Electronic Supplementary Information

Impact of Aqueous Micellar Media on Biocatalytic Transformations Involving Transaminase (ATA); Applications to Chemoenzymatic Catalysis

Jade Dussart-Gautheret,[1*] Julie Yu,[1] Krithika Ganesh,[2] Gaikwad Rajendra,[2]

Fabrice Gallou,[3] and Bruce H. Lipshutz[1*]

[1]Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA, 93106 USA

[2]Anthem Biosciences Pvt. Ltd., #49, Canara bank road, Bommasandra Industrial Area, Bommasandra, Bengaluru-560099, Karnataka, India

[3]Chemical & Analytical Development, Novartis Pharma AG, 4056 Basel, Switzerland

*Correspondence to: lipshutz@chem.ucsb.edu

Table of Contents

1. General experimental information S4
   a. TLC S4
   b. NMR S4
   c. HRMS S4
   d. Aminotransferase (ATA) and PLP cofactor S5
   e. Reagents S5
2. Experimental procedures S5
   a. TPGS-750-M preparation S5
   b. Surfactant solution preparation S6
   c. Triethanolamine buffer solution preparation S6
   d. 2 wt % TPGS-750-M in triethanolamine buffer solution preparation S7
   e. Conversion monitoring in buffer and TPGS-750-M/buffer S7
   f. Screening of the aqueous reaction medium involving various surfactants. S9
   g. Synthesis of nonracemic amines using transaminases S9
   h. General procedures for the synthesis of racemic amines S11
   i. Experimental procedure for a 3-step sequence (DMP/ATA/CbzCl) S12
   j. Experimental procedure for 1-pot sequence (ERED/ATA/S_NAr) S13
   k. Experimental procedure for (*S*)-rivastigmine S14
3. Supplementary Tables S15
   a. E-factor calculation details presented in Table 2 ..... S15
   b. Screening of transaminases in aqueous buffer S17
   c. Optimization of temperature and pH for transamination in aqueous buffer S18
   d. Concentration effect of transamination in aqueous buffer *vs.* in surfactant for 24 h ... S19
   e. Time screening of transamination in 2 wt % TPGS-750-M/buffer S21

4. Product characterization (NMR, HRMS, and chirality assessment)..... S22

5. NMR spectra..... S31

6. HPLC traces..... S51

7. References..... S69

1. General experimental information

a. TLC

Thin layer chromatography (TLC) was performed using Silica Gel 60 F254 plates (Merck, 0.25 mm thick), and visualized with a UV lamp and ninhydrin stain. Flash chromatography was done in glass columns using Silica Gel 60 (EMD, 40-63 μm).

b. NMR

^{1}H and ^{13}C NMR spectra were recorded on either a Varian Unity Inova 400 MHz (400 MHz for ^{1}H, 100 MHz for ^{13}C), a Varian Unity Inova 500 MHz (500 MHz for ^{1}H, 125 MHz for ^{13}C), a Varian Unity Inova 600 MHz (600 MHz for ^{1}H), Bruker (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F), or Bruker (500 MHz for ^{1}H, 125 MHz for ^{13}C, 471 MHz for ^{19}F).

Deuterated NMR solvents were purchased from Cambridge Isotopes Laboratories. DMSO-d_6, CD_3OD, and $CDCl_3$ were used as solvents. Residual peaks for $CHCl_3$ in $CDCl_3$ (^{1}H = 7.26 ppm, ^{13}C = 77.00 ppm), $(CH_3)_2SO$ in $(CD_3)_2SO$ (^{1}H = 2.50 ppm, ^{13}C = 39.52 ppm) or MeOH in MeOD (^{1}H = 3.31 ppm, ^{13}C = 49.00 ppm) have been assigned as internal standards. The chemical shifts are reported in ppm. The coupling constants *J* value are given in Hz. Data are reported as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, bd = broad doublet, t = triplet, q = quartet, quin = quintet, m = multiplet), coupling constant (if applicable) and integration.

c. HRMS

Mass spectra were obtained from the UC Santa Barbara and UC Irvine Mass Spectrometry Facility.

LCT-Premier (ESI)

Mass spectra were acquired via ESI-MS using a Waters LCT Premier mass spectrometer equipped with an Alliance 2695 Separations module. Samples dissolved in methanol were directly infused into the mass spectrometer with no chromatography performed. Accurate mass data was calibrated using sodiated polyethylene glycol or sodiated polyethylene glycol monomethyl ether as an internal standard for positive ions and clusters of sodium formate as an internal standard for negative ions.

GCT-Premier (GC-EI and GC-CI)

Mass spectra were acquired via GC-MS using a Waters GCT Premier mass spectrometer equipped with an Agilent 7890A GC oven and J&W Scientific DB-5ms+DG narrow bore column using

helium carrier gas. Samples dissolved in DCM were injected into the GC injector port which was maintained at 260 ℃. The GC oven temperature was maintained at 50 ℃ for one minute then raised to 290 ℃ at a rate of 10 ℃ per minute to elute the sample. Accurate mass data were calibrated using perfluorotributylamine or 2,4,6-tris(trifluoromethyl)-1,3,5-triazine as a co-injected standard. Where applicable, methane reagent gas was used to perform chemical ionization (CI) experiments.

d. Aminotransferase (ATA) and PLP cofactor

Aminetransaminase (ATA) Screening Kit containing 24 amine transaminase enzymes and PLP were purchased from Codex® and were used as received. The enzyme powder was stored at -18 °C until use. Purchasing website:https://www.codexis-estore.com/product-page/codex-amine-transaminase-ata-screening-kit.

e. Reagents

Triethanolamine was purchased from Sigma-Aldrich. Ketone reagents were purchased from Sigma-Aldrich, Combi-Blocks, Alfa Aesar, TCI, or Acros Organics and used without further purification. TPGS-750-M was synthesized according to the published procedure[1] or was obtained from PHT international. Brij 30, Tween 60, Triton X-100 were purchased from Sigma-Aldrich. PTS 600 was purchased from Cambridge Major Laboratories Inc. Solutol was purchased from Gattefosse.

2. Experimental procedures

a. TPGS-750-M preparation

DL-α-Tocopherol Succinate. To a solution of DL-α-Tocopherol (4.30 g, 10.00 mmol) and succinic anhydride (1.50 g, 15.00 mmol) in toluene (20 mL) was added Et_3N (0.35 mL, 2.50 mmol) at 22 °C with stirring, and the stirring was continued at 60 °C for 5 h. Water was added to the reaction mixture, which was then extracted with CH_2Cl_2. The combined organic layers were washed with 1 N HCl (3 x 50 mL) and water (2 x 30 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* affording a yellow liquid, which was purified by flash column chromatography on silica gel eluting with a 10% EtOAc/ hexane to 35% EtOAc/hexanes gradient

to afford DL-R-tocopherol succinate (5.25 g, 99%) as a white solid, mp 64- 67 °C. IR (neat) 2926, 1757, 1714, 1576, 1463, 1455, 1415, 1377, 1251, 1224, 1151, 1110, 1078, 926 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 2.94 (t, *J* = 6.8 Hz, 2H), 2.84 (t, *J* = 6.8 Hz, 2H), 2.59 (t, *J* = 6.8 Hz, 2H), 2.09 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H), 1.85-1.71 (m, 2H), 1.56-1.50 (m, 3H), 1.43-1.05 (m, 21H), 0.88-0.84 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 171.0, 149.7, 140.7, 126.9, 125.1, 123.2, 117.6, 75.2, 39.6, 37.8, 37.7, 37.6, 37.5, 33.0, 32.9, 31.3, 29.2, 28.8, 28.2, 25.0, 24.6, 24.0, 22.9, 22.8, 21.2, 20.8, 19.95, 19.88, 13.0, 12.2, 12.0; MS ESI+ *m/z* 554 $[M + Na]^+$. HRMS ESI+ *m/z* calcd for $C_{33}H_{54}O_5Na$ $[M + Na]^+$: 553.3869; found: 553.3876.

TPGS-750-M. A mixture containing DL-*R*-tocopherol succinate (2.97 g, 5.60 mmol), poly(ethylene glycol) monomethylether-750 (4.00 g, 5.33 mmol) and *p*-TsOH (0.15 g, 0.79 mmol) in toluene (20 mL) was refluxed for 5 h using a Dean-Stark trap. After cooling to rt, the mixture was poured into saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ (3 x 50 mL), brine (2 x 30 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to afford TPGS-750-M (6.60 g, 98%) as a waxy solid. IR (neat) 2888, 1755, 1739, 1465, 1414, 1346, 1281, 1245, 1202, 1109, 947, 845 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.28-4.26 (m, 2H), 3.71-3.54 (m, PEG), 3.38 (s, 3H), 2.93 (t, *J* = 7.2 Hz, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 6.8 Hz, 2H), 2.08 (s, 3H), 2.01 (s, 3H), 1.97 (s, 3H), 1.84-1.70 (m, 2H), 1.55-1.04 (m, 24H), 0.87-0.83 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 170.9, 149.5, 140.6, 126.7, 125.0, 123.0, 117.4, 94.5, 75.1, 72.0, 70.64, 70.56, 69.1, 64.0, 59.0, 39.4, 37.6, 37.5, 37.4, 37.3, 32.8, 32.7, 31.1, 29.2, 28.9, 28.0, 24.8, 24.5, 22.8, 22.7, 21.1, 20.6, 19.8, 19.7, 13.0, 12.1, 11.8; MS (ESI) m/z 1272 $[M + Na]^+$

b. Surfactant solution preparation

TPGS-750-M is also commercially available from Sigma-Aldrich (catalog number 733857). The 2 wt % TPGS-750-M aqueous solution was prepared by mixing TPGS-750-M wax (10.0 g) with HPLC grade water (490.0 g), and stir until dissolved.[2]

c. Triethanolamine buffer solution preparation

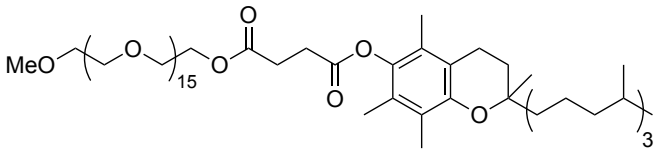
To a 500 mL beaker equipped with a magnetic stirrer, HPLC grade water (200.0 mL), triethanolamine (5.0 g), and isopropylamine (18.0 g) were added. Under gentle stirring at rt, concentrated HCl was added dropwise. After pH reached 8.5 (indicated by a pH meter), the total

volume was then adjusted to 300.0 mL by adding HPLC grade water. The buffer solution was stored at 4 °C until use.

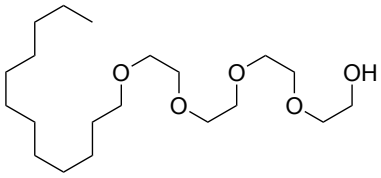
d. 2 wt % TPGS-750-M in triethanolamine buffer solution preparation

To a 500 mL beaker equipped with a magnetic stirrer, triethanolamine (5.0 g), 2 wt % TPGS-750-M aqueous solution (200.0 mL), and isopropylamine (18.0 g) were added. Under gentle stirring at room temperature, concentrated HCl was added dropwise, monitoring the pH by a pH meter. After the pH reached 8.5, the total volume was then adjusted to 300.0 mL by adding 2 wt % TPGS-750-M aqueous solution in a graduate cylinder. The buffer solution was stored under 4 °C until use.

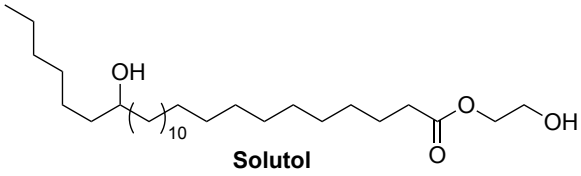
Alternative Method: Desired amount (2 wt %, 4 wt %, or 6 wt %) of non-ionic surfactant (TPGS-750-M, solutol, PTS-600, or Brij 30, Tween 60 or Triton X-100) was weighed into a beaker, then stirred in triethanolamine buffer solution (pH 8.5) until surfactant dissolved.



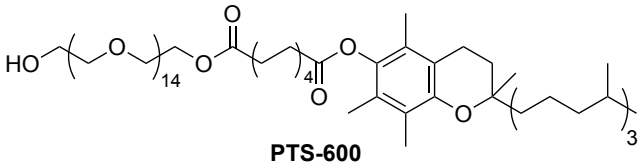
TPGS-750-M



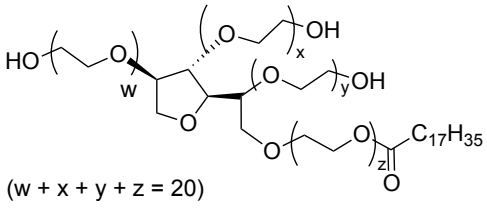
Brij 30



Solutol

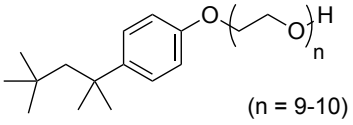


PTS-600



(w + x + y + z = 20)

Tween 60



(n = 9-10)

Triton X-100

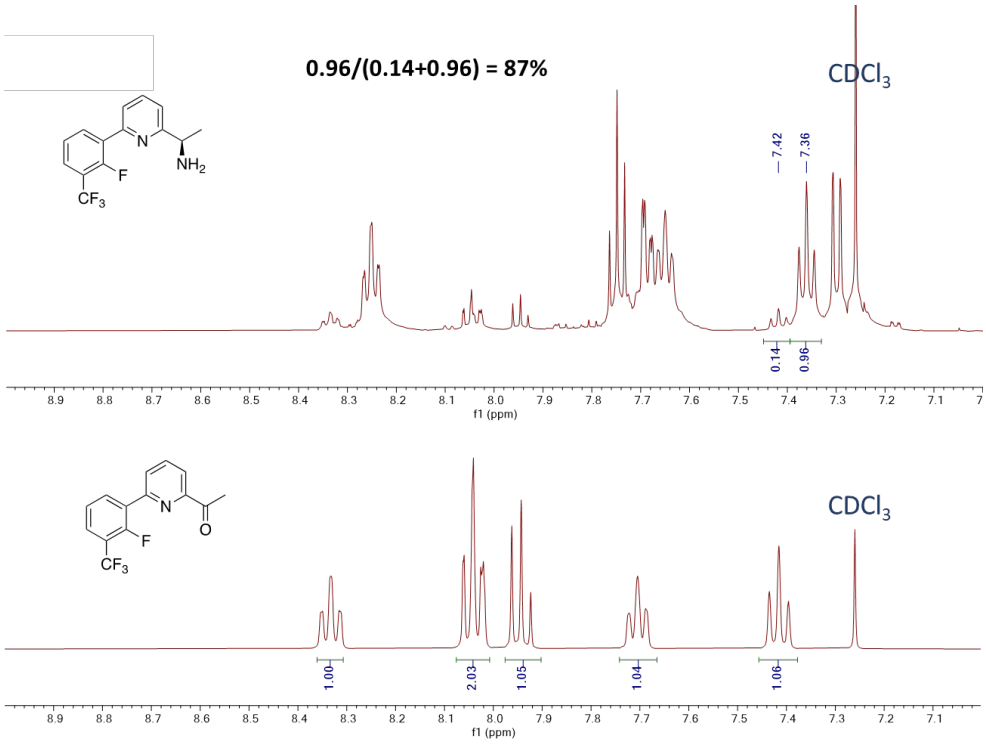
e. Conversion monitoring in buffer and TPGS-750-M/buffer

To evaluate the impact of TGPS-750-M on the conversion of different ketone substrates by transaminase, comparative monitoring has been performed. There is one time monitoring per vial

(t = 30 min, 1 h, 3 h, 5 h, and 24 h). To each of the five 5 mL vials equipped with a magnetic stir bar was added the ketone (0.01 mmol). Triethanolamine buffer at pH = 8.5 (1.0 mL) (with or without 2 wt % TPGS-750-M) was then added. Each reaction vial was capped by a screw cap and stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL or 1 mM), and transaminase (1.0 mg) were then added sequentially and stirred vigorously (1000 rpm) at 50 °C.

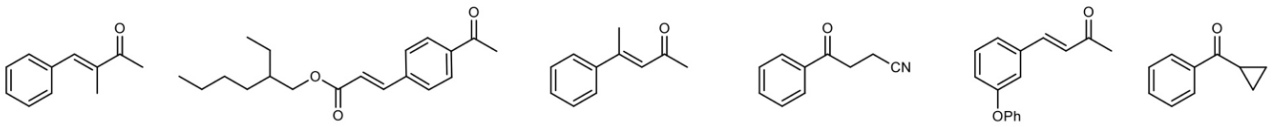
After the desired time is reached, the reaction mixture was basified with 5 N NaOH (~0.30 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (1.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (3.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

Example using the NMR spectrum to determine the extent of conversion of the nonracemic amine **8** after 24 h (7.42 ppm (t) → 7.36 ppm (t)).



f. Screening of the aqueous reaction medium involving various surfactants.

Ketone substrate (0.01 mmol) was added to a 5 mL vial equipped with a magnetic stir bar. Triethanolamine buffer at pH = 8.5 (1.0 mL) (with or without 2, 4, 6 wt % surfactant) was then added and stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL or 1 mM), and transaminase (1.0 mg) was then added sequentially and stirred vigorously (1000 rpm) at 50 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.30 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (1.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (3.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.



1 2 3 4 5 6

Substrate	Enzyme	Buffer only	2 wt % TPGS-750-M/buffer	2 wt % Solutol/buffer	4 wt % Solutol/buffer	6 wt % Solutol/buffer	2 wt % PTS600/buffer	2 wt % Brij30/buffer	2 wt % Triton X-100/buffer
1	ATA-256	46	52 (55)[a]	68	59	54	52	38	59
2	ATA-256	26	46 (56)[a]	45	48	45	13	48	44
3	ATA-260	75	82	83	80	80	79	79	70
4	ATA-256	75	72	84	72	72	70	70	71
5	ATA-260	19	35	27	38	29	25	28	24
6	ATA-025	63	38	40	38	39	37	35	32

Table 1. Screening of the aqueous reaction medium involving various surfactants. Conversions were determined by ^1H NMR. Reaction conditions: ketone substrate (0.01 mmol), isopropyl amine (1.3 M), PLP (1.0 mM), ATA (1.0 mg), aqueous buffer pH = 8.5 (1.0 mL), 50 ºC, 24 h. [a] TPGS-750-M (6 wt %) / triethanolamine (TEA) buffer was used.

g. Synthesis of nonracemic amines using transaminases

The ketone substrate (0.10 mmol) was added to a 20 mL vial equipped with a magnetic stir bar. A solution of 2 wt % TPGS-750-M in a triethanolamine buffer (10 mL, pH = 8.5) was then added and the mixture stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL or 1 mM), and transaminase (10 mg) were then added sequentially. The reaction vial was capped with a screw cap and stirred vigorously (1000 rpm) at 50 °C.

Chemical species	Concentration
ketone substrate	10.0 mM
triethanolamine	142.5 mM
isopropylamine	1.3 M
PLP	1.0 mM
ATA	10 mg per 0.1 mmol ketone

Workup: The reaction mixture was basified with 5 N NaOH (~1.5 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (5.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (30 mL x 1) and dried over anhydrous $MgSO_4$. Volatiles were evaporated under reduced pressure. The residue was analyzed by NMR, HRMS, and HPLC.

Some amine products were readily isolated and directly subjected to chiral HPLC analysis. Others, however, due to their lack of stability (e.g., air oxidation) or solubility issues (e.g., in water) required derivatization to facilitate their isolation and characterization.

Cbz protection: To a stirred solution of the crude product in DCM (1.0 mL) was added sodium carbonate (12 mg, 0.30 mmol, 3 equiv), and benzyl chloroformate (85.3 mg, 70.5 μL, 0.50 mmol, 5.0 equiv). Upon completion of the reaction, the solvents were evaporated. The Cbz-protected amines were purified *via* column chromatography with 0-10% EtOAc/hexane.

Acetyl derivatization: To a stirred solution of the extracted crude product in DCM (1.0 mL) were added triethylamine (30.3 mg, 41.8 μL, 0.30 mmol, 3 equiv) and Ac_2O (30.6 mg, 20.4 μL, 0.30 mmol, 3.0 equiv). Upon completion of the reaction, the solvents were evaporated. Purification of the crude material was done *via* flash chromatography.

h. General procedures for the synthesis of racemic amines

General procedure A was employed for preparation of the corresponding racemic amines 14_{rac} and 36_{rac} General procedure B was used for the corresponding racemic amines 8_{rac}, 10_{rac}, 12_{rac}, 13_{rac}, 16_{rac}, 17_{rac}, 18_{rac}, 19_{rac}, 20_{rac}, 21_{rac}, 22_{rac}, 23_{rac}, 24_{rac}, 25_{rac}, 26_{rac} and 31_{rac} (rac = racemic). The protecting group installation procedures are the same for both the racemic and nonracemic amines.

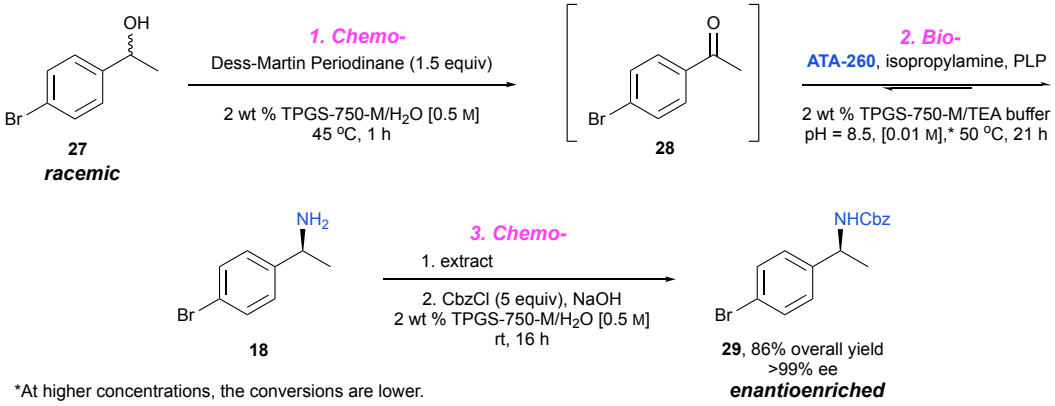
- Procedure A

Ammonium formate (5 equiv) and ketone (1.0 mmol, 1.0 equiv) were added to a 4 mL vial equipped with a magnetic stir bar. $[Ir(COD)Cl_2]_2$ (1.0 mg, 0.50 mol %) was added in a glove box. Methanol was added via syringe under argon. The vial was sealed and refluxed overnight. Upon completion, the resulting mixture was extracted with EtOAc (1 v x 5). The organic layers were separated and washed with 1 N HCl (1 v x 3). The aqueous layers were combined, basified with 5 N NaOH to pH 12–13 and extracted with EtOAc (1 v x 4). The separated organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Volatiles were evaporated under reduced pressure and analyzed by NMR.

- Procedure B

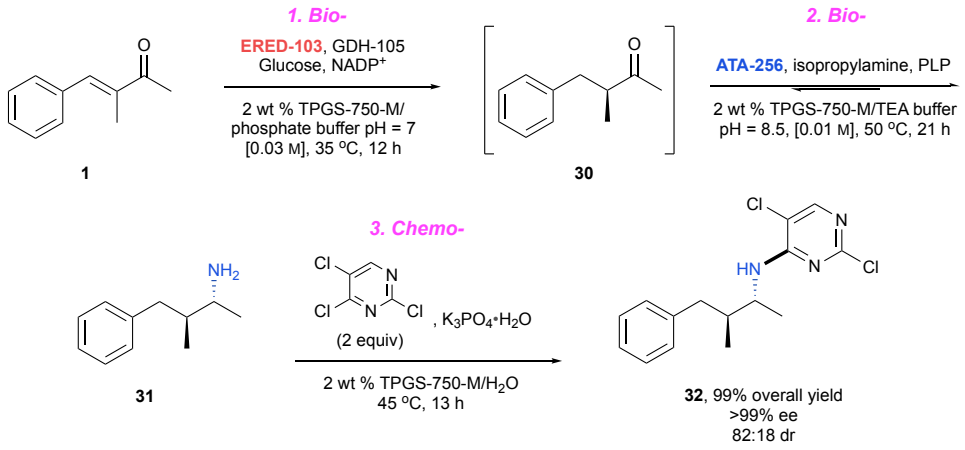
To a solution of ketone (1.0 mmol, 1.0 equiv) in methanol was added ammonium acetate (0.15 g, 2.0 mmol, 2.0 equiv) and sodium cyanoborohydride (0.31 g, 5.0 mmol, 5.0 equiv). The resulting mixture was stirred at 60 °C. (Caution: gas evolution) After 12 h, the reaction mixture was basified with 5 N NaOH to pH 12–13 (indicated by pH paper). The resulting mixture was extracted with EtOAc (1 v x 5). The organic layers were separated and washed with 1 N HCl (1 v x 3). The aqueous layers were combined, basified with 5 N NaOH to pH 12–13 and extracted with EtOAc (1 v x 4). The separated organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The racemic amine was analyzed by NMR.

i. Experimental procedure for a 3-step sequence (DMP/ATA/CbzCl)



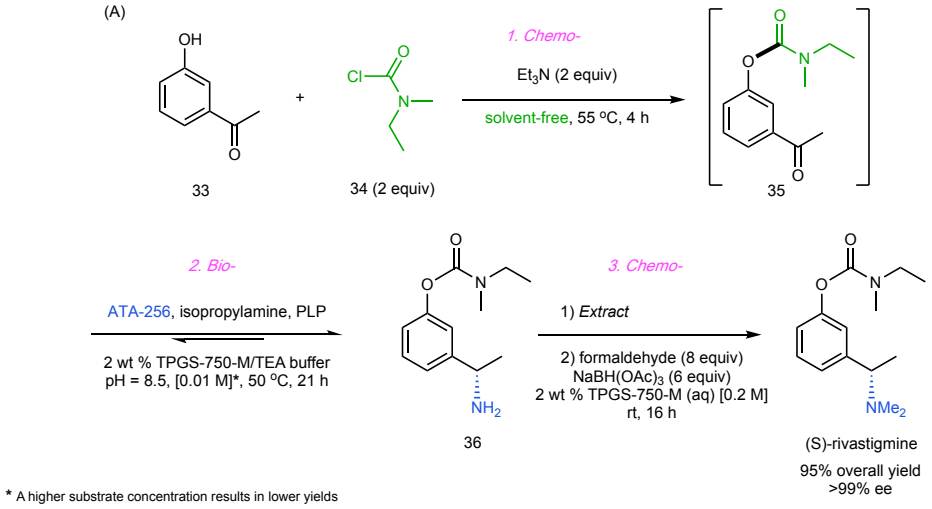
To a 4 mL vial equipped with a magnetic stirrer, 1-(4-bromophenyl)ethan-1-ol (20 mg, 0.10 mmol, 1 equiv), Dess-Martin periodinane (63.6 mg, 0.15 mmol, 1.5 equiv) and 2 wt % TPGS-750-M (0.2 mL) were added. The reaction vial was capped with a screw cap. The mixture was stirred vigorously at 45 °C until complete consumption of the starting material monitored by TLC. The reaction solution was then transferred to a 20 mL vial equipped with a magnetic stir bar, 2 wt % TPGS-750-M/triethanolamine buffer (9.8 ml, pH = 8.5), PLP (2.6 mg), and ATA-260 (5.0 mg) was added sequentially and stirred (1000 rpm) at 50 °C for 21 h. The reaction mixture was basified with 5 N NaOH (~1.5 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (5 mL x 5). The organic layer was separated with the aid of a centrifuge (low speed for 5 min). The combined organic phases were collected and dried over anhydrous $MgSO_4$. Volatiles were evaporated under reduced pressure. To a stirred solution of the crude product in 2 wt % TPGS-750-M (0.2 mL), sodium hydroxide (12.0 mg, 0.30 mmol, 3.0 equiv), and benzyl chloroformate (85.3 mg, 70.5 µL, 0.50 mmol, 5.0 equiv) were added and stirred at rt. The reaction mixture was then loaded on silica gel and purified by flash column chromatography to yield (*S*)-benzyl (1-(4-bromophenyl)ethyl)carbamate (28.7 mg, 86% yield, >99%*ee*, R_f = 0.43, 10% EtOAc/hexanes) as a white solid.

j. Experimental procedure for 1-pot sequence (ERED/ATA/S_NAr)



To a 20 mL vial equipped with a magnetic stirrer, (*E*)-3-methyl-4-phenylbut-3-en-2-one (20 mg, 0.127 mmol, 1.0 equiv), ERED-103 (40 mg), GDH-105 (8 mg), glucose (46 mg, 0.26 mmol, 2.0 equiv), and $NADP^+$ (2 mg) were suspended in 2 wt % of TPGS-750-M in phosphate buffer (pH = 7, 4 mL). The reaction was stirred at 35 °C for 12 h. The reaction progress was monitored by ^1H NMR. After the reaction reached completion, the substrate concentration was adjusted to 10 mM by adding 8.72 mL of triethanolamine buffer solution (triethanolamine, [118 mM], pH = 8.5). ATA-256 (50 mg) was then added and stirred (1000 rpm) at 50 °C for 21 h. The reaction progress was monitored by ^1H NMR. After completion, potassium phosphate tribasic monohydrate (29 mg, 0.127 mmol, 1 equiv) and 2,4,5-trichloropyrimidine (23 µL, 0.254 mmol, 2.0 equiv,) were added and the mixture was stirred at 45 °C for 21 h. The resulting mixture was extracted with EtOAc (10 mL x 5), and the combined organic extracts were dried over anhydrous $MgSO_4$. The volatiles were evaporated under reduced pressure and the crude residue was purified by flash column chromatography (0 to 25% EtOAc/hexane) to yield 2,5-dichloro-*N*-((2*R*,3*S*)-3-methyl-4-phenylbutan-2-yl)pyrimidin-4-amine. (60.5 mg, 99% yield, >99% *ee*, R_f = 0.36, 10% EtOAc/hexane).

k. Experimental procedure for (*S*)-rivastigmine



To a 5 mL vial equipped with a magnetic stir bar was added 3'-hydroxyacetophenone (0.1 mmol, 1 equiv), triethylamine (0.2 mmol, 2 equiv), and *N*-ethyl-*N*-methylcarbamoyl chloride (0.2 mmol, 2 equiv) was added sequentially. The reaction was stirred at 55 °C for 4 h. After completion of the reaction (monitored by ^{1}H NMR), 2 wt % TPGS-750-M/triethanolamine buffer (pH 8.5) was added in (3.3 mL x 3) and transferred to a 20 mL vial. To the stirred resulting reaction mixture, PLP (2.6 mg) and ATA-256 (5 mg) were added sequentially and heated to 50 °C and stirred for 21 h. After completion of the reaction, the solution was basified to pH 12–13 and extracted with EtOAc (3 x 4 mL). The combined organic layers were evaporated to provide crude amine intermediate. To the stirred solution of crude amine intermediate in 2 wt % TPGS-750-M (0.5 mL) was added formaldehyde (37% in water; 0.8 mmol, 8 equiv, 65.0 uL) and $NaBH(OAc)_3$ (0.6 mmol, 0.6 equiv). The rection was allowed to stirred at rt for 10 h. After completion, the mixture was loaded on silica gel and purified by flash column chromatography (2 v/v % MeOH in DCM + 1 v/v% Et_3N) to provide (*S*)-rivastigmine (23.7 mg, 95% yield, >99% *ee*) as a colorless oil.

3. Supplementary Tables

a. E Factor calculation details presented in Table 2

TABLE 2. COMPARISON OF LITERATURE ROUTES TO (*S*)-RIVASTIGMINE.

entry	cat. to generate chiral center	no. of rxn steps	no. of pots	total time [h][a]	yield [%][b]	ee[c] [%]	E Factor[d]
1[29]	Ir (1 mol %), H_2 (60 atm), Pd/C	4	4	49	82	96	2779
2[30]	Ir (1 mol %), H_2 (30 atm)	5	4	30	64	>99	270
3[31]	Hantzsch ester, disulfonimide	5	5	177	78	>99	3268
4[32]	ADHs in DSM 20016 whole cells	4	3	N/A	78	98	N/A
5[33]	ATA-114 or ATA-117	5	4	53	61	>99	6125
6[34]	PD-ω-TA	3	3	46	66	99	3626
7	**ATA-256**	**3**	**2**	**35**	**95**	**>99**	**561[e]**

[a]Sum of reaction time of each step. [b]Overall yield was considered. [c]Represents the % *ee* of (*S*)-rivastigmine. [d]Mass of organic solvents used in the reaction and workup divided by the mass of product. [e]The unusually high E Factor calculated up to the point of final purification (as this is highly variable) is attributed to the EtOAc needed in this particular case to extract amine **36** from the ATA reaction mixture; recovery and recycling of this solvent was not attempted.

Entry 1:
Overall Yield: 0.99*0.94*0.97*0.91 = 82%
>96% *ee*
Reaction Time: 4+.3+20+17+8 = 49.3 h
Acetone: 130 *ml* / 0.784 *g/ml* = 165.816 g
CH_2Cl_2: 10 *ml* / 1.33 g/ml = 7.519 g
MeOH: 8 *ml* / 0.792 *g/ml* = 10.101 g
Total waste: 183.436 g
Product: 66 mg
E Factor: 2779

Entry 2:
Overall Yield: = 0.85*0.82*.92 = 64%
99% *ee*
Reaction Time: 0.25+1+0.25+0.5+3+16+3+0.5+1+4 = 29.5 h
EtOH: 157 *L* / 0.789 *g/ml* = 198.986 kg
EtOAc: 736 L / 0.902 *g/ml* = 815.964 kg
THF: 135 *L* / 0.889 g/ml = 151.856 kg
Heptane: 50 *L* / 0.684 g/ml = 73.099 kg
Total waste: 1239.905 kg
Product: 4.6 kg
E Factor: 269.544

Entry 3:
Overall Yield: 0.98*0.92*0.93*0.95*0.98 = 82%
>96% *ee*
Reaction Time: 3 d+2d+40 h+12 h+5 h = 177h
EtOH: 20 *ml* / 0.789 *g/mL* = 25.348 g
mesitylene: 7 *ml* / 0.864 *g/mL* = 8.102 g
Et_2O: 10 *ml* / 0.713 g/mL = 12.399 g
EtOAc: 90 *ml* / 0.902 *g/mL* = 99.778 g
THF: 10 *ml* / 0.889 *g/mL* = 11.249 g
Total waste: 156.876 g
Product: 48 mg
E Factor: 3268

Entry 5:
Overall Yield: 0.86*0.80*0.99*0.92*0.97 = 61%
>99% *ee*
EtOAc: 147 *ml* / 0.902 *g/mL* = 162.971 g
THF: 6 *ml* / 0.889 *g/mL* = 6.748 g
CH_2Cl_2: 2.4 *ml* / 1.33 g/mL = 1.804 g
Total waste: 171.523 g
Product: 28 mg
E-factor: 6125

Entry 6:
Overall Yield: 0.89*0.76*1 = 66%
99% *ee*
Reaction Time: 5+24+16.5 = 45.5 h
THF: 100 *mL* / 0.889 *g/mL* = 112.486g
EtOAc: 130 *mL* / 0.902 *g/mL* = 144.124g
CH_2Cl_2: 6 *mL* / 1.33 g/mL = 4.511 g
Total waste: 261.121 g
Product: 72 mg
E-factor: 3626

Entry 7:
Overall Yield: 0.99*0.94*0.97*0.91 = 82%
>96% *ee*
Reaction Time: 4+21+10=35 h
EtOAc: 12 *mL* / 0.902 *g/mL* = 13.3 g
Total waste: 13.3 g
Product: 23.7 mg
E-factor: 561

b. Screening of transaminases in aqueous buffer

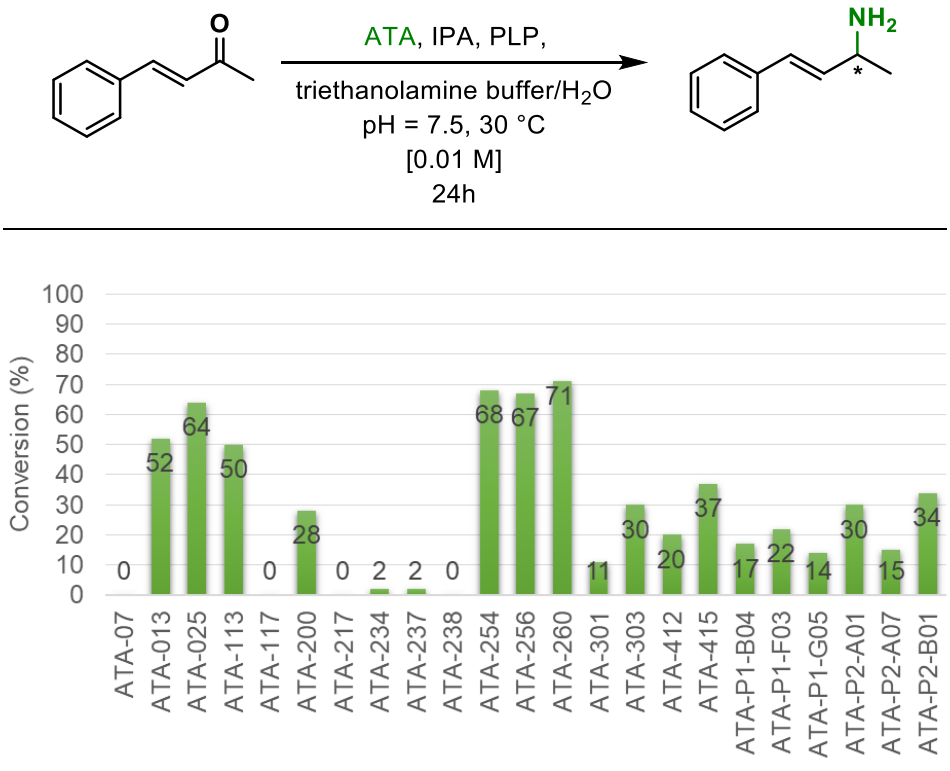
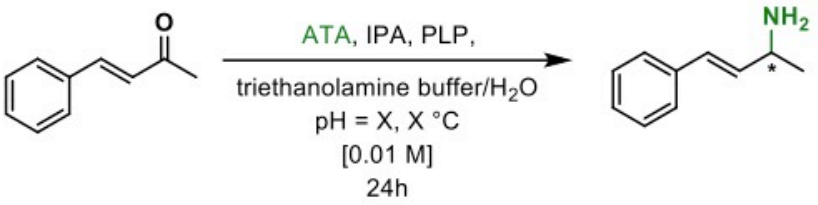


Table S1. Screening of ATAs in aqueous buffer

The ketone substrate (0.01 mmol) was added to a 4 mL vial equipped with a magnetic stir bar. Triethanolamine buffer at pH = 7.5 (1 mL) was then added and stirred at 30 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL or 1 mM), and transaminase (1.0 mg) was then added sequentially and stirred vigorously (1000 rpm) under 30 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.30 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (1.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (3.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

c. Optimization of temperature and pH for transamination in aqueous buffer



pH	Temp. (°C)	ATA-025	ATA-254	ATA-256	ATA-260
7.5	30	64%	68%	67%	71%
	40	64%	70%	69%	70%
	50	69%	70%	69%	75%
8.5	30	64%	70%	71%	61%
	40	72%	74%	70%	67%
	50	**75%**	**76%**	**71%**	**75%**

Table S2. Optimization of temperature and pH effect for transamination in aqueous buffer

The ketone substrate (0.01 mmol) was added to a 4 mL vial equipped with a magnetic stir bar. Triethanolamine buffer at pH = 7.5 or 8.5 (1 mL) was then added and stirred at 30 °C, 40 °C or 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL or 1 mM), and transaminase (1.0 mg) was then added sequentially and stirred vigorously (1000 rpm) under 30 °C, 40 °C, or 50 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.30 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (1.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (3.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

d. Concentration effect of transamination in aqueous buffer *vs.* in surfactant for 24 h

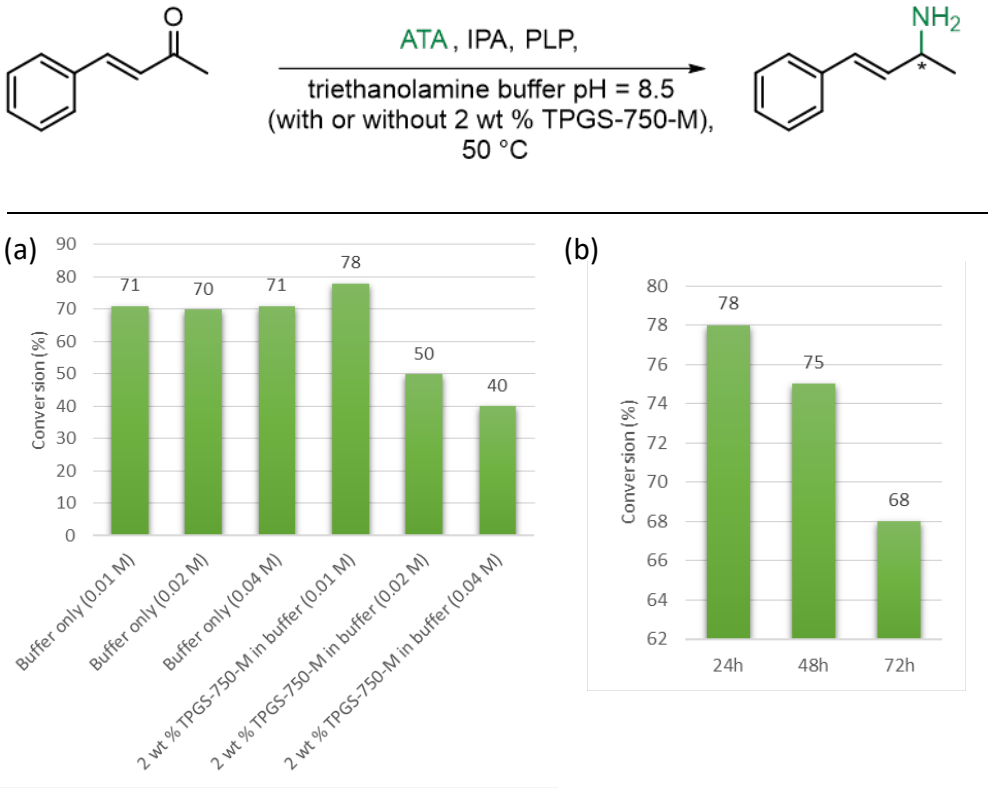


Table S3. (a) Concentration effect of transamination in aqueous buffer vs surfactant for 24 h; (b) time screening of transamination in 2 wt % TPGS-750-M/buffer (0.01 M)

To evaluate the concentration effect of transamination in aqueous buffer *vs*. that in surfactant, a triethanolamine buffer solution was prepared for each concentration (0.01 M, 0.02 M, and 0.04 M).

- For a concentration of 0.01 M

To a 50 mL beaker equipped with a magnetic stirrer, triethanolamine (0.5 g), 2 wt % TPGS-750-M aqueous solution or aqueous solution (20.0 mL), and isopropylamine (1.80 g) were added. Concentrated HCl was added dropwise under gentle stirring at rt, monitoring the pH with a pH meter. After the pH reached 8.5, the total volume was then adjusted to 30.0 mL by adding 2 wt % TPGS-750-M aqueous solution or water in a graduated cylinder. The buffer solution was stored at 4 °C until use.

The ketone substrate (0.04 mmol) was added to a 5 mL vial equipped with a magnetic stir bar. Triethanolamine buffer at pH = 8.5 (4 mL), with or without 2 wt % surfactant, was then added and stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (0.266 mg/mL), and transaminase (4.0 mg) were then added sequentially and the reaction mixture was stirred vigorously (1000 rpm) under 50 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.60 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (2.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (5.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

- For a concentration of 0.02 M

To a 50 mL beaker equipped with a magnetic stirrer, triethanolamine (0.25 g), 2 wt % TPGS-750-M aqueous solution or aqueous solution (10.0 mL), and isopropylamine (1.80 g) were added. Concentrated HCl was added dropwise under gentle stirring at rt, monitoring the pH with a pH meter. After the pH reached 8.5, the total volume was then adjusted to 15.0 mL by adding 2 wt % TPGS-750-M aqueous solution or water in a graduated cylinder. The buffer solution was stored at 4 °C until use.

Ketone substrate (0.04 mmol) was added to a 5 mL vial equipped with a magnetic stir bar. Triethanolamine buffer at pH = 8.5 (2 mL; with or without 2 wt % surfactant) was then added and the reaction mixture stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP; 0.53 mg/mL) and transaminase (4.0 mg) were then added sequentially and stirred vigorously (1000 rpm) under 50 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.60 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (2.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (5.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

- For a concentration of 0.04 M

To a 25 mL beaker equipped with a magnetic stirrer, triethanolamine (0.125 g), 2 wt % TPGS-750-M aqueous solution or aqueous solution (5.0 mL), and isopropylamine (1.80 g) were added.

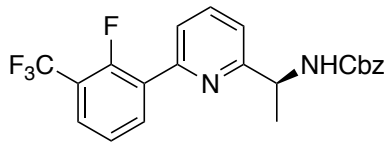
Concentrated HCl was added dropwise under gentle stirring at rt, monitoring the pH using a pH meter. After the pH reached 8.5, the total volume was then adjusted to 7.5 mL by adding 2 wt % TPGS-750-M aqueous solution or water in a graduated cylinder. The buffer solution was stored at 4 °C until use.

The ketone substrate (0.04 mmol) was added to a 5 mL vial equipped with a magnetic stirrer. Triethanolamine buffer at pH = 8.5 (1 mL), with or without 2 wt % surfactant, was then added and stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP) (1.07 mg/mL), and transaminase (4.0 mg) was then added sequentially and stirred vigorously (1000 rpm) under 50 °C. The reaction vial was capped with a screw cap, and after 24 h, the reaction mixture was basified with 5 N NaOH (~0.60 mL) to pH 12–13 (indicated by a pH indicator paper). The resulting mixture was extracted with EtOAc (2.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 minutes. The combined organic phases were collected and washed with distilled water (5.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

e. Time screening of transamination in 2 wt % TPGS-750-M/buffer

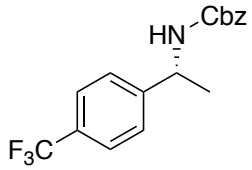
The ketone substrate (0.04 mmol) was added to a 5 mL vial equipped with a magnetic stir bar. A solution of 2 wt % TPGS-750-M in a triethanolamine buffer at pH = 8.5 (4 mL) was then added and stirred at 50 °C for 2 min to afford an emulsified solution. Pyridoxal 5'-phosphate (PLP; 0.266 mg/mL or 1 mM), and transaminase (4.0 mg) were then added sequentially and stirred vigorously (1000 rpm) under 50 °C. The reaction vial was capped with a screw cap, and after 24 h, 48 h, or 72 h, the reaction mixture was basified with 5 N NaOH (~0.60 mL) to pH 12–13 (indicated by pH indicator paper). The resulting mixture was extracted with EtOAc (2.0 mL x 5). The organic layer was separated with the aid of a low-speed centrifuge for 5 min. The combined organic phases were collected and washed with distilled water (5.0 mL x 1) and dried over anhydrous $MgSO_4$. The conversion was determined by ^1H NMR.

4. Product characterization (NMR, HRMS, and chirality assessment)



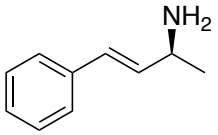
Benzyl (*S*)-(1-(6-(2-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)ethyl)carbamate 8

Following the general procedure with enzyme ATA-256, the product **16** was obtained as a white solid, 35.6 mg from a 0.1 mmol batch, 85% yield, 97% *ee.* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (t, *J* = 7.5 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.72 (ddd, *J* = 7.9, 2.5, 1.2 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.40 – 7.25 (m, 7H), 5.99 (d, *J* = 7.8 Hz, 1H), 5.18 – 5.08 (m, 2H), 5.01 (t, *J* = 7.1 Hz, 1H), 1.54 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.4, 158.7, 156.7, 155.7, 151.1, 137.4, 136.5, 135.1, 128.6, 128.5, 128.2, 128.1, 127.5, 127.0, 124.2, 123.3, 123.2, 121.6, 120.5, 66.7, 51.6, 22.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -61.26, -119.48. **HRMS** TOF MS EI+ *m/z* calcd $C_{22}H_{18}F_4N_2O_2$ $[M]^+$: 418.1304; found 418.1314. The enantioselectivity was determined by HPLC analysis Chiralcel® 5 μm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 6.697 min (minor) t_2 = 7.296 min (major).



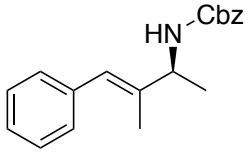
(*R*)-Benzyl (1-(4-(trifluoromethyl)phenyl)ethyl)carbamate 10

Following the general procedure with enzyme ATA-025, the product was obtained as a yellow oil, 29.1 mg from a 0.1 mmol batch, 88% yield, 79% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 7H), 5.07 – 4.89 (m, 3H), 4.86 – 4.75 (m, 1H), 1.40 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.5, 136.2, 129.7, 128.5, 128.2, 126.2, 125.7, 125.6, 125.6, 125.4, 66.9, 50.5, 22.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.49. **HRMS** TOF MS EI+ *m/z* calcd $C_{17}H_{16}F_3NO_2$ $[M+Na]^+$: 346.1031; found 346.1031. The enantioselectivity was determined by HPLC analysis (Phenomenex® 3 μm Lux Cellulose-2 column 150 x 2 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 0.416 min (minor) t_2 = 0.873 min (major).



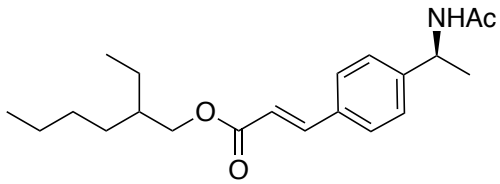
(*S*)-*E*-4-Phenylbut-3-en-2-amine 12

Following the general procedure with enzyme ATA-260, the product was obtained as a yellow oil, 90 mg from a 120 mg batch, 75% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (s, 2H), 7.44 – 7.27 (m, 5H), 6.69 (d, *J* = 16.0, 1H), 6.28 – 6.22 (m, 1H), 3.98 (s, 1H), 1.34 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 135.5, 134.7, 128.6, 126.9, 125.4, 50.1, 19.2. The enantioselectivity was determined by HPLC analysis (Chiralcel OD-H 250 mm x 4.6 mm, 5 µ column, *n*-hexane : 0.1% TFA in methanol = 95:5, flow rate 1.0 mL/min) t_1 = 18.520 min (major). Spectral data matched those previously reported.[3]



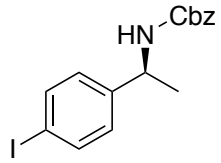
(*S*), *E*-Benzyl-(3-methyl-4-phenylbut-3-en-2-yl)carbamate 13

Following the general procedure with enzyme ATA-256, the product was obtained as a white solid, 19.2 mg from a 0.1 mmol batch, 65% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.28 (m, 7H), 7.21 (q, *J* = 7.2 Hz, 3H), 6.46 (s, 1H), 5.25 – 5.04 (m, 2H), 4.84 (s, 1H), 4.35 (s, 1H), 1.85 (s, 3H), 1.34 (d, *J* = 6.9 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.5, 138.9, 137.6, 136.6, 129.0, 128.5, 128.1, 128.1, 128.0, 126.4, 124.9, 66.7, 53.7, 20.1, 14.8. **HRMS** TOF MS EI+ *m/z* calcd $C_{19}H_{21}NO_2$ $[M]^+$: 295.1572; found 295.1564. The enantioselectivity was determined by HPLC analysis (Chiralcel® 5 µm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 10.611 min (major).



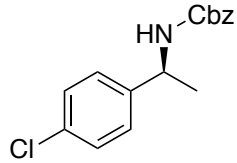
(*S*)-2-Ethylhexyl (*E*)-3-(4-(1-(((benzyloxy)carbonyl)amino)ethyl)phenyl)acrylate 14

Following the general procedure with enzyme ATA-256, the product was obtained as a colorless oil, 15.5 mg from a 0.1 mmol batch, 45% yield, >99% *ee.* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H), 7.50 (dd, *J* = 8.2, 2.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.63 (d, *J* = 7.9 Hz, 1H), 5.15 – 5.10 (m, 1H), 4.19 – 4.07 (m, 2H), 2.00 (s, 3H), 1.49 (d, *J* = 7.0 Hz, 3H), 1.41 (m, 3H), 0.95 – 0.82 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.7, 158.7, 145.4, 143.9, 133.7, 128.4, 126.7, 118.4, 67.4, 48.6, 38.9, 30.5, 29.7, 29.0, 23.8, 23.5, 23.0, 21.7, 14.0, 11.0. TOF MS CI+ *m/z* calcd $C_{21}H_{32}NO_3$ $[M]^+$: 345.2304; found 345.2313. The enantioselectivity of the unprotected primary amine was determined by HPLC analysis (Phenomenex® 5 µm Lux Cellulose-1 column 250 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 6.333 min (major).



(*S*)-Benzyl (1-(4-iodophenyl)ethyl)carbamate 16

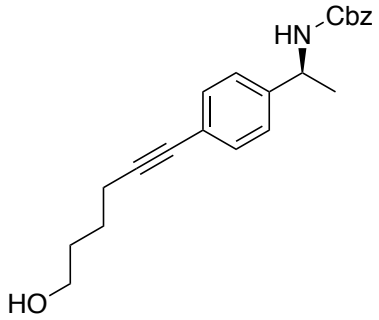
Following the general procedure with enzyme ATA-260, the product was obtained as a white solid, 28.6 mg from a 0.1 mmol batch, 75% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (s, 5H), 7.06 (d, *J* = 7.9 Hz, 2H), 5.15 – 4.99 (m, 3H), 4.86 – 4.71 (m, 1H), 1.44 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.4, 143.3, 137.7, 136.3, 128.5, 128.2, 127.9, 92.6, 66.8, 50.3, 22.4. **HRMS** TOF MS EI+ *m/z* calcd $C_{16}H_{16}INO_2$ Na $[M+Na]^+$: 404.0124; found 404.0128. The enantioselectivity was determined by HPLC analysis (Phenomenex® 5 µm Lux Cellulose-1 column 250 x 4.6 mm, isopropanol: *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 13.488 min (major).



(*S*)-Benzyl(1-(4-chlorophenyl)ethyl)carbamate 17

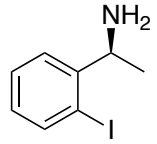
Following the general procedure with enzyme ATA-260, the product was obtained as a white solid 24.0 mg from a 0.1 mmol batch, 81% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.19 (m, 9H), 5.15 – 5.02 (m, 2H), 4.98 (s, 1H), 4.88 – 4.75 (m, 1H), 1.45 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.1, 141.1, 136.3, 133.0, 128.8, 128.5, 128.2, 127.3, 66.8, 50.8, 22.4. **HRMS** TOF

MS EI+ *m/z* calcd $C_{16}H_{16}ClNO_2$ Na $[M+Na]^+$: 312.0767; found 312.0767. The enantioselectivity was determined by HPLC analysis (Chiralcel® 5 μm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 9.987 min (major).



(*S*)-Benzyl (1-(4-(6-hydroxyhex-1-yn-1-yl)phenyl)ethyl)carbamate 19

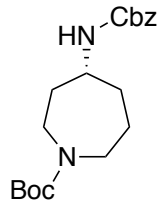
Following the general procedure with enzyme ATA-256, the product was obtained as a white solid, 26.3 mg, 75% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.0 Hz, 7H), 7.21 (d, *J* = 7.8 Hz, 2H), 5.18 – 4.74 (m, 5H), 3.71 (t, *J* = 6.1 Hz, 2H), 2.45 (t, *J* = 6.5 Hz, 2H), 1.72 (dq, *J* = 14.8, 7.8 Hz, 5H), 1.45 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.5, 142.9, 136.4, 131.8, 128.5, 128.1, 125.8, 122.9, 89.9, 80.6, 66.8, 62.5, 50.5, 31.9, 30.9, 25.0, 19.2, 14.1. **HRMS** TOF MS EI+ *m/z* calcd $C_{22}H_{25}NO_3$ Na $[M+Na]^+$: 374.1732; found 374.1732. The enantioselectivity of the unprotected primary amine was determined by HPLC analysis (Agilent® Poroshell 120 2.7 μm chiral-V column 50 x 4.6 mm, NH_4COOH pH = 3.5 (15 mM) : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 3.780 min (major).



(*S*)-1-(2-Iodophenyl)ethan-1-amine 20

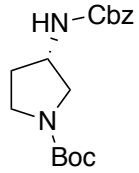
Following the general procedure with enzyme ATA-260, the product was obtained as a clear oil, 100.0 mg from a 190.0 mg batch, 52% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.87 (q, *J* = 0.8 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.27 (s, 1H), 7.07-7.03 (m, 1H), 4.73 (t, *J*= 8 Hz, 1H), 1.59 (d, *J* = 8.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.2, 140.0, 130.6, 129.4, 126.1, 98.7, 55.7, 20.0. **HRMS** TOF MS EI+ *m/z* calcd $C_8H_{11}IN$ $[M+H]^+$: 247.993626; found 247.9946. The enantioselectivity was determined by HPLC analysis (Chiralpak® AY-H 5 μ

column 250 mm x 4.6 mm, *n*-hexane: 0.1% diethylamine in ethanol = 95:5, flow rate 1.0 mL/min) t_1 = 12.579 min (major).



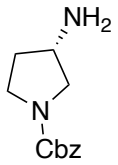
(*S*)-*t*-Butyl -4-(((benzyloxy)carbonyl)amino)azepane-1-carboxylate 21

Following the general procedure with enzyme ATA-260, the product was obtained as a colorless oil, 21.6 mg from a 0.1 mmol batch, 62% yield, 83% *ee.* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 3.5 Hz, 5H), 5.06 (s, 2H), 4.77 – 4.65 (m, 1H), 3.67 (s, 1H), 3.52 (d, *J* = 16.9 Hz, 2H), 3.33 (s, 1H), 3.14 – 3.05 (m, 1H), 2.05 – 1.97 (m, 1H), 1.91 – 1.83 (m, 1H), 1.81 (s, 1H), 1.51 (d, *J* = 39.7 Hz, 3H), 1.43 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.5, 155.4, 136.5, 128.5, 128.1, 128.1, 79.4, 66.6, 51.5, 51.3, 46.5, 45.4, 42.6, 42.3, 35.3, 35.0, 33.6, 33.3, 28.5, 24.2, 24.2. **HRMS** TOF MS EI+ *m/z* calcd $C_{19}H_{28}N_2O_4$ Na $[M+Na]^+$: 371.1947; found 371.1946. The enantioselectivity was determined by HPLC analysis (Phenomenex® 5 μm Lux Cellulose-1 column 250 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 0.5 mL/min) t_1 = 24.767 min (major) t_2 = 28.886 min (minor).



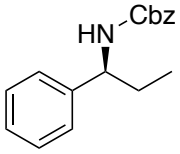
(*S*)-*t*-Butyl-3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 22

Following the general procedure with enzyme ATA-260, the product was obtained as a white solid, 24.6 mg from a 0.1 mmol batch, 75% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 5H), 5.18 (d, *J* = 13.8 Hz, 3H), 3.56 (dd, *J* = 12.5, 4.6 Hz, 2H), 3.52 – 3.35 (m, 2H), 2.13 – 2.02 (m, 2H), 1.45 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.6, 154.5, 154.4, 154.2, 140.9, 134.9, 128.7, 128.7, 128.6, 128.5, 128.4, 127.7, 127.0, 79.6, 77.7, 69.9, 65.4, 60.4, 51.8, 51.5, 43.9, 43.5, 31.5, 31.0, 30.8, 29.7, 28.5, 21.2, 14.2. (rotamer was observed). The enantioselectivity was determined by HPLC analysis (Chiralcel® 5 μm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 1.295 min (major). Spectral data matched those previously reported.[4]



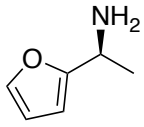
(*S*)-Benzyl 3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 23

Following the general procedure with enzyme ATA-260, the product was obtained as a black oil, 156.0 mg from a 196.0 mg batch, 80% yield, 98.4% *ee.* **^{1}H NMR** (400 MHz, d_6-DMSO) 7.96 (s, 3H), 7.37-7.31 (m, 4 H), 5.07 (d, *J* = 1.2 Hz, 2H), 3.81- 3.48 (m, 6H), 3.42-3.34 (m, 2H), 2.16 (d, *J* = 4 Hz, 1H), δ 1.94 (d, *J* = 80 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-d_6) 136.9, 128.0, 66.0, 49.3, 43.5, 40.1, 38.9, 29.0. The enantioselectivity was determined by HPLC analysis (Chiralpak® AD-H 250 mm x 4.6 mm, 5 μ column, *n*-hexane: 0.1% DEA in ethanol = 75:25, flow rate 1.0 mL/min) t_1 = 12.829 min (major) t_2 = 15.665 min (minor). Spectral data matched those previously reported.[5]



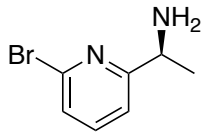
(*S*)-Benzyl-(1-phenylpropyl)carbamate 24

Following the general procedure with enzyme ATA-260, the product was obtained as a white solid, 42.6 mg from a 0.2 mmol scale batch, 79% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 9.0, 5.8 Hz, 6H), 7.12 (d, *J* = 6.4 Hz, 4H), 5.00 – 4.82 (m, 3H), 4.46 (q, *J* = 7.9 Hz, 1H), 1.65 (hept, *J* = 7.0 Hz, 2H), 0.75 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.7, 142.3, 136.5, 128.7, 128.6, 128.5, 128.1, 127.3, 126.4, 66.7, 56.9, 29.6, 10.6. The enantioselectivity was determined by HPLC analysis (Chiralcel® 5 μm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 9.777 min (major). Spectral data matched those previously reported.[6]



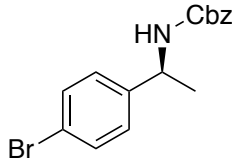
(*S*)-1-(Furan-2-yl)ethan-1-amine 25

Following the general procedure with enzyme ATA-260, the product was obtained as a yellow oil, 61 mg from an 88 mg batch, 70% yield, 98.9% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (*d*, *J* = 1.2 Hz, 1H), 6.37 – 6.33 (m, 2H), 4.42 (s, *J* = 8.0 Hz, 1H), 1.62 (d, *J* = 8.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.3, 143.5, 110.7, 108.5, 44.9, 17.1. The enantioselectivity was determined by HPLC analysis (Chiralpak® IG 250 mm x 4.6 mm, 5 µ column, *n*-hexane: 0.1% diethylamine in ethanol = 90:10, flow rate 1.0 mL/min) t_1 = 8.250 min (major) t_2 = 9.016 min (minor). Spectral data matched those previously reported.[7]



(*S*)-1-(6-Bromopyridin-2-yl)ethan-1-amine 26

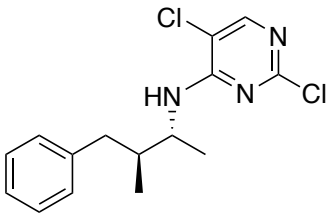
Following the general procedure with enzyme ATA-260, the product was obtained as a brown oil, 110 mg from a 160 mg batch, 69% yield, 95.7% *ee*. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.33 (s, 2H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.689 (d, *J* = 8 Hz, 1H), 7.56 (d, 7.6 Hz, 1H), 4.52 (d, *J* = 7.2Hz, 1H), 1.46 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 159.3, 158.3, 140.7, 127.8, 121.2, 39.5, 19.6. The enantioselectivity was determined by HPLC analysis (Chiralpak® AY-H 250 mm x 4.6 mm, 5 µ column, *n*-hexane: 0.1% diethylamine in isopropanol = 90:10, flow rate 0.8 mL/min) t_1 = 11.630 min (major) t_2 = 12.872 min (minor). Spectral data matched those previously reported.[87]



(*S*)-Benzyl (1-(4-bromophenyl)ethyl)carbamate 29

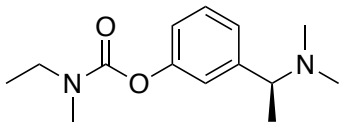
Following the general procedure with enzyme ATA-260, the product was obtained as a white solid, 29.4 mg from a 0.1 mmol batch, 88% yield, >99% *ee.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.1 Hz, 2H), 7.34 (s, 5H), 7.18 (d, *J* = 8.1 Hz, 2H), 5.16 – 4.93 (m, 3H), 4.86 – 4.72 (m, 1H), 1.45 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.4, 142.6, 136.3, 131.7, 131.5, 128.5, 128.2, 127.7, 121.1, 66.8, 50.2, 22.4. **HRMS** TOF MS EI+ *m/z* calcd $C_{16}H_{16}BrNO_2$ Na $[M+Na]^+$: 356.0262; found

356.0273. The enantioselectivity was determined by HPLC analysis (Chiralcel® 5 µm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 10.709 min (major).



2,5-Dichloro-*N*-((2*R*,3*S*)-3-methyl-4-phenylbutan-2-yl)pyrimidin-4-amine 32

Following the experimental procedure used for the 1-pot sequence (ERED/ATA/S_NAr), the product was obtained as a colorless oil, 60.5 mg from a 0.127 mmol batch, 99% yield, >99% *ee*, 82:18 dr. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.33 – 7.25 (m, 3H), 7.24 – 7.20 (m, 1H), 7.20 – 7.11 (m, 2H), 5.31 (d, *J* = 9.3 Hz, 1H), 4.37 (dqt, *J* = 8.1, 6.5, 4.2 Hz, 1H), 2.76 (dt, *J* = 13.5, 6.5 Hz, 1H), 2.44 (td, *J* = 14.1, 13.6, 8.6 Hz, 1H), 2.16 – 2.02 (m, 1H), 1.31 – 1.21 (m, 4H) (mixed with a diastereomer), 0.93 (dd, *J* = 29.4, 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.5, 158.2, 158.1, 158.0, 153.4, 153.4, 153.3, 140.3, 140.1, 129.0, 128.9, 128.5, 128.4, 128.3, 126.2, 126.1, 126.0, 113.0, 113.0, 52.2, 50.6, 50.2, 43.2, 39.9, 39.8, 39.5, 38.9, 36.0, 32.2, 31.9, 29.7, 27.7, 22., 22.5, 17.6, 16.3, 15.3, 14.6, 10.0. **HRMS** TOF MS EI+ *m/z* calcd $C_{15}H_{17}C_{l2}N_3H$ $[M+H]^+$: 310.0878; found 310.0893. The dr was determined by ^{1}H NMR (4.37 ppm int. = 1.00; 4.26 ppm int. = 0.22); the enantioselectivity was determined by HPLC analysis (Phenomenex® 5 µm Lux Cellulose-1 column 250 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 17.219 min (minor) t_2 = 20.928 (major).

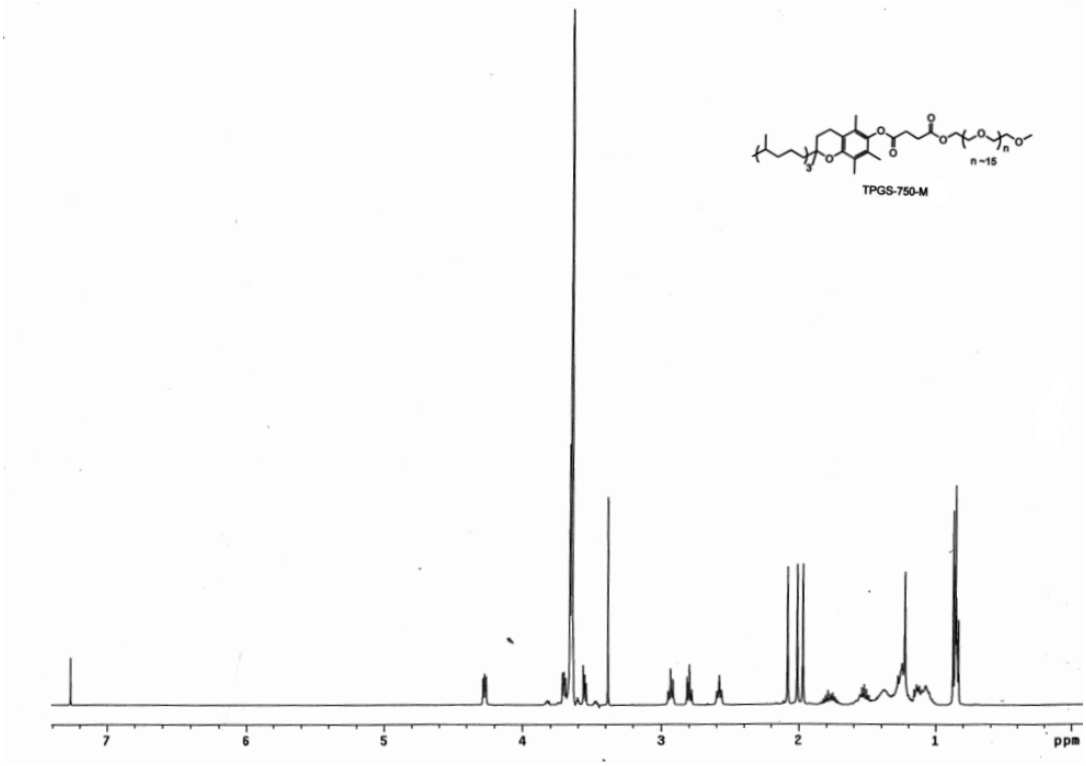


(*S*)-Rivastigmine

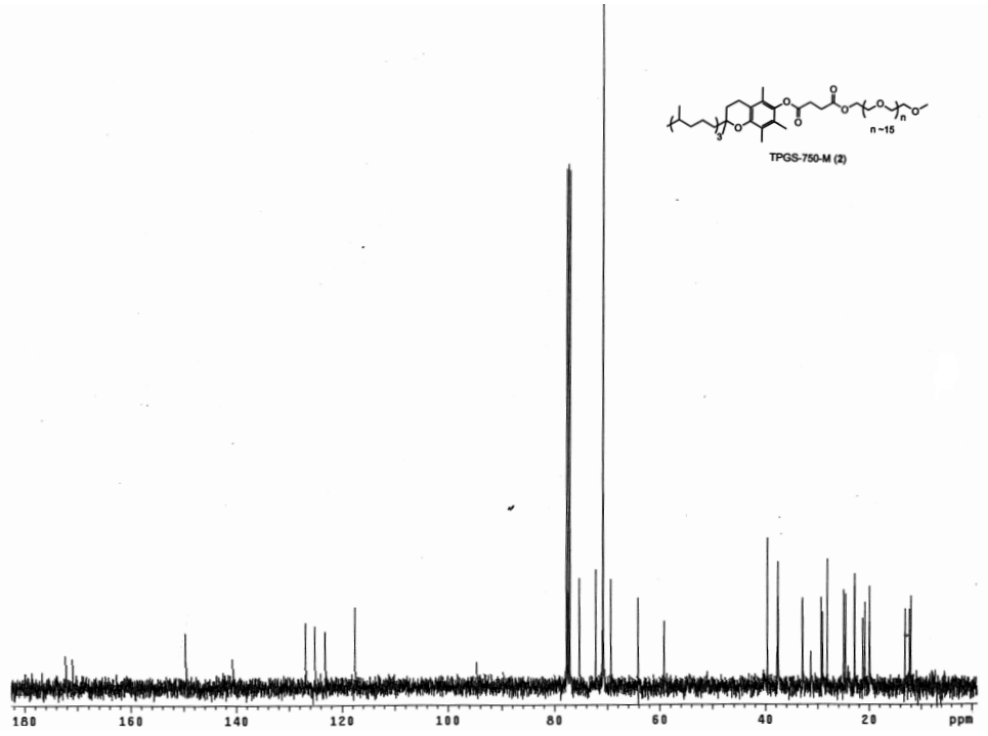
Following the experimental procedure for (*S*)-rivastigmine, the product was obtained as a colorless oil, 23.7 mg from a 0.1 mmol batch, 95% yield, >99% *ee.* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.8 Hz, 1H), 7.11 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.08 – 7.03 (m, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 3.44 (dq, *J*

= 31.3, 7.2 Hz, 2H), 3.24 (q, *J* = 6.7 Hz, 1H), 3.02 (d, *J* = 37.1 Hz, 3H), 2.20 (d, *J* = 0.9 Hz, 6H), 1.39 – 1.33 (m, 3H), 1.26 – 1.17 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.6, 154.4, 151.5, 145.8, 145.7, 128.9, 124.2, 124.2, 120.7, 120.7, 120.2, 65.6, 44.0, 43.2, 34.2, 33.8, 29.7, 27.1, 20.1, 13.2, 12.5. The enantioselectivity was determined by HPLC analysis Chiralcel® 5 μm OD-H column 150 x 4.6 mm, isopropanol : *n*-hexane = 10:90, flow rate 1.0 mL/min) t_1 = 5.565 min (major). Spectral data matched those previously reported.[9]

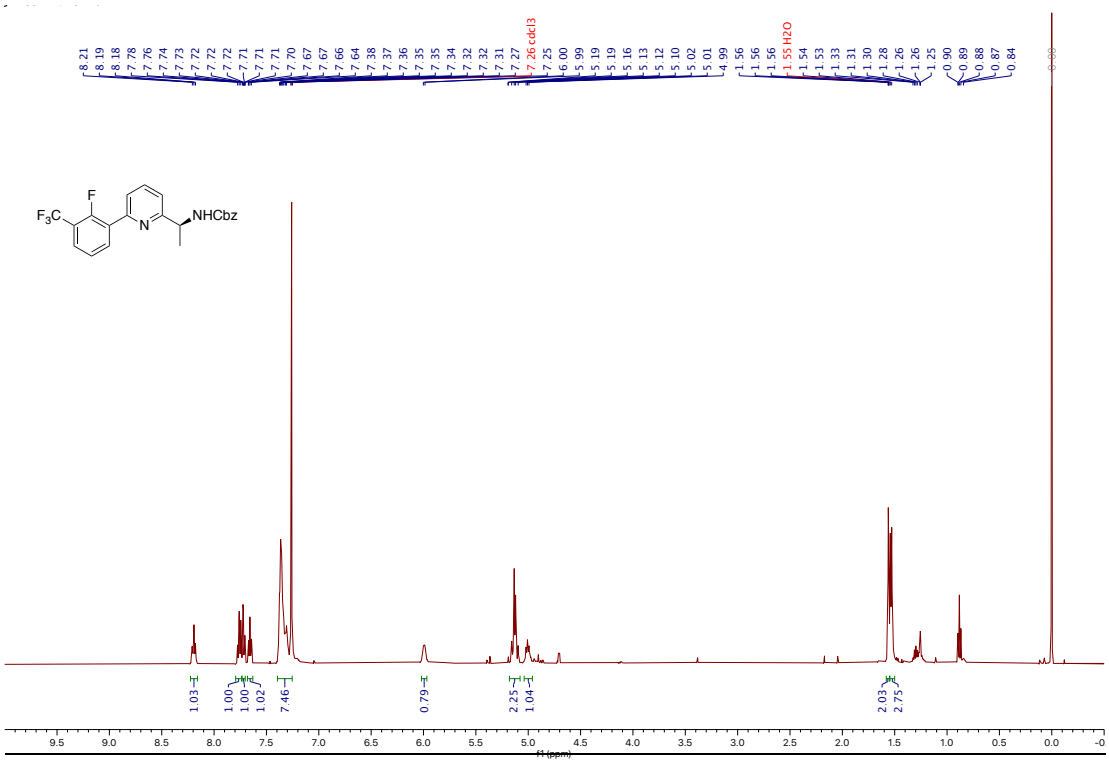
5. NMR spectra



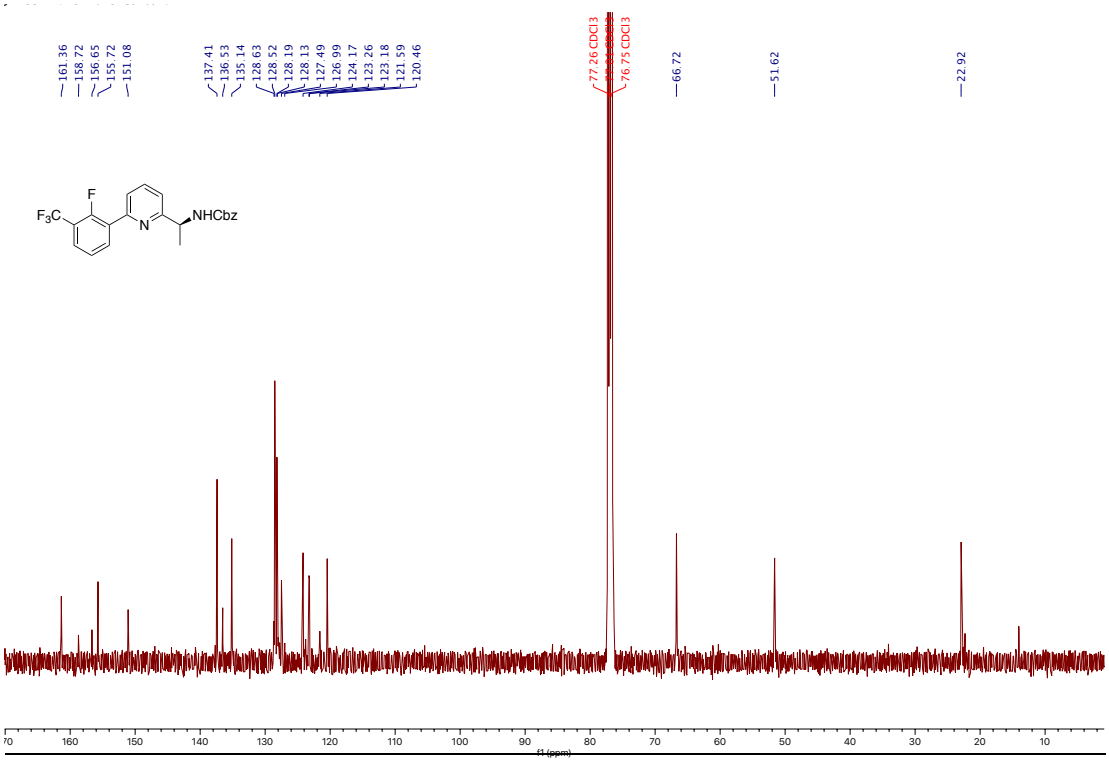
^{1}H NMR spectrum of **TPGS-750-M**



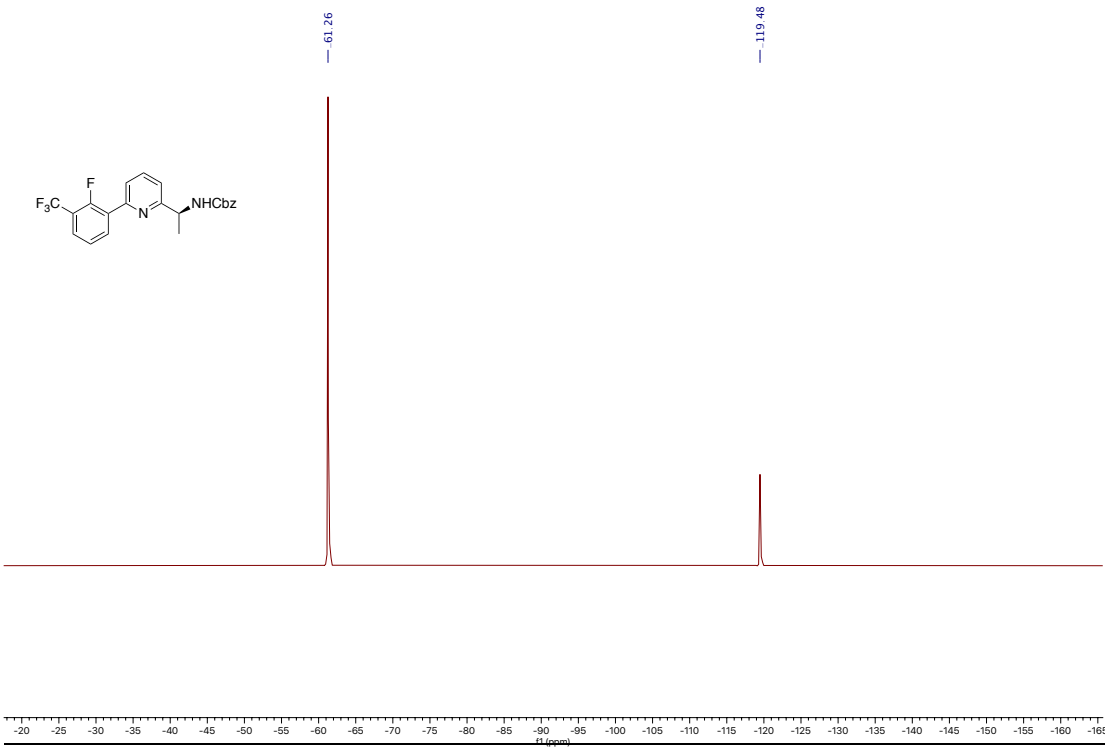
^{13}C NMR spectrum of **TPGS-750-M**



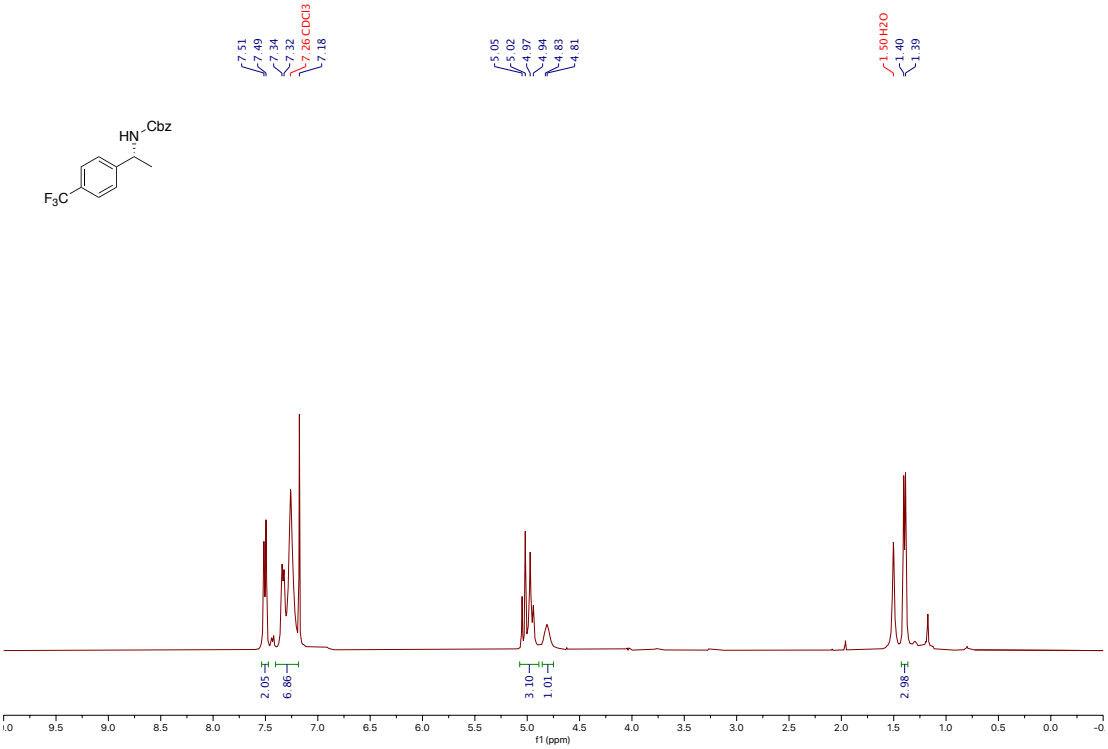
^{1}H NMR spectrum of **benzyl (*S*)-(1-(6-(2-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)ethyl)carbamate 8**



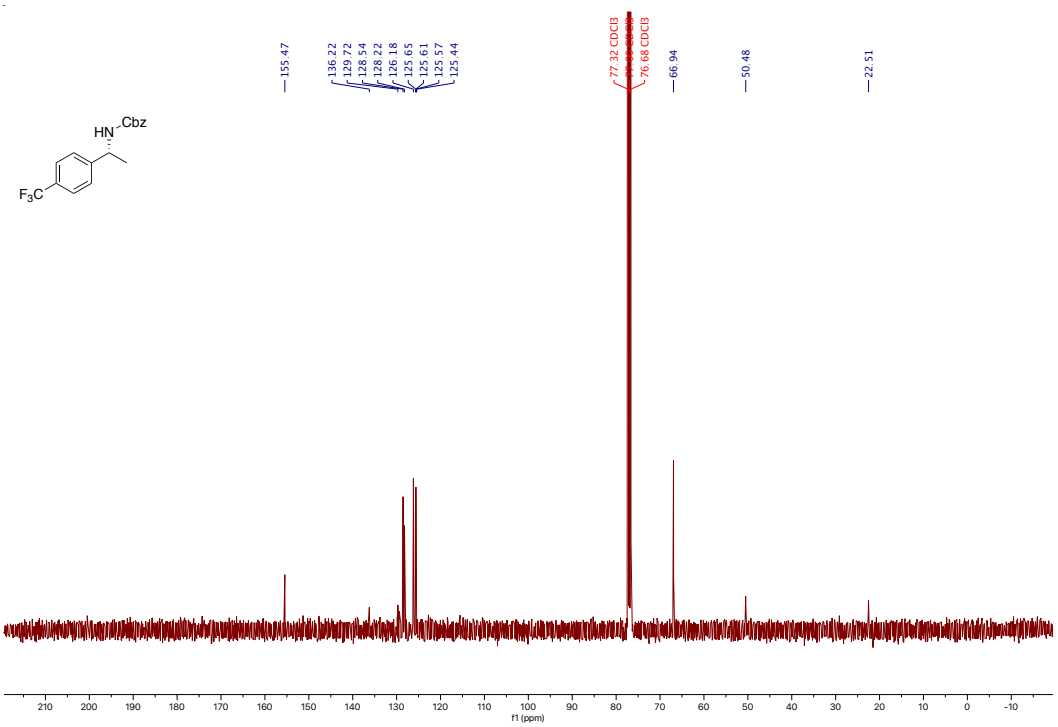
^{13}C NMR spectrum of **benzyl (*S*)-(1-(6-(2-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)ethyl)carbamate 8**



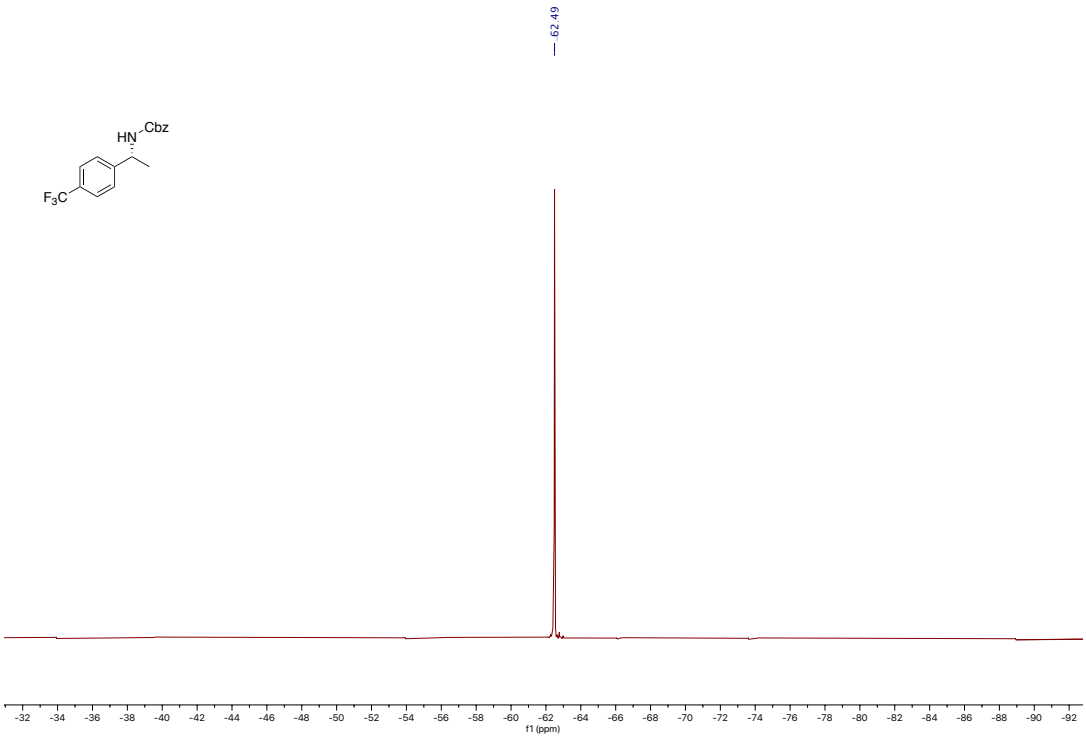
^{19}F NMR spectrum of **benzyl (*S*)-(1-(6-(2-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)ethyl)carbamate 8**



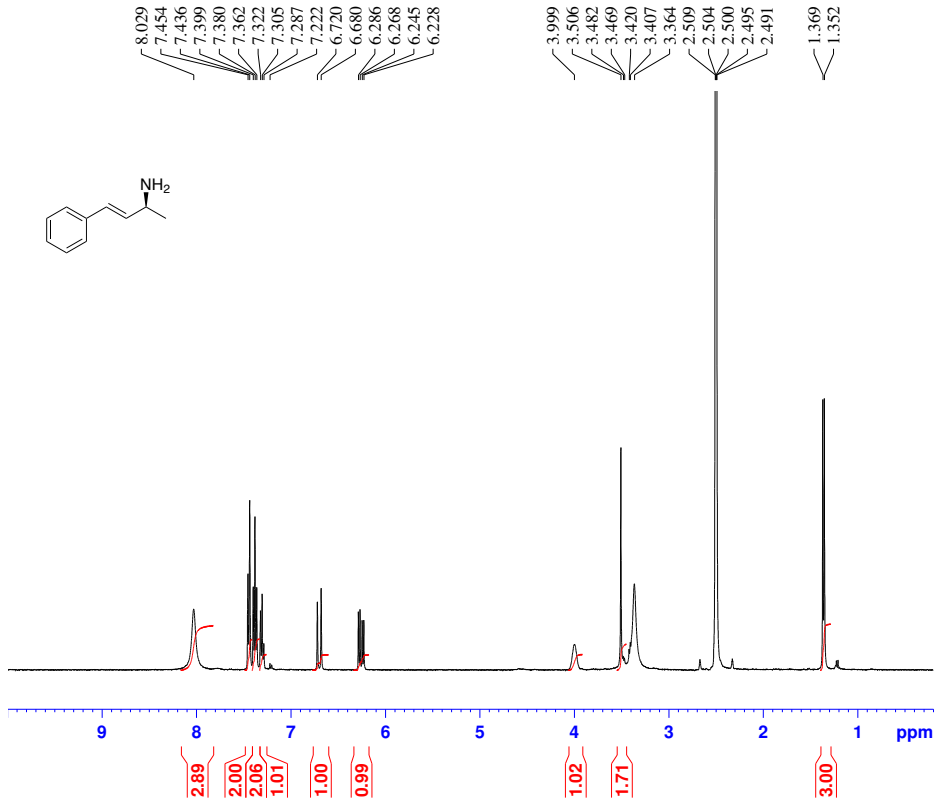
^{1}H NMR spectrum of **(*R*)-benzyl (1-(4-(trifluoromethyl)phenyl)ethyl)carbamate 10**



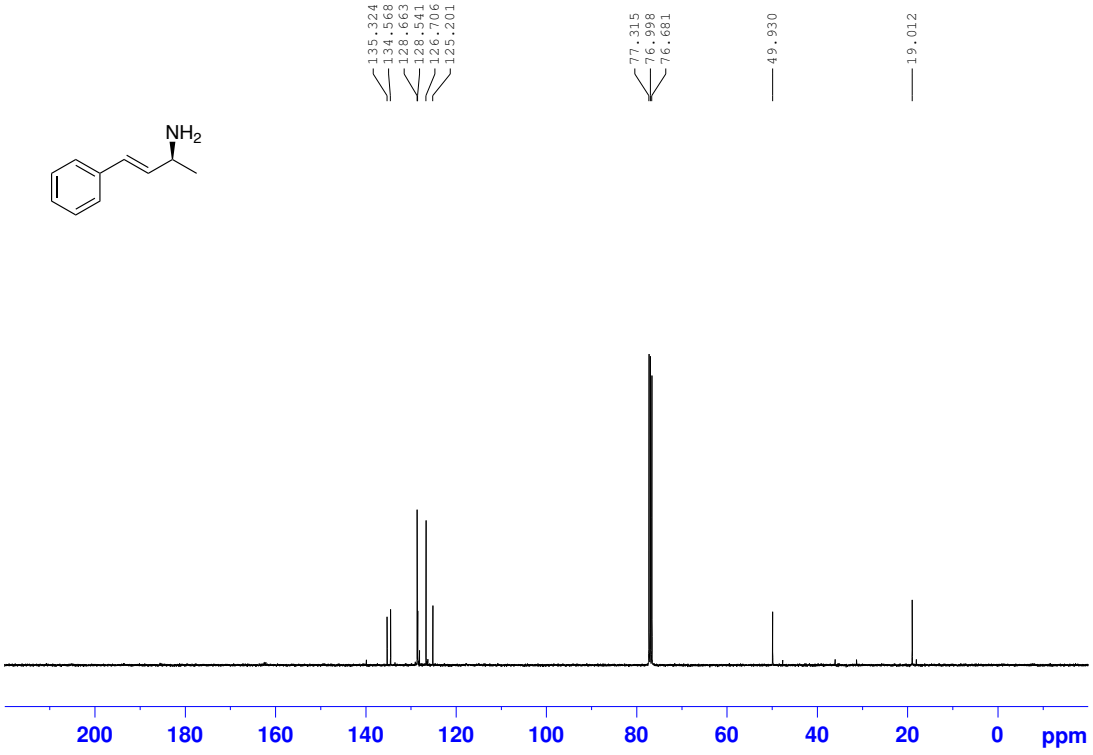
^{13}C NMR spectrum of **(*R*)-benzyl (1-(4-(trifluoromethyl)phenyl)ethyl)carbamate 10**



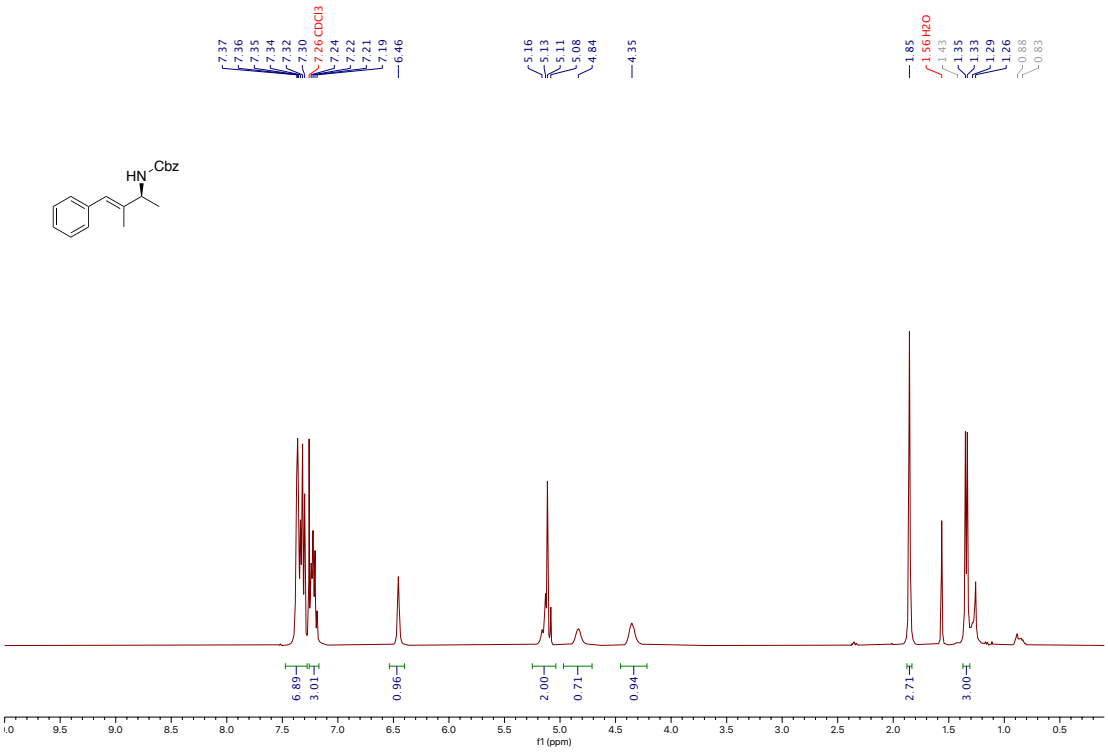
^{19}F NMR spectrum of **(*R*)-benzyl (1-(4-(trifluoromethyl)phenyl)ethyl)carbamate 10**



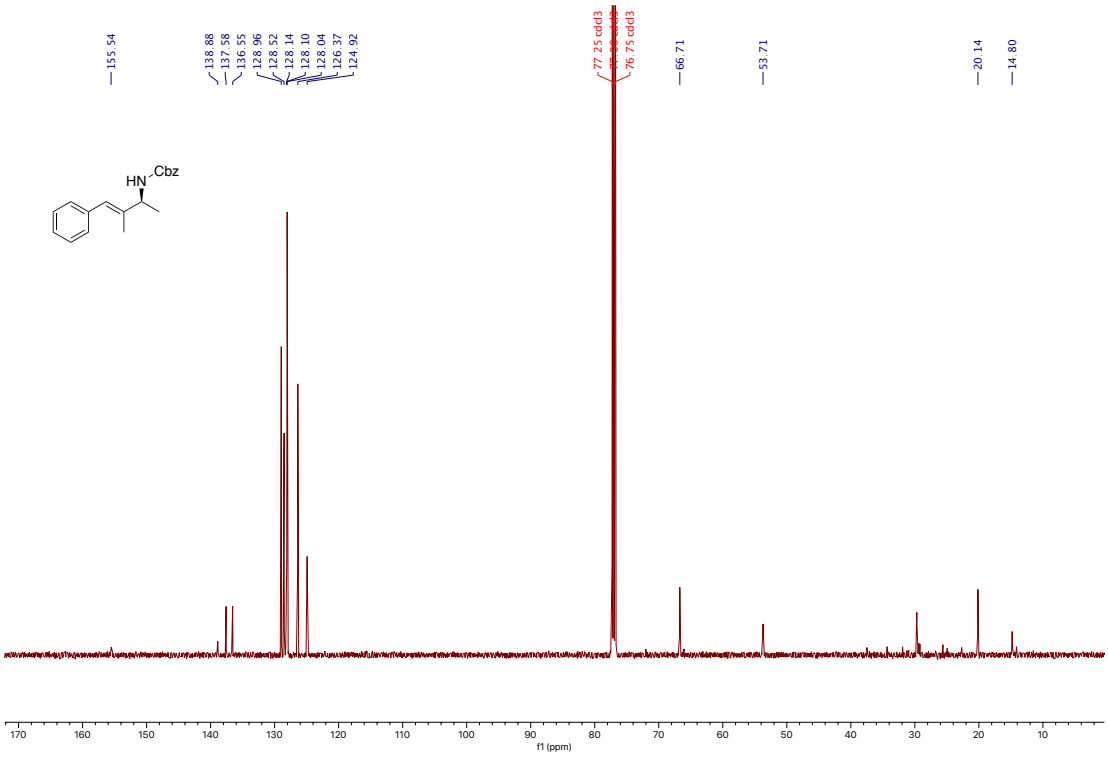
^{1}H NMR spectrum of **(*S*,*E*)-4-phenylbut-3-en-2-amine 12**



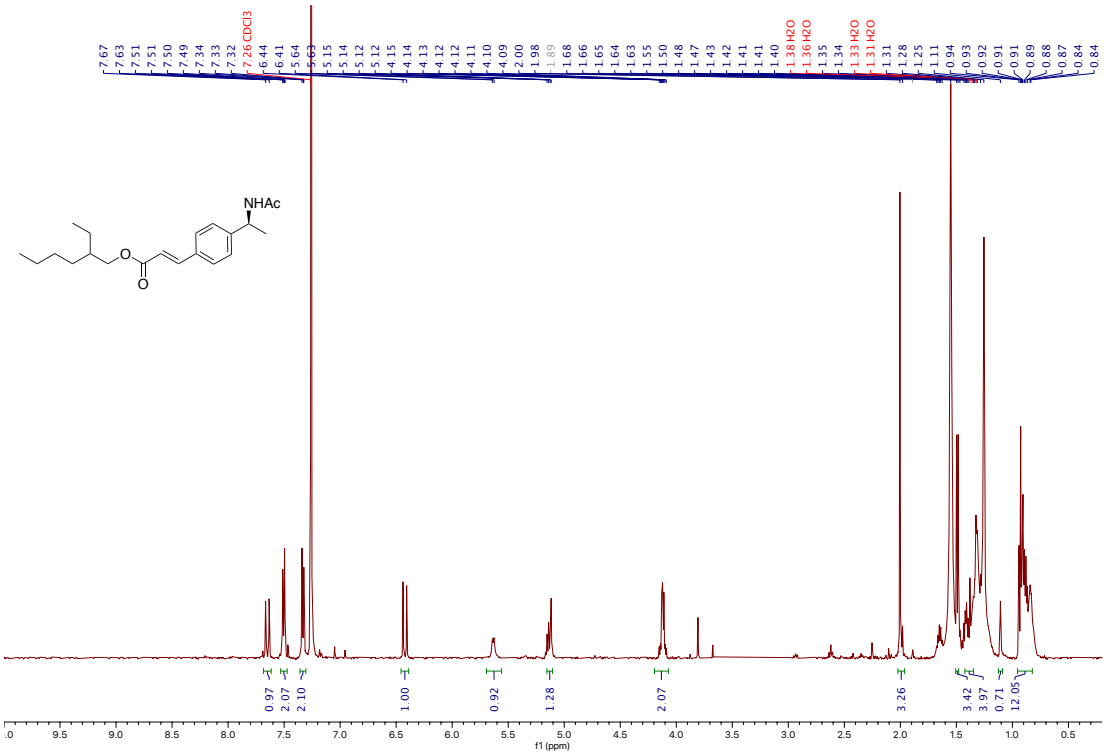
^{13}C NMR spectrum of **(*S*,*E*)-4-phenylbut-3-en-2-amine 12**



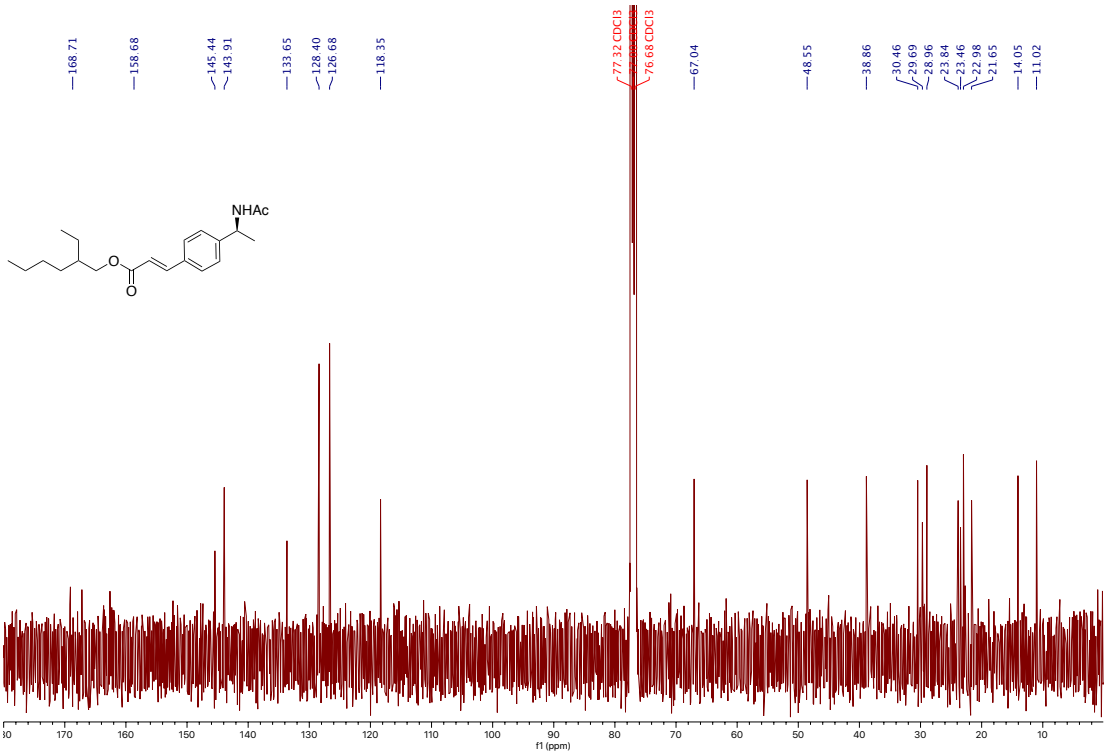
^{1}H NMR spectrum of **(*S*,*E*)-benzyl-(3-methyl-4-phenylbut-3-en-2-yl)carbamate 13**



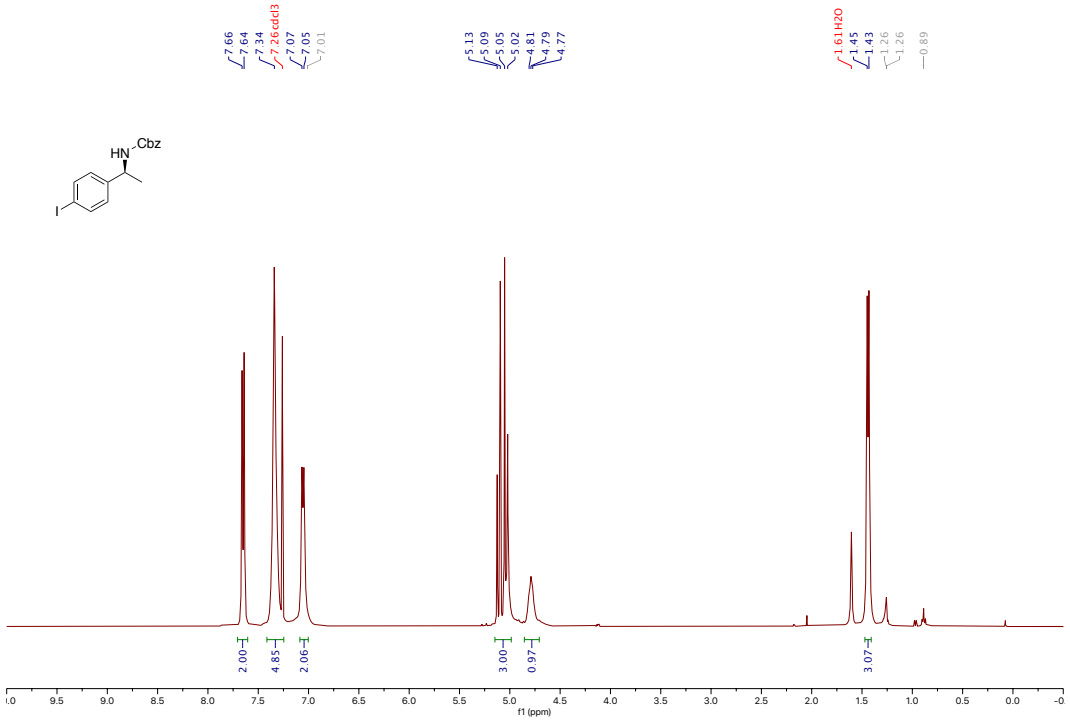
^{13}C NMR spectrum of **(*S*,*E*)-benzyl-(3-methyl-4-phenylbut-3-en-2-yl)carbamate 13**



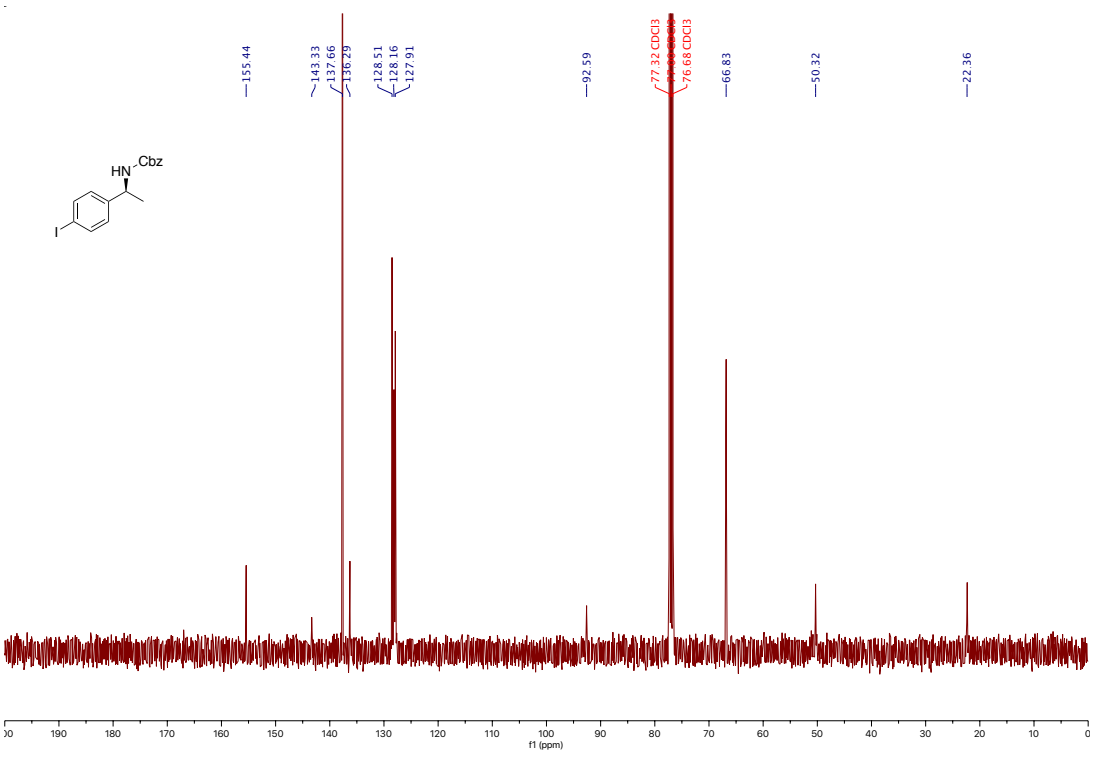
^{1}H NMR spectrum of **2-ethylhexyl (*E*)-3-(4-(1-(((benzyloxy)carbonyl)amino)ethyl)phenyl)acrylate 14**



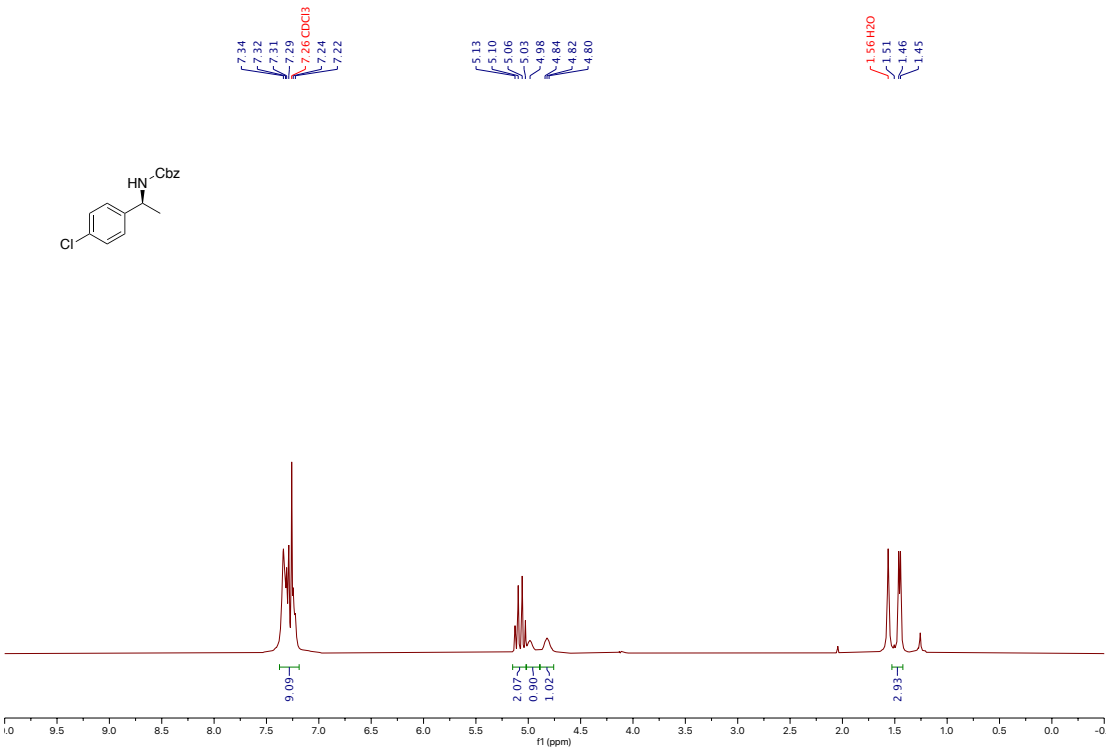
^{13}C NMR spectrum of **2-ethylhexyl (*E*)-3-(4-(1-(((benzyloxy)carbonyl)amino)ethyl)phenyl)acrylate 14**



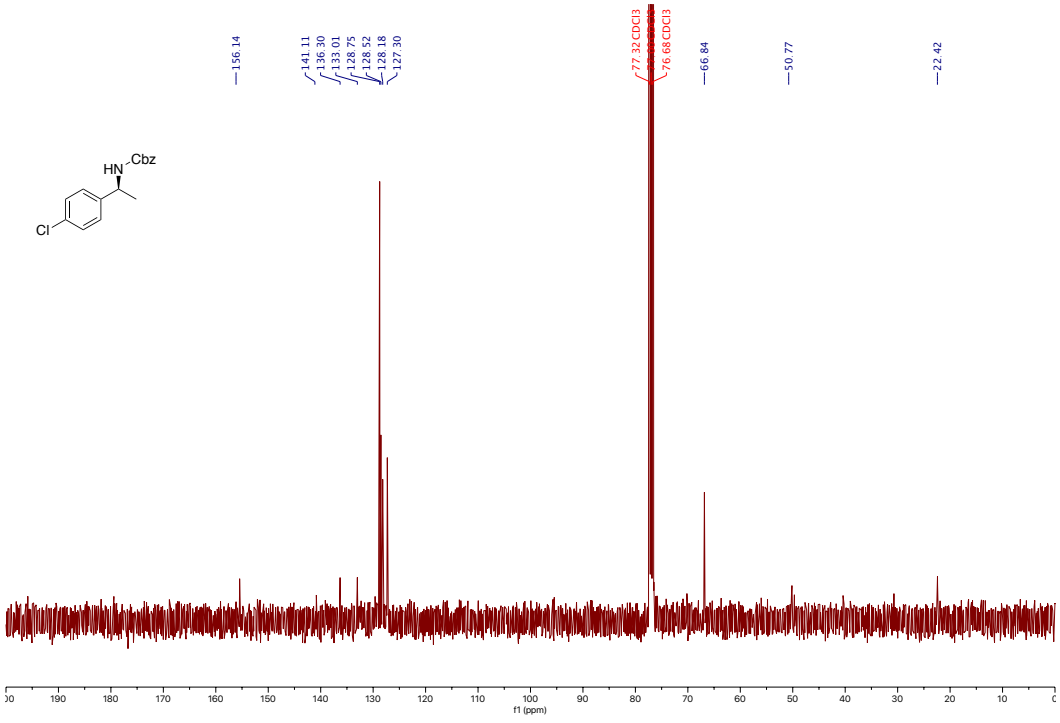
^{1}H NMR spectrum of **(*S*)-benzyl(1-(4-iodophenyl)ethyl)carbamate 16**



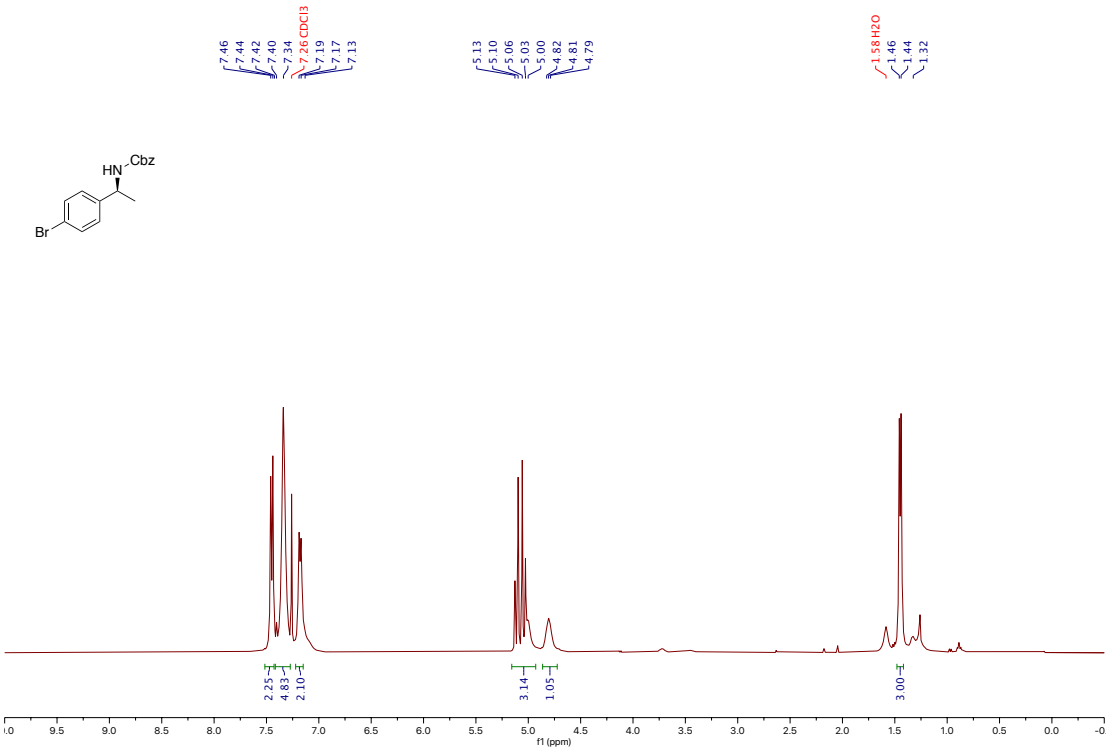
^{13}C NMR spectrum of **(*S*)-benzyl(1-(4-iodophenyl)ethyl)carbamate 16**



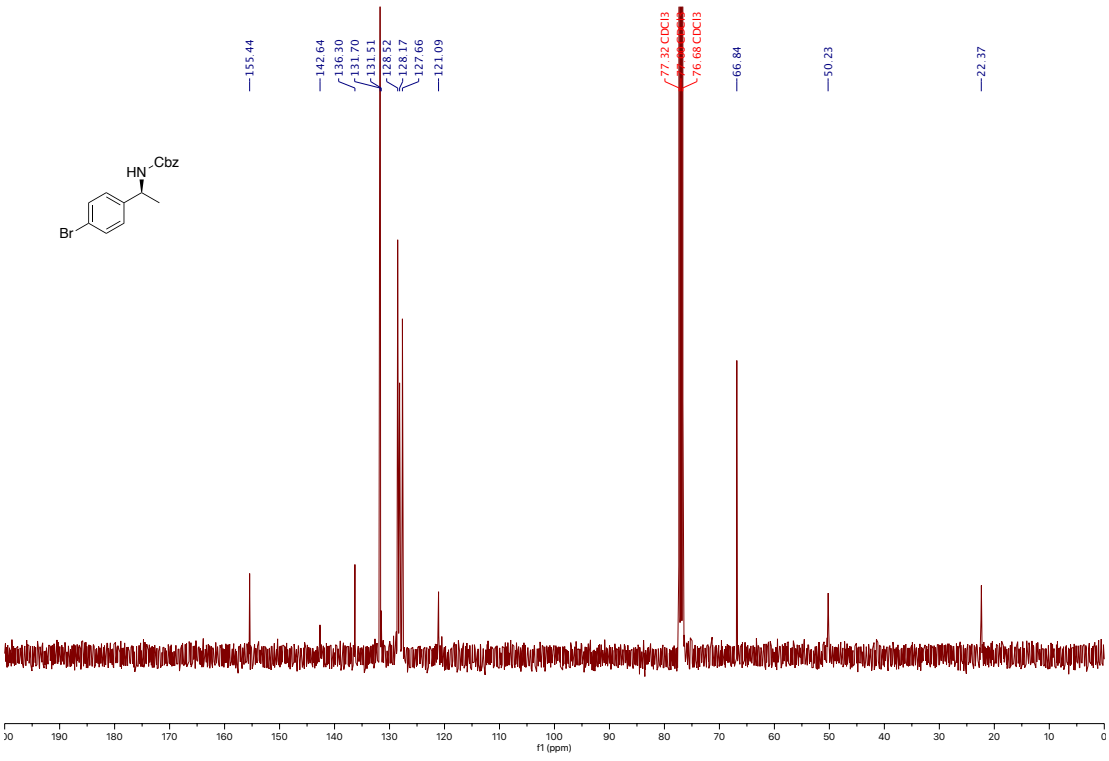
^{1}H NMR spectrum of **(*S*)-benzyl(1-(4-chlorophenyl)ethyl)carbamate 17**



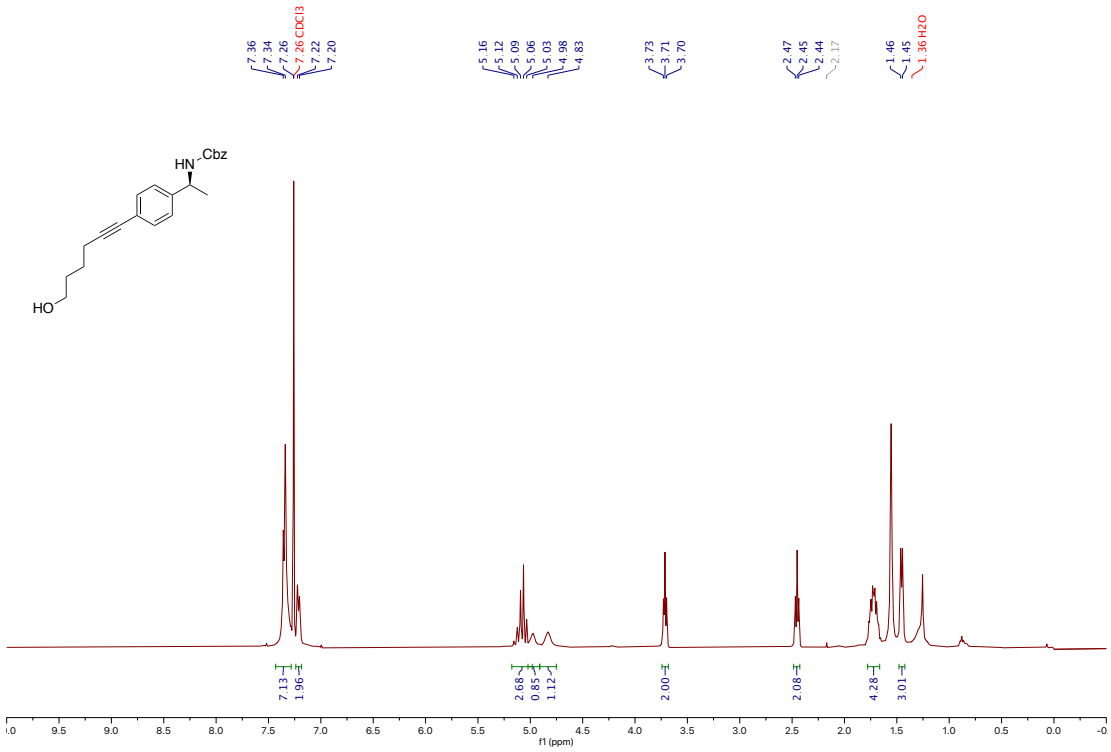
^{13}C NMR spectrum of **(*S*)-benzyl(1-(4-chlorophenyl)ethyl)carbamate 17**



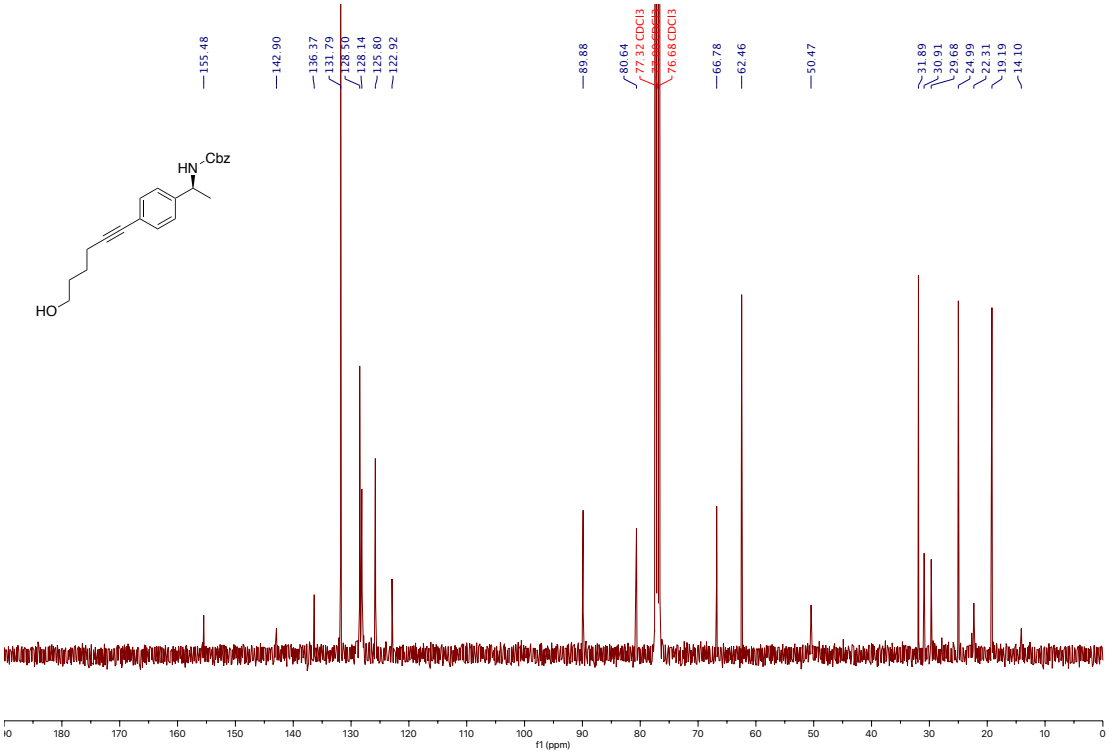
^{1}H NMR spectrum of **(*S*)-benzyl(1-(4-bromophenyl)ethyl)carbamate 18**



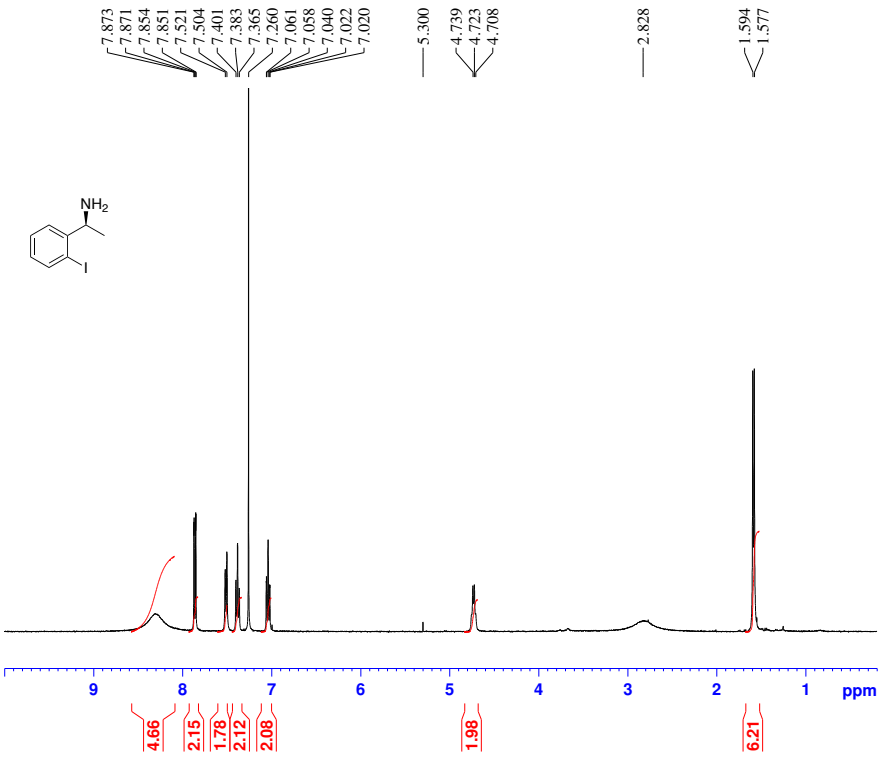
^{13}C NMR spectrum of **(*S*)-benzyl(1-(4-bromophenyl)ethyl)carbamate 18**



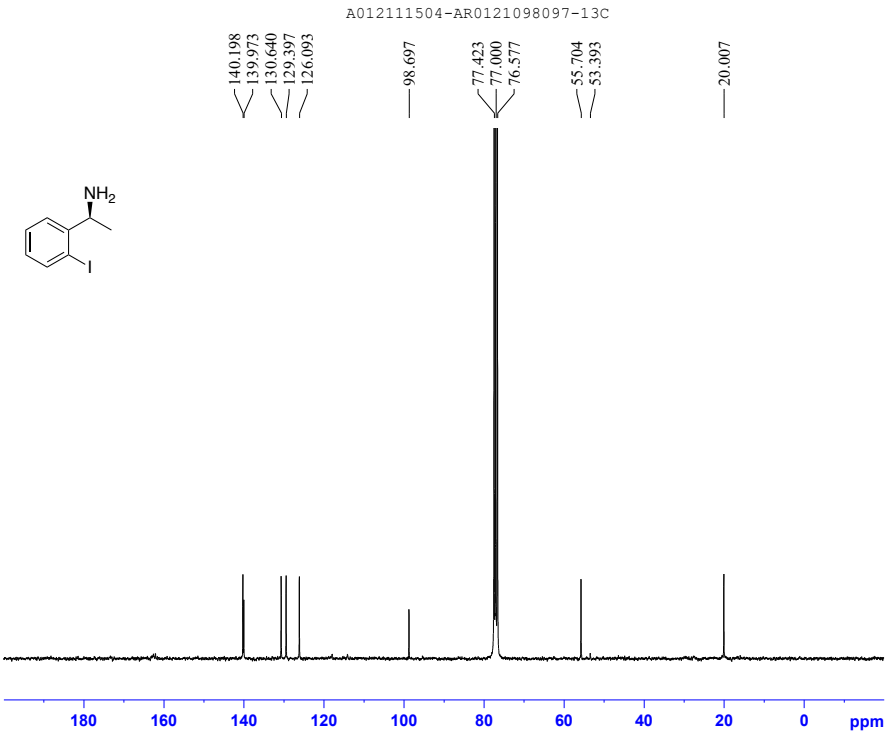
^{1}H NMR spectrum of **(*S*)-benzyl (1-(4-(6-hydroxyhex-1-yn-1-yl)phenyl)ethyl)carbamate 19**



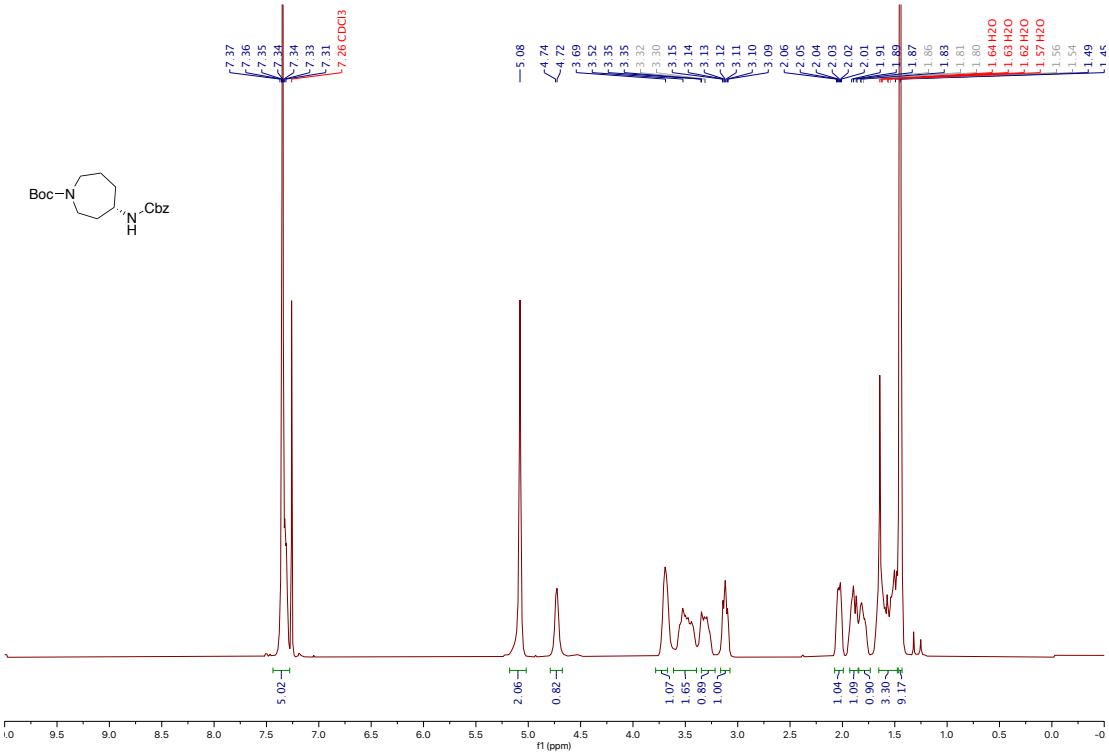
^{13}C NMR spectrum of **(*S*)-benzyl (1-(4-(6-hydroxyhex-1-yn-1-yl)phenyl)ethyl)carbamate 19**



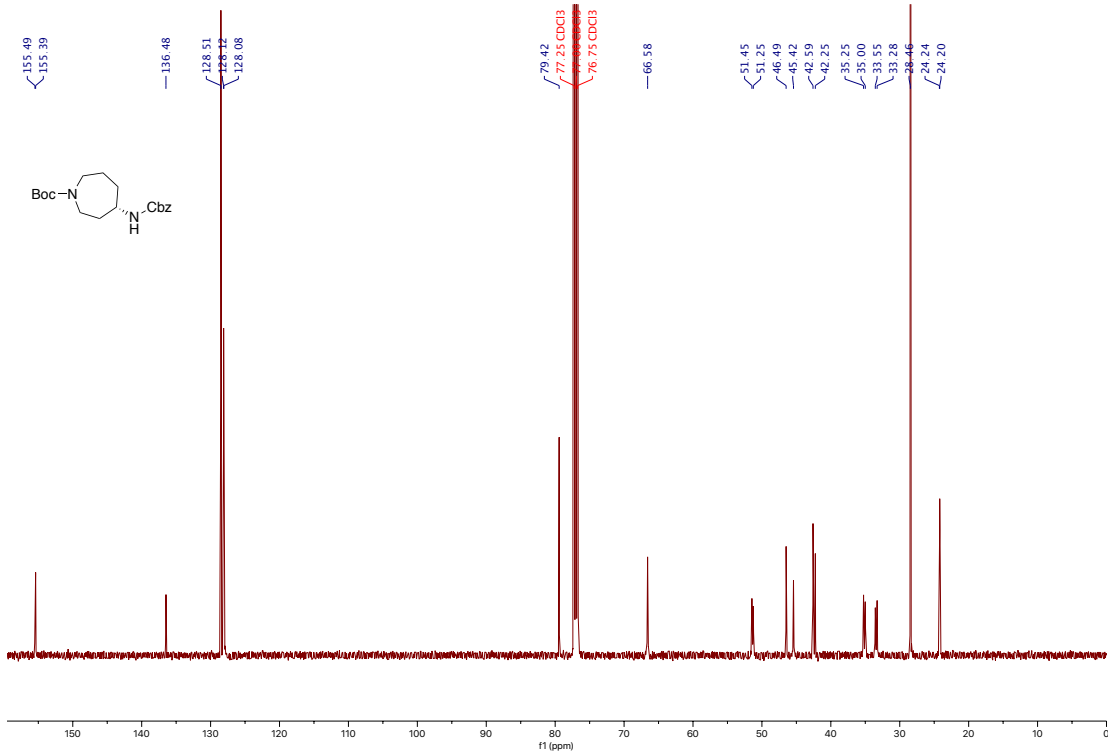
^{1}H NMR spectrum of **(*S*)-1-(2-iodophenyl)ethan-1-amine 20**



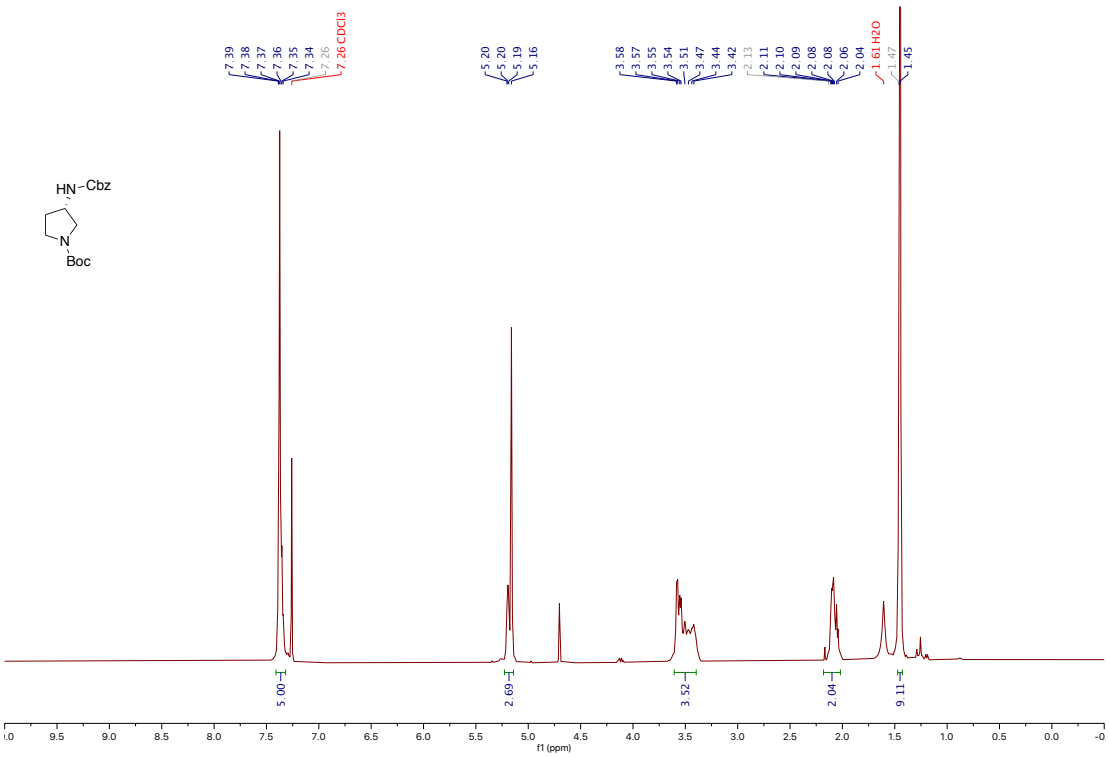
^{13}C NMR spectrum of **(*S*)-1-(2-iodophenyl)ethan-1-amine 20**



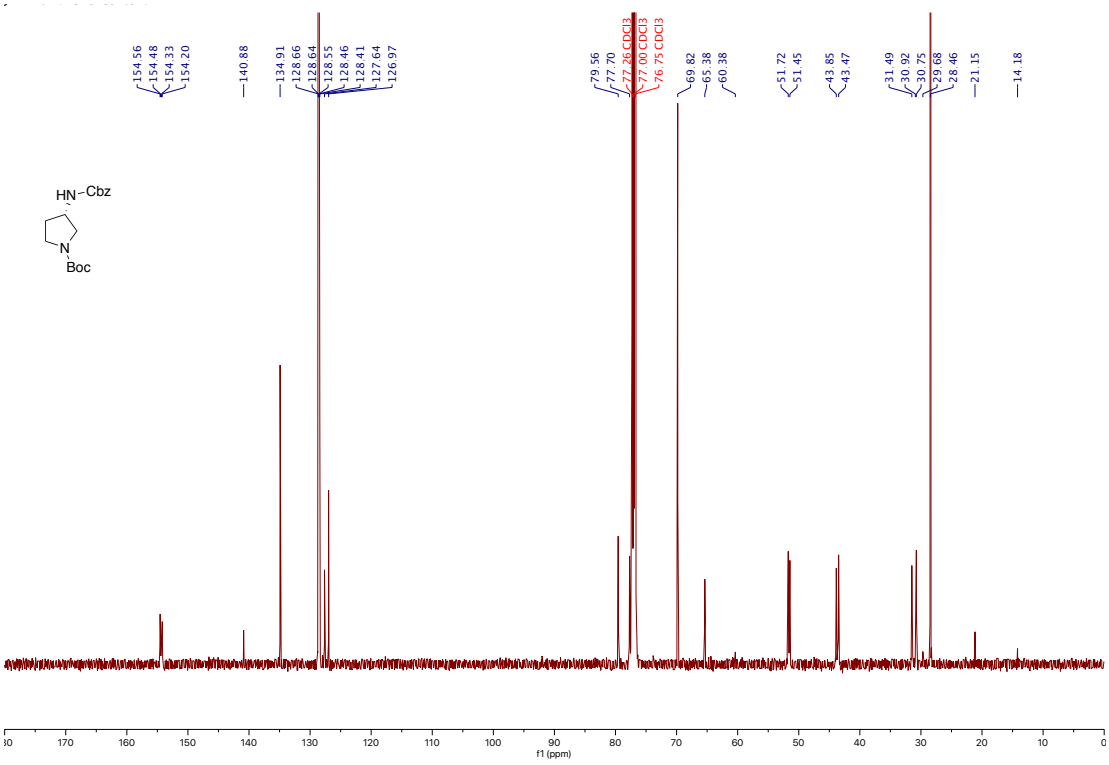
^{1}H NMR spectrum of **(*S*)-*tert*-butyl -4-(((benzyloxy)carbonyl)amino)azepane-1-carboxylate 21**



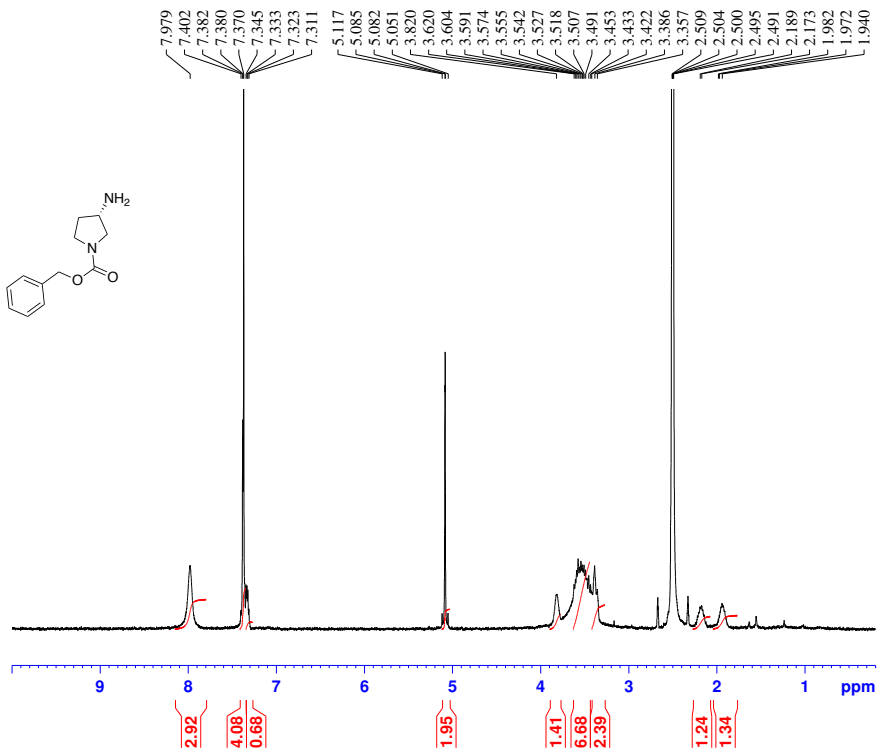
^{13}C NMR spectrum of **(*S*)-*tert*-butyl -4-(((benzyloxy)carbonyl)amino)azepane-1-carboxylate 21**



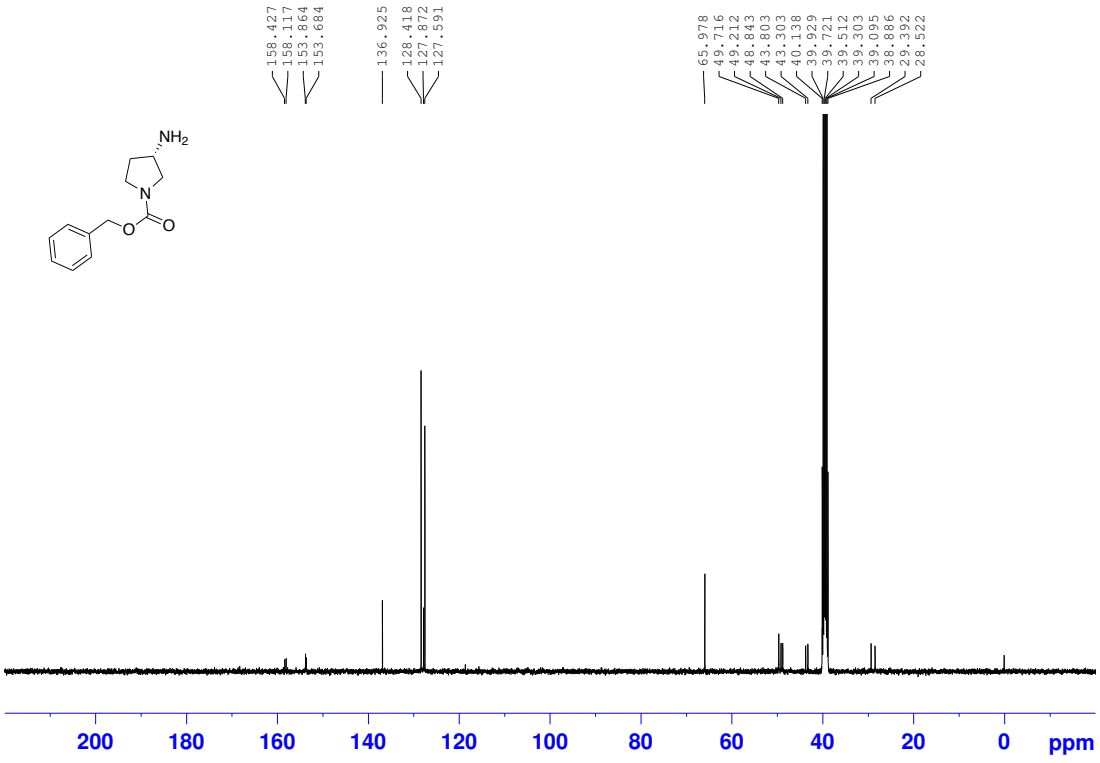
^{1}H NMR spectrum of **(*S*)-*tert*-butyl-3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 22**



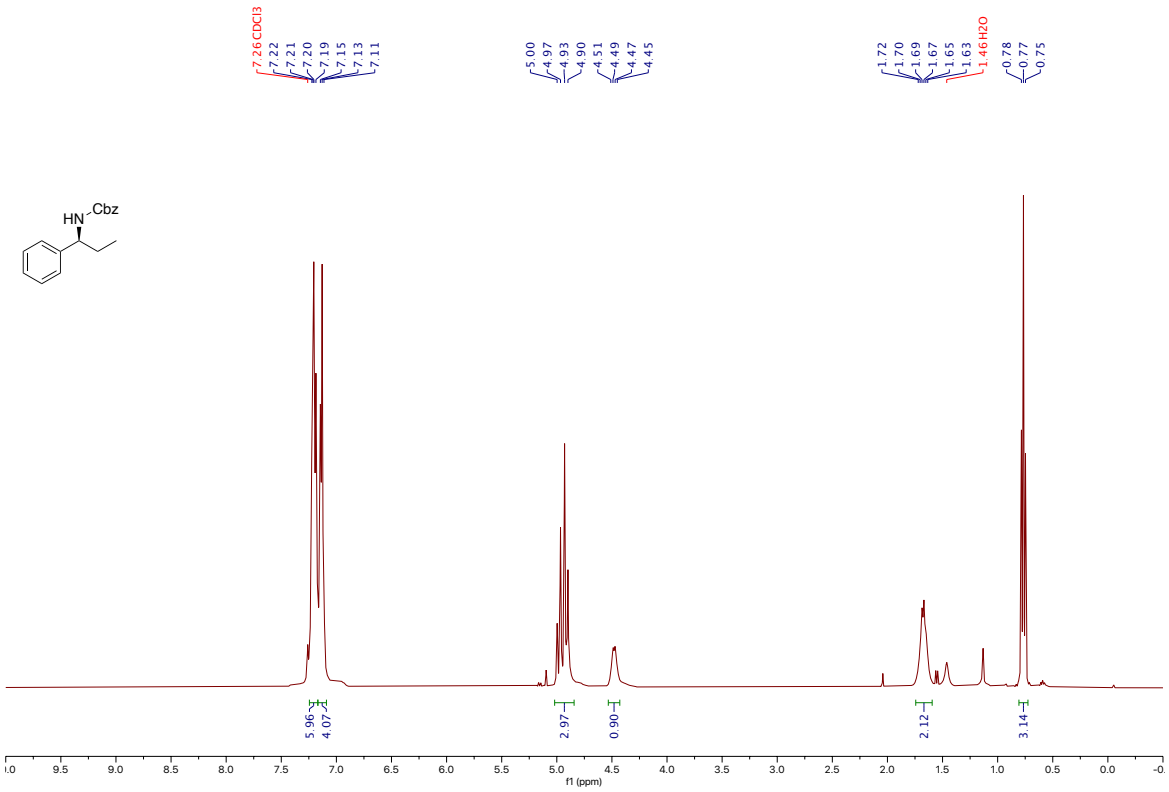
^{13}C NMR spectrum of **(*S*)-*tert*-butyl-3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 22**



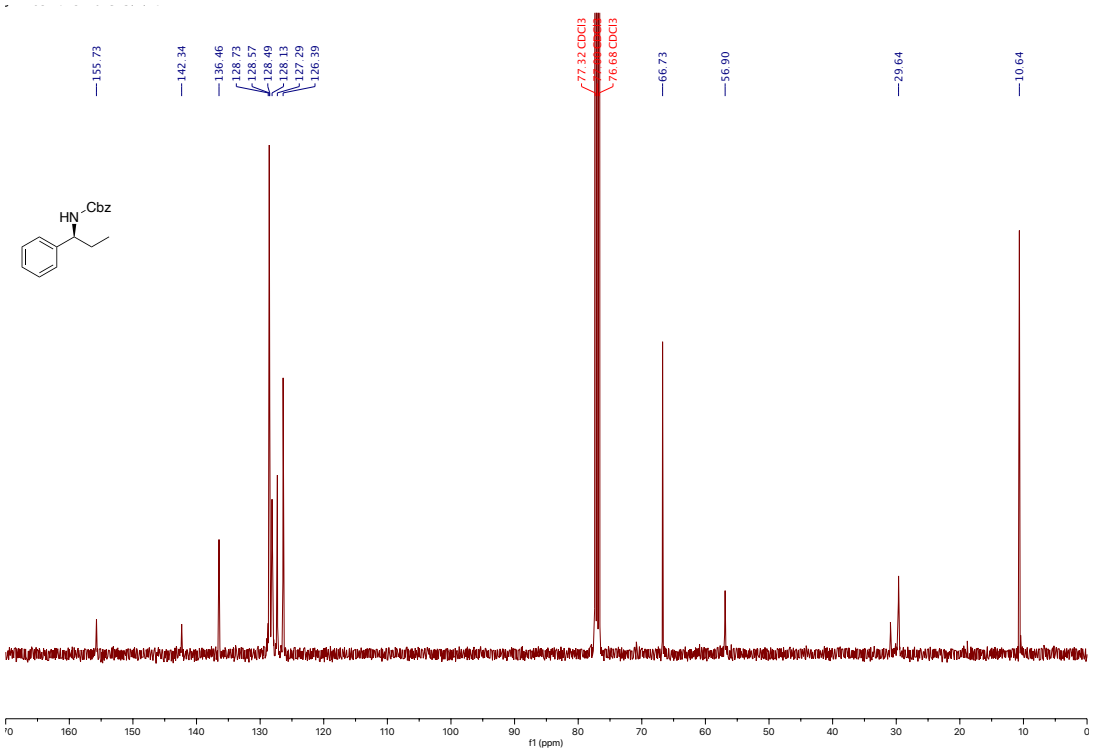
^{1}H NMR spectrum of **(*S*)-benzyl 3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 23**



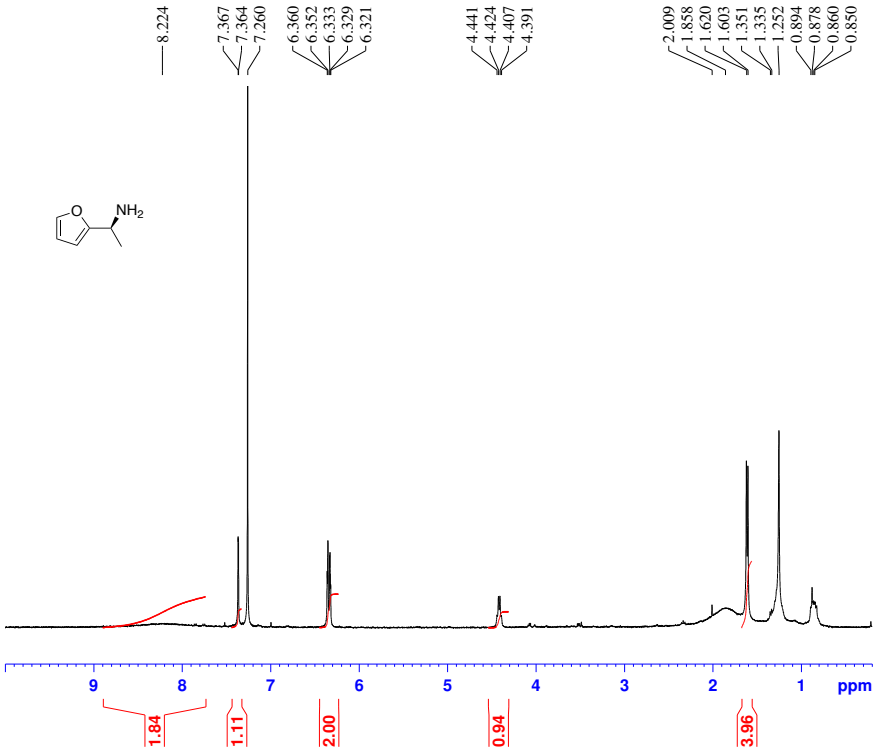
^{13}C NMR spectrum of **(*S*)-benzyl 3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 23**



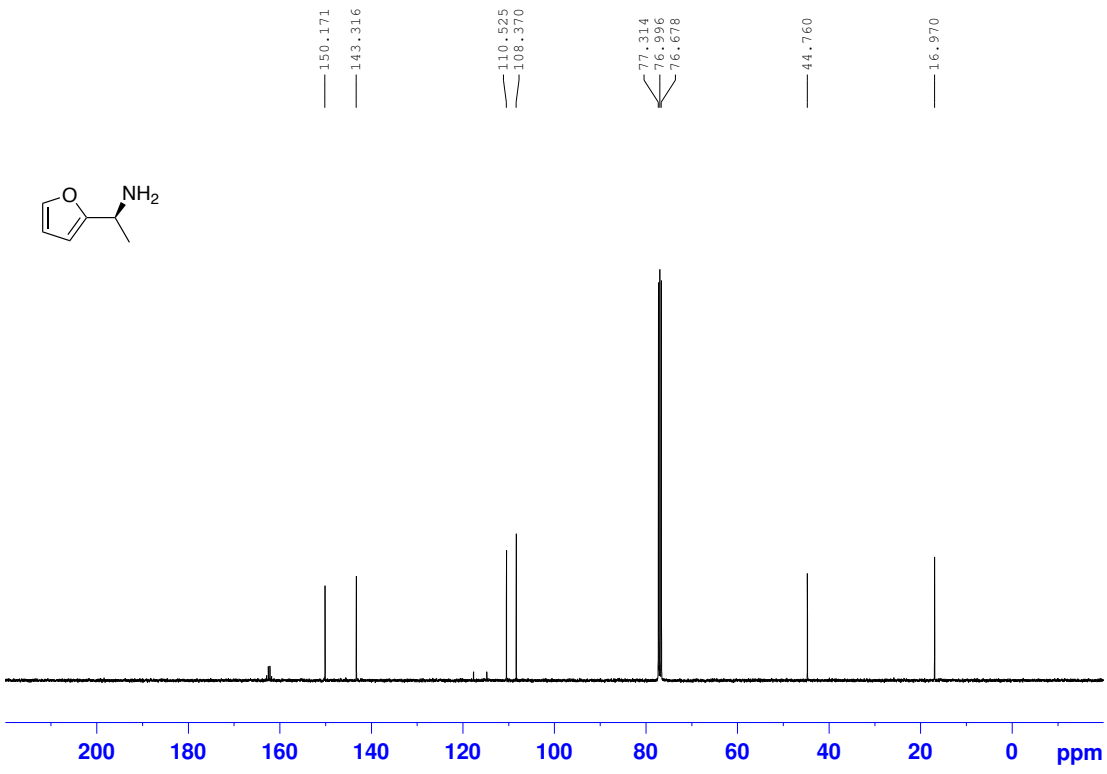
^{1}H NMR spectrum of **benzyl (*S*)-(1-phenylpropyl)carbamate 24**



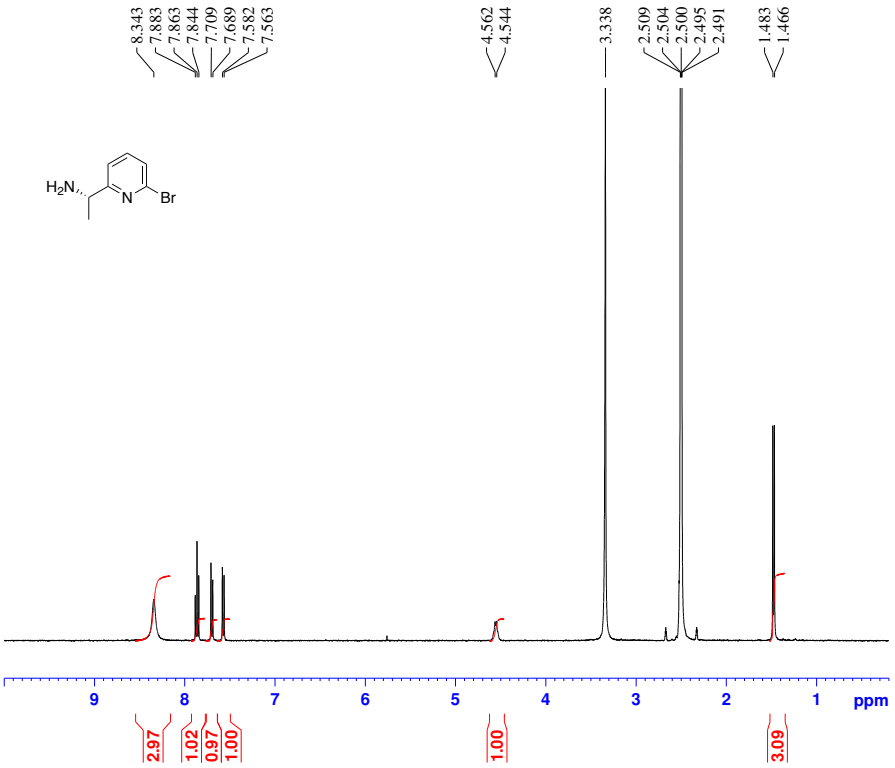
^{13}C NMR spectrum of **benzyl (*S*)-(1-phenylpropyl)carbamate 24**



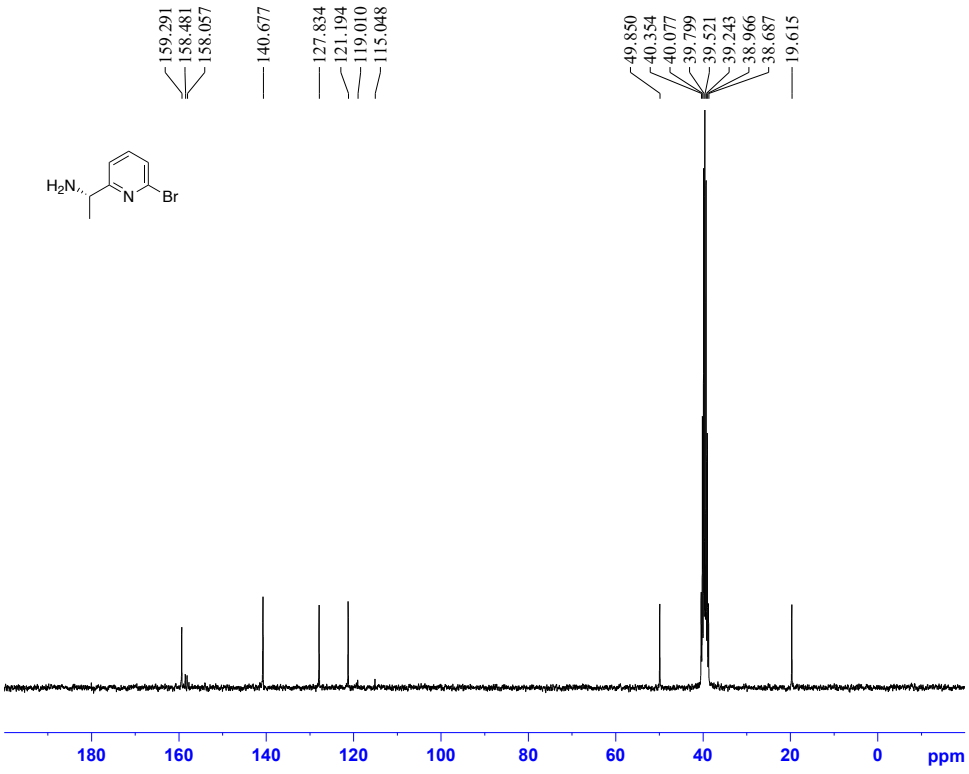
^{1}H NMR spectrum of **(*S*)-1-(furan-2-yl)ethan-1-amine 25**



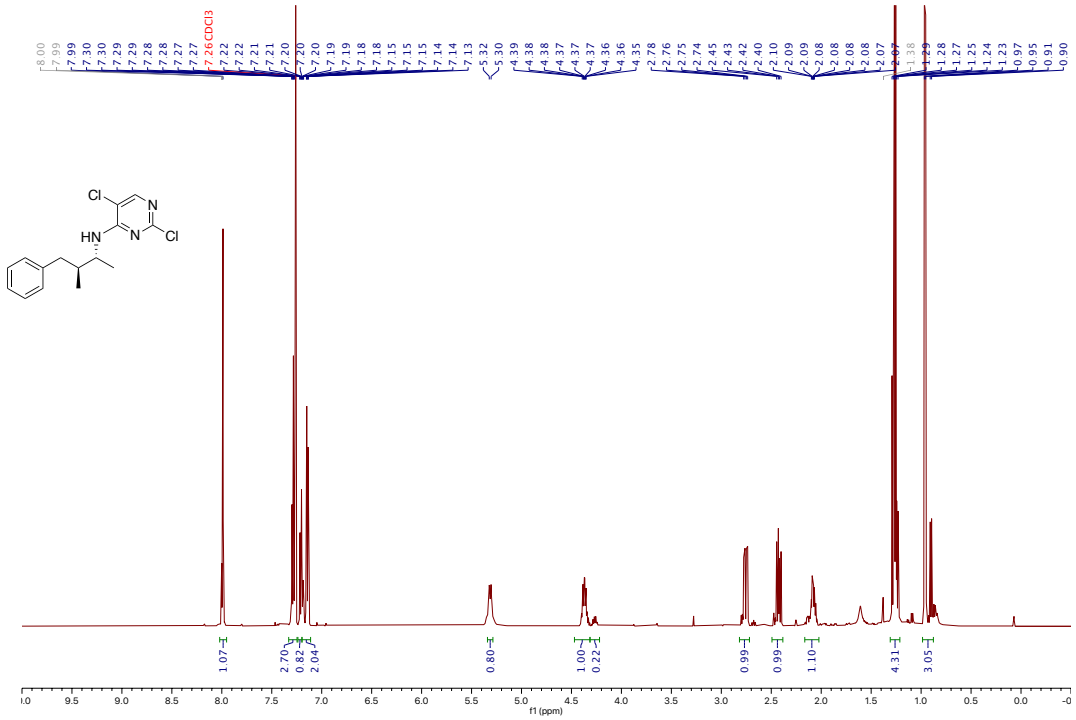
^{13}C NMR spectrum of **(*S*)-1-(furan-2-yl)ethan-1-amine 25**



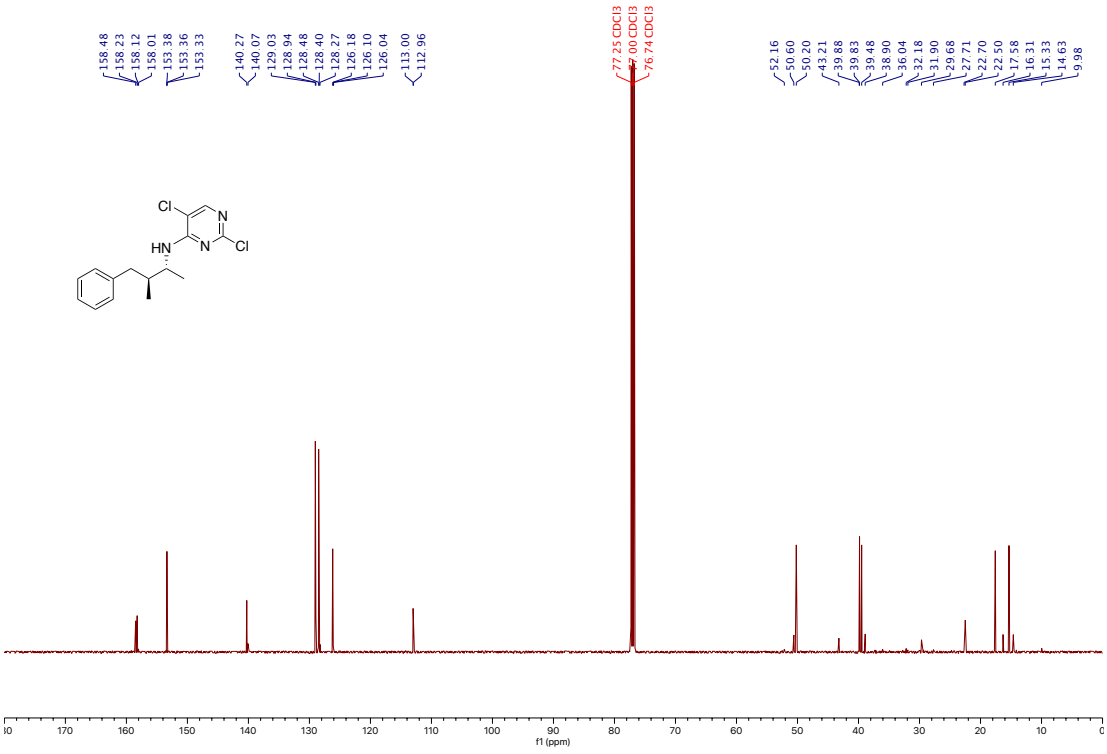
^{1}H NMR spectrum of **(*S*)-1-(6-bromopyridin-2-yl)ethan-1-amine 26**



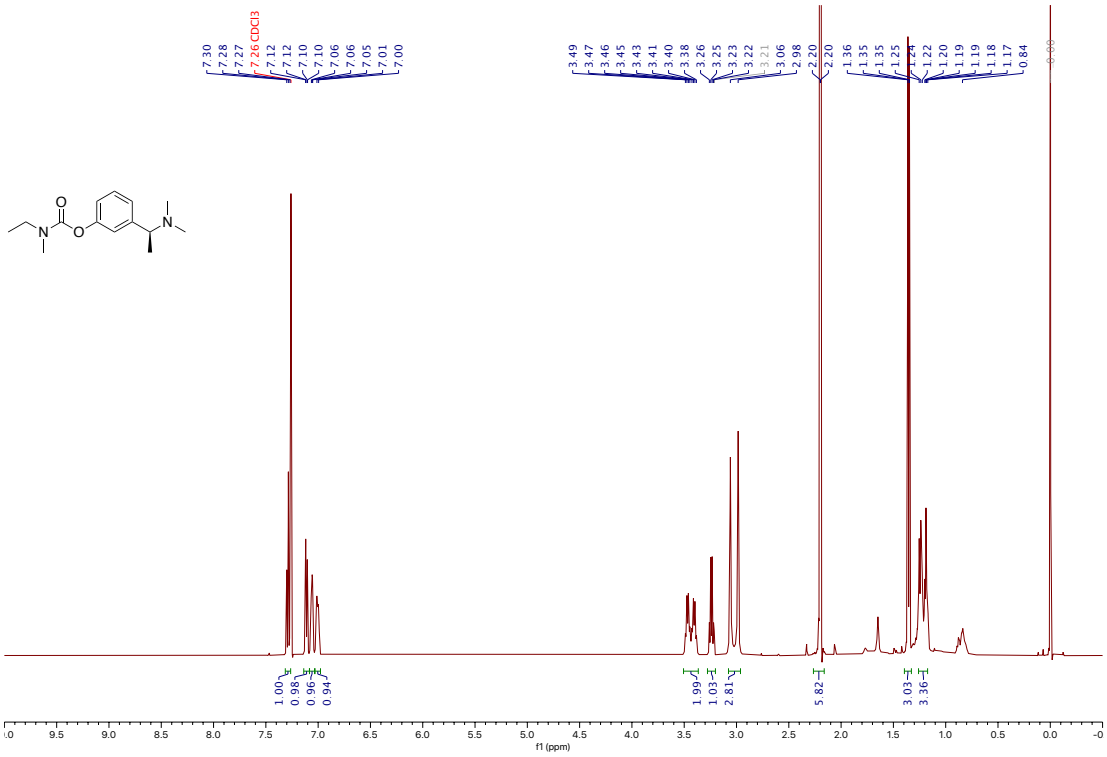
^{13}C NMR spectrum of **(*S*)-1-(6-bromopyridin-2-yl)ethan-1-amine 26**



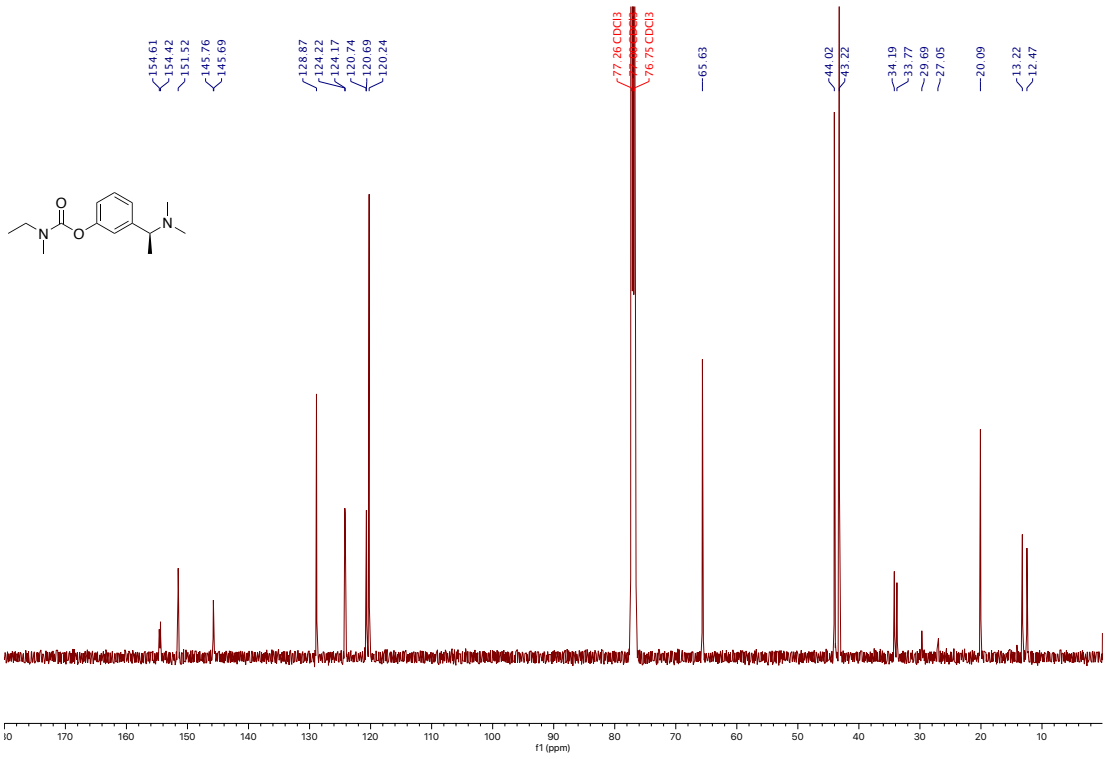
^{1}H NMR spectrum of **2,5-dichloro-*N*-((2*R*,3*S*)-3-methyl-4-phenylbutan-2-yl)pyrimidin-4-amine 32**



^{13}C NMR spectrum of **2,5-dichloro-*N*-((2*R*,3*S*)-3-methyl-4-phenylbutan-2-yl)pyrimidin-4-amine 32**

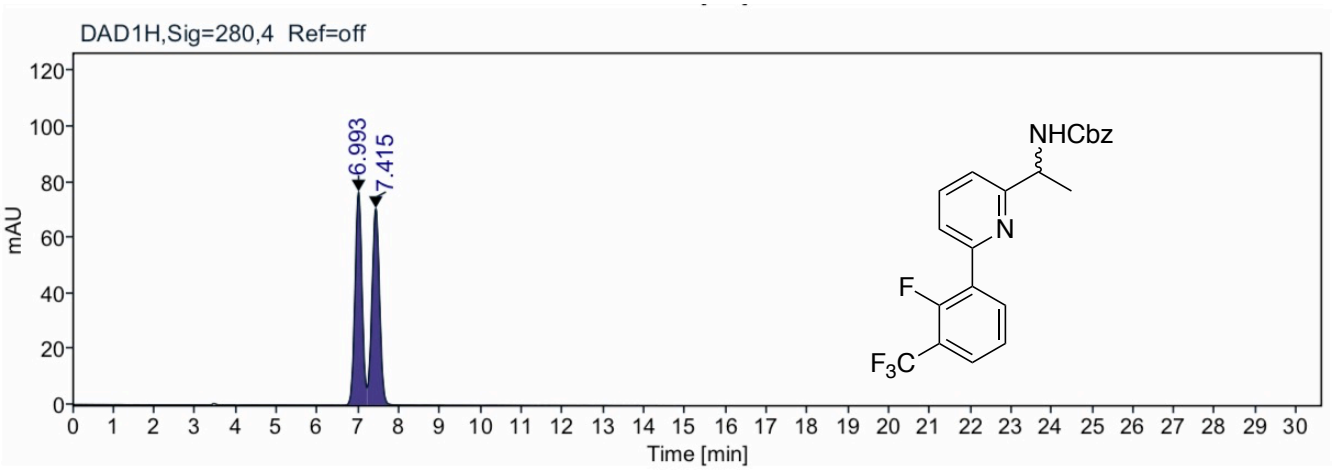


^{1}H NMR spectrum of **(*S*)-rivastigmine**

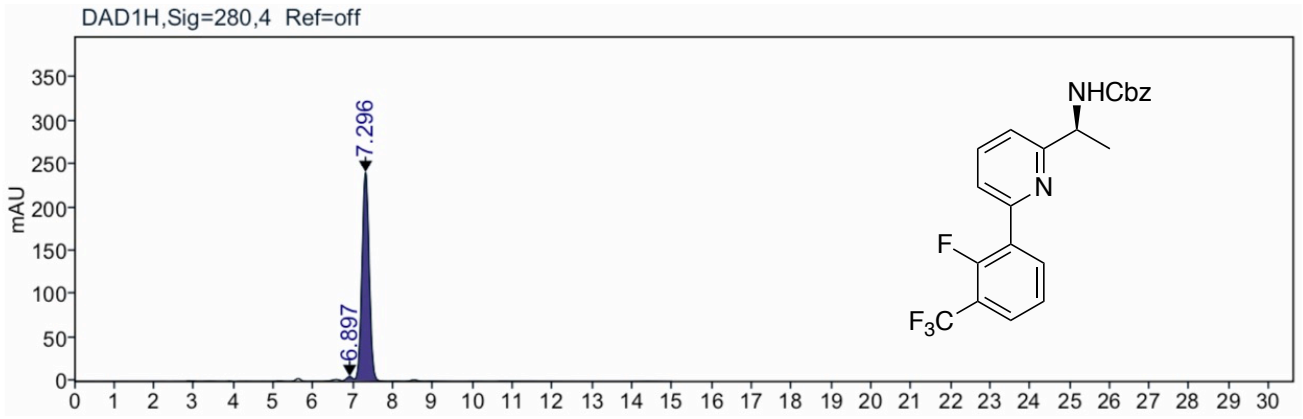


^{13}C NMR spectrum of **(*S*)-rivastigmine**

6. HPLC traces

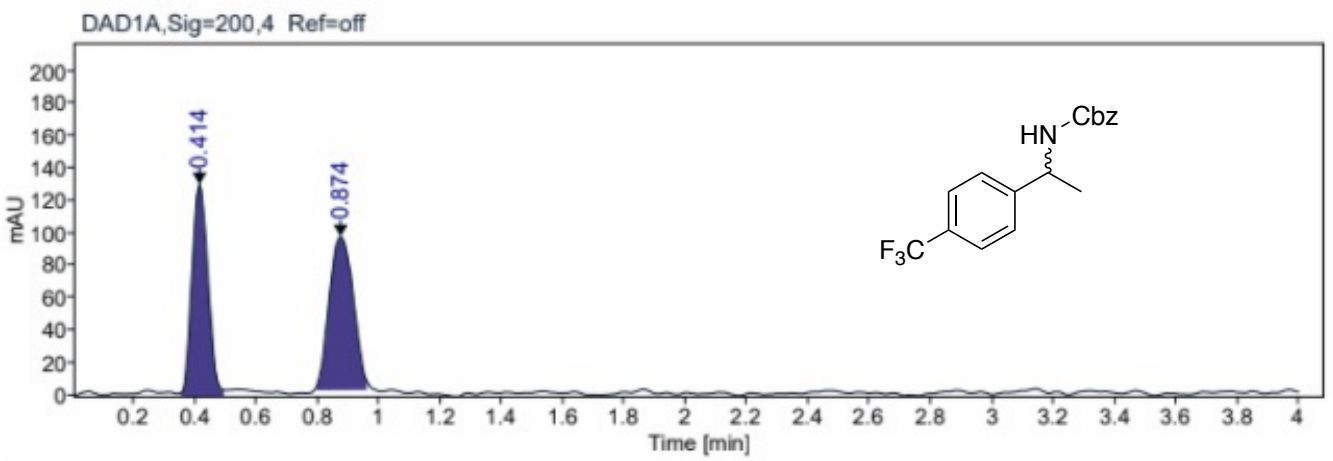


RT [min]	Area	Area%
6.993	912.0047	49.7
7.415	922.0871	50.3
Sum	1834.0918	

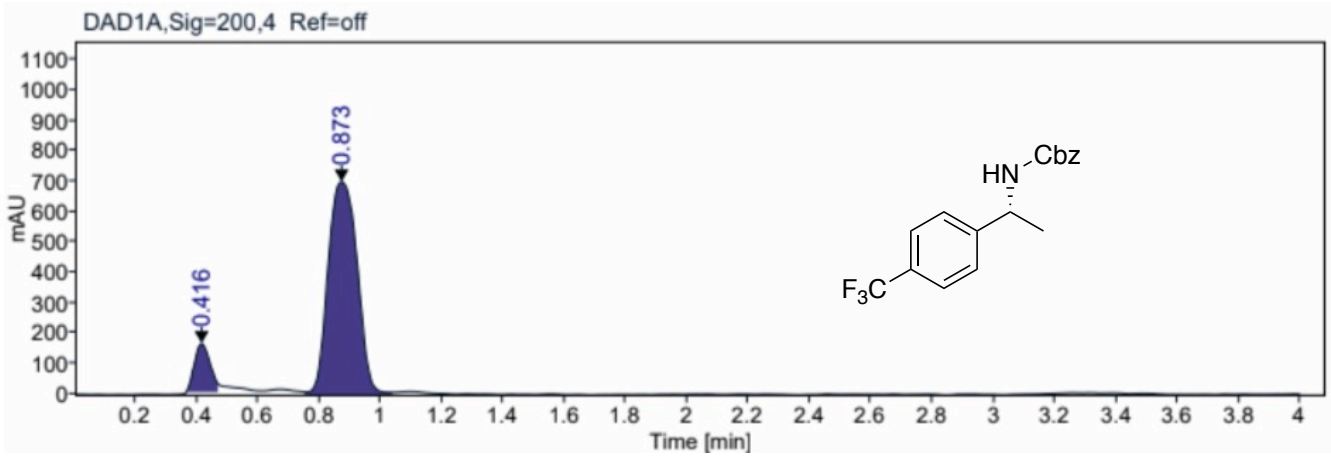


RT [min]	Area	Area%
6.897	44.0198	1.4
7.296	3013.2262	98.6
Sum	3057.2460	

HPLC analysis of **benzyl (*S*)-(1-(6-(2-fluoro-3-(trifluoromethyl)phenyl)pyridin-2-yl)ethyl)carbamate 8**

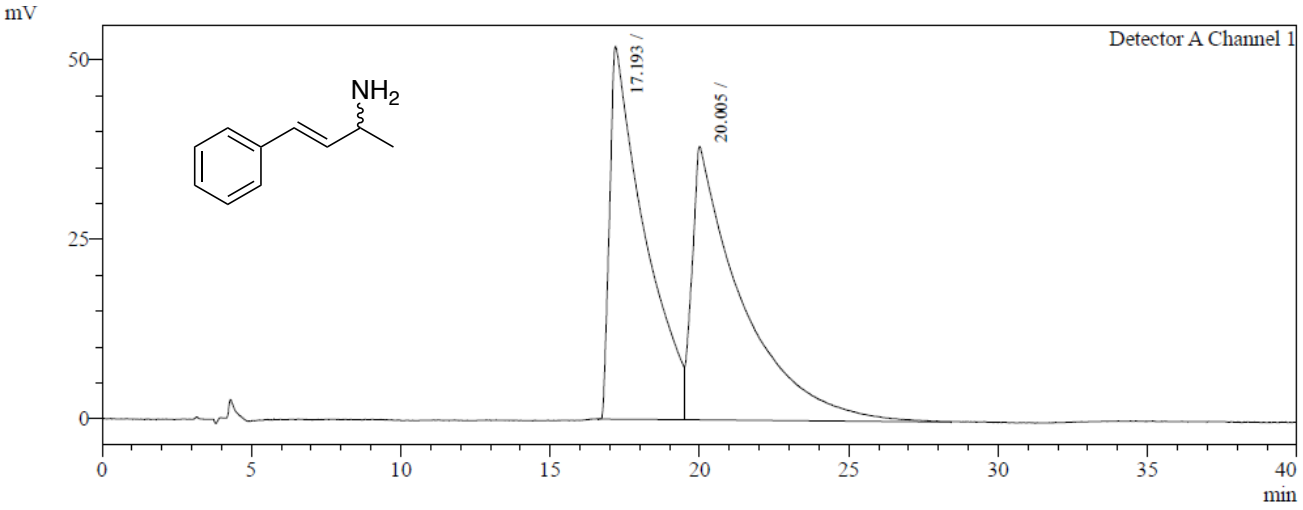


RT [min]	Area	Area%
0.414	509.8059	49.9
0.874	511.3966	50.1
Sum	1021.2025	



RT [min]	Area	Area%
0.416	564.8058	10.7
0.873	4722.5385	89.3
Sum	5287.3443	

HPLC analysis of **(*R*)-benzyl (1-(4-(trifluoromethyl)phenyl)ethyl)carbamate 10**

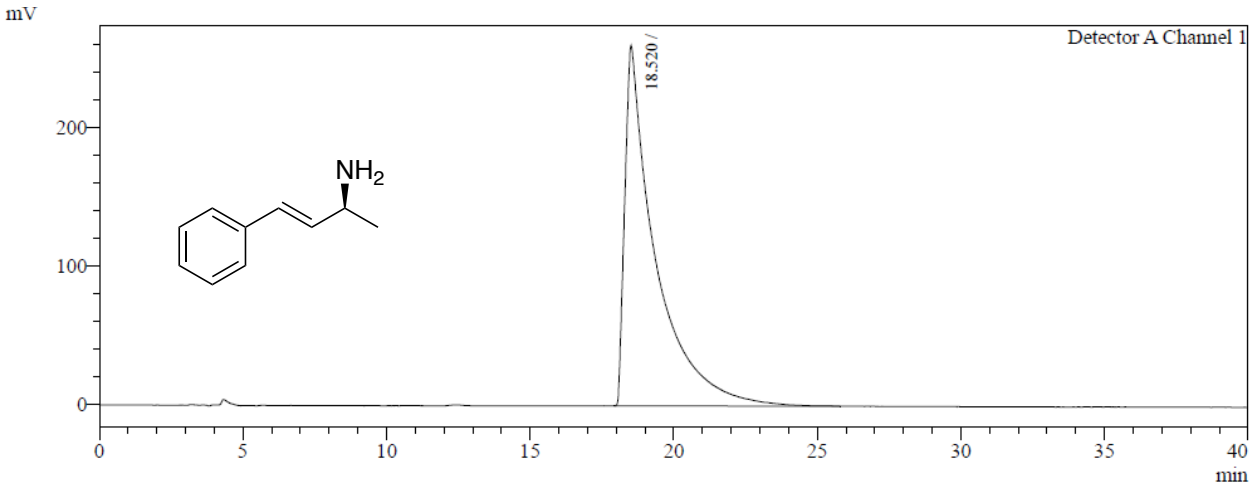


1 Detector A Channel 1 / 240nm

Peak Table

Detector A Channel 1 240nm

Peak#	Ret. Time (min)	RRT	Height	Area	Area%	Name
1	17.193	0.859	51905	4182004	48.855	
2	20.005	1.000	38099	4377981	51.145	
Total			90004	8559985	100.000	



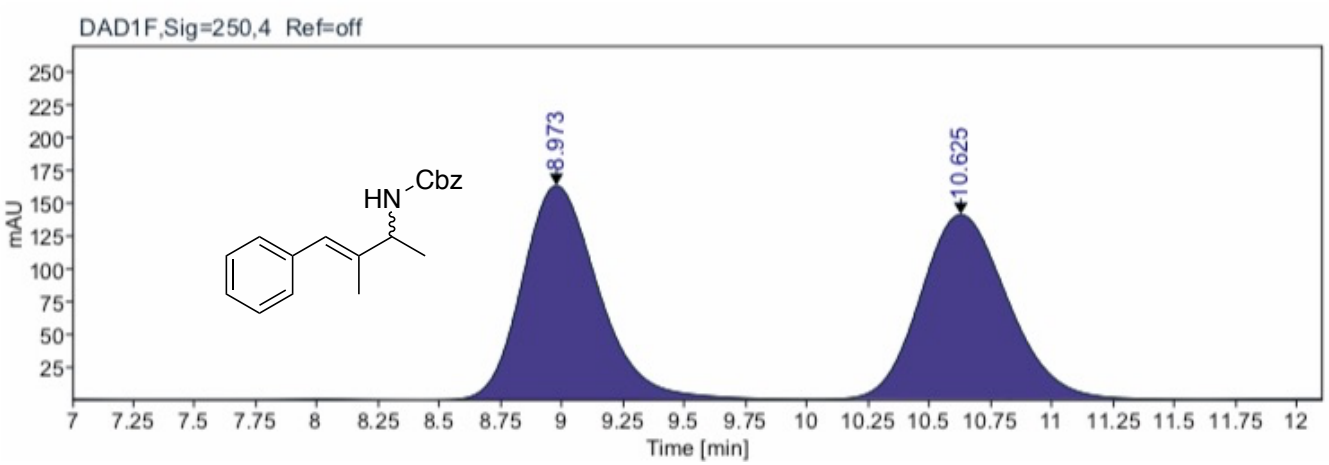
1 Detector A Channel 1 / 240nm

Peak Table

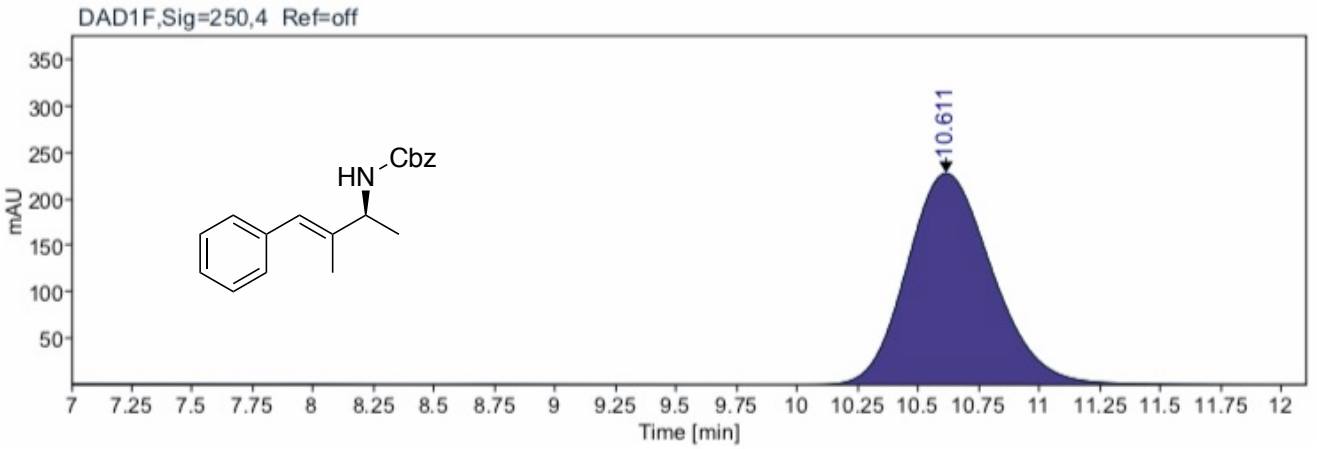
Detector A Channel 1 240nm

Peak#	Ret. Time (min)	RRT	Height	Area	Area%	Name
1	18.520	1.000	259796	19161367	100.000	
Total			259796	19161367	100.000	

HPLC analysis of **(*S*,*E*)-4-phenylbut-3-en-2-amine 12**

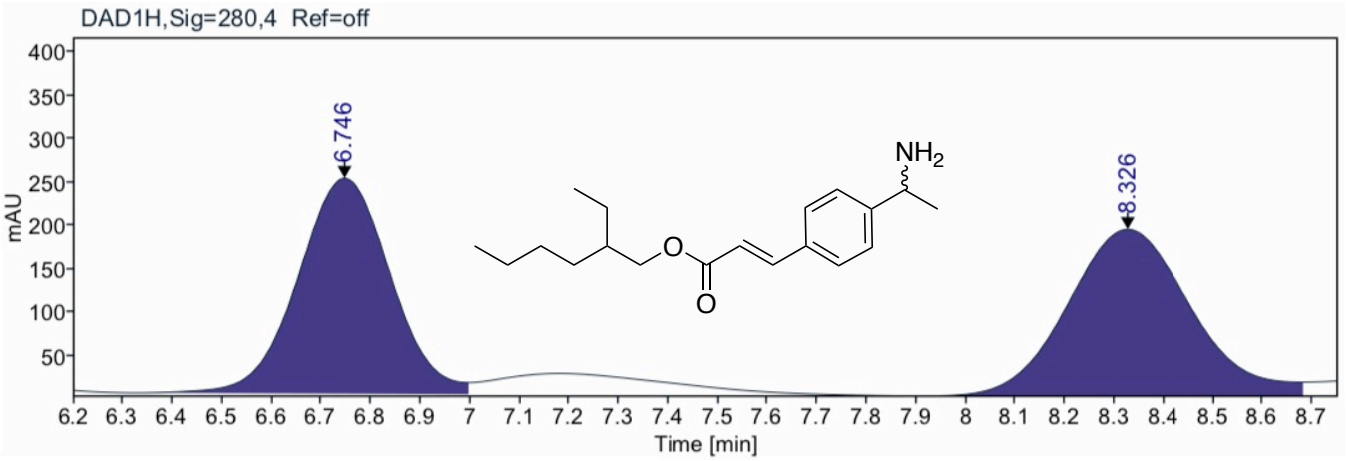


RT [min]	Area	Area%
8.973	3522.4688	50.3
10.625	3483.7551	49.7
Sum	7006.2239	

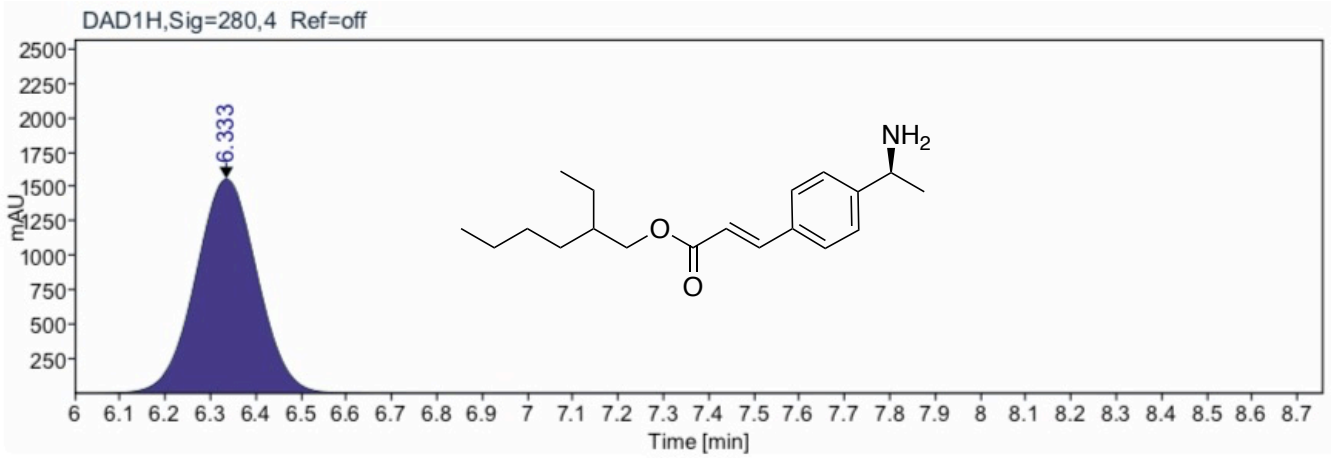


RT [min]	Area	Area%
10.611	5605.5983	100.0
Sum	5605.5983	

HPLC analysis of **(*S*,*E*)-benzyl-(3-methyl-4-phenylbut-3-en-2-yl)carbamate 13**

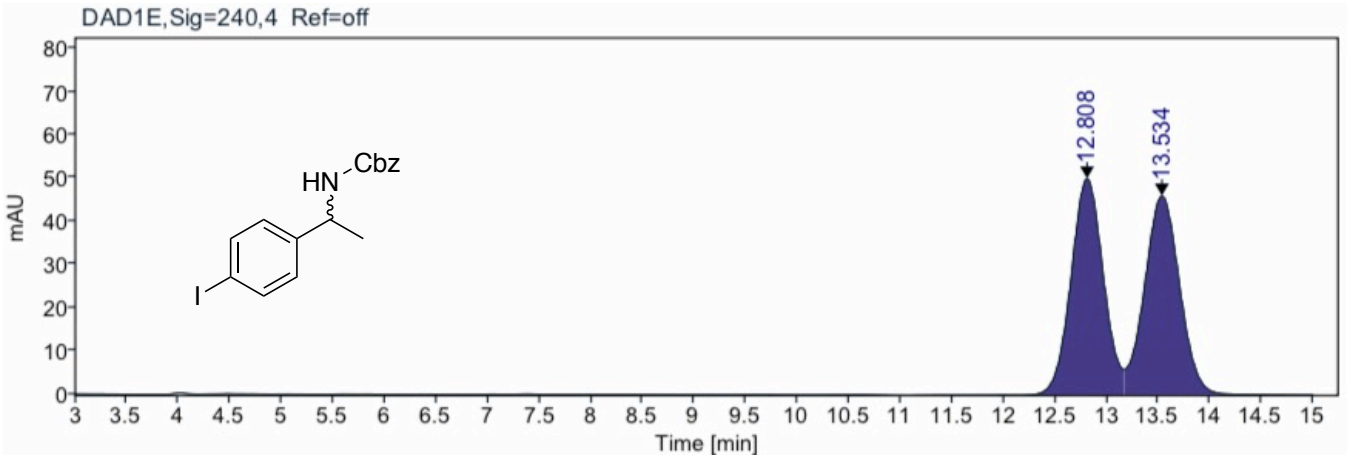


RT [min]	Area	Area%
6.746	3214.7639	49.0
8.326	3340.7536	51.0
Sum	6555.5174	

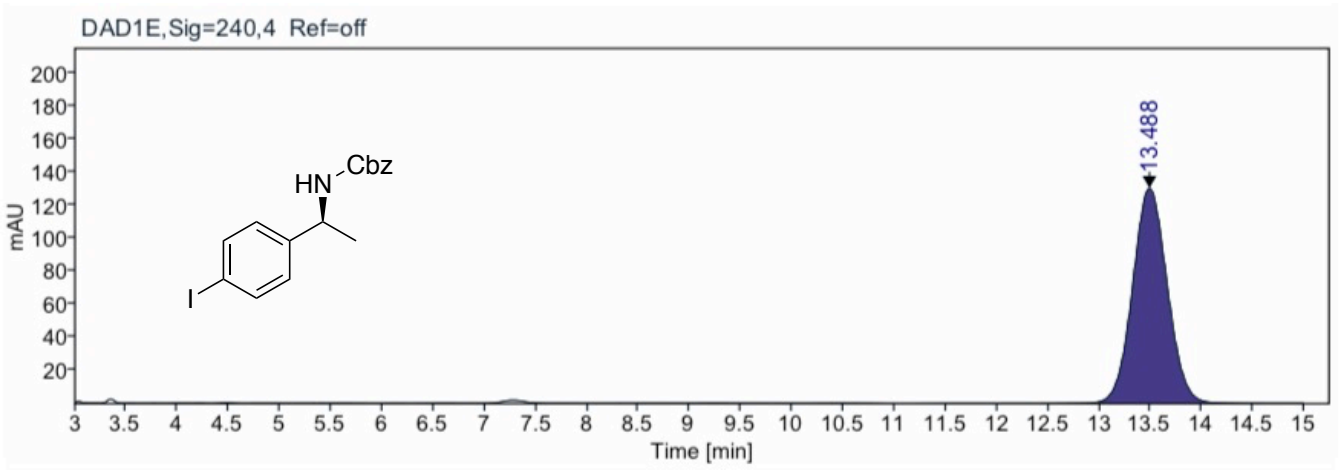


RT [min]	Area	Area%
6.333	14725.0334	100.0
Sum	14725.0334	

HPLC analysis of **(*S*)-2-ethylhexyl (*E*)-3-(4-(1-(((benzyloxy)carbonyl)amino)ethyl)phenyl)acrylate 14**



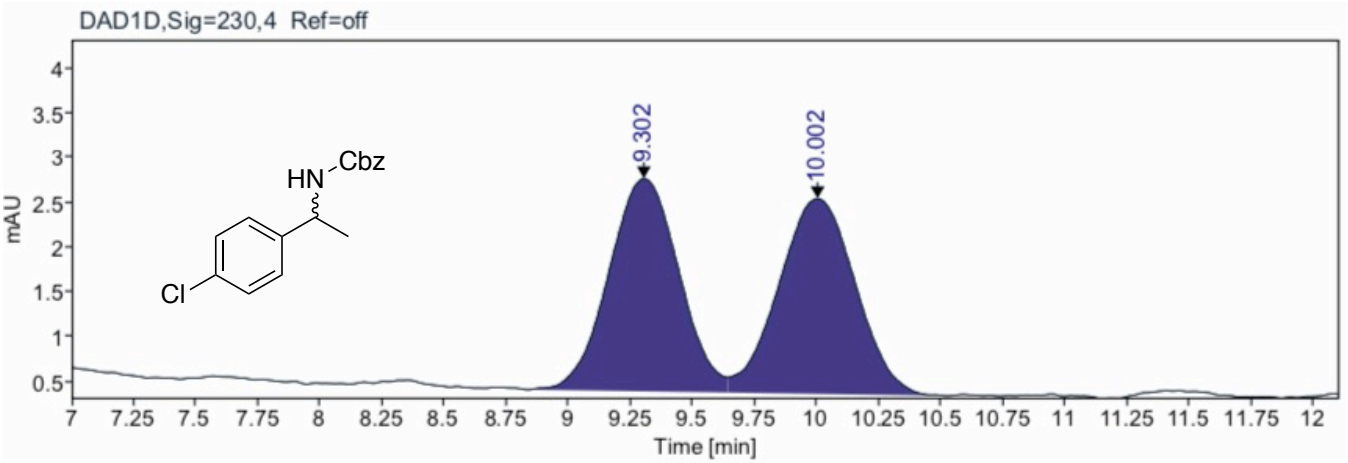
RT [min]	Area	Area%
12.808	1094.1356	50.0
13.534	1096.2754	50.0
Sum	2190.4110	



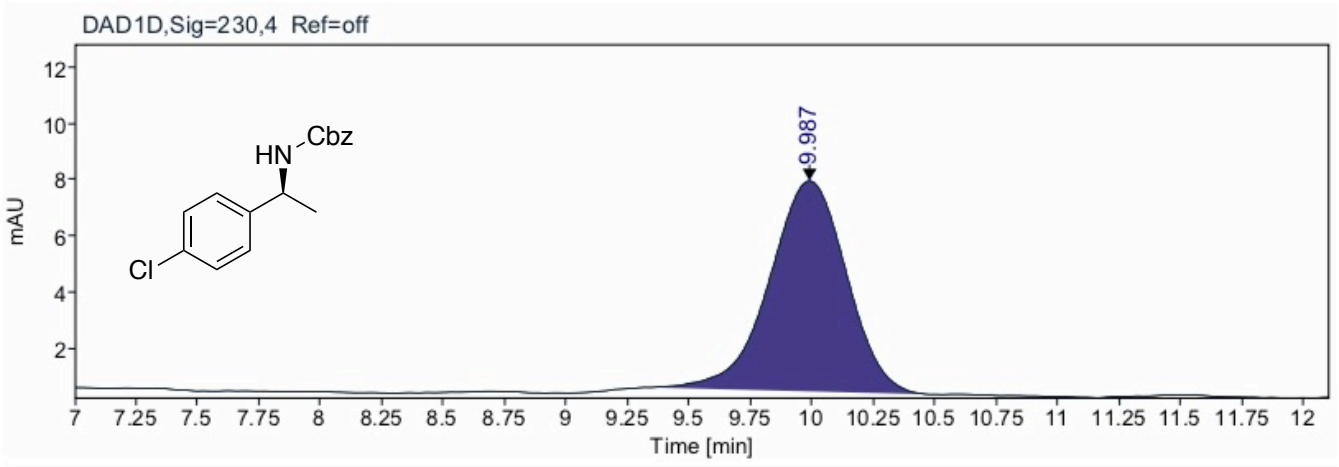
a

RT [min]	Area	Area%
13.488	3060.1331	100.0
Sum	3060.1331	

HPLC analysis of **(*S*)-benzyl(1-(4-iodophenyl)ethyl)carbamate 16**

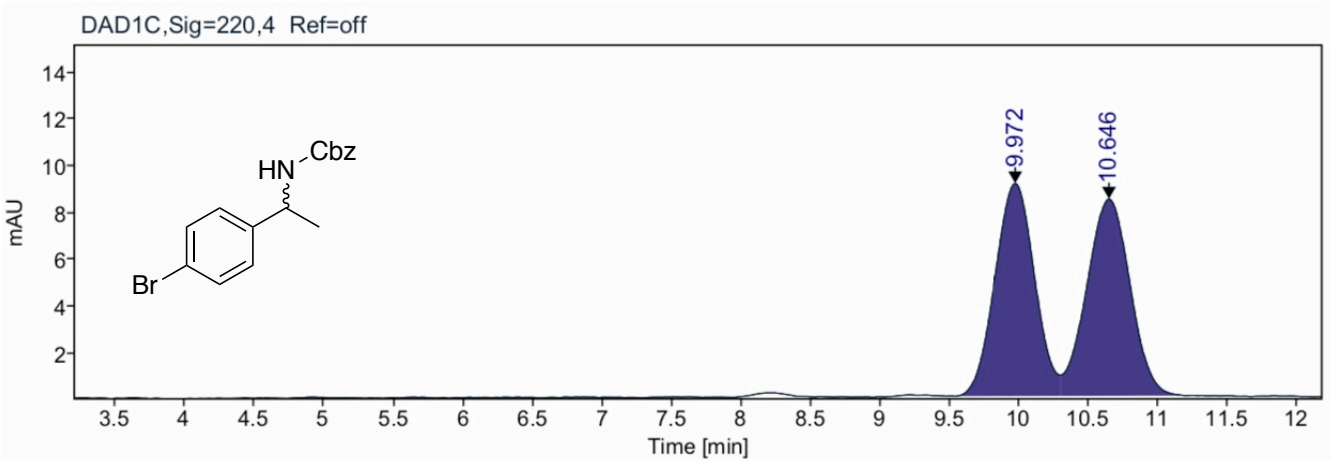


RT [min]	Area	Area%
9.302	46.7580	49.9
10.002	46.8697	50.1
Sum	93.6277	

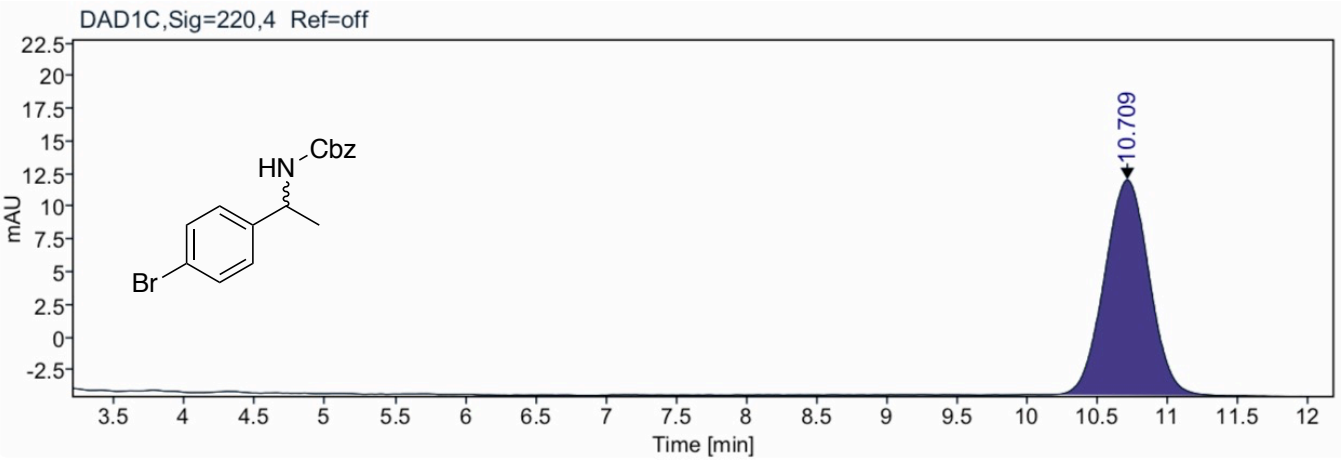


RT [min]	Area	Area%
9.987	163.1647	100.0
Sum	163.1647	

HPLC analysis of **(*S*)-benzyl(1-(4-chlorophenyl)ethyl)carbamate 17**

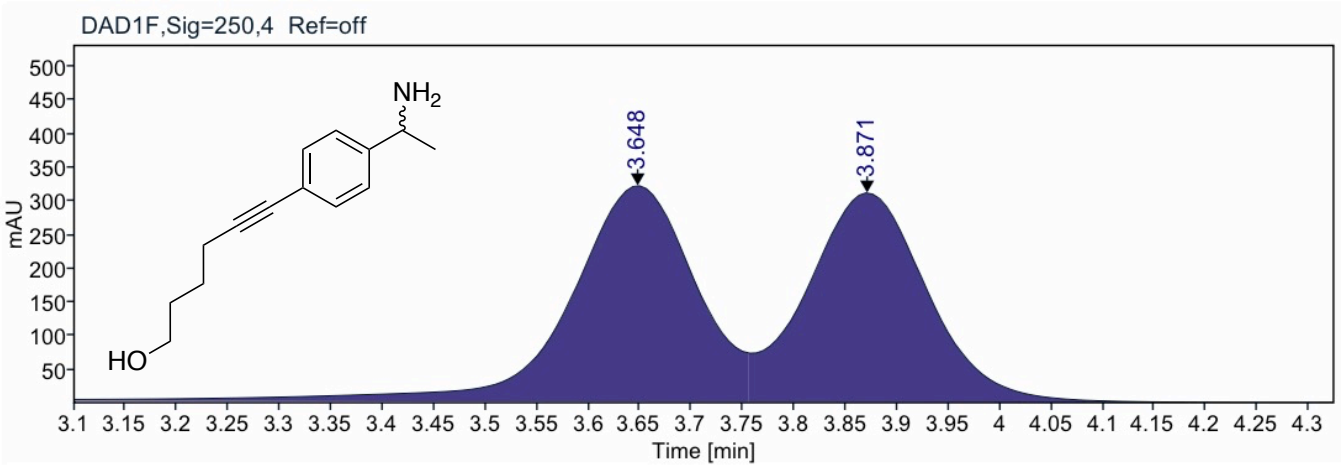


RT [min]	Area	Area%
9.972	180.7430	49.7
10.646	183.1462	50.3
Sum	363.8893	

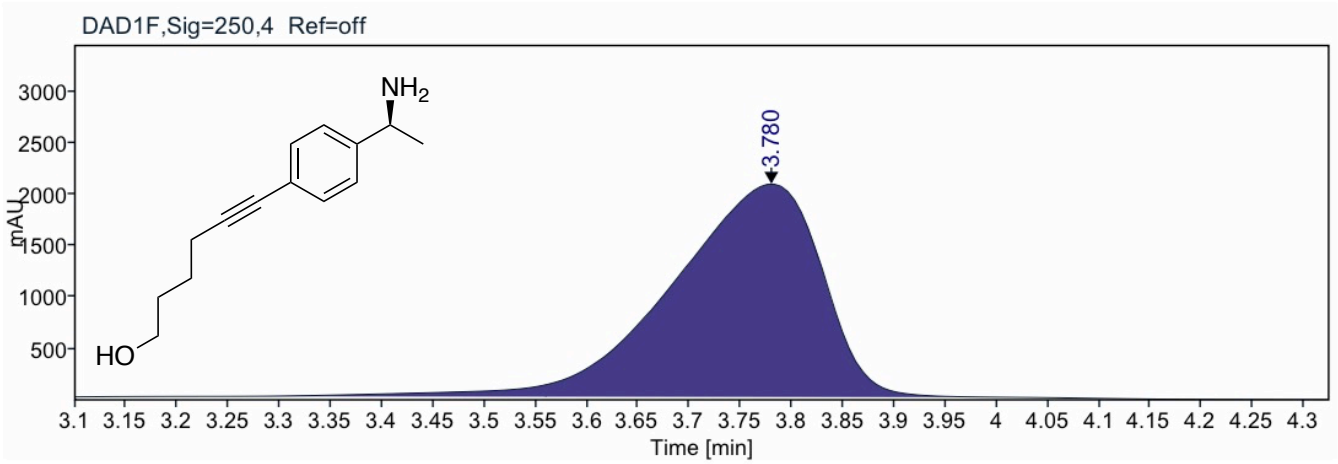


RT [min]	Area	Area%
10.709	363.4214	100.0
Sum	363.4214	

HPLC analysis of **(*S*)-benzyl(1-(4-bromophenyl)ethyl)carbamate 18**

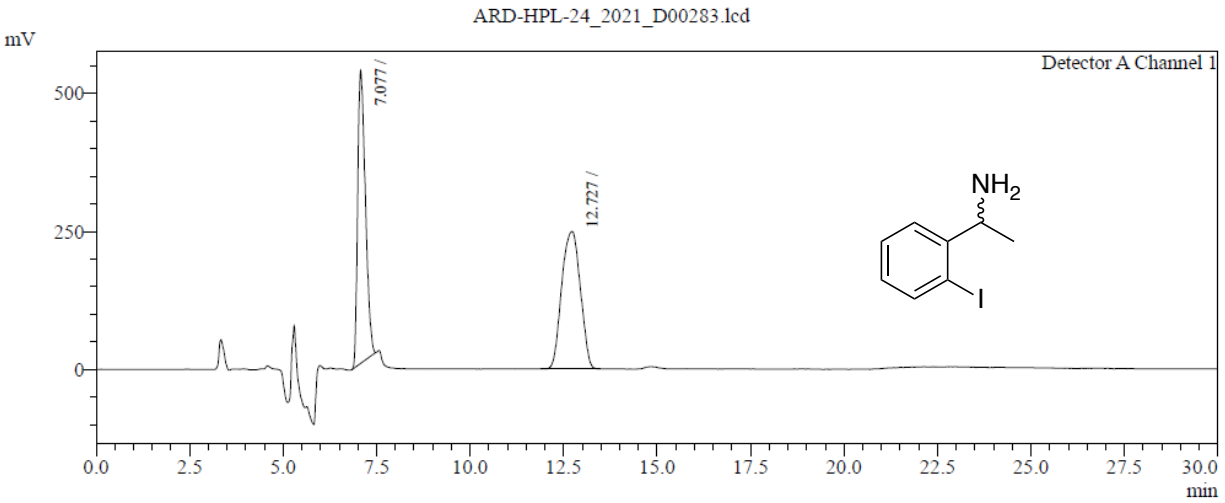


RT [min]	Area	Area%
3.648	2737.5088	51.9
3.871	2535.1423	48.1
Sum	5272.6511	



RT [min]	Area	Area%
3.780	21178.1383	100.0
Sum	21178.1383	

HPLC analysis of **(*S*)-benzyl (1-(4-(6-hydroxyhex-1-yn-1-yl)phenyl)ethyl)carbamate 19**



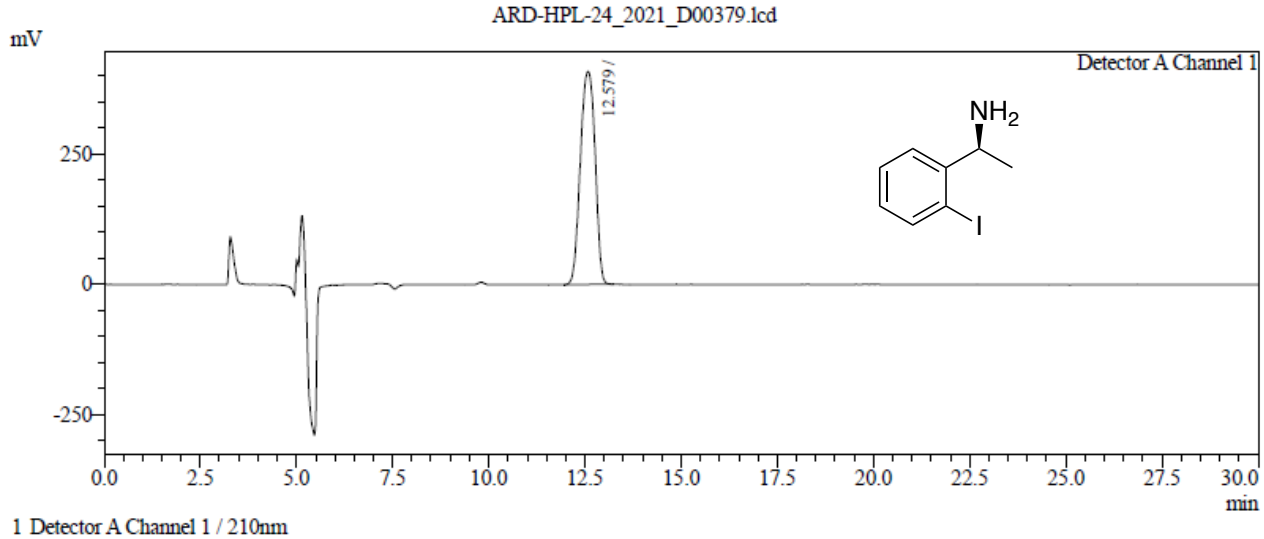
1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	7.077	1.000	530230	7617644	46.906	
2	12.727	1.798	248954	8622671	53.094	
Total			779184	16240316	100.000	

Iodo acetamine



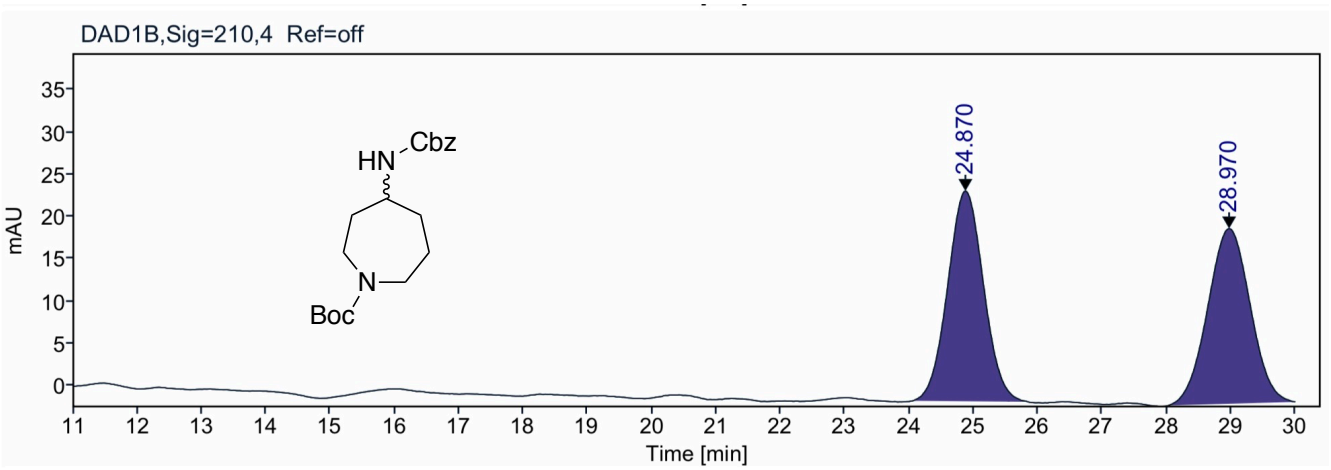
1 Detector A Channel 1 / 210nm

Peak Table

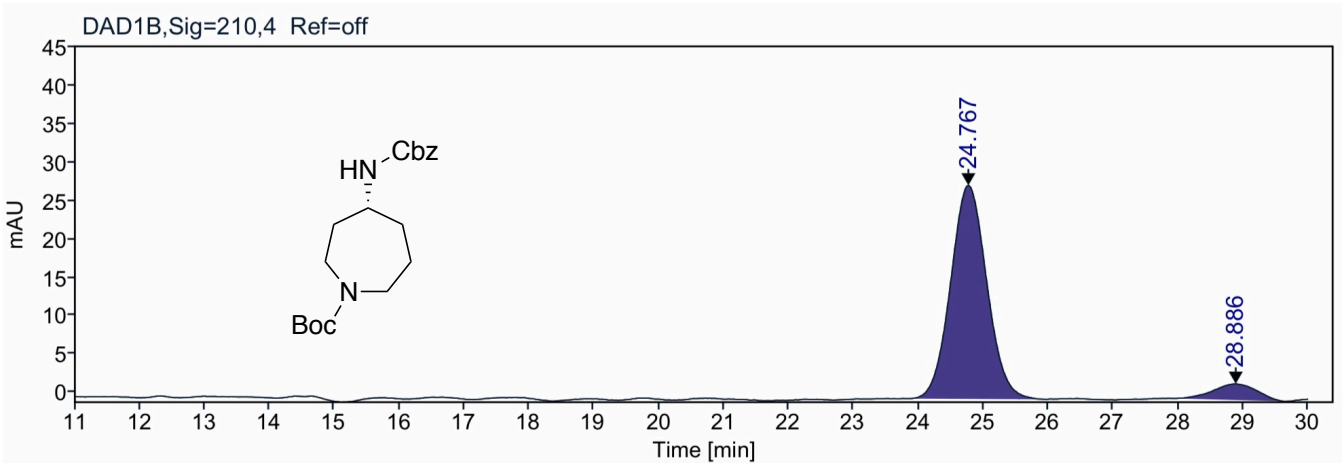
Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	12.579	1.000	408369	10870539	100.000	
Total			408369	10870539	100.000	

HPLC analysis of **(*S*)-1-(2-iodophenyl)ethan-1-amine 20**

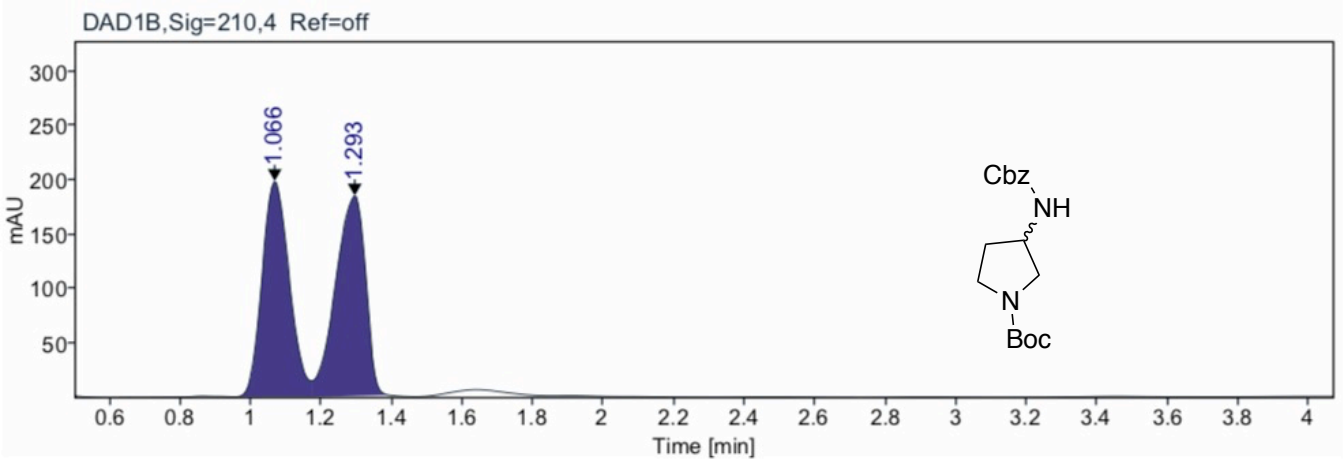


RT [min]	Area	Area%
24.870	962.1121	50.4
28.970	946.8702	49.6
Sum	1908.9823	

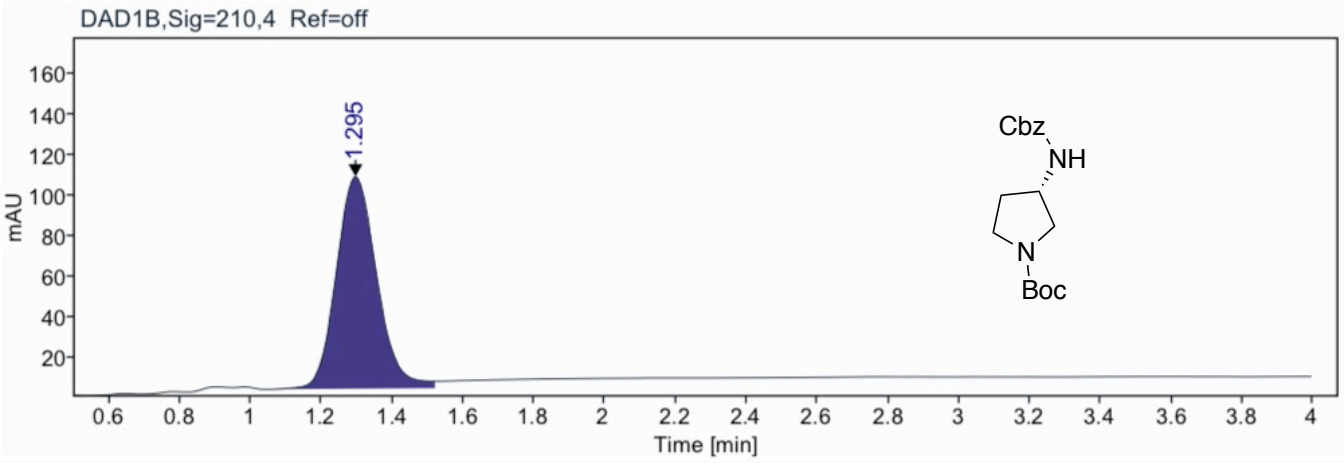


RT [min]	Area	Area%
24.767	1079.8347	91.6
28.886	99.3328	8.4
Sum	1179.1675	

HPLC analysis of **(*S*)-*tert*-butyl -4-(((benzyloxy)carbonyl)amino)azepane-1-carboxylate 21**

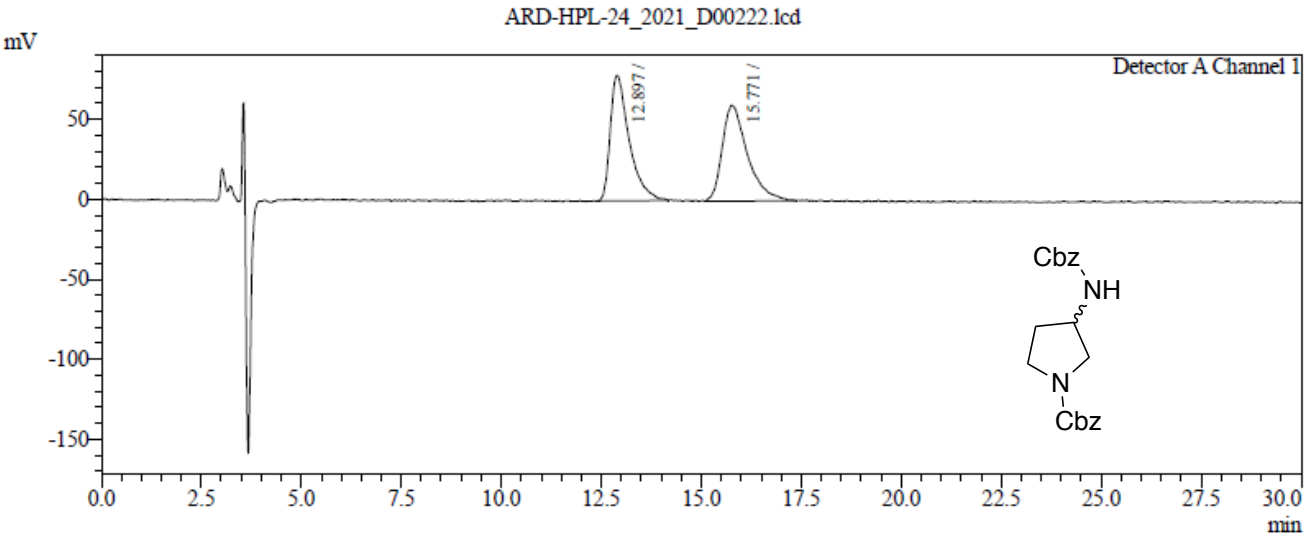


RT [min]	Area	Area%
1.066	1065.6655	49.4
1.293	1091.0728	50.6
Sum	2156.7383	



RT [min]	Area	Area%
1.295	832.8978	100.0
Sum	832.8978	

HPLC analysis of **(*S*)-*tert*-butyl-3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 22**

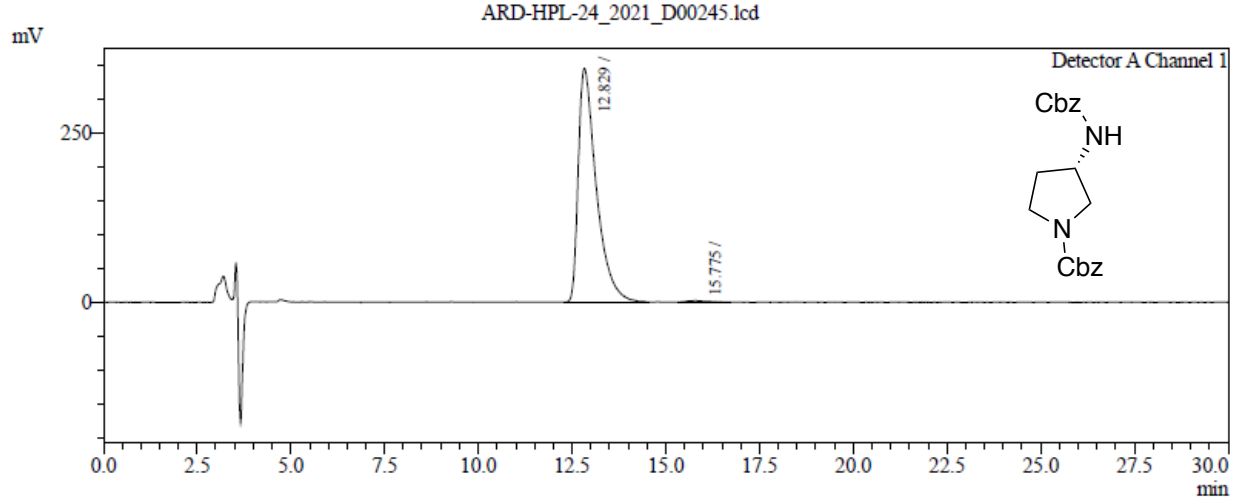


1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	12.897	1.000	78302	2576513	49.557	
2	15.771	1.223	59836	2622525	50.443	
Total			138138	5199038	100.000	



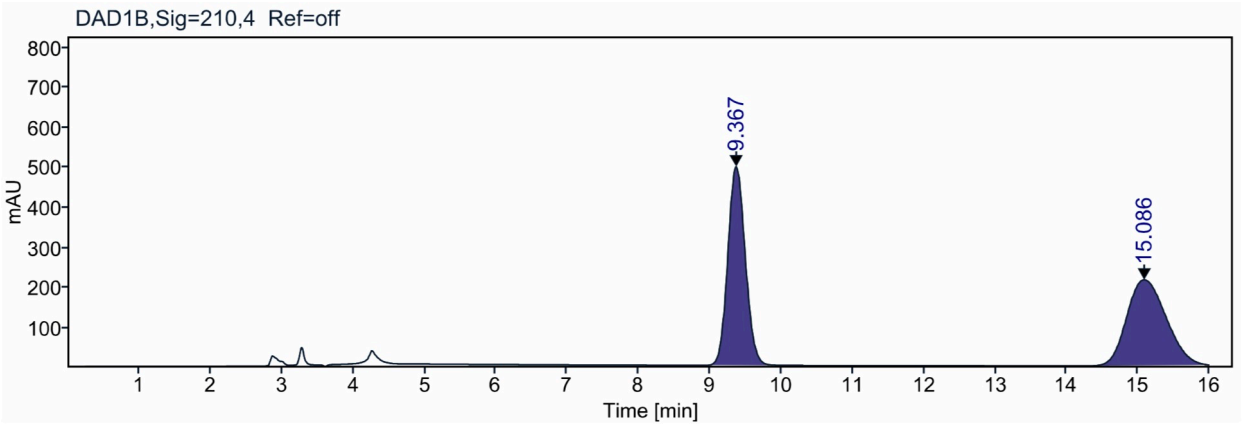
1 Detector A Channel 1 / 210nm

Peak Table

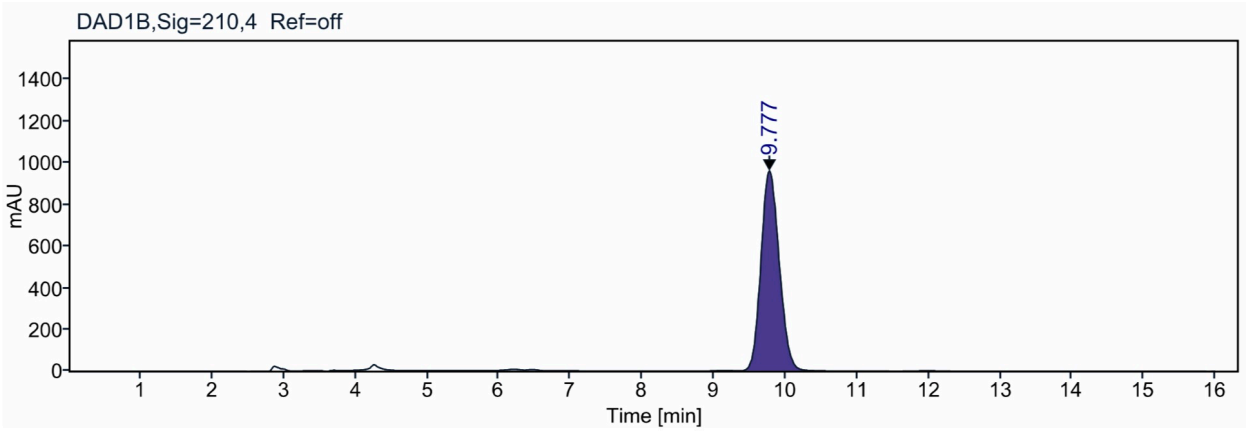
Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	12.829	1.000	344813	11575460	99.215	
2	15.775	1.230	2474	91581	0.785	
Total			347287	11667041	100.000	

HPLC analysis of**(*S*)-benzyl 3-(((benzyloxy)carbonyl)amino)pyrrolidine-1-carboxylate 23**

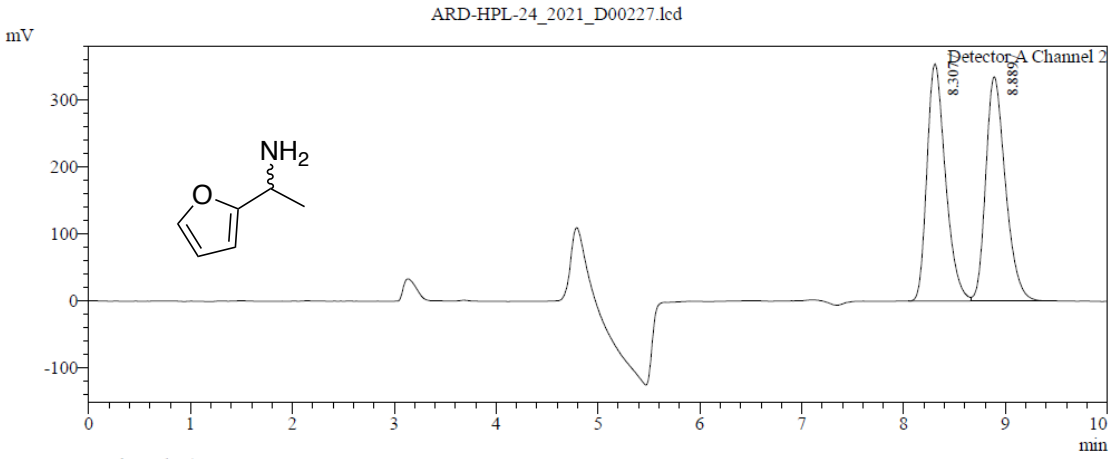


RT [min]	Area	Area%
9.367	8468.2318	50.9
15.086	8167.0223	49.1
Sum	16635.2541	



RT [min]	Area	Area%
9.777	17044.5630	100.0
Sum	17044.5630	

HPLC analysis of **(*S*)-benzyl-(1-phenylpropyl)carbamate 24**

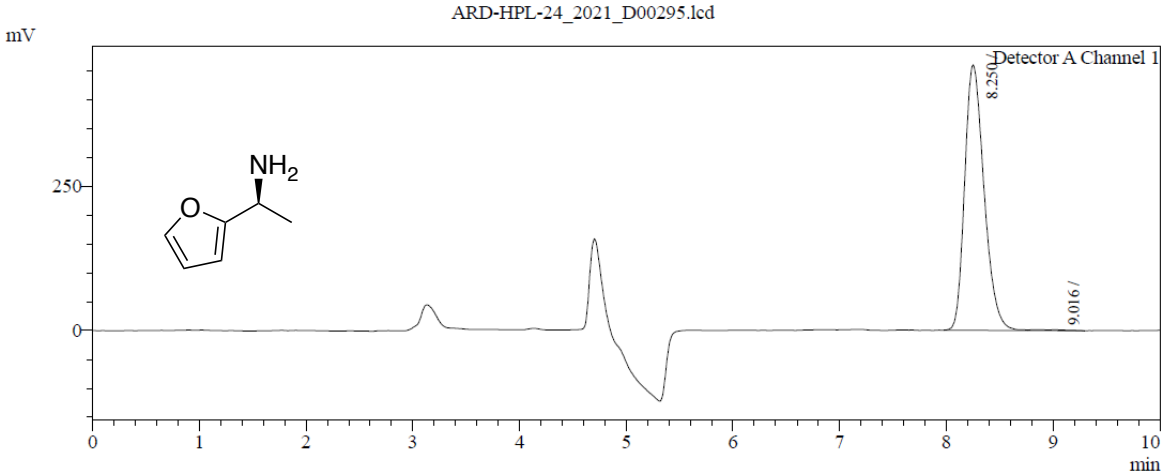


1 Detector A Channel 2 / 210nm

Peak Table

Detector A Channel 2 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	8.307	1.000	353528	4484166	49.927	
2	8.889	1.070	333989	4497219	50.073	
Total			687517	8981385	100.000	



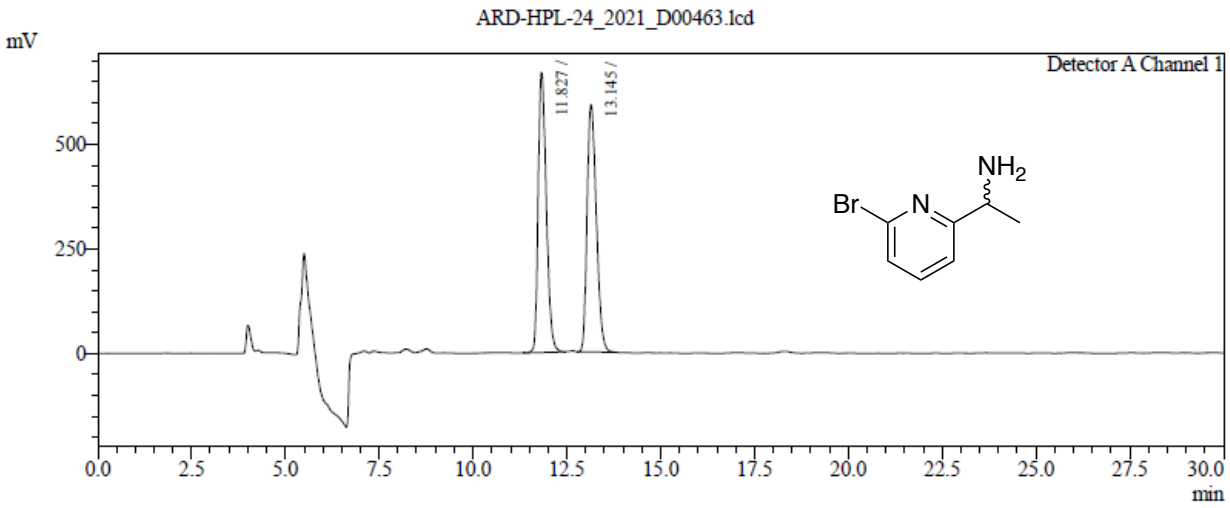
1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	8.250	1.000	460481	5820238	99.469	
2	9.016	1.093	1563	31051	0.531	
Total			462044	5851289	100.000	

HPLC analysis of **(*S*)-1-(furan-2-yl)ethan-1-amine 25**

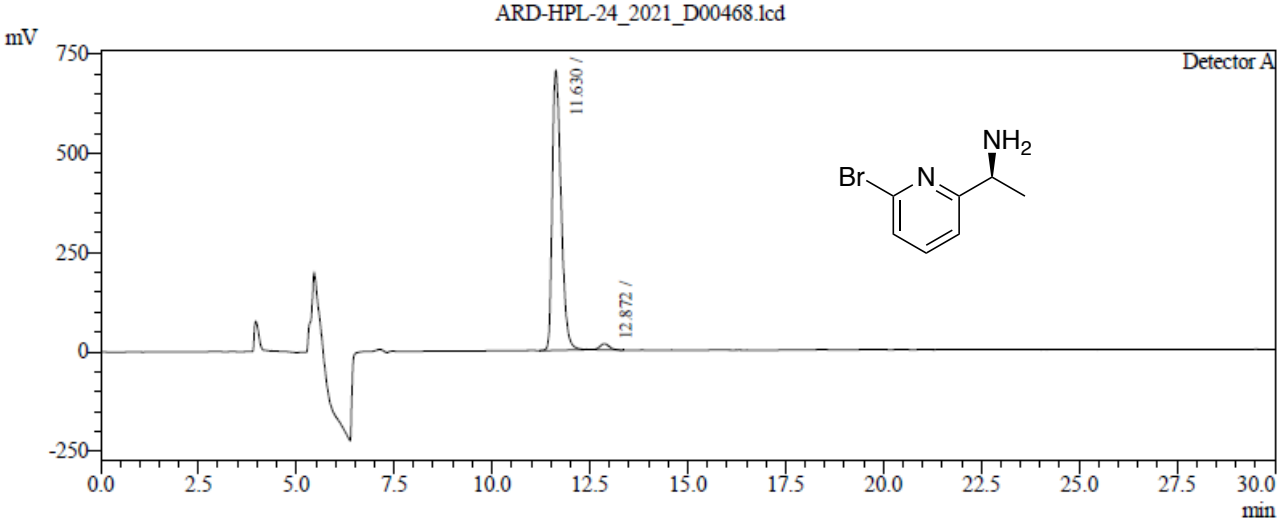


1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	11.827	1.000	668987	10105539	49.958	
2	13.145	1.111	590566	10122347	50.042	
Total			1259553	20227885	100.000	



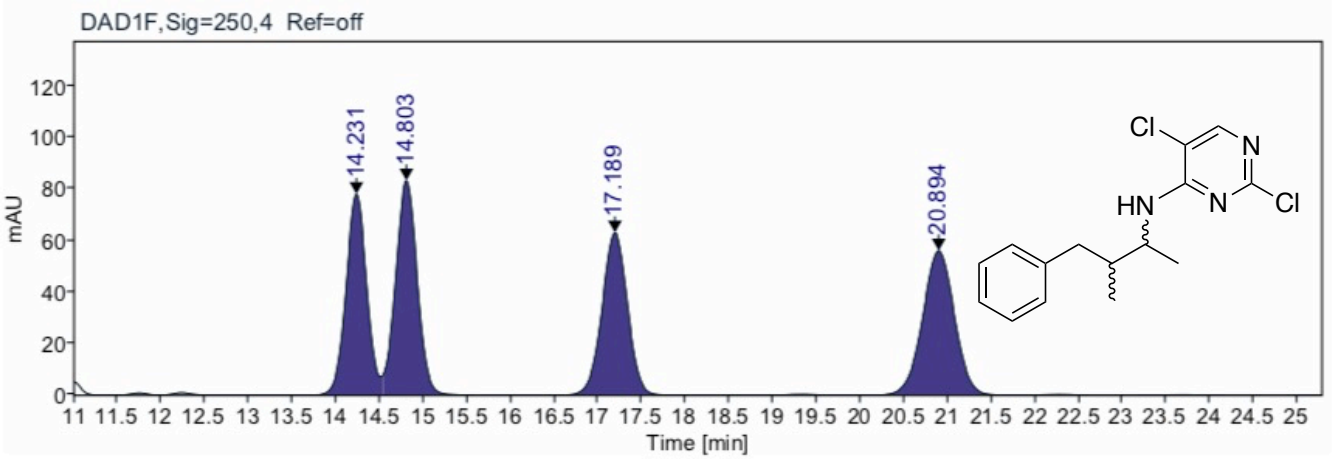
1 Detector A / 210nm

Peak Table

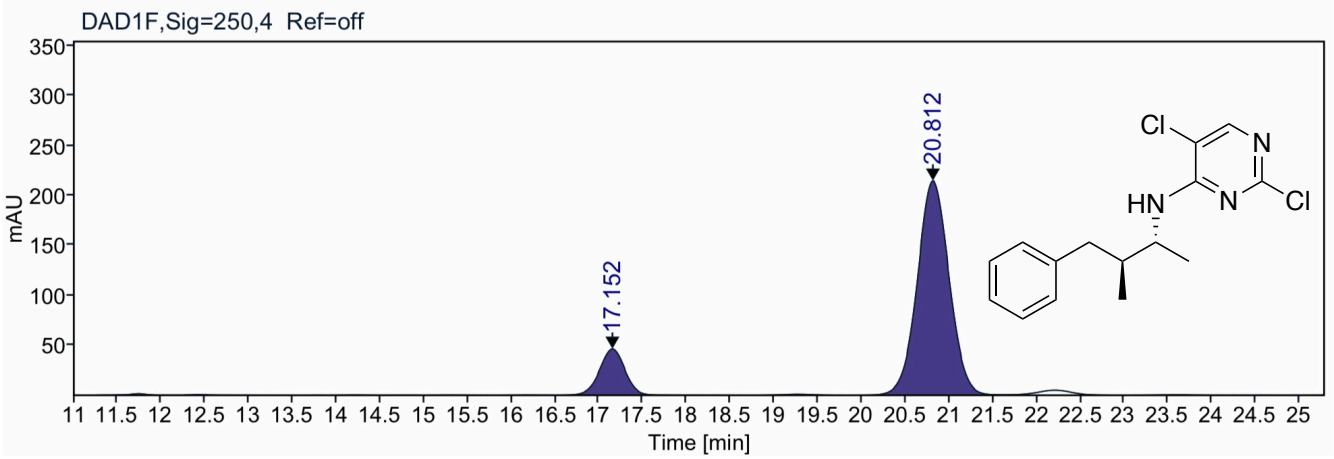
Detector A 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	11.630	1.000	703872	11057601	97.863	
2	12.872	1.107	14700	241500	2.137	
Total			718572	11299101	100.000	

HPLC analysis of **(*S*)- 1-(6-bromopyridin-2-yl)ethan-1-amine 26**

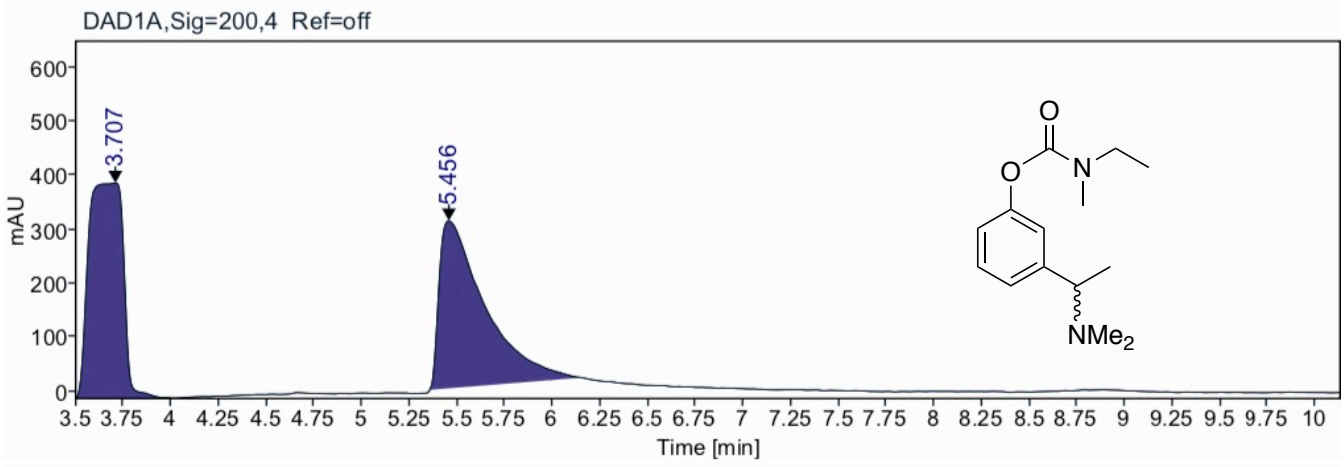


RT [min]	Area	Area%
14.231	1285.4020	23.9
14.803	1419.7391	26.4
17.189	1271.6822	23.6
20.894	1406.8956	26.1
Sum	5383.7190	

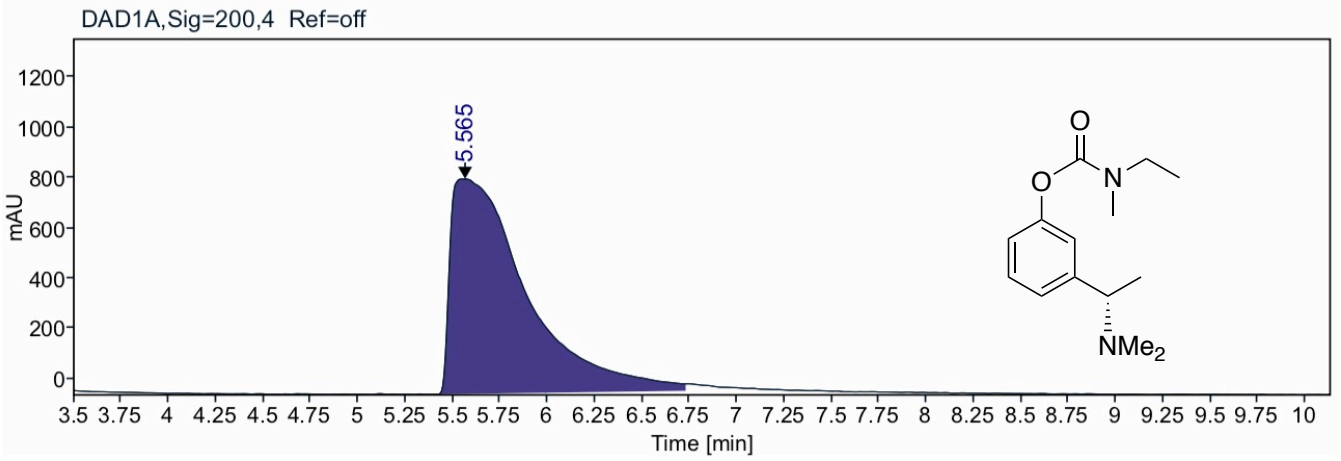


RT [min]	Area	Area%
17.152	932.9441	14.7
20.812	5420.0159	85.3
Sum	6352.9600	

HPLC analysis of **2,5-dichloro-*N*-((2*R*,3*S*)-3-methyl-4-phenylbutan-2-yl)pyrimidin-4-amine 32**



RT [min]	Area	Area%
3.707	5184.0055	50.1
5.456	5169.8312	49.9
Sum	10353.8367	



RT [min]	Area	Area%
5.565	24031.3379	100.0
Sum	24031.3379	

HPLC analysis of **(*S*)-rivastigmine**

7. References

1 Lipshutz, B. H, Ghorai, S, Abela, A. R, Moser, R, Nishikata, T, Duplais, C, Krasovskiy, A, Gaston, R. D, Gadwood, R. C, TPGS-750-M: A Second-Generation Amphiphile for Metal-Catalyzed Cross-Couplings in Water at Room Temperature, *J. Org. Chem.,* 2011**,** ***76***, 4379-4391.

2 M. P. Andersson, F. Gallou, P. Klumphu, B. S. Takale and B. H. Lipshutz, Structure of Nanoparticles Derived from Designer Surfactant TPGS-750-M in Water, As Used in Organic Synthesis, *Eur. J. Chem.,* 2018, **24**, 6778–6786.

3 J. Albarrán-Velo, I. Lavandera and V. Gotor-Fernández, Sequential Two-Step Stereoselective Amination of Allylic Alcohols through the Combination of Laccases and Amine Transaminases, *ChemBioChem*, 2020, **21**, 200–211.

4 Z.-J. Han, Y.-B. Li, B.-H. Gu, Y.-M. Li and H. Chen, Economical synthesis of *tert*- butyl (*S*)-3-aminopyrrolidine-1-carboxylate from L-aspartic acid, *Synth. Commun.*, 2018, **48**, 2452–2456.

5 T. D. Ashton, K. M. Aumann, S. P. Baker, C. H. Schiesser and P. J. Scammells, Structure–activity relationships of adenosines with heterocyclic N6-substituents, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 6779–6784.

6 M. G. Pizzuti, A. J. Minnaard and B. L. Feringa, Catalytic Enantioselective Addition of Organometallic Reagents to N-Formylimines Using Monodentate Phosphoramidite Ligands, *J. Org. Chem.*, 2008, **73**, 940–947.

7 X. Tan, S. Gao, W. Zeng, S. Xin, Q. Yin and X. Zhang, Asymmetric Synthesis of Chiral Primary Amines by Ruthenium-Catalyzed Direct Reductive Amination of Alkyl Aryl Ketones with Ammonium Salts and Molecular H2, *J. Am. Chem. Soc.*, 2018, **140**, 2024–2027.

8 W. Baratta, F. Benedetti, A. Del Zotto, L. Fanfoni, F. Felluga, S. Magnolia, E. Putignano and P. Rigo, Chiral Pincer Ruthenium and Osmium Complexes for the Fast and Efficient Hydrogen Transfer Reduction of Ketones, *Organometallics*, 2010, **29**, 3563–3570.

9 M. Fuchs, D. Koszelewski, K. Tauber, W. Kroutil and K. Faber, Chemoenzymatic asymmetric total synthesis of (S)-Rivastigmine using ω-transaminases, *ChemComm*, 2010, **46**, 5500–5502.