Direct β-Selectivity of α, β-Unsaturated γ-Butyrolactam for Asymmetric Conjugate Additions under Organocatalytic Manner

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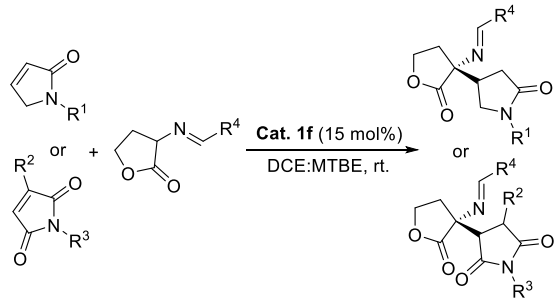
Supporting Information

Table of Content:

1. General methods

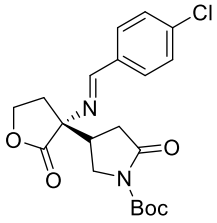
Unless stated otherwise, all reactions were carried out in flame dried glassware. All solvents and catalyst **1d-1f** were from commercial sources and used without purification unless otherwise noted. Catalysts **1a-1b**[1], **1c**[2], α,β-unsaturated γ-butyrolactam[3], cyclic imino esters[4] and maleimides[5] were prepared according to literature procedures. Reactions were monitored by thin layer chromatography (TLC). ^{1}H, ^{13}C and ^{19}F spectra were recorded on a Avance 300 (300 MHz, 75 MHz and 282 MHz, respectively), Avance 400 (400 MHz, 100 MHz and 376 MHz, respectively), Avance 500 (500 MHz, 125 MHz and 470 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data are presented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet) and coupling constant in Hertz (Hz). Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HRMS was measured with a MaXis 4G mass spectrometer. The er values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel IC-H column or Phenomenex LUX 5um Amylose-1 on Waters with a 2998 UV-detector.

2. General procedure for asymmetric Michael addition of α,β-unsaturated γ-butyrolactams or maleimides and cyclic imino esters in the presence of $(DHQD)_2AQN$

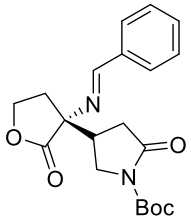


An ordinary vial equipped with a magnetic stirring bar was charged with α,β-unsaturated γ-butyrolactams or maleimides (0.2 mmol) and cyclic imino esters (0.3 mmol) and $(DHQD)_2AQN$ (15 mol %) were added in 2.2 mL a mixture of dichloroethane and methyl *tert*-butyl ether (volume ratio = 10 : 1). The stirring was maintained at room temperature for 48 hours. The reaction mixture was directly charged onto silica gel and purified through flash chromatography (CH_2Cl_2/EtOAc = 4:1) to furnish the corresponding products.

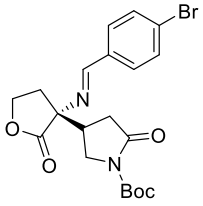
3. Characterization of products 4



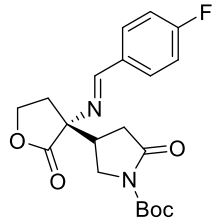
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(4-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4a**): 75% yield; White solid; $[\alpha]_D^{20}$ = +5 (*c* = 1.00 in $CHCl_3$); er = 87 : 13, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.15 min, t (minor) = 8.26 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.18 (s, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 4.45-4.38 (m, 1H), 4.16-4.08 (m, 1H), 4.00-3.93 (m, 1H), 3.77-3.71 (m, 1H), 2.99-2.84 (m, 1H), 2.81-2.65 (m, 2H), 2.56-2.39 (m, 2H), 1.42 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.4, 172.6, 160.3, 149.7, 138.1, 133.3, 129.9, 129.2, 83.0, 70.2, 65.1, 47.0, 36.6, 34.8, 34.6, 27.9; **ESI-HRMS:** calcd. for $C_{20}H_{23}ClN_2O_5+H^+$ 407.1368, found 407.1371.



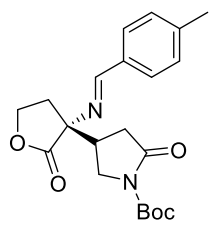
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-benzylideneamino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4b**): 73% yield; Yellow oil; $[\alpha]_D^{20}$ = +22 (*c* = 1.00 in $CHCl_3$); er = 91 : 9, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 6.93 min, t (minor) = 8.20 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.22 (s, 1H), 7.78-7.75 (m, 2H), 7.50-7.42 (m, 3H), 4.44-4.38 (m, 1H), 4.14-4.08 (m, 1H), 4.01-3.95 (m, 1H), 3.78-3.72 (m, 1H), 3.05-2.87 (m, 1H), 2.82-2.62 (m, 2H), 2.56-2.39 (m, 2H), 1.42 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.6, 172.8, 161.5, 149.7, 134.9, 131.9, 128.8, 128.7, 82.8, 70.1, 65.1, 47.0, 36.6, 34.7, 34.6, 27.8; **ESI-HRMS:** calcd. for $C_{20}H_{24}N_2O_5+H^+$ 373.1758, found 373.1768.



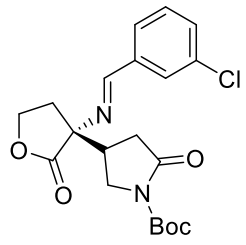
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(4-bromobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4c**): 63% yield; White solid; $[\alpha]_D^{20}$ = +17 (*c* = 1.00 in $CHCl_3$); er = 87 : 13, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.50 min, t (minor) = 8.80 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.17 (s, 1H), 7.65-7.57 (m, 4H), 4.44-4.38 (m, 1H), 4.16-4.07 (m, 1H), 4.00-3.93 (m, 1H), 3.76-3.70 (m, 1H), 2.97-2.84 (m, 1H), 2.81-2.65 (m, 2H), 2.56-2.39 (m, 2H), 1.43 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.4, 172.6, 160.5, 149.7, 133.7, 132.1, 130.1, 126.7, 83.0, 70.2, 65.1, 47.0, 36.6, 34.8, 34.5, 27.9; **ESI-HRMS:** calcd. for $C_{20}H_{23}BrN_2O_5+H^+$ 451.0863, found 451.0865.



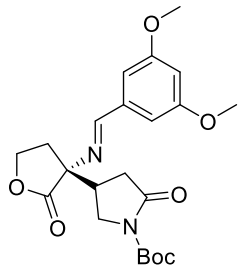
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(4-fluorobenzylidene)amino)-2-oxotetr-ahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4d**): 58% yield; White solid; $[\alpha]_D^{20}$ = +15 (*c* = 1.00 in $CHCl_3$); er = 89 : 11, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.06 min, t (minor) = 7.99 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.19 (s, 1H), 7.79-7.75 (m, 2H), 7.14 (t, *J* = 8.6 Hz, 2H), 4.44-4.38 (m, 1H), 4.16-4.08 (m, 1H), 4.00-3.93 (m, 1H), 3.78-3.73 (m, 1H), 2.98-2.85 (m, 1H), 2.81-2.63 (m, 2H), 2.56-2.39 (m, 2H), 1.42 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.5, 172.7, 165.0 ($J_{C\text{-}F}$ = 251.3 Hz), 160.1, 149.7, 131.3 ($J_{C\text{-}F}$ = 3.0 Hz), 130.8 ($J_{C\text{-}F}$ = 9.0 Hz), 116.00 ($J_{C\text{-}F}$ = 21.8 Hz), 82.9, 70.1, 65.1, 47.0, 36.6, 34.8, 34.6, 27.8; **^{19}F NMR** (282 MHz, $CDCl_3$) δ (ppm) -107.09; **ESI-HRMS:** calcd. for $C_{20}H_{23}FN_2O_5$+Na^+ 413.1483, found 413.1489.



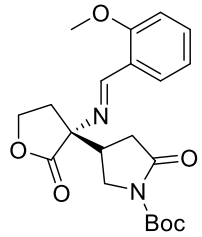
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(4-methylbenzylidene)amino)-2-oxotet-rahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4e**): 72% yield; Yellow oil; $[\alpha]_D^{20}$ = -11 (*c* = 1.00 in $CHCl_3$); er = 92 : 8, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.69 min, t (minor) = 9.41 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.09 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.34-4.28 (m, 1H), 4.07-3.98 (m, 1H), 3.92-3.85 (m, 1H), 3.68-3.62 (m, 1H), 2.90-2.82 (m, 1H), 2.73-2.55 (m, 2H), 2.47-2.33 (m, 2H), 2.31 (s, 3H), 1.34 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.7, 172.8, 161.3, 149.7, 142.5, 132.4, 129.5, 128.7, 82.8, 70.0, 65.1, 47.1, 36.7, 34.7, 34.7, 27.8, 21.6; **ESI-HRMS:** calcd. for $C_{21}H_{26}N_2O_5$+H^+ 387.1914, found 387.1919.



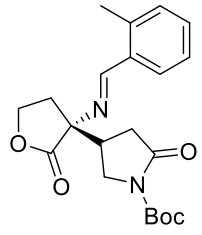
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(3-chlorobenzylidene)amino)-2-oxote-trahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4f**): 68% yield; White solid; $[\alpha]_D^{20}$ = +8 (*c* = 1.00 in $CHCl_3$); er = 90 : 10, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.35 min, t (minor) = 8.67 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.11 (s, 1H), 7.71 (s, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.40-7.29 (m, 2H), 4.38-4.31 (m, 1H), 4.09-4.00 (m, 1H), 3.94-3.87 (m, 1H), 3.67-3.61 (m, 1H), 2.88-2.80 (m, 1H), 2.76-2.57 (m, 2H), 2.51-2.32 (m, 2H), 1.37 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.2, 172.4, 160.3, 149.8, 136.6, 135.0, 131.9, 130.1, 128.2, 127.2, 83.0, 70.2, 65.1, 47.0, 36.6, 34.7, 34.4, 27.9; **ESI-HRMS:** calcd. for $C_{20}H_{23}ClN_2O_5$+Na^+ 429.1188, found 429.1193.



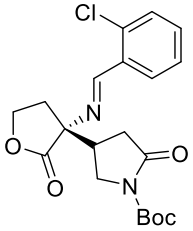
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(3,5-dimethoxybenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4g**): 71% yield; White oil; $[\alpha]_D^{20}$ = -20 (*c* = 1.00 in $CHCl_3$); er = 90 : 10, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 8.11 min, t (minor) = 9.54 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.04 (s, 1H), 6.83 (d, *J* = 2.3 Hz, 2H), 6.50 (t, *J* = 2.4 Hz, 1H), 4.36-4.29 (m, 1H), 4.08-4.00 (m, 1H), 3.90-3.84 (m, 1H), 3.78 (s, 9H), 3.76-2.78 (m, 1H), 2.84-2.78 (m, 1H), 2.71-2.60 (m, 2H), 2.45-2.34 (m, 2H), 1.32 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.5, 172.8, 161.2, 161.0, 149.7, 136.9, 106.2, 104.6, 82.8, 70.2, 65.0, 55.6, 47.00, 36.7, 35.0, 34.7, 27.8; **ESI-HRMS:** calcd. for $C_{22}H_{28}N_2O_7$+Na^+ 455.1789, found 455.1793.



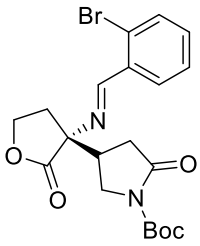
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(2-methoxybenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4i**): 72% yield; Yellow solid; $[\alpha]_D^{20}$ = +2 (*c* = 1.00 in $CHCl_3$); er = 95 :5, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.66 min, t (minor) = 9.56 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.69 (s, 1H), 7.94 (d, *J* = 6.7 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 4.42-4.36 (m, 1H), 4.18-4.10 (m, 1H), 4.02-3.94 (m, 1H), 3.86 (s, 3H), 3.78-3.72 (m, 1H), 2.98-2.91 (m, 1H), 2.81-2.63 (m, 2H), 2.53-2.37 (m, 2H), 1.44 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 176.0, 172.9, 159.2, 157.4, 149.8, 133.2, 127.2, 123.4, 120.7, 111.1, 82.7, 70.2, 65.0, 55.5, 47.1, 36.6, 34.7, 34.7, 27.9; **ESI-HRMS:** calcd. for $C_{21}H_{26}N_2O_6$+H^+ 403.1864, found 403.1877.



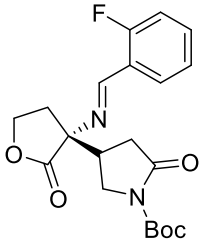
(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(2-methylbenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4j**): 68% yield; Yellow oil; $[\alpha]_D^{20}$ = +11 (*c* = 1.00 in $CHCl_3$); er = 89 : 11, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.31 min, t (minor) = 9.07 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.45 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.32-7.26 (m, 1H), 7.22-7.12 (m, 2H), 4.37-4.31 (m, 1H), 4.10-4.01 (m, 1H), 3.95-3.88 (m, 1H), 3.69-3.63 (m, 1H), 2.90-2.82 (m, 1H), 2.76-2.53 (m, 2H), 2.44 (s, 3H), 2.42-2.31 (m, 2H), 1.37 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.7, 172.7, 160.6, 149.8, 138.6, 132.9, 131.5, 131.2, 128.2, 126.4, 83.0, 70.5, 65.1, 47.1, 36.6, 34.8, 34.7, 34.7, 34.6, 27.9, 27.9, 19.7; **ESI-HRMS:** calcd. for $C_{21}H_{26}N_2O_5$+H^+ 387.1914, found 387.1925.



(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(2-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4k**): 62% yield; Yellow solid; $[\alpha]_D^{20}$ = +4 (*c* = 1.00 in $CHCl_3$); er = 94 : 6, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 7.28 min, t (minor) = 9.03 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.71 (s, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.42-7.39 (m, 2H), 7.37-7.31 (m, 1H), 4.46-4.39 (m, 1H), 4.21-4.12 (m, 1H), 4.02-3.95 (m, 1H), 3.81-3.75 (m, 1H), 2.96-2.86 (m, 1H), 2.84-2.67 (m, 2H), 2.56-2.39 (m, 2H), 1.44 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.4, 172.7, 158.8, 149.7, 136.0, 132.8, 132.1, 130.0, 128.4, 127.3, 83.0, 70.4, 64.9, 47.0, 36.6, 34.8, 34.5, 27.9; **ESI-HRMS:** calcd. for $C_{20}H_{23}ClN_2O_5$+Na^+ 429.1188, found 429.1198.

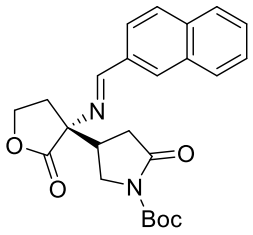


(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(2-bromobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4l**): 68% yield; Yellow solid; $[\alpha]_D^{20}$ = +10 (*c* = 1.00 in $CHCl_3$); er = 93 : 7, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 6.90 min, t (minor) = 8.68 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.65 (s, 1H), 7.95 (dd, *J* = 7.5, 2.1 Hz, 1H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.41-7.30 (m, 2H), 4.47-4.40 (m, 1H), 4.22-4.13 (m, 1H), 4.02-3.96 (m, 1H), 3.81-3.75 (m, 1H), 2.98-2.88 (m, 1H), 2.84-2.67 (m, 2H), 2.57-2.39 (m, 2H), 1.44 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.4, 172.7, 161.2, 149.7, 133.4, 133.2, 133.0, 128.9, 127.9, 125.9, 83.0, 70.3, 64.9, 47.1, 36.6, 34.8, 34.5, 27.9; **ESI-HRMS:** calcd. for $C_{20}H_{23}BrN_2O_5$+Na^+ 473.0683, found 473.0687.

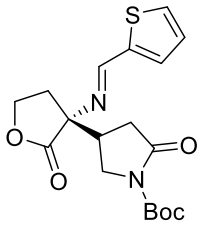


(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(2-fluorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4m**): 57% yield; Yellow oil; $[\alpha]_D^{20}$ = +10 (*c* = 1.00 in $CHCl_3$); er = 82 : 18, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 6.72 min, t (minor) = 8.07 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.48 (s, 1H), 7.89 (td, *J* = 1.7 Hz, 1H), 7.43-7.37 (m, 1H), 7.20-7.12 (m, 1H), 7.04 (t, *J* = 2.4, 8.4 Hz, 1H), 4.38-4.31 (m, 1H), 4.12-4.04 (m, 1H), 3.93-3.87 (m, 1H), 3.72-3.66 (m, 1H), 2.93-2.79 (m, 1H), 2.77-2.59 (m, 2H), 2.49-2.33 (m, 2H), 1.36 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 174.3, 171.7, 161.6 ($J_{C\text{-}F}$ = 253.5 Hz), 154.2 ($J_{C\text{-}F}$ = 4.5 Hz), 148.7, 132.7 ($J_{C\text{-}F}$ = 9.0 Hz), 126.6 ($J_{C\text{-}F}$ = 2.3 Hz), 123.6 ($J_{C\text{-}F}$ = 1.0 Hz), 121.7 ($J_{C\text{-}F}$ = 9.0 Hz), 115.0 ($J_{C\text{-}F}$ = 20.3 Hz), 82.0, 69.4, 63.9, 46.0, 35.6,

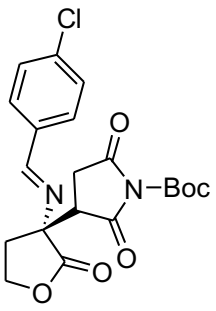
33.8, 33.6, 26.9; **^{19}F NMR** (282 MHz, $CDCl_3$) δ (ppm) -120.45; **ESI-HRMS:** calcd. for $C_{20}H_{23}FN_2O_5$+H^+ 391.1664, found 391.1674.



(*S*)-*tert*-butyl 4-((*S*)-3-((*E*)-(naphthalen-2-ylmethylene)amino)-2-oxotetrahydrofuran-3-yl)-2-oxopyrrolidine-1-carboxylate (**4n**): 78% yield; White solid; $[\alpha]_D^{20}$ = +13 (*c* = 1.00 in $CHCl_3$); er = 92 : 8, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 8.09 min, t (minor) = 9.84 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.29 (s, 1H), 8.00 (s, 1H), 7.91 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.86-7.77 (m, 3H), 7.51-7.43 (m, 2H), 4.37-4.30 (m, 1H), 4.11-4.03 (m, 1H), 3.96-3.89 (m, 1H), 3.72-3.66 (m, 1H), 2.95-2.87 (m, 1H), 2.77-2.58 (m, 2H), 2.49-2.35 (m, 2H), 1.32 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.7, 172.8, 161.6, 149.8, 135.2, 132.9, 132.7, 131.8, 128.8, 128.8, 127.9, 126.8, 123.3, 82.9, 70.2, 65.2, 47.1, 36.7, 34.8, 34.7, 27.9; **ESI-HRMS:** calcd. for $C_{24}H_{26}N_2O_5$+Na^+ 445.1734, found 445.1740.

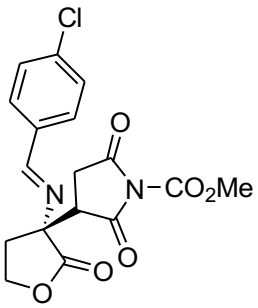


(*S*)-*tert*-butyl 2-oxo-4-((*S*)-2-oxo-3-((*E*)-(thiophen-2-ylmethylene)amino)tetrahydrofuran-3-yl)pyrrolidine-1-carboxylate (**4p**): 52% yield; Yellow solid; $[\alpha]_D^{20}$ = +10 (*c* = 1.00 in $CHCl_3$); er = 88 : 12, determined by HPLC analysis [Daicel chiralpak IC-H, EtOH, 1.0 mL/min, λ = 254 nm, t (major) = 6.74 min, t (minor) = 8.13 min]; **^{1}H NMR** (300 MHz, $CDCl_3$): δ (ppm) 8.26 (s, 1H), 7.42 (d, *J* = 5.1 Hz, 1H), 7.34 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.03 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.36-4.30 (m, 1H), 4.12-4.03 (m, 1H), 3.93-3.87 (m, 1H), 3.66-3.60 (m, 1H), 2.85-2.78 (m, 1H), 2.73-2.63 (m, 1H), 2.61-2.53 (m, 1H), 2.43-2.31 (m, 2H), 1.38 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ (ppm) 175.4, 172.6, 154.9, 149.8, 141.4, 132.8, 130.9, 127.8, 82.9, 69.7, 65.2, 47.0, 36.7, 34.6, 28.1, 27.9; **ESI-HRMS:** calcd. for $C_{18}H_{22}N_2O_5S$+Na^+ 401.1142, found 401.1147.

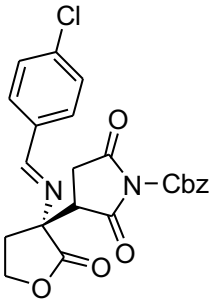


tert-butyl(S)-3-((R)-3-(((E)-4-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2,5-dioxopyrrolidine-1-carboxylate（**4r**）: 48% yield; white solid; $[\alpha]_D^{20}$ = +18 (*c* = 0.1 g/100 ml in $CHCl_3$); dr = 19 : 1, er = 65 : 35, determined by HPLC analysis [Phenomenex LUX 5um Amylose-1, Hexane : iPrOH = 7 : 3, 1.0 mL/min, λ = 254 nm, t (major) = 14.37 min, t (minor) = 18.81 min]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 4.42-4.36 (m, 1H), 4.08 (ddd, *J* = 19.1, 10.8, 7.0 Hz, 1H), 3.18 (dd, *J* = 8.8,

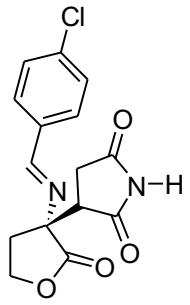
5.0 Hz, 1H), 2.94 (dt, *J* = 13.2, 8.2 Hz, 1H), 2.90-2.78 (m, 2H), 2.55 (ddd, *J* = 13.8, 6.3, 2.7 Hz, 1H), 1.52 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.5, 172.7, 171.8, 161.6, 146.3, 138.4, 133.1, 130.0, 129.2, 86.4, 69.6, 65.4, 45.7, 34.6, 31.0, 27.7; **ESI-HRMS:** calcd. for $C_{20}H_{21}ClN_2O_6+H^+$ 421.1161, found 421.1163.



methyl(S)-3-((R)-3-(((E)-4-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2,5-dioxopyrrolidine-1-carboxylate（**4s**）：55% yield; white solid; $[\alpha]_D^{20}$ = +42 (*c* = 0.2 g/100 ml in $CHCl_3$); dr = 3 : 1, er^1 = 72 : 28, er^2 = 85 : 15, determined by HPLC analysis [Phenomenex LUX 5um Amylose-1, Hexane : iPrOH = 3 : 1, 0.6 mL/min, λ = 254 nm, t^1 (major) = 34.740 min, t^1 (minor) = 44.17 min, t^2 (major) = 35.98 min, t^2 (minor) = 39.09 min]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 4.49 (ddd, *J* = 9.4, 7.0, 2.8 Hz, 1H), 4.23-4.09 (m, 1H), 4.02 (s, 3H), 3.30 (dd, *J* = 8.2, 5.9 Hz, 1H), 3.03 (ddd, *J* = 14.5, 11.2, 6.0 Hz, 3H), 2.64 (ddd, *J* = 13.9, 6.3, 2.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.5, 172.4, 171.4, 161.9, 148.6, 138.5, 132.9, 130.0, 129.2, 69.7, 65.4, 55.1, 45.7, 34.8, 31.0; **ESI-HRMS:** calcd. for $C_{17}H_{15}ClN_2O_6+H^+$ 379.0691, found 379.0689.



benzyl(S)-3-((R)-3-(((E)-4-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)-2,5-dioxopyrrolidine-1-carboxylate（**4t**）：58% yield; white solid; $[\alpha]_D^{20}$ = +21 (*c* = 0.292 g/100 ml in $CHCl_3$); dr = 2 : 1, er^1 = 64 : 36, er^2 = 13 : 87, determined by HPLC analysis [Phenomenex LUX 5um Amylose-1, Hexane : iPrOH = 7 : 3, 0.6 mL/min, λ = 254 nm, t^1 (major) = 35.830 min, t^1 (minor) = 43.78 min, t^2 (major) = 37.710 min, t^2 (minor) = 39.01 min]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.41 (ddd, *J* = 15.5, 12.3, 5.3 Hz, 5H), 7.27 (d, *J* = 8.3 Hz, 2H), 5.40 (s, 2H), 4.44 (td, *J* = 9.3, 2.7 Hz, 1H), 4.13 (td, *J* = 9.2, 6.7 Hz, 1H), 3.26 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.07-2.85 (m, 3H), 2.60 (ddd, *J* = 13.8, 6.3, 2.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.5, 172.45, 171.45, 161.85, 148.05, 138.45, 134.0, 132.9, 130.0, 129.2, 128.9, 128.8, 128.5, 70.1, 69.7, 65.4, 45.7, 34.7, 30.9; **ESI-HRMS:** calcd. for $C_{23}H_{19}ClN_2O_6+H^+$ 455.1004, found 455.1003.



(S)-3-((R)-3-(((E)-4-chlorobenzylidene)amino)-2-oxotetrahydrofuran-3-yl)pyrrolidine-2,5-dione（**4u**）：61% yield，white solid; $[\alpha]_D^{20}$=+31 (c = 0.305 g/100 ml in $CHCl_3$); er = 82 : 17, determined by chiral HPLC analysis [Phenomenex LUX 5um Amylose-1, Hexane : iPrOH = 7 : 3, 1.0 mL/min, λ = 254 nm, t (major) = 11.91 min, t (minor) = 19.72 min]; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.13 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 4.49 (t, *J* = 8.6 Hz, 1H), 4.12 (td, *J* = 9.5, 6.2 Hz, 1H), 3.60 (dd, *J* = 9.4, 5.9 Hz, 1H), 3.50 (ddd, *J* = 13.0, 10.2, 9.0 Hz, 1H), 2.83 (dd, *J* = 18.4, 5.9 Hz, 1H), 2.71 (dd, *J* = 18.4, 9.5 Hz, 1H), 2.40 (dd, *J* = 13.2, 5.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.1, 175.8, 175.0, 160.1, 138.3, 133.1, 129.9, 129.2, 70.0, 65.7, 45.2, 34.2, 32.5; **ESI-HRMS:** calcd. for $C_{15}H_{13}ClN_2O_4+H^+$ 321.0637, found 321.0638.

4. Reference

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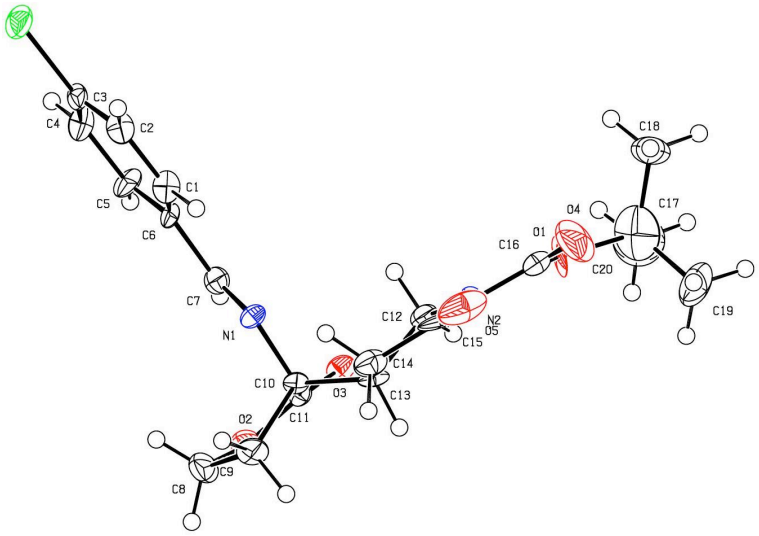
5 a) T. Sengoku, Y. Murata, Y. Aso, A. Kawakami, T. Inuzuka, M. Sakamoto, M. Takahashi, H. Yoda, *Org. Lett.*, 2015, **17**, 5846; b) L. Qin, B. Hu, D. Neumann Kiel, J. Linstad Ethan, K. McCauley, J. Veness, J. Kempinger Jayson, G. DiMagno Stephen, *Eur. J. Org. Chem.*, 2015, **2015**, 5919; c) K. Köninger, Á. Gómez Baraibar, C. Mügge, E. Paul Caroline, F. Hollmann, M. Nowaczyk Marc, R. Kourist, *Angew. Chem. Int. Ed.* 2016, **55**, 5582.

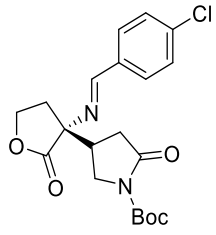
5. Crystal data and the absolute configuration for enantiopure compound 4a

CCDC number 1475321

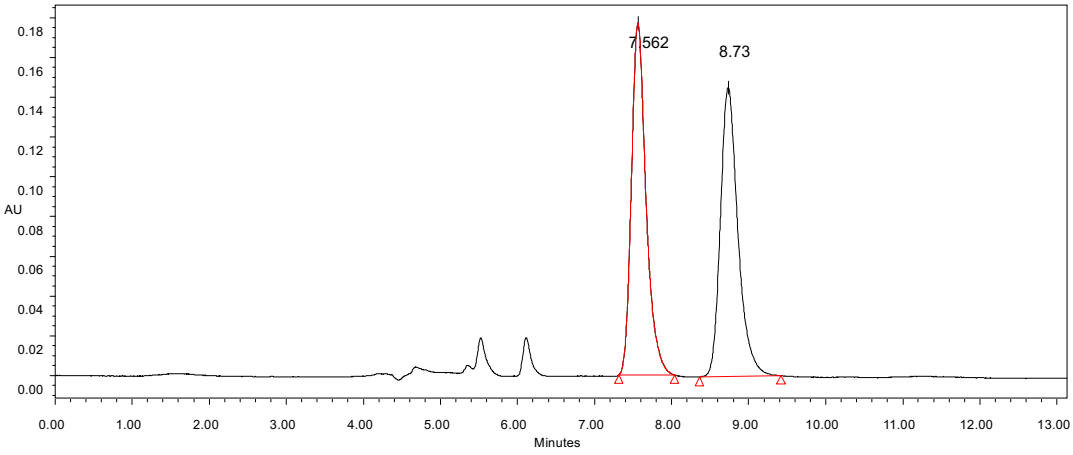


Bond precision:	C-C = 0.0127 Å	Wavelength = 0.71073	
Cell:	a = 29.349 (2)	b = 11.9764 (9)	c = 11.5790 (9)
	alpha = 90	beta = 90	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	4070.0 (5)		4070.0 (5)
Space group	P b c n		Pbcn
Hall group	-P 2n 2ab		?
Moiety formula	C20 H23 Cl N2 O5		?
Sum formula	C20 H23 Cl N2 O5		C20 H23 Cl N2 O5
Mr	406.85		406.85
Dx, g cm^{-3}	1.328		1.328
Z	8		8
Mu (mm^{-1})	0.221		0.221
F000	1712.0		1712.0
F000’	1713.99		
h, k, lmax	24, 9, 9		24, 9, 9
Nref	1234		1231
Tmin, Tmax	0.946, 0.982		0.929, 0.983
Tmin’	0.928		
Correction method = MULTI-SCAN			
Data completeness = 0.998			Theta (max) = 17.240
R (reflections) = 0.0630 (1099)			wR2 (reflections) = 0.1755 (1231)
S = 1.119			Npar = 248

6. HPLC Chromatogram of Compounds 4



4a



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
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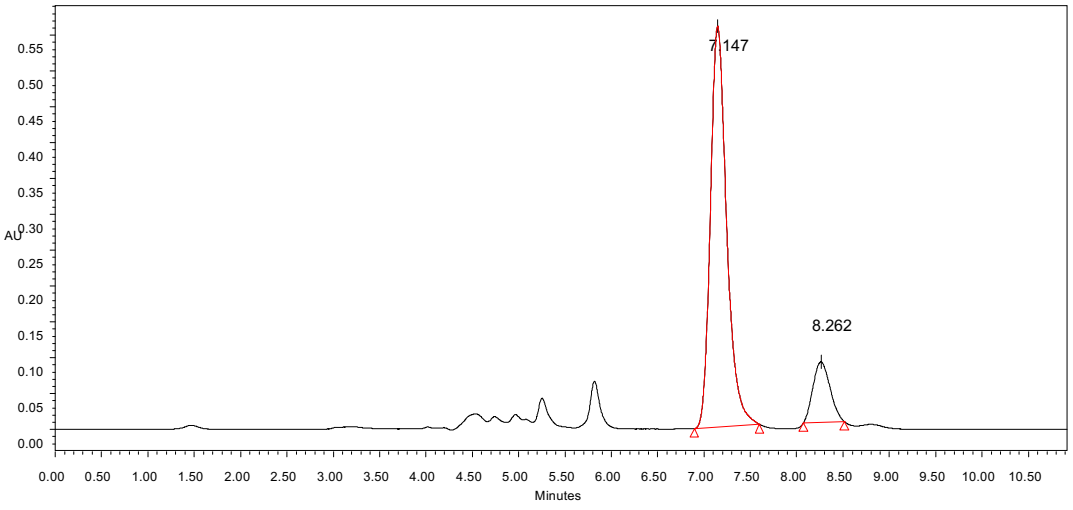
2	8.733	2297302	49.56	145358	bb	Unknown



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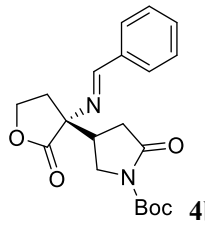
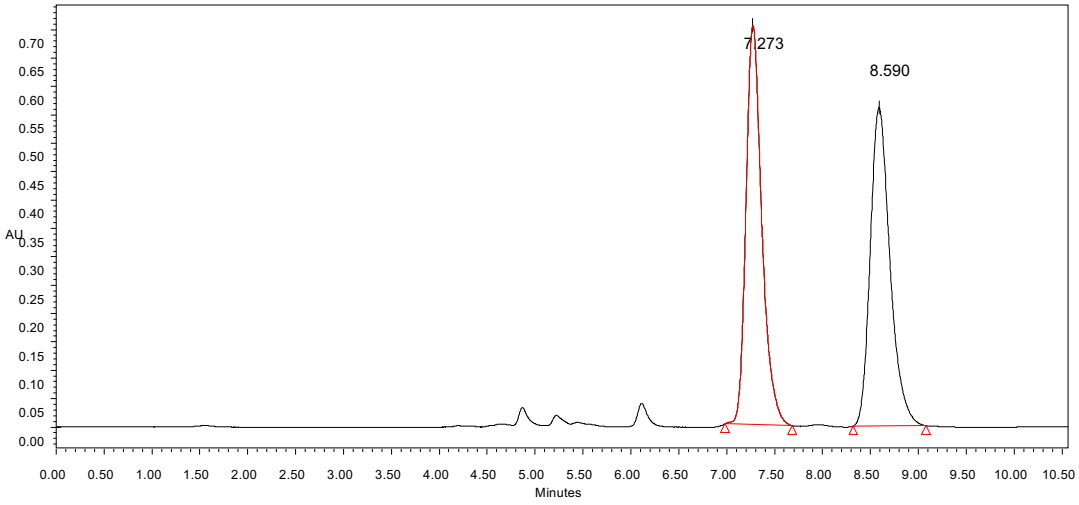


4b



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1	7.273	8103382	50.21	703661	bb	Unknown
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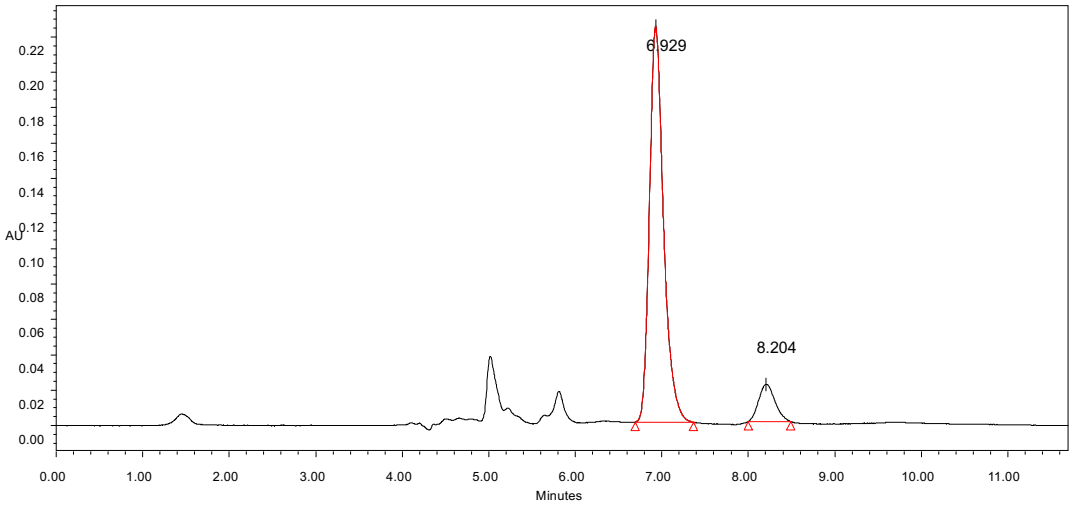

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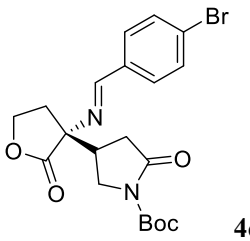

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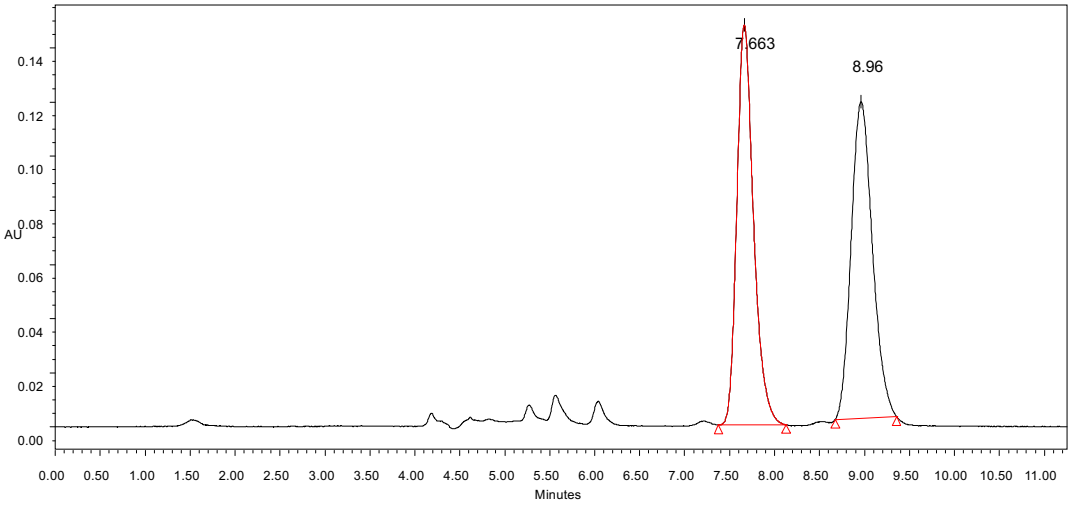

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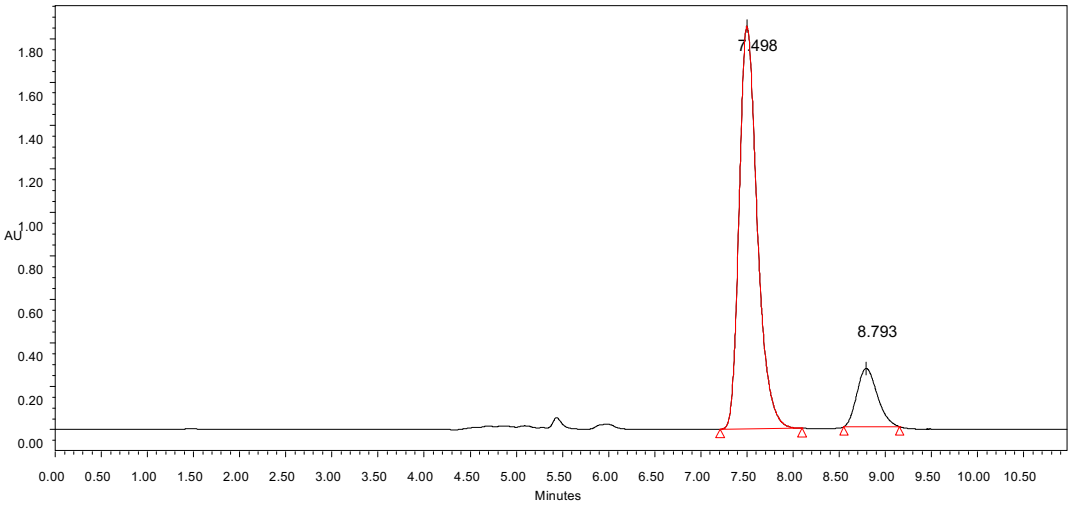

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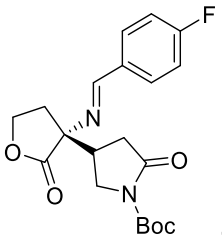
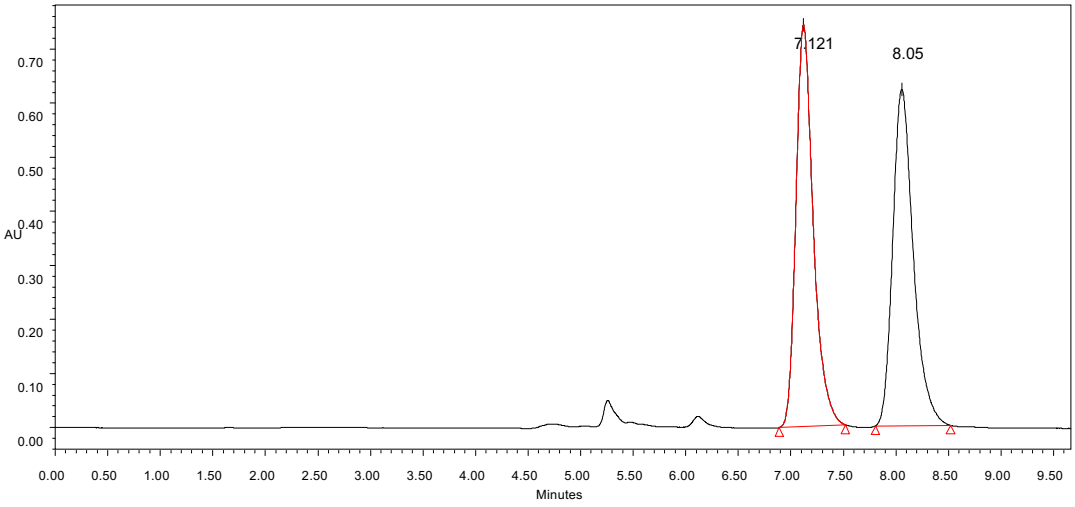


4d



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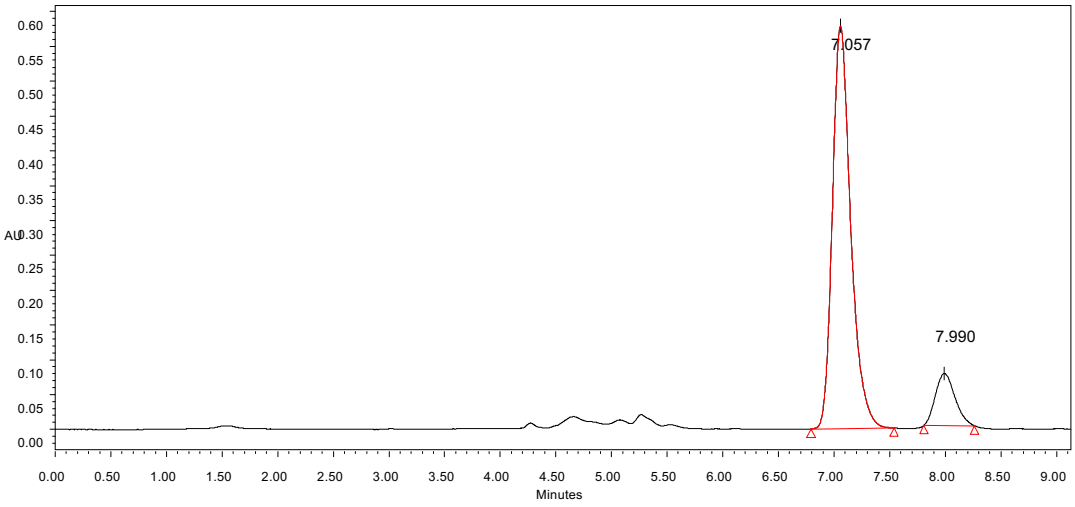

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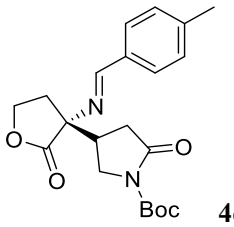
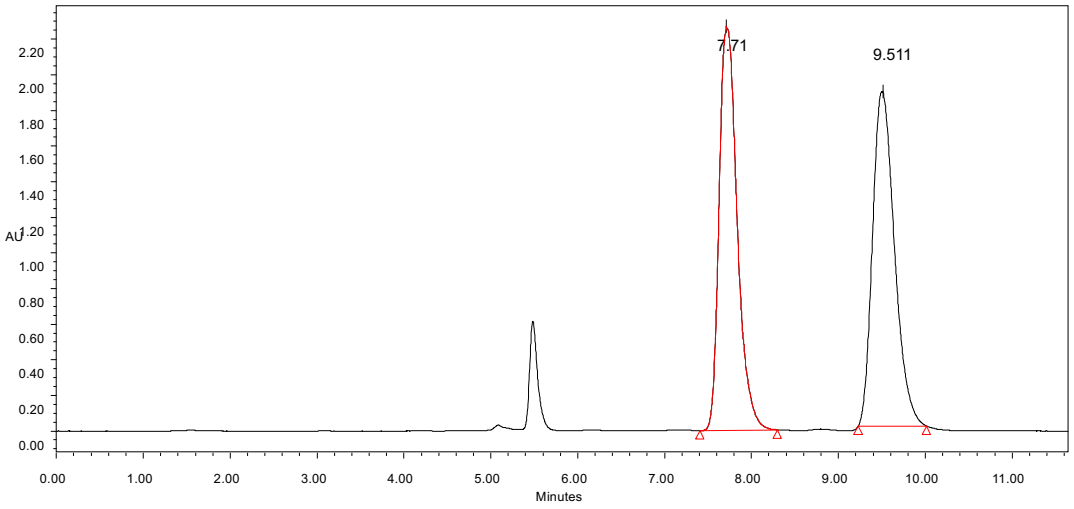


4e



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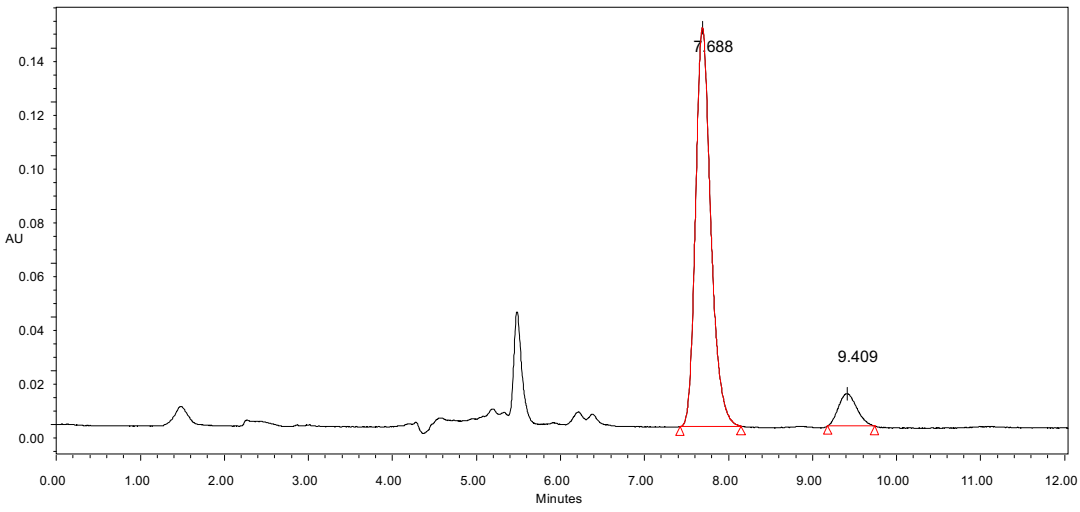
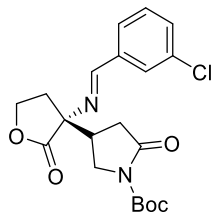


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.688	1877010	91.18	148260	bb	Unknown
2	9.409	181496	8.82	12034	bb	Unknown



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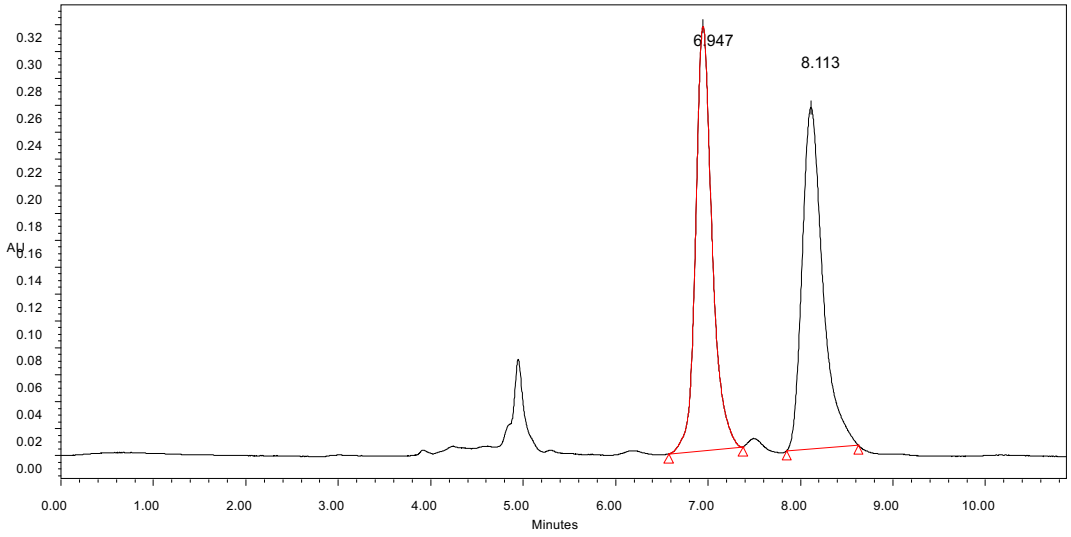
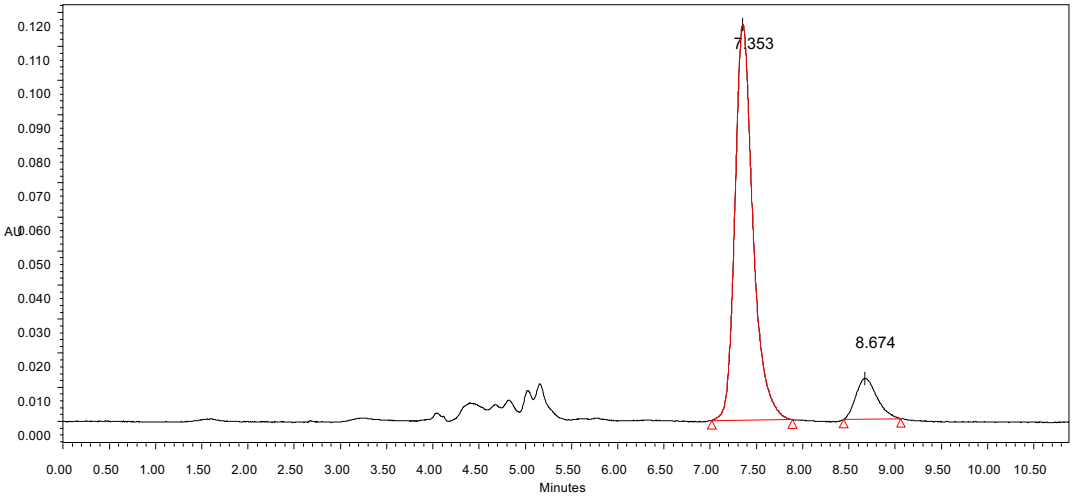
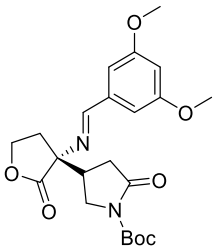


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.947	3913969	49.85	315015	bb	Unknown
2	8.113	3936859	50.15	253515	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.353	1579159	89.34	116081	bb	Unknown
2	8.674	188354	10.66	11948	bb	Unknown



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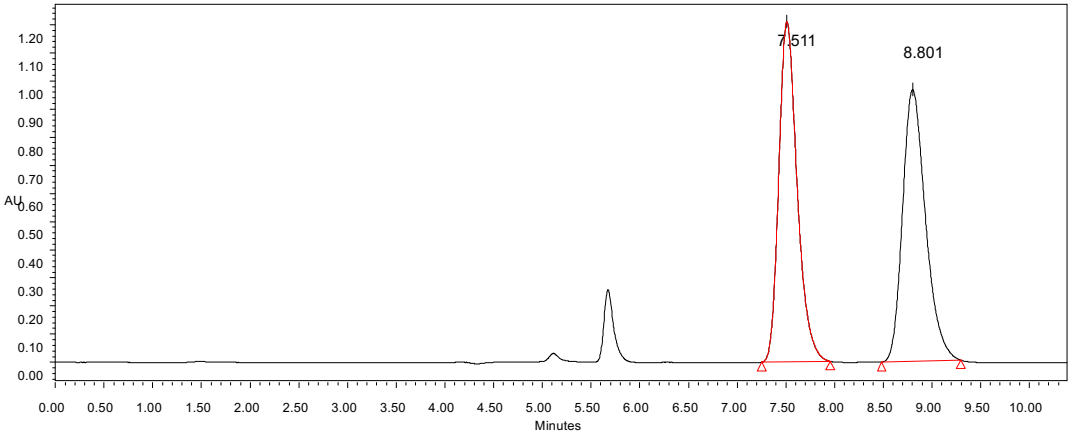
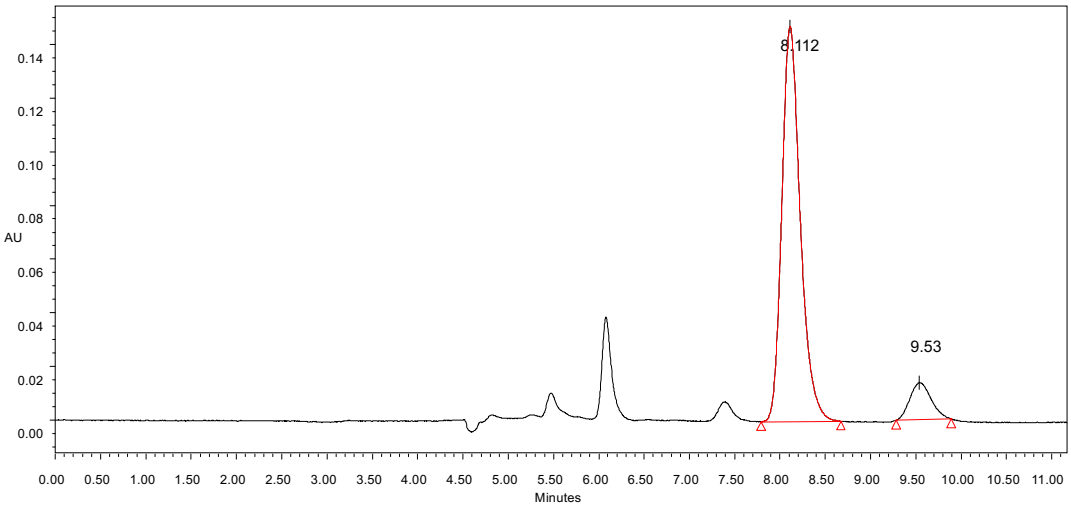
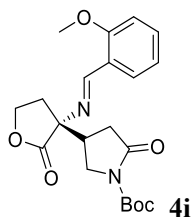


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.511	15858696	50.01	1210429	bb	Unknown
2	8.801	15852666	49.99	966403	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.112	2091887	90.24	147303	bb	Unknown
2	9.539	226141	9.76	13868	bb	Unknown



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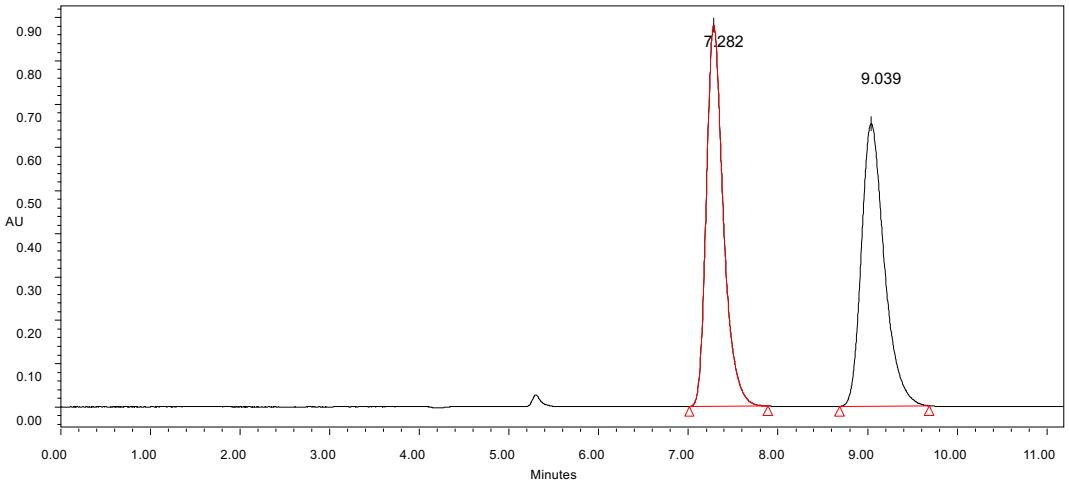
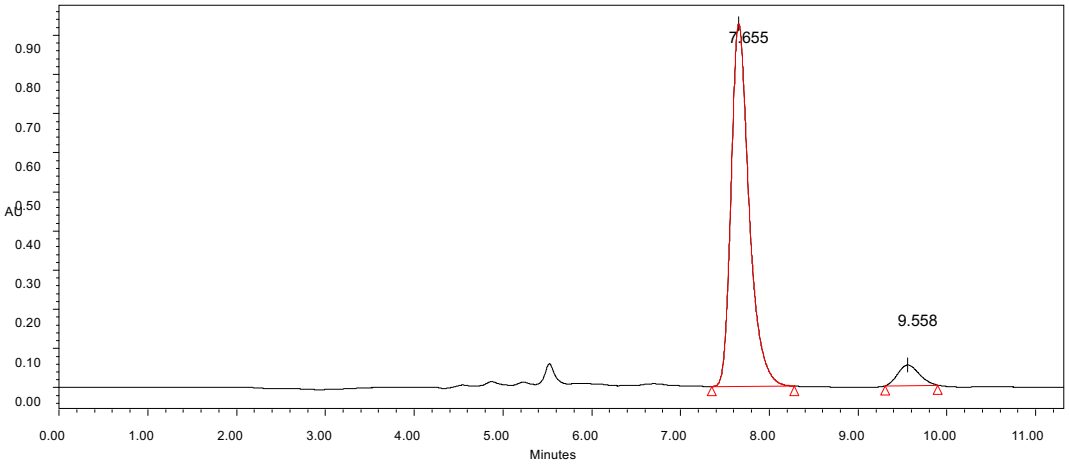
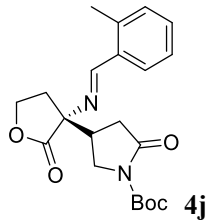


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.282	11635835	50.04	881246	bb	Unknown
2	9.039	11619104	49.96	653461	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.655	13063117	93.75	926856	bb	Unknown
2	9.558	871038	6.25	52200	bb	Unknown



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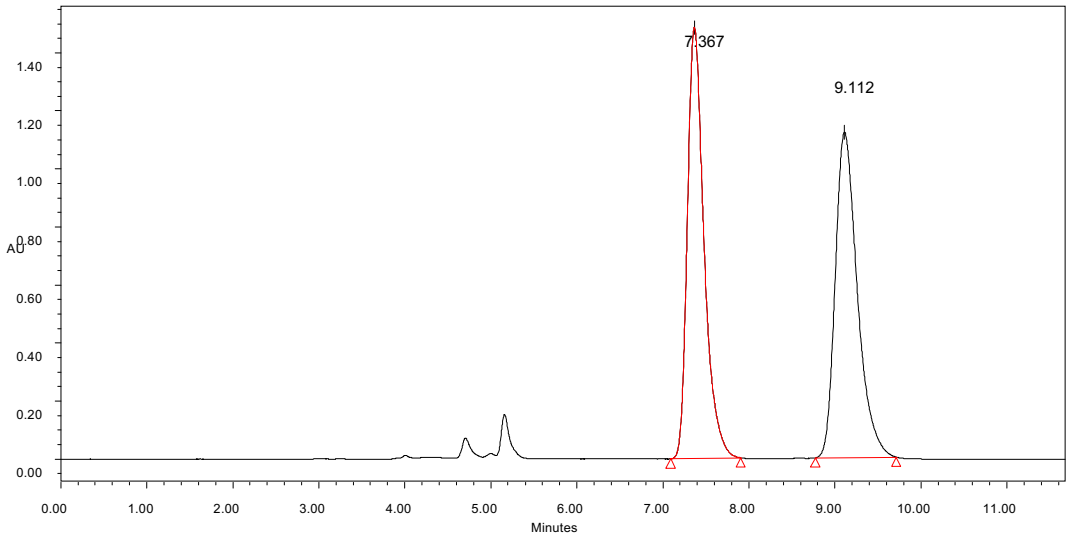
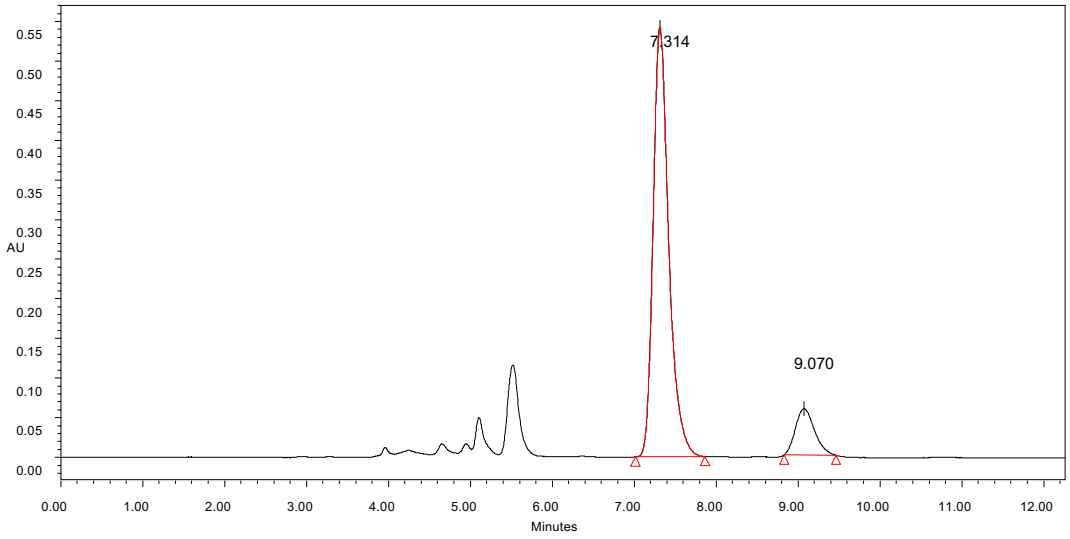
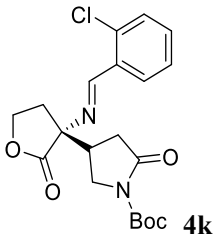


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.367	20033901	50.08	1485276	bb	Unknown
2	9.112	19971622	49.92	1121252	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.314	7168084	88.34	541993	bb	Unknown
2	9.070	946222	11.66	58577	bb	Unknown



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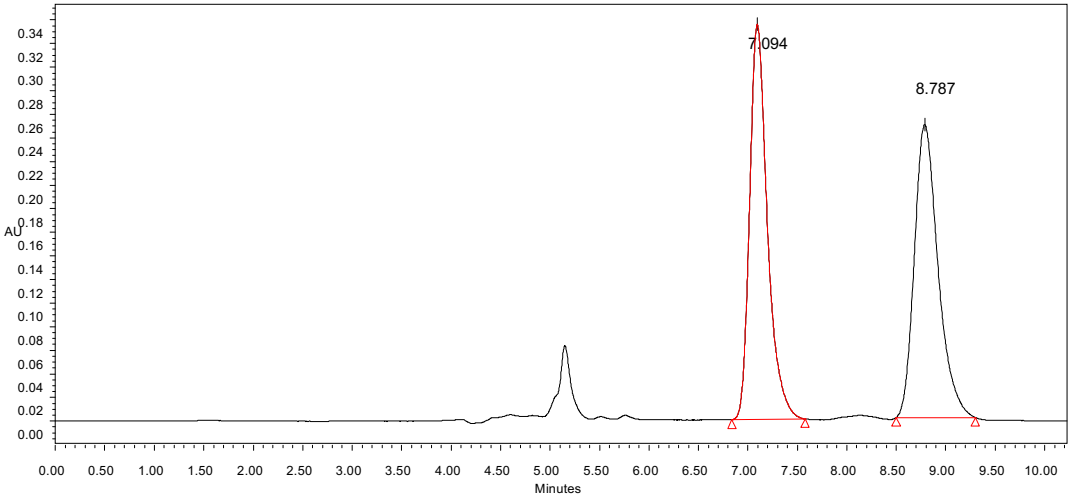
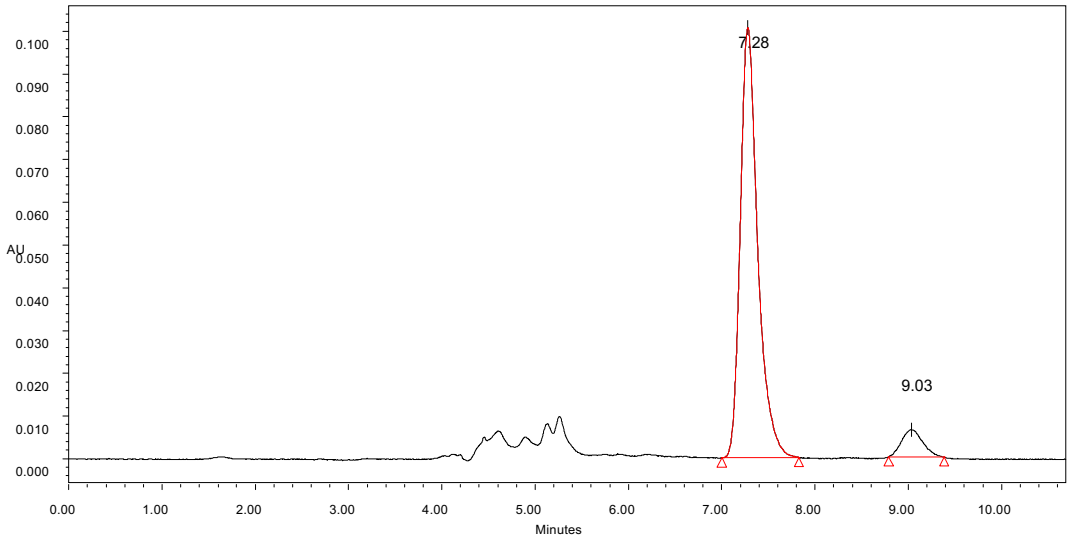
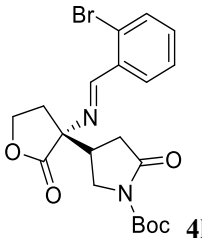


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.094	4173343	50.23	334778	bb	Unknown
2	8.787	4135908	49.77	248384	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.280	1308188	92.87	100588	bb	Unknown
2	9.033	100375	7.13	6370	bb	Unknown



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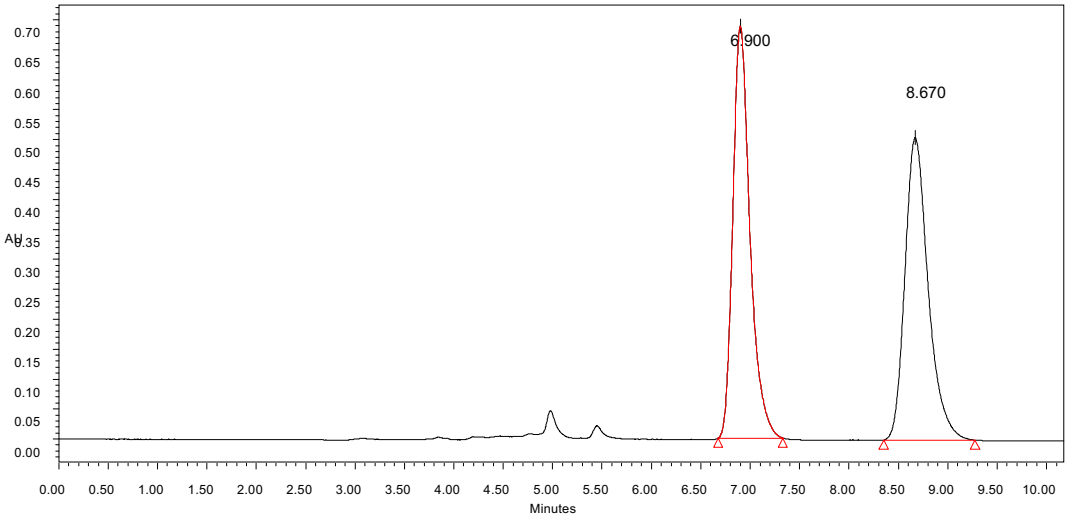
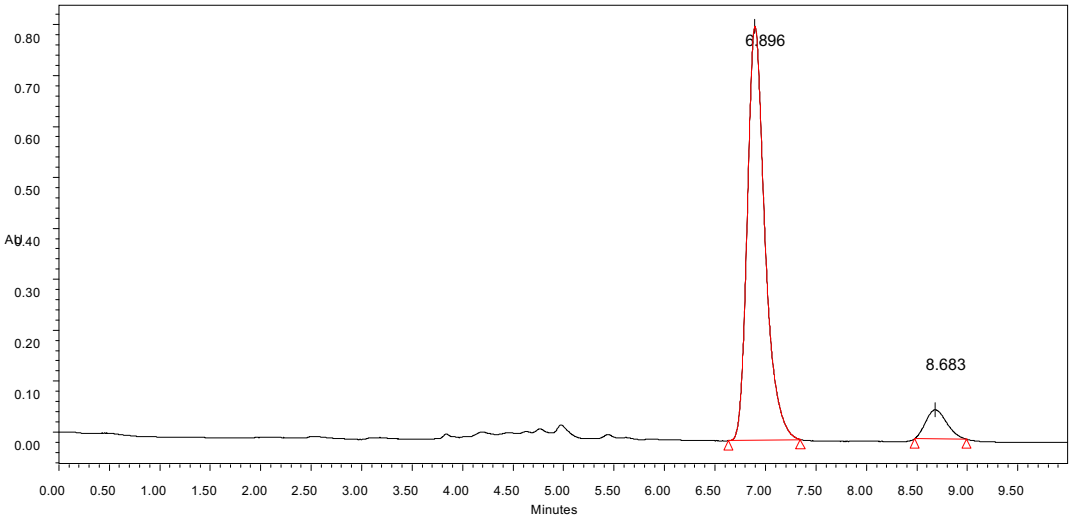
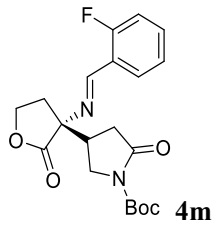


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.900	8310104	50.19	687941	bb	Unknown
2	8.670	8245621	49.81	504905	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.896	9854536	92.28	812924	bb	Unknown
2	8.683	824194	7.72	57103	bb	Unknown



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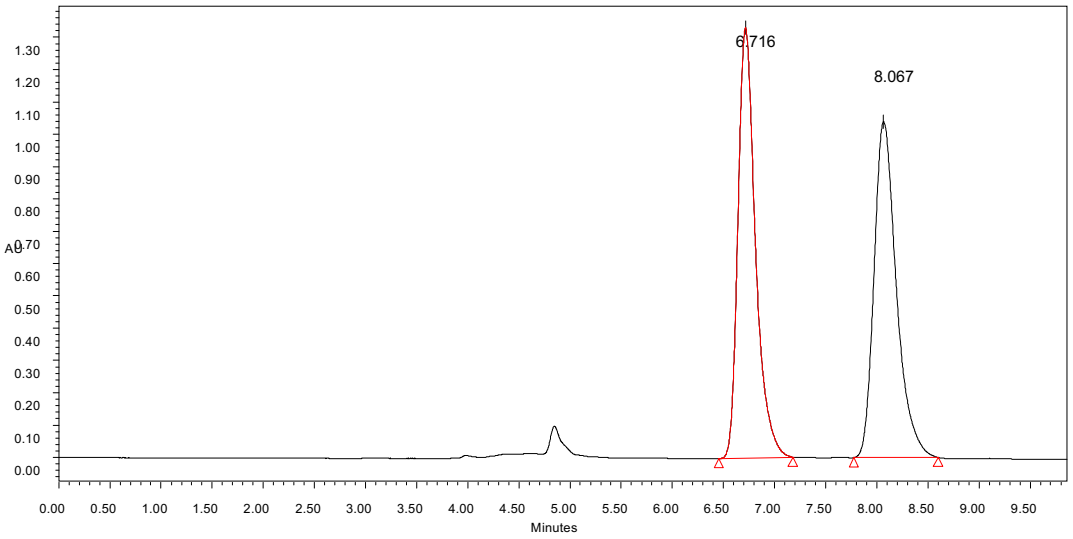
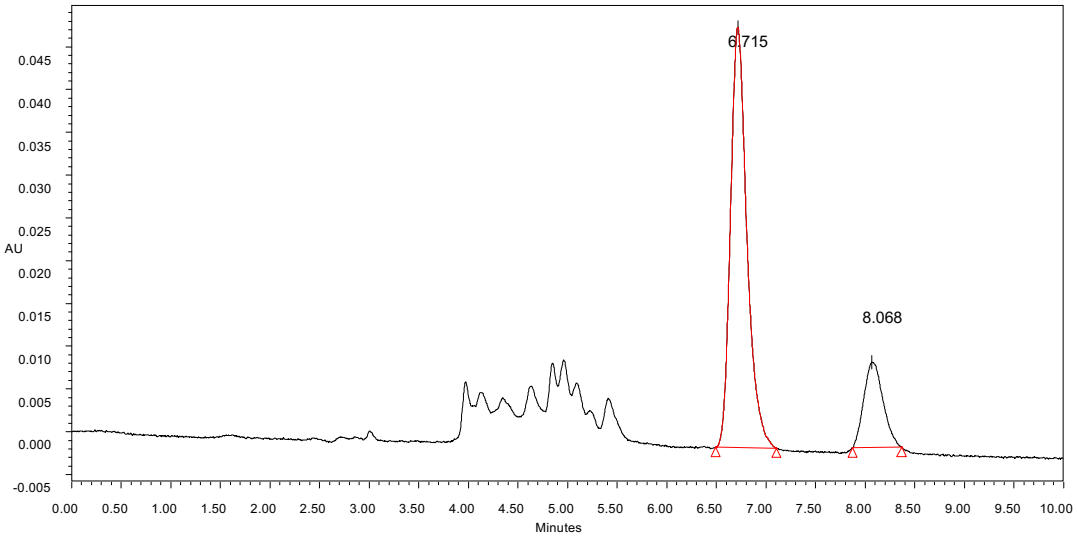
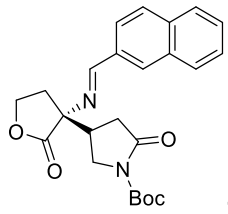


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.716	15826072	50.07	1332132	bb	Unknown
2	8.067	15784552	49.93	1039343	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.715	564930	80.78	49131	bb	Unknown
2	8.068	134384	19.22	9969	bb	Unknown



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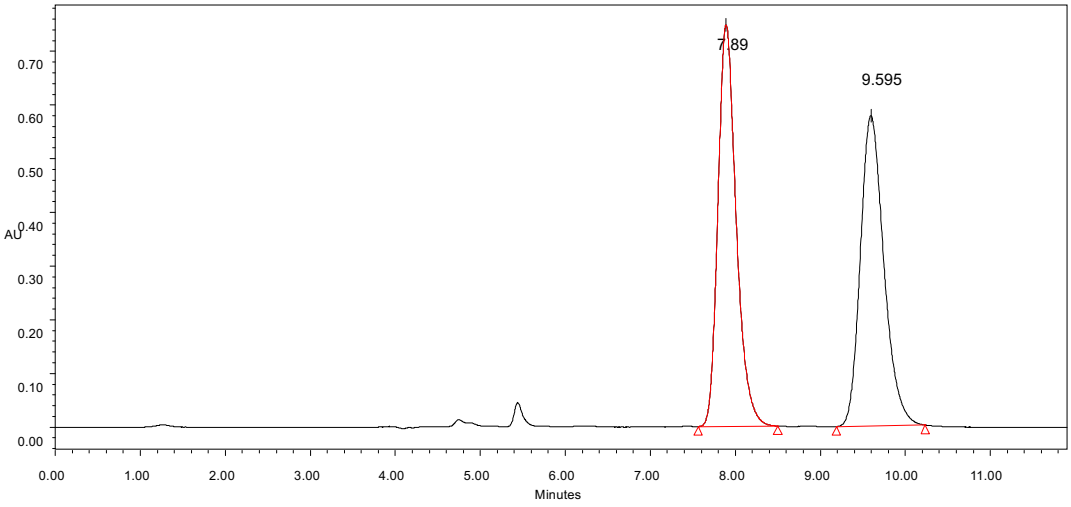
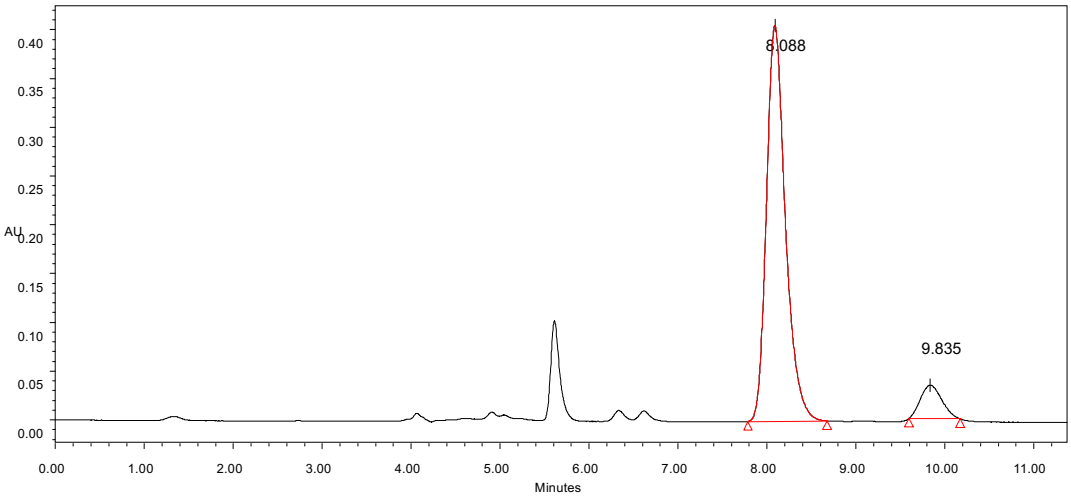
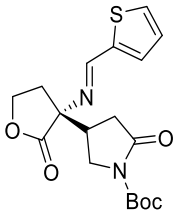


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.891	11165964	50.13	747913	bb	Unknown
2	9.595	11106190	49.87	578394	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.088	6009425	91.33	405716	bb	Unknown
2	9.835	570448	8.67	34272	bb	Unknown



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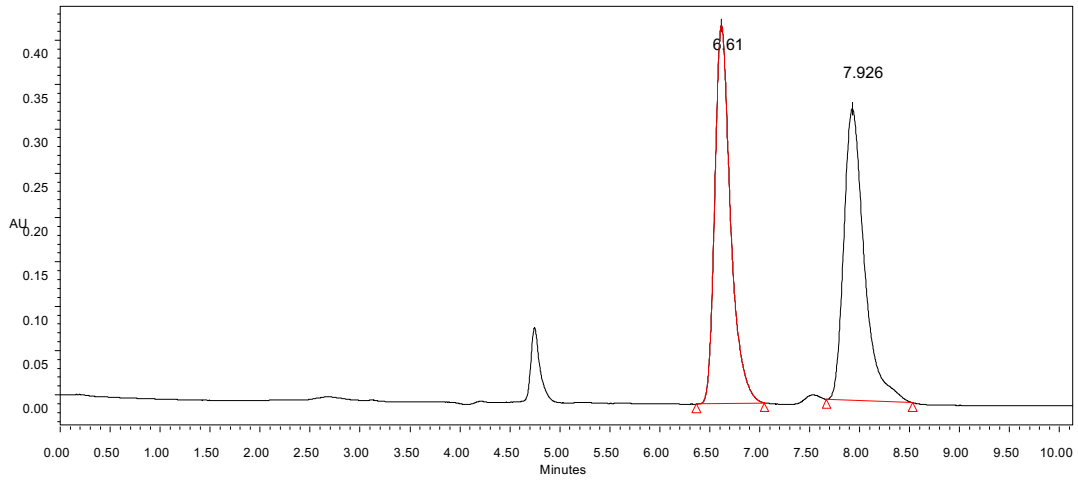
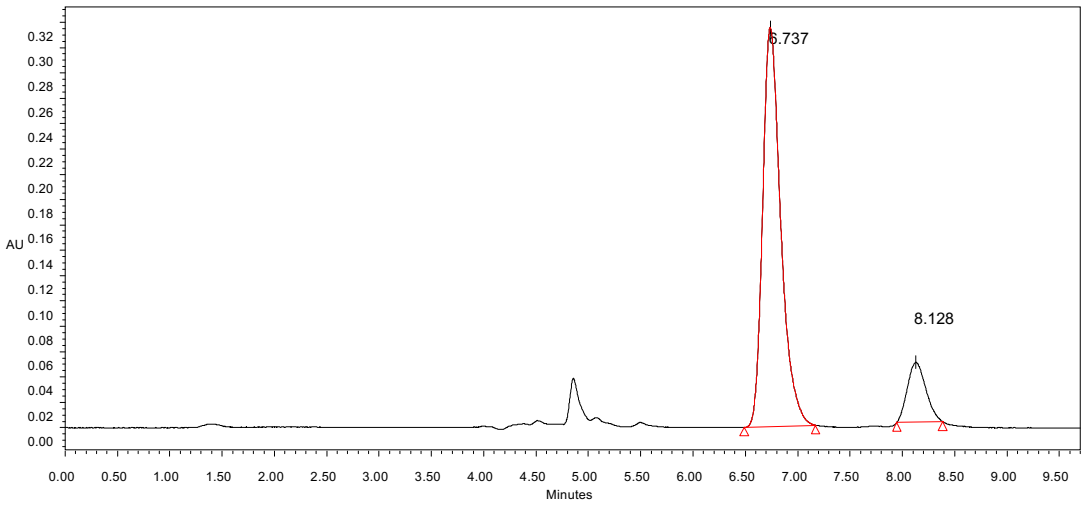
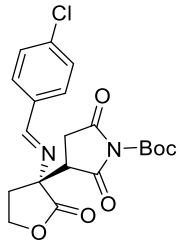


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.616	4683211	49.97	426668	bb	Unknown
2	7.926	4688049	50.03	328795	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	6.737	3788571	86.77	315234	bb	Unknown
2	8.128	577601	13.23	47204	bb	Unknown



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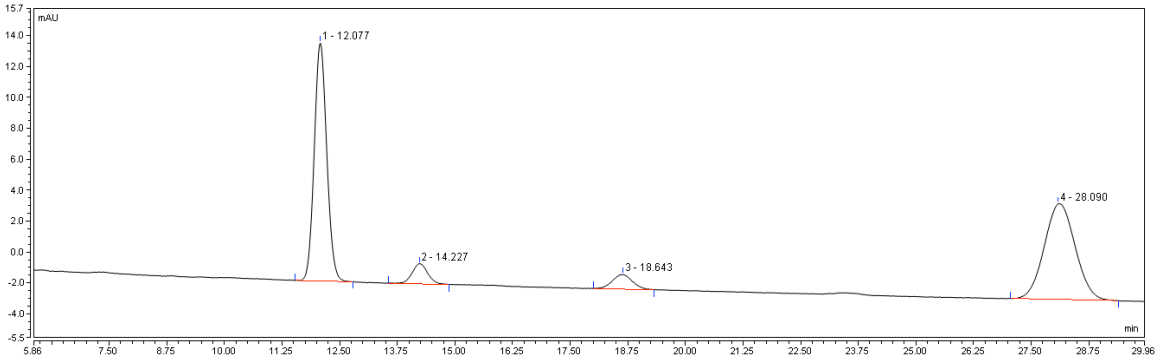
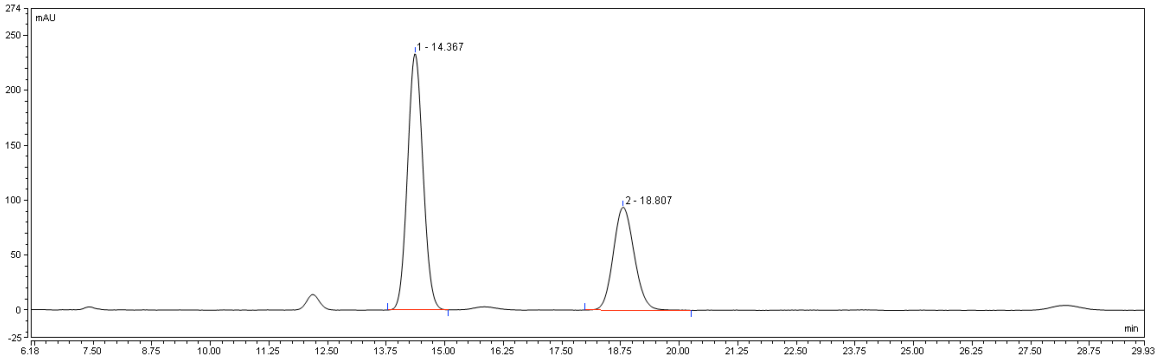
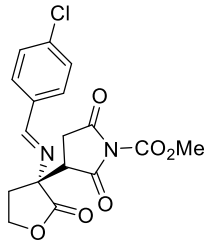


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	12.077	4.8555	45.47	15.41	bb	Unknown
2	14.227	0.5256	4.92	1.32	bb	Unknown
3	18.643	0.4865	4.56	0.96	bb	Unknown
4	28.090	4.8106	45.05	6.20	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	14.367	89.4185	65.35	233.29	bb	Unknown
2	18.807	47.4142	34.65	93.01	bb	Unknown



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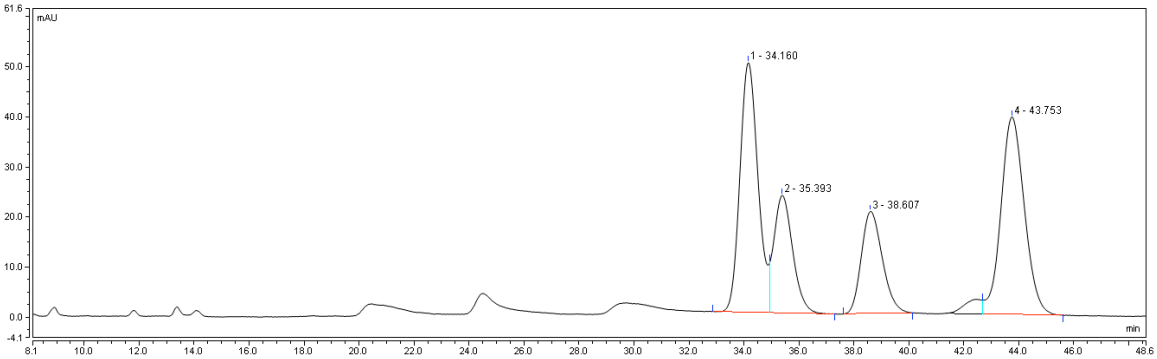
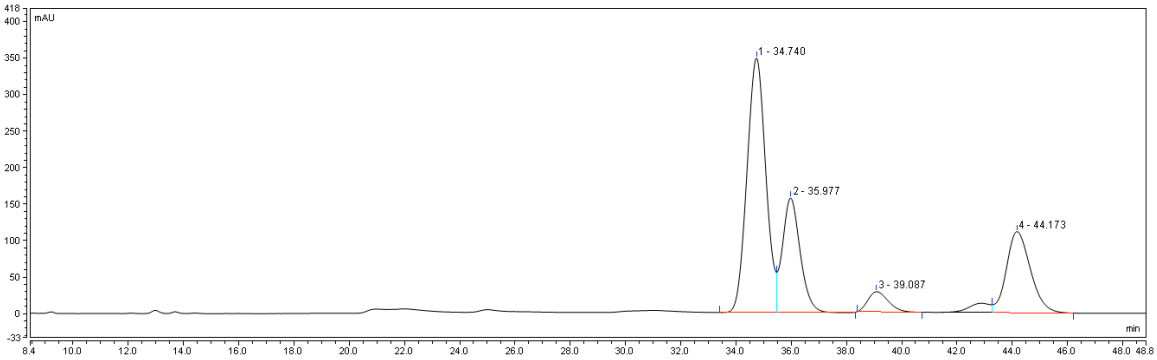
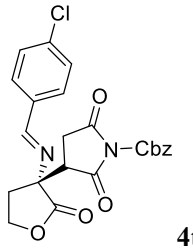


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	34.160	38.1712	33.65	49.84	bb	Unknown
2	35.393	18.2761	16.11	23.52	bb	Unknown
3	38.607	18.0189	15.88	20.39	bb	Unknown
4	43.753	38.9740	34.36	39.42	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	34.740	275.2760	52.28	348.69	bb	Unknown
2	35.977	115.5551	21.95	156.58	bb	Unknown
3	39.087	23.3078	4.43	27.53	bb	Unknown
4	44.173	112.3820	21.34	111.22	bb	Unknown



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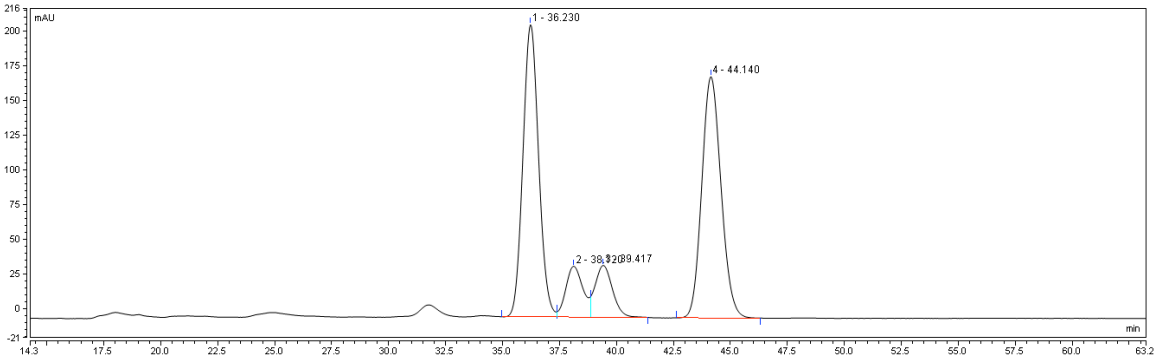
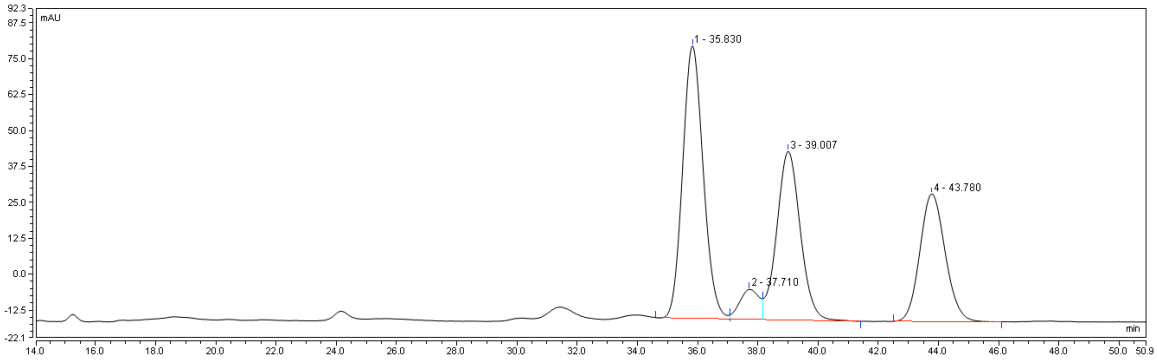
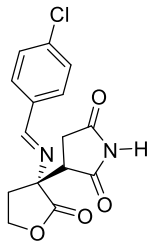


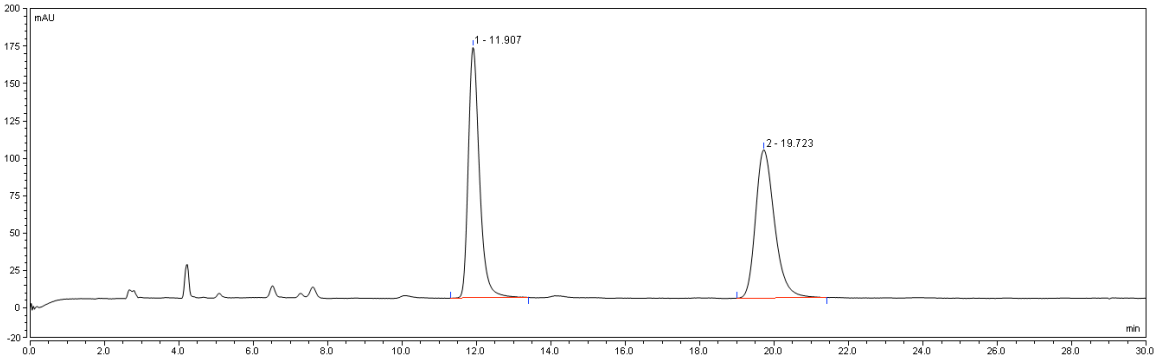
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	36.230	168.4279	41.75	210.44	bb	Unknown
2	38.120	31.9462	7.92	36.63	bb	Unknown
3	39.417	33.0339	8.19	37.32	bb	Unknown
4	44.140	170.0328	42.15	173.79	bb	Unknown



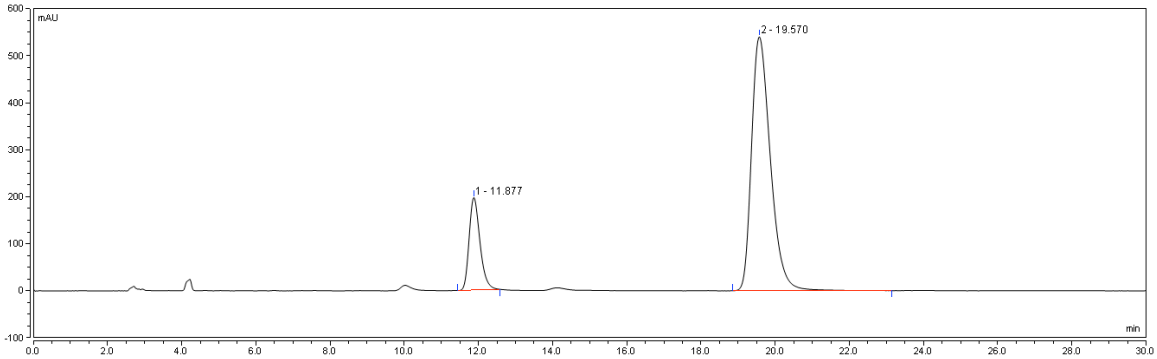
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	35.830	75.1400	41.88	94.75	bb	Unknown
2	37.710	7.8527	4.38	10.43	bb	Unknown
3	39.007	53.2742	29.70	58.66	bb	Unknown
4	43.780	43.1375	24.04	44.36	bb	Unknown



4u



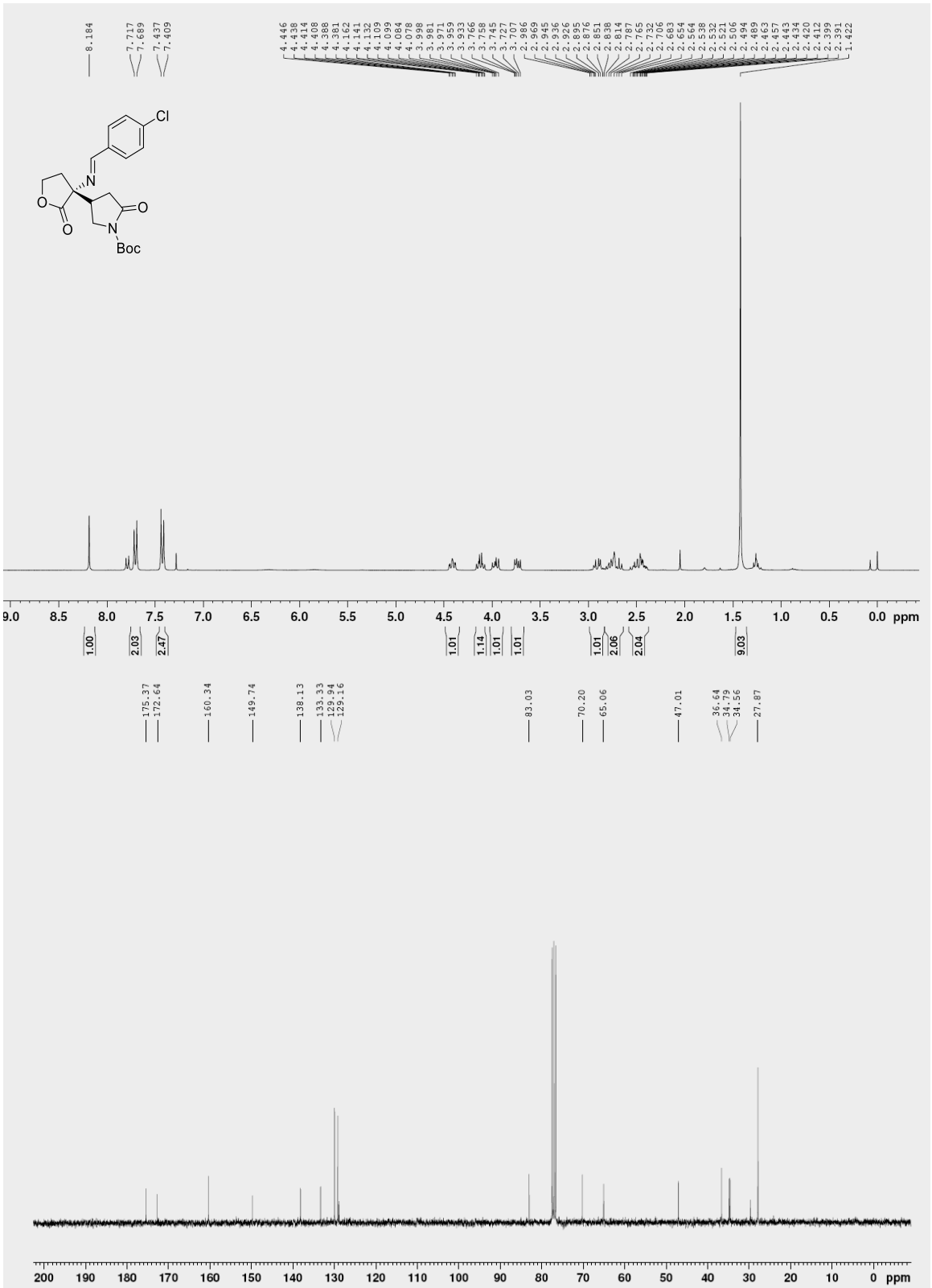
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.907	58.2539	49.88	167.73	bb	Unknown
2	19.723	58.5387	50.12	99.20	bb	Unknown



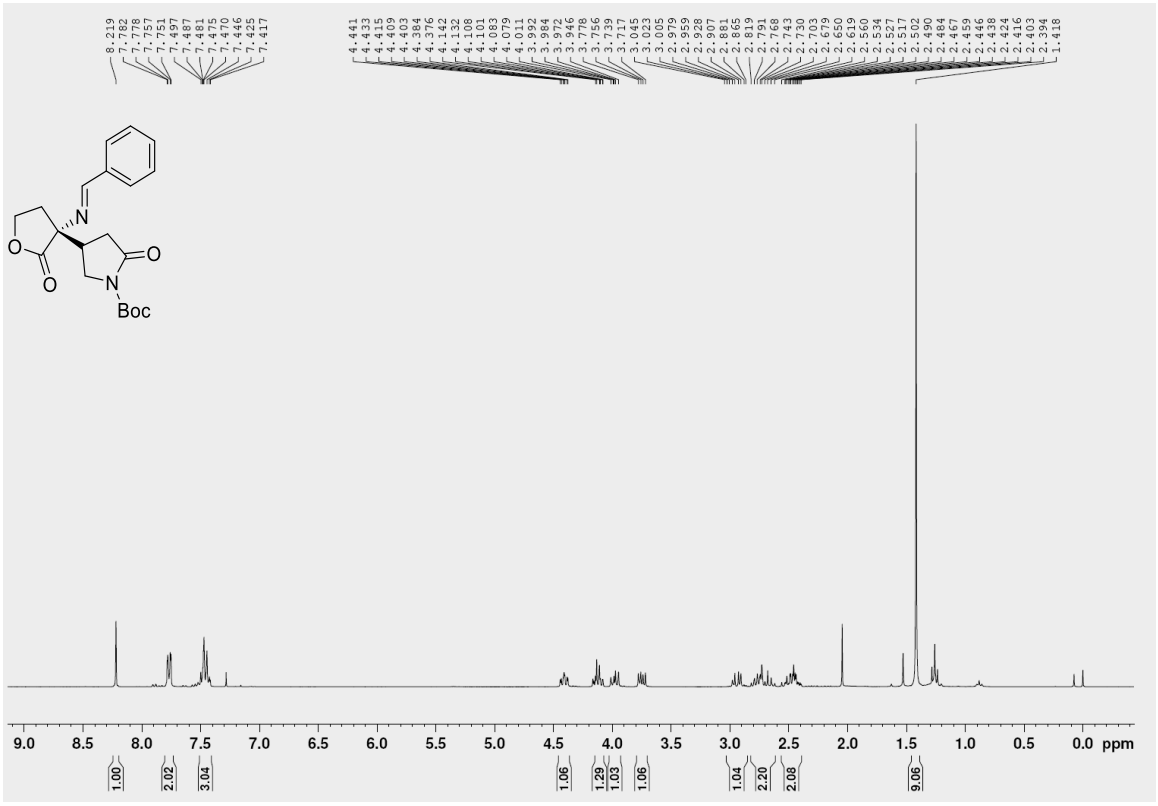
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.877	66.7407	17.34	197.05	bb	Unknown
2	19.570	318.2231	82.66	540.55	bb	Unknown

7. ^{1}H and ^{13}C NMR Spectra of compounds 4

4a



4b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N
Boc
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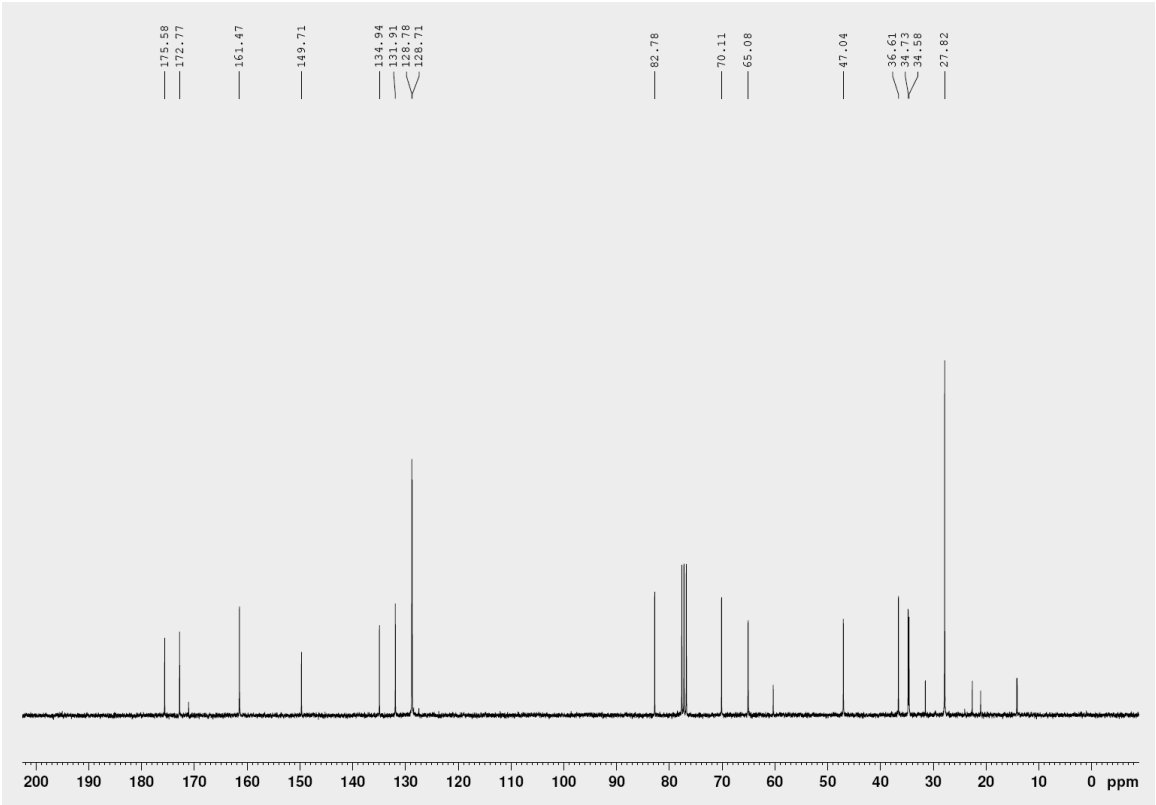
1.06
1.29
1.03
1.06
1.04
2.20
2.08
9.06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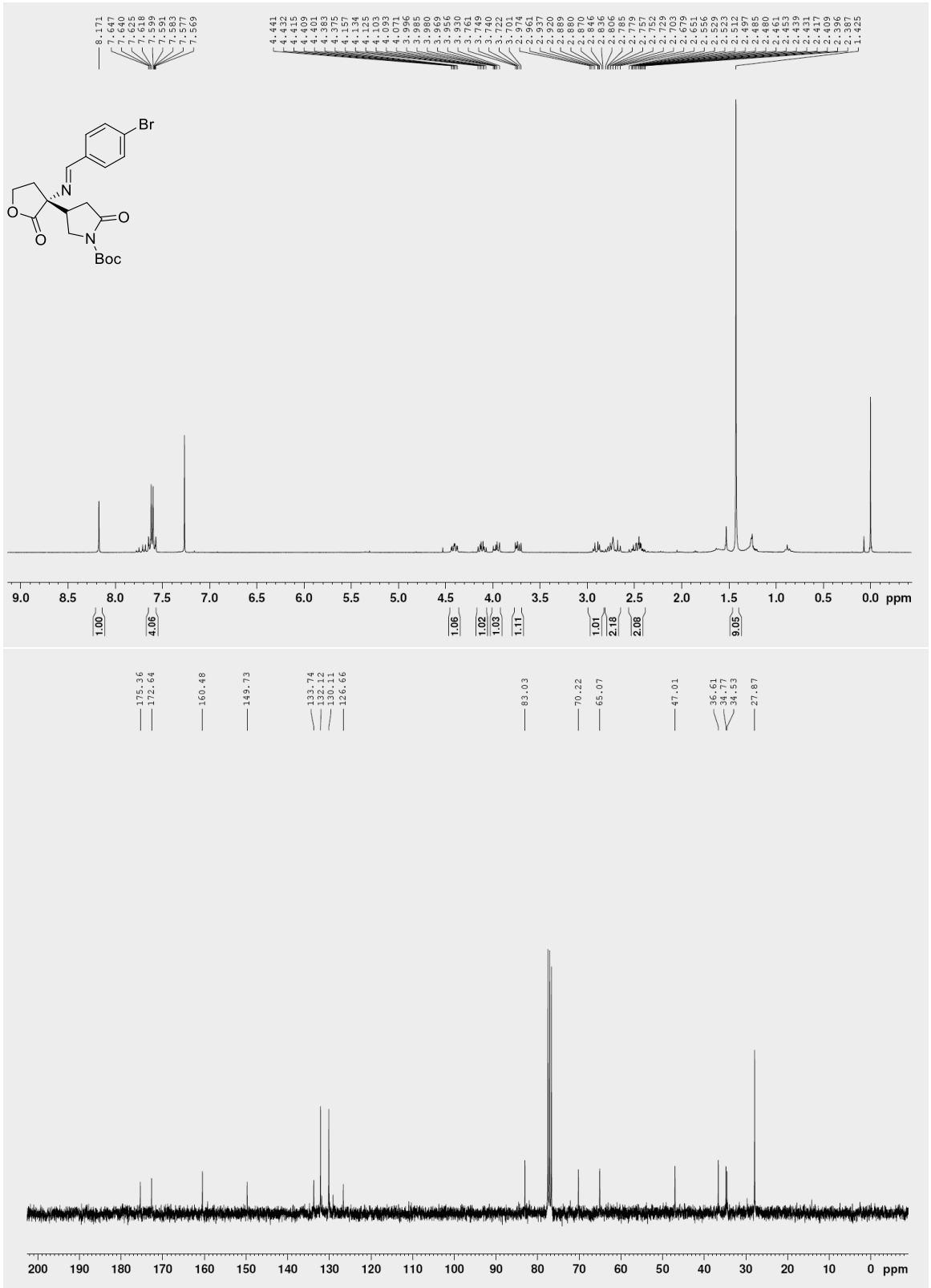
172.77
161.47
149.71
134.94
131.91
128.78
128.71
82.78
70.11
65.08
47.04
36.61
34.73
34.58
27.82
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4c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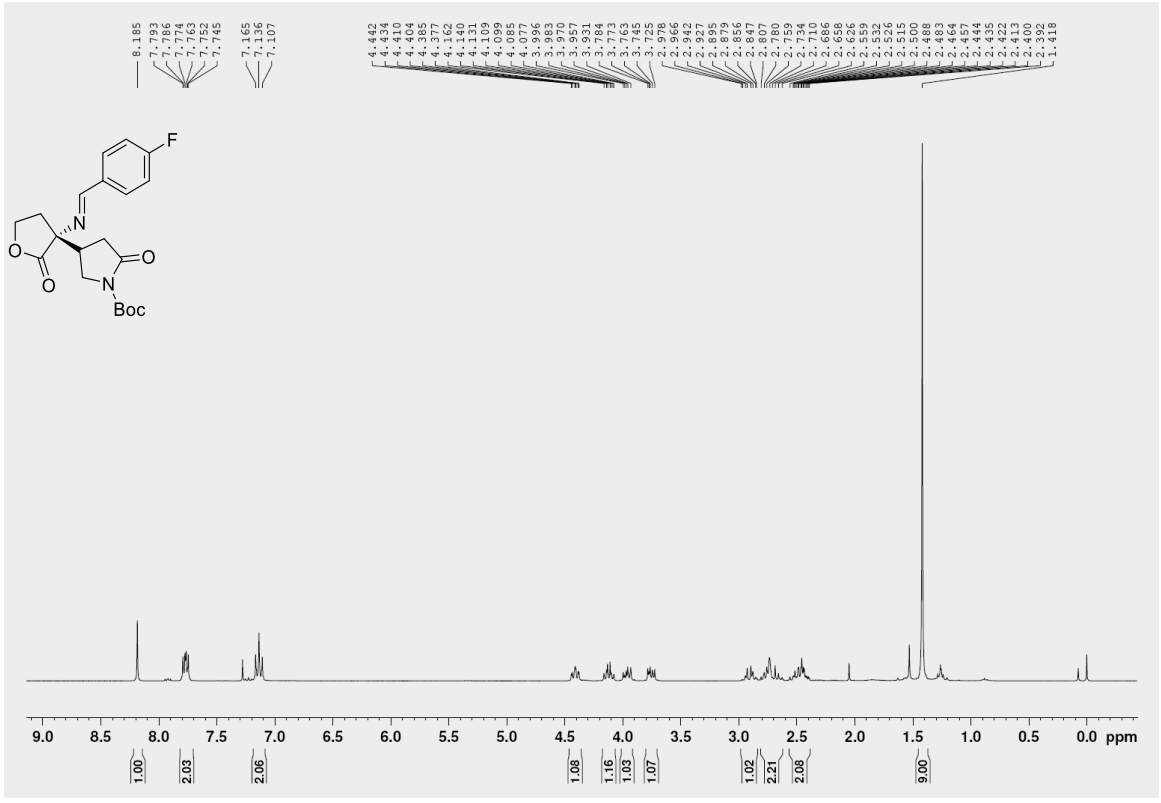
7.647
7.640
7.625
7.618
7.599
7.591
7.583
7.577
7.569
4.441
4.432
4.415
4.409
4.401
4.383
4.375
4.157
4.134
4.125
4.103
4.093
4.071
3.996
3.985
3.980
3.969
3.956
3.930
3.761
3.749
3.740
3.722
3.701
2.974
2.961
2.937
2.889
2.880
2.870
2.846
2.836
2.806
2.785
2.779
2.757
2.752
2.729
2.703
2.679
2.651
2.556
2.529
2.523
2.512
2.497
2.485
2.480
2.461
2.453
2.439
2.431
2.417
2.409
2.396
2.387
1.425
Br
N
O
O
O
N
Boc
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
4.06
1.06
1.02
1.03
1.11
1.01
2.18
2.08
9.05
175.36
172.64
160.48
149.73
133.74
132.12
130.11
126.66
83.03
70.22
65.07
47.01
36.61
34.77
34.53
27.87
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4d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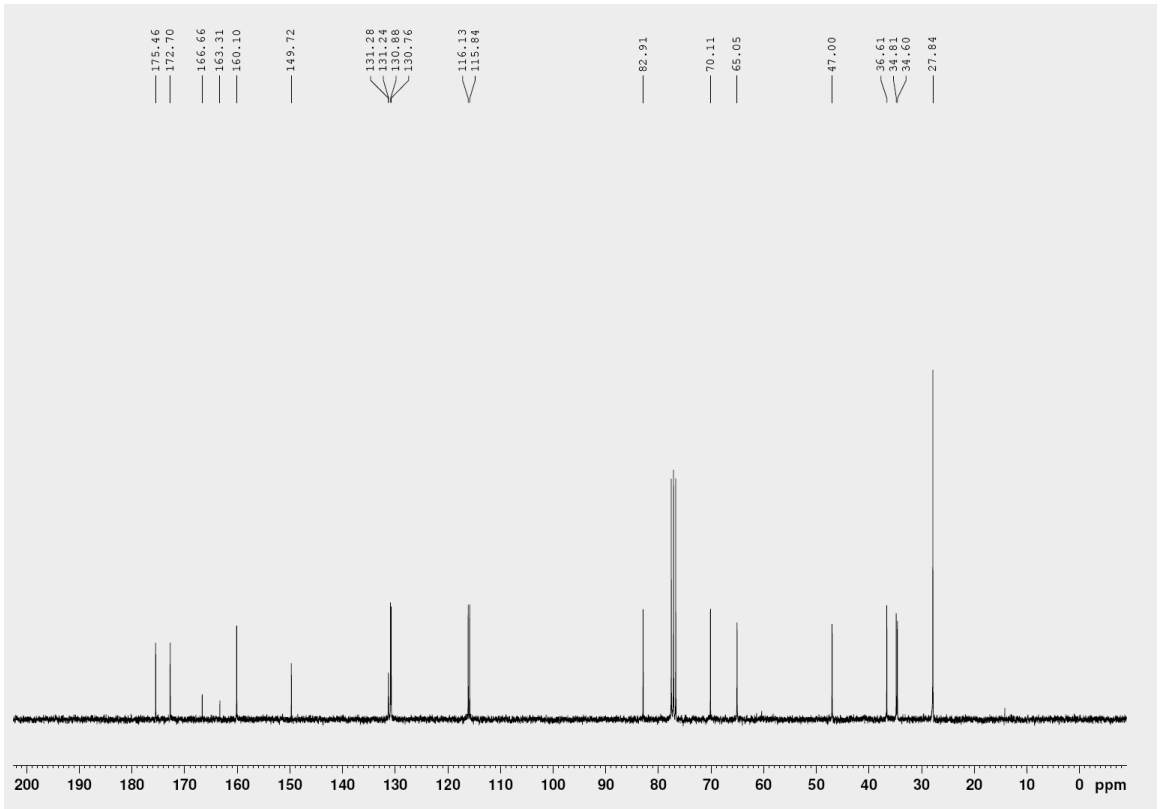
7.786
7.774
7.763
7.752
7.745
7.165
7.136
7.107
4.442
4.434
4.410
4.404
4.385
4.377
4.162
4.140
4.131
4.109
4.099
4.085
4.077
3.996
3.983
3.970
3.957
3.931
3.784
3.773
3.763
3.745
3.725
2.978
2.966
2.942
2.927
2.895
2.879
2.856
2.847
2.807
2.780
2.759
2.734
2.710
2.686
2.658
2.626
2.559
2.532
2.526
2.515
2.500
2.488
2.483
2.464
2.457
2.444
2.435
2.422
2.413
2.400
2.392
1.418
F
N
O
O
O
N
Boc
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.00
2.03
2.06
1.08
1.16
1.03
1.07
1.02
2.21
2.08
9.00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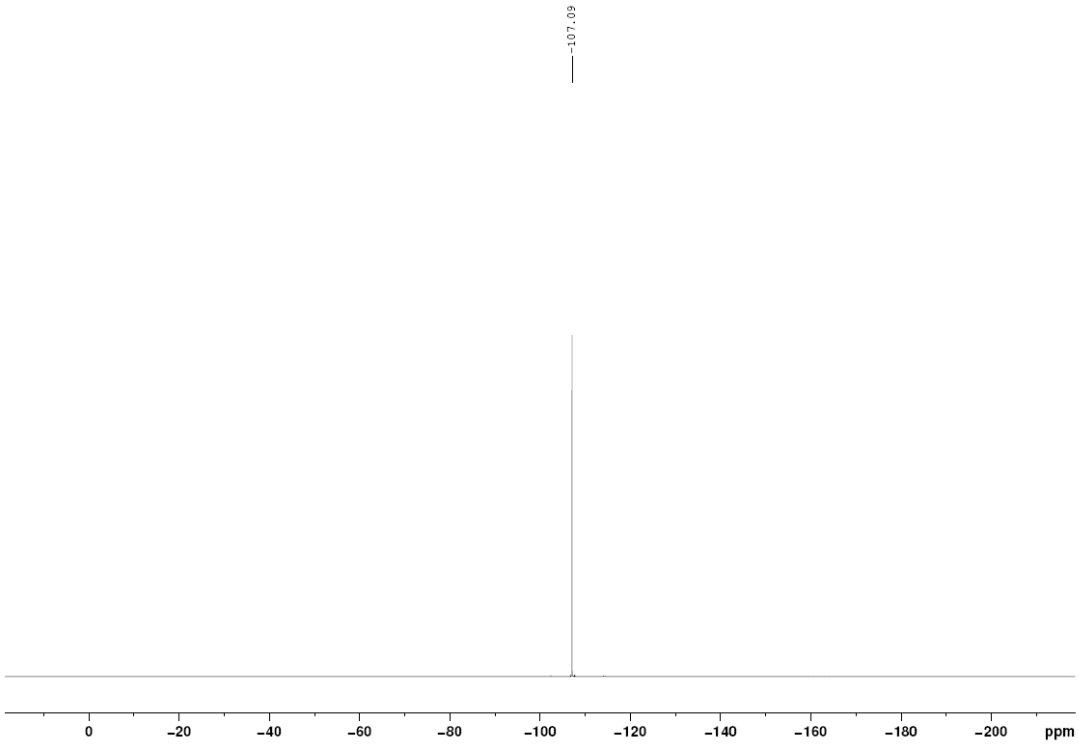
172.70
166.66
163.31
160.10
149.72
131.28
131.24
130.88
130.76
116.13
115.84
82.91
70.11
65.05
47.00
36.61
34.81
34.60
27.84
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm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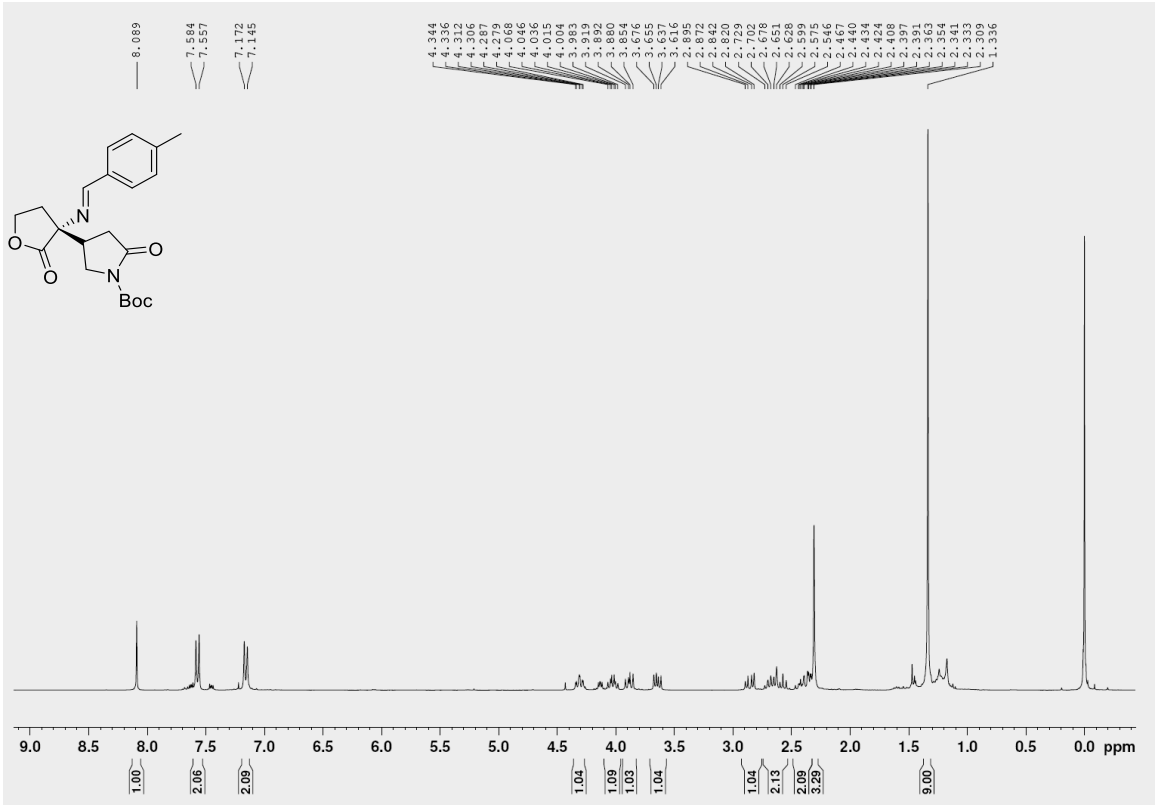
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

4e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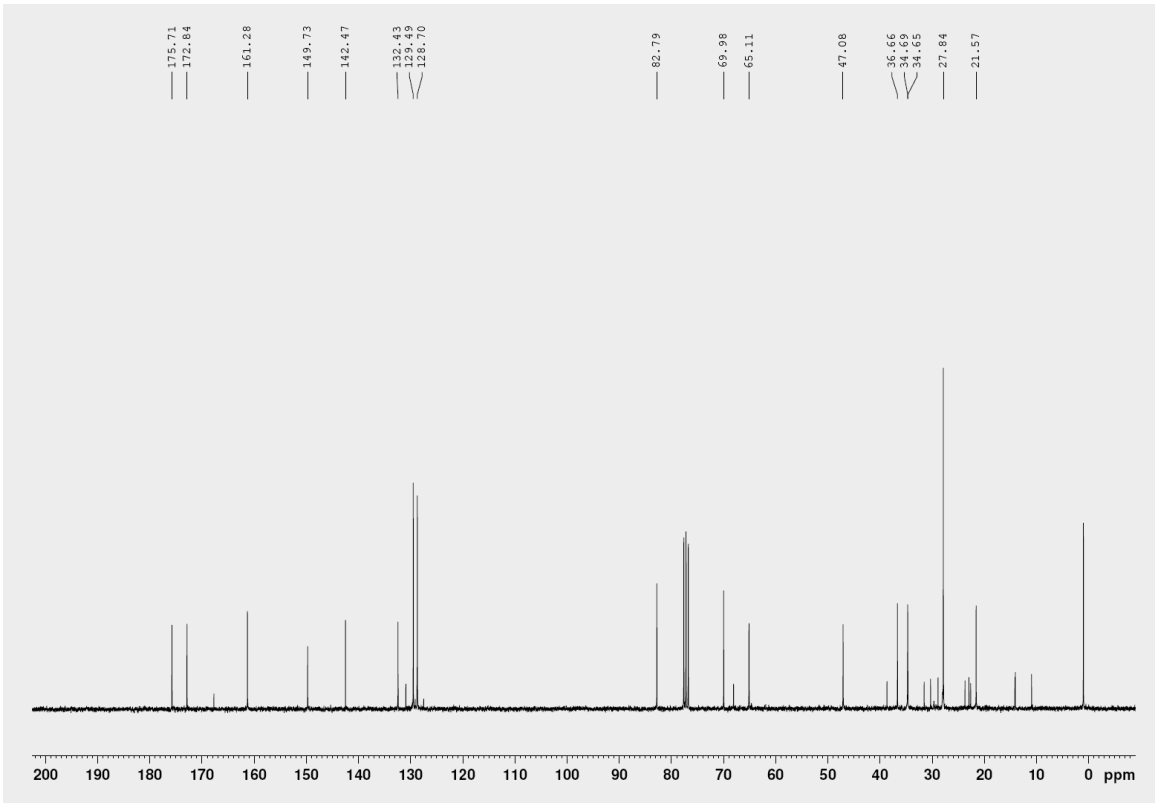
7.557
7.172
7.145
4.344
4.336
4.312
4.306
4.287
4.279
4.068
4.046
4.036
4.015
4.004
3.983
3.892
3.880
3.854
3.676
3.655
3.637
3.616
2.695
2.672
2.642
2.620
2.729
2.702
2.678
2.651
2.628
2.599
2.575
2.546
2.467
2.440
2.434
2.424
2.408
2.397
2.391
2.363
2.354
2.341
2.333
2.309
1.336
O
O
N
O
N
Boc
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.00
2.06
2.09
1.04
1.09
1.03
1.04
1.04
2.13
2.09
3.29
9.00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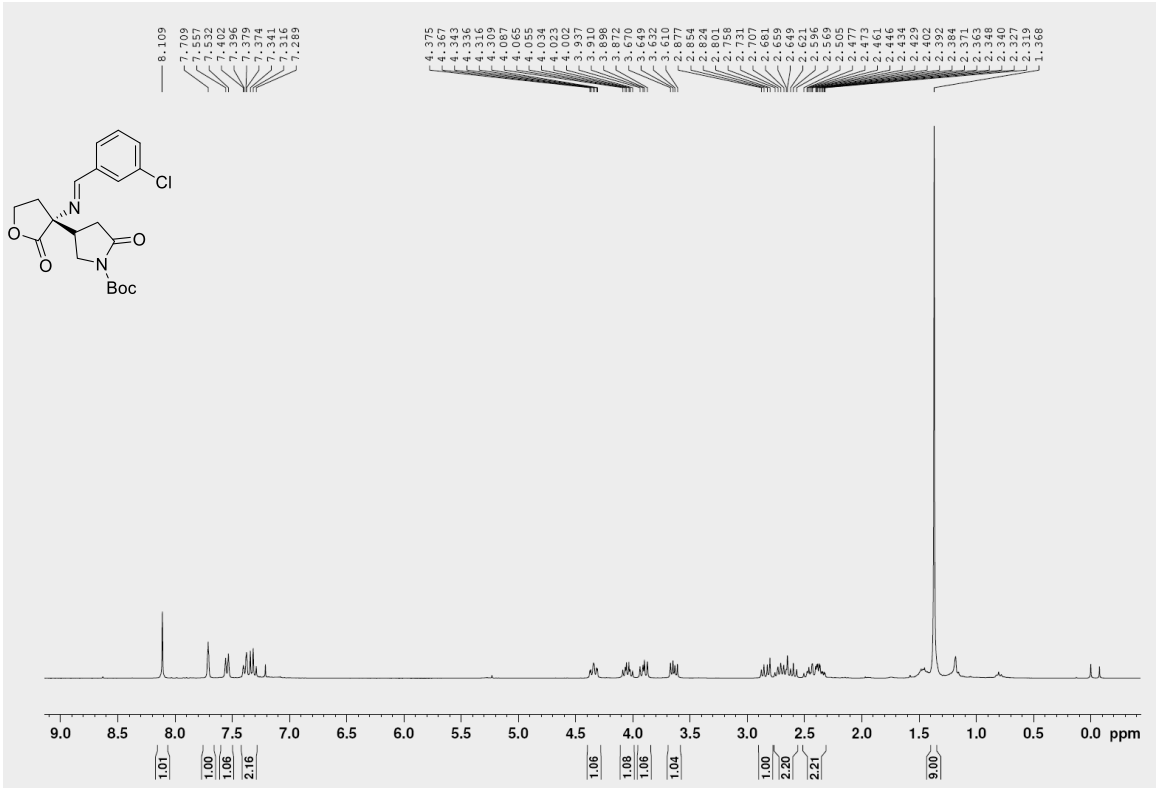
172.84
161.28
149.73
142.47
132.43
129.49
128.70
82.79
69.98
65.11
47.08
36.66
34.69
34.65
27.84
21.57
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

4f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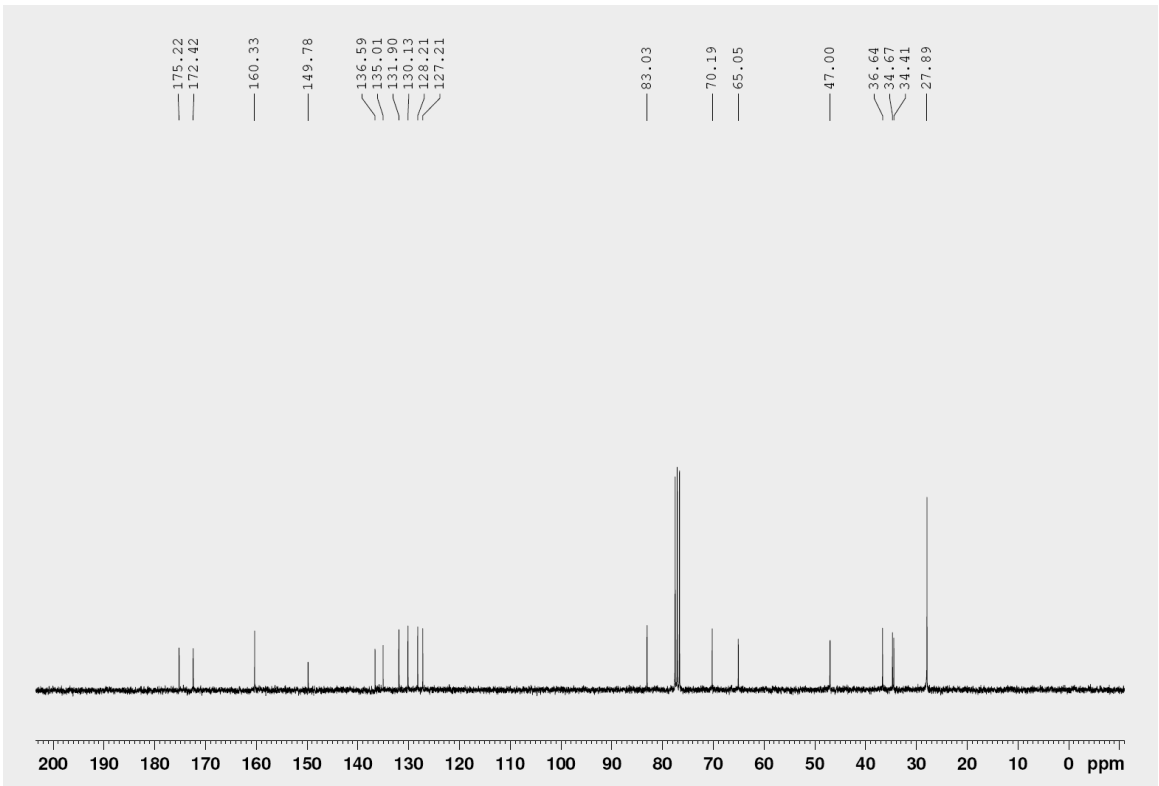
7.709
7.537
7.532
7.402
7.396
7.379
7.374
7.341
7.316
7.289
4.375
4.367
4.343
4.336
4.316
4.309
4.087
4.065
4.055
4.034
4.023
4.002
3.937
3.910
3.898
3.872
3.670
3.649
3.632
3.610
2.877
2.854
2.824
2.801
2.758
2.731
2.707
2.681
2.659
2.649
2.621
2.596
2.569
2.555
2.477
2.473
2.461
2.446
2.434
2.429
2.402
2.392
2.384
2.371
2.363
2.348
2.340
2.327
2.319
1.368
Cl
N
O
O
O
N
Boc
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.01
1.00
1.06
2.16
1.06
1.08
1.06
1.04
1.00
2.20
2.21
9.00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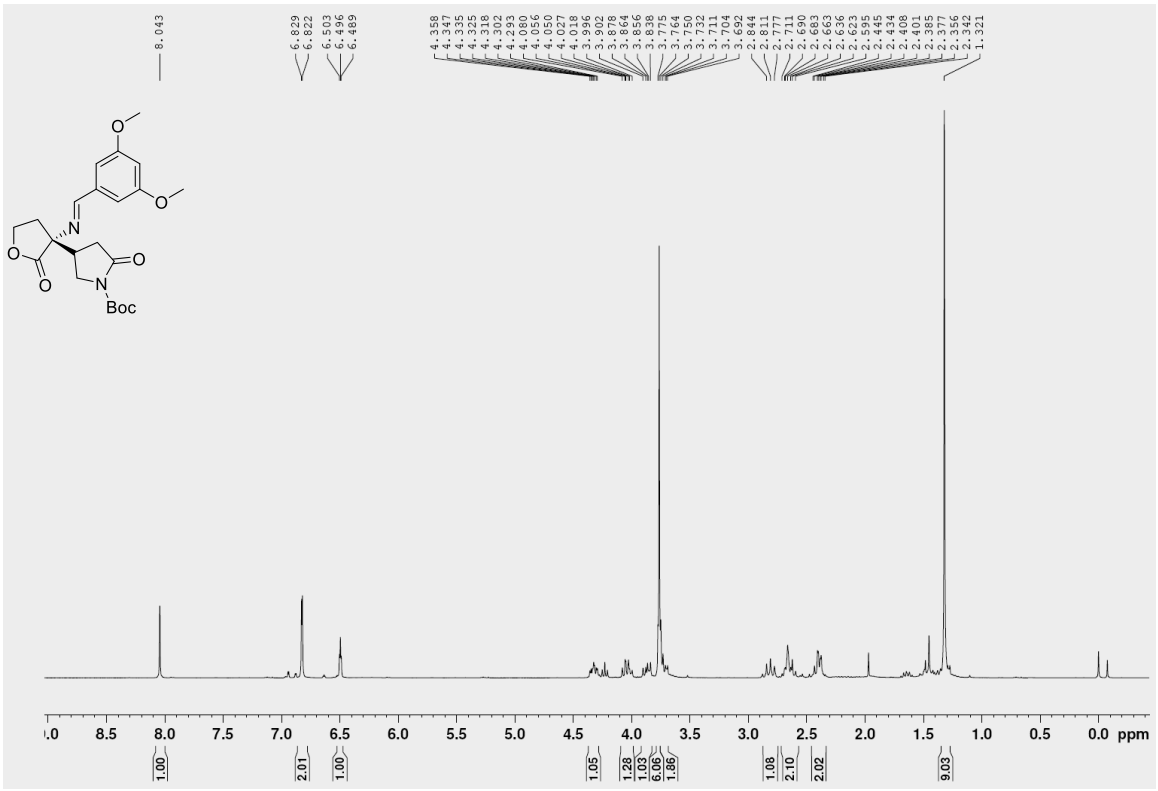
172.42
160.33
149.78
136.59
135.01
131.90
130.13
128.21
127.21
83.03
70.19
65.05
47.00
36.64
34.67
34.41
27.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4g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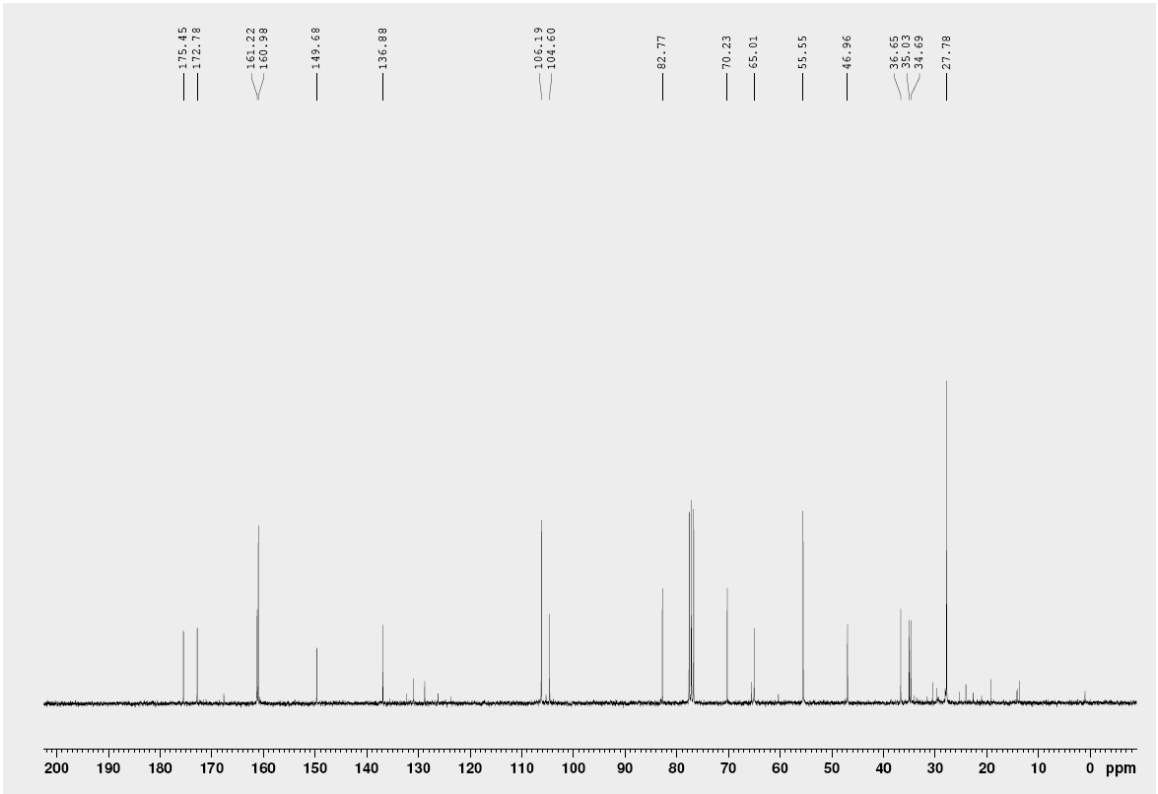
6.829
6.822
6.503
6.496
6.489
4.358
4.347
4.335
4.325
4.318
4.302
4.293
4.080
4.056
4.050
4.027
4.018
3.906
3.902
3.878
3.864
3.856
3.838
3.775
3.764
3.750
3.732
3.711
3.704
3.692
2.844
2.811
2.777
2.711
2.690
2.683
2.663
2.636
2.623
2.595
2.445
2.434
2.408
2.401
2.385
2.377
2.356
2.342
1.321
O
O
N
O
O
N
Boc
1.00
2.01
1.00
1.05
1.28
1.03
6.06
1.86
1.08
2.10
2.02
9.03
ppm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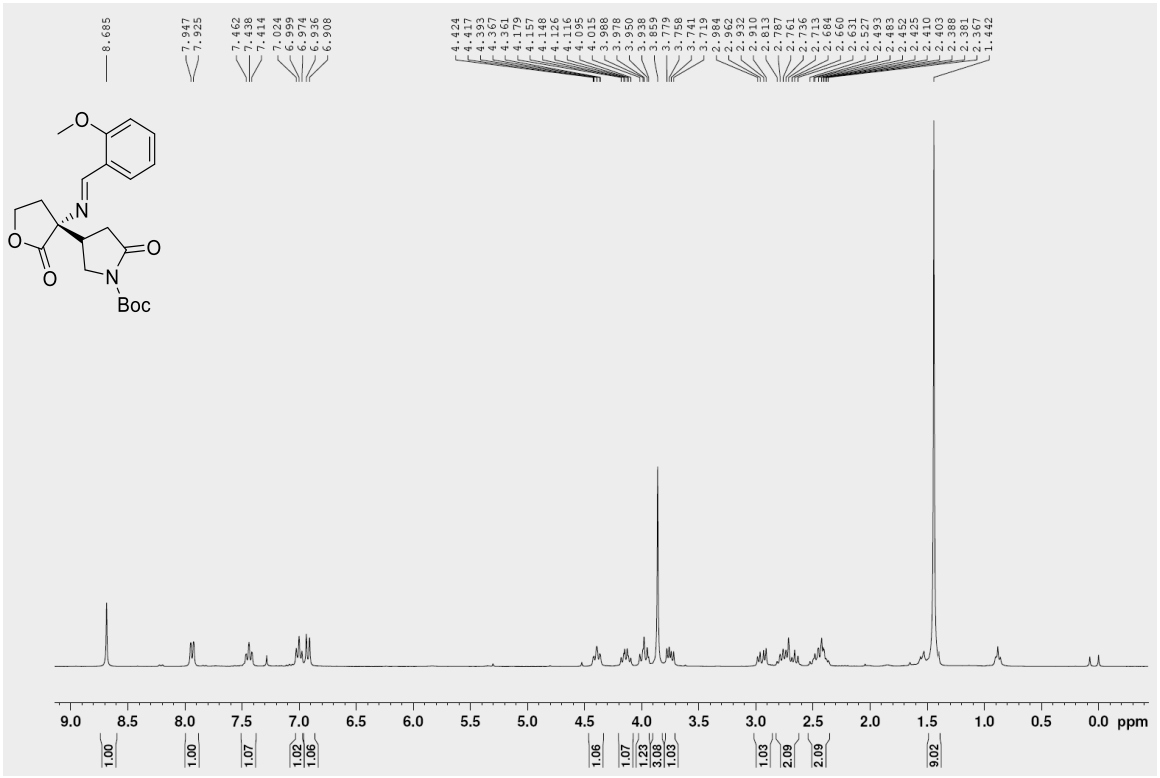
172.78
161.22
160.98
149.68
136.88
106.19
104.60
82.77
70.23
65.01
55.55
46.96
36.65
35.03
34.69
27.78
ppm

4i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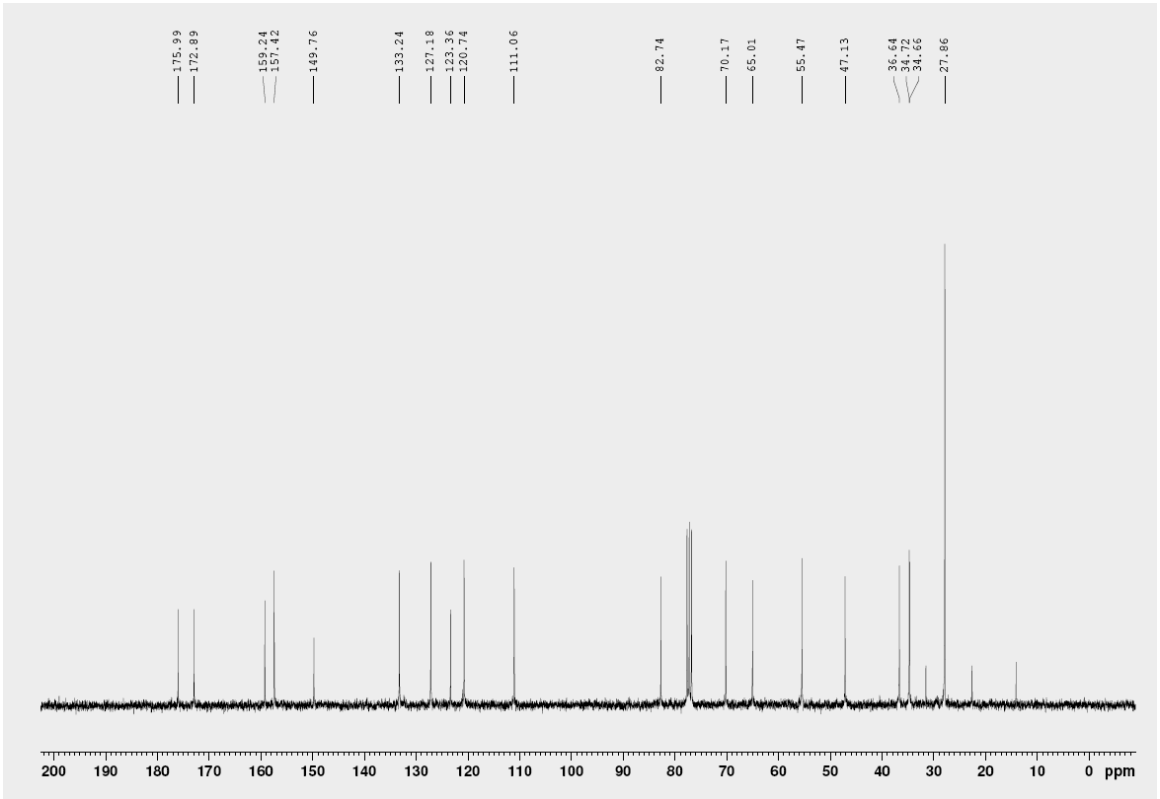
7.925
7.462
7.438
7.414
7.024
6.999
6.974
6.936
6.908
O
N
O
O
O
N
Boc
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
1.07
1.02
1.06
1.06
1.07
1.23
3.08
1.03
1.03
2.09
2.09
9.02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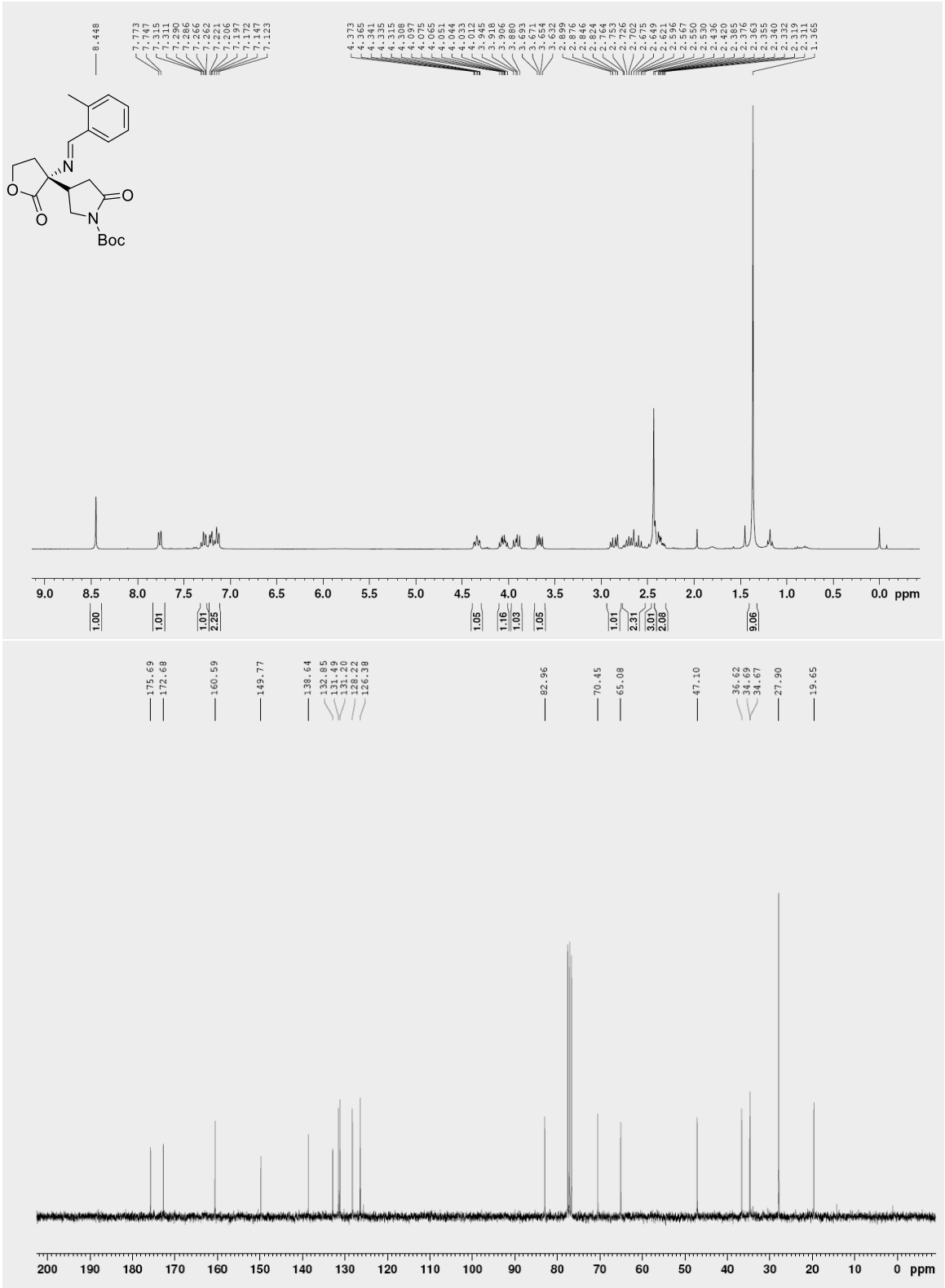
172.89
159.24
157.42
149.76
133.24
127.18
123.36
120.74
111.06
82.74
70.17
65.01
55.47
47.13
36.64
34.72
34.66
27.86
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

4j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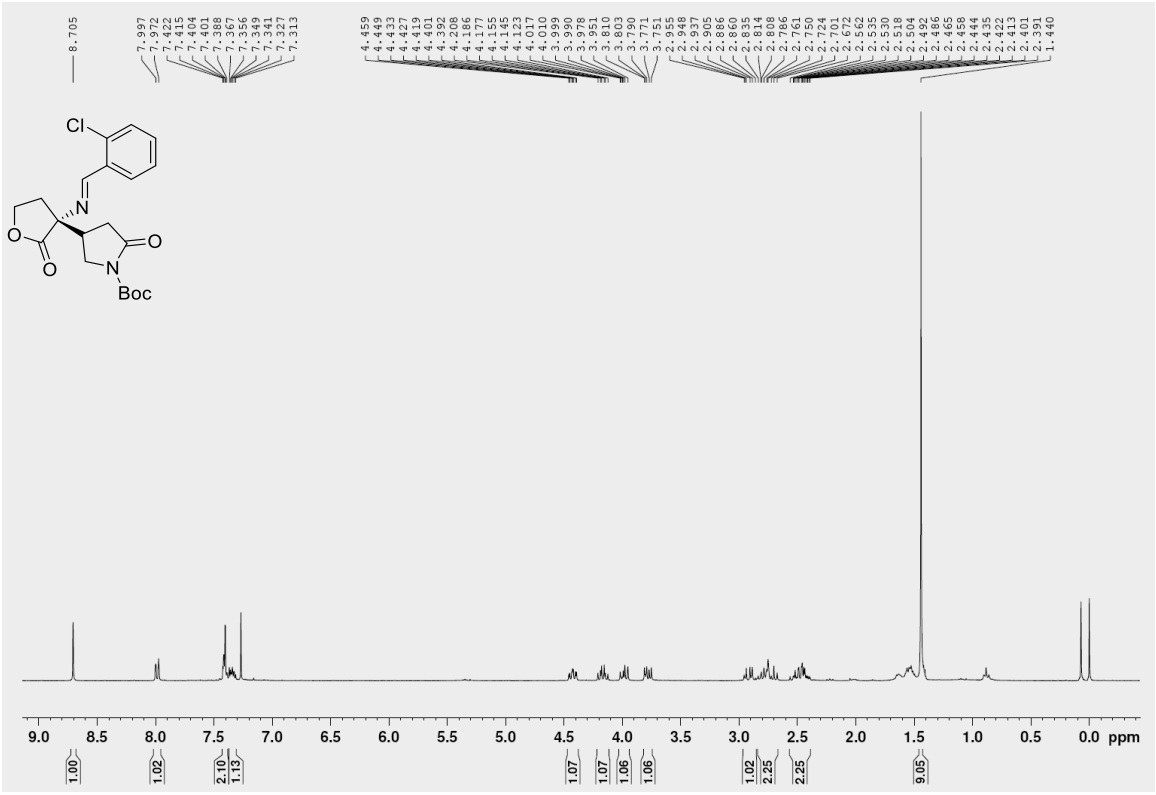
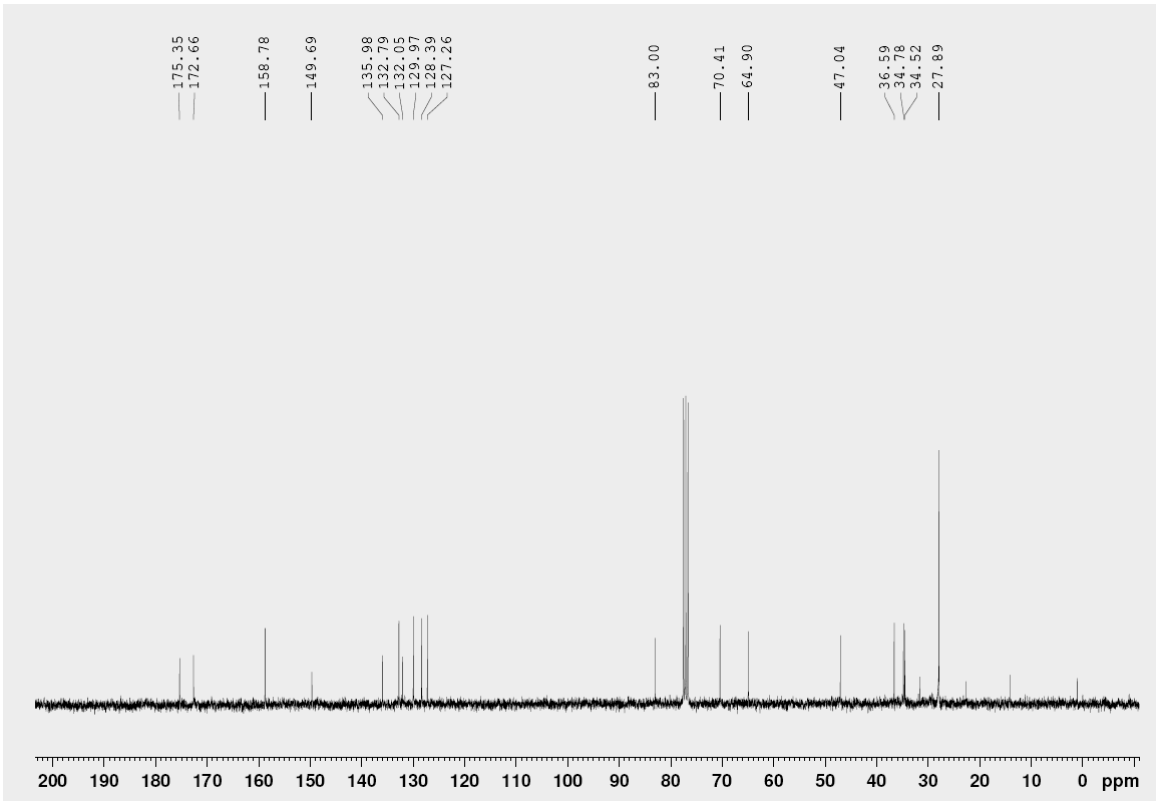
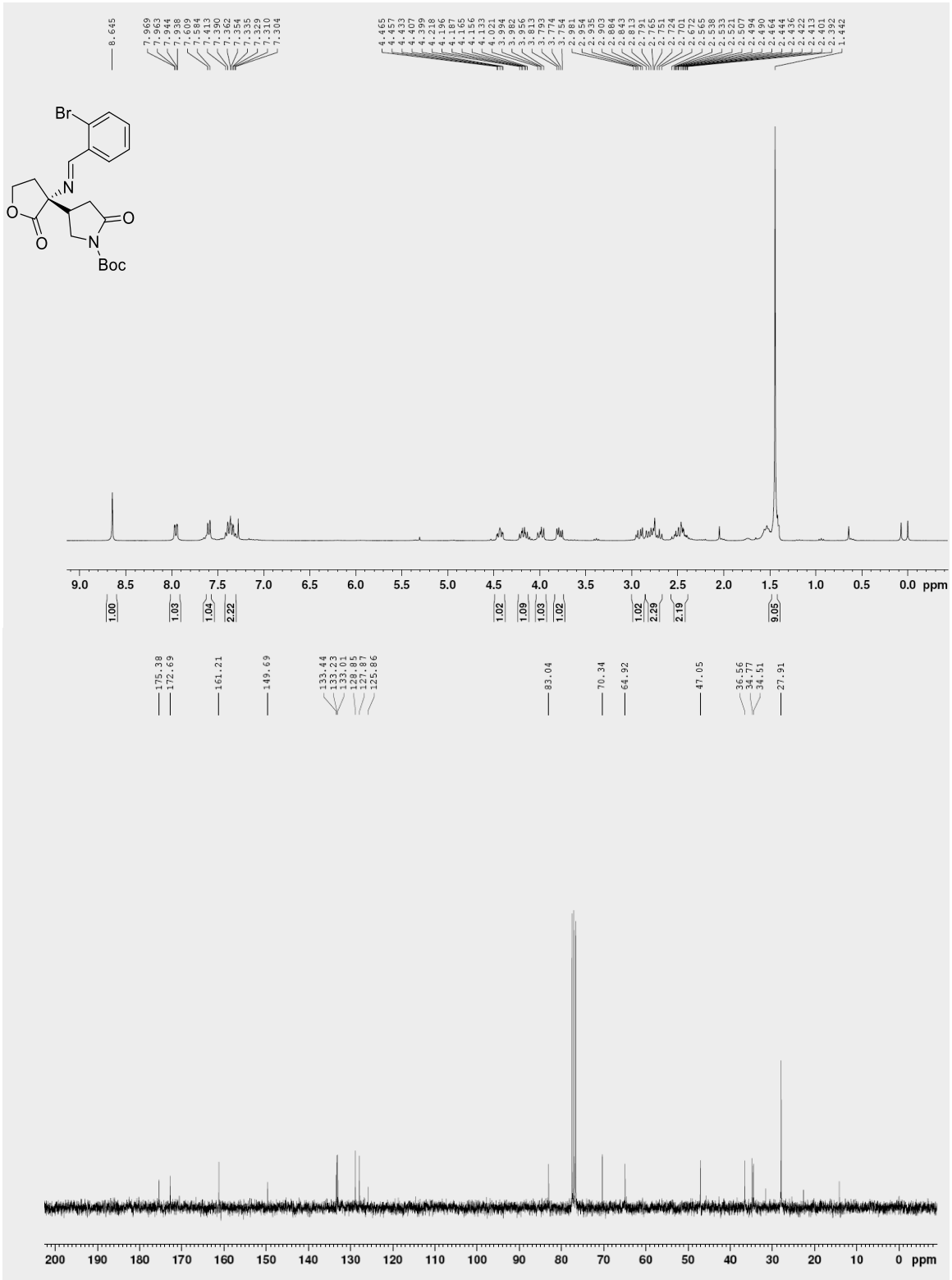
7.290
7.286
7.266
7.262
7.221
7.206
7.197
7.172
7.147
7.123
4.373
4.365
4.341
4.335
4.315
4.308
4.097
4.075
4.065
4.051
4.044
4.033
4.012
3.945
3.918
3.906
3.880
3.693
3.671
3.654
3.632
2.899
2.876
2.846
2.824
2.764
2.753
2.726
2.702
2.675
2.649
2.621
2.591
2.567
2.550
2.530
2.436
2.420
2.385
2.376
2.363
2.355
2.340
2.332
2.319
2.311
1.365
O
O
N
O
N
Boc
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.01
1.01
2.25
1.05
1.16
1.03
1.05
1.01
2.31
3.01
2.08
9.06
175.69
172.68
160.59
149.77
138.64
132.85
131.49
128.20
128.22
126.38
82.96
70.45
65.08
47.10
36.62
34.69
34.67
27.90
19.65
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4k


8.705
7.997
7.972
7.422
7.415
7.404
7.401
7.388
7.367
7.356
7.349
7.341
7.327
7.313
4.459
4.449
4.433
4.427
4.419
4.401
4.392
4.208
4.186
4.177
4.155
4.145
4.123
4.017
4.010
3.999
3.990
3.978
3.951
3.810
3.803
3.790
3.771
3.751
2.948
2.937
2.905
2.886
2.860
2.835
2.814
2.808
2.786
2.761
2.750
2.724
2.701
2.672
2.562
2.535
2.530
2.518
2.494
2.492
2.486
2.465
2.458
2.444
2.435
2.422
2.413
2.401
2.391
1.440
Cl
N
O
O
O
N
Boc
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.02
2.10
1.13
1.07
1.07
1.06
1.06
1.02
2.25
2.25
9.05


175.35
172.66
158.78
149.69
135.98
132.79
132.05
129.97
128.39
127.26
83.00
70.41
64.90
47.04
36.59
34.78
34.52
27.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4l


Br
N
O
O
O
N
Boc
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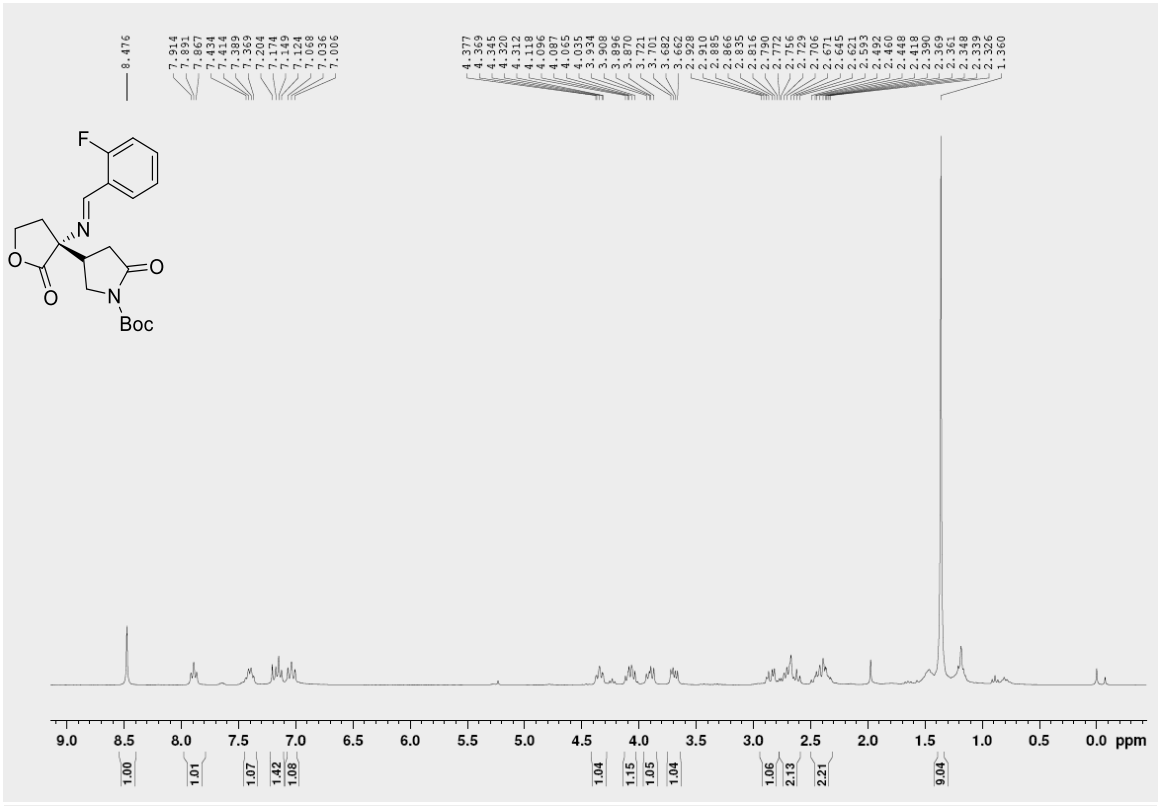
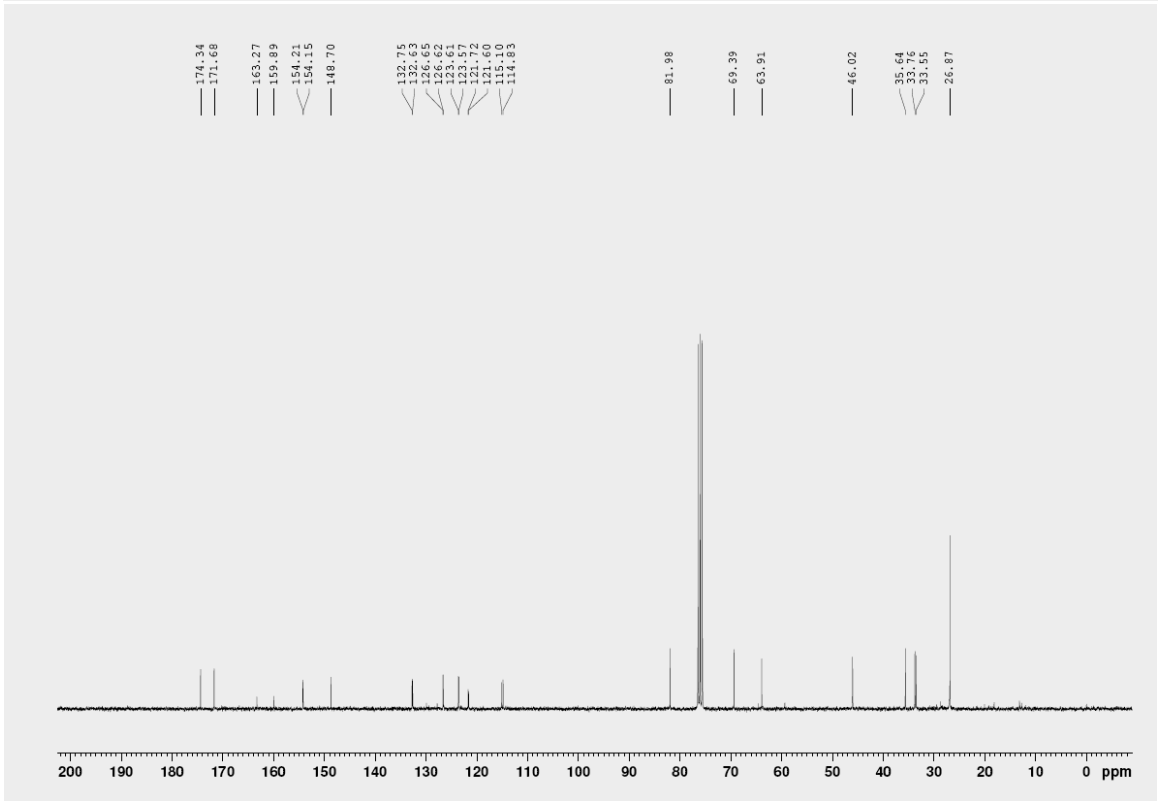
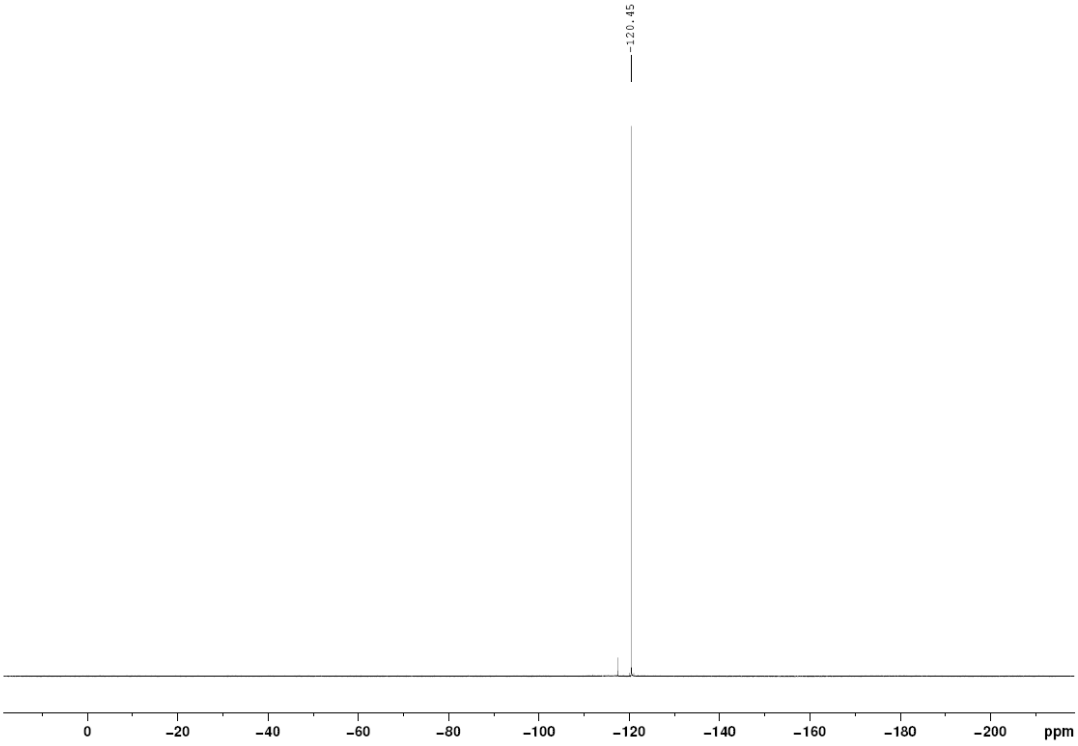
7.969
7.963
7.944
7.938
7.609
7.584
7.413
7.360
7.362
7.354
7.335
7.329
7.310
7.304
4.465
4.457
4.433
4.403
4.399
4.218
4.196
4.187
4.165
4.156
4.133
4.021
3.994
3.982
3.956
3.813
3.793
3.774
3.754
2.981
2.954
2.935
2.903
2.884
2.843
2.813
2.791
2.765
2.751
2.724
2.701
2.672
2.565
2.538
2.533
2.521
2.507
2.494
2.490
2.464
2.444
2.436
2.425
2.413
2.401
2.392
1.442
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 1.03 1.04 2.22 1.02 1.09 1.03 1.02 1.02 2.29 2.19 9.05
175.38
172.69
161.21
149.69
133.44
133.23
131.01
128.85
127.87
125.86
83.04
70.34
64.92
47.05
36.56
34.77
34.51
27.91
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

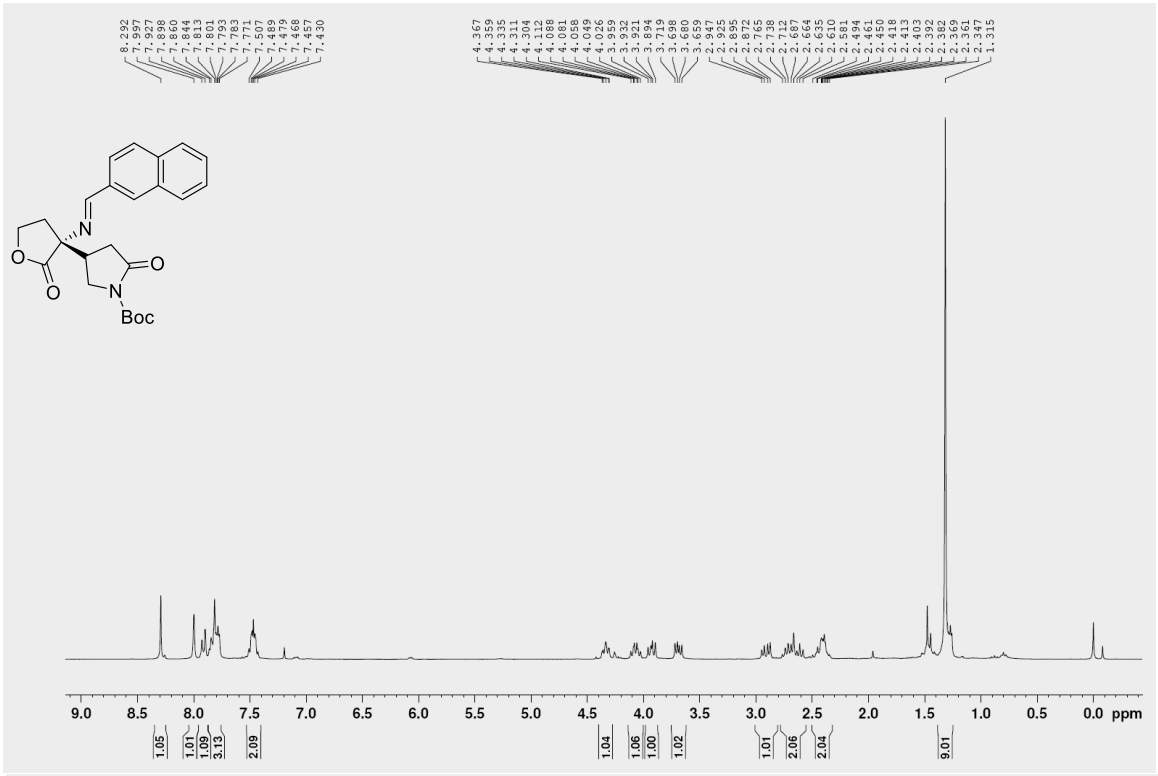
4m

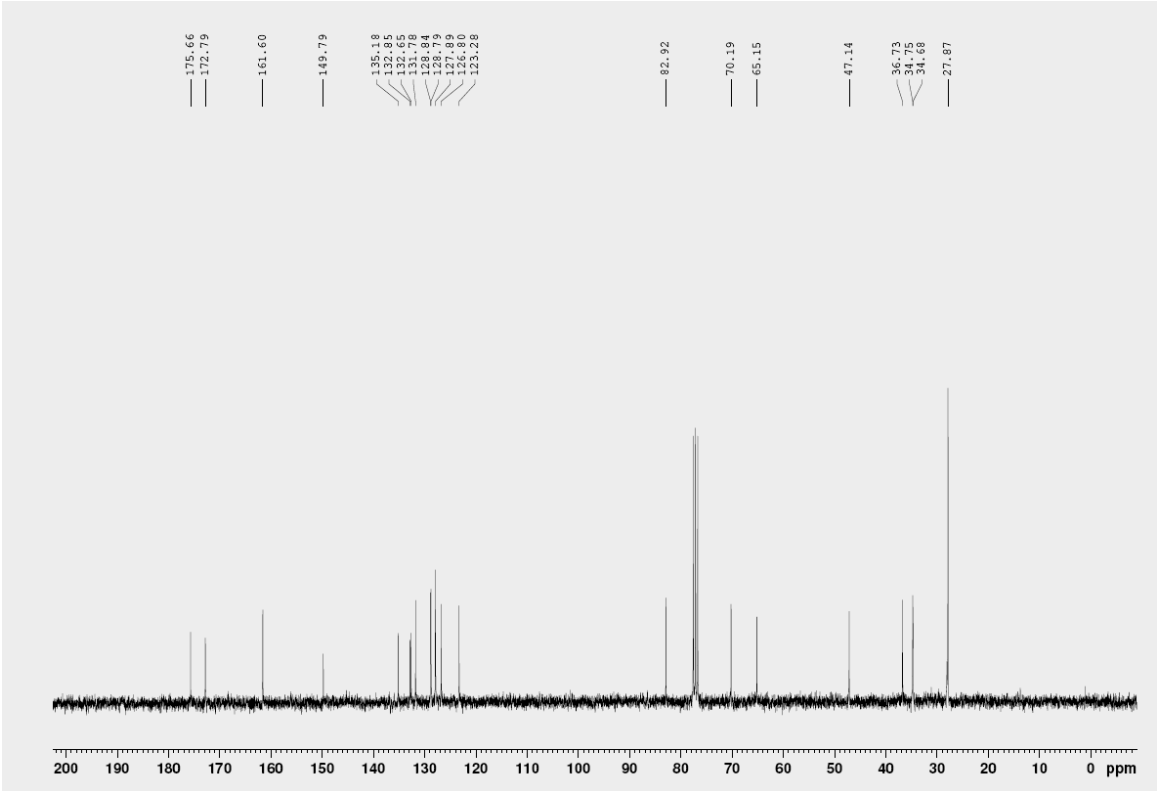

F
N
O
O
O
N
Boc
8.476
7.914
7.891
7.867
7.434
7.414
7.389
7.369
7.204
7.174
7.149
7.124
7.068
7.036
7.006
4.377
4.369
4.345
4.320
4.312
4.118
4.096
4.087
4.065
4.035
3.934
3.908
3.896
3.870
3.721
3.701
3.682
3.662
2.928
2.910
2.885
2.866
2.835
2.816
2.790
2.772
2.756
2.729
2.706
2.671
2.645
2.621
2.593
2.492
2.460
2.448
2.418
2.390
2.369
2.361
2.348
2.339
2.326
1.360
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 1.01 1.07 1.42 1.08 1.04 1.15 1.05 1.04 1.06 2.13 2.21 9.04


174.34
171.68
163.27
159.89
154.21
154.15
148.70
132.75
132.63
126.65
126.62
123.61
123.57
121.72
121.60
115.10
114.83
81.98
69.39
63.91
46.02
35.64
33.76
33.55
26.87
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

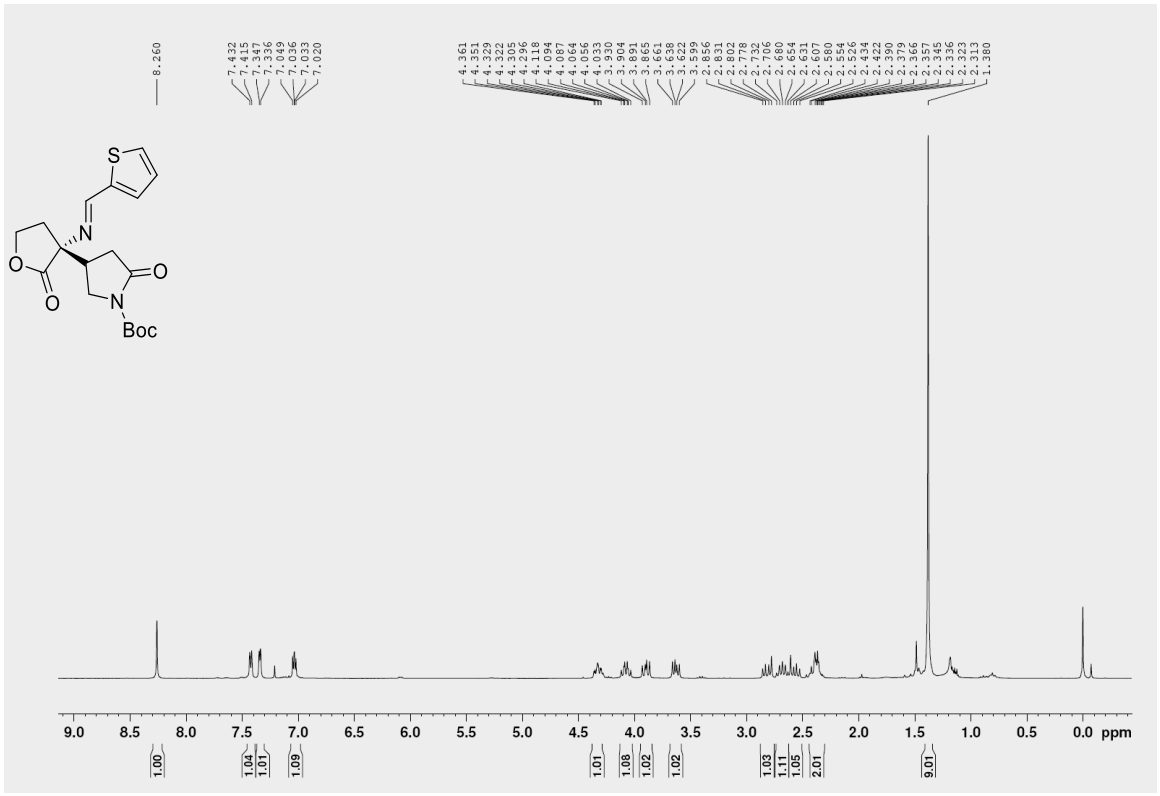

-120.45
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

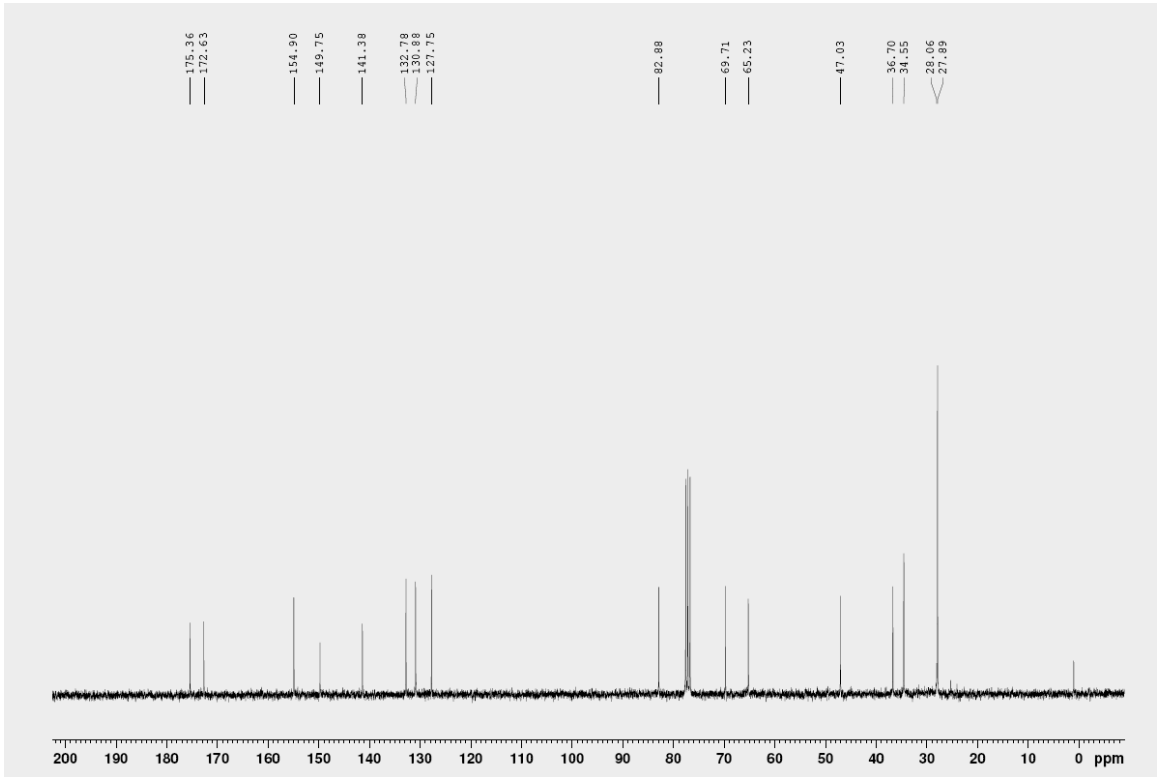
4n


8.292
7.597
7.927
7.898
7.860
7.844
7.813
7.791
7.783
7.771
7.507
7.489
7.479
7.468
7.457
7.430
4.367
4.359
4.335
4.311
4.304
4.112
4.088
4.081
4.058
4.049
4.026
3.959
3.932
3.921
3.894
3.719
3.698
3.680
3.659
2.947
2.925
2.895
2.872
2.765
2.738
2.722
2.687
2.664
2.635
2.610
2.581
2.494
2.461
2.450
2.418
2.413
2.403
2.392
2.382
2.369
2.361
2.347
1.315
O
O
N
O
N
Boc
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.05
1.01
1.09
3.13
2.09
1.04
1.06
1.00
1.02
1.01
2.06
2.04
9.01

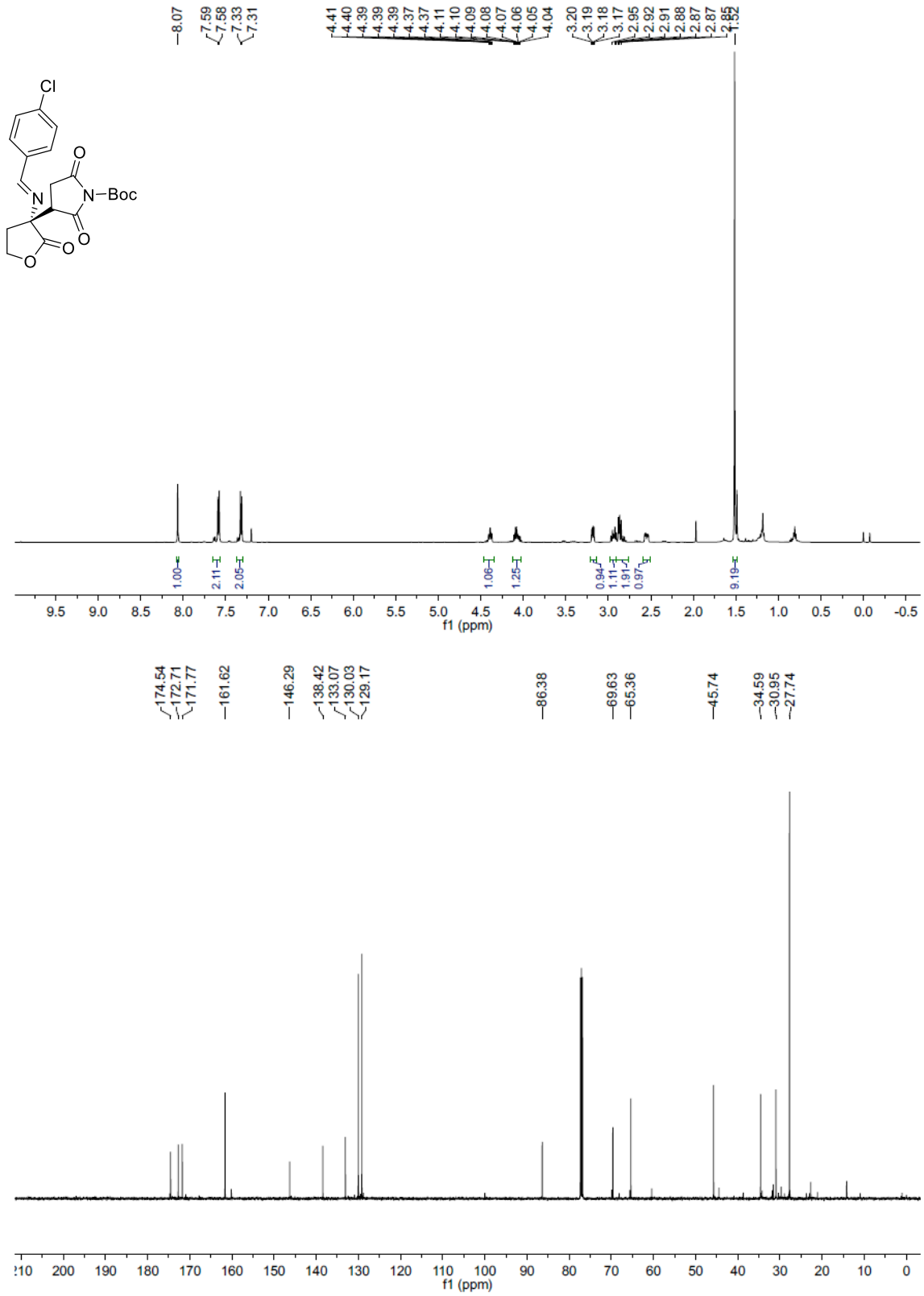

175.66
172.79
161.60
149.79
135.18
132.85
132.65
131.76
128.84
128.79
127.89
126.80
123.28
82.92
70.19
65.15
47.14
36.73
34.75
34.68
27.87
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

4p

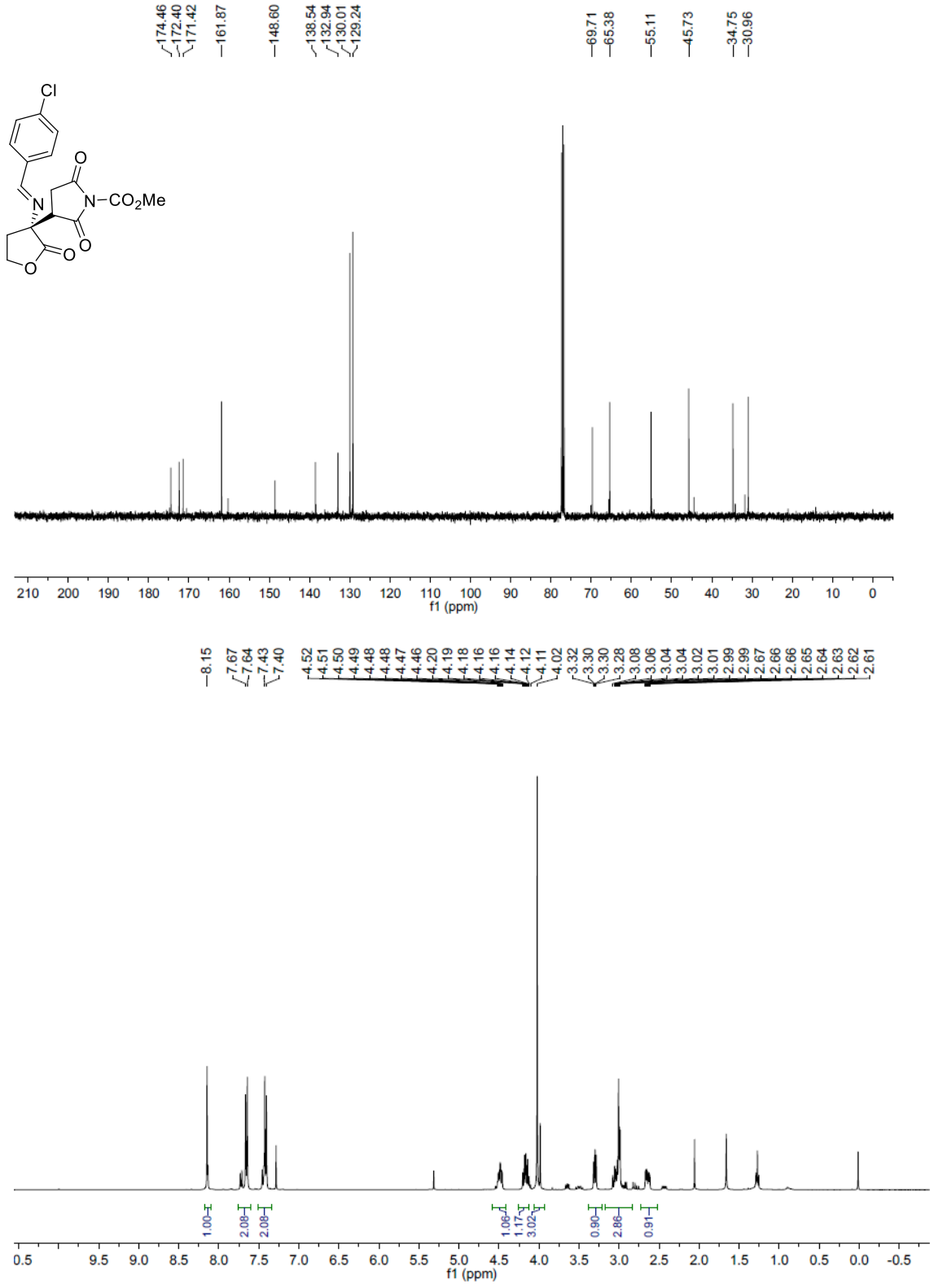

8.260
7.432
7.415
7.347
7.336
7.049
7.035
7.020
4.361
4.351
4.329
4.322
4.305
4.296
4.118
4.094
4.087
4.064
4.056
4.033
3.930
3.904
3.691
3.665
3.661
3.638
3.622
3.599
2.856
2.831
2.802
2.778
2.732
2.706
2.680
2.654
2.631
2.607
2.580
2.554
2.526
2.434
2.422
2.390
2.379
2.366
2.357
2.345
2.335
2.323
2.313
1.380
S
N
O
O
O
N
Boc
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.04
1.01
1.09
1.01
1.08
1.02
1.02
1.03
1.11
1.05
2.01
9.01


175.36
172.63
154.90
149.75
141.38
132.78
130.88
127.75
82.88
69.71
65.23
47.03
36.70
34.55
28.06
27.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

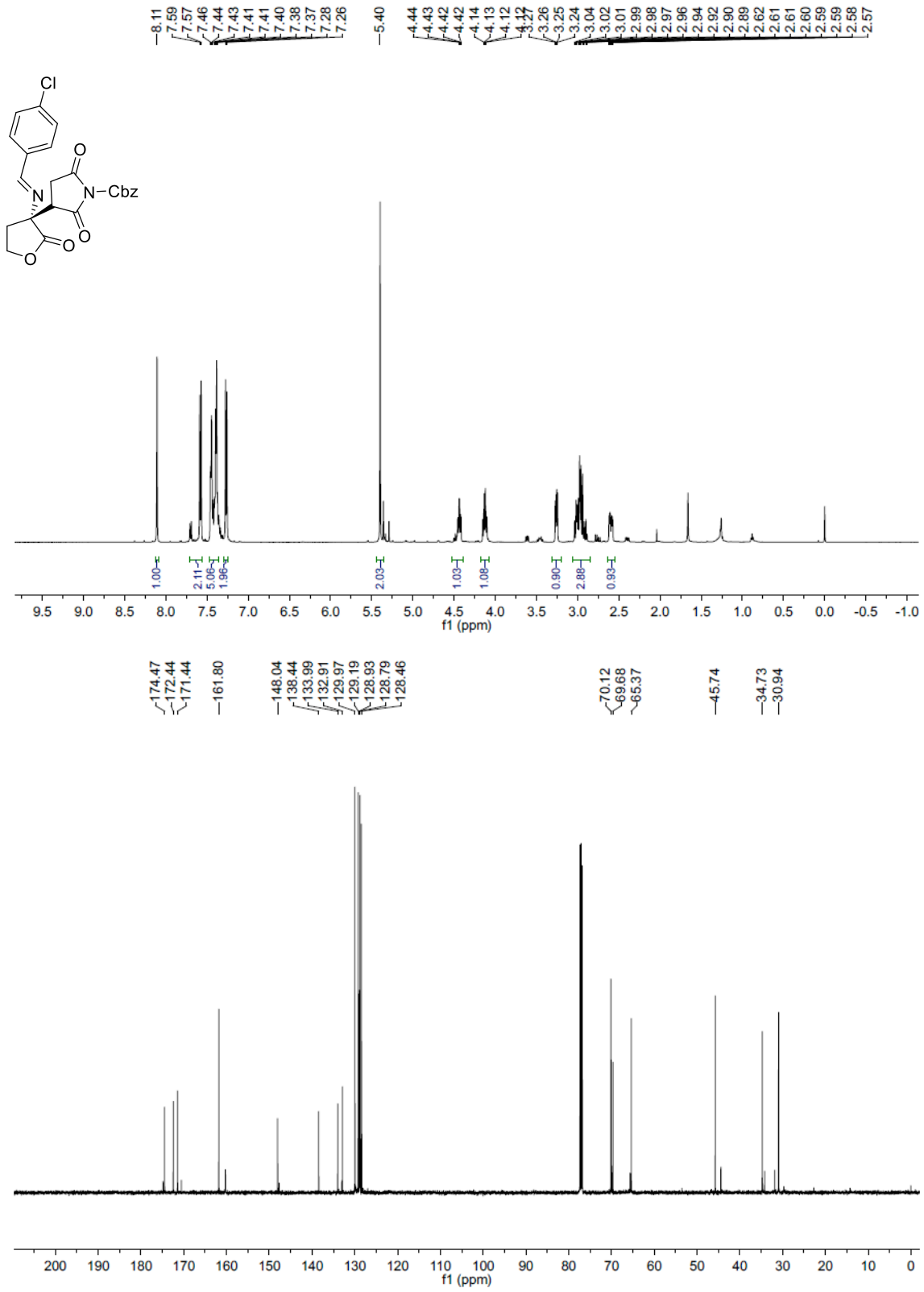
4r


Cl
O
N
N–Boc
O
O
O
8.07
7.59
7.58
7.33
7.31
4.41
4.40
4.39
4.39
4.39
4.37
4.37
4.11
4.10
4.09
4.08
4.07
4.06
4.05
4.04
3.20
3.19
3.18
3.17
2.95
2.92
2.91
2.88
2.87
2.87
2.85
1.52
1.00
2.11
2.05
1.06
1.25
0.94
1.11
1.91
0.97
9.19
f1 (ppm)
174.54
172.71
171.77
161.62
146.29
138.42
133.07
130.03
129.17
86.38
69.63
65.36
45.74
34.59
30.95
27.74
f1 (ppm)

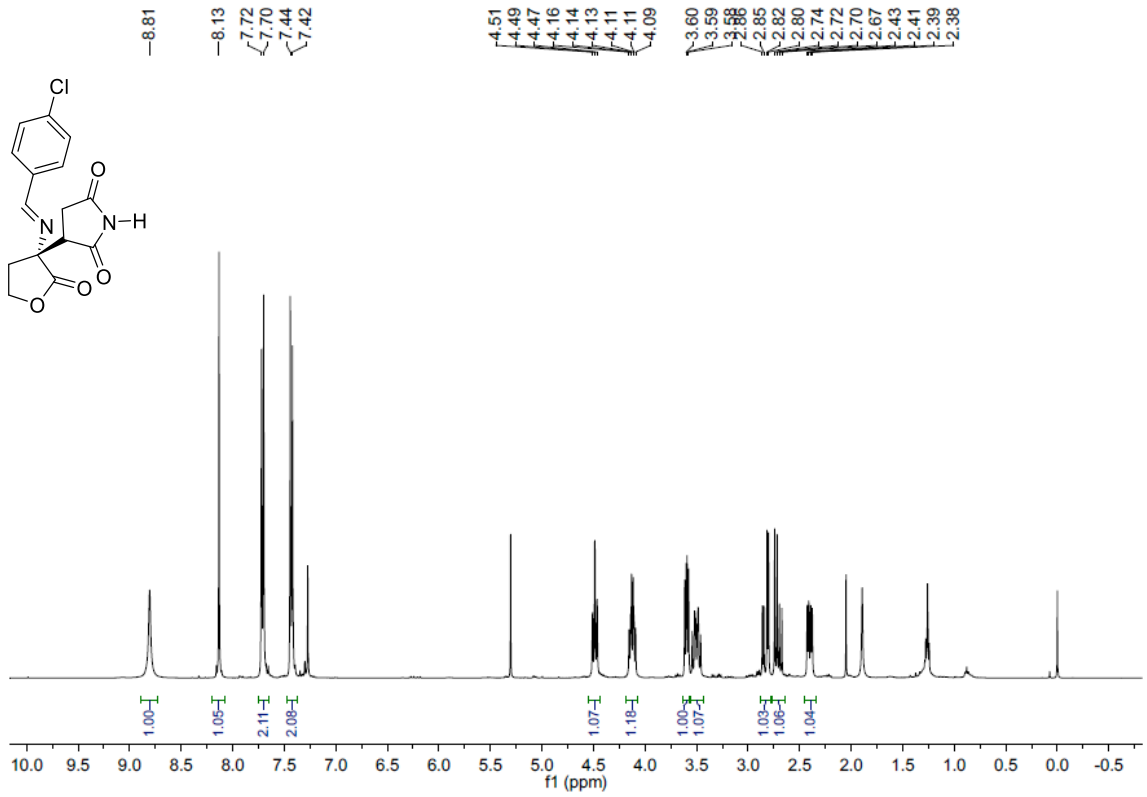
4s

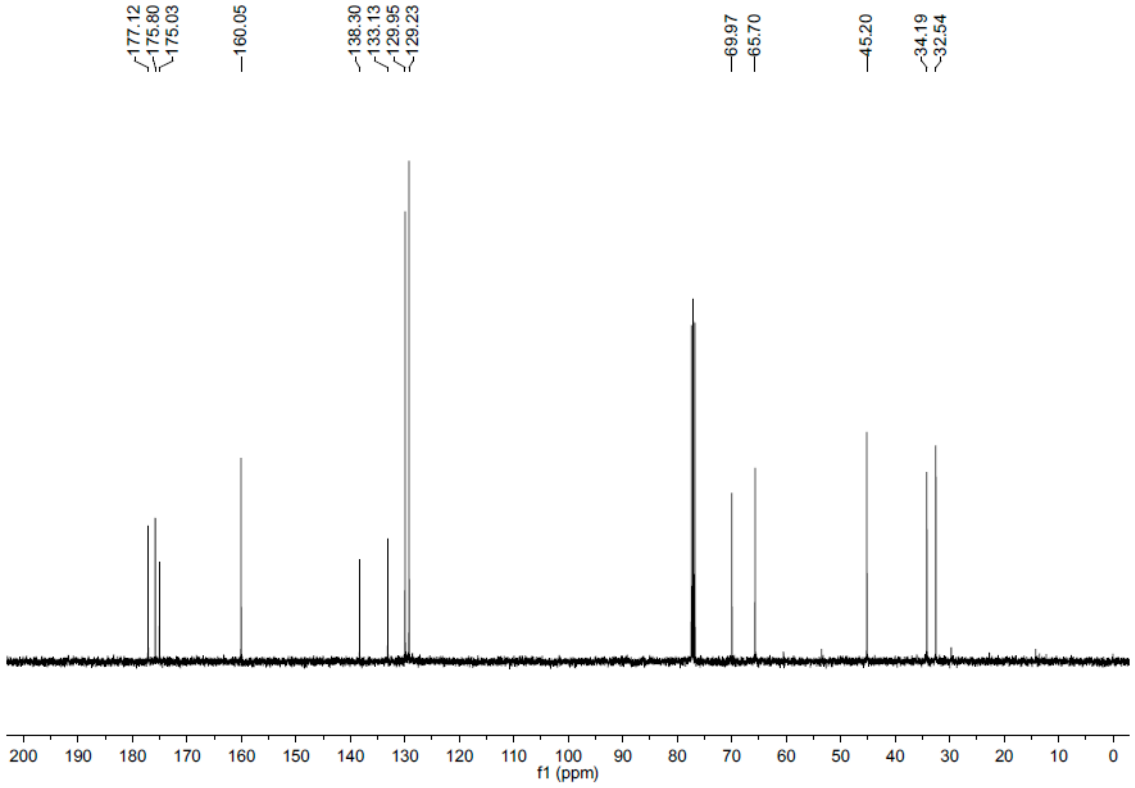

174.46
172.40
171.42
161.87
148.60
138.54
132.94
130.01
129.24
69.71
65.38
55.11
45.73
34.75
30.96
Cl
O
N
N−CO2Me
O
O
O
f1 (ppm)
8.15
7.67
7.64
7.43
7.40
4.52
4.51
4.50
4.49
4.48
4.48
4.47
4.46
4.20
4.19
4.18
4.16
4.16
4.14
4.12
4.11
4.02
3.32
3.30
3.30
3.28
3.08
3.06
3.04
3.04
3.02
3.01
2.99
2.99
2.67
2.66
2.66
2.65
2.64
2.63
2.62
2.61
1.00
2.08
2.08
1.06
1.17
3.02
0.90
2.86
0.91
f1 (ppm)

4t


8.11
7.59
7.57
7.46
7.44
7.43
7.41
7.41
7.40
7.38
7.37
7.28
7.26
5.40
4.44
4.43
4.42
4.42
4.14
4.13
4.12
3.26
3.25
3.24
3.04
3.02
3.01
2.99
2.98
2.97
2.96
2.94
2.92
2.90
2.89
2.62
2.61
2.61
2.60
2.59
2.59
2.58
2.57
Cl
O
N
N–Cbz
O
O
O
1.00
2.11
5.06
1.96
2.03
1.03
1.08
0.90
2.88
0.93
f1 (ppm)
174.47
172.44
171.44
161.80
148.04
138.44
133.99
132.91
129.97
129.19
128.93
128.79
128.46
70.12
69.68
65.37
45.74
34.73
30.94
f1 (ppm)

4u


8.81
8.13
7.72
7.70
7.44
7.42
4.51
4.49
4.47
4.16
4.14
4.13
4.11
4.11
4.09
3.60
3.59
2.85
2.82
2.80
2.74
2.72
2.70
2.67
2.43
2.41
2.39
2.38
Cl
O
N
N–H
O
O
O
1.00
1.05
2.11
2.08
1.07
1.18
1.00
1.07
1.03
1.06
1.04
f1 (ppm)


177.12
175.80
175.03
160.05
138.30
133.13
129.95
129.23
69.97
65.70
45.20
34.19
32.54
f1 (ppm)