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 ($CDCl_3$: 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 ($CDCl_3$: 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 (λ = 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

Table S1

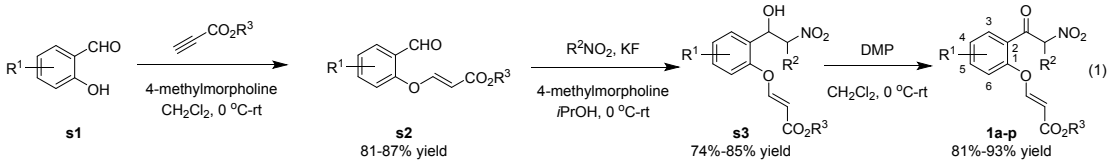
Entry	Catalyst	Amount of catalyst (mol%)	Solvent	Temp (°C)	Yield of **2a** (%)	d.r.
1	KO*t*Bu	10	THF	-40	>95	20:1
2	KO*t*Bu	5	THF	-40	>95	16.6:1
3	KO*t*Bu	2	THF	-40	>95	15.7:1
4	KO*t*Bu	20	THF	-40	92	18.3:1

2.2 Preparation and Spectral Data of Substrates

2.2.1 Preparation of Substrates

α-Nitro ketones were prepared by the following procedures.[1]

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



Reference

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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 N_2 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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{12}H_{12}NaO_4$ $[M+Na]^+$: 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 *i*PrOH (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 N_2 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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{14}H_{17}NNaO_6$ $[M+Na]^+$: 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 N_2 atmosphere. The mixture was allowed to rise to room temperature and stirred for another 18 h. The slurry was purified directly by column chromatography (CH_2Cl_2/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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 189.36, 166.07, 155.96, 154.44, 135.56, 131.78, 125.60,

125.40, 117.49, 105.66, 88.12, 60.51, 15.49, 14.18. HRMS (ESI): Calcd for $C_{14}H_{15}NNaO_6$ $[M+Na]^+$: 316.0792. Found: 316.0792.

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 86% yield from 2-hydroxy-5-methylbenzaldehyde **s1b** (5 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.30 (s, 1H), 7.80 (d, *J* = 12.2 Hz, 1H), 7.70 (d, *J* = 1.4 Hz, 1H), 7.43 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 5.56 (d, *J* = 12.2 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 188.27, 166.62, 158.61, 155.52, 136.62, 135.39, 128.93, 126.23, 118.46, 103.56, 60.29, 20.57, 14.24. HRMS (ESI): Calcd for $C_{13}H_{14}NaO_4$ $[M+Na]^+$: 257.0790. Found: 257.0804.

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, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.99, 158.46, 149.75, 135.28, 130.26, 128.49, 128.27, 117.34, 102.82, 85.09, 68.93, 60.30, 20.88, 14.21, 11.73. HRMS (ESI): Calcd for $C_{15}H_{19}NNaO_6$ $[M+Na]^+$: 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-(1-hydroxy-2-nitropropyl)-4-methyl-phenoxy)acrylate **s3b** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 $C_{15}H_{17}NNaO_6$ $[M+Na]^+$: 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 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 186.67, 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 $C_{13}H_{11}F_3NaO_4$ $[M+Na]^+$: 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 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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),

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). **^{13}C 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 $C_{15}H_{16}F_3NNaO_6$ $[M+Na]^+$: 386.0822. Found: 386.0827.

Ethyl (*E*)-3-(2-(2-nitropropanoyl)-4-(trifluoromethyl)phenoxy)acrylate **1c** was obtained as a yellowish oil in 87% yield from ethyl (E)-3-(2-(1-hydroxy-2-nitropropyl)-4-(trifluoro-methyl)-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 $C_{15}H_{14}F_3NNaO_6$ $[M+Na]^+$: 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 $C_{12}H_{11}FNaO_4$ $[M+Na]^+$: 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 (dd, *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), 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-nitro-propyl)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 (dd, *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:

334.0703.

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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 13C NMR (100 MHz, CDCl3) δ 195.93, 168.18, 159.29, 136.48, 127.63, 127.04, 119.57, 118.89, 80.47, 77.36, 77.04, 76.72, 72.34, 52.33, 41.66, 36.77, 36.32, 29.43, 18.19. HRMS (ESI): Calcd for $C_{12}H_{11}ClNaO_4$ $[M+Na]^+$: 277.0238. Found: 277.0239.

Ethyl (*E*)-3-(4-chloro-2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3e** was obtained as a yellowish oil in 83% yield from ethyl (*E*)-3-(4-chloro-2-formylphenoxy)acrylate **s2e** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 12.2 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.34 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 5.65 (s, 1H), 5.61 (d, *J* = 12.2 Hz, 1H), 4.74 (dd, *J* = 6.9, 2.6 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.17 (d, *J* = 4.2 Hz, 1H), 1.44 (d, *J* = 6.9 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.64, 157.35, 150.23, 131.04, 130.70, 129.77, 128.14, 118.50, 104.01, 84.60, 68.34, 60.53, 14.21, 11.47. HRMS (ESI): Calcd for $C_{14}H_{16}ClNNaO_6$ $[M+Na]^+$: 352.0558. Found: 352.0574.

Ethyl (*E*)-3-(4-chloro-2-(2-nitropropanoyl)phenoxy)acrylate **1e** was obtained as a yellow gum in 91% yield from ethyl (*E*)-3-(4-chloro-2-(1-hydroxy-2-nitropropyl)phen-oxy)acrylate **s3e** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{14}H_{14}ClNNaO_6$ $[M+Na]^+$: 350.0402. Found: 350.0399.

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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{12}H_{11}BrNaO_4$$[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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.83,

157.65, 151.74, 133.20, 131.44, 131.30, 119.30, 118.59, 103.93, 87.77, 69.36, 60.58, 15.99, 14.16. HRMS (ESI): Calcd for $C_{14}H_{16}BrNNaO_6$ $[M+Na]^+$: 396.0053. Found: 396.0069.

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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 187.95, 165.86, 155.29, 153.42, 138.16, 134.39, 127.05, 119.12, 118.40, 106.47, 87.81, 60.70, 15.51, 14.21. HRMS (ESI): Calcd for $C_{14}H_{14}BrNNaO_6$ $[M+Na]^+$: 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** was obtained as a yellowish oil in 84% yield from 2-hydroxy-6-methoxybenzaldehyde **s1g** (5 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 187.74, 166.70, 162.13, 158.63, 156.65, 135.77, 116.20, 111.16, 108.42, 102.93, 60.09, 56.23, 14.17. HRMS (ESI): Calcd for $C_{13}H_{14}NaO_5$ $[M+Na]^+$: 273.0739. Found: 273.0756.

Ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-3-methoxyphenoxy)acrylate **s3g** was obtained as a colorless oil in 79% yield from ethyl (*E*)-3-(2-formyl-3-methoxyphenoxy)acrylate **s2g** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.68, 158.44, 157.77, 154.21, 130.81, 116.34, 110.70, 107.94, 103.86, 87.05, 69.38, 60.29, 56.09, 16.31, 14.23. HRMS (ESI): Calcd for $C_{15}H_{19}NNaO_7$ $[M+Na]^+$: 348.1054. Found: 348.1026.

Ethyl (*E*)-3-(3-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate **1g** was obtained as a yellowish oil in 89% yield from ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-3-methoxyphenoxy)acrylate **s3g** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.67 (d, *J* = 12.2 Hz, 1H), 7.43 (dd, *J* = 8.5, 8.4 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 5.77 (q, *J* = 7.1 Hz, 1H), 5.59 (d, *J* = 12.2 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.73 (d, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0903. Found: 346.0916.

Ethyl (*E*)-3-(4-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate (1h)

Substrate **1h** was synthesized analogously to **1a**. Ethyl (*E*)-3-(2-formyl-4-methoxyphenoxy)acrylate **s2h** was obtained as a yellowish oil in 81% yield from 2-hydroxy-5-methoxy- benzaldehyde **s1h** (5 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 187.86, 166.61, 159.46, 157.04, 151.52, 127.23, 123.26, 120.58, 110.68, 103.08, 60.26, 55.85, 14.22. HRMS (ESI): Calcd for $C_{13}H_{14}NaO_5$ $[M+Na]^+$: 273.0739. Found: 273.0748.

Ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-4-methoxyphenoxy)acrylate **s3h** was obtained as a yellowish oil in 77% yield from ethyl (*E*)-3-(2-formyl-4-methoxyphenoxy)acrylate **s2h** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 167.08, 159.22, 157.13, 145.30, 130.42, 119.13, 114.69, 112.98, 102.23, 84.91, 68.78, 60.30, 55.69, 14.18, 11.47. HRMS (ESI): Calcd for $C_{15}H_{19}NNaO_7$ $[M+Na]^+$: 348.1054. Found: 348.1056.

Ethyl (*E*)-3-(4-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate **1h** was obtained as a yellowish oil in 87% yield from ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-4-methoxyphenoxy)acrylate **s3h** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 189.13, 166.28, 157.21, 156.86, 148.36, 126.28, 122.31, 119.63, 114.51, 104.69, 87.98, 60.50, 55.91, 15.57, 14.21. HRMS (ESI): Calcd for $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0903. Found: 346.0892.

Ethyl (*E*)-3-(5-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate (1i)

Substrate **1i** was synthesized analogously to **1a**. Ethyl (*E*)-3-(2-formyl-5-methoxyphenoxy)acrylate **s2i** was obtained as a yellowish oil in 83% yield from 2-hydroxy-4-methoxy- benzaldehyde **s1i** (5 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.18 (s, 1H), 7.86 (d, *J* = 8.8 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 (ESI): Calcd for $C_{13}H_{14}NaO_5$ $[M+Na]^+$: 273.0739. Found: 273.0751.

Ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-5-methoxyphenoxy)acrylate **s3i** was obtained as a yellowish oil in 74% yield from ethyl (*E*)-3-(2-formyl-5-methylphenoxy)acrylate **s2i** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 12.2 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 1H), 6.76 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.57 (d, *J* = 2.2 Hz, 1H), 5.61 (d, *J* = 12.2 Hz, 1H), 5.54 (t, *J* = 3.4 Hz, 1H), 4.73 (dd, *J* = 6.8, 3.3 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.01 (d, *J* = 4.3 Hz, 1H), 1.45 (d, *J* = 6.9 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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, 11.94. HRMS (ESI): Calcd for $C_{15}H_{19}NNaO_7$ $[M+Na]^+$: 348.1054. Found: 348.1053.

Ethyl (*E*)-3-(5-methoxy-2-(2-nitropropanoyl)phenoxy)acrylate **1i** was obtained as a yellowish oil in 92% yield from ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-5-methoxyphenoxy)acrylate **s3i** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.95 (d, *J* = 8.9 Hz, 1H), 7.71 (d, *J* = 12.2 Hz, 1H), 6.81 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.57 (d, *J* = 2.2 Hz, 1H), 5.96 (q, *J* = 7.0 Hz, 1H), 5.78 (d, *J* = 12.2 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 1.78 (d, *J* = 7.0

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 $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 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-methoxyphenoxy)acrylate **s2j** was obtained as a colorless oil in 82% yield from 2-hydroxy-3-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* = 1 2.3 Hz, 1H), 7.25 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.18 (d, *J* = 6.9 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, 2H), 3.84 (s, 3H), 3.31 (d, *J* = 4.3 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 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 $C_{15}H_{19}NNaO_7$ $[M+Na]^+$: 348.1054. Found: 348.1042.

Ethyl (*E*)-3-(2-methoxy-6-(2-nitropropanoyl)phenoxy)acrylate **1j** was obtained as a yellowish oil in 93% yield from ethyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)-6-methoxy-phenoxy)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), 1.70 (d, *J* = 7.1 Hz, 3H), 1.21 (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 $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 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-nitrobutyl)phenoxy)acrylate **s3k** was obtained as a yellowish oil in 78% yield from ethyl (*E*)-3-(2-formylphenoxy)acrylate **s2a** (4 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 $C_{15}H_{19}NNaO_6$ $[M+Na]^+$: 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). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{15}H_{17}NNaO_6$ $[M+Na]^+$: 330.0954. Found: 330.0964.

Methyl (*E*)-3-(2-(2-nitropropanoyl)phenoxy)acrylate (1l)

Substrate **1l** was synthesized analogously to **1a**. Methyl (*E*)-3-(2-formylphenoxy)acrylate **s2l** was obtained as a white solid in 85% yield from 2-hydroxybenzaldehyde **s1a** (5 mmol). m.p. 54-56 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.36 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 12.2 Hz, 1H), 7.63 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.31 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.64 (d, *J* = 12.2 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 188.03, 166.90, 158.07, 157.48, 135.97, 128.95, 126.46, 125.36, 118.15, 103.76, 51.49. HRMS (ESI): Calcd for $C_{11}H_{10}NaO_4$ $[M+Na]^+$: 229.0477. Found: 229.0489.

Methyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3l** was obtained as a yellowish oil in 78% yield from methyl (*E*)-3-(2-formylphenoxy)acrylate **s2l** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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), 3.36 (d, *J* = 4.2 Hz, 1H), 1.44 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{13}H_{15}NNaO_6$ $[M+Na]^+$: 304.0792. Found: 304.0809.

Methyl (*E*)-3-(2-(2-nitropropanoyl)phenoxy)acrylate **1l** was obtained as a yellowish oil in 85% yield from methyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3l** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{13}H_{13}NNaO_6$ $[M+Na]^+$: 302.0635. Found: 302.0654.

Butyl (*E*)-3-(2-(2-nitropropanoyl)phenoxy)acrylate (1m)

Substrate **1m** 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, 1.0 equiv) and 1-butanol (488 mg, 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 *n*-butyl propiolate which was not absolutely pure and thus used for next step directly. Butyl (*E*)-3-(2-formylphenoxy)acrylate **s2m** was obtained as a yellowish oil in 84% yield from 2-hydroxybenzaldehyde **s1a** (5 mmol) and *n*-butyl propiolate above. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.35 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 12.2 Hz, 1H), 7.63 (dd, *J* = 7.9, 7.7 Hz, 1H), 7.30 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.14 (d, *J* = 8.3 Hz,

1H), 5.62 (d, *J* = 12.2 Hz, 1H), 4.12 (t, *J* = 6.7 Hz, 2H), 1.63 (quintet, *J* =6.8 Hz, 2H), 1.38 (sextet, *J* = 7.3 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 188.04, 166.57, 157.88, 157.51, 135.96, 128.90, 126.48, 125.31, 118.22, 104.14, 64.24, 30.66, 19.09, 13.65. HRMS (ESI): Calcd for $C_{14}H_{16}NaO_4$ $[M+Na]^+$: 271.0946. Found: 271.0951.

Butyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3m** was obtained as a yellowish oil in 74% yield from butyl (*E*)-3-(2-formylphenoxy)acrylate **s2m** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.76 (d, *J* = 12.2 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.38 (dd, *J* = 7.9, 7.6 Hz, 1H), 7.26 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 5.67 (s, 1H), 5.62 (d, *J* = 12.2 Hz, 1H), 4.78 (dd, *J* = 6.9, 2.8 Hz, 1H), 4.14 (t, *J* = 6.7 Hz, 2H), 3.03 (s, 1H), 1.64 (quintet, *J* =6.8 Hz, 2H), 1.45 (d, *J* = 6.9 Hz, 3H), 1.40 (sextet, *J* =7.3 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.95, 157.78, 151.89, 129.90, 128.75, 127.98, 125.40, 117.17, 103.49, 85.00, 68.85, 64.30, 30.67, 19.12, 13.68, 11.69. HRMS (ESI): Calcd for $C_{16}H_{21}NNaO_6$ $[M+Na]^+$: 346.1261. Found: 346.1261.

Butyl (*E*)-3-(2-(2-nitropropanoyl)phenoxy)acrylate **1m** was obtained as a yellowish oil in 91% yield from butyl (E)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3m** (1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.87 (d, *J* = 7.9 Hz, 1H), 7.73 (d, *J* = 12.2 Hz, 1H), 7.63 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.31 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 5.98 (q, *J* = 7.0 Hz, 1H), 5.76 (d, *J* = 12.2 Hz, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 1.78 (d, *J* = 7.0 Hz, 3H), 1.64 (quintet, *J* =6.8 Hz, 2H), 1.39 (sextet, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 189.37, 166.26, 155.96, 154.43, 135.57, 131.78, 125.58, 125.39, 117.45, 105.64, 88.13, 64.46, 30.60, 19.07, 15.49, 13.64. HRMS (ESI): Calcd for $C_{16}H_{19}NNaO_6$ $[M+Na]^+$: 344.1105. Found: 344.1104.

Phenyl (*E*)-3-(2-(2-nitropropanoyl)phenoxy)acrylate (1n)

Substrate **1n** 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 phenol (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 phenyl propiolate which was used for next step directly. Phenyl (*E*)-3-(2-formylphenoxy)acrylate **s2n** was obtained as a white solid in 87% yield from 2-hydroxybenzaldehyde **s1a** (5 mmol) and phenyl propiolate above. m.p. 58-60 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.41 (s, 1H), 8.03 (d, *J* = 12.2 Hz, 1H), 7.96 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.71-7.65 (m, 1H), 7.42-7.33 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 2H), 5.83 (d, *J* = 12.2 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 187.95, 164.99, 159.61, 157.30, 150.44, 136.06, 129.41, 129.16, 126.58, 125.83, 125.69, 121.60, 118.43, 103.26. HRMS (ESI): Calcd for $C_{16}H_{12}NaO_4$ $[M+Na]^+$: 291.0628. Found: 291.0627.

Phenyl (*E*)-3-(2-(1-hydroxy-2-nitropropyl)phenoxy)acrylate **s3n** was obtained as a yellowish oil in 81% yield from phenyl (*E*)-3-(2-formylphenoxy)acrylate **s2n** (4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.94 (d, *J* = 12.2 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.45-7.37 (m, 3H), 7.29 (dd, *J* = 7.5, 7.4 Hz, 1H), 7.24 (dd, *J* = 8.0, 7.1 Hz, 1H), 7.13 (dd, *J* = 8.0, 2.9 Hz, 3H), 5.82 (d, *J* = 12.2 Hz, 1H), 5.40 (dd, *J* = 8.4, 5.3 Hz, 1H), 4.92-4.80 (m, 1H), 2.94 (d, *J* = 5.4 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 165.33, 159.76, 152.80, 150.43, 130.54, 129.41, 128.94, 128.52, 126.07, 125.83, 121.60, 117.90,

102.67, 87.90, 70.22, 16.21. HRMS (ESI): Calcd for $C_{18}H_{17}NNaO_6$ $[M+Na]^+$: 366.0948. Found: 366.0923.

Phenyl (*E*)-3-(2-(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). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 12.1 Hz, 1H), 7.90 (d, *J* = 6.4 Hz, 1H), 7.68-7.64 (m, 1H), 7.41-7,32 (m, 3H), 7.26-7.19 (m, 2H), 7.13 (d, *J* = 7.7 Hz, 2H), 6.01 (q, *J* = 7.1 Hz, 1H), 5.95 (d, *J* = 12.1 Hz, 1H), 1.87 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 189.25, 164.61, 157.65, 154.25, 150.33, 135.59, 131.76, 129.39 (2C), 125.87, 125.71, 125.69, 121.52 (2C), 117.66, 104.65, 88.06, 15.53. HRMS (ESI): Calcd for $C_{18}H_{15}NNaO_6$ $[M+Na]^+$: 364.0797. Found: 364.0802.

Cyclohexyl (*E*)-3-(2-(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. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.36 (s, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 12.4 Hz, 1H), 7.66-7.62 (m, 1H), 7.33-7.29 (m, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 4.85-4.81 (m, 1H), 1.89-1.86 (m, 2H), 1.75-1.72 (m, 2H), 1.57-1.33 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 188.12, 165.96, 157.76, 157.55, 135.98, 128.86, 126.50, 125.29, 118.32, 104.64, 72.67, 31.65 (2C), 25.32, 23.74 (2C). HRMS (ESI): Calcd for $C_{16}H_{18}NaO_4$ $[M+Na]^+$: 297.1097. Found: 297.1112.

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. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, *J* = 12.0 Hz, 1H), 7.64 (d, *J* = 7.6, 1H), 7.42-7.38 (m, 1H), 7.30-7.28 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 5.71-5.68 (m, 1H), 5.62 (d, *J* = 12.0 Hz, 1H), 4.87-4.83 (m, 1H), 4.82-4.78 (m, 1H), 3.19 (d, *J* = 4.0 Hz, 1H), 1.91-1.88 (m, 2H), 1.78-1.75 (m, 2H), 1.59-1.56 (m, 2H), 1.47 (d, *J* = 6.8 Hz, 1H), 1.43-1.38 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.36, 157.63, 151.85, 129.84, 128.80, 127.93, 125.32, 117.16, 103.90, 84.97, 72.70, 68.82, 31.63 (2C), 25.31, 23.73 (2C), 11.61. HRMS (ESI): Calcd for $C_{18}H_{23}NNaO_6$ $[M+Na]^+$: 372.1418. Found: 372.1419.

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). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.90 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 12.4, 1H), 7.66-7.63 (m, 1H), 7.34-7.30 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.99 (q, *J* = 7.2 Hz, 1H), 5.77 (d, *J* = 12.0 Hz, 1H), 4.87-4.83 (m, 1H), 1.91-1.87 (m, 2H), 1.81 (d, *J* = 7.2 Hz, 1H), 1.75-1.74 (m, 2H), 1.58-1.37 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 189.43, 165.60, 155.69, 154.53, 135.61, 131.88, 125.59, 125.39, 117.46, 106.30, 88.20, 72.97, 31.65 (2C), 25.32, 23.76 (2C), 15.56. HRMS (ESI): Calcd for $C_{18}H_{21}NNaO_6$ $[M+Na]^+$: 370.1261. Found: 370.1274.

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

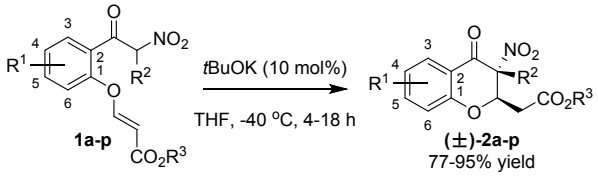
Substrate **1p** was synthesized analogously to **1a**. A catalytic amount of p-TsOH (34 mg, 0.2 mmol) was added to propiolic acid (420 mg, 6 mmol) and 1-adamantanol (1.03 g, 6.6 mmol) dissolved in toluene (5 mL). The solution was heated to reflux overnight using a Dean-Stark apparatus, concentrated 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 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 $C_{20}H_{22}NaO_4$ $[M+Na]^+$: 349.1410. Found: 349.1393.

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). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 $C_{22}H_{27}NNaO_6$ $[M+Na]^+$: 424.1731. Found: 424.1750.

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). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 $C_{22}H_{25}NNaO_6$ $[M+Na]^+$: 422.1580. Found: 422.1609.

2.3 General Procedure and Spectral Data of Products

2.3.1 General Procedure



General procedure: A catalytic amount of *t*BuOK (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. *t*BuOK 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 Na_2SO_4 and the solvent was evaporated. The diastereomeric ratios were determined by ^{1}H 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-((2*R,3*R**)-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2a)**

Prepared according to the general procedure from **1a** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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* = 16.0, 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{14}H_{15}NNaO_6$ $[M+Na]^+$: 316.0792. Found: 316.0791.

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

Prepared according to the general procedure from **1b** (1 mmol) and catalyst *t*BuOK (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, 12.5:1 d.r.). m.p. 88-92 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 185.07, 168.42, 157.75, 138.62, 132.84, 127.85, 117.88, 117.81, 92.22, 77.96, 61.45, 34.51, 20.40, 14.33, 14.09. HRMS (ESI): Calcd for $C_{15}H_{17}NNaO_6$ $[M+Na]^+$: 330.0948. Found: 330.0941.

Ethyl 2-((2*R,3*R**)-3-methyl-3-nitro-4-oxo-6-(trifluoromethyl)chroman-2-yl)acetate (2c)**

Prepared according to the general procedure from **1c** (1 mmol) and catalyst *t*BuOK (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.). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) 62.50. HRMS (ESI): Calcd for $C_{15}H_{14}F_3NNaO_6$ $[M+Na]^+$: 384.0665. Found: 384.0684.

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

Prepared according to the general procedure from **1d** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) 118.53. HRMS (ESI): Calcd for $C_{14}H_{14}FNNaO_6$ $[M+Na]^+$: 334.0697. Found: 334.0714.

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

Prepared according to the general procedure from **1e** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{14}H_{14}ClNNaO_6$ $[M+Na]^+$: 350.0407. Found: 350.0425.

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

Prepared according to the general procedure from **1f** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{14}H_{14}BrNNaO_6$ $[M+Na]^+$: 393.9897. Found: 393.9916.

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

Prepared according to the general procedure from **1g** (1 mmol) and catalyst *t*BuOK (11

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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 182.87, 168.45, 161.90, 160.97, 137.60, 109.85, 108.47, 105.29, 92.63, 77.24, 61.43, 56.33, 34.52, 14.63, 14.10. HRMS (ESI): Calcd for $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0897. Found: 346.0893.

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

Prepared according to the general procedure from **1h** (1 mmol) and catalyst *t*BuOK (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.). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0897. Found: 346.0918.

Ethyl 2-((2*R,3*R**)-7-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2i)**

Prepared according to the general procedure from **1i** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0897. Found: 346.0918.

Ethyl 2-((2*R,3*R**)-8-methoxy-3-methyl-3-nitro-4-oxochroman-2-yl)acetate (2j)**

Prepared according to the general procedure from **1j** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 185.00, 168.37, 149.90, 148.92, 122.80, 119.29, 119.04, 118.73, 92.12, 78.48, 61.51, 56.47, 34.51, 14.30, 14.04. HRMS (ESI): Calcd for $C_{15}H_{17}NNaO_7$ $[M+Na]^+$: 346.0897. Found: 346.0907.

Ethyl 2-((2*R,3*R**)-3-ethyl-3-nitro-4-oxochroman-2-yl)acetate (2k)**

Prepared according to the general procedure from **1k** (1 mmol) and catalyst *t*BuOK (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.). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{15}H_{17}NNaO_6$ $[M+Na]^+$: 330.0948. Found: 330.0939.

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

Prepared according to the general procedure from **1l** (1 mmol) and catalyst *t*BuOK (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. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{13}H_{13}NNaO_6$ $[M+Na]^+$: 302.0641. Found: 302.0659.

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

Prepared according to the general procedure from **1m** (1 mmol) and catalyst *t*BuOK (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.). **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{16}H_{19}NNaO_6$ $[M+Na]^+$: 344.1105. Found: 344.1100.

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

Prepared according to the general procedure from **1n** (1 mmol) and catalyst *t*BuOK (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. 98 -102 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) 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 $C_{18}H_{15}NNaO_6$ $[M+Na]^+$: 364.0792. Found: 364.0786.

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

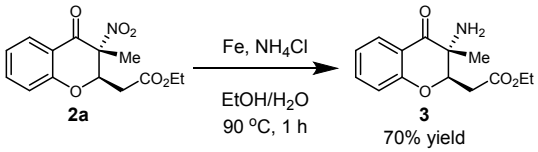
Prepared according to the general procedure from **1o** (1 mmol) and catalyst *t*BuOK (11 mg, 0.1 mmol) in THF (5 mL) at -40 °C for 4 h to provide the title compound as a colorless gum (86% yield, 16:1 d.r.). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.96 (dd, *J* = 7.6, 1.2 Hz,

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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (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 *t*BuOK (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.). m.p. 103-105 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ (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). **^{13}C NMR** (126 MHz, $CDCl_3$) δ (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_4Cl (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-((***2R*,3R****)-3-amino-3-methyl-4-oxochroman-2-yl)acetate **3** as a yellowish oil in 70% yield (37 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (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, $CDCl_3$) δ (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

1 C. Lu, B. Kirsch, C. K. Maurer, J. C. de Jong, A. Braunshausen, A. Steinbach and R. W. Hartmann, *Eur. J. Med. Chem.*, 2014, **79**, 173.

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 ^{o}C and 5% CO_2 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 ^{o}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 IC_{50} was calculated using GraphPad Software.

Reference

1 Y. D. He, S. H. Peng, J. H. Wang, H. Chen, X. N. Cong, A. Chen, M. C. Hu, M. Qin, H. G. Wu, S. M. Gao, L. G. Wang, X. Wang, Z. F. Yi and M. Y. Liu, *Nat. Commun.*, 2016, **7**, 13122.

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).

Identification code	mo_d8v17545_0m	
Empirical formula	C14 H14 Br N O6	
Formula weight	372.17	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P b c a	
Unit cell dimensions	a = 10.1785(3) Å	a= 90°
	b = 11.8901(4) Å	b= 90°
	c = 25.9949(8) Å	g = 90°
Volume	3145.99(17) $Å^3$	
Z	8	
Density (calculated)	1.572 Mg/m^3	
Absorption coefficient	2.641 mm^{-1}	
F(000)	1504	
Crystal size	0.190 x 0.150 x 0.120 mm^3	
Theta range for data collection	2.542 to 25.493°.	
Index ranges	-12<=h<=12, -14<=k<=14, -31<=l<=31	
Reflections collected	48093	
Independent reflections	2925 [R(int) = 0.0584]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.3875	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2925 / 70 / 230	
Goodness-of-fit on F^2	1.033	
Final R indices [I>2sigma(I)]	R1 = 0.0501, wR2 = 0.1251	
R indices (all data)	R1 = 0.0636, wR2 = 0.1371	
Extinction coefficient	0.0136(11)	
Largest diff. peak and hole	0.978 and -0.839 $e.Å^{-3}$	

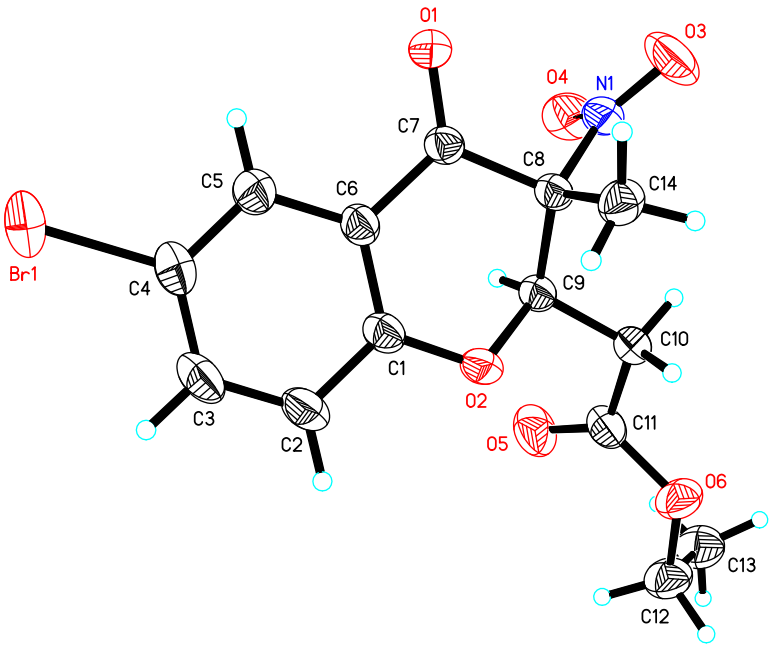


Figure S1: Molecular structure of 2f (major diastereomer)

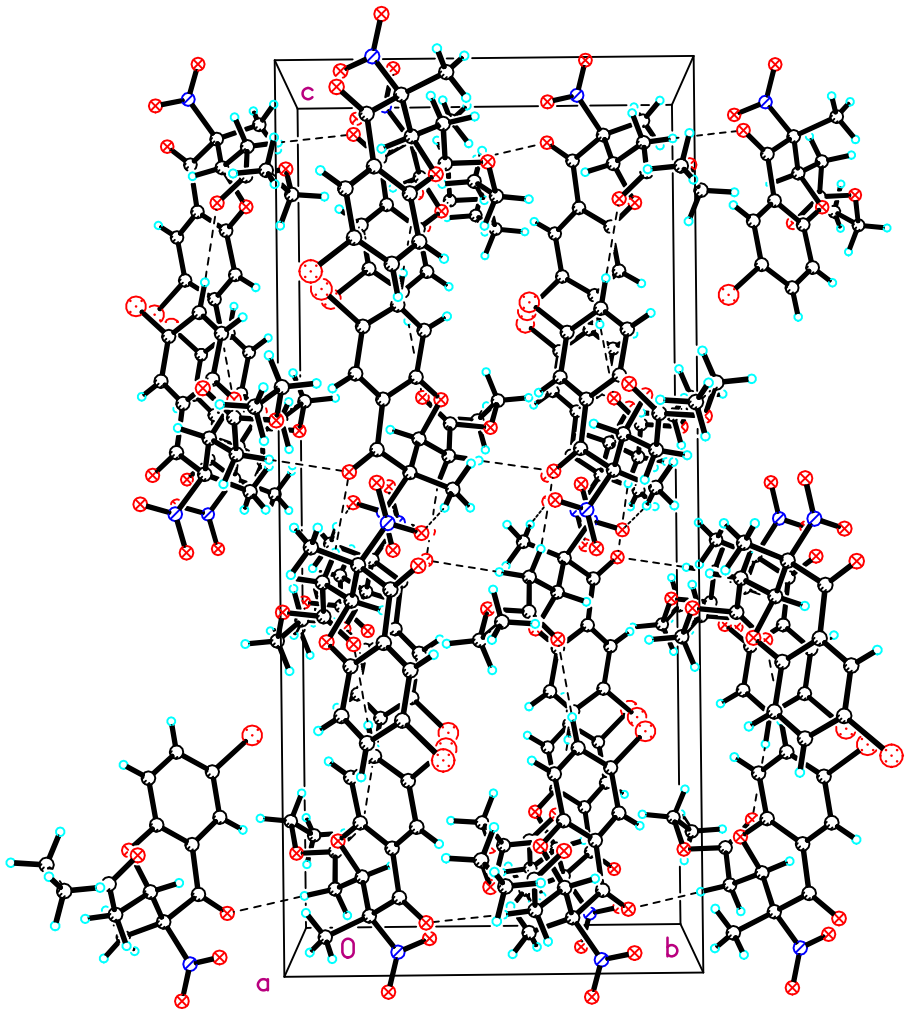
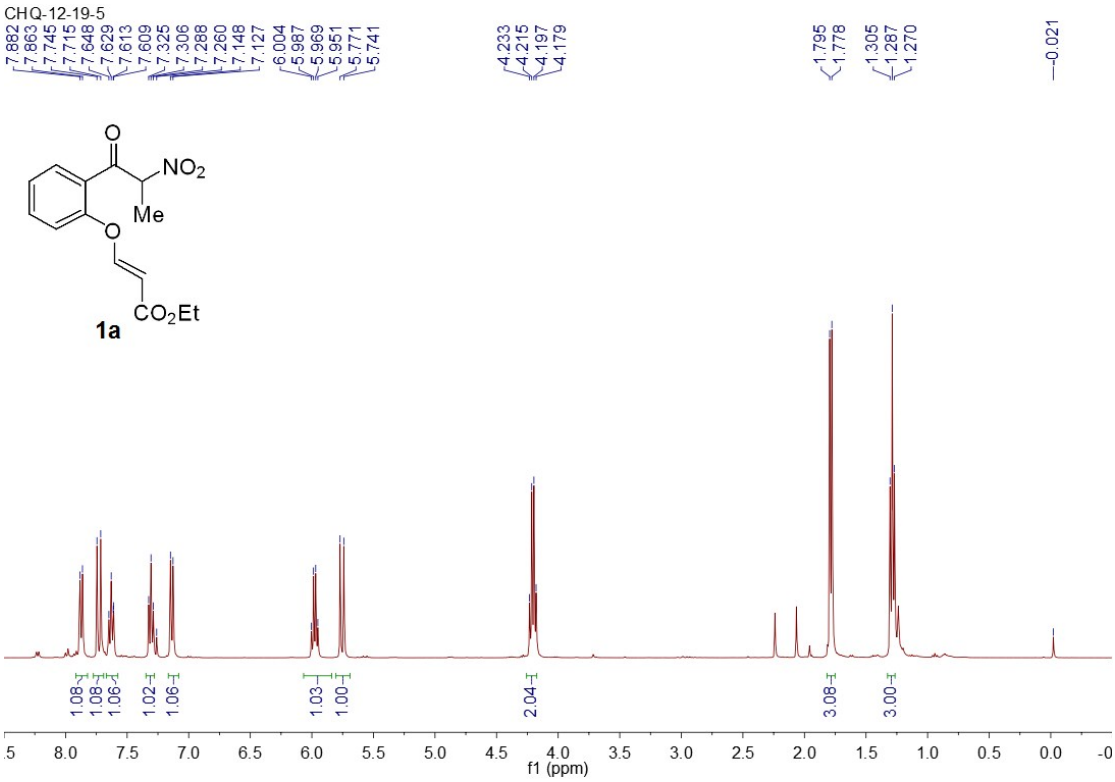


Figure S2: Unit cell molecular packing arrangement of 2f (major diastereomer)

6. NMR charts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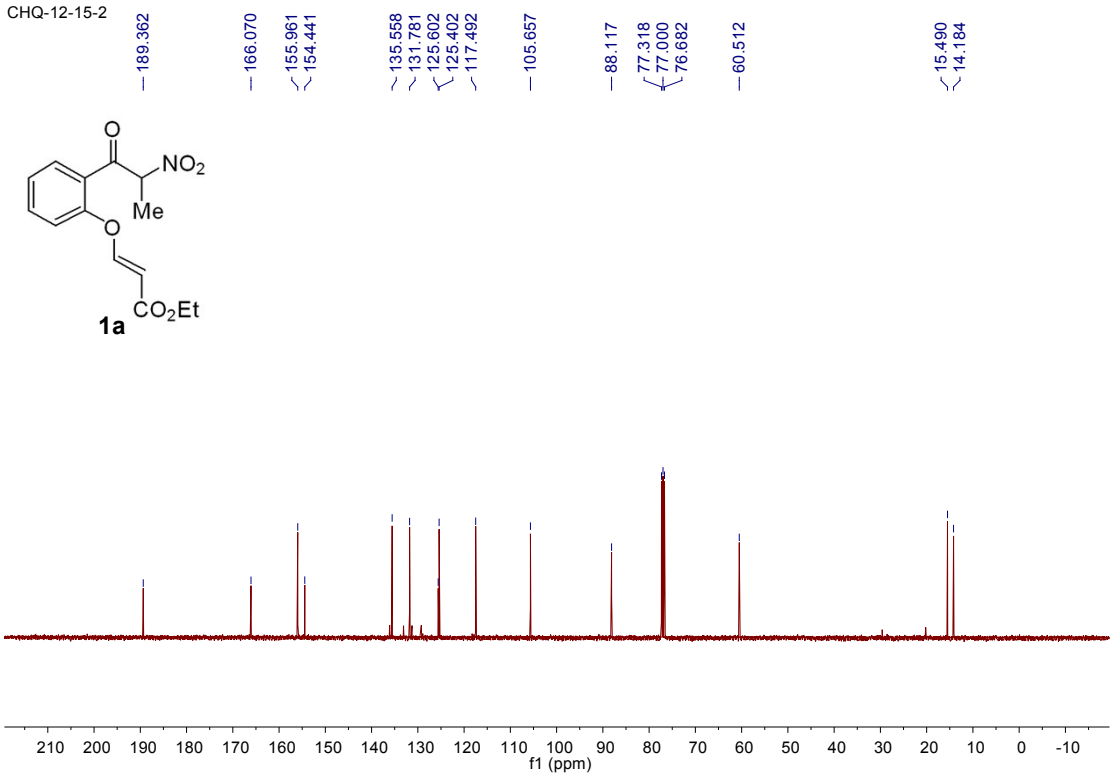
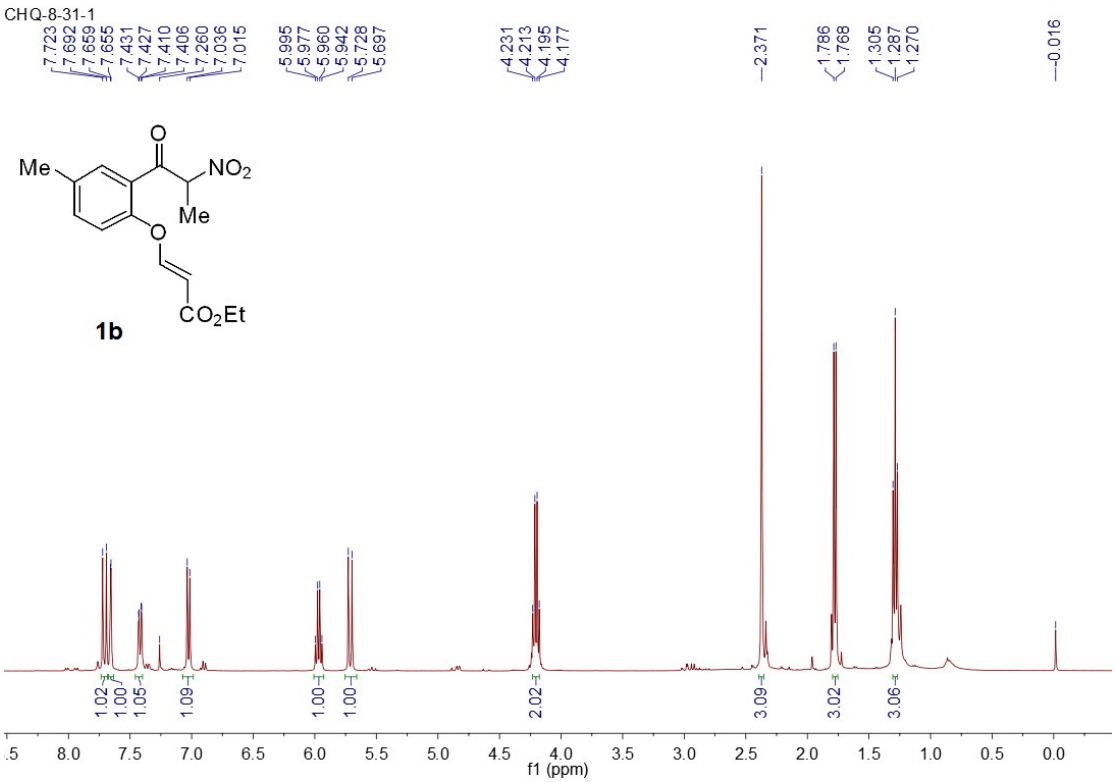
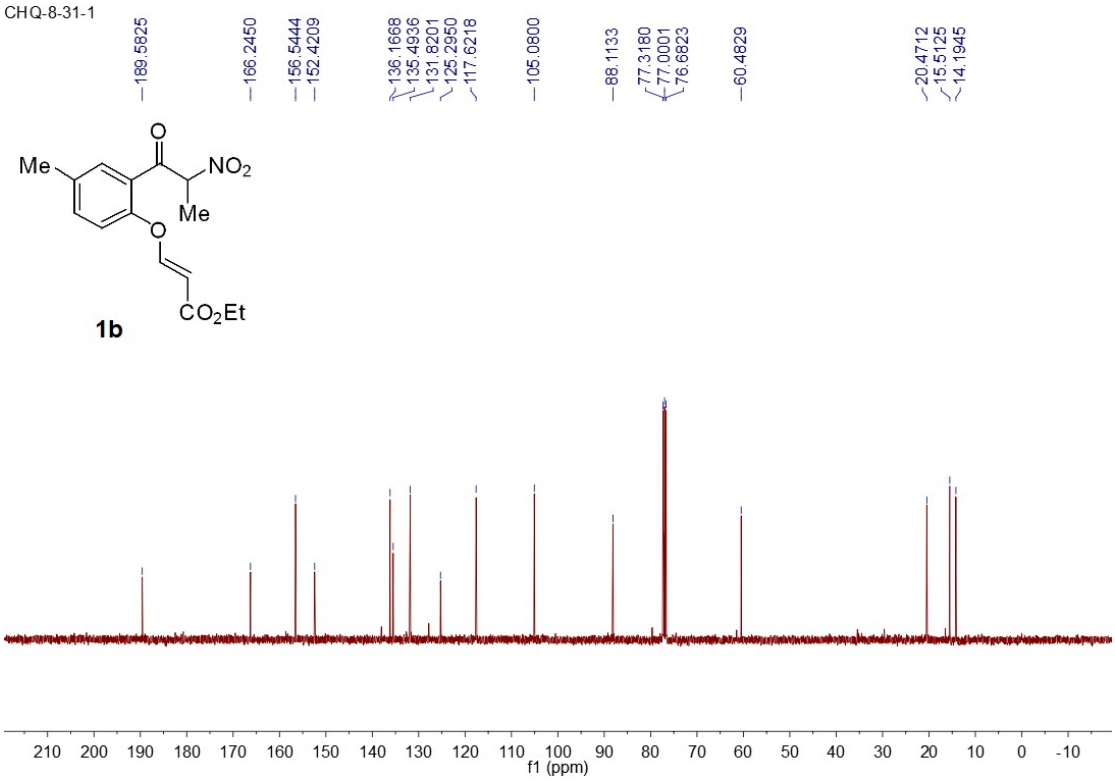
7.745
7.715
7.648
7.629
7.613
7.609
7.325
7.306
7.288
7.260
7.148
7.127
6.004
5.987
5.969
5.951
5.771
5.741
4.233
4.215
4.197
4.179
1.795
1.778
1.305
1.287
1.270
0.021
NO2
Me
O
CO2Et
1a
1.08
1.08
1.06
1.02
1.06
1.03
1.00
2.04
3.08
3.00
f1 (ppm)


CHQ-12-15-2
189.362
166.070
155.961
154.441
135.558
131.781
125.602
125.402
117.492
105.657
88.117
77.318
77.000
76.682
60.512
15.490
14.184
NO2
Me
O
CO2Et
1a
f1 (ppm)


CHQ-8-31-1
7.723
7.692
7.659
7.655
7.431
7.427
7.410
7.406
7.260
7.036
7.015
5.995
5.977
5.960
5.942
5.728
5.697
4.231
4.213
4.195
4.177
2.371
1.786
1.768
1.305
1.287
1.270
0.016
Me
NO2
Me
O
CO2Et
1b
1.02
1.00
1.05
1.09
1.00
1.00
2.02
3.09
3.02
3.06
f1 (ppm)


CHQ-8-31-1
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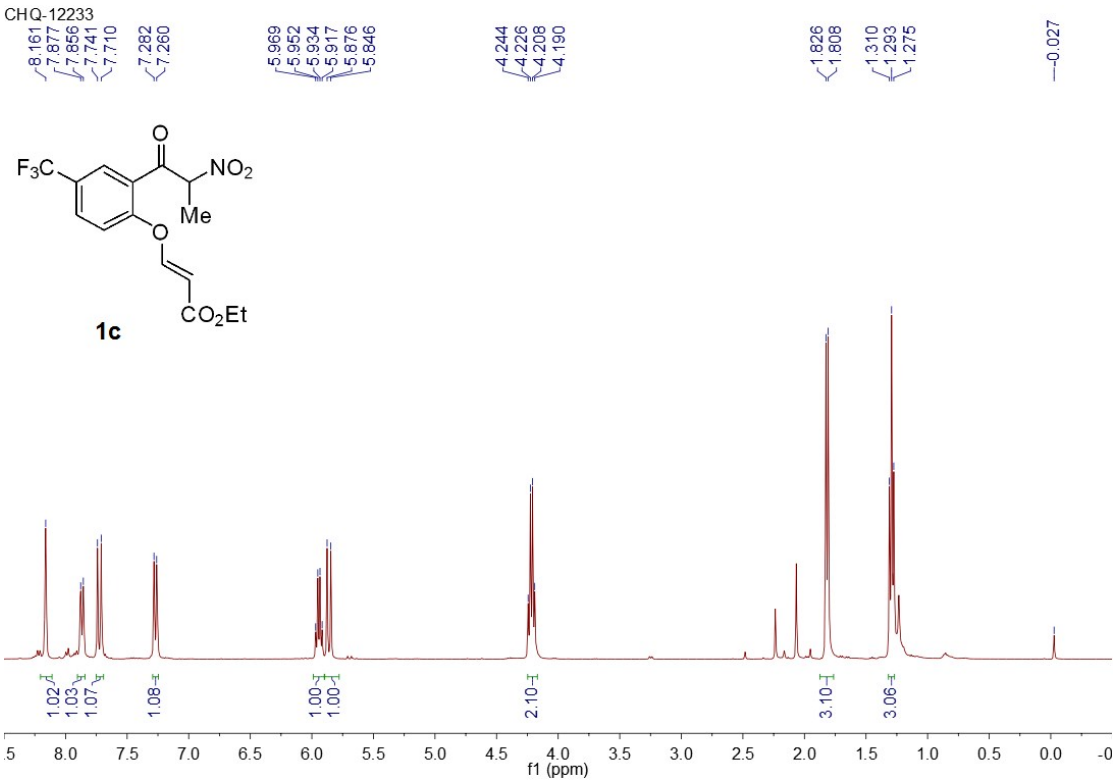
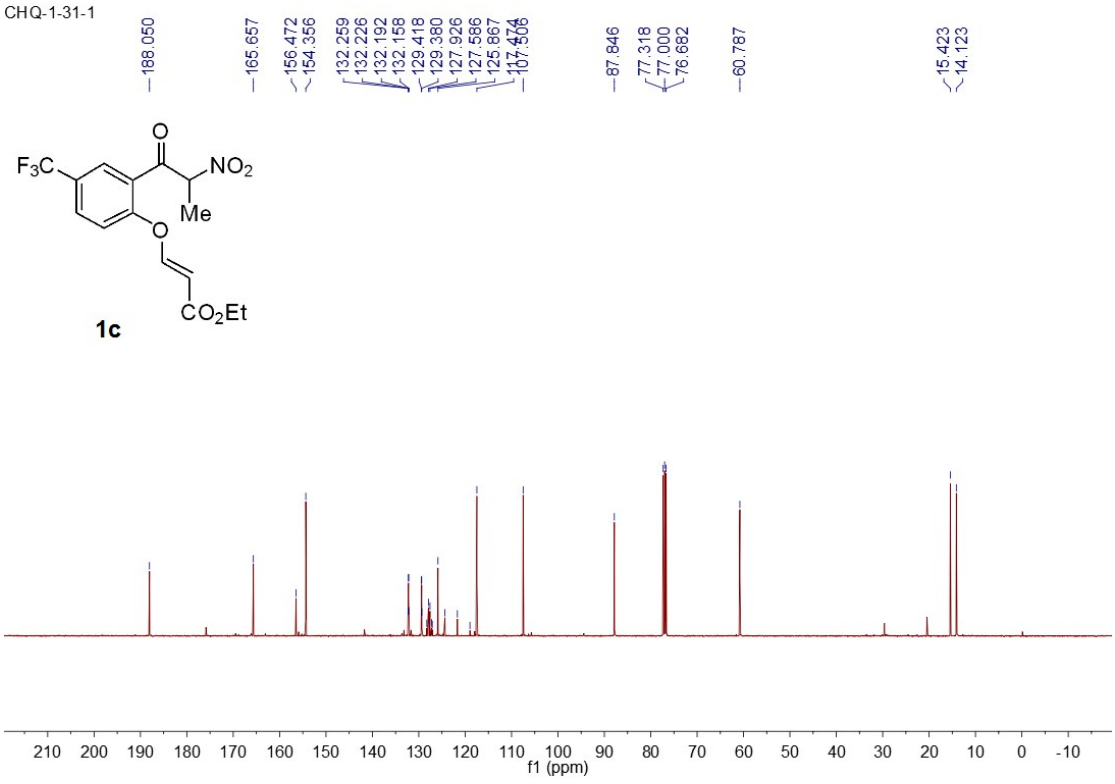
152.4209
136.1668
135.4936
131.8201
125.2950
117.6218
105.0800
88.1133
77.3180
77.0001
76.6823
60.4829
20.4712
15.5125
14.1945
Me
NO2
Me
O
CO2Et
1b
f1 (ppm)

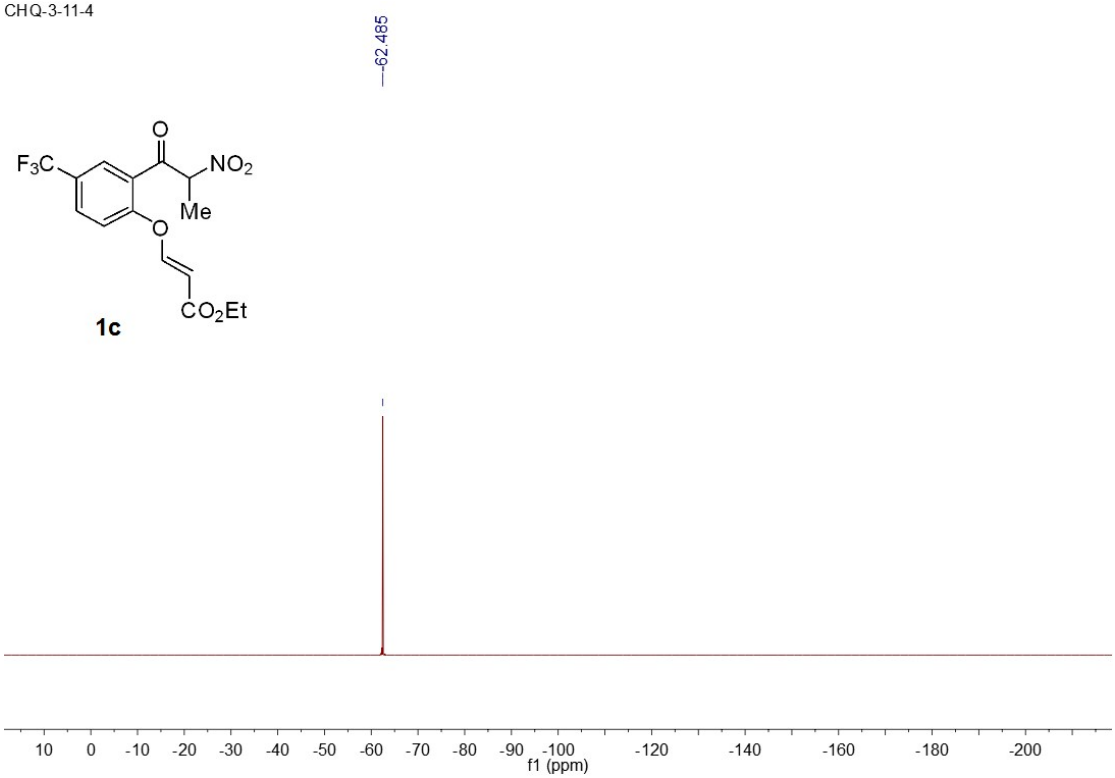
CHQ-12233

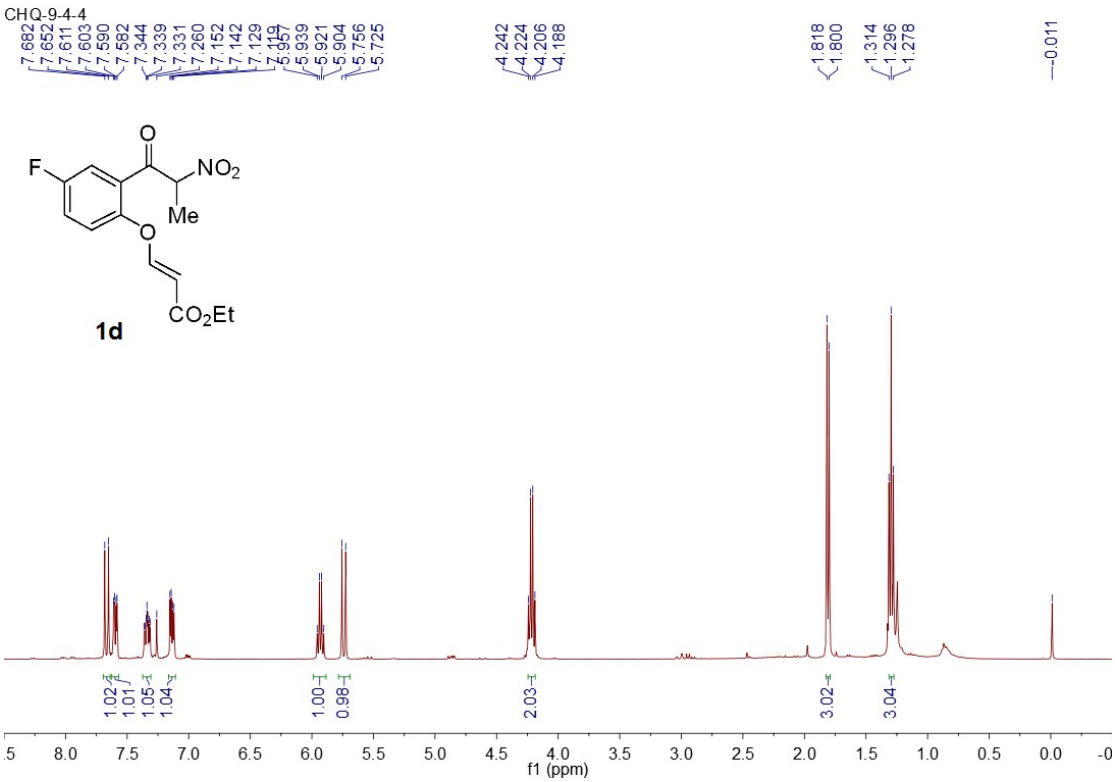


CHQ-1-31-1



CHQ-3-11-4


-62.485
F3C
O
NO2
Me
O
CO2Et
1c
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)


CHQ-9-4-4
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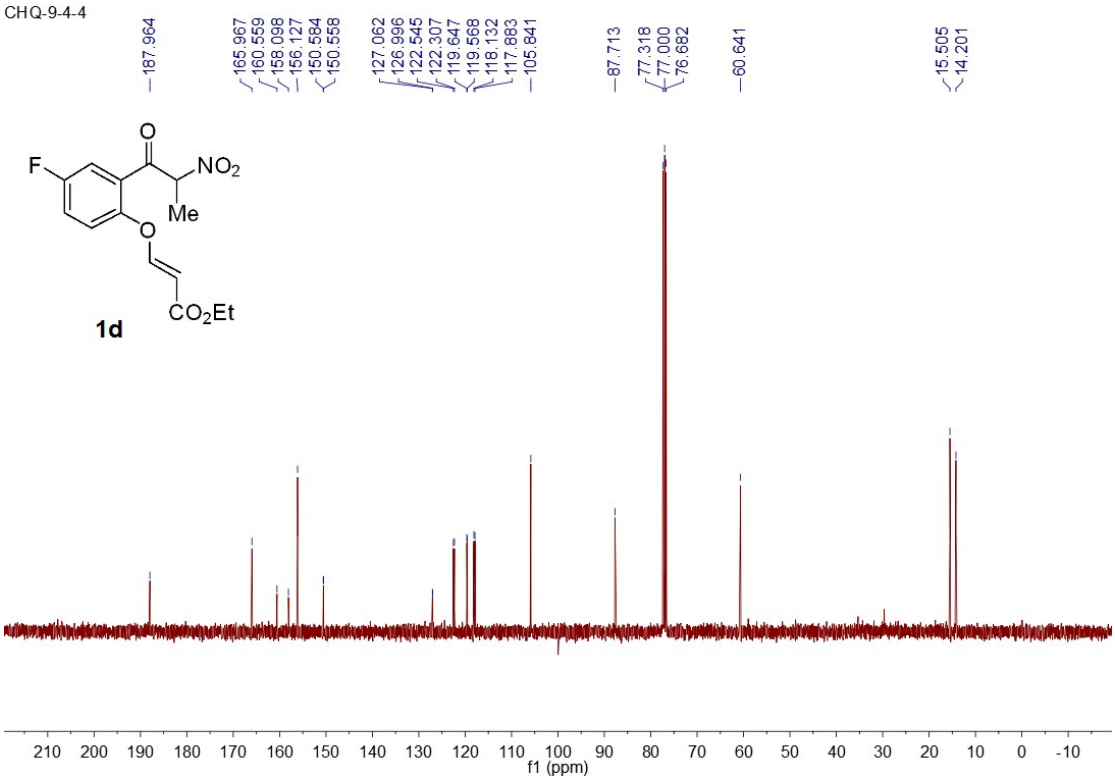
7.652
7.611
7.603
7.590
7.582
7.344
7.339
7.331
7.260
7.152
7.142
7.129
7.119
5.957
5.939
5.921
5.904
5.756
5.725
4.242
4.224
4.206
4.188
1.818
1.800
1.314
1.296
1.278
0.011
F
O
NO2
Me
O
CO2Et
1d
1.02
1.01
1.05
1.04
1.00
0.98
2.03
3.02
3.04
f1 (ppm)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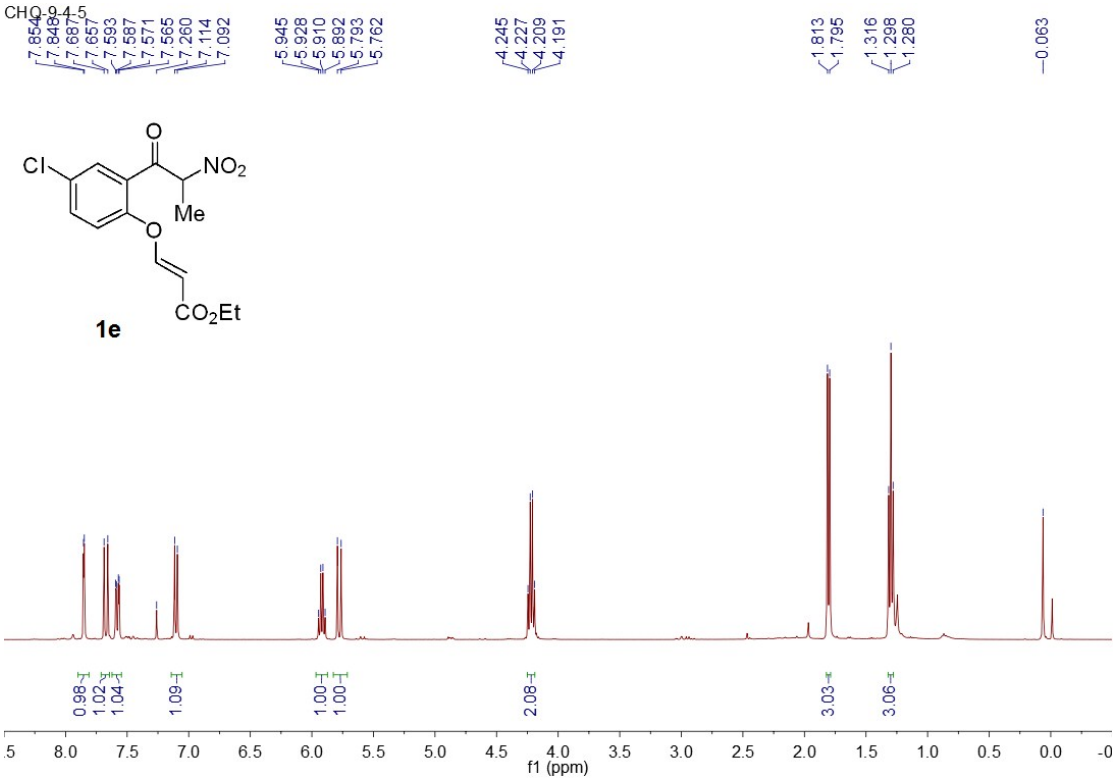
165.967
160.559
158.098
156.127
150.584
150.558
127.062
126.996
122.545
122.307
119.647
119.568
118.132
117.883
105.841
87.713
77.318
77.000
76.682
60.641
15.505
14.201
F
O
NO2
Me
O
CO2Et
1d
f1 (ppm)


CHQ-9-4-5
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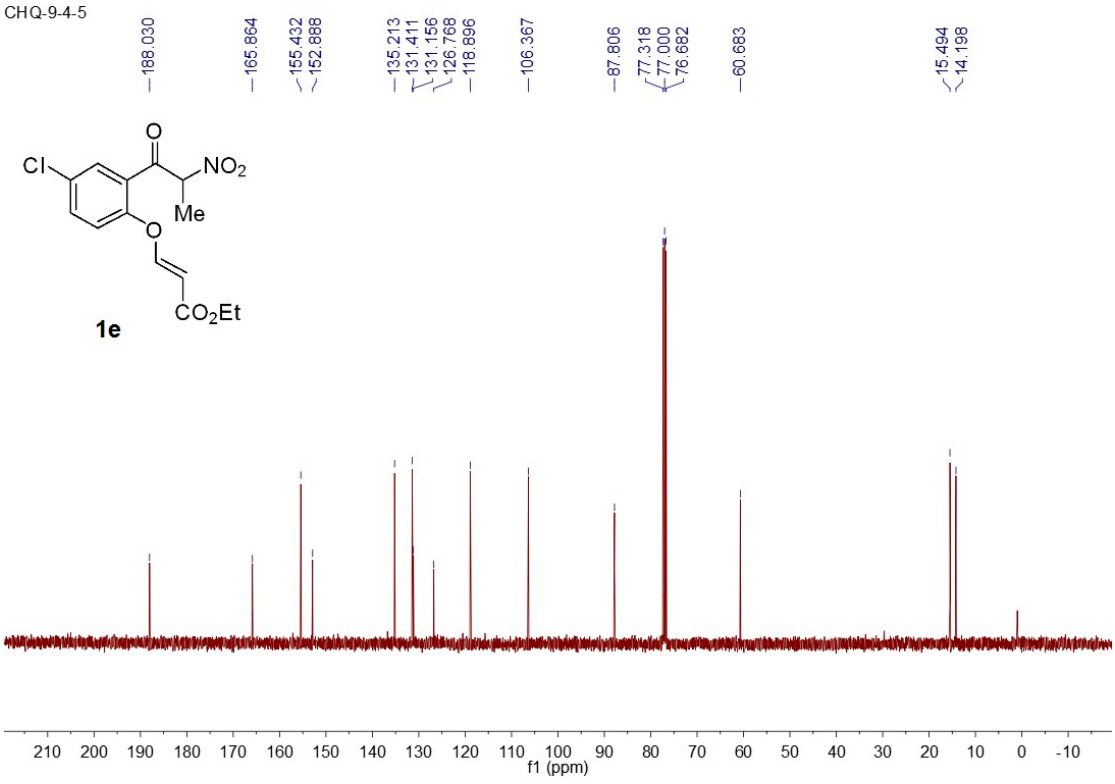
7.848
7.687
7.657
7.593
7.587
7.571
7.565
7.260
7.114
7.092
5.945
5.928
5.910
5.892
5.793
5.762
4.245
4.227
4.209
4.191
1.813
1.795
1.316
1.298
1.280
0.063
Cl
O
NO2
Me
O
CO2Et
1e
0.98
1.02
1.04
1.09
1.00
1.00
2.08
3.03
3.06
f1 (ppm)


CHQ-9-4-5
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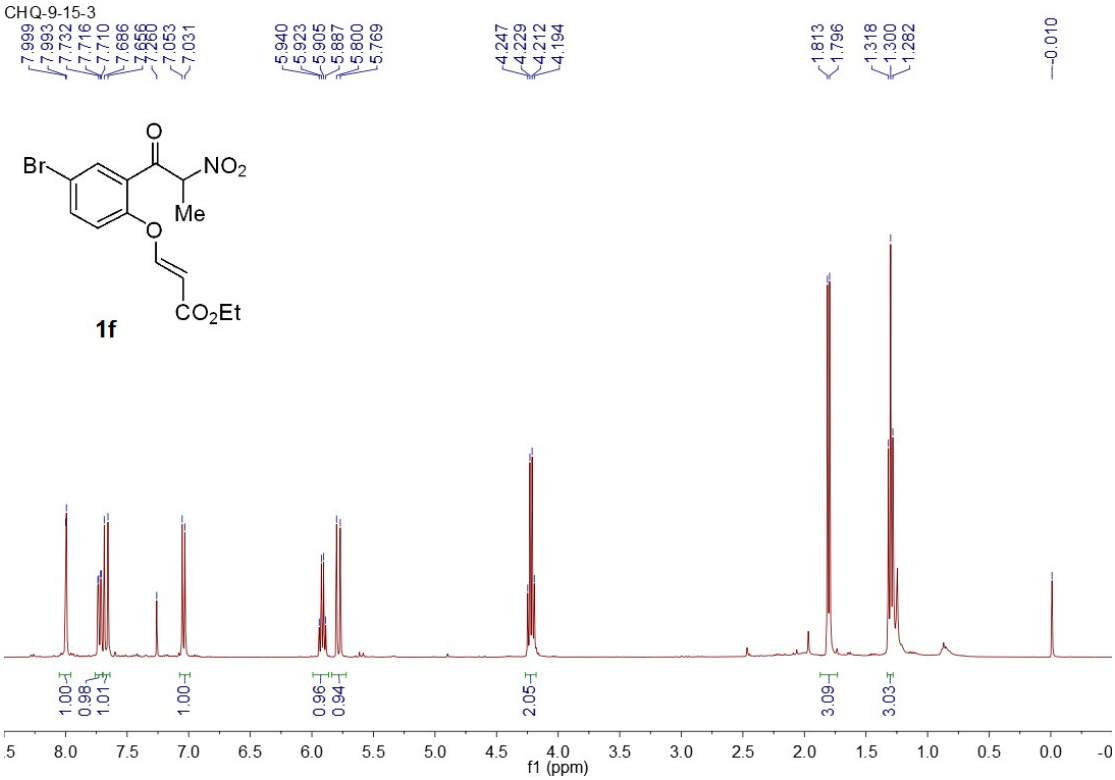
165.864
155.432
152.888
135.213
131.411
131.156
126.768
118.896
106.367
87.806
77.318
77.000
76.682
60.683
15.494
14.198
Cl
O
NO2
Me
O
CO2Et
1e
f1 (ppm)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7.993
7.732
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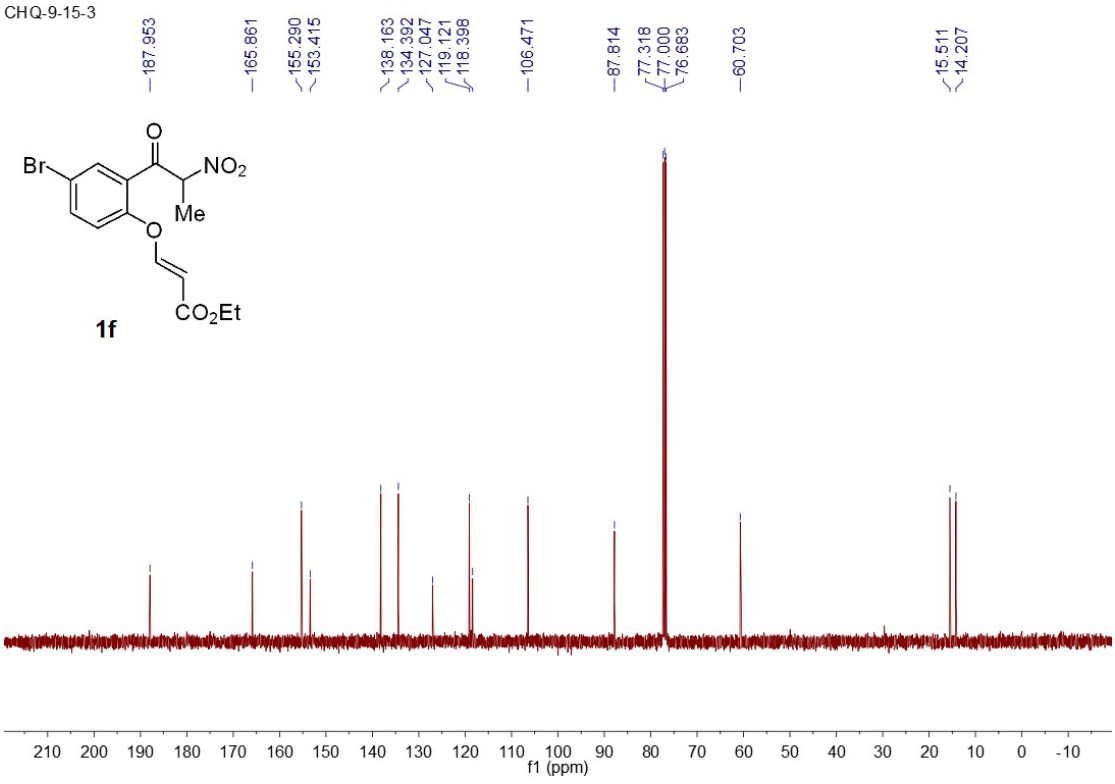
7.710
7.686
7.656
7.053
7.031
5.940
5.923
5.905
5.887
5.800
5.769
4.247
4.229
4.212
4.194
1.813
1.796
1.318
1.300
1.282
0.010
Br
O
NO2
Me
O
CO2Et
1f
1.00
0.98
1.01
1.00
0.96
0.94
2.05
3.09
3.03
f1 (ppm)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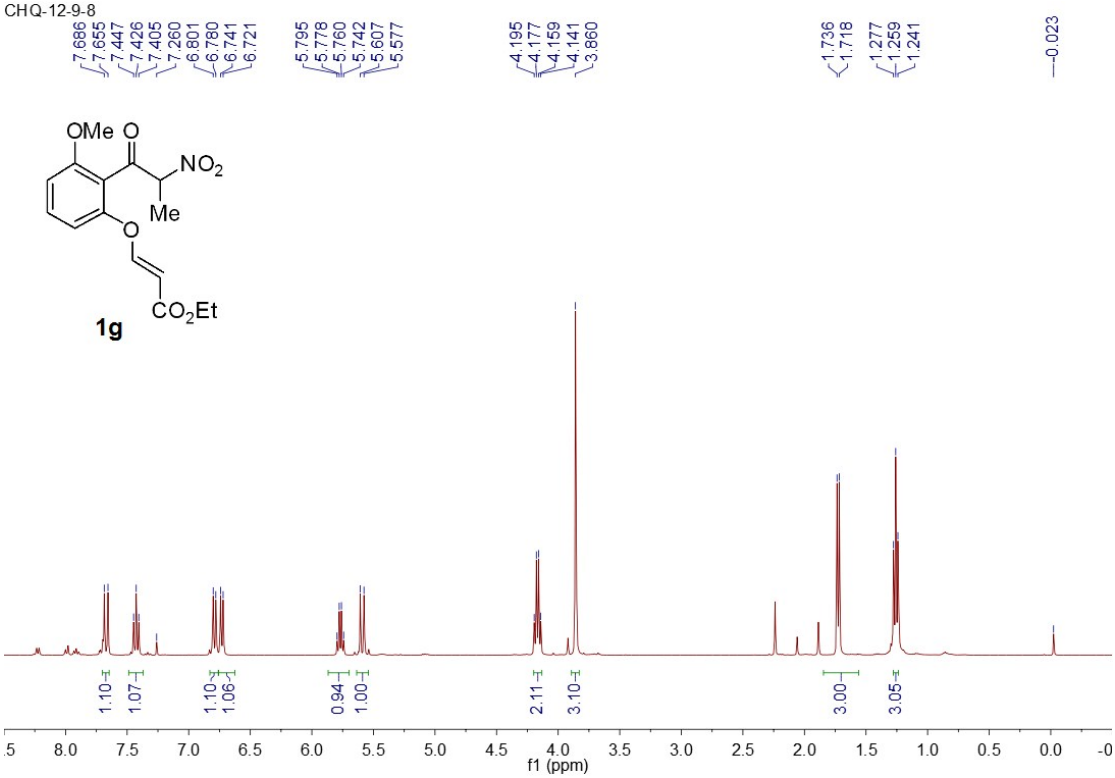
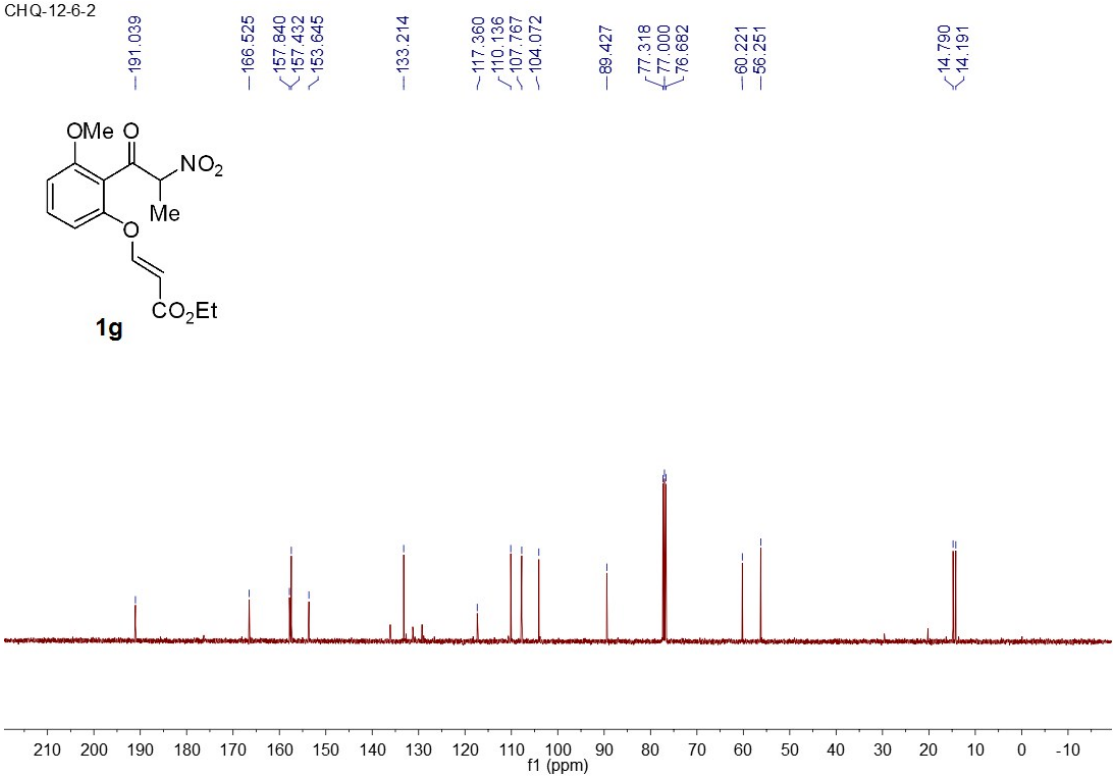
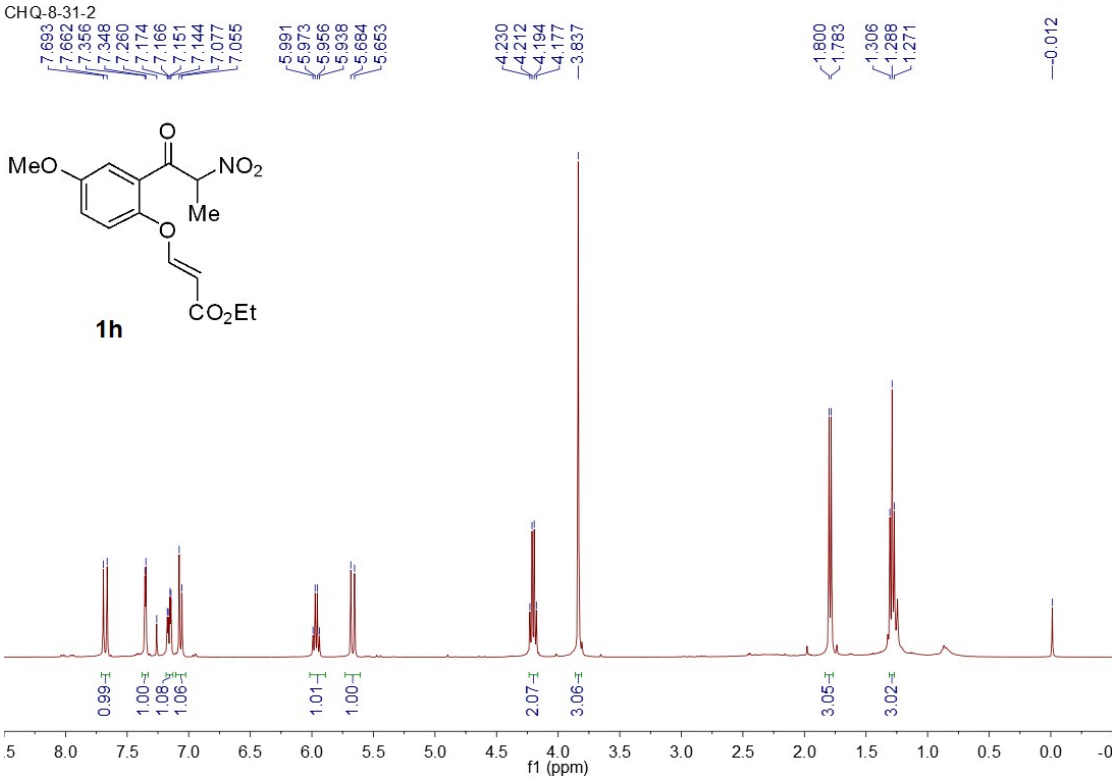
155.290
153.415
138.163
134.392
127.047
119.121
118.398
106.471
87.814
77.318
77.000
76.683
60.703
15.511
14.207
Br
O
NO2
Me
O
CO2Et
1f
f1 (ppm)

CHQ-12-9-8



CHQ-12-6-2

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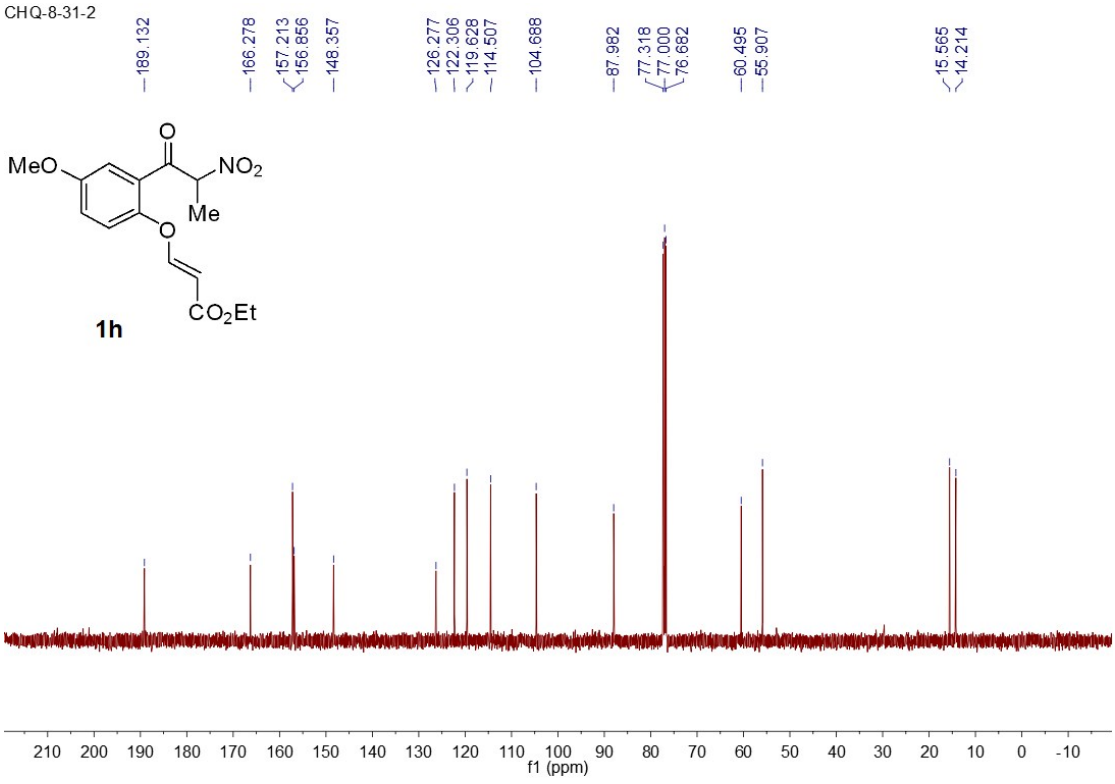
7.662
7.356
7.348
7.260
7.174
7.166
7.151
7.144
7.077
7.055
5.991
5.973
5.956
5.938
5.684
5.653
4.230
4.212
4.194
4.177
3.837
1.800
1.783
1.306
1.288
1.271
0.012
MeO
NO2
Me
O
CO2Et
1h
0.99
1.00
1.08
1.06
1.01
1.00
2.07
3.06
3.05
3.02
f1 (ppm)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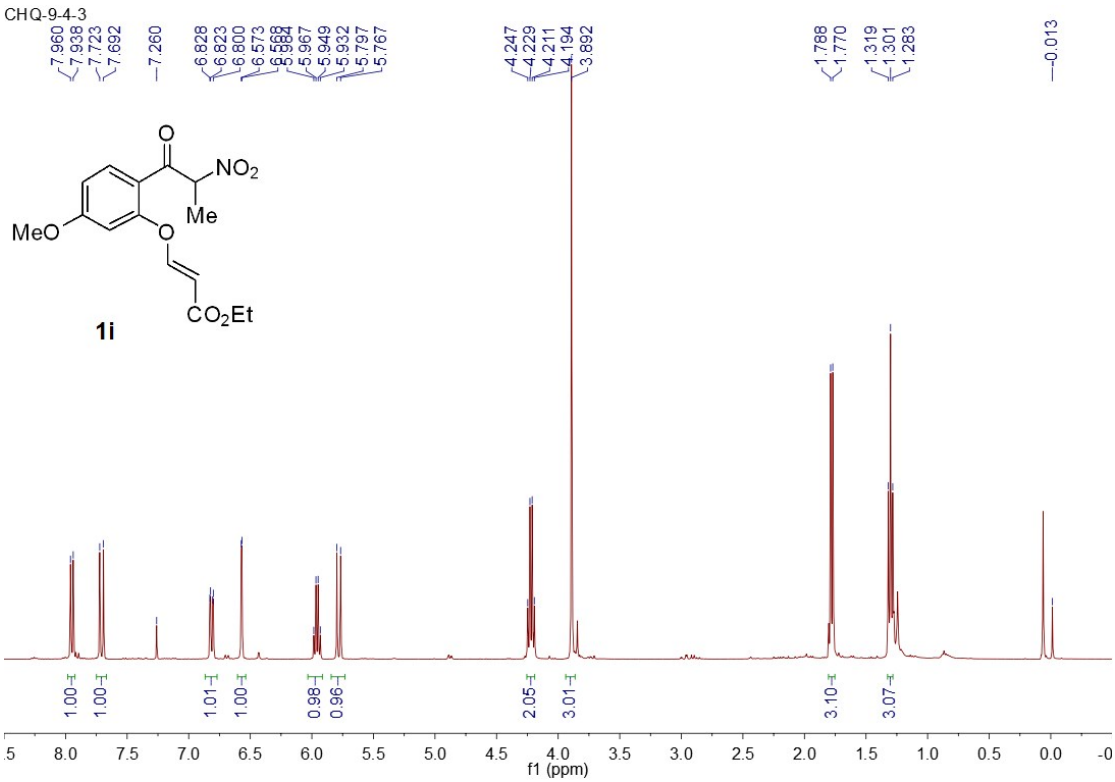
157.213
156.856
148.357
126.277
122.306
119.628
114.507
104.688
87.982
77.318
77.000
76.682
60.495
55.907
15.565
14.214
MeO
NO2
Me
O
CO2Et
1h
f1 (ppm)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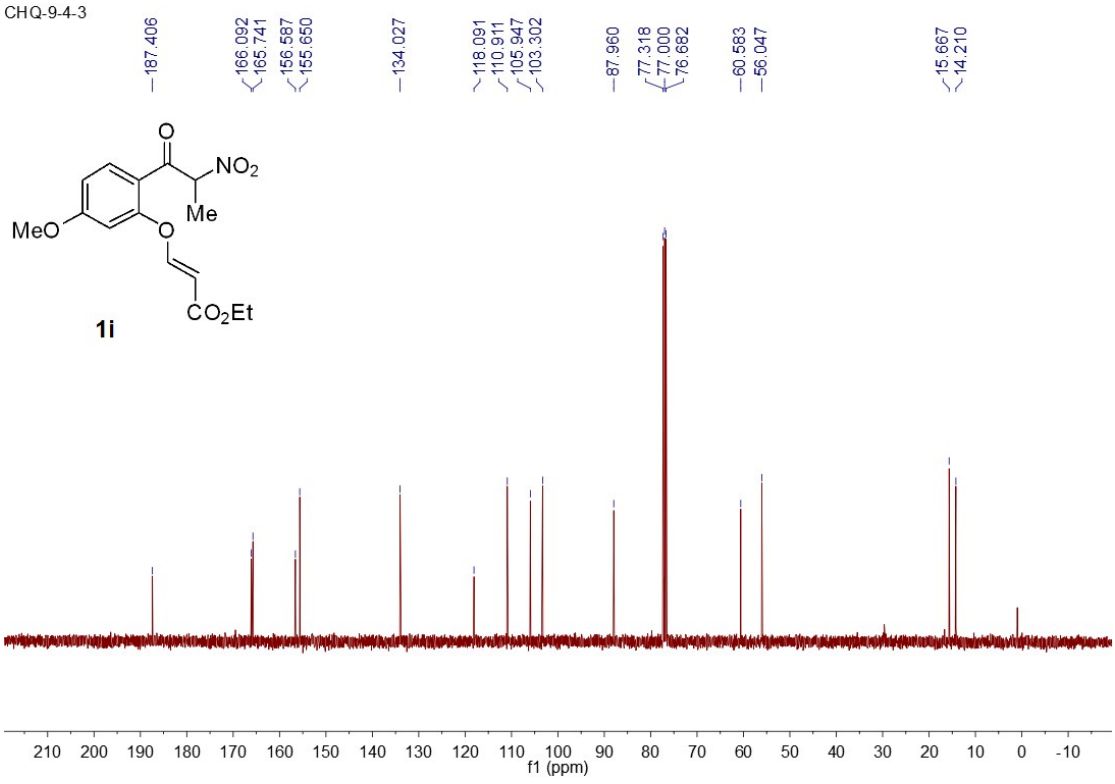
7.692
7.260
6.828
6.823
6.800
6.573
5.967
5.949
5.932
5.797
5.767
4.247
4.229
4.211
4.194
3.892
1.788
1.770
1.319
1.301
1.283
0.013
NO2
Me
MeO
O
CO2Et
1i
1.00
1.00
1.01
1.00
0.98
0.96
2.05
3.01
3.10
3.07
f1 (ppm)


CHQ-9-4-3
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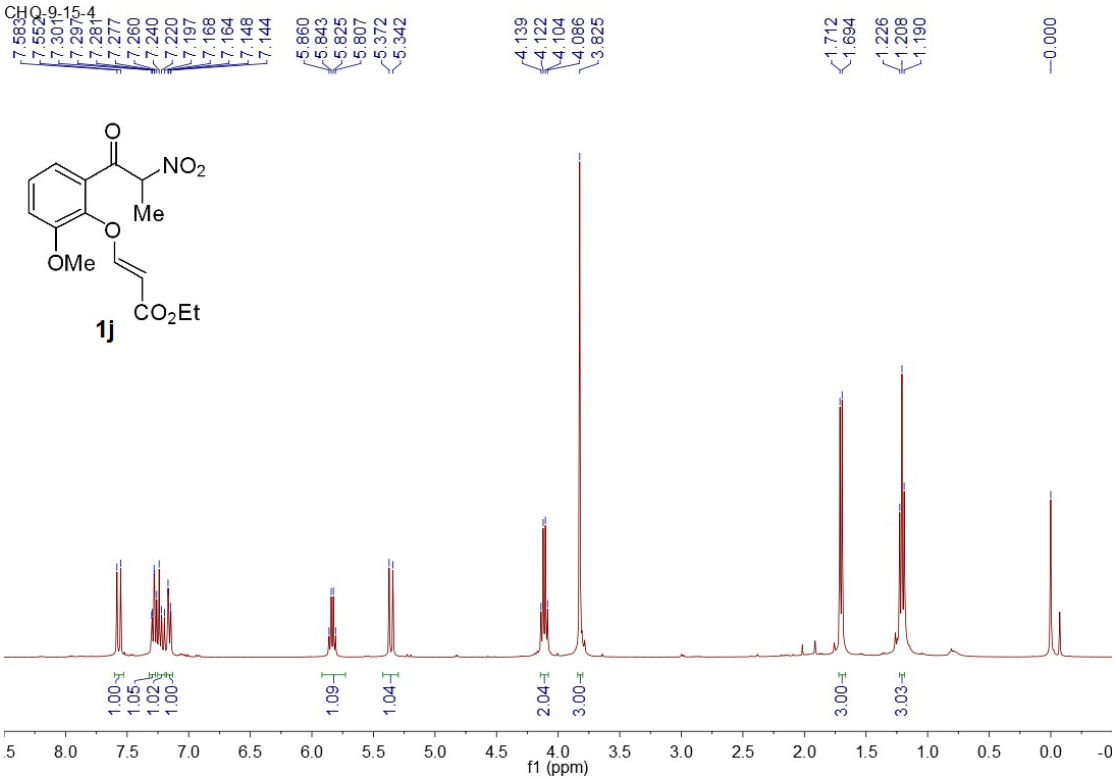
165.741
156.587
155.650
134.027
118.091
110.911
105.947
103.302
87.960
77.318
77.000
76.682
60.583
56.047
15.667
14.210
NO2
Me
MeO
O
CO2Et
1i
f1 (ppm)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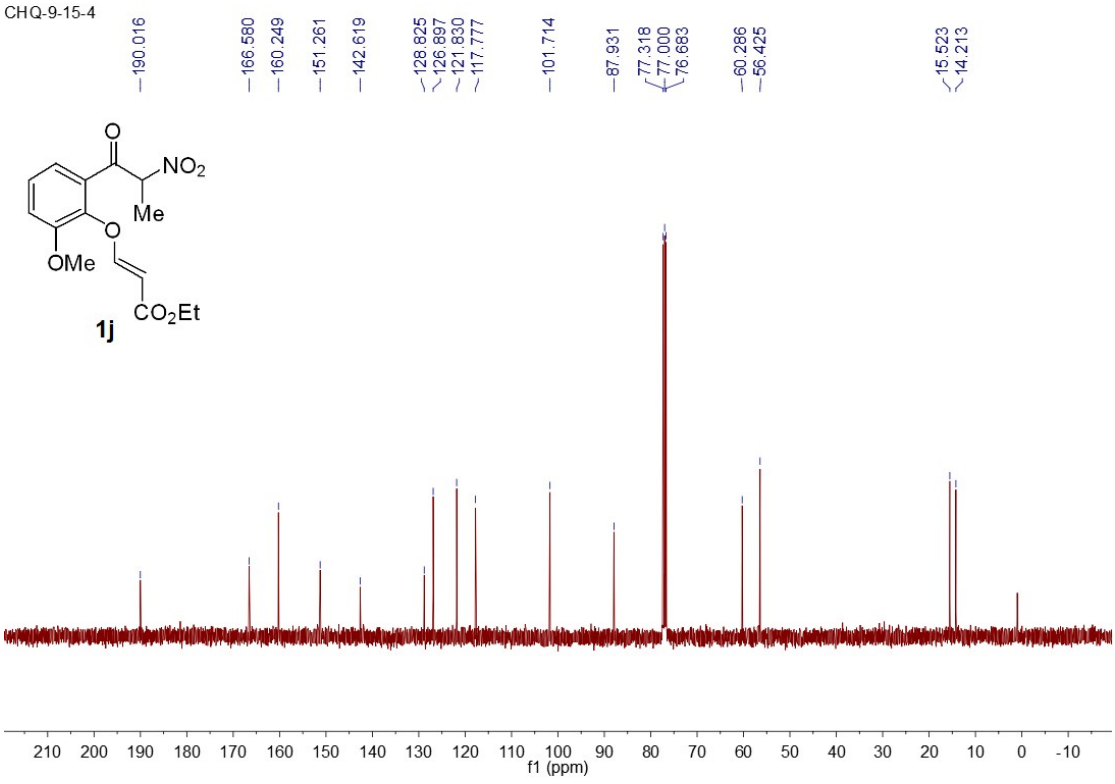
7.301
7.297
7.281
7.277
7.260
7.240
7.220
7.197
7.168
7.164
7.148
7.144
5.860
5.843
5.825
5.807
5.372
5.342
4.139
4.122
4.104
4.086
3.825
1.712
1.694
1.226
1.208
1.190
0.000
NO2
Me
O
OMe
CO2Et
1j
1.00
1.05
1.02
1.00
1.09
1.04
2.04
3.00
3.00
3.03
f1 (ppm)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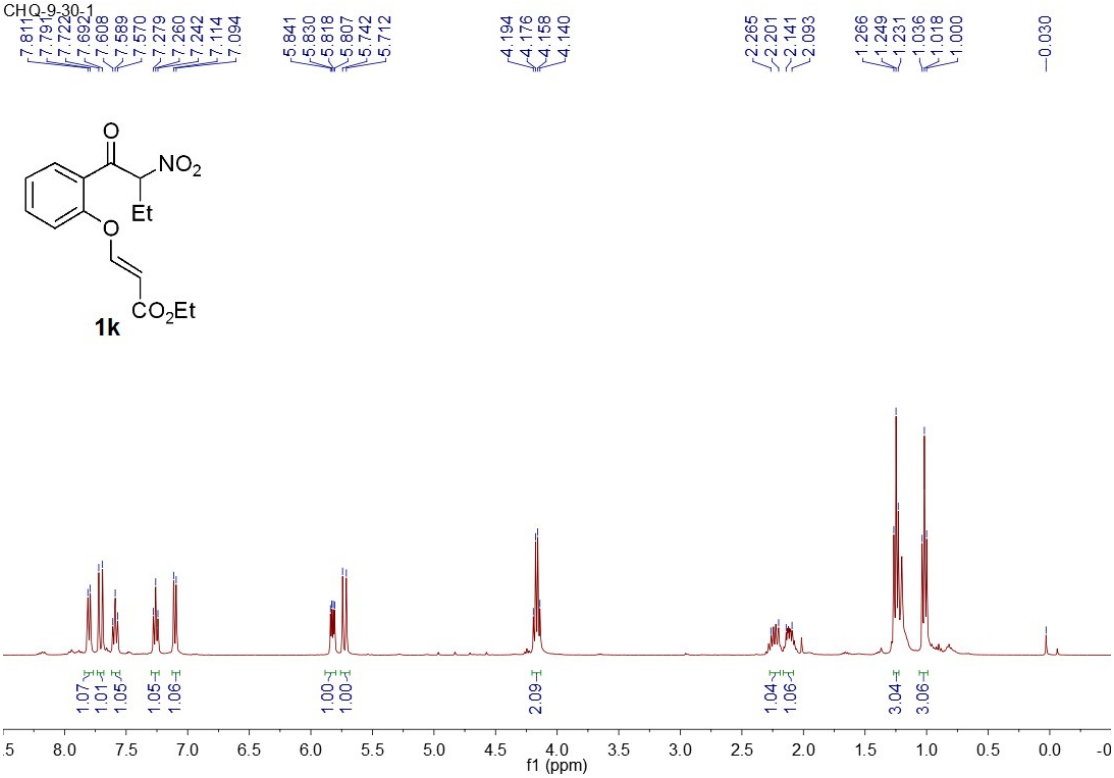
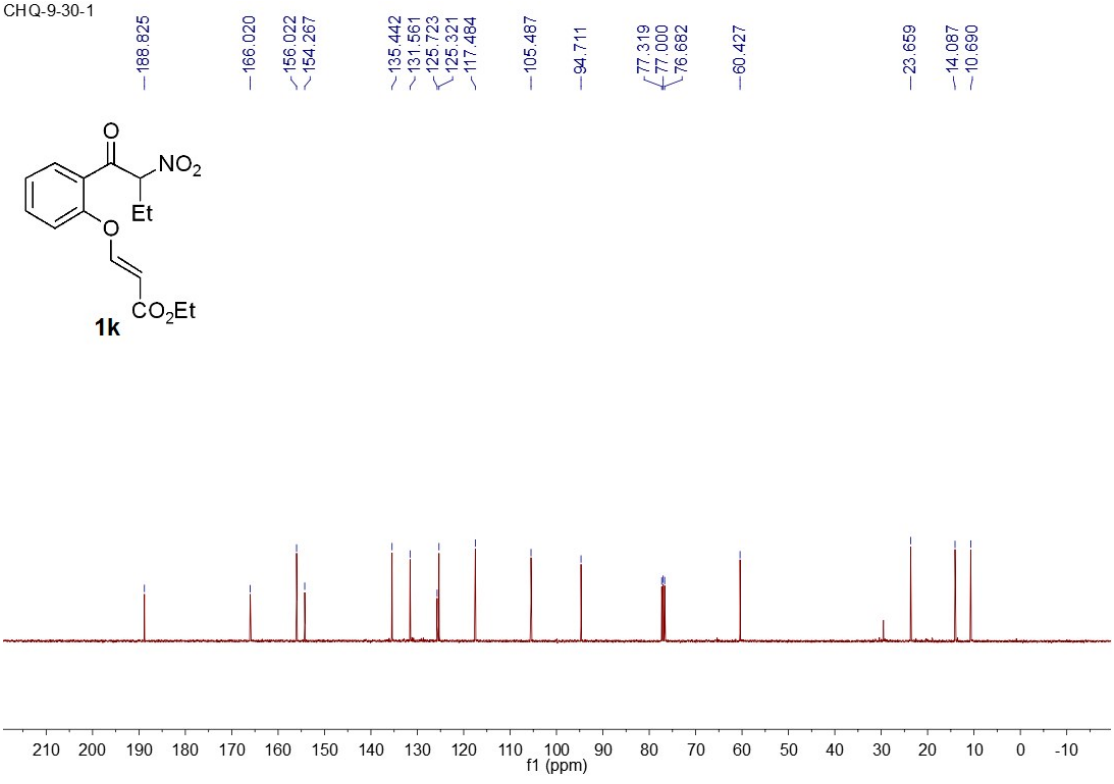
166.580
160.249
151.261
142.619
128.825
126.897
121.830
117.777
101.714
87.931
77.318
77.000
76.683
60.286
56.425
15.523
14.213
NO2
Me
O
OMe
CO2Et
1j
f1 (ppm)

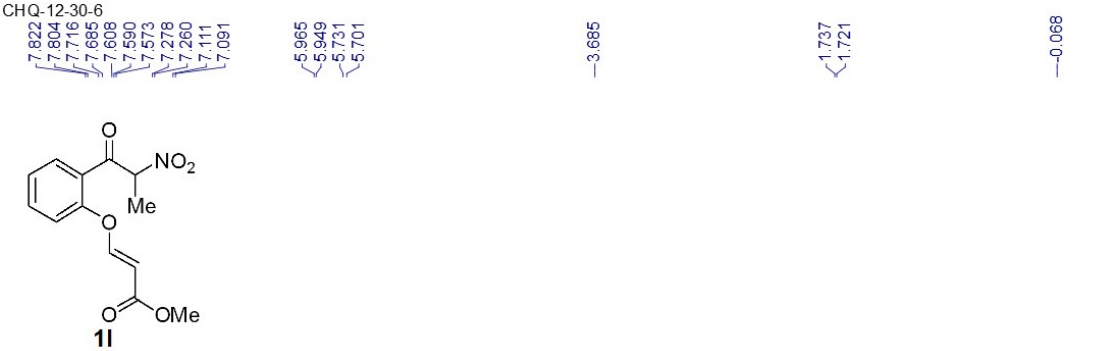
CHQ-9-30-1



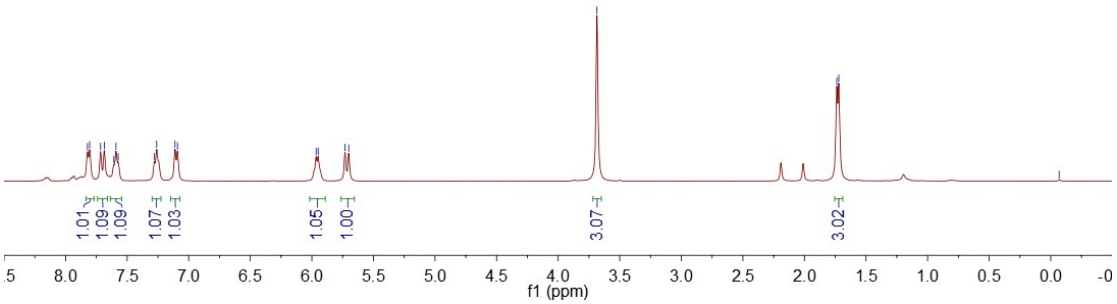
CHQ-9-30-1



CHQ-12-30-6



1l



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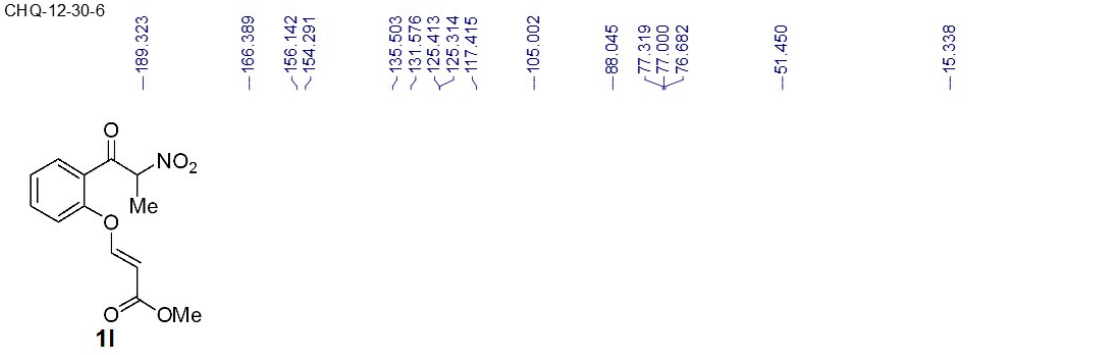

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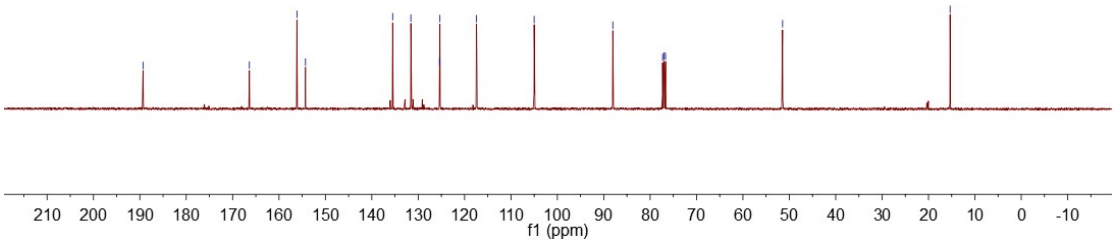

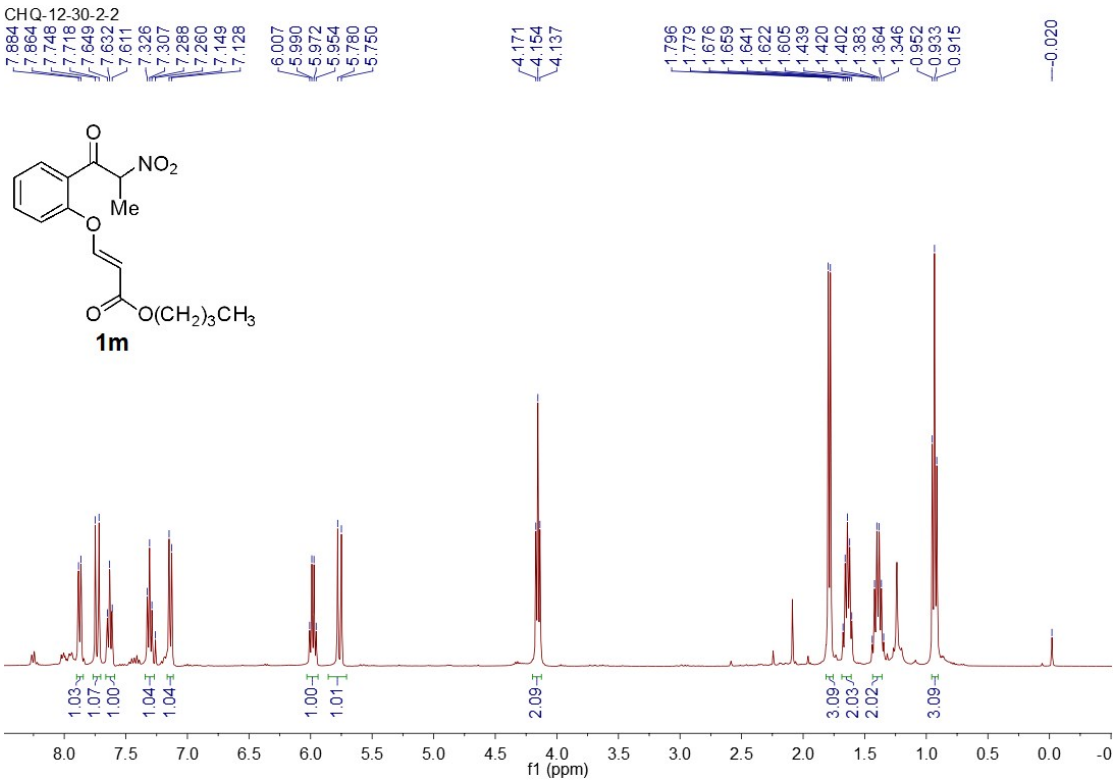
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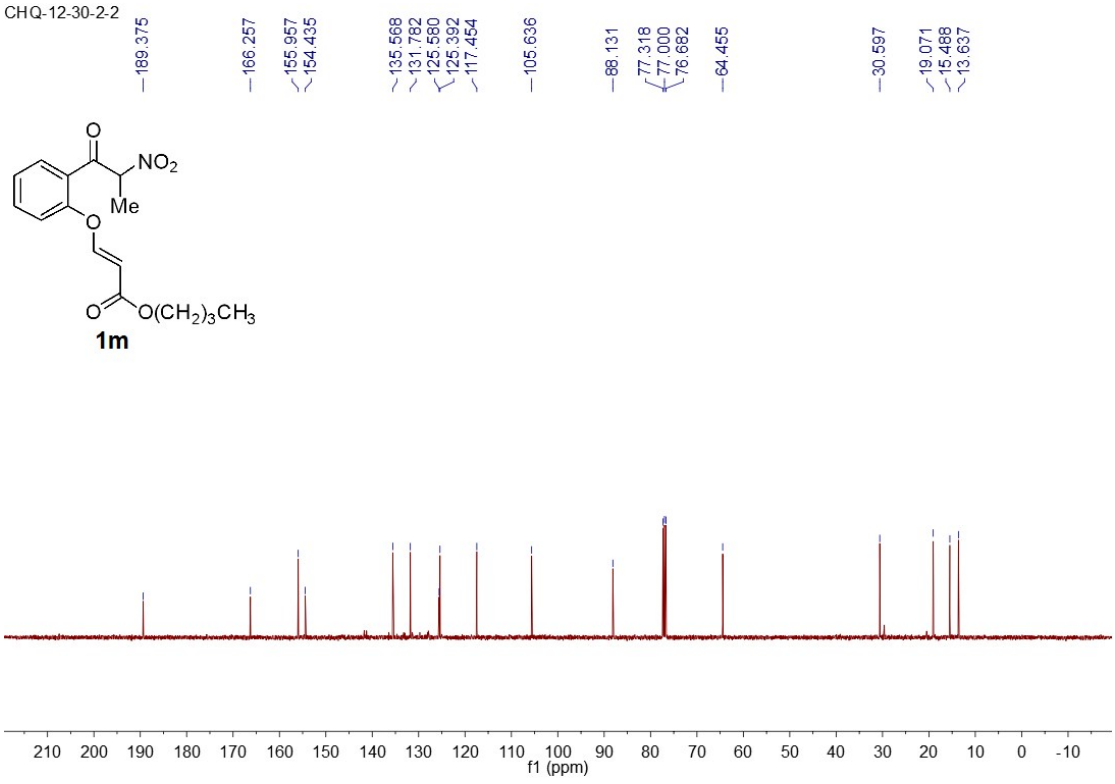
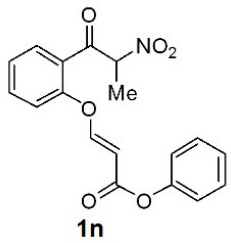
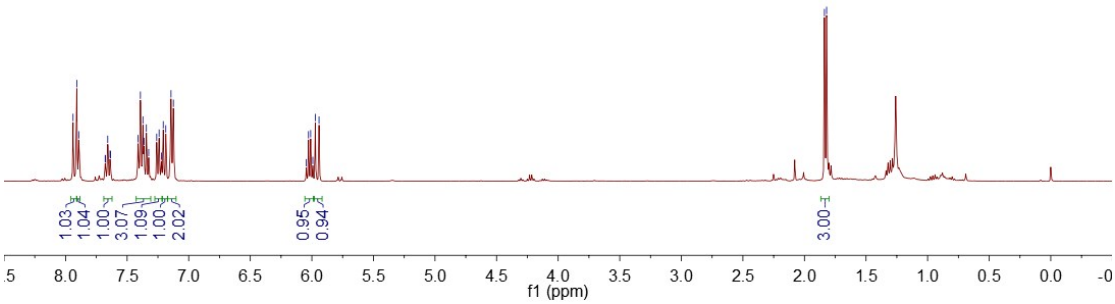
7.864
7.748
7.718
7.649
7.632
7.611
7.326
7.307
7.288
7.260
7.149
7.128
6.007
5.990
5.972
5.954
5.780
5.750
4.171
4.154
4.137
1.796
1.779
1.676
1.659
1.641
1.622
1.605
1.439
1.420
1.402
1.383
1.364
1.346
0.952
0.933
0.915
0.020
NO2
Me
O(CH2)3CH3
1m
1.03
1.07
1.00
1.04
1.04
1.00
1.01
2.09
3.09
2.03
2.02
3.09
f1 (ppm)


CHQ-12-30-2-2
189.375
166.257
155.957
154.435
135.568
131.782
125.580
125.392
117.454
105.636
88.131
77.318
77.000
76.682
64.455
30.597
19.071
15.488
13.637
NO2
Me
O(CH2)3CH3
1m
f1 (ppm)

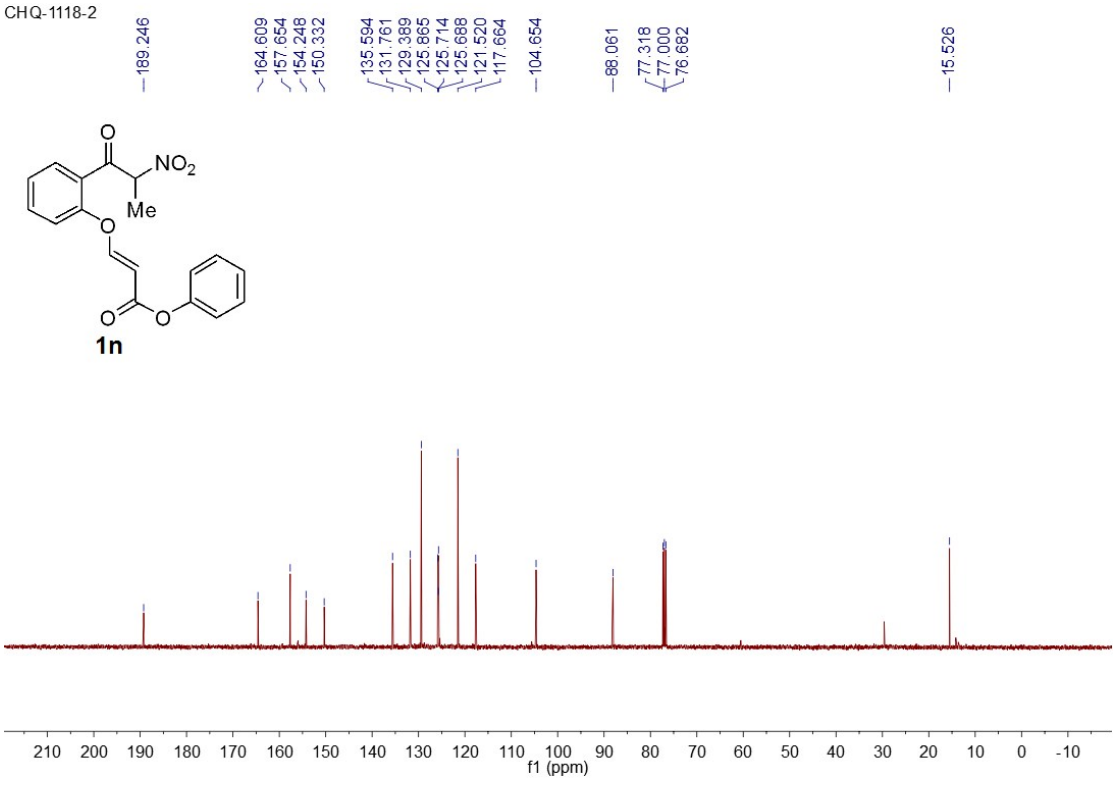
CHQ-11-15-5



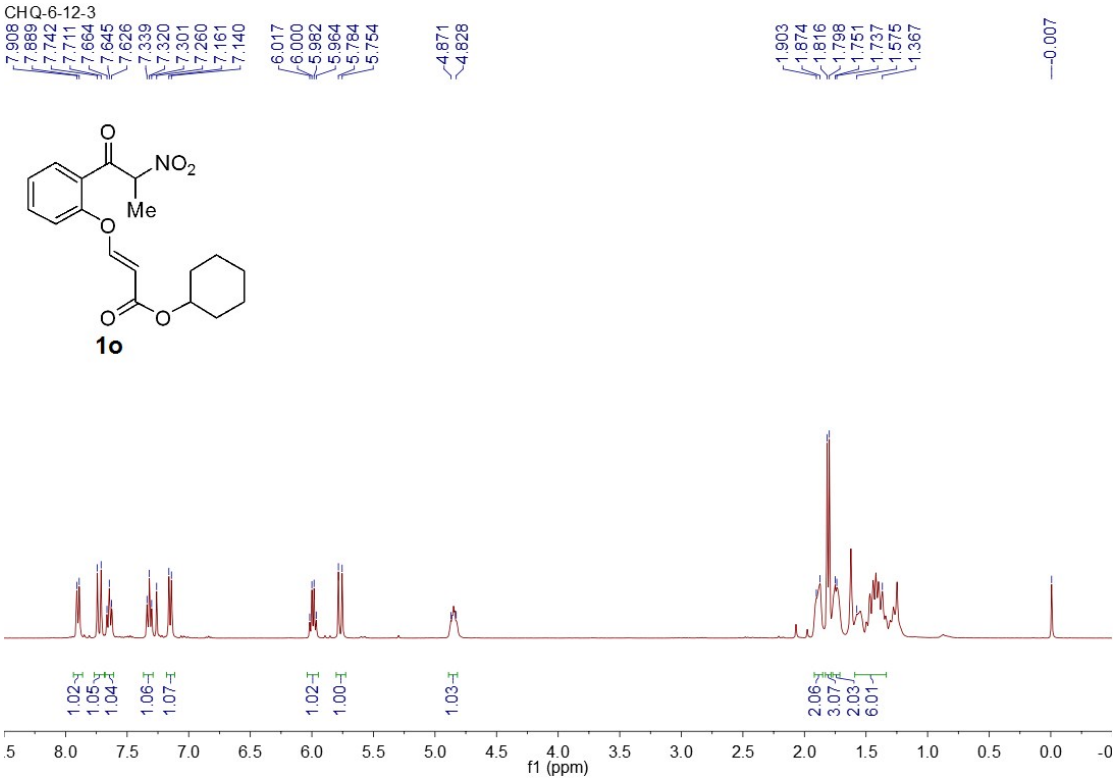
1n

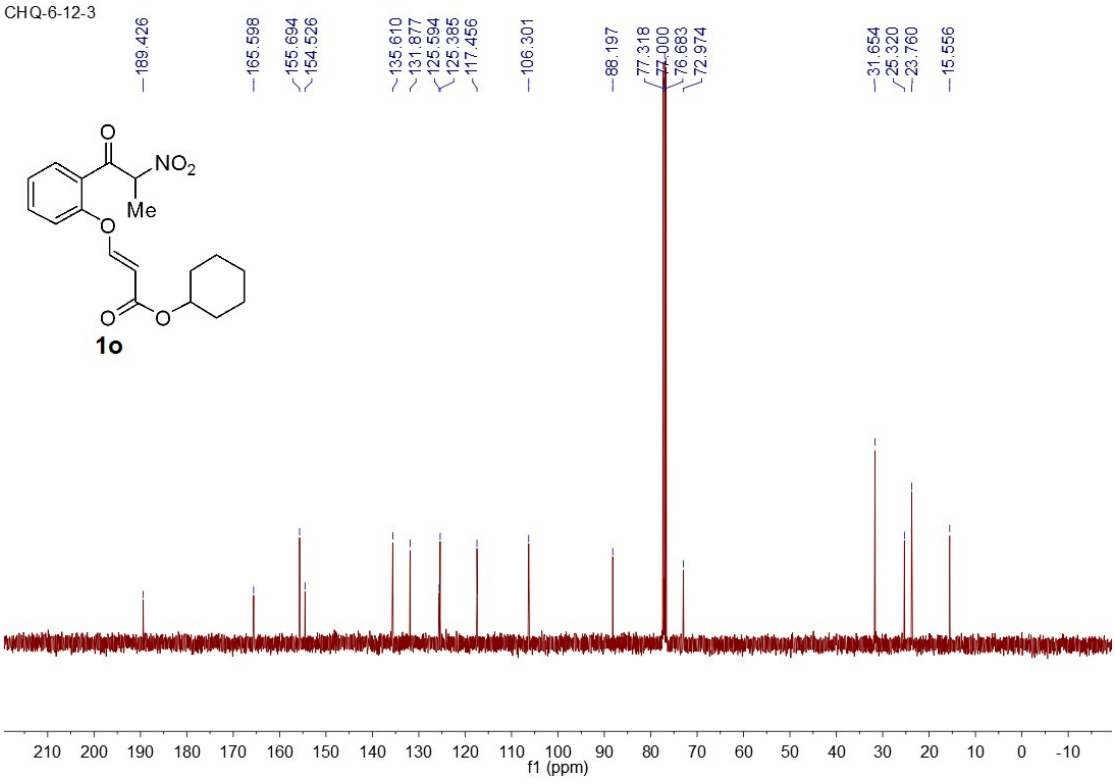


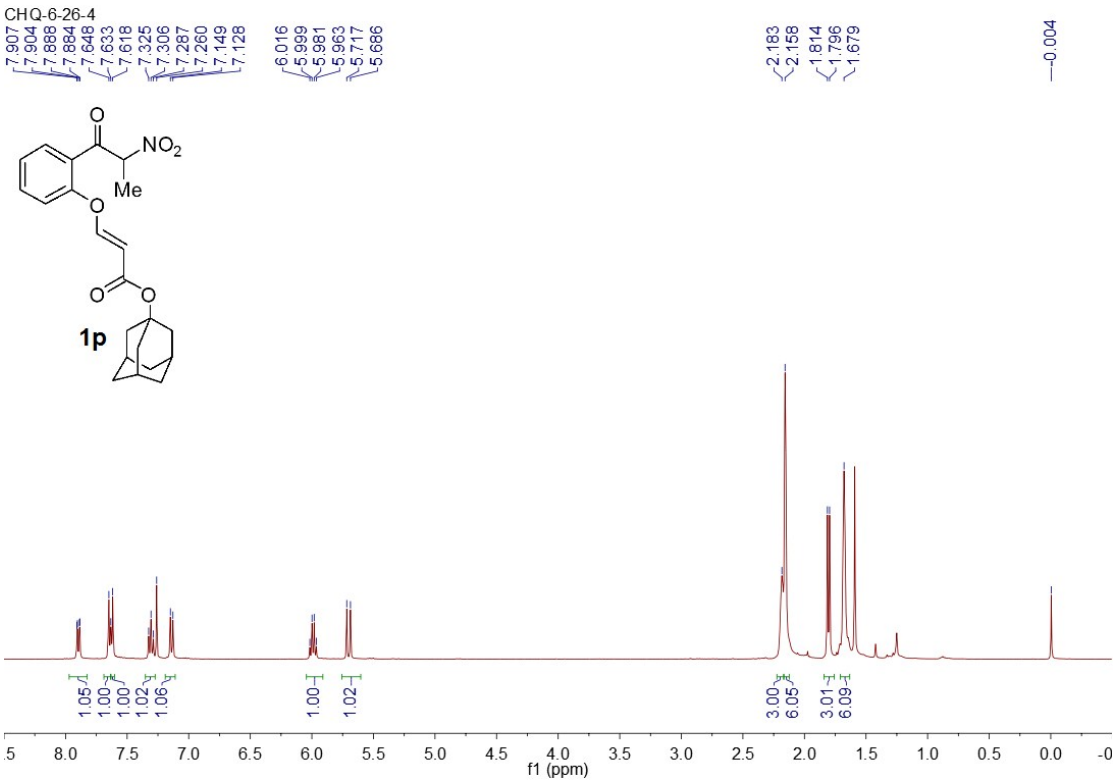
CHQ-1118-2

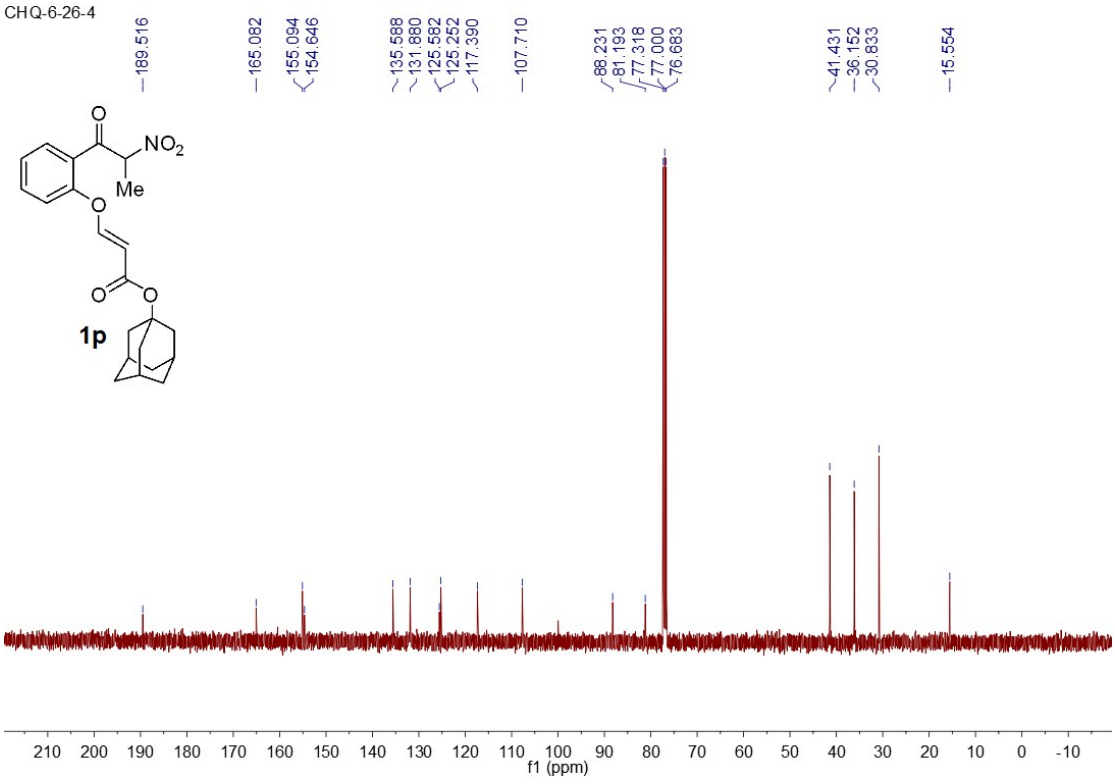


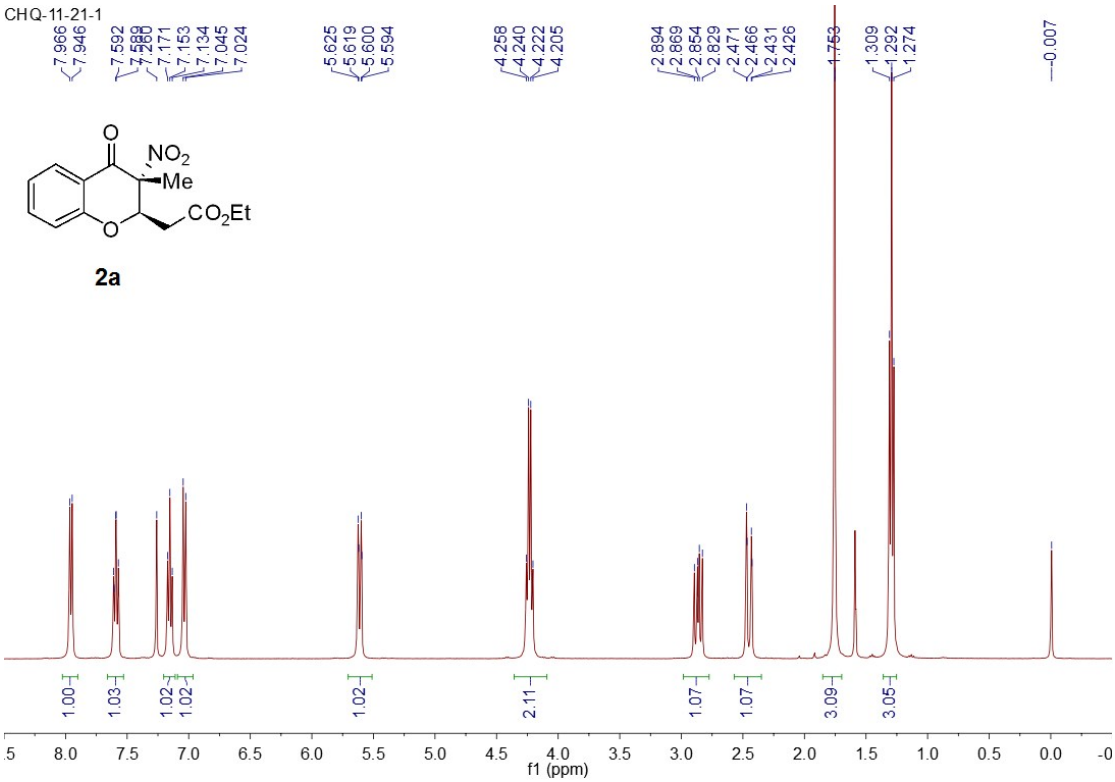
1n

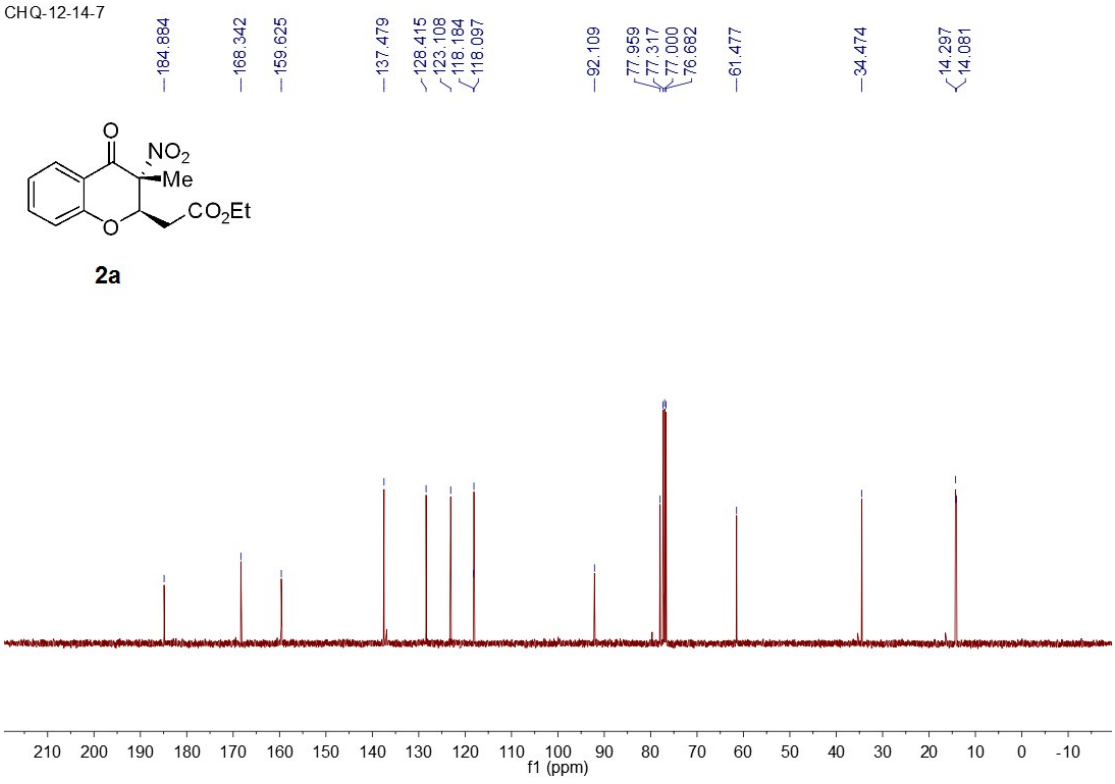

CHQ-6-12-3
7.908
7.889
7.742
7.711
7.664
7.645
7.626
7.339
7.320
7.301
7.260
7.161
7.140
6.017
6.000
5.982
5.964
5.784
5.754
4.871
4.828
1.903
1.874
1.816
1.798
1.751
1.737
1.575
1.367
0.007
NO2
Me
O
O
O
O
1o
1.02
1.05
1.04
1.06
1.07
1.02
1.00
1.03
2.06
3.07
2.03
6.01
f1 (ppm)

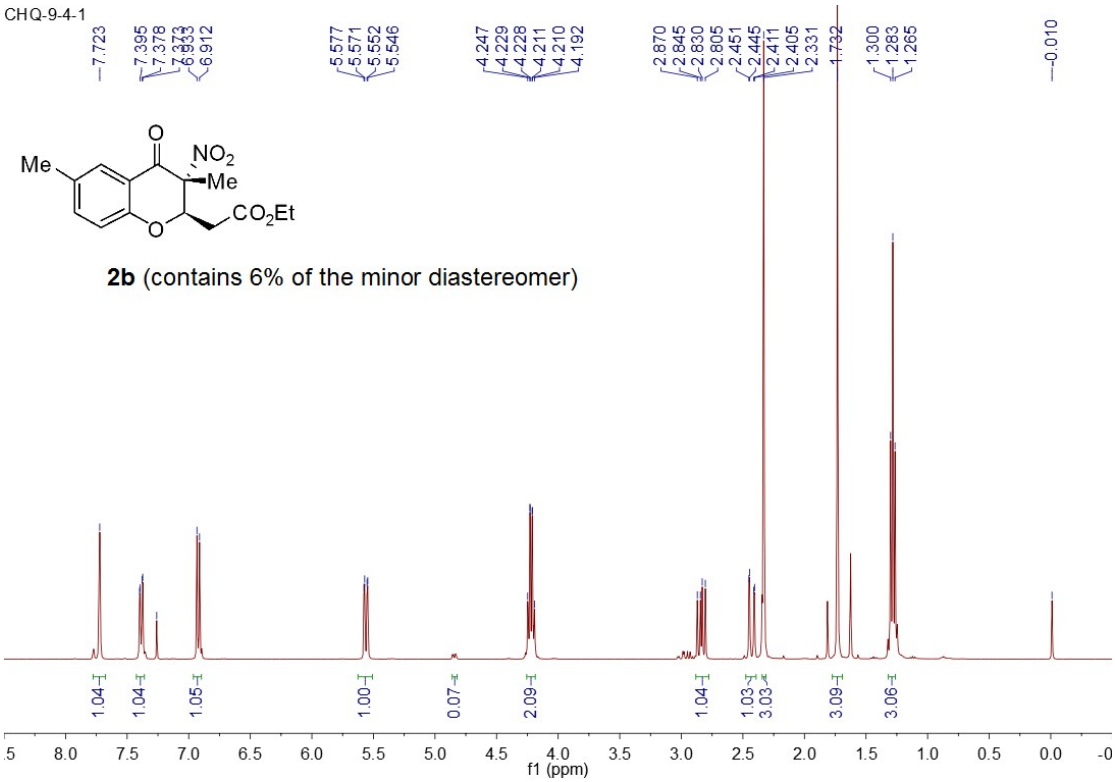

CHQ-6-12-3
189.426
165.598
155.694
154.526
135.610
131.877
125.594
125.385
117.456
106.301
88.197
77.318
77.000
76.683
72.974
31.654
25.320
23.760
15.556
NO2
Me
O
O
O
O
1o
f1 (ppm)


CHQ-6-26-4
7.907
7.904
7.888
7.884
7.648
7.633
7.618
7.325
7.306
7.287
7.260
7.149
7.128
6.016
5.999
5.981
5.963
5.717
5.686
2.183
2.158
1.814
1.796
1.679
0.004
NO2
Me
1p
1.05
1.00
1.00
1.02
1.06
1.00
1.02
3.00
6.05
3.01
6.09
f1 (ppm)

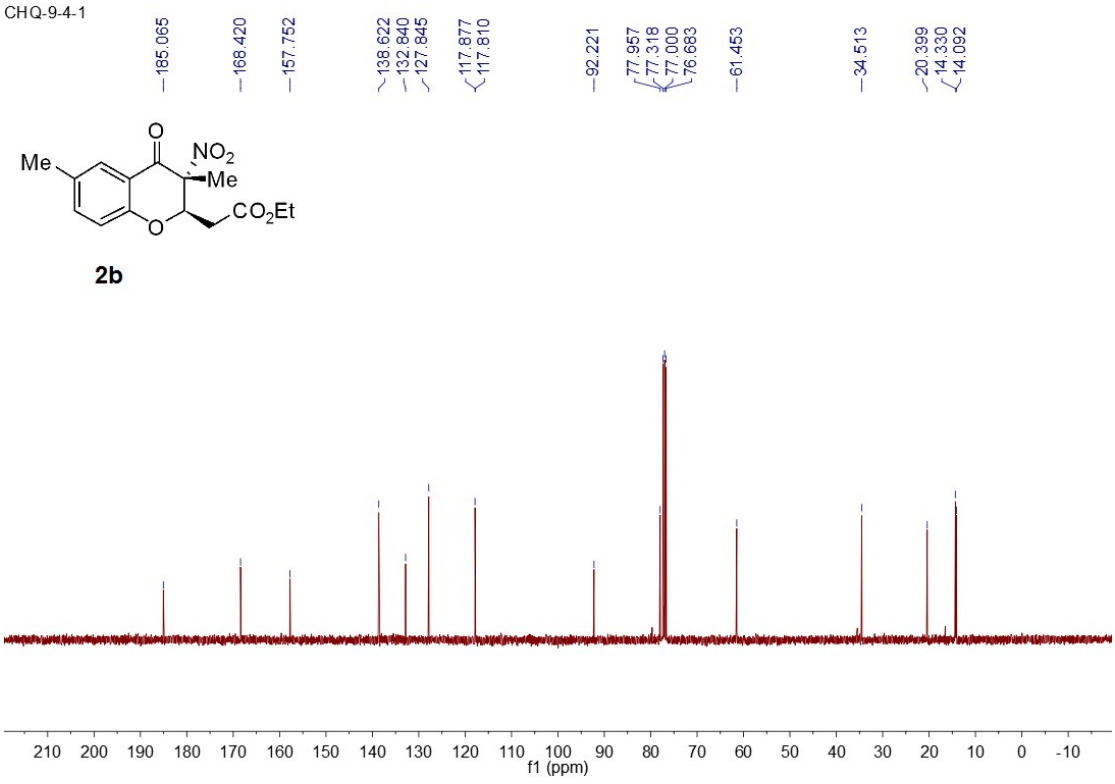

CHQ-6-26-4
189.516
165.082
155.094
154.646
135.588
131.880
125.582
125.252
117.390
107.710
88.231
81.193
77.318
77.000
76.683
41.431
36.152
30.833
15.554
NO2
Me
1p
f1 (ppm)


CHQ-11-21-1
7.966
7.946
7.592
7.171
7.153
7.134
7.045
7.024
5.625
5.619
5.600
5.594
4.258
4.240
4.222
4.205
2.894
2.869
2.854
2.829
2.471
2.466
2.431
2.426
1.753
1.309
1.292
1.274
0.007
NO2
Me
CO2Et
2a
1.00
1.03
1.02
1.02
1.02
2.11
1.07
1.07
3.09
3.05
f1 (ppm)

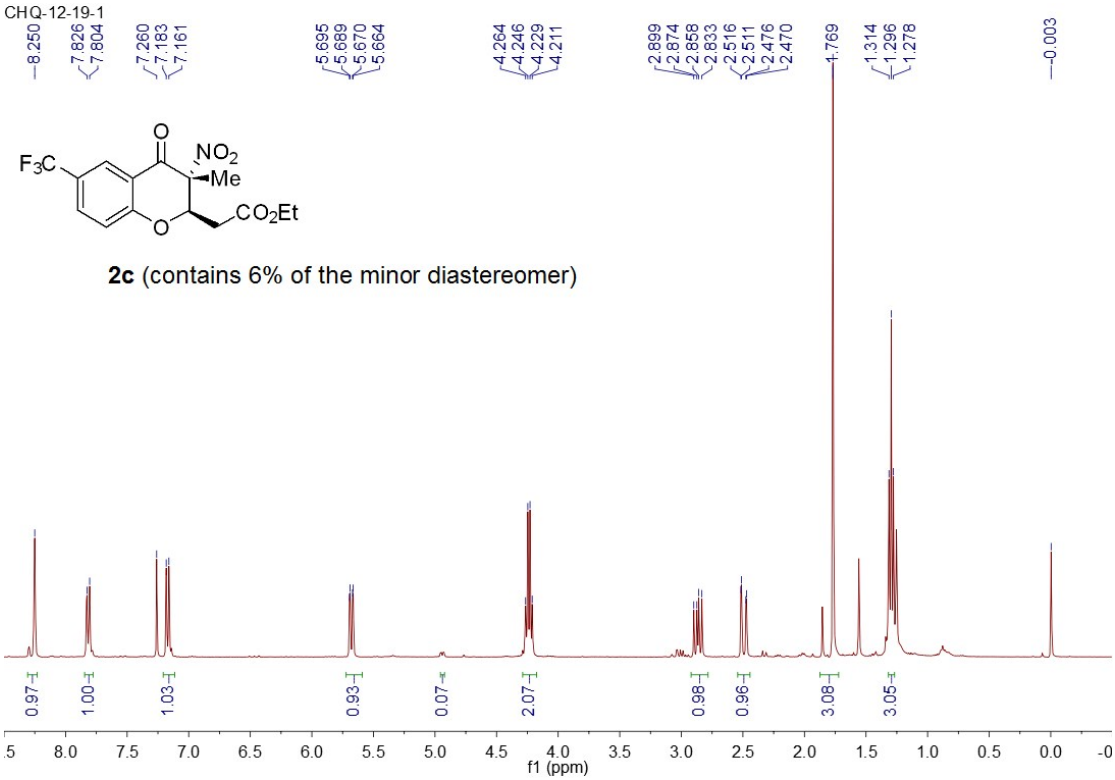

CHQ-12-14-7
184.884
168.342
159.625
137.479
128.415
123.108
118.184
118.097
92.109
77.959
77.317
77.000
76.682
61.477
34.474
14.297
14.081
NO2
Me
CO2Et
2a
f1 (ppm)



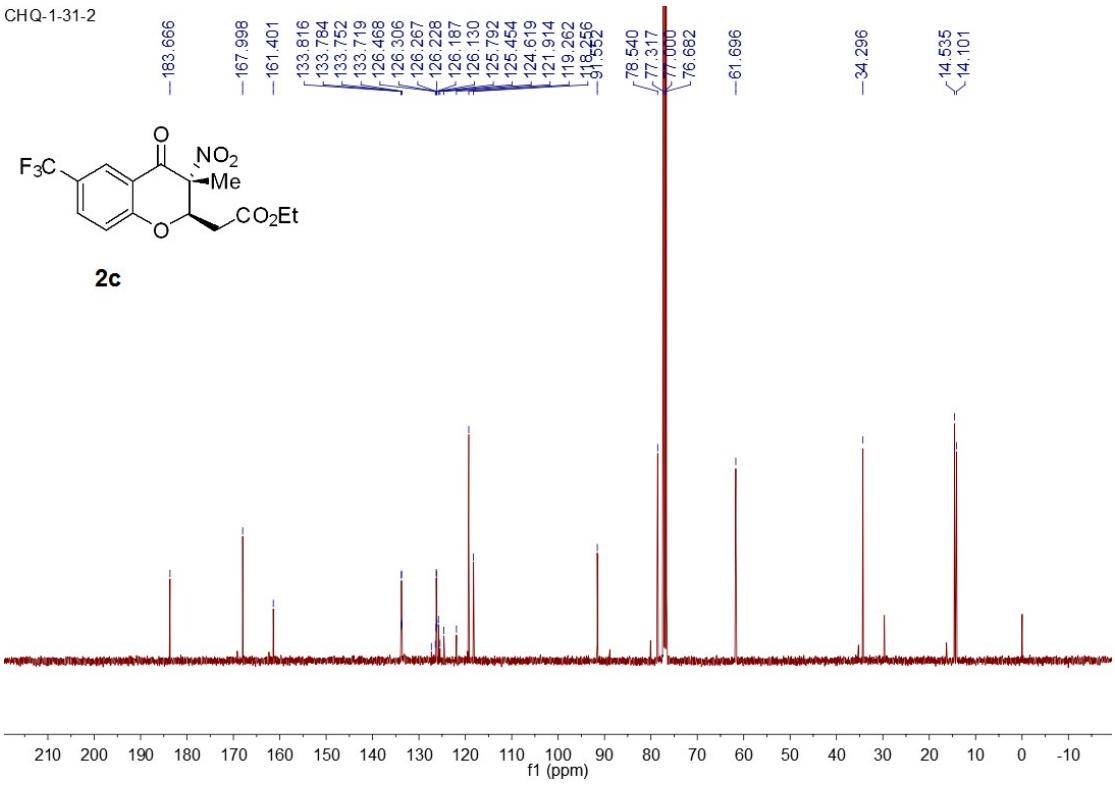
2b (contains 6% of the minor diastereomer)



2b

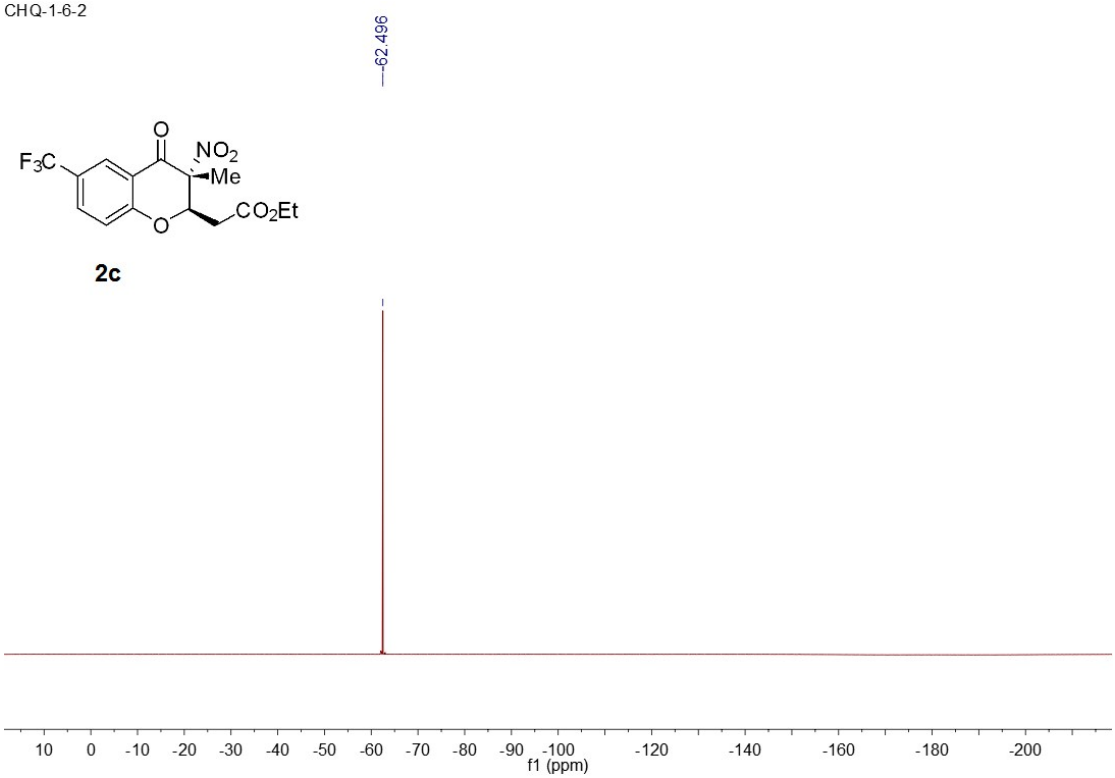


2c (contains 6% of the minor diastereomer)

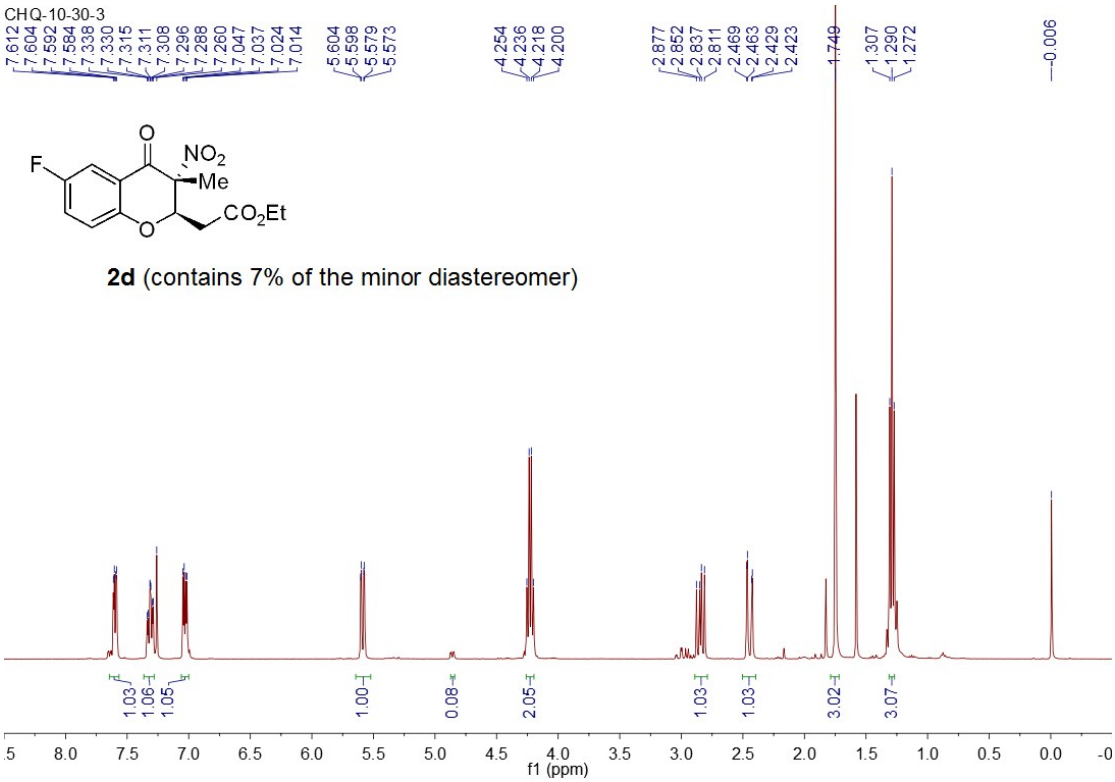


2c

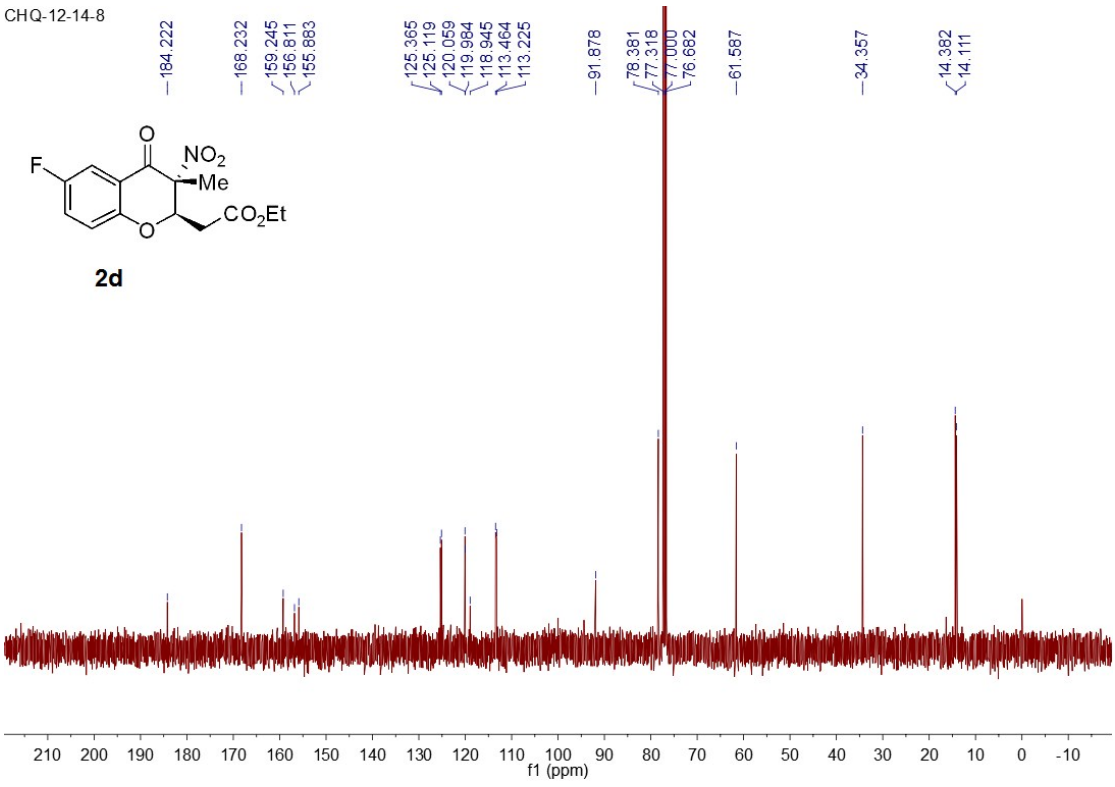
CHQ-1-6-2


-62.496
F3C
O
NO2
Me
CO2Et
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

2c

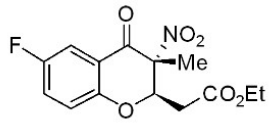


2d (contains 7% of the minor diastereomer)



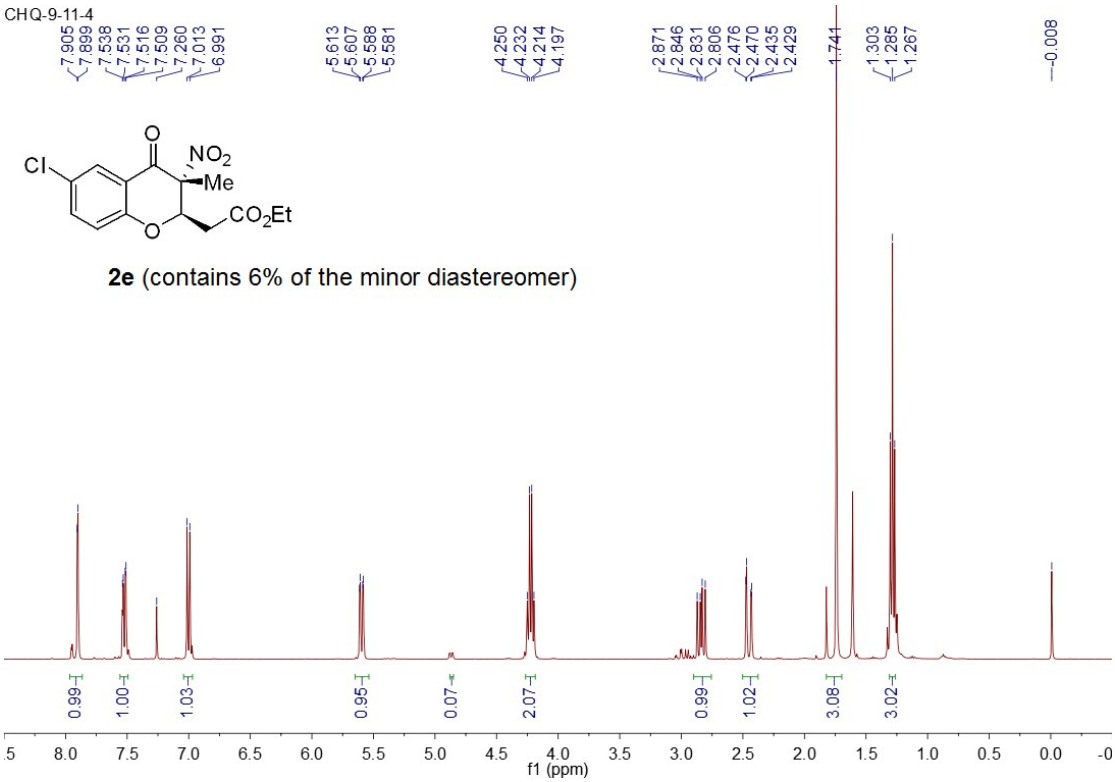
2d

CHQ-3-11-5

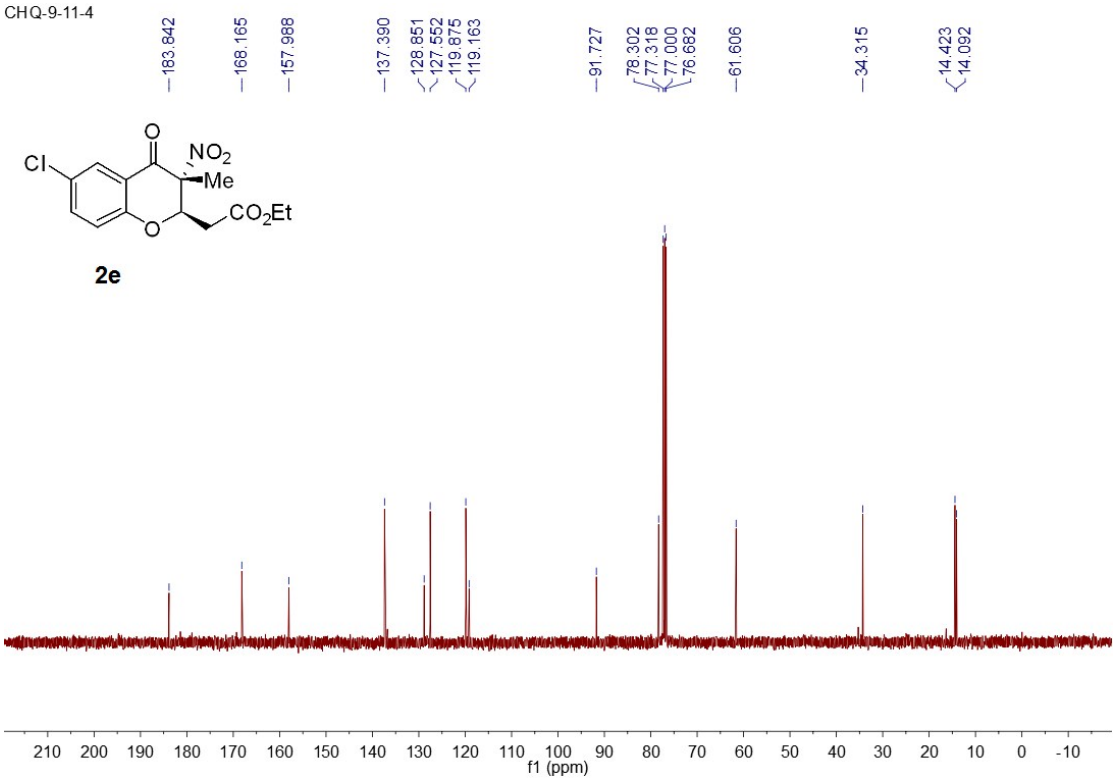

O
NO2
F
Me
CO2Et
O

2d

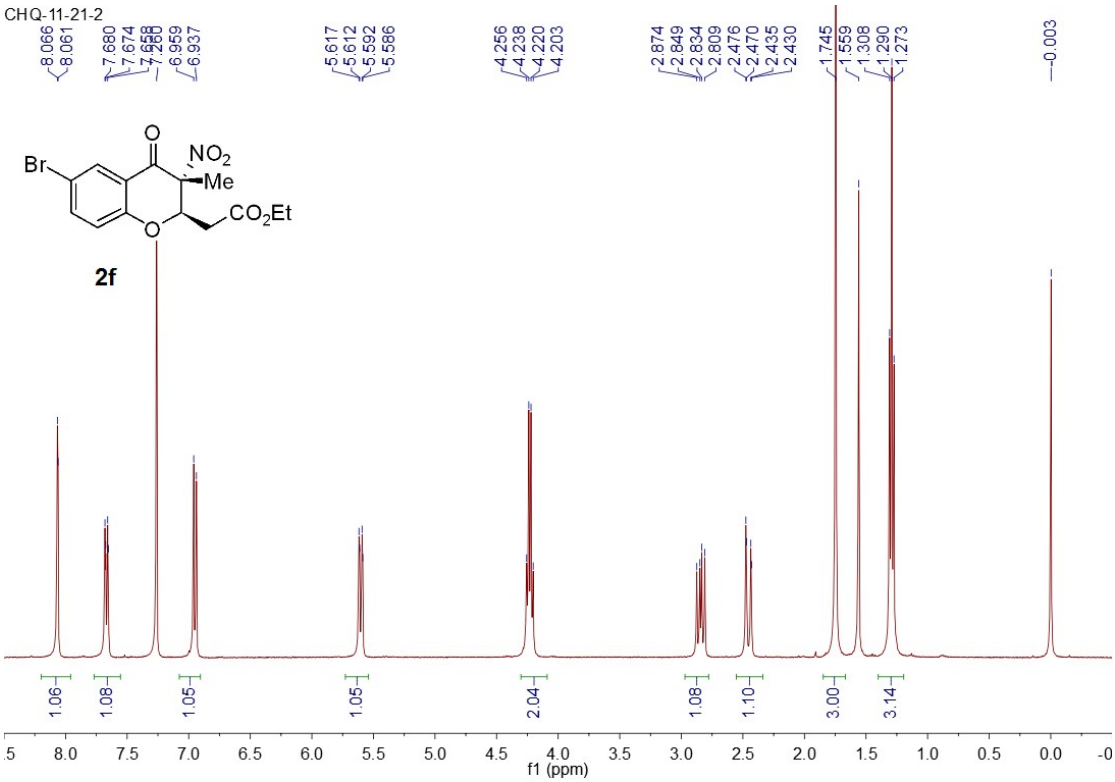
-118.526
100
-104
-108
-112
-116
-120
-124
-128
-132
-136
-140
-144
-148
f1 (ppm)

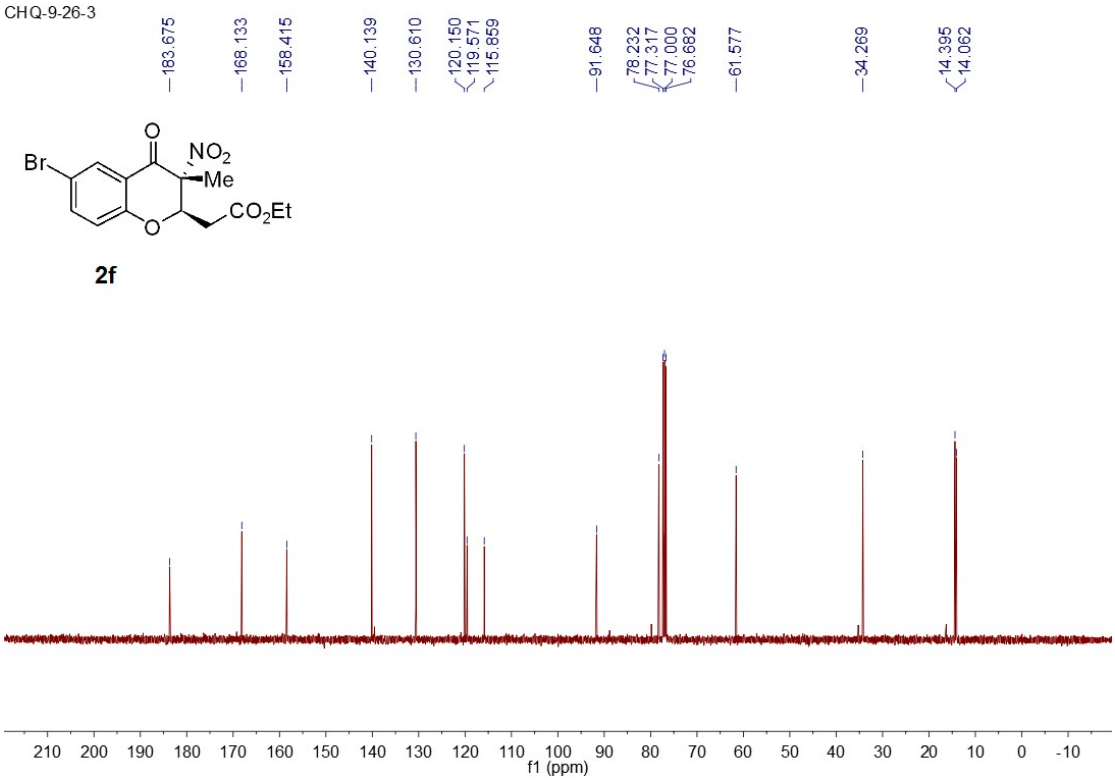


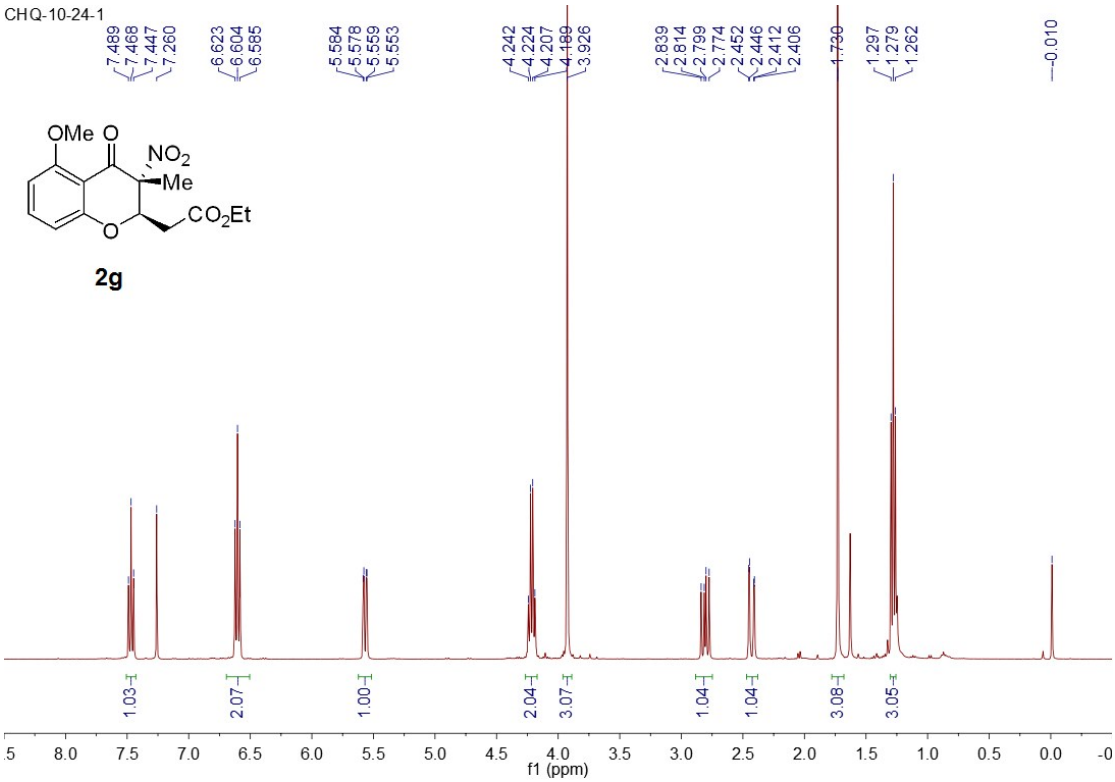
2e (contains 6% of the minor diastereomer)

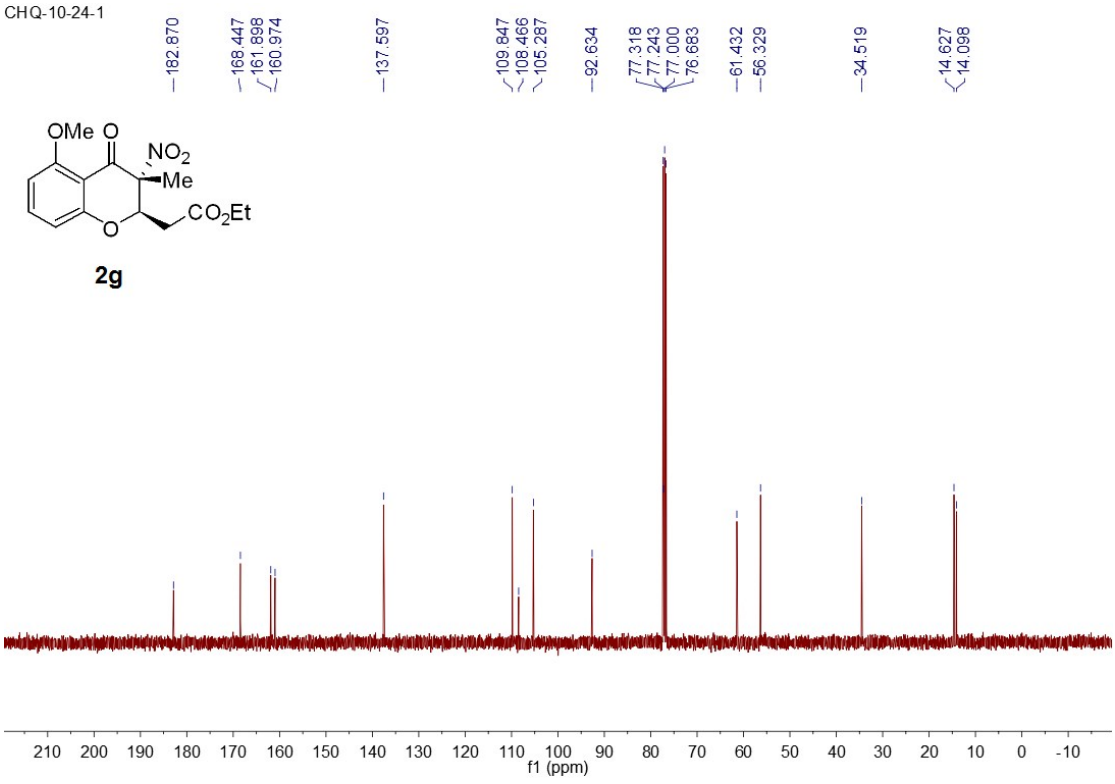


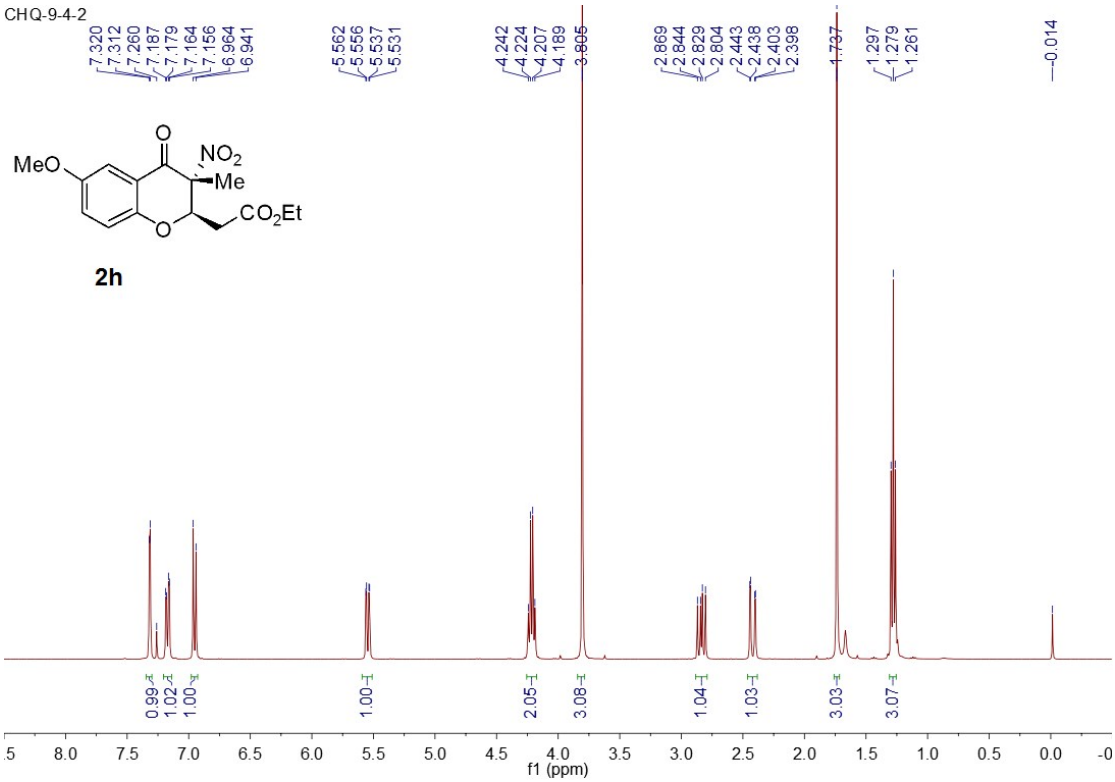
2e

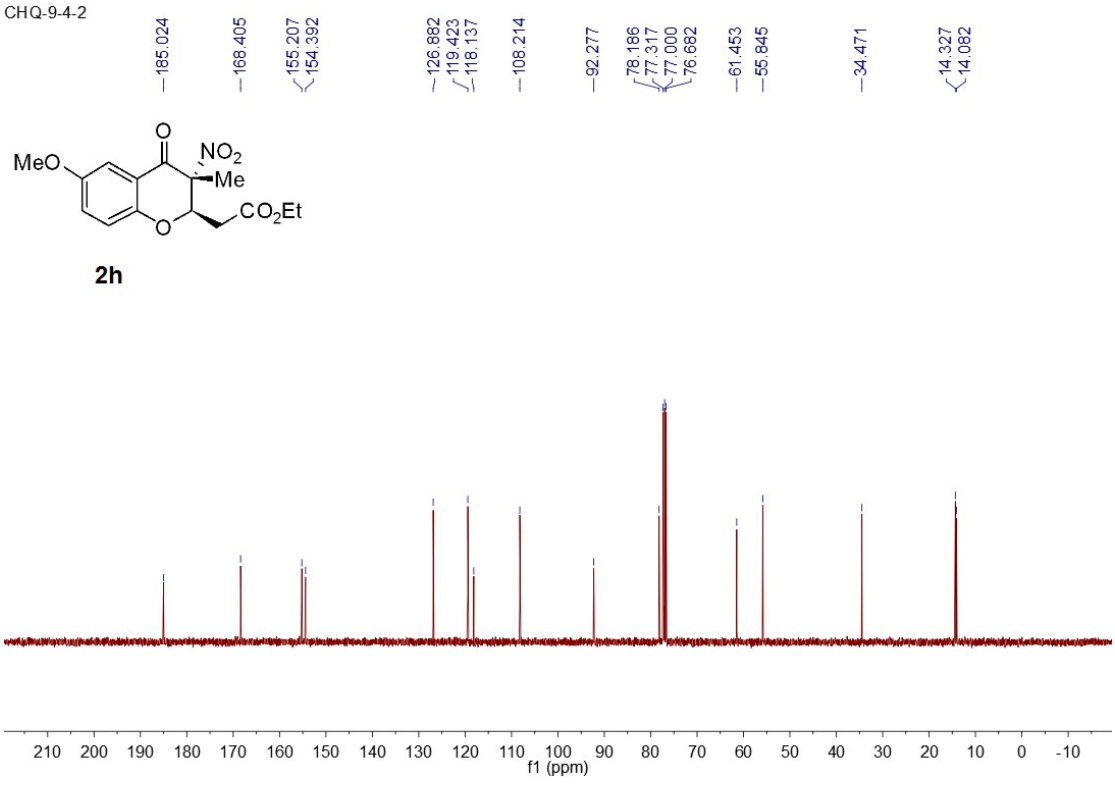

CHQ-11-21-2
8.066
8.061
7.680
7.674
7.268
6.959
6.937
5.617
5.612
5.592
5.586
4.256
4.238
4.220
4.203
2.874
2.849
2.834
2.809
2.476
2.470
2.435
2.430
1.745
1.559
1.308
1.290
1.273
0.003
Br
O
NO2
Me
CO2Et
2f
1.06
1.08
1.05
1.05
2.04
1.08
1.10
3.00
3.14
f1 (ppm)

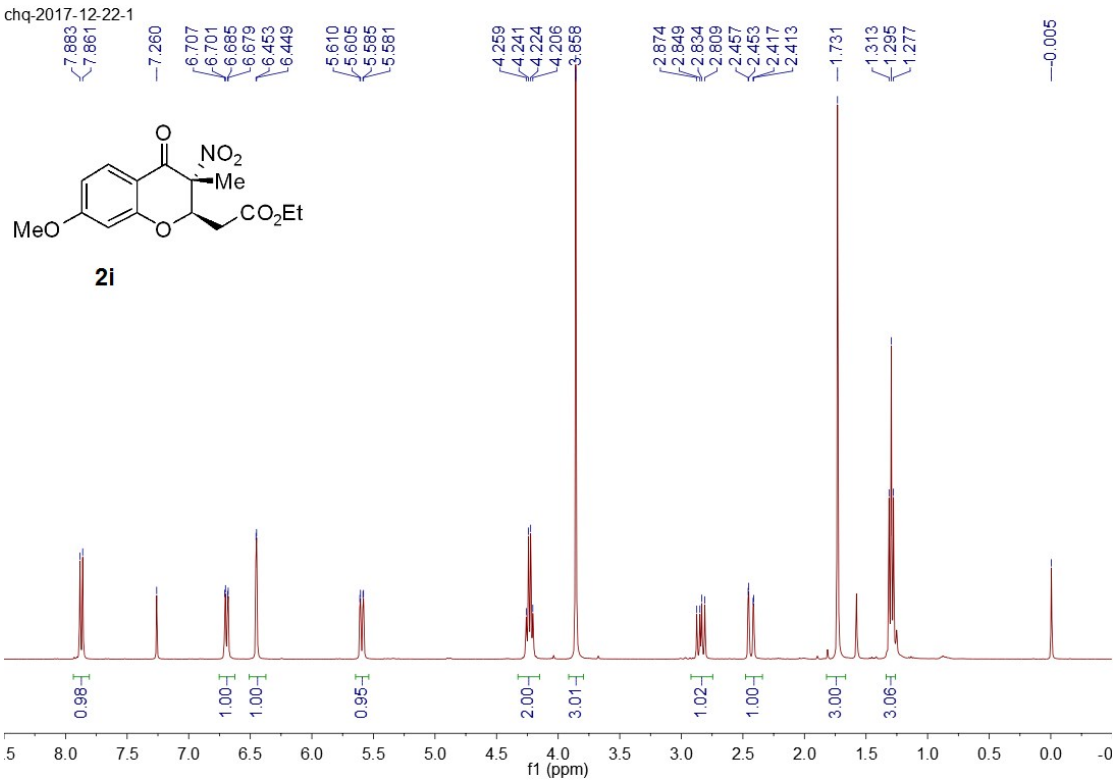

CHQ-9-26-3
183.675
168.133
158.415
140.139
130.610
120.150
119.571
115.859
91.648
78.232
77.317
77.000
76.682
61.577
34.269
14.395
14.062
Br
O
NO2
Me
CO2Et
2f
f1 (ppm)

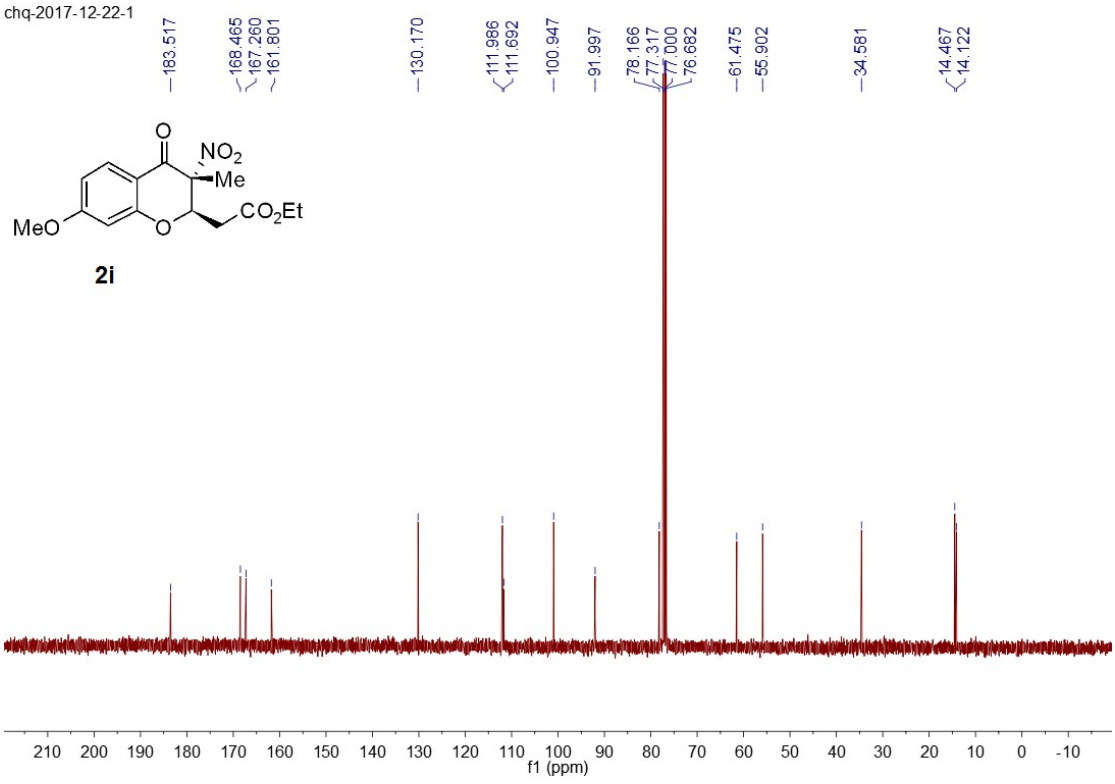

CHQ-10-24-1
7.489
7.468
7.447
7.260
6.623
6.604
6.585
5.584
5.578
5.559
5.553
4.242
4.224
4.207
4.189
3.926
2.839
2.814
2.799
2.774
2.452
2.446
2.412
2.406
1.730
1.297
1.279
1.262
0.010
OMe O
NO2
Me
CO2Et
O
2g
1.03
2.07
1.00
2.04
3.07
1.04
1.04
3.08
3.05
f1 (ppm)

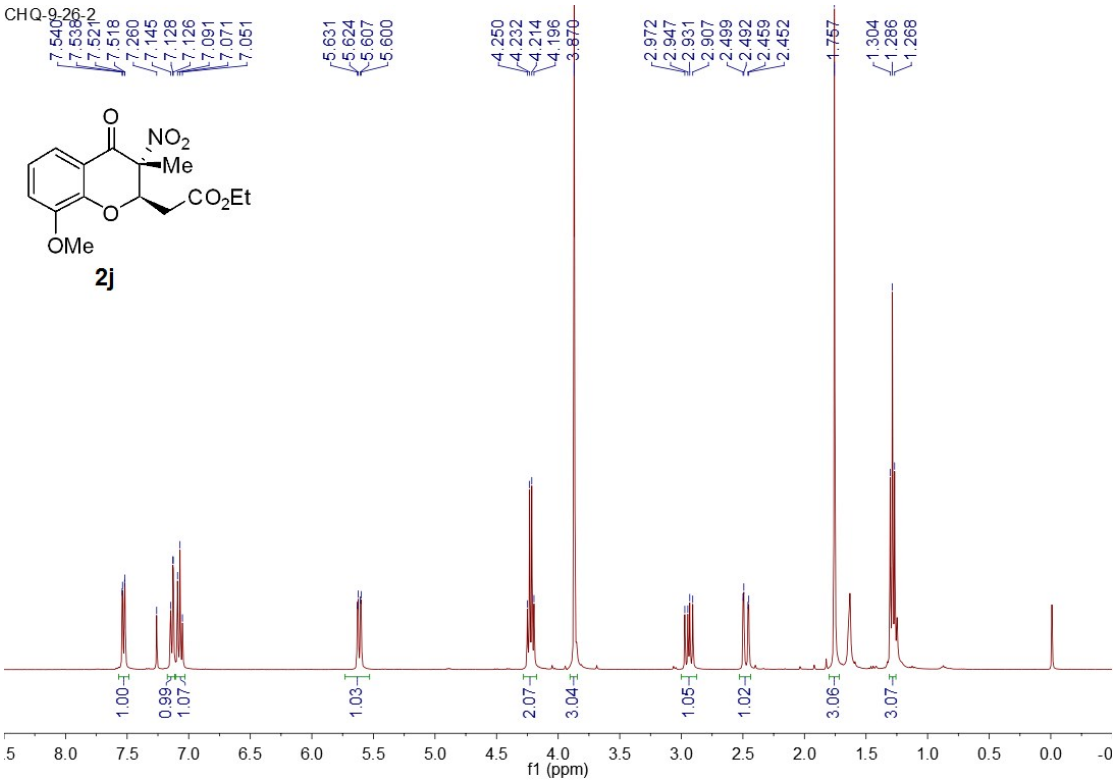

CHQ-10-24-1
182.870
168.447
161.898
160.974
137.597
109.847
108.466
105.287
92.634
77.318
77.243
77.000
76.683
61.432
56.329
34.519
14.627
14.098
OMe O
NO2
Me
CO2Et
O
2g
f1 (ppm)

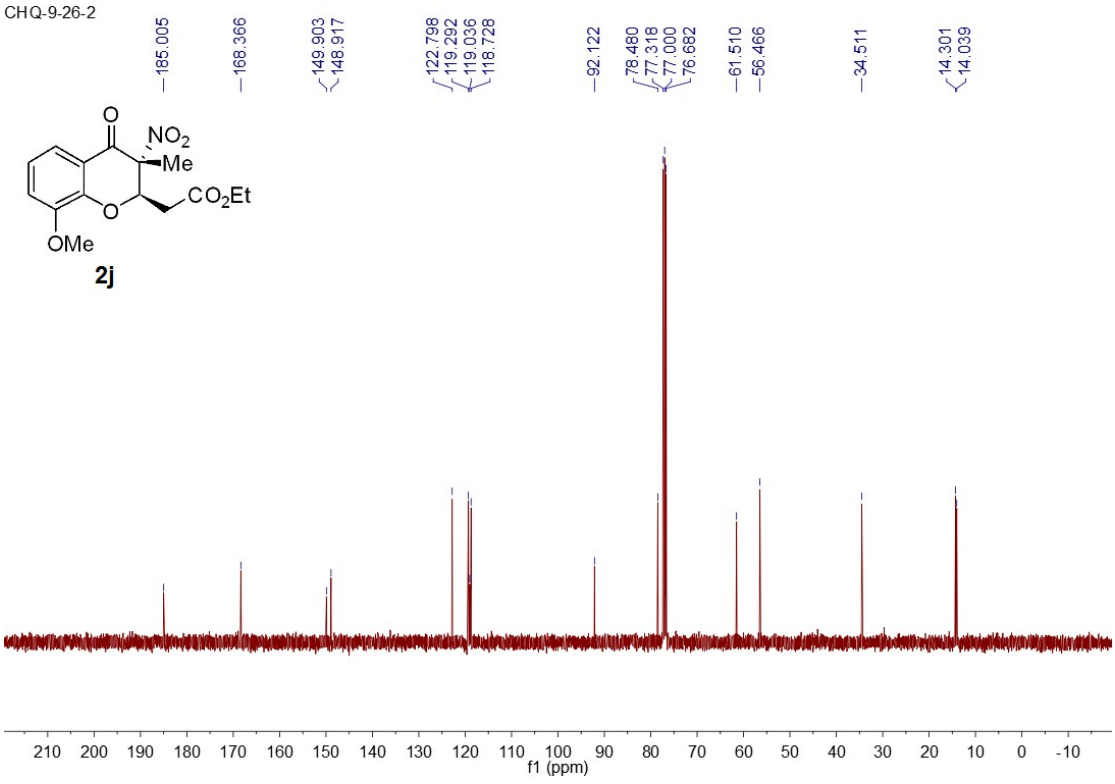

CHQ-9-4-2
7.320
7.312
7.260
7.187
7.179
7.164
7.156
6.964
6.941
5.562
5.556
5.537
5.531
4.242
4.224
4.207
4.189
3.805
2.869
2.844
2.829
2.804
2.443
2.438
2.403
2.398
1.737
1.297
1.279
1.261
0.014
MeO
NO2
Me
CO2Et
2h
0.99
1.02
1.00
1.00
2.05
3.08
1.04
1.03
3.03
3.07
f1 (ppm)


CHQ-9-4-2
185.024
168.405
155.207
154.392
126.882
119.423
118.137
108.214
92.277
78.186
77.317
77.000
76.682
61.453
55.845
34.471
14.327
14.082
MeO
NO2
Me
CO2Et
2h
f1 (ppm)

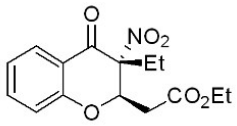

chq-2017-12-22-1
7.883
7.861
7.260
6.707
6.701
6.685
6.679
6.453
6.449
5.610
5.605
5.585
5.581
4.259
4.241
4.224
4.206
3.858
2.874
2.849
2.834
2.809
2.457
2.453
2.417
2.413
1.731
1.313
1.295
1.277
0.005
NO2
Me
CO2Et
MeO
2i
0.98
1.00
1.00
0.95
2.00
3.01
1.02
1.00
3.00
3.06
f1 (ppm)


chq-2017-12-22-1
183.517
168.465
167.260
161.801
130.170
111.986
111.692
100.947
91.997
78.166
77.317
77.000
76.682
61.475
55.902
34.581
14.467
14.122
NO2
Me
CO2Et
MeO
2i
f1 (ppm)

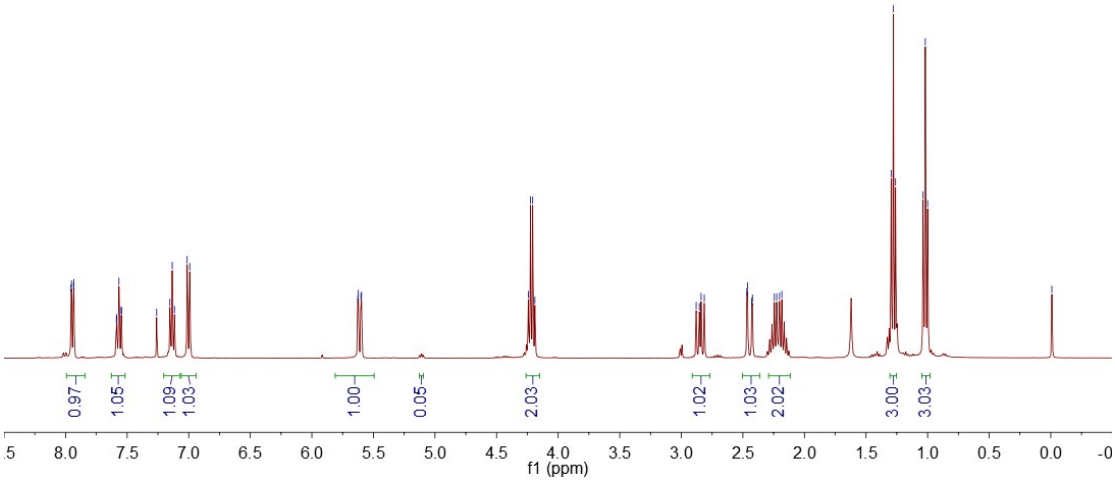

CHQ-9-26-2
7.540
7.538
7.521
7.518
7.260
7.145
7.128
7.126
7.091
7.071
7.051
5.631
5.624
5.607
5.600
4.250
4.232
4.214
4.196
3.870
2.972
2.947
2.931
2.907
2.499
2.492
2.459
2.452
1.757
1.304
1.286
1.268
NO2
Me
CO2Et
O
OMe
2j
1.00
0.99
1.07
1.03
2.07
3.04
1.05
1.02
3.06
3.07
f1 (ppm)


CHQ-9-26-2
185.005
168.366
149.903
148.917
122.798
119.292
119.036
118.728
92.122
78.480
77.318
77.000
76.682
61.510
56.466
34.511
14.301
14.039
NO2
Me
CO2Et
O
OMe
2j
f1 (ppm)

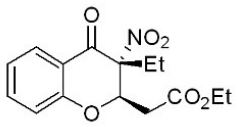
CHQ-10-6-2



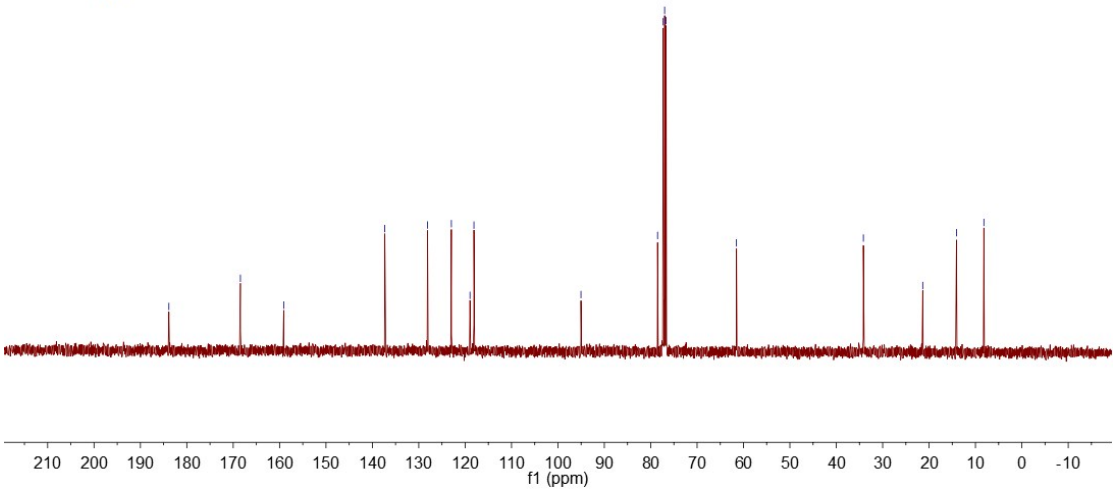
2k (contains 5% of the minor diastereomer)

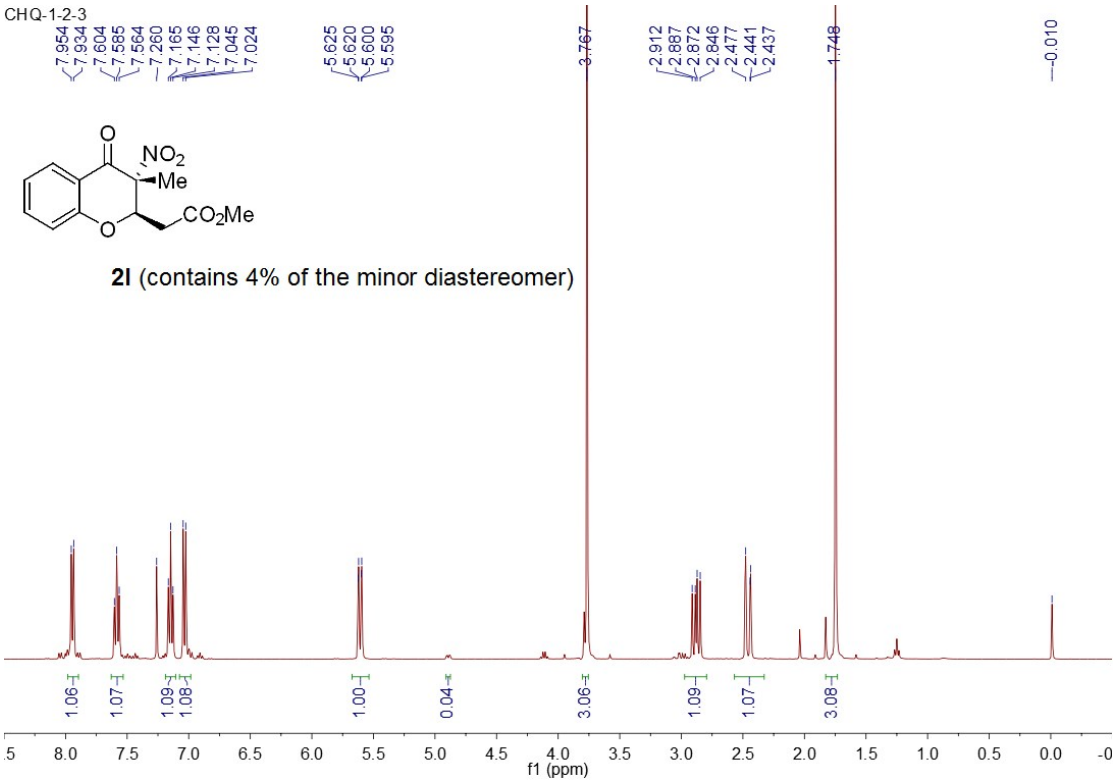


CHQ-10-6-2

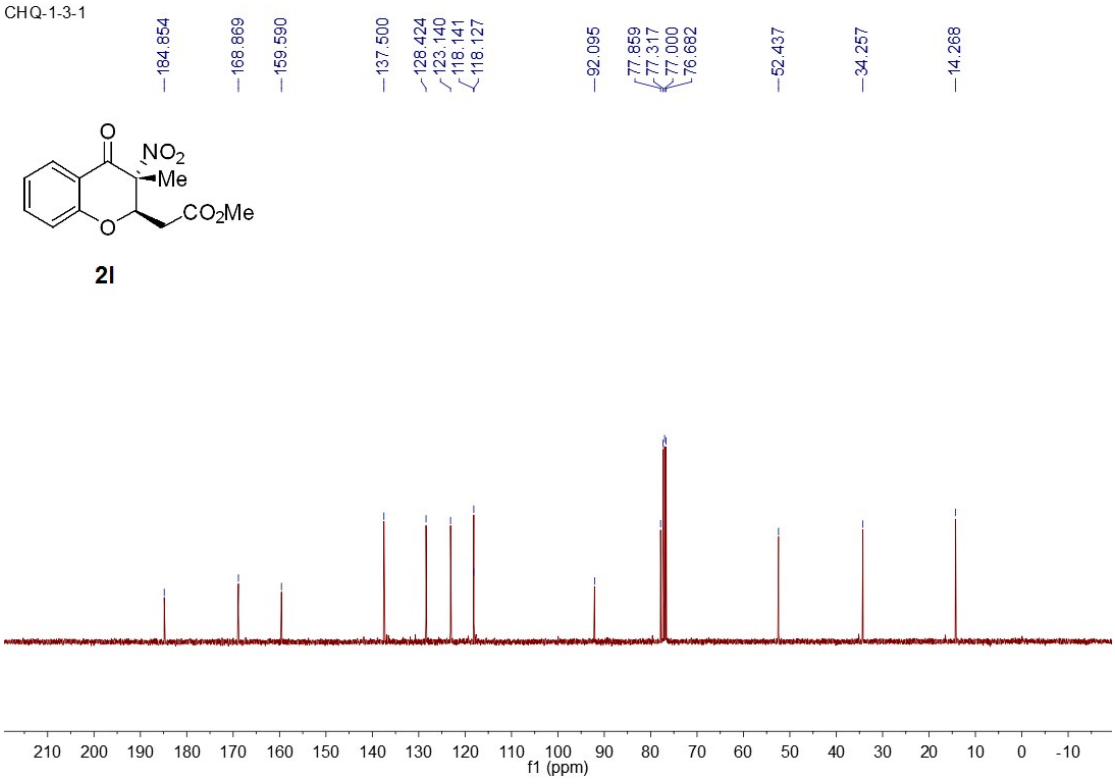


2k



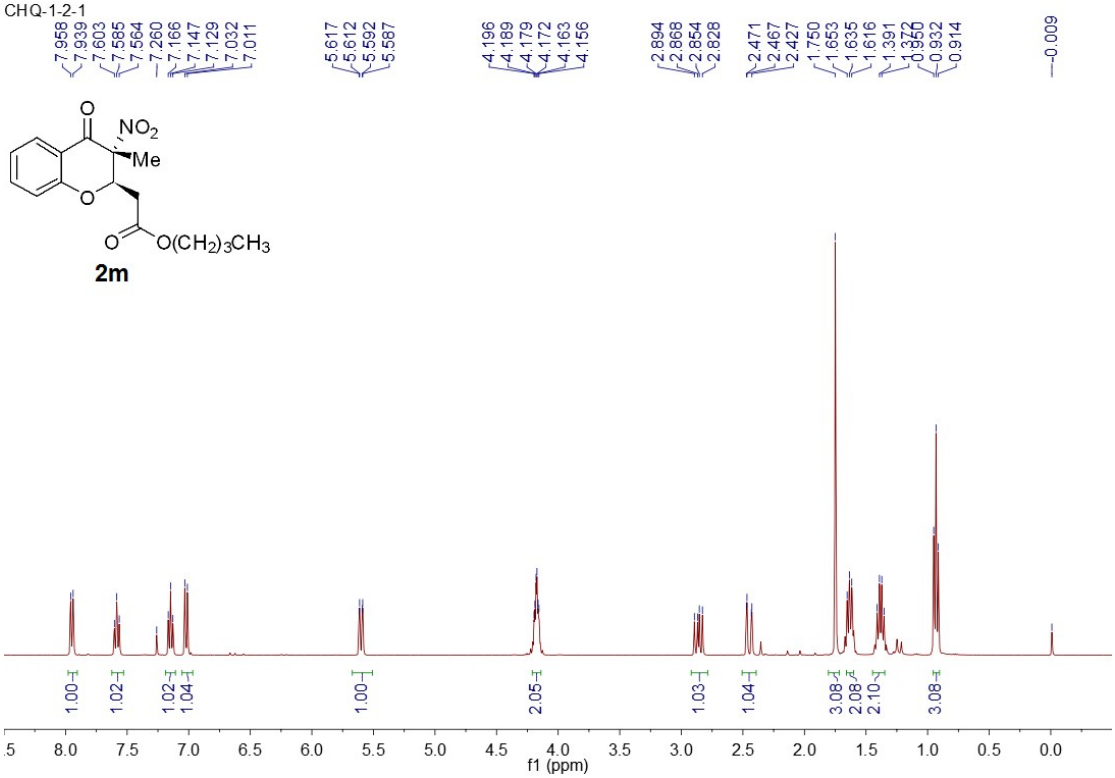


2l (contains 4% of the minor diastereomer)



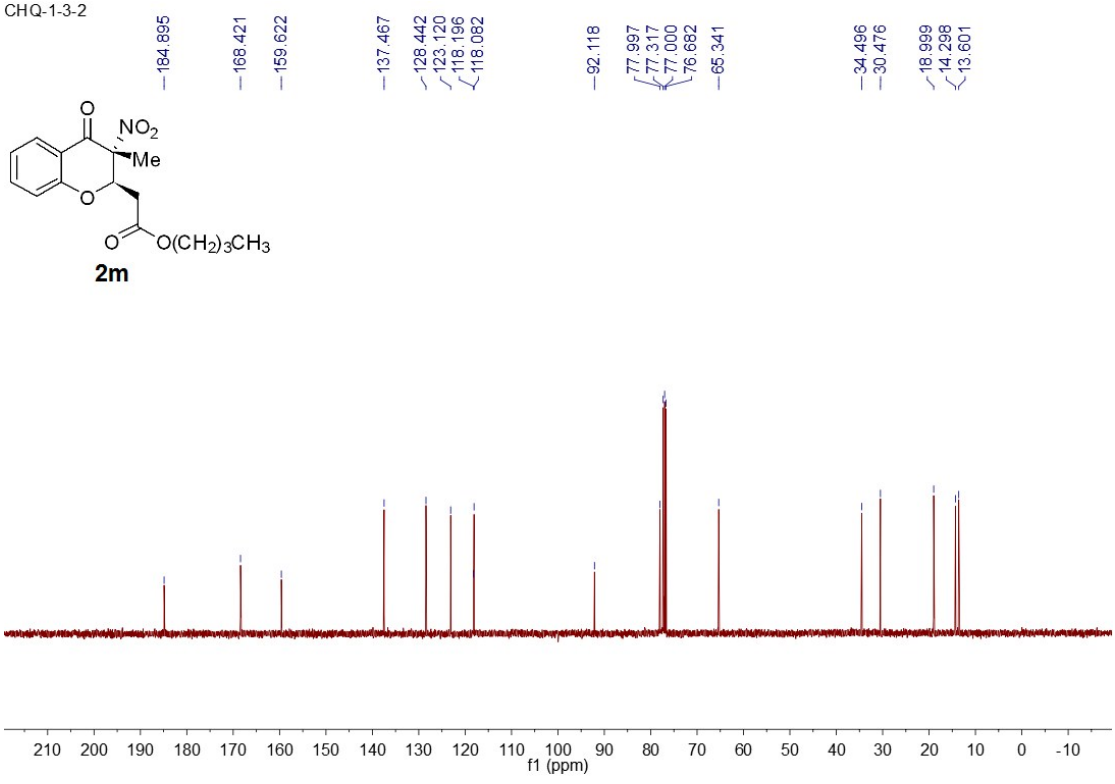
2l

CHQ-1-2-1

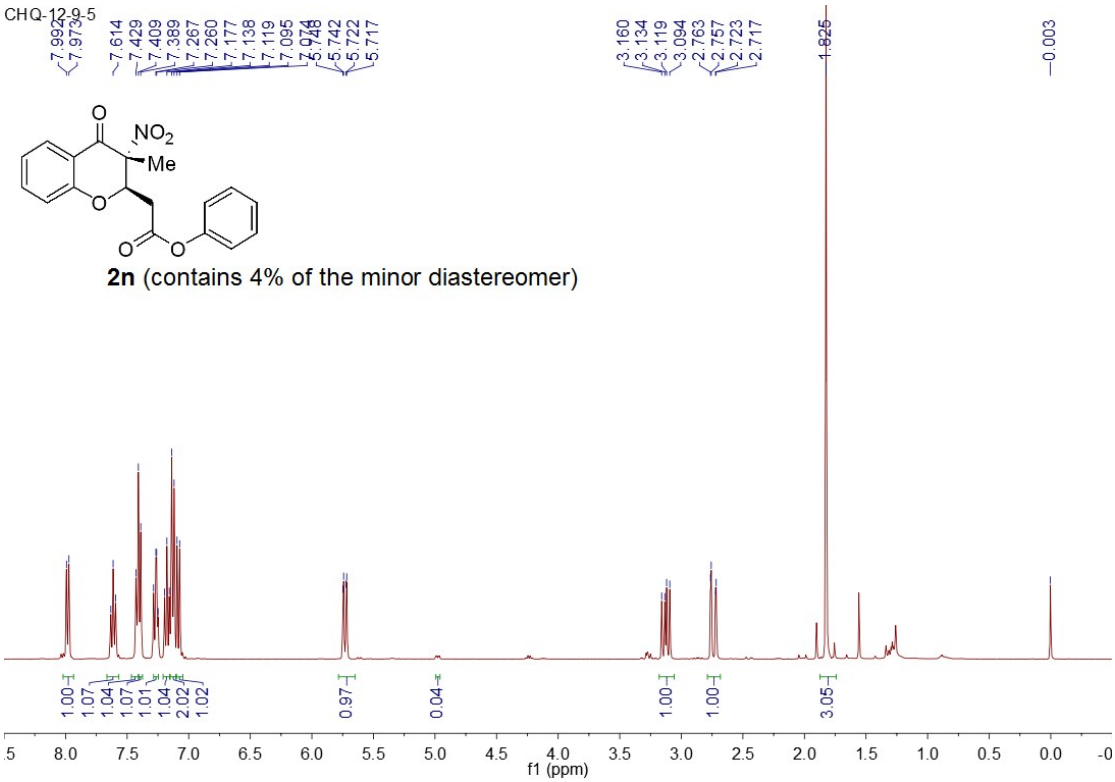


2m

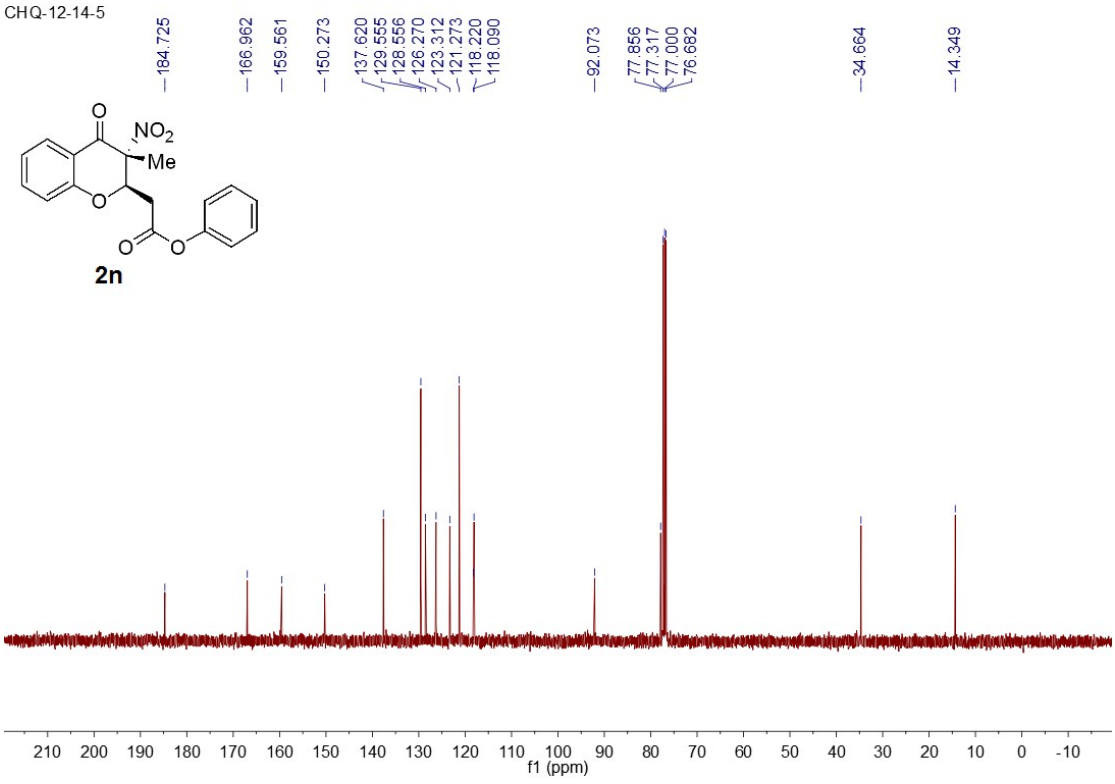
CHQ-1-3-2



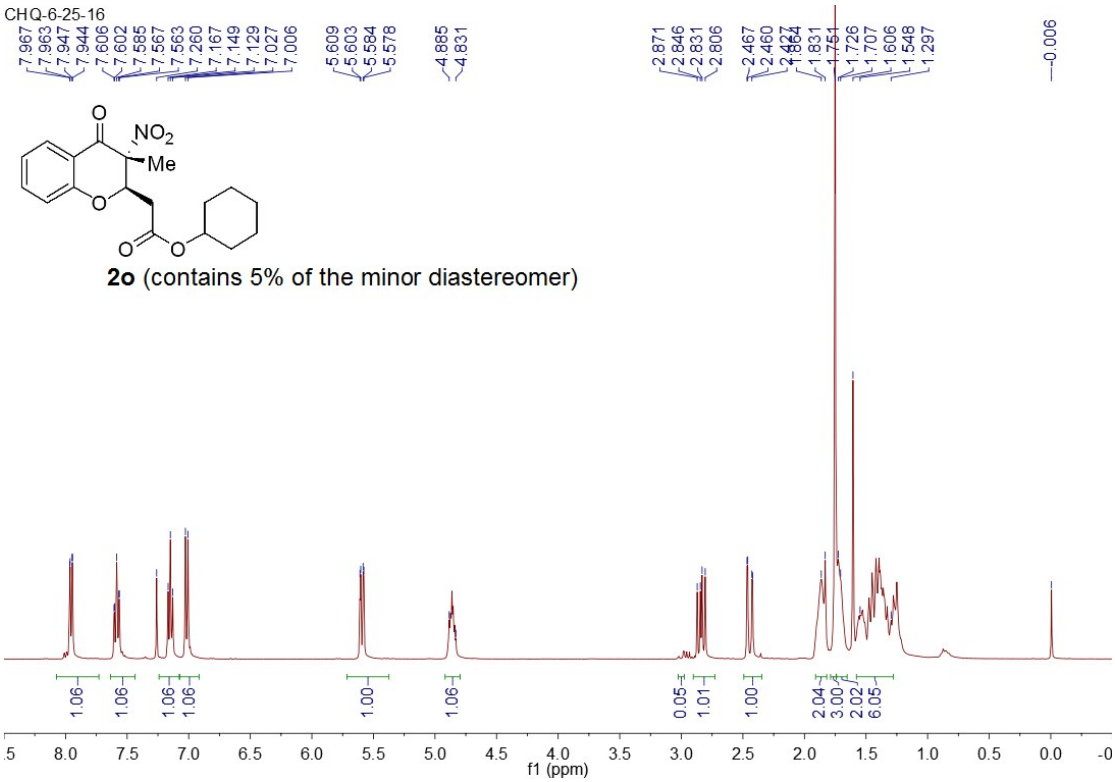
2m



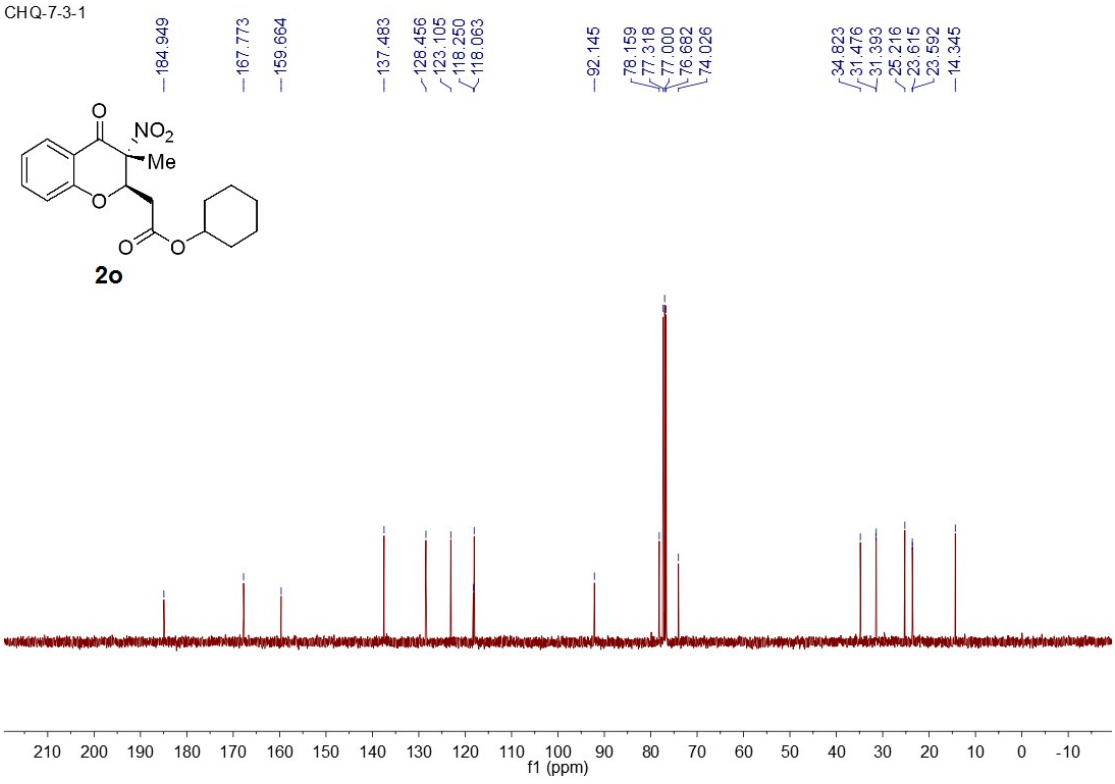
2n (contains 4% of the minor diastereomer)



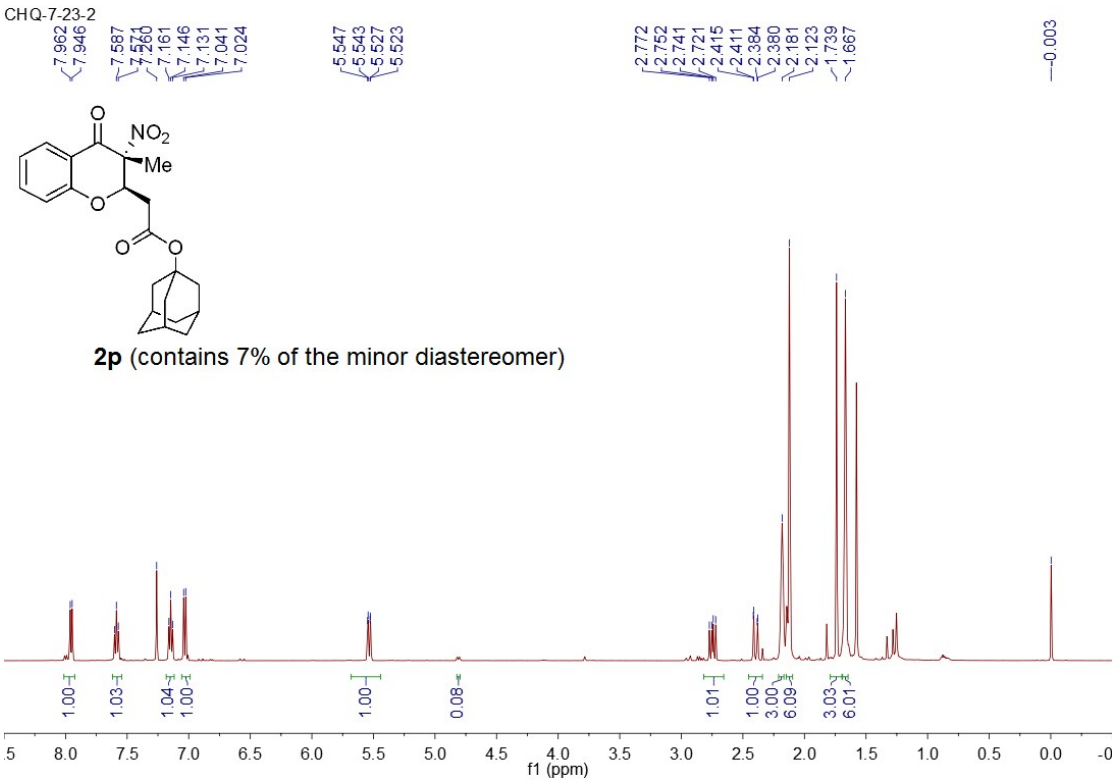
2n



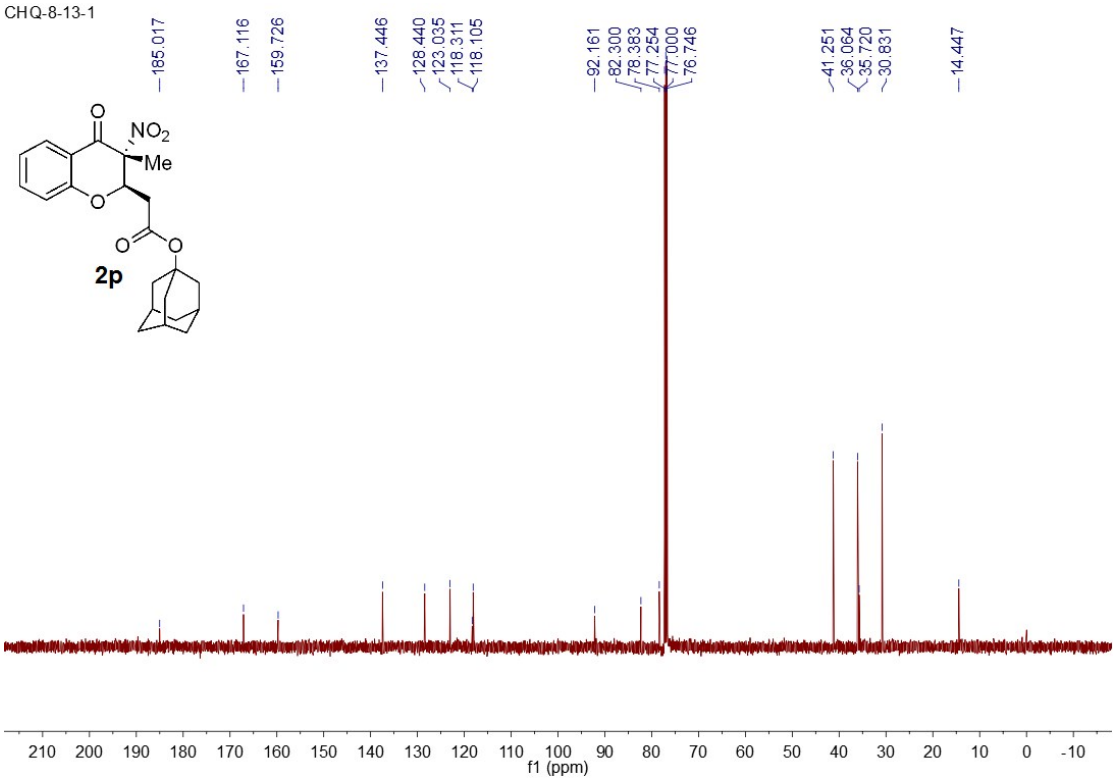
2o (contains 5% of the minor diastereomer)



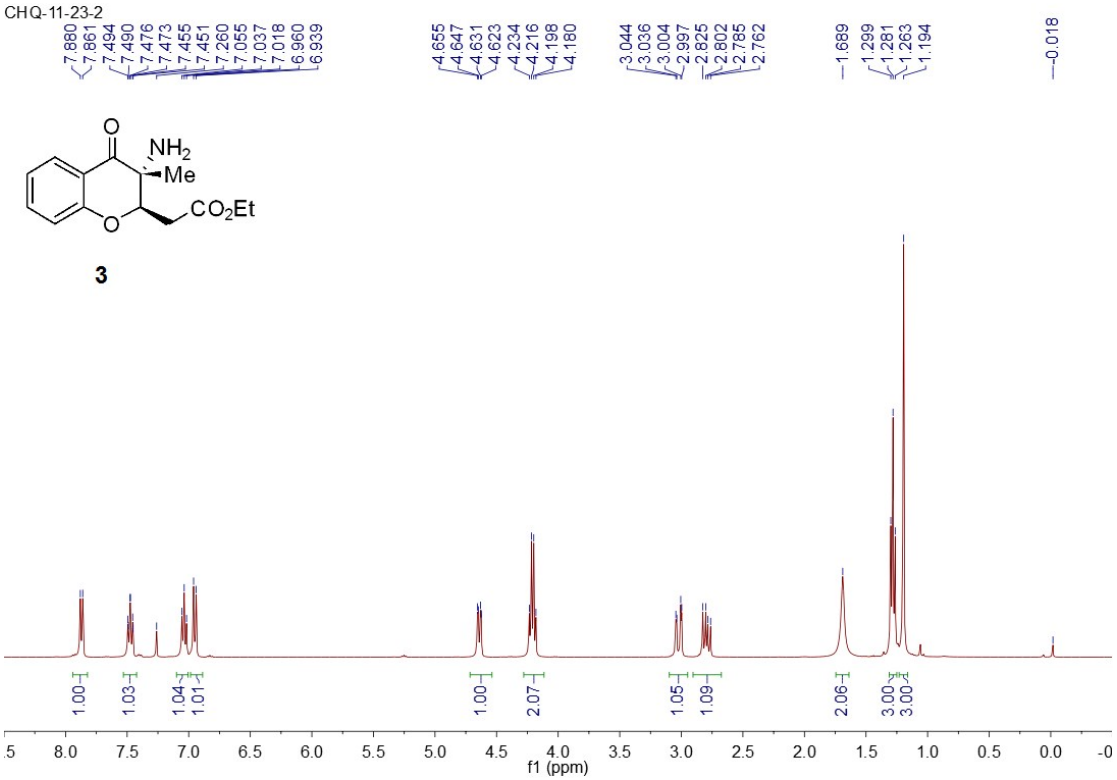
2o



2p (contains 7% of the minor diastereomer)

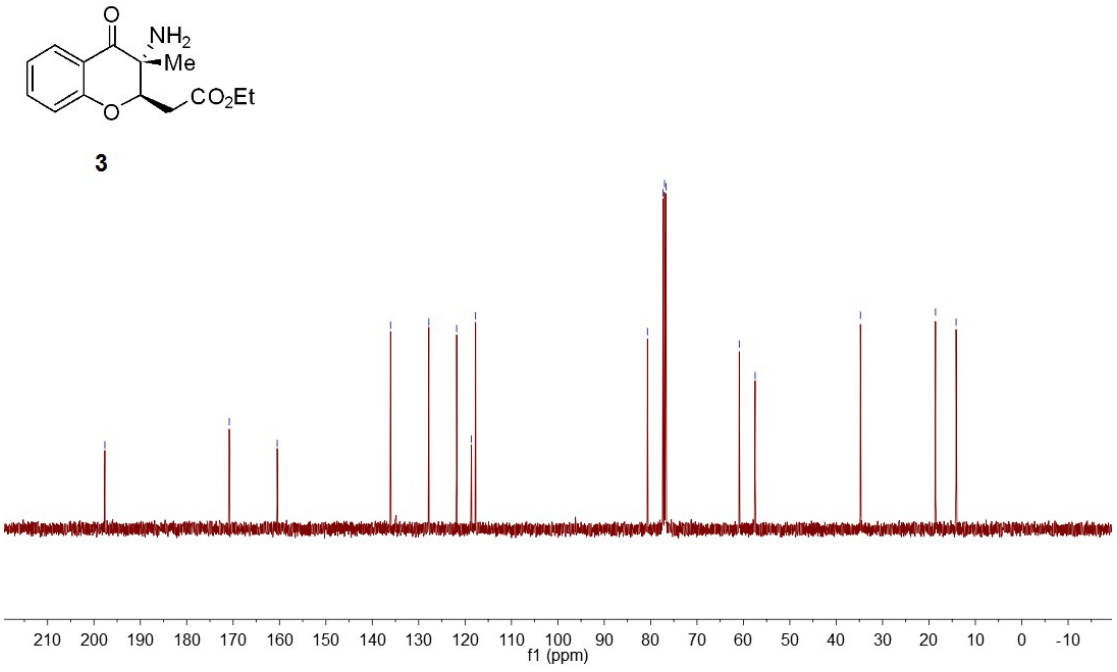


CHQ-11-23-2



3

CHQ-11-23-2



3