Supporting Information for:

Highly Enantioselective Insertion of Carbenoids into N-H Bonds Catalyzed by Copper Complexes of Chiral Spiro Bisoxazolines

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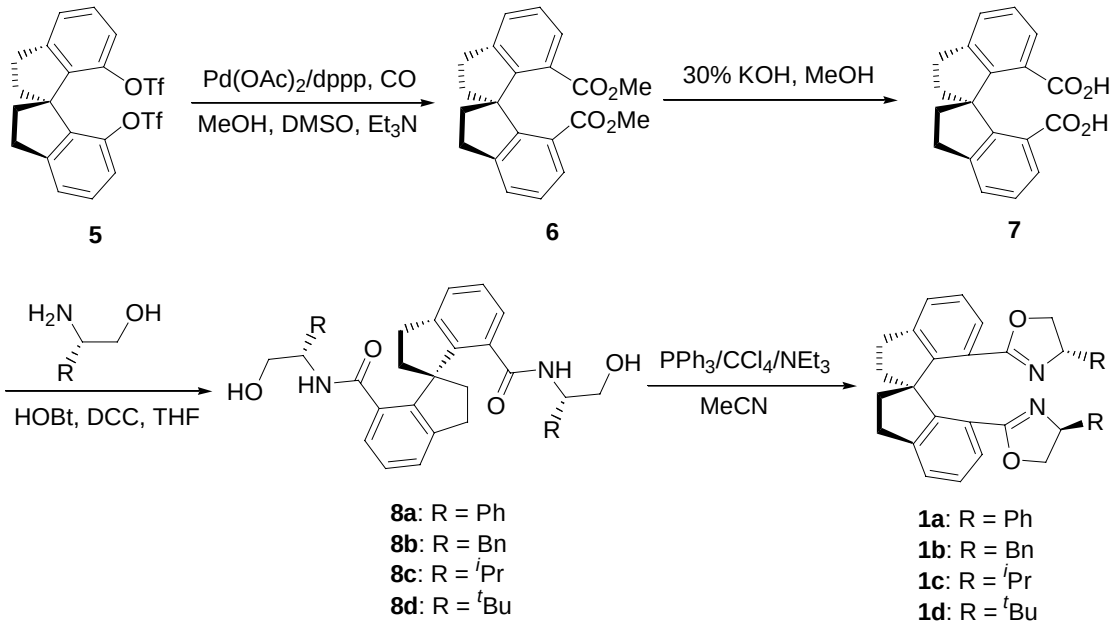
CONTENTS:

General. The reactions and manipulations were performed under an atmosphere of argon by using standard Schlenk techniques. Anhydrous dichloromethane, chloroform, acetonitrile and DMSO were distilled from calcium hydride. Anhydrous benzene and THF was distilled from sodium benzophenone ketyl prior to use. The aniline and substituted anilines were purified by distillation or recrystallization before use. The bis(triflate) **5** was synthesized according to the previous method.[1] CuCl and $CuPF_6(MeCN)_4$ were prepared according to the literature

[1] Liu, B.; Zhu, S.-F.; Wang, L.-X.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2006**, *17*, 634.

method.[2] NaBARF.$(H_2O)_{1.5}$ was prepared according to the literatures.[3] CuOTf(toluene)$_{1/2}$, CuBr(Me_2S), $CuCl_2$, $Cu(OTf)_2$, $Pd(OAc)_2$, dppp and HOBt were purchased from Aldrich or Acros company and used without further purification. NMR spectra were recorded with a Bruker or Varian spectrometer at 400 or 300 (^{1}H NMR), 100 or 75 (^{13}C NMR) MHz with $CDCl_3$ as solvent. Chemical shifts were reported in ppm down field from internal Me_4Si. HRMS were recorded on VG ZAB-HS mass spectrometer with EI resource. Optical rotations were measured using a Perkin Elmer Model 341 polarimeter. HPLC analyses were performed using a Hewlett Packard Model HP 1100 Series chromatography.

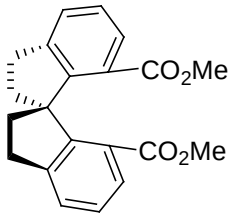
1. Preparation of Chiral Spiro Bisoxazoline Ligands 1



Synthesis of (*S*)-1,1′-spirobiindanyl-7,7′-dicarboxylic acid dimethyl ester [(*S*)-6]

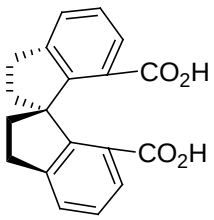
[2] Inorg. Synth. Vol. II, p. 1

[3] (a) Brookhart, M.; Grant, B.; Volpe, A. F. *Organometallics* **1992**, *11*, 3920. (b) Nishida, H.; Takada, N.; Yoshimura, M.; Sonoda, T.; Kobayashi, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2600.



A mixture of bis(triflate) (*S*)-**5** (5.2 g 10 mmol), $Pd(OAc)_2$ (225 mg, 1.0 mmol), 1,3-bis(diphenylphosphino)propane (dppp, 412 mg, 1.0 mmol), MeOH (60 mL), DMSO (90 mL) and Et_3N (24 mL) was saturated with CO and stirred under CO atmosphere at 70 ^oC for full conversion. After cooling to room temperature, the reaction mixture was concentrated in reduced pressure. The residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1:8) to afford product (*S*)-**6** (2.85 g, 85%) as a white solid. Mp 118–120 ^oC; $[\alpha]^{20}_D$ = –278 (*c* 1.0, $CHCl_3$); ^1H NMR δ 2.27–2.32 (m, 2H), 2.53–2.61 (m, 2H), 3.00–3.11 (m, 4H), 3.16 (s, 6H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR δ 30.9, 38.3, 51.3, 63.3, 126.5, 126.9, 128.3, 128.7, 145.3, 149.7, 167.9; HRMS (EI) Calcd for $C_{21}H_{20}O_4$: 336.1362; Found: 336.1367.

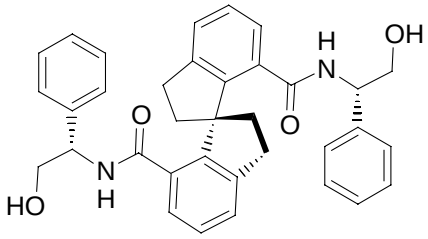
Synthesis of (*S*)-1,1′-spirobiindanyl-7,7′-dicarboxylic acid [(*S*)-7] [1]



The compound (*S*)-**6** (3.1 g, 9.2 mmol) was added to a solution of MeOH (40 mL) and 30% aqueous KOH (40 mL) and stirred at refluxing for 10 h. The resulting mixture was cooled to room temperature, diluted with water (200 mL) and adjusted pH to 4~5 with 6 M HCl, and extracted with ethyl acetate (120 mL) for three times. The combined organic layer was washed with water and saturated brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1:1) to afford product (*S*)-**7** (2.8 g, 97%). Further purification by recrystallization

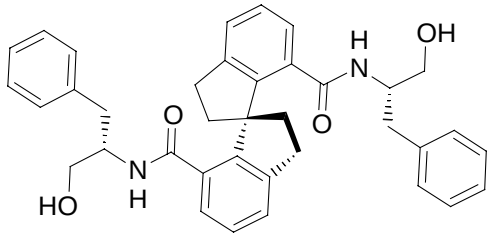
from toluene afforded white solid. Mp = 230–231 °C; ^{1}H NMR δ 2.22–2.27 (m, 2H), 2.43–2.51 (m, 2H), 2.97–3.13 (m, 4H), 7.12 (t, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 10.8 (brs, 2H).

Synthesis of (*S*$_a$,*S*,*S*)-7,7′-bis[N-(2-hydroxy-1-phenylethyl)amide]-1,1′-spirobiindane [(*S*$_a$,*S*,*S*)-8a] [1]



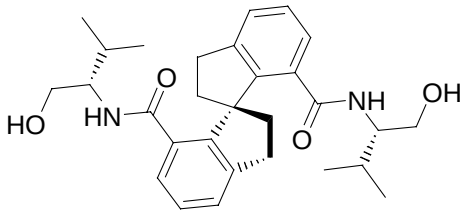
A solution of (*S*)-**7** (308 mg, 1.0 mmol), dicyclohexyl carbodiimide (870 mg, 4.2 mmol), benzotriazol-1-ol (300 mg, 2.2 mmol) and (*S*)-2-amino-2-phenylethanol (300 mg, 2.2 mmol) in dry THF was cooled to –5 °C and stirred for 1 hour. After spontaneously warmed to room temperature the mixture was stirred for over night. The resulting mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography (ethyl acetate) to afford (*S*$_a$,*S*,*S*)-**8a** (475 mg, 87%) as a white solid. Mp 104–107 °C; $[\alpha]^{20}_D$ –103 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22–1.30 (m, 2H), 2.23–2.29 (m, 2H), 2.44–2.50 (m, 2H), 2.86 (s, 2H), 2.94–3.02 (m, 4H), 3.50–3.61 (m, 4H), 4.42–4.46 (m, 2H), 6.91–6.99 (m, 6H), 7.14 (t, *J* = 7.6 Hz, 2H), 7.24–7.30 (m, 8H).

Synthesis of (*S*$_a$,*S*,*S*)-7,7′-bis[N-(1-benzyl-2-hydroxyethyl)amide]-1,1′-spirobiindane [(*S*$_a$,*S*,*S*)-8b]



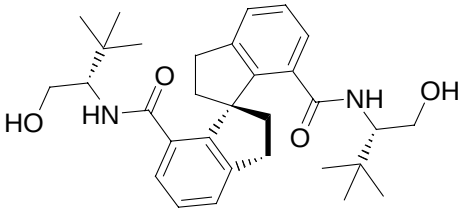
The compound (S_a,*S*,*S*)-**8b** was synthesized from (*S*)-2-amino-3-phenylpropan-1-ol in 99% yield by the same procedure as that for (S_a,*S*,*S*)-**8a**. White solid, mp 175–178 ^oC; $[\alpha]^{20}_D$ = –106 (*c* 1.0, $CHCl_3$); ^1H NMR: δ 2.23–2.27 (m, 2H), 2.35–2.49 (m, 6H), 2.98–3.00 (m, 6H), 3.18–3.28 (m, 4H), 3.68–3.69 (m, 2H), 6.90 (d, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.2 Hz, 3H), 7.15–7.19 (m, 4H), 7.22–7.28 (m, 5H); ^{13}C NMR: δ 30.7, 26.1, 40.3, 53.9, 62.2, 63.4, 126.3, 126.7, 127.4, 128.7, 129.3, 133.9, 138.2, 145.54, 170.5; HRMS (EI) Calcd for $C_{37}H_{38}N_2O_4$: 574.2832; Found: 574.2834.

Synthesis of (S_a,*S*,*S*)-7,7′-bis[N-(1-hydroxymethyl-2-methylpropyl)amide]-1,1′-spirobiindane [(S_a,*S*,*S*)-8c]



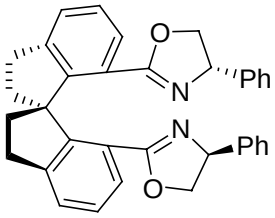
The compound (S_a,*S*,*S*)-**8c** was synthesized from (*S*)-2-amino-3-methylbutan-1-ol in 99% yield by the same procedure as that for (S_a,*S*,*S*)-**8a**. White solid, mp 166–170 ^oC; $[\alpha]^{20}_D$ = –126 (*c* 1.0, $CHCl_3$); ^1H NMR: δ 0.81 (t, *J* = 6.9Hz, 12H), 1.63–1.67 (m, 2H), 2.28–2.34 (m, 2H), 2.44–2.48 (m, 2H), 2.99–3.04 (m, 6H), 3.13–3.16 (m, 2H), 3.24–3.35 (m, 4H), 6.85 (d, 2H, *J* = 6.9 Hz), 7.17–7.32 (m, 6H); ^{13}C NMR: δ 18.9, 19.4, 28.6, 30.5, 40.1, 58.9, 63.2, 126.0, 126.3, 127.3, 134.2, 145.1, 171.0; HRMS (EI) Calcd for $C_{29}H_{38}N_2O_4$: 478.2832; Found: 478.2839.

Synthesis of (S_a,*S*,*S*)-7,7′-bis[N-(2-hydroxy-1-*tert*-butylethyl)amide]-1,1′-spirobiindane [(S_a,*S*,*S*)-8d]



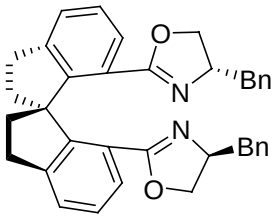
The compound (S_a,*S*,*S*)-**8d** was synthesized from (*S*)-2-amino-3,3-dimethylbutan-1-ol in 99% yield by the same procedure as that for (S_a,*S*,*S*)-**8a**. White solid, mp 200–203 °C, $[\alpha]^{20}_D$ = –66.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 0.79 (s, 18H), 2.24–2.31 (m, 2H), 2.44–2.52 (m, 2H), 2.71 (brs, 2H), 2.98–3.03 (m, 4H), 3.28–3.33 (m, 4H), 3.45–3.52 (m, 2H), 6.70 (d, *J* = 6.8 Hz, 2H), 7.22–7.29 (m, 6H); ^{13}C NMR: δ 27.1, 30.7, 33.9, 40.3, 61.5, 63.0, 126.3, 126.7, 126.5, 134.6, 145.3, 171.3; HRMS (EI) Calcd for $C_{31}H_{42}N_2O_4$: 506.3145; Found: 506.3136.

Synthesis of (S_a,*S*,*S*)-7,7′-bis[4-phenyloxazolin-2-yl]-1,1′-spirobiindane [(S_a,*S*,*S*)-1a] [1]



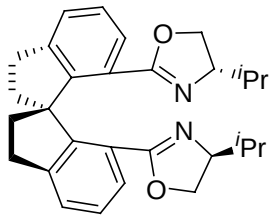
A solution of (S_a,*S*,*S*)-**8a** (234 mg, 0.42 mmol), triphenylphosphine (440 mg, 1.68 mmol), triethylamine (170 mg, 1.68 mmol), tetrachloromethane (260 mg, 1.68 mmol) in dry acetonitrile was stirred over night at room temperature. After concentrated in vacuum, the residue was dissolved in CH_2Cl_2, washed with water, dried over anhydrous magnesium sulfate, and then concentrated in vacuum. The crude product was purified by chromatography on silica gel column (ethyl acetate/petroleum ether = 1:3) to afford (S_a,*S*,*S*)-**1a** (200 mg, 93%) as a white solid. Mp 167–169 °C; $[\alpha]^{20}_D$ –321 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.31 (dd, *J* = 4.8 and 7.2 Hz, 2H), 2.60 (q, *J* = 10.8 Hz, 2H), 2.98–3.16 (m, 4H), 3.34–3.41 (m, 2H), 3.72 (t, *J* = 7.2 Hz, 2H), 4.98 (dd, *J* = 3.0 and 6.9 Hz, 2H,), 7.05–7.08 (m, 4H), 7.18–7.28 (m, 8H), 7.36 (d, *J* = 6.9 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 2H).

Synthesis of (*S*$_a$,*S*,*S*)-7,7′-bis(4-benzyloxazolin-2-yl)-1,1′-spirobiindane [(*S*$_a$,*S*,*S*)-1b]



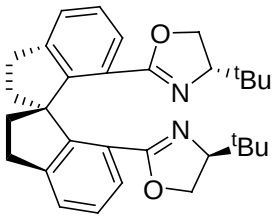
The compound (*S*$_a$,*S*,*S*)**-1c** was synthesized from (*S*$_a$,*S*,*S*)**-8c** in 80% yield by the same procedure as that for (*S*$_a$,*S*,*S*)**-1a**. White solid, mp 49–52 ^{o}C; $[\alpha]^{20}_{D}$ = –220 (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 2.03 (dd, *J* = 9.6 and 4.4 Hz, 2H), 2.24 (dd, *J* = 7.6 and 4.4 Hz, 2H), 2.63–2.68 (m, 4H), 2.92–2.98 (m, 2H), 2.96–3.04 (m, 2H), 3.27 (t, *J* = 8.8 Hz, 2H), 3.57 (t, *J* = 7.2 Hz, 2H), 4.11–4.16 (m, 2H), 7.08–7.27 (m, 14H), 7.54–7.56 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR: δ 30.7, 36.1, 40.3, 53.9, 62.2, 63.4, 126.3, 126.6, 126.7, 127.4, 128.7, 129.3, 133.9, 138.2, 145.5, 170.5; HRMS (EI) Calcd for $C_{37}H_{34}N_2O_2$: 538.2620; Found: 538.2614.

Synthesis of (*S*$_a$,*S*,*S*)-7,7′-bis(4-isopropyloxazolin-2-yl)-1,1′-spirobiindane [(*S*$_a$,*S*,*S*)-1c]



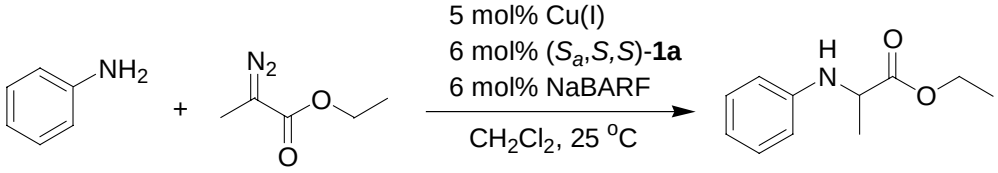
The compound (*S*$_a$,*S*,*S*)**-1c** was synthesized from (*S*$_a$,*S*,*S*)**-8c** in 73% yield by the same procedure as that for (*S*$_a$,*S*,*S*)**-1a**. White solid, mp = 64–66 ^{o}C; $[\alpha]^{20}_{D}$ = –353 (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 0.67 (d, *J* = 6.9 Hz, 6H), 0.77 (d, *J* = 6.6 Hz, 6H), 1.11–1.20 (m, 2H), 2. 23 (dd, *J* = 7.2 and 4.5 Hz, 2H), 2.62–2.72 (m, 2H), 2.91–3.07 (m, 6H), 3.33 (dd, *J* = 7.8 and 1.5 Hz, 2H), 3.48–3.62 (m, 4H), 7.15 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR: δ 17.8, 19.6, 30.6, 32.4, 38.4, 69.6, 72.3, 125.8, 126.4, 127.8, 145.1, 148.5, 163.4; HRMS (EI) Calcd for $C_{29}H_{34}N_2O_2$: 442.2620; Found: 442.2633.

Synthesis of (S_a,*S*,*S*)-7,7′-bis(4-*tert*-butyloxazolin-2-yl)-1,1′-spirobiindane [(S_a,*S*,*S*)-1d]



The compound (S_a,*S*,*S*)-**1d** was synthesized from (S_a,*S*,*S*)-**8d** in 25% yield by the same procedure as that for (S_a,*S*,*S*)-**1a**. White solid, mp 149–152 °C; $[\alpha]^{20}_D$ = –395 (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 0.75 (s, 18H), 2.19–2.25 (m, 2H), 2.46–2.57 (m, 2H), 2.91–3.07 (m, 6H), 3.58–3.64 (m, 4H), 7.16 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.71 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR: δ 25.8, 30.6, 33.7, 38.7, 68.1, 74.9, 124.2, 125.9, 126.5, 128.7, 144.9, 149.0, 164.1; HRMS (EI) Calcd for $C_{31}H_{38}N_2O_2$: 470.2933; Found: 470.2922.

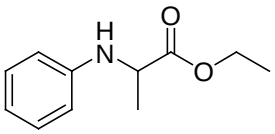
2. General Procedure for Cu-Catalyzed Asymmetric Insertion of Carbenoid into Anilines



The CuCl (1.0 mg, 0.01 mmol, 5 mol%), (S_a,*S*,*S*)-**1a** (6.1 mg, 0.012 mmol, 6 mol%) and NaBARF.$(H_2O)_{1.5}$ (11.3 mg, 0.012 mmol, 6 mol%) were introduced into an oven-dried Schlenk tube in argon-filled glovebox. CH_2Cl_2 (2 mL) was injected and the solution was stirred at room temperature under the argon atmosphere for 2 h, followed by additions of aniline (19 mg, 0.2 mmol) and ethyl α-diazopropionate (26 mg, 0.2 mmol). The resulting mixture was stirred for 2 h and the product was purified by flash chromatography (ethyl acetate/petroleum ether = 1:10).

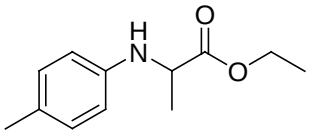
3. Analytical Data for N-H Insertion Products

(*R*)-(+)-Ethyl 2-(phenylamino)propionate (4a) [4]



Colorless oil, 94% yield, ^{1}H NMR: δ 1.25 (t, *J* = 7.2 Hz, 3H), 1.47 (d, *J* = 6.4 Hz, 3H), 4.09–4.21 (m, 4H), 6.61 (d, *J* = 8.4 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 2H); 98% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 5.65 min for major isomer, t_R = 6.26 min for minor isomer]; $[\alpha]^{20}_D$ = +98.8 (c 1.0, EtOH) and $[\alpha]^{20}_D$ = +58.7 (*c* 1.0, $CHCl_3$). [lit [5]: $[\alpha]_D$ = +5.9 (*c* 0.09, $CHCl_3$) for >75% ee, (*R*)].

(+)-Ethyl 2-(*p*-toluidino)propionate (4b) [4]



Colorless oil, 94% yield, ^{1}H NMR: δ 1.24 (t, *J* = 7.2 Hz, 3H), 1.44 (d, *J* = 6.8 Hz, 3H), 2.23 (s, 3H), 4.01–4.20 (m, 4H), 6.54 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H); 91% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 8.17 min for major isomer, t_R = 9.48 min for minor isomer]; $[\alpha]^{20}_D$ = +59.8 (*c* 0.9, EtOH).

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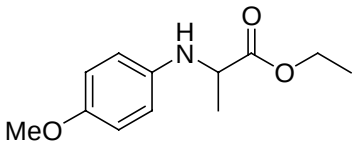
[4] Bachmann, S.; Fielenbach, D.; Jøgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044.

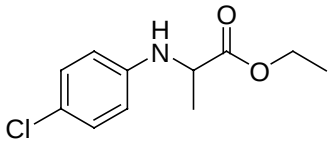
[5] Kurkin, A. V.; Nesterov, V. V.; Karchava, A. V.; Yurovskaya, M. A. *Chem. Heterocycl. Compd.* **2003**, *39*, 1466

(+)-Ethyl 2-(*p*-methoxyphenylamino)propionate (4c) [4]



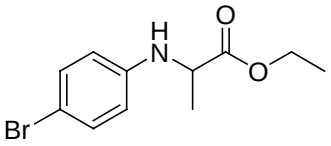
Colorless oil, 96% yield, ^{1}H NMR: δ 1.23 (t, *J* = 6.8 Hz, 3H), 1.44 (d, *J* = 6.8 Hz, 3H), 3.73 (s, 3H), 3.87 (s, 1H), 4.04 (q, *J* = 6.8 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H); 85% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 21.75 min for minor isomer, t_R = 23.36 min for major isomer]; $[\alpha]^{20}_D$ = +41.8 (*c* 1.0, EtOH).

(+)-Ethyl 2-(*p*-chlorophenylamino)propionate (4d)



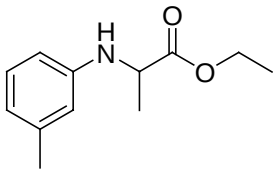
Colorless oil, 92% yield, ^{1}H NMR: δ 1.24 (t, *J* = 7.2 Hz, 3H), 1.43 (d, *J* = 6.8 Hz, 3H), 4.05 (q, *J* = 6.8 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 6.50 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR: δ 14.4, 18.9, 52.3, 61.4, 114.7, 123.0, 129.3, 145.5, 174.5; HRMS (EI) Calcd for $C_{11}H_{14}NO_2Cl$: 227.0713, Found: 227.0716; 98% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 9.40 min for minor isomer, t_R = 10.05 min for major isomer]; $[\alpha]^{20}_D$ = +101 (*c* 1.0, EtOH).

(+)-Ethyl 2-(*p*-bromophenylamino)propionate (4e)



Colorless oil, 95% yield, ^{1}H NMR: δ 1.24 (t, *J* = 7.2 Hz, 3H), 1.44 (d, *J* = 6.8 Hz, 3H), 4.02–4.09 (m, 1H), 4.15–4.24 (m, 3H), 6.46 (d, *J* = 9.2 Hz, 2H), 7.23 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR: δ 14.4, 18.9, 52.2, 61.5, 110.1, 115.2, 132.2, 145.9, 174.4; HRMS (EI) Calcd for $C_{11}H_{14}NO_2Br$: 271.0208, Found: 271.0211; 98% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 10.13 min for minor isomer, t_R = 12.21 min for major isomer]; $[\alpha]^{20}_D$ = +78.9 (*c* 1.0, EtOH).

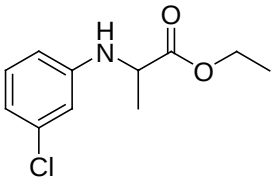
(+)-Ethyl 2-(*m*-toluidino)propionate (4f)



Colorless oil, 92% yield, ^{1}H NMR: δ 1.25 (t, *J* = 7.2 Hz, 3H), 1.46 (d, *J* = 6.4 Hz, 3H), 2.26 (s, 3H), 4.10–4.14 (m, 2H), 4.15–4.21 (m, 2H), 6.41–6.43 (m, 2H), 6.56 (d, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR: δ 14.4, 19.2, 21.7, 52.3, 61.2, 110.7, 114.5, 119.4, 129.3, 139.3, 146.9, 174.8; HRMS (EI) Calcd for $C_{12}H_{17}NO_2$: 207.1259; Found: 207.1263; 96% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.10 min for major isomer, t_R = 6.60 min for minor isomer]; $[\alpha]^{20}_D$ = +72.2 (*c* 0.8, EtOH).

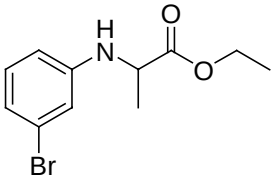
(+)-Ethyl 2-(*m*-chlorophenylamino)propionate (4g) [6]

[6] Marilena, G.; Nicola, C.; Rita, L. M.; Maurizio, M.; Massimo, M. *J. Med. Chem.* **1999**, *42*, 336.



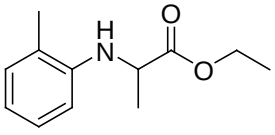
Colorless oil, 95% yield, ^{1}H NMR: δ 1.26 (t, *J* = 7.2 Hz, 3H), 1.46 (d, *J* = 6.8 Hz, 3H), 4.07–4.27 (m, 4H), 6.46 (dd, *J* = 8.4 and 2.4 Hz, 1H), 6.56–6.57 (m, 1H), 6.68–6.70 (m, 1H), 7.6 (t, *J* = 8.0 Hz, 1H); 97% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.59 min for major isomer, t_R = 8.27 min for minor isomer]; $[\alpha]^{20}_D$ = +82.6 (*c* 1.2, EtOH).

(+)-Ethyl 2-(*m*-bromophenylamino)propionate (4h)



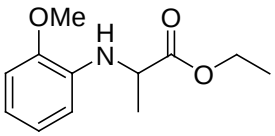
Colorless oil, 96% yield, ^{1}H NMR: δ 1.19 (t, *J* = 6.9 Hz, 3H), 1.38 (d, *J* = 6.9 Hz, 3H), 3.96–4.06 (m, 1H), 4.10–4.18 (m, 3H), 6.42–6.45 (m, 1H), 6.66–6.67 (m, 1H), 6.75–6.78 (m, 1H), 6.93 (t, *J* = 8.1 Hz, 1H); ^{13}C NMR: δ 14.2, 18.7, 51.8, 61.3, 112.1, 116,0, 121.0, 123.3, 130.5, 147.9, 174.1; HRMS (EI) Calcd for $C_{11}H_{14}NO_2Br$: 271.0208. Found: 271.0206; 98% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 7.11 min for major isomer, t_R = 8.54 min for minor isomer]; $[\alpha]^{20}_D$ = +71.7 (*c* 1.0, EtOH).

(+)-Ethyl 2-(*o*-toluidino)propionate (4i)



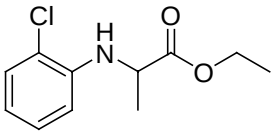
Colorless oil, 95% yield, ^{1}H NMR: δ 1.26 (t, *J* = 7.2 Hz, 3H), 1.51 (d, *J* = 6.8 Hz, 3H), 2.21 (s, 3H), 4.07–4.09 (m, 1H), 4.16–4.23 (m, 3H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.67–6.71 (m, 1H), 7.06–7.11 (m, 2H); ^{13}C NMR: δ 14.4, 17.6, 19.3, 52.2, 61.3, 110.6, 118.0, 122.8, 127.3, 130.6, 144.9, 174.9; HRMS (EI) Calcd for $C_{12}H_{17}NO_2$: 207.1259; Found: 207.1254; 98% ee [HPLC condition: Chiralpak AD-H column, *n*-Hexane/2-PrOH = 99:1, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 13.01 min for major isomer, t_R = 15.71 min for minor isomer]; $[\alpha]^{20}_D$ = +31.9 (*c* 1.0, EtOH).

(+)-Ethyl 2-(*o*-methoxyphenylamino)propionate (4j) [4]



Colorless oil, 86% yield, ^{1}H NMR: δ 1.24 (t, *J* = 7.0 Hz, 3H), 1.50 (d, *J* = 6.4 Hz, 3H), 3.85 (s, 3H), 4.11–4.21 (m, 3H), 4.70 (d, *J* = 7.2 Hz, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 6.68–6.71 (m, 1H), 6.77–6.84 (m, 2H); 98% ee [HPLC condition: Chiralpak AD-H column, *n*-Hexane/2-PrOH = 99:1, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 21.56 min for major isomer, t_R = 25.66 min for minor isomer]; $[\alpha]^{20}_D$ = +23.7 (*c* 1.1, EtOH).

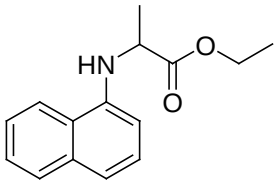
(+)-Ethyl 2-(*o*-chlorophenylamino)propanoate (4k)



Colorless oil, 95% yield, ^{1}H NMR: δ 1.25 (t, *J* = 7.2 Hz, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 4.13–4.22 (m, 3H), 4.80 (d, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.64–6.68 (m, 1H), 7.09–7.13 (m, 1H), 7.25–7.27(m, 1H); ^{13}C NMR δ 14.37, 19.01, 52.08, 61.48, 111.83, 118.31,

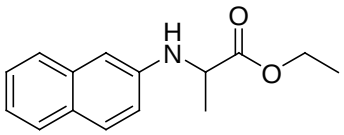
119.91, 127.95, 129.61, 142.85, 174.10; HRMS (EI) Calcd for $C_{11}H_{14}NO_2Cl$: 227.0713, Found: 227.0710; 88% ee [HPLC condition: Chiralcel OD-H column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 7.00 min for major isomer, t_R = 22.99 min for minor isomer]; $[\alpha]^{20}_D$ = +9.8 (*c* 1.1, EtOH).

(-)-Ethyl 2-(naphthalen-1-ylamino)propionate (4l) [4]



Colorless oil, 89% yield, ^{1}H NMR: δ 1.28 (t, *J* = 7.2 Hz, 3H), 1.61 (d, *J* = 6.8 Hz, 3H), 4.20–4.34 (m, 3H), 4.96 (d, *J* = 4.0 Hz, 1H), 6.54 (d, *J* = 7.2 Hz, 1H), 7.26–7.34 (m, 2H), 7.45–7.47 (m, 2H), 7.78–7.80 (m, 1H), 7.90–7.92 (m, 1H); 98% ee [HPLC condition: Chiralpak AD-H column, *n*-Hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 7.81 min for major isomer, t_R = 10.18 min for minor isomer]; $[\alpha]^{20}_D$ = –23.9 (*c* 1.1, EtOH).

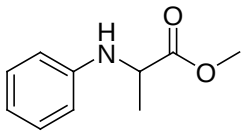
(+)-Ethyl 2-(naphthalen-2-ylamino)propionate (4m)



White solid, 91% yield, mp = 80–82 ^{o}C; ^{1}H NMR: δ 1.27 (t, *J* = 7.2 Hz, 3H), 1.54 (d, *J* = 6.8 Hz, 3H), 4.17–4.36 (m, 4H), 6.78 (s, 1H), 6.90–6.93 (m, 1H), 7.21 (t, *J* = 6.8 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.59–7.68 (m, 3H); ^{13}C NMR: δ 14.2, 18.8, 52.1, 61.2, 105.4, 118.1, 122.4, 126.1, 126.3, 127.6, 129.1, 135.0, 144.3, 174.5; HRMS (EI) Calcd for $C_{15}H_{17}NO_2$: 243.1259. Found: 243.1266; 98% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 9.20 min for major isomer, t_R = 11.26

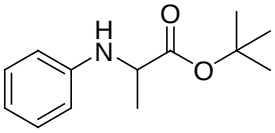
min for minor isomer]; $[\alpha]^{20}_{D}$ = +173 (c 1.0, EtOH).

(+)-Methyl 2-(phenylamino)propionate (4n) [7]



Colorless oil, 78% yield, ^{1}H NMR: δ 1.48 (d, *J* = 5.6 Hz, 3H), 3.73 (s, 3H), 4.15 (brs, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 2H); 96% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 9.79 min for major isomer, t_R = 10.94 min for minor isomer]; $[\alpha]^{20}_{D}$ = +111 (*c* 1.0, EtOH).

(+)-*tert*-Butyl 2-(phenylamino)propionate (4o) [4]



Colorless oil, 93% yield, ^{1}H NMR: δ 1.43 (s, 9H), 4.01 (q, *J* = 6.8 Hz, 1H), 4.14 (brs, 1H), 6.60 (d, *J* = 8.0 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 2H); 96% ee [HPLC condition: Chiralpak AS column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.51 min for major isomer, t_R = 8.60 min for minor isomer]; $[\alpha]^{20}_{D}$ = +43.3 (*c* 1.0, EtOH).

(+)-Ethyl 2-(phenylamino)butyrate (4p)

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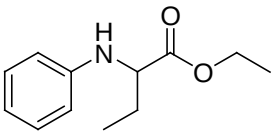
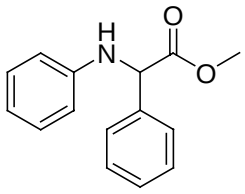
[7] Gately, D. A.; Norton, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 3479



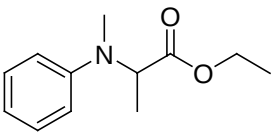
Colorless oil, 51% yield, ^{1}H NMR: δ 1.00 (t, *J* = 7.6 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.77–1.93 (m, 2H), 4.02 (t, *J* = 6.4 Hz, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 6.62 (d, *J* = 7.6 Hz, 2H), 6.72 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR: δ 10.1, 14.5, 26.3, 58.0, 61.2, 113.6, 118.4, 129.5, 147.1, 174.2; HRMS (EI) Calcd for $C_{12}H_{17}NO_2$: 207.1259; Found: 207.1266; 94% ee [HPLC condition: Chiralpak AS column, n-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.41 min for major isomer, t_R = 7.31 min for minor isomer]; $[\alpha]^{20}_D$ = +100 (*c* 1.0, EtOH).

(+)-Methyl 2-phenyl-2-(phenylamino)acetate (4q) [4]



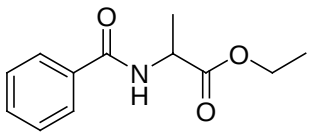
White solid, 85% yield, mp = 76–78 °C; ^{1}H NMR: δ 3.73 (s, 3H), 4.96 (s, 1H), 5.01 (s, 1H), 6.55 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 7.2 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 2H), 7.30–7.37 (m, 3H), 7.49 (d, *J* = 7.2 Hz, 2H); 8% ee [HPLC condition: Chiralpak AS column, n-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 8.68 min for major isomer, t_R = 10.29 min for minor isomer]; $[\alpha]^{20}_D$ = –7.3 (c 1.0, EtOH).

Ethyl 2-(methyl(phenyl)amino)propionate (4r) [4]



Colorless oil, 93% yield, ^{1}H NMR: δ 1.22 (t, *J* = 6.9 Hz, 3H), 1.47 (d, *J* = 7.2 Hz, 3H), 2.89 (s, 3H), 4.14–4.17 (m, 2H), 4.47–4.54 (m, 1H), 6.75–6.80 (m, 3H), 7.21–7.26 (m, 2H); rac. [HPLC condition: Chiralpak AD-H column, *n*-Hexane/2-PrOH = 98:2, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.67 min, t_R = 7.04 min].

Ethyl 2-benzamidopropionate (4s) [8]

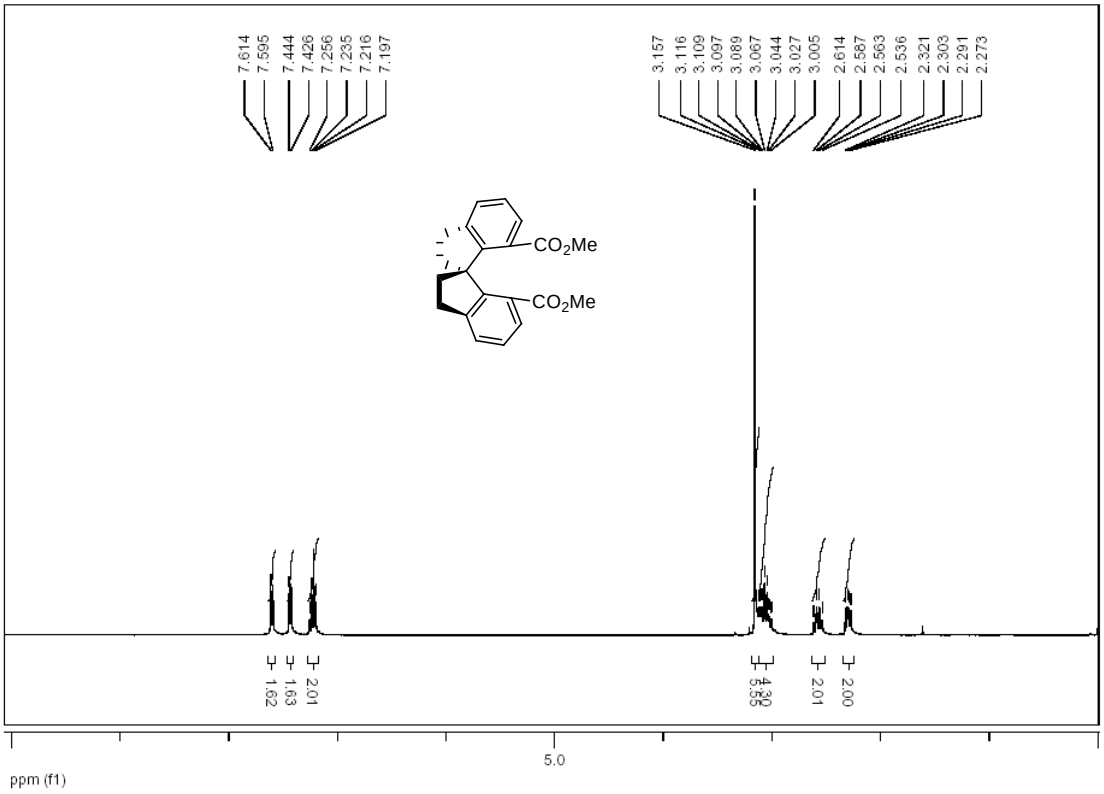


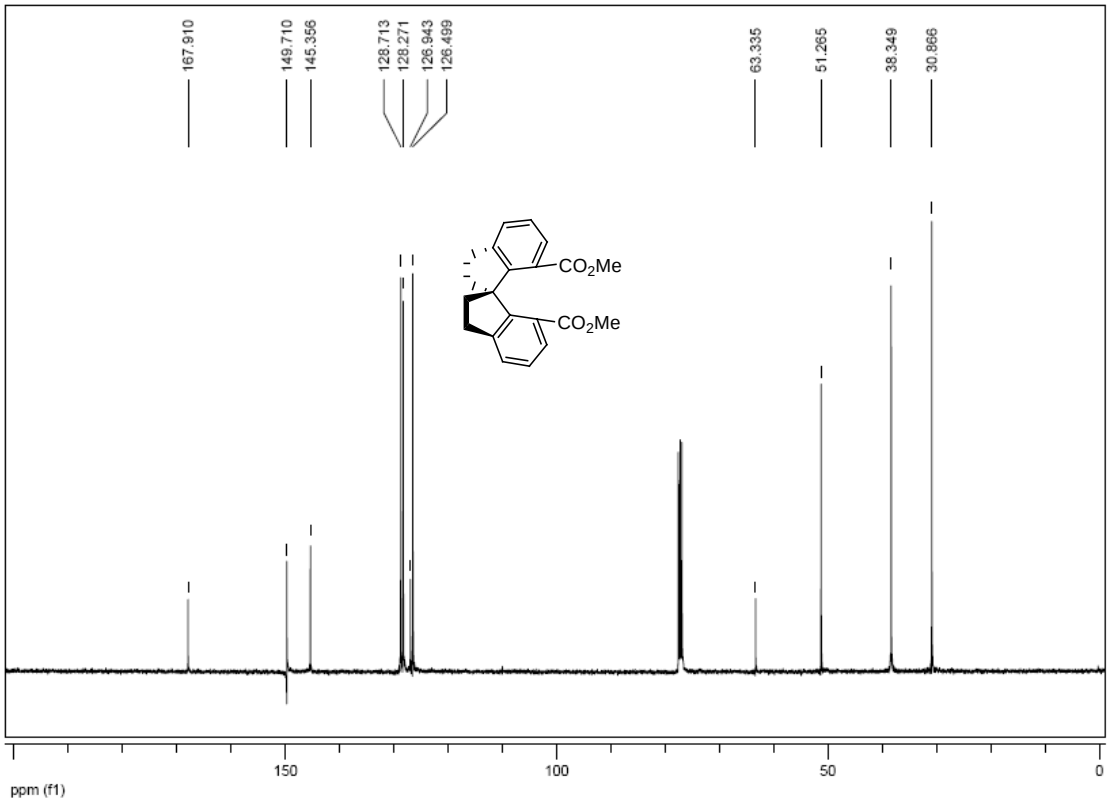
White solid, 55% yield, mp = 74–76 °C; ^{1}H NMR: δ 1.31 (t, *J* = 7.2 Hz, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 4.21–4.27 (m, 2H), 4.74–4.79 (m, 1H), 6.76 (m, 1H), 7.42–7.45 (m, 2H), 7.51–7.56 (m, 3H); rac. [HPLC condition: Chiralcel OB column, *n*-Hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min, wavelength = 235 nm, t_R = 21.22 min, t_R = 27.98 min].

[8] Benati, L.; Nanni, D.; Sangiorgi, C.; Spagnolo, P. *J. Org. Chem* **1996**, *64*, 7836.

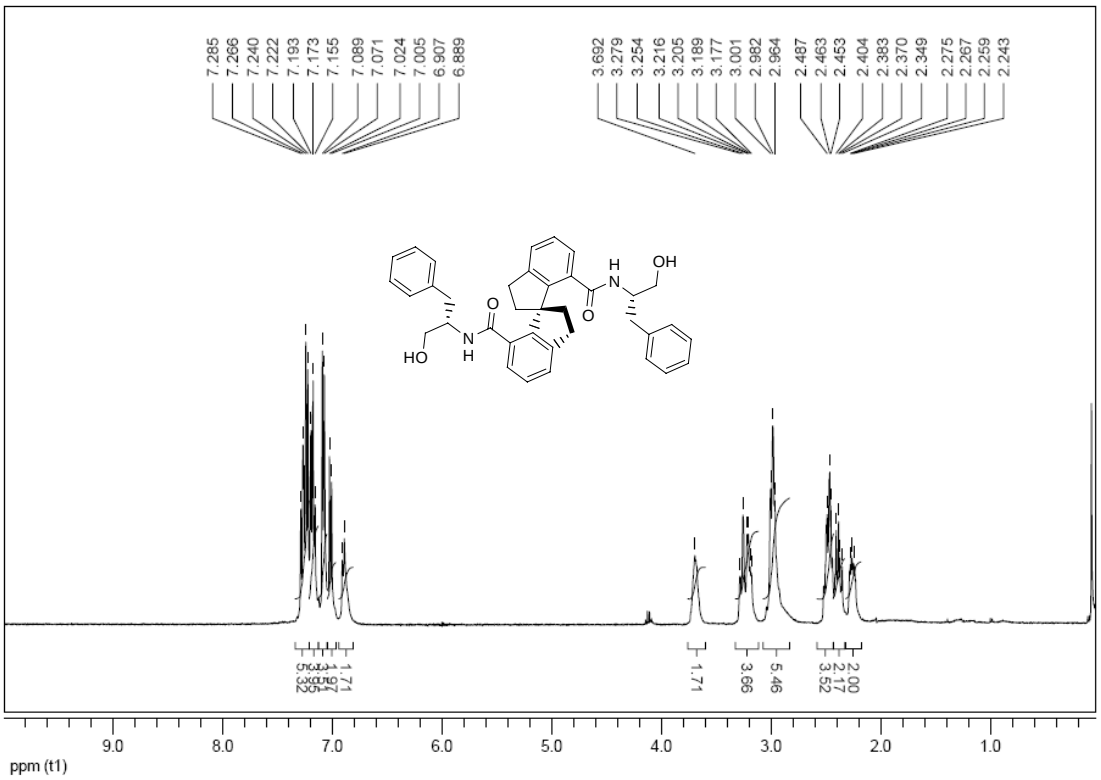
4. NMR Spectra for New Ligands and Intermediates

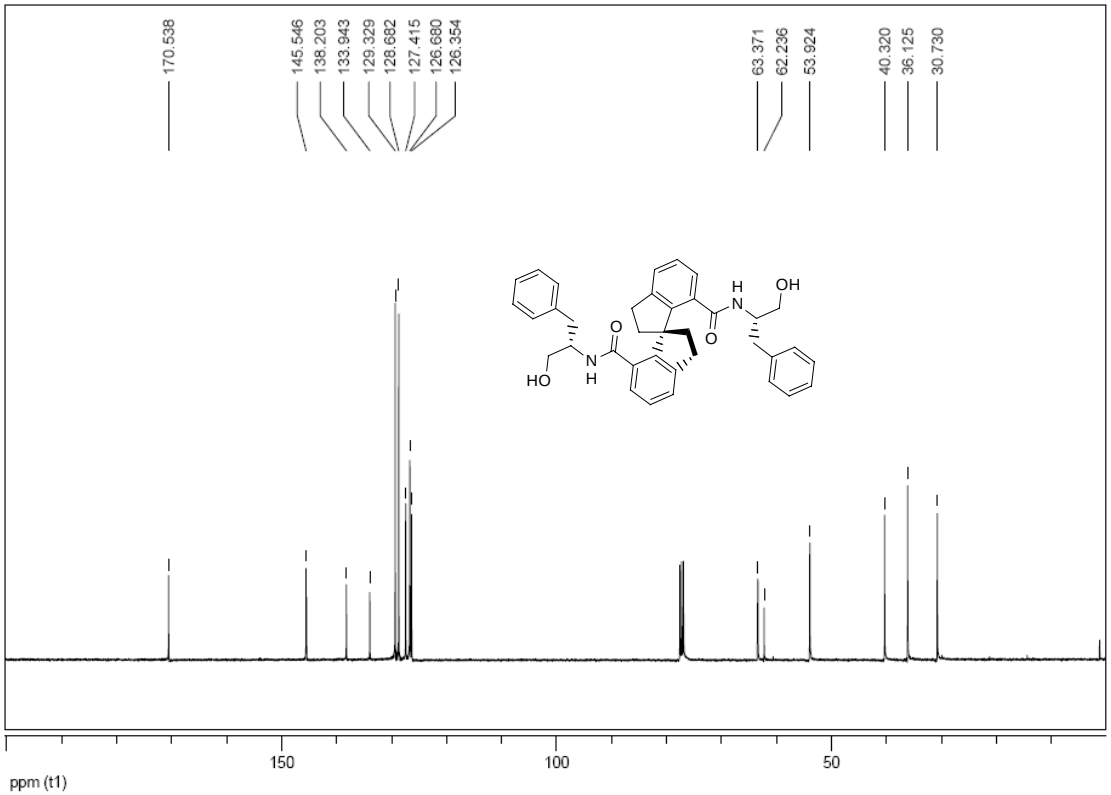
(*S*)-1,1′-Spirobiindanyl-7,7′-dicarboxylic acid dimethyl ester



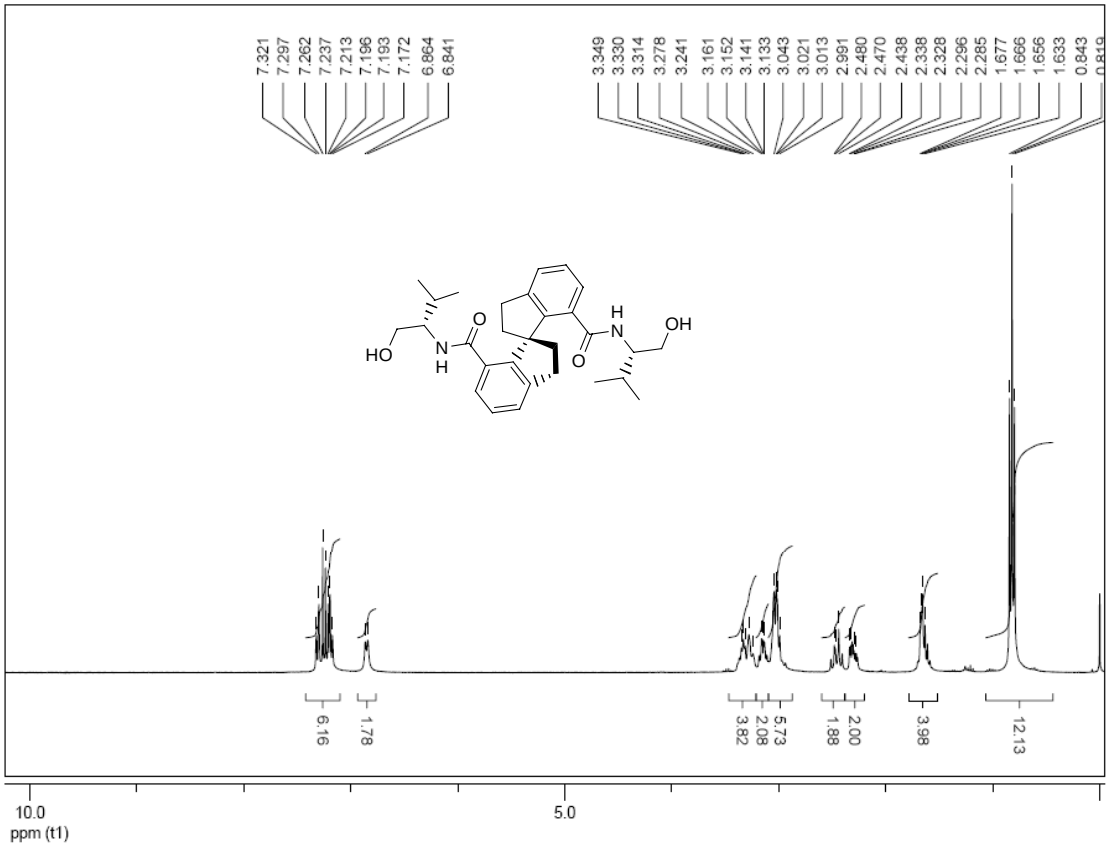


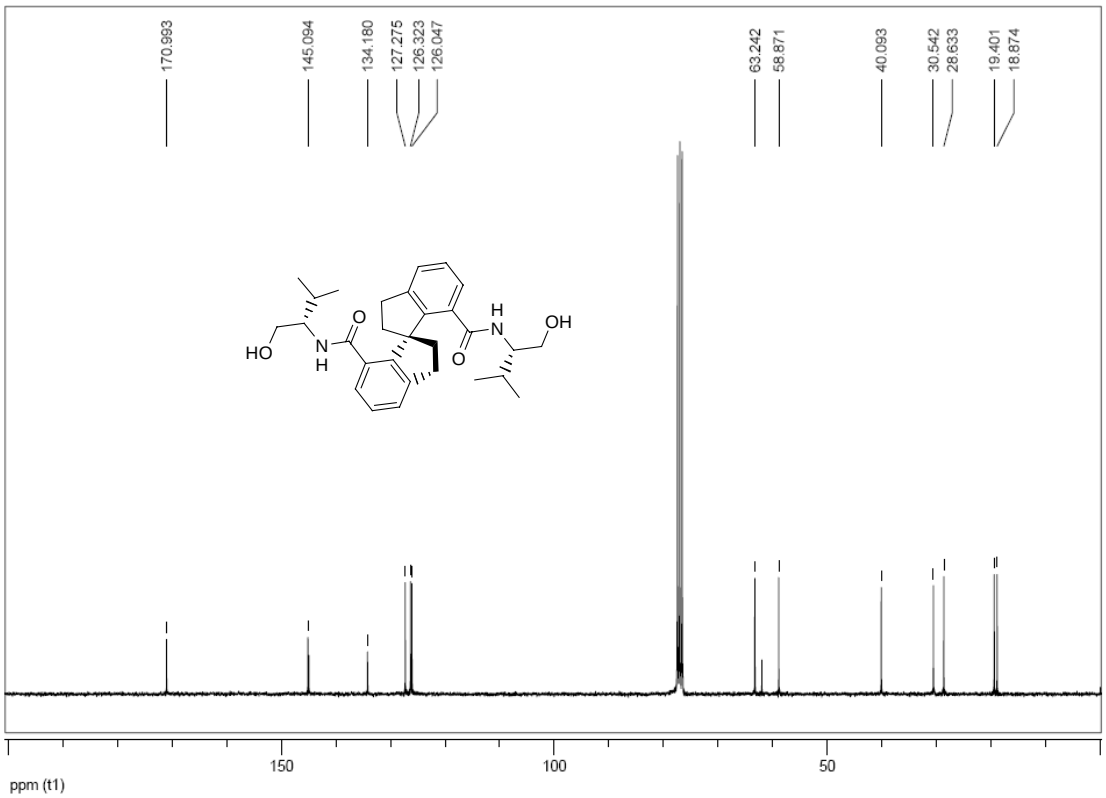
(S_a,*S*,*S*)-7,7′-Bis[N-(1-benzyl-2-hydroxyethyl)amide]-1,1′-spirobiindane



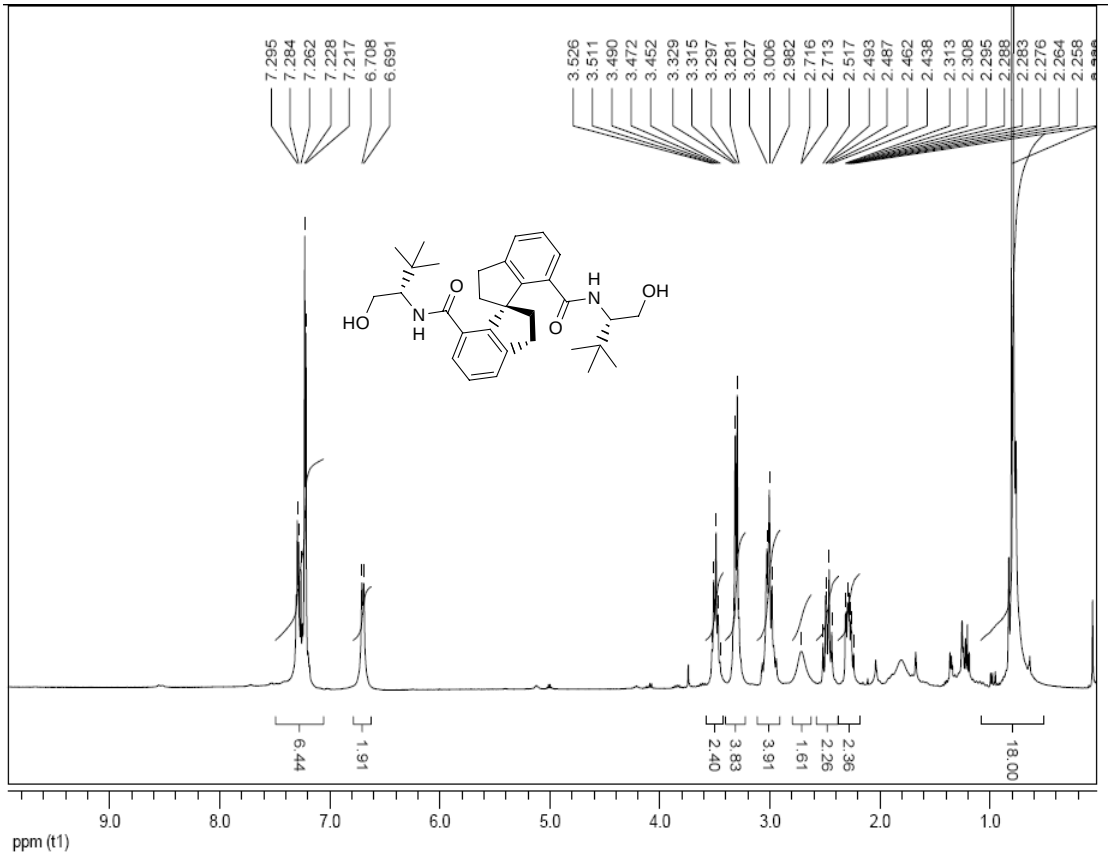


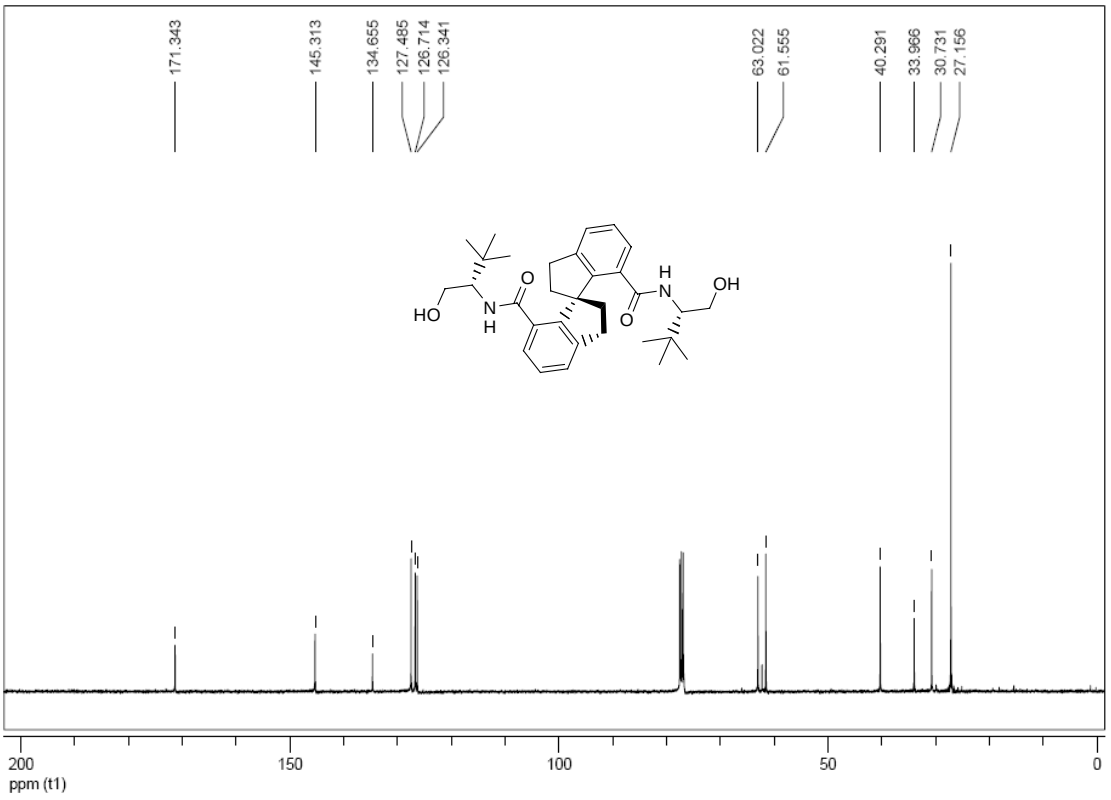
(S_a,*S*,*S*)-7,7′-Bis[N-(1-hydroxymethyl-2-methylpropyl)amide]-1,1′-spirobiindane



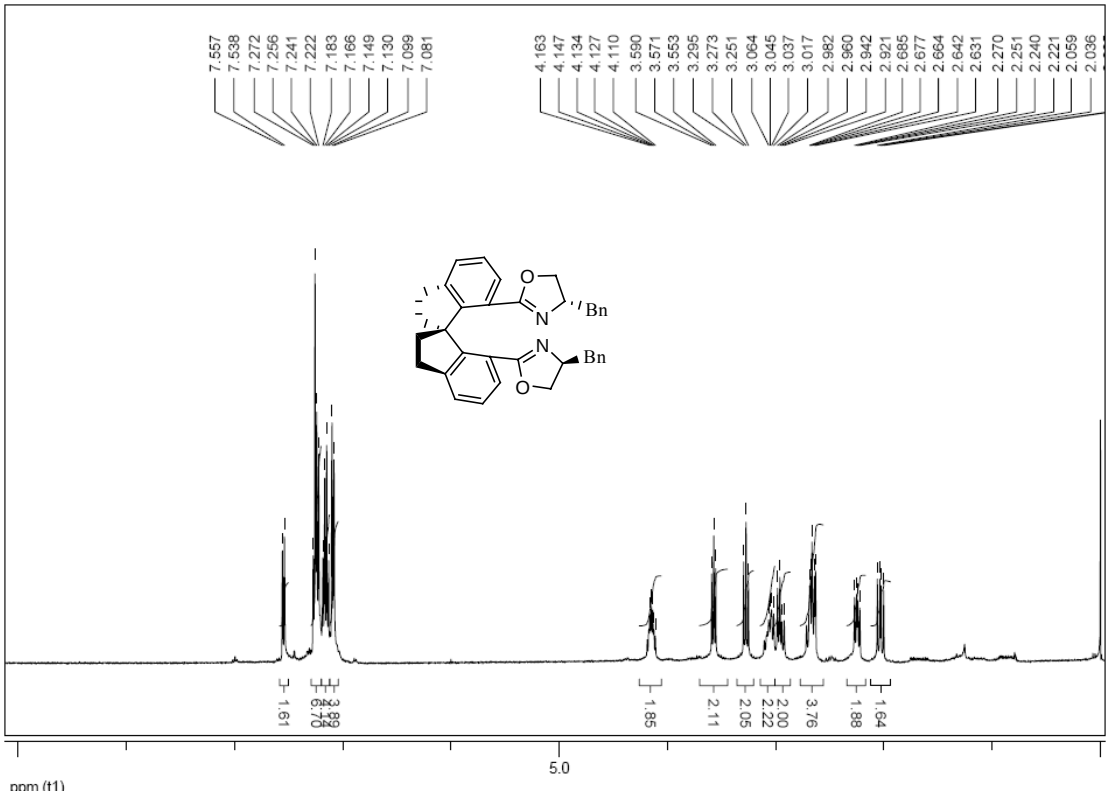


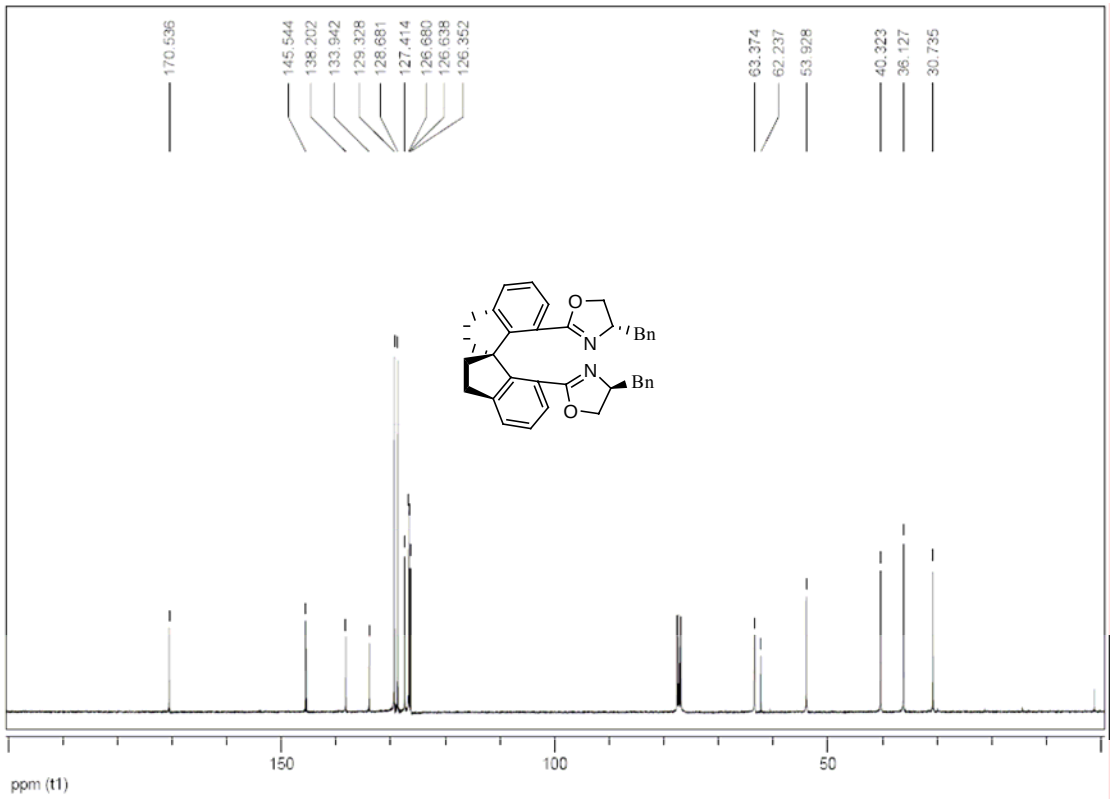
(S_a,*S*,*S*)-7,7′-Bis[N-(2-hydroxy-1-*tert*-butylethyl)amide]-1,1′-spirobiindane



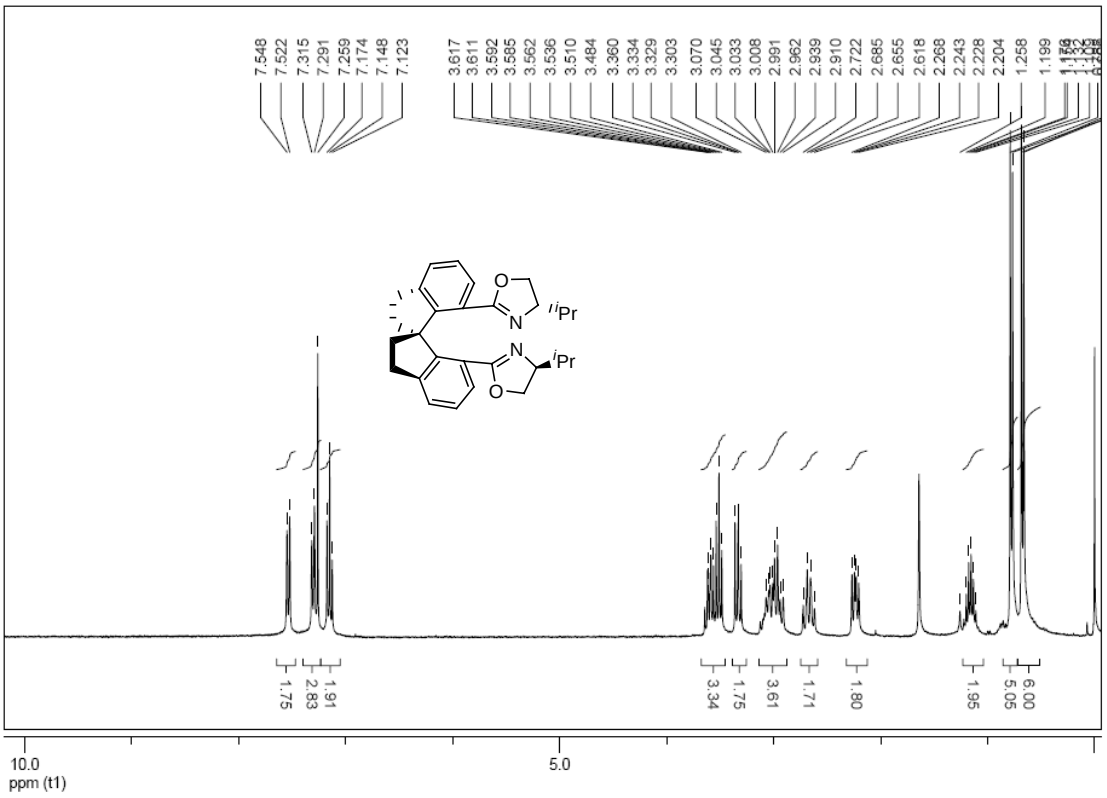


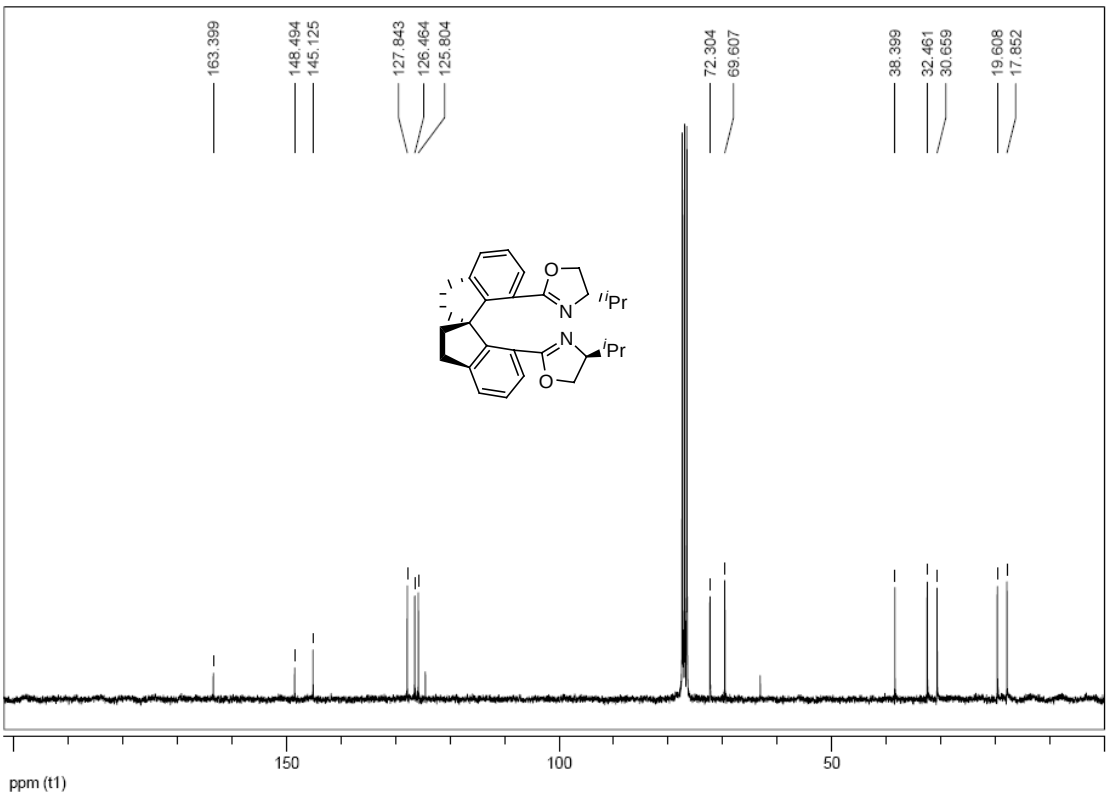
(S_a,*S*,*S*)-7,7′-Bis(4-benzyloxazolin-2-yl)-1,1′-spirobiindane



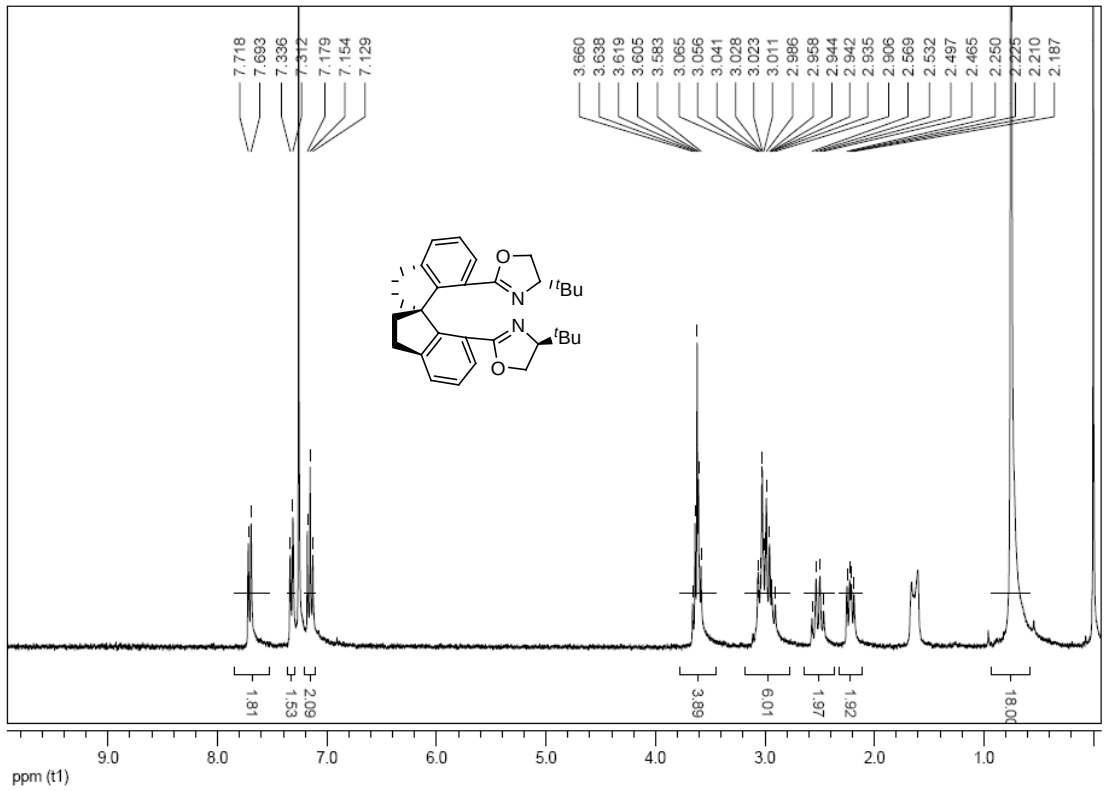


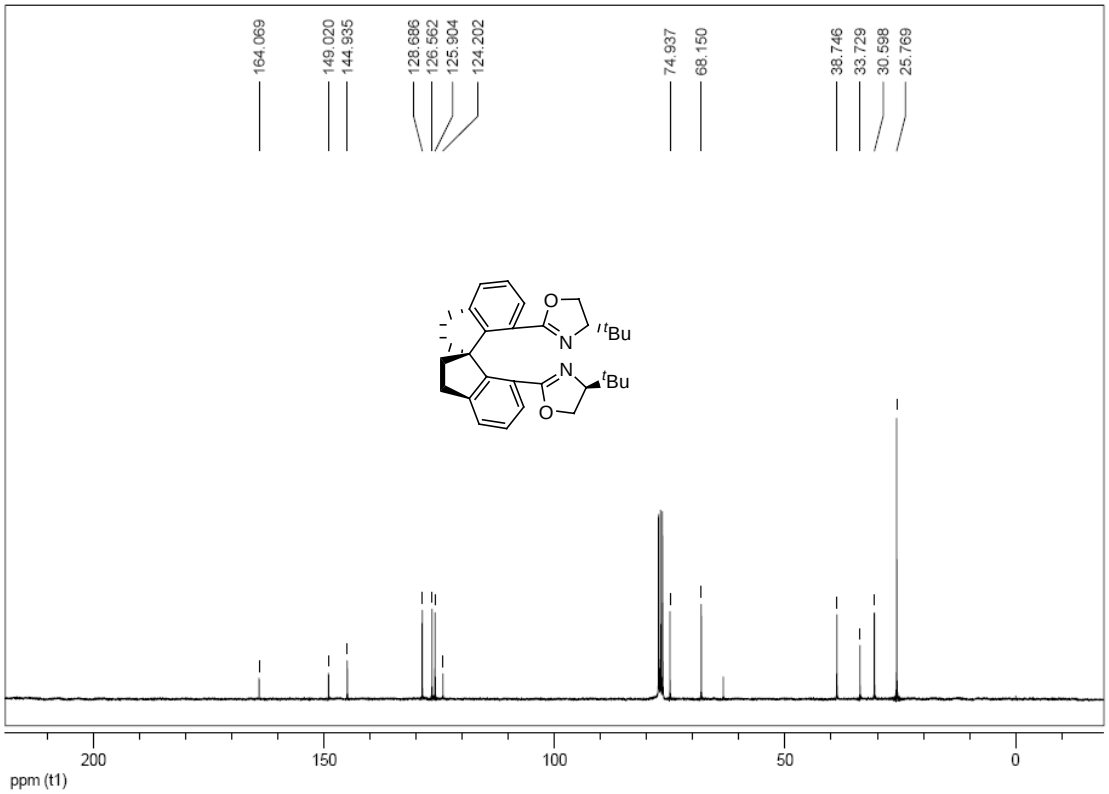
(S_a,*S*,*S*)-7,7′-Bis(4-isopropyloxazolin-2-yl)-1,1′-spirobiindane





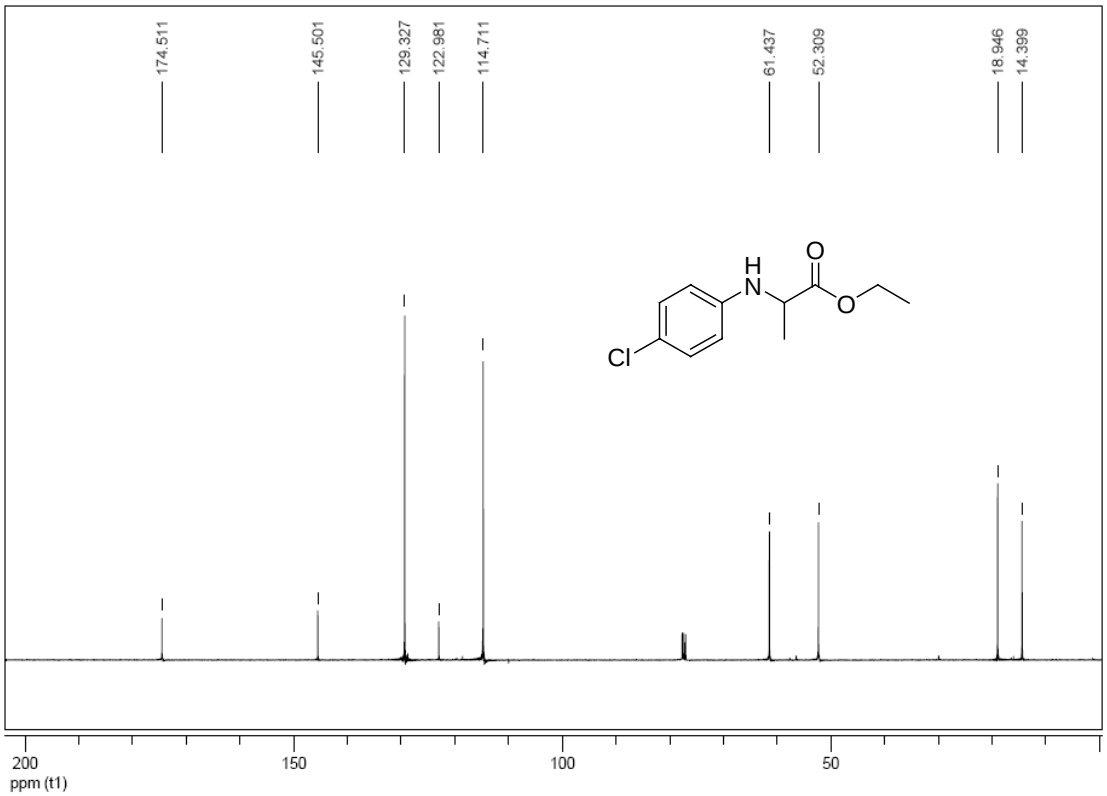
(S_a,*S*,*S*)-7,7′-Bis (4-*tert*-butyloxazolin-2-yl)-1,1′-spirobiindane



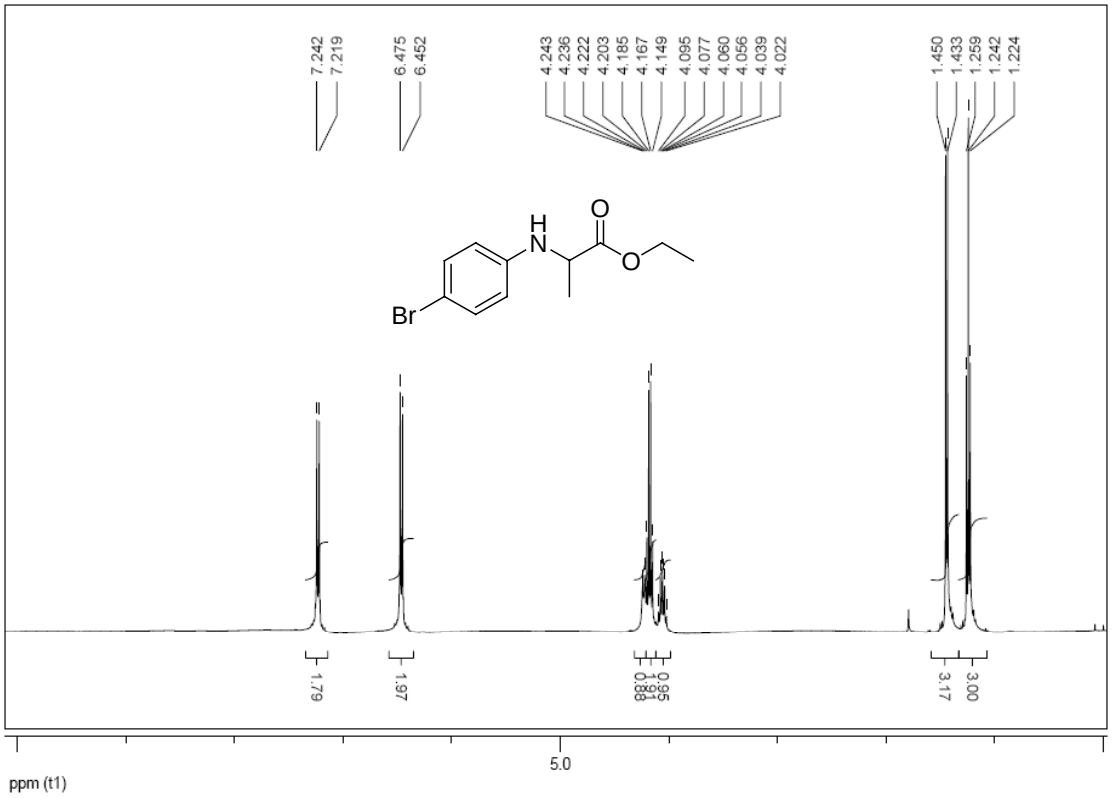


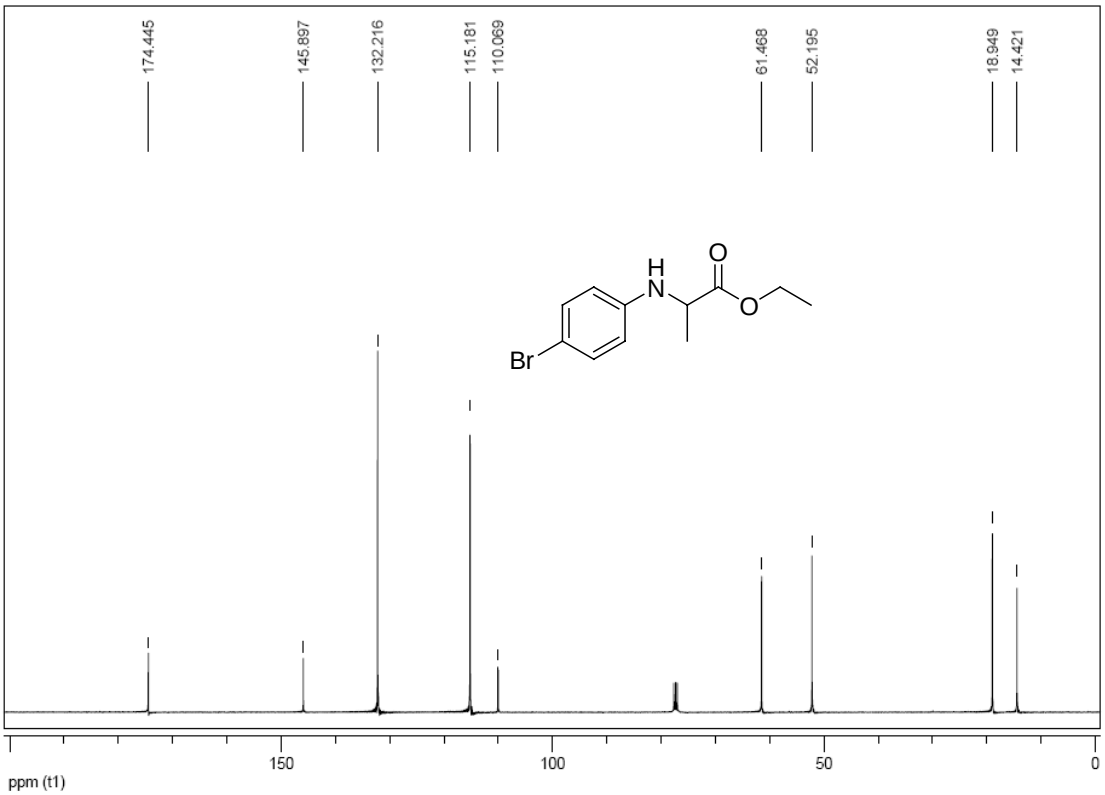
5. NMR Spectra for New N-H Insertion Products

(+)-Ethyl 2-(*p*-chlorophenylamino)propionate (4d)

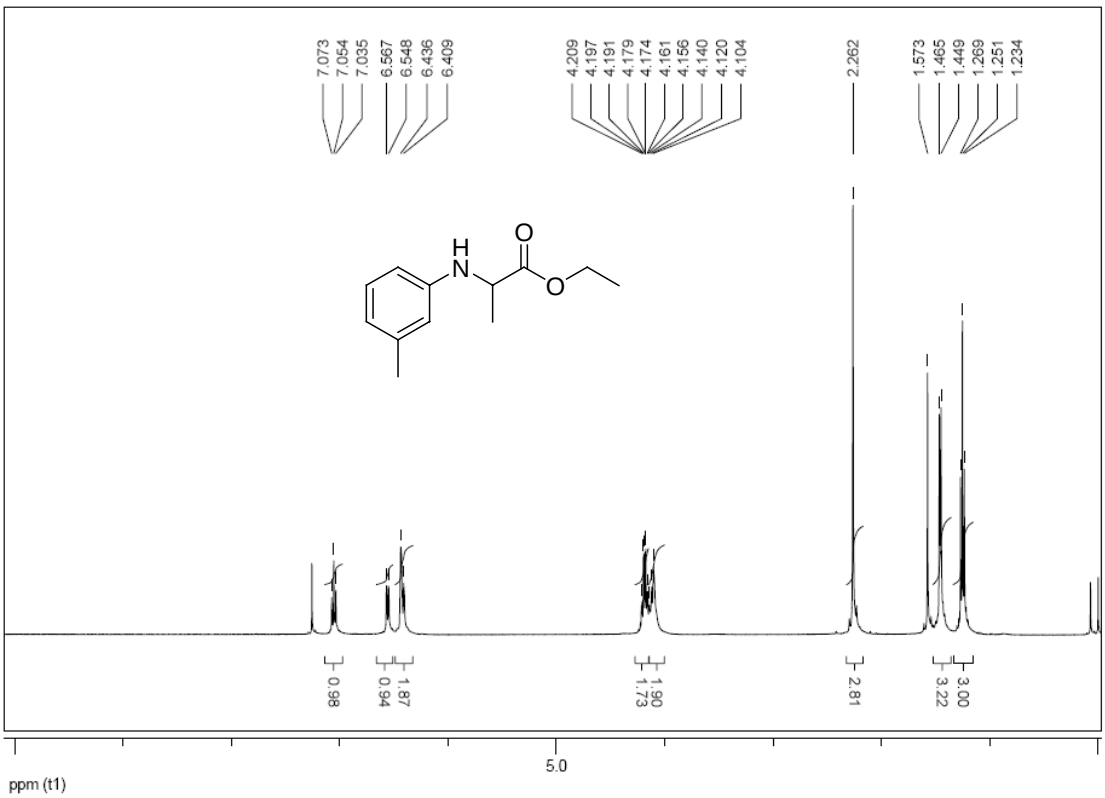


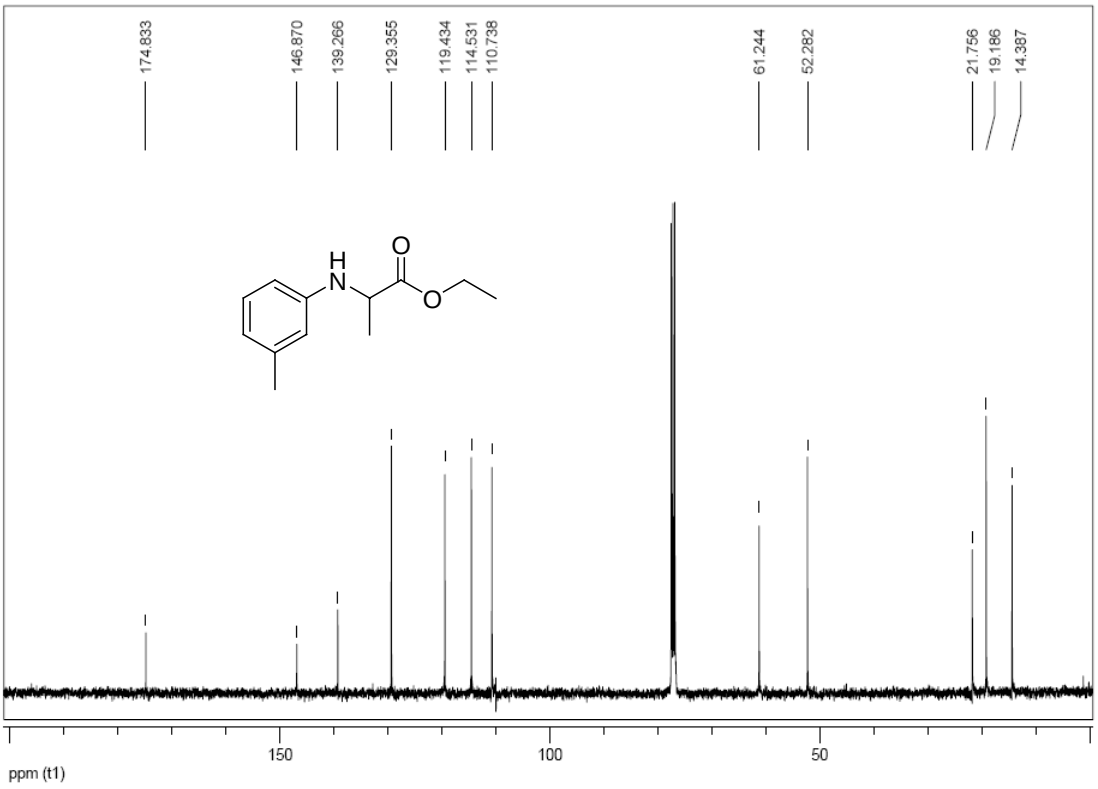
(+)-Ethyl 2-(*p*-bromophenylamino)propionate (4e)



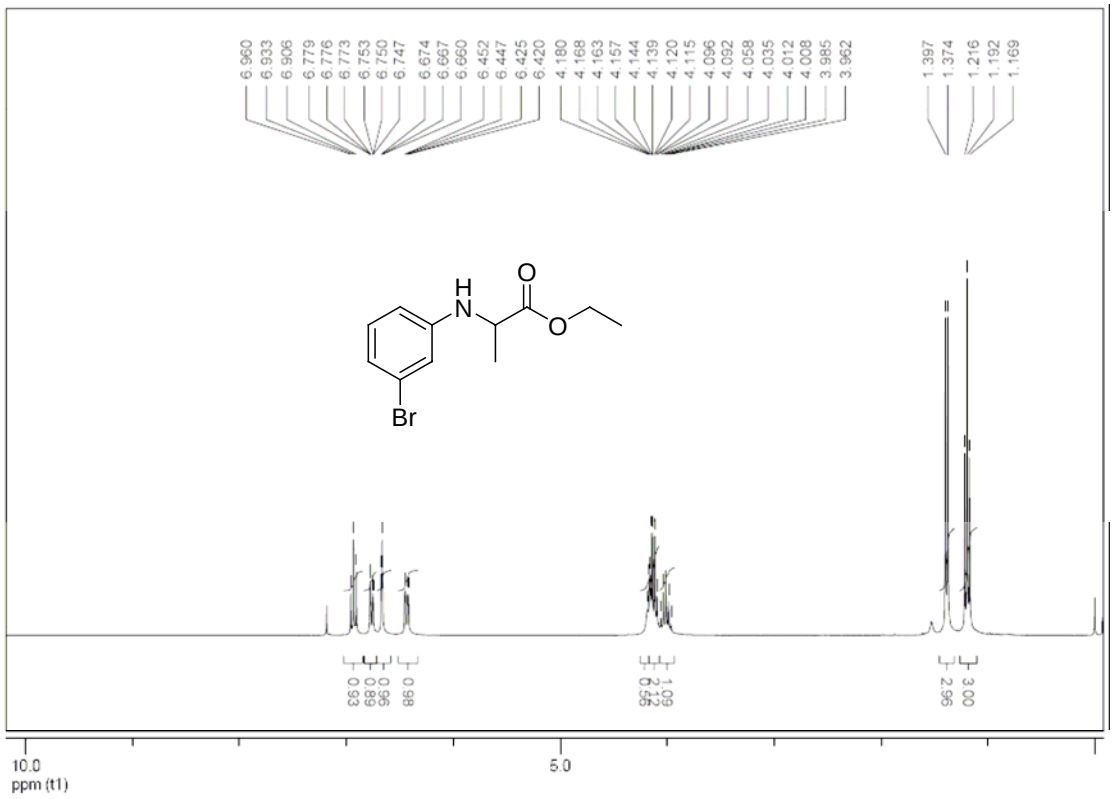


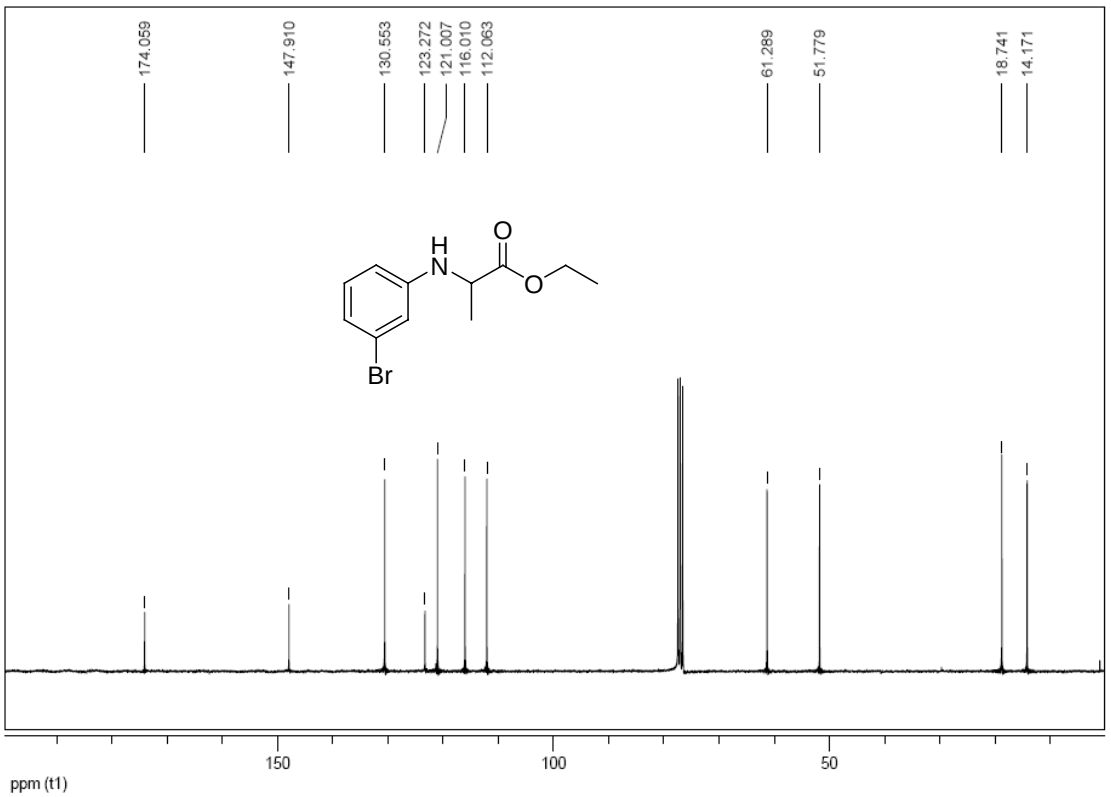
(+)-Ethyl 2-(*m*-toluidino)propionate (4f)



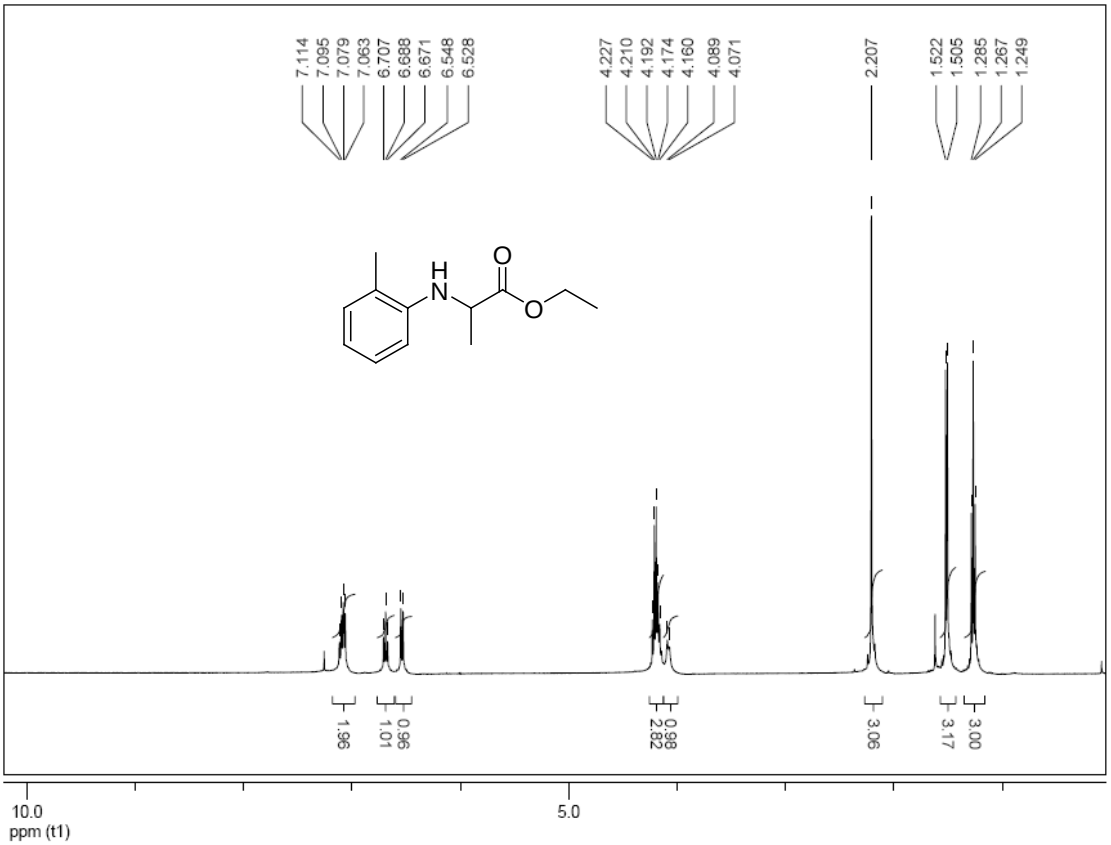


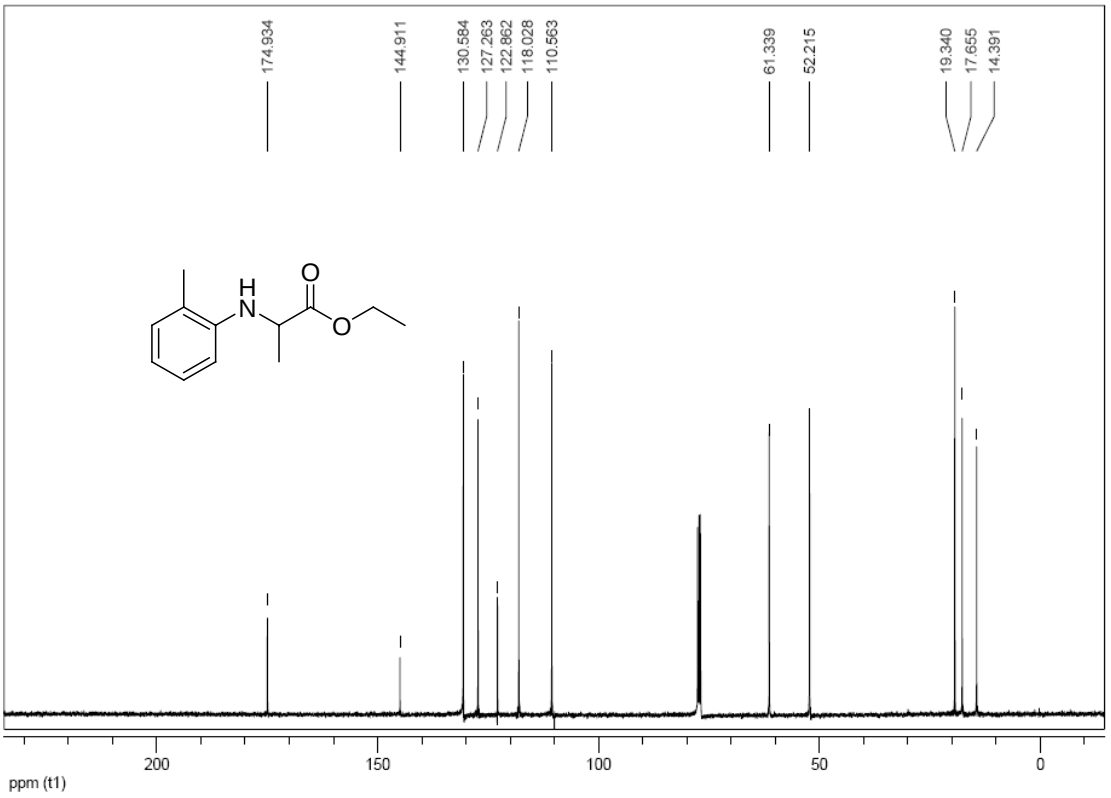
(+)-Ethyl 2-(*m*-bromophenylamino)propionate (4h)



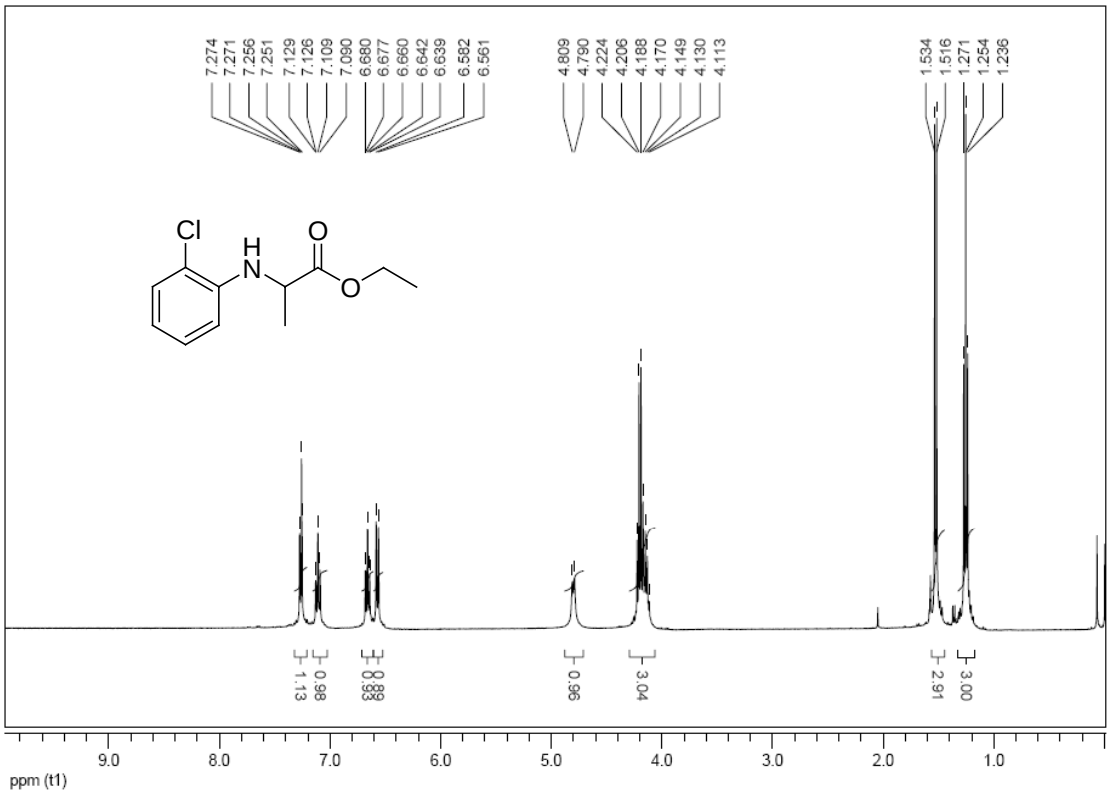


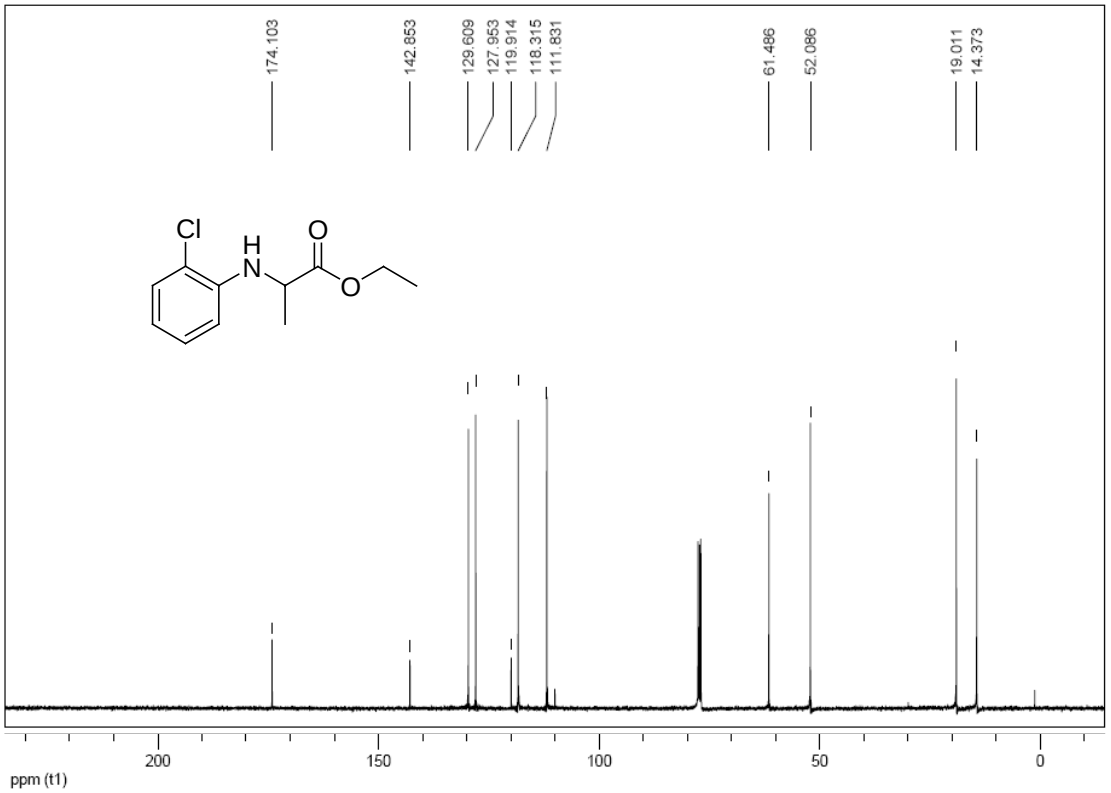
(+)-Ethyl 2-(*o*-toluidino)propionate (4i)



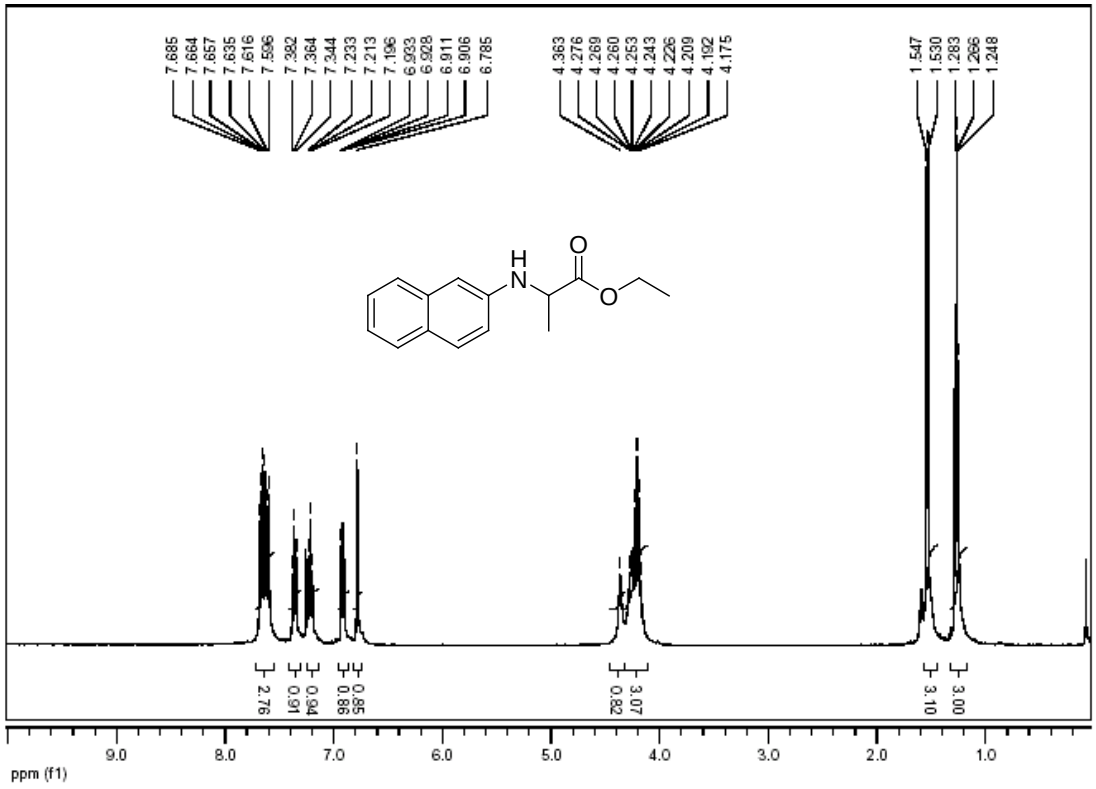


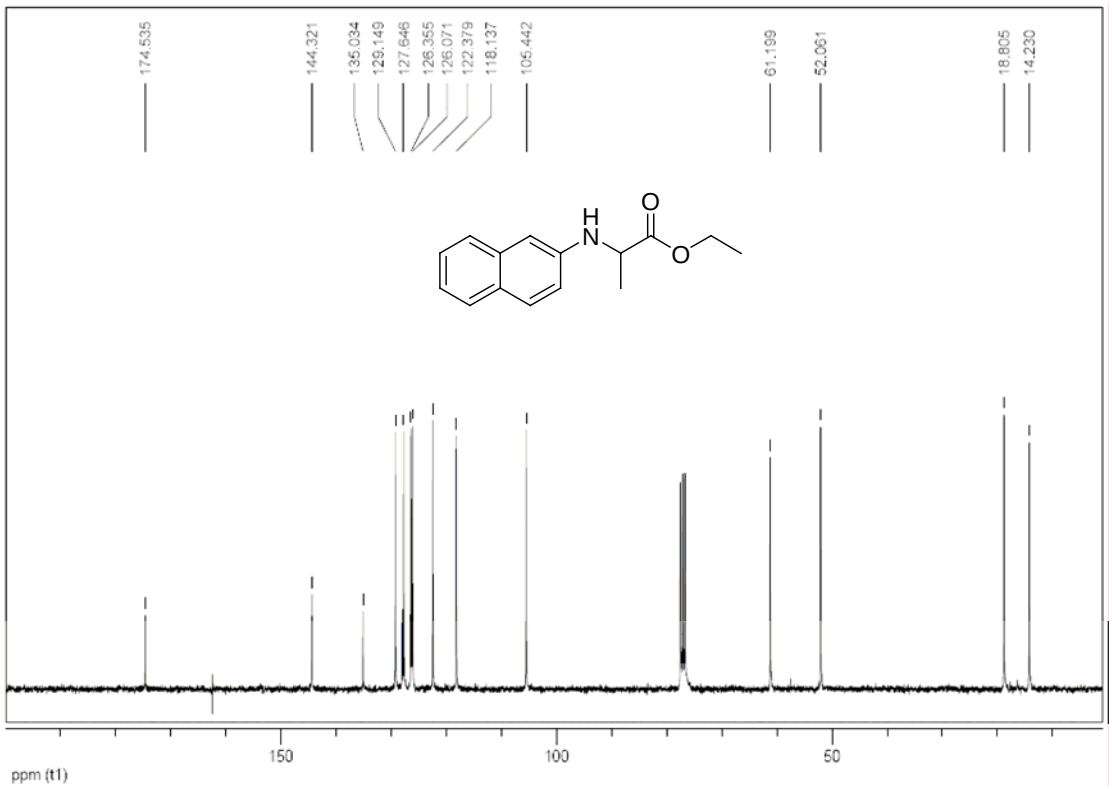
(+)-Ethyl 2-(*o*-chlorophenylamino)propionate (4k)



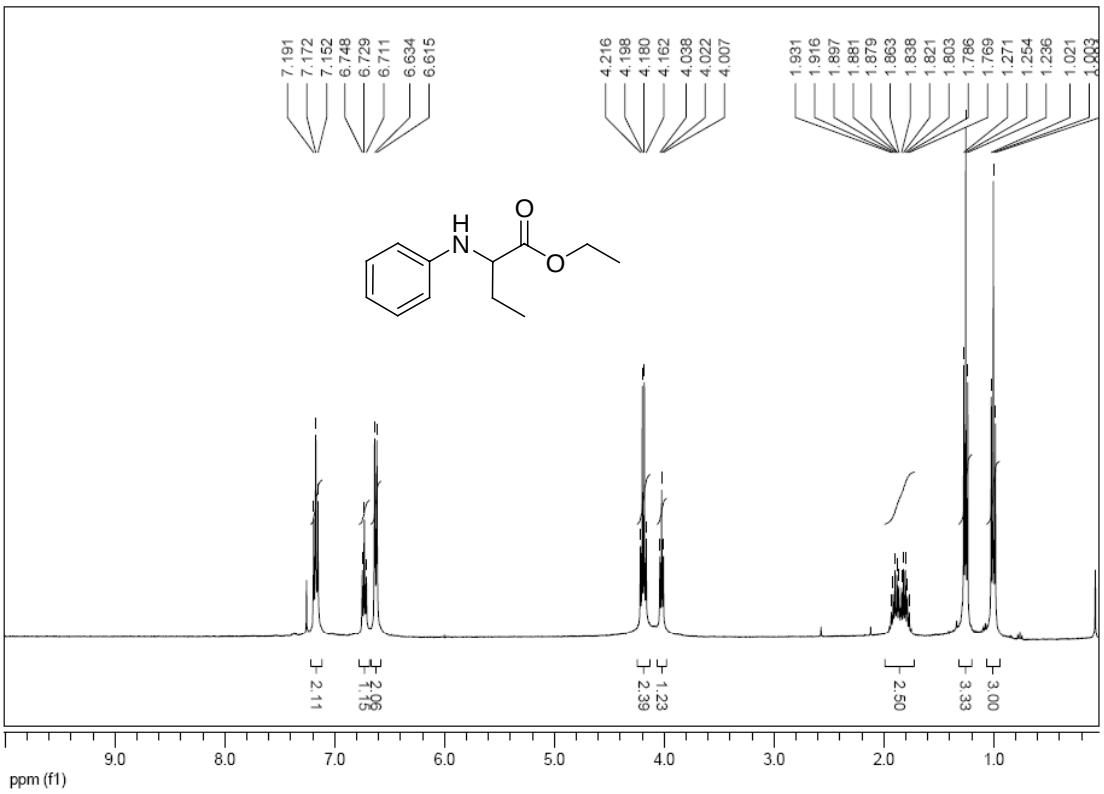


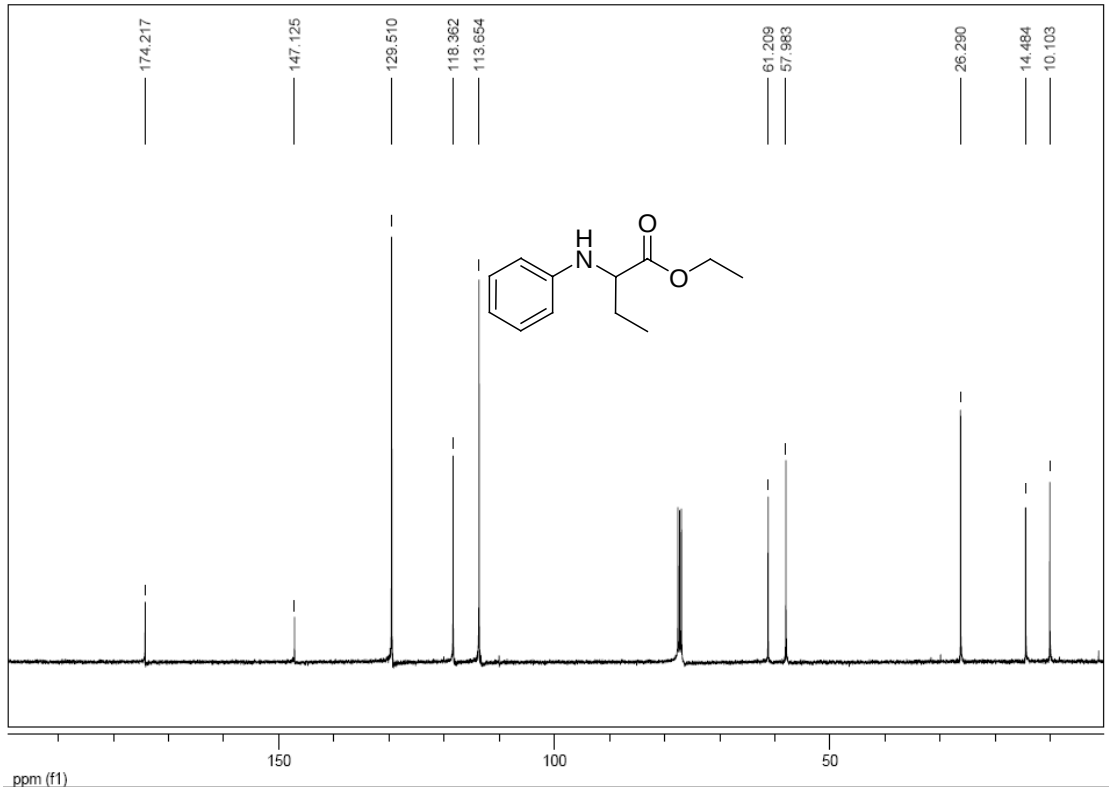
(+)-Ethyl 2-(naphthalen-2-ylamino)propionate (4m)





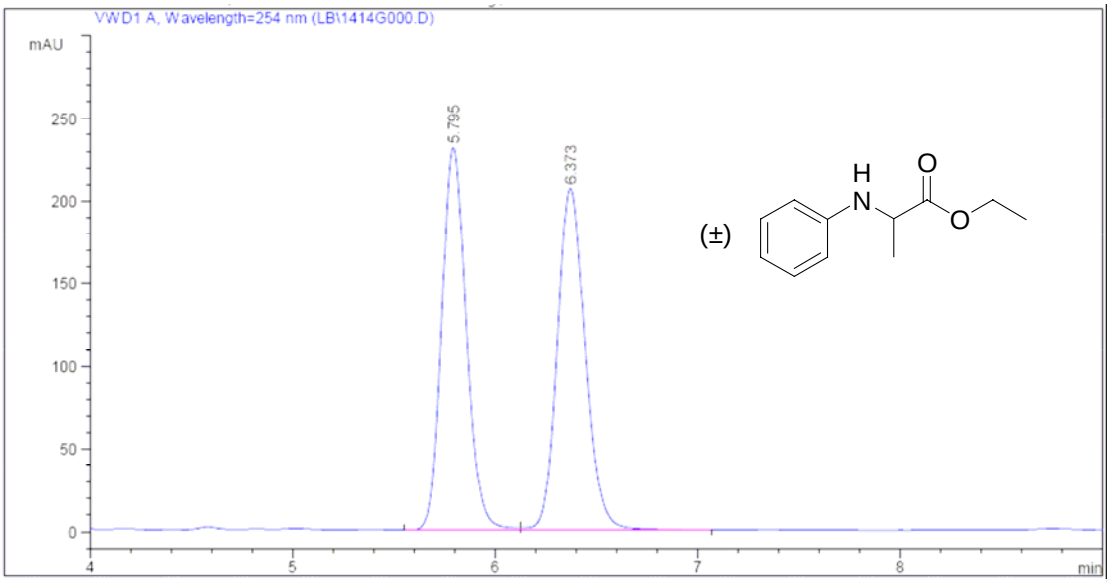
(+)-Ethyl 2-(phenylamino)butyrate (4p)

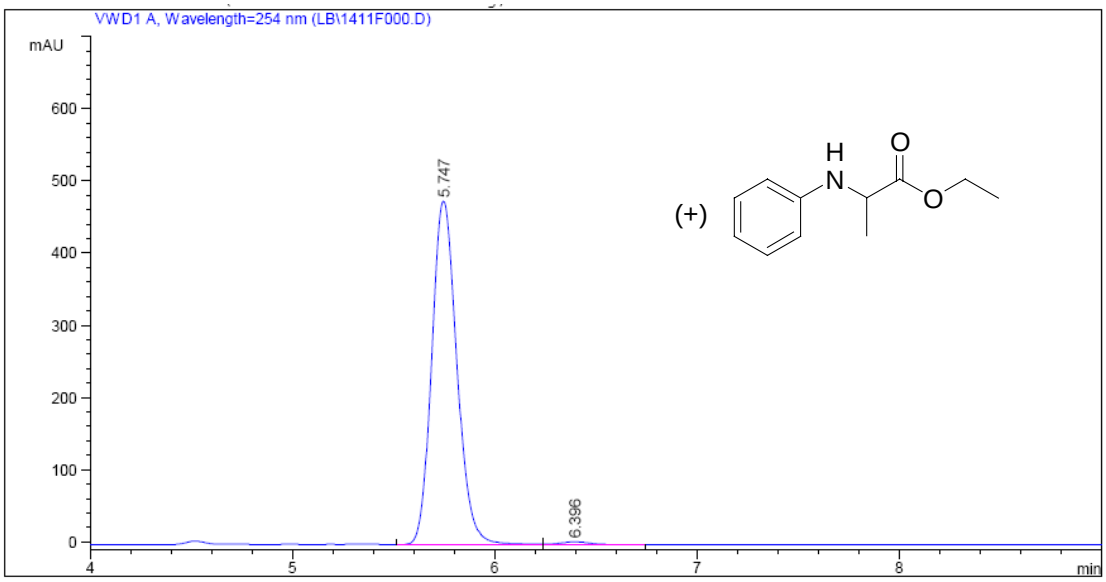




6. HPLC Charts for N-H Insertion Products

(+)-Ethyl 2-(phenylamino)propionate (4a)

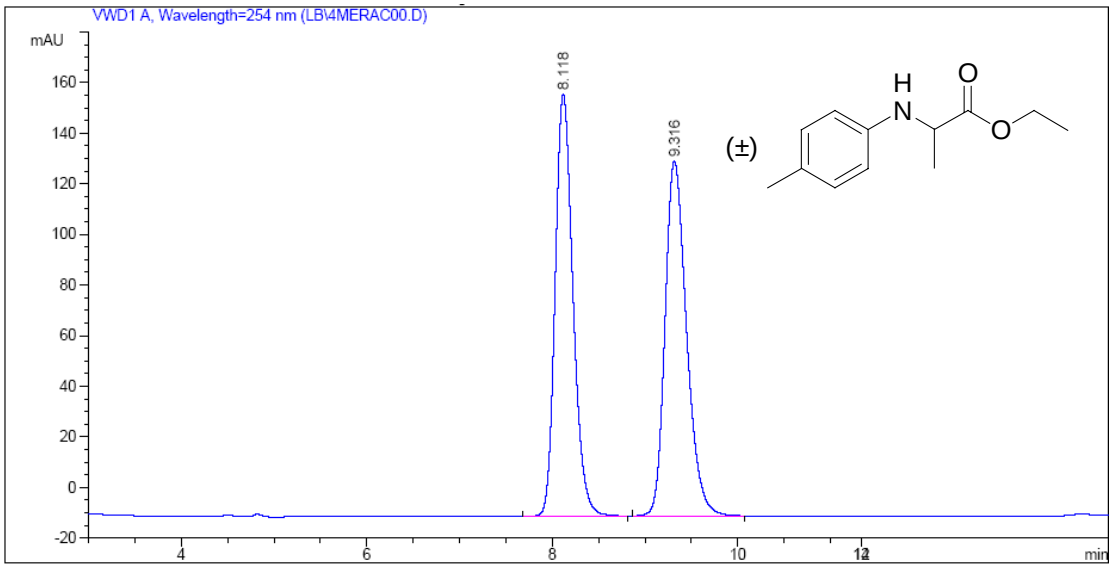


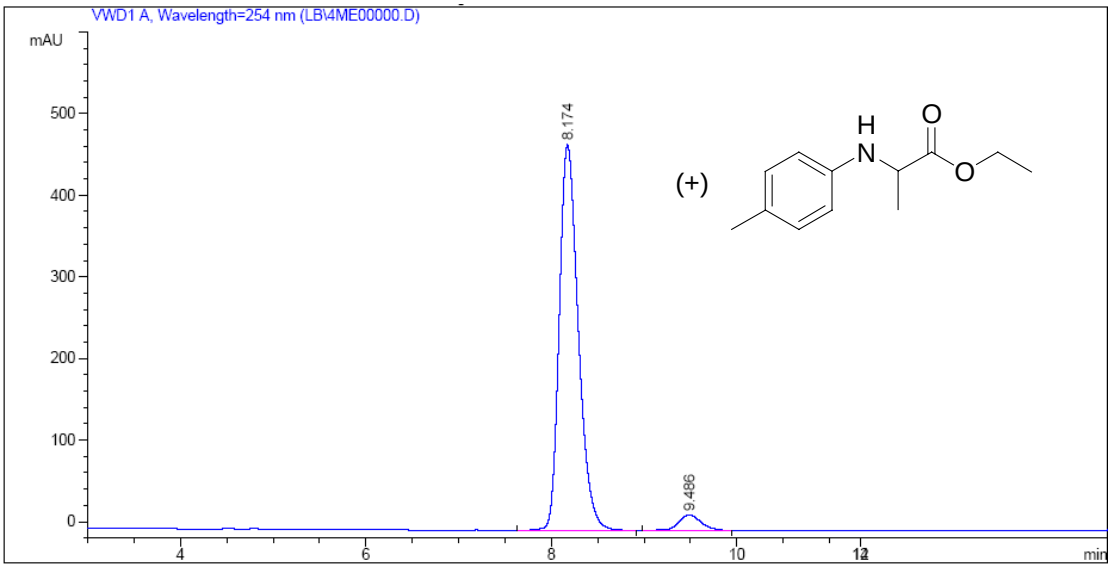


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.747	VV	0.1360	4114.32178	475.11868	98.9342
2	6.396	VB	0.1634	44.32206	4.11814	1.0658

(+)-Ethyl 2-(*p*-toluidino)propionate (4b)

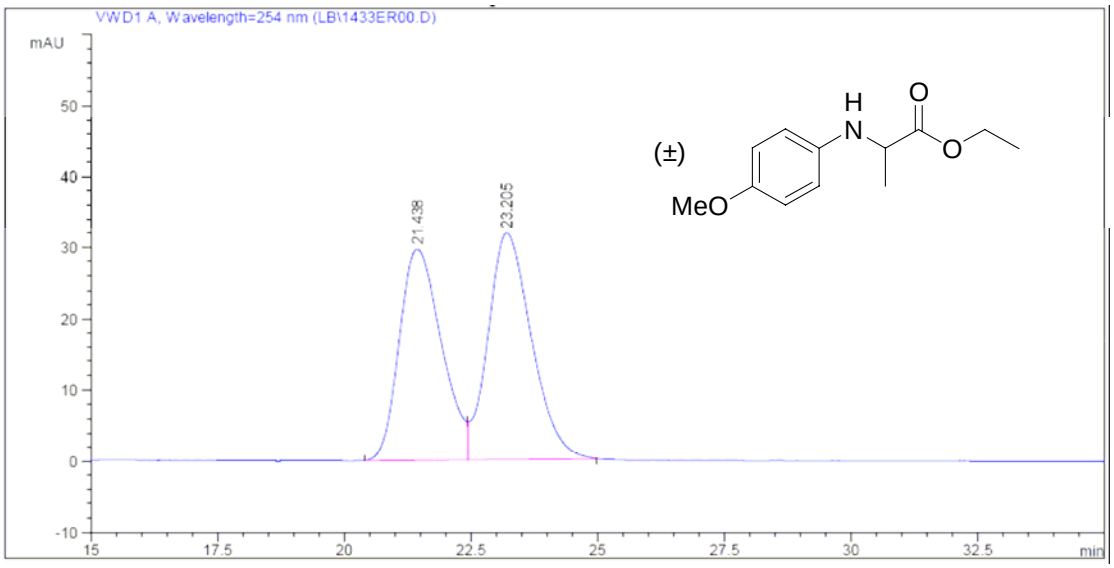


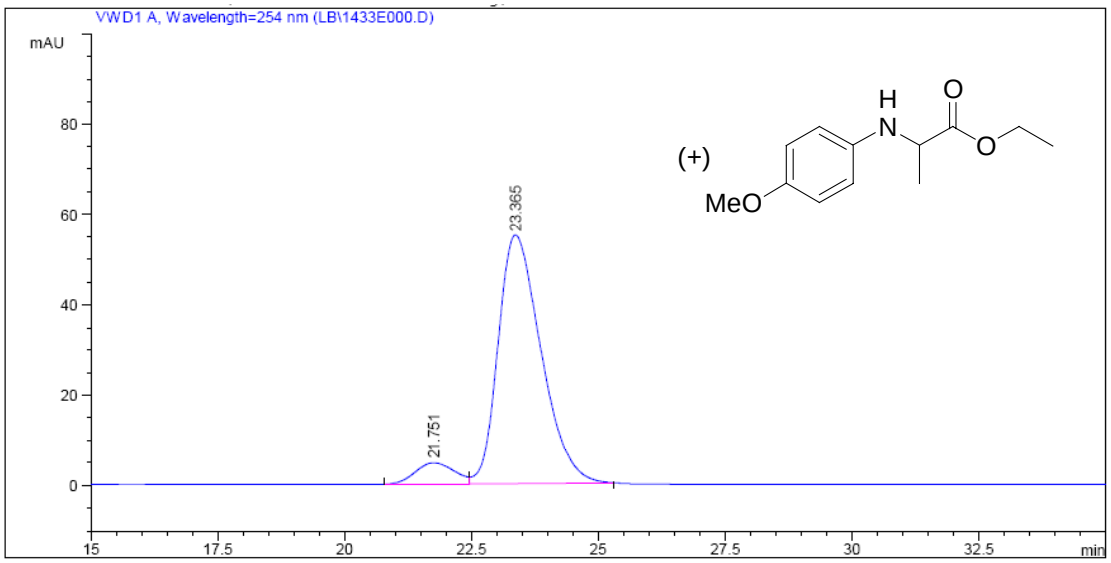


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.174	BB	0.2197	6719.87109	472.69507	95.6029
2	9.486	BB	0.2550	309.06802	18.60299	4.3971

(+)-Ethyl 2-(4-methoxyphenylamino)propionate (4c)

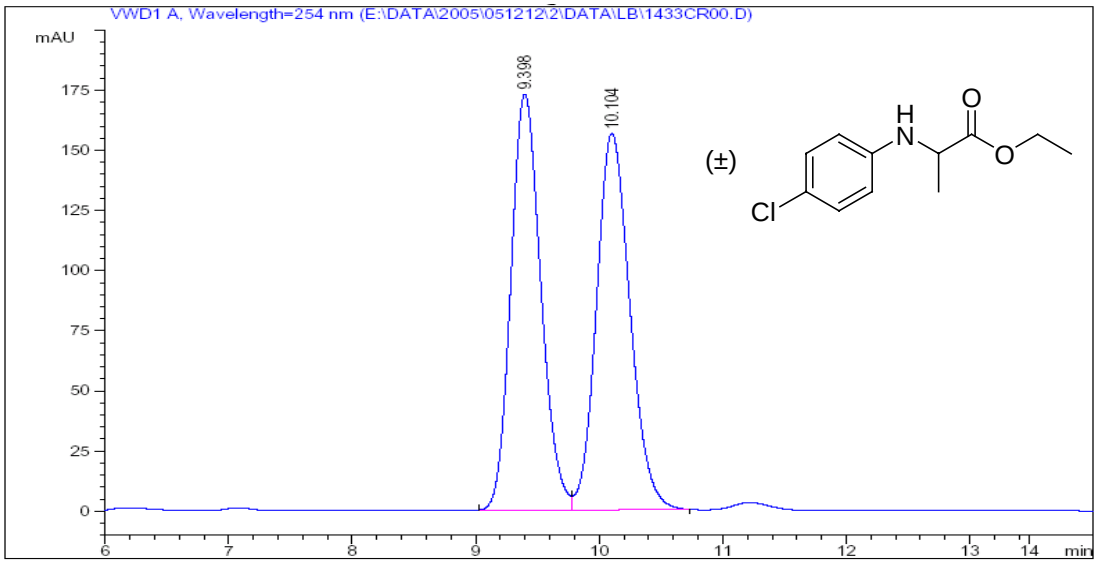


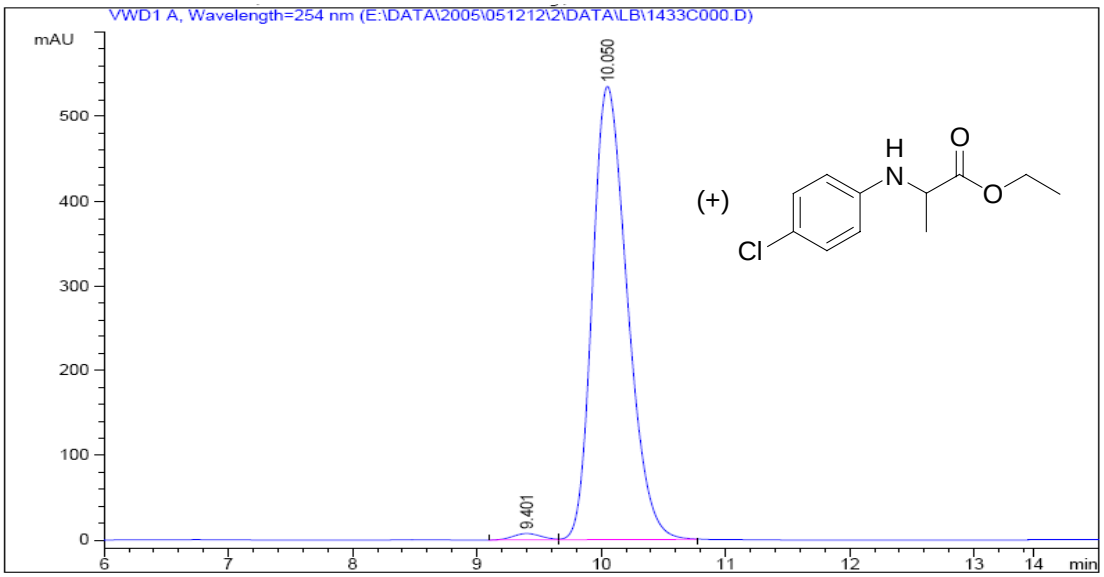


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.751	BV	0.7731	250.44537	4.65630	7.1595
2	23.365	VB	0.9000	3247.62183	54.99705	92.8405

(+)-Ethyl 2-(*p*-chlorophenylamino)propionate (4d)

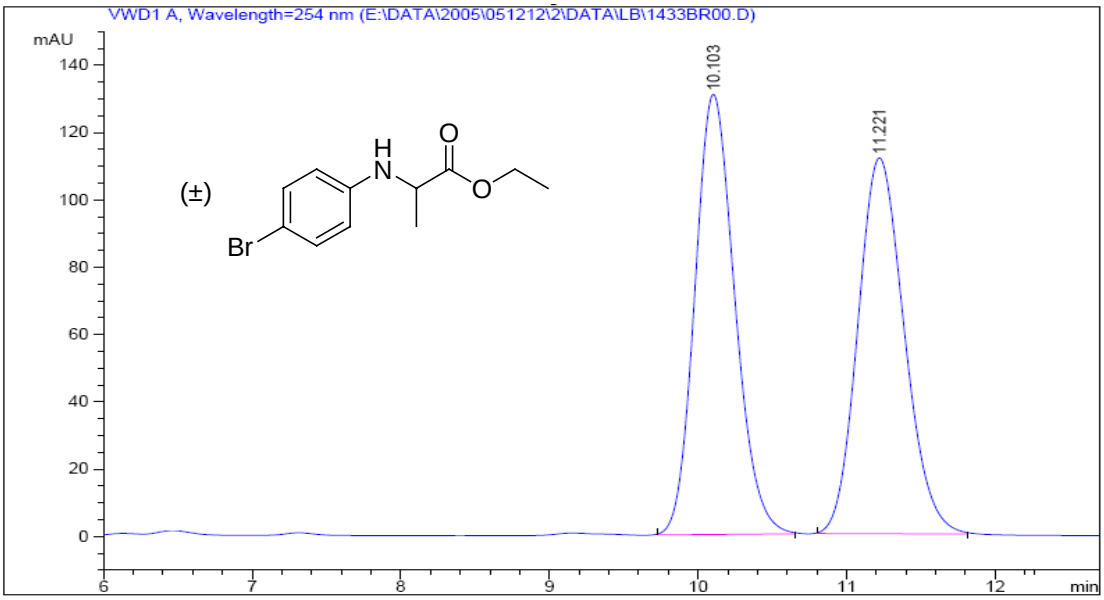


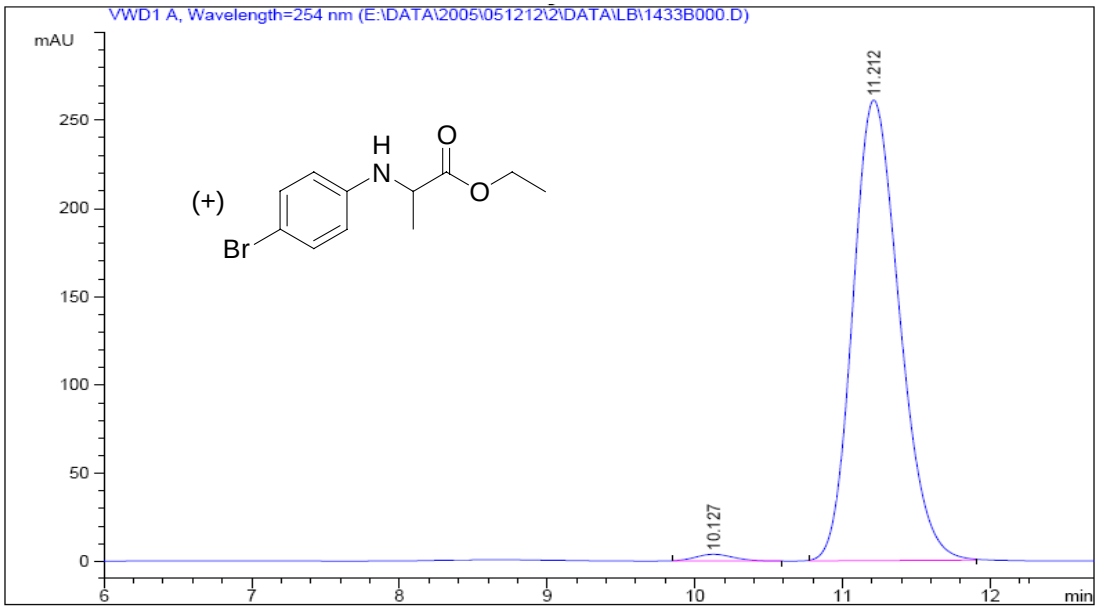


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.401	PV	0.2502	120.26642	7.53814	1.1384
2	10.050	VB	0.3017	1.04438e4	535.74323	98.8616

(+)-Ethyl 2-(*p*-bromophenylamino)propionate (4e)

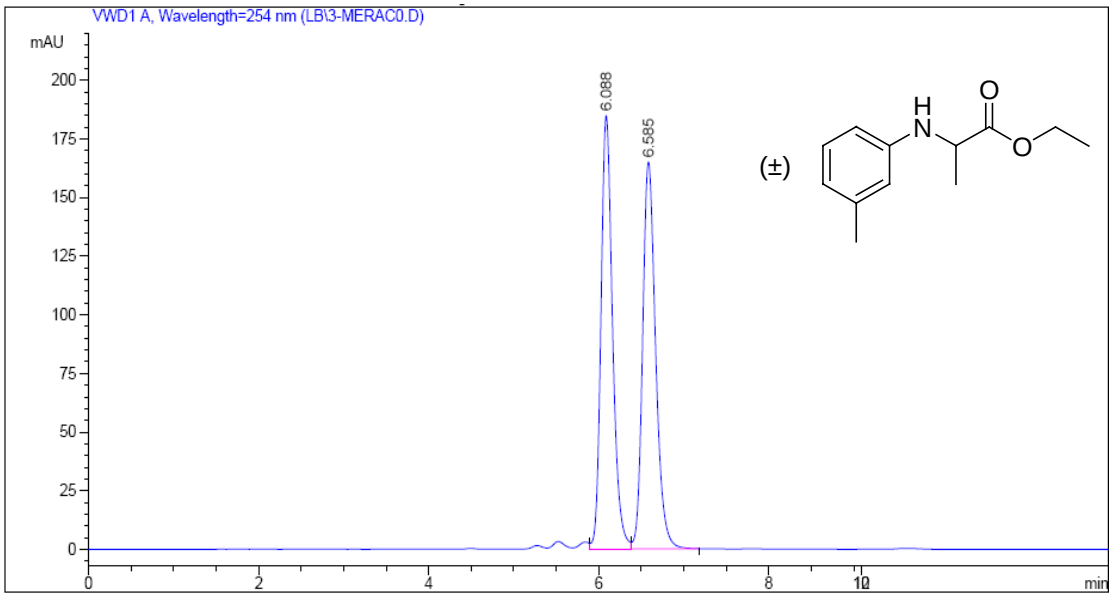




Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.127	BP	0.2806	69.01994	3.79613	1.1864
2	11.212	BB	0.3409	5748.64648	261.48798	98.8136

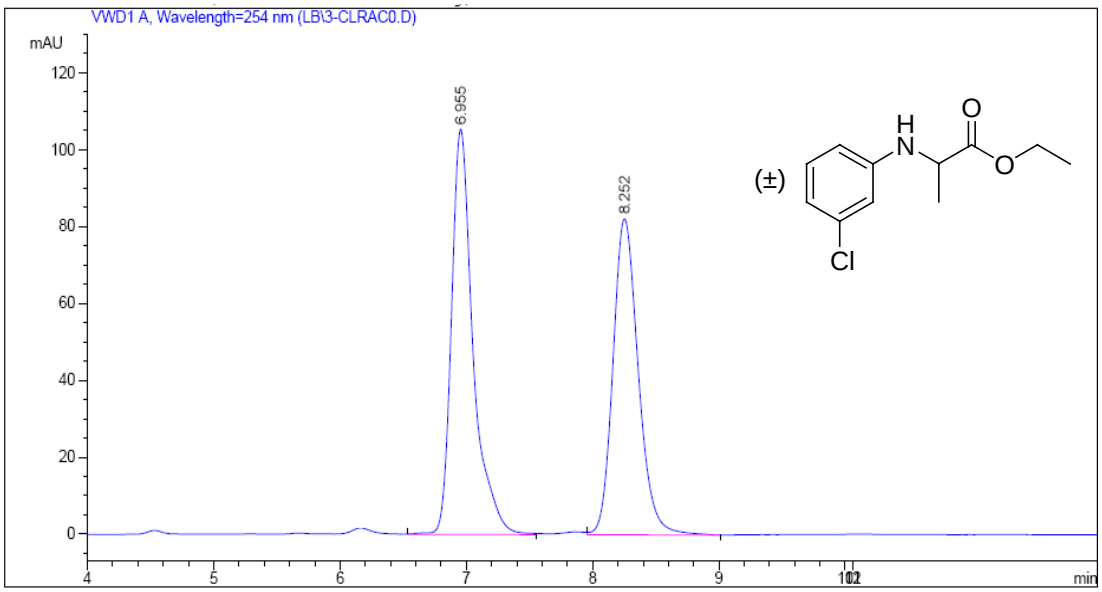
(+)-Ethyl 2-(*m*-toluidino)propionate (4f)

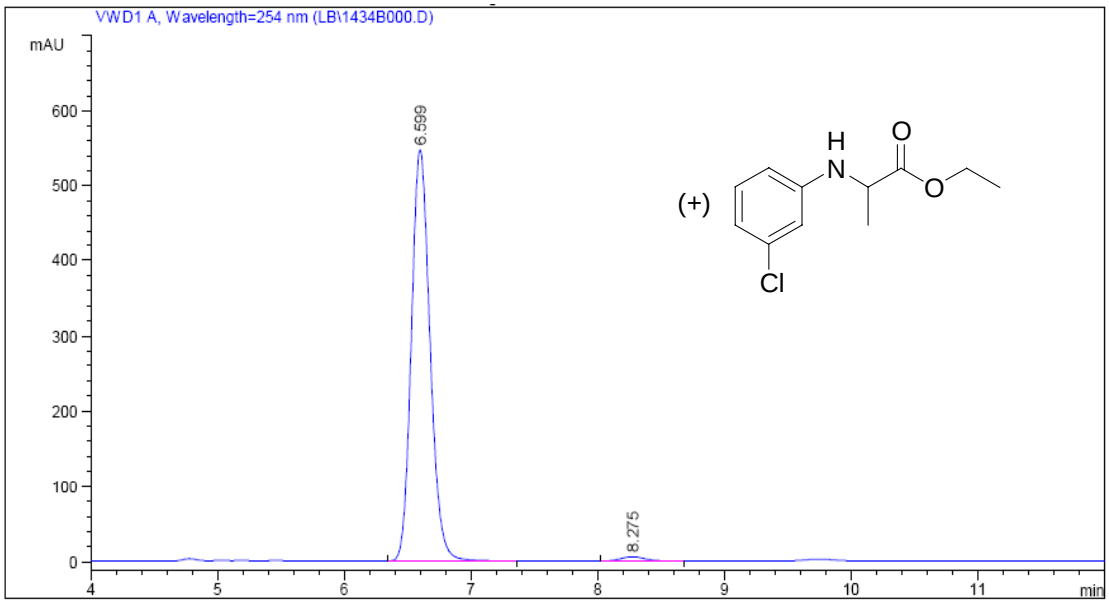


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.100	VV	0.1474	8456.84082	877.09113	98.3239
2	6.605	VB	0.1730	144.15909	12.30999	1.6761

(+)-Ethyl 2-(*m*-chlorophenylamino)propionate (4g)

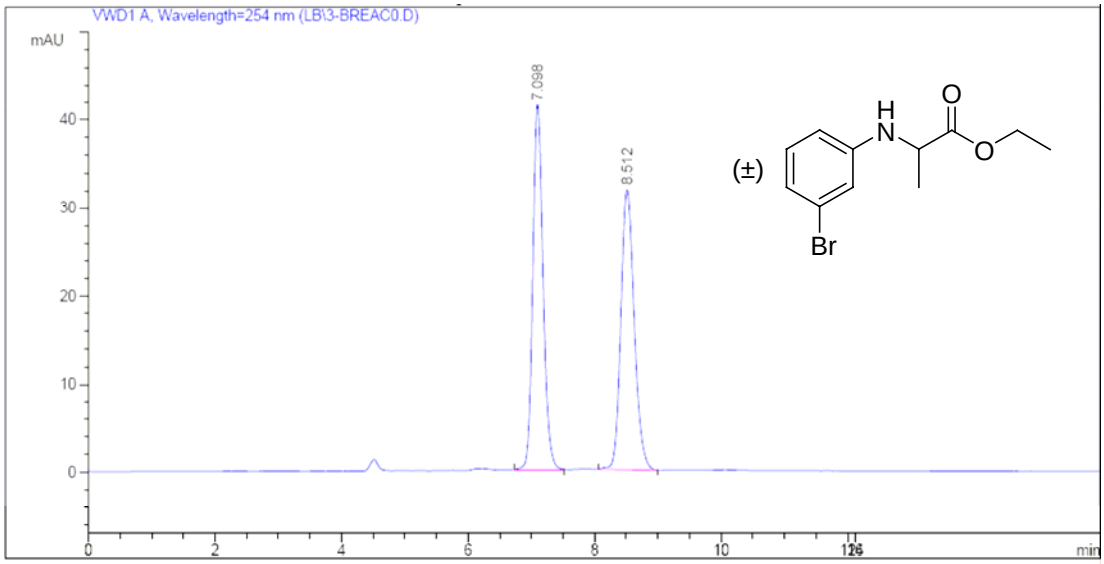


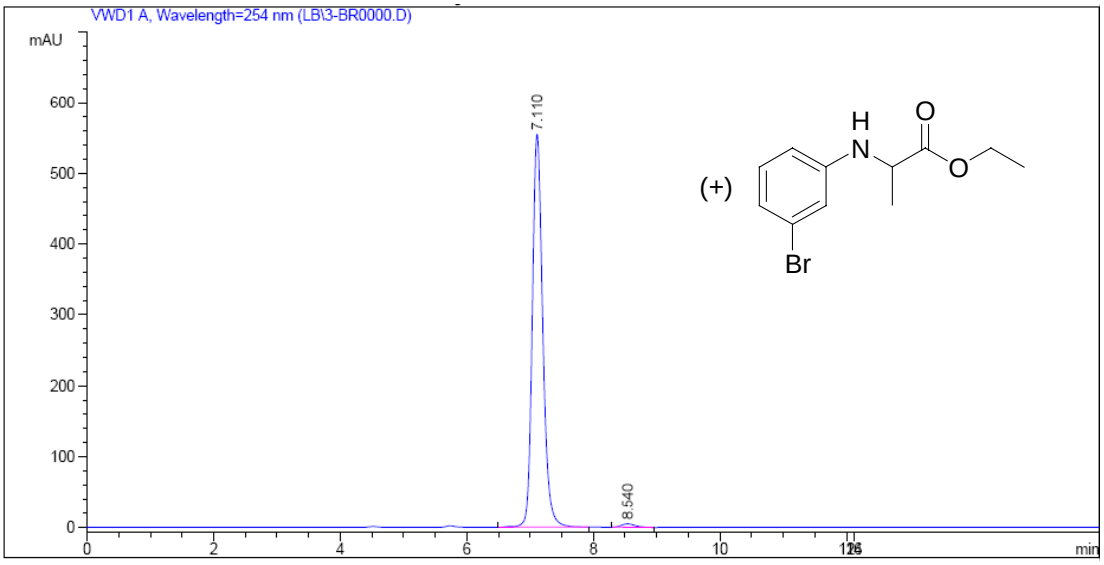


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.600	VB	0.1602	5585.03516	545.76575	98.6678
2	8.276	BP	0.2059	75.40966	5.73133	1.3322

(+)-Ethyl 2-(*m*-bromophenylamino)propionate (4h)

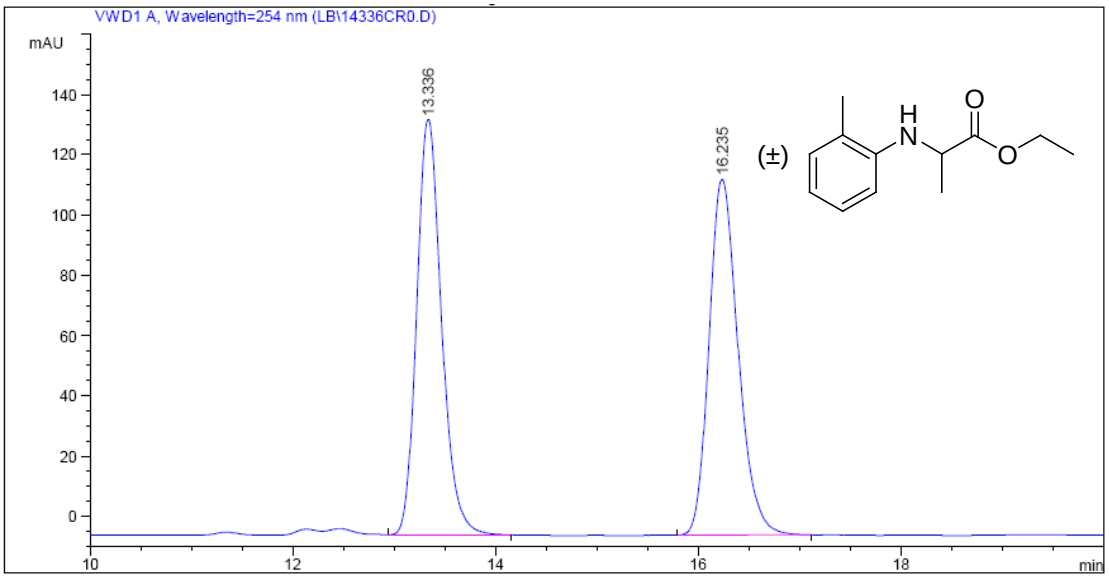


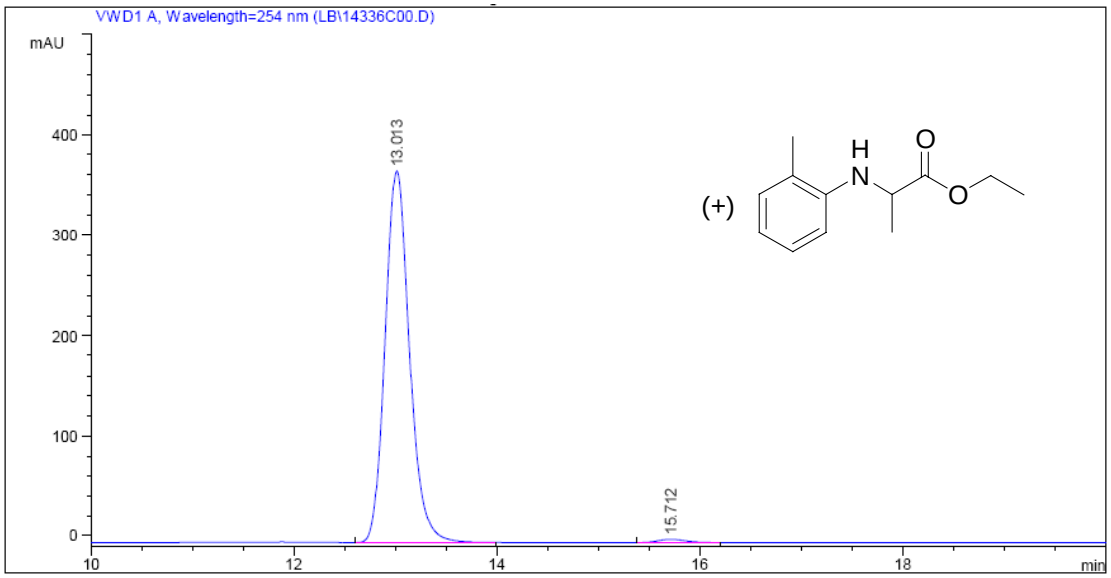


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.421	VB	0.1587	5914.82666	577.94360	99.0084
2	7.850	BB	0.2004	59.24116	4.57974	0.9916

(+)-Ethyl 2-(*o*-toluidino)propionate (4i)

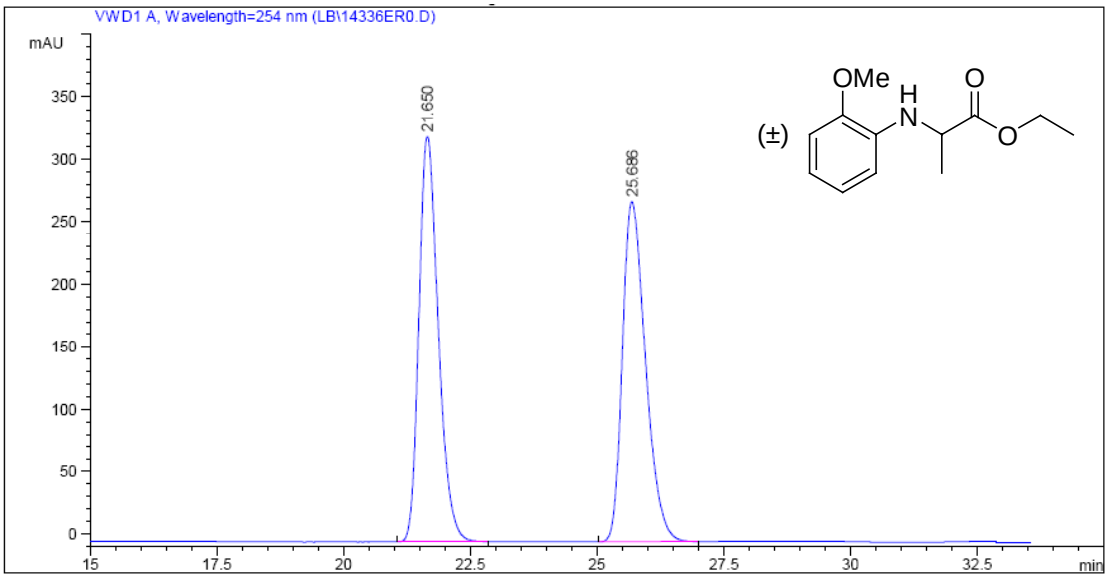


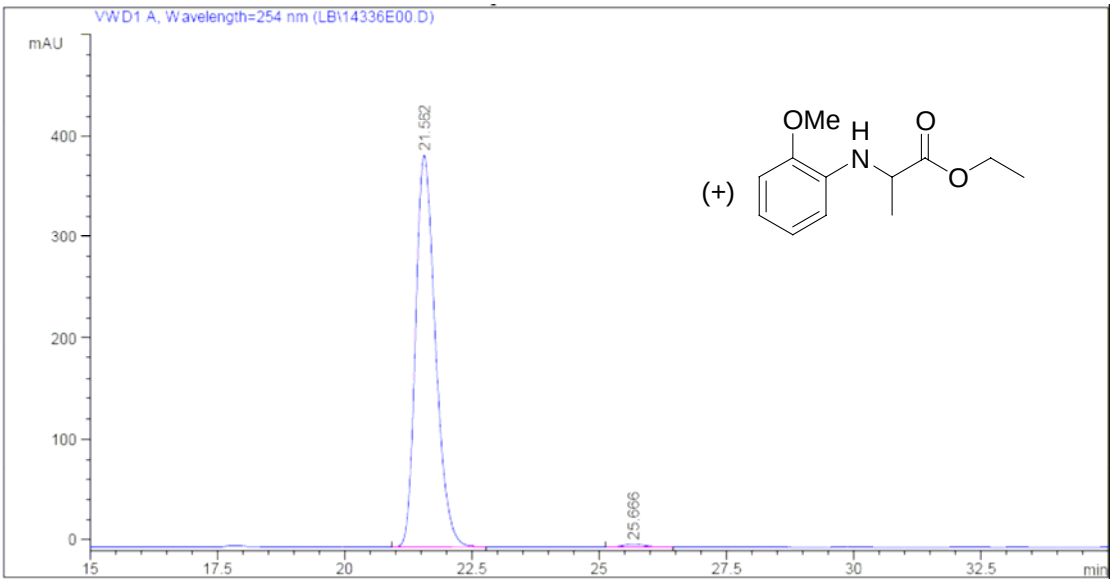


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.013	PB	0.2641	6214.55713	370.52734	98.9876
2	15.712	BB	0.2846	63.56122	3.36291	1.0124

(+)-Ethyl 2-(*o*-methoxyphenylamino)propionate (4j)

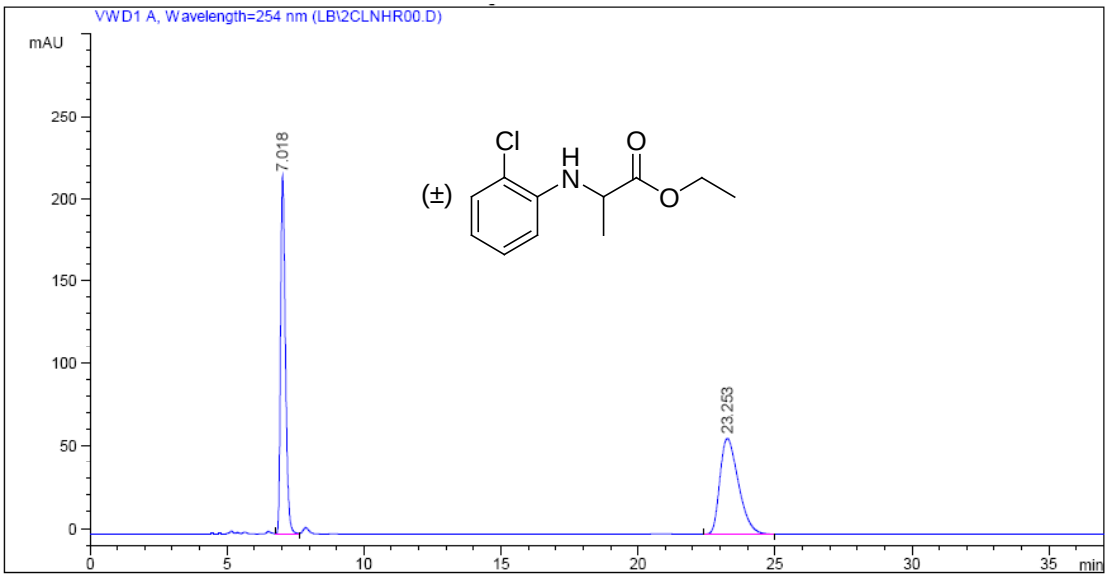


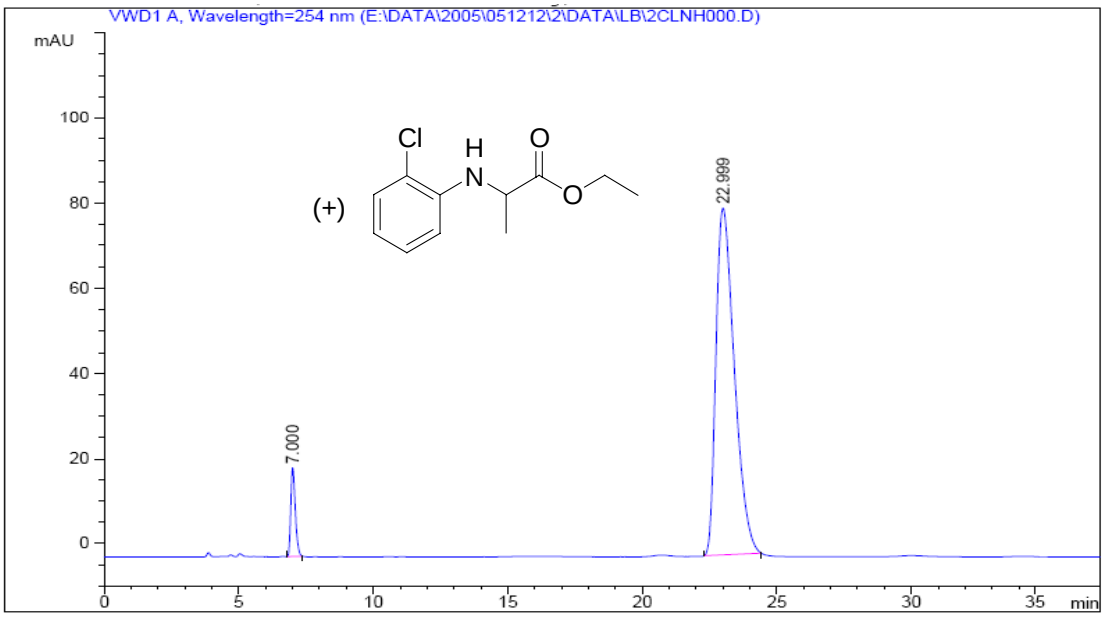


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.562	VB	0.4137	1.04953e4	387.34448	99.1011
2	25.666	BB	0.4462	95.19795	3.17255	0.8989

(+)-Ethyl 2-(*o*-fluorophenylamino)propionate (4k)

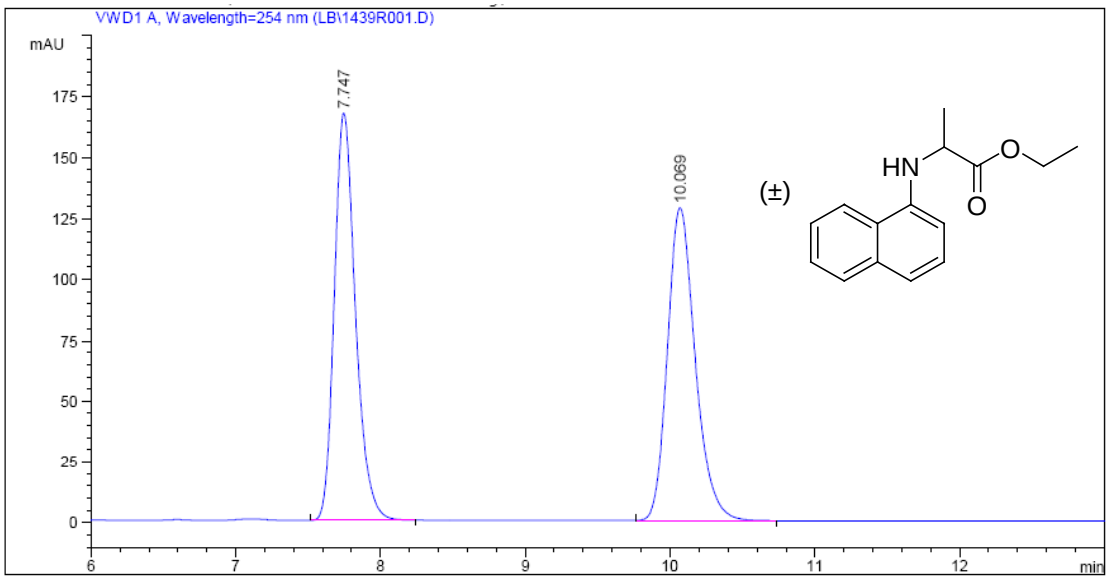


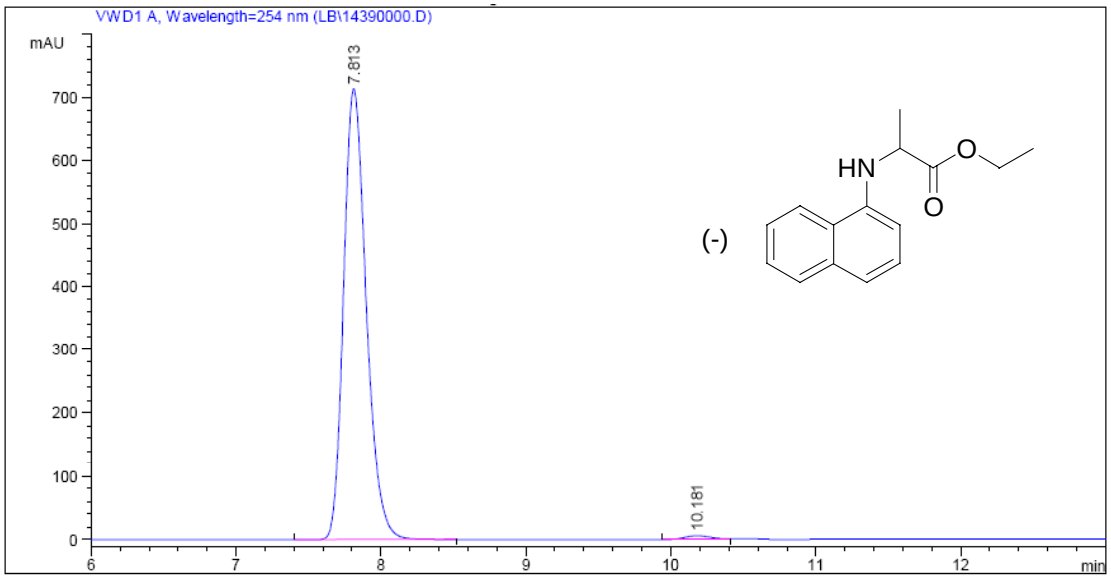


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.000	BB	0.1776	244.41809	21.05807	5.9205
2	22.999	BB	0.7318	3883.90918	81.54900	94.0795

(-)-Ethyl 2-(naphthalen-1-ylamino)propionate (4l)

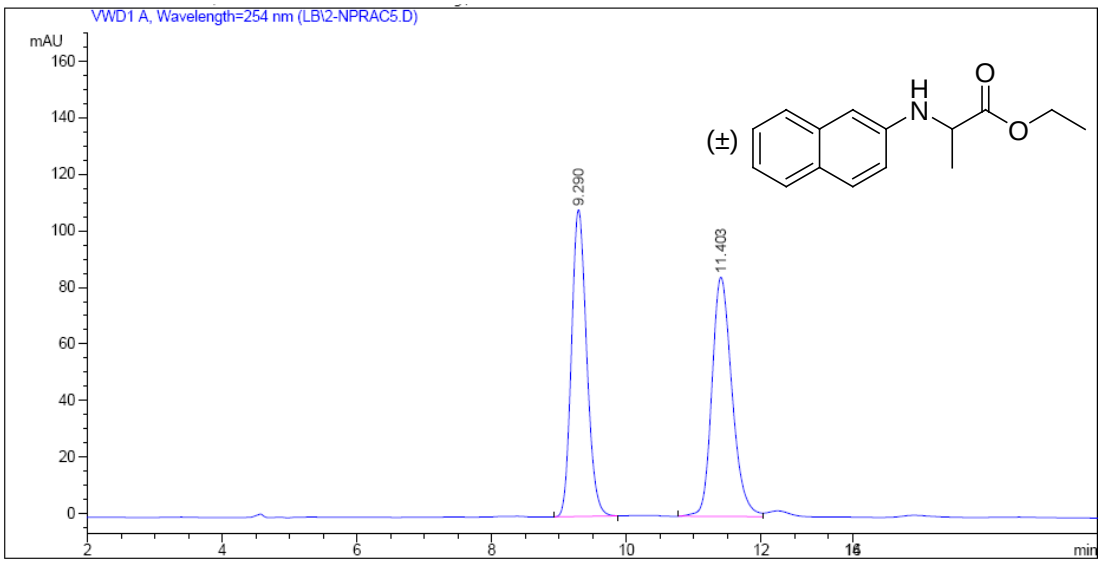


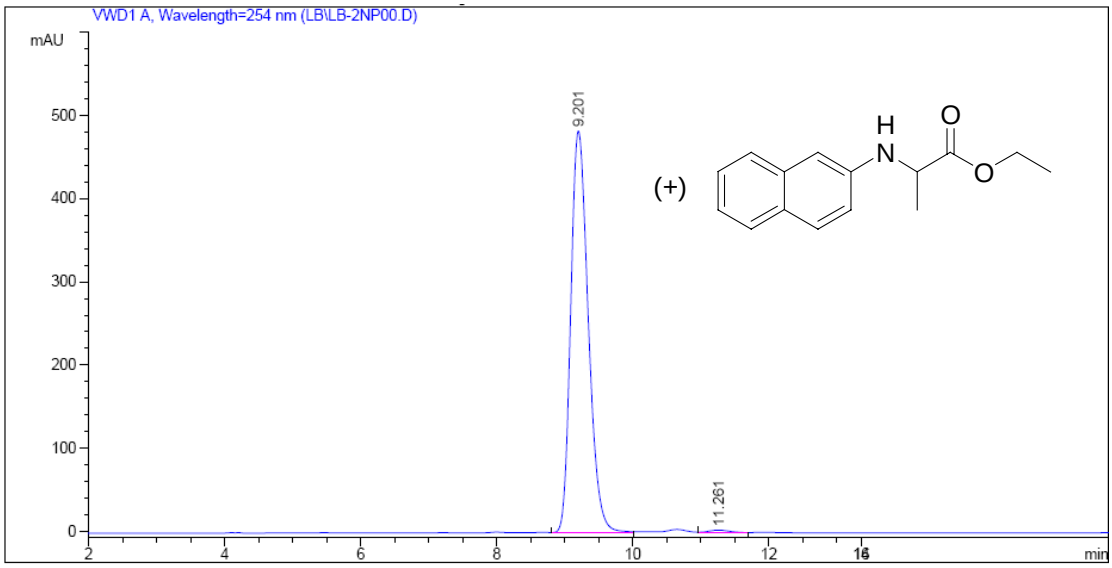


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.813	PB	0.1670	7727.17773	714.31036	98.9074
2	10.181	BV	0.2080	85.35999	6.22620	1.0926

(+)-Ethyl 2-(naphthalen-2-ylamino)propionate (4m)

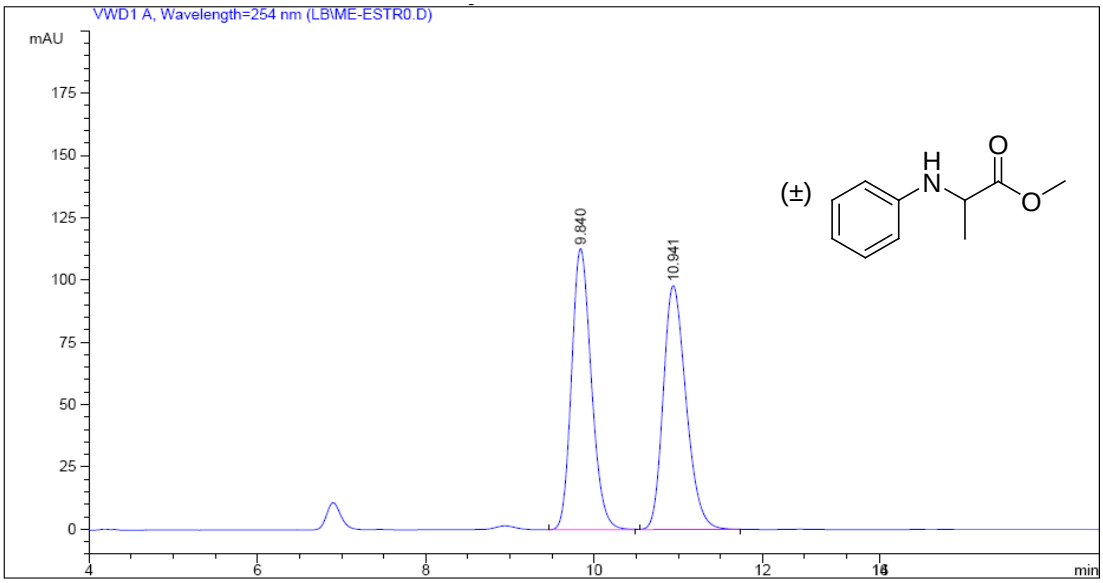


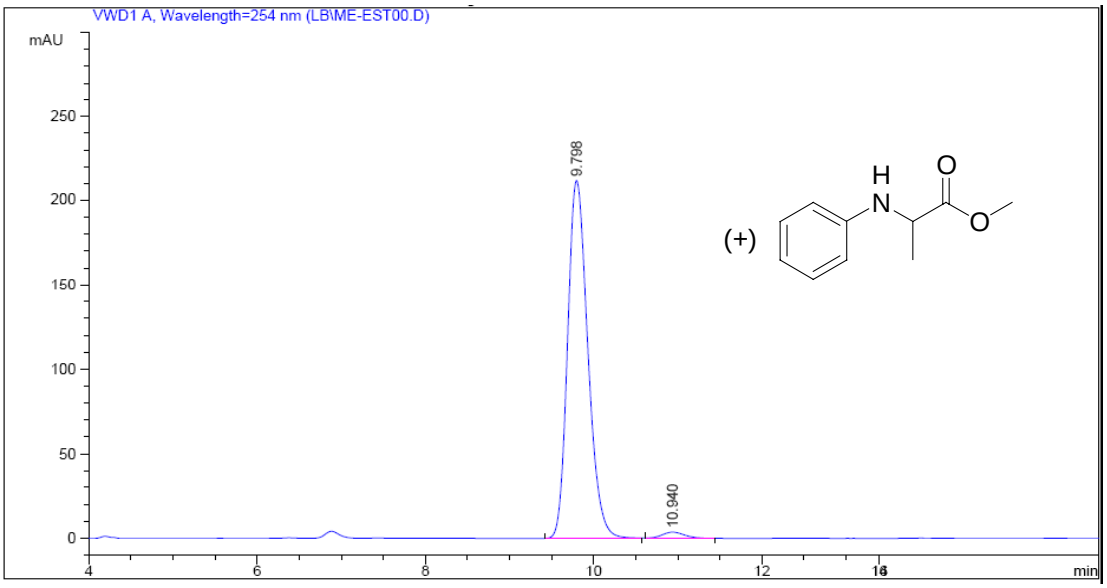


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.201	VB	0.2776	8651.52441	482.45346	99.0633
2	11.261	VV	0.3638	81.80889	3.41706	0.9367

(+)-Methyl 2-(phenylamino)propionate (4n)

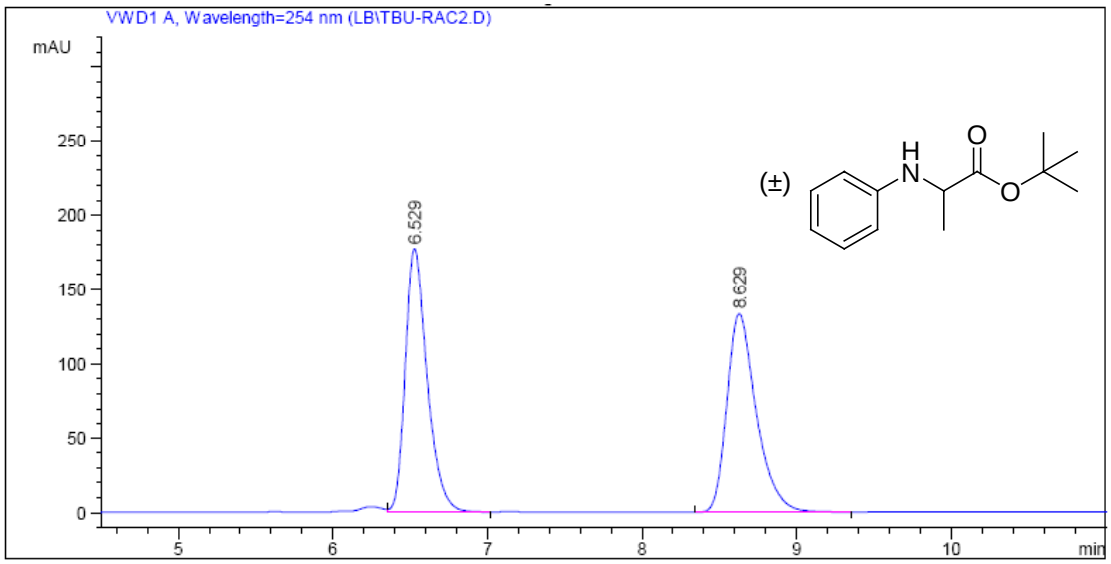


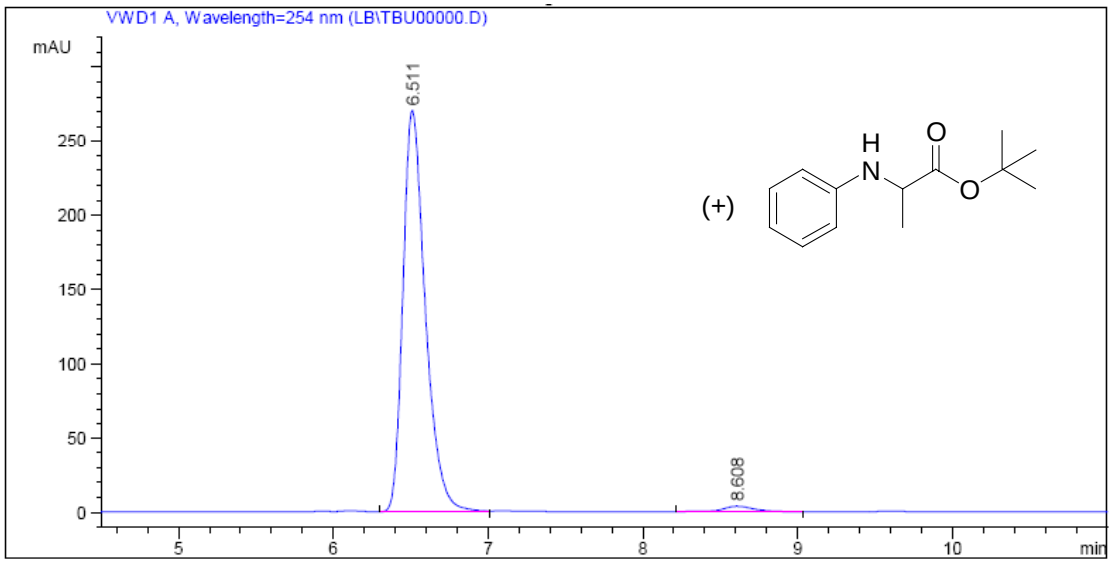


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.798	BB	0.2584	3533.63672	212.12744	98.0540
2	10.940	BB	0.2926	70.12914	3.67348	1.9460

(+)-*tert*-Butyl 2-(phenylamino)propionate (4o)

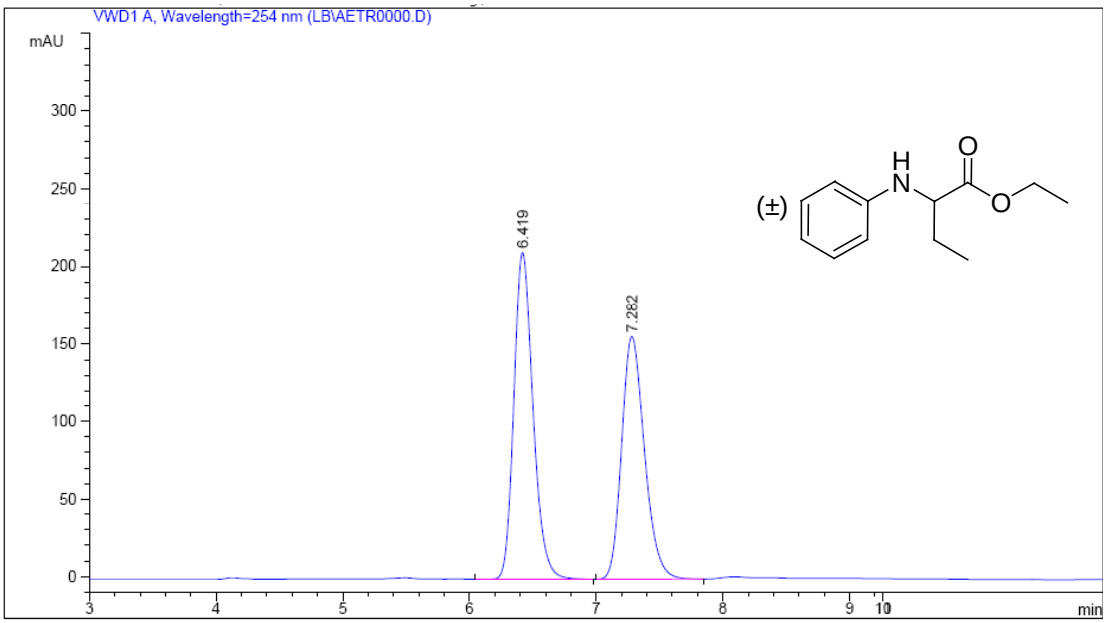


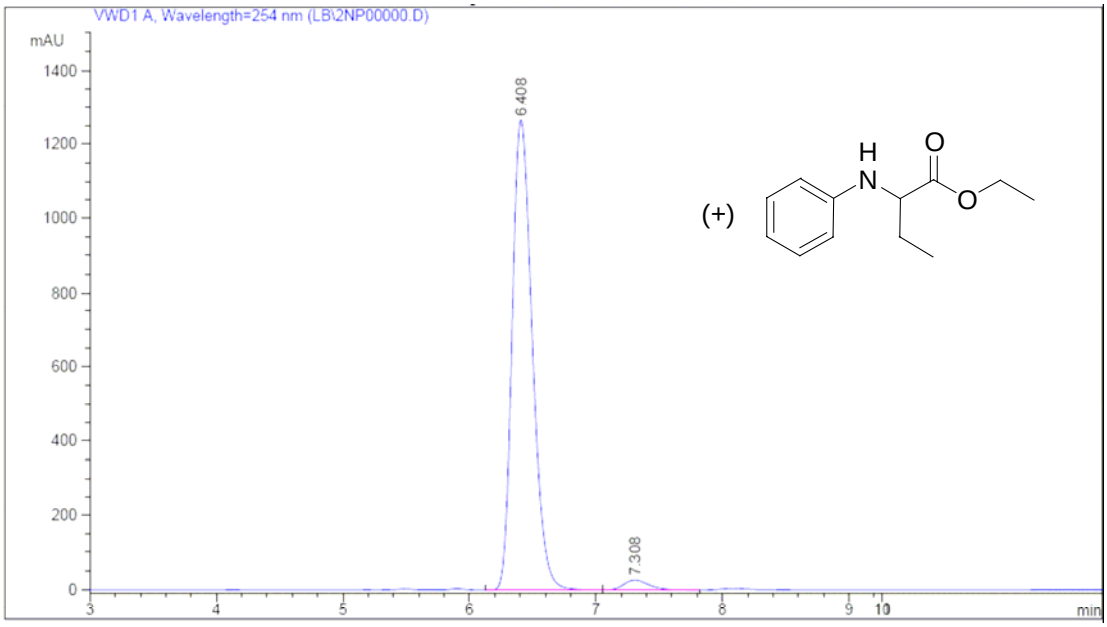


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.511	VV	0.1520	2711.87036	270.28592	98.0637
2	8.608	BP	0.2111	53.54787	3.73179	1.9363

(+)-Ethyl 2-(phenylamino)butyrate (4p)

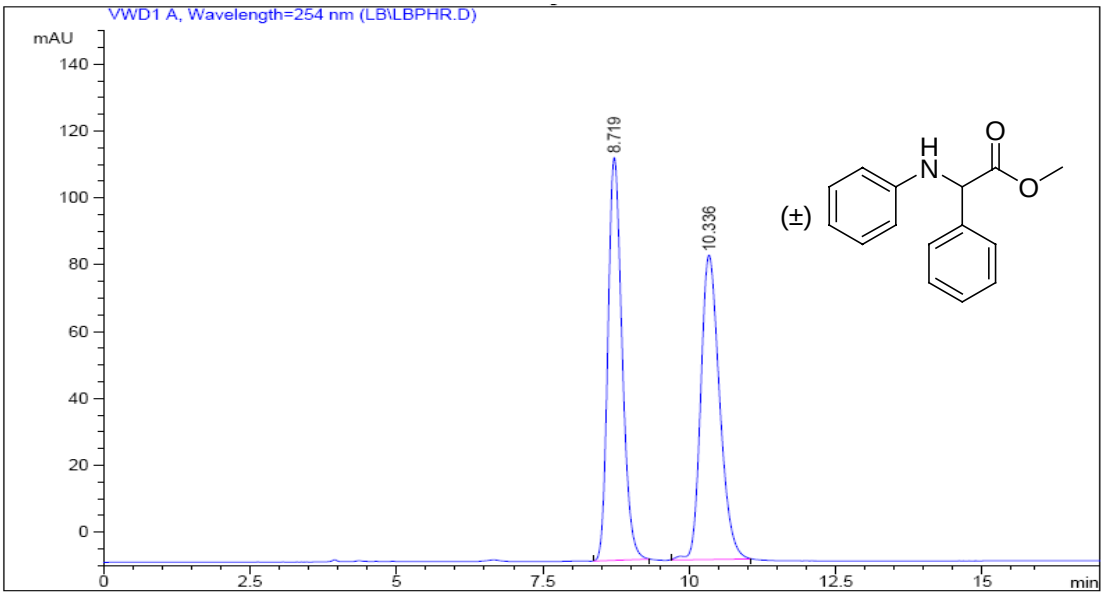


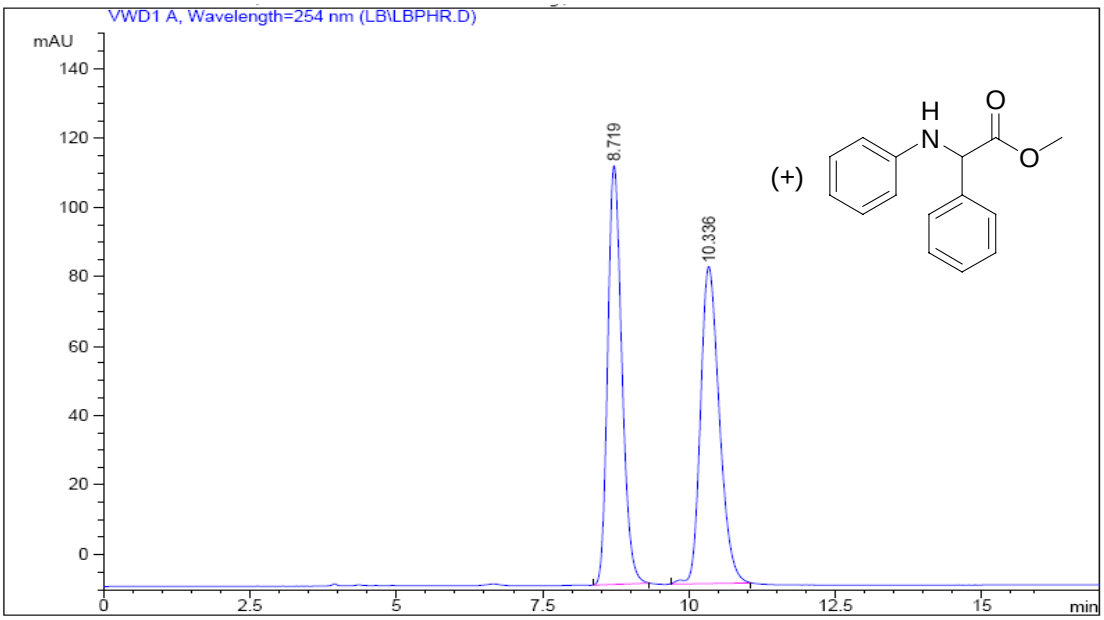


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.408	VV	0.1726	1.40023e4	1267.18677	97.2162
2	7.308	VV	0.2207	400.95395	27.56659	2.7838

(+)-Methyl 2-phenyl-2-(phenylamino)acetate (4q)





Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.687	BB	0.2551	1169.48169	70.89153	54.0120
2	10.292	VB	0.3374	995.74396	45.92213	45.9880