N,N-Dimethylaminobenzoates Enable Highly Enantioselective

Sharpless Dihydroxylations of 1,1-Disubstituted Alkenes

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1. General Information

All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF and toluene were distilled from sodium-benzophenone, and dichloromethane, and acetonitrile were distilled from calcium hydride. Thin-layer chromatography (TLC) was conducted with 0.25 mm Tsingdao silica gel plates (60F-254) and visualized by exposure to UV light (254 nm) or stained with potassium permanganate. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040-0.063 mm). Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. The 2-methylprop-2-en-1-ol was purchased from Adamas. Other alcohols were synthesized from literature¹, unless otherwise stated. ¹H NMR spectra were recorded on Brueker spectrometers (at 300, 400 or 500 MHz) and are reported relative to deuterated solvent signals. Data for 1 H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ¹³C NMR spectrawere recorded on Brueker Spectrometers (at 75, 100 or 125 MHz). Data for ¹³C NMR spectra are reported in terms of chemical shift. Mass spectrometric data were obtained using Bruker Apex IV RTMS. The following abbreviations were used to explain the multiplicities: s =singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

⁽¹⁾ Erkkila, A.; Pihko, P. M. J. Org. Chem. 2006, 71, 2538.

2. General Procedure for the Preparation of the Olefin Substrate

A solution of the *N*,*N*-dimethyl amino benzoic acid (1.5 equiv.), 4-(dimethylamino) pyridine (DMAP) (0.5 equiv.) in dried methylene chloride (0.1 M) was treated with EDC HCl (1.5 equiv.) and Et₃N (1.5 equiv.) at 23 °C under nitrogen atmosphere. The resulting mixture was stirred for 30 min and then was treated with the corresponding alcohol. After completion (monitored by TLC analysis), the reaction mixture was quenched with saturated NaHCO₃ (aq.), and extracted with methylene chloride. The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated *in vacuo* to give crude product, which was purified by flash chromatography to afford the indicated yield of product.

3. ¹H NMR and ¹³C NMR spectra data of compounds 1a-1f, 3a-19a



2-methylallyl 6-methoxy-2-naphthoate (**1a**): Following the general procedure, 2-methylprop-2-en-1-ol (104 mg, 1.21 mmol) and the corresponding acid afforded the olefin **1a** (248 mg, 80% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.56 (s, 1H), 8.06 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.20 (dd, *J* = 2.4, 8.8 Hz, 2H), 7.15 (d, *J* = 2.4 Hz, 1H), 5.13 (s, 1H), 5.02 (s, 1H), 4.81 (s, 2H), 3.94 (s, 3H), 1.88 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 159.5, 140.1, 137.2, 130.9, 130.8, 127.9, 126.8, 125.9, 125.2, 119.6, 112.9, 105.6, 68.1, 55.3, 19.6; HRMS calculated for C₁₆H₁₇O₃ (M + H⁺): 257.1172, found: 257.1175.



2-methylallyl benzo[d][1,3]dioxole-5-carboxylate (**1b**): Following the general procedure, 2-methylprop-2-en-1-ol (104 mg, 1.21 mmol) and the corresponding acid afforded the olefin **1b** (223 mg, 79% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 1H), 6.84 (d, *J* = 8.4Hz, 1H), 6.04 (s, 2H),

5.05 (s, 1H), 4.97 (s, 1H), 4.70 (s, 2H), 1.82 (s, 3H); 13 C NMR (100 MHz, CDCl₃) δ 166.5, 151.6, 147.7, 140.0, 125.4, 124.1, 109.5, 107.9, 101.7, 68.0, 19.5; HRMS calculated for C₁₂H₁₃O₄ (M + H⁺): 221.0808, found: 221.0809.



2-methylallyl 4-phenoxybenzoate (**1c**): Following the general procedure, 2-methylprop-2-en-1-ol (104 mg, 1.21 mmol) and the corresponding acid afforded the olefin **1c** (269 mg, 83% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 8.8 Hz, 2H), 7.41-7.37 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.07 (dd, *J* = 1.2, 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.07 (s, 1H), 4.98 (s, 1H), 4.73 (s, 2H), 1.83 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.7, 161.8, 155.6, 140.0, 131.7, 130.0, 124.5, 124.4, 120.0, 117.3, 112.8, 67.9, 19.5; HRMS calculated for C₁₇H₁₇O₃ (M + H⁺): 269.1172, found: 269.1173.



2-methylallyl 4-ethoxybenzoate (**1d**): Following the general procedure, 2-methylprop-2-en-1-ol (104 mg, 1.21 mmol) and the corresponding acid afforded the olefin **1d** (200 mg, 75% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.06 (s , 1H), 4.96 (s , 1H), 4.71 (s , 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.83 (s , 3H), 1.43 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.0, 162.8, 140.2, 131.6, 122.3, 114.0, 112.6, 67.7, 63.6, 19.5, 14.6; HRMS calculated for C₁₃H₁₇O₃ (M + H⁺): 221.1172, found: 221.1173.



2-methylallyl 4-methoxybenzoate (1e): Following the general procedure, 2-methylprop-2-en-1-ol (104 mg, 1.21 mmol) and the corresponding acid afforded the

olefin **1e** (220 mg, 88% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 5.06 (s , 1H), 4.97 (s, 1H), 4.72 (s, 2H), 3.86 (s, 3H), 1.83 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.9, 163.4, 140.2, 131.6, 122.6, 113.6, 112.6, 67.8, 55.4, 19.5; HRMS calculated for C₁₂H₁₅O₃ (M + H⁺): 207.1016, found: 207.1012.



2-methylallyl 4-(dimethylamino)benzoate (1f): Following the general procedure, 2-methylprop-2-en-1-ol (113mg, 1.57 mmol) and the corresponding acid afforded the olefin **1f** (258 mg, 75% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.95 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 9.0 Hz, 2H), 5.06 (s, 1H), 4.95 (s, 1H), 4.70 (s, 2H), 3.01 (s, 6H), 1.83 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.6, 153.3, 140.6, 131.3, 116.9, 112.2, 110.7, 67.3, 40.0, 19.6; HRMS calculated for C₁₃H₁₈NO₂ (M + H⁺): 220.1332, found: 220.1335.



2-methylenebutyl 4-(dimethylamino)benzoate (**3a):** Following the general procedure, the alcohol¹ (91 mg, 1.05 mmol) and the corresponding acid afforded the olefin **3a** (163 mg, 70% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 9.2 Hz, 2H), 6.64 (d, *J* = 9.2 Hz, 2H), 5.10 (s, 1H), 4.96 (s, 1H), 4.74 (s, 2H), 3.03 (s, 6H), 2.16 (q, *J* = 7.2 Hz, 2H), 1.11 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 146.2, 131.3, 116.9, 110.7, 110.4, 66.6, 40.0, 26.1, 12.0; HRMS calculated for C₁₄H₂₀NO₂ (M + H⁺): 234.1489, found: 234.1488.



2-methylenepentyl 4-(dimethylamino)benzoate (4a): Following the general procedure, the alcohol¹ (150 mg, 1.50 mmol) and the corresponding acid afforded the olefin **5a** (203 mg, 55% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.94 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 9.0 Hz, 2H), 5.11 (s, 1H), 4.96 (s, 1H), 4.72 (s, 2H), 3.04 (s, 6H), 2.12 (q, *J* = 7.2 Hz, 2H), 1.60-1.47 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.6, 153.3, 144.6, 131.3, 116.9, 111.6, 110.7, 66.5, 40.0, 35.5, 20.7, 13.8; HRMS calculated for C₁₅H₂₂NO₂ (M + H⁺): 248.1645, found: 248.1646.



2-methylenehexyl 4-(dimethylamino)benzoate (5a): Following the general procedure, the alcohol¹ (114 mg, 1.00 mmol) and the corresponding acid afforded the olefin **5a** (144 mg, 55% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 5.10 (s, 1H), 4.95 (s, 1H), 4.73 (s, 2H), 3.04 (s, 6H), 2.14 (t, *J* = 7.2 Hz, 2H), 1.51-1.45 (m, 2H), 1.38-1.33 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 144.7, 131.3, 117.0, 111.4, 110.7, 66.5, 40.0, 33.0, 29.7, 22.4, 13.9; HRMS calculated for C₁₆H₂₄NO₂ (M + H⁺): 262.1802, found: 262.1802.



2-methyleneheptyl 4-(dimethylamino)benzoate (**6a):** Following the general procedure, the alcohol¹ (200 mg, 1.58 mmol) and the corresponding acid afforded the olefin **6a** (259 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.10 (d, *J* = 1.2 Hz, 1H), 4.95 (d, *J* = 1.2 Hz, 1H), 4.72 (s, 2H), 3.04 (s, 6H), 2.13 (t, *J* = 8.0 Hz, 2H), 1.51-1.47 (m, 2H), 1.34 -1.29 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 144.7, 131.3, 117.0, 111.4, 110.7, 66.5, 40.0, 33.3, 31.5, 27.2, 22.5, 14.0; HRMS calculated for C₁₇H₂₆NO₂ (M + H⁺): 276.1958, found: 276.1957.



2-methyleneoctyl 4-(dimethylamino)benzoate (**7a):** Following the general procedure, the alcohol¹ (195 mg, 1.50 mmol) and the corresponding acid afforded the olefin **7a** (340 mg, 82% yield). ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.10 (s, 1H), 4.95 (s, 1H), 4.72 (s, 2H), 3.04 (s, 6H), 2.13 (t, *J* = 8.0 Hz, 2H), 1.54-1.46 (m, 2H), 1.35-1.26 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 144.7, 131.3, 117.0, 111.4, 110.7, 66.5, 40.0, 33.4, 31.7, 29.0, 27.5, 22.6, 14.0; HRMS calculated for C₁₈H₂₈NO₂ (M + H⁺): 290.2120, found: 290.2123.



2-(((tert-butyldimethylsilyl)oxy)methyl)allyl 4-(dimethylamino)benzoate (**8a):** Following the general procedure, the alcohol¹ (244 mg, 1.20 mmol) and the corresponding acid afforded the olefin **8a** (267mg, 62% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.10 (t, *J* = 0.8 Hz, 1H), 4.95 (d, *J* = 1.2 Hz, 1H), 4.79 (s, 2H), 4.25 (s, 2H), 3.04 (s, 6H), 0.91 (d, *J* = 2.8 Hz, 9H), 0.08 (t, *J* = 2.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 143,8, 131.3, 116.9, 112.3, 110.7, 64.4, 63.9, 40.0, 25.9, 18.4, 5.4; HRMS calculated for C₁₉H₃₂NO₃Si (M + H⁺): 350.2146, found: 350.2142.



2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl 4-(dimethylamino)benzoate (**9**a): Following the general procedure, the $alcohol^{1}$ (200 mg, 0.61 mmol) and the corresponding acid afforded the olefin **9a** (284 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 9.2 Hz, 2H), 7.72-7.66 (m, 4H), 7.46-7.36 (m, 6H), 6.64 (d, *J* = 9.2 Hz, 2H), 5.37 (s, 1H), 5.27 (s, 1H), 4.81 (s, 2H), 4.31 (s, 2H), 3.05 (s, 6H), 1.09 (s, S7) 9H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.3, 143.4, 135.5, 133.4, 131.3, 129.6, 127.7, 116.9, 112.5, 110.6, 64.6, 64.4, 40.0, 26.8, 19.2; HRMS calculated for C₂₉H₃₆NO₃Si (M + H⁺): 474.2459, found: 474.2455.



2-(((triisopropylsilyl)oxy)methyl)allyl 4-(dimethylamino)benzoate (10a): Following the general procedure, the alcohol¹ (243 mg, 1.00 mmol) and the corresponding acid afforded the olefin **10a** (300 mg, 77% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.92 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.32 (s, 1H), 5.22 (s, 1H), 4.80 (s, 2H), 4.34 (s, 2H), 3.04 (s, 6H), 1.16-1.11 (m, 3H), 1.09 (s, 12H), 1.07 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.3, 143.9, 131.3, 116.9, 111.9, 110.7, 64.5, 64.1, 40.0, 18.0, 12.0; HRMS calculated for C₂₂H₃₈NO₃Si (M + H⁺): 392.6215, found: 392.6212.



2-(methoxymethyl)allyl 4-(dimethylamino)benzoate (11a): Following the general procedure, the alcohol¹ (153 mg, 1.50 mmol) and the corresponding acid afforded the olefin **11a** (224 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J* = 9.2 Hz, 2H), 6.65 (d, *J* = 9.2 Hz, 2H), 5.29 (s, 1H), 5.25 (s, 1H), 4.80 (s, 2H), 4.01 (s, 2H), 3.35 (s, 3H), 3.04 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.4, 141.2, 131.3, 116.8, 114.4, 110.7, 73.3, 64.3, 58.0, 40.0; HRMS calculated for C₁₄H₂₀NO₃ (M + H⁺): 250.1438, found: 250.1435.



2-((benzyloxy)methyl)allyl 4-(dimethylamino)benzoate (12a): Following the general procedure, the alcohol¹ (216 mg, 1.20 mmol) and the corresponding acid afforded the olefin **12a** (213 mg, 65% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, J

= 8.8 Hz, 2H), 7.36-7.28 (m, 5H), 6.65 (d, J = 8.8 Hz, 2H), 5.33 (s, 1H), 5.30 (s, 1H), 4.85 (s, 2H), 4.55 (s, 2H), 4.13 (s, 2H), 3.04 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.4, 141.3, 138.1, 131.3, 128.4, 127.7, 127.6, 116.8, 114.7, 110.7, 72.2, 70.9, 64.4, 40.0; HRMS calculated for C₂₀H₂₄NO₃ (M + H⁺): 326.1751, found: 326.1752.



2-((prop-2-yn-1-yloxy)methyl)allyl 4-(dimethylamino)benzoate (13a): Following the general procedure, the alcohol¹ (254 mg, 2.00 mmol) and the corresponding acid afforded the olefin **13a** (431 mg, 78% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.93 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 9.0 Hz, 2H), 5.33 (s, 1H), 5.29 (s, 1H), 4.18-4.17 (overlapped, 4H), 3.04 (s, 6H), 2.42 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 153.4, 140.5, 131.3, 116.7, 115.5, 110.7, 79.5, 74.6, 70.2, 64.2, 57.2, 40.0; HRMS calculated for C₁₆H₂₀NO₃ (M + H⁺): 274.1438, found: 274.1440.



4-(benzyloxy)-2-methylenebutyl 4-(dimethylamino)benzoate (**14a**): Following the general procedure, the alcohol¹ (384 mg, 2.00 mmol) and the corresponding acid afforded the olefin **14a** (427 mg, 63% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.94 (dd, *J*= 3.3, 8.6 Hz, 2H), 7.36-7.28 (overlapped, 5H), 6.65 (d, *J*= 8.6 Hz, 2H), 5.20 (s, 1H), 5.06 (s, 1H), 4.77 (s, 2H), 4.54 (d, *J*= 1.8 Hz, 2H), 3.66 (td, *J*= 1.8, 6.6 Hz, 2H), 3.04 (s, 6H), 2.50 (t, *J*= 6.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 153.3, 141.7, 138.3, 131.3, 128.4, 127.6, 127.5, 116.8, 113.4, 110.7, 73.0, 68.7, 66.6, 40.0, 33.7; HRMS calculated for C₂₁H₂₆NO₃ (M + H⁺): 340.1907, found: 340.1911.



4-((tert-butyldiphenylsilyl)oxy)-2-methylenebutyl 4-(dimethylamino)benzoate

(15a): Following the general procedure, the alcohol¹ (1702 mg, 5.00 mmol) and the corresponding acid afforded the olefin **15a** (1485 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.95-7.92 (m, 2H), 7.70-7.68 (overlapped, 4H), 7.44-7.40 (overlapped, 6H), 6.65 (dd, *J*= 1.6, 8.8 Hz, 2H), 5.18 (s, 1H), 5.00 (s, 1H), 4.72 (s, 2H), 3.88-3.84 (m, 2H), 3.04 (s, 6H), 2.42 (t, *J*= 6.4 Hz, 2H), 1.08 (d, *J*= 3.2 Hz, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.3, 141.7, 135.6, 133.8, 131.3, 129.6, 127.6, 117.0, 113.7, 110.7, 66.6, 62.7, 40.0, 36.6, 26.8, 19.2; HRMS calculated for C₃₀H₃₈NO₃Si (M + H⁺): 488.2615, found: 488.2615.



4-hydroxy-2-methylenebutyl 4-(dimethylamino)benzoate (S15): To a solution of **15a** (2.26 g, 4.65 mmol) in acetonitrile at 0°C, HF aqueous solution (4.65 mL) was added dropwise. Then the mixture was allowed elevated to room temperature. After completion (monitored by TLC analysis), the reaction was quenched by satureated aqueous NaHCO₃, diluted with Et₂O, washed with brine, and dried over Na₂SO₄. Concentration in reduced pressure afforded the crude product. Purification by flash column chromatograpy to deliver the hydroxy product **S15** (1.1g, 95% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J*= 9.2 Hz, 2H), 6.64 (d, *J*= 9.2 Hz, 2H), 5.22 (s, 1H), 5.06 (s, 1H), 4.75 (s, 2H), 3.79 (t, *J*= 5.6 Hz, 2H), 3.03 (s, 6H), 2.41 (t, *J*= 5.6 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 166.7, 153.4, 141.3, 131.3, 116.6, 114.3, 110.7, 66.2, 60.8, 40.0, 36.7; HRMS calculated for C₁₄H₂₀NO₃ (M + H⁺): 250.1438, found: 250.1442.



4-((tert-butyldimethylsilyl)oxy)-2-methylenebutyl 4-(dimethylamino)benzoate (16a): To a solution of S15 (114 mg, 0.45 mmol) in dried DCM (5 mL) was added Et_3N (90 mg, 0.90 mmol) and DMAP (18 mg, 0.15 mmol) at 0°C. Subsequently, TBSCl (135 mg, 0.90 mmol) was added as one portion. The resulting mixture was allowed to reach room temperature. After completion (monitored by TLC analysis), the reaction was quenched with saturated aqueous NH₄Cl, extracted with DCM. The combined organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated to afford the crude product. Purification via flash column chromatography gave **16a** (142 mg, 87% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J*= 9.2 Hz, 2H), 6.64 (d, *J*= 9.2 Hz, 2H), 5.16 (d, *J*= 1.2 Hz, 1H), 5.00 (d, *J*= 1.2 Hz, 1H), 4.74 (s, 2H), 3.78 (t, *J*= 6.8 Hz, 2H), 3.04 (s, 6H), 2.37 (t, *J*= 6.8 Hz, 2H), 0.89 (s, 9H), 0.06 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.3, 141.9, 131.3, 116.9, 113.4, 110.7, 66.7, 62.1, 40.0, 36.9, 25.9, 25.6, 18.3; HRMS calculated for C₂₀H₃₄NO₃Si (M + H⁺): 364.2302, found: 364.2303.



4-chloro-2-methylenebutyl 4-(dimethylamino)benzoate (17a): To a stirred solution of **S15** (80 mg, 0.32 mmol) and PPh₃ (168 mg, 0.64 mmol) in dried DCM (6 mL) was added hexachloroacetone (169 mg, 0.64 mmol) at room temperature. The resulting mixture was maintained at this temperature for 2h. The reaction was quenched with cold water, extracted with DCM. The combined organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated to afford the crude product. Purification via flash column chromatography afforded **17a** (80 mg, 93% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.92 (d, *J*= 9.0 Hz, 2H), 6.65 (d, *J*= 9.0 Hz, 2H), 5.27 (s, 1H), 5.09 (s, 1H), 4.75 (s, 2H), 3.69 (t, *J*= 7.2 Hz, 2H), 3.04 (s, 6H), 2.63 (t, *J*= 7.2 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 153.4, 140.7, 131.3, 116.5, 115.3, 110.7, 66.2, 42.4, 40.0, 36.5; HRMS calculated for C₁₄H₁₉NO₂Cl (M + H⁺): 268.1099, found: 268.1094.



4-fluoro-2-methylenebutyl 4-(dimethylamino)benzoate (18a): To a solution of **S15** (80 mg, 0.32 mmol) in dried DCM (6 mL) was added DAST (128 mg, 0.8 mmol) at

-78°C. The resulting mixture was maintained at this temperature until completion (monitored by TLC analysis). The reaction was quenched with saturated aqueous NaHCO₃, extracted with DCM. The combined organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated to afford the crude product. Purification via flash column chromatography afforded **18a** (37 mg, 46% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J*= 8.8 Hz, 2H), 6.65 (d, *J*= 8.8 Hz, 2H), 5.25 (s, 1H), 5.10 (s, 1H), 4.77 (s, 2H), 4.67 (t, *J*= 6.0 Hz, 1H), 4.55 (t, *J*= 6.0 Hz, 1H), 3.04 (s, 6H), 2.58 (t, *J*= 6.0 Hz, 1H), 2.52 (t, *J*= 6.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 166.5, 153.4, 140.0, 140.0, 131.3, 116.6, 114.8, 110.7, 82.9, 81.3, 66.4, 40.0, 34.3, 34.1; HRMS calculated for C₁₄H₁₉NO₂F (M + H⁺): 252.1394, found: 252.1393.



2-phenylallyl 4-(dimethylamino)benzoate (19a): Following the general procedure, the alcohol (134 mg, 1.00 mmol) prepared from oxidation of prop-1-en-2-ylbenzene via SeO₂ and the corresponding acid afforded the olefin **19a** (166 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 9.2 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.38-7.30 (m, 3H), 6.63 (d, *J* = 9.2 Hz, 2H), 5.58 (s, 1H), 5.45 (s, 1H), 5.17 (s, 2H), 3.03 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 153.4, 143.0, 138.4, 131.4, 131.2, 128.4, 127.9, 126.0, 116.8, 114.6, 110.7, 65.4, 40.0; HRMS calculated for C₁₈H₂₀NO₂ (M + H⁺): 282.1489, found: 282.1490.

4. General Procedure for the Asymmetric Dihydroxylation

A suspension of AD-mix- β in ^{*t*}BuOH/H₂O (0.1M, 1:1) was cooled to 0°C, and treated with the corresponding olefin (0.1 mmol). The resulting mixture was stirred vigorously and maintained at 0°C until the starting material disappeared by TLC analysis. After completion, the reaction mixture was quenched with saturated Na₂SO₃ (aq.), stirred for 10 min, and warmed to room temperature. Then the mixture was diluted with EtOAc and minimal water, extracted with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo* to give crude product, which was purified by flash chromatography to afford the indicated yield of product.

5. ¹H NMR and ¹³C NMR spectra data of compounds 2a-2f, 3b-20b



(*S*)-2,3-dihydroxy-2-methylpropyl 6-methoxy-2-naphthoate (2a): Compound 2a was obtained via the general procedure in 68% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 85:15 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 39.7 min., t_R (*S*)-enantiomer (major) = 41.6 min.; 29:71 er. ¹H NMR (500 MHz, CDCl₃) δ 8.49 (s, 1H), 7.98 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.18 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.12 (d, *J* = 2.5 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.29 (d, *J* = 11.5 Hz, 1H), 3.92 (s, 3H), 3.63 (d, *J* = 11.5 Hz, 1H), 3.52 (d, *J* = 11.5 Hz, 1H), 1.31 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.4, 159.8 137.4, 131.2, 130.9, 127.8, 127.0, 125.8, 124.5, 119.8, 105.7, 72.2, 68.4, 67.0, 55.4, 21.4; HRMS calculated for C₁₆H₁₈O₅Na (M + Na⁺): 313.1046, found: 313.4048.







(*S*)-2,3-dihydroxy-2-methylpropyl benzo[d][1,3]dioxole-5-carboxylate (2b): Compound 2b was obtained via the general procedure in 67% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 70:30 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 25.7 min., t_R (*S*)-enantiomer (major) = 27.3 min.; 15:85 er. ¹H NMR (300 MHz, CDCl₃) δ 7.62 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.42 (d, *J* = 1.5 Hz, 1H), 6.81 (d, *J* = 8.1Hz, 1H), 4.14 (d, *J* = 11.2 Hz, 1H), 6.02 (s, 2H), 4.32 (d, *J* = 11.4 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.36 (d, *J* = 11.4 Hz, 1H), 3.45 (d, *J* = 11.4 Hz, 1H), 1.24 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.4, 151.9, 147.7, 125.6, 123.4, 109.5, 108.0, 101.9, 72.1, 68.2, 66.9, 21.3; HRMS calculated for C₁₂H₁₄O₆Na (M + Na⁺): 277.0683, found: 277.0687.





(*S*)-2,3-dihydroxy-2-methylpropyl 4-phenoxybenzoate (2c): Compound 2c was obtained via the general procedure in 83% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 85:15 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 23.1 min., t_R (*S*)-enantiomer (major) = 21.7 min.; 18:82 er. ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 8.8 Hz, 2H), 7.41-7.37 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.05 (dd, *J* = 1.2, 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.37 (d, *J* = 11.2 Hz, 1H), 4.21 (d, *J* = 11.2 Hz, 1H), 3.57 (d, *J* = 11.2 Hz, 1H), 3.47 (d, *J* = 11.2 Hz, 1H), 1.26 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.6, 162.2, 155.3, 131.8, 130.0, 124.6, 123.6, 120.1, 117.3, 72.1, 68.1, 66.8, 21.3; HRMS calculated for







(*S*)-2,3-dihydroxy-2-methylpropyl 4-ethoxybenzoate (2d): Compound 2d was obtained via the general procedure in 76% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 85:15 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 32.4 min., t_R (*S*)-enantiomer (major) = 30.2 min.; 16:84 er. ¹H NMR (300 MHz, CDCl₃) δ 7.96 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 4.35 (d, *J* = 11.4 Hz, 1H), 4.18 (d, *J* = 11.4 Hz, 1H), 4.06 (d, *J* = 7.2 Hz, 2H), 3.56 (d, *J* = 11.4 Hz, 1H), 3.45 (d, *J* = 11.4 Hz, 1H), 1.42 (d, *J* = 7.2 Hz, 1H), 1.25 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.9, 163.1, 131.8, 121.5, 114.1, 72.2, 68.0, 66.8, 21.3, 14.6; HRMS calculated for C₁₃H₁₈O₅Na (M + Na⁺): 277.1046, found: 277.1046.





(*S*)-2,3-dihydroxy-2-methylpropyl 4-methoxybenzoate (2e): Compound 2e was obtained via the general procedure in 88% yield. Chiral HPLC analysis (CHIRALCEL OD-H column), 95:5 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 23.8 min., t_R (*S*)-enantiomer (major) = 25.1 min.; 7:93 er. ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.35 (d, *J* = 11.2 Hz, 1H), 4.19 (d, *J* = 11.2 Hz, 1H), 3.84 (s, 3H), 3.56 (d, *J* = 11.6 Hz, 1H), 3.45 (d, *J* = 11.6 Hz, 1H), 1.25 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.8, 163.7, 131.8, 121.8, 113.7, 72.1, 68.0, 66.8, 55.4, 21.3; HRMS calculated for C₁₂H₁₆O₅Na (M + Na⁺): 263.0890, found: 263.0893.





(*S*)-2,3-dihydroxy-2-methylpropyl 4-(dimethylamino)benzoate (2f): Compound 2f was obtained via the general procedure in 92% yield. Chiral HPLC analysis (CHIRALCEL AS-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 14.8 min., t_R (*S*)-enantiomer (major) = 15.6 min.; 2:98 er. AD-mix- α : Chiral HPLC analysis (CHIRALCEL AS-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; tR (S)-enantiomer (minor) = 14.8 min., tR (R)-enantiomer (minor) = 14.8 min., tR (S)-enantiomer (minor) = 14.8 min., tR (R)-enantiomer (major) = 15.6 min.; 3:97 er. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 9.2 Hz, 2H), 6.61 (d, *J* = 9.2 Hz, 2H), 4.34 (d, *J* = 11.2 Hz, 1H), 4.14 (d, *J* = 11.2 Hz, 1H), 3.53 (d, *J* = 11.2 Hz, 1H), 3.42 (d, *J* = 11.2 Hz, 1H), 3.02 (s, 6H), 1.24 (s, S18)

3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 153.6, 131.5, 115.8, 110.7, 72.2, 67.6, 66.8, 40.0, 21.3; HRMS calculated for C₁₃H₁₉NO₄Na (M + Na⁺): 276.1206, found: 276.1027.





(*S*)-2-hydroxy-2-(hydroxymethyl)butyl 4-(dimethylamino)benzoate (3b): Compound 3b was obtained via the general procedure in 85% yield. Chiral HPLC analysis (CHIRALCEL AS-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; $t_R(R)$ -enantiomer (minor) = 12.0 min., $t_R(S)$ -enantiomer (major) = 14.8 min.; 5:95 er. ¹H NMR (300 MHz, CDCl₃) δ 7.89 (d, *J* = 9.0 Hz, 2H), 6.64 (d, *J* = 9.0 Hz, 2H), 4.40

(d, J = 11.4 Hz, 1H), 4.17 (d, J = 11.4 Hz, 1H), 3.53 (d, J = 11.4 Hz, 1H), 3.43 (d, J = 11.4 Hz, 1H), 3.05 (s, 6H), 1.61 (q, J = 7.8 Hz, 2H), 0.99 (t, J = 7.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 167.7, 153.6, 131.5, 115.8, 110.7, 73.9, 66.6, 65.2, 40.0, 27.0, 7.1; HRMS calculated for C₁₄H₂₁NO₄Na (M + Na⁺): 290.1363, found: 290.1360.







1H), 3.44 (dd, J = 11.6, 5.6 Hz, 1H), 3.04 (s, 6H), 2.99 (s, 1H), 2.84 (s, 1H), 1.57-1.42 (m, 4H), 0.94 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 153.6, 131.5, 116.9, 115.9, 110.7, 73.8, 66.0, 65.4, 40.0, 36.8, 16.0, 14.7; HRMS calculated for C₁₅H₂₃NO₄Na (M + Na⁺): 304.1519, found: 304.1519.



(*S*)-2-hydroxy-2-(hydroxymethyl)hexyl 4-(dimethylamino)benzoate (5b): Compound 4b was obtained via the general procedure in 90% yield. Chiral HPLC analysis (CHIRALCEL AS-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; $t_R(R)$ -enantiomer (minor) = 9.7 min., $t_R(S)$ -enantiomer (major) = 10.3 min.; 8:92 er. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 9.2 Hz, 2H), 6.64 (d, *J* = 9.2 Hz, 2H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.17 (d, *J* = 11.6 Hz, 1H), 3.53 (d, *J* = 11.6 Hz, 1H), 3.44 (d, *J* =

11.4 Hz, 1H), 3.04 (s, 6H), 1.57-1.44 (m, 2H), 1.42-1.36 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 153.6, 131.5, 115.9, 110.7, 73.8, 65.9, 65.5, 40.0, 34.1, 24.8, 23.3, 14.0; HRMS calculated for C₁₆H₂₅NO₄Na (M + H⁺): 318.1676, found: 318.1674.



(S)-2-hydroxy-2-(hydroxymethyl)heptyl 4-(dimethylamino)benzoate (6b): Compound 6b was obtained via the general procedure in 85% yield. Chiral HPLC analysis (CHIRALCEL OJ-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 16.8 min., t_R (*S*)-enantiomer (major) = 17.9 min.; 8:92 er.

¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 8.8 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.17 (d, *J* = 11.6 Hz, 1H), 3.54-3.51 (m, 1H), 3.46-3.41 (m, 1H), 3.04 (s, 6H), 2.95 (s, 1H), 2.81 (s, 1H), 1.58-1.53 (m, 2H), 1.45-1.41 (m, 2H), 1.34 -1.25 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 153.6, 131.5, 115.9, 110.7, 73.8, 65.9, 65.5, 40.0, 34.4, 32.4, 22.5, 22.3, 14.0; HRMS calculated for C₁₇H₂₇NO₄Na (M + Na⁺): 332.1832, found: 332.1832.







t_R (*R*)-enantiomer (minor) = 9.5 min., t_R (*S*)-enantiomer (major) = 15.0 min.; 14:86 er. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.16 (d, *J* = 11.6 Hz, 1H), 3.54-3.50 (m, 1H), 3.46-3.41 (m, 1H), 3.05 (s, 6H), 2.92 (t, *J* = 6.4 Hz, 1H), 2.77 (s, 1H), 1.58-1.54 (m, 2H), 1.44-1.41 (m, 2H), 1.32-1.25 (m, 6H), 0.88 (t, *J* = 6.8 Hz , 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 153.6, 131.5, 115.8, 110.7, 73.8, 65.9, 65.5, 40.0, 34.4, 31.7, 29.8, 22.6, 22.5, 14.0; HRMS calculated for C₁₈H₂₉NO₄Na (M + Na⁺): 346.1989, found: 346.1992.



(S)-3-((tert-butyldimethylsilyl)oxy)-2-hydroxy-2-(hydroxymethyl)propyl4-(dimethylamino)benzoate (8b): Compound 8b was obtained via the general

procedure in 90% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 9.1 min., t_R (*S*)-enantiomer (major) = 13.1 min.; 1:99 er. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 9.2 Hz, 2H), 6.65 (d, *J* = 9.2 Hz, 2H), 4.35 (d, *J* = 11.2 Hz, 1H), 4.30 (d, *J* = 11.2 Hz, 1H), 3.70 (s, 2H), 3.62 (d, *J* = 6.4 Hz, 2H), 3.17 (s, 1H), 3.03 (s, 6H), 3.72 (t, *J* = 6.8 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 153.5, 131.4, 116.0, 110.7, 73.9, 64.7, 64.4, 64.1, 39.9, 25.8, 18.2, 5.6; HRMS calculated for C₁₉H₃₃NO₅NaSi (M + Na⁺): 406.2020, found: 406.2022.





(S)-3-((tert-butyldiphenylsilyl)oxy)-2-hydroxy-2-(hydroxymethyl)propyl

4-(dimethylamino)benzoate (9b): Compound 9b was obtained via the general

procedure in 70% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 11.5 min., t_R (*S*)-enantiomer (major) = 18.5 min.; 2:98 er. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 9.2 Hz, 2H), 7.68-7.66 (m, 4H), 7.43-7.34 (m, 6H), 6.63 (d, *J* = 9.2 Hz, 2H), 4.42-4.42 (m, 2H), 3.75 (s, 2H), 3.66 (d, *J* = 6.4 Hz, 2H), 3.04 (s, 6H), 2.50 (t, *J* = 6.4 Hz, 2H), 1.08 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 153.5, 135.5, 132.7, 132.6, 131.5, 129.8, 127.8, 116.0, 110.6, 74.3, 64.8, 64.6, 64.1, 40.0, 26.8, 19.2; HRMS calculated for C₂₉H₃₇NO₅NaSi (M + Na⁺): 530.2333, found: 530.2332.







(S)-2,3-dihydroxy-2-(((triisopropylsilyl)oxy)methyl)propyl

4-(dimethylamino)benzoate (10b): Compound 10b was obtained via the general

procedure in 83% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (R)-enantiomer (minor) = 8.3 min., t_R (S)-enantiomer (major) = 12.6 min.; 2:98 er. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, J = 9.2 Hz, 2H), 6.63 (d, J = 9.2 Hz, 2H), 4.39 (d, J = 11.6 Hz, 1H), 4.33 (d, J = 11.6Hz, 1H), 3.80 (s, 2H), 3.65 (d, J = 6.8 Hz, 2H), 3.22 (s, 1H), 3.01 (s, 6H), 3.69 (t, J = 6.8 Hz, 1H), 1.17-1.10 (m, 3H), 1.09-1.06 (overlapped, 18H); ¹³C NMR (100 MHz, CDCl₃) & 167.4, 153.5, 131.5, 116.0, 110.6, 74.0, 64.7, 64.2, 40.0, 17.9, 11.8; HRMS calculated for $C_{22}H_{39}NO_5NaSi (M + Na^+)$: 448.2490, found: 448.2488.



Tes



(*R*)-2,3-dihydroxy-2-(methoxymethyl)propyl 4-(dimethylamino)benzoate (11b): Compound 11b was obtained via the general procedure in 81% yield. Chiral HPLC

analysis (CHIRALCEL OD-H column), 85:15 hexane/ethanol at 1.0 mL/min flow rate; t_R (*S*)-enantiomer (minor) = 13.8 min., t_R (*R*)-enantiomer (major) = 17.2 min.; 2:98 er. ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 12.0 Hz, 2H), 6.64 (d, *J* = 12.0 Hz, 2H), 4.34 (s, 2H), 3.64 (dd, *J* = 8.8, 2.0 Hz, 2H), 3.50 (s, 2H), 3.40 (s, 3H), 3.17 (s, 1H), 3.04 (s, 6H), 2.75 (t, *J* = 8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 153.6, 131.5, 115.9, 110.7, 74.2, 73.6, 64.9, 64.2, 59.6, 40.0; HRMS calculated for C₁₄H₂₁NO₅Na (M + Na⁺): 306.1312, found: 306.1310.





(R) - 3 - (benzy loxy) - 2 - hydroxy - 2 - (hydroxy methyl) propyl

4-(dimethylamino)benzoate (12b): Compound **4b** was obtained via the general procedure in 78% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 70:30

hexane/ethanol at 1.0 mL/min flow rate; t_R (*S*)-enantiomer (minor) = 24.7 min., t_R (*R*)-enantiomer (major) = 21.1 min.; >1:99 er. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, J = 8.8 Hz, 2H), 7.34-7.30 (m, 5H), 6.62 (d, J = 8.8 Hz, 2H), 4.58 (d, J = 1.2 Hz, 2H), 4.38 (d, J = 1.2 Hz, 2H), 3.64 (dd, J = 6.8, 2.4 Hz, 2H), 3.59 (s, 2H), 3.17 (s, 1H), 3.04 (s, 6H), 2.68 (t, J = 6.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 153.5, 137.7, 131.5, 128.4, 127.8, 127.7, 116.0, 110.7, 73.8, 73.7, 71.5, 64.9, 64.3, 40.0; HRMS calculated for C₂₀H₂₅NO₅Na (M + Na⁺): 382.1625, found: 382.1628.





(R)-2,3-dihydroxy-2-((prop-2-yn-1-yloxy)methyl)propyl

4-(dimethylamino)benzoate (13b): Compound 13b was obtained via the general procedure in 77% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10

hexane/ethanol at 1.0 mL/min flow rate; t_R (*S*)-enantiomer (minor) = 20.7 min., t_R (*R*)-enantiomer (major) = 25.1 min.; 2:98 er. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J*= 8.8 Hz, 2H), 6.63 (d, *J*= 8.8 Hz, 2H), 4.36 (s, 2H), 4.21 (d, *J*= 2.4 Hz, 2H), 3.65-3.63 (overlapped, 4H), 3.19 (s, 1H), 3.04 (s, 6H), 2.73 (s, 1H), 2.43 (d, *J*= 2.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 153.6, 131.5, 115.9, 110.7, 79.2, 75.0, 71.0, 64.8, 64.0, 58.8, 40.0; HRMS calculated for C₁₆H₂₁NO₅Na (M + Na⁺): 330.1312, found: 330.1312.



(S)-4-(benzyloxy)-2-hydroxy-2-(hydroxymethyl)butyl 4-(dimethylamino)benzoate (14b): Compound 14b was obtained via the general procedure in 80% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; $t_R(R)$ -enantiomer (minor) = 21.3 min., $t_R(S)$ -enantiomer (major) = 22.8

min.; 2:98 er. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J*= 8.8 Hz, 2H), 7.37-7.26 (overlapped, 5H), 6.63 (d, *J*= 8.8 Hz, 2H), 4.55 (d, *J*= 11.6 Hz, 1H), 4.31 (s, 2H), 3.83-3.78 (m, 2H), 3.75-3.71 (m, 2H), 3.57 (d, *J*= 6.4 Hz, 2H), 3.04 (s, 6H), 2.03-1.97 (m, 1H), 1.91-1.85 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.2, 153.5, 137.4, 131.4, 128.5, 127.9, 127.7, 116.0, 110.6, 73.7, 73.4, 66.4, 66.3, 65.8, 39.9, 33.5; HRMS calculated for C₂₁H₂₇NO₅Na (M + Na⁺): 396.1781, found: 396.1779.





(S)-4-((tert-butyldiphenylsilyl)oxy)-2-hydroxy-2-(hydroxymethyl)butyl

4-(dimethylamino)benzoate (15b): Compound 15b was obtained via the general procedure in 69% yield. Chiral HPLC analysis (CHIRALCEL AD-H column), 80:20 hexane/ethanol at 1.0 mL/min flow rate; $t_R(R)$ -enantiomer (minor) = 9.3 min., t_R S31

(*S*)-enantiomer (major) = 7.1 min.; >1:99 er. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J*= 8.8 Hz, 2H), 7.70-7.67 (overlapped, 4H), 7.45-7.39 (overlapped, 6H), 6.62 (d, *J*= 8.8 Hz, 2H), 4.39 (d, *J*= 11.2 Hz, 1H), 4.35 (d, *J*= 11.2 Hz, 1H), 4.07 (s, 1H), 4.03-3.99 (m, 1H), 3.95-3.91 (m, 1H), 3.62 (d, *J*= 6.8 Hz, 2H), 3.04 (s, 6H), 1.99-1.93 (m, 1H), 1.87-1.77 (m, 1H), 1.07 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 167.2, 153.5, 135.5, 132.6, 131.5, 130.0, 127.9, 127.9, 116.1, 110.7, 74.0, 66.4, 66.0, 60.7, 40.0, 35.3, 26.8, 19.0; HRMS calculated for C₃₀H₃₉NO₅NaSi (M + Na⁺): 544.2490, found: 544.2488.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.131	5630045	671416	49.683	62.926
2	9,260	5701835	395580	50.317	37.074
Total	1	11331880	1066996	100.000	100.000



DA Chi 28	0mm 4mm	PeakTable			
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.118	19418783	2451444	99.232	99.582
2	9,309	150203	10295	0.768	0.418
Total		19568986	2461739	100.000	100.000



(S) - 4 - ((tert-butyldimethylsilyl) oxy) - 2 - hydroxy - 2 - (hydroxymethyl) butyl

4-(dimethylamino)benzoate (16b): Compound 16b was obtained via the general

procedure in 88% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 9.9 min., t_R (*S*)-enantiomer (major) = 11.3 min.; >1:99 er. ¹H NMR (300 MHz, CDCl₃) δ 7.90 (d, *J*= 9.0 Hz, 2H), 6.62 (d, *J*= 9.0 Hz, 2H), 4.35 (d, *J*= 11.4 Hz, 1H), 4.26 (d, *J*= 11.4 Hz, 1H), 4.12 (s, 1H), 4.01-3.94 (m, 1H), 3.92-3.85 (m, 1H), 3.57 (d, *J*= 5.4 Hz, 1H), 3.10 (t, *J*= 6.0 Hz, 1H), 3.03 (s, 6H), 2.03-1.87 (m, 1H), 1.82-1.74 (m, 1H), 0.90 (s, 9H), 0.09 (d, *J*= 2.1 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 167.2, 153.5, 131.5, 116.1, 110.6, 74.0, 66.3, 65.9, 59.7, 40.0, 35.1, 25.8, 18.0, 5.6; HRMS calculated for C₂₀H₃₆NO₅Si (M + H⁺): 398.2357, found: 398.2357.



(S)-4-chloro-2-hydroxy-2-(hydroxymethyl)butyl 4-(di

4-(dimethylamino)benzoate

S33

(17b): Compound 17b was obtained via the general procedure in 70% yield. Chiral HPLC analysis (CHIRALCEL IB-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; $t_R(R)$ -enantiomer (minor) = 19.7 min., $t_R(S)$ -enantiomer (major) = 24.8 min.; 6:94 er. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J*= 9.2 Hz, 2H), 6.64 (d, *J*= 9.2 Hz, 2H), 4.41 (d, *J*= 11.6 Hz, 1H), 4.17 (d, *J*= 11.6 Hz, 1H), 3.76-3.71 (m, 2H), 3.57-3.53 (m, 1H), 3.49-3.44 (m, 1H), 309 (s, 1H), 3.04 (s, 6H), 2.22-2.04 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 153.7, 131.6, 115.4, 110.7, 73.5, 65.7, 65.1, 40.0, 39.4, 35.6; HRMS calculated for C₁₄H₂₀NO₄NaCl (M + Na⁺): 324.0973, found: 324.0976.



(S)-4-fluoro-2-hydroxy-2-(hydroxymethyl)butyl

4-(dimethylamino)benzoate

S34

(18b): Compound 18b was obtained via the general procedure in 73% yield. Chiral HPLC analysis (CHIRALCEL AS-H column), 90:10 hexane/ethanol at 1.0 mL/min flow rate; t_R (*R*)-enantiomer (minor) = 18.7 min., t_R (*S*)-enantiomer (major) = 23.2 min.; 6:94 er. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J*= 9.2 Hz, 2H), 6.64 (d, *J*= 9.2 Hz, 2H), 4.79 (t, *J*= 6.4 Hz, 1H), 4.67 (t, *J*= 6.4 Hz, 1H), 4.45 (d, *J*= 11.6 Hz, 1H), 4.22 (d, *J*= 11.6 Hz, 1H), 3.54 (q, *J*= 11.6 Hz, 1H), 3.04 (s, 6H), 2.04 (t, *J*= 6.0 Hz, 1H), 1.97 (t, *J*= 6.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 153.7, 131.6, 115.5, 110.7, 81.0, 79.4, 73.1, 66.3, 66.4, 40.0, 35.1, 34.9; HRMS calculated for C₁₄H₂₁NO₄F (M + H⁺): 286.1449, found: 286.1451.



2,3-dihydroxy-2-phenylpropyl 4-(dimethylamino)benzoate (19b): Compound 19b

was obtained via the general procedure in 65% yield. Chiral HPLC analysis (CHIRALCEL OJ-H column), 85:15 hexane/ethanol at 1.0 mL/min flow rate; t_R minor-enantiomer = 38.1 min., t_R major-enantiomer = 48.1 min.; 29:72 er. ¹H NMR (300 MHz, CDCl₃) δ 7.84 (d, J = 9.0 Hz, 2H), 7.54 (d, J = 6.9 Hz, 2H), 7.39-7.29 (m, 3H), 6.60 (d, J = 9.0 Hz, 2H), 4.62 (d, J = 11.7 Hz, 1H), 4.50 (d, J = 11.7 Hz, 1H), 3.88 (d, J = 11.7 Hz, 1H), 3.74 (d, J = 8.1 Hz, 2H), 3.13 (s, 1H), 3.01 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 167.6, 153.6, 141.2, 131.2, 128.3, 127.6, 125.6, 115.8, 110.7, 76.0, 68.0, 67.1, 40.0; HRMS calculated for C₁₈H₂₁NO₄Na (M + Na⁺): 338.1368, found: 338.1362.





PDA Chi 30	4am 4am	PeakTable			
Peak#	Ret. Time	Area	Height	Area %	Height %
1	38,102	3783071	60366	28,633	42.231
2	48.060	9429343	82576	71.367	57,769
Total	01	13212414	142943	100.000	100.000




210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm







210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm





210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm









































210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


























210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm





210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



7,875 7,876 7,876 7,770 688 7,770 688 7,756 665 44,005 7,424 4,005 7,425







