

Nickel-Catalyzed Enantioselective Hydrogenation of β -(Acylamino)-acrylates: Synthesis of Chiral β -Amino Acid Derivatives

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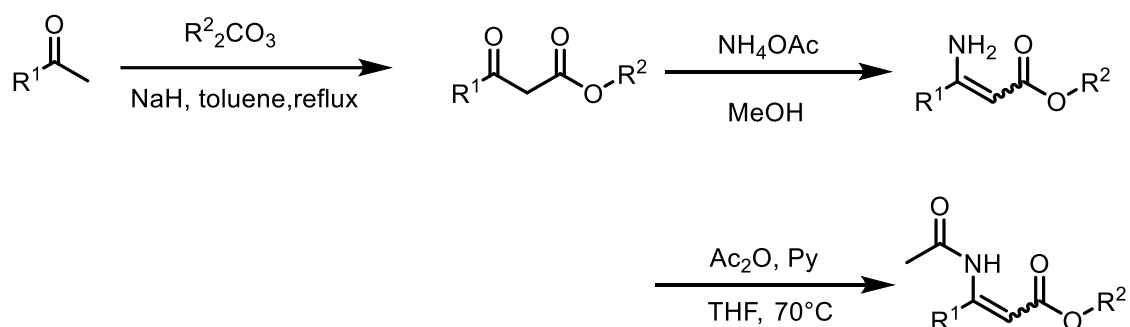
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1. General Information

Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification. NMR spectra were recorded on Bruker ADVANCE III (400 MHz) spectrometers for ^1H NMR and ^{13}C NMR. CDCl_3 was the solvent used for the NMR analysis, with tetramethylsilane as the internal standard. Chemical shifts were reported upfield to TMS (0.00 ppm) for ^1H NMR and relative to CDCl_3 (77.3 ppm) for ^{13}C NMR. Optical rotation was determined using a Perkin Elmer 343 polarimeter. HPLC analysis was conducted on an Agilent 1260 Series instrument. Column Chromatography was performed with silica gel Merck 60 (300-400 mesh).

2. General procedure for the synthesis of compound 1¹

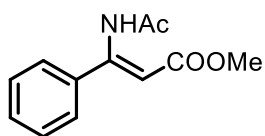


Step 1. To a dried 100-mL three-necked flask were added NaH (2.2 g, 60% w/w, 56 mmol), dimethyl carbonate or diethyl carbonate (40 mmol) and toluene (20 mL) under nitrogen. After the mixture was heated to reflux, a solution of acetophenone (20 mmol) in toluene (10 mL) was added dropwise over 0.5 h. After the evolution of hydrogen ceased (30-45 min), the reaction was cooled down to room temperature. Glacial acetic acid (6 mL) was added dropwise and a heavy pasty solid separated. Ice-cold water was slowly added until the solid was dissolved completely. Then, the reaction system was dilute with EtOAc . The organic layer was separated, washed with water (20 mL) and brine (20 mL) and dried over Na_2SO_4 . After the solvent was evaporated, the residue was purified by flash chromatography on silica gel with EtOAc /hexanes.

Step 2. A solution of β -ketoesters (12 mmol) and NH_4OAc (4.6 g, 60 mmol) in methanol (12 mL) was stirred under reflux for overnight. After the solvent was evaporated under reduced pressure, the residue was dilute with CH_2Cl_2 (50 mL). The resulting solid was filtered off and washed with CH_2Cl_2 (2 x 30 mL). The combined

filtrate was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent gave the enamine intermediate, which was used directly in the next step without further purification.

Step 3. To a solution of the enamine intermediate from the above step (about 12 mmol) in THF (12 mL) were added acetic anhydride (3.6 mL, 36 mmol) and pyridine (0.19g, 2.4 mmol). The reaction mixture was then heated to reflux until the starting material completely disappeared. After the mixture was cooled to room temperature, the volatiles were evaporated. The residue was dissolved in EtOAc (200 mL), and the solution was washed with water, 1N HCl, saturated NaHCO₃ and brine. After the solution was dried over sodium sulfate, the solvent was evaporated. The residue was purified by flash chromatography on silica gel with EtOAc/hexanes to afford desired products. (Some products are *Z/E* mixtures, which can not be separated by chromatography)



methyl (*Z*)-3-acetamido-3-phenylacrylate (1a): Step 1. To a dried 100-mL three-necked flask were added NaH (2.2 g, 60% w/w, 56 mmol), dimethyl carbonate (3.6g, 40 mmol) and toluene (20 mL) under nitrogen. After the mixture was heated to reflux, a solution of acetophenone (2.4 g, 20 mmol) in toluene (10 mL) was added dropwise over 0.5 h. After the evolution of hydrogen ceased (30 min), the reaction was cooled down to room temperature. Glacial acetic acid (6 mL) was added dropwise and a heavy pasty solid separated. Ice-cold water was slowly added until the solid was dissolved completely. Then, the reaction system was diluted with EtOAc. The organic layer was separated, washed with water (20 mL) and brine (20 mL) and dried over Na₂SO₄. After the solvent was evaporated, the residue was purified by flash chromatography on silica gel with EtOAc/hexanes to afford methyl 3-oxo-3-phenylpropanoate (2.2 g, yield: 60%).

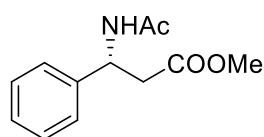
Step 2. A solution of methyl 3-oxo-3-phenylpropanoate (2.2 g, 12 mmol) and NH₄OAc (4.6 g, 60 mmol) in methanol (12 mL) was stirred under reflux for overnight. After the solvent was evaporated under reduced pressure, the residue was diluted with

CH₂Cl₂ (50 mL). The resulting solid was filtered off and washed with CH₂Cl₂ (2 x 30 mL). The combined filtrate was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent gave the enamine intermediate, which was used directly in the next step without further purification.

Step 3. To a solution of the enamine intermediate from the above step (about 12 mmol) in THF (12 mL) were added acetic anhydride (3.6 mL, 36 mmol) and pyridine (0.19 g, 2.4 mmol). The reaction mixture was then heated to reflux until the starting material completely disappeared. After the mixture was cooled to room temperature, the volatiles were evaporated. The residue was dissolved in EtOAc (200 ml), and the solution was washed with water, 1N HCl, saturated NaHCO₃ and brine. After the solution was dried over sodium sulfate, the solvent was evaporated. The residue was purified by flash chromatography on silica gel with EtOAc/hexanes to afford methyl (Z)-3-acetamido-3-phenylacrylate (2.2 g, yield: 83%). The physical data were identical in all respect to those previously reported. ^{[1][2]}

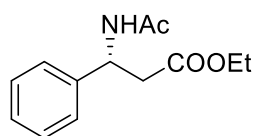
3. General Procedure for Asymmetric Hydrogenation of compound 1

A stock solution was made by mixing Ni(OAc)₂ (1.8 mg, 0.01 mmol) with (*S*)-Binapine (8.0 mg, 0.011mmol) in a 1:1.1 molar ratio in CF₃CH₂OH (1 ml) at room temperature for 30 min in a nitrogen-filled glovebox. An aliquot of the catalyst solution (0.1 mL, 0.001 mmol) was transferred by syringe into the vials charged with different substrates (0.1 mmol for each) in anhydrous CF₃CH₂OH (0.9 mL). The vials were subsequently transferred into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H₂ (50 atm) at 50 °C for 24 h. The hydrogen gas was released slowly and carefully. The solution was concentrated and passed through a short column of silica gel (eluant: EtOAc) to remove the metal complex. The ee values of all compounds **2** were determined by HPLC analysis on a chiral stationary phase. The physical data were identical in all respect to those previously reported. ^{[1][2]}

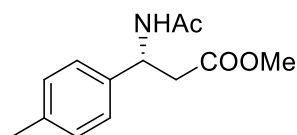


methyl (R)-3-acetamido-3-phenylpropanoate (2a): ^{[1a][2]} colorless oil; 215 mg,

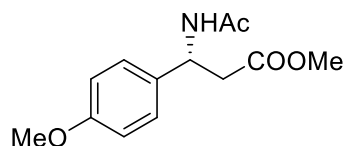
isolated yield: 97%; 99% ee; $[\alpha]_{20}^D = 77.2$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 28.6$ min (major), 31.4 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 7.35-7.26 (m, 5H), 6.67 (d, $J = 5.9$ Hz, 1H), 5.43 (dt, $J = 8.4, 6.0$ Hz, 1H), 3.61 (s, 3H), 2.93 (dd, $J = 15.8, 5.9$ Hz, 1H), 2.83 (dd, $J = 15.8, 6.0$ Hz, 1H) 2.01 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.8, 169.7, 140.7, 128.8, 127.8, 126.5, 52.0, 49.8, 40.0, 23.4 ppm.



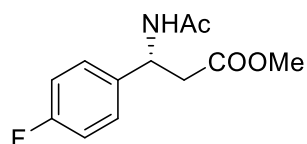
ethyl (R)-3-acetamido-3-phenylpropanoate (2b): $^{[1b]}$ colorless oil; 226 mg, isolated yield: 96%; 99% ee; $[\alpha]_{20}^D = 67.8$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 26.8$ min (major), 33.7 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 7.41-7.16 (m, 5H), 6.95 (d, $J = 7.7$ Hz, 1H), 5.50-5.31 (m, 1H), 4.05 (q, $J = 7.1$ Hz, 2H), 3.01-2.71 (m, 2H), 1.97 (d, $J = 2.3$ Hz, 3H), 1.15 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.3, 169.6, 140.8, 128.8, 127.7, 126.5, 60.9, 49.8, 40.3, 23.4, 14.2 ppm.



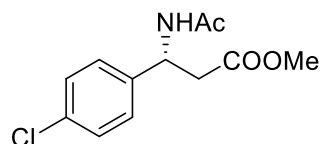
methyl (R)-3-acetamido-3-(p-tolyl)propanoate (2c): $^{[1c] [2]}$ colorless oil; 225 mg, isolated yield: 96%; 99% ee; $[\alpha]_{20}^D = 88.6$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 28.2$ min (major), 36.4 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 7.14 (dd, $J = 22.4, 8.1$ Hz, 4H), 6.80 (s, 1H), 5.37 (dd, $J = 14.5, 6.2$ Hz, 1H), 3.60 (s, 3H), 3.02-2.72 (m, 2H), 2.31 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.8, 169.6, 137.8, 137.4, 129.5, 126.4, 52.0, 49.6, 40.0, 23.5, 21.2 ppm.



methyl (R)-3-acetamido-3-(4-methoxyphenyl)propanoate (2d): ^[1c] ^[2] colorless oil; 246 mg, isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 89.4$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 52.4$ min (major), 65.7 min (minor). ¹H NMR (400 MHz, CDCl₃) δ : 7.21 (d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.7$ Hz, 2H), 6.78 (d, $J = 6.3$ Hz, 1H), 5.35 (dd, $J = 14.5, 6.3$ Hz, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 2.84 (ddd, $J = 49.5, 15.6, 6.3$ Hz, 2H), 1.97 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ : 171.8, 169.6, 159.1, 132.8, 127.7, 114.2, 55.4, 52.0, 49.3, 40.1, 23.5 ppm.

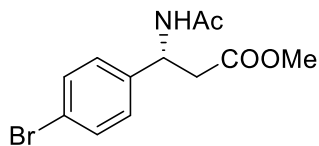


methyl (R)-3-acetamido-3-(4-fluorophenyl)propanoate (2e): ^[1c] ^[2] colorless oil; 230 mg, isolated yield: 96%; 99% ee; $[\alpha]_{20}^D = 62.8$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 29.7$ min (major), 35.3 min (minor). ¹H NMR (400 MHz, CDCl₃) δ : 7.29-7.25 (m, 2H), 7.02-6.97 (m, 3H), 5.51-5.30 (m, 1H), 3.61 (s, 3H), 2.84 (ddd, $J = 40.7, 15.8, 6.2$ Hz, 2H), 1.98 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ : 171.7, 169.7, 162.2 (d, $J = 246.0$ Hz), 136.7 (d, $J = 3.2$ Hz), 128.2 (d, $J = 8.1$ Hz), 115.7 (d, $J = 21.5$ Hz), 52.1, 49.2, 40.0, 23.4 ppm.

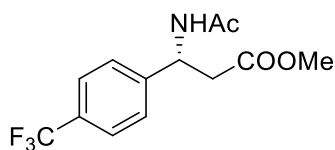


methyl (R)-3-acetamido-3-(4-chlorophenyl)propanoate (2f): ^[1c] colorless oil; 242 mg, isolated yield: 95%; 97% ee; $[\alpha]_{20}^D = 64.0$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 32.8$ min (major), 40.7 min (minor). ¹H NMR (400 MHz, CDCl₃) δ : 7.25 (dd, $J = 24.0, 8.5$ Hz, 4H), 6.99 (s, 1H), 5.39-5.34 (m, 1H), 3.62 (s, 3H), 2.83 (ddd, $J = 36.3, 15.9, 6.1$ Hz, 2H), 1.99 (s, 3H). ¹³C

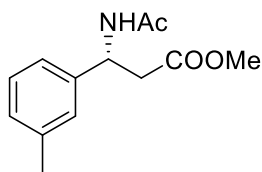
NMR (101 MHz, CDCl₃) δ : 171.6, 169.7, 139.4, 133.5, 129.0, 127.9, 52.1, 49.2, 39.8, 23.4 ppm.



methyl (R)-3-acetamido-3-(4-bromophenyl)propanoate (2g): ^[1c] ^[2] white solid; 290 mg, isolated yield: 97%; 99% ee; $[\alpha]_{20}^D = 75.2$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 36.2$ min (major), 45.9 min (minor). ¹H NMR (400 MHz, CDCl₃) δ : 7.47-7.40 (m, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8.1$ Hz, 1H), 5.35 (dt, $J = 8.4, 6.1$ Hz, 1H), 3.62 (s, 3H), 2.83 (ddd, $J = 35.5, 15.9, 6.1$ Hz, 2H), 1.98 (d, $J = 1.7$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ : 171.6, 169.8, 139.9, 131.9, 128.3, 121.6, 52.1, 49.2, 39.8, 23.4 ppm.

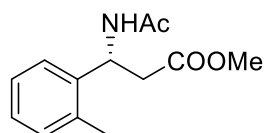


methyl (R)-3-acetamido-3-(4-(trifluoromethyl)phenyl)propanoate (2h): ^[2] colorless oil; 292 mg, isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 65.2$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 27.1$ min (major), 35.1 min (minor). ¹H NMR (400 MHz, CDCl₃) δ 7.57 (d, $J = 8.2$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 7.12 (d, $J = 3.3$ Hz, 1H), 5.45 (dd, $J = 14.1, 6.1$ Hz, 1H), 3.63 (s, 3H), 2.87 (qd, $J = 16.0, 6.0$ Hz, 2H), 2.01 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ : 171.6, 169.9, 145.0, 130.0 (q, $J = 32.5$ Hz), 126.9, 125.8 (q, $J = 3.7$ Hz), 124.2 (d, $J = 272.0$ Hz), 52.2, 49.4, 39.7, 23.4 ppm.

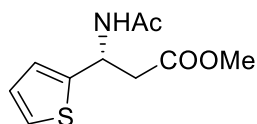


methyl (R)-3-acetamido-3-(m-tolyl)propanoate (2i): ^[2] colorless oil; 230 mg, isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 66.0$ ($c = 1.0$, MeOH); The enantiomeric excess

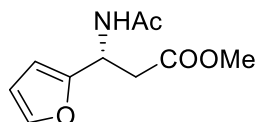
was determined by HPLC on Chiralpak OD-H column, hexane: isopropanol = 92:8; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R = 20.4 min (major), 29.0 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 7.20 (t, J = 7.5 Hz, 1H), 7.13-7.02 (m, 3H), 6.83 (s, 1H), 5.51-5.31 (m, 1H), 3.61 (s, 3H), 3.02-2.69 (m, 2H), 2.32 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.8, 169.6, 140.7, 138.5, 128.7, 128.5, 127.3, 123.4, 52.0, 49.8, 40.1, 23.5, 21.6 ppm.



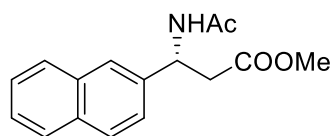
methyl (R)-3-acetamido-3-(o-tolyl)propanoate (2j): $^{[1c]}$ colorless oil; 232 mg, Isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 56.8$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R = 17.0 min (major), 20.4 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 7.24-7.22 (m, 1H), 7.20-7.13 (m, 3H), 6.61 (s, 1H), 5.60 (dd, J = 14.7, 6.8 Hz, 1H), 3.60 (s, 3H), 2.82 (qd, J = 15.4, 6.7 Hz, 2H), 2.41 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.7, 169.5, 138.9, 136.1, 131.0, 127.8, 126.5, 125.2, 52.0, 46.6, 39.5, 23.4, 19.4 ppm.



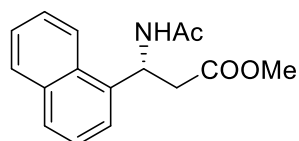
methyl (R)-3-acetamido-3-(thiophen-2-yl)propanoate (2k): $^{[2]}$ colorless oil; 222 mg, isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 77.4$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R = 30.0 min (minor), 30.8 min (major). ^1H NMR (400 MHz, CDCl_3): δ 7.20 (dd, J = 4.0, 2.2 Hz, 1H), 6.94-6.93 (m, 2H), 6.68 (d, J = 7.7 Hz, 1H), 5.71-5.67 (m, 1H), 3.67 (s, 3H), 2.98 (dd, J = 16.1, 5.4 Hz, 1H), 2.90 (dd, J = 16.1, 5.8 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 171.6, 169.3, 144.4, 127.0, 124.7, 124.5, 52.1, 45.6, 40.0, 23.4 ppm.



methyl (R)-3-acetamido-3-(furan-2-yl)propanoate (2l): ^[2] colorless oil; 203 mg, isolated yield: 95%; 99% ee; $[\alpha]_{20}^D = 99.2$ (c = 1.0, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 23.9$ min (minor), 26.8 min (major). ¹H NMR (400 MHz, CDCl₃) δ 7.33 (dd, $J = 1.6, 0.6$ Hz, 1H), 6.55 (d, $J = 7.6$ Hz, 1H), 6.31 (dd, $J = 3.2, 1.9$ Hz, 1H), 6.20 (d, $J = 3.3$ Hz, 1H), 5.54-5.49 (m, 1H), 3.67 (s, 3H), 2.95 (dd, $J = 16.0, 5.3$ Hz, 1H), 2.83 (dd, $J = 16.0, 6.2$ Hz, 1H), 2.02 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.6, 169.6, 153.1, 142.2, 110.6, 106.6, 52.1, 44.1, 37.7, 23.5 ppm.

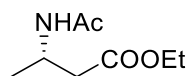


methyl (R)-3-acetamido-3-(naphthalen-2-yl)propanoate (2m): ^[2] colorless oil; 260 mg, isolated yield: 96%; 98% ee; $[\alpha]_{20}^D = 104.1$ (c = 1.0, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 92:8; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 22.1$ min (major), 27.3 min (minor). ¹H NMR (400 MHz, CDCl₃) δ : 7.83-7.76 (m, 4H), 7.53-7.37 (m, 3H), 7.07 (d, $J = 4.7$ Hz, 1H), 5.60 (dd, $J = 14.5, 6.2$ Hz, 1H), 3.61 (s, 3H), 3.09-2.83 (m, 2H), 2.02 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ : 171.8, 169.74, 138.2, 133.4, 132.9, 128.7, 128.1, 127.8, 126.4, 126.2, 125.2, 124.7, 52.0, 49.9, 40.0, 23.5 ppm.



methyl (R)-3-acetamido-3-(naphthalen-1-yl)propanoate (2n): ^[2] colorless oil; 265 mg, isolated yield: 98%; 99% ee; $[\alpha]_{20}^D = 30.9$ (c = 1.0, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 29.5$ min (minor), 40.3 min (major). ¹H NMR (400 MHz, CDCl₃) δ : 8.10-8.05 (m, 1H), 7.87-7.80 (m, 1H), 7.76 (d, $J = 7.8$ Hz, 1H), 7.56-7.45 (m, 2H), 7.44-7.34 (m, 2H), 6.77 (d, $J = 5.6$ Hz, 1H), 6.19 (dd, $J = 14.9, 6.6$ Hz, 1H), 3.56 (d, $J = 3.9$ Hz, 3H), 2.98 (t, $J = 6.6$ Hz, 2H),

1.91 (d, $J = 5.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.8, 169.5, 136.2, 134.1, 130.9, 129.1, 128.7, 126.9, 126.1, 125.3, 123.2, 123.0, 52.0, 46.1, 39.5, 23.3 ppm.



ethyl (S)-3-acetamidobutanoate (2o): ^[1a-b]^[2] colorless oil ; 173 mg, isolated yield: 95%; 98% ee; $[\alpha]_{20}^{\text{D}} = -38.9$ ($c = 1.0$, MeOH); The enantiomeric excess was determined by HPLC on Chiralpak OJ-H column, hexane: isopropanol = 95:5; flow rate = 0.5 mL/min; UV detection at 210 nm; $t_{\text{R}} = 24.2$ min (major), 26.6 min (minor). ^1H NMR (400 MHz, CDCl_3) δ : 6.30 (d, $J = 5.8$ Hz, 1H), 4.34-4.19 (m, 1H), 4.13-3.98 (m, 2H), 2.44 (d, $J = 5.5$ Hz, 2H), 1.89 (s, 3H), 1.22-1.14 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ : 171.9, 169.5, 60.8, 42.2, 40.2, 23.6, 20.2, 14.4 ppm.

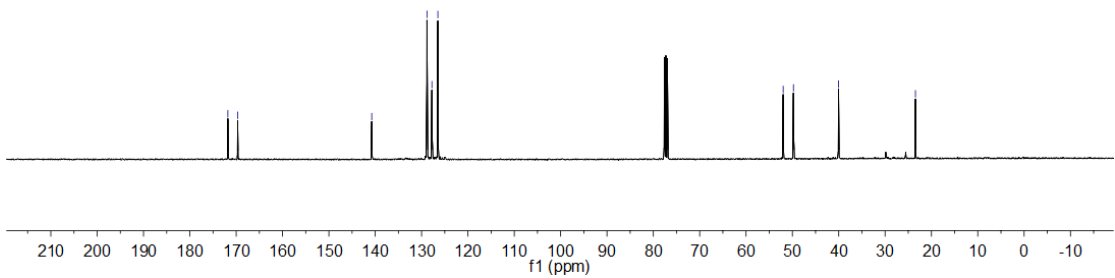
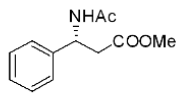
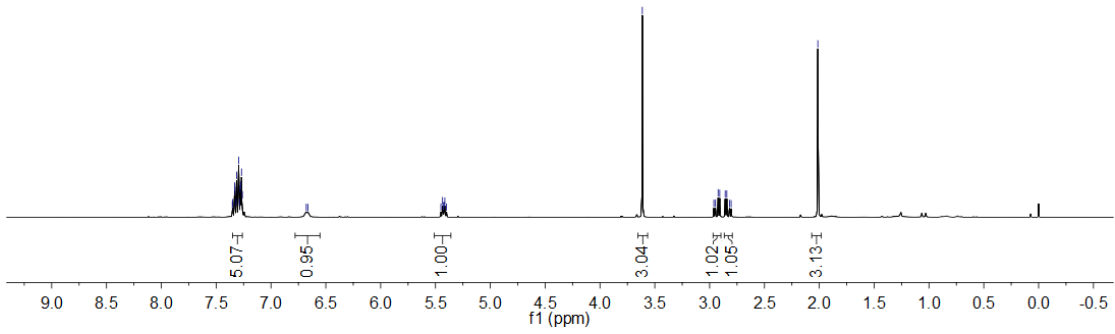
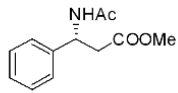
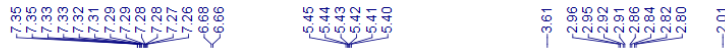
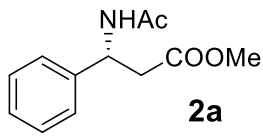
4. General procedure for gram-scale asymmetric hydrogenation with 0.2 mol% catalysis loading

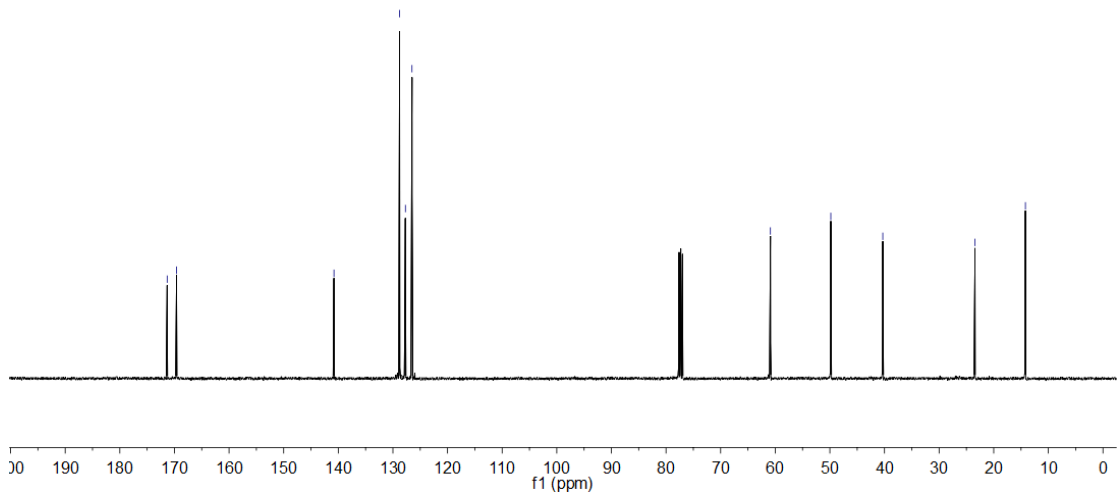
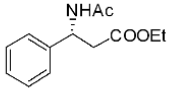
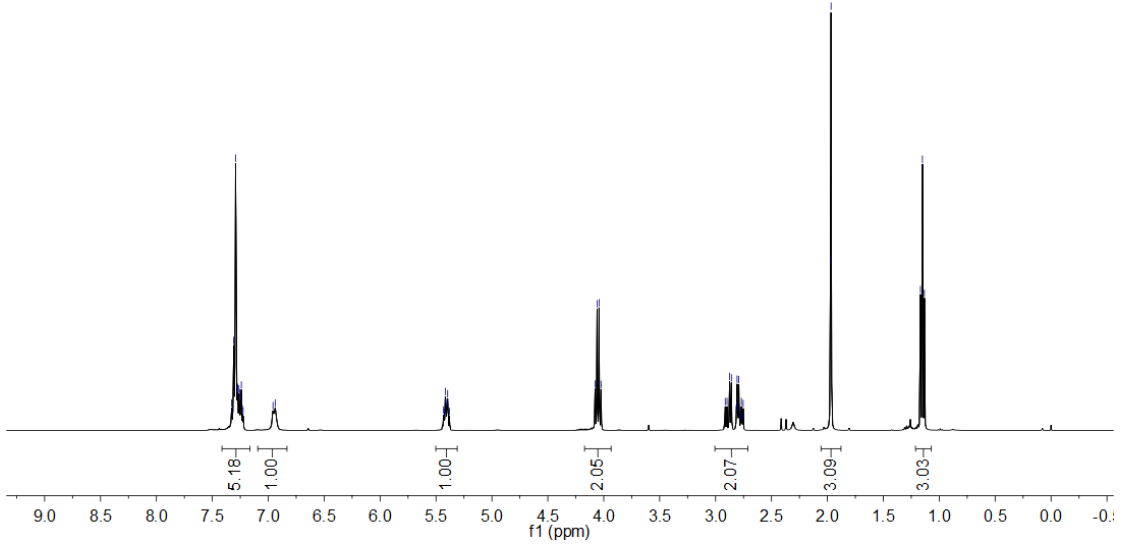
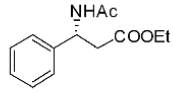
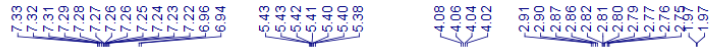
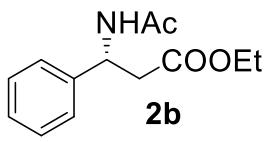
A stock solution was made by mixing $\text{Ni}(\text{OAc})_2$ (1.8 mg, 0.01 mmol) with (*S*)-Binapine (8.0 mg, 0.011 mmol) in a 1:1.1 molar ratio in $\text{CF}_3\text{CH}_2\text{OH}$ (1 mL) at room temperature for 30 min in a nitrogen-filled glovebox. Then the catalyst solution (1.0 mL, 0.01 mmol) was transferred by syringe into the vials charged with substrate **1b** (5 mmol, 1.17 g) in anhydrous $\text{CF}_3\text{CH}_2\text{OH}$ (12 mL). The vials were subsequently transferred into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H_2 (80 atm) at 50°C for 70 h. The hydrogen gas was released slowly and carefully. The solution was concentrated and passed through a short column of silica gel (eluant: EtOAc) to remove the metal complex. The ee values of all compounds **2b** were determined by HPLC analysis on Chiralpak OD-H column.

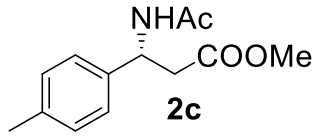
5. References

- [1] (a) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907. (b) Zhou, Y.-G.; Tang, W.; Wang, W.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952. (c) Tang, W.; Wang, W.; Chi, Y.; Zhang, X. *Angew. Chem. Int. Ed.* **2003**, *42*, 3509.
- [2] Yang, P., Xu, H., Zhou, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 12210.

6. NMR spectra of 2



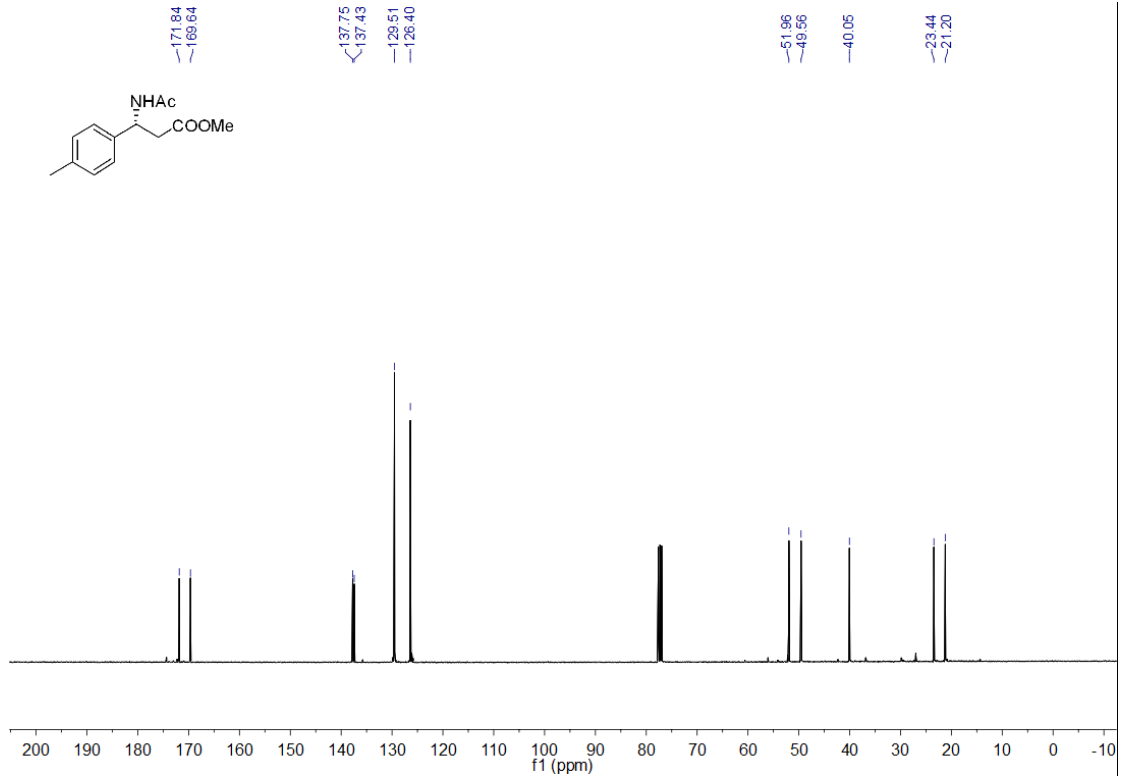
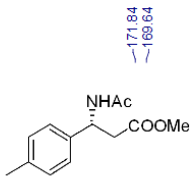
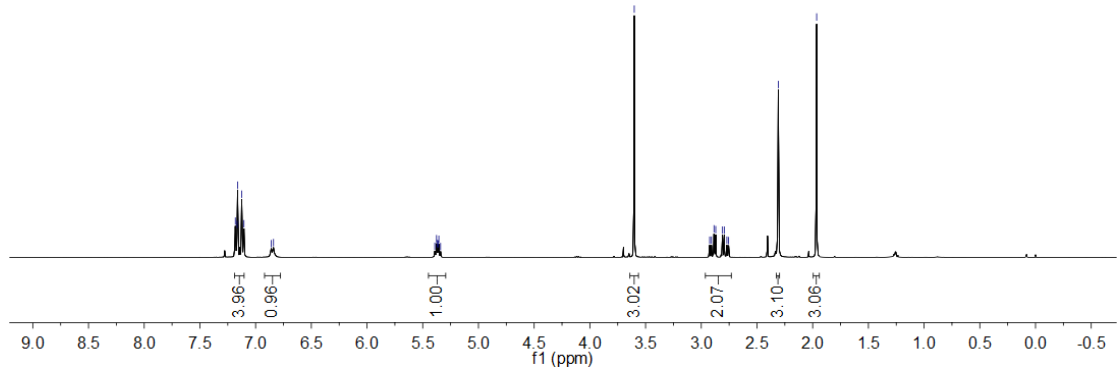
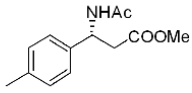


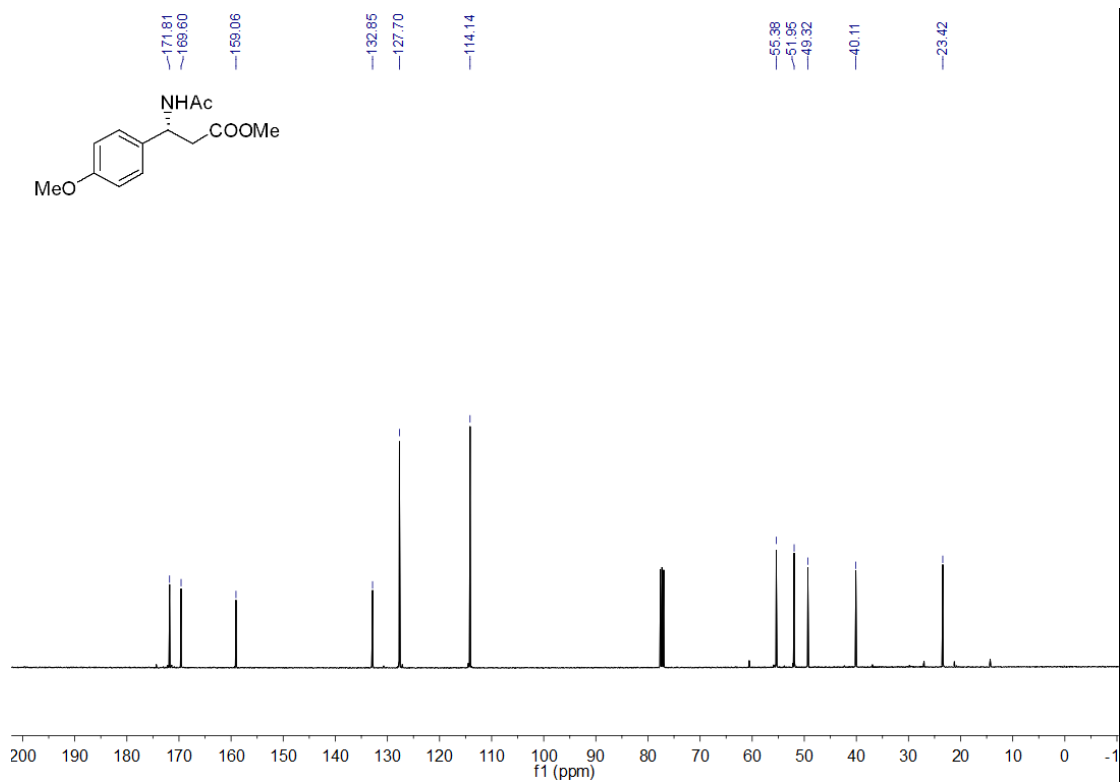
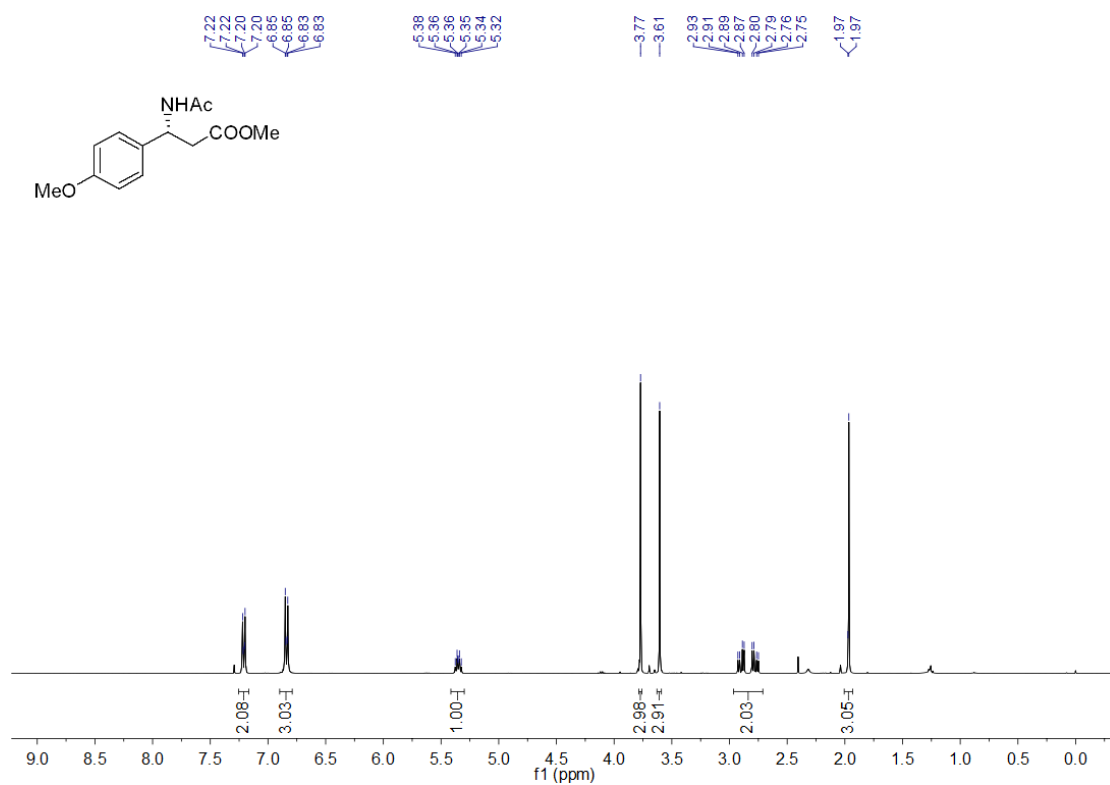
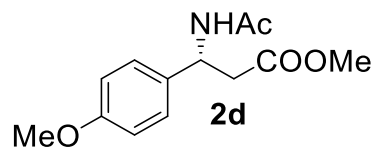


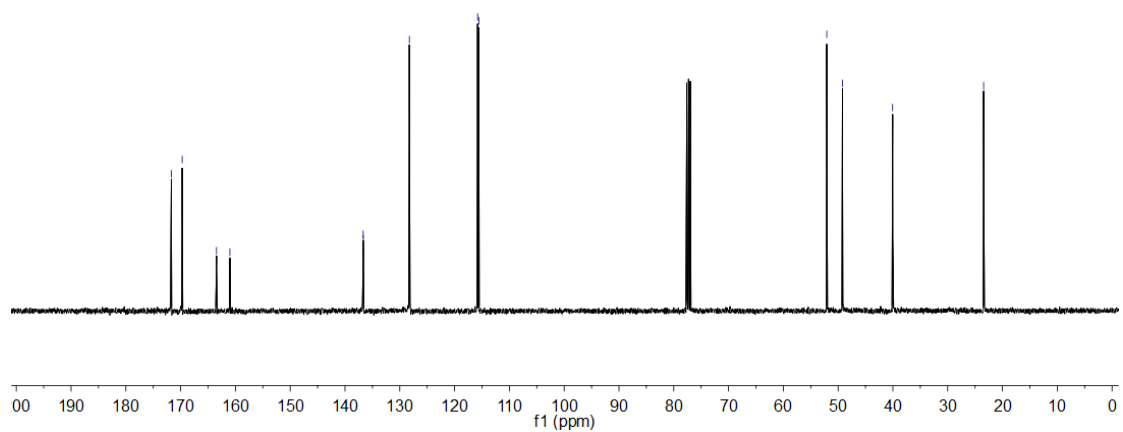
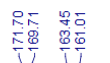
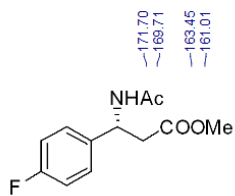
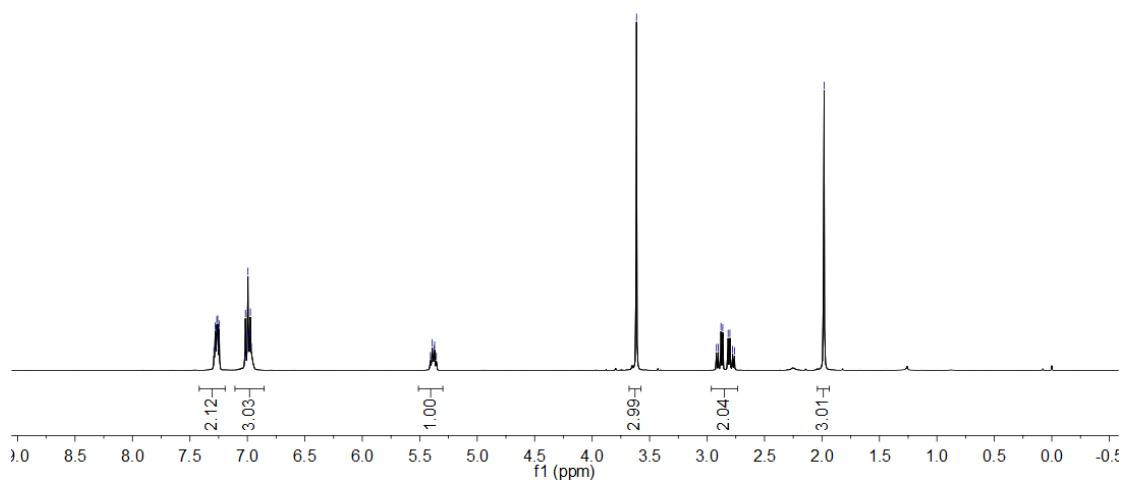
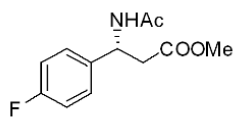
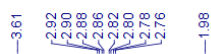
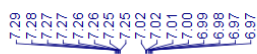
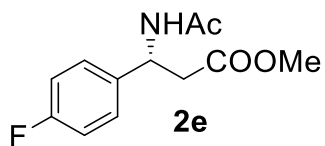
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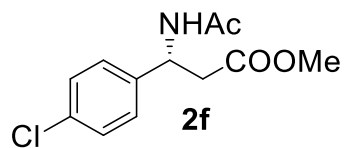
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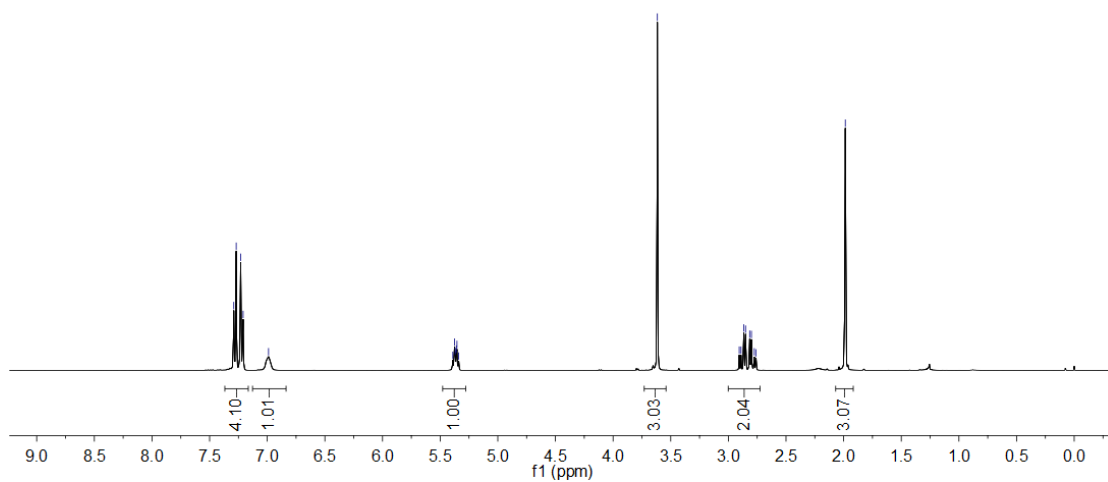
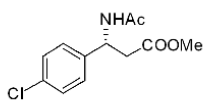




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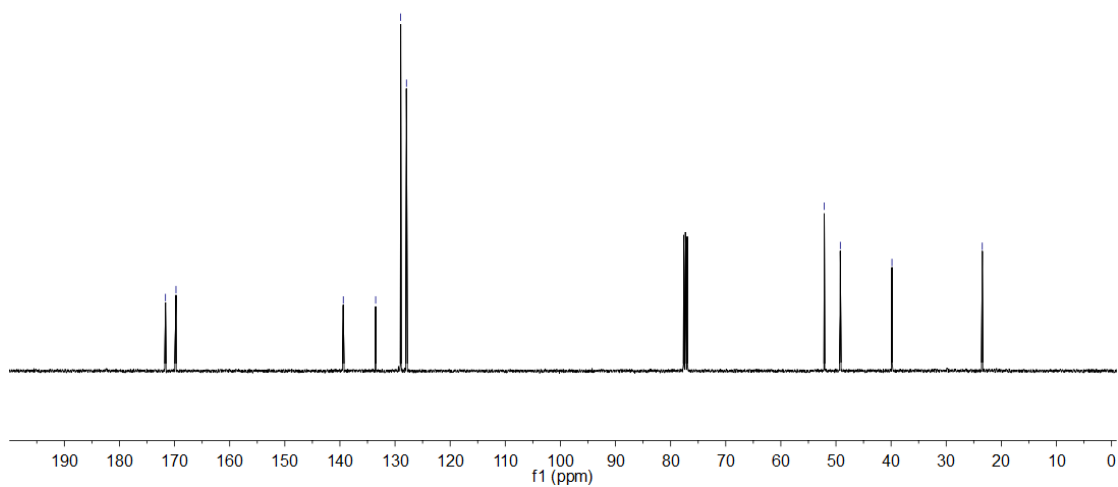
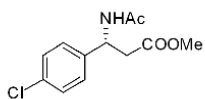
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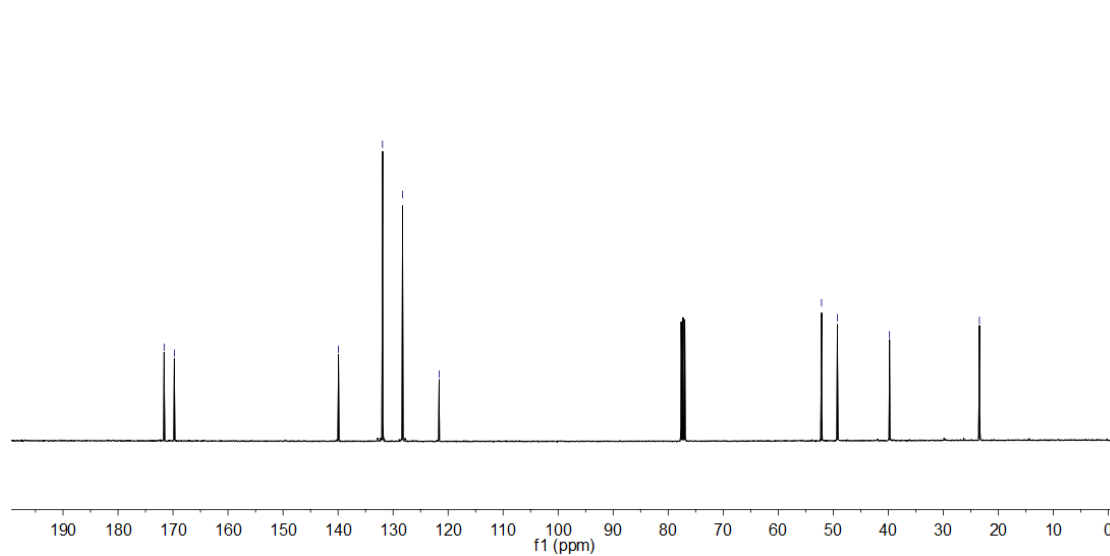
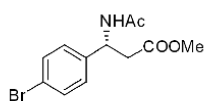
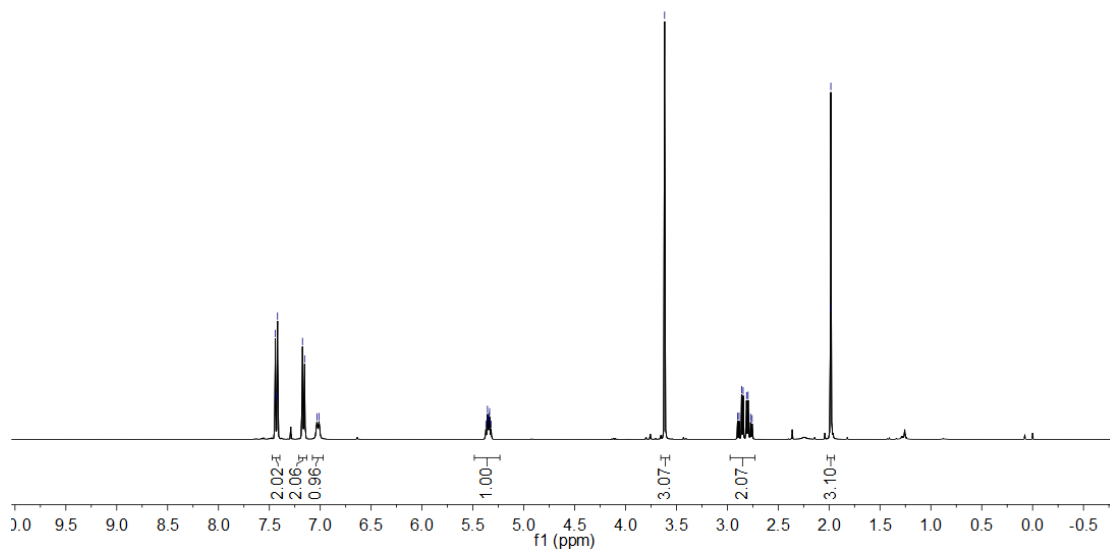
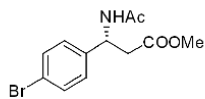
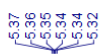
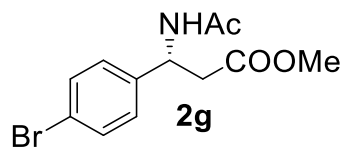


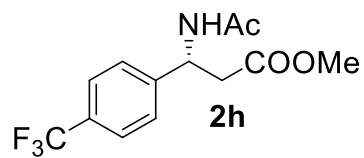
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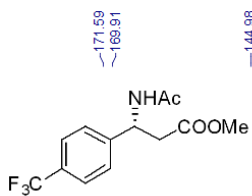
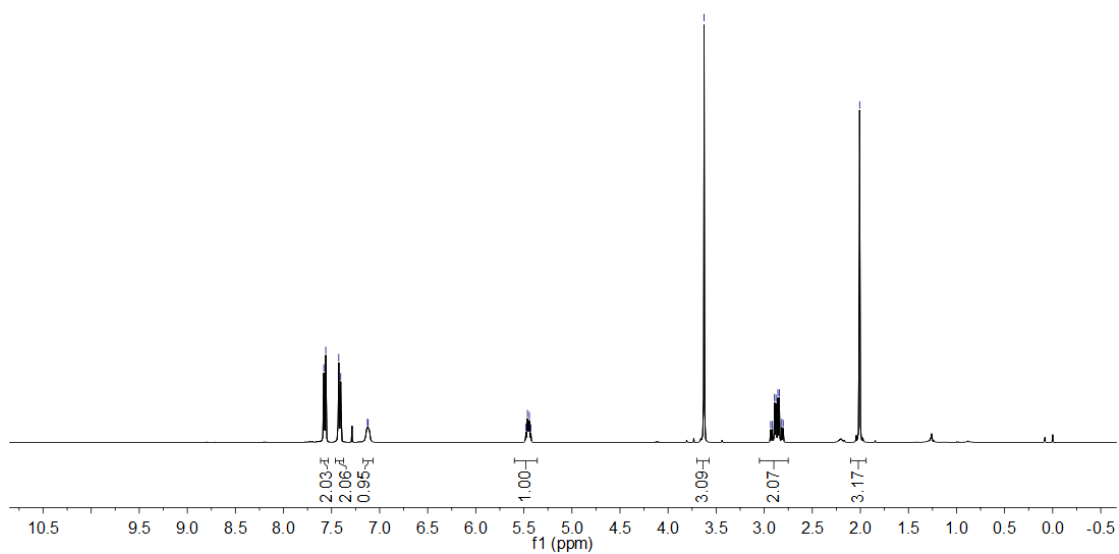
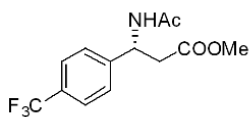


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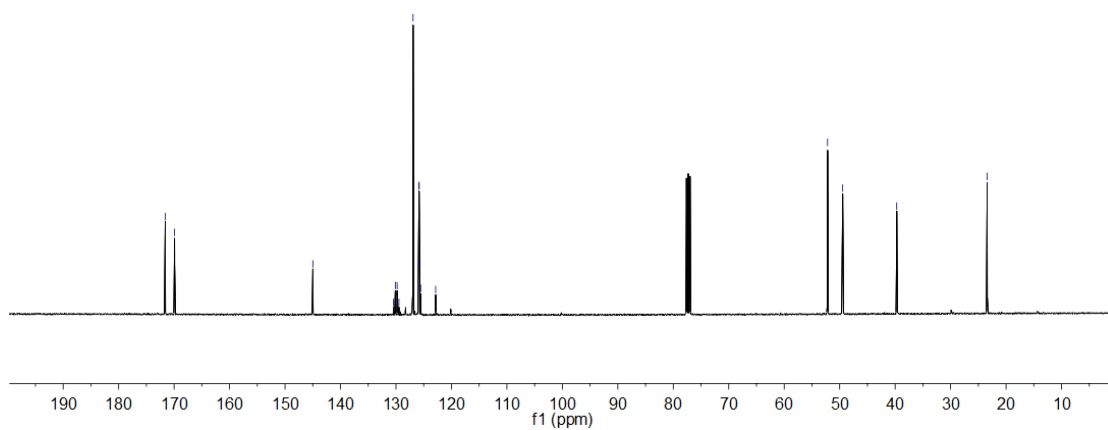
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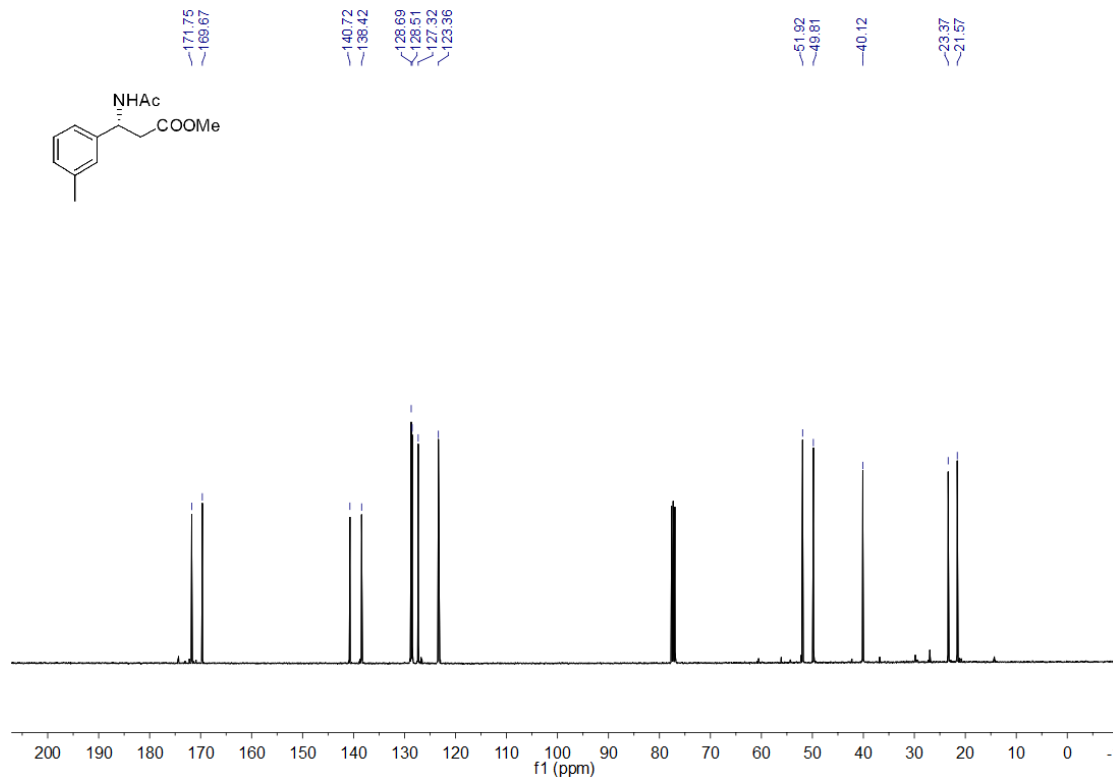
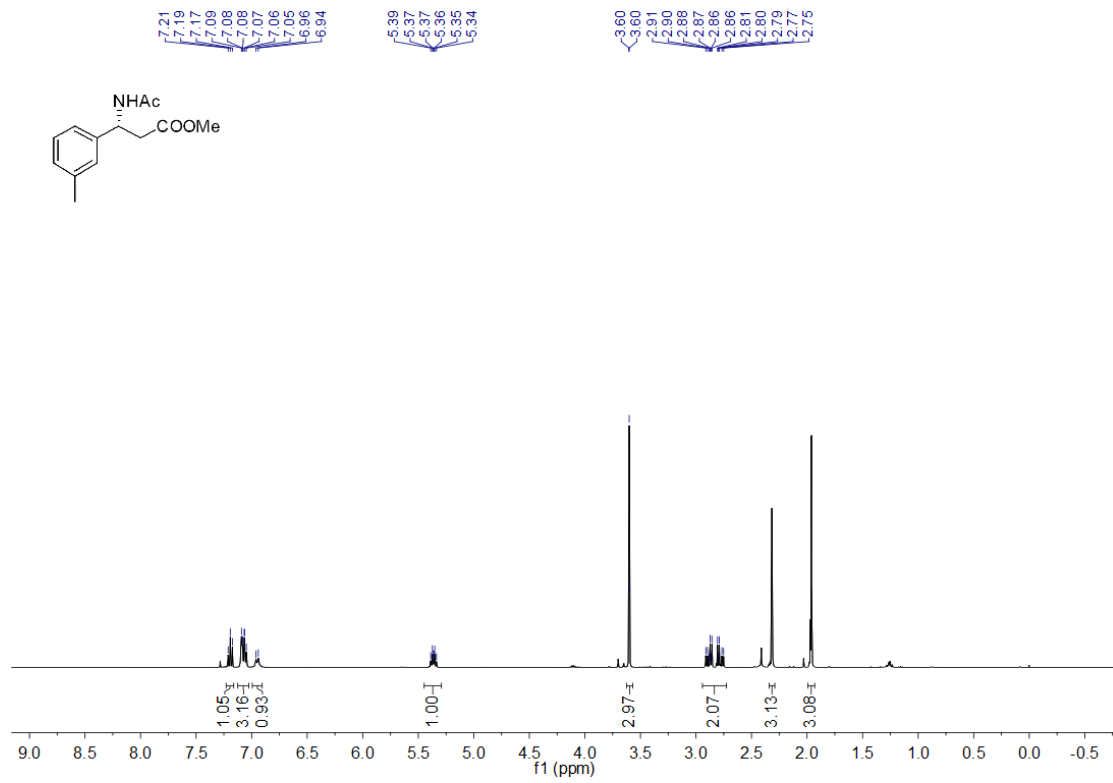
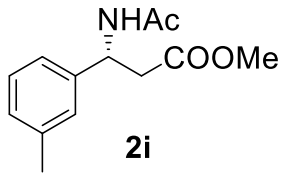
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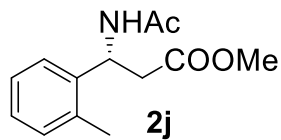
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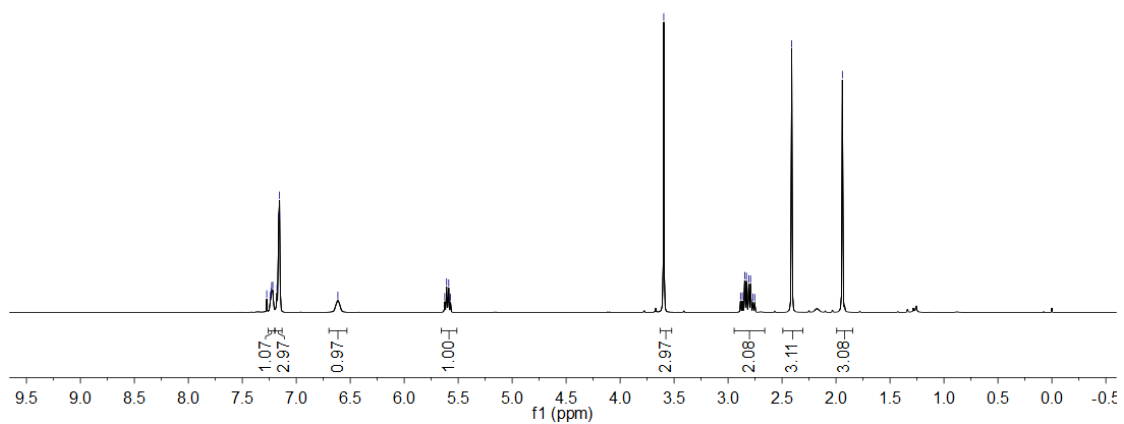
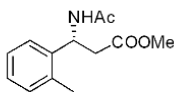


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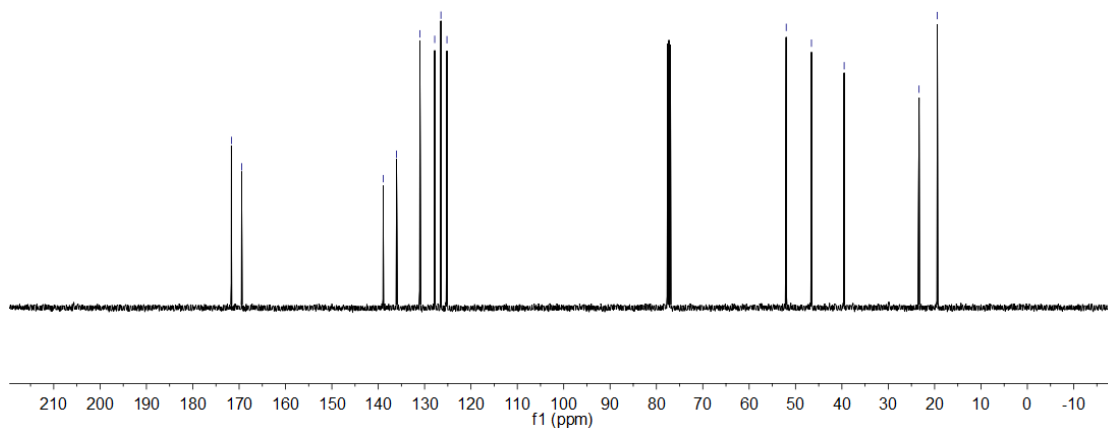
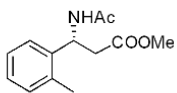


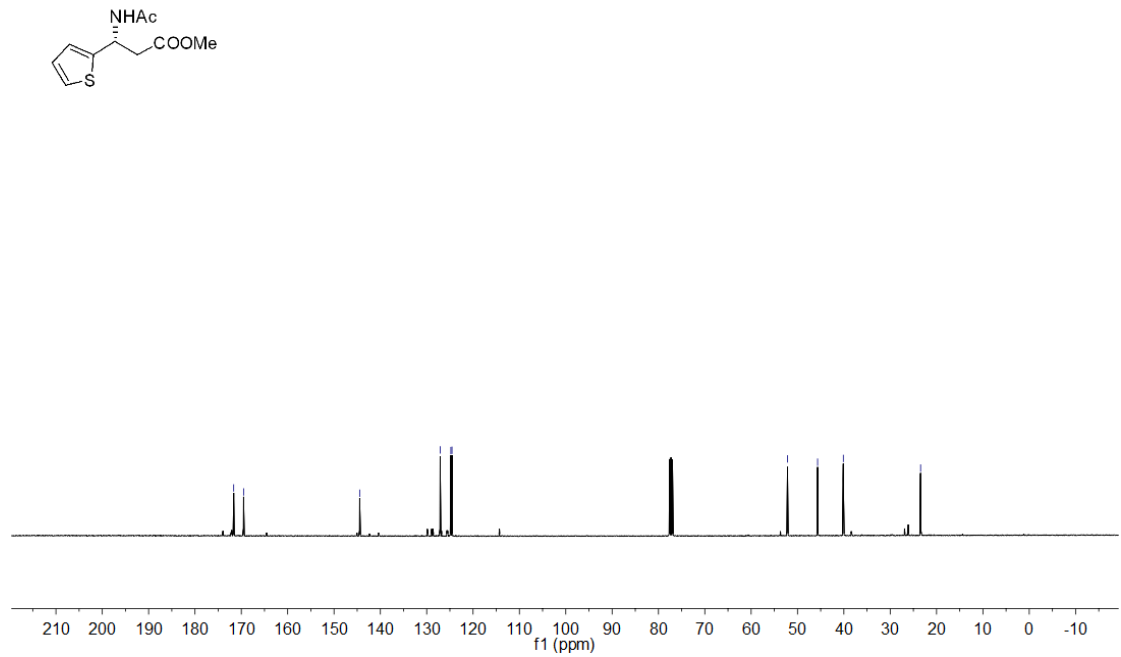
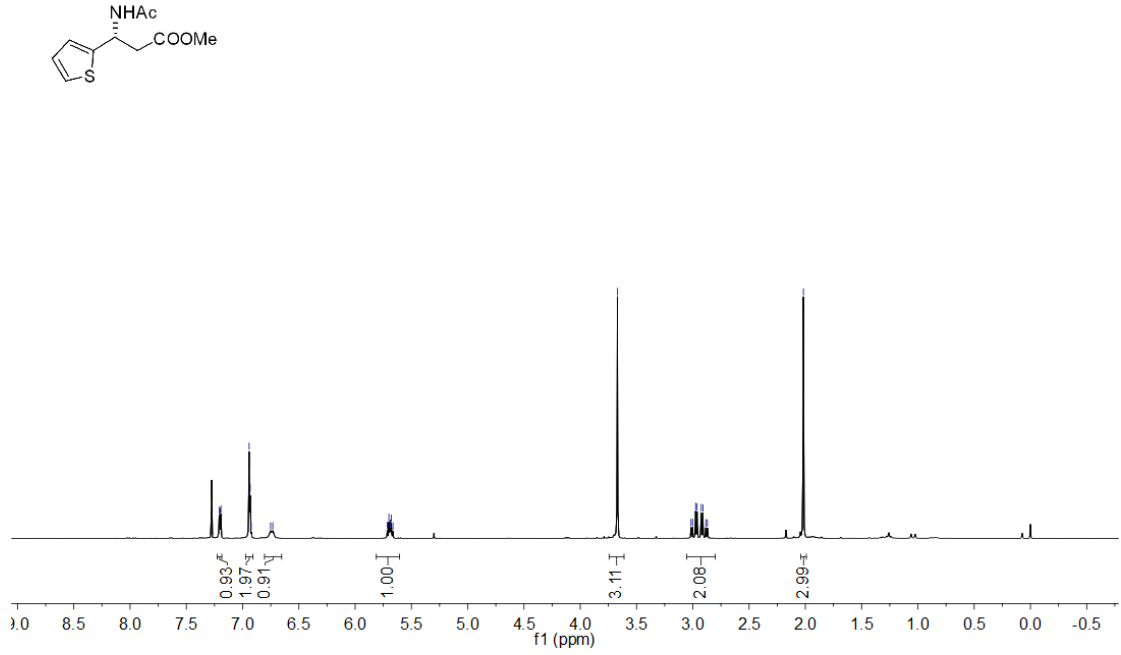
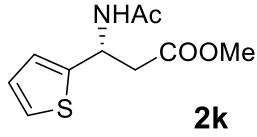
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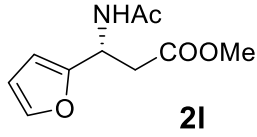
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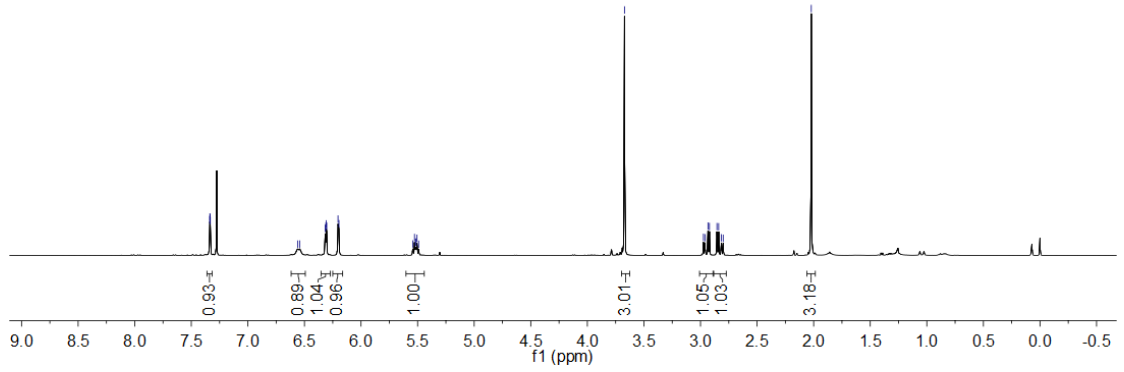
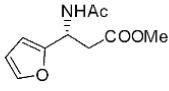




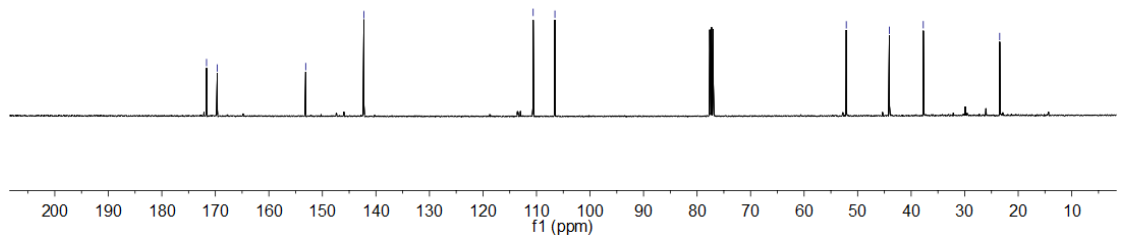
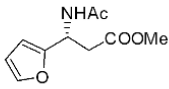


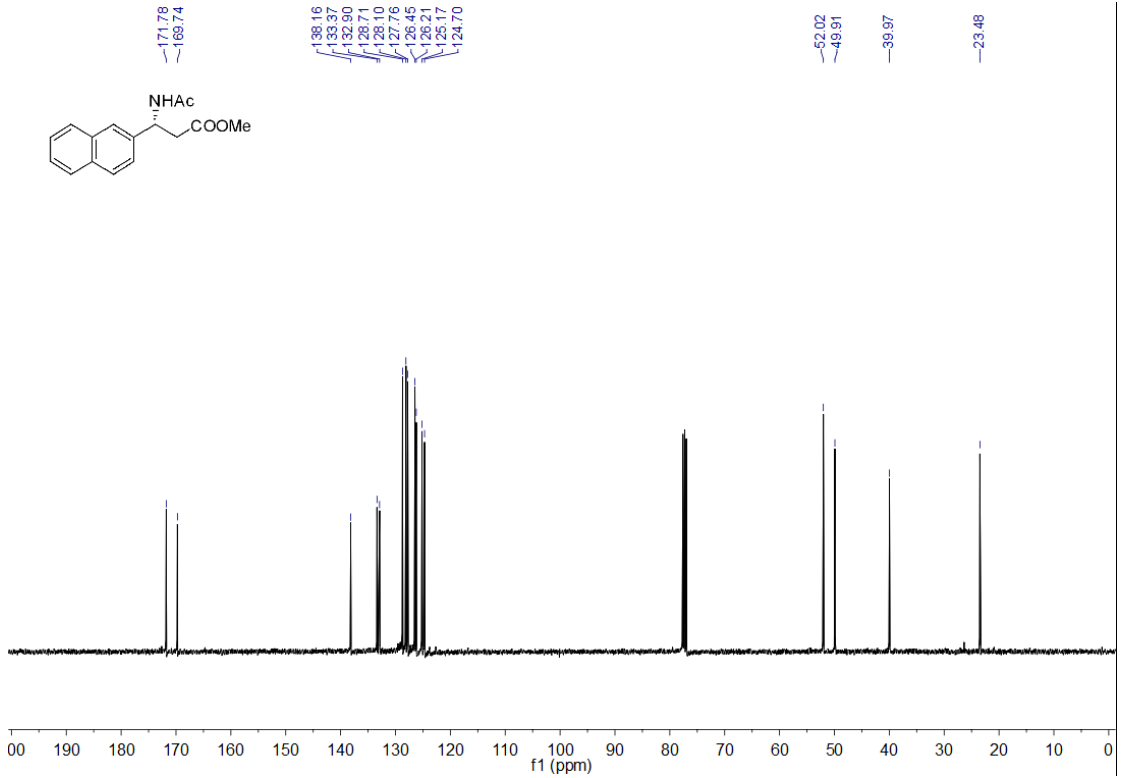
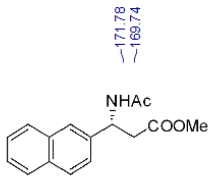
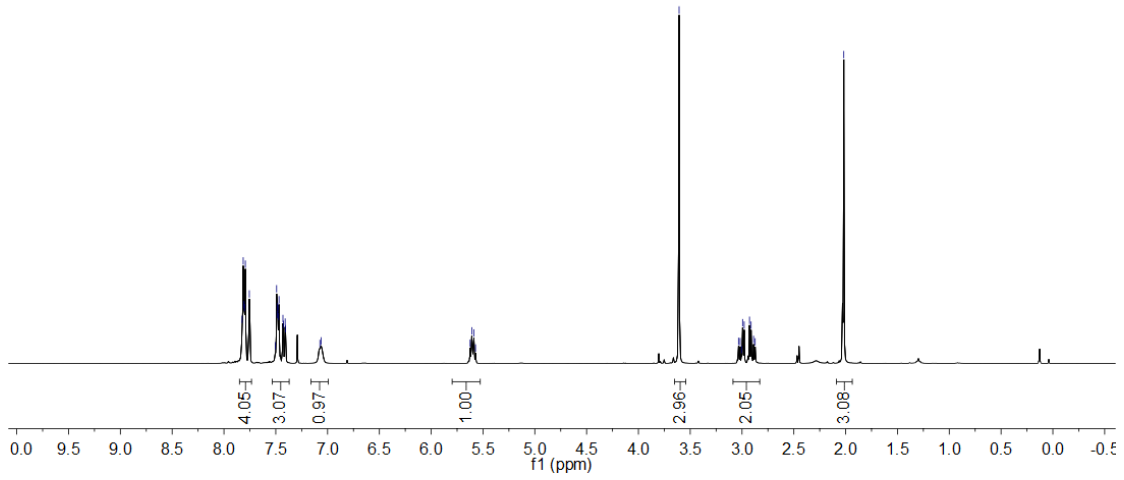
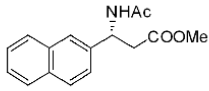
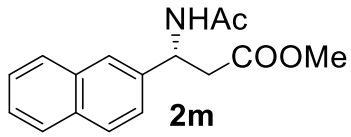
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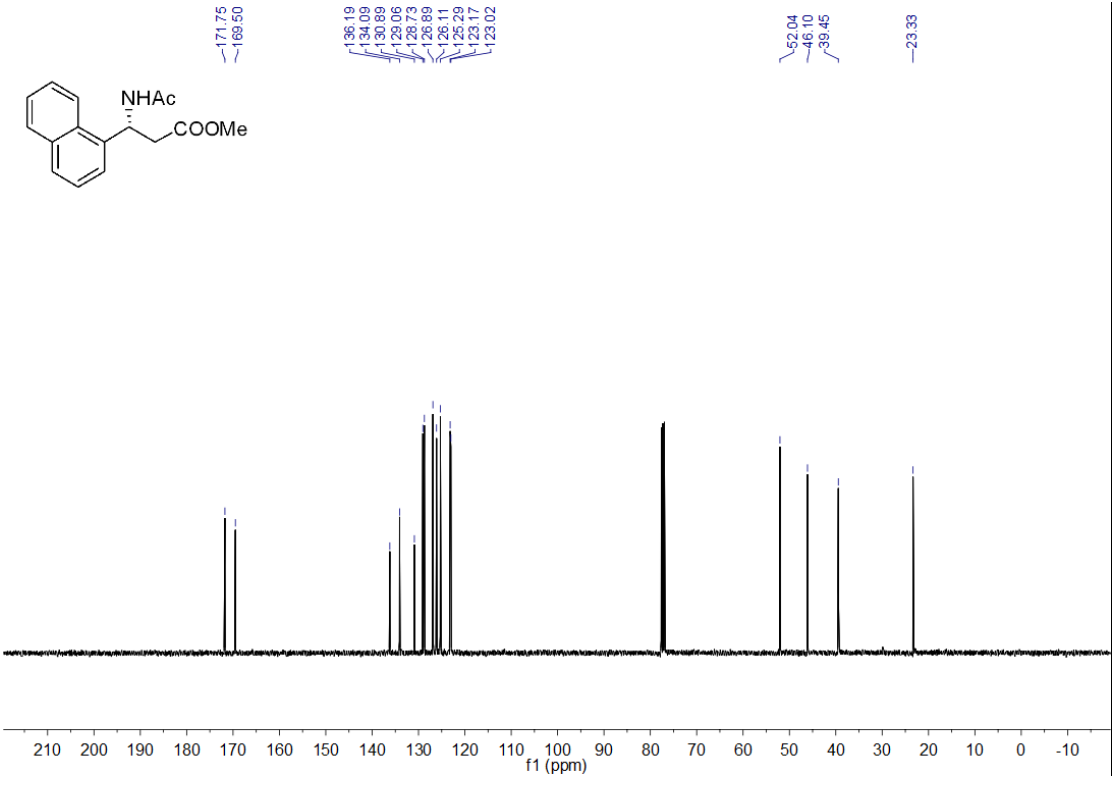
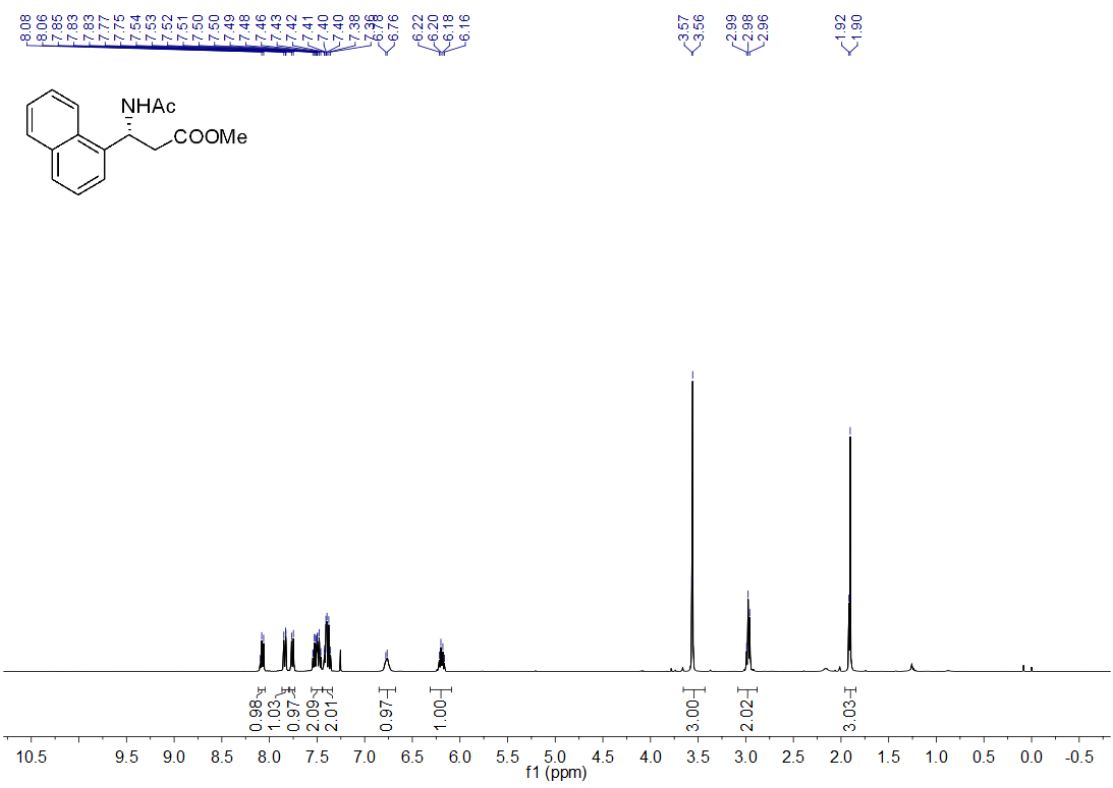
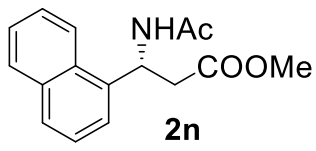
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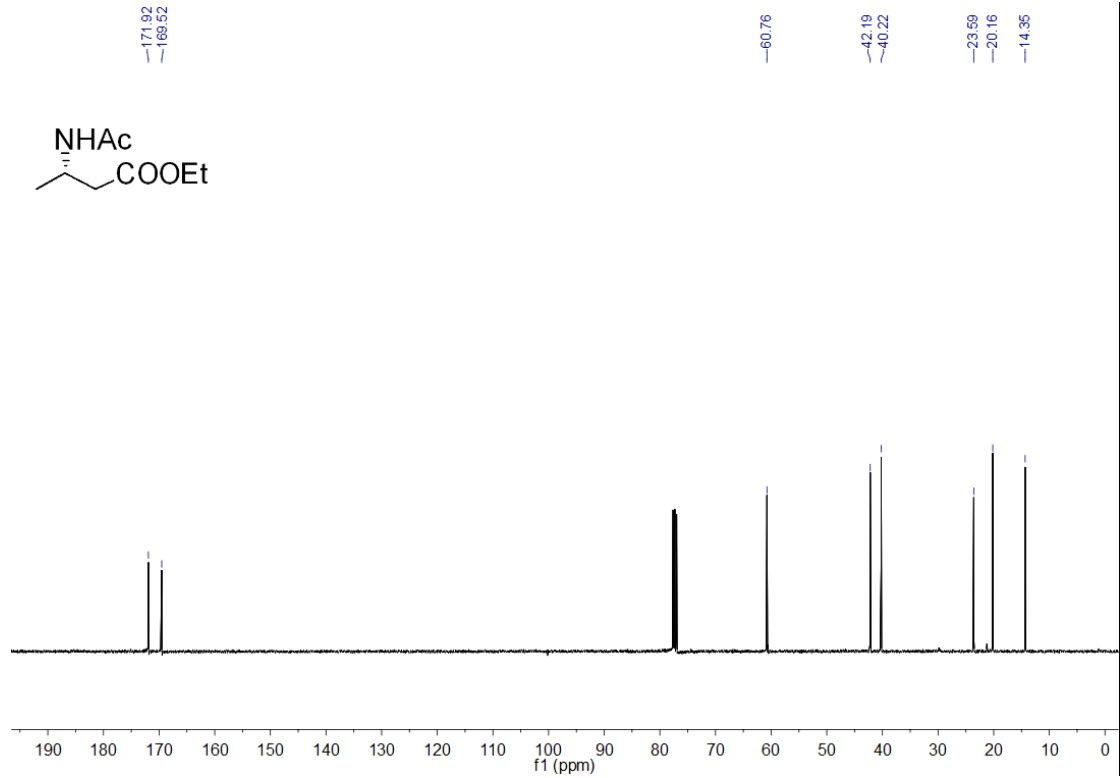
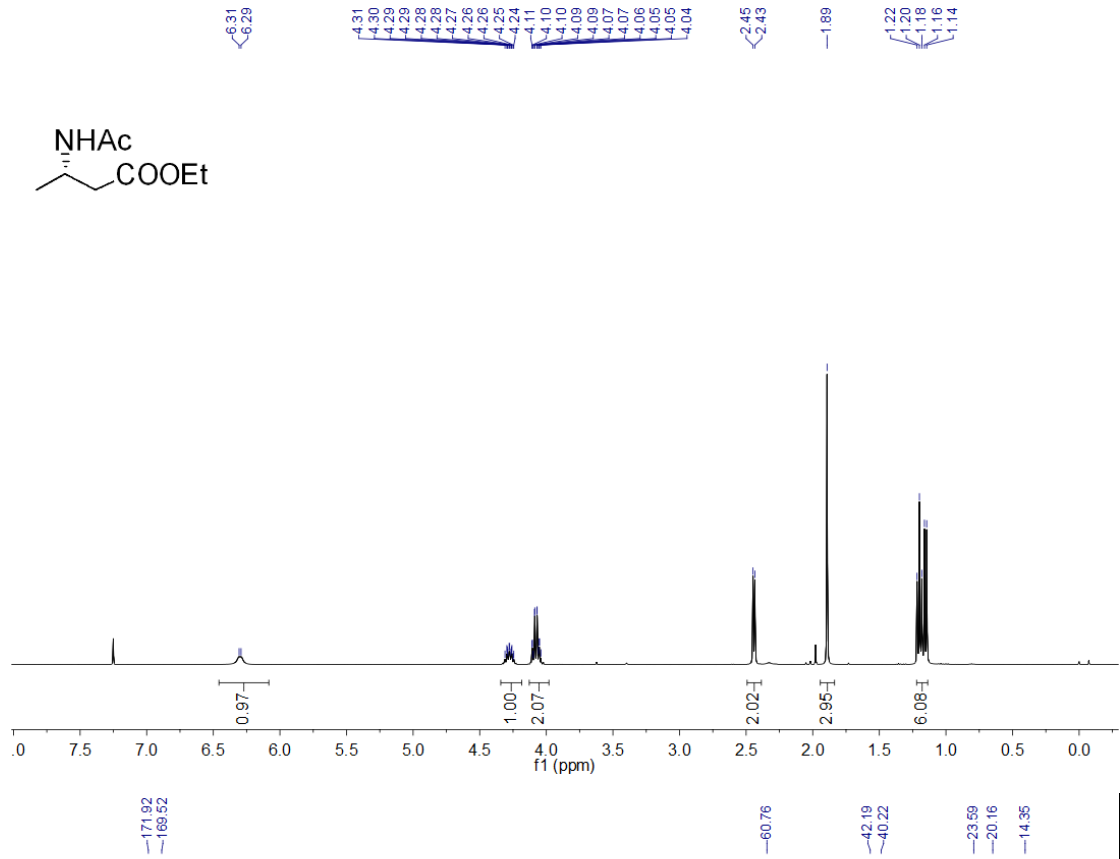
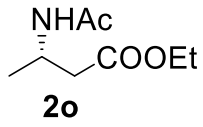


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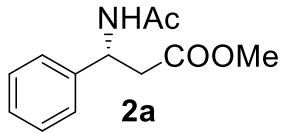








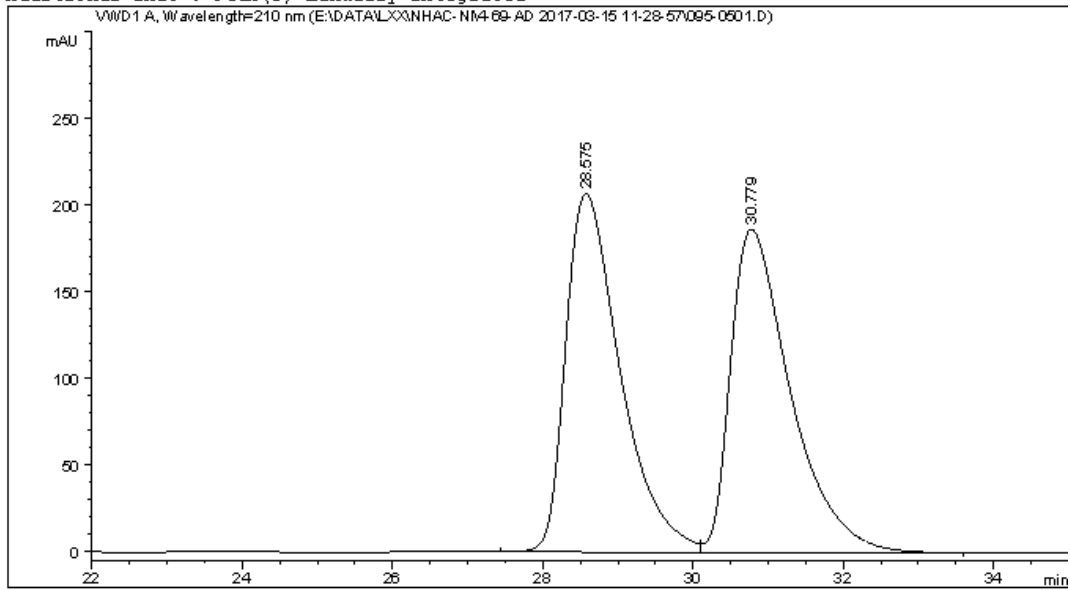
7 HPLC spectra of 2



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Last changed    : 3/15/2017 11:28:58 AM by SYSTEM
Analysis Method : E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\VWD-AD(1-2)-95-5-1ML-3UL
                  -210NM-35MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:41:21 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

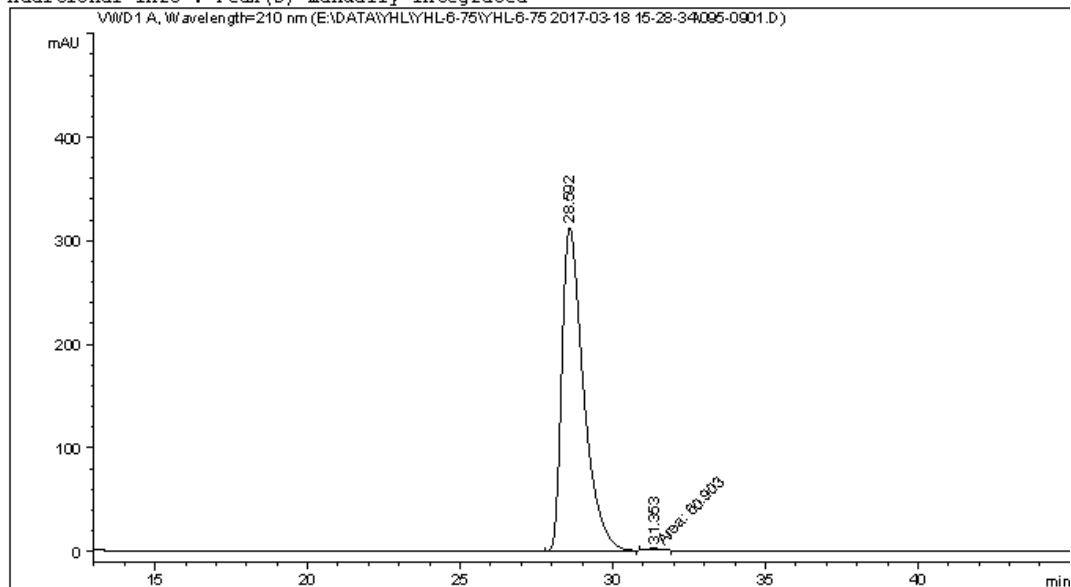
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 28.575 | BV | 0.7678 | 1.04297e4 | 206.66759 | 50.3075 |
| 2 | 30.779 | VB | 0.8381 | 1.03022e4 | 186.59975 | 49.6925 |

Totals : 2.07318e4 393.26733

=====
 *** End of Report ***

Data File E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\095-0901.D
Sample Name: LXX-4-75-4

```
=====
Acq. Operator   : SYSTEM                      Seq. Line :    9
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 95
Injection Date  : 3/18/2017 9:00:07 PM        Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
3UL-210NM-50MIN.M
Last changed    : 3/18/2017 3:44:42 PM by SYSTEM
Analysis Method : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:32:57 AM by SYSTEM
                (modified after loading)
Additional Info : Peak(s) manually integrated
=====
```



```
=====
                          Area Percent Report
=====
```

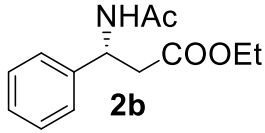
```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 28.592 | BB | 0.7421 | 1.53984e4 | 312.35544 | 99.6060 |
| 2 | 31.353 | MM | 0.5525 | 60.90300 | 1.83714 | 0.3940 |

```
Totals :                      1.54593e4  314.19258
```

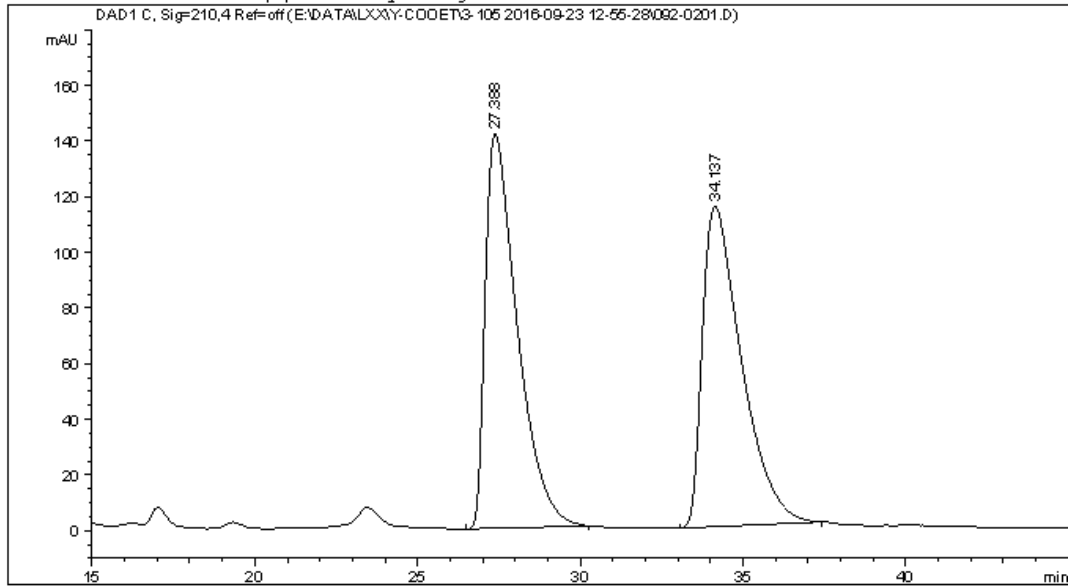
```
=====
*** End of Report ***
```



Data File E:\DATA\LXX\Y-COOET\3-105 2016-09-23 12-55-28\092-0201.D
 Sample Name: Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 92
Injection Date  : 9/23/2016 1:12:23 PM        Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\Y-COOET\3-105 2016-09-23 12-55-28\DAD-OD(1-2)-95-5-1.OML-3UL
                  -40MIN.M
Last changed    : 9/23/2016 1:39:39 PM by SYSTEM
                  (modified after loading)
Analysis Method : E:\DATA\LXX\Y-COOET\3-105 2016-09-23 12-55-28\DAD-OD(1-2)-95-5-1.OML-3UL
                  -40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:39:02 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

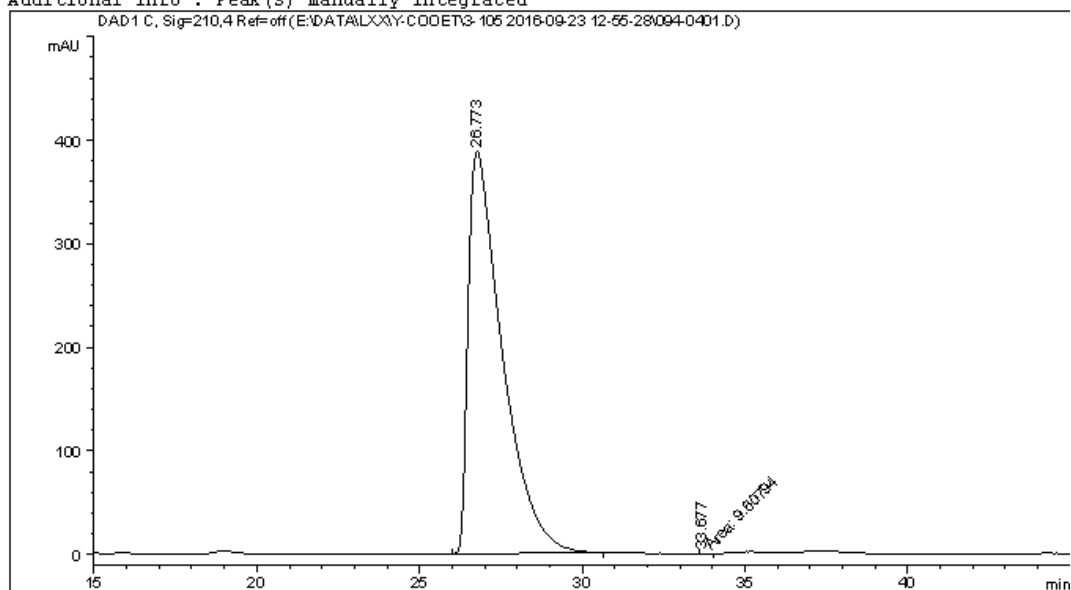
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 27.388 | BB | 0.9787 | 9711.58691 | 141.85748 | 50.2375 |
| 2 | 34.137 | BB | 1.1551 | 9619.76074 | 115.33123 | 49.7625 |

Totals : 1.93313e4 257.18871

```
=====
Acq. Operator   : SYSTEM                      Seq. Line :    4
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 94
Injection Date  : 9/23/2016 2:54:15 PM        Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\Y-COOET\3-105 2016-09-23 12-55-28\DAD-OD(1-2)-95-5-1.OML-3UL
                  -40MIN.M
Last changed    : 9/23/2016 1:39:39 PM by SYSTEM
Analysis Method : E:\DATA\LXX\Y-COOET\3-105 2016-09-23 12-55-28\DAD-OD(1-2)-95-5-1.OML-3UL
                  -40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:43:47 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
=====
```



=====
Area Percent Report
=====

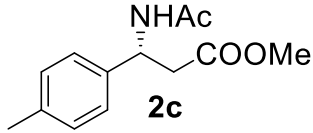
```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 26.773 | BB | 1.0258 | 2.82769e4 | 388.21286 | 99.9660 |
| 2 | 33.677 | MM | 0.3646 | 9.60794 | 4.39151e-1 | 0.0340 |

Totals : 2.82865e4 388.65201

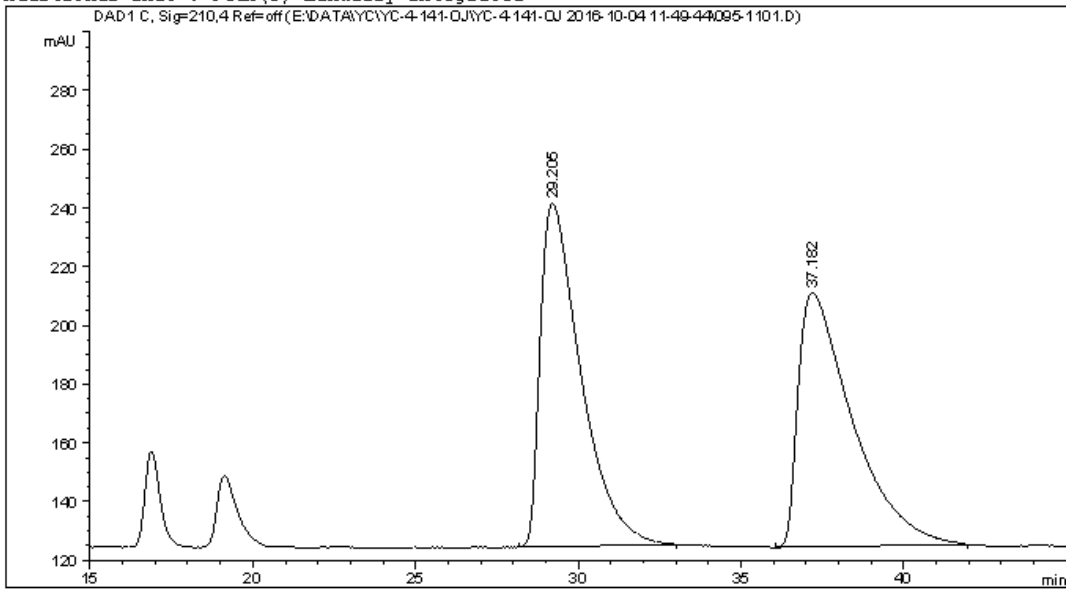
=====
*** End of Report ***



Data File E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\095-1101.D
 Sample Name: p-CH3-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :   11
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 95
Injection Date  : 10/4/2016 3:56:12 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\DAD-0D(1-2)-95-5-
                  1.0ML-3UL-40MIN.M
Last changed    : 10/4/2016 11:59:28 AM by SYSTEM
Analysis Method : E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\DAD-0D(1-2)-95-5-
                  1.0ML-3UL-40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:29:51 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



```

=====
                          Area Percent Report
=====
  
```

```

Sorted By       :      Signal
Multiplier      :      1.0000
Dilution        :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

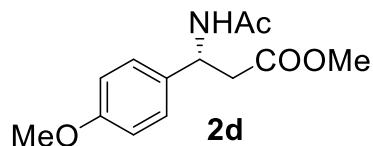
Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 29.205 | BB | 1.1505 | 1.01225e4 | 116.87374 | 50.3463 |
| 2 | 37.182 | BB | 1.3771 | 9983.25391 | 86.45850 | 49.6537 |

Totals : 2.01058e4 203.33224

```

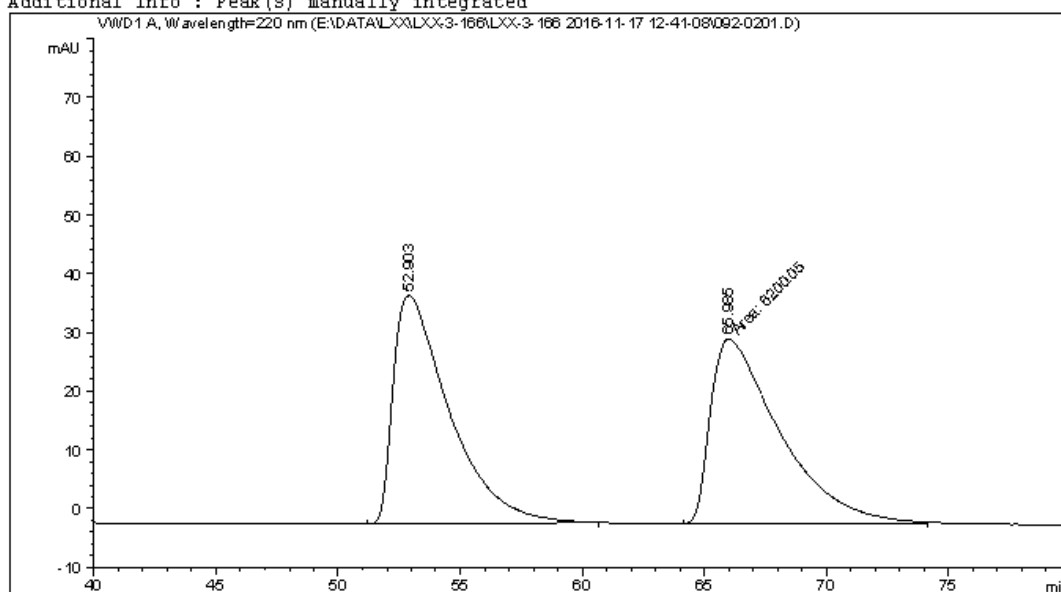
=====
*** End of Report ***
  
```

Data File E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\092-0201.D
 Sample Name: LXX-3-166-4-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 92
Injection Date  : 11/17/2016 12:57:39 PM      Inj       :    1
                                           Inj Volume: 1.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-OD (1-2)-95-5-
                  1ML3UL-210NM-80MIN.M
Last changed    : 11/17/2016 12:41:08 PM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-OD (1-2)-95-5-
                  1ML3UL-210NM-80MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:50:17 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



```

=====
                          Area Percent Report
=====
  
```

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

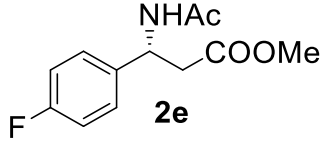
Signal 1: VWD1 A, Wavelength=220 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 52.903 | BB | 2.2351 | 6204.22607 | 38.80886 | 50.0168 |
| 2 | 65.985 | MM | 3.2745 | 6200.05127 | 31.55764 | 49.9832 |

Totals : 1.24043e4 70.36650

```

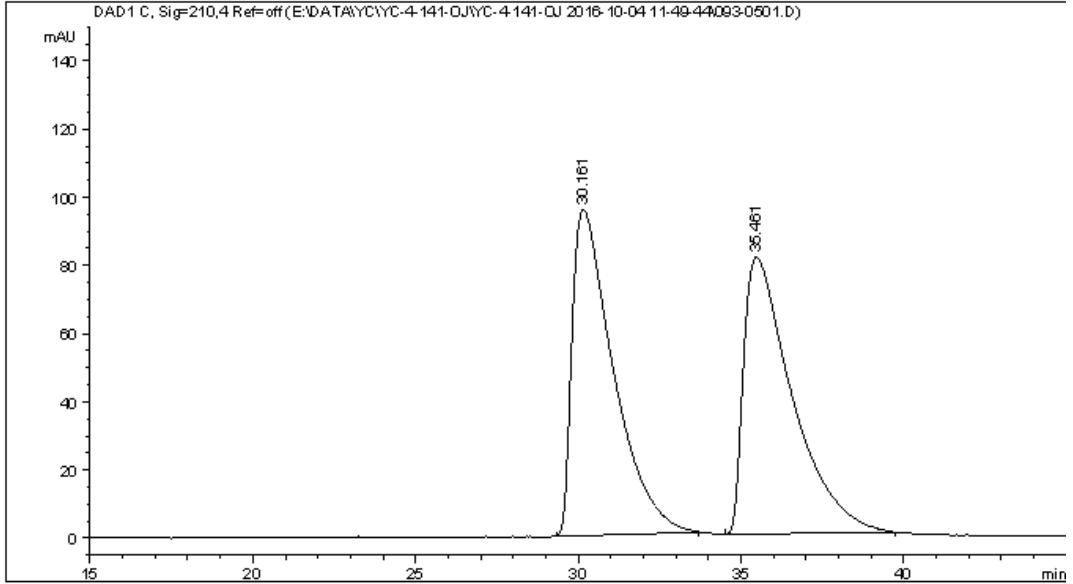
=====
*** End of Report ***
  
```

Data File E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\093-0501.D
 Sample Name: p-F-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    5
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 93
Injection Date  : 10/4/2016 1:20:19 PM        Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\DAD-OD(1-2)-95-5-
                  1.OML-3UL-40MIN.M
Last changed    : 10/4/2016 1:29:48 PM by SYSTEM
                  (modified after loading)
Analysis Method : E:\DATA\YC\YC-4-141-0J\YC-4-141-0J 2016-10-04 11-49-44\DAD-OD(1-2)-95-5-
                  1.OML-3UL-40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:27:02 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

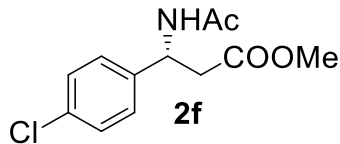
```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 30.161 | BB | 1.0480 | 8421.93555 | 95.57661 | 50.0074 |
| 2 | 35.461 | BB | 1.3524 | 8419.44922 | 81.15081 | 49.9926 |

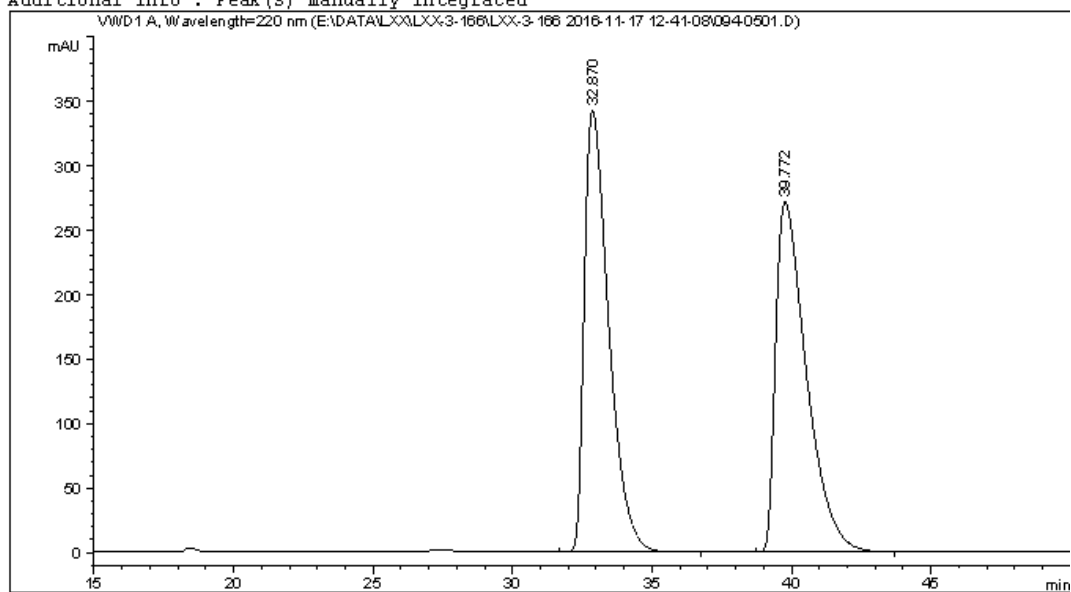
Totals : 1.68414e4 176.72742



Data File E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\094-0501.D
 Sample Name: LXX-3-166-2-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    5
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 94
Injection Date  : 11/17/2016 4:04:58 PM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-AD (1-6)-95-5-1ML
                  -3UL-50MIN-220NM.M
Last changed    : 11/17/2016 12:41:08 PM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-AD (1-6)-95-5-1ML
                  -3UL-50MIN-220NM.M (Sequence Method)
Last changed    : 5/4/2017 10:52:44 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By       :      Signal
Multiplier      :      1.0000
Dilution        :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

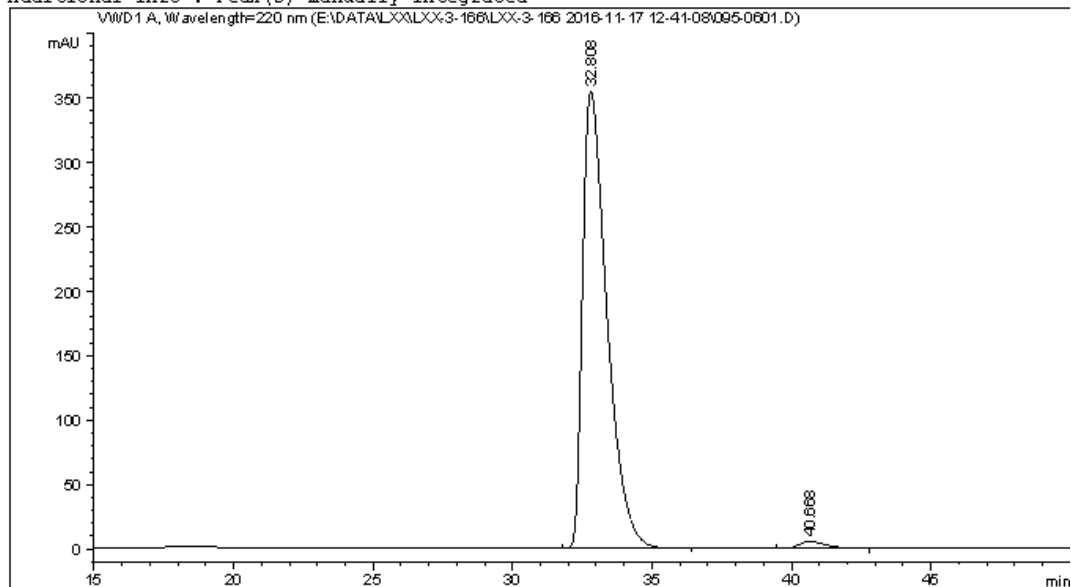
Signal 1: VWD1 A, Wavelength=220 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 32.870 | BB | 0.9322 | 2.07651e4 | 342.57419 | 50.0049 |
| 2 | 39.772 | BB | 1.1551 | 2.07611e4 | 271.49887 | 49.9951 |

Totals : 4.15262e4 614.07306

=====
 *** End of Report ***

```
=====
Acq. Operator   : SYSTEM                      Seq. Line :    6
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 95
Injection Date  : 11/17/2016 4:55:42 PM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-AD(1-6)-95-5-1ML
                  -3UL-50MIN-220NM.M
Last changed    : 11/17/2016 12:41:08 PM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-3-166\LXX-3-166 2016-11-17 12-41-08\VWD-AD(1-6)-95-5-1ML
                  -3UL-50MIN-220NM.M (Sequence Method)
Last changed    : 5/4/2017 10:52:44 AM by SYSTEM
                  (modified after loading)
Additional Info  : Peak(s) manually integrated
=====
```



=====
Area Percent Report
=====

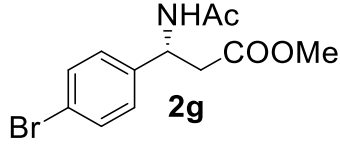
```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=220 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 32.808 | BB | 0.9242 | 2.14892e4 | 354.50406 | 98.3530 |
| 2 | 40.668 | BB | 0.9525 | 359.85889 | 5.34478 | 1.6470 |

Totals : 2.18491e4 359.84884

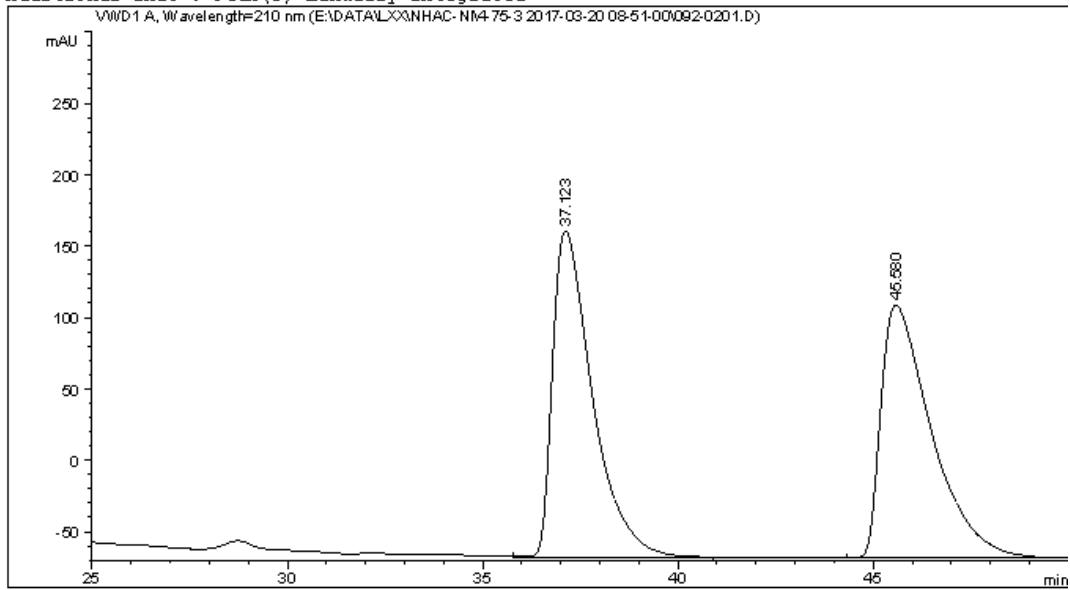
=====
*** End of Report ***



Data File E:\DATA\LXX\NHAC-NI\4-75-3 2017-03-20 08-51-00\092-0201.D
 Sample Name: 4-75-3-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 92
Injection Date  : 3/20/2017 9:07:32 AM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\NHAC-NI\4-75-3 2017-03-20 08-51-00\VWD-AD(1-2)-95-5-1ML-3UL-
                210NM-50MIN.M
Last changed    : 3/20/2017 8:51:00 AM by SYSTEM
Analysis Method : E:\DATA\LXX\NHAC-NI\4-75-3 2017-03-20 08-51-00\VWD-AD(1-2)-95-5-1ML-3UL-
                210NM-50MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:34:09 AM by SYSTEM
                (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



```

=====
                          Area Percent Report
=====
  
```

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 37.123 | BB | 1.0920 | 1.60969e4 | 228.18394 | 50.3350 |
| 2 | 45.580 | BBA | 1.3126 | 1.58826e4 | 177.21634 | 49.6650 |

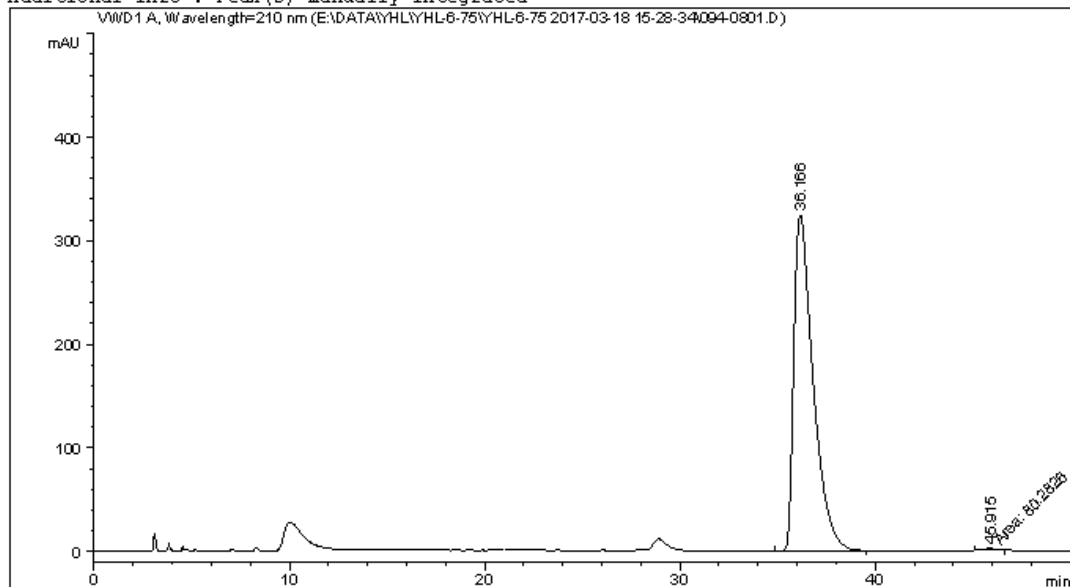
```
Totals :                      3.19794e4  405.40028
```

```

=====
*** End of Report ***
  
```

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    8
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 94
Injection Date  : 3/18/2017 8:09:23 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M
Last changed    : 3/18/2017 3:44:42 PM by SYSTEM
Analysis Method : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 8/21/2017 9:45:43 PM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

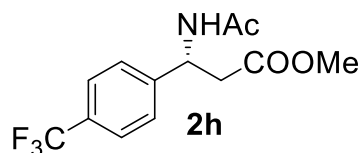
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 36.166 | BB | 1.0270 | 2.23269e4 | 324.38647 | 99.6417 |
| 2 | 45.915 | MM | 0.6749 | 80.28262 | 1.44389 | 0.3583 |

Totals : 2.24072e4 325.83036

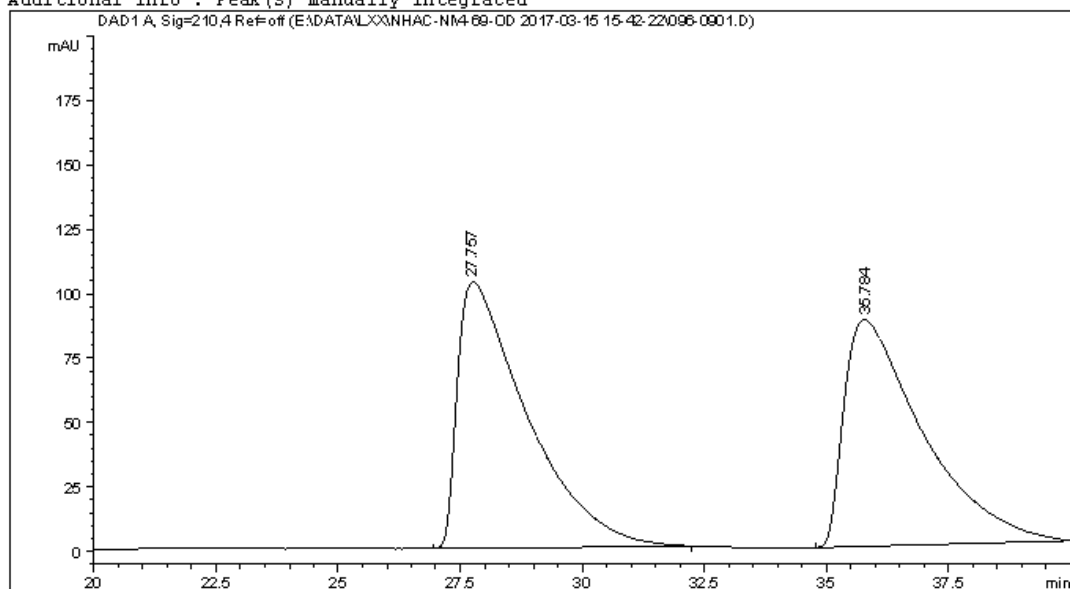
=====
 *** End of Report ***



Data File E:\DATA\LXX\NHAC-NI\4-69-OD 2017-03-15 15-42-22\096-0901.D
 Sample Name: 4-69-5

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    9
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 96
Injection Date  : 3/15/2017 8:05:55 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\NHAC-NI\4-69-OD 2017-03-15 15-42-22\DAD-OD(1-2)-95-5-1ML-3UL
                  -45MIN.M
Last changed    : 3/15/2017 8:44:43 PM by SYSTEM
                  (modified after loading)
Analysis Method : E:\DATA\LXX\NHAC-NI\4-69-OD 2017-03-15 15-42-22\DAD-OD(1-2)-95-5-1ML-3UL
                  -45MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:22:14 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

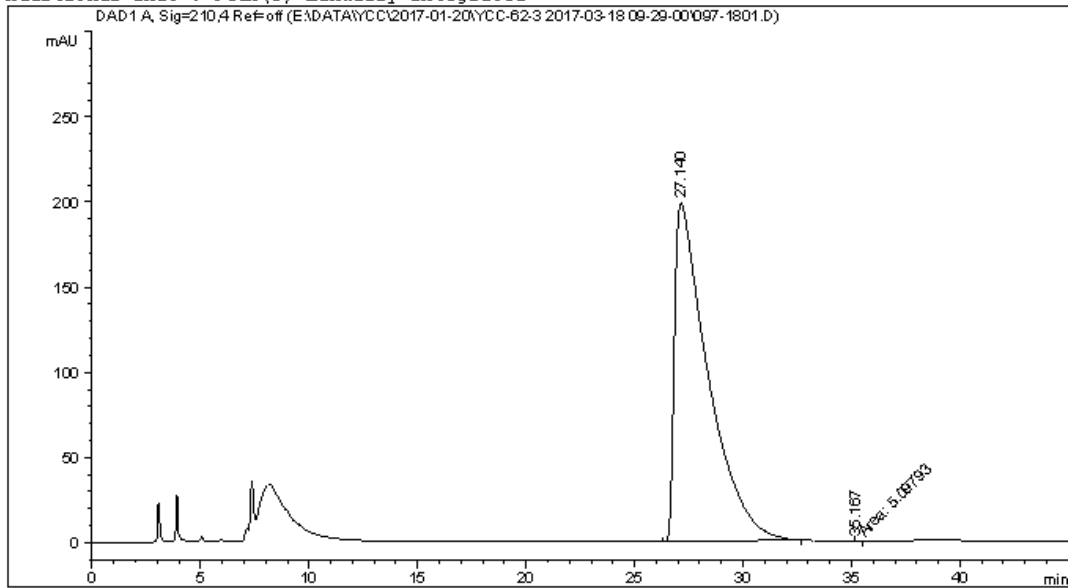
Signal 1: DAD1 A, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 27.757 | BB | 1.3087 | 1.02080e4 | 103.31514 | 50.9250 |
| 2 | 35.784 | BBA | 1.4772 | 9837.18359 | 87.93222 | 49.0750 |

Totals : 2.00452e4 191.24736

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :   18
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 97
Injection Date  : 3/18/2017 4:35:52 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YCC\2017-01-20\YCC-62-3 2017-03-18 09-29-00\DAD-OD(1-2)-95-5-1ML
                                           -3UL-45MIN.M
Last changed    : 3/18/2017 3:47:13 PM by SYSTEM
Analysis Method : E:\DATA\YCC\2017-01-20\YCC-62-3 2017-03-18 09-29-00\DAD-OD(1-2)-95-5-1ML
                                           -3UL-45MIN.M (Sequence Method)
Last changed    : 8/21/2017 9:42:48 PM by SYSTEM
                                           (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

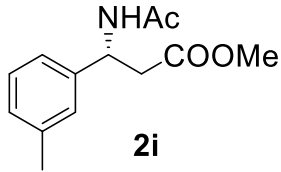
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 A, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 27.140 | BB | 1.3794 | 2.12284e4 | 198.55215 | 99.9760 |
| 2 | 35.167 | MM | 0.2408 | 5.09793 | 3.52880e-1 | 0.0240 |

Totals : 2.12335e4 198.90503

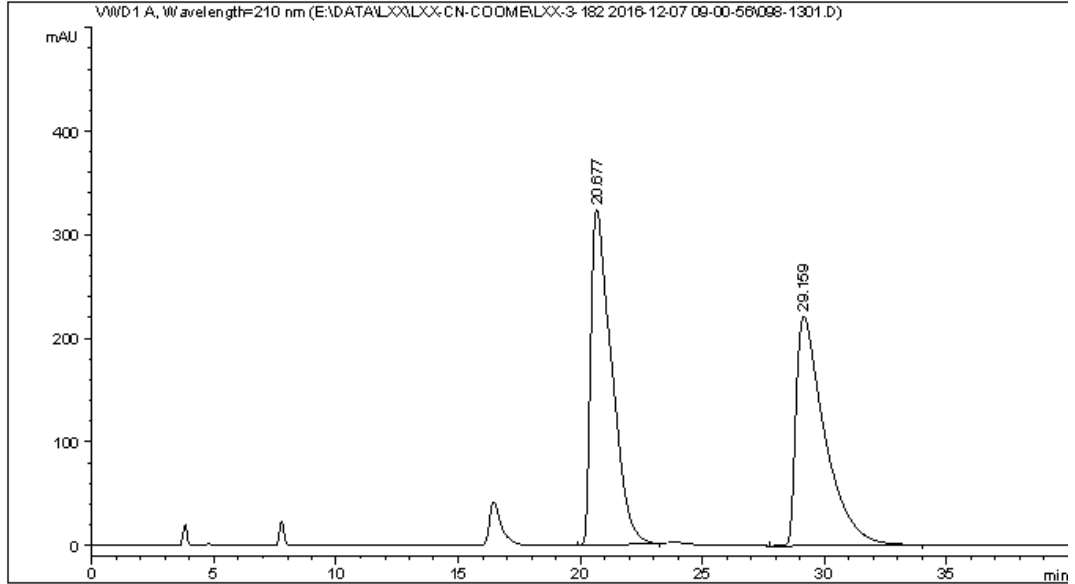
=====
 *** End of Report ***



Data File E:\DATA\LXX\LXX-CN-COOME\LXX-3-182 2016-12-07 09-00-56\098-1301.D
 Sample Name: LXX-3-177-1-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :   13
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 98
Injection Date  : 12/7/2016 3:52:16 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-CN-COOME\LXX-3-182 2016-12-07 09-00-56\VWD-OD(1-6)-92-8-
                  0.8ML3UL-210NM-50MIN.M
Last changed    : 12/7/2016 3:05:58 PM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-CN-COOME\LXX-3-182 2016-12-07 09-00-56\VWD-OD(1-6)-92-8-
                  0.8ML3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 5/4/2017 11:04:40 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
=====
  
```



=====
 Area Percent Report
 =====

```

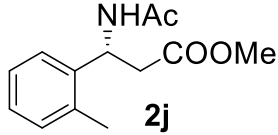
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 20.677 | BB | 0.8492 | 1.91351e4 | 323.93301 | 51.4765 |
| 2 | 29.159 | BB | 1.1906 | 1.80374e4 | 221.59834 | 48.5235 |

Totals : 3.71725e4 545.53136

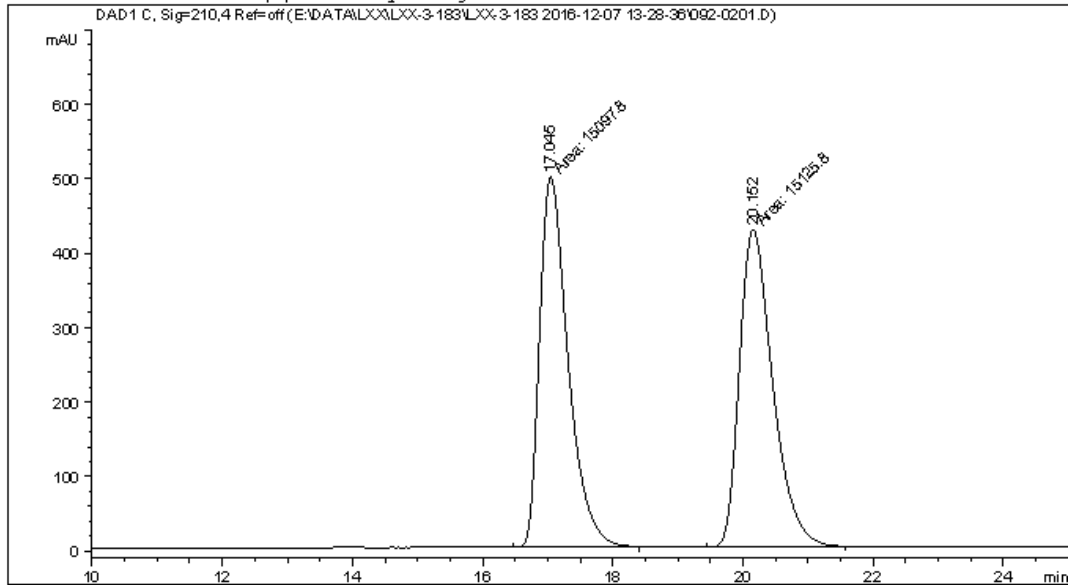
=====
 *** End of Report ***



Data File E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\092-0201.D
 Sample Name: LXX-3-177-2-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 92
Injection Date  : 12/7/2016 1:45:33 PM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-95-5-1.
                                           OML-3UL-40MIN.M
Last changed    : 12/7/2016 2:08:13 PM by SYSTEM
                                           (modified after loading)
Analysis Method : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-95-5-1.
                                           OML-3UL-40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:57:38 AM by SYSTEM
                                           (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

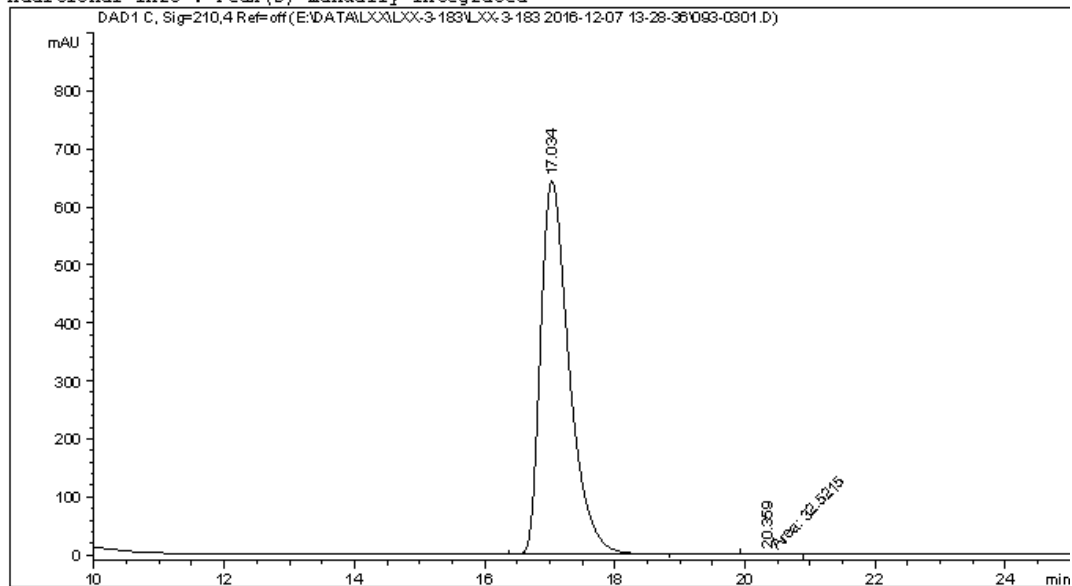
Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 17.045 | MM | 0.5063 | 1.50978e4 | 497.04028 | 49.9538 |
| 2 | 20.152 | MM | 0.5912 | 1.51258e4 | 426.40335 | 50.0462 |

Totals : 3.02236e4 923.44363

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    3
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 93
Injection Date  : 12/7/2016 2:11:29 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-95-5-1.
                                           OML-3UL-40MIN.M
Last changed    : 12/7/2016 2:12:11 PM by SYSTEM
                                           (modified after loading)
Analysis Method : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-95-5-1.
                                           OML-3UL-40MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:58:36 AM by SYSTEM
                                           (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



Area Percent Report

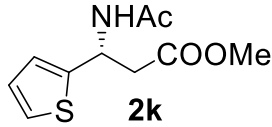
```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 17.034 | BB | 0.4640 | 1.95118e4 | 643.10095 | 99.8336 |
| 2 | 20.359 | MM | 0.4987 | 32.52153 | 1.08685 | 0.1664 |

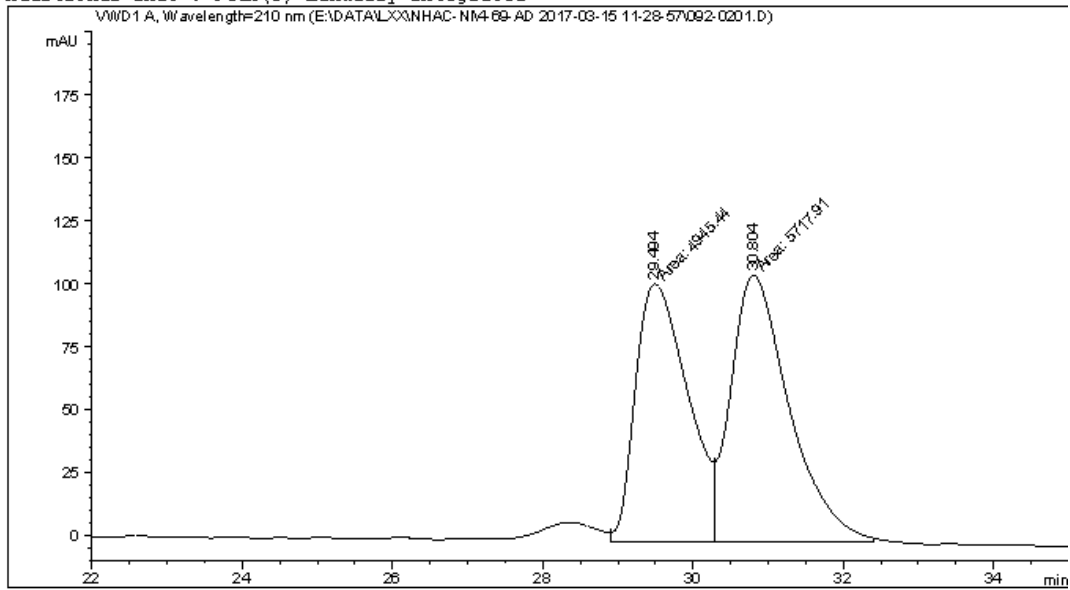
Totals : 1.95443e4 644.18780



Data File E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\092-0201.D
 Sample Name: 4-69-1

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 92
Injection Date  : 3/15/2017 11:45:32 AM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\VWD-AD(1-2)-95-5-1ML-3UL
                  -210NM-35MIN.M
Last changed    : 3/15/2017 11:28:58 AM by SYSTEM
Analysis Method : E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\VWD-AD(1-2)-95-5-1ML-3UL
                  -210NM-35MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:38:08 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



```

=====
                          Area Percent Report
=====
  
```

```

Sorted By      : Signal
Multiplier     : 1.0000
Dilution      : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 29.494 | MF | 0.8057 | 4945.44434 | 102.29678 | 46.3780 |
| 2 | 30.804 | FM | 0.9011 | 5717.90771 | 105.76258 | 53.6220 |

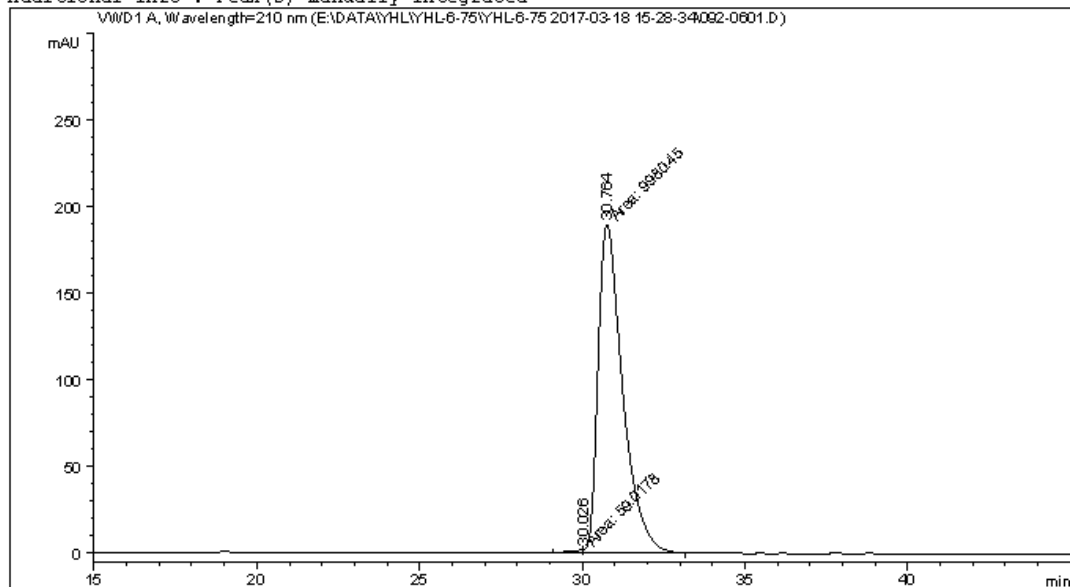
```
Totals :                      1.06634e4  208.05936
```

```

=====
*** End of Report ***
  
```

Data File E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\092-0601.D
Sample Name: LXX-4-75-1

```
=====
Acq. Operator   : SYSTEM                      Seq. Line :    6
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 92
Injection Date  : 3/18/2017 6:27:56 PM       Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M
Last changed    : 3/18/2017 3:44:42 PM by SYSTEM
Analysis Method : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:28:44 AM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
=====
```



```
=====
                          Area Percent Report
=====
```

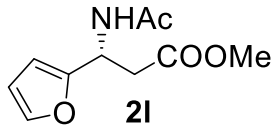
```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 30.026 | MF | 0.5357 | 59.01775 | 1.83632 | 0.5879 |
| 2 | 30.764 | FM | 0.8768 | 9980.45117 | 189.71786 | 99.4121 |

Totals : 1.00395e4 191.55419

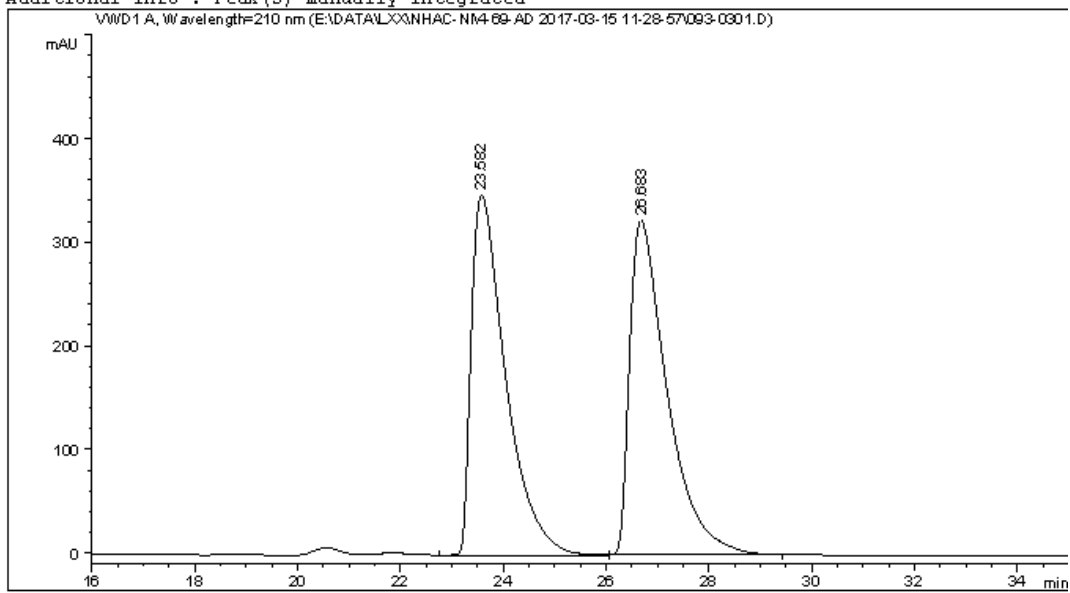
```
=====
*** End of Report ***
```



Data File E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\093-0301.D
 Sample Name: 4-69-2

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    3
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 93
Injection Date  : 3/15/2017 12:21:16 PM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\VWD-AD(1-2)-95-5-1ML-3UL
                  -210NM-35MIN.M
Last changed    : 3/15/2017 11:28:58 AM by SYSTEM
Analysis Method : E:\DATA\LXX\NHAC-NI\4-69-AD 2017-03-15 11-28-57\VWD-AD(1-2)-95-5-1ML-3UL
                  -210NM-35MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:39:55 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

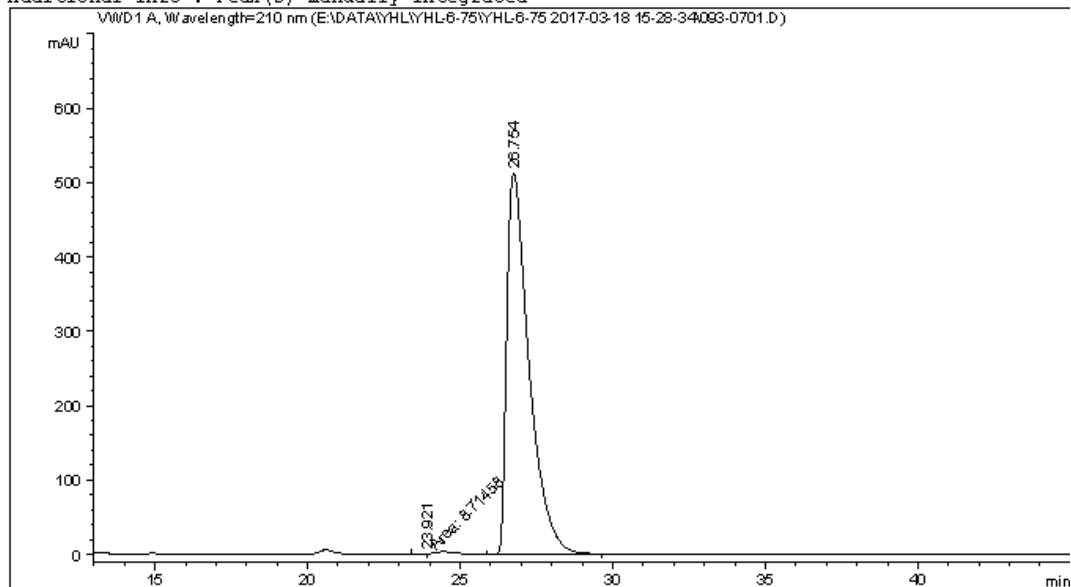
Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 23.582 | BB | 0.6970 | 1.61545e4 | 347.71820 | 49.7255 |
| 2 | 26.683 | BB | 0.7501 | 1.63328e4 | 322.89972 | 50.2745 |

Totals : 3.24873e4 670.61792

=====
 *** End of Report ***

```
=====
Acq. Operator   : SYSTEM                               Seq. Line :    7
Acq. Instrument : 1260HPLC-VWD                       Location  : Vial 93
Injection Date  : 3/18/2017 7:18:38 PM              Inj       :    1
                                                    Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M
Last changed    : 3/18/2017 3:44:42 PM by SYSTEM
Analysis Method : E:\DATA\YHL\YHL-6-75\YHL-6-75 2017-03-18 15-28-34\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 3/20/2017 10:31:14 AM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
=====
```



```
=====
                          Area Percent Report
=====
```

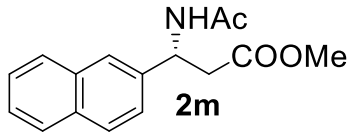
```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 23.921 | MF | 0.2833 | 8.71458 | 5.12678e-1 | 0.0337 |
| 2 | 26.754 | BB | 0.7572 | 2.58685e4 | 512.20599 | 99.9663 |

Totals : 2.58772e4 512.71867

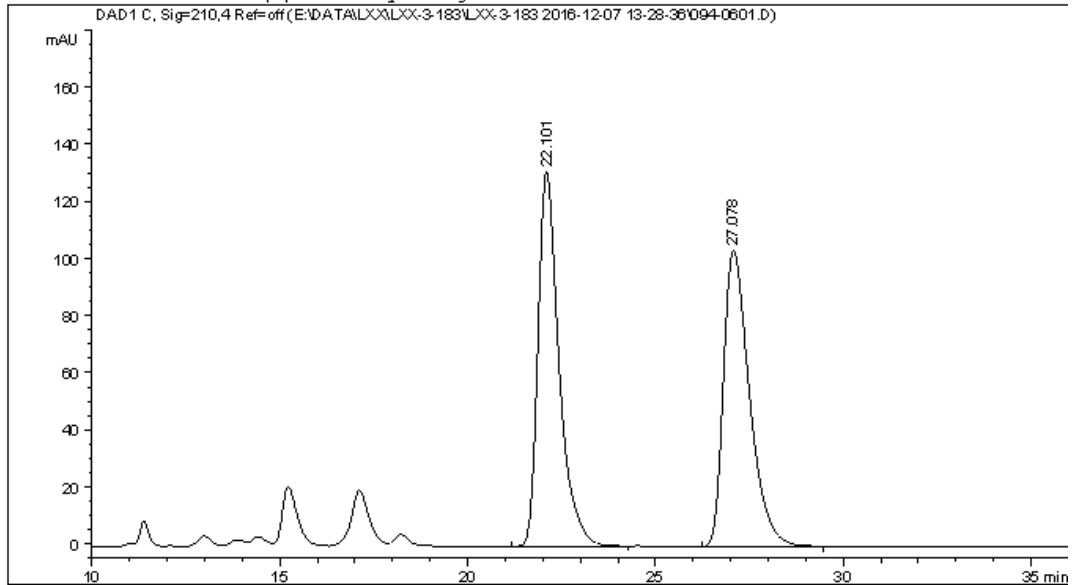
```
=====
*** End of Report ***
```



Data File E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\094-0601.D
 Sample Name: LXX-3-177-3-Rac

```

=====
Acq. Operator   : SYSTEM                               Seq. Line :    6
Acq. Instrument : 1260HPLC-DAD                         Location  : Vial 94
Injection Date  : 12/7/2016 3:39:19 PM                Inj       :    1
                                                    Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-92-8-1.
                  OML-3UL-40MIN.M
Last changed    : 12/7/2016 4:16:49 PM by SYSTEM
                  (modified after loading)
Analysis Method : E:\DATA\LXX\LXX-3-183\LXX-3-183 2016-12-07 13-28-36\DAD-AD (1-2)-92-8-1.
                  OML-3UL-40MIN.M (Sequence Method)
Last changed    : 5/4/2017 11:00:03 AM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

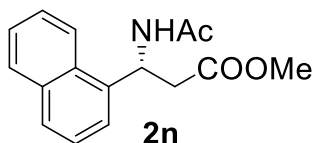
```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 C, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 22.101 | BB | 0.5865 | 5108.32080 | 131.13869 | 50.5745 |
| 2 | 27.078 | BB | 0.7318 | 4992.25635 | 103.67726 | 49.4255 |

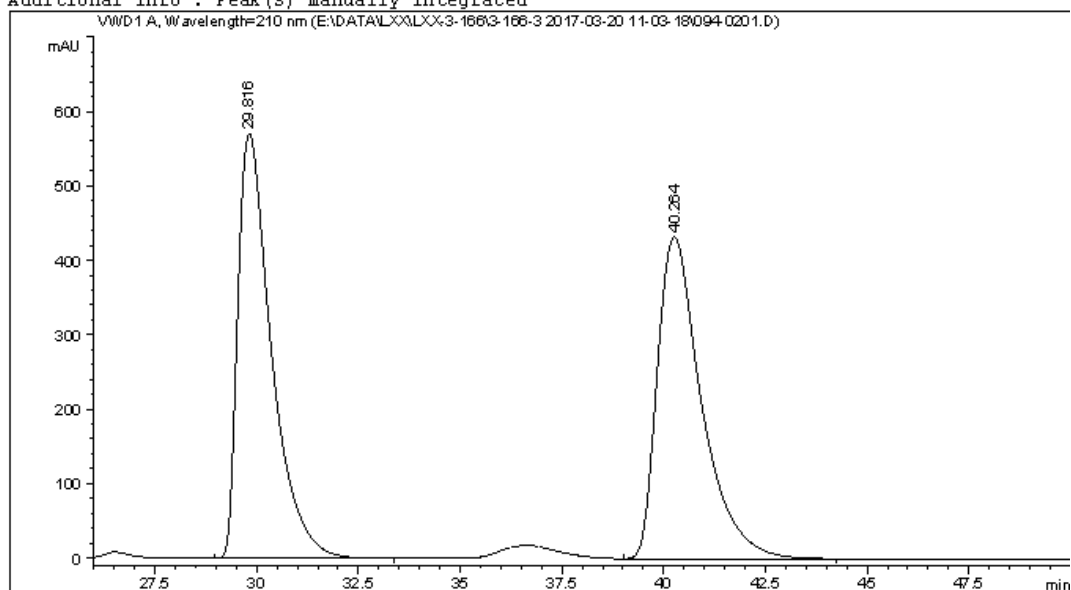
Totals : 1.01006e4 234.81595



Data File E:\DATA\LXX\LXX-3-166\3-166-3 2017-03-20 11-03-18\094-0201.D
 Sample Name: 3-166-3-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    2
Acq. Instrument : 1260HPLC-VWD                 Location  : Vial 94
Injection Date  : 3/20/2017 11:19:47 AM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-166\3-166-3 2017-03-20 11-03-18\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M
Last changed    : 3/20/2017 11:03:18 AM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-3-166\3-166-3 2017-03-20 11-03-18\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:46:47 AM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

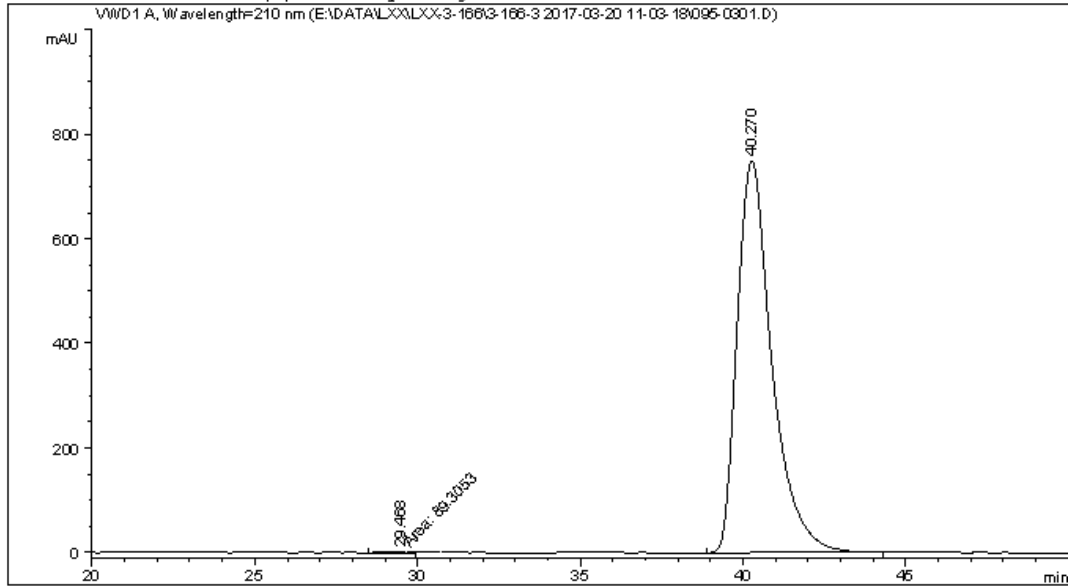
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 29.816 | BB | 0.8666 | 3.26645e4 | 570.84601 | 50.0452 |
| 2 | 40.264 | BB | 1.1399 | 3.26055e4 | 432.31717 | 49.9548 |

Totals : 6.52700e4 1003.16318

=====
 *** End of Report ***

```

=====
Acq. Operator   : SYSTEM                      Seq. Line :    3
Acq. Instrument : 1260HPLC-VWD                Location  : Vial 95
Injection Date  : 3/20/2017 12:10:32 PM      Inj       :    1
                                           Inj Volume: 3.000 µl
Acq. Method     : E:\DATA\LXX\LXX-3-166\3-166-3 2017-03-20 11-03-18\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M
Last changed    : 3/20/2017 11:03:18 AM by SYSTEM
Analysis Method : E:\DATA\LXX\LXX-3-166\3-166-3 2017-03-20 11-03-18\VWD-AD(1-2)-95-5-1ML-
                 3UL-210NM-50MIN.M (Sequence Method)
Last changed    : 5/4/2017 10:48:13 AM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

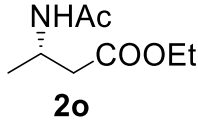
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: VWD1 A, Wavelength=210 nm

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 29.468 | MM | 0.7641 | 89.30527 | 1.94801 | 0.1604 |
| 2 | 40.270 | BB | 1.1289 | 5.55796e4 | 749.71729 | 99.8396 |

Totals : 5.56689e4 751.66530

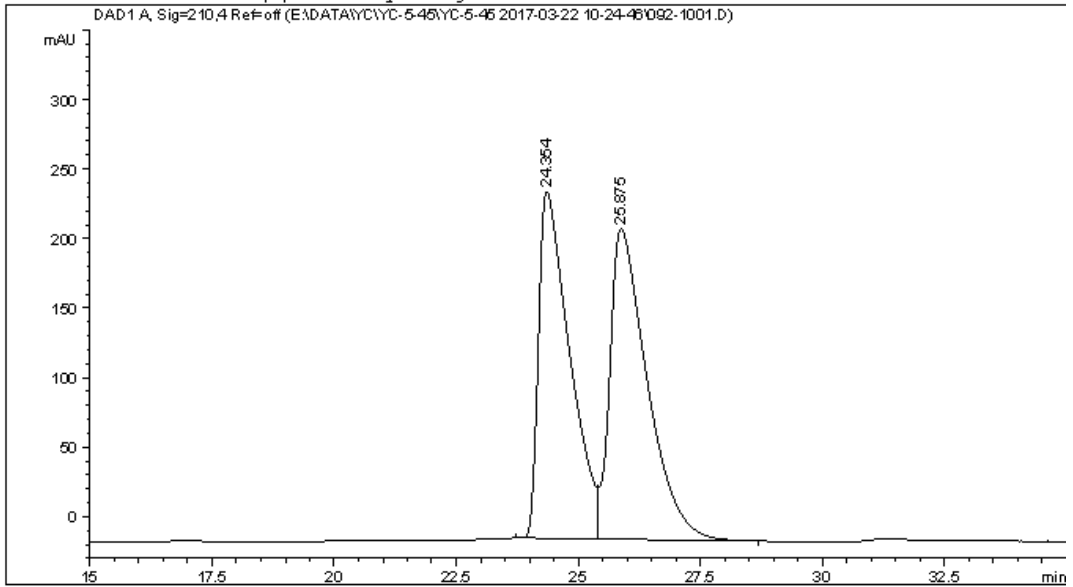
=====
 *** End of Report ***



Data File E:\DATA\YC\YC-5-45\YC-5-45 2017-03-22 10-24-46\092-1001.D
 Sample Name: LXX-4-75-6-Rac

```

=====
Acq. Operator   : SYSTEM                      Seq. Line : 10
Acq. Instrument : 1260HPLC-DAD                Location  : Vial 92
Injection Date  : 3/22/2017 4:39:25 PM       Inj       : 1
                                           Inj Volume: 5.000 µl
Acq. Method     : E:\DATA\YC\YC-5-45\YC-5-45 2017-03-22 10-24-46\DAD-0J(1-6)-95-5-0.5ML-
3UL-200MM-50MIN.M
Last changed    : 3/22/2017 5:22:52 PM by SYSTEM
                 (modified after loading)
Analysis Method : E:\DATA\YC\YC-5-45\YC-5-45 2017-03-22 10-24-46\DAD-0J(1-6)-95-5-0.5ML-
3UL-200MM-50MIN.M (Sequence Method)
Last changed    : 5/4/2017 11:21:40 AM by SYSTEM
                 (modified after loading)
Additional Info : Peak(s) manually integrated
  
```



=====
 Area Percent Report
 =====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
  
```

Signal 1: DAD1 A, Sig=210,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 24.354 | BV | 0.6187 | 1.09966e4 | 249.27791 | 48.0948 |
| 2 | 25.875 | VB | 0.7684 | 1.18679e4 | 223.15918 | 51.9052 |

Totals : 2.28645e4 472.43709

