Supporting Information

for Importance of Chiral Phase–Transfer Catalysts with Dual Functions in Obtaining High Enantioselectivity in the Michael Reaction of Malonates and Chalcone Derivatives

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Preparation and Characterization of Chiral Quaternary Ammonium Bromide 2. To a solution of **1** (50 mg, 0.025 mmol)[1] in CH_2Cl_2 (5.0 mL) was added boron trifluoride-diethyl etherate (16 μL, 0.125 mmol) dropwise at 0 °C under argon atmosphere. After being stirred for 2 h at room temperature, triethylsilane (40 μL, 0.25 mmol) was introduced. The reaction mixture was then heated to reflux and stirred there for 24 h. The resulting mixture was poured into water and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and concentrated. The residual crude ammonium salt was passed through a column of ion exchange resin, Amberlyst A-26 (OH^-), with MeOH as eluant to convert it into the corresponding hydroxide, which was subsequently neutralized with 2 equiv of 1 N HBr solution. After removal of solvents, the residue was purified by column chromatography on silica gel (MeOH/CH_2Cl_2 = 1:10 as eluant) to give **2** (22.4 mg, 0.012 mmol, 48% yield): $[\alpha]_D^{29}$ –7.92 ° (*c* 0.42, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J* = 8.4 Hz, Ar-H), 7.89 (2H, s, Ar-H), 7.73-7.52 (18H, m, Ar-H), 7.48-7.33 (24H, m, Ar-H), 7.29-7.22 (20H, m, Ar-H), 7.18-7.16 (12H, m, Ar-H), 7.11-7.08 (12H, m, Ar-H), 6.92 (4H, s, Ar-H), 5.88 (2H, s, Ar_3CH), 4.77 (2H, d, *J* = 13.6 Hz, CH_2), 4.66 (2H, d, *J* = 12.8 Hz, CH_2), 4.51 (2H, d, *J* = 13.6 Hz, CH_2), 4.08 (2H, d, *J* = 12.8 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 143.6, 142.9, 142.7, 142.1, 141.9, 141.8, 140.6, 139.9, 139.8, 139.6, 135.6, 132.2, 132.0, 131.9, 131.8, 131.2, 130.8, 129.0, 128.6, 128.5, 128.4, 128.2, 127.7, 127.5, 127.3, 127.2, 126.9, 126.8, 126.6, 126.4, 126.2, 125.7, 125.6, 124.5, 124.3, 64.9, 60.3, 53.1, 29.6; IR (neat) 3057, 3034, 2924, 2853, 1593, 1576, 1497, 1454, 1429, 1029, 912, 883, 758, 696 cm^{-1}; HRMS (ESI) Calcd for $C_{146}H_{104}N$ (M^+): 1870.8163, Found: 1870,8172.

General Procedure for Enantioselective Michael Addition of Diethyl Malonate to Chalcone Derivative Using Designer Chiral Phase–Transfer Catalyst 1. To a mixture of 1,4-diarylenone **3** (0.1 mmol), K_2CO_3 (1.6 mg, 10 mol%) and chiral quaternary ammonium salt **1** (6 mg, 3 mol%) in toluene (0.2 mL) was added diethyl malonate (72 μL, 0.4 mmol) at –20 °C under argon atmosphere. The reaction mixture was stirred for 24 h at that temperarure, and then water and ether were added sequentially. The ethereal phase was separated, washed with brine and dried over Na_2SO_4. Evaporation of solvents gave the crude product, which was purified by column chromatography on silica gel (ethyl acetate/hexane as eluant) to afford the corresponding Michael adduct **4**. An

enantiomeric excess of **4** was determined by chiral stationary-phase HPLC analysis.

Characterization of Michael Adduct 4.

2-(1-Naphthalen-2-yl-3-oxo-3-phenylpropyl)malonic Acid Diethyl Ester (4b): $[\alpha]_D^{20}$ –8.37 ° [*c* 0.87, $CHCl_3$ (91% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (2H, d, *J* = 7.9 Hz, Ar-H), 7.75-7.70 (4H, m, Ar-H), 7.49 (1H, t, *J* = 7.9 Hz, Ar-H), 7.45-7.36 (5H, m, Ar-H), 4.37 (1H, dt, *J* = 9.1, 5.1 Hz, $COCH_2C\underline{H}$), 4.20 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.94 (1H, d, *J* = 9.9 Hz, $CHCO_2$), 3.89 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.63 (1H, dd, *J* = 16.6, 5.1 Hz, $COCH_2$), 3.58 (1H, dd, *J* = 16.6, 9.1 Hz, $COCH_2$), 1.22 (3H, t, *J* = 7.1 Hz, CH_3), 0.92 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 137.9, 136.6, 133.1, 132.8, 132.4, 128.4, 127.9, 127.9, 127.6, 127.4, 126.9, 126.2, 125.8, 125.5, 61.6, 61.3, 42.6, 40.8, 14.1, 13.8; IR (neat) 1728, 1684, 1597, 1506, 1449, 1368, 1256, 1219, 1152, 1096, 1028, 858, 820, 748, 691, 650 cm^{-1}; HRMS (ESI) Calcd for $C_{26}H_{26}NaO_5$ ($[M+Na]^+$): 441.1672, Found: 441.1673; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 4:1, flow rate = 1.0 mL/min, retention time; 28.5 min (minor) and 31.4 min (major).

2-[1-(4-Methoxyphenyl)-3-oxo-3-phenylpropyl]malonic Acid Diethyl Ester (4c): $[\alpha]_D^{19}$ –16.5 ° [*c* 3.40, $CHCl_3$ (87% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (2H, d, *J* = 7.5 Hz, Ar-H), 7.52 (1H, t, *J* = 7.5 Hz, Ar-H), 7.41 (2H, t, *J* = 7.5 Hz, Ar-H), 7.17 (2H, t, *J* = 8.7 Hz, Ar-H), 6.76 (2H, t, *J* = 8.7 Hz, Ar-H), 4.24-4.15 (2H, m, CO_2CH_2), 4.13 (1H, dt, *J* = 9.9, 4.4 Hz, $COCH_2C\underline{H}$), 3.96 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.78 (1H, d, *J* = 9.9 Hz, $CHCO_2$), 3.73 (3H, s, OCH_3), 3.51 (1H, dd, *J* = 16.6, 7.1 Hz, $COCH_2$), 3.40 (1H, dd, *J* = 16.6, 9.9 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 1.03 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 168.2, 167.5, 158.3, 136.7, 132.8, 132.2, 129.1, 128.4, 127.9, 113.6, 61.6, 61.3, 57.8, 55.1, 42.8, 40.2, 14.1, 13.9; IR (neat) 1728, 1684, 1611, 1597, 1581, 1514, 1464, 1449, 1368, 1248, 1179, 1152, 1113, 1096, 1032, 916, 860, 831, 733, 691 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{26}NaO_6$ ($[M+Na]^+$): 421.1622, Found: 421.1621; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 20:1, flow rate = 1.0 mL/min, retention time; 117 min (minor) and 155 min (major).

2-(1-[1,3]-Benzodioxol-5-yl-3-oxo-3-phenylpropyl)malonic Acid Diethyl Ester (4d): $[\alpha]_D^{21}$ –14.1 ° [*c* 1.96, $CHCl_3$ (89% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (2H, d, *J* = 7.5 Hz, Ar-H), 7.52 (1H, t, *J* = 7.5 Hz, Ar-H), 7.42 (2H, t, *J* = 7.5 Hz, Ar-H), 6.76 (1H, s, Ar-H), 6.71 (1H, d, *J* = 7.9 Hz, Ar-H), 6.65 (1H, d, *J* = 7.9 Hz, Ar-H), 5.87 (2H, s, OCH_3), 4.23-4.16 (2H, m, CO_2CH_2), 4.11 (1H, dt, *J* = 9.4, 4.4 Hz, $COCH_2C\underline{H}$), 4.00 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.75 (1H, d, *J* = 9.4 Hz, $CHCO_2$), 3.50 (1H, dd, *J* = 16.6, 4.4 Hz, $COCH_2$), 3.39 (1H, dd, *J* = 16.6, 9.4 Hz, $COCH_2$), 1.25 (3H, t, *J* = 7.1 Hz, CH_3), 1.07 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 168.0, 167.4, 147.3, 146.3, 136.6, 134.0, 132.9, 128.4, 127.9, 121.3, 108.5, 108.0, 100.8, 61.6, 61.3, 57.7, 42.7, 40.6, 14.1, 13.9; IR (neat) 1728, 1684, 1506, 1489, 1447, 1368, 1339, 1236, 1179, 1153, 1099, 1036, 934, 910, 858, 810, 729, 691 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{24}NaO_7$ ($[M+Na]^+$): 435.1414,

Found: 435.1412; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 4:1, flow rate = 1.0 mL/min, retention time; 47.3 min (minor) and 53.5 min (major).

2-[1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl]malonic Acid Diethyl Ester (4e): $[\alpha]_D^{22}$ –22.7 ° [*c* 0.60, $CHCl_3$ (85% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (2H, d, *J* = 7.5 Hz, Ar-H), 7.53 (1H, t, *J* = 7.5 Hz, Ar-H), 7.42 (2H, t, *J* = 7.5 Hz, Ar-H), 7.21 (4H, s, Ar-H), 4.24-4.13 (3H, m, $COCH_2C\underline{H}$ and CO_2CH_2), 3.98 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.78 (1H, d, *J* = 9.8 Hz, $CHCO_2$), 3.53 (1H, dd, *J* = 16.6, 4.4 Hz, $COCH_2$), 3.43 (1H, dd, *J* = 16.6, 9.8 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 1.05 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 167.9. 167.3, 138.9, 136.5, 133.0, 132.7, 129.6, 128.5, 128.4, 127.9, 61.7, 61.5, 57.3, 42.4, 40.2, 14.1, 13.9; IR (neat) 1728, 1686, 1597, 1580, 1491, 1449, 1414, 1368, 1252, 1227, 1153, 1094, 1030, 1015, 860, 829, 754, 691 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{23}ClNaO_5$ ($[M+Na]^+$): 425.1126, Found: 425.1128; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 20:1, flow rate = 1.0 mL/min, retention time; 65.5 min (minor) and 90.8 min (major).

2-[3-(4-Chlorophenyl)-3-oxo-1-phenylpropyl]malonic Acid Diethyl Ester (4f): $[\alpha]_D^{19}$ –17.2 ° [*c* 3.70, $CHCl_3$ (86% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.7 Hz, Ar-H), 7.38 (2H, d, *J* = 8.7 Hz, Ar-H), 7.26-7.15 (5H, m, Ar-H), 4.24-4.11 (3H, m, $COCH_2C\underline{H}$ and CO_2CH_2), 3.95 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.81 (1H, d, *J* = 9.5 Hz, $CHCO_2$), 3.52 (1H, dd, *J* = 16.6, 4.4 Hz, $COCH_2$), 3.40 (1H, dd, *J* = 16.6, 9.5 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 1.00 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 168.1, 167.4, 140.0, 139.3, 135.0, 129.4, 128.7, 128.3, 128.0, 127.1, 61.7, 61.4, 57.5, 42.6, 40.9, 14.1, 13.8; IR (neat) 1728, 1686, 1589, 1495, 1454, 1400, 1368, 1254, 1225, 1175, 1152, 1092, 1013, 860, 829, 764, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{23}ClNaO_5$ ($[M+Na]^+$): 425.1126, Found: 425.1127; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 20:1, flow rate = 1.0 mL/min, retention time; 47.1 min (minor) and 51.5 min (major).

2-(3-Oxo-3-phenyl-1-pyridin-2-ylpropyl)malonic Acid Diethyl Ester (4g): $[\alpha]_D^{21}$ –16.2 ° [*c* 2.13, $CHCl_3$ (90% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (1H, d, *J* = 4.7 Hz, Ar-H), 7.90 (2H, d, *J* = 7.9 Hz, Ar-H), 7.54 (1H, t, *J* = 7.9 Hz, Ar-H), 7.49 (1H, d, *J* = 7.5 Hz, Ar-H), 7.40 (1H, t, *J* = 7.5 Hz, Ar-H), 7.38 (2H, t, *J* = 7.9 Hz, Ar-H), 7.05 (1H, dd, *J* = 7.5 Hz, Ar-H), 4.32 (1H, dd, *J* = 9.9, 3.6 Hz, $CHCO_2$), 4.24-4.18 (2H, m, CO_2CH_2), 4.08 (1H, d, *J* = 9.9 Hz, $COCH_2C\underline{H}$), 4.03-3.95 (2H, m, CO_2CH_2), 3.80 (1H, dd, *J* = 17.4, 9.9 Hz, $COCH_2$), 3.42 (1H, dd, *J* = 17.4, 3.6 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 1.05 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 168.3, 167.7, 160.1, 148.7, 136.5, 135.9, 132.8, 128.3, 127.8, 124.7, 121.6, 61.5, 61.2, 41.7, 41.5, 14.0, 13.8; IR (neat) 1728, 1684, 1591, 1474, 1449, 1437, 1368, 1300, 1256, 1227, 1209, 1152, 1096, 1030, 1001, 860, 787, 750, 691 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{24}NO_5$ ($[M+H]^+$): 370.1649, Found: 370.1649. HPLC analysis: DAICEL Chiralpak OJ-H, hexane/ethanol = 9:1, flow rate = 1.0 mL/min, retention time; 12.6 min (minor) and 14.0 min (major).

2-(1-Furan-2-yl-3-oxo-3-phenylpropyl)malonic Acid Diethyl Ester (4h): $[\alpha]_D^{29}$ –1.34 ° [*c* 0.37, $CHCl_3$ (86% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (2H, d, *J* = 8.0 Hz, Ar-H), 7.55 (1H, t, *J* = 8.0 Hz, Ar-H), 7.43 (2H, t, *J* = 8.0 Hz, Ar-H), 7.26 (2H, s, Ar-H), 6.21 (1H, m, Ar-H), 6.11 (2H, d, *J* = 3.6 Hz, Ar-H), 4.33 (1H, ddd, *J* = 8.8, 8.0, 4.8 Hz, $COCH_2C\underline{H}$), 4.23-4.15 (2H, m, CO_2CH_2), 4.10 (2H, q, *J* = 7.2 Hz, CO_2CH_2), 3.90 (2H, d, *J* = 8.0 Hz, $CHCO_2$), 3.58 (1H, dd, *J* = 17.2, 8.8 Hz, $COCH_2$), 3.47 (1H, dd, *J* = 17.2, 4.8 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.2 Hz, CH_3), 1.16 (3H, t, *J* = 7.2 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 167.8, 167.6, 153.4, 141.4, 136.6, 133.0, 128.5, 128.0, 110.1, 107.0, 61.6, 61.5, 55.2, 39.9, 34.3, 14.1, 14.0; IR (neat) 1730, 1686, 1597, 1449, 1368, 1255, 1223, 1153, 1096, 1013, 860, 737, 690 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{22}NaO_6$ ($[M+Na]^+$): 381.1309, Found: 381.1305; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 20:1, flow rate = 0.5 mL/min, retention time; 49.9 min (major) and 54.1 min (minor).

2-(3-Oxo-3-phenyl-1-thiophen-2-ylpropyl)malonic Acid Diethyl Ester (4i): $[\alpha]_D^{20}$ -13.5 ° [*c* 1.66, $CHCl_3$ (94% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (1H, d, *J* = 4.7 Hz, Ar-H), 7.57 (1H, d, *J* = 4.7 Hz, Ar-H), 7.28-7.21 (4H, m, Ar-H), 7.16 (1H, t, *J* = 6.7 Hz, Ar-H), 7.07 (1H, dd, *J* = 8.7, 4.7 Hz, Ar-H), 4.24-4.13 (3H, m, $COCH_2C\underline{H}$ and CO_2CH_2), 3.94 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.83 (1H, d, *J* = 9.5 Hz, $CHCO_2$), 3.46 (1H, dd, *J* = 16.2, 4.7 Hz, $COCH_2$), 3.37 (1H, dd, *J* = 16.2, 9.5 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 0.99 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 168.0, 167.4, 143.9, 139.9, 133.4, 131.9, 128.2, 128.0, 127.9, 127.0, 61.6, 61.3, 57.4, 43.3, 41.2, 14.0, 13.8; IR (neat) 1728, 1661, 1518, 1497, 1454, 1414, 1368, 1256, 1233, 1152, 1096, 1028, 912, 858, 727, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{22}NaO_5S$ ($[M+Na]^+$): 397.1080, Found: 397.1078; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 4:1, flow rate = 1.0 mL/min, retention time; 19.9 min (minor) and 22.3 min (major).

2-(3-Oxo-1-phenyl-3-thiophen-2-ylpropyl)malonic Acid Diethyl Ester (4j): $[\alpha]_D^{18}$ –14.3 ° [*c* 1.39, $CHCl_3$ (94% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (1H, d, *J* = 3.6 Hz, Ar-H), 7.57 (1H, d, *J* = 5.1 Hz, Ar-H), 7.28-7.21 (4H, m, Ar-H), 7.16 (1H, t, *J* = 6.7 Hz, Ar-H), 7.07 (1H, dd, *J* = 5.1, 3.6 Hz, Ar-H), 4.24-4.13 (3H, m, $COCH_2C\underline{H}$ and CO_2CH_2), 3.94 (2H, q, *J* = 7.1 Hz, CO_2CH_2), 3.83 (1H, d, *J* = 9.4 Hz, $CHCO_2$), 3.46 (1H, dd, *J* = 16.2, 4.7 Hz, $COCH_2$), 3.37 (1H, dd, *J* = 16.2, 9.4 Hz, $COCH_2$), 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 1.00 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 168.0, 167.4, 143.9, 139.9, 133.5, 131.9, 128.2, 128.0, 127.9, 127.0, 61.6, 61.3, 57.4, 43.3, 41.2, 14.1, 13.8; IR (neat) 1728, 1661, 1518, 1454, 1414, 1368, 1256, 1234, 1152, 1096, 1028, 912, 858, 727, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{22}NaO_5S$ ($[M+Na]^+$): 397.1080, Found: 397.1065; HPLC analysis: DAICEL Chiralpak AD-H, hexane/ethanol = 4:1, flow rate = 1.0 mL/min, retention time; 19.5 min (minor) and 21.9 min (major).

Reference

(1) Ooi, T.; Ohara, D.; Tamura, M.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 6844.