Enantioselective Equilibration – Access to Chiral Aldol Adducts of Mandelic Acid Esters.

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Experimental Procedures and Characterization of the Products

Toluene was distilled, dried and stored over molecular sieves (3A). $\text{Ti}(\text{O}i\text{Bu})_4$ and $\text{Ti}(\text{O}i\text{Pr})_4$ purchased from Merck chemical company was used without prior purification. Aldehydes were freshly distilled before use. ^1H -NMR und ^{13}C -NMR spectra were recorded at 300 and 75 MHz in CDCl_3 (if not stated otherwise), respectively using a AC-300 spectrometer. Chemical shifts are given in ppm. Purification of products was accomplished by flash chromatography. Thin layer chromatography was performed with Merck Silica Gel 60 F₂₅₄ TLC plates.

General Procedure A:

Aldol addition in the presence of $\text{Ti}(\text{O}i\text{Pr})_4$ and NEt_3

1.9 g Isopropyl mandelate (10.0 mmol) and 3.0 ml $\text{Ti}(\text{O}i\text{Pr})_4$ (or 4.0 ml $\text{Ti}(\text{O}t\text{Bu})_4$) (10 mmol) were dissolved in appr. 15 ml abs. toluene. 10 mmol of the corresponding aldehyde **1a-h** were added together with 73 mg triethylamine (1 mmol). The reaction was continuously monitored by thin layer chromatography (hexane / ethyl acetate – 8 / 2). At the end of the reaction the resulting mixture was extracted by diethylether and successively by saturated aq. NH_4Cl - and NaHCO_3 -solution. The organic layers were separated, dried (MgSO_4) and the solvent was removed in vacuo. The residue was purified by flash column chromatography.

General Procedure B:

Aldol addition in the presence of $\text{Ti}(\text{O}t\text{Bu})_4$ and N-methylephedrine

1.7 g Methyl mandelate (10.0 mmol) and 4.0 ml $\text{Ti}(\text{O}t\text{Bu})_4$ (10 mmol) were dissolved in appr. 10 ml abs. toluene. 10 mmol of the corresponding aldehyde **1a-k** were added together with 5.4 g (+)- or (-)-methylephedrine (30 mmol). The reaction was continuously monitored by thin layer chromatography (hexane / ethyl acetate – 8 / 2). At the end of the reaction the resulting mixture was extracted by diethylether and successively by saturated aq. NH_4Cl - and NaHCO_3 -solution. The organic layers were separated, dried (MgSO_4) and the solvent was removed in vacuo. The residue was purified by flash column chromatography.

Studies of controlled racemization of (*R*)-methyl mandelate

3.0 ml $\text{Ti}(\text{O}i\text{Pr})_4$ (10 mmol) were added to a solution of 1.7 g (*R*)-methyl mandelate (10 mmol) in 50 ml abs. toluene at r.t. The enantioselectivities were determined by ^1H NMR experiments of the corresponding Mosher-ester.

syn-Isopropyl-2,3-dihydroxy-2,3-diphenylpropanoate (**syn-3a**)

m.p.: 133 °C

^1H NMR: δ =1.24 (d, J =6.2 Hz, 3H, CH_3), 1.32 (d, J =6.2 Hz, 3H, CH_3), 2.82 (d, J =8.6 Hz, 1H, OH), 3.99 (s, 1H, OH), 5.12 (spt, J =6.2Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 5.30 (d, J =8.6 Hz,

1H, CHOH), 7.03 (m, 10H, Ph). ^{13}C NMR: δ =21.6, 21.7, 71.2, 78.1, 81.6, 125.8, 127.4, 127.6, 127.7, 127.8, 127.9, 138.1, 138.2, 173.5.

HRMS (ESI) cal. for $\text{C}_{18}\text{H}_{20}\text{O}_4\text{Na}$: 323.1259. found: 323.1262.

anti-Isopropyl-2,3-dihydroxy-2,3-diphenylpropanoate (***anti*-3a**)

m.p.: 123 °C

^1H NMR: δ =1.00 (d, J =6.4 Hz, 3H, CH_3), 1.10 (d, J = 6.4Hz, 3H, CH_3), 2.58 (d, J =7.1 Hz, 1H, OH), 3.71 (s, 1H, OH), 4.80 (spt, J =6.4 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 5.28 (d, J =7.1 Hz, 1H, CHOH), 7.23 (m, 8H, Ph), 7.72 (m, 2H, Ph). ^{13}C NMR: δ =21.3, 21.4, 71.0, 77.9, 80.9, 126.4, 127.8, 128.0, 128.1, 128.2, 128.3, 138.5, 138.7, 172.0

syn- Isopropyl-2,3-dihydroxy-4,4-dimethyl-2-phenylpentanoate (***syn*-3b**)

^1H NMR: δ =0.66 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.10 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.24 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 2.55 (d, J =11.1 Hz, 1H, OH), 4.06 (d, J = 11.1 Hz, 1H, CHOH), 4.1 (s, 1H, OH), 4.96 (spt, J =6.3 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.1 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =21.4, 21.6, 28.1, 36.9, 71.1, 81.2, 82.8, 126.2, 127.7, 127.8, 139.5, 174.6. HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_4\text{Na}$: 303.1572. found: 303.1568.

anti- Isopropyl-2,3-dihydroxy-4,4-dimethyl-2-phenylpentanoate (***anti*-3b**)

m.p.: 66°C

^1H NMR: δ =0.68 (s, 9H, C(CH₃)₃), 1.16 (d, J=6.3 Hz, 3H, CH(CH₃)₂), 1.28 (d, J=6.3 Hz, 3H, CH(CH₃)₂), 2.40 (s, 1H, OH), 4.00 (s, 1H, CHOH), 4.07 (s, 1H, OH), 4.95 (spt, J=6.3 Hz, 1H, CH(CH₃)₂), 7.2 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =21.3, 21.6, 28.0, 36.8, 71.3, 81.2, 82.7, 126.1, 127.7, 127.8, 139.4, 174.6

syn-Isopropyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (***syn*-3c**)

m.p.: 63°C

^1H NMR: δ =0.78 (d, J =6.8 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 0.82 (d, J =6.8 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.19 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.33 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.55 (dspt, J =2.9, 6.8 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 2.31 (d, J =11.1 Hz, 1H, OH), 4.10 (s, 1H, OH), 4.22 (dd, J =2.9, 11.1 Hz, 1H, CHOH), 5.05 (spt, J =6.3 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.26 (m, 3H, Ph), 7.60 (m, 2H, Ph). ^{13}C NMR: δ =15.9, 21.3, 21.6, 21.8, 28.6, 71.1, 78.7, 82.0, 125.5, 127.7, 128.1, 139.0, 174.3.

HRMS (ESI) cal. for $\text{C}_{15}\text{H}_{22}\text{O}_4\text{Na}$: 289.1416 . found: 289.1415.

anti-Isopropyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (***anti*-3c**)

^1H NMR: δ =0.99 (d, J =6.8 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.02 (d, J =6.8 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.16 (d, J =6.4 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.29 (d, J =6.4 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.83 (d, J =8.0 Hz, 1H, OH), 1.92 (dspt, J =3.8, 6.8 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.81 (s, 1H, OH), 4.11 (dd, J =3.8, 8.0 Hz, 1 H, CHOH), 5.04 (spt, J =6.4 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.3 (m, 3H, Ph), 7.60 (m, 2H, Ph). ^{13}C NMR: δ =17.6, 21.4, 21.5, 21.6, 30.7, 70.7, 79.1, 81.0, 125.6, 125.9, 127.8, 140.2, 173.4

syn- Isopropyl-2,3-dihydroxy-2-phenylpentanoate (***syn*-3d**)

^1H NMR: δ =0.80 (t, J =7.3 Hz, 3H, CH_3), 1.15 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.27 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.31 (m, J =2.4, 7.3 Hz, 1H, CH_2), 1.89 (s, 1H, OH), 3.90 (s, 1H, OH), 4.06 (t, J =2.4 Hz, 1H, CHOH), 5.02 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.2 (m, 3H, Ph), 7.5 (m, 2H, Ph). ^{13}C NMR: δ =10.5, 21.5, 21.7, 23.5, 71.0, 77.6, 81.4, 125.6, 127.8, 128.3, 138.7, 173.1

calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_4$

C: 66.65, H 7.99; found C: 66.37, H 7.73.

anti- Isopropyl-2,3-dihydroxy-2-phenylpentanoate (**anti-3d**)

^1H NMR: δ =0.96 (t, J =7.4 Hz, 3H, CH_3), 1.14 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.22 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.51 (m, J =2.6, 7.4 Hz, 1H, CH_2), 1.76 (s, 1H, OH), 3.74 (s, 1H, OH), 4.03 (t, J =2.6 Hz, 1H, CHOH), 5.01 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.2 (m, 3H, Ph), 7.5 (m, 2H, Ph). ^{13}C NMR: δ =10.9, 21.5, 21.6, 24.6, 70.8, 77.4, 80.7, 126.1, 128.0, 128.3, 139.3, 174.1.

syn-Isopropyl-3-cyclohexyl-2,3-dihydroxy-2-phenylpropanoate (**syn-3e**)

^1H NMR: δ =1.15 (m, 8H, cHex), 1.18 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.31 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.55 (m, 3H, cHex), 2.33 (d, J =10.9 Hz, 1H, OH), 4.11 (s, 1H, OH), 4.16 (dd, J =2.3, 10.9 Hz, 1H, CHOH), 5.04 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.2 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =21.3, 21.6, 25.9, 26.0, 26.3, 26.4, 31.5, 38.8, 71.0, 78.9, 82.2, 125.6, 127.7, 128.1, 138.9, 174.4.

HRMS (ESI) cal. for $\text{C}_{18}\text{H}_{26}\text{O}_4\text{Na}$: 329.1729 . found: 329.1725.

anti-Isopropyl-3-cyclohexyl-2,3-dihydroxy-2-phenylpropanoate (**anti-3e**)

^1H NMR: δ =1.10 (m, 8H, cHex), 1.17 (d, J = 6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.29 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.50 (m, 3H, cHex), 1.82 (d, J =8.3 Hz, 1H, OH), 3.80 (s, 1H, OH), 4.07 (dd, J =4.1, 8.3 Hz, 1H, CHOH), 5.03 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.2 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =21.4, 21.6, 25.5, 26.2, 26.6, 27.9, 31.3, 40.8, 70.6, 79.2, 81.0, 125.9, 127.8, 128.2, 140.2, 173.3.

syn- Isopropyl-2,3-dihydroxy-2-phenylbutanoate (***syn*-3f**)

^1H NMR: δ =1.22 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.25 (d, J =6.3 Hz, 3H, CH_3), 1.31 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 2.33 (s, 1H, OH), 4.01 (s, 1H, OH), 4.43 (q, J =6.3 Hz, 1H, CHOH), 5.03 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.3 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =17.3, 21.5, 21.6, 70.7, 71.9, 80.6, 126.3, 128.0, 128.2, 139.3, 172.9.

calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_4$ C: 66.53, H 7.61; found C: 65.60, H 7.41.

anti- Isopropyl-2,3-dihydroxy-2-phenylbutanoate (***anti*-3f**)

^1H NMR: δ =0.95 (d, J =6.4 Hz, 3H, CH_3), 1.23 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.33 (d, J =6.2 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 2.51 (s, 1H, OH), 4.13 (s, 1H, OH), 4.50 (q, J =6.4 Hz, 1H, CHOH), 5.04 (spt, J =6.2 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.3 (m, 3H, Ph), 7.6 (m, 2H, Ph). ^{13}C NMR: δ =16.7, 21.5, 21.6, 70.8, 72.3, 81.3, 125.6, 127.8, 128.2, 138.8, 174.0

syn- Isopropyl-2,3-dihydroxy-2,5-diphenylpentanoate (***syn*-3g**)

^1H NMR: δ =0.76 (m, 1H, CH_2), 1.00 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.08 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.49 (m, 1H, CH_2), 2.54 (m, 1H, CH_2), 2.78 (m, 1H, CH_2), 3.93 (s, 1H, OH), 4.11 (dd, 1.8, 10.4 Hz, 1H, CHOH), 4.86 (spt, J =6.3 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.0 (m, 8H, Ph), 7.4 (m, 2H, Ph). ^{13}C NMR: δ =21.4, 21.5, 32.3, 33.5, 70.8, 74.9, 80.9, 125.7, 126.2, 128.3, 128.5, 128.7, 139.4, 173.0

calcd. for $\text{C}_{20}\text{H}_{24}\text{O}_4$ C: 73.15, H 7.37; found C: 72.92, H 7.15.

anti- Isopropyl-2,3-dihydroxy-2,5-diphenylpentanoate (***anti*-3g**)

^1H NMR: δ =1.06 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.19 (d, J =6.3 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.31 (m, 1H, CH_2), 1.83 (m, 1H, CH_2), 2.36 (m, 1H, CH_2), 2.68 (m, 1H, CH_2), 4.09 (s, 1H, OH), 4.21 (dd, 2.3, 10.4 Hz, 1H, CHOH), 4.86 (spt, J =6.3 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 7.0 (m, 8H, Ph), 7.4 (m, 2H, Ph). ^{13}C NMR: δ =21.5, 21.7, 32.1, 32.2, 71.0, 75.6, 81.6, 125.8, 125.9, 128.3, 128.5, 128.7, 138.6, 174.0.

syn- Isopropyl-2,3-dihydroxy-2,5-diphenylpenten-(4)-oate (***syn*-3h**)

mp: 133°C

IR(KBr) ν_{max} : 3470 (OH), 1713 (CO), 1256 (C-O-C)

calcd for $\text{C}_{18}\text{H}_{18}\text{O}_4$: C 72.47; H 6.08; found: C 72.27; H 6.07.

^1H NMR: δ =2.82 (d, J =8.1 Hz, 1H, OH), 3.90 (s, 1H, OCH_3), 4.15 (s, 1H, OH), 5.08 (t, J =6.3 Hz, 1H, CHOH), 6.01 (dd, J =6.3, 16.0 Hz, 1H, CHCHOH), 6.53 (dd, J =2.1, 16.0 Hz, 1H, CH=CH), 7.21 (m, 8H, Ph), 7.67 (m, 2H, Ph).

^{13}C NMR: δ =53.7, 76.7, 81.5, 125.8, 126.6, 127.7, 128.2, 128.4, 133.5, 136.5, 137.8, 174.4.

anti- Isopropyl-2,3-dihydroxy-2,5-diphenylpenten-(4)-oate (***anti*-3h**)

^1H NMR: δ =2.55 (s, 1H, OH), 3.79 (s, 1H, OCH_3), 3.97 (s, 1H, OH), 4.96 (t, J =7.1 Hz, 1H, CHOH), 6.28 (dd, J =7.1, 15.9 Hz, 1H, CHCHOH), 6.70 (d, J =15.9 Hz, 1H, CH=CH), 7.29 (m, 8H, Ph), 7.74 (m, 2H, Ph).

^{13}C NMR: δ =53.4, 77.1, 81.1, 126.0, 126.3, 126.7, 128.1, 128.3, 128.5, 128.6, 134.0, 136.4, 138.2, 173.3.

rac-syn-Methyl-2,3-dihydroxy-2,3-diphenylpropanoate (*rac-syn-5a*)¹

m.p.: 144°C

IR(KBr) ν_{max} : 3487, 3316 (OH), 1710 (CO), 1268 (C-O-C).

¹H NMR: δ =2.94 (d, J=6.8 Hz, 1H, OH), 3.94 (s, 3H, OCH₃), 4.02 (s, 1H, OH), 5.44 (d, J=6.8 Hz, 1H, CHOH), 7.1 (m, 8H, Ph), 7.5 (m, 2H, Ph). ¹³C NMR: δ =53.7, 78.2, 81.9, 125.7, 127.6, 127.8, 127.9, 128.0, 128.1, 137.8, 138.0, 174.6.

calcd. for C₁₆H₁₆O₄ C: 70.57, H 5.92; found C: 70.55, H 6.07.

rac-anti-Methyl-2,3-dihydroxy-2,3-diphenylpropanoate (*rac-anti-5a*)¹

m.p.: 165°C

¹H NMR: δ =2.68 (d, J=6.6 Hz, 1H, OH), 3.67 (s, 3H, OCH₃), 3.7 (s, 1H, OH), 5.45 (d, J=6.6 Hz, 1H, CHOH), 7.3 (m, 8H, Ph), 7.8 (m, 2H, Ph). ¹³C NMR: δ =53.2, 77.7, 81.3, 126.6, 127.6, 128.1, 128.4, 128.5, 138.1, 138.4, 173.1

(*S,S*)-Methyl-2,3-dihydroxy-2,3-diphenylpropanoate (*S,S-5a*)

HPLC: hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm

t_{major} = 29.5 min, t_{minor} = 45.3 min

$[\alpha]_D^{25}$ (93%ee) = - 8.5° (c = 0.5g/100ml, CH₂Cl₂)

(R,R)-Methyl-2,3-dihydroxy-2,3-diphenylpropanoate (**R,R-5a**)

HPLC: hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm
 $t_{\text{major}} = 45.5 \text{ min}$, $t_{\text{minor}} = 29.9 \text{ min}$

$[\alpha]_D^{25}$ (75%ee) = + 7.0° (c = 0.5g/100ml, CH₂Cl₂)

rac-syn-Methyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (*rac-syn-5c*)¹

m.p.: 55°C

IR(KBr) ν_{max} : 3500 (OH), 1726 (CO), 1253 (C-O-C)

calcd. for C₁₃H₁₈O₄

C: 65.53, H 7.61; found C: 65.41, H 7.61.

^1H NMR: δ =0.82 (d, J =6.8 Hz, 3H, CH_3), 0.86 (d, J =6.8 Hz, 3H, CH_3), 1.58 (m, J =6.8, 2.4 Hz, 1H, CH), 2.38 (d, 1H, OH), 3.85 (s, 3H, OCH_3), 4.29 (d, J =2.4 Hz, 1H, CHOH), 7.32 (m, 3H, Ph), 7.65 (m, 2H, Ph). ^{13}C NMR: δ =17.5, 20.8, 30.1, 53.5, 79.8, 81.5, 125.8, 126.5, 128.4, 128.7, 129.2, 139.9, 175.2

rac-anti-Methyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (***rac-anti-5c***)

m.p.: 65°C

^1H NMR: δ =1.0 (d, J =6.8 Hz, 3H, CH_3), 1.05 (d, J =6.8 Hz, 3H, CH_3), 1.9 (m, J =6.8, ~4 Hz, 1H, CH), 3.81 (s, 3H, OCH_3), 4.15 (d, J =4.4 Hz, 1H, CHOH), 7.28 (m, 3H, Ph), 7.68 (m, 2H, Ph). ^{13}C NMR: δ =17.8, 21.1, 30.8, 53.2, 79.3, 81.0, 125.6, 126.0, 128.0, 128.3, 128.4, 140.0, 174.4

(*S,S*)-Methyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (***S,S-5c***)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm
 $t_{\text{major}} = 10.7$ min, $t_{\text{minor}} = 16.8$ min

$[\alpha]_{\text{D}}^{25}$ (72%ee) = - 2.0° ($c = 0.5\text{g}/100\text{ml}$, CH_2Cl_2)

(*R,R*)-Methyl-2,3-dihydroxy-4-methyl-2-phenylpentanoate (***R,R-5c***)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm
 $t_{\text{major}} = 17.1$ min, $t_{\text{minor}} = 11.0$ min

$[\alpha]_D^{25}$ (64%ee) = + 1.8° (c = 0.5g/100ml, CH₂Cl₂)

rac-syn-Methyl-2,3-dihydroxy-2-phenylpentanoate (*rac-syn-5d*)¹

m.p.: 77°C

IR(KBr) $\nu_{\max}$: 3502, 3471 (OH), 1726 (CO), 1252 (C-O-C)

¹H NMR: δ =0.89 (t, J=7.3 Hz, 3H, CH₃), 1.15 (m, 1H, CH₂), 1.29 (m, 1H, CH₂), 2.3 (s, 1H, OH), 3.85 (s, 3H, OCH₃), 4.09 (s, 1H, OH), 4.23 (dd, J=2.5, 10.1 Hz, 1H, CHOH), 7.31 (m, 3H, Ph), 7.62 (m, 2H, Ph). ¹³C NMR: δ =10.5, 23.3, 53.6, 77.7, 81.8, 125.6, 128.0, 128.4, 138.4, 175.1.

calcd. for C₁₂H₁₆O₄

C: 64.27, H 7.19;

found C: 64.15, H 7.27.

rac-anti-Methyl-2,3-dihydroxy-2-phenylpentanoate (*rac-anti*-5d)¹

m.p.: 99°C

¹H NMR: δ=1.04 (t, J=7.4 Hz, 3H, CH₃), 1.42 (m, 1H, CH₂), 1.61 (m, 1H, CH₂), 2.2 (s, 1H, OH), 3.82 (s, 3H, OCH₃), 3.93 (s, 1H, OH), 4.15 (dd, J=2.5, 10.1 Hz, 1H, CHOH), 7.29 (m, 3H, Ph), 7.62 (m, 2H, Ph). ¹³C NMR: δ=10.8, 24.6, 53.3, 77.3, 81.1, 126.1, 128.1, 128.5, 139.2, 173.9

(*S,S*)-Methyl-2,3-dihydroxy-2-phenylpentanoate (*S,S*-5d)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm
t_{major} = 16.0 min, t_{minor} = 19.7 min

[α]_D²⁵ (61%ee) = - 4.3° (c = 0.5g/100ml, CH₂Cl₂)

(*R,R*)-Methyl-2,3-dihydroxy-2-phenylpentanoate (*R,R*-5d)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm
t_{major} = 21.1 min, t_{minor} = 17.1 min

[α]_D²⁵ (56%ee) = + 1.9° (c = 0.5g/100ml, CH₂Cl₂)

rac-syn-Methyl-2,3-dihydroxy-3-cyclohexyl-2-phenylpropanoate (*rac-syn-5e*)

m.p.: 121-123°C

IR(KBr) ν_{max} : 3483 (OH), 1717 (CO), 1252 (C-O-C)

^1H NMR: δ =0.95 (m, 3H, cHex), 1.21 (m, 4H, cHex), 1.52 (m, 4H, cHex), 2.26 (s, 1H, OH), 3.84 (s, 3H, OCH₃), 4.04 (s, 1H, OH), 4.23 (s, 1H, CHOH), 7.32 (m, 3 H, Ph), 7.62 (m, 2H, Ph). ^{13}C NMR: δ =25.9, 26.1, 26.4, 26.6, 31.6, 38.8, 53.7, 79.0, 82.5, 125.6, 127.9, 128.3, 138.9, 175.6

calcd. for C₁₆H₂₂O₄

C: 69.04, H 7.97;

found C: 68.84, H 7.75.

rac-anti-Methyl-2,3-dihydroxy-3-cyclohexyl-2-phenylpropanoate (*rac-anti-5e*)

m.p.: 142-144°C

^1H NMR: δ =1.16 (m, 3H, cHex), 1.52 (m, 8H, cHex), 3.69 (s, 1H, OH), 3.81 (s, 1H, OCH₃), 4.12 (s, 1H, CHOH), 7.31 (m, 3 H, Ph), 7.68 (m, 2H, Ph). ^{13}C NMR: δ =25.9, 26.0, 26.3, 26.4, 31.5, 38.7, 53.7, 79.0, 82.5, 125.5, 127.9, 128.3, 138.6, 175.4

(S,S)-Methyl-2,3-dihydroxy-3-cyclohexyl-2-phenylpropanoate (**S,S-5e**)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm

$t_{\text{major}} = 11.9 \text{ min}$, $t_{\text{minor}} = 20.1 \text{ min}$

$[\alpha]_{\text{D}}^{25}$ (58%ee) = -1.9° ($c = 0.5\text{g}/100\text{ml}$, CH_2Cl_2)

(R,R)-Methyl-2,3-dihydroxy-3-cyclohexyl-2-phenylpropanoate (**R,R-5e**)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm

$t_{\text{major}} = 19.7 \text{ min}$, $t_{\text{minor}} = 11.8 \text{ min}$

$[\alpha]_{\text{D}}^{25}$ (48%ee) = $+1.0^{\circ}$ ($c = 0.5\text{g}/100\text{ml}$, CH_2Cl_2)

rac-syn-Methyl-2,3-dihydroxy-2-phenylhexanoate (**rac-syn-5i**)

m.p.: 92-94°C

IR(KBr) ν_{max} : 3501 (OH), 1721 (CO), 1244 (C-O-C)

^1H NMR: $\delta=0.81$ (t, $J=7.2$ Hz, 3H, CH_2CH_3), 1.05 (m, 1H, CH_2), 1.27 (m, 2H, CH_2), 1.46 (m, 1H, CH_2), 2.03 (d, $J=10.0$ Hz, 1H, OH), 3.86 (s, 3H, OCH_3), 3.98 (s, 1H, OH), 4.33 (t, 8.8 Hz, 1H, CHOH), 7.30 (m, 3H, Ph), 7.61 (m, 2H, Ph)
 ^{13}C NMR: $\delta=14.0, 19.3, 33.7, 53.3, 75.5, 81.0, 126.2, 128.2, 128.4, 139.0, 173.9$

calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_4$ C: 65.53, H 7.61; found C: 65.57, H 7.54.

rac-anti-Methyl-2,3-dihydroxy-2-phenylhexanoate (*rac-anti-5i*)

m.p.: 99-101°C

^1H NMR: $\delta=0.94$ (t, $J=7.2$ Hz, 3H, CH_2CH_3), 1.26 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 1.85 (d, $J=7.3$ Hz, 1H, OH), 3.74 (s, 1H, OH), 3.83 (s, 3H, OCH_3), 4.23 (dt, $J=2.1, 9.6$ Hz, 1H, CHOH), 7.31 (m, 3H, Ph), 7.61 (m, 2H, Ph). ^{13}C NMR: $\delta=14.0, 19.3, 33.7, 53.3, 75.5, 81.0, 126.2, 128.2, 128.4, 139.0, 173.9$

(*S,S*)-Methyl-2,3-dihydroxy-2-phenylhexanoate (*S,S-5i*)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm

$t_{\text{major}} = 14.2 \text{ min}$, $t_{\text{minor}} = 22.9 \text{ min}$.

$[\alpha]_{\text{D}}^{25}$ (67%ee) = - 4.2° ($c = 0.5\text{g}/100\text{ml}$, CH_2Cl_2)

(R,R)-Methyl-2,3-dihydroxy-2-phenylhexanoate (**R,R-5i**)

HPLC : hexane (96 Vol.%) / isopropanol (4 Vol.%), 1mL/min, 220 nm

$t_{\text{major}} = 21.5 \text{ min}$, $t_{\text{minor}} = 13.7 \text{ min}$

$[\alpha]_{\text{D}}^{25}$ (66%ee) = + 3.7° ($c = 0.5\text{g}/100\text{ml}$, CH_2Cl_2)

rac-syn-Methyl-2,3-dihydroxy-2-phenyl-3-(4-bromophenyl)-propanoate (**rac-syn-5k**)²

mp.: 158-160°C

IR(KBr) $\nu_{\max}$: 3479 (OH), 1715 (CO), 1259 (C-O-

calcd. for C ₁₆ H ₁₅ BrO ₄	C: 54.72	H: 4.31	Br: 22.75
found	C: 54.61	H: 4.28	Br: 22.48

¹H NMR: δ = 2.92 (s, 1H, OH), 3.92 (s, 3H, OCH₃), 4.00 (s, 1H, OH), 5.38 (s, 1H, CHOH), 6.94 (m, 10H, Ph). ¹³C NMR: δ = 53.8, 78.1, 81.8, 125.7, 128.2, 128.3, 129.6, 130.6, 130.7, 137.1, 137.5, 175.2.

rac-anti-Methyl-2,3-dihydroxy-2-phenyl-3-(4-bromophenyl)-propanoate (*rac-anti*-5k)

mp: 140-142°C

¹H NMR: δ = 2.65 (d, J=6.4 Hz, 1H, OH), 3.67 (s, 1H, OH), 3.69 (s, 3H, OCH₃), 5.36 (d, J=6.4 Hz, 1H, CHOH), 7.24 (m, 10H, Ph). ¹³C NMR: δ = 53.3, 77.8, 81.1, 126.4, 127.6, 128.1, 128.5, 129.5, 131.1, 137.3, 137.8, 172.9.

(S,S)-Methyl-2,3-dihydroxy-2-phenyl-3-(4-bromophenyl)-propanoate (**S,S-5k**)

HPLC: hexane (96 Vol.%) / isopropanol (4 Vol.%), 1ml/min, 220 nm, t_{major} = 31.5 min, t_{minor} = 53.2 min

$[\alpha]_{\text{D}}^{25}$ (92%ee) = - 30.3° (c = 0.5g/100ml, CH_2Cl_2)

Literature and References

- (1) (a) Clerici, A., Porta, O. *J. Org. Chem.* **1982**, 47, 2852-2856. (b) Clerici, A., Clerici, L., Malpezzi, L., Porta, O. *Tetrahedron*, **1995**, 51, 13385-13400.
- (2) Clerici, A.; Pastori, N.; Porta, O. *J. Org. Chem.* **2005**, 70, 4174 - 4176
- (3) Crystallographic data of compound **3c** (CCDC 621427) and **5k** (CCDC 621428) have been deposited at the Cambridge Crystal Data Centre. This

Material can be obtained upon request to CCDC, 12 Union Road, Cambridge, 1EZ, UK (<http://www.ccdc.cam.ac.uk> email: deposit@ccdc.cam.ac.uk).

The structure was refined with SHELX97 (Sheldrick, G.M.; programme for crystal structure refinement, Universität Göttingen.)