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Enantiospecific on-water bromination: a mild and efficient protocol for the preparation of alkyl bromides

Francesco Alletto and Mauro F. A. Adamo*

Centre for Synthesis and Chemical Biology (CSCB), Department of Chemistry, Royal College of Surgeons in Ireland, 123 St. Stephen's Green, Dublin 2, Ireland

email: *madamo@rcsi.ie*

Supporting Information

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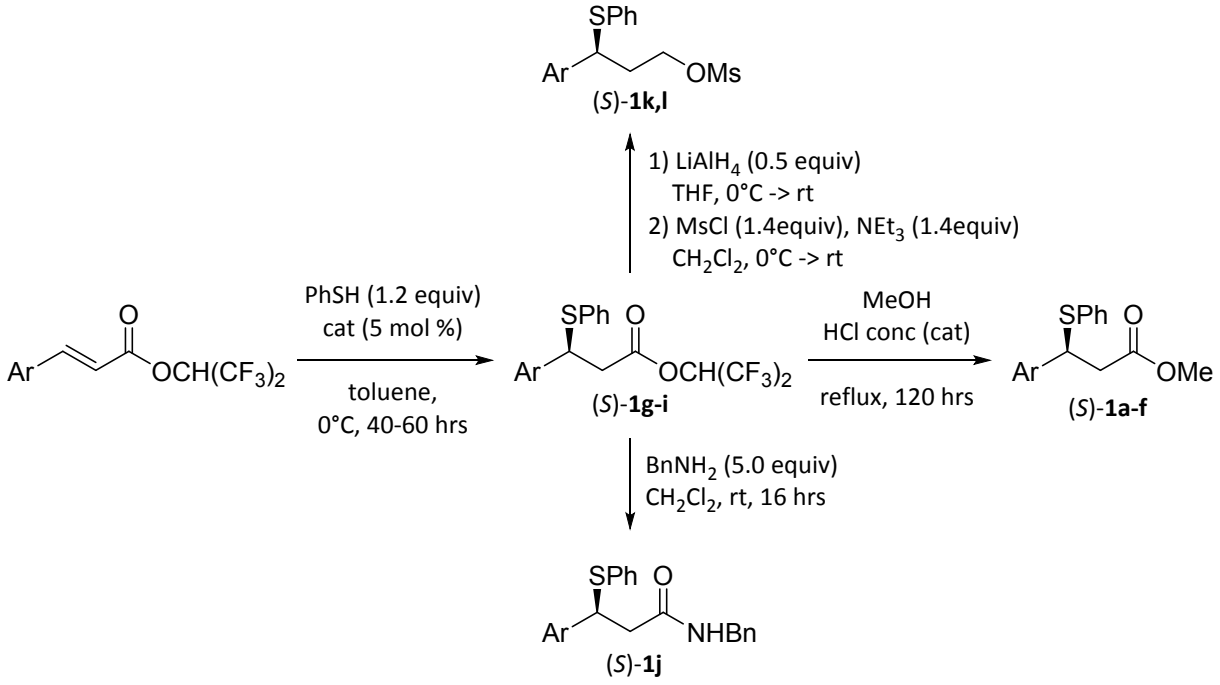
1. General remarks

Vigorous stirring was achieved with an Ika C-MAG HS 7 magnetic stirrer. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals for ^{1}H and ^{13}C NMR (^{1}H NMR: 7.26 ppm for $CDCl_3$, ^{13}C NMR: 77.00 ppm for $CDCl_3$). ^{13}C NMR spectra were acquired with ^{1}H broad band decoupled mode. Coupling constants (J) are in Hz. Melting points were measured using a Stuart scientific melting point apparatus and are uncorrected. High resolution mass spectra were obtained on a Bruker micrOTOF-Q III LC-MS spectrometer interfaced to a Dionex UltiMate 3000 LC (APCI method). Optical rotations were measured on a Perkin-Elmer 343 polarimeter. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Shimadzu SIL-20AHT HPLC instrument.

2. Materials

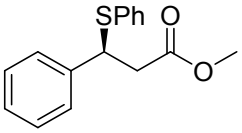
Analytical grade solvents and commercially available reagents were used as received. Dry CH_2Cl_2, DCE, toluene, MeCN and DMF were purchased from commercial sources. Dry THF was obtained from an Inert Pure Solv Micro drying solvent system. Reactions were monitored by TLC analysis (Merck, aluminum plates, silica gel 60 F254) and/or ^{1}H NMR spectroscopy. Flash column chromatography was performed using silica gel 60 (0.040-0.063 mm, 230-400 mesh). Cinnamate esters, 1,1,1,3,3,3-hexafluoropropan-2-yl cinnamates, were synthesized according to published procedure.[1]

3. Preparation of sulphides



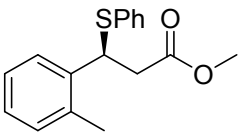
Enantioenriched sulphides (*S*)-**1g-i** were prepared according to published procedure.[1] Synthesis of methyl esters (*S*)-**1a-f** was achieved with known procedure.[1] Amide (*S*)-**1j** was obtained according to procedure.[1] Mesylates (*S*)-**1k,l** were synthesized following published procedure.[2]

Methyl (*S*)-3-phenyl-3-(phenylthio)propanoate – (*S*)-1a



Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a colourless oil (95% yield). All analytical data are consistent with those reported in the literature.[1] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 13.9 min; tr (minor) = 8.9 min: 98.07% ee.

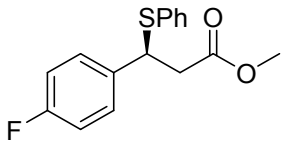
Methyl (*S*)-3-(phenylthio)-3-(o-tolyl)propanoate – (*S*)-1b



Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a yellow oil (89% yield). All analytical data are

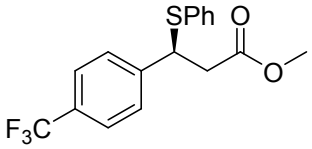
consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 12.9 min; tr (minor) = 6.1 min: 78.86% ee.

Methyl (*S*)-3-(4-fluorophenyl)-3-(phenylthio)propanoate – (*S*)-1c



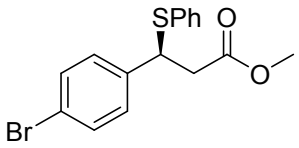
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a colourless oil (91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.17 (m, 7H), 6.93 (t, J = 8.5 Hz, 2H), 4.63 (t, J = 7.7 Hz, 1H), 3.57 (s, 3H), 2.95 (dd, J = 15.8, 6.9 Hz, 1H), 2.88 (dd, J = 15.8, 8.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.05, 162.03 (d, J = 246.2 Hz), 136.30 (d, J = 3.2 Hz), 133.55, 133.27, 129.29 (d, J = 8.1 Hz) 128.97, 128.04, 115.38 (d, J = 21.5 Hz), 51.88, 48.40, 40.48. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.51. $[\alpha]D^{20}$ = -141.0 (c 1.05, $CHCl_3$). HRMS (APCI): $C_{16}H_{16}FO_2S$ $[M + H]^+$, calculated: 291.0855, found: 291.0850. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 5°C, 210 nm): tr (major) = 8.4 min; tr (minor) = 12.5 min: 97.66% ee.

Methyl (*S*)-3-(phenylthio)-3-(4-(trifluoromethyl)phenyl)propanoate – (*S*)-1d



Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a white solid (93% yield).. All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 7.2 min; tr (minor) = 10.3 min: 98.21% ee.

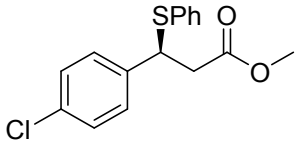
Methyl (*S*)-3-(4-bromophenyl)-3-(phenylthio)propanoate – (*S*)-1e



Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a white solid (99% yield). Mp: 43-45 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.3 Hz, 2H), 7.31 – 7.21 (m, 5H), 7.10 (d, J = 8.3 Hz, 2H), 4.59 (t, J = 7.6 Hz, 1H), 3.59 (s, 3H), 2.95 (dd, J = 15.9, 6.9 Hz, 1H), 2.87 (dd, J = 15.9, 8.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.97, 139.66, 133.57, 133.05, 131.61, 129.36, 129.01, 128.13, 121.40,

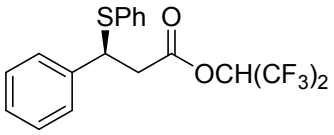
51.96, 48.54, 40.52. $[\alpha]D^{20}$ = -139.2 (c 1.02, $CHCl_3$). HRMS (APCI): $C_{16}H_{14}BrO_2S$ $[M - H]^-$, calculated: 348.9898, found: 348.9903. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 7.8 min; tr (minor) = 10.8 min: 98.57% ee.

Methyl (*S*)-3-(4-chlorophenyl)-3-(phenylthio)propanoate – (*S*)-1f



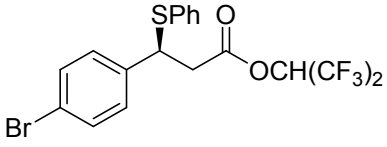
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 9552) as a white solid (73% yield). All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 7.3 min; tr (minor) = 9.4 min: 98.36% ee.

1,1,1,3,3,3-hexafluoropropan-2-yl (*S*)-3-phenyl-3-(phenylthio)propanoate – (*S*)-1g



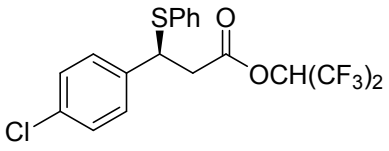
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a white solid (97% yield). All analytical data are consistent with those reported in the literature.[1] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.5 mL/min, 5 °C, 210 nm): tr (major) = 10.3 min; tr (minor) = 11.2 min: 97.31%.

1,1,1,3,3,3-hexafluoropropan-2-yl (*S*)-3-(4-bromophenyl)-3-(phenylthio)propanoate – (*S*)-1h



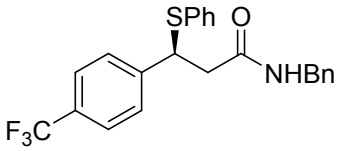
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a white solid (94% yield). All analytical data are consistent with those reported in the literature.[1] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm): tr (major) = 8.6 min; tr (minor) = 10.0 min: 99.11% ee.

1,1,1,3,3,3-hexafluoropropan-2-yl (*S*)-3-(4-chlorophenyl)-3-(phenylthio)propanoate – (*S*)-1i



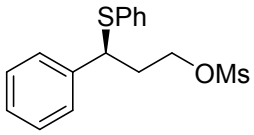
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) as a white solid (91% yield). All analytical data are consistent with those reported in the literature.[1] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.5 mL/min, 5 °C, 210 nm): tr (major) = 10.3 min; tr (minor) = 12.3 min: 98.77% ee.

(*S*)-N-benzyl-3-(phenylthio)-3-(4-(trifluoromethyl)phenyl)propenamide – (*S*)-1j



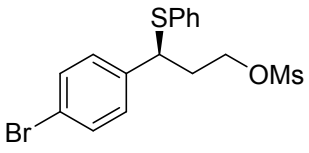
Synthesized according to published procedure.[1] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 70:30) as a white solid (90% yield). Mp: 100-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.29 – 7.20 (m, 8H), 7.02 – 6.97 (m, 2H), 5.81 (bs, 1H), 4.78 (dd, J = 8.5, 6.8 Hz, 1H), 4.40 (dd, J = 14.8, 6.2 Hz, 1H), 4.22 (dd, J = 14.8, 5.2 Hz, 1H), 2.89 (dd, J = 14.5, 6.5 Hz, 1H), 2.70 (dd, J = 14.5, 8.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.12, 145.12, 137.68, 133.17, 133.01, 129.65 (q, J = 32.4 Hz), 129.05, 128.66, 128.12, 128.02, 127.59, 127.55, 125.51 (q, J = 3.7 Hz), 49.32, 43.60, 43.18. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.40. [α]D20 = -105.7 (c 1.06, $CHCl_3$). HRMS (APCI): $C_{23}H_{21}F_3NOS$ $[M + H]^+$, calculated: 416.1296, found: 416.1290. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 80:20, 1.0 mL/min, 5°C, 210 nm): tr (major) = 8.3 min; tr (minor) = 11.8 min: 95.02% ee.

(*S*)-3-phenyl-3-(phenylthio)propyl methanesulphonate – (*S*)-1k



Synthesized according to published procedure.[2] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) as a colourless oil (67% yield). All analytical data are consistent with those reported in the literature.[2] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 16.0 min; tr (minor) = 17.5 min: 97.90% ee.

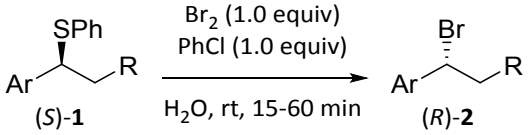
(*S*)-3-(4-bromophenyl)-3-(phenylthio)propyl methanesulphonate – (*S*)-1l



Synthesized according to published procedure.[2] The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) as a colourless oil (70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (t, J = 7.9 Hz, 2H), 7.23 (s, 5H), 7.09 (d, J = 8.2 Hz, 2H), 4.38 – 4.31 (m, 1H), 4.24 (t, J = 7.7 Hz, 1H), 4.18 – 4.08 (m, 1H), 2.93 (s, 3H), 2.37 (td, J = 13.8, 6.8 Hz, 1H), 2.25 (td, J = 14.2, 6.0 Hz, 1H). [α]D20 = -127.0 (c 1.15, $CHCl_3$). HRMS (APCI): $C_{16}H_{18}BrO_3S_2$ $[M + H]^+$, calculated: 400.9881, found: 400.9875. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 16.7 min; tr (minor) = 22.6 min: 98.80% ee.

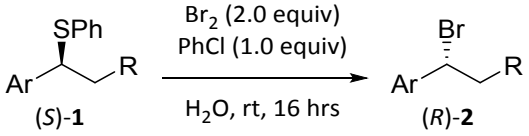
4. Enantiospecific on-water bromination

4.1. General procedure for small-scale bromination of active substrates (GP1)



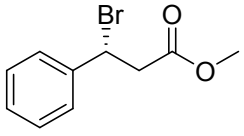
(*S*)-**1** (0.2 mmol, 1.0 equiv) was charged in a 10 mL vial, followed by addition of PhCl (0.2 mmol, 1.0 equiv) and water (2.0 mL) with formation of two unmixable phases. Under vigorous magnetic stirring at 1500 rpm, neat Br_2 (0.2 mmol, 1.0 equiv) was added with immediate colour change of the organic phase to brick-orange. During the reaction time a gradual disappearance of the colour was observed. Upon complete consumption of (*S*)-**1** the organic phase was extracted with Et_2O (3 x 1 mL), dried over Na_2SO_4, concentrated and purified via flash column chromatography on silica gel.

4.2. General procedure for small-scale bromination of deactivated substrates (GP2)



(*S*)-**1** (0.2 mmol, 1.0 equiv) was charged in a 10 mL vial, followed by addition of PhCl (0.2 mmol, 1.0 equiv) and water (2.0 mL) with formation of two unmixable phases. Under vigorous stirring at 1500 rpm, neat Br_2 (0.4 mmol, 2.0 equiv) was added with immediate colour change of the organic phase to brick-orange. During the reaction time a gradual disappearance of the colour was observed. Upon complete consumption of (*S*)-**1** the organic phase was extracted with CH_2Cl_2 (3 x 1 mL), dried over Na_2SO_4, concentrated and purified via flash column chromatography on silica gel.

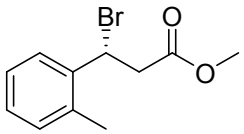
Methyl (*R*)-3-bromo-3-phenylpropanoate – (*R*)-2a



Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (48 mg, 99% yield). All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-

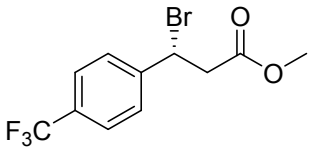
hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 8.5 min; tr (minor) = 15.6 min: 72.49% ee.

Methyl (*R*)-3-bromo-3-(o-tolyl)propanoate – (*R*)-2b



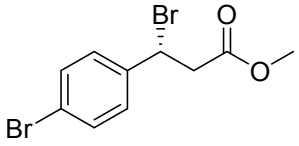
Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (42 mg, 81% yield). All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 5.9 min; tr (minor) = 10.6 min: 55.97% ee.

Methyl (*R*)-3-bromo-3-(4-(trifluoromethyl)phenyl)propanoate – (*R*)-2c



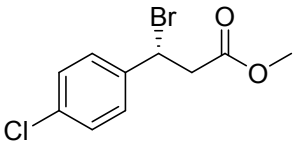
Prepared according to GP2. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (50 mg, 80% yield). All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm): tr (major) = 8.7 min; tr (minor) = 9.3 min: 92.33% ee.

Methyl (*R*)-3-bromo-3-(4-bromophenyl)propanoate – (*R*)-2d



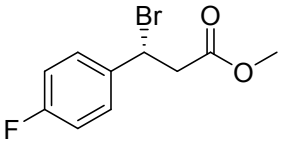
Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (52 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 5.34 (dd J = 8.4, 6.6 Hz, 1H), 3.70 (s, 3H), 3.32 (dd, J = 16.3, 8.6 Hz, 1H), 3.19 (dd, J = 16.3, 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.90, 139.79, 132.05, 128.88, 122.73, 52.22, 46.60, 44.49. [α]D20 = +51.0 (c 1.02, $CHCl_3$). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 5 °C, 210 nm): tr (major) = 10.8 min; tr (minor) = 11.6 min: 79.04% ee.

Methyl (*R*)-3-bromo-3-(4-chlorophenyl)propanoate – (*R*)-2e



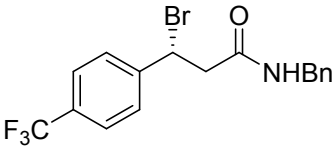
Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (55 mg, 99% yield). All analytical data are consistent with those reported in the literature.[3] Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 8.6 min; tr (minor) = 9.0 min: 82.83% ee.

Methyl (*R*)-3-bromo-3-(4-fluorophenyl)propanoate – (*R*)-2f



Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (47 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 8.5, 5.3 Hz, 2H), 7.04 (t, J = 8.6 Hz, 2H), 5.39 (dd, J = 8.4, 6.8 Hz, 1H), 3.70 (s, 3H), 3.34 (dd, J = 16.3, 8.7 Hz, 1H), 3.20 (dd, J = 16.3, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.00, 162.58 (d, J = 248.5 Hz), 136.70 (d, J = 3.3 Hz), 129.03 (d, J = 8.4 Hz), 115.86 (d, J = 21.8 Hz), 52.19, 46.85, 44.80. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.37. [α]D20 = +55.5 (c 0.99, $CHCl_3$). HRMS (APCI): $C_{10}H_{10}FO_2$ $[M - Br]^+$, calculated: 181.0659, found: 181.0641. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 10 °C, 210 nm): tr (major) = 14.0 min; tr (minor) = 15.0 min: 72.84% ee.

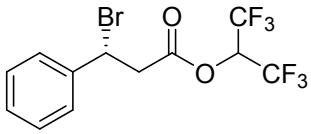
(*R*)-N-benzyl-3-bromo-3-(4-(trifluoromethyl)phenyl)propenamide – (*R*)-2g



Prepared according to GP2. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 75:25) as a white solid (61 mg, 79% yield). Mp: 127-129 °C ^{1}H NMR (400 MHz, CDCl3) δ 7.60 (d, J = 8.2 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.28 (t, J = 7.4 Hz, 3H), 7.15 (d, J = 7.5 Hz, 2H), 5.87 (br s, 1H), 5.52 (dd, J = 8.3, 6.5 Hz, 1H), 4.42 (d, J = 5.7 Hz, 2H), 3.16 (dd, J = 14.8, 8.6 Hz, 1H), 3.06 (dd, J = 14.8, 6.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.23, 144.81, 137.54, 130.74 (q, J = 32.8 Hz), 128.76, 127.76, 127.73, 127.72, 125.90 (q, J = 3.7 Hz), 47.59, 47.09, 43.79.^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69. [α]D20 = +46.0 (c 1.03, $CHCl_3$). HRMS (APCI): $C_{17}H_{16}{}^{79}BrF_3NO$ $[M + H]^+$, calculated: 386.0367, found: 386.0362. Enantiomeric excess was

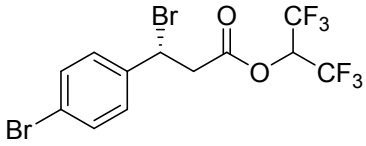
determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 15.3 min; tr (minor) = 18.7 min: 67.23% ee.

1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-3-bromo-3-phenylpropanoate – (*R*)-2h



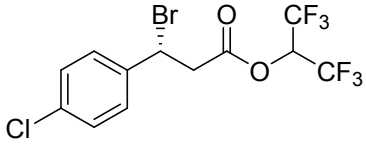
Prepared according to GP1. The title compound was isolated as an inseparable mixture with 1,1,1,3,3,3- hexafluoropropan-2-yl cinnamate (5%) by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (65 mg, 99% yield). All analytical data are consistent with those reported in the literature[3]. [α]D20 = +42.7 (c 1.03, $CHCl_3$). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm): tr (major) = 11.1 min; tr (minor) = 9.8 min: 84.13% ee.

1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-3-bromo-3-(4-bromophenyl)propanoate – (*R*)-2i



Prepared according to GP1. The title compound was isolated as an inseparable mixture with 1,1,1,3,3,3- hexafluoropropan-2-yl cinnamate (14%) by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (97 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 5.74 (hept, J = 6.0 Hz, 1H), 5.32 (dd, J = 8.4, 6.9 Hz, 1H), 3.53 (dd, J = 16.6, 8.8 Hz, 1H), 3.41 (dd, J = 16.6, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.34, 138.73, 132.23, 128.71, 123.18, 120.15 (qd, J = 281.9, 2.9 Hz), 66.78 (dt, J = 69.9, 34.9 Hz), 44.71, 43.72. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.16. [α]D20 = +33.0 (c 0.97, $CHCl_3$). HRMS (APCI): $C_{12}H_6BrF_6O_2$ $[M - HBr - H]^-$, calculated: 374.9455, found: 374.9461. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm): tr (major) = 10.2 min; tr (minor) = 10.7 min: 90.93% ee.

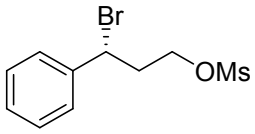
1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-3-bromo-3-(4-chlorophenyl)propanoate – (*R*)-2j



Prepared according to GP1. The title compound was isolated as an inseparable mixture with 1,1,1,3,3,3- hexafluoropropan-2-yl cinnamate (6%) by flash column chromatography (silica gel; petroleum ether/EtOAc, 99:1) as a colourless oil (80 mg, 97% yield). ^{1}H NMR (400 MHz, CDCl3) δ

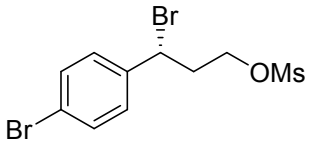
7.38 – 7.31 (m, 4H), 5.73 (hept, J = 6.0 Hz, 1H), 5.34 (virt t, J = 7.73 Hz, 1H), 3.53 (dd, J = 16.6, 8.8 Hz, 1H), 3.42 (dd, J = 16.6, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.36, 138.22, 135.02, 129.26, 128.45, 120.15 (qd, J = 282.1, 3.0 Hz), 66.78 (dt, J = 69.9, 35.0), 44.69, 43.79. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.19. [α]D20 = +50.4 (c 1.19, $CHCl_3$). HRMS (APCI): $C_{12}H_6ClF_6O_2$ [M – HBr – H]$^-$, calculated: 330.9961, found: 330.9966. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK AD-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 5.6 min; tr (minor) = 5.0 min: 92.14% ee.

(*R*)-3-bromo-3-phenylpropyl methanesulphonate – (*R*)-2k



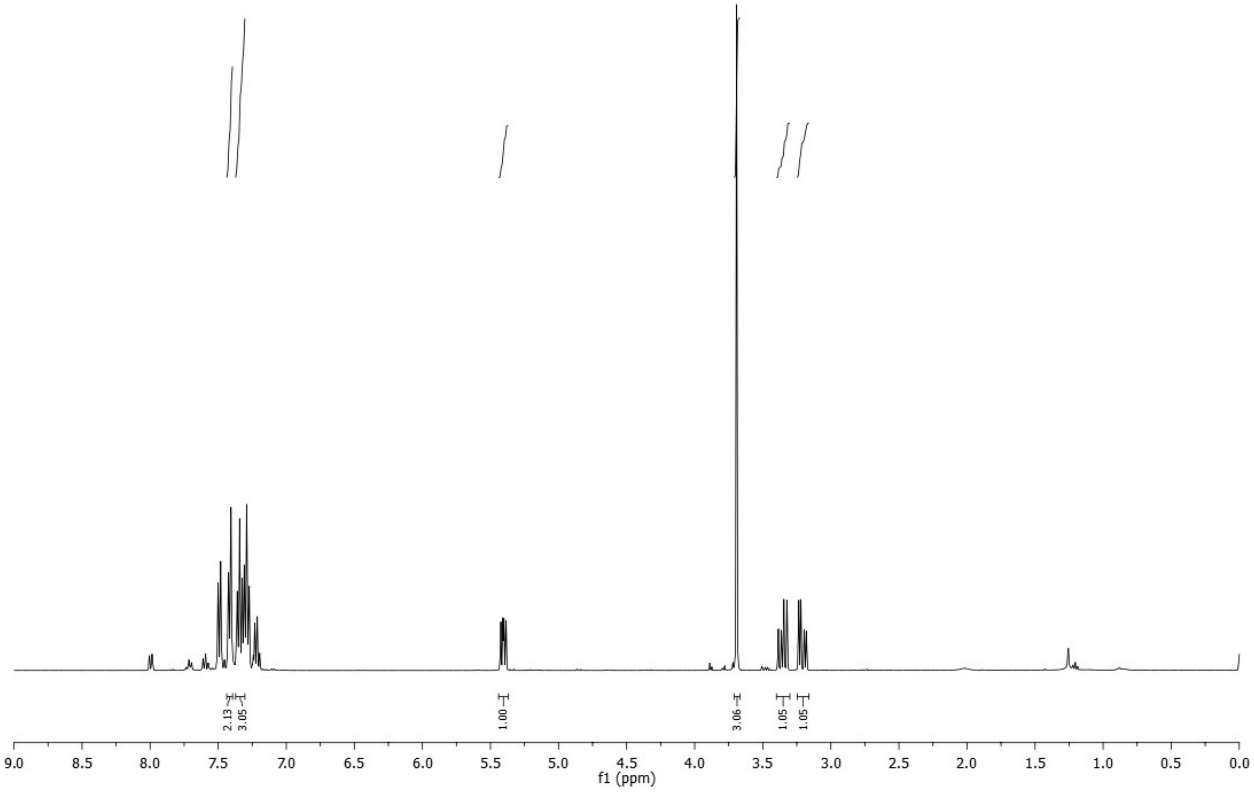
Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) as a colourless oil (55 mg, 93% yield). All analytical data are consistent with those reported in the literature[3]. [α]D20 = +63.3 (c 0.98, $CHCl_3$). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 13.2 min; tr (minor) = 14.4 min: 67.06% ee.

(*R*)-3-bromo-3-(4-bromophenyl)propyl methanesulphonate – (*R*)-2l



Prepared according to GP1. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) as a colourless oil (63 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 5.08 (dd, J = 9.5, 5.4 Hz, 1H), 4.44 – 4.38 (m, 1H), 4.32 (dt, J = 10.3, 5.2 Hz, 1H), 3.04 (s, 3H), 2.60 (ddt, J = 14.6, 9.6, 4.8 Hz, 1H), 2.53 – 2.44 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.78, 132.16, 128.98, 122.79, 67.54, 49.03, 38.88, 37.38. [α]D20 = +46.3 (c 0.95, $CHCl_3$). HRMS (APCI): $C_{10}H_{12}{}^{79}Br_2O_3SNa$ [M + Na]$^+$, calculated: 392.8772, found: 392.8766. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm): tr (major) = 21.7 min; tr (minor) = 20.6 min: 72.41% ee.

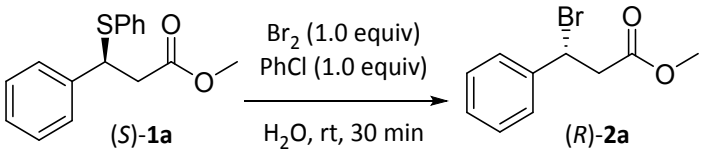
4.3. Copy of ^{1}H NMR spectra of 2a crude of reaction



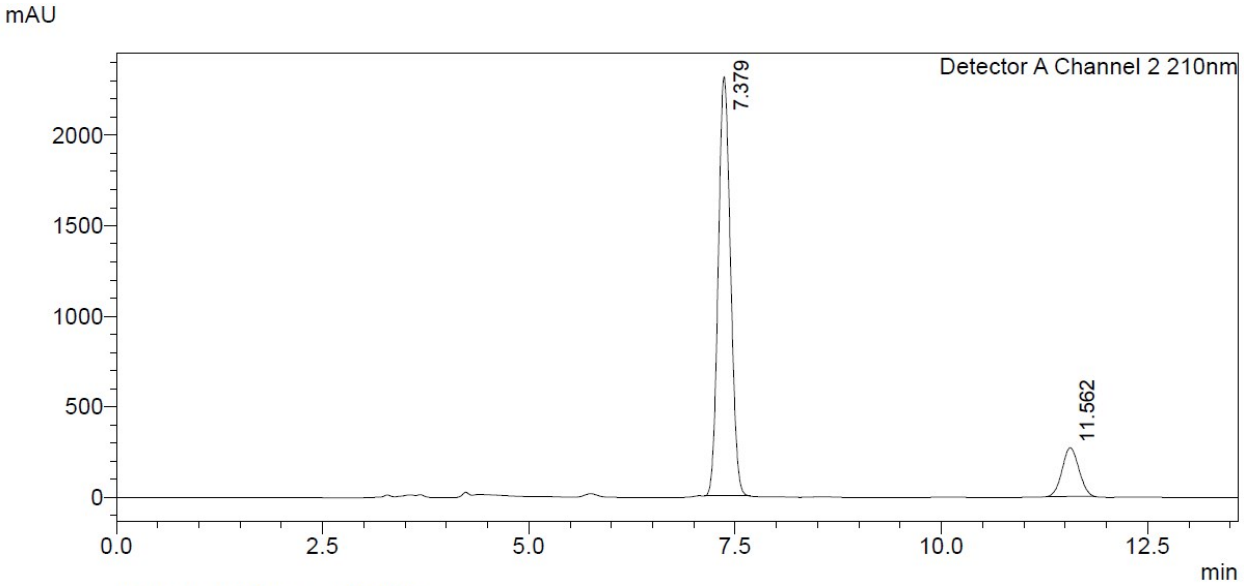
4.4. Recycle of residual waters for consecutive brominations

1a (0.2 mmol, 1.0 equiv) was charged in a 10 mL vial, followed by addition of PhCl (0.2 mmol, 1.0 equiv) and water (2.0 mL) with formation of two unmixable phases. Under vigorous magnetic stirring at 1500 rpm, neat Br_2 (0.2 mmol, 1.0 equiv) was added with immediate colour change of the organic phase to brick-orange. During the reaction time a gradual disappearance of the colour was observed. After 20 minutes, the organic phase was extracted with Et_2O (1 x 1 mL), dried over Na_2SO_4, concentrated and the product distribution was analysed via ^1H NMR. The residual waters were then collected and re-used in a consecutive experiment. Fresh **1a** (0.2 mmol, 1.0 equiv) was charged in a 10 mL vial, followed by addition of PhCl (0.2 mmol, 1.0 equiv) and the collected residual waters (2.0 mL). Under vigorous magnetic stirring at 1500 rpm, neat Br_2 (0.2 mmol, 1.0 equiv) was added. After 20 minutes, the organic phase was extracted with Et_2O (1 x 1 mL), dried over Na_2SO_4, concentrated and the product distribution was analysed via ^1H NMR. The residual waters were then collected and re-used in a following experiment. The consecutive use of residual waters gradually impaired the rate of conversion requiring greater amounts of Br_2 to achieve complete conversion; *i.e.* after four cycles the bromination of **1a** required 1.4 equiv of Br_2 to reach complete consumption of the substrate.

4.5. Gram-scale enantiospecific on-water bromination

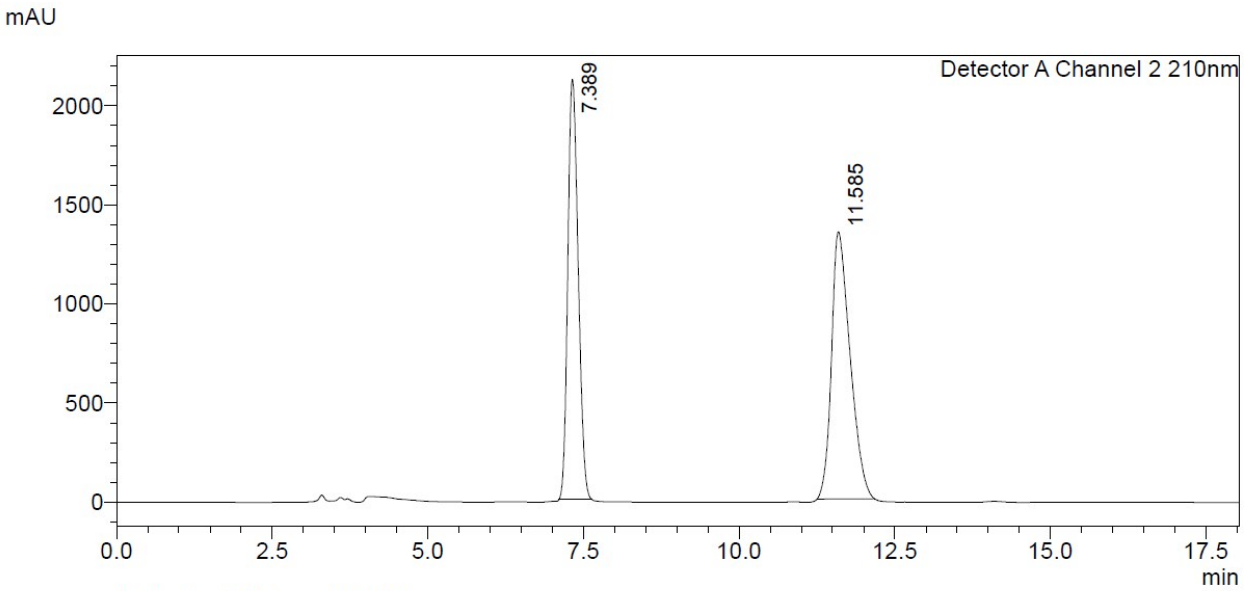


(*S*)-**1a** (10.0 mmol, 1.0 equiv) was charged in a 25 mL round flask, followed by addition of PhCl (10.0 mmol, 1.0 equiv) and water (5 mL) with formation of two unmixable phases. Under vigorous stirring at 1500 rpm, neat Br_2 (10 mmol, 1.0 equiv) was added with immediate colour change of the organic phase to brick-orange. During the reaction time a gradual disappearance of the colour was observed. Upon complete consumption of (*S*)-**1a** the aqueous phase was carefully removed via high-vacuum (pressure ≤ 1.0 mbar) evaporation without further handling and the residual non-viscous organic crude was collected and directly charged in a flash column chromatography for purification (silica gel; petroleum ether/EtOAc, 98:2). Product (*R*)-**2a** was isolated as a colourless oil (1.90 g, 78%). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.8 mL/min, 25 °C, 210 nm): tr (major) = 7.4 min; tr (minor) = 11.6 min: 72.56% ee.



Detector A Channel 2 210nm

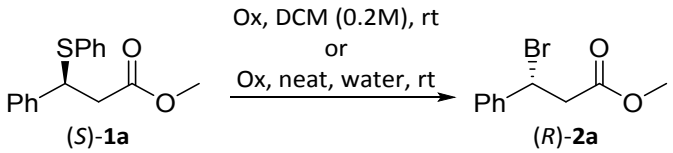
Peak#	Ret. Time	Area	Height	Conc.
1	7.379	23917170	2311482	86.282
2	11.562	3802754	268487	13.718
Total		27719923	2579970	



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.389	22355734	2125197	50.035
2	11.585	22324601	1388826	49.965
Total		44680335	3514023	

5. Comparison of reaction times and ees of in-solution vs on-water



(*S*)-**1a** (*R*)-**2a**

5.1. Procedure for in-solution desulphurative bromination

To a stirred solution of (*S*)-**1a** (0.2 mmol, 1.0 equiv) in dry DCM (1.0 mL) was added the oxidant (quantities as reported in Table S1) at rt under N_2 atmosphere. Upon completion of the reaction – or at stopping of conversion – monitored via ^{1}H NMR analysis, the solvent was evaporated and the residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) to afford (*R*)-**2a** in yields and ees as reported in Table S1. Ees were determined by HPLC analysis on chiral stationary phase.

5.2. Procedure for on-water desulphurative bromination

To a stirred suspension of (*S*)-**1a** (0.2 mmol, 1.0 equiv) in water (1.0 mL) was added the oxidant (quantities as reported in Table S1) at rt. Upon completion of the reaction monitored via ^{1}H NMR analysis, the organic phase was extracted with Et_2O (3 x 1 mL), dried over Na_2SO_4, concentrated and purified via flash column chromatography (silica gel; petroleum ether/EtOAc, 98:2) to afford (*R*)-**2a** in yields and ees as reported in Table S1. Ees were determined by HPLC analysis on chiral stationary phase.

Table S1 Comparison of reaction times and ees of in-solution vs on-water

			In-DCM				On-water			
Entry	Oxidant	Ox equiv	Time	Conv	Yield	ee	Time	Conv	Yield	ee
1	DBI	1.0	15 min	100%	98%	61	5 min	100%	97%	63
2	NBS	2.0	60 hrs	80%	73%	81	2 hrs	100%	97%	68
3	Br_2	1.0	25 min	100%	99%	83	10 min	100%	99%	67

6. References

1 X. Fang, J. Li and C. J. Wang, *Org. Lett.*, 2013, **15**, 3448–3451.

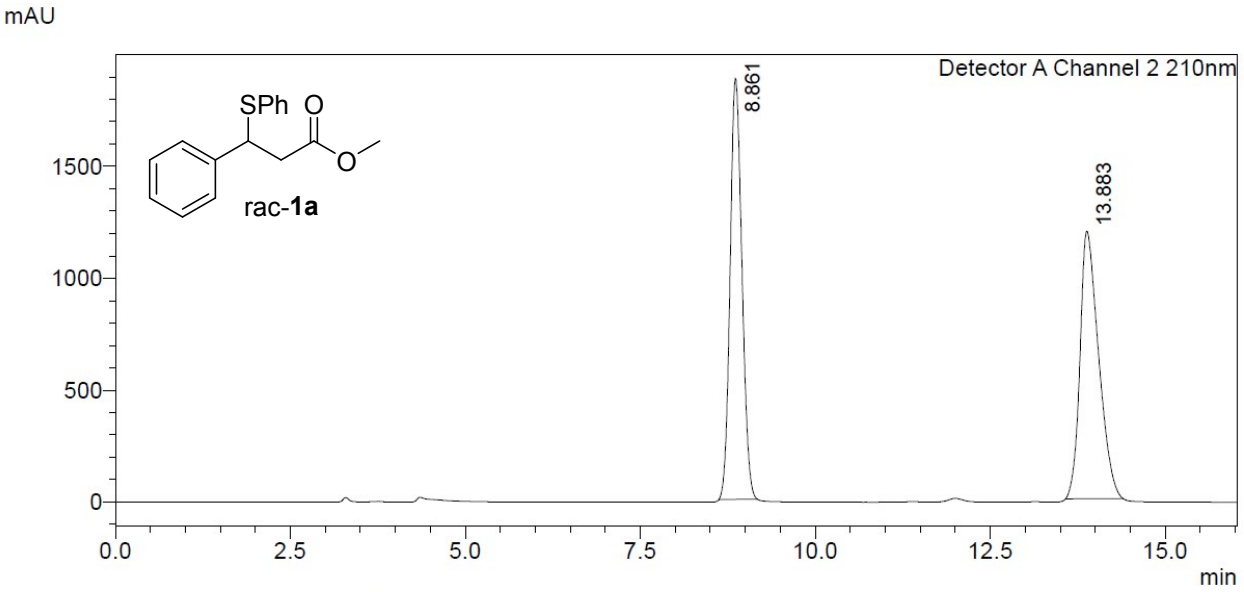
2 D. Canestrari, S. Lancianesi, E. Badiola, C. Strinna, H. Ibrahim and M. F. A. Adamo, *Org. Lett.*, 2017, **19**, 918–921.

3 D. Canestrari, C. Cioffi, I. Biancofiore, S. Lancianesi, L. Ghisu, M. Ruether, J. O'Brien, M. F. A. Adamo and H. Ibrahim, *Chem. Sci.*, 2019, **10**, 9042–9050.

7. HPLC traces of optically active compounds

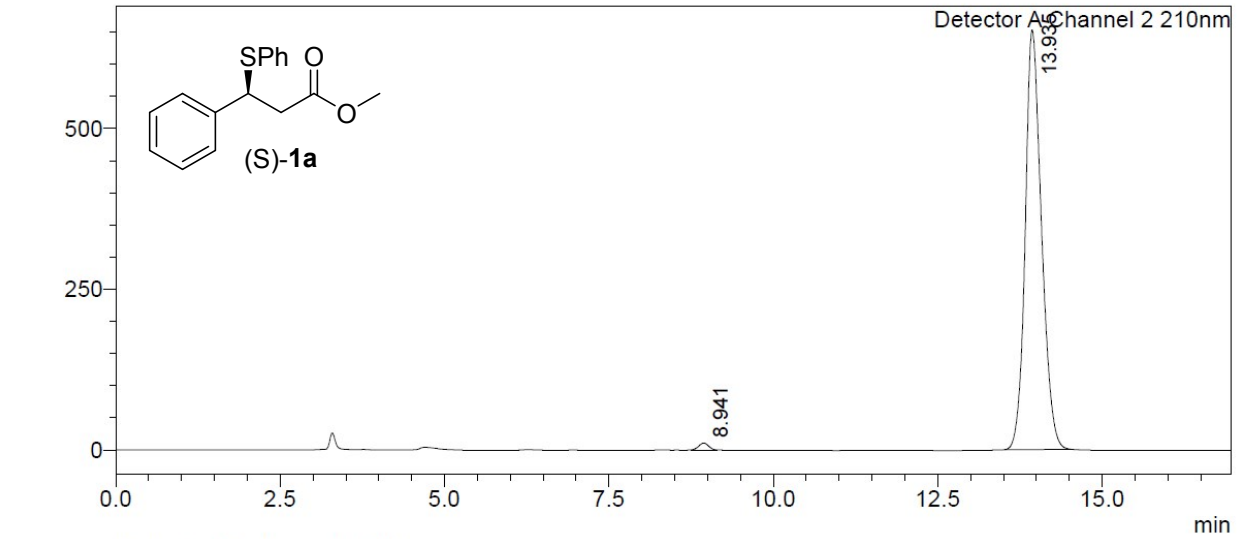
7.1. HPLC traces of (±)-1a and (–)-(S)-1a

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.861	22073554	1878617	50.000
2	13.883	22073201	1195494	50.000
Total		44146755	3074111	

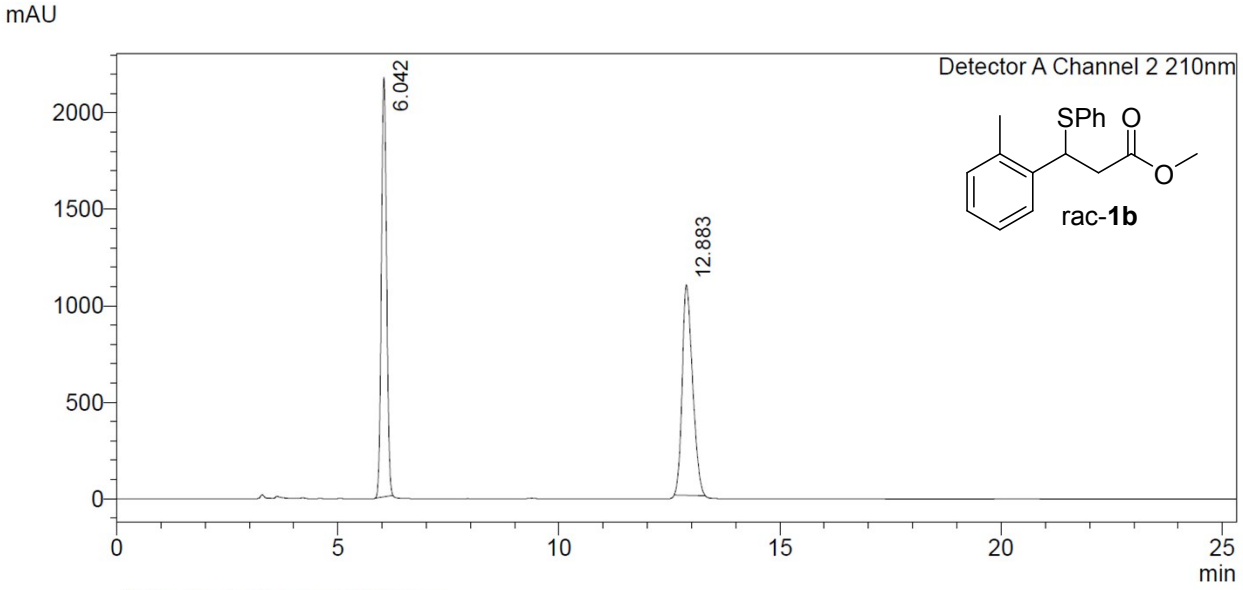


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.941	109467	10661	0.965
2	13.935	11236568	652210	99.035
Total		11346035	662871	

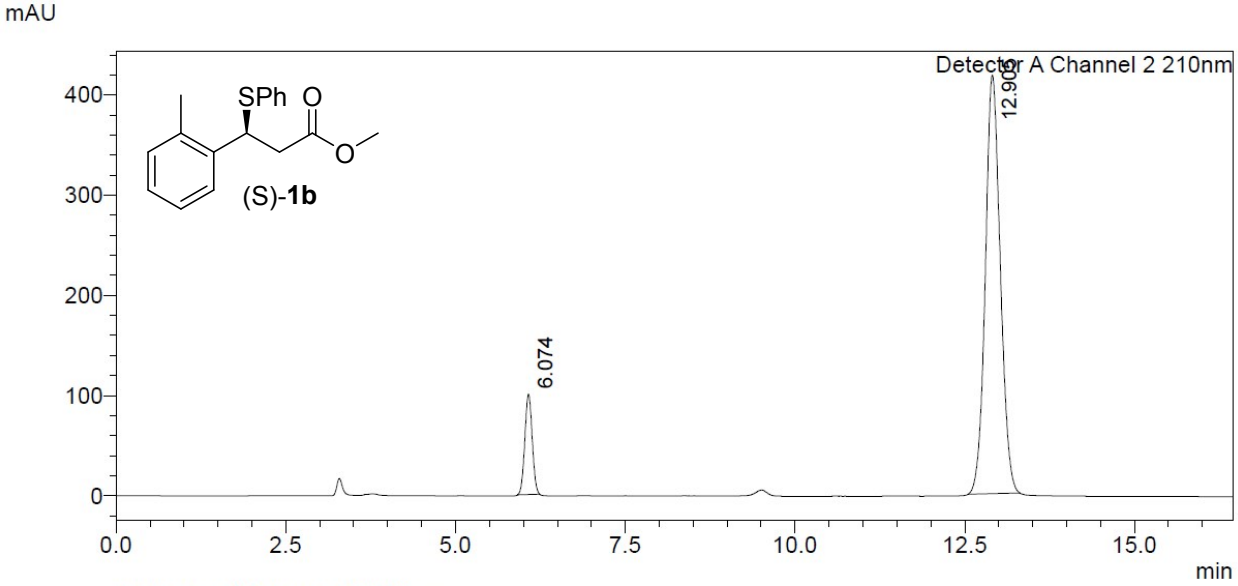
7.2. HPLC traces of (±)-1b and (–)-(S)-1b

CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	6.042	17760006	2171744	49.966
2	12.883	17784336	1090525	50.034
Total		35544342	3262269	

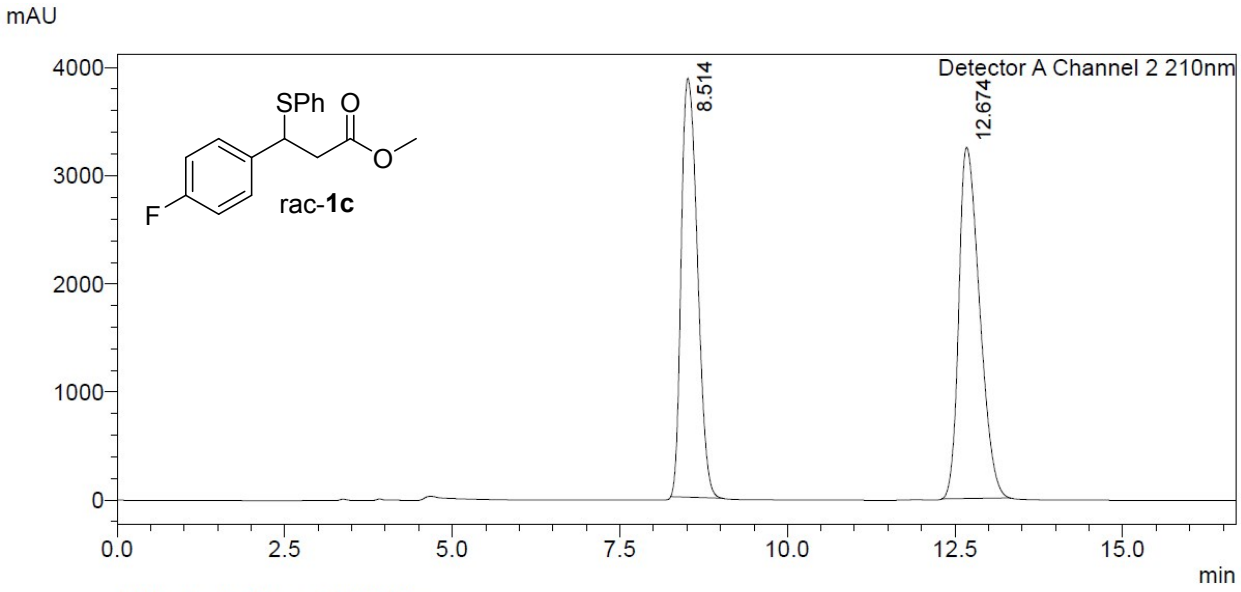


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	6.074	757338	99940	10.571
2	12.905	6406815	417517	89.429
Total		7164153	517457	

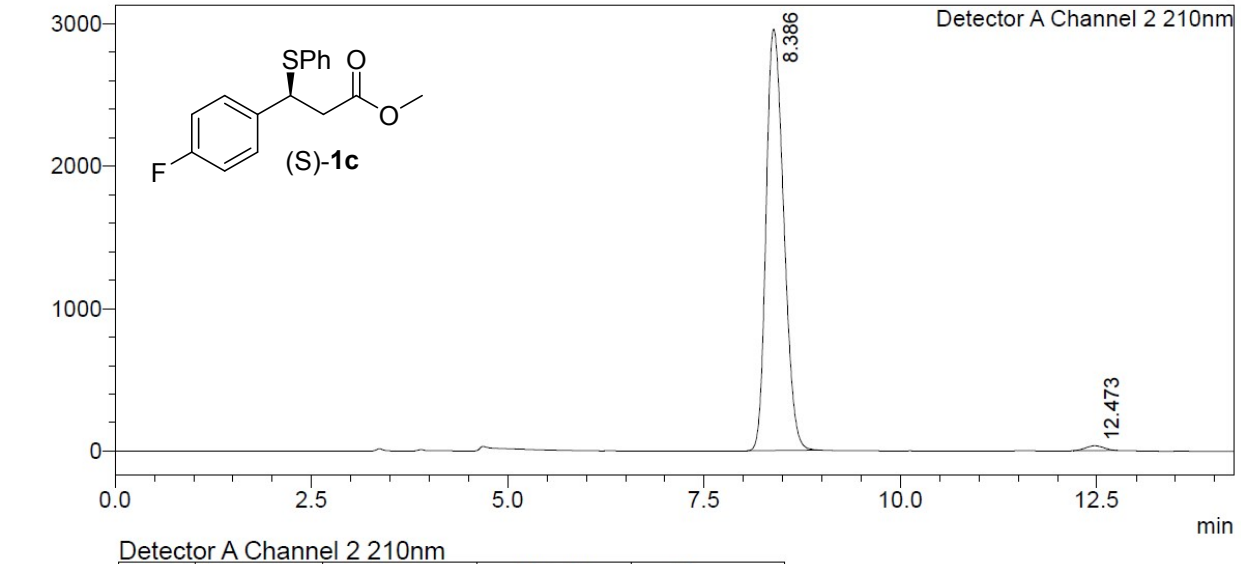
7.3. HPLC traces of (±)-1c and (–)-(S)-1c

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 5°C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.514	64975265	3871292	48.106
2	12.674	70090971	3245145	51.894
Total		135066236	7116437	

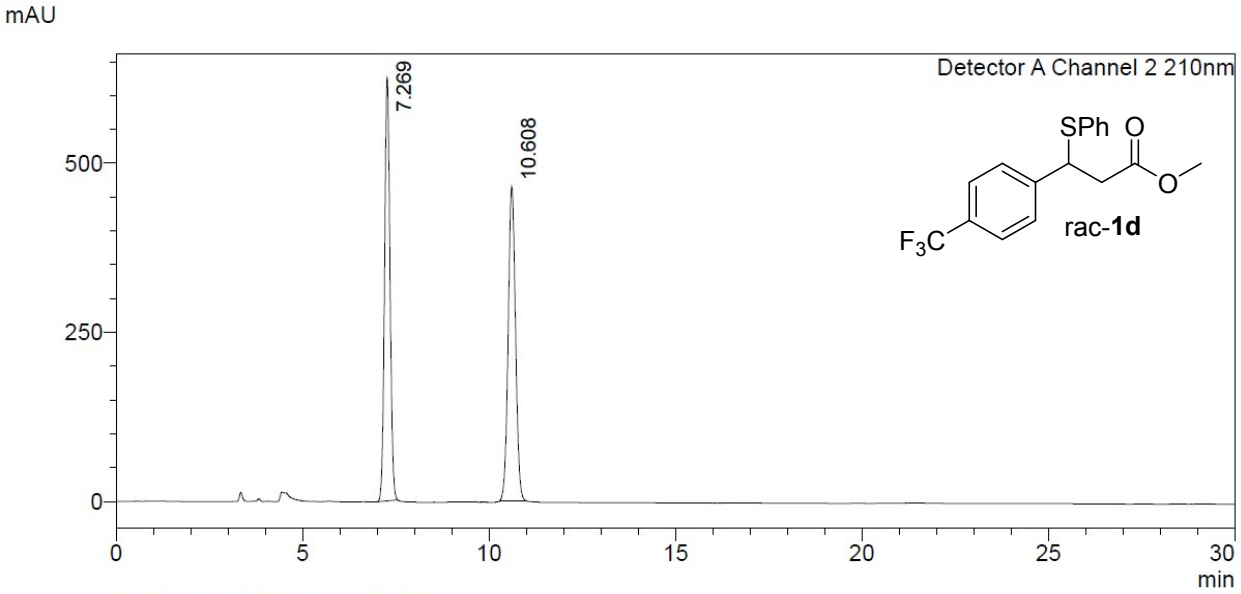


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.386	46260707	2959783	98.828
2	12.473	548497	33429	1.172
Total		46809204	2993213	

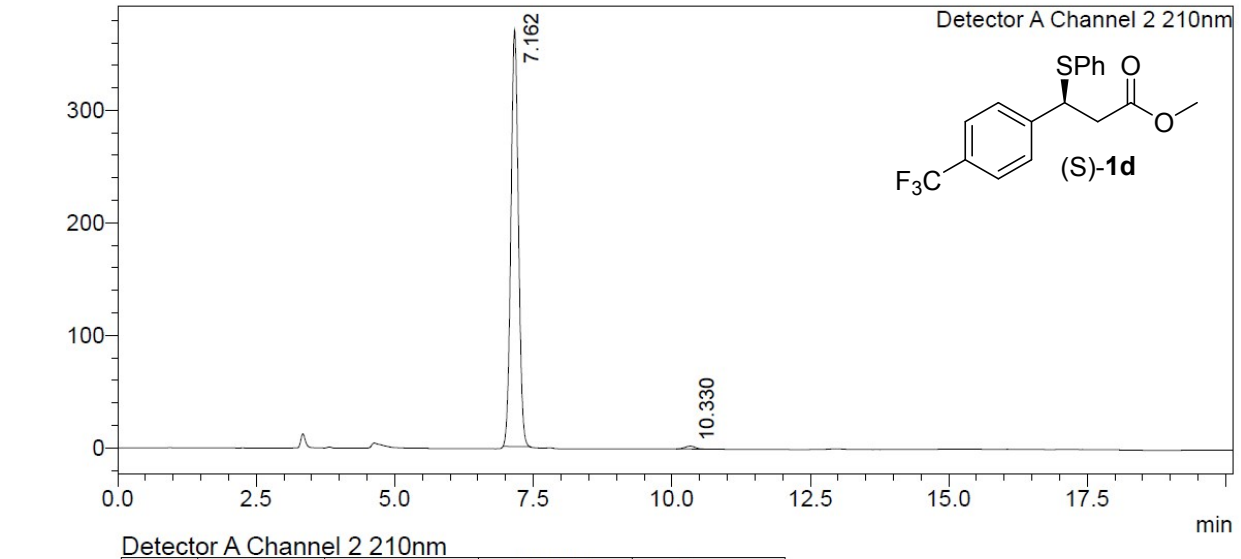
7.4. HPLC traces of (±)-1d and (–)-(S)-1d

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.269	6344916	624948	50.142
2	10.608	6309084	464180	49.858
Total		12654001	1089128	

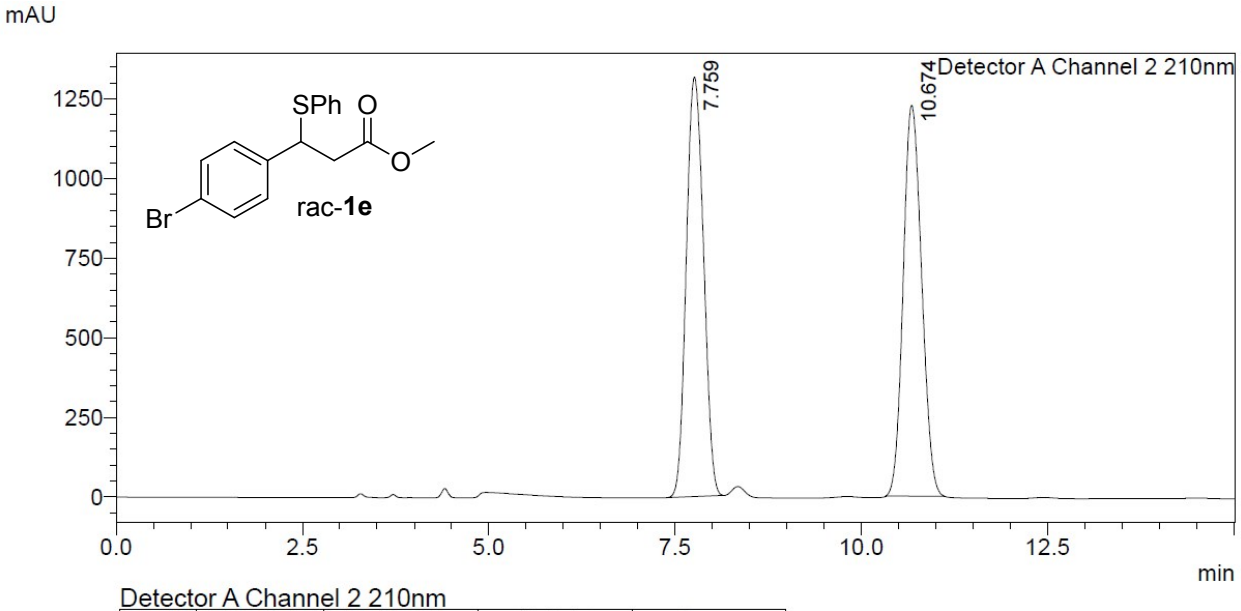


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.162	3491818	369681	99.107
2	10.330	31475	2473	0.893
Total		3523293	372154	

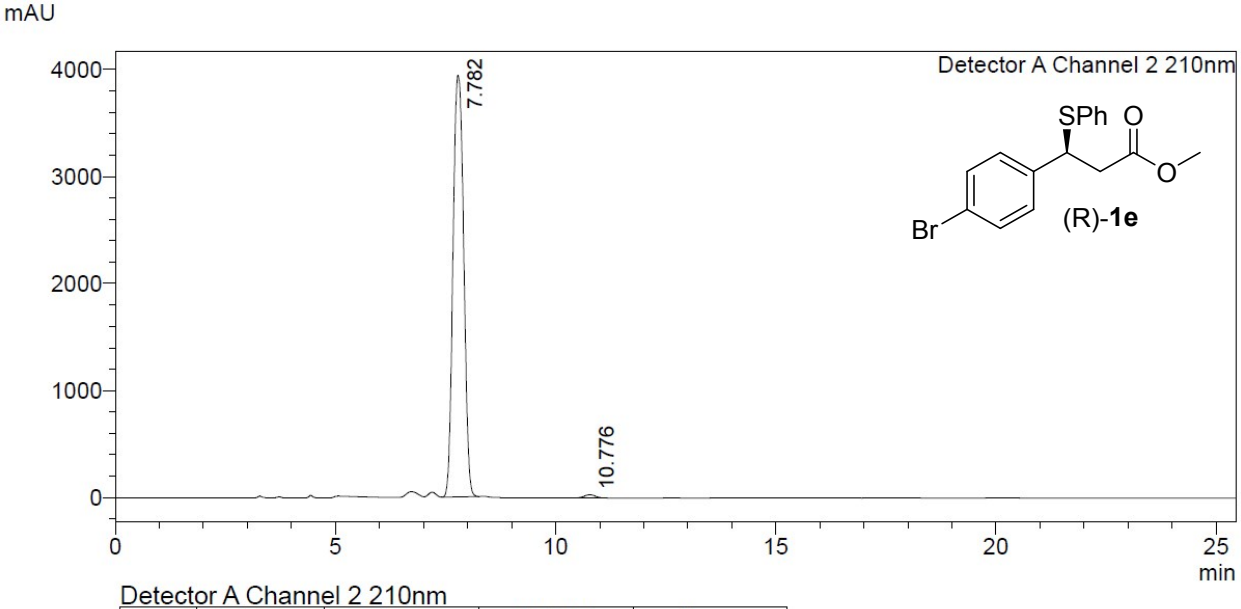
7.5. HPLC traces of (±)-1e and (–)-(S)-1e

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.759	21196132	1316343	50.087
2	10.674	21122884	1226826	49.913
Total		42319016	2543169	

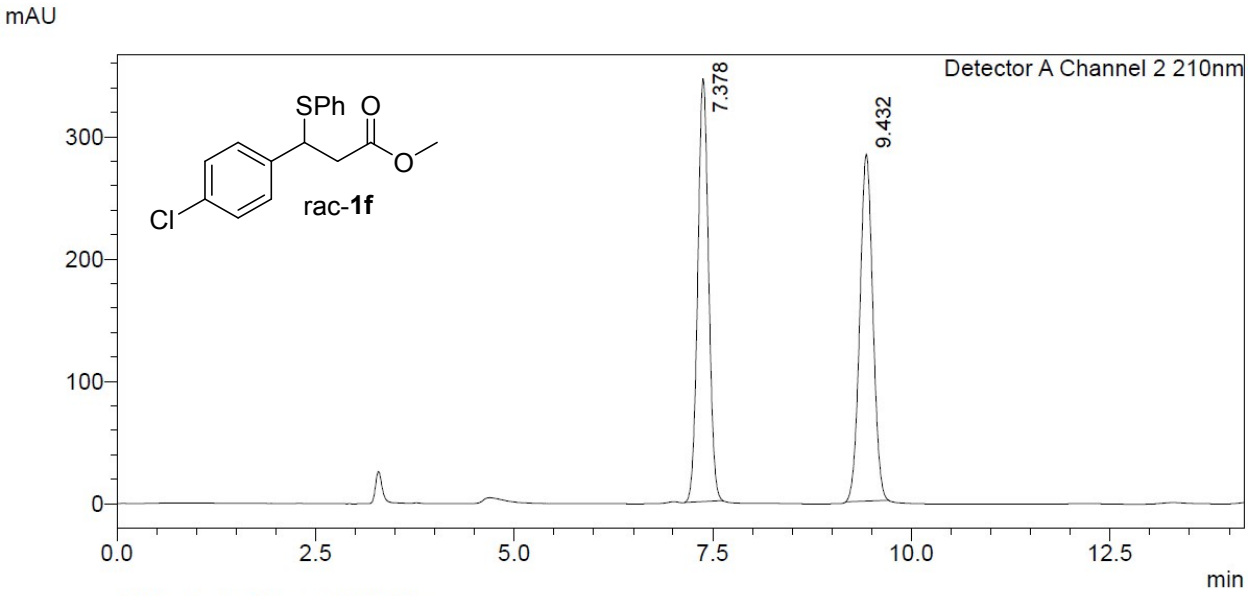


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.782	66351561	3937060	99.284
2	10.776	478605	29400	0.716
Total		66830166	3966460	

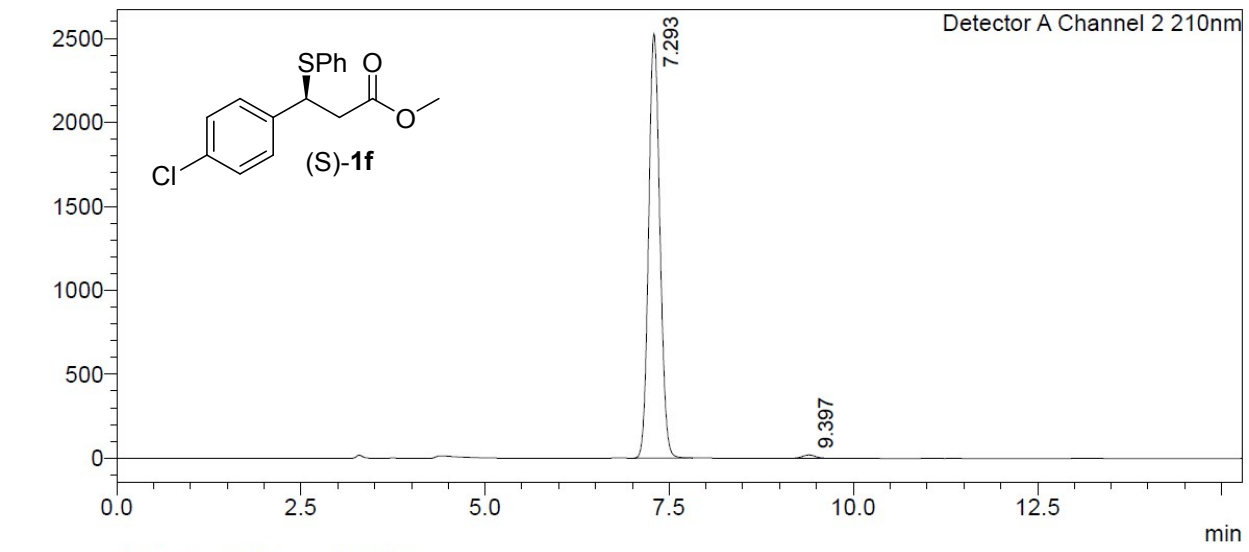
7.6. HPLC traces of (±)-1f and (–)-(S)-1f

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.378	3268579	345796	50.159
2	9.432	3247860	283812	49.841
Total		6516439	629607	

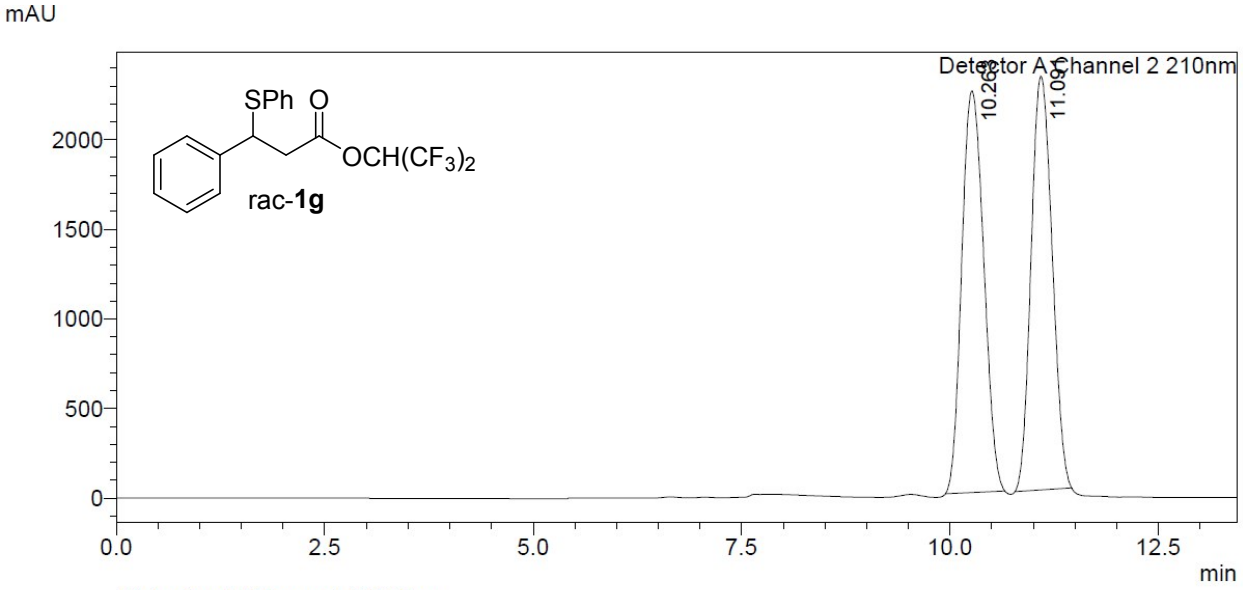


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	7.293	26845431	2525125	99.178
2	9.397	222520	19316	0.822
Total		27067950	2544441	

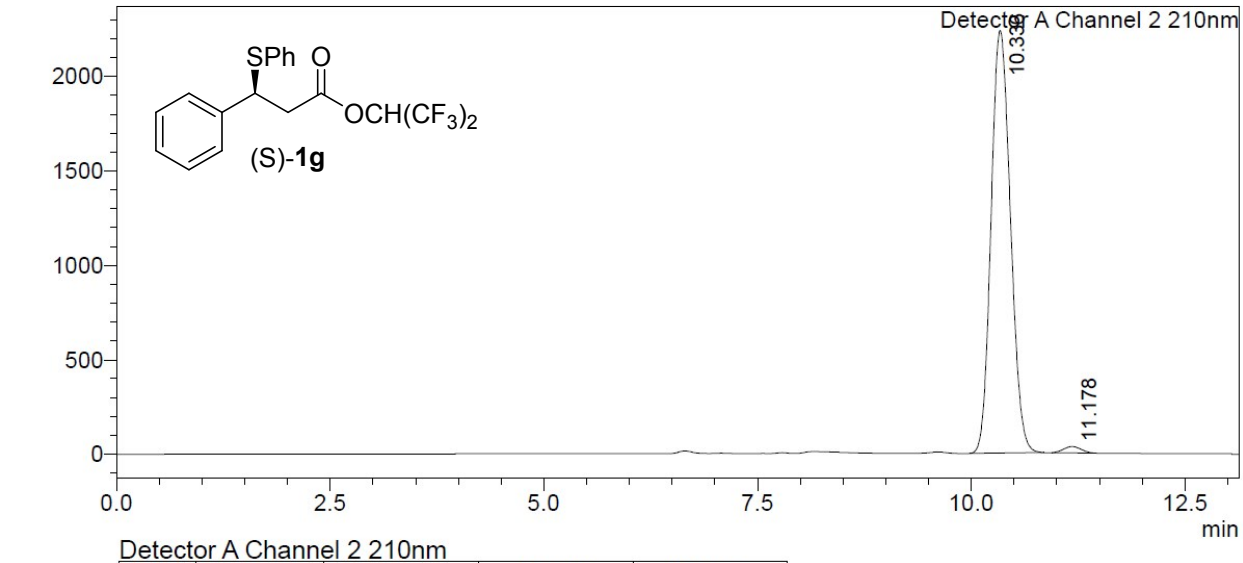
7.7. HPLC traces of (±)-1g and (–)-(S)-1g

CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.5 mL/min, 5 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.263	41064401	2240372	50.363
2	11.091	40472828	2308481	49.637
Total		81537229	4548853	

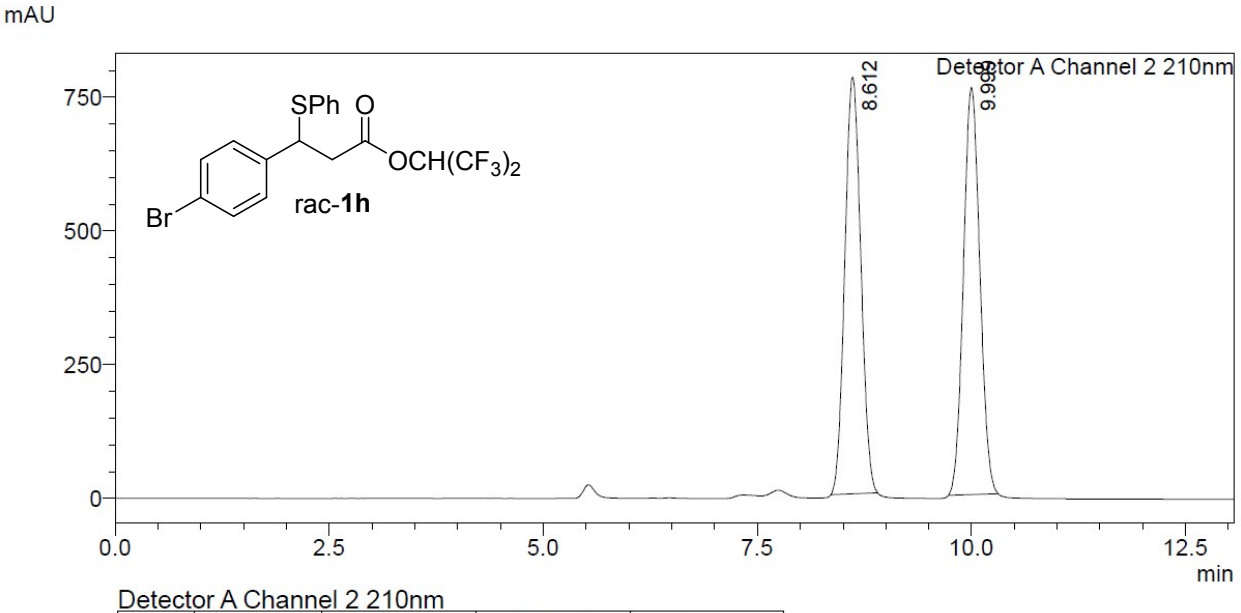


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.336	35277734	2236272	98.655
2	11.178	481057	33652	1.345
Total		35758792	2269924	

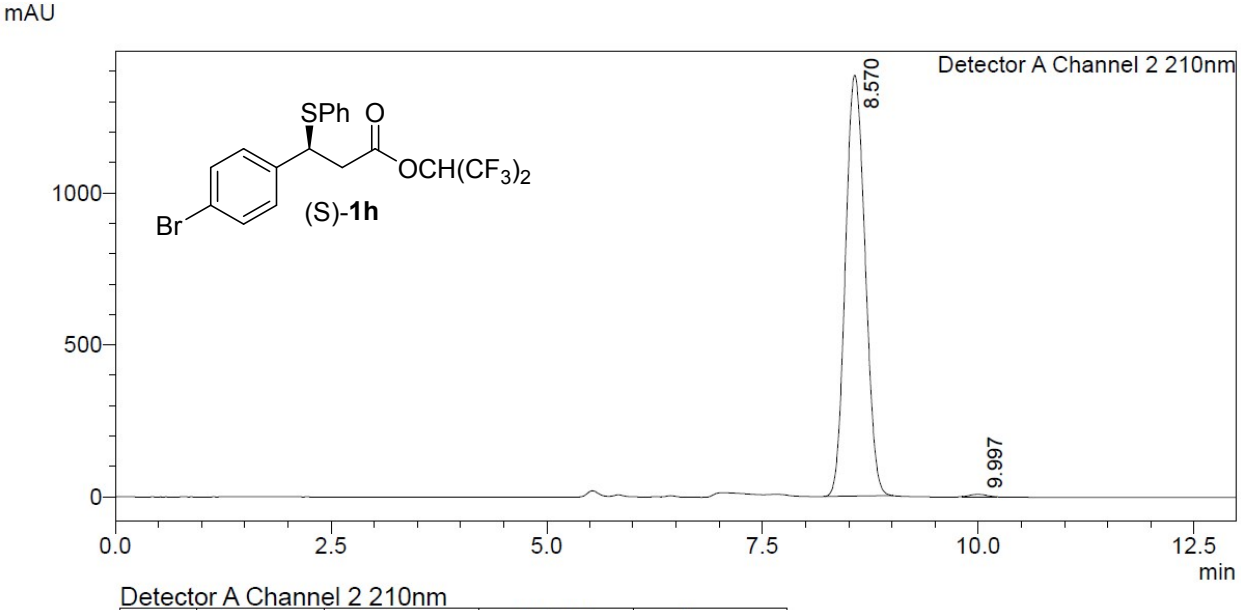
7.8. HPLC traces of (±)-1h and (–)-(S)-1h

CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.612	10111216	778867	49.968
2	9.999	10124245	761403	50.032
Total		20235461	1540270	

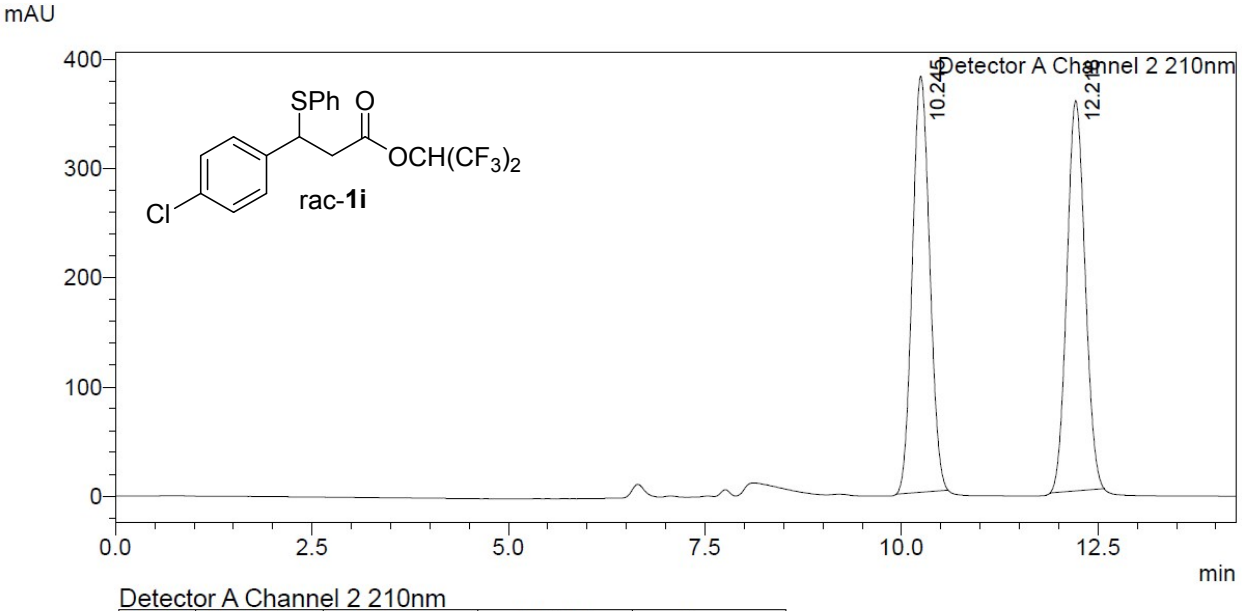


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.570	21946722	1384148	99.556
2	9.997	97921	7774	0.444
Total		22044643	1391922	

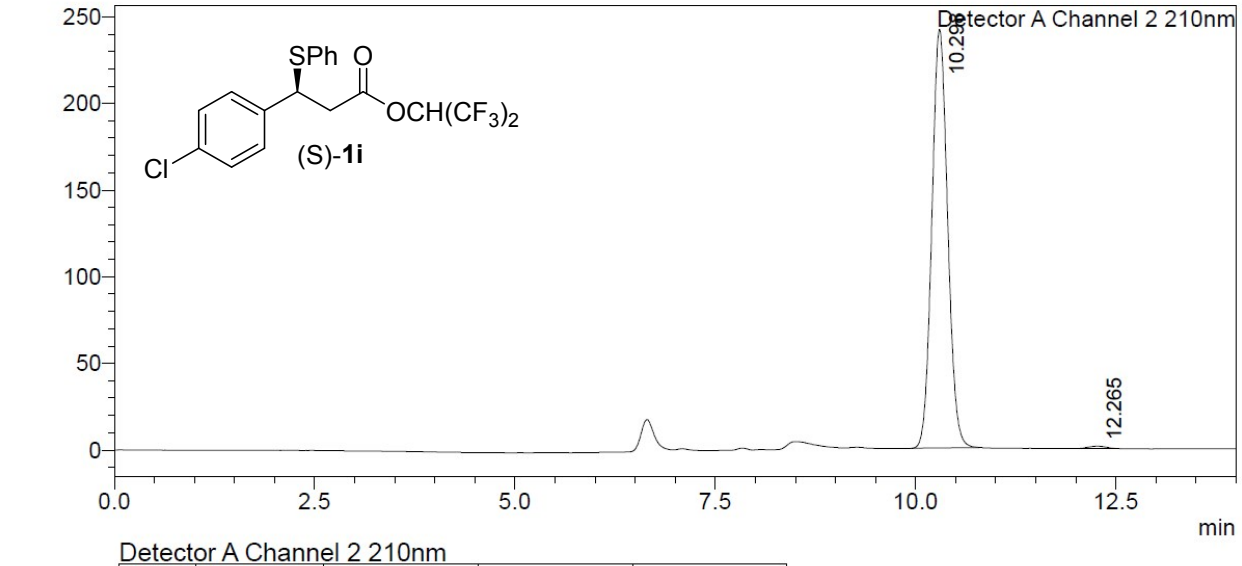
7.9. HPLC traces of (±)-1i and (–)-(S)-1i

CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.5 mL/min, 5 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.245	5821561	381011	50.302
2	12.216	5751635	357285	49.698
Total		11573196	738295	

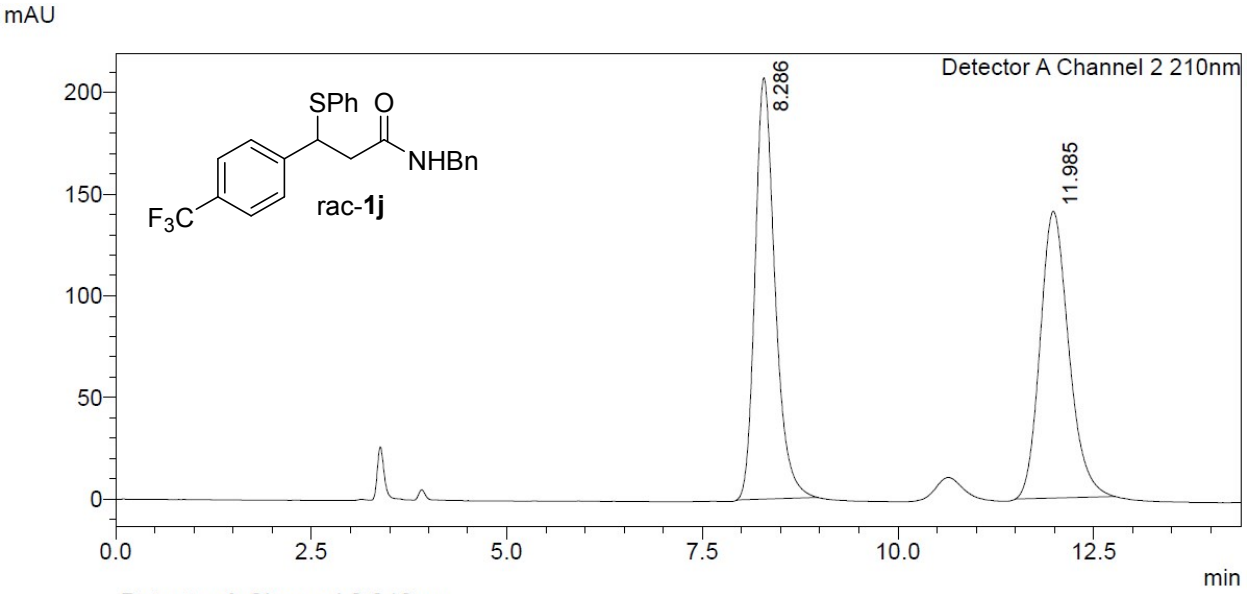


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.298	3318273	241479	99.387
2	12.265	20479	1416	0.613
Total		3338752	242895	

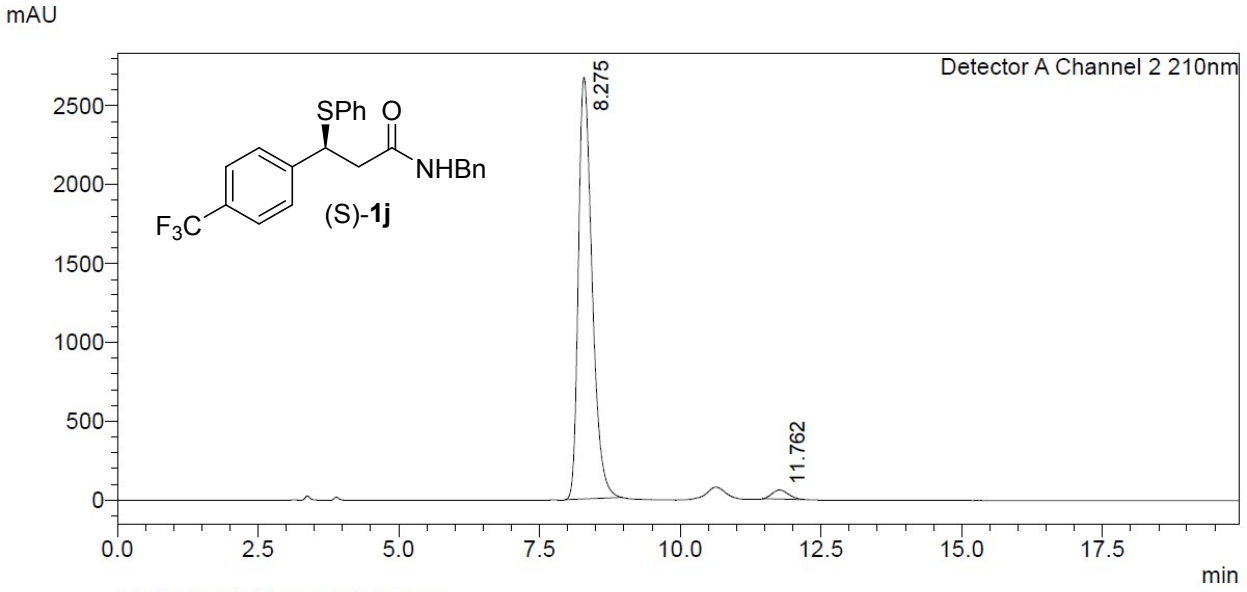
7.10. HPLC traces of (±)-1j and (–)-(S)-1j

CHIRALPAK IB-H, n-hexane/i-PrOH, 80:20, 1.0 mL/min, 5°C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.286	3680023	207128	50.581
2	11.985	3595530	140992	49.419
Total		7275552	348120	

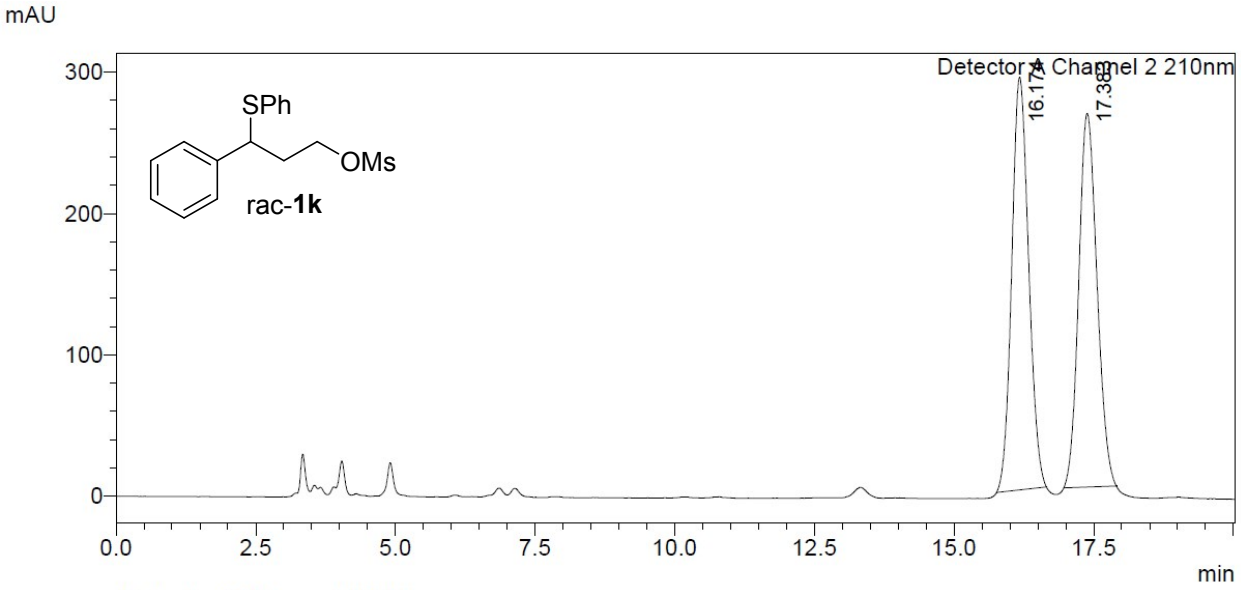


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.275	45377576	2670416	97.511
2	11.762	1158184	57317	2.489
Total		46535760	2727733	

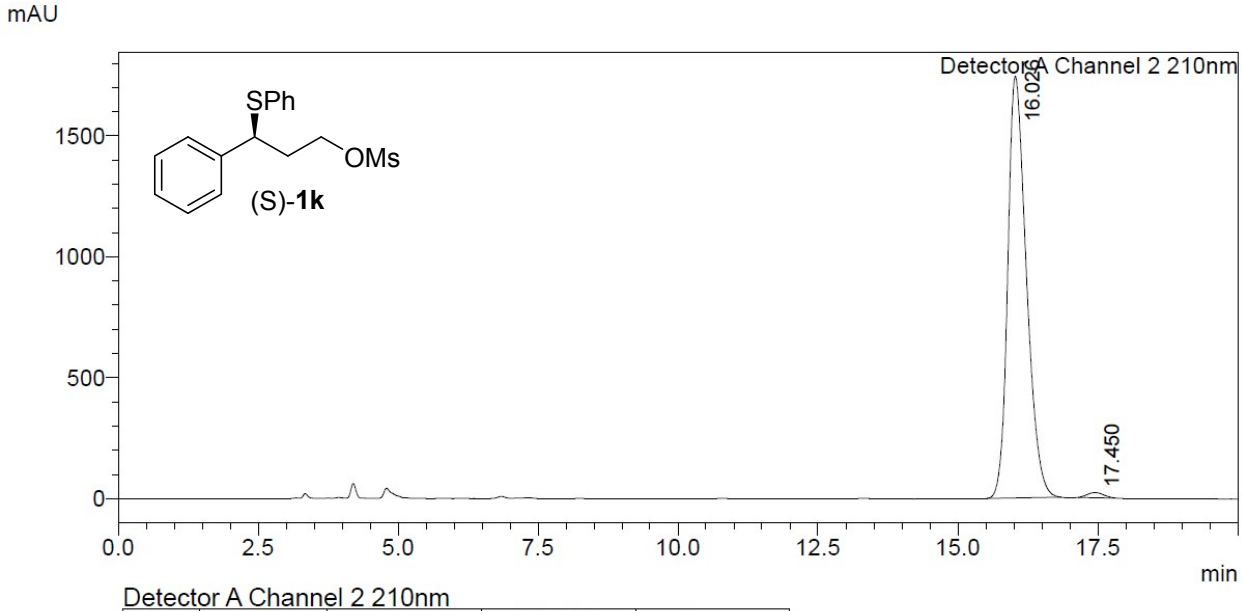
7.11. HPLC traces of (±)-1k and (–)-(S)-1k

CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	16.174	6128632	291728	50.459
2	17.383	6017118	264217	49.541
Total		12145750	555945	

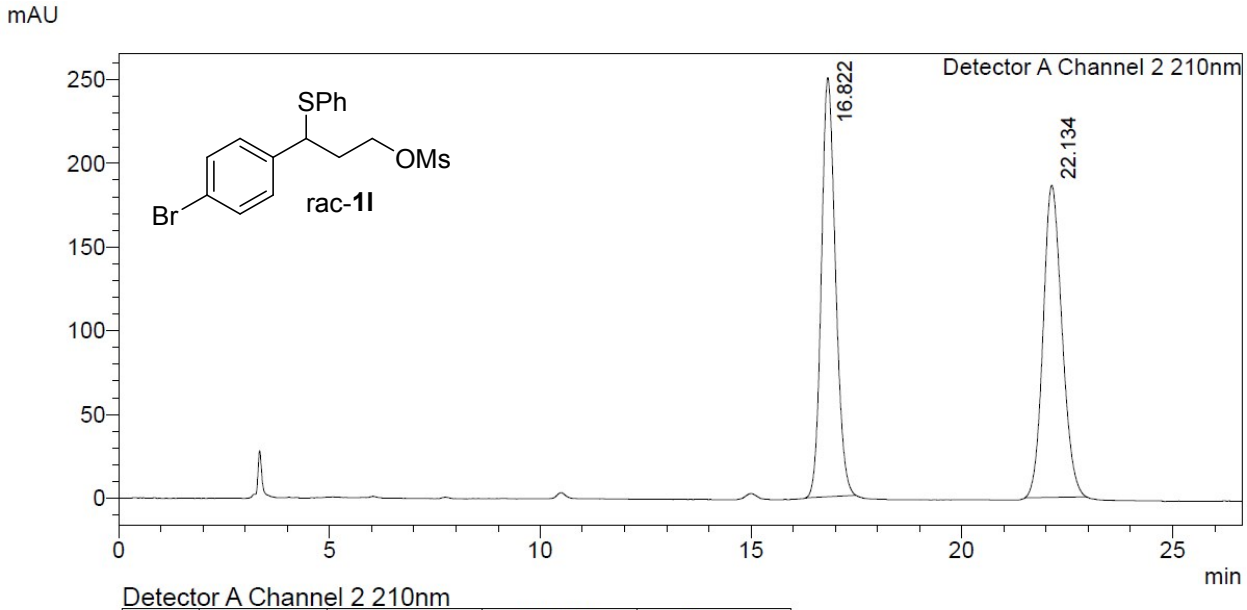


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	16.026	40414864	1742884	98.949
2	17.450	429409	21333	1.051
Total		40844273	1764218	

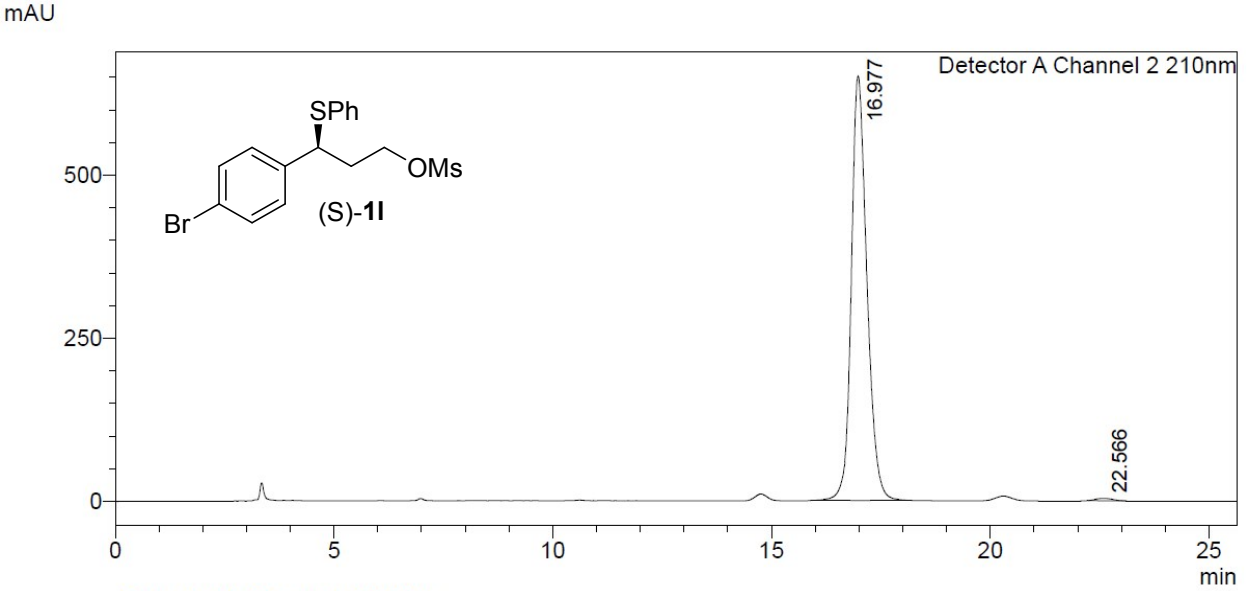
7.12. HPLC traces of (±)-1l and (–)-(S)-1l

CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	16.822	5834506	250260	50.132
2	22.134	5803760	186388	49.868
Total		11638266	436648	

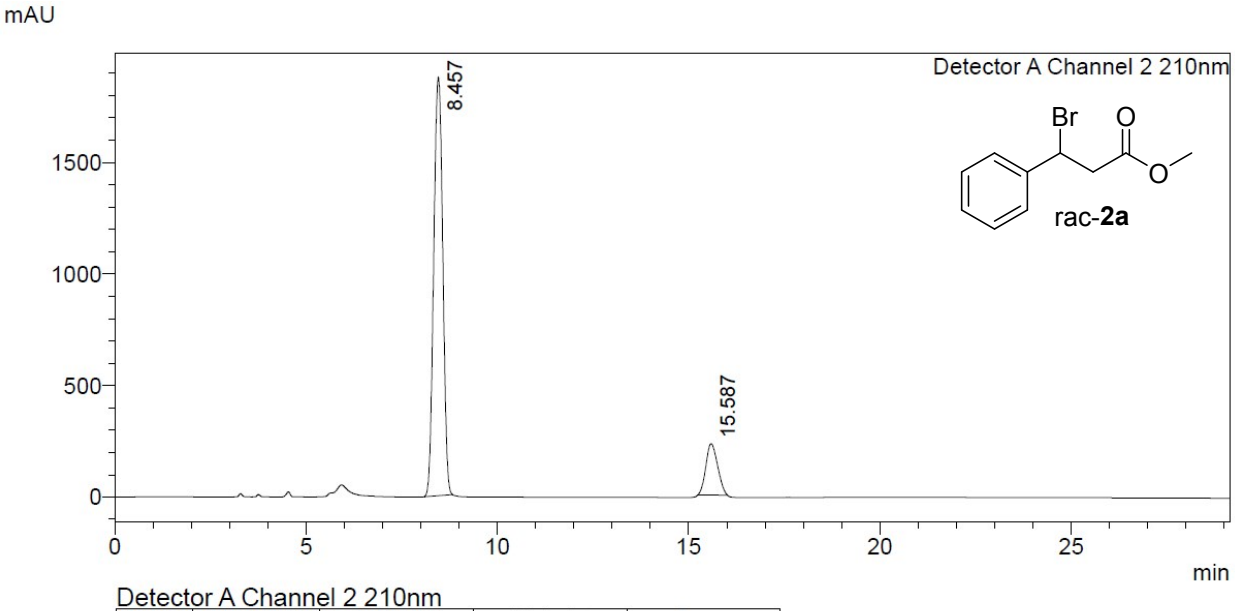


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	16.977	16293782	650250	99.401
2	22.566	98150	3801	0.599
Total		16391931	654052	

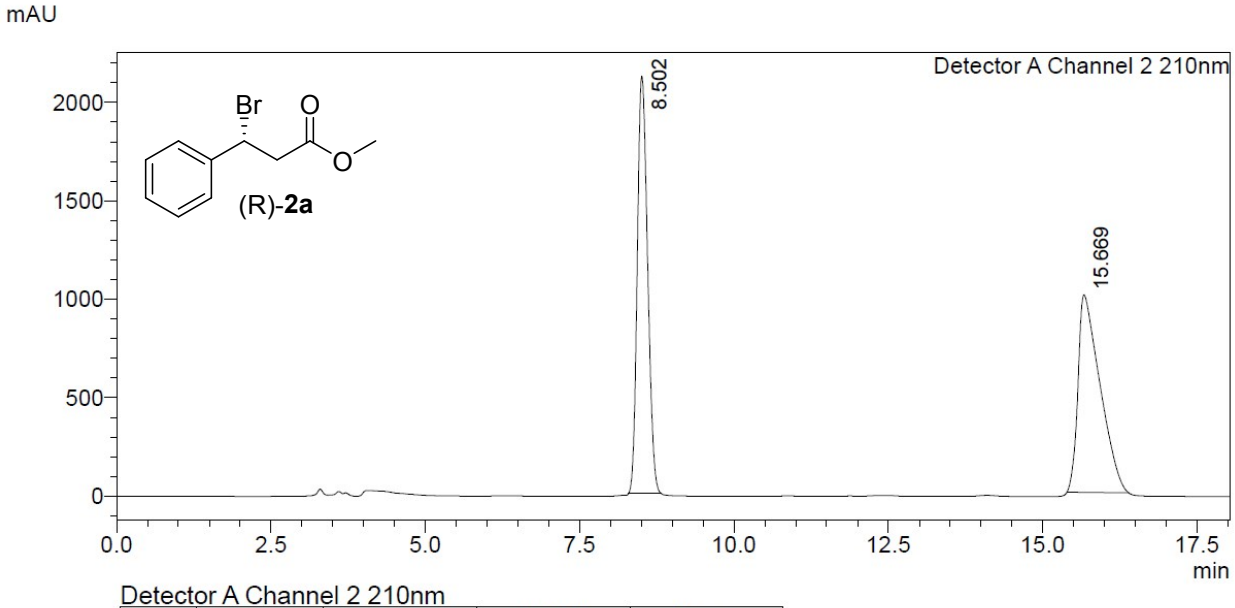
7.13. HPLC traces of (±)-2a and (+)-(R)-2a

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.457	30876522	1876713	86.245
2	15.587	4924491	230773	13.755
Total		35801013	2107486	

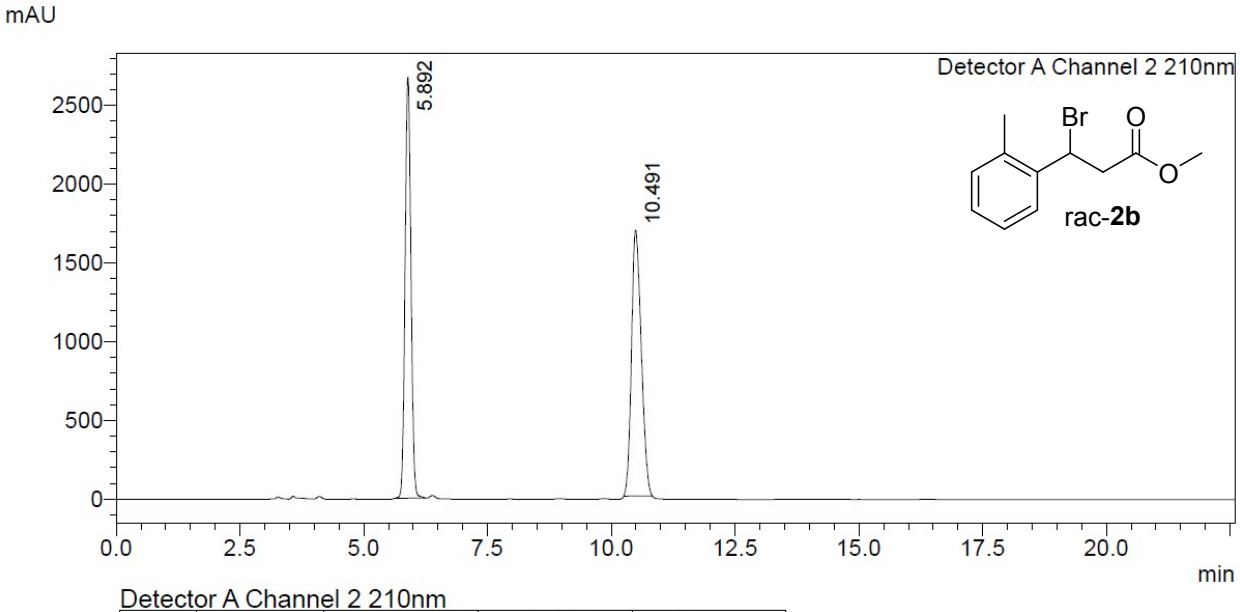


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.502	24504930	2117795	49.655
2	15.669	24845738	1001810	50.345
Total		49350668	3119605	

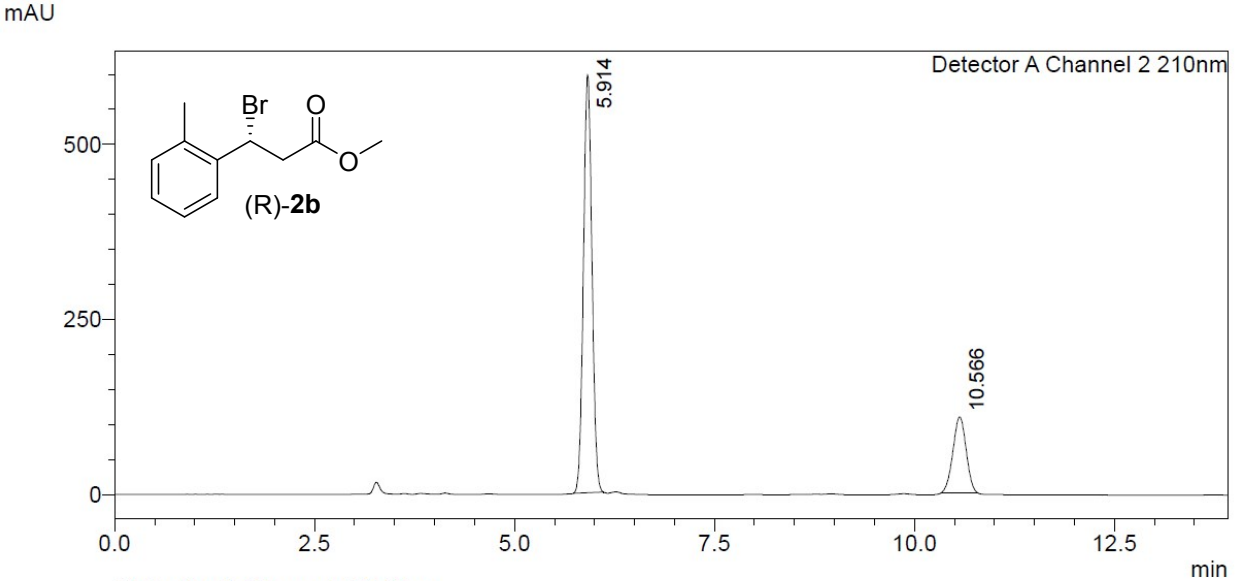
7.14. HPLC traces of (±)-2b and (+)-(R)-2b

CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	5.892	22132188	2670174	48.935
2	10.491	23095338	1686633	51.065
Total		45227526	4356807	

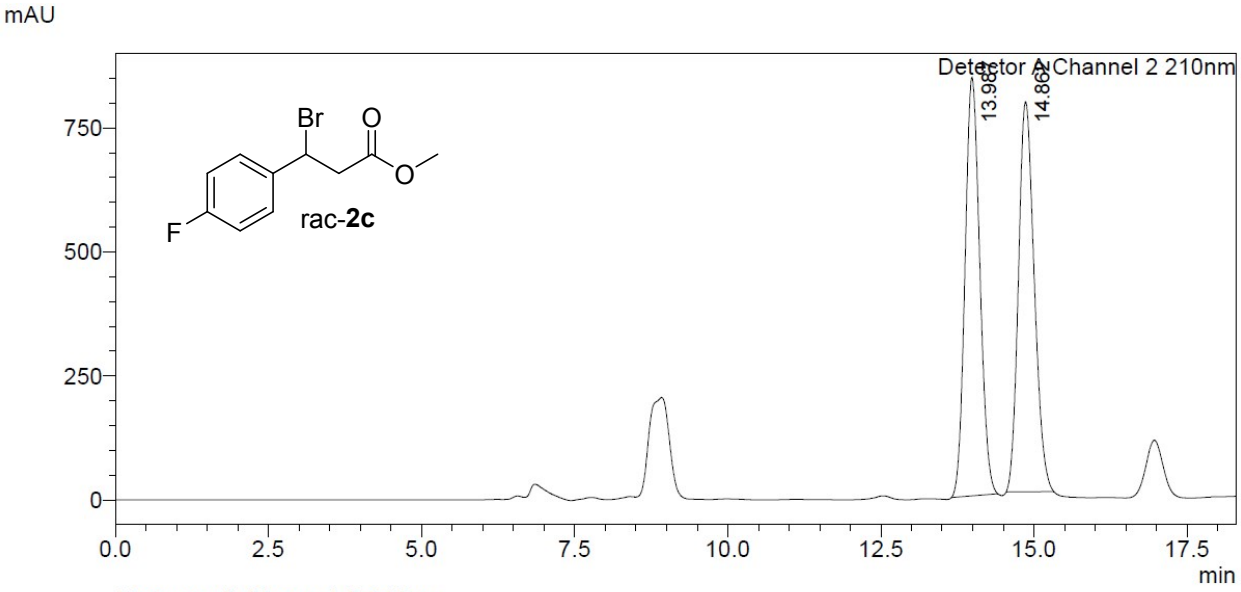


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	5.914	4420798	595737	77.985
2	10.566	1247988	108625	22.015
Total		5668785	704362	

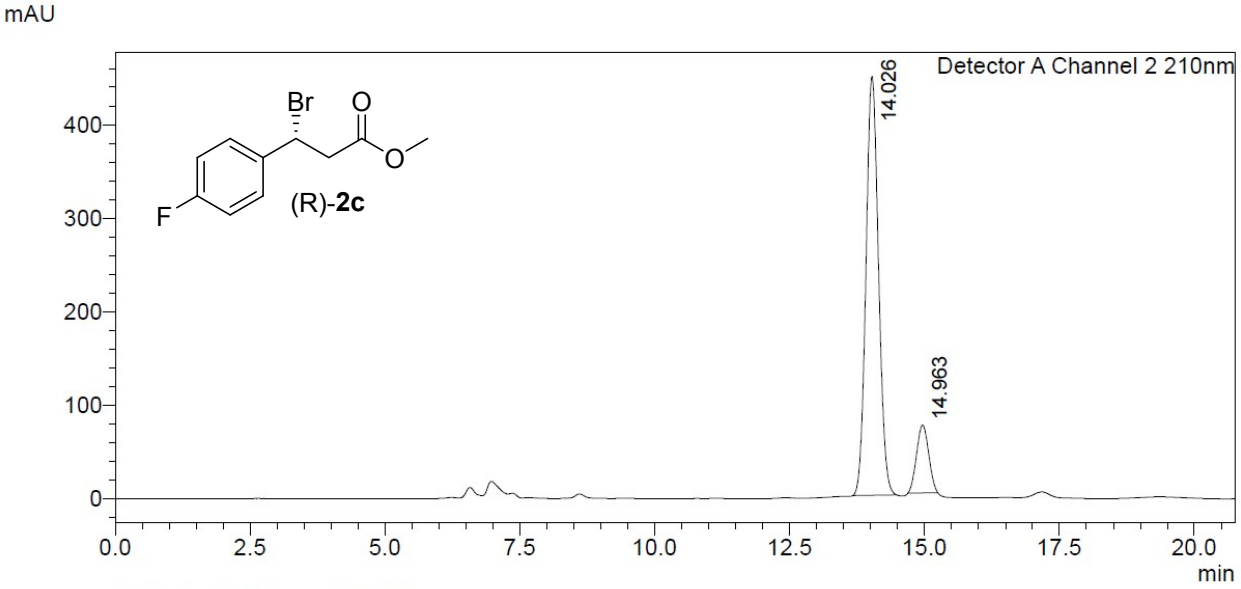
7.15. HPLC traces of (±)-2c and (+)-(R)-2c

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 25 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13.987	14085118	842748	49.976
2	14.862	14098597	786197	50.024
Total		28183715	1628946	

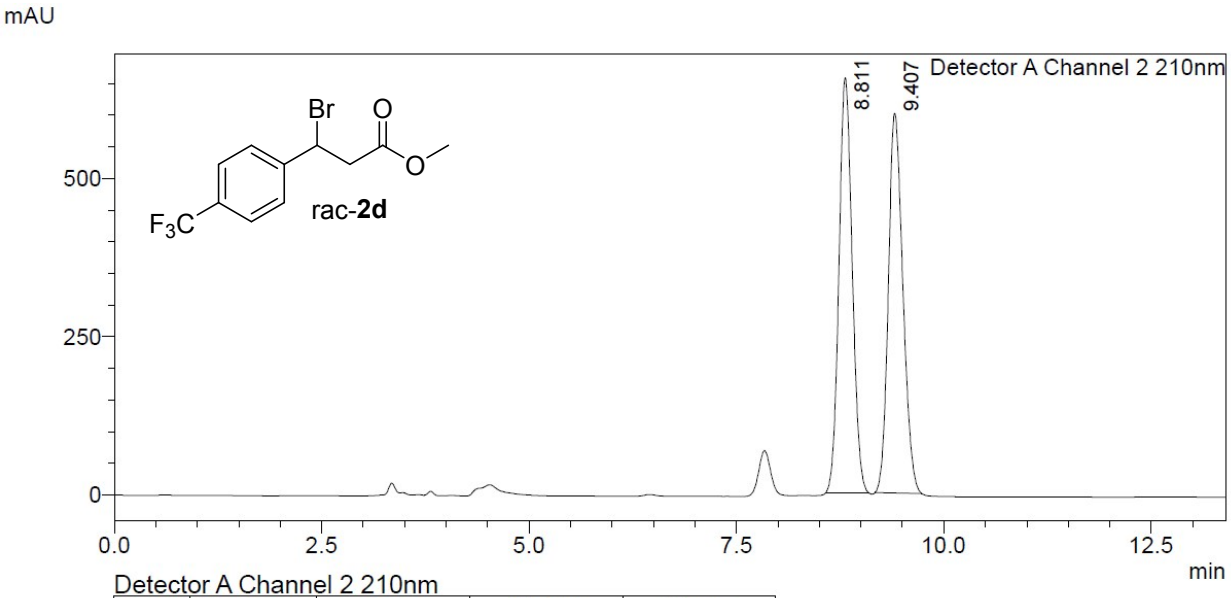


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	14.026	7227709	447903	86.418
2	14.963	1135940	72669	13.582
Total		8363648	520572	

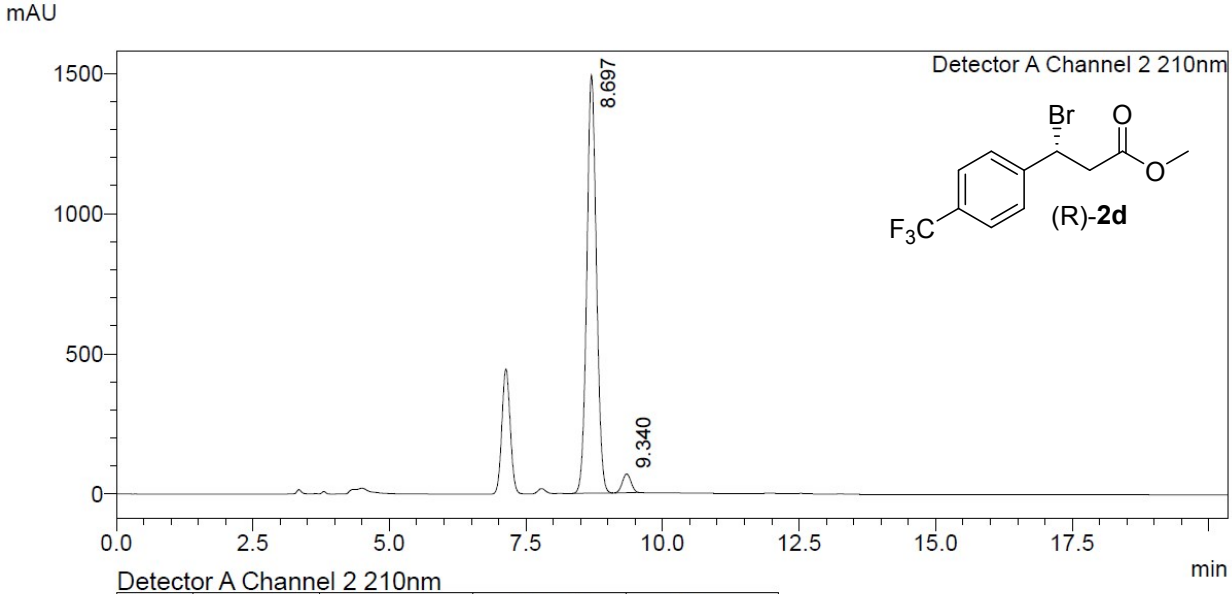
7.16. HPLC traces of (±)-2d and (+)-(R)-2d

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 5 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.811	7313130	655785	50.079
2	9.407	7290098	599187	49.921
Total		14603228	1254972	

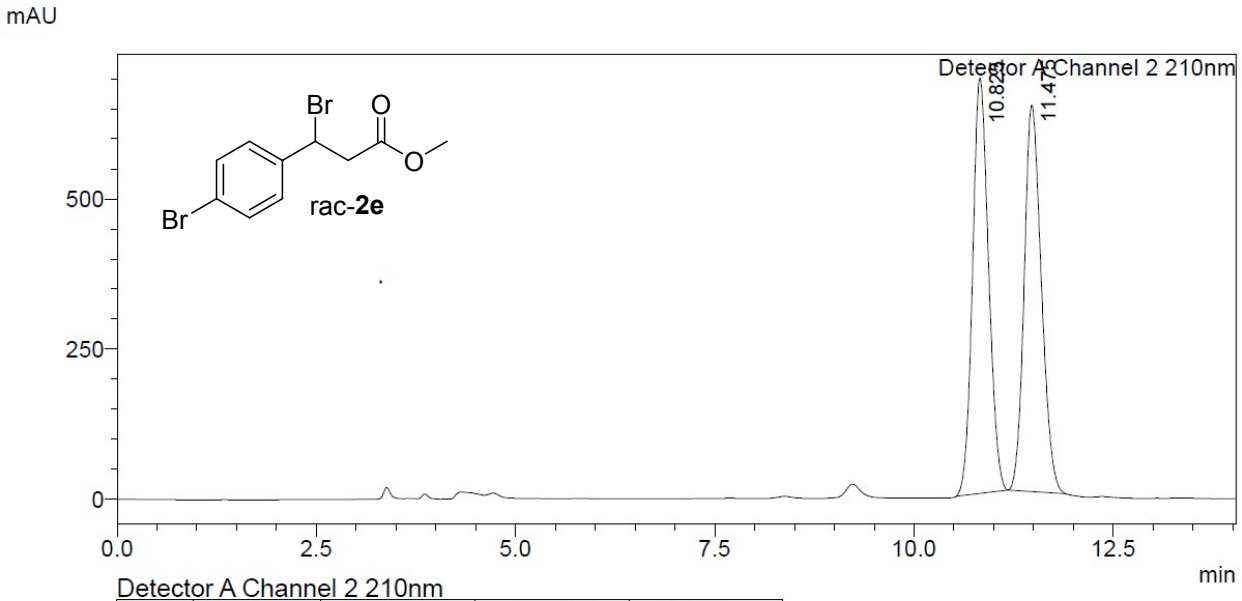


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.697	18290682	1491073	96.163
2	9.340	729799	66642	3.837
Total		19020481	1557715	

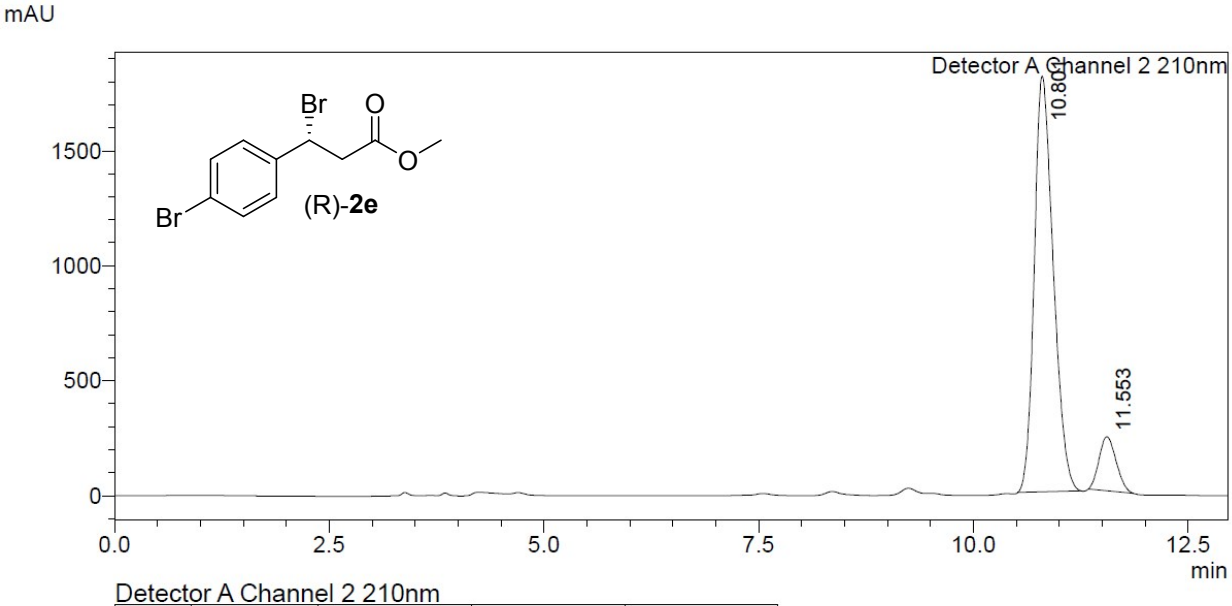
7.17. HPLC traces of (±)-2e and (+)-(R)-2e

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.825	9655687	691314	50.005
2	11.475	9653850	642936	49.995
Total		19309537	1334249	

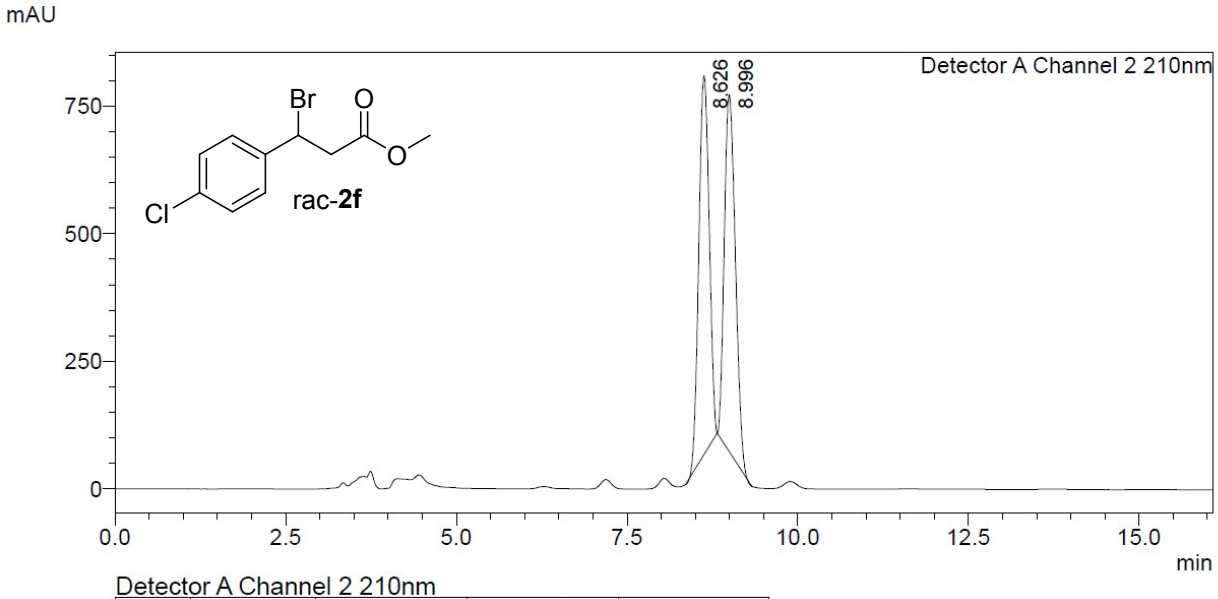


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.801	27848688	1808023	89.522
2	11.553	3259575	235130	10.478
Total		31108263	2043153	

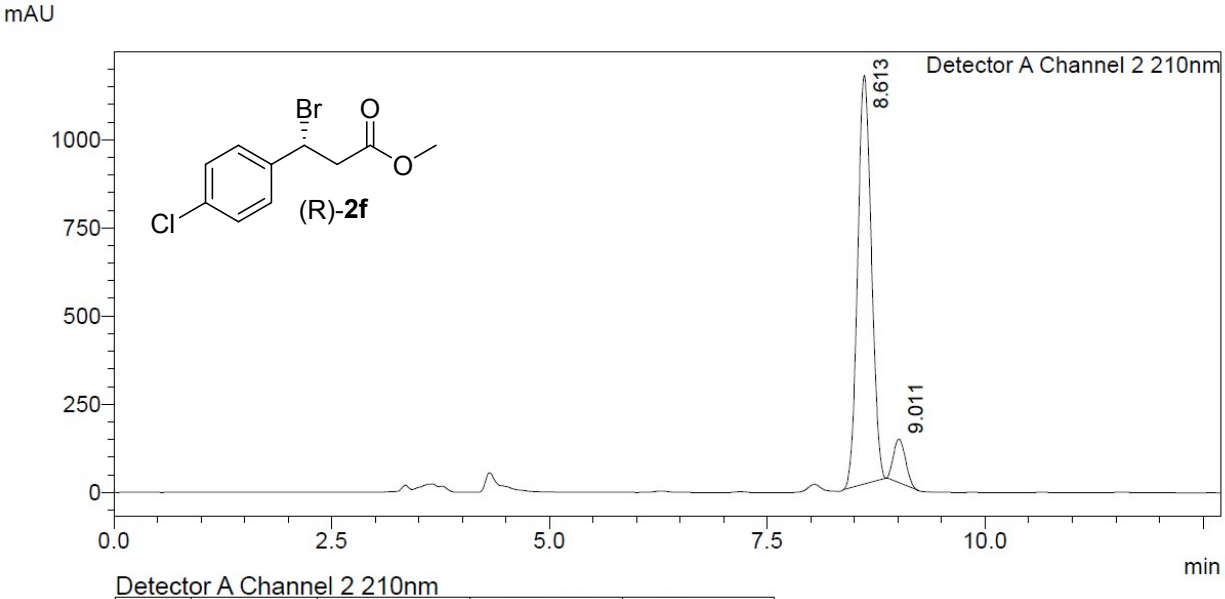
7.18. HPLC traces of (±)-2f and (+)-(R)-2f

CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.626	7873812	741604	50.102
2	8.996	7841905	698762	49.898
Total		15715717	1440365	

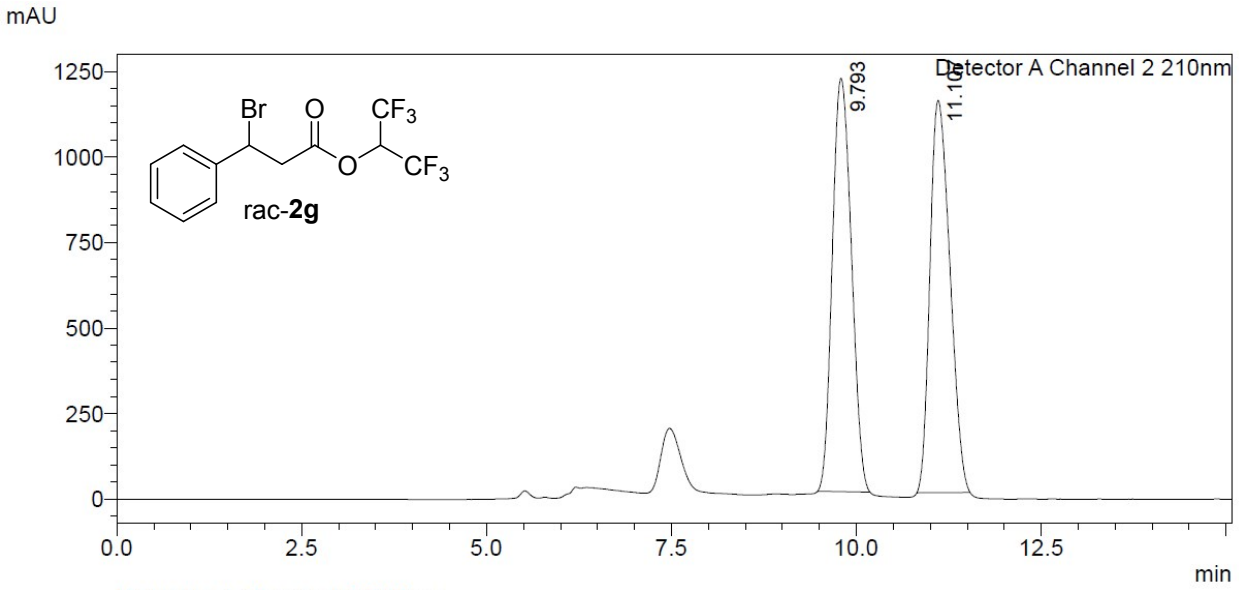


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	8.613	12685149	1158192	91.416
2	9.011	1191155	124057	8.584
Total		13876304	1282249	

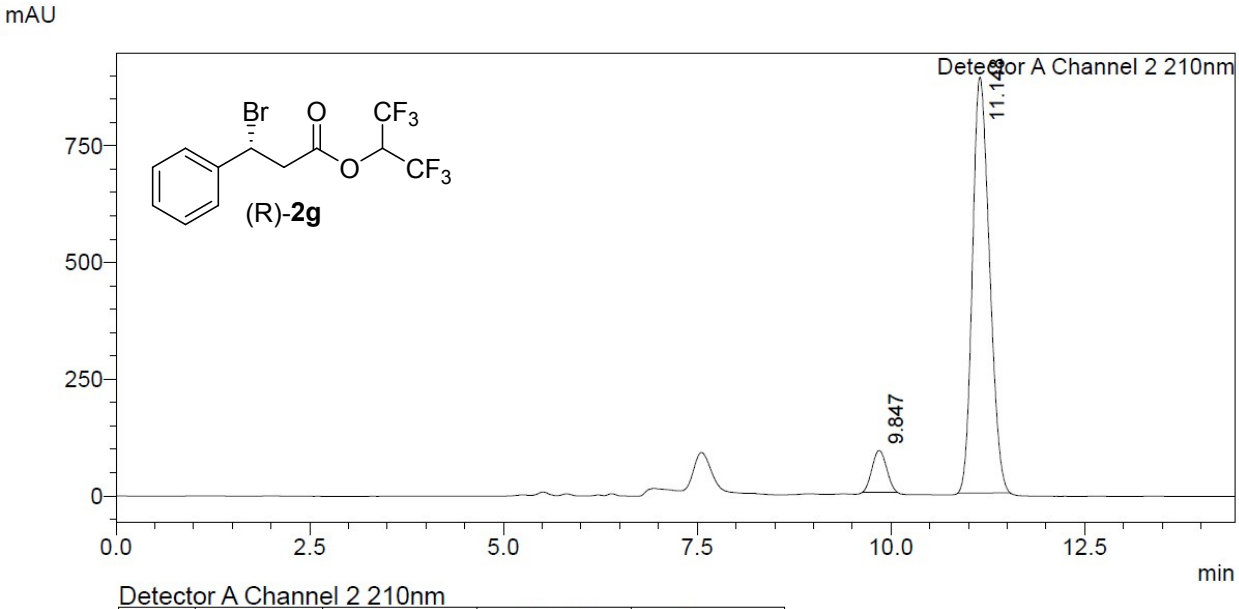
7.19. HPLC traces of (±)-2g and (+)-(R)-2g

CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	9.793	21631108	1208300	50.103
2	11.107	21542546	1146187	49.897
Total		43173653	2354487	

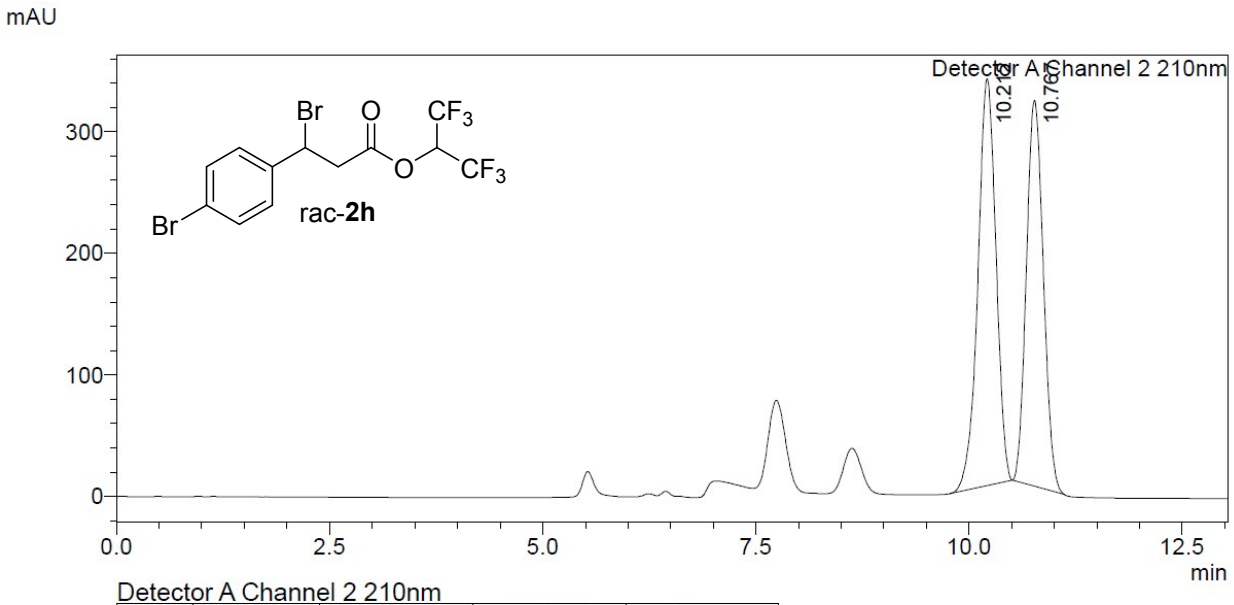


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	9.847	1175533	90217	7.935
2	11.148	13639589	890118	92.065
Total		14815122	980335	

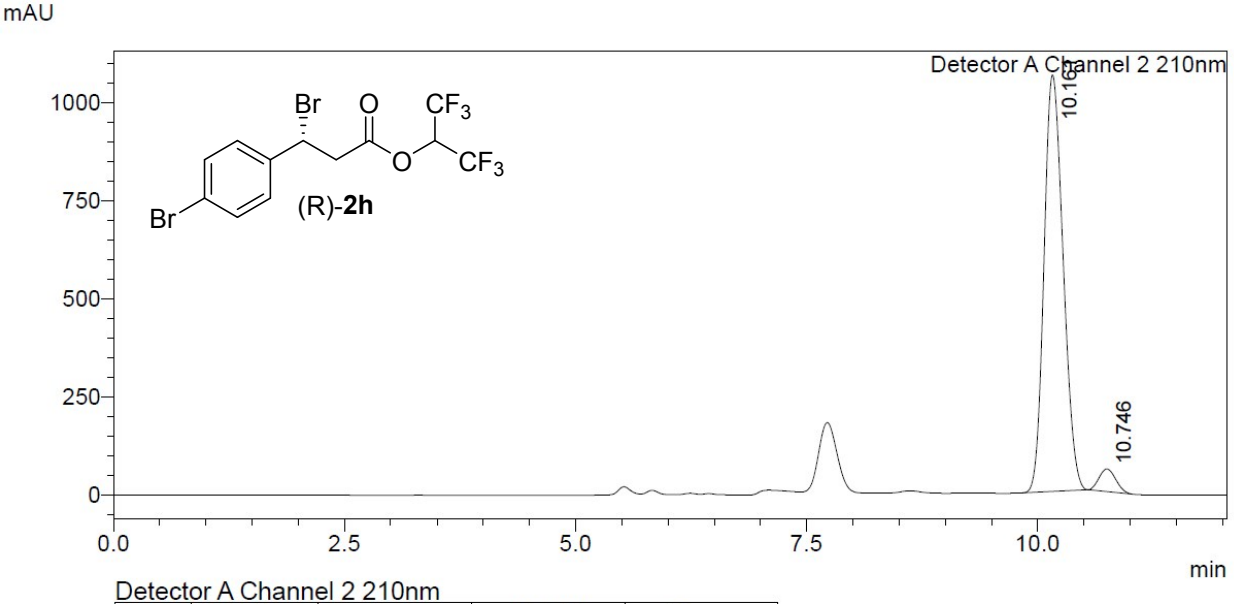
7.20. HPLC traces of (±)-2h and (+)-(R)-2h

CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.213	2363371	171606	50.796
2	10.765	2289330	166659	49.204
Total		4652701	338265	

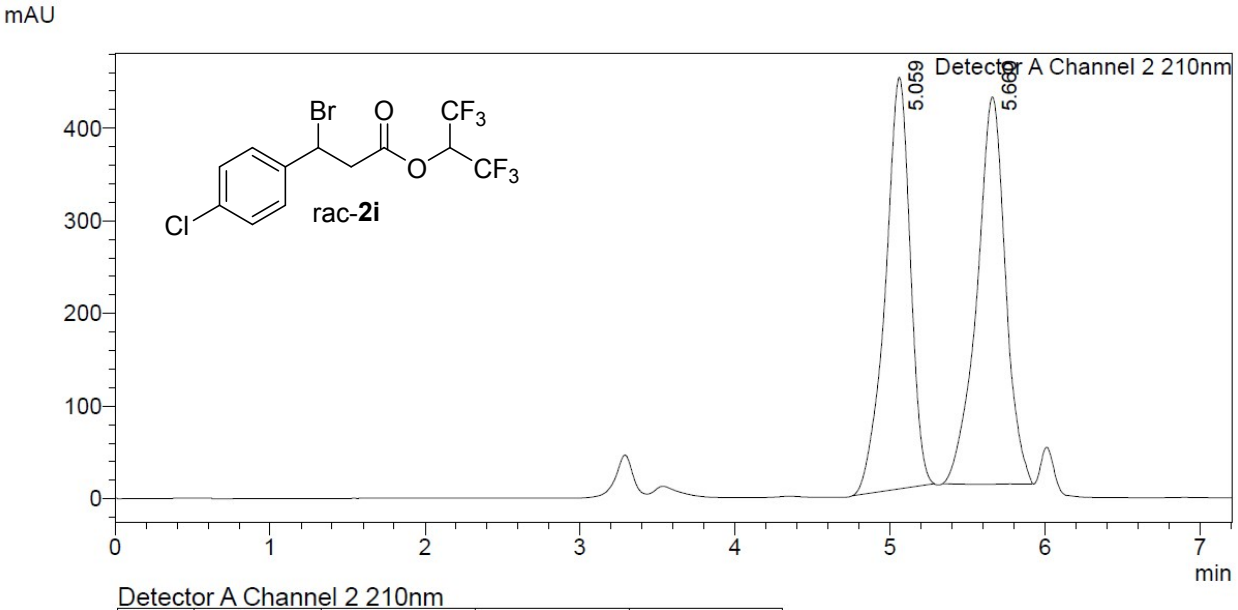


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10.161	15298262	1061681	95.472
2	10.746	725528	57664	4.528
Total		16023790	1119345	

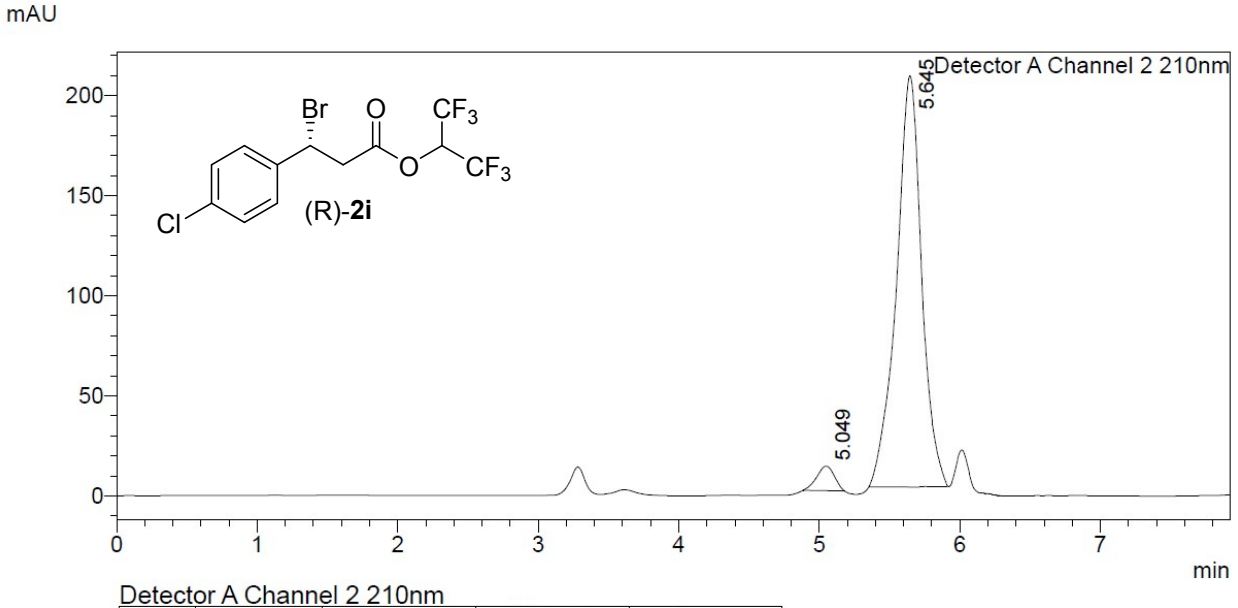
7.21. HPLC traces of (±)-2i and (+)-(R)-2i

CHIRALPAK IB-H, n-hexane/i-PrOH, 99.2:0.8, 0.6 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	5.059	4971246	444047	50.210
2	5.660	4929716	398005	49.790
Total		9900963	842053	

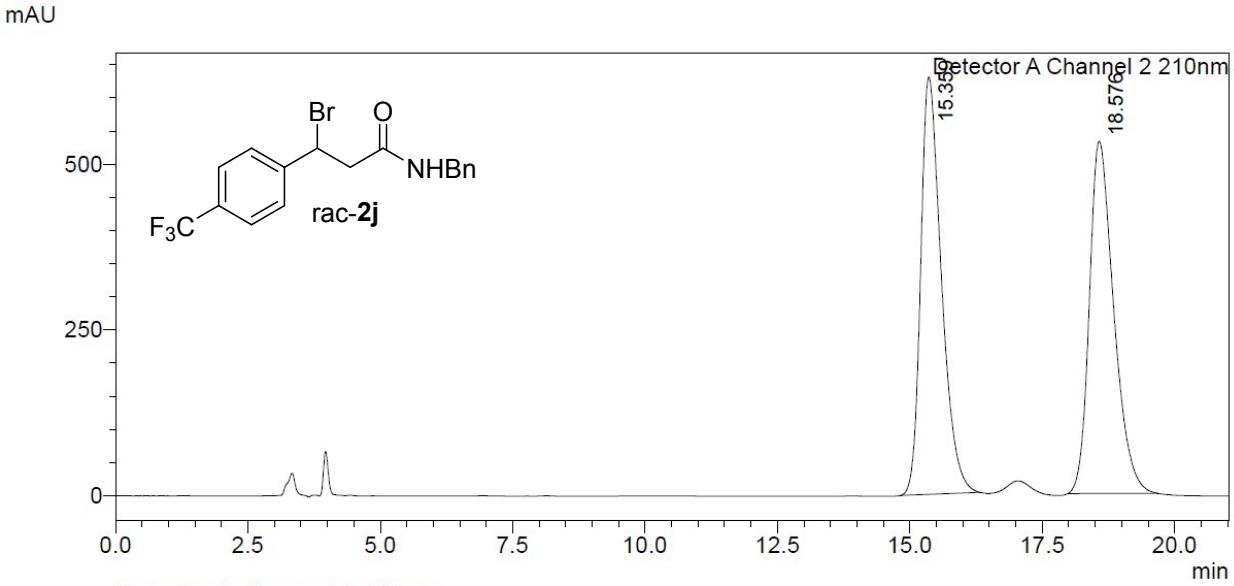


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	5.049	106288	12181	3.932
2	5.645	2596735	205482	96.068
Total		2703022	217663	

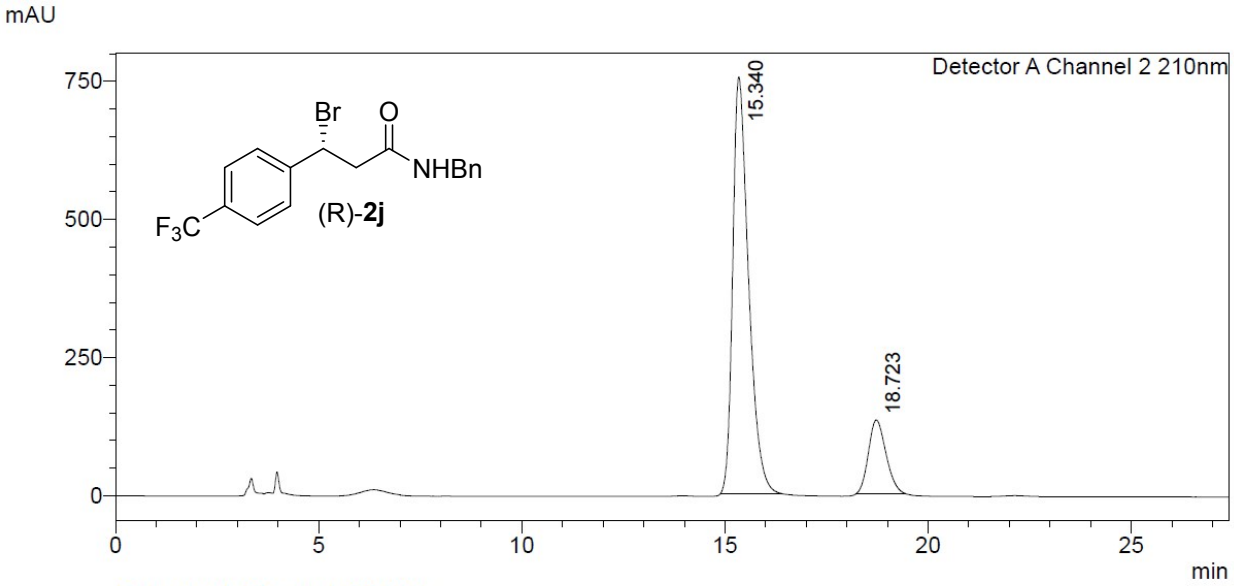
7.22. HPLC traces of (±)-2j and (+)-(R)-2j

CHIRALPAK AD-H, n-hexane/i-PrOH, 98:2, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	15.359	17116768	629282	50.149
2	18.576	17015192	531036	49.851
Total		34131960	1160318	

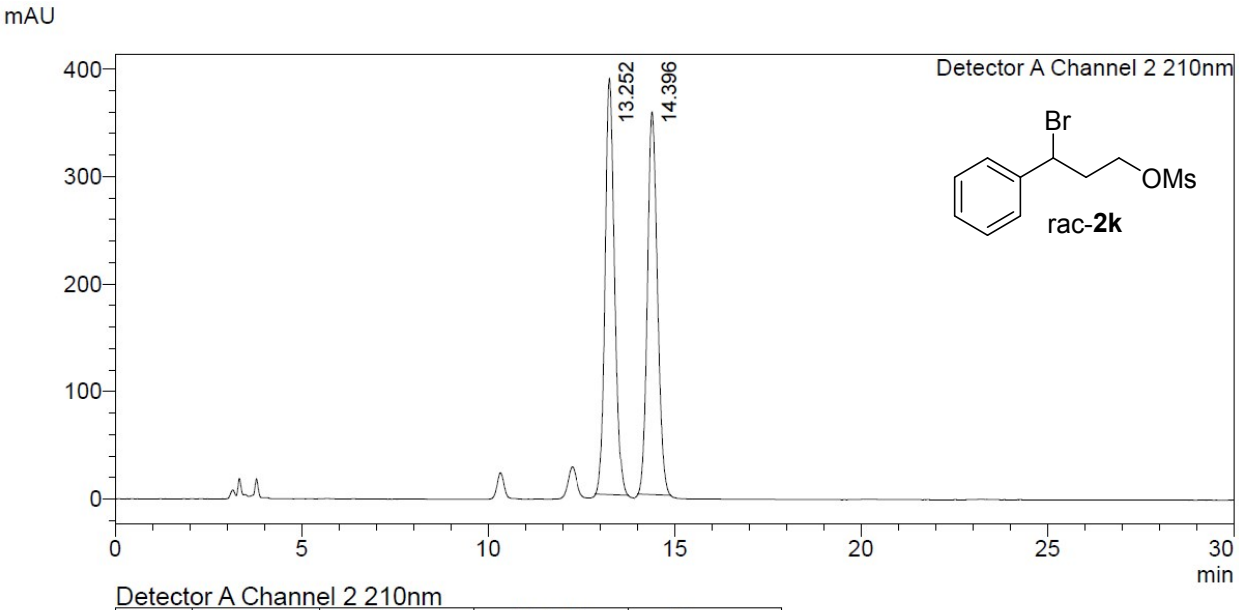


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	15.340	20371234	753375	83.616
2	18.723	3991626	133229	16.384
Total		24362859	886605	

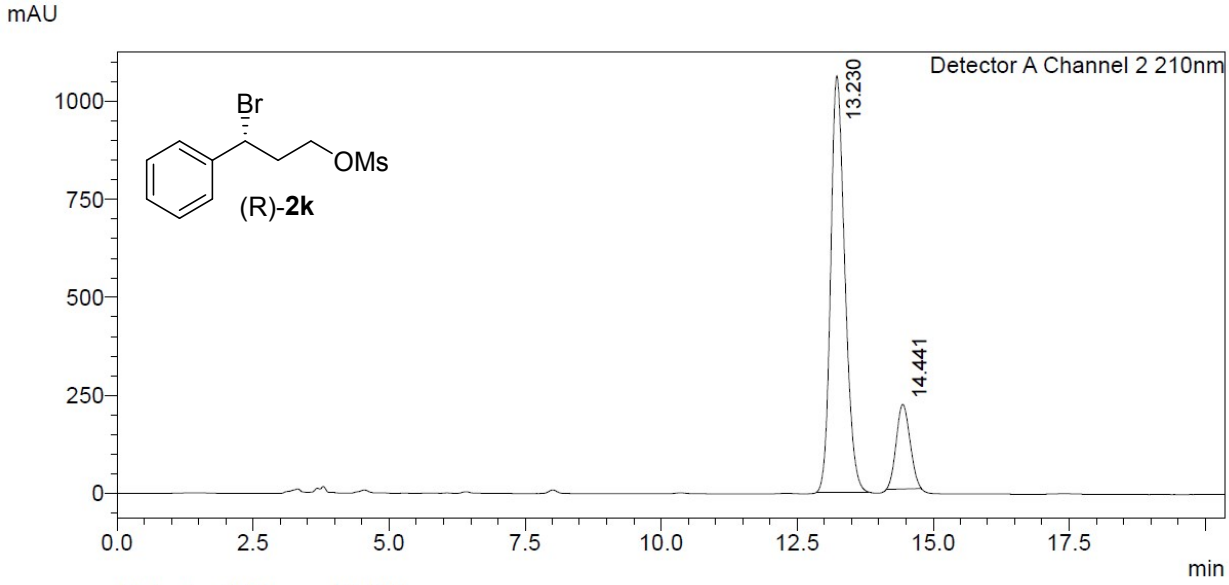
7.23. HPLC traces of (±)-2k and (+)-(R)-2k

CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13.252	6617291	381000	49.814
2	14.396	6666668	356091	50.186
Total		13283959	737091	

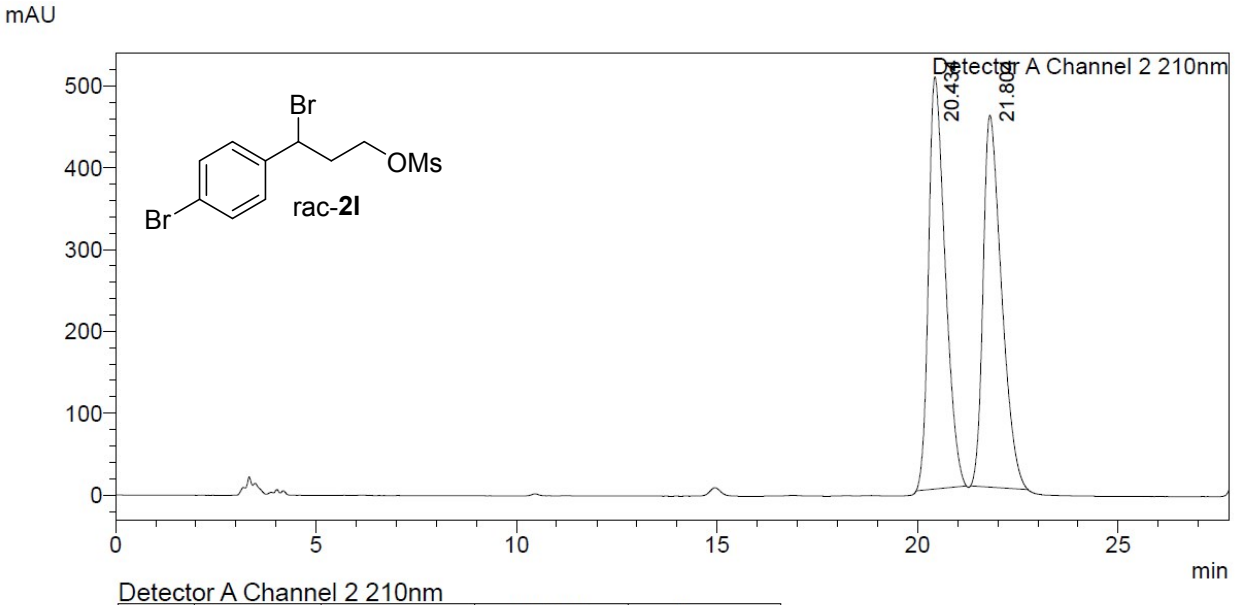


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13.230	19226792	1061373	83.529
2	14.441	3791353	215828	16.471
Total		23018145	1277202	

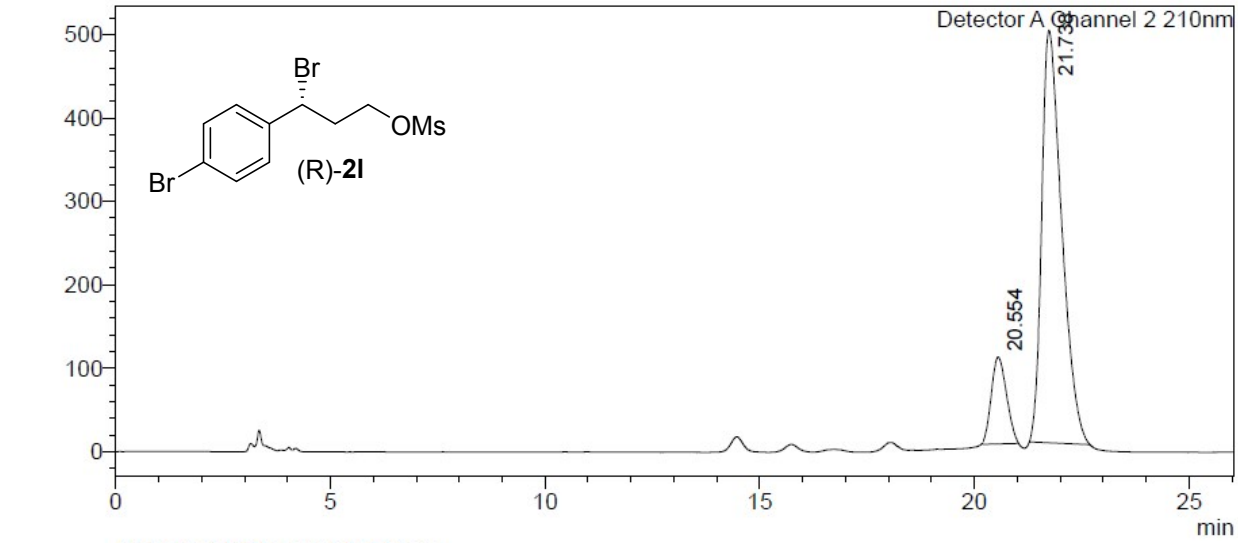
7.24. HPLC traces of (±)-2l and (+)-(R)-2l

CHIRALPAK IB-H, n-hexane/i-PrOH, 85:15, 1.0 mL/min, 10 °C, 210 nm



Detector A Channel 2 210nm

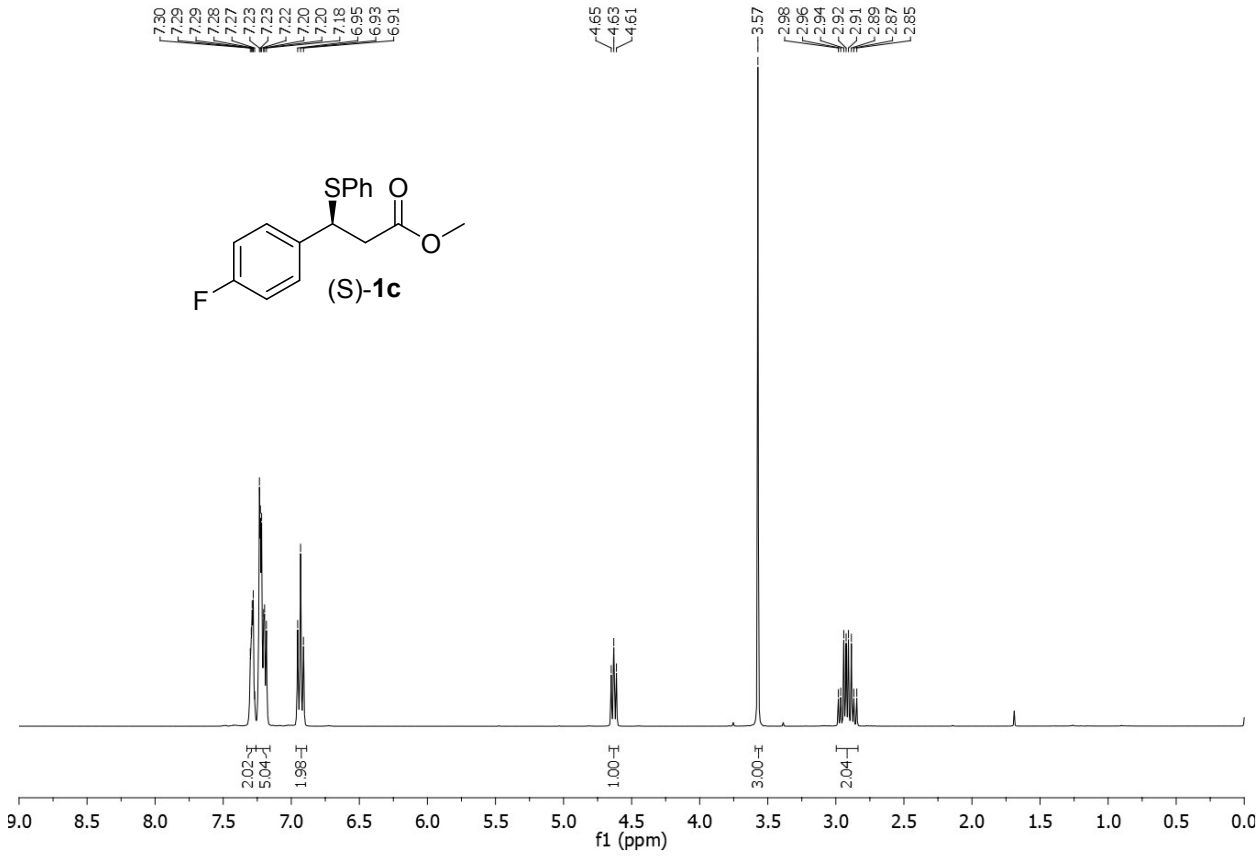
Peak#	Ret. Time	Area	Height	Conc.
1	20.434	14559551	503852	49.977
2	21.804	14573219	454823	50.023
Total		29132771	958675	

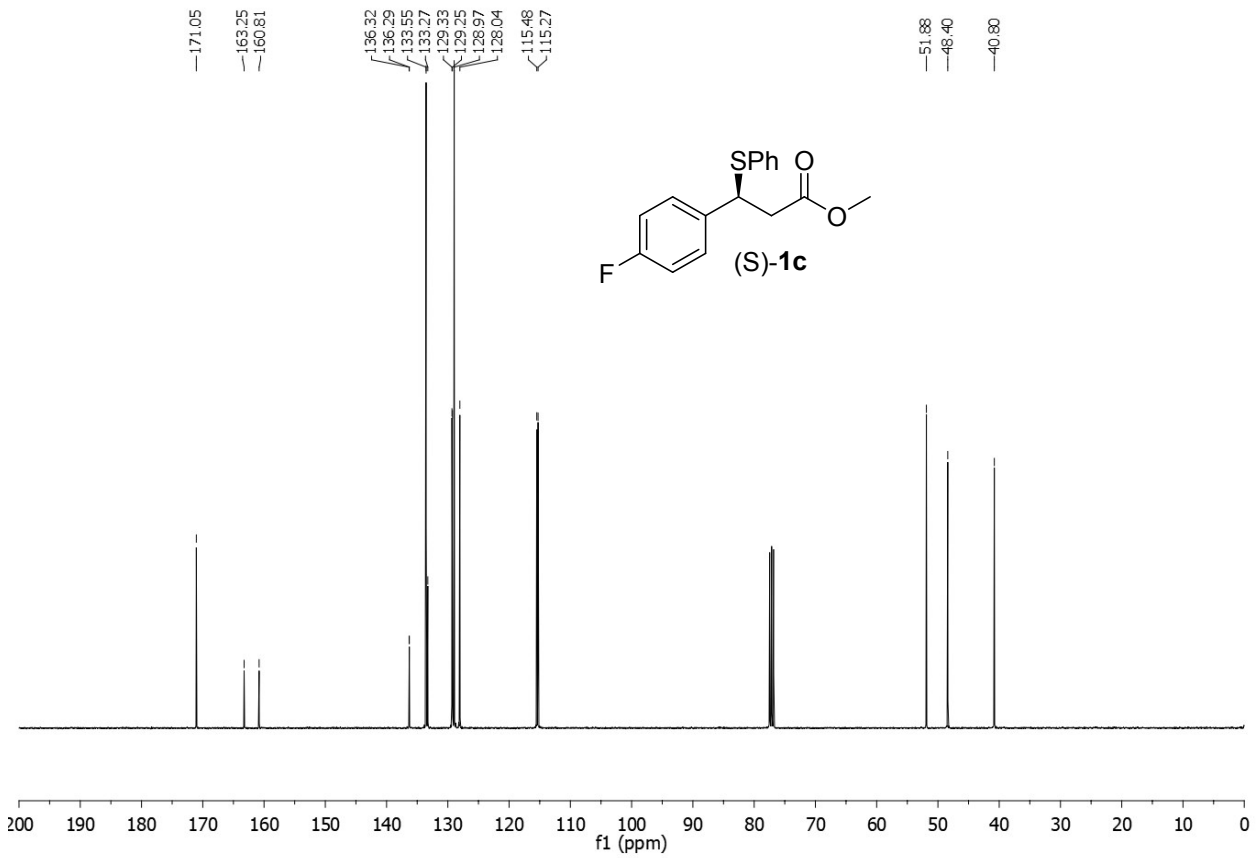


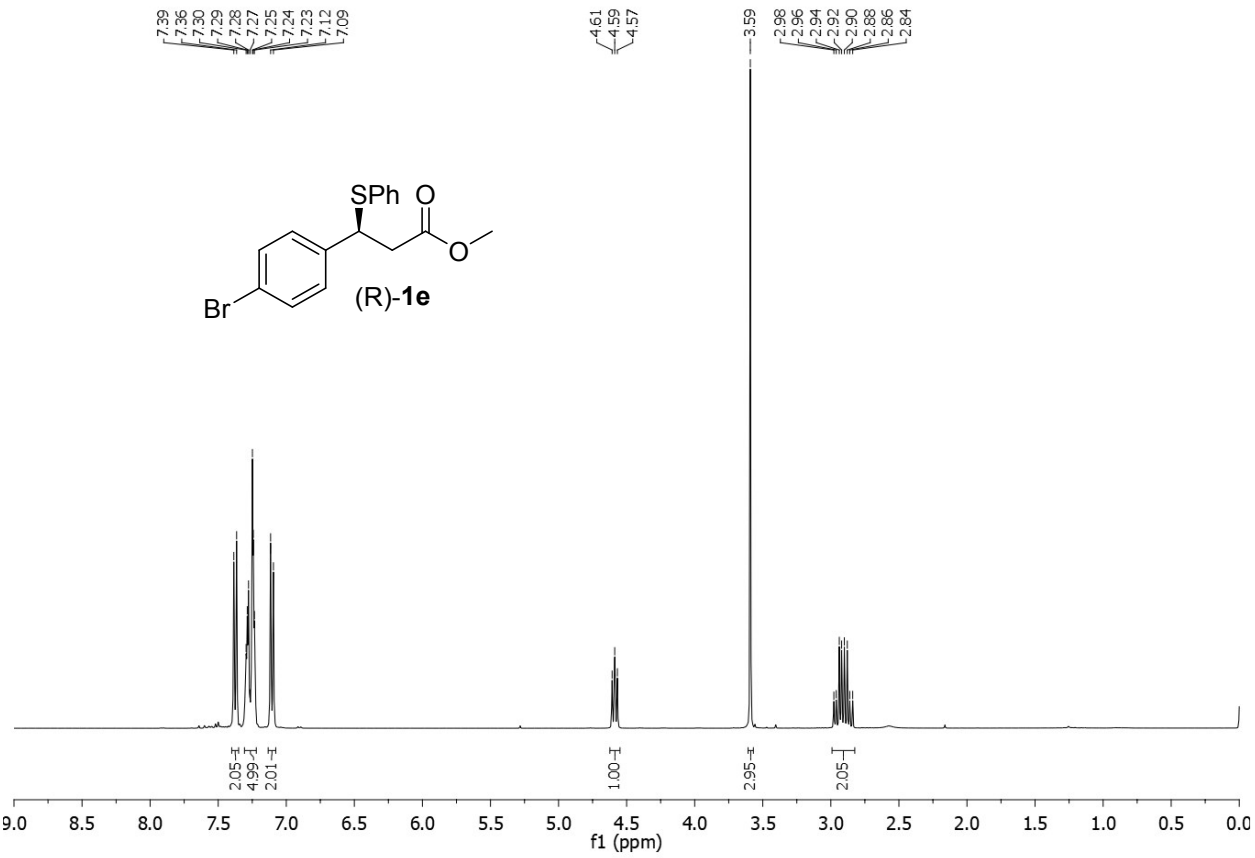
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	20.554	2563004	104007	13.793
2	21.738	16019343	494443	86.207
Total		18582347	598450	

8. Copies of ^{1}H NMR and ^{13}C NMR spectra



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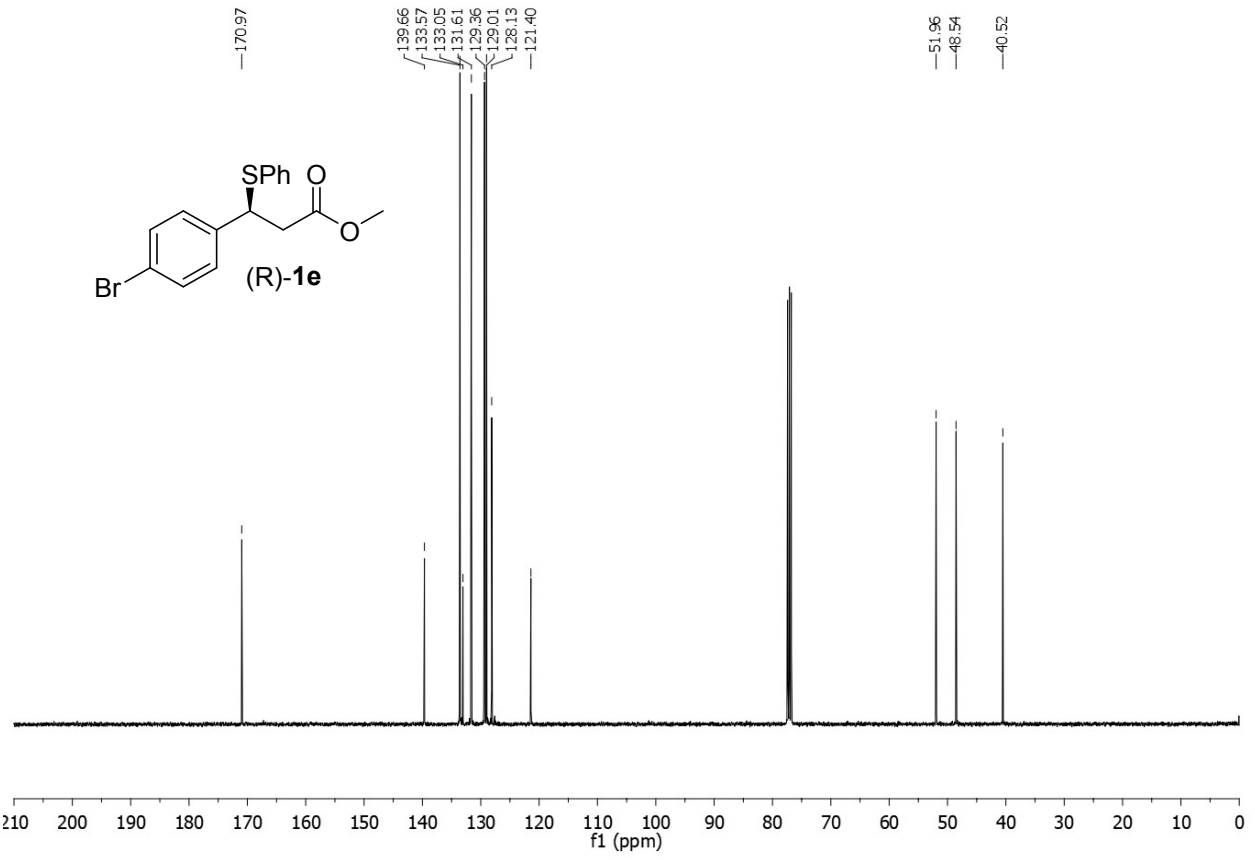
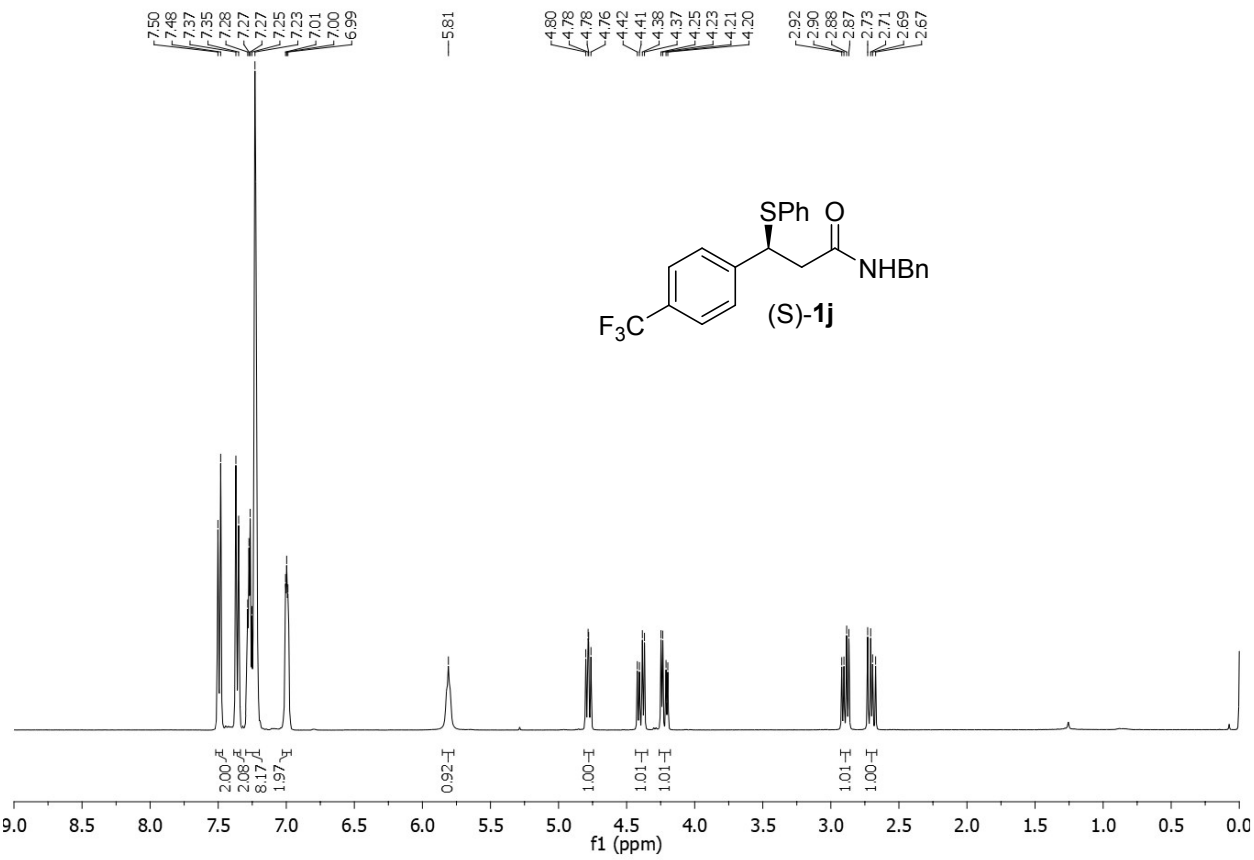
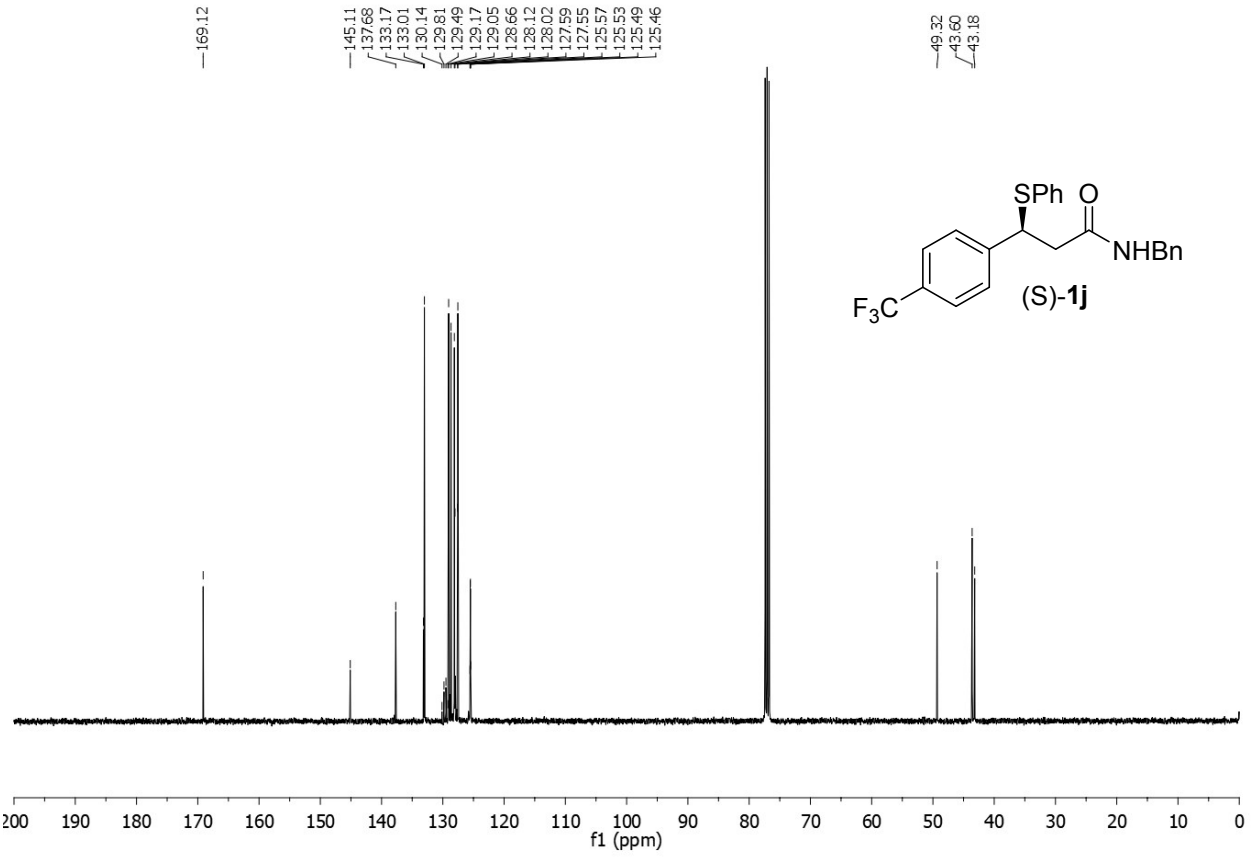
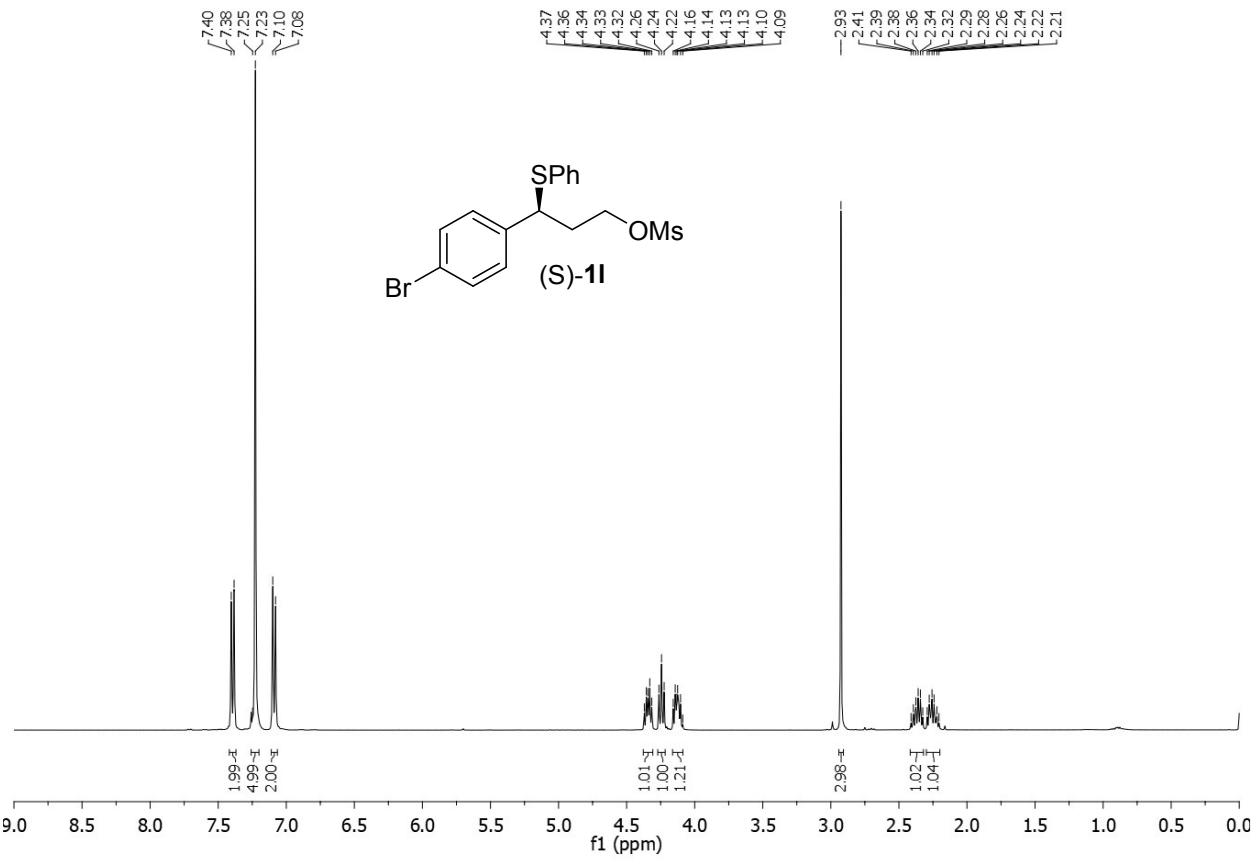
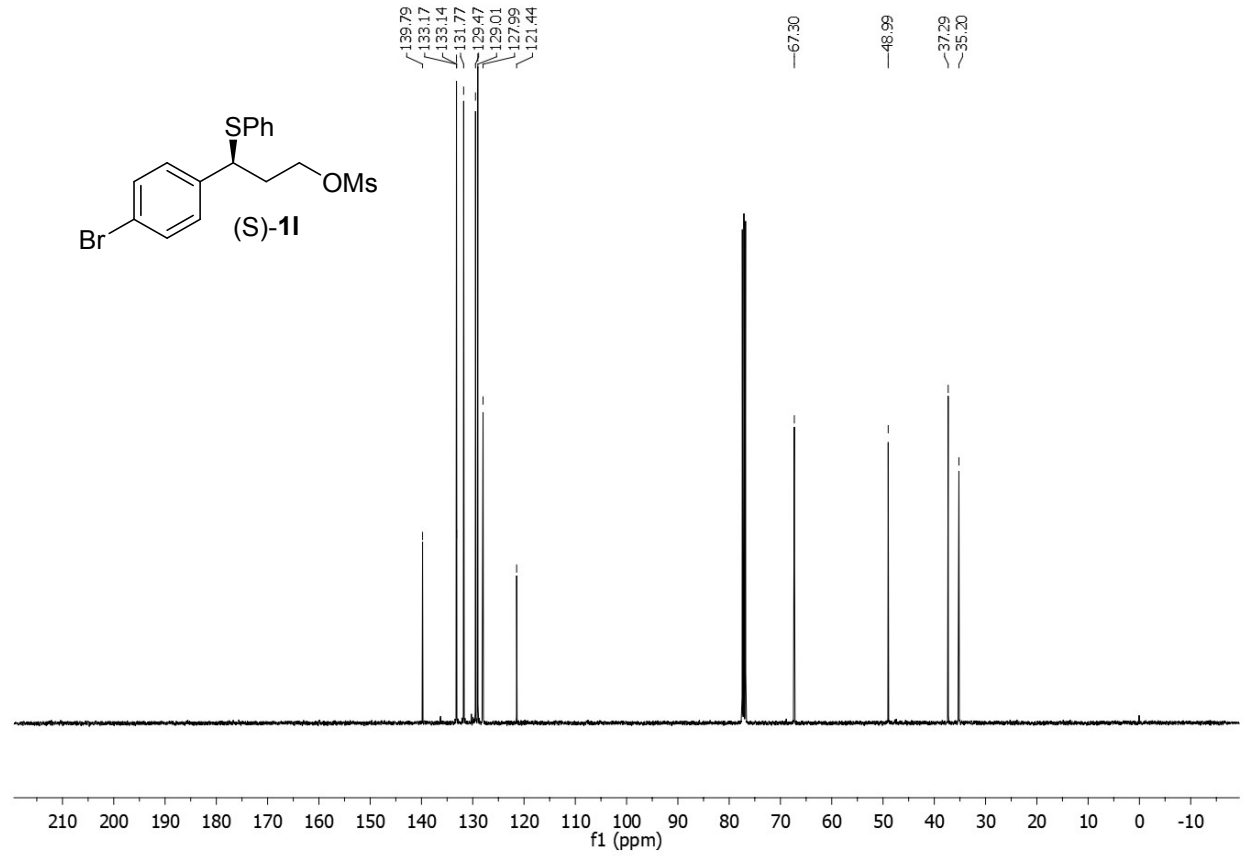
7.36
7.30
7.29
7.28
7.27
7.25
7.24
7.23
7.12
7.09
4.61
4.59
4.57
3.59
2.98
2.96
2.94
2.92
2.90
2.88
2.86
2.84
SPh
O
O
Br
(R)-1e
2.05
4.99
2.01
1.00
2.95
2.05
f1 (ppm)

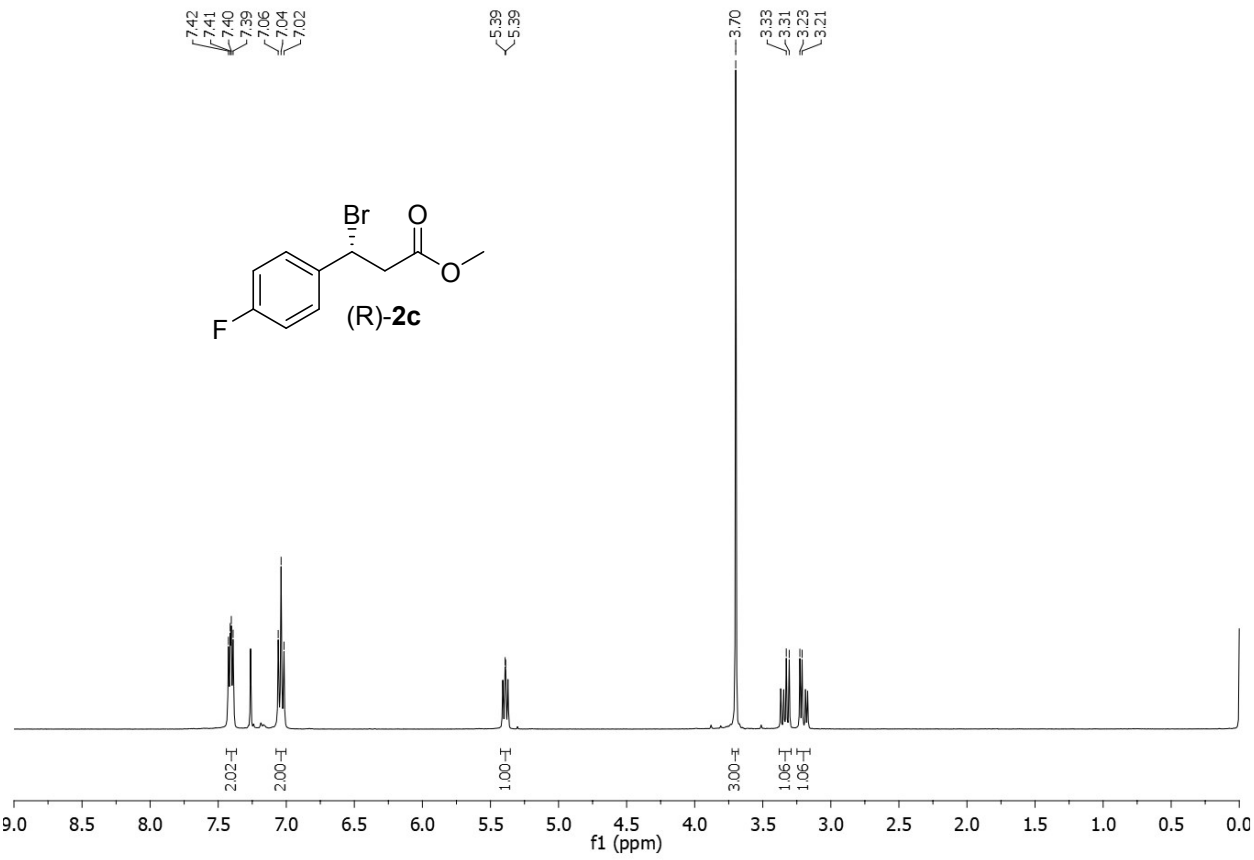

170.97
139.66
133.57
133.05
131.61
129.36
129.01
128.13
121.40
51.96
48.54
40.52
SPh
O
O
Br
(R)-1e
f1 (ppm)

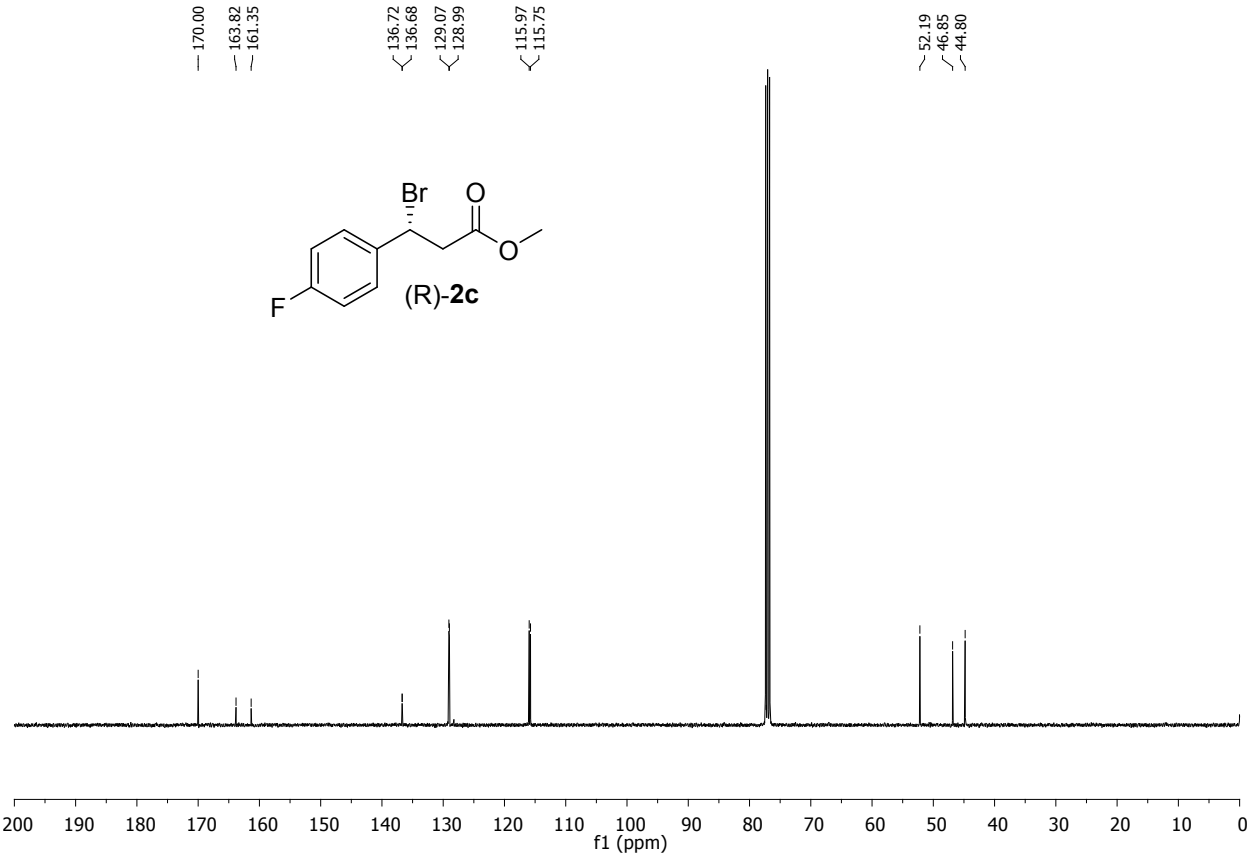

7.50
7.48
7.37
7.35
7.28
7.27
7.27
7.25
7.23
7.01
7.00
6.99
5.81
4.80
4.78
4.78
4.76
4.42
4.41
4.38
4.37
4.25
4.23
4.21
4.20
2.92
2.90
2.88
2.87
2.73
2.71
2.69
2.67
SPh
O
NHBn
F3C
(S)-1j
2.00
2.08
8.17
1.97
0.92
1.00
1.01
1.01
1.01
1.00
f1 (ppm)

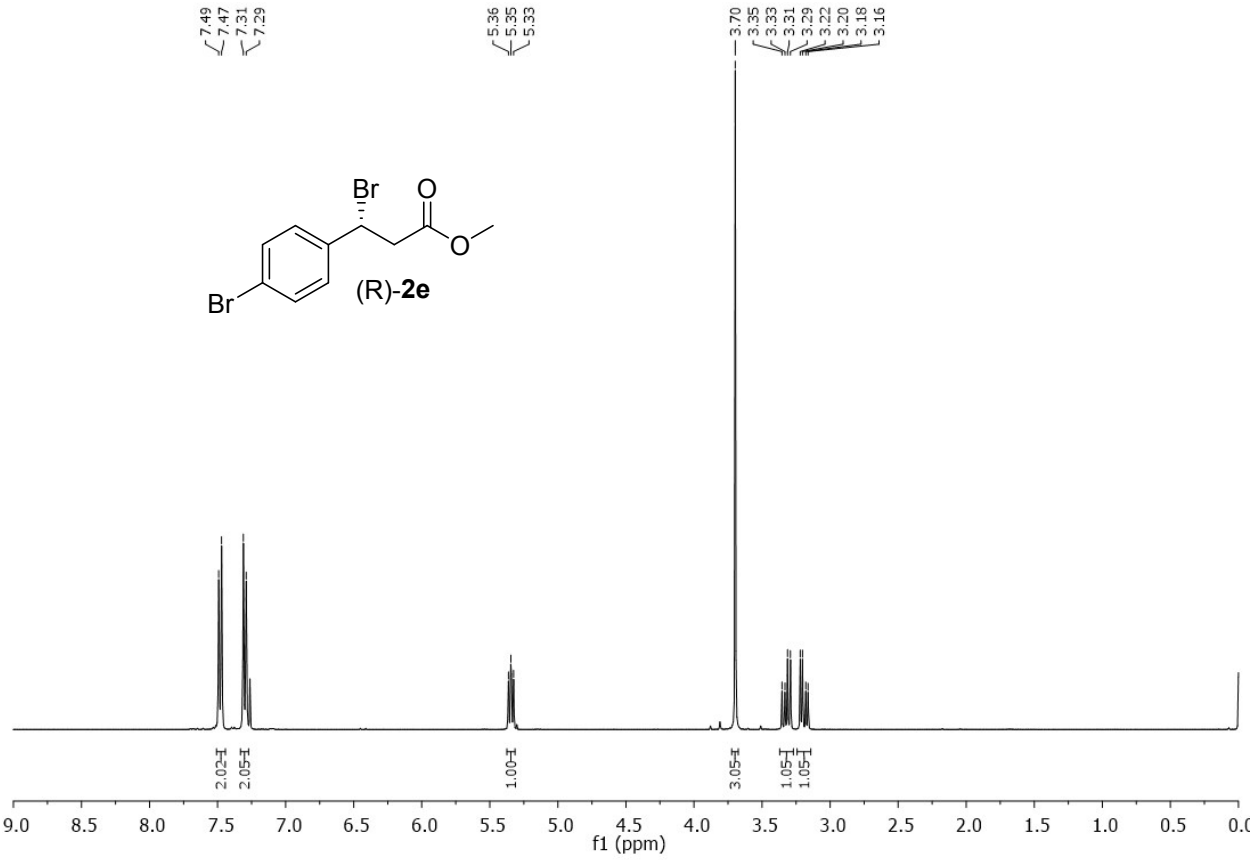

169.12
145.11
137.68
133.17
133.01
130.14
129.81
129.49
129.17
129.05
128.66
128.12
128.02
127.59
127.55
125.57
125.53
125.49
125.46
49.32
43.60
43.18
SPh
O
NHBn
F3C
(S)-1j
f1 (ppm)

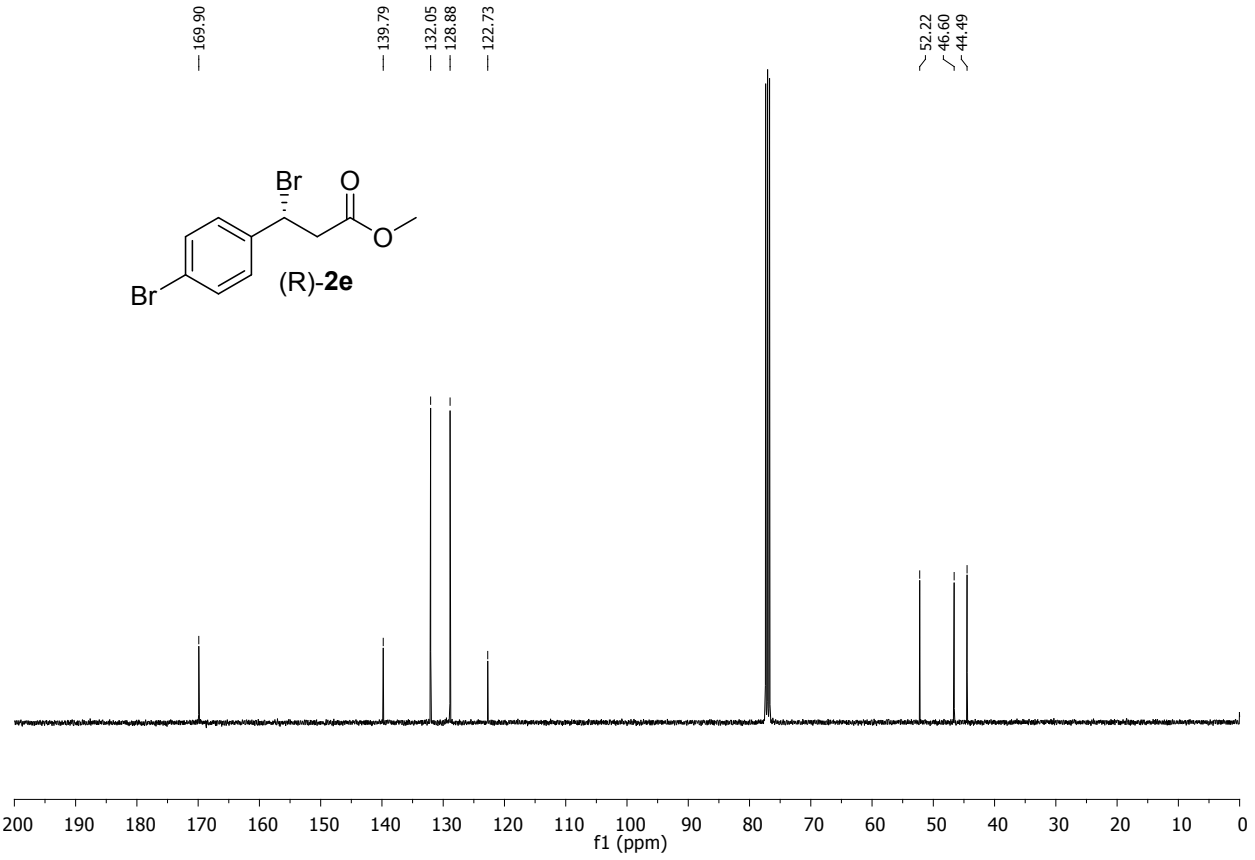

7.40
7.38
7.25
7.23
7.10
7.08
4.37
4.36
4.34
4.33
4.32
4.26
4.24
4.22
4.16
4.14
4.13
4.10
4.09
2.93
2.41
2.39
2.38
2.36
2.34
2.32
2.29
2.28
2.26
2.24
2.22
2.21
SPh
OMs
Br
(S)-1l
1.99
4.99
2.00
1.01
1.00
1.21
2.98
1.02
1.04
f1 (ppm)

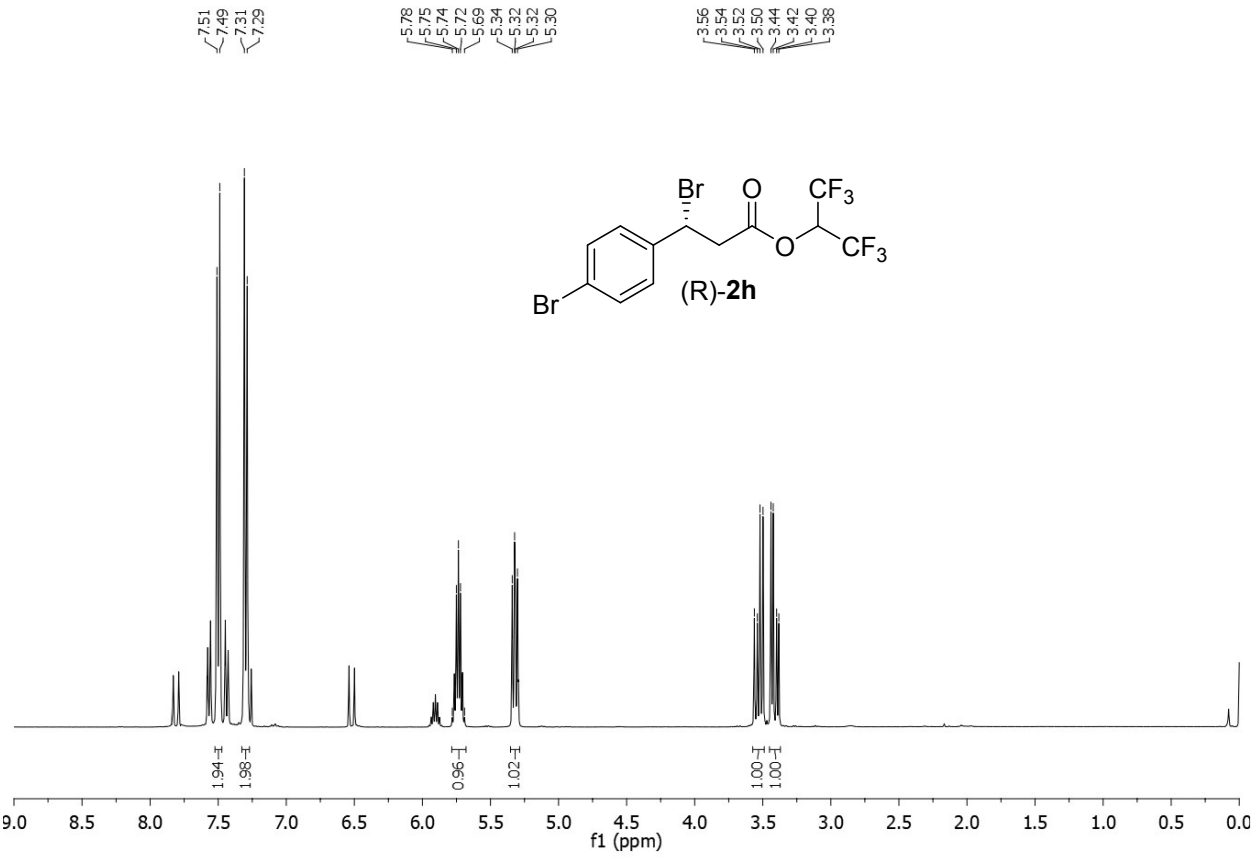

139.79
133.17
133.14
131.77
129.47
129.01
127.99
121.44
67.30
48.99
37.29
35.20
SPh
OMs
Br
(S)-1l
f1 (ppm)


7.42
7.41
7.40
7.39
7.06
7.04
7.02
5.39
5.39
3.70
3.33
3.31
3.23
3.21
Br
O
O
F
(R)-2c
2.02
2.00
1.00
3.00
1.06
1.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.00
163.82
161.35
136.72
136.68
129.07
128.99
115.97
115.75
52.19
46.85
44.80
Br
O
O
F
(R)-2c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.49
7.47
7.31
7.29
5.36
5.35
5.33
3.70
3.35
3.33
3.31
3.29
3.22
3.20
3.18
3.16
Br
O
O
Br
(R)-2e
2.02
2.05
1.00
3.05
1.05
1.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


169.90
139.79
132.05
128.88
122.73
52.22
46.60
44.49
Br
O
O
Br
(R)-2e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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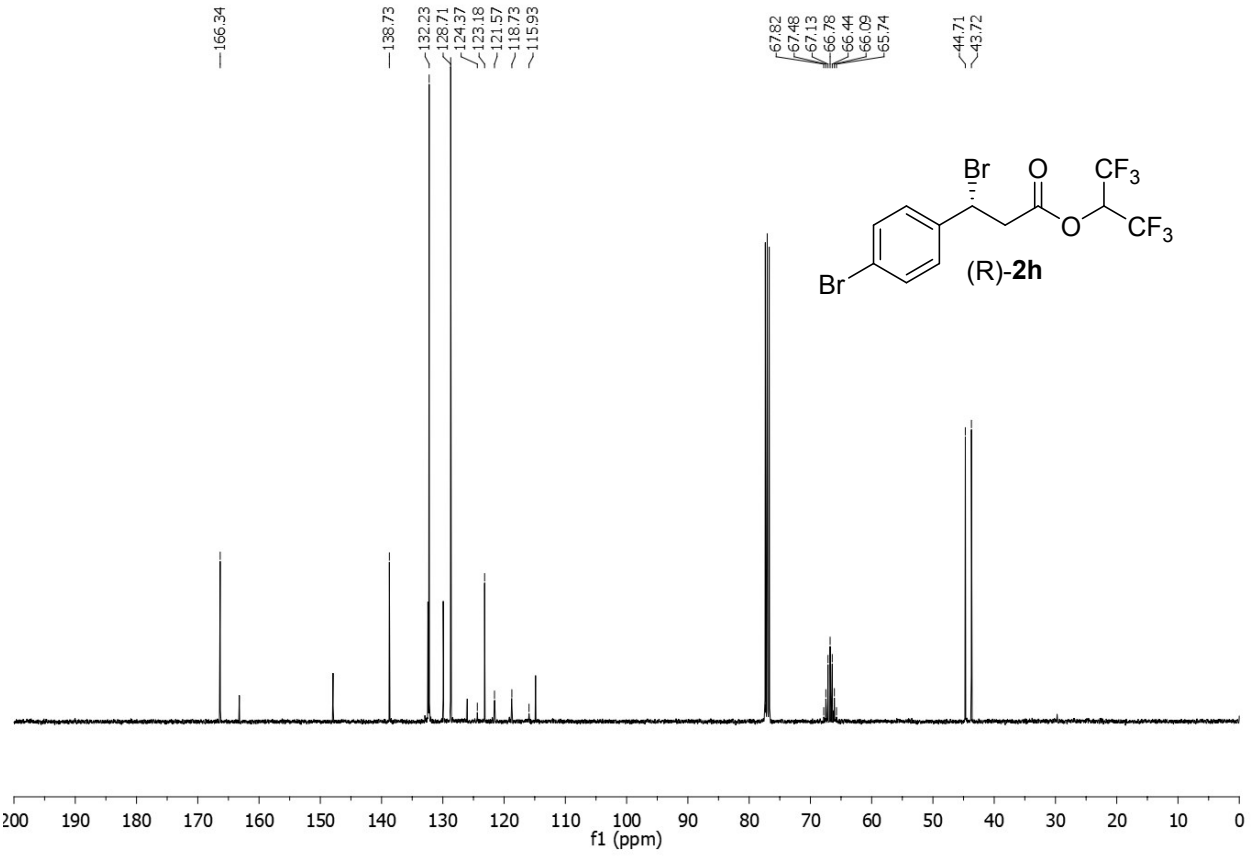
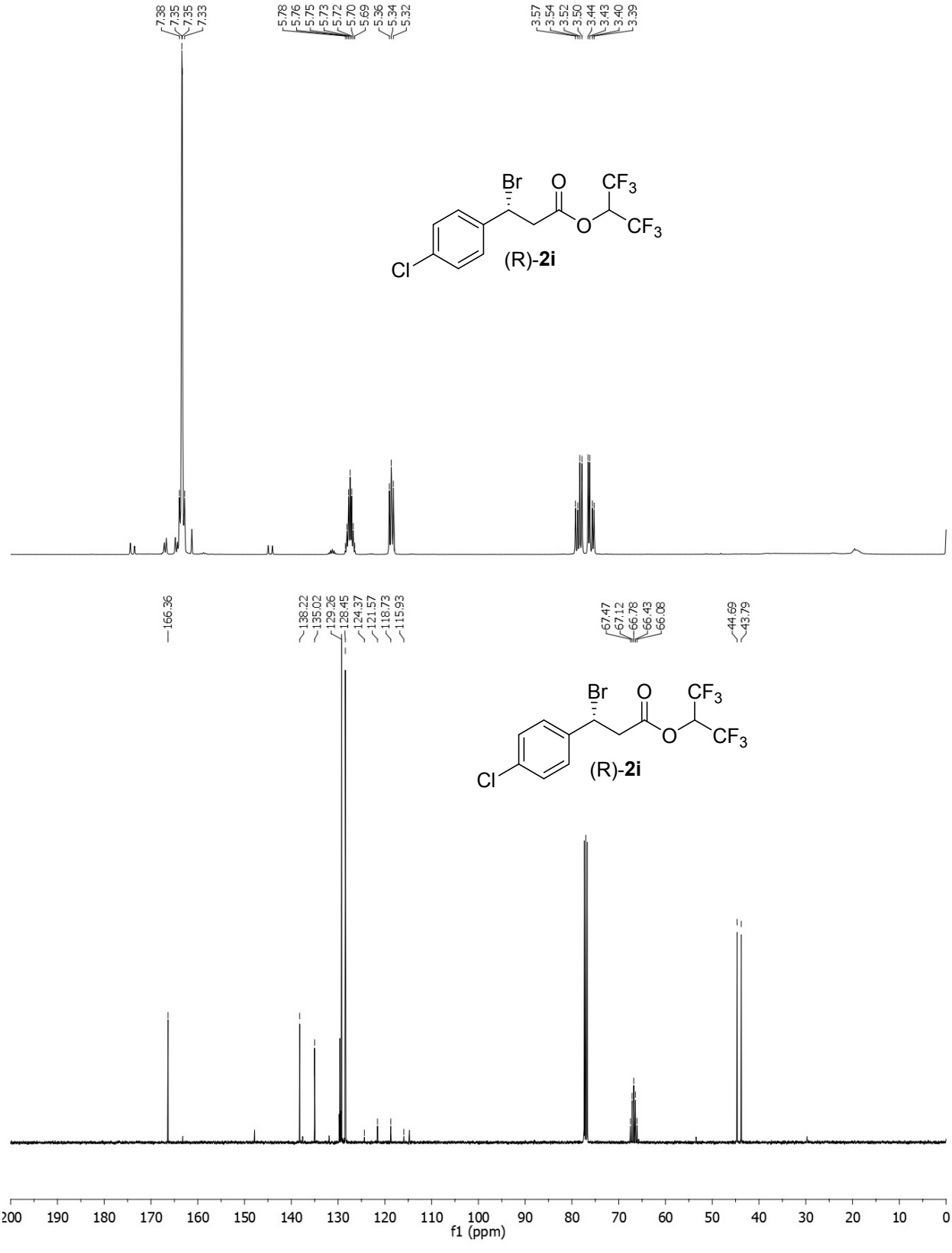
7.49
7.31
7.29
5.78
5.75
5.74
5.72
5.69
5.34
5.32
5.30
3.56
3.54
3.52
3.50
3.44
3.42
3.40
3.38
Br
O
CF3
O
CF3
Br
(R)-2h
1.94
1.98
0.96
1.02
1.00
1.00
f1 (ppm)


166.34
138.73
132.23
128.71
124.37
123.18
121.57
118.73
115.93
67.82
67.48
67.13
66.78
66.44
66.09
65.74
44.71
43.72
Br
O
CF3
O
CF3
Br
(R)-2h
f1 (ppm)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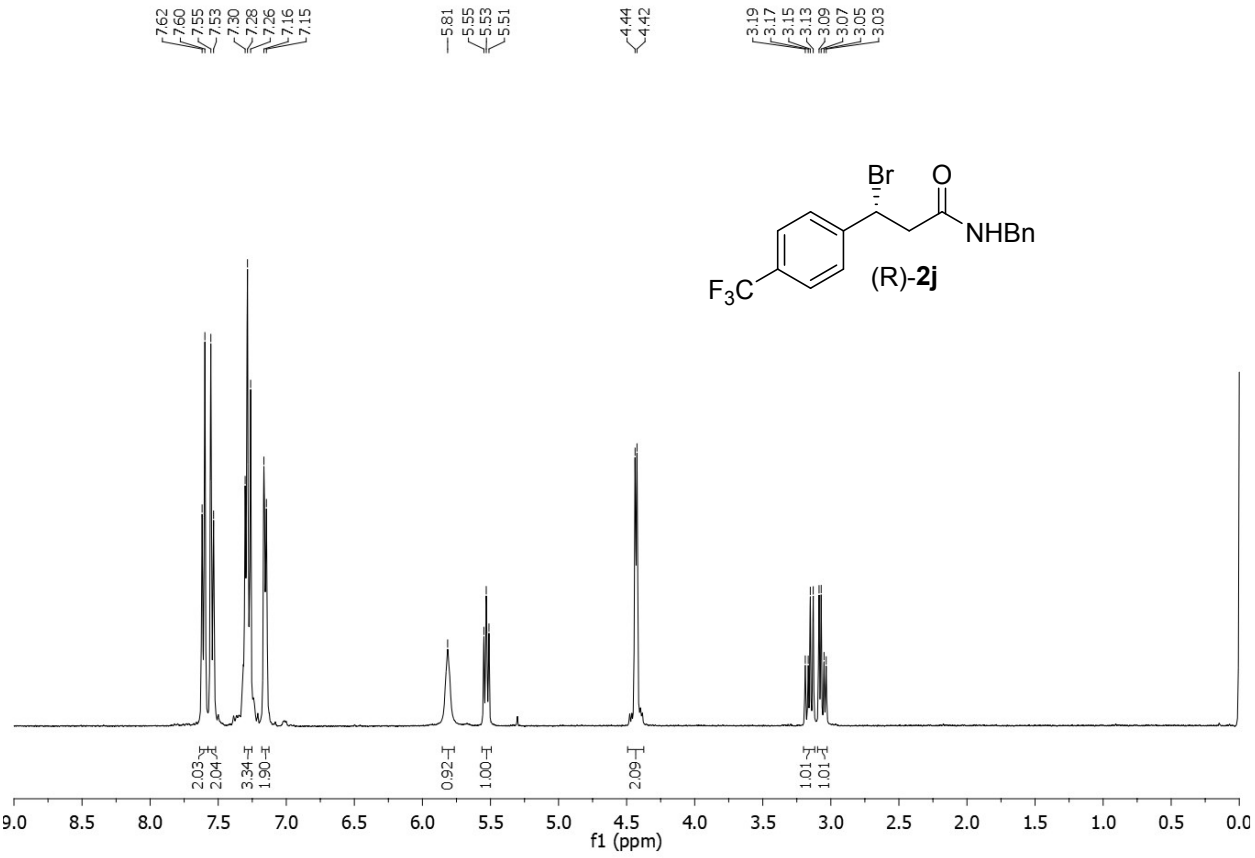
7.35
7.35
7.33
5.78
5.76
5.75
5.73
5.72
5.70
5.69
5.36
5.34
5.32
3.57
3.54
3.52
3.50
3.44
3.43
3.40
3.39
Br
O
CF3
O
CF3
Cl
(R)-2i
166.36
138.22
135.02
129.26
128.45
124.37
121.57
118.73
115.93
67.47
67.12
66.78
66.43
66.08
44.69
43.79
Br
O
CF3
O
CF3
Cl
(R)-2i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.62
7.60
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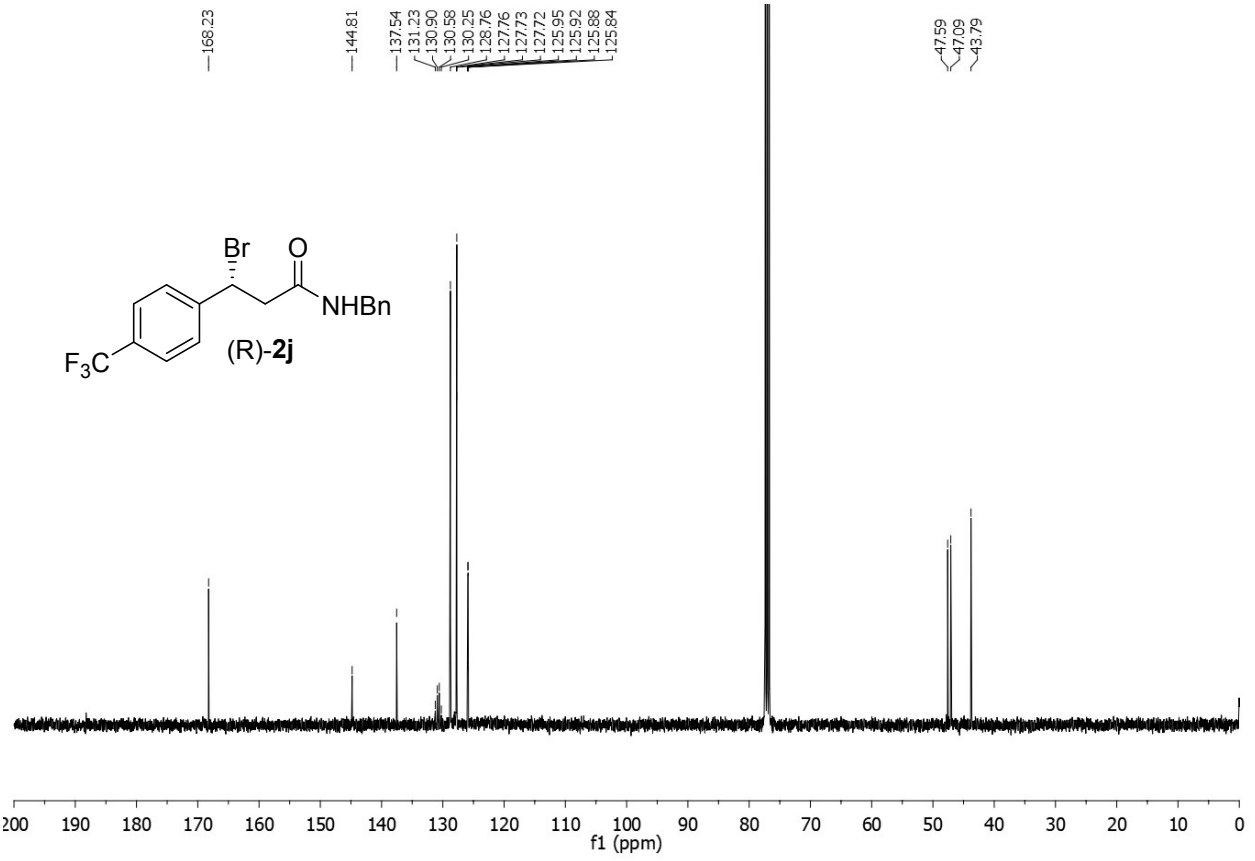
7.53
7.30
7.28
7.26
7.16
7.15
5.81
5.55
5.53
5.51
4.44
4.42
3.19
3.17
3.15
3.13
3.09
3.07
3.05
3.03
Br
O
NHBn
F3C
(R)-2j
2.03
2.04
3.34
1.90
0.92
1.00
2.09
1.01
1.01
f1 (ppm)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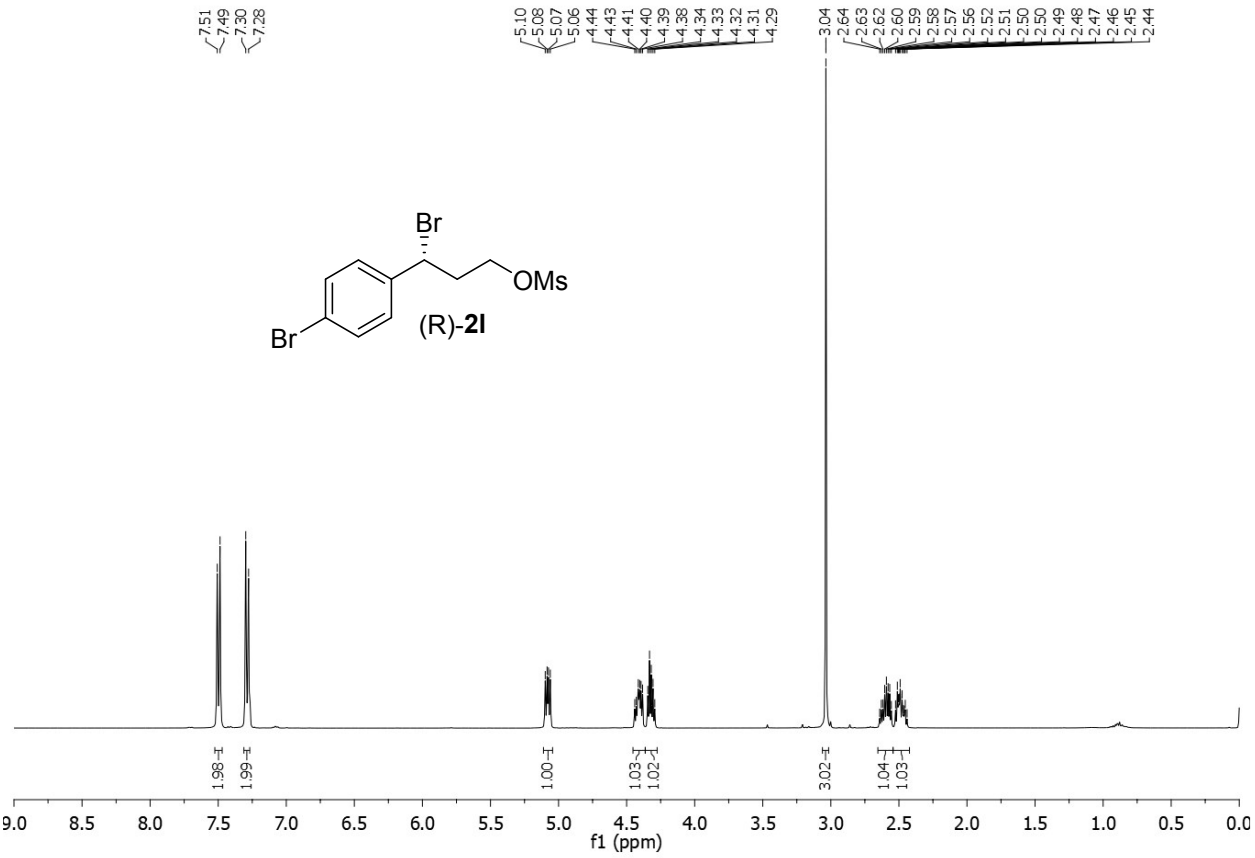
144.81
137.54
131.23
130.90
130.58
130.25
128.76
127.76
127.73
127.72
125.95
125.92
125.88
125.84
47.59
47.09
43.79
Br
O
NHBn
F3C
(R)-2j
f1 (ppm)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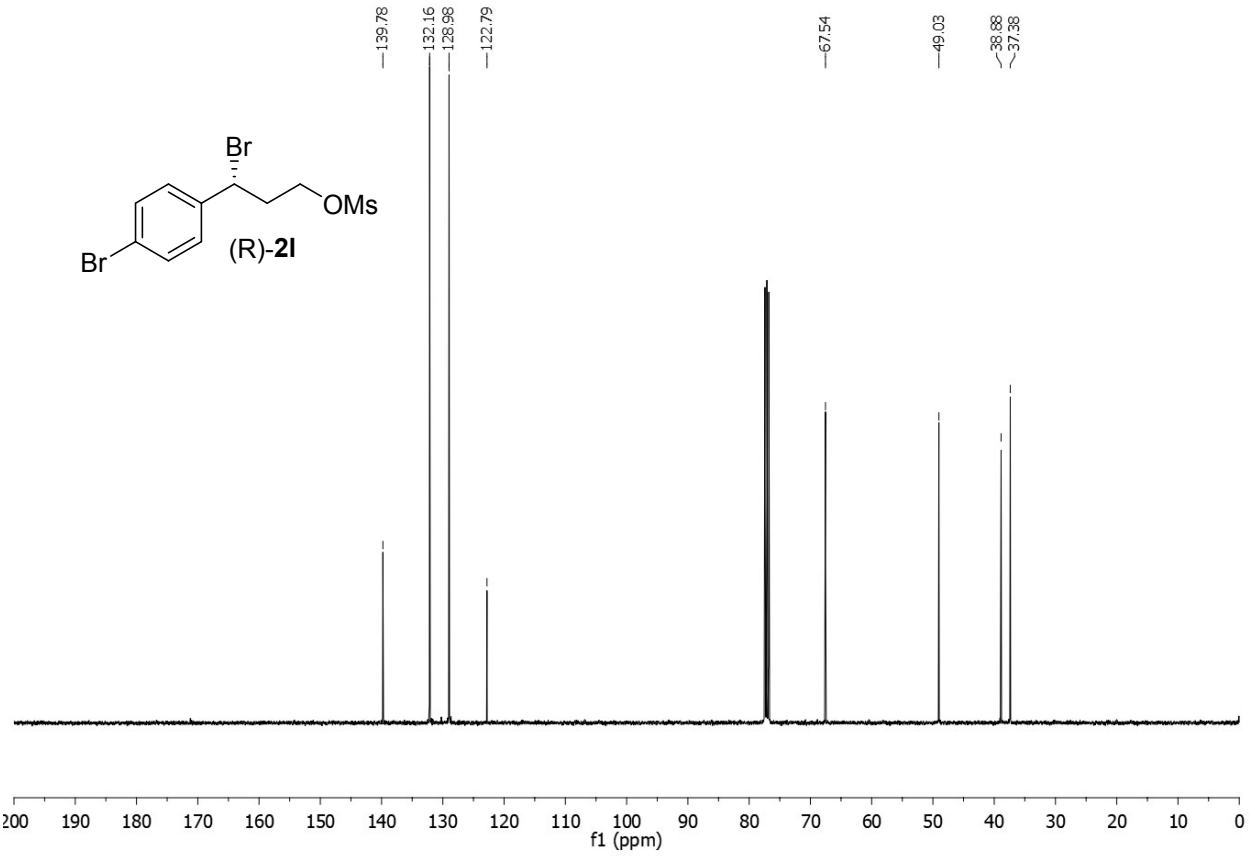
7.49
7.30
7.28
5.10
5.08
5.07
5.06
4.44
4.43
4.41
4.40
4.39
4.38
4.34
4.33
4.32
4.31
4.29
3.04
2.64
2.63
2.62
2.60
2.59
2.58
2.57
2.56
2.52
2.51
2.50
2.50
2.49
2.48
2.47
2.46
2.45
2.44
Br
OMs
Br
(R)-2l
1.98
1.99
1.00
1.03
1.02
3.02
1.04
1.03
f1 (ppm)


139.78
132.16
128.98
122.79
67.54
49.03
38.88
37.38
Br
OMs
Br
(R)-2l
f1 (ppm)