

Chemoselective esterification of α -hydroxyacids catalyzed by salicylaldehyde through induced intramolecularity

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SUPPLEMENTARY MATERIAL

Representative experimental procedures, analytical datas, spectral data (20 pages)

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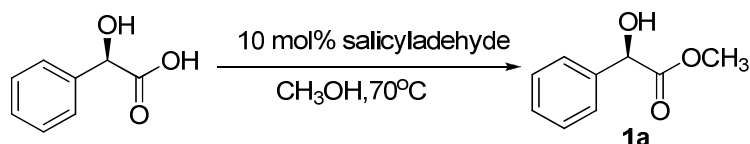
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General.

^1H and ^{13}C NMR spectra were recorded in CDCl_3 using a Jeol JNMEX400 spectrometer (400 MHz, ^1H ; 100 MHz, ^{13}C) and Bruker AVANCE 500 spectrometer (500 MHz, ^1H ; 125 MHz, ^{13}C), respectively, with CHCl_3 as internal reference. Electron-impact (ESI) mass spectra were recorded using a Thermo Finnigan spectrometer equipped with LCQ Advantage ionization and Spectra System detector systems. Analytical GC was carried out using an Agilent 6890C GC system equipped with an Agilent DB-WAX column (30 m $\times$ 0.25 mm $\times$ 0.25 mm). Analytical TLC plates were visualized under UV light or by spraying with phosphomolybdic acid (PMA) and KMnO_4 staining agents. All the reactions were performed in nitrogen or argon atmosphere, and the end products were isolated as pure materials. Aldehyde **2**,¹ racemic *N*-Benzoyl-3-phenylisoserine,² 2-(4-nitrophenylamino)-2-phenylacetic acid,³ and α -substituted α -hydroxyacids⁴ were prepared according to the literature reports. (*R*)-Mandelic acid, racemic 4-bromomandelic acid, (*R*)-lactic acid, racemic 2-methyl-2-hydroxyl-propanoic acid, racemic tropic acid, *L*-tartaric acid, *L*-malic acid were purchased from ALDRICH or ACROS and used without further purification. All the liquid aldehydes and alcohols used in this study were distilled under reduced pressure from anhydrous CaSO_4 or activated magnesium metal before use.

Experimental:

Representative procedure for the esterification of α -hydroxyacids catalyzed by salicylaldehyde (Table 2):



(*R*)-Mandelic acid (**1**, 153 mg, 1 mmol) was dissolved in methanol (1.0 mL) in a 5-mL single-neck round-bottom flask. Salicylaldehyde (12.2 mg, 11 μL , 0.10 mmol) was added to the flask via a syringe, at room temperature under nitrogen atmosphere. The resulting mixture was heated to 70°C , and the reaction progress was monitored by TLC, ^1H NMR spectroscopy, and GC analysis. After

completion of the reaction, the mixture was gradually cooled to room temperature, and the organic solvent was evaporated to give the crude product. The salicylaldehyde was recovered through vacuum distillation using a Kügelrohr apparatus (1 torr, 50°C). The remaining material was extracted with ethyl acetate (20 mL) and the organic layer was washed with saturated aqueous NaHCO₃ (10 mL × 2), dried with Na₂SO₄, and filtrated. Evaporation of the organic solvent provided pure methyl mandelate **1a** (153 mg, 92% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.43-7.33 (m, 5H), 5.18 (d, *J* = 5.2, 1H), 3.76 (s, 3H), 3.45 (d, *J* = 5.6, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 174.1, 138.2, 128.6, 128.5, 126.6, 72.9, 53.0; MS C₉H₁₀O₃ (EI, 166) 166 (M⁺, 13), 107 (100), 79 (51), 77 (43), 40 (12); TLC R_f 0.32 (EtOAc/hexane, 1/3); GC conditions: Agilent DB-WAX column (30 m × 0.25 mm × 0.25 mm), flow rate: 1 mL/min; 90°C, 1 min; 10°C/min to 140°C; retention time (*t*_R) 19.78 min; internal standard: 1,3,5-trimethylbenzene. HPLC for racemic methyl mandelate: *t*_R 27.4 min (*R*, 50%), 31.2 min (*S*, 50%) (CHIRALCEL AD-H, *i*-PrOH/hexane, 6/94, 1.0 mL/min, λ = 254 nm). [α]_D²⁴ -142 (c 1.0, MeOH) for 99% ee (lit. [α]_D²⁰ -144 (c 1.0, MeOH) for (*R*)). The absolute configuration was deduced to be *R* according to the sign of the optical rotation.^{5a} Mp: 56-58°C.

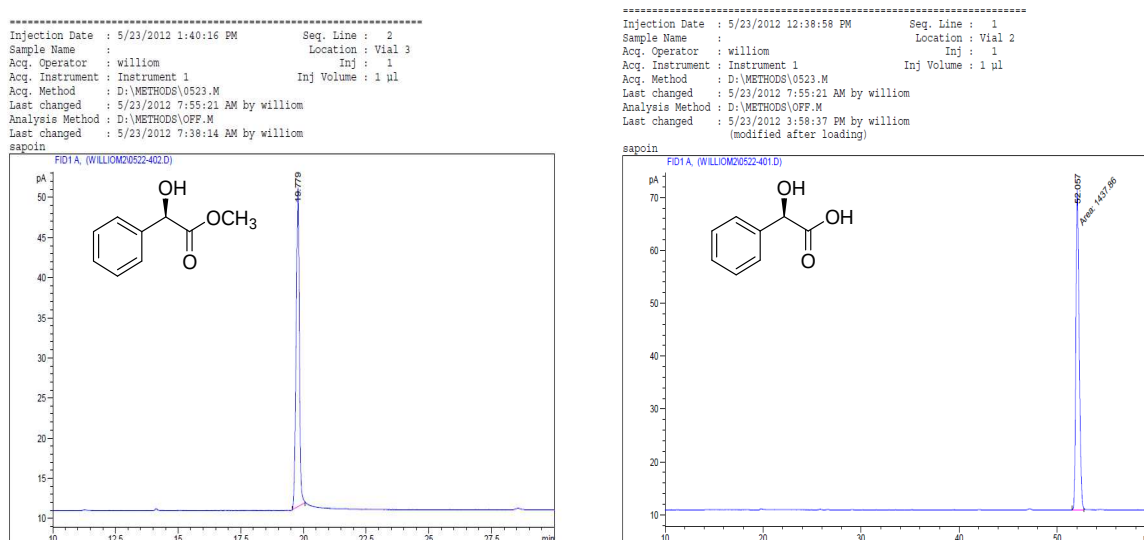


Figure S1. GC spectra of (*R*)-methyl mandelate and (*R*)-mandelic acid.

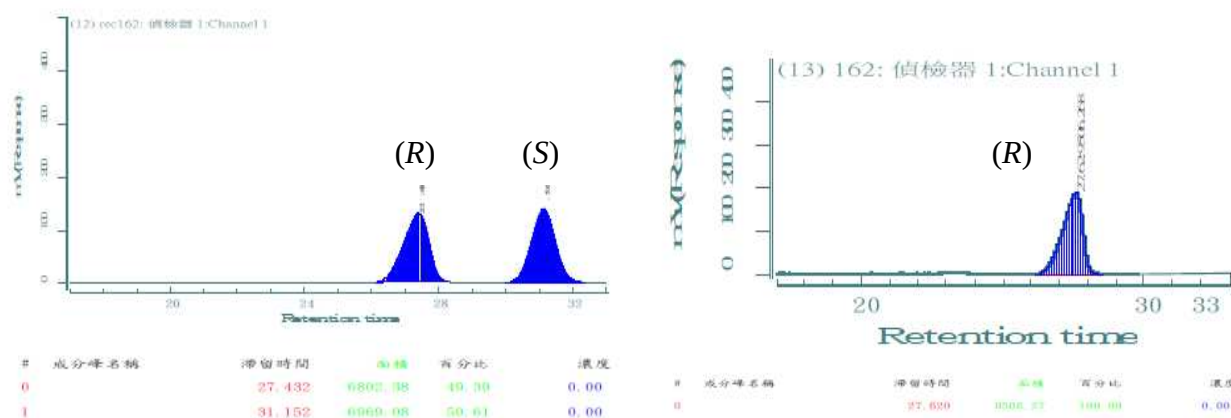
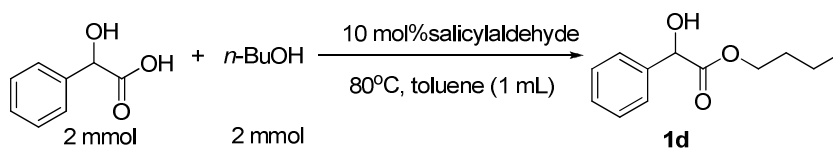


Figure S2. HPLC diagrams of racemic methyl mandelate and (*R*)-methyl mandelate.

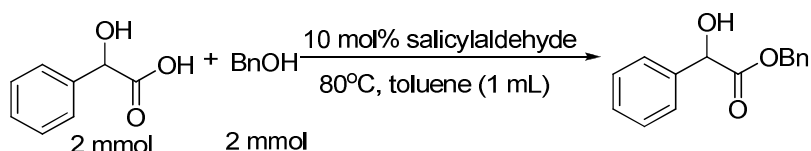
Representative procedure for the esterification of mandelic acid with *n*-butanol catalyzed by salicylaldehyde in toluene (concentration study, Table 3, entry 5):



To a 5-mL single-neck round-bottom flask was added mandelic acid (306 mg, 2 mmol) in 1 mL toluene at room temperature under nitrogen atmosphere. Solutions of *n*-butanol (149 mg, 184 μ L, 2 mmol) and salicylaldehyde (24.4 mg, 22 μ L, 0.20 mmol, 10 mol%) were added successively via syringe. The resulting mixture was heated to 70°C and the reaction progress was monitored by TLC and ^1H NMR spectroscopy analysis. After completion of the reaction, the salicylaldehyde was recovered through vacuum distillation using a Kügelrohr apparatus (1 torr, 50°C). The remaining material was extracted with ethyl acetate (20 mL) and the organic layer was washed with saturated aqueous NaHCO_3 (10 mL $\times$ 2), dried with Na_2SO_4 , and filtrated. Evaporation of the organic solvent provided pure *n*-butyl mandelate **1d** (387 mg, 93% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.43-7.34 (m, 5H), 5.16 (d, J = 5.2, 1H), 4.15 (m, 2H), 3.57 (d, J = 5.6, 1H, OH), 1.56 (m, 2H), 1.26 (m, 2H), 0.85 (t, J = 7.2, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.7, 138.4, 128.5, 128.3, 126.5, 72.8, 66.0,

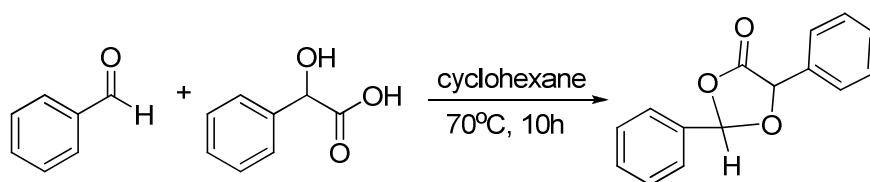
30.3, 18.8, 13.5; MS $C_{12}H_{16}O_3$ (EI, 208) 208 (M^+ , 21), 191 (58), 107 (100), 79 (62), 77 (47); TLC R_f 0.28 (EtOAc/Hexane, 1/5).^{5c}

Representative procedure for the esterification of α -hydroxyacids with benzyl alcohol catalyzed by salicylaldehyde in concentrated toluene (Table 4):



To a 5-mL single-neck round-bottom flask was added α -hydroxyacid (2 mmol) in 1 mL toluene at room temperature under nitrogen atmosphere. Solutions of benzyl alcohol (216mg, 208 μ L, 2 mmol) and salicylaldehyde (24.4 mg, 22 μ L, 0.20 mmol, 10 mol%) were added successively via syringe. The resulting mixture was heated to 70°C and the reaction progress was monitored by TLC and 1H NMR spectroscopy analysis. The salicylaldehyde was recovered through vacuum distillation using Kugelrohr apparatus (1 torr, 50°C). The remaining material was extracted with ethyl acetate (20 mL) and the organic layer was purified by column chromatography on a shot pad of silica gel (hexane/EtOAc = 1/5) to provide the pure benzyl mandelate **1f** (455 mg, 94% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.30 (m, 7H), 7.21-7.19 (m, 2H), 5.24 (d, J = 12.0, 1H), 5.22 (d, J = 5.2, 1H), 5.14 (d, J = 12.0, 1H), 3.41 (d, J = 5.2, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 138.2, 135.0, 128.6, 128.5, 128.4, 127.9, 126.6, 73.0, 67.6; MS $C_{15}H_{14}O_3$ (EI, 242) 242 (M^+ , 4), 226 (12), 107 (100), 92(18), 90(24), 80(12), 79(19), 77(11); TLC R_f 0.34 (EtOAc/Hexane, 1/5); Mp: 96-98°C.^{5a}

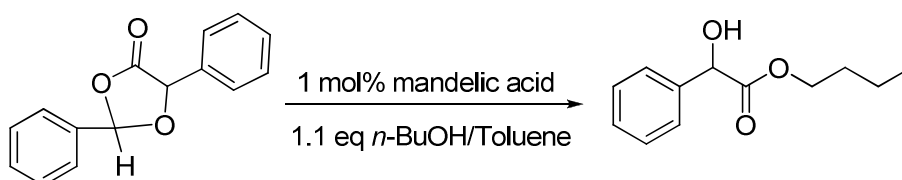
Synthesis of dioxolanone III from mandelic acid and benzaldehyde (equation 1):



Mandelic acid (608 mg, 4 mmol) was placed in a 10 mL single-neck round-bottomed flask and

benzaldehyde (415 μ L, 2 mmol) in cyclohexane (5 mL) was added to the flask via a syringe, at room temperature under nitrogen atmosphere. The resulting mixture was refluxed (70°C) for 10 h. The reaction mixture was gradually cooled to room temperature, and the organic solvent and unreacted benzaldehyde were evaporated under vacuum to give the crude product. The crude product was dissolved in ether (30 mL) and washed with saturated aqueous NaHCO₃ (10 mL $\times$ 2) to remove the unreacted mandelic acid. The organic layer was dried with Na₂SO₄ and filtrated. Evaporation of the organic solvent provided pure 2,5-diphenyl-[1,3]dioxolan-4-one (dioxolanone **III**, 442 mg, 46% yield), with 99.6% of *cis* isomers. ¹H NMR (400 MHz, CDCl₃) δ 7.61-7.43 (m, 10H), 6.57 (s, H), 5.43 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 171.3, 134.3, 133.3, 130.7, 129.3, 128.79, 128.75, 127.0, 126.8, 103.2, 77.19; MS C₁₅H₁₂O₃ (EI, 240) 240 (M⁺, 16), 151(32) 105 (100), 93(23), 90(24), 79(43), 77(76); Mp: 102-104°C. ⁶

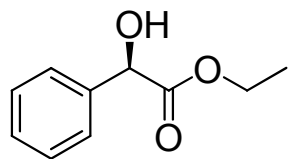
Synthesis of *n*-butyl mandelate **1d from dioxolanone **III** (equation 2):**



To a dry 25 mL, two-neck round-bottom flask was added 2,5-diphenyl-[1,3]dioxolan-4-one (dioxolanone **III**, 240 mg, 1.0 mmol), *n*-butanol (82 mg, 102 μ L, 1.1 mmol), and 1 mol% of mandelic acid (1.5 mg, 0.01 mmol) in anhydrous toluene (10 mL) under nitrogen atmosphere. The reaction mixture was heated at 70°C for 10 h. The mixture was cooled to room temperature, washed with saturated aqueous NaHCO₃ (10 mL $\times$ 2), dried with Na₂SO₄, and filtrated. Evaporation of the organic solvent gave pure *n*-butyl mandelate **1d** (196 mg, 94 % yield).

Analytical data for mandelate **1b**, **1c**, **1e**, **1g-1i**:

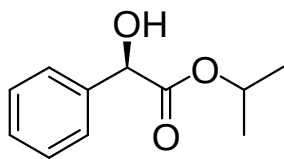
2-Hydroxy-2-phenyl-acetic acid ethyl ester^{5a}-**1b**



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.32 (m, 5H, ArH), 5.16 (d, *J* = 5.6, 1H), 4.31-4.14 (m, 2H), 3.44 (d, *J* = 5.6, 1H, OH), 1.23 (t, *J* = 6.8, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.6, 138.4, 128.5, 128.3,

126.5, 72.8, 62.1, 14.0 ; MS C₁₀H₁₂O₃ (EI, 70 eV, 180.2): 180 (M⁺, 3), 107 (100), 79 (26), 77 (22), 32 (46); TLC R_f 0.31 (EtOAc/Hexane, 1/5); [α]³² -125.68 (c 1.0, CHCl₃) (lit.^{5a} [α]²⁵ -130 (c 1.0, CHCl₃); The absolute configuration was deduced to be *R* according to the sign of optical rotation.

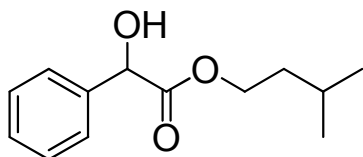
2-Hydroxy-2-phenyl-acetic acid isopropyl ester^{5a}-**1c**



Data: ¹HNMR (400 MHz, CDCl₃) δ 7.43-7.31 (m, 5H) 5.12-5.02 (m, 2H), 3.45 (bs, 1H, OH), 1.28 (d, *J* = 6.4, 3H), 1.11 (d, *J* = 6.4, 3H); ¹³C NMR (100 MHz, CDCl₃) 173.2, 138.6, 128.4, 128.2, 126.4, 72.9,

70.1, 21.6, 21.3; MS C₁₁H₁₄O₃ (EI, 70 eV, 194): 194 (M⁺, 2), 107 (100), 79 (40), 77 (27), 43 (14); TLC R_f 0.38 (EtOAc/Hexane, 1/5); [α]²¹ -89.12 (c 1.0, MeOH) (lit.^{5a} [α]²⁰ -91.6 (c 1.0, MeOH); The absolute configuration was deduced to be *R* according to the sign of optical rotation.

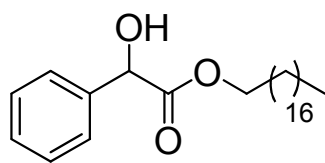
2-Hydroxy-2-phenyl-acetic acid isoarmyl ester^{5c}-**1e**



Data: ¹HNMR (400 MHz, CDCl₃) δ 7.43-7.33 (m, 5H), 5.16 (d, *J* = 5.6, 1H), 4.24-4.13 (m, 2H), 3.58 (bs, 1H, OH), 1.57-1.47 (m, 3H), 0.85 (d, *J* = 6.4, 3H), 0.83 (d, *J* = 6.4, 3H); ¹³C NMR (100

MHz, CDCl₃) 173.7, 138.4, 128.5, 128.3, 126.5, 72.8, 64.8, 36.9, 24.8, 22.2; MS C₁₃H₁₈O₃ (EI, 70 eV, 222): 222 (M⁺, 4), 107 (100), 87 (56), 77 (35); TLC R_f 0.32 (EtOAc/Hexane, 1/5);

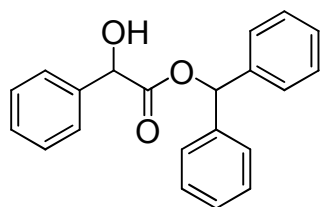
2-Hydroxy-2-phenyl-acetic acid octadodecyl ester⁷-**1g**



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.44-7.31 (m, 5H), 5.16 (d, J)
5.7, 1H), 4.17-4.14 (m, 2H), 3.46 (d, J) 6.2, 1H), 1.57 (quint, J)
6.8, 2H), 1.30-1.20 (m, 30H), 0.88 (t, J) 7.0, 3H); ^{13}C NMR (100

MHz, CDCl_3) δ 173.8, 138.5, 128.5, 128.4, 126.5, 72.8, 66.3, 31.9, 29.69, 29.65, 29.61, 29.5, 29.42,
29.35, 29.0, 28.4, 25.6, 22.7, 14.1; MS (FAB^+): calcd for $\text{C}_{26}\text{H}_{44}\text{O}_3+\text{Na}$: 427.3188, found: 427.3191;
TLC R_f 0.26 (EtOAc/hexane, 1/10);

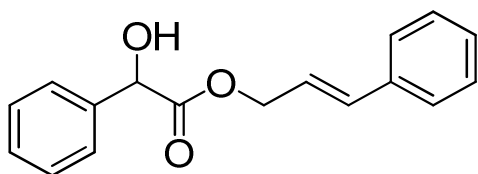
2-Hydroxy-2-phenyl-acetic acid benzhydryl ester^{5a}-1h



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.45-7.31 (m, 10H), 7.21-7.15
(m, 3H), 6.94-6.90 (m, 3H), 5.30 (d, J = 5.6, 1H), 3.54 (d, J = 5.6,
1H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.6, 139.2, 139.1, 138.0,
128.53, 128.51, 128.45, 128.2, 127.7, 127.3, 126.8, 126.2, 78.6, 73.1;

MS $\text{C}_{21}\text{H}_{18}\text{O}_3$ (EI, 318.): 318 (12), 277 (M^+ , 100), 165 (66), 148 (70); TLC R_f 0.35 (EtOAc/Hexane,
1/5); mp: 56-57°C.

2-Hydroxy-2-phenyl-acetic acid cinnamyl ester-1i

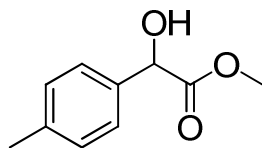


Oil solid, Data: ^1H NMR (400 MHz, CDCl_3) δ 7.45 (d, J =
8.0, 1H), 7.40-7.27 (m, 9H), 6.50 (dt, J = 16.0, 1.2, 1H),
6.19 (dt, J = 16.0, 6, 1H), 5.22 (d, J = 5.2, 1H), 4.85 (ddd,

J = 12.8, 6.3, 1.2, 1H), 4.79 (ddd, J = 12.8, 6.4, 1.2, 1H), 3.47 (d, J = 5.2, 1H); ^{13}C NMR (100 MHz,
 CDCl_3) 173.5, 138.2, 135.9, 134.6, 128.63, 128.59, 128.52, 128.2, 126.6, 122.0, 73.0, 66.4; HR-MS
(FAB^+) calcd for $\text{C}_{17}\text{H}_{16}\text{O}_3+\text{Na}$: 291.0997, found: 291.0994; Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{O}_3$: C, 76.10; H,
6.01; Found: C, 75.92; H, 6.16; TLC R_f 0.36 (EtOAc/Hexane, 1/5).

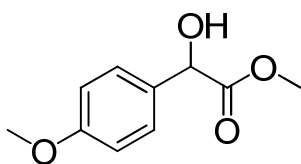
Analytical data for α -hydroxyacids 3a-3t:

2-Hydroxy-2-(*p*-tolyl)-acetic acid methyl ester⁸-3a



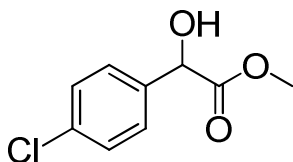
Data: ¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, J = 8.0, 2H), 7.17 (d, J = 8.0, 2H), 5.16 (d, J = 5.6, 1H), 3.96 (d, J = 5.6, 1H, OH), 3.71 (s, 3H), 2.35 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.9, 137.9, 135.3, 130.0, 126.3, 72.6, 52.4, 20.8; MS C₁₀H₁₂O₃ (ESI, 180): 204 (M+Na⁺+H⁺, 100), 504 (2M+Na⁺+H⁺, 72); TLC R_f 0.32 (EtOAc/Hexane, 1/5).

2-Hydroxy-2-(4-methoxy-phenyl)-acetic acid methyl ester⁸-3b



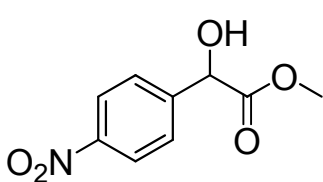
Data: ¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, J = 8.8, 2H), 6.88 (d, J = 8.8, 2H), 5.12 (d, J = 5.6, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 3.52 (m, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 174.2, 159.7, 130.4, 127.8, 114.0, 72.4, 55.2, 52.8; MS C₁₀H₁₂O₄: (EI, 70 eV, 196.2): 196 (M⁺, 13), 137 (100), 109 (19), 77 (10); TLC R_f 0.31 (EtOAc/Hexane, 1/3).

2-(4-BromoChloro-phenyl)-2-hydroxy-acetic acid methyl ester⁹-3c



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.51-7.49 (m, 2H), 7.32-7.30 (m, 2H), 5.14 (d, J = 5.2, 1H), 3.77 (s, 3H), 3.44 (d, J = 5.2, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 173.6, 137.2, 131.7, 128.2, 122.5, 72.2, 53.0; MS C₉H₉BrClO₃ (EI, 70 eV, 200.6): 200 (M⁺, 31), 227 (44), 79 (51), 187 (100), 77 (83), 43 (100); TLC R_f 0.32 (EtOAc/Hexane, 1/5).

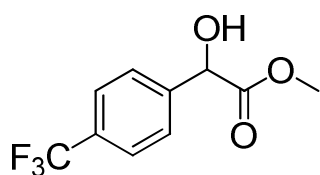
2-Hydroxy-2-(4-nitro-phenyl)-acetic acid methyl ester⁸-3d



Data: ¹H NMR (400 MHz, CDCl₃) δ 8.24 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 5.31 (s, 1H), 3.80 (s, 3H), 3.65 (br, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 173.9, 164.4, 161.1, 133.9, 128.3, 115.6, 72.1, 53.1; MS C₉H₉NO₅: (EI, 70 eV, 211.2): 212 (M⁺+1, 2), 152 (96), 150 (50), 134 (48), 104 (100), 77 (54);

TLC R_f 0.28 (EtOAc/Hexane, 1/3). $C_9H_9NO_5$: 211.17.

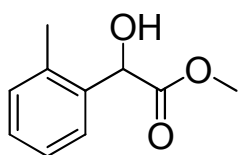
2-Hydroxy-2-(4-trifluoromethyl-phenyl)-acetic acid methyl ester¹⁰-3e



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0, 2H), 7.57 (d, J = 8.0, 2H), 5.26 (s, 1H), 3.79 (s, 3H), 3.58 (br, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 142.0, 130.7, 126.9, 125.45, 125.41, 72.3, 53.0;

MS $C_{10}H_9F_3O_3$ (EI, 70 eV, 234.2): 234 (M^+ , 16), 217 (35), 175 (23), 147 (100); TLC R_f 0.28 (EtOAc/Hexane, 1/3).

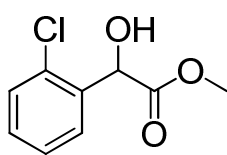
2-Hydroxy-2-(o-tolyl)-acetic acid methyl ester¹¹-3f



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.18 (m, 5H), 5.38 (d, J = 5.2, 1H), 3.77 (s, 3H), 3.48 (d, J = 5.2, 1H, OH), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 136.5, 136.3, 130.8,

128.5, 126.8, 126.2, 70.4, 52.9, 19.2; MS $C_{10}H_{12}O_3$ (ESI, 180): 204 ($M+Na^++H^+$, 66), 384 ($2M+Na^++H^+$, 100); TLC R_f 0.36 (EtOAc/Hexane, 1/5).

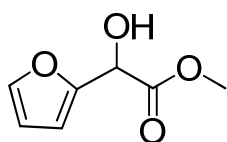
2-(2-Chloro-phenyl)-2-hydroxy-acetic acid methyl ester¹¹-3g



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.29-7.27 (m, 2H), 5.57 (s, 1H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 135.9, 133.3, 129.7, 129.6, 128.7, 127.0, 70.2,

50.3; MS $C_9H_9ClO_3$ (EI, 70 eV, 200.62): 200 (M^+ , 5), 143 (25), 141 (96), 77 (100), 51 (23), 32 (49); TLC R_f 0.39 (EtOAc/Hexane, 1/5).

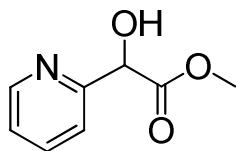
2-(Furan-2-yl)-2-hydroxy-acetic acid methyl ester¹²-3h



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 1.6, 1H), 6.35-6.32 (m, 2H), 5.19 (s, 1H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 150.6, 142.9, 110.4, 108.6, 66.7, 53.0; MS $C_7H_8O_4$ (ESI, 156):

179 (M+Na⁺,35), 335 (2M+Na⁺, 100);TLC R_f 0.40 (EtOAc/Hexane, 1/19).

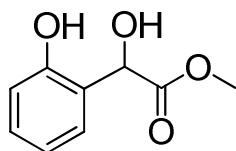
Hydroxy-2-pyridyl-acetic acid methyl ester¹²-3i



Data: ¹H NMR (400 MHz, CDCl₃) δ 8.56 (dd, *J* = 4.8, 1.2, 1H), 7.73 (td, *J* = 7.6, 1.6, 1H), 7.48 (d, *J* = 8.0, 1H), 7.26 (dd, *J* = 4.8, 1.2, 1H), 5.29 (s, 1H), 3.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.6,

141.1, 132.1, 128.2, 123.9, 113.7, 73.2, 52.9; MS C₈H₉NO₃ (ESI, 167.1): 190 (M+Na⁺,29), 357 (2M+Na⁺,100); TLC R_f 0.28 (EtOAc/Hexane, 1/3).

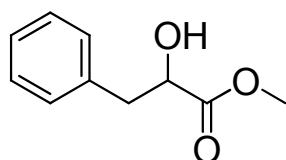
2-(2-Hydroxyl-phenyl)-2-hydroxy-acetic acid methyl ester¹²-3j



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.20-7.16 (m, 2H), 6.89-6.83 (m, 2H), 5.03 (s, 1H), 3.74 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.7, 154.8, 130.1, 129.1, 122.8, 120.4, 117.0, 72.2, 53.1; MS C₉H₁₀O₄

(ESI, 182.2): 205 (M+Na⁺, 33), 423 (2M+Na⁺, 100); TLC R_f 0.37 (EtOAc/Hexane, 1/2).

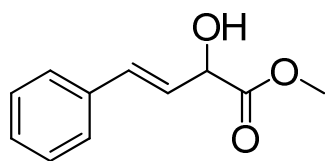
2-hydroxy-3-phenyl-propionic acid methyl ester⁹-3k



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.21 (m, 5H), 4.48-4.44 (m, 1H), 3.78 (s, 3H), 3.13 (dd, *J* = 14.0, 4.4, 1H), 2.97 (dd, *J* = 14.0, 7.2, 1H), 2.73 (d, *J* = 6.0, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 174.4, 136.3, 129.3, 128.3, 126.7, 71.2, 52.2, 40.4; MS C₁₀H₁₂O₃ (EI, 70 eV,

180.2): 180 (M⁺, 4), 162 (19), 103 (27), 91 (100), 32 (28); TLC R_f 0.30 (EtOAc/Hexane, 1/6).

2-Hydroxy-4-phenyl-but-3-enoic acid methyl ester¹³-3l

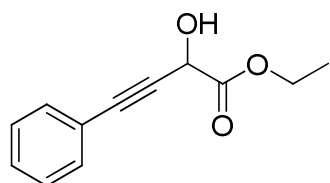


Data: ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.39 (d, *J* = 7.2, 2H), 7.35-7.31 (t, *J* = 7.2, 2H), 7.28-7.24 (t, *J* = 7.2, 1H), 6.81 (d, *J* = 16.0, 1H), 6.26 (dd, *J* = 16.0, 5.6, 1H), 4.86 (d, *J* = 5.6, 1H), 3.83 (s, 3H),

3.16 (bs, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 173.7, 136.0, 132.3, 128.5, 128.0, 126.6, 125.2,

71.3, 52.9; MS $C_{11}H_{12}O_3$ (EI, 70 eV, 192.2): 192 (M^+ , 2), 147 (28), 133 (15), 131 (100), 102 (41), 77 (34), 51 (21); TLC R_f 0.30 (EtOAc/Hexane, 1/3);

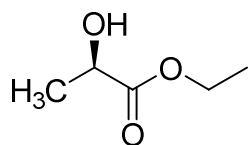
2-Hydroxy-4-phenyl-but-3-ynoic acid ethyl ester^{5a}-3m



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 7.6, 1.6, 2H), 7.34-7.31 (m, 3H), 5.06 (s, 1H), 4.36 (q, J = 7.2, 2H), 1.36 (t, J = 7.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 131.8, 128.8, 128.2, 121.8,

85.3, 84.2, 62.8, 61.9, 14.0; MS $C_{12}H_{12}O_3$ (ESI, 204): 227 ($M+Na^+$, 28), 431 ($2M+Na^+$, 67), 635 ($3M+Na^+$, 100); TLC R_f 0.36 (EtOAc/Hexane, 1/5).

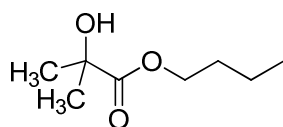
(R)-lactic acid ethyl ester^{5b}-3n



Data: 1H NMR (400 MHz, $CDCl_3$) δ 4.35 (q, J = 7.2, 1H), 4.21 (q, J = 1.2, 2H), 2.86 (br, 1H, OH), 1.36 (d, J = 7.2, 3H), 1.24 (t, J = 1.2, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 66.7, 61.6, 20.5, 14.0; MS

$C_5H_{10}O_3$ (ESI, 118): 141 ($M+Na^++H^+$, 29), 259 ($2M+Na^+$, 63), 377 ($3M+Na^+$, 100); TLC R_f 0.36 (EtOAc/Hexane, 1/2); $[\alpha]^{28}_{D}$ -10.8 (c 3.0, CH_3CN); (lit. $[\alpha]^{24}_{D}$ -13.4 (c 3.0, CH_3CN) for (*R*))

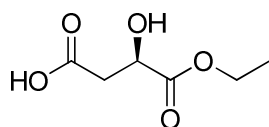
2-Hydroxy-2-methyl-propanoic acid *n*-butyl ester^{5b}-3o



Data: 1H NMR (400 MHz, $CDCl_3$) δ 4.14 (t, J = 6.4, 2H), 1.61 (quin, J = 7.2, 2H), 1.39 (s, 3H), 1.32 (m, 2H), 0.91 (t, J = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 72.0, 65.6, 30.5, 27.1, 18.9, 13.5; MS

$C_8H_{16}O_3$ (ESI, 160) 183 ($M+Na^+$, 30), 343 ($2M+Na^+$, 100); TLC R_f 0.35 (EtOAc/Hexane, 1/5).

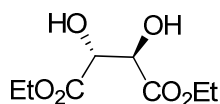
(R)-2-hydroxybutanedioic acid 1-methylester^{5e}-3p



Data: 1H NMR (400 MHz, $CDCl_3$) δ 6.18 (br, 1H, OH), 4.49 (dd, J = 6.4, 4.4, 1H), 4.25 (ddd, J = 14.4, 7.2, 2.4, 2H), 2.89 (dd, J = 16.8, 4.0, 2.4, 1H), 2.81 (dd, J = 16.8, 6.4, 2H), 1.28 (t, J = 6.8, 3H); ^{13}C NMR

(100 MHz, CDCl₃) δ 175.3, 173.3, 67.1, 62.2, 38.4, 29.6, 14.0; MS C₆H₁₀O₅ (ESI, 162) 185 (M+Na⁺, 19), 167 (M+Na⁺-H₂O, 100); TLC R_f 0.23 (EtOAc/MeOH, 20/1); [α]²⁷ -5.5 (c 2.0, CH₃OH); lit. [α]²⁴ -5.2 (c 2.0, CH₃OH) for (R));

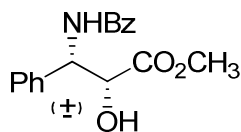
D-(-)-tartaric acid diethyl ester^{5b}-3q



Data: ¹H NMR (400 MHz, CDCl₃) δ 4.50 (s, 2H), 4.25 (dd, *J* = 7.2, 1.2, 2H), 4.22 (dd, *J* = 6.8, 1.2, 2H), 3.97 (br, 1H, OH), 1.25 (t, *J* = 7.2, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 171.5, 72.1, 62.1, 13.9; MS C₈H₁₄O₆

(ESI, 206.2): 229 (M+Na⁺, 28), 435 (2M+Na⁺, 100); TLC R_f 0.36 (EtOAc/Hexane, 1/2); [α]²⁷ +8.9 (c 2.5, EtOH); (lit. [α]²⁰ +8.5 (c 2.46, EtOH).

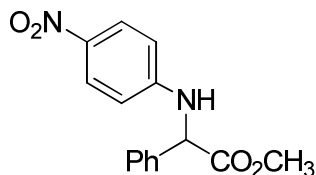
Racemic-methyl (2R, 3S)- N-Benzoylamino-2-hydroxy-3-phenyl-propanoate^{5a}-3r



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 7.4, 2H), 7.53-7.30 (m, 8H), 7.01 (d, *J* = 8.8, 1H, NH), 5.74 (d, *J* = 8.8, 1.9, 1H), 4.63 (d, *J* = 1.9, 1H), 3.84 (s, 3H, OCH₃), 3.41 (bs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ

173.4, 166.9, 138.7, 134.1, 131.8, 128.7, 128.6, 127.9, 127.1, 127.0, 73.2, 55.8, 53.3; MS C₁₇H₁₇NO₄ (ESI, 299): 621 (M₂+Na⁺, 100), 323 (M+Na⁺+1, 35); TLC R_f 0.22 (EtOAc/hexane,1/2).

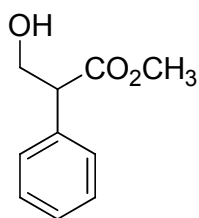
(4-Nitrophenylamino)-phenyl-acetic acid methyl ester³-3s



Data: ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, *J* = 9.2, 2H), 7.45-7.32 (m, 5H), 6.50 (d, *J* = 9.2, 2H), 5.84 (d, *J* = 5.2, 1H), 6.14 (d, *J* = 5.6, 2H), 3.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.1, 150.8, 135.9, 129.2, 128.9, 127.0, 126.2, 112.1, 59.8, 53.3; MS C₁₅H₁₄N₂O₄ (ESI,

286.2): 309 (M+Na⁺, 21), 295 (2M+Na⁺, 70), 881 (3M+Na⁺, 100); TLC R_f 0.25 (EtOAc/MeOH, 2/1)

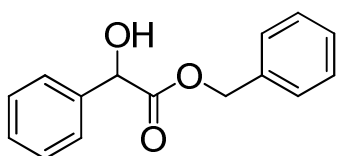
Methyl-2-phenyl-3-hydroxypropionate¹⁴-3t



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.24 (m, 5H), 4.14 (t, *J* = 9.6, 1H), 3.83 (dd, *J* = 8.8, 5.2, 2H), 3.7 (br, 1H, OH), 3.67 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.5, 135.5, 128.7, 128.0, 127.6, 64.4, 53.9, 52.1; MS C₁₀H₁₂O₃ (ESI, 180.2) 203 (M+Na⁺, 43), 186 (M+H₂O+Na⁺, 100), 635 (3M+Na⁺, 100); TLC R_f 0.34 (EtOAc/Hexane, 1/5).

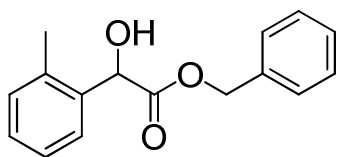
Analytical data for α-hydroxyacids 4a-4o:

2-Hydroxy-2-phenyl-acetic acid benzyl ester^{5a}-4a



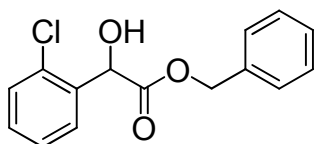
Data: ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.30 (m, 7H), 7.21-7.19 (m, 2H), 5.24 (d, *J* = 12.0, 1H), 5.22 (d, *J* = 5.2, 1H), 5.14 (d, *J* = 12.0, 1H), 3.41 (d, *J* = 5.2, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 173.5, 138.2, 135.0, 128.6, 128.5, 128.5, 128.4, 127.9, 126.6, 73.0, 67.6; MS C₁₅H₁₄O₃ (EI, 242): 242 (M⁺, 4), 226 (12), 107 (100), 92(18), 90(24), 80(12), 79(19), 77(11); TLC R_f 0.34 (EtOAc/Hexane, 1/5); mp: 96-98°C.

2-Hydroxy-2-(*o*-tolyl)-acetic acid benzyl ester^{5a}-4b



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.28 (m, 4H), 7.23-7.17 (m, 5H), 5.42 (d, *J* = 5.2, 1H), 5.25 (d, *J* = 12.4, 1H), 5.15 (d, *J* = 5, 12.4, 1H), 3.35 (d, *J* = 5.2, 1H, OH), 2.40(s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.9, 136.5, 136.3, 135.0, 130.7, 128.44, 128.38, 128.3, 127.8, 126.7, 126.2, 70.4, 67.4, 19.2; TLC R_f 0.38 (EtOAc/Hexane, 1/6); MS C₁₆H₁₆O₃ (EI, 70eV, 256): 256 (M⁺, 1), 120 (100), 90 (38).

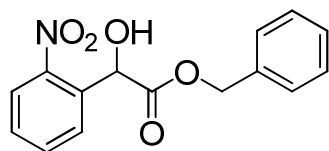
2-(2-Chloro-phenyl)-2-hydroxy-acetic acid benzyl ester^{5a}-4c



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.25 (m, 2H), 7.20-7.10 (m, 7H), 5.53 (d, *J* = 5.2, 1H), 5.14 (d, *J* = 12.4, 1H), 5.07 (d, *J* = 12.4, 1H),

3.54 (d, $J = 5.2$, 1H, OH); ^{13}C NMR (100 MHz, CDCl_3) δ 173.0, 135.9, 134.9, 133.5, 129.9, 129.7, 128.7, 128.4, 128.3, 127.7, 127.1, 70.4, 67.7; MS $\text{C}_{15}\text{H}_{13}\text{ClO}_3$ (ESI, 275): 299 ($\text{M}+\text{Na}^++\text{H}^+$, 6), 572 ($2\text{M}+\text{Na}^+$, 51); TLC R_f 0.39 (EtOAc/Hexane, 1/4).

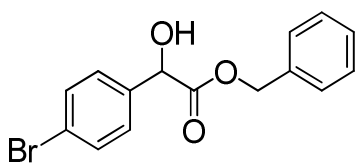
2-Hydroxy-2-(2-nitro-phenyl)-acetic acid benzyl ester^{5d}-4d



Data: ^1H NMR (400 MHz, CDCl_3) δ 8.00 (d, $J = 8.0$, 1H), 7.66-7.60 (m, 2H), 7.50 (td, $J = 8.0$, 1.6, 1H), 7.32-7.30 (m, 3H), 7.22-7.20 (m, 2H), 5.89 (d, $J = 4.8$, 1H), 5.22 (d, $J = 12.0$, 1H),

5.16 (d, $J = 12.0$, 1H), 3.59 (d, $J = 5.2$, 1H, OH); ^{13}C NMR (100 MHz, CDCl_3) δ 171.6, 147.9, 134.6, 133.4, 132.9, 129.8, 129.3, 128.6, 128.1, 125.2, 70.2, 68.2; TLC R_f 0.36 (EtOAc/Hexane, 1/3); MS $\text{C}_{15}\text{H}_{15}\text{NO}_5$ (EI, 70 eV, 287.1): 287 (M^+ , 3), 122 (100), 107 (65), 90 (33); mp: 89-91°C.

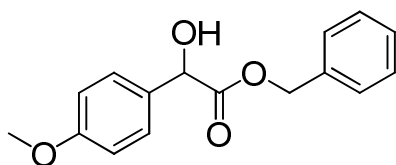
2-(4-Bromo-phenyl)-2-hydroxy-acetic acid benzyl ester^{5a}-4e



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.49-7.47 (m, 2H), 7.43-7.29 (m, 5H), 7.22-7.21 (m, 2H), 5.23(d, $J = 12.0$, 1H), 5.17 (d, $J = 5.6$, 1H), 5.14 (d, $J = 12.0$, 1H), 3.43 (d, $J = 5.6$, 1H, OH); ^{13}C NMR (100

MHz, CDCl_3) δ 172.9, 137.1, 134.7, 131.6, 128.5, 128.48, 128.0, 122.4, 72.3, 67.8; MS $\text{C}_{15}\text{H}_{13}\text{BrO}_3$ (EI, 70 eV, 320): 320 (M^+ , 8), 186 (100), 107 (72), 90 (28); TLC R_f 0.38 (EtOAc/Hexane, 1/4); mp: 107-109°C.

2-Hydroxy-2-(4-methoxy-phenyl)-acetic acid benzyl ester^{5a}-4f

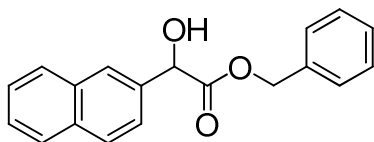


Data: ^1H NMR (400 MHz, CDCl_3) δ 7.34-7.31 (m, 5H), 7.23-7.21 (m, 2H), 6.89-6.87 (m, 2H), 5.24 (d, $J = 12.4$, 1H), 5.17 (d, $J = 6.0$, 1H), 5.13 (d, $J = 12.4$, 1H), 3.81(s, 3H), 3.42 (d, $J = 6.0$, 1H); ^{13}C

NMR (100 MHz, CDCl_3) δ 173.6, 159.7, 135.0, 130.4, 128.5, 128.4, 127.9, 127.85, 114.0, 72.5, 67.5, 55.2; TLC R_f 0.39 (EtOAc/Hexane, 1/3); MS $\text{C}_{16}\text{H}_{16}\text{O}_4$ (EI, 70 eV, 272.1): 272 (M^+ , 8),

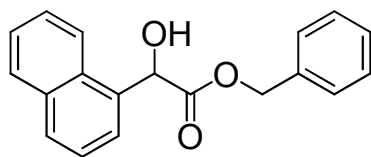
165 (21), 120 (100), 107 (60), 91 (30); mp: 94-96°C.

2-Hydroxy-1-(naphthalen-1-yl)-acetic acid benzyl ester^{5a}-4g



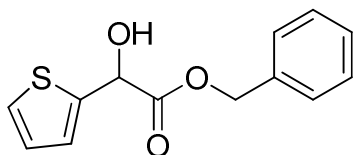
Data: ¹H NMR (400 MHz, CDCl₃) δ 7.91(s, 1H), 7.86-7.82 (m, 2H), 7.54-7.50 (m, 3H), 7.31-7.29 (m, 3H), 7.22-7.20 (m, 2H), 5.41 (s, 1H), 5.27 (d, *J* = 12.3, 1H), 5.15 (d, *J* = 12.3, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 135.5, 134.9, 133.3, 133.1, 128.5, 128.4, 128.39, 128.1, 128.0, 127.6, 126.28, 126.27, 125.9, 124.2, 73.1, 67.7; MS C₁₉H₁₆O₃ (ESI, 292): 315(M+Na⁺, 6), 607 (2M+Na⁺); TLC R_f 0.32 (EtOAc/Hexane, 1/4); mp: 121-124°C.

2-Hydroxy-2-(naphthalen-1-yl)-acetic acid benzyl ester^{5a}-4h



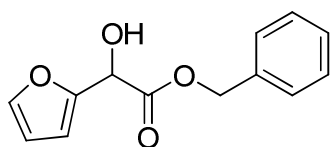
Data: ¹H NMR (400 MHz, CDCl₃) δ 8.17-8.14 (m, 1H), 7.89-7.84 (m, 2H), 7.53-7.42 (m, 4H), 7.25-7.21 (m, 3H), 7.10-7.08 (m, 2H), 5.88 (d, *J* = 5.2, 1H), 5.25 (d, *J* = 12.4, 1H), 5.13 (d, *J* = 12.4, 1H), 5.48 (d, *J* = 5.2, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 134.8, 133.87, 133.86, 130.9, 129.3, 128.6, 128.3, 128.1, 127.7, 126.4, 125.7, 125.6, 125.1, 123.7, 71.3, 67.4; MS C₁₉H₁₆O₃ (EI, 292): 292 (M⁺, 13), 157 (100), 129 (48), 128 (50), 91 (18); TLC R_f 0.34 (EtOAc/Hexane, 1/4); mp: 128-130°C.

2-Hydroxy-2-(thiophen-2-yl)-acetic acid benzyl ester^{5a}-4i



Data: ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.34 (m, 3H), 7.31-7.28 (m, 3H), 7.09 (dd, *J* = 6.6, 1.0, 1H), 6.98 (dd, *J* = 5.4, 4, 1H), 5.47 (s, 1H), 5.25 (q, *J* = 13.2, 2H), 3.47 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 172.3, 141.2, 134.7, 128.6, 128.55, 128.17, 126.8, 125.7, 125.4, 69.1, 68.0; MS C₁₃H₁₂O₃S (ESI, 248): 519 (2M+Na⁺, 100); TLC R_f 0.22 (EtOAc/Hexane, 1/19).

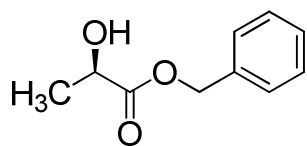
2-(Furan-2-yl)-2-hydroxy-acetic acid benzyl ester^{5a}-4j



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.39 (d, $J = 1.2$, 1H), 7.37-7.32 (m, 3H), 7.31-7.26 (m, 2H), 6.53 (d, $J = 1.6$, 2H), 5.27 (d, $J = 12.4$ H), 5.25 (s, 1H), 5.24 (d, $J = 12.4$ H); ^{13}C NMR (100 MHz, CDCl_3) δ

171.3, 150.6, 143.0, 134.8, 128.56, 128.5, 128.1, 110.5, 108.7, 67.9, 66.9; MS $\text{C}_{13}\text{H}_{12}\text{O}_4$ (ESI, 232): 255 ($\text{M}+\text{Na}^+$, 30), 487 ($2\text{M}+\text{Na}^+$, 100); TLC R_f 0.20 (EtOAc/Hexane, 1/19).

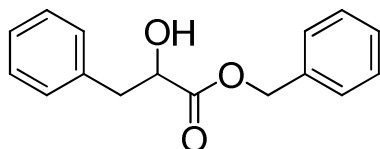
(R)-2-Hydroxy-propionic acid benzyl ester^{5a}-4k



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.40-7.34 (m, 5H), 5.21 (s, 2H), 4.32 (q, $J = 6.8$, 1H), 2.84 (bs, 1H, OH), 1.44 (d, $J = 6.8$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.5, 135.2, 128.6, 128.5, 128.2, 67.3,

66.8, 20.3; MS $\text{C}_{10}\text{H}_{12}\text{O}_3$ (ESI, 180) 204 ($\text{M}+\text{Na}^++\text{H}^+$, 100), 383 ($2\text{M}+\text{Na}^+$, 84); TLC R_f 0.30 (EtOAc/Hexane, 1/7). $[\alpha]^{30}_{\text{D}}$ -12.4 (c 1.02, CHCl_3); (lit. $[\alpha]^{23}_{\text{D}}$ -15.5 (c 1.02, CHCl_3))

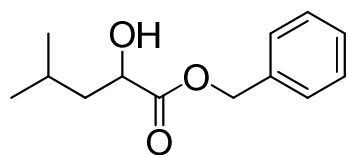
2-hydroxy-3-phenyl-propionic acid benzyl ester^{5a}-4l



Data: ^1H NMR (400 MHz, CDCl_3) δ 7.43-7.35 (m, 5H), 7.31-7.28 (m, 3H), 7.20-7.19 (m, 2H), 5.23 (d, $J = 12.0$, 1H), 5.19 (d, $J = 12.0$, 1H), 4.52 (td, $J = 4.8, 4.8$, 1H), 3.16 (dd, $J = 12.0, 4.8$, 1H, OH), 3.04-2.96 (m, 2H); ^{13}C NMR (100 MHz,

CDCl_3) δ 173.9, 136.1, 134.9, 129.4, 128.5, 128.48, 128.3, 126.7, 71.2, 67.2, 40.4; MS $\text{C}_{16}\text{H}_{16}\text{O}_3$ (EI, 70 eV, 256.3): 256 (M^+ , 2), 238 (25), 192 (38), 121 (84), 103 (26), 91 (100), 77 (15); TLC R_f 0.38 (EtOAc/Hexane, 1/5).

2-Hydroxyl-4-methyl-pentanoic acid benzyl ester^{5a}-4m

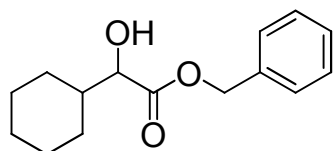


Data: ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.35 (m, 5H), 5.21 (s, 2H), 4.25 (dt, $J = 8.0, J = 5.6$, 1H), 2.69-2.66 (m, 1H, OH), 1.89 (heptet, $J = 6.8$, 1H), 1.60-1.56 (m, 2H), 0.94 (s, $J = 6.8$, 3H), 0.93 (d, $J = 6.8$,

3H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.7, 135.2, 128.6, 128.5, 128.3, 69.2, 67.3, 43.4, 24.4, 23.2,

21.5; MS $C_{13}H_{18}O_3$ (EI, 222): 222 (M^+ , 3), 91 (100), 87 (31), 69 (36); TLC R_f 0.30 (EtOAc/Hexane, 1/15).

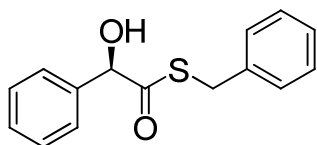
2-Cyclohexyl-2-hydroxyl-acetic acid benzyl ester^{5a}-4n



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.38- 7.34 (m, 5H), 5.22 (s, 2H), 4.06 (dd, J = 6.0, 3.6, 1H), 2.74 (d, J = 6.0, 1H, OH), 1.77-1.63 (m, 5H), 1.38-1.16 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 135.2,

128.6, 128.5, 128.3, 74.8, 67.2, 42.0, 29.0, 26.2, 26.18, 26.0, 25.9; MS $C_{15}H_{20}O_3$ (EI, 248): 248 (M^+ , 3), 113 (49), 95 (100) , 92 (13), 91 (61); TLC R_f 0.35 (EtOAc/Hexane, 1/15).

(R)-2-Hydroxy-2-phenyl-thioacetic acid S-benzyl ester.¹⁵-4o



Data: 1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.37 (m, 5H, ArH), 7.30-7.27 (m, 5H), 5.21 (s, 1H), 4.16 (d, J = 13.6, 1H), 4.10 (d, J = 13.6, 1H), 3.57 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4,

137.8, 136.7, 128.8, 128.79, 128.7, 128.6, 127.3, 127.0, 79.7, 33.2; MS $C_{15}H_{14}O_2S$ (EI, 70 eV, 258.3): 259 (M^++1 , 5), 213 (23), 124 (26) , 107 (100), 91 (31) , 79 (25), 77 (16); TLC R_f 0.37 (EtOAc/Hexane, 1/6); mp: 83-85°C.

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