# Kinetic Resolution of β-Chromenyl-β-Hydroxy Esters for Asymmetric Preparation of Flavene Derivatives

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Functionalized *2H*-chromenes are widely distributed in biologically important natural products and pharmaceutical agents.[1] While a variety of synthetic methods for chromene derivatives has become well developed, asymmetric synthetic methods for optically active chromene derivatives remain limited.[2] We describe in this paper our approach for the asymmetric preparation of 2,3-disubstituted chromene derivatives using the kinetic resolution of β-chromenyl-β-hydroxy esters.

For the preparation of enantioenriched chromene derivative **2**, we initially examined an asymmetric Reformatsky reaction of *2H*-chromene 3-carbaldehyde (**1**) with chiral ligand **3**. Treatment of **1** with BrZnCH₂CO₂t-Bu in the presence of chiral ligand **3** (30 mol%) for 1 h at room temperature provided β-chromenyl-β-hydroxy ester **2** with no detectable enantioselectivity. We recently reported that enantioenriched β-hydroxy esters can alternatively be prepared from asymmetric dehydration.[3] Based on our previous investigation, we carried out the reaction of racemic β-hydroxy ester **2** with chiral ligand **3** (5 mol%) and BrZnCH₂CO₂t-Bu (8 equiv) for 4 h in refluxing THF. As shown in Scheme 1, the dehydration of **2** gave the eliminated product and enantioenriched (*R*)-**2** with 87% ee in 53% conversion (s = 22).[4] The efficiency of the catalyst drastically decreased with less than 8 equiv of BrZnCH₂CO₂t-Bu. When 4 equiv of BrZnCH₂CO₂t-Bu

was used, (*R*)-**2** was obtained with 45% ee in 44% conversion (s = 6).

To develop a more efficient ligand for the kinetic resolution, *p*-fluoro substituted chiral ligand **4** has been tested for asymmetric dehydration of various β-hydroxy esters as shown in Table 1. When β-chromenyl-β-hydroxy ester **2** was treated with chiral ligand **4**, the reaction provided a higher selectivity compared to the reaction with chiral ligand **3** (Entry 1). However, dehydrations of β-aryl-β-hydroxy esters **5-7** and β-styryl-β-hydroxy esters **8-10** with *p*-fluoro substituted chiral

**Table 1.**



| Entry | R | Time (h) | Conv. (%)[a] | % ee[b] | s ($k_S/k_R$)[c] |
|-------|---|----------|--------------|---------|------------------|
| 1 | (**2**) | 1 | 50 | 90 | 43 |
| 2 | MeO— (**5**) | 2 | 54 | 88 | 23 |
| 3 | MeO— (**6**) | 3 | 58 | 60 | 6 |
| 4 | Cl— (**7**) | 3 | 57 | 80 | 10 |
| 5 | (**8**) | 1 | 50 | 85 | 30 |
| 6 | (**9**) | 1.5 | 50 | 70 | 12 |
| 7 | —OCH₃ (**10**) | 1.5 | 51 | 64 | 8 |

[a]Determined by ¹H NMR analysis of crude mixture with hexamethyl benzene as an internal integration standard. [b]The % ee values are determined by CSP-HPLC. [c]Selectivity (s) values represent an average of at least two experiments, while conversion and ee value are for specific cases.
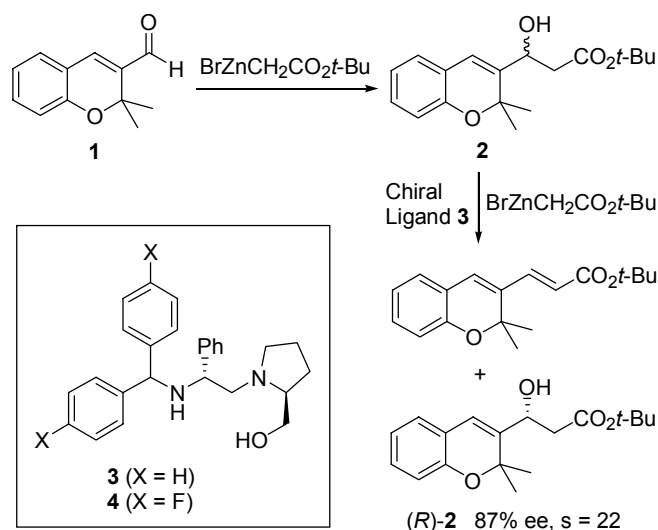


**Scheme 1**

ligand **4** gave lower selectivities compared to the previously reported results with ligand **3**[3b,3c] (Entries 2-7).
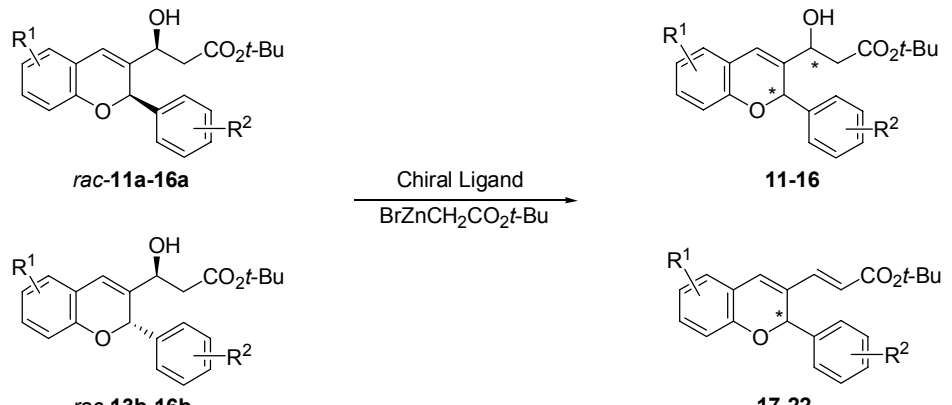
In our continuing studies for synthetic elaboration of flavene (2-phenyl-2*H*-chromene) derivatives,[3d] we have prepared racemic β-flavenyl-β-hydroxy esters **11-16** by the substrate controlled diastereoselective addition of Reformatsky reagent to flavene-3-carbaldehydes.[5] The major and minor diastereomers were separated by column chromatography on silica gel and subjected to asymmetric dehydration as shown in Table 2. When the major diastereomers **11a-16a** were dehydrated with $BrZnCH_2CO_2t$-Bu and chiral ligand **3** (5 mol%), the elimination afforded 3-alkenyl flavenes (*R*)-**17-22** and unreacted β-hydroxy esters **11a-16a** with selectivity values ranging from 22 to 7.[4] Limited results in Table 2 suggest that the selectivity is dependent on the substitution pattern and electronic properties of substituents on both aryl rings. In addition, the same experimental procedure was applied to the kinetic resolution of minor diastereomers **13b-16b**. The reactions of minor diastereomers **13b-16b** with chiral ligand **3** produced 3-alkenyl flavenes (*S*)-**19-22** with the selectivity values lower than those of major diastereomers **13a-16a** (Entries 4, 6, 9 and 12). Consistent with the results obtained in the reaction of chromene derivative **2** (Table 1, Entry 1), flavenes **14b, 15a,** and **16b** were kinetically resolved

with higher efficiencies with *p*-fluoro substituted chiral ligand **4** than those with chiral ligand **3** (Entries 7, 10 and 13). Exceptionally high selectivity (*s* = 50) in kinetic resolution was obtained with 6-methyl substituted **16a** and chiral ligand **4** (Entry 10).

We then examined whether 2-methyl-2*H*-chromene **23** and 4-chloro substituted flavene **24** might be good substrates for asymmetric dehydration as shown in Scheme 2. When the diastereomeric mixture of racemic **23** (79:21 dr) was treated with $BrZnCH_2CO_2t$-Bu and chiral ligand **3** (5 mol%) in refluxing THF for 10 h, the unconverted diastereomeric mixture of **23** was recovered from the comparatively slow reaction in 40% yield based on 36% conversion. The dr of recovered **23** was 80:20 as determined by analysis of the ^{1}H NMR spectrum of reaction mixture and the enantiopurities of major and minor diastereomers were 52% ee (*s* = 43) and 40% ee (*s* = 9), respectively. These results reflect both diastereomers were dehydrated at a similar rate but with different enantioselectivities under the reaction condition. Also, the dehydration of 4-chloro substituted flavene derivative **24** (94:6 dr) for 3.5 h under the same condition gave the diastereomeric mixture of **24** (93:7 dr) with 77% ee (*s* = 21) and 60% ee (*s* = 8), respectively, as shown in Scheme 2.

We here reported catalytic asymmetric dehydration of two

**Table 2.**



| Entry | Substrate | $R^1$ | $R^2$ | ligand | % ee[b] of **11-16** | % ee[b] of **17-22** | Conv.[c](%) | $s$[c] |
|---|---|---|---|---|---|---|---|---|
| 1 | **11a** | 6-Cl | *p*-MeO | **3** | 98 | 54 (**17**, *R*) | 65 | 18 |
| 2 | **12a** | 8-Cl-6-F | *o*-MeO | **3** | 32 | 80 (**18**, *R*) | 29 | 11 |
| 3[a] | **13a** | H | *o*-MeO | **3** | 96 | 70 (**19**, *R*) | 58 | 21 |
| 4 | **13b** | H | *o*-MeO | **3** | 74 | 70 (**19**, *S*) | 51 | 12 |
| 5[a] | **14a** | 8-MeO | H | **3** | 89 | 77 (**20**, *R*) | 54 | 22 |
| 6 | **14b** | 8-MeO | H | **3** | 54 | 79 (**20**, *S*) | 41 | 14 |
| 7[a] | **14b** | 8-MeO | H | **4** | 88 | 77 (**20**, *S*) | 53 | 23 |
| 8 | **15a** | 6-Me | *o*-MeO | **3** | 80 | 50 (**21**, *R*) | 62 | 7 |
| 9 | **15b** | 6-Me | *o*-MeO | **3** | 58 | 42 (**21**, *S*) | 58 | 4 |
| 10 | **15a** | 6-Me | *o*-MeO | **4** | 98 | 85 (**21**, *R*) | 54 | 50 |
| 11 | **16a** | 8-MeO | *o*-MeO | **3** | 31 | 72 (**22**, *R*) | 30 | 8 |
| 12 | **16b** | 8-MeO | *o*-MeO | **3** | 37 | 59 (**22**, *S*) | 39 | 5 |
| 13 | **16b** | 8-MeO | *o*-MeO | **4** | 59 | 78 (**22**, *S*) | 43 | 15 |

[a]Previously reported results in ref. 3d. [b]The ee values of **11-22** are determined by CSP-HPLC. [c]Determined from ee values of **11-22** as in ref. 4.
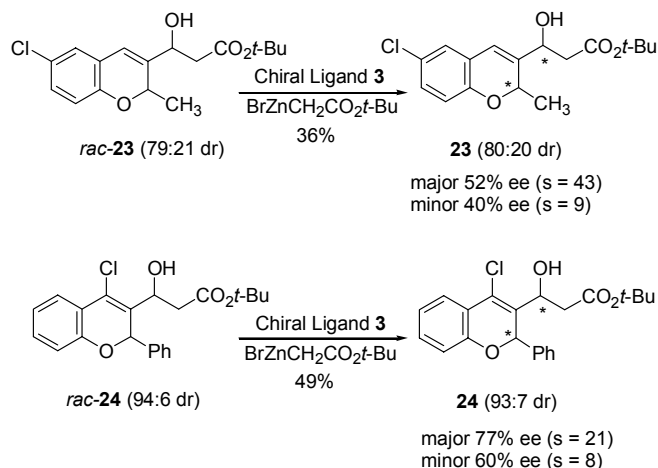
**Scheme 2**

diastereomers of various β-(2*H*-3-chromenyl)-β-hydroxy esters. Kinetic resolutions of major diastereomers of 2,3-disubstituted chromene derivatives **11-16** and **23-24** showed better selectivities compared to the reactions of minor diastereomers. In the dehydration of all chromene substrates examined, *p*-fluoro substituted chiral ligand **4** generally gave better selectivities than chiral ligand **3**. The resulting enantioenriched chromene derivatives contain several functionalities that allow further transformations into more complex molecules and its application to the syntheses of biologically interesting molecules is underway.

## Experimental

**General procedure for asymmetric dehydration.** Trimethylchlorosilane (0.4 equiv) was added to a suspension of zinc metal (8 equiv) in anhydrous THF. After the mixture was refluxed for 50 min, a solution of chiral ligand (5 mol%), *tert*-butyl bromoacetate (8 equiv) and racemic β-chromenyl-β-hydroxy ester (1 equiv) in THF was slowly added. The mixture was stirred at reflux for 1-10 h and then quenched with saturated NH$_4$Cl aqueous solution. The resulting mixture was extracted with CH$_2$Cl$_2$ (3×5 mL) and combined extracts were washed with brine. The solvents were removed and the residue was purified by flash column chromatography to give enantioenriched products.

**t-Butyl (*R*)-3-hydroxy-3-(2,2-dimethyl-2*H*-chromen-3-yl) propanoate (2):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.10-6.77 (m, 4H), 6.36 (s, 1H), 4.76 (s, 2H), 4.58 (m, 1H), 3.48 (d, *J* = 3.9 Hz, 1H), 2.55 (d, *J* = 6.4 Hz, 2H), 1.46 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 171.9, 153.9, 135.0, 129.5, 127.2, 122.7, 121.9, 120.0, 115.9, 82.2, 69.2, 65.9, 40.9, 28.5; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 87% ee, 14.5 min (major), 13.1 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*S*)-6-chloro-2-(*p*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (11a):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.97 (m, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.59 (d, *J* = 8.5 Hz, 1H), 6.54 (s, 1H), 5.88 (s, 1H), 4.43 (m, 1H), 3.73 (s, 3H), 3.39 (d, *J* = 5.0 Hz, 1H), 2.46 (m, 2H), 1.42 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 172.0, 160.5,

150.8, 138.1, 130.8, 129.6, 129.4, 126.5, 126.2, 123.5, 119.1, 118.0, 114.6, 82.2, 77.4, 68.2, 55.6, 41.0, 28.5; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 98% ee, 60.8 min (major), 81.9 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*S*)-8-chloro-6-fluoro-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (12a):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.30-7.15 (m, 2H), 6.94-6.70 (m, 4H), 6.64 (s, 1H), 6.53 (s, 1H), 4.51 (m, 1H), 3.91 (s, 3H), 3.33 (d, *J* = 4.4 Hz, 1H), 2.42 (m, 2H), 1.41 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 171.8, 157.6, 156.7 (d, *J* = 239.4 Hz), 144.9, 138.9, 130.9, 128.8, 126.1, 124.2 (d, *J* = 9.1 Hz), 121.8 (d, *J* = 11.5 Hz), 121.0, 119.7, 116.7 (d, *J* = 26.1 Hz), 112.0, 111.8 (d, *J* = 23.3 Hz), 82.2, 71.6, 68.3, 56.4, 41.0, 28.4; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 32% ee, 54.7 min (major), 48.6 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*R*)-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (13b):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.31 (m, 2H), 7.06-6.67 (m, 7H), 6.35 (s, 1H), 4.32 (m, 1H), 3.89 (s, 3H), 3.32 (d, *J* = 4.3 Hz, 1H), 2.60 (dd, *J* = 3.1 and 16.2 Hz, 1H), 2.42 (dd, *J* = 8.8 and 16.2 Hz, 1H), 1.43 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 172.2, 156.9, 152.6, 136.9, 130.5, 129.6, 129.2, 127.3, 127.0, 122.0, 121.5, 121.3, 120.1, 116.4, 111.4, 82.1, 70.6, 68.1, 56.2, 41.5, 28.5; CSP- HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 74% ee, 50.5 min (major), 42.8 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*S*)-6-methyl-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (15a):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.25 (m, 2H), 6.92-6.78 (m, 4H), 6.63 (s, 1H), 6.57 (d, *J* = 8.6 Hz, 1H), 6.45 (s, 1H), 4.44 (m, 1H), 3.90 (s, 3H), 3.10 (d, *J* = 4.5 Hz, 1H), 2.48 (m, 2H), 2.23 (s, 3H), 1.41 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 172.0, 157.2, 150.4, 136.3, 130.5, 130.4, 130.3, 129.1, 127.5, 127.1, 121.9, 121.1, 120.8, 116.4, 111.6, 81.9, 70.4, 68.6, 56.3, 41.2, 28.5, 21.0; CSP-HPLC (Chiralcel OD column; 5% 2-propanol in hexane; 0.5 mL/min): 80% ee, 52.4 min (major), 40.2 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*R*)-6-methyl-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (15b):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.28 (m, 2H), 6.92-6.81 (m, 4H), 6.74 (s, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 6.31 (s, 1H), 4.31 (m, 1H), 3.90 (s, 3H), 3.27 (d, *J* = 4.2 Hz, 1H), 2.60 (dd, *J* = 3.0 and 16.1 Hz, 1H), 2.42 (dd, *J* = 9.0 and 16.3 Hz, 1H), 2.24 (s, 3H), 1.44 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 172.2, 156.6, 150.3, 136.9, 130.6, 130.4, 130.1, 129.2, 127.5, 127.3, 121.7, 121.3, 120.2, 116.1, 111.4, 82.1, 70.4, 68.2, 56.2, 41.5, 28.5, 21.0; CSP-HPLC (Chiralpak OD column; 5% 2-propanol in hexane; 0.5 mL/min): 58% ee, 22.6 min (major), 27.4 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*S*)-8-methoxy-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propanoate (16a):** $^1$H NMR (CDCl$_3$, 400 MHz) δ 7.29-7.22 (m, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.79 (m, 2H), 6.70 (m, 2H), 6.65 (s, 1H), 6.55 (s, 1H), 4.46 (m, 1H), 3.88 (s, 3H), 3.68 (s, 3H), 3.13 (d, *J* = 4.6 Hz, 1H), 2.43 (m, 2H), 1.41 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 171.9, 157.2, 148.6, 142.0, 136.5, 130.4, 129.0, 127.4, 122.9, 121.1, 121.0, 120.4, 119.7, 113.8, 111.6, 81.8, 70.8, 68.5, 56.8, 56.2, 41.2, 28.5; CSP-HPLC (Chiralcel OD column; 5% 2-propanol in hexane; 0.5 mL/min): 31% ee, 87.5 min (major), 78.4 min (minor).

**t-Butyl (*R*)-3-hydroxy-3-[(*R*)-8-methoxy-2-(*o*-methoxy-

**phenyl)-2*H*-chromen-3-yl] propanoate (16b):** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.35-7.25 (m, 2H), 6.90-6.72 (m, 6H), 6.41 (s, 1H), 4.33 (m, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 3.31 (d, *J* = 4.4 Hz, 1H), 2.63 (dd, *J* = 3.0 and 16.2 Hz, 1H), 2.53 (dd, *J* = 8.8 and 16.2 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 172.2, 156.9, 148.3, 141.8, 137.2, 130.4, 129.0, 127.7, 122.7, 121.3, 121.1, 119.7, 119.6, 113.5, 111.3, 82.1, 70.8, 67.9, 56.8, 56.0, 41.4, 28.5; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 59% ee, 67.2 min (major), 54.8 min (minor).

**t-Butyl 3-[(*R*)-6-chloro-2-(*p*-methoxyphenyl)-2*H*-chromen-3-yl] propenoate (17):** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.31 (d, *J* = 16.0 Hz, 1H), 7.26 (m, 2H), 7.09 (d, *J* = 2.5 Hz, 1H), 7.04 (m, 2H), 6.87 (s, 1H), 6.82 (m, 2H), 6.65 (d, *J* = 8.6 Hz, 1H), 6.02 (s, 1H), 5.61 (d, *J* = 16.0 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.3, 160.5, 151.4, 141.1, 132.0, 130.8, 129.8, 129.5, 129.4, 127.3, 126.6, 123.6, 121.5, 118.5, 114.5, 81.2, 76.6, 55.6, 28.5; CSP-HPLC (Chiralcel OD column; 10% 2-propanol in hexane; 0.5 mL/min): 54% ee, 11.4 min (major), 17.8 min (minor).

**t-Butyl 3-[(*R*)-8-chloro-6-fluoro-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propenoate (18):** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.26 (m, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.91 (m, 2H), 6.79 (m, 2H), 6.71 (s, 1H), 5.67 (d, *J* = 16.0 Hz, 1H), 3.98 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.2, 157.7, 156.5 (d, *J* = 239.4 Hz), 144.9, 140.4, 133.1, 131.2, 129.2, 128.5, 125.2, 124.0 (d, *J* = 9.1 Hz), 122.7, 122.1, 120.9, 118.1 (d, *J* = 26.2 Hz), 112.3 (d, *J* = 23.4 Hz), 111.9, 81.2, 71.2, 56.4, 28.5; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 80% ee, 36.9 min (major), 27.9 min (minor).

**t-Butyl 3-[(*R*)-6-methyl-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propenoate (21):** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.28-6.58 (m, 10H), 5.58 (d, *J* = 16.0 Hz, 1H), 3.97 (s, 3H), 2.25 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.6, 157.1, 151.1, 141.6, 131.9, 131.2, 131.0, 130.9, 130.7, 128.8, 128.3, 126.3, 121.9, 121.0, 120.0, 116.9, 111.5, 80.8, 70.0, 56.2, 28.5, 20.9; CSP-HPLC (Chiralcel OD column; 2% 2-propanol in hexane; 0.5 mL/min): 50% ee, 22.8 min (major), 20.1 min (minor).

**t-Butyl 3-[(*R*)-8-methoxy-2-(*o*-methoxyphenyl)-2*H*-chromen-3-yl] propenoate (22):** ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.27-6.73 (m, 10H), 5.64 (d, *J* = 16.0 Hz, 1H), 3.95 (s, 3H), 3.69 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.6, 157.2, 148.8, 142.7, 141.4, 131.2, 130.7, 128.8, 126.4, 122.9, 121.3, 120.9, 120.4, 120.3, 115.1, 111.5, 80.8, 70.3, 56.9, 56.1, 28.5; CSP-HPLC (Chiralpak AD-H column; 10% 2-propanol in hexane; 0.5 mL/min): 78% ee, 15.9 min (major), 34.9 min (minor).

**t-Butyl 3-hydroxy-3-(6-chloro-2-methyl-2*H*-chromen-3-yl) propanoate (23):** The mixture of two diastereomers (80:20 dr) was recovered in 40% yield based on 36% conversion. ^{1}H NMR (CDCl$_3$, 400 MHz) δ major diastereomer; 7.05 (m, 1H), 6.95 (m, 1H), 6.73 (d, *J* = 8.5 Hz, 2H), 6.22 (s, 1H), 5.05 (q, *J*

= 6.5 Hz, 1H), 4.61 (m, 1H), 3.56 (br, 1H), 2.62 (m, 2H), 1.46 (s, 9H), 1.37 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ major diastereomer; 172.0, 150.8, 140.5, 129.5, 126.5, 126.1, 123.6, 118.4, 118.1, 82.4, 71.8, 69.0, 41.3, 28.5, 20.2; CSP-HPLC (Chiralpak AD-H column; 5% 2-propanol in hexane; 0.5 mL/min): major diastereomer, 52% ee, 40.1 min (major), 36.0 min (minor); minor diastereomer, 40% ee, 13.9 min (major), 10.9 min (minor).

**t-Butyl 3-hydroxy-(4-chloro-2-phenyl-2*H*-chromen-3-yl) propanoate (24):** The mixture of two diastereomers (93:7 dr) was recovered in 29% yield based on 49% conversion. ^{1}H NMR (CDCl$_3$, 400 MHz) δ major diastereomer; 7.49 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.22 (m, 3H), 7.07 (m, 1H), 6.88 (m, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.05 (s, 1H), 5.36 (m, 1H), 3.08 (br, 1H), 2.73 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ major diastereomer; 172.1, 152.8, 139.1, 132.1, 130.9, 129.3, 128.8, 128.3, 124.8, 124.4, 122.2, 121.9, 117.2, 82.3, 76.4, 68.2, 40.9, 28.5; CSP-HPLC (Chiralpak AD-H column; 5% 2-propanol in hexane; 0.5 mL/min): major diastereomer, 77% ee, 23.2 min (major), 46.0 min (minor); minor diastereomer, 60% ee, 59.9 min (major), 51.3 min (minor).

**References and Notes**

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