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Enantioselective Direct Synthesis of *syn*- and *anti*-*α,β*-Dihydroxy *γ*-Ketoesters by a Dinuclear Zinc-AzePhenol Complex

Zhao-Fei Zhang,[a] Xiao-Chao Yang,[a] Hui-Jie Lu,[a] and Min-Can Wang*[a]

Abstract: A one-step enantioselective direct synthesis of both *syn*- and *anti*-*α,β*-dihydroxy *γ*-ketoesters by a dinuclear zinc-AzePhenol complex is presented. This asymmetric *α*-hydroxyacetate aldol reaction proceeds in moderate to good yield and with excellent enantioselectivity of up to 99% ee. The desired products could be versatile intermediates for several transformations.

Introduction

Chiral *α,β*-dihydroxy esters are important chiral synthons and pharmacophores that serve as the core structures of bioactive polyketide natural products and drugs (Figure 1).[1] Examples of bioactive agents include the **Peloruside A**,[1a,b] which could be served as a potent microtubule stabilizer that acts in a manner synergistic to that of paclitaxel and the antifungal agent **Altermaric acid**.[1d] Thus, significant attention has been devoted to their construction. The asymmetric dihydroxylation of *α,β*-unsaturated esters developed by Sharpless[2] has been demonstrated as an efficient method for the synthesis of *syn*-*α,β*-dihydroxy esters, however, the toxic Os catalyst is used; the *anti*-*α,β*-dihydroxy esters can be accessed by asymmetric epoxidation and ring opening process.[3] While several catalytic methods have been reported, their applications in synthesis have been limited due to utilizing chiral auxiliaries[4] or needing multi steps.[5] Through the Bayer-Villager oxidation of the asymmetric aldol reaction products, *α,β*-dihydroxy esters can be accessed by Shibasaki and co-workers.[6] Using as donor substrates 5*H*-Oxazol-4-ones, surrogate of the activated aster, which may be transformed to *α,β*-dihydroxy esters, Sugimura[7] realized a catalytic direct aldol reaction. Novel methods for the synthesis *α,β*-dihydroxy esters should meet these qualities: environmentally friendly, high efficiency and atom economy. Direct synthesis of highly enantioselective both *syn*- and *anti*-*α,β*-dihydroxy esters holds great potential, and remains to be developed.

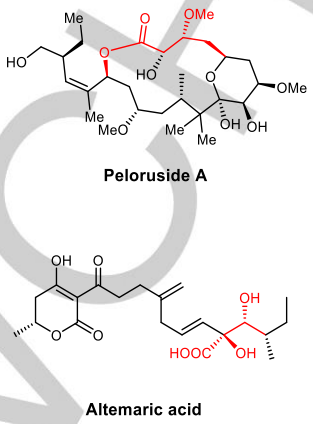
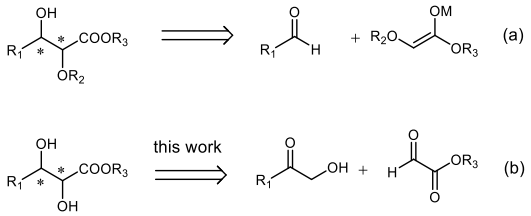


Figure 1. Examples of *α,β*-dihydroxy ester-bearing natural products and drugs

The glycolate aldol reaction[8] is regarded as an efficient route to the preparation of *α,β*-dihydroxy carboxylic compounds. Stereoselective glycolate aldol reaction using auxiliaries have been described.[8c-8e] However, the catalytic enantioselective glycolate aldol reaction is far less developed. In 2008, a highly stereoselective glycolate aldol reaction was realized by Demnmark,[9] but the corresponding *syn*- and *anti*-*α,β*-dihydroxy esters were obtained in a protected form (Scheme 1, reaction a). Inspired by this work, we assumed that *α,β*-dihydroxy ester can be traced back to the simple ethyl glyoxylate as the electronic acceptor with hydroxy ketone as the donor substrate. The aldol reation products will be directly acheived with simple reagents within one step by employing an efficient catalytic system (Scheme 1, reaction b).



Scheme 1. Retrosynthetic analysis

In recent years, Trost's dinuclear zinc-ProPhenol complex **1** (**L**/Et_2Zn) has been successfully applied to a variety of catalytic asymmetric reaction[10] and the synthesis of natural products.[11] Very recently, through the micro adjustment of **L**, changing pyrrolidine to a more rigid azetidine ring, we can get **L'** (Figure 2), another kind of semi-crown ligand, and it has been proved that this ligand can also bind zincs to form dinuclear zinc complex **2** *in situ*. The novel AzePhenol complex has been employed in the asymmetric copolymerization reaction[10] of CO_2 and cyclohexene oxide, and domino Michael/hemiketalization[12] reaction of *α*-hydroxyacetophenone

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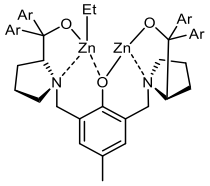
with *β,γ*-unsaturated *α*-ketoesters and gives better enantioselectivities than complex **1**.[10d] Given the importance of synthesis of chiral *α,β*-dihydroxy esters and the development of the AzePhenol dinuclear zinc complex, herein we report an asymmetric *α*-hydroxyacetate aldol reaction of *α*-hydroxy ketones with ethyl glyoxylate, affording a series of chiral *syn*- and *anti*-*α,β*-dihydroxy *γ*-ketoesters in moderate to good yields and with high enantioselectivities.



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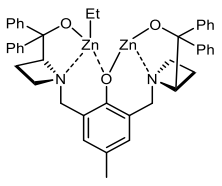

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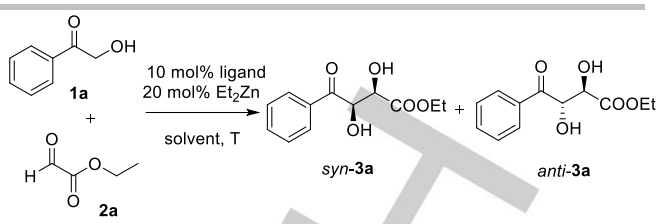
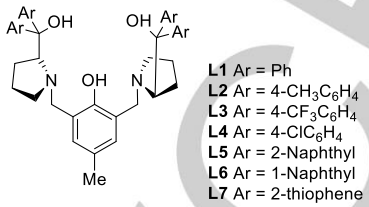
Figure 2**.** Dinuclear zinc catalysts.

Results and Discussion

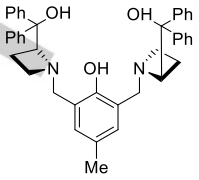
Initially, the reaction of 2-hydroxyacetophenone **1a** with ethyl glyoxylate **2a** was investigated in the presence of the Trost's dinuclear zinc-ProPhenol complex derived from $ZnEt_2$ and **L1** (Table 1). To our delight, the *syn* and *anti*-**3a** could be separated in column chromatography: the desired *syn*-**3a** could be not only isolated in 41% yield and with 36% ee, but also *anti*-**3a** in 45% yield and with 65% ee (Table 1, entry 1). Encouraged by the result, we began to optimize the reaction. First, a series of Trost's ligands[8b, 8c, 14] (**L2**-**L7**), varied with different substituents on (*S*)-prolinol, were examined (Table 1, entries 2-7). However, the yield and enantioselectivity of **3a** did not change significantly. Then, the AzePhenol ligand **L8** was employed (Table 1, entry 8). Surprisingly, the ee values of *syn*-**3a** and *anti*-**3a** were improved to 78% and 69%, respectively. Screening the solvent reveals that DCM was the best choice (Table 1, entries 9-13) in terms of the enantioselectivity. Lowering the temperature to 0℃ (Table 1, entry 14), the *syn*-**3a** can be obtained with 91% ee. However, further lowering the reaction temperature to -20℃ (Table 1, entry 15), the reaction became not only obviously slow, but also the enantioselectivity was decreased. Furthermore, introduction of 4Å MS[10b] (Table 1, entry 16) did not provide additional benefit. It is notable that increasing the amount of **2a** to 1.3 equiv. led to better enantioselectivity (Table 1, entry 17). Variation of ligand loading (Table 1, entry 18) and substrate concentration (Table 1, entry 19) showed no improvement.

Table 1**.** Reaction optimization [a]





L1-7



L8

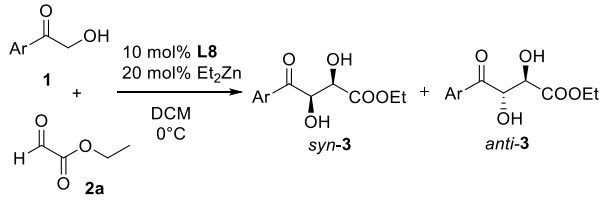
entry	Solvent	Ligand	T [°C]	Yield (*syn*/*anti*) [%][b]	Ee (*syn*/*anti*) [%][c]
1	toluene	**L1**	rt	41, 45	36, 65
2	toluene	**L2**	rt	32, 32	15, 66
3	toluene	**L3**	rt	46, 49	55, 65
4	toluene	**L4**	rt	38, 49	7, 66
5	toluene	**L5**	rt	31, 40	39, 52
6	toluene	**L6**	rt	33, 36	14, 4
7	toluene	**L7**	rt	26, 37	5, 59
8	toluene	**L8**	rt	42, 38	78, 69
9	THF	**L8**	rt	30, 31	73, 50
10	Dioxane	**L8**	rt	34, 36	89, 74
11	DCM	**L8**	rt	50, 41	88, 77
12	$CHCl_3$	**L8**	rt	40, 44	81, 84
13	CH_3CN	**L8**	rt	39, 36	85, 76
14	DCM	**L8**	0	46, 41	91, 80
15	DCM	**L8**	-20	21, 22	81, 81
16[d]	DCM	**L8**	0	33, 39	88, 38
17[e]	DCM	**L8**	0	34, 58	94, 93
18[e,f]	DCM	**L8**	0	42, 51	87, 90
19[e,g]	DCM	**L8**	0	38, 50	90, 86

[a] The reaction was run on 0.2 mmol scale. [b] Isolated yield. [c] Determined by HPLC analysis with a chiral column (Sino-Chiral AS). [d] 40 mg 4A MS was added. [e] 1.3 equiv. of **2a** was used. [f] 5 mol% of **L8** was used. [g] 2 mL of DCM was used.

With the optimized conditions in hand, we evaluated the scope of this reaction. The results were summarized in Table 2. Performing the reaction with the *para*-tolyl substrate gave *syn*-**3b** in 33% yield, 96% ee and *anti*-**3b** in 57% yield, 93% ee (Table 2, entry 2), while the *para*-methoxy substrate afforded *syn*-**3c** in 41% yield, with 96% ee and *anti*-**3c** in 53% yield, with 87% ee (Table 2, entry 3). The *ortho*-methoxy and *ortho*-methyl donors resulted in the corresponding products **3d** and **3e** with excellent enantioselectivities (Table 2, entries 4-5). The 2,5-dimethoxy substrate was converted to product **3f** with outstanding enantioselectivity (Table 2, entry 6). Several *meta* substituents were well tolerated, giving the corresponding products in good yields and enantioselectivities (Table 2, entries 7-9). The electron-withdrawing bromide substituent at the *para* position slightly decreased the enantioselectivity

(Table 2, entry 10). Notably, the absolute configuration of *syn*-**3j** was unambiguously established as (2*R*,3*R*)-configuration by single crystal X-ray analysis (Figure 3). Substrates bearing other electron-withdrawing substituents led to the decrease in the enantioselectivities (Table 2, entries 11-12). This effect was even more pronounced by a nitro group (*syn*-**3m**, 4% yield, 4% ee) (Table 2, entry 13). Donors containing heteroaromatic rings were also possible (Table 2, entries 14-15), especially in the thiophene case, the corresponding product **3o** could be obtained with excellent enantioselectivity.

Table 2**.** Substrate scope [a]



entry	Ar	t [h]	3	Yield (*syn*/*anti*) [%][b]	Ee (*syn*/*anti*) [%] [c]
1	Ph (**1a**)	12	**3a**	34, 58	94, 93
2	4-Me-C_6H_4 (**1b**)	12	**3b**	33, 57	96, 93
3	4-MeO-C_6H_4 (**1c**)	12	**3c**	41, 53	96, 87
4	2-Me-C_6H_4 (**1d**)	12	**3d**	46, 47	96, 99
5	2-MeO-C_6H_4 (**1e**)	12	**3e**	43, 55	98, 94
6	2,5-OMe-C_6H_3(**1f**)	12	**3f**	33, 53	98, ND
7	3-MeO-C_6H_4 (**1g**)	12	**3g**	55, 42	88, 88
8	3-Br-C_6H_4 (**1h**)	12	**3h**	40, 58	89, 82
9	3-Cl-C_6H_4 (**1i**)	12	**3i**	49, 41	86, 72
10	4-Br-C_6H_4 (**1j**)	12	**3j**	31, 58	91, 90
11	4-Cl-C_6H_4 (**1k**)	12	**3k**	32, 55	76, 72
12	4-F-C_6H_4 (**1l**)	12	**3l**	48, 40	81, 76
13	4-NO_2-C_6H_4 (**1m**)	48	**3m**	4, ND	4, ND
14	2-Furyl (**1n**)	8	**3n**	48, 58	77, 84
15	2-Thienyl (**1o**)	8	**3o**	40, 57	89, 97

[a] General reaction conditions: **1a** (0.2 mmol), **2a** (0.26 mmol) in 1.5 mL toluene, **L8** (0.02 mmol), Et_2Zn (0.04 mmol) at 0 °C. [b] Isolated yield. [c] Determined by HPLC analysis.

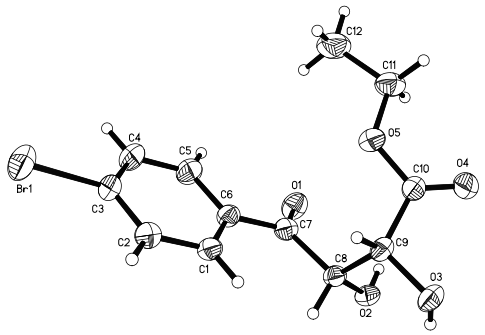
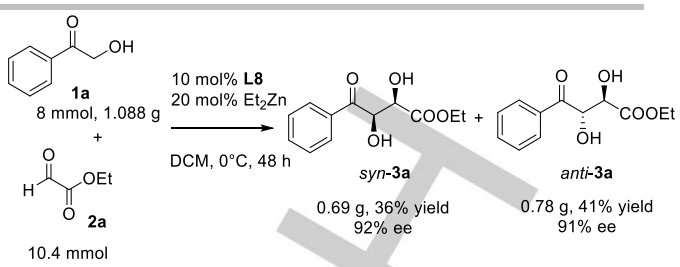
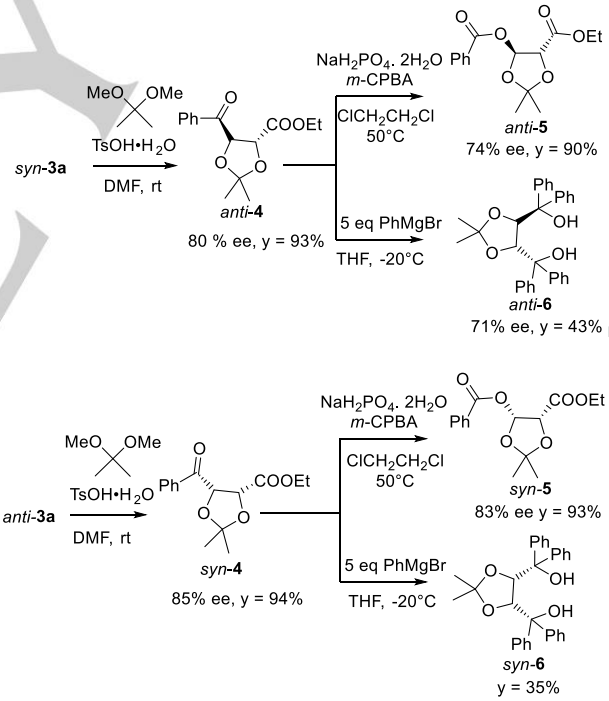


Figure 3**.** Single crystal X-ray diffraction analysis of *syn*-**3j**



Scheme 2**.** Scale-up reaction

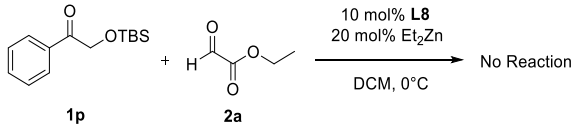
To further demonstrate the synthetic utility of this methodology, the aldol reaction of 2-hydroxyacetophenone with ethyl glyoxylate was performed on a gram scale (Scheme 2). The reaction was completed in 48 hours, and satisfying results were acheived. After seperation and recrystallization, *syn*-**3a** can be obtained in 36% yield and with 92% ee, meanwhile the *anti*-**3a** can be obtained in 41% yield and with 91% ee. Since all the materials of the reaction can be easily prepared or commercially avaliable, the present catalytic system has provided a practical and economical protocol for the direct synthesis of chiral *syn*- and *anti*-*α,β*-dihydroxy *γ*-ketoesters.



Scheme 3**.** Transformation of *syn*-**3a** and *anti*-**3a**

As shown in Scheme 3, *α,β*-dihydroxy *γ*-ketoesters can be converted to the protected acetonide in excellent yield and with slight loss of enantioselectivity. Subsequent Baeyer-Villiger oxidation proceeded smoothly by treating the *syn*- and *anti*-**4** with *m*-CPBA to give compounds *syn*- and *anti*-**5**, respectively. Furthermore, **6**[15] were obtained from **4** by the treatment with a Grignard reagent, the *syn*-**4** gave the expected TADDOL *syn*-6

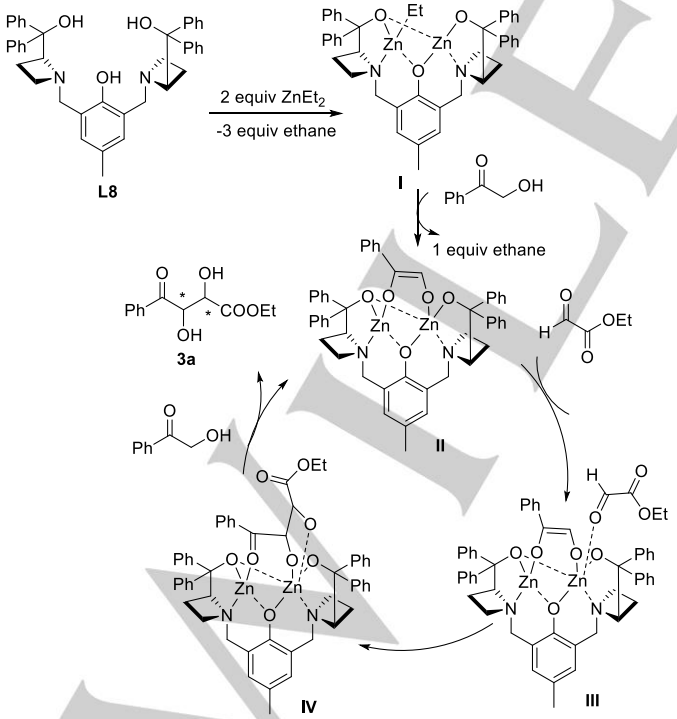
without optical rotation value, for it is a *meso* compound. The expected chiral *anti*-**6** was also prepared. The specific rotation value of resulting *anti*-**6** is +19.3º. Since the specific rotation value of reported compound (*R*,*R*)-Taddol[15] is +69º, this result can further suggest that the absolute configuration of the *syn*-**3a** is (*R,R*).



Scheme 4**.** Asymmetric aldol reaction of **1p** and **2a**

When TBS-protected 2-hydroxyacetophenone **1p** was employed, no reaction was observed (Scheme 4), thereby demonstrating that the process of 2-hydroxyphenone deprotonated by an ethyl zinc species to form the zinc enolate with the bidentate coordination plays an important role for the present system.[16]

Our proposed catalytic cycle is described in Scheme 5. Similar to the ProPhenol ligand, **L8** binds two equiv. of Et_2Zn *in situ* to give dinuclear zinc catalytic system **I**. Then, 2-hydroxyacetophenone is deprotonated by an ethyl zinc species to afford dinuclear zinc-AzePhenol complex **II**. Ethyl glyoxylate coordinates the Lewis acid zinc nucleus to form intermediate **III**, and then undergoes aldol reaction. We assume that high reactive flexible ethyl glyoxylate could not bind the zinc strictly, which led to a mixture of diasteroisomer in the aldol reaction. Finally, proton transfer with an incoming molecule of nucleophile would release product **3a**, and complete the catalytic cycle.



Scheme 5**.** Proposed mechanism of the aldol reaction

Conclusions

In conclusion, we have developed a highly enantioselective direct synthesis of both *syn*- and *anti*-*α,β*-dihydroxy *γ*-ketoesters via a dinuclear zinc-AzePhenol complex catalyzed aldol reaction of 2-hydroxyacetophenone with ethyl glyoxylate. The reaction can be carried out on gram scale without obvious sacrifice of the enatioselectivity. The resulting product can be versatile intermediates for a variety of functionalization reactions, including conversion to carboxylic acid derivatives, alcohols, and TADDOL. The further application of the AzePhenol ligand in the asymmetric synthesis is currently underway in our lab.

Experimental Section

General Remarks

^{1}H NMR spectra were performed on a Bruker DPX 400 (400 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si). ^{13}C NMR spectra were performed on a Bruker DPX 400 (100 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si). The data are reported as (s = single, d = double, t = triple, q = quarte, m = multiple or unresolved, coupling constant(s) in Hz, integration). The enantiomeric purity was determined by HPLC using a chiral column with hexane/propan-2-ol as the eluent. The chromatographic system consisted of a JASCO model PU-1580 intelligent HPLC pump and a JASCO model UV-1575 intelligent UV-vis detector (254 nm). Chiralcel AD, OD-H, OJ, AD-H, or AS column (250 × 4.6 mm, Daicel Chemical Ind., LTD, Japan). The column was operated at ambient temperature. Diethylzinc (1.0 mol/L in hexane) was purchased from Aldrich and used as received. Chiral ligands **L1-L6**[17], **L7**[18], **L8**[19] was synthesized according to the literature procedure. Other reagents were obtained from commercial sources and used as received without further purification.

General Procedure for Catalytic Asymmetric aldol reaction of α-hydroxy ketones with ethyl glyoxylate catalyzed by Et_2Zn/ L8 complex

In a flame-dried Schlenk tube, a solution of diethylzinc (40 uL, 1.0 mol/L in hexane, 0.04 mmol) was added to a solution of the chiral ligand **L8** (12.4 mg, 0.02 mmol) in dry dichloromethane (0.7 mL) under nitrogen at 0 ºC. The mixture was stirred at room temperature for 30 min. Then a solution of α-hydroxy ketones (0.2 mmol, 1.0 equiv) and ethyl glyoxylate (0.26 mmol, 1.3 equiv) in dry dichloromethane (0.8 mL) was added to the mixture at 0 ºC. The solution was stirring at the same temperature for the necessary reaction times, and then quenched with aqueous NH_4Cl (5 mL), extracted three times with DCM (3 x 10 mL). The combined organics were washed with brine before dried by Na_2SO_4, filtered and concentrated in vacuo. The crude product was separated by flash column chromatography.

ethyl (2R, 3R)-2,3-dihydroxy-4-oxo-4-phenylbutanoate (*syn*-3a). Yield: 34%, 16.1 mg; white solid, m.p.= 55-56℃; $[\alpha]_D^{25}$ = +36.1 (*c* 0.182, in $CHCl_3$); 94% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 19.46 min, t_{minor} = 28.19 min). ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (d, *J* = 7.4 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 5.45 (d, *J* = 5.6 Hz, 1H), 4.57 (d, *J* = 6.2 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.08 (d, *J* = 6.8 Hz, 1H), 3.05 (d, *J* = 7.8 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 197.72, 171.88, 134.77, 133.50, 129.55, 128.96, 74.87, 72.70, 63.04, 14.66. HRMS (EI): calcd for $C_{12}H_{14}O_5Na$

[M+Na]$^+$: 261.0739, found 261.0737; IR: v=3385.38, 1742.61, 1627.05, 1598.13, 1233.11, 1097.76, 767.18, 694.49 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-oxo-4-phenylbutanoate (*anti*-3a): Yield: 58%, 27.6 mg; white solid, m.p.= 61-62℃; $[\alpha]_D^{25}$ = -20.5 (*c* 0.205, in $CHCl_3$); 93% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 27.19 min, t_{minor} = 36.46 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 19.5, 7.9 Hz, 2H), 7.76 – 7.63 (m, 1H), 7.52 (dd, *J* = 21.5, 13.9 Hz, 2H), 5.35 (s, 1H), 4.65 (d, *J* = 1.8 Hz, 1H), 4.05 (dq, *J* = 10.8, 7.2 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.94, 170.80, 134.62, 134.45, 129.47, 128.82, 76.77, 73.93, 62.54, 14.32. HRMS (EI): calcd for $C_{12}H_{14}O_5Na$ [M+Na]$^+$: 261.0739, found 261.0737; IR: v=3385.38, 1742.61, 1627.05, 1598.13, 1233.11, 1097.76, 767.18, 694.49 cm^{-1}

ethyl (2R, 3R)-2,3-dihydroxy-4-oxo-4-(p-tolyl)butanoate (*syn*-3b): Yield: 33%, 16.6 mg; colorless oil; $[\alpha]_D^{25}$ = +23.9 (*c* 0.197, in $CHCl_3$); 96% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 16.68 min, t_{minor} = 24.69 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.88 (d, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 5.41 (s, 1H), 4.55 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.23 – 3.92 (m, 1H), 2.44 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.99, 169.47, 144.33, 130.51, 128.74, 127.56, 75.23, 72.69, 61.03, 20.80, 12.92. HRMS(EI): calcd for $C_{13}H_{16}O_5Na$ [M+Na]$^+$: 275.0895, found 275.0892; IR: v=3346.10, 1743.20, 1623.67, 1597.79, 1449.46, 1383.97, 1098.03, 767.01, 695.28 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-oxo-4-(p-tolyl)butanoate (*anti*-3b): Yield: 57%, 28.7 mg; white solid, m.p.= 72-74℃; $[\alpha]_D^{25}$ = -85 (*c* 0.146, in $CHCl_3$); 93% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ=254 nm, t_{major} = 25.35 min, $t_{mino\ r}$= 31.95 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.31 (s, 1H), 4.59 (d, *J* = 31.1 Hz, 1H), 4.22 – 3.90 (m, 2H), 3.68 – 3.25 (m, 1H), 2.44 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.81, 170.57, 144.47, 129.60, 128.81, 127.69, 73.33, 71.48, 61.53, 20.81, 13.25. HRMS (EI): calcd for $C_{13}H_{16}O_5Na$ [M+Na]$^+$: 275.0895, found 275.0892; IR: v=3346.10, 1743.20, 1623.67, 1597.79, 1449.46, 1383.97, 1098.03, 767.01, 695.28 cm^{-1}

ethyl (2R, 3R)-2,3-dihydroxy-4-(4-methoxyphenyl)-4-oxobutanoate (*syn*-3c): Yield: 41%, 21.9 mg; colorless oil; $[\alpha]_D^{25}$ = +30.0 (*c* 0.199, in $CHCl_3$); 96% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 44.25 min, t_{minor} = 51.25 min). ^{1}H NMR (400 MHz, CDCl3) δ 7.98 (d, *J* = 8.9 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 5.39 (dd, *J* = 6.8, 1.5 Hz, 1H), 4.58 – 4.52 (m, 1H), 4.37 (q, *J* = 7.1 Hz, 1H), 4.14 (d, *J* = 6.8 Hz, 1H), 3.89 (s, 1H), 3.06 (d, *J* = 7.9 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.37, 171.54, 164.42, 130.92, 125.77, 114.31, 73.91, 72.54, 62.45, 55.55, 14.18. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ [M+Na]$^+$:291.0845, found 291.0844; IR: v=3415.26, 1744.38, 1574.08, 1513.36, 1463.03,1176.42, 1114.37, 789.54 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-(4-methoxyphenyl)-4-oxobutanoate (*anti*-3c): Yield: 53%, 28.4 mg; white solid, m.p.= 60-62℃; $[\alpha]_D^{25}$ = -22.0 (*c* 0.110, in $CHCl_3$); 87% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 36.65 min, t_{minor} = 45.79 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 7.71 (m, 2H), 7.19 – 6.67 (m, 2H), 5.29 (s, 1H), 4.63 (s, 1H), 4.28 – 3.97 (m, 2H), 3.90 (s, 3H), 1.18 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.54, 170.44, 164.31, 130.77, 126.72, 114.23, 75.48, 73.71, 61.90, 55.54, 13.85. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ [M+Na]$^+$:291.0845, found 291.0844; IR: v=3415.26, 1744.38, 1574.08, 1513.36, 1463.03,1176.42, 1114.37, 789.54 cm^{-1}

ethyl (2R,3R)-2,3-dihydroxy-4-oxo-4-(o-tolyl)butanoate (*syn*-3d): Yield: 46% 23.1 mg; colorless oil; $[\alpha]_D^{25}$ = +37.0 (*c* 0.199, in $CHCl_3$); 96% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate=1.0 mL/min, λ=254 nm, t_{major}=11.48 min, t_{minor}=16.12 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 5.34 (d, *J* = 3.9 Hz, 1H), 4.38 – 4.32 (m, 2H), 4.09 (d, *J* = 5.4 Hz, 1H), 3.04 (d, *J* = 6.0 Hz, 1H), 2.52 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.88, 171.58, 139.57, 133.77, 132.46, 132.41, 127.91, 125.91, 75.93, 72.02, 62.57, 20.66, 14.27. HRMS (EI): calcd for $C_{13}H_{16}O_5Na$ [M+Na]$^+$: 275.0895, found 275.0892; IR: v=3346.10, 1743.20, 1623.67, 1597.79, 1449.46, 1383.97, 1098.03, 767.01, 695.28 cm^{-1}

ethyl (2R,3S)-2,3-dihydroxy-4-oxo-4-(o-tolyl)butanoate (*anti*-3d): Yield: 47%, 23.6 mg; colorless oil; $[\alpha]_D^{25}$ = -21.1 (*c* 0.199, in $CHCl_3$); 99% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 46.20 min, t_{minor} = 47.20 min). ^{1}H NMR (400 MHz, CDCl3) δ 7.63 (t, *J* = 7.9 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.37 – 7.31 (m, 2H), 5.34 (s, 1H), 4.56 (s, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 2.55 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.91, 170.61, 139.73, 133.78, 132.67, 132.47, 128.57, 125.85, 77.21, 73.64, 62.35, 20.79, 14.17. HRMS (EI): calcd for $C_{13}H_{16}O_5Na$ [M+Na]$^+$: 275.0895, found 275.0892; IR: v=3346.10, 1743.20, 1623.67, 1597.79, 1449.46, 1383.97, 1098.03, 767.01, 695.28 cm^{-1}

ethyl (2R, 3R)-2,3-dihydroxy-4-(2-methoxyphenyl)-4-oxobutanoate (*syn*-3e): Yield: 43%, 23.0 mg; white solid, m.p.= 84-86℃; $[\alpha]_D^{25}$ = -17.8 (*c* 0.294, in $CHCl_3$); 98% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ=254 nm, t_{major} = 42.20 min, t_{minor} = 46.55 min). ^{1}H NMR (400 MHz, CDCl3) δ 7.97 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.57 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H), 7.11 – 7.05 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.51 (dd, *J* = 6.2, 1.3 Hz, 1H), 4.57 (d, *J* = 8.3 Hz, 1H), 4.41 – 4.29 (m, 2H), 4.18 (d, *J* = 6.2 Hz, 1H), 3.98 (s, 3H), 2.98 (d, *J* = 8.7 Hz, 1H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.11, 172.12, 158.89, 135.39, 131.84, 123.01 121.40, 111.62, 78.11, 71.07, 62.10, 55.36, 14.17. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ [M+Na]$^+$: 291.0845, found 291.0845; IR: v=3368.34 1755.15, 1662.94, 1598.11, 1486.27, 1127.20, 1082.07, 770.05, 723.21 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-(2-methoxyphenyl)-4-oxobutanoate (*anti*-3e): Yield: 55%, 29.4 mg; colorless oil; $[\alpha]_D^{25}$ = -88.2 (*c* 0.304, in $CHCl_3$); 94% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 9:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 15.60 min, t_{minor} = 19.99 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.61 – 7.50 (m, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 5.39 (d, *J* = 1.8 Hz, 1H), 4.58 (d, *J* = 2.0 Hz, 1H), 4.17 – 4.00 (m, 3H), 3.97 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.13, 170.99, 158.53, 135.00, 131.58, 124.13, 121.17, 111.66, 80.03, 73.14, 61.83, 55.70, 13.90. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ [M+Na]$^+$: 291.0845, found 291.0845; IR: v=3368.34, 1755.15, 1662.94, 1598.11, 1486.27, 1127.20, 1082.07, 770.05, 723.21 cm^{-1}

ethyl (2R, 3R)-4-(2,5-dimethoxyphenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3f): Yield: 33%, 19.6 mg; pale-yellow solid, m.p.= 98-100℃; $[\alpha]_D^{25}$ = +3.0 (*c* 0.288, in $CHCl_3$); 98% ee, determined by HPLC analysis (Chiralpak AD column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 23.70 min, t_{minor} = 33.91 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 3.2 Hz, 1H), 7.14 (dd, *J* = 9.1, 3.2 Hz, 1H), 6.96 (d, *J* = 9.1 Hz, 1H), 5.53 (dd, *J* = 6.4, 1.2 Hz, 1H), 4.58 (t, *J* = 16.4 Hz, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.15 (t, *J* = 12.1 Hz, 1H), 3.94 (s, 3H), 3.82 (s, 3H), 3.01 (d, *J* = 8.6 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.09, 173.54, 155.22, 154.86, 124.18, 115.66, 114.47, 79.46, 72.46, 63.52, 57.15, 57.10, 15.56. HRMS (EI):

calcd for $C_{14}H_{18}O_7Na$ $[M+Na]^+$:321.0950, found 321.0948; IR: v=3373.12, 1752.03, 1608.26, 1581.34, 1496.17, 1113.60, 734.54 cm^{-1}

ethyl (2S, 3R)-4-(2,5-dimethoxyphenyl)-2,3-dihydroxy4-oxobutanoate (*anti*-3f): Yield: 53%, 31.5 mg; pale-yellow solid, m.p.= 106-108℃; $[\alpha]_D^{25}$ = -110.2 (*c* 0.288, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 3.2 Hz, 1H), 7.14 (dd, *J* = 9.1, 3.3 Hz, 1H), 6.97 (d, J = 9.1 Hz, 1H), 5.40 (dd, J = 5.0, 2.1 Hz, 1H), 4.62 – 4.57 (m, 1H), 4.24 – 4.11 (m, 2H).., 3.94 (s, 3H), 3.82 (s, 3H), 3.35 (d, *J* = 8.1 Hz, 1H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.14, 172.40, 155.13, 154.44, 125.54, 123.25, 116.02, 114.47, 81.40, 74.56, 63.24, 57.49, 57.16, 15.32. HRMS (EI): calcd for $C_{14}H_{18}O_7Na$ $[M+Na]^+$:321.0950, found 321.0948; IR: v=3373.12, 1752.03, 1608.26, 1581.34, 1496.17, 1113.60, 734.54 cm^{-1}

ethyl (2R, 3R)-2,3-dihydroxy-4-(3-methoxyphenyl)-4-oxobutanoate (*syn*-3g): Yield: 55%, 29.4 mg; colorless oil; $[\alpha]_D^{25}$ = +30.0 (*c* 0.143, in $CHCl_3$); 88% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 22.63 min, t_{minor} = 34.64 min). ^1H NMR (400 MHz, CDCl3) δ 7.52 (m, 2H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.19 (dd, *J* = 8.1, 2.2 Hz, 1H), 5.42 (s, 1H), 4.57 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 1H), 3.88 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.23, 170.50, 159.20, 133.46, 129.08, 119.84, 103.61, 73.59, 71.40, 61.60, 54.55, 13.25. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ $[M+Na]^+$: 291.0845, found 291.0842; IR: v=3457.84, 1743.73, 1587.91, 1582.88, 1466.18, 1119.83, 1094.35, 788.29, 747.82 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-(3-methoxyphenyl)-4-oxobutanoate (*anti*-3g): Yield: 42%, 22.5 mg; colorless oil; $[\alpha]_D^{25}$ = -25.9 (*c* 0.173, in $CHCl_3$); 88% ee, determined by HPLC analysis (Chiralpak OJ column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 67.19 min, t_{minor} = 73.44 min). ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.6 Hz, 1H), 7.42 (m, 2H), 7.17 (dt, *J* = 15.6, 7.9 Hz, 1H), 5.31 (d, *J* = 2.1 Hz, 1H), 4.66 (d, *J* = 2.2 Hz, 1H), 4.11 (m, 2H). 3.89 (s, 3H), 1.29 – 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.44, 169.42, 159.13, 134.41, 129.04, 119.79, 119.44, 112.06, 75.45, 72.66, 61.09, 54.55, 12.94. HRMS (EI): calcd for $C_{13}H_{16}O_6Na$ $[M+Na]^+$: 291.0845, found 291.0842; IR: v=3457.84, 1743.73, 1587.91, 1582.88, 1466.18, 1119.83, 1094.35, 788.29, 747.82 cm^{-1}

ethyl (2R, 3R)-4-(3-bromophenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3h): Yield: 40% 25.2 mg; coloress liquid; $[\alpha]_D^{25}$ = +18.5 (*c* 0.196, in $CHCl_3$); 89% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 26.22 min, t_{minor} = 31.05 min). ^1H NMR (400 MHz, CDCl3) δ 8.11 (t, *J* = 1.7 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 5.39 (s, 1H), 4.53 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.99 (d, *J* = 6.1 Hz, 1H), 3.11 (s, 1H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.59, 172.57, 138.46, 136.28, 132.85, 131.93, 128.26, 124.81, 75.98, 73.39, 64.07, 31.01, 15.55. HRMS (EI): calcd for $C_{12}H_{13}O_5BrNa$ $[M+Na]^+$:338.9844, found 338.9840; IR: v=3406.11, 1746.66, 1591.10, 1567.31, 1425.76, 1250.90, 1111.46, 790.43, 703.83 cm^{-1}

ethyl (2S, 3R)-4-(3-bromophenyl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3h): Yield: 58%, 36.5 mg; white solid, m.p.= 57-58℃; $[\alpha]_D^{25}$ = -29.4 (*c* 0.275, in $CHCl_3$); 82% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ =254 nm, t_{major} = 59.35 min, t_{minor} = 66.11 min). ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.6 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.81 – 7.74 (t, *J* = 7.9 Hz 1H), 7.50 – 7.32 (m, 1H), 5.29 (s, 1H), 4.62 (d, *J* = 1.8 Hz, 1H), 4.29 – 4.02 (m, 2H), 3.94 (d, *J* = 10.7 Hz, 1H), 3.46 (s, 1H), 1.20 (t, *J* = 7.1 Hz, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.84, 171.57, 138.32, 132.70, 131.90, 128.19, 124.66, 77.70, 74.64, 63.64, 15.26. HRMS (EI): calcd for $C_{12}H_{13}O_5BrNa$ $[M+Na]^+$:338.9844, found 338.9840; IR: v=3406.11, 1746.66, 1591.10, 1567.31, 1425.76, 1250.90, 1111.46, 790.43, 703.83 cm^{-1}

ethyl (2R, 3R)-4-(3-chlorophenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3i): Yield: 49% 26.7 mg; colorless oil; $[\alpha]_D^{25}$ = +4.0 (*c* 0.286, in $CHCl_3$); 86% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 23.63 min, t_{minor} = 36.00 min). ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.83 (t, *J* = 11.3 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.53 – 7.41 (m, 1H), 5.39 (s, 1H), 4.54 (s, 1H), 4.39 (q, *J* = 6.7 Hz, 2H), 1.50 – 1.33 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.39, 170.28, 134.59, 133.81, 133.22, 129.42, 127.64, 125.53, 73.75, 71.11, 61.74, 13.25. HRMS (EI): calcd for $C_{12}H_{13}O_5ClNa$ $[M+Na]^+$:295.0349, found 295.0344; IR: v=3390.17, 1738.71, 1595.82, 1572.12, 1463.79, 1249.40, 1119.52, 788.54, 721.61 cm^{-1}

ethyl (2S, 3R)-4-(3-chlorophenyl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3i): Yield: 41%, 22.3 mg; colorless oil; $[\alpha]_D^{25}$ = -7.9 (*c* 0.287, in $CHCl_3$); 72% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 105.400 min, t_{minor} = 121.967 min). ^1H NMR (400 MHz, CDCl3) δ 7.90 (s, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.9 Hz, 1H), 5.29 (d, J = 1.8 Hz, 1H), 4.61 (d, J = 2.0 Hz, 1H), 4.21 – 4.06 (m, 2H), 1.21 (t, J = 7.1 Hz, 3H).;^{13}C NMR (100 MHz, $CDCl_3$) δ 195.63, 169.28, 134.80, 134.49, 133.09, 129.36, 127.52, 125.46, 75.43, 72.37, 61.30, 12.95. HRMS(EI): calcd for $C_{12}H_{13}O_5ClNa$ $[M+Na]^+$:295.0349, found 295.0344; IR: v=3390.17, 1738.71, 1595.82, 1572.12, 1463.79, 1249.40, 1119.52, 788.54, 721.61 cm^{-1}

ethyl (2R, 3R)-4-(4-bromophenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3j): Yield: 31%, 19.6 mg; pale-yellow solid, m.p.= 74-77℃; $[\alpha]_D^{25}$ = +21.3 (*c* 0.15, in $CHCl_3$); 91% ee, determined by HPLC analysis (Chiralpak OJ column, hexane/*i*-PrOH = 9:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 19.91 min, t_{minor} = 23.07 min). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 5.39 (d, *J* = 5.3 Hz, 1H), 4.52 (d, *J* = 4.4 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.98 (d, J = 6.9 Hz, 1H), 3.07 (d, *J* = 6.6 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.78, 172.61, 133.83, 133.12, 131.27, 130.99, 75.80, 73.47, 64.05, 15.56. HRMS (EI): calcd for $C_{12}H_{13}O_5BrNa$ $[M+Na]^+$: 338.9844, found 338.9842; IR: v=3405.98, 1747.01, 1586.64, 1463.25, 1213.64, 1111.64, 1027.87, 800.98, 699.17 cm^{-1}

ethyl (2S, 3R)-4-(4-bromophenyl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3j): Yield: 58%, 36.6 mg; pale-yellow solid, m.p.= 63-65℃; $[\alpha]_D^{25}$ = -28.6 (*c* 0.255, in $CHCl_3$); 90% ee, determined by HPLC analysis (Chiralpak OJ column, hexane/*i*-PrOH = 9:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 25.50 min, t_{minor} = 33.18 min). ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 5.28 (d, *J* = 2.3 Hz, 1H), 4.60 (s, 1H), 4.24 – 4.03 (m, 2H), 4.00 – 3.88 (m, 1H), 3.43 (s, 1H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.96, 171.55, 134.12, 133.75, 131.17, 130.84, 77.59, 74.69, 63.55, 15.25. HRMS (EI): calcd for $C_{12}H_{13}O_5BrNa$ $[M+Na]^+$: 338.9844, found 338.9842; IR: v=3405.98, 1747.01, 1586.64, 1463.25, 1213.64, 1111.64, 1027.87, 800.98, 699.17 cm^{-1}

ethyl (2R, 3R)-4-(4-chlorophenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3k): Yield: 32%, 17.4 mg; white solid, m.p.= 79-80℃; $[\alpha]_D^{25}$ = +25.3 (*c* 0.253, in $CHCl_3$); 76% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 19.13min, t_{minor} = 24.38min). ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.87 (m, 2H), 7.62 – 7.42 (m, 2H), 5.39 (d, *J* = 4.8 Hz, 1H), 4.52 (s, 1H), 4.45 – 4.30 (m, 2H), 4.18 – 3.82 (m, 1H), 3.08 (s, 1H), 1.39 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.26, 170.32, 139.93, 130.54, 128.94, 128.53, 73.53, 71.21, 61.71, 13.25. HRMS (EI): calcd for $C_{12}H_{13}O_5ClNa$ $[M+Na]^+$: 295.0349, found 295.0344; IR: v=3490.52,

1747.04, 1590.43, 1570.30, 1491.02, 1400.77, 1111.71, 748.81, 701.14 cm^{-1}

ethyl (2S, 3R)-4-(4-chlorophenyl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3k): Yield: 55%, 29.9 mg; colorless oil; $[\alpha]_D^{25}$ = -12.0 (*c* 0.061, in $CHCl_3$); 72% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 29.42 min, t_{minor} = 33.00 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.87 (m, 2H), 7.57 (dd, *J* = 8.5, 3.8 Hz, 2H), 5.30 (d, *J* = 29.6 Hz, 1H), 4.65 (d, *J* = 2.4 Hz, 1H), 4.25 - 4.09 (m, 2H), 4.00 (d, *J* = 18.8 Hz, 1H), 1.24 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.47, 169.29, 139.79, 131.44, 128.84, 128.45, 75.31, 72.42, 61.21, 12.94. HRMS (EI): calcd for $C_{12}H_{13}O_5ClNa$ $[M+Na]^+$: 295.0349, found 295.0344; IR: v=3490.52, 1747.04, 1590.43, 1570.30, 1491.02, 1400.77, 1111.71, 748.81, 701.14 cm^{-1}

ethyl (2R, 3R)-4-(4-fluorophenyl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3l): Yield: 48%, 24.5 mg; white solid, m.p.= 52-53℃; $[\alpha]_D^{25}$ = +16.0 (*c* 0.265, in $CHCl_3$); 81% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 9:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 26.98 min, t_{minor} = 37.65 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.92 (m, 2H), 7.32 – 7.17 (m, 2H), 5.45 – 5.34 (m, 1H), 4.53 (d, *J* = 1.1 Hz, 1H), 4.46 – 4.28 (m, 2H), 1.46 – 1.33 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.77, 170.38, 164.11 (d, *J* = 247.70 Hz), 131.82 (d, *J* = 9.09 Hz), 130.38 (d, *J* = 10.1 Hz), 128.63, 115.43 (d, *J* = 22.22 Hz), 114.70 (d, *J* = 22.22 Hz), 75.70, 73.41, 61.68, 13.24. HRMS (EI): calcd for $C_{12}H_{13}O_5FNa$ $[M+Na]^+$: 279.0645, found 279.0642; IR: v=3441.03, 1716.69, 1598.47, 1507.90, 1401.07, 1160.94, 735.37, 704.23 cm^{-1}

ethyl (2S, 3R)-4-(4-fluorophenyl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3l): Yield: 40%, 21.0 mg; colorless oil; $[\alpha]_D^{25}$ = -19.9 (*c* 0.279, in $CHCl_3$); 76% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 19.11 min, t_{minor} = 23.58min). ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (dd, *J* = 8.6, 5.4 Hz, 1H), 7.21 (t, *J* = 8.5 Hz, 1H), 5.29 (d, *J* = 2.4 Hz, 1H), 4.61 (d, *J* = 2.4 Hz, 1H), 4.12 (m, 2H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.00, 169.34, 166.43 (d, *J* = 257.55 Hz), 131.82 (d, *J* = 10.10 Hz), 130.22 (d, *J* = 10.10 Hz), 115.35 (d, *J* = 22.22 Hz), 114.79 (d, *J* = 22.22 Hz), 75.21, 72.48, 61.15, 12.93. HRMS (EI): calcd for $C_{12}H_{13}O_5FNa$ $[M+Na]^+$: 279.0645, found 279.0642; IR: v=3441.03, 1716.69, 1598.47, 1507.90, 1401.07, 1160.94, 735.37, 704.23 cm^{-1}

ethyl (2R,3R)-2,3-dihydroxy-4-(4-nitrophenyl)-4-oxobutanoate (*syn*-3m): Yield: 4%, 2.3 mg; colorless oil; 4% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 19.11 min, t_{minor} = 23.58min). ^{1}H NMR (400 MHz, CDCl3) δ 8.39 (d, *J* = 8.7 Hz, 2H), 8.17 (d, *J* = 8.7 Hz, 2H), 5.35 (s, 1H), 4.73 (d, *J* = 5.9 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). HRMS (EI): calcd for $C_{12}H_{13}NO_7Na$ $[M+Na]^+$: 283.0692, found 283.0689; IR: v=3441.03, 1716.69, 1598.47, 1507.90, 1401.07, 1160.94, 735.37, 704.23 cm^{-1}

ethyl (2R, 3R)-4-(furan-2-yl)-2,3-dihydroxy-4-oxobutanoate (*syn*-3n): Yield: 48%, 21.8 mg; brown solid, m.p.= 98-99℃; $[\alpha]_D^{25}$ = +11.6 (*c* 0.151, in $CHCl_3$); 77% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 22.90min, t_{minor} = 27.91min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.61 (m, 1H), 7.42 (t, *J* = 5.8 Hz, 1H), 6.71 – 6.50 (m, 1H), 5.19 (d, *J* = 1.0 Hz, 1H), 4.81 (t, *J* = 7.6 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.50 – 1.33 (q, *J* = 7.1 Hz,, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.56, 170.56, 149.08, 146.29, 127.34, 124.89, 118.48 111.96, 73.98, 71.10, 61.59, 13.22. HRMS (EI): calcd for $C_{10}H_{12}O_6Na$ $[M+Na]^+$: 251.0532, found 251.0531; IR: v=3468.11, 1735.23, 1566.17, 1469.58, 1124.16, 728.67 cm^{-1}

ethyl (2S, 3R)-4-(furan-2-yl)-2,3-dihydroxy-4-oxobutanoate (*anti*-3n): Yield: 58%, 26.4 mg; brown solid, m.p.= 91-92℃; $[\alpha]_D^{25}$ =-15.7 (*c* 0.176, in $CHCl_3$); 84% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 28.20 min, t_{minor} = 35.83 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 1.0 Hz, 1H), 7.42 (dd, *J* = 7.1, 4.0 Hz, 1H), 6.64 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.08 (d, *J* = 2.8 Hz, 1H), 4.83 (d, *J* = 2,8 Hz, 1H), 4.26 – 4.06 (m, 2H), 1.23 – 1.12 (t, *J* = 7.1, Hz 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 184.34, 169.64, 149.52, 146.28, 118.24, 111.89, 75.55, 72.23, 61.10, 12.89. HRMS (EI): calcd for $C_{10}H_{12}O_6Na$ $[M+Na]^+$: 251.0532, found 251.0531; IR: v=3468.11, 1735.23, 1566.17, 1469.58, 1124.16, 728.67 cm^{-1}

ethyl (2R, 3R)-2,3-dihydroxy-4-oxo-4-(thiophen-2-yl)butanoate (*syn*-3o): Yield: 40%, 19.5 mg; colorless oil; $[\alpha]_D^{25}$ = +25.0 (*c* 0.220, in $CHCl_3$); 89% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 22.5 min, t_{minor} = 27.28min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 3.9, 1.0 Hz, 1H), 7.78 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.21 (dd, *J* = 4.9, 3.9 Hz, 1H), 5.23 (d, *J* = 1.8 Hz, 1H), 4.67 (dd, *J* = 10.1, 2.4 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.48 – 1.31 (*J* = 7.1 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 188.64, 170.45, 134.33, 132.21, 127.50, 124.91, 74.19, 72.12, 61.65, 13.23. HRMS(EI): calcd for $C_{10}H_{12}O_5SNa$ $[M+Na]^+$: 267.0303, found 267.0301; IR: v=3365.09, 1759.65, 1516.99, 1411.02, 1119.16, 752.87 cm^{-1}

ethyl (2S, 3R)-2,3-dihydroxy-4-oxo-4-(thiophen-2-yl)butanoate (*anti*-3o): Yield: 57%, 27.8 mg; white solid, m.p.= 71-72℃; $[\alpha]_D^{25}$ = -25.9 (*c* 0.241, in $CHCl_3$); 97% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 52.76 min, t $_{minor}$ = 57.96 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 3.8 Hz, 1H), 7.77 (d, *J* = 4.9 Hz, 1H), 7.24 – 7.16 (m, 1H), 5.14 (d, *J* = 2.8 Hz, 1H), 4.67 (t, *J* = 5.3 Hz, 1H), 4.25 – 4.02 (m, 2H), 3.87 (d, *J* = 35.6 Hz, 1H), 1.25 – 1.05 (t, *J* = 7.1 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.80, 169.53, 139.15, 134.28, 132.30, 127.43, 75.72, 73.03, 61.17, 12.88. HRMS (EI): calcd for $C_{10}H_{12}O_5SNa$ $[M+Na]^+$: 267.0303 found 267.0301; IR: v=3365.09, 1759.65, 1516.99, 1411.02, 1119.16, 752.87 cm^{-1}

Scale-up reaction

In a flame-dried Schlenk tube, a solution of diethylzinc (1.6 ml, 1.0 mol/L in hexane, 1.6 mmol) was added to a solution of the chiral ligand **L8** (500 mg, 0.8 mmol) in dry dichloromethane (2 mL) under nitrogen at 0 ºC. The mixture was stirred at room temperature for 30 min. Then a solution of α-hydroxy ketones (8.0 mmol, 1.0 equiv) and ethyl glyoxylate (10.3 mmol, 1.3 equiv) in dry dichloromethane (4 mL) was added to the mixture at 0 ºC. The solution was stirring at the same temperature for the necessary reaction times, and then quenched with aqueous NH_4Cl (10 mL), extracted three times with DCM (3 x 10 mL). The combined organics were washed with brine before dried by Na_2SO_4, filtered and concentrated in vacuo. The crude product was separated by flash column chromatography and recrystallization from ethyl acetate and petroleum ether to afford the *syn*-**3a** in 36% yield and with 92% ee and *anti*-**3a** in 41% yield and with 91% ee, respectively.

Procedures for Transformations of the products

Into a 10 ml round bottom flask was placed *syn*-**3a** (71.4 mg, 0.3 mmol, 1 equiv) in 1.5 ml DMF and dimethoxypropane (1.5 ml, 3 mmol, 10 equiv) was added, followed by *p*-toluenesulfonic acid mono hydrate (10 mg, 0.03 mmol, 0.1 equiv). The mixture was stirred at room temperature for 6 h. H_2O and ether were added to the mixture and the aqueous layer was separated and extracted with ether (×4). The combined organic layers were washed with aqueous $NaHCO_3$ and with brine (×4) and dried over Na_2SO_4. The solvent was removed under

reduced pressure and the resulting residue was purified by flash silica gel column chromatography with 10:1 petroleum ether:EtOAc as eluent to give *anti*-**4** in 93% yield.

ethyl (4R,5R)-5-benzoyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (*anti*-4): 93% yield, 77.5 mg; colorless oil; $[\alpha]_D^{25}$ = +35.1 (*c* 0.220, in $CHCl_3$); 80% ee, determined by HPLC analysis (Chiralpak AS column, hexane/*i*-PrOH=9:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 5.3 min, t_{minor} = 6.1 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 7.99 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.46 (d, *J* = 4.8 Hz, 1H), 5.18 (d, *J* = 4.8 Hz, 1H), 4.36 – 4.07 (m, 2H), 1.54 (s, 3H), 1.38 (s, 3H), 1.33 – 1.22 (t, *J* = 8.0 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 195.01, 170.76, 134.76, 133.89, 129.54, 128.68, 80.45, 75.53, 61.85, 26.62, 26.50, 14.14. HRMS (EI): calcd for $C_{15}H_{18}O_5Na$ $[M+Na]^+$: 301.1052, found 301.1050; IR: v=2987.74, 1758.39, 1688.19, 1598.24, 1581.85, 1203.43,1108.88, 790.60, 691.57 cm^{-1}

To a stirred solution of *anti*-**4** (106.4 mg, 0.45 mmol) in dichloroethane (5 mL) at room temperature was added $NaH_2PO_4 \cdot 2H_2O$ (209.2 mg, 1.2 mmol)and *m*-chloroperbenzoic acid (*m*-CPBA) (77.2 mg, 0.900 mmol, >70%). After being stirred for 4h at 50 ºC, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$. The resulting mixture was extracted with diethyl ether (10 mL x 3). The combined organic extracts were washed with ice cooled saturated aqueous $NaHCO_3$ (8 mL x 2) and brine, and then dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by flash silica gel column chromatography with 20:1 petroleum ether:EtOAc as eluent to give *anti*-**5** in 90% yield.

ethyl (4S,5R)5-(benzoyloxy)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (*anti*-5): 90% yield, 119.0 mg; colorless oil; $[\alpha]_D^{25}$ = +3.6 (*c* 0. 778, in $CHCl_3$); 74% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/i-PrOH=19:1, flow rate=1.0 mL/min, λ=254 nm, t_{major}=5.7 min, t_{minor}= 6.8 min). ^{1}H NMR (400 MHz, CDCl3) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 6.66 (s, 1H), 4.81 (d, *J* = 7.7 Hz, 1H), 4.28 – 4.07 (m, 2H), 1.51 (s, 6H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 168.76, 165.37, 133.68, 129.86, 129.32, 128.60, 113.59, 97.43, 80.75, 62.05, 27.95, 27.20, 14.17. HRMS (EI): calcd for $C_{15}H_{18}O_6Na$ $[M+Na]^+$: 317.1001, found 317.0999; IR: v= 3073.57, 1766.73, 1730.21, 1601.28, 1584.09, 1215.12, 1125.82, 784.89, 715.81 cm^{-1}

To the Grignard reagent solution prepared from 0.76 g (5.0 mmol) bromobenzene in 8 mL THF and 115 mg (5.0 mmol) magnesium in 8 mL THF was gradually added 278 mg (1.0 mmol) *anti*-**4** dissolved in 8 mL THF at -20 ºC over a period of 30 min. The mixture was then allowed to room temperature. After stirring for 24 h, the reaction was quenched with saturated aqueous NH_4Cl (10 mL) at -20 ºC. The product was separated and the aqueous phase extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4, and concentrated in vacuo. The resulting residue by flash silica gel column chromatography with 7:1 petroleum ether:EtOAc as eluent to give *anti*-**6** in 43% yield.

(2R,3R)-(-)-1,1,4,4-Tetraphenyl-2,3-(2-propylidenedioxy)butane-1,4-diol (*anti*-6): 43% Yield, 200.3 mg; white solid, m.p.= 207-210℃; $[\alpha]_D^{25}$ = +19.3 (*c* 0.320, in $CHCl_3$); 71% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 98:2, flow rate = 1.0 mL/min, λ = 254 nm, t_{minor} = 6.7 min, t_{major} = 8.4 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 6.8 Hz, 4H), 7.43 – 7.15 (m, 16H), 4.59 (s, 2H), 4.00 (d, *J* = 20.8 Hz, 2H), 1.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.96, 142.72, 128.65, 128.18, 127.66, 127.35, 109.60, 81.00, 78.22, 76.76, 27.19. HRMS (EI): calcd for $C_{31}H_{30}O_4Na$ $[M+Na]^+$: 489.2042, found 489.2038; IR: v=3439.87, 3222.05, 3056.68, 1599.38, 1494.14, 1218.17, 1166.98, 741.86, 788.60 cm^{-1}.

Into a 10 ml round bottom flask was placed *anti*-**3a** (71.4 mg, 0.3 mmol, 1 equiv) in 1.5 ml DMF and dimethoxypropane (1.5 ml, 3 mmol, 10 equiv) was added, followed by *p*-toluenesulfonic acid mono hydrate (10 mg, 0.03 mmol, 0.1 equiv). The mixture was stirred at room temperature for 6 h. H_2O and ether were added to the mixture and the aqueous layer was separated and extracted with ether (×4). The combined organic layers were washed with aqueous $NaHCO_3$ and with brine (×4) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting residue was purified by flash silica gel column chromatography with 8:1 petroleum ether:EtOAc as eluent to give *syn*-**4** in 94% yield.

ethyl (4R,5S)-5-benzoyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (*syn*-4): 94% yield, 77.8 mg; white solid, m.p.= 83-84℃; $[\alpha]_D^{25}$ = -18.1 (*c* 0.182, in $CHCl_3$); 85% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/i-PrOH=4:1, flow rate=1.0 mL/min, λ=254 nm, t_{major}=6.8 min, t_{minor}=8.2 min). 1H NMR (400 MHz, CDCl3) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.58 (d, *J* = 6.8 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 4.12 – 3.88 (m, 2H), 1.60 (s, 3H), 1.47 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.68, 168.59, 135.40, 133.66, 128.89, 128.63, 79.41, 76.30, 61.41, 26.81, 25.86, 13.76. HRMS (EI): calcd for $C_{15}H_{18}O_5Na$ $[M+Na]^+$: 301.1052, found 301.1050; IR: v=2987.74, 1758.39, 1688.19, 1598.24, 1581.85, 1203.43,1108.88, 790.60, 691.57 cm^{-1}

To a stirred solution of *syn*-**4** (106.4 mg, 0.45 mmol) in dichloroethane (5 mL) at room temperature was added $NaH_2PO_4 \cdot 2H_2O$ (209.2 mg, 1.2 mmol)and *m*-chloroperbenzoic acid (*m*-CPBA) (77.2 mg, 0.900 mmol, >70%). After being stirred for 4h at 50 ºC, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$. The resulting mixture was extracted with diethyl ether (10 mL x 3). The combined organic extracts were washed with ice cooled saturated aqueous $NaHCO_3$ (8 mL x 2) and brine, and then dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by flash silica gel column chromatography with 19:1 petroleum ether:EtOAc as eluent to give *syn*-**5** in 93% yield.

ethyl (4R,5S)-5-(benzoyloxy)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (*syn*-5): 93% yield, 119.0 mg; white solid, m.p.= 58-59℃; $[\alpha]_D^{25}$ = +16.6 (*c* 0.826, in $CHCl_3$); 83% ee, determined by HPLC analysis (Chiralpak OD-H column, hexane/*i*-PrOH = 4:1, flow rate = 1.0 mL/min, λ = 254 nm, t_{major} = 5.0 min, t_{minor} = 6.9 min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 2H), 6.71 (d, *J* = 3.8 Hz, 1H), 4.82 (d, *J* = 3.9 Hz, 1H), 4.32 – 3.95 (m, 1H), 1.56 (s, 3H), 1.41 (s, 3H), 1.05 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.55, 164.97, 133.69, 129.79, 129.20, 128.61, 114.39, 93.89, 78.60, 76.78, 61.63, 28.01, 26.40, 14.15. HRMS (EI): calcd for $C_{15}H_{18}O_6Na$ $[M+Na]^+$: 317.1001, found 317.0999; IR: v= 3073.57, 1766.73, 1730.21, 1601.28, 1584.09, 1215.12, 1125.82, 784.89, 715.81 cm^{-1}

To a stirred solution 278 mg (1.0 mmol) *syn*-**4** in 8 mL THF was slowly added 5 mL 1M PhMgBr solution at -20 ºC. The mixture was then allowed to room temperature. After stirring for 24 h, the reaction was quenched with saturated aqueous NH_4Cl (10 mL) at -20 ºC. The product was separated and the aqueous phase extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4, and concentrated in vacuo. The resulting residue by flash silica gel column chromatography with 7:1 petroleum ether:EtOAc as eluent to give *syn*-**6** in 35% yield.

(4R,5S)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(diphenylmethanol) (*syn*-6): 35% yield, 163.1 mg; white solid, m.p.= 207-210℃; $[\alpha]_D^{25}$ = 0 (*c* 0.320, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.9 Hz, 4H),

7.23 (t, *J* = 7.5 Hz, 4H), 7.10 (t, *J* = 7.5 Hz, 6H), 6.98 – 6.79 (m, 6H), 5.55 (s, 2H), 4.19 (d, *J* = 10.3 Hz, 2H), 1.57 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.86, 144.29, 128.76, 128.35, 126.81, 126.62, 125.57, 124.65, 81.73, 26.77, 25.71. HRMS (EI): calcd for $C_{31}H_{30}O_4Na$ $[M+Na]^+$: 489.2042, found 489.2038; IR: v=3439.87, 3222.05, 3056.68, 1599.38, 1494.14, 1218.17, 1166.98, 741.86, 788.60 cm^{-1}

Crystal data

CCDC 1573105 (*syn*-**3j**) contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from TheCambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif.

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Keywords: direct aldol reaction • Aze-Phenol complex • *syn*-*α,β*-Dihydroxy *γ*-Ketoesters • *anti*-*α,β*-Dihydroxy *γ*-Ketoesters • TADDOL

[1] a) A. Author, B. Coauthor, *ChemSusChem* **2008**, *1*, 1-10; b) A. Author, B. Coauthor, *Angew. Chem.* **2006**, *118*, 1-5; *Angew. Chem. Int. Ed.* **2006**, *45*, 1-5; c) L. M. West, P. T. Northcote, C. N. Battershill, *J. Org. Chem.* 2000, *65*, 445-449; d) D. A. Evans, D. S. Welch, A. W. H. Speed, G. A. Moniz, A. Reichelt, S. Ho, *J. Am. Chem. Soc.* 2009, *131*, 3840-3841; e) P. W. Brian, P. J. Curtis, H. G. Hemming, E. G. Jefferts, C. H. Unwin, J. M. Wrught, *Microbiology* 1951, *5*, 619-632; f) B. M. Trost, G. D. Probst, A. Schoop, *J. Am. Chem. Soc.* 1998, *120*, 9228-9236.

[2] a) L. Wang, K. B. Sharpless, *J. Am. Chem. Soc.* **1992**, *114*, 7568-7570; b) H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483-2547.

[3] a) Y. Shi, *Acc. Chem. Res.* **2004**, *37*, 488-496; b) D. Yang, *Acc. Chem. Res.* **2004**, *37*, 497-505; c) Q. H. Xia, H. Q. Ge, C.- P. Ye, Z. M. Liu, K. X. Su, *Chem. Rev.* **2005**, *105*, 1603-1662.

[4] a) Y. Murata, T. Kamino, S. Hosokawa, S. Kobayashi, *Tetrahedron Lett.* **2002**, *43*, 8121-8123; b) A. Battaglia, E. Baldelli, G. Barbaro, P. Giorgianni, A. Guerrini, M. Monari, S. Selva, *Tetrahedron: Asymmetry* **2002**, *13*, 1825-1832; c) N. M. Neisius, B. Plietker, *J. Org. Chem.* **2008**, *73*, 3218-3227; d) N. C. Giampietro, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2009**, *131*, 12556-12557.

[5] a) I. Shiina, Y.-I. Kawakita, R. Ibuka, K. Yokoyama, Y.-S. Yamai, *Chem. Commun*. **2005**, 4062-4064; b) B. M. Trost, S. Malhotra, B. A. Fried, *J. Am. Chem. Soc*. **2009**, *131*, 1674-1675; c) T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, N. Abe, T. Ooi, K. Maruoka, *Chem. Asian J*. **2010**, *5*, 562-570; d) C. Liu, X. Dou, Y. Lu, *Org. Lett*. **2011**, *13*, 5248-5251; e) B. M. Trost, S. Malhotra, P. Koschker, P. Ellerbrock, *J. Am. Chem. Soc*. **2012**, *134*, 2075-2084; f) B. M. Trost, D. J. Michaelis, M. I. Truica, *Org. Lett*. **2013**, *15*, 4516-4519.

[6] N. Kumagai, S. Matsunaga, T. Kinoshita, S. Harada, S. Okada, S. Sakamoto, K. Yamaguchi, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 2169-2178

[7] T. Misaki, G. Takimoto, T. Sugimura, *J. Am. Chem. Soc*. **2010**, *132*, 6286-6287

[8] a) D. Haigh, H. C. Birrell, B. C. C. Cantello, D. S. Eggleston, R. C. Haltiwanger, R. M. Hindley, A. Ramaswamy, N. C. Stevens, *Tetrahedron: Asymmetry* **1999**, *10*, 1353-1367; b) W. Zhang, R. G. Carter, A. F. T. Yokochi, *J. Org. Chem.* **2004**, *69*, 2569-2572; c) M. B. Andrus, B. B. V. S. Sekhar, E. L. Meredith, N. K. Dalley, *Org. Lett.* **2000**, *2*, 3035-3037; d) Z. Li, R. Wu, R. Michalczyk, R. B. Dunlap, J. D. Odom, L. A. P. Silks, *J. Am. Chem. Soc.* **2000**, *122*, 386-387; e) M. T. Crimmins, P. J. McDougall, *Org. Lett.* **2003**, *5*, 591-594; f) T. R. Hoover, S. R. Hitchcock, *Tetrahedron: Asymmetry* **2003**, *14*, 3233-3241; g) S. Kobayashi, M. Horibe, *J. Am. Chem. Soc.* **1994**, *116*, 9805-9806; h) S. Kobayashi, T. Hayashi, *J. Org. Chem.* **1995**, *60*, 1098-1099; i) S. Kobayashi, M. Horibe, *Chem. Eur. J.* **1997**, *3*, 1472-1481.

[9] a) S. E. Denmark, W.-j. Chung, *Angew. Chem*. **2008**, *120*, 1916 –1918; *Angew. Chem. Int. Ed*. **2008**, *47*, 1890-1892S; b) E. Denmark, W.-j. Chung, *J. Org. Chem*. **2008**, *73*, 4582-4595.

[10] a) B. M. Trost, M. J. Bartlett, *Acc. Chem. Res.* **2015**, *48*, 688-701; b) B. M. Trost, H. Ito, *J. Am. Chem. Soc.* **2000**, *122*, 12003-12004; c) B. M. Trost, L. R. Terrell, *J. Am. Chem. Soc.* **2003**, *125*, 338-339; d) Y. Xiao, Z. Wang, K. Ding, *Chem. Eur. J.* **2005**, *11*, 3668-3678; e) B. M. Trost, C. Müller, *J. Am. Chem. Soc.* **2008**, *130*, 2438-2439; f) D. Zhao, L. Wang, D. Yang, Y. Zhang, R. Wang, *Angew. Chem*. 2012, *124*, 7641 –7645; *Angew. Chem. Int. Ed.* **2012**, *51*, 7523-7527; g) B. M. Trost, F. Miege, *J. Am. Chem. Soc.* **2014**, *136*, 3016-3019; h) B. M. Trost, T. Saget, C.-I. Hung, *J. Am. Chem. Soc.* **2016**, *138*, 3659-3662; i) B. M. Trost, T. Saget, C.-I. Hung, *Angew. Chem*. 2017, *129*, 2480 –2484; *Angew. Chem. Int. Ed.* **2017**, *56*, 2440-2444; j) B. M. Trost, V. S. C. Yeh, H. Ito, N. Bremeyer, *Org. Lett.* **2002**, *4*, 2621-2623.

[11] a) B. M. Trost, V. S. C. Yeh, *Org. Lett.* **2002**, *4*, 3513-3516; b) B. M. Trost, M. U. Frederiksen, J. P. N. Papillon, P. E. Harrington, S. Shin, B. T. Shireman, *J. Am. Chem. Soc.* **2005**, *127*, 3666-3667; c) B. M. Trost, A. H. Weiss, *Org. Lett.* **2006**, *8*, 4461-4464; d) B. M. Trost, A. H. Weiss, *Angew. Chem*. 2007, *119*, 7808 –7810; *Angew. Chem. Int. Ed.* **2007**, *46*, 7664-7666; e) B. M. Trost, D. J. Michaelis, S. Malhotra, *Org. Lett.* **2013**, *15*, 5274-5277; f) B. M. Trost, A. Quintard, *Org. Lett.* **2012**, *14*, 4698-4700; g) B. M. Trost, B. Biannic, C. S. Brindle, B. M. O'Keefe, T. J. Hunter, M.-Y. Ngai, *J. Am. Chem. Soc.* **2015**, *137*, 11594-11597.

[12] a) Y.-Z. Hua, L.-J. Lu, P.-J. Huang, D.-H. Wei, M.-S. Tang, M.-C. Wang, J.-B. Chang, *Chem. Eur. J*. **2014**, *20*, 12394-12398; b) Y.-Z. Hua, X.-C. Yang, M.-M. Liu, X. Song, M.-C. Wang, J.-B. Chang, *Macromolecules* **2015**, 48, 1651-1657.

[13] Y.-Z. Hua, M.-M. Liu, P.-J. Huang, X. Song, M.-C. Wang, J.-B. Chang, *Chem. Eur. J.* **2015**, *21*, 11994-11998.

[14] D. Zhao, Y. Yuan, A. S. C. Chan, R. Wang, *Chem. Eur. J.* **2009**, *15*, 2738-2741.

[15] D. Seebach, A. K.Beck, A. Heckel, *Angew. Chem.* 2001, *113*, 96-142; *Angew. Chem. Int. Ed*. **2001**, *40*, 92-138.

[16] D. A. Evans, M. C. Kozlowski, J. A. Murry, C. S. Burgey, K. R. Campos, B. T. Connell, R. J. Staples, *J. Am. Chem. Soc*. **1999**, *121*, 669-685.

[17] a) B. M. Trost, H. Ito, *J. Am. Chem. Soc.* **2000**, *122*, 12003-12004; b) B. M. Trost, V. S. C. Yeh, H. Ito, N. Bremeyer, *Org. Lett*. 2002, *4*, 2621.

[18] D.-P. Zhao, L.-J. Mao, D.-X. Yang, R. Wang, *J. Org. Chem.* **2010**, *75*, 6756–6763

[19] Y.-Z. Hua, L.-J. Lu, P.-J. Huang, D.-H. Wei, M.-S. Tang, M.-C. Wang, J.-B. Chang, *Chem. Eur. J.* **2014**, *20*, 12394-12398.

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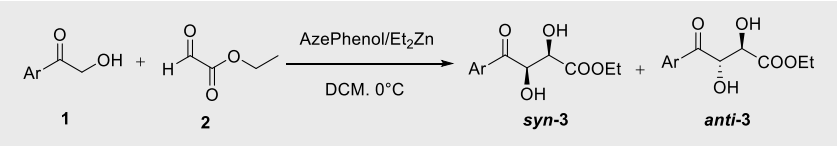

Synthesis of Chiral *α,β*-Dihydroxy *γ*-Ketoesters

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Enantioselective Direct Synthesis of *syn*- and *anti*-*α,β*-Dihydroxy *γ*-Ketoesters by a Dinuclear Zinc-AzePhenol Complex

A one-step enantioselective direct synthesis of both *syn*- and *anti*-*α,β*-dihydroxy *γ*-ketoesters by a dinuclear zinc-AzePhenol complex is presented. This asymmetric *α*-hydroxyacetate aldol reaction proceeds in moderate to good yield and with excellent enantioselectivity of up to 99% ee. The desired products could be versatile intermediates for several transformations.

*Chiral Lewis acid catalysis