Bio-inspired Water-Driven Catalytic Enantioselective Protonation

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Supporting Information

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General Information

Chemicals

Chemicals were purchased from various companies (including Acros, Aldrich, TCI, Alfa Aesar and Fluka) as reagent grade and used without further purification. The glyoxals **1a**, **1e–1g** and **1m** were obtained as a hydrate commercially and used without further purification. The glyoxals **1b–1d**, **1h–1l, 1n** and **1o** were prepared from the corresponding ketone[1] or aldehyde[2] according to the literature procedure.

Solvents

Dried solvents (including CH_2Cl_2, THF, toluene, and xylenes) were purchased from various companies (including Merck, Aldrich, and Alfa Aesar) and used without further purification. Additional solvents were purchased from various commercial suppliers.

Inert Gas

Dry argon was purchased from Hanmi Gas with > 99.99% purity.

Glassware

All non-aqueous reactions were performed in flame-dried glassware under Ar. Solvents were removed under reduced pressure at 30 °C using a rotary evaporator and were dried under high vacuum (10^{-1} mbar).

Thin Layer Chromatography

Thin-layer chromatography (TLC) was performed using silica gel plates (Merck, Kieselgel 60 F254 0.25 mm).

Column chromatography

Column chromatography was carried out using Merck silica gel (60 Å, 230−400 mesh, particle size 0.040−0.063 mm) with technical grade solvents. Elution was accelerated using compressed air.

Nuclear Magnetic Resonance Spectroscopy

^{1}H, ^{13}C and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Ascend™ 500 spectrometer in a suitable deuterated solvent. The solvent employed and the respective measuring frequency are indicated for each experiment. Chemical shifts are reported with tetramethylsilane (TMS) serving as an internal reference for ^{1}H and ^{13}C NMR analysis and with two or one digits after the comma. The resonance multiplicity is described as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and bs (broad singlet). All spectra were recorded at 298 K unless otherwise noted and processed with the MestReNova 6.0.2 suites of programs, and the coupling constants are reported as observed. The residual deuterated solvent signal relative to tetramethylsilane was used as the internal reference in the ^{1}H NMR spectra ($CDCl_3$ δ 7.26), and are reported as follows: chemical shift δ in ppm (multiplicity, coupling constant J in Hz, number of protons). ^{13}C NMR spectra are reported in ppm from tetramethylsilane (TMS), with the solvent resonance as the internal standard ($CDCl_3$ δ 77.2). All spectra are broadband decoupled unless otherwise noted. ^{19}F NMR (470.4 MHz) spectra were recorded using a Bruker

Ascend™ 500 spectrometer with benzotrifluoride ($C_6H_5CF_3$) as the external standard. All spectra are broadband decoupled unless otherwise noted.

Mass Spectrometry
High-resolution mass spectrometry (HRMS) was recorded using a Bruker Compact mass spectrometer.

Infrared Spectroscopy
Infrared (IR) spectroscopy was performed using a Bruker Vertex 70 spectrometer with the MIRacle Micro ATR accessory.

Specific Rotations
Specific rotations ($[\alpha]_D^T$) were measured with a PerkinElmer Polarimeter 343 Plus at room temperature with a sodium lamp (sodium D line, λ = 589 nm).

High Performance Liquid Chromatography
High performance liquid chromatography (HPLC) was performed on a YL9100 Plus HPLC System instrument equipped with an isostatic pump using a chiral column (CHIRALPAK AD-H, CHIRALCEL OD-H, CHIRALCEL OX-3, CHIRALPAK IA, CHIRALPAK IC; 250 × 4.6 mm).

Magnetic stirrer
The stirring rate (rpm) was controlled using a CORNING PC-420D.

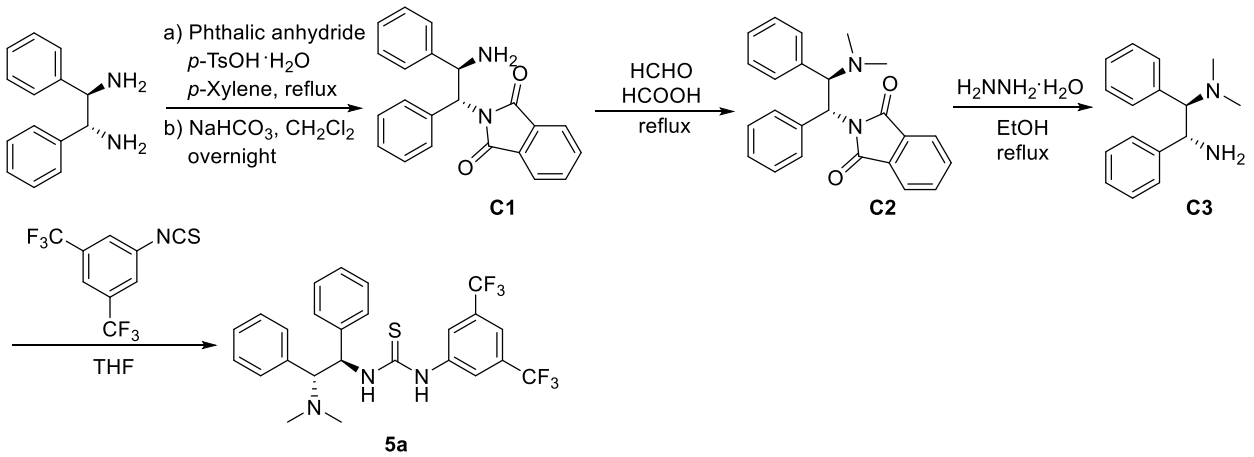
Syringe Pump
The injection speed (flow rate) was controlled with a KD Scientific Legato 200 syringe pump.

Tubing
FEP tubing was used (250, 500, 750 and 1000 μm ID).

Synthetic procedures and analytical data

Catalyst preparation

Catalysts were prepared according to the published procedures.[3]



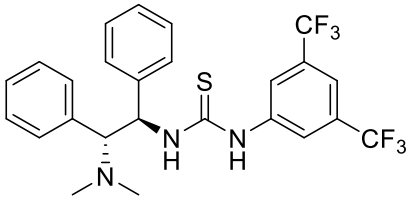
Preparation of **C1**: *p*-TsOH·H_2O (3.8 g, 20 mmol, 1 equiv) was dissolved in *p*-xylene (50 mL). The reaction mixture was stirred at 60 °C for 30 minutes, which generated a pink solution. After cooling to room temperature, (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (4.25 g, 20 mmol, 1 equiv) was added to the solution followed by phthalic anhydride (2.96 g, 20 mmol, 1 equiv). The reaction mixture was stirred under reflux for 3 hours. After the solution was cooled to room temperature, the colorless solid was collected by filtration and washed with 1:1 mixture of *p*-xylene and hexane. The solid was then dried under vacuum for 30 minutes. Subsequently, DCM (50 mL) and saturated $NaHCO_3$ (aq.) (32 mL) were added, and the solution was stirred overnight. The organic layer was separated, washed with brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* to give product **C1** as a white solid (5.53 g, 81% yield), which was used without further purification.

Preparation of **C2**: A solution of **C1** (5.53 g, 16.1 mmol) in HCHO (37 % aq., 12.1 mL) and HCOOH (80 % aq., 9.7 mL) was stirred under reflux for 12 hours. After cooling to room temperature, saturated Na_2CO_3 (aq.) (30 mL) was added dropwise at 0 °C. The solution was extracted with DCM, and dried over anhydrous Na_2SO_4. The reaction mixture was concentrated *in vacuo*, and purified by silica gel column chromatography (hexanes/EtOAc = 1:4) to yield a yellow solid (5.56 g, 92 % yield).

Preparation of **C3**: To a solution of **C2** (5.56 g, 15 mmol) in ethanol (80 mL), hydrazine monohydrate (2.2 mL, 45 mmol, 3 equiv) was added dropwise. The mixture was stirred under reflux for 6 hours. After the solution was cooled to room temperature, it was diluted with diethyl ether and filtered to remove the precipitate. The filtrate was washed with DI water twice to remove excess hydrazine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. **C3** was obtained as a yellow solid (2.95 g, 82% yield), which was used without further purification.

Preparation of **5a**: In a flame-dried RBF, **C3** (2.4 g, 10 mmol) was dissolved in THF (anhydrous, 25 mL), and cooled down to 0 °C. Subsequently, the corresponding isothiocyanate (13 mmol, 1.3 equiv) was added to the reaction mixture dropwise, which was then stirred at RT for 24 hours. The reaction mixture was concentrated *in vacuo*, and purified by silica gel column chromatography (hexanes/acetone = 1:8) to yield a white solid (4.757 g, 93% yield).

Catalyst 5a: white solid

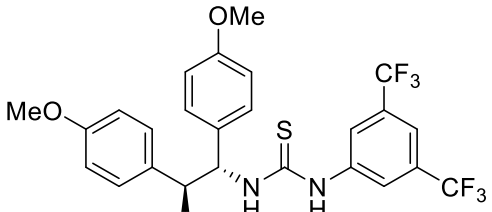


(*R*,*R*)-**5a**

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (br s, 2H), 7.84 – 7.62 (m, 2H), 7.29 – 7.02 (m, 10H), 5.42 (br s, 1H), 3.83 (d, J = 11.0 Hz, 2H), 2.20 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 180.47, 139.58, 139.17, 132.56 (q, $^2J_{C\text{-}F}$ = 33.57 Hz), 131.34, 129.91, 128.54, 128.07, 127.95, 127.84, 123.75, 122.93 (q, $^1J_{C\text{-}F}$ = 273.00 Hz), 119.03, 73.94, 59.43, 40.52.

The analytical data was identical to the reported value.[3]

Catalyst 5b: New compound, white solid; mp: 95 °C



(*S*,*S*)-**5b**

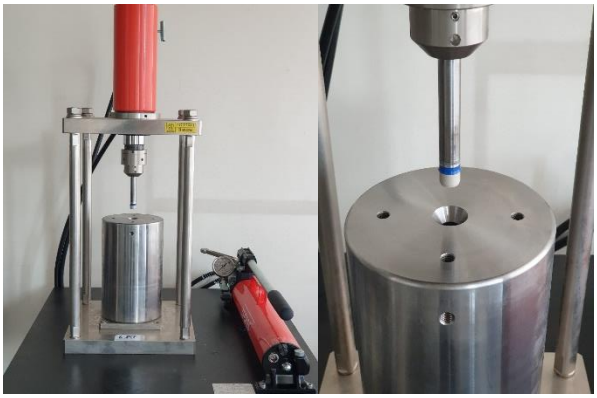
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (br s, 2H), 7.73 (s, 2H), 7.65 (s, 1H), 7.07 (d, J = 8.2 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 8.0 Hz, 2H), 5.14 (s, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 2.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.17, 130.94, 128.96, 123.41, 122.94 (q, $^1J_{C\text{-}F}$ = 272.8 Hz), 118.77, 114.23, 113.32, 73.53, 59.08, 55.14, 40.44.
IR (neat): ν 1611, 1512, 1469, 1382, 1277, 1249, 1177, 1134, 1037.
HRMS (m/z, ESI): $[M+H]^+$ cald. for $C_{27}H_{28}F_6N_3O_2S$, 572.1807; found, 572.1803.

General procedure for the enantioselective protonation reaction under various conditions

Under on-water batch conditions: The corresponding thiol **2** (1 mmol, 10 equiv) was added to a mixture of glyoxal **1** (0.1 mmol), catalyst **5** (0.03 mmol, 30 mol%), eucalyptol (1 mmol, 10 equiv) and brine (2.0 mL). The reaction mixture was stirred vigorously with a magnetic bar at 1150 rpm and the temperature was set to 20 °C. After completion of the reaction (96 h), the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel eluting with a hexanes/ethyl acetate mixture, affording the desired product **4**.

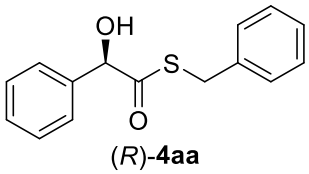
Under on-water microfluidic conditions: The organic solutions (solution 1: in-situ-generated hemithioacetal **3** (0.2 mmol) made by heating a mixture of phenylglyoxal **1** and thiol **2** (10 equiv) in eucalyptol (16.7 mL); solution 2: catalyst **5a** (0.06 mmol, 30 mol%) in eucalyptol (16.7 mL)) and the aqueous solution (brine, 5.13 M)) were loaded into separate syringes, then injected onto the static mixing connector. The brine and organic solutions were brought together at the mixing connector, then coflowed and compartmentalized into droplets by flow focusing of the aqueous phase with the organic phase. After the tube was filled with the reaction mixture, the flows of brine and organic solutions were stopped, and the outlet of the tube was then sealed tightly with a paraffin film. The other end of the tube was also sealed with a paraffin film. The biphasic plugs were kept inside the FEP tubing at 20 ^{o}C without any shaking. After 96 h, the reaction mixture was collected from the outlet of the tubing by flushing with argon. The organic phase was then purified by chromatography to determine the *ee* value (92% *ee*). Conversion of the reaction mixture was determined using ^{1}H NMR spectroscopy by comparing the product peak integration with the reactant peak integration.

Typical high-pressure experimental procedure: Phenylglyoxal **1a** (15.2mg, 0.1 mmol), tertiary butyl thiol **2d** (112 μL, 1 mmol), catalyst **5a** (15.3 mg, 0.03 mmol) and anhydrous eucalyptol or dichloromethane (2 mL) were added to a 4 mL Teflon tube at 20 ^{o}C and the tube was capped with exclusion of air. This tube was placed in a high-pressure reactor vessel (1.5 cm inner diameter; 12 cm vessel diameter; 27.5 cm height) (see photographs below). The cylinder was filled with water and the vessel was pressurized with a hydraulic press to subject the Teflon tube to the necessary pressure. After a specific time had elapsed, the pressure was removed by pulling up the ram of the hydraulic press, and the Teflon tube was recovered from the vessel. The reaction mixture was directly used to measure conversion by ^{1}H NMR.



Hydraulic press and high-pressure reactor vessel for high pressure experiments

Compound 4aa: Isolated yield: 24.1 mg (93%); colorless liquid

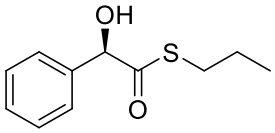


(*R*)-**4aa**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.32 (m, 5H), 7.28 – 7.20 (m, 5H), 5.20 (d, J = 4.4 Hz, 1H), 4.10 (dd, J = 34.2, 13.7 Hz, 2H), 3.52 (d, J = 4.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.38, 137.93, 136.72, 128.99, 128.91, 128.84, 128.69, 127.49, 127.13, 79.91, 33.36.
HPLC analysis: Chiralpak AD-H, Hex/IPA = 96/4, 1.0 mL/min, 220 nm; t_R = 33.3 min (major, *R*), 27.0 min (minor, *S*)

The analytical data was identical to the reported value.[4]

Compound 4ab: Isolated yield: 15.4 mg (74%); colorless liquid

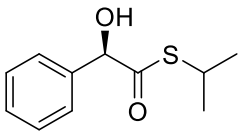


(*R*)-**4ab**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 – 7.32 (m, 5H), 5.22 (d, J = 4.4 Hz, 1H), 3.66 – 3.50 (m, 1H), 3.02 – 2.74 (m, 2H), 1.70 – 1.46 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.98, 138.22, 128.84, 128.74, 127.08, 79.95, 30.84, 22.64, 13.29.
HPLC analysis: Chiralcel OD-H, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 8.8 min (minr, *S*), 13.6 min (major, *R*)

The analytical data was identical to the reported value.[4]

Compound 4ac: Isolated yield: 19.5 mg (93%); colorless liquid

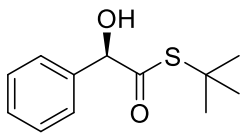


(*R*)-**4ac**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 – 7.34 (m, 5H), 5.18 (d, J = 4.4 Hz, 1H), 3.72 – 3.63 (m, 1H), 3.60 (t, J = 4.2 Hz, 1H), 1.28 (dd, J = 16.5, 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.79, 138.27, 128.86, 128.78, 127.18, 79.96, 35.22, 22.90, 22.84.
HPLC analysis: Chiralcel OD-H, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 8.1 min (minor, *S*), 14.9 min (major, *R*)

The analytical data was identical to the reported value.[4]

Compound 4ad: Isolated yield: 20.3 mg (90%); colorless liquid

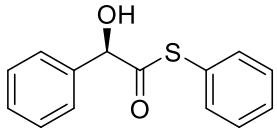


(*R*)-**4ad**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 – 7.31 (m, 5H), 5.11 (d, J = 4.7 Hz, 1H), 3.75 (d, J = 4.7 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.94, 138.61, 128.74, 127.26, 79.96, 49.03, 29.86.
HPLC analysis: Chiralcel OD-H, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 6.9 min (minor, *S*), 12.5 min (major, *R*)

The analytical data was identical to the reported value.[4]

Compound 4ae: Isolated yield: 23.7 mg (97%); colorless liquid

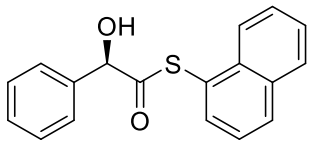


(*R*)-**4ae**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 – 7.32 (m, 10H), 5.34 (d, J = 4.3 Hz, 1H), 3.47 (d, J = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.13, 137.72, 134.64, 129.67, 129.31, 129.10, 128.92, 127.21, 126.54, 80.03.
HPLC analysis: Chiralcel OD-H, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 18.5 min (minor, *S*), 22.2 min (major, *R*)

The analytical data was identical to the reported value.[4]

Compound 4af: Isolated yield: 28.1 mg (96%); white solid

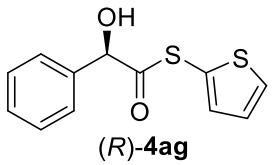


(*R*)-**4af**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 – 7.80 (m, 3H), 7.71 – 7.58 (m, 1H), 7.55 – 7.36 (m, 8H), 5.38 (s, 1H), 3.60 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.90, 137.85, 135.28, 134.25, 134.21, 131.22, 129.15, 128.99, 128.74, 127.32, 127.24, 126.53, 125.63, 125.00, 123.93, 80.17.
HPLC analysis: Chiralcel OD-H, Hex/IPA = 90/10, 1.0 mL/min, 220 nm; t_R = 18.0 min (major, *R*), 27.5 min (minor, *S*)

The analytical data was identical to the reported value.[4]

Compound 4ag: Isolated yield: 3 mg (12%); colorless liquid

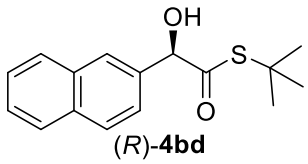


(*R*)-**4ag**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 – 7.51 (m, 1H), 7.47 – 7.44 (m, 2H), 7.42 – 7.38 (m, 3H), 7.13 – 7.04 (m, 2H), 5.33 (s, 1H), 3.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.08, 137.24, 136.09, 132.11, 129.22, 128.99, 127.92, 127.15, 123.35, 79.92.
HPLC analysis: Chiralpak IC, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 11.8 min (major, *R*), 14.4 min (minor, *S*)

The analytical data was identical to the reported value.[4]

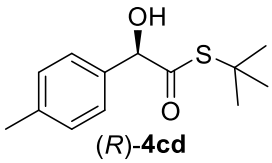
Compound 4bd: New compound, isolated yield: 22.6 mg (82%); white solid; mp: 123 ^{o}C; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.51; $[\alpha]_D^{20}$ = -209 (c = 0.8 in $CHCl_3$);



(*R*)-**4bd**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 – 7.74 (m, 4H), 7.56 – 7.38 (m, 3H), 5.27 (d, J = 4.6 Hz, 1H), 3.88 (d, J = 4.6 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.90, 135.98, 133.46, 133.24, 128.69, 128.20, 127.79, 127.07, 126.44, 126.35, 124.33, 80.13, 49.11, 29.87.
IR (neat): ν 1669, 1507, 1456, 1363, 1155, 973, 955, 810.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{16}H_{18}OS_2Na$, 297.0925; found, 297.0922.
HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 13.2 min (minor, *S*), 15.0 min (major, *R*)

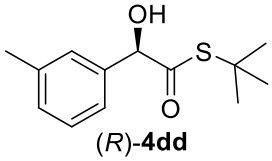
Compound 4cd: New compound, isolated yield: 14.3 mg (60%); white solid; mp: 73 °C; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.48; $[\alpha]_D^{20}$ = -142 (c = 0.5 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 5.06 (d, *J* = 4.7 Hz, 1H), 3.67 (d, *J* = 4.8 Hz, 1H), 2.35 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.11, 138.58, 135.70, 129.45, 127.20, 79.82, 48.92, 29.87, 21.28.



(*R*)-**4cd**

IR (neat): ν 1677, 1609, 1479, 1455, 1365, 1260, 1156, 1051, 969, 902, 779.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{16}H_{18}OS_2Na$, 261.0925; found, 261.0922.
HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 9.1 min (minor, *S*), 11.6 min (major, *R*)

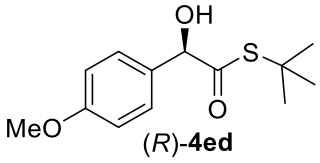
Compound 4dd: New compound, isolated yield: 15.5 mg (65%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.47; $[\alpha]_D^{20}$ = -166 (c = 0.5 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.24 (m, 1H), 7.20 – 7.13 (m, 3H), 5.06 (d, *J* = 4.5 Hz, 1H), 3.70 (d, *J* = 4.7 Hz, 1H), 2.36 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.02, 138.53, 138.46, 129.50, 128.60, 127.87, 124.39, 80.00, 48.94, 29.88, 21.44.



(*R*)-**4dd**

IR (neat): ν1677, 1607, 1477, 1455, 1365, 1155, 1078, 1054, 969, 901, 776, 760, 718.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{16}H_{18}OS_2Na$, 261.0925; found, 261.0923.
HPLC analysis: Chiralpak IA, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 16.8 min (minor, *S*), 18.9 min (major, *R*)

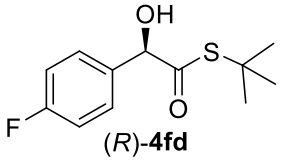
Compound 4ed: New compound, isolated yield: 10.1 mg (40%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.50; $[\alpha]_D^{20}$ = -94 (c = 1.0 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.29 (m, 2H), 6.92 – 6.89 (m, 2H), 5.05 (d, *J* = 4.6 Hz, 1H), 3.81 (s, 3H), 3.64 (d, *J* = 4.6 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.28, 159.93, 130.78, 128.62, 114.15, 79.52, 55.27, 48.83, 29.88.



(*R*)-**4ed**

IR (neat): ν 1675, 1600, 1489, 1455, 1365, 1260, 1157, 1045, 972, 901, 830.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{13}H_{18}O_3SNa$, 277.0874; found, 277.0871.
HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 13.2 min (minor, *S*), 16.4 min (major, *R*)

Compound 4fd: New compound, isolated yield: 17.7 mg (73%); white solid; mp: 40 °C; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.52; $[\alpha]_D^{20}$ = -62.5 (c = 1.2 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.35 (m, 2H), 7.08–7.04 (m, 2H), 5.09 (d, *J* = 4.49 Hz, 1H), 3.74 (d, *J* = 4.51 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.81, 162.93 (d, $^1J_{C\text{-}F}$ = 247.39 Hz), 134.44 (d, $^4J_{C\text{-}F}$ = 3.17 Hz), 129.01 (d, $^3J_{C\text{-}F}$ = 8.40 Hz), 115.68 (d, $^2J_{C\text{-}F}$ = 21.72 Hz), 79.21, 49.10, 29.84; ^{19}F NMR (470 MHz, $CDCl_3$): δ −113.04.

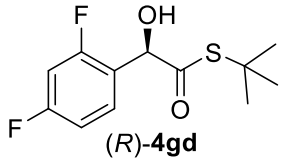


(*R*)-**4fd**

IR (neat): ν 2364, 2338, 1667, 1602, 1509, 1364, 1233, 1186, 1156, 1104, 1078, 1014, 971, 937, 851, 808.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{15}FO_2SNa$, 265.0675; found, 265.0672.

HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 7.8 min (minor, *S*), 9.1 min (major, *R*)

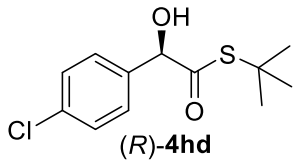
Compound 4gd: New compound, isolated yield: 27.5 mg (95%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.63; $[\alpha]_D^{20}$ = -75 (c = 1.0 in $CHCl_3$);



(*R*)-**4gd**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.30 (m, 1H), 6.92–6.82 (m, 2H), 5.32 (d, *J* = 4.70 Hz, 1H), 3.82 (d, *J* = 4.70 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.90, 163.18, (dd, $^{1,3}J_{C\text{-}F}$ = 12.06, 250.42 Hz), 160.82 (dd, $^{1,3}J_{C\text{-}F}$ = 12.15, 251.26 Hz), 130.07 (dd $^{3,3}J_{C\text{-}F}$ = 5.11, 9.96 Hz), 122.34 (dd, $^{2,4}J_{C\text{-}F}$ = 3.81, 13.61 Hz), 111.81 (dd, $^{2,4}J_{C\text{-}F}$ = 3.68, 21.45 Hz), 104.29 (t, $^{2,2}J_{C\text{-}F}$ = 25.47, 25.47 Hz), 73.58 (d, $^{4}J_{C\text{-}F}$ = 2.26 Hz), 49.27, 29.82; ^{19}F NMR (470 MHz, $CDCl_3$): δ −108.78 (d, *J* = 8.2 Hz), −113.40 (d, *J* = 8.11 Hz).
IR (neat): ν 2364, 2338, 1667, 1602, 1509, 1364, 1233, 1186, 1156, 1104, 1078, 1014, 971, 937, 851, 808.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{14}F_2O_2SNa$, 283.0580; found, 283.0579.
HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 8.4 min (minor, *S*), 9.9 min (major, *R*)

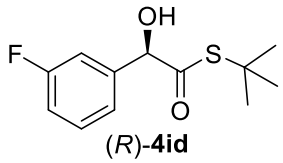
Compound 4hd: New compound, isolated yield: 18.1 mg (70%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.51; $[\alpha]_D^{20}$ = -160 (c = 0.63 in $CHCl_3$);



(*R*)-**4hd**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.30 (m, 4H), 5.08 (s, 1H), 3.77 (s, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.45, 137.08, 134.61, 128.91, 128.56, 79.23, 49.29, 29.84.
IR (neat): ν 1672, 1491, 1455, 1407, 1392, 1365, 1189, 1167, 1089, 1055, 1015, 969, 847, 802, 744.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{15}ClO_2SNa$, 281.0379; found, 281.0375.
HPLC analysis: Chiralpak IA, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 19.8 min (minor, *S*), 23.2 min (major, *R*)

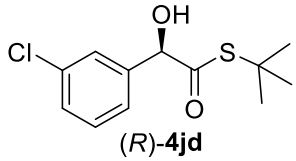
Compound 4id: New compound, isolated yield: 23.1 mg (95%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.42; $[\alpha]_D^{20}$ = -52 (c = 0.25 in $CHCl_3$);



(*R*)-**4id**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.30 (m, 1H), 7.21 – 7.16 (m, 1H), 7.13 – 7.09 (m, 1H), 7.08 – 6.99 (m, 1H), 5.10 (d, *J* = 4.6 Hz, 1H), 3.80 (d, *J* = 4.7 Hz, 1H), 1.45 (s, 9H).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.28, 162.90 (d, $^{1}J_{C\text{-}F}$ = 246.8 Hz), 140.98 (d, $^{3}J_{C\text{-}F}$ = 7.1 Hz), 130.20 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 122.91 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 115.64 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 114.07 (d, $^{2}J_{C\text{-}F}$ = 22.4 Hz), 79.27 (d, $^{4}J_{C\text{-}F}$ = 1.8 Hz), 49.27, 29.83.
IR (neat): ν 1674, 1592, 1486, 1452, 1366, 1249, 1162, 1137, 1064, 975, 921, 756.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{15}FO_2SNa$, 265.0675; found, 265.0673.
HPLC analysis: Chiralcel OX-3, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 12.6 min (minor, *S*), 15.1 min (major, *R*)

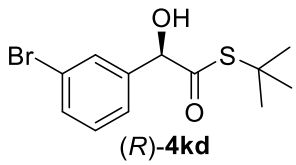
Compound 4jd: New compound, isolated yield: 24.8 mg (96%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.42; $[\alpha]_D^{20}$ = -122 (c = 0.5 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.38 (m, 1H), 7.33 – 7.27 (m, 3H), 5.07 (d, J = 4.7 Hz, 1H), 3.80 (d, J = 4.7 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.22, 140.51, 134.61, 129.92, 128.85, 127.29, 125.38, 79.25, 49.36, 29.85.



(*R*)-**4jd**

IR (neat): ν 1672, 1595, 1576, 1475, 1457, 1431, 1365, 1192, 1164, 1076, 969, 779, 744, 729, 685, 630.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{15}ClO_2SNa$, 281.0379; found, 281.0976.
HPLC analysis: Chiralcel OX-3, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 14.1 min (minor, *S*), 15.0 min (major, *R*)

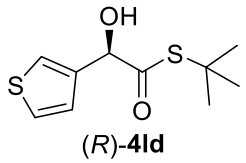
Compound 4kd: New compound, isolated yield: 28.4 mg (94%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.55; $[\alpha]_D^{20}$ = -105 (c = 0.95 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.57 – 7.54 (m, 1H), 7.49 – 7.45 (m, 1H), 7.34 – 7.31 (m, 1H), 7.26 – 7.22 (m, 1H), 5.06 (d, J = 4.5 Hz, 1H), 3.79 (d, J = 4.7 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.18, 140.74, 131.76, 130.19, 130.17, 125.84, 122.74, 79.18, 49.37, 29.84.



(*R*)-**4kd**

IR (neat): ν 2360, 1671, 1593, 1571, 1474, 1456, 1427, 1365, 1186, 1166, 1098, 1071, 1055, 968.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{12}H_{15}BrO_2SNa$, 324.9874; found, 324.9870.
HPLC analysis: Chiralcel OX-3, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 14.6 min (minor, *S*), 16.2 min (major, *R*)

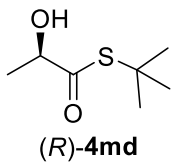
Compound 4ld: New compound, isolated yield: 22.1 mg (97%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.57; $[\alpha]_D^{20}$ = -61 (c = 1.0 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.34 (m, 1H), 7.34 – 7.31 (m, 1H), 7.09 (dd, J = 5.0, 1.1 Hz, 1H), 5.21 (d, J = 5.0 Hz, 1H), 3.57 (d, J = 5.2 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.38, 139.32, 126.49, 125.94, 123.77, 75.96, 48.92, 29.85.



(*R*)-**4ld**

IR (neat): ν 1676, 1476, 11455, 1364, 1154, 1082, 1050, 975, 927, 913, 837, 778, 744.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{10}H_{14}O_2SNa$, 253.0333; found, 253.0331.
HPLC analysis: Chiralpak IA, Hex/IPA = 95/5, 1.0 mL/min, 220 nm; t_R = 11.2 min (minor, *S*), 12.7 min (major, *R*)

Compound 4md: New compound, isolated yield: 3.9 mg (24%); ^1H NMRconversion: 80%; colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.43; $[\alpha]_D^{20}$ = +60 (c = 0.13 in $CHCl_3$);



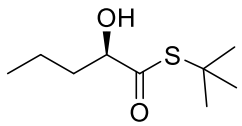
(*R*)-**4md**

^1H NMR (500 MHz, $CDCl_3$): δ 4.24 (q, J = 6.8 Hz, 1H), 2.94 (s, 1H), 1.50 (s, 9H), 1.42 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.46, 73.84, 48.30, 29.91, 21.52.

IR (neat): ν 1668, 1455, 1365, 1148, 1139, 1037, 964, 915, 887, 738, 666, 652, 638, 626.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_7H_{14}O_2SNa$, 185.0612; found, 185.0610.

HPLC analysis: Chiralcel OX-3, Hex/IPA = 99/1, 0.7 mL/min, 220 nm; t_R = 12.4 min (minor, *S*), 12.9 min (major, *R*)

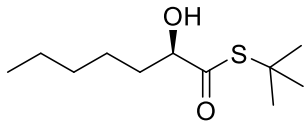
Compound 4nd: New compound, isolated yield: 15.6 mg (83%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.52; $[\alpha]_D^{20}$ = -33 (c = 0.75 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.18 – 4.12 (m, 1H), 2.92 (d, *J* = 5.4 Hz, 1H), 1.83 – 1.72 (m, 1H), 1.65 – 1.55 (m, 1H), 1.50 – 1.40 (m, 11H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.18, 77.33, 48.30, 37.69, 29.92, 17.86, 13.84.



(*R*)-**4nd**

IR (neat): ν 1676, 1477, 1456, 1391, 1364, 1163, 1141, 1068, 1033, 993, 940, 931, 740, 732.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_9H_{18}O_2SNa$, 213.0925; found, 213.0923.
HPLC analysis: Chiralpak IA-3, Hex/IPA = 99/1, 1.0 mL/min, 220 nm; t_R = 12.0 min (minor, *S*), 12.9 min (major, *R*)

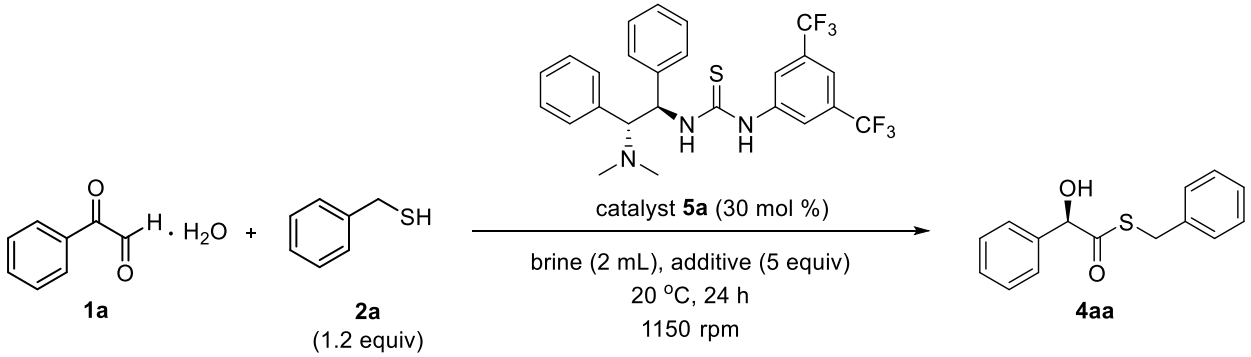
Compound 4od: New compound, isolated yield: 18.3 mg (24%); colorless liquid; TLC (EtOAc/*n*-hexane, 1/4 v/v): R_f = 0.55; $[\alpha]_D^{20}$ = -105 (c = 0.8 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.17 – 4.12 (m, 1H), 2.88 (d, *J* = 5.4 Hz, 1H), 1.85 – 1.76 (m, 1H), 1.66 – 1.57 (m, 2H), 1.50 (s, 9H), 1.48 – 1.39 (m, 3H), 1.32 – 1.29 (m, 2H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.15, 77.51, 48.33, 35.58, 31.53, 29.93, 24.13, 22.46, 13.97.



(*R*)-**4od**

IR (neat): ν 1676, 1477, 1456, 1391, 1379, 1365, 1163, 1139, 1079, 1058, 965, 910, 732.
HRMS (m/z, ESI): $[M+Na]^+$ cald. for $C_{11}H_{22}O_2SNa$, 241.1238; found, 241.1236.
HPLC analysis: Chiralpak IA, Hex/IPA = 99/1, 0.5 mL/min, 220 nm; t_R = 18.8 min (minor, *S*), 20.0 min (major, *R*)

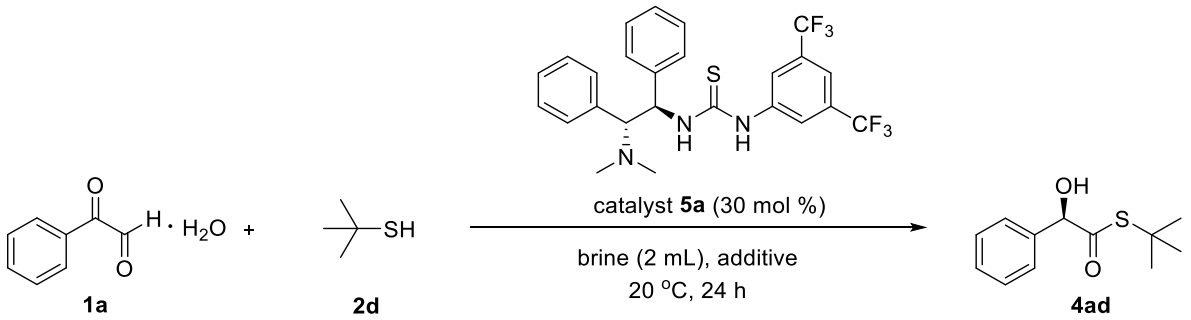
Table S1. Screening of hydrophobic cosolvents[a]



Entry	Additive	Conversion (%)[b]	*ee* (%)[c]
1	toluene	82	39
2	*o*-xylene	77	40
3	*m*-xylene	74	43
4	*p*-xylene	77	41
5	chlorobenzene	82	39
6	bromobenzene	75	*43*
7	1,2-dichlorobenzene	79	41
8	CH_2Cl_2	82	31
9	diethyl ether	69	56
10	diisopropyl ether	36	67
11	dibuthyl ether	50	66
12	dipentyl ether	43	68
13	MTBE (20 equiv)	32	75
14	methoxy cyclohexane	66	71
15	methyl propargyl ether	91	39
16	THF	82	51
17	2-methyl THF	62	62
18	CPME	60	74
19	CPME (2.5 equiv)/THF (2.5 equiv)	63	64
20	1,2-dimethyxy ethane	90	39
21	eucalyptol	51	77
22	(*R*)-(+)-limonene (20 equiv)	26	71
23	(*S*)-(-)-limonene (20 equiv)	38	60
24	(+)-(α)-pinene (20 equiv)	47	51
25	(-)-(α)-pinene (20 equiv)	32	53

[a]General reaction conditions: **1a** (0.1 mmol), **2** (0.12 mmol), and catalyst **5a** (30 mol%) on 2.0 mL of media at 20 °C. [b]The conversion was determined by ^{1}H NMR integration. [c]Enantiomeric excess (% *ee*) was determined by high-performance liquid chromatography (HPLC).

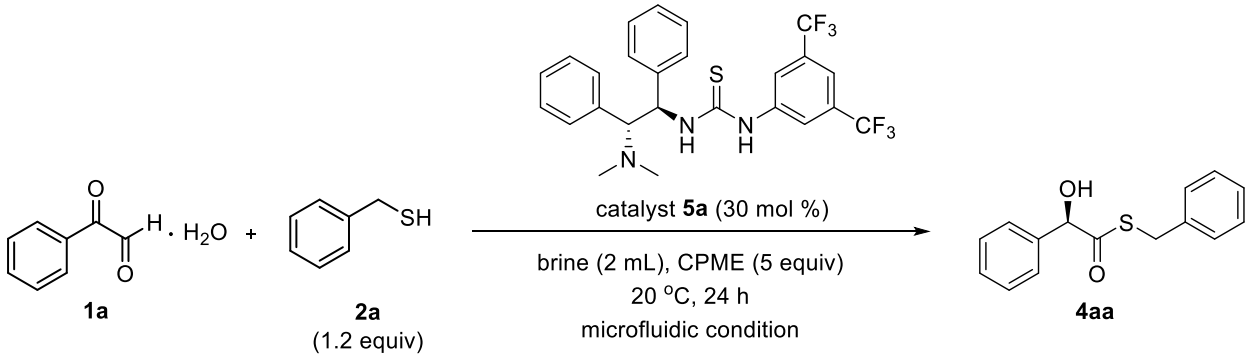
Table S2. Equivalent screening



1a 2d 4ad

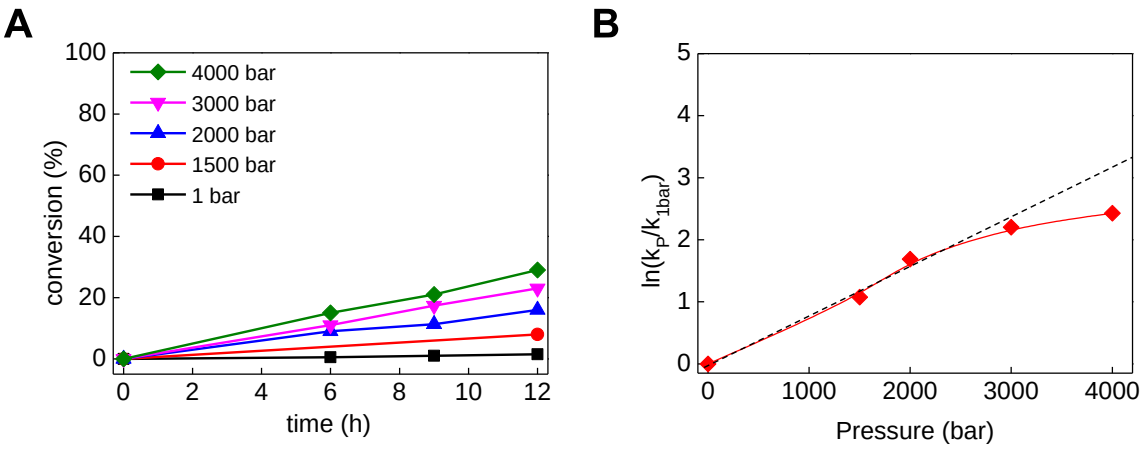
Entry	Thiol	Additive	Conversion (%)	*ee* (%)	condition
1	*t*-BuSH (2 equiv)	eucalyptol (5 equiv)	32	89	on-water
2	*t*-BuSH (6 equiv)	eucalyptol (5 equiv)	47	91	on-water
3	*t*-BuSH (10 equiv)	eucalyptol (5 equiv)	61	90	on-water
4	*t*-BuSH (20 equiv)	eucalyptol (5 equiv)	64	90	on-water
5	*t*-BuSH (6 equiv)	-	68	70	on-water
6	*t*-BuSH (10 equiv)	-	79	73	on-water
7	*t*-BuSH (20 equiv)	-	81	78	on-water

Table S3. Effect of droplet size under the biphasic microfluidic conditions



conditions	conversion (%)	*ee* (%)
0.5 mm tube, Q_w:Q_o=20:1	53	79
0.5 mm tube, Q_w:Q_o=1:20	54	79

Table S4. High-pressure experiments for the determination of activation volume



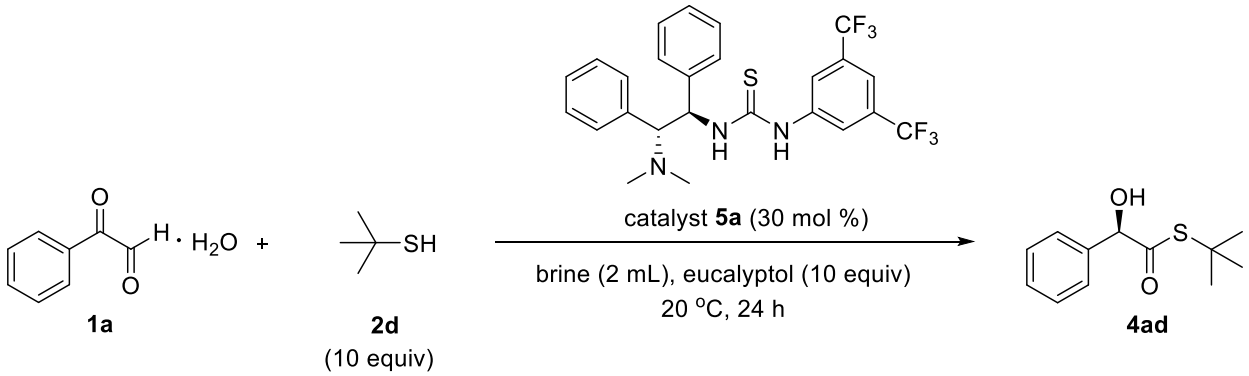
Pressure (bar)	Conversion (%)					k_{rel}
	6 h	9 h	12 h	24 h	36 h	
1	<1	1	-	2	-	1
1500	-	-	8	15	22	2.93
2000	9	11	16	-	-	5.40
3000	11	17	23	-	-	9.05
4000	15	21	29	-	-	11.33

(A) Effect of pressure on the reaction rate. k_{rel} = 1.0 (1 bar), k_{rel} = 2.93 (1.5 kbar), k_{rel} = 5.40 (2 kbar), k_{rel} = 9.05 (3 kbar), k_{rel} = 11.33 (4 kbar) (B) Determination of activation volume according to the equation $\ln(k_P/k_{1bar}) = -(\Delta\Delta V^{\ddagger}/RT)(P-1)+C$.

*__Comment 1__: The kinetic analysis is proposed in terms of the formation of the thioester product **4aa**, which leads to the same results as the analysis for the consumption of starting material.

**__Comment 2__: Plotting In (k_P-k_{1bar}) *vs.* (*P*-1) shows a typical curve with a linear dependence in the low-pressure region, leveling off at higher pressures. This may be due to the increased viscosity of the solvent at higher pressures.

Table S5. Study of the effect of catalyst optical purity on product optical purity[a]



ee of catalyst **5a** [%]	3	23	42	60	81	100
ee of product **4ad** [%]	2	21	38	55	74	91

[a]General reaction conditions: **1a** (0.1 mmol), **2d** (1 mmol), and catalyst **5a** (30 mol%) on brine (2.0 mL) and eucalyptol (1 mmol) at 20 °C. Enantiomeric excess (% *ee*) was determined by high-performance liquid chromatography (HPLC).

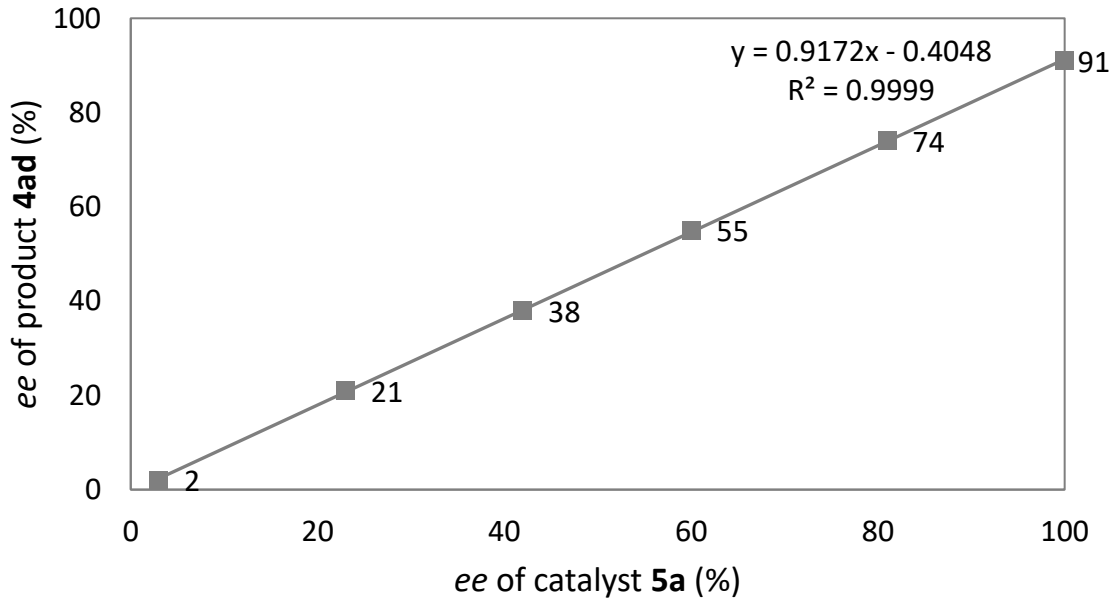
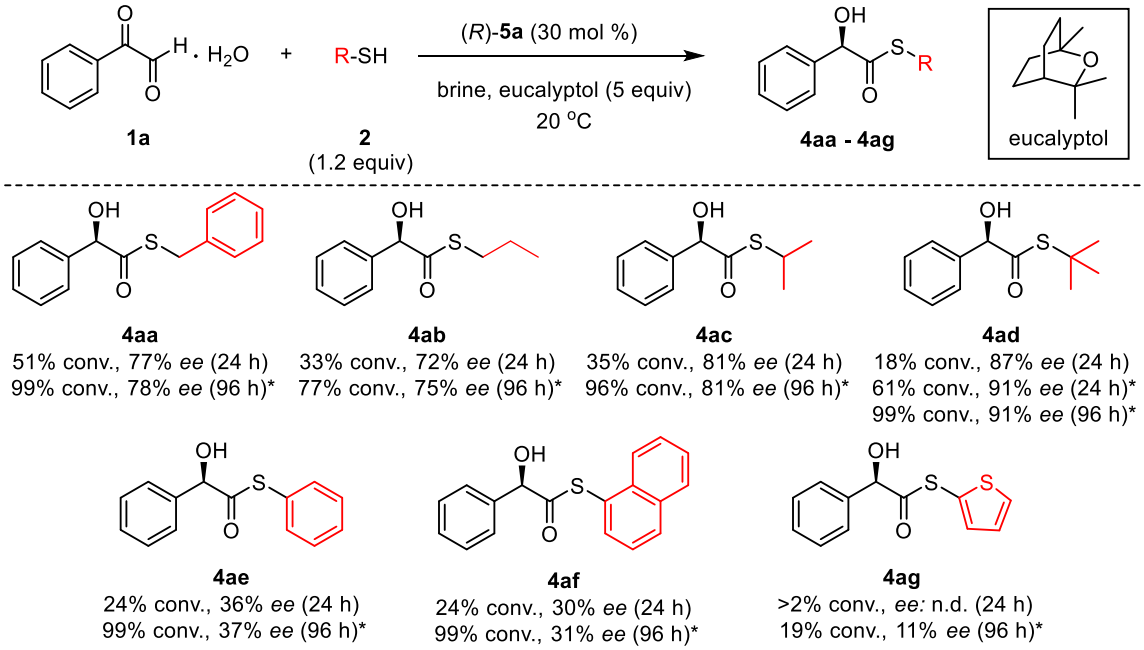


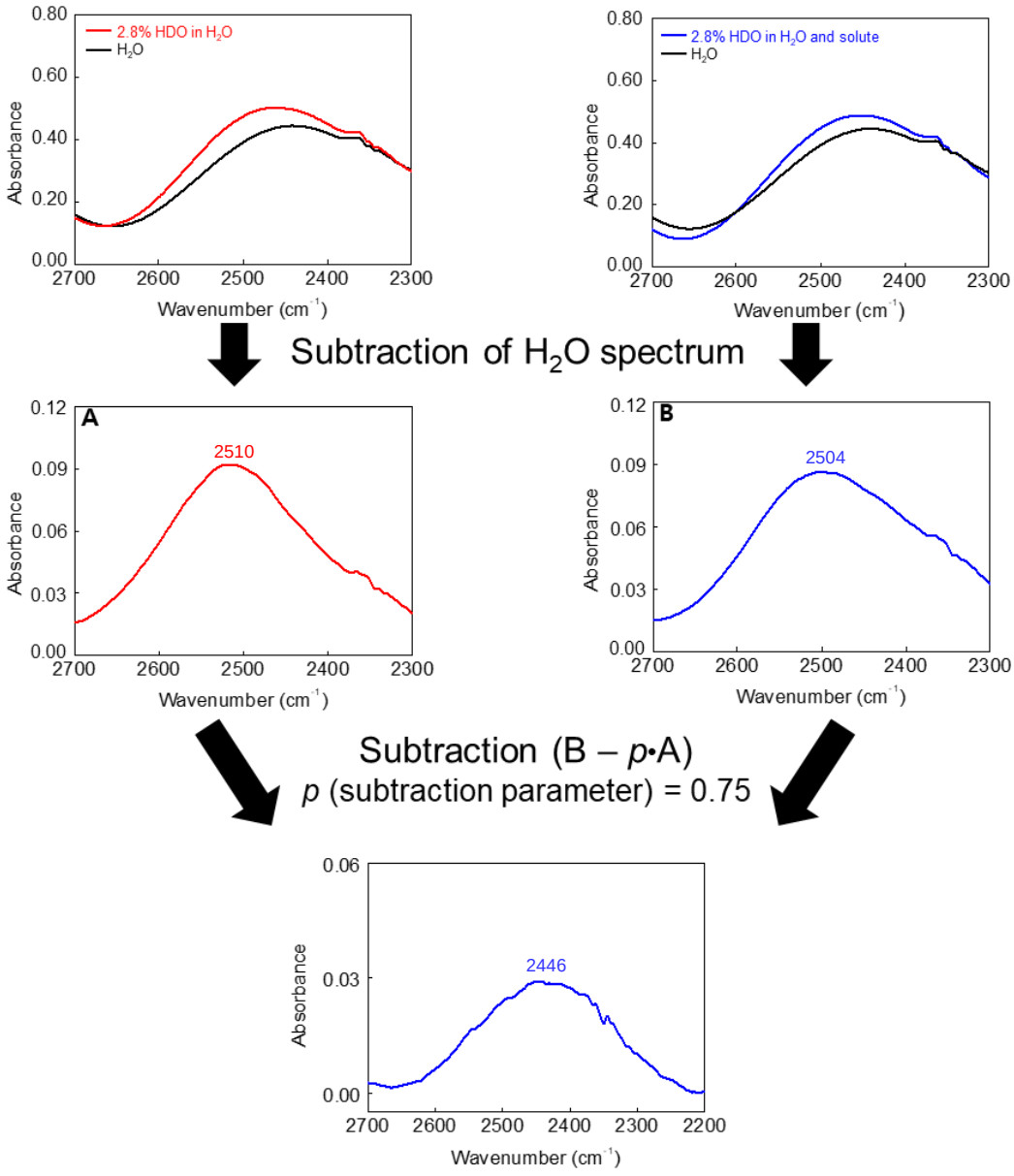
Figure S1. Thiol screening



*10 equiv of R-SH was used.

***Comments:** Regardless of the degree of substitution, alkyl thiols were found to serve as suitable GSH surrogates in terms of enantioselectivity. However, aromatic and heteroaromatic thiols were markedly inferior for enantioselectivity.

Figure S2. Schematic representation of the double-subtraction procedure of IR spectra

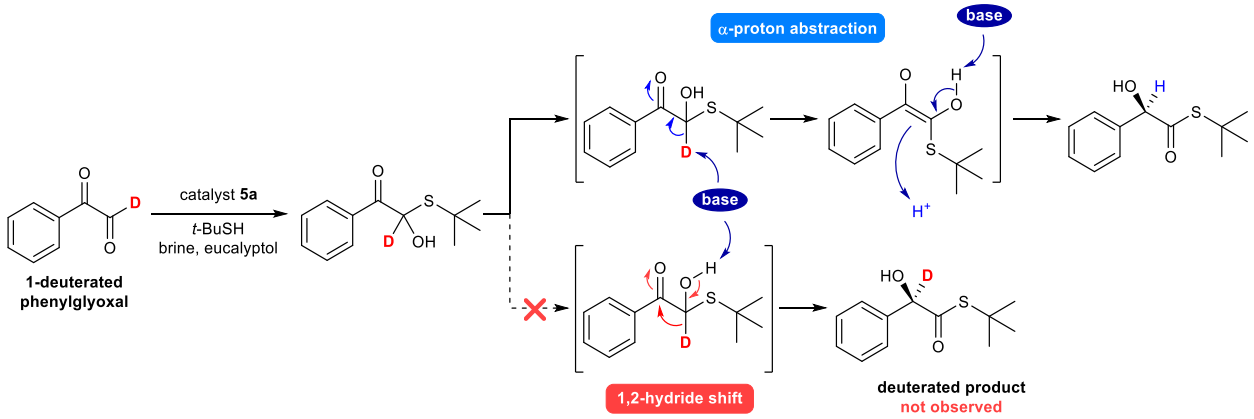


*The subtraction procedure developed by Lindgren and coworkers was used to determine the hydrogen bond strength of water molecules near the hydrophobic reaction mixture under on-water conditions.[5]

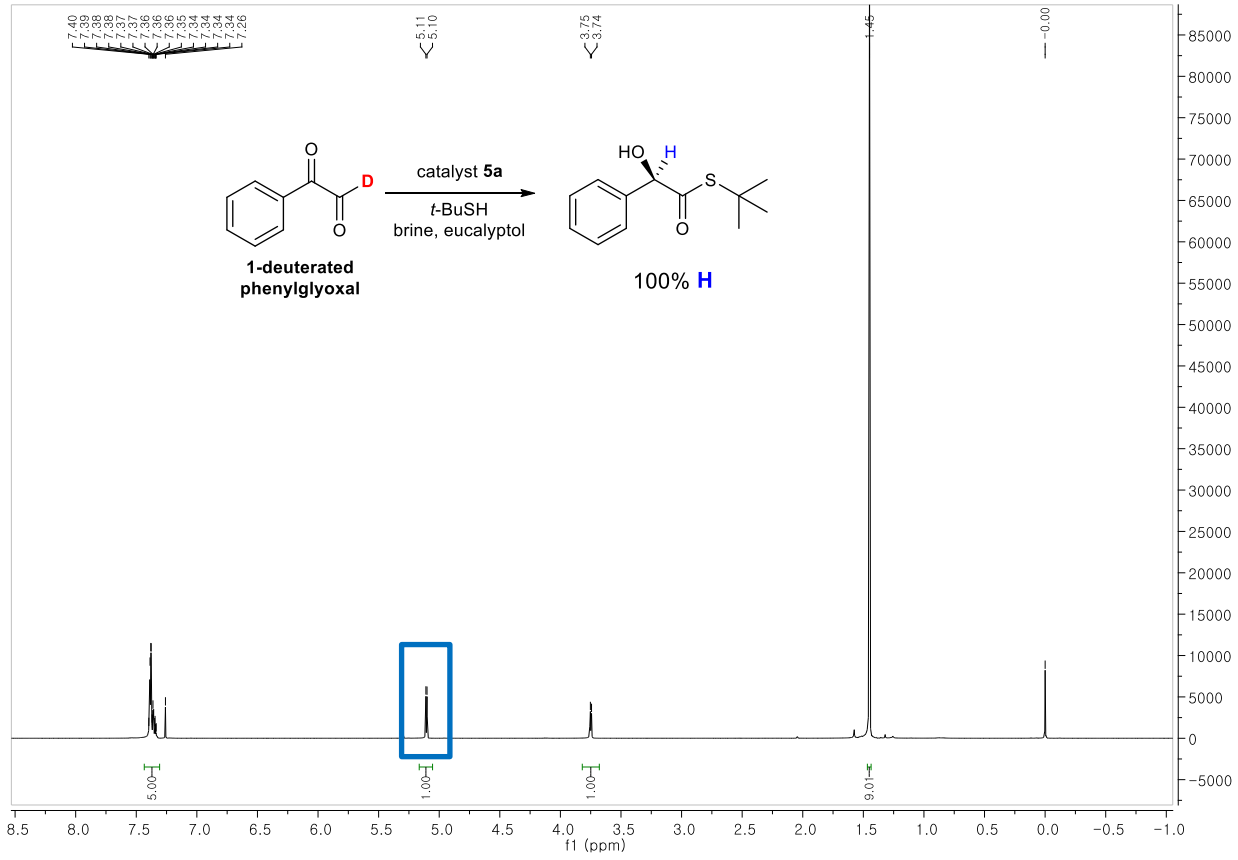
*Solutions of 2.8% (by volume) HDO in H_2O were used for all IR measurements. The solution was prepared by mixing 1.4% D_2O and 98.6% H_2O. A demountable flow cell (Specac, ZnSe window, GS20586) was used as a sample cell and deuterated triglycine sulphate (DTGS) as a detector. The spectra were collected in the transmission mode with a resolution of 4 cm^{-1}. Thirty two interferograms were measured and apodized using the Gapp-Henzel function. The aperture of the IR beam was set to 2 mm. Sample was injected into the cavity generated by 6 μm thick Mylar spacers between the ZnSe windows mounted in the flow cell. OPUS software (Ver. 6.5) was used for subtraction of spectra.

Figure S3. Isotope experiment with [1-^{2}H]-phenylglyoxal

A

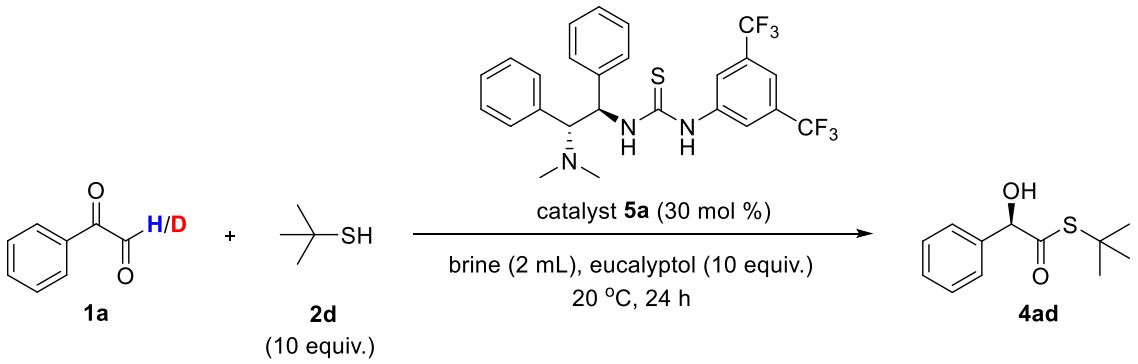


B

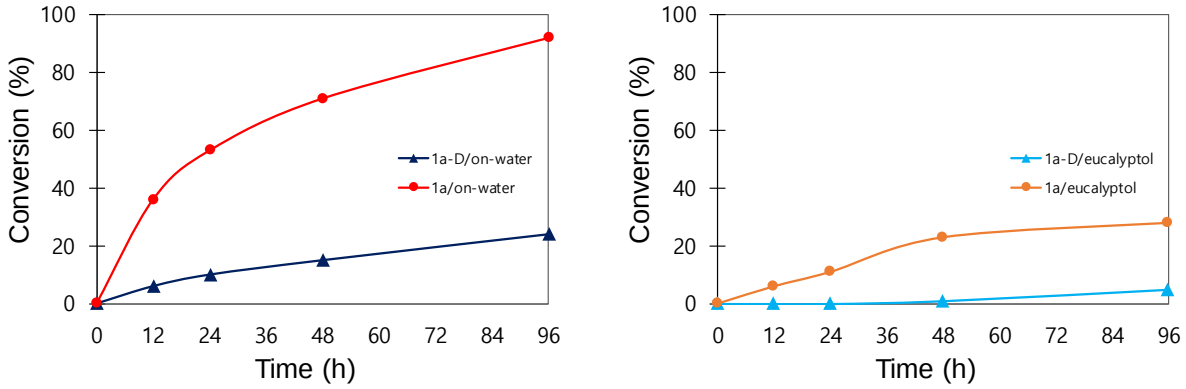


(A) Two possible mechanisms. (B) NMR spectrum of the isotope experiment with deuterated-phenylglyoxal. The reaction was performed with [1-^{2}H]-phenylglyoxal (0.1 mmol), **2d** (1 mmol), and catalyst **5a** (30 mol%) on brine (2.0 mL) and eucalyptol (1 mmol) at 20 ºC.

Figure S4. Study of the rate determining step for isomerization of hemithioacetals

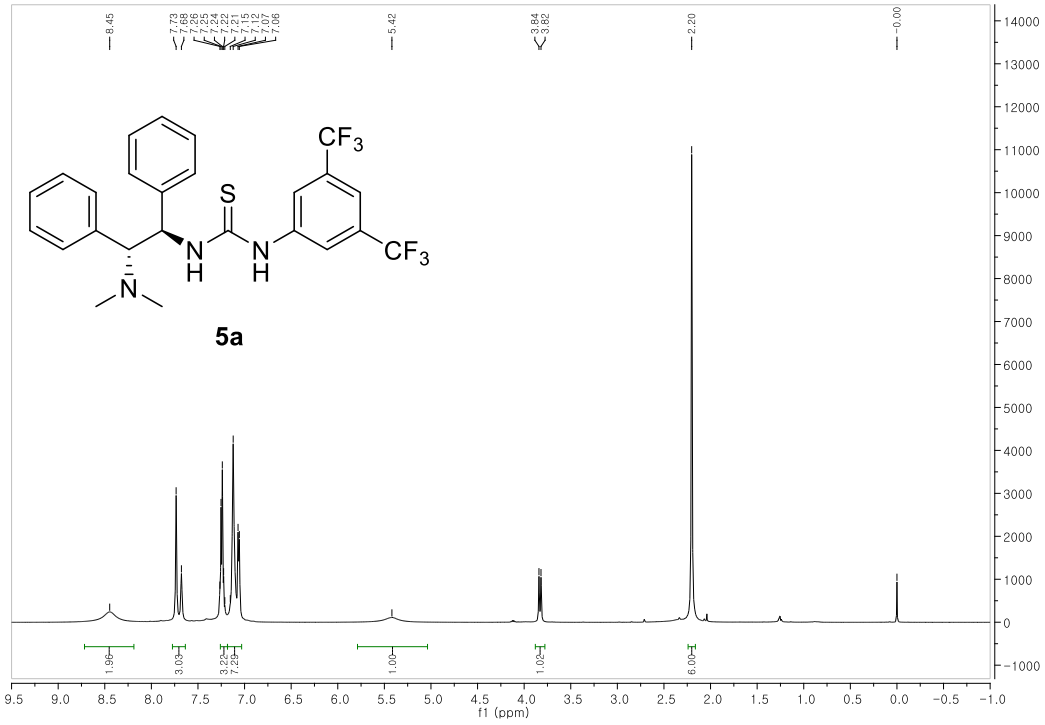


Time [h]	0	12	24	48	96
(1) Phenylglyoxal-D / Brine, eucalyptol	0	6	10	15	24
(2) Phenylglyoxal-H / Brine, eucalyptol	0	36	53	71	92
(3) Phenylglyoxal-D / eucalyptol (dry)	0	0	0	1	5
(4) Phenylglyoxal-H / eucalyptol (dry)	0	6	11	23	28

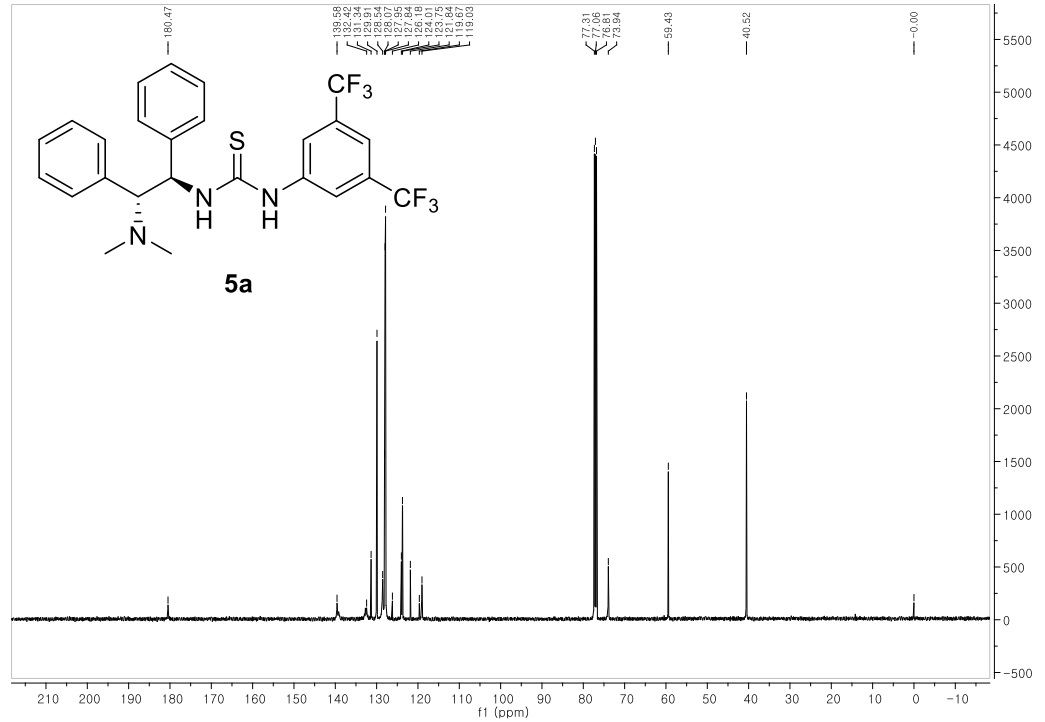


NMR spectra

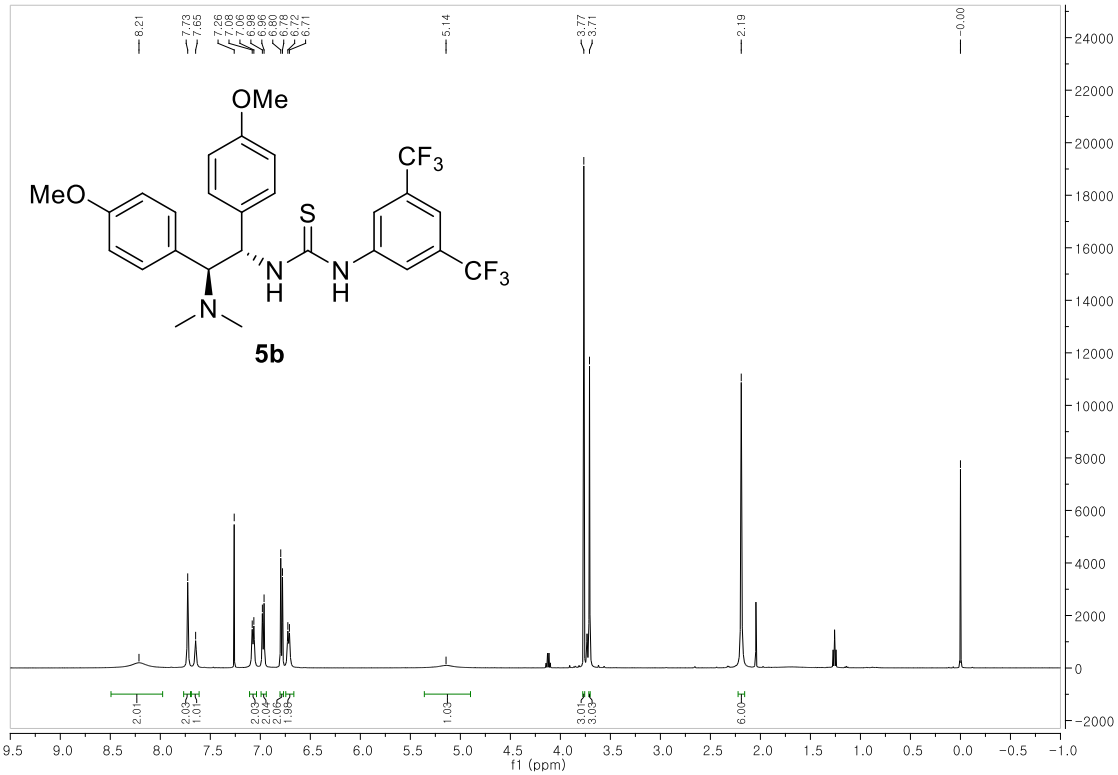
NMR Spectra of catalysts



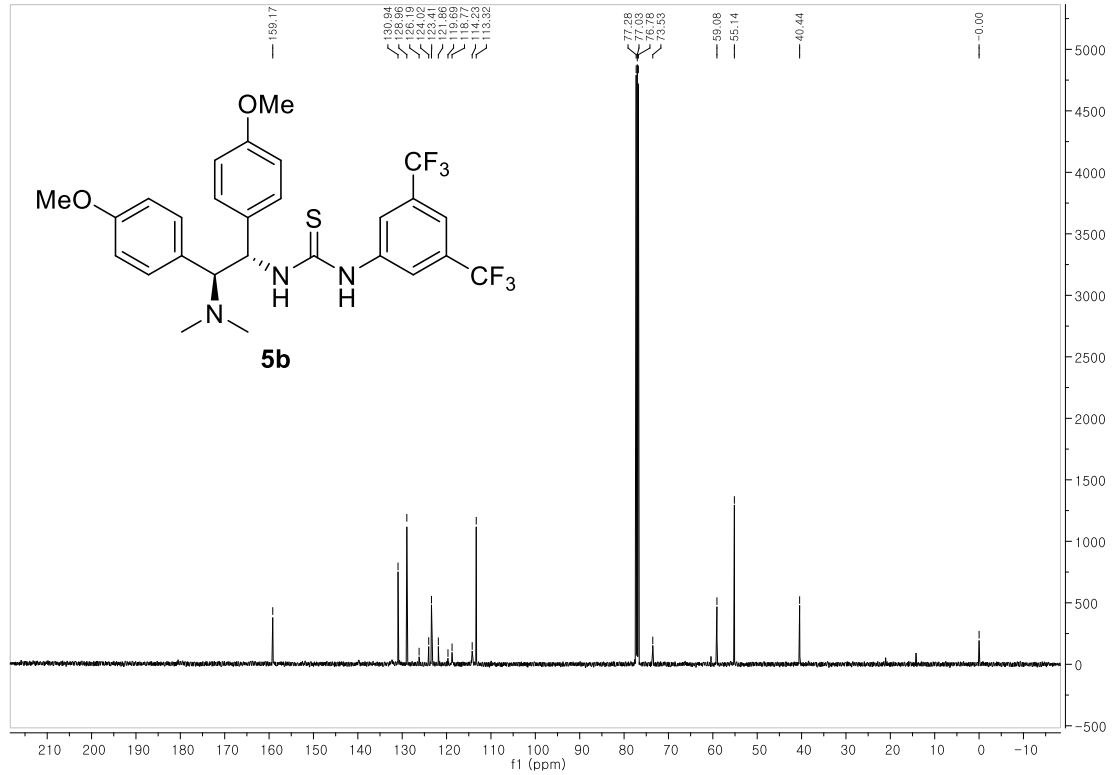
^{1}H NMR spectra of **5a**



^{13}C NMR spectra of **5a**

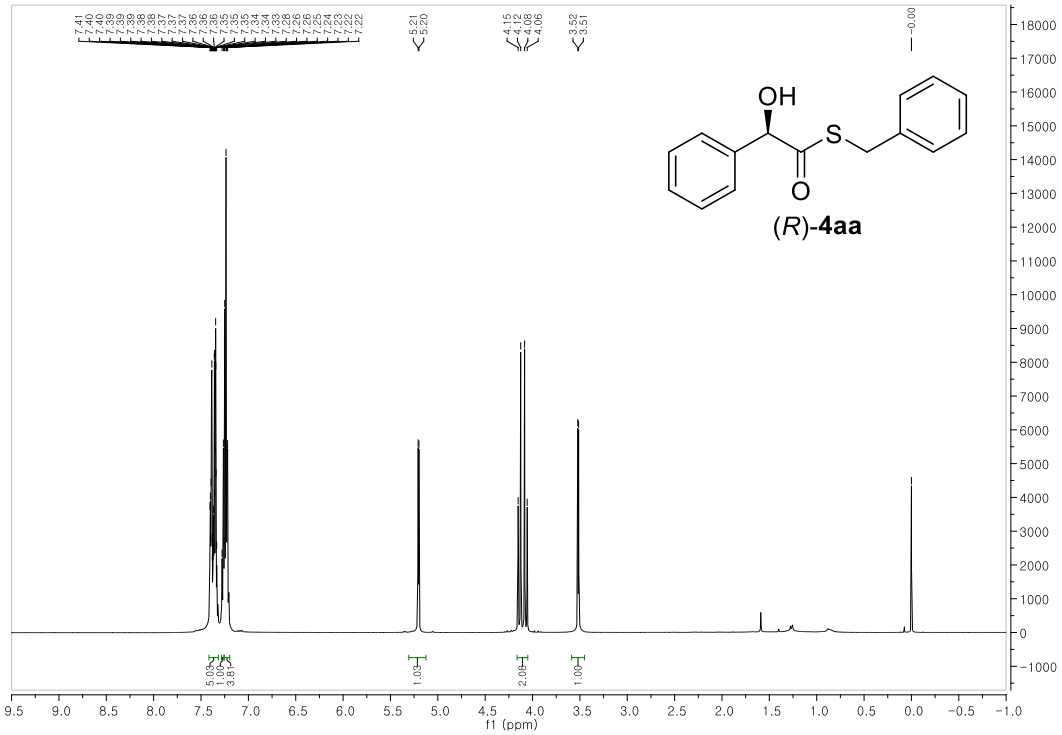


^{1}H NMR spectra of **5b**

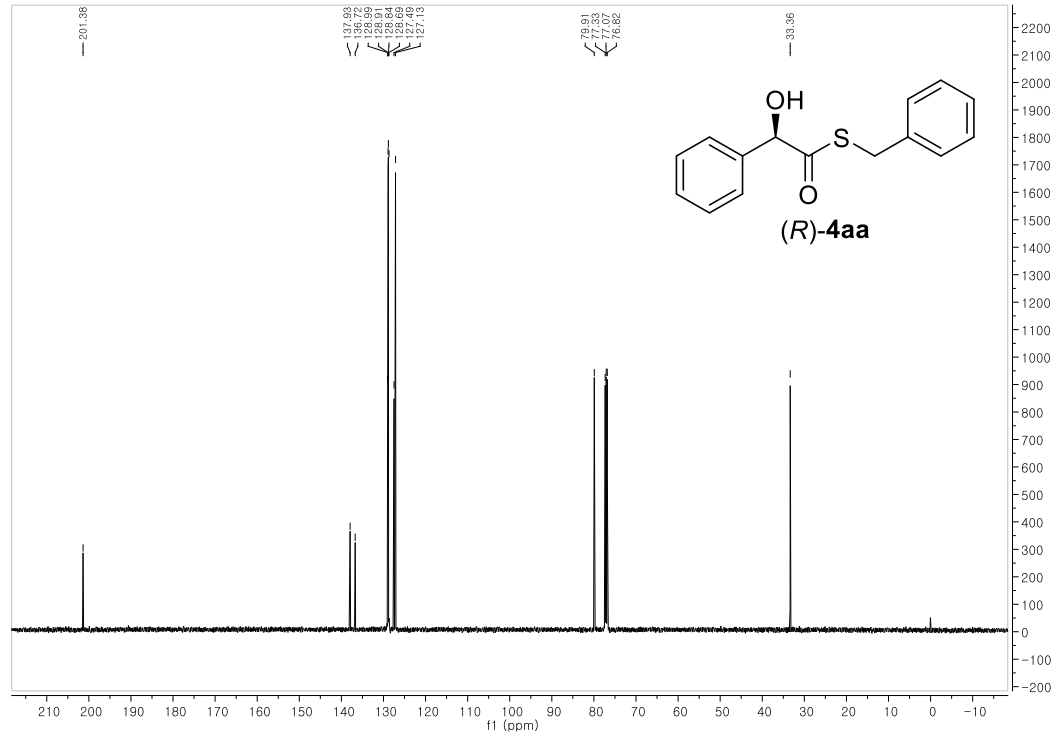


^{13}C NMR spectra of **5b**

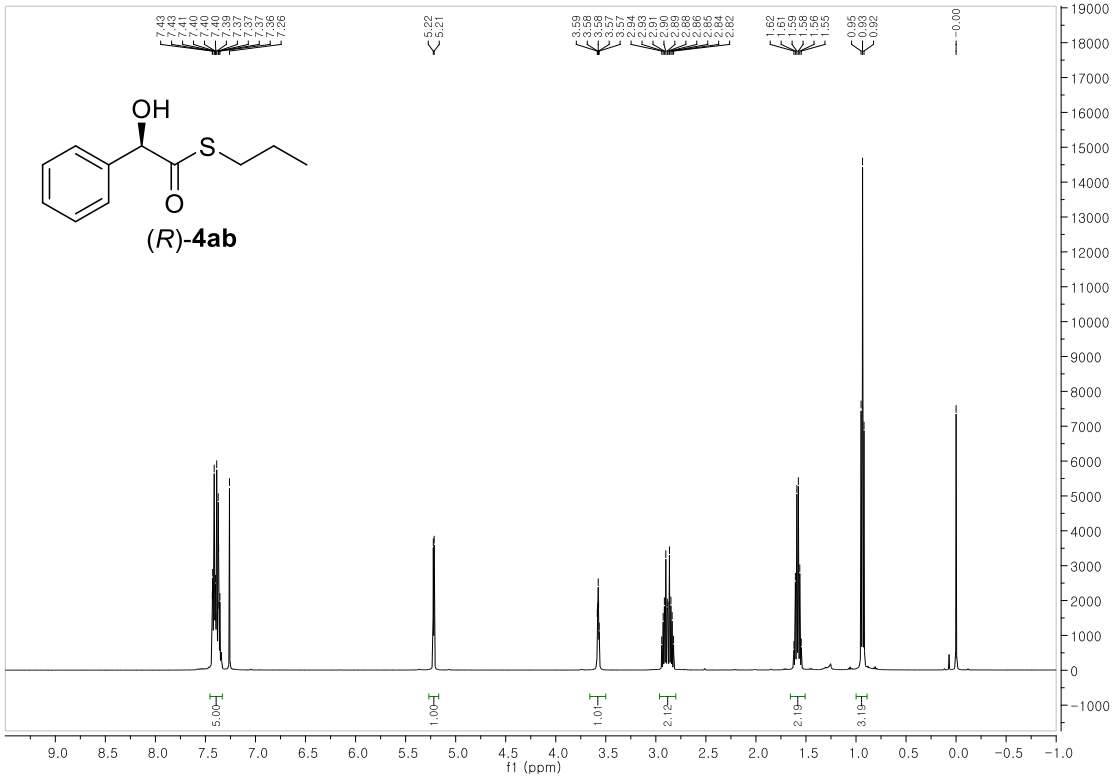
NMR spectra of products **4**



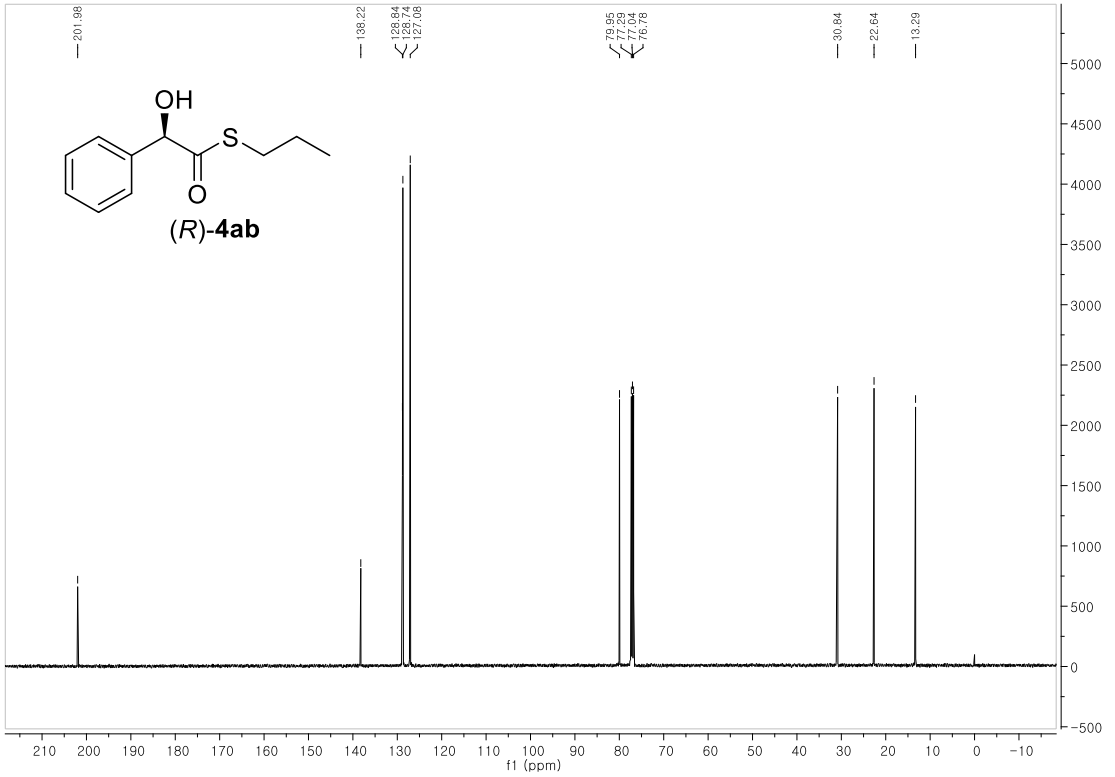
^{1}H NMR spectra of **4aa**



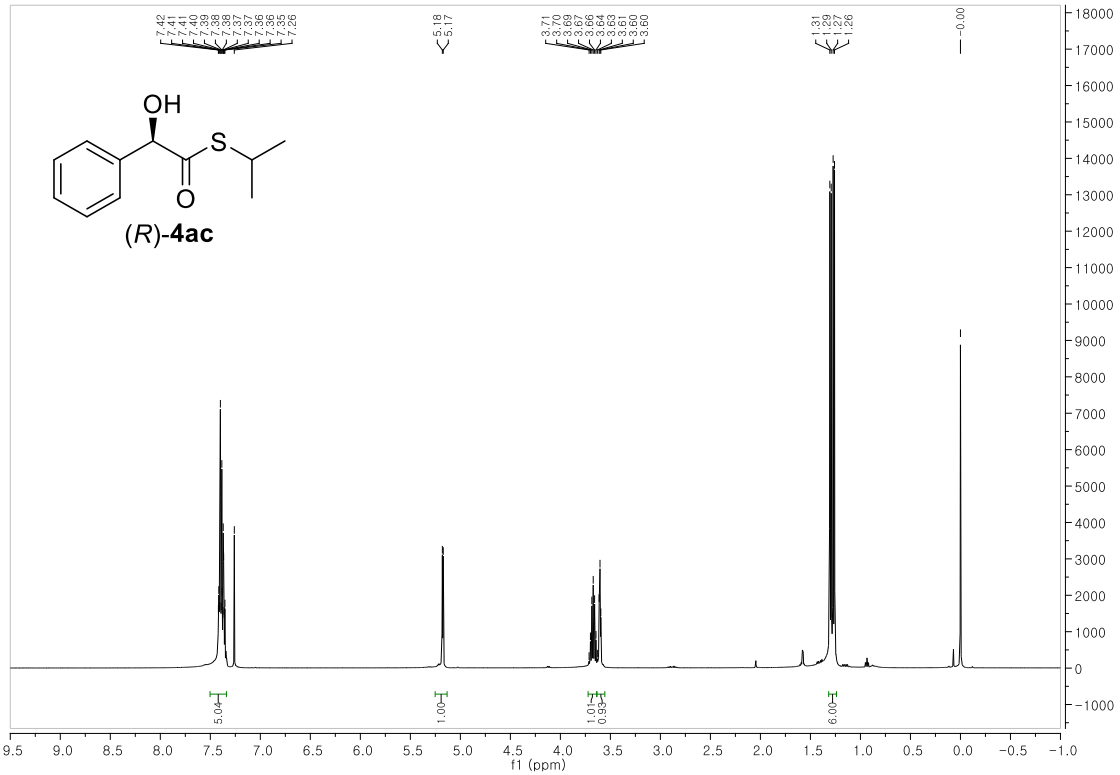
^{13}C NMR spectra of **4aa**



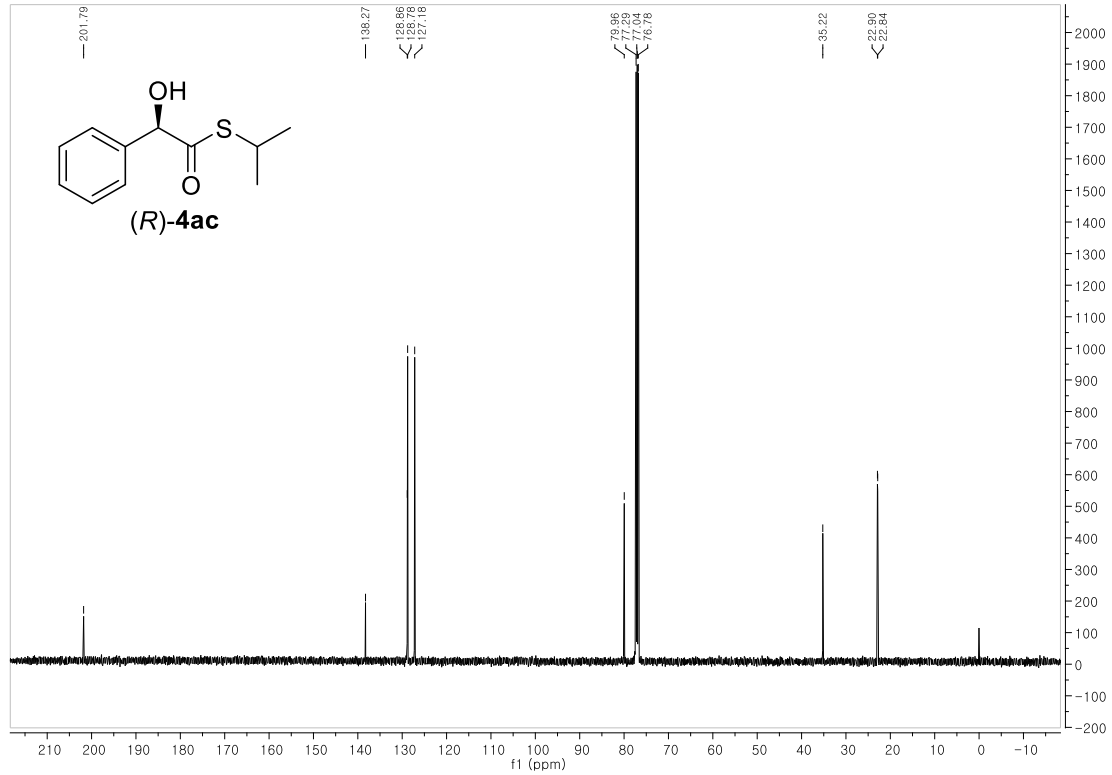
^{1}H NMR spectra of **4ab**



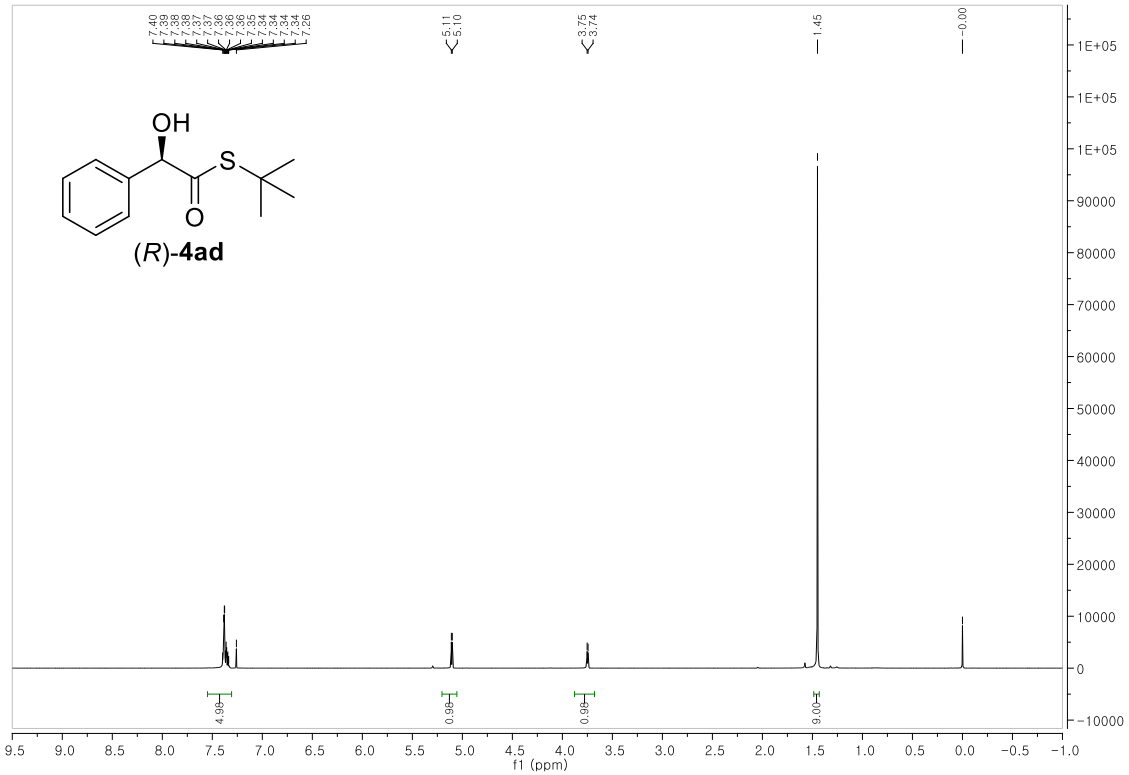
^{13}C NMR spectra of **4ab**



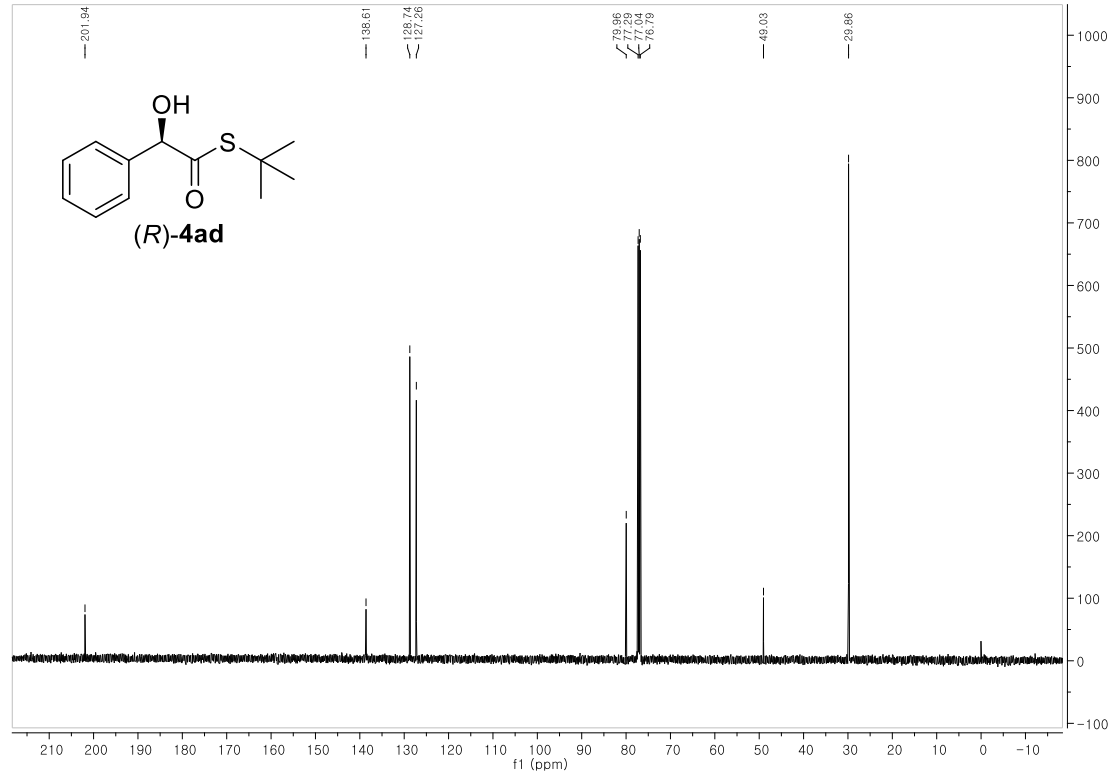
^{1}H NMR spectra of **4ac**



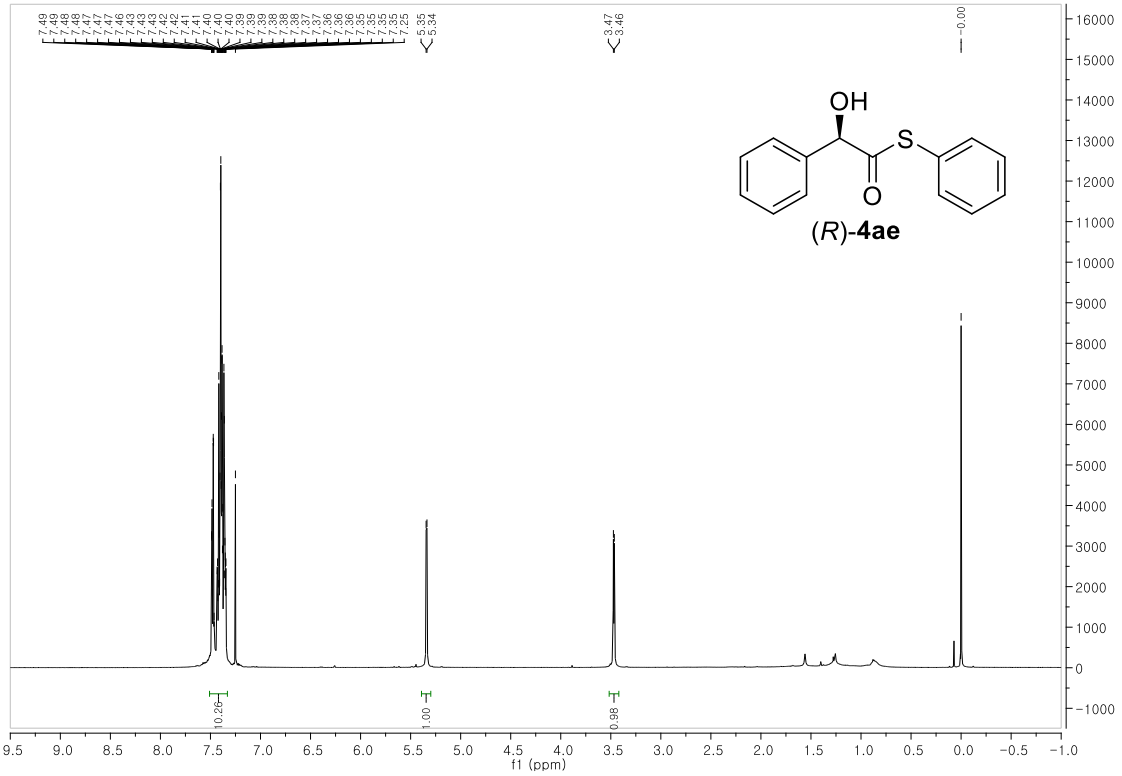
^{13}C NMR spectra of **4ac**



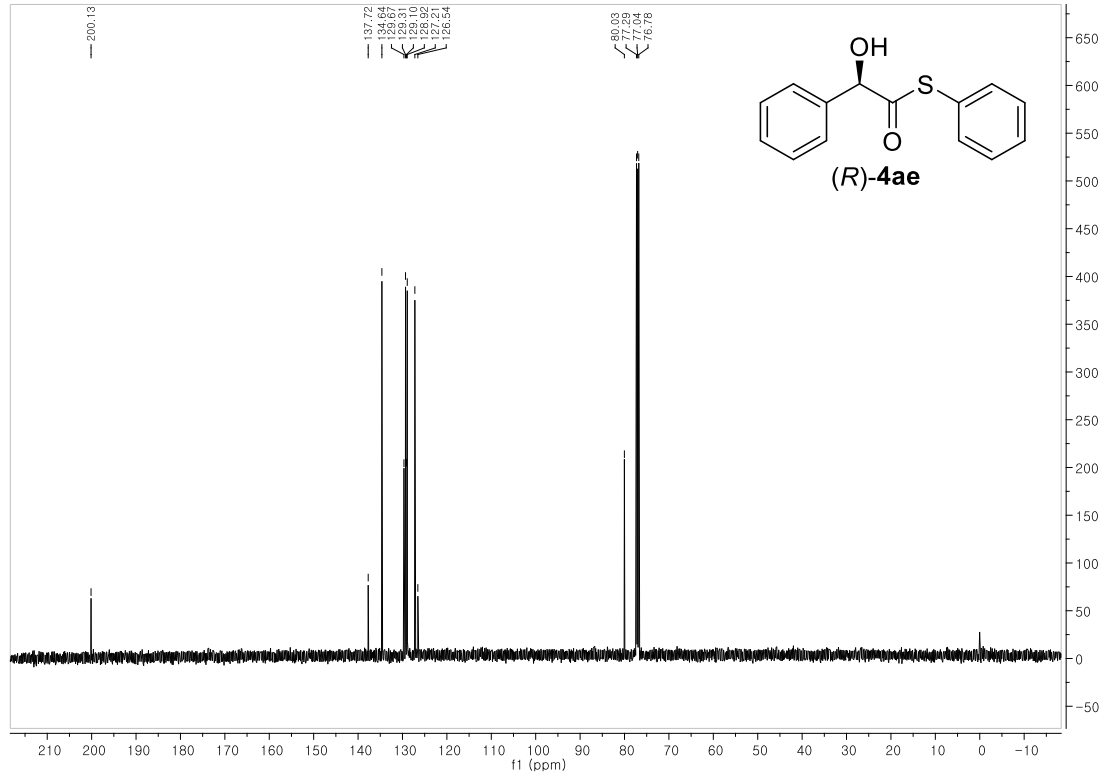
^{1}H NMR spectra of **4ad**



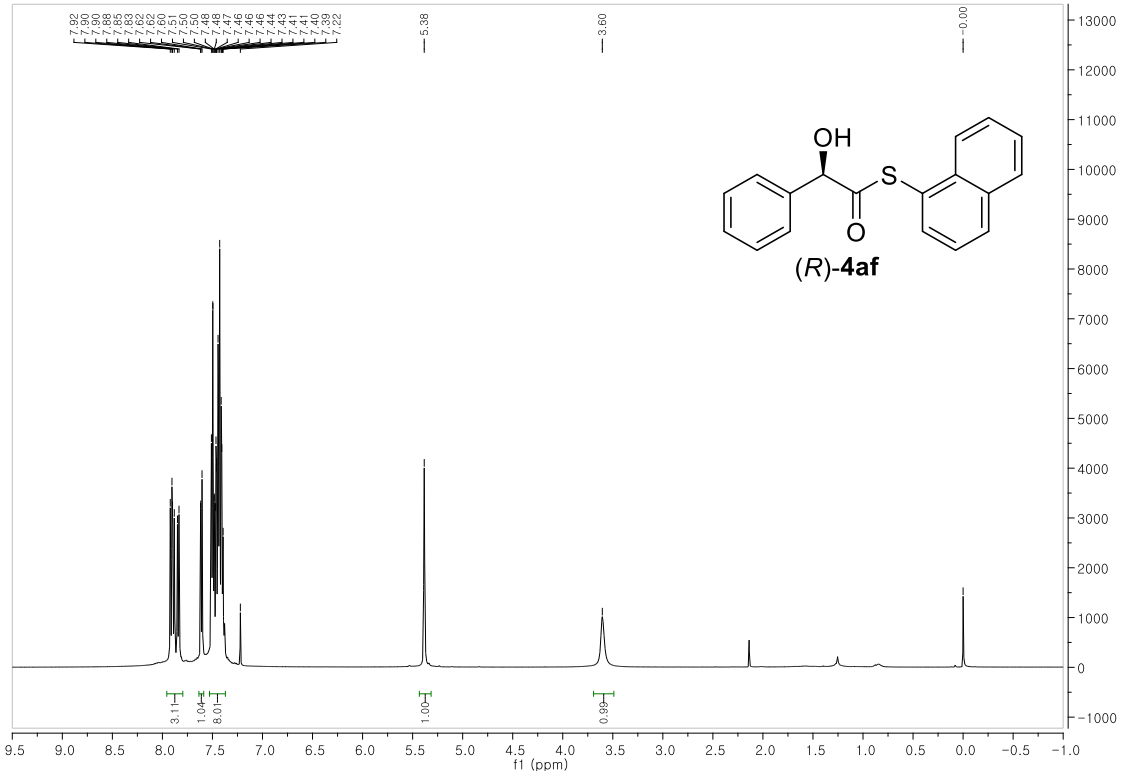
^{13}C NMR spectra of **4ad**



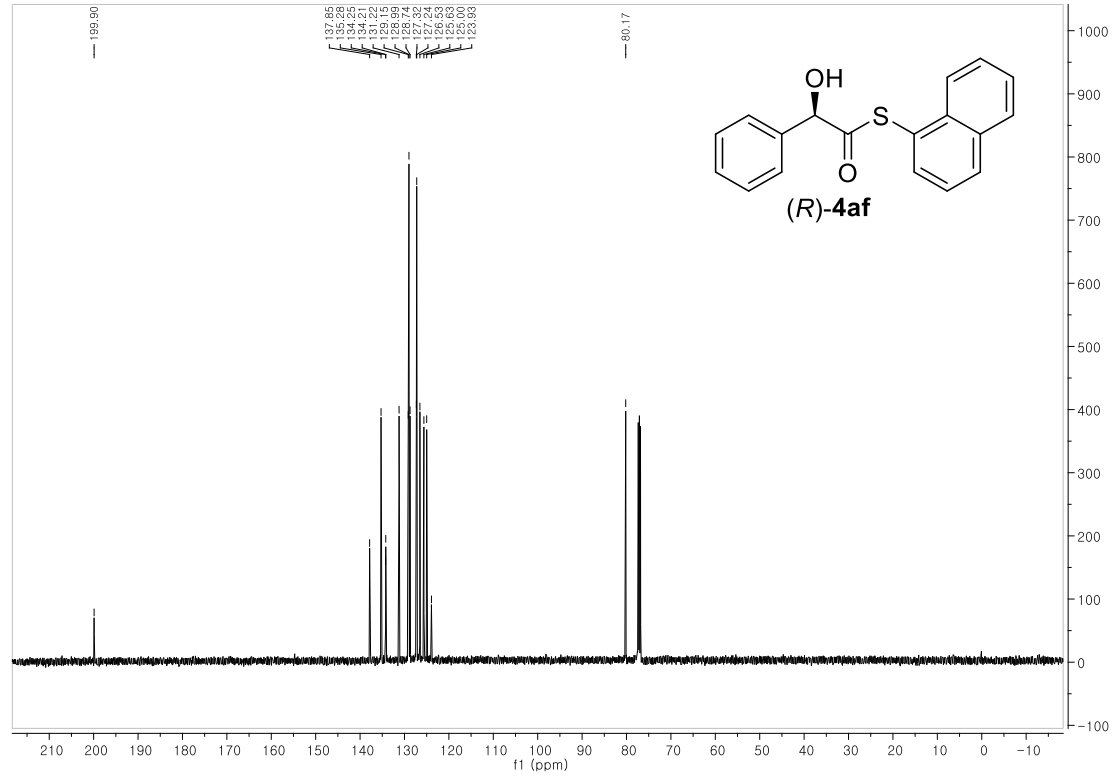
^{1}H NMR spectra of **4ae**



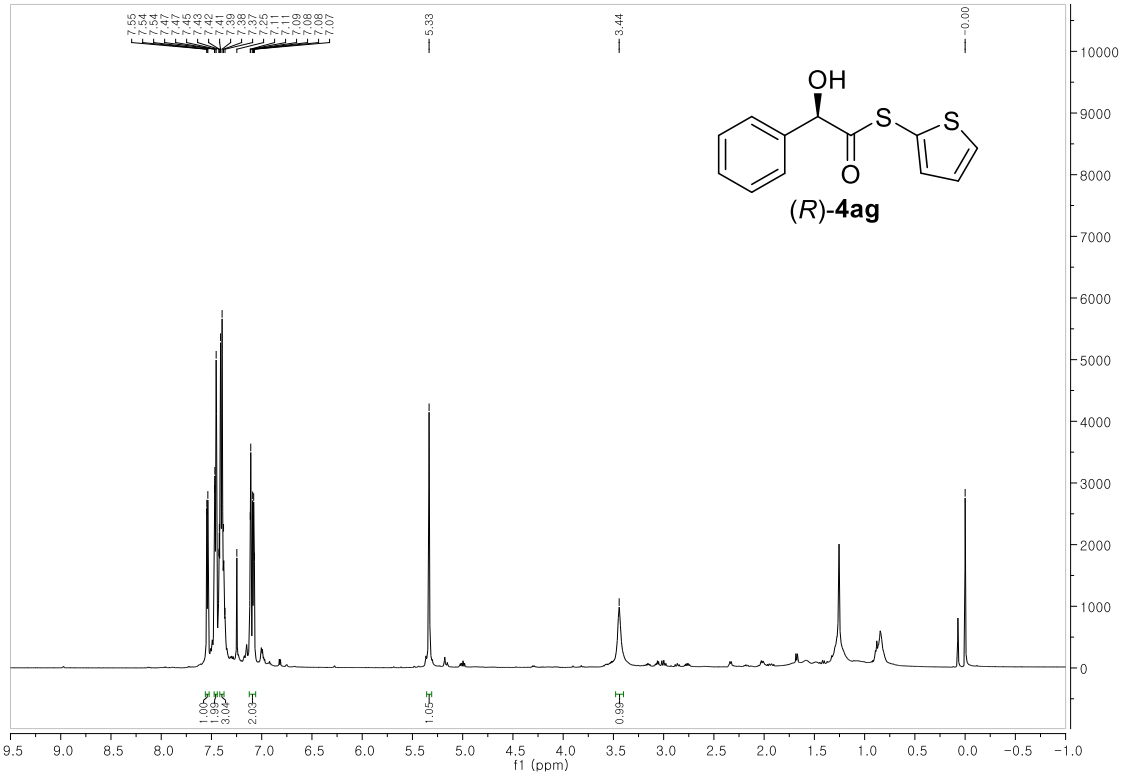
^{13}C NMR spectra of **4ae**



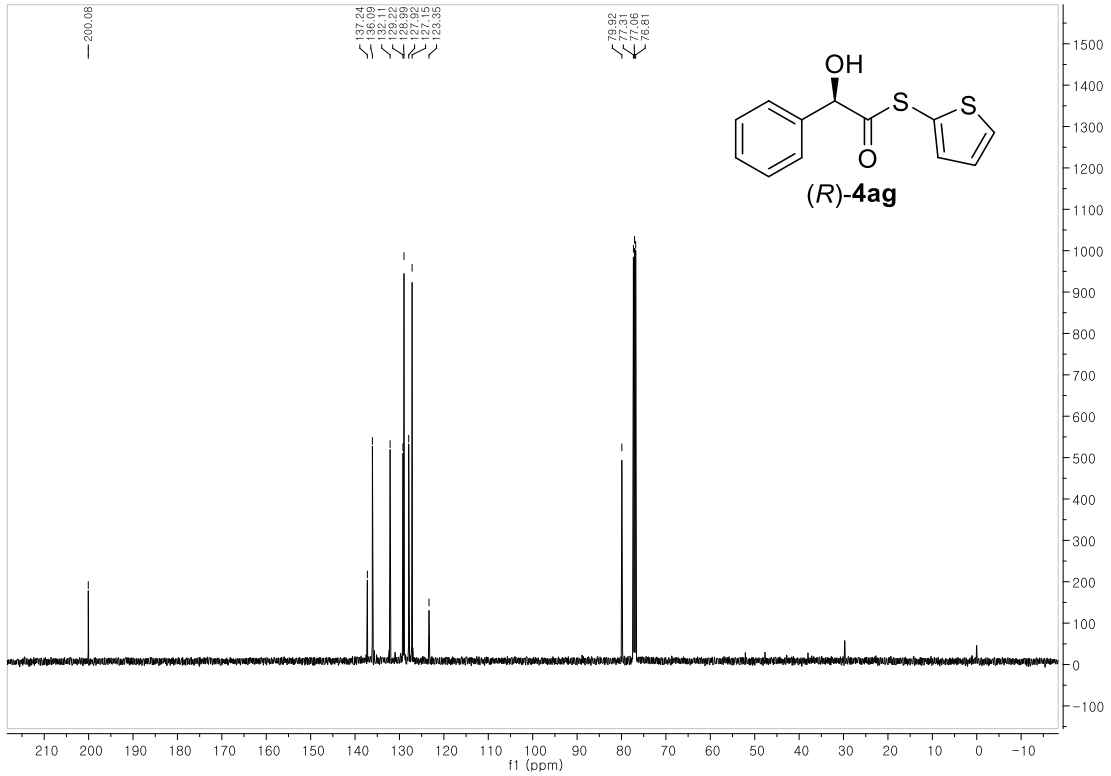
^{1}H NMR spectra of **4af**



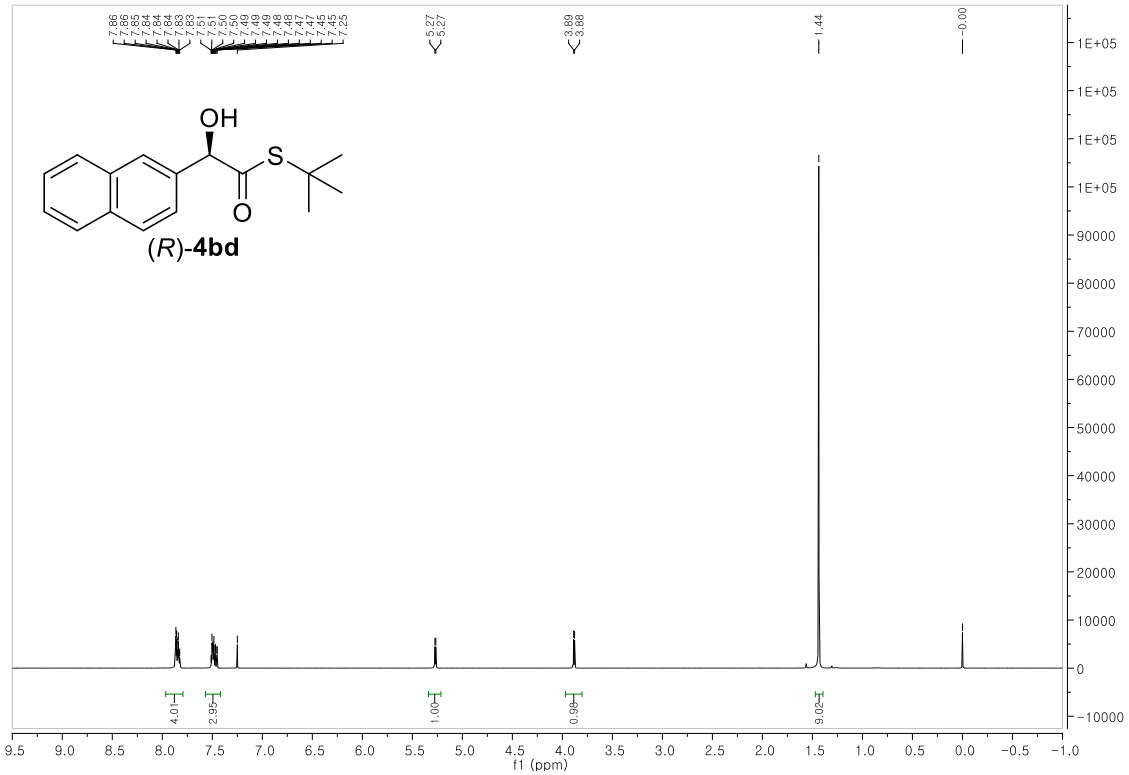
^{13}C NMR spectra of **4af**



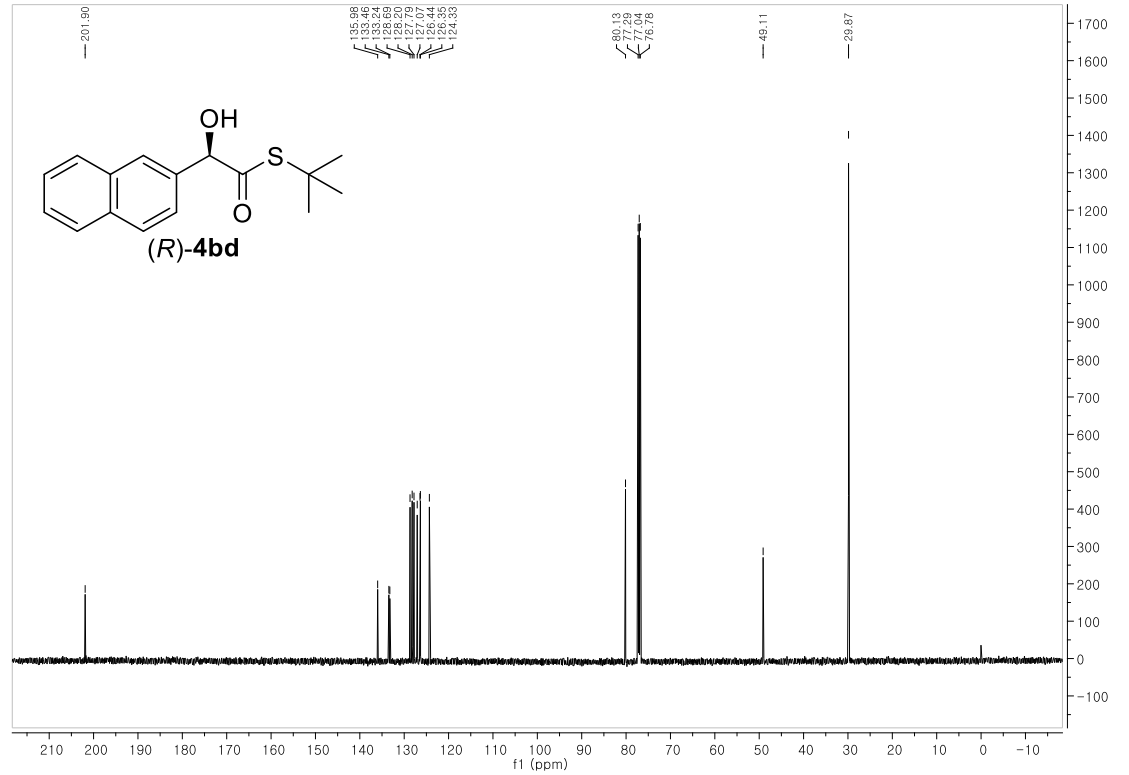
^{1}H NMR spectra of **4ag**



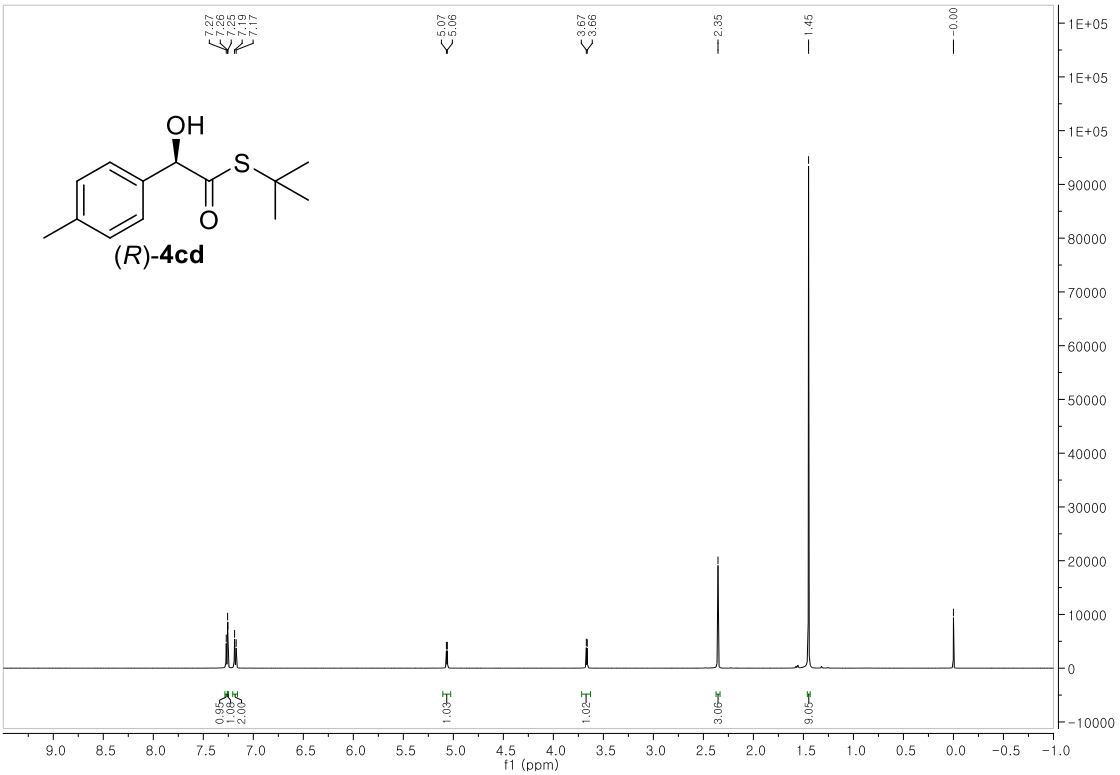
^{13}C NMR spectra of **4ag**



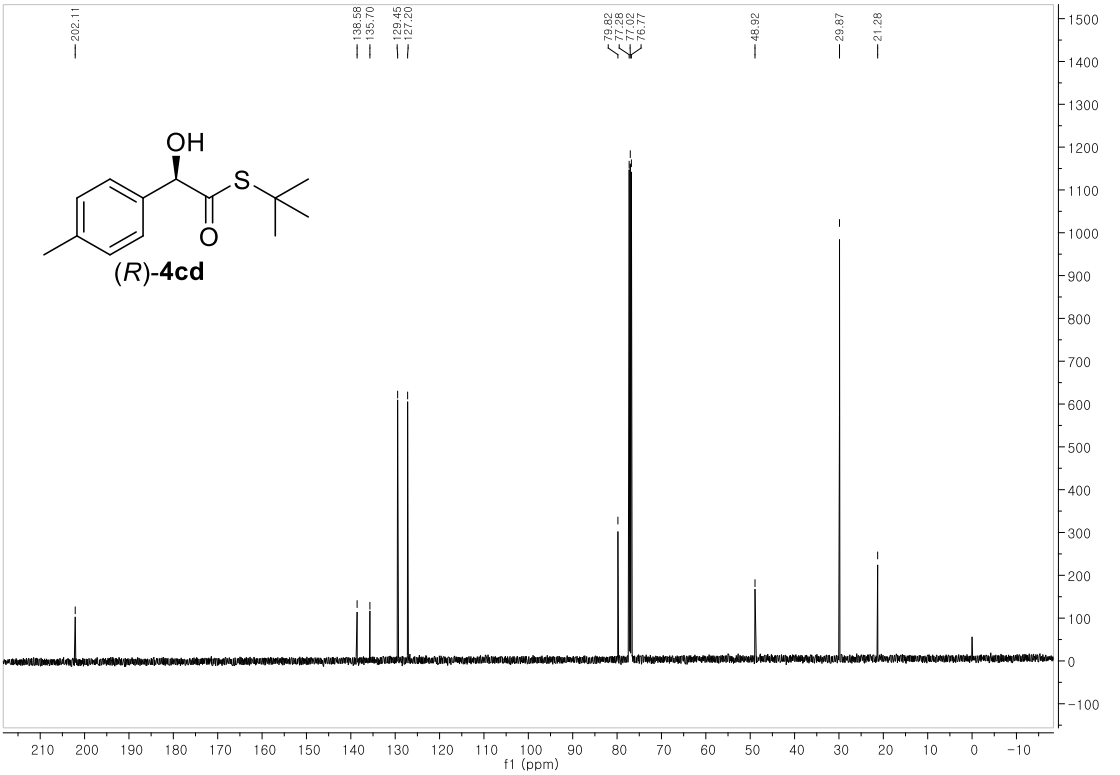
^{1}H NMR spectra of **4bd**



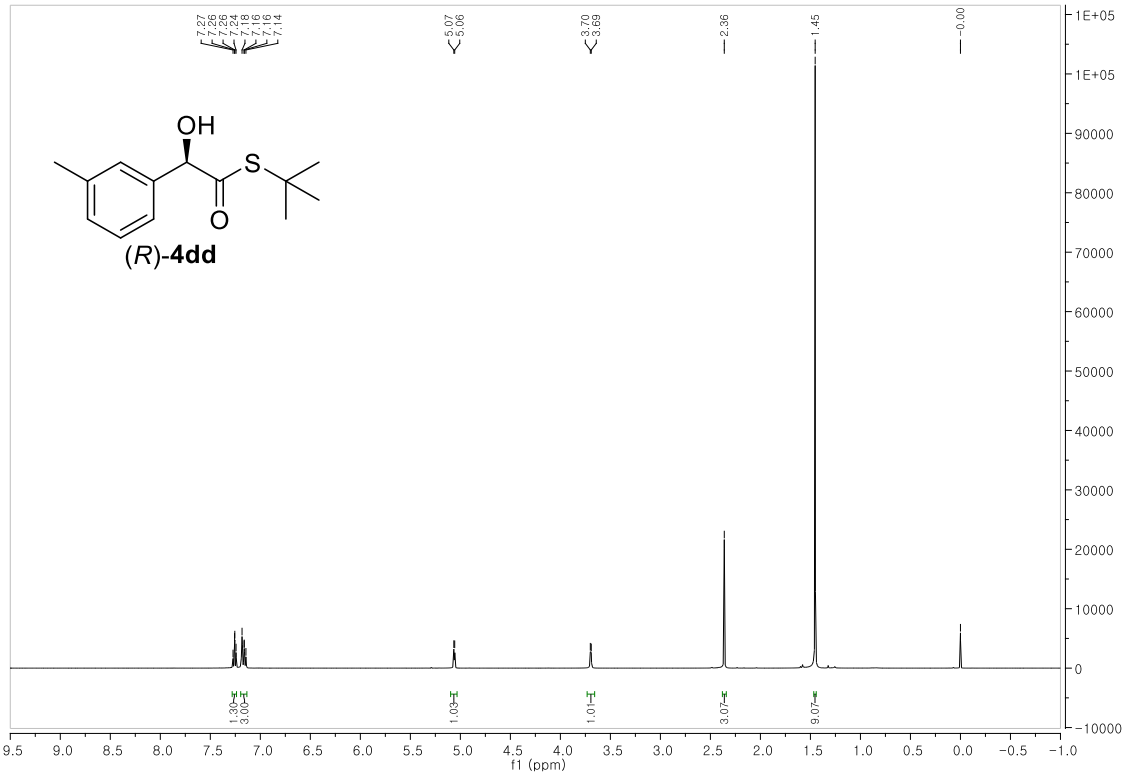
^{13}C NMR spectra of **4bd**



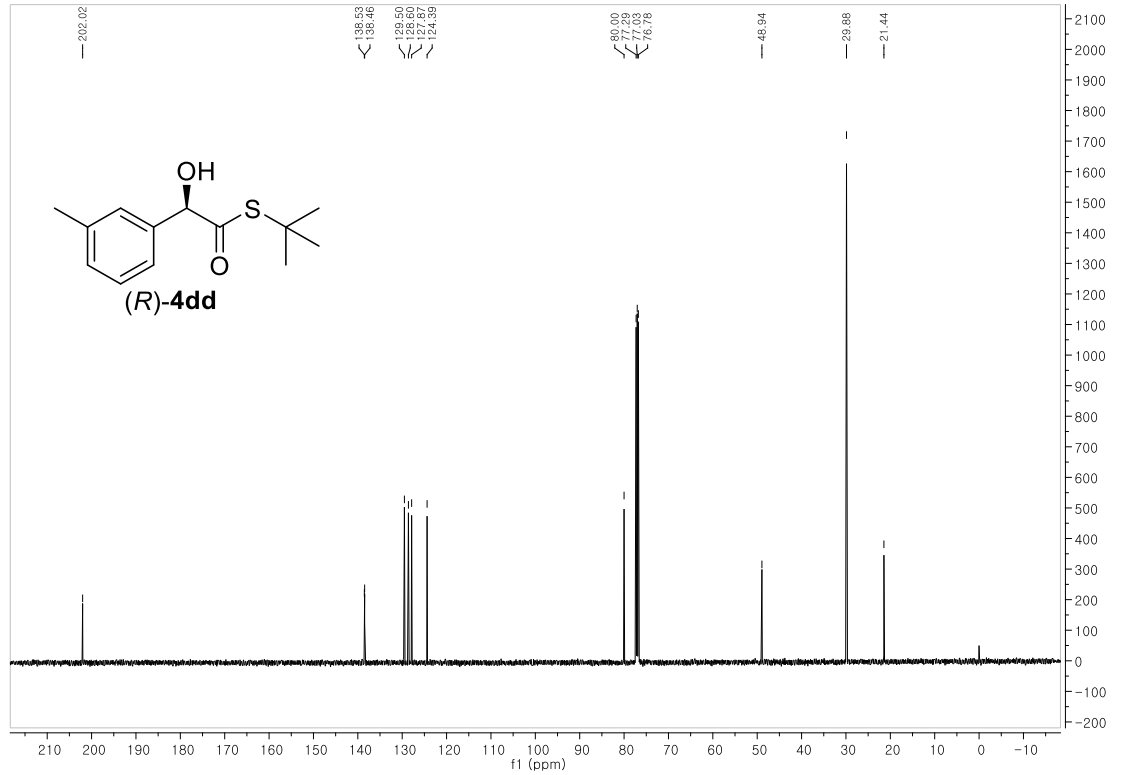
^{1}H NMR spectra of **4cd**



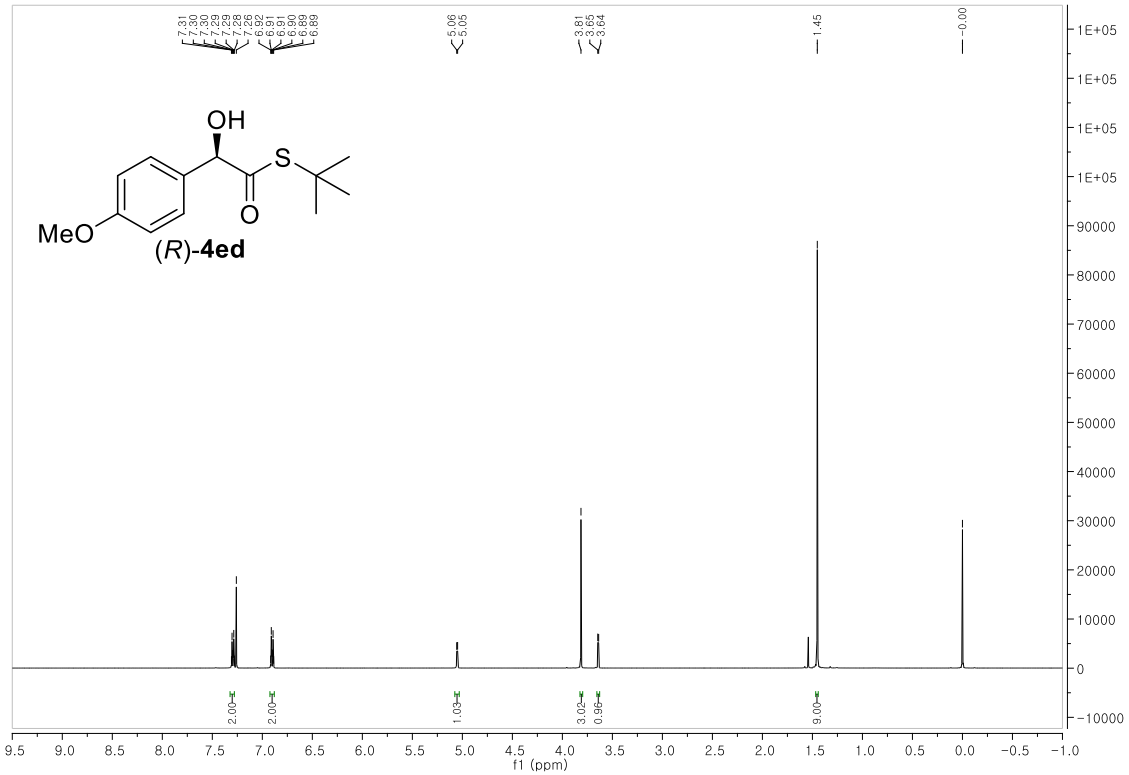
^{13}C NMR spectra of **4cd**



^{1}H NMR spectra of **4dd**



^{13}C NMR spectra of **4dd**



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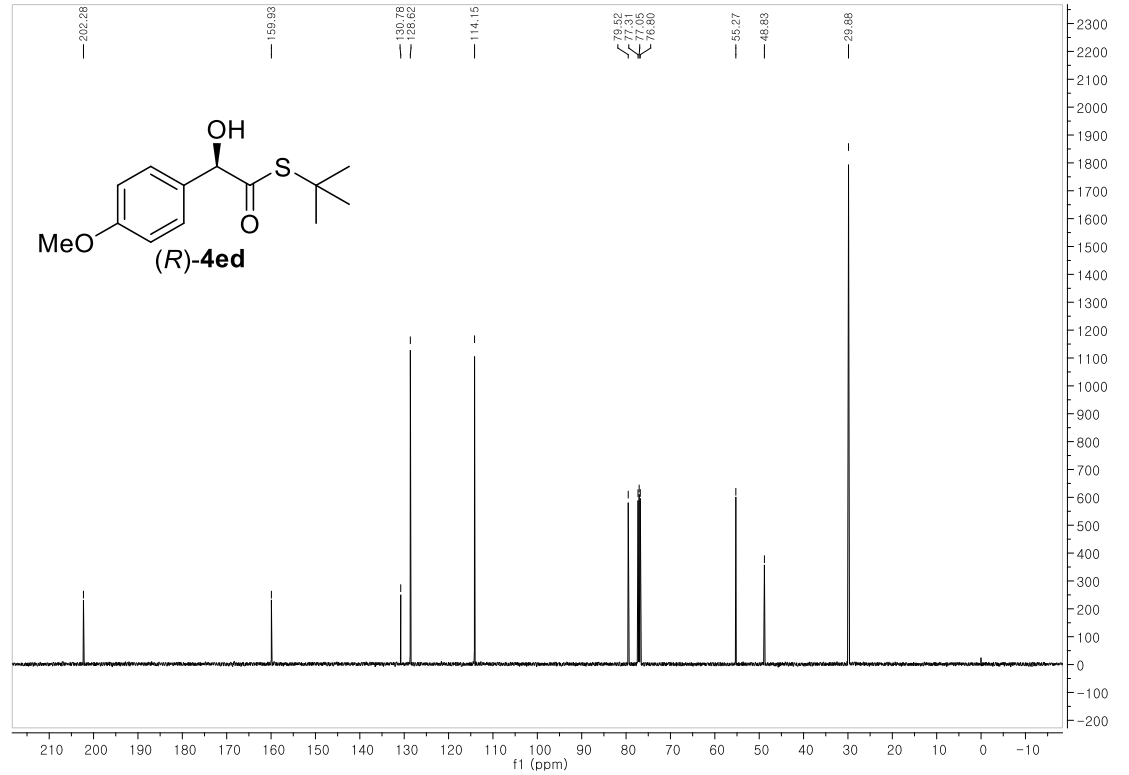

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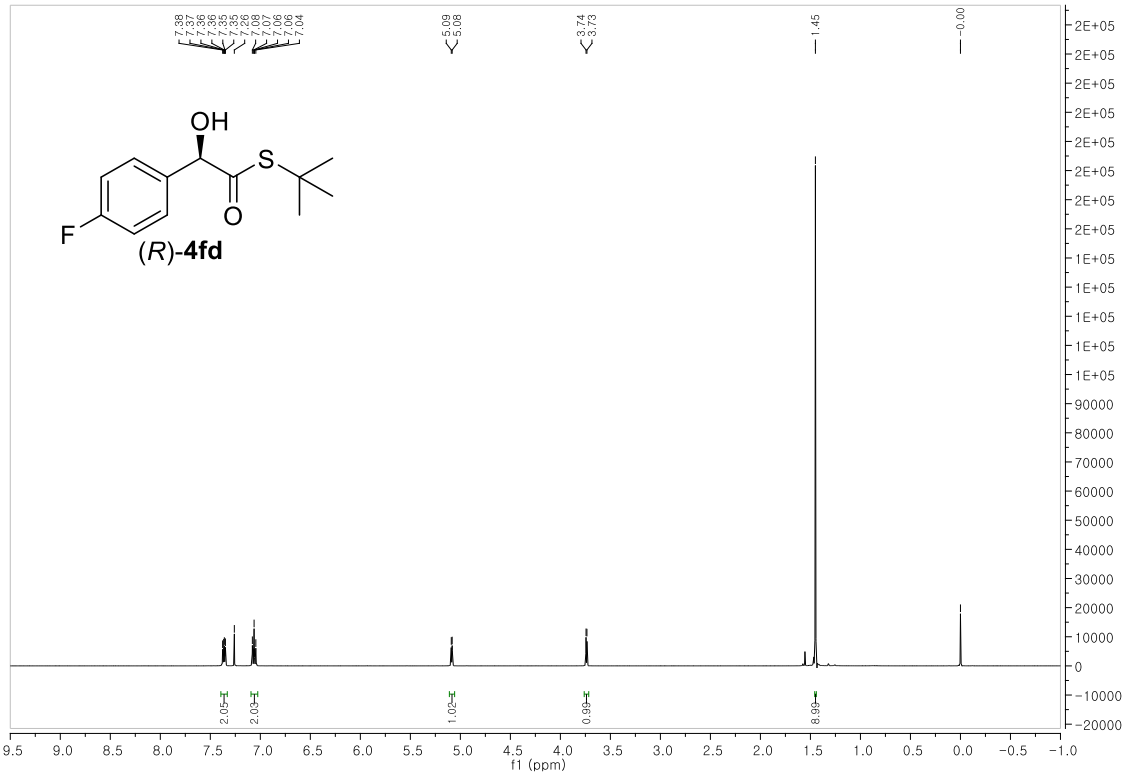
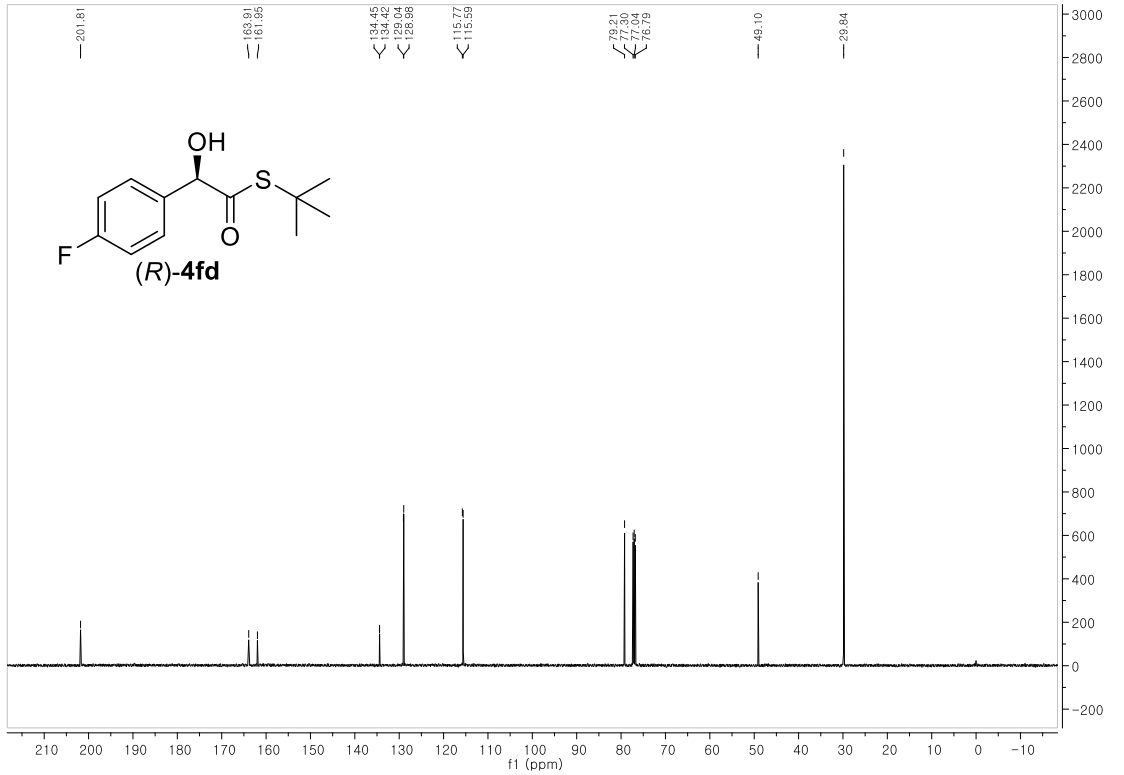
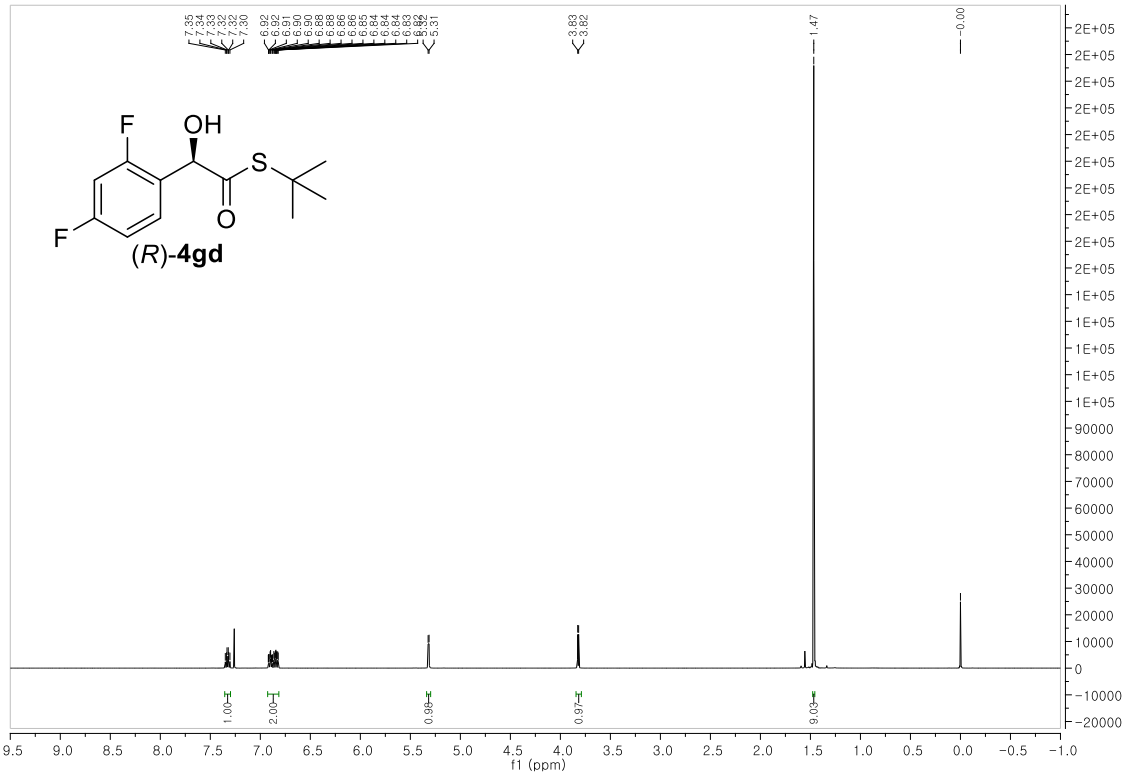


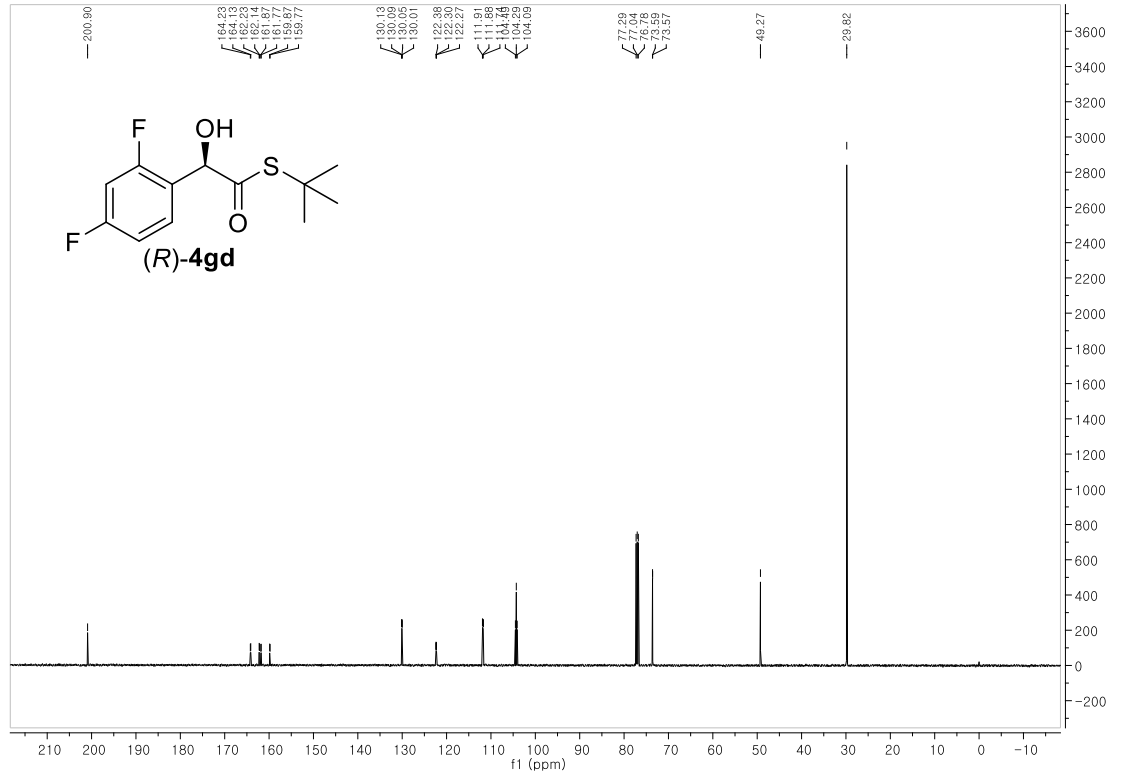
^{1}H NMR spectra of **4fd**



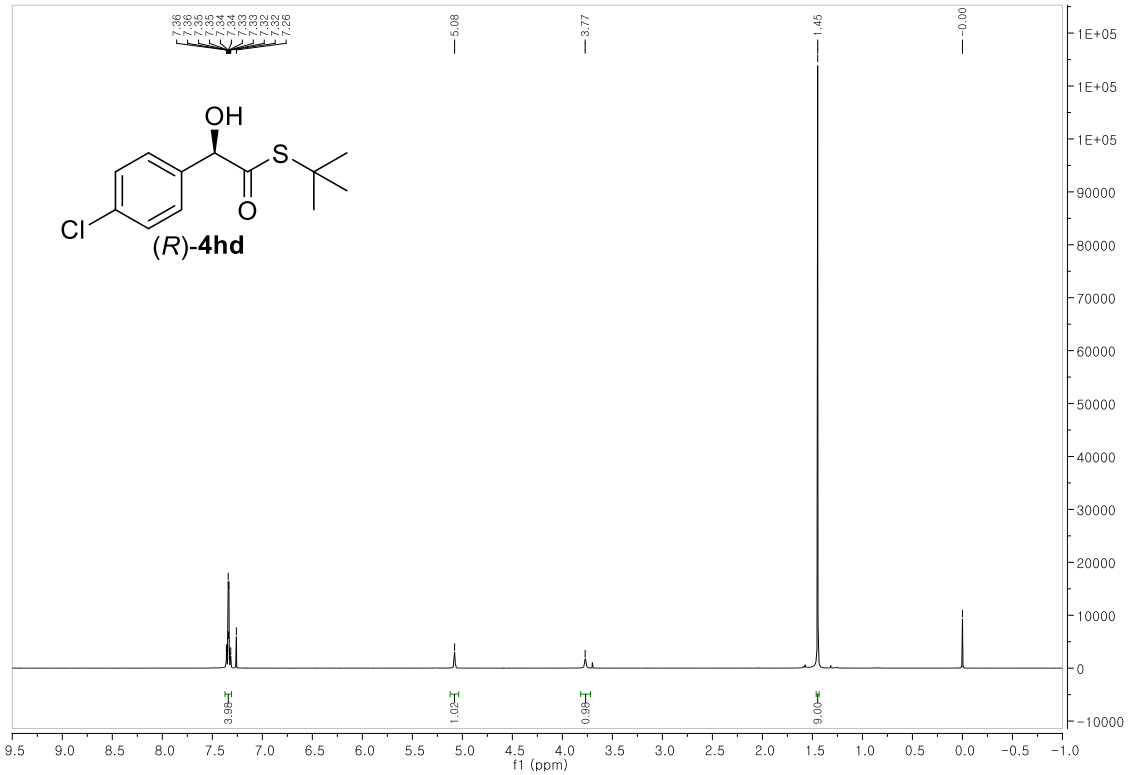
^{13}C NMR spectra of **4fd**



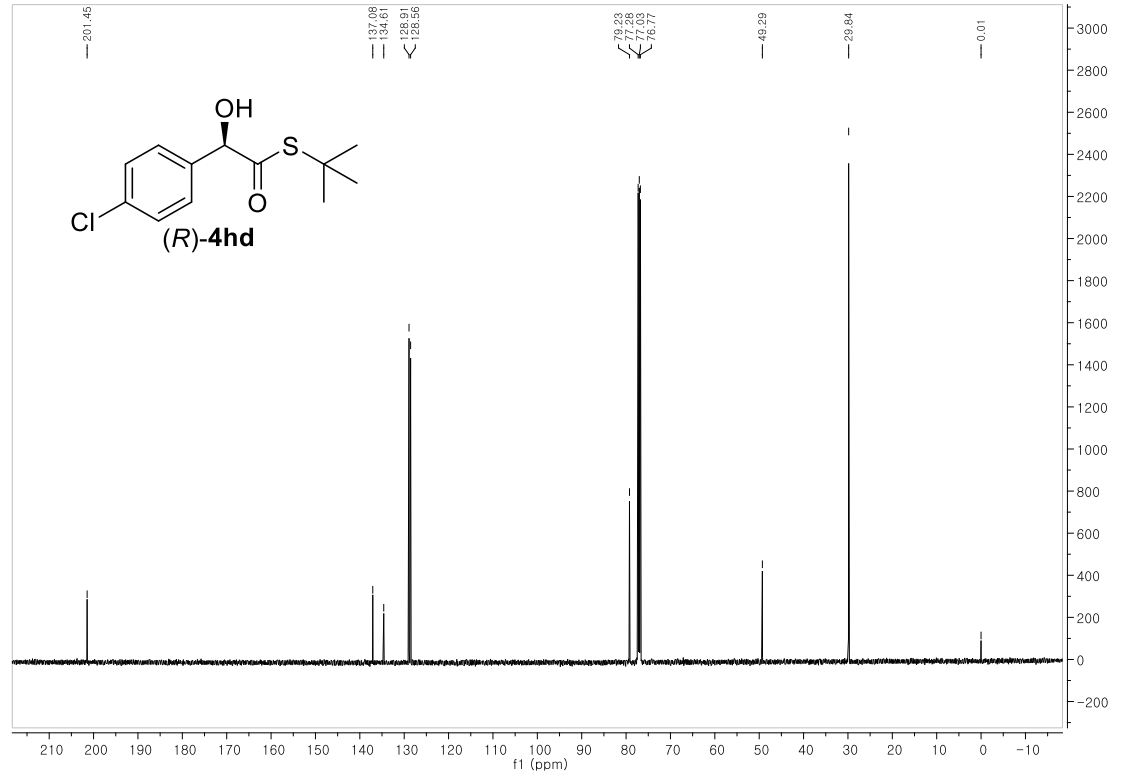
^{1}H NMR spectra of **4gd**



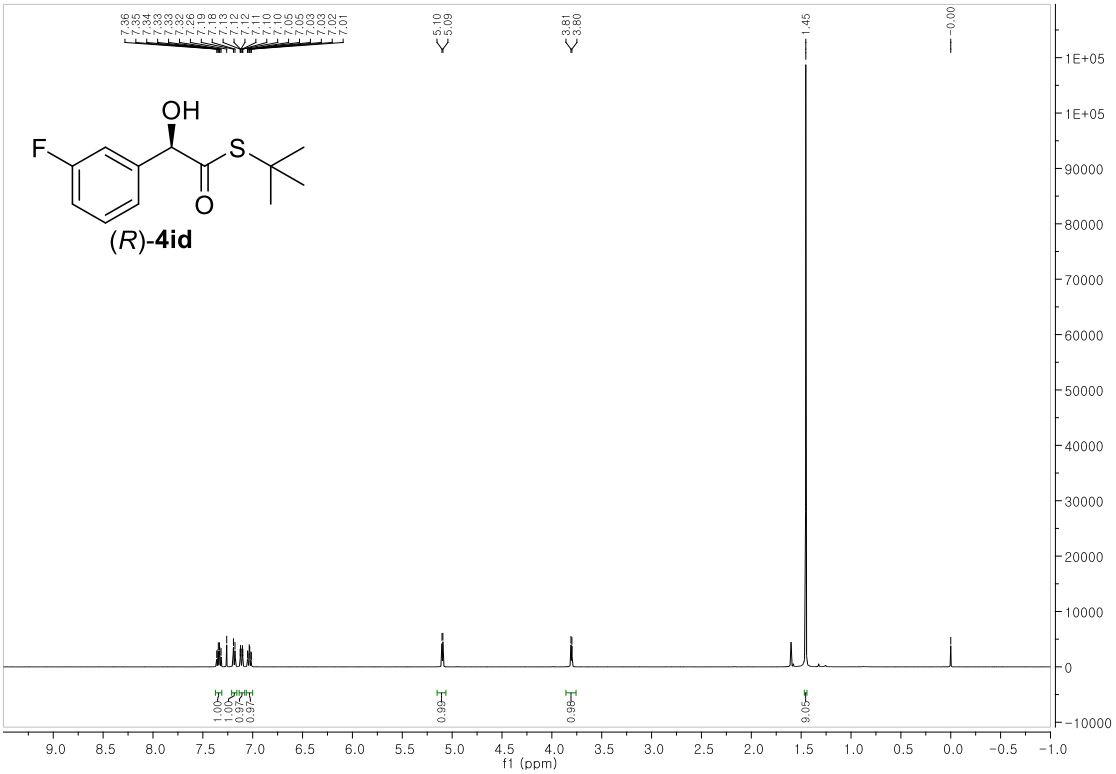
^{13}C NMR spectra of **4gd**



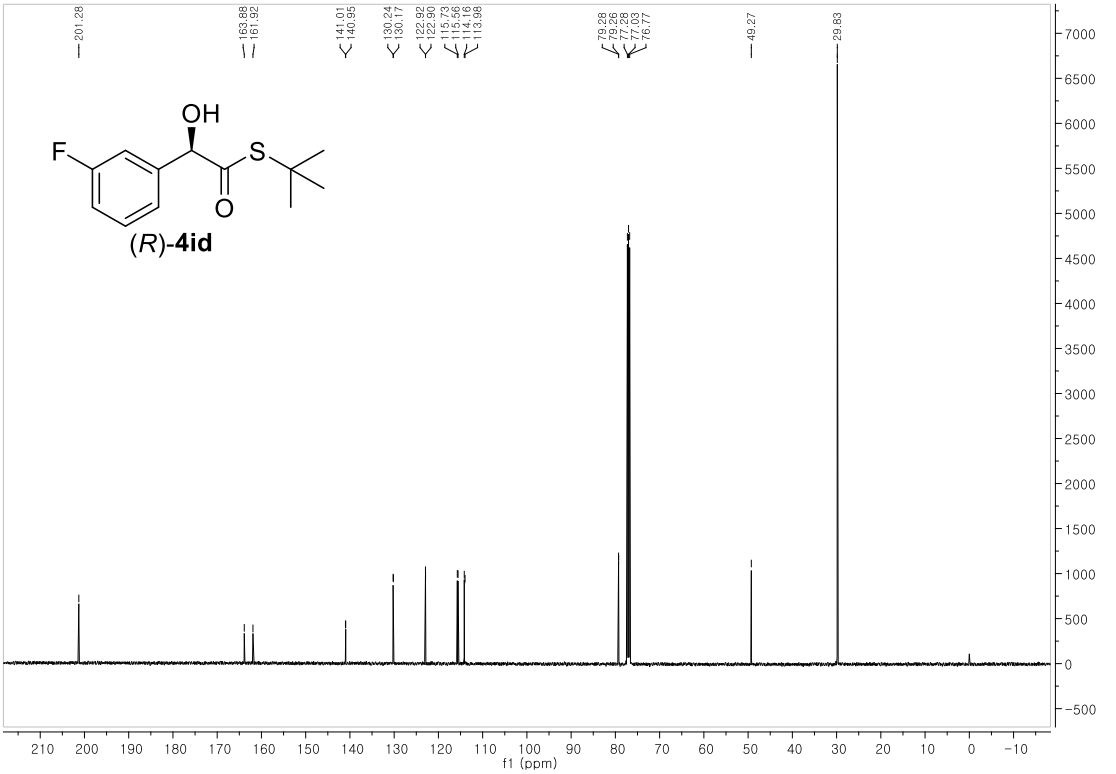
^{1}H NMR spectra of **4hd**



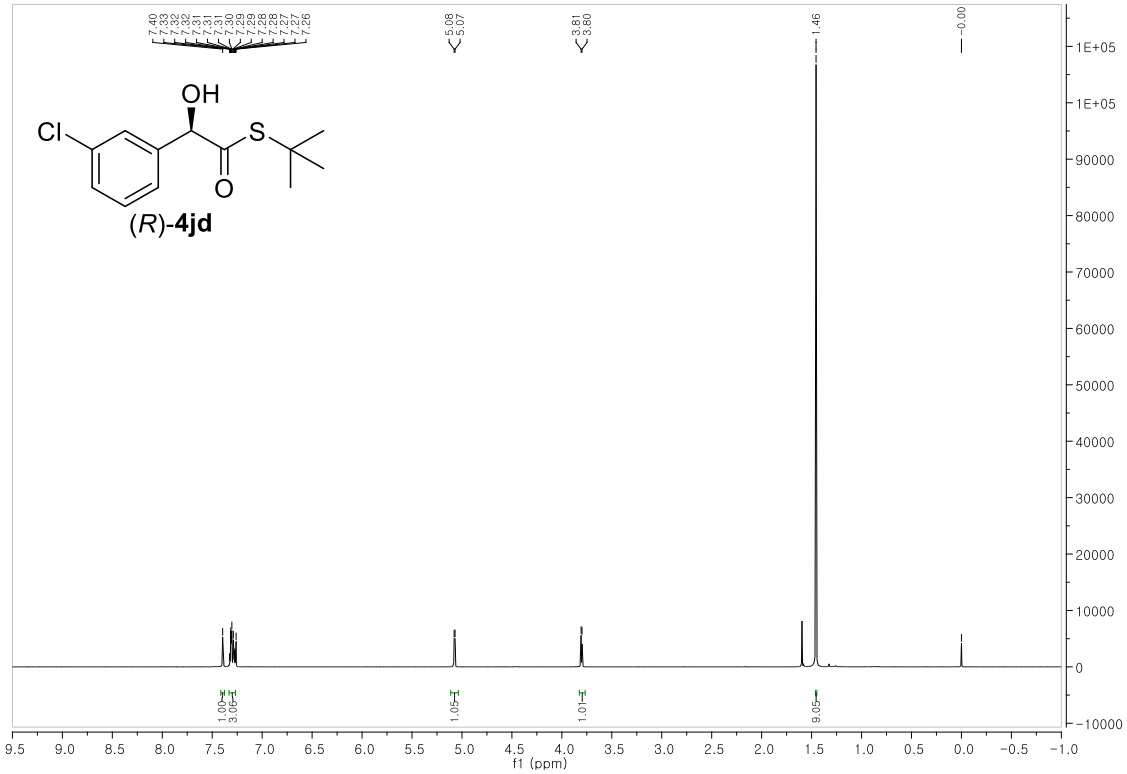
^{13}C NMR spectra of **4hd**



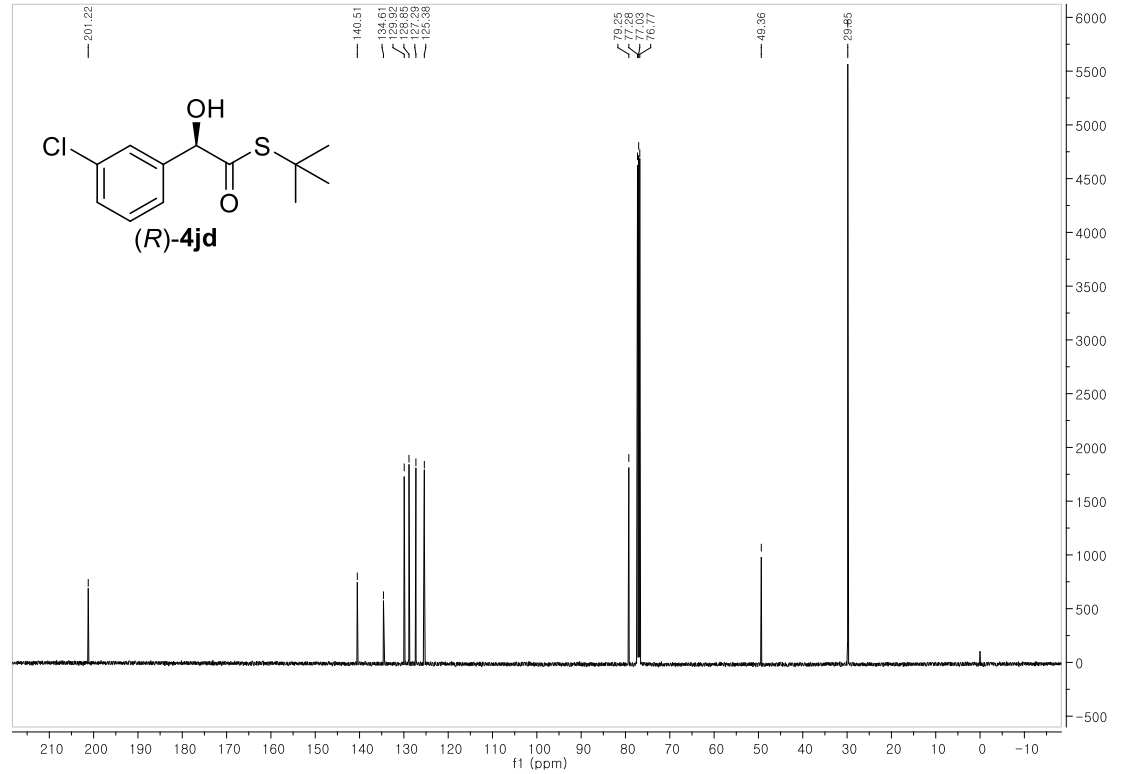
^{1}H NMR spectra of **4id**



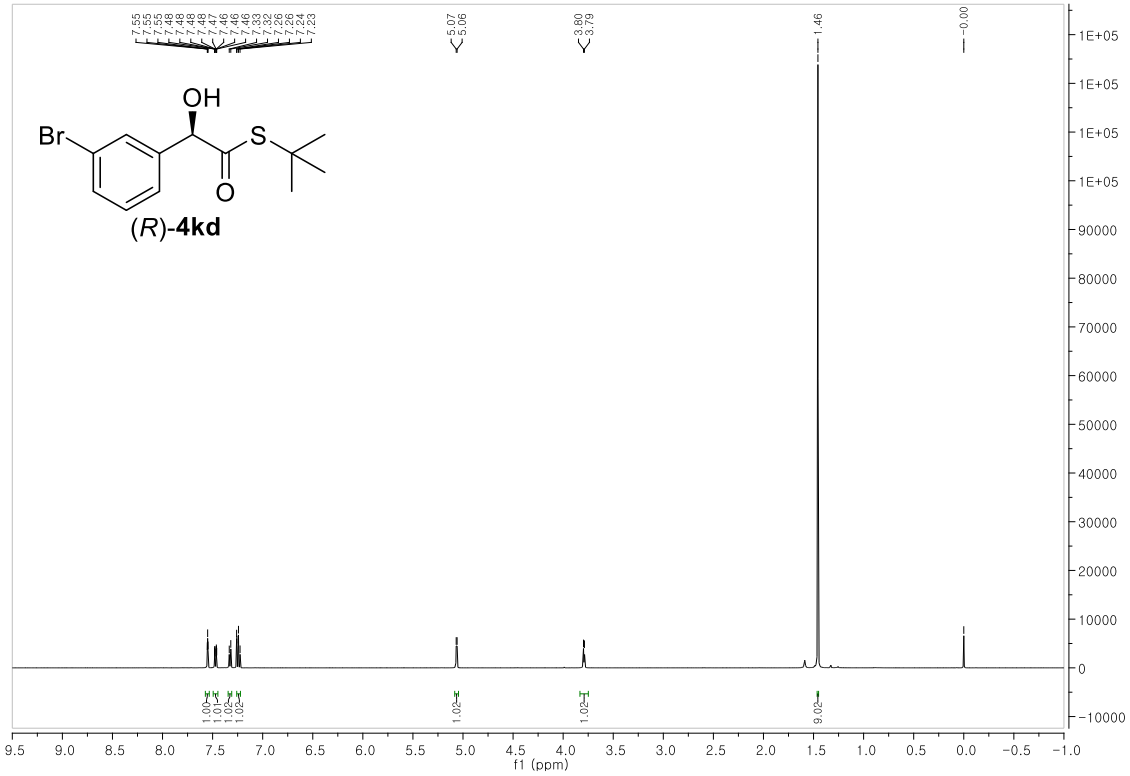
^{13}C NMR spectra of **4id**



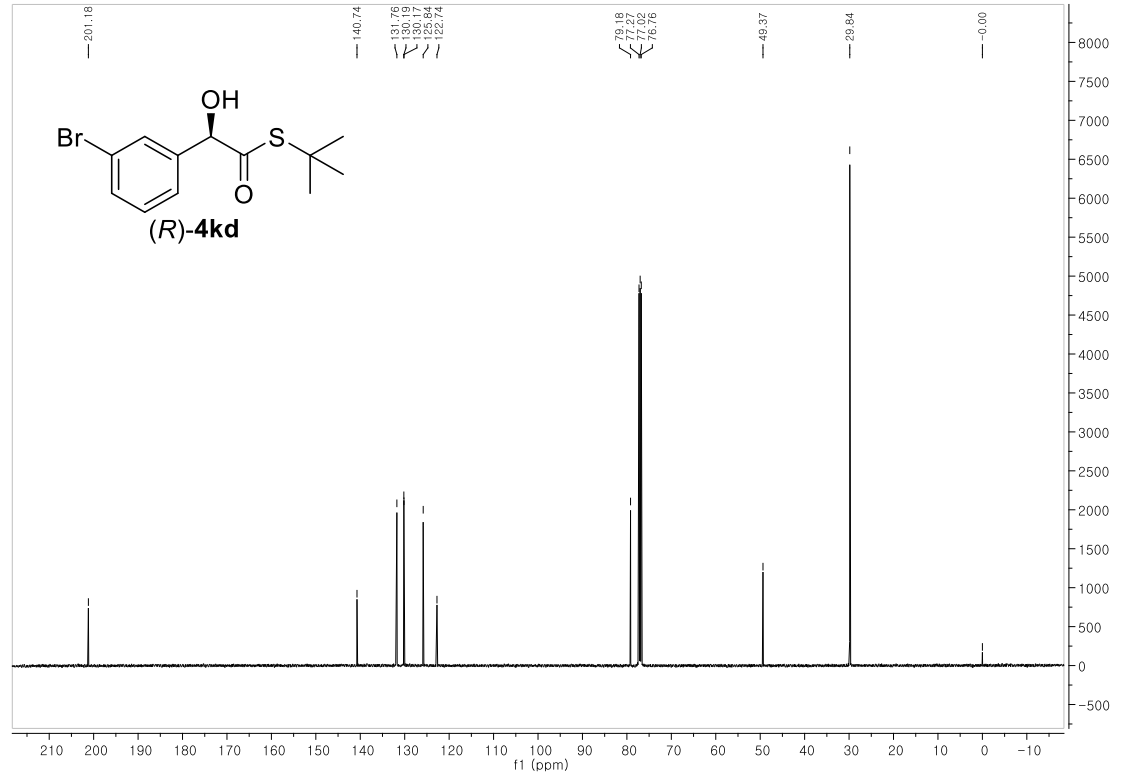
^{1}H NMR spectra of **4jd**



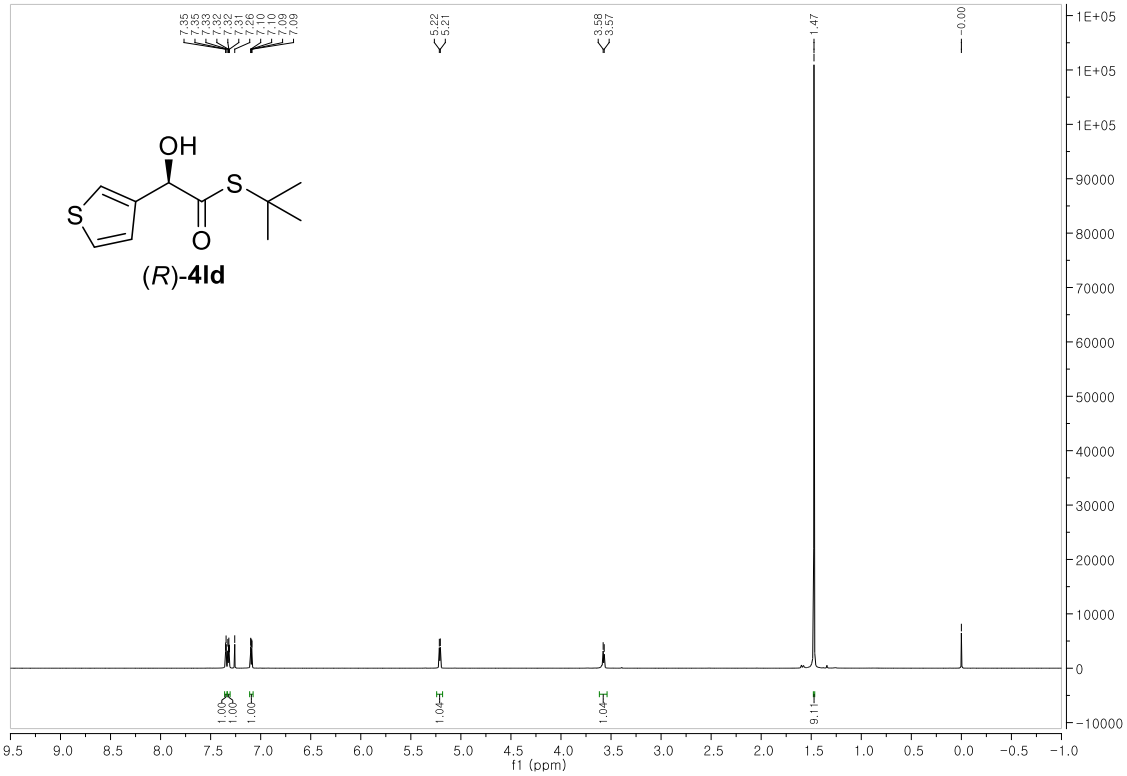
^{13}C NMR spectra of **4jd**



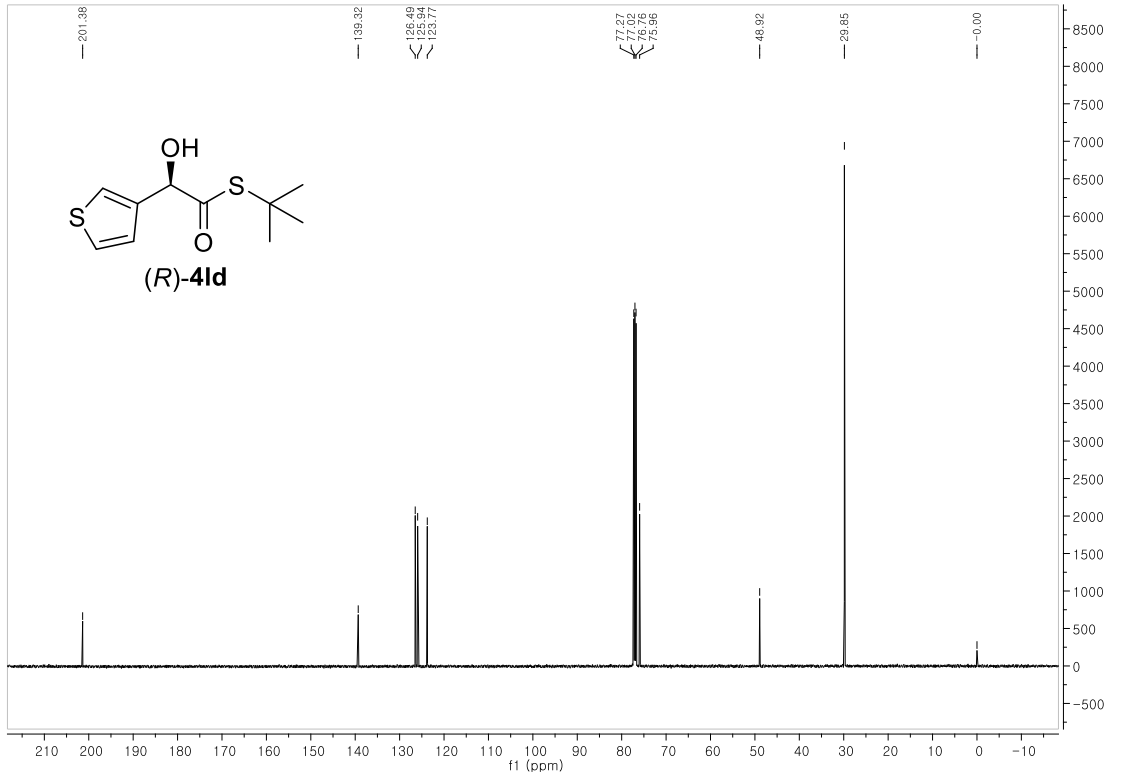
^{1}H NMR spectra of **4kd**



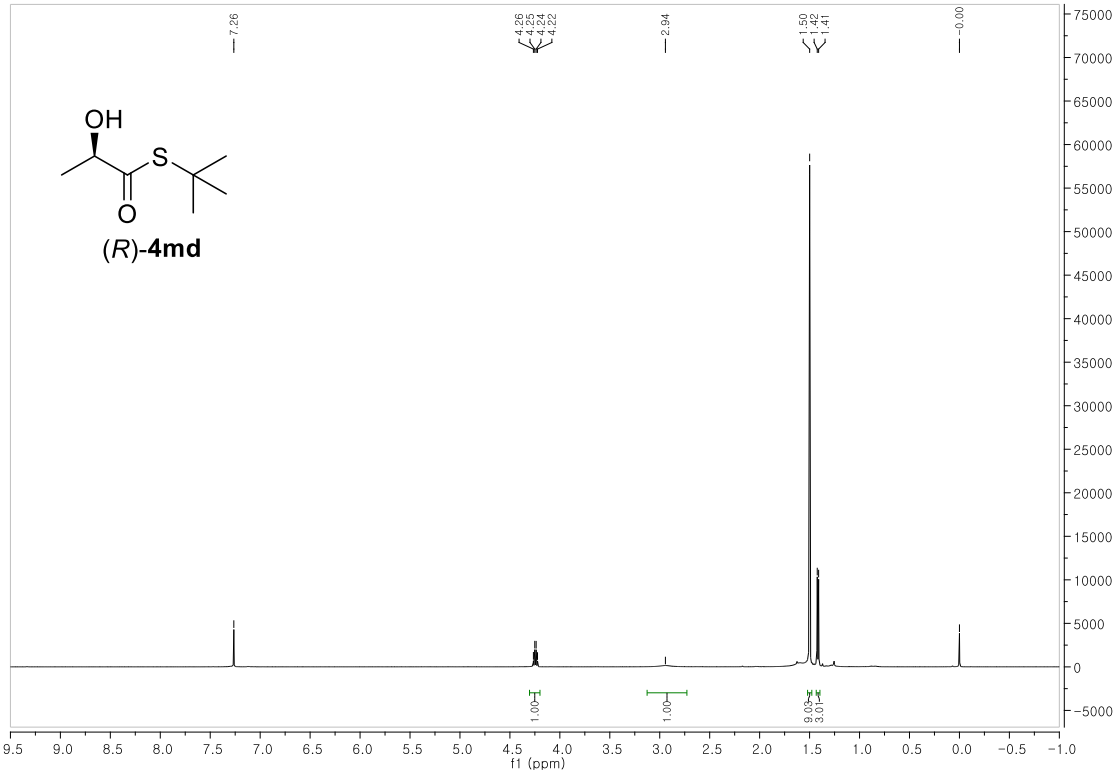
^{13}C NMR spectra of **4kd**



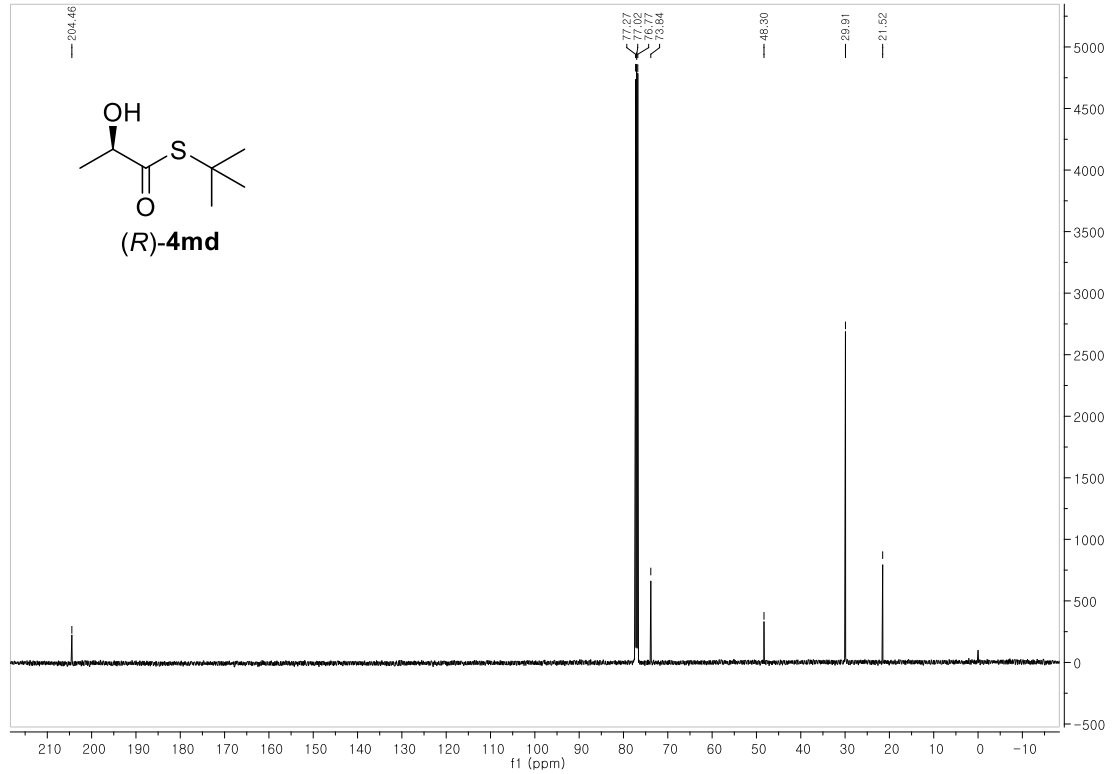
^{1}H NMR spectra of **4ld**



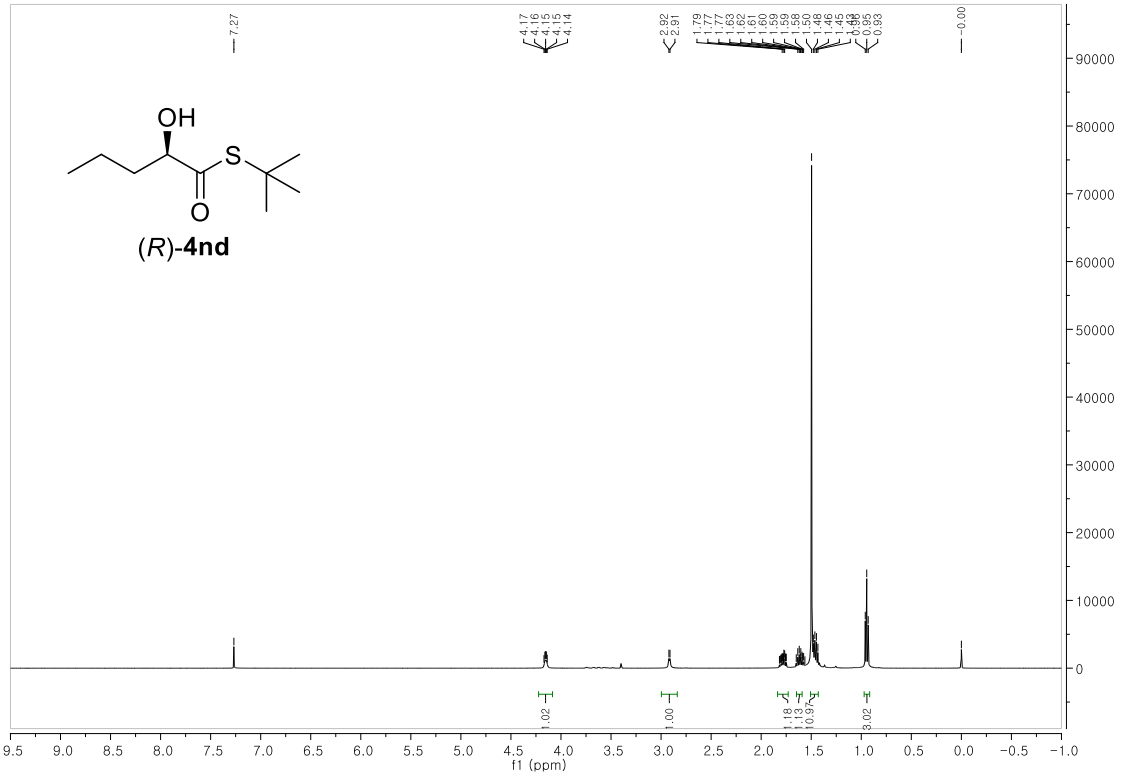
^{13}C NMR spectra of **4ld**



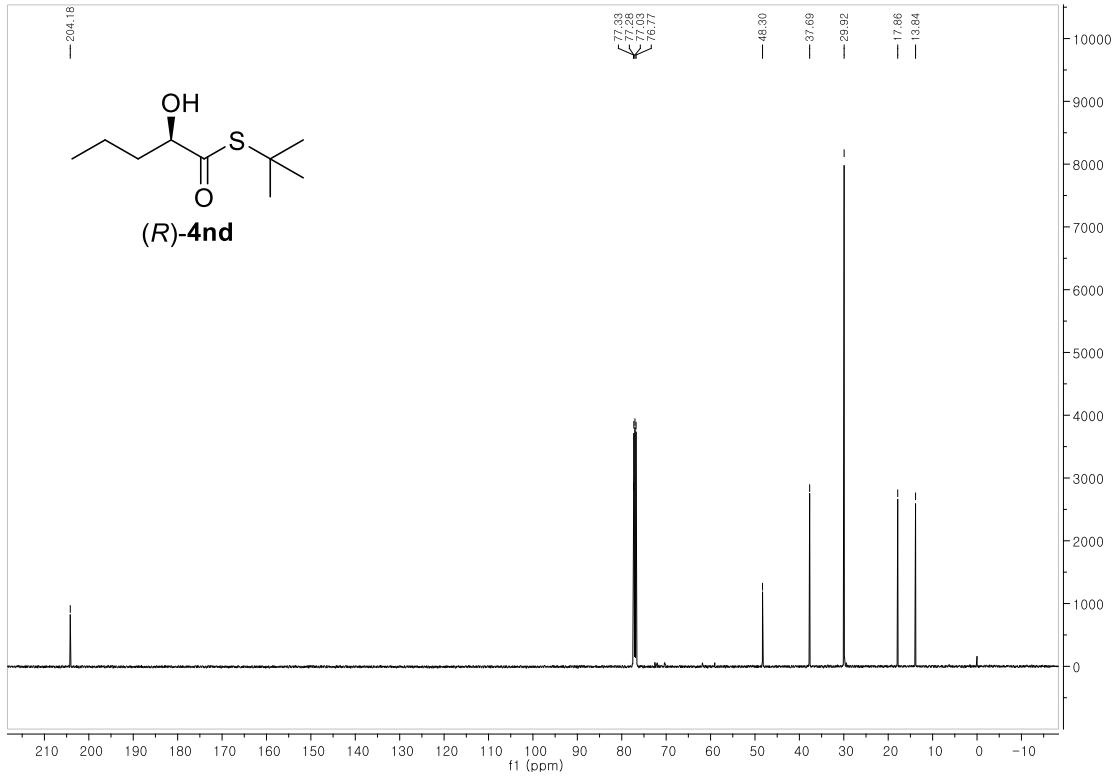
^{1}H NMR spectra of **4md**



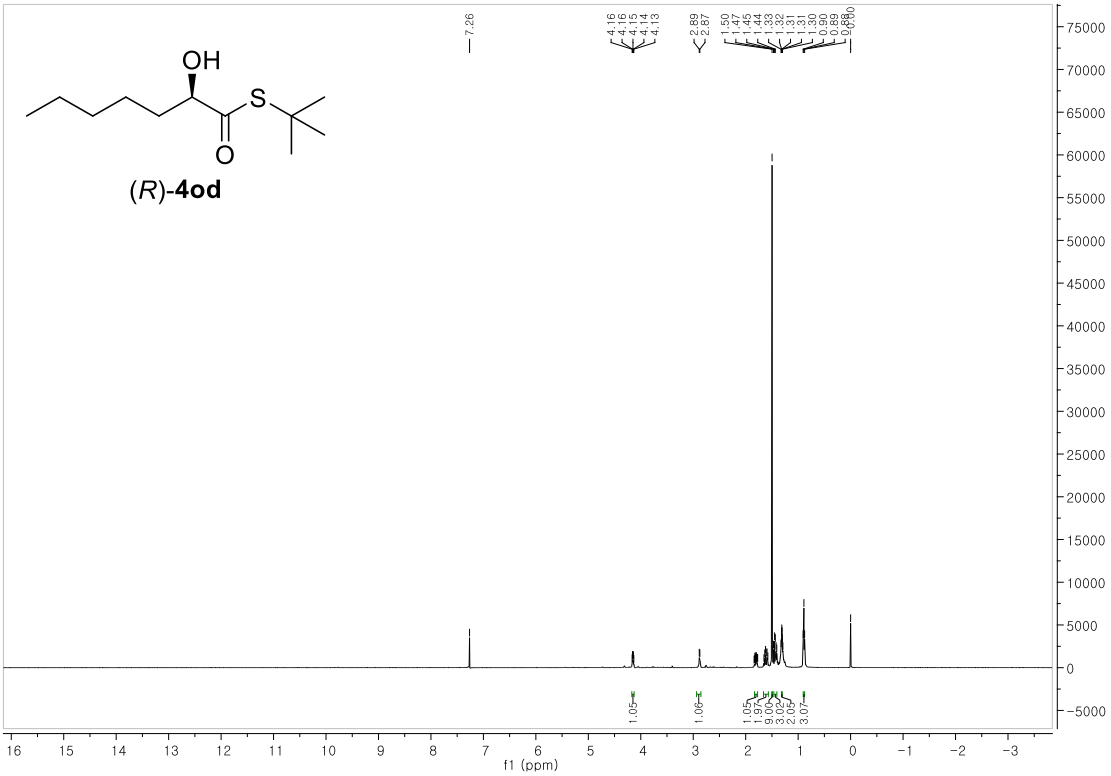
^{13}C NMR spectra of **4md**



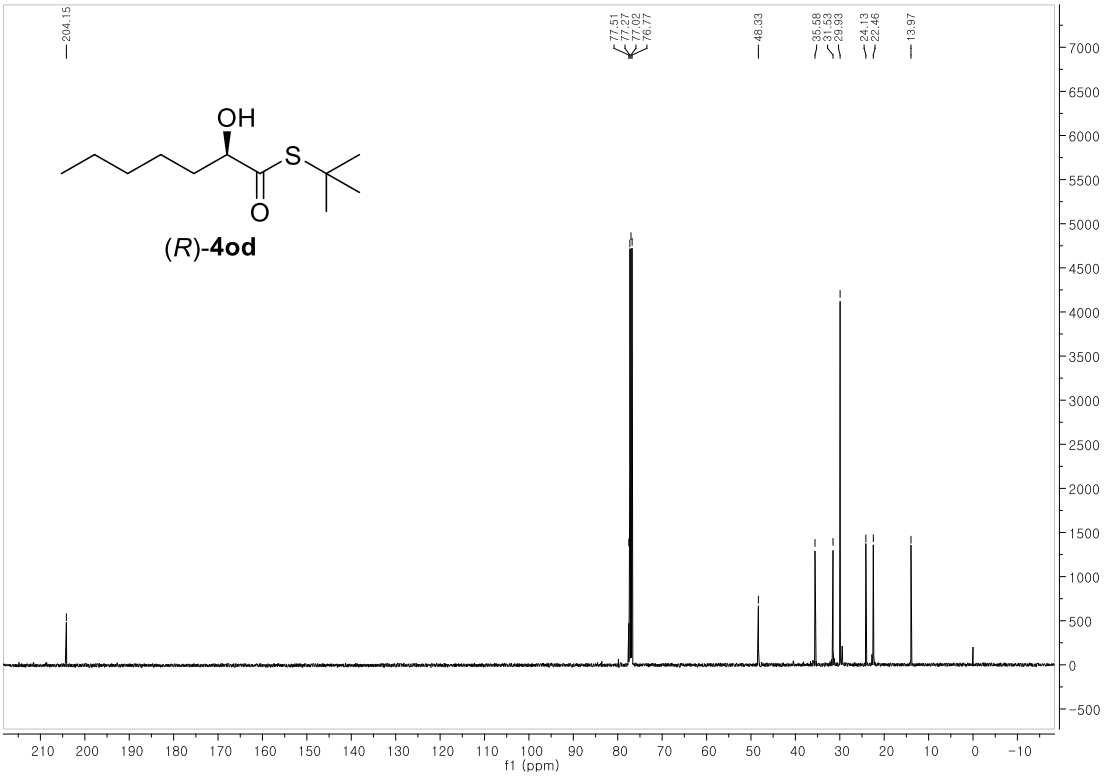
^{1}H NMR spectra of **4nd**



^{13}C NMR spectra of **4nd**



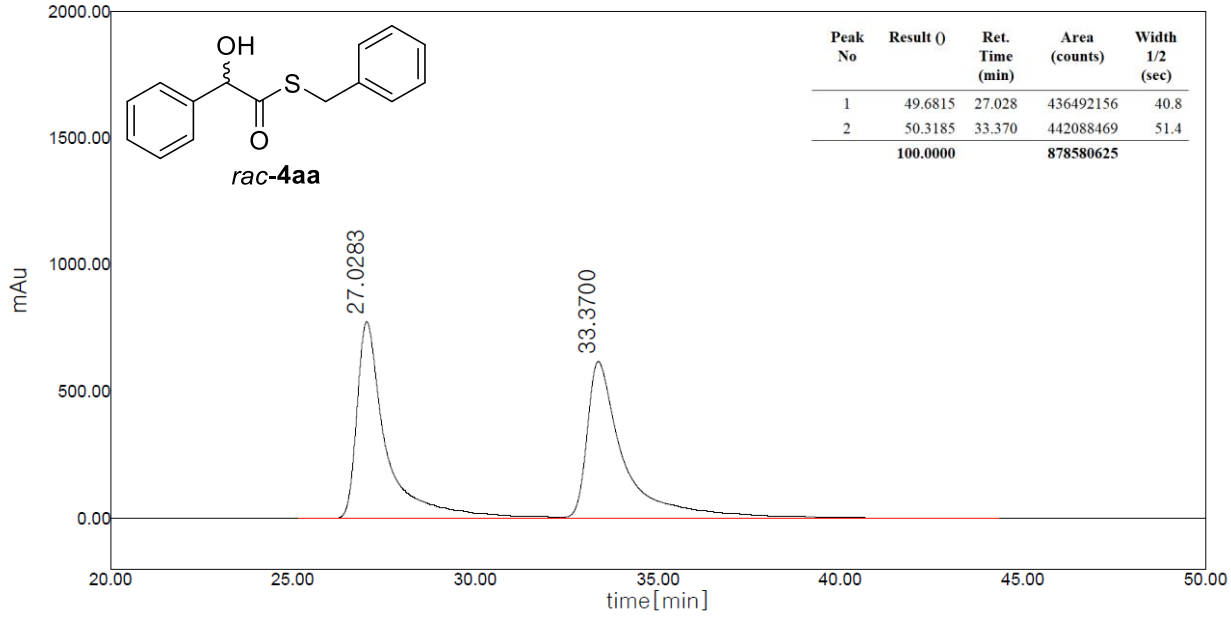
^{1}H NMR spectra of **4od**



^{13}C NMR spectra of **4od**

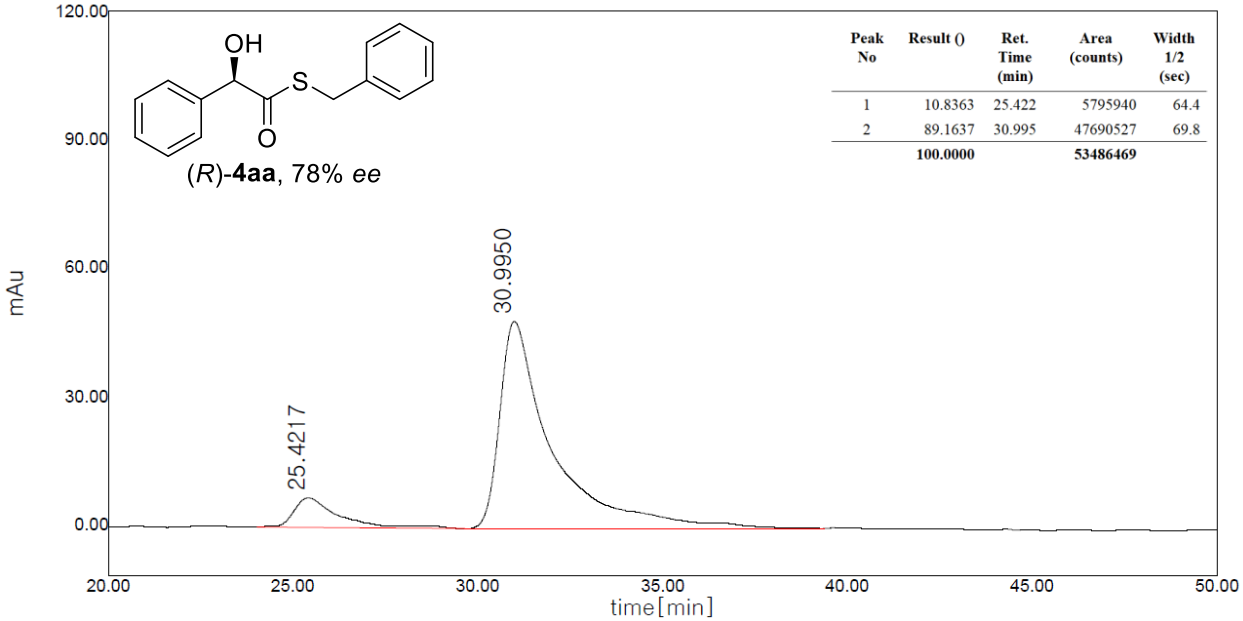
HPLC Traces

HPLC traces of Scheme 1B



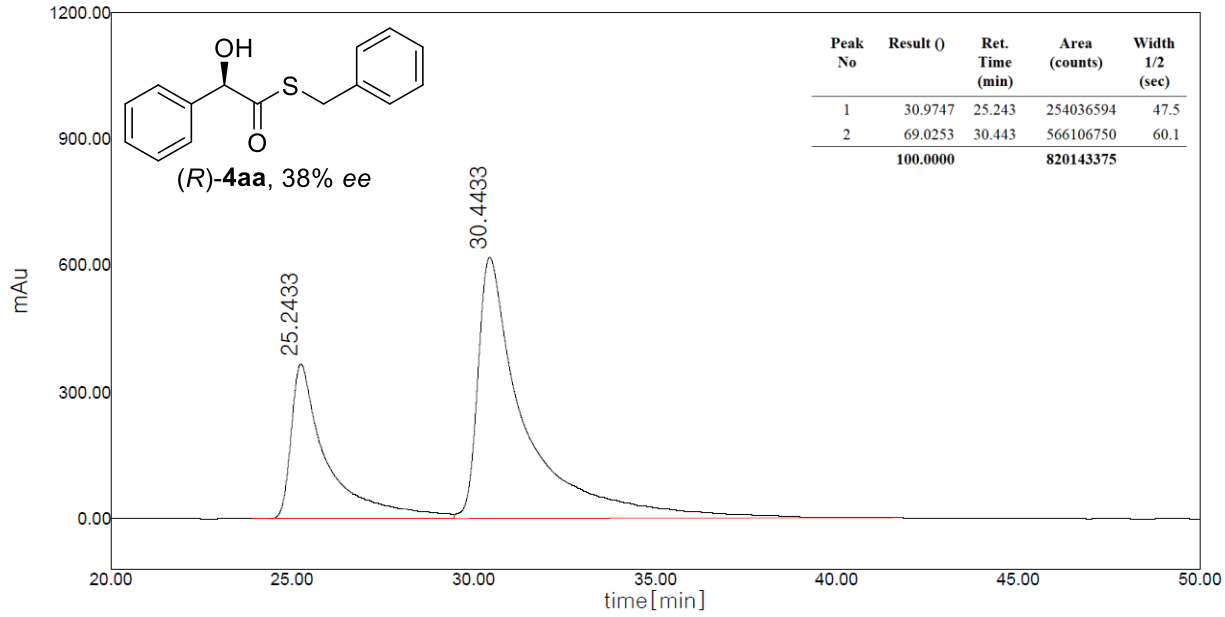
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6815	27.028	436492156	40.8
2	50.3185	33.370	442088469	51.4
	100.0000		**878580625**	

HPLC trace of *rac*-**4aa**



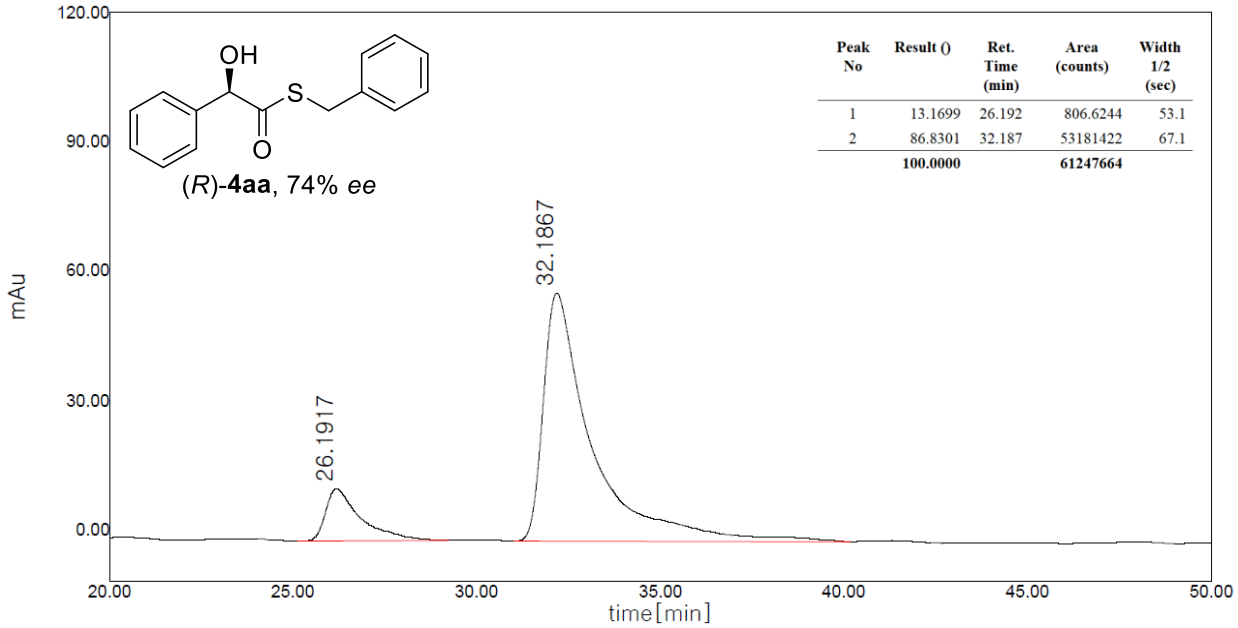
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.8363	25.422	5795940	64.4
2	89.1637	30.995	47690527	69.8
	100.0000		**53486469**	

HPLC trace of **4aa** (catalyst **5a**, in CPME)



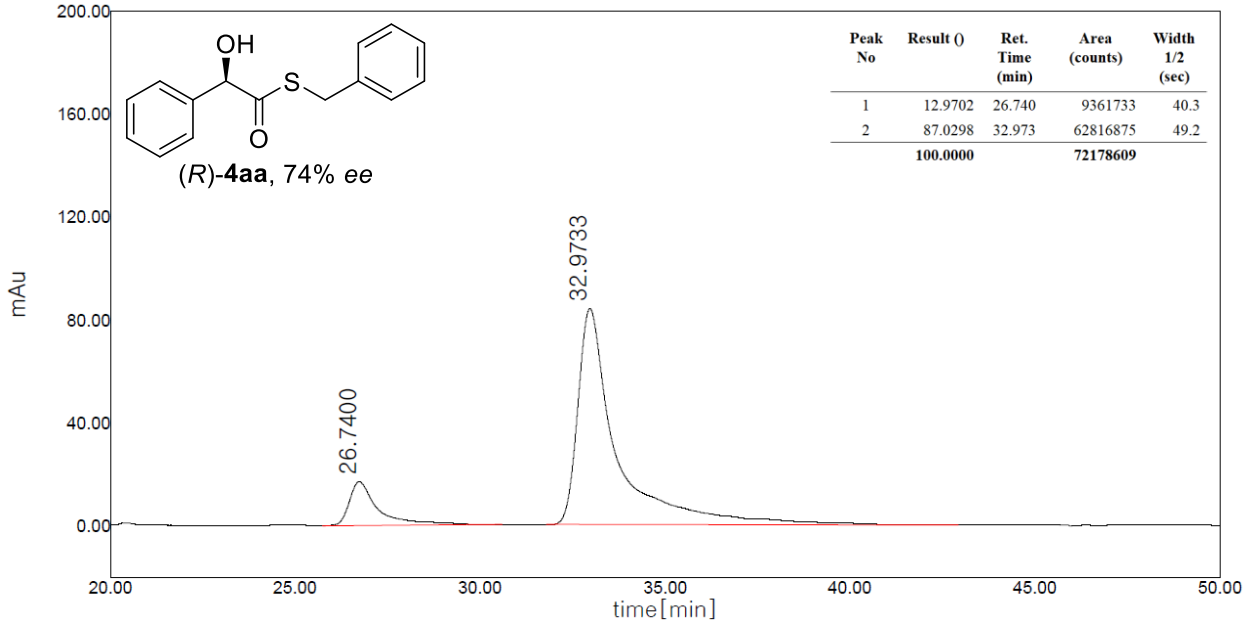
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	30.9747	25.243	254036594	47.5
2	69.0253	30.443	566106750	60.1
	100.0000		**820143375**	

HPLC trace of **4aa** (catalyst **5a**, in H_2O)

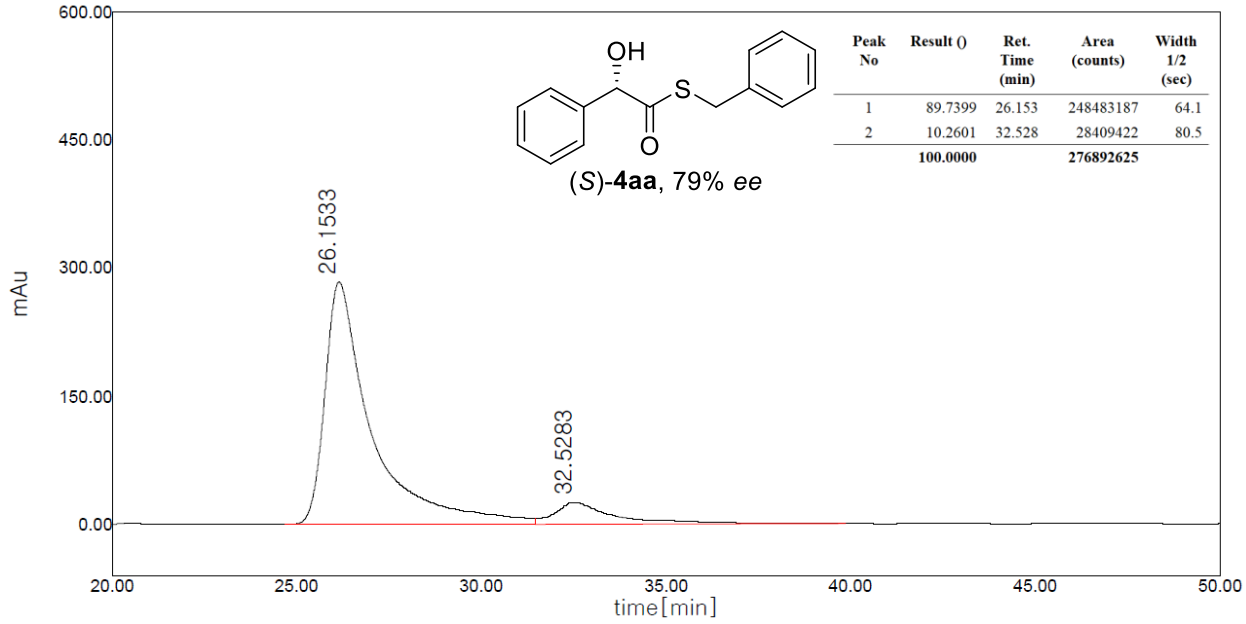


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	13.1699	26.192	806.6244	53.1
2	86.8301	32.187	53181422	67.1
	100.0000		**61247664**	

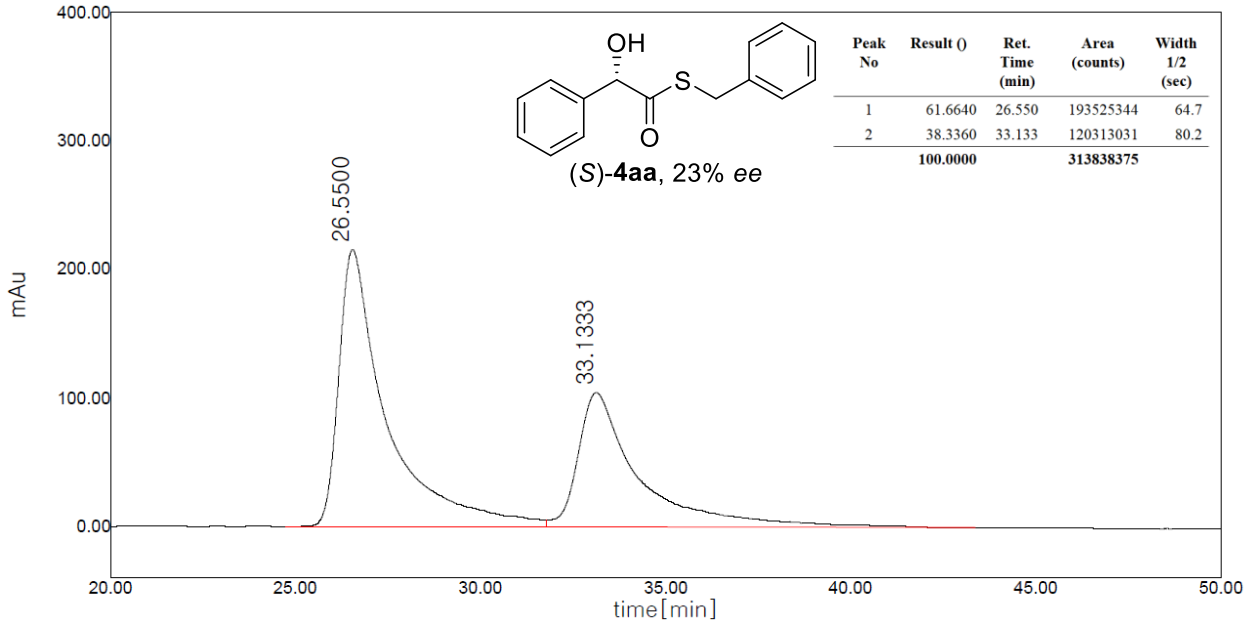
HPLC trace of **4aa** (catalyst **5a**, in H_2O/CPME)



HPLC trace of **4aa** (catalyst **5a**, in brine/CPME)

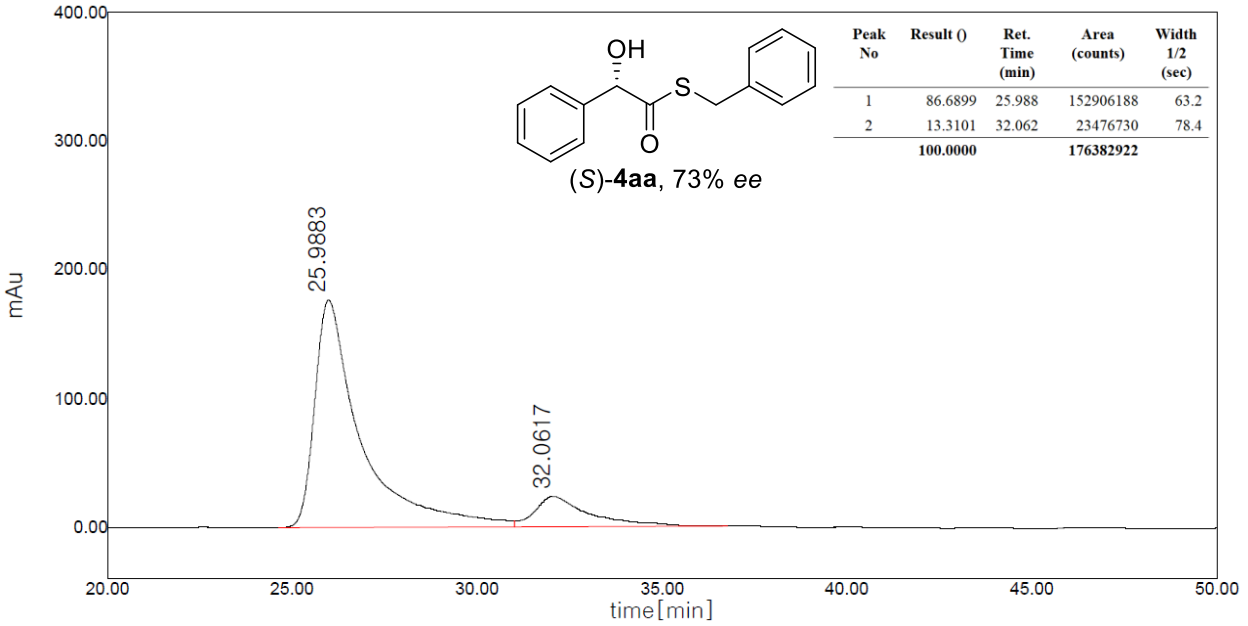


HPLC trace of **4aa** (catalyst **5b**, in CPME)



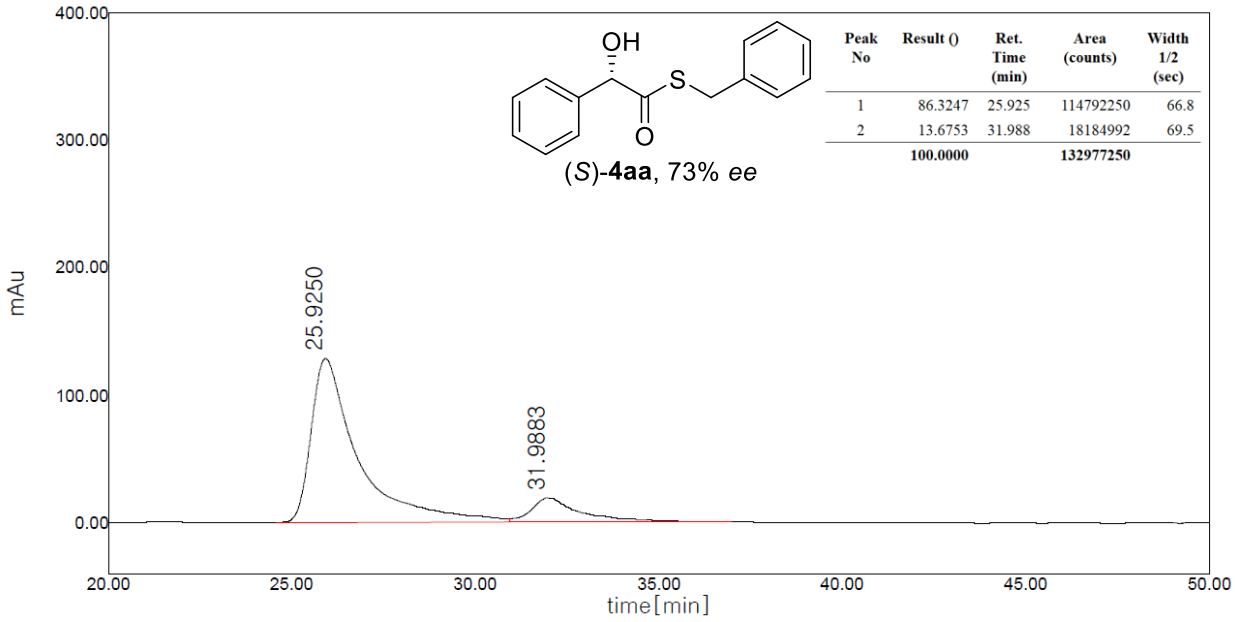
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	61.6640	26.550	193525344	64.7
2	38.3360	33.133	120313031	80.2
	100.0000		**313838375**	

HPLC trace of **4aa** (catalyst **5b**, in H_2O)



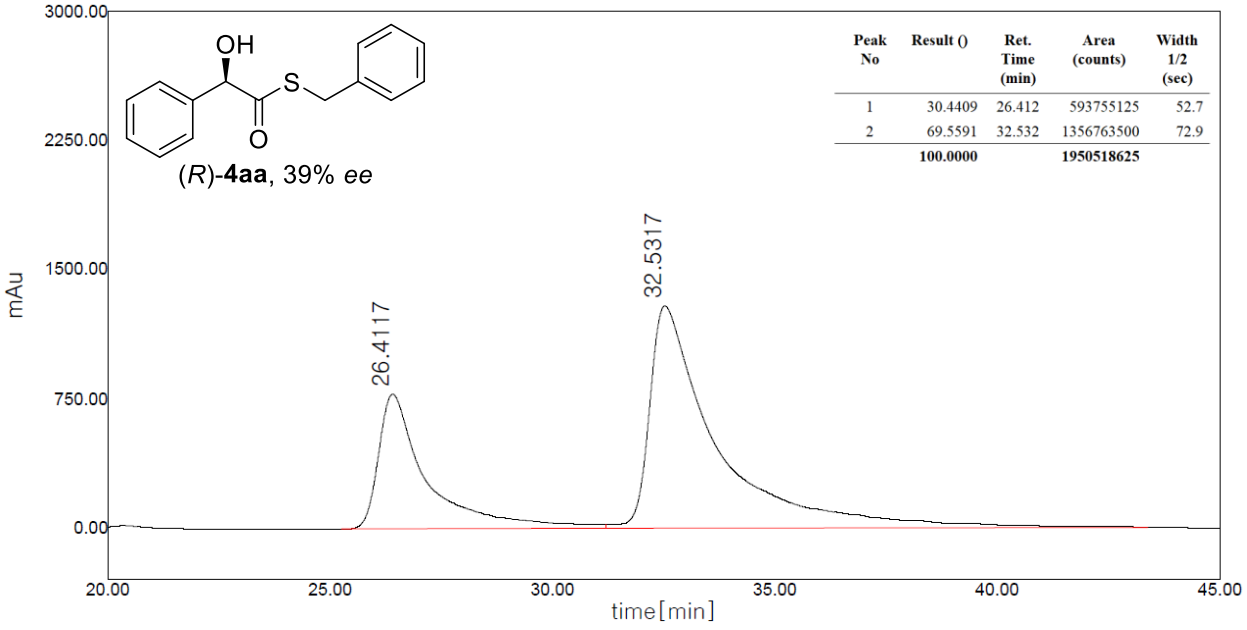
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	86.6899	25.988	152906188	63.2
2	13.3101	32.062	23476730	78.4
	100.0000		**176382922**	

HPLC trace of **4aa** (catalyst **5b**, in H_2O/CPME)



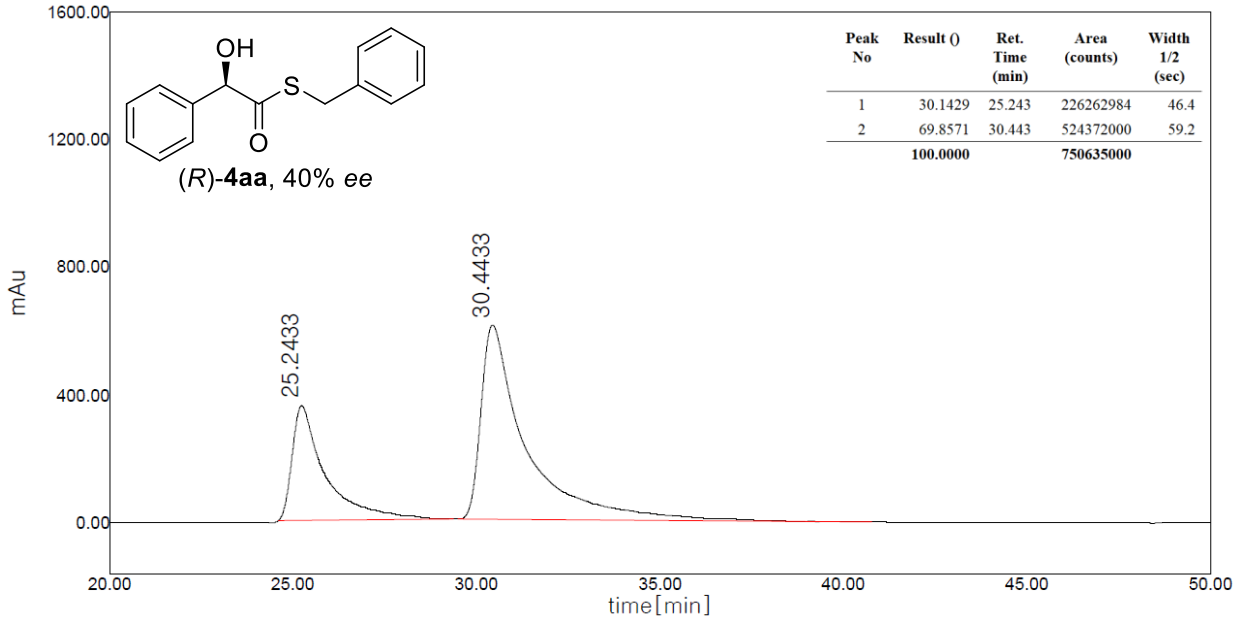
HPLC trace of **4aa** (catalyst **5b**, in brine/CPME)

HPLC traces of Table S1



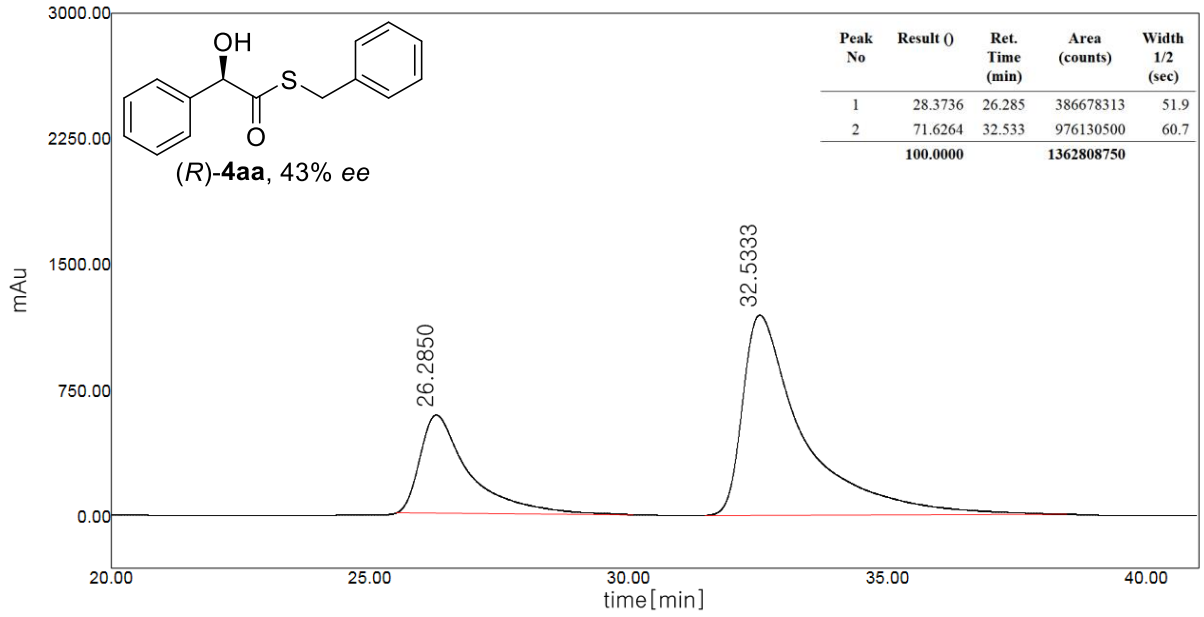
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	30.4409	26.412	593755125	52.7
2	69.5591	32.532	1356763500	72.9
	100.0000		**1950518625**	

HPLC trace of **4aa** (in toluene)



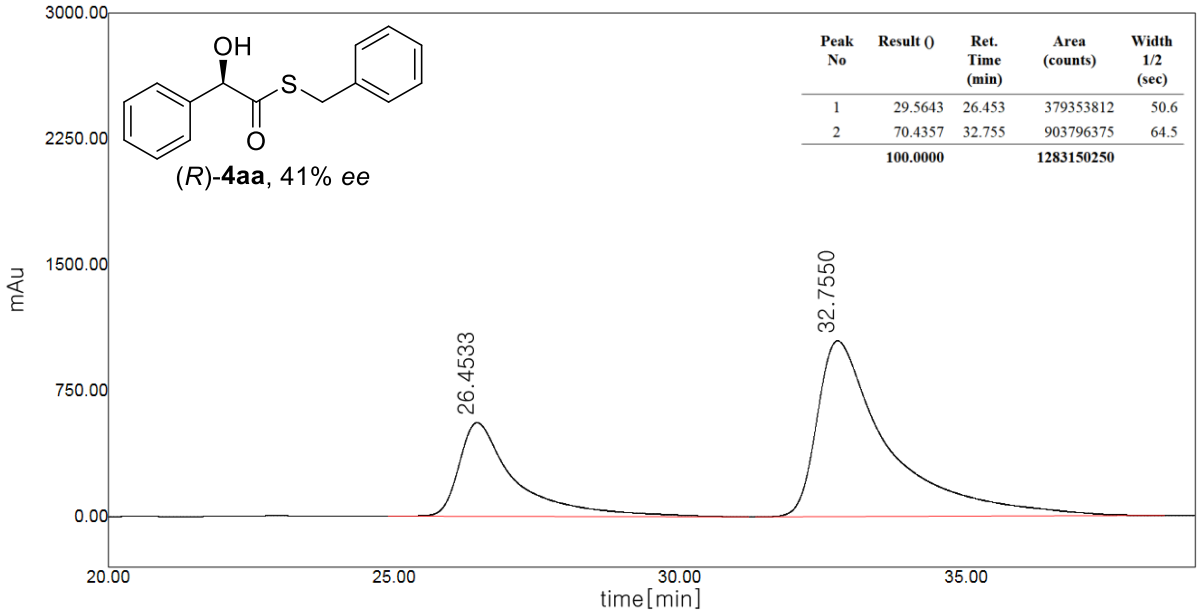
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	30.1429	25.243	226262984	46.4
2	69.8571	30.443	524372000	59.2
	100.0000		**750635000**	

HPLC trace of **4aa** (in *o*-xylene)



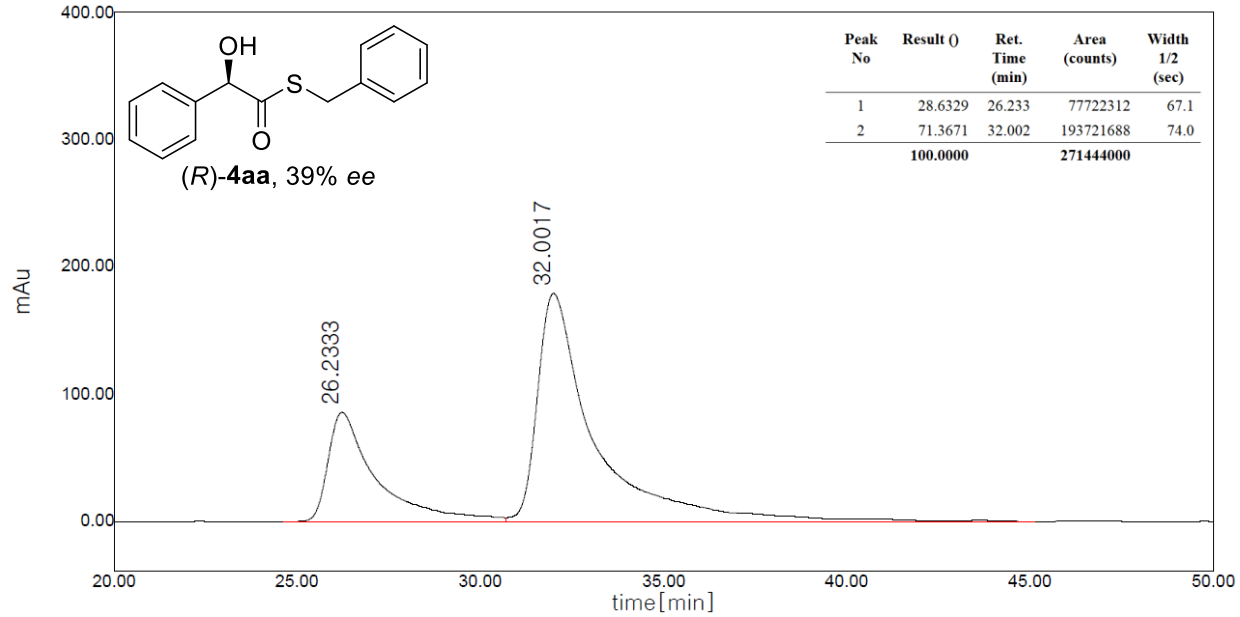
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	28.3736	26.285	386678313	51.9
2	71.6264	32.533	976130500	60.7
	100.0000		**1362808750**	

HPLC trace of **4aa** (in *m*-xylene)

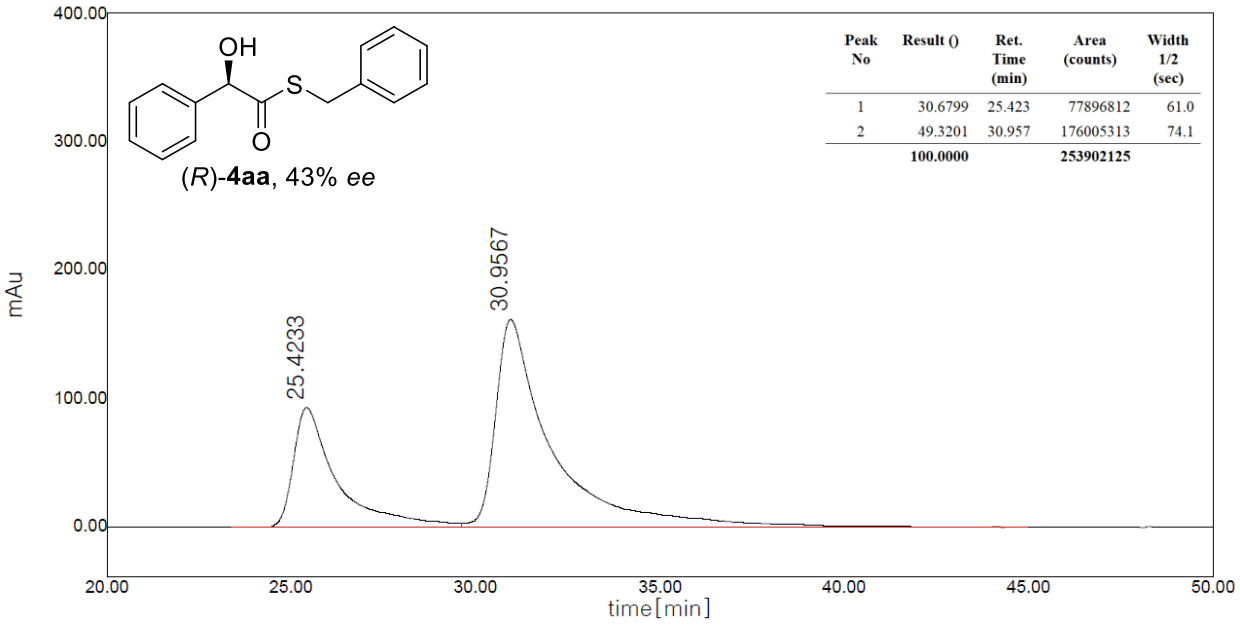


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	29.5643	26.453	379353812	50.6
2	70.4357	32.755	903796375	64.5
	100.0000		**1283150250**	

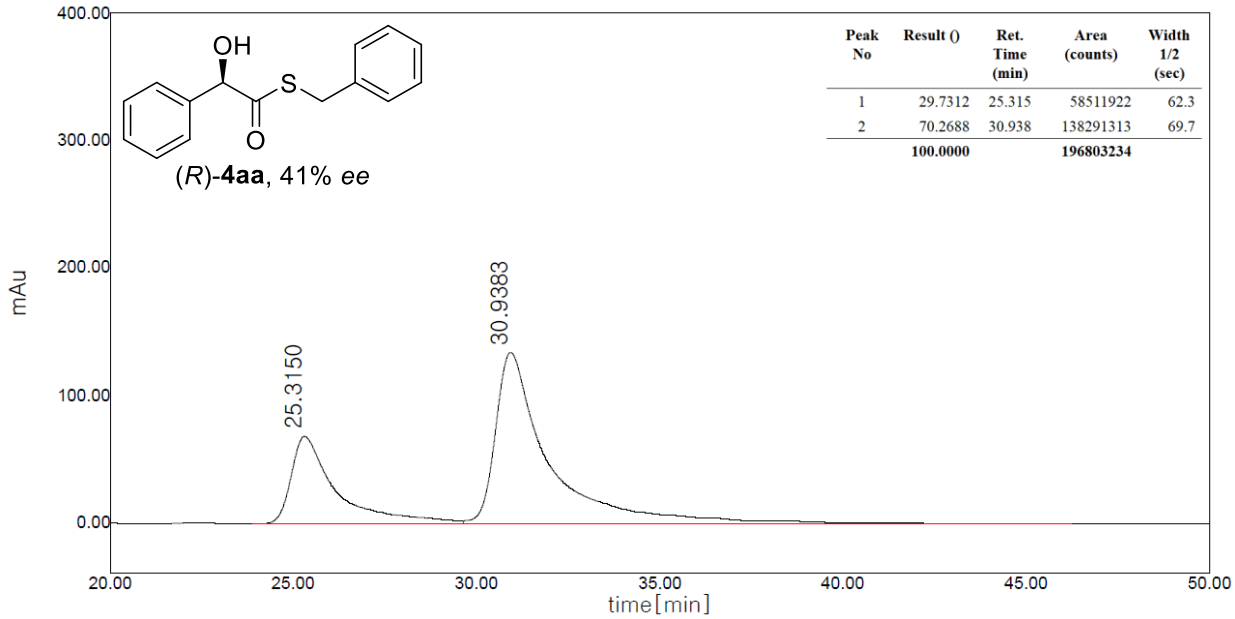
HPLC trace of **4aa** (in *p*-xylene)



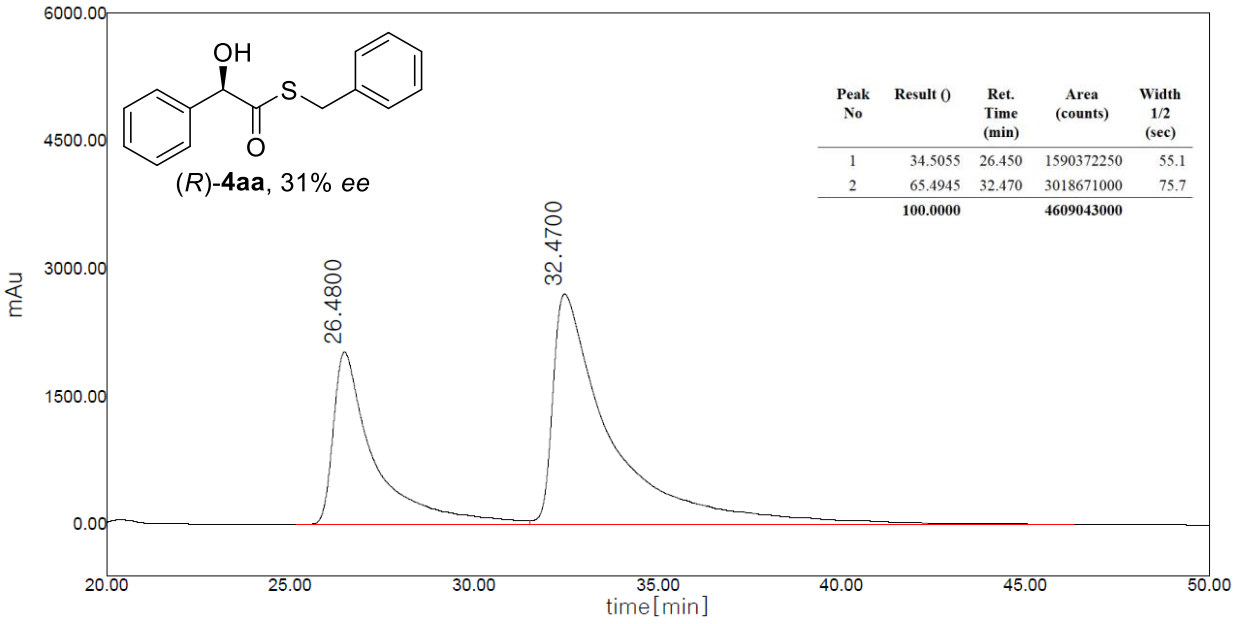
HPLC trace of **4aa** (in chlorobenzene)



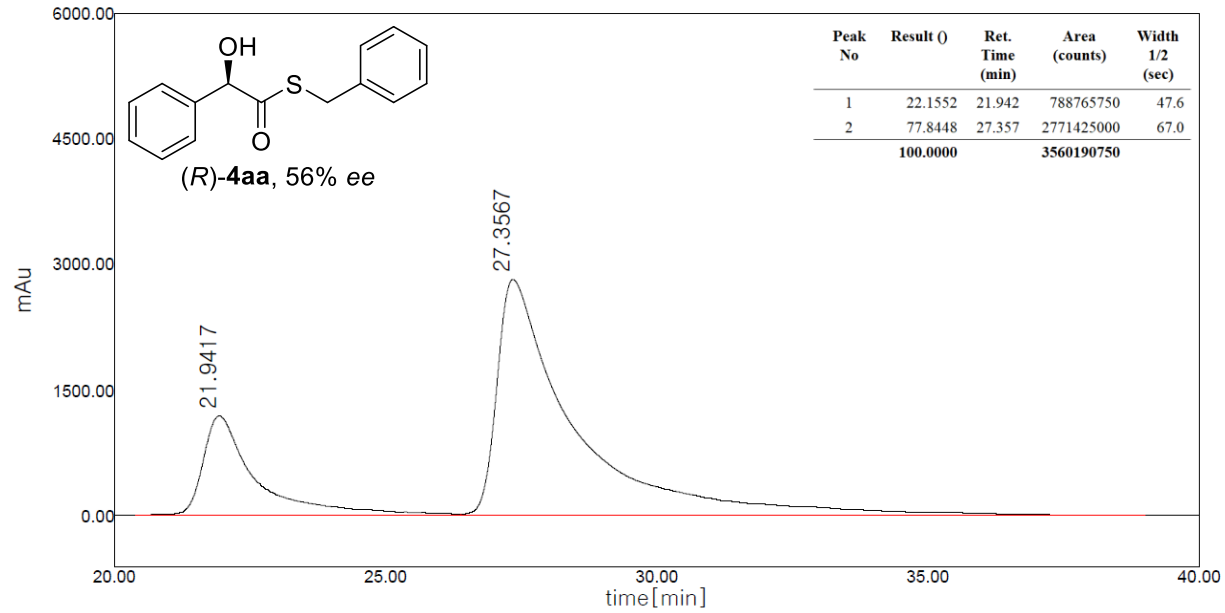
HPLC trace of **4aa** (in bromobenzene)



HPLC trace of **4aa** (in 1,2-dibromobenzene)

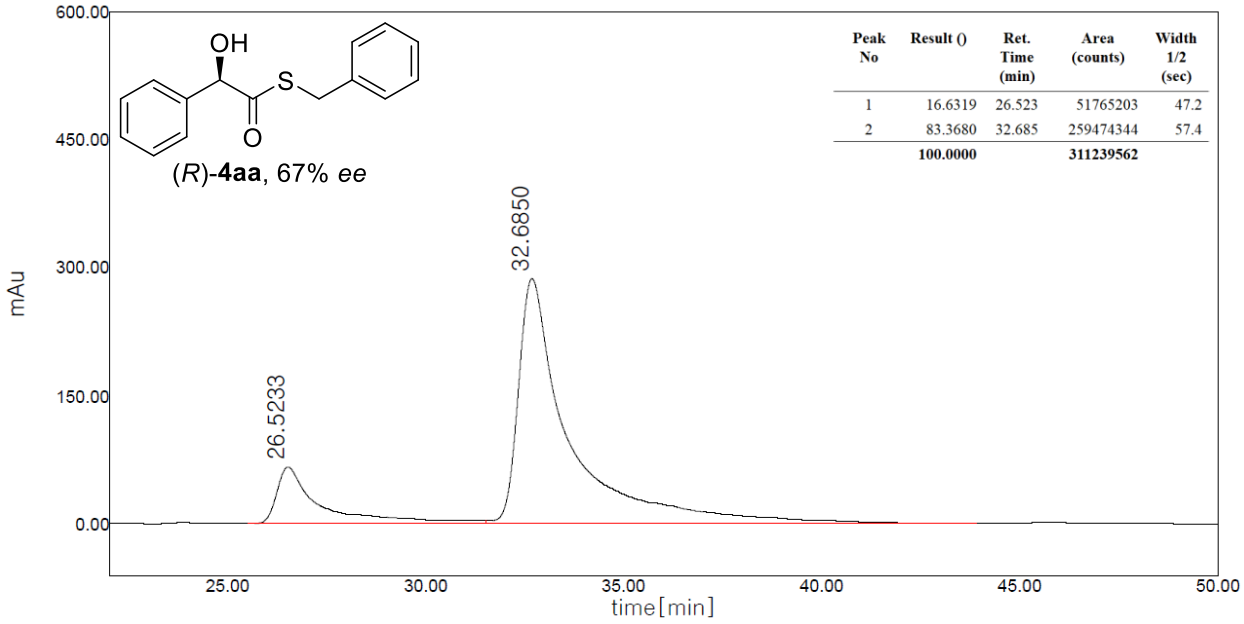


HPLC trace of **4aa** (in CH_2Cl_2)



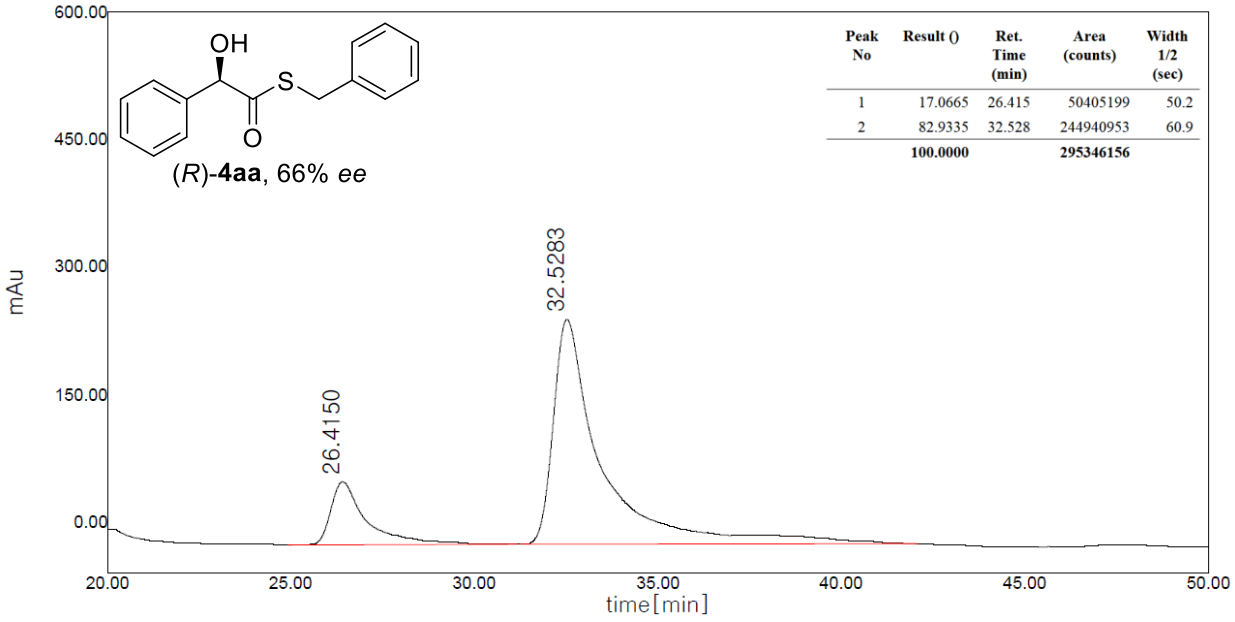
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	22.1552	21.942	788765750	47.6
2	77.8448	27.357	2771425000	67.0
	100.0000		**3560190750**	

HPLC trace of **4aa** (in diethyl ether)

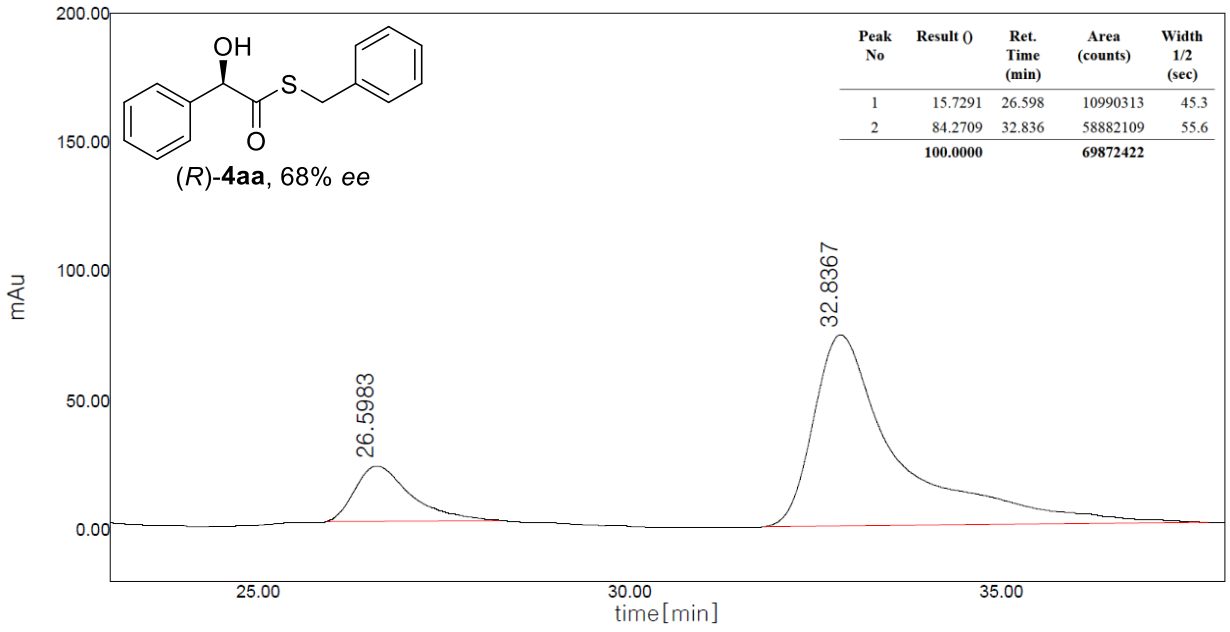


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	16.6319	26.523	51765203	47.2
2	83.3680	32.685	259474344	57.4
	100.0000		**311239562**	

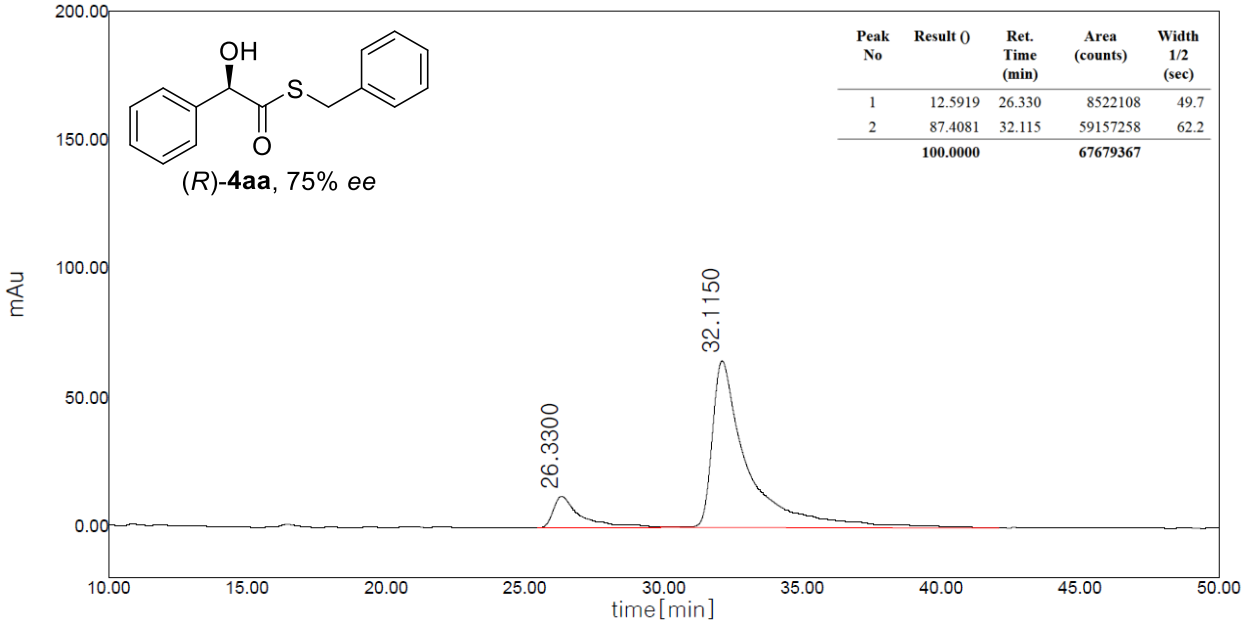
HPLC trace of **4aa** (in diisopropyl ether)



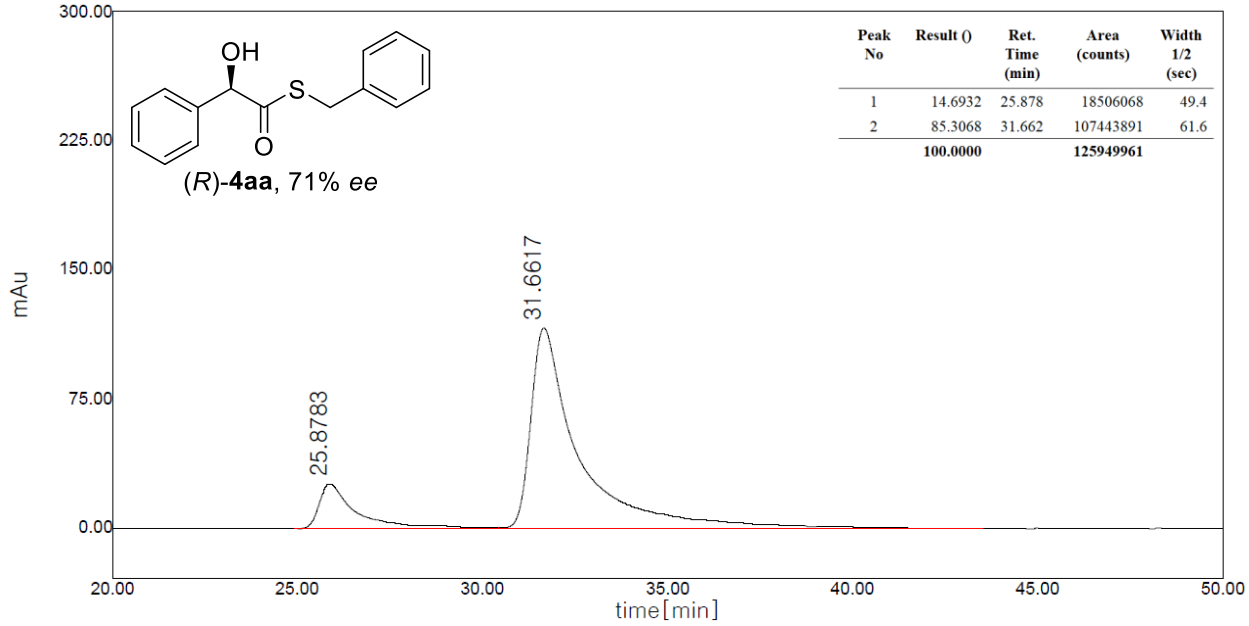
HPLC trace of **4aa** (in dibutyl ether)



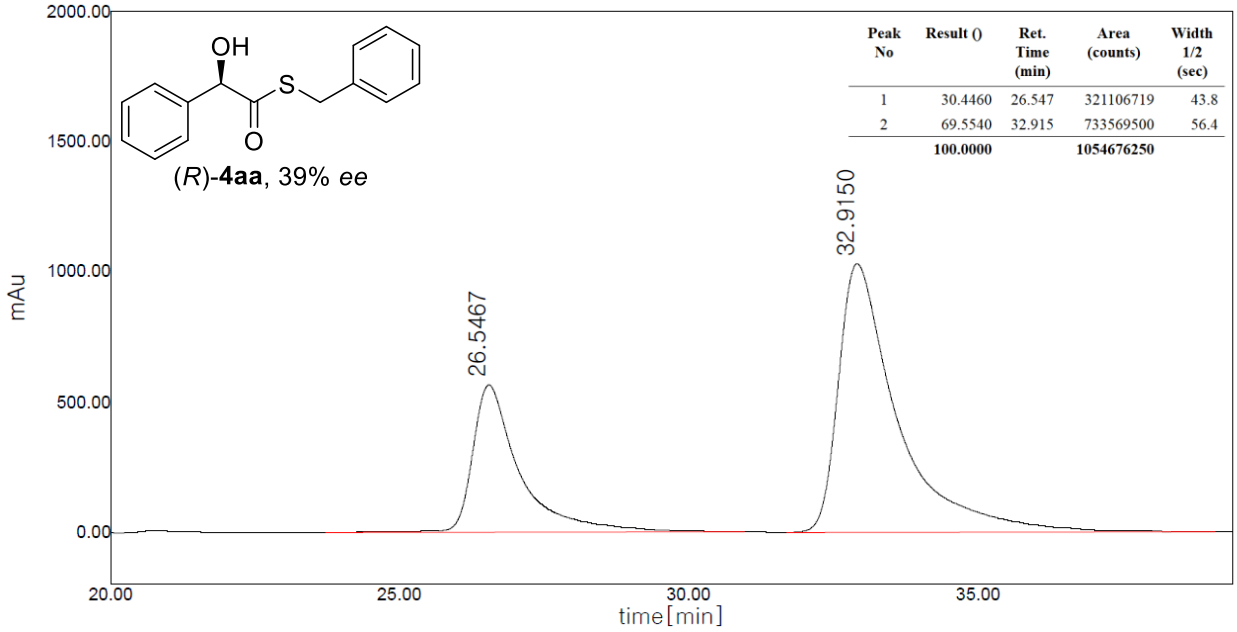
HPLC trace of **4aa** (in dipentyl ether)



HPLC trace of **4aa** (in MTBE)

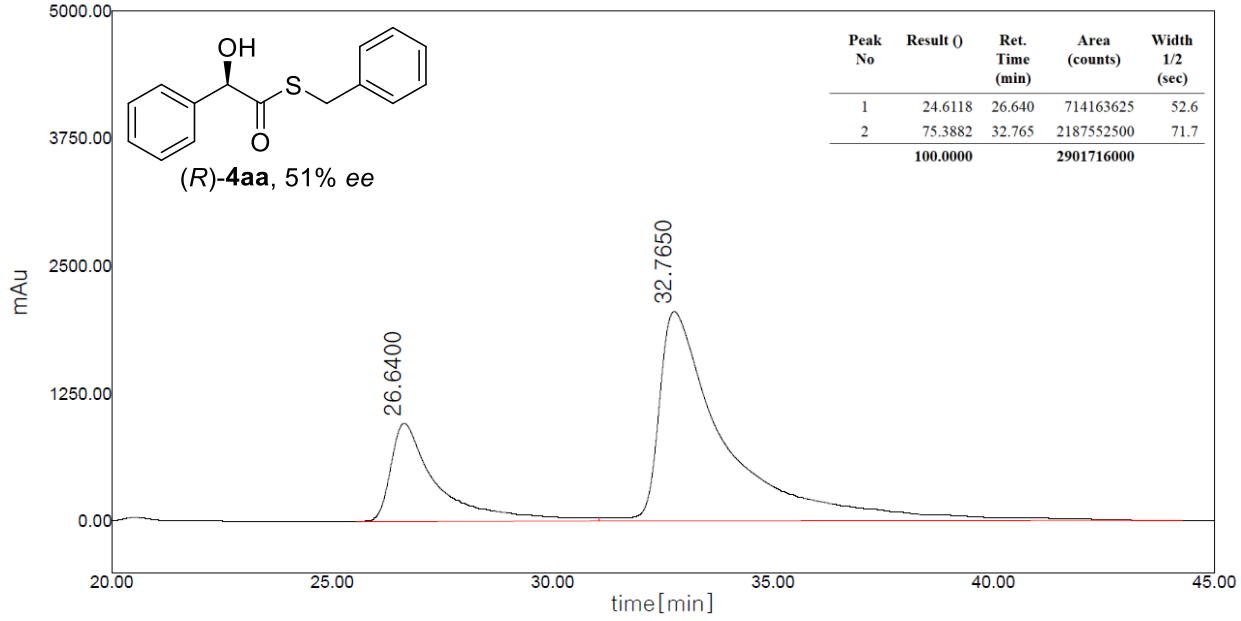


HPLC trace of **4aa** (in methoxy cyclohexane)



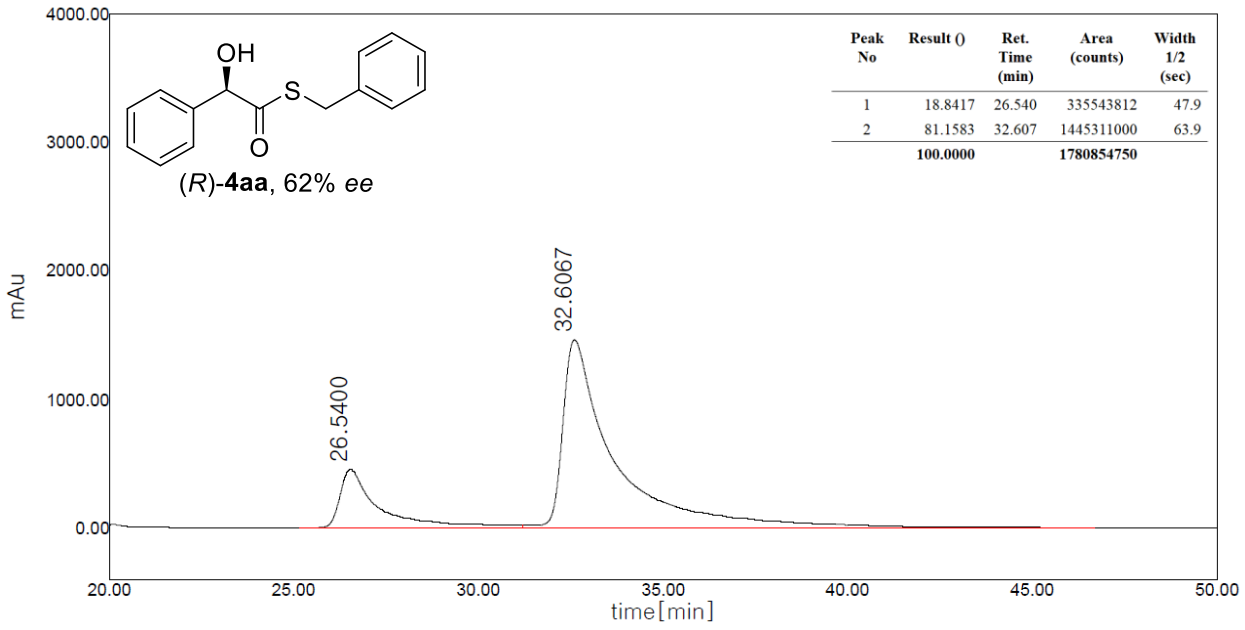
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	30.4460	26.547	321106719	43.8
2	69.5540	32.915	733569500	56.4
	100.0000		**1054676250**	

HPLC trace of **4aa** (in methyl propargyl ether)

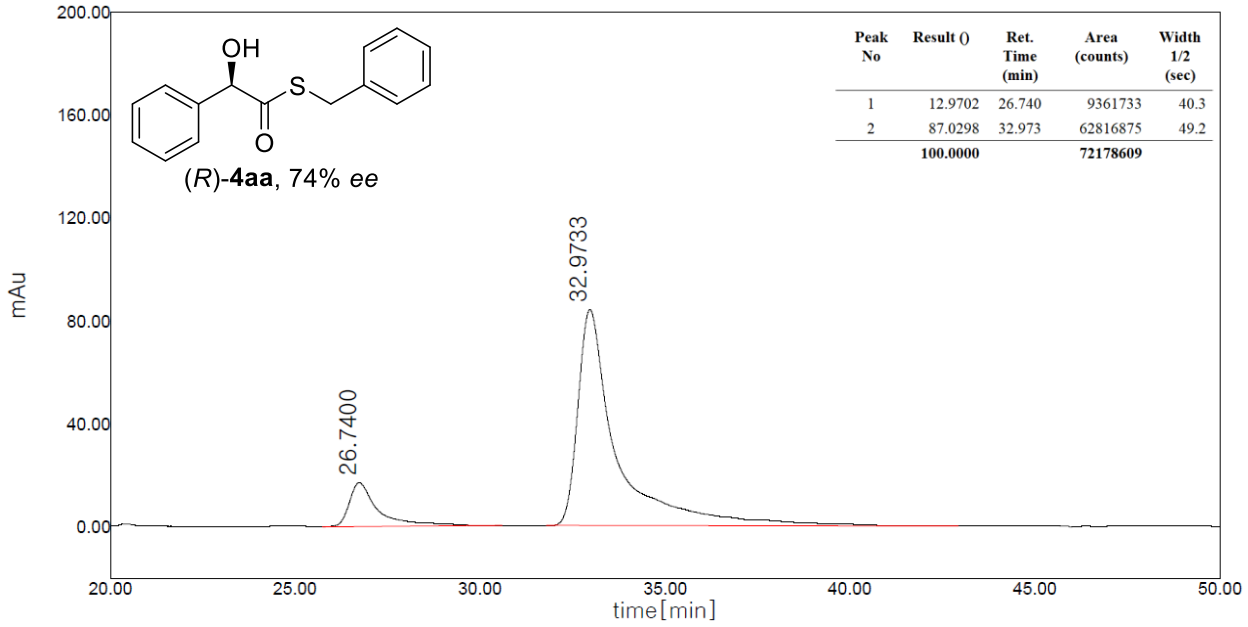


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	24.6118	26.640	714163625	52.6
2	75.3882	32.765	2187552500	71.7
	100.0000		**2901716000**	

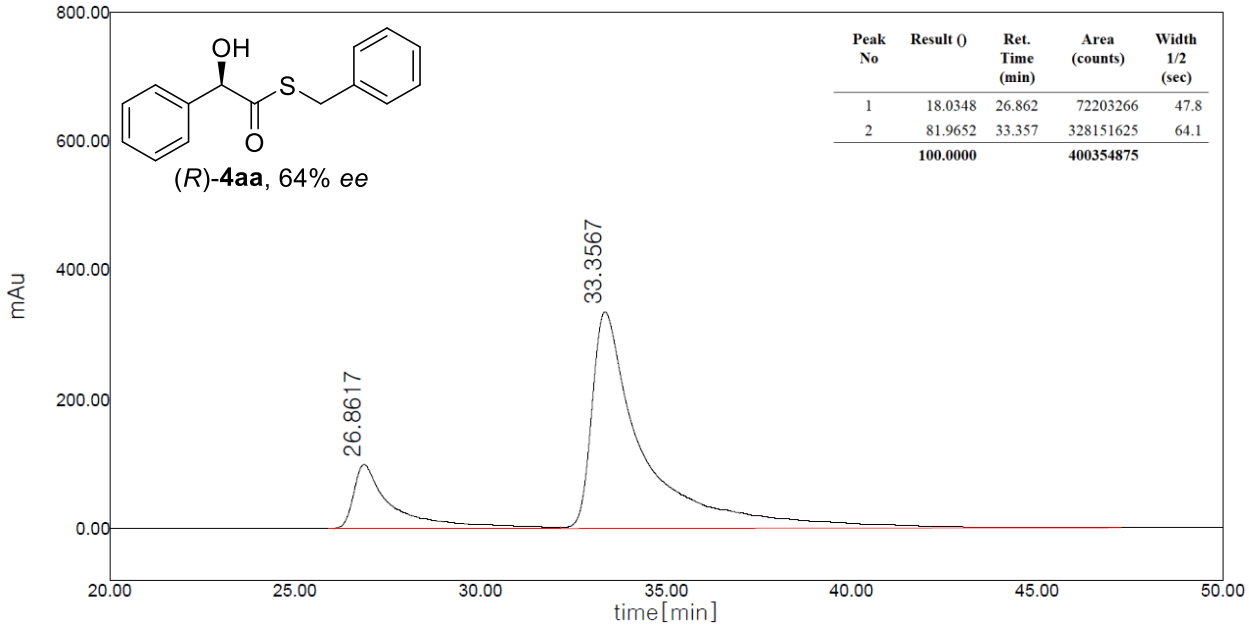
HPLC trace of **4aa** (in THF)



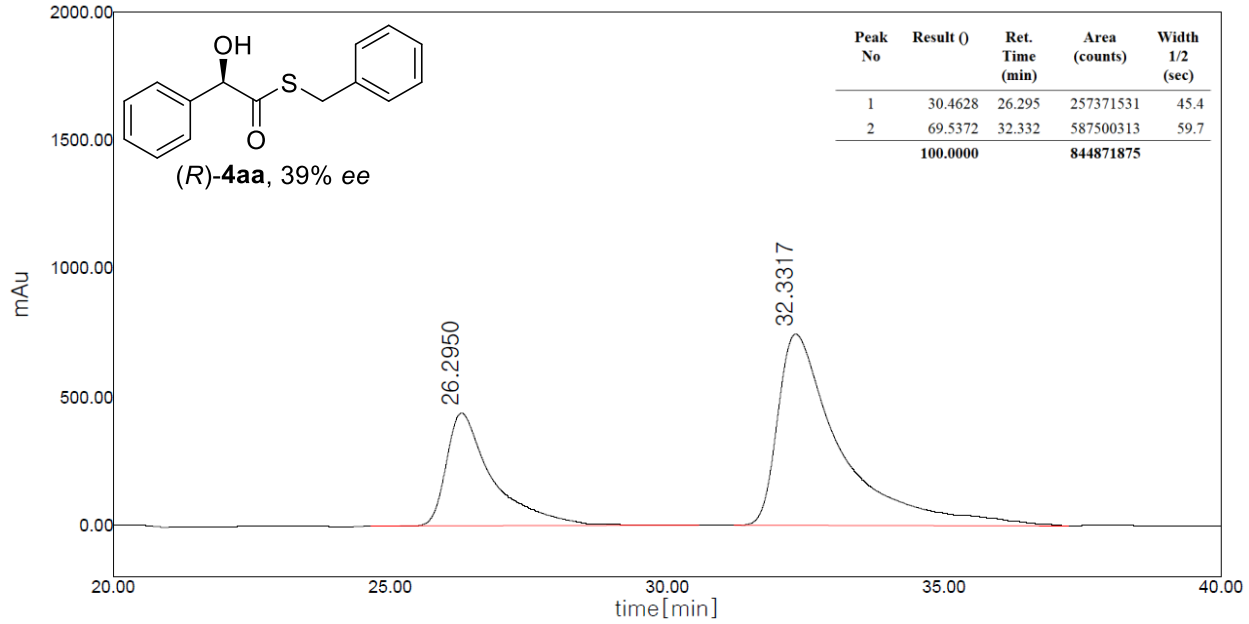
HPLC trace of **4aa** (in 2-methyl THF)



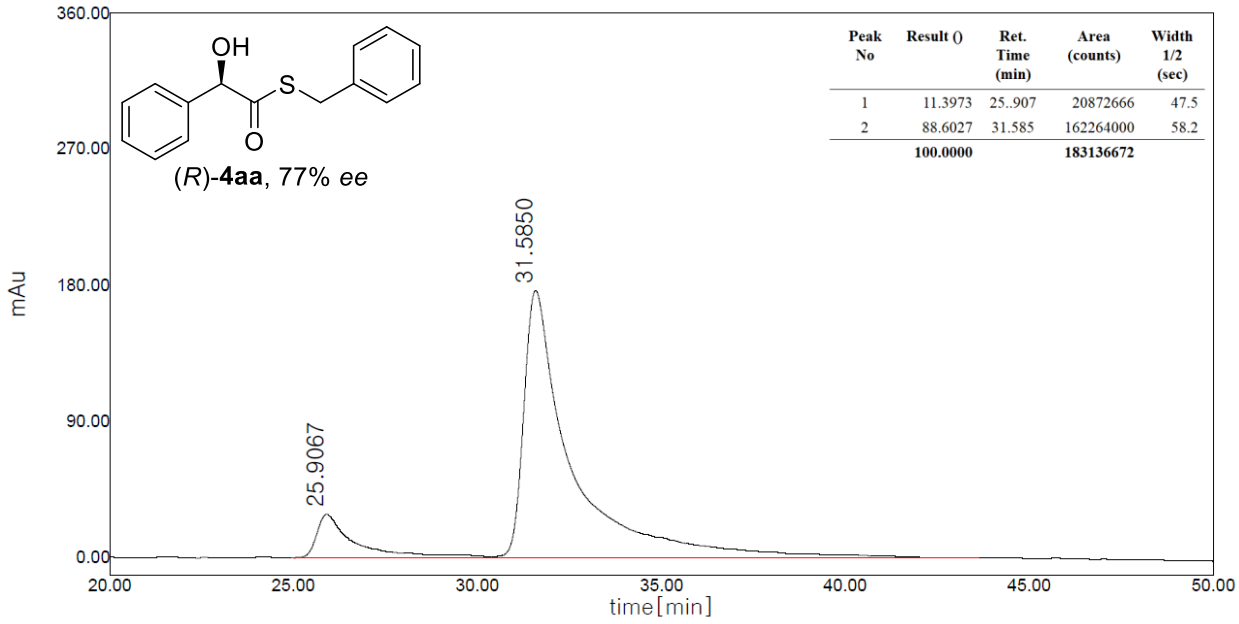
HPLC trace of **4aa** (in CPME)



HPLC trace of **4aa** (in CPME/THF)

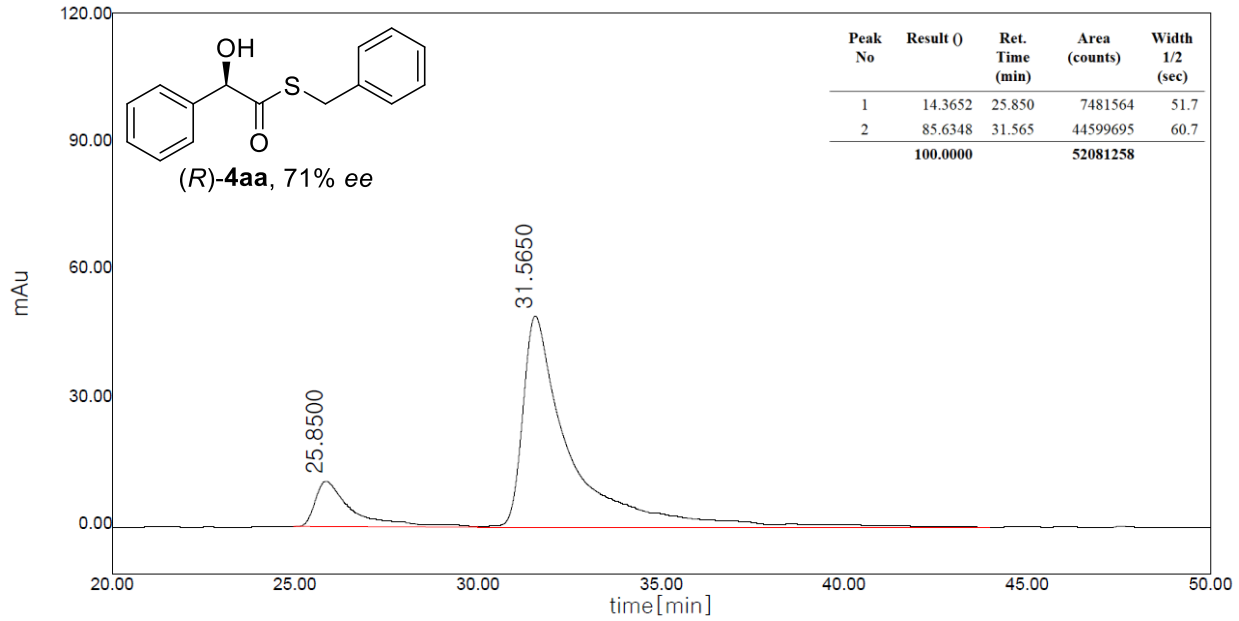


HPLC trace of **4aa** (in 1,2-dimethoxy ethane)



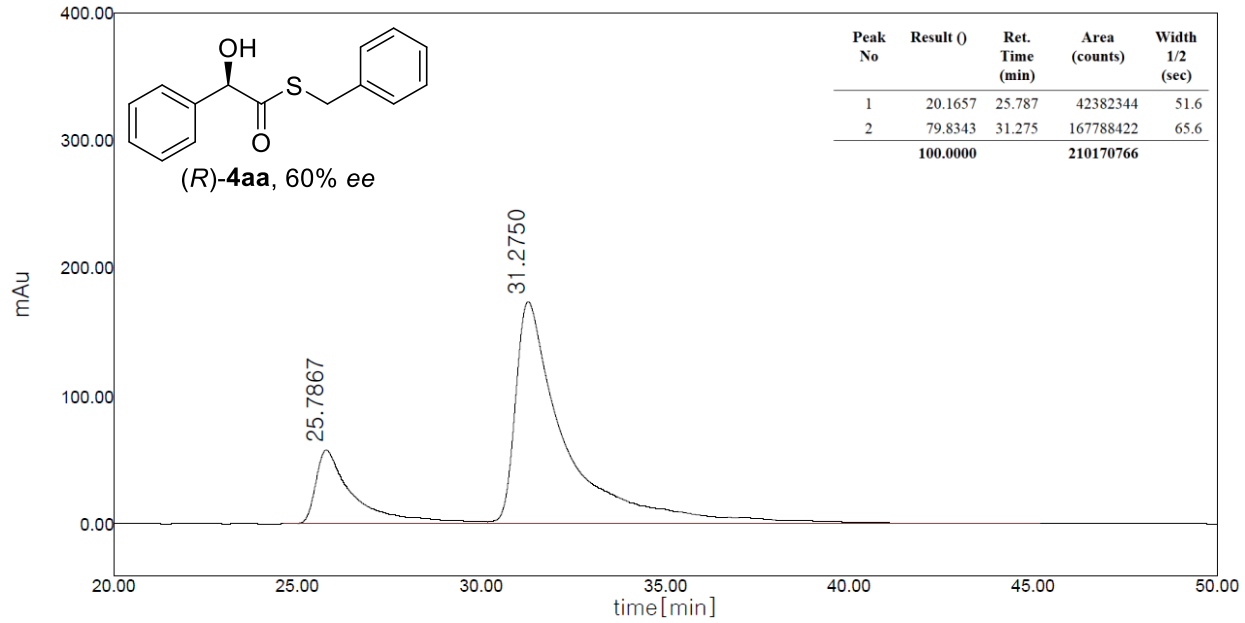
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	11.3973	25..907	20872666	47.5
2	88.6027	31.585	162264000	58.2
	100.0000		**183136672**	

HPLC trace of **4aa** (in eucalyptol)



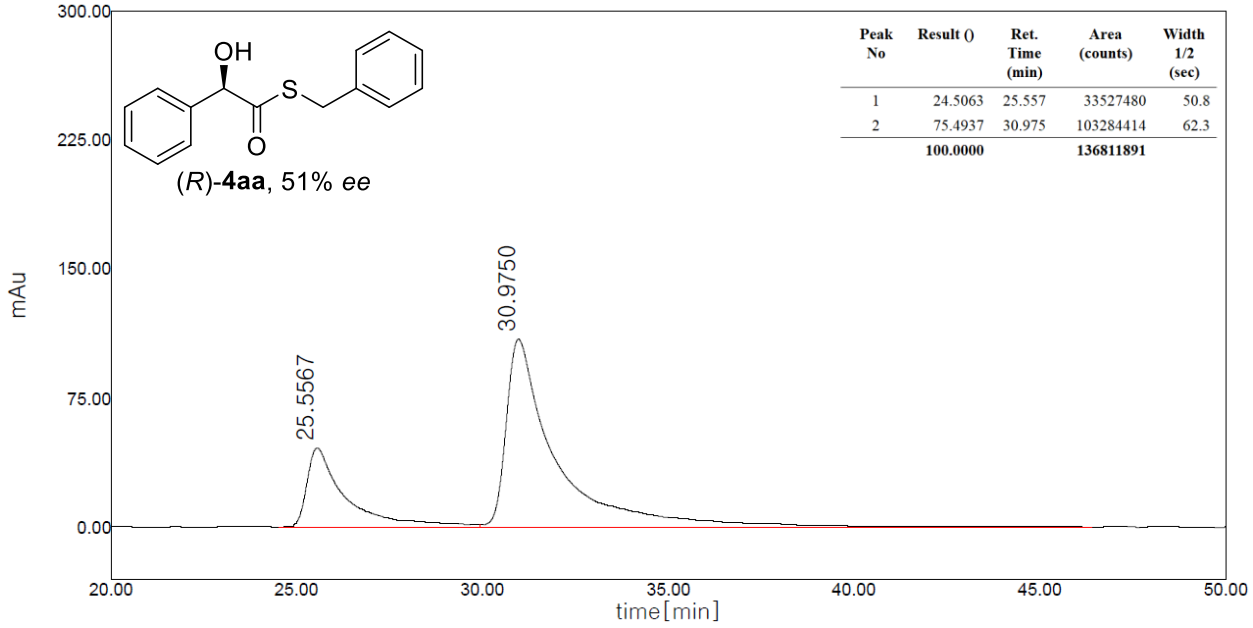
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	14.3652	25.850	7481564	51.7
2	85.6348	31.565	44599695	60.7
	100.0000		**52081258**	

HPLC trace of **4aa** (in (*R*)-(+)-limonene)



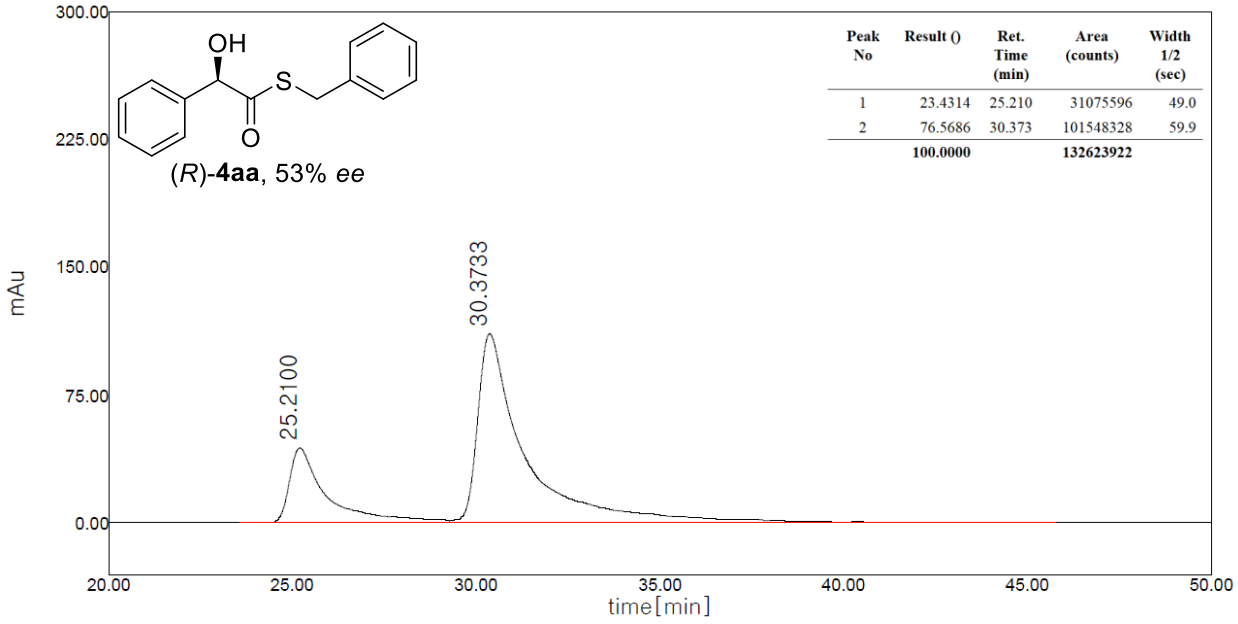
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	20.1657	25.787	42382344	51.6
2	79.8343	31.275	167788422	65.6
	100.0000		**210170766**	

HPLC trace of **4aa** (in (*S*)-(-)-limonene)



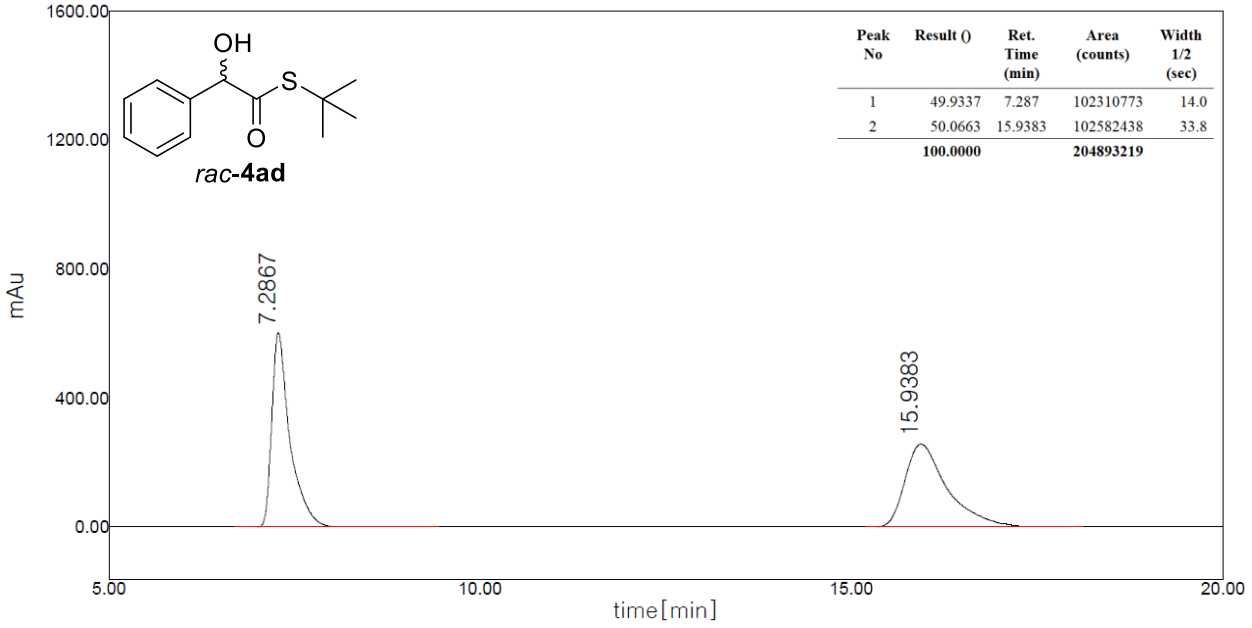
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	24.5063	25.557	33527480	50.8
2	75.4937	30.975	103284414	62.3
	100.0000		**136811891**	

HPLC trace of **4aa** (in (+)-(α)-pinene)



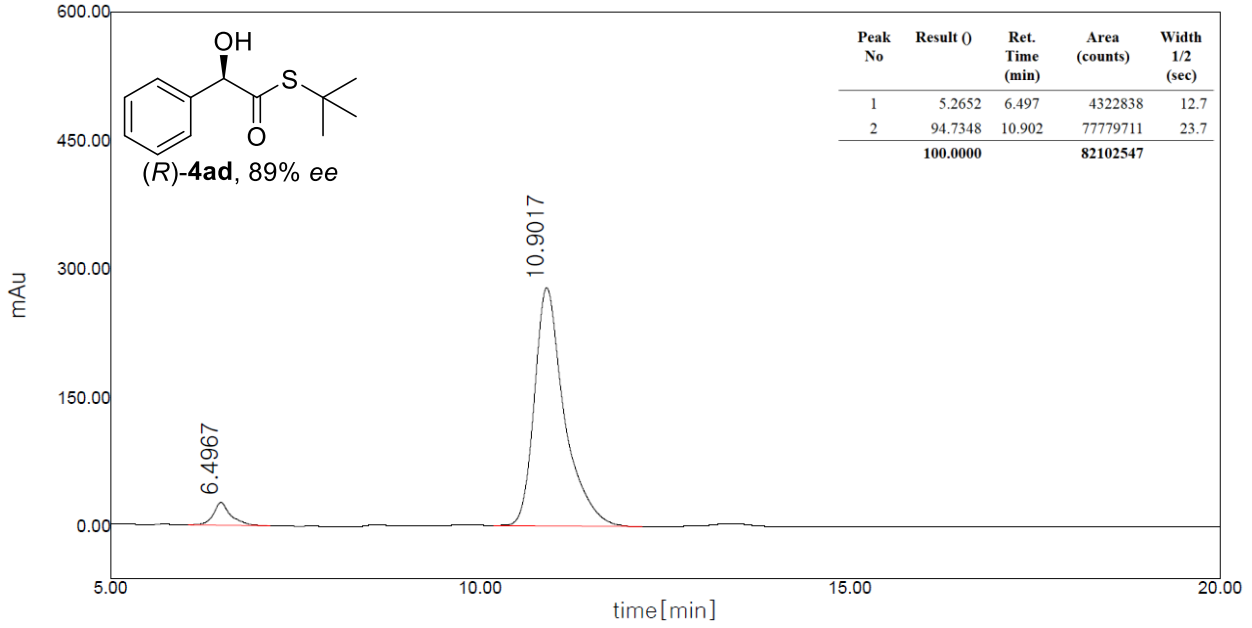
HPLC trace of **4aa** (in (-)-(α)-pinene)

HPLC traces of Table S2



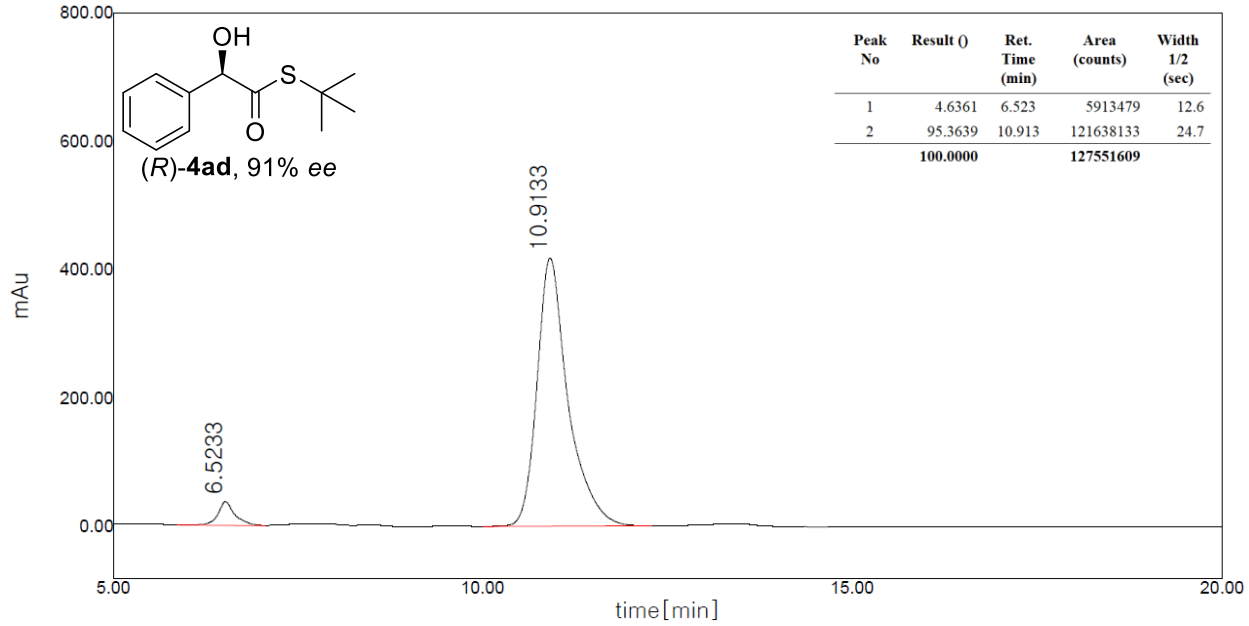
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.9337	7.287	102310773	14.0
2	50.0663	15.9383	102582438	33.8
	100.0000		**204893219**	

HPLC trace of *rac*-**4ad**



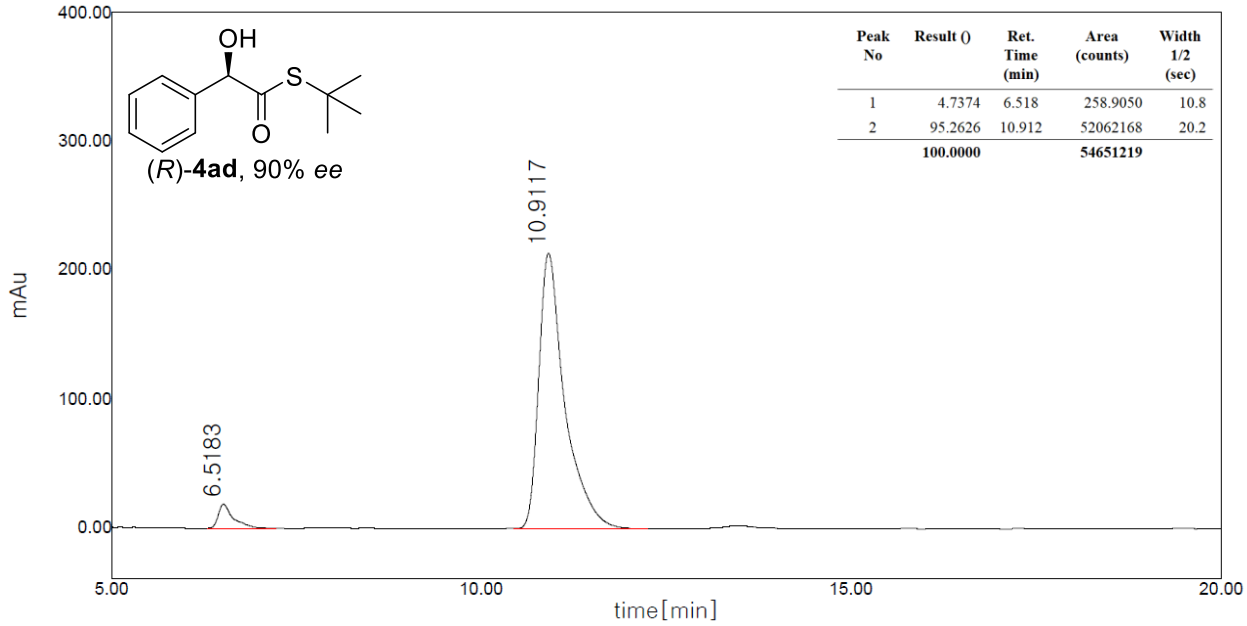
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	5.2652	6.497	4322838	12.7
2	94.7348	10.902	77779711	23.7
	100.0000		**82102547**	

HPLC trace of **4ad** (in *t*-BuSH (2 equiv)/Eucalyptol (5 equiv))



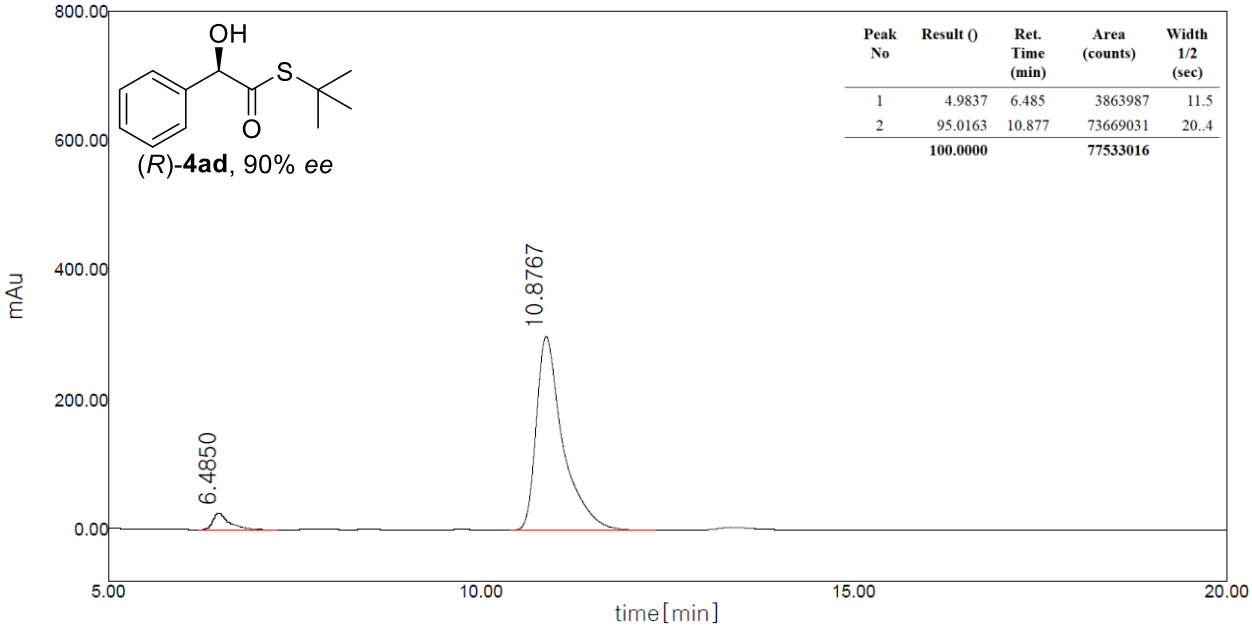
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.6361	6.523	5913479	12.6
2	95.3639	10.913	121638133	24.7
	100.0000		**127551609**	

HPLC trace of **4ad** (in *t*-BuSH (6 equiv)/Eucalyptol (5 equiv))



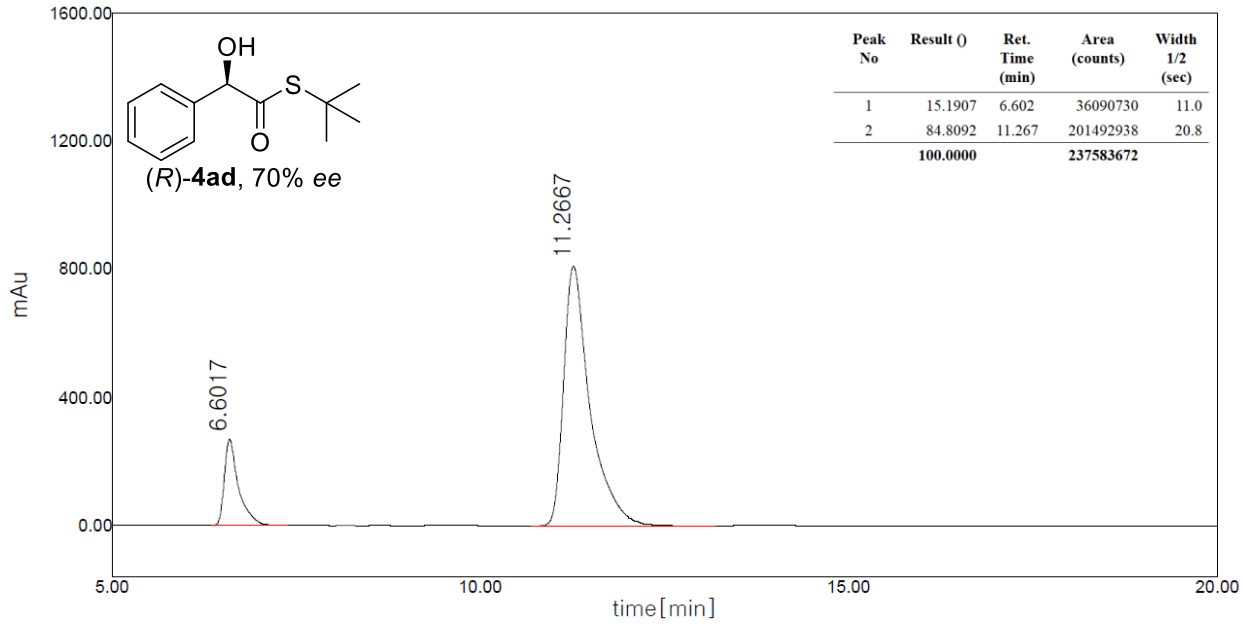
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.7374	6.518	258.9050	10.8
2	95.2626	10.912	52062168	20.2
	100.0000		**54651219**	

HPLC trace of **4ad** (in *t*-BuSH (10 equiv)/Eucalyptol (5 equiv))



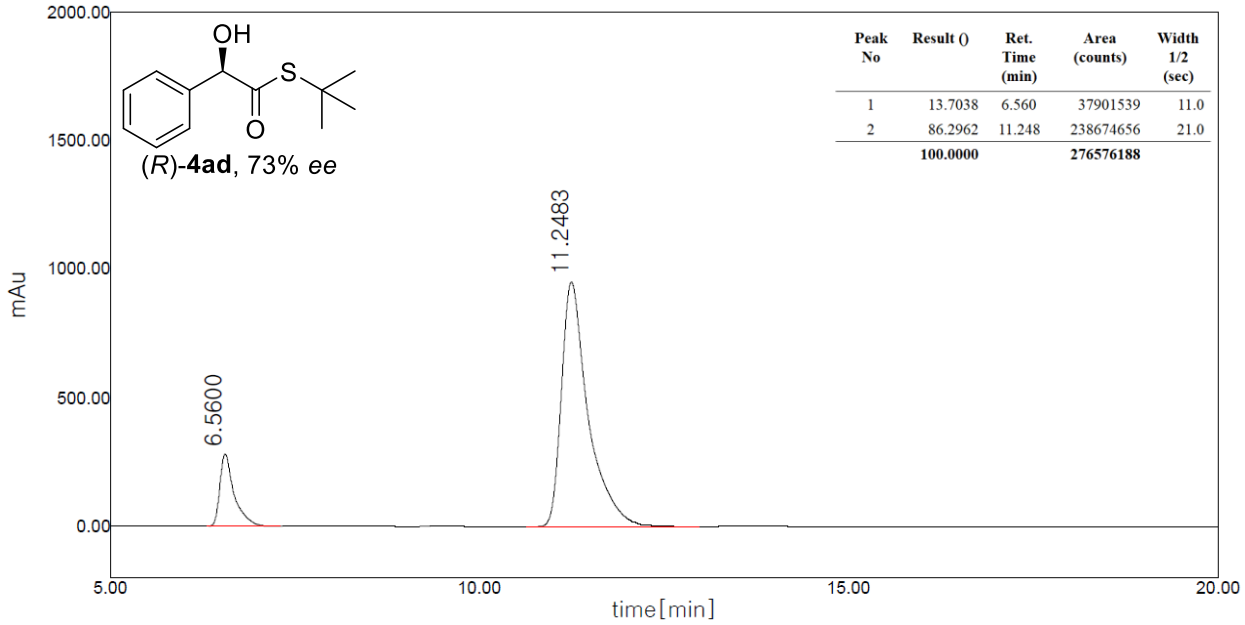
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.9837	6.485	3863987	11.5
2	95.0163	10.877	73669031	20..4
	100.0000		**77533016**	

HPLC trace of **4ad** (in *t*-BuSH (20 equiv)/Eucalyptol (5 equiv))



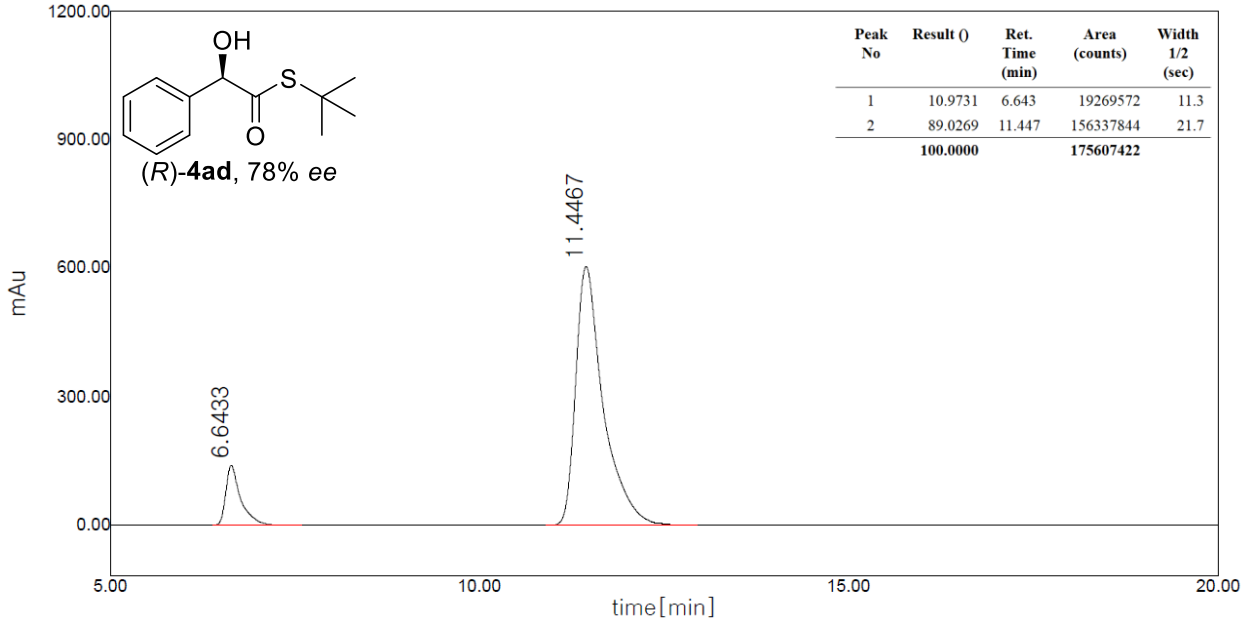
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	15.1907	6.602	36090730	11.0
2	84.8092	11.267	201492938	20.8
	100.0000		**237583672**	

HPLC trace of **4ad** (in *t*-BuSH (6 equiv))



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	13.7038	6.560	37901539	11.0
2	86.2962	11.248	238674656	21.0
	100.0000		**276576188**	

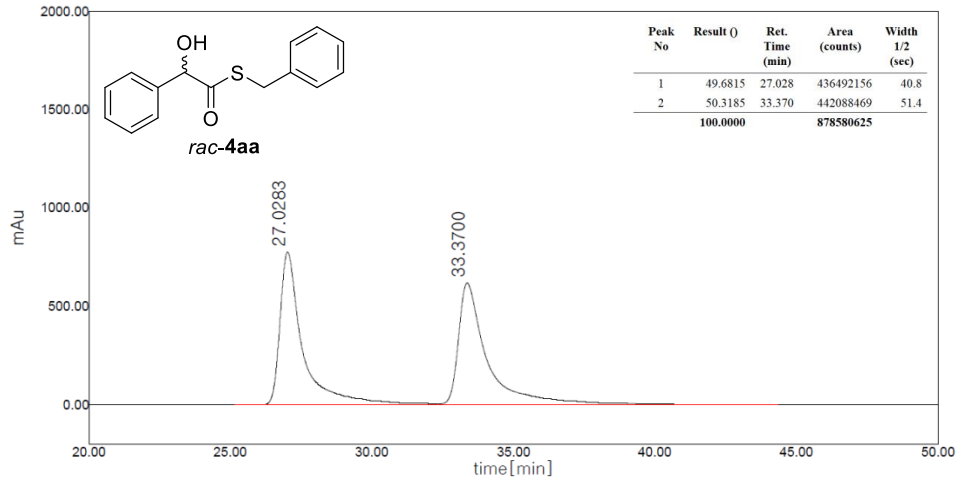
HPLC trace of **4ad** (in *t*-BuSH (10 equiv))



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.9731	6.643	19269572	11.3
2	89.0269	11.447	156337844	21.7
	100.0000		**175607422**	

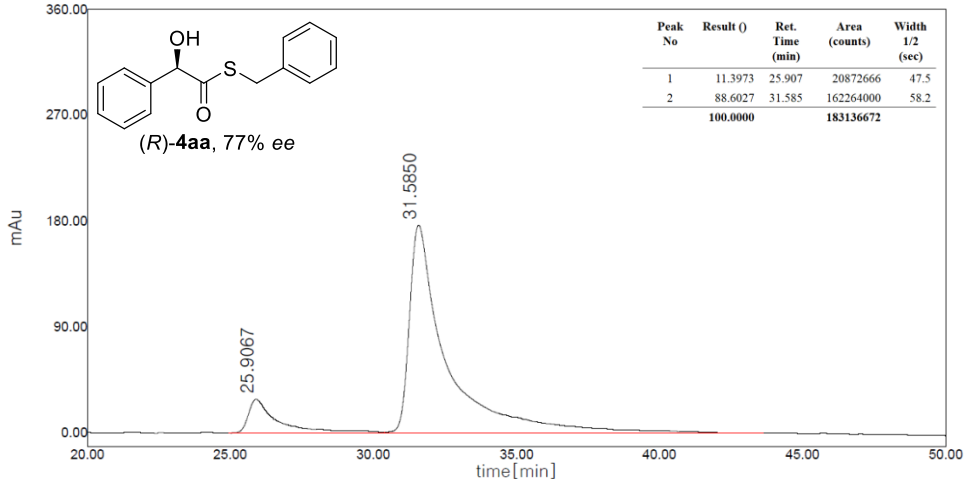
HPLC trace of **4ad** (in *t*-BuSH (20 equiv))

HPLC trace of Scheme 1C/Figure S1



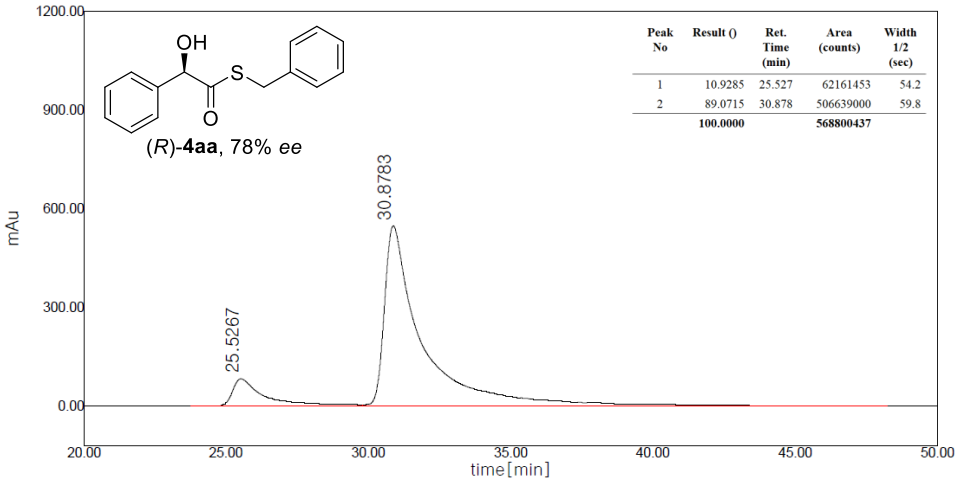
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6815	27.028	436492156	40.8
2	50.3185	33.370	442088469	51.4
	100.0000		878580625	

HPLC trace of *rac*-**4aa**



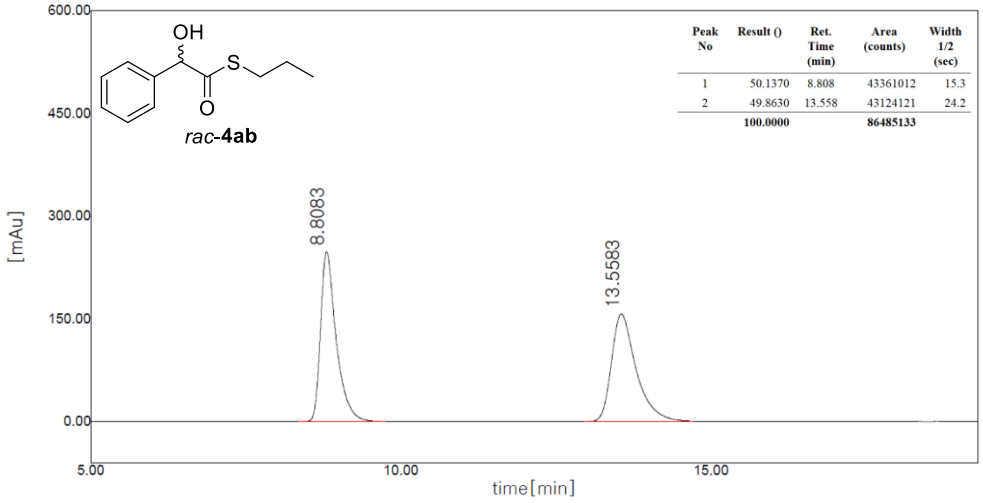
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	11.3973	25.907	20872666	47.5
2	88.6027	31.585	162264000	58.2
	100.0000		183136672	

HPLC trace of **4aa**-1.2 equiv. of **2a**/5 equiv. of eucalyptol



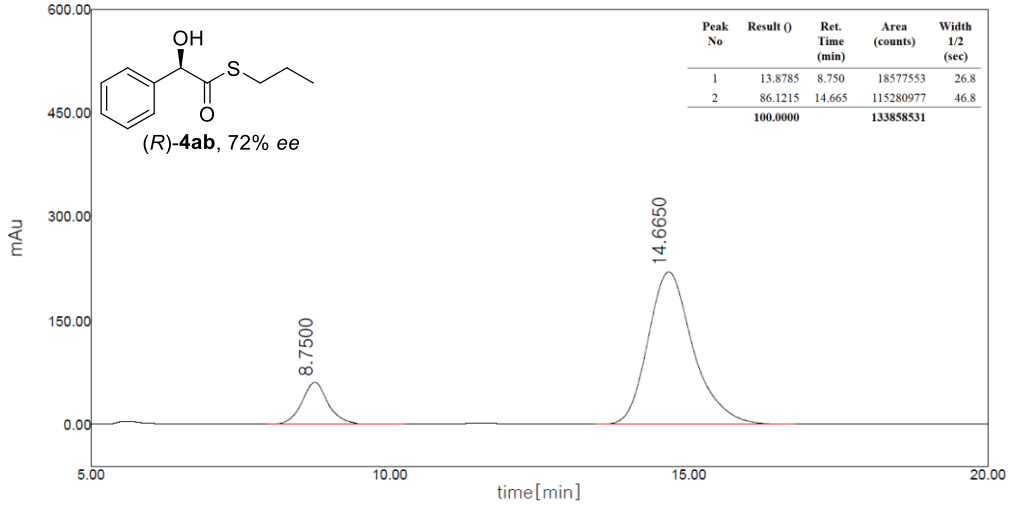
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.9285	25.527	62161453	54.2
2	89.0715	30.878	506639000	59.8
	100.0000		568800437	

HPLC trace of **4aa**-10 equiv. of **2a**/10 equiv. of eucalyptol



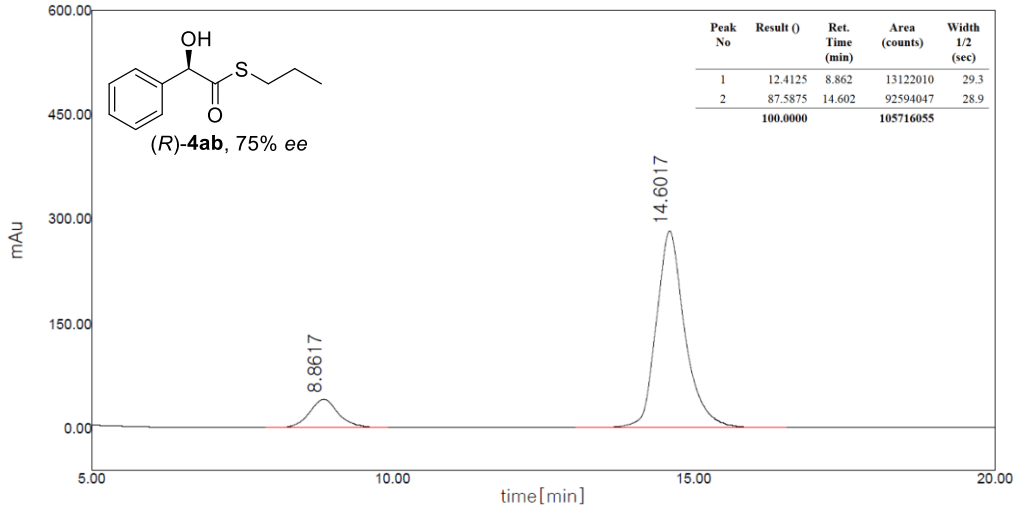
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.1370	8.808	43361012	15.3
2	49.8630	13.558	43124121	24.2
	100.0000		86485133	

HPLC trace of *rac*-**4ab**



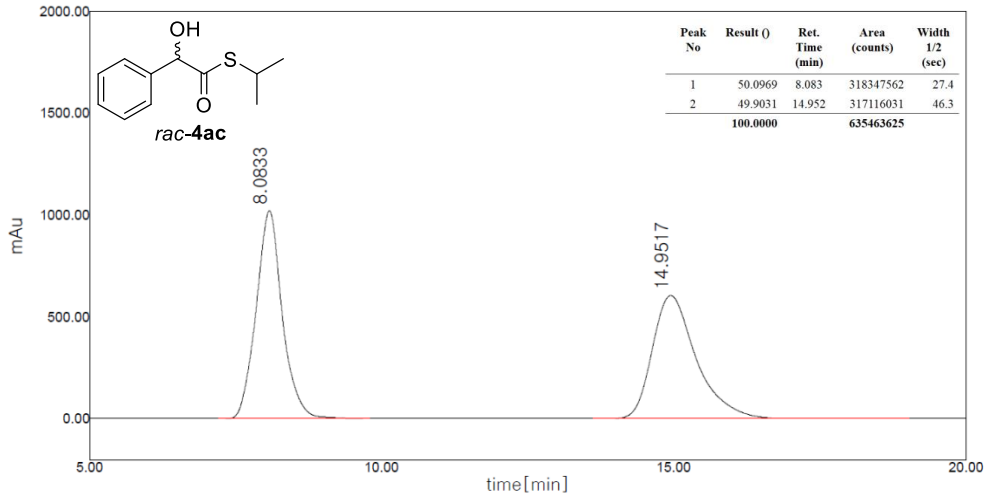
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	13.8785	8.750	18577553	26.8
2	86.1215	14.665	115280977	46.8
	100.0000		133858531	

HPLC trace of **4ab**-1.2 equiv. of **2a**/5 equiv. of eucalyptol



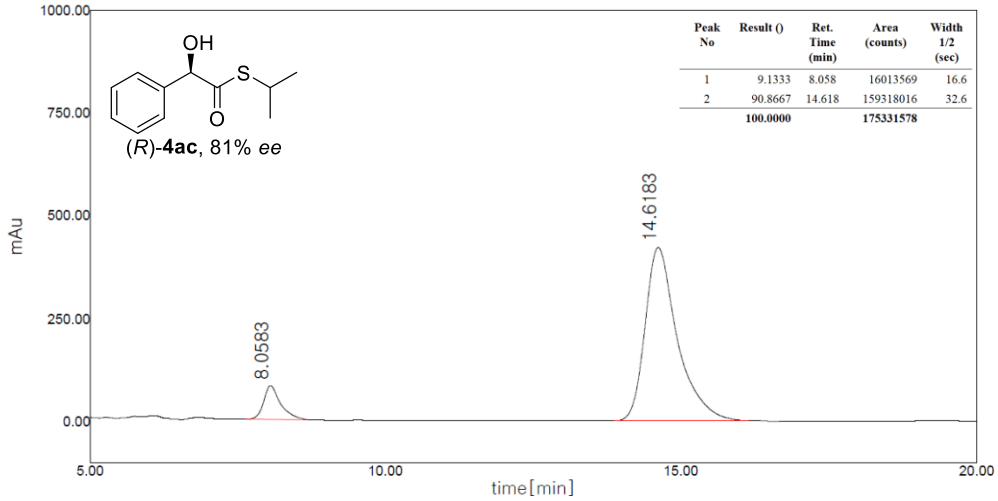
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	12.4125	8.862	13122010	29.3
2	87.5875	14.602	92594047	28.9
	100.0000		105716055	

HPLC trace of **4ab**-10 equiv. of **2a**/10 equiv. of eucalyptol



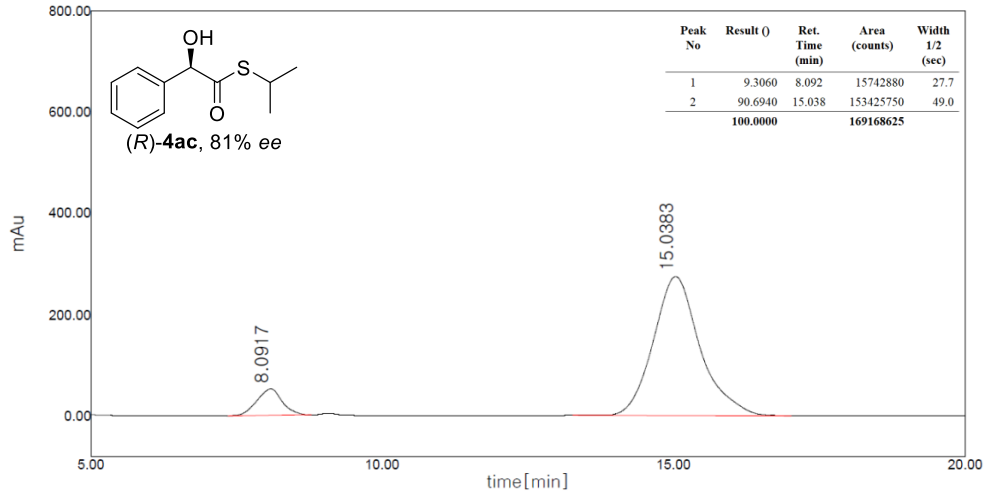
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0969	8.083	318347562	27.4
2	49.9031	14.952	317116031	46.3
	100.0000		635463625	

HPLC trace of *rac*-**4ac**



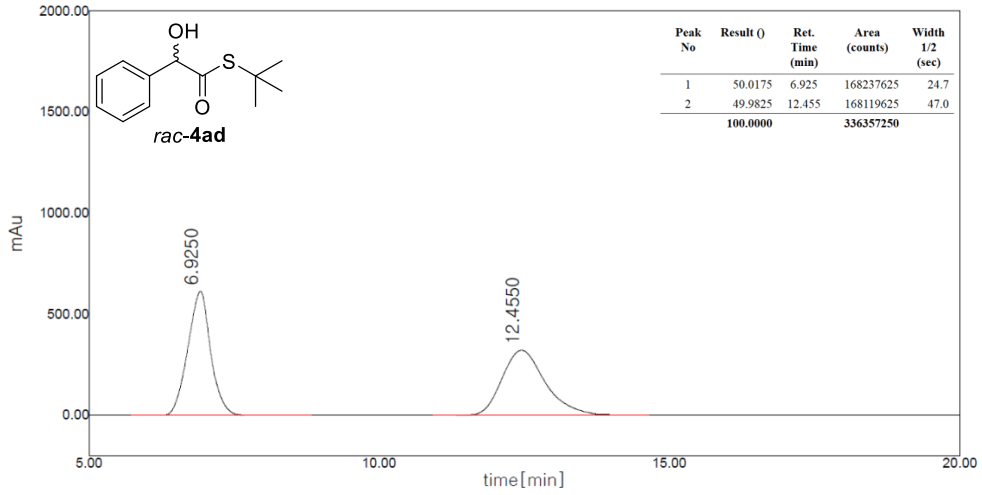
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	9.1333	8.058	16013569	16.6
2	90.8667	14.618	159318016	32.6
	100.0000		175331578	

HPLC trace of **4ac**-1.2 equiv. of **2a**/5 equiv. of eucalyptol



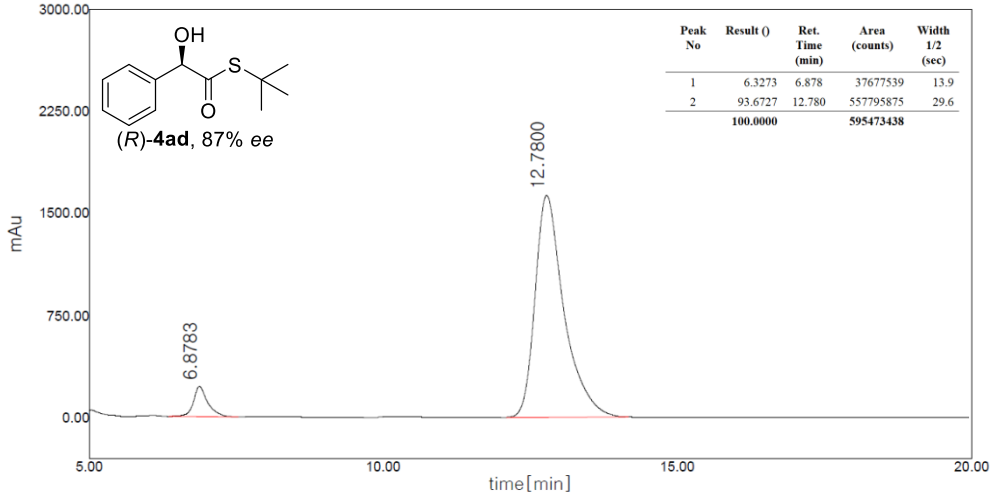
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	9.3060	8.092	15742880	27.7
2	90.6940	15.038	153425750	49.0
	100.0000		169168625	

HPLC trace of **4ac**-10 equiv. of **2a**/10 equiv. of eucalyptol



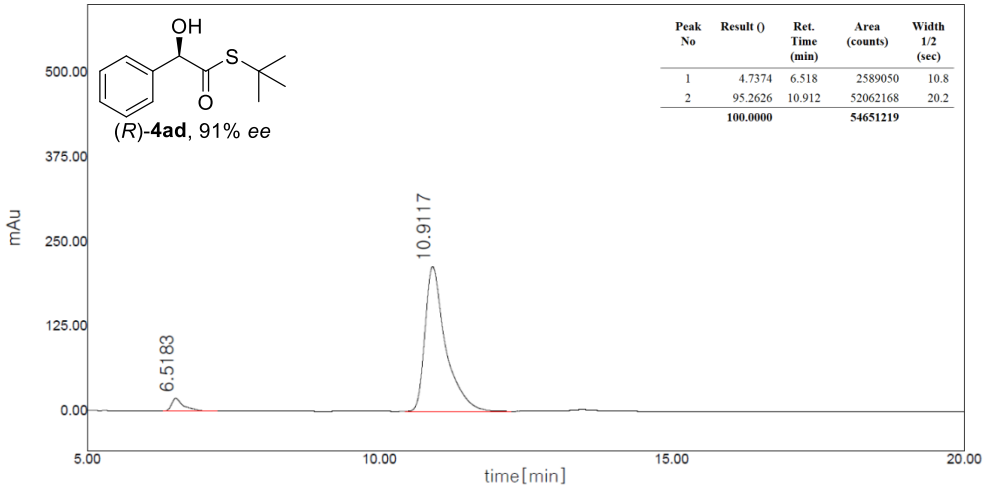
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0175	6.925	168237625	24.7
2	49.9825	12.455	168119625	47.0
	100.0000		**336357250**	

HPLC trace of *rac*-**4ad**



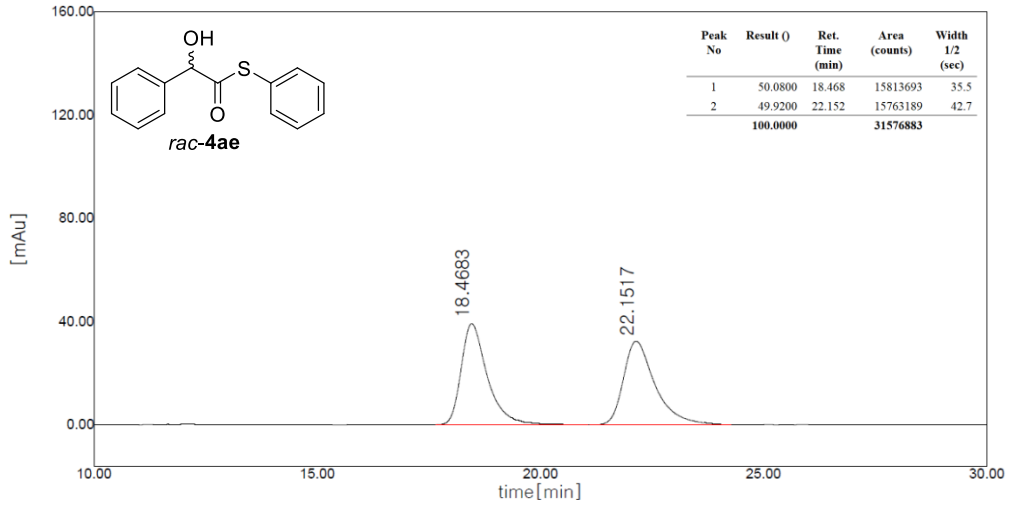
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.3273	6.878	37677539	13.9
2	93.6727	12.780	557795875	29.6
	100.0000		**595473438**	

HPLC trace of **4ad**-1.2 equiv. of **2a**/5 equiv. of eucalyptol

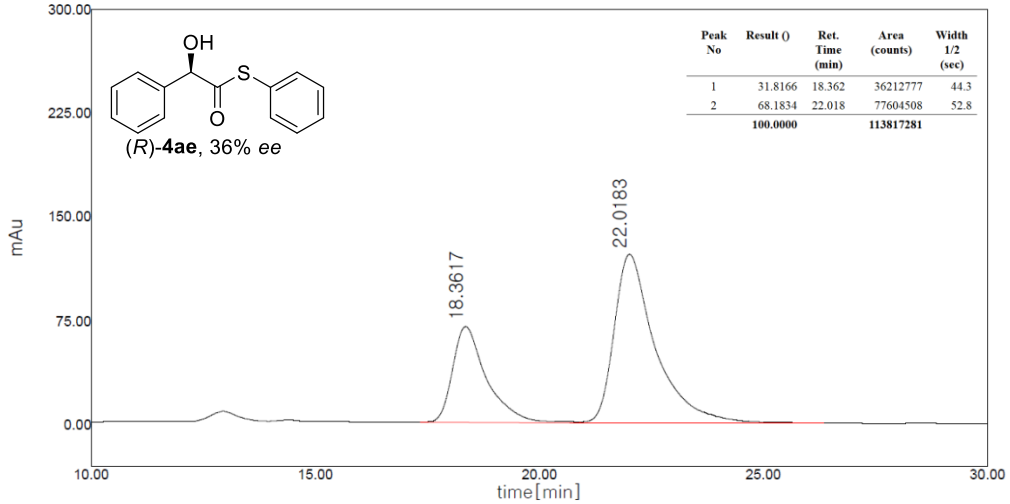


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.7374	6.518	2589050	10.8
2	95.2626	10.912	52062168	20.2
	100.0000		**54651219**	

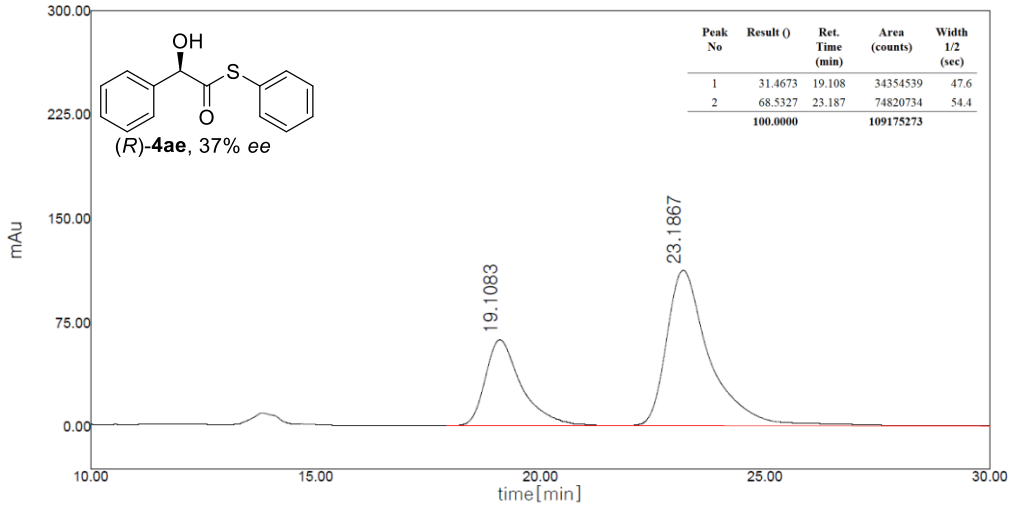
HPLC trace of **4ad**-10 equiv. of **2a**/10 equiv. of eucalyptol



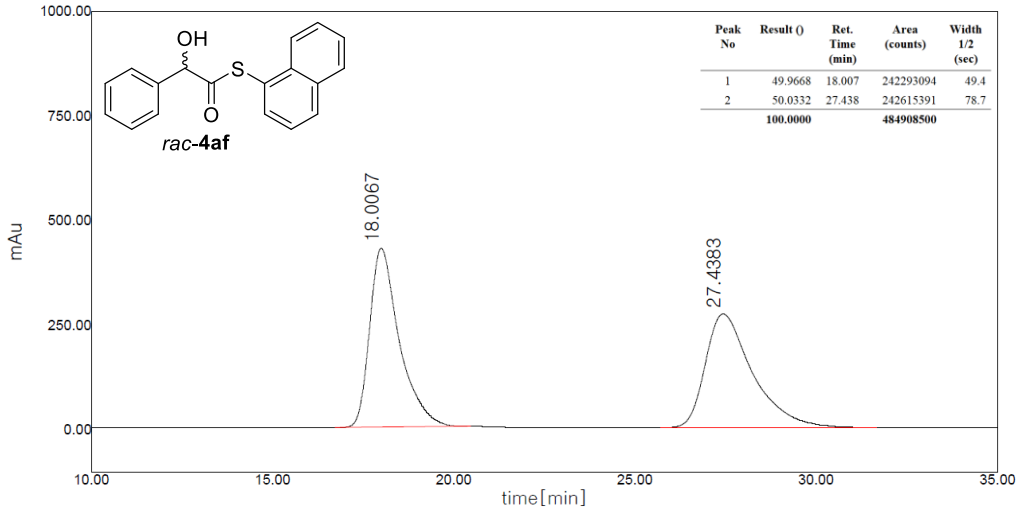
HPLC trace of *rac*-**4ae**



HPLC trace of **4ae**-1.2 equiv. of **2a**/5 equiv. of eucalyptol

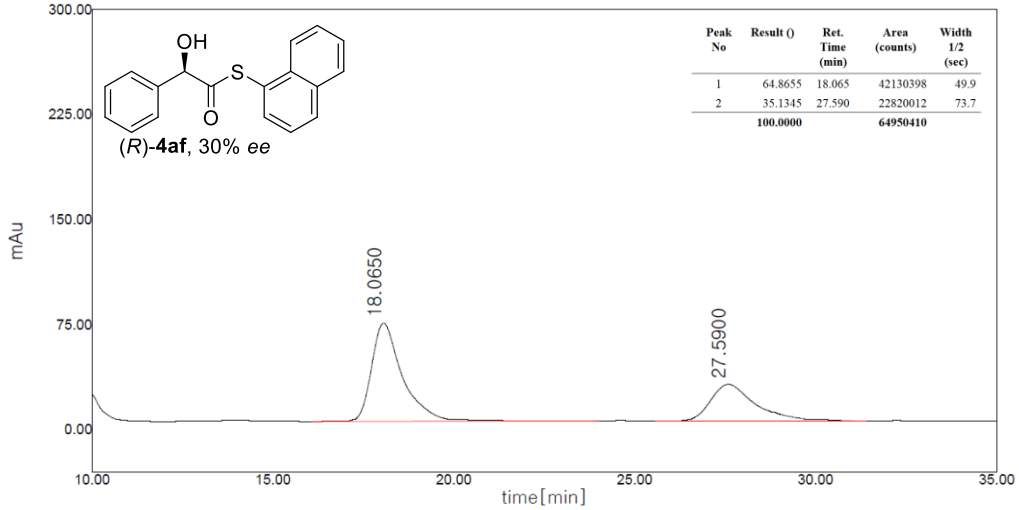


HPLC trace of **4ae**-10 equiv. of **2a**/10 equiv. of eucalyptol



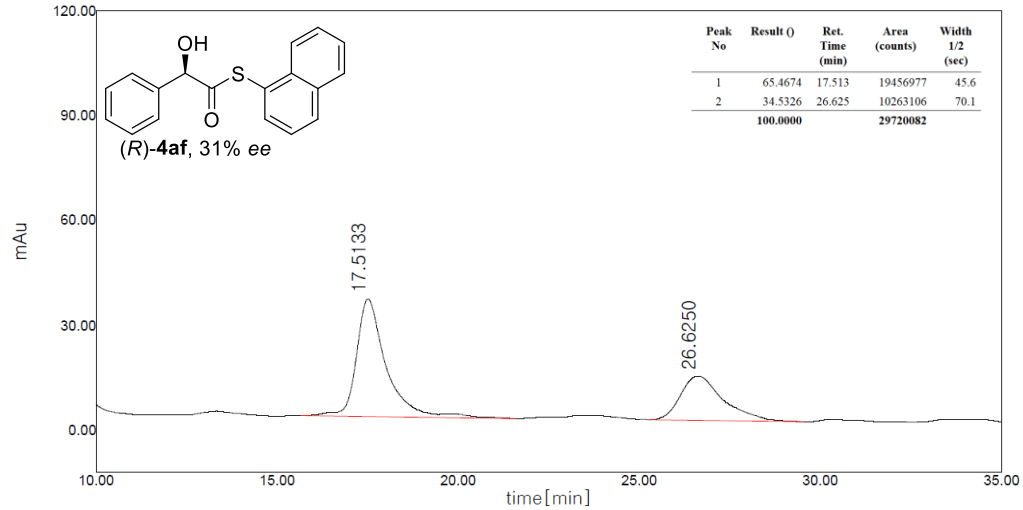
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.9668	18.007	242293094	49.4
2	50.0332	27.438	242615391	78.7
	100.0000		484908500	

HPLC trace of *rac*-**4af**



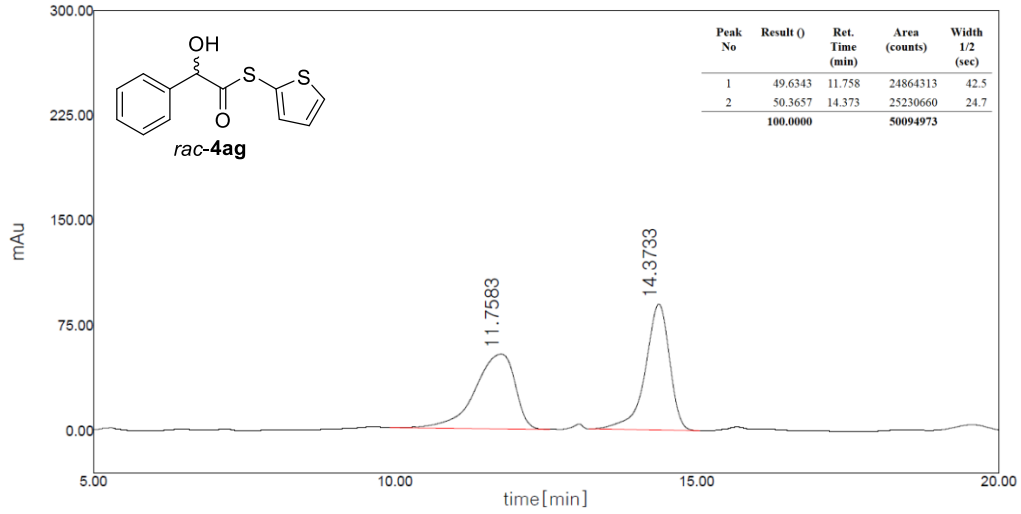
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	64.8655	18.065	42130398	49.9
2	35.1345	27.590	22820012	73.7
	100.0000		64950410	

HPLC trace of **4af**-1.2 equiv. of **2a**/5 equiv. of eucalyptol



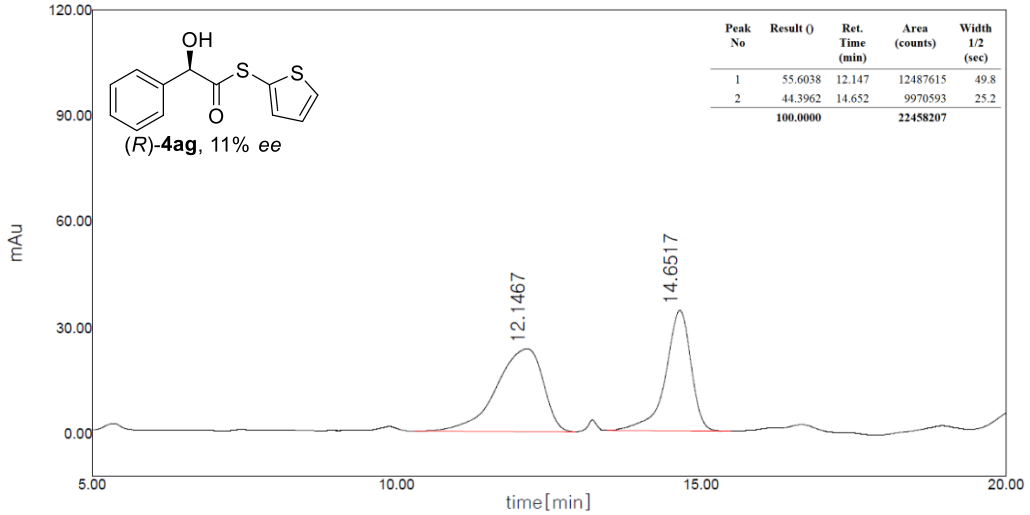
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	65.4674	17.513	19456977	45.6
2	34.5326	26.625	10263106	70.1
	100.0000		29720082	

HPLC trace of **4af**-10 equiv. of **2a**/10 equiv. of eucalyptol



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6343	11.758	24864313	42.5
2	50.3657	14.373	25230660	24.7
	100.0000		**50094973**	

HPLC trace of *rac*-**4ag**

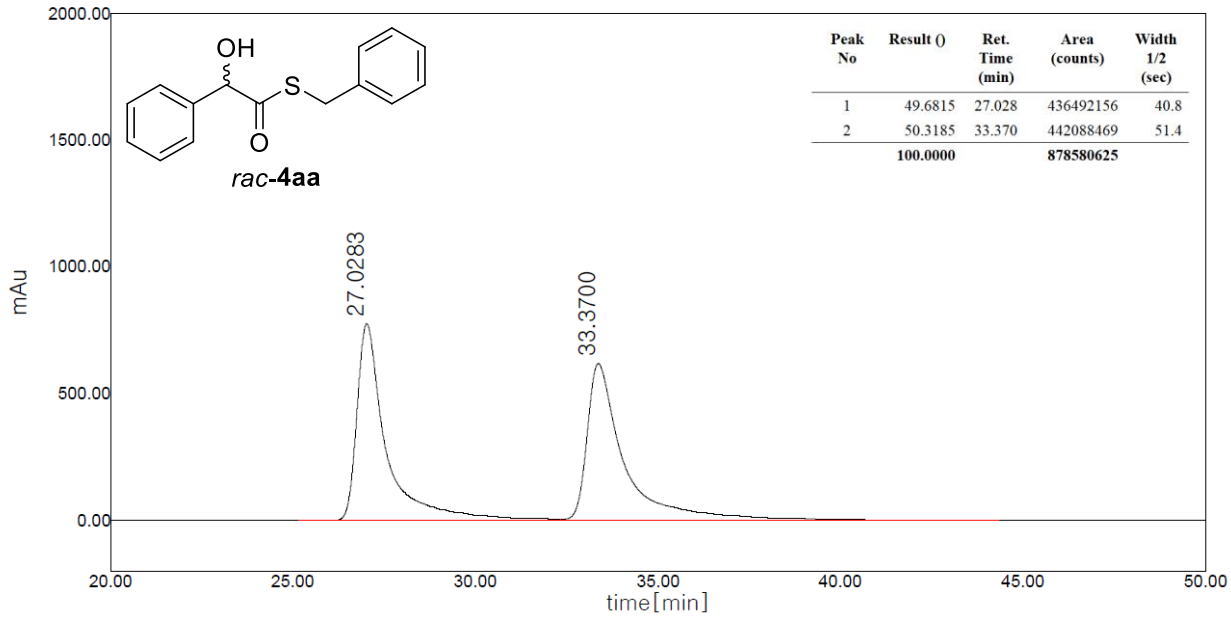


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	55.6038	12.147	12487615	49.8
2	44.3962	14.652	9970593	25.2
	100.0000		**22458207**	

HPLC trace of **4ag**-10 equiv. of **2a**/10 equiv. of eucalyptol

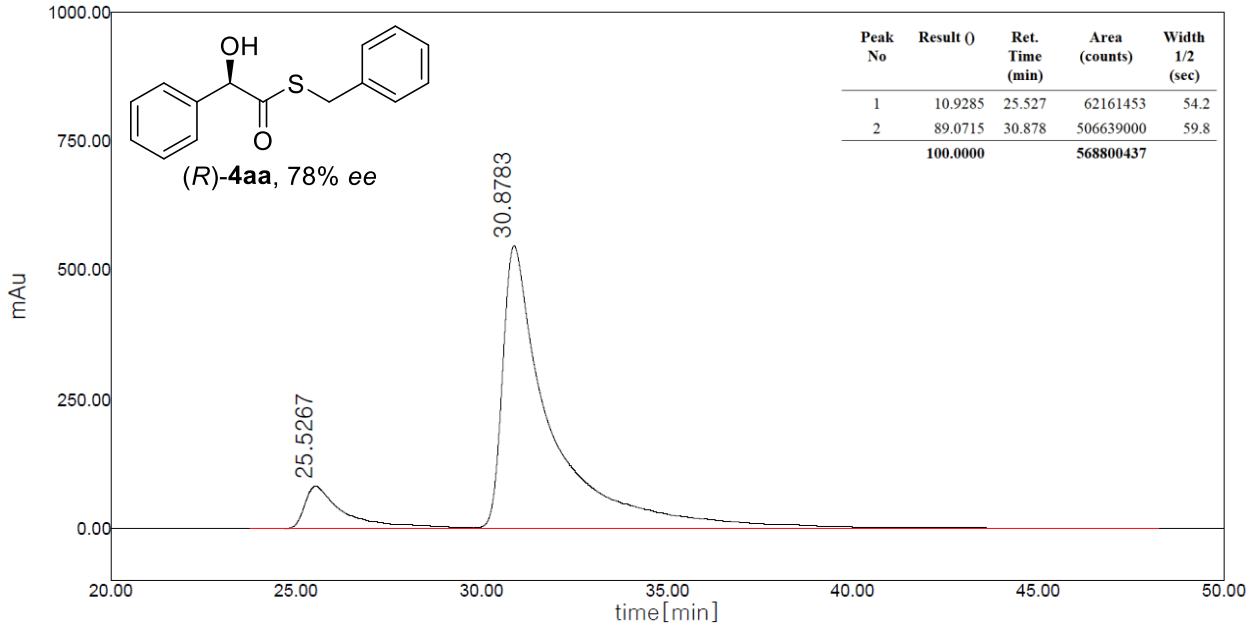
HPLC traces of Scheme 2C

10 equiv. of thiol/10 equiv. of eucalyptol



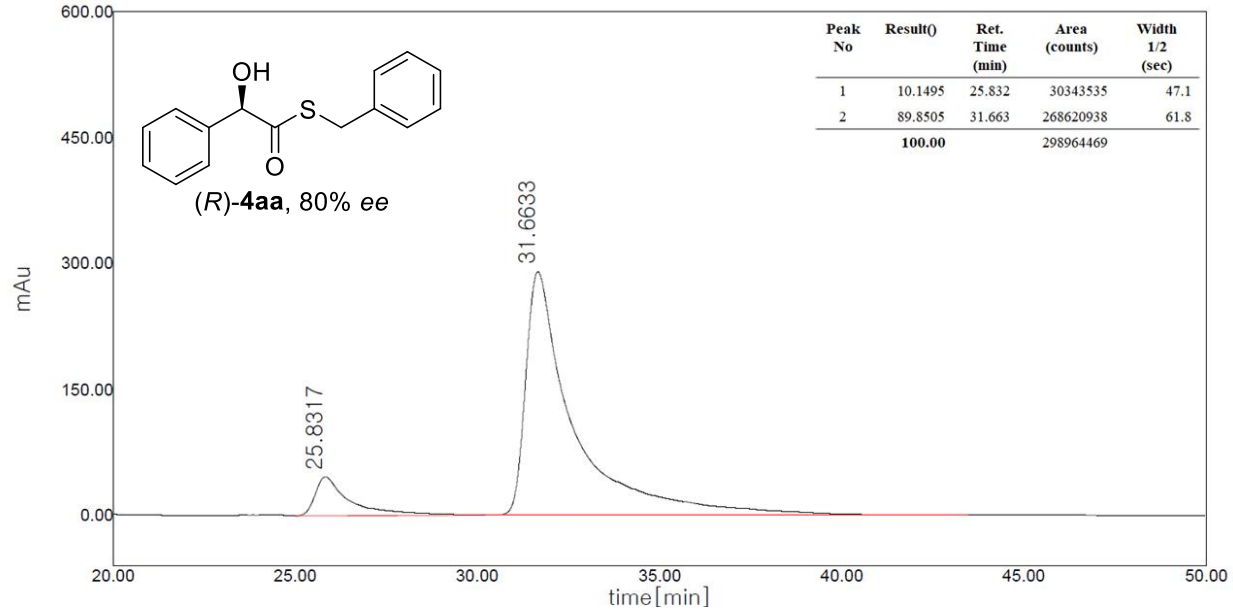
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6815	27.028	436492156	40.8
2	50.3185	33.370	442088469	51.4
	100.0000		**878580625**	

HPLC trace of *rac*-**4aa**



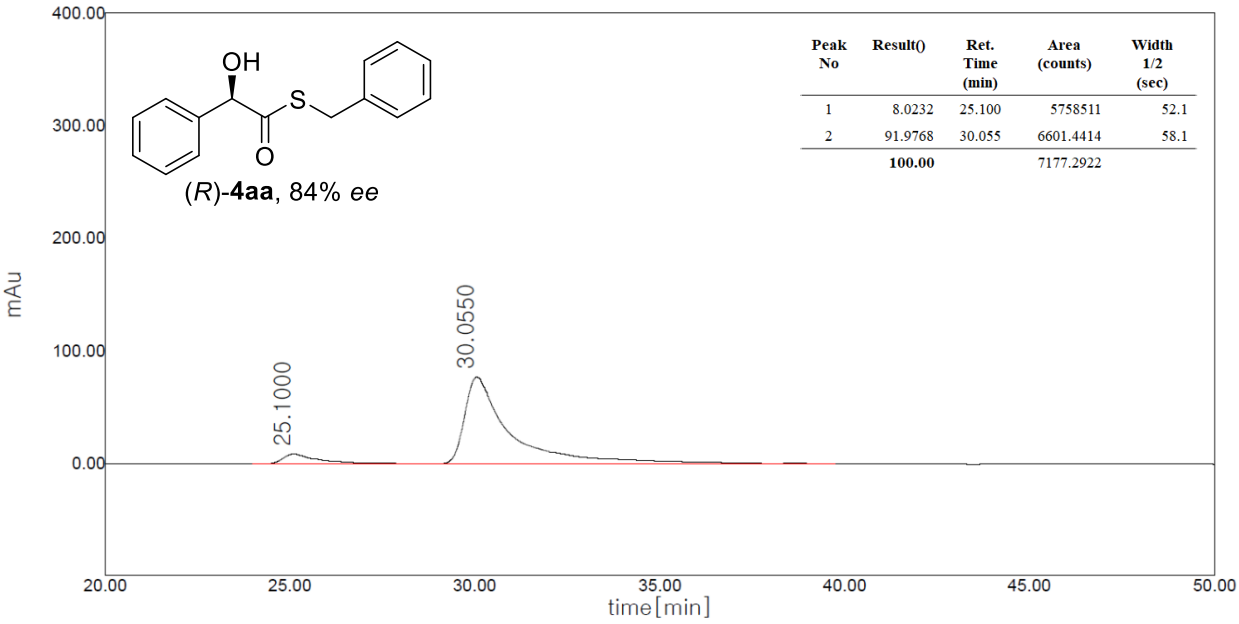
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.9285	25.527	62161453	54.2
2	89.0715	30.878	506639000	59.8
	100.0000		**568800437**	

HPLC trace of **4aa** (condition a)



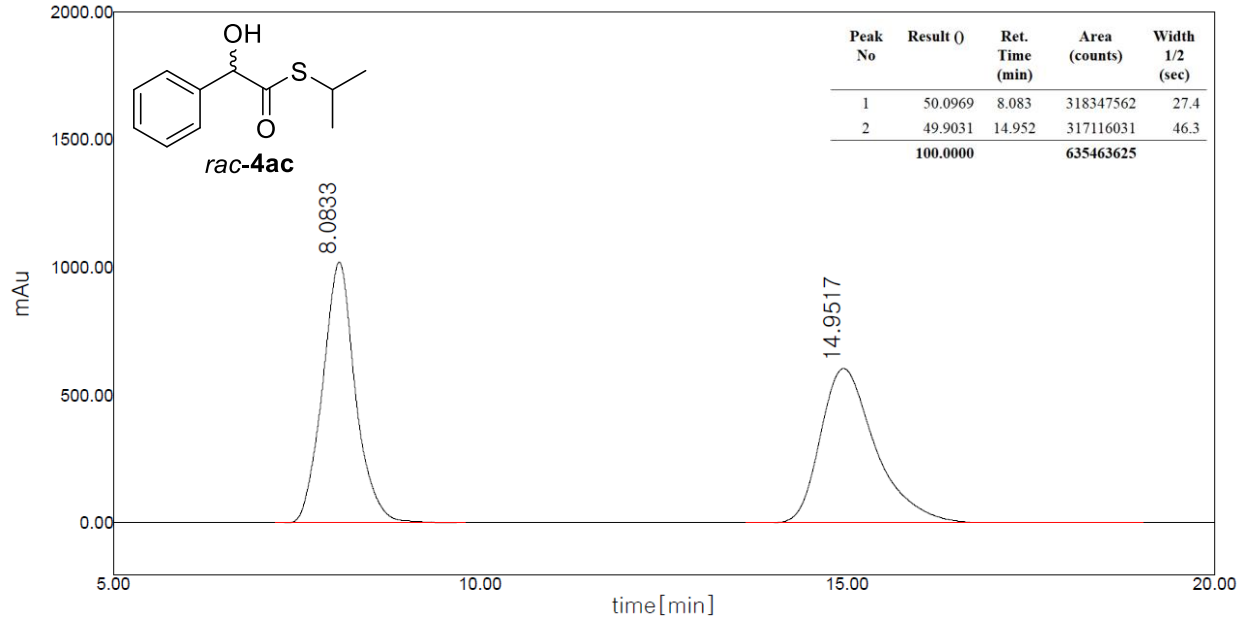
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.1495	25.832	30343535	47.1
2	89.8505	31.663	268620938	61.8
	100.00		298964469	

HPLC trace of **4aa** (condition b)



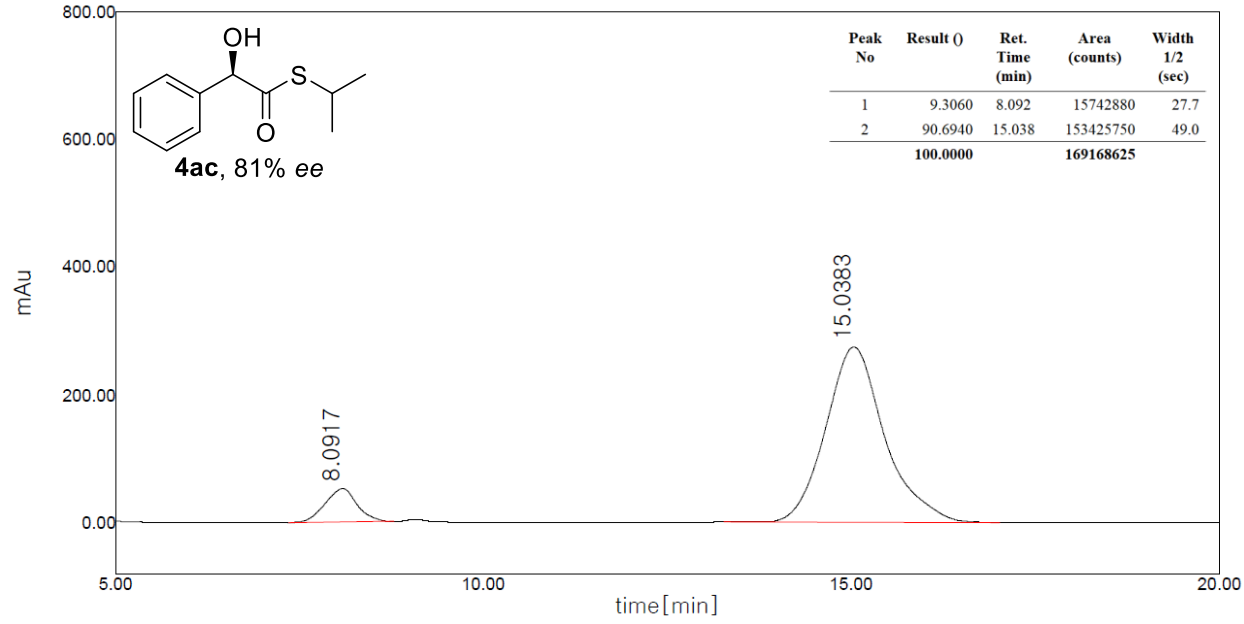
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	8.0232	25.100	5758511	52.1
2	91.9768	30.055	6601.4414	58.1
	100.00		7177.2922	

HPLC trace of **4aa** (condition c)



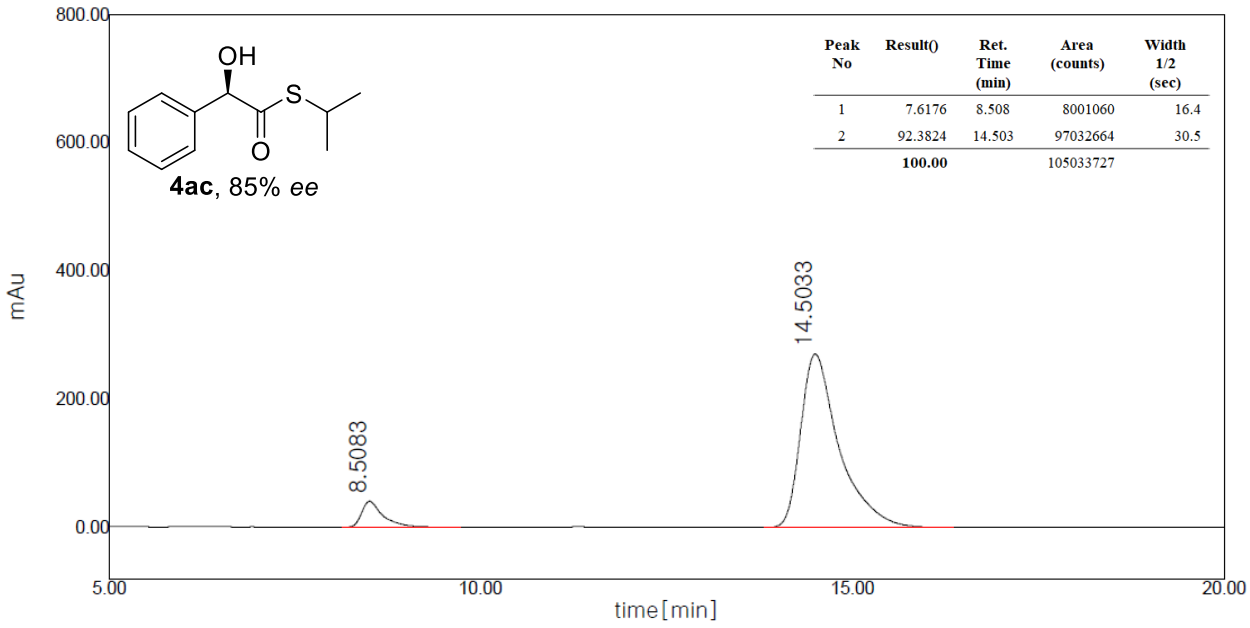
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0969	8.083	318347562	27.4
2	49.9031	14.952	317116031	46.3
	100.0000		**635463625**	

HPLC trace of *rac*-**4ac**

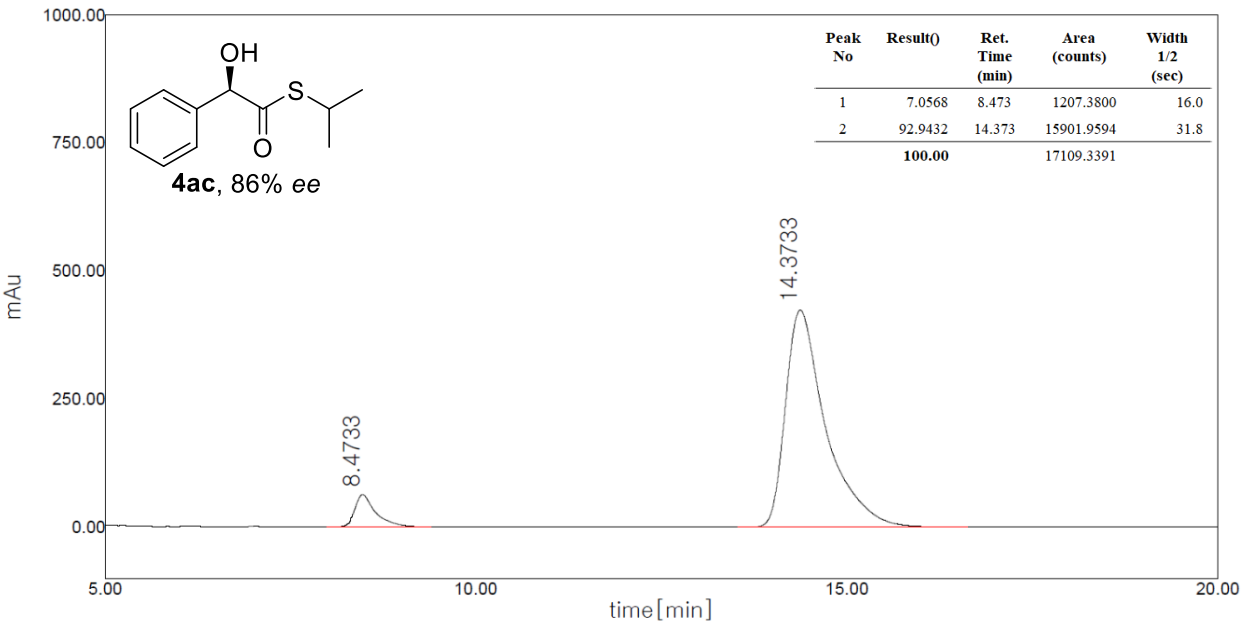


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	9.3060	8.092	15742880	27.7
2	90.6940	15.038	153425750	49.0
	100.0000		**169168625**	

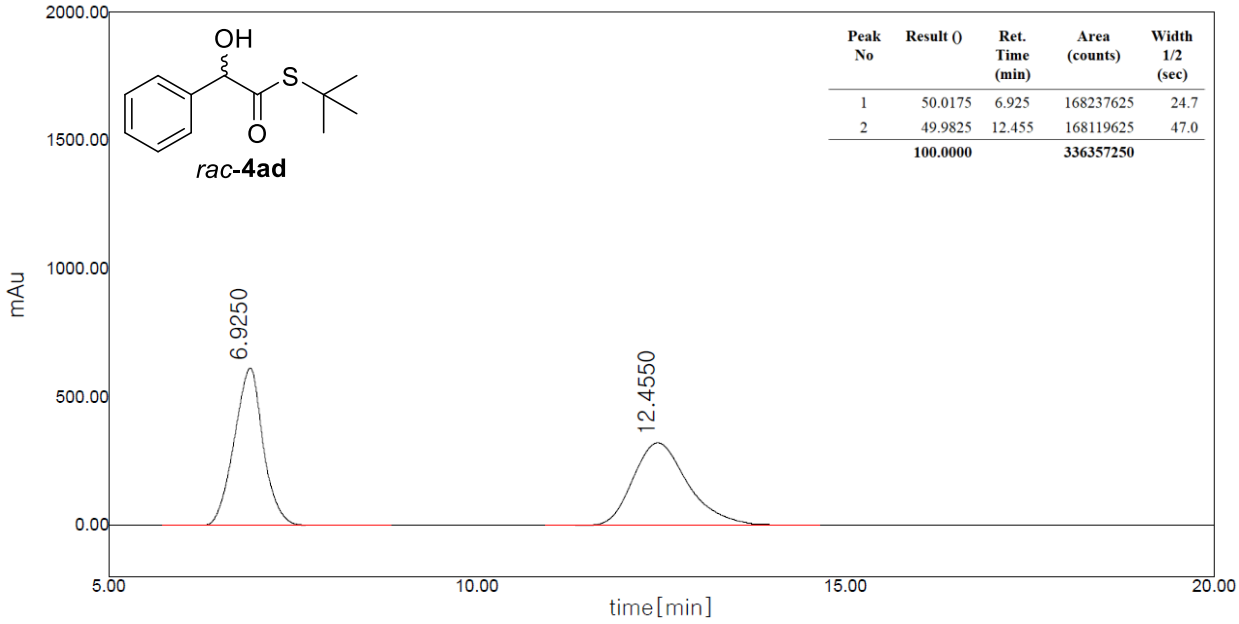
HPLC trace of **4ac** (condition a)



HPLC trace of **4ac** (condition b)

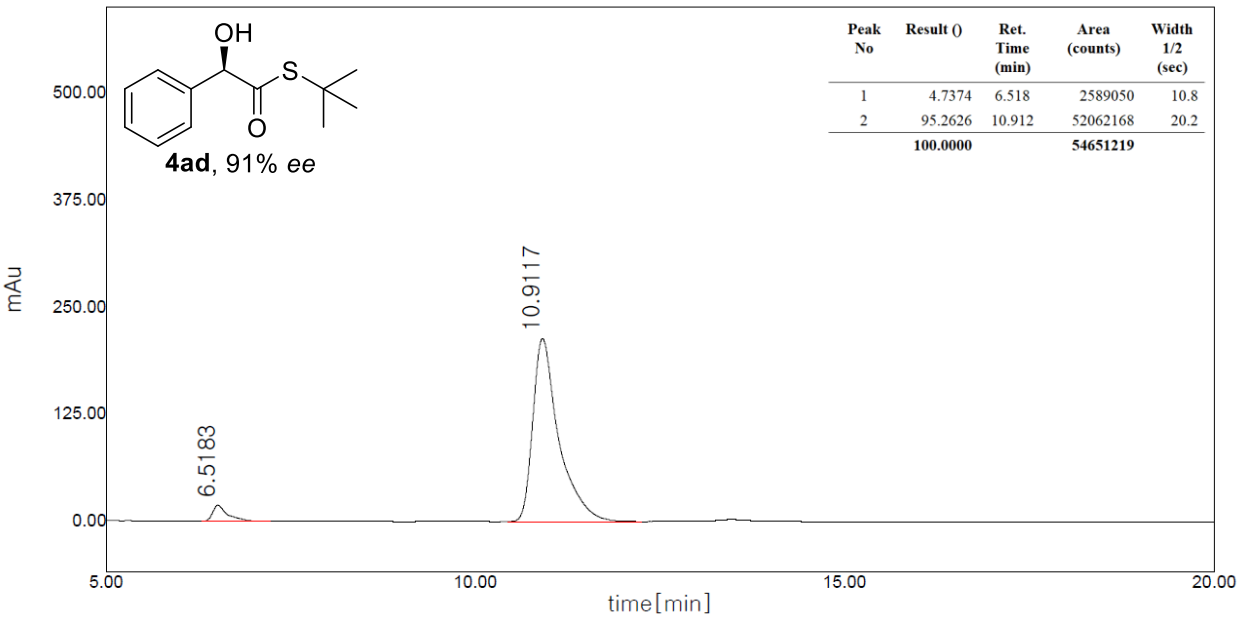


HPLC trace of **4ac** (condition c)



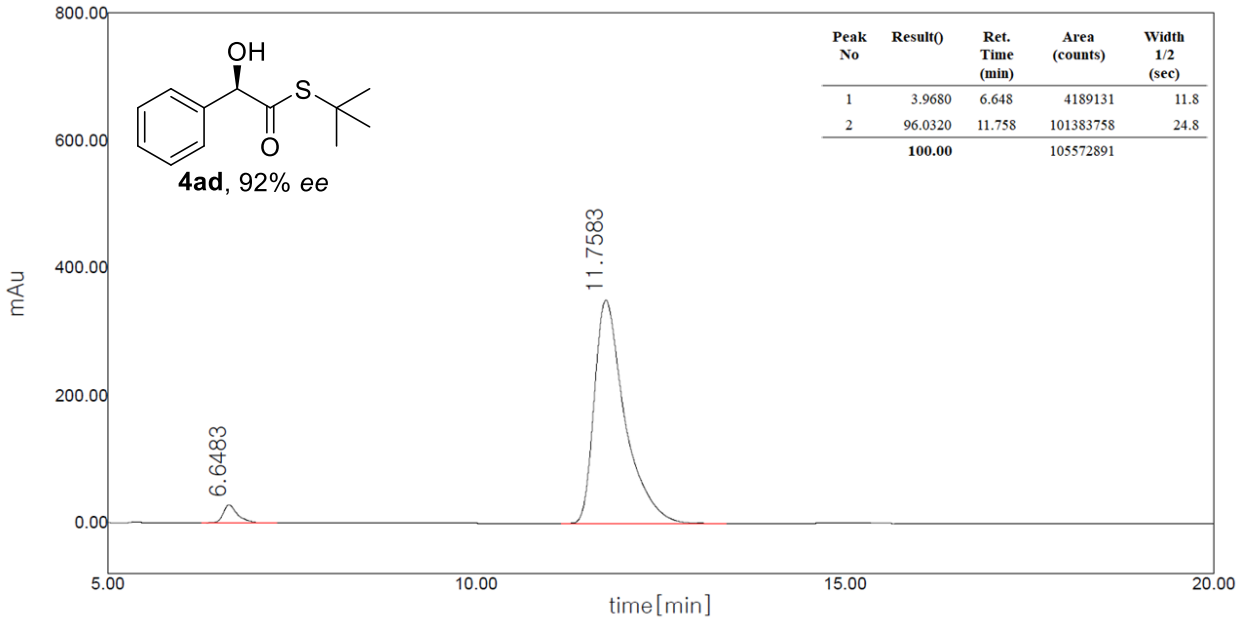
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0175	6.925	168237625	24.7
2	49.9825	12.455	168119625	47.0
	100.0000		**336357250**	

HPLC trace of *rac*-**4ad**



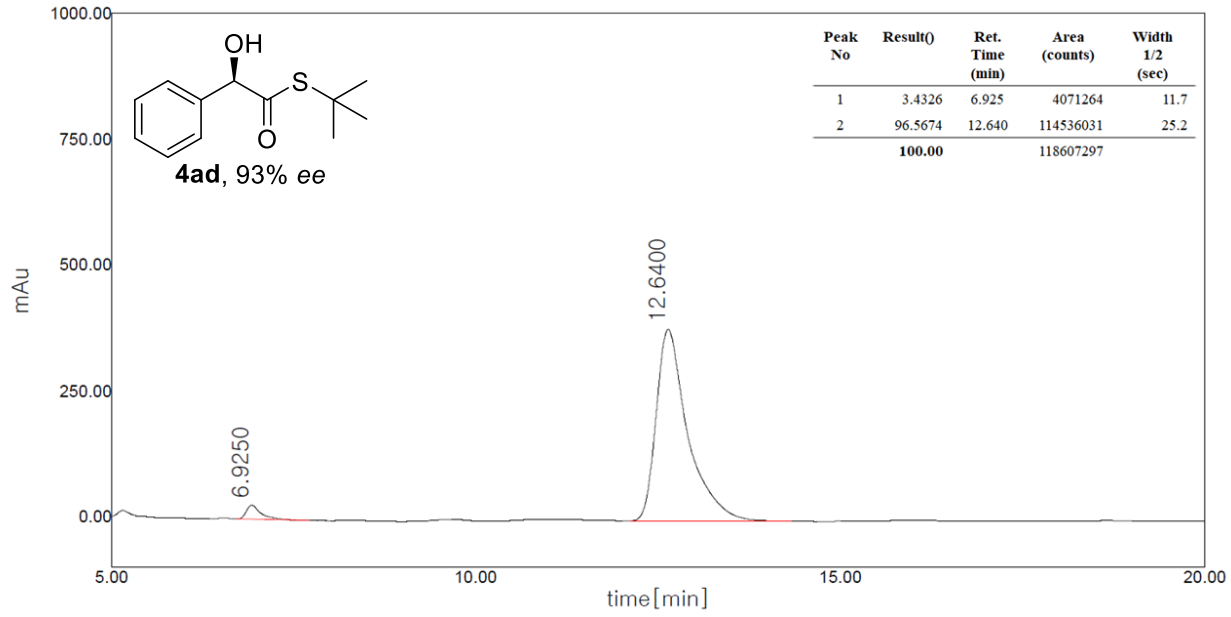
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.7374	6.518	2589050	10.8
2	95.2626	10.912	52062168	20.2
	100.0000		**54651219**	

HPLC trace of **4ad** (condition a)



Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	3.9680	6.648	4189131	11.8
2	96.0320	11.758	101383758	24.8
	100.00		105572891	

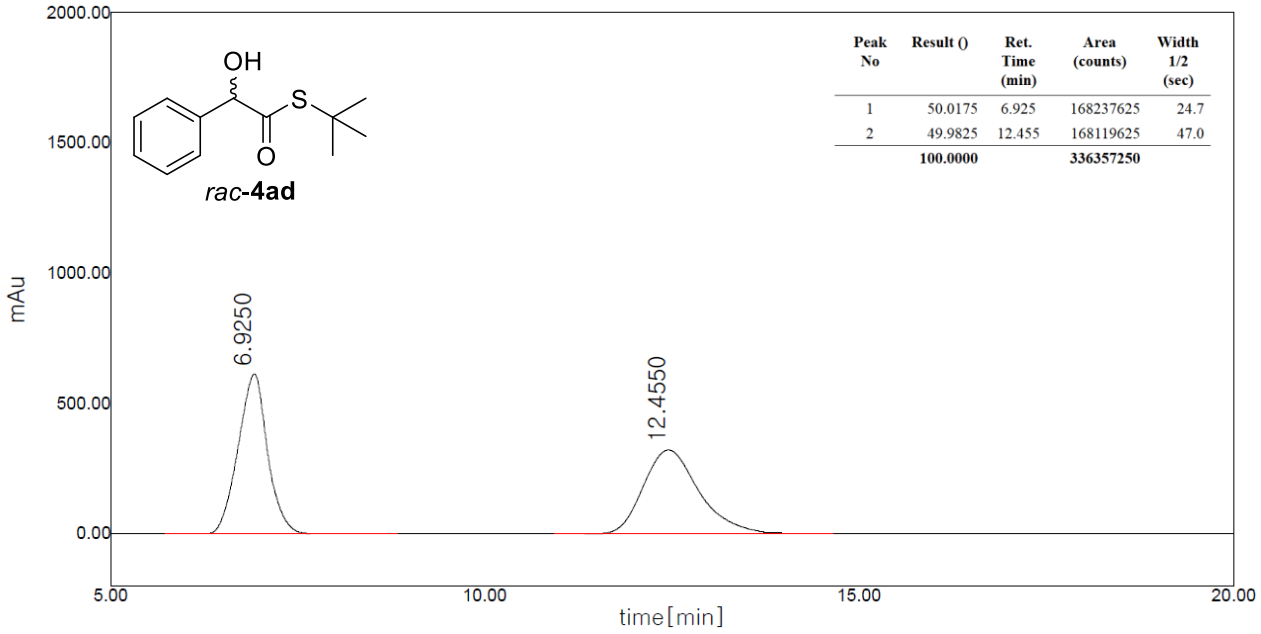
HPLC trace of **4ad** (condition b)



Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	3.4326	6.925	4071264	11.7
2	96.5674	12.640	114536031	25.2
	100.00		118607297	

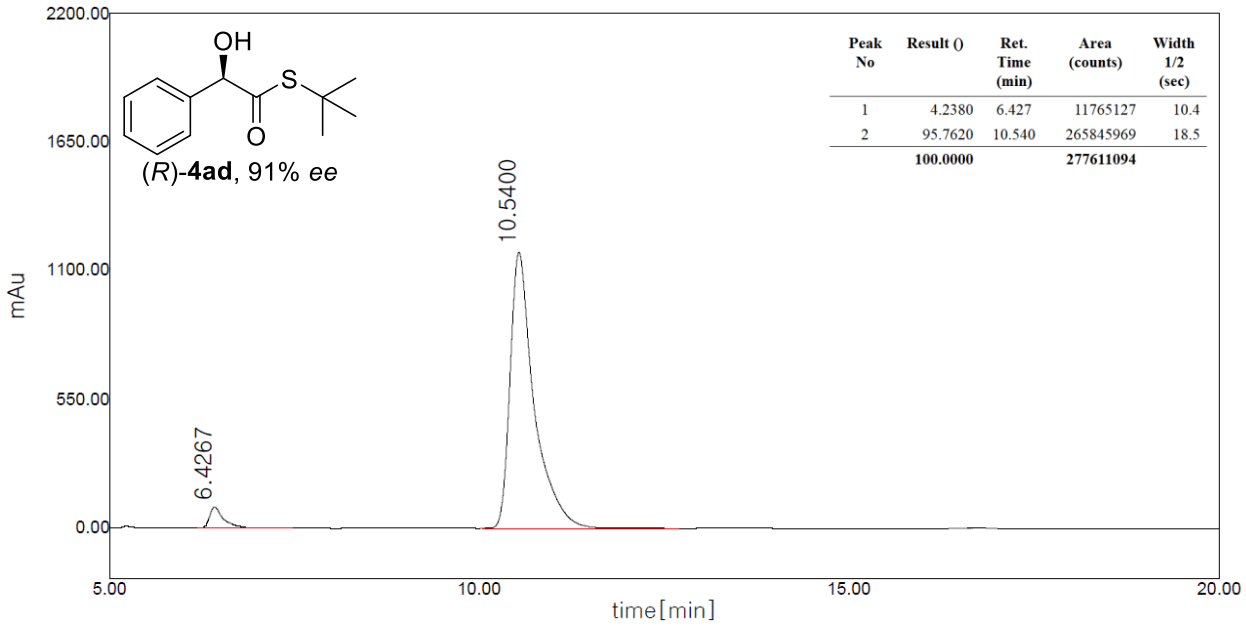
HPLC trace of **4ad** (condition c)

HPLC trace of Scheme 3



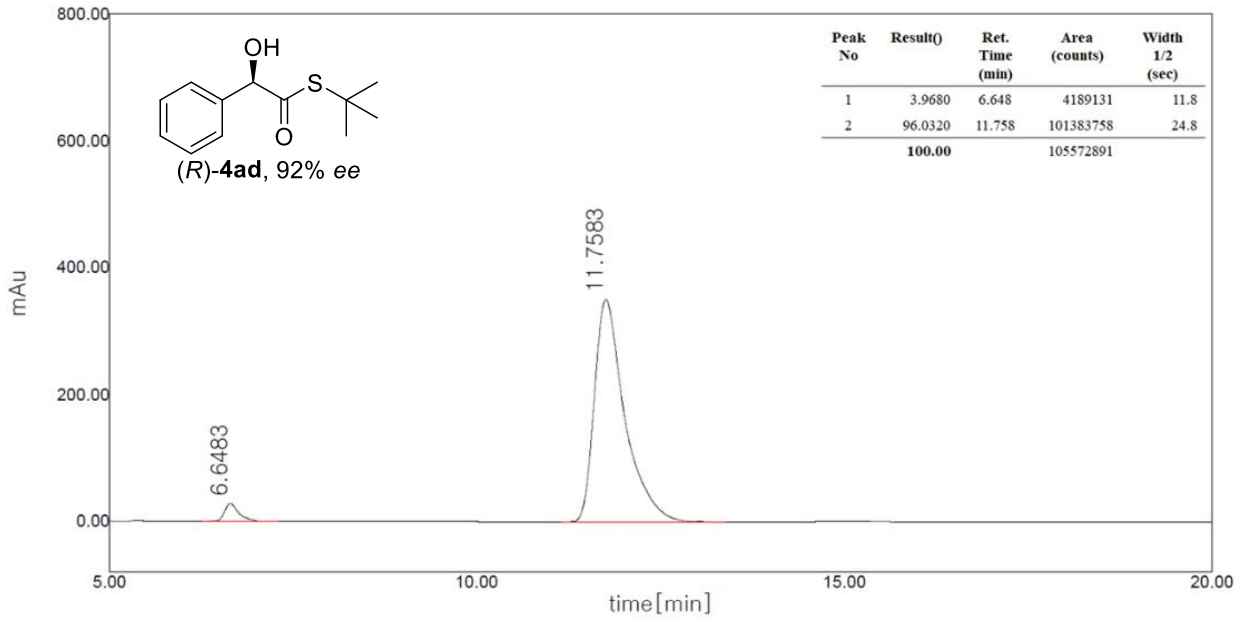
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0175	6.925	168237625	24.7
2	49.9825	12.455	168119625	47.0
	100.0000		**336357250**	

HPLC trace of *rac*-**4ad**

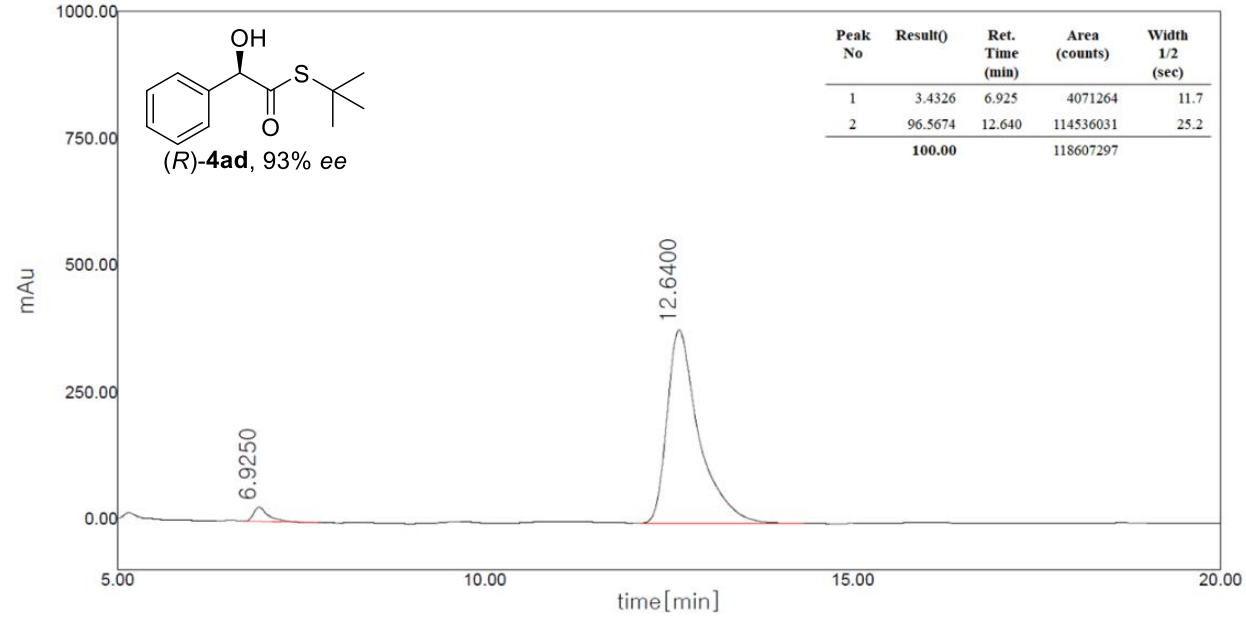


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.2380	6.427	11765127	10.4
2	95.7620	10.540	265845969	18.5
	100.0000		**277611094**	

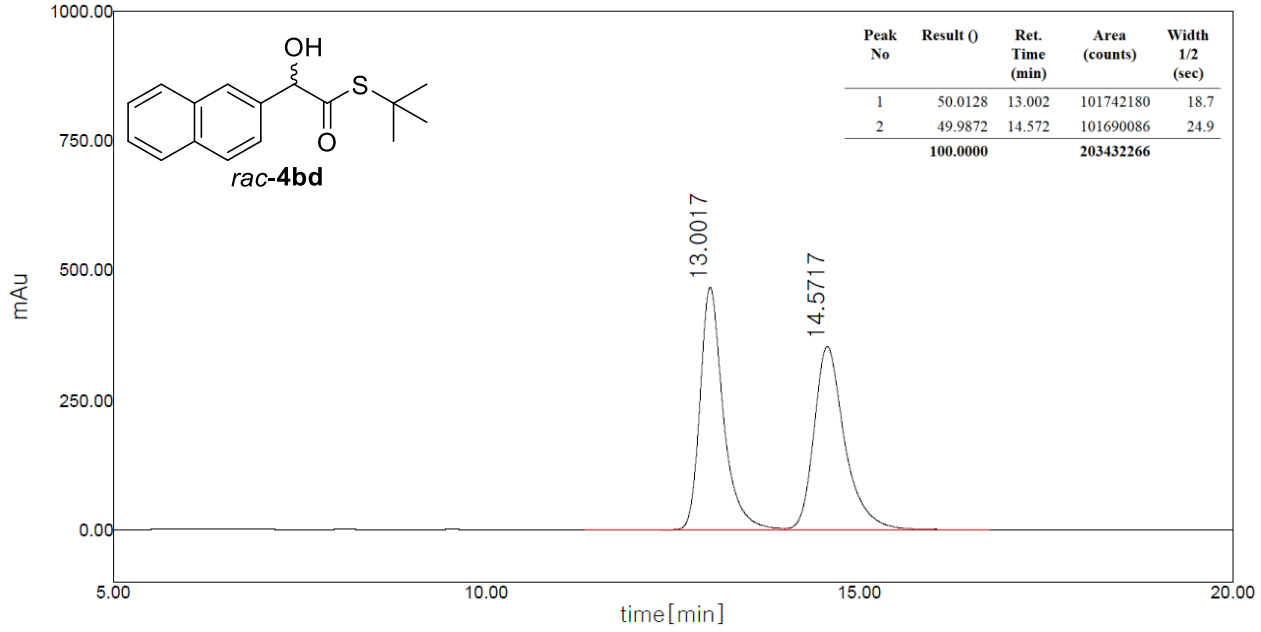
HPLC trace of **4ad** (condition a)



HPLC trace of **4ad** (condition b)

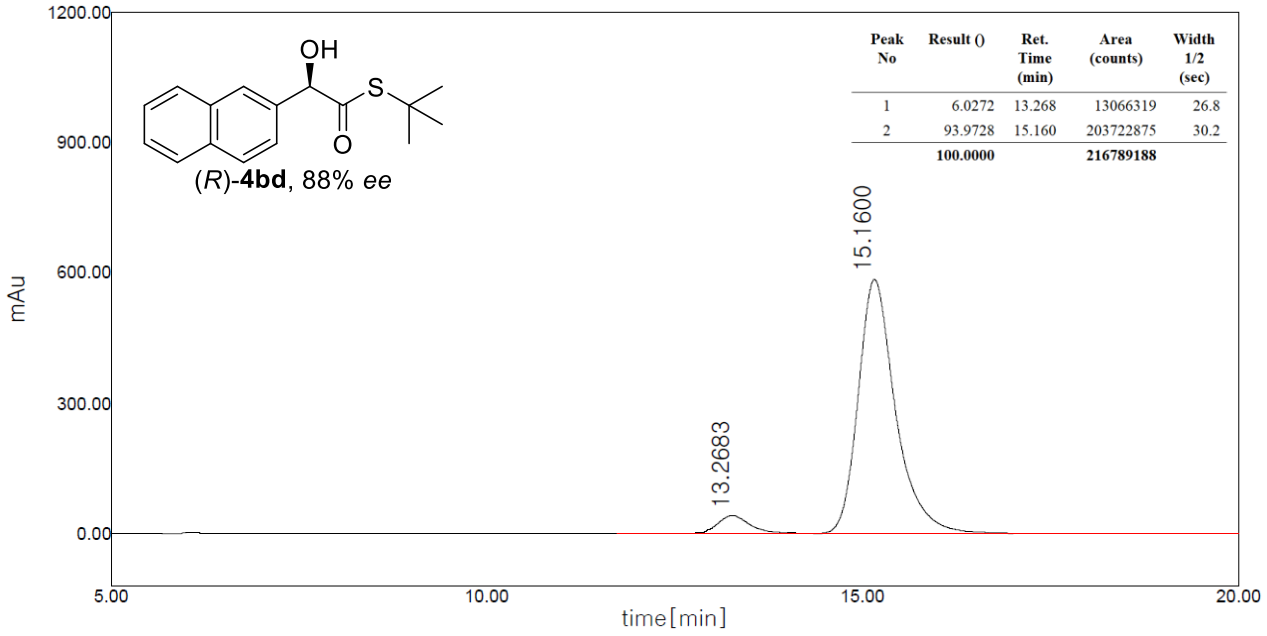


HPLC trace of **4ad** (condition c)



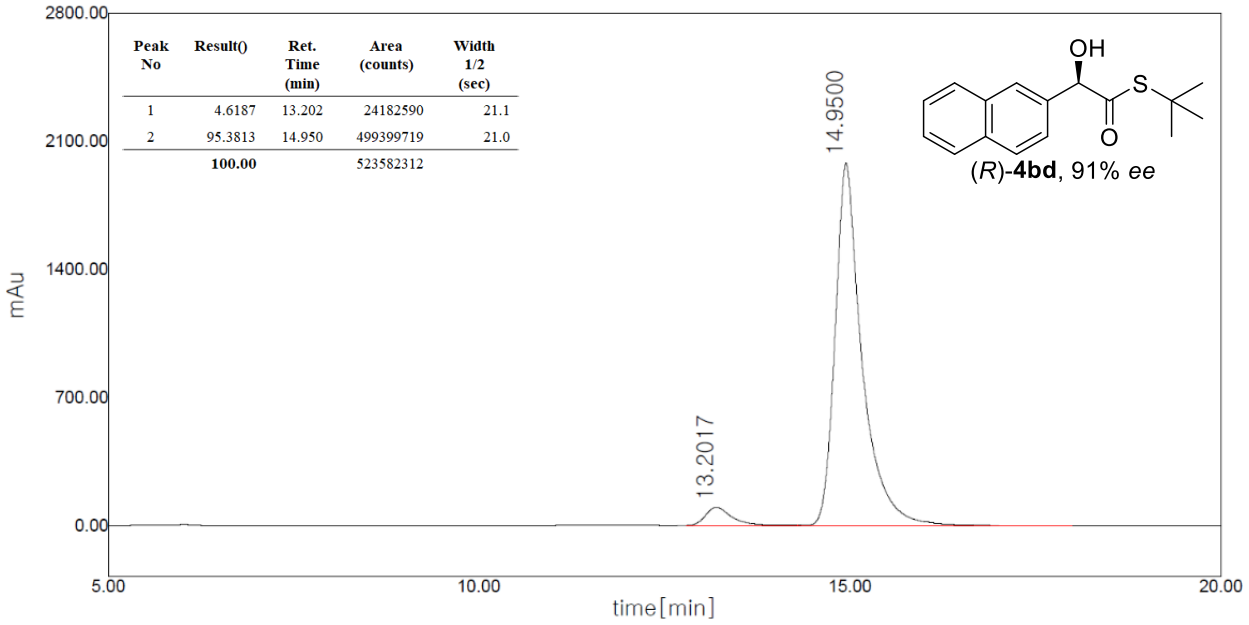
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0128	13.002	101742180	18.7
2	49.9872	14.572	101690086	24.9
	100.0000		**203432266**	

HPLC trace of *rac*-**4bd**

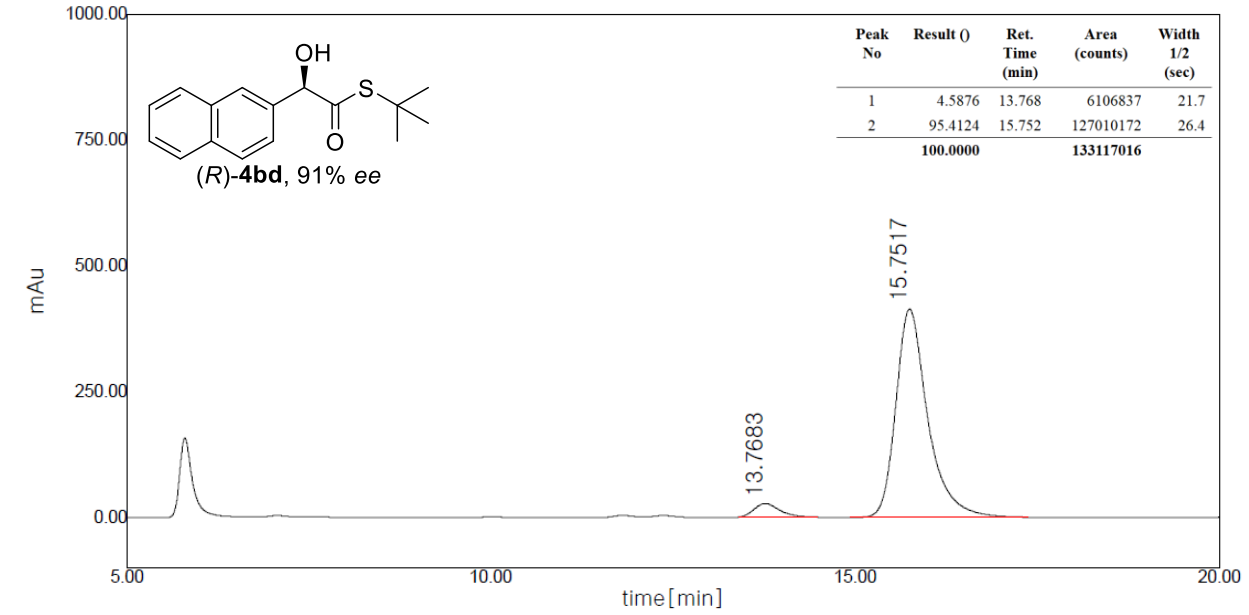


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.0272	13.268	13066319	26.8
2	93.9728	15.160	203722875	30.2
	100.0000		**216789188**	

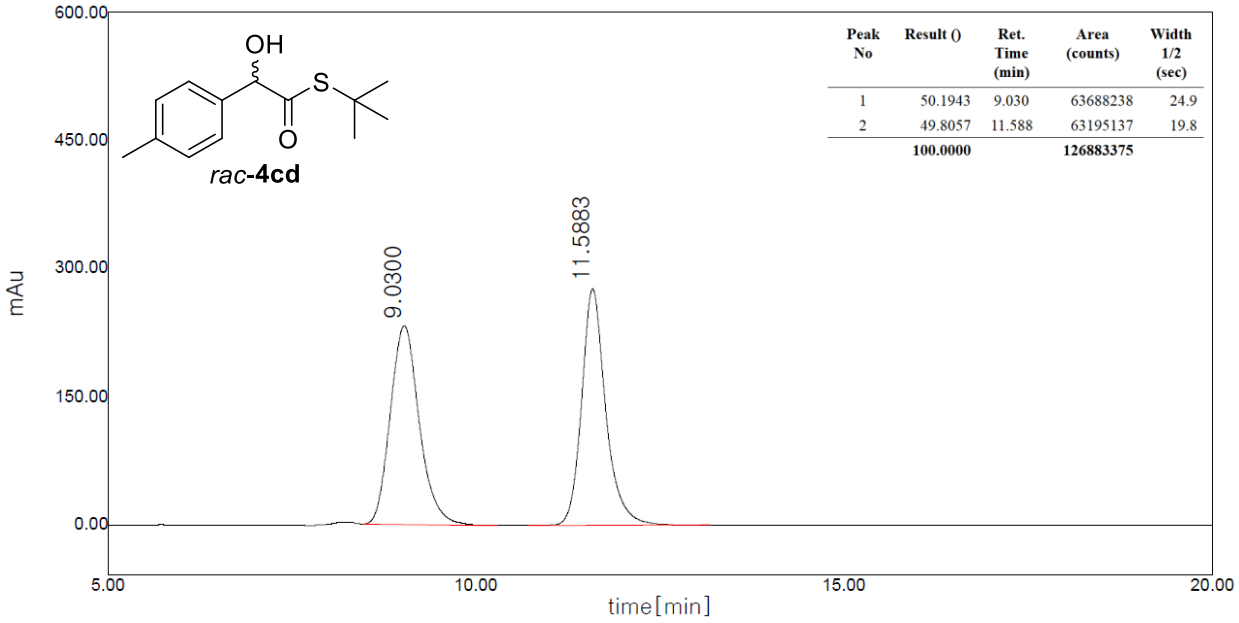
HPLC trace of **4bd** (condition a)



HPLC trace of **4bd** (condition b)

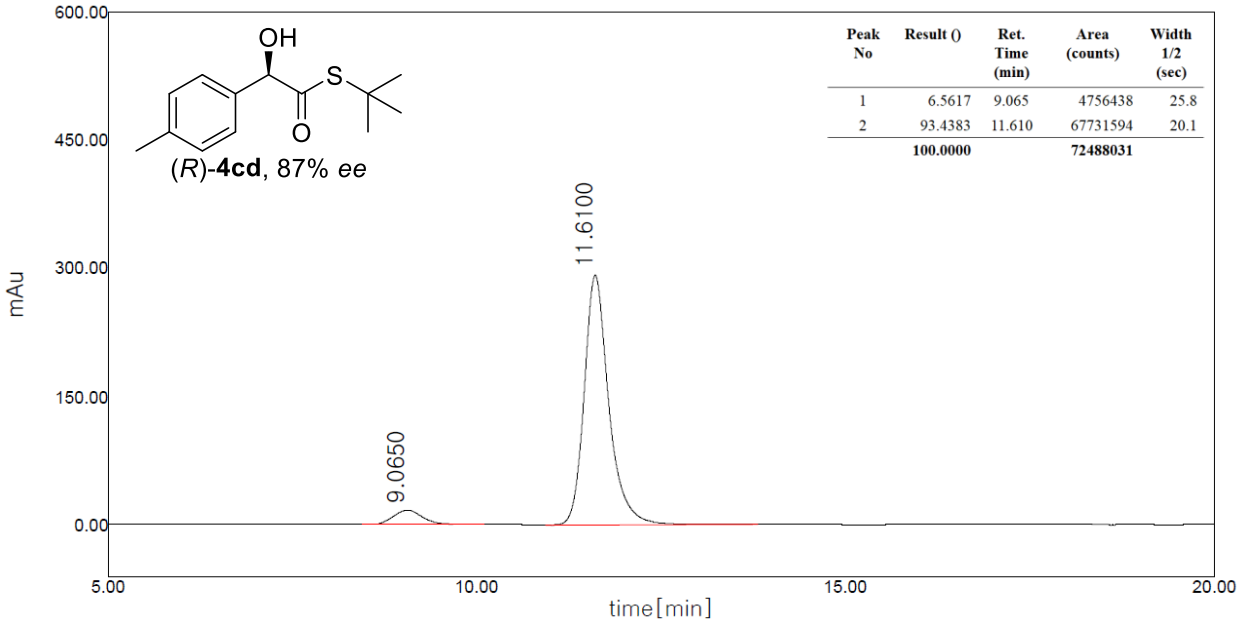


HPLC trace of **4bd** (condition c)



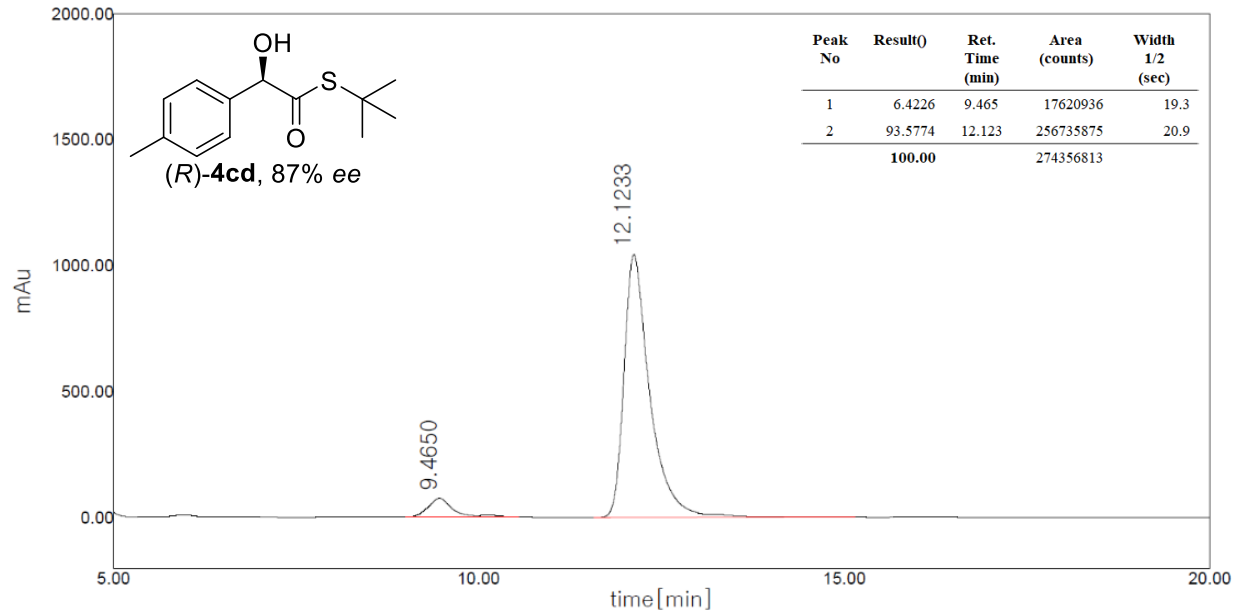
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.1943	9.030	63688238	24.9
2	49.8057	11.588	63195137	19.8
	100.0000		**126883375**	

HPLC trace of *rac*-**4cd**



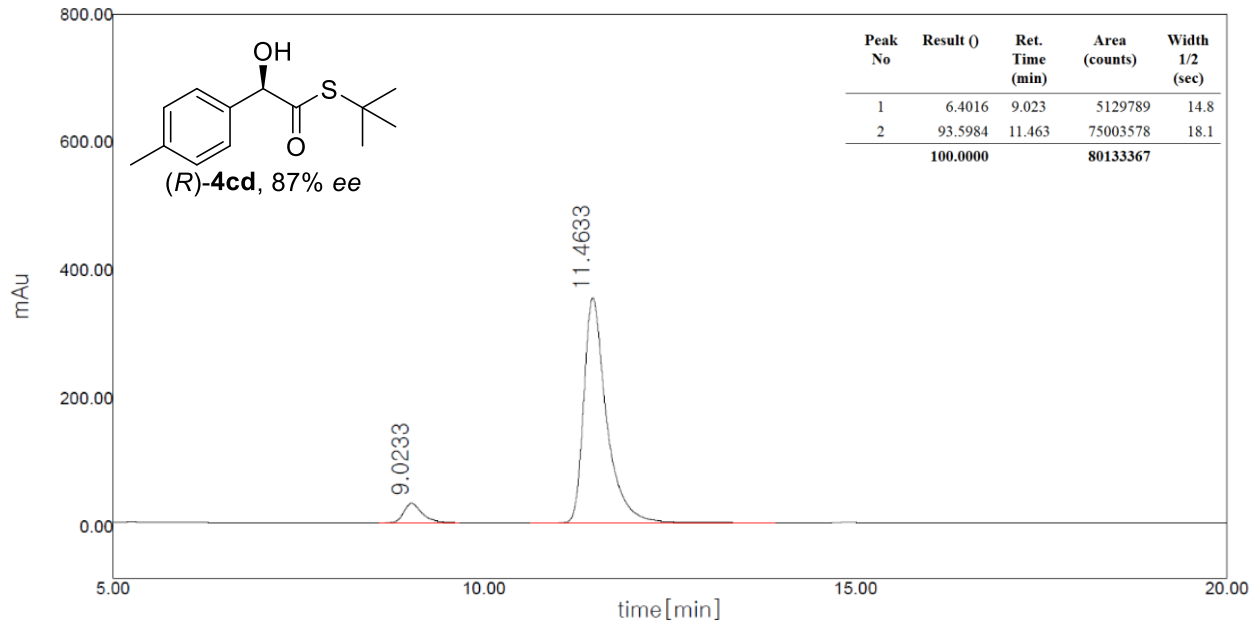
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.5617	9.065	4756438	25.8
2	93.4383	11.610	67731594	20.1
	100.0000		**72488031**	

HPLC trace of **4cd** (condition a)



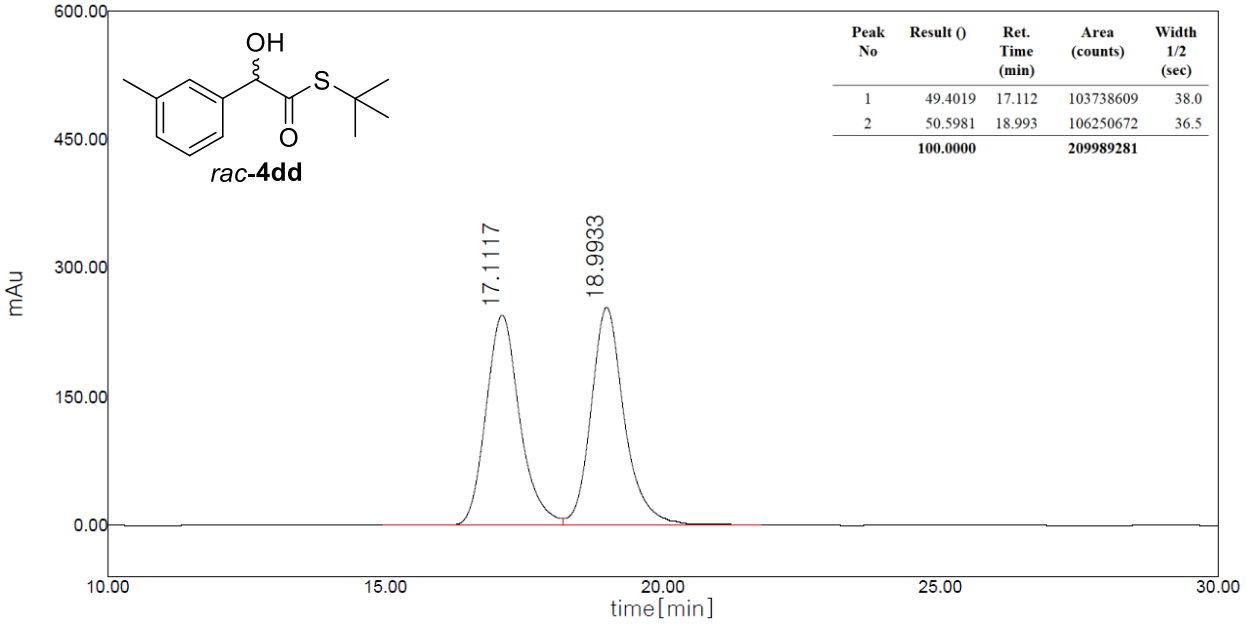
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.4226	9.465	17620936	19.3
2	93.5774	12.123	256735875	20.9
	100.00		274356813	

HPLC trace of **4cd** (condition b)



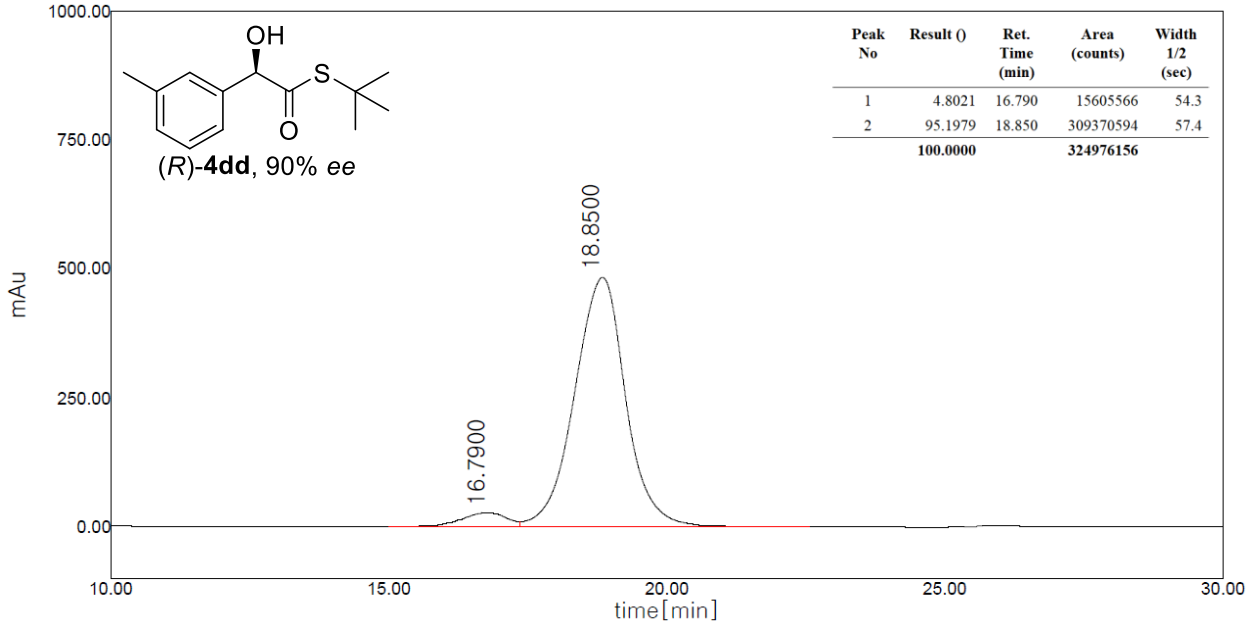
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.4016	9.023	5129789	14.8
2	93.5984	11.463	75003578	18.1
	100.0000		**80133367**	

HPLC trace of **4cd** (condition c)



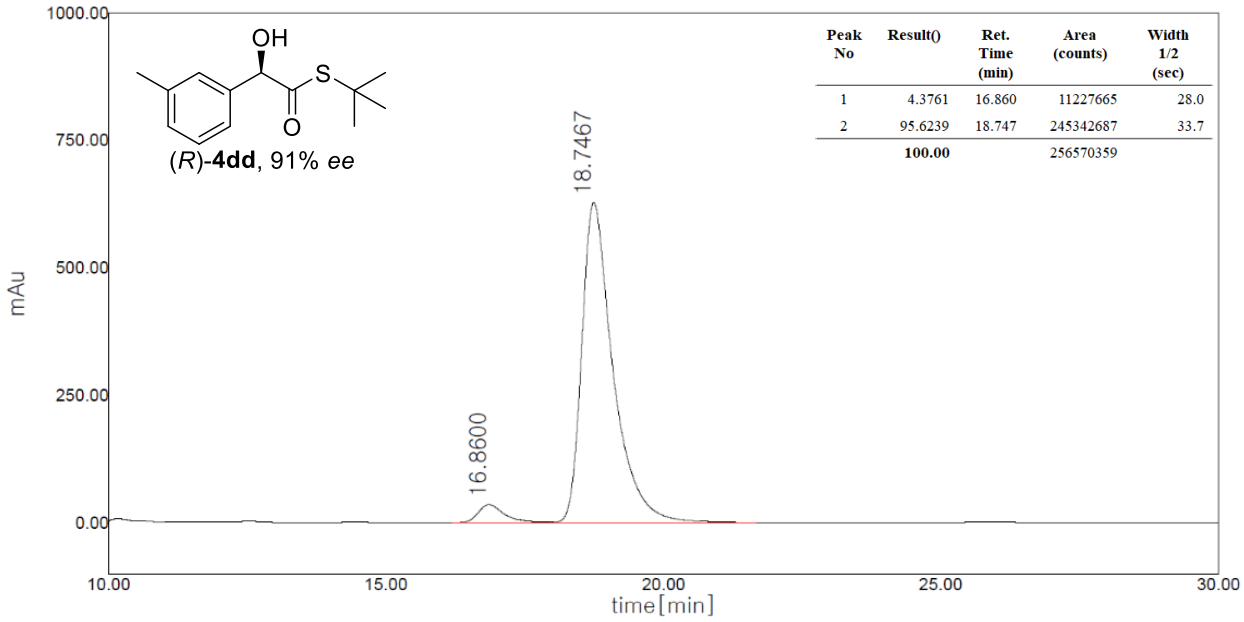
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.4019	17.112	103738609	38.0
2	50.5981	18.993	106250672	36.5
	100.0000		**209989281**	

HPLC trace of *rac*-**4dd**



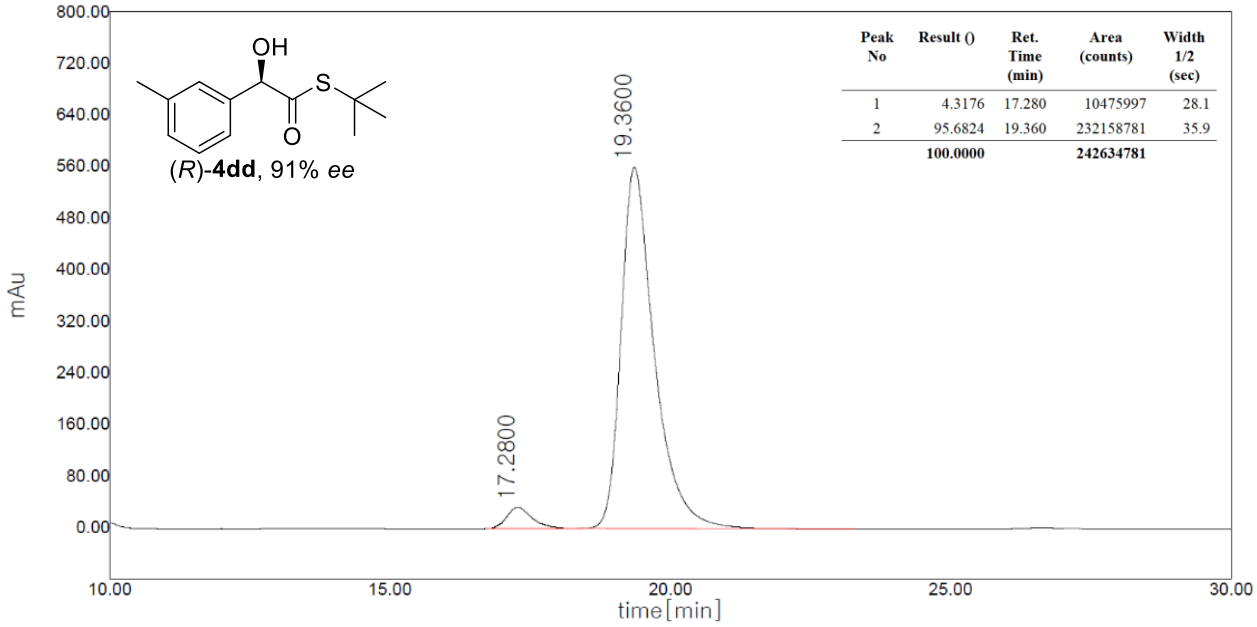
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.8021	16.790	15605566	54.3
2	95.1979	18.850	309370594	57.4
	100.0000		**324976156**	

HPLC trace of **4dd** (condition a)



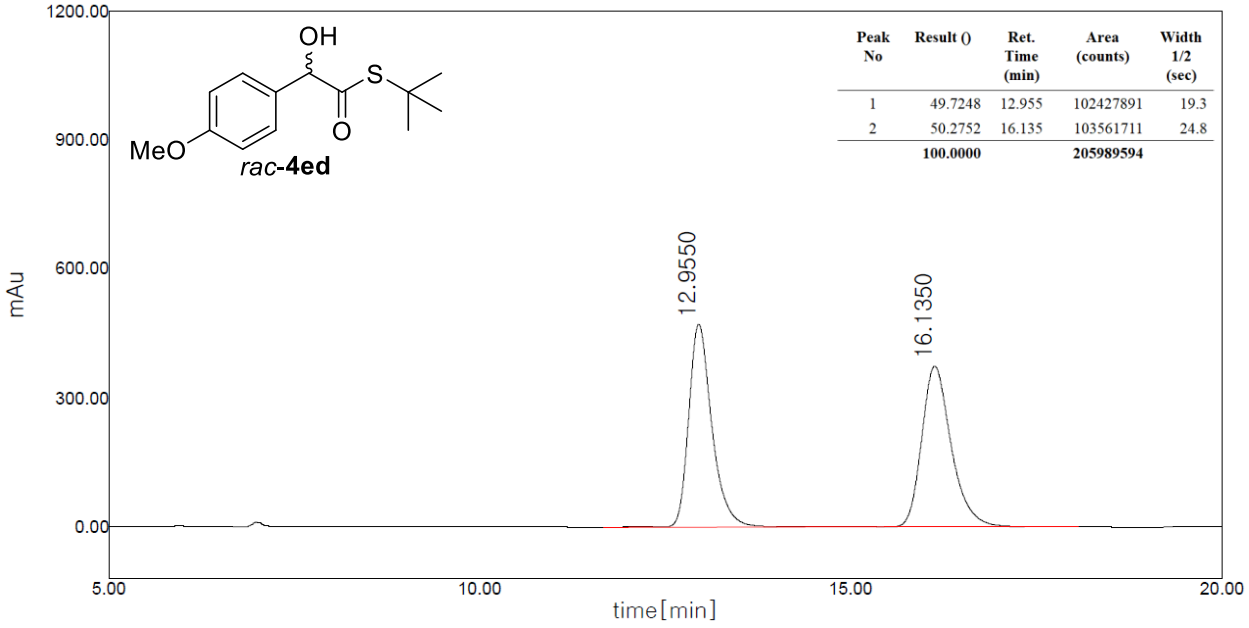
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.3761	16.860	11227665	28.0
2	95.6239	18.747	245342687	33.7
	100.00		256570359	

HPLC trace of **4dd** (condition b)

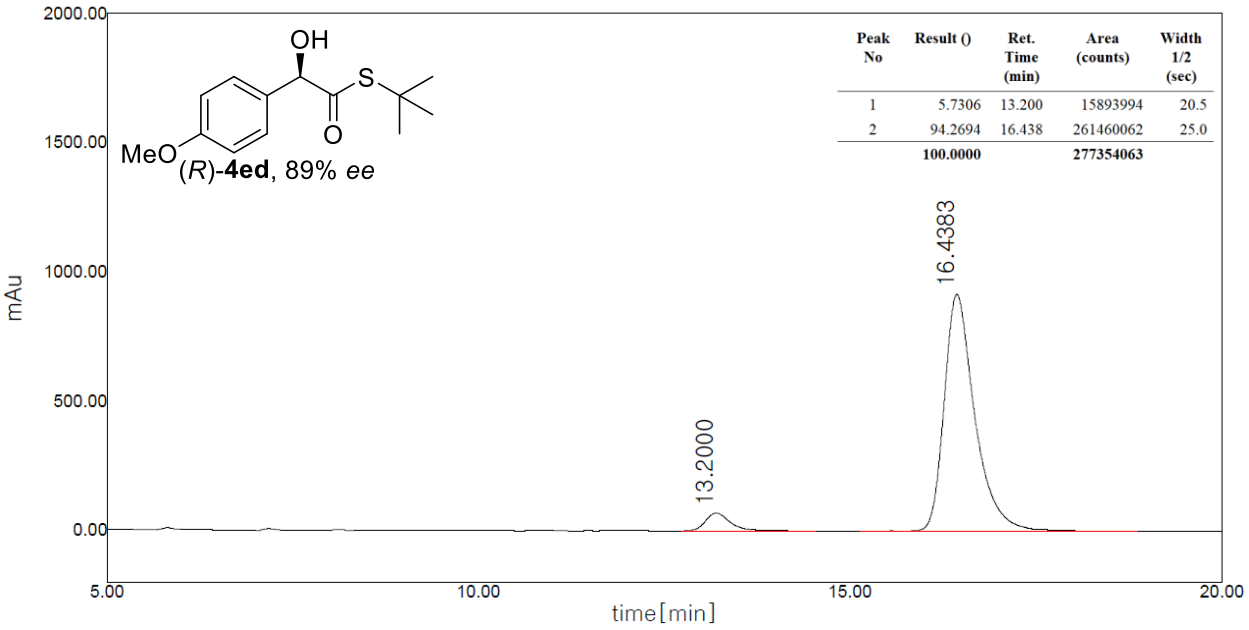


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.3176	17.280	10475997	28.1
2	95.6824	19.360	232158781	35.9
	100.0000		**242634781**	

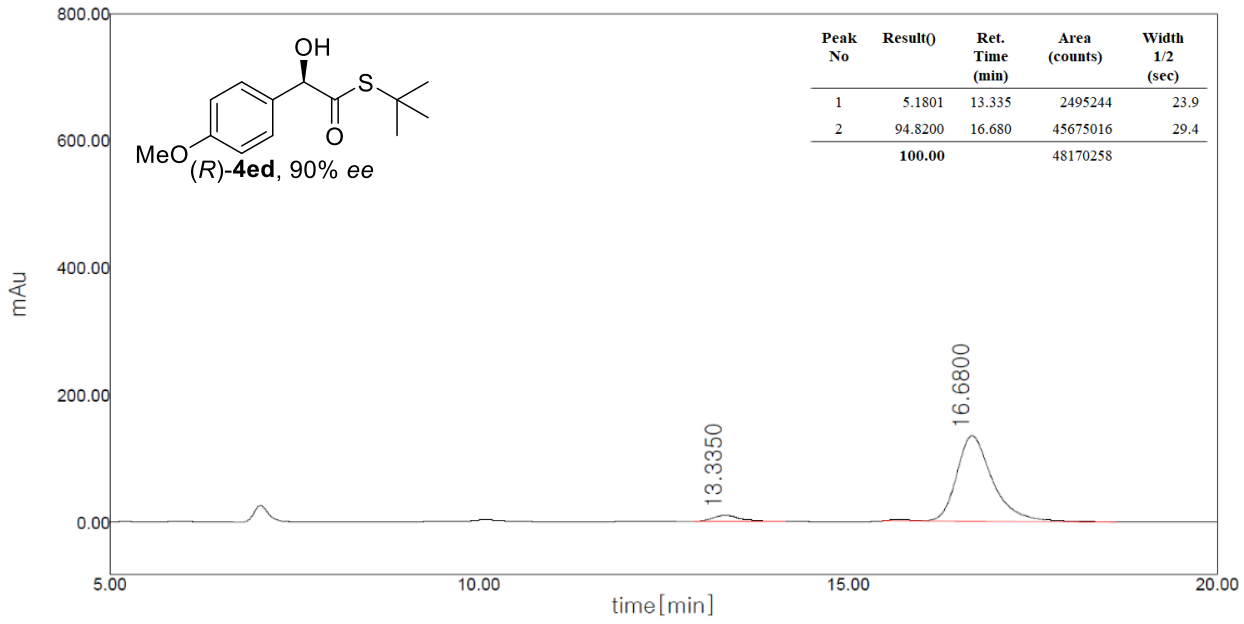
HPLC trace of **4dd** (condition c)



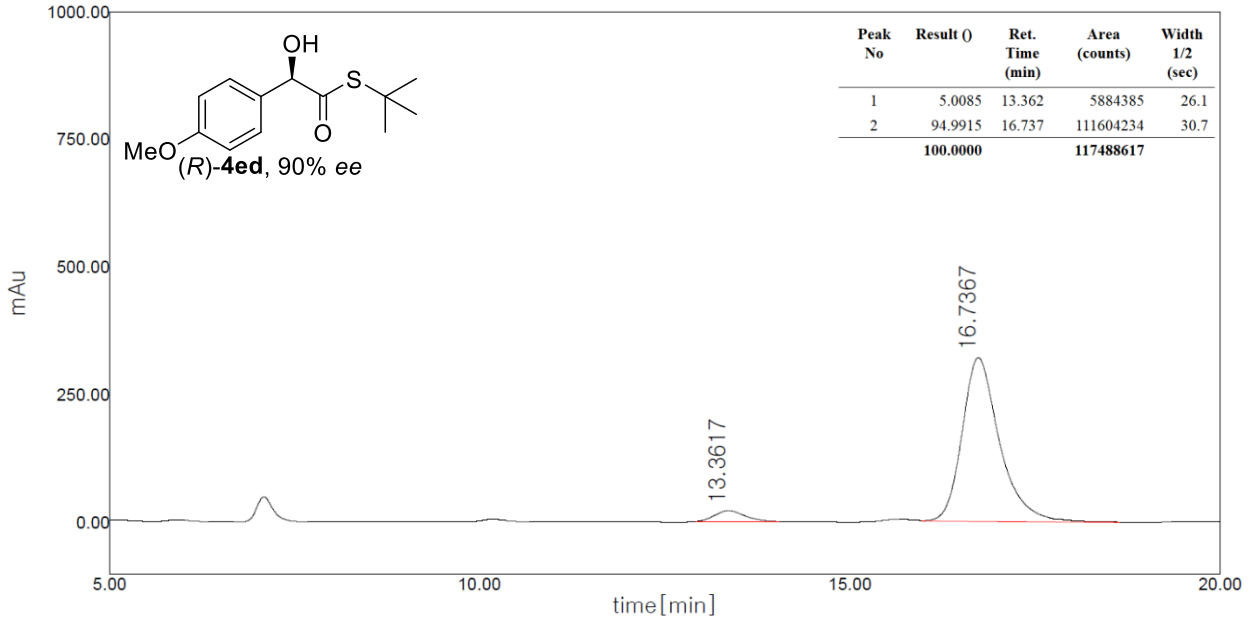
HPLC trace of *rac*-**4ed**



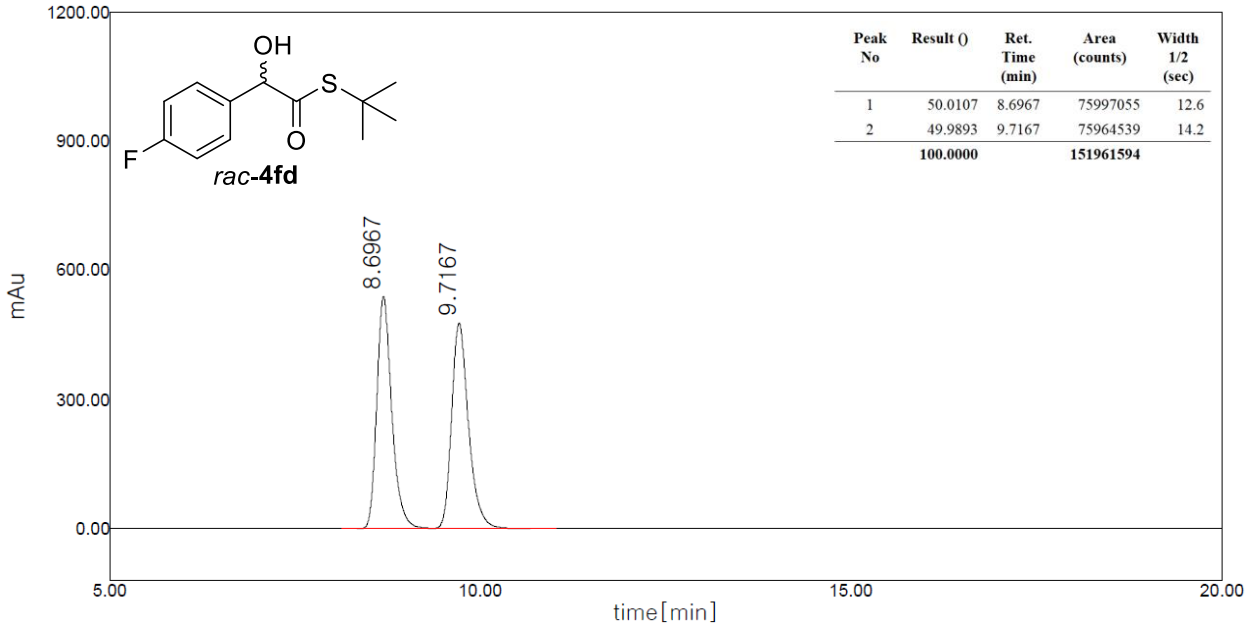
HPLC trace of **4ed** (condition a)



HPLC trace of **4ed** (condition b)

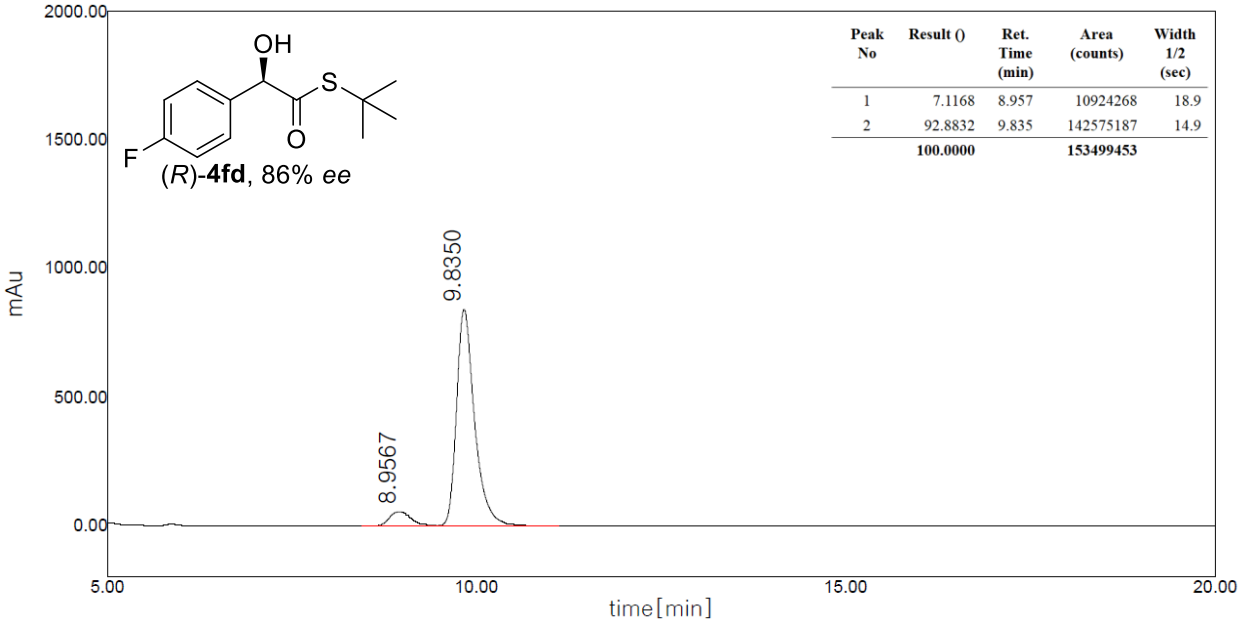


HPLC trace of **4ed** (condition c)



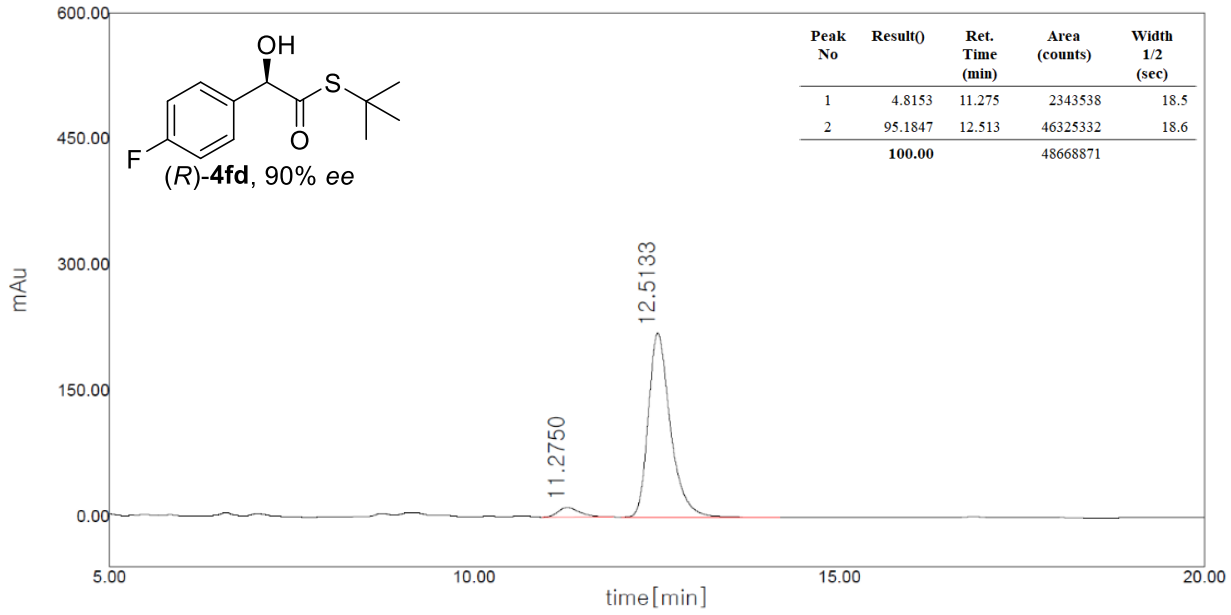
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0107	8.6967	75997055	12.6
2	49.9893	9.7167	75964539	14.2
	100.0000		**151961594**	

HPLC trace of *rac*-**4fd**



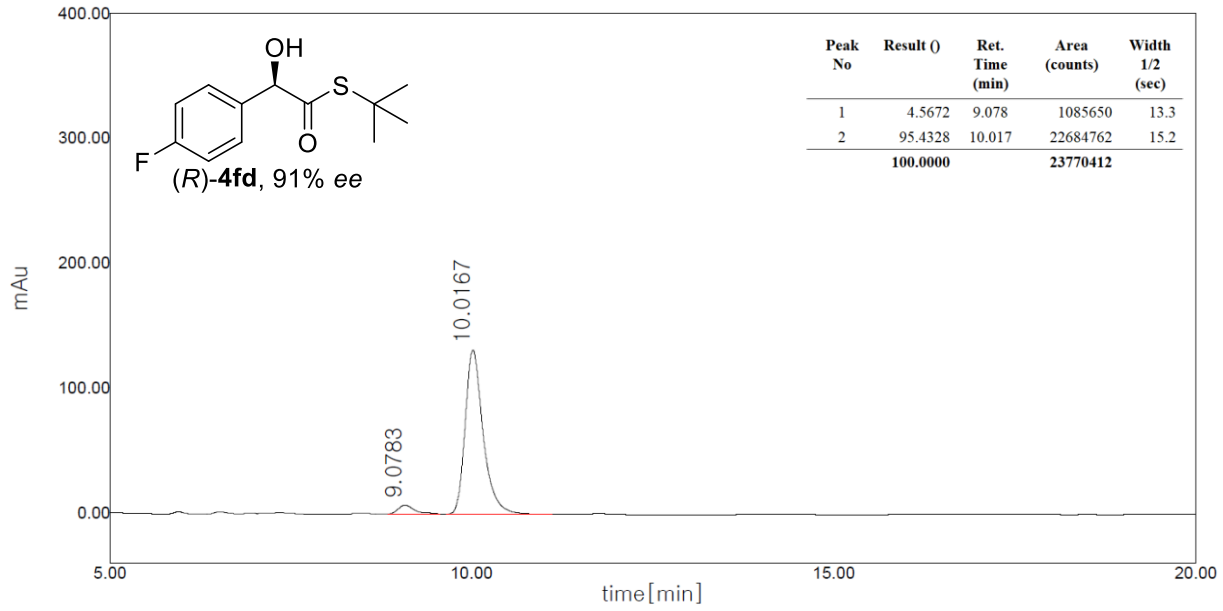
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	7.1168	8.957	10924268	18.9
2	92.8832	9.835	142575187	14.9
	100.0000		**153499453**	

HPLC trace of **4fd** (condition a)



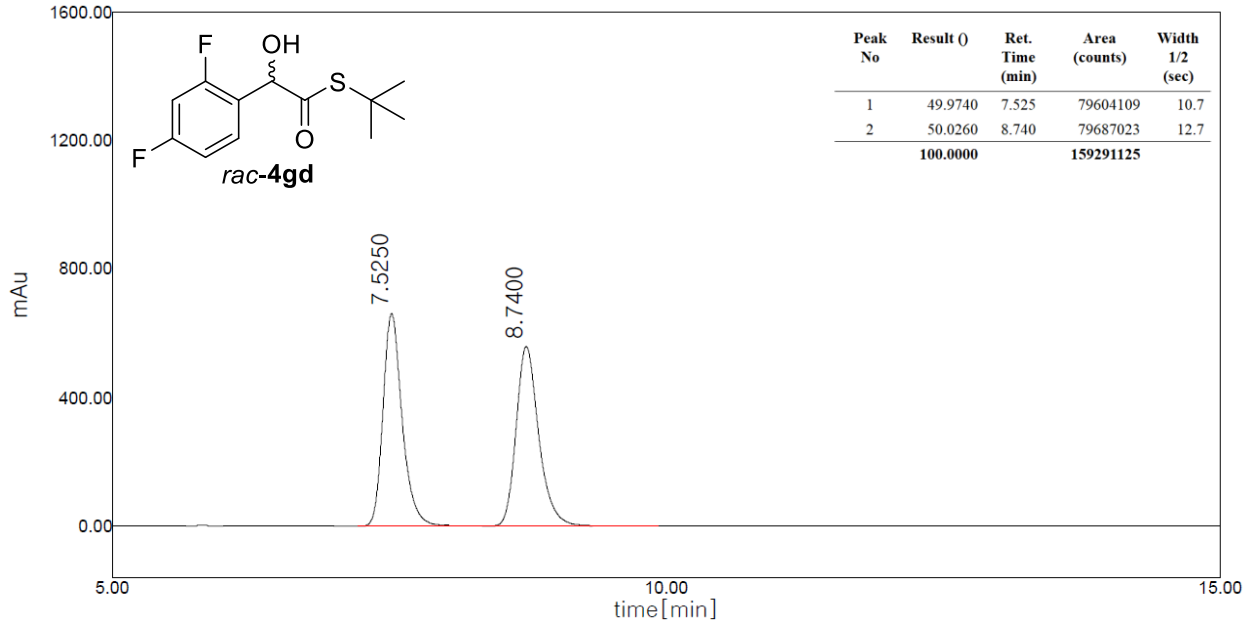
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.8153	11.275	2343538	18.5
2	95.1847	12.513	46325332	18.6
	100.00		48668871	

HPLC trace of **4fd** (condition b)



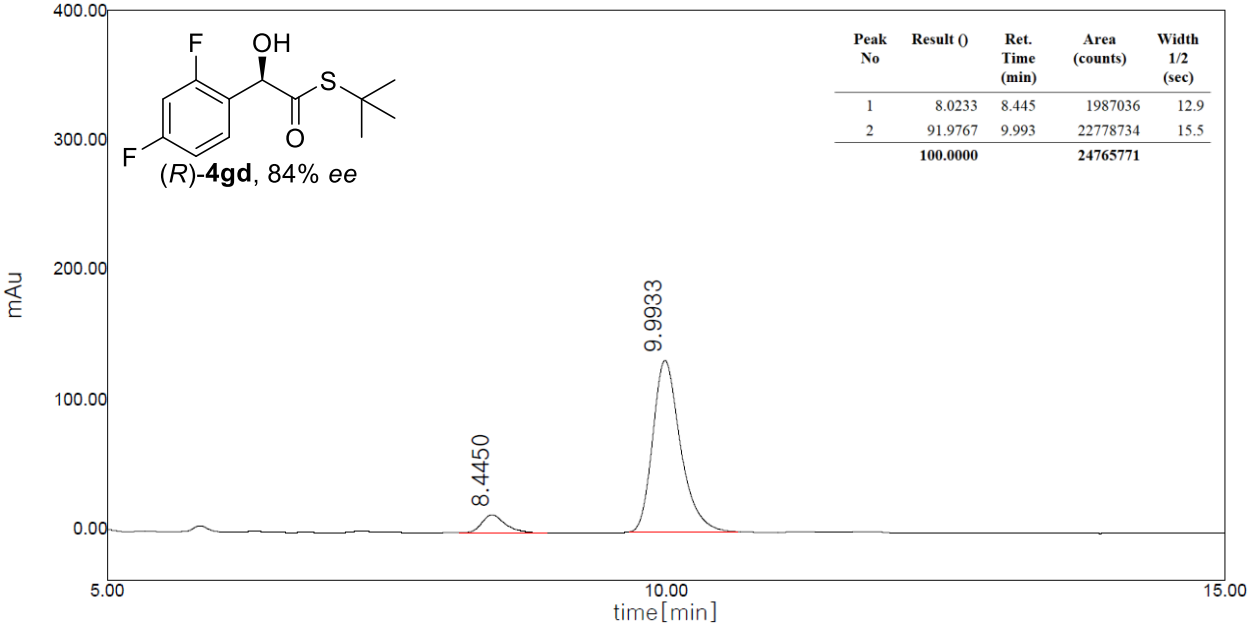
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.5672	9.078	1085650	13.3
2	95.4328	10.017	22684762	15.2
	100.0000		**23770412**	

HPLC trace of **4fd** (condition c)



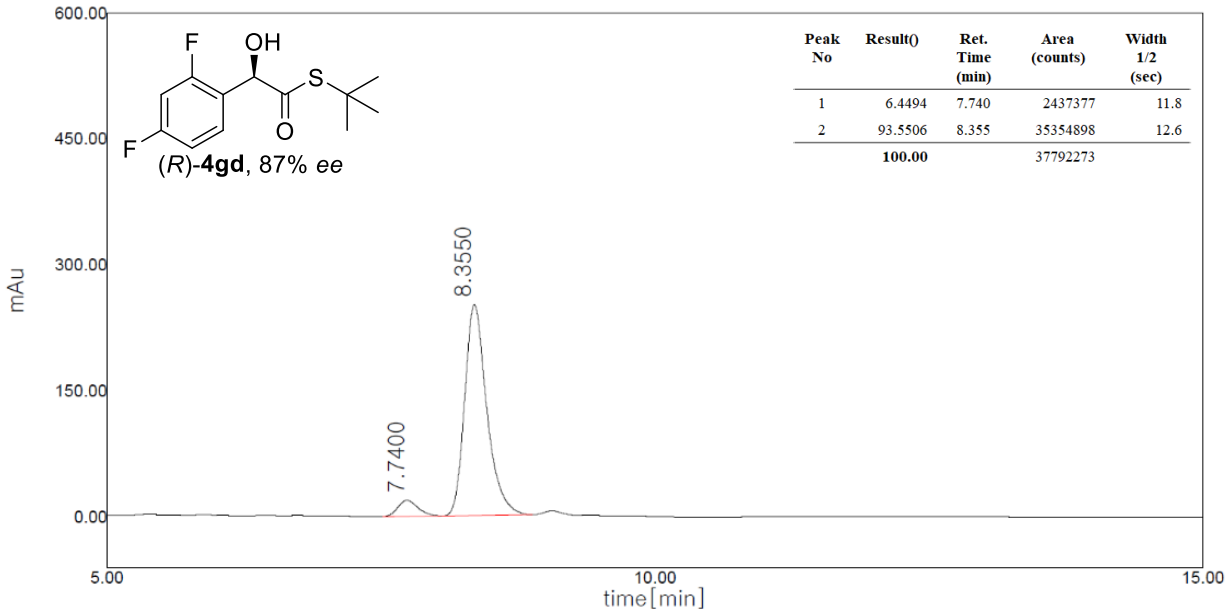
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.9740	7.525	79604109	10.7
2	50.0260	8.740	79687023	12.7
	100.0000		**159291125**	

HPLC trace of *rac*-**4gd**



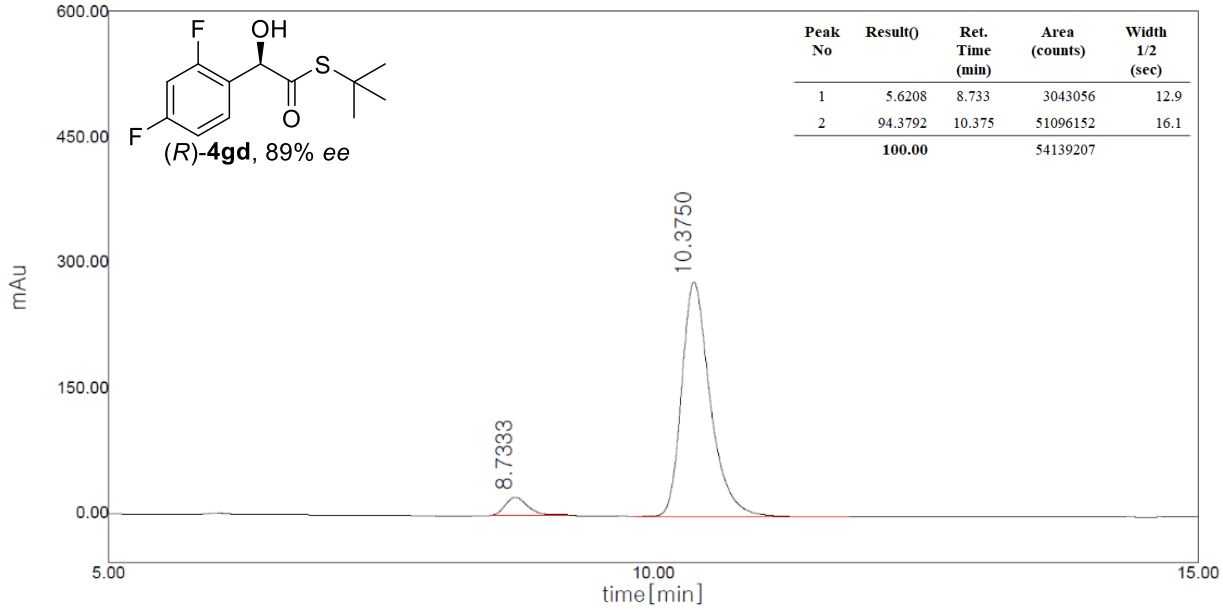
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	8.0233	8.445	1987036	12.9
2	91.9767	9.993	22778734	15.5
	100.0000		**24765771**	

HPLC trace of **4gd** (condition a)



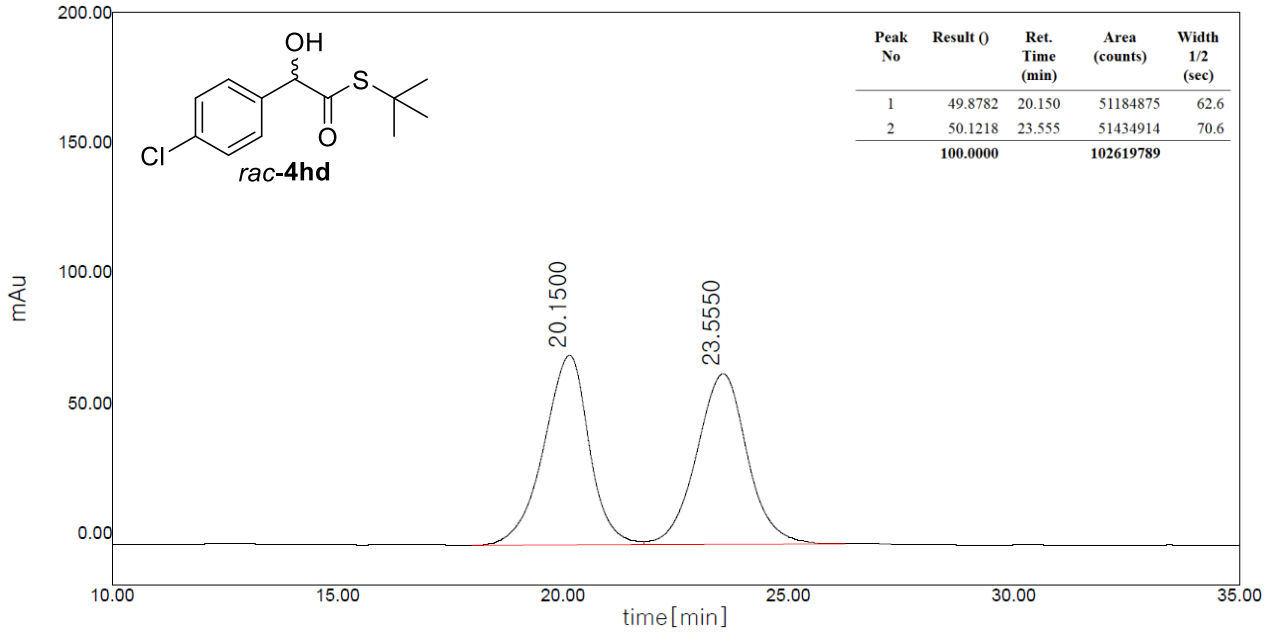
Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	6.4494	7.740	2437377	11.8
2	93.5506	8.355	35354898	12.6
	100.00		37792273	

HPLC trace of **4gd** (condition b)

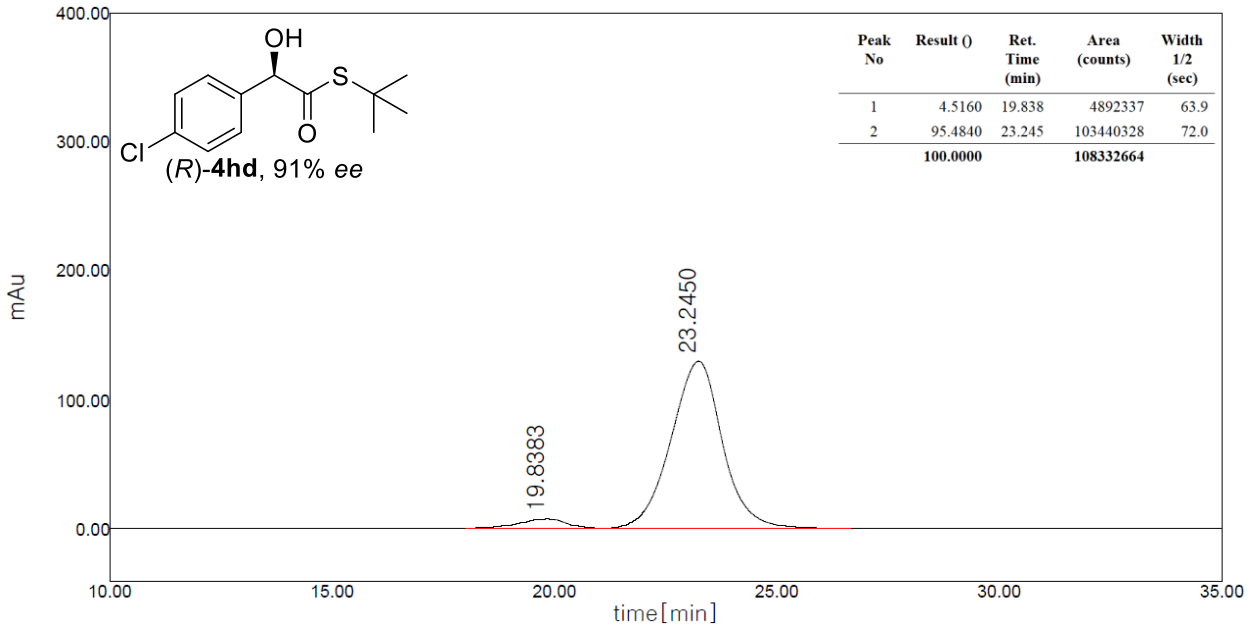


Peak No	Result()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	5.6208	8.733	3043056	12.9
2	94.3792	10.375	51096152	16.1
	100.00		54139207	

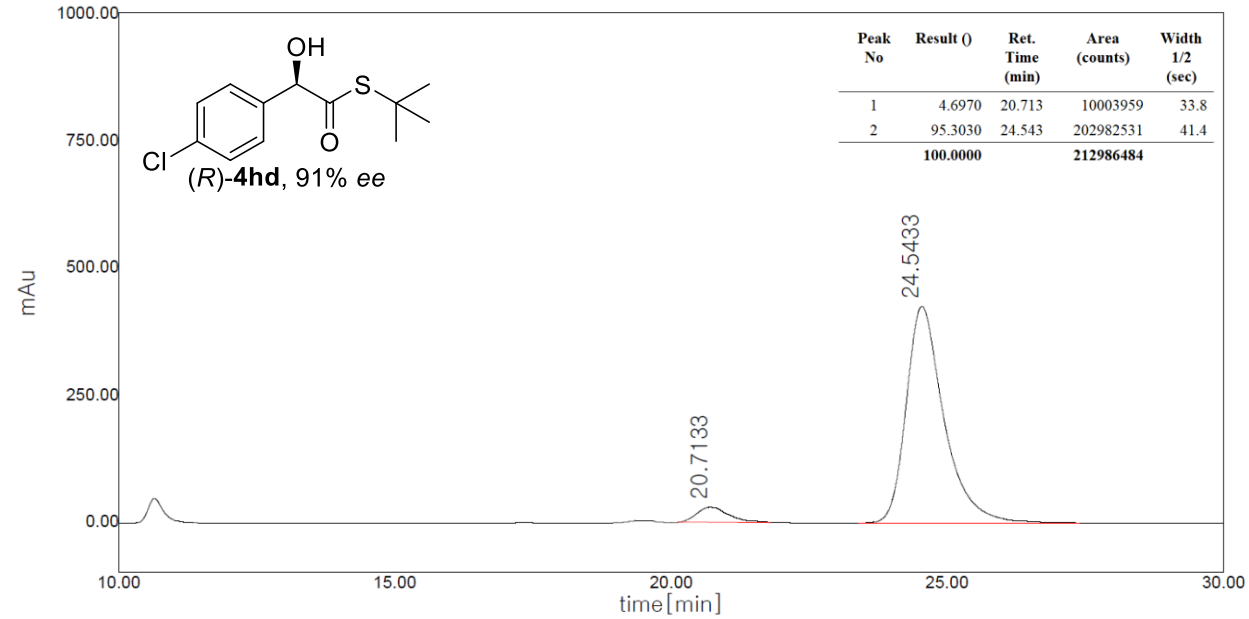
HPLC trace of **4gd** (condition c)



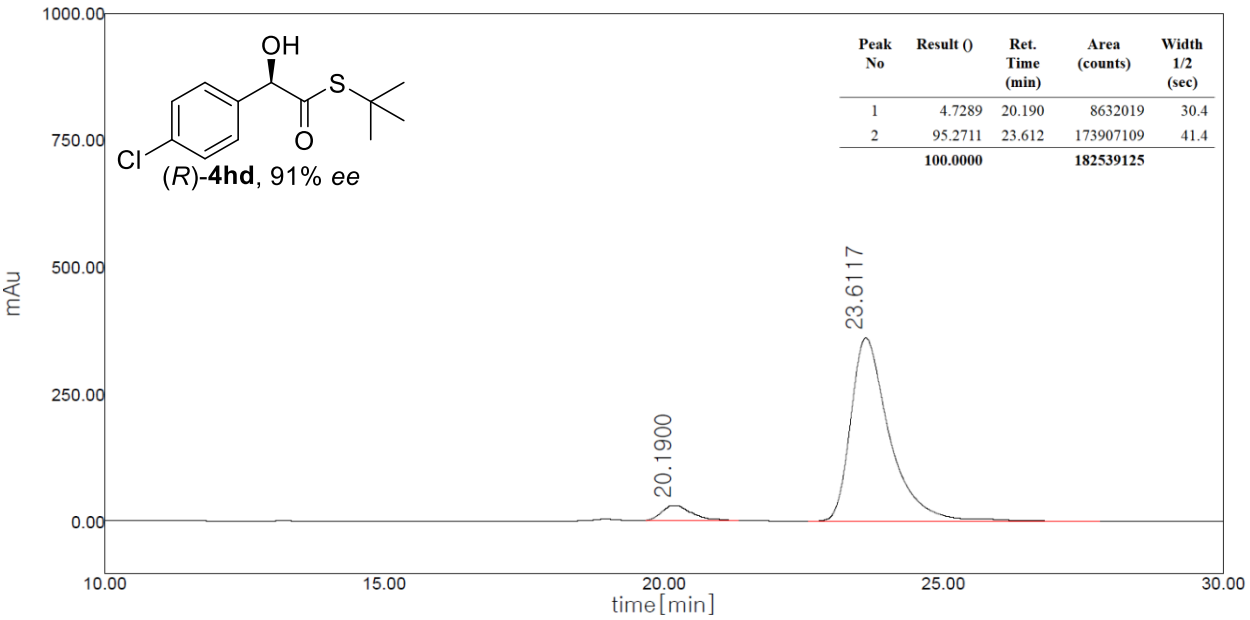
HPLC trace of *rac*-**4hd**



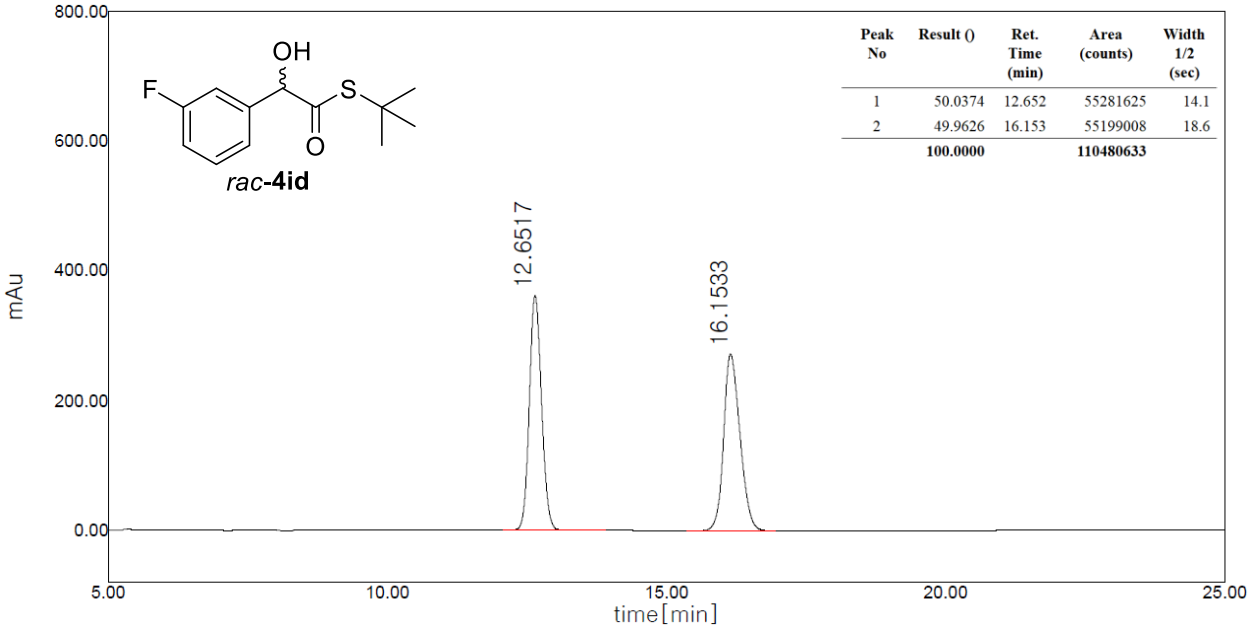
HPLC trace of **4hd** (condition a)



HPLC trace of **4hd** (condition b)

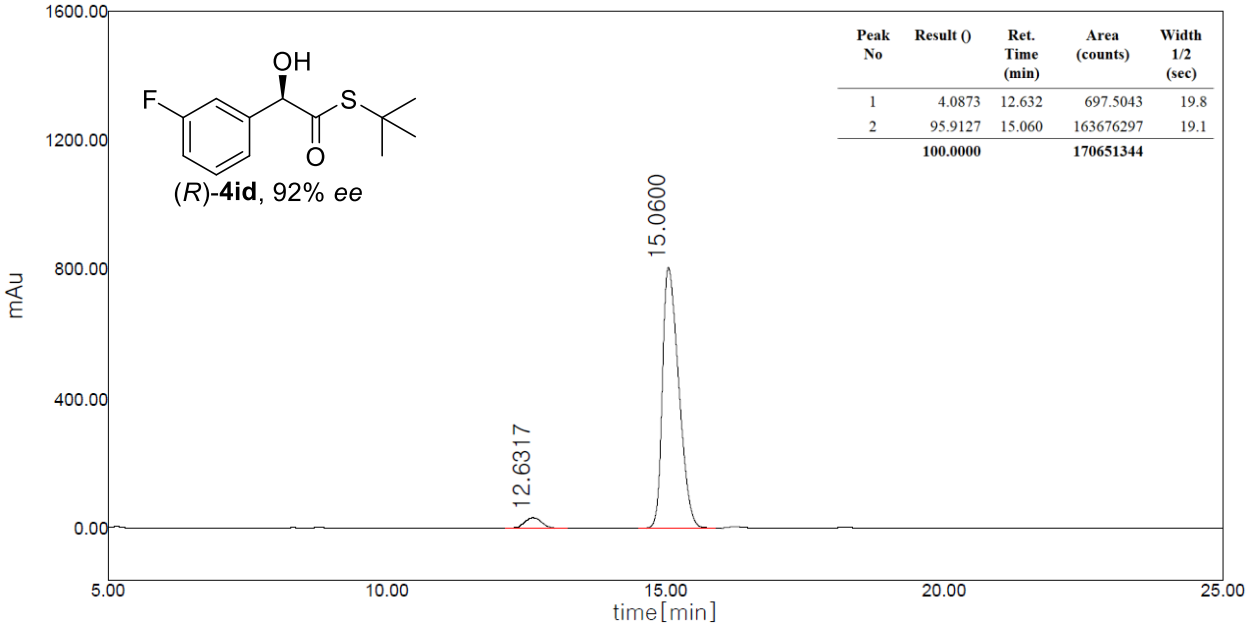


HPLC trace of **4hd** (condition c)



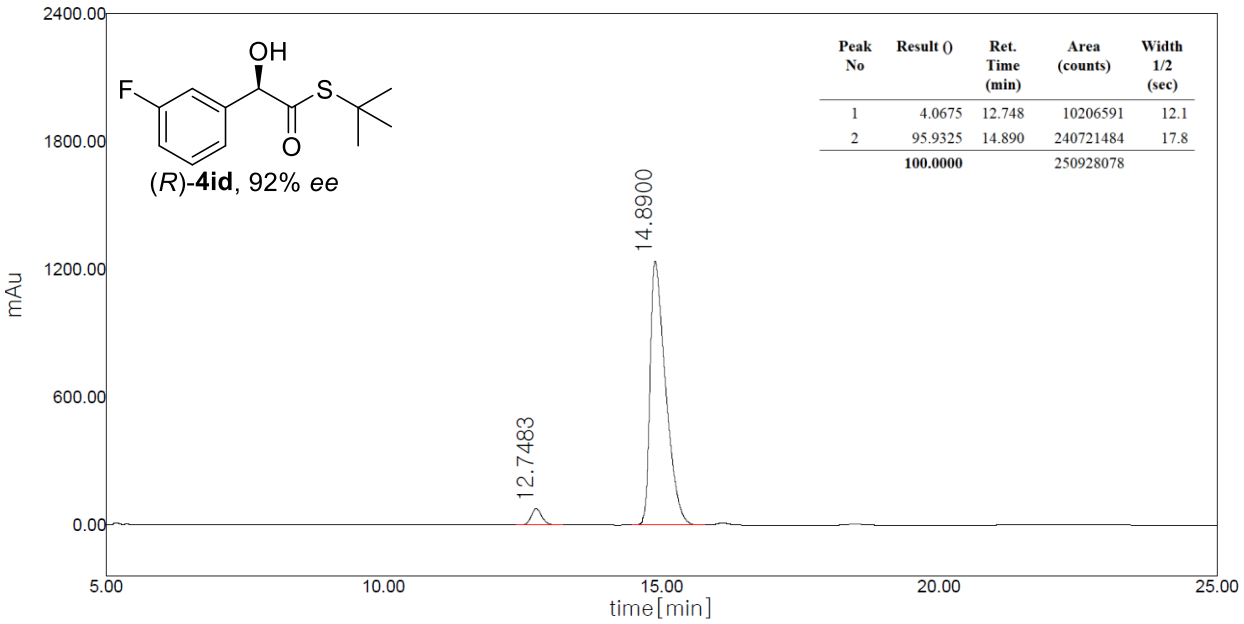
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.0374	12.652	55281625	14.1
2	49.9626	16.153	55199008	18.6
	100.0000		**110480633**	

HPLC trace of *rac*-**4id**



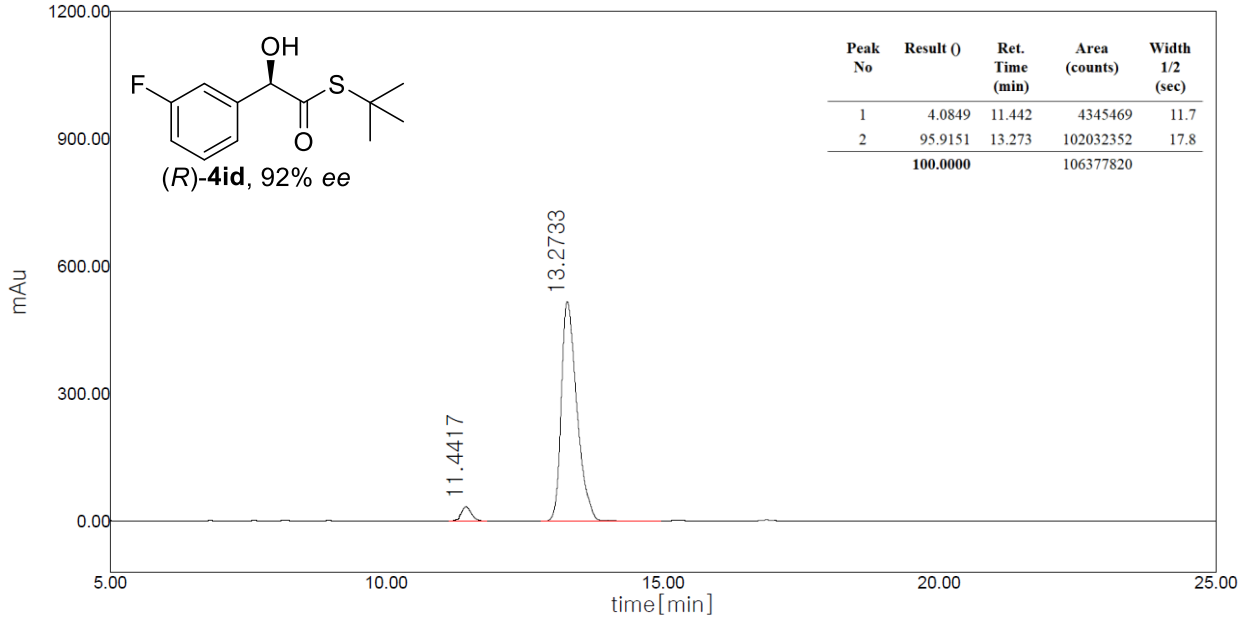
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.0873	12.632	697.5043	19.8
2	95.9127	15.060	163676297	19.1
	100.0000		**170651344**	

HPLC trace of **4id** (condition a)



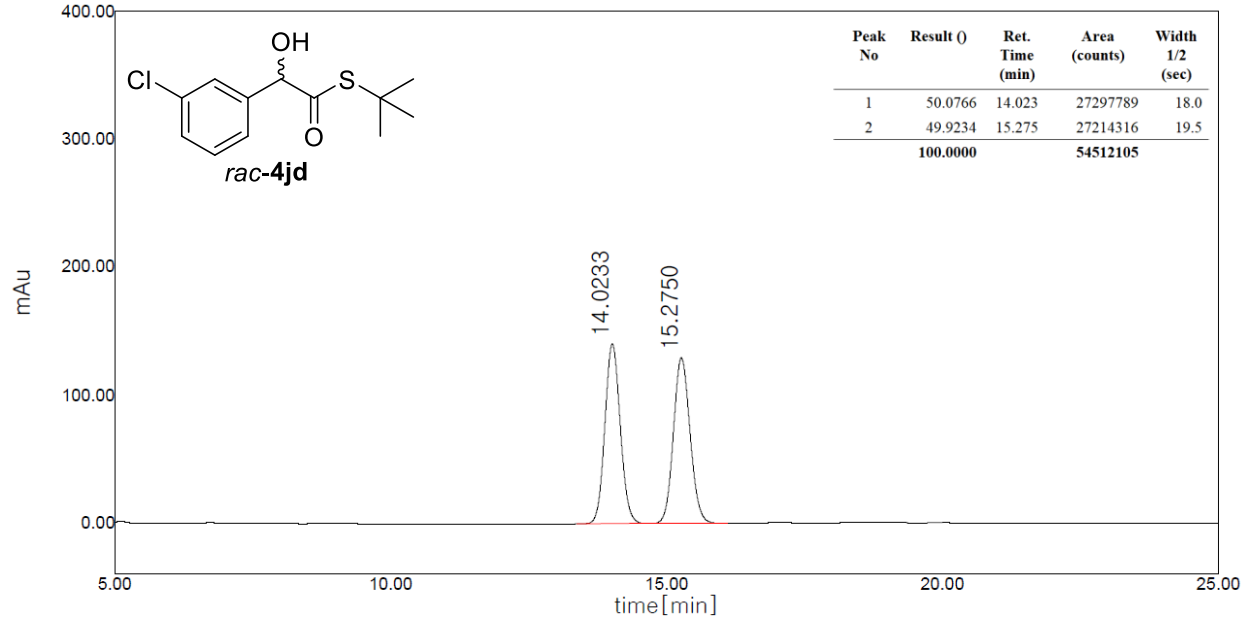
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.0675	12.748	10206591	12.1
2	95.9325	14.890	240721484	17.8
	100.0000		250928078	

HPLC trace of **4id** (condition b)

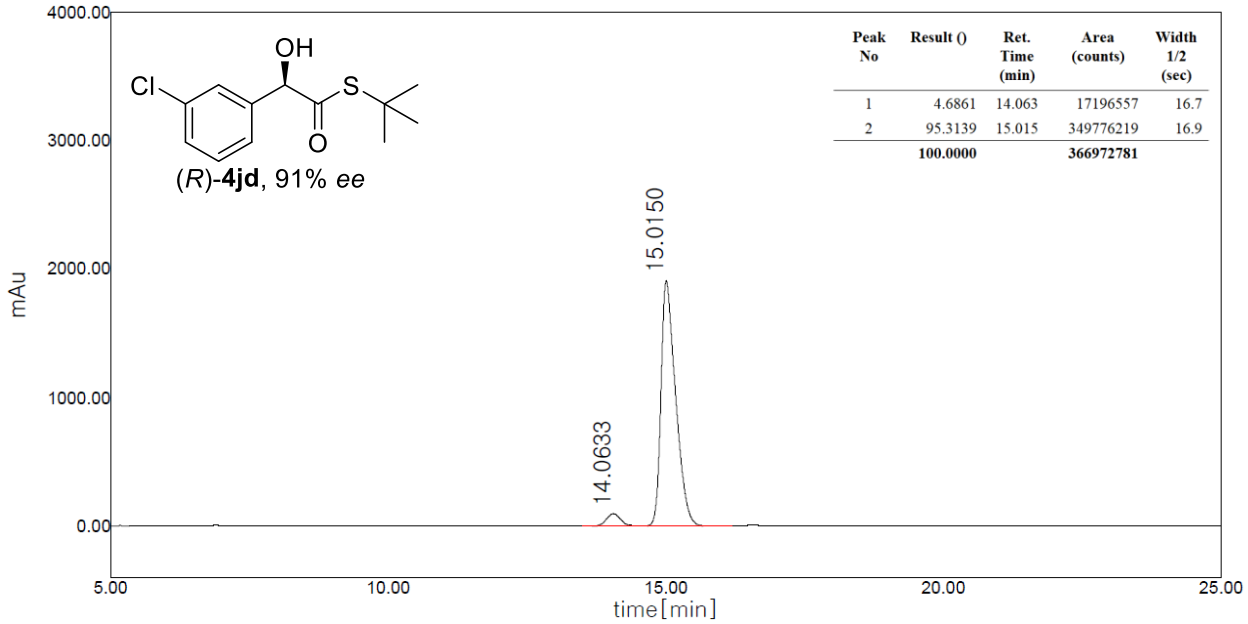


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	4.0849	11.442	4345469	11.7
2	95.9151	13.273	102032352	17.8
	100.0000		106377820	

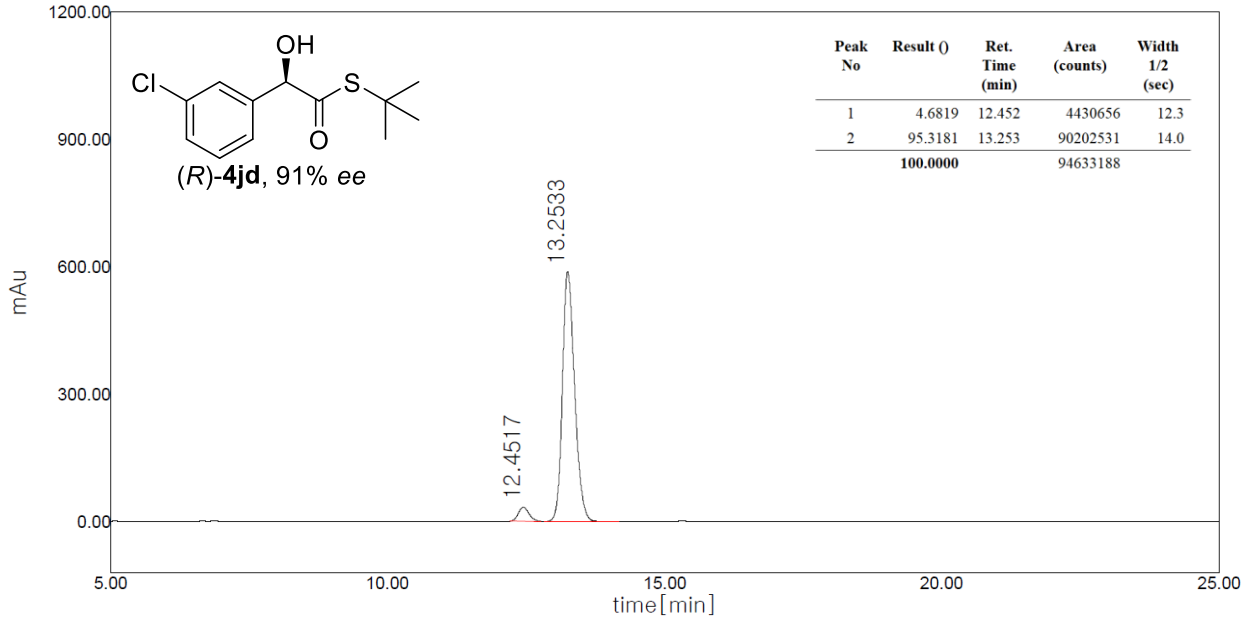
HPLC trace of **4id** (condition c)



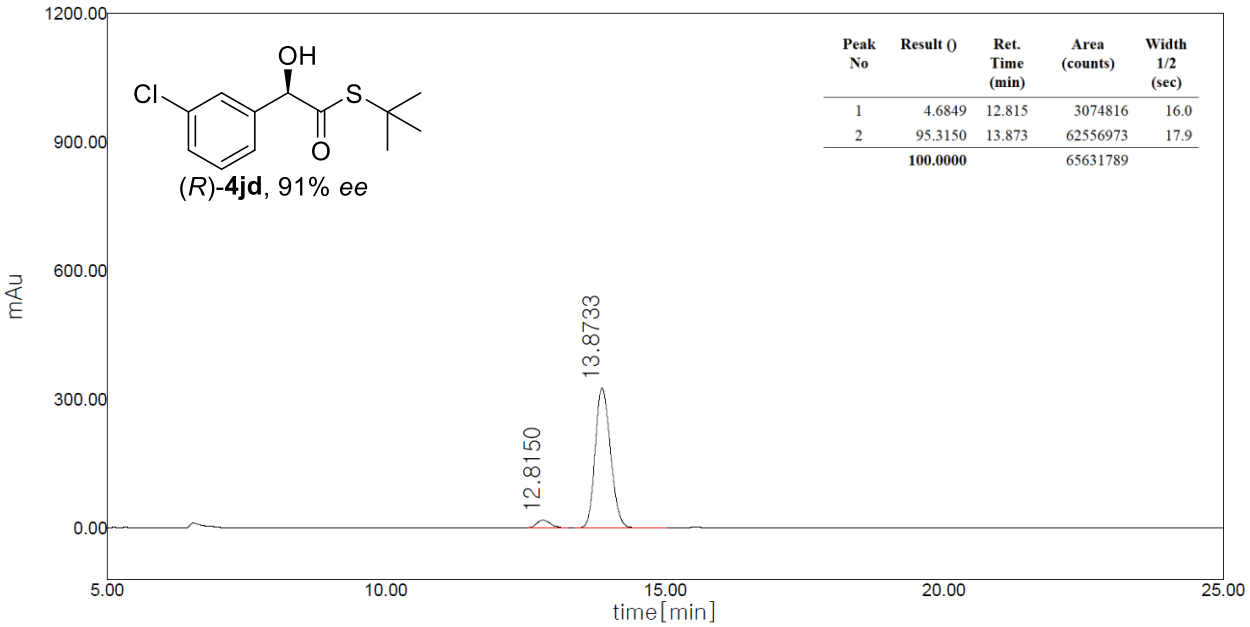
HPLC trace of *rac*-**4jd**



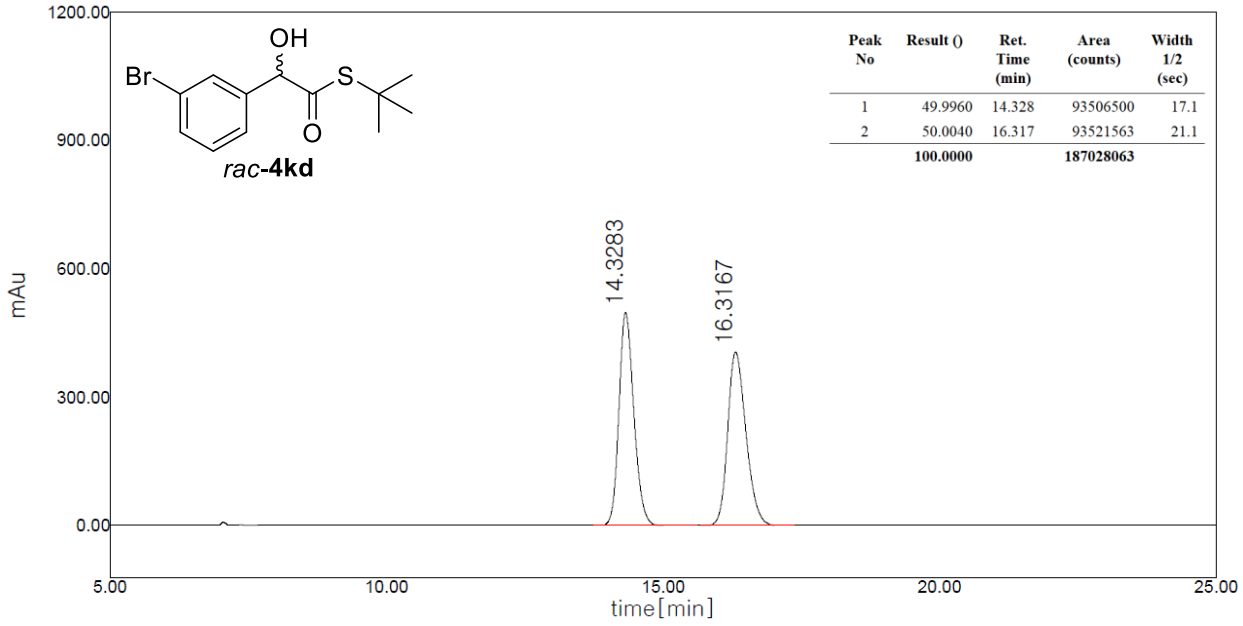
HPLC trace of **4jd** (condition a)



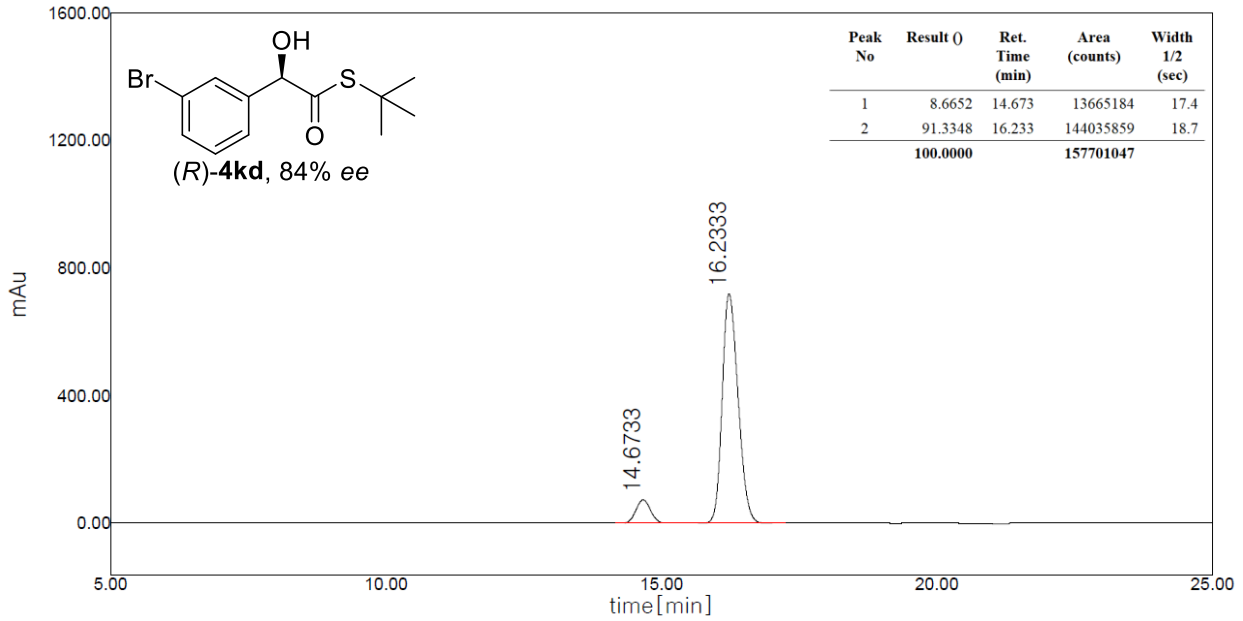
HPLC trace of **4jd** (condition b)



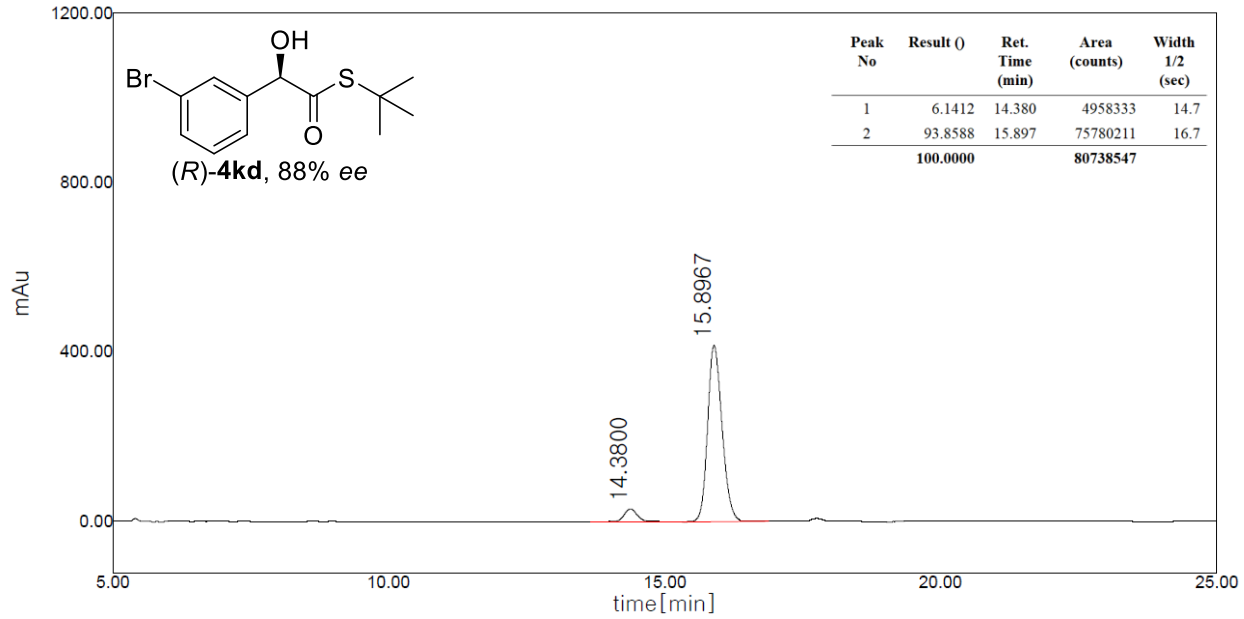
HPLC trace of **4jd** (condition c)



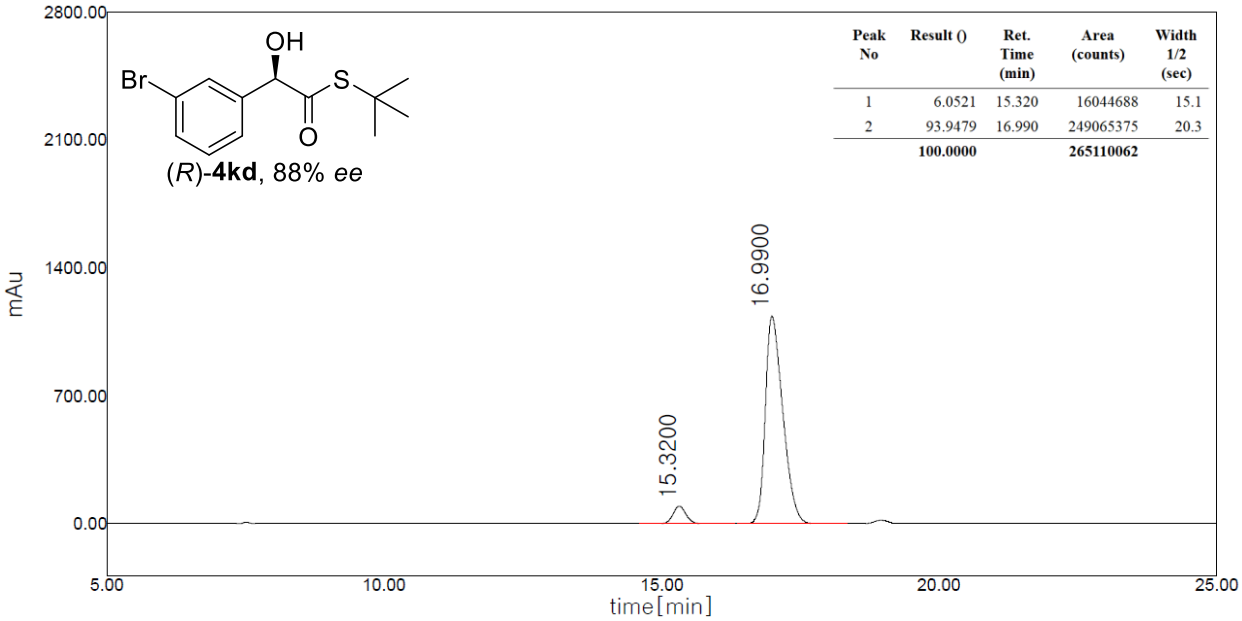
HPLC trace of *rac*-**4kd**



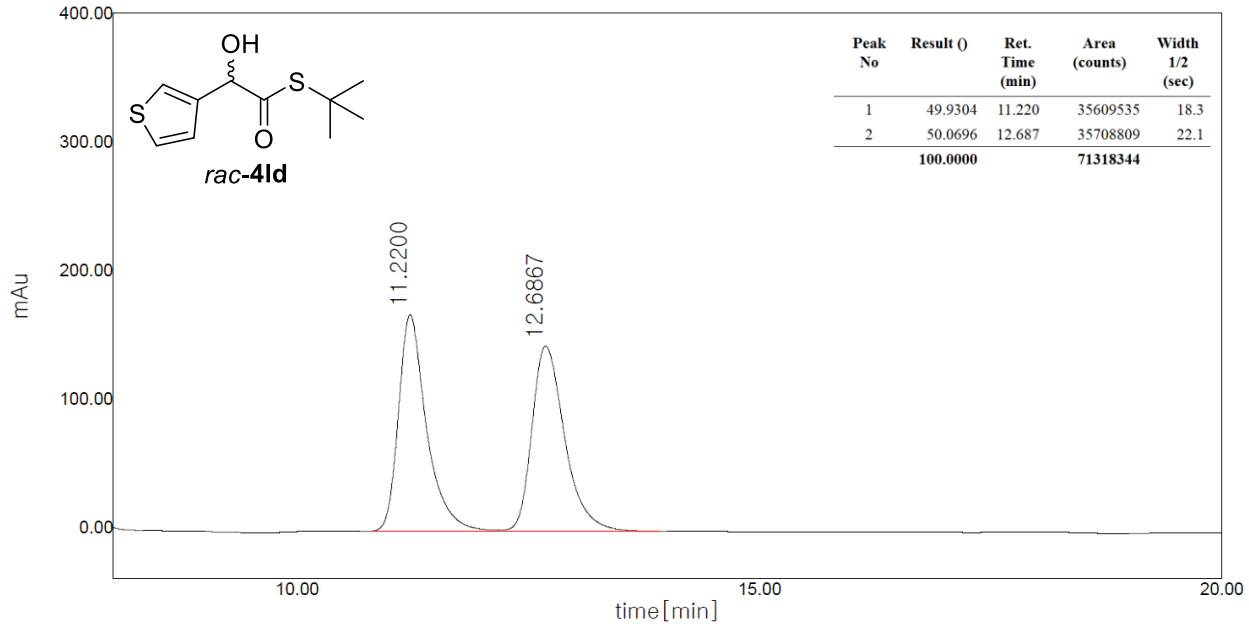
HPLC trace of **4kd** (condition a)



HPLC trace of **4kd** (condition b)

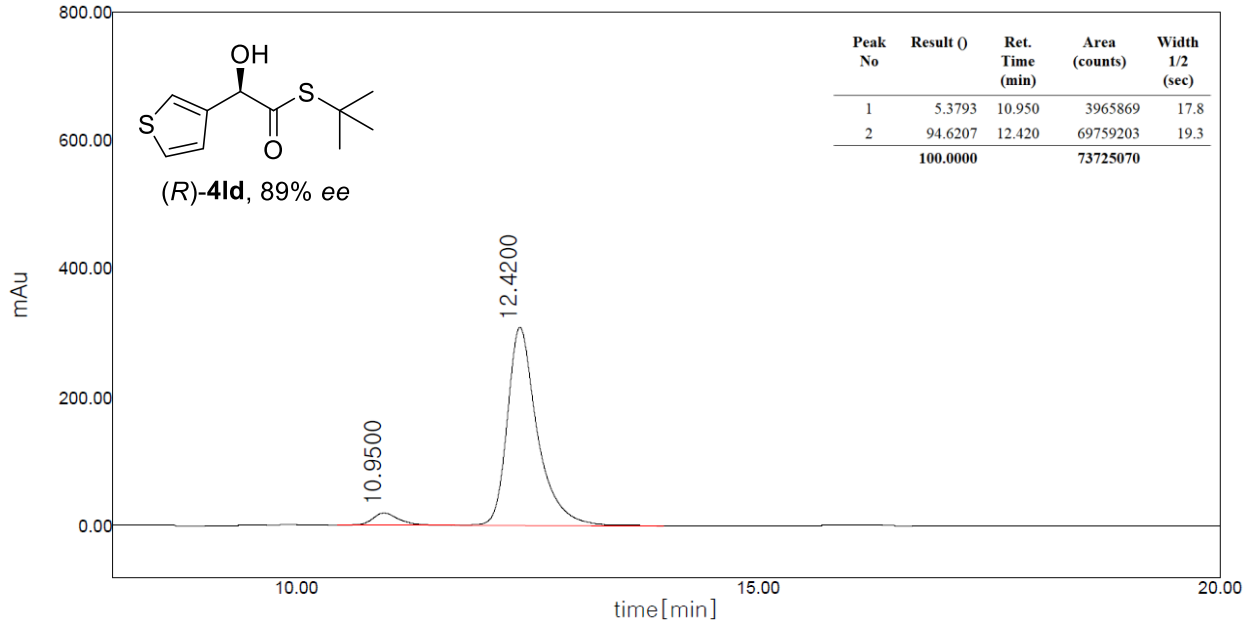


HPLC trace of **4kd** (condition c)



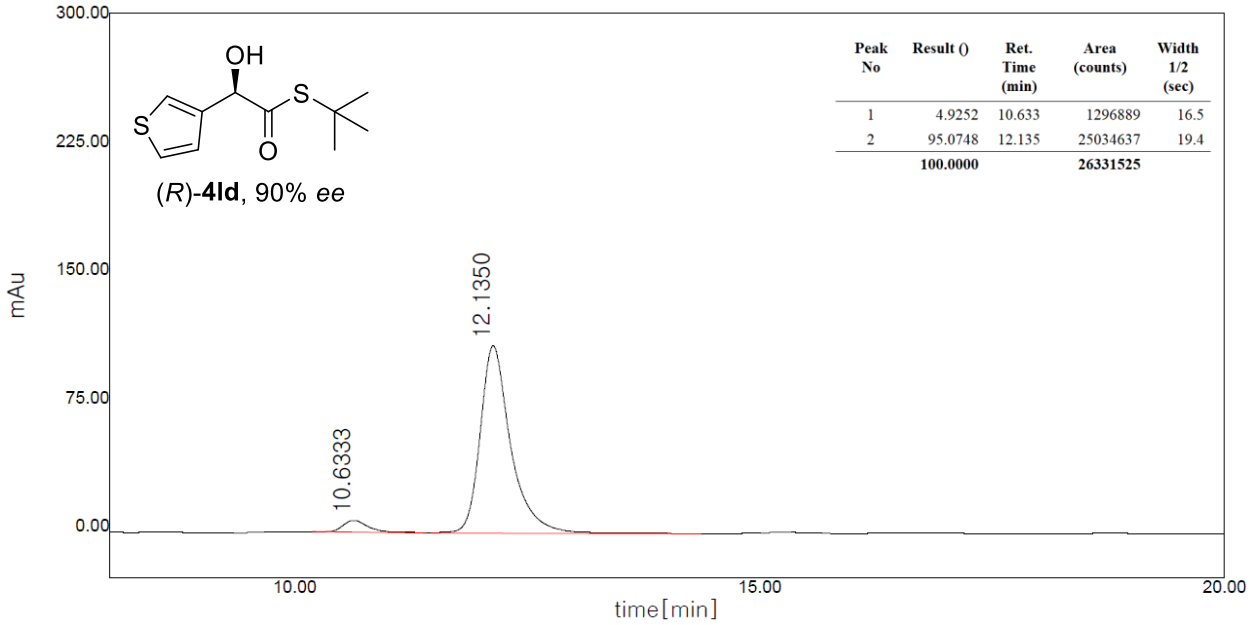
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.9304	11.220	35609535	18.3
2	50.0696	12.687	35708809	22.1
	100.0000		**71318344**	

HPLC trace of *rac*-**4ld**

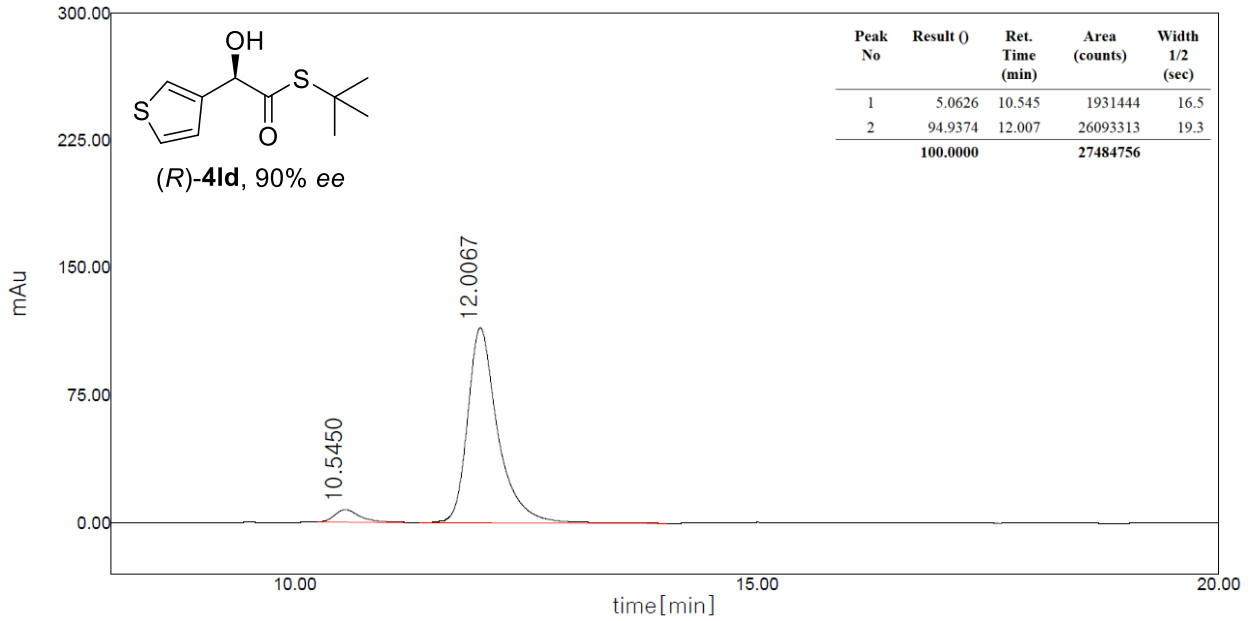


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	5.3793	10.950	3965869	17.8
2	94.6207	12.420	69759203	19.3
	100.0000		**73725070**	

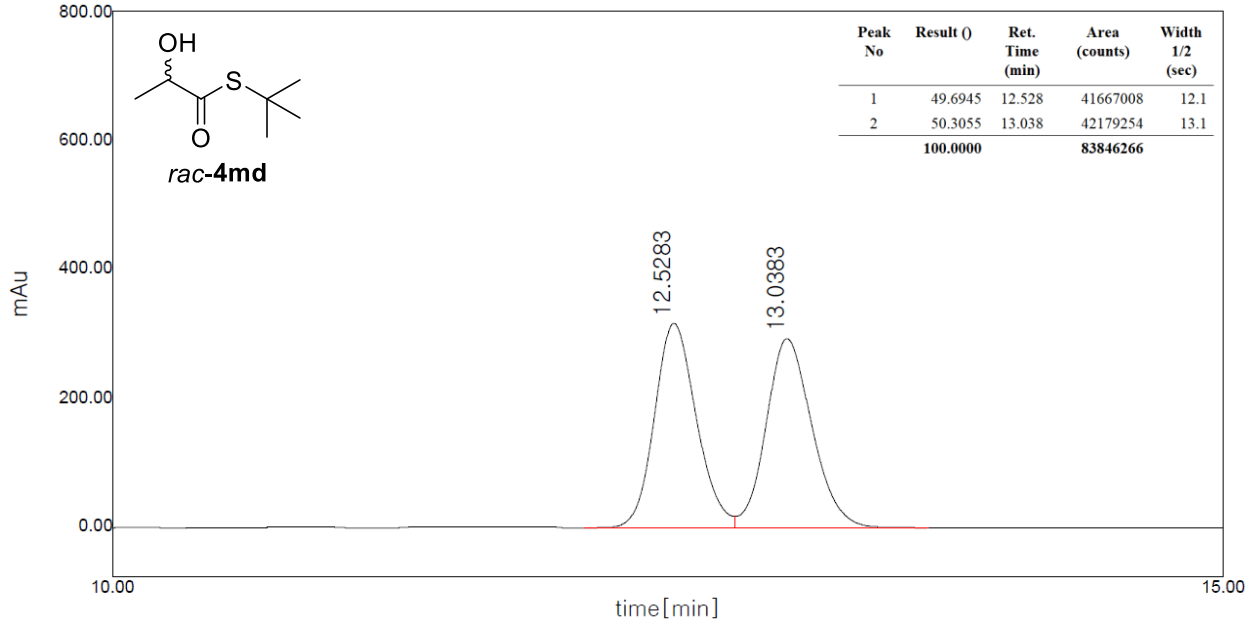
HPLC trace of **4ld** (condition a)



HPLC trace of **4ld** (condition b)

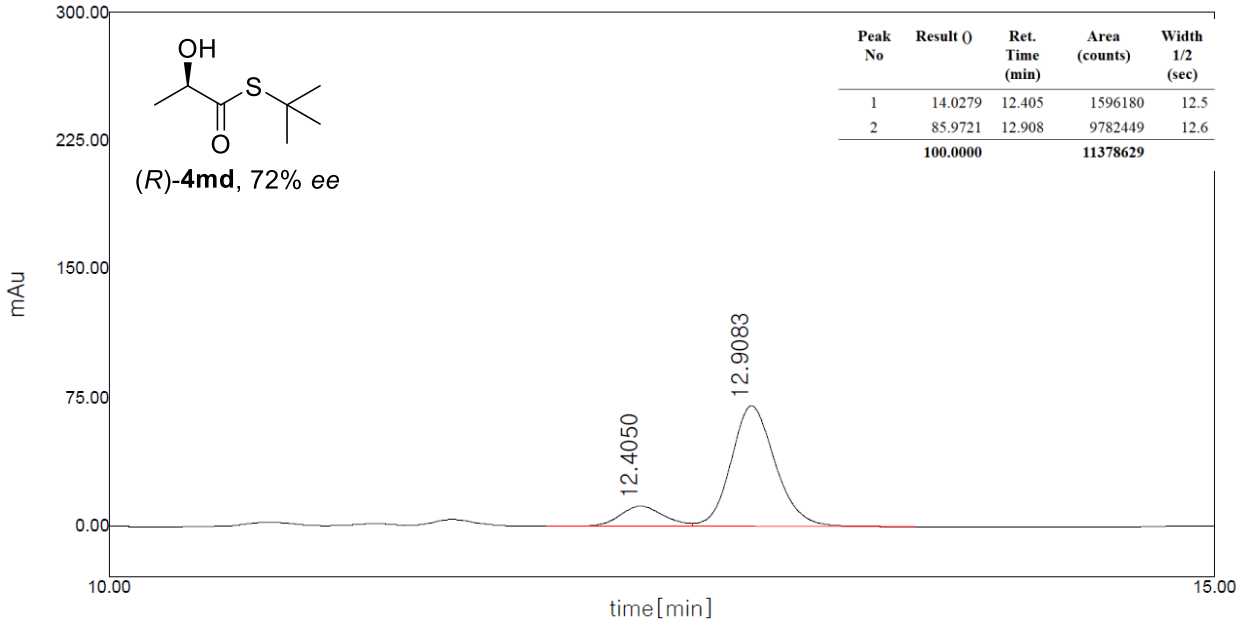


HPLC trace of **4ld** (condition c)



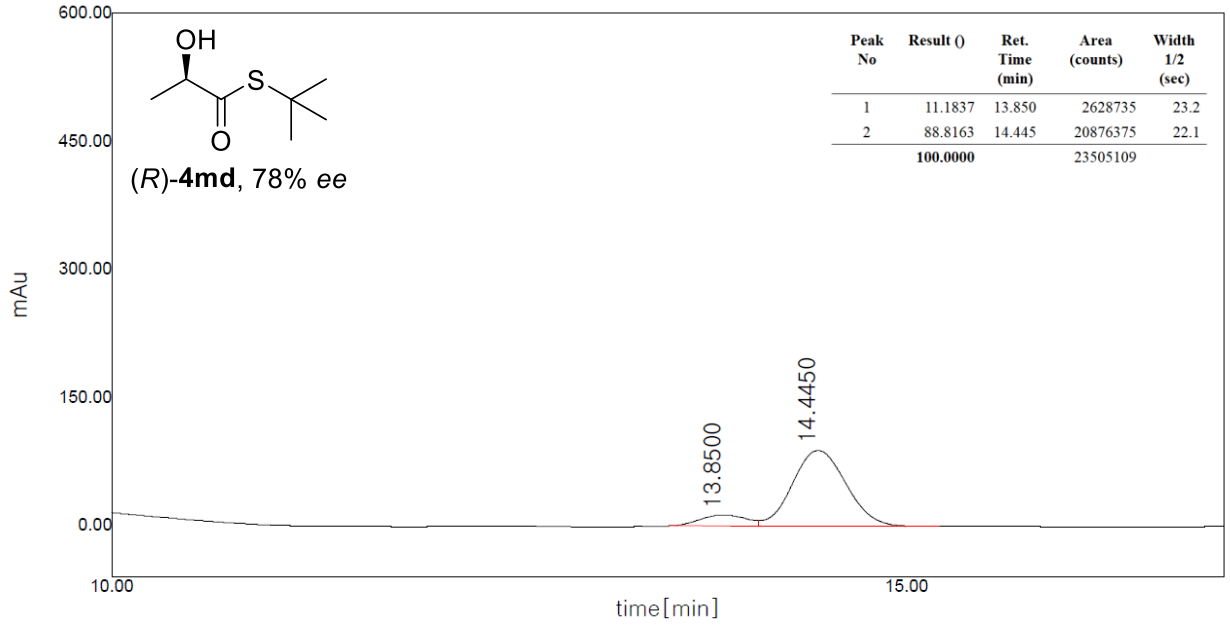
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.6945	12.528	41667008	12.1
2	50.3055	13.038	42179254	13.1
	100.0000		**83846266**	

HPLC trace of *rac*-**4md**



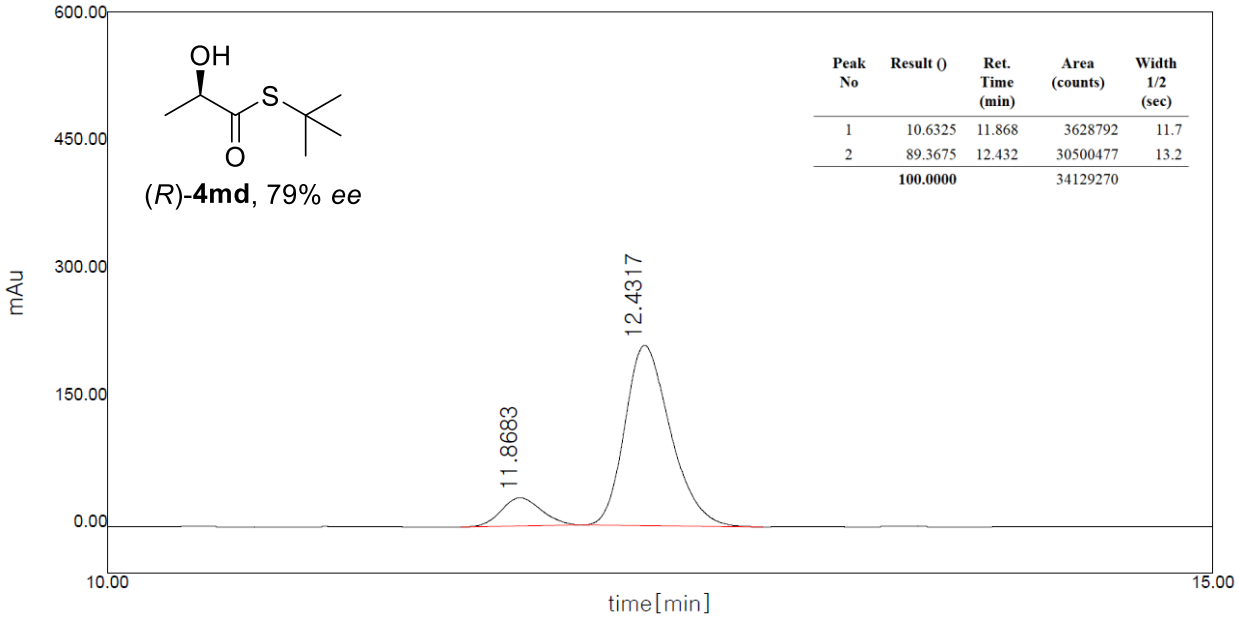
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	14.0279	12.405	1596180	12.5
2	85.9721	12.908	9782449	12.6
	100.0000		**11378629**	

HPLC trace of **4md** (condition a)



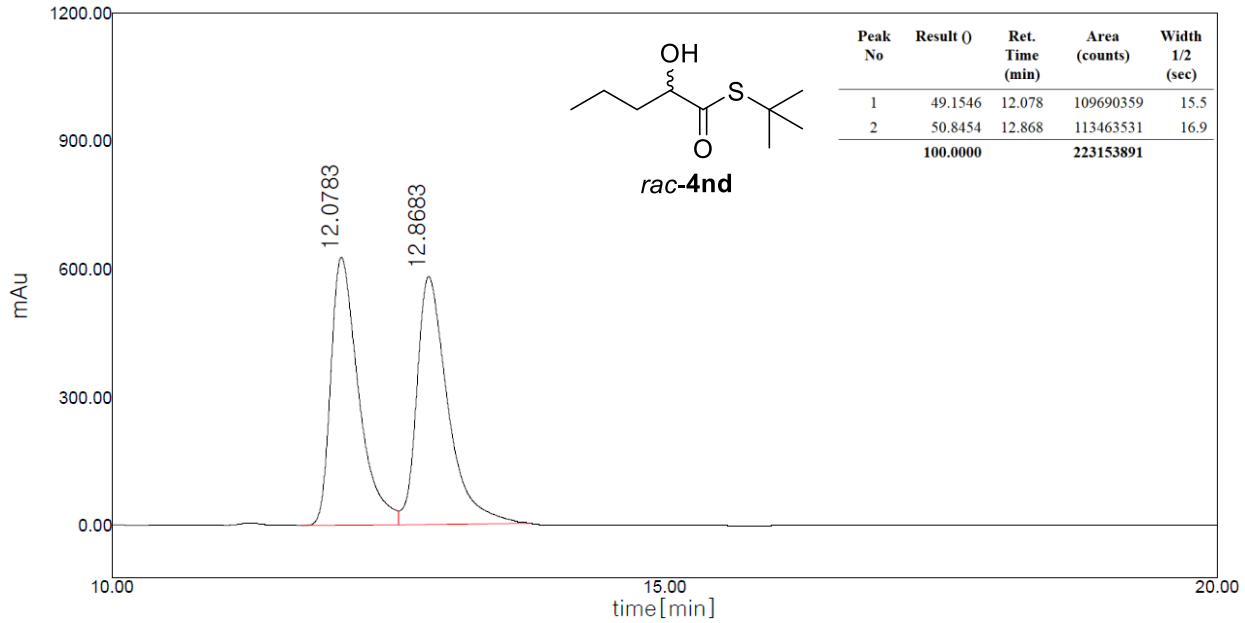
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	11.1837	13.850	2628735	23.2
2	88.8163	14.445	20876375	22.1
	100.0000		23505109	

HPLC trace of **4md** (condition b)



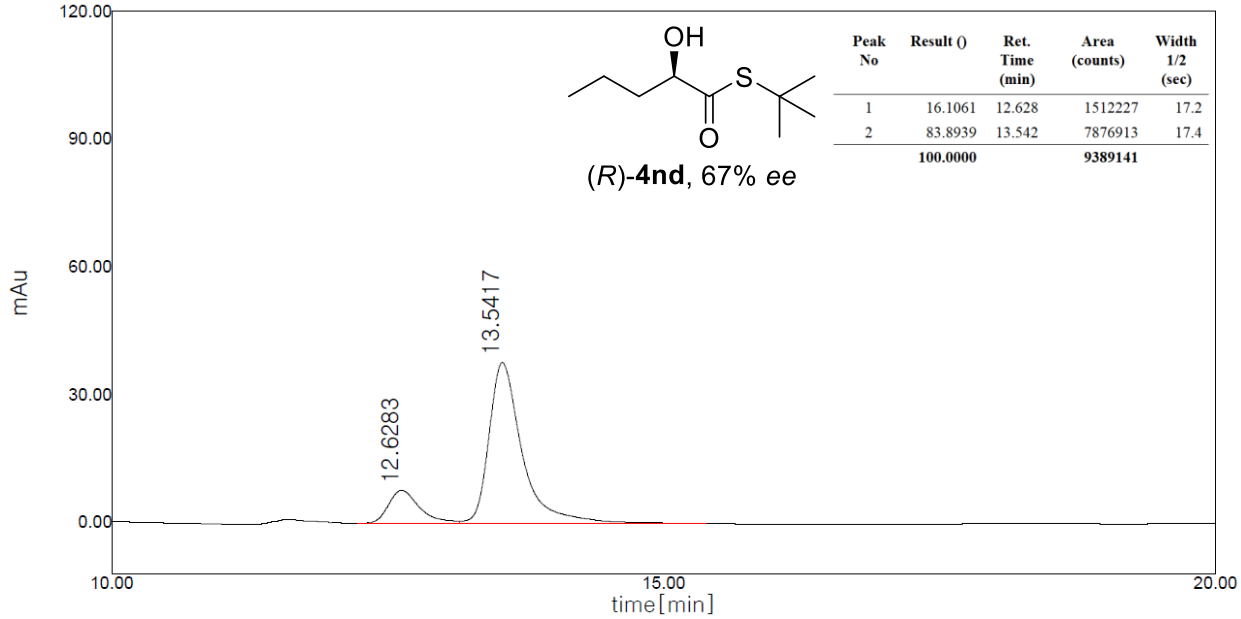
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	10.6325	11.868	3628792	11.7
2	89.3675	12.432	30500477	13.2
	100.0000		34129270	

HPLC trace of **4md** (condition c)



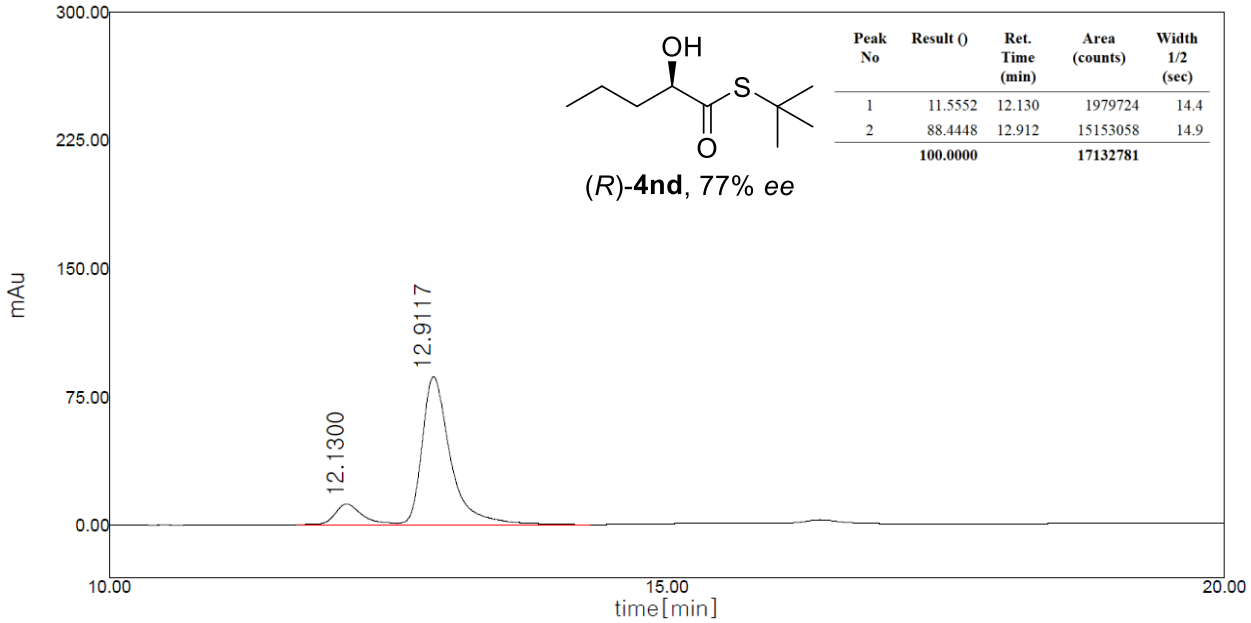
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	49.1546	12.078	109690359	15.5
2	50.8454	12.868	113463531	16.9
	100.0000		**223153891**	

HPLC trace of *rac*-**4nd**

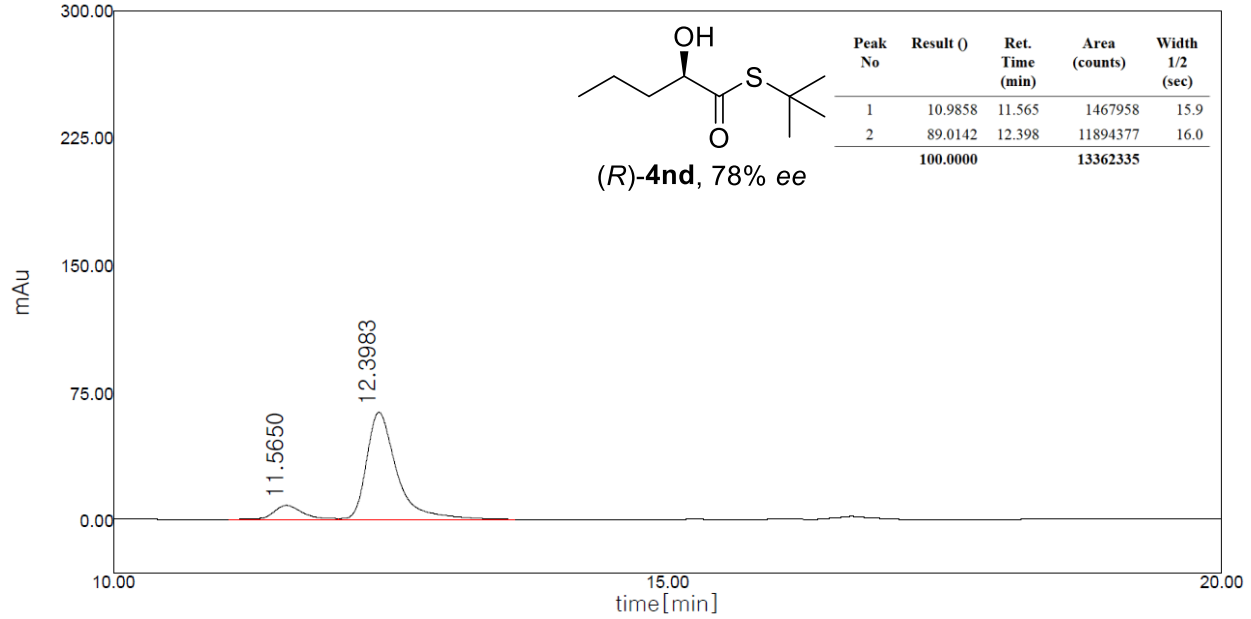


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	16.1061	12.628	1512227	17.2
2	83.8939	13.542	7876913	17.4
	100.0000		**9389141**	

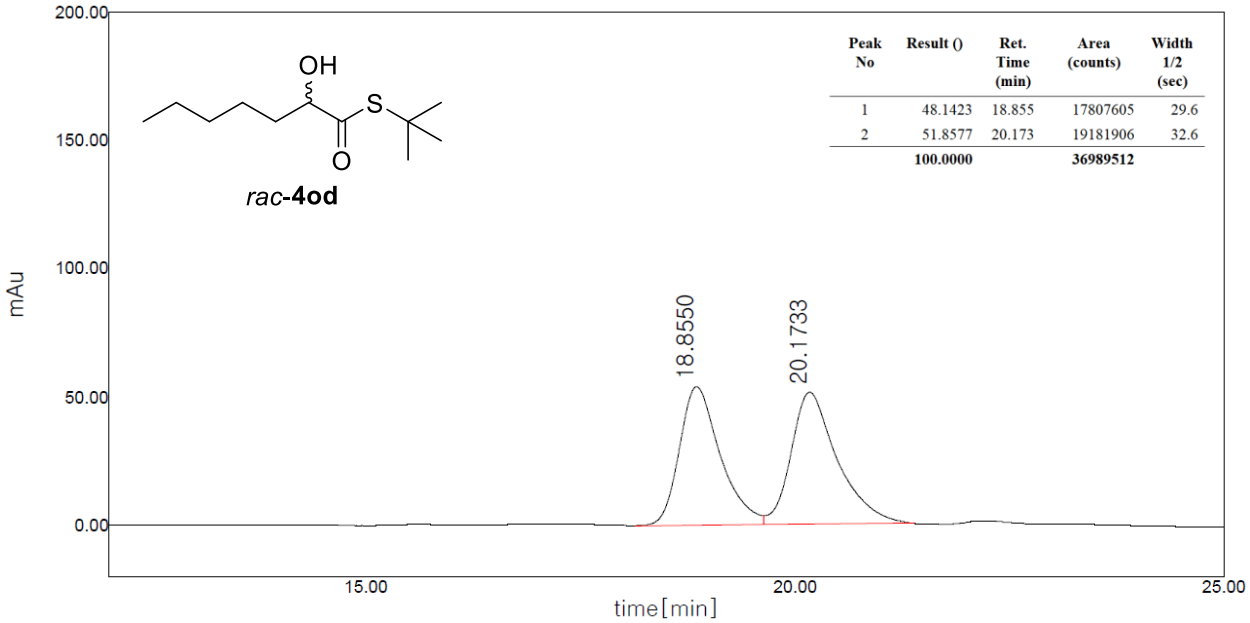
HPLC trace of **4nd** (condition a)



HPLC trace of **4nd** (condition b)

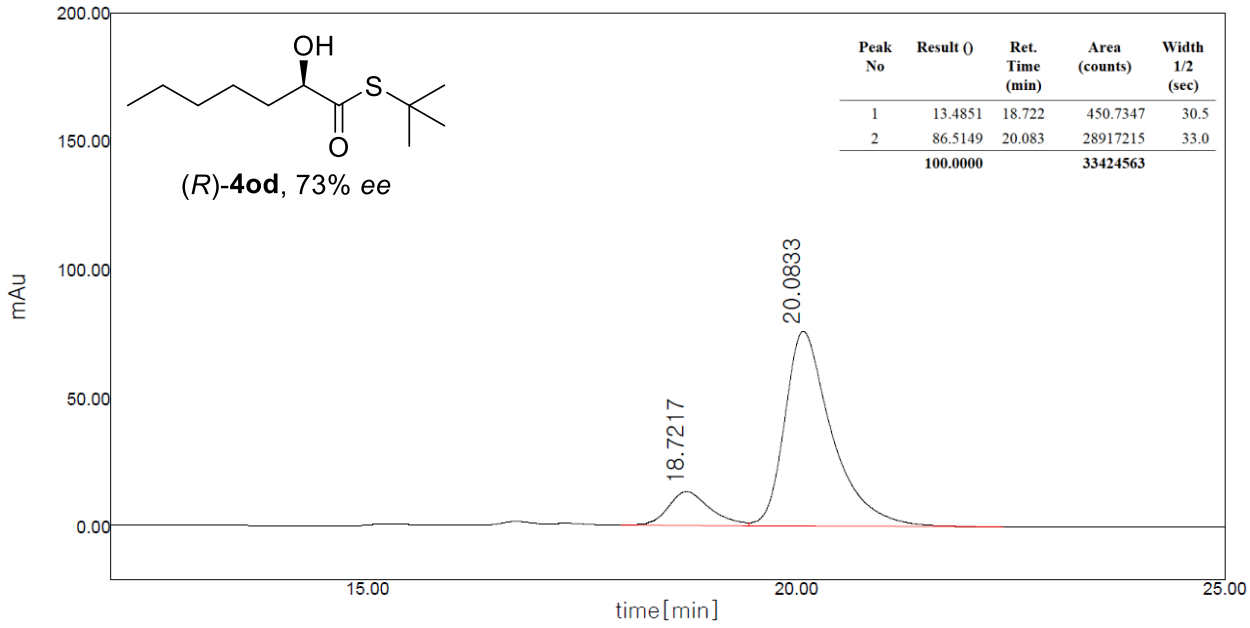


HPLC trace of **4nd** (condition c)



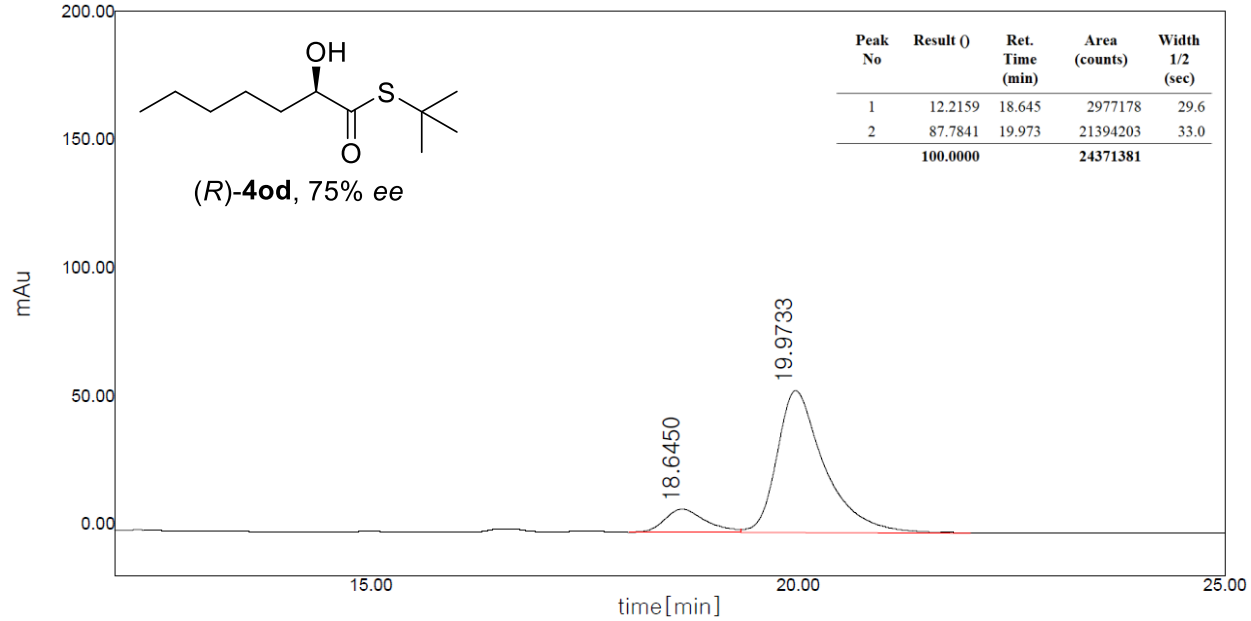
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	48.1423	18.855	17807605	29.6
2	51.8577	20.173	19181906	32.6
	100.0000		**36989512**	

HPLC trace of *rac*-**4od**

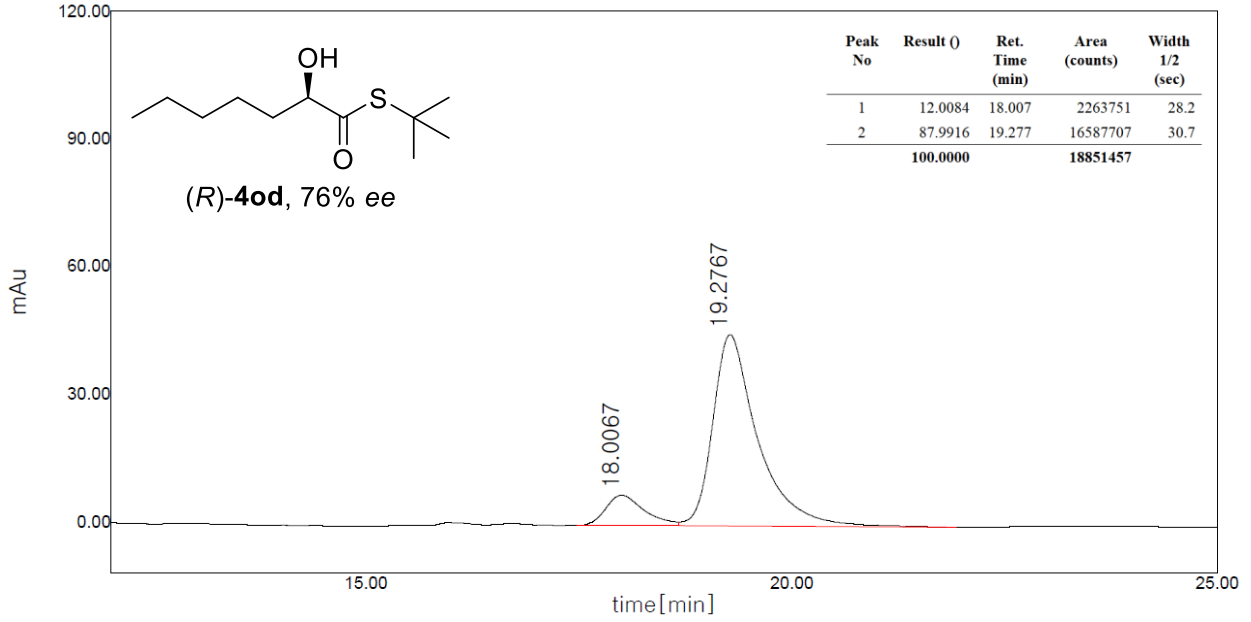


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	13.4851	18.722	450.7347	30.5
2	86.5149	20.083	28917215	33.0
	100.0000		**33424563**	

HPLC trace of **4od** (condition a)



HPLC trace of **4od** (condition b)



HPLC trace of **4od** (condition c)

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2. Zheng, Q.; Maksimovic, I.; Upad, A.; Guber, D.; David, Y. Synthesis of an Alkynyl Methylglyoxal Probe to Investigate Nonenzymatic histone Glycation. *J. Org. Chem.* **2020,** *85*, 1691−1697.

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