JOC The Journal of Organic Chemistry

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# Organocatalyzed Michael–Michael Cascade Reaction: Asymmetric Synthesis of Polysubstituted Chromans

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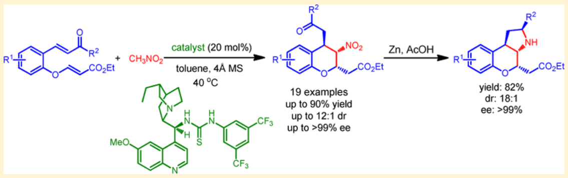
Supporting Information

**ABSTRACT:** An enantioselective cascade Michael–Michael reaction between chalcones enolates and nitromethane catalyzed by a bifunctional thiourea is developed. This reaction provides a mild but efficient approach to chiral benzopyrans bearing three consecutive stereocenters in high yields with excellent stereoselectivities, and the benzopyrans can be easily transformed to the corresponding tricyclic product.



## INTRODUCTION

It is well-known that chiral chroman and benzopyran structures belong to an important class of heterocycles that constitute the core of numerous natural products and synthetic analogs possessing an extensive array of biological activities (Figure 1).[1]

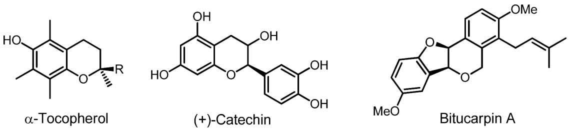


**Figure 1.** Examples of biologically active chroman derivatives.

For example, α-tocopherol, as one of the most well-known chiral chromans, is an important member of the vitamin E family, which serve as natural lipophilic antioxidants and radical scavengers.[2] (+)-Catechin, commonly found in land plants such as the traditional Chinese medicine plant *Uncaria rhynchophylla* and green alga *Myriophyllum spicatum*, displays modest antitumor and antioxidant activity.[3] Bitucarpin A, isolated from the aerial parts of Mediterranean plants *Bituminaria bituminosa* (*Leguminosae*), exhibited potent antibacterial and anticlastogenic activity against both mytomicin C and bleomycin C.[4] Due to the importance of the chiral chroman frameworks, the development of new and more general catalytic asymmetric strategies for their preparation has become an active field of research.[5]

Over the past a few years, organocatalyzed cascade reactions have emerged as powerful synthetic tools for the construction of new multiple bonds and newly created stereocenters, which are characterized by the highly efficient, facile, and stereoselective assembly of complex and diverse molecules without the need for costly protection/deprotection processes as well as the purification of the intermediates.[6] Recently, our group has developed some methods for the organocatalytic asymmetric cascade reaction.[7] In particular, we could make substituted tetrahydroquinolines with diverse stereochemical features through a cascade Michael–aza-Henry reaction and a cascade aza-Michael–Michael reaction.[8] Inspired by the previous work, we reasoned that the chiral polysubstituted chromans **3** could be directly constructed from commercially available raw materials nitromethane and chalcones enolates **2** via a cascade Michael–Michael reaction using suitable chiral bifunctional thiourea catalyst **1**.

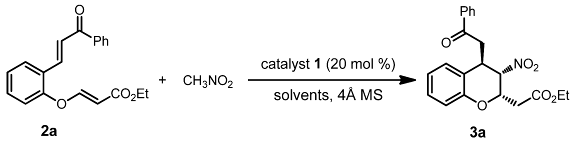
## RESULTS AND DISCUSSION

For the preliminary study, chalcone enolate **2a** and nitromethane were chosen as model substrates for the feasibility of the proposed cascade double Michael reaction in the presence of various chiral bifunctional organocatalysts in toluene. Initially, organocatalyst **1a** was investigated at room temperature. To our delight, the expected product **3a** was formed with excellent enantioselectivity (98% enantiomeric excess (ee)), albeit in low yield (Table 1, entries 1 and 2). When the reaction temperature was increased to 40 °C, the reaction yield was improved to 66% (Table 1, entry 3). In order to reduce the reaction time and further improve the reaction yield, a 4 Å molecular sieve (MS) was added to the reaction system. The results showed the yield was improved, even with reduced reaction time, when a 4 Å MS was added (Table 1, entry 4). On the basis of these results, several commonly used bifunctional organocatalysts (Figure 2) were screened for this cascade reaction for their reactivity and selectivity. Among them, organocatalyst **1a** was identified as the best catalyst for this double Michael reaction process (Table 1, entries 4–11). Subsequently, the reaction medium was investigated for this cascade reaction. It was found that the solvents had little

**Received:** March 13, 2013
**Revised:** May 31, 2013
**Accepted:** June 10, 2013
**Published:** June 10, 2013

dx.doi.org/10.1021/jo400476b | *J. Org. Chem.* 2013, 78, 6488–6494

### Table 1. Conditions Optimization for the Double Michael Cascade Reaction



| entry[a] | catalyst | solvent | time (d) | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|---|---|
| 1[e,f] | **1a** | toluene | 4 | 36 | | |
| 2[e,f] | **1a** | toluene | 6 | 57 | 9:1 | 98 |
| 3[f] | **1a** | toluene | 6 | 66 | 9:1 | 98 |
| 4 | **1a** | toluene | 4 | 86 | 9:1 | >99 |
| 5 | **1b** | toluene | 5 | 78 | 8:1 | 98 |
| 6 | **1c** | toluene | 5 | 75 | 8:1 | >99 |
| 7 | **1d** | toluene | 5 | 70 | 8:1 | 96 |
| 8 | **1e** | toluene | 4 | 80 | 8:1 | 96 |
| 9 | **1f** | toluene | 5 | 56 | 4:1 | >99 |
| 10 | **1g** | toluene | 5 | 45 | 3:1 | 93 |
| 11 | **1h** | toluene | 5 | 50 | 6:1 | 95 |
| 12 | **1a** | DCM | 4 | 84 | 9:1 | 98 |
| 13 | **1a** | THF | 4 | 78 | 10:1 | 98 |
| 14 | **1a** | $CHCl_3$ | 4 | 85 | 9:1 | >99 |
| 15 | **1a** | DCE | 4 | 81 | 9:1 | 98 |
| 16 | **1a** | $CH_3CN$ | 4 | 80 | 8:1 | 98 |
| 17 | **1a** | xylene | 4 | 84 | 9:1 | >99 |

[a] Unless otherwise specified, the reaction was carried out with nitromethane (4 mmol), **2a** (0.2 mmol), organocatalyst (20 mol %), and a 4 Å MS (60 mg) in the indicated solvent (1.0 mL) at 40 °C. [b] The yields are the combined yields of the mixtures of diastereomers after flash chromatography. [c] Determined by $^1H$ NMR analysis of the crude products. [d] Determined by chiral-phase HPLC analysis (OD-H column). [e] The reaction was conducted at room temperature. [f] The reaction was carried out without a 4 Å MS added.

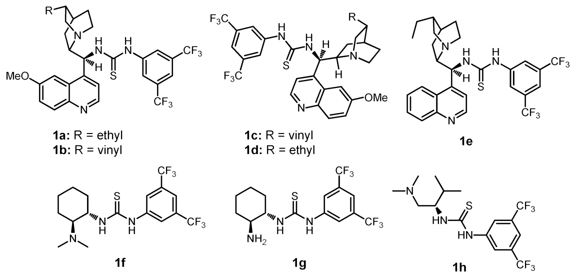
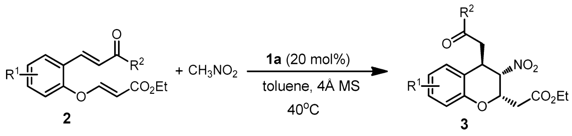


**Figure 2.** Bifunctional thiourea catalysts examined in this study.

influence on the reaction. The corresponding product **3a** could be obtained in either a polar solvent or a nonpolar solvent in high yields with excellent enantioselectives (Table 1, entries 12−17). Given the above results, the optimal conditions were found to be using catalyst **1a** (20 mol %) in toluene at 40 °C.

Based on the established optimal reaction conditions, the scope of the double Michael addition reaction was explored by employing a variety of chalcones enolates **2** with different steric and electronic properties. As shown in Table 2, all the reactions afforded the corresponding chromans in high yields with excellent enantioselectivities. Electronic properties ($R^2$ substituents) had an apparent effect on this cascade reaction. Substrates with electron-deficient substituents had higher reactivity than those with electron-rich substituents. Although all the substrates tested could afford products in high yields with excellent enantioselectivities (78 to 88% yields, 97 to >99% ee), it took less time for the reaction to complete with the electron-deficient substituents (Table 2, entries 2−5 versus entries 6−10). Furthermore, corresponding products could also be obtained in high yields with excellent enantioselectivities with various substituents in the phenyl ring ($R^1$ substituents) (Table 2, entries 11−15). Chalcones with heteroaromatic groups could also be employed to afford the products with excellent results (Table 2, entries 16 and 17). However, when an aliphatic chalcone was tested, the reaction did not occur, which is probably due to its low reactivity (Table 2, entry 18).

### Table 2. Substrates Scope of the Double Michael Addition Reaction



| entry[a] | $R^1$ | $R^2$ | time (d) | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|---|---|
| 1 | H | Ph | 4 | 86 (**3a**) | 9:1 | >99 |
| 2 | H | 4-$CH_3C_6H_4$ | 5 | 88 (**3b**) | 9:1 | >99 |
| 3 | H | 4-$CH_3OC_6H_4$ | 5 | 85 (**3c**) | 8:1 | >99 |
| 4 | H | 3-$CH_3OC_6H_4$ | 5 | 84 (**3d**) | 9:1 | >99 |
| 5 | H | 2-$CH_3OC_6H_4$ | 6 | 78 (**3e**) | 6:1 | 97 |
| 6 | H | 4-$BrC_6H_4$ | 4 | 85 (**3f**) | 10:1 | >99 |
| 7 | H | 4-$ClC_6H_4$ | 4 | 90 (**3g**) | 9:1 | 97 |
| 8 | H | 3-$BrC_6H_4$ | 4 | 87 (**3h**) | 10:1 | >99 |
| 9 | H | 2-$ClC_6H_4$ | 4 | 80 (**3i**) | 9:1 | 97 |
| 10 | H | 2-$FC_6H_4$ | 3 | 85 (**3j**) | 9:1 | >99 |
| 11 | 4-Cl | Ph | 4 | 84 (**3k**) | 7:1 | >99 |
| 12 | 4-Br | Ph | 4 | 84 (**3l**) | 7:1 | >99 |
| 13 | 4-$CH_3$ | Ph | 4 | 86 (**3m**) | 9:1 | >99 |
| 14 | 4-$CH_3O$ | Ph | 5 | 82 (**3n**) | 12:1 | >99 |
| 15 | 5-$CH_3$ | Ph | 4 | 87 (**3o**) | 8:1 | 95 |
| 16 | H | furyl | 4 | 80 (**3p**) | 8:1 | >99 |
| 17 | H | thienyl | 4 | 85 (**3q**) | 7:1 | >99 |
| 18 | H | $CH_3$ | 6 | nr (**3r**) | nd | nd |
| 19 | 4-Br | 4-Br | 4 | 82 (**3s**) | 9:1 | >99 |

[a] Unless otherwise specified, the reaction was carried out with nitromethane (4 mmol), **2** (0.2 mmol), **1a** (20 mol %), and a 4 Å MS (60 mg) in toluene (1.0 mL) at 40 °C. [b] The yields are the combined yields of the mixtures of diastereomers after flash chromatography. [c] Determined by $^1H$ NMR analysis of the crude products. [d] Determined by chiral-phase HPLC analysis.

Fortunately, a single crystal of **3s** was obtained, and the absolute configuration was determined as (2*S*,3*S*,4*R*) by X-ray crystallographic analysis (see Supporting Information).[9]

A mechanism similar to that of the Michael addition reaction of chalcones with nitromethane catalyzed by the bifunctional organocatalysts was proposed for the double Michael reaction.[10] As outlined in Figure 3, $\alpha,\beta$-unsaturated ketones **2** activated by catalyst **1a** containing H-bond donors and nitromethane activated by the tertiary amine moiety react to form intermediate **A**, which undergoes the Michael reaction to afford the intermediate **B**. Then the intermediate **B** undergoes an intramolecular Michael addition to generate a cyclized intermediate to deliver the product **3** and regenerate the catalyst **1a**.

The polycyclic frameworks of chiral chromans play an important role in various therapeutic areas.[4,11] We tried to apply this cascade reaction to the synthesis of tricyclic chromans. The reduction amination of product **3a** with zinc powder and acetic acid, shown in Scheme 1, successfully

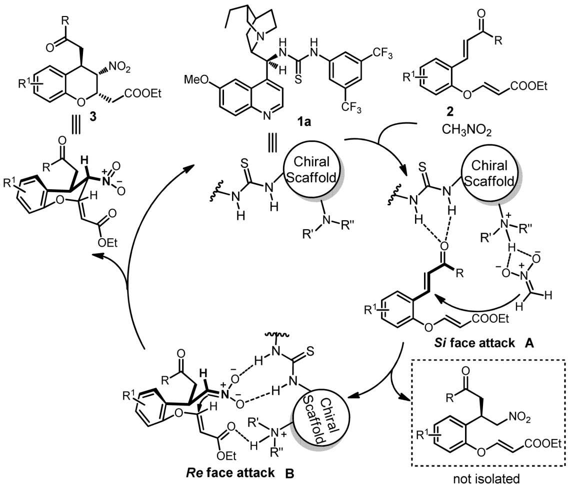
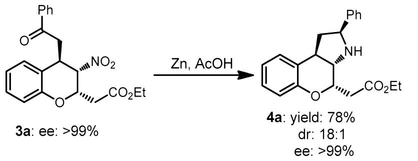


**Figure 3.** Proposed catalytic cycle for the cascade reaction.

**Scheme 1. Synthetic Application of the Chiral Chromans 3**



afforded the tricyclic framework **4a** in good yield with excellent diastereoselectivity and enantioselectivity (78% yield, 18:1 dr, >99% ee). The ring-fused benzopyran **4a** contained a new chiral center with the configuration determined by an NOE experiment.

## ■ CONCLUSION

In summary, we have developed a highly enantioselective cascade double Michael addition reaction for the synthesis of chiral chromans in good yields from starting materials chalcones enolates and nitromethane using the commonly available bifunctional organocatalysts. This cascade reaction showed remarkably broad substrate scope and generated the products with three consecutive stereogenic carbons, which are synthetically useful. Furthermore, these products can be transformed into tricyclic chromans in good yields with high diastereo- and enantioselectivity. This synthetic method is a powerful strategy for constructing multiple stereocenters of polysubstituted chromans.

## ■ EXPERIMENTAL SECTION

**General Procedure for Synthesis of Chalcones Enolates (2a–2s).** Aryl ketone (10 mmol) was added to a solution of 50% KOH (5 mL) in MeOH (25 mL). After complete dissolution, substituted salicyaldehyde (10 mmol) was added slowly. The mixture was then stirred overnight at room temperature; the product was formed as a precipitate. The precipitate was filtered out and then washed with $H_2O$, cold MeOH, and ethyl acetate. The residue was dried to obtain chalcones.

*N*-Methylmorpholine (36 mg, 0.36 mmol) was added to a mixture of chalcones (6 mmol), ethyl propiolate (8 mmol), and $CH_3CN$ (5 mL). The mixture was stirred for 2 h, and deionized water was added. The mixture was then extracted with $CH_2Cl_2$. The combined organic phase was dried over $Na_2SO_4$, filtered, concentrated in vacuo, and purified with flash chromatography (eluent, 1/9 ethyl acetate/petroleum ether) to yield *Z* chalcones enolates.

*(E)-Ethyl 3-(2-((E)-3-Oxo-3-phenylprop-1-en-1-yl)phenoxy)-acrylate (**2a**).* White solid in a 45% yield of two steps (870 mg). Mp: 78–79 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02–7.95 (m, 3H), 7.81–7.73 (m, 2H), 7.60–7.56 (m, 2H), 7.50 (t, $J$ = 7.2 Hz, 2H), 7.45–7.41 (m, 1H), 7.26 (t, $J$ = 7.2 Hz, 1H), 7.09 (dd, $J$ = 0.4 Hz, 8.0 Hz, 1H), 5.56 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 190.3, 166.7, 158.6, 154.4, 137.9, 137.8, 132.8, 131.7, 128.7, 128.6, 128.5, 126.1, 125.4, 124.3, 118.7, 103.1, 103.0, 60.1, 14.2. IR (KBr): 3437, 3077, 1705, 1603, 1484, 1284, 1211, 1152, 1044, 984, 755 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{19}O_4$ [M + H]$^+$: calcd, 323.1278; found, 323.1293.

*(E)-Ethyl 3-(2-((E)-3-Oxo-3-(p-tolyl)prop-1-en-1-yl)phenoxy)-acrylate (**2b**).* White solid in a 51% yield of two steps (1.03 g). Mp: 106–108 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.97–7.91 (m, 3H), 7.79 (d, $J$ = 12.0 Hz, 1H), 7.74 (dd, $J$ = 1.2 Hz, 7.6 Hz, 1H), 7.57 (d, $J$ = 16.0 Hz, 1H), 7.44–7.40 (m, 1H), 7.31–7.23 (m, 3H), 7.10 (d, $J$ = 8.0 Hz, 1H), 5.56 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 2.43 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}$CNMR (100 MHz, $CDCl_3$): $\delta$ 189.8, 166.7, 158.7, 154.4, 143.7, 137.4, 135.4, 131.6, 129.3, 128.7, 128.6, 126.3, 125.4, 124.4, 118.7, 103.1, 60.1, 21.6, 14.2. IR (KBr): 3441, 2985, 1709, 1658, 1604, 1482, 1283, 1214, 1047, 850, 767 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{21}O_4$ [M + H]$^+$: calcd, 337.1434; found, 337.1449.

*(E)-Ethyl 3-(2-((E)-3-(4-Methoxyphenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate (**2c**).* White solid in a 48% yield of two steps (1.01 g). Mp: 92–93 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03–8.01 (m, 2H), 7.94 (d, $J$ = 12.0 Hz, 1H), 7.79 (d, $J$ = 12.0 Hz, 1H), 7.74 (dd, $J$ = 1.2 Hz, 8.0 Hz, 1H), 7.58 (d, $J$ = 16.0 Hz, 1H), 7.44–7.40 (m, 1H), 7.28–7.23 (m, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 6.99–6.96 (m, 2H), 5.56 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 3.88 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 188.5, 166.8, 163.4, 158.7, 154.3, 137.0, 131.5, 130.8, 130.7, 128.7, 126.3, 125.4, 124.2, 118.7, 113.8, 103.0, 102.9, 60.1, 55.4, 14.2. IR (KBr): 3441, 2961, 1709, 1602, 1483, 1301, 1218, 1172, 1042, 847, 754 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{21}O_5$ [M + H]$^+$: calcd, 353.1384; found, 353.1396.

*(E)-Ethyl 3-(2-((E)-3-(3-Methoxyphenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate (**2d**).* Light yellow oil in a 50% yield of two steps (1.06 g). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, $J$ = 16.0 Hz, 1H), 7.78 (d, $J$ = 12.4 Hz, 1H), 7.74 (d, $J$ = 7.6 Hz, 1H), 7.59–7.53 (m, 3H), 7.42 (dd, $J$ = 8.0 Hz, 18.4 Hz, 2H), 7.27–7.24 (m, 1H), 7.14–7.09 (m, 2H), 5.57 (d, $J$ = 12.0 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 3.88 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 190.0, 166.7, 159.9, 158.6, 154.5, 139.3, 137.9, 131.7, 129.5, 128.8, 126.2, 125.4, 124.4, 121.0, 119.4, 118.7, 112.8, 103.1, 60.2, 55.4, 14.2. IR (KBr): 3324, 2976, 1712, 1663, 1596, 1485, 1225, 1123, 1042, 848, 756 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{21}O_5$ [M + H]$^+$: calcd, 353.1384; found, 353.1396.

*(E)-Ethyl 3-(2-((E)-3-(2-Methoxyphenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate (**2e**).* Yellow solid in a 42% yield of two steps (887 mg). Mp: 38–40 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.81–7.75 (m, 2H), 7.70–7.68 (m, 1H), 7.63 (dd, $J$ = 1.6 Hz, 7.6 Hz, 1H), 7.49–7.438 (m, 3H), 7.27–7.21 (m, 1H), 7.08–6.98 (m, 3H), 5.51 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 3.89 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 192.5, 166.8, 158.8, 158.2, 154.3, 136.0, 133.0, 131.4, 130.5, 129.1, 129.0, 128.7, 126.5, 125.4, 120.7, 118.8, 111.6, 102.9, 60.1, 55.6, 14.2. IR (KBr): 3443, 2980, 1710, 1645, 1485, 1326, 1224, 1119, 1031, 844, 750 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{21}O_5$ [M + H]$^+$: calcd, 353.1384; found, 353.1399.

*(E)-Ethyl 3-(2-((E)-3-(4-Bromophenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate (**2f**).* Light yellow solid in a 52% yield of two steps (1.25 g). Mp: 111–112 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, $J$ = 16.0 Hz, 1H), 7.87 (d, $J$ = 8.4 Hz, 2H), 7.78 (d, $J$ = 12.4 Hz, 1H), 7.73 (d, $J$ = 7.2 Hz, 1H), 7.63 (d, $J$ = 7.6 Hz, 2H), 7.51 (d, $J$ = 16.0 Hz, 1H), 7.47–7.42 (m, 1H), 7.26 (d, $J$ = 7.2 Hz, 1H), 7.10 (d, $J$ = 7.6 Hz, 1H), 5.57 (d, $J$ = 12.0 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 189.1, 166.7, 158.5, 154.5, 138.4, 136.7, 132.0, 131.9, 130.0, 128.8, 128.0, 125.9, 125.4, 123.7, 118.7, 103.3, 60.2, 14.2. IR (KBr): 3440, 3078, 1702, 1662, 1601, 1482, 1284, 1213, 1154, 1040, 1006, 839, 752 cm$^{-1}$.

HRMS (ESI) for $C_{20}H_{18}BrO_4$ $[M + H]^+$: calcd, 401.0383; found, 401.0396.

*(E)-Ethyl 3-(2-((E)-3-(4-Chlorophenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate* ***(2g)***. White solid in a 50% yield of two steps (1.07 g). Mp: 127−128 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (t, $J$ = 8.4 Hz, 3H), 7.78 (d, $J$ = 12.4 Hz, 1H), 7.73 (d, $J$ = 6.8 Hz, 1H), 7.55−7.43 (m, 4H), 7.28−7.24 (m, 1H), 7.10 (d, $J$ = 8.4 Hz, 1H), 5.57 (d, $J$ = 12.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 189.0, 166.7, 158.6, 154.5, 139.3, 138.4, 136.2, 132.0, 129.9, 128.9, 128.8, 125.9, 125.4, 123.7, 118.7, 103.2, 60.2, 14.2. IR (KBr): 3439, 3062, 1705, 1661, 1602, 1483, 1284, 1213, 1041, 840, 752 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}ClO_4$ $[M + H]^+$: calcd, 357.0888; found, 357.1161.

*(E)-Ethyl 3-(2-((E)-3-(3-Bromophenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate* ***(2h)***. White solid in a 43% yield of two steps (1.03 g). Mp: 98−99 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.12 (s, 1H), 7.99−7.91 (m, 2H), 7.81−7.70 (m, 3H), 7.52−7.43 (m, 2H), 7.38 (t, $J$ = 7.6 Hz, 1H), 7.28−7.25 (m, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 5.58 (d, $J$ = 12.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 188.8, 166.7, 158.5, 154.5, 139.7, 138.7, 135.6, 132.0, 131.5, 130.2, 128.7, 127.0, 125.9, 125.4, 123.6, 122.9, 118.7, 103.3, 60.2, 14.2. IR (KBr): 3441, 3075, 1707, 1641, 1599, 1480, 1288, 1209, 1153, 1039, 858, 751 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}BrO_4$ $[M + H]^+$: calcd, 401.0383; found, 401.0399.

*(E)-Ethyl 3-(2-((E)-3-(2-Chlorophenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate* ***(2i)***. White solid in a 47% yield of two steps (1.0 mg). Mp: 68−70 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.74−7.66 (m, 3H), 7.49−7.40 (m, 4H), 7.38−7.34 (m, 1H), 7.27−7.17 (m, 2H), 7.08 (d, $J$ = 8.0 Hz, 1H), 5.49 (d, $J$ = 12.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 193.4, 166.7, 158.5, 154.4, 139.0, 138.8, 132.1, 131.5, 131.3, 130.3, 129.5, 128.7, 128.1, 126.8, 125.7, 125.5, 118.7, 103.2, 60.2, 14.2. IR (KBr): 3441, 2996, 1657, 1605, 1485, 1329, 1226, 1135, 1066, 979, 846, 744 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}ClO_4$ $[M + H]^+$: calcd, 357.0888; found, 357.1180.

*(E)-Ethyl 3-(2-((E)-3-(2-Fluorophenyl)-3-oxoprop-1-en-1-yl)-phenoxy)acrylate* ***(2j)***. Yellow solid in a 49% yield of two steps (998 mg). Mp: 68−69 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.89 (d, $J$ = 1.2 Hz, 1H), 7.85−7.80 (m, 1H), 7.78 (d, $J$ = 12.0 Hz, 1H), 7.72 (dd, $J$ = 1.2 Hz, 8.0 Hz, 1H), 7.56−7.50 (m, 1H), 7.48−7.41 (m, 2H), 7.28−7.23 (m, 2H), 7.16 (dd, $J$ = 8.8 Hz, 10.8 Hz, 1H), 7.09 (d, $J$ = 8.0 Hz, 1H), 5.55 (d, $J$ = 12.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 188.7, 188.6, 166.7, 162.5, 160.0, 158.5, 154.5, 137.8, 134.1, 134.0, 131.9, 131.0, 130.9, 128.8, 127.7, 127.6, 126.9, 126.8, 126.0, 125.4, 124.5, 124.4, 118.6, 116.6, 116.4, 103.2, 60.1, 14.2. IR (KBr): 3440, 1708, 1649, 1609, 1451, 1333, 1232, 1185, 1128, 1016, 847, 756 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}FO_4$ $[M + H]^+$: calcd, 341.1184; found, 341.1189.

*(E)-Ethyl 3-(4-Chloro-2-((E)-3-oxo-3-phenylprop-1-en-1-yl)-phenoxy)acrylate* ***(2k)***. Light yellow solid in a 46% yield of two steps (982 mg). Mp: 41−42 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.01 (d, $J$ = 7.6 Hz, 2H), 7.88 (d, $J$ = 16.0 Hz, 1H), 7.75−7.71 (m, 2H), 7.62−7.49 (m, 4H), 7.38 (dd, $J$ = 2.4 Hz, 8.8 Hz, 1H), 7.05 (d, $J$ = 8.4 Hz, 1H), 5.56 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 189.7, 166.5, 158.2, 152.8, 137.7, 136.3, 133.1, 131.3, 130.9, 128.7, 128.5, 128.1, 127.8, 125.2, 120.1, 103.7, 60.3, 14.2. IR (KBr): 3442, 2979, 1718, 1645, 1605, 1484, 1321, 1223, 1134, 992, 826, 685 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}ClO_4$ $[M + H]^+$: calcd, 357.0888; found, 357.0894.

*(E)-Ethyl 3-(4-Bromo-2-((E)-3-oxo-3-phenylprop-1-en-1-yl)-phenoxy)acrylate* ***(2l)***. White solid in a 51% yield of two steps (1.22 g). Mp: 109−110 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02−8.00 (m, 2H), 7.89−7.85 (m, 2H), 7.73 (d, $J$ = 12.4 Hz, 1H), 7.62−7.49 (m, 5H), 6.99 (d, $J$ = 8.4 Hz, 1H), 5.57 (d, $J$ = 12.0 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 189.7, 166.5, 158.0, 153.3, 137.7, 136.2, 134.3, 133.1, 131.1, 128.7, 128.5, 128.2, 125.2, 120.3, 118.3, 103.8, 60.3, 14.2. IR (KBr): 3441, 2977, 1717, 1646, 1605, 1481, 1321, 1223, 1137, 993, 826, 687 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{18}BrO_4$ $[M + H]^+$: calcd, 401.0383; found, 401.0396.

*(E)-Ethyl 3-(4-Methyl-2-((E)-3-oxo-3-phenylprop-1-en-1-yl)-phenoxy)acrylate* ***(2m)***. White solid in a 44% yield of two steps (885 mg). Mp: 91−92 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02−8.00 (m, 2H), 7.91 (d, $J$ = 16.0 Hz, 1H), 7.76 (d, $J$ = 12.4 Hz, 1H), 7.60−7.48 (m, 5H), 7.22 (dd, $J$ = 1.6 Hz, 8.0 Hz, 1H), 6.98 (d, $J$ = 8.4 Hz, 1H), 5.50 (d, $J$ = 12.0 Hz, 1H), 4.18 (q, $J$ = 7.2 Hz, 2H), 2.38 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 190.3, 166.8, 159.2, 152.4, 138.0, 137.9, 135.2, 132.8, 132.4, 128.9, 128.6, 128.5, 125.8, 124.1, 118.8, 102.6, 102.5, 60.1, 20.7, 20.6, 14.2. IR (KBr): 3441, 3057, 2974, 1708, 1664, 1603, 1488, 1291, 1204, 1040, 960, 859, 797, 686 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{21}O_4$ $[M + H]^+$: calcd, 337.1434; found, 337.1446.

*(E)-Ethyl 3-(4-Methoxy-2-((E)-3-oxo-3-phenylprop-1-en-1-yl)-phenoxy)acrylate* ***(2n)***. White solid in a 45% yield of two steps (950 mg). Mp: 104−105 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.00−7.98 (m, 2H), 7.86 (d, $J$ = 16.0 Hz, 1H), 7.74 (d, $J$ = 12.4 Hz, 1H), 7.60−7.56 (m, 1H), 7.54−7.48 (m, 3H), 7.21 (d, $J$ = 2.8 Hz, 1H), 7.03 (d, $J$ = 9.2 Hz, 1H), 6.96 (dd, $J$ = 2.8 Hz, 8.8 Hz, 1H), 5.43 (d, $J$ = 12.4 Hz, 1H), 4.18 (q, $J$ = 7.2 Hz, 2H), 3.85 (s, 3H), 1.27 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 190.3, 166.9, 160.0, 157.0, 148.3, 137.9, 137.8, 132.9, 128.6, 128.5, 127.2, 124.6, 120.6, 117.2, 112.9, 102.1, 60.1, 55.8, 55.7, 14.2. IR (KBr): 3442, 2974, 1703, 1645, 1599, 1490, 1293, 1231, 1132, 1031, 859, 694 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{21}O_5$ $[M + H]^+$: calcd, 353.1384; found, 353.1397.

*(E)-Ethyl 3-(5-Methyl-2-((E)-3-oxo-3-phenylprop-1-en-1-yl)-phenoxy)acrylate* ***(2o)***. Light yellow solid in a 36% yield of two steps (726 mg). Mp: 68−70 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (d, $J$ = 8.0 Hz, 2H), 7.93 (d, $J$ = 15.6 Hz, 1H), 7.78 (d, $J$ = 12.0 Hz, 1H), 7.61 (d, $J$ = 8.0 Hz, 1H), 7.59−7.47 (m, 4H), 7.05 (d, $J$ = 8.0 Hz, 1H), 6.90 (s, 1H), 5.56 (d, $J$ = 12.0 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 2.39 (s, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 190.4, 166.9, 158.8, 154.5, 142.9, 138.1, 138.0, 132.7, 128.6, 128.5, 126.3, 123.3, 123.2, 119.3, 103.0, 60.1, 21.4, 14.2. IR (KBr): 3443, 2981, 1708, 1644, 1601, 1253, 1129, 1013, 784, 689 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{21}O_4$ $[M + H]^+$: calcd, 337.1434; found, 337.1447.

*(E)-Ethyl 3-(2-((E)-3-(Furan-2-yl)-3-oxoprop-1-en-1-yl)phenoxy)-acrylate* ***(2p)***. White solid in a 39% yield of two steps (730 mg). Mp: 78−79 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, $J$ = 16.0 Hz, 1H), 7.79 (d, $J$ = 13.2 Hz, 1H), 7.74 (d, $J$ = 7.6 Hz, 1H), 7.66 (s, 1H), 7.49 (d, $J$ = 16.0 Hz, 1H), 7.43 (t, $J$ = 7.6 Hz, 1H), 7.33 (d, $J$ = 3.6 Hz, 1H), 7.29−7.23 (m, 1H), 7.09 (d, $J$ = 8.0 Hz, 1H), 6.60 (t, $J$ = 2.0 Hz, 1H), 5.57 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 177.7, 166.7, 158.6, 154.5, 153.6, 146.6, 137.0, 131.8, 128.8, 125.9, 125.4, 123.4, 118.6, 117.6, 112.5, 103.2, 103.1, 60.1, 14.2. IR (KBr): 3442, 3119, 2995, 1711, 1660, 1466, 1397, 1289, 1213, 1158, 1046, 956, 839, 758 cm$^{-1}$. HRMS (ESI) for $C_{18}H_{17}O_5$ $[M + H]^+$: calcd, 313.1071; found, 313.1085.

*(E)-Ethyl 3-(2-((E)-3-Oxo-3-(thiophen-2-yl)prop-1-en-1-yl)-phenoxy)acrylate* ***(2q)***. Light yellow solid in a 42% yield of two steps (827 mg). Mp: 84−85 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 15.6 Hz, 1H), 7.85 (dd, $J$ = 0.8 Hz, 3.6 Hz, 1H), 7.79 (d, $J$ = 12.4 Hz, 1H), 7.72 (dd, $J$ = 1.2 Hz, 8.0 Hz, 1H), 7.69 (dd, $J$ = 0.8 Hz, 4.8 Hz, 1H), 7.50−7.41 (m, 2H), 7.28−7.24 (m, 1H), 7.18 (dd, $J$ = 4.0 Hz, 4.8 Hz, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 5.58 (d, $J$ = 12.4 Hz, 1H), 4.19 (q, $J$ = 7.2 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 181.8, 166.7, 158.5, 154.5, 145.3, 137.2, 134.0, 131.9, 131.8, 129.0, 128.2, 125.9, 125.4, 124.0, 118.7, 103.2, 60.2, 14.2. IR (KBr): 3442, 2985, 1959, 1707, 1646, 1596, 1485, 1328, 1226, 1133, 979, 841, 754, 720 cm$^{-1}$. HRMS (ESI) for $C_{18}H_{17}O_4S$ $[M + H]^+$: calcd, 329.0842; found, 329.0855.

*(E)-Ethyl 3-(2-((E)-3-Oxobut-1-en-1-yl)phenoxy)acrylate* ***(2r)***. Light yellow oil in a 40% yield of two steps (624 mg). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.78 (d, $J$ = 12.0 Hz, 1H), 7.70 (d, $J$ = 16.4 Hz, 1H), 7.65−7.63 (m, 1H), 7.45−7.41 (m, 1H), 7.23 (t, $J$ = 7.6 Hz, 1H), 7.09 (d, $J$ = 8.4 Hz, 1H), 6.73 (d, $J$ = 16.4 Hz, 1H), 5.56 (d, $J$ = 12.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 2.38 (s, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 198.1, 166.6, 158.5, 154.1, 136.2, 131.7, 129.0, 128.1, 125.6, 125.4, 118.6, 103.1, 103.0, 60.1, 27.4, 14.2. IR (KBr): 3407, 2982, 1712, 1650, 1483, 1364, 1227, 1124, 976,

839, 753, 569 cm$^{-1}$. HRMS (ESI) for $C_{15}H_{17}O_4$ [M + H]$^+$: calcd, 261.1121; found, 261.1133.

*(E)-Ethyl 3-(4-Bromo-2-((E)-3-(4-bromophenyl)-3-oxoprop-1-en-1-yl)phenoxy)acrylate (**2s**).* White solid in a 54% yield of two steps (1.55 g). Mp: 95−96 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.90−7.85 (m, 4H), 7.73 (d, *J* = 12.0 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.55−7.48 (m, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 5.58 (d, *J* = 12.0 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 188.6, 166.5, 157.9, 153.4, 136.7, 136.3, 134.5, 132.0, 131.0, 130.0, 128.3, 127.8, 124.4, 120.2, 118.3, 103.9, 60.3, 14.2. IR (KBr): 3439, 2979, 1713, 1642, 1603, 1481, 1398, 1319, 1222, 1136, 1033, 1008, 829, 740 cm$^{-1}$. HRMS (ESI) for $C_{20}H_{17}Br_2O_4$ [M + H]$^+$: calcd, 478.9488; found, 478.9494.

**Typical Experimental Procedure for the Synthesis of Chromans (3a−3s).** A mixture of chalcone enolate (**2a**; 0.2 mmol, 64 mg), nitromethane (4.0 mmol, 214 μL), organocatalyst **1a** (0.04 mmol, 23 mg), and a 4 Å MS (60 mg) in toluene (1.0 mL) was stirred at 40 °C. The reaction was stirred until **2a** was completely consumed, as monitored by TLC. The crude mixture was purified by flash chromatography on silica gel to afford product **3a** as a colorless oil in 86% yield (66 mg), >99% ee, dr = 9:1.

*Ethyl 2-((2S,3S,4R)-3-Nitro-4-(2-oxo-2-phenylethyl)chroman-2-yl)acetate (**3a**).* Colorless oily solid in an 86% yield (66 mg), >99% ee, dr = 9:1. $[\alpha]_D^{20}$ = −34.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (90/10 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 44.9 min, $t_{R(major)}$ = 47.6 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.98−7.96 (m, 2H), 7.63−7.59 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.20−7.16 (m, 2H), 7.03−6.99 (m, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 5.07 (t, *J* = 1.2 Hz, 1H), 4.69−4.65 (m, 1H), 4.23−4.15 (m, 3H), 3.57 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.38 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.99−2.85 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 196.2, 169.9, 153.4, 135.9, 133.9, 128.8, 128.7, 128.1, 128.0, 122.3, 122.1, 117.1, 83.5, 68.4, 61.2, 45.3, 36.3, 33.2, 14.0. IR (KBr): 3063, 2957, 1733, 1683, 1490, 1355, 1231, 1191, 758 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{25}N_2O_6$ [M + $NH_4$]$^+$: calcd, 401.1707; found, 401.1711.

*Ethyl 2-((2S,3S,4R)-3-Nitro-4-(2-oxo-2-(p-tolyl)ethyl)chroman-2-yl)acetate (**3b**).* Colorless oily solid in an 88% yield (70 mg), >99% ee, dr = 9:1. $[\alpha]_D^{20}$ = −50.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 14.3 min, $t_{R(major)}$ = 24.0 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.29−7.26 (m, 2H), 7.18 (t, *J* = 8.0 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.06 (s, 1H), 4.67 (t, *J* = 6.4 Hz, 1H), 4.22−4.15 (m, 3H), 3.54 (dd, *J* = 3.2 Hz, 18.4 Hz, 1H), 3.35 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.98−2.85 (m, 2H), 2.42 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 195.8, 169.9, 153.4, 144.9, 133.5, 129.5, 128.8, 128.2, 128.0, 122.3, 122.2, 117.1, 83.6, 68.4, 61.2, 45.2, 36.4, 33.3, 21.7, 14.1. IR (KBr): 2956, 1733, 1678, 1490, 1353, 1282, 1185, 1025, 810, 759 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_6$ [M + $NH_4$]$^+$: calcd, 415.1864; found, 415.1873.

*Ethyl 2-((2S,3S,4R)-4-(2-(4-Methoxyphenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3c**).* Colorless oily solid in an 85% yield (70 mg), >99% ee, dr = 8:1. $[\alpha]_D^{20}$ = −52.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 33.4 min, $t_{R(major)}$ = 45.2 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.95−7.93 (m, 2H), 7.19−7.15 (m, 2H), 7.02−6.98 (m, 1H), 6.95−6.92 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.07 (t, *J* = 1.2 Hz, 1H), 4.69−4.65 (m, 1H), 4.21−4.15 (m, 3H), 3.87 (s, 3H), 3.51 (dd, *J* = 3.2 Hz, 18.4 Hz, 1H), 3.32 (dd, *J* = 10.8 Hz, 18.4 Hz, 1H), 2.97−2.84 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 194.6, 169.8, 164.0, 153.4, 130.4, 129.0, 128.8, 128.0, 122.3, 122.2, 117.0, 113.9, 83.6, 68.4, 61.1, 55.5, 44.9, 36.4, 33.3, 14.0. IR (KBr): 2957, 2925, 2847, 1733, 1673, 1600, 1552, 1512, 1354, 1262, 1242, 1174, 1112, 1027, 834, 760 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_7$ [M + $NH_4$]$^+$: calcd, 431.1813; found, 431.1821.

*Ethyl 2-((2S,3S,4R)-4-(2-(3-Methoxyphenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3d**).* Colorless oily solid in an 84% yield (69 mg), >99% ee, dr = 9:1. $[\alpha]_D^{20}$ = −30.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 20.6 min, $t_{R(major)}$ = 27.3 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.53−7.50 (m, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.20−7.13 (m, 3H), 7.03−6.99 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 5.07 (s, 1H), 4.68−4.64 (m, 1H), 4.22−4.15 (m, 3H), 3.85 (s, 3H), 3.56 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.37 (dd, *J* = 10.8 Hz, 18.4 Hz, 1H), 2.99−2.85 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 196.1, 169.8, 159.9, 153.4, 137.2, 129.8, 128.7, 128.1, 122.3, 122.0, 120.6, 120.4, 117.1, 112.2, 83.5, 68.4, 61.2, 55.5, 45.4, 36.3, 33.3, 14.1. IR (KBr): 2956, 1733, 1682, 1586, 1457, 1352, 1283, 1191, 1041, 759 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_7$ [M + $NH_4$]$^+$: calcd, 431.1813; found, 431.1807.

*Ethyl 2-((2S,3S,4R)-4-(2-(2-Methoxyphenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3e**).* Colorless oily solid in a 78% yield (64 mg), ee = 97%, dr = 6:1. $[\alpha]_D^{20}$ = −38.0 (*c* 1.0, $CH_2Cl_2$, 97% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 10.4 min, $t_{R(major)}$ = 12.7 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.82 (dd, *J* = 1.6 Hz, 7.6 Hz, 1H), 7.54−7.50 (m, 1H), 7.26−7.15 (m, 2H), 7.07−6.97 (m, 3H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.06 (s, 1H), 4.71−4.68 (m, 1H), 4.23−4.17 (m, 3H), 3.90 (s, 3H), 3.57 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.43 (dd, *J* = 10.8 Hz, 18.4 Hz, 1H), 2.98−2.85 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.2, 169.9, 159.0, 153.4, 134.5, 130.7, 128.9, 127.9, 126.8, 122.5, 122.2, 120.9, 117.0, 111.6, 83.9, 68.4, 61.1, 55.6, 50.4, 36.6, 33.8, 14.1. IR (KBr): 3072, 2925, 1734, 1667, 1551, 1487, 1286, 1188, 1023, 759 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_7$ [M + $NH_4$]$^+$: calcd, 431.1813; found, 431.1822.

*Ethyl 2-((2S,3S,4R)-4-(2-(4-Bromophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3f**).* Colorless oily solid in an 85% yield (78 mg), >99% ee, dr = 10:1. $[\alpha]_D^{20}$ = −63.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 25.4 min, $t_{R(major)}$ = 36.6 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.18 (t, *J* = 6.8 Hz, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.05 (s, 1H), 4.65 (dd, *J* = 6.4 Hz, 6.8 Hz, 1H), 4.21−4.15 (m, 3H), 3.53 (dd, *J* = 3.6 Hz, 18.8 Hz, 1H), 3.35 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.99−2.86 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 195.3, 169.9, 153.4, 134.6, 132.2, 129.5, 129.2, 128.7, 128.2, 122.4, 121.9, 117.1, 83.4, 68.4, 61.2, 45.2, 36.2, 33.1, 14.1. IR (KBr): 2957, 1732, 1684, 1551, 1489, 1398, 1281, 1191, 1071, 814, 759 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}BrN_2O_6$ [M + $NH_4$]$^+$: calcd, 479.0812; found, 479.0811.

*Ethyl 2-((2S,3S,4R)-4-(2-(4-Chlorophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3g**).* Colorless oily solid in a 90% yield (75 mg), 97% ee, dr = 9:1. $[\alpha]_D^{20}$ = −49.0 (*c* 1.0, $CH_2Cl_2$, 97% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 22.8 min, $t_{R(major)}$ = 28.8 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.20−7.17 (m, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 5.05 (s, 1H), 4.67−4.64 (m, 1H), 4.22−4.16 (m, 3H), 3.54 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.35 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 3.00−2.86 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 195.0, 169.9, 153.4, 140.4, 134.2, 129.5, 129.2, 128.7, 128.2, 122.4, 121.9, 117.1, 83.4, 68.4, 61.2, 45.3, 36.2, 33.1, 14.1. IR (KBr): 2957, 1732, 1684, 1552, 1490, 1402, 1282, 1023, 821, 760 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}ClN_2O_6$ [M + $NH_4$]$^+$: calcd, 435.1317; found, 435.1304.

*Ethyl 2-((2S,3S,4R)-4-(2-(3-Bromophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3h**).* Colorless oily solid in an 87% yield (80 mg), >99 ee, dr = 10:1. $[\alpha]_D^{20}$ = −31.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 14.9 min, $t_{R(major)}$ = 16.5 min. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.09 (t, *J* = 2.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 0.8 Hz, 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.20−7.17 (m, 2H), 7.03−6.99 (m, 1H), 6.89−6.87 (m, 1H), 5.05 (s, 1H), 4.67−4.63 (m, 1H), 4.23−4.15 (m, 3H), 3.54 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.36 (dd, *J* = 10.8 Hz, 19.2 Hz, 1H), 3.00−2.86 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 194.9, 169.9, 153.4, 137.5, 136.7, 131.2, 130.4, 128.7, 128.2, 126.6, 123.2, 122.4, 121.8, 117.1, 83.4, 68.4, 61.2, 45.4, 36.2, 33.1, 14.1. IR

(KBr): 2959, 1732, 1688, 1552, 1490, 1353, 1226, 1194, 1024, 791, 758 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}BrN_2O_6$ $[M + NH_4]^+$: calcd, 479.0812; found, 479.0823.

*Ethyl 2-((2S,3S,4R)-4-(2-(2-Chlorophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3i**).* Colorless oily solid in an 80% yield (67 mg), ee = 97%, dr = 9:1. $[\alpha]_D^{20}$ = −51.0 (*c* 1.0, $CH_2Cl_2$, 97% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 12.0 min, $t_{R(major)}$ = 14.0 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.54 (d, *J* = 7.6 Hz, 1H), 7.44−7.43 (m, 2H), 7.38−7.34 (m, 1H), 7.22−7.18 (m, 1H), 7.17−7.15 (m, 1H), 7.02−6.98 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.13 (s, 1H), 4.69−4.65 (m, 1H), 4.24−4.19 (m, 3H), 3.55 (dd, *J* = 3.6 Hz, 18.8 Hz, 1H), 3.39 (dd, *J* = 10.4 Hz, 18.8 Hz, 1H), 3.02−2.89 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.6, 169.8, 153.3, 138.0, 132.5, 131.0, 130.7, 129.2, 128.7, 128.2, 127.2, 122.4, 121.7, 117.1, 83.2, 68.5, 61.2, 49.4, 36.2, 33.5, 14.1. IR (KBr): 3066, 2957, 1733, 1699, 1552, 1489, 1352, 1282, 1191, 1028, 758 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}ClN_2O_6$ $[M + NH_4]^+$: calcd, 435.1317; found, 435.1316.

*Ethyl 2-((2S,3S,4R)-4-(2-(2-Fluorophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3j**).* Colorless oily solid in an 85% yield (68 mg), >99% ee, dr = 9:1. $[\alpha]_D^{20}$ = −41.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 9.7 min, $t_{R(major)}$ = 15.2 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.99−7.94 (m, 1H), 7.60−7.55 (m, 1H), 7.30−7.26 (m, 1H), 7.22−7.13 (m, 3H), 7.03−6.99 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.08 (s, 1H), 4.69−4.65 (m, 1H), 4.23−4.16 (m, 3H), 3.63−3.57 (m, 1H), 3.42−3.34 (m, 1H), 2.99−2.86 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 194.5, 194.4, 169.8, 163.5, 161.0, 153.4, 135.6, 135.5, 130.8, 128.8, 128.0, 124.8, 124.7, 124.5, 124.3, 122.3, 121.9, 117.0, 116.9, 116.7, 83.5, 68.4, 61.1, 50.1, 50.0, 36.3, 33.3, 33.2, 14.1. IR (KBr): 3070, 2957, 1734, 1683, 1552, 1454, 1357, 1282, 1191, 1026, 761 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}FN_2O_6$ $[M + NH_4]^+$: calcd, 419.1613; found, 419.1624.

*Ethyl 2-((2S,3S,4R)-6-Chloro-3-nitro-4-(2-oxo-2-phenylethyl)-chroman-2-yl)acetate (**3k**).* Colorless oily solid in an 84% yield (70 mg), >99% ee, dr = 7:1. $[\alpha]_D^{20}$ = −10.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 12.0 min, $t_{R(major)}$ = 22.6 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.97−7.95 (m, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 2.4 Hz, 1H), 7.13 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 5.06 (d, *J* = 1.2 Hz, 1H), 4.66−4.62 (m, 1H), 4.16 (dd, *J* = 7.2 Hz, 14.4 Hz, 3H), 3.54 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.38 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.97−2.84 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 195.8, 169.7, 152.0, 135.7, 134.0, 128.9, 128.4, 128.2, 128.1, 127.1, 123.8, 118.5, 83.1, 68.6, 61.2, 45.1, 36.2, 33.2, 14.0. IR (KBr): 3063, 2957, 1732, 1683, 1553, 1484, 1354, 1235, 1194, 1025, 818, 757 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}ClN_2O_6$ $[M + NH_4]^+$: calcd, 435.1317; found, 435.1313.

*Ethyl 2-((2S,3S,4R)-6-Bromo-3-nitro-4-(2-oxo-2-phenylethyl)-chroman-2-yl)acetate (**3l**).* Colorless oily solid in an 84% yield (78 mg), >99% ee, dr = 7:1. $[\alpha]_D^{20}$ = −5.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 10.5 min, $t_{R(major)}$ = 19.6 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.33−7.26 (m, 2H), 6.76 (d, *J* = 8.8 Hz, 1H), 5.06 (s, 1H), 4.64 (t, *J* = 6.8 Hz, 1H), 4.17 (dd, *J* = 7.2 Hz, 14.4 Hz, 3H), 3.54 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.38 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.97−2.84 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 195.8, 169.7, 152.6, 135.7, 134.0, 131.4, 131.1, 128.9, 128.1, 124.3, 118.9, 114.4, 83.1, 68.6, 61.3, 45.1, 36.2, 33.1, 14.0. IR (KBr): 3062, 2956, 1732, 1683, 1552, 1481, 1354, 1275, 1193, 1025, 817, 752, 691 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{20}BrNaNO_6$ $[M + Na]^+$: calcd, 484.0366; found, 484.0371.

*Ethyl 2-((2S,3S,4R)-6-Methyl-3-nitro-4-(2-oxo-2-phenylethyl)-chroman-2-yl)acetate (**3m**).* Colorless oily solid in an 86% yield (68 mg), >99% ee, dr = 9:1. $[\alpha]_D^{20}$ = −11.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 10.6 min, $t_{R(major)}$ = 14.7 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98−7.96 (m, 2H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.51−7.47 (m, 2H), 6.98 (d, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 1H), 5.04 (d, *J* = 1.2 Hz, 1H), 4.65−4.61 (m, 1H), 4.17 (dd, *J* = 7.2 Hz, 14.4 Hz, 3H), 3.58 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.38 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.98−2.84 (m, 2H), 2.29 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 196.3, 169.9, 151.3, 135.9, 133.9, 131.7, 129.0, 128.9, 128.8, 128.1, 121.7, 116.8, 83.6, 68.4, 61.1, 45.4, 36.4, 33.2, 20.6, 14.1. IR (KBr): 3060, 2957, 1732, 1683, 1552, 1450, 1355, 1226, 1189, 1025, 818, 758 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_6$ $[M + NH_4]^+$: calcd, 415.1864; found, 415.1871.

*Ethyl 2-((2S,3S,4R)-6-Methoxy-3-nitro-4-(2-oxo-2-phenylethyl)-chroman-2-yl)acetate (**3n**).* Colorless oily solid in an 82% yield (68 mg), >99% ee, dr = 12:1. $[\alpha]_D^{20}$ = −11.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an AS-H column (80/20 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(major)}$ = 24.7 min, $t_{R(minor)}$ = 30.3 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, *J* = 7.2 Hz, 2H), 7.63−7.59 (m, 1H), 7.48 (t, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.76−6.70 (m, 2H), 5.03 (s, 1H), 4.64−4.60 (m, 1H), 4.21−4.13 (m, 3H), 3.74 (s, 3H), 3.57 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.39 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.96−2.84 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 196.2, 169.9, 154.6, 147.4, 135.9, 133.9, 128.8, 128.0, 122.7, 117.8, 114.2, 113.0, 83.5, 68.6, 61.1, 55.6, 55.5, 45.2, 36.3, 33.5, 14.0. IR (KBr): 3062, 2956, 1731, 1682, 1552, 1354, 1276, 1040, 812, 758, 690 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_7$ $[M + NH_4]^+$: calcd, 431.1813; found, 431.1819.

*Ethyl 2-((2S,3S,4R)-7-Methyl-3-nitro-4-(2-oxo-2-phenylethyl)-chroman-2-yl)acetate (**3o**).* Colorless oily solid in an 87% yield (69 mg), dr = 8:1. $[\alpha]_D^{20}$ = −47.0 (*c* 1.0, $CH_2Cl_2$, 95% ee). The enantiomeric excess was determined by HPLC with an OD-H column (90/10 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 22.4 min, $t_{R(major)}$ = 25.6 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.96 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.71 (s, 1H), 5.05 (s, 1H), 4.65 (t, *J* = 6.8 Hz, 1H), 4.17 (dd, *J* = 7.2 Hz, 14.0 Hz, 3H), 3.45 (dd, *J* = 7.2 Hz, 18.8 Hz, 1H), 3.35 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.97−2.83 (m, 2H), 2.29 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 196.3, 169.9, 153.2, 138.3, 135.9, 133.8, 128.8, 128.5, 128.0, 123.4, 118.9, 117.4, 83.7, 68.4, 61.1, 45.3, 36.4, 33.0, 21.0, 20.9, 14.1. IR (KBr): 3060, 2957, 1733, 1683, 1552, 1450, 1352, 1189, 1026, 807, 745 cm$^{-1}$. HRMS (ESI) for $C_{22}H_{27}N_2O_6$ $[M + NH_4]^+$: calcd, 415.1864; found, 415.1870.

*Ethyl 2-((2S,3S,4R)-4-(2-(Furan-2-yl)-2-oxoethyl)-7-methyl-3-nitrochroman-2-yl)acetate (**3p**).* Colorless oily solid in an 80 yield (60 mg), dr = 8:1. $[\alpha]_D^{20}$ = −79.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an AS-H column (90/10 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(major)}$ = 44.1 min, $t_{R(minor)}$ = 51.0 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.60 (d, *J* = 1.2 Hz, 1H), 7.27 (d, *J* = 3.6 Hz, 1H), 7.22−7.15 (m, 2H), 7.02−6.98 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.57 (dd, *J* = 1.6 Hz, 3.6 Hz, 1H), 5.08 (s, 1H), 4.71−4.67 (m, 1H), 4.23−4.15 (m, 3H), 3.55 (dd, *J* = 3.6 Hz, 18.0 Hz, 1H), 3.22 (dd, *J* = 10.8 Hz, 18.0 Hz, 1H), 3.00−2.86 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 185.5, 169.8, 153.3, 152.0, 146.9, 128.8, 128.1, 122.3, 121.8, 117.9, 117.1, 112.7, 83.4, 68.4, 61.2, 44.9, 36.3, 33.0, 14.0. IR (KBr): 3135, 2983, 1733, 1673, 1552, 1466, 1397, 1283, 1189, 1024, 761 cm$^{-1}$. HRMS (ESI) for $C_{19}H_{23}N_2O_7$ $[M + NH_4]^+$: calcd, 391.1500; found, 391.1490.

*Ethyl 2-((2S,3S,4R)-7-Methyl-3-nitro-4-(2-oxo-2-(thiophen-2-yl)-ethyl)chroman-2-yl)acetate (**3q**).* Colorless oily solid in an 85% yield (66 mg), >99% ee, dr = 7:1. $[\alpha]_D^{20}$ = −60.0 (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an AS-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(major)}$ = 21.1 min, $t_{R(minor)}$ = 24.3 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.74−7.70 (m, 2H), 7.26−7.15 (m, 3H), 7.03−6.99 (m, 1H), 6.89−6.87 (m, 1H), 5.10 (t, *J* = 1.2 Hz, 1H), 4.71−4.67 (m, 1H), 4.19 (dd, *J* = 7.2 Hz, 14.0 Hz, 3H), 3.52 (dd, *J* = 3.6 Hz, 18.0 Hz, 1H), 3.31 (dd, *J* = 10.8 Hz, 18.0 Hz, 1H), 3.00−2.87 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 189.1, 169.9, 153.4, 143.0, 134.7, 132.5, 128.8, 128.4, 128.2, 122.4, 121.8, 117.1, 83.4, 68.4, 61.2, 45.7, 36.4, 33.4, 14.1. IR (KBr): 3094, 2958, 1773, 1660, 1552, 1415, 1282, 1190, 1026, 856, 759, cm$^{-1}$. HRMS (ESI) for $C_{19}H_{23}N_2O_6S$ $[M + NH_4]^+$: calcd, 407.1271; found, 407.1279.

*Ethyl 2-((2S,3S,4R)-6-Bromo-4-(2-(4-bromophenyl)-2-oxoethyl)-3-nitrochroman-2-yl)acetate (**3s**).* White solid in an 82% yield (86 mg), >99% ee, dr = 9:1. Mp: 99−101 °C. $[\alpha]_D^{20} = -15.0$ (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (70/30 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(minor)}$ = 15.5 min, $t_{R(major)}$ = 35.9 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.83 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.33−7.29 (m, 2H), 6.77 (d, *J* = 8.8 Hz, 1H), 5.04 (s, 1H), 4.62 (t, *J* = 6.4 Hz, 1H), 4.18 (q, *J* = 6.8 Hz, 3H), 3.51 (dd, *J* = 3.2 Hz, 18.8 Hz, 1H), 3.35 (dd, *J* = 10.8 Hz, 18.8 Hz, 1H), 2.98−2.85 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 194.8, 169.8, 152.5, 134.4, 132.2, 132.1, 131.3, 131.2, 129.5, 129.3, 124.1, 118.9, 114.5, 82.9, 68.6, 45.0, 36.1, 33.0, 14.1. IR (KBr): 3436, 2927, 1724, 1688, 1551, 1416, 1237, 1192, 1071, 811 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{19}Br_2NO_6Na$ $[M + Na]^+$: calcd, 561.9471; found, 561.9469.

**Synthesis of Tricyclic Chroman 4a by Reductive Amination Reaction.** Zinc powder (30 equiv, 390 mg) was added in portions to a solution of **3a** (77 mg, 0.2 mmol) in AcOH (2 mL) at 55 °C. The resultant mixture was stirred for 2.0 h at 65 °C (monitored by TLC). After the zinc powder was filtered off, the filtrate was cooled to 0 °C. The filtrate was diluted with ethyl acetate and neutralized by the addition of saturated sodium hydrogen carbonate. The mixture was extracted with dichloromethane, washed with brine, and dried with sodium sulfate. Concentration and flash chromatography (1:4 ethyl acetate/hexane) afforded **4a** as a colorless oil in a 78% yield (53 mg), >99% ee, dr = 18:1.

*Ethyl 2-((2S,3aS,4S,9bR)-2-Phenyl-1,2,3,3a,4,9b-hexahydrochromeno[3,4-b]pyrrol-4-yl)acetate (**4a**).* Colorless oil in a 78% yield (53 mg), >99% ee, dr = 18:1. $[\alpha]_D^{20} = -80.0$ (*c* 1.0, $CH_2Cl_2$, >99% ee). The enantiomeric excess was determined by HPLC with an OD-H column (80/20 *n*-hexane/*i*-PrOH), 1.0 mL/min, $t_{R(major)}$ = 11.5 min, $t_{R(minor)}$ = 17.3 min. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.34−7.31 (m, 4H), 7.28−7.25 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.6 Hz, 2H), 5.13−5.09 (m, 1H), 4.55 (dd, *J* = 6.4 Hz, 9.6 Hz, 1H), 4.18 (dd, *J* = 7.2 Hz, 14.0 Hz, 2H), 3.75 (dd, *J* = 5.2 Hz, 11.6 Hz, 1H), 3.05−2.97 (m, 1H), 2.91 (dd, *J* = 4.8 Hz, 16.0 Hz, 1H), 2.85−2.79 (m, 1H), 2.60 (dd, *J* = 4.8 Hz, 16.0 Hz, 1H), 1.92−1.84 (m, 1H), 1.74 (s, 1H), 1.26 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.7, 152.9, 145.8, 128.9, 127.9, 127.4, 126.4, 125.9, 124.6, 120.1, 116.4, 63.2, 61.2, 60.6, 38.2, 37.3, 34.9, 14.2. IR (KBr): 3352, 2957, 1733, 1485, 1299, 115, 1033, 758, 701 cm$^{-1}$. HRMS (ESI) for $C_{21}H_{24}NO_3$ $[M + H]^+$: calcd, 338.1751; found, 338.1756.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Chiral HPLC chromatograms of **3** and **4a**, X-ray crystallographic data for **3s** (CIF), and $^1$H and $^{13}$C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We are grateful for the NSFC (21032005, 21172097, 21202070), the International S&T Cooperation Program of China (2013DFR70580), the National Basic Research Program of China (2010CB833203), the "111" program from MOE of P. R. China, and a Syngenta fellowship to Z.-X.J.

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