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Asymmetric Construction of α-Substituted β-Hydroxy Lactones via Ni Catalyzed Decarboxylative Addition Reaction

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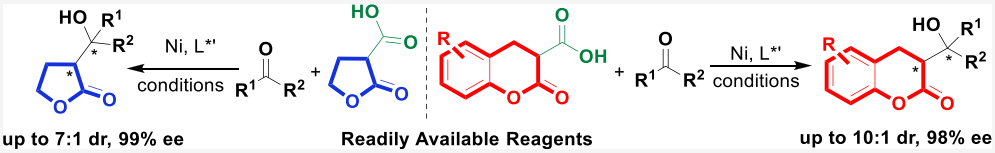


ABSTRACT: We described a Ni-bidentate oxazoline catalyzed highly enantio- and diastereoselective decarboxylative aldol reaction of 2-oxotetrahydrofuran-3-carboxylic acid/2-oxochromane-3-carboxylic acid derivatives with different kinds of carbonyls. Under optimal reaction conditions, α-substituted β-hydroxy butyrolactones and dihydrocoumarins with an all-carbon quaternary stereocenter have been generated with high levels of functional-group compatibility. Furthermore, proficient transformations of products were also described, in which an aliphatic tertiary alcohol and a multi-substituted 1,4-diol were smoothly constructed through hydrogenation and ring-opening reaction, respectively.

Enantioenriched butyrolactones[1] and dihydrocoumarins[2] specifically α-functionalized scaffolds symbolize significant lactone moieties which are wildly found in natural products and pharmaceuticals as exemplified by microtermolides B,[3] virginiae butanolides,[4] and salprzelactone[5] (Figure 1). Besides, they are

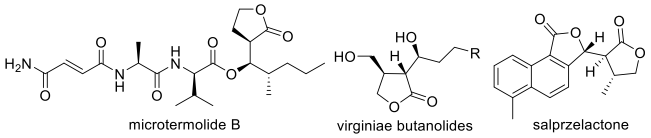
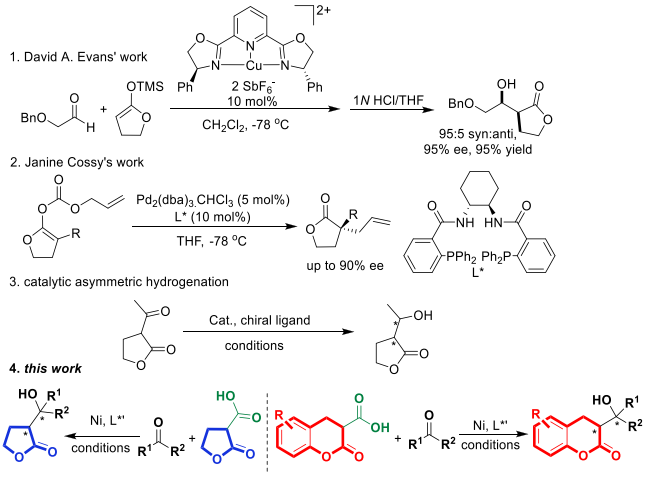


Figure 1. Natural products and pharmaceuticals containing chiral cyclic ester moieties.

also versatile building blocks for the synthesis of alcohols with great structure diversity via ring-opening reactions.[6] Thus, the exploration of efficient methods to construct enantioenriched lactones becomes an attractive target in organic synthesis.

Obviously, the direct catalytic asymmetric α-functionalization of lactones would be an ideal approach to enantioenriched α-substituted lactones. However, it is a very challenging task due to the high pK_a value of lactones' α-proton, which makes them difficult to enolize under mild conditions; besides, the ring-opening possibility of a cyclic ester moiety brings additional difficulties to the target. Accordingly, multiple operations were always required for the asymmetric synthesis of α-substituted lactones, and attempts to develop catalytic asymmetric methodologies for this target were mainly focused on Mukaiyama-type addition reactions (Scheme 1, eq 1)[7] or functional group transformation of multi-substituted lactones (Scheme 1, eqs 2 and 3).[6a]

Scheme 1. Catalytic Asymmetric Synthesis of α-Substituted Cyclic Esters



Hence, developments of direct catalytic α-functionalizations of lactones are constantly in high demand, which may provide a general and convenient access to versatile α-substituted lactones

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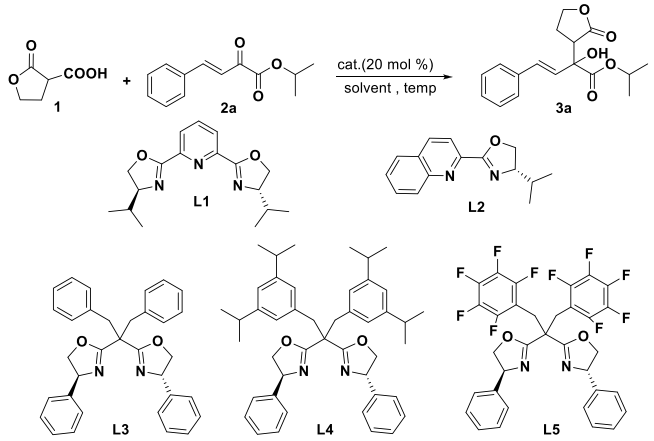
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	solvent	T (°C/h)	yield (%)[b]	ee (%)[c]	dr[c]
1	$Cu(OAc)_2$	THF	60/24	20		1:1
2	$Ni(OAc)_2{\cdot}4H_2O$	THF	60/24	33		1.2:1
3	[Ni]/**L1**	THF	10/72	38	16	1:1
4	[Ni]/**L2**	THF	10/72	79	63	6.6:1
5	[Ni]/**L3**	THF	10/72	52	81	1.3:1
6	[Ni]/**L4**	THF	10/72	53	76	1.4:1
7	[Ni]/**L5**	THF	10/72	57	92	1.5:1
8	[Ni]/**L5**	EtOH	10/72	78	99	7:1
9	[Ni]/**L5**	EtOH	0/72	70	98	7.1:1

[a]General reaction conditions: **1** (0.2 mmol), **2a** (0.1 mmol), ligand (22 mol %), and catalyst (20 mol %) in 1 mL of solvent at a specific temperature for a specific time. [b]Isolated yield of major diastereoisomer. [c]Determined by chiral HPLC analysis. [Ni] = $Ni(OAc)_2{\cdot}4H_2O$.

from simple starting materials. However, related studies were rarely reported so far.

Inspired by nature's way to synthesize polyketide and fatty acids,[8] we are particularly interested in catalytic asymmetric decarboxylative addition reactions for the synthesis of chiral carboxylic acid derivatives. Since Shair et al. reported the asymmetric decarboxylative aldol reaction of methylmalonic acid half-thioester and aldehydes in 2005,[9] β-keto acids, malonic acid half-thioesters (MAHTs), and 2-cyanoacetic acid have been successfully employed in decarboxylative addition reactions.[10] In contrast, malonic acid and malonic acid half-oxyesters (MAHOs), which can act as nucleophilic equivalents of acetic acid/ester via decarboxylation process, remain largely unexplored and unexploited in catalytic asymmetric decarboxylative additions due to their poorer nucleophilic abilities.[11,12] Recently, we made our initial efforts to address this problem: in the promotion of Ni-oxazoline complexes, we successfully achieved novel catalytic asymmetric decarboxylative aldol reactions of malonic acid and half-oxyesters with various carbonyls.[13]

Encouraged by these results as well as the importance of chiral α-substituted lactones, two types of nucleophilic cyclic esters surrogates, 2-oxotetrahydrofuran-3-carboxylic acid (OTHFCA)[14] and 2-oxochromane-3-carboxylic acid as (OCCA)),[15] were designed as potential decarboxylative donors for the construction of α-substituted cyclic esters. Herein, we report a nickel-oxazoline complex catalyzed highly enantio- and diastereoselective decarboxylative aldol reaction of OTHFCA/OCCA with various carbonyls, affording a facile access to α-substituted β-hydroxy lactones in good yield with high stereoselectivity (Scheme 1, eq 4).

OTHFCA **1** was readily synthesized according to the previous literature.[14] With this cyclic ester precursor in hand, our research commenced with exploring the catalytic ability of different metal salts in the decarboxylative aldol reaction of **1** and isopropyl (*E*)-2-oxo-4-phenylbut-3-enoate **2a**. Different Lewis acids such as $Cu(OAc)_2$ and $Ni(OAc)_2{\cdot}4H_2O$ were evaluated in THF at 60 °C (for the full evaluation of metal salts, see the Supporting Information). Fortunately, the desired decarboxylative addition product **3a** was obtained in 20% yield and 1:1 dr in 24 h when 20 mol % of $Cu(OAc)_2$ was employed as catalyst (entry 1, Table 1), while $Zn(OTf)_2$, $MnSO_4$, and $FeCl_3$ failed to give any product. Noticeably, $Ni(OAc)_2{\cdot}4H_2O$ exhibited the best catalytic ability and resulted in product **3a** with higher yield and diastereoselectivity (entry 2). Next, the effects of different chiral oxazoline ligands were studied (for the full evaluation of ligands, see the Supporting Information). Generally, improvements in reaction performance were always observed when oxazoline ligands were added in the reaction. It is worth noting that the introduction of a pyridine moiety to the bidentate oxazoline ligand brought a good effect on diastereoselectivity (entry 4), while bidentate oxazoline ligands with bulky substituents on the methylene carbon exhibited better enantiocontrol (entries 5−7). Noticeably, bidentate oxazoline **L5** bearing a 5F-benzyl group afforded the desired product with the highest enantioselectivity, albeit with poor diastereoselectivity (entry 7). To improve the result, further optimization of reaction conditions was carried out by employing **L5** as ligand (for the full evaluation of solvents, temperature, and additives, see the Supporting Information). It was revealed that solvent played an important role in stereocontrol, while the addition of organic or inorganic base decreased the reaction conversion as well as enantioselectivity. Finally, the best result was obtained when the reaction was conducted in EtOH at 10 °C for 72 h (entry 8, 78% yield, 99% ee, 7:1 dr).

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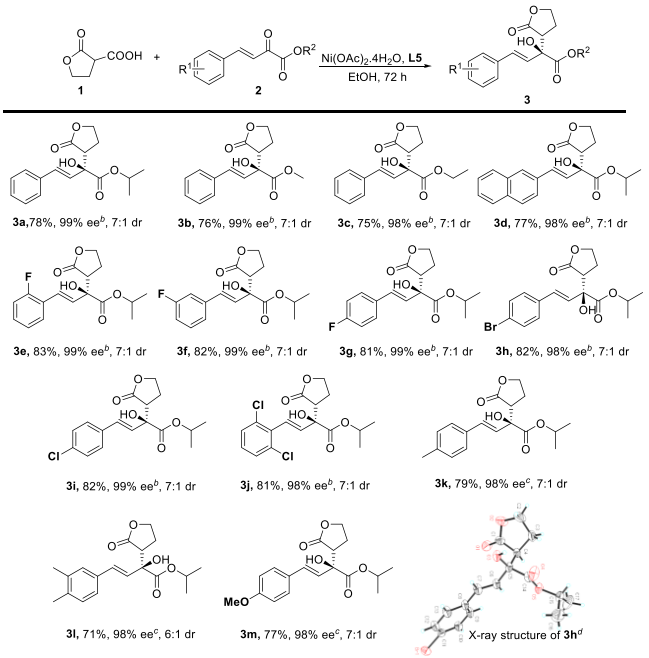
With the optimal conditions in hand, the versatility of this reaction was examined with respect to carbonyl substrates by using **1** as donor, as described in Scheme 2. First, we studied the

Scheme 2. Catalytic Asymmetric Decarboxylative Aldol Reaction of OTHFCA 1 and (*E*)-2-oxo-4-arylbut-3-enoates 2[a]

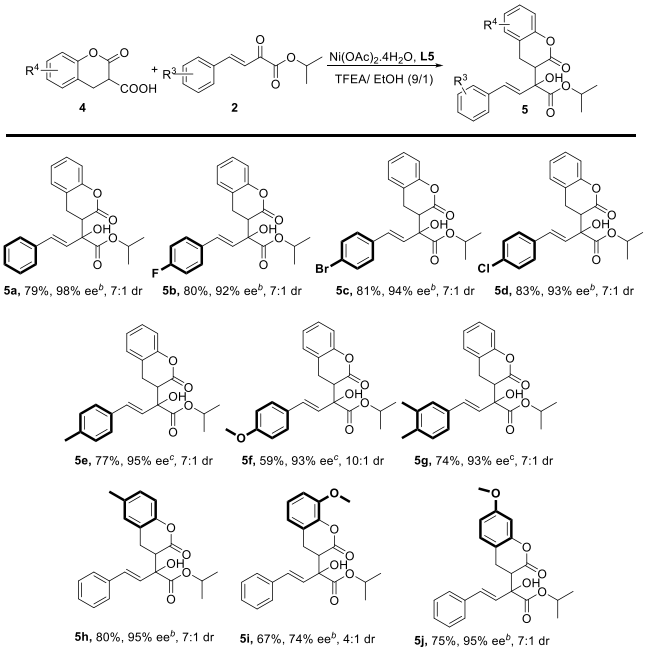


[a]General reaction conditions: **1** (0.2 mmol), **2** (0.1 mmol), **L5** (22 mol %), and $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %) in 1 mL of EtOH at a specific temperature for 72 h; given are isolated yields of major diastereoisomer. ee was determined by chiral HPLC analysis. [b]Reaction was carried out at 10 °C. [c]Reaction was carried out at 20 °C. [d]X-ray structure of **3h** (ellipsoid contour at 30% probability).

effect of the ester moiety of **2** and found that changing ^{i}Pr to Me or Et brought little influence on the reaction conversion as well as stereoselectivities. As a result, both **2b** and **2c** gave the desired products **3b** and **3c** with good yields, diastereoselectivities and excellent enantioselectivities. Subsequently, aryl substituents of **2** were also examined. It was shown that placing various functional groups on the aromatic ring had very limited effect on the reaction outcomes: isopropyl (*E*)-2-oxo-4-arylbut-3-enoate bearing either an electron-donating or an electron-withdrawing group on different positions of the benzene ring generally furnished products in high yields and stereoselectivities (**3d**−**3m**, 71−83%, 6:1−7:1 dr, 98−99% ee). The absolute configuration of product **3h** was assigned as (*S*,*S*)-configuration by X-ray analysis (CCDC 2035137; see the Supporting Information).

Further application of this asymmetric decarboxylative aldol reaction was carried out by employing OCCAs as reactants. However, the desired product **5a** was obtained in moderate yield and enantioselectivity and low diastereoselectivity when the reaction of **4a** and **2a** was carried out under the standard conditions described in Scheme 2. To improve the reaction outcomes, a careful evaluation of solvents was next conducted, which revealed that binary solvents of TFEA/EtOH (9/1) could dramatically enhance the reaction outcomes, leading to **5a** in 79% yield, 7:1 dr, and 98% ee (Scheme 3, product **5a**; for further details of screening optimal conditions, see the Supporting

Scheme 3. Catalytic Asymmetric Decarboxylative Aldol Reaction of OCCA 4 and (*E*)-2-oxo-4-arylbut-3-enoates 2[a]



[a]General reaction conditions: **4** (0.2 mmol), **2** (0.1 mmol), **L5** (22 mol %), and $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %) in 1 mL of mixed solvents (TFEA·EtOH = 9:1) at a specific temperature for 72 h; given are isolated yield of major diastereoisomer. ee was determined by chiral HPLC analysis. [b]Reaction was carried out at 20 °C. [c]Reaction was carried out at 30 °C.

Information). With these optimized conditions in hand, we next examined the substrate scope, and a series of OCCAs as well as (*E*)-2-oxo-4-arylbut-3-enoates were employed. As shown in Scheme 3, different functional groups on carbonyl acceptors **2** were well tolerated and afforded the desired products in good to excellent yields with high stereoselectivities in most cases (**5a**−**5g**, 59−83%, 7:1−10:1 dr, 92−98% ee). However, the substituents of OCCAs had an obvious influence on reaction results. For example, OCCA with a methoxyl group at the 8-position led to a decreased enantio- and diastereoselectivity value of product **5i**, while the 7-substituted one afforded the desired product in satisfactory result (**5j**, 75%, 7:1 dr, 95% ee).

Additionally, 4-nitrobenzaldehyde and isatin also fit well under modified conditions. In the presence of 20 mol % Ni (II)-**L3** complex, 4-nitrobenzaldehyde **6** and OTHFCA **1** were smoothly converted into 3-(hydroxy(4-nitrophenyl)methyl)-dihydrofuran-2(3*H*)-one **7** in 52% yield (major diastereomer) with high enantioselectivity, albeit with 1.3:1 dr (Scheme 4). When isatin acted as electrophile, 3-hydroxy-3-(2-oxotetrahydrofuran-3-yl)indolin-2-one was constructed with higher reaction conversion as well as stereoselectivity (major diastereomer, 87%, 7:1 dr, 96% ee). Unfortunately, other aldehydes than nitro-substituted ones exhibited low reactivities, while activated ketones such as α-keto esters and 1*H*-indene-1,2(3*H*)-dione failed to give any products under the present reaction conditions.

Noticeably, a 5 mmol scale catalytic procedure was performed in this reaction. As shown in Scheme 5, treatment of OTHFCA **1** (1.3 g, 10 mmol) with isopropyl (*E*)-4-(4-chlorophenyl)-2-oxobut-3-enoate (1.26 g, 5 mmol) in the promotion of 10 mol %

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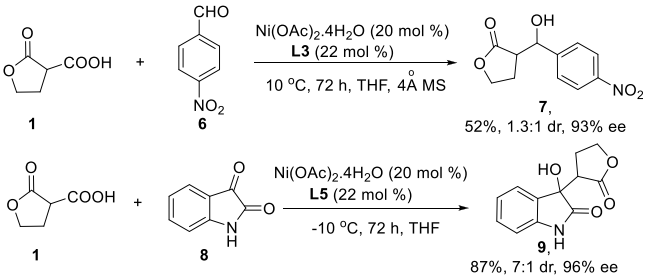
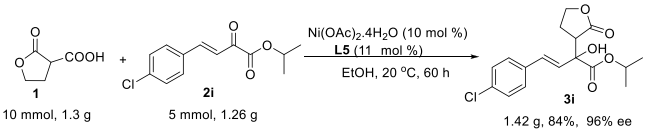
Scheme 4. Catalytic Asymmetric Decarboxylic Aldol Reaction of OTHFCA 1 and Different Carbonyls[a]



[a]Isolated yield for 0.1 mmol scale reaction.

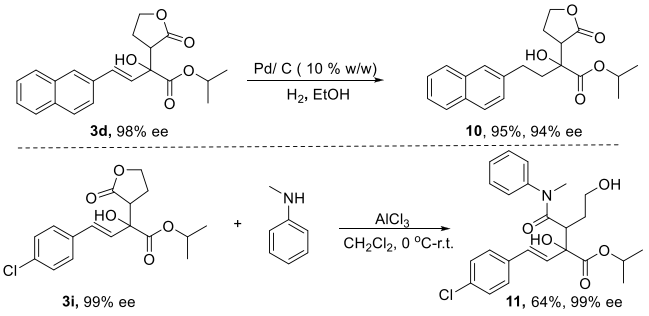
Scheme 5. 5 mmol-Scale Catalytic Procedure



Ni-**L5** catalyst led to the corresponding product **3i** in high yield and enantioselectivity (for major diastereomer, 84%, 96% ee).

To demonstrate the synthetic utilities of our methodology, further transformations of obtained adducts were next carried out, as underlined in Scheme 6. For example, in the presence of

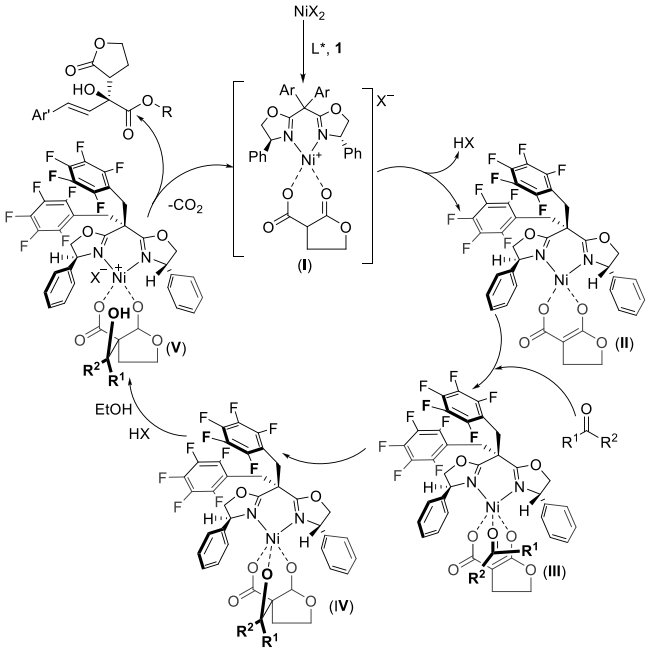
Scheme 6. Transformation of α-Substituted β-Hydroxy Butyrolactone Products



Pd/C (10% w/w), **3d** can be smoothly reduced to a aliphatic tertiary alcohol **10** with a dihydrofuran-2(3*H*)-one substituent in high yield and enantioselectivity. Besides, $AlCl_3$ catalyzed ring-opening reaction of adduct **3i** by *N*-methylaniline afforded multi-substituted 1,4-diol **11** with good yield and maintained enantioselectivity.

On the basis of previous work[13b] and obtained results herein, a nickel catalyzed aldol-decarboxylation mechanism was proposed. As shown in Scheme 7, OTHFCA was efficiently activated by Ni-bidentate oxazoline catalyst via nickel-dicarbonyl interaction (I), thus affording the nucleophilic intermediate (II) after enolization and deprotonation; subsequently, intermediate (II) enantioselectively attacked carbonyl acceptors **2** from the *Si* face and produced corresponding aldol-type adducts, which then cleaved CO_2 to produce the desired α-substituted β-hydroxy with an (*S*,*S*)-configuration. The fact that higher yield and stereoselectivity were obtained when EtOH was employed as solvent suggested EtOH may not only play an important role in the H-transfer step[18] but also act as ligand/hydrogen-bond donor to stabilize the catalytic transition state.[19] As regards the outstanding enantiocontrol

Scheme 7. Plausible Mechanism of Asymmetric Decarboxylative Aldol Reaction



ability of ligand **L5** exhibited in this aldol-decarboxylation transformation, we suppose that the introduction of electron-deficient pentafluorobenzyls into oxazoline may obviously affect C−H/π interactions in catalytic transition states,[20] thus enabling a better stereochemical model and affording the desired products in high stereoselectivity. To gain more insight into this decarboxylative process, the high resolution mass spectroscopy (HRMS) analysis of the reaction between **1** and isopropyl (*E*)-4-(3-fluorophenyl)-2-oxobut-3-enoate was carried out. Under standard conditions, two peaks at *m*/*z* 1089.1777 and 1091.1844 were observed, indicating intermediates (IV) and (V) were reasonable.

In summary, a highly enantioselective generation of α-substituted butyrolactones and dihydrocoumarins with an all-carbon quaternary stereocenter has been realized. The newly decarboxylative aldol reaction of OTHFCA/OCCA took place smoothly with a variety of carbonyl electrophiles via Ni-bidentate oxazoline catalysis under mild conditions. The afforded results demonstrated high levels of functional-group compatibility attainable with this method. Remarkably, the resulting adducts can be smoothly converted into corresponding chiral alcohol derivatives through simple operations. Thus, the present method provides access to synthetically relevant building blocks with a fully substituted carbon stereocenter that was hitherto difficult to prepare in enantioenriched form. Further researches toward broadening this methodology are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. Chemicals were received from commercial sources without further purification or prepared by literature methods. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz Bruker spectrometer, using $CDCl_3$, DMSO, or acetone as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity, integration, and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm), multiplicity, and coupling constant (Hz). HRMS (Micromass GCTMS) spectra were

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recorded on a P-SIMS-Gly of Bruker Daltonics Inc. HPLC analysis was performed on a Shimdzu LC-20A. Chiralpak AS, AD, OD, were purchased from Daicel Chemical Industries, Ltd. X-ray crystallographic analysis was performed at the Bruker D8 Venture X-ray single crystal diffractometer, at Shanghai Institute of Organic Chemistry (SIOC), Chinese Academy of Sciences (CAS). Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Flash column chromatographic purification of products was accomplished using forced-flow chromatography on silica gel (300−400 mesh).

General Procedure for the Synthesis of 2-Oxotetrahydrofuran-3-carboxylic Acid (OTHFCA) 1.[14] The 2-oxotetrahydrofuran-3-carboxylic acid (OTHFCA) was prepared as follows: Under a N_2 atmosphere, triethylamine hydrobromide (1.4 g, 7.7 mmol) was added to a solution of cyclopropane-1,1-dicarboxylic acid (1 g, 7.7 mmol) in CH_3CN (20 mL). The mixture was heated to 75 °C in an oil bath and left overnight (16 h) until the reaction completed. Afterward, the reaction mixture was evaporated under vacuum, and the remaining solid was dissolved in H_2O, which was extracted with DCM (3 × 20 mL). Then, 10 mL of 10% of aqueous HCl was added into the aqueous phase, and extracted with EtOAc (3 × 20 mL). The combined organic layer was washed with saturated NaCl solution, dried over Na_2SO_4, and concentrated to give the desired product **1** as an oil (0.9 g, 90% yield).

General Procedure for the Synthesis of β,γ-Unsaturated α-Keto Esters 2a.[16] A 100 mL round-bottom flask was charged with a mixture of pyruvic acid (1.32 g, 15 mmol) and benzaldehyde (1.59 g, 15 mmol) in 5 mL of MeOH, and KOH (1.29 g, 23 mmol) dissolved in 5 mL of methanol, which was dropped to the mixture while maintaining the temperature at 25 °C. Next, the yellow color of the solution darkened to orange-red. A voluminous precipitate of yellow potassium benzylidenepyruvate was accumulated when the temperature rose to 40 °C. The precipitate was filtered using a Buchner funnel and washed with cold methanol to give potassium 2-oxo-4-phenylbut-3-enoate. The solid was used in the next step without further purification.

The formed potassium 2-oxo-4-phenylbut-3-enoate (2.68 g, 12.5 mmol) was dissolved in isopropanol (17.5 mL), and then acetyl chloride (3 mL, 35 mmol) was added dropwise with constant stirring at 0 °C. The reaction mixture was left to react for an additional 2 h at room temperature. Afterward, the reaction mixture was heated to reflux overnight until the reaction completed. The excess amount of isopropanol was removed under reduced pressure. Then 8.5 mL of H_2O was added to the crude mixture, which was extracted with DCM (3 × 25 mL). The combined organic layers were washed with $NaHCO_3$ solution, followed by saturated NaCl aqueous solution (30 mL). The organic layers were collected, dried over anhydrous $MgSO_4$, and then concentrated under reduced pressure, to give the final product as a yellow, viscous oil **2a** (2.45 g, 90% yield).

General Procedure for the Synthesis of 2-Oxochromane-3-carboxylic Acid 4.[15] A Schlenk tube was equipped with a stirring bar and charged with salicyaldehyde (61 mg, 0.5 mmol), malonic acid cyclic isopropylidene ester (72 mg, 0.5 mmol), diethyl 1,4-dihydro-2,6-dimethyl-3, and 5-pyridine dicarboxylate (129 mg, 0.5 mmol). 1 mL of H_2O was then added to the mixture. After reacting at room temperature for 6 h, a saturated aqueous $NaHCO_3$ solution was added to the reaction until the pH is 8−9. The mixture was extracted with EtOAc (3 × 6 mL); 10% of aqueous HCl was then added to the aqueous layer until the pH is 3−4. The solution was extracted with EtOAc (3 × 6 mL) as well. The combined EtOAc was washed with saturated NaCl solution, dried over Na_2SO_4, and concentrated to give a white solid of product **4** (70% yield).

General Procedure for the Catalytic Decarboxylative Aldol Reaction of 1 and 2. A clean and dried Schlenk tube was charged with $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %), ligand **L5** (22 mol %), and 1.0 mL of EtOH. The mixture was stirred vigorously at room temperature for half an hour. Subsequently, **1** (0.2 mmol, 2 equiv) and **2a** (0.1 mmol, 1 equiv) were added, and the resulting mixture was stirred at a temperature of 10 °C for 72 h until the reaction completed. The reaction mixture was then purified through flash column chromatography on a silica gel to yield the target products.

General Procedure for the Catalytic Decarboxylative Aldol Reaction of 4 and 2. A clean and dried Schlenk tube was charged with $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %), ligand **L5** (22 mol %), and 1.0 mL of mixed solvents (TFEA:EtOH = 9:1). The mixture was stirred vigorously at room temperature for half an hour. Subsequently, **4** (0.2 mmol, 2 equiv) and **2** (0.1 mmol, 1 equiv) were added, and the resulting mixture was stirred at a specific temperature for 72 h until the reaction completed. The reaction mixture was then purified through flash column chromatography on a silica gel to yield the target products.

General Procedure for Millimole-Scale Catalytic Synthesis of 3i. A clean and dried 100 mL round-bottom flask was charged with $Ni(OAc)_2{\cdot}4H_2O$ (10 mol %), ligand (11 mol %), and 25 mL of EtOH. The mixture was stirred vigorously at room temperature for 1 h; then **1** (1.3 g, 10 mmol) and **2i** (1.26 g, 5 mmol) were added. The resulting mixture was stirred at 20 °C for 60 h. After completion of reaction (monitored by TLC), the remaining solvent was removed in vacuum. The crude product was purified by flash chromatography on silica gel using hexanes/EtOAc (15:1−5:1) as eluent to give the desired product **3i** as a white solid (1.42 g, 84% yield, 96% ee).

General Procedure for the Catalytic Asymmetric Synthesis of 7. A clean and dried Schlenk tube was charged with $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %), ligand **L3** (22 mol %), and 1.0 mL of EtOH. The mixture was stirred vigorously at room temperature for half an hour. Subsequently, **1** (0.2 mmol, 2 equiv), **6** (0.1 mmol, 1 equiv), and 50 mg of 4A molecular sieves were added, and the resulting mixture was stirred at 10 °C for 72 h until the reaction completed. The reaction mixture was then purified through flash column chromatography on a silica gel to yield the target products **7**.

General Procedure for the Catalytic Asymmetric Synthesis of 9. A clean and dried Schlenk tube was charged with $Ni(OAc)_2{\cdot}4H_2O$ (20 mol %), ligand **L5** (22 mol %), and 1.0 mL of THF. The mixture was stirred vigorously at room temperature for half an hour. Subsequently, **1** (0.2 mmol, 2 equiv) and **8** (0.1 mmol, 1 equiv) were added, and the resulting mixture was stirred at −10 °C for 72 h until the reaction completed. The reaction mixture was then purified through flash column chromatography on a silica gel to yield the target products **9**.

Experimental Procedure for the Synthesis of Isopropyl 2-Hydroxy-4-(naphthalene-2-yl)-2-(2-oxotetrahydrofuran-3-yl)-butanoate 10. Compound **3d** (36 mg, 0.1 mmol, 98% ee) was dissolved in EtOH and allowed to react in the presence of Pd/C catalyst (3.6 mg, 10% loading in 50% water) under a hydrogen atmosphere at ambient temperature for 1 h. The catalyst was removed via filtration through Celite, followed by removal of the solvent under vacuum. The crude product was purified via flash chromatography on silica gel using petroleum ether/EtOAc (15:1−8:1) as eluent, to give the final product **10** as a colorless liquid (33.8 mg, 95%, 94% ee).

Experimental Procedure for the Synthesis of Isopropyl (*E*)-2-(4-Chlorostyryl)-2,5-dihydroxy-3-(methyl(phenyl)carbamoyl)-pentanoate 11.[17] To a solution of $AlCl_3$ (73.2 mg, 0.4 mmol, 2 equiv) in CH_2Cl_2 (1 mL) was added *N*-methylaniline (81 μL, 80 mg, 0.75 mmol, 3.75 equiv) slowly at 0 °C. When the solution turned dark, **3i** (64 mg, 0.2 mmol, 99% ee) in CH_2Cl_2 (0.5 mL) was added at 0 °C, and the mixture was stirred for 5 h at room temperature. To the gray-brown suspension was added 1 mL of H_2O, and the mixture was stirred for 30 min at 0 °C. The mixture was filtered through Celite, and the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2, and the combined organic layers were washed with H_2O, saturated aqueous NaCl, NH_4Cl solution, and finally with $NaHCO_3$ (10%). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified via flash column chromatography on silica gel using petroleum ether/EtOAc (2:1−1:1) as eluent and concentrated to give the product **11** as a colorless liquid (57.1 mg, 64% yield, 99% ee).

*iso-Propyl-(E)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)-4-phenylbut-3-enoate (**3a**).* The compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (23.7 mg, 78% yield) as a white solid. MP = 90.6.8−92.5 °C, $[\alpha]_D^{25}$ = +35.2 (*c* = 0.1 in EtOAc); enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 19.305 min, t_R (minor) = 12.709

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min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.37 (m, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.28−7.22 (m, 2H), 6.86 (d, J = 15.9 Hz, 1H), 6.42 (d, J = 15.9 Hz, 1H), 5.14−5.12 (m, 1H), 4.40 (td, J = 8.6, 5.4 Hz, 1H), 4.24 (td, J = 8.4, 7.1 Hz, 1H), 3.95 (s, 1H), 3.13 (dd, J = 9.4, 7.8 Hz, 1H), 2.41−2.23 (m, 2H), 1.31 (dd, J = 6.3, 4.1 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.3, 172.2, 136.10, 131.5, 128.5, 128.0, 126.9, 126.9, 77.7, 71.1, 66.7, 46.7, 24.76, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{21}O_5$ 305.1384; found: 305.1371.

*Methyl-(E)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)-4-phenyl-but-3-enoate (**3b**).* The compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (4:1, v/v) as eluent, obtained (21.0 mg, 76% yield) as a colorless liquid; $[\alpha]_D^{25}$ = +27.4 (c = 0.11 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 24.220 min, t_R (minor) = 16.429 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46−7.38 (m, 2H), 7.36−7.29 (m, 2H), 7.27−7.26 (m, 1H), 6.86 (d, J = 15.9 Hz, 1H), 6.41 (d, J = 15.9 Hz, 1H), 4.40 (td, J = 8.5, 5.4 Hz, 1H), 4.24 (dt, J = 8.8, 7.6 Hz, 1H), 4.02 (s, 1H), 3.85 (s, 3H), 3.12 (dd, J = 9.4, 8.1 Hz, 1H), 2.50−2.20 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.5, 173.2, 135.8, 131.6, 128.6, 128.1, 126.9, 126.5, 77.9, 66.8, 53.6, 46.9, 24.8. HRMS (ESI-TOF) m/z:[M + Na]$^+$ Calcd for $C_{15}H_{16}O_5Na$ 299.0890; found: 299.0882.

*Ethyl-(E)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)-4-phenylbut-3-enoate (**3c**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (4:1, v/v) as eluent, obtained (21.8 mg, 75% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +28.9 (c = 0.12 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 21.578 min, t_R (minor) = 14.063 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.38 (m, 2H), 7.35−7.29 (m, 1H), 7.29−7.23 (m, 2H), 6.86 (d, J = 15.9 Hz, 1H), 6.43 (d, J = 15.9 Hz, 1H), 4.40 (td, J = 8.6, 5.4 Hz, 1H), 4.36−4.27 (m, 2H), 4.24 (dt, J = 8.7, 7.4 Hz, 1H), 3.99 (s, 1H), 3.13 (dd, J = 9.4, 7.9 Hz, 1H), 2.54−2.18 (m, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.4, 172.7, 136.0, 131.5, 128.5, 128.1, 126.94, 126.8, 77.8, 66.8, 62.9, 46.8, 24.7, 14.1. HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{16}H_{19}O_5$ 291.1227; found: 291.1224.

*iso-Propyl-(E)-2-hydroxy-4-(naphthalen-2-yl)-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3d**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (27.3 mg, 77% yield) as a white solid. MP = 126.0−127.1 °C, $[\alpha]_D^{25}$ = +42.1 (c = 0.1 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 27.805 min, t_R (minor) = 16.296 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86−7.70 (m, 4H), 7.61 (dd, J = 8.4, 1.8 Hz, 1H), 7.49−7.40 (m, 2H), 7.02 (d, J = 15.9 Hz, 1H), 6.55 (d, J = 15.9 Hz, 1H), 5.17−5.12 (m, 1H), 4.41 (td, J = 8.5, 5.4 Hz, 1H), 4.25 (td, J = 8.3, 7.1 Hz, 1H), 4.00 (s, 1H), 3.17 (dd, J = 9.5, 7.8 Hz, 1H), 2.51−2.17 (m, 2H), 1.32 (dd, J = 6.3, 2.8 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.4, 172.3, 133.5, 133.5, 133.2, 131.6, 128.2, 128.1, 127.6, 127.3, 127.1, 126.3, 126.0, 123.8, 77.8, 71.2, 66.8, 46.7, 24.7, 21.6, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{23}O_5$ 355.1540; found: 355.1532.

*iso-Propyl-(E)-4-(2-fluorophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3e**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (26.7 mg, 83% yield) as a white solid. MP = 86.8−88.2 °C, $[\alpha]_D^{25}$ = +30.8 (c = 0.1 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 16.467 min, t_R (minor) = 12.147 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (td, J = 7.7, 1.8 Hz, 1H), 7.22 (dd, J = 8.5, 1.7 Hz, 1H), 7.10 (td, J = 7.5, 1.2 Hz, 1H), 7.03 (d, J = 11.0, 8.3, 1.2 Hz, 1H), 6.98 (d, J = 16.1 Hz, 1H), δ 6.55 (d, J = 16.1 Hz, 1H), 5.15−5.13 (m, 1H), 4.40 (td, J = 8.6, 5.5 Hz, 1H), 4.25 (td, J = 8.3, 7.0 Hz, 1H), 3.95 (s, 1H), 3.15 (dd, J = 9.5, 7.7 Hz, 1H), 2.53−2.21 (m, 2H), 1.32 (dd, J = 6.3, 3.4 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.2, 172.1, 160.4 (d, J = 250.1 Hz), 129.7 (d, J = 5.5 Hz), 129.3 (d, J = 8.3 Hz), 128.2 (d, J = 3.2 Hz), 124.2 (d, J = 3.2 Hz), 124.1 (d, J = 3.6 Hz), 123.9 (d, J = 12.0 Hz), 115.7 (d, J = 22.1 Hz), 77.8, 71.2, 66.7, 46.6, 24.6, 21.6, 21.6; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{20}FO_5$ 323.1289; found: 323.1302.

*iso-Propyl-(E)-4-(3-fluorophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3f**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (26.5 mg, 82% yield) as a white solid. MP = 89.6−91.1 °C, $[\alpha]_D^{25}$ = +31.9 (c = 0.1 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 11.077 min, t_R (minor) = 19.346 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.20 (m, 1H), 7.17 (dt, J = 7.7, 1.2 Hz, 1H), 7.11 (dt, J = 10.1, 2.1 Hz, 1H), 7.02−6.90 (m, 1H), 6.84 (d, J = 15.8 Hz, 1H), 6.42 (d, J = 15.8 Hz, 1H), 5.15−5.12 (m, 1H), 4.40 (td, J = 8.6, 5.4 Hz, 1H), 4.25 (td, J = 8.4, 6.9 Hz, 1H) 3.96 (s, 1H), 3.13 (dd, J = 9.5, 7.6 Hz, 1H), 2.56−1.98 (m, 2H), 1.32 (dd, J = 6.3, 4.2 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ175.1, 172.1, 163.0 (d, J = 245.3 Hz), 138.4 (d, J = 7.8 Hz), 130.4 (d, J = 2.6 Hz), 130.0 (d, J = 8.3 Hz), 128.3, 122.9 (d, J = 2.7 Hz), 114.8 (d, J = 21.4 Hz), 113.3 (d, J = 21.8 Hz), 77.6, 71.3, 66.7, 46.6, 24.6, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{20}FO_5$ 323.1289; found: 323.1289.

*iso-Propyl-(E)-4-(4-fluorophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3g**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (26.2 mg, 81% yield) as a white solid. MP = 88.0−89.2 °C, $[\alpha]_D^{25}$ = +32.9 (c = 0.1 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 21.355 min, t_R (minor) = 13.094 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, J = 8.6, 5.5 Hz, 2H), 7.00 (t, J = 8.6 Hz, 2H), 6.82 (d, J = 15.8 Hz, 1H), 6.34 (d, J = 15.9 Hz, 1H), 5.28−5.02 (m, 1H), 4.50−4.32 (m, 1H), 4.25 (td, J = 8.4, 6.8 Hz, 1H), 3.93 (s, 1H), 3.13 (dd, J = 9.6, 7.6 Hz, 1H), 2.42−2.22 (m, 2H), 1.31 (dd, J = 6.3, 4.0 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.2, 172.2, δ 162.5 (d, J = 247.3 Hz), 132.2 (d, J = 3.3 Hz), 130.3, 128.5 (d, J = 8.1 Hz), 126.7 (d, J = 2.3 Hz), 115.5, 115.4, 77.7, 71.2, 66.7, 46.6, 24.6, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{20}FO_5$ 323.1289; found: 323.1300.

*iso-Propyl-(E)-4-(4-bromophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3h**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (31.4 mg, 82% yield) as a white solid. MP = 134−135.5 °C, $[\alpha]_D^{25}$ = +41.0 (c = 0.1 in EtOAc) enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 22.992 min, t_R (minor) = 14.100 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 8.4 Hz, 2H), 7.30−7.23 (m, 2H), 6.80 (d, J = 15.8 Hz, 1H), 6.41 (d, J = 15.8 Hz, 1H), 5.16−5.11 (m, 1H), 4.51−4.33 (m, 1H), 4.33−4.13 (m, 1H), 3.92 (s, 1H), 3.12 (dd, J = 9.5, 7.6 Hz, 1H), 2.49−2.10 (m, 2H), 1.31 (d, J = 5.7 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.1, 172.1, 135.0, 131.6, 130.3, 128.4, 127.7, 121.9, 77.7, 71.3, 66.7, 46.5, 24.6, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{20}BrO_5$ 383.0489; found: 383.0497.

*iso-Propyl-(E)-4-(4-chlorophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3i**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (27.8 mg, 82% yield) as a white solid. MP = 139.6−141.5 °C, $[\alpha]_D^{25}$ = +32.4 (c = 0.1 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 21.083 min, t_R (minor) = 13.688 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 6.81 (d, J = 15.9 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 5.16−5.11 (m, 1H), 4.40 (td, J = 8.6, 5.4 Hz, 1H), 4.27-4.24 (m, 1H), 3.95 (s, 1H), 3.13 (dd, J = 9.5, 7.6 Hz, 1H), 2.37−2.26 (m, 2H), 1.31 (t, J = 5.6 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.2, 172.1, 134.6, 133.7, 130.3, 128.7, 128.1, 127.6, 77.7, 71.3, 66.7, 46.6, 24.6, 21.6. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{20}ClO_5$ 361.0813; found: 361.0824.

*iso-Propyl-(E)-4-(2,6-dichlorophenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3j**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1) as eluent, obtained (30.2 mg, 81% yield) as a white

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solid. MP = 142−143.1 °C, $[\alpha]_D^{25}$ = +34.0 (*c* = 0.1 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 12.418 min, t_R (minor) = 10.922 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 16.2 Hz, 1H), 6.47 (d, *J* = 16.2 Hz, 1H), 5.19−5.14 (m, 1H), 4.42 (td, *J* = 8.4, 5.4 Hz, 1H), 4.28−4.24 (m, 1H), 3.14 (t, *J* = 8.8 Hz, 1H), 2.43−2.31 (m, 2H), 1.32 (dd, *J* = 6.2, 2.6 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.2, 171.9, 135.3, 134.5, 133.7, 128.5, 128.4, 128.4, 125.5, 77.6, 71.2, 66.7, 46.6, 24.7, 21.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{17}H_{19}Cl_2O_5$ 373.0604; found: 373.0605.

iso-Propyl-(E)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)-4-(p-tolyl)but-3-enoate (**3k**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1) as eluent, obtained (25.2 mg, 79% yield) as a white solid. MP = 109.3−111.2 °C, $[\alpha]_D^{25}$ = +37.6 (*c* = 0.1 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 m/min, 25 °C: t_R (major) = 16.798 min, t_R (minor) = 12.242 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.81 (d, *J* = 15.9 Hz, 1H), 6.37 (d, *J* = 15.8 Hz, 1H), 5.15−5.10 (m, 1H), 4.39 (td, *J* = 8.5, 5.4 Hz, 1H), 4.28−4.19 (m, 1H), 3.93 (s, 1H), 3.12 (dd, *J* = 9.4, 7.9 Hz, 1H), 2.38−2.35 (m, 1H), 2.34 (s, 3H) 2.32−2.24 (m, 1H), 1.31 (dd, *J* = 6.3, 4.6 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.4, 172.3, 137.9, 133.3, 131.3, 129.2, 126.8, 125.8, 77.7, 71.0, 66.7, 46.7, 24.8, 21.6, 21.2. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{22}O_5Na$ 341.1359; found: 341.1363.

iso-Propyl-(E)-4-(3,4-dimethylphenyl)-2-hydroxy-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3l**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (23.6 mg,71% yield) as a white solid. MP = 113.8−113.9 °C, $[\alpha]_D^{25}$ = +35.4 (*c* = 0.1 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 13.479 min, t_R (minor) = 10.328 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 1.8 Hz, 1H), 7.14 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.78 (d, *J* = 15.8 Hz, 1H), 6.36 (d, *J* = 15.9 Hz, 1H), 5.15−5.10 (m, 1H), 4.39 (td, *J* = 8.5, 5.4 Hz, 1H), 4.28−4.19 (m, 1H), 3.91 (s, 1H), 3.12 (dd, *J* = 9.4, 8.0 Hz, 1H), 2.42−2.28 (m, 2H), 2.25 (d, *J* = 4.1 Hz, 6H), 1.31 (dd, *J* = 6.3, 4.0 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.4, 172.3, 136.6, 136.6, 133.7, 131.4, 129.8, 128.0, 125.7, 124.4, 77.7, 71.0, 66.7, 46.8, 24.8, 21.6, 21.6, 19.7, 19.5. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{19}H_{25}O_5$ 333.1697; found: 333.1693.

iso-Propyl-(E)-2-hydroxy-4-(4-methoxyphenyl)-2-(2-oxotetrahydrofuran-3-yl)but-3-enoate (**3m**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (5:1, v/v) as eluent, obtained (25.7 mg, 77% yield) as a white solid. MP = 107.3−109.2 °C, $[\alpha]_D^{25}$ = +34.2 (*c* = 0.1 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 30.843 min, t_R (minor) = 24.951 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 15.9 Hz, 1H), 6.29 (d, *J* = 15.9 Hz, 1H), 5.17−5.06 (m, 1H), 4.39 (td, *J* = 8.6, 5.4 Hz, 1H), 4.28−4.18 (m, 1H), 3.92 (s, 1H), 3.80 (s, 3H), 3.12 (dd, *J* = 9.4, 7.8 Hz, 1H), 2.39−2.25 (m, 2H), 1.31 (dd, *J* = 6.3, 3.5 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ δ 175.4, 172.4, 159.6, 130.9, 128.9, 128.2, 124.7, 114.0, 77.8, 71.0, 66.7, 55.3, 46.8, 24.8, 21.7, 21.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{23}O_6$ 335.1489; found: 335.1485.

iso-Propyl-(E)-2-hydroxy-2-(2-oxochroman-3-yl)-4-phenylbut-3-enoate (**5a**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (28.9 mg, 79% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +21.7 (*c* = 0.11 in EtOAc), enantiomeric excess: 98%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 20.555 min, t_R (minor) = 14.958 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.7 Hz, 2H), 7.34 (dd, *J* = 8.4, 6.7 Hz, 2H), 7.30−7.22 (m, 2H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.3 Hz, 1H), 7.07−7.02 (m, 1H), 6.93 (d, *J* = 15.8 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 5.19−5.16 (m, 1H), 3.93 (s, 1H), 3.41 (dd, *J* = 15.4, 12.9 Hz, 1H), 3.18 (dd, *J* = 12.9, 6.1 Hz, 1H), 3.05 (dd, *J* = 15.4, 6.1 Hz, 1H), 1.33 (dd, *J* = 6.3, 2.3 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.2, 168.4, 151.1, 136.0, 131.8, 128.6, 128.3, 128.2, 127.9, 126.8, 126.7, 124.5, 122.5, 116.6, 77.1, 70.8, 48.9, 26.9, 21.7, 21.6. HRMS (ESI): HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{23}O_5$ 367.1540; found: 367.1542.

iso-Propyl-(E)-4-(4-fluorophenyl)-2-hydroxy-2-(2-oxochroman-3-yl)but-3-enoate (**5b**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (30.7 mg, 80% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +26.0 (*c* = 0.12 in EtOAc), enantiomeric excess: 92%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 20.407 min, t_R (minor) = 15.720 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.29−7.21 (m, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.11−7.08 (m, 3H), 7.07−6.98 (m, 1H), 6.89 (dd, *J* = 16.0, 3.0 Hz, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 5.19−5.15 (m, 1H), 3.91 (s, 1H), 3.39 (dd, *J* = 15.5, 12.7 Hz, 1H), 3.19 (dd, *J* = 12.6, 6.1 Hz, 1H), 3.04 (dd, *J* = 15.5, 6.1 Hz, 1H), 1.33 (d, *J* = 6.2 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.1, 168.2, 151.1, 132.2, 130.6, 128.5, 128.4, 127.9, 126.5, 124.6, 122.4, 116.6, 115.7, 115.5, 77.2 70.9, 48.8, 26.8, 21.7, 21.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{22}FO_5$ 385.1446; found: 385.1441.

iso-Propyl-(E)-4-(4-bromophenyl)-2-hydroxy-2-(2-oxochroman-3-yl)but-3-enoate (**5c**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (36.1 mg, 81% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +29.5 (*c* = 0.1 in EtOAc), enantiomeric excess: 94%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 19.537 min, t_R (minor) = 15.728 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.39 (m, 2H), 7.27−7.25 (m, 3H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.09 (td, *J* = 7.5, 1.2 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 15.9 Hz, 1H), 6.38 (d, *J* = 15.8 Hz, 1H), 5.20−5.15 (m, 1H), 3.91 (s, 1H), 3.39 (dd, *J* = 15.4, 12.7 Hz, 1H), 3.19 (dd, *J* = 12.6, 6.1 Hz, 1H), 3.03 (dd, *J* = 15.5, 6.1 Hz, 1H), 1.33 (dd, *J* = 6.3, 1.8 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.0, 168.1, 151.1, 134.9, 131.7, 130.6, 128.3, 127.9, 127.5, 124.6, 122.3, 122.0, 116.6, 77.2, 71.0, 48.7, 26.7, 21.6, 21.6. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{22}H_{21}BrO_5Na$ 467.0465; found: 467.0451.

iso-Propyl-(E)-4-(4-chlorophenyl)-2-hydroxy-(2-oxochroman-3-yl)but-3-enoate (**5d**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (33.3 mg, 83% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +24.2 (*c* = 0.11 in EtOAc), enantiomeric excess: 93%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 20.345 min, t_R (minor) = 15.018 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.28 (m, 4H), 7.28−7.23 (m, 1H), 7.19−7.14 (m, 1H), 7.09 (td, *J* = 7.5, 1.2 Hz, 1H), 7.05 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.88 (d, *J* = 15.9 Hz, 1H), 6.36 (d, *J* = 15.8 Hz, 1H), 5.19−5.16 (m, 1H), 3.91 (s, 1H), 3.39 (dd, *J* = 15.5, 12.6 Hz, 1H), 3.19 (dd, *J* = 12.6, 6.1 Hz, 1H), 3.03 (dd, *J* = 15.5, 6.1 Hz, 1H), 1.33 (dd, *J* = 6.3, 1.5 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.0, 168.1, 151.1, 134.5, 133.8, 130.6, 128.8, 128.3, 128.0, 127.9, 127.4, 124.6, 122.3, 116.6, 77.2, 71.0, 48.8, 26.7, 21.6, 21.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{22}ClO_5$ 401.1150; found: 401.1164.

iso-Propyl-(E)-2-hydroxy-2-(2-oxochroman-3-yl)-4-(p-tolyl)but-3-enoate (**5e**). This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (29.3 mg, 77% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +24.5 (*c* = 0.1 in EtOAc), enantiomeric excess: 95%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 17.772 min, t_R (minor) = 13.253 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 5.3 Hz, 1H), 7.17−7.14 (m, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.89 (d, *J* = 15.9 Hz, 1H), 6.33 (d, *J* = 15.8 Hz, 1H), 5.20−5.15 (m, 1H), 3.93 (s, 1H), 3.42 (dd, *J* = 15.3, 13.1 Hz, 1H), 3.17 (dd, *J* = 13.0, 6.1 Hz, 1H), 3.05 (dd, *J* = 15.4, 6.1 Hz, 1H), 2.35 (s, 3H), 1.32 (dd, *J* = 6.3, 3.3 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.2, 168.5, 151.1, 138.1, 133.2, 131.6, 129.3, 128.6, 128.3, 127.9, 126.7, 126.5, 125.6, 124.5, 122.5, 116.5, 77.1, 70.7, 49.0, 26.9, 21.7, 21.6, 21.2. HRMS (ESI): HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{23}H_{25}O_5$ 381.1697; found: 381.1696.

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*iso-Propyl-(E)-2-hydroxy-4(4-methoxyphenyl)-2-(2-oxochroman-3-yl)but-3-enoate (**5f**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (23.4 mg, 59% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +24.0 (*c* = 0.1 in EtOAc), enantiomeric excess: 93%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 30.448 min, t_R (minor) = 36.755 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.31 (m, 2H), 7.28−7.21 (m, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.05−7.04 (m, 1H), 6.90−6.82 (m, 3H), 6.24 (d, *J* = 15.8 Hz, 1H), 5.17 (m, 1H), 3.92 (s, 1H), 3.82 (s, 3H), 3.50−3.36 (m, 1H), 3.16 (dd, *J* = 12.9, 6.1 Hz, 1H), 3.06 (d, *J* = 15.5, 6.1 Hz, 1H), 1.33 (dd, *J* = 6.3, 3.4 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.3, 168.5, 159.6, 151.1, 131.2, 128.7, 128.3, 128.1, 127.9, 124.5, 124.3, 122.5, 116.5, 114.0, 77.1, 70.7, 55.3, 49.0, 29.7, 26.9, 21.7, 21.6. HRMS (ESI): HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{23}H_{25}O_6$ 397.1646; found: 397.1653.

*iso-Propyl-(E)-4-(3,4-dimethylphenyl)-2-hydroxy-2-(2-oxochroman-3-yl)but-3-enoate (**5g**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (29.2 mg, 74% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +20.7 (*c* = 0.1 in EtOAc), enantiomeric excess: 93%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 17.323 min, t_R (minor) = 11.383 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.22 (m, 1H), 7.22−7.12 (m, 3H), 7.12−7.06 (m, 2H), 7.04 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.86 (d, *J* = 15.8 Hz, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 5.18−5.16 (m, 1H), 3.92 (s, 1H), 3.42 (dd, *J* = 15.4, 13.1 Hz, 1H), 3.16 (dd, *J* = 13.0, 6.1 Hz, 1H), 3.05 (dd, *J* = 15.5, 6.1 Hz, 1H), 2.26 (d, *J* = 4.9 Hz, 6H), 1.32 (dd, *J* = 6.3, 4.8 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.3, 168.5, 151.1, 136.8, 136.8, 133.6, 131.8, 129.9, 128.3, 128.0, 127.9, 125.4, 124.5, 124.4, 122.6, 116.5, 77.0, 70.7, 49.1, 26.9, 21.7, 21.6, 19.7, 19.5. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{24}H_{27}O_5$ 395.1853; found: 395.1858.

*iso-Propyl-(E)-2-hydroxy-2-(6-methyl-2-oxochroman-3-yl)-4-phenylbut-3-enoate(**5h**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (30.5 mg, 80% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +29.1 (*c* = 0.1 in EtOAc), enantiomeric excess: 95%. Daicel Chiralpak AS, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 °C: t_R (major) = 23.600 min, t_R (minor) = 13.961 min. ^{1}H NMR (500 MH, $CDCl_3$) δ 7.45−7.38 (m, 2H), 7.36−7.30 (m, 2H), 7.31−7.23 (m, 1H), 7.03 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.95 (dd, *J* = 11.8, 2.0 Hz, 2H), 6.91 (d, *J* = 5.7 Hz, 1H), 6.38 (d, *J* = 15.9 Hz, 1H), 5.18−5.16 (m, 1H), 3.95 (s, 1H), 3.45−3.30 (m, 1H), 3.16 (dd, *J* = 12.9, 6.1 Hz, 1H), 3.00 (dd, *J* = 15.5, 6.1 Hz, 1H), 2.29 (s, 3H), 1.32 (dd, *J* = 6.2, 1.8 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.2, 168.6, 149.0, 136.0, 134.2, 131.7, 128.7, 128.6, 128.4, 128.1, 126.8, 126.8, 122.1, 116.2, 77.2, 70.7, 49.1, 26.8, 21.7, 21.6, 20.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{23}H_{25}O_5$ 381.1697; found: 381.1698.

*iso-Propyl-(E)-2-hydroxy-2-(8-methoxy-2-oxochroman-3-yl)-4-phenylbut-3-enoate (**5i**).* This compound was prepared according to the typical procedure, which was purified using PE (petroleum ether)/EtOAc (15:1, v/v) as eluent, obtained (26.5 mg, 67% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +27.7 (*c* = 0.1 in EtOAc), enantiomeric excess: 74%. Daicel Chiralpak OD, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 30.363 min, t_R (minor) = 23.653 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.3 Hz, 2H), 7.35 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.30−7.25 (m, 1H), 7.04 (t, *J* = 7.9 Hz, 1H), 6.93 (d, *J* = 15.8 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.38 (d, *J* = 15.9 Hz, 1H), 5.20−5.15 (m, 1H), 3.95 (s, 1H), 3.88 (s, 3H), 3.53−3.36 (m, 1H), 3.16 (dd, *J* = 13.3, 6.0 Hz, 1H), 3.04 (dd, *J* = 15.5, 6.0 Hz, 1H), 1.32 (dd, *J* = 6.2, 3.6 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.1, 167.8, 147.5, 140.4, 136.1, 131.8, 128.6, 128.2, 126.9, 126.8, 124.5, 123.8, 119.4, 111.2,77.1 70.7, 56.1, 49.0, 27.1, 21.7, 21.6. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{23}H_{25}O_6$ 397.1646; found: 397.1643.

*iso-Propyl-(E)-2-hydroxy-2-(7-methoxy-2-oxochroman-3-yl)-4-phenylbut-3-enoate (**5j**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (15:1, v/v) as eluent, obtained (29.8 mg, 75% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +31.1 (*c* = 0.1 in EtOAc), enantiomeric excess: 95%. Daicel Chiralpak AS, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (major) = 28.661 min, t_R (minor) = 18.116 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46−7.38 (m, 2H), 7.37−7.31 (m, 2H), 7.30−7.27 (m, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 15.9 Hz, 1H), 6.64 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 6.37 (d, *J* = 15.8 Hz, 1H), 5.20−5.15 (m, 1H), 3.92 (s, 1H), 3.78 (s, 3H), 3.33 (ddd, *J* = 15.2, 12.9, 1.1 Hz, 1H), 3.16 (dd, *J* = 12.8, 6.1 Hz, 1H), 2.99 (dd, *J* = 15.2, 6.1 Hz, 1H), 1.32 (dd, *J* = 6.3, 2.7 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.2, 168.3, 159.7, 151.8, 136.0, 131.7, 128.6, 128.4, 128.1, 126.8, 126.7, 114.1, 110.6, 102.2, 77.1, 70.8, 55.5, 49.2, 26.2, 21.7, 21,6. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{23}H_{25}O_6$ 397.1646; found: 397.1647.

*3-Hydroxy(4-nitrophenyl)methyl)dihydrofuran-2-(3H)-one (**7**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (3:1, v/v) as eluent, obtained (12.4 mg, 52% yield) as a yellow solid. MP = 139.8−141.6 °C, $[\alpha]_D^{25}$ = +17.9 (*c* = 0.1 in EtOAc), enantiomeric excess: 93%. Daicel Chiralpak AS-H, hexane/iso-propanol = 80/20, flow rate 1.0 mL/min, 25 °C: t_R (major) = 14.462 min, t_R (minor) = 21.597 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 4.97 (d, *J* = 8.7 Hz, 1H), 4.52 (s, 1H), 4.39−4.35 (m, 1H), 4.22−4.06 (m, 1H), 2.88 (dt, *J* = 11.5, 8.9 Hz, 1H), 2.17−1.92 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.4, 147.9, 147.4, 127.4, 123.9, 73.7, 67.0, 46.1, 25.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{11}H_{12}NO_5$ 238.0710; found: 238.0709.

*3-Hydroxy-3-(2-oxotetrahydrofuran-3-yl)indolin-2-one (**9**).* This compound was prepared according to the typical procedure, which was purified using DCM/EtOAc (3:1, v/v) as eluent, obtained (20.4 mg, 87 yield) as an off-white solid, enantiomeric excess: 96%. Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C: t_R (major) = 25.897 min, t_R (minor) = 21.243 min. ^{1}H NMR (500 MHz, Acetone-d_6) δ 9.46 (s, 1H), 7.53 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.27 (td, *J* = 7.7, 1.3 Hz, 1H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 5.44 (s, 1H), 4.36 (td, *J* = 8.7, 3.8 Hz, 1H), 4.27 (td, *J* = 8.8, 7.6 Hz, 1H), 3.42 (t, *J* = 9.8 Hz, 1H), 2.51−2.34 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ178.1, 176.7, 143.5, 130.8, 129.9, 125.7, 122.9, 110.9, 76.2, 67.4, 46.2, 24.6. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{11}H_{12}NO_5$ 234.0761; found: 234.0763.

*iso-Propyl-2-hydroxy-4-(naphthalen-2-yl)-2-(2-oxotetrahydrofuran-3-yl)butanoate (**10**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (10:1, v/v) as eluent, obtained (33.8 mg, 95% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +38.2 (*c* = 0.12 in EtOAc), enantiomeric excess: 94%. Daicel Chiralpak OD, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C: t_R (major) = 19.05 min, t_R (minor) = 18 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.72 (m, 3H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.45−7.41 (m, 2H), 7.32 (dd, *J* = 8.3, 1.8 Hz, 1H), 5.11−5.09 (m, 1H), 4.38 (td, *J* = 8.4, 5.2 Hz, 1H), 4.26−4.17 (m, 1H), 3.86 (s, 1H), 3.03−2.89 (m, 2H), 2.74−2.70 (m, 1H), 2.64−2.53 (m, 1H), 2.30−2.17 (m, 3H), 1.31 (dd, *J* = 6.3, 4.3 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.9, 173.5, 138.5, 133.5, 132.0, 128.0, 127.6, 127.4, 127.1, 126.4, 125.9, 125.2, 77.5, 70.7, 66.6, 46.0, 37.8, 30.1, 24.7, 21.7, 21.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{21}H_{25}O_5$ 357.1697; found: 357.1709.

*iso-Propyl-(E)-2,5-dihydroxy-3-(methyl(phenyl)carbamoyl)-2-styrylpentanoate (**11**).* This compound was prepared according to the typical procedure, which was purified using petroleum ether/EtOAc (2:1, v/v) as eluent, obtained (57.1 mg; 64 yield) as a colorless liquid. $[\alpha]_D^{25}$ = +28.1 (*c* = 0.1 in EtOAc), enantiomeric excess: 99%. Daicel Chiralpak AS, hexane/iso-propanol = 80/20, flow rate 1.0 mL/min, 25 °C: t_R (major) = 6.548 min, t_R (minor) = 5.040 min. ^{1}H NMR (500 MHz, Acetone-d_6) δ 7.53−7.46 (m, 4H), 7.45−7.37 (m, 3H), 7.35−7.25 (m, 2H), 6.75 (d, *J* = 15.8 Hz, 1H), 6.31 (d, *J* = 15.8 Hz, 1H), 5.15 (s, 1H), 4.96−4.90 (m, 1H), 3.51−3.64 (m, 2H), 3.45 (s, 1H), δ 3.24 (dd, *J* = 10.4, 3.5 Hz, 1H), 3.14 (s, 3H), 2.21−2.10 (m, 1H), 1.71−1.60 (m, 1H), 1.17 (d, *J* = 6.3 Hz, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.9, 171.4, 143.0, 134.5, 133.6, 130.1, 129.7, 129.4, 128.8, 128.3, 127.9, 127.49, 79.2, 69.9, 60.4, 45.6, 37.7, 32.2, 21.6, 21.4. HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{24}H_{28}ClNO_5Na$ 468.1548; found: 468.1563.

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■ ASSOCIATED CONTENT

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NMR and HPLC spectra, and crystallographic data for **3h** (PDF)

Accession Codes

CCDC 2035137 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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