Supporting Information

A Simple Method for the Preparation of Esters from Grignard Reagents and Alkyl 1-Imidazolecarboxylates

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General Remarks. All Grignard reagents were commercially available. The spectroscopic data of compounds **1f**,¹ **2a**,² **2b**,³ **2e**,⁴ **4a**,⁵ **4c**,⁶ **4d**,⁷ **4i**,⁸ **4j**,⁷ **4k**,⁹ **4m**,¹⁰ **6**,¹¹ were in agreement with the literature.

General Procedure for the preparation of 1-imidazolecarboxylates **2 (GP1).** CDI (3 equiv) was added with stirring to alcohol **1** (1 equiv) in dry THF ($c = 0.7 \text{ mmol mL}^{-1}$). After 14 h at 23 °C, the mixture was diluted with Et₂O (3.5 mL mmol⁻¹), washed with H₂O (2 x 1.8 mL mmol⁻¹), dried (MgSO₄) and rotary evaporated to afford the corresponding 1-imidazolecarboxylate **2**.

General Procedure for the addition of Grignard reagents **3 to 1-imidazolecarboxylates **2** (GP2).** The Grignard reagent **3** (1 equiv) was added dropwise to the 1-imidazolecarboxylate **2** (1 equiv) in dry THF ($c = 0.14 \text{ mmol mL}^{-1}$) at 0 °C. The reaction mixture was warmed to room temperature over 14 h, poured on ice, acidified with hydrochloric acid (1 M) and extracted with Et₂O (3 x 10 mL mmol⁻¹). The combined organic layers were dried (MgSO₄) and rotary evaporated to afford the corresponding ester **4**.

(*R*)-3-(*tert*-Butyldimethylsilanyloxy)butanol (1f**).** Imidazole (453 mg, 6.66 mmol) and DMAP (10 mg, 82 μmol) were added to (*R*)-1,3-butandiol (300 mg, 3.33 mmol) in dry DMF (8.0 mL). The mixture was cooled to 0 °C and *t*-BuMe₂SiCl (552 mg 3.66 mmol) in dry CH₂Cl₂ (4.0 mL) was added. The mixture was allowed to warm to 23 °C over 24 h, diluted with H₂O (40 mL) and extracted with Et₂O (5 x 10 mL). The combined organic layers were dried (Na₂SO₄), rotary evaporated and chromatographed (SiO₂, cyclohexane:EtOAc 10:1) to afford silyl ether **1f** (527 mg, 77%) as a colorless oil: R_f 0.10 (cyclohexane:EtOAc 10:1) ¹H NMR (300 MHz, CDCl₃) δ 0.05 (s, 6 H), 0.87 (s, 9 H), 1.16 (d, $J = 6.3$ Hz, 3 H), 1.6 – 1.66 (m, 2 H), 3.38 (s, 1 H), 3.74 – 3.90 (m, 2 H), 3.95 – 4.03 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ –5.8, –5.7, 17.9, 23.1, 25.6, 40.1, 62.1, 67.3.

Benzyl 1-imidazolecarboxylate (2b**).** According to **GP1**, CDI (3.89 g, 24.0 mmol) was allowed to react with alcohol **1b** (875 mg, 8.09 mmol) in dry THF (12.0 mL). After aqueous work up, 1-imidazolecarboxylate **2b** (1.36 g, 83%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.39 (s, 2 H), 7.03 (s, 1 H), 7.39 – 7.40 (m, 6 H), 8.12 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 69.8,

117.1, 128.7, 128.8, 129.1, 130.7, 133.9, 137.1, 148.6; LRMS (CI, NH₃) 203 (100%) (M + H)⁺, 159 (29%), 108 (12%), 69 (13%).

4-Phenyl-2-butyl 1-imidazolecarboxylate (2c). According to **GP1**, CDI (1.62 g, 9.99 mmol) was allowed to react with alcohol **1c** (500 mg, 3.33 mmol) in dry THF (5.0 mL). After aqueous work up, the title compound **2c** (693 mg, 85%) was obtained as a colorless oil: IR (neat) 1757, 1471, 1392, 1290, 1241, 1178 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.46 (d, *J* = 6.3 Hz, 3 H), 1.96 – 2.07 (m, 1 H), 2.10 – 2.22 (m, 1 H), 2.76 (t, *J* = 7.3 Hz, 2 H), 5.14 – 5.20 (m, 1 H), 7.09 (s, 1 H), 7.18 – 7.32 (m, 5 H), 7.40 (s, 1 H), 8.10 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 19.9, 31.6, 37.1, 75.9, 117.0, 126.2, 128.2, 128.5, 130.4, 137.0, 140.6, 148.2; LRMS (CI, NH₃) 245 (100%) (M + H)⁺, 132 (8%), 108 (10%), 69 (18%); HRMS (CI, NH₃) (M + H)⁺ calcd 245.1290; found 245.1283. Anal. calcd for C₁₄H₁₆N₂O₂: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.96; H, 6.68; N, 11.48.

3-Pentyl 1-imidazolecarboxylate (2d). According to **GP1**, CDI (1.10 g, 6.79 mmol) was allowed to react with alcohol **1d** (250 mg, 2.84 mmol) in dry THF (5.0 mL). After aqueous work up, the 1-imidazolecarboxylate **2d** (471 mg, 91%) was obtained as a colorless oil: IR (neat) 1756, 1469, 1393, 1289, 1243, 1180 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.93 (t, *J* = 7.6 Hz, 6 H), 1.66 – 1.76 (m, 4 H), 4.88 – 4.97 (m, 1 H), 7.03 (s, 1 H), 7.39 (s, 1 H), 8.10 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 9.3, 26.2, 82.1, 117.0, 130.4, 136.9, 148.5; LRMS (CI, NH₃) 200 (19%) (M + NH₄)⁺, 183 (100%) (M + H)⁺, 69 (38%); HRMS (CI, NH₃) (M + H)⁺ calcd 183.1134; found 183.1137.

Cyclohexyl 1-imidazolecarboxylate (2e). According to **GP1**, CDI (1.540 g, 9.50 mmol) was allowed to react with alcohol **1e** (381 mg, 3.80 mmol) in dry THF (6.0 mL). After aqueous work up, the 1-imidazolecarboxylate **2e** (612 mg, 83%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 1.29 – 1.48 (m, 3 H), 1.54 – 1.65 (m, 3 H), 1.73 – 1.75 (m, 2 H), 1.93 – 1.95 (m, 2 H), 4.94 – 5.00 (m, 1

H), 7.03 (s, 1 H), 7.39 (s, 1 H), 8.10 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 23.1, 24.8, 31.0, 77.2, 116.8, 130.1, 136.7, 147.8; LRMS (CI, NH_3) 212 (9%) ($\text{M} + \text{NH}_4$) $^+$, 195 (100%) ($\text{M} + \text{H}$) $^+$, 123 (4%), 69 (15%).

(*R*)-4-(*tert*-butyldimethylsilyloxy)-2-butyl 1-imidazolecarboxylate (2f). According to **GP1**, CDI (349 mg, 2.15 mmol) was allowed to react with alcohol **1f** (176 mg, 0.861 mmol) in dry THF (5.0 mL). After aqueous work up, the 1-imidazolecarboxylate **2f** (237 mg, 92%) was obtained as a colorless oil: $[\alpha_D]^{25} = -48.7$ ($c = 1.35$ in CH_2Cl_2); IR (neat) 1761, 1393, 1290, 1241, 1093 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ -0.03 (s, 3 H), -0.02 (s, 3 H), 0.83 (s, 9 H), 1.41 (d, $J = 6.3$ Hz, 3 H), 1.77 – 1.98 (m, 1 H), 1.90 – 2.01 (m, 1 H), 3.68 (t, $J = 6.1$ Hz, 2 H), 5.22 – 5.32 (m, 1 H), 7.04 (s, 1 H), 7.39 (s, 1 H), 8.11 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ -5.8, 18.0, 19.9, 25.6, 38.4, 58.8, 73.8, 116.9, 130.3, 136.8, 150.0; LRMS (CI, NH_3) 299 (100%) ($\text{M} + \text{H}$) $^+$, 241 (3%), 197 (3%), 142 (3%); HRMS (CI, NH_3) ($\text{M} + \text{H}$) $^+$ calcd 299.1791; found 299.1788. Anal. calcd for $\text{C}_{14}\text{H}_{26}\text{N}_2\text{O}_3\text{Si}$: C, 56.34; H, 8.78; N, 9.39. Found: C, 56.33; H, 8.84; N, 9.35.

Methyl (3*R*)-3-(imidazole-1-carboxy)-butanoate (2g). According to **GP1**, CDI (4.12 g, 25.4 mmol) was allowed to react with alcohol **1g** (1.00 g, 8.47 mmol) in dry THF (12.0 mL). After aqueous work up, the 1-imidazolecarboxylate **2g** (1.54 g, 86%) was obtained as a colorless oil: $[\alpha_D]^{25} = -31.7$ ($c = 1.35$ in CH_2Cl_2); IR (neat) 1759, 1740, 1394, 1318, 1291, 1243, 1177 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.46 (d, $J = 6.3$ Hz, 3 H), 2.64 (dd, $J = 16.2, 5.2$ Hz, 1 H), 2.79 (dd, $J = 16.2, 7.8$ Hz, 1 H), 3.66 (s, 3 H), 5.41 – 5.52 (m, 1 H), 7.03 (s, 1 H), 7.37 (s, 1 H), 8.08 (s, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 19.7, 40.2, 52.0, 72.1, 117.1, 130.5, 137.0, 147.8, 169.9; LRMS (CI, NH_3) 213 (100%) ($\text{M} + \text{H}$) $^+$, 69 (8%); HRMS (CI, NH_3) calcd 213.0875; found 213.0878. Anal. calcd for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_4$: C, 50.94; H, 5.70; N, 13.20. Found: C, 51.02; H, 5.76; N, 13.27.

3-Phenyl-1-propyl pentanoate (4b). According to **GP2**, Grignard reagent **3b** (2 M; 0.40 mL, 0.8 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (150 mg, 0.651 mmol) in dry THF (5.0 mL). After aqueous work up, the crude product was purified by Kugelrohr distillation (140 – 150 °C, 2 mbar) to afford the ester **4b** (120 mg, 85%) as a colorless oil: IR (neat) 1735, 1455, 1257, 1173, 1108 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.93 (t, J = 7.3 Hz, 3 H), 1.32 – 1.41 (m, 2 H), 1.58 – 1.66 (m, 2 H), 1.93 – 2.00 (m, 2 H), 2.30 – 2.34 (m, 2 H), 2.67 – 2.71 (m, 2 H), 4.10 (t, J = 6.5 Hz, 2 H), 7.18 – 7.22 (m, 3 H), 7.26 – 7.31 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 13.7, 22.4, 27.0, 30.2, 32.1, 34.0, 63.5, 125.9, 128.3, 128.4, 141.2, 173.9; LRMS (CI, NH_3) 238 (100%) ($\text{M} + \text{NH}_4$) $^+$, 135 (10%), 118 (86%); HRMS ($\text{M} + \text{NH}_4$) $^+$ calcd 238.1807; found 238.1805. Anal. calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.33; H, 9.15. Found: C, 76.27; H, 9.05.

3-Phenyl-1-propyl 2-methylpropanoate (4c). According to **GP2**, Grignard reagent **3c** in THF (2 M; 0.37 mL, 0.74 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (170 mg, 0.738 mmol) in dry THF (5.0 mL). After aqueous work up, the ester **4c** (146 mg, 96%) was obtained as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 1.20 (d, J = 6.9 Hz, 6 H), 1.94 – 2.03 (m, 2 H), 2.63 (sept., J = 6.9 Hz, 1 H), 2.71 (t, J = 7.6 Hz, 2 H), 4.11 (t, J = 6.6 Hz, 2 H), 7.20 – 7.34 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3) δ 18.9, 30.2, 32.0, 33.9, 63.4, 125.9, 128.3, 128.3, 141.1, 177.0; LRMS (CI, NH_3) 224 (100%) ($\text{M} + \text{NH}_4$) $^+$, 207 (4%) ($\text{M} + \text{H}$) $^+$, 135 (3%), 118 (10%).

3-Phenyl-1-propyl 2,2-dimethylpropanoate (4d). According to **GP2**, Grignard reagent **3d** in THF (1 M; 0.77 mL, 0.77 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (160 mg, 0.696 mmol) in dry THF (5.0 mL). After aqueous work up, the ester **4d** (144 mg, 94%) was obtained as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 1.24 (s, 9 H), 1.93 – 2.03 (m, 2 H), 2.72 (t, J = 7.3 Hz, 2 H), 4.10 (t, J = 6.3 Hz, 2 H), 7.19 – 7.33 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3) δ 27.1, 30.2, 32.0, 38.6, 63.4, 125.9,

128.3, 141.1, 178.4; LRMS (CI, NH₃) 238 (100%) (M + NH₄)⁺, 221 (24%) (M + H)⁺, 198 (17%), 135 (11%), 118 (50%).

3-Phenyl-1-propyl 4-dimethylaminobenzoate (4e). According to **GP2**, Grignard reagent **3e** in THF (0.4 M; 1.7 mL, 0.85 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (175 mg, 0.760 mmol) in dry THF (3.0 mL). After aqueous work up, the ester **4e** (201 mg, 94%) was obtained as a colorless oil: IR (neat) 1700, 1607, 1528, 1452, 1368, 1278, 1183 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.06 – 2.15 (m, 2 H), 2.81 (t, *J* = 7.6 Hz, 2 H), 3.07 (s, 6 H), 4.31 (t, *J* = 6.3 Hz, 2 H), 6.68 – 6.71 (m, 2 H), 7.23 – 7.34 (m, 5 H), 7.93 – 7.96 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 30.4, 32.2, 39.9, 63.3, 110.5, 117.0, 125.7, 128.2, 128.3, 131.1, 141.3, 153.1, 166.9; LRMS (CI, NH₃) 284 (100%) (M + H)⁺, 231 (14%), 165 (16%), 148 (6%); HRMS (M + H)⁺ calcd 284.1651; found 284.1642. Anal. calcd for C₁₈H₂₁NO₂: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.37; H, 7.45; N, 4.86.

3-Phenyl-1-propyl 2,4-dimethoxybenzoate (4f). According to **GP2**, Grignard reagent **3f** in THF (0.5 M; 1.7 mL, 0.85 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (187 mg, 0.812 mmol) in dry THF (5.0 mL). After aqueous work up, the crude product was chromatographed (SiO₂, cyclohexane:EtOAc 5:1) to afford the ester **4f** (158 mg, 65%) as a colorless oil: R_f 0.16 (cyclohexane:EtOAc 5:1); IR (neat) 1719, 1694, 1608, 1436, 1272, 1252, 1211 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.04 – 2.13 (m, 2 H), 2.78 – 2.83 (m, 2 H), 3.88 (s, 3 H), 3.89 (s, 3 H), 4.29 (t, *J* = 6.3 Hz, 2 H), 6.51 – 6.53 (m, 2 H), 7.23 – 7.34 (m, 5 H), 7.84 – 7.88 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 30.4, 32.3, 55.4, 55.9, 63.6, 98.9, 104.5, 112.5, 125.9, 128.3, 128.4, 133.7, 141.4, 161.3, 164.2, 165.6; LRMS (CI, NH₃) 301 (100%) (M + H)⁺, 182 (11%), 165 (5%), 118 (3%); HRMS (M + H)⁺ calcd 301.1440; found 301.1438. Anal. calcd for C₁₈H₂₀O₄: C, 71.98; H, 6.71. Found: C, 72.04; H, 6.64.

3-Phenyl-1-propyl 3-thiophenecarboxylate (4g). According to **GP2**, Grignard reagent **3g** in THF (0.3 M; 2.1 mL, 0.63 mmol) was allowed to react with 1-imidazolecarboxylate **2a** (135 mg, 0.586 mmol) in dry THF (1.6 mL). After aqueous work up, the crude product was chromatographed (SiO₂, cyclohexane:EtOAc 10:1) to afford ester **4g** (115 mg, 80%) as a colorless oil: *R*_f 0.47 (cyclohexane:EtOAc 5:1); IR (neat) 1728, 1723, 1602, 1523, 1410, 1273, 1188 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.96 – 2.10 (m, 2 H), 2.67 – 2.77 (m, 2 H), 4.27 (t, *J* = 6.6 Hz, 2 H), 7.17 – 7.29 (m, 6 H), 7.49 – 7.50 (m, 1 H), 8.05 – 8.06 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 30.3, 32.3, 64.0, 126.0, 127.9, 128.4, 132.6, 133.7, 141.2, 162.8; LRMS (CI, NH₃) 264 (100%) (*M* + NH₄)⁺, 254 (16%), 135 (12%), 118 (37%); HRMS (*M* + NH₄)⁺ calcd 247.0790; found 247.0792. Anal. calcd for C₁₄H₁₄O₂S: C, 68.26; H, 5.73. Found: C, 68.28; H, 5.71.

Benzyl benzoate (4i). According to **GP2**, Grignard reagent **3a** in THF (2 M; 0.85 mL, 1.7 mmol) was allowed to react with 1-imidazolecarboxylate **2b** (287 mg, 1.42 mmol) in dry THF (10.0 mL). After aqueous work up, the ester **4i** (282 mg, 94%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.35 (s, 2 H), 7.32 – 7.44 (m, 5 H), 7.51 – 7.59 (m, 1 H), 8.05 – 8.07 (m, 2 H), ¹³C NMR (75 MHz, CDCl₃) δ 66.5, 127.9, 128.0, 128.2, 128.4, 129.5, 129.9, 132.9, 135.9, 166.2; LRMS (CI, NH₃) 230 (100%) (*M* + NH₄)⁺, 213 (*M* + H)⁺ (12%), 203 (13%), 108 (26%) 105 (15%). Anal. calcd for C₁₄H₁₂O₂: C, 79.22; H, 5.70. Found: C, 79.23; H, 5.72.

4-Phenyl-2-butyl benzoate (4j). According to **GP2**, Grignard reagent **3a** in THF (2 M; 0.28 mL, 0.56 mmol) was allowed to react with 1-imidazolecarboxylate **2c** (132 mg, 0.54 mmol) in dry THF (5.0 mL). After aqueous work up, the ester **4j** (126 mg, 92%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 1.41 (d, *J* = 6.0 Hz, 3 H), 1.88 – 2.03 (m, 1 H), 2.06 – 2.19 (m, 1 H), 2.67 – 2.85 (m, 2 H), 5.15 – 5.25 (m, 1 H), 7.20 – 7.32 (m, 5 H), 7.45 – 7.50 (m, 2 H), 7.57 – 7.61 (m, 1 H), 8.06 – 8.09 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 20.1, 31.8, 37.7, 71.1, 125.9, 128.3, 128.4, 129.5, 130.7, 132.8, 141.5,

166.1; LRMS (CI, NH₃) 272 (100%) (M + NH₄)⁺, 255 (2%) (M + H)⁺, 245 (25%), 132 (20%). Anal. calcd for C₁₇H₁₈O₂: C, 80.28; H, 7.13. Found: C, 80.16; H, 7.05.

4-Phenyl-2-butyl 2-methylpropanoate (4k). According to **GP2**, Grignard reagent **3c** in THF (2 M; 0.25 mL, 0.50 mmol) was allowed to react with 1-imidazolecarboxylate **2c** (108 mg, 0.442 mmol) in dry THF (4.0 mL). After aqueous work up, the ester **4k** (84 mg, 86%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 1.17 (d, *J* = 6.9 Hz, 3 H), 1.18 (d, *J* = 6.9 Hz, 3 H), 1.18 (d, *J* = 6.3 Hz, 3 H), 1.74 – 1.90 (m, 1 H), 1.19 – 2.00 (m, 1 H), 2.48 – 2.57 (m, 1 H), 2.60 – 2.73 (m, 2 H), 4.88 – 4.99 (m, 1 H), 7.16 – 7.31 (m, 5 H); ¹³C NMR (75 MHz, CDCl₃) δ 18.9, 19.1, 20.0, 31.8, 34.2, 37.7, 70.0, 125.9, 128.3, 128.4, 141.6, 176.7; LRMS (CI, NH₃) 238 (100%) (M + NH₄)⁺, 221 (6%) (M + H)⁺, 132 (41%). Anal. calcd for C₁₄H₂₀O₂: C, 76.33; H, 9.15. Found: C, 76.25; H, 8.99.

3-Pentyl benzoate (4l). According to **GP2**, Grignard reagent **3a** in THF (2 M; 0.8 mL, 1.6 mmol) was allowed to react with 1-imidazolecarboxylate **2d** (243 mg, 1.33 mmol) in dry THF (10.0 mL). After aqueous work up, the ester **4l** (234 mg, 92%) was obtained as a colorless oil: IR (neat) 1716, 1451, 1274, 1175, 1101 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.93 (t, *J* = 7.6 Hz, 6 H), 1.64 – 1.73 (m, 4 H), 4.95 – 5.03 (m, 1 H), 7.32 – 7.44 (m, 3 H), 7.50 – 7.58 (m, 2 H), 8.05 – 8.08 (m, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 9.6, 26.5, 77.2, 128.2, 129.5, 130.8, 132.6, 166.4; LRMS (CI, NH₃) 210 (100%) (M + NH₃)⁺, 193 (8%) (M + H)⁺, 154 (32%), 139 (14%), 105 (79%); HRMS (CI, NH₃) (M + NH₄)⁺ calcd 210.1494; found 210.1488.

Cyclohexyl benzoate (4m). According to **GP2**, Grignard reagent **3a** in THF (2 M; 0.41 mL, 0.82 mmol) was allowed to react with 1-imidazolecarboxylate **2e** (157 mg, 0.808 mmol) in dry THF (5.0 mL). After aqueous work up, the ester **4m** (156 mg, 95%) was obtained as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 1.29 – 1.58 (m, 6 H), 1.75 – 1.89 (m, 4 H), 4.97 – 5.03 (m, 1 H), 7.32 – 7.43 (m, 2 H),

7.49 – 7.54 (m, 1 H), 8.01 – 8.03 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 23.6, 25.4, 31.5, 72.9, 128.2, 129.4, 130.9, 132.6, 165.9; LRMS (CI, NH_3) 222 (100%) ($\text{M} + \text{NH}_4$) $^+$, 205 (45%) ($\text{M} + \text{H}$) $^+$, 166 (13%), 105 (18%).

(2R)-4-(tert-Butyldimethylsilyloxy)-butyl benzoate (4n). According to **GP2**, Grignard reagent **3a** in THF (2 M; 0.37 mL, 0.74 mmol) was allowed to react with 1-imidazolecarboxylate **2f** (211 mg, 0.707 mmol) in dry THF (5.0 mL). After aqueous work up, the crude product was chromatographed (SiO_2 , cyclohexane:EtOAc 20:1) to afford the ester **4n** (195 mg, 89%) as a colorless oil: R_f 0.63 (cyclohexane:EtOAc 5:1); $[\alpha_D]^{25} = -41.9$ ($c = 1.55$ in CH_2Cl_2); IR (neat) 1720, 1471, 1451, 1276, 1258, 1096; ^1H NMR (500 MHz, CDCl_3) δ -0.02 (s, 3 H), -0.01 (s, 3 H), 0.84 (s, 9 H), 1.35 (d, $J = 6.1$ Hz, 3 H), 1.79 – 1.85 (m, 1 H), 1.92 – 1.98 (m, 1 H), 3.69 – 3.71 (m, 2 H), 5.21 – 5.28 (m, 1 H), 7.38 – 7.42 (m, 2 H), 7.50 – 7.53 (m, 1 H), 7.99 – 8.01 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ -5.5, -5.4, 18.2, 20.4, 25.9, 39.1, 59.4, 69.1, 128.3, 129.5, 130.8, 132.7, 166.0; LRMS (CI, NH_3) 309 (100%) ($\text{M} + \text{H}$) $^+$, 251 (17%), 196 (23%), 179 (24%), 177 (28%), 132 (10%), 105 (23%); HRMS ($\text{M} + \text{H}$) $^+$ calcd 309.1886; found 309.1883. Anal. calcd for $\text{C}_{17}\text{H}_{28}\text{O}_3\text{Si}$: C, 66.19; H, 9.15. Found: C, 66.16; H, 9.20.

Methyl (3R)-3-(benzoyloxy)butanoate (4o). According to **GP2**, Grignard reagent **3a** (0.90 mL, 1.80 mmol, 2 M in THF) was allowed to react with 1-imidazolecarboxylate **2g** (360 mg, 1.70 mmol) in dry THF (12.0 mL). After aqueous work up, the crude product was purified by Kugelrohr distillation (100 – 120 °C, 2 mbar) to afford the ester **4o** (244 mg, 65%) as a colorless oil: R_f 0.13 (cyclohexane:EtOAc 5:1); $[\alpha_D]^{25} = -30.5$ ($c = 1.65$ in CH_2Cl_2); IR (neat) 1740, 1719, 1451, 1314, 1276, 1199, 1113; ^1H NMR (300 MHz, CDCl_3) δ 1.41 (d, $J = 6.3$ Hz, 3 H), 2.61 (dd, $J = 15.5, 5.8$ Hz, 1 H), 2.78 (dd, $J = 15.5, 7.3$ Hz, 1 H), 3.65 (s, 3 H), 5.44 – 5.54 (m, 1 H), 7.38 – 7.43 (m, 2 H), 7.50 – 7.55 (m, 1 H), 7.98 – 8.00 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 20.0, 40.8, 51.8, 68.0, 128.3, 129.6, 130.4, 132.9, 165.7, 170.7; LRMS (CI, NH_3) 240 ($\text{M} + \text{NH}_4$) $^+$, (100%), 223 ($\text{M} + \text{H}$) $^+$, 176 (12%), 139 (7%), 122 (6%), 105 (20%);

HRMS ($M + H$)⁺ calcd 223.0970; found 223.0975. Anal. calcd for C₁₂H₁₄O₄: C, 64.85; H, 6.35. Found: C, 64.90; H, 6.28.

Preparation of Grignard reagent **3h** and ester **4h**

The Grignard reagent **3h** was prepared starting from the commercially available bromide **5**. Lithium-halogen exchange, followed by the addition of *R*-propylene oxide gave alcohol **6** (80%).¹² The reaction of arene **6** with NIS gave iodide **7** (86%),¹³ which was subsequently protected by *t*-butyldimethylsilylation to give ether **8** (82%).¹⁴ Conversion of iodide **8** under Knochel conditions¹⁵ gave the Grignard reagent **3h**, which was used directly in the addition to 1-imidazolecarboxylate **2a** to afford ester **4h**.

(a) i) *t*-BuLi, Et₂O, −78 °C, 1 h, ii) *R*-propylene oxide, −78 °C to −30 °C, 5 h, 23 °C, 30 min; (b) NIS, CCl₄, 45 – 50 °C, 16 h; (c) *t*-BuMe₂SiOTf, pyridine, CH₂Cl₂, 5 h, 0 °C to 23 °C; (d) i) *i*PrMgCl, THF, −30 °C, 2 h, ii) **2a**, THF, 0 °C to 50 °C for 10 min; 16 h, 23 °C.

1,3-Dimethoxy-5-(2*R*-hydroxypropyl)benzene (6). *t*BuLi in pentane (1.7 M; 31.0 mL, 52.7 mmol) was added dropwise to **5** (5.00 g 23.0 mmol) in dry THF (60 mL) at $-78\text{ }^{\circ}\text{C}$. After the mixture was stirred for 1 h, *R*-propylene oxide (1.85 g, 31.9 mmol) was added and the mixture warmed to $-30\text{ }^{\circ}\text{C}$ over 5 h. The mixture was stirred for another 30 min at $23\text{ }^{\circ}\text{C}$, poured onto a mixture of saturated aqueous NH_4Cl (50 mL) and ice (50 g), extracted with Et_2O (4 x 50 mL), dried (MgSO_4) and rotary evaporated. The crude product was chromatographed (SiO_2 , cyclohexane:EtOAc 2:1) to afford alcohol **6** (3.89 g, 86%) as a colorless oil: R_f (cyclohexane :EtOAc 1:1) = 0.26; ^1H NMR (300 MHz, CDCl_3) δ 1.22 (d, $J = 6.0\text{ Hz}$, 3 H), 1.61 (s, 1 H), 2.58 (dd, $J = 13.6, 8.3\text{ Hz}$, 1 H), 2.71 (dd, $J = 13.2, 4.6\text{ Hz}$, 1 H), 3.75 (s, 6 H), 3.93 – 4.04 (m, 1 H), 6.32 – 6.34 (m, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.8, 46.1, 55.3, 68.7, 98.4, 107.3, 140.8, 160.9; LRMS (CI, NH_3) 197 (100%) ($\text{M} + \text{H}$) $^+$, 179 (7%), 152 (18%), 139 (3%).

1,3-Dimethoxy-5-(2*R*-hydroxypropyl)-6-iodobenzene (7). NIS (292 mg, 1.30 mmol) and $\text{TsOH}\cdot\text{H}_2\text{O}$ (20 mg, 120 μmol) were added to alcohol **6** (240 mg, 1.22 mmol) in CCl_4 (10 mL). The reaction mixture was stirred for 16 h at $45\text{--}50\text{ }^{\circ}\text{C}$, diluted with CH_2Cl_2 (10 mL), washed with H_2O (2 x 15 mL), dried (MgSO_4) and rotary evaporated. The crude product was chromatographed (SiO_2 , cyclohexane:EtOAc 5:1) to afford the title compound **7** (196 mg, 82%) as a colorless oil: R_f 0.06 (cyclohexane:EtOAc 5:1); $[\alpha_D]^{25} = -28.3$ ($c = 1.10$ in CH_2Cl_2); IR (neat) 1579, 1454, 1324, 1205, 1160 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.26 (d, $J = 6.3\text{ Hz}$, 3 H), 1.57 (d, $J = 3.0\text{ Hz}$, 1 H), 2.81 (dd, $J = 13.2, 8.3\text{ Hz}$, 1 H), 2.97 (dd, $J = 13.5, 4.3\text{ Hz}$, 1 H), 3.77 (s, 3 H), 3.82 (s, 3 H), 4.06 – 4.11 (m, 1 H, CH), 6.30 (d, $J = 2.6\text{ Hz}$, 1 H), 6.48 (d, $J = 2.3\text{ Hz}$, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.8, 50.2, 55.4, 56.4, 67.4, 82.2, 97.0, 107.8, 143.4, 158.9, 160.6; LRMS (CI, NH_3) 340 (41%) ($\text{M} + \text{NH}_4$) $^+$, 323 (100%) ($\text{M} + \text{H}$) $^+$, 197 (71%), 153 (39%); HRMS ($\text{M} + \text{H}$) $^+$ calcd 323.0144; found 323.0142.

1,3-Dimethoxy-5-(2*R*-(*tert*-butyldimethylsilyloxy)propyl)-6-iodobenzene (8). Pyridine (0.30 mL, 293 mg, 3.70 mmol) was added dropwise to alcohol **7** (345 mg, 1.07 mmol) in dry CH₂Cl₂ (5.0 mL) at 0 °C. The mixture was stirred for 10 min followed by the dropwise addition of *t*-BuMe₂SiOTf (0.74 mL, 849 mg, 3.21 mmol). The mixture was stirred for 5 h at 23 °C, diluted with Et₂O (10 mL), quenched with saturated aqueous NaHCO₃ (10 mL) and extracted with Et₂O (2 x 10 mL). The combined organic layers were dried (MgSO₄), rotary evaporated and chromatographed (SiO₂, cyclohexane:EtOAc 5:1) to afford ether **8** (408 mg, 87%) as a colorless oil: R_f 0.53 (cyclohexane:EtOAc 5:1); [α_D]²⁵ = -25.3 (*c* = 0.91 CH₂Cl₂); IR (neat) 1588, 1455, 1329, 1255, 1163, 1127 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ -0.27 (s, 3 H), -0.14 (s, 3 H), 0.79 (s, 9 H), 1.19 (d, *J* = 6.0 Hz, 3 H), 2.76 – 2.91 (m, 2 H), 3.76 (s, 3 H), 3.82 (s, 3 H), 4.05 – 4.16 (m, 1 H), 6.28 (d, *J* = 2.3 Hz, 1 H), 6.47 (d, *J* = 1.9 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ -5.1, -5.01, 17.9, 23.9, 25.8, 50.7, 55.3, 56.4, 67.9, 82.1, 96.9, 108.8, 144.1, 158.6, 160.3; LRMS (CI, NH₃) 437 (100%) (M + H)⁺, 311 (85%), 132 (12%); HRMS (M + H)⁺ calcd 437.1009; found 437.1010.

3-Phenyl-1-propyl 2,4-dimethoxy-6-(2*R*-(*tert*-butyldimethylsilyloxy)propyl)benzoate (4h). *i*PrMgCl in THF (2 M; 0.32 mL, 0.64 mmol) was added dropwise to **8** (238 mg, 0.545 mmol) in dry THF (5.0 mL) at -30 °C, stirred for 2 h and added to 1-imidazolecarboxylate **2a** (125 mg, 0.545 mmol) in dry THF (1.0 mL) at 0 °C. The reaction mixture was warmed to 23 °C over 5 min, heated at 50 °C for 10 min and cooled to 23 °C over 16 h. The mixture was poured onto ice, acidified with hydrochloric acid (1 M), extracted with Et₂O (3 x 10 mL), dried (MgSO₄), rotary evaporated and chromatographed twice (SiO₂, cyclohexane:EtOAc 10:1 and 20:1) to afford ester **4h** (80 mg, 31%) as a colorless oil: R_f 0.38 (cyclohexane:EtOAc 5:1); [α_D]²⁵ = -15.8 (*c* = 1.65 in CH₂Cl₂); IR (neat) 3086, 3062, 3027, 2958, 2853, 1725 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ -0.21 (s, 3 H), -0.11 (s, 3 H), 0.80 (s, 9 H), 1.11 (d, *J* = 6.1 Hz, 3 H), 1.99 – 2.05 (m, 2 H), 2.64 – 2.68 (m, 2 H), 2.72 – 2.75 (m, 2 H), 3.77 (s, 3 H), 3.78 (s, 3 H), 3.99 – 4.04 (m, 1 H), 4.23 – 4.32 (m, 2 H), 6.32 (d, *J* = 2.2 Hz, 1 H), 1.11 (d, *J* = 2.2 Hz, 1 H), 7.17

– 7.26 (m, 5 H); ^{13}C NMR (125 MHz, CDCl_3) δ –5.1, 18.0, 24.0, 25.8, 30.4, 32.1, 44.1, 55.3, 55.9, 64.2, 69.3, 96.8, 107.8, 117.1, 126.0, 128.4, 139.5, 141.3, 158.1, 160.8, 168.4; LRMS (CI, NH_3) 473 (100%) ($\text{M} + \text{H}$) $^+$, 415 (49%), 337 (41%), 316 (50%), 297 (14%), 186 (10%), 118 (21%); HRMS ($\text{M} + \text{H}$) $^+$ calcd 473.2723 found 473.2714. Anal. calcd for $\text{C}_{17}\text{H}_{28}\text{O}_3\text{Si}$: C, 68.61; H, 8.53. Found: C, 68.66; H, 8.48.

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t w . i . 1 2 5 . 1 j 7 3 4 1 e x p 1 2

S16

t w. i. 125.1

tw.ii.200 o1691 exp10

S18

tw, i i, 154.1 a8325 exp12

twi.149 a8195 exp10

t w. i. 149 a8195 exp11

tw.ii.198 01598 exp10

t w. i i . 198

tw.i.111 j7048 exp11

S24

tw. i. 111 j 7059 exp12

tw.ii.155.1 a8325 exp11

S26

tw.iii.155.1 a8325 exp14

tw. i i . 237 j 1337 exp10

tw. i. 141 a8116 exp12

tw.iii.238 j1337 exp11

S30

T Werner tw.ii.238 in CDCl₃ ; ¹³C{¹H} spectrum using DRX400 ; Jan26/181

tw.ii.210A n1260 exp10

tw.iii.210a n1345 exp13

T Werner tw.ii.247 in CDCl₃ ; ¹H spectrum using DRX400 ; Feb17/280

T Werner tw.ii.247 in CDCl₃ ; ¹³C{¹H} spectrum using DRX400 ; Feb17/281

tw.ii.193 ol250 exp22

tw.ii.193 o1263 exp12

tw.ii.189 o1080 exp11

t w. i i . 189

tw.ii.203 o1740 exp12

t w . i i . 2 0 3 n 1 0 4 0 e x p 1 1

tw.ii.233.1 j1318 exp12

4f

Thomas Werner - ^{13}C of tw.ii.233.1 in CDCl_3

tw.ii.204.4 n1153 exp10

t w. i i . 2 0 4 p r p 4 **4g**

T. Werner - 1H of tw.ii.217.3.2 in CDCl₃.

T. Werner - ^{13}C of tw.ii.217.3.2 in CDCl_3 .

tw.ii.151 a8220 exp11

t w. i i . 151 a 8251 e x p 10

tw.ii.211 n1311 expl1

tw.ii.211 n1358 exp10

tw.ii.201 o1692 exp10

t w . i . 1 2 4 j 7 3 1 8 e x p 1 0

t w. i. 124 j 7326 exp10

tw.ii.220 d1173 exp13

tw.iii.220 d1190 exp12

T. Werner - ¹H of tw.ii.242.1 in CDCl₃.

T. Werner - ^{13}C of tw.ii.242.1 in CDCl_3 .

tw.ii.246 f1177 exp10

t w. i i . 246 f 1060 e x p 13

t w . i . 72 . 2 m5119 exp10

t w. i. 72.2 m5133 exp12

t w. i i . 1 6 9 . 1

tw.iii.168.1 s9156 exp11

tw.ii.181.1 s9464 exp10

S66

t w. i i . 181. 1