Electronic Supplementary Information

Enantioselective Synthesis of α-Deuterium Labelled Chiral α-Amino Acids via Dynamic Kinetic Resolution of Racemic Azlactones

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Contents

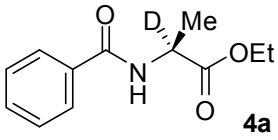
1. General remarks and materials

Cinchona alkaloids and commercially available racemic amino acids were purchased from Aldrich and used without further purification. The squaramide-base dimeric cinchona alkaloid catalysts **2a-c** were synthesized according to the procedure reported by us.[1] The azlactones **3a-j** were prepared from the corresponding amino acids according to the literature procedure.[2] *O*-Methylated *rac*-*N*-benzoyl m-tyrosine and *O,O'*-dimethylated *rac*-*N*-benzoyl DOPA were prepared according to the Erlenmeyer protocol for amino acid synthesis; (i) the reaction of 4-methoxybenzaldehyde and 3,4-dimethoxybenzaldehyde, respectively, with *N*-benzoyl glycine, (ii) hydrolysis and (iii) hydrogenation.[3] All other chemicals used in this study were obtained from commercial sources and used without further purification.
The chromatographic purification of the products was carried out by flash chromatography using Merck silica gel 60 (230–400 mesh). Thin-layer chromatography was carried out on Merck silica gel 60F plates. HPLC analyses were performed on a Varian Pro Star Series instrument equipped with an isostatic pump using a CHIRALCEL Column (250 × 4.6 mm). The melting points (Mps) were determined on a Buchi B-540 melting point apparatus and were uncorrected. The optical rotation was measured on a PerkinElmer Polarimeter 343 plus. The ^{1}H and ^{13}C NMR spectra were recorded on Varian 300 or Varian 500 spectrometers. The IR spectra were obtained using a Bruker Vertex 70 spectrometer with MIRacle Micro ATR accessory. The MS spectra (APCI) were recorded on a Varian 500-MS LC Ion Trap Mass Spectrometer.

2. General procedure for the DKR reaction of the azlactones

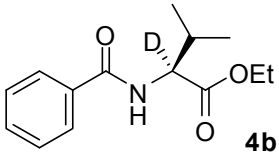
Ethyl alcohol-d_6 (3.0 mL, 50 mmol) was added to a stirred solution of the azlactones (**3**, 1.0 mmol) and catalysts (**2a-2c**) (10 mol%) in anhydrous CH_2Cl_2 (2 mL). The reaction mixture was stirred until the disappearence of **3**, as monitored by TLC. After completion of the reaction, aqueous solution of HCl (2 N, 3 mL) was added to the reaction mixture, which was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phase was washed with water, dried over anhydrous $MgSO_4$, and concentrated. The obtained crude product was purified by column chromatography on silica gel (EtOAc:Hexane = 1:4) to give the α-deuterated *N*-acylated α-amino allyl ester **4**. The enantiomeric excess value was determined by the chiral HPLC analysis (OD-H).

3. Analytical data of products



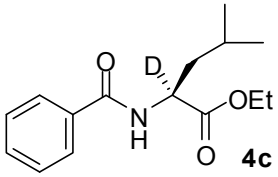
4a

mp 88 °C; $[\alpha]^{20}_{D}$: 38.16 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, *J* = 7.1 Hz, 3H), 1.37 (s, 3H), 4.09 (q, *J* = 7.1Hz, 2H) 7.11 (s, 1H), 7.23-7.38 (m, 3H), 7.68-7.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.83, 17.85, 47.74, 48.03, 61.17, 126.85, 128.14, 131.29, 133.59, 166.74, 172.94; LR-MS (APCI) Calcd for $[C_{12}H_{14}DNO_3+H]^+$: 223 (100.0 %); IR (liquid) 3316, 2925, 1737, 1643, 1531, 1487, 1273, 1136, 1095, 1024, 714,, 693 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 7.9 min (major), t_S = 10.5 min.



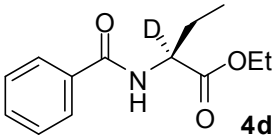
4b

mp 72 °C; $[\alpha]^{20}_{D}$: 47.92 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 2.16 (hept, *J* = 6.9 Hz, 1H), 4.10 (sym.m, 2H), 6.82 (s, 1H), 7.25-7.40 (m, 3H), 7.69-7.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.93, 17.72, 31.13, 56.95, 60.94, 126.82, 128.18, 131.30, 133.89, 167.05, 171.85; LR-MS (APCI) Calcd for $[C_{14}H_{18}DNO_3+H]^+$: 251 (100.0 %); IR (liquid) 3322, 2967, 1734, 1647, 1580, 1485, 1391, 1370, 1263, 1095, 1058, 754, 693 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 5.9 min (major), t_S = 7.5 min.



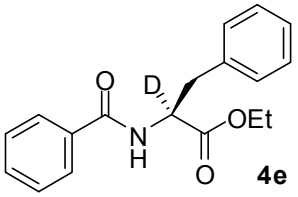
4c

mp 68 °C; $[\alpha]^{20}_{D}$: 39.52 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (d, *J* = 6.0 Hz, 3H), 0.97 (d, *J* = 6.0 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.65-1.81 (m, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 7.07 (s, 1H), 7.32-7.47 (m, 3H), 7.77-7.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.91, 21.71, 22.63, 24.72, 41.16, 50.73, 61.07, 126.89, 128.15, 131.28, 133.66, 166.97, 173.15; LR-MS (APCI) Calcd for $[C_{15}H_{20}DNO_3+H]^+$: 265 (100.0 %); IR (liquid) 3321, 2958, 1738, 1641, 1529, 1244, 1058, 1025, 800, 712, 693 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 6.1 min (major), t_S = 10.2 min.



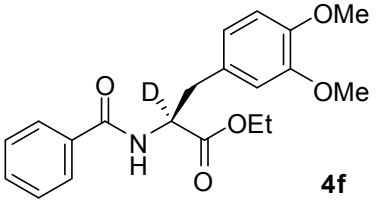
4d

Mp 68 °C; $[\alpha]^{20}_{D}$: 65.84 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.5 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.82 (dt, *J* = 7.2 Hz, $1H_A$ of AB-spin system), 1.99 (dt, *J* = 7.2 Hz, $1H_B$ of AB-spin system), 4.12-4.28 (sym.m, 2H), 7.14 (s, 1H) 7.34-7.48 (m, 3H), 7.80-7.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.38, 13.85, 25.15, 53.23, 61.03, 126.82, 128.11, 133.69, 166.92, 172.30; LR-MS (APCI) Calcd for $[C_{13}H_{16}DNO_3+H]^+$: 237 (100.0 %); IR (liquid) 3316, 2975, 2936, 1736, 1643, 1528, 1298, 1251, 1177, 1104, 754, 713 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 6.7 min (major), t_S = 9.5 min.



4e

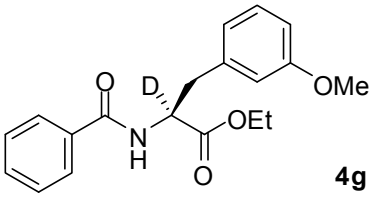
mp 92 °C; $[\alpha]^{20}_{D}$: 115.4 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (t, *J* = 7.1 Hz, 3H), 3.17 (d, *J* = 13.8 Hz, $1H_A$ of AB-spin system), 3.25 (d, *J* = 13.8 Hz, $1H_B$ of AB-spin system), 4.14 (q, *J* = 7.1 Hz, 2H), 6.98 (s, 1H), 7.13-7.44 (m, 8H), 7.69-7.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.79, 37.43, 53.14, 61.16, 126.70, 126.75, 128.17, 129.02, 131.31, 133.59, 135.83, 166.67, 171.38; LR-MS (APCI) Calcd for $[C_{18}H_{18}DNO_3+H]^+$: 299 (100.0 %); IR (liquid) 3318, 2927, 1737, 1642, 1527, 1486, 1265, 1221, 1202, 745, 698 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 9.1 min (major), t_S = 12.8 min.



4f

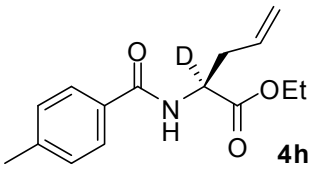
mp 98 °C; $[\alpha]^{20}_{D}$: 45.44 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H), 3.13 (d, *J* = 14.1 Hz, $1H_A$ of AB-spin system), 3.22 (d, *J* = 14.1 Hz, $1H_B$ of AB-spin system), 3.72 (s, 3H), 3.78 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 6.69-6.77 (m, 3H), 7.09 (s, 1H), 7.30-7.45 (m, 3H), 7.72-7.76 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.61, 36.59, 53.07, 55.08, 55.20, 60.88, 110.74, 112.02, 120.87, 126.50, 127.92, 128.12, 131.10, 133.34, 147.52, 148.28, 166.37, 171.20; LR-MS (APCI) Calcd for $[C_{20}H_{22}DNO_5+H]^+$: 359 (100.0 %); IR (liquid) 3324, 2938, 1745, 1635, 1517, 1312, 1295, 1156, 1083, 1027, 801, 723 cm^{-1};

Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 17.6 min (major), t_S = 20.6 min.



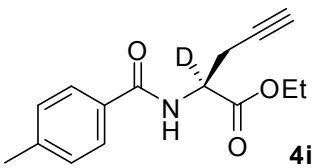
4g

mp 112 °C; $[\alpha]^{20}_D$: 87.76 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.1 Hz, 3H), 3.18 (d, *J* = 13.8 Hz, $1H_A$ of AB-spin system), 3.25 (d, *J* = 13.8 Hz, $1H_B$ of AB-spin system), 3.70 (s, 3H), 4.19 (q, *J* = 7.1 Hz, 2H), 6.69-6.78 (m, 3H), 7.15-7.21 (m,1H), 7.35-7.50 (m, 3H), 7.70-7.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.98, 37.62, 53.13, 54.59, 61.42, 112.48, 114.78, 121.50, 126.85, 128.38, 129.34, 131.54, 133.76, 137.32, 159,52, 166.72, 171.43; LR-MS (APCI) Calcd for $[C_{19}H_{20}DNO_4+H]^+$: 329 (100.0 %); IR (liquid) 3330, 2935, 1740, 1634, 1521, 1490, 1186, 1171, 1030, 780, 729, 690 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: Chiralcel OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 11.8 min (major), t_S = 14.5 min.



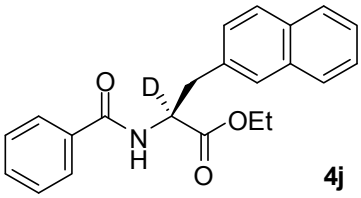
4h

mp 60 °C; $[\alpha]^{20}_D$: 70.56 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.0 Hz, 3H), 2.38 (s, 3H), 2.58–2.78 (m, 2H), 2.60 (dd, *J* = 14.5 Hz and 7.0 Hz, $1H_A$ of AB-spin system), 2.72 (dd, *J* = 14.5 Hz and 7.0 Hz, $1H_B$ of AB-spin system), 4.18-4.28 (sym.m. 2H), 5.12-5.17 (m, 2H), 5.71–5.80 (sym.m, 1H), 6.75 (s, 1H), 7.21 (d, *J* = 8,0 Hz, 2H), 7.69 (d, *J* = 8,0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.16, 21.37, 36.61, 51.92, 61.49, 119.11, 126.97, 129.14, 131.14, 132.27, 142.06, 166.73, 171.82; LR-MS (APCI) Calcd for $[C_{15}H_{18}DNO_3+H]^+$: 263 (100.0 %); IR (liquid) 3320, 2982, 1738, 1637, 1531, 1503, 1187, 1157, 1021, 920, 835, 752, 649 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: CHIRALPAK OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 5.8 min, t_S =9.3 min.



4i

mp 58 °C; $[\alpha]^{20}_D$: 46.0 (*c* = 0.25 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.1 Hz, 3H), 2.05 (t, *J* = 2.7 Hz, 1H), 2.40 (s, 3H), 2.85 (dd, *J* = 17.5 Hz and 2.5 Hz, $1H_A$ of AB-spin system), 2.92 (dd, *J* = 17.5 Hz and 2.5 Hz, $1H_B$ of AB-spin system), 4.22–4.34 (sym.m, 2H), 6.97 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.13, 21.42, 22.58, 50.94, 61.97, 71.53, 78.53, 127.09, 129.21, 130.93, 142.29, 166.83, 170.47; LR-MS (APCI) Calcd for $[C_{15}H_{16}DNO_3+H]^+$: 261 (100.0 %); IR (liquid) 3296, 2929, 1737, 1644, 1531, 1274, 1229, 1096, 1025, 837, 752 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: CHIRALPAK OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 7.8 min, t_S =10.5 min.

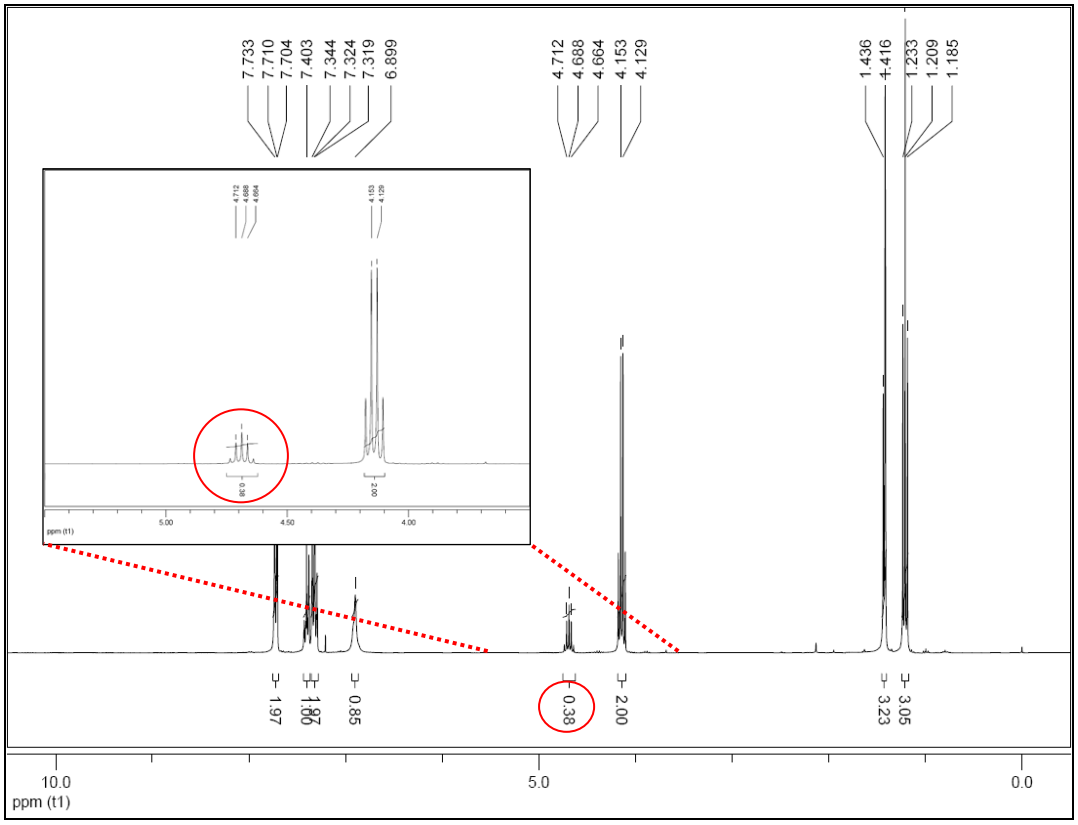


4j

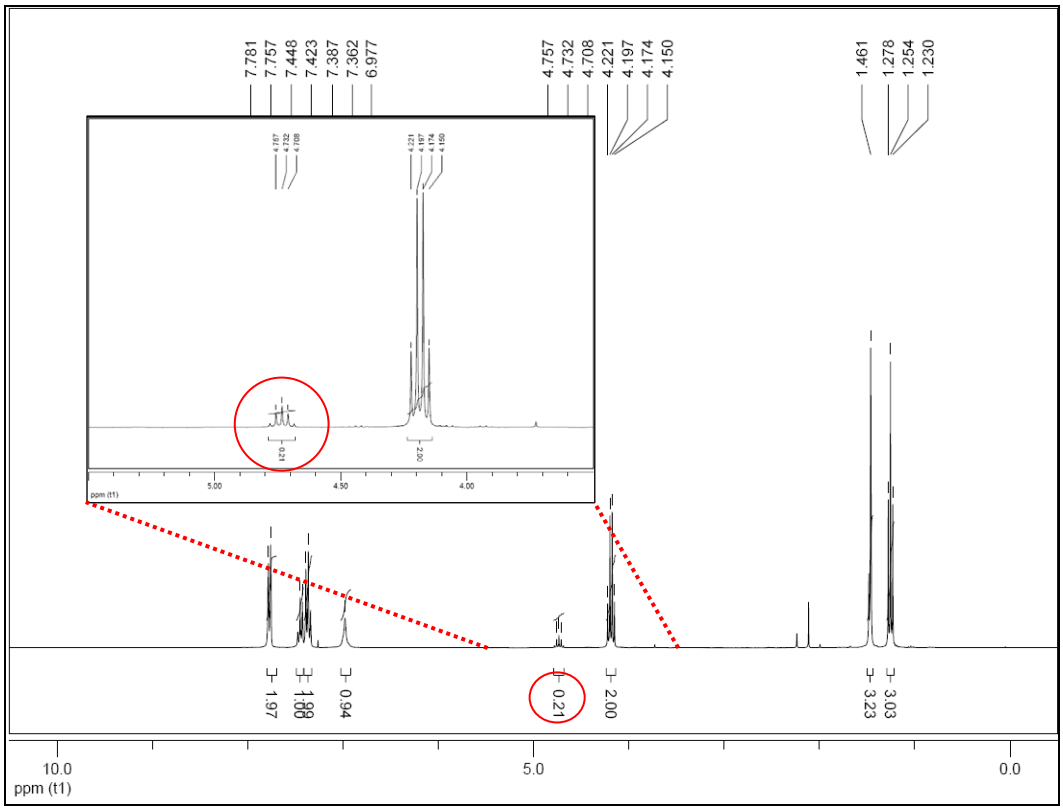
mp120 °C; $[\alpha]^{20}_D$: 41.60 (*c* = 0.25 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, *J* = 7.1 Hz, 3H), 3.37 (d, *J* = 14.0 Hz, $1H_A$ of AB-spin system), 3.42 (d, *J* = 14.0 Hz, $1H_B$ of AB-spin system), 4.14-4.21 (sym.m, 2H), 6.75 (br. s, 1H), 7.27–7.45 (m, 6H), 7.59 (br s, 1H), 7.69–7.79 (m, 5H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.91, 37.80, 53.55, 61.39, 125.50, 125.94, 126.84, 127.26, 127.30, 127.44, 127.93, 127.96, 128.31, 131.46, 132.28, 133.21, 133.44, 133.71, 166.81, 171.44; LR-MS (APCI) Calcd for $[C_{22}H_{20}DNO_3+H]^+$: 349 (100.0 %); IR (powder) 3705, 2980, 2865, 1745, 1632, 1275, 1126, 1031, 1018, 812, 721 cm^{-1}; Enantiomeric excess was determined by using HPLC analysis: CHIRALPAK OD-H; Hexane: Isopropyl alcohol=90:10; flow rate: 1.0 mL/min; 220 nm; t_R = 12.1 min, t_S =14.8 min.

4. NMR Spectra for Table 1

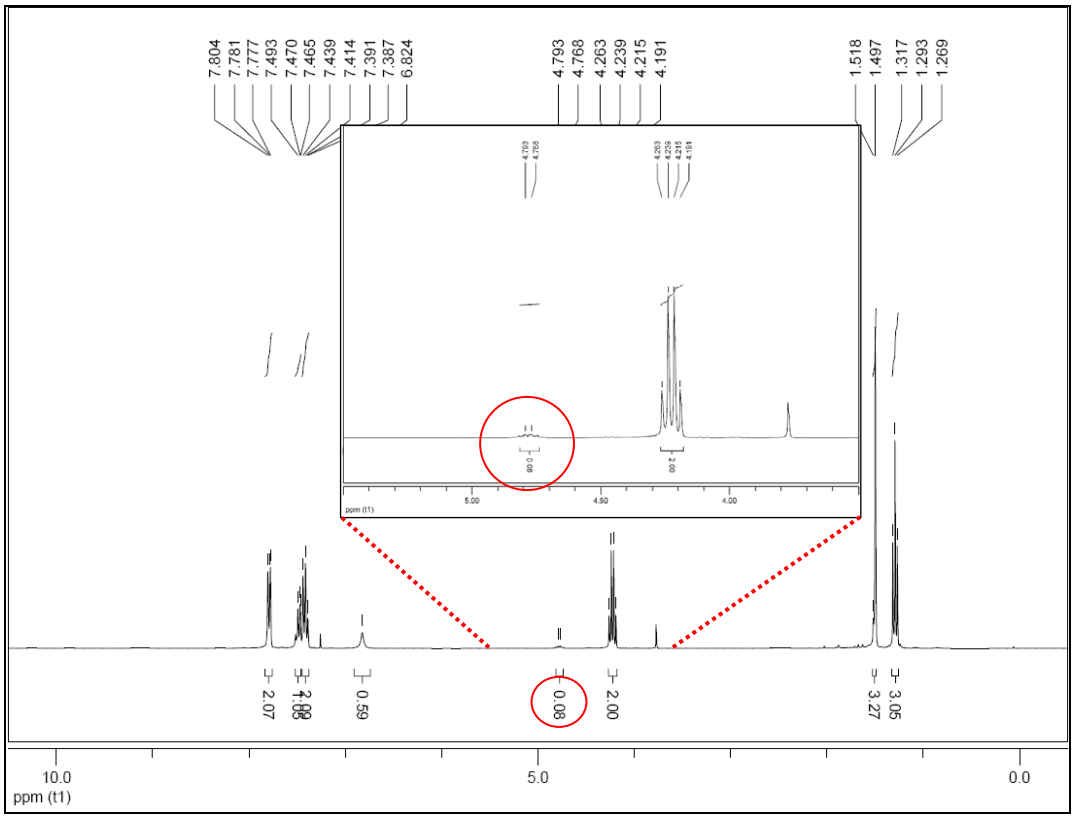
Entry 1 (^{1}H NMR)



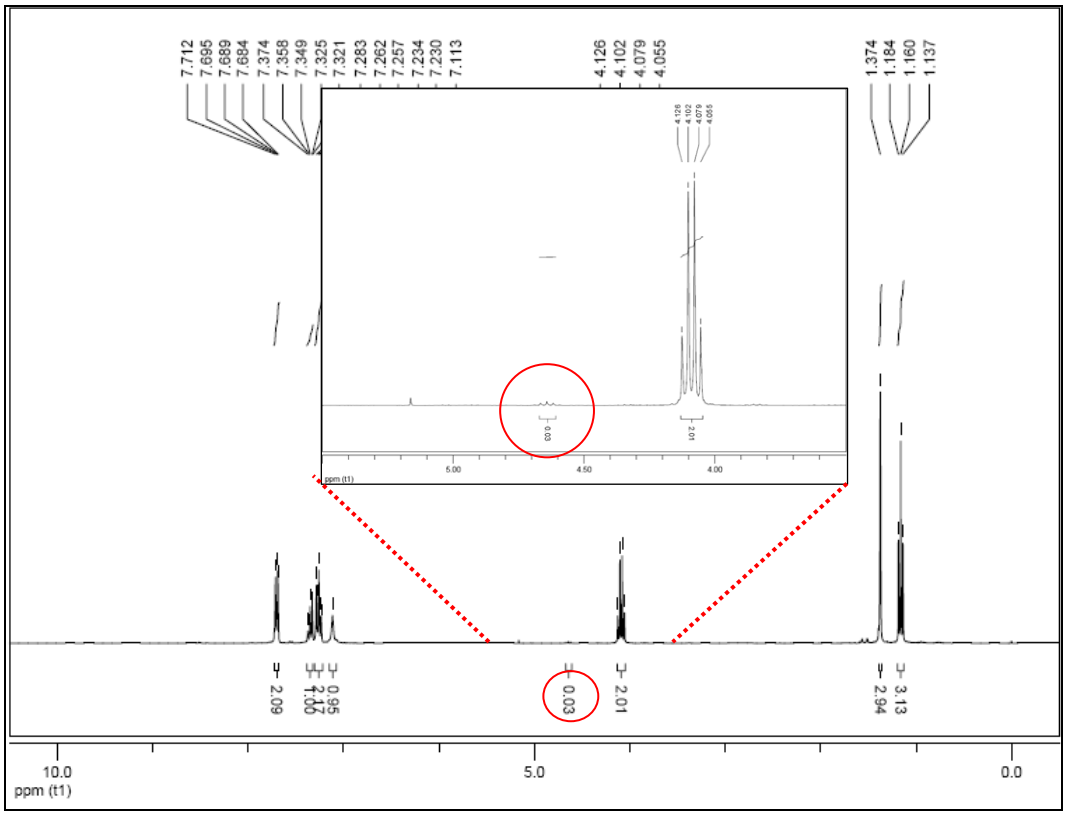
Entry 2 (^{1}H NMR)



Entry 3 (^{1}H NMR)

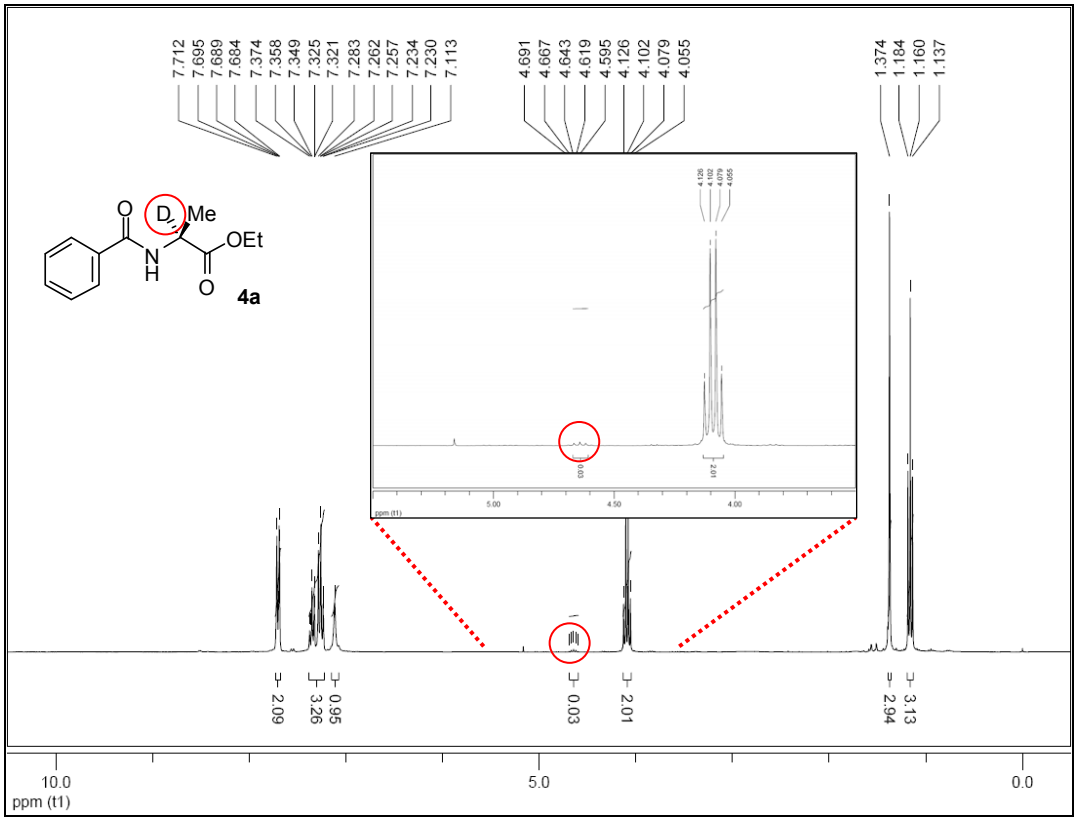


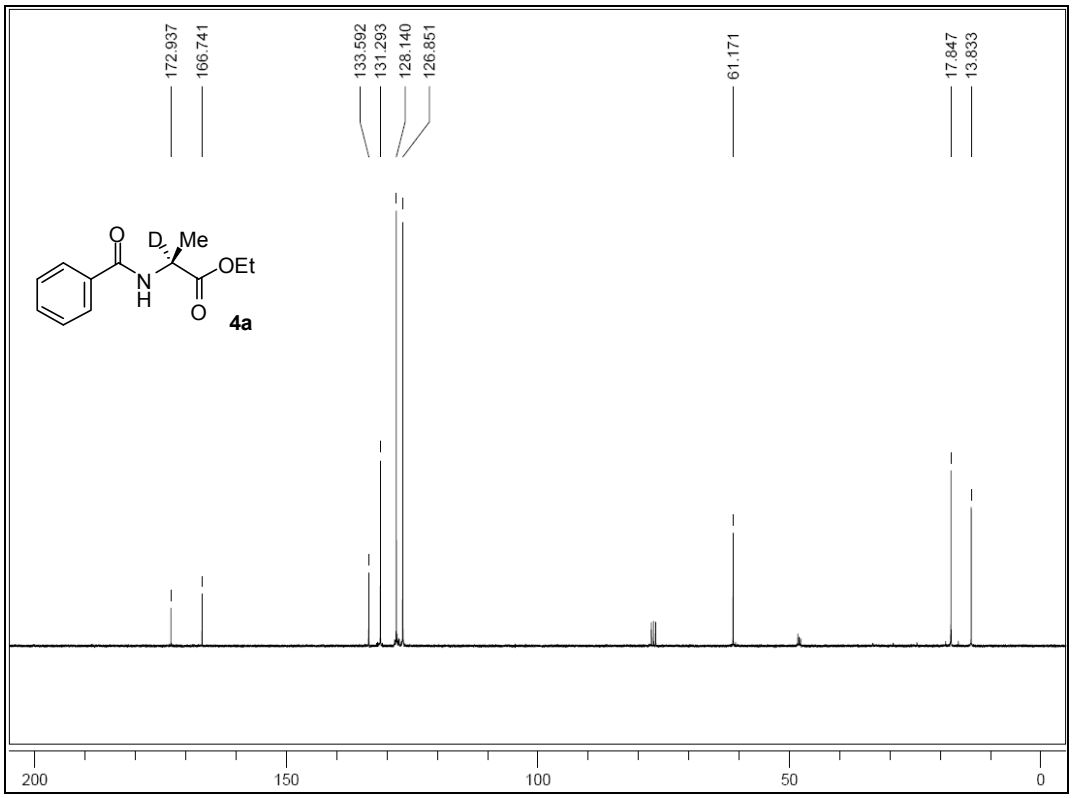
Entry 4 (^{1}H NMR)



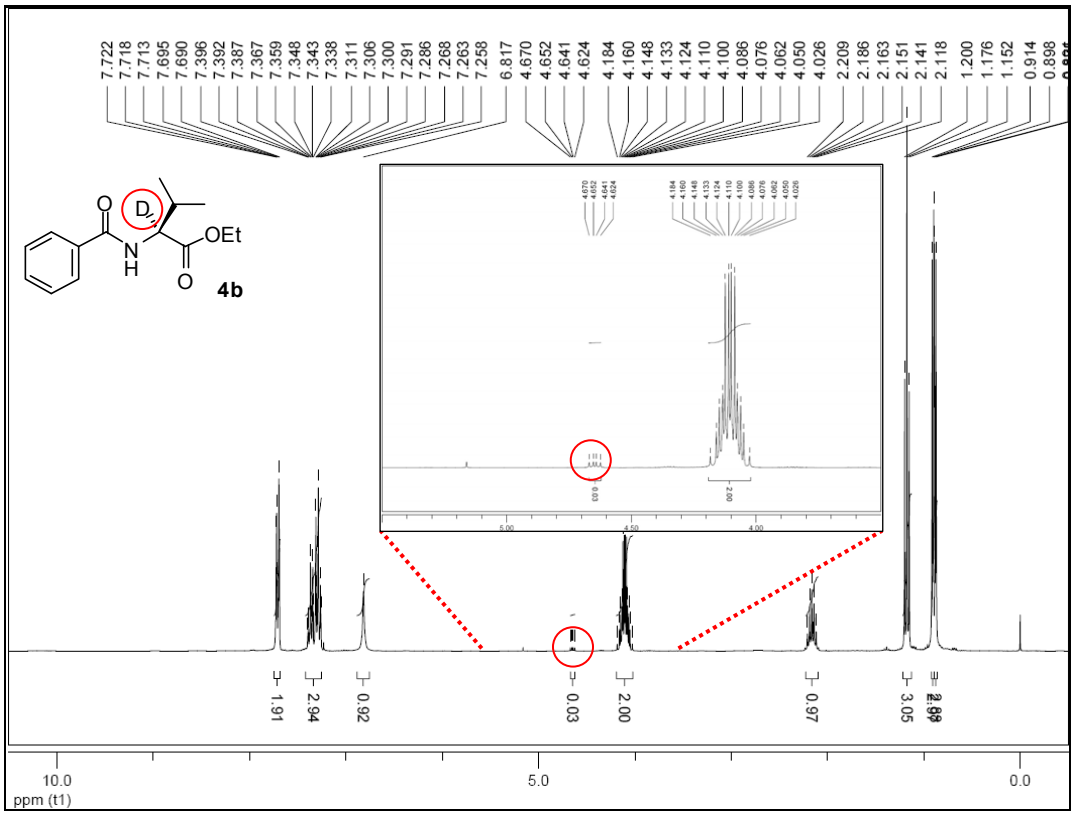
5. NMR Spectra for 4a-4j (Table 2)

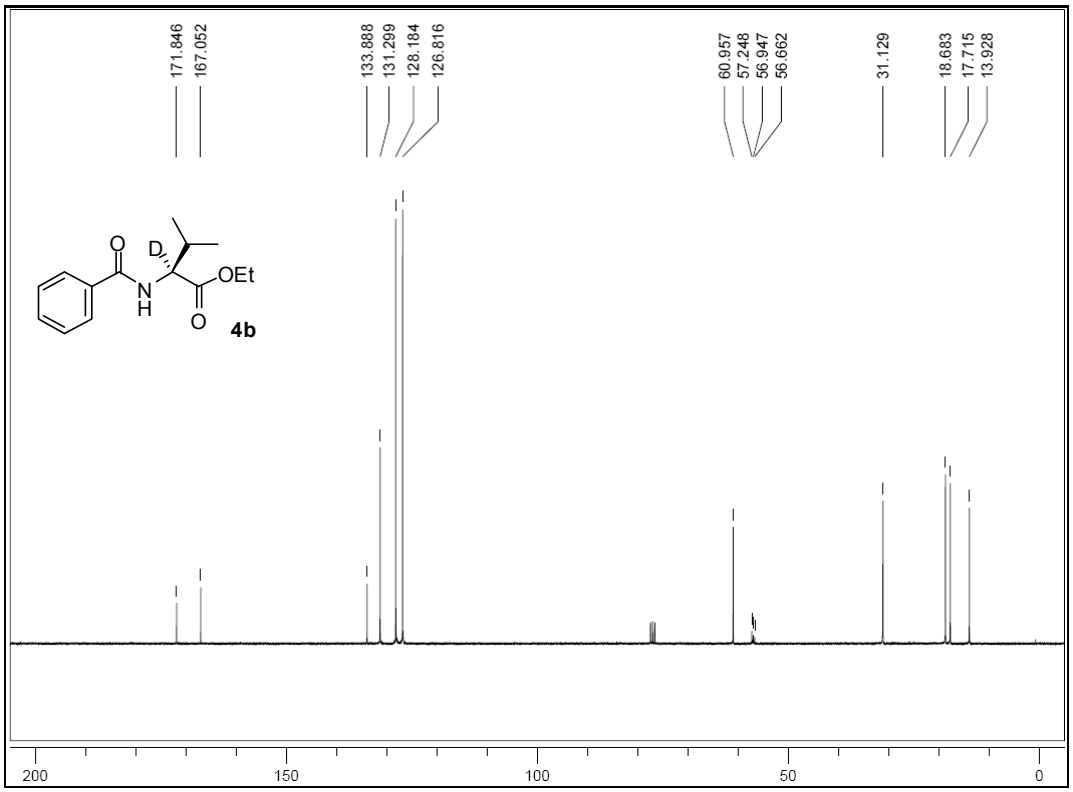
^{1}H and ^{13}C NMR of **4a**



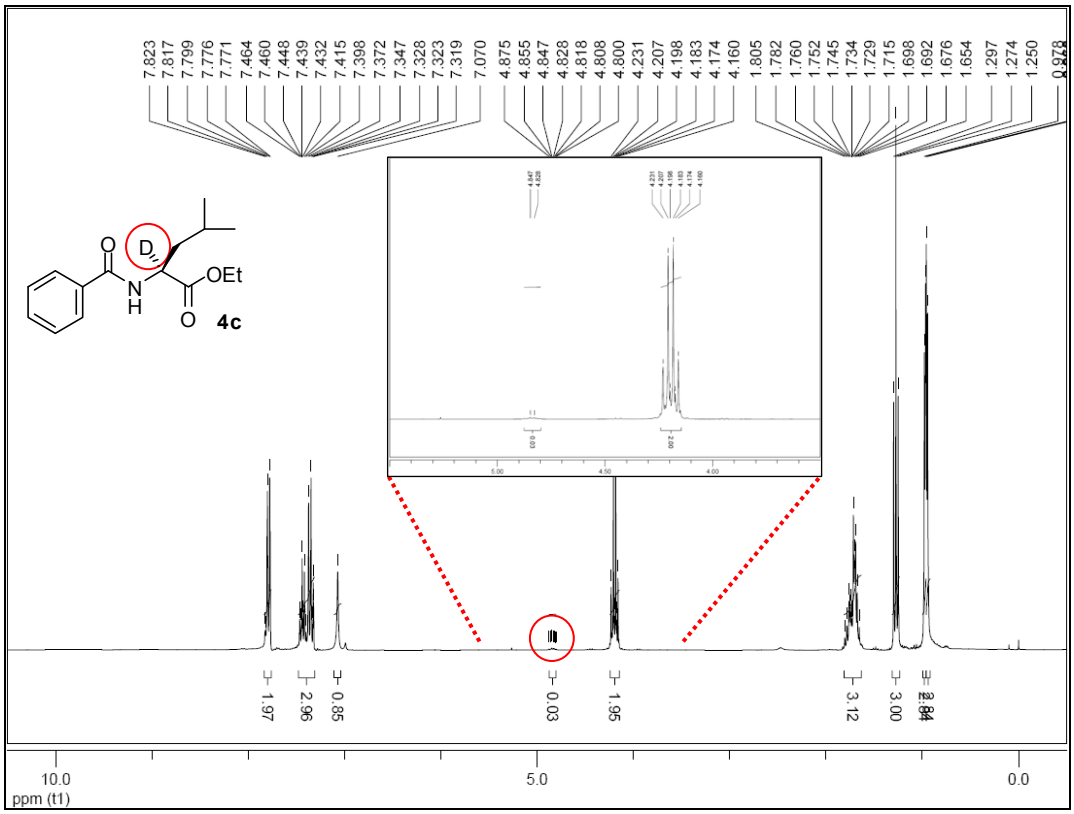


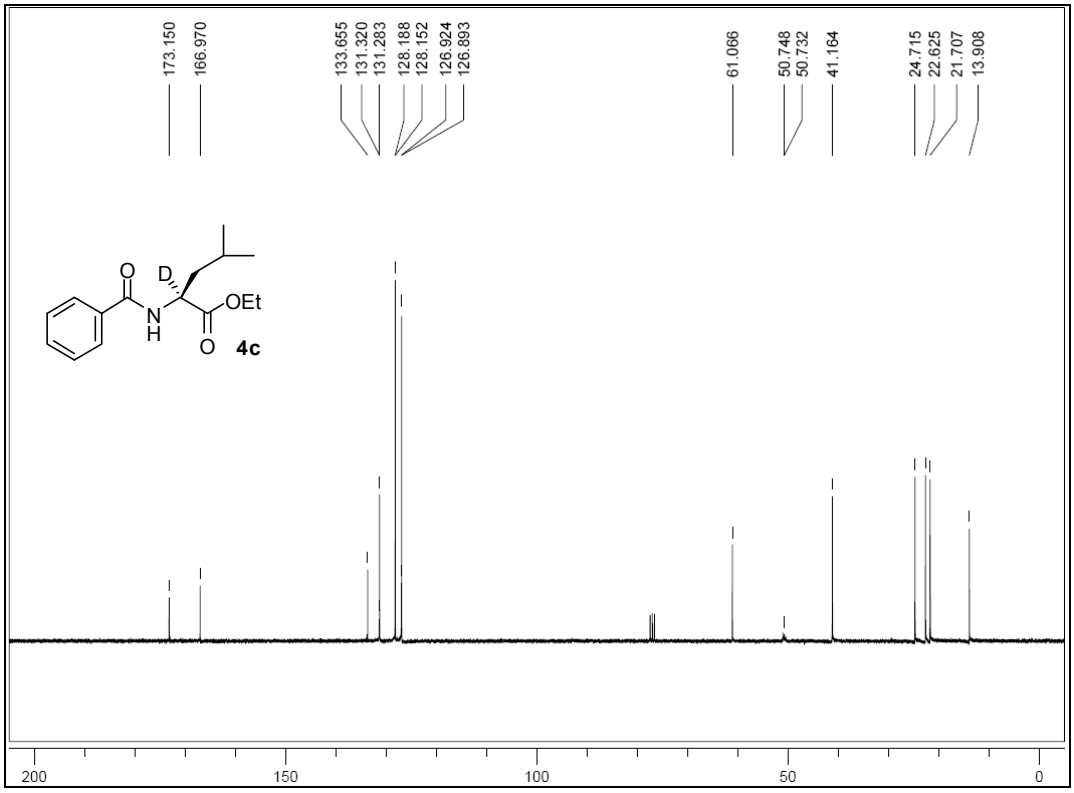
^{1}H and ^{13}C NMR of **4b**



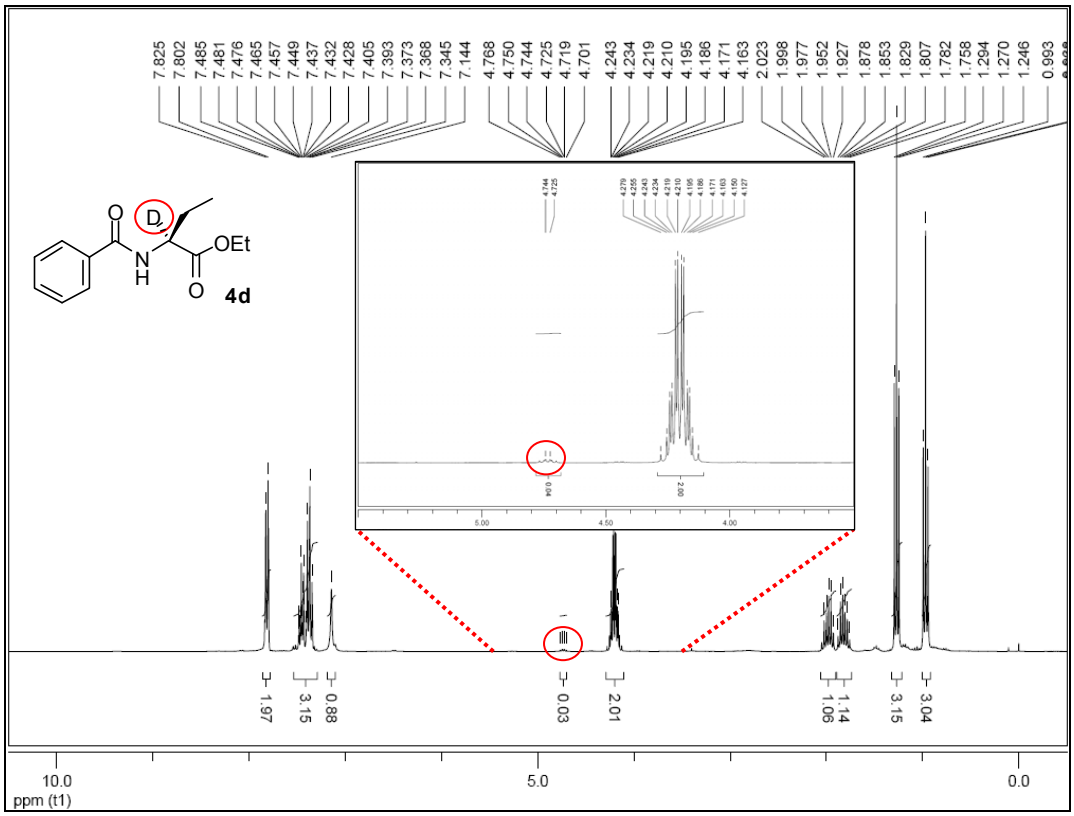


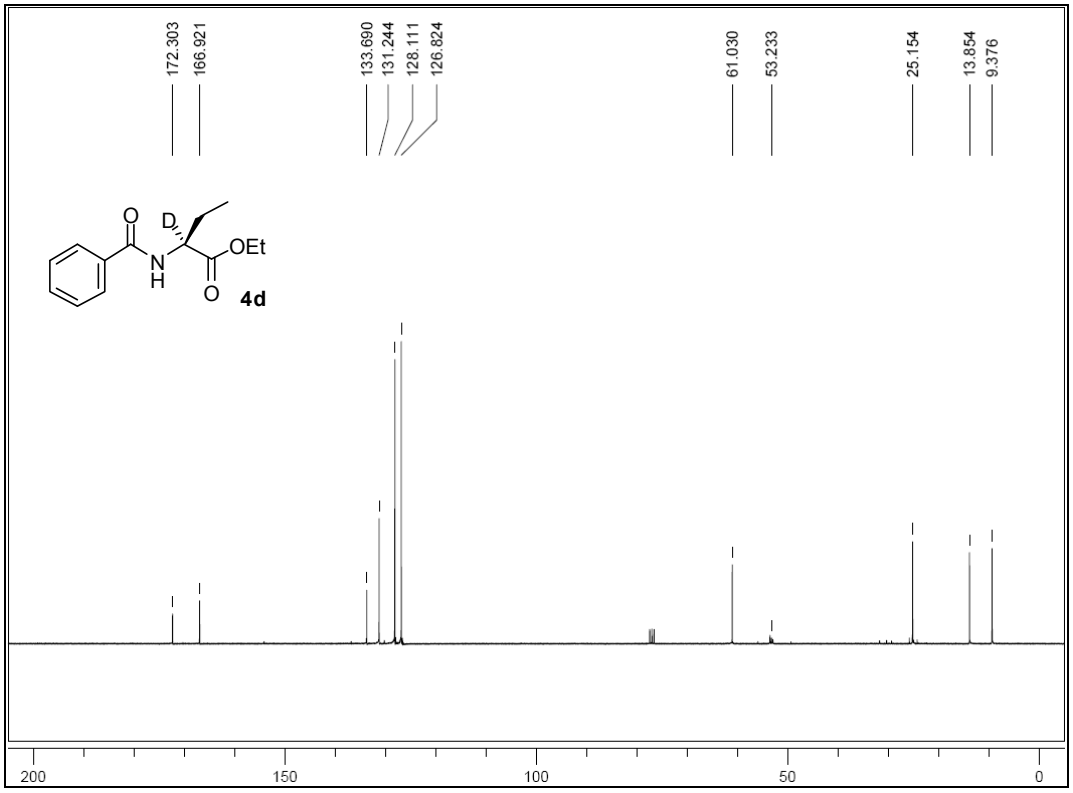
^{1}H and ^{13}C NMR of **4c**



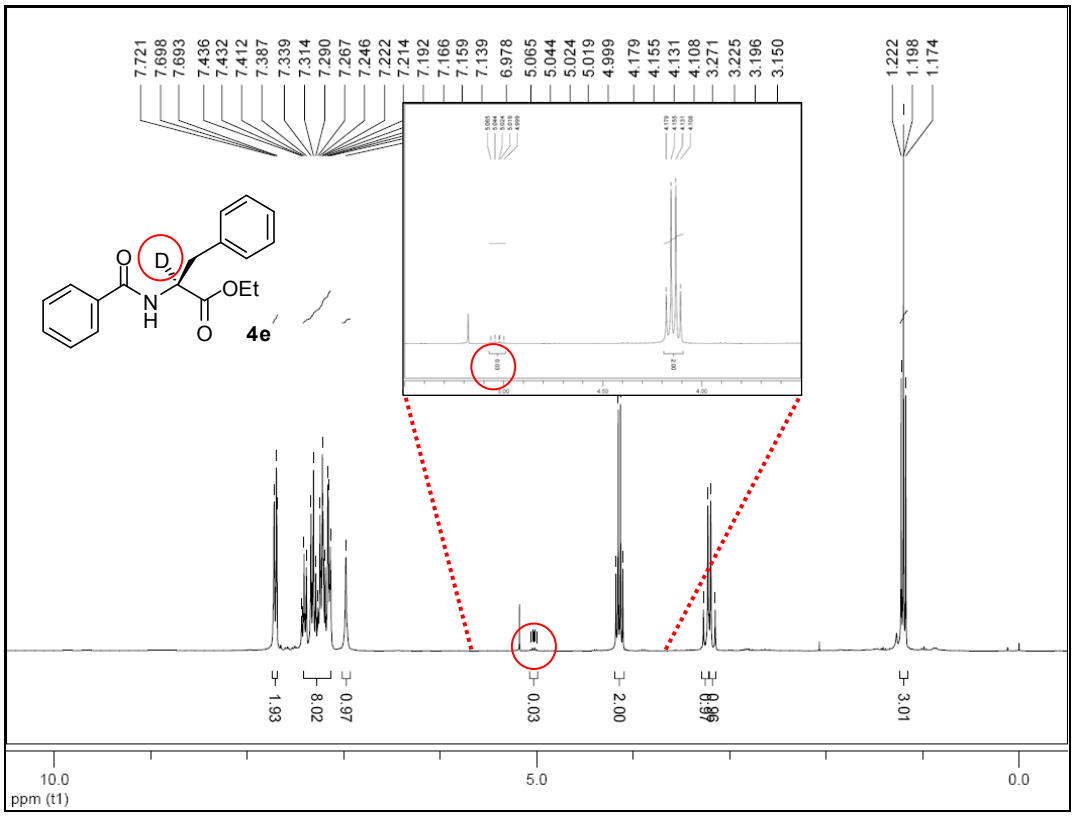


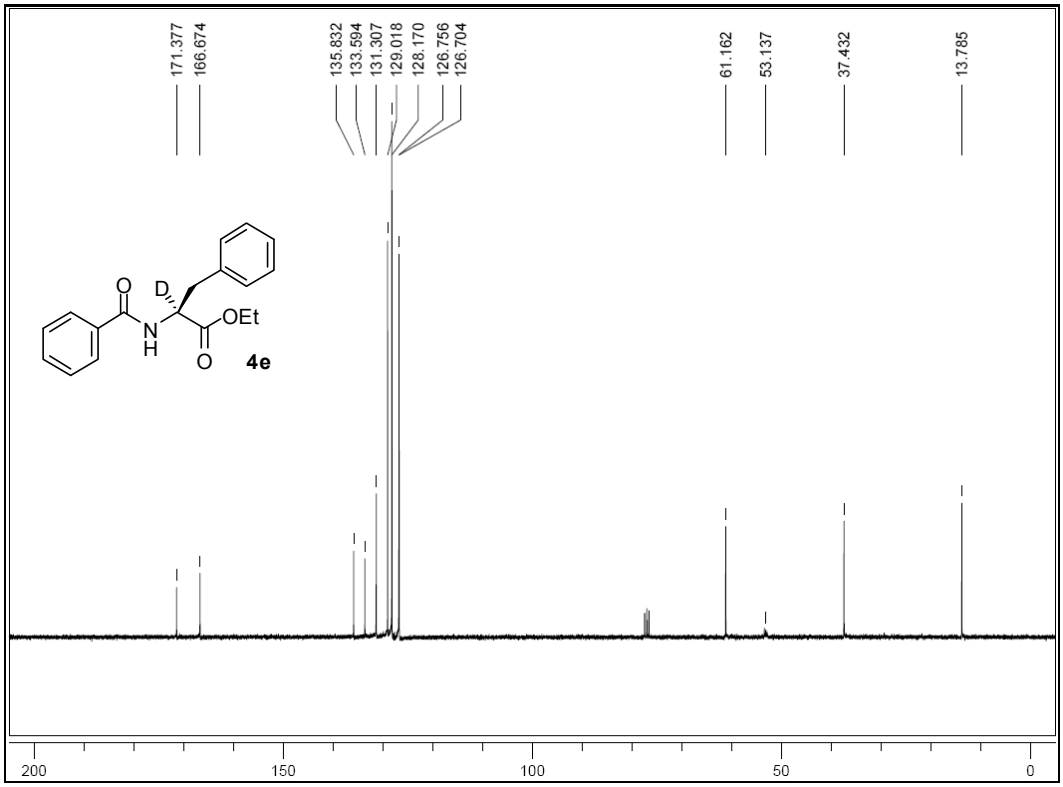
^{1}H and ^{13}C NMR of **4d**



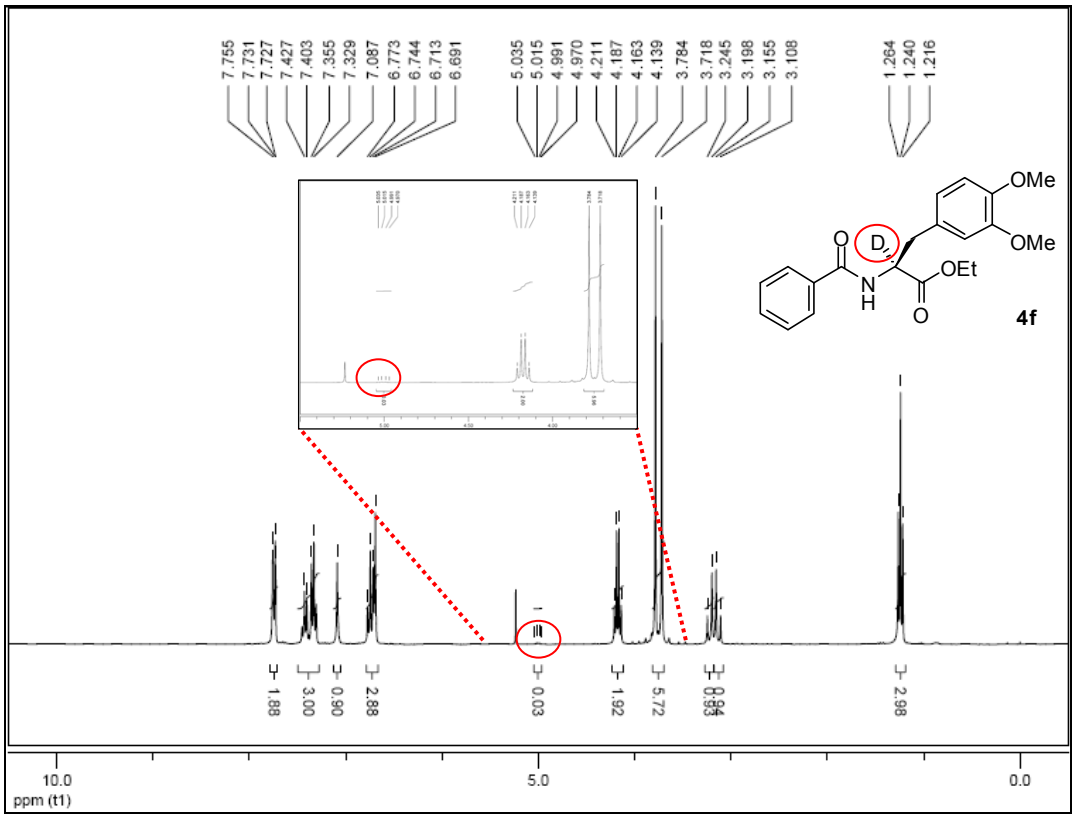


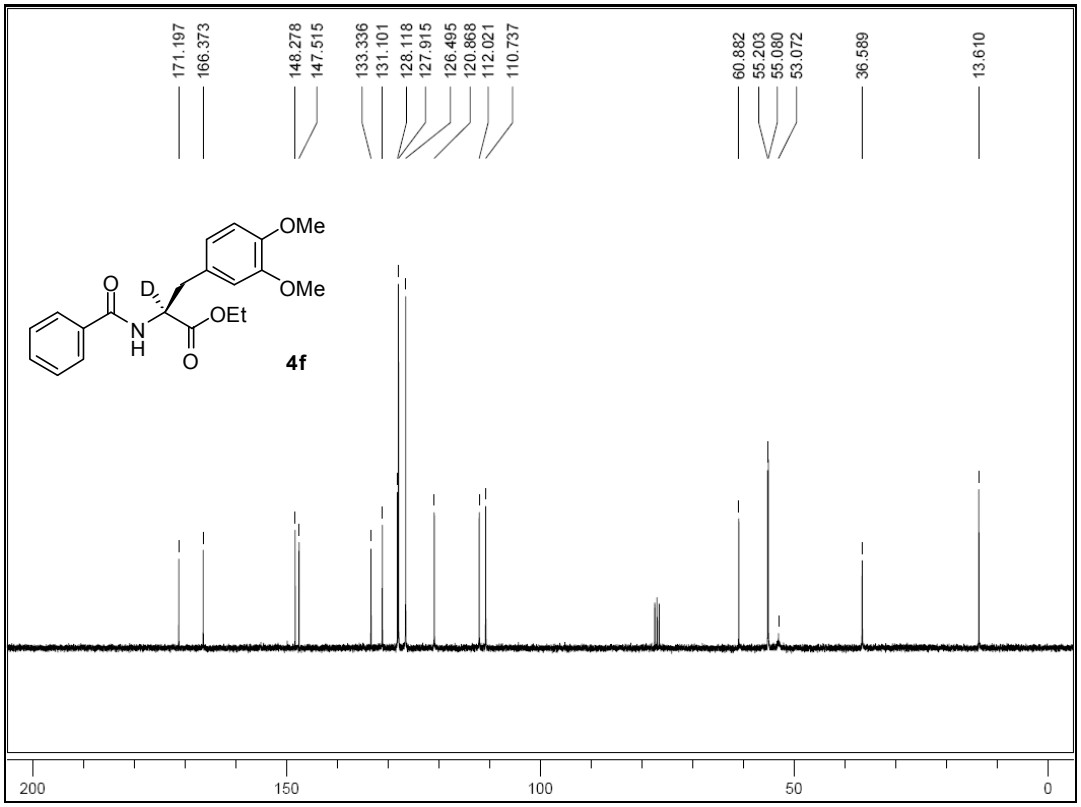
^{1}H and ^{13}C NMR of **4e**



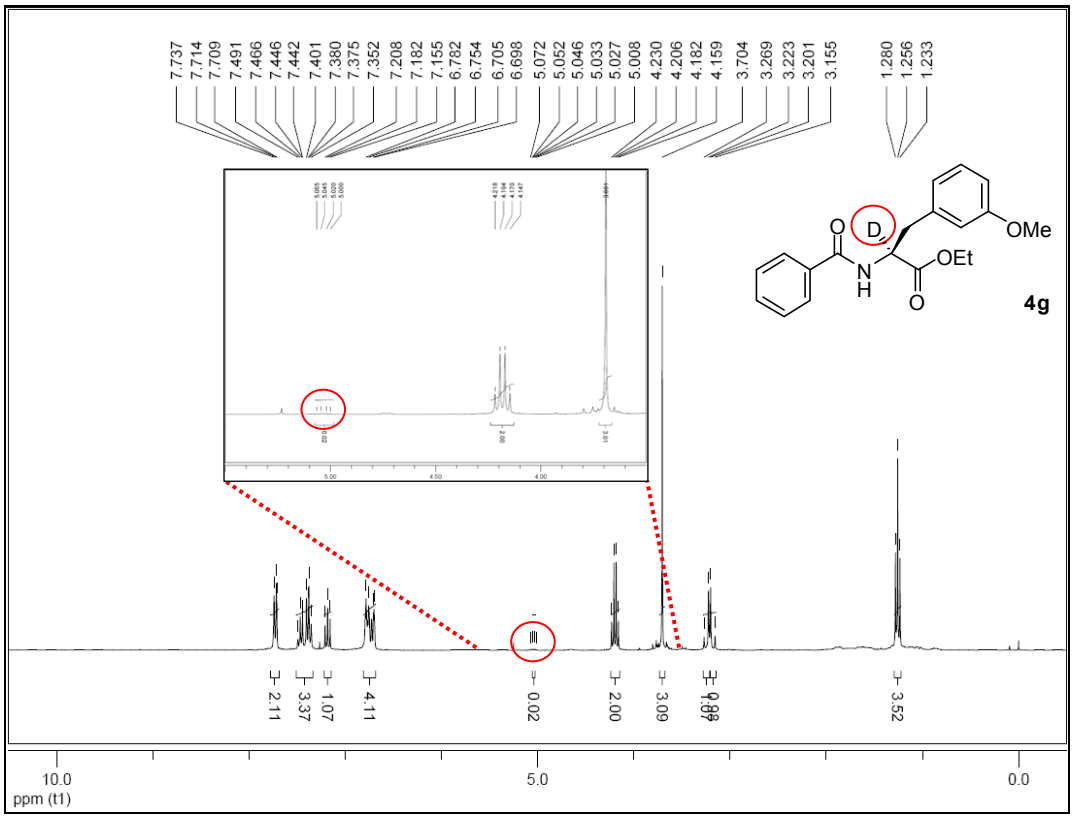


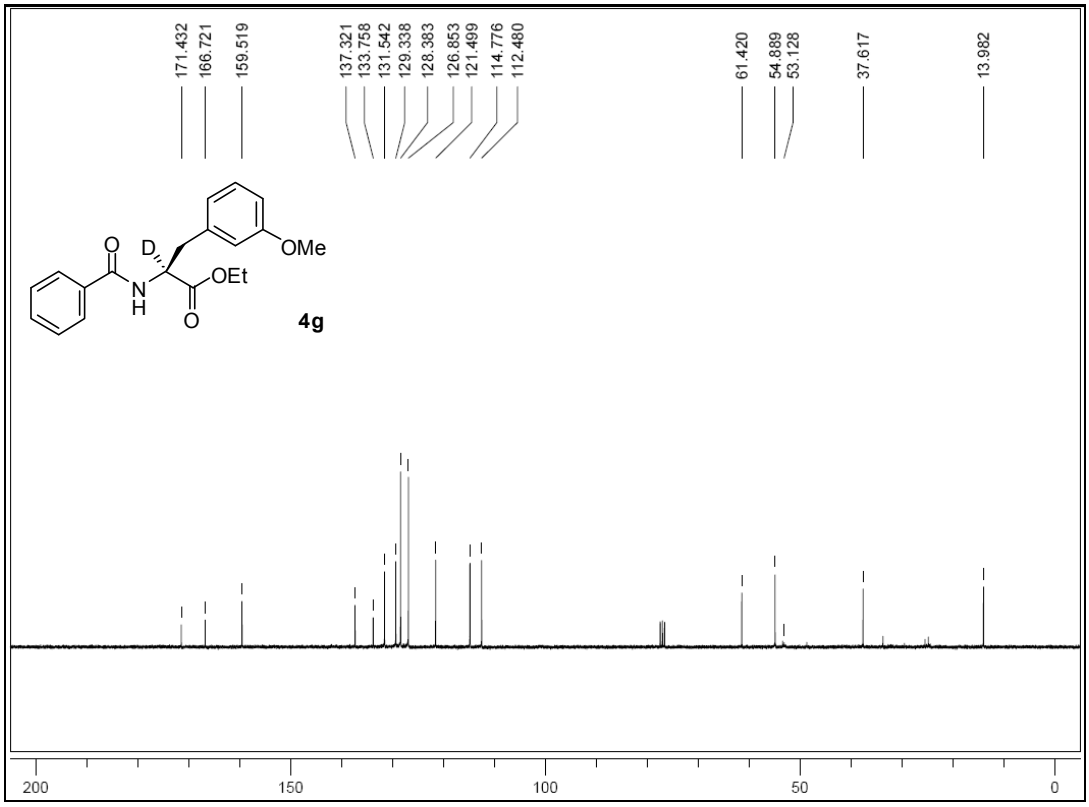
^{1}H and ^{13}C NMR of **4f**



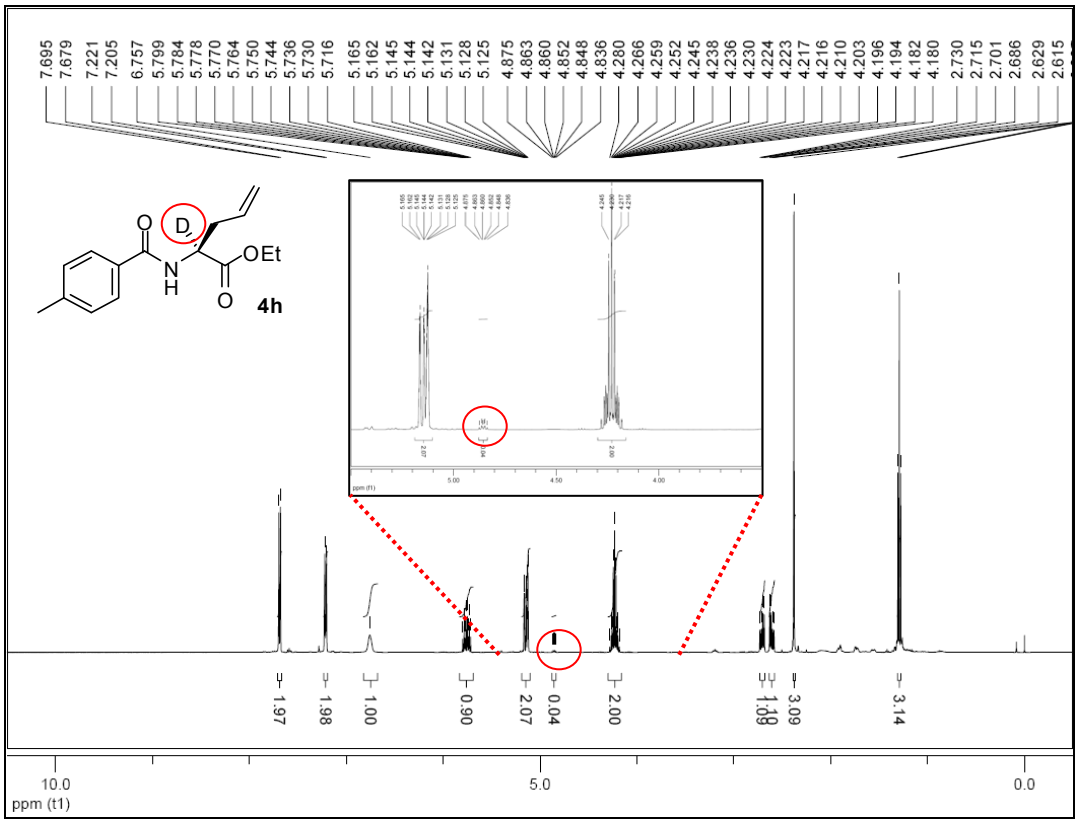


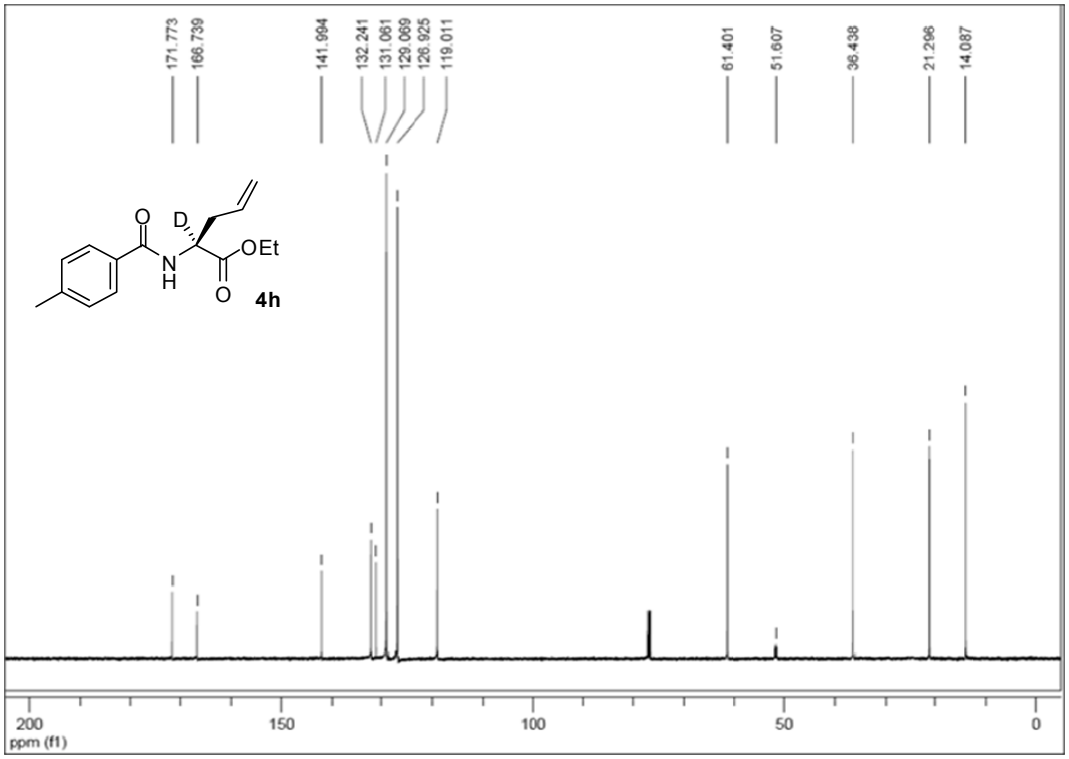
^{1}H and ^{13}C NMR of **4g**



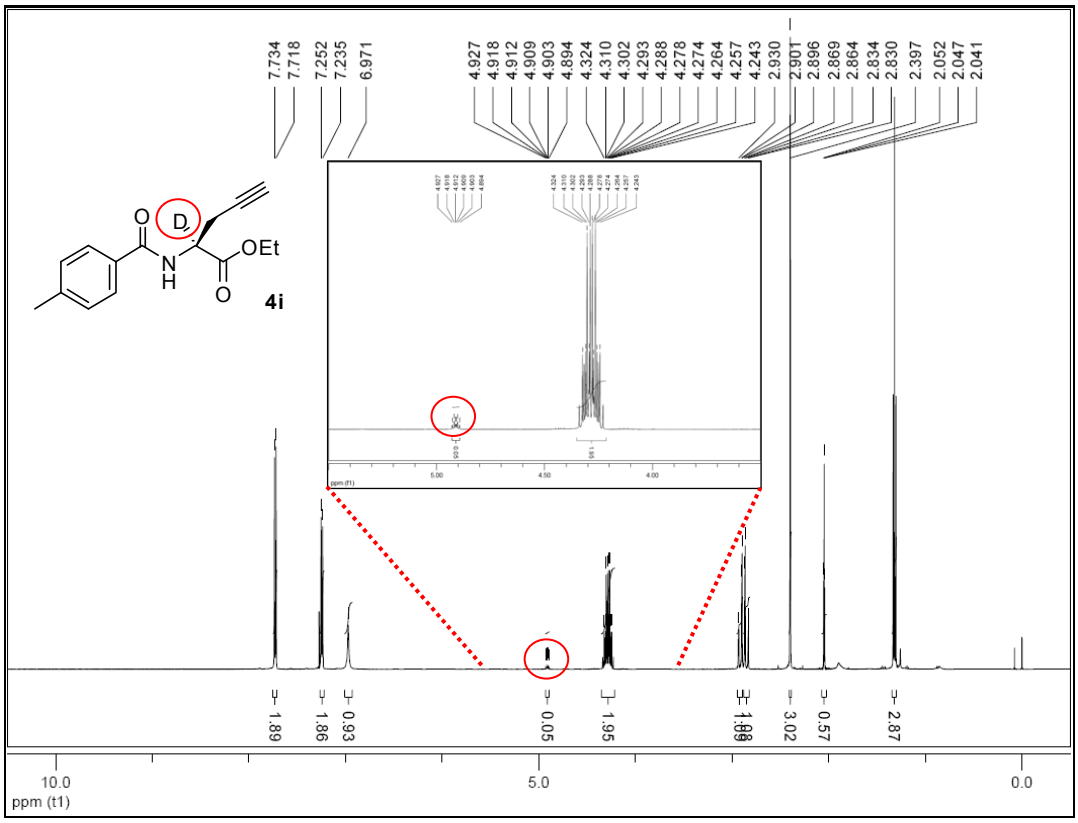


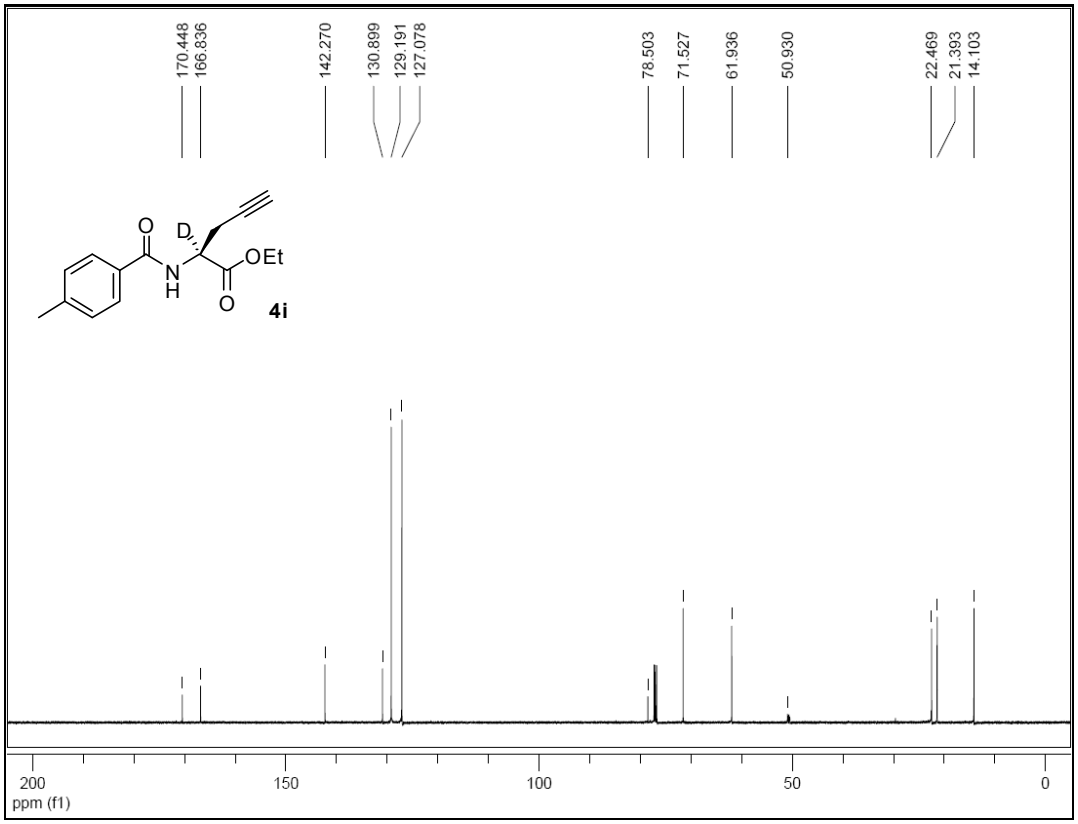
^{1}H and ^{13}C NMR of **4h**



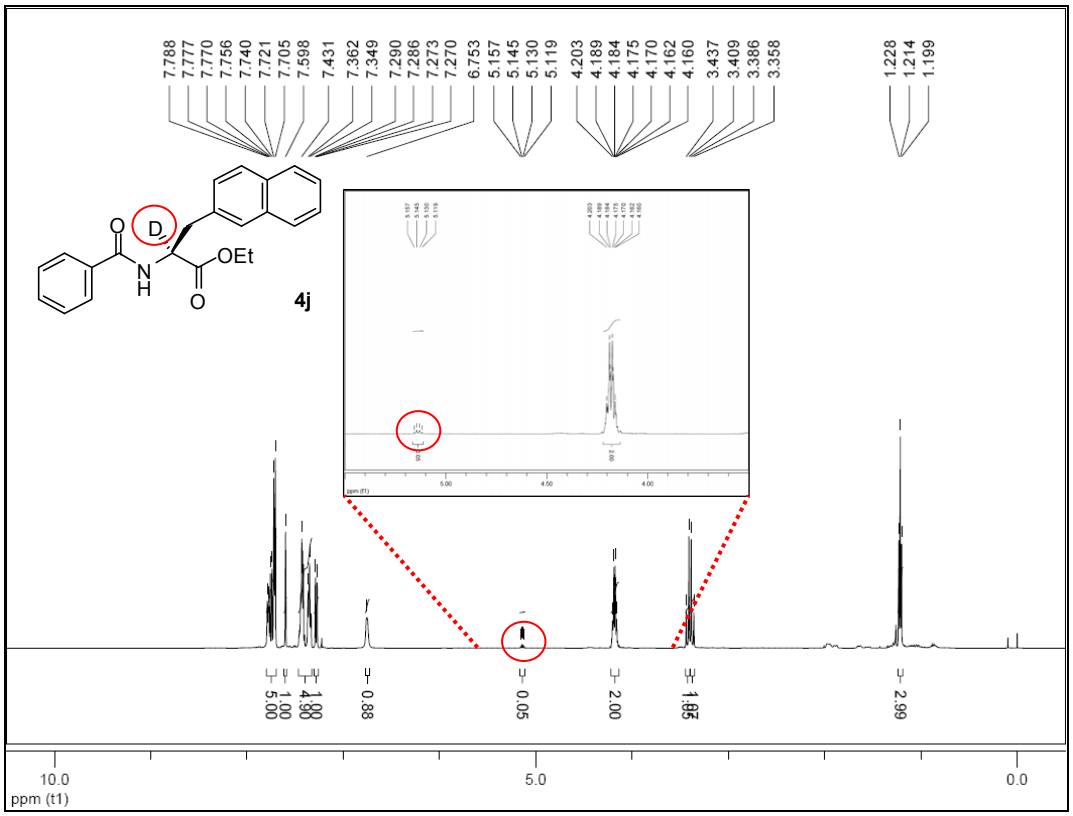


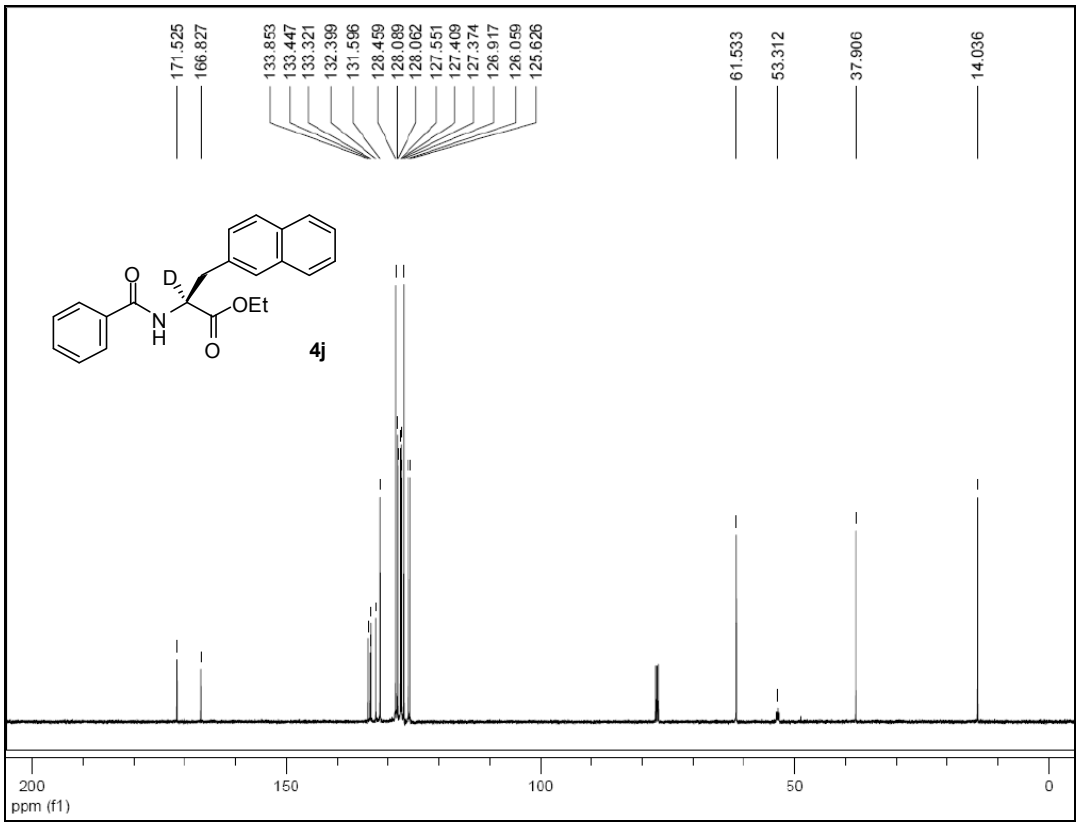
^{1}H and ^{13}C NMR of **4i**





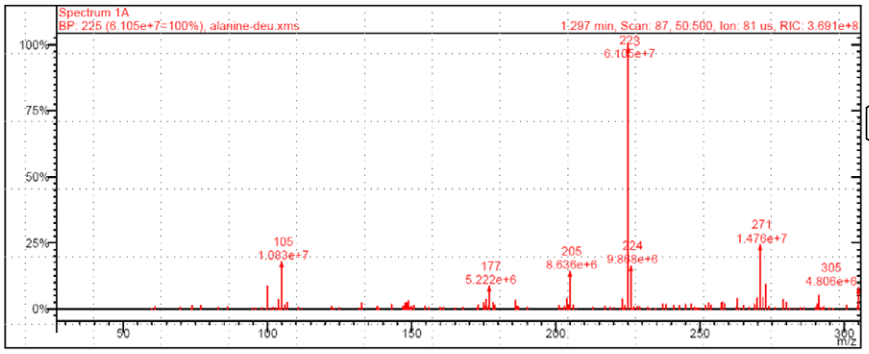
^{1}H and ^{13}C NMR of **4j**

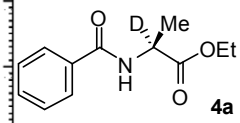




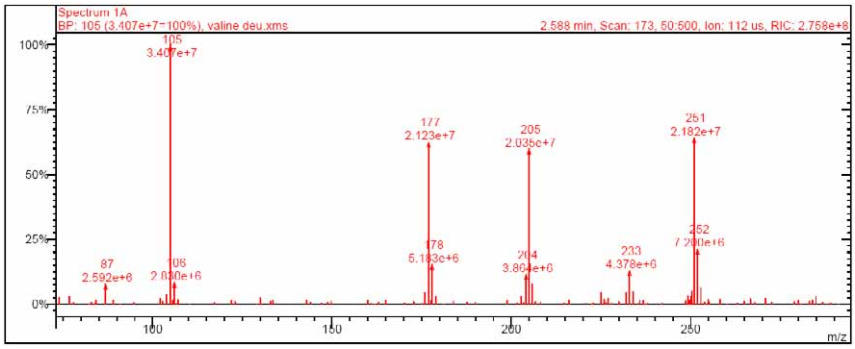
6. LR-MS (APCI) Spectra for 4a-4j (Table 2)

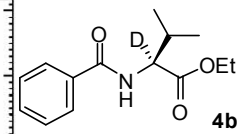
LR-MS of **4a**



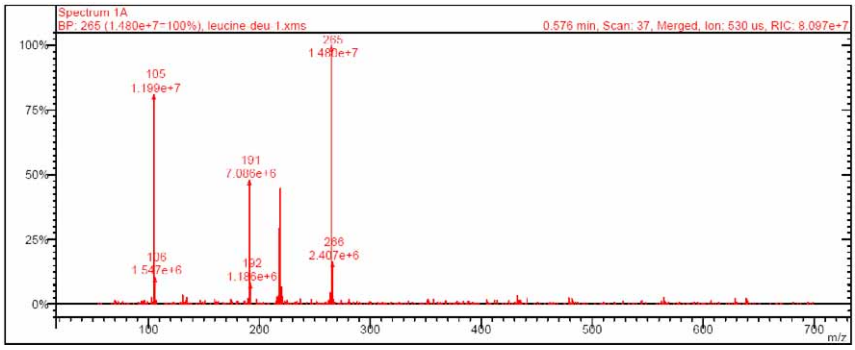


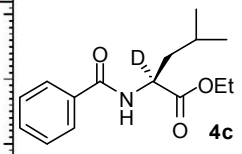
LR-MS of **4b**



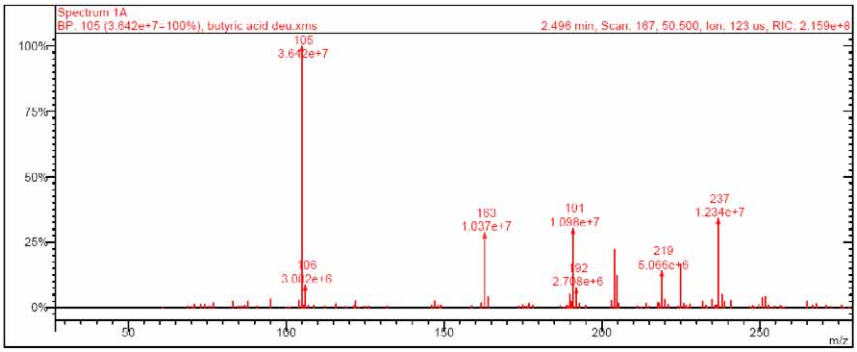


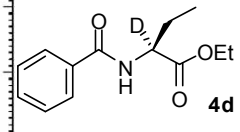
LR-MS of **4c**



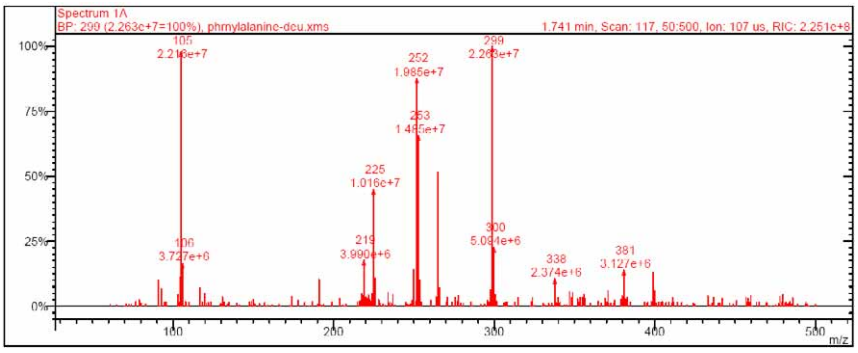


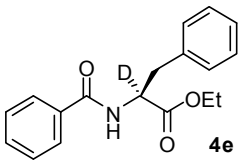
LR-MS of **4d**



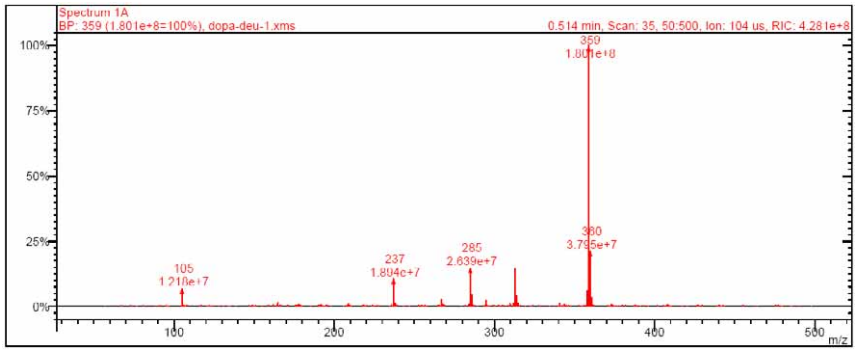


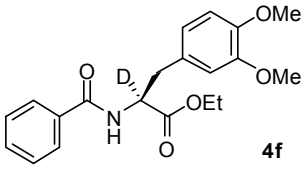
LR-MS of **4e**



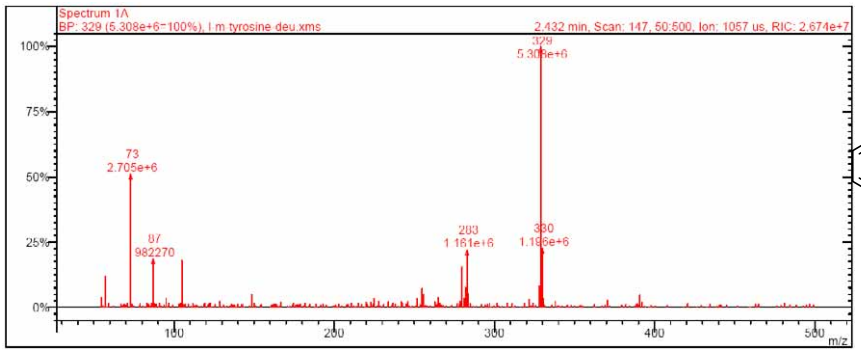


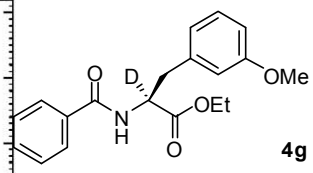
LR-MS of **4f**



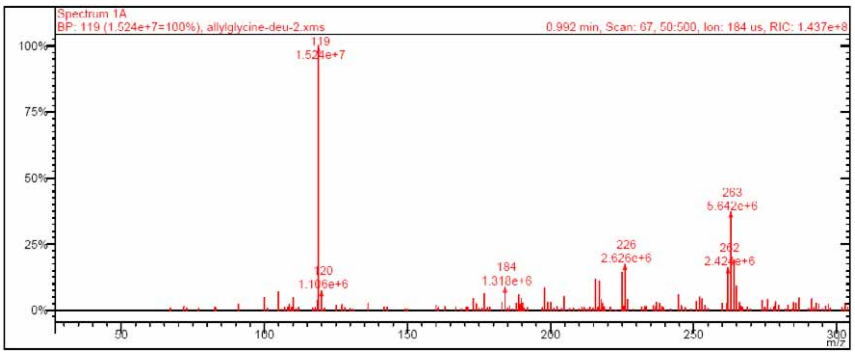


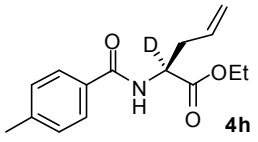
LR-MS of **4g**



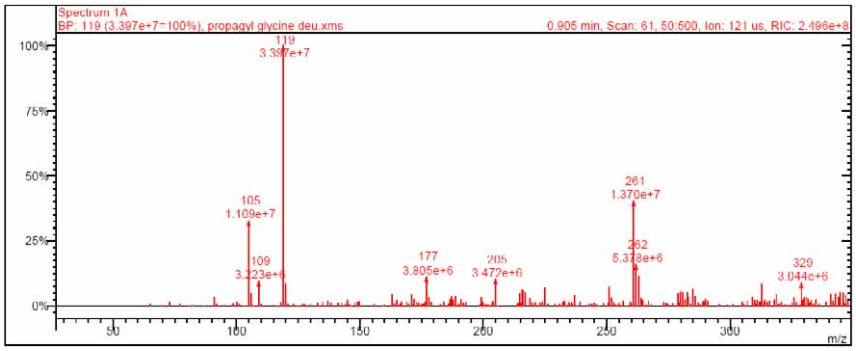


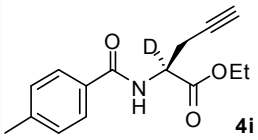
LR-MS of **4h**





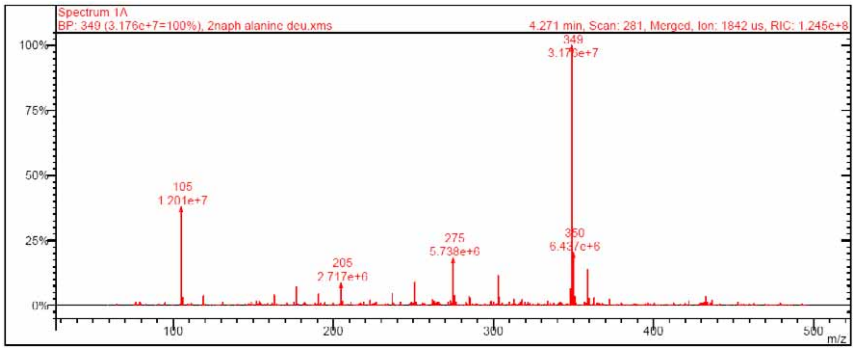
LR-MS of **4i**

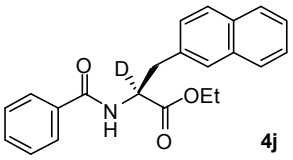




4i

LR-MS of **4j**

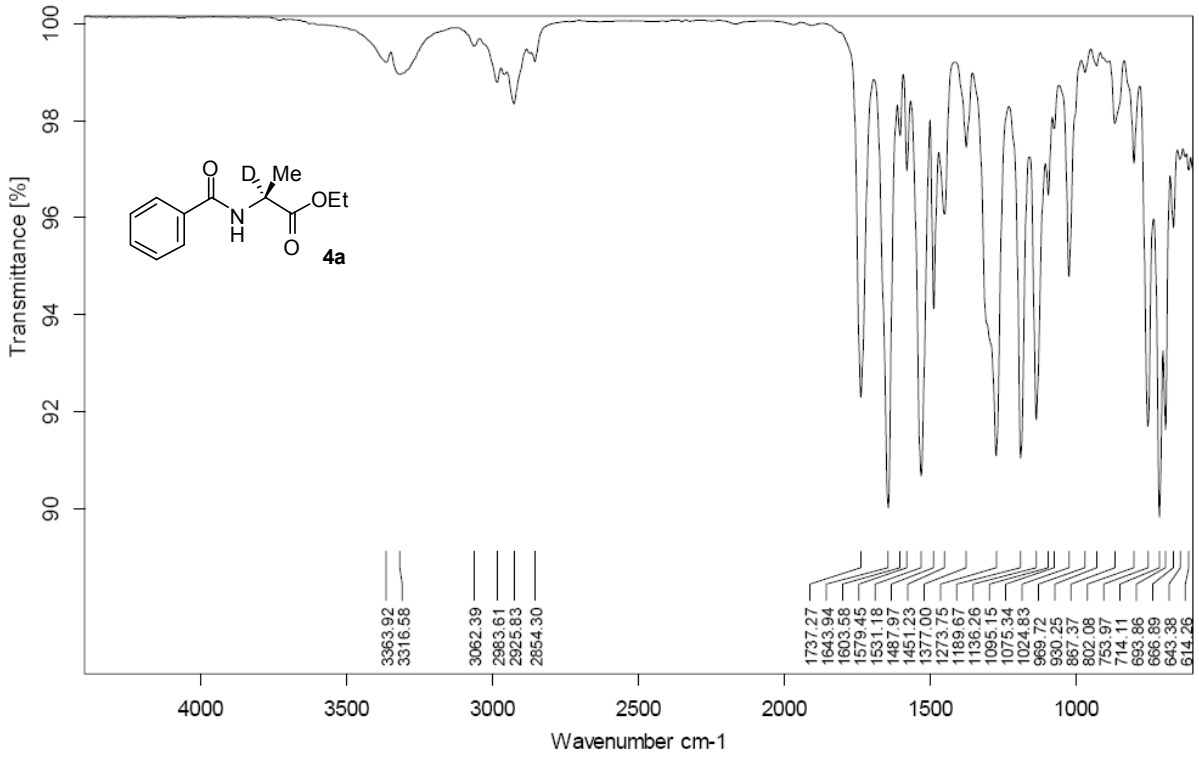




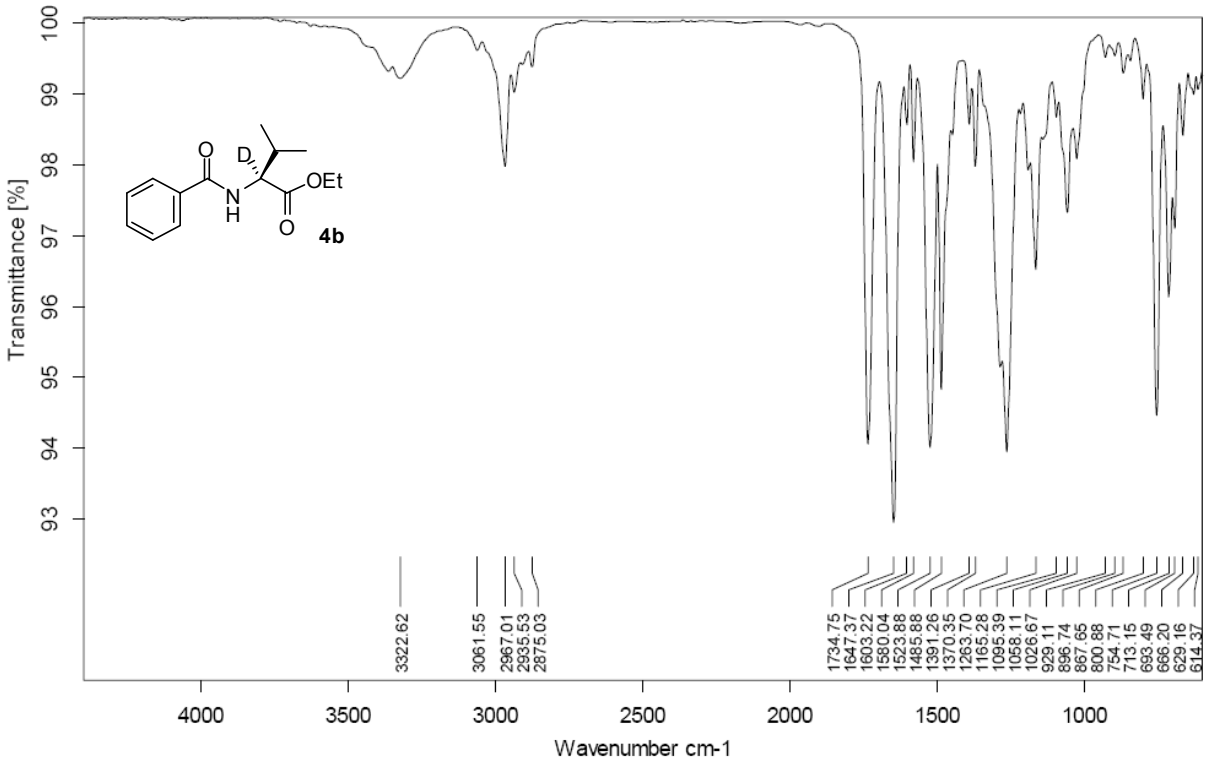
4j

7. IR Spectra for 4a-4j (table2)

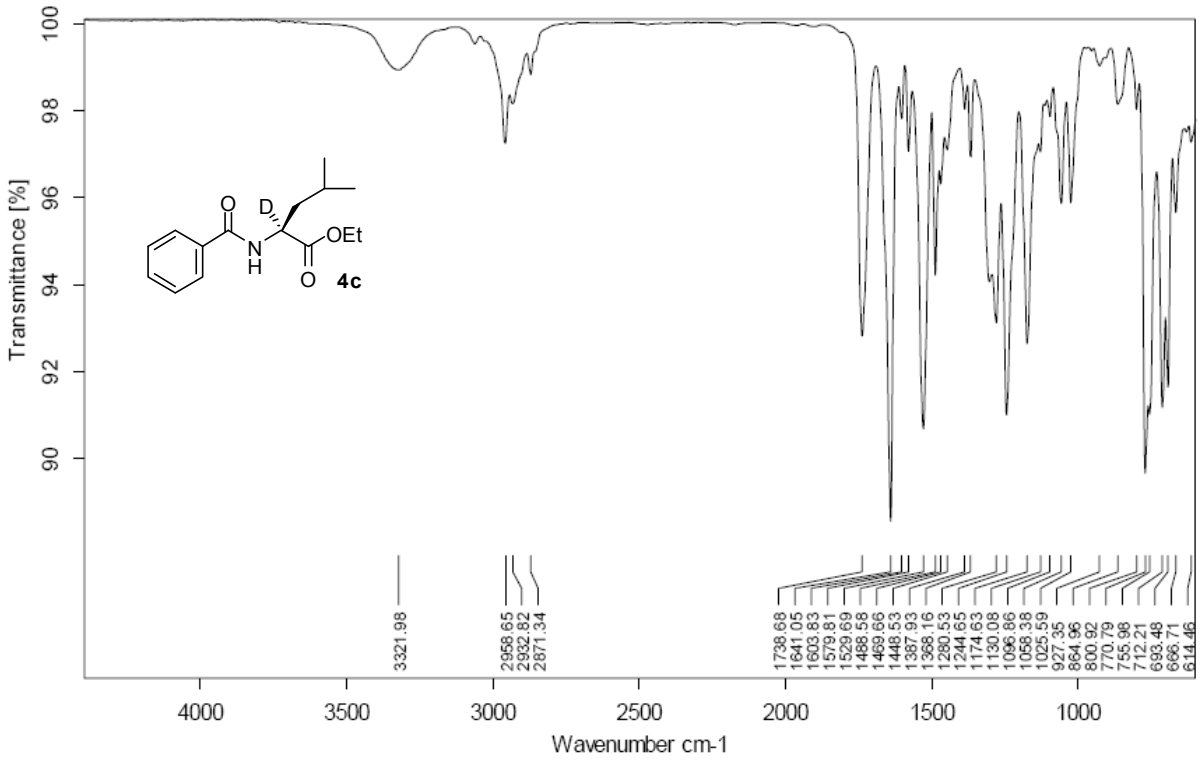
IR of **4a**



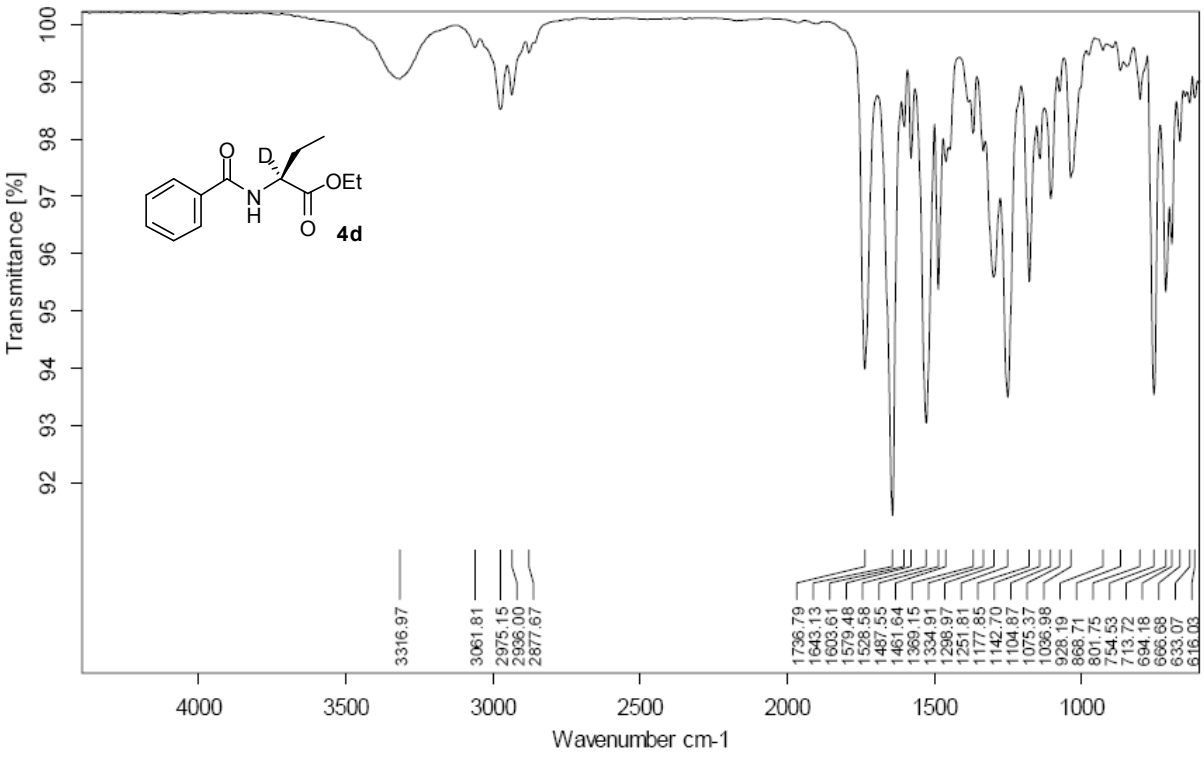
IR of **4b**



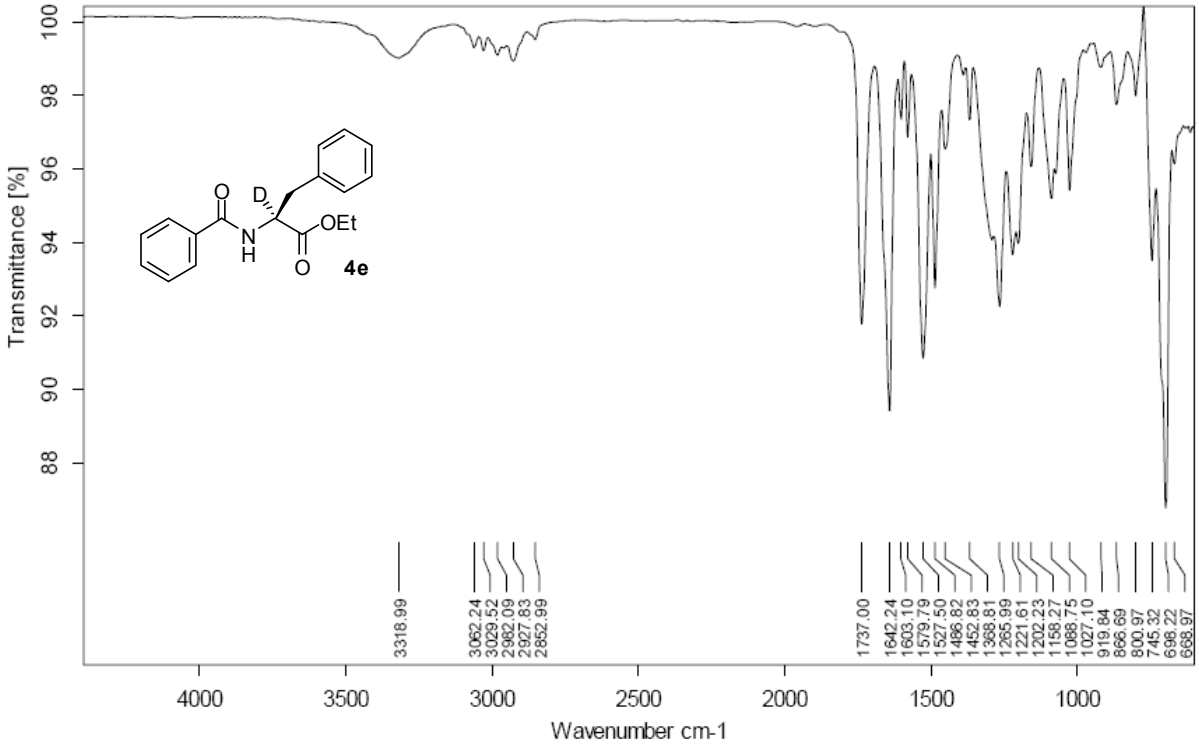
IR of **4c**



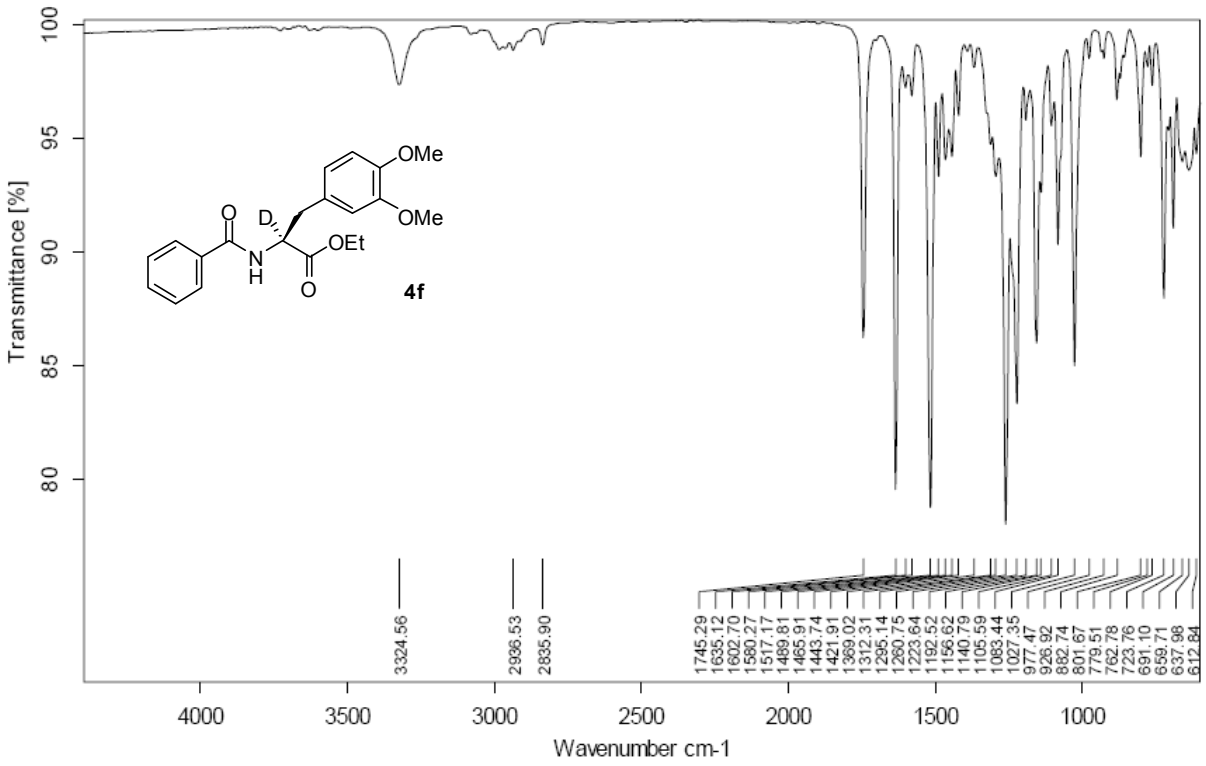
IR of **4d**



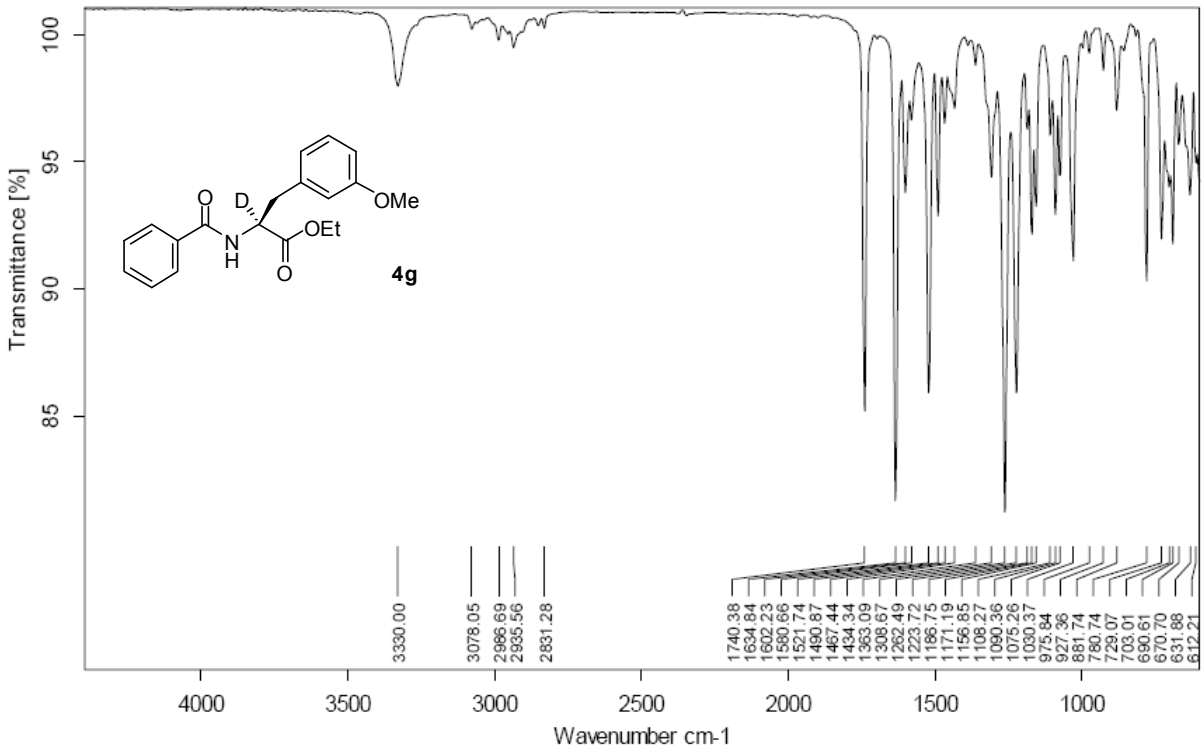
IR of **4e**



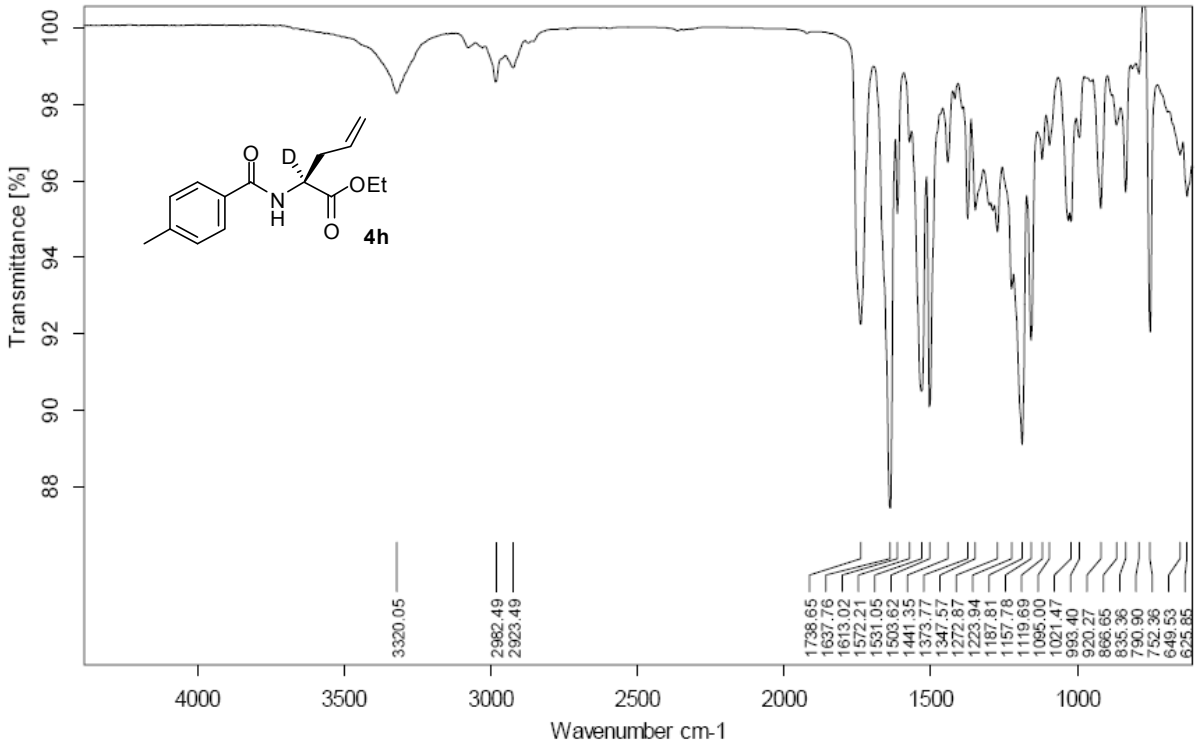
IR of **4f**



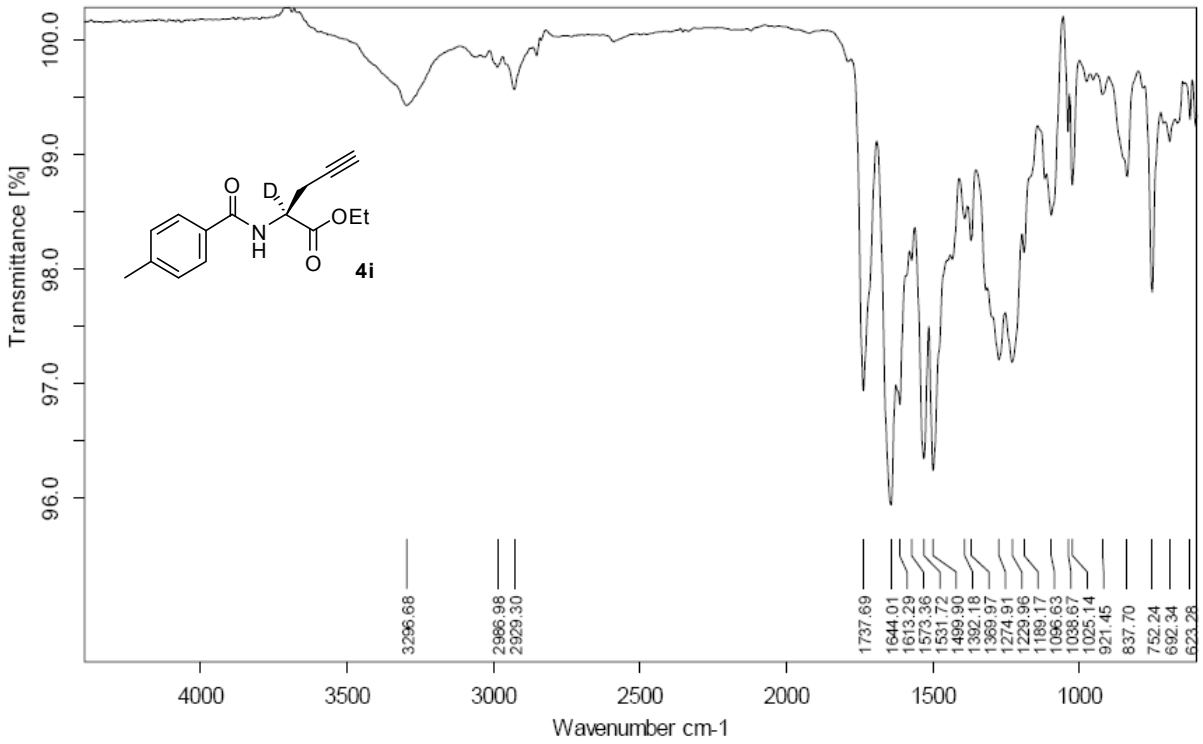
IR of **4g**



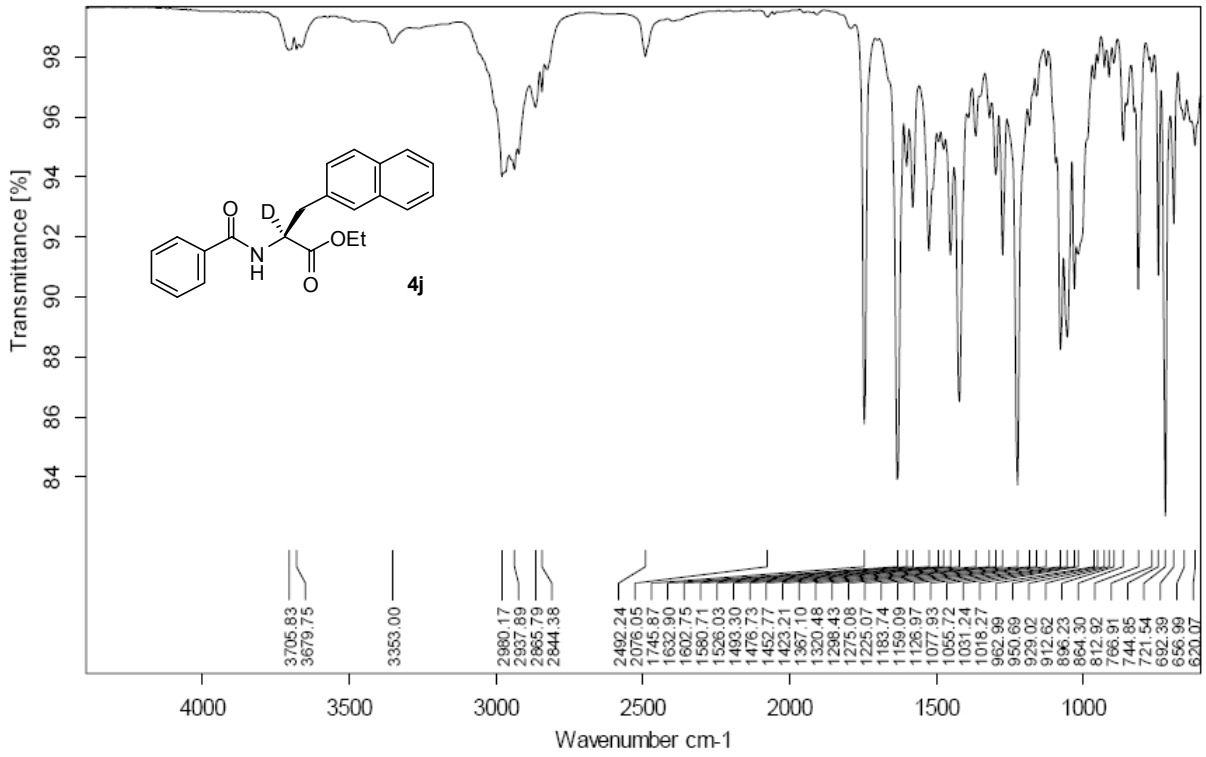
IR of **4h**



IR of **4i**

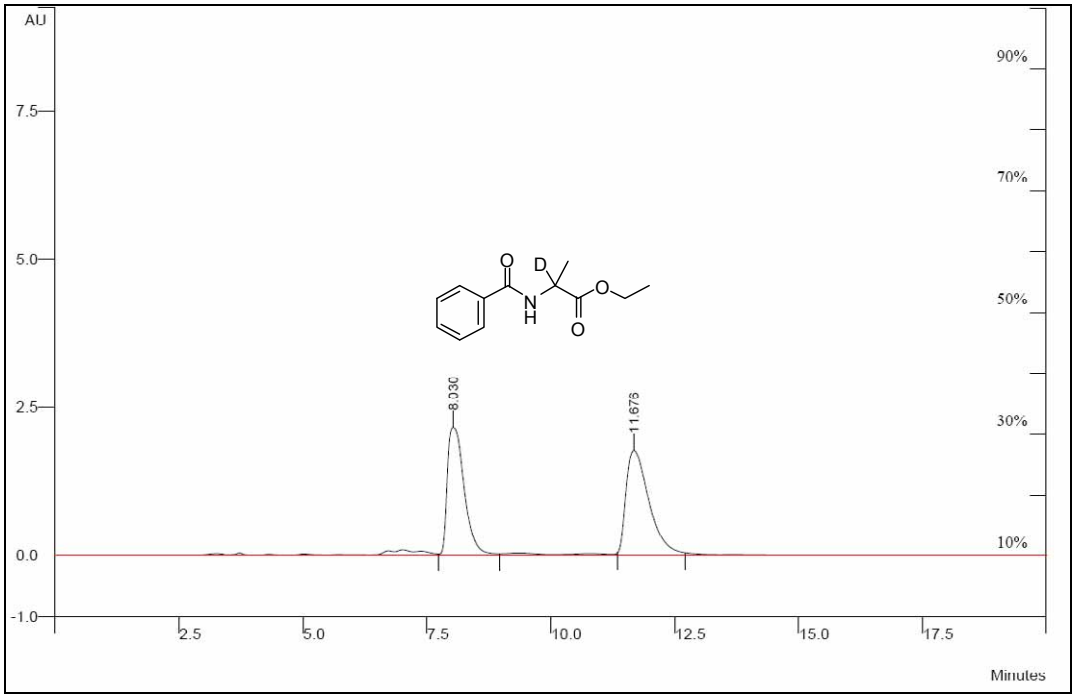


IR of **4j**

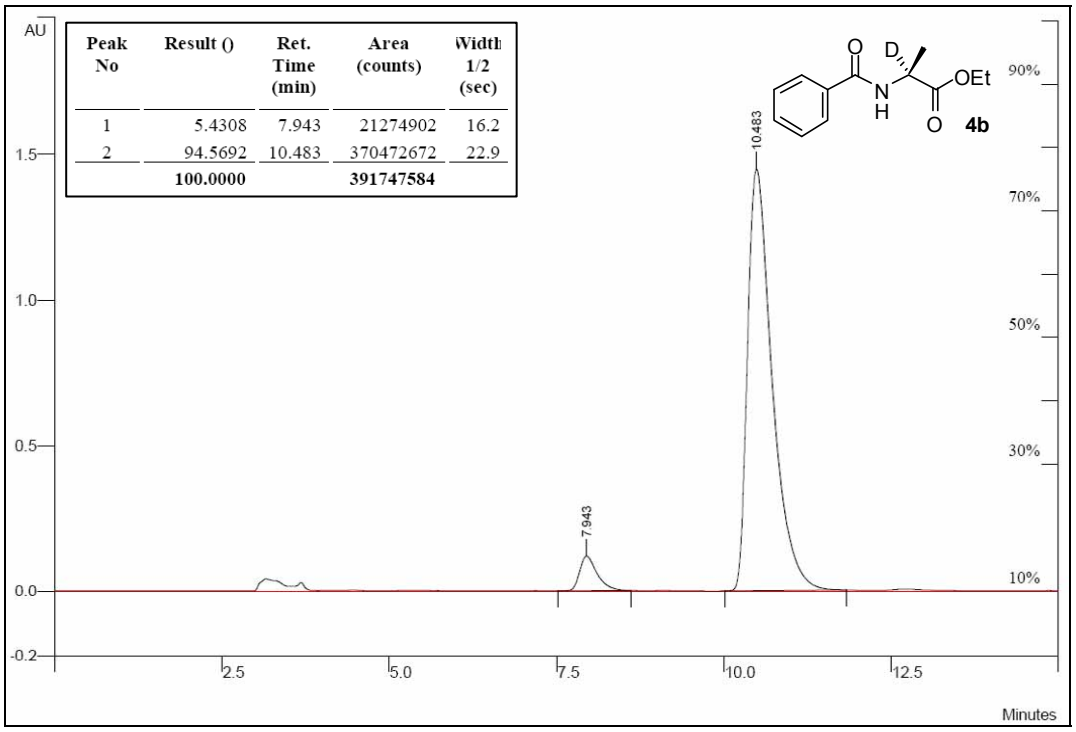


8. HPLC spectra for Table 1

Entry 1 (racemic sample)

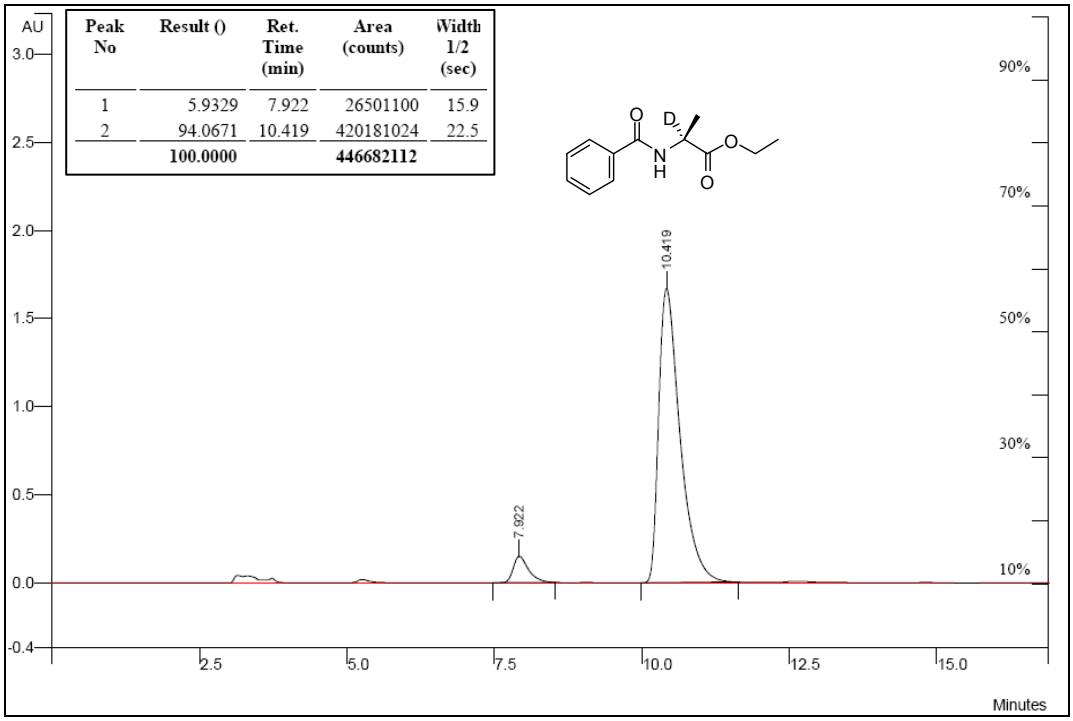


Entry 1



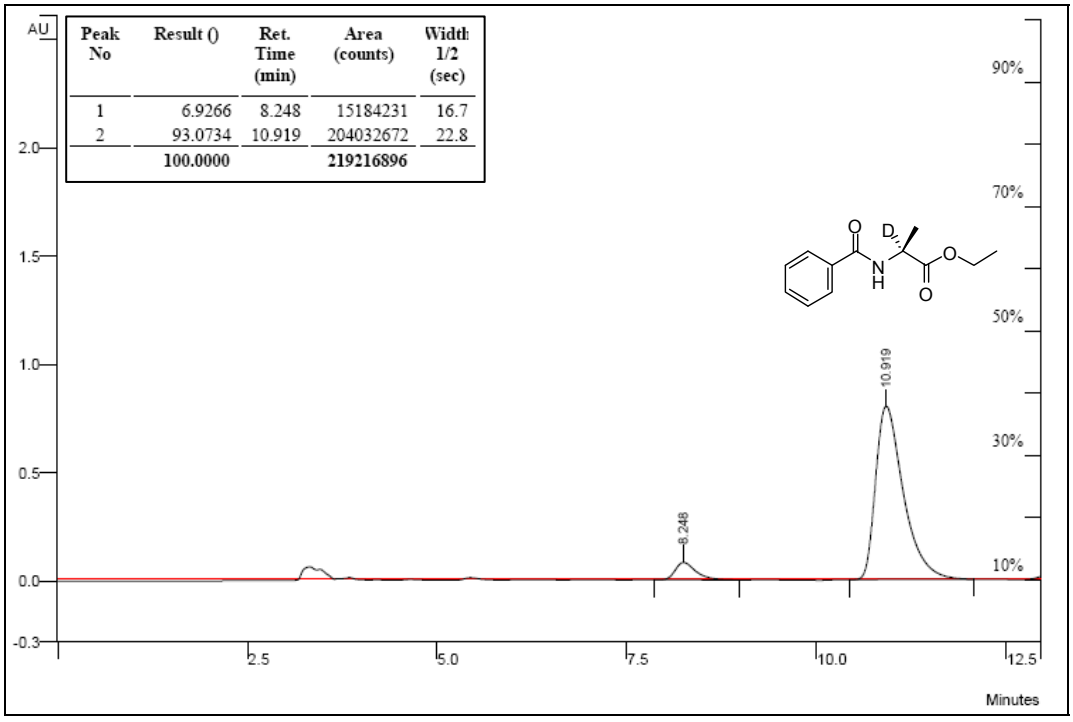
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	5.4308	7.943	21274902	16.2
2	94.5692	10.483	370472672	22.9
	100.0000		**391747584**	

Entry 2



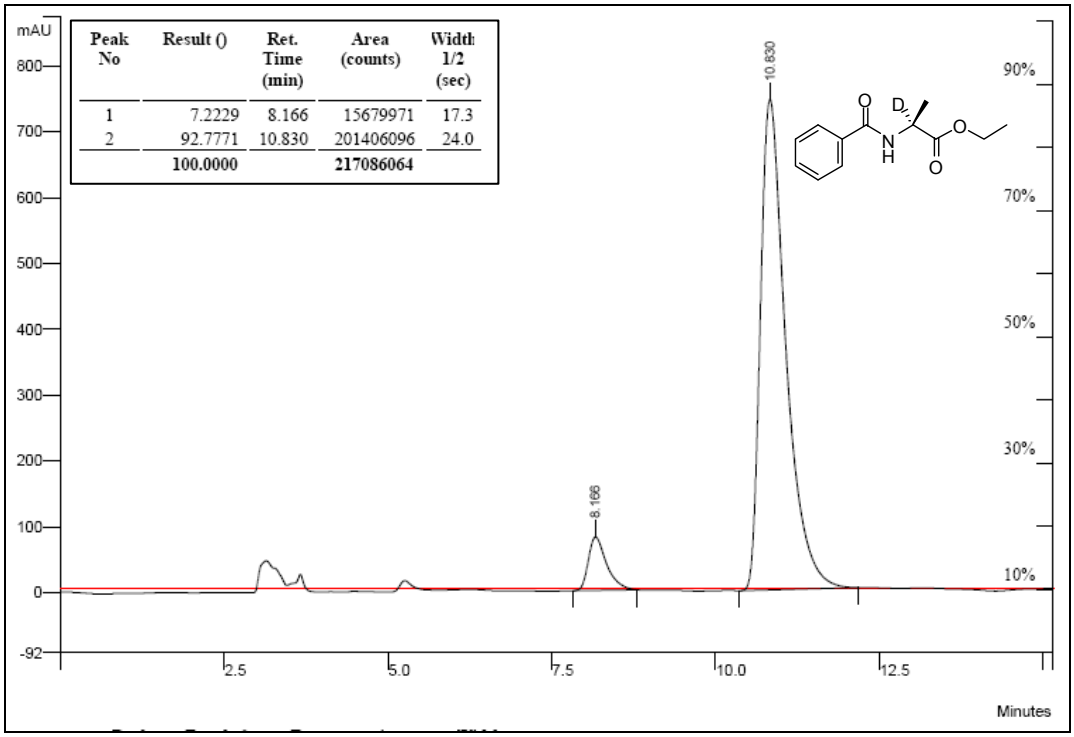
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	5.9329	7.922	26501100	15.9
2	94.0671	10.419	420181024	22.5
	100.0000		**446682112**	

Entry 3



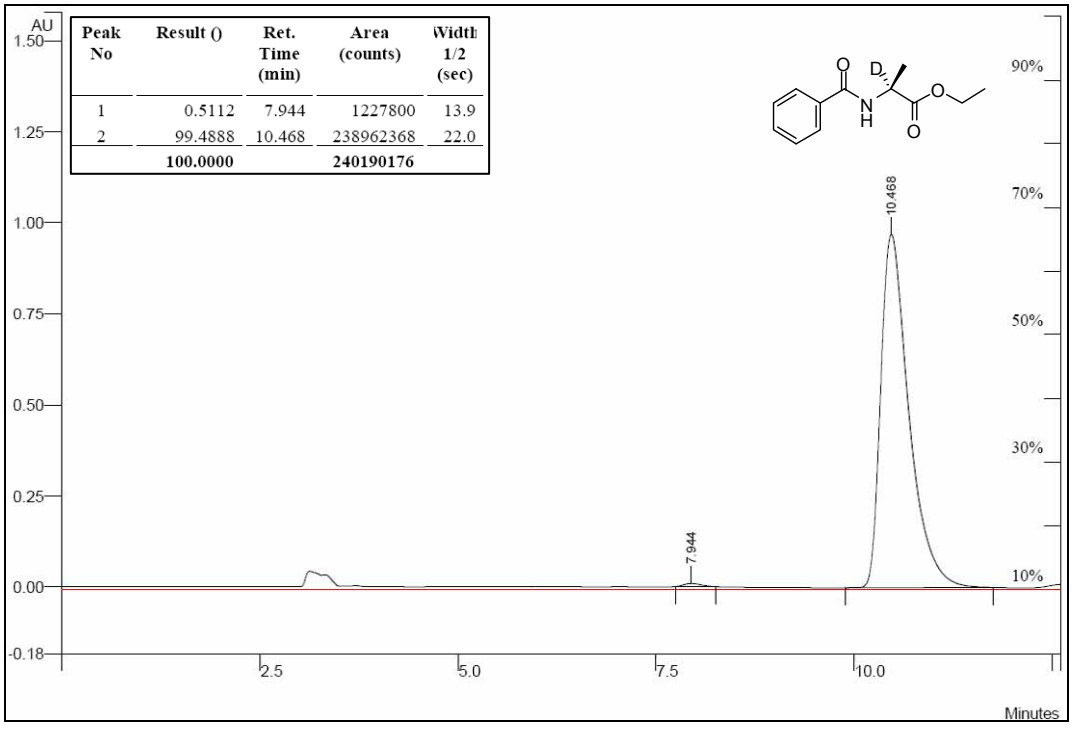
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.9266	8.248	15184231	16.7
2	93.0734	10.919	204032672	22.8
	100.0000		**219216896**	

Entry 4 (before recrystallization)



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	7.2229	8.166	15679971	17.3
2	92.7771	10.830	201406096	24.0
	100.0000		**217086064**	

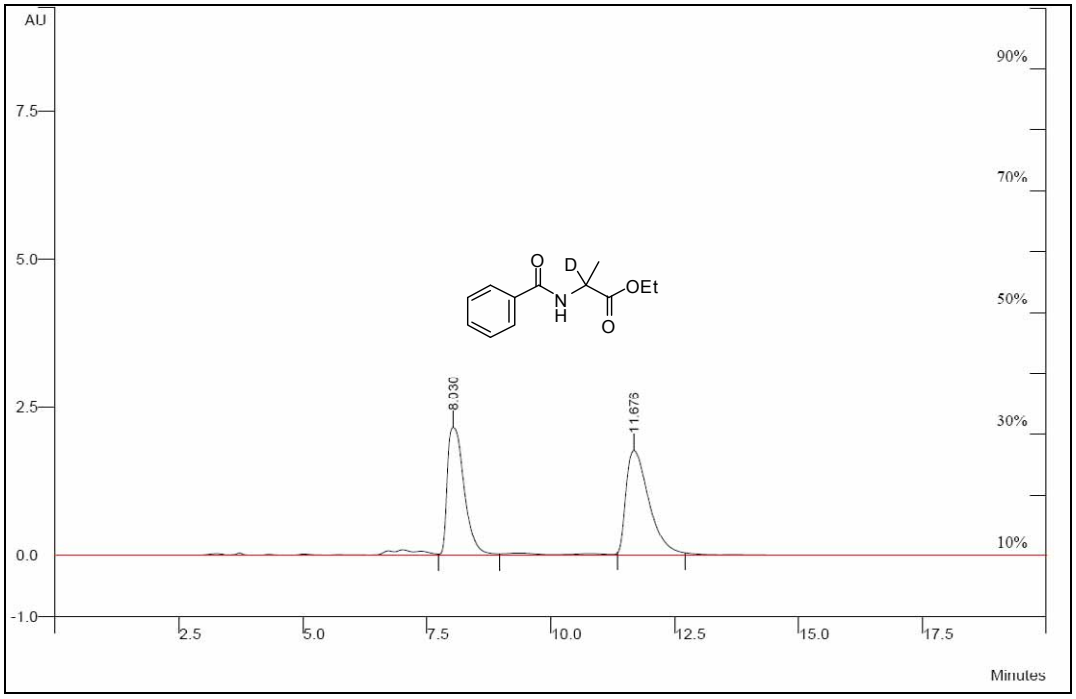
Entry 4 (after recrystallization)



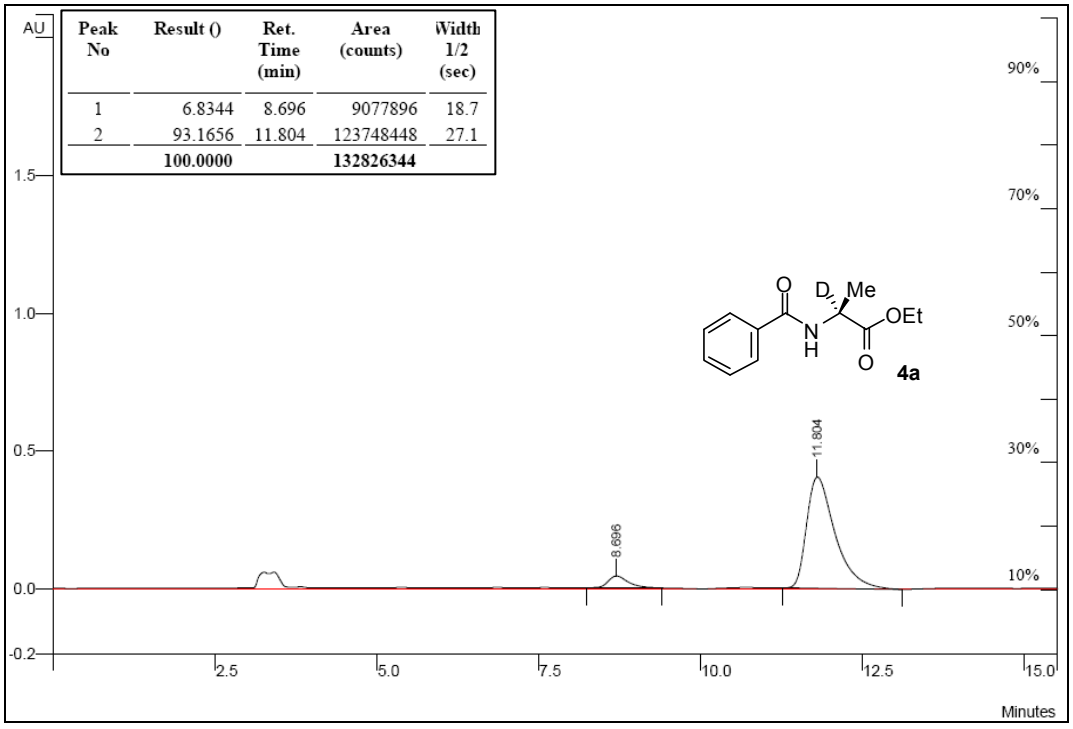
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.5112	7.944	1227800	13.9
2	99.4888	10.468	238962368	22.0
	100.0000		**240190176**	

9. HPLC spectra for Table 2

Entry 1 (racemic sample)

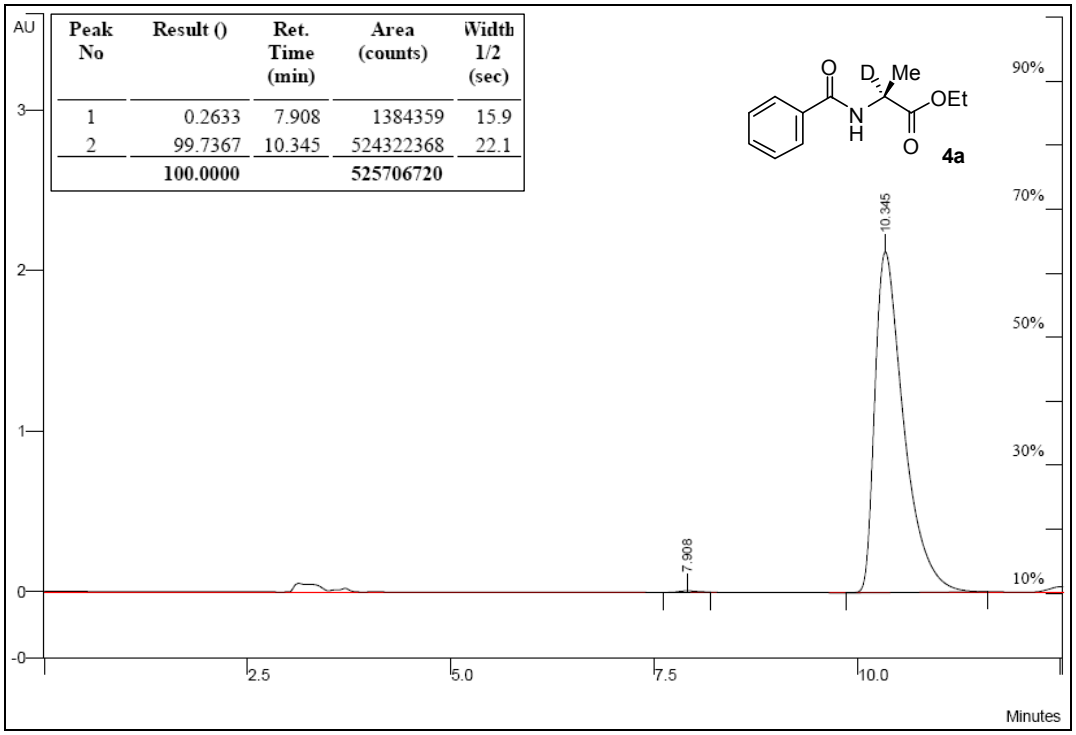


Entry 1 (before recrystallization)



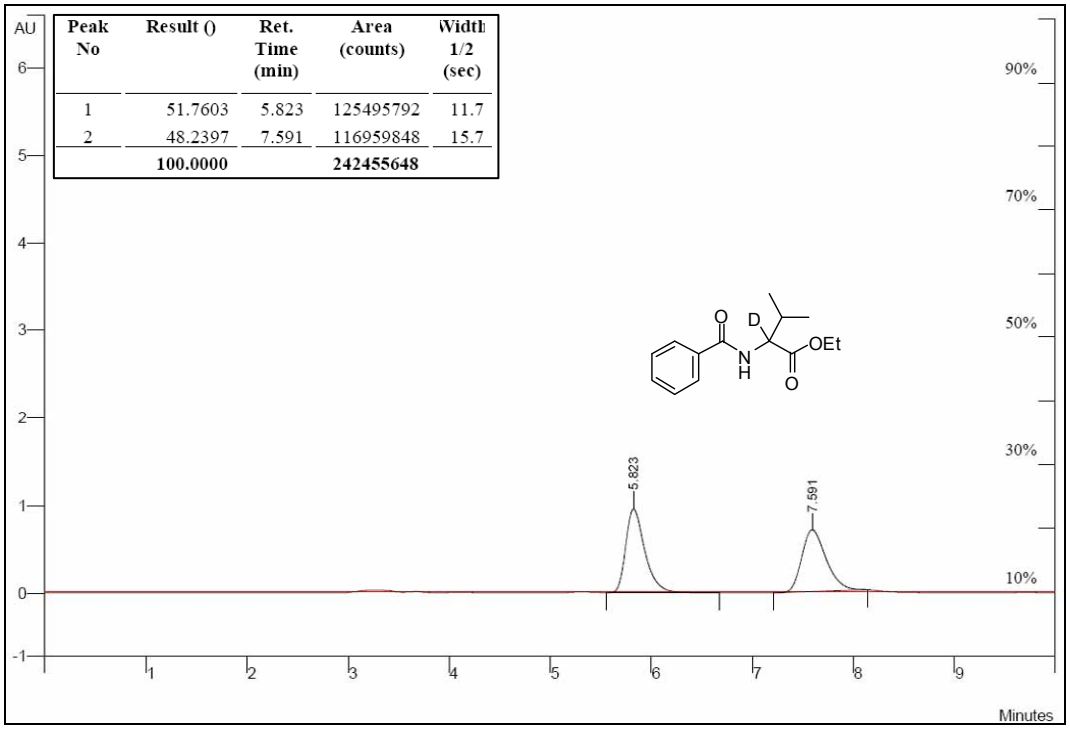
Entry 1 (after recrystallization)

Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.2633	7.908	1384359	15.9
2	99.7367	10.345	524322368	22.1
	100.0000		**525706720**	

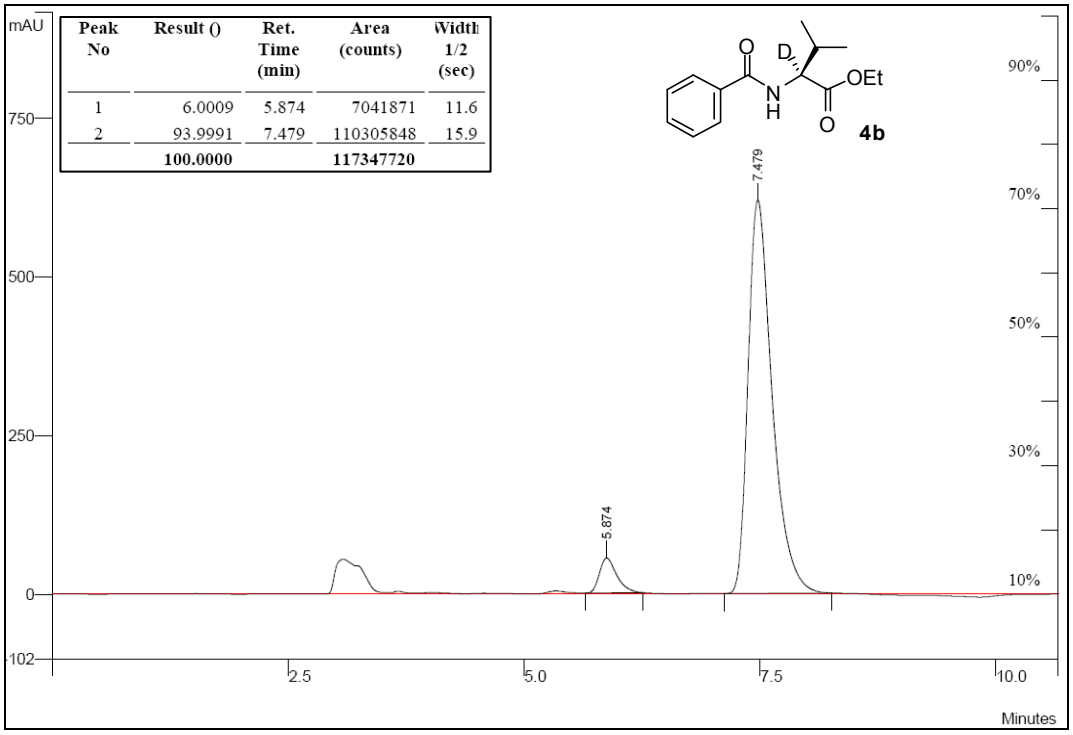


Entry 2 (racemic sample)

Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	51.7603	5.823	125495792	11.7
2	48.2397	7.591	116959848	15.7
	100.0000		**242455648**	

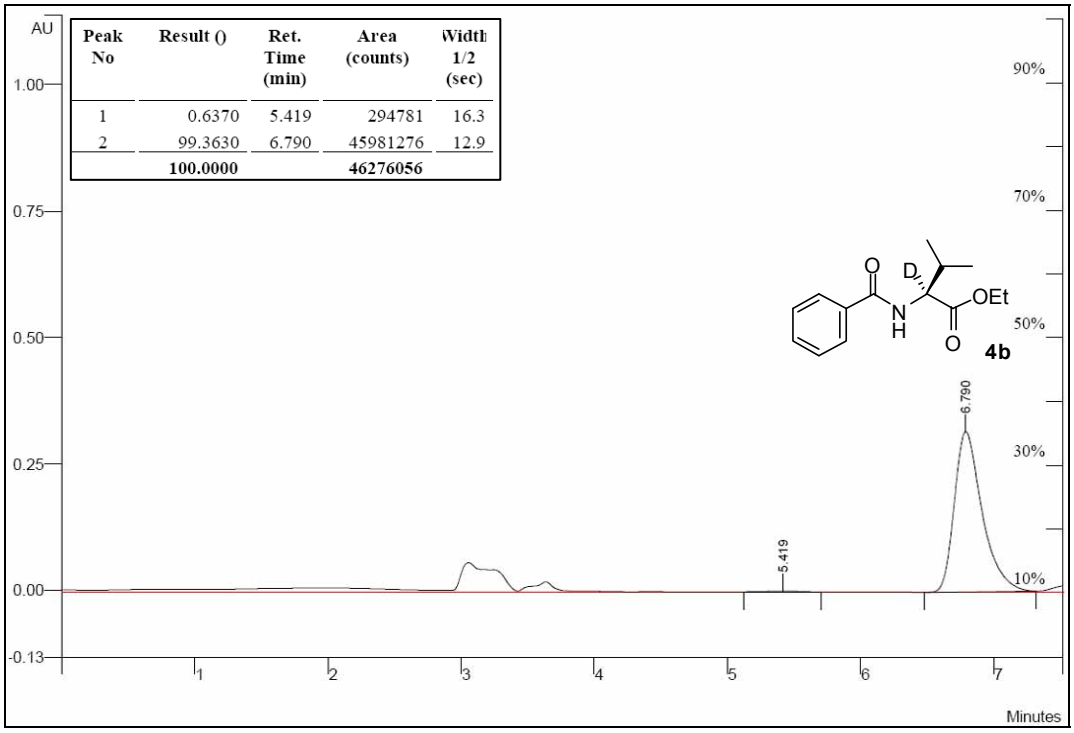


Entry 2 (before recrystallization)



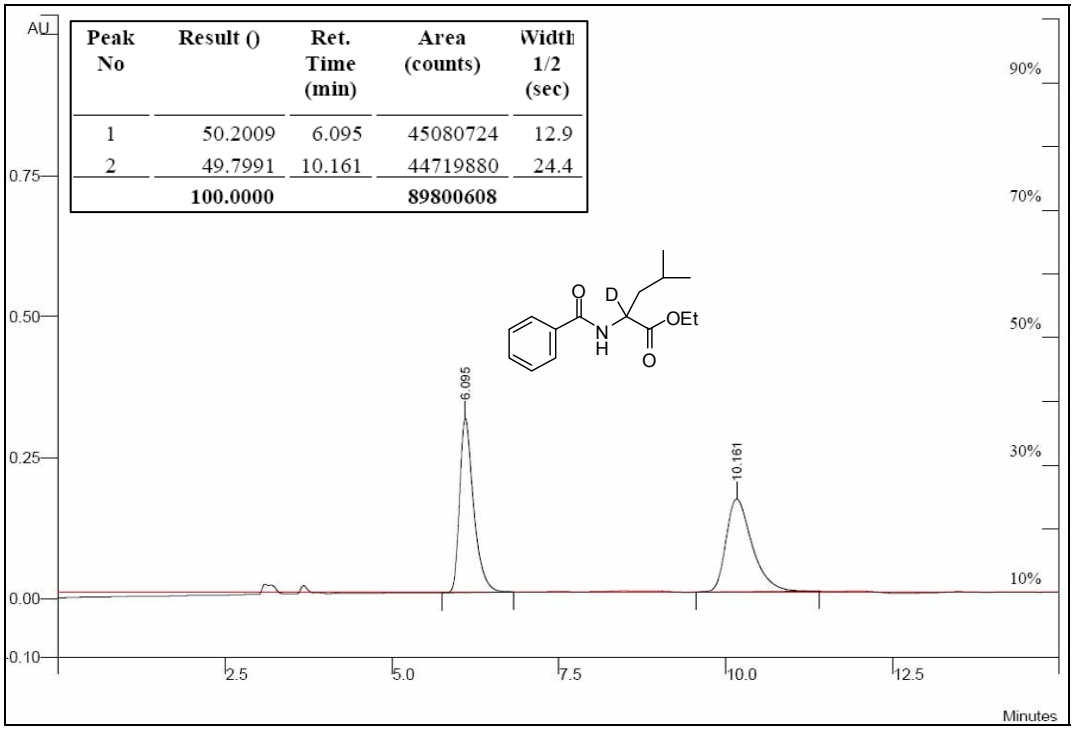
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.0009	5.874	7041871	11.6
2	93.9991	7.479	110305848	15.9
	100.0000		**117347720**	

Entry 2 (after recrystallization)



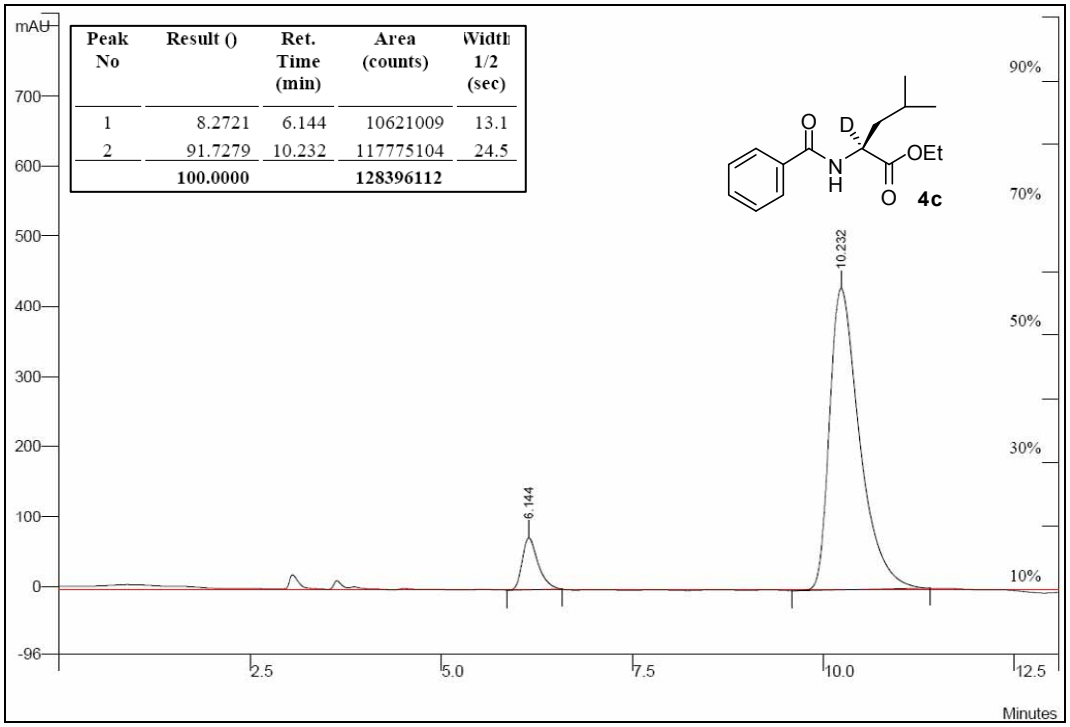
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.6370	5.419	294781	16.3
2	99.3630	6.790	45981276	12.9
	100.0000		**46276056**	

Entry 3 (racemic sample)



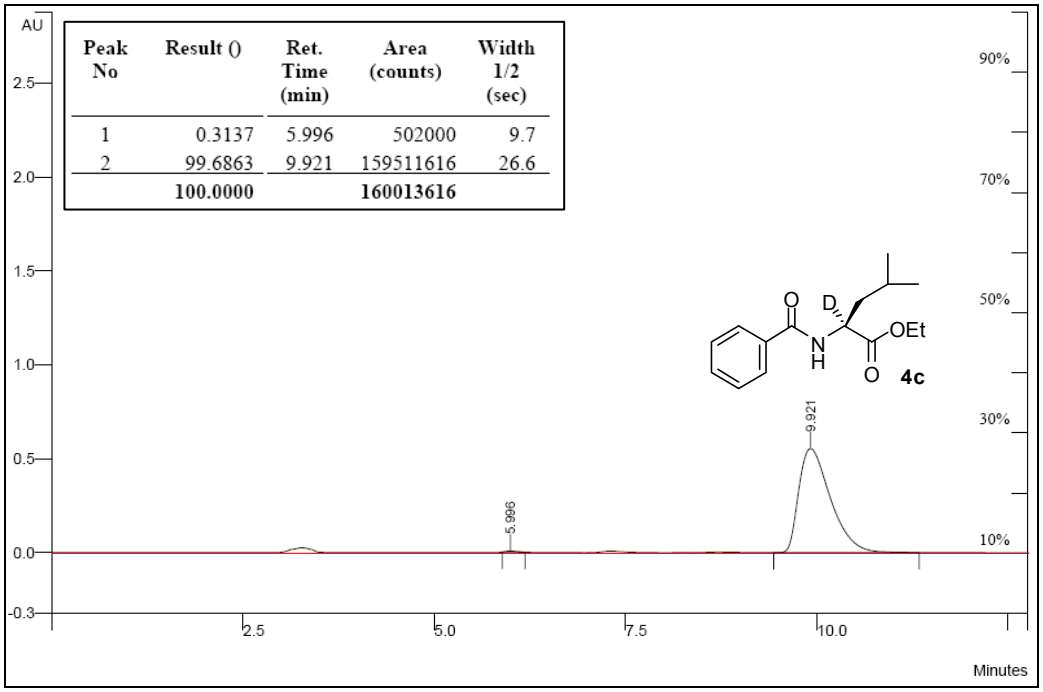
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.2009	6.095	45080724	12.9
2	49.7991	10.161	44719880	24.4
	100.0000		**89800608**	

Entry 3 (before recrystallization)



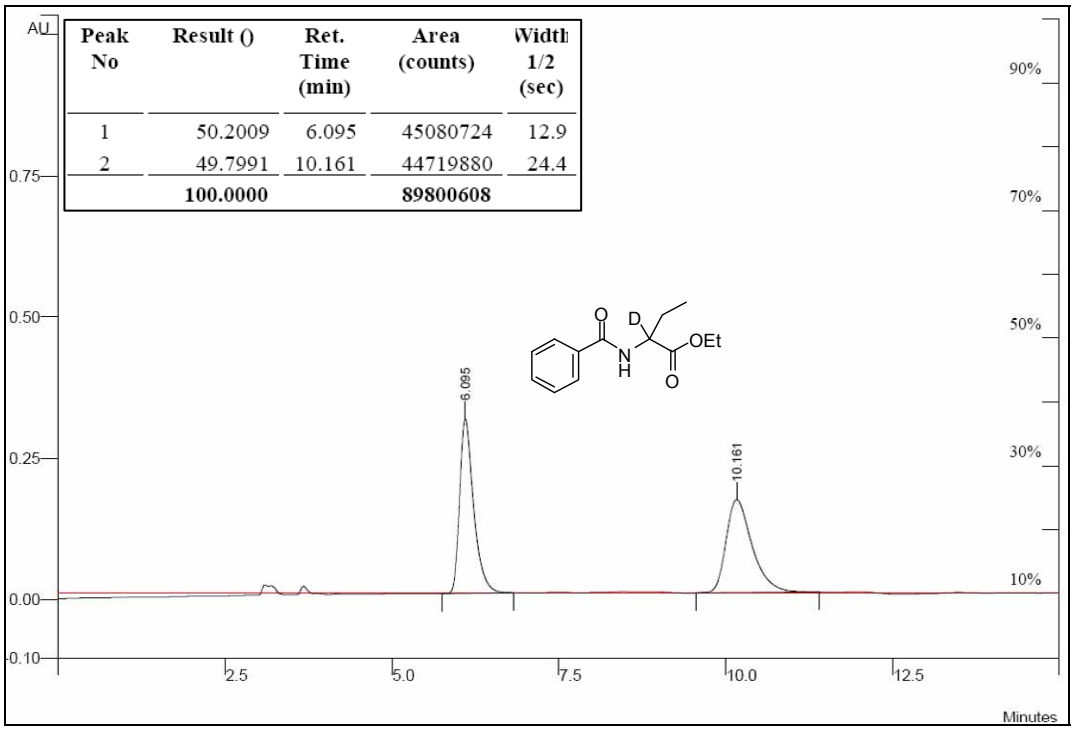
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	8.2721	6.144	10621009	13.1
2	91.7279	10.232	117775104	24.5
	100.0000		**128396112**	

Entry 3 (after recrystallization)



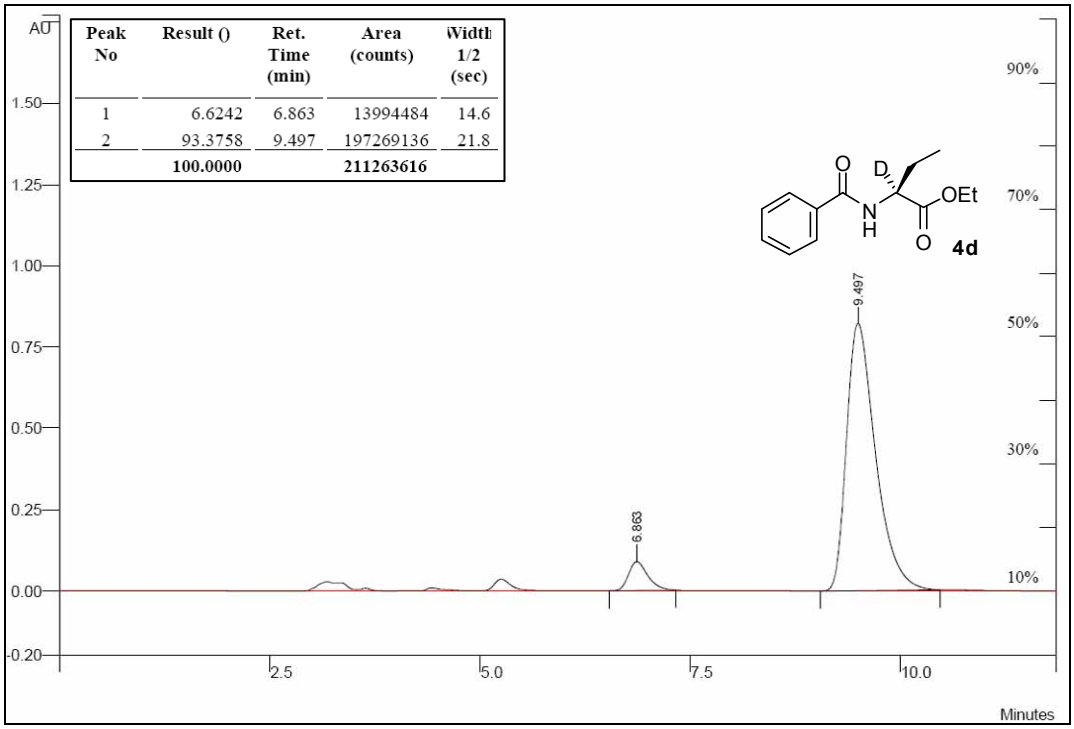
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.3137	5.996	502000	9.7
2	99.6863	9.921	159511616	26.6
	100.0000		**160013616**	

Entry 4 (racemic sample)



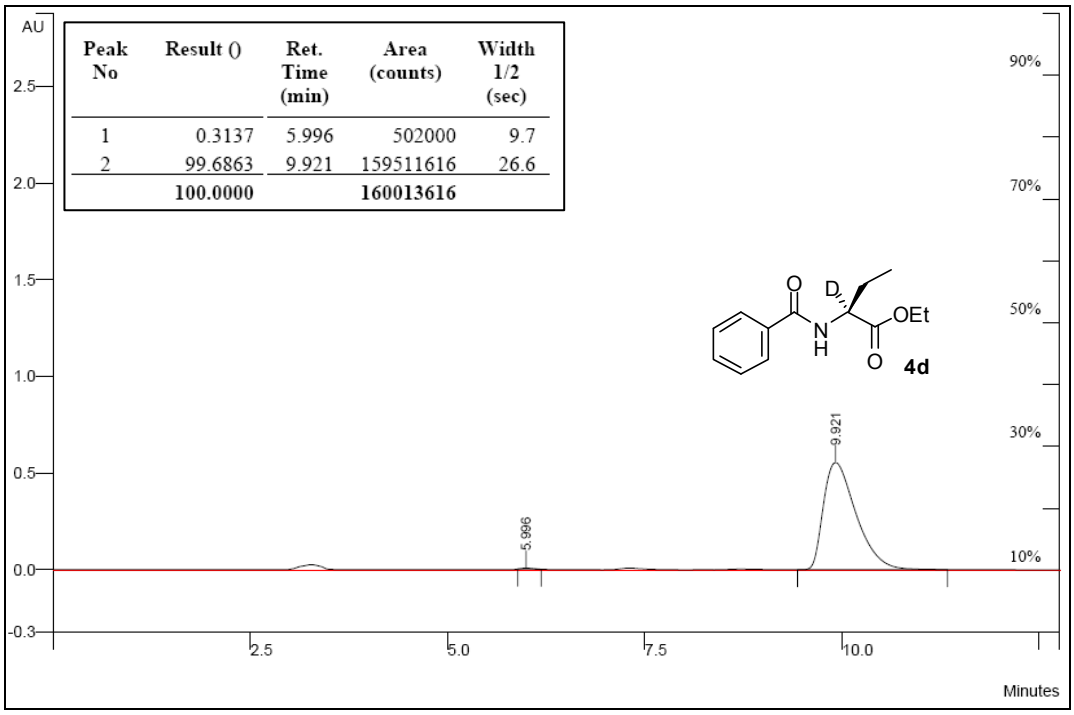
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.2009	6.095	45080724	12.9
2	49.7991	10.161	44719880	24.4
	100.0000		**89800608**	

Entry 4 (before recrystallization)



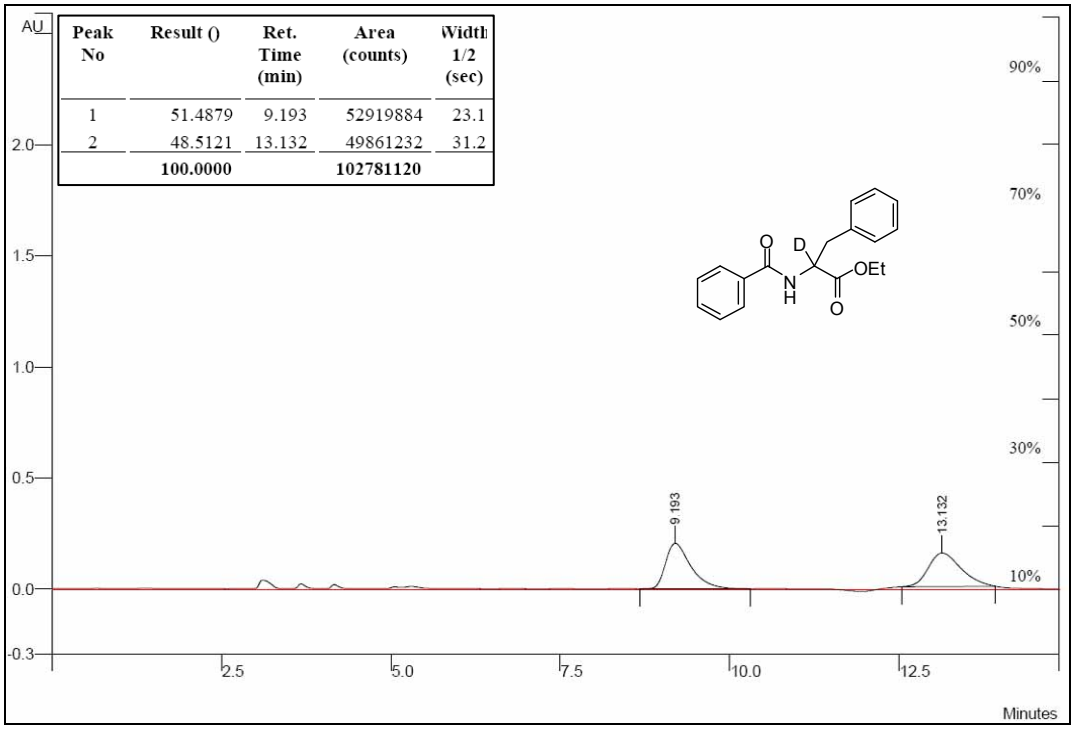
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.6242	6.863	13994484	14.6
2	93.3758	9.497	197269136	21.8
	100.0000		**211263616**	

Entry 4 (after recrystallization)



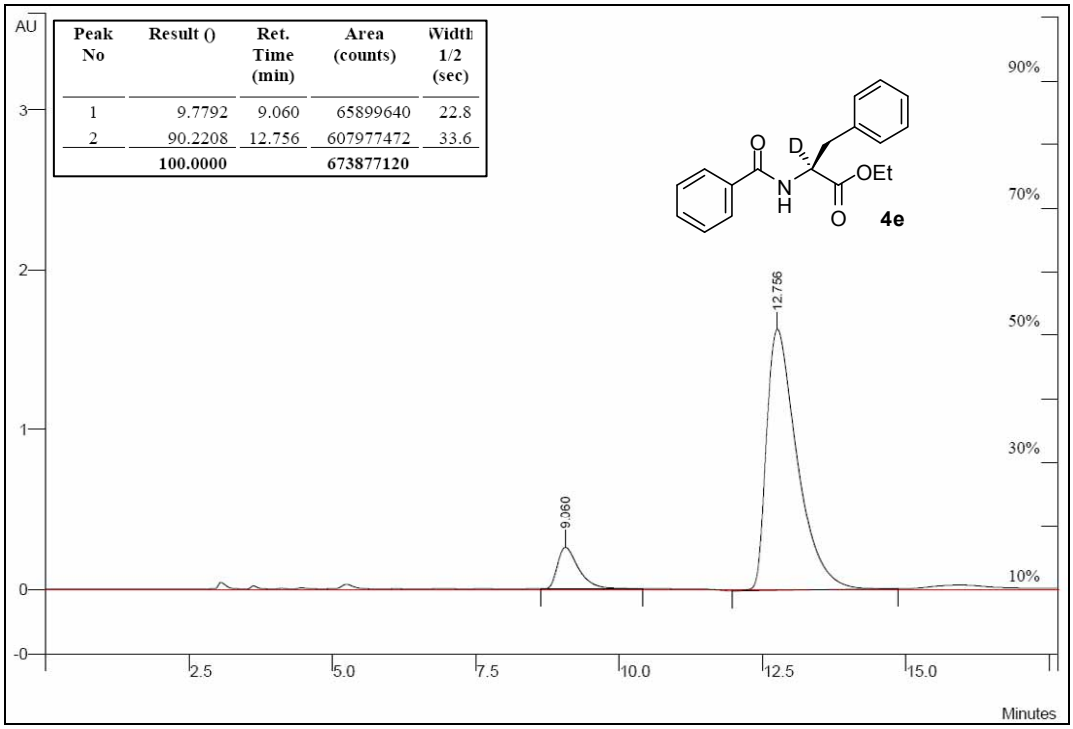
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.3137	5.996	502000	9.7
2	99.6863	9.921	159511616	26.6
	100.0000		**160013616**	

Entry 5 (racemic sample)



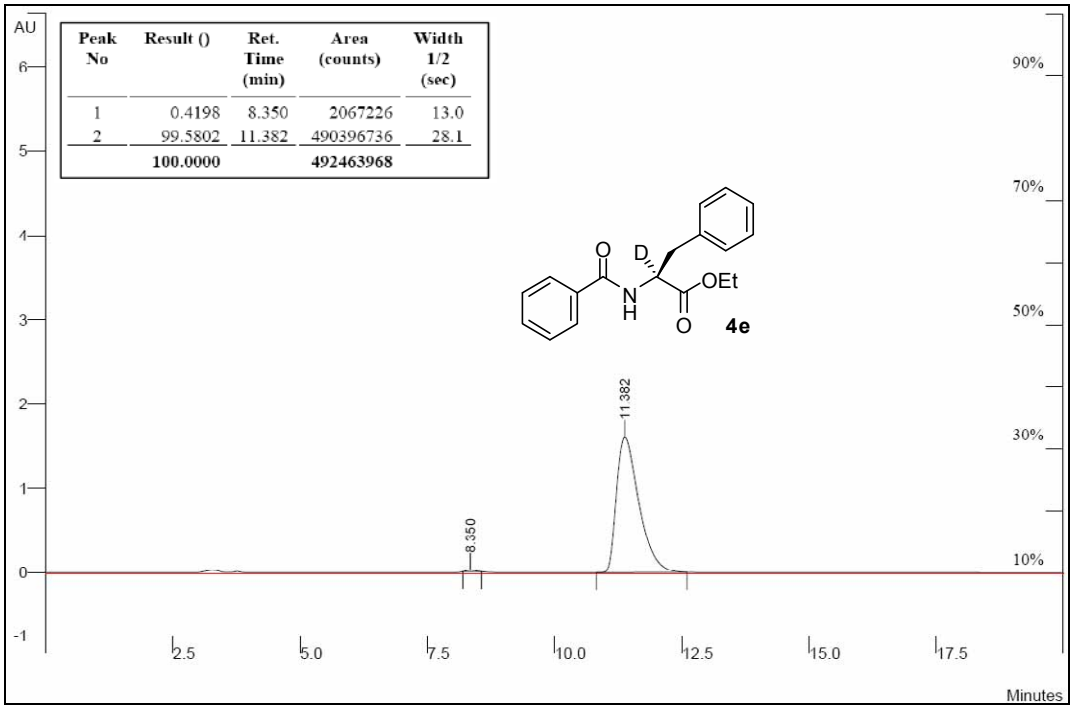
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	51.4879	9.193	52919884	23.1
2	48.5121	13.132	49861232	31.2
	100.0000		**102781120**	

Entry 5 (before recrystallization)



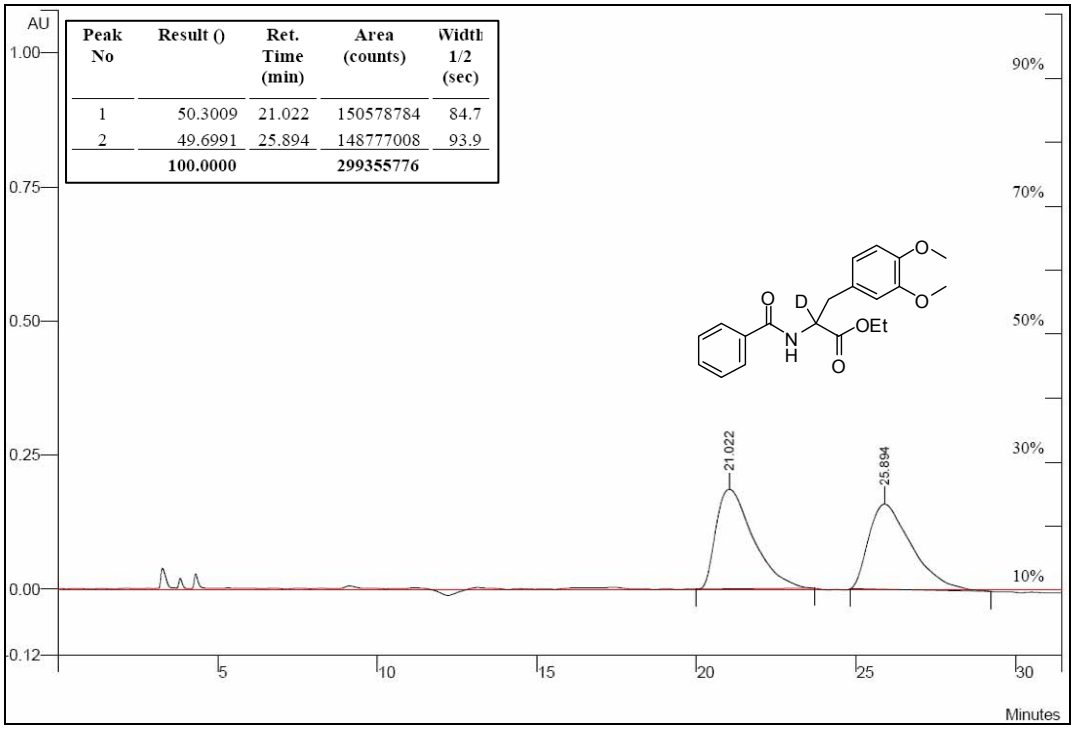
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	9.7792	9.060	65899640	22.8
2	90.2208	12.756	607977472	33.6
	100.0000		**673877120**	

Entry 5 (after recrystallization)



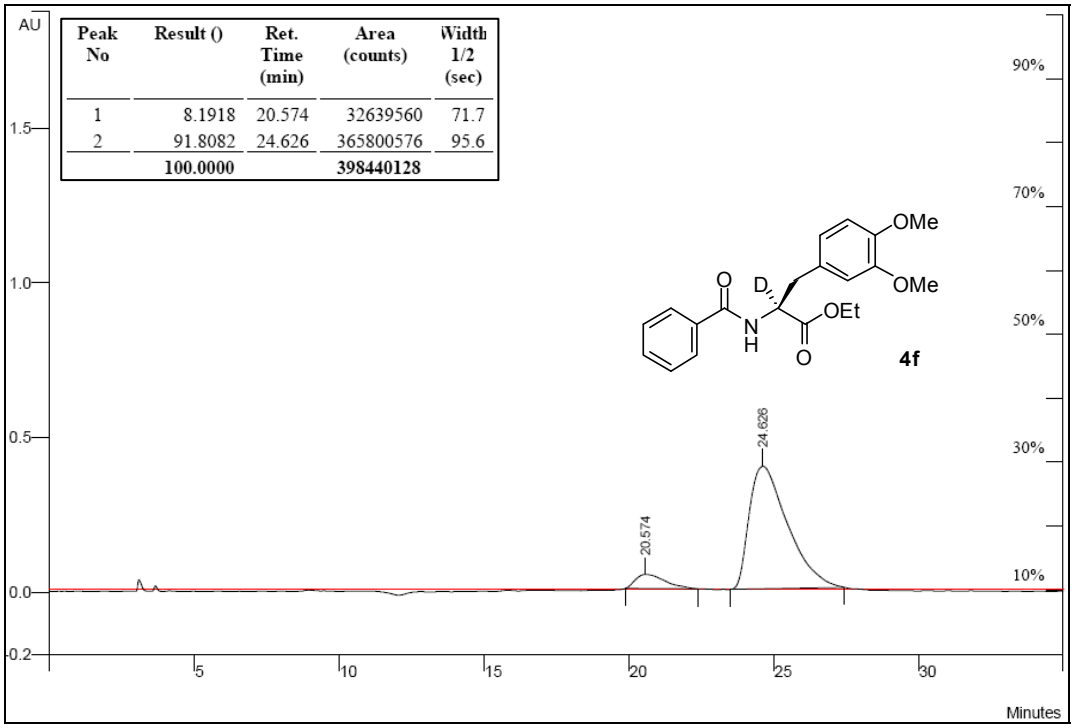
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.4198	8.350	2067226	13.0
2	99.5802	11.382	490396736	28.1
	100.0000		**492463968**	

Entry 6 (racemic sample)

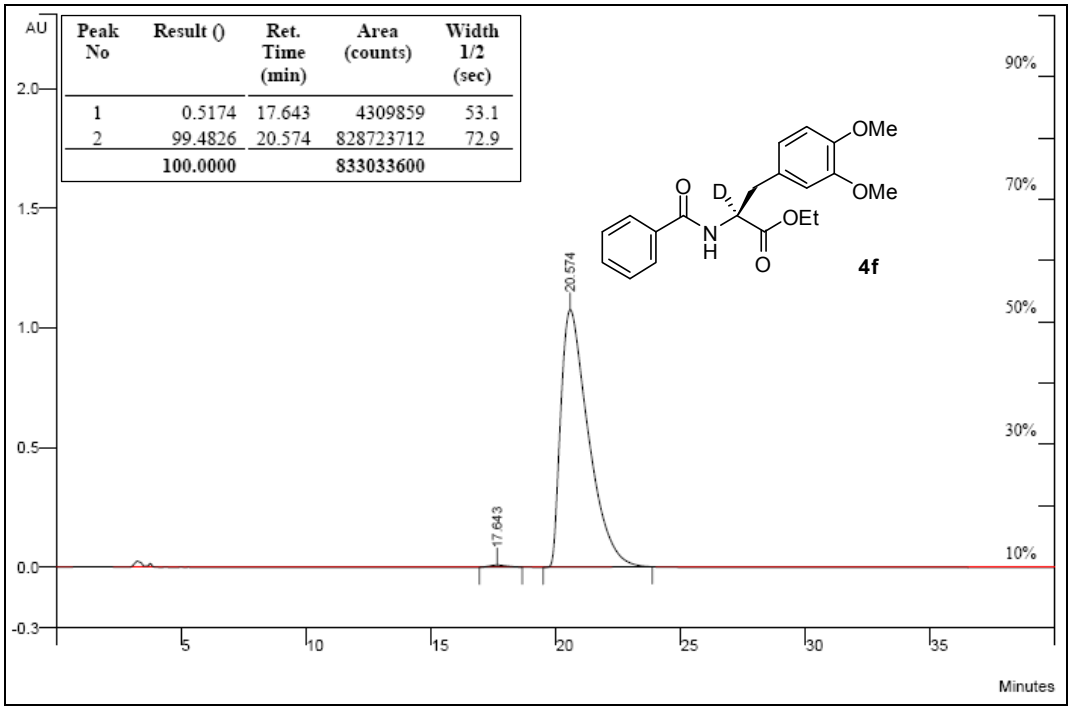


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.3009	21.022	150578784	84.7
2	49.6991	25.894	148777008	93.9
	100.0000		**299355776**	

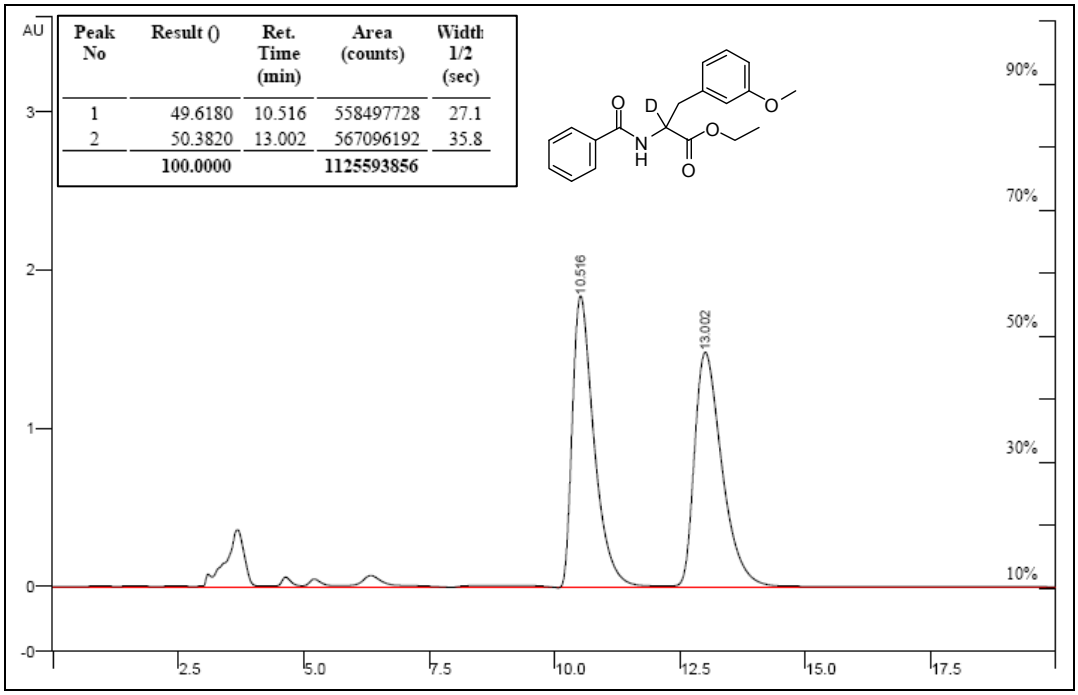
Entry 6 (before recrystallization)



Entry 6 (after recrystallization)

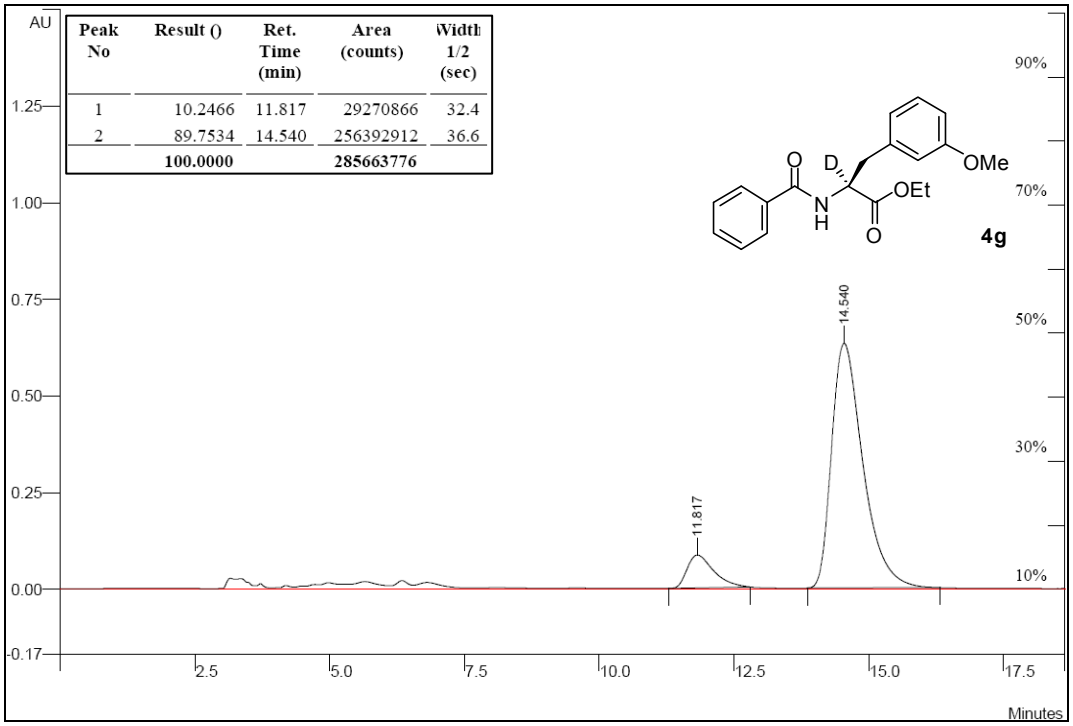


Entry 7 (racemic sample)



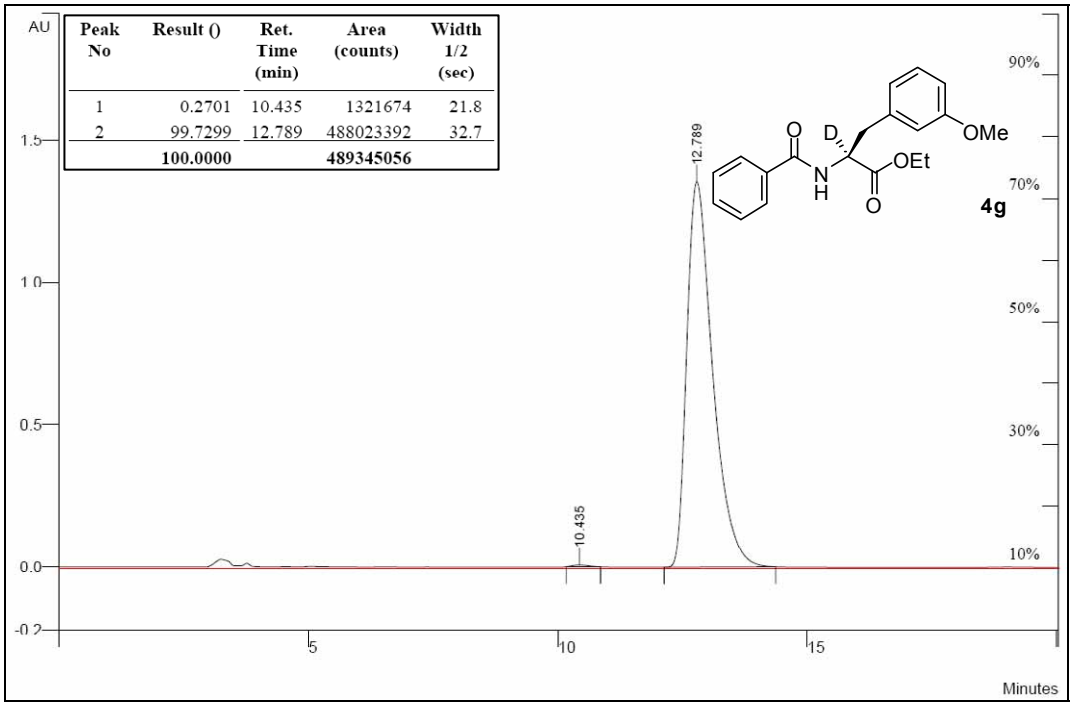
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6180	10.516	558497728	27.1
2	50.3820	13.002	567096192	35.8
	100.0000		**1125593856**	

Entry 7 (before recrystallization)



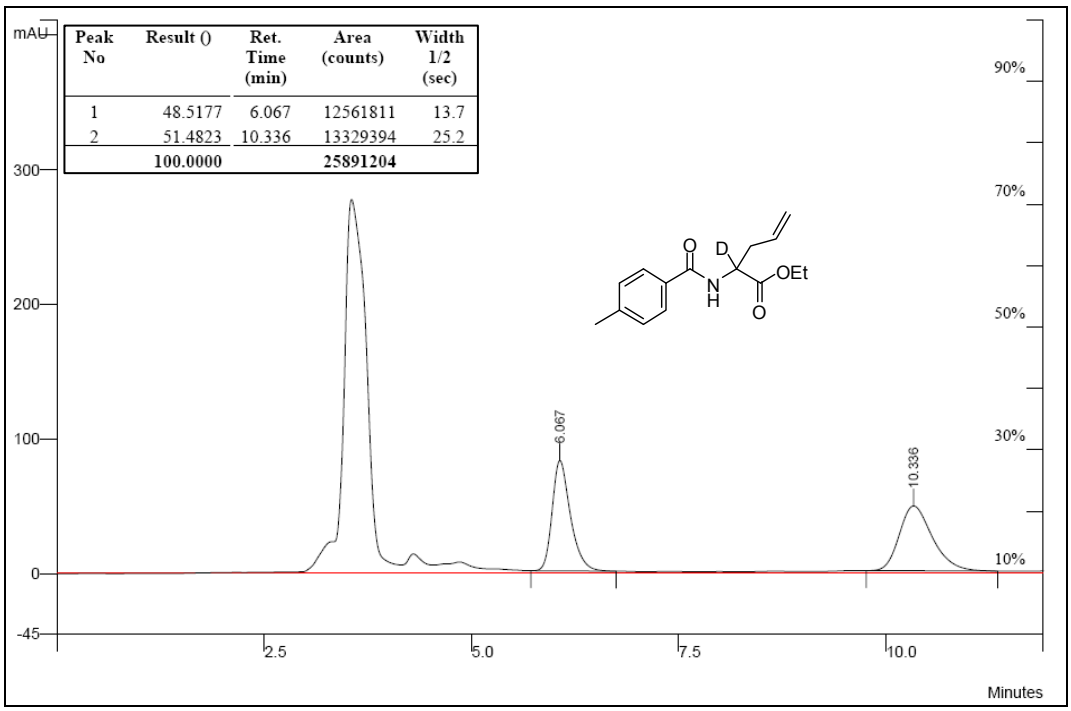
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.2466	11.817	29270866	32.4
2	89.7534	14.540	256392912	36.6
	100.0000		**285663776**	

Entry 7 (after recrystallization)



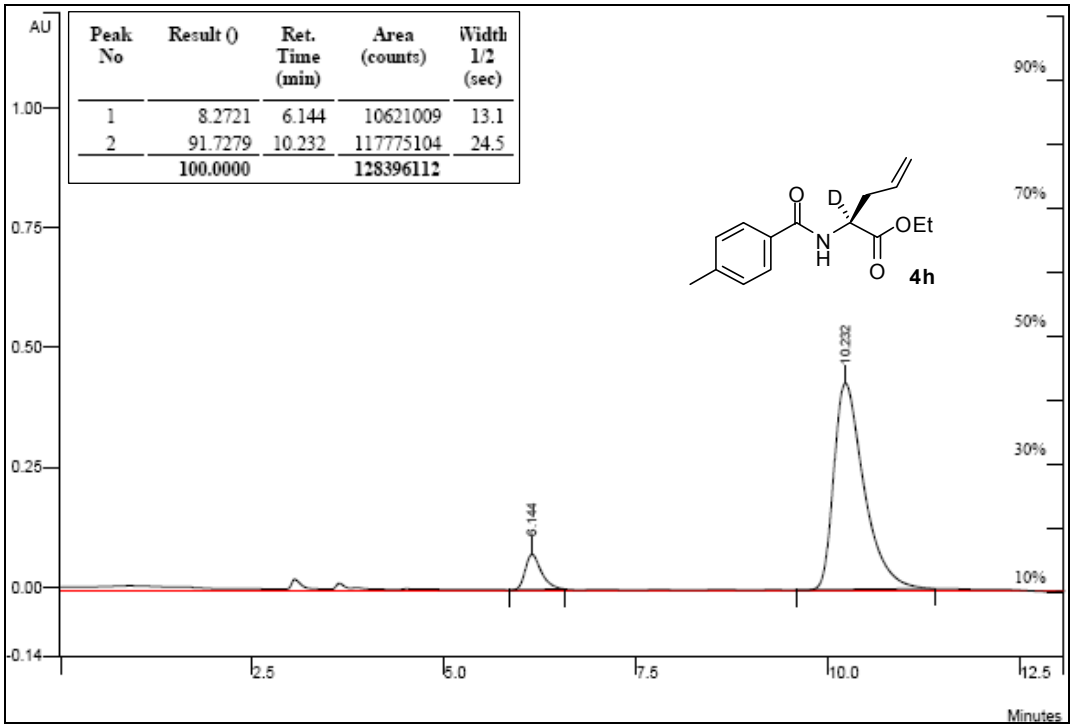
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.2701	10.435	1321674	21.8
2	99.7299	12.789	488023392	32.7
	100.0000		489345056	

Entry 8 (racemic sample)



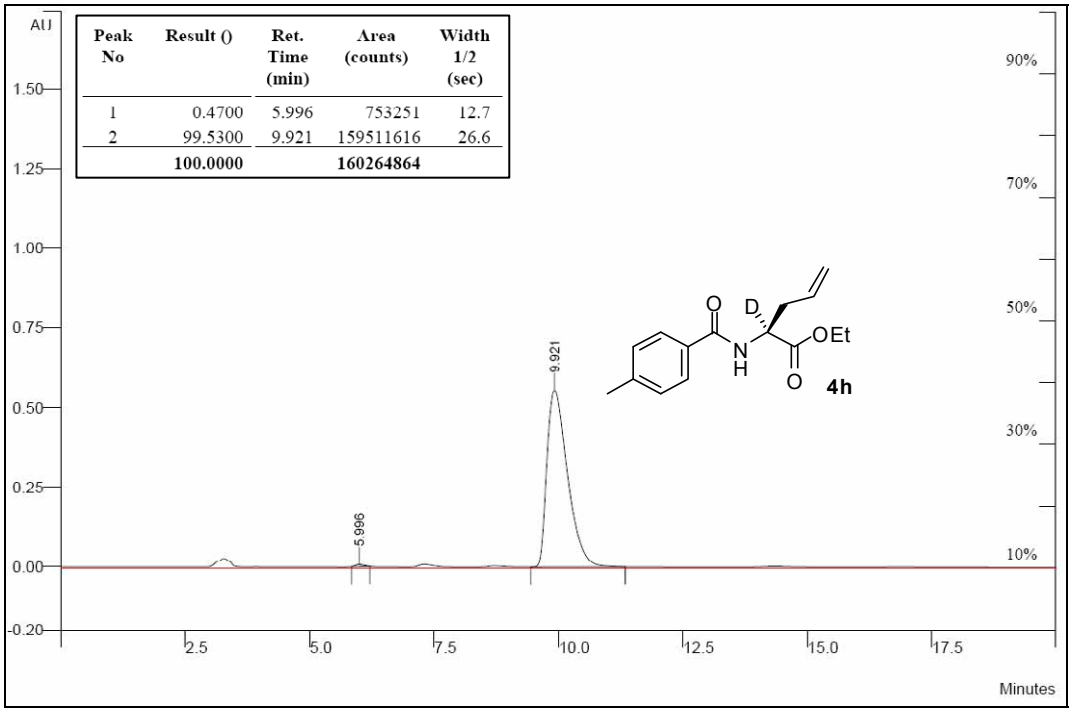
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	48.5177	6.067	12561811	13.7
2	51.4823	10.336	13329394	25.2
	100.0000		25891204	

Entry 8 (before recrystallization)



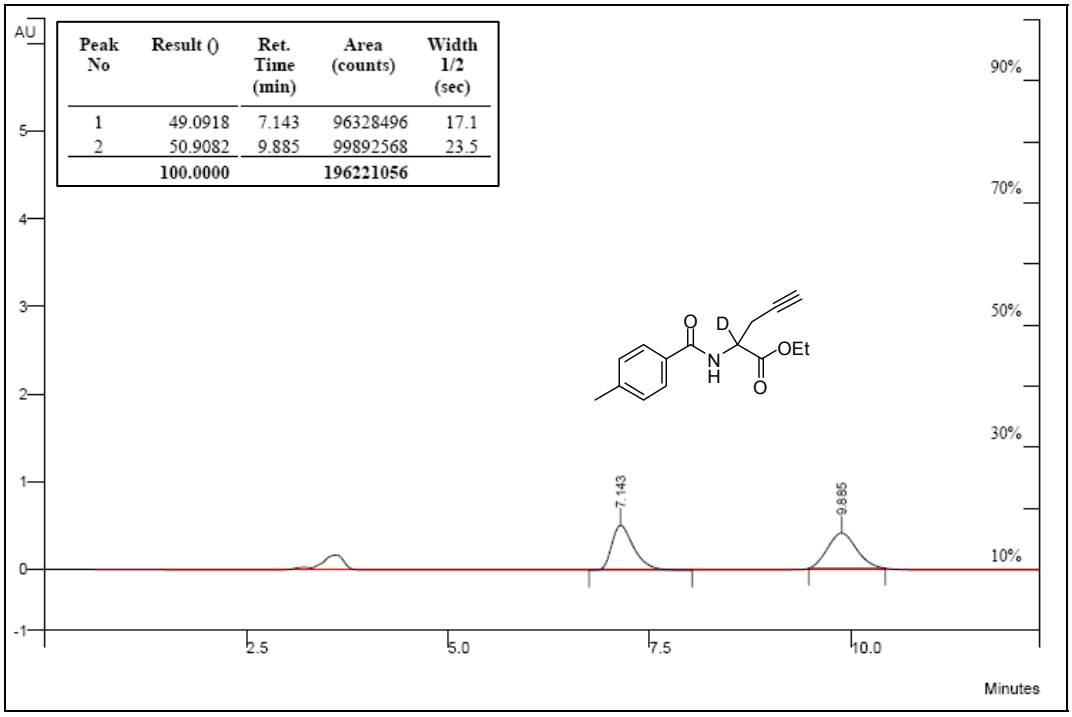
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	8.2721	6.144	10621009	13.1
2	91.7279	10.232	117775104	24.5
	100.0000		**128396112**	

Entry 8 (after recrystallization)



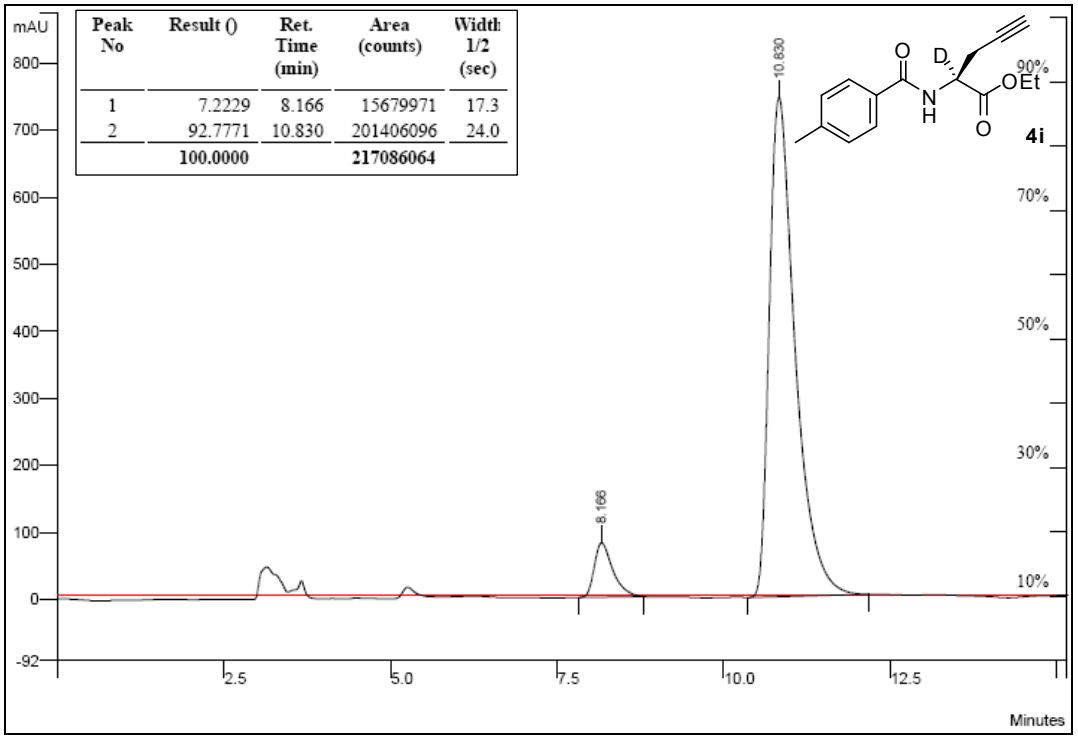
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.4700	5.996	753251	12.7
2	99.5300	9.921	159511616	26.6
	100.0000		**160264864**	

Entry 9 (racemic sample)



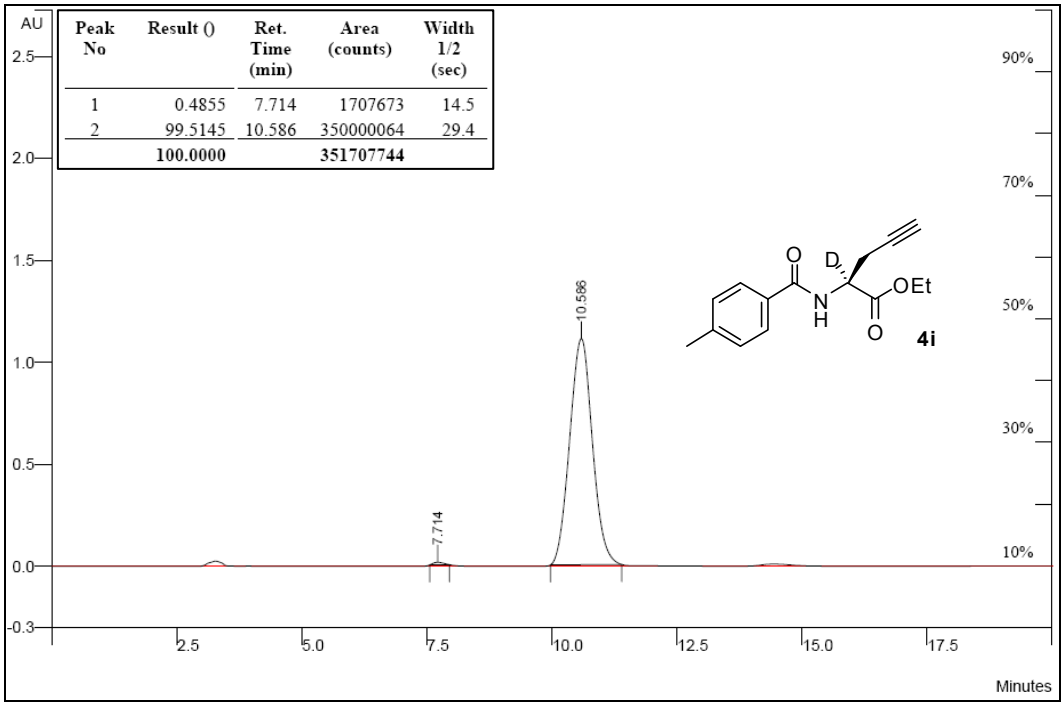
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.0918	7.143	96328496	17.1
2	50.9082	9.885	99892568	23.5
	100.0000		**196221056**	

Entry 9 (before recrystallization)

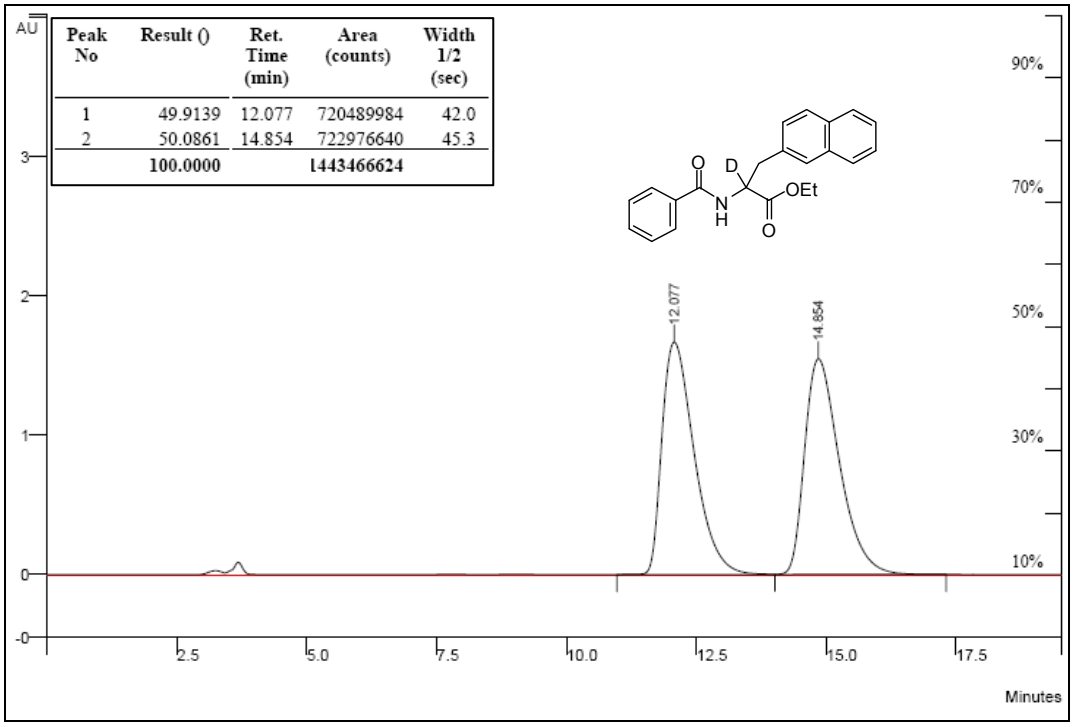


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	7.2229	8.166	15679971	17.3
2	92.7771	10.830	201406096	24.0
	100.0000		**217086064**	

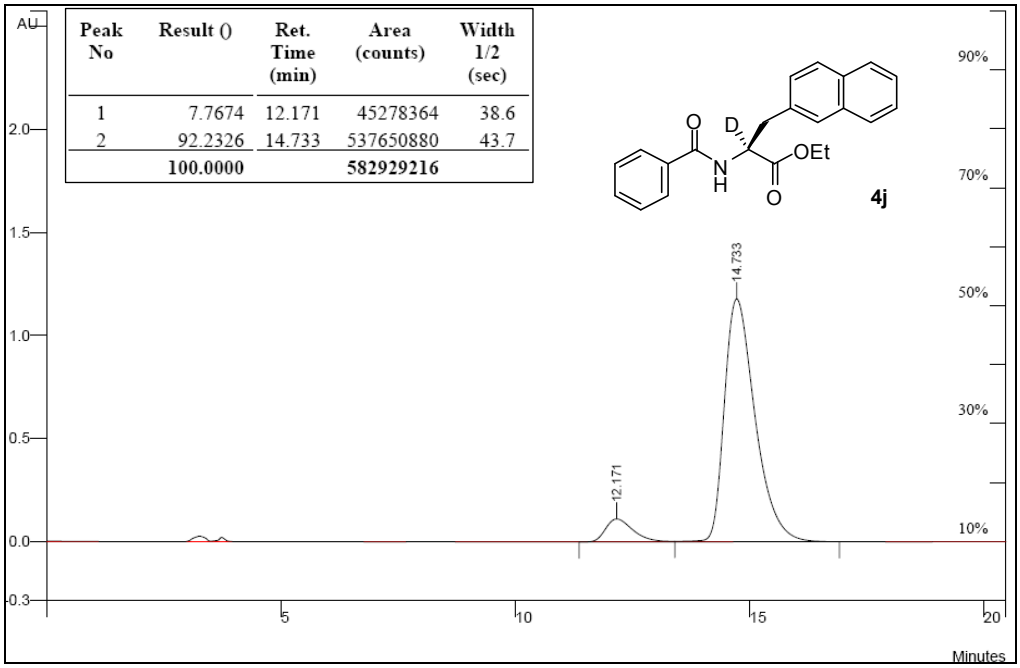
Entry 9 (after recrystallization)



Entry 10 (racemic sample)

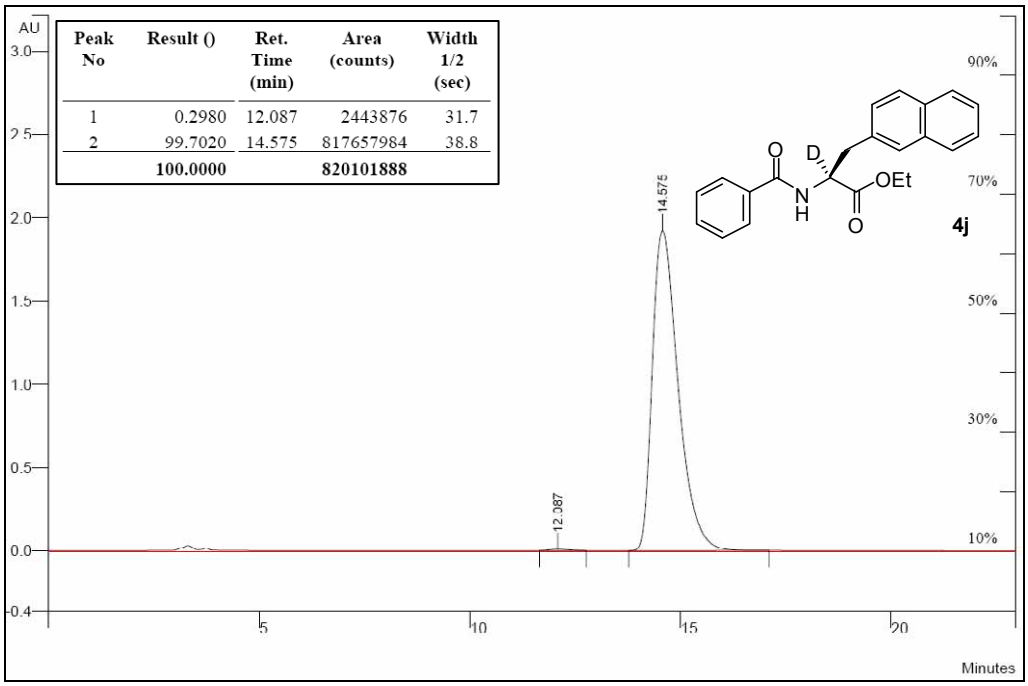


Entry 10 (before recrystallization)



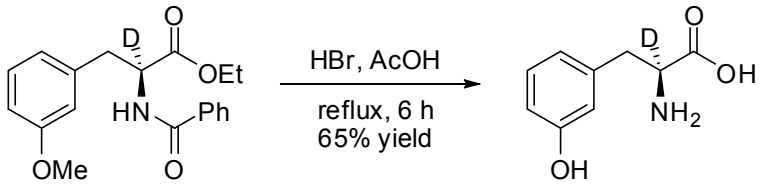
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	7.7674	12.171	45278364	38.6
2	92.2326	14.733	537650880	43.7
	100.0000		**582929216**	

Entry10 (after recrystallization)



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	0.2980	12.087	2443876	31.7
2	99.7020	14.575	817657984	38.8
	100.0000		**820101888**	

10. A gram-scale synthesis of α-deutrated L-*m*-tyrosine

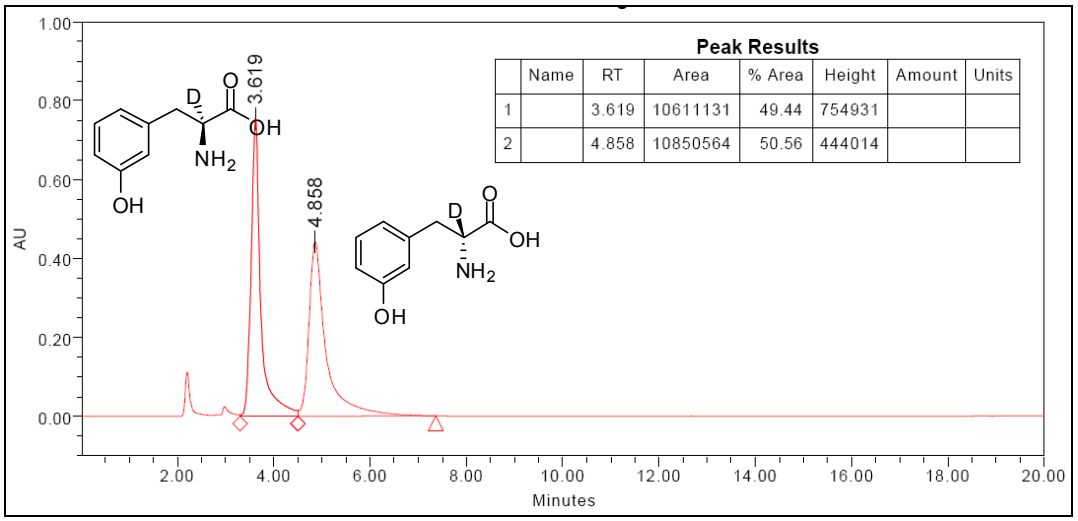


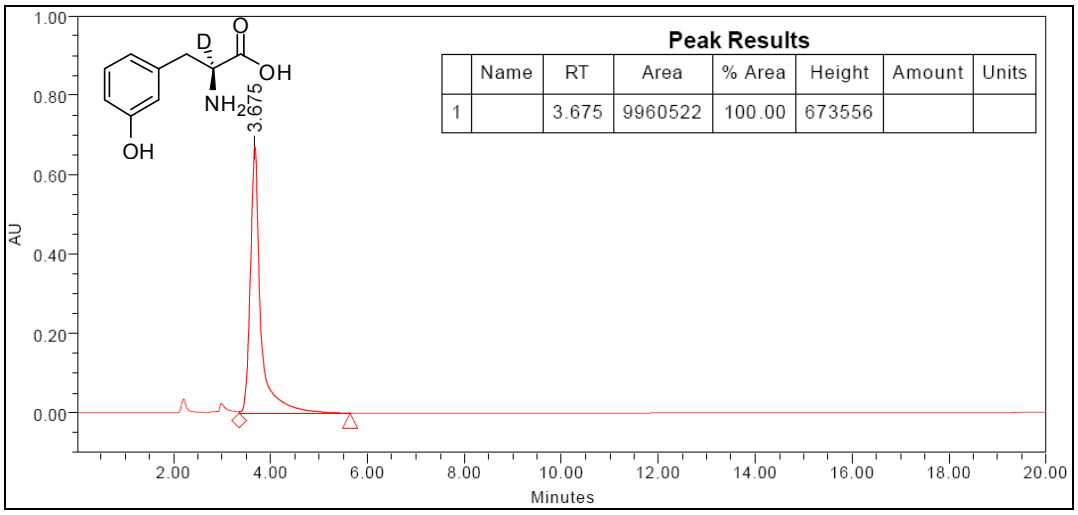
(*S*)-**4g**
>99% ee
96:4 D/H ratio
(3.90 g scale)

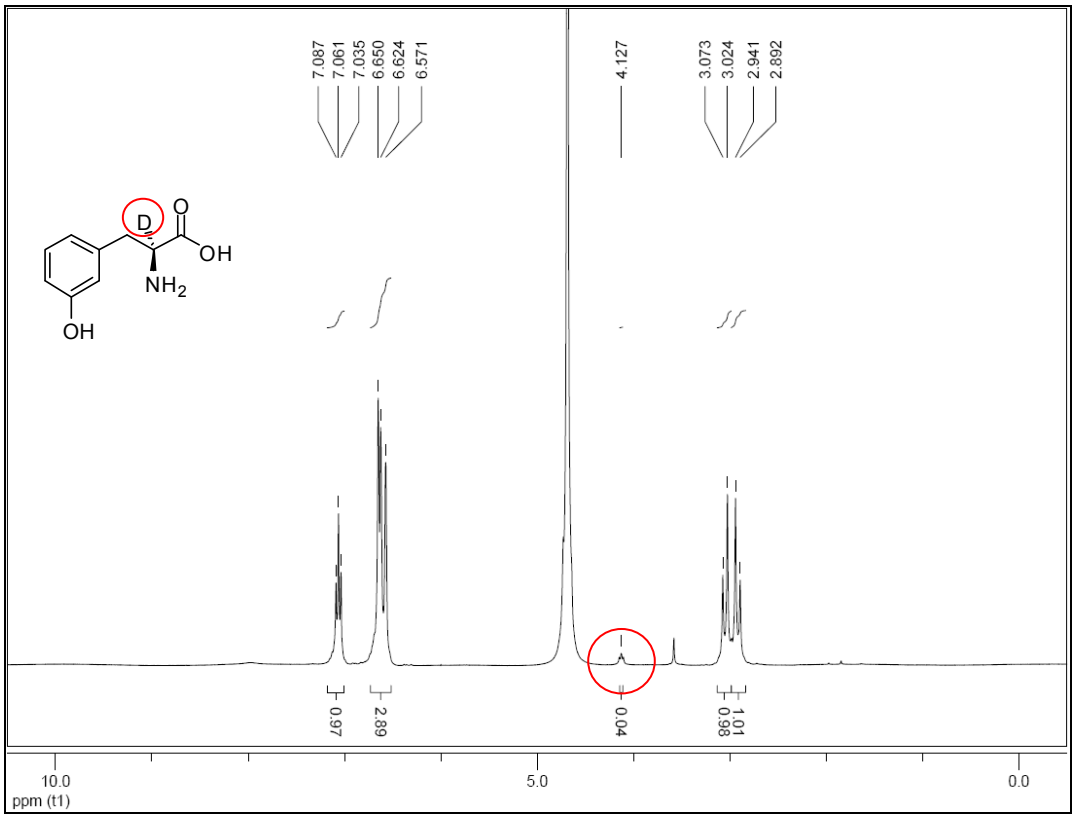
L-*m*-tyrosine
(> 99.9% ee)
96:4 D/H ratio

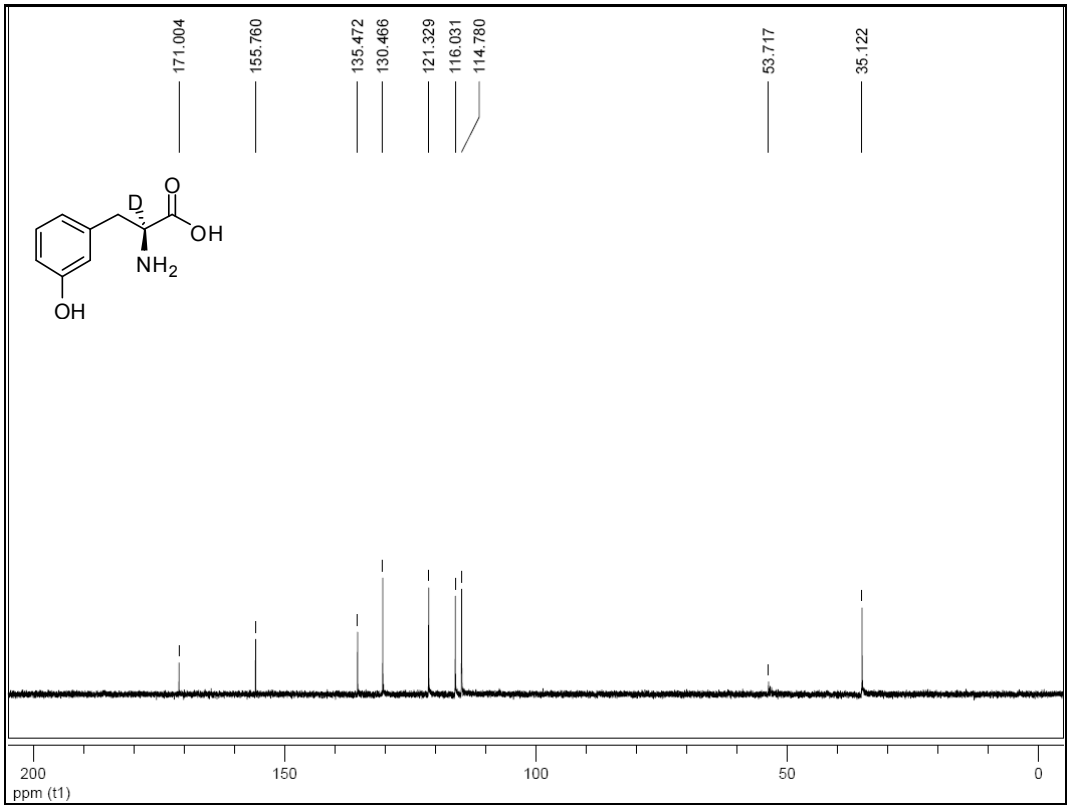
A suspension of (*S*)-**4g** (3.90 g, 11.88 mmol) in mixture of HBr (9 mL) and AcOH (8 mL) was refluxed for 6 h, followed by complete evaporation of the liquid. The residue was redissolved in water (12 mL), and extracted with CH_2Cl_2 (12 mL X 2). The pH of the aqueous layer was then adjusted to 5.5-6 by adding 4 N NaOH solution. The precipitate formed was filtered and dried in vacuo to yield α-deutrated L-*m*-tyrosine (1.4 g, 65%) as colorless crystals.

^{1}H NMR (300 MHz, D_2O, DCl) δ 2.92 (d, J = 14.7 Hz, $1H_A$ of AB-spin system), 3.05 (d, J = 14.7 Hz, $1H_B$ of AB-spin system), 6.50-6.76 (m, 3H), 7.0-7.15 (m, 1H); ^{13}C NMR (75 MHz, D_2O, DCl) δ 35.12, 53.71, 114.78, 116.03, 121.33, 130.47, 135.47, 155.76, 171.00.
Enantiomeric excess was determined by using HPLC analysis: ChiroSil RCA-51002546, 250*4.6mm (5um); : 80% MeOH & 20%, 10mM $HClO_4$ in H_2O; flow rate: 1.0 mL/min; 210 nm; t_S = 3.6 min, t_R =4.9 min.


Peak Results
Name RT Area % Area Height Amount Units
1 3.619 10611131 49.44 754931
2 4.858 10850564 50.56 444014
3.619
4.858
AU
Minutes


Peak Results
Name RT Area % Area Height Amount Units
1 3.675 9960522 100.00 673556
3.675
AU
Minutes





11. Crystal data for the compound Bis-Qn-SQ·2H_2O

Identification code	2	
Empirical formula	$C_{44}H_{52}N_6O_6$	
Formula weight	760.92	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 10.2837(2) Å	α = 90°.
	b = 16.8731(3) Å	β = 109.1920(10)°.
	c = 12.5611(2) Å	γ = 90°.
Volume	2058.44(6) Å^3	
Z	2	
Density (calculated)	1.228 Mg/m^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	812	
Crystal size	0.56 × 0.52 × 0.40 mm^3	
θ range for data collection	2.10 to 28.29°.	
Index ranges	$-11 \le h \le 13$, $-22 \le k \le 22$, $-16 \le l \le 16$	
Reflections collected	28370	
Independent reflections	9930 [R(int) = 0.0570]	
Completeness to theta = 28.29°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9677 and 0.9552	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9930 / 1 / 522	
Goodness-of-fit on F^2	0.935	
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0432, $wR2$ = 0.0963	
R indices (all data)	$R1$ = 0.0721, $wR2$ = 0.1060	
Absolute structure parameter	0.2(7)	
Extinction coefficient	0.0025(7)	
Largest diff. peak and hole	0.152 and –0.153 e·Å^{-3}	

12. References

1. J. W. Lee, T. H. Ryu, J. S. Oh,H. Y. Bae, H. B. Jang, C. E. Song, *Chem. Commun*. **2009**, 7224–7226.
2. J. Liang, J. C. Ruble and G. C. Fu, *J. Org. Chem.* **1998**, *63*, 3154-3155.
3. (a) E. Erlenmeyer, Justus Liebigs Ann. Chem. 1893, 275, 1-20; (b) C. E. Humphrey, M. Furegati, K. Laumen, L. L. Vecchia, T. Leutert, J. C. D. Müller-Hartwieg and M. Vögtle, *Org. Process. Res. Dev*. **2007**, *11*, 1069-1075.