Supporting information

Diastereoselective synthesis of 3,3-disubstituted 3-nitro- 4-
chromanone derivatives as potential antitumor agents

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1. General experimental details

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. The progress of reactions was monitored by silica gel thin layer chromatography (TLC) plates, visualized under UV. Flash column chromatography was performed using Qingdao Haiyang 200-300 mesh silica gel. $^1$H NMR spectra were recorded on Bruker Ascend 400 (400 MHz) or Bruker AVANCE III (500 MHz) spectrophotometers. Chemical shifts (δ) are reported in ppm from the solvent resonance as the internal standard (CDCl₃: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), coupling constants (Hz) and integration. $^{13}$C NMR spectra were recorded on Bruker Ascend 400 (100 MHz) or Bruker AVANCE III (126 MHz) with complete proton decoupling spectrophotometers (CDCl₃: 77.0 ppm). High resolution mass spectra were performed using a Bruker micrOTOF II high resolution mass spectrometer. Melting points were uncorrected and were recorded on a WRR melting point apparatus. Single crystal X-ray diffraction data were collected on a Bruker Apex II CCD diffractometer using Mo-Kα radiation ($\lambda$ = 0.71073 Å) at 296 K. Complete crystallographic data, in CIF format, have been deposited with the Cambridge Crystallographic Data Center. CCDC 1873098 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. For details on the individual structures, see the Single Crystal X-ray Crystallography section of this document.

2. General procedure and spectral data

2.1 Condition Optimization on the amount of catalyst

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<th>Temp (°C)</th>
<th>Yield of 2a (%)</th>
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2.2 Preparation and Spectral Data of Substrates

2.2.1 Preparation of Substrates

$\alpha$-Nitro ketones were prepared by the following procedures.$^1$

Substrates 1a-p were synthesized according to equation 1.

![R1 CO2R2 + 4-methylmorpholine (CH32OCl) 0°-rt](s1)

81-87% yield

![R1 CHO + R1NO2, KF](s2)

4-methylmorpholine (CH32OCl) 0°-rt

74%-85% yield

![R1 R2 NO2 + DMP](s3)

CH32O, 0°-rt

81%-93% yield

Reference

2.2.2 Spectral Data of Substrates

Ethyl (E)-3-(2-(2-nitropropanoyl)phenoxy)acrylate (1a)

To a mixture of Salicylaldehyde s1a (610 mg, 5 mmol, 1 equiv.) and ethyl propiolate (540 mg, 5.5 mmol, 1 equiv.) in DCM (20 mL) at 0 °C was added 4-methylmorpholine (50 mg, 0.5 mmol, 0.1 equiv.) under N₂ atmosphere. The mixture was allowed to rise to room temperature and stirred for another 2 h. The mixture was quenched with 1N HCl and extracted 3 times with EtOAc. Combined organic phases were dried over sodium sulfate, filtered and purified by column chromatography (petroleum ether/ethyl acetate = 20:1) on silica gel to afford ethyl (E)-3-(2-formylphenoxy)acrylate s2a as a yellowish oil in 81% yield (890 mg).

1H NMR (400 MHz, CDCl₃) δ (ppm) 10.35 (s, 1H), 7.91 (dd, J = 7.7, 1.4 Hz, 1H), 7.82 (d, J = 12.2 Hz, 1H), 7.65-7.61 (m, 1H), 7.30 (dd, J = 7.6, 7.5 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 5.62 (d, J = 12.2 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H).

13C NMR (100 MHz, CDCl₃) δ (ppm) 188.05, 166.48, 157.94, 157.50, 135.96, 128.90, 126.48, 125.32, 118.24, 104.13, 60.33, 14.21. HRMS (ESI): Calcd for C₁₂H₁₁NaO₄ [M+Na⁺]: 243.0633. Found: 243.0645.

To a mixture of ethyl (E)-3-(2-formylphenoxy)acrylate s2a (880 mg, 4 mmol, 1 equiv.) and nitroethane (900 mg, 12 mmol, 3 equiv.) in iPrOH (20 mL) at 0 °C was added 4-methylmorpholine (40 mg, 0.4 mmol, 0.1 equiv.) and KF (24 mg, 0.4 mmol, 0.1 equiv.) under N₂ atmosphere. The mixture was allowed to rise to room temperature and stirred for another 18 h. The mixture was quenched with 1N HCl and extracted 3 times with EtOAc. Combined organic phases were dried over sodium sulfate, filtered and purified by column chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3a as a colorless oil in 85% yield (1 g).

1H NMR (400 MHz, CDCl₃) δ (ppm) 7.78 (d, J = 12.2 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.40 (dd, J = 7.3, 7.2 Hz, 1H), 7.07 (d, J = 8.1 Hz, 1H), 5.69 (s, 1H), 5.63 (d, J = 12.2 Hz, 1H), 4.80 (dd, J = 6.9, 2.9 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.17 (d, J = 4.3 Hz, 1H), 1.46 (d, J = 6.9 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H).

13C NMR (100 MHz, CDCl₃) δ (ppm) 166.90, 157.90, 151.87, 129.86, 128.85, 127.97, 125.39, 117.20, 103.39, 85.01, 68.85, 60.38, 14.21, 11.64. HRMS (ESI): Calcd for C₁₄H₁₇NNaO₆ [M+Na⁺]: 318.0948. Found: 318.0946.

To a solution of ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3a (590 mg, 2 mmol) in DCM (20 mL) at 0 °C was added Dess-Martin periodinane (1060 mg, 2.5 mmol,) under N₂ atmosphere. The mixture was allowed to rise to room temperature and stirred for another 18 h. The slurry was purified directly by column chromatography (CH₂Cl₂/HOAc = 100:1) on silica gel. The eluent fractions were collected and washed with water. Combined organic phases were dried over sodium sulfate and concentrated. Removal of the residual acetic acid in vacuo by azeotroping with toluene to afford ethyl (E)-3-(2-(2-nitropropanoyl)phenoxy)acrylate 1a as a yellowish oil in 88% yield (556 mg).

1H NMR (400 MHz, CDCl₃) δ (ppm) 7.87 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 12.2 Hz, 1H), 7.65-7.61 (m, 1H), 7.30 (dd, J = 7.4, 7.3 Hz, 1H), 7.14 (d, J = 8.1 Hz, 1H), 5.98 (q, J = 7.0 Hz, 1H), 5.76 (d, J = 12.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.79 (d, J = 7.0 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H).

13C NMR (100 MHz, CDCl₃) δ (ppm) 189.36, 166.07, 155.96, 154.44, 135.56, 131.78, 125.60,
Ethyl \((E)-3\)-(4-methyl-2-(2-nitropropanoyl)phenoxy)acrylate (1b)

Substrate 1b was synthesized analogously to 1a. Ethyl \((E)-3\)-(2-formyl-4-methylphenoxy)acrylate s2b was obtained as a yellowish oil in 81% yield from ethyl \((E)-3\)-(2-formyl-4-methylphenoxy)acrylate s2b (4 mmol). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.72 (d, \(J = 12.2\) Hz, 1H), 7.39 (s, 1H), 7.14 (dd, \(J = 8.2, 1.2\) Hz, 1H), 6.92 (d, \(J = 8.3\) Hz, 1H), 5.60 (t, \(J = 3.4\) Hz, 1H), 5.54 (d, \(J = 12.2\) Hz, 1H), 4.75 (qd, \(J = 6.7, 3.0\) Hz, 1H), 4.17 (q, \(J = 7.1\) Hz, 2H), 3.13 (d, \(J = 4.3\) Hz, 1H), 2.35 (s, 3H), 1.44 (d, \(J = 6.9\) Hz, 3H), 1.27 (t, \(J = 7.1\) Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 166.99, 158.46, 147.75, 135.28, 130.26, 128.49, 128.39, 128.93, 126.23, 118.46, 103.56, 60.29, 20.57, 14.24. HRMS (ESI): Calcd for C\(_{13}\)H\(_{14}\)NaO\(_4\) [M+Na]\(^+\): 325.0790. Found: 325.0804.

Ethyl \((E)-3\)-(2-(1-hydroxy-2-nitropropyl)-4-methylphenoxy)acrylate s3b was obtained as a colorless oil in 81% yield from ethyl \((E)-3\)-(2-formyl-4-methylphenoxy)acrylate s2b (4 mmol). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.71 (d, \(J = 12.2\) Hz, 1H), 7.66 (d, \(J = 1.4\) Hz, 1H), 7.42 (dd, \(J = 8.4, 1.6\) Hz, 1H), 7.03 (d, \(J = 8.4\) Hz, 1H), 5.97 (q, \(J = 7.0\) Hz, 1H), 5.71 (d, \(J = 12.2\) Hz, 1H), 4.20 (q, \(J = 7.1\) Hz, 2H), 2.37 (s, 3H), 1.78 (d, \(J = 7.1\) Hz, 3H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 169.59, 158.46, 147.75, 135.24, 130.26, 128.49, 128.39, 128.93, 126.23, 118.46, 103.56, 60.29, 20.57, 14.24. HRMS (ESI): Calcd for C\(_{13}\)H\(_{14}\)NaO\(_4\) [M+Na]\(^+\): 332.1110. Found: 332.1088.

Ethyl \((E)-3\)-(4-methyl-2-(2-nitropropanoyl)phenoxy)acrylate 1b was obtained as a yellowish oil in 86% yield from ethyl \((E)-3\)-(2-formyl-4-methylphenoxy)acrylate s2b (5 mmol). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 10.40 (s, 1H), 8.18 (s, 1H), 7.88 (d, \(J = 8.6\) Hz, 1H), 7.83 (d, \(J = 12.1\) Hz, 1H), 7.29 (d, \(J = 8.6\) Hz, 1H), 5.77 (d, \(J = 12.1\) Hz, 1H), 4.22 (q, \(J = 7.1\) Hz, 2H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^1\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 189.58, 166.25, 156.54, 152.42, 136.17, 135.49, 131.82, 125.30, 117.62, 105.08, 88.11, 60.48, 20.47, 15.51, 14.19. HRMS (ESI): Calcd for C\(_{13}\)H\(_{14}\)NaO\(_4\) [M+Na]\(^+\): 330.0948. Found: 330.0942.

Ethyl \((E)-3\)-(2-(2-nitropropanoyl)-4-(trifluoromethyl)phenoxy)acrylate (1c)

Substrate 1c was synthesized analogously to 1a. Ethyl \((E)-3\)-(2-formyl-4-(trifluoromethyl)phenoxy)acrylate s2c was obtained as a white solid in 85% yield from 2-hydroxy-5-(trifluoromethyl)benzaldehyde s1c (5 mmol). m.p. 46-48 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 10.40 (s, 1H), 8.18 (s, 1H), 7.88 (d, \(J = 8.6\) Hz, 1H), 7.83 (d, \(J = 12.1\) Hz, 1H), 7.29 (d, \(J = 8.6\) Hz, 1H), 5.77 (d, \(J = 12.1\) Hz, 1H), 4.22 (q, \(J = 7.1\) Hz, 2H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 166.67, 165.98, 159.45, 156.01, 132.55 (q, \(J = 3.5\) Hz), 127.62 (q, \(J = 3.7\) Hz), 126.48 (q, \(J = 3.7\) Hz), 123.18 (q, \(J = 270.6\) Hz), 118.01, 106.12, 77.32, 77.00, 76.68, 60.61, 14.20. HRMS (ESI): Calcd for C\(_{13}\)H\(_{11}\)F\(_3\)NaO\(_4\) [M+Na]\(^+\): 311.0502. Found: 311.0493.

Ethyl \((E)-3\)-(2-(1-hydroxy-2-nitropropyl)-4-(trifluoromethyl)phenoxy)acrylate s3c was obtained as a white solid in 74% yield from ethyl \((E)-3\)-(2-formyl-4-methylphenoxy)acrylate s2c (4 mmol). m.p. 86-90 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.94 (s, 1H), 7.76 (d, \(J = 12.2\) Hz, 1H), 7.65 (d, \(J = 8.5\) Hz, 1H), 7.17 (d, \(J = 8.5\) Hz, 1H), 5.73 (d, \(J = 12.2\) Hz, 2H), 2.35 (d, \(J = 7.1\) Hz, 3H), 1.27 (t, \(J = 7.1\) Hz, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 189.58, 166.25, 156.54, 152.42, 136.17, 135.49, 131.82, 125.30, 117.62, 105.08, 88.11, 60.48, 20.47, 15.51, 14.19. HRMS (ESI): Calcd for C\(_{13}\)H\(_{11}\)F\(_3\)NaO\(_4\) [M+Na]\(^+\): 330.0942. Found: 330.0942.

4.77 (qd, J = 6.8, 2.4 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.19 (d, J = 4.0 Hz, 1H), 1.44 (d, J = 6.9 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H). $^1$H NMR (100 MHz, CDCl$_3$) δ (ppm) 166.40, 156.11, 154.05, 129.62, 127.61 (q, J = 32.9 Hz), 127.17 (q, J = 3.8 Hz), 125.58 (q, J = 3.8 Hz), 123.60 (q, J = 270.3 Hz), 116.69, 105.31, 84.49, 68.25, 60.66, 14.20, 11.44. HRMS (ESI): Calcd for C$_{16}$H$_{17}$FNaNaO$_5$ [M+Na]$^+$: 386.0822. Found: 386.0827.

Ethyl (E)-3-(2-(2-nitropropanoyl)-(trifluoromethyl)phenoxy)acrylate 1c was obtained as a yellowish oil in 87% yield from ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-(trifluoromethyl)-phenoxy)acrylate s3c (1 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 8.16 (s, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.73 (d, J = 12.1 Hz, 1H), 7.27 (d, J = 8.7 Hz, 1H), 5.94 (q, J = 7.0 Hz, 1H), 5.86 (d, J = 12.1 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.82 (d, J = 7.0 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 188.05, 165.66, 156.47, 154.36, 132.21 (q, J = 3.4 Hz), 129.40 (q, J = 3.8 Hz), 127.75 (q, J = 34.0 Hz), 125.87, 123.04 (q, J = 270.9 Hz), 117.47, 107.51, 87.85, 60.79, 15.42, 14.12. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) 62.49. HRMS (ESI): Calcd for C$_{15}$H$_{18}$F$_3$NaNaO$_6$ [M+Na]$^+$: 384.0665. Found: 384.0668.

Ethyl (E)-3-(4-fluoro-2-(2-nitropropanoyl)phenoxy)acrylate (1d)

Substrate 1d was synthesized analogously to 1a. Ethyl (E)-3-(4-fluoro-2-formylphenoxy)acrylate s2d was obtained as a yellowish oil in 86% yield from 5-fluoro-2-hydroxybenzaldehyde s1d (5 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 10.28 (d, J = 2.9 Hz, 1H), 7.78 (d, J = 12.2 Hz, 1H), 7.58 (dd, J = 8.0, 3.2 Hz, 1H), 7.34 (ddd, J = 8.9, 7.4, 3.2 Hz, 1H), 7.15 (dd, J = 9.0, 4.0 Hz, 1H), 5.57 (d, J = 12.2 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 186.87, 166.33, 159.61 (d, J = 246.1 Hz), 158.32, 153.50 (d, J = 2.6 Hz), 127.84 (d, J = 6.4 Hz), 122.85 (d, J = 24.2 Hz), 120.59 (d, J = 7.8 Hz), 114.73 (d, J = 23.8 Hz), 104.16, 60.43, 14.22. HRMS (ESI): Calcd for C$_{12}$H$_{12}$F$_3$NaN$_2$O$_4$ [M+Na]$^+$: 261.0534. Found: 261.0550.

Ethyl (E)-3-(4-fluoro-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3d was obtained as a yellowish oil in 80% yield from ethyl (E)-3-(4-fluoro-2-formylphenoxy)acrylate s2d (4 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.69 (d, J = 12.2 Hz, 1H), 7.36 (ddd, J = 8.9, 2.5 Hz, 1H), 7.05 (ddd, J = 8.1, 5.8, 2.8 Hz, 1H), 7.02 (dd, J = 8.8, 4.6 Hz, 1H), 5.64 (s, 1H), 5.55 (d, J = 12.2 Hz, 1H), 4.75 (qd, J = 6.8, 2.4 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.24 (d, J = 4.2 Hz, 1H), 1.43 (d, J = 6.9 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 166.79, 159.93 (d, J = 243.8 Hz), 158.20, 147.56 (d, J = 2.7 Hz), 131.36 (d, J = 7.4 Hz, 1H), 119.15 (d, J = 8.5 Hz), 116.37 (d, J = 23.6 Hz), 115.07 (d, J = 25.1 Hz), 103.30, 84.61, 68.34, 60.48, 14.20, 11.37. HRMS (ESI): Calcd for C$_{14}$H$_{16}$FNNaO$_6$ [M+Na]$^+$: 336.0854. Found: 336.0855.

Ethyl (E)-3-(4-fluoro-2-(2-nitropropanoyl)phenoxy)acrylate 1d was obtained as a yellowish oil in 90% yield from ethyl (E)-3-(4-fluoro-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3d (1 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.67 (d, J = 12.2 Hz, 1H), 7.60 (dd, J = 8.4, 3.1 Hz, 1H), 7.34 (ddd, J = 6.5, 4.0, 3.2 Hz, 1H), 7.14 (ddd, J = 9.0, 4.1 Hz, 1H), 5.93 (q, J = 7.0 Hz, 1H), 5.74 (d, J = 12.2 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.81 (d, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 187.96, 165.97, 159.33 (d, J = 246.1 Hz), 156.13, 150.57 (d, J = 2.6 Hz), 127.00 (d, J = 6.6 Hz), 122.42 (d, J = 23.8 Hz), 119.61 (d, J = 7.9 Hz), 118.11 (d, J = 24.9 Hz), 105.84, 87.71, 60.64, 15.51, 14.20. HRMS (ESI): Calcd for C$_{14}$H$_{14}$FNNaO$_6$ [M+Na]$^+$: 334.0697. Found:
Ethyl (E)-3-(4-chloro-2-(2-nitropropanoyl)phenoxy)acrylate (1e)

Substrate 1e was synthesized analogously to 1a. Ethyl (E)-3-(4-chloro-2-formylphenoxy)acrylate s2e was obtained as a yellow gum in 84% yield from 5-chloro-2-hydroxybenzaldehyde s1e (5 mmol). 1H NMR (400 MHz, CDCl3) δ (ppm) 10.29 (s, 1H), 7.87 (d, J = 2.6 Hz, 1H), 7.78 (d, J = 12.2 Hz, 1H), 7.58 (dd, J = 8.7, 2.6 Hz, 1H), 7.12 (d, J = 8.8 Hz, 1H), 5.64 (d, J = 12.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 139.63, 131.63, 127.65, 119.99, 118.56, 60.50, 14.23. HRMS (ESI): Calcd for C14H10ClNaO4 [M+Na]⁺: 352.0574. Found: 352.0585.

Ethyl (E)-3-(4-chloro-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3e (1 mmol). 1H NMR (400 MHz, CDCl3) δ (ppm) 7.85 (d, J = 2.5 Hz, 1H), 7.67 (d, J = 12.2 Hz, 1H), 7.58 (dd, J = 8.8, 2.6 Hz, 1H), 7.10 (d, J = 8.8 Hz, 1H), 5.92 (q, J = 7.1 Hz, 1H), 5.78 (d, J = 12.1 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.80 (d, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 188.03, 165.86, 155.43, 152.89, 135.21, 131.41, 131.16, 126.77, 118.90, 106.37, 87.81, 60.68, 15.49, 14.20. HRMS (ESI): Calcd for C14H10ClNaO4 [M+Na]⁺: 350.0402. Found: 350.0403.

Ethyl (E)-3-(4-bromo-2-(2-nitropropanoyl)phenoxy)acrylate (1f)

Substrate 1f was synthesized analogously to 1a. Ethyl (E)-3-(4-bromo-2-formylphenoxy)acrylate s2f was obtained as a white solid in 85% yield from 5-bromo-2-hydroxybenzaldehyde s1f (5 mmol). m.p. 59-61 °C. 1H NMR (400 MHz, CDCl3) δ (ppm) 10.28 (s, 1H), 8.01 (d, J = 2.4 Hz, 1H), 7.78 (d, J = 12.2 Hz, 1H), 7.73 (dd, J = 8.7, 2.5 Hz, 1H), 7.06 (d, J = 8.7 Hz, 1H), 5.65 (d, J = 12.2 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 186.64, 166.22, 157.25, 156.37, 138.55, 131.63, 127.65, 119.99, 118.56, 104.90, 60.50, 14.23. HRMS (ESI): Calcd for C14H10BrNaO4 [M+Na]⁺: 320.9733. Found: 320.9725.

Ethyl (E)-3-(4-bromo-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3f was obtained as a colorless oil in 76% yield from ethyl (E)-3-(4-bromo-2-formylphenoxy)acrylate s2f (4 mmol). 1H NMR (400 MHz, CDCl3) δ (ppm) 7.67 (d, J = 5.8 Hz, 1H), 7.65 (d, J = 4.2 Hz, 1H), 7.48 (dd, J = 8.7, 2.3 Hz, 1H), 6.95 (d, J = 8.7 Hz, 1H), 5.59 (d, J = 12.2 Hz, 1H), 5.33 (d, J = 7.8 Hz, 1H), 4.76 (dd, J = 8.3, 7.0 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.56 (s, 1H), 1.37 (d, J = 6.9 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 166.83,
Ethyl (E)-3-(4-bromo-2-(2-nitropropanoyl)phenoxy)acrylate 1f was obtained as a yellowish oil in 89% yield from ethyl (E)-3-(4-bromo-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3f (1 mmol). 1H NMR (400 MHz, CDCl₃) δ (ppm) 8.00 (d, J = 2.4 Hz, 1H), 7.72 (dd, J = 8.8, 2.5 Hz, 1H), 7.67 (d, J = 12.1 Hz, 1H), 7.04 (d, J = 8.8 Hz, 1H), 5.91 (q, J = 7.0 Hz, 1H), 5.78 (d, J = 12.1 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.80 (d, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 187.95, 165.86, 153.29, 151.68, 135.18, 116.34, 110.71, 107.94, 103.86, 87.05, 69.38, 60.29, 56.09, 14.19. HRMS (ESI): Calcd for C₁₅H₁₃BrNNaO₅ [M+Na]⁺: 393.9897. Found: 393.9916.

Ethyl (E)-3-(3-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate (1g)

Substrate 1g was synthesized analogously to 1a. Ethyl (E)-3-(2-formyl-3-methoxyphenoxy)acrylate s2g (5 mmol). 1H NMR (400 MHz, CDCl₃) δ (ppm) 10.39 (s, 1H), 7.70 (d, J = 12.3 Hz, 1H), 7.49 (s, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 5.49 (d, J = 12.3 Hz, 1H), 4.15 (d, J = 7.1 Hz, 2H), 3.91 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 187.74, 166.70, 162.13, 158.63, 156.65, 135.77, 116.20, 111.16, 108.42, 102.93, 60.09, 56.25, 14.17. HRMS (ESI): Calcd for C₁₅H₁₃NaO₅ [M+Na]⁺: 273.0739. Found: 273.0756.

Ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-3-methoxyphenoxy)acrylate s3g (4 mmol). 1H NMR (400 MHz, CDCl₃) δ (ppm) 7.72 (d, J = 12.2 Hz, 1H), 7.34 (dd, J = 8.4, 8.3 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.73 (d, J = 8.3 Hz, 1H), 5.65 (d, J = 12.2 Hz, 1H), 5.44 (dd, J = 10.7, 10.2 Hz, 1H), 5.08 (qd, J = 6.8, 2.8 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 3.70 (d, J = 11.2 Hz, 1H), 1.30 (d, J = 6.8 Hz, 3H), 1.28 (t, J = 6.8 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 166.68, 158.44, 157.77, 154.21, 130.81, 116.34, 110.70, 103.86, 87.05, 69.38, 60.29, 56.09, 16.31, 14.23. HRMS (ESI): Calcd for C₁₅H₁₃NaO₅ [M+Na]⁺: 348.1054. Found: 348.1026.

Ethyl (E)-3-(3-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate 1h was obtained as a yellowish oil in 89% yield from ethyl (E)-3-(2-formyl-3-methoxyphenoxy)acrylate s2h (5 mmol). 1H NMR (400 MHz, CDCl₃) δ (ppm) 10.26 (s, 1H), 7.78 (d, J = 12.3 Hz, 1H), 7.36 (d, J = 3.0 Hz, 1H), 7.17 (dd, J = 8.9, 3.1 Hz, 1H), 7.07 (d, J = 9.0 Hz, 1H), 5.48 (d, J = 12.3 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 191.04, 166.52, 157.84, 157.43, 153.64, 133.21, 117.36, 110.14, 107.77, 104.07, 89.43, 60.22, 56.25, 14.79, 14.19. HRMS (ESI): Calcd for C₁₅H₁₃NaO₅ [M+Na]⁺: 346.0903. Found: 346.0916.
Ethyl (E)-3-(2-[(1-hydroxy-2-nitropropyl)-4-methoxyphenoxy)acrylate was obtained as a yellowish oil in 77% yield from ethyl (E)-3-(2-formyl-4-methoxyphenoxy)acrylate (4 mmol). \(^1{\text{H}}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.69 (d, \(J = 12.3\) Hz, 1H), 7.13 (d, \(J = 2.9\) Hz, 1H), 6.95 (d, \(J = 8.9\) Hz, 1H), 6.85 (dd, \(J = 8.9, 3.0\) Hz, 1H), 5.60-5.59 (m, 1H), 5.47 (d, \(J = 12.3\) Hz, 1H), 4.75 (qd, \(J = 6.8, 2.9\) Hz, 1H), 4.15 (q, \(J = 7.1\) Hz, 2H), 3.80 (s, 3H), 3.27 (d, \(J = 4.3\) Hz, 1H), 1.42 (d, \(J = 6.9\) Hz, 3H), 1.26 (t, \(J = 7.1\) Hz, 3H). \(^1{\text{C}}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 166.82, 160.86, 157.74, 152.77, 128.75, 120.70, 110.40, 103.84, 103.54, 85.33, 68.88, 60.37, 55.62, 14.22. HRMS (EI): Calcd for C\(_{13}\)H\(_9\)NaO\(_5\) [M+Na]: 273.0739. Found: 273.0748.

Ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-4-methoxyphenoxy)acrylate was obtained as a yellowish oil in 87% yield from ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-4-methoxyphenoxy)acrylate (1 mmol). \(^1{\text{H}}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.68 (d, \(J = 12.2\) Hz, 1H), 7.35 (d, \(J = 3.1\) Hz, 1H), 7.16 (dd, \(J = 9.0, 3.1\) Hz, 1H), 7.07 (d, \(J = 9.0\) Hz, 1H), 5.96 (q, \(J = 7.0\) Hz, 1H), 5.67 (d, \(J = 12.2\) Hz, 1H), 4.20 (q, \(J = 7.1\) Hz, 2H), 3.84 (s, 3H), 1.79 (d, \(J = 7.1\) Hz, 3H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^1{\text{C}}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 186.76, 166.49, 165.84, 159.26, 157.74, 130.71, 120.16, 111.12, 104.21, 103.66, 60.34, 55.93, 14.22. HRMS (EI): Calcd for C\(_{13}\)H\(_9\)NaO\(_5\) [M+Na]: 346.0903. Found: 346.0892.

Ethyl (E)-3-(2-formyl-4-methoxyphenoxy)acrylate (1i) was synthesized analogously to 1a. Ethyl (E)-3-(2-formyl-5-methoxyphenoxy)acrylate was obtained as a yellowish oil in 83% yield from 2-hydroxy-4-benzaldehyde (5 mmol). \(^1{\text{H}}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.95 (d, \(J = 8.9\) Hz, 1H), 7.79 (d, \(J = 12.2\) Hz, 1H), 6.80 (dd, \(J = 8.7, 1.5\) Hz, 1H), 6.58 (d, \(J = 2.1\) Hz, 1H), 5.63 (d, \(J = 12.2\) Hz, 1H), 4.19 (q, \(J = 7.1\) Hz, 2H), 3.88 (s, 3H), 1.28 (t, \(J = 7.1\) Hz, 3H). \(^1{\text{C}}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 189.13, 166.28, 157.21, 156.86, 148.36, 122.31, 119.63, 114.51, 104.69, 87.98, 60.50, 55.91, 15.57, 14.21. HRMS (EI): Calcd for C\(_{15}\)H\(_{13}\)NNaO\(_7\) [M+Na]: 348.1054. Found: 348.1056.
Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 187.41, 166.09, 165.74, 156.59, 155.65, 134.03, 118.09, 110.91, 105.95, 103.30, 87.96, 60.58, 56.05, 15.67, 14.21. HRMS (ESI): Calcd for C$_{15}$H$_{17}$NaO$_7$ [M+Na]$^+$: 346.0903. Found: 346.0912.

**Ethyl (E)-3-(2-methoxy-6-(2-nitropropanoyl)phenoxy)acrylate (1j)**

Substrate 1j was synthesized analogously to 1a. Ethyl (E)-3-(2-formyl-6-methoxybenzaldehyde s1j (5 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 10.21 (s, 1H), 7.77 (d, J = 12.3 Hz, 1H), 7.46 (s, 1H), 7.30 (dd, J = 8.2, 7.8 Hz, 1H), 7.22 (dd, J = 8.1, 1.2 Hz, 1H), 5.27 (d, J = 12.3 Hz, 1H), 4.15 (d, J = 7.1 Hz, 2H), 3.88 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 188.23, 166.76, 161.22, 151.29, 145.83, 128.92, 126.67, 119.63, 118.38, 101.02, 60.13, 56.30, 14.20. HRMS (ESI): Calcd for C$_{13}$H$_{14}$NaO$_5$ [M+Na]$^+$: 273.0739. Found: 273.0744.

Ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-6-methoxyphenoxy)acrylate s3j was obtained as a yellowish oil in 81% yield from ethyl (E)-3-(2-formyl-6-methoxyphenoxy)acrylate s2j (4 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.67 (d, J = 12.3 Hz, 1H), 7.25 (dd, J = 8.0, 5.2 Hz, 1H), 6.97 (dd, J = 8.0, 1.1 Hz, 1H), 5.56 (t, J = 3.4 Hz, 1H), 5.28 (d, J = 12.3 Hz, 1H), 4.74 (dd, J = 6.9, 3.0 Hz, 1H), 4.14 (q, J = 7.1 Hz, 1H), 3.84 (s, 3H), 3.31 (d, J = 4.3 Hz, 1H), 1.41 (d, J = 6.9 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 167.23, 160.73, 150.66, 139.75, 131.98, 126.67, 118.93, 112.63, 100.20, 85.02, 68.86, 60.17, 55.97, 14.14, 11.41. HRMS (ESI): Calcd for C$_{15}$H$_{19}$NaO$_7$ [M+Na]$^+$: 348.1054. Found: 348.1042.

Ethyl (E)-3-(2-methoxy-6-(2-nitropropanoyl)phenoxy)acrylate was obtained as a yellowish oil in 93% yield from ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-6-methoxyphenoxy)acrylate s3j (1 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.57 (d, J = 12.3 Hz, 1H), 7.29 (dd, J = 7.9, 1.6 Hz, 1H), 7.23 (dd, J = 8.0, 8.0 Hz, 1H), 7.16 (dd, J = 8.0, 1.5 Hz, 1H), 5.83 (q, J = 7.1 Hz, 1H), 5.36 (d, J = 12.3 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 3.31 (d, J = 4.3 Hz, 1H), 1.41 (d, J = 6.9 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 190.02, 166.58, 160.25, 151.26, 142.62, 128.82, 126.90, 121.83, 117.78, 101.71, 87.93, 60.29, 56.43, 15.52, 14.21. HRMS (ESI): Calcd for C$_{15}$H$_{17}$NaO$_7$ [M+Na]$^+$: 346.0897. Found: 346.0913.

**Ethyl (E)-3-(2-(2-nitrobutanoyl)phenoxy)acrylate (1k)**

Substrate 1k was synthesized analogously to 1a. Ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-6-methoxyphenoxy)acrylate s3k (1 mmol). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.75 (d, J = 12.2 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.37 (dd, J = 8.1, 7.5 Hz, 1H), 7.23 (dd, J = 7.8, 7.4 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 5.62 (d, J = 12.2 Hz, 1H), 5.43 (s, 1H), 4.65 (dt, J = 10.8, 3.5 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.19 (s, 1H), 2.20-2.12 (m, 1H), 1.80-1.74 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 166.86, 157.85, 152.24, 130.03, 128.66, 128.22, 125.36, 117.30, 103.51, 92.49, 69.42, 60.36, 20.67, 14.23, 10.45. HRMS (ESI): Calcd for C$_{15}$H$_{19}$NaO$_6$ [M+Na]$^+$: 332.1110. Found: 332.1099.

Ethyl (E)-3-(2-(2-nitrobutanoyl)phenoxy)acrylate 1k was obtained as a yellowish oil in
81% yield from ethyl (E)-3-(2-(1-hydroxy-2-nitrobutyl)phenoxy)acrylate s3k (1 mmol). 1H NMR (400 MHz, CDCl3) δ (ppm) 7.80 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 12.2 Hz, 1H), 7.59 (dd, J = 7.7, 7.6 Hz, 1H), 7.26 (dd, J = 7.7, 7.3 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 5.82 (dd, J = 9.2, 4.4 Hz, 1H), 5.73 (d, J = 12.2 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 2.23 (m, 1H), 2.12 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.3 Hz, 3H).

13C NMR (100 MHz, CDCl3) δ (ppm) 188.82, 166.02, 156.02, 154.27, 135.44, 131.56, 125.72, 125.32, 117.48, 105.49, 94.71, 60.43, 23.66, 14.09, 10.69. HRMS (ESI): Calcd for C15H17NNaO6 [M+Na]+: 330.0954. Found: 330.0964.

Methyl (E)-3-(2-(2-nitropropanoyl)phenoxy)acrylate s3l was obtained as a yellowish oil in 78% yield from methyl (E)-3-(2-formylphenoxy)acrylate s2l (4 mmol).

1H NMR (400 MHz, CDCl3) δ (ppm) 7.77 (d, J = 12.2 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.37 (dd, J = 7.6, 7.5 Hz, 1H), 7.26 (dd, J = 7.8, 7.5 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 5.67 (d, J = 3.0 Hz, 1H), 5.62 (d, J = 12.2 Hz, 1H), 4.78 (dd, J = 6.8, 2.9 Hz, 1H), 3.72 (s, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 167.43, 158.18, 151.81, 129.81, 128.95, 127.93, 125.39, 117.10, 102.83, 85.00, 68.81, 51.49, 11.52. HRMS (ESI): Calcd for C13H15NNaO6 [M+Na]+: 304.0792. Found: 304.0809.

Methyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3l was obtained as a yellow oil in 78% yield from methyl (E)-3-(2-formylphenoxy)acrylate s2l (4 mmol).

1H NMR (400 MHz, CDCl3) δ (ppm) 7.81 (d, J = 7.1 Hz, 1H), 7.70 (d, J = 12.1 Hz, 1H), 7.59 (dd, J = 7.0, 6.9 Hz, 1H), 7.26 (dd, J = 7.2, 7.0 Hz, 1H), 7.10 (d, J = 7.9 Hz, 1H), 5.95 (q, J = 6.6 Hz, 1H), 5.71 (d, J = 12.1 Hz, 1H), 3.68 (s, 3H), 1.73 (d, J = 6.4 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 189.32, 166.39, 156.14, 154.29, 135.50, 131.58, 125.41, 125.31, 117.42, 105.00, 88.05, 51.45, 15.34. HRMS (ESI): Calcd for C13H13NNaO6 [M+Na]+: 302.0635. Found: 302.0654.

Butyl (E)-3-(2-(2-nitropropanoyl)phenoxy)acrylate s2m was obtained as a yellow oil in 84% yield from 2-hydroxybenzaldehyde s1a (5 mmol) and n-butyl propiolate above.

1H NMR (400 MHz, CDCl3) δ (ppm) 7.81 (d, J = 7.1 Hz, 1H), 7.70 (d, J = 12.1 Hz, 1H), 7.59 (dd, J = 7.0, 6.9 Hz, 1H), 7.26 (dd, J = 7.2, 7.0 Hz, 1H), 7.10 (d, J = 7.9 Hz, 1H), 5.95 (q, J = 6.6 Hz, 1H), 5.71 (d, J = 12.1 Hz, 1H), 3.68 (s, 3H), 1.73 (d, J = 6.4 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 189.32, 166.39, 156.14, 154.29, 135.50, 131.58, 125.41, 125.31, 117.42, 105.00, 88.05, 51.45, 15.34. HRMS (ESI): Calcd for C13H13NNaO6 [M+Na]+: 302.0635. Found: 302.0654.
Butyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate was obtained as a yellowish oil in 74% yield from butyl (E)-3-(2-formylphenoxy)acrylate. 

Butyl (E)-3-(2-formylphenoxy)acrylate was synthesized analogously to 1n. A catalytic amount of p-TsOH (34 mg, 0.2 mmol, 0.05 equiv) was added to propiolic acid (420 mg, 6 mmol, 1.0 equiv) and phenol (5 mmol) and phenyl propiolate above. m.p. 58-60 °C.

Phenyl (E)-3-(2-formylphenoxy)acrylate was obtained as a yellowish oil in 81% yield from phenyl (E)-3-(2-formylphenoxy)acrylate. 

Phenyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate was obtained as a yellowish oil in 74% yield from butyl (E)-3-(2-formylphenoxy)acrylate.
Phenyl (E)-3-(2-(nitropropanoyl)phenoxy)acrylate 1n was obtained as a amber oil in 86% yield from phenyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3n (1 mmol).  

\[ \text{Phenyl (E)}-3-(2-(2-nitropropanoyl)phenoxy)acrylate} \]

\[ 102.67, 87.90, 70.22, 16.21. \]  


Phenyl (E)-3-(2-(nitropropanoyl)phenoxy)acrylate 1n was obtained as a amber oil in 86% yield from phenyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3n (1 mmol).  

\[ \text{Phenyl (E)}-3-(2-(2-nitropropanoyl)phenoxy)acrylate} \]

\[ 102.67, 87.90, 70.22, 16.21. \]  


**Cyclohexyl (E)-3-(2-(nitropropanoyl)phenoxy)acrylate (1o)**

Substrate 1o was synthesized analogously to 1a. A catalytic amount of p-TsOH (34 mg, 0.2 mmol, 0.05 equiv) was added to propiolic acid (420 mg, 6 mmol, 1.0 equiv) and cyclohexanol (660 mg, 6.6 mmol, 1.1 equiv) dissolved in toluene (5 mL). The solution was heated to reflux overnight using a Dean-Stark apparatus, concentrated in vacuo, and the crude product was purified by column chromatography to afford cyclohexyl propiolate which was used for next step directly. Cyclohexyl (E)-3-(2-formylphenoxy)acrylate s2o was obtained as a colorless oil in 82% yield from 2-hydroxybenzaldehyde s1a (5 mmol) and cyclohexyl propiolate above.

Cyclohexyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3o was obtained as a white solid in 80% yield from cyclohexyl (E)-3-(2-formylphenoxy)acrylate s2o (4 mmol), m.p. 109-112 °C.  


Cyclohexyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3o was obtained as a white solid in 80% yield from cyclohexyl (E)-3-(2-formylphenoxy)acrylate s2o (4 mmol), m.p. 109-112 °C.  


Cyclohexyl (E)-3-(2-(2-nitropropanoyl)phenoxy)acrylate 1o was obtained as a yellowish oil in 87% yield from cyclohexyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate s3o (1 mmol).  

\[ \text{Cyclohexyl (E)}-3-(2-(2-nitropropanoyl)phenoxy)acrylate} \]

\[ 102.67, 87.90, 70.22, 16.21. \]  

Adamantan-1-yl \((E)\)-3-(2-(2-nitropropanoyl)phenoxy)acrylate \((1p)\)

Substrate \(1p\) was synthesized analogously to \(1a\). A catalytic amount of p-TsOH (34 mg, 0.2 mmol) was added to propiolic acid (420 mg, 6 mmol) and 1-adamantanol (1.03 g, 6.6 mmol) dissolved in toluene (5 mL). The solution was heated to reflux overnight using a Dean-Stark apparatus, concentrated in vacuo, and the crude product was purified by column chromatography to afford 1-adamantyl propiolate which was used for next step directly.

Adamantan-1-yl \((E)\)-3-(2-formylphenoxy)acrylate \((s2p)\) was obtained as a white solid in 85% yield from 2-hydroxybenzaldehyde \((s1a)\) (5 mmol) and 1-adamantyl propiolate. m.p. 83-85 °C.

\[\begin{align*}
\text{\textsuperscript{1}H NMR} & (400 \text{ MHz, CDCl}_3) \delta (ppm) 10.35 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.72 (d, J = 12.4, 1H), 7.64-7.60 (m, 1H), 7.30-7.27 (m, 1H), 7.13 (d, J = 8.4 Hz, 1H), 5.52 (d, J = 12.0 Hz, 1H), 2.15 (s, 3H), 2.13 (s, 6H), 1.65 (s, 6H). \\
\text{\textsuperscript{13}C NMR} & (100 \text{ MHz, CDCl}_3) \delta (ppm) 188.17, 165.47, 157.64, 157.21, 135.94, 128.76, 126.48, 125.14, 118.30, 105.95, 80.78, 41.39 (3C), 36.12 (3C), 30.77 (3C). HRMS (ESI): Calcd for C\textsubscript{20}H\textsubscript{22}NO\textsubscript{4} [M+Na]+: 349.1410. Found: 349.1393.
\end{align*}\]

Adamantan-1-yl \((E)\)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate \((s3p)\) was obtained as a colorless oil in 78% yield from adamantan-1-yl \((E)\)-3-(2-formylphenoxy)acrylate \((s2p)\) (4 mmol).

\[\begin{align*}
\text{\textsuperscript{1}H NMR} & (400 \text{ MHz, CDCl}_3) \delta (ppm) 7.65 (d, J = 12.0 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.38-7.34 (m, 1H), 7.26-7.22 (m, 1H), 7.04 (d, J = 8.4 Hz, 1H), 5.67-5.65 (m, 1H), 5.52 (d, J = 12.0 Hz, 1H), 4.80-4.75 (m, 1H), 3.07 (d, J = 4.0 Hz, 1H), 2.16 (s, 3H), 2.13 (s, 6H), 1.66 (s, 6H), 1.44 (d, J = 7.2 Hz, 1H). \\
\text{\textsuperscript{13}C NMR} & (100 \text{ MHz, CDCl}_3) \delta (ppm) 165.86, 157.03, 151.96, 129.83, 128.74, 127.92, 125.20, 117.15, 105.28, 84.98, 80.83, 68.88, 41.42 (3C), 36.15 (3C), 30.81 (3C), 11.67. HRMS (ESI): Calcd for C\textsubscript{22}H\textsubscript{27}NNaO\textsubscript{6} [M+Na]+: 424.1731. Found: 424.1750.
\end{align*}\]

Adamantan-1-yl \((E)\)-3-(2-(2-nitropropanoyl)phenoxy)acrylate \((1p)\) was obtained as a yellowish oil in 81% yield from adamantan-1-yl \((E)\)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate \((s3p)\) (1 mmol).

\[\begin{align*}
\text{\textsuperscript{1}H NMR} & (400 \text{ MHz, CDCl}_3) \delta (ppm) 7.90 (dd, J = 8.0, 1.6 Hz, 1H), 7.63 (d, J = 12.0 Hz, 1H), 7.65-7.62 (m, 1H), 7.33-7.29 (m, 1H), 7.14 (d, J = 8.4 Hz, 1H), 5.99 (q, J = 7.2 Hz, 1H), 5.70 (d, J = 12.4 Hz, 1H), 2.18 (s, 3H), 2.16 (s, 6H), 1.81 (d, J = 7.2 Hz, 1H), 1.68 (s, 6H). \\
\text{\textsuperscript{13}C NMR} & (100 \text{ MHz, CDCl}_3) \delta (ppm) 189.52, 165.08, 155.09, 154.65, 135.59, 131.88, 125.58, 125.25, 117.39, 107.71, 88.23, 81.19, 41.43 (3C), 36.15 (3C), 30.83 (3C), 15.55. HRMS (ESI): Calcd for C\textsubscript{22}H\textsubscript{27}NNaO\textsubscript{6} [M+Na]+: 422.1580. Found: 422.1609.
\end{align*}\]
2.3 General Procedure and Spectral Data of Products

2.3.1 General Procedure

General procedure: A catalytic amount of tBuOK (11 mg, 0.1 mmol, 0.1 equiv.) was added to the corresponding α-nitro-acetophenone 1 (1 mmol, 1 equiv.) dissolved in THF (5 mL) at -40 °C. tBuOK was insoluble and a suspension was formed, however, as the reaction proceeded, the system turned into a clean solution with light yellow color. The reaction was monitored by TLC analysis and was completed in 4 h. To the crude reaction mixture was added 1N HCl (1 mL) and extracted with EtOAc. The organic phase was combined, dried over Na₂SO₄ and the solvent was evaporated. The diastereomeric ratios were determined by ¹H NMR spectroscopy of the crude reaction mixture. The crude product was purified by column chromatography. The yields are isolated materials for the mixtures of the diastereomers.

2.3.2 Spectral Data of Products

Ethyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2a)

Prepared according to the general procedure from 1a (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a colorless solid (95% yield, 20:1 d.r.). m.p. 55-57 °C. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.96 (dd, J = 7.9, 1.4 Hz, 1H), 7.61-7.57 (m, 1H), 7.15 (dd, J = 7.8, 7.3 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 5.61 (dd, J = 10.0, 2.4 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.86 (dd, J = 10.1, 10.1 Hz, 1H), 2.45 (dd, J = 16.0, 2.3 Hz, 1H), 1.75 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 184.88, 168.34, 159.62, 137.48, 128.42, 123.11, 118.18, 118.10, 92.11, 77.96, 61.48, 34.47, 14.30, 14.08. HRMS (ESI): Calcd for C₁₄H₁₅NNaO₆ [M+Na]⁺: 316.0792. Found: 316.0791.

Ethyl 2-((2R*,3R*)-3,6-dimethyl-3-nitro-4-oxochroman-2-yl)acetate (2b)

Prepared according to the general procedure from 1b (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (92% yield, 20:1 d.r.). m.p. 88-92 °C. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.72 (s, 1H), 7.39 (dd, J = 8.5, 1.7 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 5.56 (dd, J = 10.1, 2.4 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.84 (dd, J = 16.0, 10.1 Hz, 1H), 2.43 (dd, J = 16.0, 2.3 Hz, 1H), 2.33 (s, 3H), 1.73 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 185.07, 168.42, 157.75, 138.62, 135.84, 127.85, 117.85, 117.81, 92.22, 77.96, 61.45, 34.51, 20.40, 14.33, 14.09. HRMS (ESI): Calcd for C₁₅H₁₇NNaO₆ [M+Na]⁺: 330.0948. Found: 330.0941.

Ethyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxo-6-(trifluoromethyl)chroman-2-yl)acetate (2c)
Prepared according to the general procedure from 1e (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a colorless oil (92% yield, 10.4:1 d.r.). 1H NMR (400 MHz, CDCl3) δ (ppm) 8.25 (s, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.17 (d, J = 8.7 Hz, 1H), 5.68 (dd, J = 10.0, 2.2 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 2.87 (dd, J = 16.2, 10.1 Hz, 1H), 2.49 (dd, J = 16.2, 2.2 Hz, 1H), 1.77 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 183.67, 168.00, 161.40, 133.77 (q, J = 3.2 Hz), 126.25 (q, J = 3.9 Hz), 125.96 (q, J = 33.8 Hz), 123.26 (q, J = 270.5 Hz), 119.26, 118.26, 91.55, 78.54, 61.70, 34.30, 14.53, 14.10. 19F NMR (376 MHz, CDCl3) δ (ppm) 62.50. HRMS (ESI): Calcd for C13H14F3NNaO6 [M+Na]+: 384.0665. Found: 384.0684.

Ethyl 2-((2R*,3R*)-6-fluoro-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2d)

Prepared according to the general procedure from 1d (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (92% yield, 10.1:1 d.r.). m.p. 64-68 °C. 1H NMR (400 MHz, CDCl3) δ (ppm) 7.60 (dd, J = 7.8, 3.1 Hz, 1H), 7.34-7.29 (m, 1H), 7.03 (dd, J = 9.1, 4.1 Hz, 1H), 5.59 (dd, J = 10.0, 2.2 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.84 (dd, J = 16.1, 10.1 Hz, 1H), 2.45 (dd, J = 16.1, 2.2 Hz, 1H), 1.75 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 184.22, 168.23, 159.24, 156.35 (d, J = 92.8 Hz), 125.24 (d, J = 24.6 Hz), 120.02 (d, J = 7.5 Hz), 118.91 (d, J = 7.1 Hz), 113.34 (d, J = 23.9 Hz), 91.88, 78.38, 61.59, 34.36, 14.38, 14.11. 19F NMR (376 MHz, CDCl3) δ (ppm) 118.53. HRMS (ESI): Calcd for C13H14F3NNaO6 [M+Na]+: 334.0714. Found: 334.0714.

Ethyl 2-((2R*,3R*)-6-chloro-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2e)

Prepared according to the general procedure from 1e (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellowish solid (92% yield, 11.3:1 d.r.). m.p. 86-89 °C. 1H NMR (400 MHz, CDCl3) δ (ppm) 7.90 (d, J = 2.5 Hz, 1H), 7.52 (dd, J = 8.9, 2.6 Hz, 1H), 7.00 (d, J = 8.9 Hz, 1H), 5.60 (dd, J = 10.0, 2.4 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.84 (dd, J = 16.1, 10.1 Hz, 1H), 2.45 (dd, J = 16.1, 2.4 Hz, 1H), 1.74 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 183.84, 168.17, 157.99, 137.39, 128.85, 127.55, 119.87, 119.16, 91.73, 78.30, 61.61, 34.31, 14.42, 14.09. HRMS (ESI): Calcd for C14H15ClNNaO6 [M+Na]+: 350.0407. Found: 350.0425.

Ethyl 2-((2R*,3R*)-6-bromo-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2f)

Prepared according to the general procedure from 1f (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (93% yield, 11.4:1 d.r.). m.p. 99-102 °C. 1H NMR (400 MHz, CDCl3) δ (ppm) 8.03 (d, J = 2.4 Hz, 1H), 7.67 (dd, J = 8.9, 2.5 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 5.60 (dd, J = 10.0, 2.4 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 2.84 (dd, J = 16.1, 10.1 Hz, 1H), 2.45 (dd, J = 16.1, 2.4 Hz, 1H), 1.74 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 183.68, 168.13, 158.41, 140.14, 130.61, 120.15, 119.57, 115.86, 91.65, 78.23, 61.58, 34.27, 14.39, 14.06. HRMS (ESI): Calcd for C14H14BrNNaO6 [M+Na]+: 393.9897. Found: 393.9916.

Ethyl 2-((2R*,3R*)-5-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2g)

Prepared according to the general procedure from 1g (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (92% yield, 10.4:1 d.r.). 1H NMR (400 MHz, CDCl3) δ (ppm) 8.36 (s, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 5.68 (dd, J = 10.0, 2.2 Hz, 1H), 4.24 (q, J = 7.6 Hz, 2H), 2.84 (dd, J = 16.1, 2.2 Hz, 1H), 1.74 (s, 3H), 1.29 (t, J = 7.6 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ (ppm) 183.70, 168.20, 158.42, 140.13, 130.62, 120.16, 119.58, 115.87, 91.66, 78.23, 61.59, 34.26, 14.38, 14.06. HRMS (ESI): Calcd for C14H15O2NNaO6 [M+Na]+: 357.0457. Found: 357.0471.
mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellowish solid (94% yield, 13:1 d.r.). m.p. 115-119 °C. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.49-7.45 (m, 1H), 6.62-6.59 (m, 2H), 5.57 (dd, J = 10.1, 2.4 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 2.81 (dd, J = 16.0, 10.1 Hz, 1H), 2.43 (dd, J = 16.0, 2.4 Hz, 1H), 1.73 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).¹³C NMR (100 MHz, CDCl₃) δ (ppm) 182.87, 168.45, 161.90, 160.97, 137.60, 109.85, 108.47, 92.29, 92.63, 77.24, 61.43, 56.33, 34.52, 14.63, 14.10. HRMS (ESI): Calcd for C₁₅H₁₇NNaO₇ [M+Na]+: 346.0897. Found: 346.0893.

Ethyl 2-((2R*,3R*)-6-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2h)
Prepared according to the general procedure from 1h (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellowish oil (93% yield, 17.3:1 d.r.). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.32 (d, J = 3.1 Hz, 1H), 7.17 (dd, J = 9.1, 3.1 Hz, 1H), 6.95 (d, J = 9.1 Hz, 1H), 5.55 (dd, J = 10.1, 2.3 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 2.84 (dd, J = 16.0, 10.1 Hz, 1H), 2.42 (dd, J = 16.0, 2.3 Hz, 1H), 1.74 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).¹³C NMR (100 MHz, CDCl₃) δ (ppm) 185.02, 168.40, 155.21, 154.39, 126.88, 119.42, 118.14, 108.21, 92.28, 78.19, 61.45, 55.85, 34.47, 14.33, 14.08. HRMS (ESI): Calcd for C₁₅H₁₇NNaO₇ [M+Na]+: 346.0897. Found: 346.0918.

Ethyl 2-((2R*,3R*)-7-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2i)
Prepared according to the general procedure from 1i (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellow solid (95% yield, 13:1 d.r.). m.p. 97-103 °C. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.87 (d, J = 8.9 Hz, 1H), 6.69 (dd, J = 8.9, 2.1 Hz, 1H), 6.45 (d, J = 1.8 Hz, 1H), 5.60 (dd, J = 9.9, 1.8 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 2.84 (dd, J = 16.1, 10.1 Hz, 1H), 2.43 (dd, J = 16.0, 1.8 Hz, 1H), 1.73 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H).¹³C NMR (100 MHz, CDCl₃) δ (ppm) 183.52, 168.47, 167.26, 161.80, 130.17, 111.99, 111.69, 100.95, 92.00, 78.17, 61.48, 55.90, 34.58, 14.47, 14.12. HRMS (ESI): Calcd for C₁₅H₁₇NNaO₇ [M+Na]+: 346.0897. Found: 346.0918.

Ethyl 2-((2R*,3R*)-8-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2j)
Prepared according to the general procedure from 1j (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellow solid (94% yield, 44:1 d.r.). m.p. 110-113 °C. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.53 (dd, J = 7.9, 1.1 Hz, 1H), 7.13 (dd, J = 7.9, 0.8 Hz, 1H), 7.07 (dd, J = 8.0, 7.9 Hz, 1H), 5.62 (dd, J = 9.7, 2.6 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 2.94 (dd, J = 16.0, 9.7 Hz, 1H), 2.48 (dd, J = 16.0, 2.7 Hz, 1H), 1.76 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H).¹³C NMR (100 MHz, CDCl₃) δ (ppm) 185.00, 168.47, 167.26, 161.80, 130.17, 111.99, 111.69, 100.95, 92.00, 78.17, 61.48, 55.90, 34.58, 14.47, 14.12. HRMS (ESI): Calcd for C₁₅H₁₇NNaO₇ [M+Na]+: 346.0897. Found: 346.0907.

Ethyl 2-((2R*,3R*)-3-ethyl-3-nitro-4-oxochroman-2-yl)acetate (2k)
Prepared according to the general procedure from 1k (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellowish oil (92% yield, 14:1 d.r.). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.94 (dd, J = 7.9, 1.1 Hz, 1H),
7.57 (dd, J = 8.4, 7.1 Hz, 1H), 7.13 (dd, J = 7.7, 7.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 5.61 (dd, J = 10.3, 2.2 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.85 (dd, J = 16.0, 10.4 Hz, 1H), 2.45 (dd, J = 16.0, 2.2 Hz, 1H), 2.28-2.15 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 183.87, 168.44, 159.11, 137.32, 128.10, 122.97, 118.95, 118.10, 95.03, 78.52, 61.51, 34.16, 21.36, 14.09, 8.18. HRMS (ESI): Calcd for C₁₅H₁₃NNaO₆ [M+Na]+: 330.0948. Found: 330.0939.

**Methyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2l)**

Prepared according to the general procedure from 1l (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (92% yield, 20:1 d.r.). m.p. 91-94 °C. 1H NMR (400 MHz, CDCl₃) δ (ppm) 7.94 (d, J = 7.9 Hz, 1H), 7.58 (dd, J = 8.3, 7.4 Hz, 1H), 7.15 (dd, J = 7.6, 7.5 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 5.61 (dd, J = 10.0, 1.8 Hz, 1H), 3.77 (s, 3H), 2.88 (dd, J = 16.1, 10.1 Hz, 1H), 2.46 (dd, J = 16.0, 1.7 Hz, 1H), 1.75 (s, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 184.85, 168.87, 159.59, 137.50, 128.42, 123.14, 118.14, 118.13, 92.10, 77.86, 52.44, 34.26, 14.27. HRMS (ESI): Calcd for C₁₅H₁₃NNaO₆ [M+Na]+: 302.0641. Found: 302.0659.

**Butyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2m)**

Prepared according to the general procedure from 1m (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a yellowish oil (92% yield, 11.5:1 d.r.). m.p. 91-94 °C. 1H NMR (400 MHz, CDCl₃) δ (ppm) 7.95 (d, J = 7.9 Hz, 1H), 7.58 (dd, J = 8.2, 7.4 Hz, 1H), 7.15 (dd, J = 7.6, 7.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 5.60 (dd, J = 10.1, 1.8 Hz, 1H), 4.21-4.14 (m, 2H), 2.86 (dd, J = 16.0, 10.1 Hz, 1H), 2.45 (dd, J = 16.0, 1.8 Hz, 1H), 1.75 (s, 3H), 1.66-1.60 (m, 2H), 1.43-1.35 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 184.90, 168.42, 159.62, 137.47, 128.44, 123.12, 118.20, 118.08, 92.12, 78.00, 65.34, 34.50, 30.48, 19.00, 14.30, 13.60. HRMS (ESI): Calcd for C₁₈H₁₉NNaO₈ [M+Na]+: 344.1105. Found: 344.1100.

**Phenyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2n)**

Prepared according to the general procedure from 1n (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a white solid (92% yield, 18:1 d.r.). m.p. 91-94 °C. 1H NMR (400 MHz, CDCl₃) δ (ppm) 7.98 (d, J = 7.9 Hz, 1H), 7.61 (dd, J = 8.3, 7.3 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H), 7.39 (d, J = 7.7 Hz, 1H), 7.29-7.25 (m, 1H), 7.18 (dd, J = 7.9, 7.4 Hz, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 8.4 Hz, 1H), 5.73 (dd, J = 10.2, 2.3 Hz, 1H), 3.13 (dd, J = 16.1, 10.2 Hz, 1H), 2.74 (dd, J = 16.1, 2.3 Hz, 1H), 1.79 (s, 3H). 13C NMR (100 MHz, CDCl₃) δ (ppm) 184.73, 166.96, 159.56, 150.27, 137.62, 129.56 (2C), 128.56, 126.27, 123.31, 121.27 (2C), 118.22, 118.09, 92.07, 77.86, 34.66, 14.35. HRMS (ESI): Calcd for C₁₅H₁₃NNaO₆ [M+Na]+: 364.0792. Found: 364.0786.

**Cyclohexyl 2-((2R*,3R*)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2o)**

Prepared according to the general procedure from 1o (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a colorless gum (86% yield, 16:1 d.r.). 1H NMR (400 MHz, CDCl₃) δ (ppm) 7.96 (dd, J = 7.6, 1.2 Hz,
1H), 7.61-7.56 (m, 1H), 7.5 (dd, \(J = 7.8, 7.3\) Hz, 1H), 7.02 (d, \(J = 8.3\) Hz, 1H), 5.59 (dd, \(J = 10.0, 2.4\) Hz, 1H), 4.89-4.83 (m, 1H), 2.84 (dd, \(J = 16.0, 10.0\) Hz, 1H), 2.44 (dd, \(J = 16.0, 2.4\) Hz, 1H), 1.86-1.83 (m, 2H), 1.75 (s, 3H), 1.73-1.71 (m, 2H), 1.55-1.30 (m, 6H). \(1^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 184.95, 167.77, 159.66, 137.48, 128.46, 123.11, 118.25, 118.06, 92.14, 78.16, 74.03, 34.82, 31.48, 31.39, 25.22, 23.62, 23.59, 14.34. HRMS (ESI): Calcd for C\(_{18}\)H\(_{21}\)NNaO\(_6\) [M+Na]\(^{+}\): 370.1267. Found: 370.1269.

Adamantan-1-yl 2-((2\(R^*\),3\(R^*\))-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2p)

Prepared according to the general procedure from 1p (1 mmol) and catalyst tBuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 18 h to provide the title compound as a white solid (77% yield, 9:1 d.r.). \(1^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.95 (d, \(J = 7.9\) Hz, 1H), 7.59 (dd, \(J = 7.9, 7.7\) Hz, 1H), 7.15 (dd, \(J = 7.6, 7.5\) Hz, 1H), 7.03 (d, \(J = 8.4\) Hz, 1H), 5.54 (dd, \(J = 10.0, 2.0\) Hz, 1H), 2.75 (dd, \(J = 15.5, 10.0\) Hz, 1H), 2.40 (dd, \(J = 15.8, 2.1\) Hz, 1H), 2.18 (br s, 3H), 2.12 (br s, 6H), 1.74 (s, 3H), 1.67 (br s, 6H). \(1^{13}C\) NMR (126 MHz, CDCl\(_3\)) \(\delta\) (ppm) 185.02, 167.12, 159.73, 137.45, 128.44, 123.04, 118.31, 118.10, 92.16, 82.30, 78.38, 41.25 (3C), 36.06 (3C), 35.72, 30.83 (3C), 14.45. HRMS (ESI): Calcd for C\(_{22}\)H\(_{25}\)NNaO\(_6\) [M+Na]\(^{+}\): 422.1574. Found: 422.1579.
3. Derivatization of the product 2a and spectral data

A suspension of 2a (60 mg, 0.2 mmol, 1.0 equiv) in ethanol (5 mL) was heated at reflux. Iron powder (110 mg, 2.0 mmol) and an aqueous solution of NH$_4$Cl (100 mg dissolved in 0.8 mL of water) were added. The reaction was stirred at reflux to completeness. The warm mixture was filtered through a Celite patch and the remaining solids were washed several times with warm EtOH. The filtrates were combined and concentrated.$^1$ The residue was purified by column chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford ethyl 2-((2$^R$,3$^R$)-3-amino-3-methyl-4-oxochroman-2-yl)acetate 3 as a yellowish oil in 70% yield (37 mg).$^1$ H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.87 (d, $J$=7.8 Hz, 1H), 7.48 (dd, $J$= 8.0, 7.5 Hz, 1H), 7.04 (dd, $J$= 7.7, 7.3 Hz, 1H), 6.95 (d, $J$= 8.3 Hz, 1H), 4.64 (dd, $J$= 9.3, 2.5 Hz, 1H), 4.21 (q, $J$= 7.0 Hz, 2H), 3.02 (dd, $J$= 16.0, 3.0 Hz, 1H), 2.79 (dd, $J$= 16.0, 9.3 Hz, 1H), 1.69 (br s, 2H), 1.27 (t, $J$= 7.0 Hz, 3H), 1.19 (s, 3H).$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 197.64, 170.83, 160.49, 136.05, 127.81, 121.82, 118.63, 117.73, 80.68, 60.90, 57.46, 34.77, 18.59, 14.15. HRMS (ESI): Calcd for C$_{14}$H$_{18}$NO$_4$ [M+H]$^+$: 264.1230. Found: 264.1225.

Reference
4. Biology materials and methods

4.1 Cell lines and culture conditions
The cell lines used in this study were obtained from the American Type Culture Collection (ATCC). DU145 and PC3 cell lines were cultured in RPMI 1640 medium, which was supplemented with 10% FBS. Moreover, the human fibroblast cell line HAF was cultured in DMEM medium with 1% glutamine and 10% FBS. All cells were incubated at 37 °C and 5% CO₂ incubator.

4.2 Cell viability assay
The cell viability of cell lines in the presence of this series of compounds was determined by Sulforhodamine B (SRB) assay (Sigma Aldrich) which was described previously.\(^1\) In brief, cells (including DU145, PC3) were seeded into 96-well plates at the appropriate cell densities during the experiment. After 24 h, the cells were treated with various concentrations of the compound for 96 h. Control group were exposed to DMSO at a concentration equivalent to that of the compound-treated cells. After treatment, 25 µL of 50% TCA was added for cell fixation at 4 °C. At least 1 h later or more, the plates were washed by water for five times. The plates were allowed to dry using hair dryer followed by being dyed with 100 µL 0.4% SRB for 10 min. After dying, the plates were washed by 1% acetic acid to remove the dye and allowed to dry using hair dryer. 100 µL of 10 mM Tris-based solution was added to each well, and absorbance was measured using a 96-well plate reader at 515 nm. Three independent experiments were carried out in triplicate. The IC₅₀ was calculated using GraphPad Software.

Reference
5. X-Ray crystallography of 2f (CCDC1873098)

A single crystal of 2f was obtained from EtOAc solvent at room temperature. Diffraction data were collected on Bruker CCD-APEX X-ray diffractometer. Refinement was carried out on F^2.

Table S1 Crystal data and structure refinement for 2f (major diastereomer).

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<td>Z</td>
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</table>
Figure S1: Molecular structure of 2f (major diastereomer)
Figure S2: Unit cell molecular packing arrangement of 2f (major diastereomer)
6. NMR charts
S31
2b (contains 5% of the minor diastereomer)
2c (contains 6% of the minor diastereomer)
2d (contains 7% of the minor diastereomer)
2e (contains 6% of the minor diastereomer)
**2k** (contains 5% of the minor diastereomer)
2I (contains 4% of the minor diastereomer)
2n (contains 4% of the minor diastereomer)
2p (contains 7% of the minor diastereomer)