Enantioselective Conjugate Addition of Boronic Acids to Enones
Catalyzed by O-Monoacyltartaric Acids

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Supplementary Information
### General Methods

Melting points (mp) are uncorrected. $^1$H and $^{13}$C NMR spectra were measured in CDCl$_3$ or DMSO-$d_6$ with JEOL JNM-ECX400 spectrometer. Tetramethylsilane (TMS) ($\delta = 0$ ppm) and CDCl$_3$ ($\delta = 77.0$ ppm) or DMSO-$d_6$ ($\delta = 39.52$ ppm) served as internal standards for $^1$H and $^{13}$C NMR, respectively. Infrared spectra were recorded on JEOL JIR-6500W. Mass spectra were measured with JEOL JMS-DX303HF mass spectrometer. Optical rotations were recorded on JASCO P-1010 polarimeter. High-pressure liquid chromatography (HPLC) was performed on JASCO P-980 and UV-1575. Thin-layer chromatography (TLC) analysis was carried out using Merck silica gel plates. Visualization was accomplished with UV light, phosphomolybdic acid and/or anisaldehyde. Column chromatography was performed using Kanto Chemical Silica Gel 60N (spherical, neutral, 63-210 µm).

Chalcone (2a) was purchased from Tokyo Kasei Kogyo (TCI) and used without purification. Benzalacetone (2b) was purchased from TCI and used after vacuum distillation. Enone 2c was prepared via addition of phenylmagnesium bromide to crotonaldehyde and subsequent MnO$_2$-oxidation. Enone 2d was prepared by TsOH-catalyzed aldol condensation of acetophenone with ethyl glyoxylate (polymer form) according to the literature. Enones 2e and 2f were prepared by NaOH-promoted aldol condensation of acetophenone with the corresponding aldehyde. ($E$)-Styrylboronic acid (3a) and ($E$)-1-octenylboronic acid (3b) were purchased from Sigma-Aldrich and used without purification. 2-Furanboronic acid (3c) and 2-benzofuranboronic acid (3e) were purchased from Wako Pure Chemical Industries and used without purification. Dichloromethane (dehydrated) and toluene (99%) were purchased from Kanto Chemical and nacalai tesque, respectively and stored over 4Å MS prior to use. All other solvents were purified based on standard procedures.
Synthesis of Catalyst 1k

(R,R)-Dibenzyl tartrate mono-3,5-di(tert-butyl)benzoate

To a solution of (R,R)-dibenzyl tartrate (495.8 mg, 1.50 mmol), triethylamine (0.33 mL, 2.34 mmol) and DMAP (4.5 mg, 2 mol %) in dry dichloromethane (6 mL) was added dropwise 3,5-di(tert-butyl)benzoyl chloride (379 mg, 1.0 equiv) in dry dichloromethane (4 mL) at rt. The reaction was stirred at rt for 19 h and quenched with water (10 mL). The mixture was extracted with dichloromethane (3 ×). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, evaporated, and purified by silica gel column chromatography (SiO₂18g, hexane/Et₂O/CH₂Cl₂ = 5/1/3) to give (R,R)-dibenzyl tartrate mono-3,5-di(tert-butyl)benzoate (594.8 mg, 73%).

1H-NMR (400 MHz, CDCl₃): δ 1.34 (s, 18H), 3.41 (d, J = 7.4 Hz, 1H), 4.92 (dd, J = 1.8, 7.4 Hz, 1H), 5.10 (d, J = 11.9 Hz, 1H), 5.24 (d, J = 11.9 Hz, 1H), 5.26 (d, J = 11.9 Hz, 1H), 5.67 (d, J = 1.8 Hz, 1H), 7.05 - 7.38 (m, 10 H), 7.65 (s, 1H), 7.82 (s, 2H).

(R,R)-Tartaric acid mono-3, 5-di(tert-butyl)benzoate (1k)

A suspension of (R,R)-dibenzyl tartrate mono-3, 5-di(tert-butyl)benzoate (594.8 mg, 1.09 mmol) and 10% Pd/C (59.4 mg) in ethyl acetate (20 mL) was vigorously stirred under hydrogen atmosphere at rt for 18 h. The mixture was filtered through a Celite pad with ethyl acetate and concentrated under vacuum to give (R,R)-tartaric acid mono-3,5-di(tert-butyl)benzoate (1k) (411.5 mg, quant).

mp 178-181 °C; [α]D²⁷ −4.3 (c 1.00, ethanol); IR (KBr, cm⁻¹) 3408, 2964, 1732, 1230, 1120, 1063, 895, 769, 702; 1H-NMR (400 MHz, DMSO-d₆) δ 1.32 (s, 18H), 4.66 (d, J = 2.3 Hz, 1H), 5.42 (d, J = 2.3 Hz, 1H), 7.71 (s, 1H), 7.84 (s, 2H); 13C-NMR (100 MHz, DMSO-d₆) δ 31.1, 34.6, 70.2, 74.1, 123.5, 127.6, 128.5, 151.0, 165.6, 168.3, 172.0; Anal. Calcd. for C₁₉H₂₆O₇·0.8H₂O C, 59.92; H, 7.31; Found: C, 59.79; H, 7.17.
General Procedure for Conjugate Addition of Boronic Acids to Enones Catalyzed by 1k

Under an argon atmosphere, a 20-mL screw-top test tube was charged with an enone 2 (0.3 mmol), a boronic acid 3 (0.36 mmol, 1.2 equiv), catalyst 1k (11.1 mg, 10 mol %), methanol (0.72 mmol) and toluene (1 mL) at rt. Then, the mixture was heated at 50 °C for the indicated time (monitored by TLC analysis). The reaction mixture was cooled to rt and concentrate under vacuum. The residue was purified by silica gel column chromatography (hexane/AcOEt) to give an adduct 4. The enantiomeric excess of 4 was determined by HPLC analysis using a chiral stationary phase column.

(3S,4E)-1,3,5-Triphenylpent-4-en-1-one (4a)
According to the general procedure, the reaction of chalcone (2a) (62.3 mg) and (E)-styrylboronic acid (3a) (53.5 mg) at 50 °C for 24 h gave adduct 4a (86.0 mg, 92%, 87% ee (S)). The spectral data were consistent with the literature. The absolute configuration was determined to be S in comparison with HPLC data. HPLC (Chiralpak AD-H, hexane/2-propanol = 200/1, flow rate = 1.0 mL/min, UV detection at 254 nm) \( t_R = 50.7 \) min (R, minor), 55.0 min (S, major).

(E)-4,6-Diphenylhex-5-en-2-one (4b)
According to the general procedure, the reaction of benzalacetone (2b) (43.9 mg) and (E)-styrylboronic acid (3a) (53.3 mg) at 60 °C for 48 h gave adduct 4b (34.6 mg, 46%, 81% ee). The spectral data were consistent with the literature. \([\alpha]_D^{28} = -15.6 \) (c 2.07, CHCl₃ for 81% ee); HPLC (Chiralpak AD-H, hexane/2-propanol = 300/1, flow rate = 1.0 mL/min, UV detection at 254 nm) \( t_R = 32.1 \) min (minor), 37.0 min (major).

(E)-1,5-Diphenyl-3-methylpent-4-en-1-one (4c)
According to the general procedure, the reaction of (E)-1-phenylbut-2-en-1-one (2c) (44.2 mg) and (E)-styrylboronic acid (3a) (53.3 mg) at 50 °C for 24 h gave adduct 4c (69.3 mg, 92%, 81% ee). The spectral data were consistent with the literature.\(^5\)

\[ \alpha \] D\(^{29} \) +45.3 (c 1.09, CHCl\(_3\) for 81% ee); HPLC (Chiralpak AD-H, hexane/2-propanol = 99/1, flow rate = 1.0 mL/min, UV detection at 254 nm) \( t_R = 10.2 \) min (major), 11.7 min (minor).

**Ethyl 4-oxo-4-phenyl-2-((E)-2-pheneylethenyl)butanote (4d)**

According to the general procedure, the reaction of (E)-ethyl 4-oxo-4-phenylbut-2-enoate (2d) (61.4 mg) and (E)-styrylboronic acid (3a) (53.1 mg) at 50 °C for 48 h gave adduct 4d (68.4 mg, 74%, 85% ee).

mp 71-73 °C; \([\alpha]_D^{28} +86.8\) (c 1.01, CHCl\(_3\) for 85% ee); IR (KBr, cm\(^{-1}\)) 3059, 3028, 2981, 1728, 1687, 1597, 1448, 1215, 1163, 966, 756, 692; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \)

1.27 (t, \( J \) = 7.3 Hz, 3H), 3.25 (dd, \( J \) = 4.6, 17.9 Hz, 1H), 3.69 (dd, \( J \) = 9.2, 17.9 Hz, 1H), 3.88 (ddd, \( J \) = 4.6, 8.2, 9.2 Hz, 1H), 4.19 (m, 2H), 6.28 (dd, \( J \) = 8.2, 16.0 Hz, 1H), 6.60 (d, \( J \) = 16.0 Hz, 1H), 7.24 (t, \( J \) = 7.8 Hz, 1H), 7.31 (t, \( J \) = 7.8 Hz, 2H), 7.37 (d, \( J \) = 7.8 Hz, 2H), 7.47 (t, \( J \) = 7.8 Hz, 2H), 7.57 (t, \( J \) = 7.8 Hz, 1H), 7.98 (d, \( J \) = 7.8 Hz, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \)

14.1, 40.8, 44.2, 61.0, 126.1, 126.3, 127.7, 128.0, 128.5, 128.6, 132.7, 133.2, 136.43, 136.48, 173.2, 197.4; HRMS (FAB) Calcd. for C\(_20\)H\(_{21}\)O\(_3\) (M+H\(^+\)) 309.1491, found 309.1484; HPLC (Chiralpak AD-H, hexane/2-propanol = 19/1, flow rate = 1.0 mL/min, UV detection at 254nm) \( t_R = 16.1 \) min (minor), 19.8 min (major).

\( (E)\)-3-(p-Methoxyphenyl)-1,5-diphenylpent-4-en-1-one (4e)

According to the general procedure, the reaction of (E)-3-(p-methoxyphenyl)-1-phenylprop-2-en-1-one (2e) (71.5 mg) and (E)-styrylboronic acid (3a) (53.3 mg) at 50 °C for 24 h gave adduct 4e (71.5 mg, 84%, 87% ee).

mp 64-66 °C; [\( \alpha \)]\(_D^{28} \) –7.7 (c 0.97, CHCl\(_3\) for 87% ee); IR (KBr, cm\(^{-1}\)) 3352, 3059, 2933, 2835, 1693, 1597, 1514, 1446, 1257, 1178, 1034, 966, 829, 750, 692; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \)

3.44 (dd, \( J \) = 6.9, 16.5 Hz, 1H), 3.49 (dd, \( J \) = 7.4, 16.5 Hz, 1H), 3.78 (s, 3H), 4.25 (ddd, \( J \) = 5.5, 6.9, 7.4 Hz, 1H), 6.35 (d, \( J \) = 16.0 Hz, 1H), 6.40 (dd, \( J \) = 5.5, 16.0 Hz, 1H), 6.85 (d, \( J \) =
8.7 Hz, 2H), 7.15 - 7.32 (m, 7H), 7.44 (t, J = 7.6 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.93 (d, J = 7.3 Hz, 2H); \'H NMR (100 MHz, CDCl3) δ 43.0, 44.5, 55.1, 113.9, 126.1, 127.1, 128.0, 128.4, 128.5, 128.6, 129.6, 132.9, 133.0, 135.2, 137.0, 137.1, 158.1, 158.2, 198.2; HRMS (FAB) : Calcd. for C_{24}H_{22}O_{2}Na (M+Na^+) 365.1517, found 365.1530; HPLC (Chiralpak AS-H, hexane/2-propanol = 19/1, flow rate = 1.0 mL/min, UV detection at 254 nm) t_R = 14.5 min (major), 16.9 min (minor).

\[(E)-3-(p-Nitrophenyl)-1,5-diphenylpent-4-en-1-one (4f)\]

According to the general procedure, the reaction of (E)-3-(p-nitrophenyl)-1-phenylprop-2-en-1-one (2f) (76.2 mg) and (E)-styrylboronic acid (3a) (53.1 mg) at 50 °C for 24 h gave adduct 4f (72.7 mg, 68%, 88% ee).

\([\alpha]_{D}^{29} +29.7 (c 1.415, \text{CHCl}_3 \text{ for } 87\% \text{ ee}); \text{IR (neat, cm}^{-1}\text{)} 3059, 2926, 2852, 1687, 1680, 1597, 1514, 1495, 1448, 1344, 1205, 1111, 968, 856, 746, 692; \H NMR (400 MHz, CDCl3) δ 3.54 (dd, J = 7.4, 17.0 Hz, 1H), 3.59 (dd, J = 6.9, 17.0 Hz, 1H), 4.43 (ddd, J = 6.9, 6.9, 7.4 Hz, 1H), 6.37 (dd, J = 6.9, 16.0 Hz, 1H), 6.44 (d, J = 16.0 Hz, 1H), 7.20-7.35 (m, 5H), 7.40-7.60 (m, 5H), 7.94 (d, J = 7.8 Hz, 2H), 8.18 (d, J = 8.7 Hz, 2H); \C NMR (100 MHz, CDCl3) δ 43.6, 43.9, 123.9, 126.3, 127.7, 128.0, 128.6, 128.71, 128.73, 130.8, 131.3, 133.4, 136.5, 136.6, 146.7, 150.9, 197.1; HPLC (Chiralpak AS-H, hexane/2-propanol = 9/1, flow rate = 1.0 mL/min, UV detection at 254 nm) t_R = 29.7 min (major), 34.8 min (minor).

\[(E)-1,3-Diphenylundec-4-en-1-one (4g)\]

According to the general procedure, the reaction of chalcone (2a) (62.4 mg) and (E)-1-octenylboronic acid (3b) (56.0 mg) at 60 °C for 120 h gave adduct 4g (46.1 mg, 48%, 69% ee (S)). The spectral data were consistent with the literature.\textsuperscript{3} The absolute configuration was determined to be S in comparison with HPLC data.\textsuperscript{3} HPLC (Chiralcel OD-H, hexane/2-propanol = 99/1, flow rate = 1.0 mL/min, UV detection at 254nm) t_R = 6.8 min (R, minor), 7.6 min (S, major).
3-(Furan-2-yl)-1,3-diphenylpropan-1-one (4h)

According to the general procedure, the reaction of chalcone (2a) (62.5 mg) and 2-furanboronic acid (3c) (40.1 mg) at 50 °C for 24 h gave adduct 4h (45.6 mg, 55%, 68% ee). 

\([\alpha]_D^{28} -35.7 \text{ (c 0.955, CHCl}_3 \text{ for 68% ee); IR (neat, cm}^{-1}) 3061, 3028, 2924, 1684, 1597, 1508, 1448, 1144, 1078, 688; ^1H NMR (400 MHz, CDCl}_3) \delta 3.56 (dd, J = 6.9, 17.0 Hz, 1H), 3.82 (dd, J = 6.9, 7.3 Hz, 1H), 4.84 (dd, J = 6.9, 7.3 Hz, 1H), 5.10 (dt, J = 7.3, 7.8 Hz, 2H), 6.03 (d, J = 3.2 Hz, 1H), 6.26 (dd, J = 1.8, 3.2 Hz, 1H), 7.19 - 7.32 (m, 6H), 7.44 (dd, J = 7.3, 7.8 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.93 (d, J = 7.8 Hz, 2H); ^13C NMR (100 MHz, CDCl}_3) \delta 40.2, 43.5, 105.7, 110.1, 126.8, 127.8, 128.0, 128.6, 133.1, 136.8, 141.5, 141.9, 156.7, 197.4 (one carbon is overlapped); HRMS (FAB) Calcd. for C_{19}H_{16}O_2Na (M+Na) + 299.1048, found 299.1038; HPLC (Chiralcel OD-3, hexane/2-propanol = 49/1, flow rate = 1.0 mL/min, UV detection at 254 nm) \(t_R = 9.8 \text{ min (minor), 10.2 min (major).}

3-(Benzofuran-2-yl)-1,3-diphenylpropan-1-one (4i)

According to the general procedure, the reaction of chalcone (2a) (62.3 mg) and 2-benzofuranboronic acid (3d) (58.4 mg) at 50 °C for 24 h gave adduct 4i (77.3 mg, 79%, 81% ee).

\([\alpha]_D^{28} -73.2 \text{ (c 0.715, CHCl}_3 \text{ for 81% ee); IR (neat, cm}^{-1}) 3032, 2891, 1676, 1599, 1579, 1495, 1454, 1236, 1165, 700; ^1H NMR (400 MHz, CDCl}_3) \delta 3.67 (dd, J = 7.3, 17.4 Hz, 1H), 3.94 (dd, J = 7.3, 17.4 Hz, 1H), 4.98 (t, J = 7.3 Hz, 1H), 6.43 (s, 1H), 7.12 - 7.58 (m, 12H), 7.96 (d, J = 7.4 Hz, 2H); ^13C NMR (400 MHz, CDCl}_3) \delta 40.5, 43.2, 102.9, 110.9, 120.5, 122.5, 123.5, 127.0, 127.9, 128.0, 128.5, 128.58, 128.65, 133.2, 136.6, 141.2, 154.7, 159.8, 197.1; HRMS (FAB) Calcd. for C_{23}H_{18}O_2Na (M+Na) + 349.1204, found 349.1202; HPLC (Chiralpak AD-H, hexane/2-propanol = 39/1, flow rate = 1.0 mL/min, UV detection at 254 nm) \(t_R = 19.0 \text{ min (major), 25.2 min (minor).}
$^1$H and $^{13}$C NMR Spectra of New Compounds
**HPLC Traces of Optically Active Compounds**

1. Racemic

2. Optically active (87% ee)
1. Racemic

CHIRALPAK AD-H
Hexane/iPrOH = 300/1
1.0 mL/min, 254 nm

Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2010

2. Optically active (81% ee)

Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2010
1. Racemic

2. Optically active (81% ee)
1. Racemic

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** CALCULATION REPORT **

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2. Optically active (87% ee)
1. Racemic

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2. Optically active (69% ee)

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1.0 mL/min, 254 nm

2. Optically active (68% ee)
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