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Supporting Information

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Catalytic Asymmetric Reaction with Water: Enantioselective Synthesis of α-Hydroxyesters by Copper-carbenoid O–H Insertion Reaction

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CONTENTS:

General. All reactions and manipulations were performed using standard Schlenk techniques. All solvents were purified and dried using standard procedures. CuCl and $CuPF_6(MeCN)_4$ were prepared according to the literature procedures.[1] The other copper salts were purchased and used without further purification. Ligands **1**,[2] (S_a,*S*,*S*)-Ph-Binabox and (R_a,*S*,*S*)-Ph-Binabox,[3] (*S*,*S*)-Ph-Box,[4] (*S*,*S*)-^{i}Pr-Pybox,[5] (*R*)-BINAP,[6] (*S*)-SDP,[7] (*S*)-Phox,[8] and SIPHOX[9]

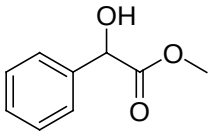
[1] Inorg. Synth. Vol. II, p. 1
[2] a) B. Liu, S.-F. Zhu, L.-X. Wang, Q.-L. Zhou, *Tetrahedron: Asymmetry* **2006**, *17*, 634. b) B. Liu, S.-F. Zhu, W. Zhang, C. Chen, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, *129*, 5834.
[3] Y. Uozumi, H. Kyota, E. Kishi, K. Kitayama, T. Hayashi, *Tetrahedron: Asymmetry* **1996**, *7*, 1603.
[4] D. A. Evans, K. A. Woerpel, M. M. Hinman, M. M. Faul, *J. Am. Chem. Soc.* **1991**, *113*, 726.
[5] H. Nishiyama, H. Sakaguchi, T. Nakamura, M. Horihata, M. Kondo, K. Itoh, *Organometallics* **1989**, *8*, 846.
[6] D. Cai, J. F. Payack, D. R. Bender, D. L. Hughes, T. R. Verhoeven, P. J. Reider, *J. Org. Chem.* **1994**, *59*, 7180.

were prepared by literature methods. All the 2-diazophenylacetates were prepared according to the literature procedure.[10] Melting points were measured on a RY–I apparatus and uncorrected. NMR spectra were recorded on a Bruker or Varian spectrometer at 400 or 300 (^{1}H NMR), 100 or 75 (^{13}C NMR) MHz. Chemical shifts (δ values) were reported in ppm down field from internal Me_4Si (^{1}H and ^{13}C NMR). Optical rotations were determined using a Perkin Elmer 341 MC polarimeter. HRMS were recorded on VG ZAB-HS mass spectrometer with EI resource. HPLC analyses were performed on a Hewlett Packard Model HP 1100 Series chromatography. SFC analyses were performed on Mettler-Toledo Model Analytix SFC.

1. Typical Procedure for Cu-catalyzed Asymmetric Insertion of Carbenoid into Water

The $CuSO_4$ (2.4 mg, 0.015 mmol, 5 mol%), (S_a,*S*,*S*)-**1a** (9.1 mg, 0.018 mmol, 6 mol%) and NaBARF (16.9 mg, 0.018 mmol, 6 mol%) were introduced into an oven-dried Schlenk tube in argon-filled glovebox. After $CHCl_3$ (3 mL) was injected into the Schlenk tube, the solution was stirred at room temperature under the argon atmosphere for 4 h. Then the Schlenk tube was heated to 40 ^{o}C, H_2O (27 mg, 1.5 mmol) and diazoesters (0.3 mmol) were injected. The resulting mixture was stirred at 40 ^{o}C for 15 min and the product was purified by flash chromatography (ethyl acetate/petroleum ether = 1:5). The analytical data for α-hydroxyesters are listed below.

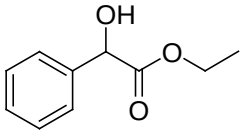
2. Analytical Data for Insertion Products



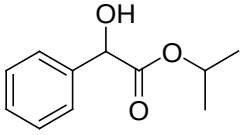
(*R*)-(–)-Methyl 2-hydroxy-2-phenylacetate (3a).[11] Colorless oil; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.33 (m, 5H), 5.18 (d, *J* = 4.8 Hz, 1H), 3.76 (s, 3H), 3.46 (d, *J* = 5.2 Hz, 1H); 90% ee [SFC condition:

[7] J.-H. Xie, L.-X. Wang, Y. Fu, S.-F. Zhu, B.-M. Fan, H.-F. Duan, Q.-L. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 4404.
[8] J. V. Allen, G. J. Dawson, C. G. Frost, J. M. J. Willams, S. J. Coote, *Tetrahedron* **1994**, *50*, 799.
[9] S.-F. Zhu; J.-B. Xie, Y.-Z. Zhang, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 12886.
[10] a) M. Regitz, *Angew. Chem.* **1967**, *79*, 786; *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 733; b) T. C. Maier, G. C. Fu, *J. Am. Chem. Soc.* **2006**, *128*, 4594.
[11] O. Kuisle, E. Quiñoá, R. Riguera, *J. Org. Chem.* **1999**, *64*, 8063.

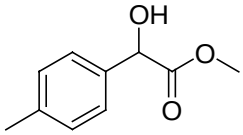
Chiralcel OD-H column, sc CO_2/*i*-PrOH = 80:20, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 2.35 min for (*S*)-enantiomer, t_R = 2.87 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –122 (*c* 1.00, EtOH) [lit: $[\alpha]_D^{20}$ = –130 (*c* 1.03, EtOH) for (*R*)].[12]



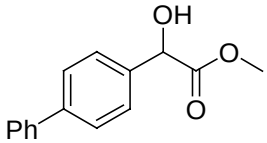
(*R*)-(–)-Ethyl 2-hydroxy-2-phenylacetate (3b).[13] Colorless oil; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.30 (m, 5H), 5.15 (d, *J* = 5.6 Hz, 1H), 4.31–4.13 (m, 2H), 3.47 (d, *J* = 5.6 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); 88% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 4.15 min for (*S*)-enantiomer, t_R = 5.71 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –104 (*c* 1.00, $CHCl_3$) [lit: $[\alpha]_D^{25}$ = –126 (*c* 2.01, $CHCl_3$) for (*R*)].[14]



(*R*)-(–)-Isopropyl 2-hydroxy-2-phenylacetate (3c).[13] Colorless oil; 81% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44–7.31 (m, 5H), 5.13–5.03 (m, 1H), 3.48 (d, *J* = 6.0 Hz, 1H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); 86% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.46 min for (*S*)-enantiomer, t_R = 4.71 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –96.1 (*c* 1.15, $CHCl_3$) [lit: $[\alpha]_D^{25}$ = –98.9 (*c* 1.00, $CHCl_3$) for (*R*)].[15]



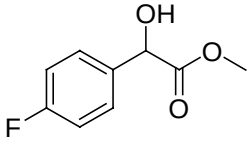
(*R*)-(–)-Methyl 2-hydroxy-2-*p*-tolylacetate (3d).[13] Colorless oil; 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.14 (d, *J* = 5.2 Hz, 1H), 3.75 (s, 3H), 3.40 (brs, 1H), 2.35 (s, 3H); 92% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.41 min for (*S*)-enantiomer, t_R = 3.89 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –108 (*c* 0.90, EtOH).



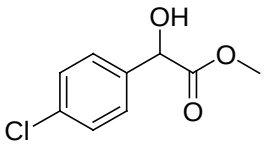
(–)-Mehtyl 2-hydroxy-2-(4-biphenyl)acetate (3e). White solid; 87% yield; mp = 103–104 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.24 (m, 9H), 5.13 (s, 1H), 3.66 (s, 3H), 3.53 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (75

[12] A. Ohno, M. Ikeguchi, T. Kimura, S. Oka, *J. Am. Chem. Soc.* **1979**, *101*, 7036.
[13] D. Basavaiah, P. R. Krishna, *Tetrahedron* **1995**, *51*, 2403.
[14] R. Roger, *J. Chem. Soc.* **1932**, 2168.
[15] H. C. Brown, G. G. Pai, *J. Org. Chem.* **1985**, *50*, 1384.

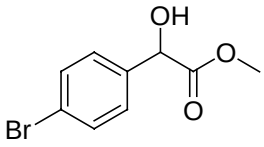
MHz, $CDCl_3$): δ 174.1, 141.5, 140.6, 137.3, 128.8, 127.5, 127.4, 127.1, 72.8, 53.0; HRMS (EI) Calcd for $C_{15}H_{14}O_3$: 242.0943; Found: 242.0969; 92% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 18.69 min for minor isomer, t_R = 20.47 min for major isomer]; $[\alpha]_D^{25}$ = –135 (*c* 1.80, $CHCl_3$).



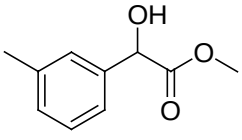
(–)-Methyl 2-(4-fluorophenyl)-2-hydroxyacetate (3f).[16] Colorless oil; 90% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 5.4 and 8.4 Hz, 2H), 6.97 (t, *J* = 8.7 Hz, 2H), 5.09 (s, 1H), 3.68 (s, 3H), 3.47 (brs, 1H); 92% ee [SFC condition: Chiralpak AD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.61 min for minor isomer, t_R = 3.90 min for major isomer]; $[\alpha]_D^{25}$ = –89.4 (*c* 0.70, acetone).



(*R*)-(–)-Methyl 2-(4-chlorophenyl)-2-hydroxyacetate (3g).[16] Colorless oil; 83% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39–7.32 (m, 4H), 5.16 (d, *J* = 5.4 Hz, 1H), 3.77 (s, 3H), 3.45 (d, *J* = 5.4 Hz, 1H); 92% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 5.80 min for (*S*)-enantiomer, t_R = 6.26 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –61.4 (*c* 0.35, acetone).



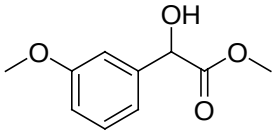
(*R*)-(–)-Methyl 2-(4-bromophenyl)-2-hydroxyacetate (3h).[16] Colorless oil; 86% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.14 (s, 1H), 3.77 (s, 3H), 3.48 (brs, 1H); 91% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 7.07 min for (*S*)-enantiomer, t_R = 7.65 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –71.2 (*c* 0.70, acetone).



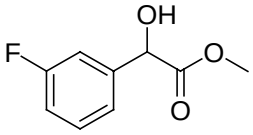
(–)-Methyl 2-hydroxy-2-*m*-tolylacetate (3i). Colorless oil; 87% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19–7.04 (m, 4H), 5.04 (d, *J* = 5.7 Hz, 1H), 3.66 (s, 3H), 3.45 (d, *J* = 5.7 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.2, 138.4, 138.3, 129.3, 128.5, 127.2, 123.8, 73.0, 52.9, 21.4; HRMS (EI) Calcd for $C_{10}H_{12}O_3$: 180.0786; Found: 180.0789; 92% ee [SFC condition: Chiralcel OD-H

[16] R. Chênevert, M. Létourneau, *Can. J. Chem.* **1990**, *68*, 314.

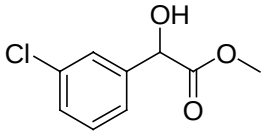
column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 4.68 min for minor isomer, t_R = 5.78 min for major isomer]; $[\alpha]_D^{25}$ = –112 (*c* 0.35, EtOH).



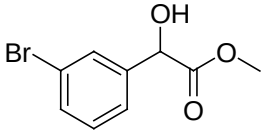
(*R*)-(–)-Methyl 2-hydroxy-2-(3-methoxyphenyl)acetate (3j).[16] Colorless oil; 89% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23–7.18 (m, 1H), 6.94–6.89 (m, 2H), 6.81–6.78 (m. 1H), 5.08 (s, 1H), 3.73 (s, 3H), 3.69 (s, 3H), 3.41 (d, *J* = 3.9 Hz, 1H); 91% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 4.42 min for (*S*)-enantiomer, t_R = 5.11 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –97.3 (*c* 0.75, EtOH).



(–)-Methyl 2-(3-fluorophenyl)-2-hydroxyacetate (3k). Colorless oil; 85% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25–7.05 (m, 3H), 6.96–6.90 (m, 1H), 5.09 (d, *J* = 3.3 Hz, 1H), 3.69 (s, 3H), 3.59 (d, *J* = 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.6, 164.5, 161.3, 140.7, 140.6, 130.1, 130.0, 122.2, 115.5, 115.2, 113.8, 113.5, 72.3, 53.1; HRMS (EI) Calcd for $C_9H_9FO_3$: 184.0536; Found: 184.0534; 89% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 95:5, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 4.15 min for minor isomer, t_R = 4.64 min for major isomer]; $[\alpha]_D^{25}$ = –117 (*c* 0.70, $CHCl_3$).



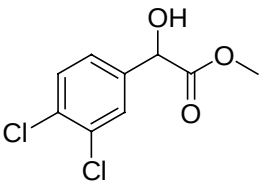
(*R*)-(–)-Methyl 2-(3-chlorophenyl)-2-hydroxyacetate (3l). [17] Colorless oil; 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.31 (m, 4H), 5.15 (s, 1H), 3.78 (s, 3H), 3.51 (brs, 1H); 88% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.93 min for (*S*)-enantiomer, t_R = 4.20 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –111 (*c* 1.80, $CHCl_3$).



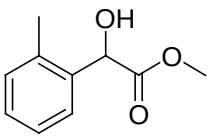
(–)-Methyl 2-(3-bromophenyl)-2-hydroxyacetate (m). [18] Colorless oil; 92% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61–7.26 (m, 4H), 5.16 (d, *J* = 5.4 Hz, 1H), 3.80 (s, 3H), 3.52 (d, *J* = 5.4 Hz, 1H); 88% ee [SFC condition: Chiralcel OJ-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0 mL/min,

[17] G. C. Lloyd-Jones, P. D. Wall, J. L. Slaughter, A. J. Parker, D. P. Laffan, *Tetrahedron* **2006**, *62*, 11402.
[18] B. M. Bocknack, L.-C. Wang, F. W. Hughes, M. J. Krische, *Tetrahedron* **2005**, *61*, 6266.

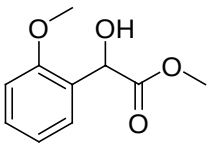
wavelength = 220 nm, pressure = 100 bar, t_R = 5.42 min for major isomer, t_R = 5.94 min for minor isomer]; $[\alpha]_D^{26}$ = –100 (*c* 0.90, EtOH).



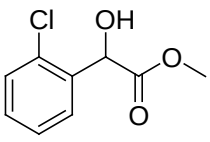
(*R*)-(–)-Methyl 2-(3,4-dichlorophenyl)-2-hydroxyacetate (3n). Colorless oil; 91% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (d, *J* = 2.1 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.21–7.17 (m, 1H), 5.06 (d, *J* = 5.1 Hz, 1H), 3.69 (s, 3H), 3.65 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.2, 138.3, 132.8, 132.6, 130.5, 128.6, 125.9, 71.7, 53.3; HRMS (EI) Calcd for $C_9H_8Cl_2O_3$: 233.9850; Found: 233.9851; 94% ee [SFC condition: Chiralpak AD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 6.86 min for (*S*)-enantiomer, t_R = 7.57 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –123 (*c* 0.65, $CHCl_3$). The absolute configuration was determined by comparing the specific rotation of corresponding acid with the literature data. See next section for details.



(–)-Methyl 2-hydroxy-2-*o*-tolylacetate (3o). Colorless oil; 81% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.14 (m, 4H), 5.36 (d, *J* = 5.1 Hz, 1H), 3.72 (s, 3H), 3.53 (d, *J* = 5.1 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.6, 136.6, 136.4, 130.8, 128.5, 126.9, 126.3, 70.5, 52.8, 19.2; HRMS (EI) Calcd for $C_{10}H_{12}O_3$: 180.0786; Found: 180.0782; 89% ee [SFC condition: Chiralcel OJ-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.34 min for major isomer, t_R = 3.74 min for minor isomer]; $[\alpha]_D^{25}$ = –87.0 (*c* 0.40, EtOH).

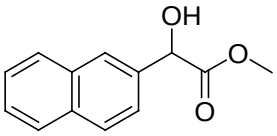


(*R*)-(–)-Methyl 2-hydroxy-2-(2-methoxyphenyl)acetate (3p).[13] Colorless oil; 71% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35–7.28 (m, 2H), 7.00–6.90 (m, 2H), 5.29 (d, *J* = 7.2 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H), 3.53 (d, *J* = 6.9 Hz, 1H); 50% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 4.48 min for (*S*)-enantiomer, t_R = 4.88 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –70.7 (*c* 0.40, EtOH).

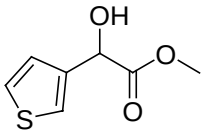


(*R*)-(–)-Methyl 2-(2-chlorophenyl)-2-hydroxyacetate (3q).[17] Colorless oil; 90% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41–7.38 (m, 2H), 7.30–7.26 (m, 2H), 5.57 (d, *J* = 5.1 Hz, 1H), 3.77 (s, 3H), 3.57 (d, *J* = 4.8 Hz, 1H); 36% ee [SFC condition: Chiralcel OJ-H column, sc CO_2/*i*-PrOH = 94:6, flow rate = 2.0

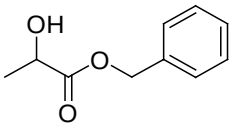
mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 5.43 min for (*R*)-enantiomer, t_R = 6.12 min for (*S*)-enantiomer]; $[\alpha]_D^{25}$ = –84.6 (*c* 0.92, $CHCl_3$).



(*R*)-(–)-Methyl 2-hydroxy-2-naphthalen-2-ylacetate (3r).[19] White solid; 76% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90–7.82 (m, 4H), 7.53–7.48 (m, 3H), 5.35 (d, *J* = 5.4 Hz, 1H), 3.76 (s, 3H), 3.55 (d, *J* = 5.7 Hz, 1H); 90% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 9.76 min for (*S*)-enantiomer, t_R = 10.60 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = –144 (*c* 1.00, $CHCl_3$).



(–)-Methyl 2-hydroxy-2-thiophene-3-ylacetate (3s). Colorless oil; 70% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22–7.15 (m, 2H), 7.00 (d, *J* = 4.8 Hz, 1H), 5.17 (d, *J* = 5.7 Hz, 1H), 3.87 (d, *J* = 6.0 Hz, 1H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.5, 139.3, 126.3, 125.9, 122.7, 69.5, 52.8; HRMS (EI) Calcd for $C_7H_8O_3S$: 172.0194; Found: 172.0194; 90% ee [SFC condition: Chiralcel OD-H column, sc CO_2/*i*-PrOH = 90:10, flow rate = 2.0 mL/min, wavelength = 220 nm, pressure = 100 bar, t_R = 3.79 min for minor isomer, t_R = 4.21 min for major isomer]; $[\alpha]_D^{25}$ = –108 (*c* 0.65, $CHCl_3$).



(*R*)-(+)-Benzyl 2-hydroxypropionate (3t).[20] Colorless oil; 78% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.33 (m, 5H), 5.21 (s, 2H), 4.36–4.28 (m, 1H), 2.85 (d, *J* = 5.1 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 3H); 78% ee [HPLC condition: Chiralcel OD-H column, *n*-Hex/*i*-PrOH = 96:4, flow rate = 1.0 mL/min, wavelength = 220 nm, t_R = 20.95 min for (*S*)-enantiomer, t_R = 21.86 min for (*R*)-enantiomer]; $[\alpha]_D^{25}$ = +13.2 (*c* 0.72, MeOH).

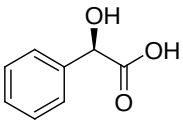
3. Typical Procedure for Hydrolysis of Methyl 2-Hydroxyphenylacetate

A solution of methyl 2-hydroxyphenylacetate (170 mg, 1.02 mmol) in EtOH (3 mL) was added to an aqueous solution of NaOH (4 mL, 1.25 M) at 0 °C. After being stirred for 2 h, the reaction mixture was acidified by 3 M hydrochloric acid and extracted with EtOAc (10 mL X

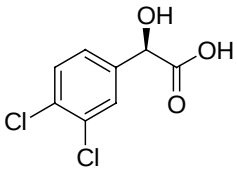
[19] M. Kimura, A. Kuboki, T. Sugai, *Tetrahedron: Asymmetry* **2002**, *13*, 1059.
[20] I. Shin, M. Lee, J. Lee, M. Jung, W. Lee, J. Yoon, *J. Org. Chem.* **2000**, *65*, 7667.

3). The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuum to give mandelic acid (**4a**) (154 mg, quant.) as a white solid which was recrystallized from DCE to give a optically pure (*R*)-mandelic acid in 74% yield. The analytical data for 2-hydroxyphenylacetic acids are listed below.

4. Analytical Data for Mandelic Acids



(*R*)-(–)-Mandelic acid (4a).[21] White solid; 74% yield; mp = 132–133 °C; ^{1}H NMR (300 MHz, Acetone-d_6): δ 7.52–7.27 (m, 7H), 5.22 (s, 1H); $[\alpha]_D^{25}$ = –157 (*c* 2.00, EtOH).

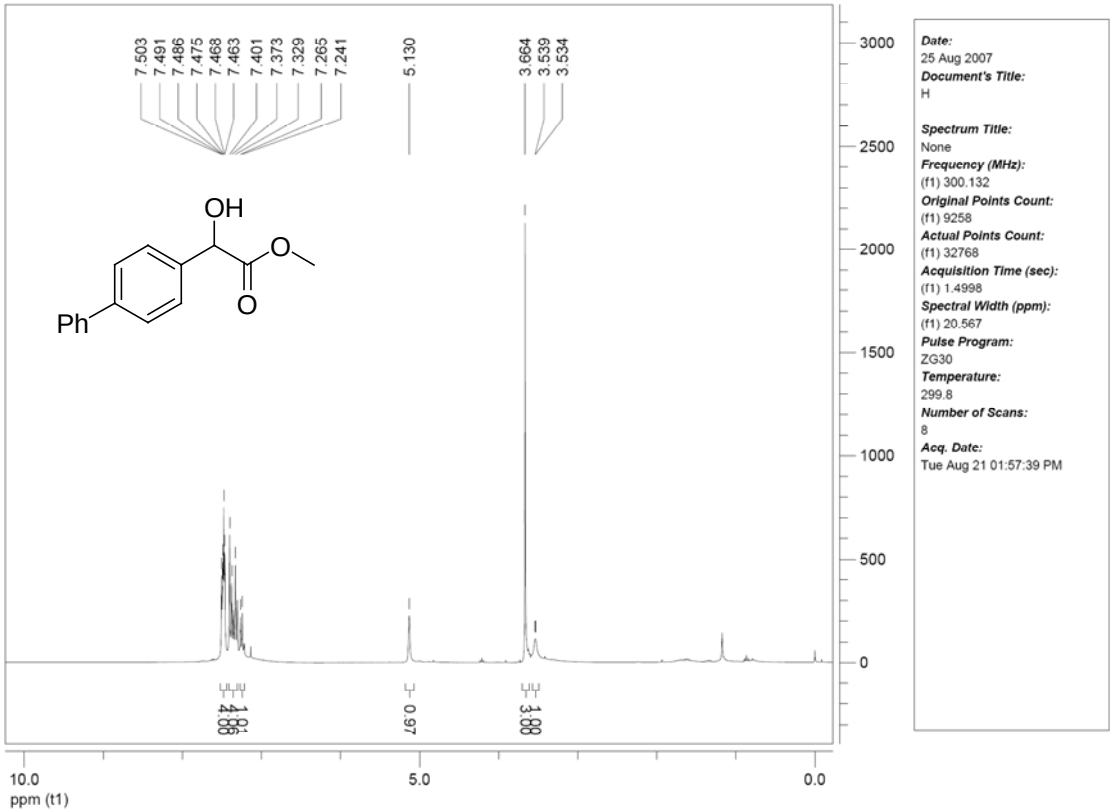


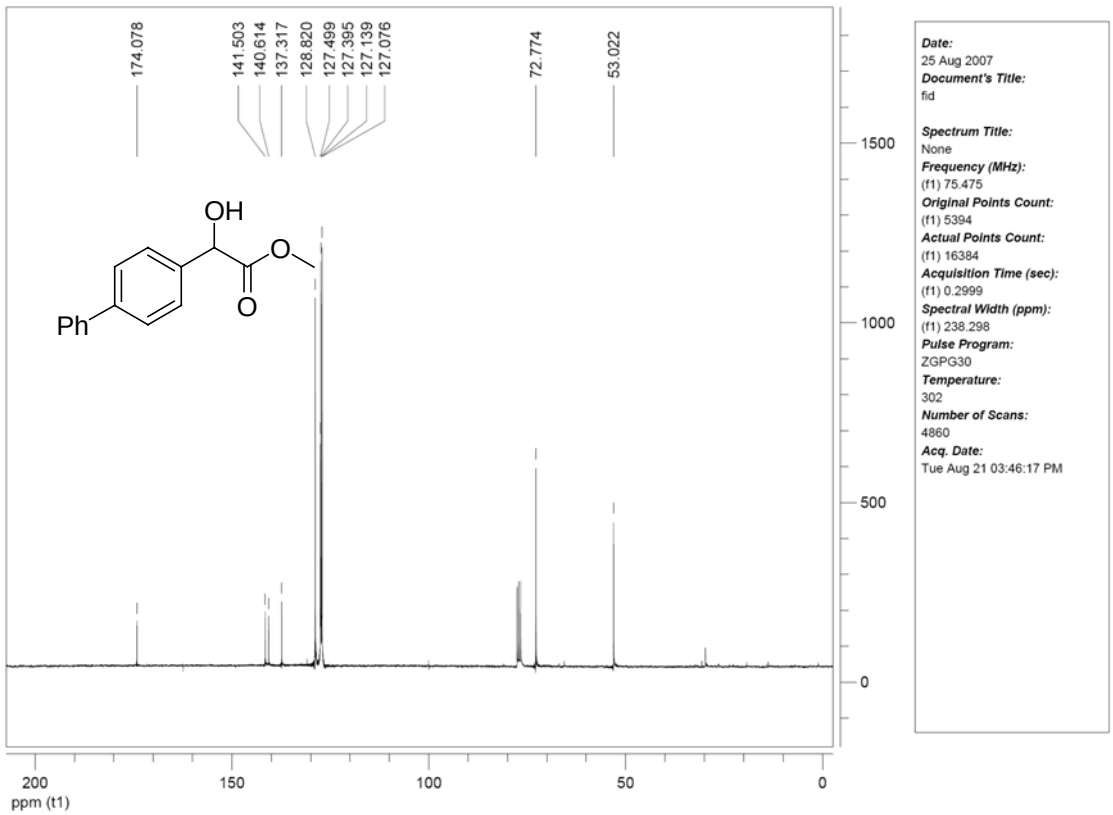
(*R*)-(–)-2-(3,4-Dichlorophenyl)-2-hydroxyacetic acid (4n). [22] White solid; 65% yield; mp = 117–118 °C; ^{1}H NMR (300 MHz, Acetone-d_6): δ 7.72–7.49 (m, 5H), 5.29 (s, 1H); $[\alpha]_D^{25}$ = –115 (*c* 0.50, H_2O).

[21] P. L. Polavarapu, L. P. Fontana, H. E. Smith, *J. Am. Chem. Soc.* **1986**, *108*, 94.
[22] J. R. E. Hoover, G. L. Dunn, D. R. Jakas, L. L. Lam, J. J. Taggart, J. R. Guarini, L. Phillips, *J. Med. Chem.* **1974**, *17*, 34.

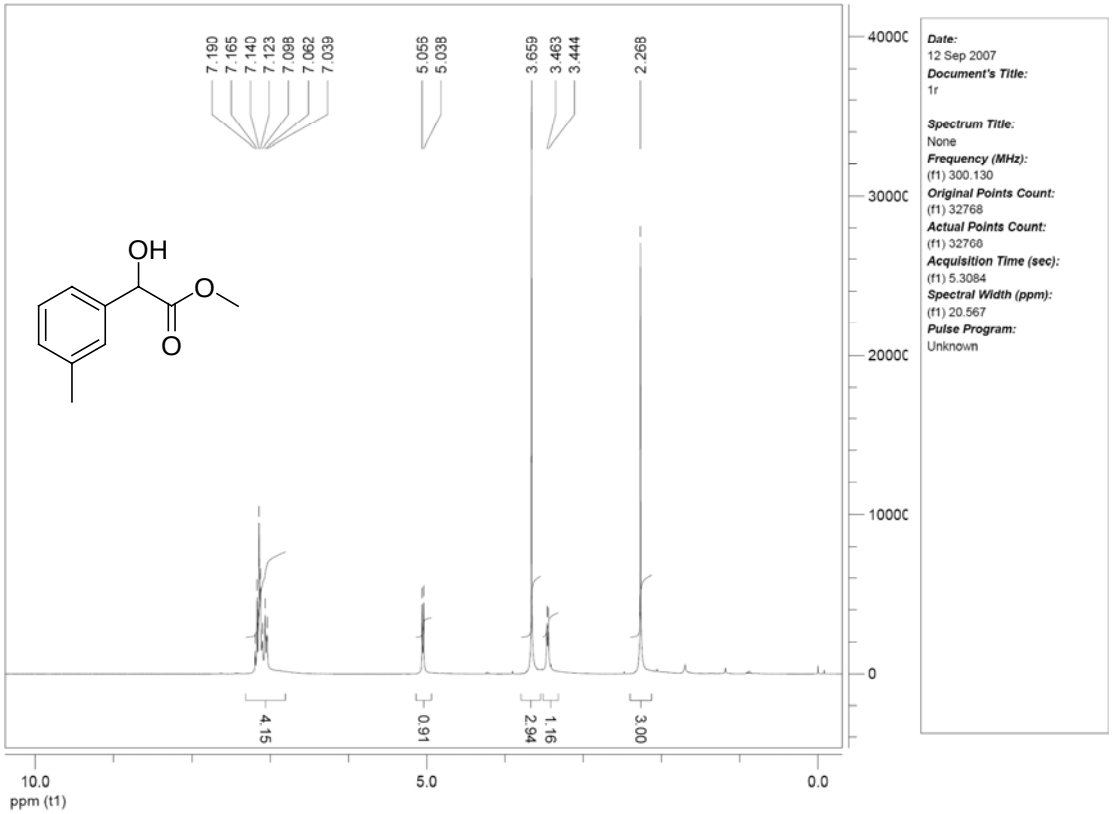
5. NMR Spectra for New Compounds

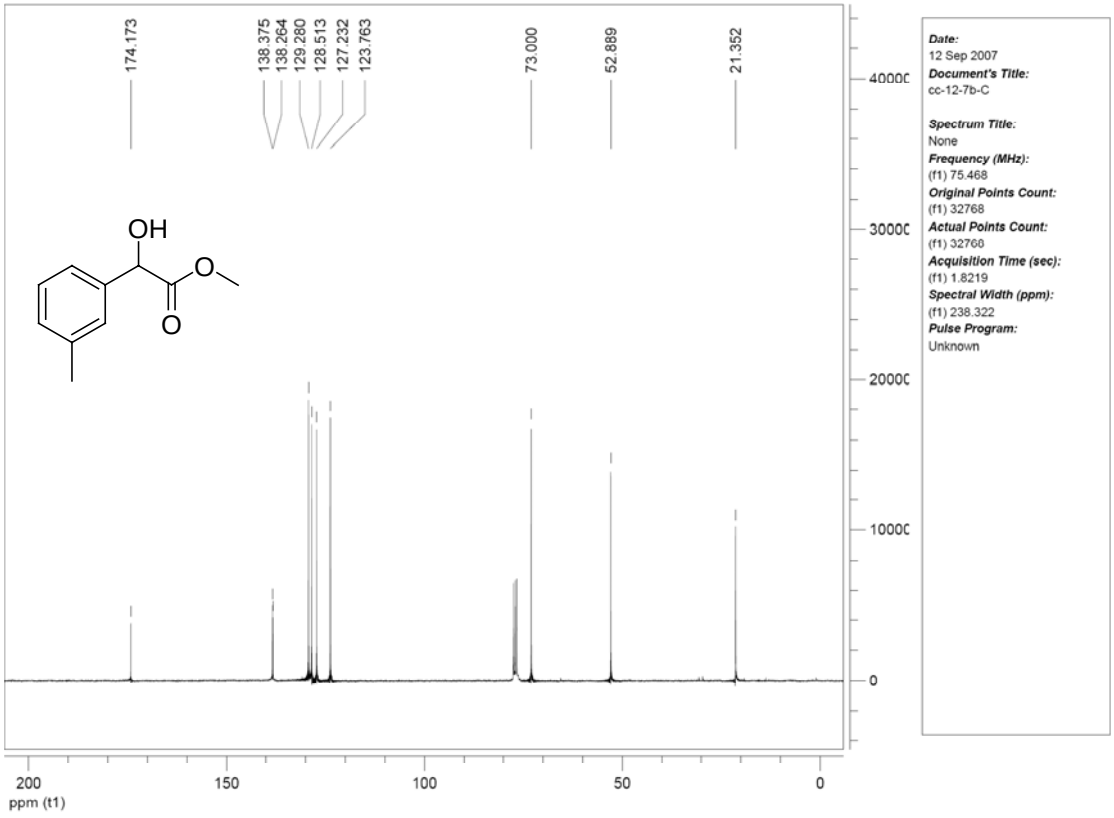
Mehtyl 2-hydroxy-2-biphenylacetate (3e)



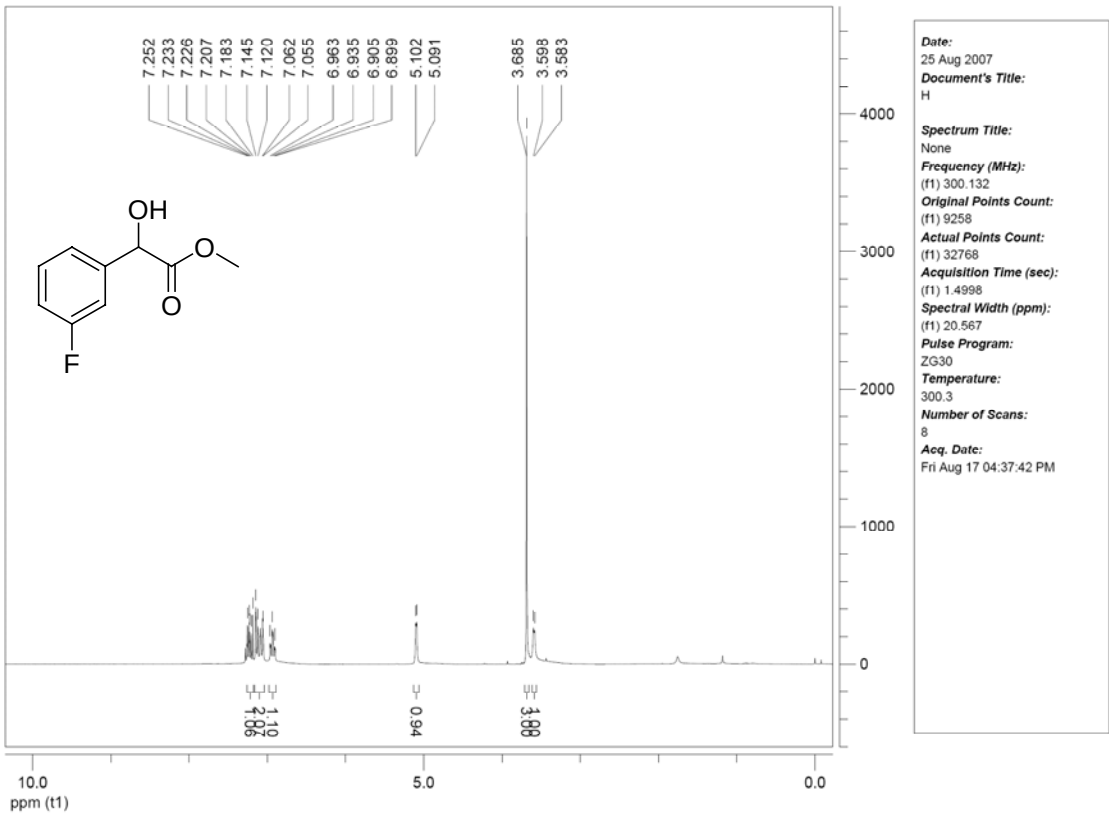


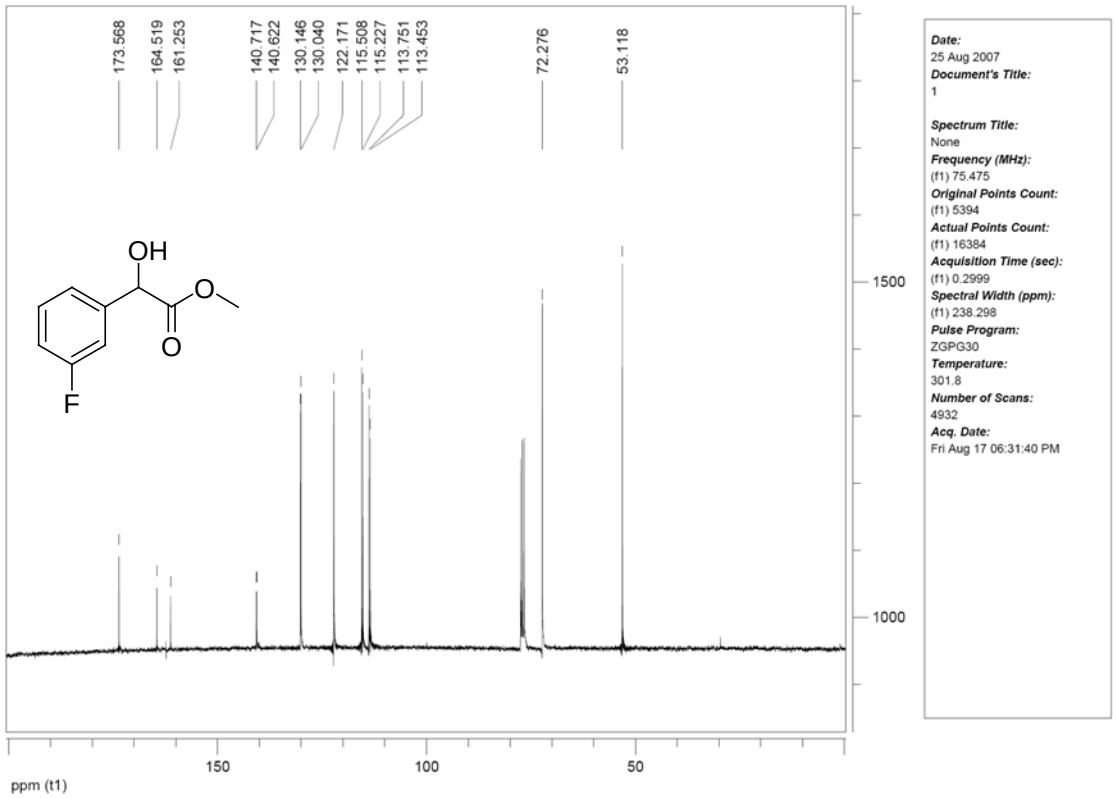
Methyl 2-hydroxy-2-*m*-tolylacetate (3i)



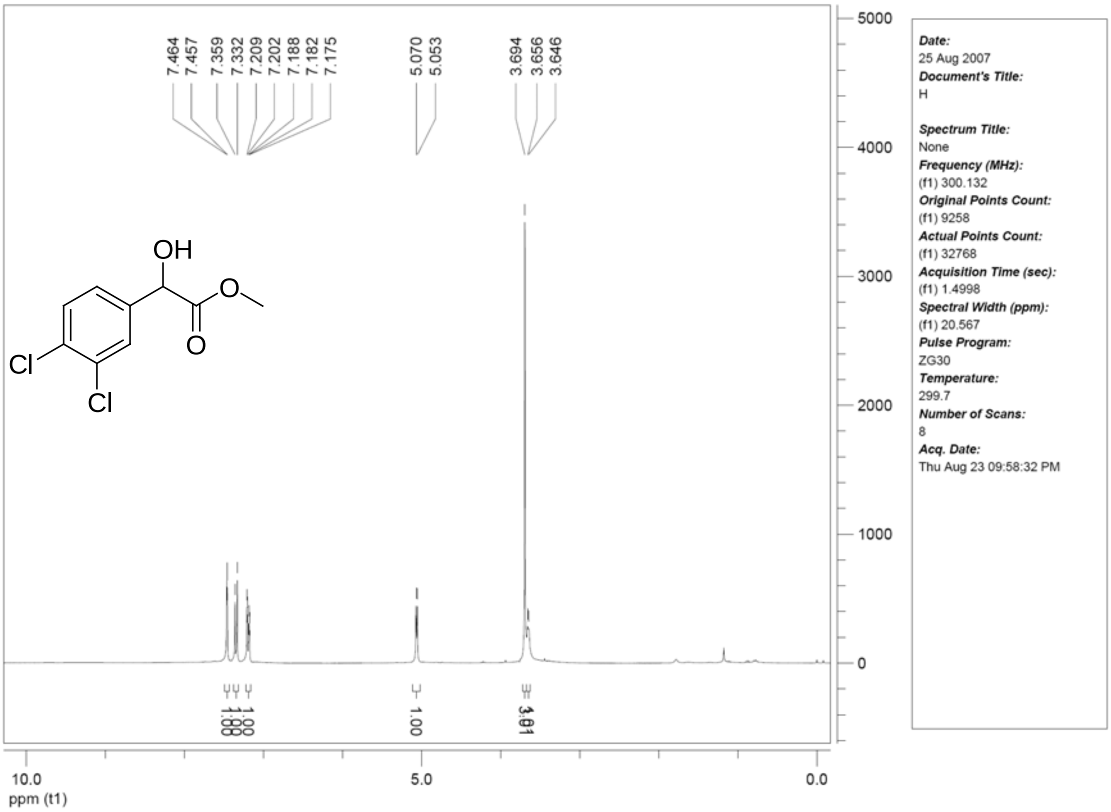


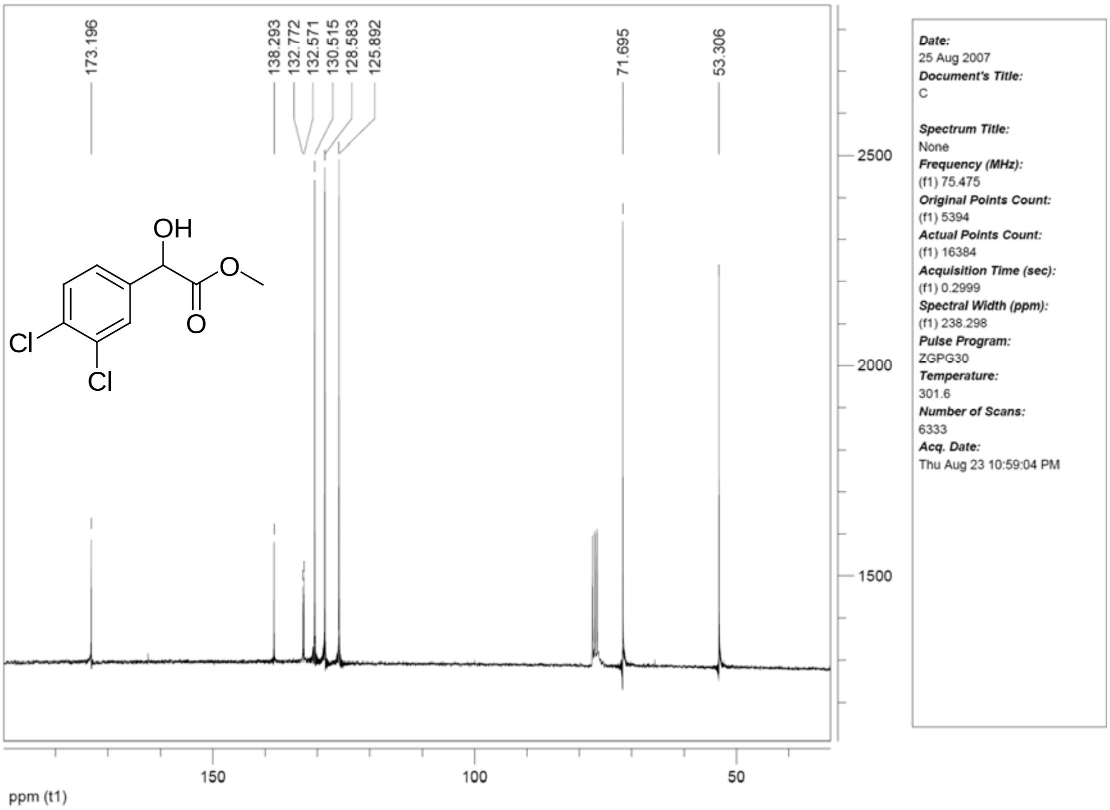
Methyl 2-(3-fluorophenyl)-2-hydroxyacetate (3k)



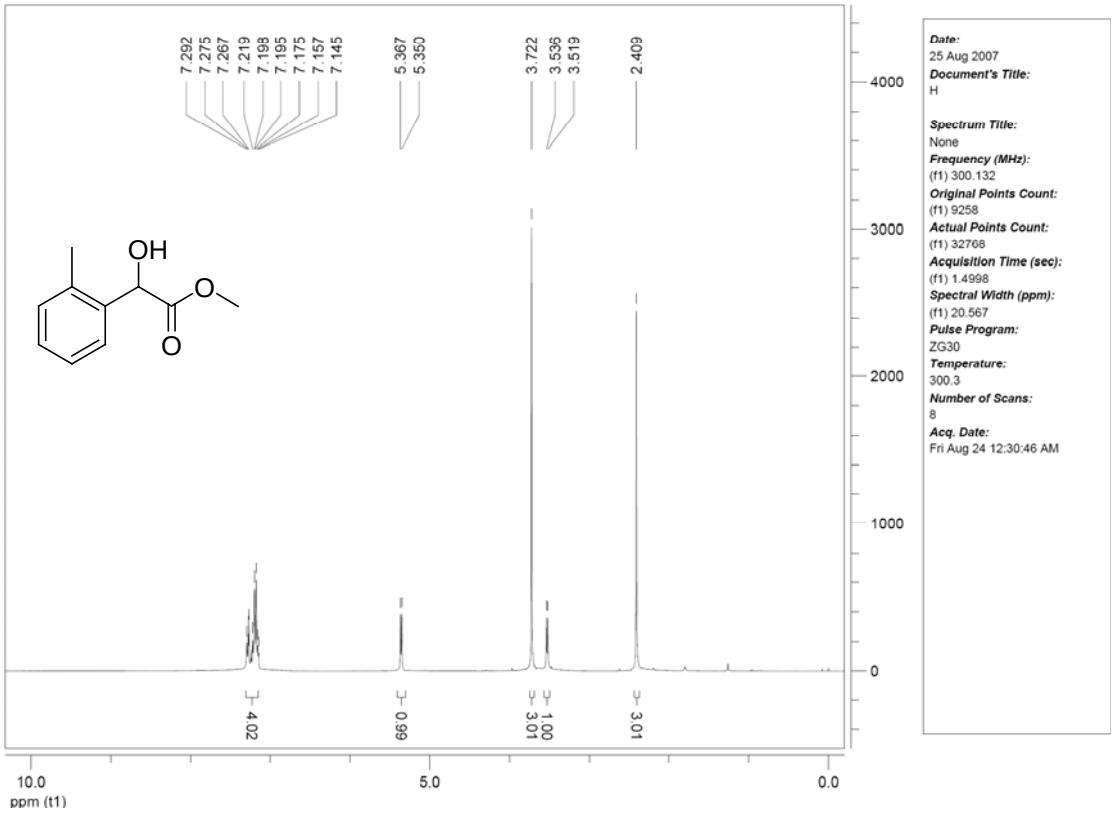


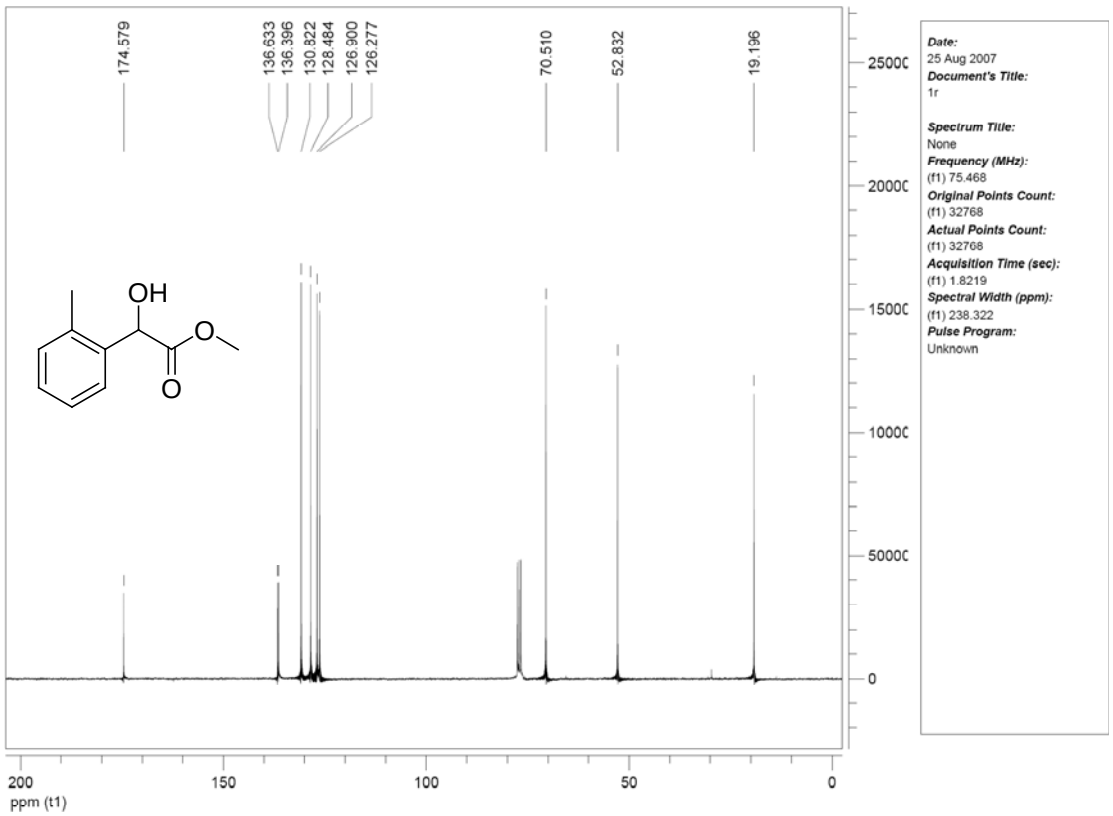
Methyl 2-(3,4-dichlorophenyl)-2-hydroxyacetate (3n)



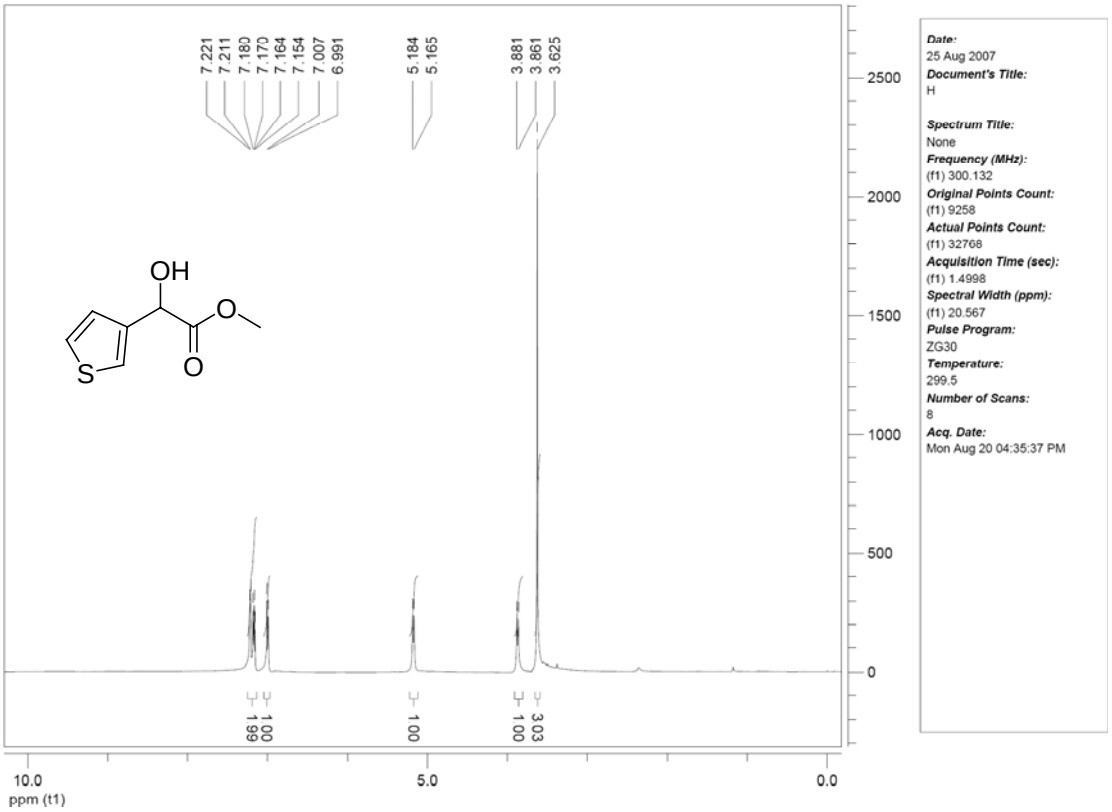


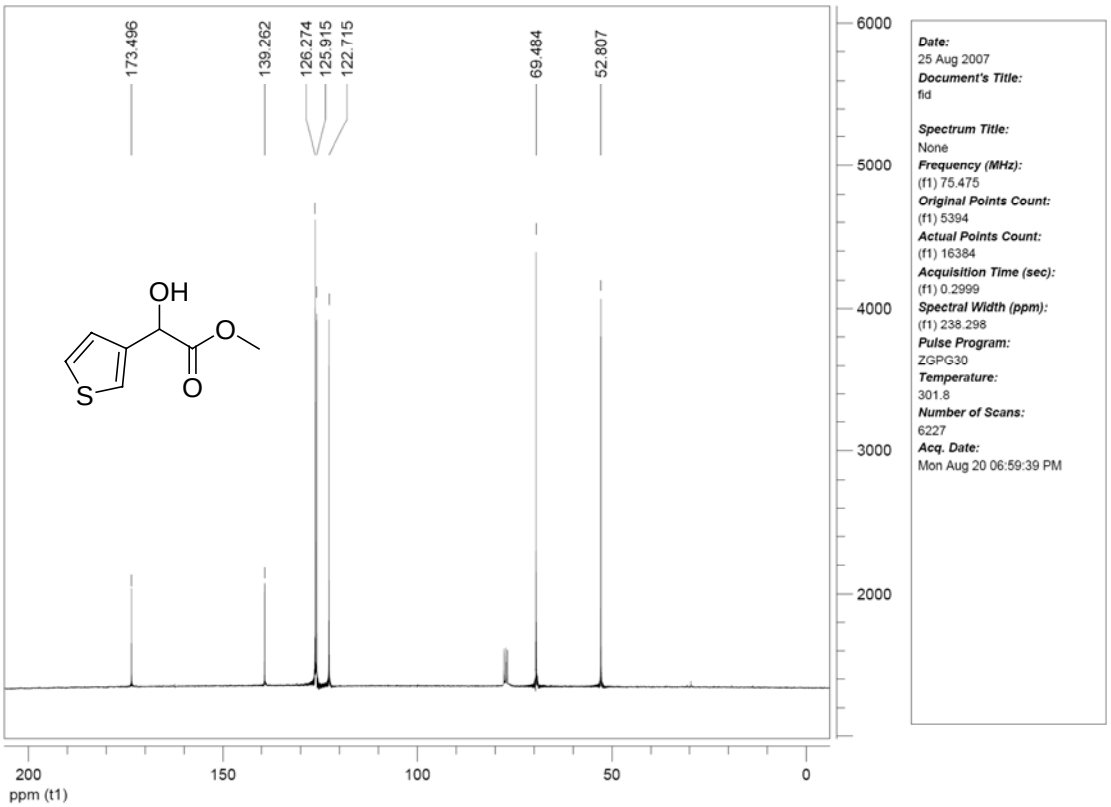
Methyl 2-hydroxy-2-*o*-tolylacetate (3o)





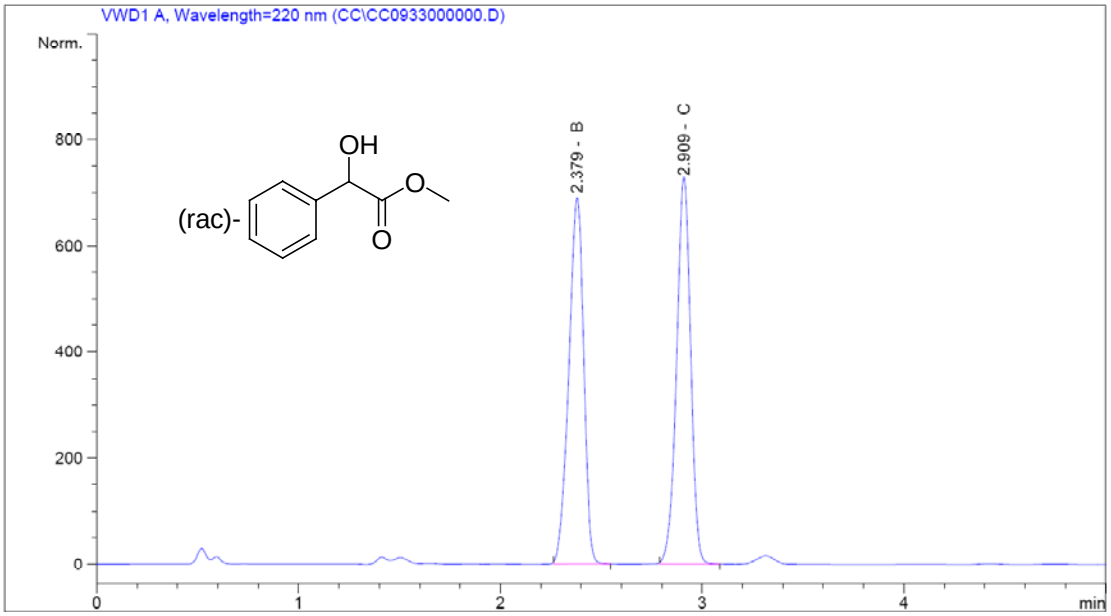
Methyl 2-hydroxy-2-thiophene-3-ylacetate (3s)

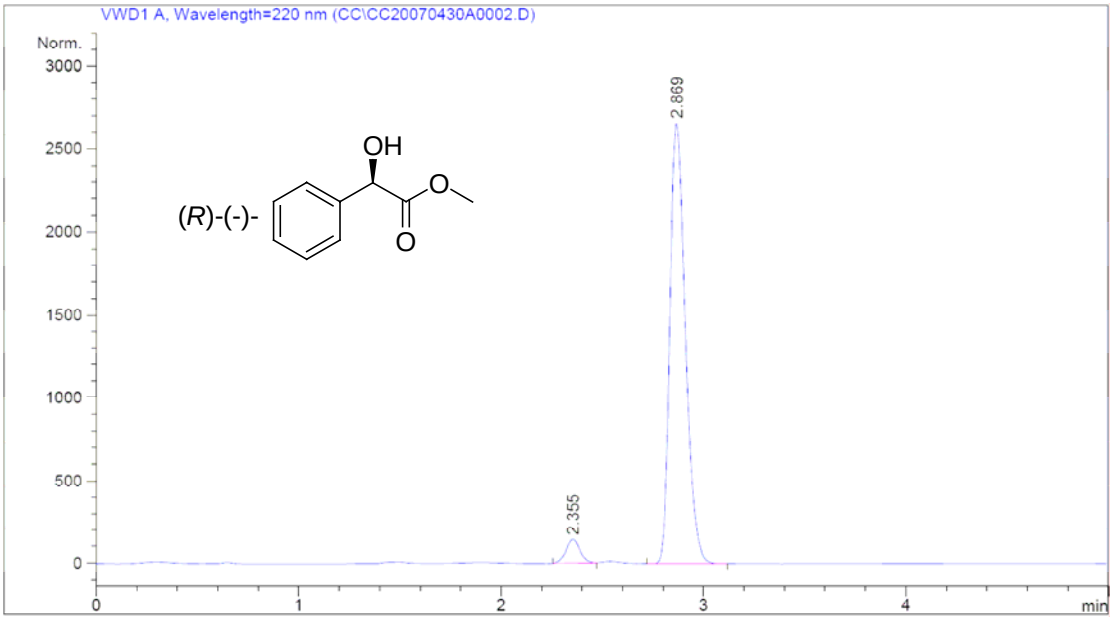




6. HPLC and SFC Charts for O–H Insertion Products

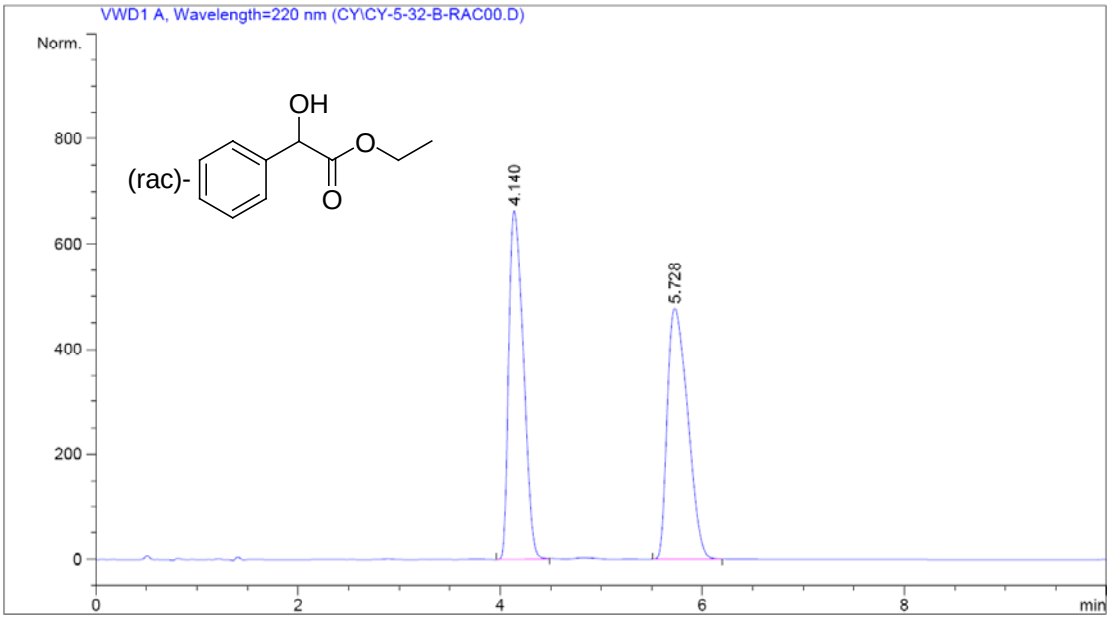
Methyl 2-hydroxy-2-phenylacetate (3a)

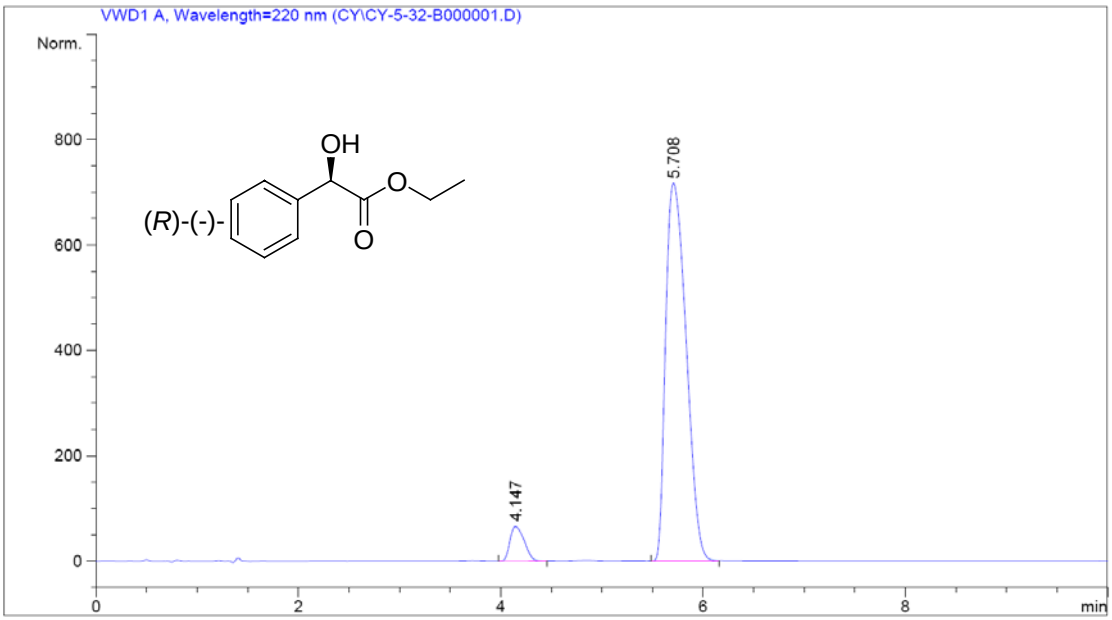




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	2.355	BV	0.0750	706.05042	4.7537	?
2	2.867	VB	0.0825	1.41465e4	95.2463	?
Uncalib. totals :				1.48525e4	100.0000	

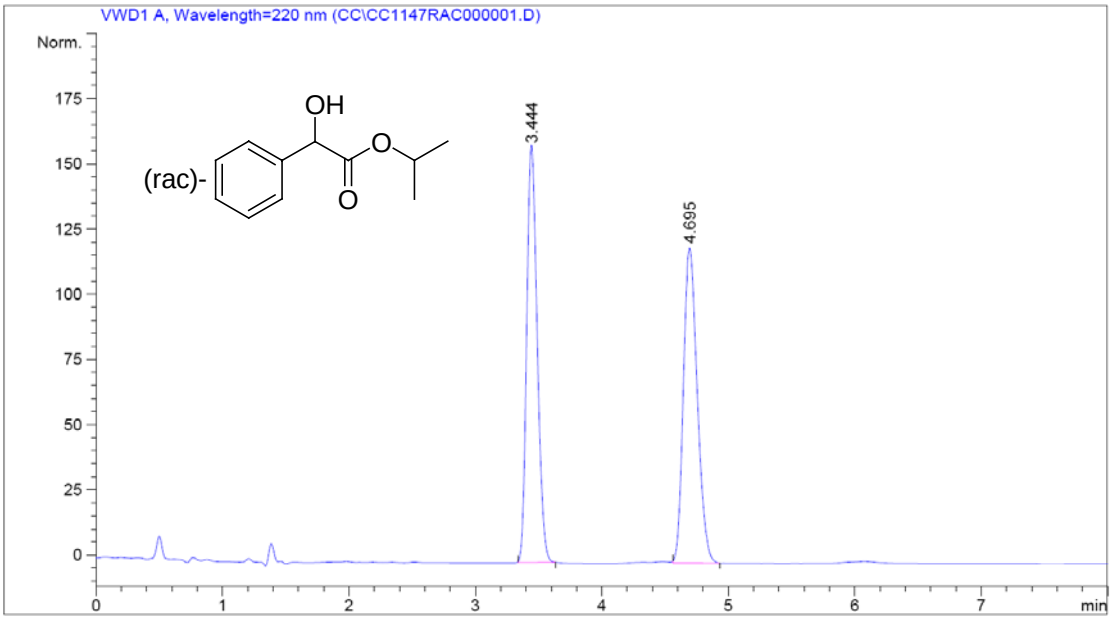
Ethyl 2-hydroxy-2-phenylacetate (3b)

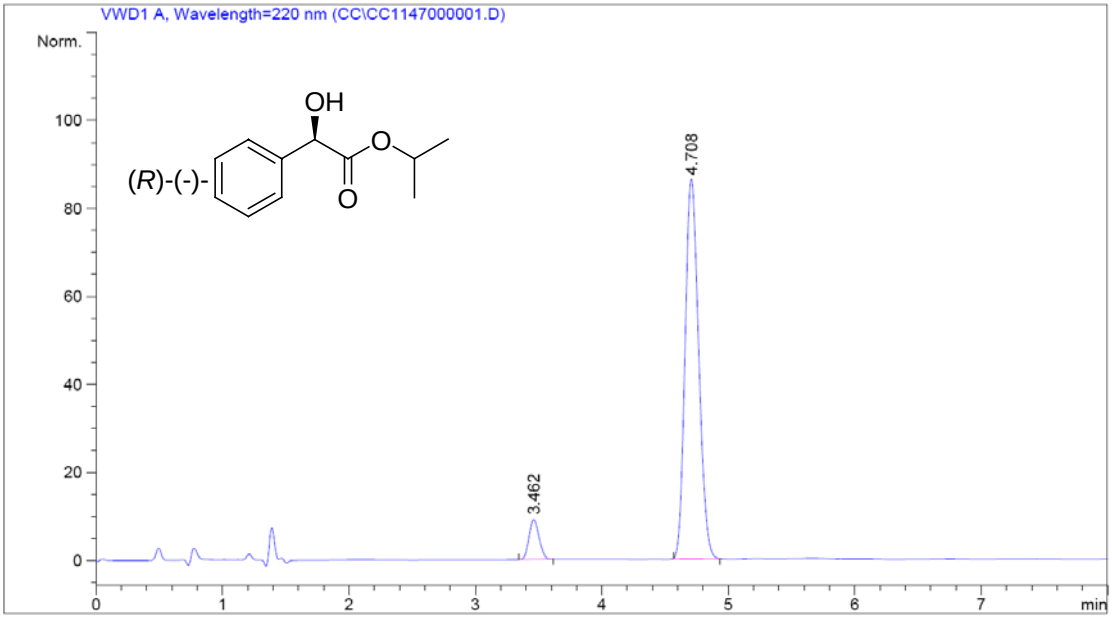




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	4.147	BB	0.1602	640.73077	5.9798	?
2	5.708	BB	0.2310	1.00742e4	94.0202	?
Uncalib. totals :				1.07149e4	100.0000	

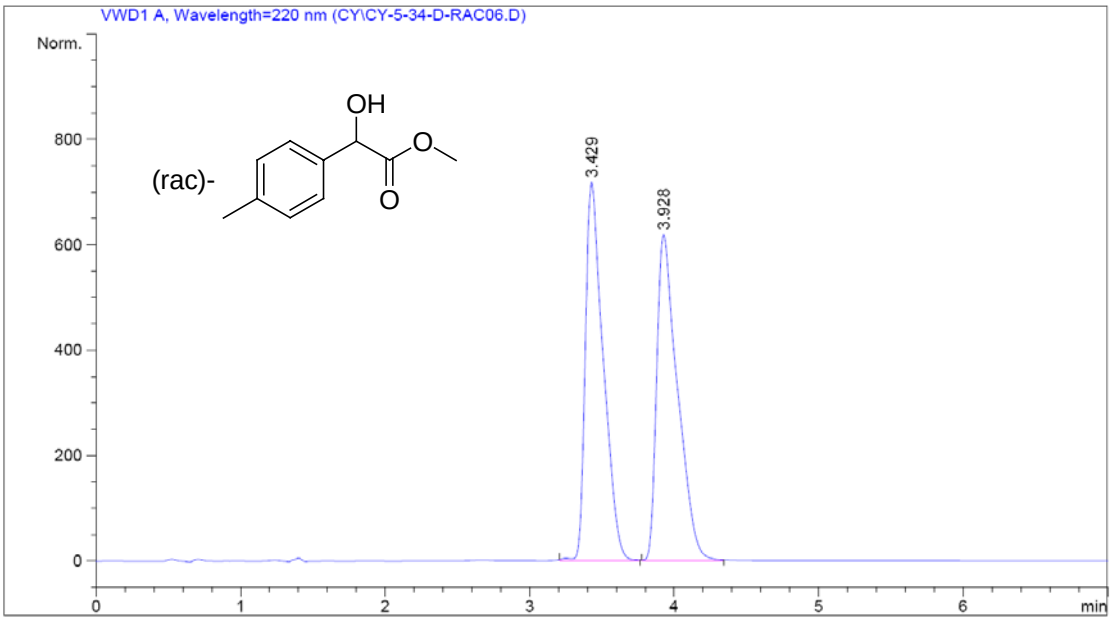
Isopropyl 2-hydroxy-2-phenylacetate (3c)

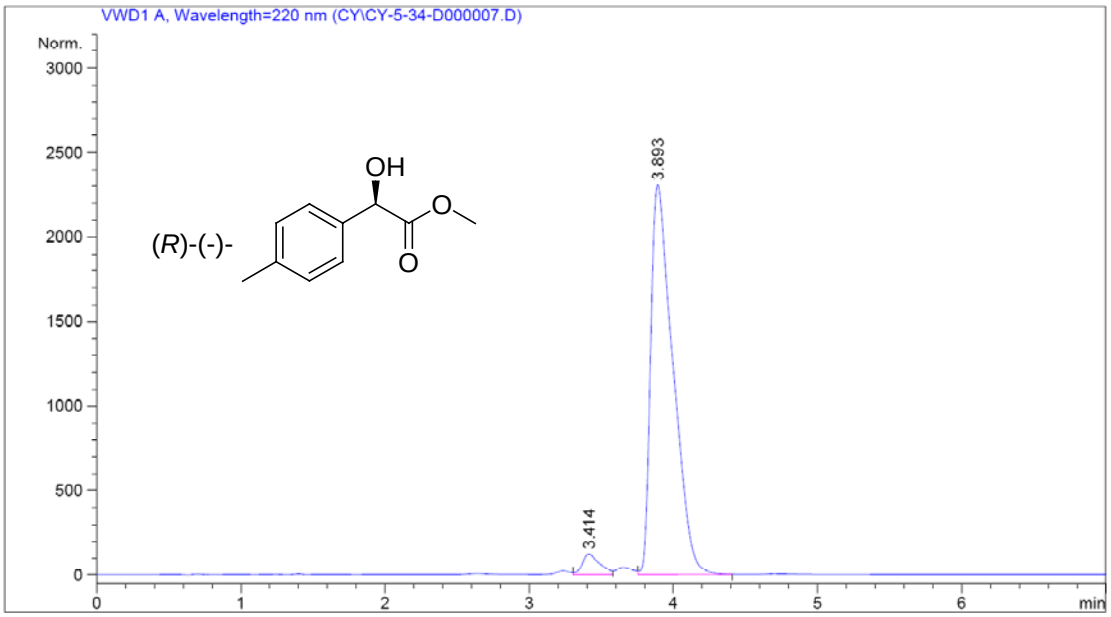




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.462	BB	0.0877	49.80808	7.1859	?
2	4.708	BB	0.1191	643.32587	92.8141	?
Uncalib. totals :				693.13395	100.0000	

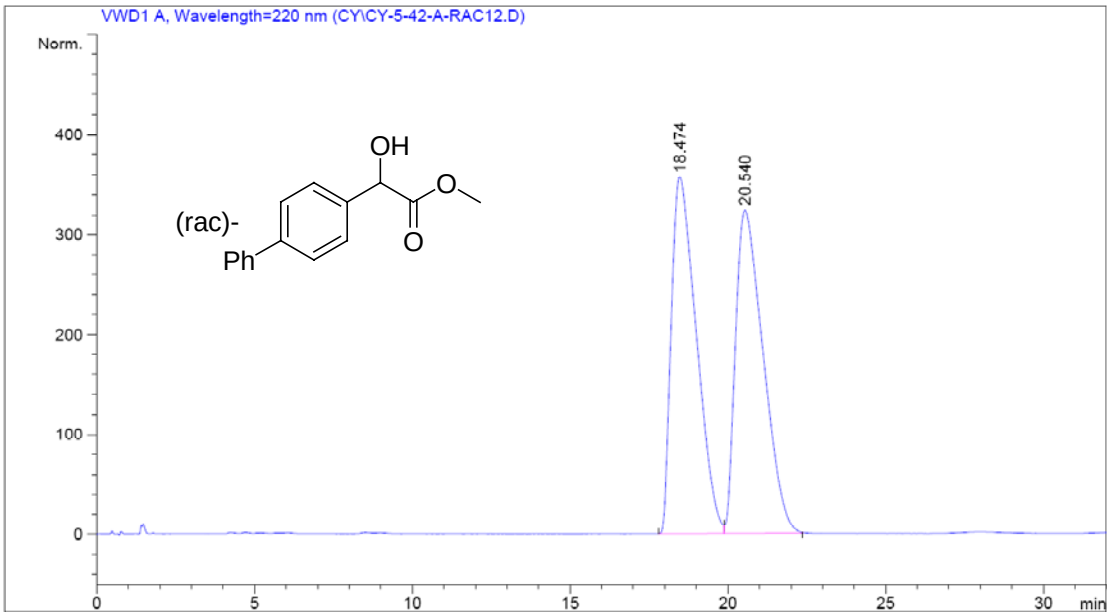
Methyl 2-hydroxy-2-*p*-tolylacetate (3d)

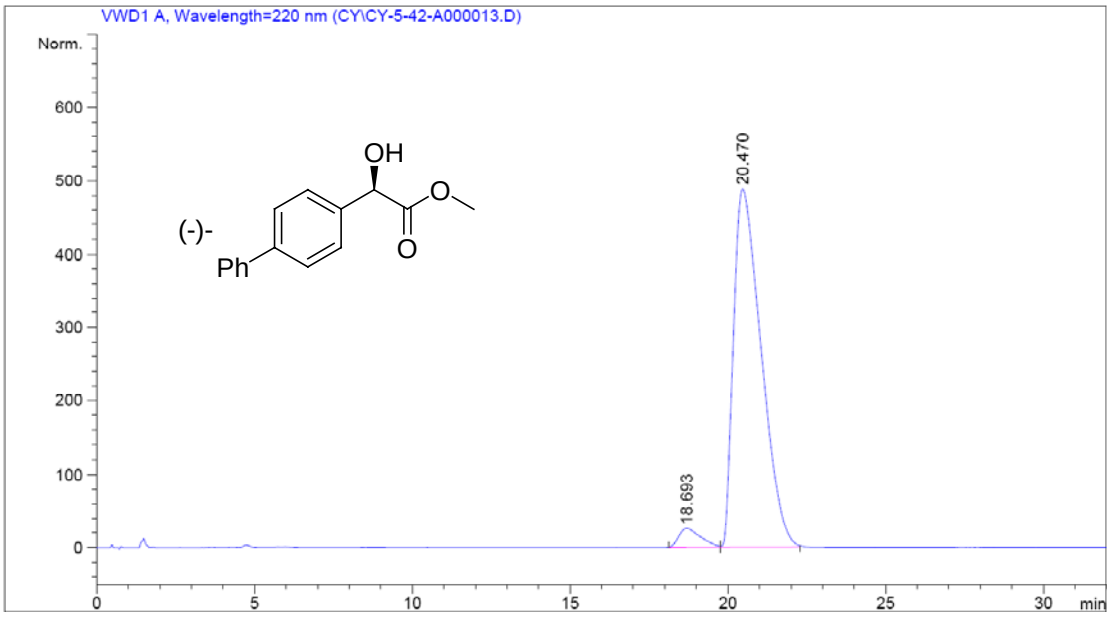




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.414	VV	0.1226	1062.66467	4.1174	?
2	3.893	VB	0.1556	2.47464e4	95.8826	?
Uncalib. totals :				2.58090e4	100.0000	

Mehtyl 2-hydroxy-2-biphenylacetate (3e)

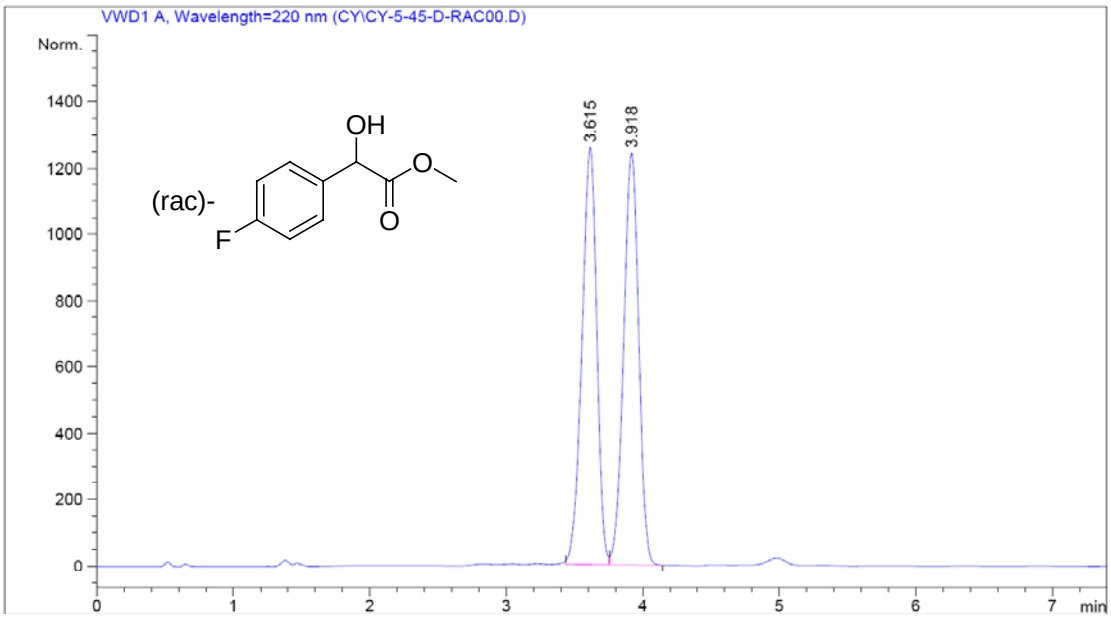


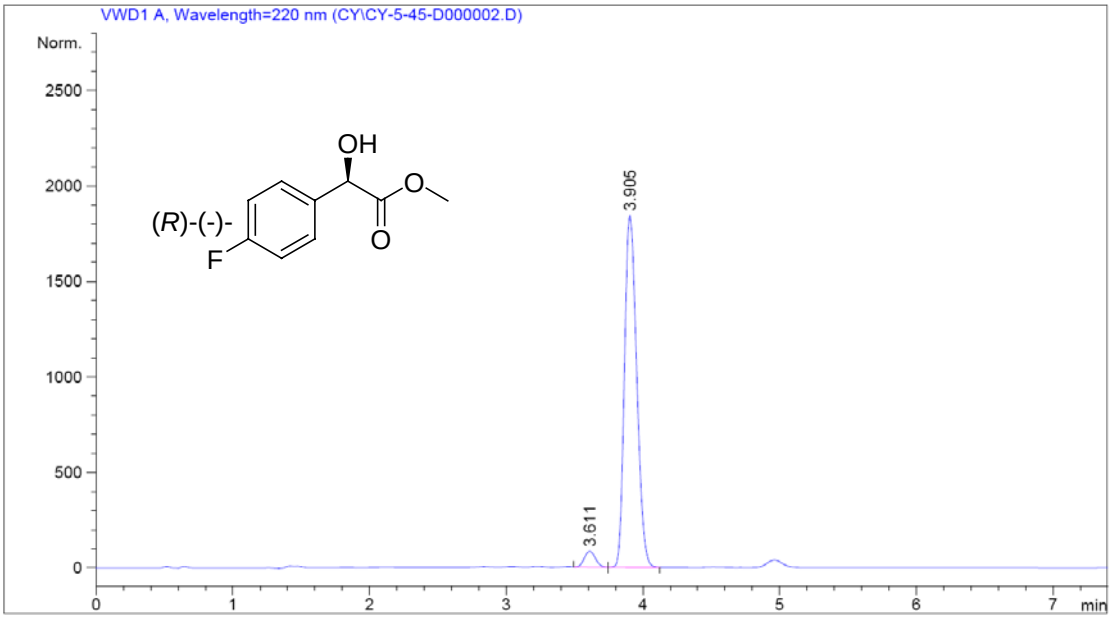


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	18.693	BV	0.6932	1212.89990	3.9385	?
2	20.470	VB	0.8907	2.95829e4	96.0615	?

Uncalib. totals : 3.07958e4 100.0000

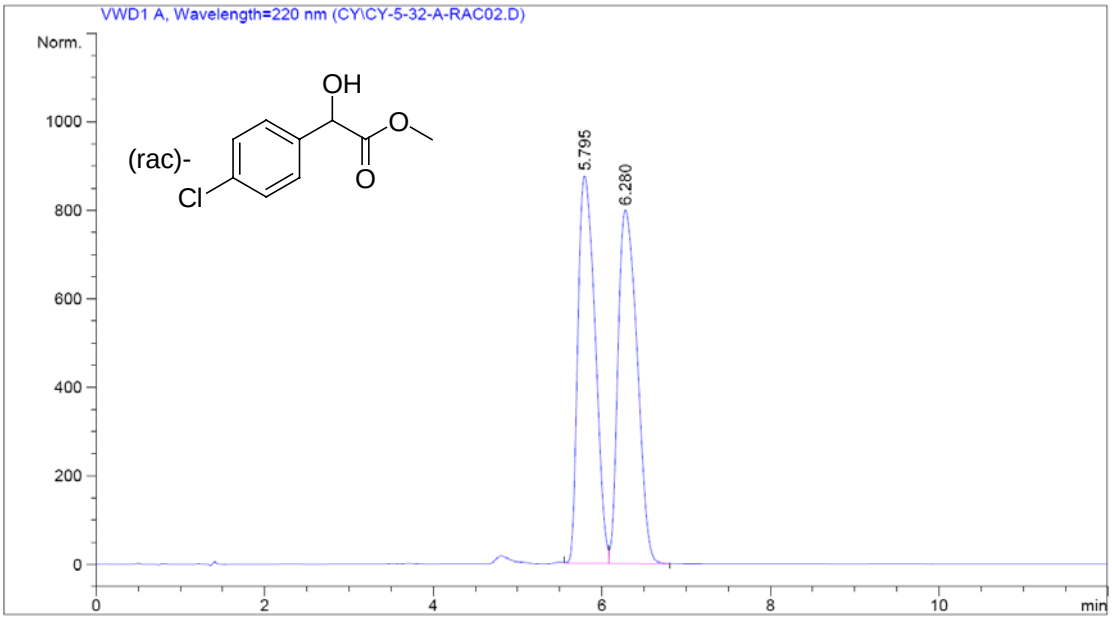
Methyl 2-(4-fluorophenyl)-2-hydroxyacetate (3f)

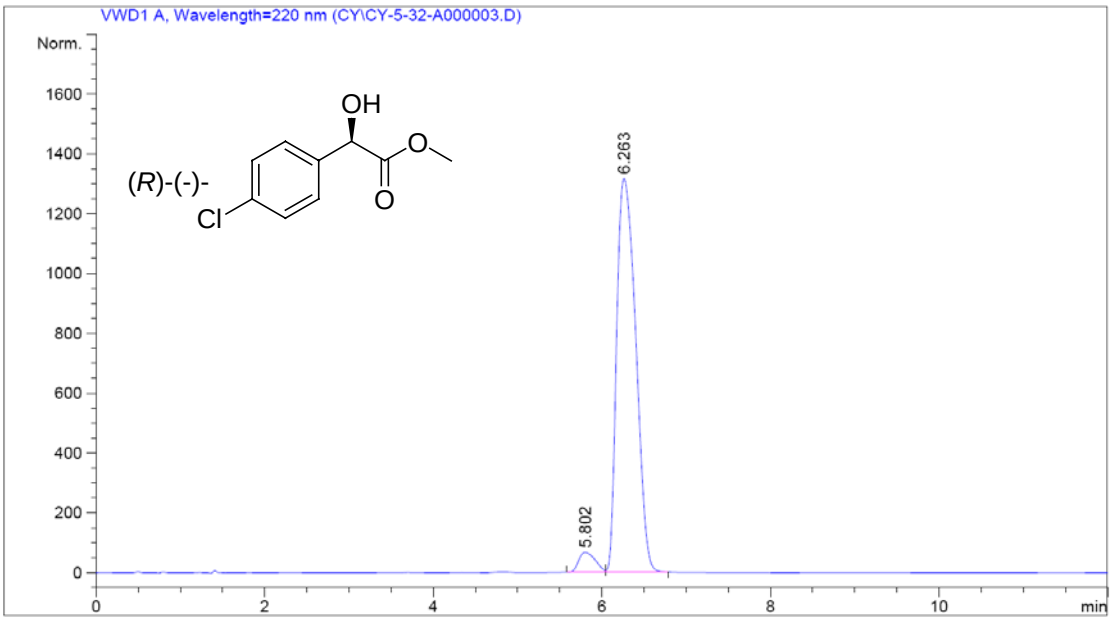




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.611	BV	0.0907	473.03259	3.9603	?
2	3.905	VB	0.0974	1.14712e4	96.0397	?
Uncalib. totals :				1.19443e4	100.0000	

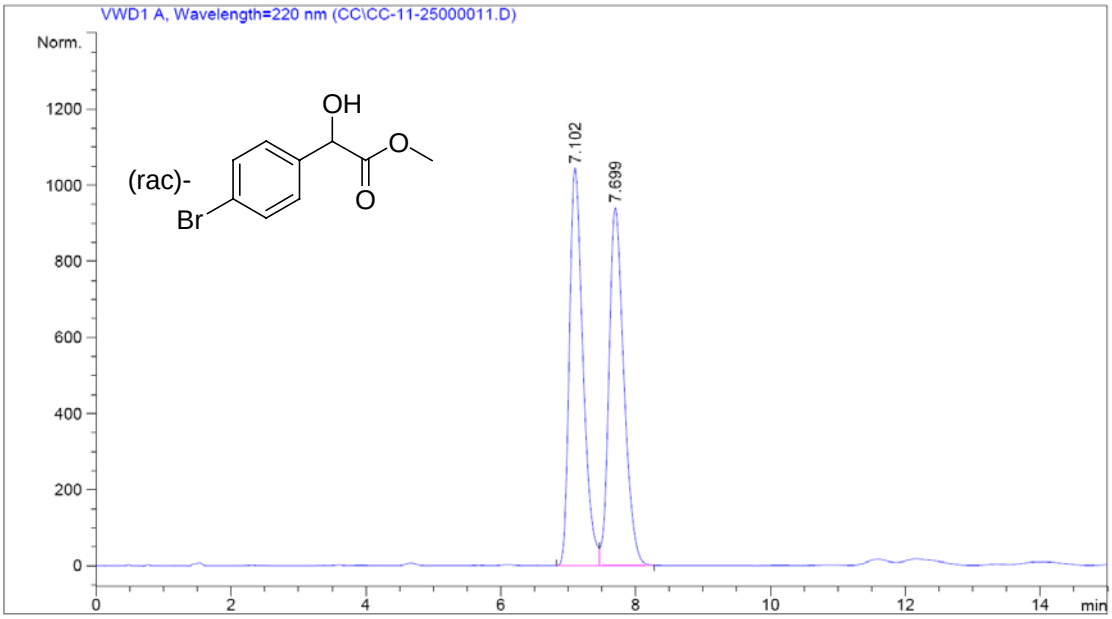
Methyl 2-(4-chlorophenyl)-2-hydroxyacetate (3g)

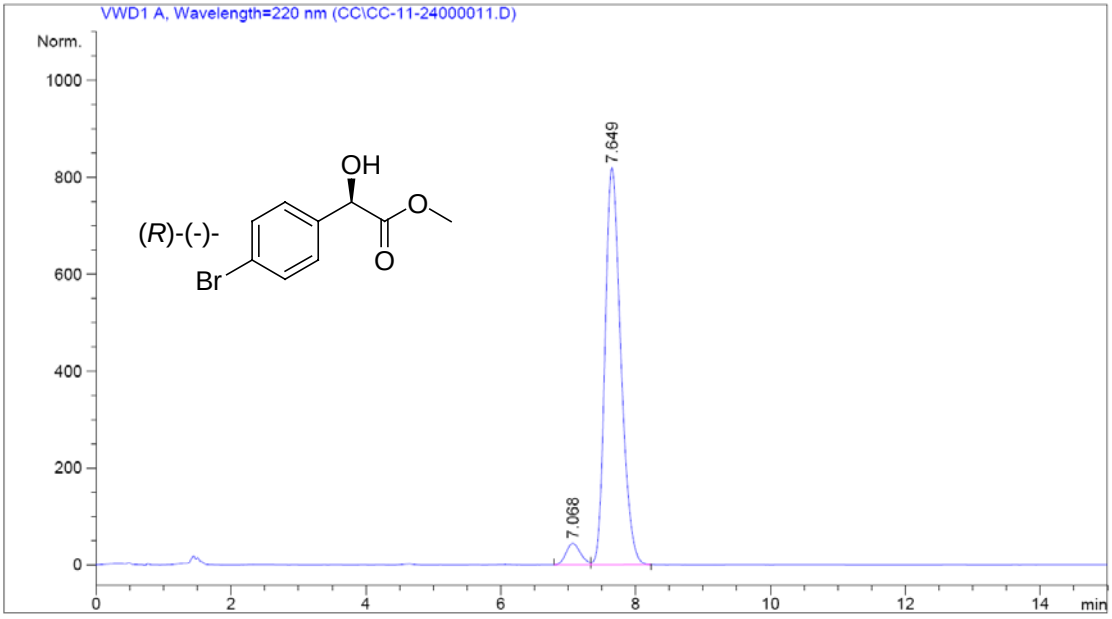




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	5.802	BV	0.2306	900.09546	4.1837	?
2	6.263	VB	0.2613	2.06141e4	95.8163	?
Uncalib. totals :				2.15142e4	100.0000	

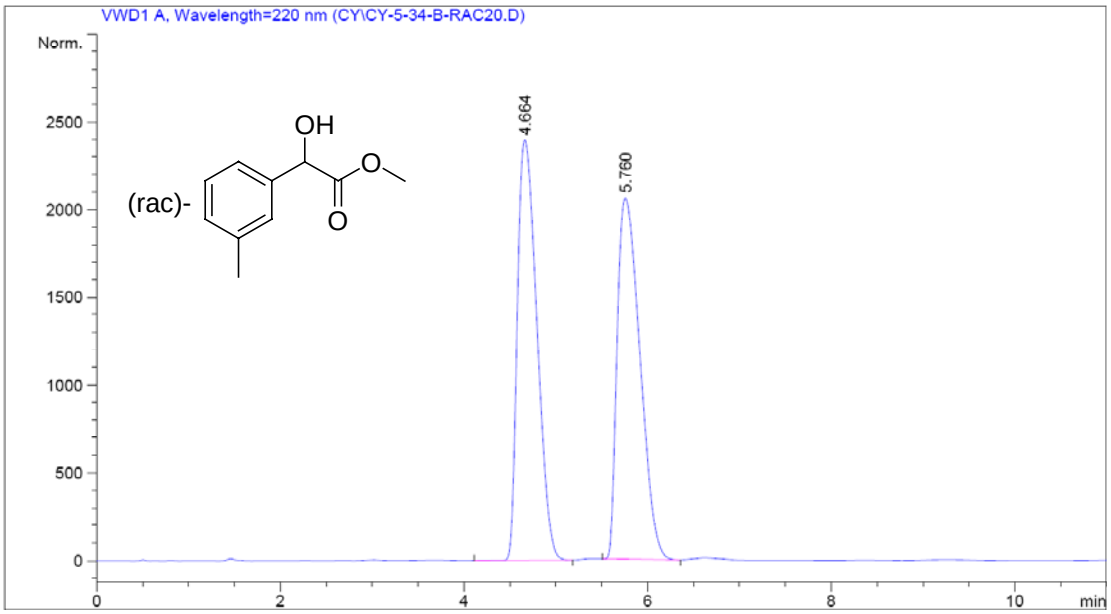
Methyl 2-(4-bromophenyl)-2-hydroxyacetate (3h)

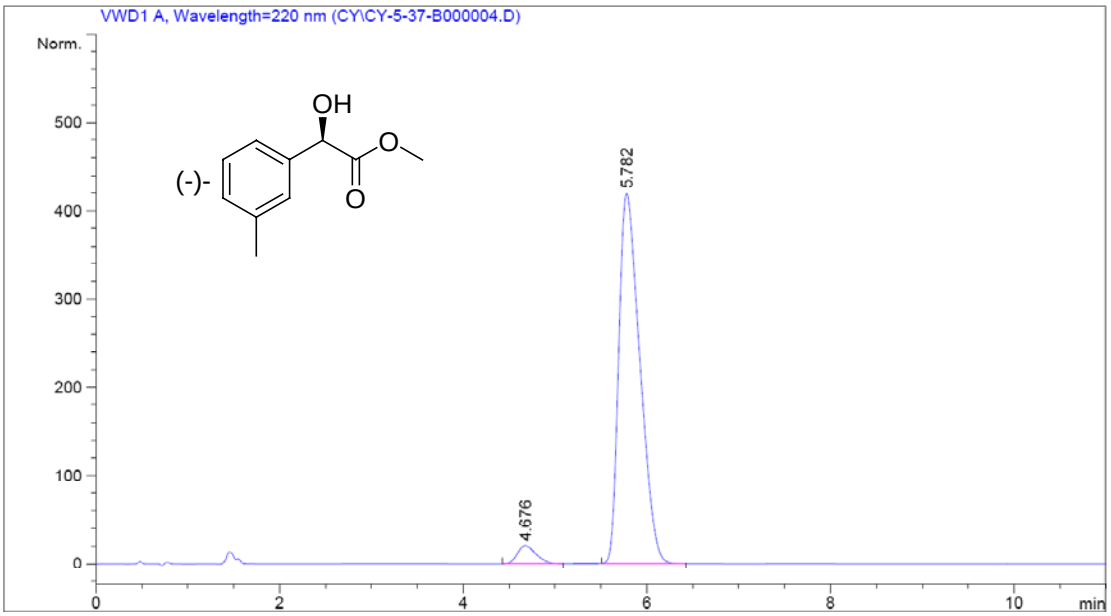




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	7.068	BV	0.2304	657.94080	4.7047	?
2	7.649	VB	0.2495	1.33267e4	95.2953	?
Uncalib. totals :				1.39846e4	100.0000	

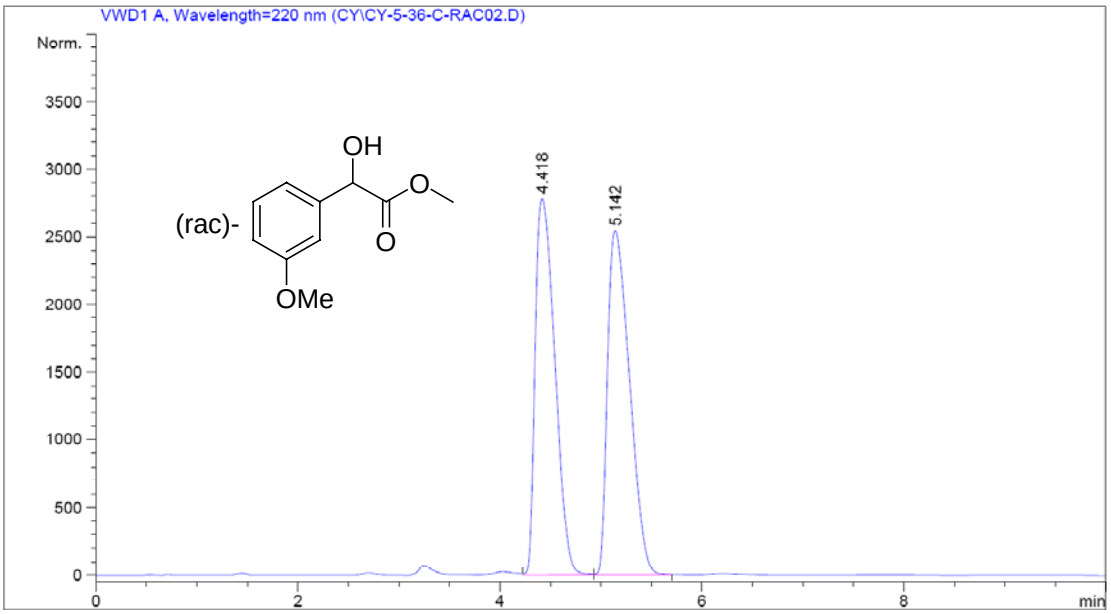
Methyl 2-hydroxy-2-*m*-tolylacetate (3i)

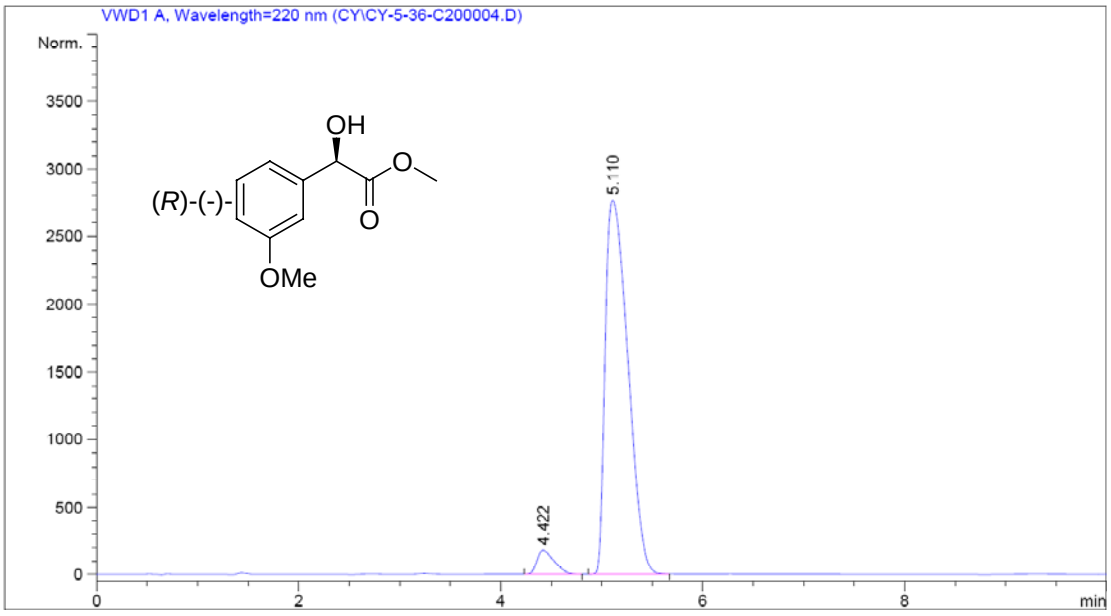




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	4.676	BB	0.2146	281.81863	4.0539	?
2	5.782	BB	0.2438	6669.95361	95.9461	?
Uncalib. totals :				6951.77225	100.0000	

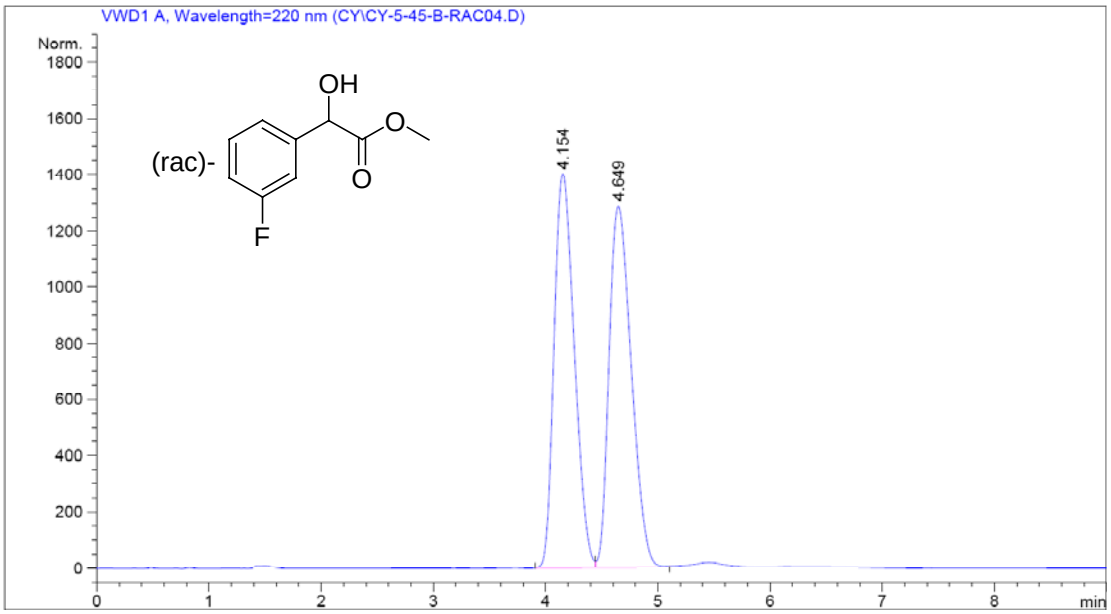
Methyl 2-hydroxy-2-(3-methoxyphenyl)acetate (3j)

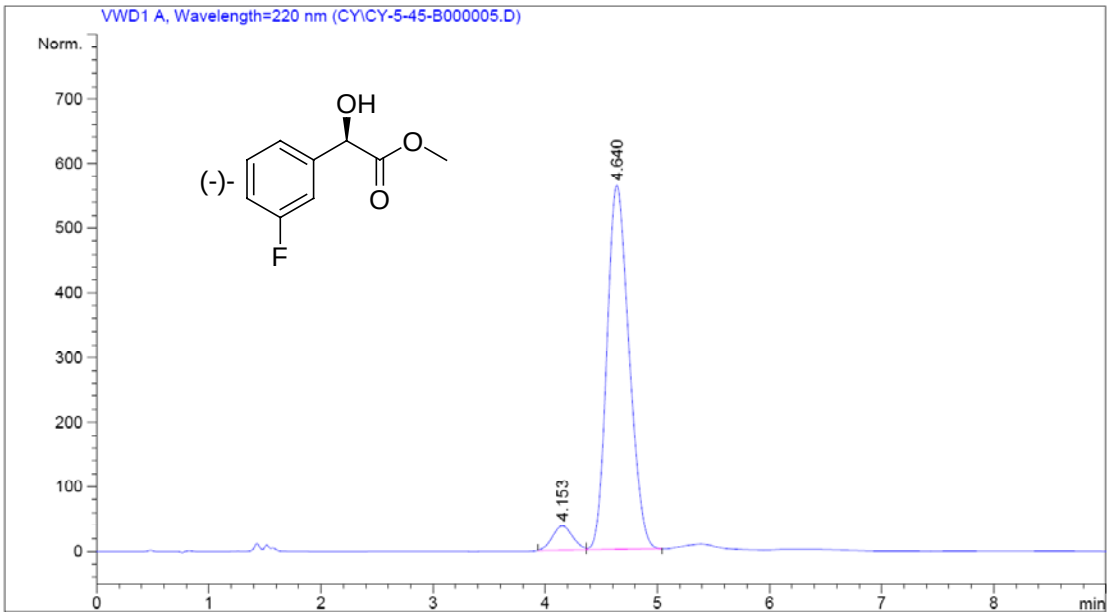




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	4.422	BB	0.1739	2121.41138	4.7026	?
2	5.110	BB	0.2540	4.29896e4	95.2974	?
Uncalib. totals :				4.51110e4	100.0000	

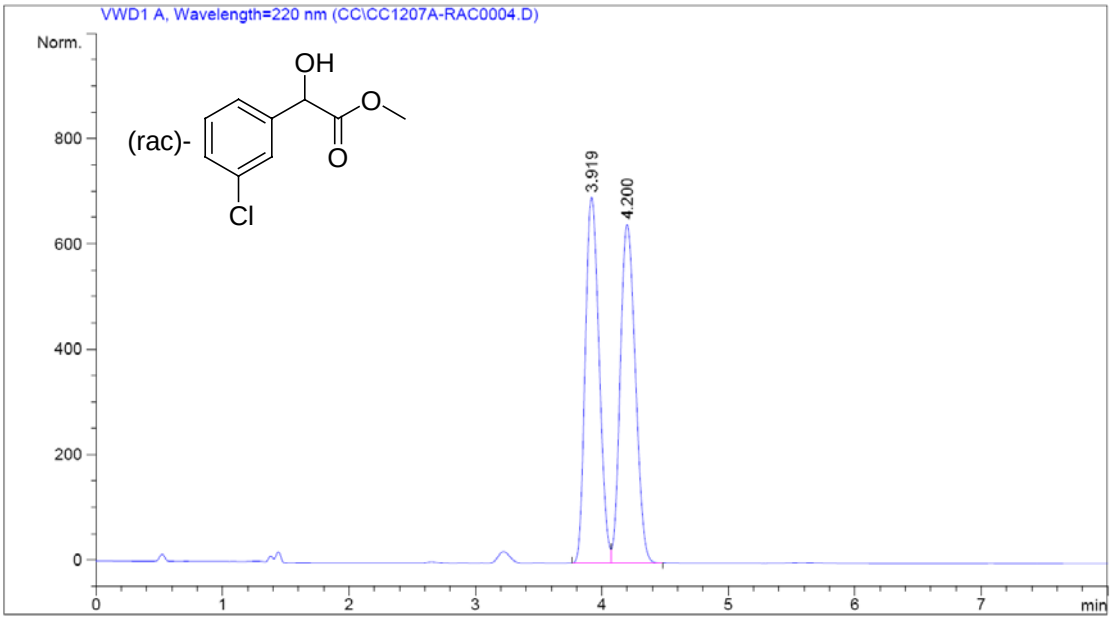
Methyl 2-(3-fluorophenyl)-2-hydroxyacetate (3k)

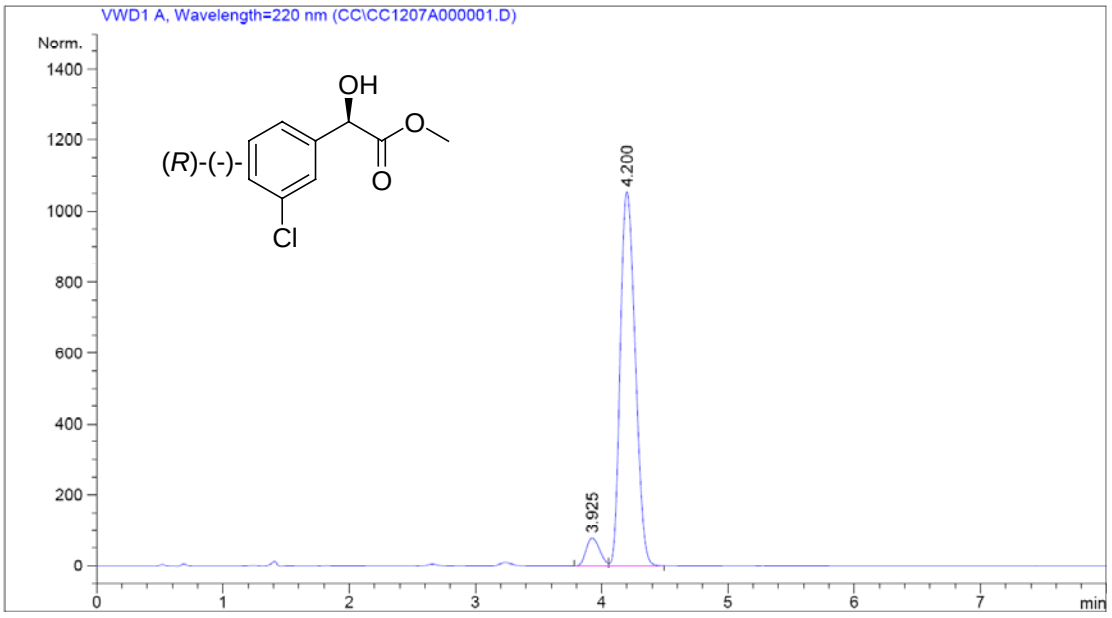




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	4.153	BV	0.1940	467.53360	5.7116	?
2	4.640	VB	0.2124	7718.12891	94.2884	?
Uncalib. totals :				8185.66251	100.0000	

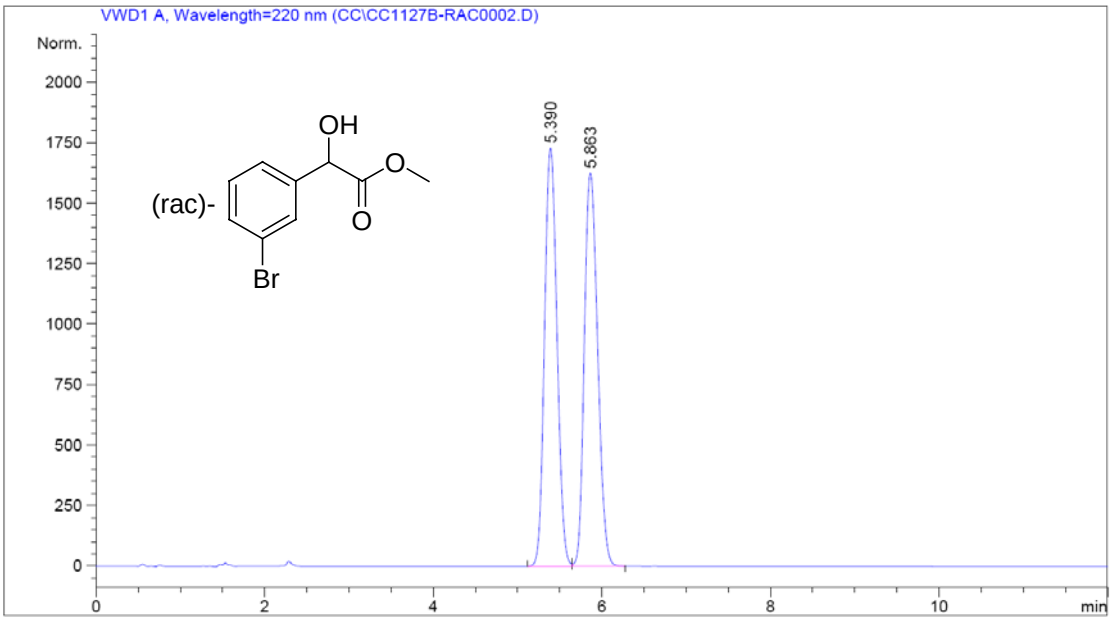
(–)-Methyl 2-(3-chlorophenyl)-2-hydroxyacetate (3l)

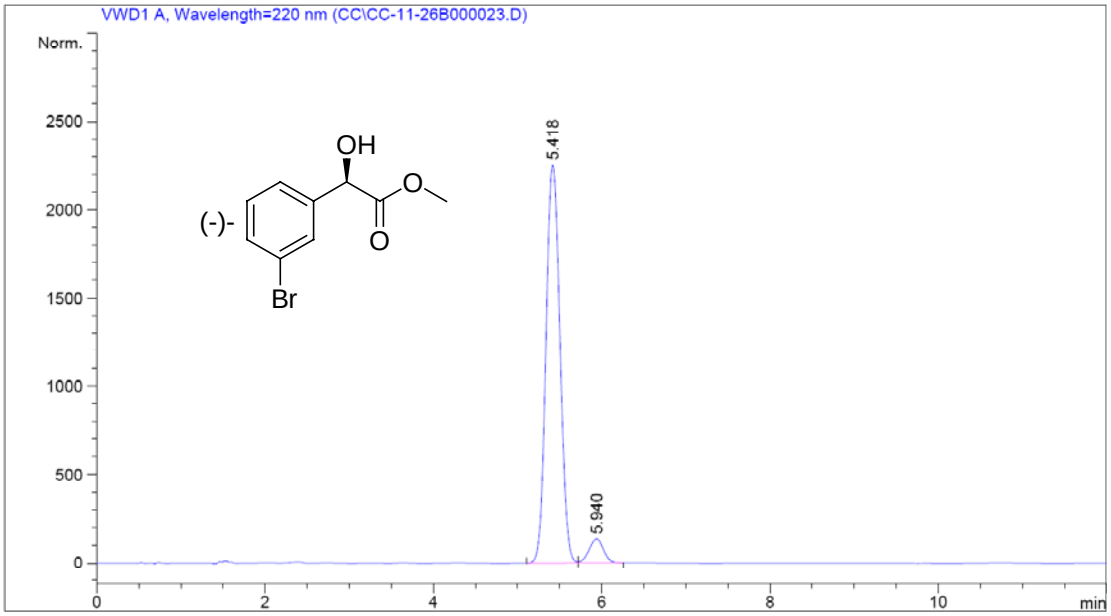




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.925	BV	0.1186	576.97192	6.2340	?
2	4.200	VB	0.1323	8678.22070	93.7660	?
Uncalib. totals :				9255.19263	100.0000	

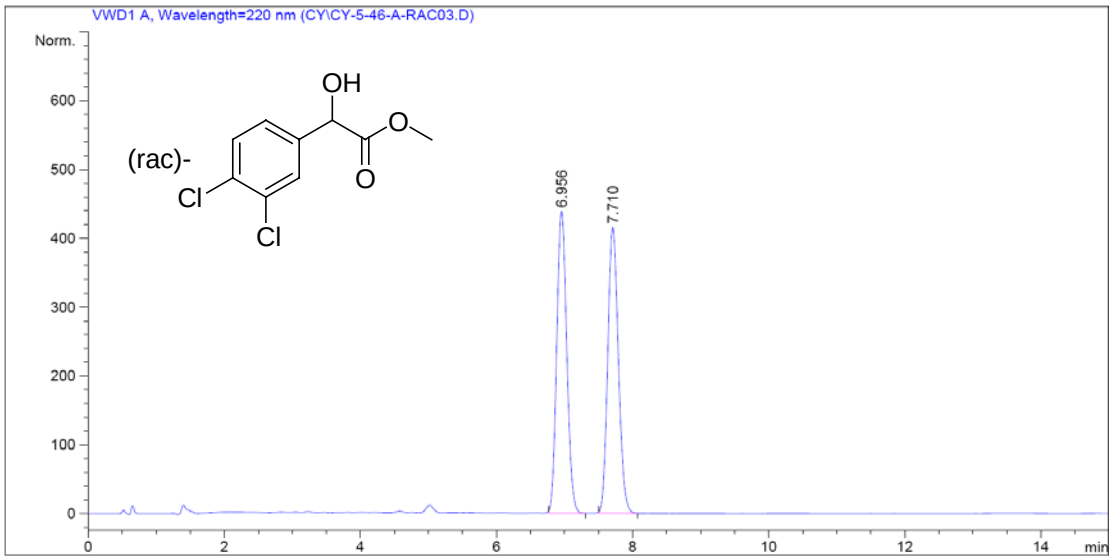
Methyl 2-(3-bromophenyl)-2-hydroxyacetate (3m)

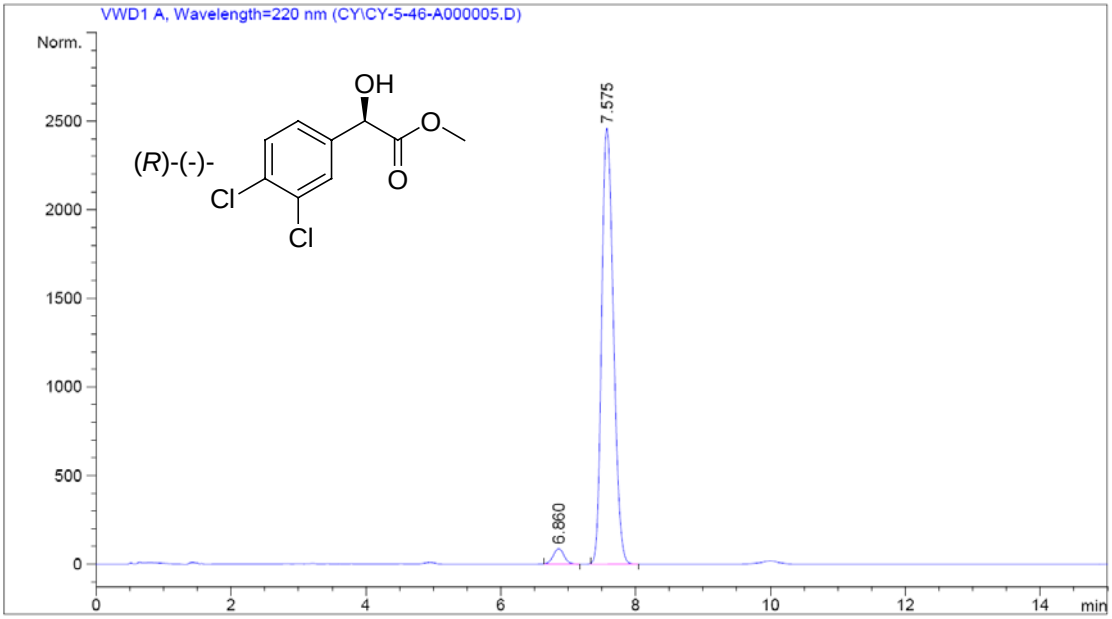




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	5.418	BV	0.1819	2.58546e4	94.1936	?
2	5.940	VB	0.1838	1593.75732	5.8064	?
Uncalib. totals :				2.74483e4	100.0000	

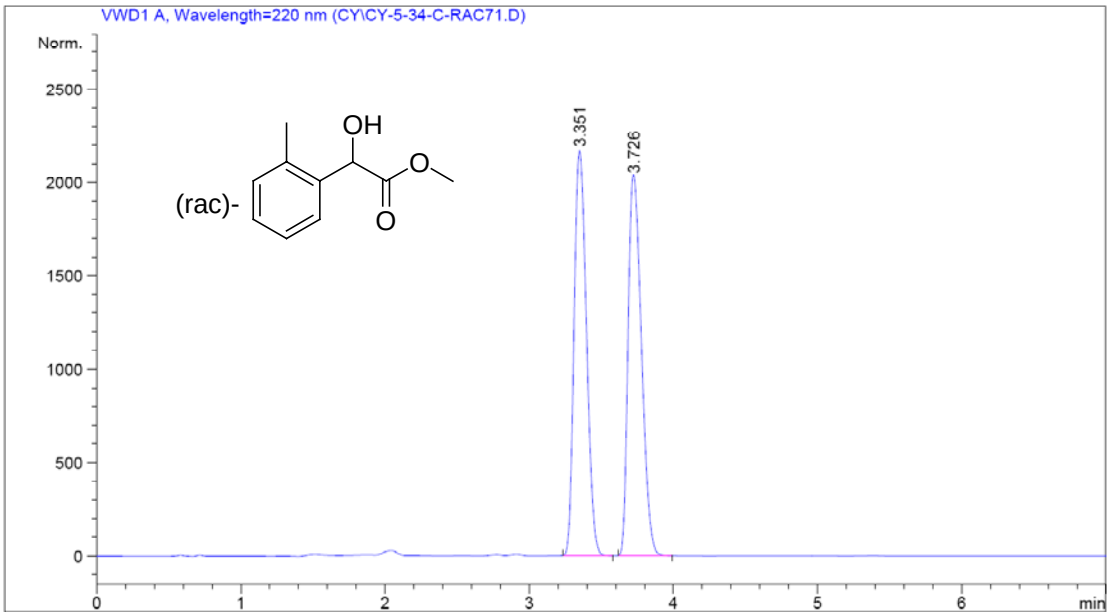
Methyl 2-(3,4-dichlorophenyl)-2-hydroxyacetate (3n)

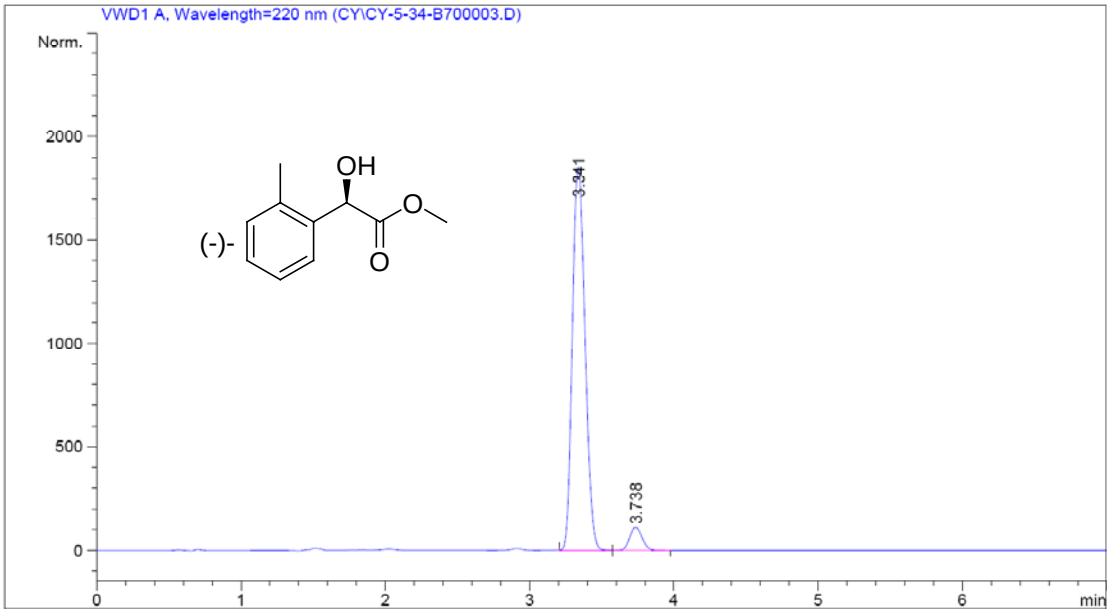




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	6.860	BB	0.1785	975.15881	3.1712	?
2	7.575	BB	0.1937	2.97758e4	96.8288	?
Uncalib. totals :				3.07509e4	100.0000	

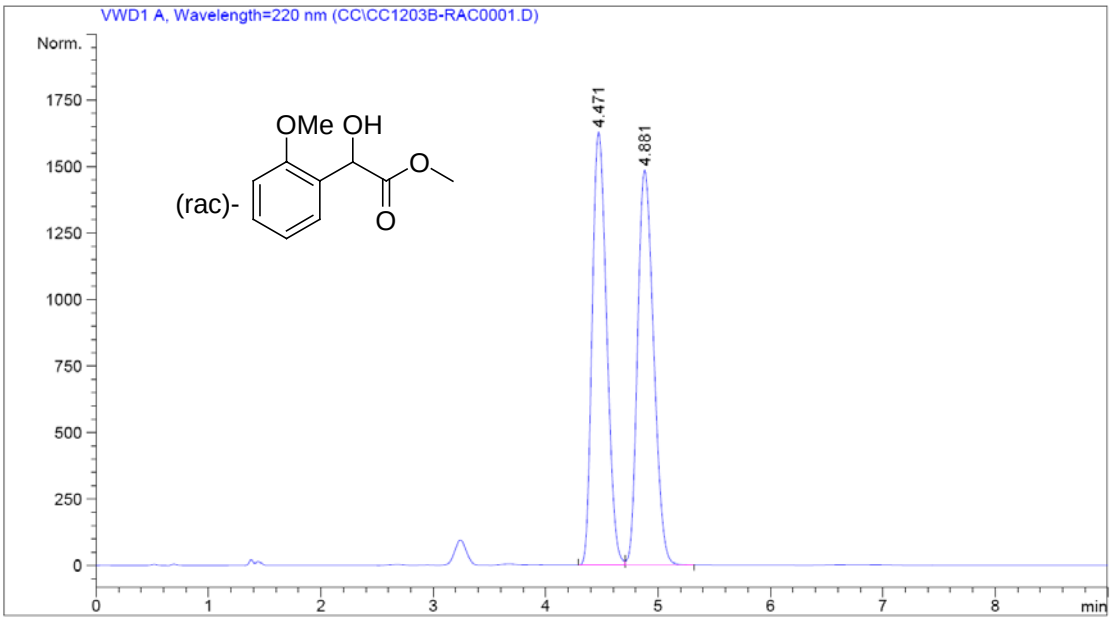
Methyl 2-hydroxy-2-*o*-tolylacetate (3o)

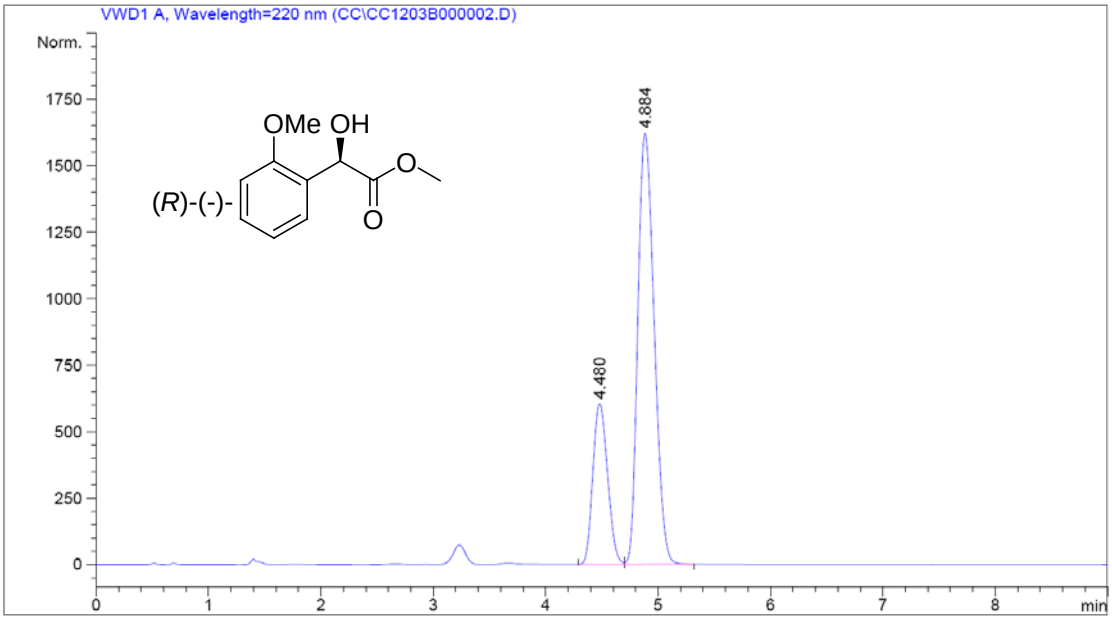




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.341	BB	0.1015	1.12703e4	94.5132	?
2	3.738	BB	0.1080	654.27826	5.4868	?
Uncalib. totals :				1.19246e4	100.0000	

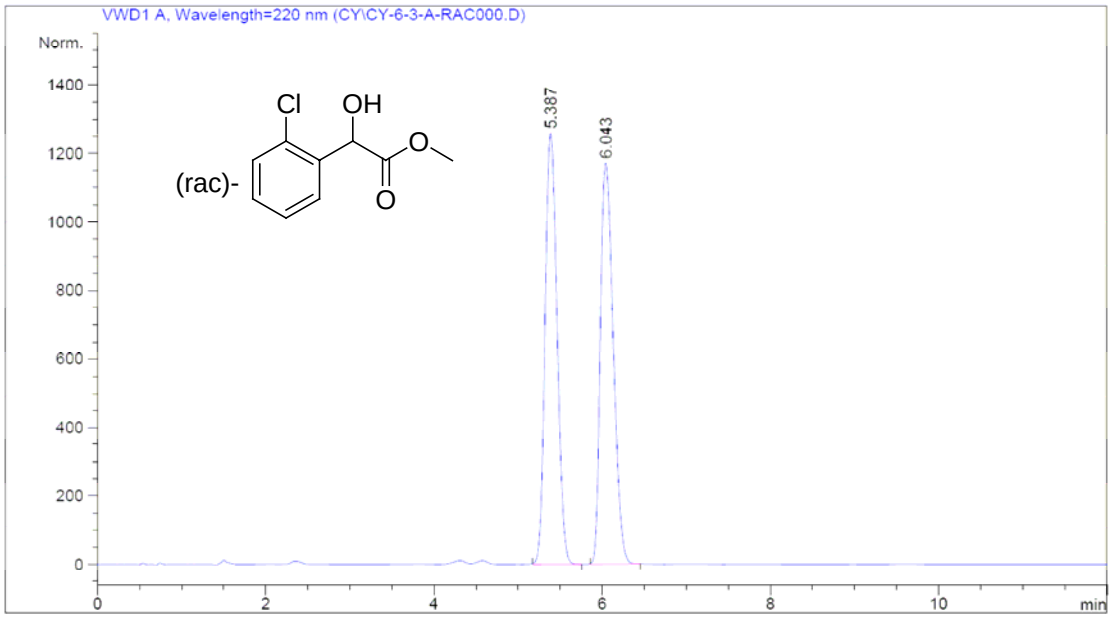
Methyl 2-hydroxy-2-(2-methoxyphenyl)acetate (3p)

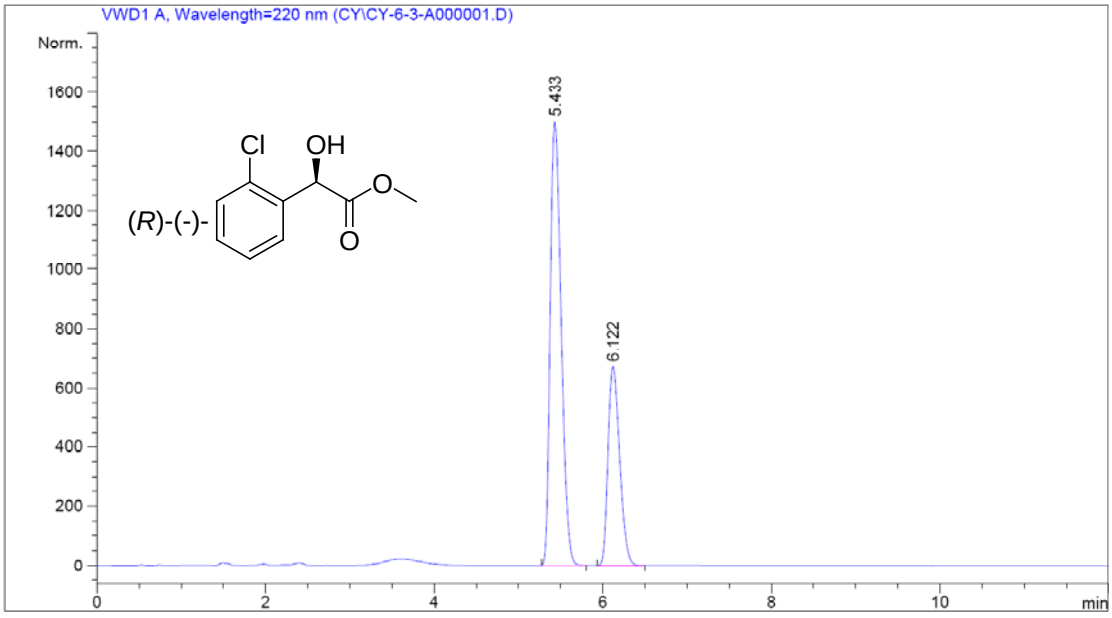




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	4.480	BV	0.1441	5507.33936	25.1827	?
2	4.884	VB	0.1600	1.63622e4	74.8173	?
Uncalib. totals :				2.18695e4	100.0000	

Methyl 2-(2-chlorophenyl)-2-hydroxyacetate (3q)



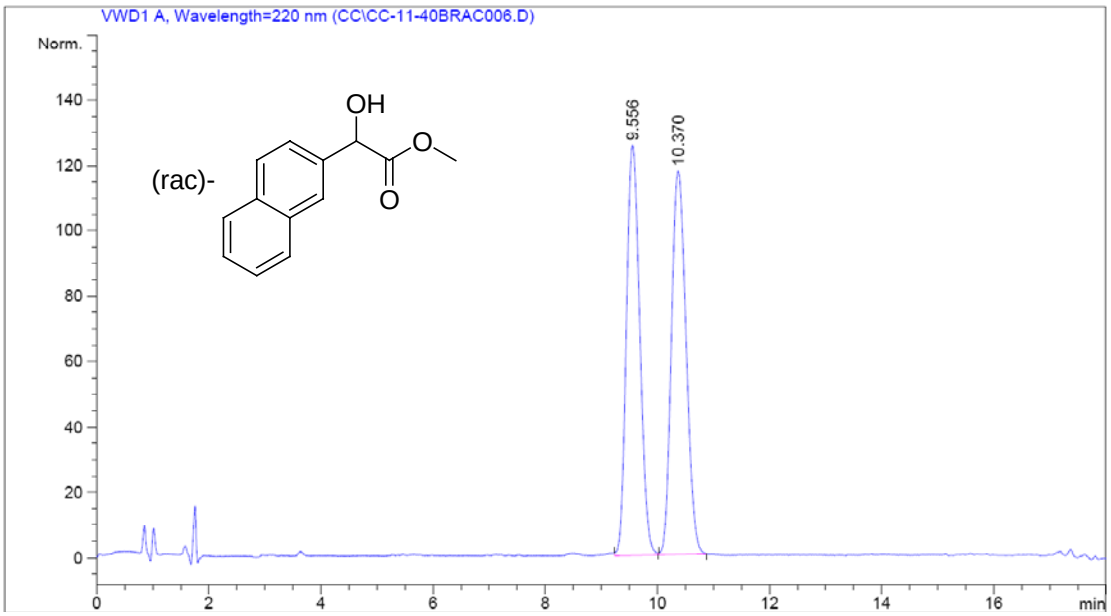


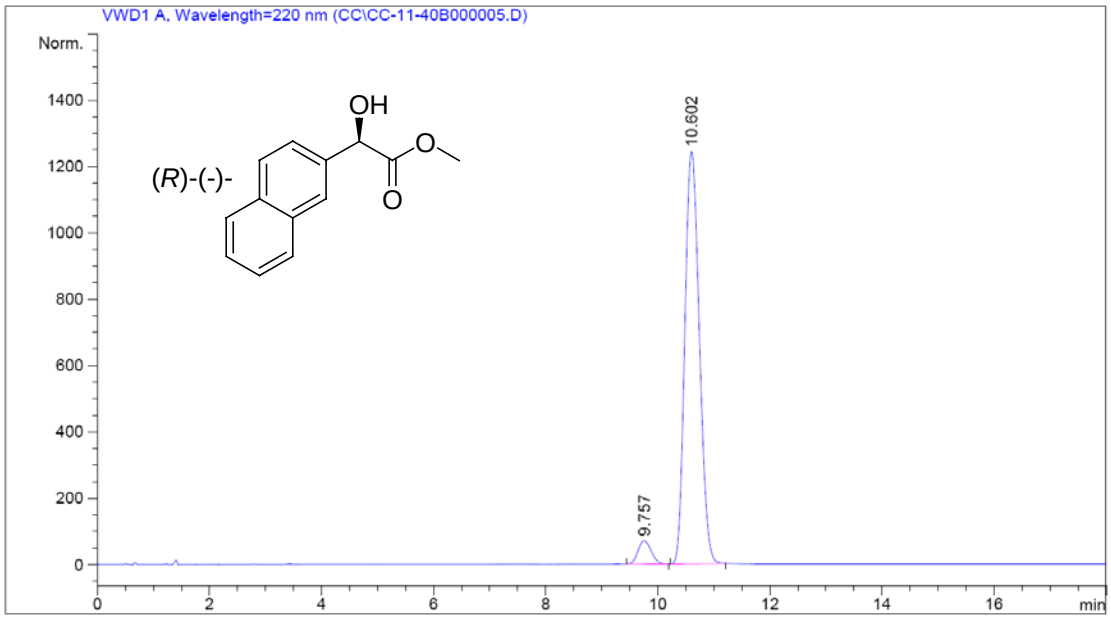
Uncalibrated Peaks:

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	5.433	BB	0.1427	1.34908e4	67.8844	?
2	6.122	BB	0.1517	6382.38525	32.1156	?

Uncalib. totals : 1.98732e4 100.0000

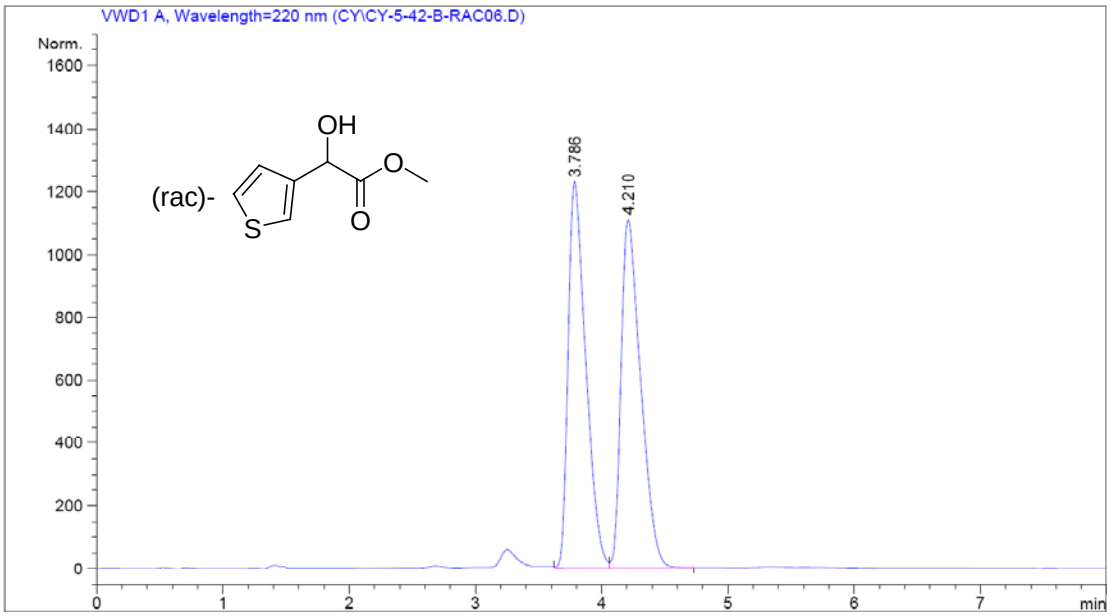
Methyl 2-hydroxy-2-naphthalen-2-ylacetate (3r)

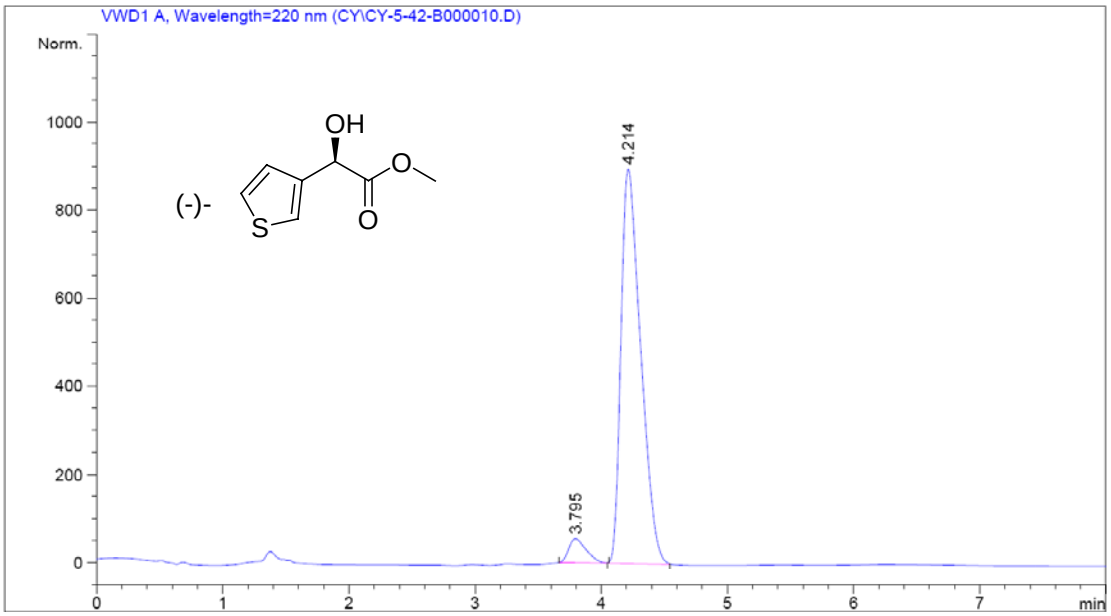




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	9.757	BB	0.2542	1125.72778	4.8067	?
2	10.602	BB	0.2820	2.22943e4	95.1933	?
Uncalib. totals :				2.34200e4	100.0000	

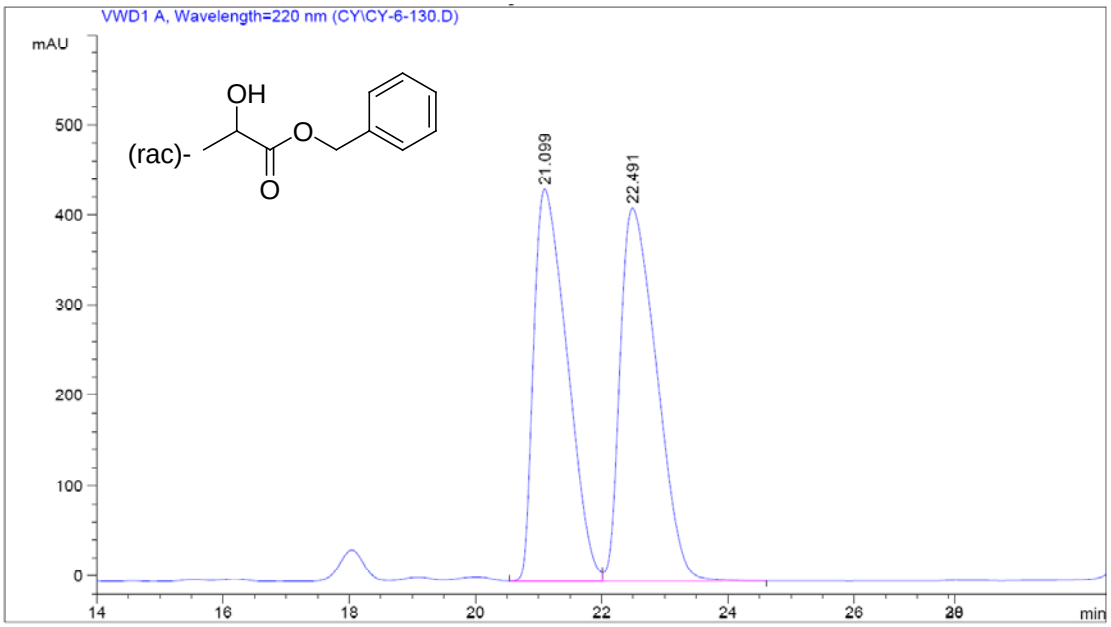
Methyl 2-hydroxy-2-thiophene-3-ylacetate (3s)

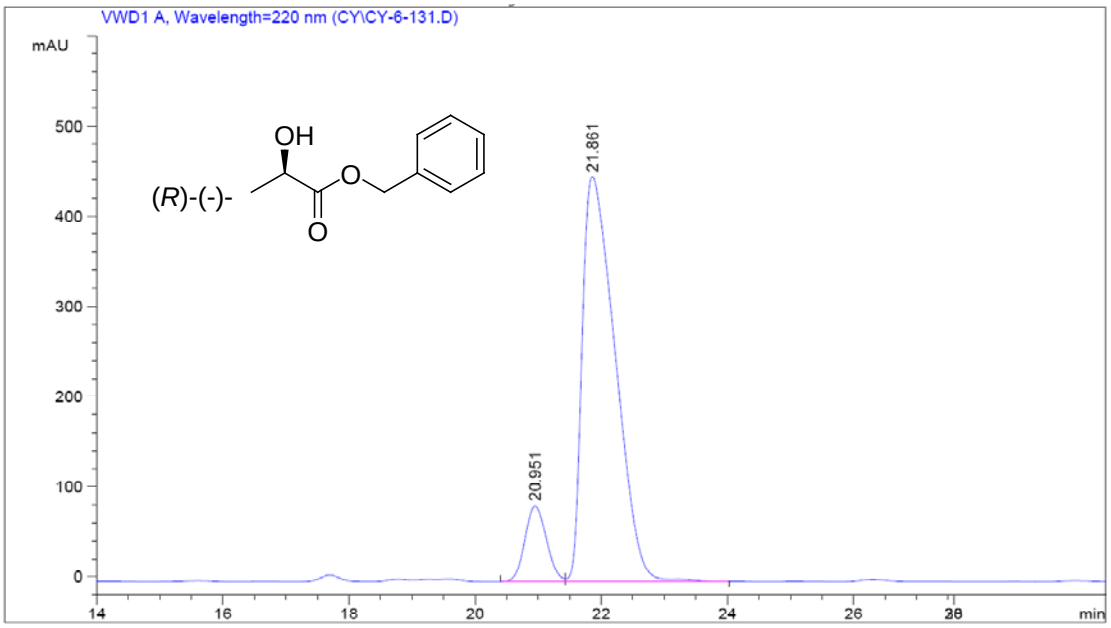




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.795	BB	0.1443	514.14624	5.0422	?
2	4.214	BB	0.1610	9682.80273	94.9578	?
Uncalib. totals :				1.01969e4	100.0000	

Benzyl 2-hydroxypropionate (3t)





Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.951	BV	0.3742	2010.90552	84.34593	10.9802
2	21.861	VB	0.5926	1.63030e4	448.93365	89.0198
Totals :				1.83139e4	533.27959	