Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Ethyl Acetate as Acyl Donor on the Continuous Flow Kinetic Resolution of (+/-)-1-phenylethylamine Catalyzed by Lipases

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Supporting Information

1. Experimental

1.1. General:

Toluene and Ethyl Acetate were purchased from Vetec and used as received. (+/-)-1-phenylethylamine was purchased from Sigma-Aldrich and distilled and stored under Argon atmosphere. (*S*)-1-Phenylethylamine was purchased from Fluka, Methyl 2-methoxyacetate and Isopropenyl Acetate was purchased from Sigma-Aldrich and all were used as received. All enzymes were purchased from Novozymes and used as received.

Reactions under continuous flow were performed using an Asia Flow system which consists of a syringe pump, a solid phase glass column reactor (d = 1.0000 cm^2) with adjustable ends and a heater. All equipments were purchased from Syrris.

Chiral GC analysis was performed on a Shimadzu GC-2010 chromatograph equipped with a FID, an AOC-20i autosampler and a chiral CP-Chirasil-Dex CB (25 m X 0.25 mm ID) or a chiral β-Dex325 (30 m X 0.24 mm ID) column using hydrogen as carrier gas. Injector and detector temperatures were set at 220 °C. GC-FID temperature program for 1-phenylethylamine (**1**) using β-Dex325 column: 90°C | 30 min → 180°C, 40°C/min |10 min. GC-FID temperature program for 1-phenylethylamine (**1**) using CP-Chirasil-Dex CB column: 90°C | 30 min → 180°C, 40°C/min |10 min. GC-FID temperature program for *N*-(1-phenylethyl)acetamide (**3a**) using β-Dex325 column: 100°C | 5 min → 160°C, 1.5 °C/min | 5min → 200 °C, 20 °C/min | 5 min. GC-FID temperature program for 2-methoxy-*N*-(1-phenylethyl)acetamide (**3b**) using CP-Chirasil-Dex CB column: 105°C | 9 min → 180°C, 140 °C/min | 10 min. GC-MS analysis were performed on a Shimadzu GC-MS-QP2010 Plus chromatograph mass spectrometer equipped with an AOC-20i autosampler and a 5-(Phenyl)Methylpolysiloxane Quadrex (29.6 m X 0.25 mm ID) column using Helium as carrier gas.. Injector temperature was set at 250 °C. GC-MS temperature program: 60°C | 2 min → 280°C, 20 °C/min | 15min.

1.2. Synthesis of (+/-)-*N*-(1-phenylethyl)acetamide (3a):[1]

Acetic anhydride (0.60 mL, 2 mmol) was added dropwise to a solution of (+/-)-1-phenylethylamine (**1**) (0.50 mL, 4 mmol) in $CHCl_3$ (3.50 mL) at 0 °C. After completion of the reaction, ice water (3.5 mL) was added and the mixture was extracted with $CHCl_3$ (3 X 3.5 mL). The organic layer was washed with 1N aqueous solution of NaOH (2.5 mL), dried over $MgSO_4$,

filtered and concentrated under reduced pressure. After evaporation of $CHCl_3$ the title compound was obtained (0.522 g, 80 %) as colourless crystals and was analyzed by GC-MS and used for optimization of chiral GC-FID temperature program.

1.3. Synthesis of (+/-)-2-methoxy-*N*-(1-phenylethyl)acetamide (3b):

A solution of racemic (+/-)-1-phenylethylamine (0.24 mmol) and methyl 2-methoxyacetate 0.96 mmol) in toluene (3 mL) was stirred at 70°C for 24h. The reaction media was washed with a 10% aqueous solution of HCl and dried over Na_2SO_4. An aliquot of 300 µL was collected, diluted in 700 µL of toluene and directly analyzed by GC-MS spectrometer and used for optimization of chiral GC-FID temperature program.

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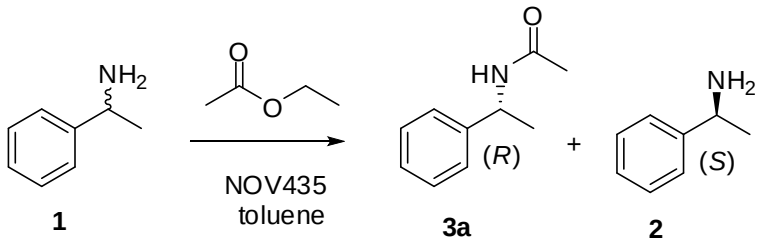
1.4. General procedure for enzymatic kinetic resolution of (+/-)-1-phenylethylamine (1) under continuous flow conditions:

A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and acyl donor (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized enzyme (1.4 g; volume = 3.927 cm^3) at different flow rates (1.0; 0.5 and 0.1 $mL.min^{-1}$, corresponding to residence times of 4, 8 and 40 minutes, respectively) and temperatures (25, 35, 50 and 70°C). Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product (ee_p). The *ee* of substrate (ee_s) was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Comparison between substrate chromatograms and (*S*)-1-phenylethylamine and (*R*)-1-phenylethylamine chromatograms indicated that (*R*)-1-phenylethylamine was consumed, thus producing (*R*)-N-(1-phenylethyl)acetamide, as expected from previous reported data.[2-4] Some reactions were chosen for analysis by GC-MS in order to confirm the structure of products and identify byproducts. Conversion (*C*) was calculated as $C = ee_s / (ee_p + ee_s)$ and enantiomeric ratio (*E*) was calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$.[5] When byproducts were detected, their percentages were calculated from relative area of theirs peaks in chromatograms of products (i.e. these obtained from aliquots without addition of trifluoracetic anhydride and triethylamine).

1.4.1. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Ethyl Acetate under continuous flow conditions:



A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and Ethyl Acetate (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at different flow rates (1.0; 0.5 and 0.1 mL.min^{-1}, corresponding to residence times of 4, 8 and 40 minutes, respectively) and temperatures (35, 35, 50 and 70°C). Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 1.

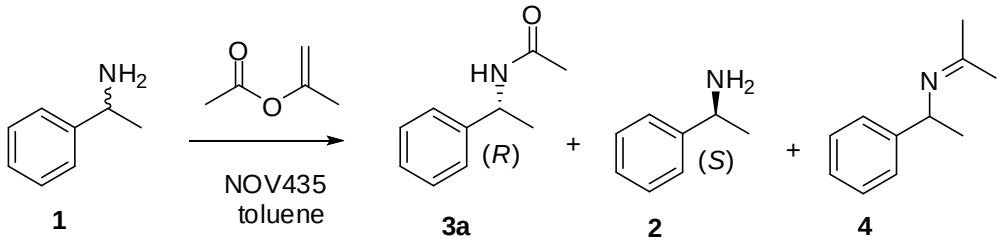
Table 1. Kinetic resolution of (+/-)-1-phenylethylamine with Ethyl Acetate as acyl donor under continuous flow conditions.

Temperature (°C)	Residence Time (min.)	ee_p (%)	ee_s (%)	*C* (%)	*E*
25°C	4	>99	10	9	>200
	8	>99	19	16	>200
	40	>99	45	31	>200
35°C	4	>99	16	14	>200
	8	>99	24	19	>200
	40	>99	62	38	>200
50°C	4	>99	21	17	>200
	8	>99	33	25	>200
	40	>99	79	44	>200
70°C	4	>99	31	24	>200

	8	>99	52	34	>200
	40	99	94	48	>200

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

1.4.2 Kinetic resolution of (+/-)-1-phenylethylamine (1) with Isopropenyl Acetate under continuous flow conditions:



A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and Isopropenyl Acetate (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at different flow rates (1.0; 0.5 and 0.1 $mL.min^{-1}$, corresponding to residence times of 4, 8 and 40 minutes, respectively) and temperatures (35, 35, 50 and 70°C). Aliquots of 300 µL were taken at the exit of the reactor and diluted toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 2.

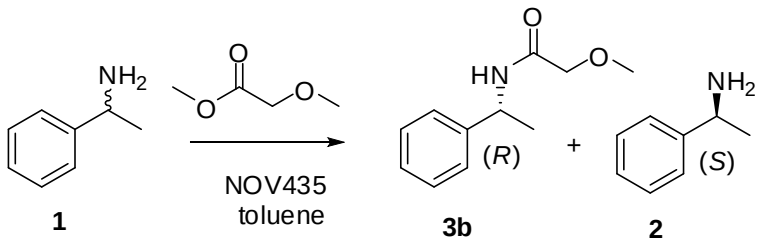
Table 2. Kinetic resolution of (+/-)-1-phenylethylamine with Isopropenyl Acetate as acyl donor under continuous flow conditions

Temperature (°C)	Residence Time (min.)	ee_p (%)	ee_s (%)	*C* (%)	*E*	Percentage of by product **4**
	4	84	38	31	17	3
25°C	8	82	86	51	27	5
	40	79	91	54	28	9
35°C	4	72	61	46	11	5

	8	79	69	47	18	6
	40	81	80	50	24	12
	4	64	55	46	8	4
50°C	8	64	58	48	8	7
	40	68	70	51	11	7
	4	52	53	50	5	5
70°C	8	54	60	53	6	6
	40	59	67	57	9	3

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess and percentage of byproducts were determined by chiral GC.

1.4.3. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Methyl 2-methoxyacetate under continuous flow conditions:



A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and Methyl 2-methoxyacetate (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at different flow rates (1.0; 0.5 and 0.1 $mL.min^{-1}$, corresponding to residence times of 4, 8 and 40 minutes, respectively) and temperatures (35, 35, 50 and 70°C). Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 3. The same procedure was carried out at room temperature with 3.6, 10.8 and 18.0 mmol of Methyl 2-methoxyacetate (Table 4).

Table 3. Kinetic resolution of (+/-)-1-phenylethylamine with Methyl 2-methoxyacetate as acyl donor under continuous flow conditions.

Temperature (°C)	Residence Time (min.)	ee_p (%)	ee_s (%)	*C* (%)	*E*
25°C	4	>99	20	17	>200
	8	>99	78	44	>200
	40	99	96	49	>200
35°C	4	>99	74	43	>200
	8	99	90	47	>200
	40	97	99	50	>200
50°C	4	99	83	46	>200
	8	98	94	49	>200
	40	94	>99	51	146
70°C	4	98	92	48	>200
	8	98	99	50	>200
	40	90	>99	52	83

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)]/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

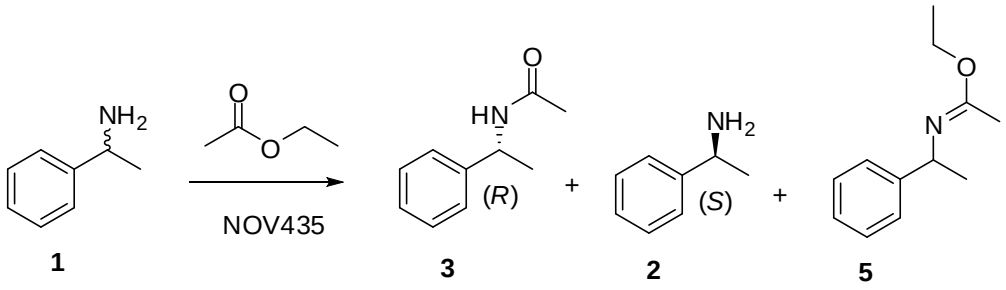
Tabela 4. Variation of acyl dono:substrate ratio in the kinetic resolution of (+/-)-1-phenylethylamine with Methyl 2-methoxyacetate as acyl donor under continuous flow conditions.

Acyl donor:substrate ratio	Residence Time (min.)	ee_p (%)	ee_s (%)	*C* (%)	*E*
1:1	4	>99	62	38	>200
	8	>99	74	43	>200
	40	99	96	49	>200
3:1	4	>99	62	38	>200
	8	>99	82	45	>200
	40	>99	95	49	>200

	4	>99	88	47	>200
5:1	8	99	96	49	>200
	40	97	99	50	>200

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

1.4.5. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Ethyl Acetate as solvent under continuous flow conditions:



A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) in Ethyl Acetate (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at different flow rates (0.1; 0.5 and 1.0 $mL.min^{-1}$) and temperatures (35, 35, 50 and 70°C). Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 5.

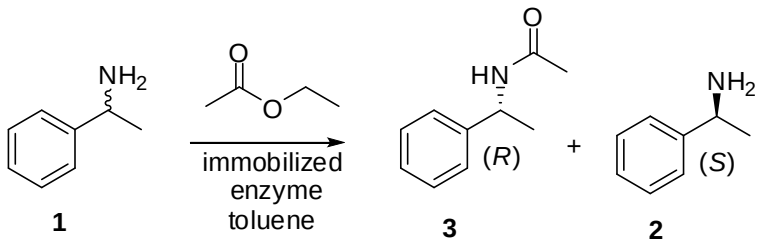
Tabela 5. Kinetic resolution of (+/-)-1-phenylethylamine with Ethyl Acetate as solvent under continuous flow conditions.

Temperature (°C)	Residence Time (min.)	ee_p (%)	ee_s (%)	*C* (%)	*E*	Percentage of by product **5**
25°C	4	98	13	12	113	5
	8	98	19	16	118	5

	40	98	53	35	168	1
	4	92	17	16	28	1
35°C	8	93	19	17	33	1
	40	96	57	37	87	1
	4	87	18	17	17	4
50°C	8	90	23	20	24	4
	40	95	71	43	84	3
	4	82	23	22	13	3
70°C	8	94	35	27	45	3
	40	90	89	50	58	3

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess and percentage fo byproducts were determined by chiral GC.

1.4.6. Kinetic resolution of (+/-)-1-phenylethylamine (1) with different immobilized enzymes under continuous flow conditions:



A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and Ethyl Acetate (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized enzyme (1.4 g) at 50 °C and 70 °C at flow rate of 0.1 $mL.min^{-1}$.Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to 1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Resultas are summarized in Table 6.

Tabela 6. Kinetic resolution of (+/-)-1-phenylethylamine with different immobilized enzymes under continuous flow conditions.

Enzyme	Temperature (°C)	ee_p (%)	ee_s (%)	*C* (%)	*E*
RMIM	50	>99	0,3	0,3	199
	70	>99	0,2	0,2	199
TLIM	50	-	0,6	-	-
	70	-	1,9	-	-
PS"amano"IM	50	4,6	0,6	11	1
	70	>99	1,5	1,5	202

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)]/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

1.4.7. Evaluation of continuous flow system stability during kinetic resolution of (+/-)-1 phenylethylamine (1):

A solution of (+/-)-1-phenylethylamine (**1**) (3.6 mmol) and Ethyl Acetate (14.4 mmol) in toluene (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at 70°C and flow rate of 0.1 $mL.min^{-1}$. Aliquots of 300 µL were taken at the exit of the reactor every one hour and diluted in toluene (1.0 mL). Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 7.

Tabela 7. Evaluation of continuous flow system stability during kinetic resolution of (+/-)-1-phenylethylamine

Time (h)	ee_p (%)	ee_s (%)	*C* (%)	*E*
1	99	89	47	>200
2	98	96	50	>200
3	99	97	49	>200
4	97	97	50	>200

5	99	97	50	>200
6	97	98	50	>200
7	99	98	50	>200
8	99	98	50	>200
9	>99	98	50	>200

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

1.4.8. Evaluation of continuous flow system capability of operating with high concentration of substrate:

A solution of (+/-)-1-phenylethylamine (**1**) (3.6-40.5 mmol) and acyl donor (14.4-162 mmol) in toluene (45 mL) was pumped through a column packed with immobilized *Candida antartica* lipase B (NOV435) (1.4 g) at 70°C and flow rate of 0.1 mL.min^{-1}. Aliquots of 300 µL were taken at the exit of the reactor and diluted in toluene to1.0 mL. Aliquots were analyzed by GC directly for *ee* of product. The *ee* of substrate was determined by GC after derivatization with 5 µL of trifluoracetic anhydride and 5 µL of triethylamine. Results are summarized in Table 8.

Tabela 8. Evaluation of continuous flow system capability of operating with high concentration of substrate

Concentration (mol.L^{-1})	ee_p (%)	ee_s (%)	*C* (%)	*E*
0.80	>99	94	48	>200
0.150	99	85	46	>200
0.300	99	76	43	>200
0.450	99	69	41	>200
0.600	99	78	44	>200
0.750	99	72	42	>200
0.900	99	72	42	>200

Conversions (*C*) were calculated as $C = ee_s/(ee_p + ee_s)$, where ee_r and ee_p are the enantiomeric excess of amine 2 and amide 3, respectively. Enantiomeric ratios (*E*) are calculated as $E = \ln[1 - C(1-ee_p)/\ln[1-C(1 + ee_p)]$. Enantiomeric excess were determined by chiral GC.

References:

(1) Palecek, J.; Zweigerdt, R.; Olmer, R.; Martin, U.; Kirschning, A.; Dräger, G. *Org. Biomol. Chem.* **2011**, *9*, 5503.

(2) Pilissao, C.; Carvalho, P. d. O.; Nascimento, M. d. G. *Process Biochemistry* **2009**, *44*, 1352.

(3) Munoz, L.; Rodriguez, A. M.; Rosell, G.; Bosch, M. P.; Guerrero, A. *Organic & Biomolecular Chemistry* **2011**, *9*, 8171.

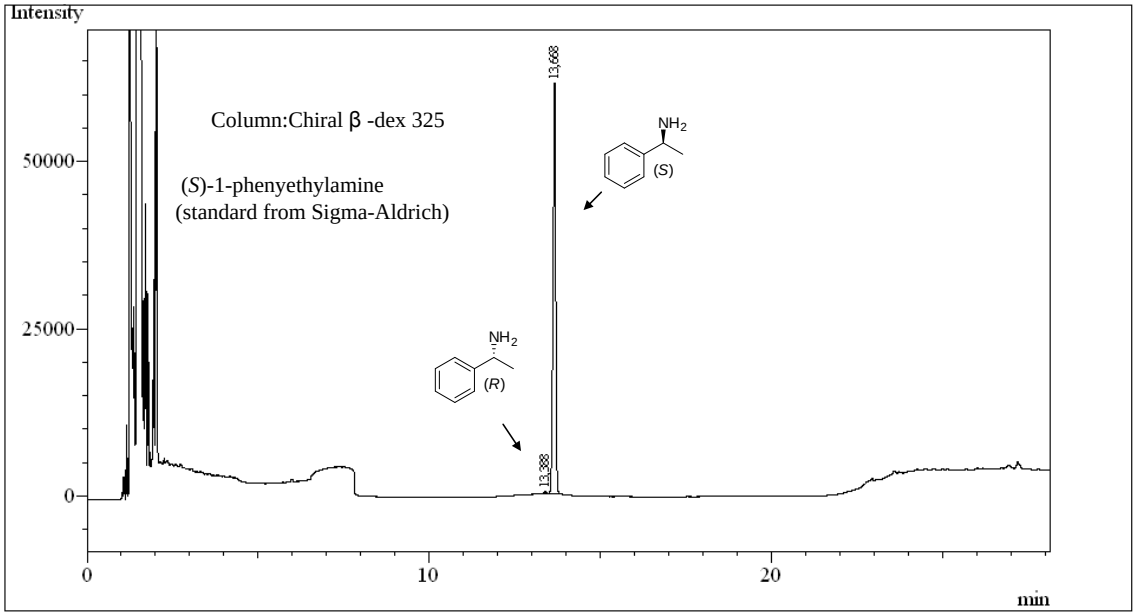
(4) Sontakke, J. B.; Yadav, G. D. *J. Chem. Technol. Biotechnol.* **2011**, *86*, 739.

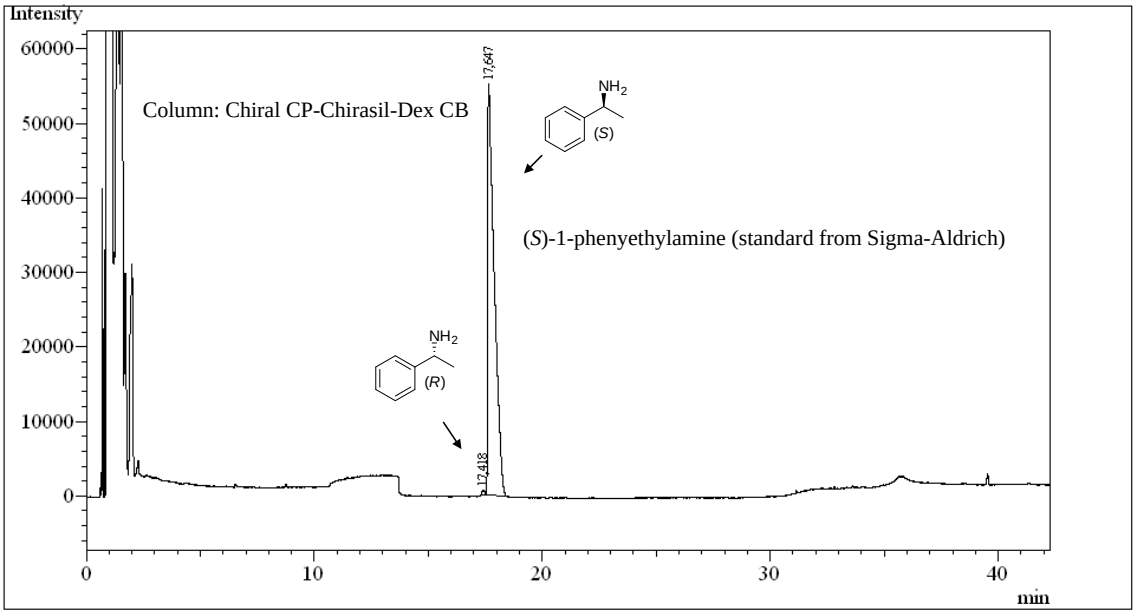
(5) Faber, K. *Biotransformations in Organic Chemistry*, 5th Ed. Springer-Verlag, **2005**.

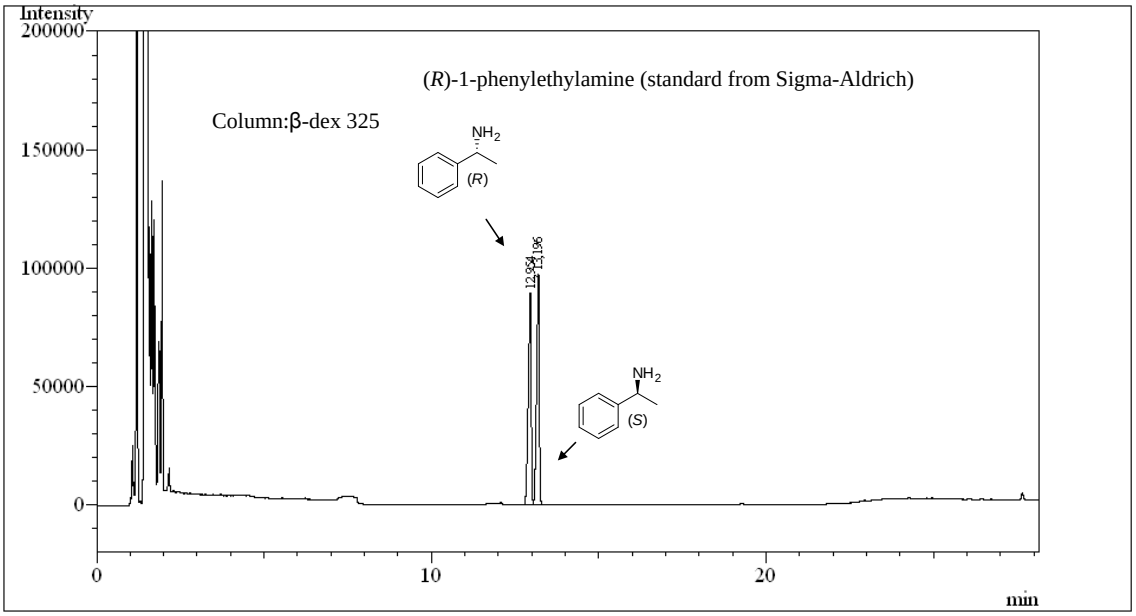
2. Chromatograms

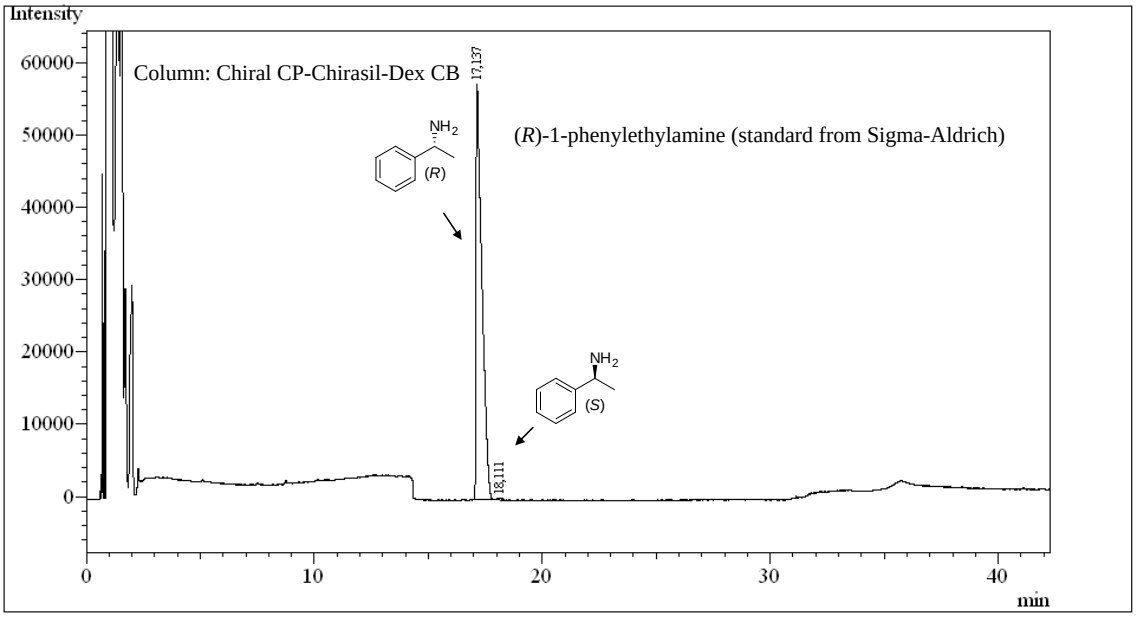
2.1. Chromatograms obtained from chiral gas chromatograph

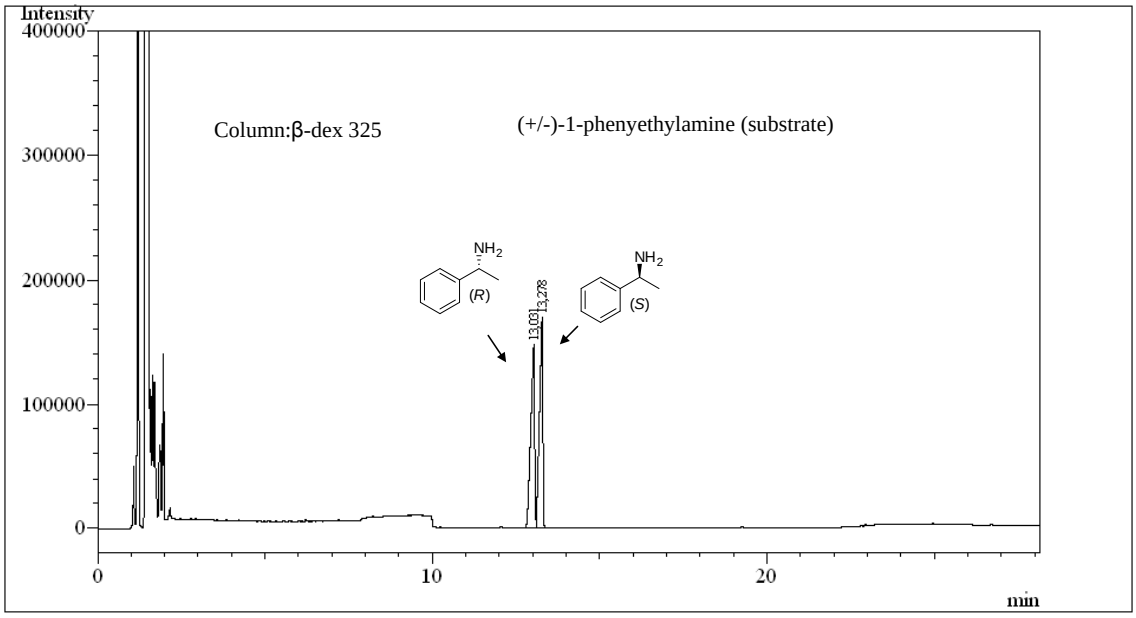
2.1.1. Standard compounds

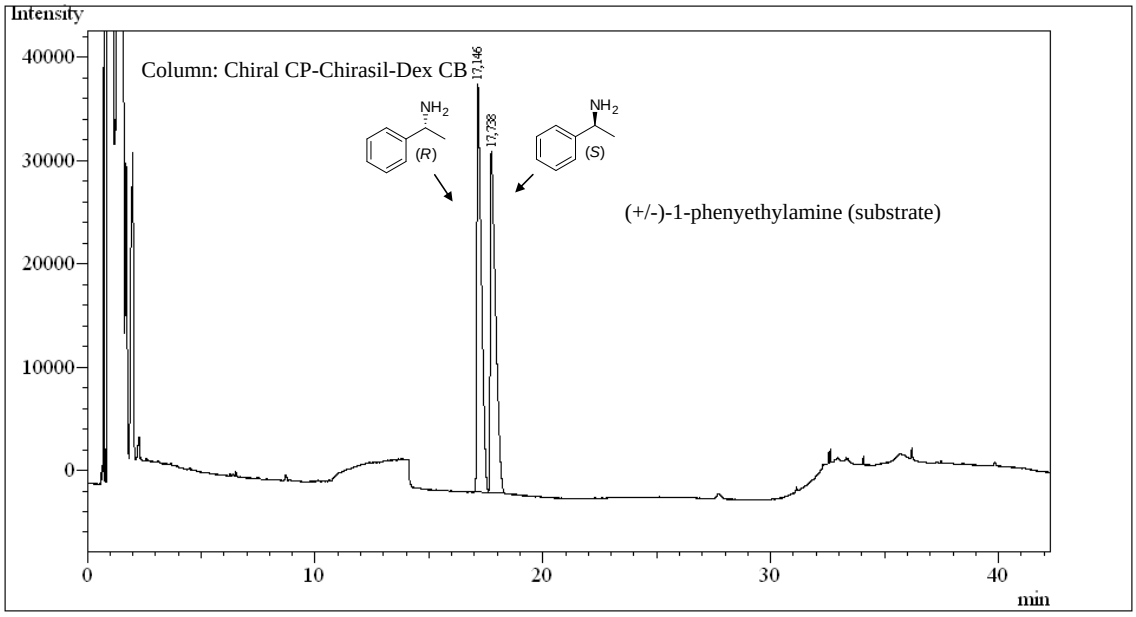


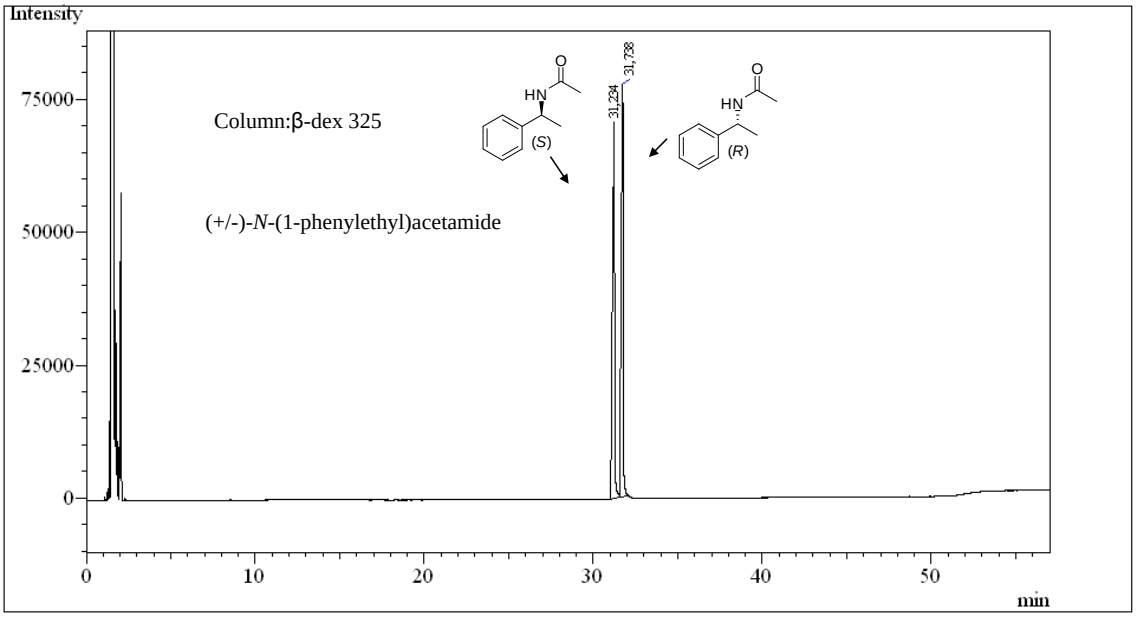


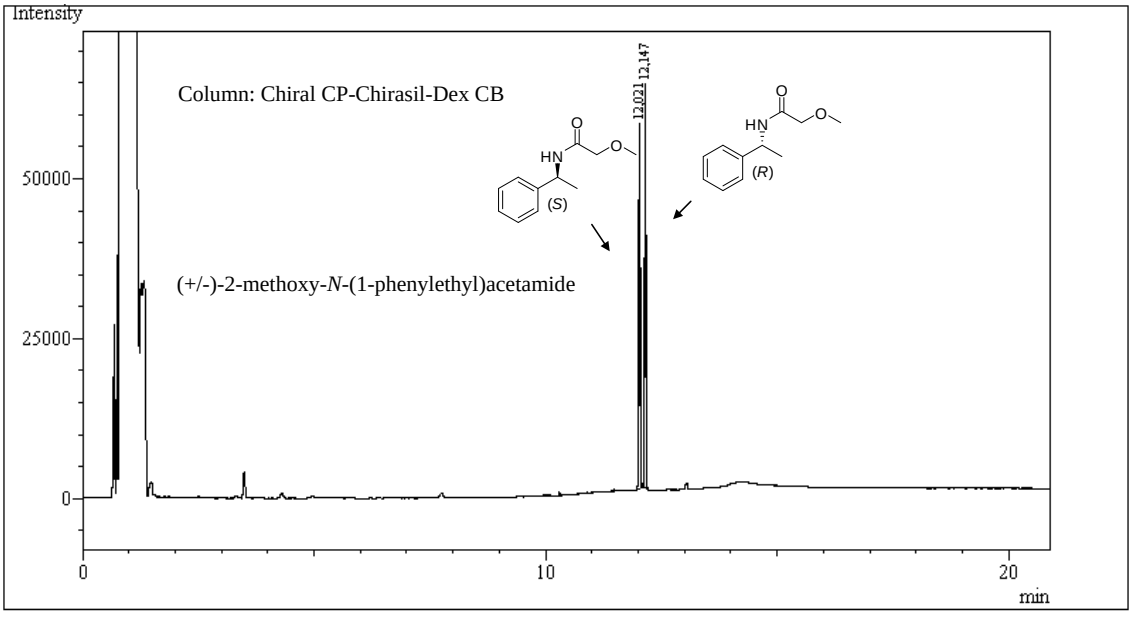




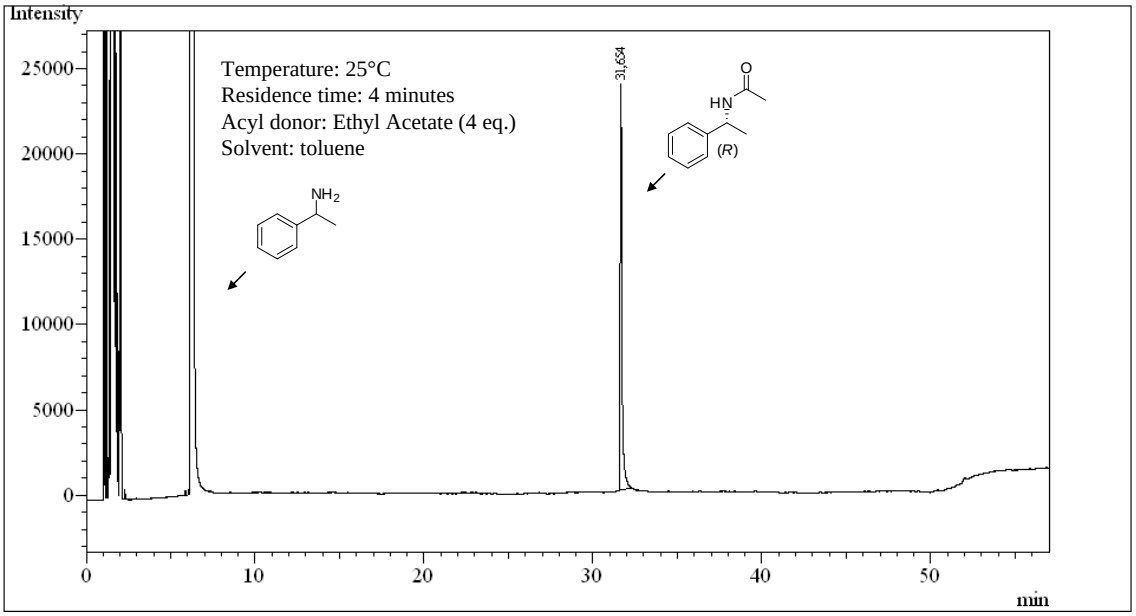


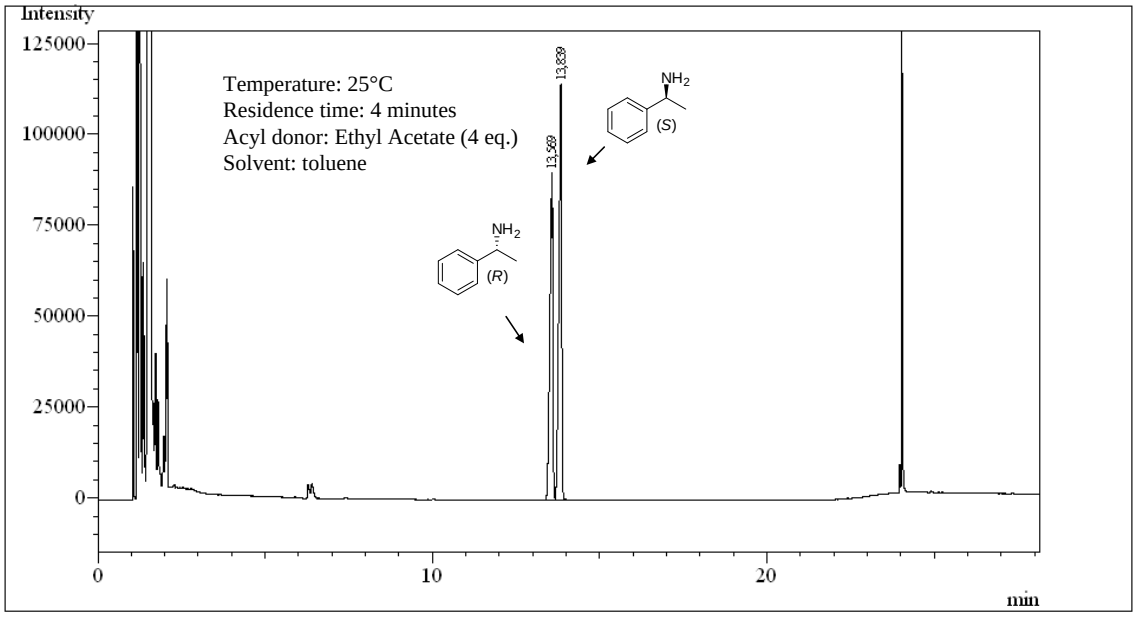


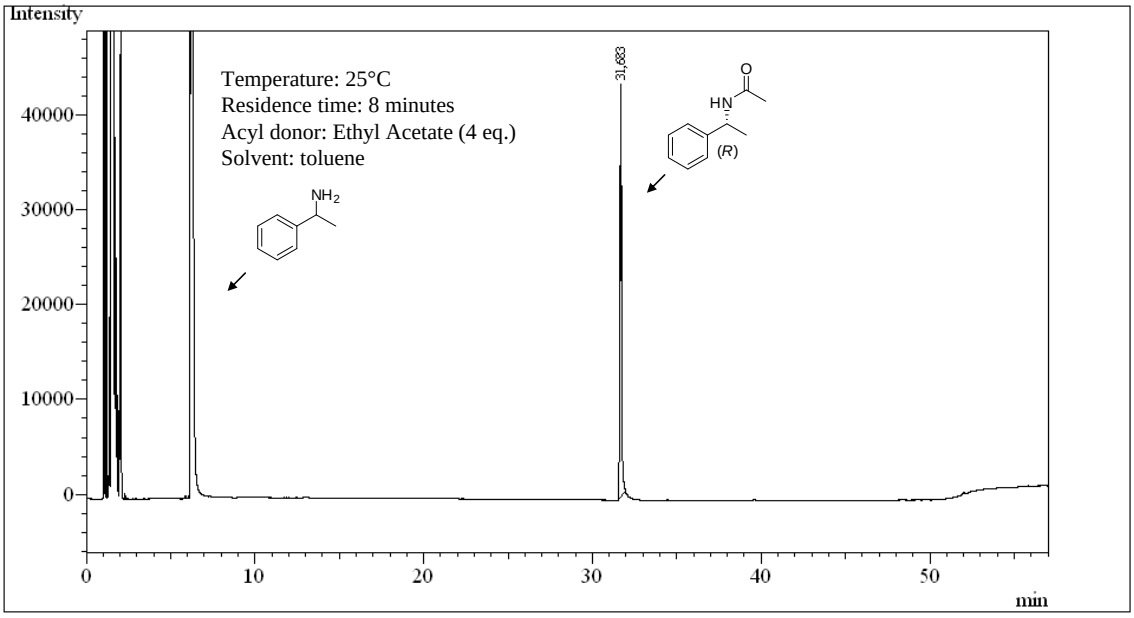


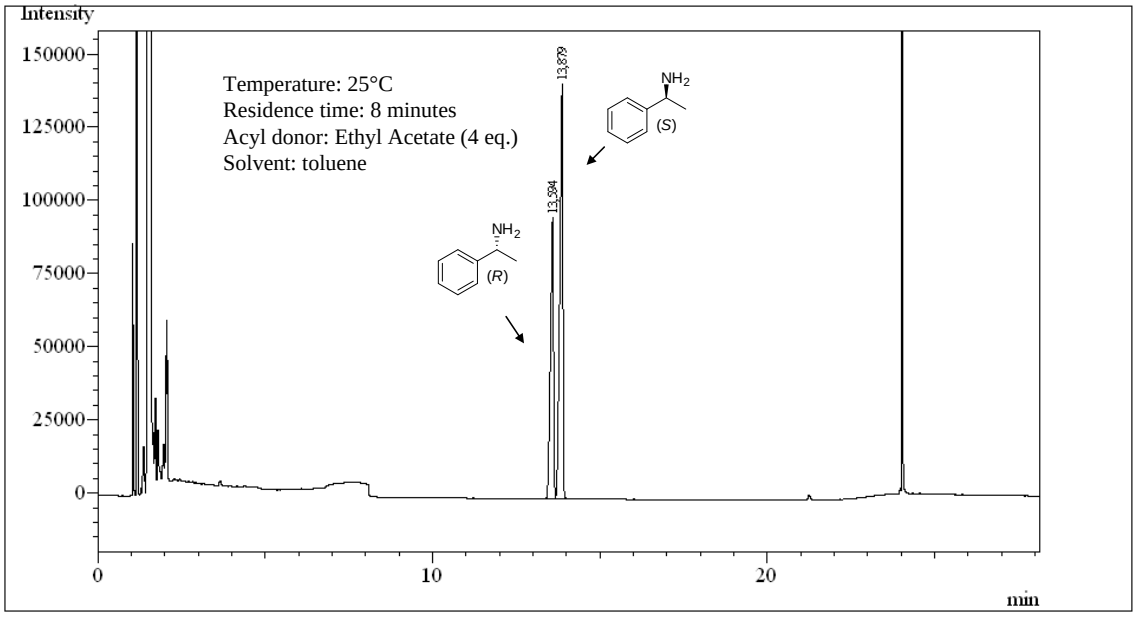


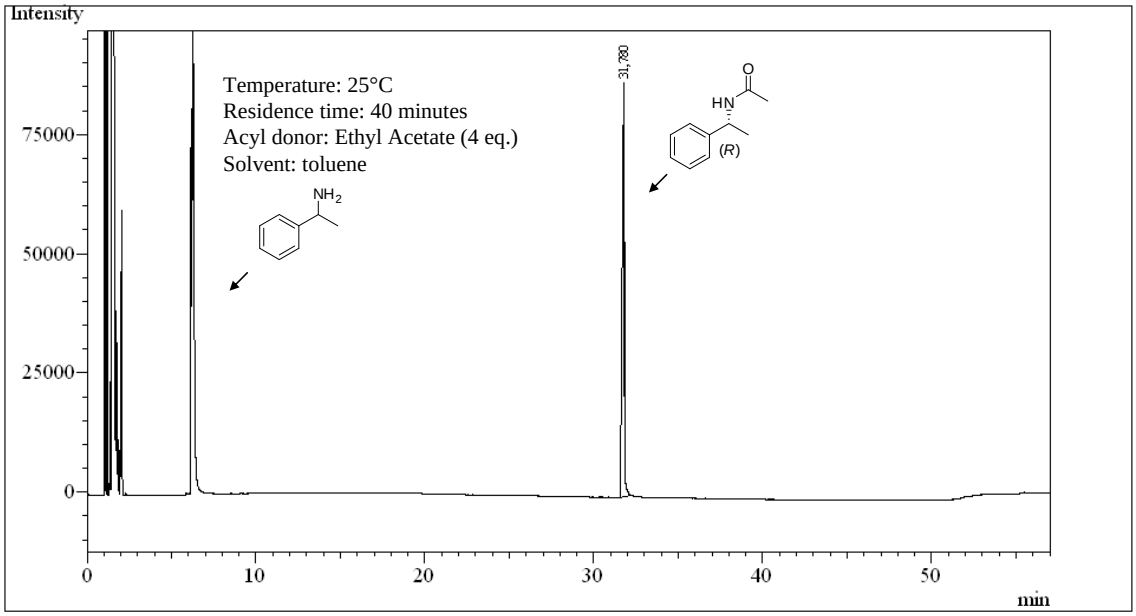
2.1.2. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Ethyl Acetate under continuous flow conditions

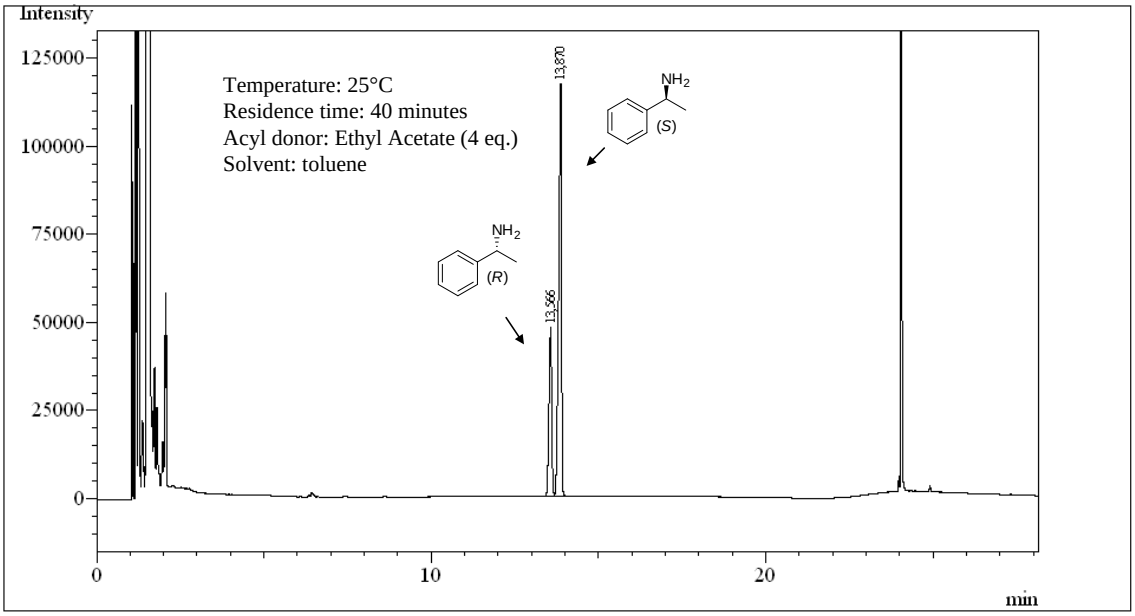


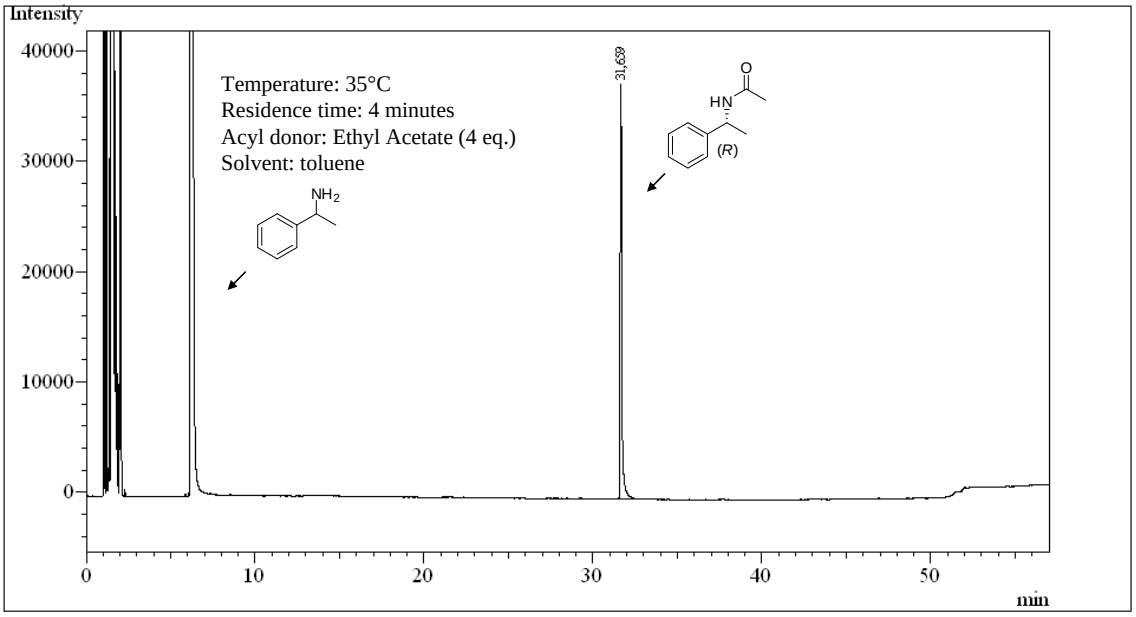


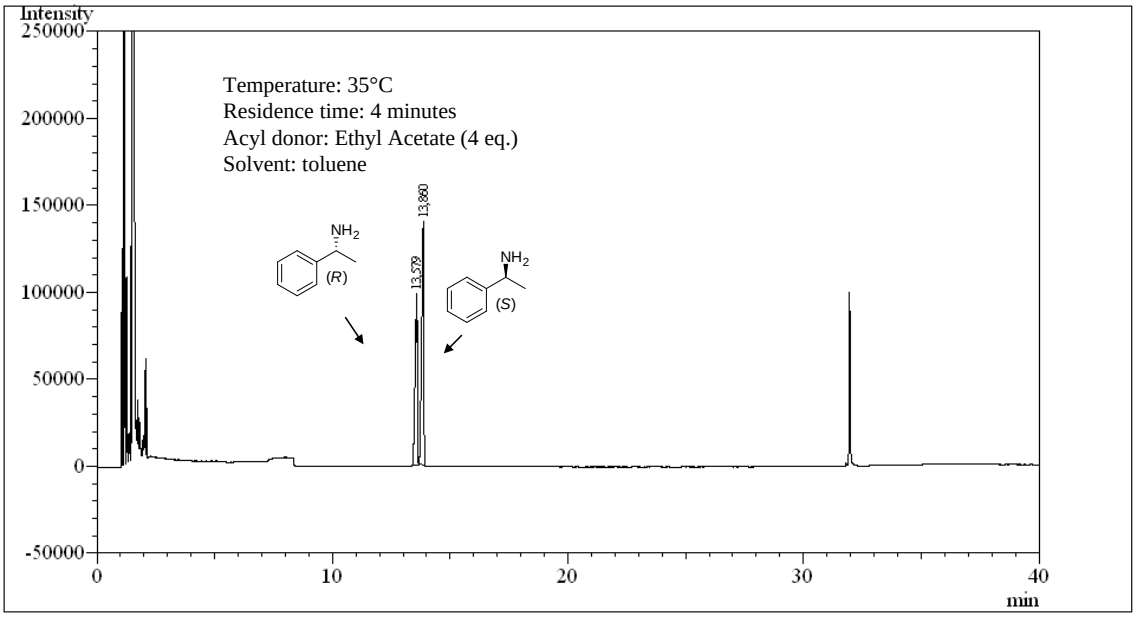


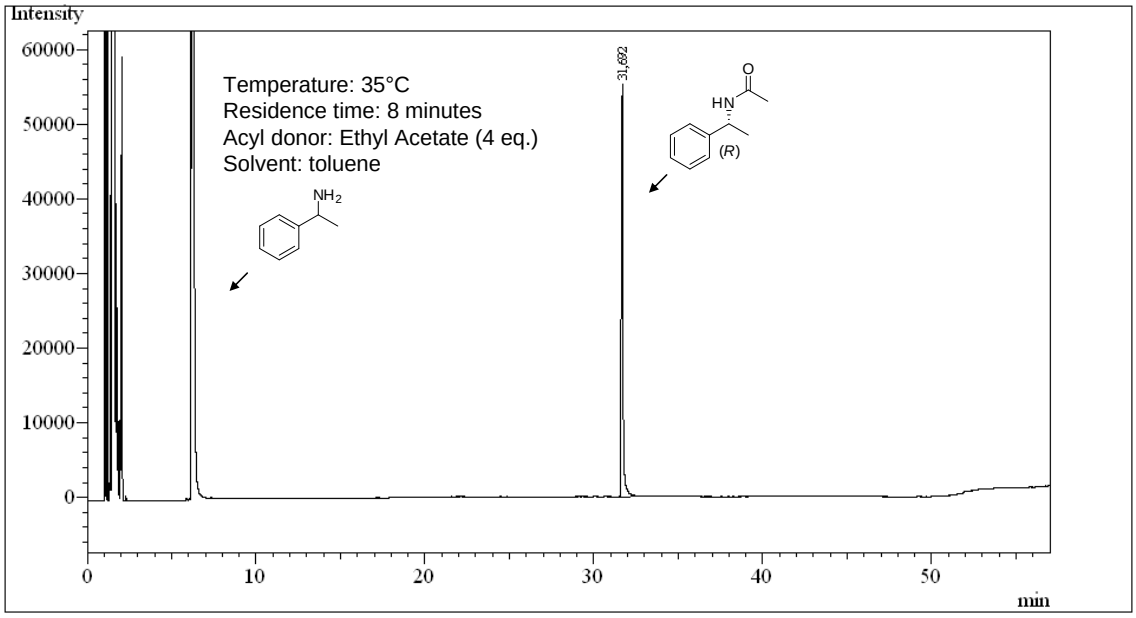


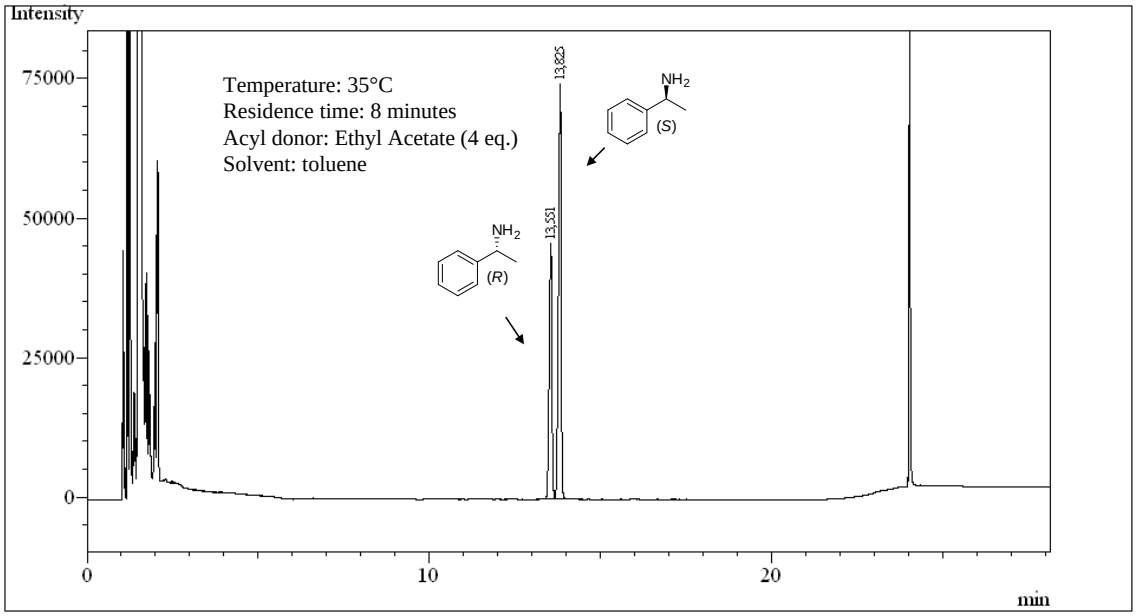


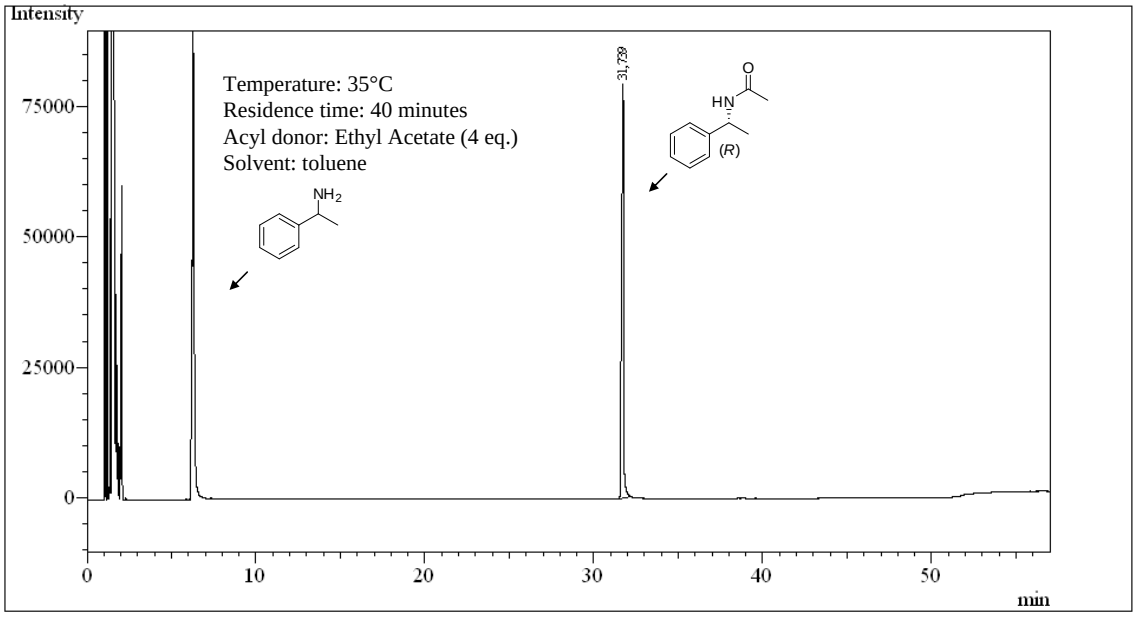


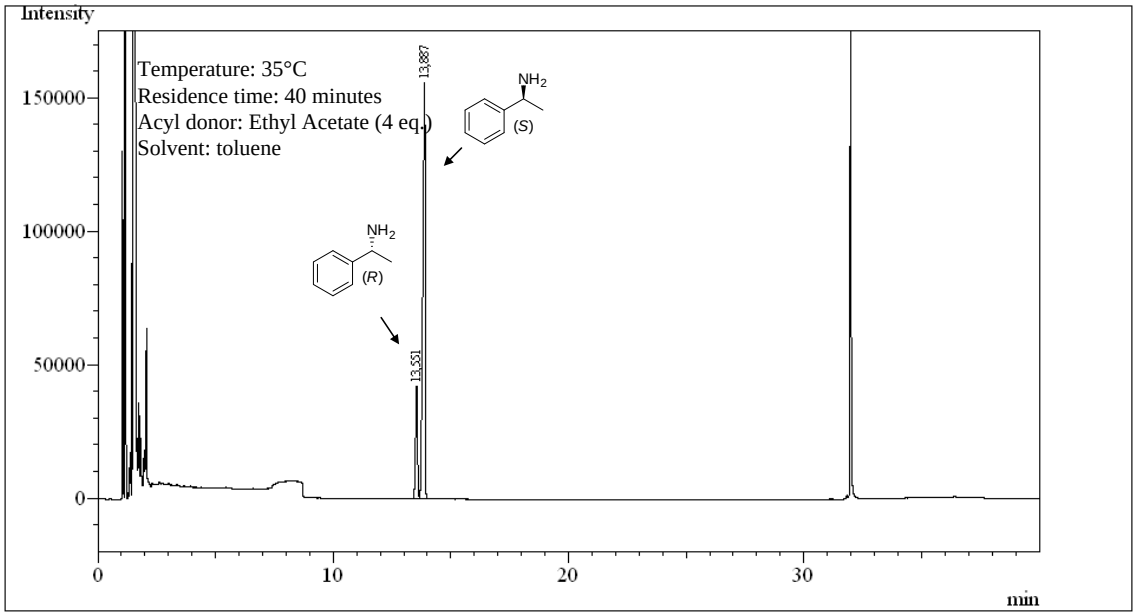


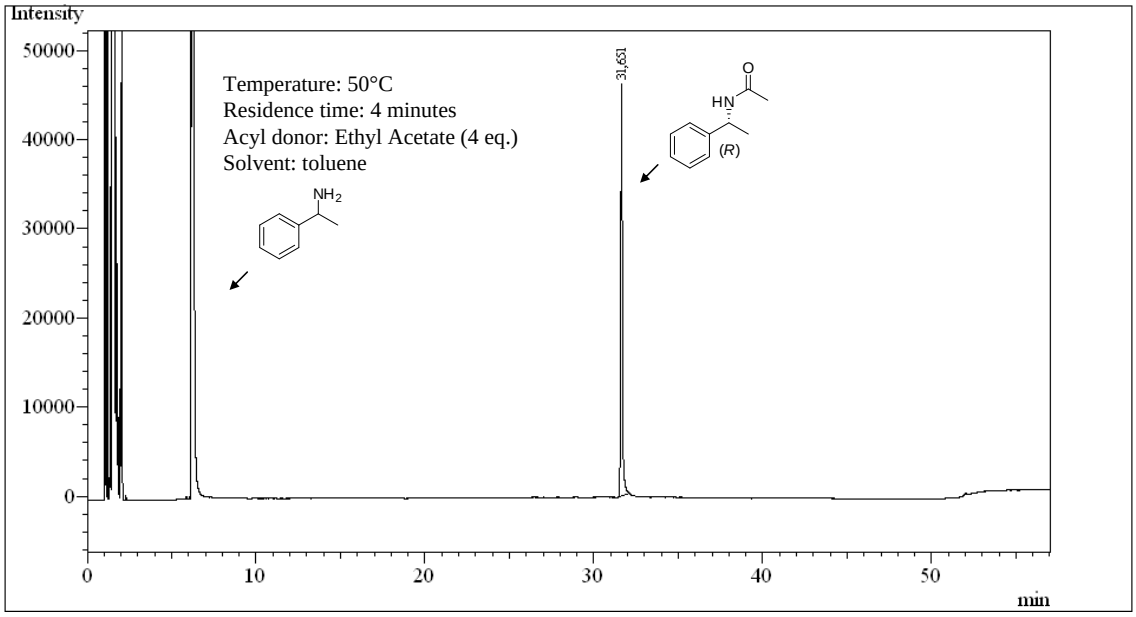


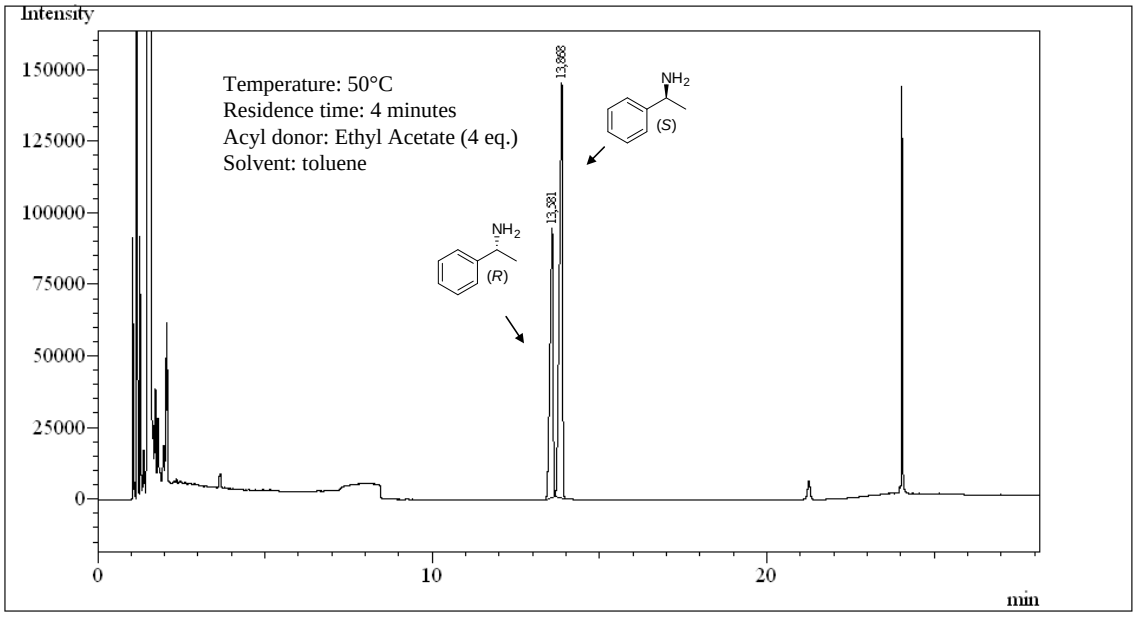


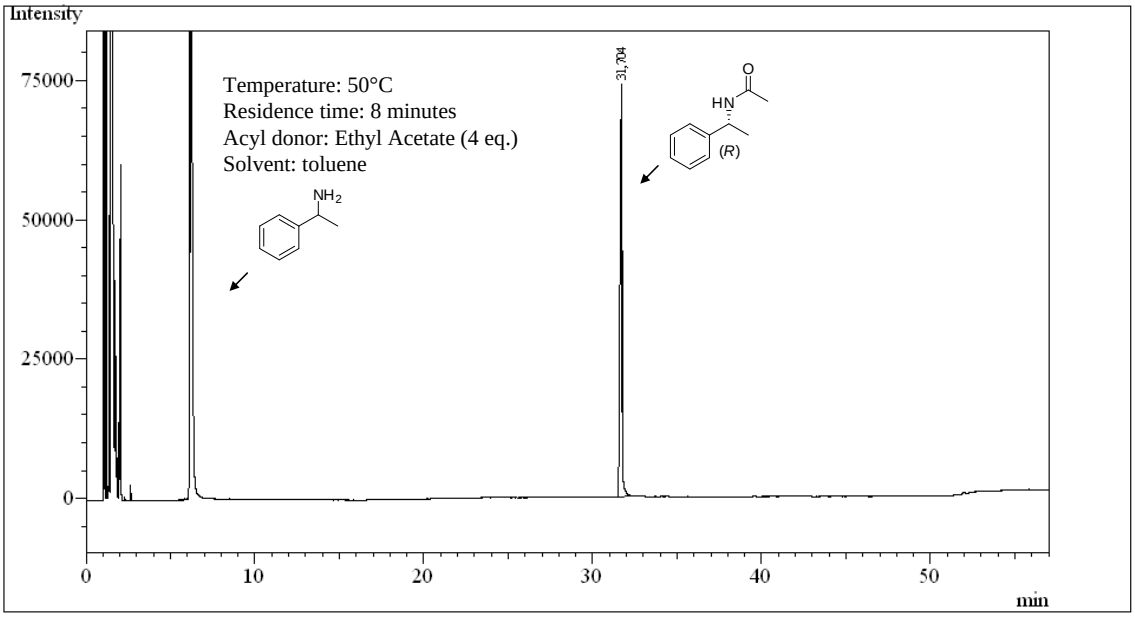


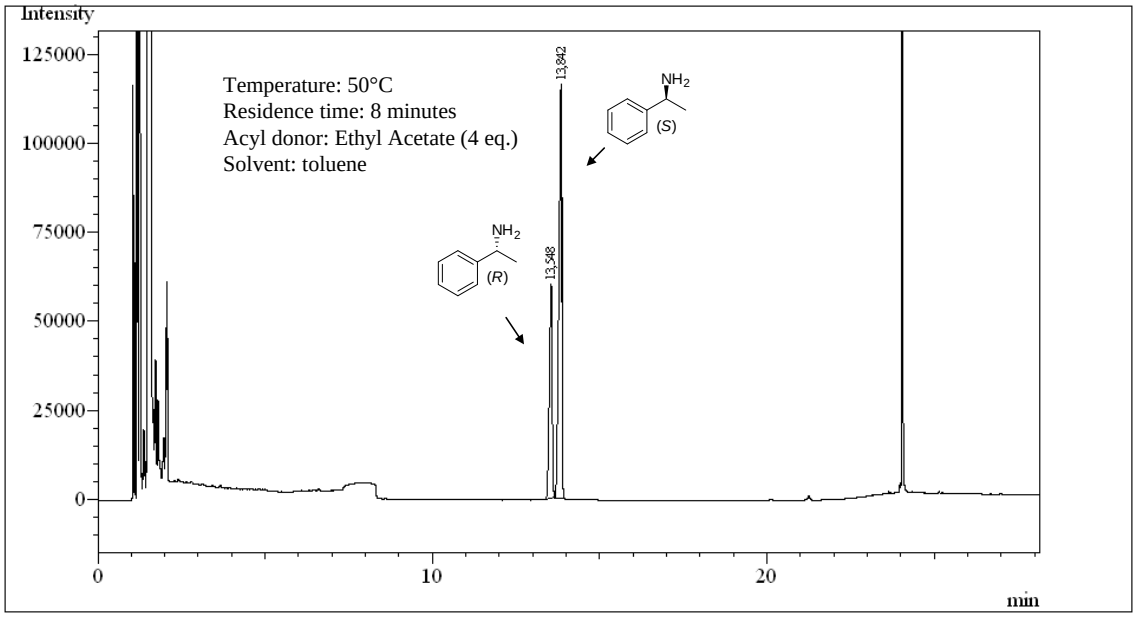


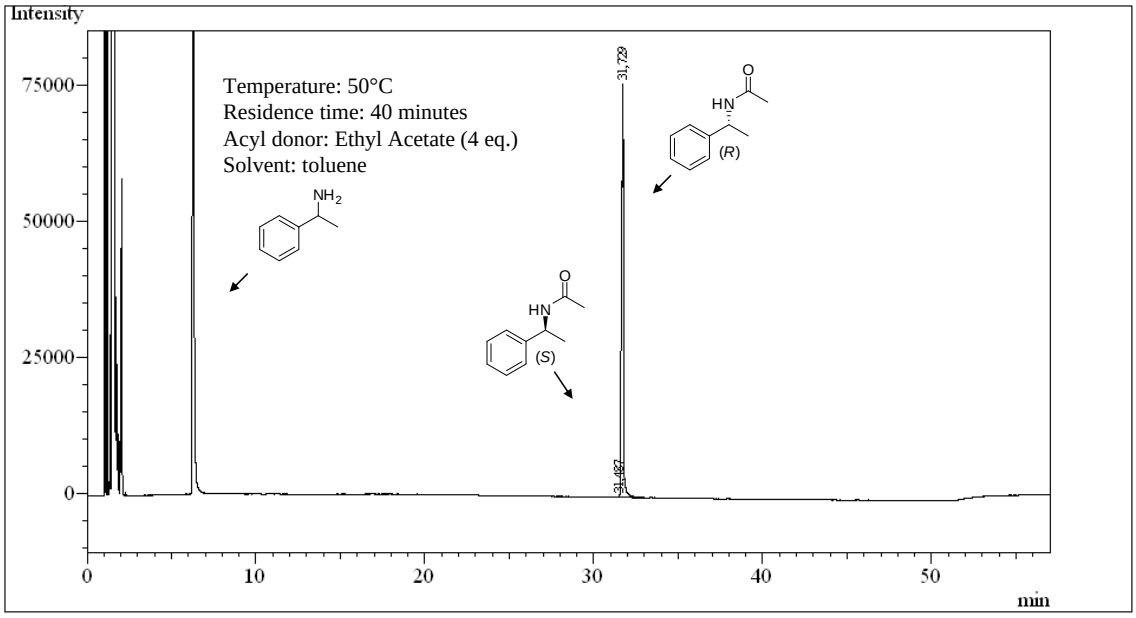


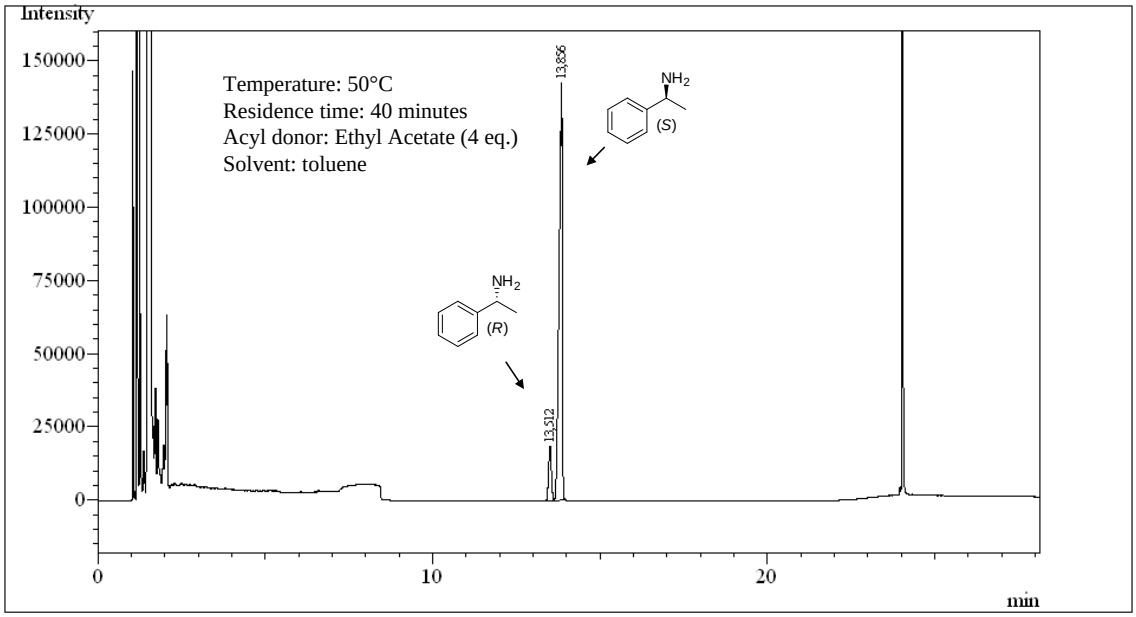


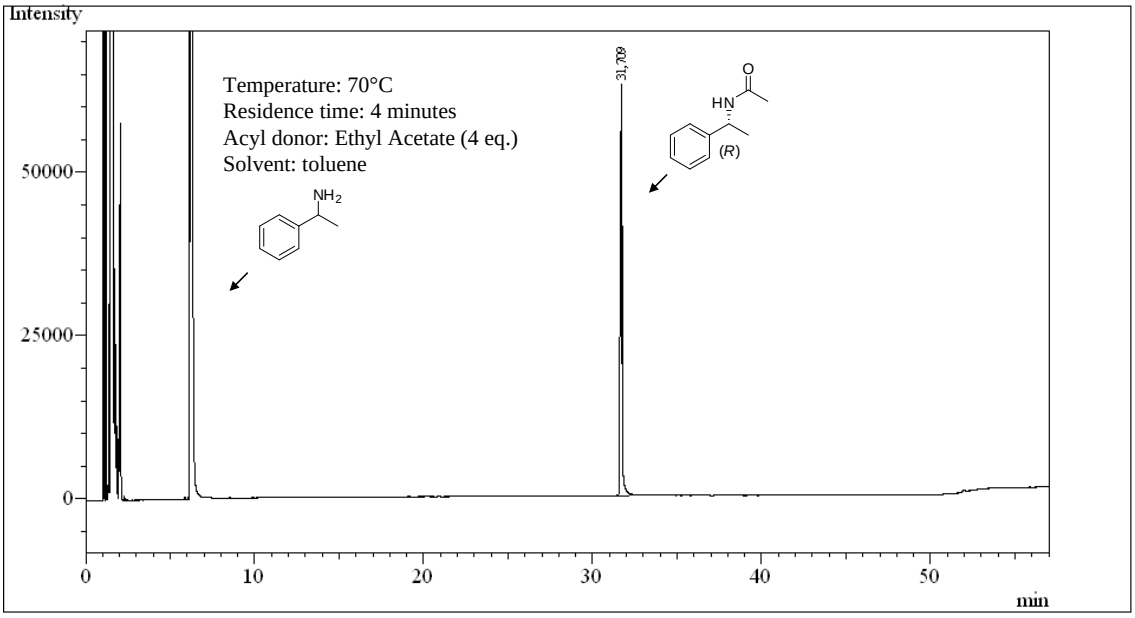


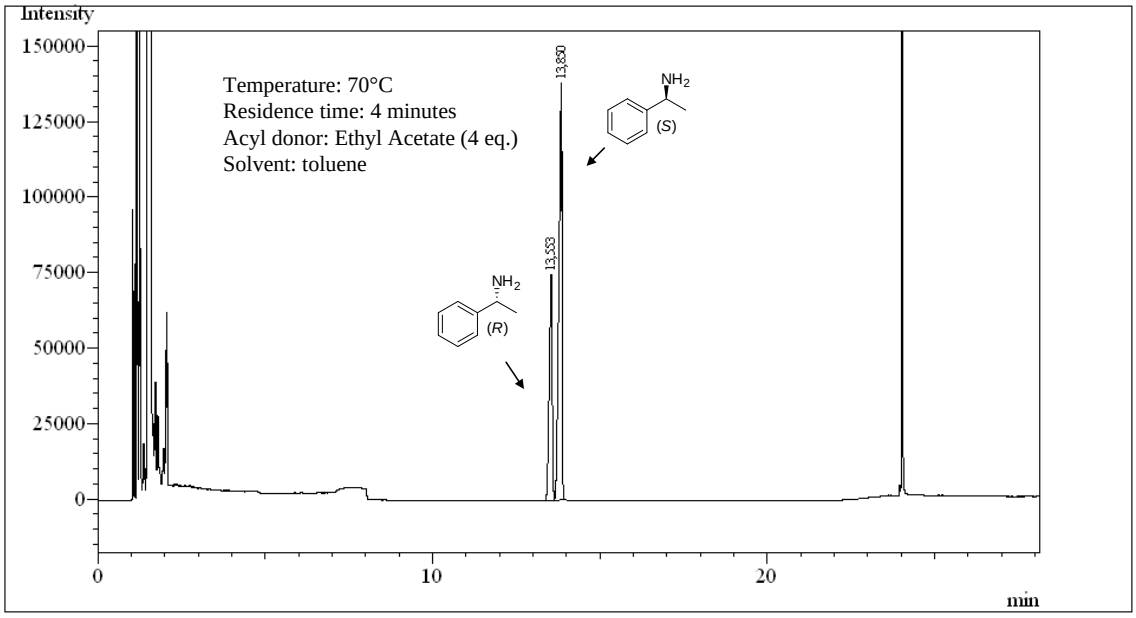


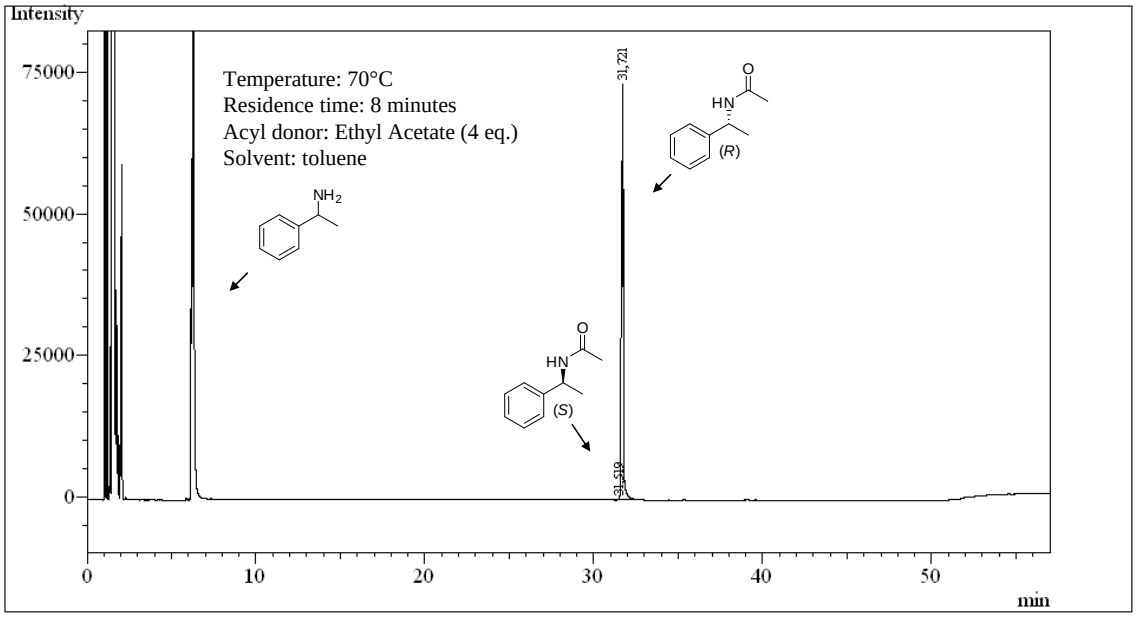


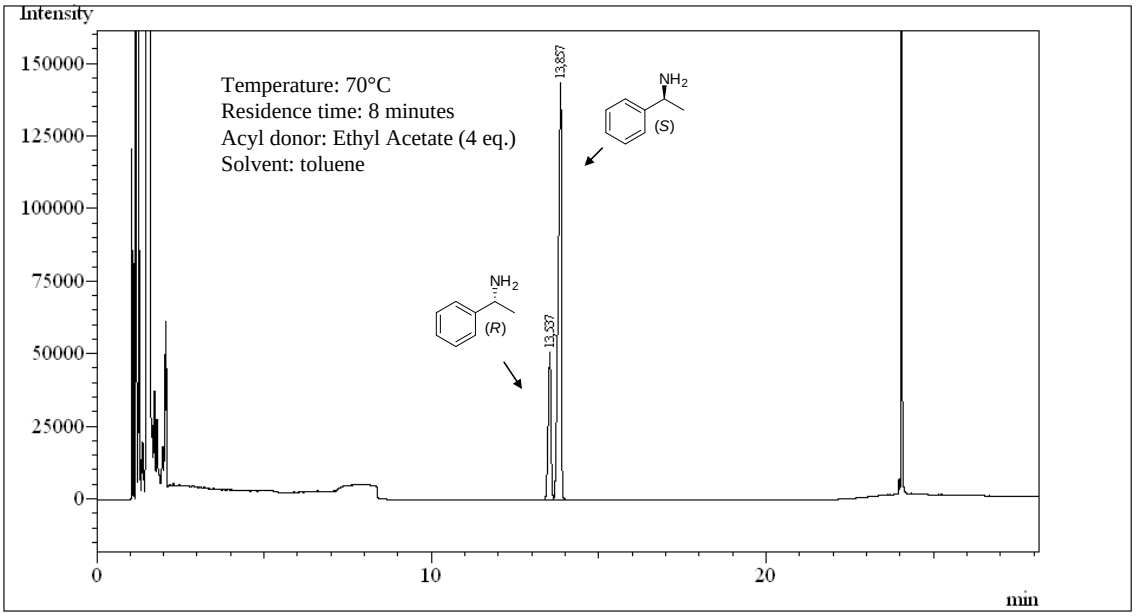


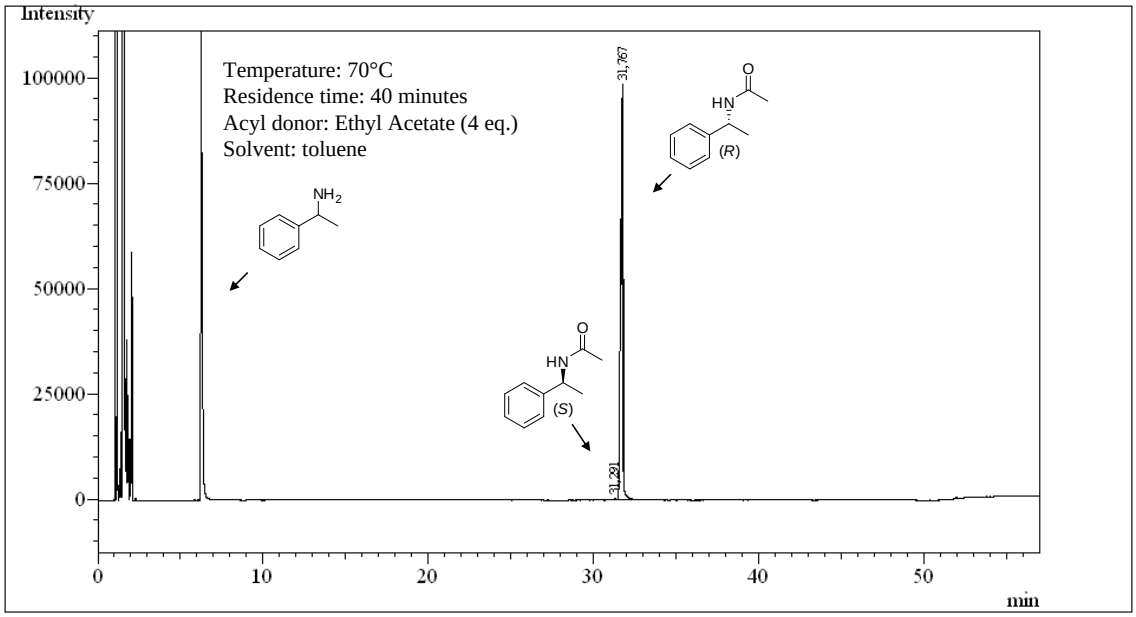


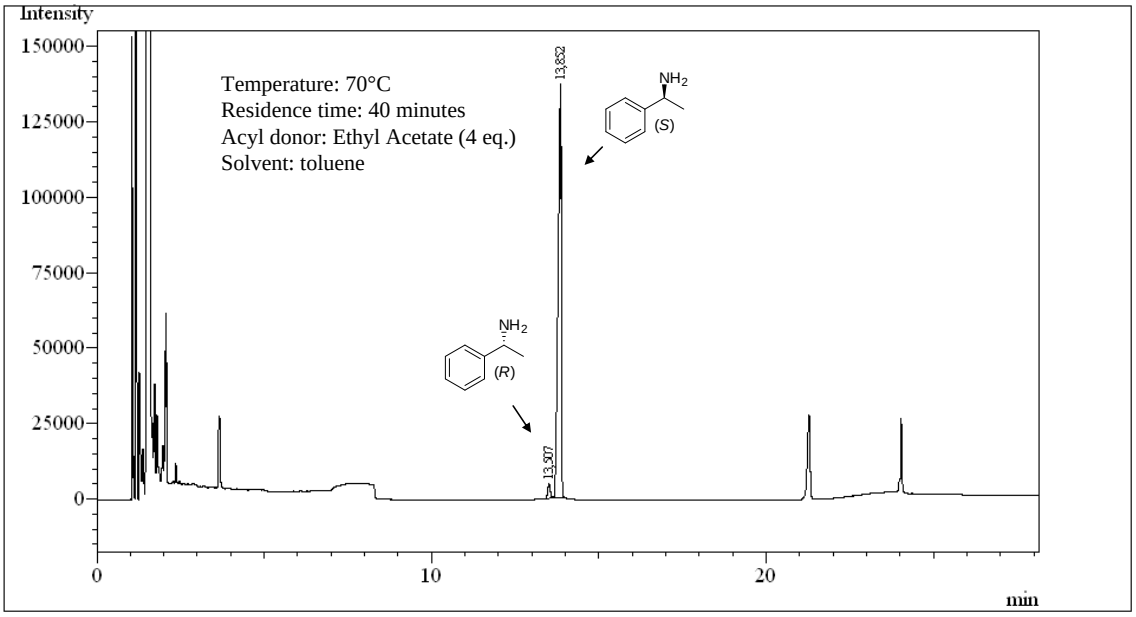




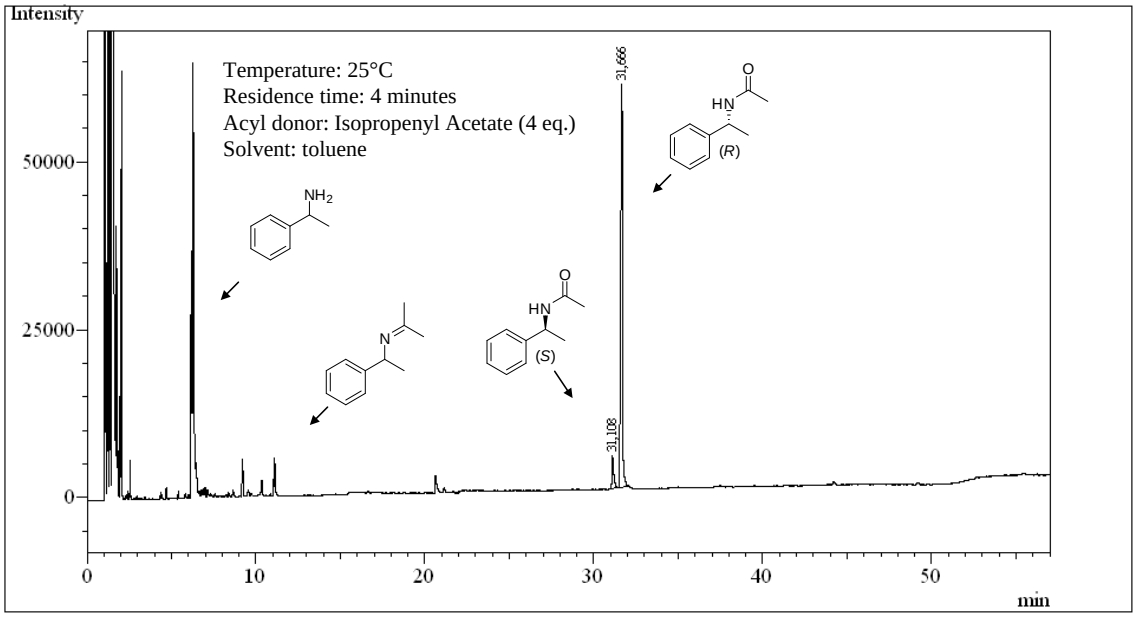


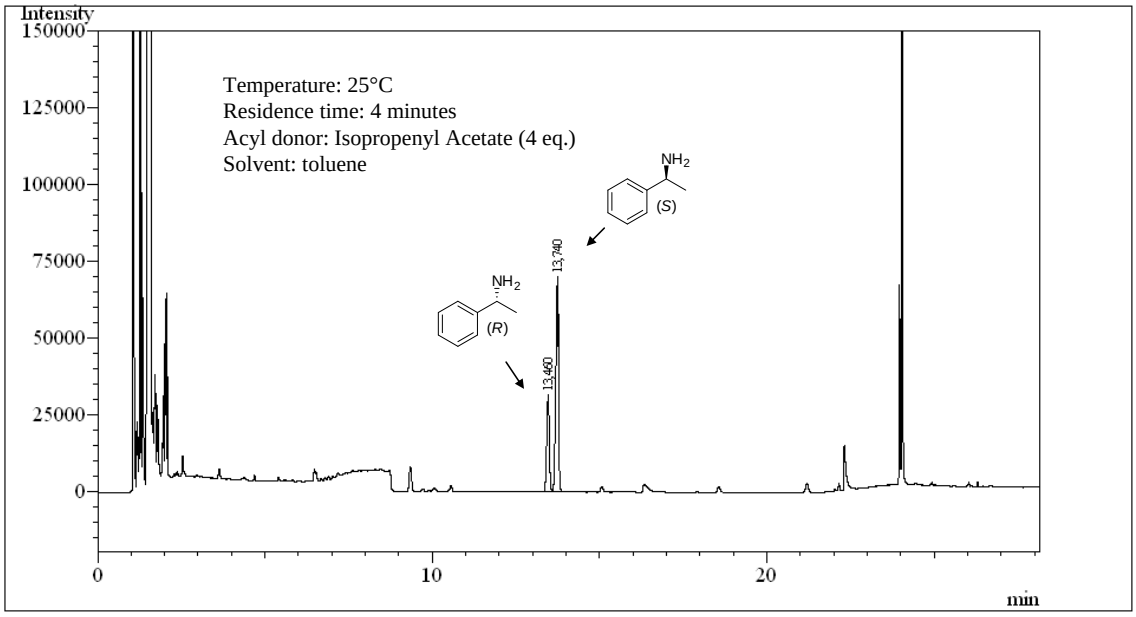


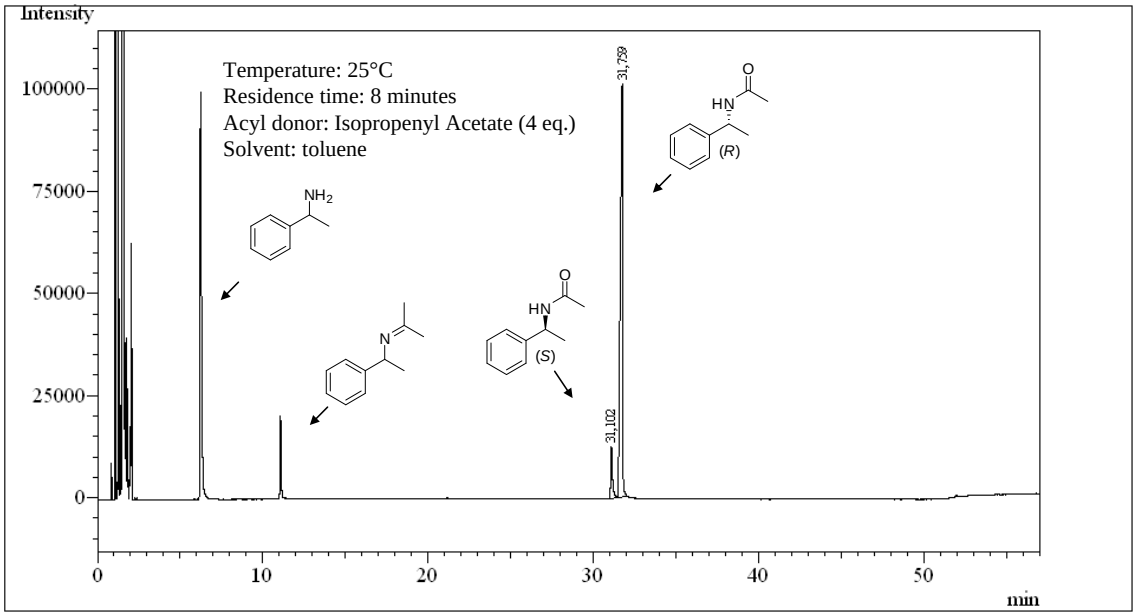


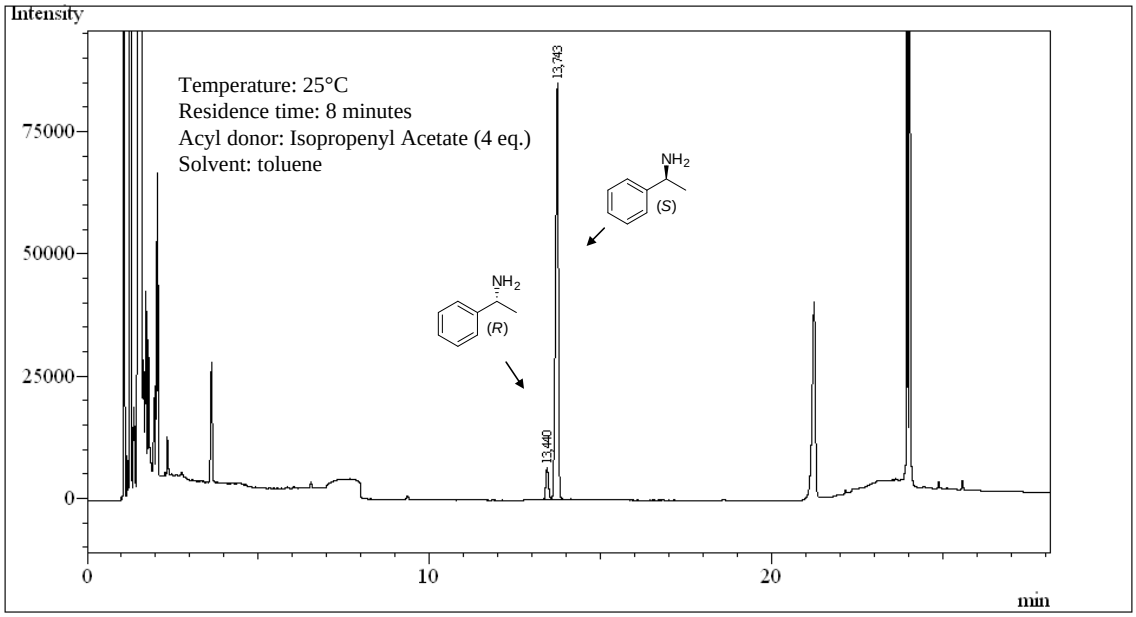


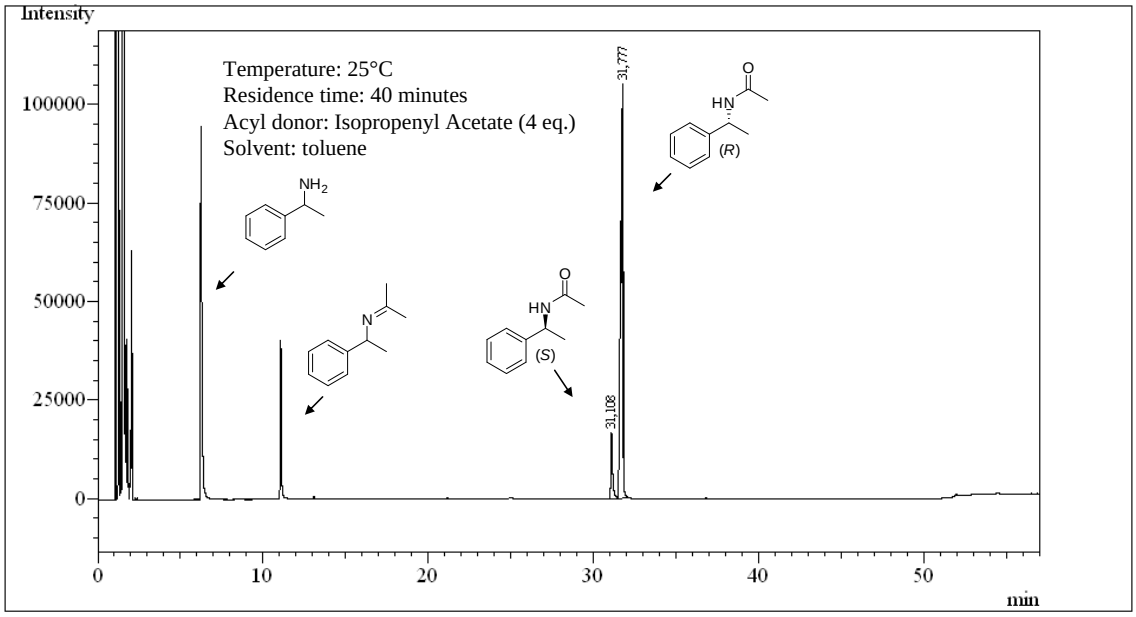
2.1.3. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Isopropenyl Acetate under continuous flow conditions:

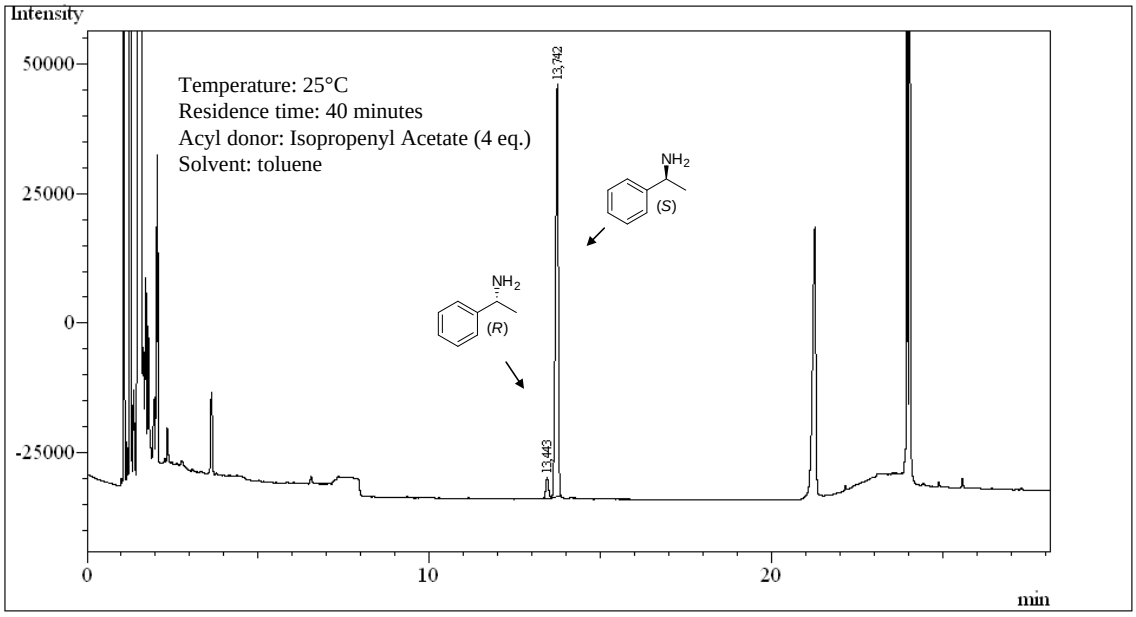


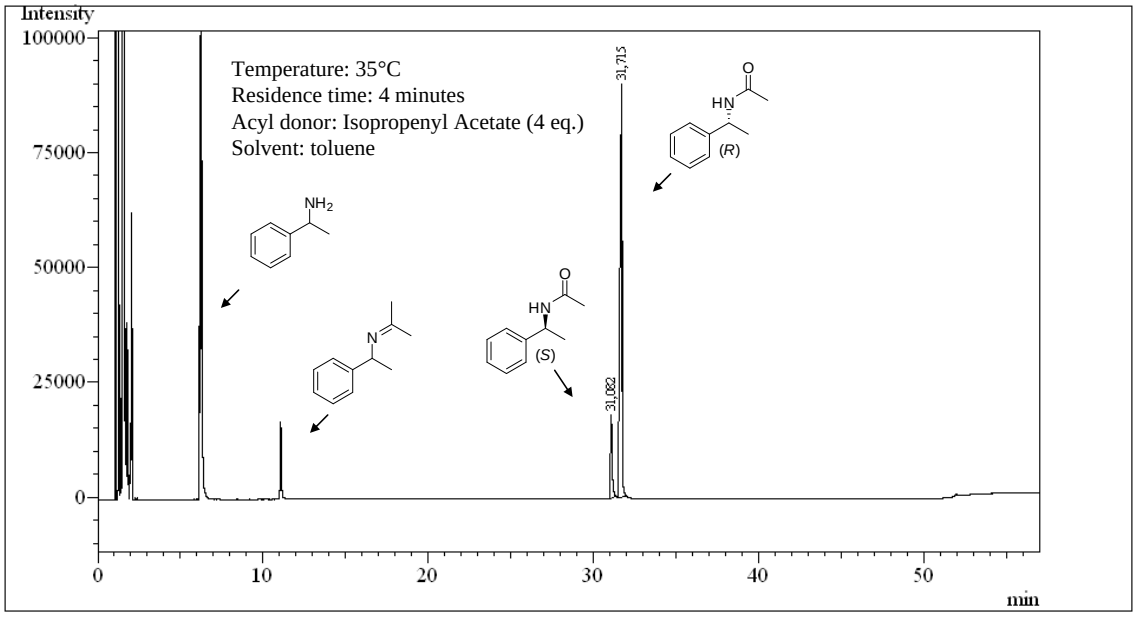


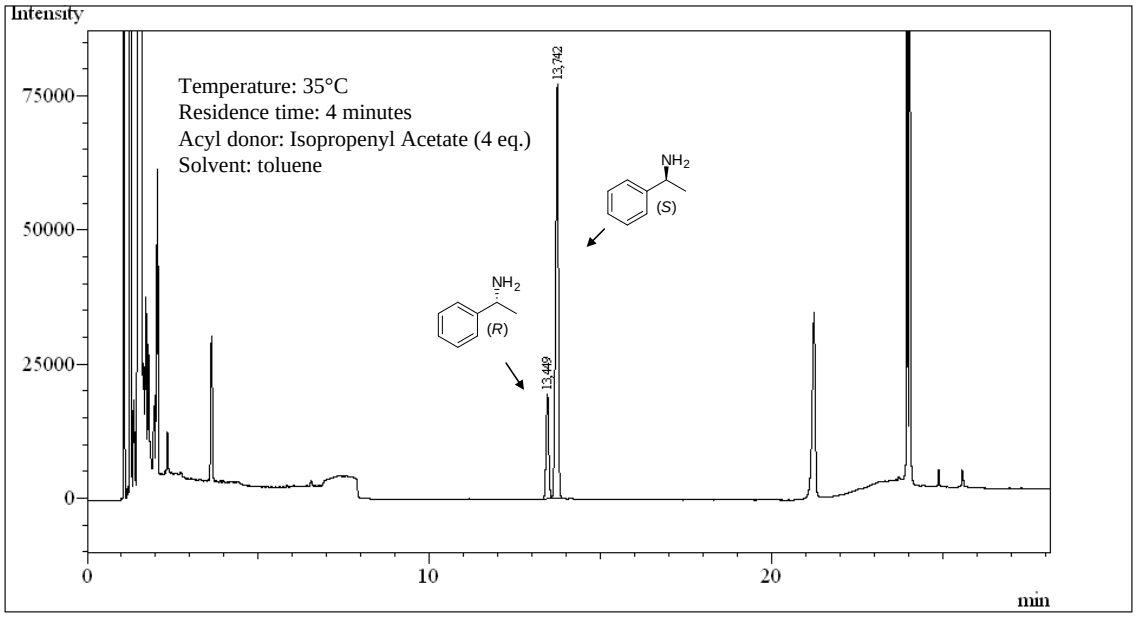


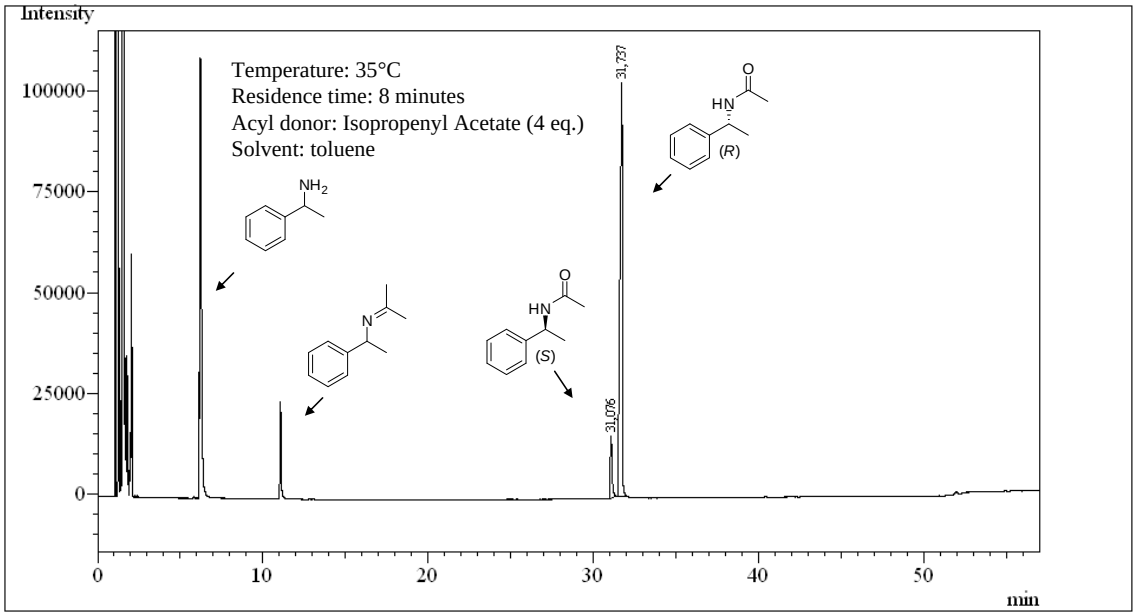


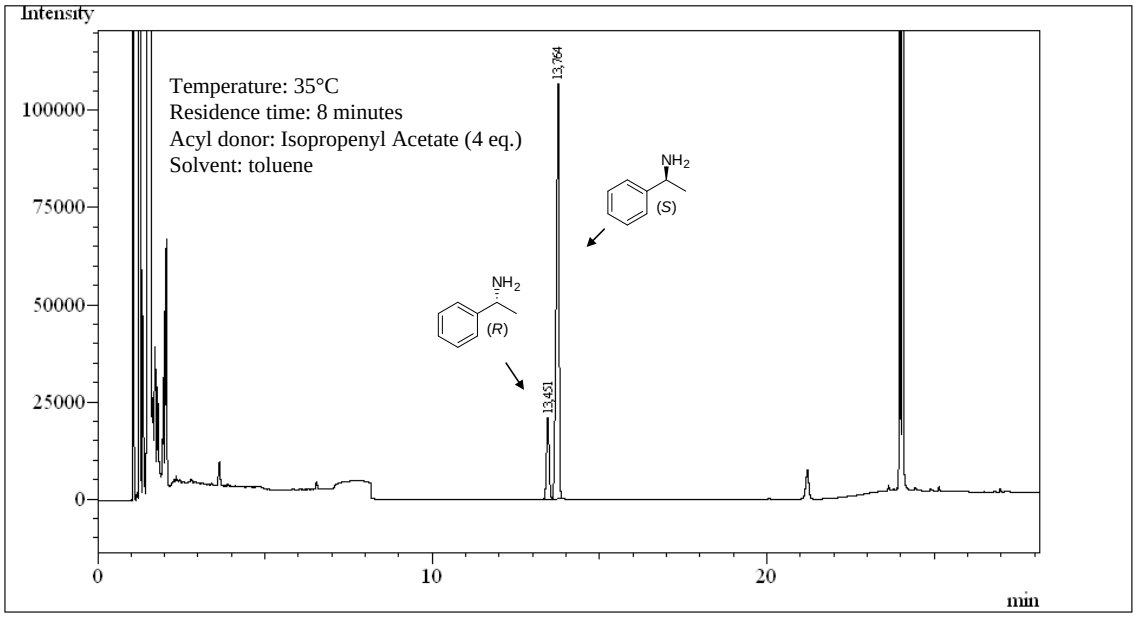


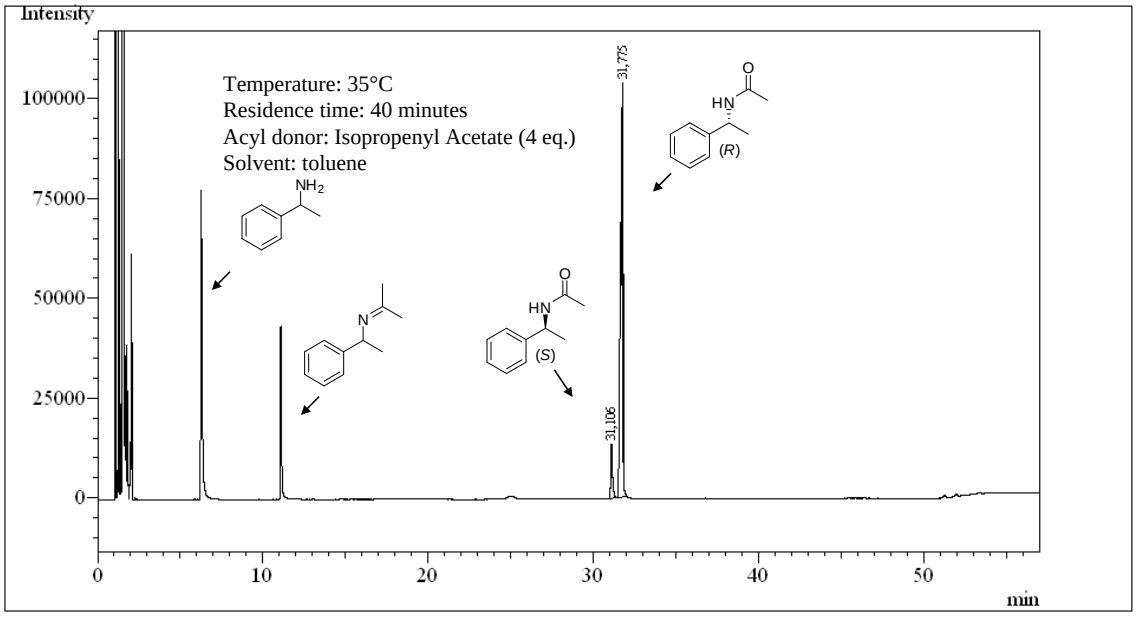


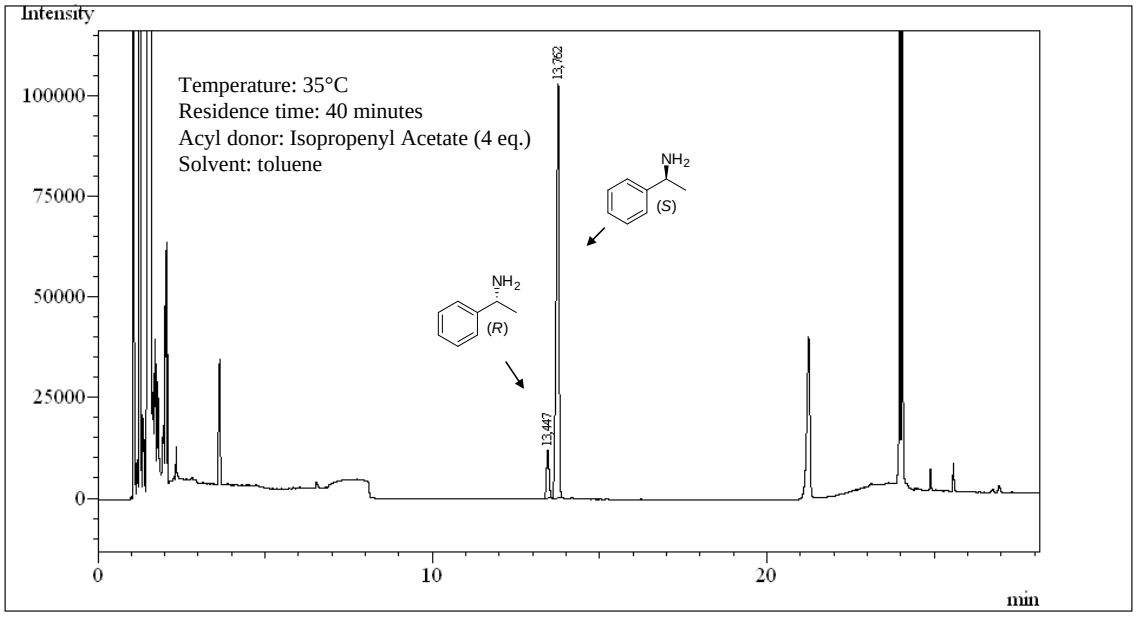


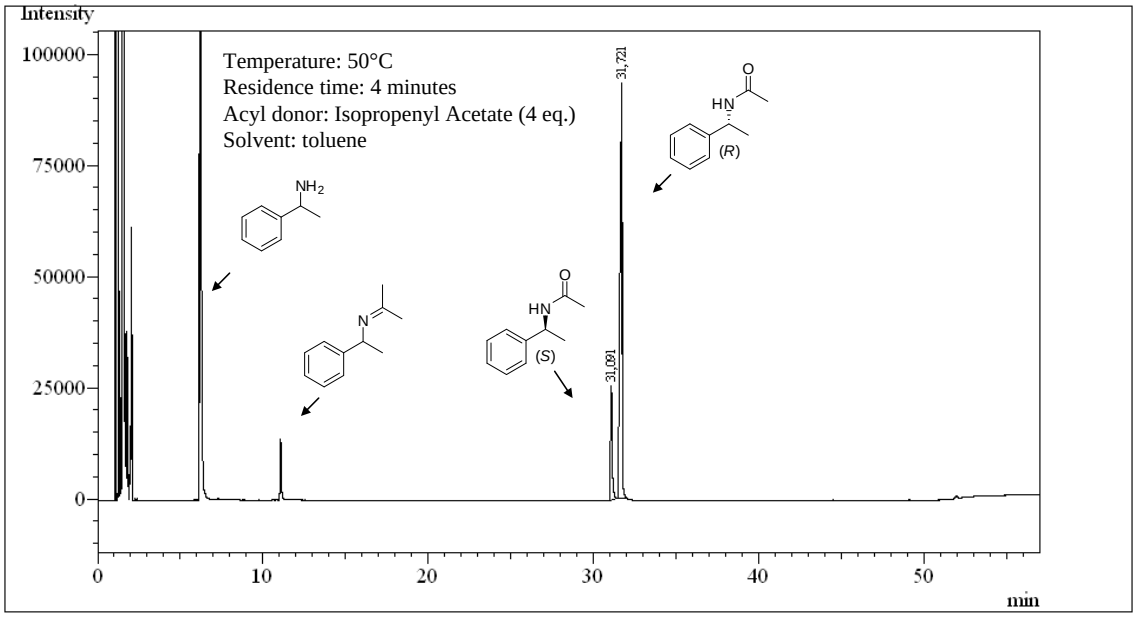


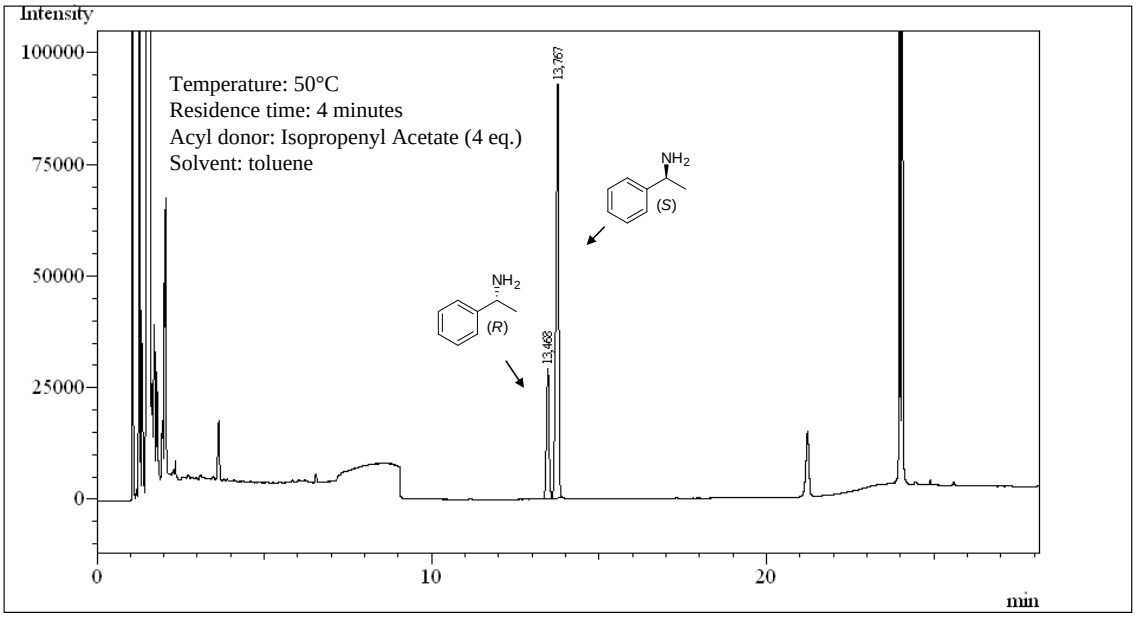


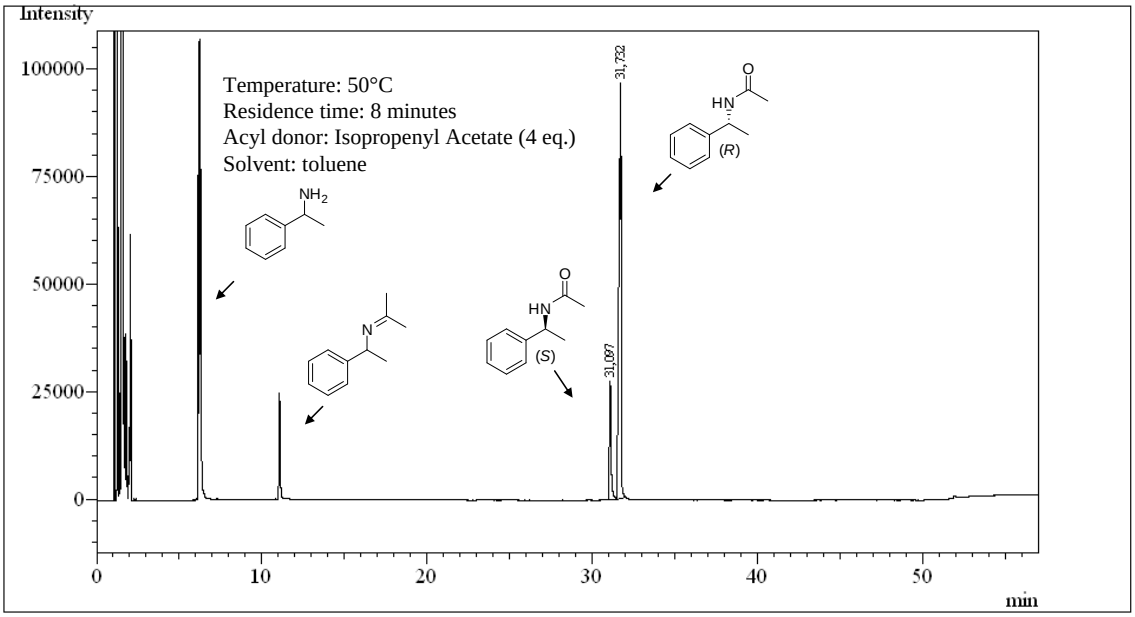


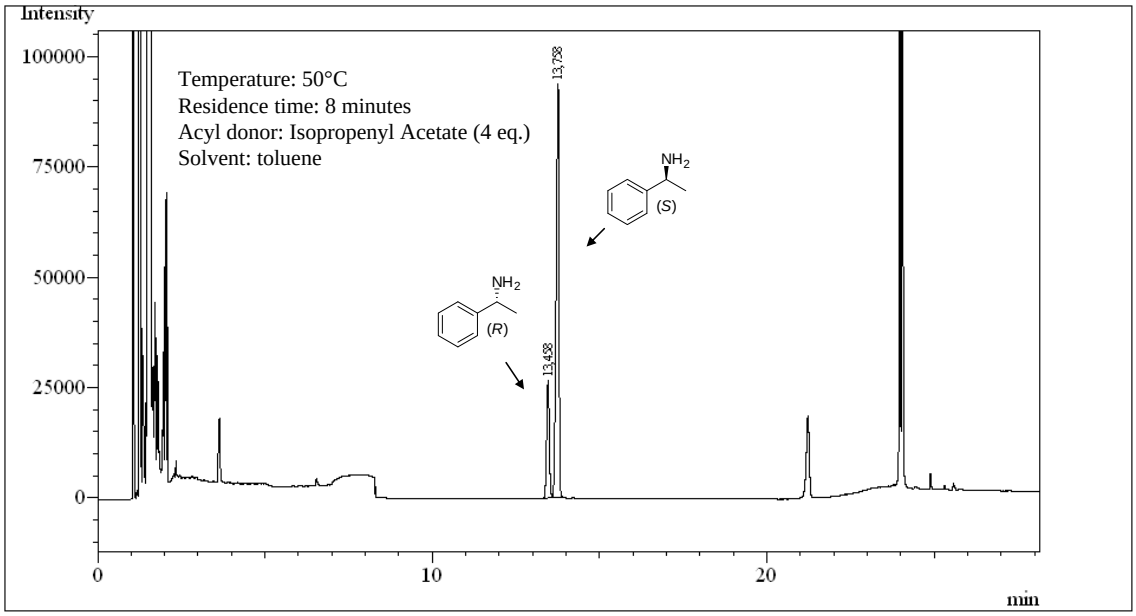


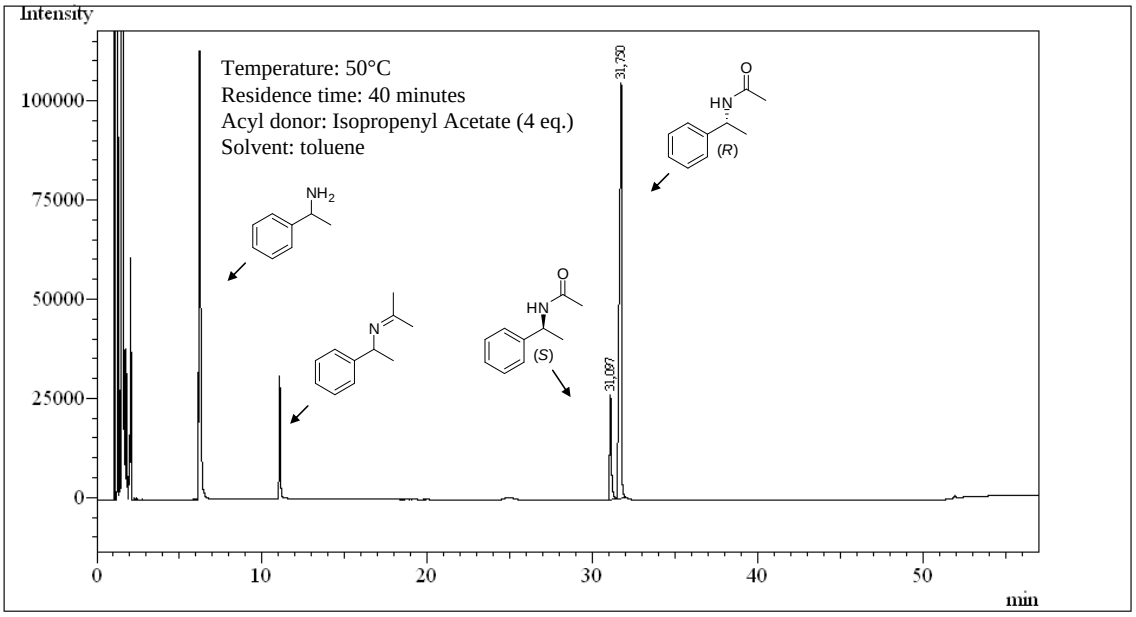


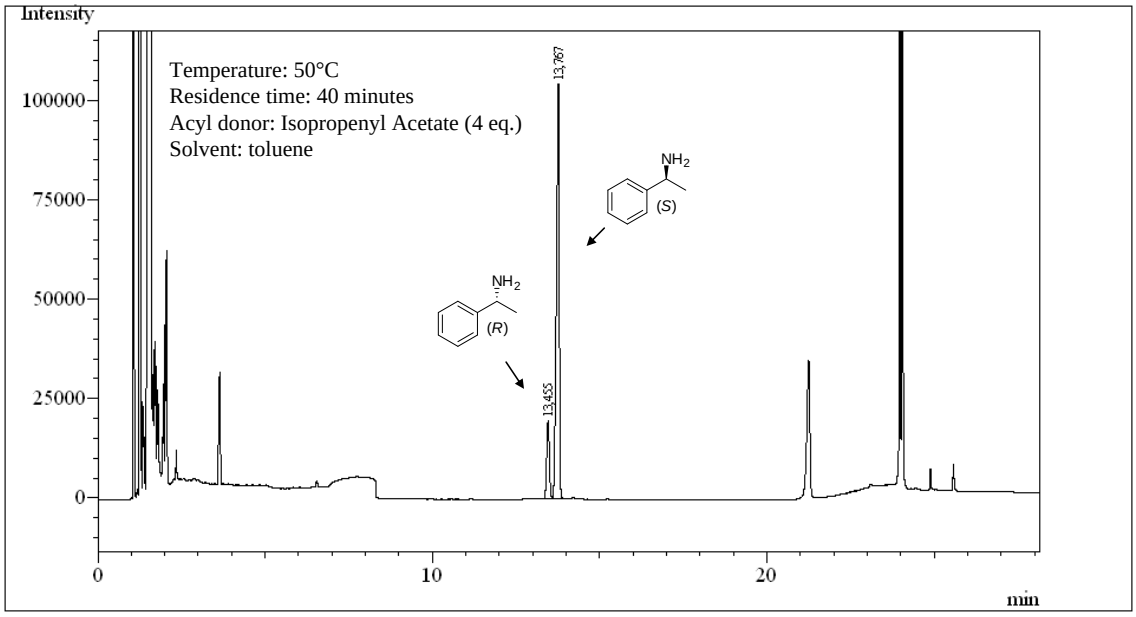


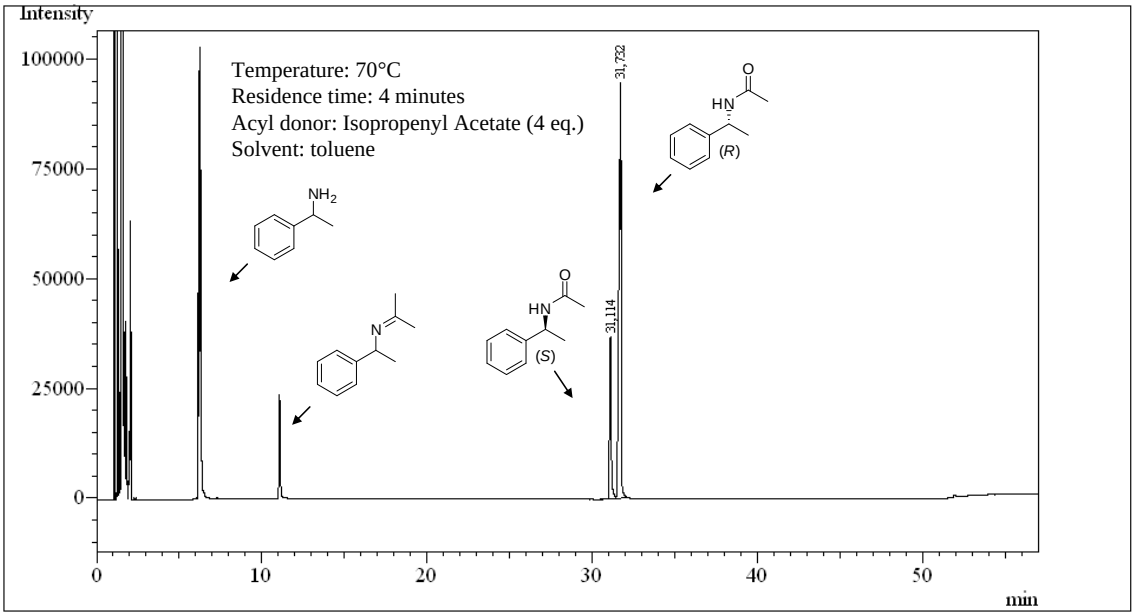


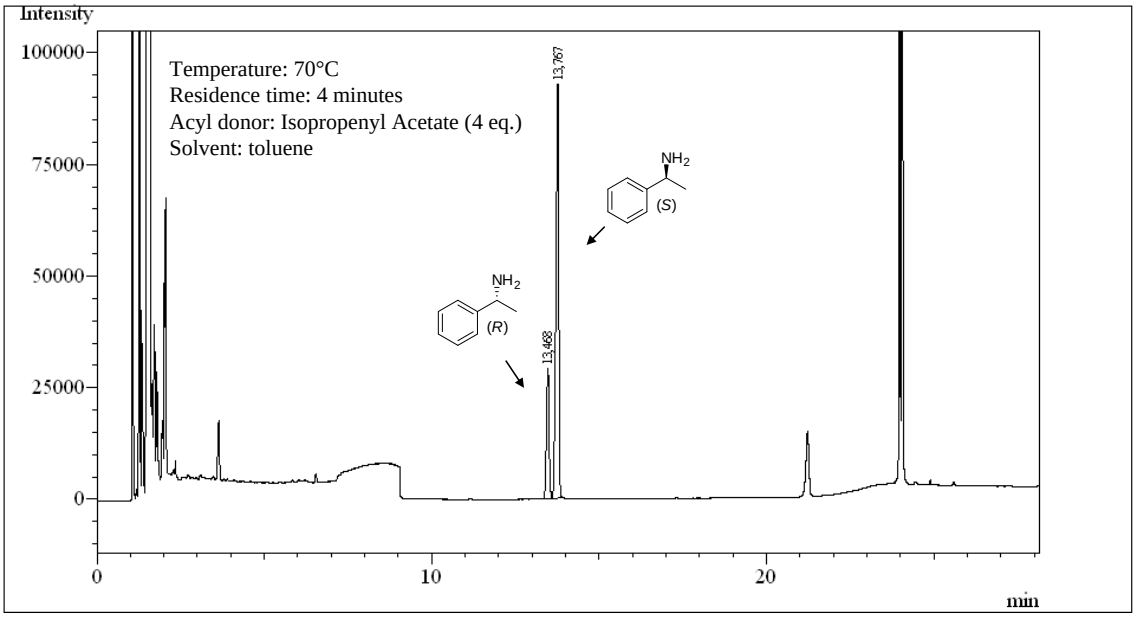


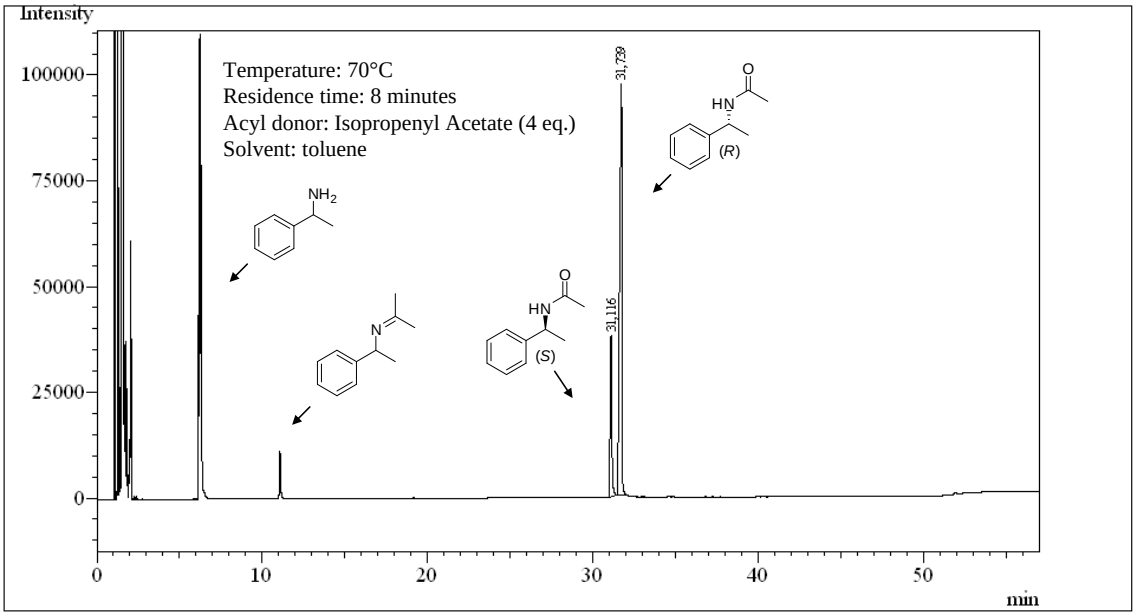


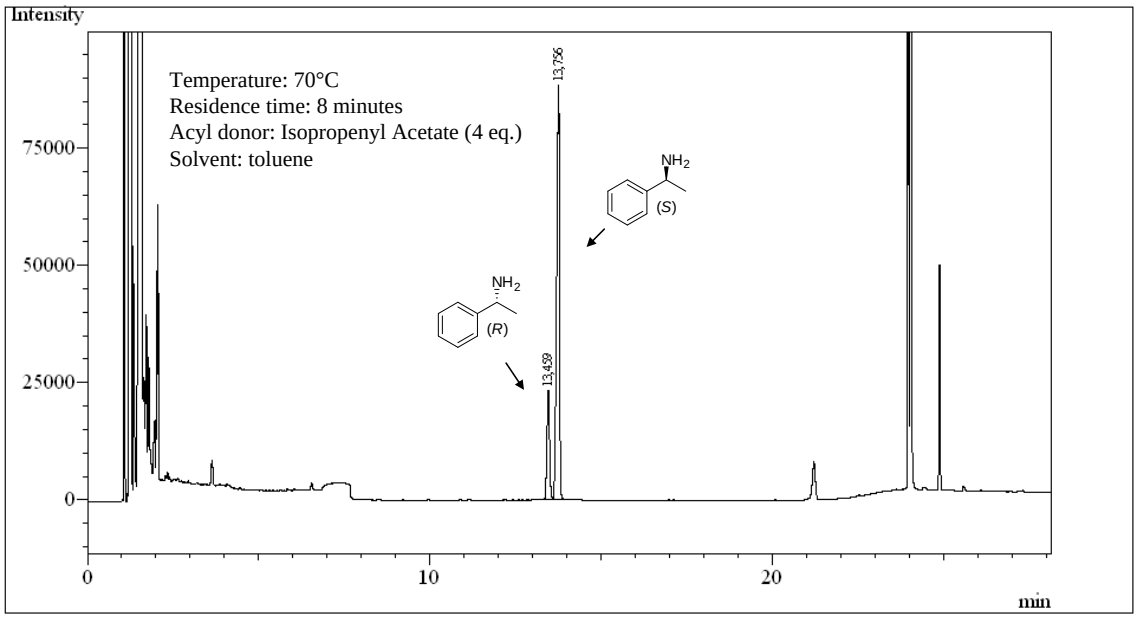


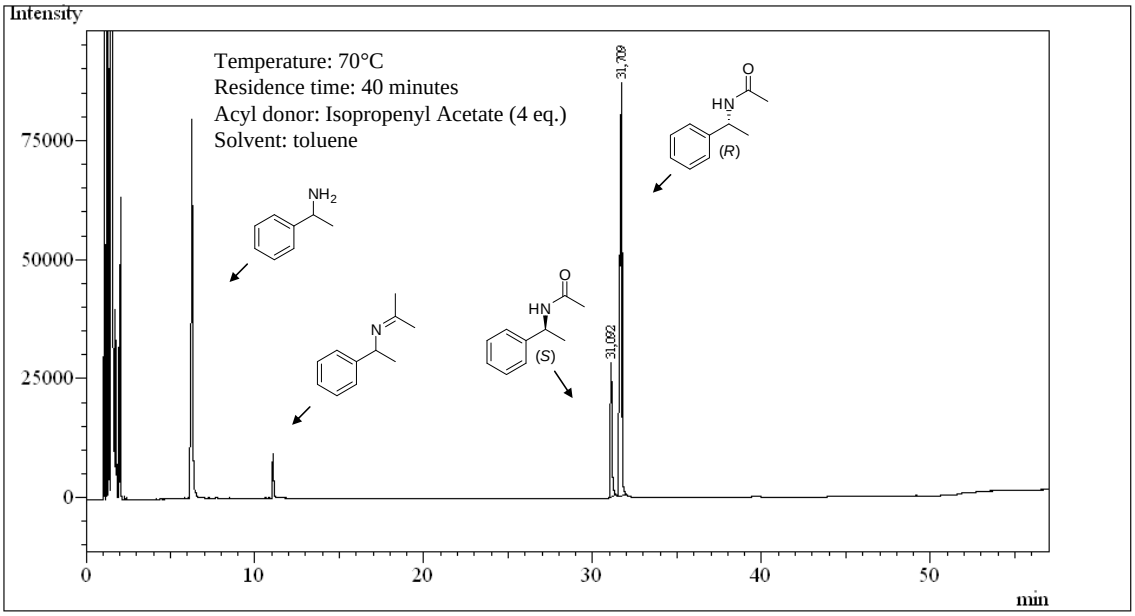


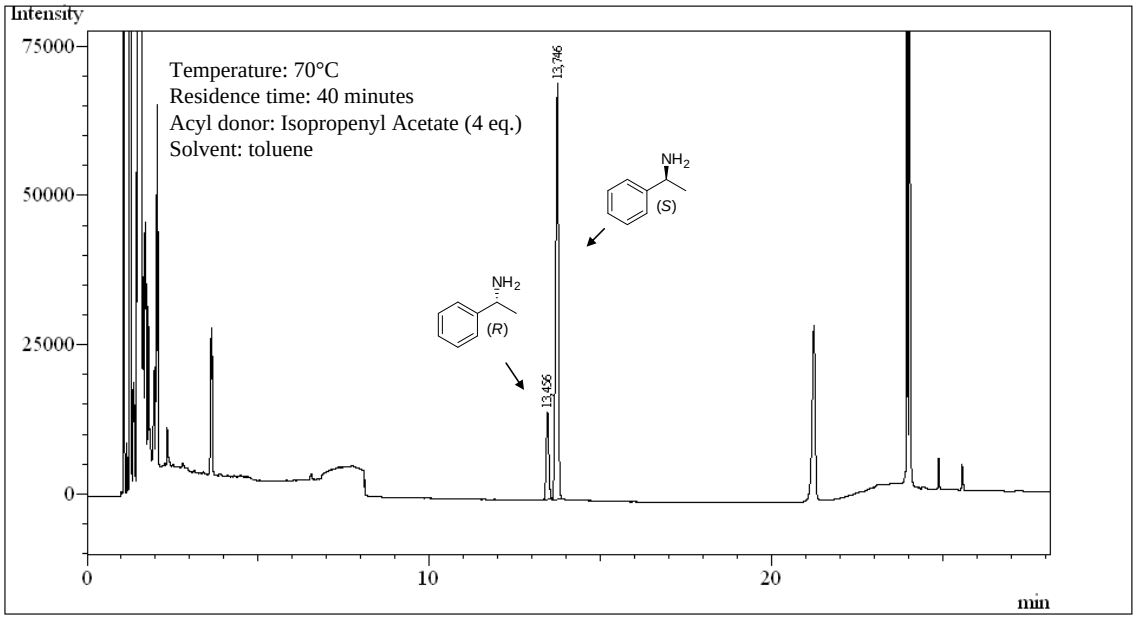




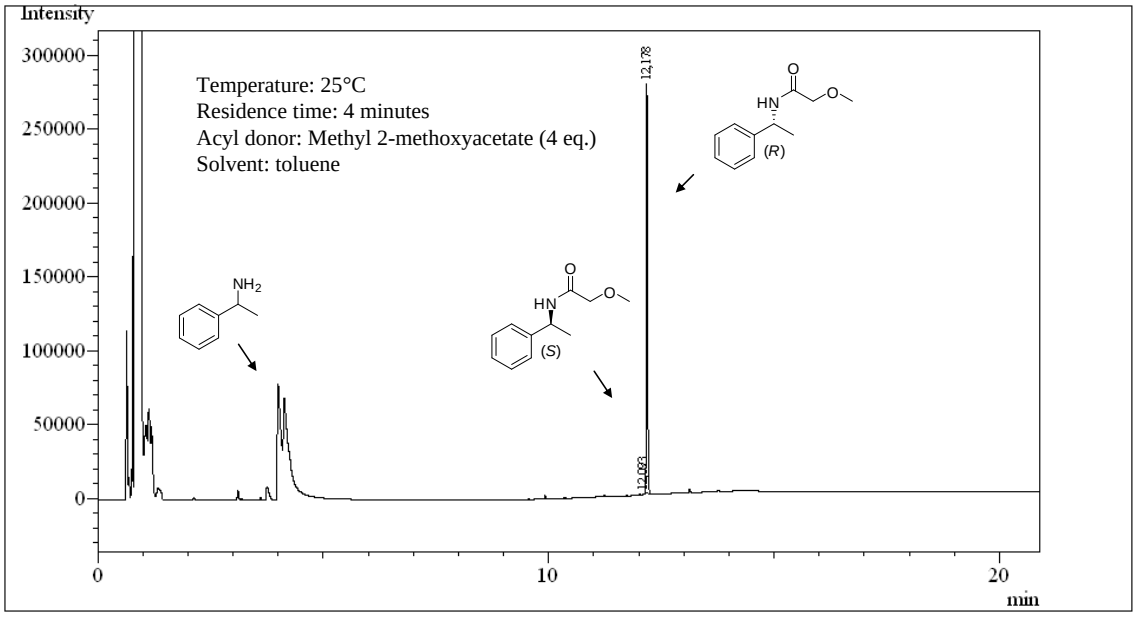


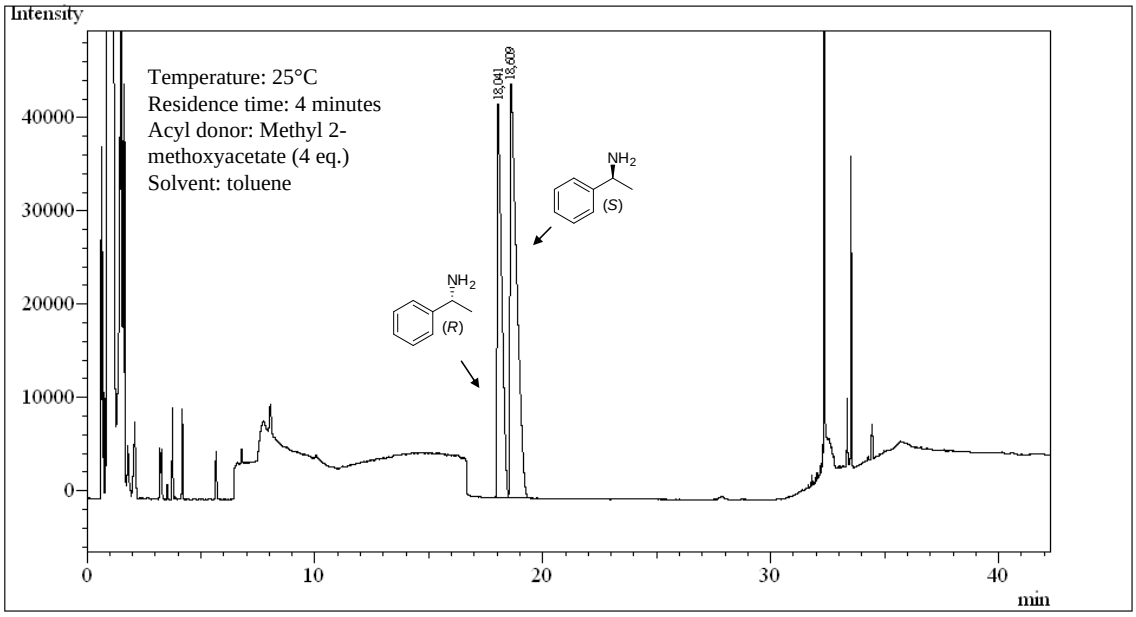


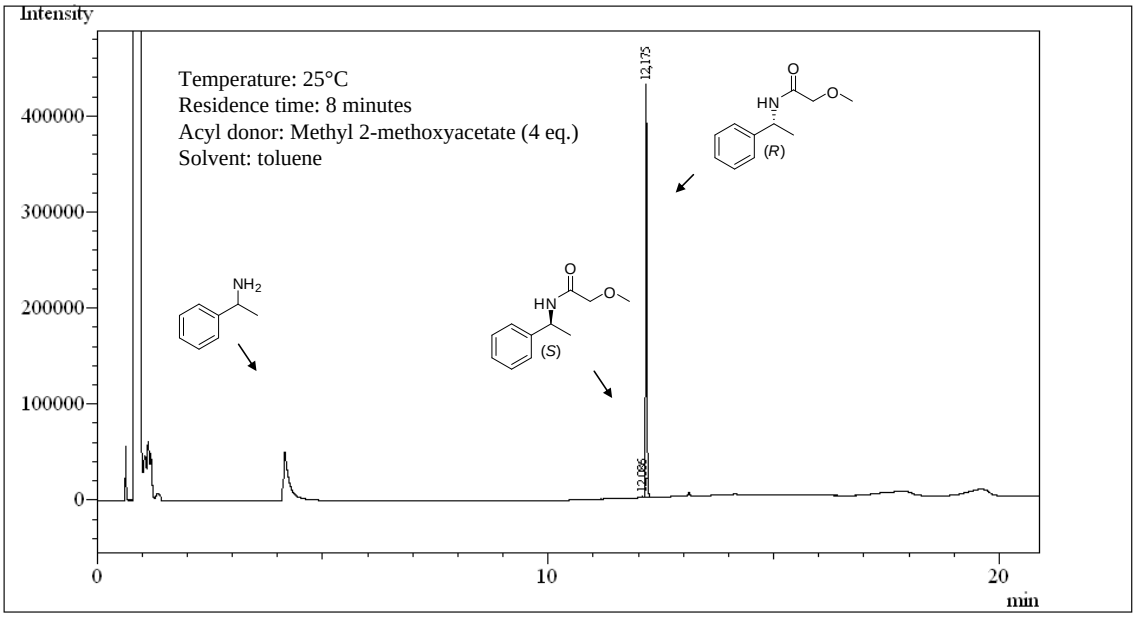


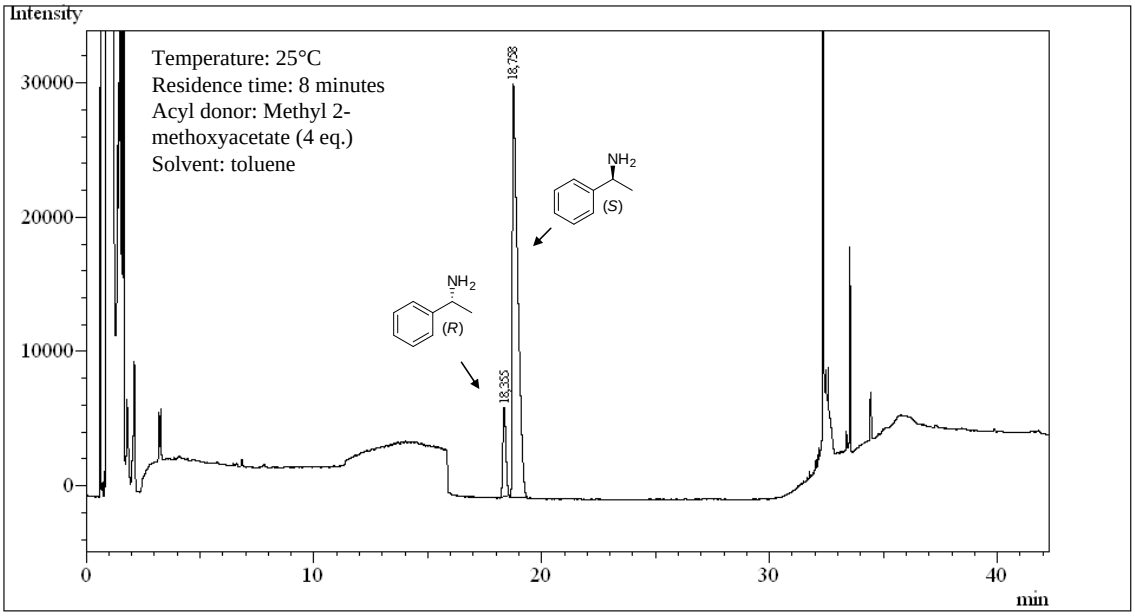


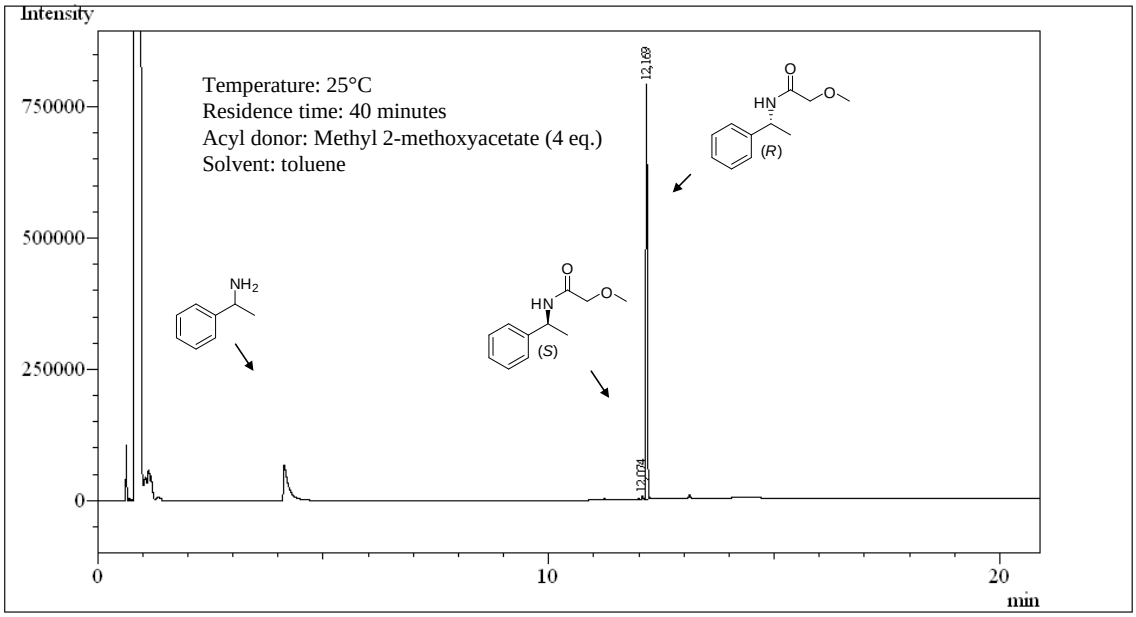
2.1.4. Kinetic resolution of (+/-)-1-phenylethylamine (1) with Methyl 2-methoxyacetate under continuous flow conditions

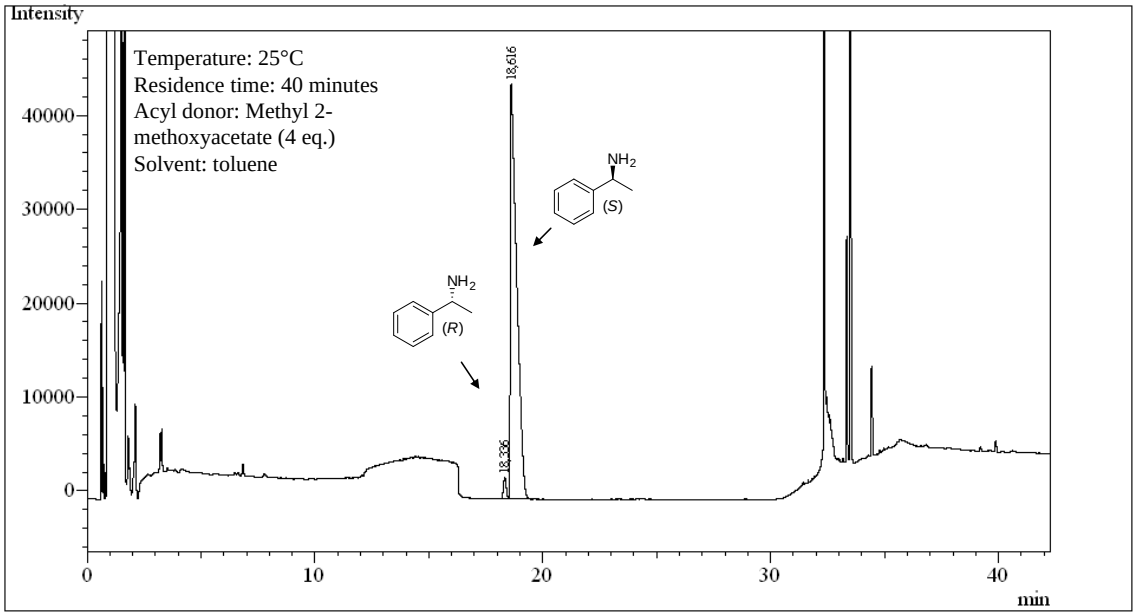


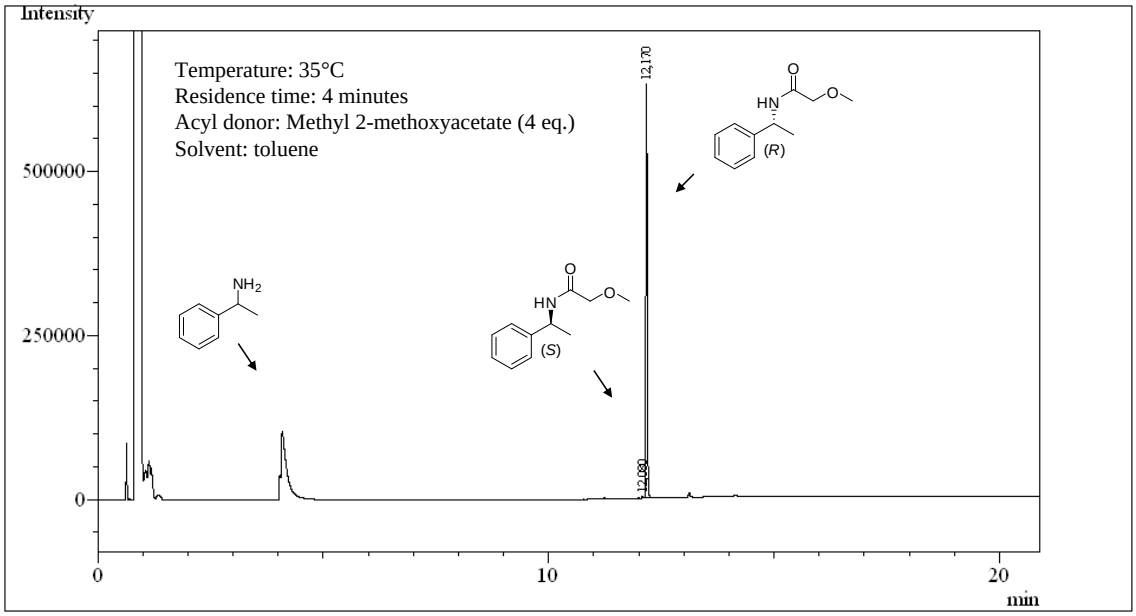


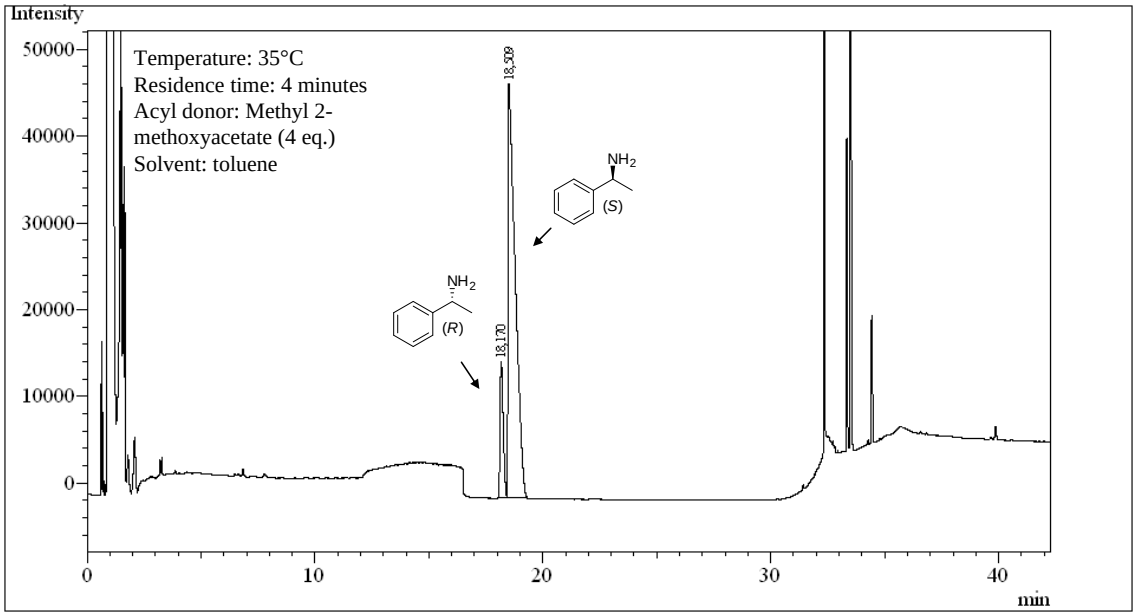


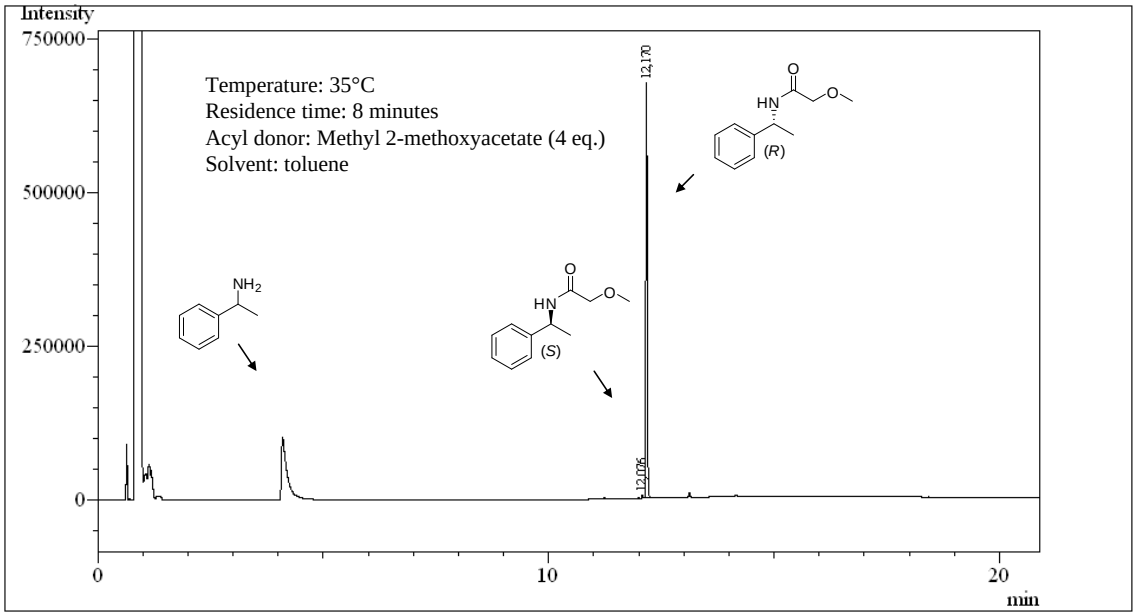


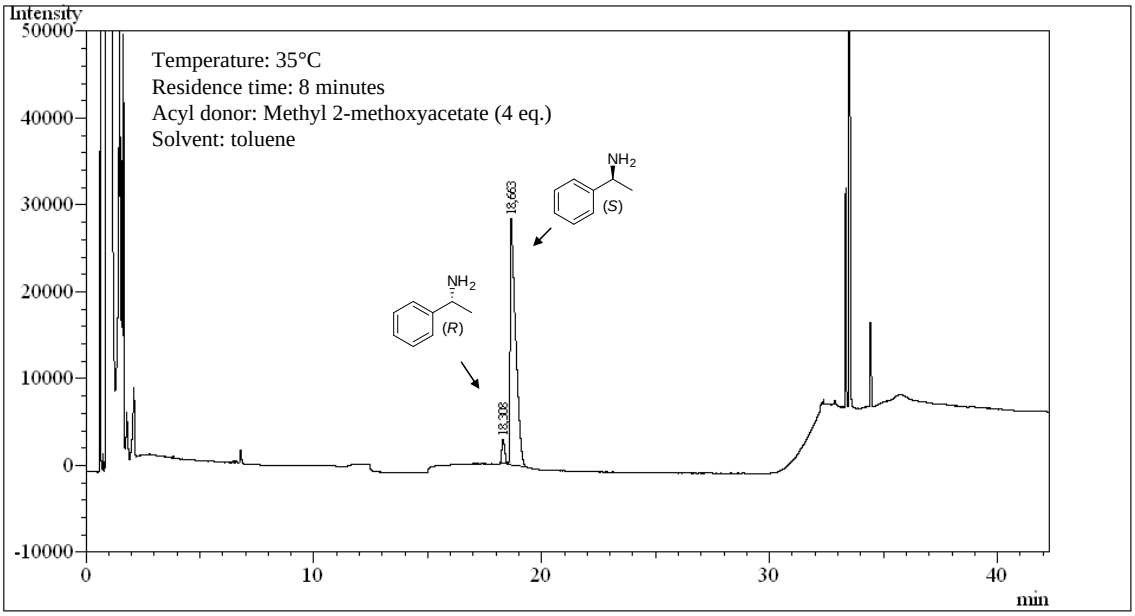


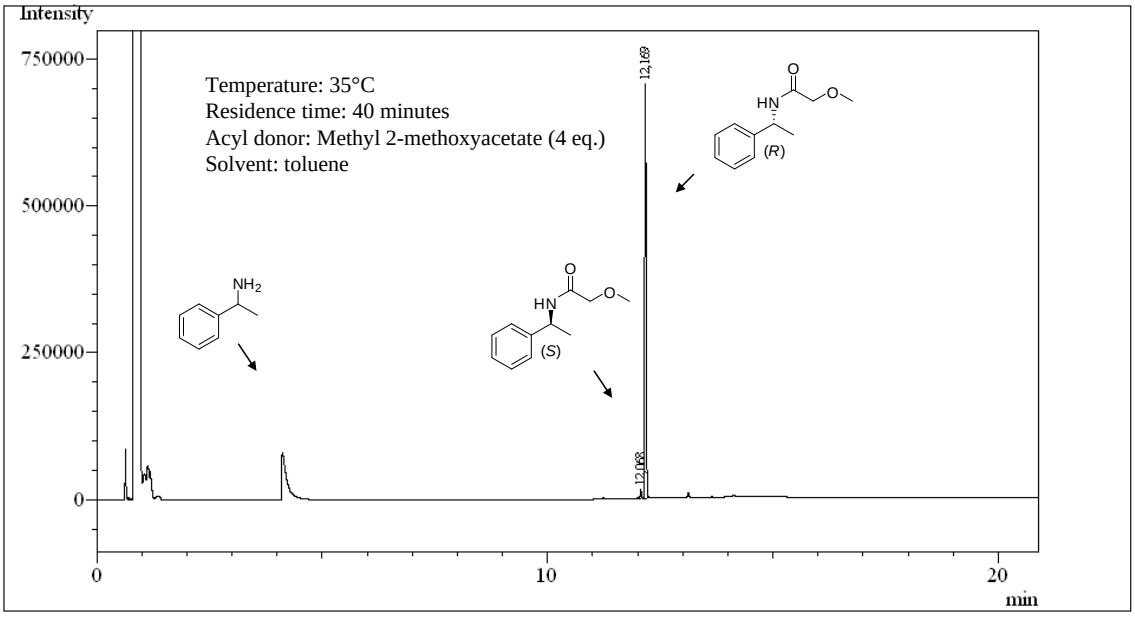


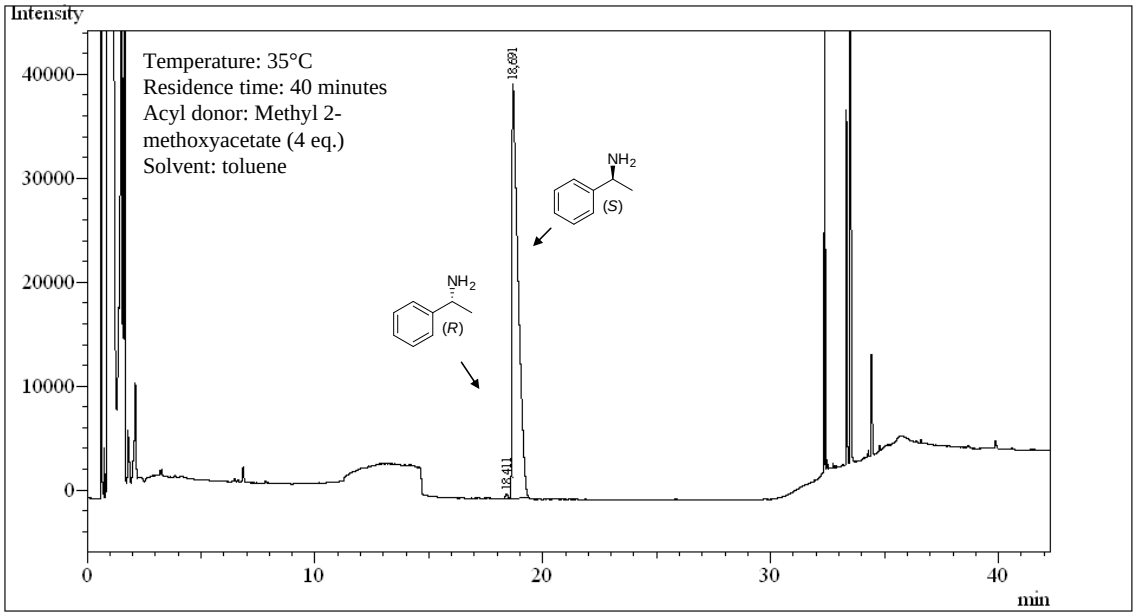


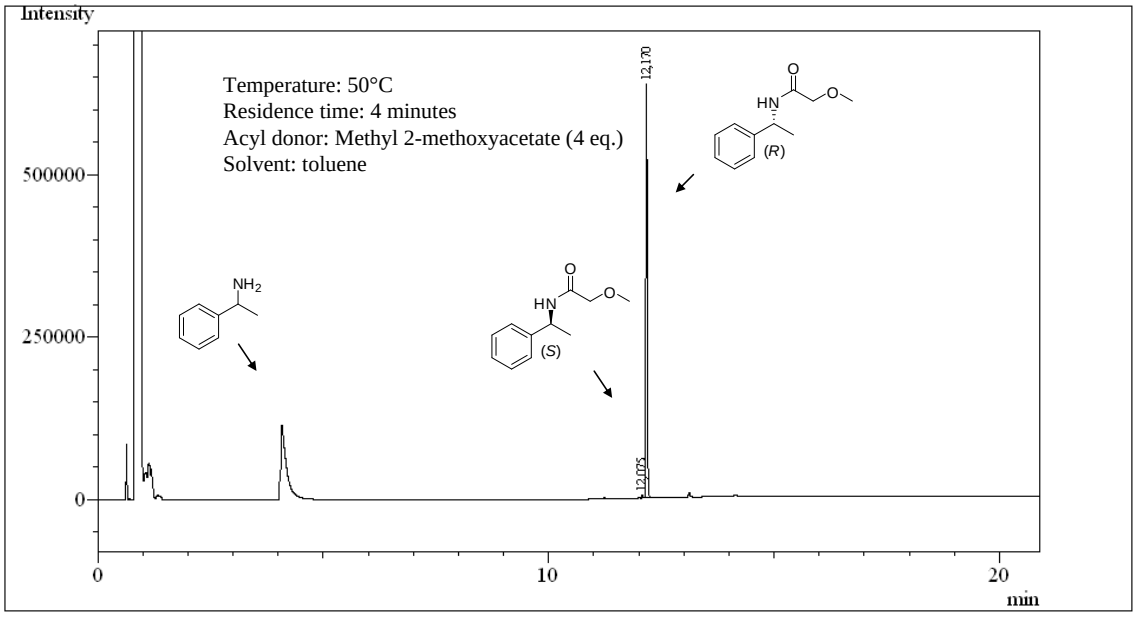


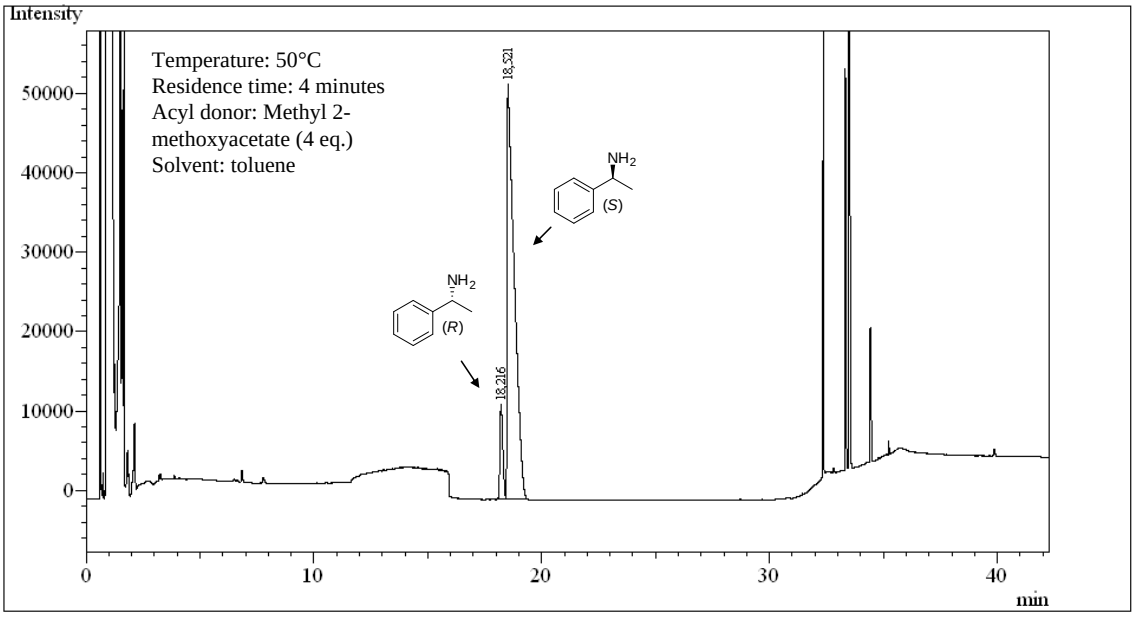


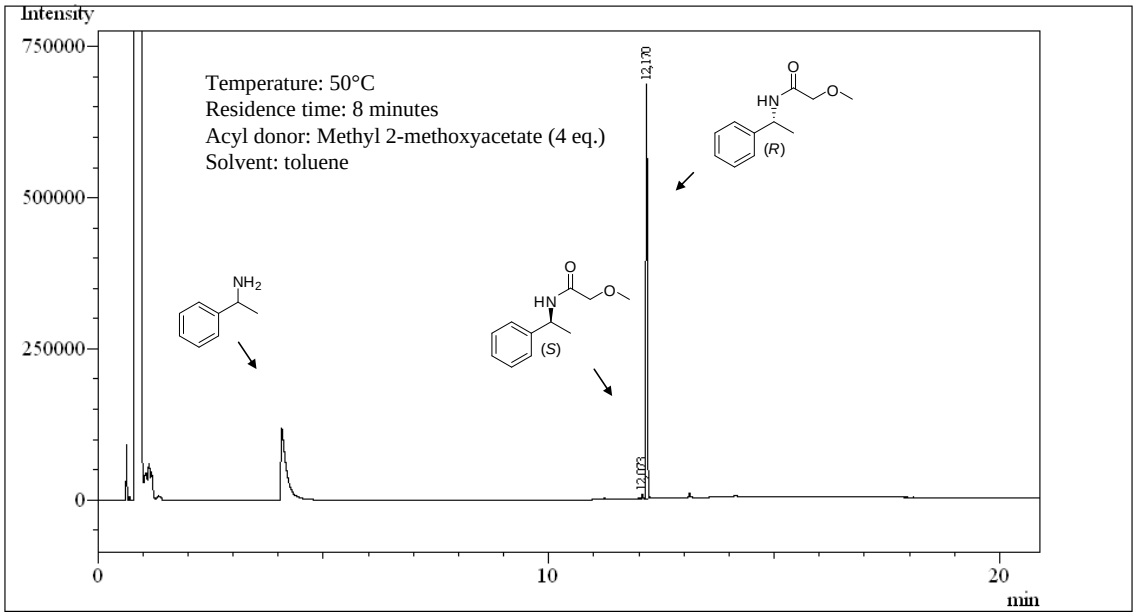


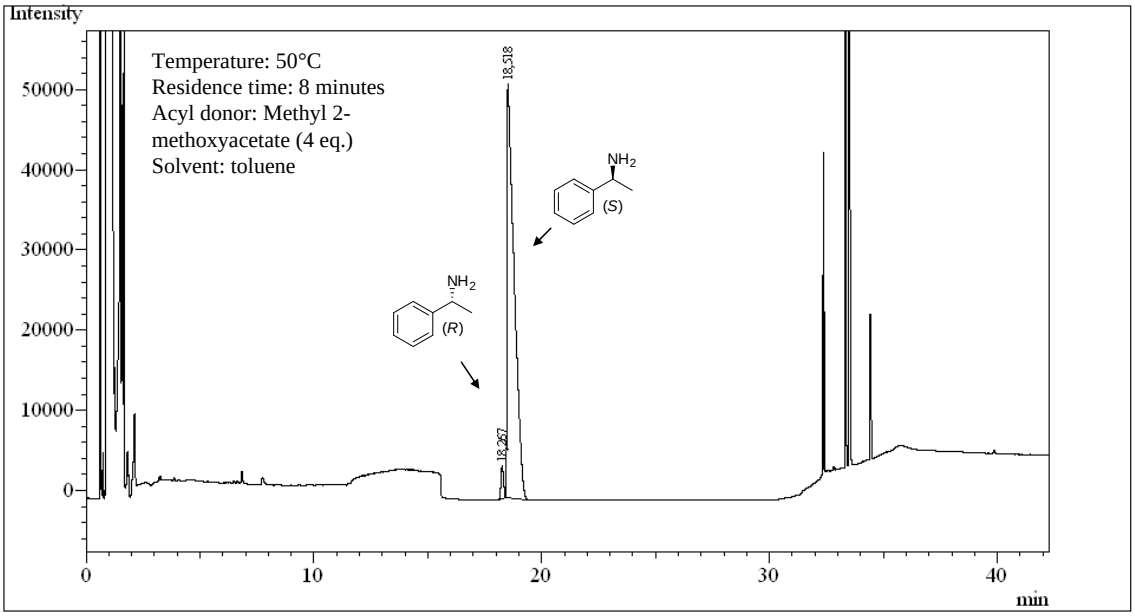


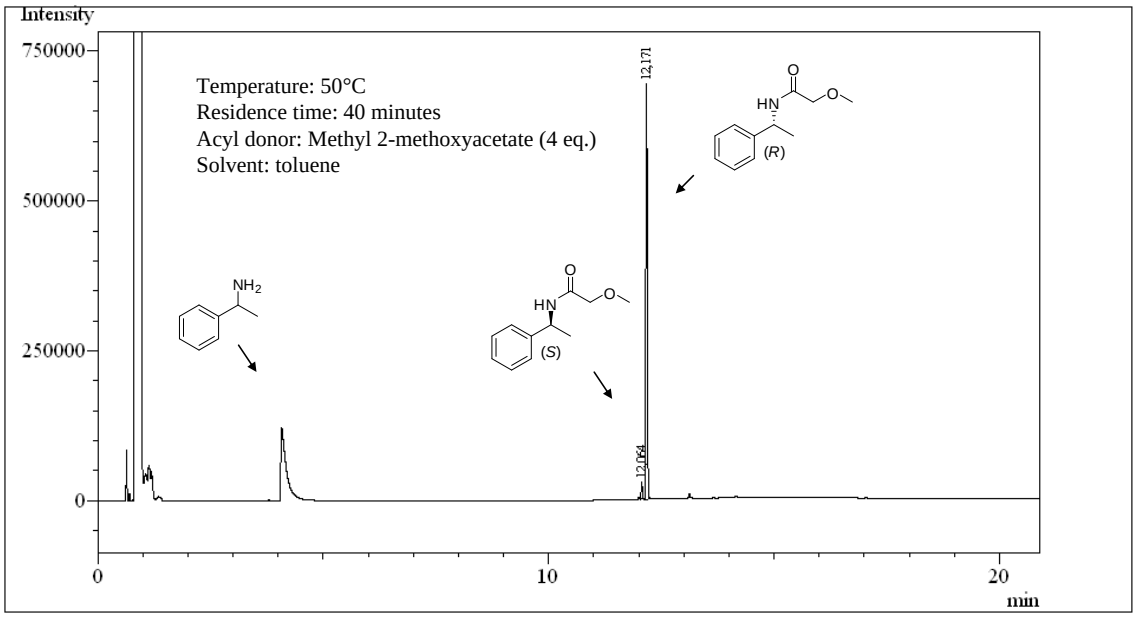


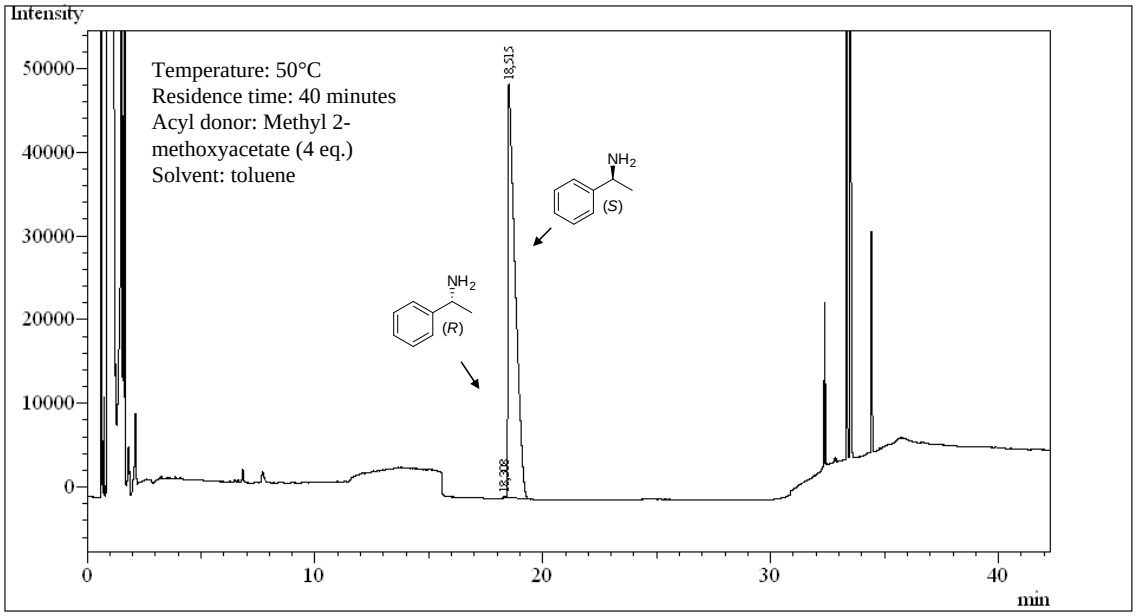


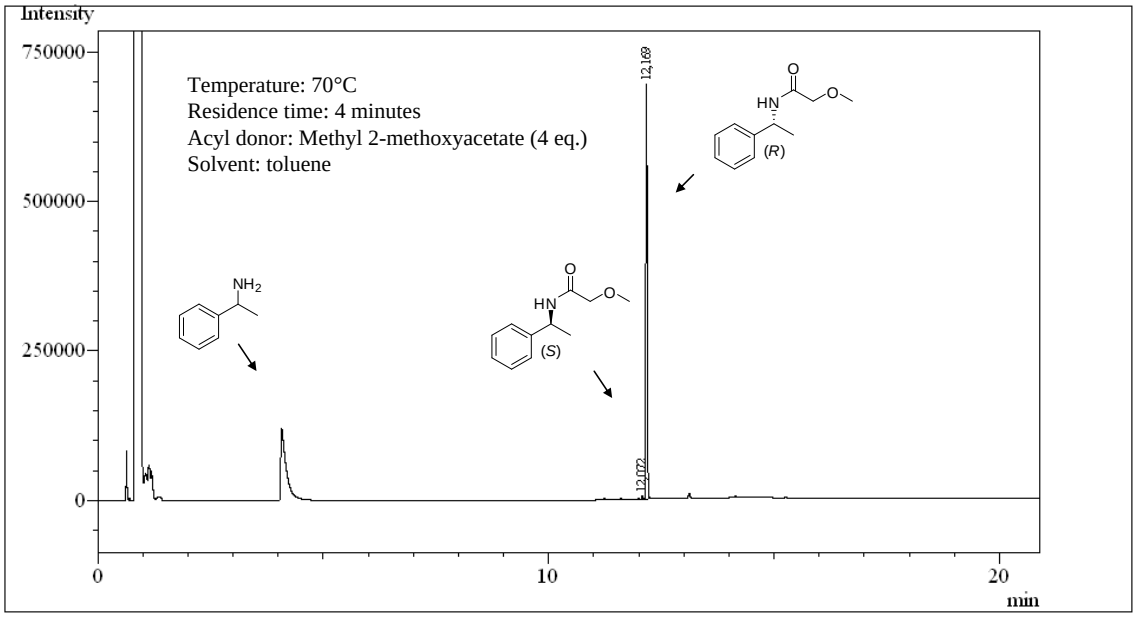


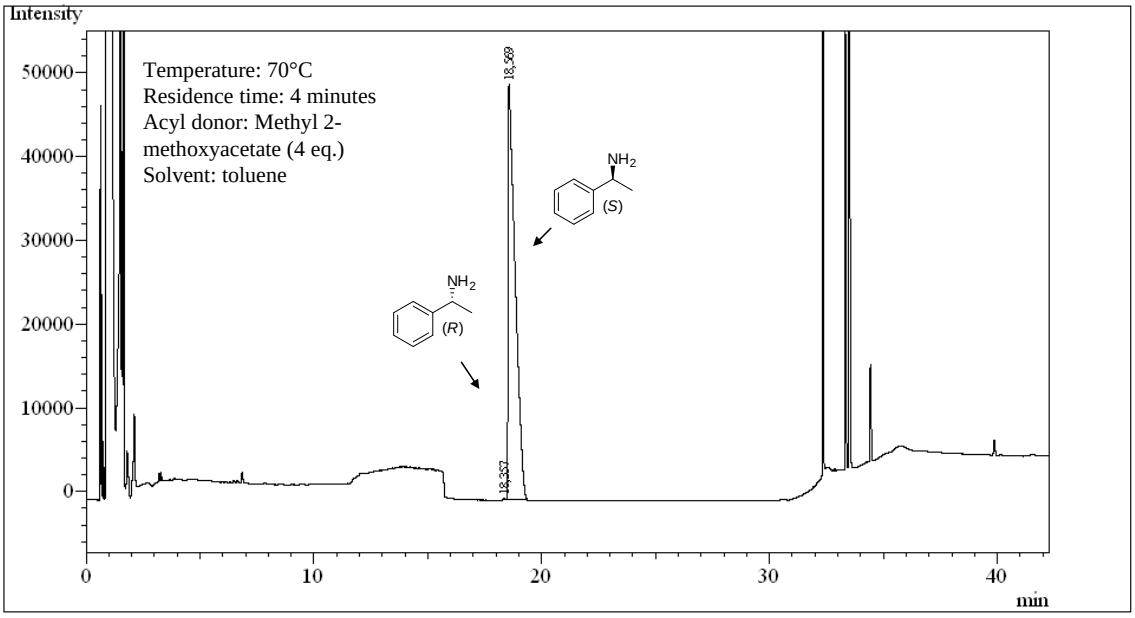


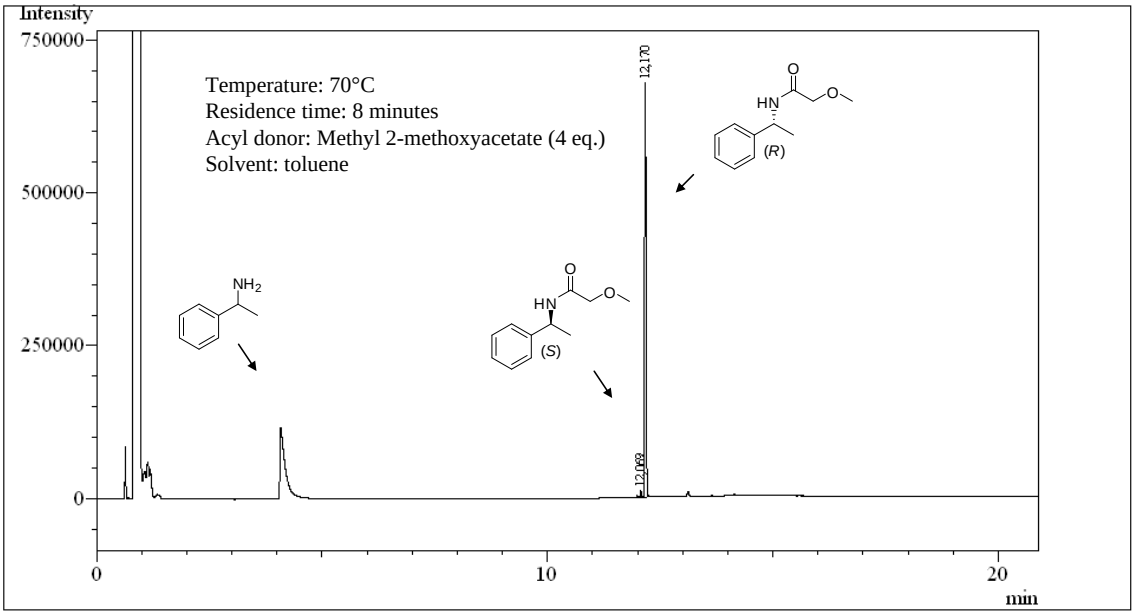


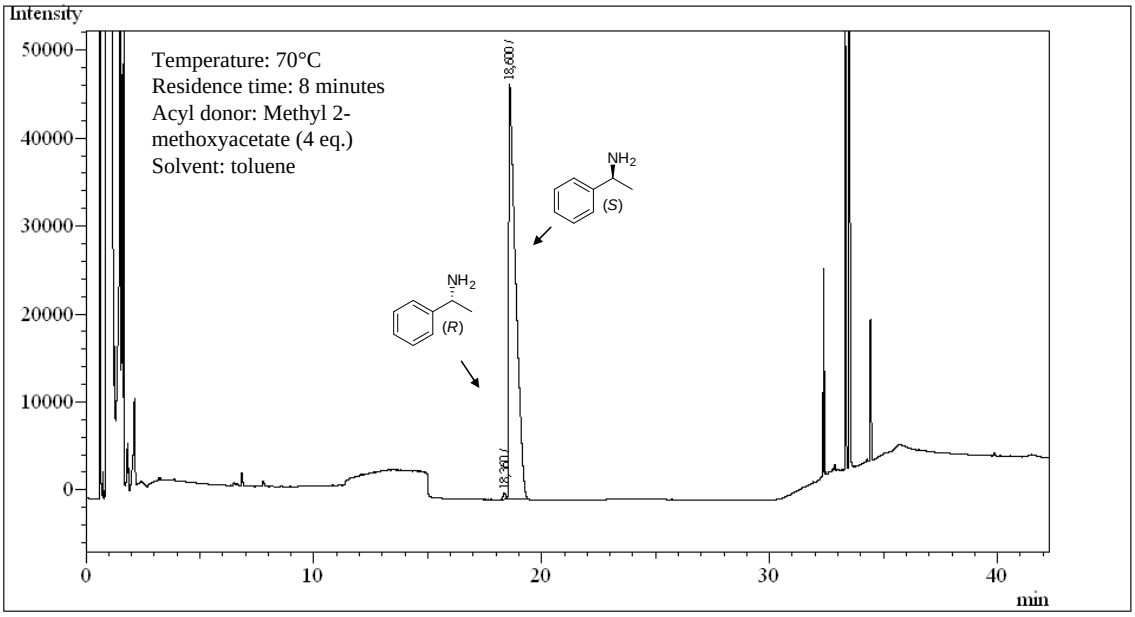


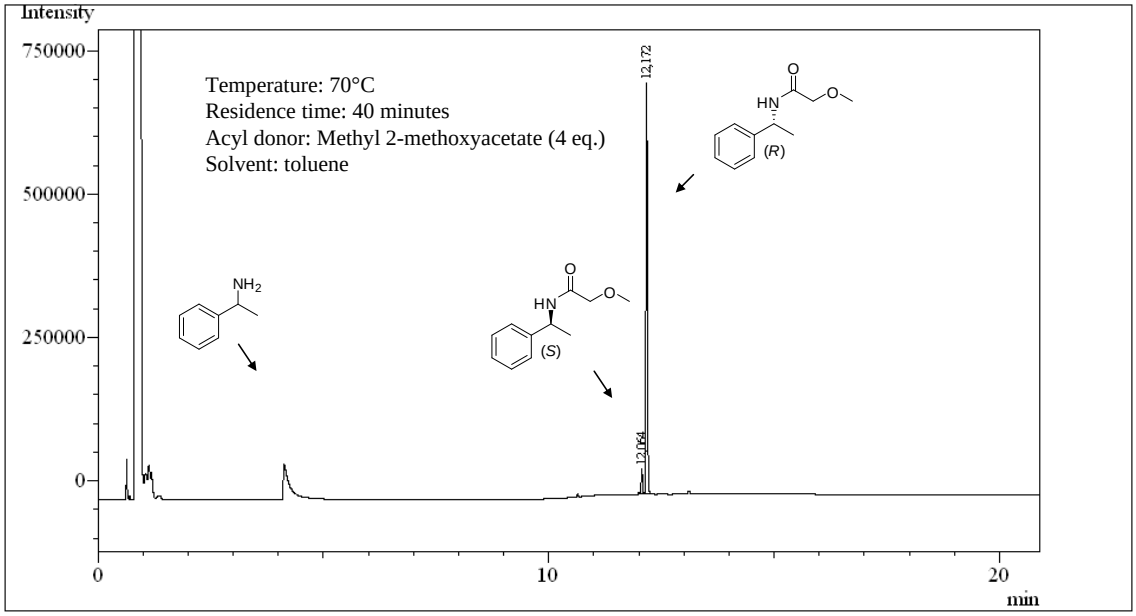


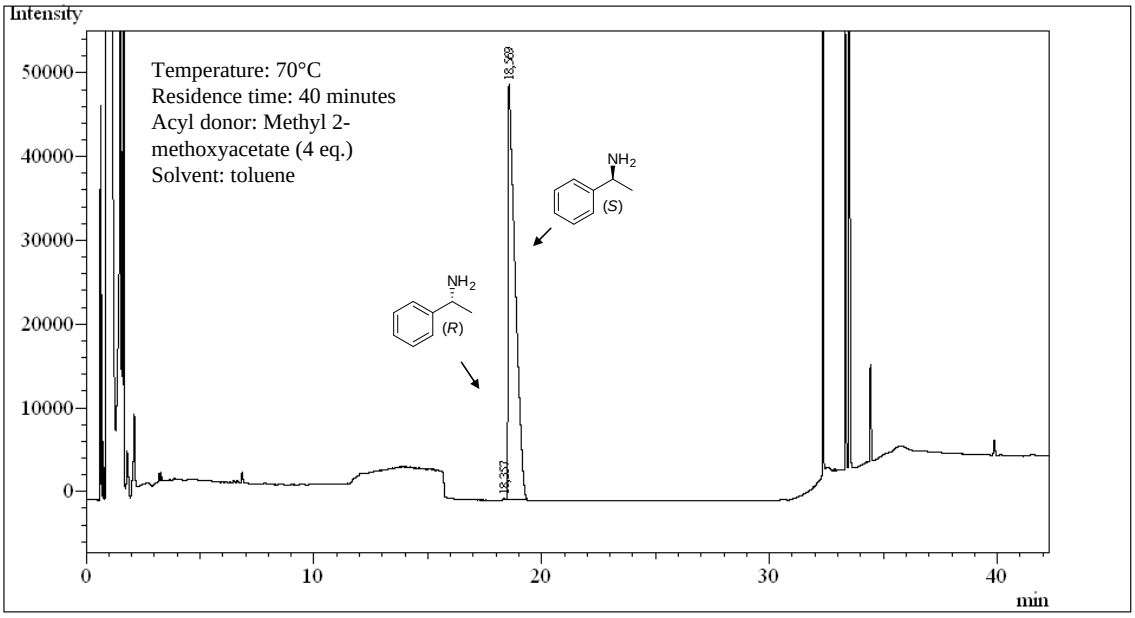




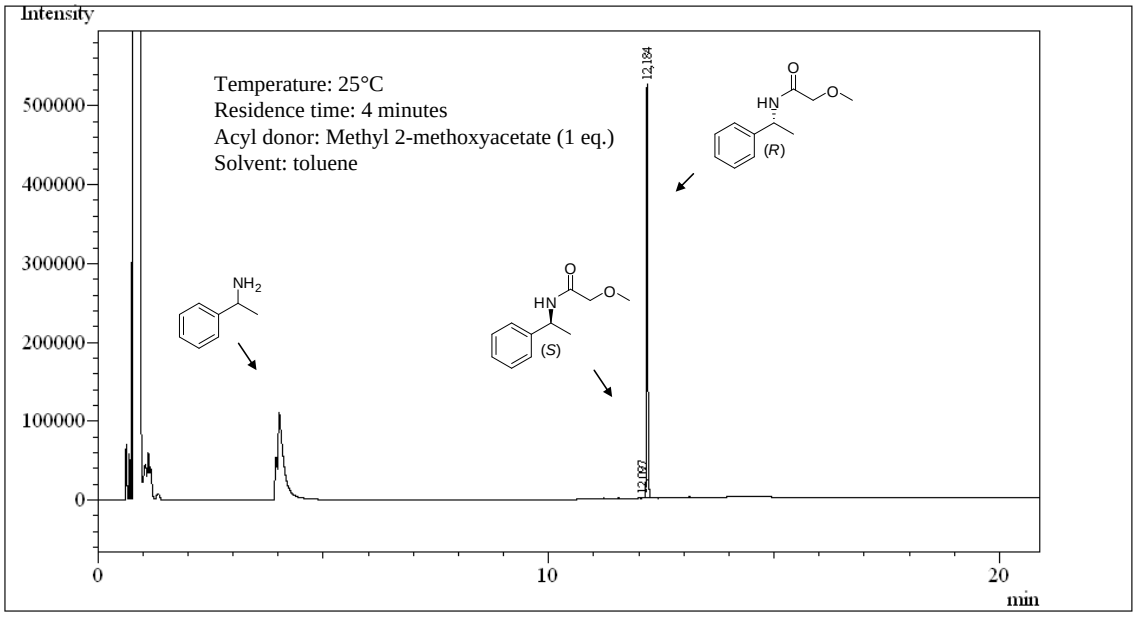


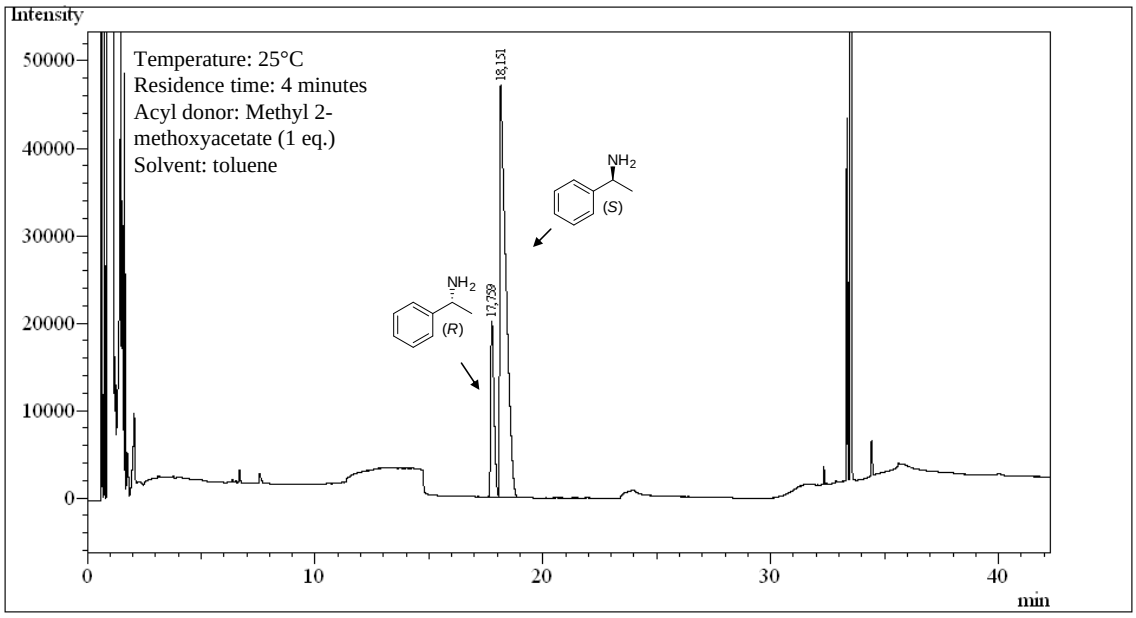


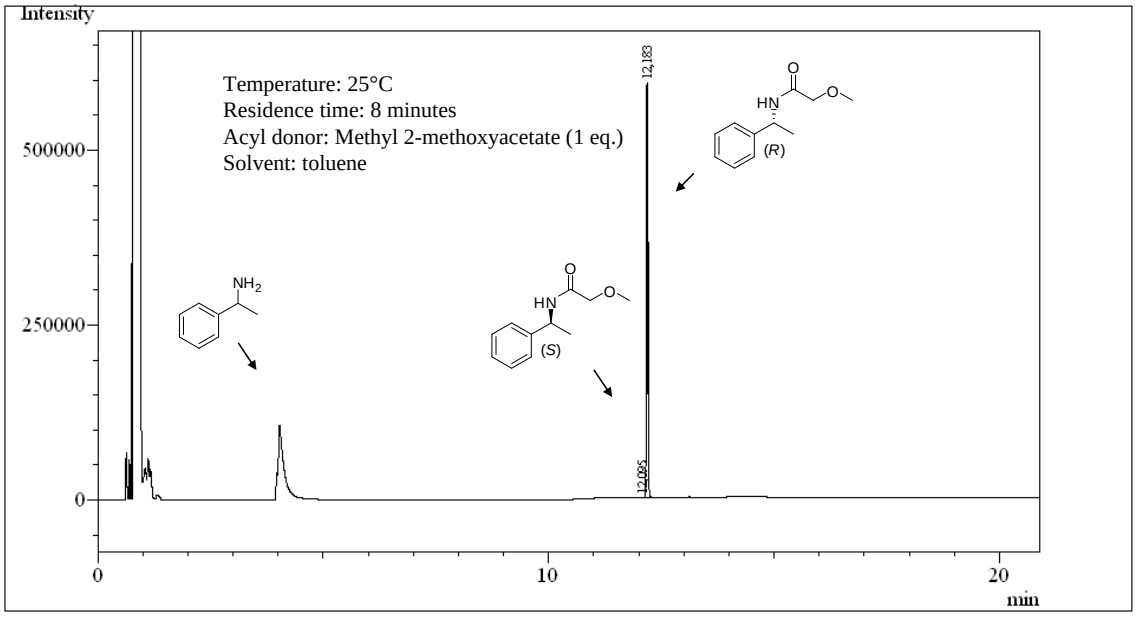


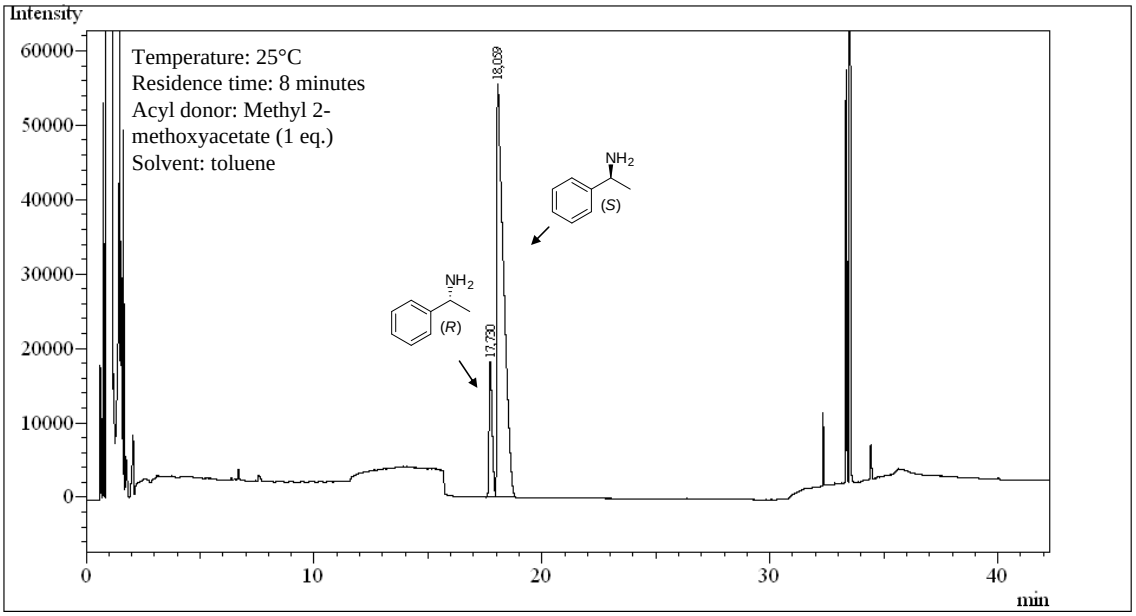


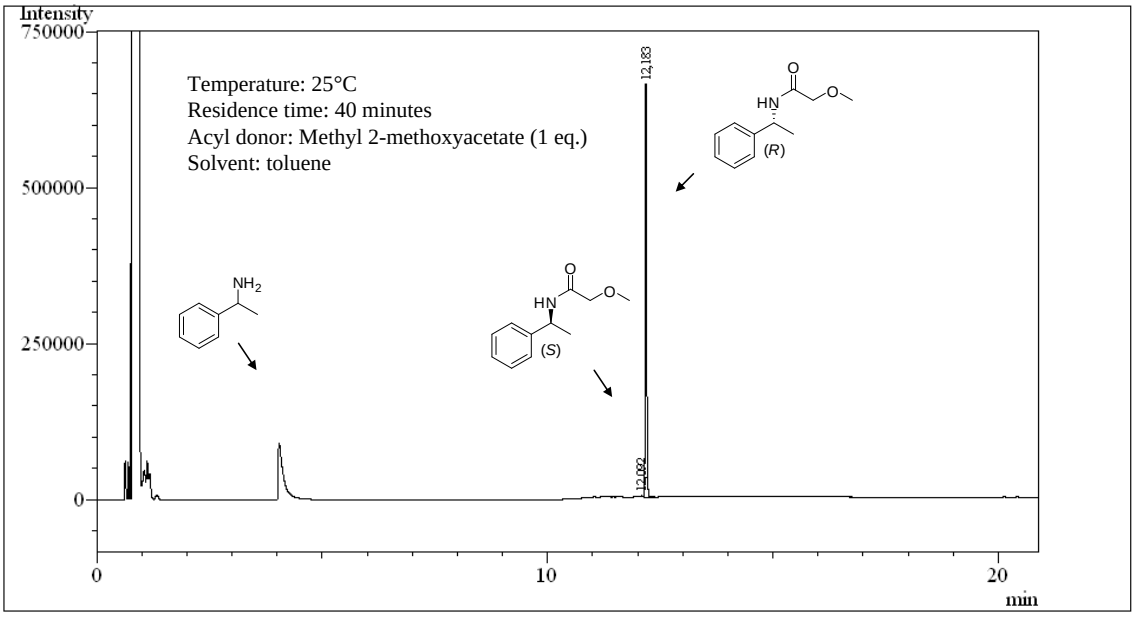
2.1.5. Variation of acyl dono:substrate ratio in the kinetic resolution of (+/-)-1-phenylethylamine with Methyl 2-methoxyacetate as acyl donor under continuous flow conditions

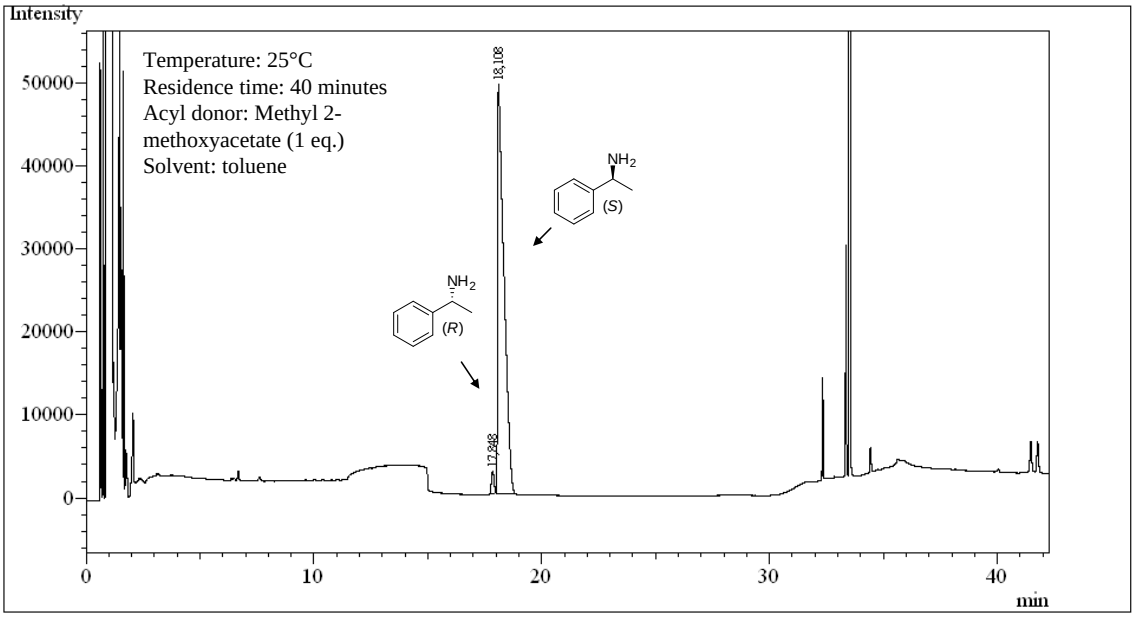


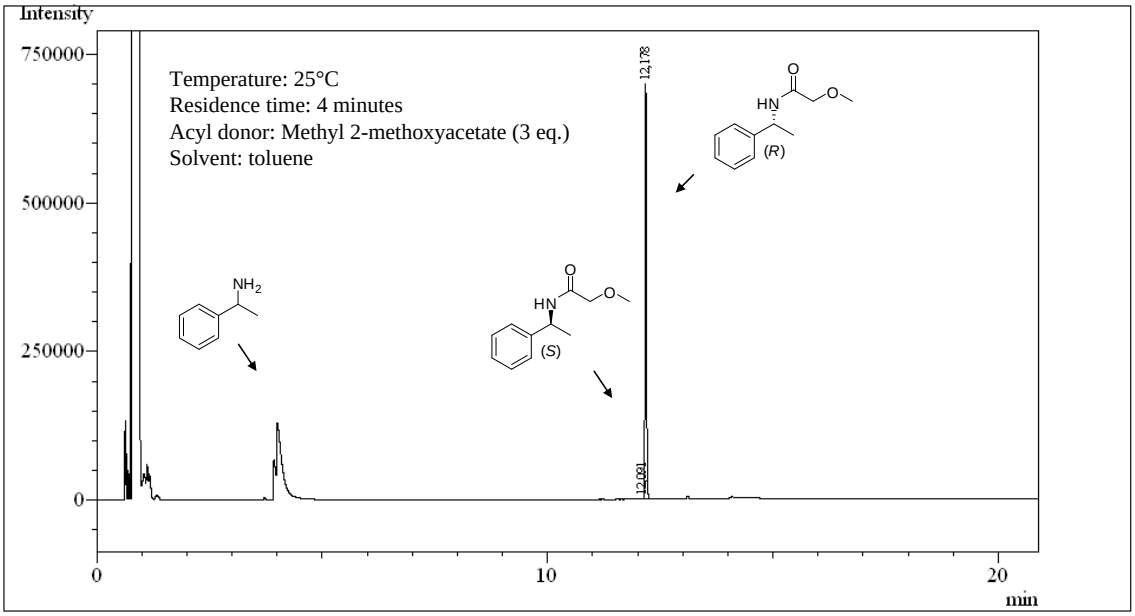


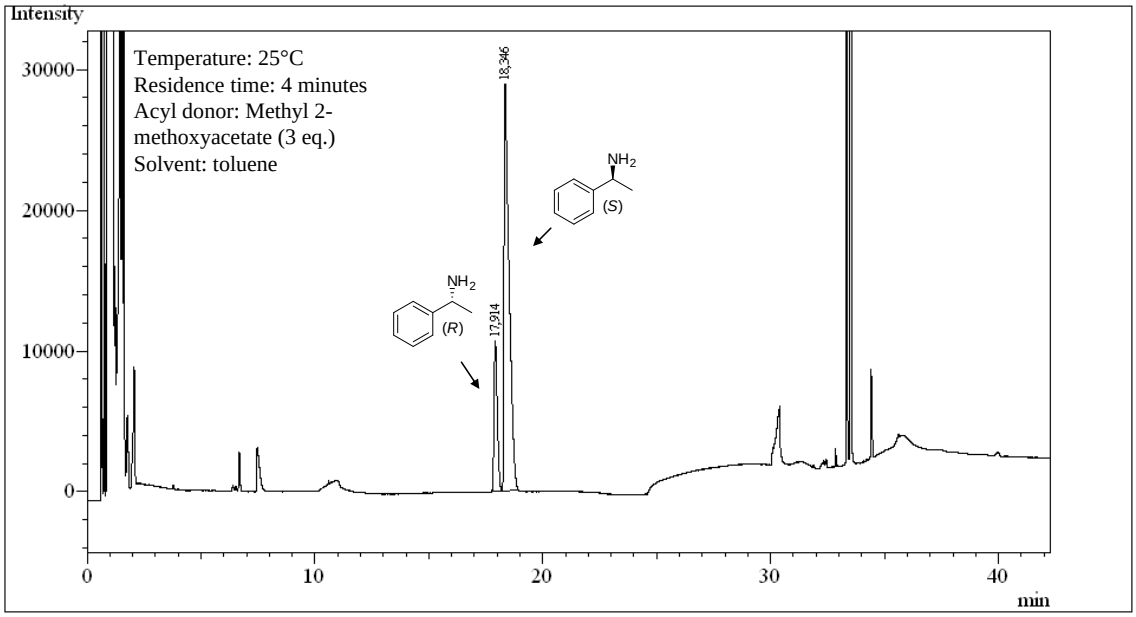


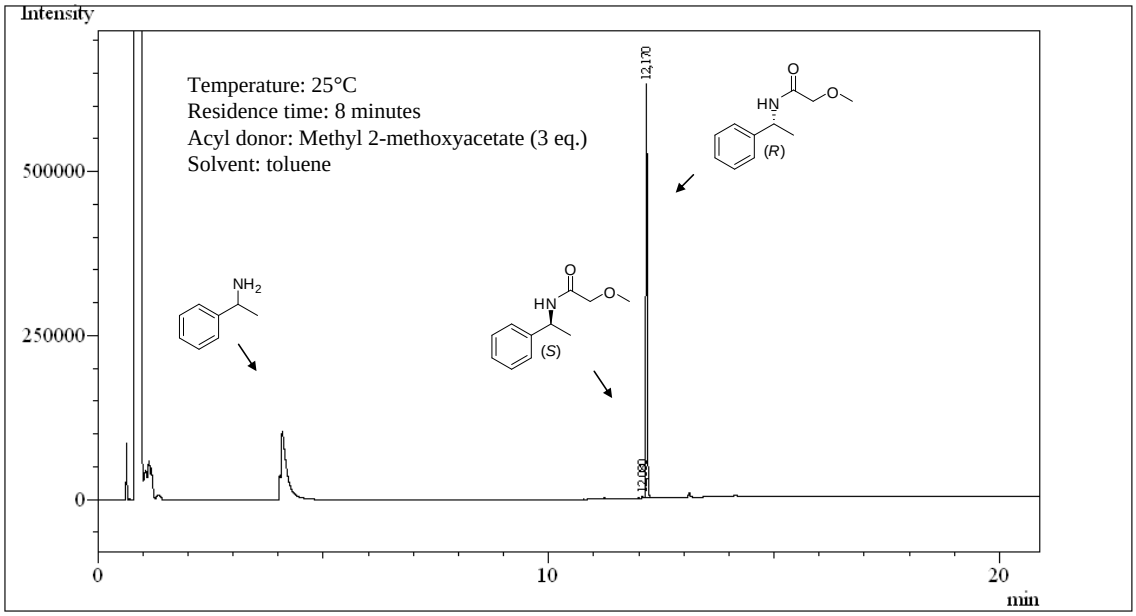


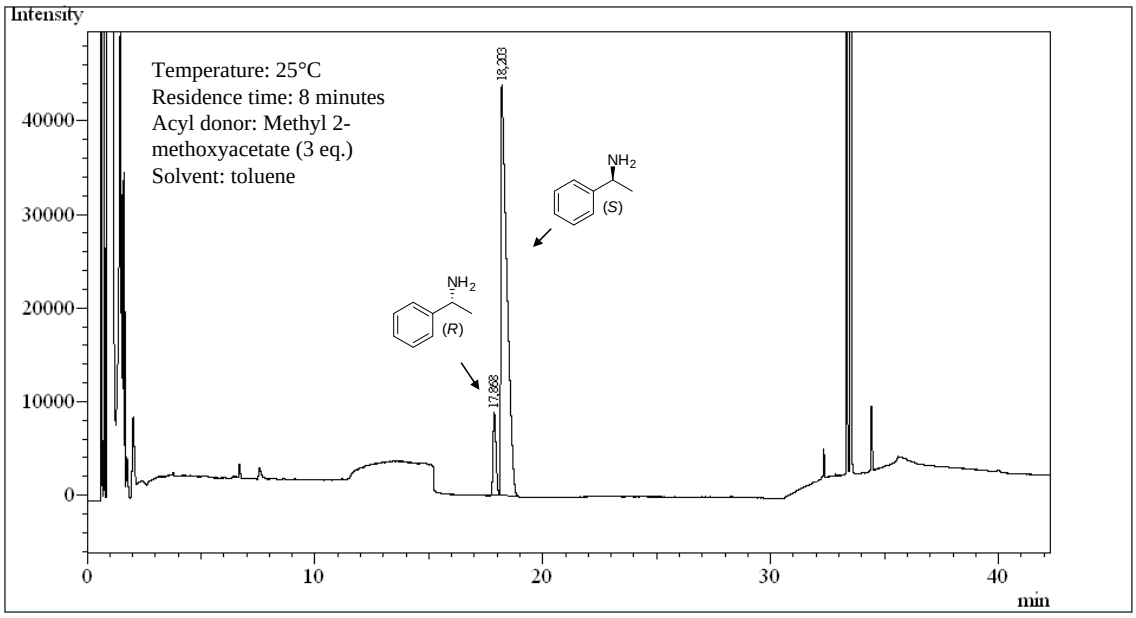


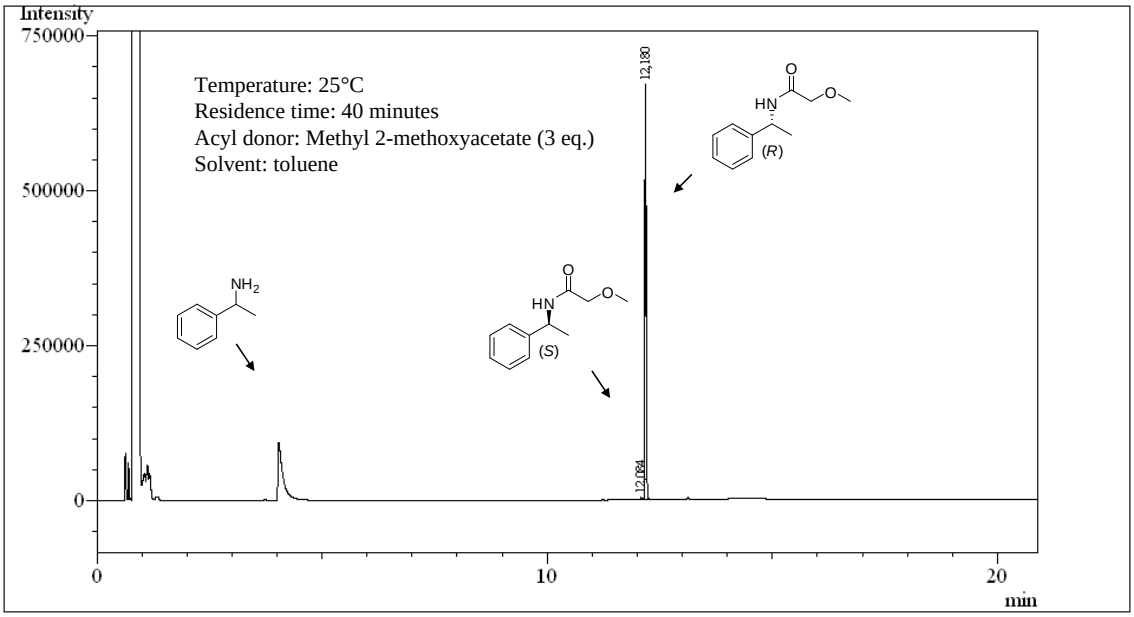


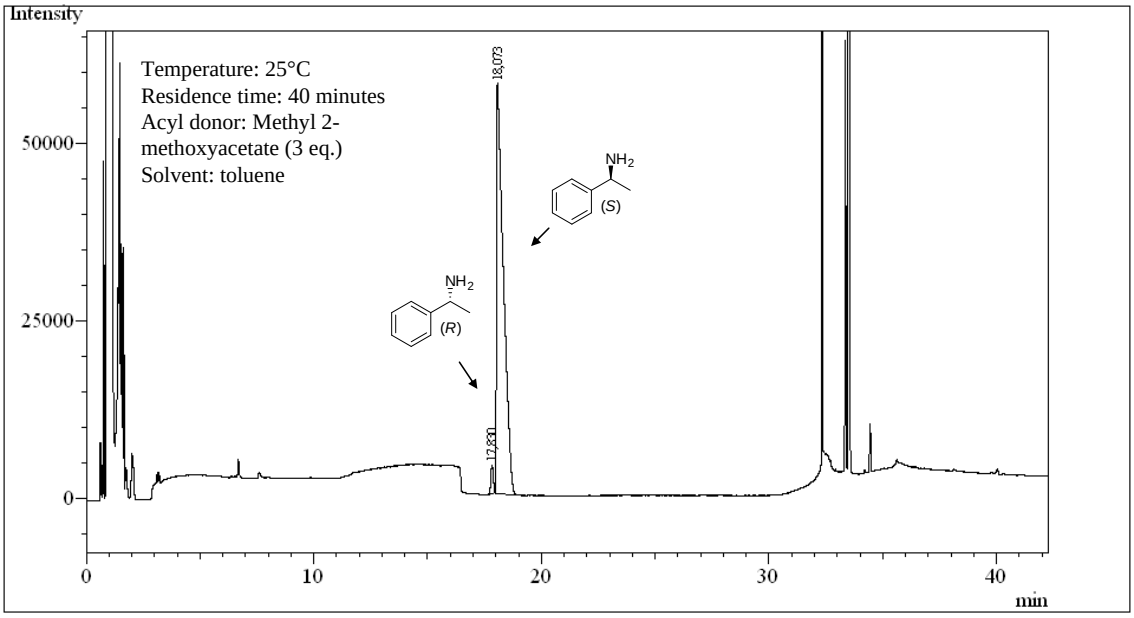


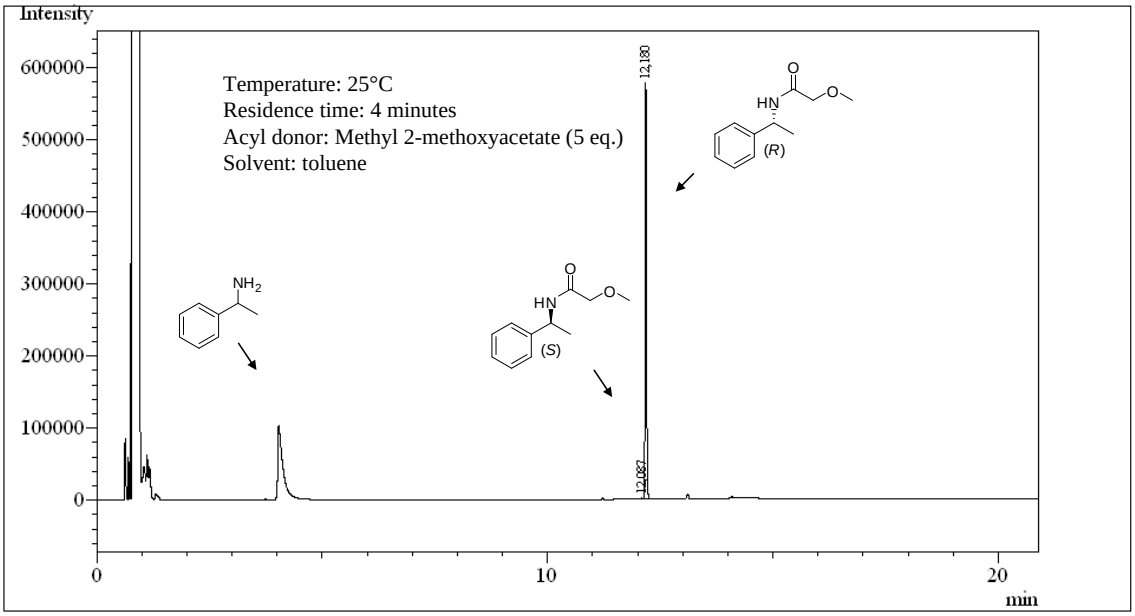


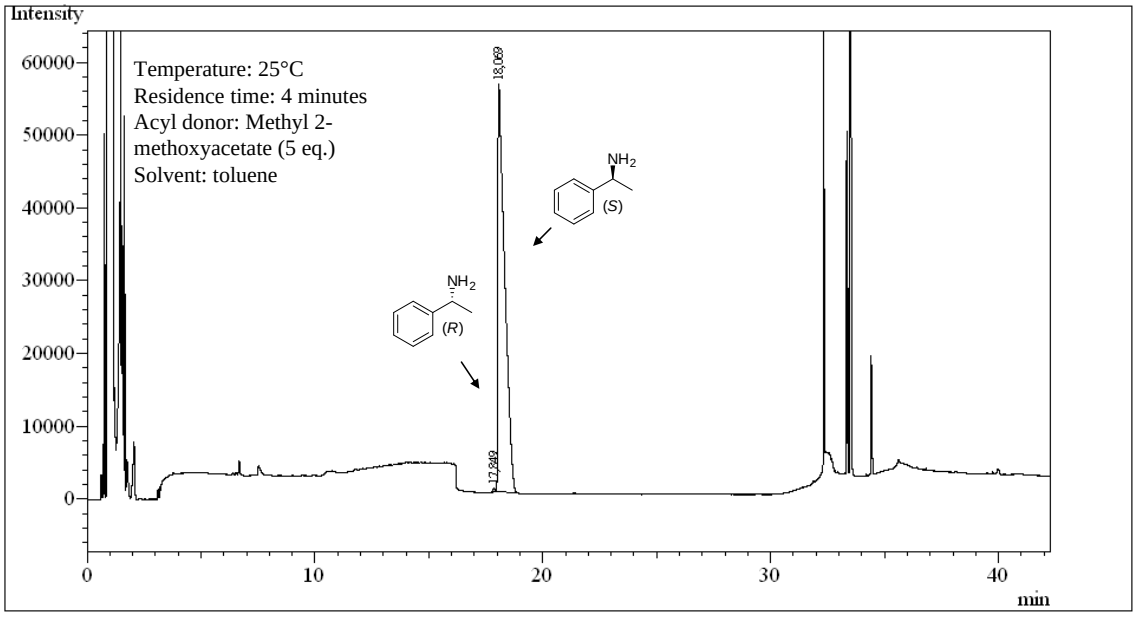


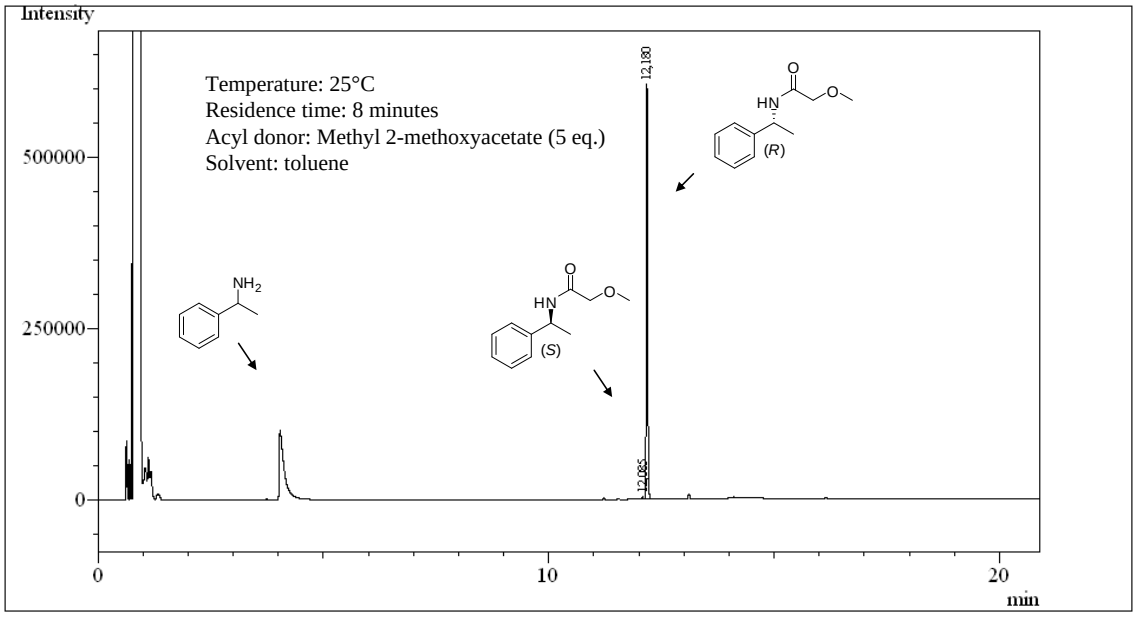


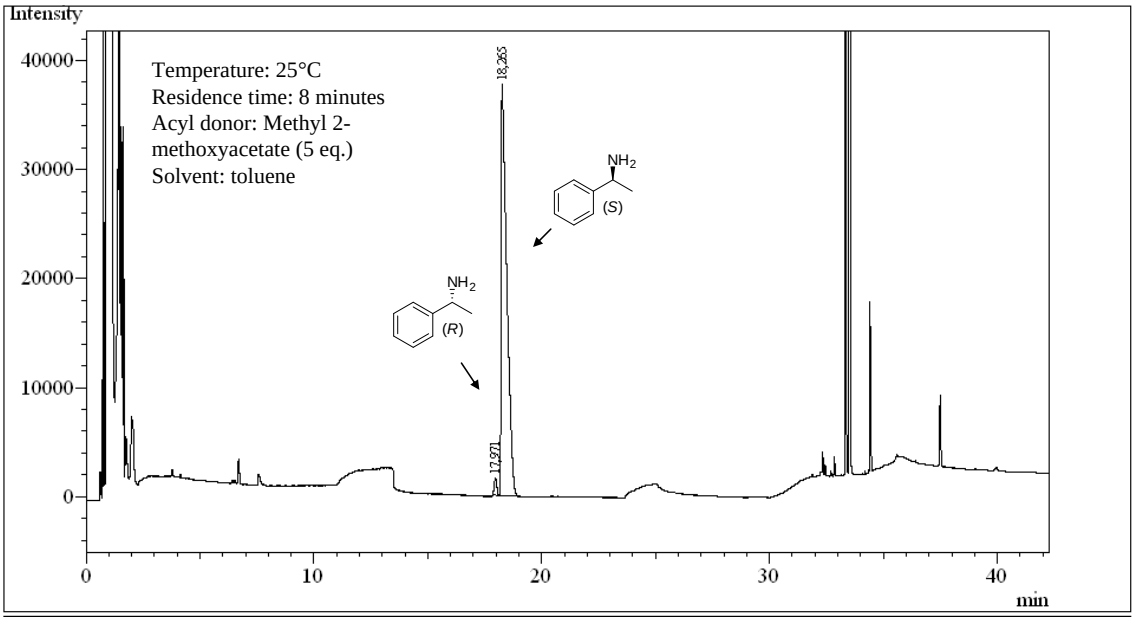


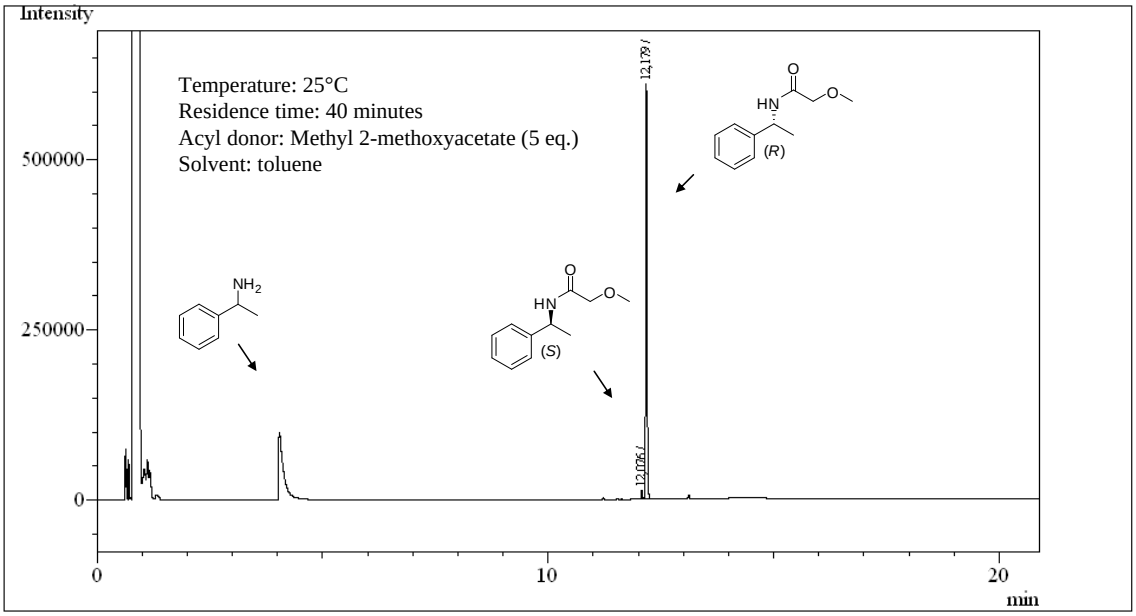


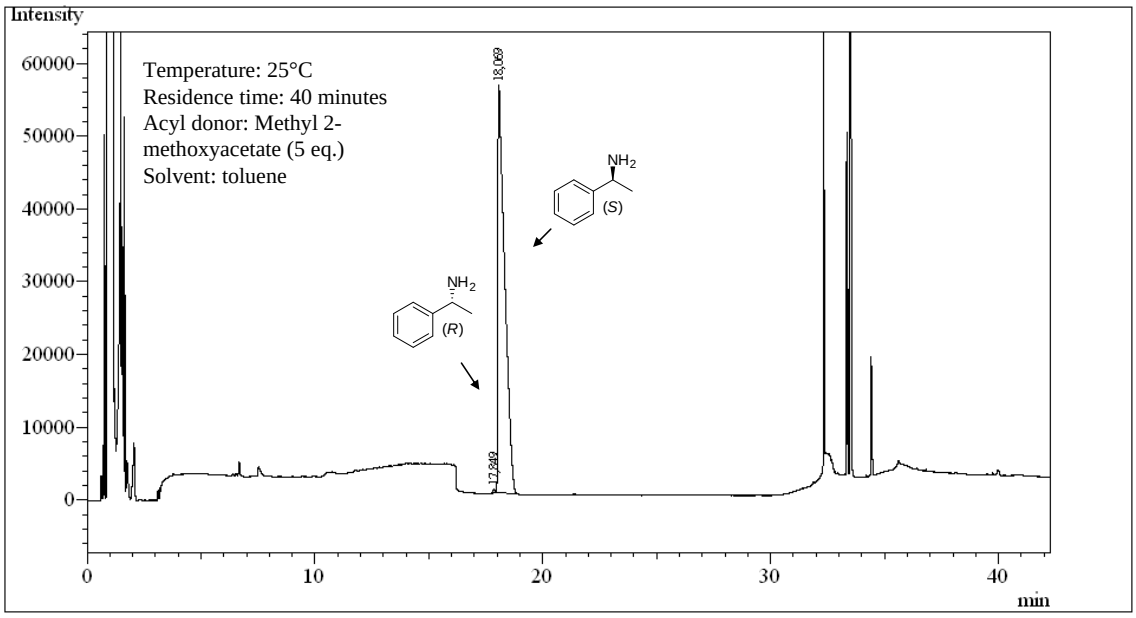




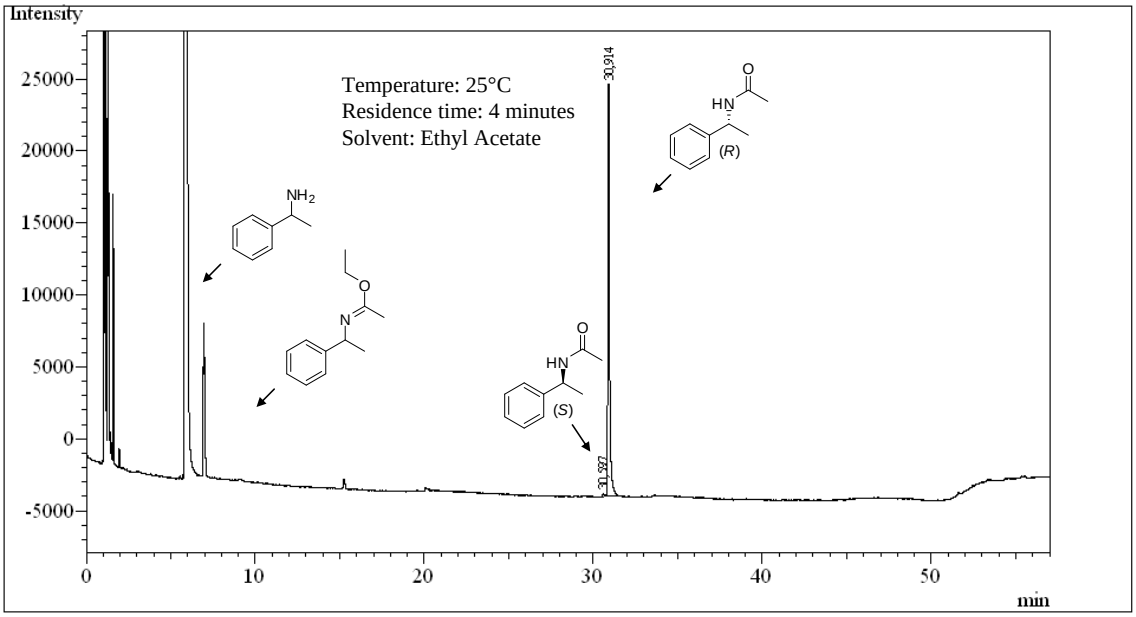


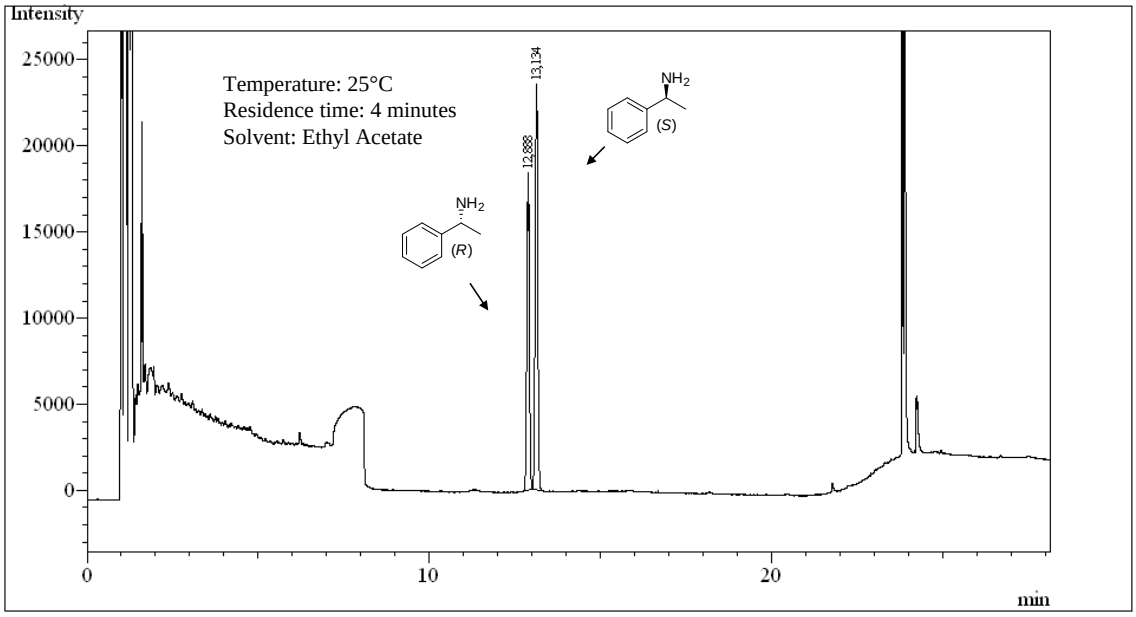


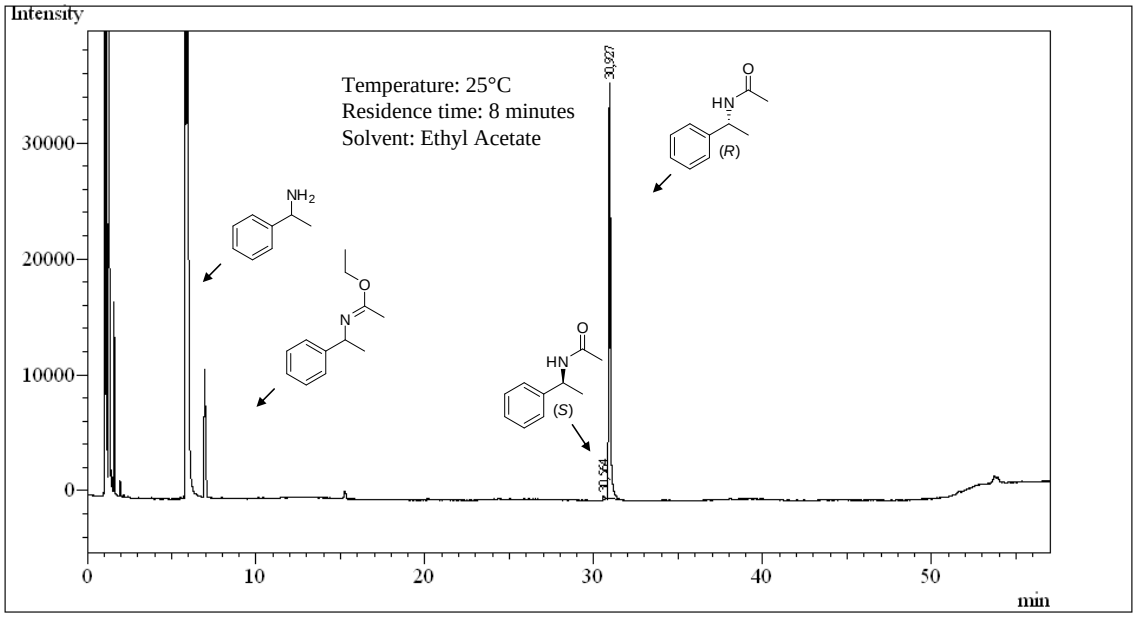


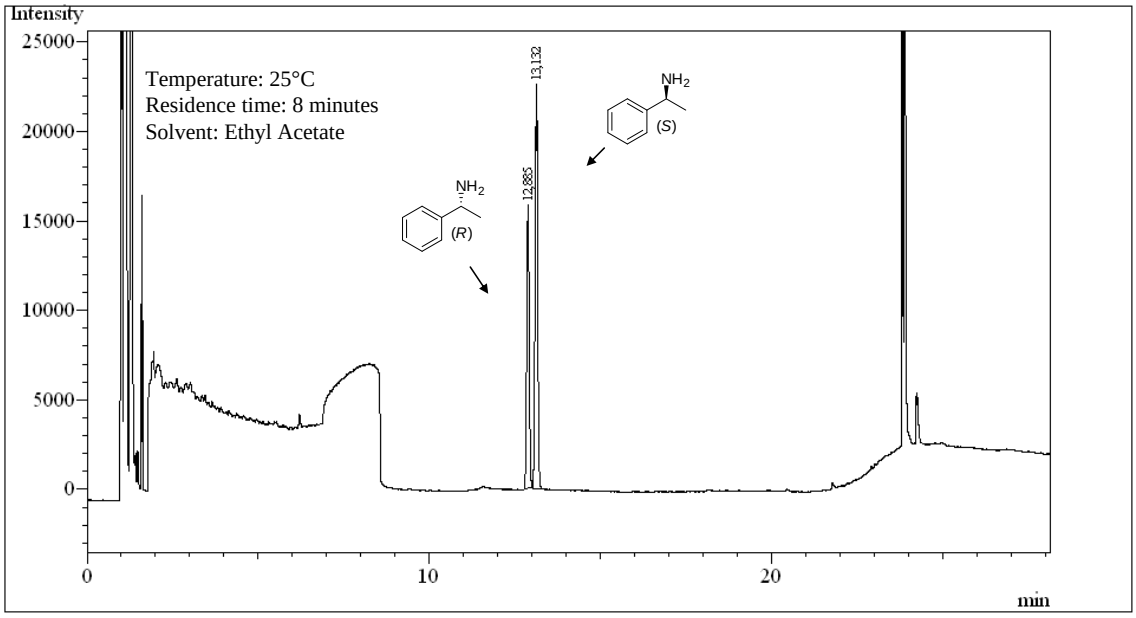


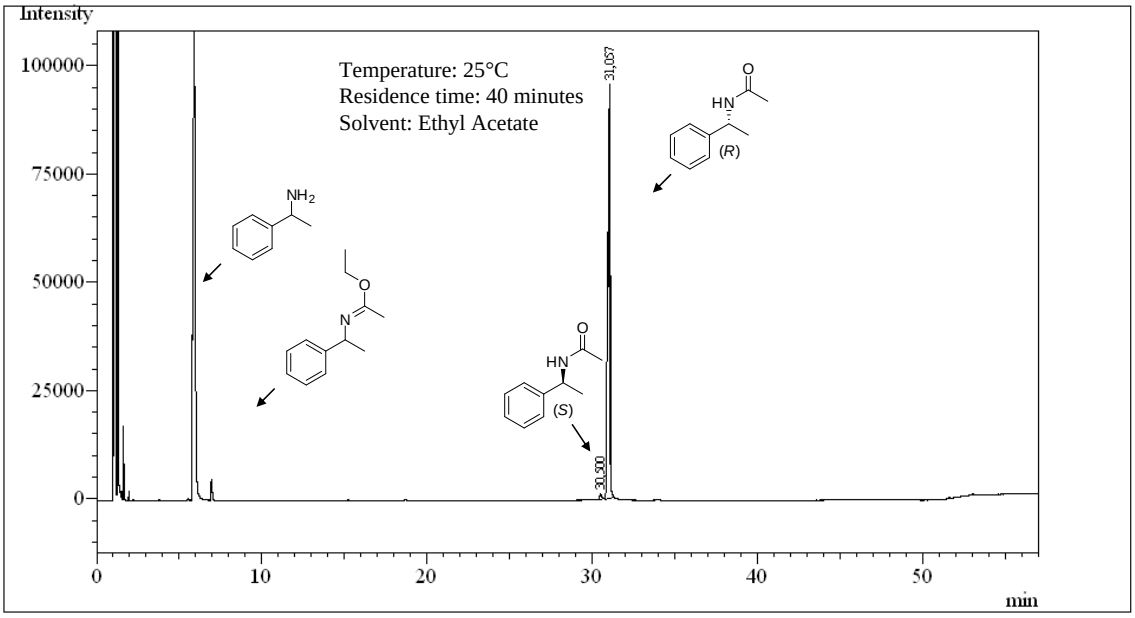
2.1.5 Kinetic resolution of (+/-)-1-phenylethylamine (1) with Ethyl Acetate as solvent under continuous flow conditions

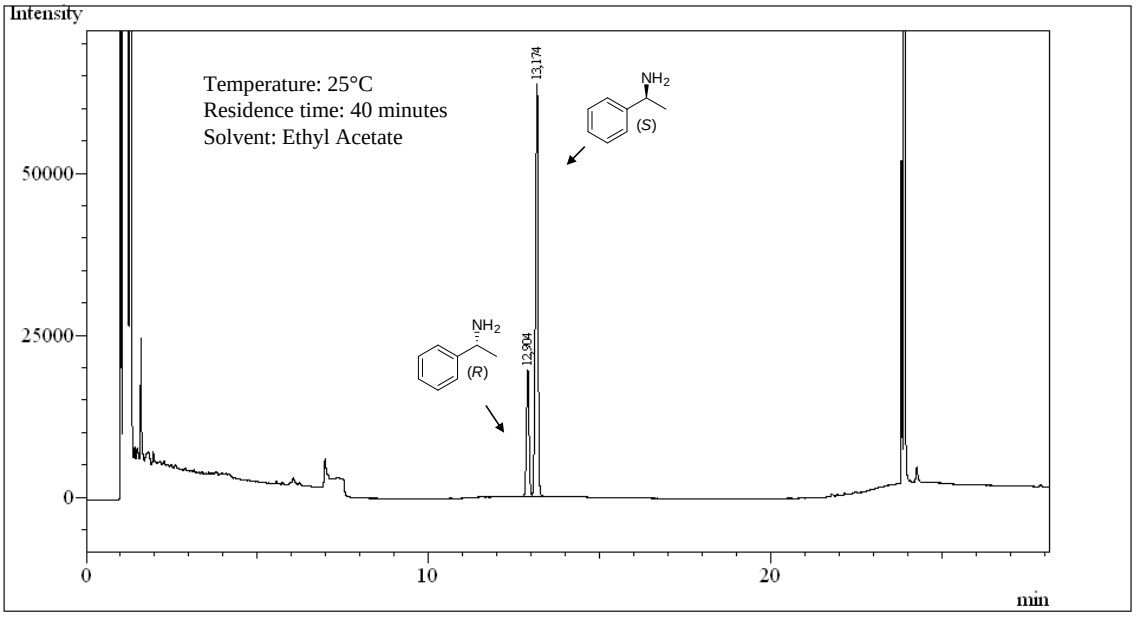


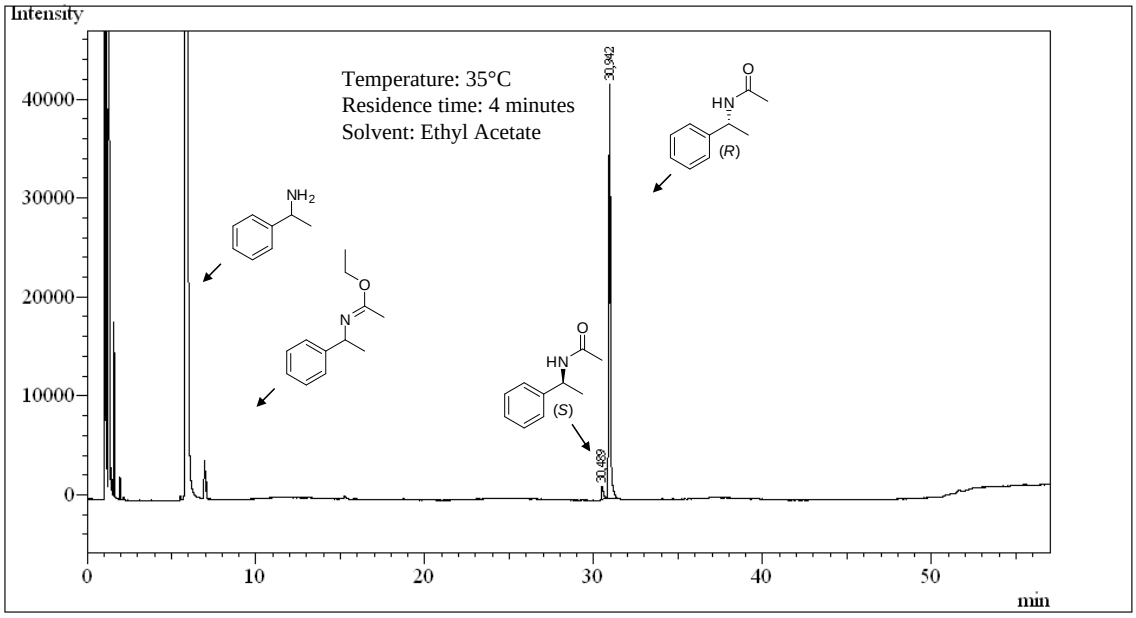


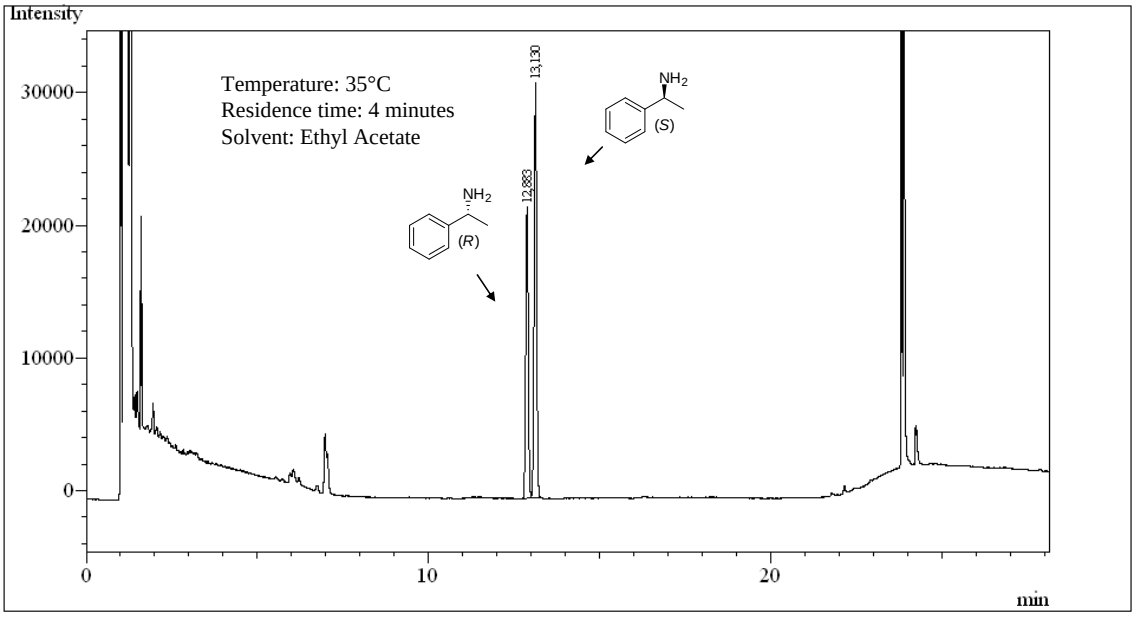


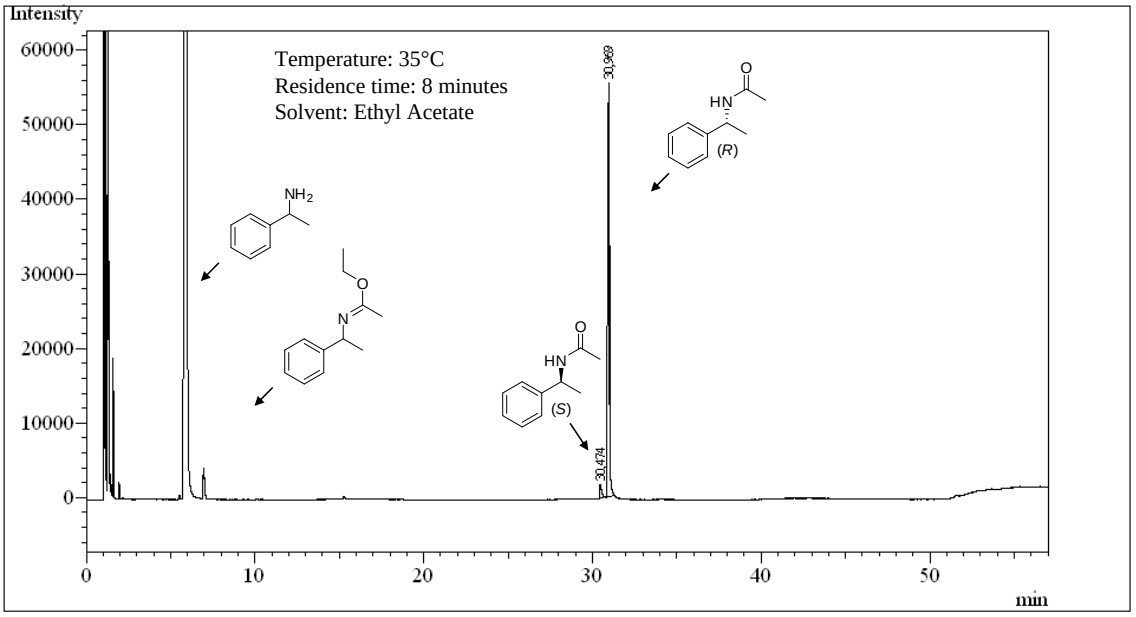


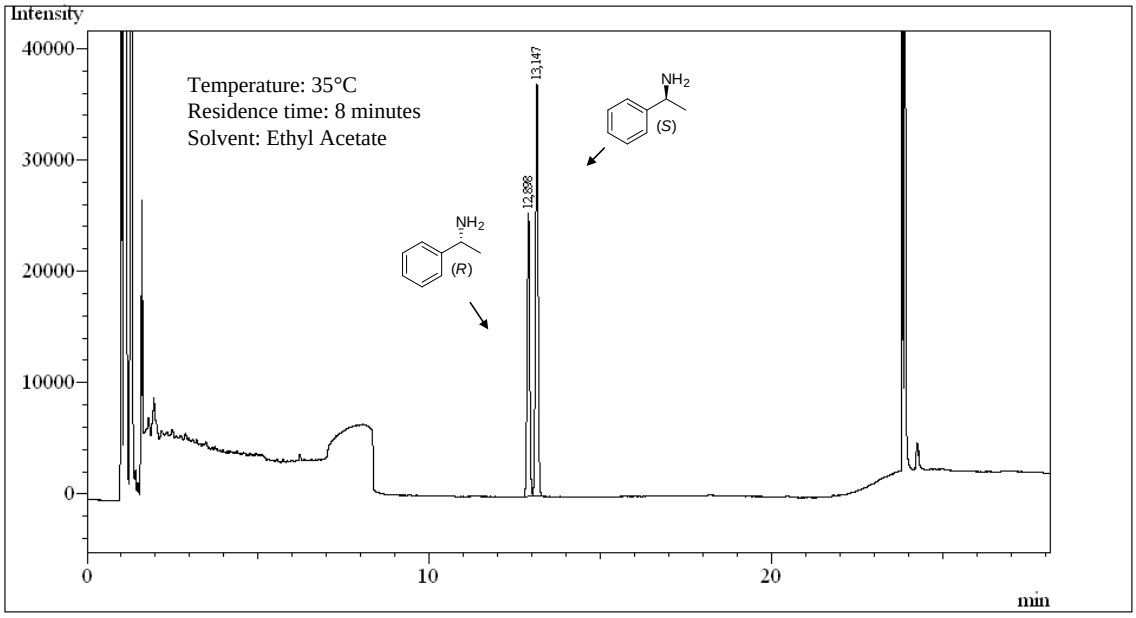


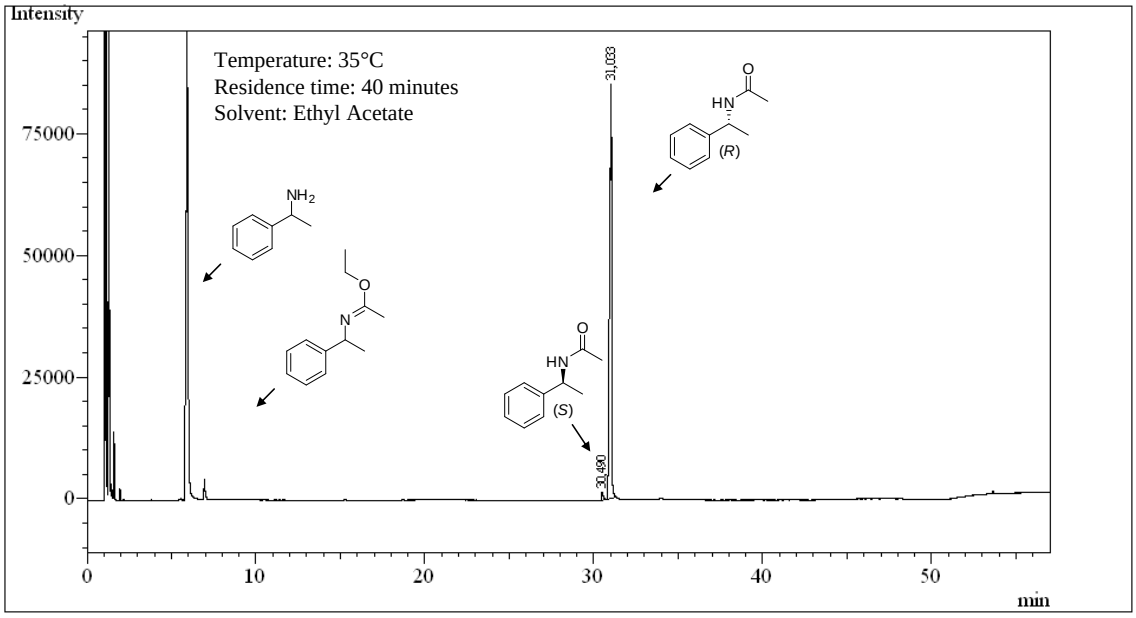


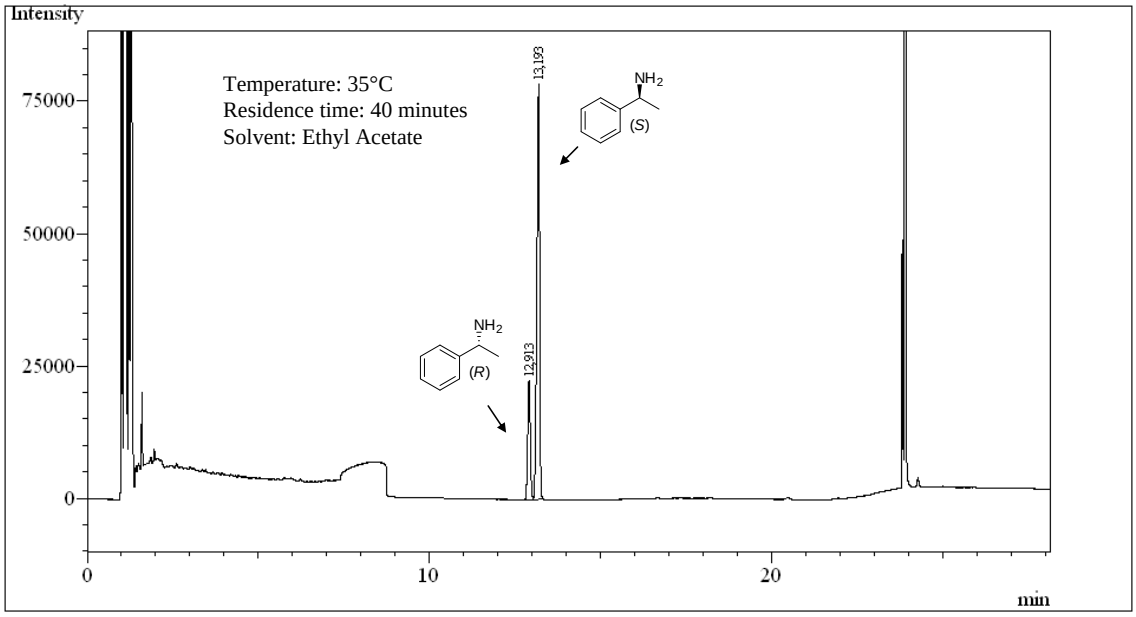


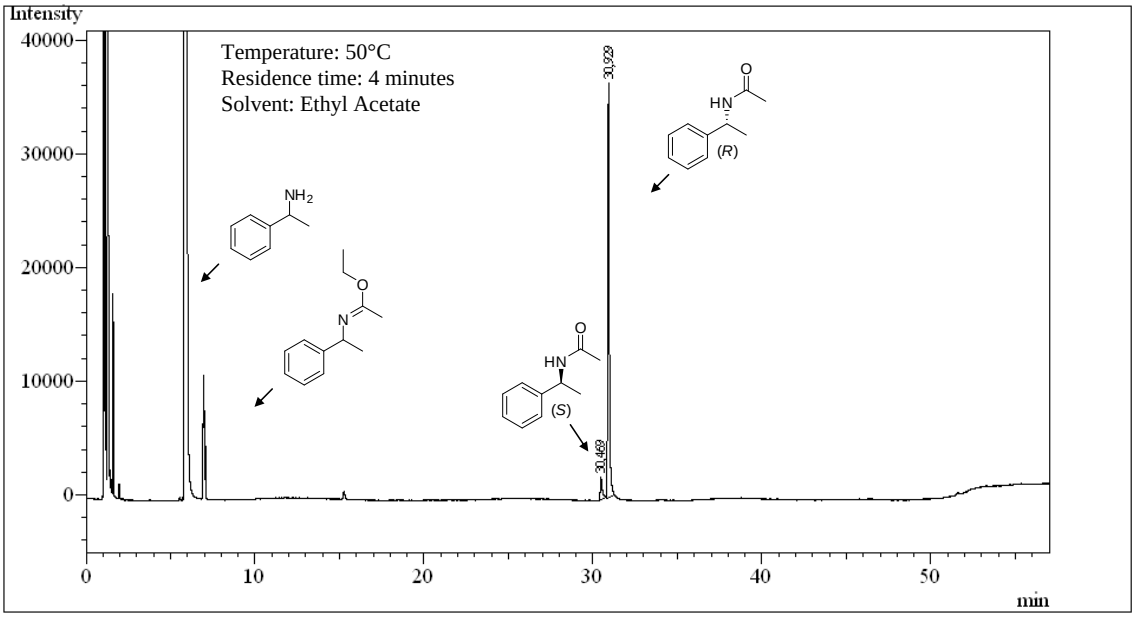


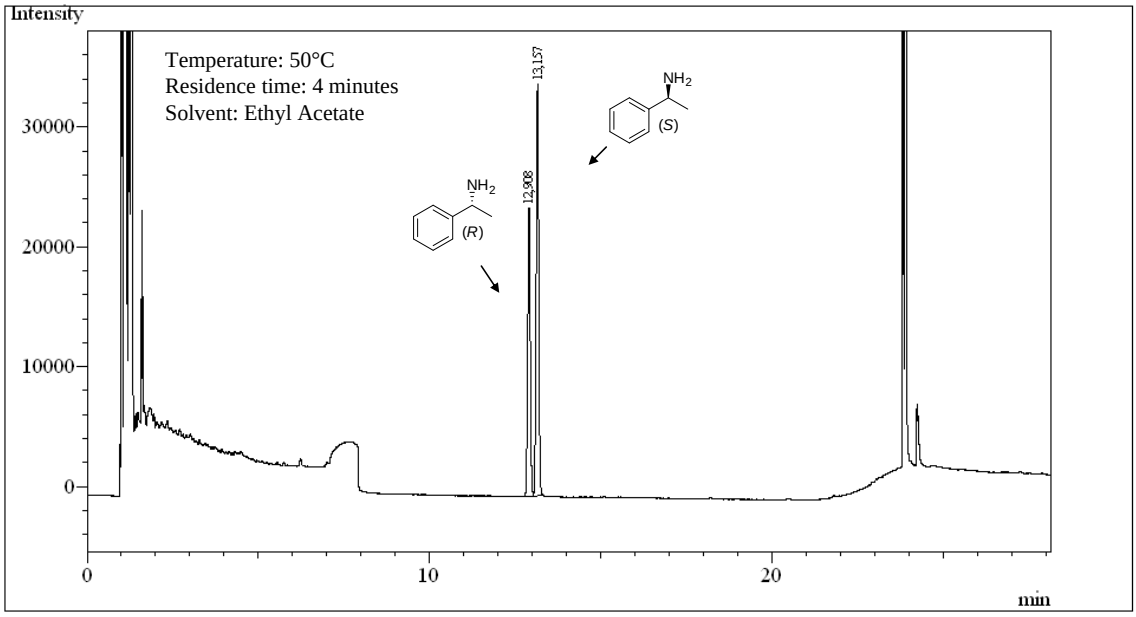


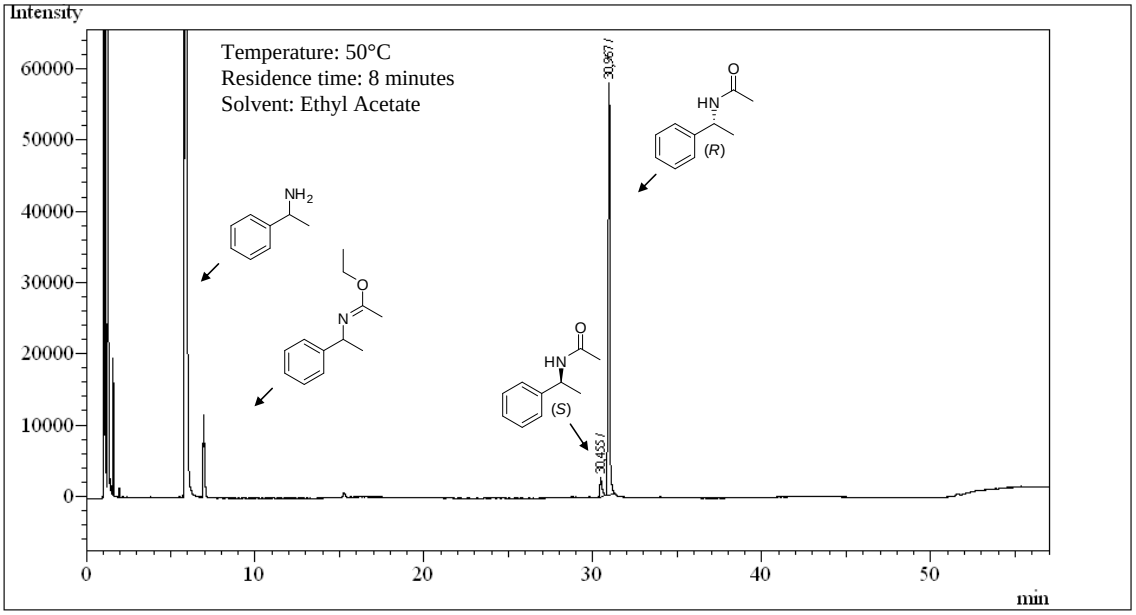


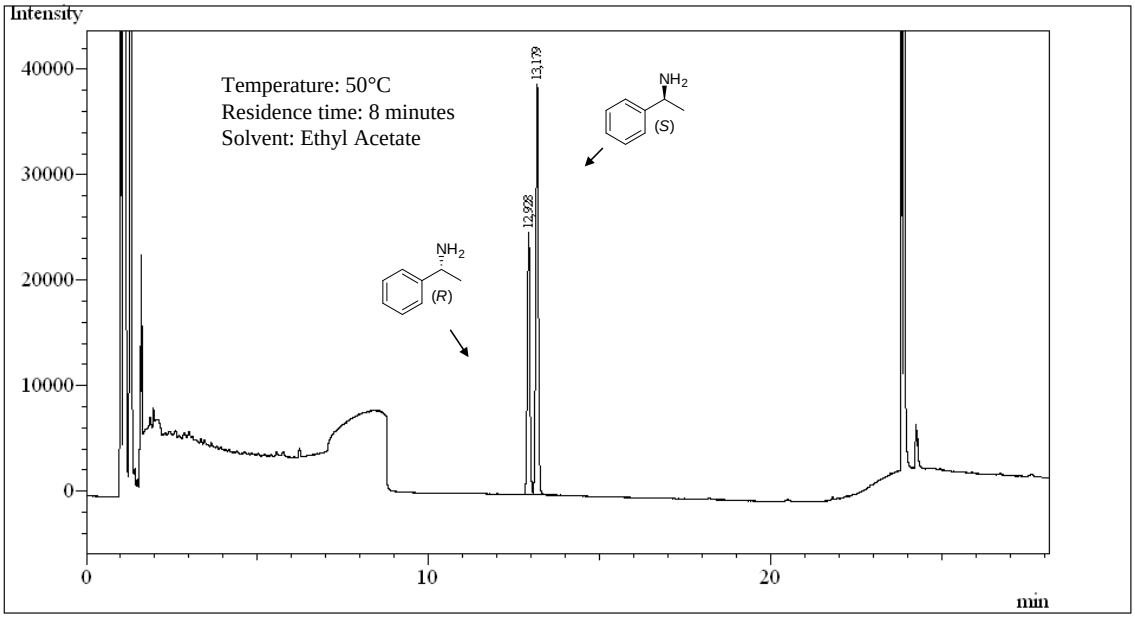


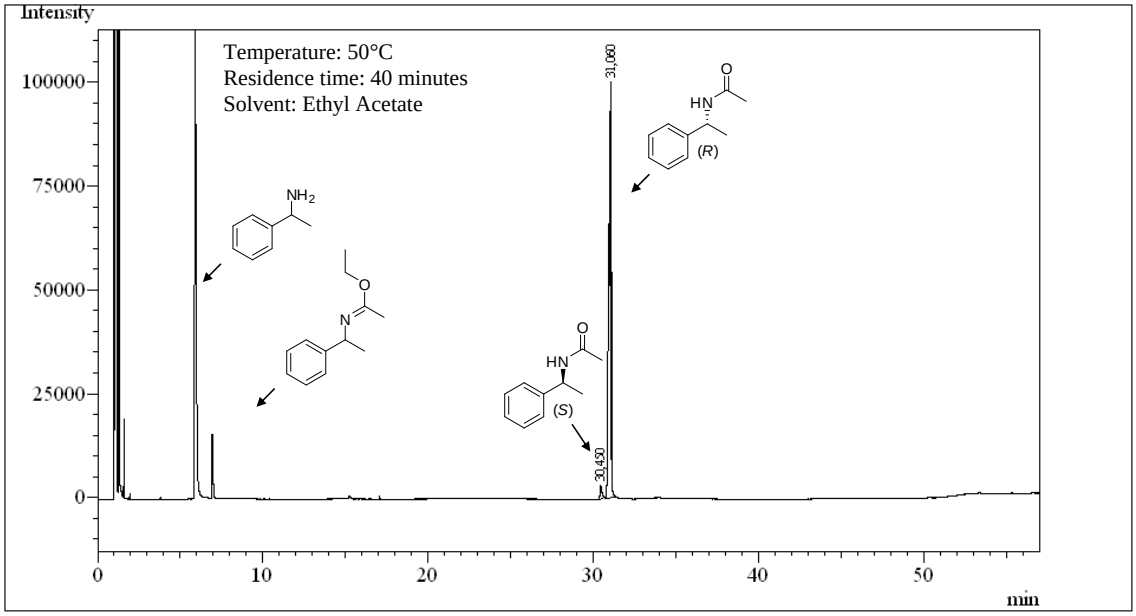


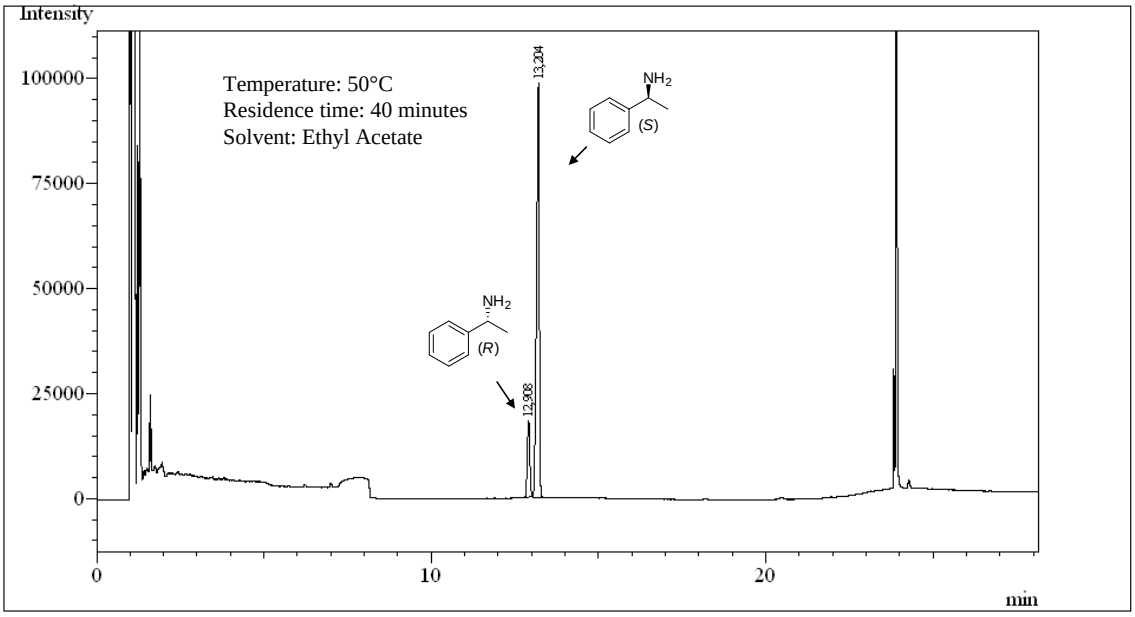


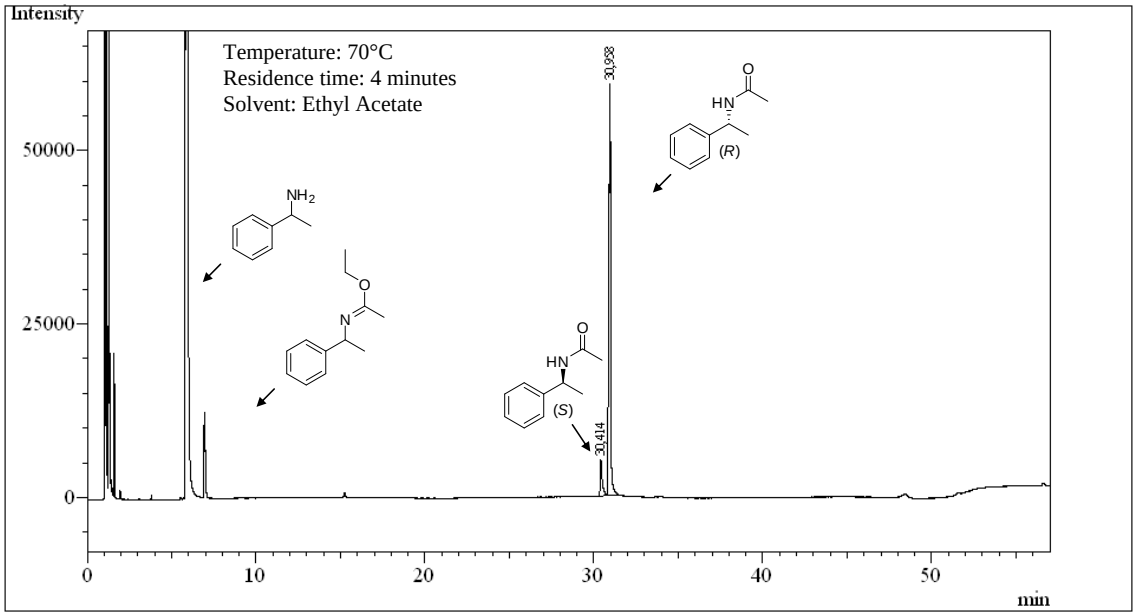


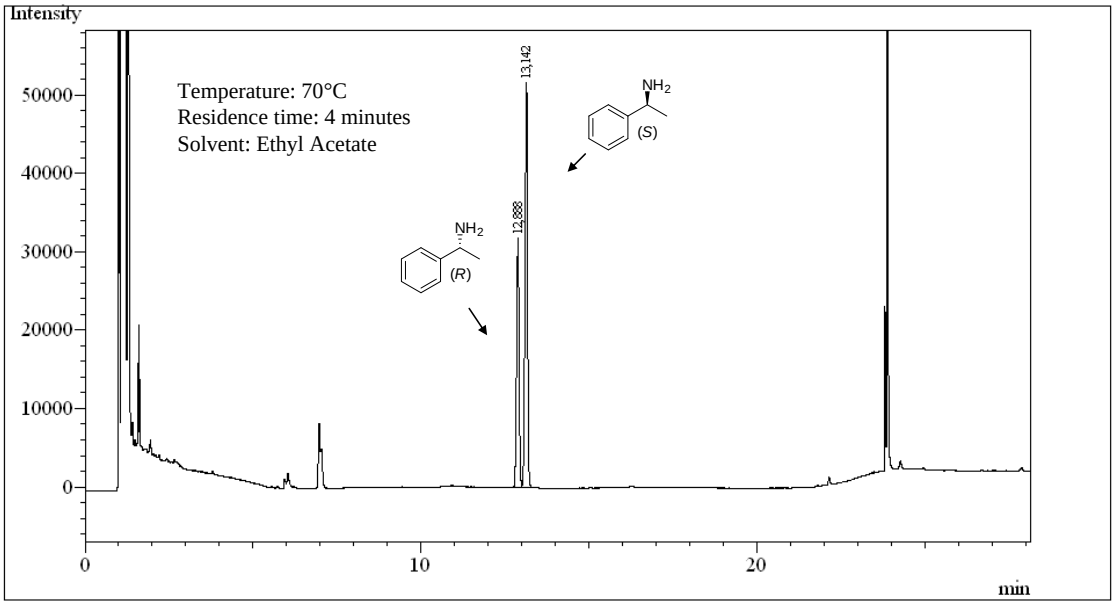


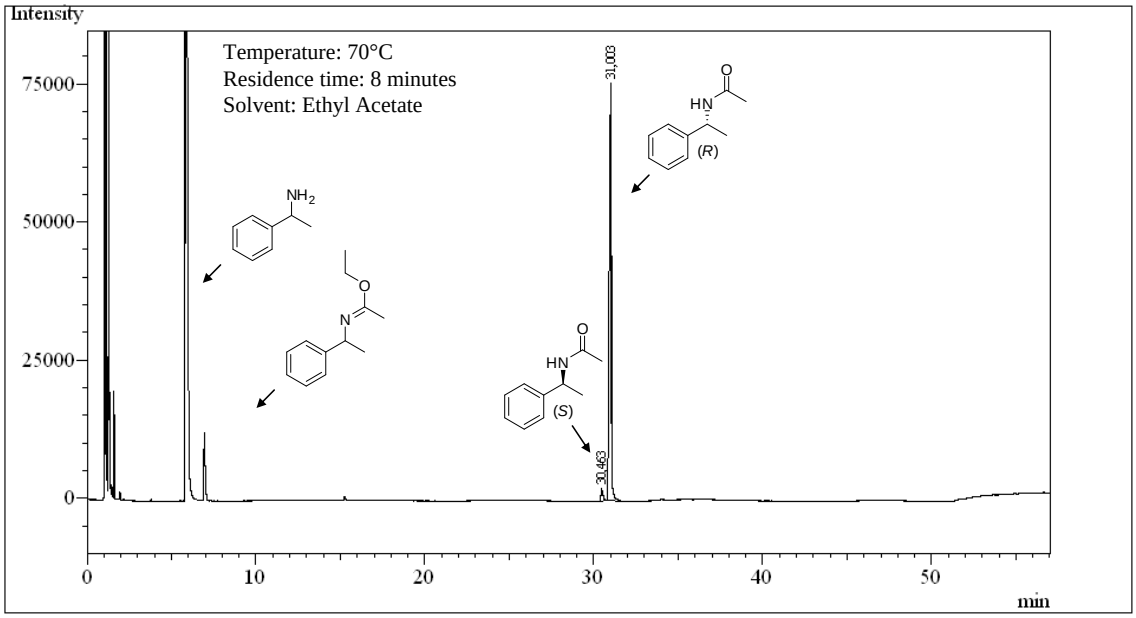


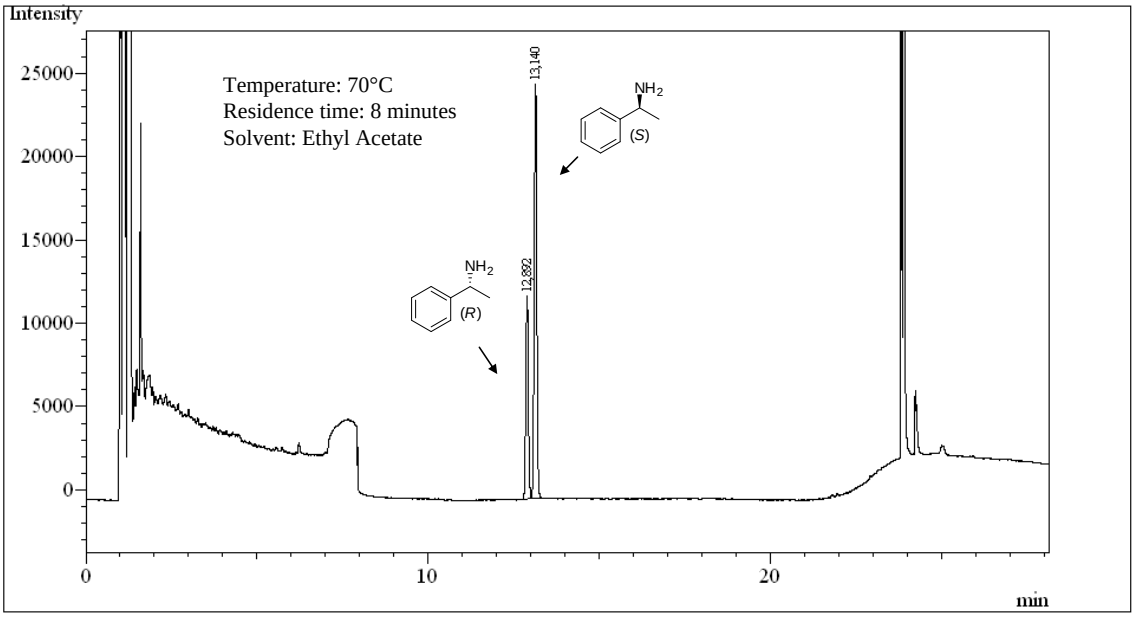


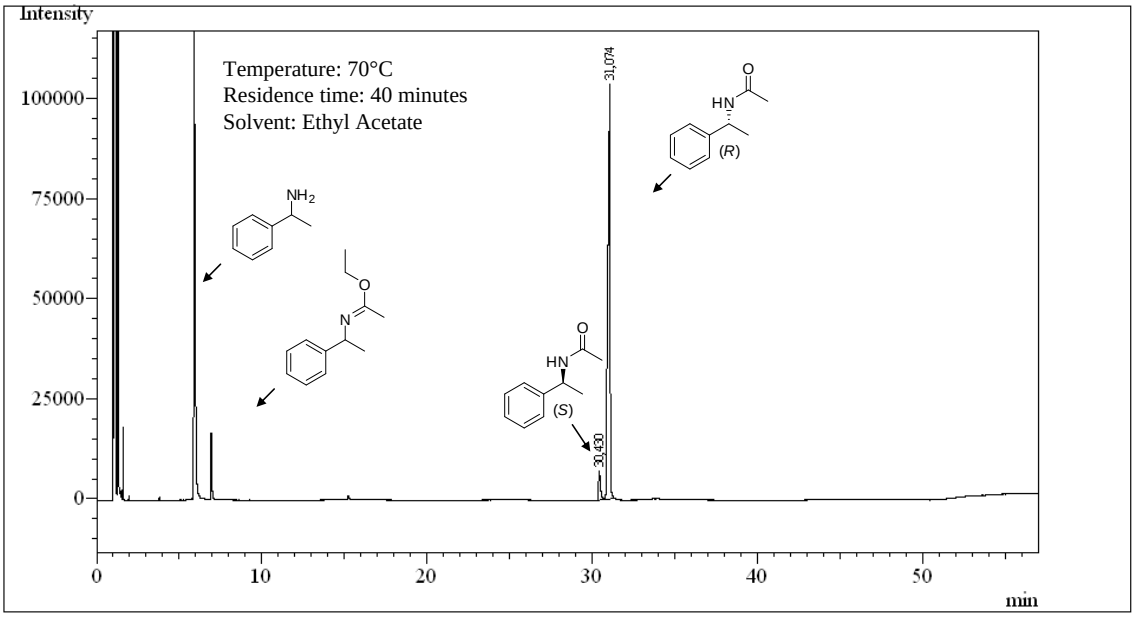


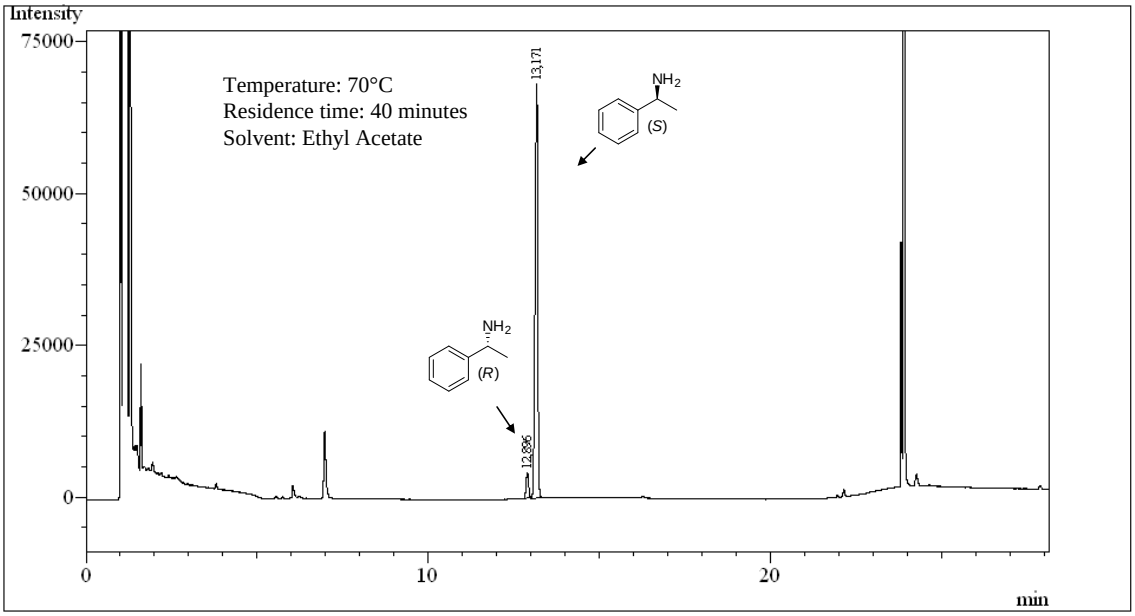




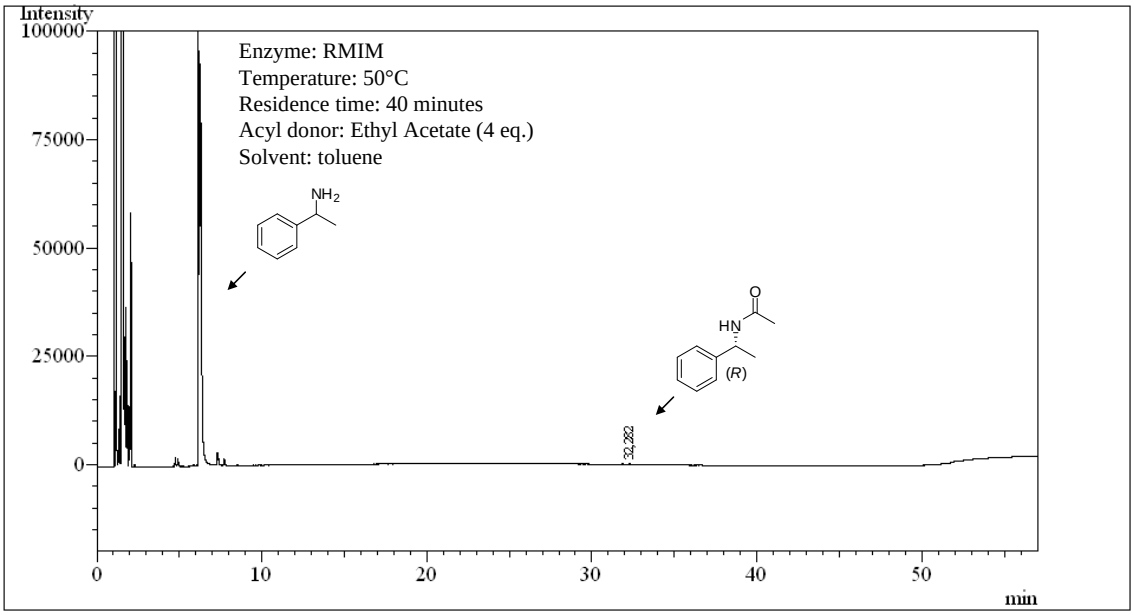


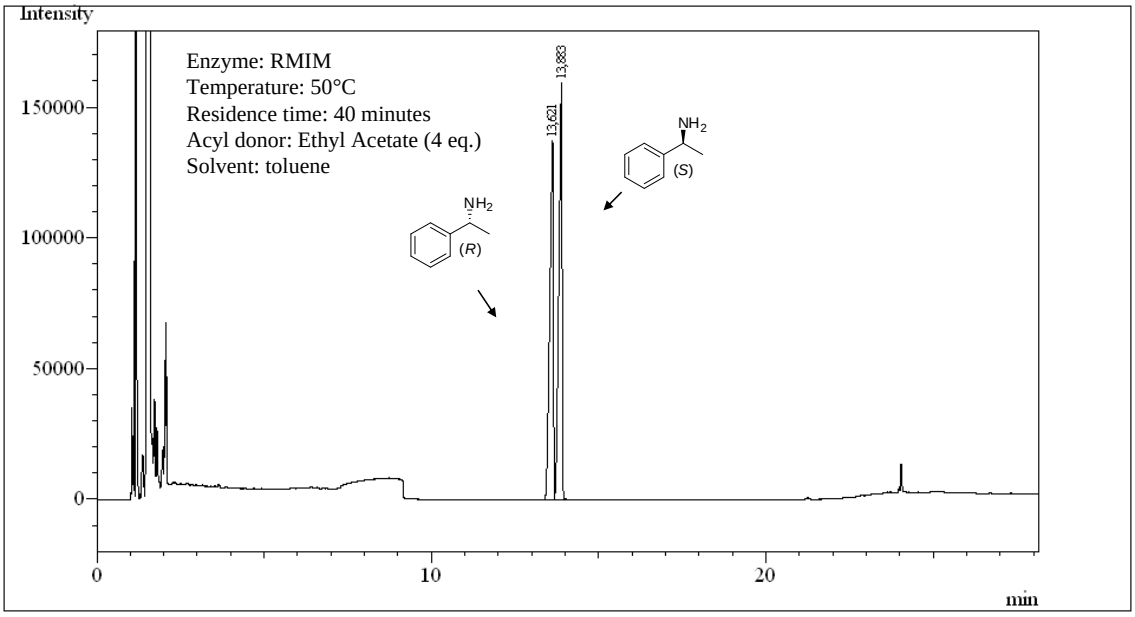


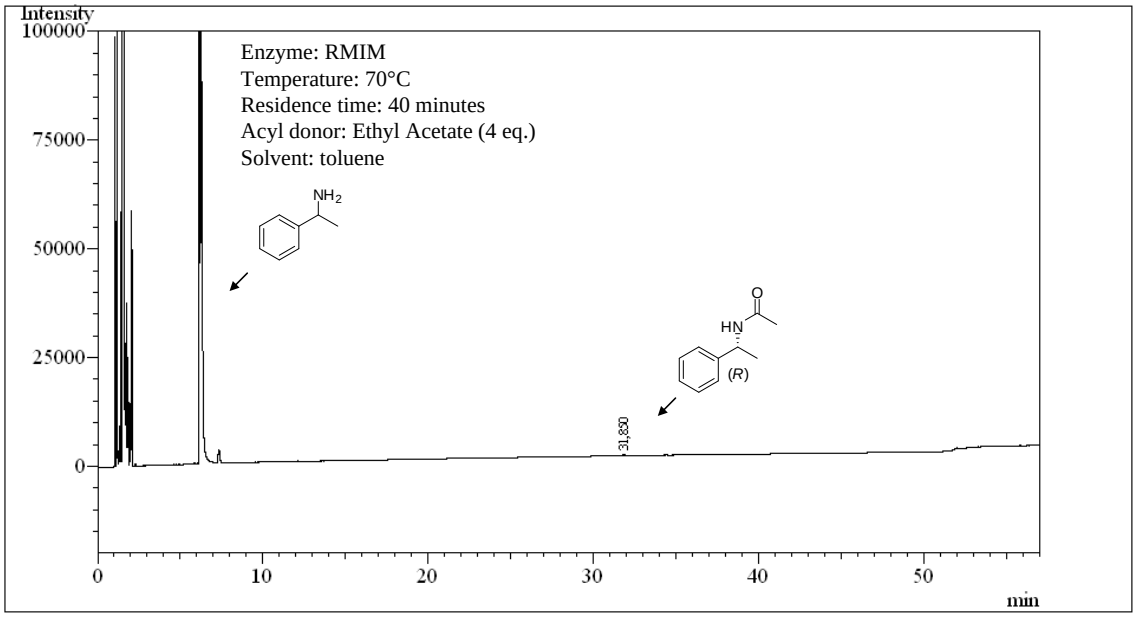


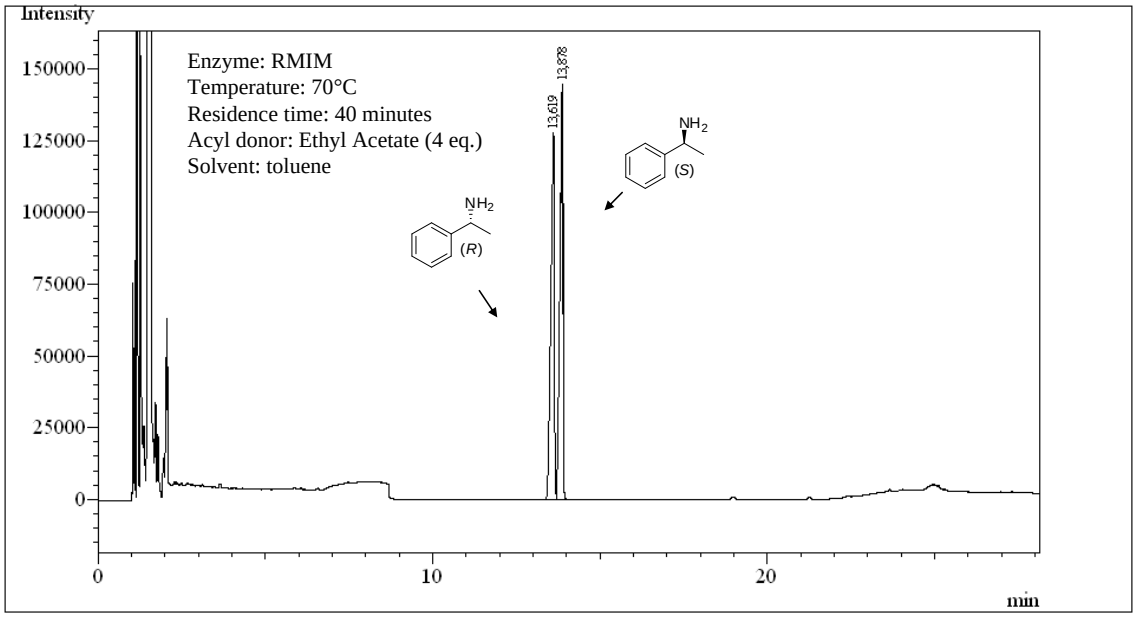


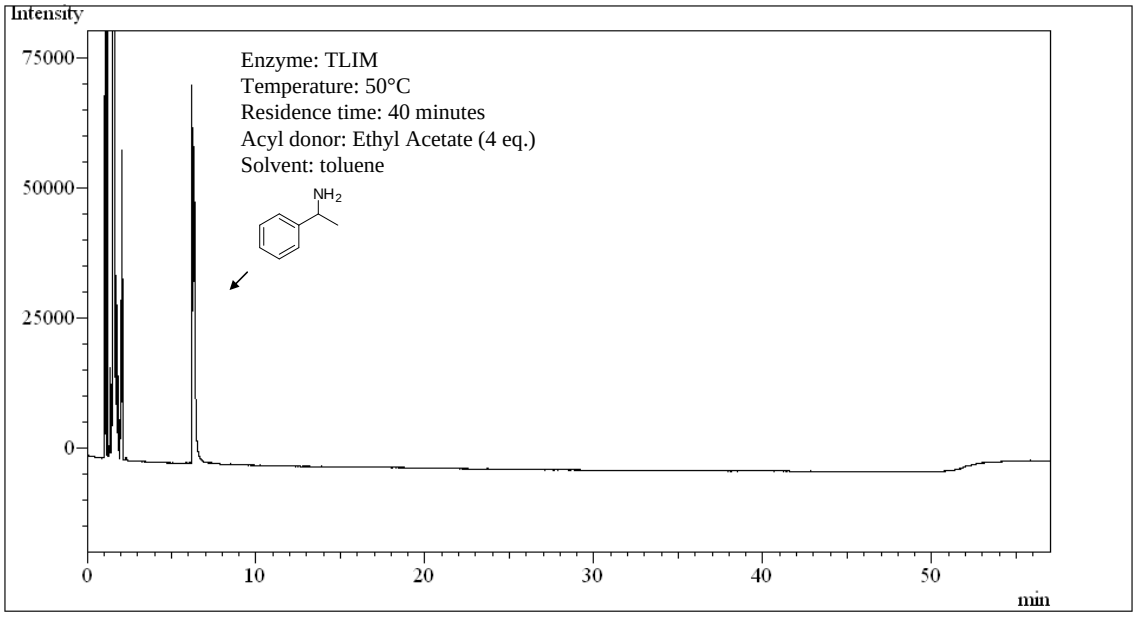
2.1.6. Kinetic resolution of (+/-)-1-phenylethylamine with different immobilized enzymes under continuous flow conditions

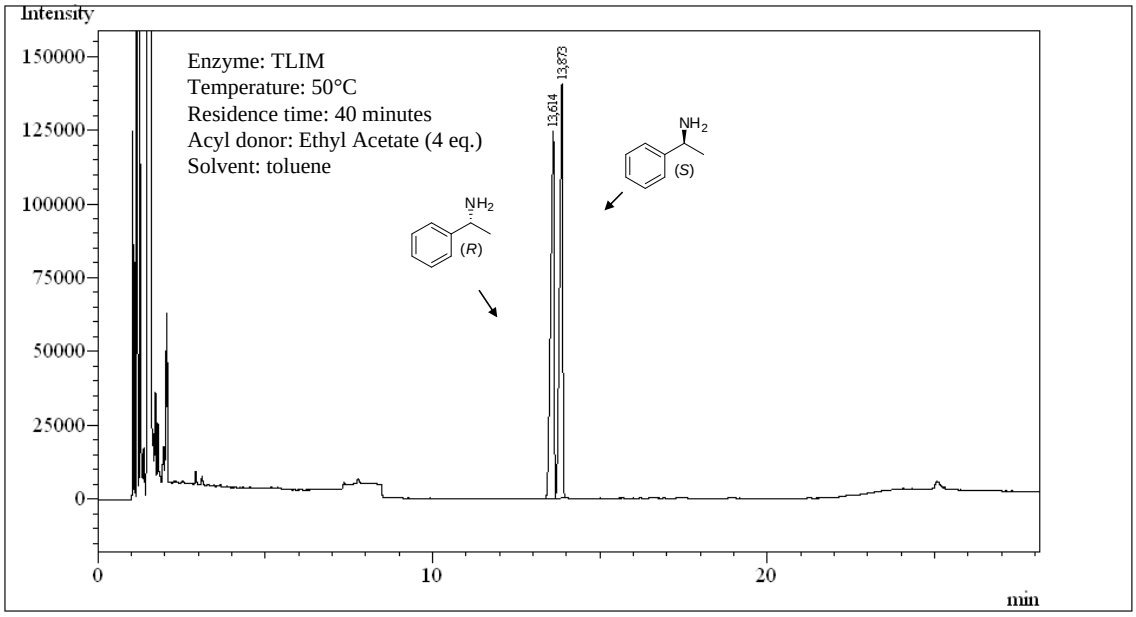


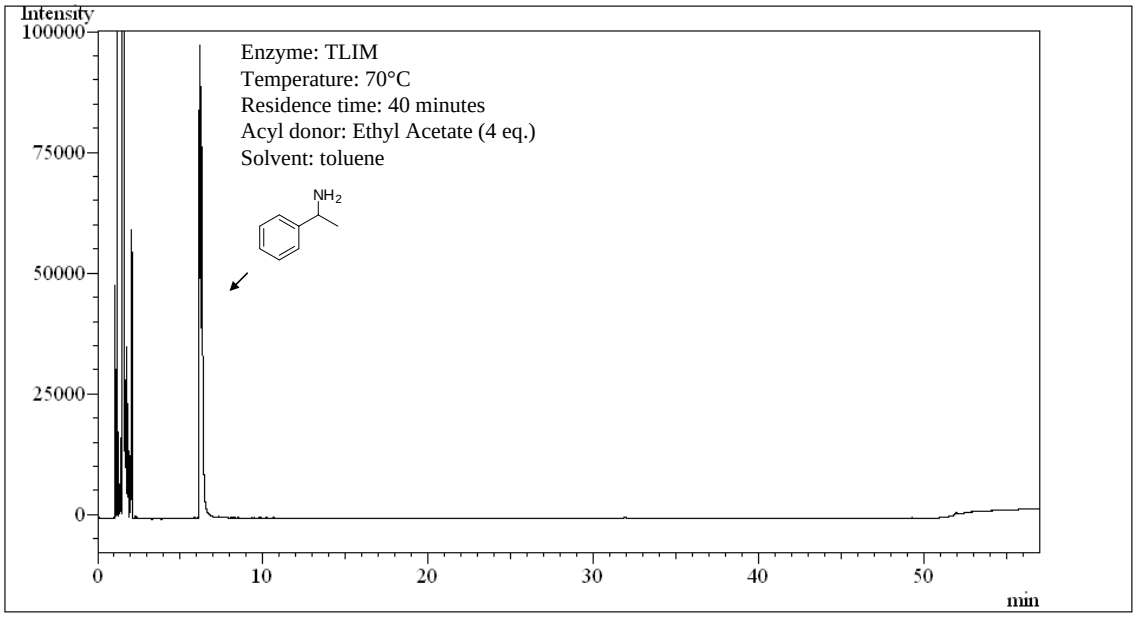


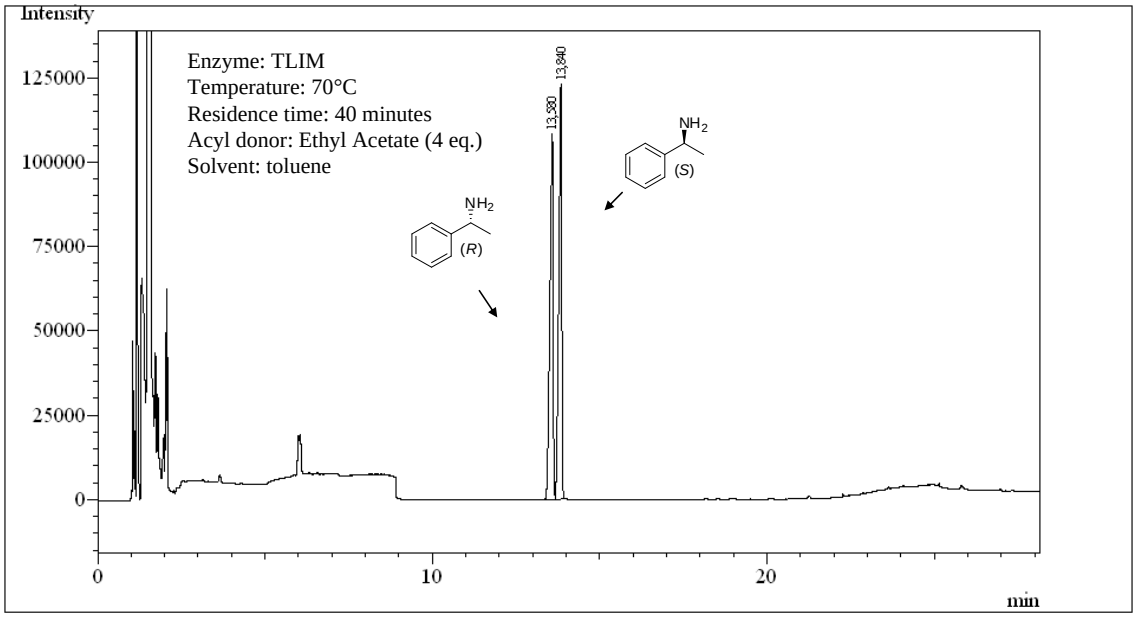


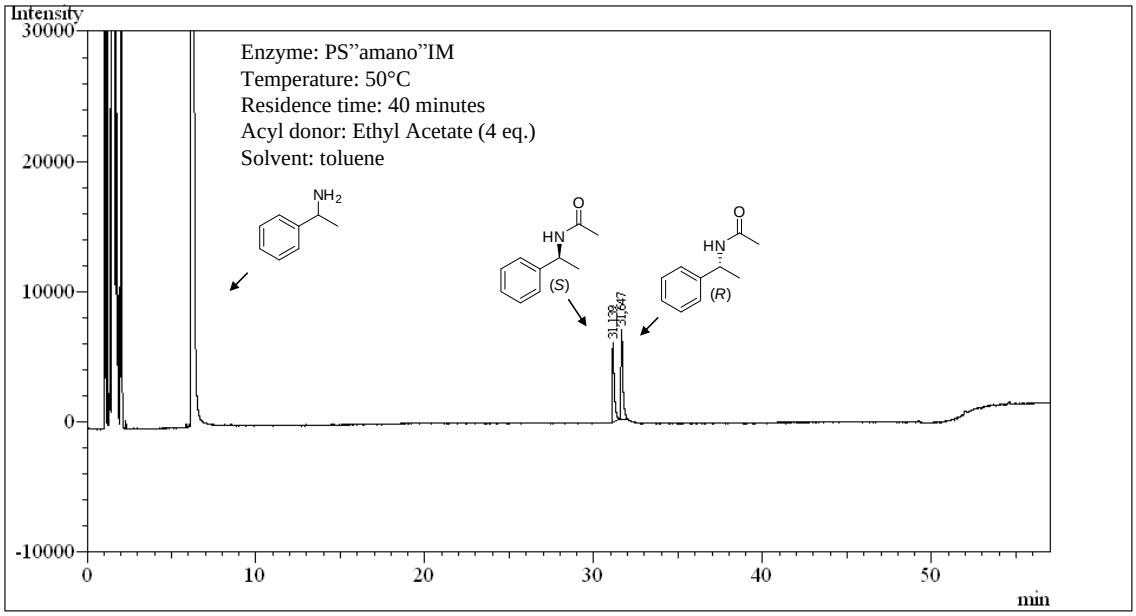


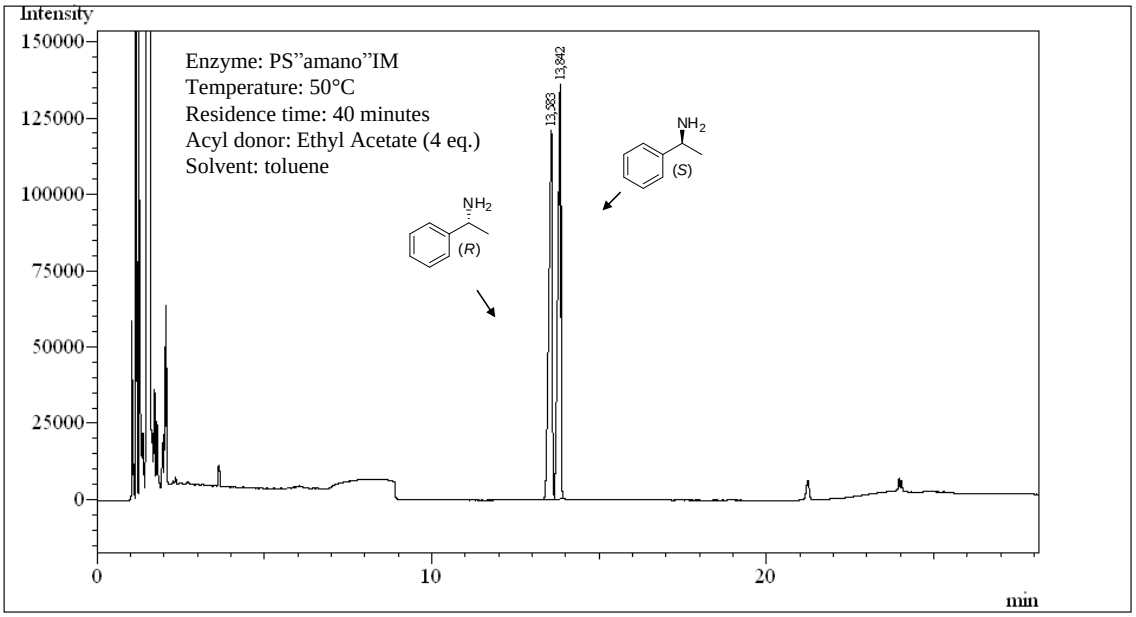


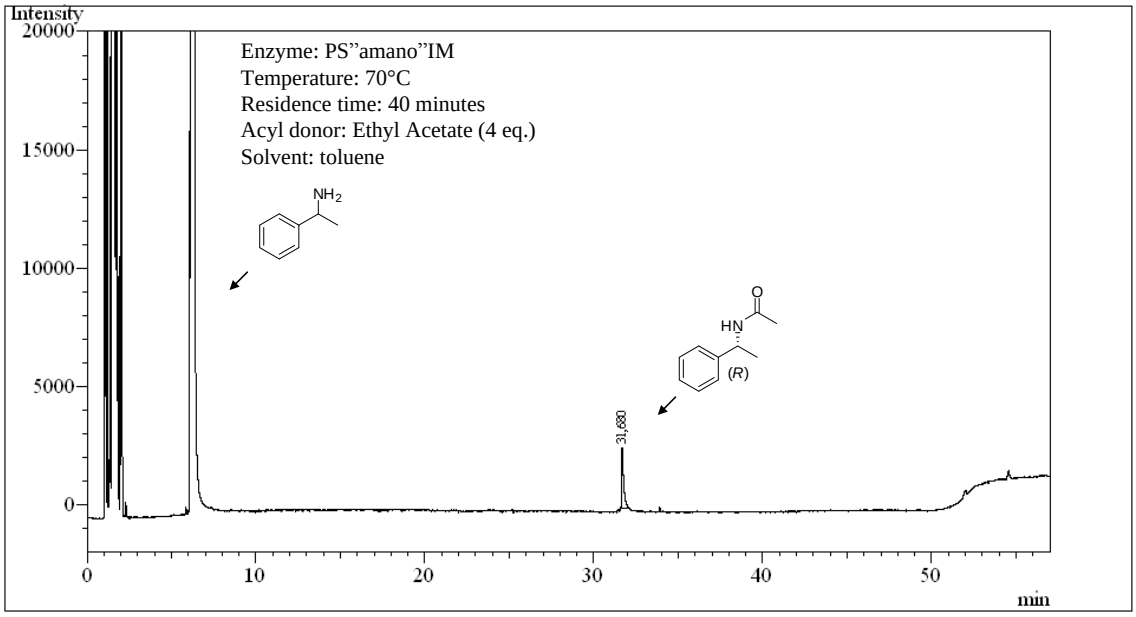


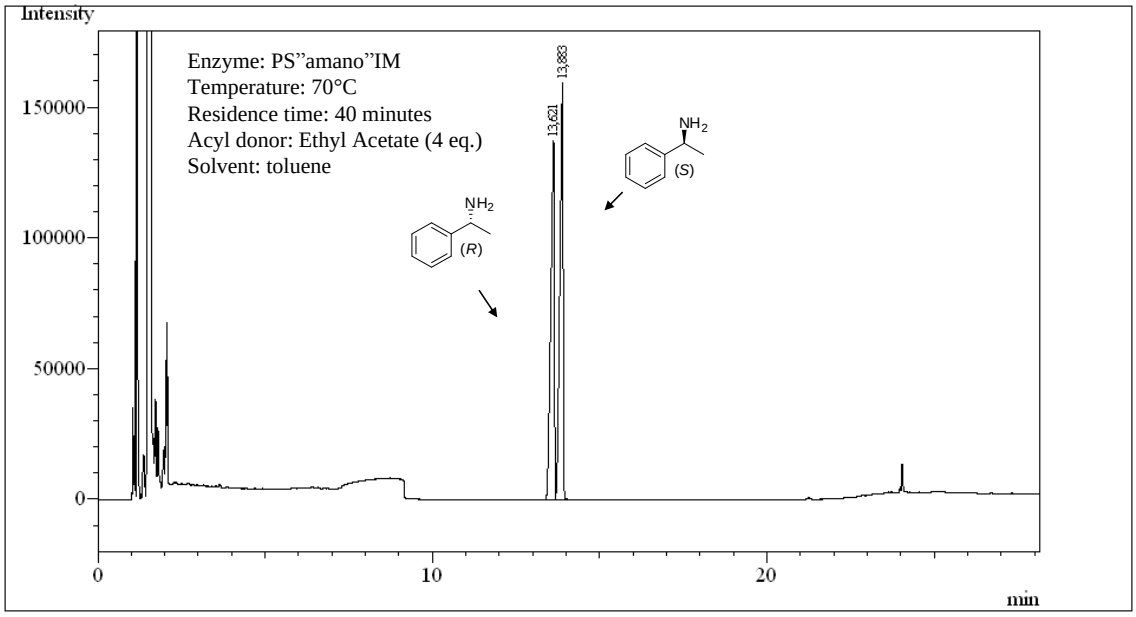




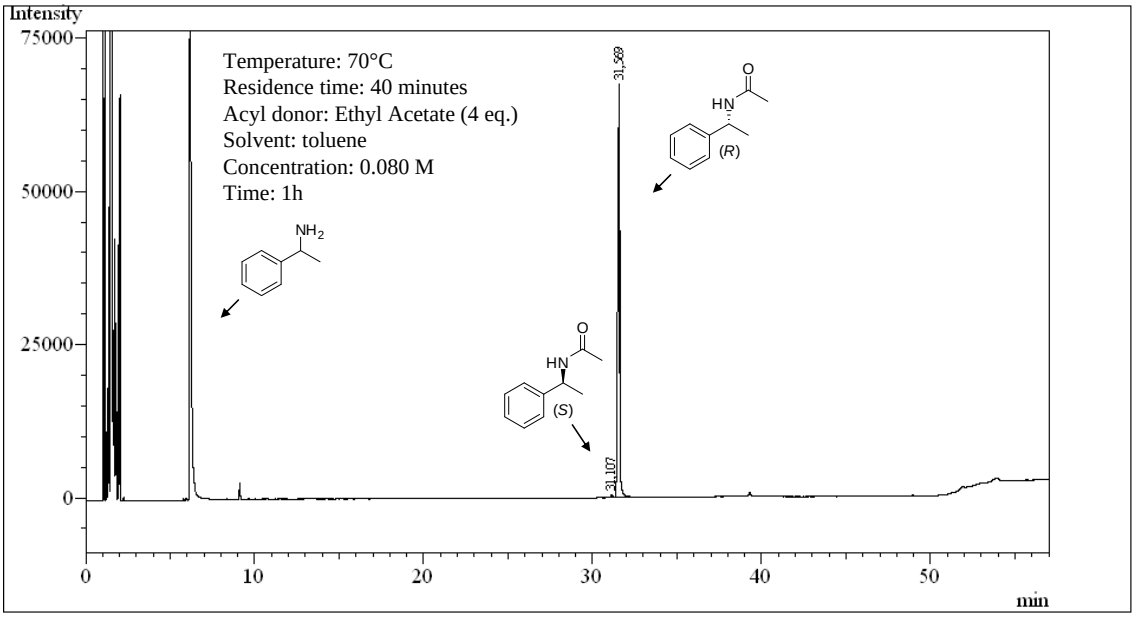


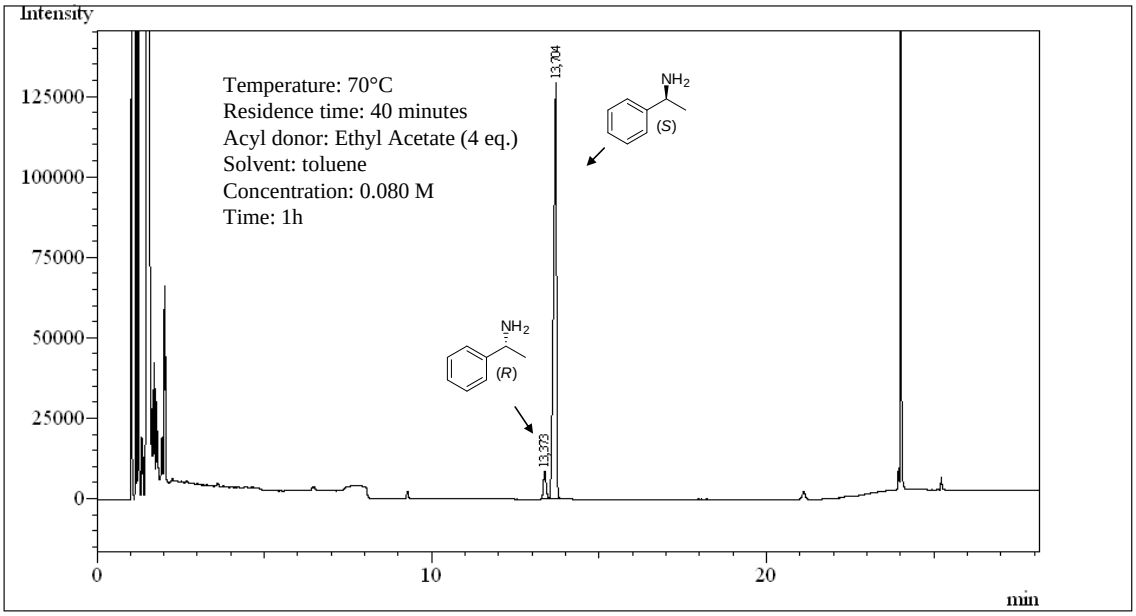


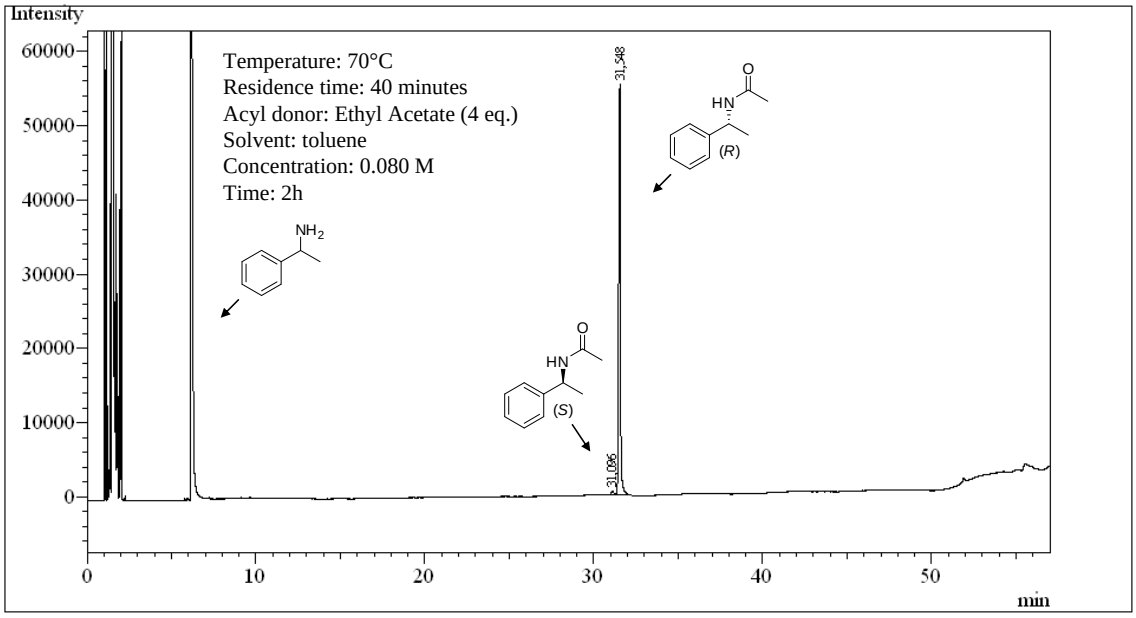


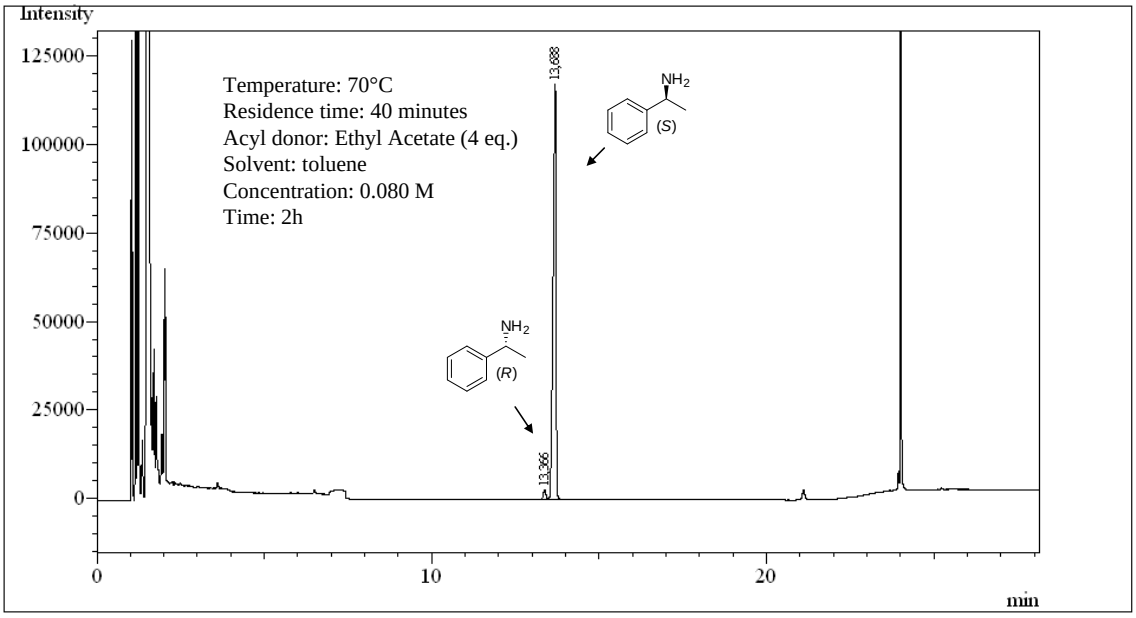


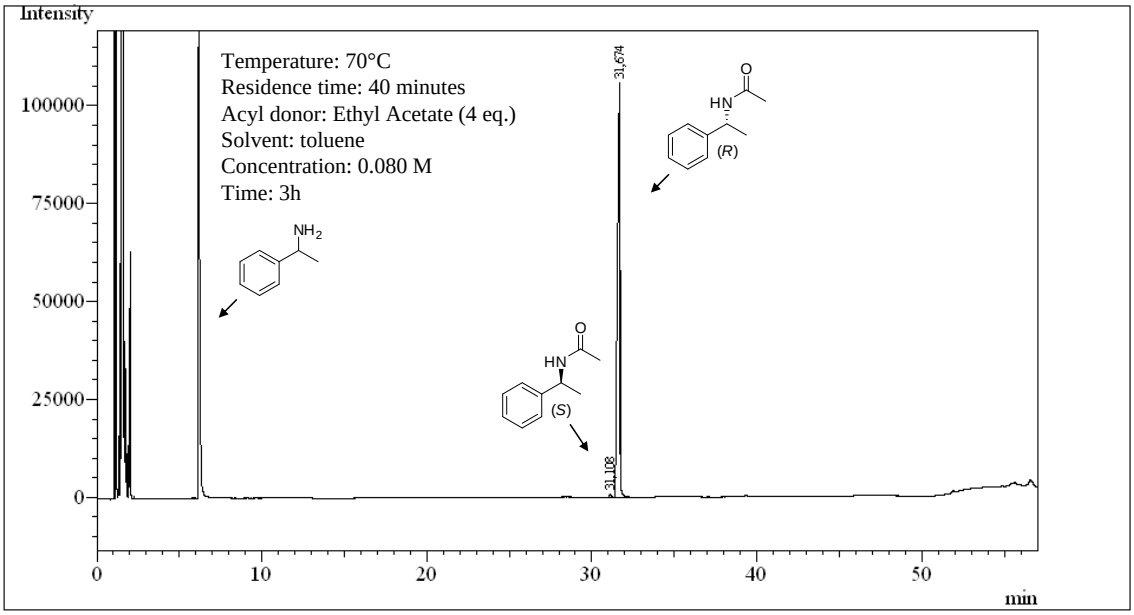
2.1.7. Evaluation of continuous flow system stability during kinetic resolution of (+/-)-1 phenylethylamine

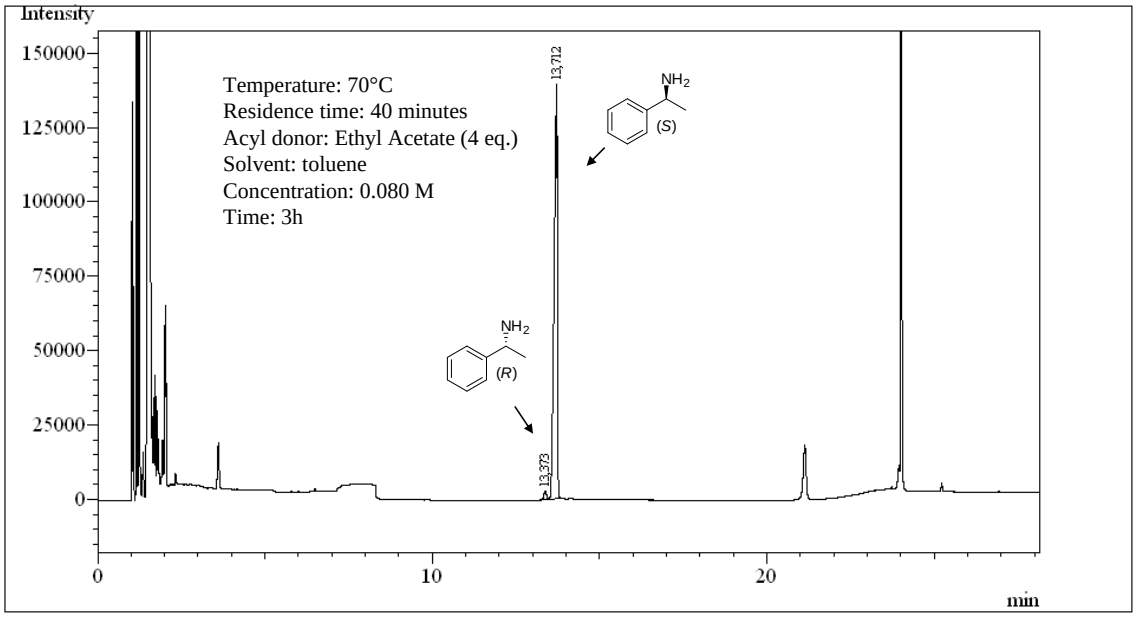


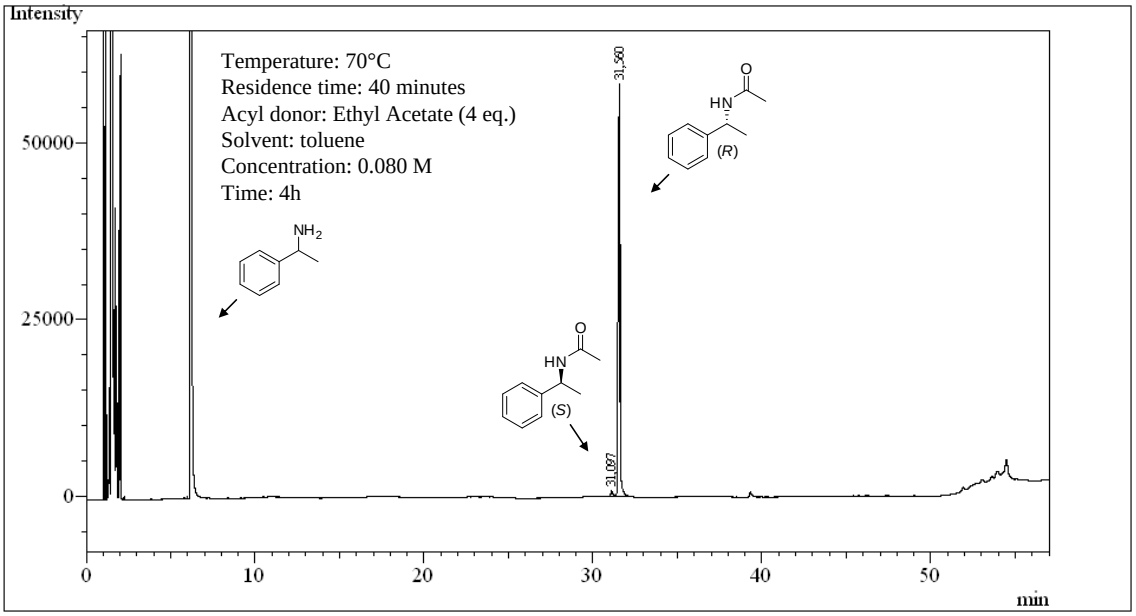


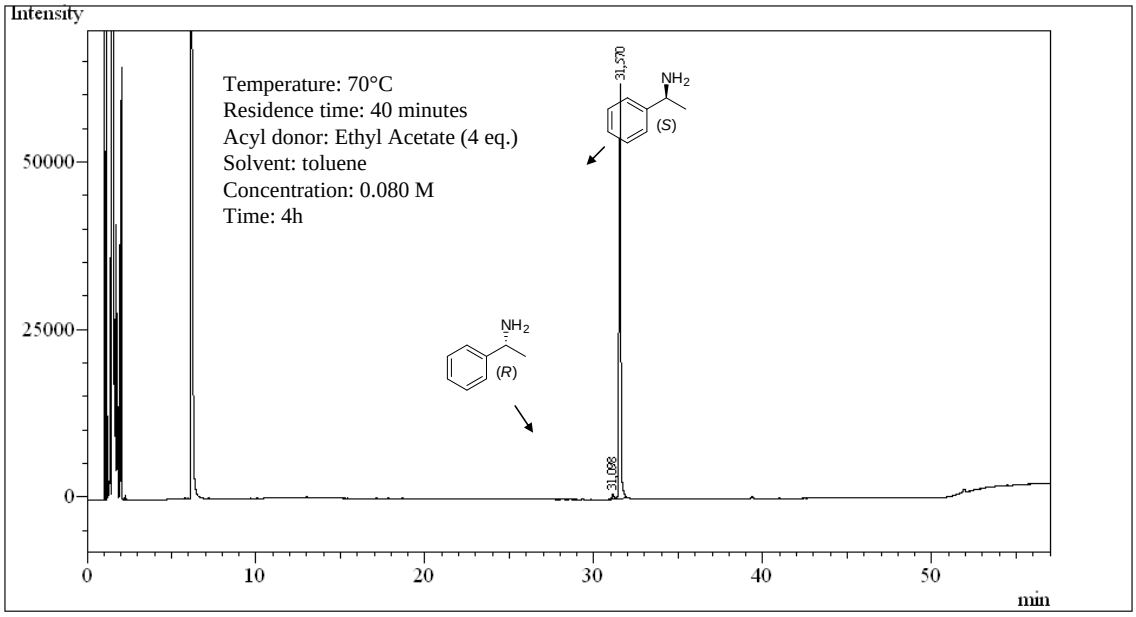


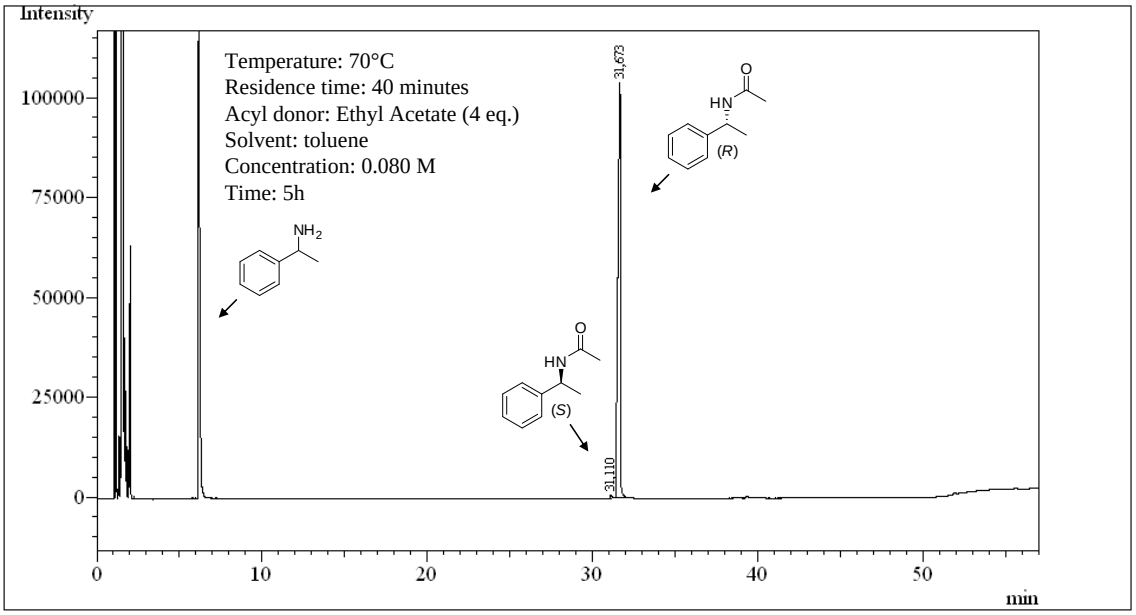


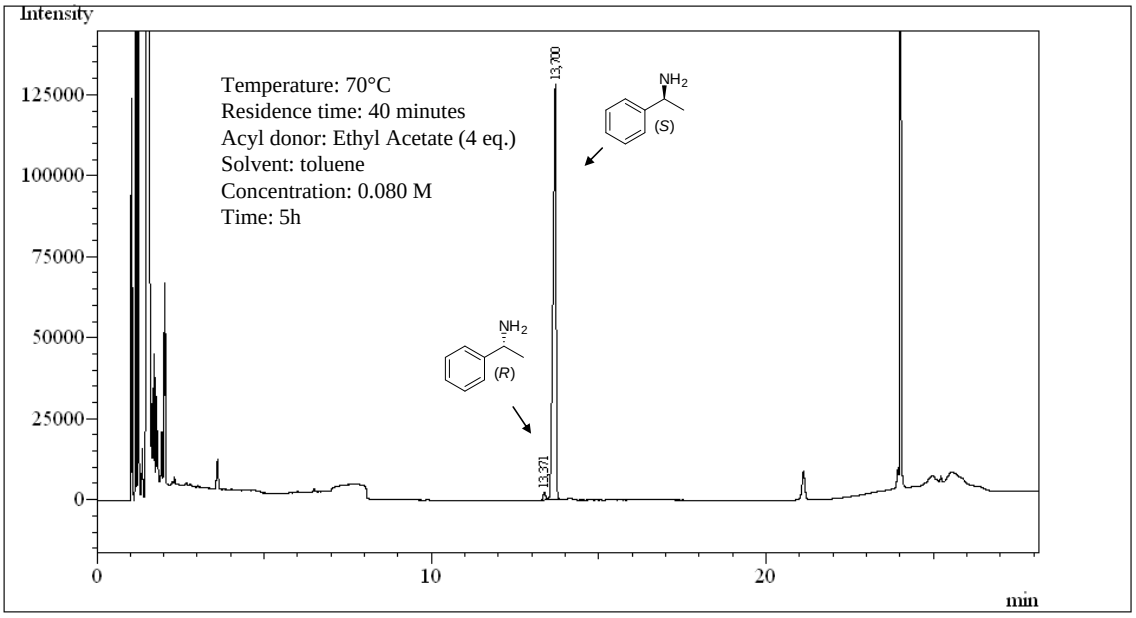


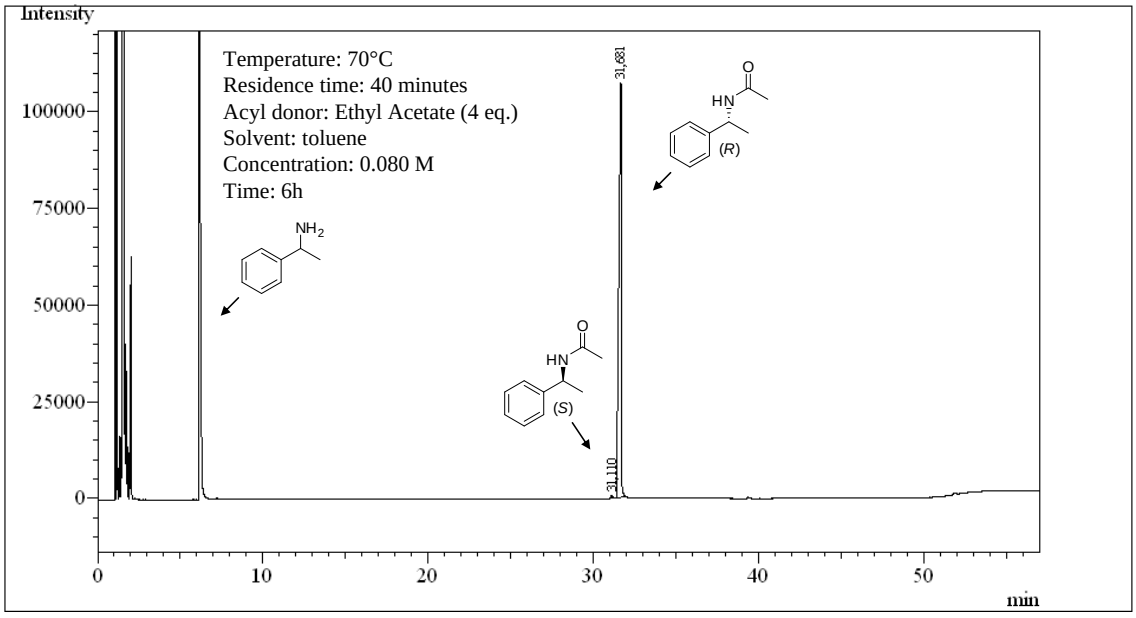


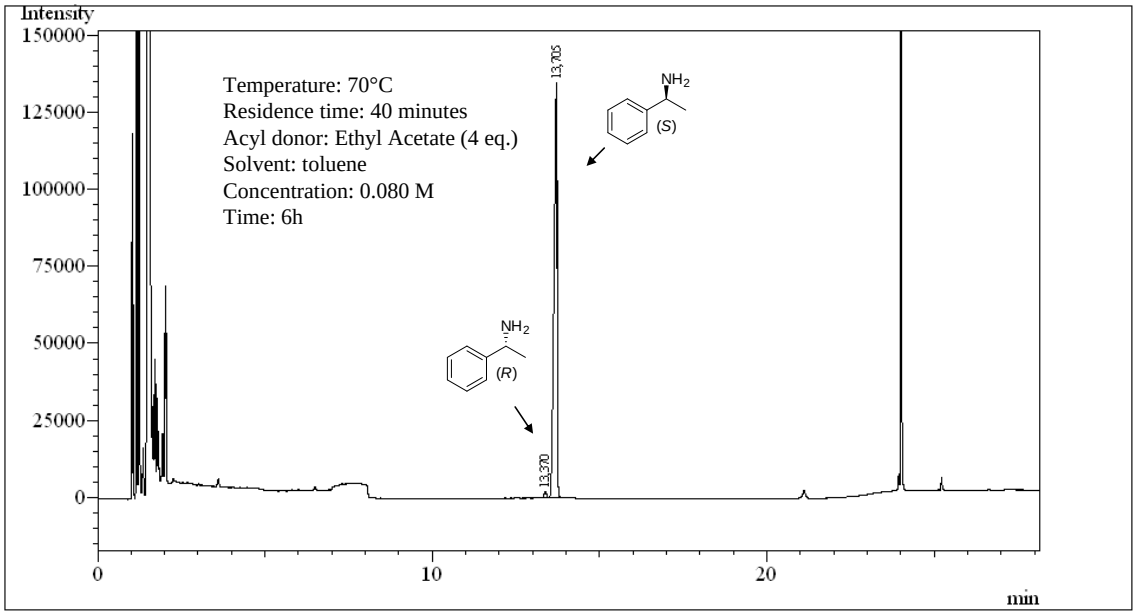


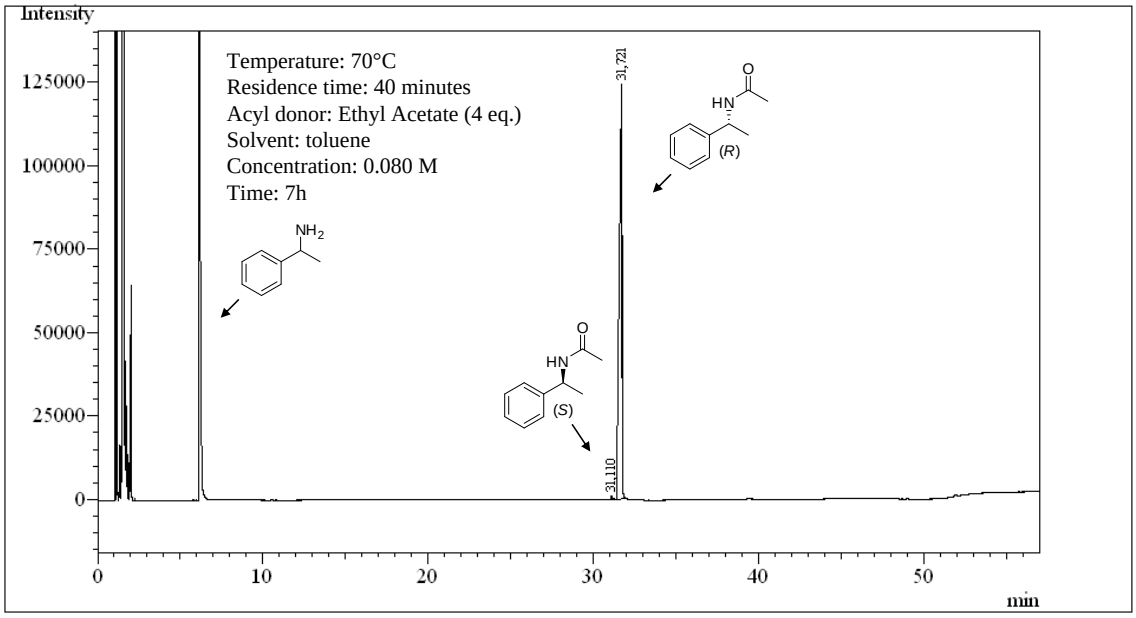


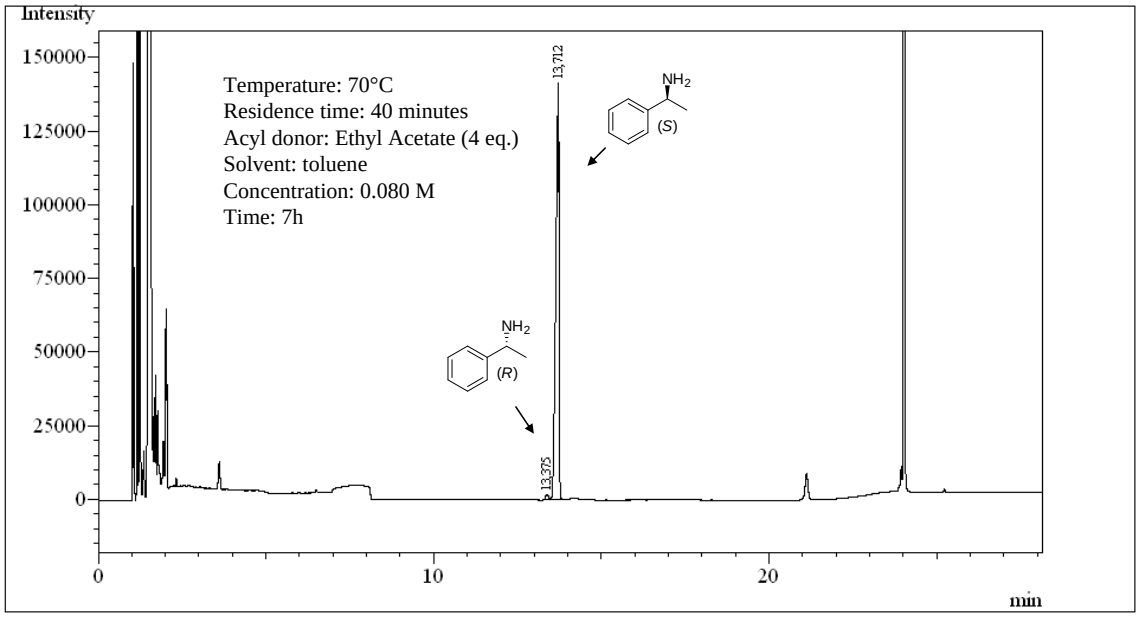


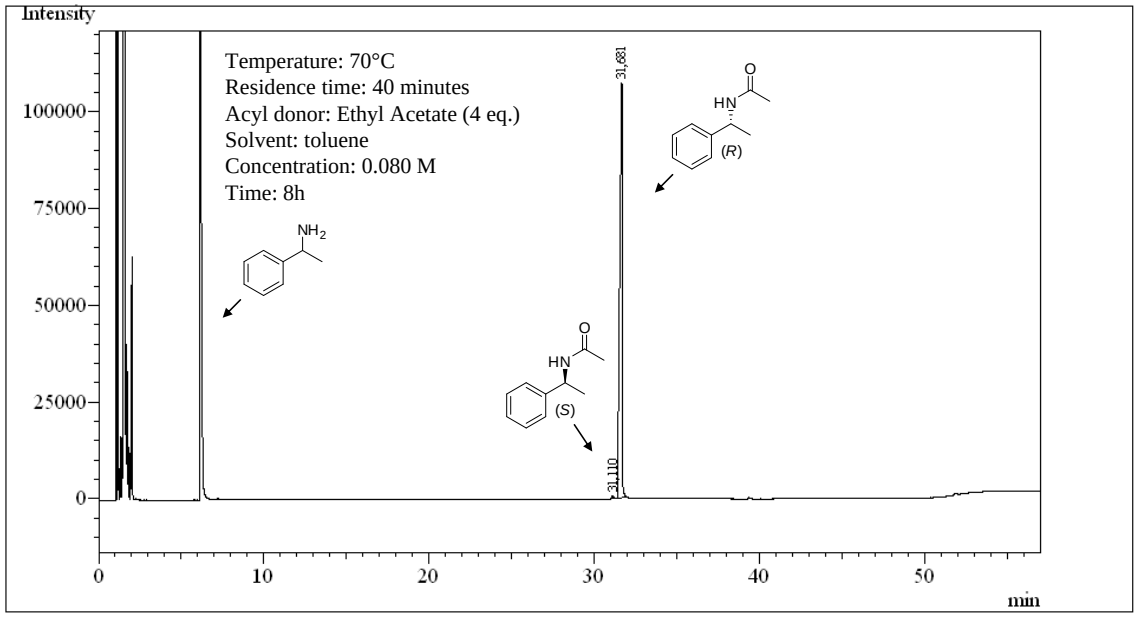


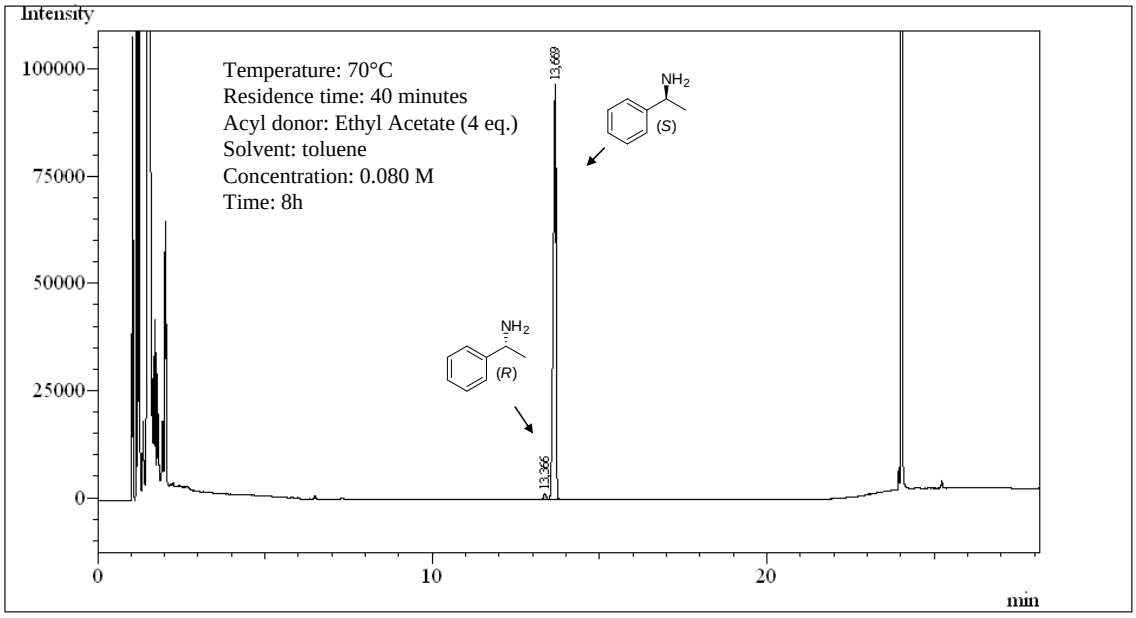


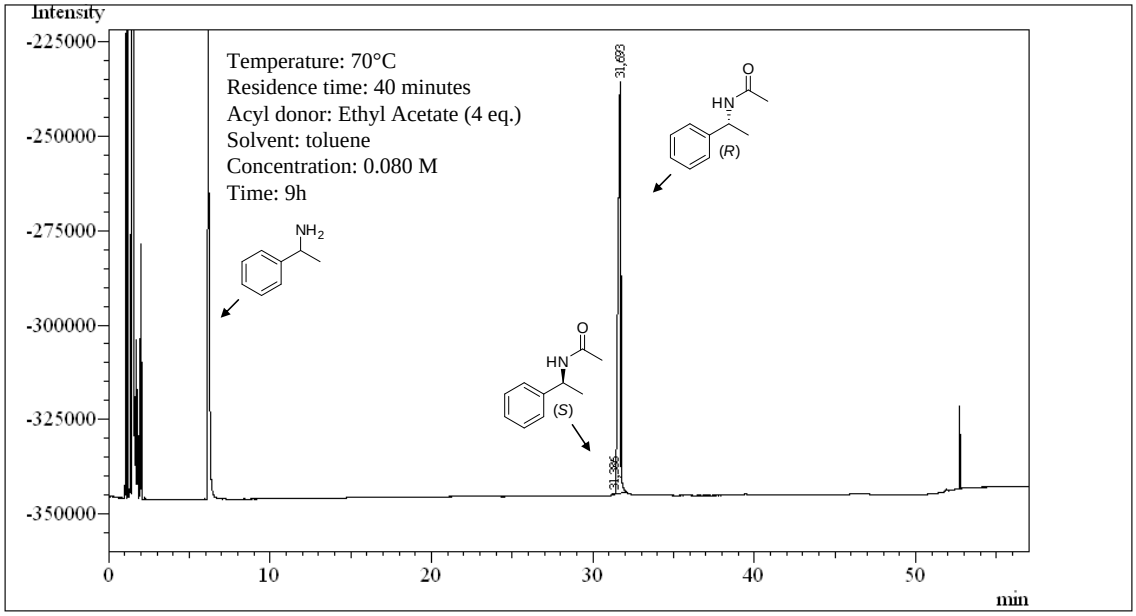


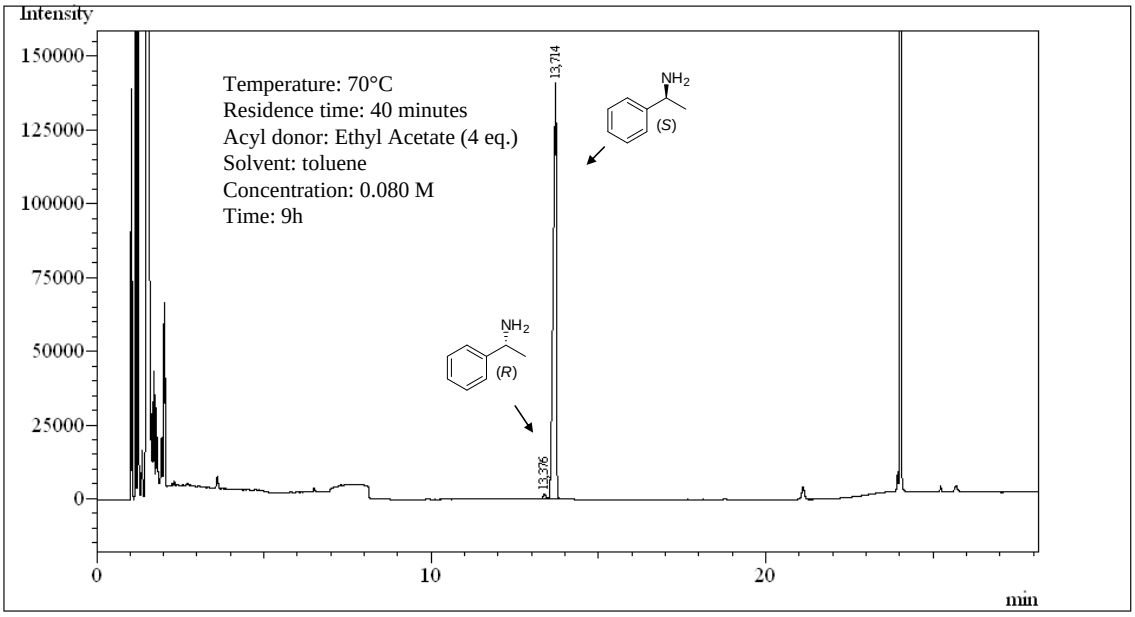




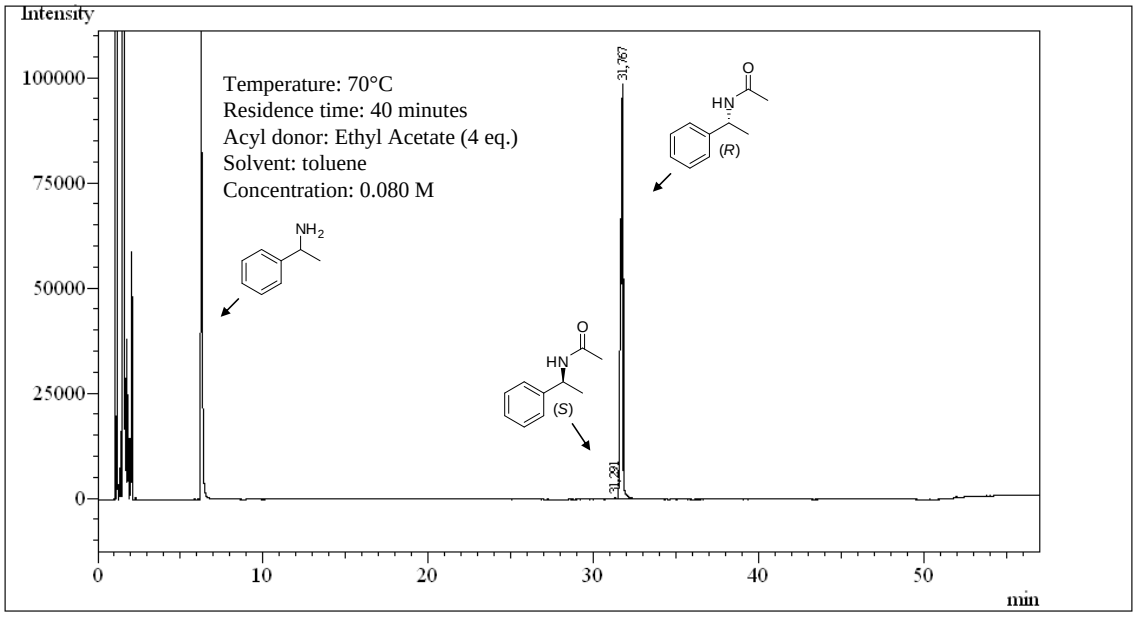


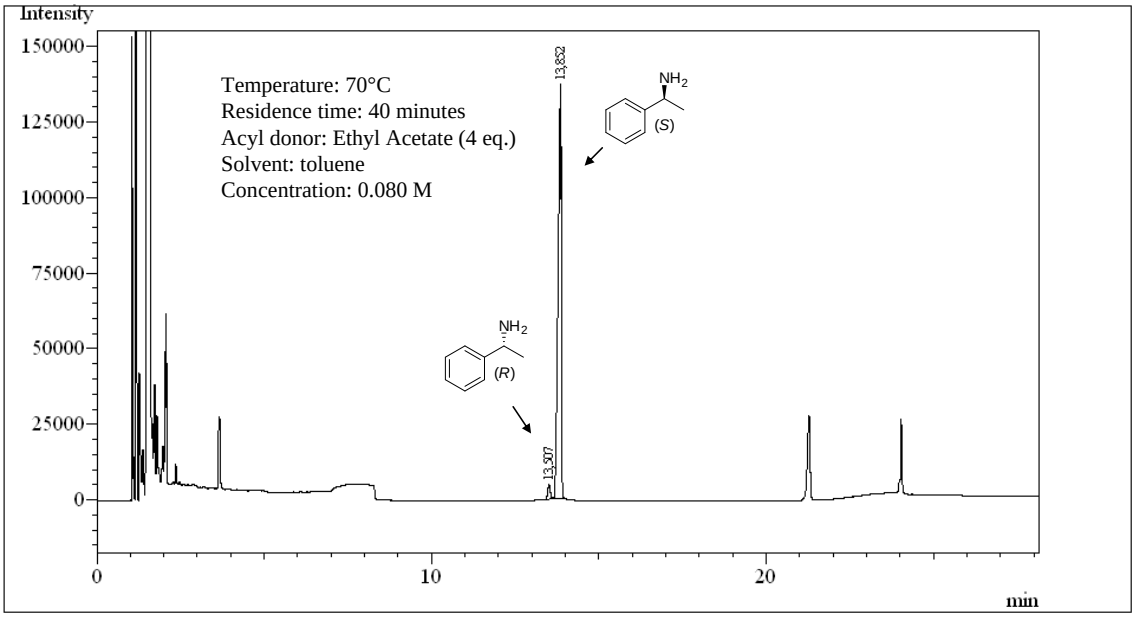


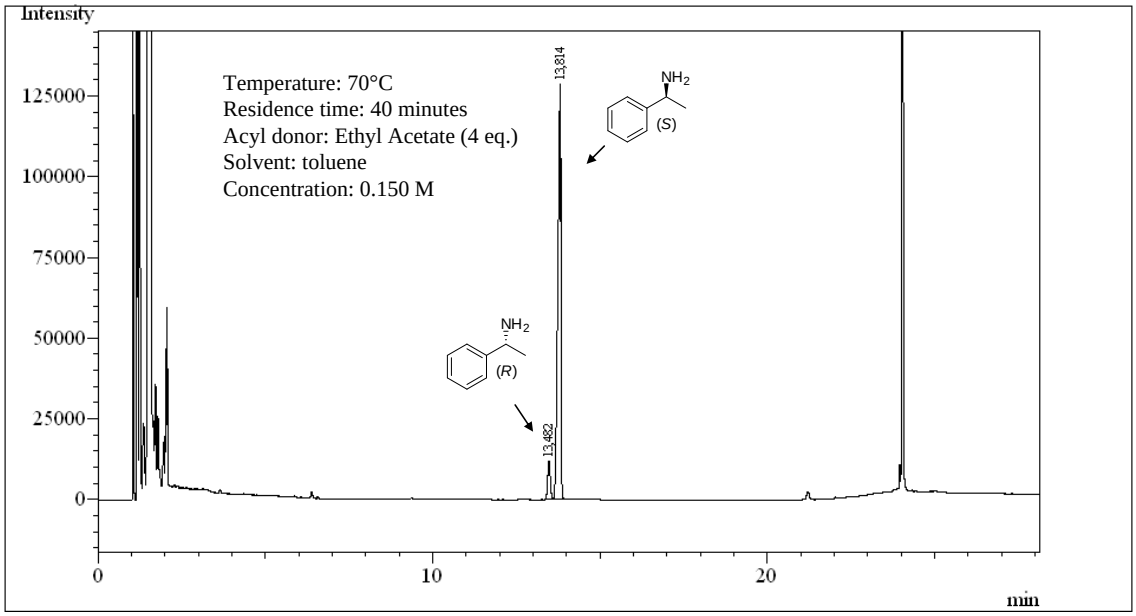


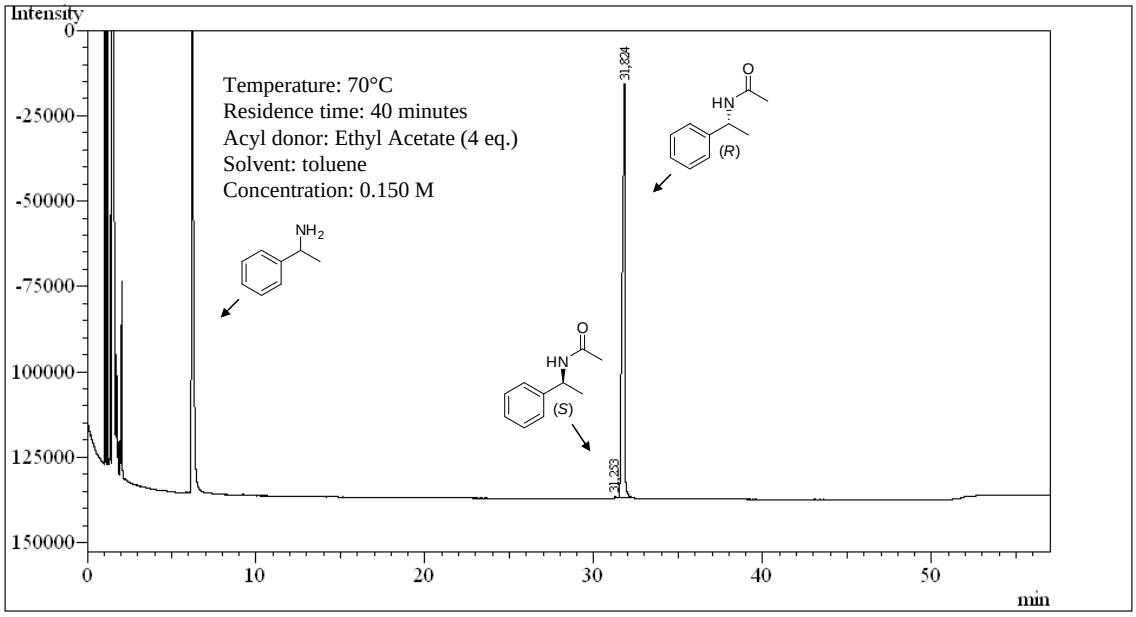


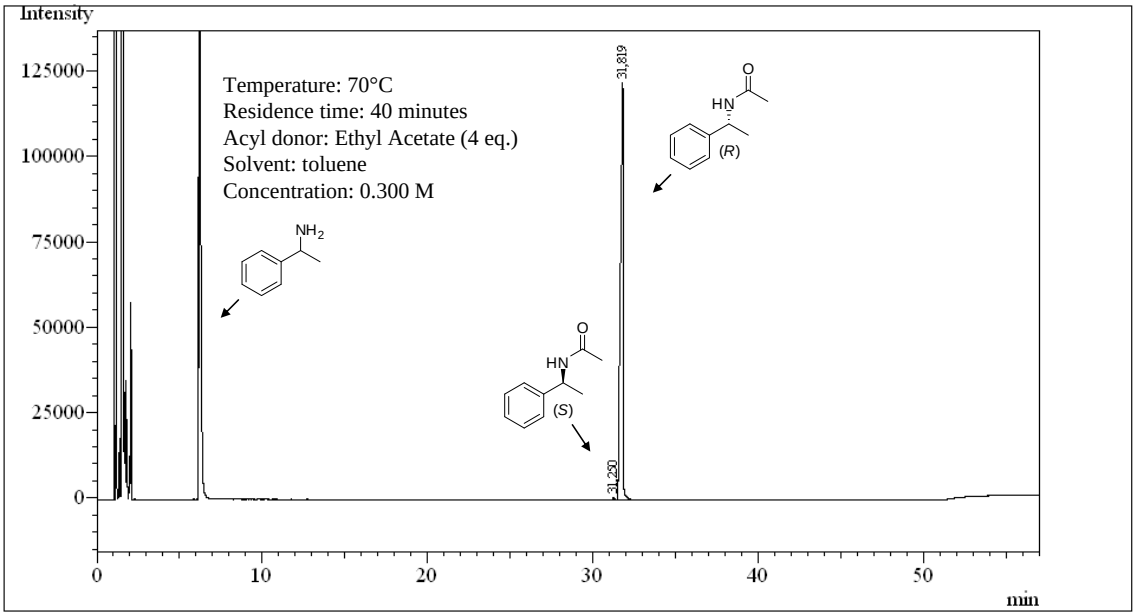
2.1.8. Evaluation of continuous flow system capability of operating with high concentration of substrate

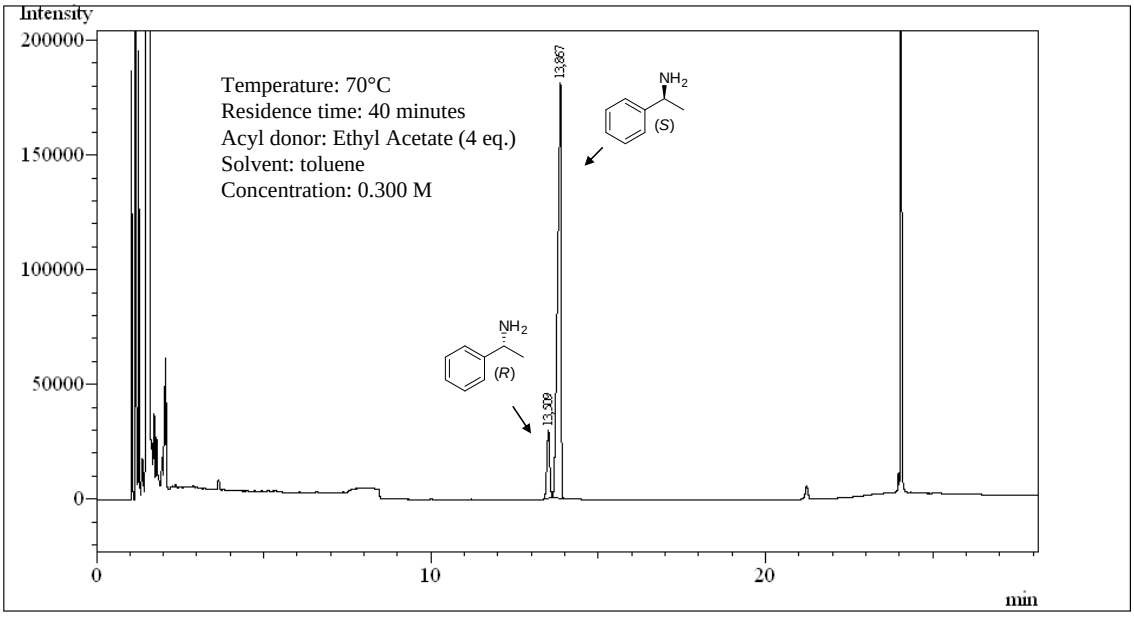


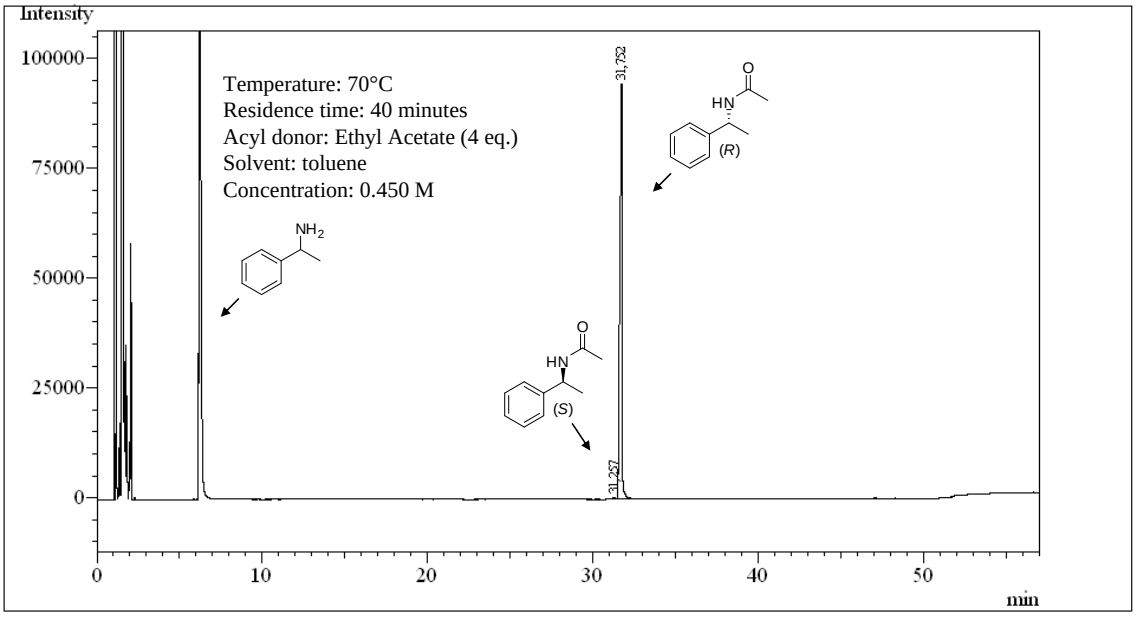


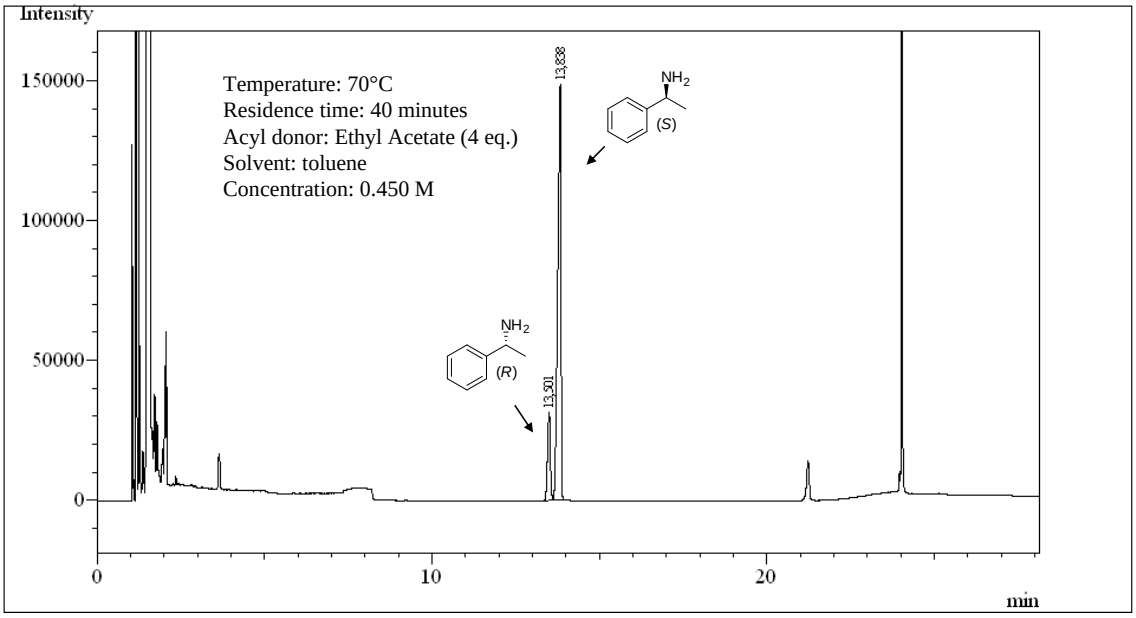


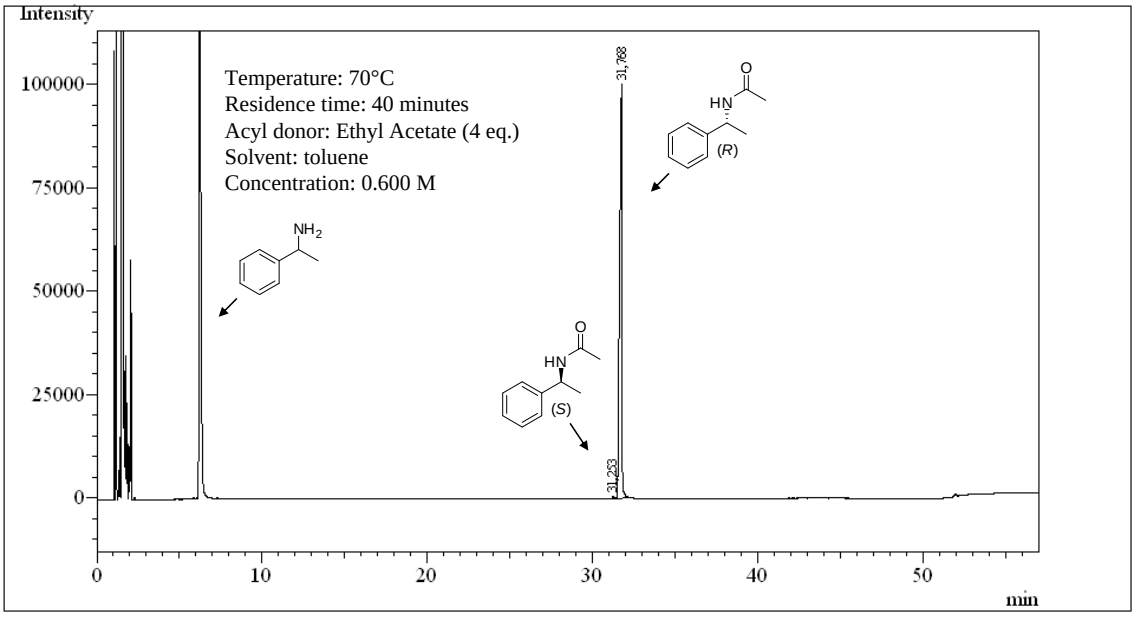


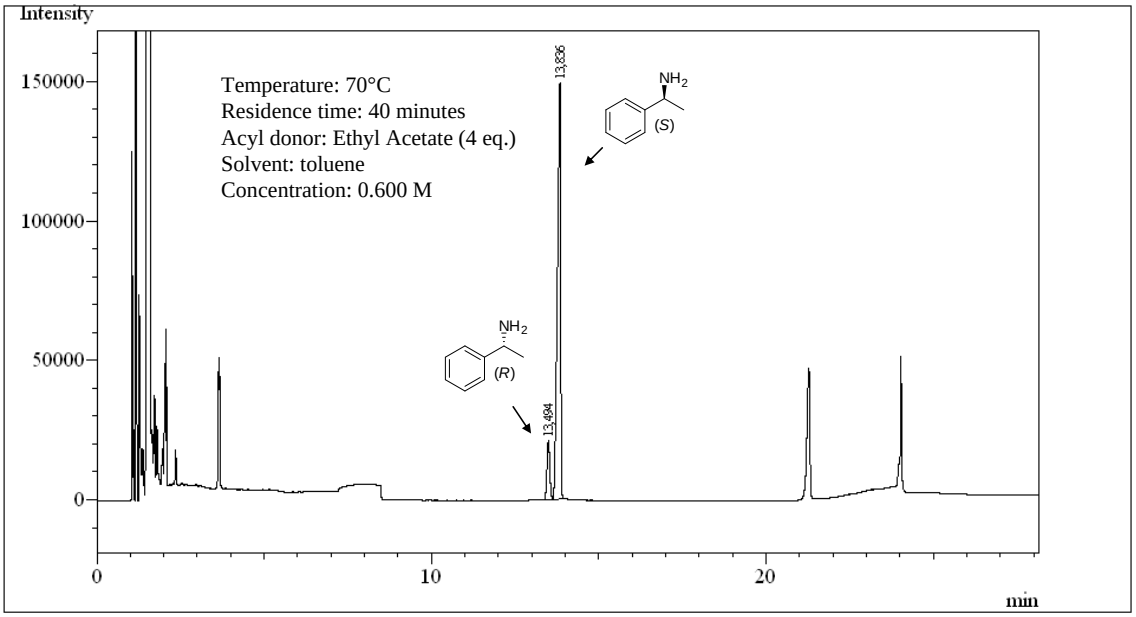


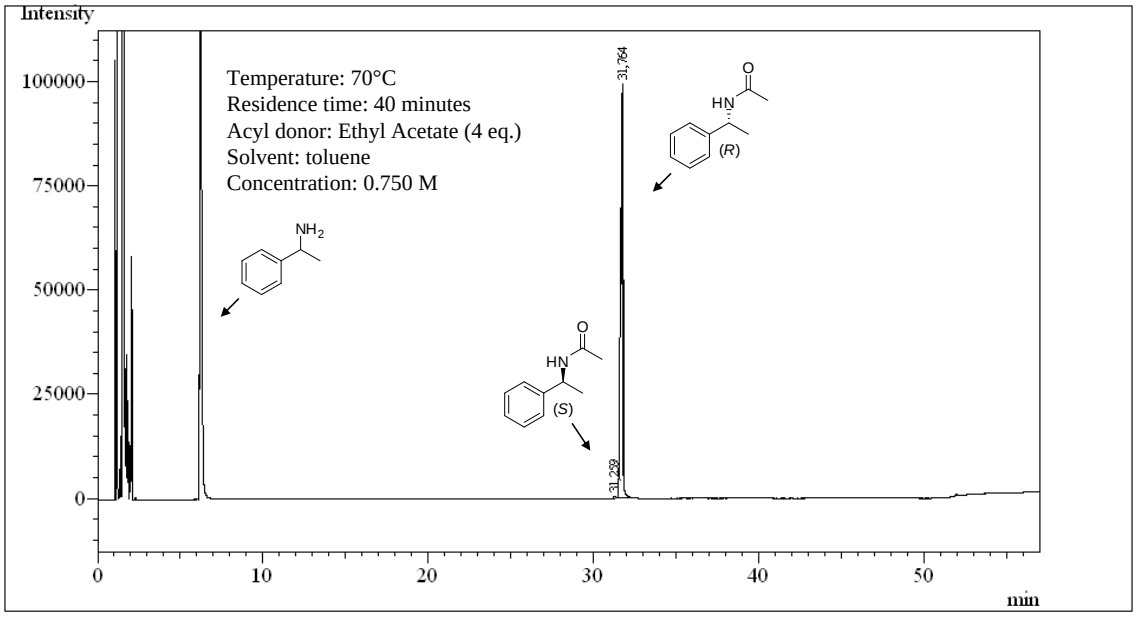


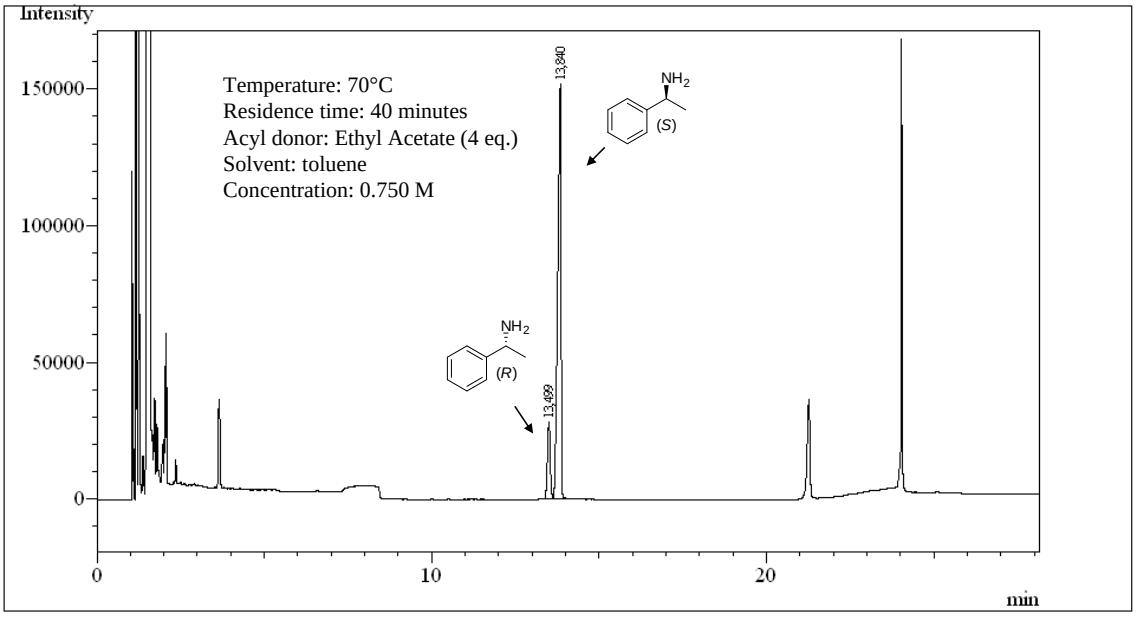


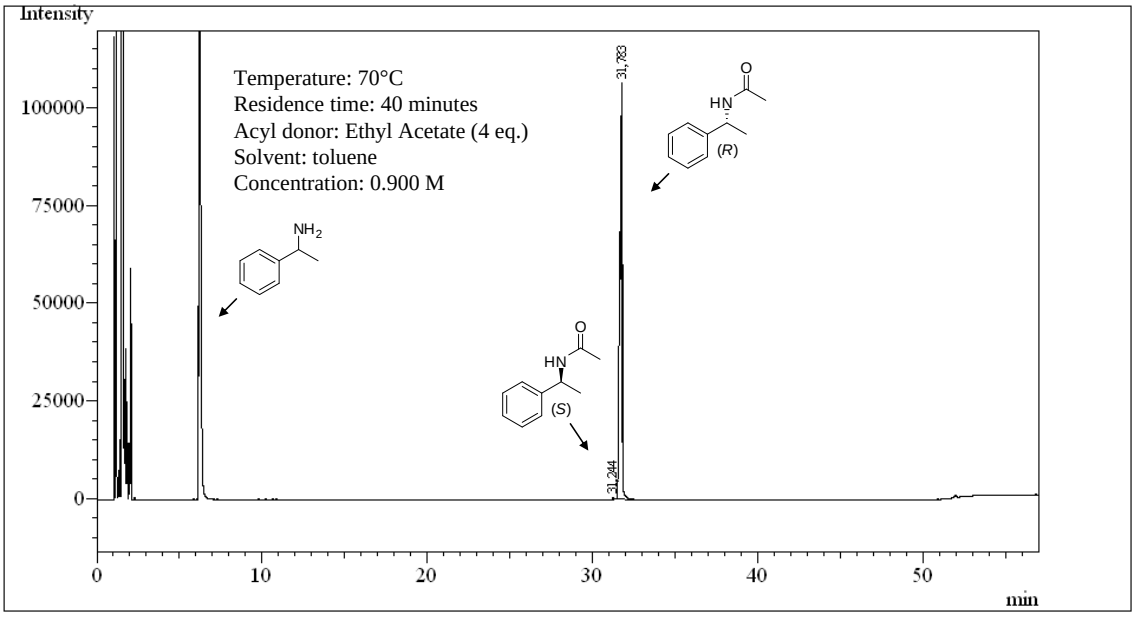


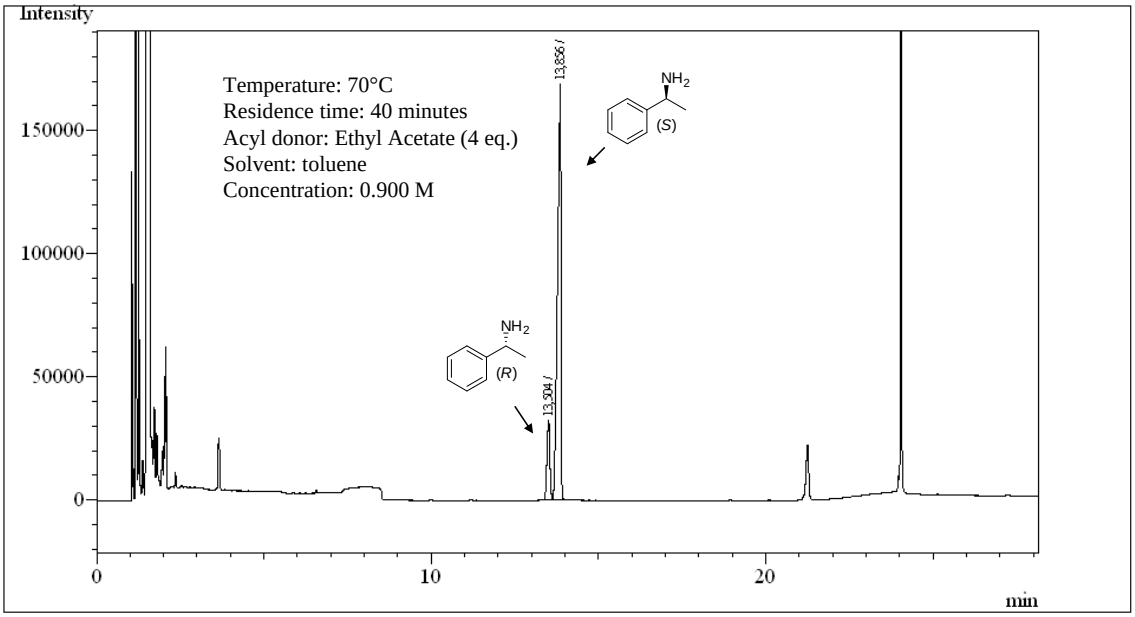




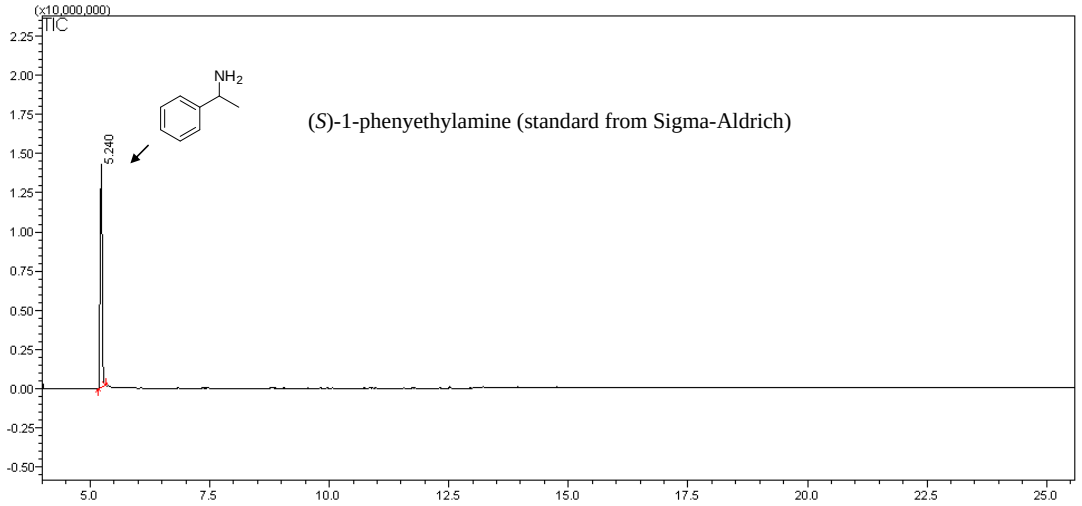




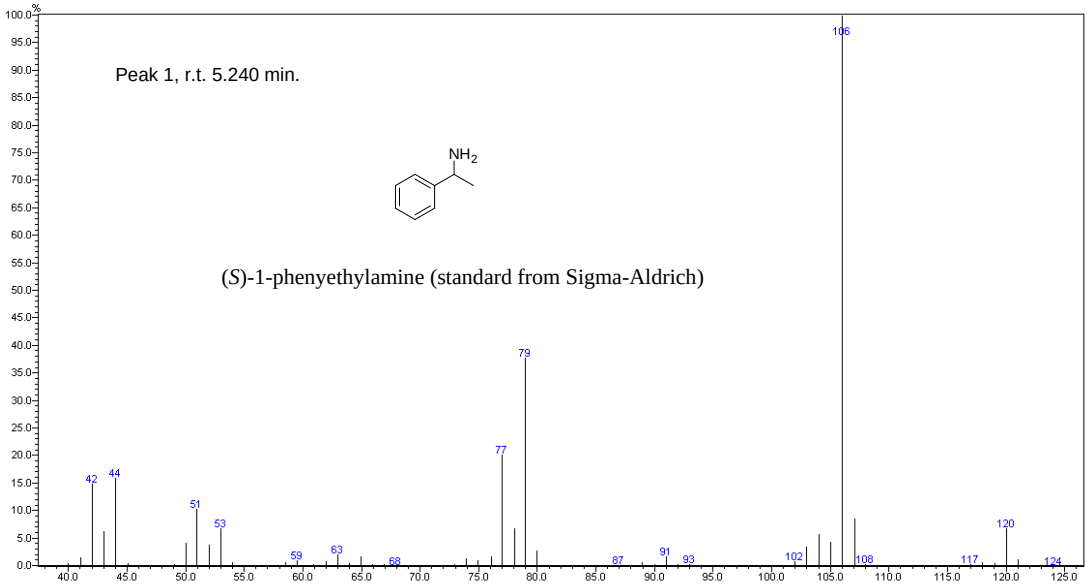




3. GC-MS Chromatograms and mass spectra



(*S*)-1-phenyethylamine (standard from Sigma-Aldrich)



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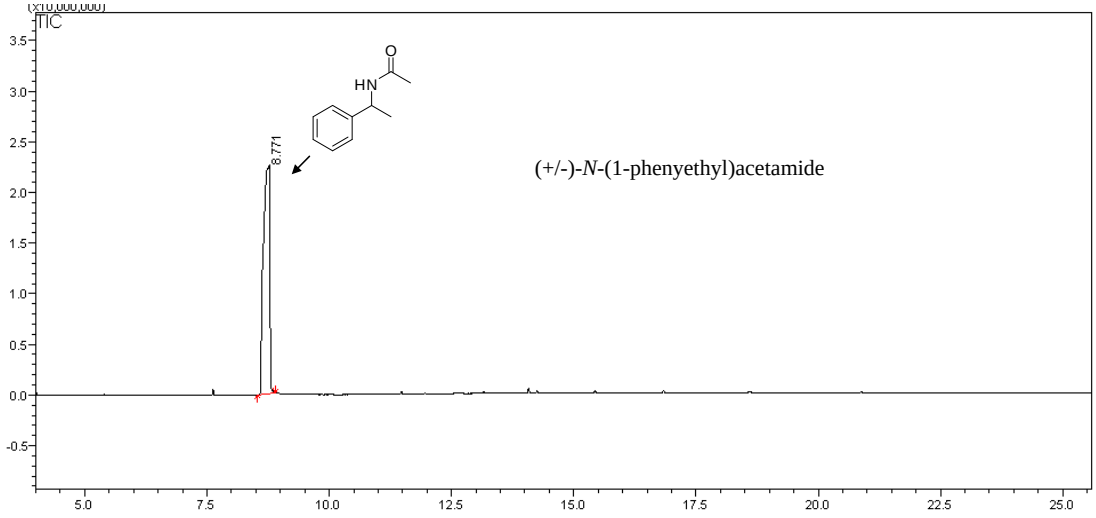

(+/-)-*N*-(1-phenyethyl)acetamide