

SUPPORTING INFORMATION

Asymmetric phase-transfer catalysed β -addition of isoxazolidin-5-ones to MBH carbonates

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1. Experimental

1.1 General information

¹H- and ¹³C-NMR spectra were recorded on a Bruker Avance III 300 MHz spectrometer with a broad band observe probe, a Bruker Avance III HD 600 and a Bruker Avance-400 at room temperature. All NMR spectra were referenced to residual CHCl₃ (7.26 ppm, ¹H; 77.00 ppm, ¹³C). The following abbreviations are used to indicate the multiplicity in NMR spectra: s = singlet; d = doublet; t = triplet; q = quartet; dd = double doublet; ddd = double doublet of doublet; m = multiplet; bs = broad signal.

Optical rotation of compounds was performed on a Jasco P-2000 digital polarimeter and a Schmidt + Haensch Polarimeter Model UniPol L 1000.

High resolution mass spectra (HRMS) were acquired using a Bruker solariX XR Fourier transform ion cyclotron resonance mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a 7 T refrigerated actively-shielded superconducting magnet. The samples were ionized in positive ion mode using a MALDI ion source.

FTIR spectra were recorded as thin films on KBr plates using Bruker Tensor 27 spectrometer.

HPLC analyses were performed using a Waters-Breeze 2487, UV dual λ absorbance detector and 1525 Binary HPLC Pump and a Thermo Scientific Dionex Ultimate 3000 system with diode array detector, using a Chiralpak AD-H (250 x 4.6 mm, 5 μm), IC (250 x 4.6 mm, 5 μm), IA-3 (250 x 4.6 mm, 5 μm) or a YMC Cellulose-SB (250 x 4.6 mm, 5 μm) chiral stationary phase.

All chemicals were purchased from commercial suppliers and used without further purification. All reactions were performed under an Ar atmosphere.

Catalysts **A1-2**, **B**, **C**, **D1-3** were either commercial or prepared as described previously.^{1,2,3,4}

¹ M .Parvez, N. Haraguchi, S. Itsuno, *Macromolecules*, **2014**, 47, 1922–1928.

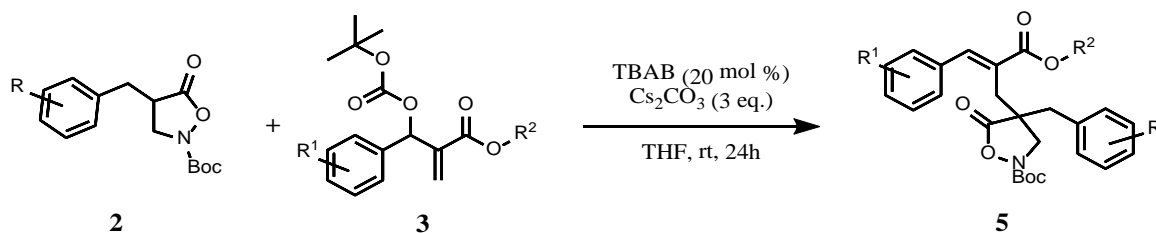
² P .Nun, V. Pérez, M. Calmès, J. Martinez, F. Lamaty, *Chem. Eur. J.*, **2012**, 18, 3773-3779.

³ M. Tiffner, J. Novacek, A. Busillo, K. Gratzner, A. Massa, M. Waser, *RSC Adv.*, **2015**, 5, 78941.

⁴ M.Waser, K. Gratzner, R. Herchl, N. Müller, *Org. Biomol. Chem.*, **2012**, 10, 251.

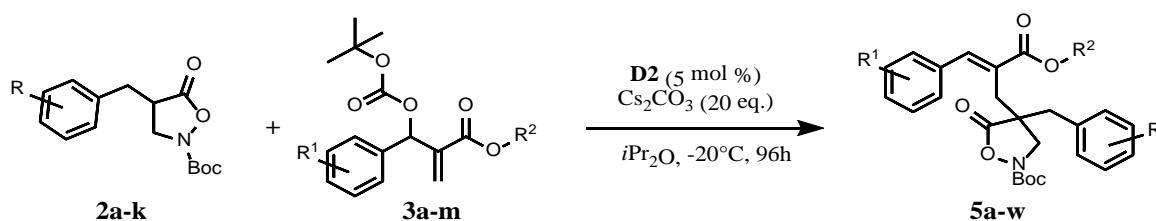
1.2 Experimental procedures and compounds characterization

1.2.1 General procedure for the synthesis of racemic compounds **5**:

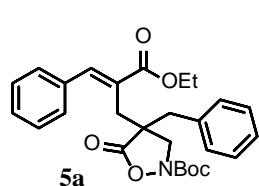


In a Schlenk tube, under argon atmosphere, the Baylis-Hillman carbonate **3** (1.5 eq., 0.15 mmol), benzyl-substituted isoxazolidin-5-one **2** (1.0 eq., 0.10 mmol) and tetrabutylammonium bromide (0.20 eq., 0.020 mmol, 6.4 mg) were dissolved in THF (2 ml). Then, Cs₂CO₃ (3.0 eq., 0.30 mmol, 98 mg) was added and the resulting heterogeneous solution was stirred (1000 rpm) at room temperature for 24 h. Then, the mixture was filtered over a pad of Na₂SO₄, the solvent evaporated and the residue dried in vacuo. The resulting crude product was purified by chromatography (silica gel, heptane-ethyl acetate, 15/1 to 10/1) to afford racemic products **5**.

1.2.2 General procedure A for the asymmetric β -addition of isoxazolidin-5-ones to MBH carbonates to obtain enantioenriched products **5a-w**:

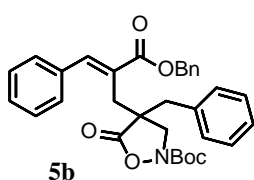


In a Schlenk tube, under argon atmosphere, the Baylis-Hillman carbonate **3a-m** (1.5 eq., 0.15 mmol), benzyl-substituted isoxazolidin-5-one **2a-k** (1.0 eq., 0.10 mmol) and catalyst **D2** (0.05 eq., 0.005 mmol, 5.4 mg) were charged and dissolved in 2.0 ml of isopropyl ether, and the mixture cooled at -20°C. After 20 minutes, Cs₂CO₃ (3.0 eq., 0.30 mmol, 97.7 mg) was quickly added and the mixture was stirred (1000 rpm) for 96 h. Then, the mixture was filtered over a pad of Na₂SO₄, washed with DCM, the solvent evaporated, and the residue dried in vacuo. The resulting crude product was purified by chromatography (silica gel, heptane-ethyl acetate, 15/1 to 10/1) to afford enantioenriched products **5a-w**.



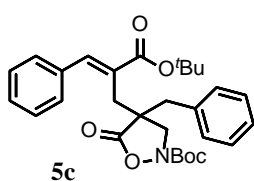
tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5a): Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5 eq.), the title compound **5a** was obtained as a colorless oil (41.9 mg, 90%, E/Z= 10:1, e.r.= 94:6 (major diastereomer)). $[\alpha]_D^{25} = 43.9^\circ$ (c = 0.41, CHCl₃). ¹H NMR (300 MHz, Chloroform-d, 298 K)

δ 7.83 (s, 1H), 7.30 – 7.06 (m, 8H), 7.04 – 6.94 (m, 2H), 4.21 (q, $J = 7.1$ Hz, 2H), 3.82 – 3.70 (m, 2H), 3.06 (s, 2H), 2.96 (d, $J = 13.9$ Hz, 1H), 2.58 (d, $J = 13.9$ Hz, 1H), 1.40 (s, 9H), 1.28 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 175.5, 167.7, 154.9, 143.5, 134.9, 134.9, 130.4, 128.9, 128.8, 128.7, 128.7, 128.0, 127.4, 83.6, 61.4, 54.4, 49.8, 40.8, 31.7, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2977, 2938, 1794, 1712, 1454, 1369, 1254, 1202, 1146, 1095, 1022, 848, 754, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₁NNaO₆ [M+Na]⁺ = 488.20456, found: 488.20359; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 95:5, 0.5 mL/min, 10 °C, t_{major} = 46.8 min, t_{minor} = 61.4 min).



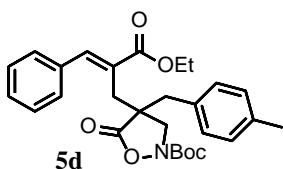
tert-butyl (E)-4-benzyl-4-(2-((benzyloxy)carbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5b): Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and benzyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3b** (55.2 mg, 0.15 mmol, 1.5 eq.), the title compound **5b** was obtained as a colorless oil (35.9 mg, 68%, E/Z = 8:1, e.r. = 78:22 (major diastereomer)).

$[\alpha]_D^{25} = 22.3^\circ$ ($c = 0.22$, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.85 (s, 1H), 7.46 – 7.04 (m, 13H), 7.04 – 6.89 (m, 2H), 5.22 (d, $J = 12.3$ Hz, 1H), 5.15 (d, $J = 12.3$ Hz, 1H), 3.79 (d, $J = 11.1$ Hz, 1H), 3.73 (d, $J = 11.1$ Hz, 1H), 3.08 (s, 2H), 2.95 (d, $J = 13.9$ Hz, 1H), 2.57 (d, $J = 13.9$ Hz, 1H), 1.38 (s, 9H) ppm; ^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 175.4, 167.6, 154.9, 143.8, 135.8, 134.8, 134.8, 130.4, 128.9, 128.8, 128.7, 128.6, 128.6, 128.3, 127.8, 127.4, 83.6, 67.1, 54.5, 49.9, 40.7, 31.8, 28.1 ppm; **IR** (film): ν (cm⁻¹) 2920, 2852, 1794, 1713, 1633, 1497, 1456, 1369, 1253, 1146, 1030, 848, 753, 700; **HRMS (MALDI-FT ICR)**: m/z calcd for C₃₂H₃₃NNaO₆ [M+Na]⁺ = 550.22001, found: 550.21909; The enantioselectivity was determined by **HPLC** (YMC Cellulose-SB column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, 10 °C, t_{minor} = 21.1 min, t_{major} = 26.7 min).



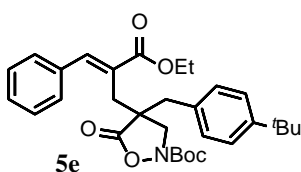
tert-butyl (E)-4-benzyl-4-(2-(tert-butoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5c): Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and tert-butyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3c** (50.2 mg, 0.15 mmol, 1.5 eq.), the title compound **5c** was obtained as a colorless oil (26.2 mg, 53%, E/Z = 8:1, e.r. = 91:9 (major diastereomer)).

$[\alpha]_D^{24} = 33.0^\circ$ ($c = 1.00$, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.82 (s, 1H), 7.40 – 7.14 (m, 8H), 7.10 – 7.00 (m, 2H), 3.83 (d, $J = 10.9$ Hz, 1H), 3.76 (d, $J = 10.9$ Hz, 1H), 3.11 (s, 2H), 3.02 (d, $J = 13.9$ Hz, 1H), 2.63 (d, $J = 13.9$ Hz, 1H), 1.54 (s, 9H), 1.46 (s, 9H) ppm; ^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 175.2, 166.8, 154.9, 142.5, 135.3, 135.0, 130.4, 129.5, 128.8, 128.7, 128.7, 128.4, 127.4, 83.6, 81.9, 54.6, 50.0, 40.7, 31.5, 28.1, 28.0 ppm; **IR** (film): ν (cm⁻¹) 2976, 2933, 1798, 1711, 1495, 1477, 1455, 1394, 1369, 1255, 1147, 1017, 850, 758, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₉H₃₅NNaO₆ [M+Na]⁺ = 516.23566, found: 516.23499; The enantioselectivity was determined by **HPLC** (Chiralpak IA-3 column, n-hexane:i-PrOH = 80:20, 0.8 mL/min, t_{major} = 6.4 min, t_{minor} = 8.6 min).



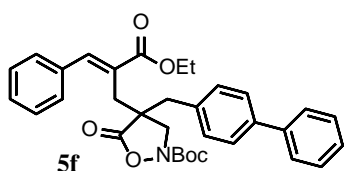
tert-butyl (E)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-4-(4-methylbenzyl)-5-oxoisoxazolidine-2-carboxylate (5d): Following the general procedure A with tert-butyl 4-(4-methylbenzyl)-5-oxoisoxazolidine-2-carboxylate **2b** (29.1 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5

eq.), the title compound **5d** was obtained as a colorless oil (44.1 mg, 92%, E/Z= 8:1, e.r.= 92:8 (major diastereomer)). $[\alpha]_D^{25} = 30.9^\circ$ ($c = 0.80$, CHCl_3). $^1\text{H NMR}$ (300 MHz, Chloroform- d , 298 K) δ 7.82 (s, 1H), 7.30 – 7.15 (m, 3H), 7.14 – 7.06 (m, 2H), 6.97 (d, $J = 7.8$ Hz, 2H), 6.87 (d, $J = 7.8$ Hz, 2H), 4.20 (q, $J = 7.2$ Hz, 2H), 3.76 (s, 2H), 3.04 (s, 2H), 2.91 (d, $J = 14.0$ Hz, 1H), 2.54 (d, $J = 14.0$ Hz, 1H), 2.24 (s, 3H), 1.39 (s, 9H), 1.28 (d, $J = 7.2$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (75 MHz, Chloroform- d , 298 K) δ 175.7, 167.7, 154.9, 143.5, 137.0, 134.9, 131.7, 130.2, 129.4, 128.9, 128.7, 128.6, 128.0, 83.6, 61.4, 54.4, 49.8, 40.5, 31.7, 28.1, 21.0, 14.1 ppm; **IR** (film): ν (cm^{-1}) 2978, 2937, 1197, 1715, 1629, 1446, 1369, 1254, 1202, 1147, 1023, 848, 813, 763, 700; **HRMS (MALDI-FT ICR):** m/z calcd for $\text{C}_{28}\text{H}_{33}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+ = 502.22001$, found: 502.21955; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, $t_{\text{major}} = 11.9$ min, $t_{\text{minor}} = 16.0$ min).



tert-butyl (E)-4-(4-(tert-butyl)benzyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5e): Following the general procedure A with tert-butyl 4-(4-(tert-butyl)benzyl)-5-oxoisoxazolidine-2-carboxylate **2c** (33.3 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg,

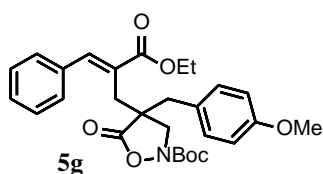
0.15 mmol, 1.5 eq.), the title compound **5e** was obtained as a colorless oil (40.2 mg, 77%, E/Z= 11:1, e.r.= 95:5 (major diastereomer)). $[\alpha]_D^{24} = 41.8^\circ$ ($c = 1.00$, CHCl_3). $^1\text{H NMR}$ (300 MHz, Chloroform- d , 298 K) δ 7.82 (s, 1H), 7.25 – 7.16 (m, 5H), 7.16 – 7.09 (m, 2H), 6.92 (d, $J = 7.9$ Hz, 2H), 4.20 (d, $J = 7.2$ Hz, 2H), 3.77 (s, 2H), 3.06 (s, 2H), 2.91 (d, $J = 14.0$ Hz, 1H), 2.54 (d, $J = 14.0$ Hz, 1H), 1.41 (s, 9H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.22 (s, 9H) ppm; $^{13}\text{C NMR}$ (75 MHz, Chloroform- d , 298 K) δ 175.6, 167.7, 155.0, 150.2, 143.5, 135.0, 131.7, 130.2, 129.0, 128.7, 128.6, 128.0, 125.6, 83.6, 61.4, 54.4, 49.7, 40.2, 34.4, 31.6, 31.3, 28.1, 14.1 ppm; **IR** (film): ν (cm^{-1}) 2968, 2869, 1797, 1745, 1714, 1629, 1494, 1477, 1394, 1446, 1369, 1318, 1254, 1202, 1147, 1099, 1020, 850, 757, 701; **HRMS (MALDI-FT ICR):** m/z calcd for $\text{C}_{31}\text{H}_{39}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+ = 544.26696$, found: 544.26614; The enantioselectivity was determined by **HPLC** (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, $t_{\text{minor}} = 11.0$ min, $t_{\text{major}} = 17.7$ min).



tert-butyl (E)-4-([1,1'-biphenyl]-4-ylmethyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5f): Following the general procedure A with tert-butyl 4-([1,1'-biphenyl]-4-ylmethyl)-5-oxoisoxazolidine-2-carboxylate **2d** (35.3 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0

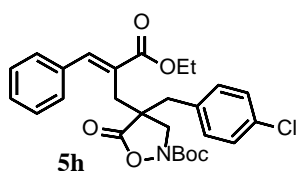
mg, 0.15 mmol, 1.5 eq.), the title compound **5f** was obtained as a colorless oil (40.1 mg, 74%, E/Z= 9:1, e.r.= 92:8 (major diastereomer)). $[\alpha]_D^{25} = 19.8^\circ$ ($c = 0.36$, CHCl_3). $^1\text{H NMR}$ (300 MHz, Chloroform- d , 298 K) δ 7.91 (s, 1H), 7.56 (d, $J = 7.8$ Hz, 2H), 7.50 – 7.41 (m, 4H), 7.39 – 7.34 (m, 1H), 7.31 – 7.23 (m, 3H), 7.19 (s, 2H), 7.14 (d, $J = 7.8$ Hz, 2H), 4.29 (q, $J = 7.1$ Hz, 2H), 3.88 (s, 2H), 3.16 (s, 2H), 3.06 (d, $J = 13.9$ Hz, 1H), 2.71 (d, $J = 13.9$ Hz, 1H), 1.47 (s, 9H), 1.36 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (75 MHz, Chloroform- d , 298 K) δ 175.6, 167.7, 155.0, 143.6, 140.5,

140.3, 134.9, 133.9, 130.8, 128.8, 128.8, 128.6, 128.0, 127.4, 127.4, 127.0, 83.7, 61.5, 54.4, 49.8, 40.5, 31.6, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2979, 2935, 1796, 1713, 1636, 1488, 1447, 1369, 1253, 1202, 1149, 1008, 848, 754, 698; **HRMS (MALDI-FT ICR)**: m/z calcd for C₃₃H₃₅NNaO₆ [M+Na]⁺ = 564.23566, found: 564.23488; The enantioselectivity was determined by **HPLC** (YMC Cellulose-SB column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, t_{minor} = 25.5 min, t_{major} = 29.1 min).



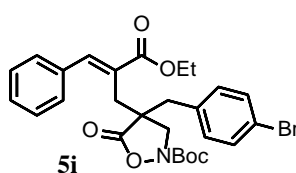
tert-butyl (E)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-4-(4-methoxybenzyl)-5-oxoisoxazolidine-2-carboxylate (5g): Following the general procedure A with tert-butyl 4-(4-methoxybenzyl)-5-oxoisoxazolidine-2-carboxylate **2e** (30.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg,

0.15 mmol, 1.5 eq.), the title compound **5g** was obtained as a colorless oil (38.1 mg, 77%, E/Z = 10:1, e.r. = 93:7 (major diastereomer)). $[\alpha]_D^{25}$ = 23.1° (c = 0.30, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.89 (s, 1H), 7.35 – 7.27 (m, 3H), 7.21 – 7.14 (m, 2H), 6.98 (d, J = 8.2 Hz, 2H), 6.77 (d, J = 8.2 Hz, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.83 (s, 2H), 3.78 (s, 3H), 3.11 (s, 2H), 2.97 (d, J = 14.1 Hz, 1H), 2.59 (d, J = 14.1 Hz, 1H), 1.46 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.7, 167.7, 158.9, 154.9, 143.5, 143.4, 134.9, 131.4, 128.9, 128.7, 128.6, 128.0, 126.7, 114.1, 83.6, 61.4, 55.2, 54.3, 49.9, 40.1, 31.7, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2979, 2930, 1797, 1715, 1612, 1514, 1458, 1369, 1303, 1252, 1202, 1181, 1146, 1034, 847, 763, 700; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₈H₃₃NNaO₇ [M+Na]⁺ = 518.21492, found: 518.21471; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, 10 °C, t_{major} = 23.0 min, t_{minor} = 31.3 min).



tert-butyl (E)-4-(4-chlorobenzyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5h): Following the general procedure A with tert-butyl 4-(4-chlorobenzyl)-5-oxoisoxazolidine-2-carboxylate **2f** (31.2 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5

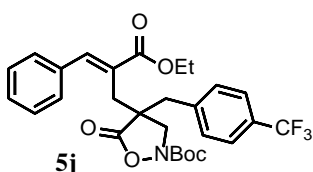
eq.), the title compound **5h** was obtained as a colorless oil (40.0 mg, 80%, E/Z = 6:1, e.r. = 88/12 (major diastereomer)). $[\alpha]_D^{25}$ = 19.0° (c = 0.37, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.91 (s, 1H), 7.38 – 7.27 (m, 3H), 7.24 – 7.14 (m, 4H), 6.97 (d, J = 8.0 Hz, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.84 (d, J = 11.1 Hz, 1H), 3.76 (d, J = 11.1 Hz, 1H), 3.09 (s, 2H), 2.97 (d, J = 14.0 Hz, 1H), 2.61 (d, J = 14.0 Hz, 1H), 1.47 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.4, 167.6, 154.8, 143.7, 134.9, 133.5, 133.3, 131.6, 128.9, 128.8, 128.7, 128.7, 127.9, 83.8, 61.5, 54.4, 49.7, 40.1, 31.6, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2983, 2936, 1795, 1714, 1632, 1494, 1446, 1369, 1253, 1202, 1146, 1095, 1016, 847, 756, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₀ClKNNaO₆ [M+Na]⁺ = 538.13932, found: 538.13875; The enantioselectivity was determined by **HPLC** (YMC Cellulose-SB column, n-hexane:i-PrOH = 90:10, 0.5 mL/min, 10 °C, t_{minor} = 22.7 min, t_{major} = 31.0 min).



tert-butyl (E)-4-(4-bromobenzyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5i): Following the general procedure A with tert-butyl 4-(4-bromobenzyl)-5-oxoisoxazolidine-2-carboxylate **2g** (35.6 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15

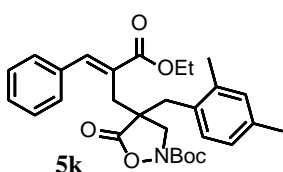
mmol, 1.5 eq.), the title compound **5i** was obtained as a colorless oil (38.1 mg, 70%, E/Z = 10:1,

e.r.= 84:16 (major diastereomer)). $[\alpha]_D^{24} = 24.4^\circ$ (c= 1.00, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.91 (s, 1H), 7.40 – 7.28 (m, 5H), 7.21 – 7.13 (m, 2H), 6.91 (d, J = 8.0 Hz, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.84 (d, J = 11.1 Hz, 1H), 3.76 (d, J = 11.1 Hz, 1H), 3.09 (s, 2H), 2.95 (d, J = 14.0 Hz, 1H), 2.60 (d, J = 14.0 Hz, 1H), 1.47 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.3, 167.6, 154.8, 143.7, 134.9, 133.8, 132.0, 131.8, 128.8, 128.7, 127.9, 121.7, 83.8, 61.5, 54.4, 49.6, 40.12, 31.6, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2980, 2937, 1795, 1712, 1490, 1369, 1253, 1146, 1074, 1012, 846, 755, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₀BrNNaO₆ [M+Na]⁺ = 566.11487, found: 566.11407; The enantioselectivity was determined by **HPLC** (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, t_{minor} = 12.7 min, t_{major} = 24.8 min).



tert-butyl (E)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxo-4-(4-(trifluoromethyl)benzyl)isoxazolidine-2-carboxylate (5j): Following the general procedure A with tert-butyl 5-oxo-4-(4-(trifluoromethyl)benzyl)isoxazolidine-2-carboxylate **2h** (34.5 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-

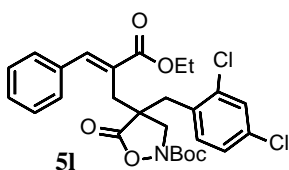
butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5 eq.), the title compound **5j** was obtained as a colorless oil (43.8 mg, 82%, E/Z= 10:1, e.r.= 85:15 (major diastereomer)). $[\alpha]_D^{26} = 25.2^\circ$ (c = 0.50, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.93 (s, 1H), 7.48 (d, J = 7.9 Hz, 2H), 7.34 – 7.27 (m, 3H), 7.23 – 7.11 (m, 4H), 4.28 (q, J = 7.1 Hz, 2H), 3.87 (d, J = 11.1 Hz, 1H), 3.74 (d, J = 11.1 Hz, 1H), 3.11 (s, 2H), 3.04 (d, J = 13.9 Hz, 1H), 2.70 (d, J = 13.9 Hz, 1H), 1.47 (s, 9H), 1.36 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.1, 167.5, 154.8, 143.8, 139.0, 134.9, 130.6, 129.7 (q, J= 32.6 Hz), 128.8, 128.7, 128.7, 127.8, 125.6 (q, J= 3.7 Hz), 124.0 (q, J= 272.0 Hz), 83.9, 61.5, 54.6, 49.7, 40.4, 31.6, 28.0, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2919, 2849, 1798, 1714, 1634, 1447, 1370, 1326, 1255, 1203, 1163, 1125, 1068, 1019, 850, 764, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₈H₃₀F₃NNaO₆ [M+Na]⁺ = 556.19174, found: 556.19087; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, t_{major} = 14.3 min, t_{minor} = 25.6 min).



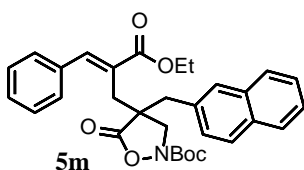
tert-butyl (E)-4-(2,5-dimethylbenzyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5k): Following the general procedure A with tert-butyl 4-(2,5-dimethylbenzyl)-5-oxoisoxazolidine-2-carboxylate **2i** (30.5 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-

butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5 eq.), the title compound **5k** was obtained as a colorless oil (32.1 mg, 65%, E/Z= 8:1, e.r.= 89:11 (major diastereomer)). $[\alpha]_D^{24} = 66.9^\circ$ (c= 1.00, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.93 (s, 1H), 7.37 – 7.28 (m, 3H), 7.28 – 7.19 (m, 2H), 7.00 (d, J = 7.5 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 4.37 – 4.21 (m, 2H), 3.94 (d, J = 10.9 Hz, 1H), 3.56 (d, J = 10.9 Hz, 1H), 3.23 – 3.08 (m, 2H), 2.96 (d, J = 14.4 Hz, 1H), 2.73 (d, J = 14.4 Hz, 1H), 2.21 (s, 3H), 2.07 (s, 3H), 1.47 (s, 9H), 1.37 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.7, 167.6, 154.8, 143.5, 136.0, 135.1, 133.8, 133.6, 130.8, 130.6, 128.9, 128.8, 128.6, 128.3, 128.0, 83.6, 61.4, 54.2, 50.3, 36.3, 32.2, 28.1, 20.9, 19.5, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2981, 2932, 1796, 1714, 1629, 1504, 1447, 1369, 1257, 1201, 1147, 1099, 1022, 848, 813, 755, 701; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₉H₃₅NNaO₆ [M+Na]⁺ = 516.23566, found:

516.23513; The enantioselectivity was determined by **HPLC** (Chiralpak IC column, n-hexane:i-PrOH = 90:10, 0.5 mL/min, $t_{\text{minor}} = 31.4$ min, $t_{\text{major}} = 46.0$ min).

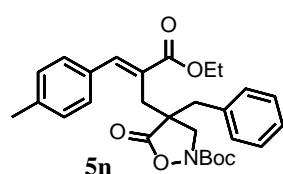


tert-butyl (E)-4-(2,4-dichlorobenzyl)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-5-oxoisoxazolidine-2-carboxylate (5l): Following the general procedure A with tert-butyl 4-(2,4-dichlorobenzyl)-5-oxoisoxazolidine-2-carboxylate **2j** (34.6 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg, 0.15 mmol, 1.5 eq.), the title compound **5l** was obtained as a colorless oil (40.1 mg, 75%, E/Z = 9:1, e.r. = 84:16 (major diastereomer)). $[\alpha]_D^{26} = 37.4^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.96 (s, 1H), 7.45 – 7.27 (m, 6H), 7.12 (s, 2H), 4.29 (q, J = 7.2 Hz, 2H), 3.98 (d, J = 11.2 Hz, 1H), 3.55 (d, J = 11.2 Hz, 1H), 3.25 – 3.10 (m, 2H), 3.02 – 2.95 (m, 2H), 1.46 (s, 9H), 1.36 (d, J = 7.2 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.1, 167.5, 154.7, 143.8, 135.8, 135.0, 134.1, 132.6, 131.9, 129.5, 128.8, 128.8, 128.3, 127.8, 127.7, 83.8, 61.5, 54.4, 50.4, 36.0, 32.3, 28.0, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2979, 1796, 1717, 1475, 1370, 1255, 1202, 1146, 1020, 849, 759, 700; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₂₉Cl₂NNaO₆ [M+Na]⁺ = 556.12641, found: 556.12767; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, $t_{\text{minor}} = 13.7$ min, $t_{\text{major}} = 15.8$ min).



tert-butyl (E)-4-(2-(ethoxycarbonyl)-3-phenylallyl)-4-(naphthalen-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate (5m): Following the general procedure A with tert-butyl 4-(naphthalen-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate **2k** (32.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate **3a** (46.0 mg,

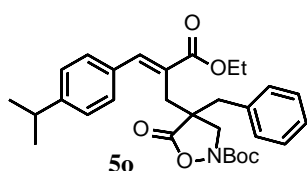
0.15 mmol, 1.5 eq), the title compound **5m** was obtained as a colorless oil (40.2 mg, 78%, E/Z = 9:1, e.r. = 91:9 (major diastereomer)). $[\alpha]_D^{25} = 22.0^\circ$ (c = 0.37, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.91 (s, 1H), 7.87 – 7.78 (m, 1H), 7.78 – 7.70 (m, 2H), 7.54 (s, 1H), 7.52 – 7.43 (m, 2H), 7.22 – 7.08 (m, 6H), 4.29 (q, J = 6.8 Hz, 2H), 3.96 – 3.83 (m, 2H), 3.26 – 3.14 (m, 3H), 2.83 (d, J = 13.9 Hz, 1H), 1.39 (d, J = 16.1 Hz, 12H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.7, 167.7, 154.8, 143.6, 134.8, 133.4, 132.6, 132.4, 129.3, 128.7, 128.6, 128.6, 128.4, 128.2, 128.0, 127.8, 127.6, 126.8, 126.1, 83.6, 61.5, 54.4, 50.0, 41.0, 31.8, 28.0, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2981, 2936, 1796, 1711, 1631, 1369, 1251, 1202, 1147, 1099, 1020, 849, 757, 700; **HRMS (MALDI-FT ICR)**: m/z calcd for C₃₁H₃₂NNaO₆ [M+Na]⁺ = 538.22001, found: 538.21925; The enantioselectivity was determined by **HPLC** (YMC Cellulose-SB column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, 10 °C, $t_{\text{minor}} = 19.2$ min, $t_{\text{major}} = 25.6$ min).



tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-(p-tolyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5n): Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(p-tolyl)methyl)acrylate **3d** (48.0 mg, 0.15 mmol, 1.5 eq.), the title compound

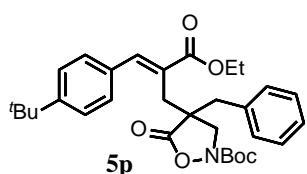
5n was obtained as a colorless oil (39.8 mg, 83%, E/Z = 7:1, e.r. = 92:8 (major diastereomer)). $[\alpha]_D^{25} = 48.8^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.87 (s, 1H), 7.30 – 7.23 (m, 3H), 7.13 – 7.03 (m, 6H), 4.27 (q, J = 7.1 Hz, 2H), 3.90 – 3.77 (m, 2H), 3.15 (s, 2H), 3.04 (d, J = 14.0 Hz, 1H), 2.68 (d, J = 14.0 Hz, 1H), 2.35 (s, 3H), 1.46 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H)

ppm; ^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 175.7, 167.8, 154.9, 143.6, 138.9, 134.9, 131.9, 130.4, 129.5, 129.0, 128.7, 127.4, 127.0, 83.6, 61.4, 54.4, 49.8, 40.9, 31.8, 28.1, 21.3, 14.1 ppm; IR (film): ν (cm $^{-1}$) 2979, 2928, 1797, 1715, 1629, 1497, 1369, 1292, 1147, 1021, 848, 813, 759, 703; HRMS (MALDI-FT ICR): m/z calcd for $\text{C}_{28}\text{H}_{33}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+= 502.22001$, found: 502.21964; The enantioselectivity was determined by HPLC (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, $t_{\text{minor}} = 15.8$ min, $t_{\text{major}} = 25.2$ min).



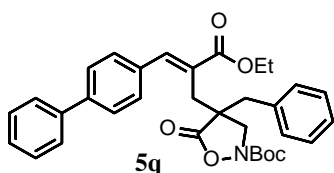
tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-(4-isopropylphenyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5o):

Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(4-isopropylphenyl)methyl)acrylate **3e** (52.3 mg, 0.15 mmol, 1.5 eq.), the title compound **5o** was obtained as a colorless oil (34.0 mg, 67%, E/Z= 6:1, e.r.= 91:9 (major diastereomer)). $[\alpha]_D^{24} = 45.7^\circ$ ($c = 1.00$, CHCl_3). ^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.85 (s, 1H), 7.29 – 7.22 (m, 3H), 7.15 – 7.05 (m, 6H), 4.27 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 2H), 3.22 – 3.09 (m, 2H), 3.05 (d, $J = 14.0$ Hz, 1H), 2.96 – 2.83 (m, 1H), 2.71 (d, $J = 14.0$ Hz, 1H), 1.46 (s, 9H), 1.35 (t, $J = 7.1$ Hz, 3H), 1.26 (s, 3H), 1.24 (s, 3H). ppm; ^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 175.8, 167.9, 154.9, 149.8, 143.6, 134.9, 132.2, 130.5, 129.2, 128.8, 128.7, 127.4, 126.9, 83.6, 61.4, 54.4, 49.7, 41.1, 33.9, 31.8, 28.1, 23.8, 23.8, 14.1 ppm; IR (film): ν (cm $^{-1}$) 2979, 1797, 1714, 1635, 1455, 1369, 1253, 1146, 1017, 848, 703; HRMS (MALDI-FT ICR): m/z calcd for $\text{C}_{30}\text{H}_{37}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+= 530.25131$, found: 530.25046; The enantioselectivity was determined by HPLC (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, $t_{\text{major}} = 14.2$ min, $t_{\text{minor}} = 15.6$ min).



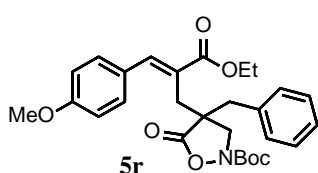
tert-butyl (E)-4-benzyl-4-(3-(4-(tert-butyl)phenyl)-2-(ethoxycarbonyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5p):

Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(4-(tert-butyl)phenyl)methyl)acrylate **3f** (54.4 mg, 0.15 mmol, 1.5 eq.), the title compound **5p** was obtained as a colorless oil (40.2 mg, 77%, E/Z= 8:1, e.r.= 91:9 (major diastereomer)). $[\alpha]_D^{26} = 63.4^\circ$ ($c = 0.80$, CHCl_3). ^1H NMR (400 MHz, Chloroform-d, 298 K) δ 7.84 (s, 1H), 7.32 – 7.22 (m, 5H), 7.11 (d, $J = 7.8$ Hz, 4H), 4.33 – 4.21 (m, 2H), 3.91 – 3.83 (m, 2H), 3.23 – 3.10 (m, 2H), 3.05 (d, $J = 13.9$ Hz, 1H), 2.73 (d, $J = 13.9$ Hz, 1H), 1.47 (s, 9H), 1.38 – 1.29 (m, 12H) ppm; ^{13}C NMR (100 MHz, Chloroform-d, 298 K) δ 175.8, 167.8, 154.8, 152.0, 143.4, 134.9, 131.7, 130.4, 128.9, 128.6, 127.3, 126.8, 125.6, 83.5, 61.3, 54.4, 49.5, 40.9, 34.6, 31.7, 31.1, 28.0, 14.0 ppm; IR (film): ν (cm $^{-1}$) 3023, 2966, 2929, 2856, 1798, 1713, 1456, 1394, 1319, 1295, 1255, 1216, 1192, 1147, 1023, 849, 758, 703, 667; HRMS (MALDI-FT ICR): m/z calcd for $\text{C}_{31}\text{H}_{39}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+= 544.26696$, found: 544.26616; The enantioselectivity was determined by HPLC (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, $t_{\text{minor}} = 12.2$ min, $t_{\text{major}} = 19.9$ min).



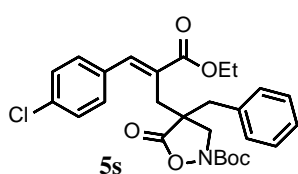
tert-butyl (E)-4-(3-([1,1'-biphenyl]-4-yl)-2-(ethoxycarbonyl)allyl)-4-benzyl-5-oxoisoxazolidine-2-carboxylate (5q): Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-([1,1'-biphenyl]-4-yl)((tert-butoxycarbonyl)oxy)methyl)acrylate **3g** (57.4 mg, 0.15 mmol, 1.5 eq.),

the title compound **5q** was obtained as a colorless oil (49.8 mg, 92%, E/Z= 8:1, e.r.= 92:8 (major diastereomer)). $[\alpha]_D^{23} = 44.1^\circ$ (c = 1.00, CHCl₃). ¹H NMR (300 MHz, Chloroform-d, 298 K) δ 7.92 (s, 1H), 7.61 (d, J = 7.7 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 7.7 Hz, 2H), 7.40 (d, J = 7.4 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.25 (d, J = 6.3 Hz, 4H), 7.15 – 7.04 (m, 2H), 4.30 (q, J = 7.1 Hz, 2H), 3.89 (s, 2H), 3.27 – 3.13 (m, 2H), 3.07 (d, J = 13.9 Hz, 1H), 2.74 (d, J = 13.9 Hz, 1H), 1.47 (s, 9H), 1.37 (t, J = 7.1 Hz, 3H). ppm; ¹³C NMR (75 MHz, Chloroform-d, 298 K) δ 175.7, 167.7, 154.9, 143.1, 141.4, 140.1, 134.9, 133.7, 130.4, 129.6, 128.9, 128.8, 127.8, 127.5, 127.4, 127.0, 127.0, 83.7, 61.5, 54.5, 49.8, 40.9, 31.8, 28.1, 14.1 ppm; IR (film): ν (cm⁻¹) 2978, 2924, 2849, 1797, 1713, 1628, 1604, 1488, 1455, 1369, 1291, 1253, 1146, 1097, 1007, 848, 763, 700; HRMS (MALDI-FT ICR): m/z calcd for C₃₃H₃₅NNaO₆ [M+Na]⁺ = 564.23566, found: 564.23490; The enantioselectivity was determined by HPLC (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, t_{minor} = 17.1 min, t_{major} = 25.6 min).



tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-(4-methoxyphenyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5r):

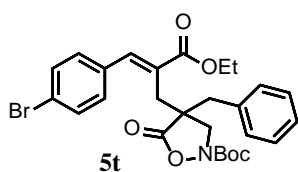
Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(4-methoxyphenyl)methyl)acrylate **3h** (50.4 mg, 0.15 mmol, 1.5 eq.), the title compound **5r** was obtained as a colorless oil (40.1 mg, 81%, E/Z= 11:1, e.r.= 92:8 (major diastereomer)). $[\alpha]_D^{24} = 39.6^\circ$ (c = 1.00, CHCl₃). ¹H NMR (400 MHz, Chloroform-d, 298 K) δ 7.82 (s, 1H), 7.31 – 7.26 (m, 3H), 7.17 – 7.08 (m, 4H), 6.79 (d, J = 8.8 Hz, 2H), 4.26 (m, 2H), 3.87 (s, 2H), 3.82 (s, 3H), 3.16 (s, 2H), 3.06 (d, J = 13.9 Hz, 1H), 2.74 (d, J = 13.9 Hz, 1H), 1.46 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (150 MHz, Chloroform-d, 298 K) δ 175.8, 168.0, 160.0, 154.9, 143.2, 135.0, 130.9, 130.5, 128.7, 127.4, 127.2, 125.6, 114.2, 83.6, 61.3, 55.3, 54.4, 49.8, 41.0, 31.7, 28.1, 14.1 ppm; IR (film): ν (cm⁻¹) 2981, 2921, 2850, 1796, 1709, 1605, 1512, 1456, 1369, 1303, 1255, 1176, 1146, 1030, 847, 759, 700; HRMS (MALDI-FT ICR): m/z calcd for C₂₈H₃₃NNaO₆ [M+Na]⁺ = 518.21492, found: 518.21503; The enantioselectivity was determined by HPLC (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, t_{minor} = 21.8 min, t_{major} = 32.6 min).



tert-butyl (E)-4-benzyl-4-(3-(4-chlorophenyl)-2-(ethoxycarbonyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5s):

Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate **3i** (51.1 mg, 0.15 mmol, 1.5 eq.), the title compound **5s** was obtained as a colorless oil (39.0 mg, 78%, E/Z= 5:1, e.r.= 92:8 (major diastereomer)). $[\alpha]_D^{24} = 37.9^\circ$ (c = 1.00, CHCl₃). ¹H NMR (300 MHz, Chloroform-d, 298 K) δ 7.81 (s, 1H), 7.33 – 7.19 (m, 5H), 7.14 – 7.01 (m, 4H), 4.27 (q, J = 7.1 Hz, 2H), 3.88 – 3.75 (m, 2H), 3.07 (s, 2H), 3.02 (d, J = 14.0 Hz, 1H), 2.69 (d, J = 14.0 Hz, 1H), 1.47 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (75 MHz, Chloroform-d, 298 K) δ 175.5, 167.4, 154.9,

142.1, 134.7, 134.6, 133.2, 130.4, 130.1, 129.0, 128.8, 128.6, 127.5, 83.8, 61.6, 54.4, 49.8, 40.8, 31.4, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2981, 1798, 1713, 1634, 1490, 1369, 1253, 1146, 1093, 1013, 762, 703; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₀ClNNaO₆ [M+Na]⁺ = 522.16539, found: 522.16470; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, t_{major} = 15.1 min, t_{minor} = 17.9 min).



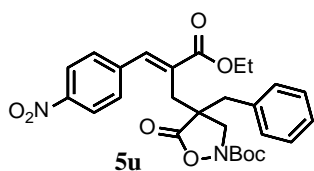
tert-butyl

(E)-4-benzyl-4-(3-(4-bromophenyl)-2-

(ethoxycarbonyl)allyl)-5-oxoisoxazolidine-2-carboxylate

(5t):

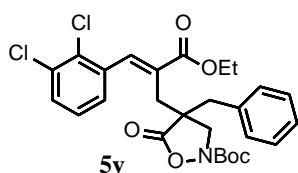
Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-((4-bromophenyl)((tert-butoxycarbonyl)oxy)methyl)acrylate **3j** (57.8 mg, 0.15 mmol, 1.5 eq.), the title compound **5t** was obtained as a colorless oil (44.1 mg, 81%, E/Z = 5:1, e.r. = 91:9 (major diastereomer)). $[\alpha]_D^{26} = 27.0^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 7.78 (s, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.30 – 7.22 (m, 3H), 7.08 – 7.04 (m, 2H), 7.01 (d, J = 8.2 Hz, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.87 – 3.74 (m, 2H), 3.06 (s, 2H), 3.01 (d, J = 13.9 Hz, 1H), 2.68 (d, J = 13.9 Hz, 1H), 1.47 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.5, 167.4, 154.9, 142.2, 134.7, 133.7, 132.0, 130.3, 128.8, 128.7, 127.5, 122.8, 83.8, 61.6, 54.4, 49.8, 40.8, 31.4, 28.1, 14.1 ppm; **IR** (film): ν (cm⁻¹) 2978, 1797, 1712, 1636, 1487, 1456, 1393, 1369, 1308, 1252, 1146, 1074, 1010, 847, 811, 762, 703; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₀BrNNaO₆ [M+Na]⁺ = 566.11487, found: 566.11408; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, t_{major} = 15.1 min, t_{minor} = 18.8 min).



tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-(4-nitrophenyl)allyl)-

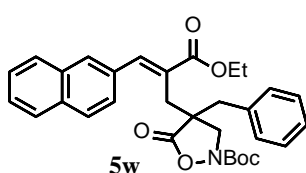
5-oxoisoxazolidine-2-carboxylate (5u):

Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(4-nitrophenyl)methyl)acrylate **3k** (52.7 mg, 0.15 mmol, 1.5 eq.), the title compound **5u** was obtained as a colorless oil (28.1 mg, 55%, E/Z = 5:1, e.r. = 93:7 (major diastereomer)). $[\alpha]_D^{26} = 19.5^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (400 MHz, Chloroform-d, 298 K) δ 8.11 (d, J = 8.5 Hz, 2H), 7.86 (s, 1H), 7.28 (d, J = 8.5 Hz, 2H), 7.27 – 7.20 (m, 3H), 7.04 (d, J = 7.3 Hz, 2H), 4.37 – 4.22 (m, 2H), 3.82 (d, J = 11.0 Hz, 1H), 3.79 (d, J = 11.0 Hz, 1H), 3.03 (s, 2H), 2.99 (d, J = 14.0 Hz, 1H), 2.70 (d, J = 14.0 Hz, 1H), 1.48 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (100 MHz, Chloroform-d, 298 K) δ 175.1, 166.8, 154.8, 147.3, 141.4, 140.7, 134.5, 131.1, 130.2, 129.4, 128.7, 127.5, 123.8, 83.9, 61.8, 54.4, 49.7, 40.8, 31.2, 28.0, 13.9 ppm; **IR** (film): ν (cm⁻¹) 2983, 2933, 2850, 1794, 1719, 1710, 1600, 1476, 1456, 1394, 1370, 1347, 1302, 1254, 1205, 1146, 1110, 1015, 852, 756, 703; **HRMS (MALDI-FT ICR)**: m/z calcd for C₂₇H₃₂N₂NaO₈ [M+2H+Na]⁺ = 535.20509, found: 535.20425; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, t_{major} = 26.3 min, t_{minor} = 30.0 min).



tert-butyl (E)-4-benzyl-4-(3-(2,3-dichlorophenyl)-2-(ethoxycarbonyl)allyl)-5-oxoisoxazolidine-2-carboxylate (5v):

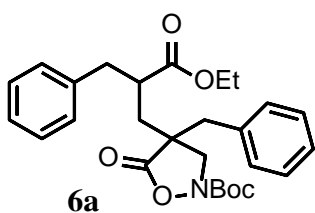
Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(2,3-dichlorophenyl)methyl)acrylate **3l** (56.3 mg, 0.15 mmol, 1.5 eq.), the title compound **5v** was obtained as a colorless oil (41.9 mg, 90%, E/Z= 4:1, e.r.= 93:7 (major diastereomer)). $[\alpha]_D^{26} = 25.3^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (400 MHz, Chloroform-d, 298 K) δ 7.81 (s, 1H), 7.41 (d, J = 7.9 Hz, 1H), 7.23 – 7.17 (m, 3H), 7.14 (t, J = 7.9 Hz, 1H), 7.04 – 6.96 (m, 3H), 4.36 – 4.21 (m, 2H), 3.82 (d, J = 11.0 Hz, 1H), 3.77 (d, J = 11.0 Hz, 1H), 2.99 – 2.92 (m, 3H), 2.59 (d, J = 13.9 Hz, 1H), 1.47 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H). ppm; **¹³C NMR** (100 MHz, Chloroform-d, 298 K) δ 175.2, 166.8, 154.9, 140.2, 135.8, 134.6, 133.6, 131.6, 130.7, 130.3, 130.1, 128.5, 127.7, 127.4, 127.3, 83.7, 61.6, 54.4, 49.7, 40.4, 31.6, 28.0, 14.0. ppm; **IR** (film): ν (cm⁻¹) 3017, 2928 2856, 1795, 1717, 1641, 1559, 1456, 1411, 1395, 1371, 1216, 1184, 1149, 1098, 1049, 1024, 848, 760, 702, 668; **HRMS (MALDI-FT ICR)**: *m/z* calcd for C₂₇H₂₉Cl₂NNaO₆ [M+Na]⁺ = 556.12641, found: 556.12582; The enantioselectivity was determined by **HPLC** (Chiralpak IC column, n-hexane:i-PrOH = 80:20, 1.0 mL/min, *t*_{minor} = 13.0 min, *t*_{major} = 17.2 min).



tert-butyl (E)-4-benzyl-4-(2-(ethoxycarbonyl)-3-(naphthalen-2-yl)allyl)-5-oxoisoxazolidine-2-carboxylate (5w):

Following the general procedure A with tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate **2a** (27.7 mg, 0.10 mmol, 1.0 eq.) and ethyl 2-(((tert-butoxycarbonyl)oxy)(naphthalen-2-yl)methyl)acrylate **3m** (53.5 mg, 0.15 mmol, 1.5 eq.), the title compound **5w** was obtained as a colorless oil (32.0 mg, 62%, E/Z= 7:1, e.r.= 91:9 (major diastereomer)). $[\alpha]_D^{25} = 45.3^\circ$ (c = 0.80, CHCl₃). **¹H NMR** (300 MHz, Chloroform-d, 298 K) δ 8.06 (s, 1H), 7.89 – 7.68 (m, 4H), 7.59 – 7.47 (m, 2H), 7.40 – 7.20 (m, 2H), 7.16 – 7.07 (m, 2H), 7.05 – 6.92 (m, 2H), 4.31 (q, J = 7.1 Hz, 2H), 3.89 (d, J = 11.0 Hz, 1H), 3.80 (d, J = 11.0 Hz, 1H), 3.22 (s, 2H), 3.05 (d, J = 13.9 Hz, 1H), 2.65 (d, J = 13.9 Hz, 1H), 1.45 (s, 9H), 1.38 (t, J = 7.1 Hz, 3H) ppm; **¹³C NMR** (75 MHz, Chloroform-d, 298 K) δ 175.5, 167.7, 154.9, 143.6, 134.8, 133.1, 133.0, 132.4, 130.2, 128.8, 128.6, 128.5, 128.4, 128.2, 127.7, 127.4, 126.9, 126.6, 125.9, 83.63, 61.49, 54.60, 49.93, 40.79, 31.96, 28.05, 14.13. ppm; **IR** (film): ν (cm⁻¹) 3017, 2928, 2856, 1795, 1717, 1641, 1456, 1411, 1395, 1371, 1216, 1184, 1149, 1098, 1049, 1024, 848, 760, 702, 668; **HRMS (MALDI-FT ICR)**: *m/z* calcd for C₃₁H₃₃NNaO₆ [M+Na]⁺ = 538.22001, found: 538.21934; The enantioselectivity was determined by **HPLC** (Chiralpak AD-H column, n-hexane:i-PrOH = 80:20, 0.5 mL/min, *t*_{major} = 18.6 min, *t*_{minor} = 21.4 min).

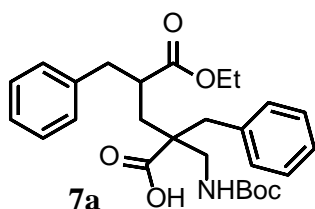
tert-butyl 4-benzyl-4-(2-benzyl-3-ethoxy-3-oxopropyl)-5-oxoisoxazolidine-2-carboxylate (6a):



5a (22.7 mg, 0.05 mmol, 1 eq.) was dissolved in MeOH and Pd/C (10% w/w, 2.1 mg, 0.002 mmol, 0.04 eq.) was added followed by three freeze-pump-thaw cycles to remove any remaining oxygen. The reaction mixture was flushed with hydrogen, and then vigorously stirred under a hydrogen atmosphere (balloon) over night at room temperature. The catalyst was filtered off over a pad of Celite® and washed 3 times with

DCM. The filtrate was concentrated to give (**6a**) as a colourless oil (22.4 mg, 0.05 mmol, quant., d.r.=2:1). ¹H NMR (700 MHz, δ, CDCl₃, 298 K): *Major*: 1.12 (t, *J* = 7.1 Hz, 3H), 1.46 (s, 9H), 1.77 (dd, *J* = 14.6, 1.8 Hz, 1H), 2.19-2.26 (m, 1H), 2.68-2.72 (m, 1H), 2.73 (d, *J* = 13.9 Hz, 1H), 2.84-2.91 (m, 1H), 2.92-2.96 (m, 1H), 2.95 (d, *J* = 13.9 Hz, 1H), 3.71 (d, *J* = 11.1 Hz, 1H), 3.88 (d, *J* = 11.1 Hz, 1H), 4.00-4.08 (m, 2H), 6.98-7.00 (m, 1H), 7.08 (d, *J* = 11.1 Hz, 1H), 7.13-7.15 (m, 1H), 7.22-7.31 (m, 7H). *Minor*: 1.15 (t, *J* = 7.1 Hz, 3H), 1.48 (s, 9H), 1.86 (dd, *J* = 14.8, 2.6 Hz, 1H), 2.19-2.26 (m, 1H), 2.68-2.72 (m, 1H), 2.80 (d, *J* = 13.9 Hz, 1H), 2.84-2.91 (m, 1H), 2.92-2.96 (m, 1H), 3.00 (d, *J* = 13.9 Hz, 1H), 3.75 (d, *J* = 11.0 Hz, 1H), 3.90 (d, *J* = 11.0 Hz, 1H), 4.00-4.08 (m, 2H), 6.98-7.00 (m, 1H), 7.12-7.15 (m, 2H), 7.22-7.31 (m, 7H). ¹³C NMR (176 MHz, δ, CDCl₃, 298 K): *Major*: 14.1, 28.2, 35.4, 40.0, 40.5, 43.5, 48.9, 56.0, 61.0, 84.0, 127.0, 127.6, 128.7, 128.9, 129.3, 130.2, 134.7, 138.0, 155.7, 174.7, 175.7. *Minor*: 14.1, 28.2, 29.8, 36.3, 39.7, 40.1, 43.1, 48.8, 55.3, 61.1, 84.0, 126.9, 127.7, 128.7, 128.8, 129.1, 130.3, 134.7, 138.1, 155.5, 174.8, 175.4. IR (film): ν (cm⁻¹) 3326, 3030, 2979, 2926, 2853, 1792, 1719, 1455, 1369, 1275, 1146, 1029, 847, 747, 700. HRMS (ESI): *m/z* calcd for C₂₇H₃₃NO₆: 468.2381[M+H]⁺; found: 468.2370.

2,4-dibenzyl-2-(((tert-butoxycarbonyl)amino)methyl)-5-ethoxy-5-oxopentanoic acid (7a):

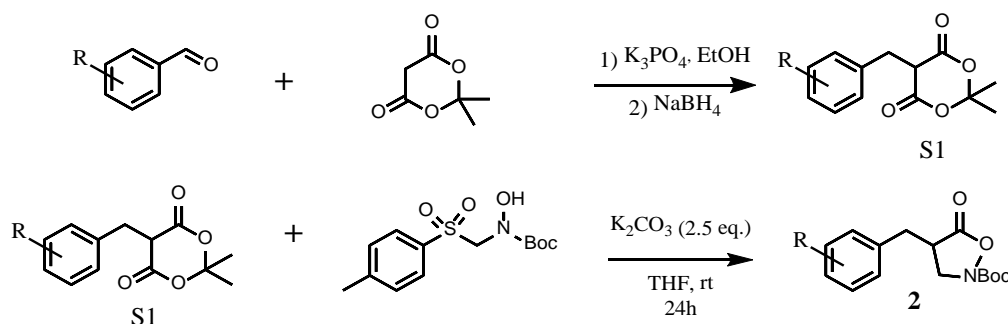


5a (57.6 mg, 0.12 mmol, 1 eq.) was dissolved in MeOH and Pd/C (10% w/w, 13.2 mg, 0.012 mmol, 0.1 eq.) was added followed by three freeze-pump-thaw cycles to remove any remaining oxygen. The reaction mixture was flushed with hydrogen, and then vigorously stirred under a hydrogen atmosphere (balloon) over night at room temperature. The catalyst was filtered off over a pad of Celite® and washed 3 times with DCM. The

filtrate was concentrated to give (**7a**) as a colourless oil (57.1 mg, 0.12 mmol, quant., d.r.=2:1). Mixture of diastereomers (ratio 2:1): ¹H NMR (300 MHz, δ, CDCl₃, 298 K): 0.88-0.98 (m, 3H), 1.48 (s, 9H), 1.66-1.84 (m, 1H), 2.23-2.34 (m, 1H), 2.67-2.99 (m, 6H), 3.33-3.55 (m, 1H), 3.88-3.99 (m, 2H), 7.10-7.27 (m, 10H). ¹³C NMR (75 MHz, δ, CDCl₃, 298 K): 13.9, 28.4, 35.8, 40.7, 41.1, 43.4, 43.7, 51.4, 60.6, 79.5, 126.6, 126.8, 128.3, 128.4, 129.1, 130.1, 130.2, 136.1, 138.3, 138.4, 156.2, 176.1, 180.5. IR (film): ν (cm⁻¹) 3370, 2978, 2927, 2854, 1712, 1497, 1454, 1392, 1366, 1325, 1248, 1163, 1046, 1023, 990, 851, 700. HRMS (ESI): *m/z* calcd for C₂₇H₃₃NO₆: 470.2537[M+H]⁺; found: 470.2528.

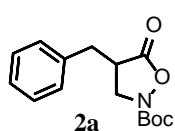
1.2.3 General procedure for the synthesis of benzyl-substituted isoxazolidin-5-one 2a-k:

The benzyl-substituted isoxazolidin-5-one **2** were prepared according to literature.^{5,6}



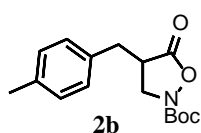
To a stirred solution of Meldrum's acid (1.0 eq., 2.08 mmol) in ethanol (10 ml) was added potassium phosphate (0.20 eq., 0.416 mmol) and the appropriate substituted benzaldehyde (1.0 eq., 2.08 mmol). After 24-48 h the temperature of the reaction mixture was cooled at 0 °C and sodium borohydride (1.05 eq., 2.18 mmol) was added and the mixture was stirred overnight at room temperature. Afterward, 1 M aqueous HCl was added drop by drop until the pH value to 7 (or 6-5). Ethanol was removed by using a rotary evaporator and the crude product was extracted with ethyl acetate (3x60 mL). The combined organic phases washed with brine and dried over Na₂SO₄, the solvent evaporated and the residue dried in vacuo to yield derivatives of meldrum's acid **S1**.

To a solution of crude **S1** in THF (0.1 M) were added *tert*-butyl hydroxy(tosylmethyl)carbamate (1.0 eq.) and K₂CO₃(2.5 eq.) at 25 °C. After 24h, the reaction mixture was filtered through a pad of sodium sulphate, washed with DCM and the filtrates were evaporated under reduced pressure to give the crude residue that was purified by chromatography (silica gel, heptane-ethyl acetate, 25/1 to 15/1) to yield benzyl-substituted isoxazolidin-5-one **2** as a oil or a white/yellow solid.



tert-butyl 4-benzyl-5-oxoisoxazolidine-2-carboxylate (2a):

Known compound⁷



tert-butyl 4-(4-methylbenzyl)-5-oxoisoxazolidine-2-carboxylate (2b):

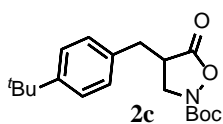
¹H NMR (300 MHz, Chloroform-d, 298 K) δ 7.14 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 4.24 – 4.03 (m, 1H), 3.81 – 3.60 (m, 1H), 3.31 – 3.04 (m, 2H), 2.76 (dd, J = 13.7, 9.4 Hz, 1H), 2.33 (s, 3H), 1.51 (s, 9H) ppm;

¹³C NMR (75 MHz, Chloroform-d, 298 K): δ 174.3, 156.0, 136.9, 133.8, 129.6, 128.6, 84.1, 52.9, 42.2, 34.0, 28.0, 21.0 ppm.

⁵ U. V. Desai, D. M. Pore, R. B. Mane, S. B. Solabannavar, P. P. Wadgaonkar, *Synthetic Communications*, **2004**, 34, 25-32.

⁶ T. Cadart, C. Berthonneau, V. Levacher, S. Perrio, J.-F. Brière, *Chem. Eur. J.*, **2016**, 22, 15261-15264.

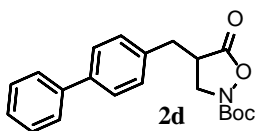
⁷ T. Tite, M. Sabbah, V. Levacher, J. F. Brière, *Chem. Commun.*, **2013**, 49, 11569-11571.



tert-butyl 4-(4-(tert-butyl)benzyl)-5-oxoisoxazolidine-2-carboxylate (2c):

^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.35 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 4.16 (dd, J = 11.0, 8.3 Hz, 1H), 3.82 – 3.62 (m, 1H), 3.33 – 3.03 (m, 2H), 2.76 (dd, J = 13.7, 9.6 Hz, 1H), 1.52 (s, 9H), 1.31 (s, 9H) ppm;

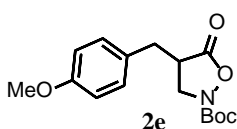
^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 174.4, 156.0, 150.2, 133.9, 128.4, 125.9, 84.1, 53.0, 42.2, 34.5, 34.0, 31.3, 28.1 ppm.



tert-butyl 4-([1,1'-biphenyl]-4-ylmethyl)-5-oxoisoxazolidine-2-carboxylate (2d):

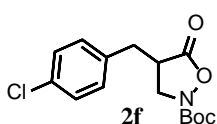
^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.64 – 7.52 (m, 4H), 7.45 (t, J = 7.4 Hz, 2H), 7.37 (d, J = 7.4 Hz, 1H), 7.27 (d, J = 7.9 Hz, 2H), 4.20 (dd, J = 11.1, 8.2 Hz, 1H), 3.85 – 3.66 (m, 1H), 3.36 – 3.12 (m, 2H), 2.86 (dd, J = 13.7, 9.4 Hz, 1H), 1.53 (s, 9H) ppm;

^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 174.2, 156.0, 140.5, 140.2, 136.0, 129.2, 128.9, 127.7, 127.5, 127.0, 84.2, 53.0, 42.2, 34.1, 28.1 ppm.



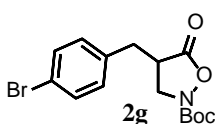
tert-butyl 4-(4-methoxybenzyl)-5-oxoisoxazolidine-2-carboxylate (2e):

Known compound⁷



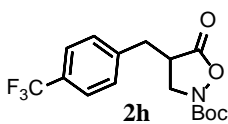
tert-butyl 4-(4-chlorobenzyl)-5-oxoisoxazolidine-2-carboxylate (2f):

Known compound⁸



tert-butyl 4-(4-bromobenzyl)-5-oxoisoxazolidine-2-carboxylate (2g):

Known compound⁸

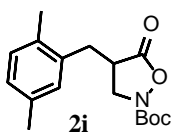


tert-butyl 5-oxo-4-(4-(trifluoromethyl)benzyl)isoxazolidine-2-carboxylate (2h):

^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.60 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.17 (dd, J = 11.1, 8.4 Hz, 1H), 3.77 – 3.59 (m, 1H), 3.37 – 3.11 (m, 2H), 2.89 (dd, J = 13.9, 9.2 Hz, 1H), 1.51 (s, 9H) ppm;

^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 173.8, 155.8, 140.9, 129.7 (q, J = 32.6 Hz), 129.2, 126.0 (q, J = 3.7 Hz), 124.0 (q, J = 272.0 Hz), 84.4, 52.8, 41.8, 34.2, 28.0 ppm.

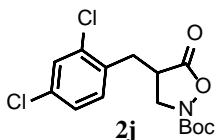
⁸ J. S. Yu, H. Noda, M. Shibasaki, *Angew. Chem. Int. Ed.*, **2018**, 57, 818-822.



tert-butyl 4-(2,5-dimethylbenzyl)-5-oxoisoxazolidine-2-carboxylate (2i):

^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.07 (d, $J = 7.7$ Hz, 1H), 6.99 (d, $J = 7.7$ Hz, 1H), 6.92 (s, 1H), 4.15 (dd, $J = 11.1, 8.3$ Hz, 1H), 3.79 – 3.67 (m, 1H), 3.28 (dd, $J = 14.3, 4.3$ Hz, 2H), 3.21 – 3.05 (m, 1H), 2.72 (dd, $J = 14.3, 10.4$ Hz, 1H), 2.31 (s, 3H), 2.29 (s, 3H), 1.53 (s, 9H) ppm;

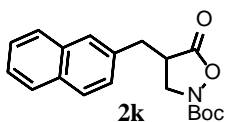
^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 174.4, 156.0, 136.0, 135.1, 132.9, 130.7, 129.8, 128.1, 84.2, 53.3, 41.1, 31.9, 28.1, 21.0, 18.9 ppm.



tert-butyl 4-(2,4-dichlorobenzyl)-5-oxoisoxazolidine-2-carboxylate (2j):

^1H NMR (300 MHz, Chloroform-d, 298 K) δ 7.40 (s, 1H), 7.21 (s, 2H), 4.17 (dd, $J = 11.1, 8.2$ Hz, 1H), 3.77 – 3.63 (m, 1H), 3.45 – 3.14 (m, 2H), 2.90 (dd, $J = 13.6, 8.2$ Hz, 1H), 1.50 (s, 9H) ppm;

^{13}C NMR (75 MHz, Chloroform-d, 298 K) δ 173.8, 155.8, 134.7, 134.0, 133.3, 131.9, 129.7, 127.7, 84.4, 52.9, 40.4, 31.5, 28.0 ppm.

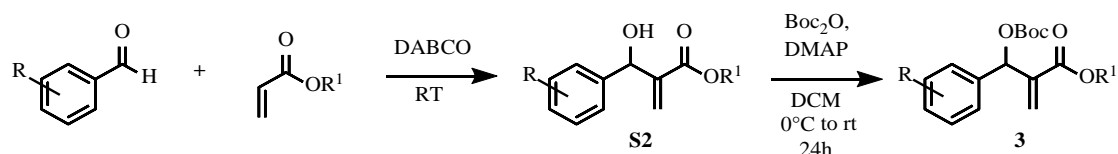


tert-butyl 4-(naphthalen-2-ylmethyl)-5-oxoisoxazolidine-2-carboxylate (2k):

Known compound⁷

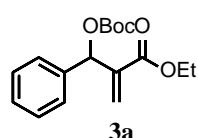
1.2.4 Preparation of Morita-Baylis-Hillman Carbonates **3a-m**:

The Morita-Baylis-Hillman carbonates **3** were prepared according to the literature.^{9,10}



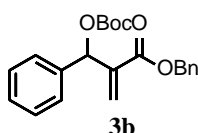
A mixture of aldehyde (1.0 eq, 4.41 mmol), acrylate (2.0 eq., 8.81 mmol) and DABCO (0.40 eq., 1.76 mmol) was stirred for 3-7 days at rt. Then, the mixture was diluted with Et₂O (30 mL) and washed with water (2x20 mL), 1M HCl (1x20 mL) and brine (10 mL). The organic phase was dried with sodium sulphate and evaporated in vacuo to yield alcohols **S2**.

Then, alcohols **S2** were converted to the corresponding carbonates **3a-m**: alcohol S1 (1.0 eq., 1.0 mmol) and Boc₂O (1.1 eq., 1.1 mmol) were dissolved in DCM (2.0 mL) and the solution was cooled to 0°C. Afterward, DMAP (0.10 eq., 0.10 mmol) was added and the reaction mixture stirred at room temperature for 24h. After 24h, the reaction mixture was diluted with CH₂Cl₂. The combined organic phase was washed with 4 N aq. HCl solution, saturated aq. NaHCO₃ and brine. The organic layer, dried over anhydrous Na₂SO₄, filtered and vacuum at rotary evaporator to obtain an oil. The crude product was purified by chromatography (silica gel, heptane-ethyl acetate, 50/1 to 20/1) to afford an oil or a white/pale yellow solid.



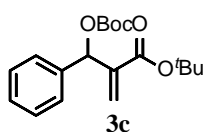
ethyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate (3a):

Known compound¹⁰



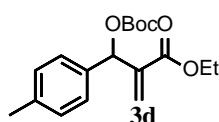
benzyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate (3b):

Known compound¹¹



tert-butyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate (3c):

Known compound¹²



ethyl 2-(((tert-butoxycarbonyl)oxy)(p-tolyl)methyl)acrylate (3d):

Known compound¹³

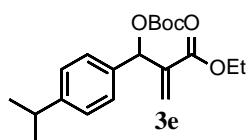
⁹ M. Kalyva, A. L. Zografos, E. Kapourani, E. Giambazolias, L. Devel, A. Papakyriakou, V. Dive, Y. G. Lazarou, D. Georgiadis, *Chem. Eur. J.*, **2015**, 21, 3278-3289.

¹⁰ S. J. Singha Roy, S. Mukherjee, *Chem. Commun.*, **2014**, 50, 121-123.

¹¹ L. Zhang, H. Liu, G. Qiao, Z. Hou, Y. Liu, Y. Xiao, H. Guo, *J. Am. Chem. Soc.*, **2015**, 137, 4316-4319.

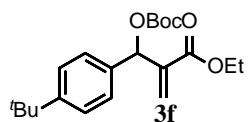
¹² S. Jayakumar, S. Muthusamy, M. j Prakash, V. Kesavan, *Eur. J. Org. Chem.*, **2014**, 1893-1898.

¹³ S. Kayal, S. Mukherjee, *Org. Lett.*, **2017**, 19, 4944-4947.



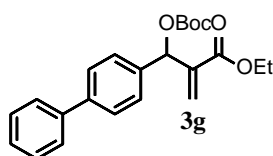
ethyl 2-(((tert-butoxycarbonyl)oxy)(4-isopropylphenyl)methyl)acrylate (3e):

Known compound¹³



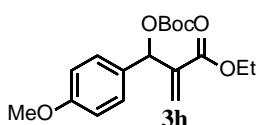
ethyl 2-(((tert-butoxycarbonyl)oxy)(4-(tert-butyl)phenyl)methyl)acrylate (3f):

¹H NMR (300 MHz, Chloroform-d, 298 K) δ 7.39 – 7.27 (m, 4H), 6.47 (s, 1H), 6.39 (s, 1H), 5.89 (s, 1H), 4.23 – 4.10 (m, 2H), 1.46 (s, 9H), 1.30 (s, 9H), 1.23 (t, J = 7.1, 3H) ppm.



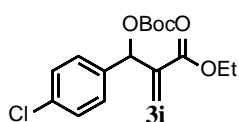
ethyl 2-([1,1'-biphenyl]-4-yl((tert-butoxycarbonyl)oxy)methyl)acrylate (3g):

¹H NMR (300 MHz, Chloroform-d, 298 K) δ 7.57 – 7.49 (m, 4H), 7.45 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 7.1 Hz, 1H), 6.52 (s, 1H), 6.40 (s, 1H), 5.92 (s, 1H), 4.14 (d, J = 7.2 Hz, 2H), 1.44 (s, 9H), 1.20 (t, J = 7.2 Hz, 3H) ppm.



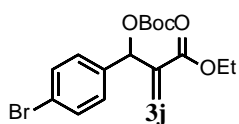
ethyl 2-(((tert-butoxycarbonyl)oxy)(4-methoxyphenyl)methyl)acrylate (3h):

Known compound¹³



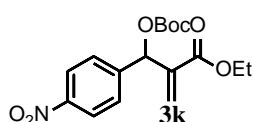
ethyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (3i):

Known compound¹³



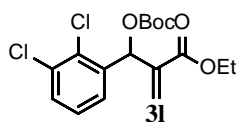
ethyl 2-((4-bromophenyl)((tert-butoxycarbonyl)oxy)methyl)acrylate (3j):

Known compound¹³



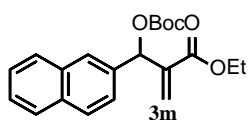
ethyl 2-(((tert-butoxycarbonyl)oxy)(4-nitrophenyl)methyl)acrylate (3k):

¹H NMR (300 MHz, Chloroform-d, 298 K) δ 8.18 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 6.51 (s, 1H), 6.45 (s, 1H), 5.98 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 1.44 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H) ppm.



ethyl 2-(((tert-butoxycarbonyl)oxy)(2,3-dichlorophenyl)methyl)acrylate (3l):

$^1\text{H NMR}$ (300 MHz, Chloroform-d, 298 K) δ 7.44 (d, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 7.8$ Hz, 1H), 7.21 (t, $J = 7.8$ Hz, 1H), 6.89 (s, 1H), 6.47 (s, 1H), 5.63 (s, 1H), 4.20 (q, $J = 7.1$ Hz, 2H), 1.47 (s, 9H), 1.24 (t, $J = 7.1$ Hz, 3H) ppm.

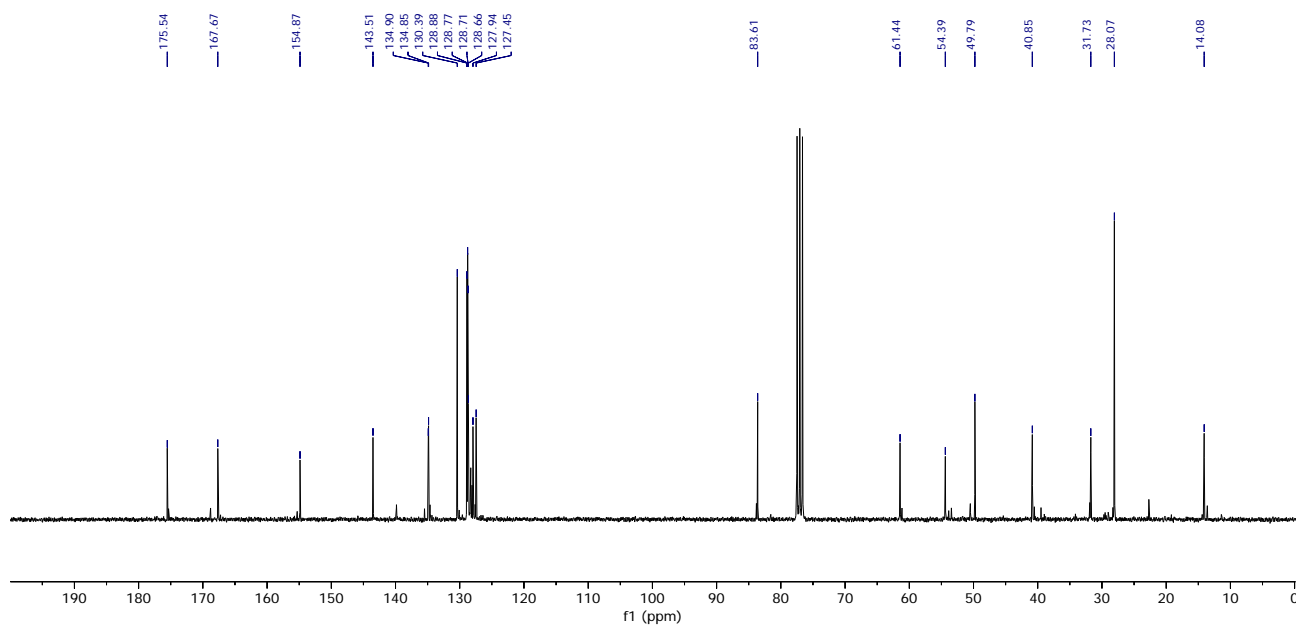
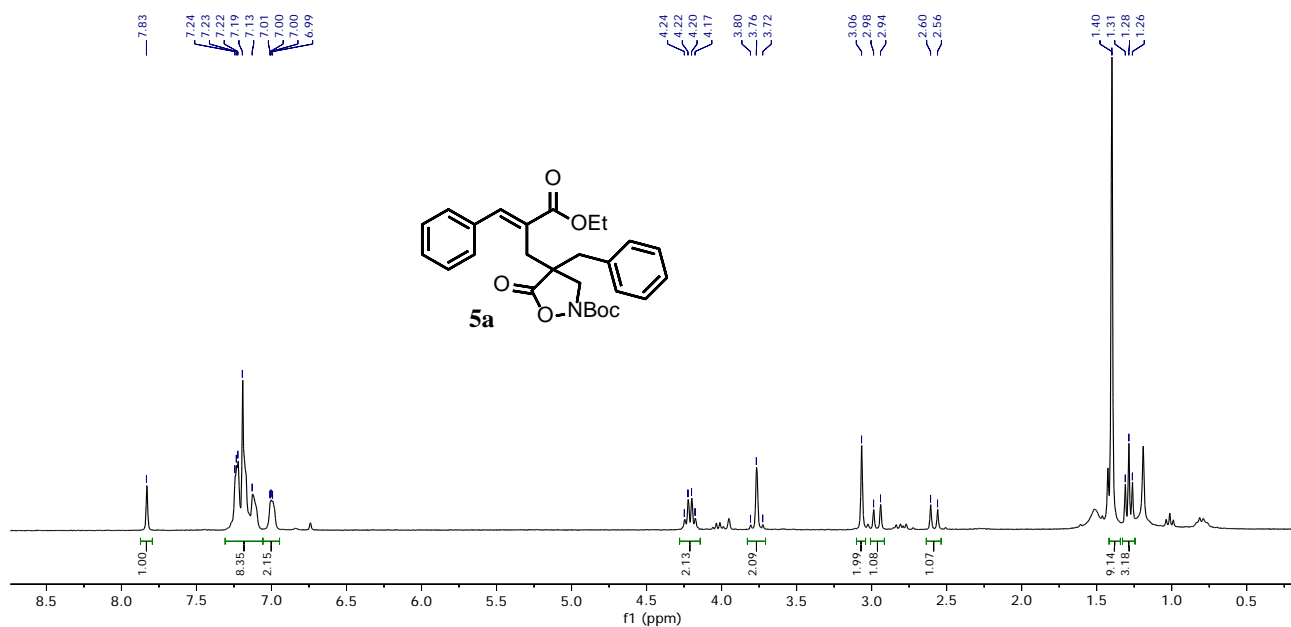


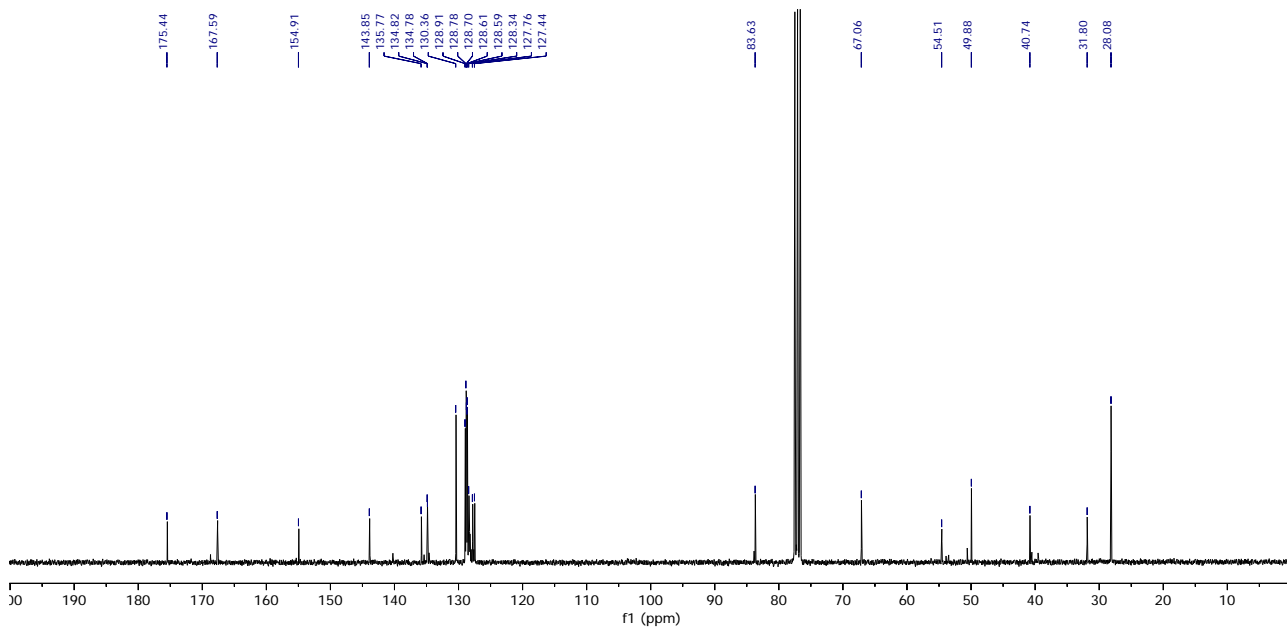
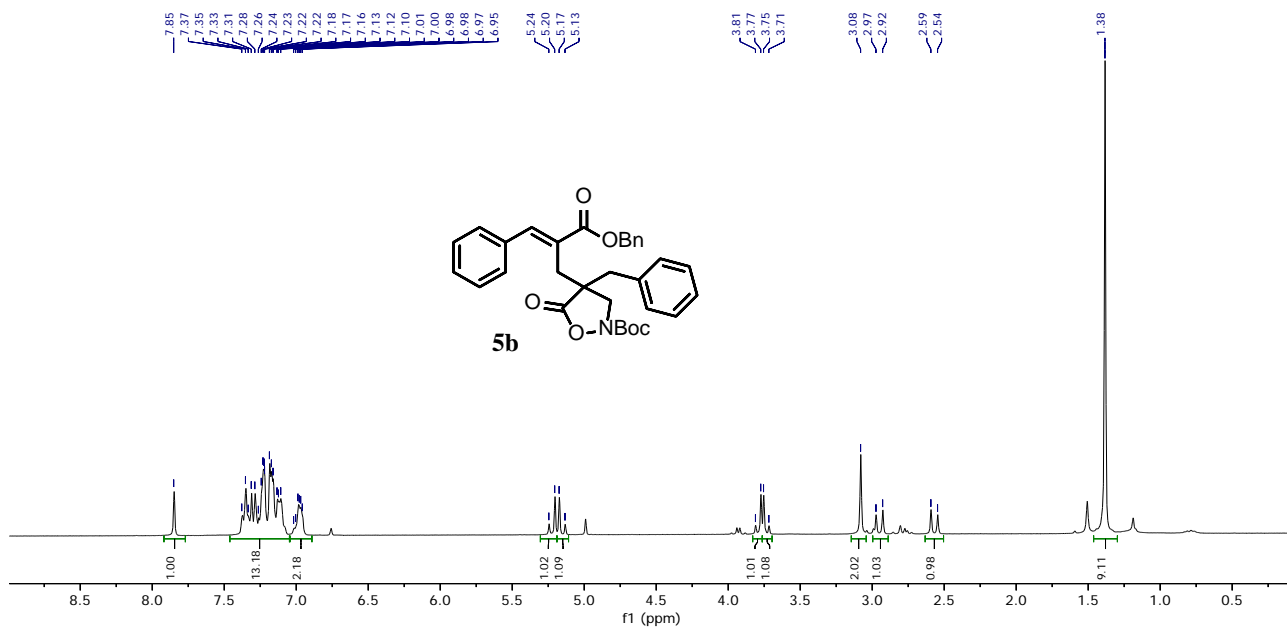
ethyl 2-(((tert-butoxycarbonyl)oxy)(naphthalen-2-yl)methyl)acrylate (3m):

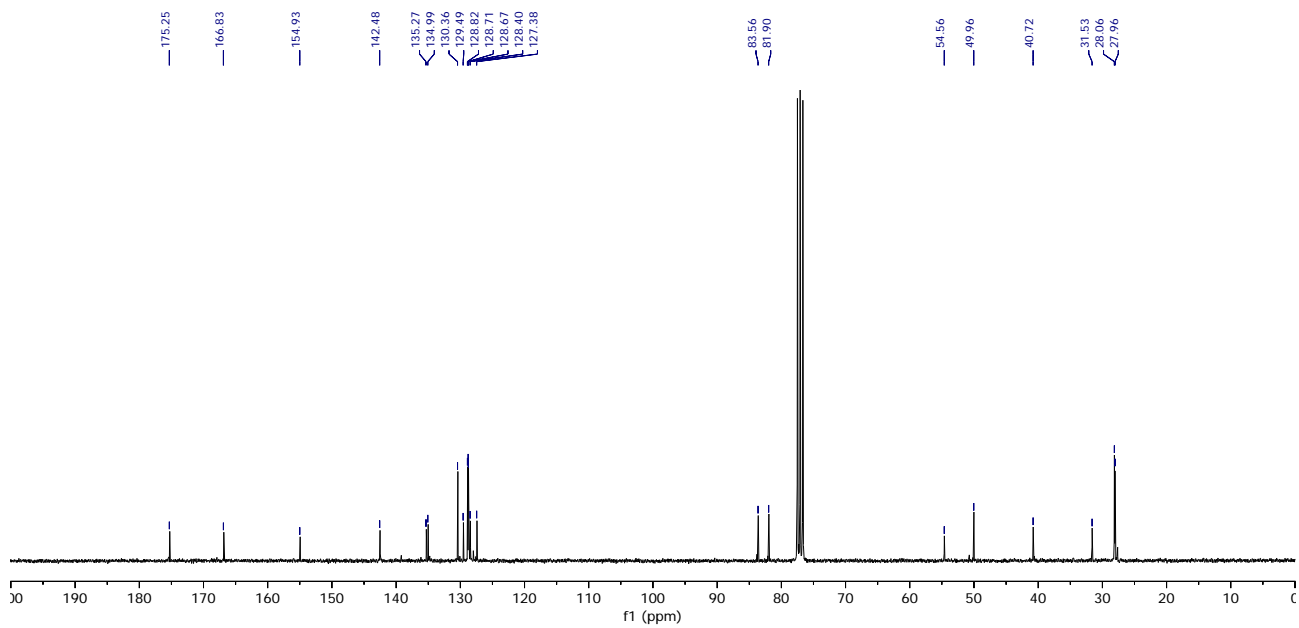
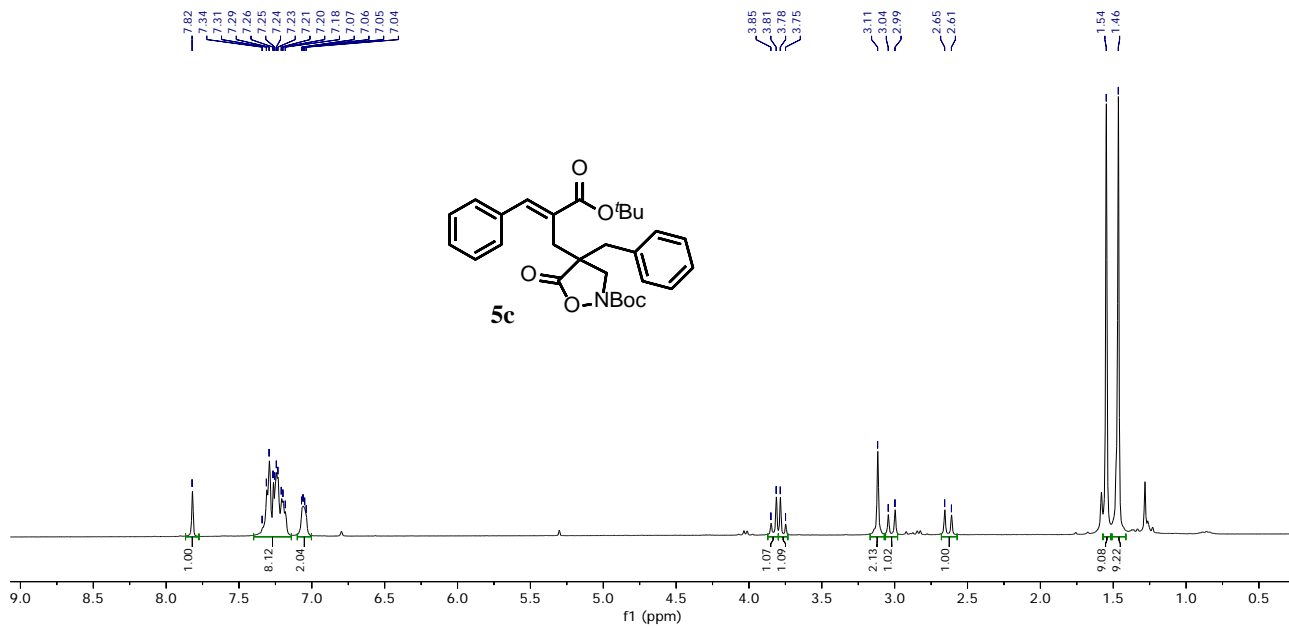
Known compound¹⁰

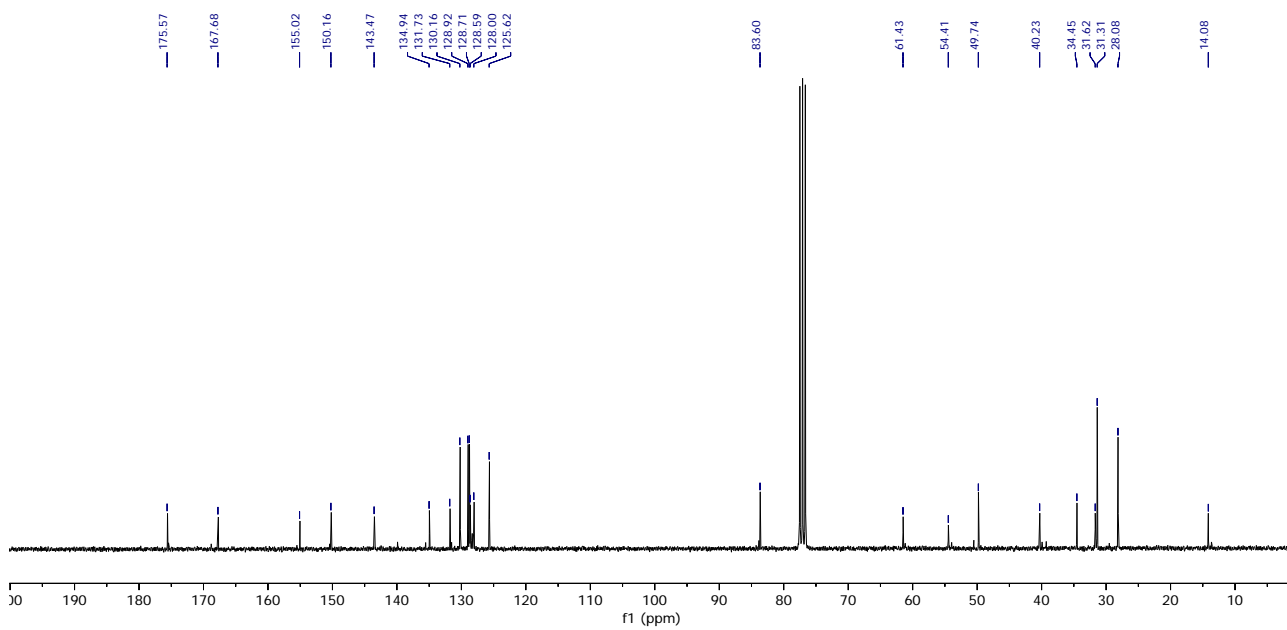
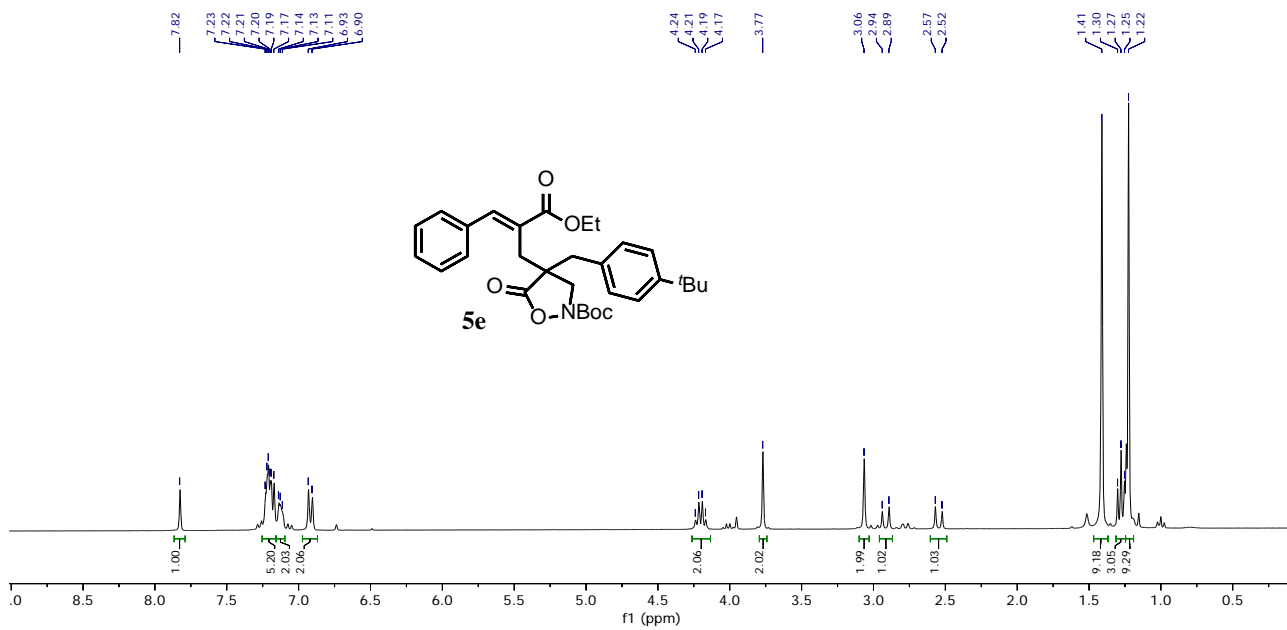
2. Copies of NMR-Spectra

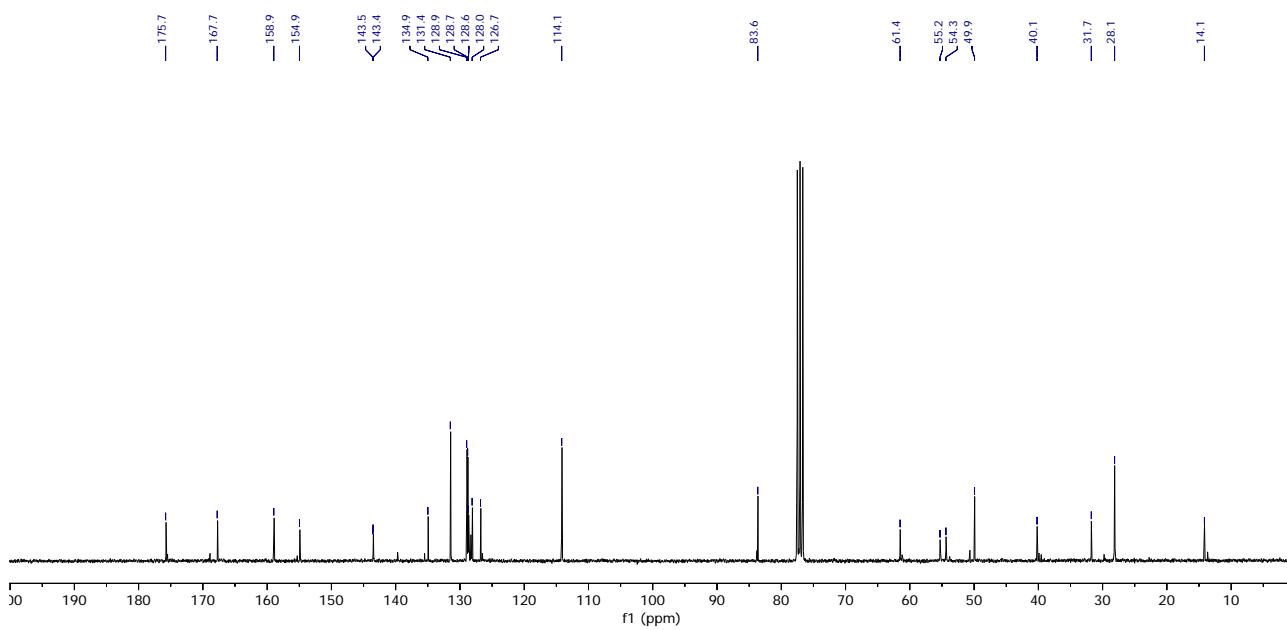
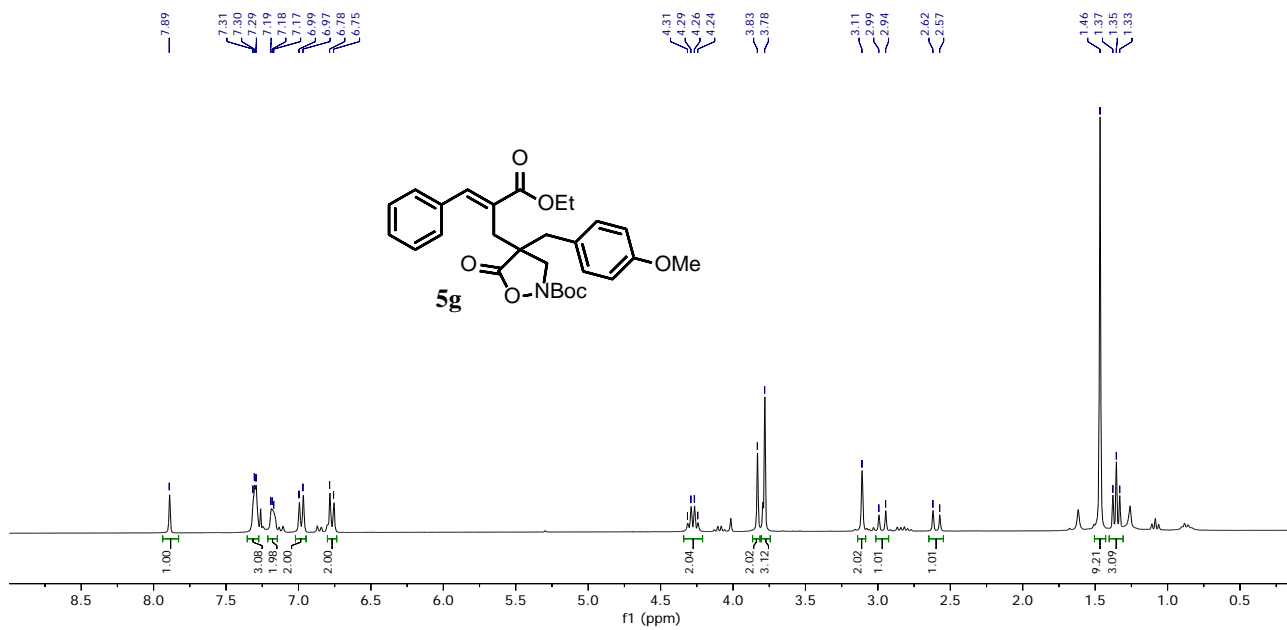
Spectra contain traces of the 2nd diastereomer (not integrated!)

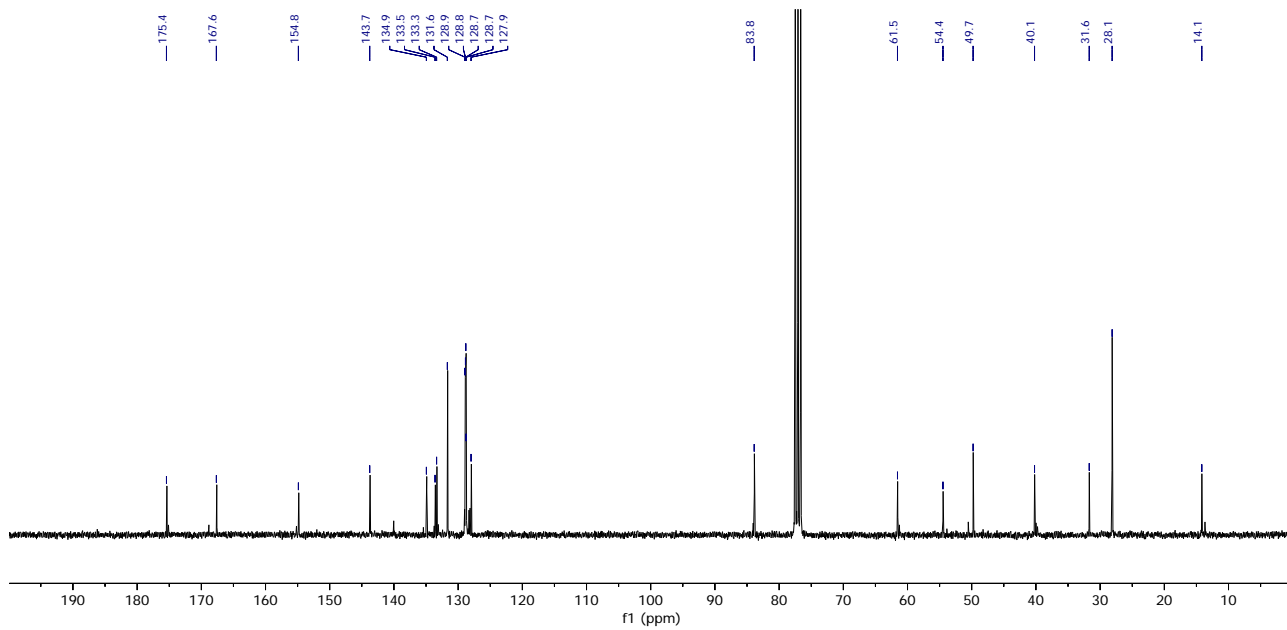
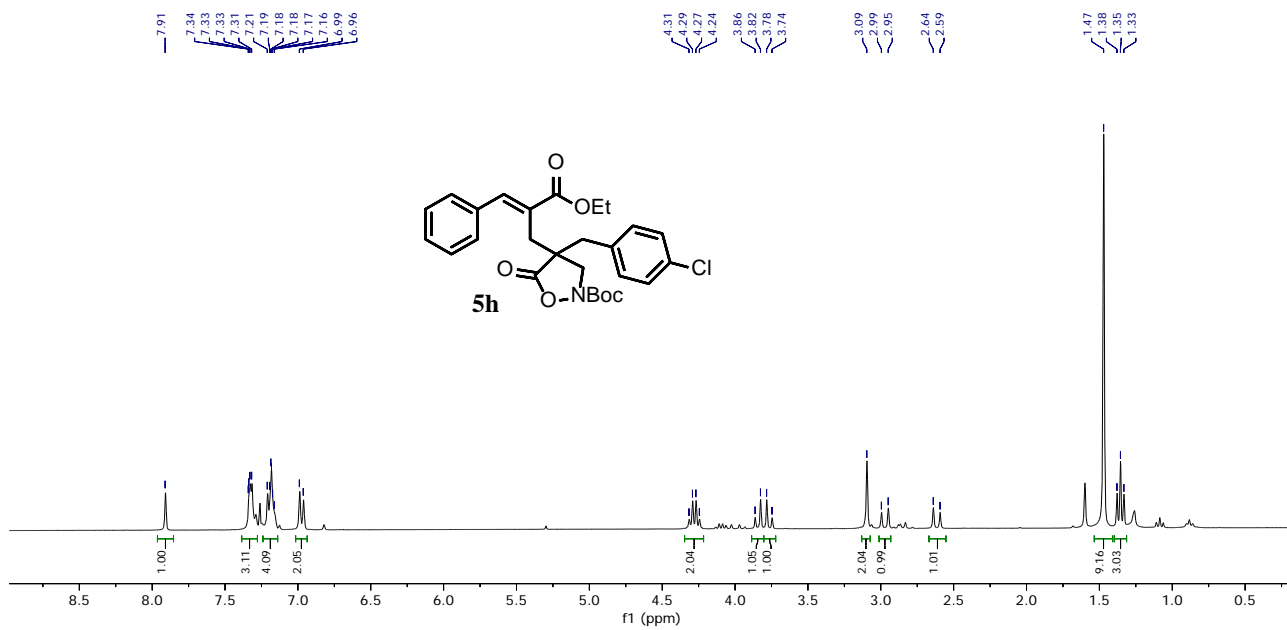


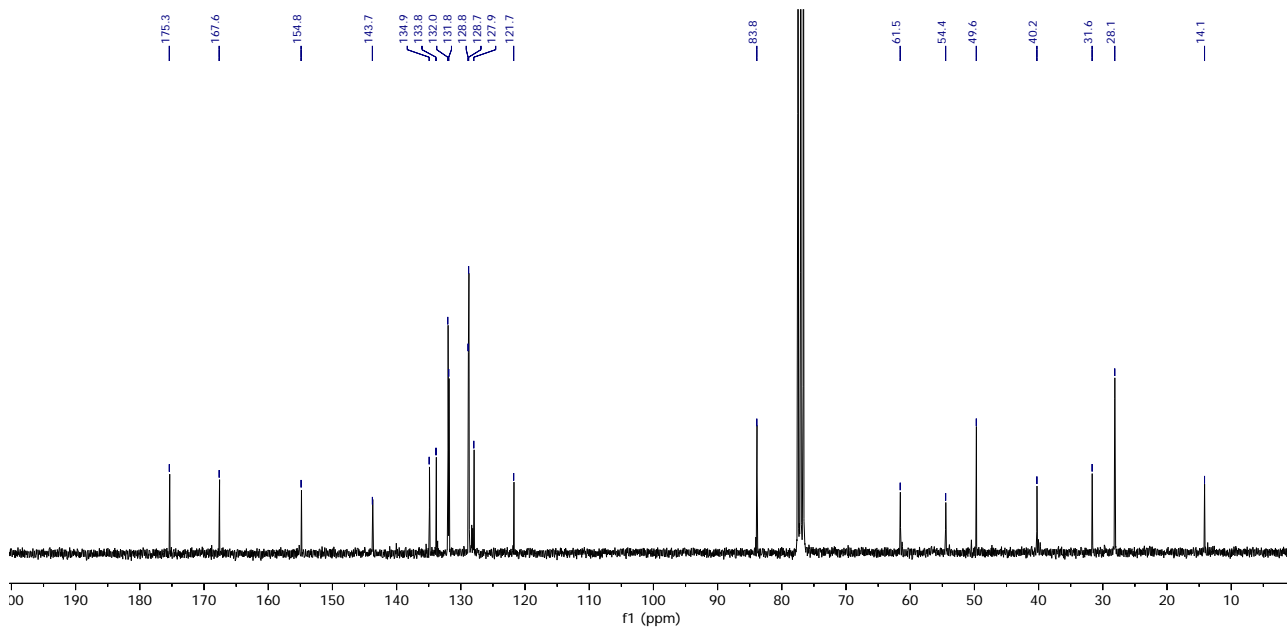
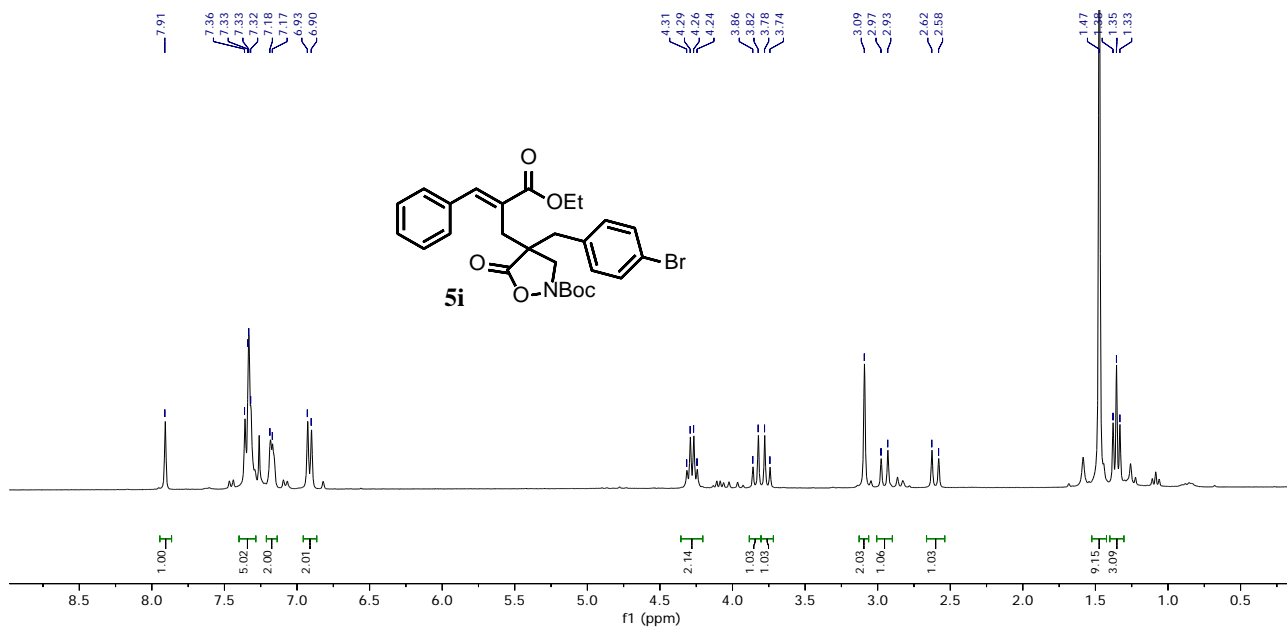


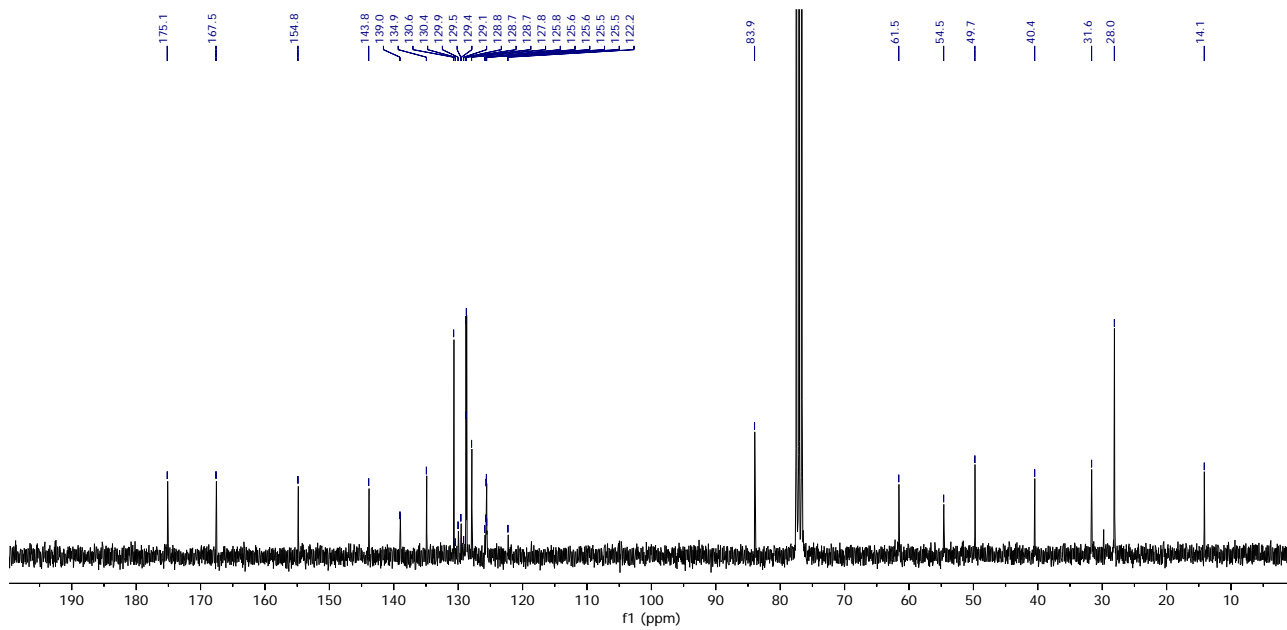
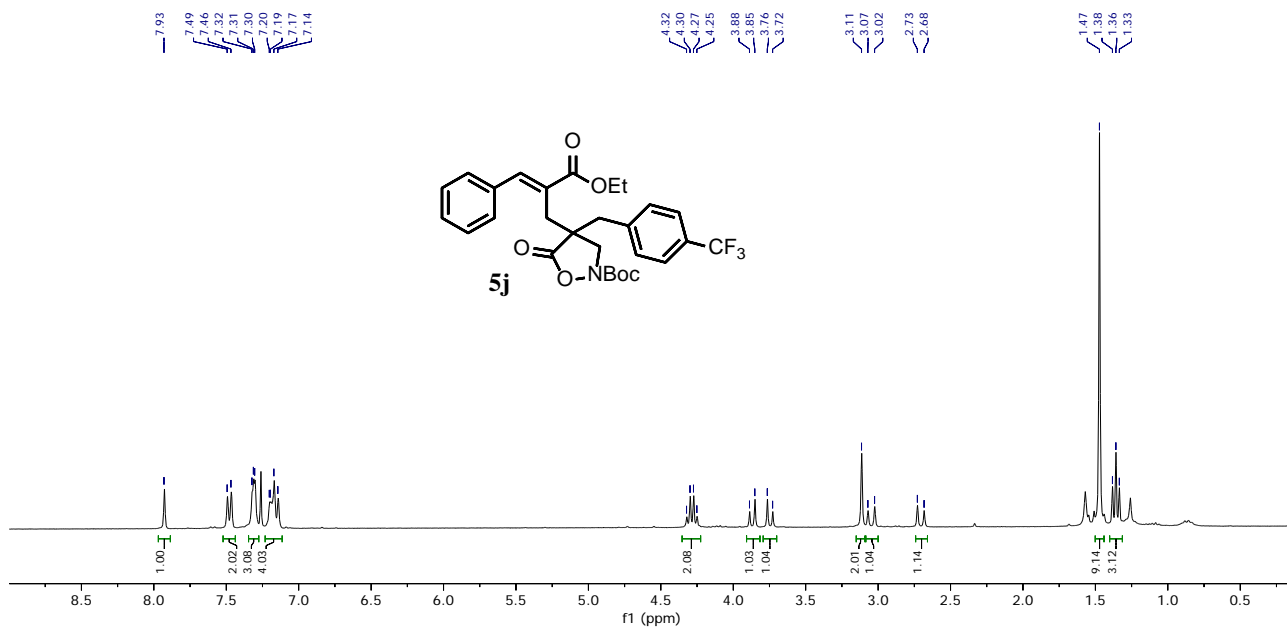


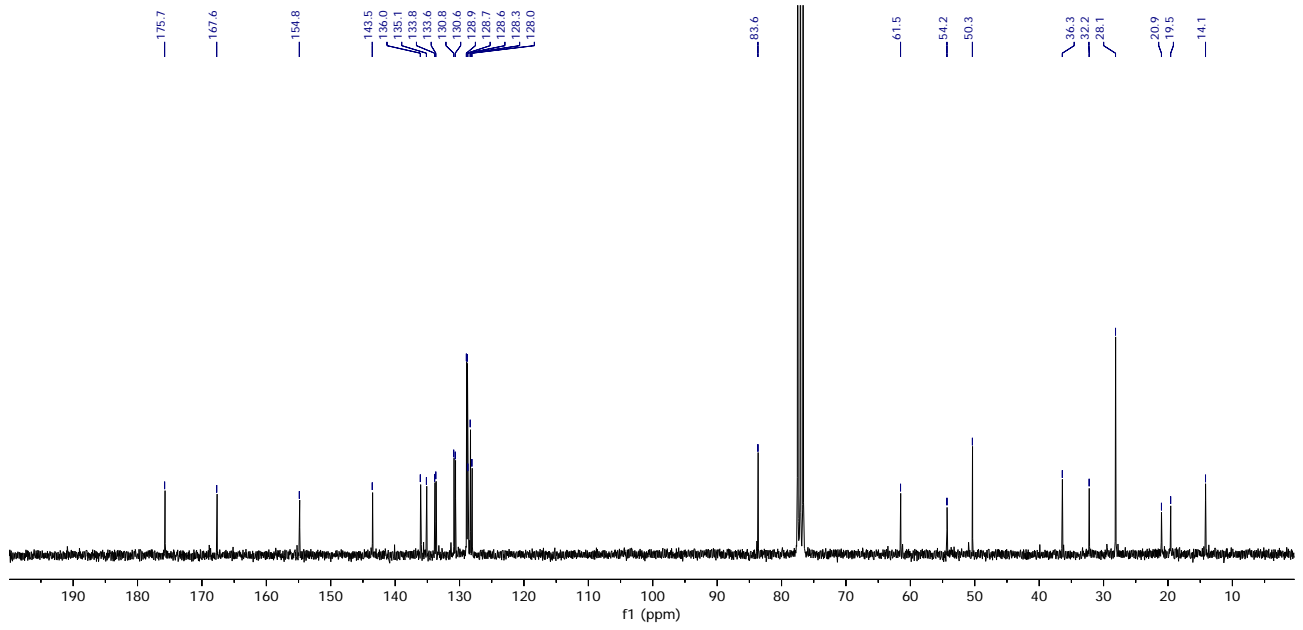
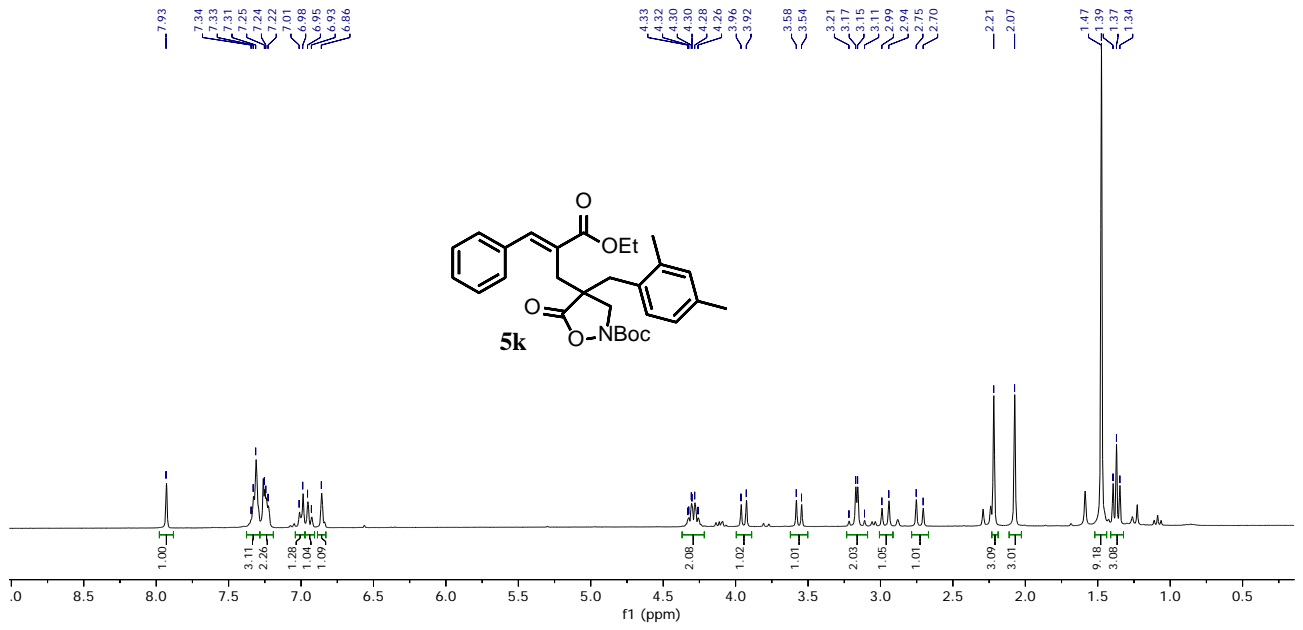


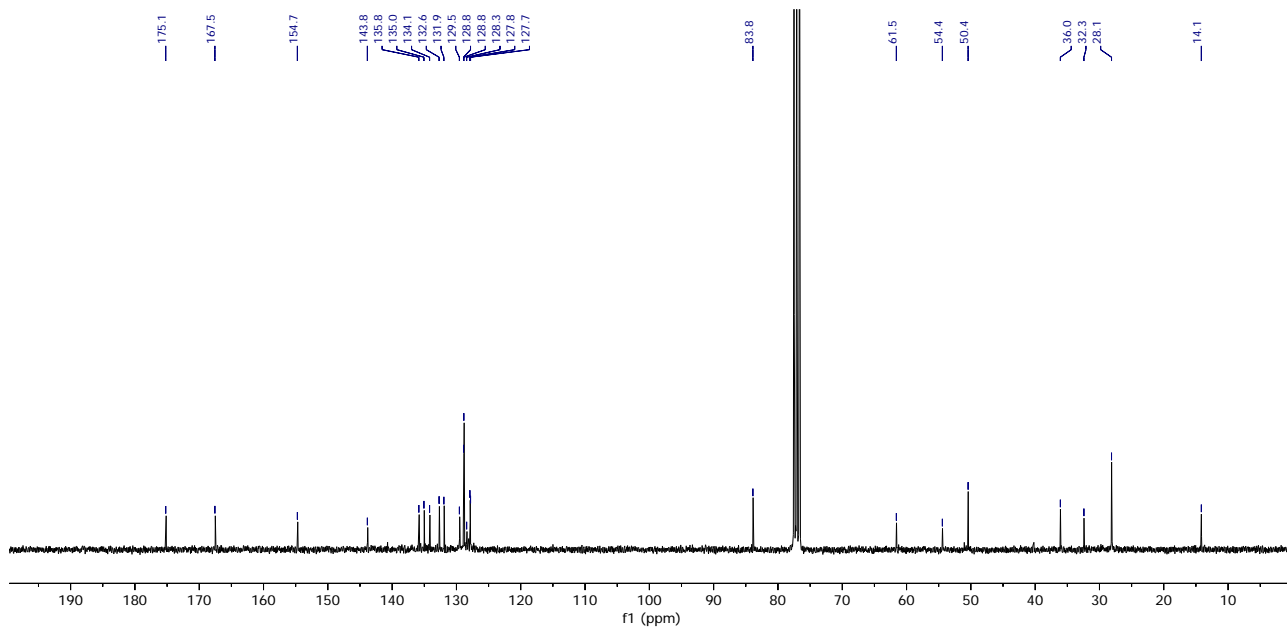
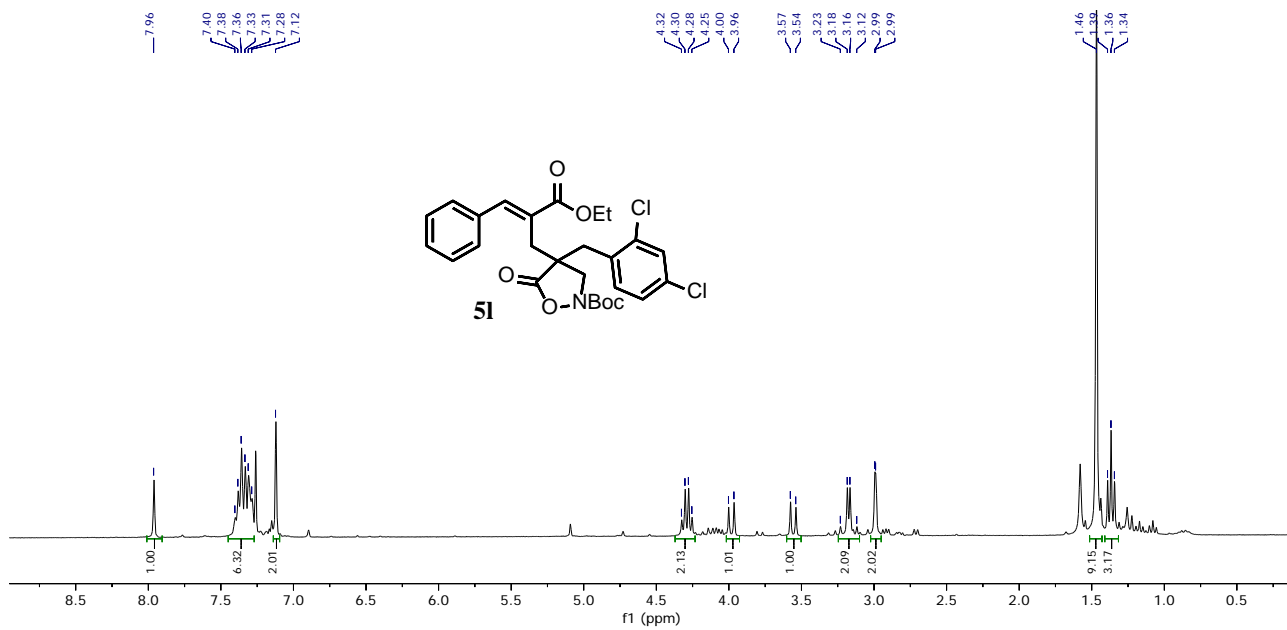


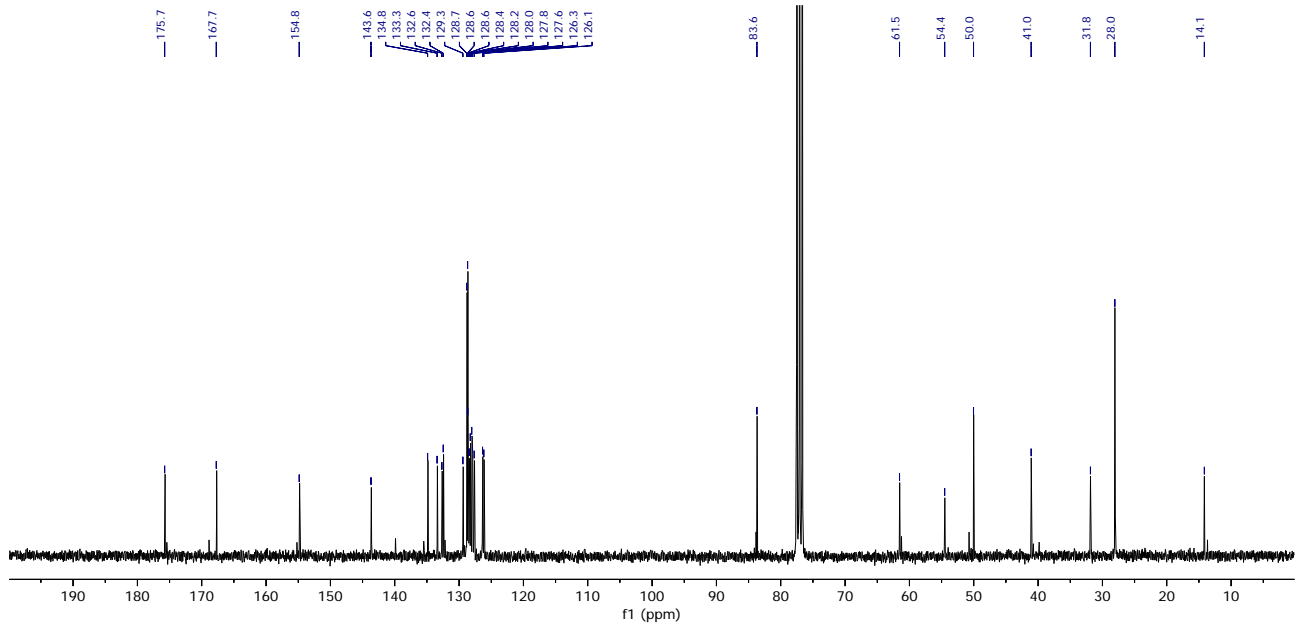
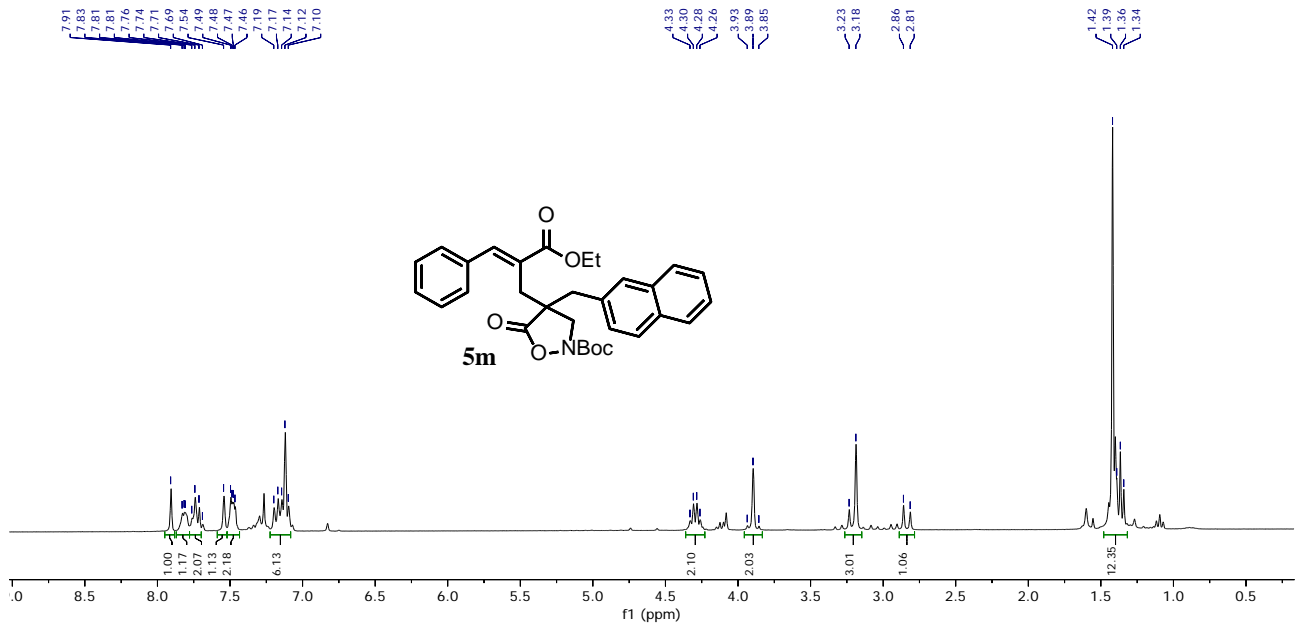


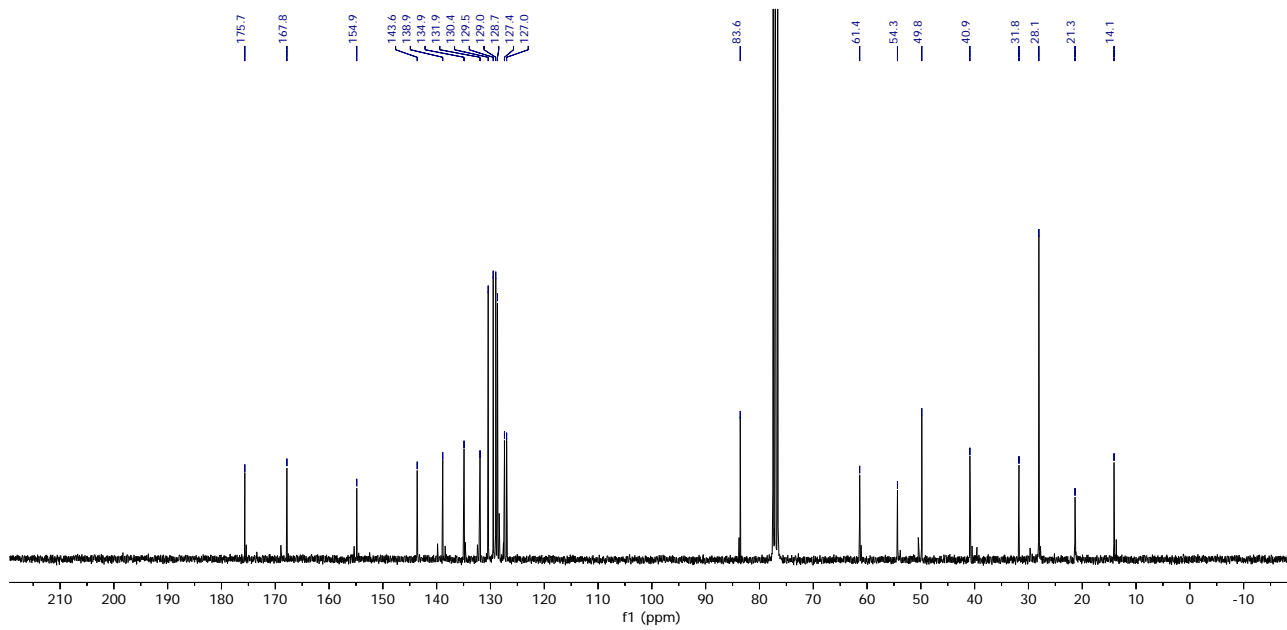
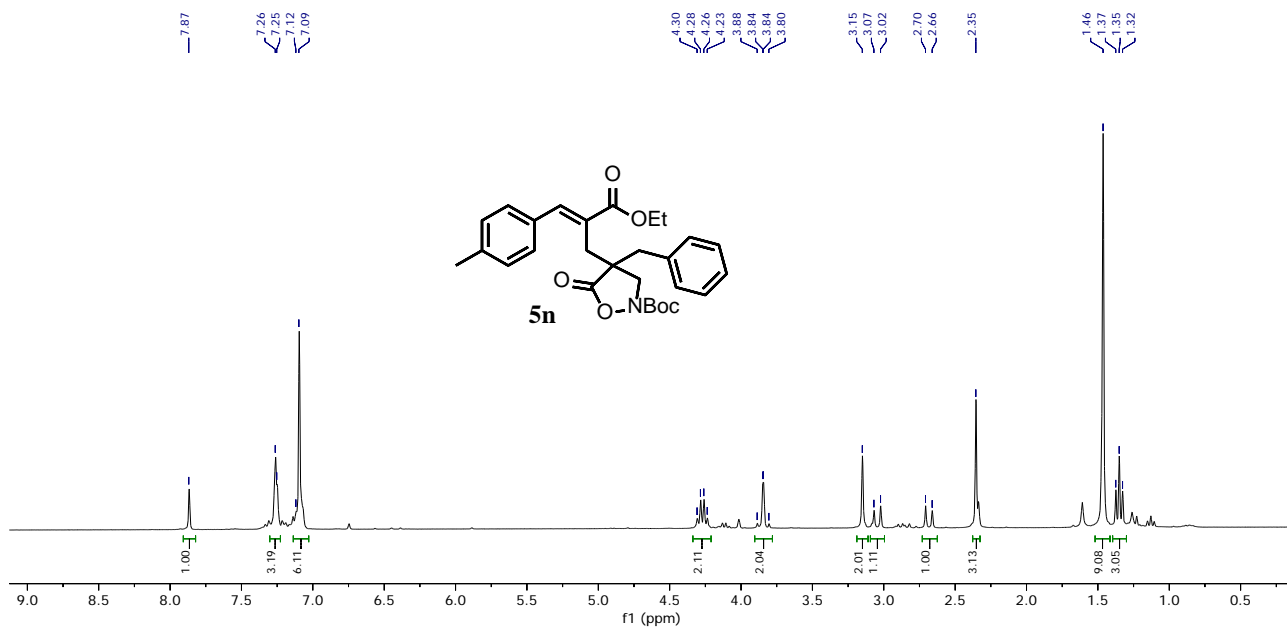


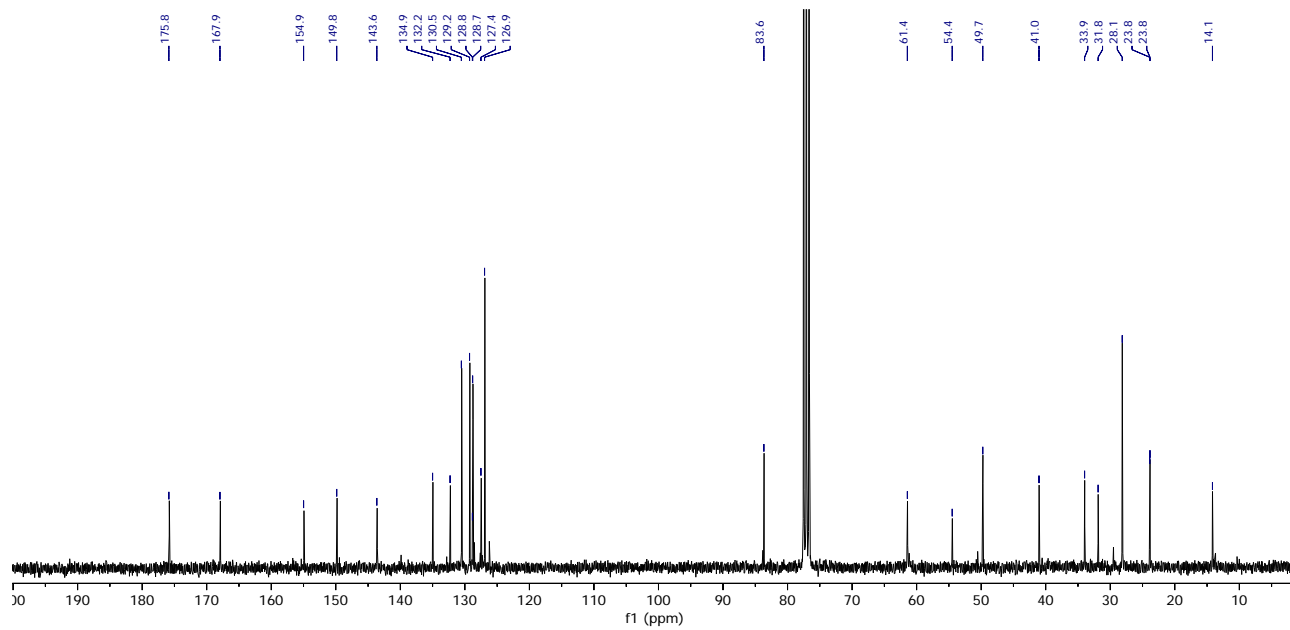
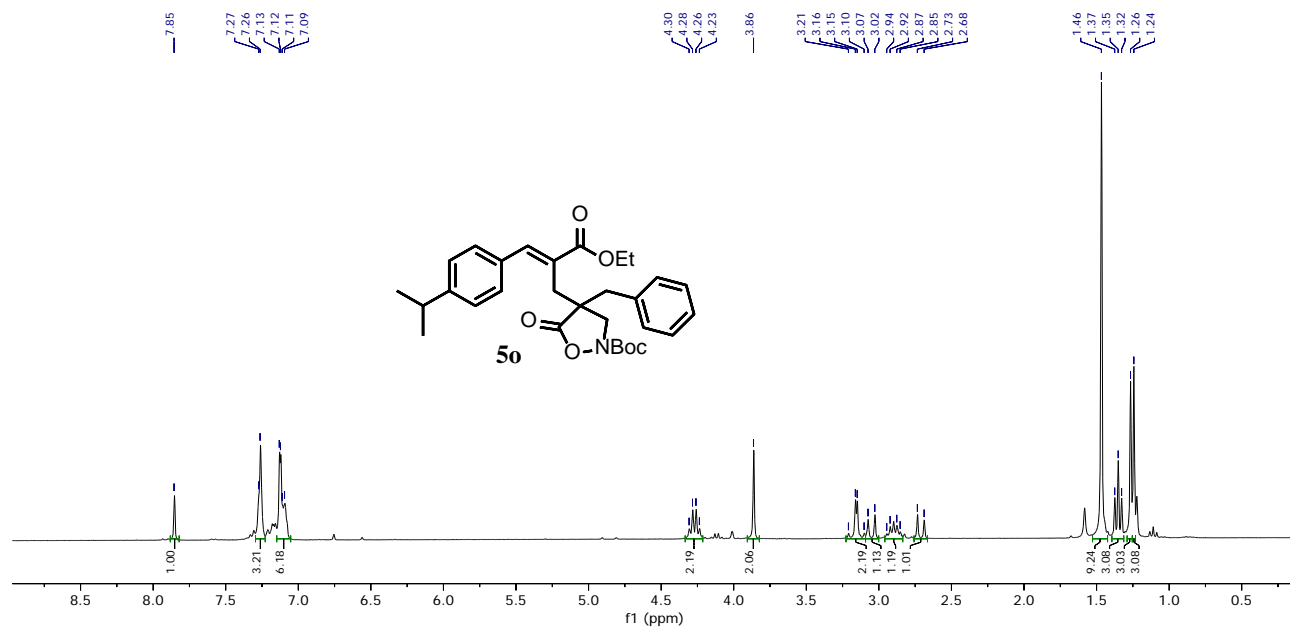


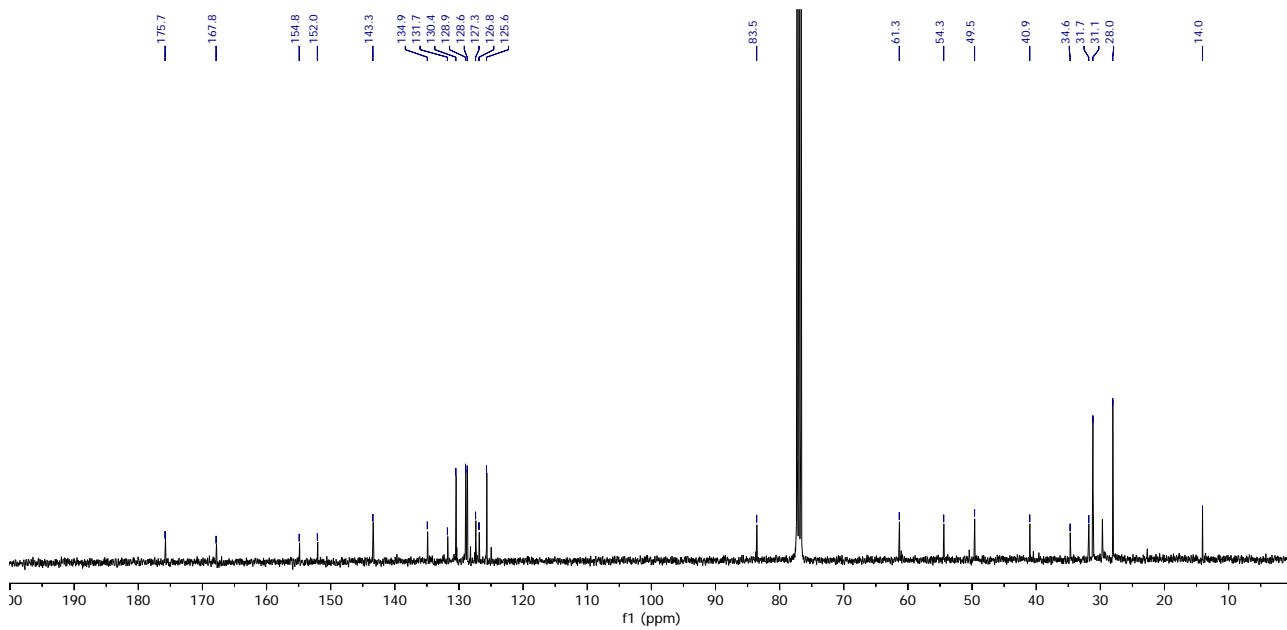
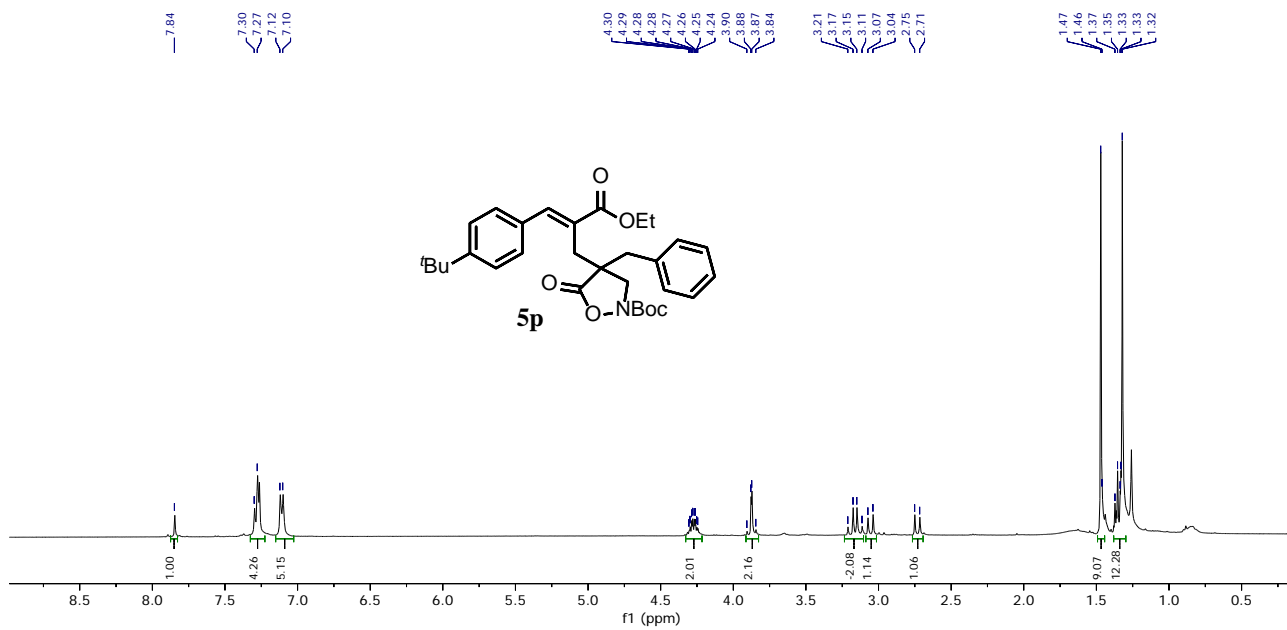


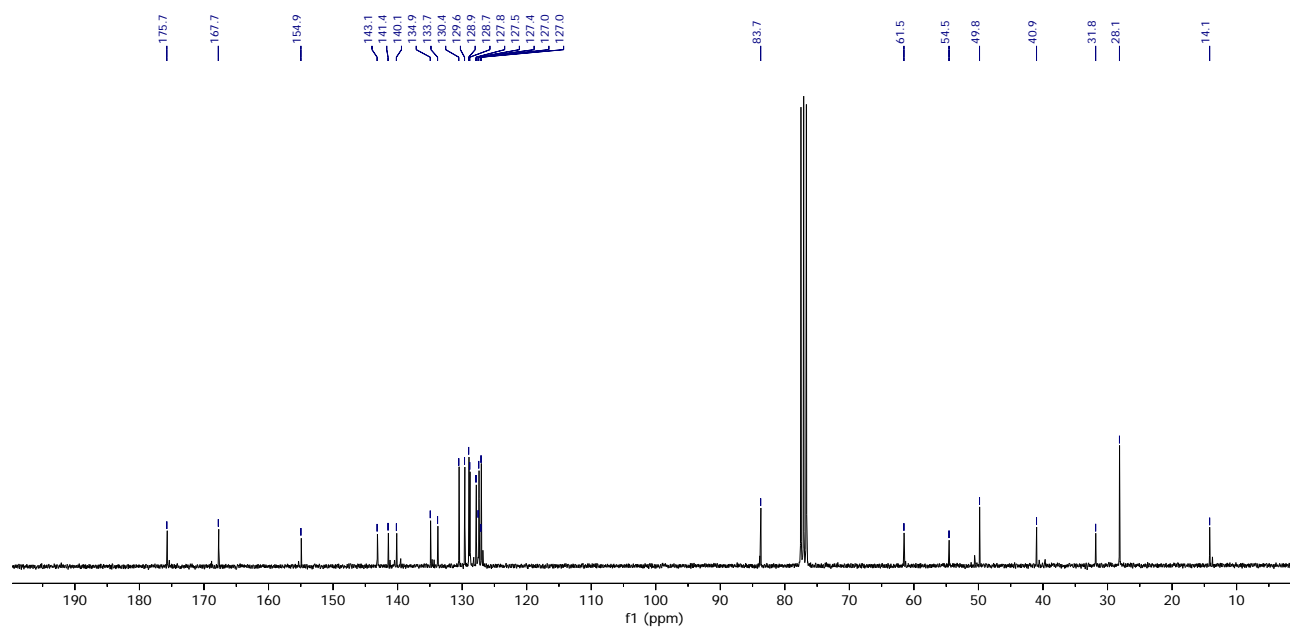
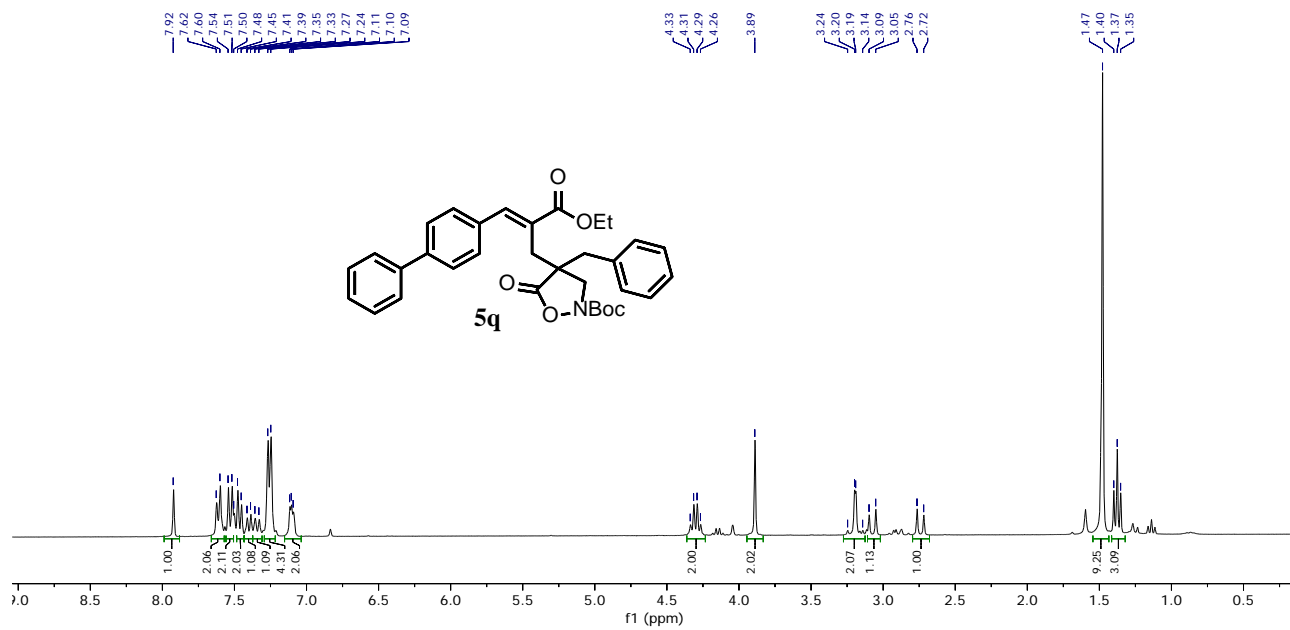


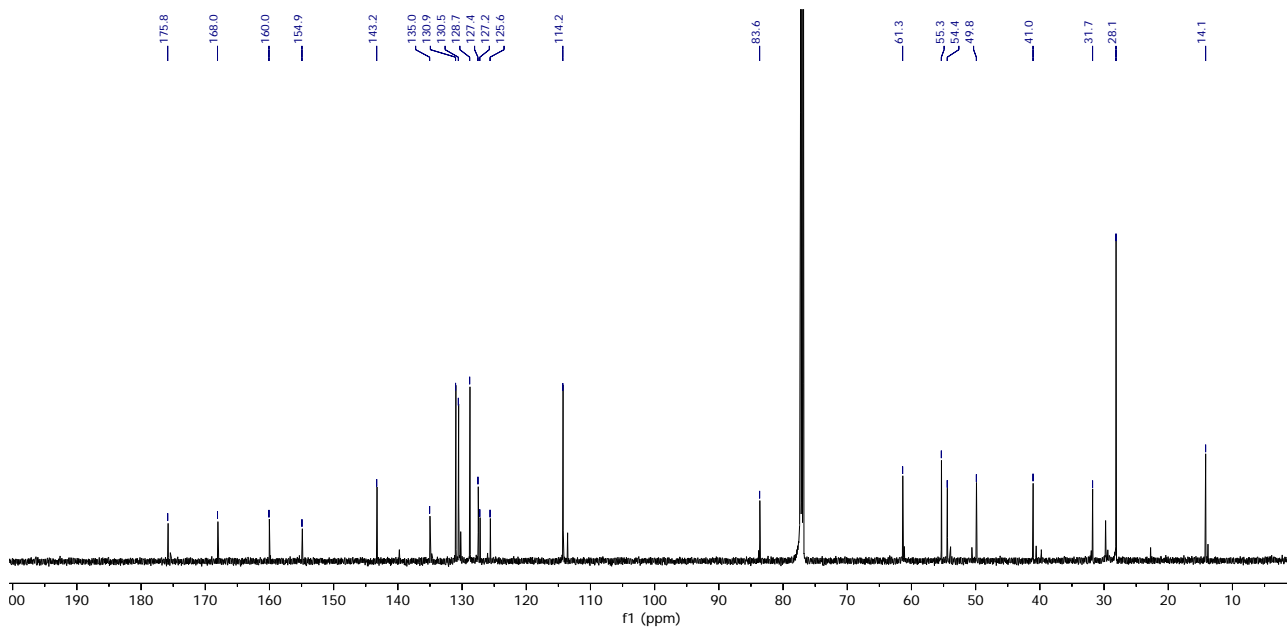
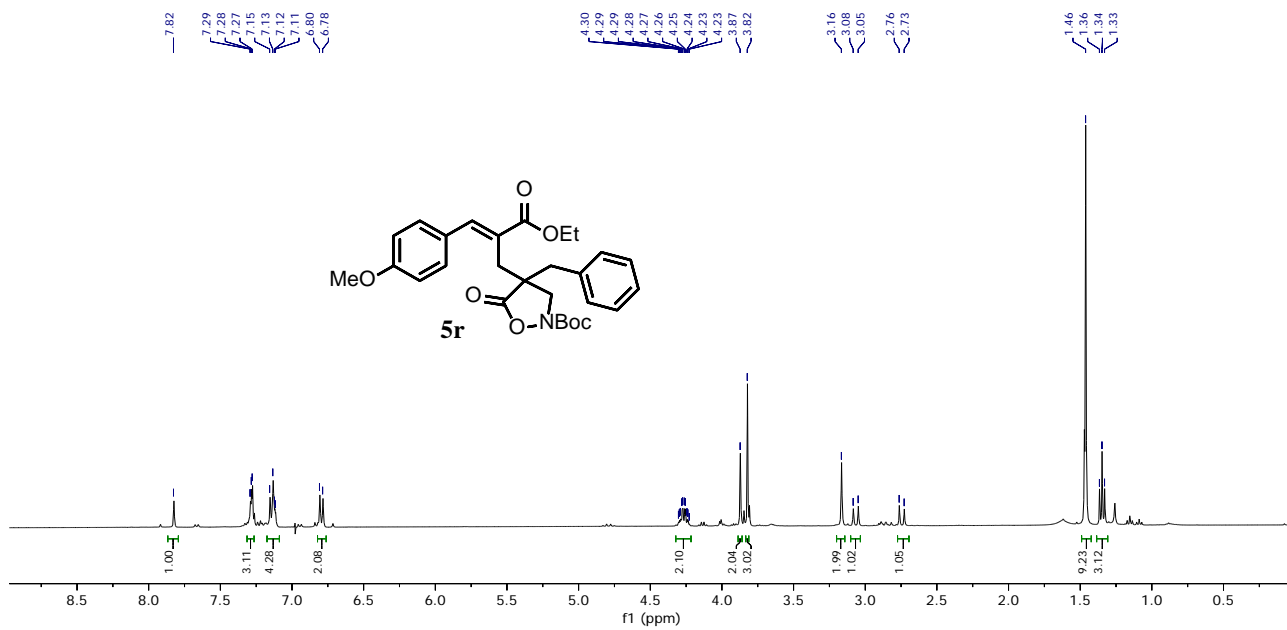


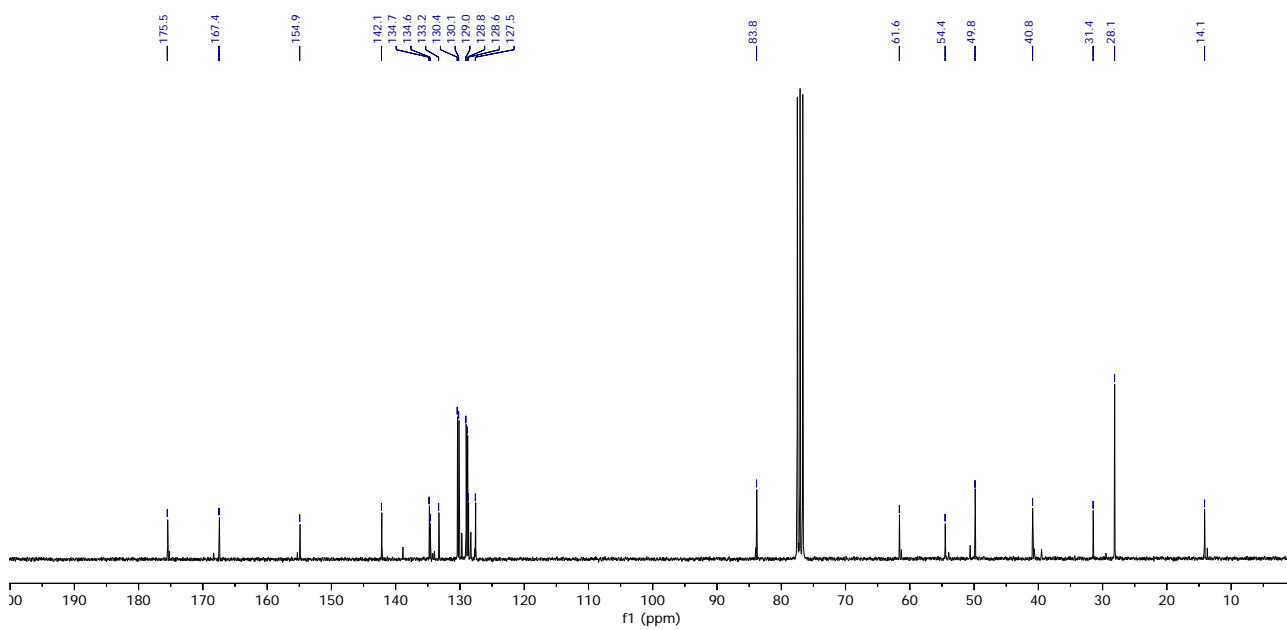
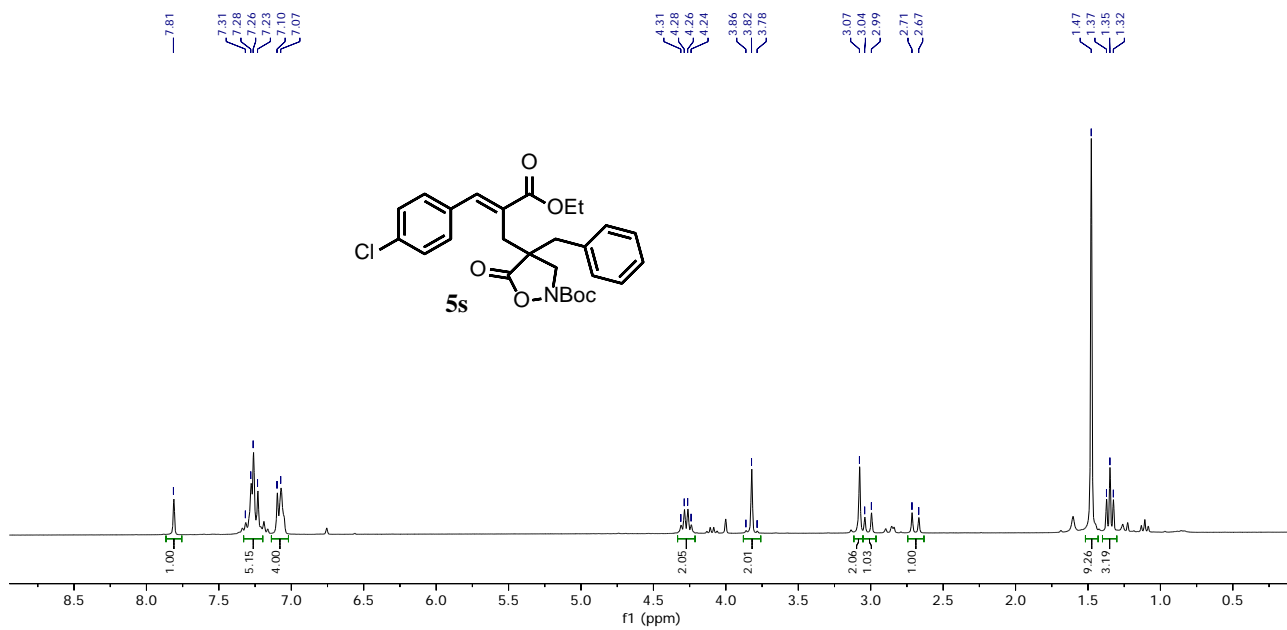


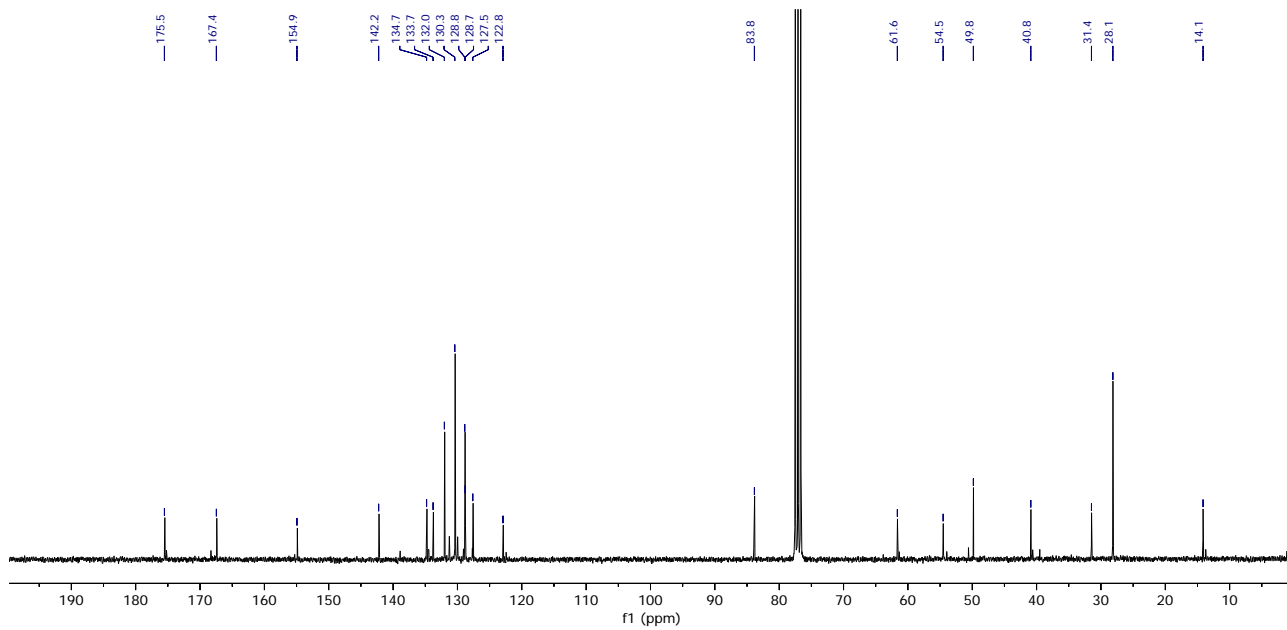
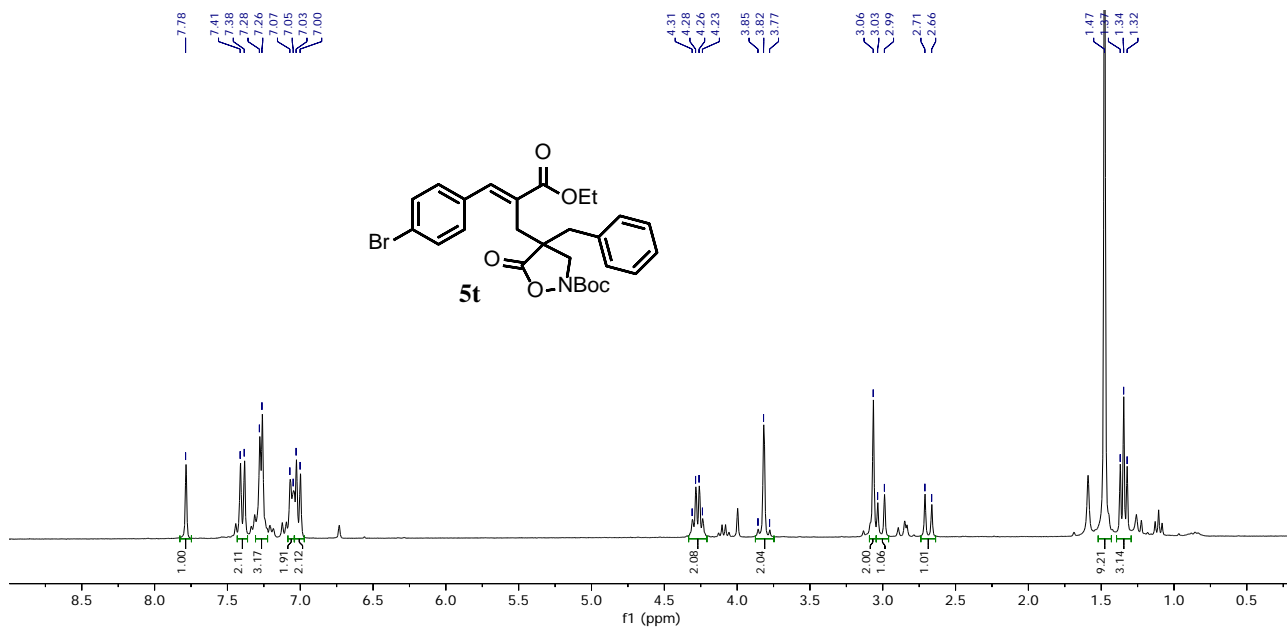


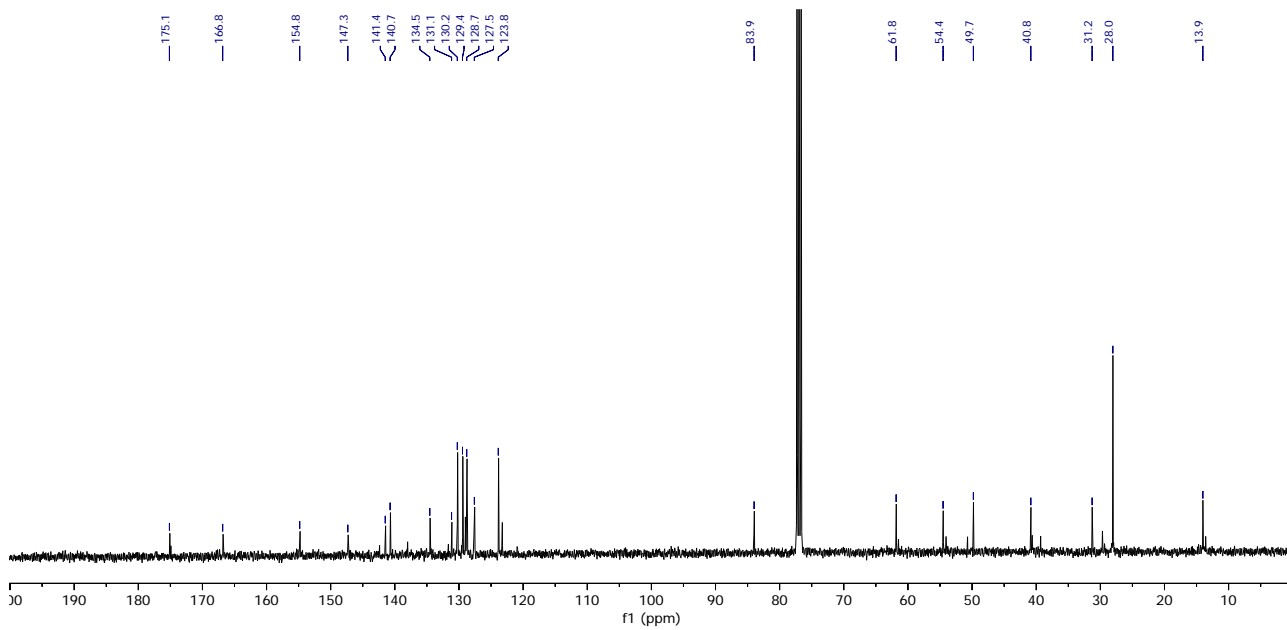
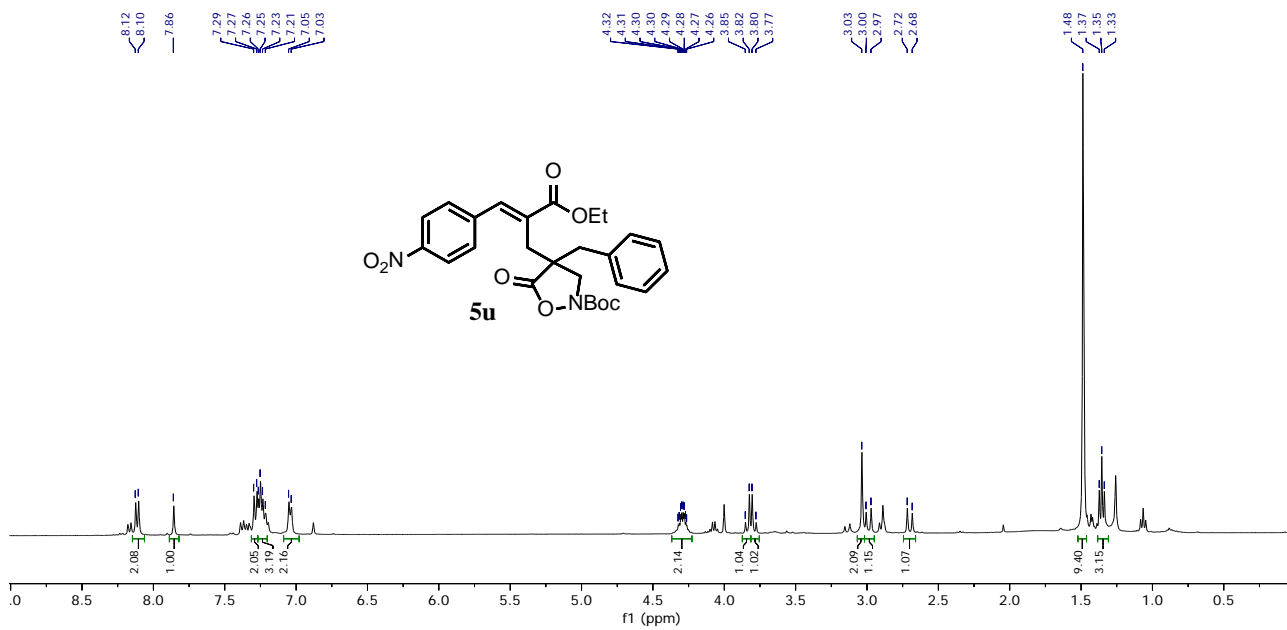


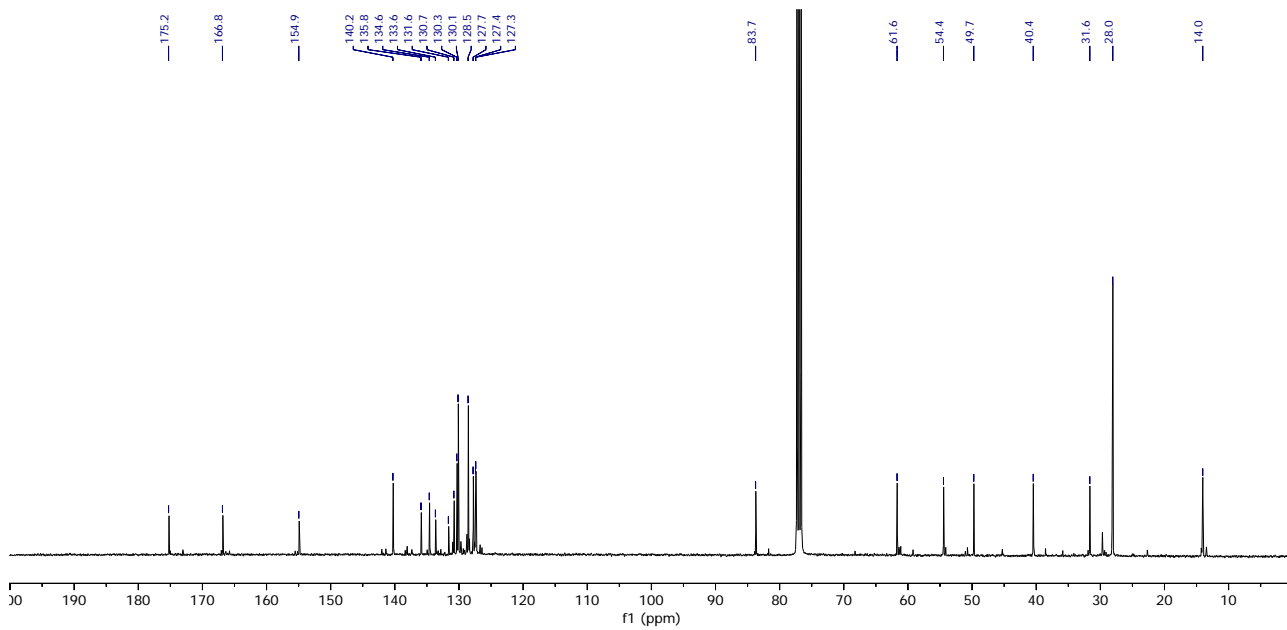
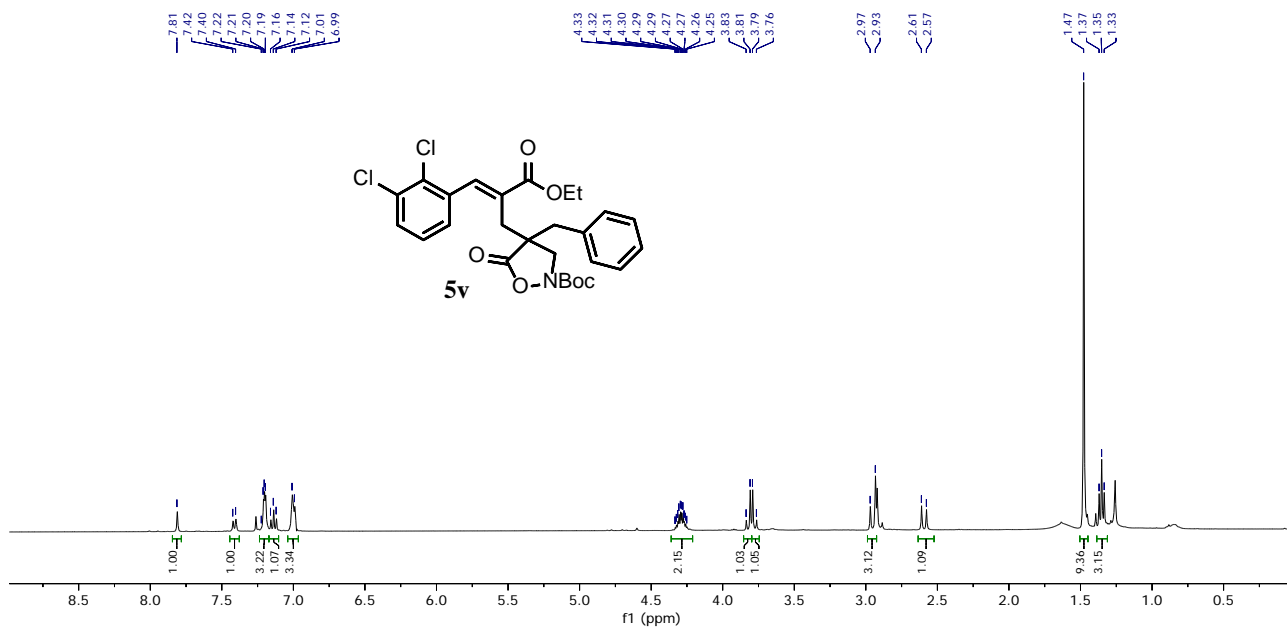


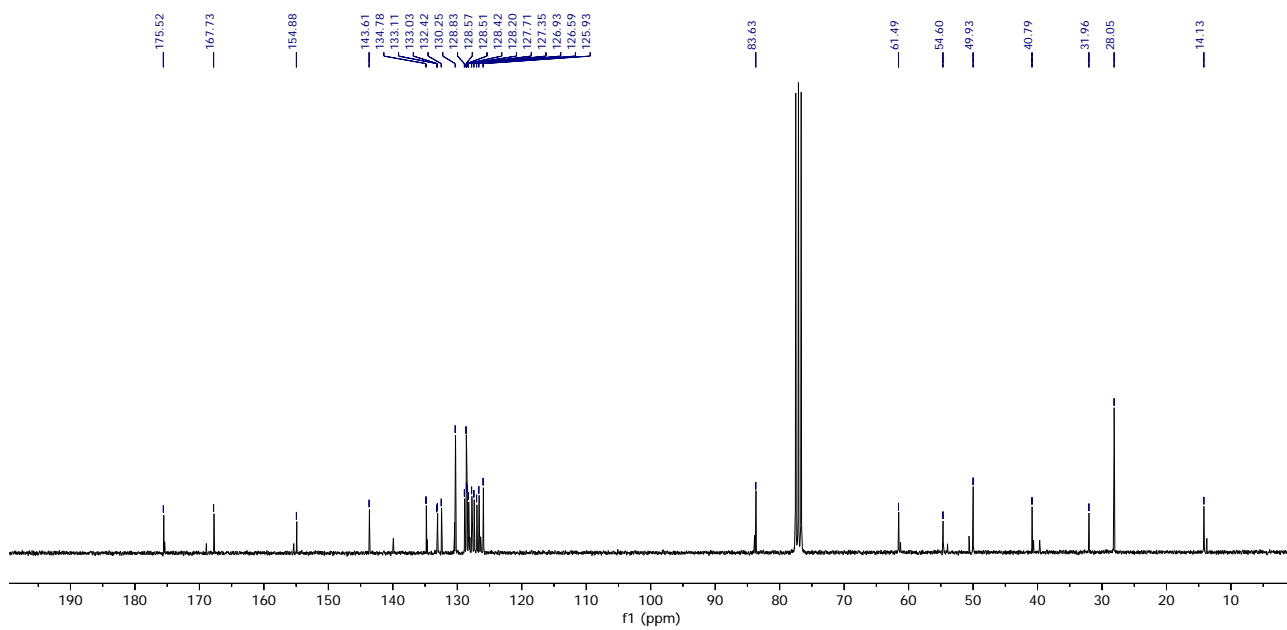
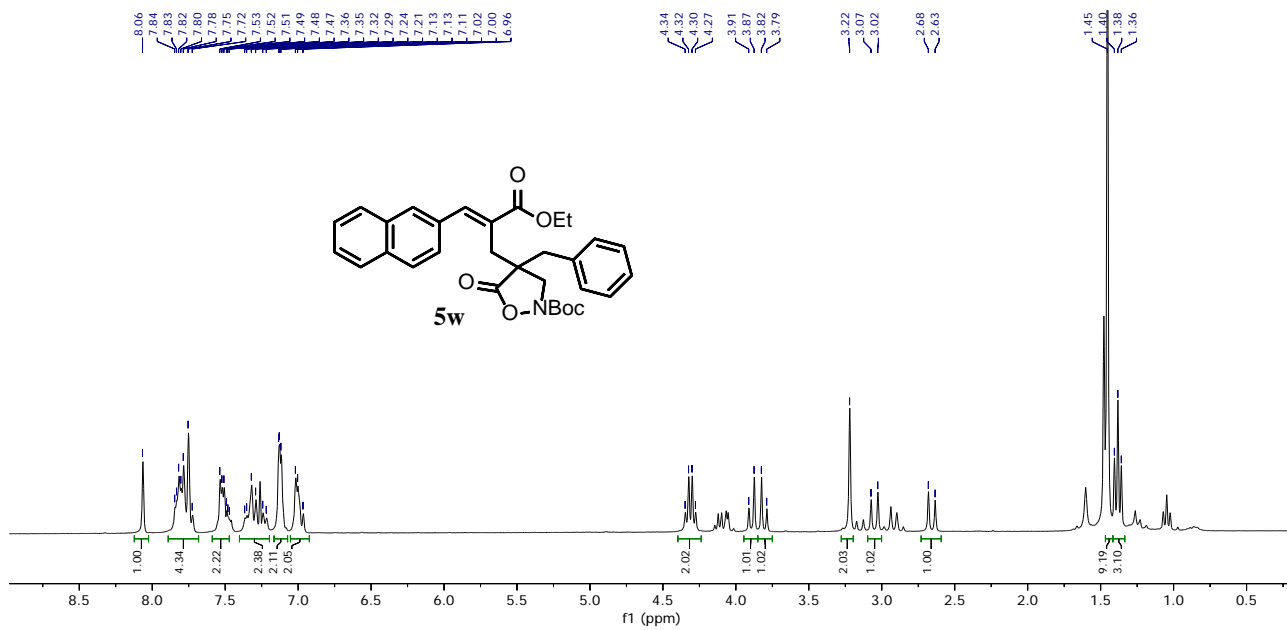


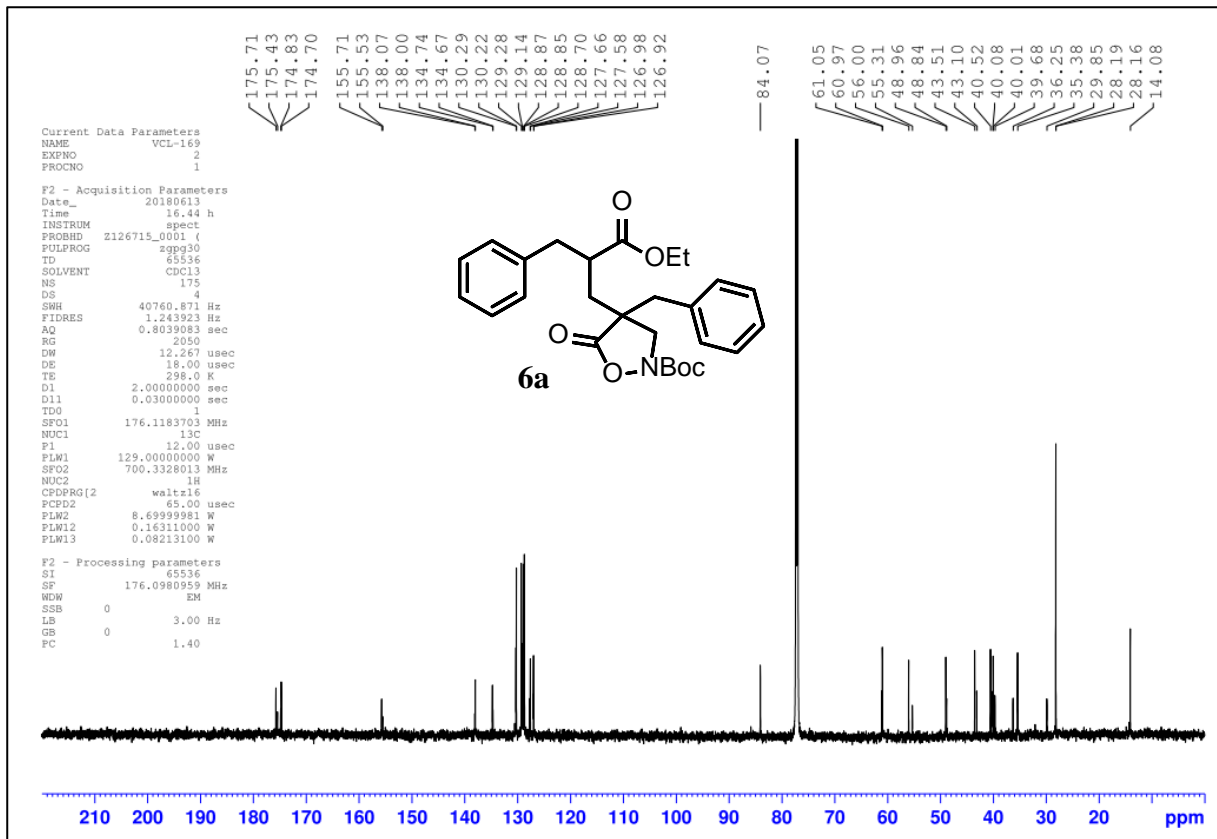
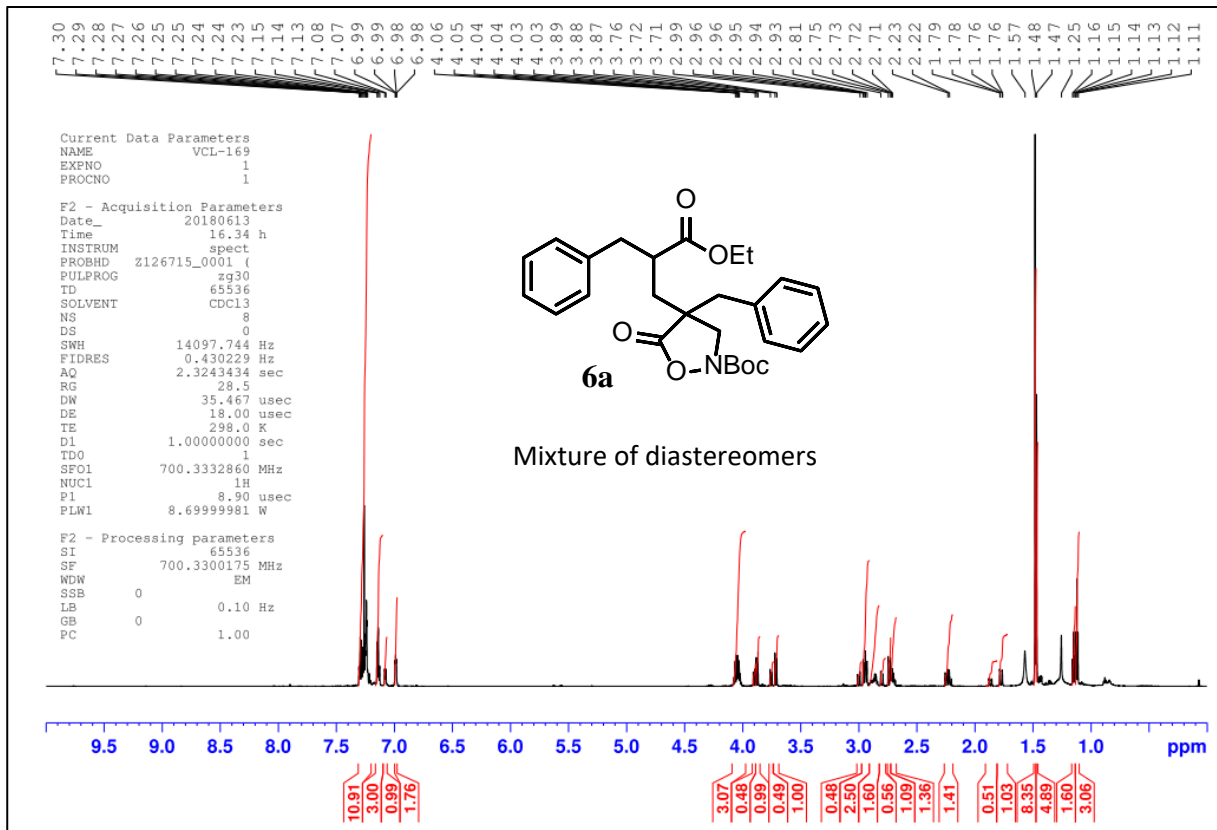










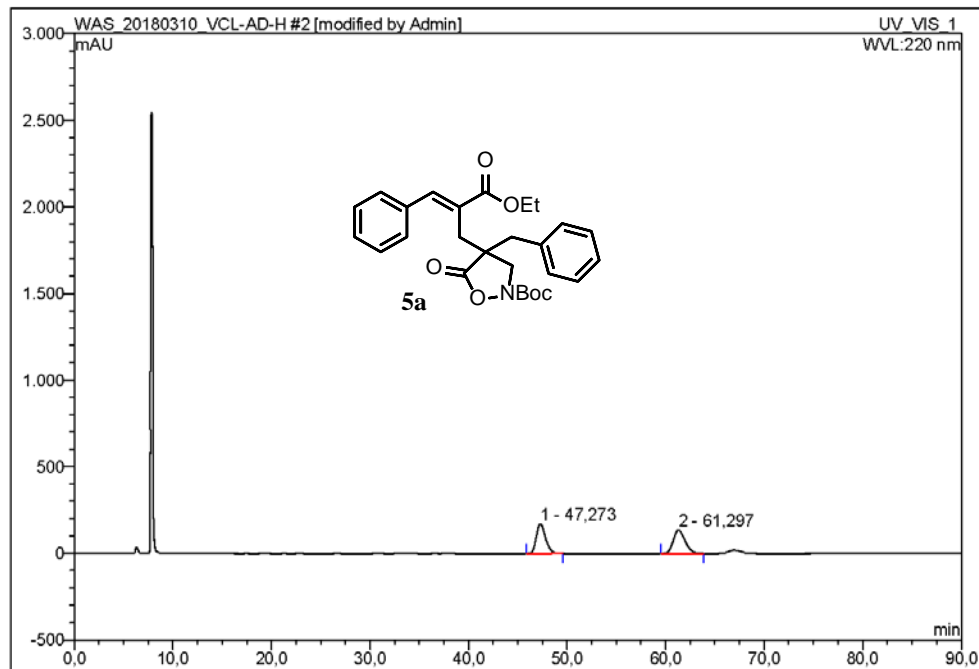


3. Copies of HPLC Chromatograms

Operator:Admin Timebase:U-3000_DAD Sequence:WAS_20180310_VCL-AD-H

Page 1-2
28.6.2018 7:21 PM

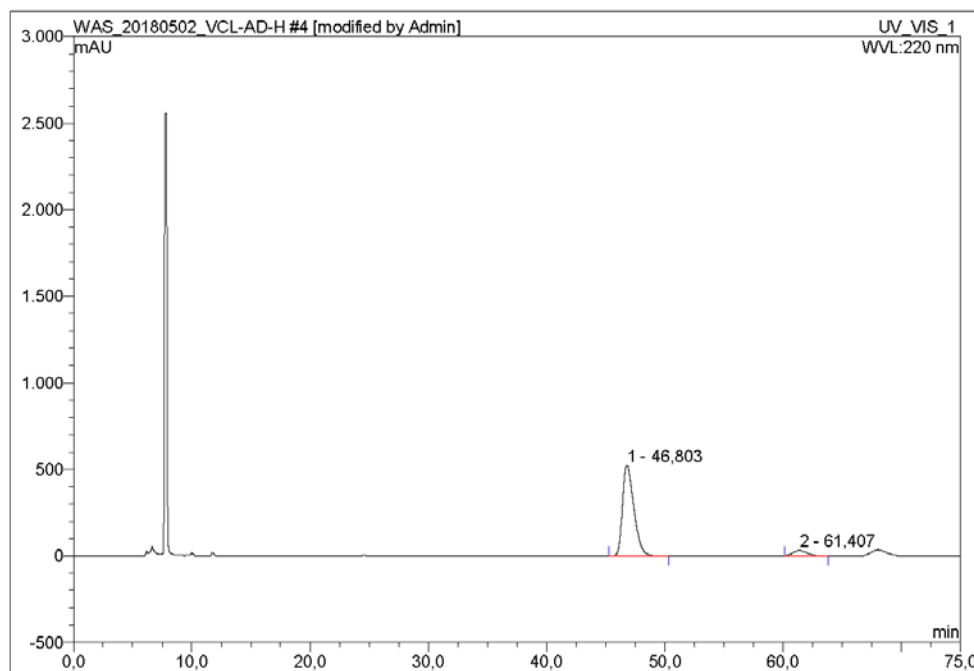
2 VCL-66-01-01 95/5 0,5 ml/min			
Sample Name:	VCL-66-01-01 95/5 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC90min_95-5_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	10.3.2018 13:38	Flow ml/min:	0,500
Run Time (min):	90,00	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	47,27	n.a.	170,848	185,289	49,86	n.a.	BMB
2	61,30	n.a.	134,840	186,360	50,14	n.a.	BMB
Total:			305,688	371,648	100,00	0,000	

4 VCL-189-01-01 95/5 0,5 ml/min

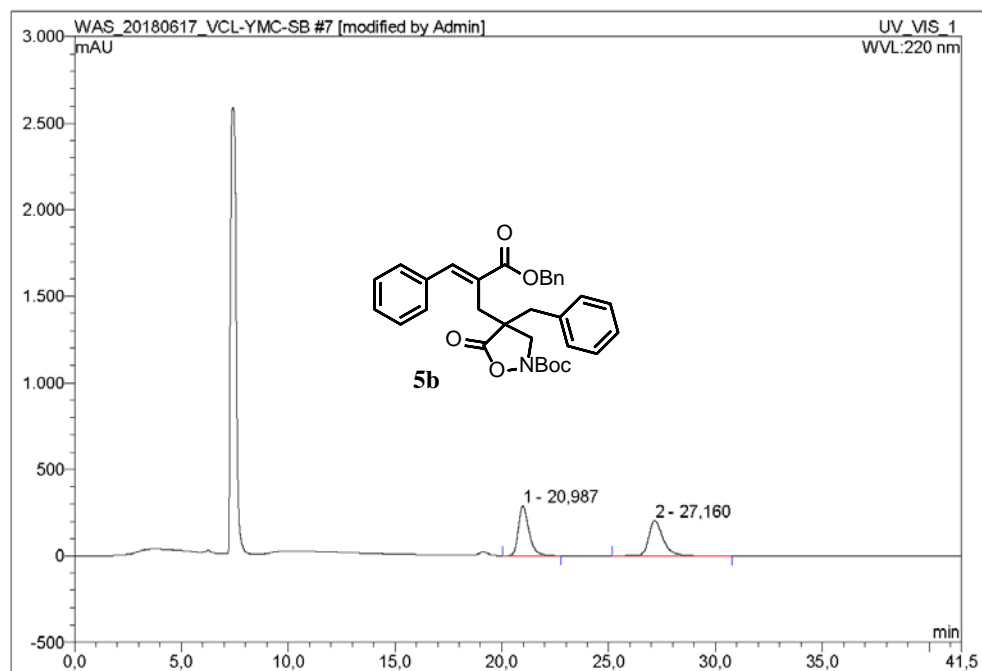
Sample Name:	VCL-189-01-01 95/5 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC75min_95-5_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	16.5.2018 14:44	Flow ml/min:	0,500
Run Time (min):	75,00	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	46,80	n.a.	524,094	582,612	93,69	n.a.	BMB*
2	61,41	n.a.	29,717	39,236	6,31	n.a.	BMB*
Total:			553,811	621,848	100,00	0,000	

7 VCL-115-01-01 80/20 0,5 ml/min

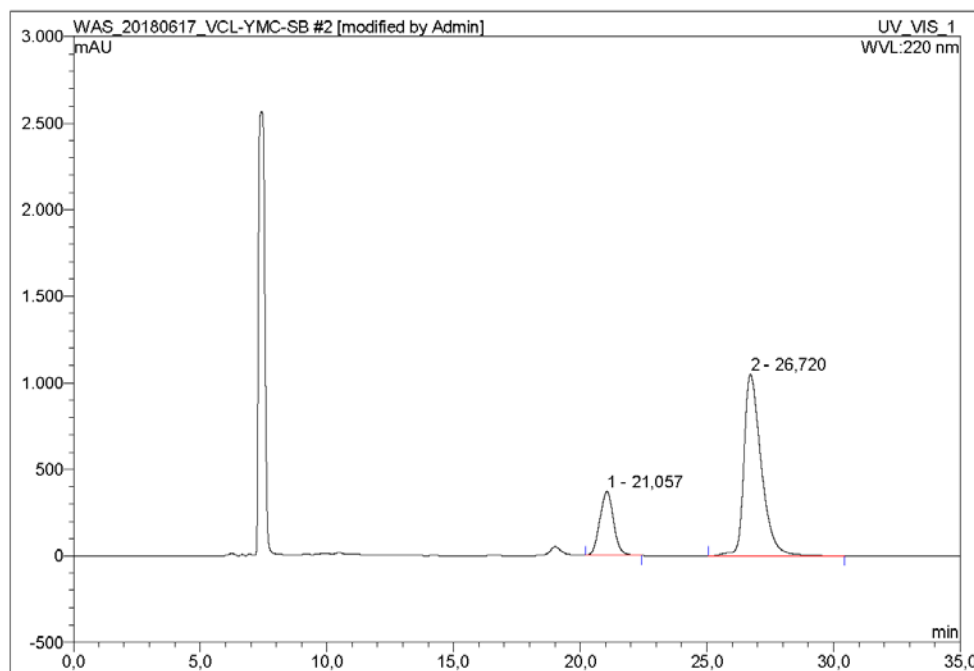
Sample Name:	VCL-115-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RB1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC60min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	11.6.2018 17:47	Flow ml/min:	0,500
Run Time (min):	41,50	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	20,99	n.a.	286,327	163,234	50,74	n.a.	BMB*
2	27,16	n.a.	204,069	158,475	49,26	n.a.	BMB*
Total:			490,396	321,709	100,00	0,000	

2 VCL-242-01-01 80/20 0,5 ml/min

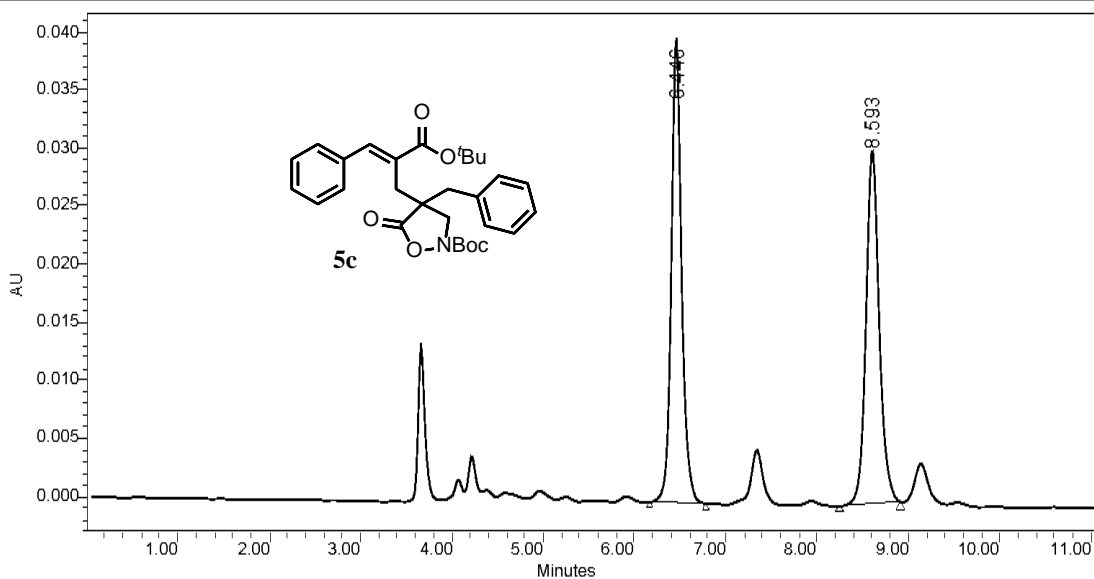
Sample Name:	VCL-242-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC35min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	18.6.2018 13:46	Flow ml/min:	0,500
Run Time (min):	35,00	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	21,06	n.a.	370,156	232,453	21,96	n.a.	BMB*
2	26,72	n.a.	1050,232	826,094	78,04	n.a.	BMB
Total:			1420,388	1058,546	100,00	0,000	

SAMPLE INFORMATION

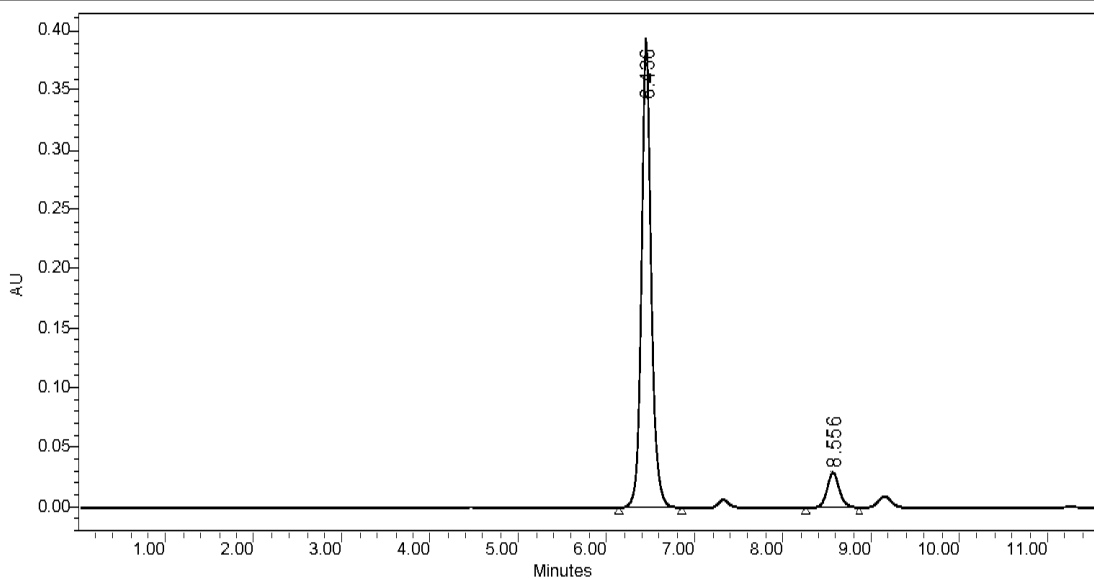
Sample Name:	VCL-114 rac IA-3	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/4/2018 10:55:34 AM
Vial:	1	Acq. Method:	80 20 a 08 ml
Injection #:	1	Date Processed:	9/4/2018 11:25:33 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	6.446	312847	50.36	39925	56.70
2	8.593	308353	49.64	30486	43.30

SAMPLE INFORMATION

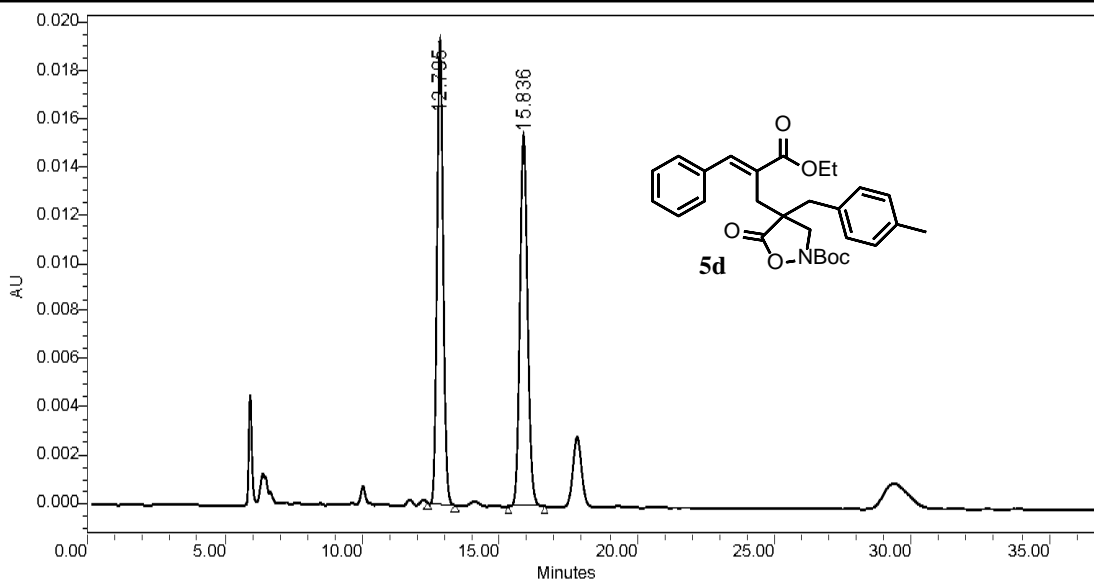
Sample Name:	VCL-304 IA-3	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/4/2018 11:11:00 AM
Vial:	1	Acq. Method:	80 20 a 08 ml
Injection #:	2	Date Processed:	9/4/2018 11:25:51 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	6.436	3007416	91.14	392781	92.96
2	8.556	292491	8.86	29738	7.04

SAMPLE INFORMATION

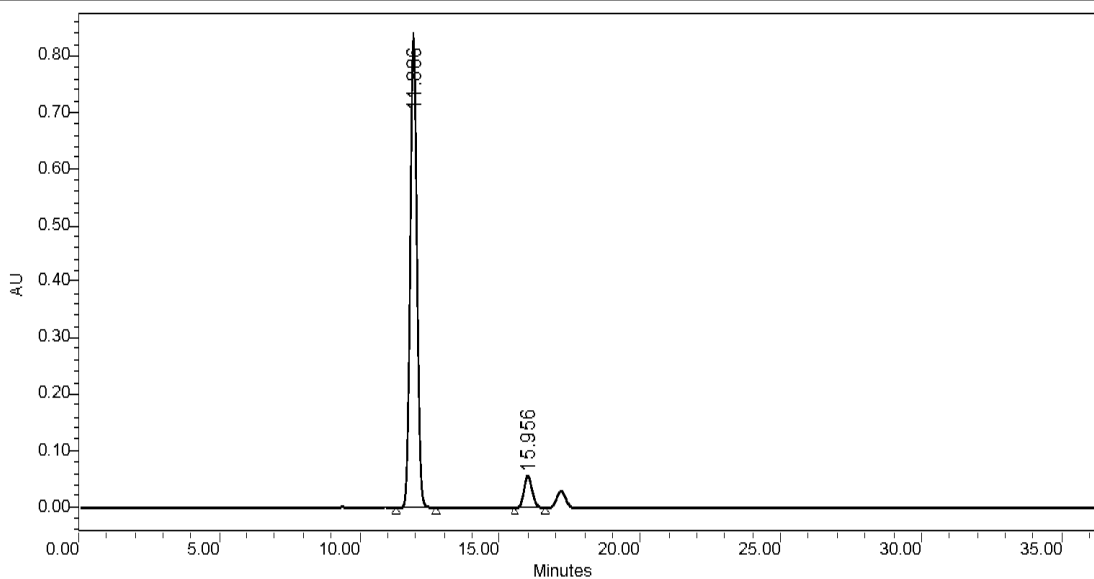
Sample Name:	VCL-252 RAC2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	7/7/2018 12:16:07 PM
Vial:	1	Acq. Method:	80 a 20 05
Injection #:	3	Date Processed:	8/3/2018 6:29:55 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	12.795	301488	49.98	19273	55.59
2	15.836	301694	50.02	15396	44.41

SAMPLE INFORMATION

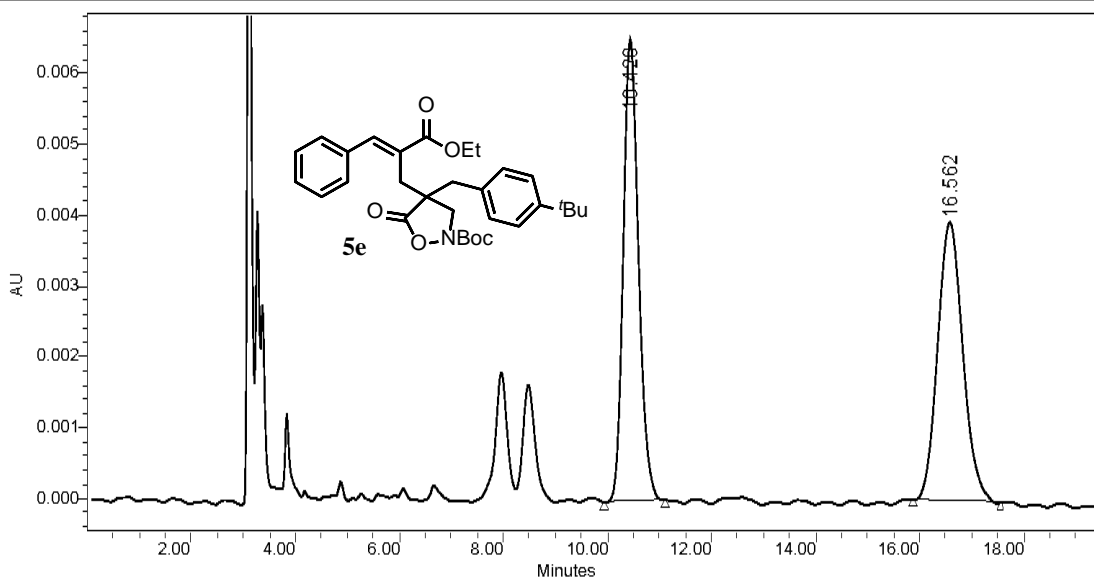
Sample Name:	VCL-281-5d	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/9/2018 3:58:30 PM
Vial:	1	Acq. Method:	80 20 05ml 254e270 nm
Injection #:	2	Date Processed:	10/9/2018 6:55:28 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (Δ*sec)	% Area	Height (Δ)	% Height
1	11.886	13940446	92.25	833274	93.70
2	15.956	1171345	7.75	56009	6.30

SAMPLE INFORMATION

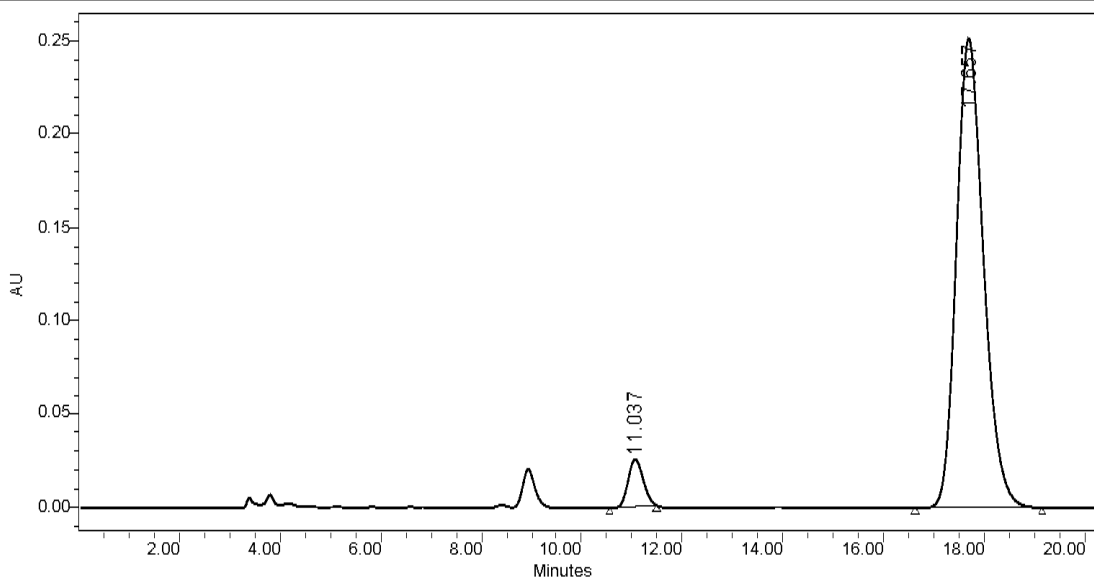
Sample Name:	VCL-275 RAC 4 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/2/2018 9:50:48 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	1	Date Processed:	8/3/2018 6:37:08 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	10.420	132581	50.04	6533	62.44
2	16.562	132343	49.96	3930	37.56

SAMPLE INFORMATION

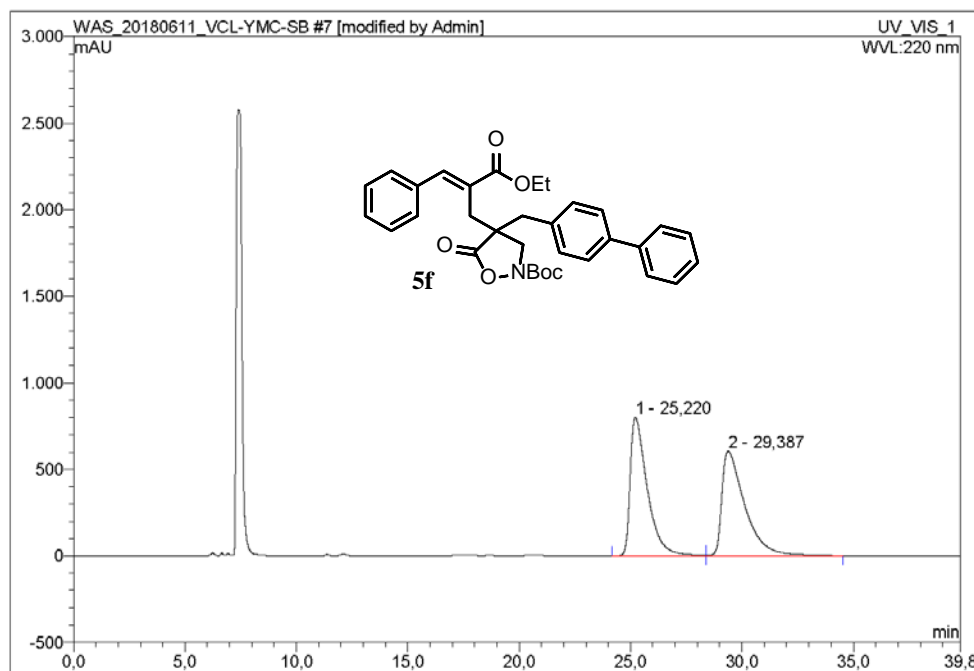
Sample Name:	VCL-302 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/28/2018 1:02:00 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	4	Date Processed:	8/30/2018 1:22:45 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	11.037	539117	5.41	25625	9.24
2	17.657	9430589	94.59	251845	90.76

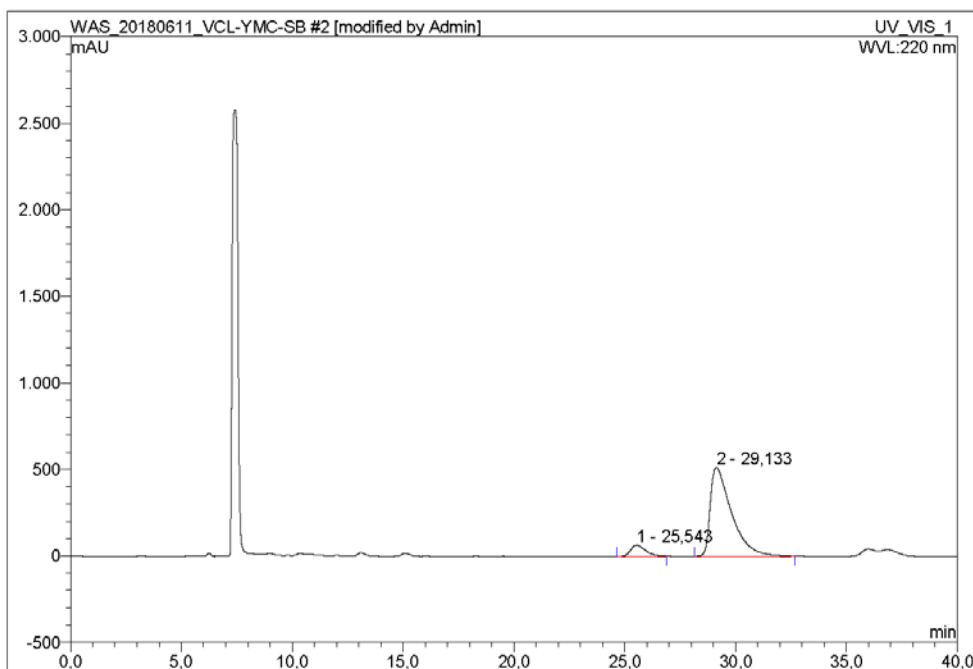
7 VCL-244-01-01 80/20 0,5 ml/min

Sample Name:	VCL-244-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA2	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC60min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	11.6.2018 16:31	Flow ml/min:	0,500
Run Time (min):	39,80	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25,22	n.a.	802,474	709,989	49,75	n.a.	BM
2	29,39	n.a.	604,830	717,046	50,25	n.a.	MB
Total:			1407,304	1427,035	100,00	0,000	

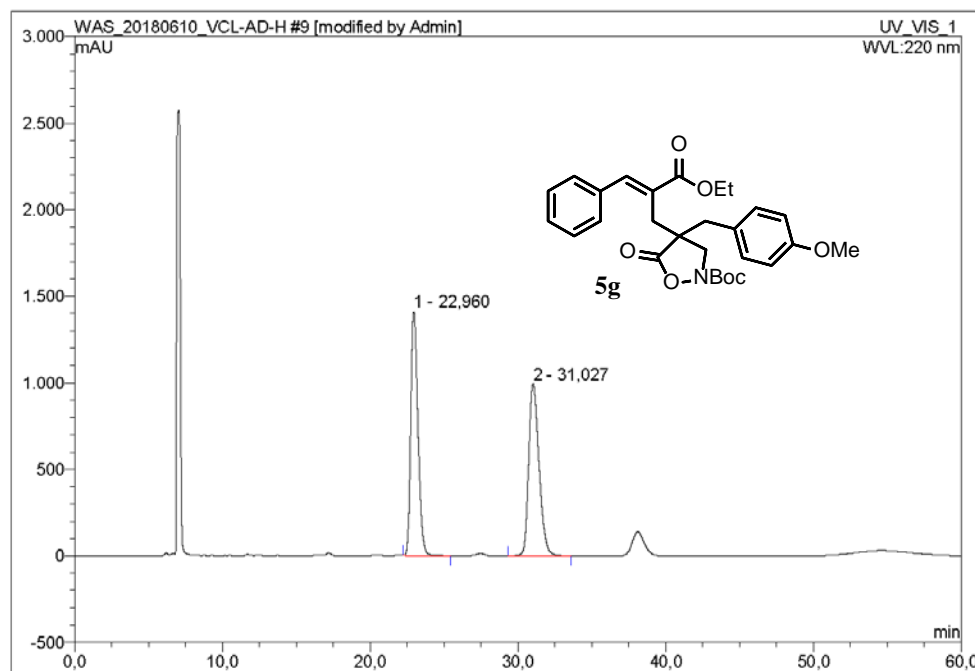
2 VCL-263-01-01 90/10 0,5 ml/min		
Sample Name:	VCL-263-01-01 90/10 0,5 ml/min	Injection Volume: 20,0
Vial Number:	RA1	Channel: UV_VIS_1
Sample Type:	unknown	Wavelength: 220
Control Program:	YMC40min_80-20_flow0,5	Bandwidth: 4
Quantif. Method:	default	Temperature/Column: 10
Recording Time:	27.6.2018 14:41	Flow ml/min: 0,500
Run Time (min):	40,00	Sample Amount: 1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25,54	n.a.	64,315	49,968	8,06	n.a.	BMB*
2	29,13	n.a.	513,895	570,107	91,94	n.a.	BMB*
Total:			578,210	620,075	100,00	0,000	

9 VCL-246-01-01 80/20 0,5 ml/min

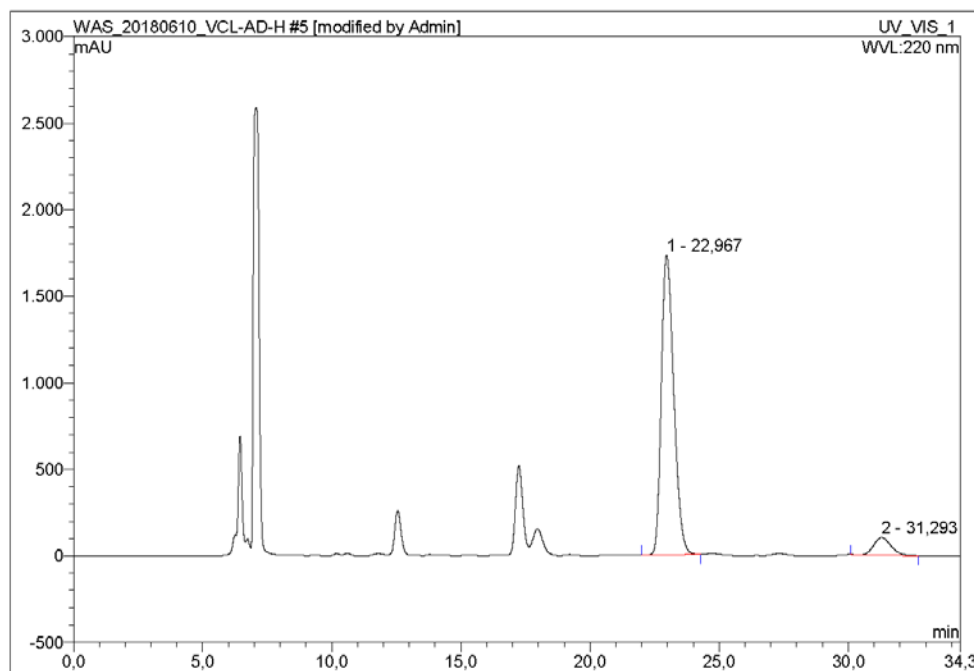
Sample Name:	VCL-246-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA4	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC60min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	11.6.2018 13:33	Flow ml/min:	0,500
Run Time (min):	60,00	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22,96	n.a.	1410,541	793,666	49,69	n.a.	BMB
2	31,03	n.a.	994,045	803,564	50,31	n.a.	BMB
Total:			2404,586	1597,230	100,00	0,000	

5 VCL-258-01-01 80/20 0,5 ml/min

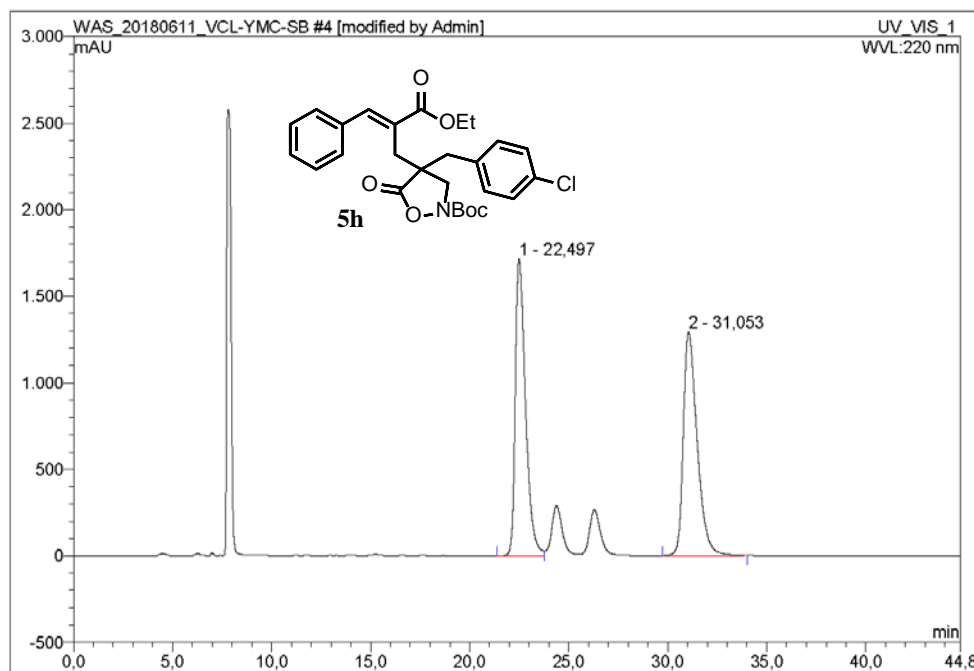
Sample Name:	VCL-258-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC60min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	18.6.2018 17:28	Flow ml/min:	0,500
Run Time (min):	34,34	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22,97	n.a.	1732,781	968,815	92,58	n.a.	BMB*
2	31,29	n.a.	103,647	77,620	7,42	n.a.	BMB*
Total:			1836,428	1046,435	100,00	0,000	

4 VCL-245-01-01 90/10 0,5 ml/min

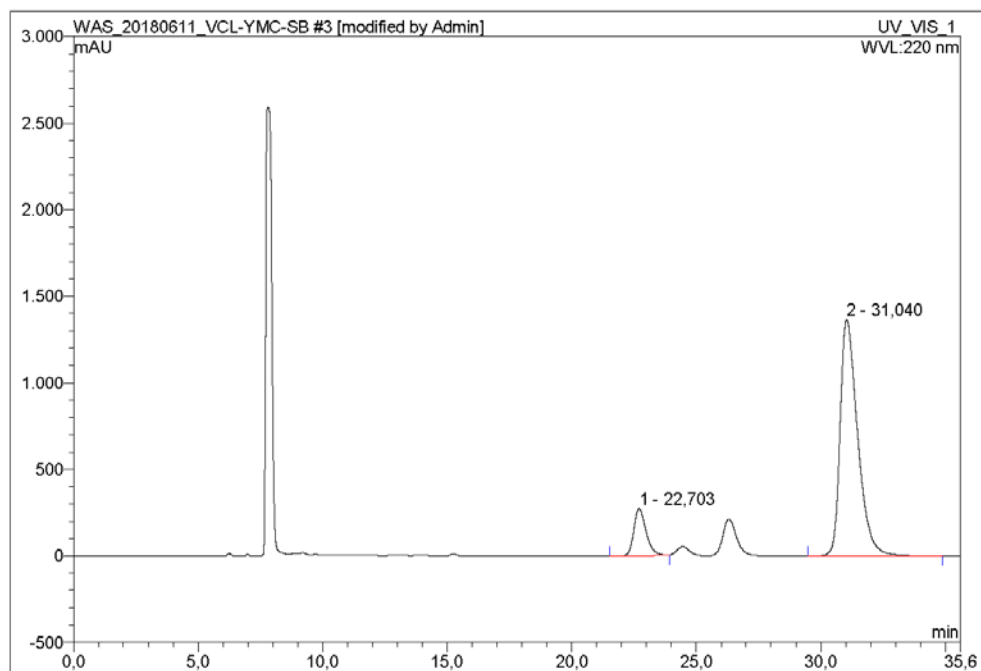
Sample Name:	VCL-245-01-01 90/10 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA2	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC75min_90-10_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	18.6.2018 14:50	Flow ml/min:	0,500
Run Time (min):	44,77	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22,50	n.a.	1717,597	1026,634	49,60	n.a.	BM *
2	31,05	n.a.	1291,391	1043,342	50,40	n.a.	BMB*
Total:			3008,988	2069,976	100,00	0,000	

3 VCL-257-01-01 90/10 0,5 ml/min

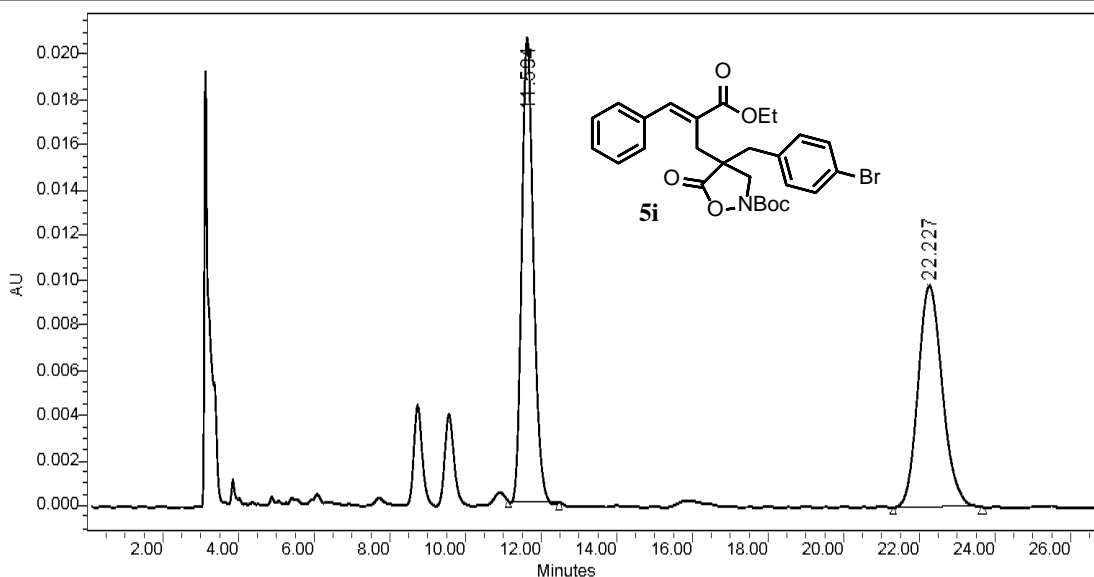
Sample Name:	VCL-257-01-01 90/10 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA3	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC75min_90-10_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	18.6.2018 15:41	Flow ml/min:	0,500
Run Time (min):	35,60	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	22,70	n.a.	272,411	152,708	12,05	n.a.	BMB*
2	31,04	n.a.	1367,472	1114,483	87,95	n.a.	BMB
Total:			1639,882	1267,190	100,00	0,000	

SAMPLE INFORMATION

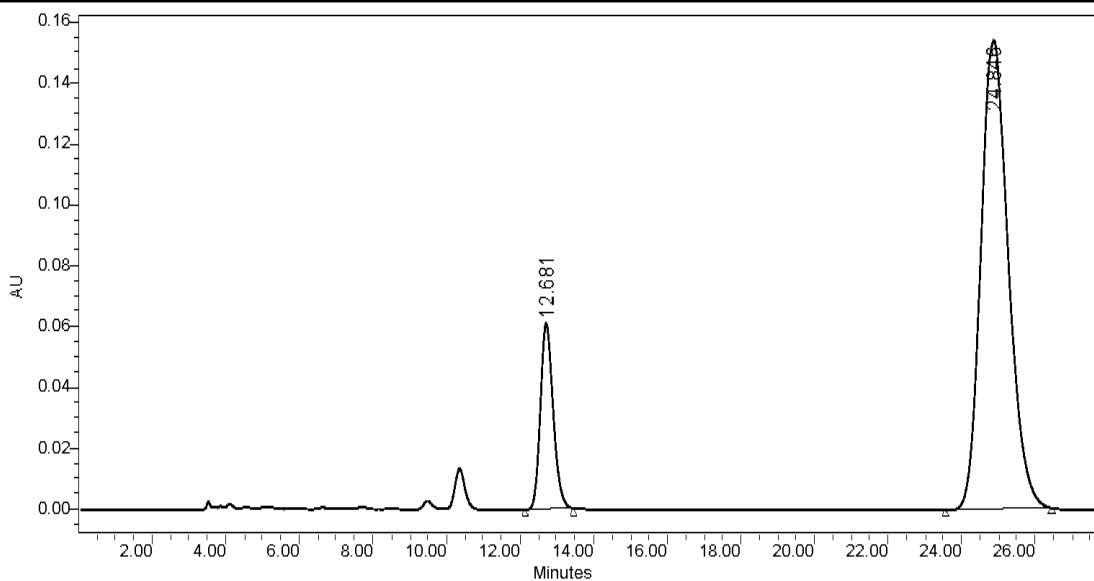
Sample Name:	VCL-250 RAC IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/2/2018 10:13:34 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	2	Date Processed:	8/3/2018 6:39:12 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	11.594	440524	49.95	20569	67.63
2	22.227	441343	50.05	9845	32.37

SAMPLE INFORMATION

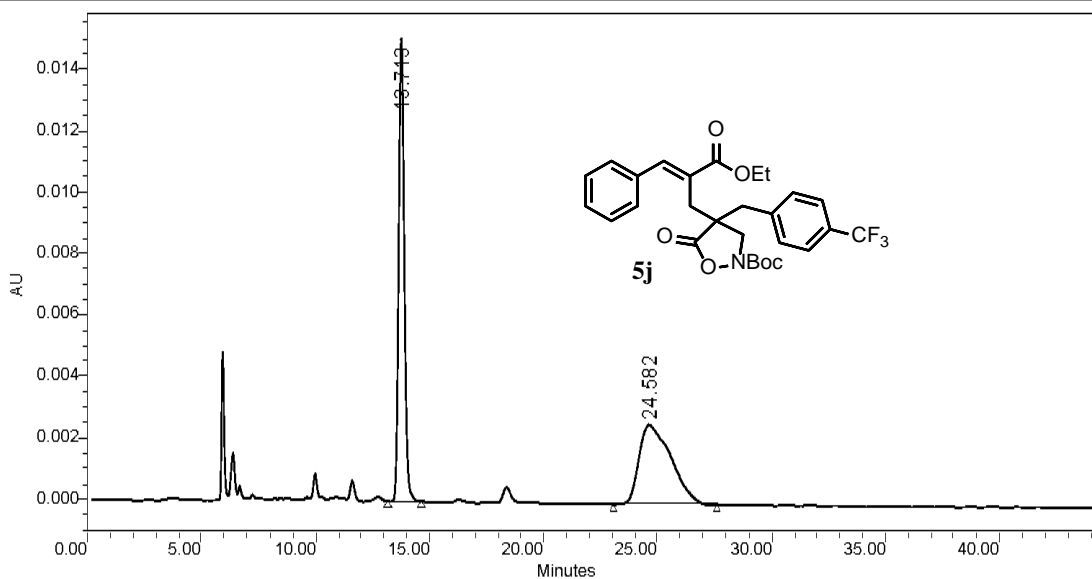
Sample Name:	VCL-301 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/27/2018 5:15:30 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	1	Date Processed:	8/30/2018 1:20:42 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	12.681	1470326	15.54	60969	28.36
2	24.846	7992438	84.46	154043	71.64

SAMPLE INFORMATION

Sample Name:	VCL-274 RAC2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	7/7/2018 12:56:17 PM
Vial:	1	Acq. Method:	80 a 20 05
Injection #:	4	Date Processed:	8/6/2018 5:20:10 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

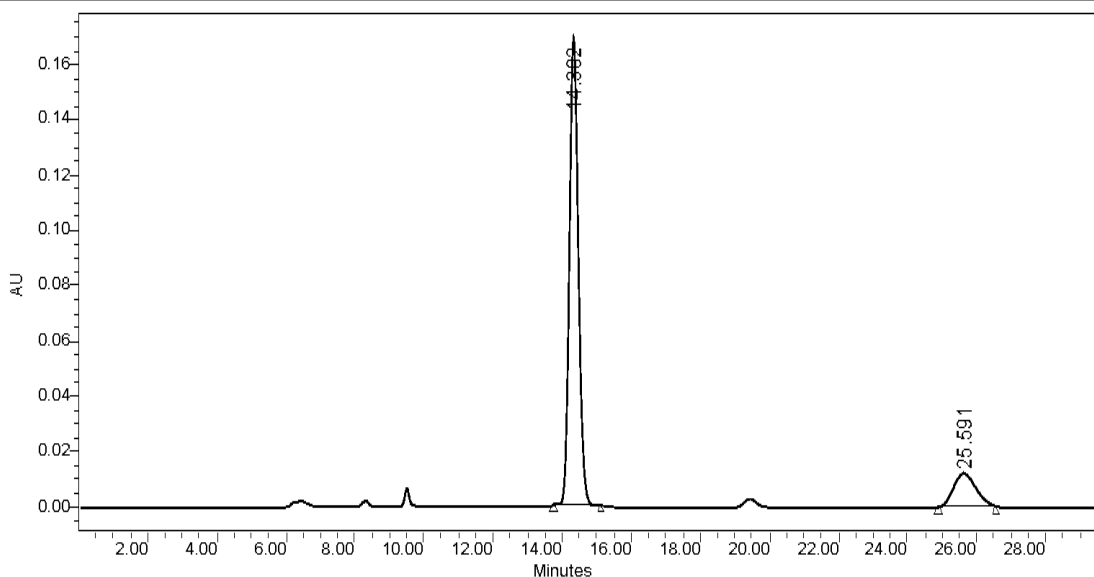


	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	13.713	255064	50.18	15078	85.36
2	24.582	253185	49.82	2585	14.64



SAMPLE INFORMATION

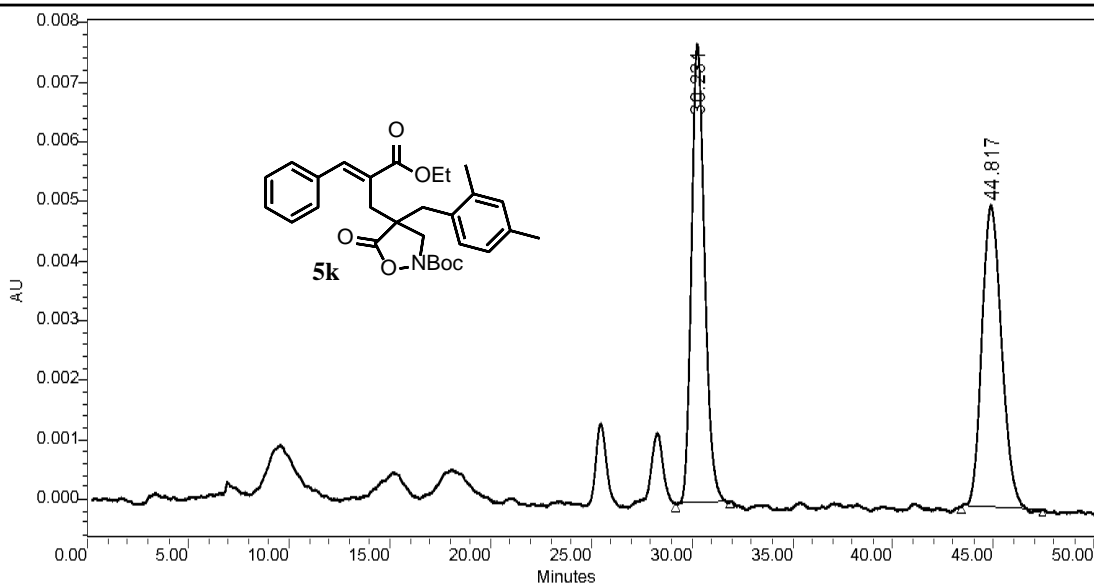
Sample Name:	VCL-280-2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/9/2018 4:48:29 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	3	Date Processed:	10/9/2018 6:54:42 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	14.302	3043075	84.82	168756	93.35
2	25.591	544549	15.18	12024	6.65

SAMPLE INFORMATION

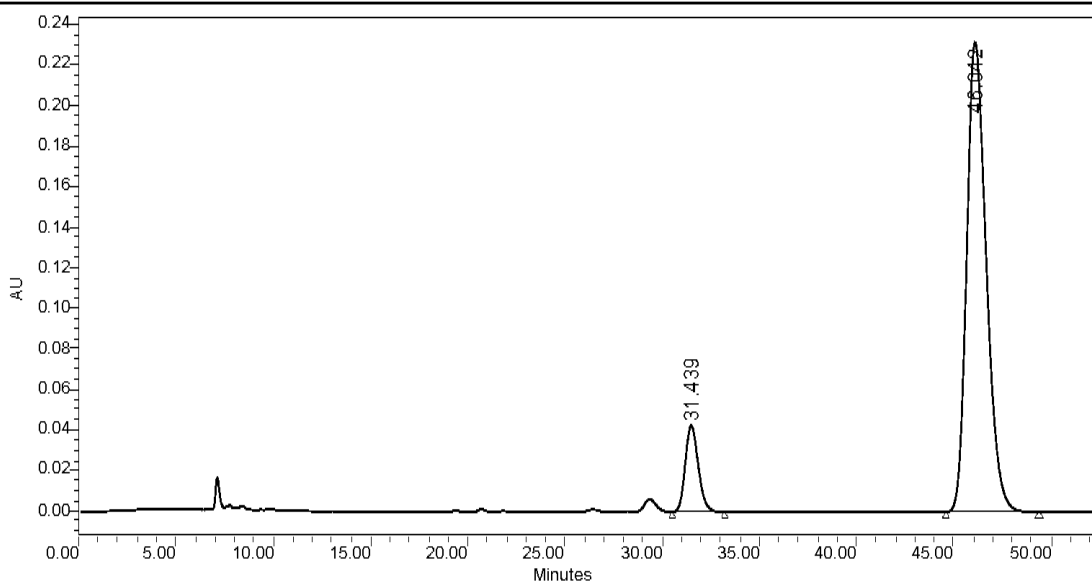
Sample Name:	VCL-276-5 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/27/2018 4:03:38 PM
Vial:	1	Acq. Method:	90 a 10 05ml 220 254
Injection #:	2	Date Processed:	8/27/2018 4:54:10 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	30.231	349445	50.21	7691	60.25
2	44.817	346483	49.79	5074	39.75

SAMPLE INFORMATION

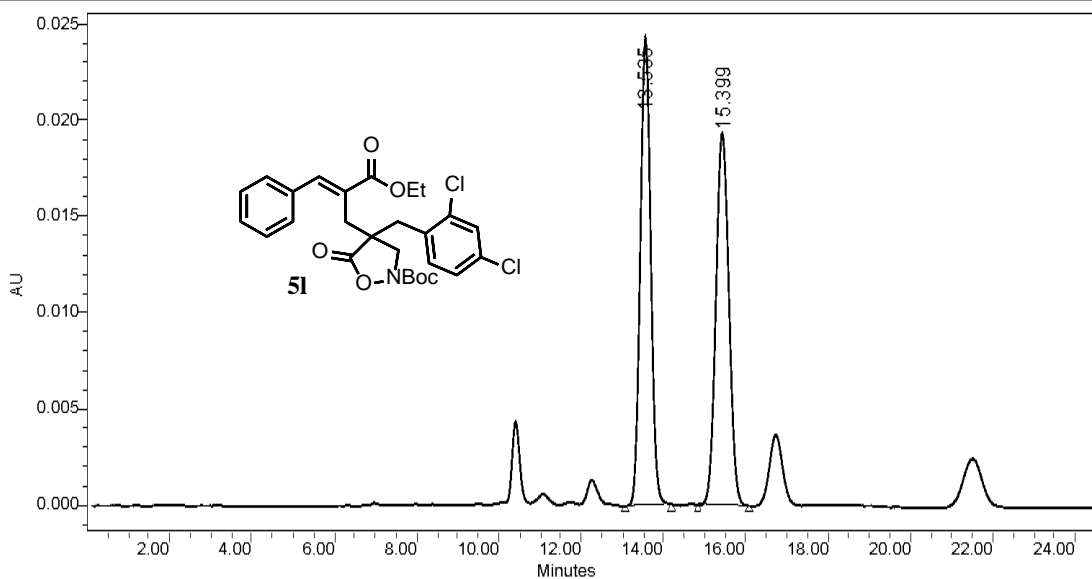
Sample Name:	VCL-299 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/27/2018 3:04:46 PM
Vial:	1	Acq. Method:	90 a 10 05ml 220 254
Injection #:	1	Date Processed:	8/27/2018 4:54:45 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (Δ*sec)	% Area	Height (Δ)	% Height
1	31.439	1989204	10.97	42587	15.54
2	46.042	16137731	89.03	231454	84.46

SAMPLE INFORMATION

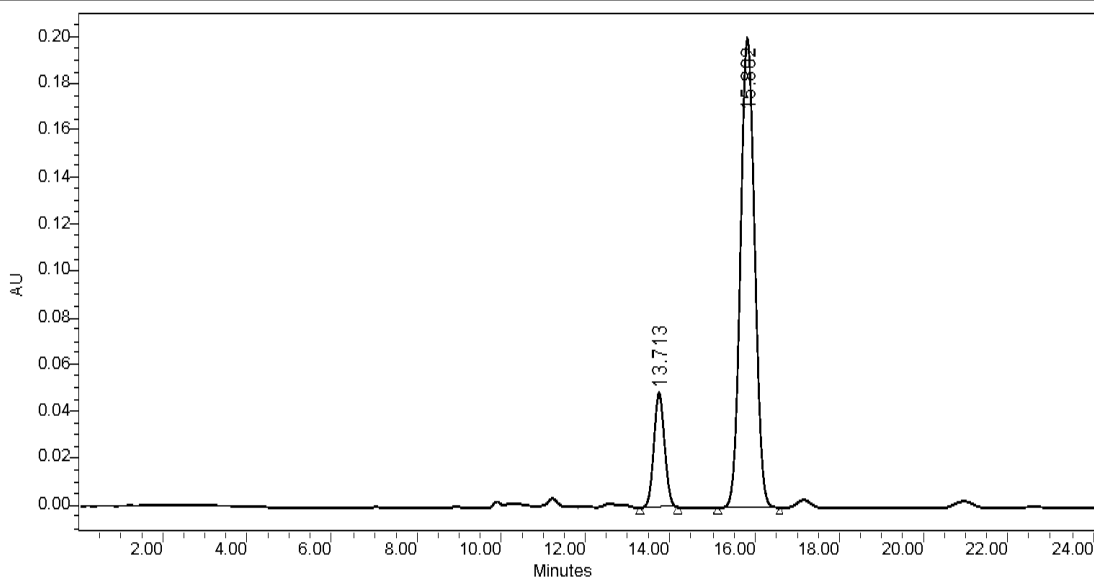
Sample Name:	VCL-251-2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 4:37:48 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	3	Date Processed:	8/30/2018 1:11:04 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	13.535	428075	50.20	24244	55.63
2	15.399	424651	49.80	19339	44.37

SAMPLE INFORMATION

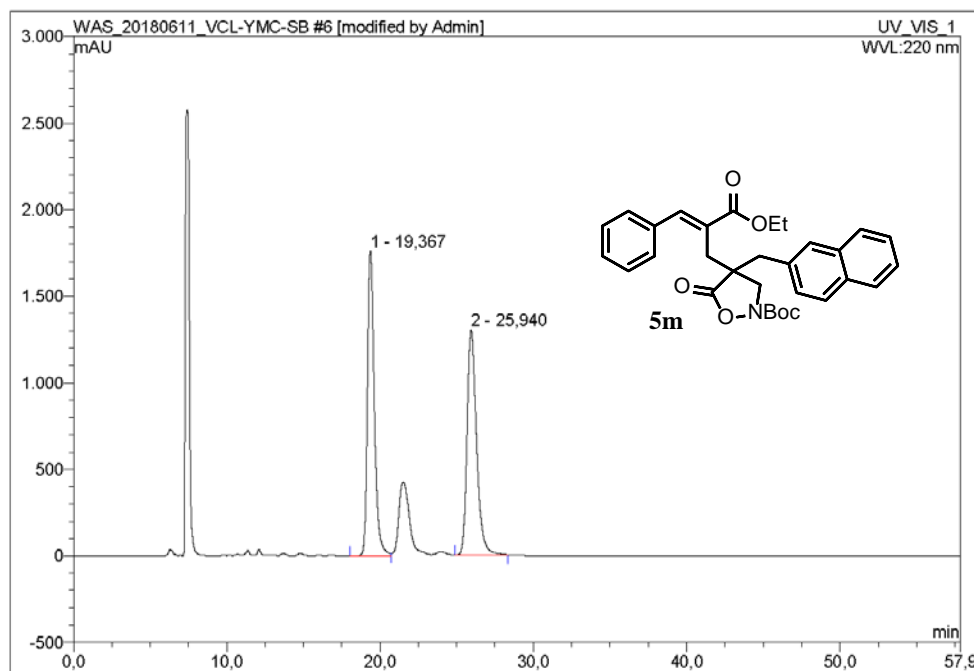
Sample Name:	VCL-293-6 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 3:41:20 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	1	Date Processed:	8/30/2018 1:18:56 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	13.713	863178	15.51	48854	19.61
2	15.802	4702193	84.49	200323	80.39

6 VCL-243-01-01 80/20 0,5 ml/min

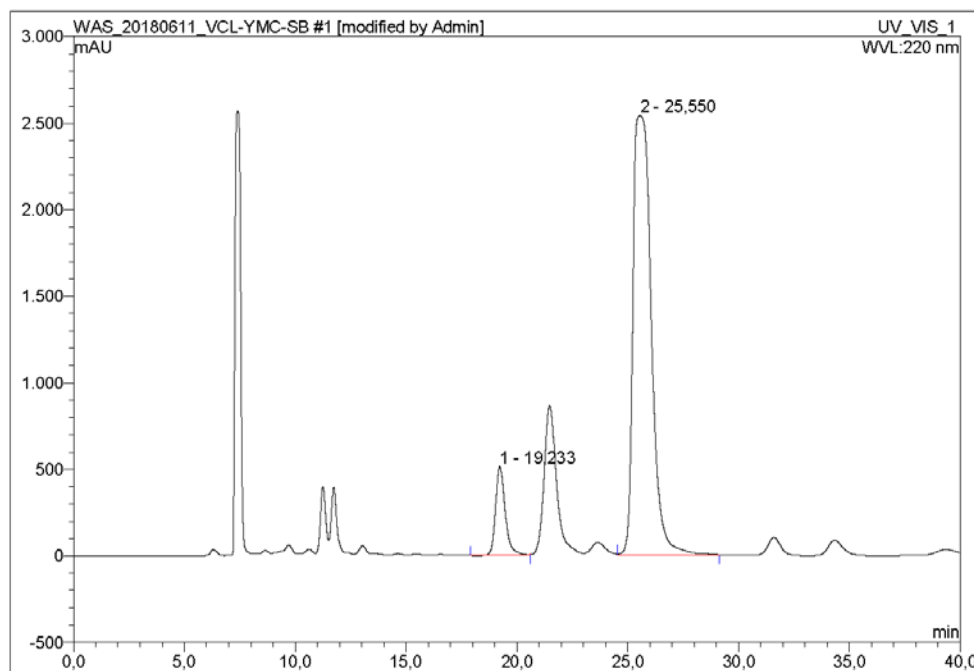
Sample Name:	VCL-243-01-01 80/20 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA1	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC60min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	11.6.2018 15:32	Flow ml/min:	0,500
Run Time (min):	57,85	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,37	n.a.	1760,992	917,903	49,55	n.a.	BM *
2	25,94	n.a.	1301,805	934,714	50,45	n.a.	BMB*
Total:			3062,798	1852,618	100,00	0,000	

1 VCL-264-01-01 90/10 0,5 ml/min

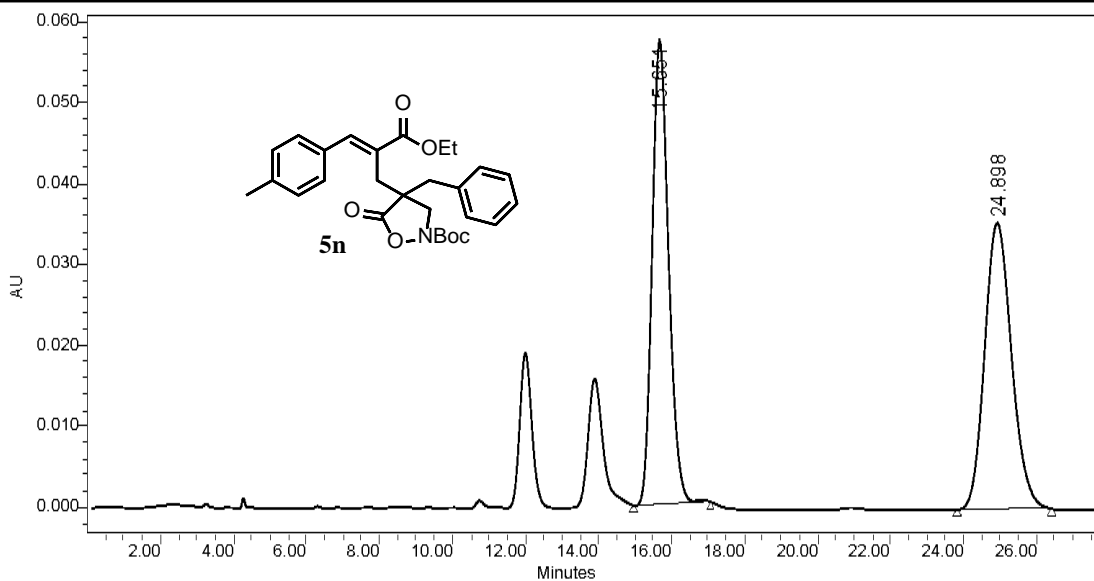
Sample Name:	VCL-264-01-01 90/10 0,5 ml/min	Injection Volume:	20,0
Vial Number:	RA2	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	220
Control Program:	YMC40min_80-20_flow0,5	Bandwidth:	4
Quantif. Method:	default	Temperature/Column:	10
Recording Time:	27.6.2018 14:01	Flow ml/min:	0,500
Run Time (min):	40,00	Sample Amount:	1,0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,23	n.a.	511,766	254,128	9,49	n.a.	BMB*
2	25,55	n.a.	2541,047	2422,918	90,51	n.a.	MB*
Total:			3052,813	2677,046	100,00	0,000	

SAMPLE INFORMATION

Sample Name:	VCL-256 racemo	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/10/2018 12:00:15 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	4	Date Processed:	10/10/2018 12:36:35 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

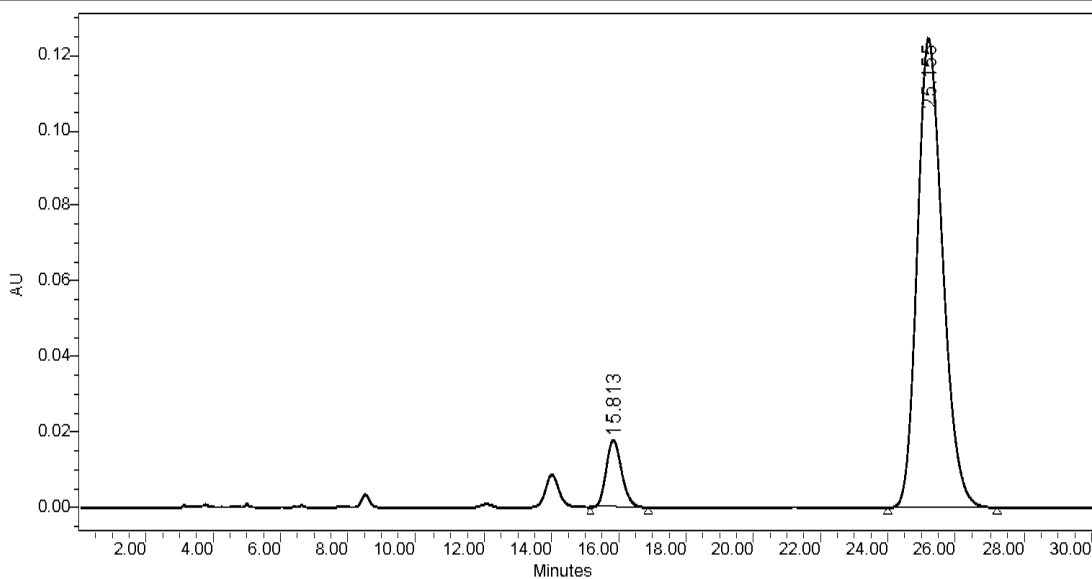


	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	15.651	1795796	49.74	57282	61.82
2	24.898	1814284	50.26	35371	38.18



SAMPLE INFORMATION

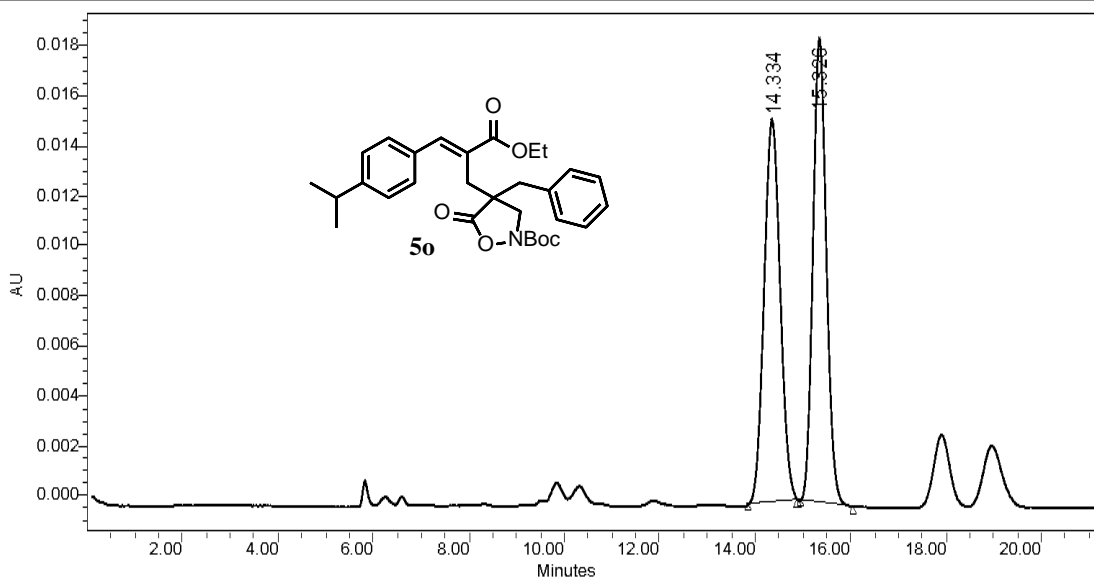
Sample Name:	5N-295	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/10/2018 11:28:18 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	3	Date Processed:	10/10/2018 12:37:24 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	15.813	575139	8.08	17845	12.50
2	25.155	6543151	91.92	124890	87.50

SAMPLE INFORMATION

Sample Name:	VCL-278 RAC AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	7/27/2018 1:04:43 PM
Vial:	1	Acq. Method:	80 20 05ml 254e270 nm
Injection #:	3	Date Processed:	8/3/2018 6:32:56 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

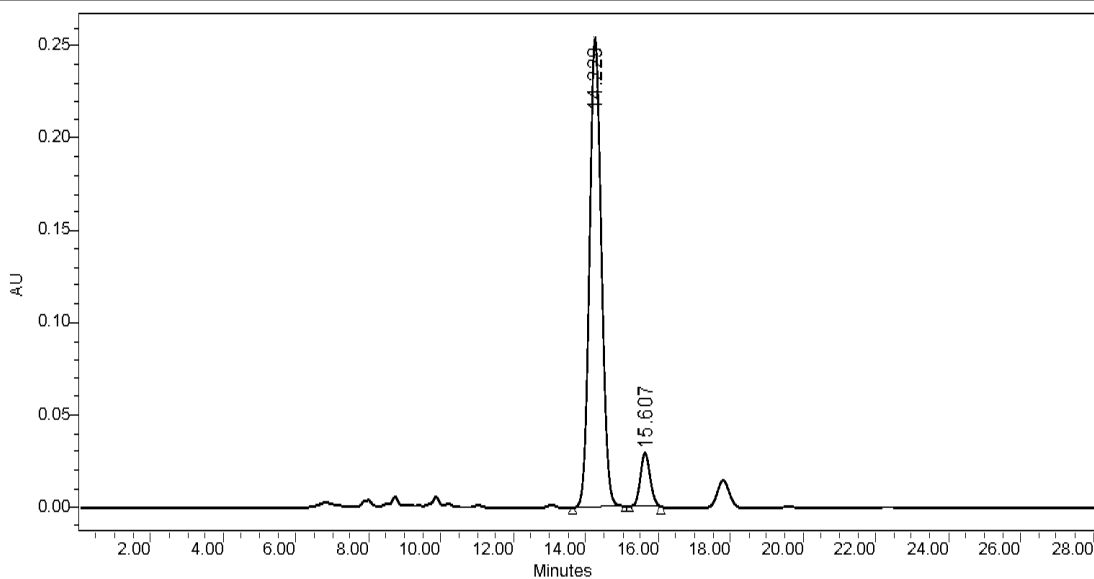


	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	14.334	359303	49.90	15301	45.17
2	15.326	360782	50.10	18571	54.83



SAMPLE INFORMATION

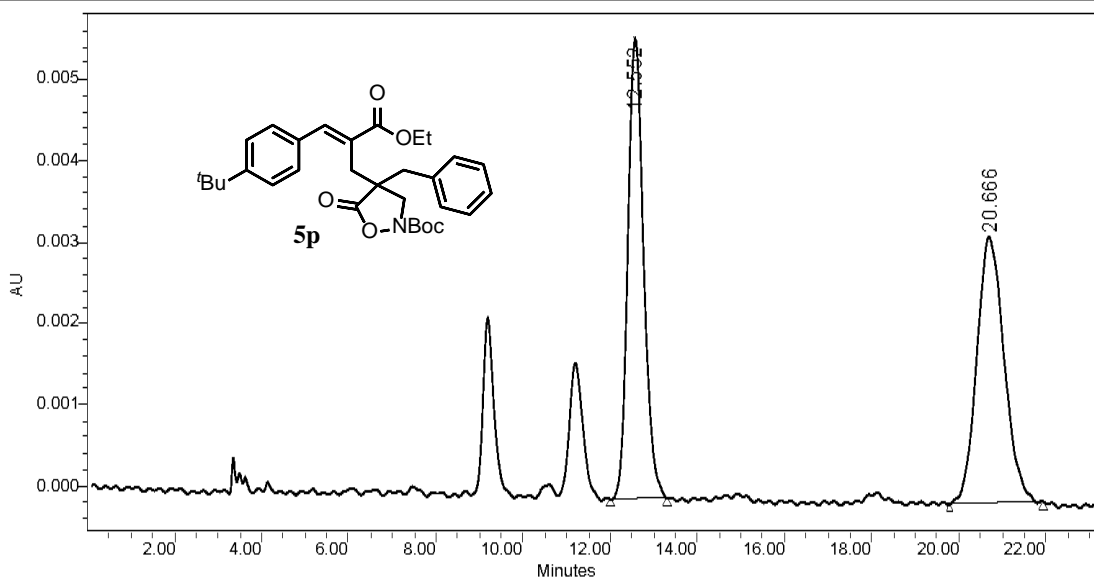
Sample Name:	VCL-294-2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/24/2018 3:31:39 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	1	Date Processed:	8/30/2018 1:19:57 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	14.229	5829252	91.46	254208	89.73
2	15.607	544339	8.54	29100	10.27

SAMPLE INFORMATION

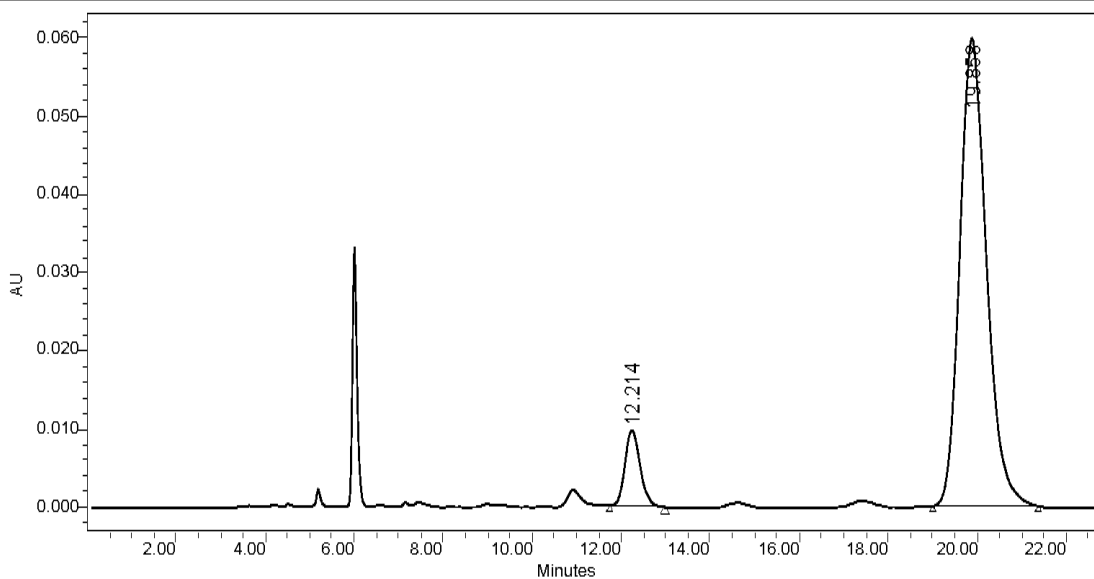
Sample Name:	VCL-291-2 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 2:03:16 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	5	Date Processed:	8/30/2018 1:12:23 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	12.552	142829	49.93	5663	63.33
2	20.666	143215	50.07	3279	36.67

SAMPLE INFORMATION

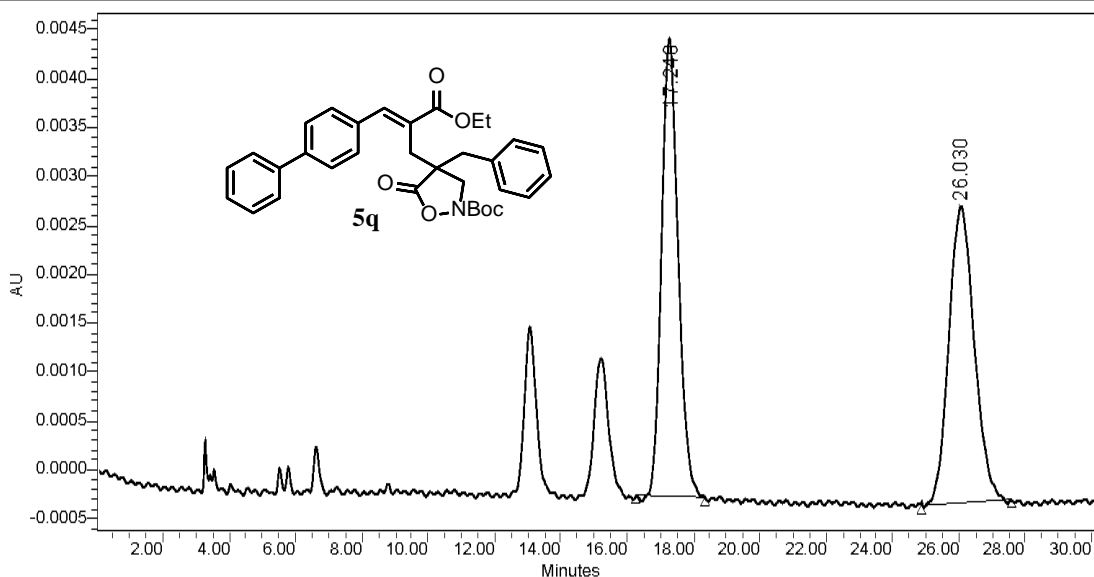
Sample Name:	VCL-297-6-2 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 1:35:34 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	4	Date Processed:	8/30/2018 1:12:51 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	12.214	231651	8.52	9721	13.98
2	19.858	2486329	91.48	59830	86.02

SAMPLE INFORMATION

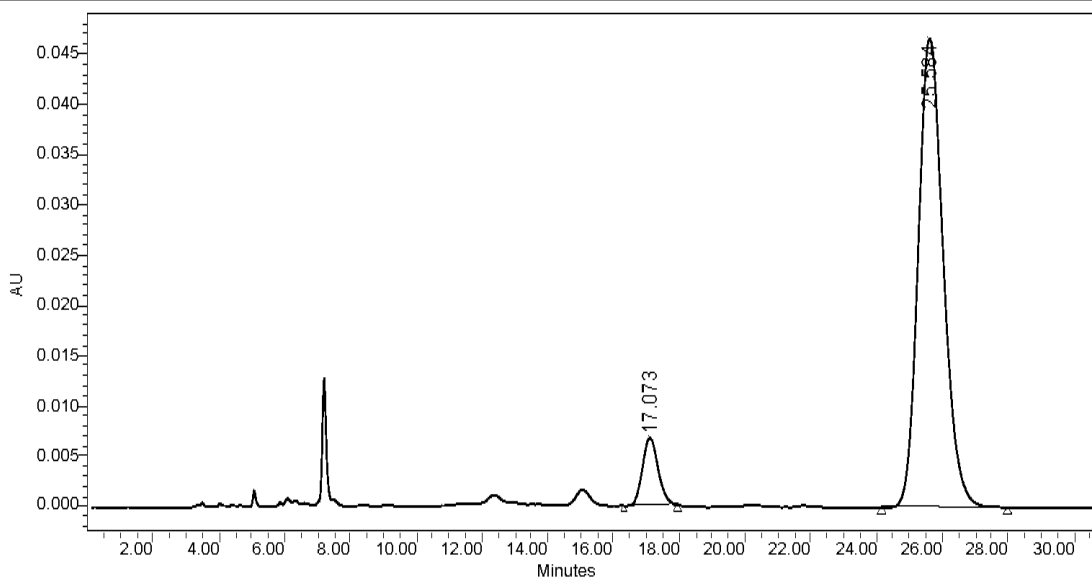
Sample Name:	VCL-277-2 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/23/2018 11:47:51 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	1	Date Processed:	8/30/2018 1:08:05 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	17.240	163544	50.02	4692	60.60
2	26.030	163409	49.98	3050	39.40

SAMPLE INFORMATION

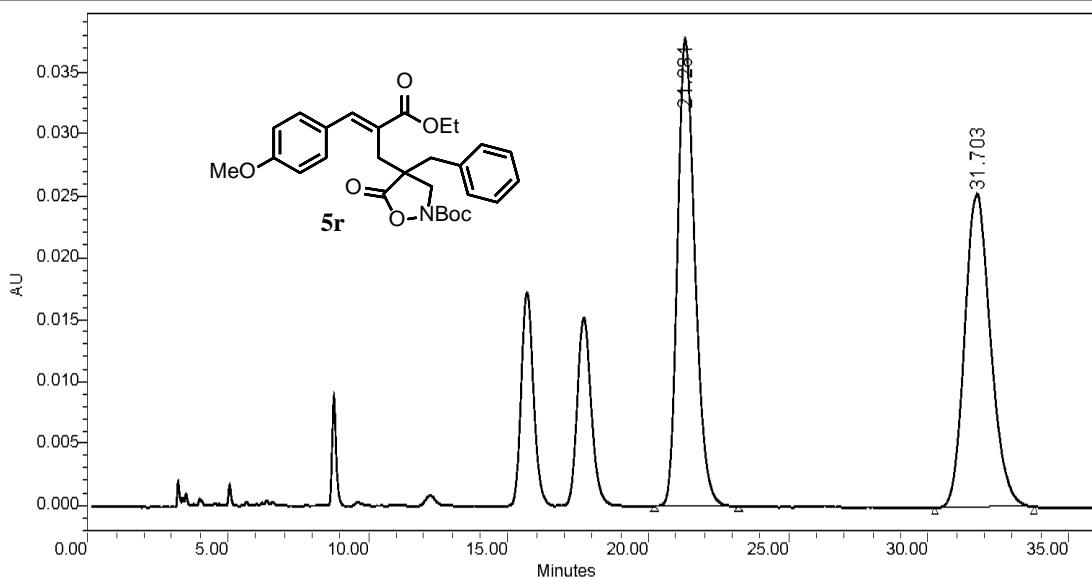
Sample Name:	VCL-282-5 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/23/2018 12:21:27 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	2	Date Processed:	8/23/2018 1:05:22 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	17.073	225519	8.38	6707	12.58
2	25.584	2466599	91.62	46608	87.42

SAMPLE INFORMATION

Sample Name:	VCL-288-6 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/28/2018 12:20:55 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	3	Date Processed:	8/30/2018 1:03:57 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

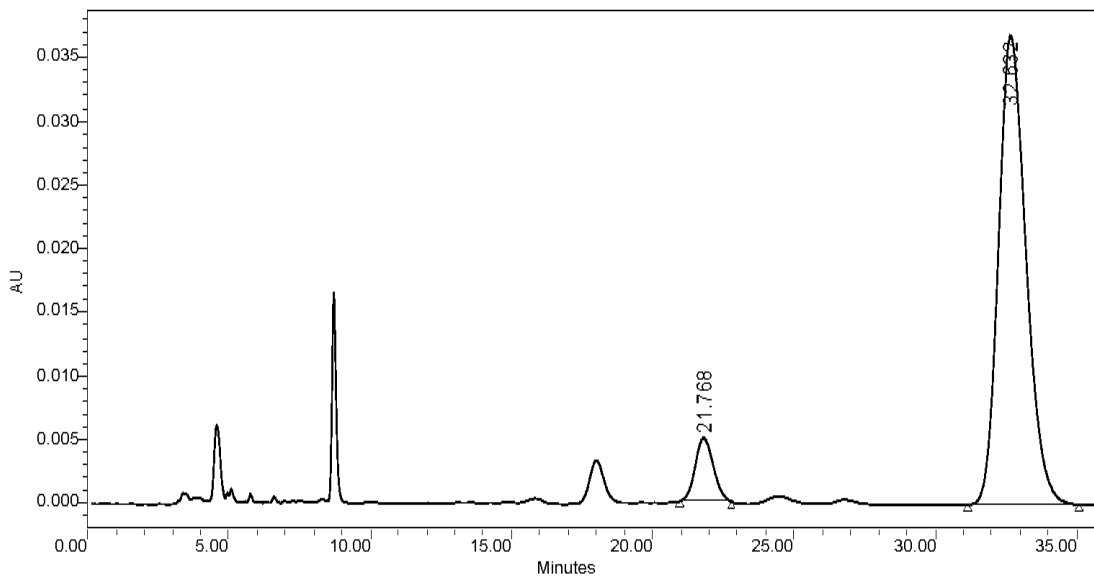


	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	21.281	1633086	50.03	37790	59.88
2	31.703	1631309	49.97	25317	40.12



SAMPLE INFORMATION

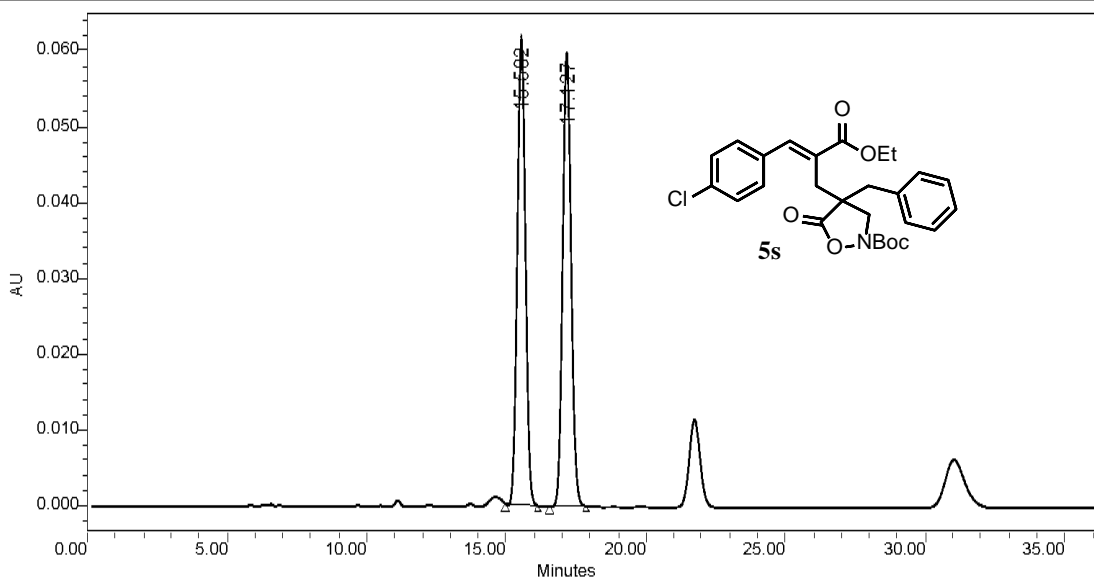
Sample Name:	5R-298	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/10/2018 12:32:56 PM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	5	Date Processed:	10/10/2018 1:10:08 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	21.768	225104	8.29	5006	11.95
2	32.632	2491626	91.71	36876	88.05

SAMPLE INFORMATION

Sample Name:	VCL-253 RAC AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/1/2018 11:14:35 AM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	4	Date Processed:	8/3/2018 6:28:21 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

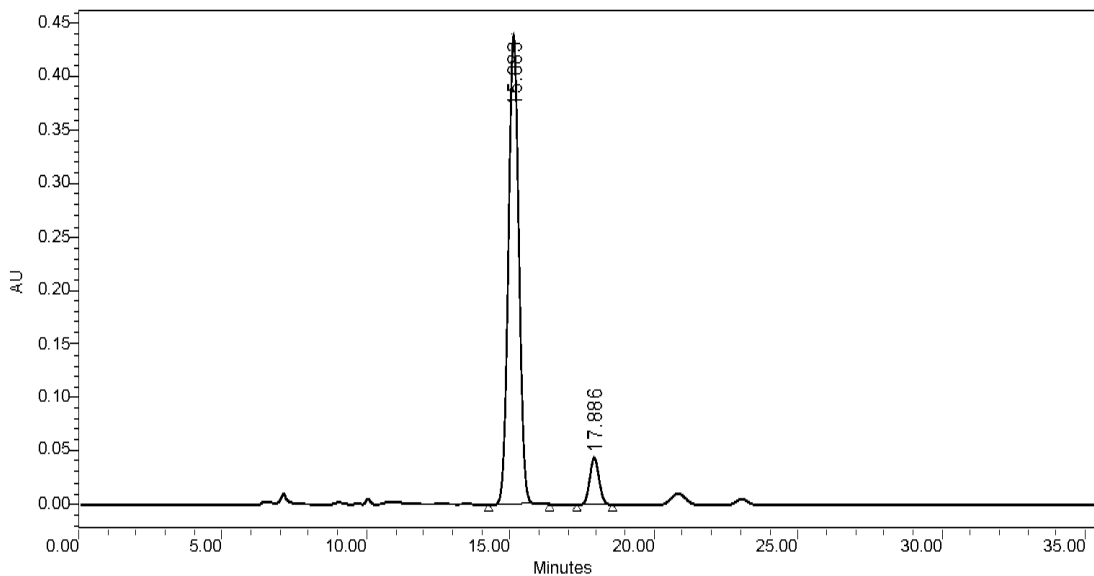


	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	15.502	1249429	49.74	61495	50.69
2	17.127	1262489	50.26	59812	49.31



SAMPLE INFORMATION

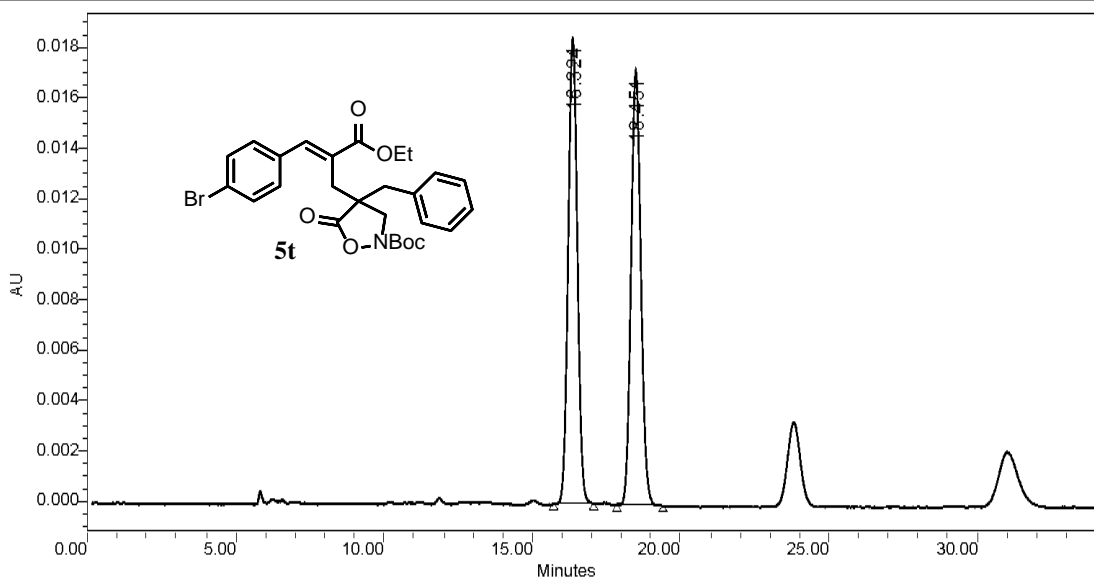
Sample Name:	VCL-300 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/28/2018 1:46:11 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	1	Date Processed:	8/28/2018 2:33:33 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (Δ*sec)	% Area	Height (Δ)	% Height
1	15.083	11136016	91.72	439088	90.82
2	17.886	1005129	8.28	44387	9.18

SAMPLE INFORMATION

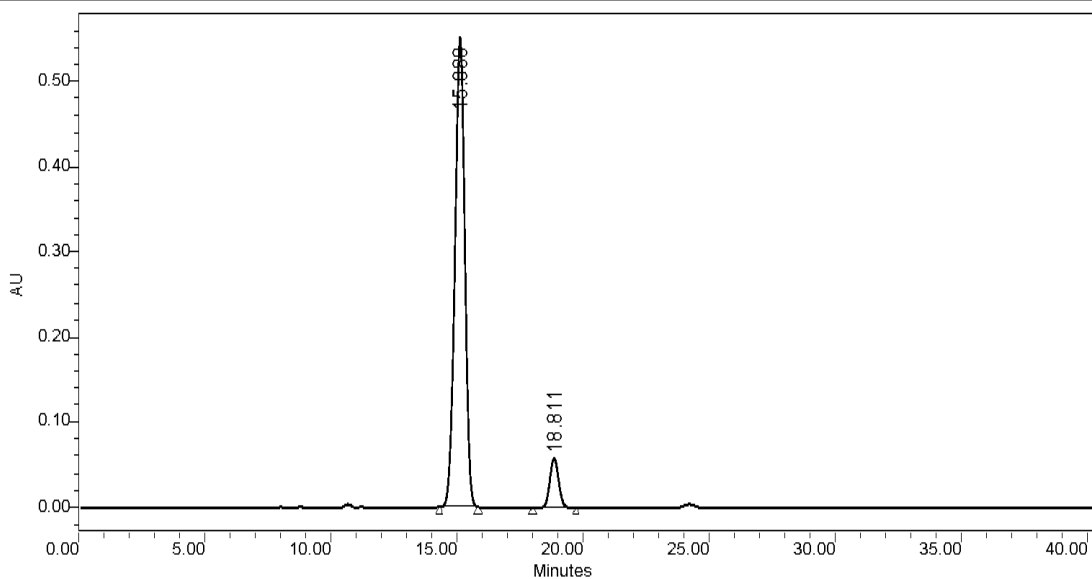
Sample Name:	VCL-254 RAC AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/1/2018 10:10:19 AM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	2	Date Processed:	8/3/2018 6:20:12 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (AU*sec)	% Area	Height (AU)	% Height
1	16.324	397613	49.99	18476	51.70
2	18.451	397744	50.01	17260	48.30

SAMPLE INFORMATION

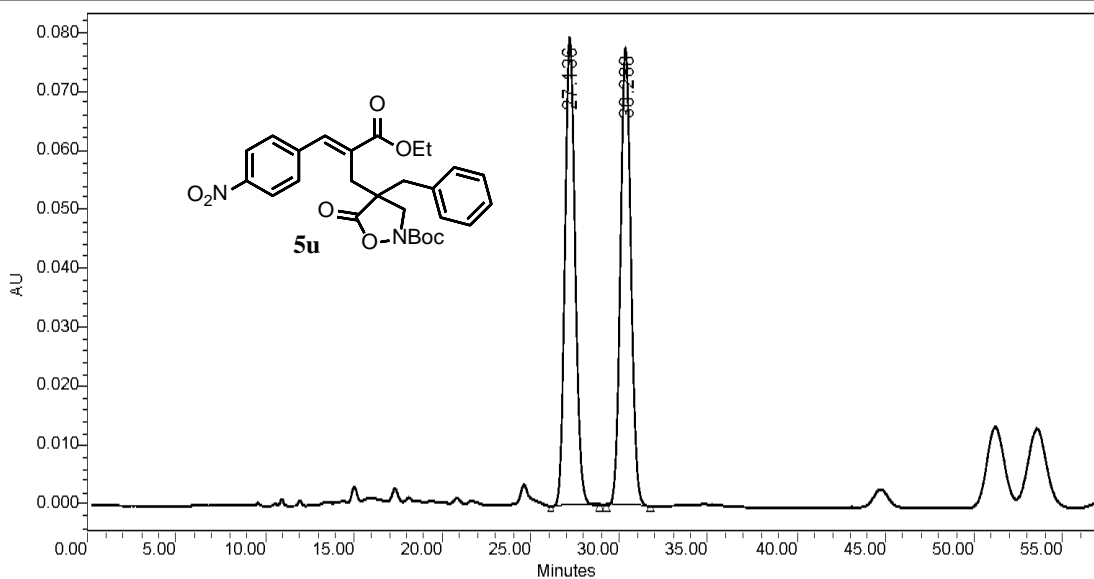
Sample Name:	VCL-296-5t	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	10/9/2018 5:12:41 PM
Vial:	1	Acq. Method:	80 20 05ml 254e270 nm
Injection #:	4	Date Processed:	10/9/2018 6:58:28 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (Δ*sec)	% Area	Height (Δ)	% Height
1	15.088	15036734	91.24	550360	90.41
2	18.811	1442844	8.76	58386	9.59

SAMPLE INFORMATION

Sample Name:	VCL-287 RAC-2 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/3/2018 3:18:47 PM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	1	Date Processed:	8/3/2018 6:43:40 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

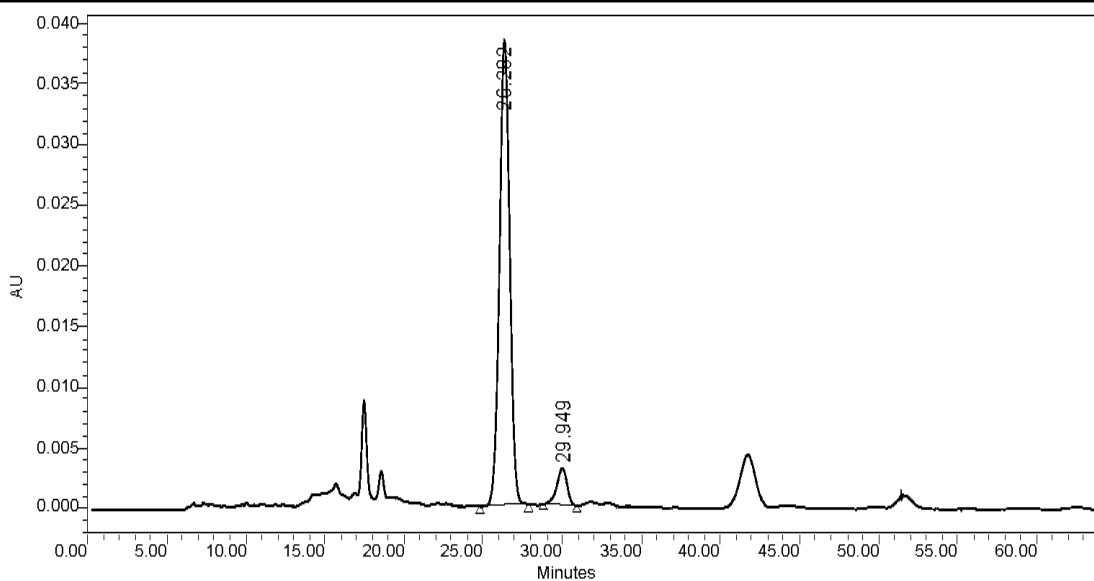


	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	27.136	3175290	49.92	79198	50.53
2	30.280	3185627	50.08	77548	49.47



SAMPLE INFORMATION

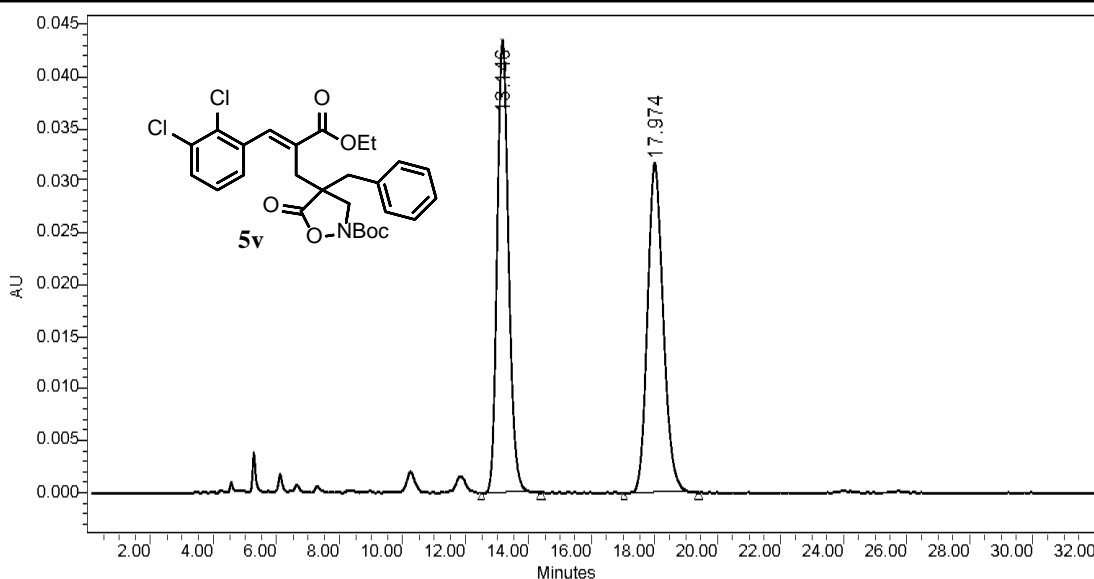
Sample Name:	VCL-285-7 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/24/2018 11:31:04 AM
Vial:	1	Acq. Method:	80 a 20 05ml 254 220
Injection #:	1	Date Processed:	8/30/2018 1:19:35 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	26.282	1723515	92.63	38339	92.64
2	29.949	137030	7.37	3045	7.36

SAMPLE INFORMATION

Sample Name:	VCL-290 rac IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 11:17:13 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	1	Date Processed:	8/30/2018 1:14:16 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

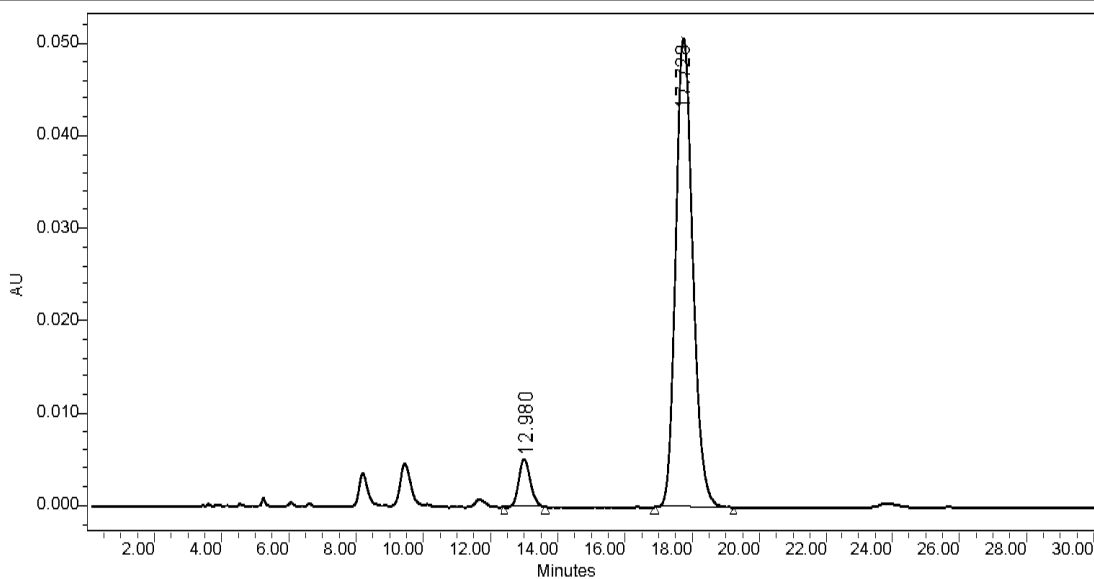


	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	13.146	1097996	49.82	43538	57.82
2	17.974	1105718	50.18	31755	42.18



SAMPLE INFORMATION

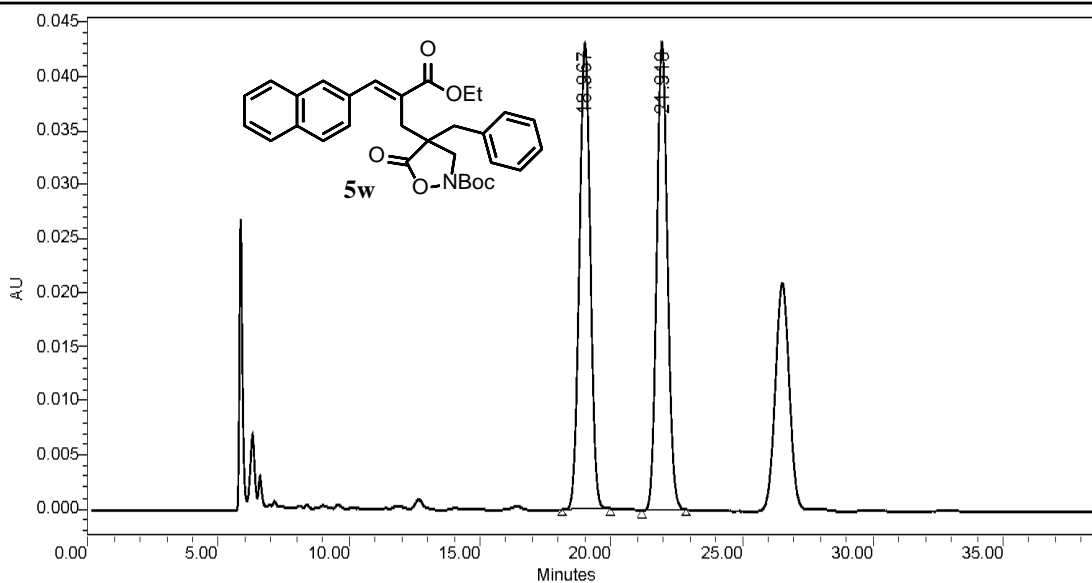
Sample Name:	VCL-284-5 IC	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	8/22/2018 11:54:04 AM
Vial:	1	Acq. Method:	80 20 1 ml 254 nm
Injection #:	2	Date Processed:	8/30/2018 1:15:46 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	12.980	126506	6.55	5168	9.24
2	17.728	1803580	93.45	50791	90.76

SAMPLE INFORMATION

Sample Name:	VCL-255 RAC AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	7/27/2018 12:20:37 PM
Vial:	1	Acq. Method:	80 20 05ml 254e270 nm
Injection #:	2	Date Processed:	8/3/2018 6:31:24 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	

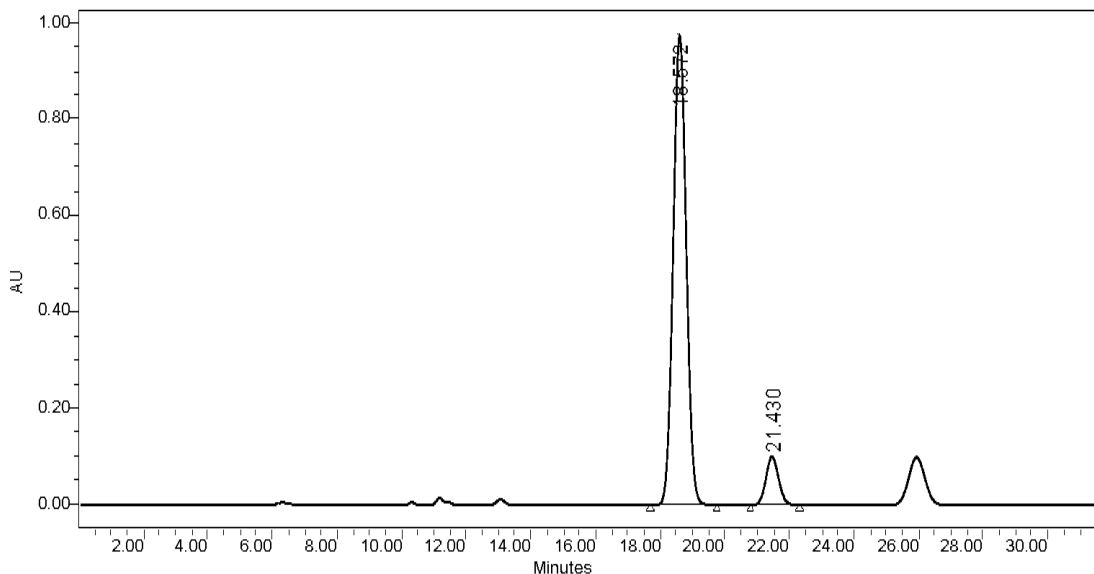


	RT (min)	Area (∇*sec)	% Area	Height (∇)	% Height
1	18.967	1248874	50.30	43001	49.86
2	21.910	1234037	49.70	43237	50.14



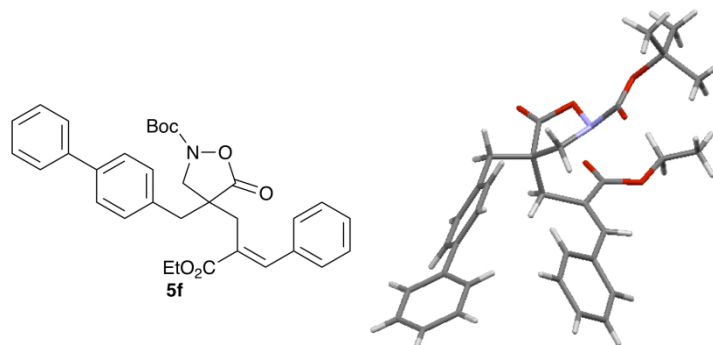
SAMPLE INFORMATION

Sample Name:	VCL-283 AD-H	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	7/27/2018 3:54:13 PM
Vial:	1	Acq. Method:	80 20 05ml 254e270 nm
Injection #:	1	Date Processed:	8/3/2018 7:06:52 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	120.00 Minutes	Channel Desc.:	
Column Type:		Sample Set Name:	



	RT (min)	Area (Δ*sec)	% Area	Height (Δ)	% Height
1	18.572	27387298	90.78	974793	90.60
2	21.430	2780372	9.22	101124	9.40

4. X-Ray Analysis of 5f



X-ray quality crystals were selected in Fomblin[®] Y H-VAC 140/13 perfluoropolyether at ambient temperature. The data was collected at 296(2) K on a *Bruker D8 Quest Eco* diffractometer using graphite monochromated Mo K_α radiation ($\lambda = 0.71073 \text{ \AA}$). The data was processed using APEX3,¹⁴ the structures were solved by intrinsic phasing (SHELXT, Version 2014/5),¹⁵ and refined by full matrix least squares procedures on F^2 (SHELXL, Version 2014/7)¹⁶ using the graphical interface Shelxle¹⁷ within the SHELXTL suite of programs by Bruker. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were calculated geometrically, and a riding model was applied in the refinement process.

Due to the absence of heavy atoms, compound **5f** is a weak anomalous scatterer, rendering the Flack parameter meaningless. Detailed crystallographic and refinement data can be found in Table S1.

1870182 contains the supplementary crystallographic data for **5f**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk.

¹⁴ Bruker (2016), *APEX3 v2016.9-0, SAINT V8.37A, SHELXTL-2014*, Bruker AXS Inc.: Madison (WI), USA, **2016**.

¹⁵ a) G. M. Sheldrick, *SHELXT-2014: Program for the Solution of Crystal Structures*, University of Göttingen, Germany, **2014**. b) G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *64*, 112–122. c) G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.* **2015**, *71*, 3–8.

¹⁶ a) G. M. Sheldrick, *SHELXL-2014: Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, **2014**. b) G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.* **2015**, *71*, 3–8.

¹⁷ C. B. Hübschle, G. M. Sheldrick, B. Dittrich, *Shelxle: a Qt graphical user interface for SHELXL*, *J. Appl. Crystallogr.* **2011**, *44*, 1281–1284.

Table S1: Crystal data, data collection and structure refinement details for compounds **5f**.

Compound	5f
Empirical formula	C ₃₃ H ₃₅ NO ₆
Formula weight [g/mol]	541.62
Color	colorless
Crystal size [mm]	0.70 × 0.53 × 0.07
Crystal system	monoclinic
Space group	Cc
<i>a</i> [Å]	9.900(3)
<i>b</i> [Å]	34.441(10)
<i>c</i> [Å]	9.602(3)
α [°]	90
β [°]	116.727(10)
γ [°]	90
<i>V</i> [Å ³]	2924.2(15)
<i>Z</i>	4
<i>D</i> _{calc} [g/cm ³]	1.230
μ [mm ⁻¹]	0.08
<i>T</i> [K]	296
θ range [°]	2.5-23.3
No. of reflections measured	30621
No. of independent reflections	4190
Obs. Reflections with <i>I</i> > 2 σ (<i>I</i>)	2414
No. of Parameters refined/restraints	365/2
Absorption correction	Multi-scan
<i>T</i> _{min} , <i>T</i> _{max}	0.77, 0.99
$\Delta\rho_{\min}/\Delta\rho_{\max}$ [e Å ⁻³]	-0.24/0.20
F(000)	1152
<i>R</i> _{int}	0.172
<i>R</i> ₁ (<i>R</i> [<i>F</i> ² ≥ 2 σ (<i>F</i> ²)])	0.086
<i>wR</i> ₂ (<i>wR</i> (<i>F</i> ²))	0.174
Goof	1.12
CCDC no.	1870182