Copper-Catalyzed Asymmetric [4+1] Cycloadditions of Enones with Diazo Compounds to Form Dihydrofurans

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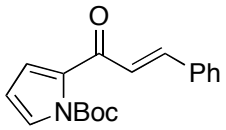
Supporting Information

1. General

All reactions were carried out in oven-dried glassware under an atmosphere of nitrogen. CH_2Cl_2 was purified by passage through a neutral alumina column under argon. $CuOTf{\cdot}0.5C_6H_5CH_3$ was purchased from Aldrich, and the diazo esters[1] and bpy*[2] were prepared according to literature procedures. All other chemicals were purchased from commercial suppliers and used as received, unless noted otherwise.

HPLC analyses were carried out on an Agilent 1100 Series system with Daicel Chiralpak® columns in hexane/isopropanol mixtures. Melting points were measured on a Hoover melting point apparatus and are uncorrected.

2. Preparation of Starting Material



***tert*-Butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate.** A 100-mL flask was charged with 2-acetylpyrrole (3.27 g, 30.0 mmol), 4-(dimethylamino)pyridine (73 mg, 0.60 mmol), NEt_3 (4.2 mL, 30 mmol), and THF (30 mL). To this mixture was added a solution of Boc anhydride (dropwise; 30 mL, 1.0 M in THF, 30.0 mmol). The reaction mixture was stirred overnight, and then a saturated solution of $NaHCO_3$ (30 mL) was added. The resulting mixture was extracted with Et_2O (30 mL x 3), and the combined extracts were dried over $MgSO_4$ and concentrated. The product was purified by column chromatography (hexanes/EtOAc 5:1), which furnished 5.64 g (90%) of *N*-Boc-2-acetylpyrrole.

N-Boc-2-acetylpyrrole (5.64 g, 27.0 mmol) was added to a stirred solution of LiHMDS (1.0 M in THF; 28 mL, 28 mmol) at –78 °C under argon, and the resulting mixture was stirred for 2 h. Then, benzaldehyde (2.8 mL, 27 mmol) was added, and the reaction mixture was stirred for an additional 2 h. The reaction was then quenched by the addition of saturated aq NH_4Cl (40 mL), and the mixture was extracted with Et_2O

(30 mL x 3). The combined extracts were dried over $MgSO_4$, concentrated, and purified by column chromatography (hexanes/EtOAc 5:1), which furnished *N*-Boc-2-(3-hydroxy-1-oxo-3-phenylpropyl)pyrrole (6.82 g, 80%).

NEt_3 (9.0 mL, 65 mmol) and MsCl (1.65 mL, 21.7 mmol) were added to a solution of *N*-Boc-2-(3-hydroxy-1-oxo-3-phenylpropyl)pyrrole (6.82 g, 21.7 mmol) in THF (20 mL). This reaction mixture was stirred overnight, and then it was quenched by the addition of saturated aq NH_4Cl (40 mL). The mixture was extracted with Et_2O (30 mL x 3), and the combined extracts were dried over $MgSO_4$, concentrated, and purified by column chromatography (hexanes/EtOAc 5:1), which furnished *tert*-butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate (5.89 g, 91%).

mp 75-76 °C;

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.60-7.57 (m, 2H), 7.43-7.40 (m, 4H), 7.12 (d, *J* = 16.0 Hz, 1H), 6.86 (dd, *J* = 3.5, 1.6 Hz, 1H), 6.25 (t, *J* = 3.3 Hz, 1H), 1.56 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.8, 149.0, 143.7, 135.0, 134.3, 130.6, 129.1, 128.5, 127.4, 125.7, 120.8, 110.5, 85.2, 27.0;

IR (film) 2981, 1748, 1661, 1639, 1606, 1440, 1415, 1315, 1150 cm^{-1};

HRMS (ESI) calcd for $C_{18}H_{19}NO_3Na$ ($M + Na^+$) 320.1257, found 320.1266.

All other materials have been reported previously.

3. Copper-Catalyzed Asymmetric [4+1] Cycloadditions (Table 3)

All yields, dr's, and ee's are the average of two runs, one with (–)-bpy* and one with (+)-bpy*. All dr's were determined through analysis of the ^{1}H NMR spectra of the unpurified reaction mixtures.

General Procedure A. The catalyst was prepared by adding a solution of (–)-bpy* (8.4 mg, 0.013 mmol) in CH_2Cl_2 (4 mL) to CuOTf·0.5$C_6H_5CH_3$ (2.6 mg, 0.010 mmol) and stirring the resulting mixture for 20 min. This solution was then added to the enone (1.0 mmol), and the mixture was stirred for 5 min. Then, a solution of the diazoacetate (1.1 mmol) in CH_2Cl_2 (1.0 mL) was added. After 1 h of stirring at room temperature, the reaction mixture was filtered through a plug of silica gel (50% Et_2O/hexane as the eluant).

General Procedure B. The catalyst was prepared by adding a solution of (–)-bpy* (7.7 mg, 0.012 mmol) in CH_2Cl_2 (10 mL) to CuOTf·0.5$C_6H_5CH_3$ (2.6 mg, 0.010 mmol) and stirring the resulting mixture for 20 min. This solution was then added to the enone (1.0 mmol) in CH_2Cl_2 (60 mL), and the mixture was stirred for 5 min. Then, a solution of the diazoacetate (1.4 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After 1 h of stirring at room temperature, the reaction mixture was filtered through a plug of silica gel (50% Et_2O/hexane as the eluant).

(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3,5-diphenylfuran-2-carboxylate (Table 3, entry 1). General Procedure A was followed, with (–)-bpy*, *trans*-chalcone (208 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 341 mg (80%; 86% de, 84% ee); run 2, 328 mg (77%; 86% de, 86% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min) with t_r(major) 12.2 min, t_r(minor) 13.0 min.

$[\alpha]^{20}_D$ = –106 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.75-7.73 (m, 2H), 7.33-7.31 (m, 2H), 7.18-7.04 (m, 9H), 5.35 (d, *J* = 2.9 Hz, 1H), 5.26 (d, *J* = 4.9 Hz, 1H), 4.83 (dd, *J* = 4.8, 1.8 Hz, 1H), 3.14 (septet, *J* = 6.8 Hz, 2H), 1.16 (d, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6, 157.4, 146.5, 143.3, 141.1, 130.7, 129.6, 129.0, 128.9, 127.5, 126.4, 124.7, 99.5, 86.6, 54.4, 28.3, 23.6;

IR (film) 3064, 3029, 2965, 2931, 2870, 1774, 1753, 1649, 1602, 1494, 1449, 1213 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{30}O_3Na$ (M + Na^+) 449.2087, found 449.2102.

(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-phenyl-5-(4-trifluoromethylphenyl)furan-2-carboxylate (Table 3, entry 2). General Procedure A was followed, with (–)-bpy*, *trans*-4′-(trifluoromethyl)chalcone (276 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1,

282 mg (57%; 90% de, 76% ee); run 2, 297 mg (60%; 90% de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 7.8 min, t_r(minor) 10.0 min.

$[\alpha]^{20}_D$ = –90.1 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.54-7.52 (m, 2H), 7.33-7.27 (m, 4H), 7.18-7.04 (m, 6H), 5.29 (d, *J* = 2.9 Hz, 1H), 5.23 (d, *J* = 4.9 Hz, 1H), 4.79 (dd, *J* = 4.5, 3.1 Hz, 1H), 3.20-3.00 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.3, 156.0, 146.3, 142.8, 140.9, 129.7, 128.3, 128.0, 127.6, 126.6, 126.4, 126.0, 125.9, 124.8, 123.7, 101.9, 86.5, 54.4, 28.3, 23.6;

IR (film) 3066, 3030, 2966, 2932, 2872, 1773, 1755, 1647, 1619, 1493, 1457, 1326, 1165, 1070 cm^{-1};

HRMS (ESI) calcd for $C_{30}H_{29}F_3O_3Na$ (M + Na^+) 517.1961, found 517.1977.

(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-phenyl-5-(4-chlorophenyl)furan-2-carboxylate (Table 3, entry 3). General Procedure A was followed, with (–)-bpy*, *trans*-4′-chlorochalcone (243 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 360 mg (78%; 92% de, 88% ee); run 2, 350 mg (76%; 88% de, 87% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 6.5 min, t_r(minor) 8.3 min.

$[\alpha]^{20}_D$ = –108 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.46-7.43 (m, 2H), 7.30-7.28 (m, 2H), 7.18-7.04 (m, 8H), 5.23 (d, *J* = 3.3 Hz, 1H), 5.22 (d, *J* = 5.1 Hz, 1H), 4.79 (dd, *J* = 4.8, 3.0 Hz, 1H), 3.10 (septet, *J* = 6.4 Hz, 2H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 156.3, 146.4, 143.1, 141.0, 135.4, 129.6, 129.2, 129.1, 128.5, 128.1, 127.7, 127.5, 124.8, 100.1, 86.5, 54.4, 28.3, 23.7;

IR (film) 3065, 3030, 2965, 2931, 2871, 1773, 1755, 1648, 1598, 1490, 1456, 1163 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{29}ClO_3Na$ (M + Na^+) 483.1697, found 483.1720.

(2*R*,3*S*)-2,6-Diisopropylphenyl 2-acetoxy-5-(4-methoxyphenyl)-5-oxo-3-phenylpentanoate (Table 3, entry 4). General Procedure A was followed, with (–)-bpy*, *trans*-4′-methoxychalcone (238 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). To the unpurified reaction mixture was added CH_3CN (2 mL) and 10% aq HBF_4 (2 mL). The mixture was stirred for 10 min, and then it was diluted with water and extracted with Et_2O (20 mL x 3). The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated. The resulting hydroxyketone was dissolved in CH_2Cl_2 (10 mL), and NEt_3 (0.84 mL, 6.0 mmol), DMAP (24.4 mg, 0.20 mmol), and Ac_2O (0.47 mL, 5.0 mmol) were added to the stirred solution. After 15 min, the reaction mixture was diluted with water and extracted with CH_2Cl_2 (20 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. After chromatography on silica gel (hexanes/ethyl ether 20:1), the title compound was isolated as a white solid: run 1, 360

mg (85%; 90% de, 92% ee); run 2, 350 mg (83%; 90% de, 91% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 17.8 min, t_r(minor) 26.0 min.

mp 158-161 C;

$[\alpha]^{20}_D$ = –58.8 (c = 1.00, CH_2Cl_2);

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.97-7.94 (m, 2H), 7.48-7.46 (m, 2H), 7.35-7.31 (m, 2H), 7.27-7.20 (m, 2H), 7.14-7.13 (m, 2H), 6.95-6.91 (m, 2H), 5.64 (d, *J* = 3.8 Hz, 1H), 4.39 (dt, *J* = 10.2, 3.5 Hz, 1H), 3.87 (s, 3H), 3.82 (dd, *J* = 18.0, 10.4 Hz, 1H), 3.40 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.10-2.80 (m, 1H), 2.80-2.50 (m, 1H), 2.21 (s, 3H), 1.14 (d, *J* = 6.8 Hz, 6H), 1.30-0.80 (m, 6H);

^{13}C NMR (C_6D_6, 100 MHz) δ 195.4, 170.3, 168.2, 163.8, 145.1, 140.2, 130.5, 130.0, 128.8, 128.5, 127.6, 127.0, 124.1, 113.9, 76.0, 55.7, 41.8, 38.9, 27.3, 24.0, 22.8, 20.8;

IR (film) 2964, 2929, 2872, 1765, 1749, 1677, 1597, 1510, 1456, 1257 cm^{-1};

HRMS (ESI) calcd for $C_{32}H_{36}O_6Na$ (M + Na^+) 539.2404, found 539.2396.

(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-(4-chlorophenyl)-5-phenyl-furan-2-carboxylate (Table 3, entry 5). General Procedure A was followed, with (–)-bpy*, *trans*-4-chlorochalcone (243 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 360 mg (78%; 90% de, 88% ee); run 2, 383 mg (83%; 94% de, 88% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 0.9 mL/min) with t_r(major) 8.1 min, t_r(minor) 5.9 min.

$[\alpha]^{20}_D$ = –126 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.74-7.71 (m, 2H), 7.16-7.00 (m, 10H), 5.23 (d, *J* = 2.9 Hz, 1H), 5.11 (d, *J* = 4.9 Hz, 1H), 4.69 (dd, *J* = 4.7, 3.0 Hz, 1H), 3.12 (septet, 2H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.7, 146.4, 141.7, 141.0, 133.9, 130.5, 129.8, 129.7, 129.5, 129.0, 127.5, 126.4, 124.8, 99.0, 86.3, 53.6, 28.3, 23.6;

IR (film) 3065, 3029, 2965, 2931, 2871, 1775, 1752, 1648, 1601, 1577, 1492, 1163 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{29}ClO_3Na$ (M + Na^+) 483.1697, found 483.1716.

(2*R*,3*S*)-2,6-Diisopropylphenyl 2,3-dihydro-3-(4-methoxyphenyl)-5-phenyl-furan-2-carboxylate (Table 3, entry 6). General Procedure A was followed, with (–)-bpy*, *trans*-4-methoxychalcone (238 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 384 mg (84%; 80% de, 93% ee); run 2, 379 mg (83%; 80% de, 93% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 7.4 min, t_r(minor) 9.6 min.

$[\alpha]^{20}_D$ = –130 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.77-7.75 (m, 2H), 7.26-7.24 (m, 2H), 7.16-7.04 (m, 6H), 6.81-6.79 (m, 2H), 5.39 (d, *J* = 2.9 Hz, 1H), 5.29 (d, *J* = 5.0 Hz, 1H), 4.84 (dd, *J* = 5.0, 2.9 Hz, 1H), 3.33 (s, 3H), 3.16 (septet, *J* = 6.7 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.7, 160.0, 157.2, 146.5, 141.1, 135.3, 130.8, 129.6, 129.2, 129.0, 127.5, 126.4, 124.7, 115.0, 99.8, 86.8, 55.2, 53.8, 28.3, 23.7;

IR (film) 3065, 3029, 2965, 2932, 2870, 1773, 1752, 1648, 1610, 1584, 1512, 1462, 1448, 1251, 1145, 1033 cm^{-1};

HRMS (ESI) calcd for $C_{30}H_{32}O_4Na$ ($M + Na^+$) 479.2193, found 479.2216.

***tert*-Butyl 2-((4*S*,5*R*)-5-((2,6-diisopropylphenoxy)carbonyl)-4,5-dihydro-4-phenylfuran-2-yl)-1*H*-pyrrole-1-carboxylate (Table 3, entry 7).** General Procedure A was followed, with (–)-bpy*, *tert*-butyl 2-((*E*)-3-phenylacryloyl)-1*H*-pyrrole-1-carboxylate (297 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 347 mg (66%; >90% de, 94% ee); run 2, 368 mg (70%; >90% de, 92% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 99:1, flow 0.9 mL/min) with t_r(major) 5.2 min, t_r(minor) 4.8 min.

$[\alpha]^{20}_D$ = –129 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.54-7.52 (m, 2H), 7.26 (dd, *J* = 3.2, 1.8 Hz, 1H), 7.21-7.17 (m, 2H), 7.11-7.03 (m, 4H), 6.82 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.03 (t, *J* = 3.4 Hz, 1H), 5.77 (d, *J* = 2.8 Hz, 1H), 5.31 (d, *J* = 5.8 Hz, 1H), 4.90 (dd, *J* = 5.8, 2.7 Hz, 1H), 3.13 (septet, 2H), 1.25 (s, 9H), 1.15 (d, *J* = 6.8 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6, 150.3, 149.0, 146.5, 143.5, 141.1, 129.5, 128.5, 128.0, 127.4, 125.6, 124.8, 124.7, 117.9, 111.3, 103.4, 86.3, 84.0, 55.0, 28.2, 28.0, 23.7;

IR (film) 2966, 2932, 2871, 1754, 1652, 1456, 1306, 1144 cm^{-1};

HRMS (ESI) calcd for $C_{32}H_{37}NO_5Na$ ($M + Na^+$) 538.2564, found 538.2554.

(2*R*,3*S*)-2,6-Diisopropylphenyl 3-(furan-3-yl)-2,3-dihydro-5-phenylfuran-2-carboxylate (Table 3, entry 8). General Procedure A was followed, with (–)-bpy*, (*E*)-1-(3-furyl)-3-phenyl-2-propen-1-one (198 mg, 1.0 mmol), and 2,6-diisopropylphenyl-diazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 258 mg (62%; 68% de, 85% ee); run 2, 262 mg (63%; 70% de, 88% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min) with t_r(major) 12.5 min, t_r(minor) 13.1 min.

$[\alpha]^{20}_D$ = –97.1 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.72-7.70 (m, 2H), 7.14-7.00 (m, 8H), 6.23 (s, 1H), 5.27 (d, *J* = 2.9 Hz, 1H), 5.21 (d, *J* = 5.3 Hz, 1H), 4.73 (dd, *J* = 5.3, 2.8 Hz, 1H), 3.12 (septet, 2H), 1.16 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.2, 146.4, 144.4, 141.0, 139.9, 130.7, 129.6, 129.0, 127.5, 127.3, 126.3, 124.8, 110.1, 98.5, 85.6, 45.0, 28.3, 23.7;

IR (film) 3065, 2965, 2871, 1774, 1753, 1650, 1578, 1448, 1162 cm^{-1};

HRMS (ESI) calcd for $C_{27}H_{28}O_4Na$ ($M + Na^+$) 439.1880, found 439.1870.

(2*R*,3*R*)-2,6-Diisopropylphenyl 2,3-dihydro-5-phenyl-3-(*E*)-styrylfuran-2-carboxylate (Table 3, entry 9). General Procedure A was followed, with (–)-bpy*, *trans,trans*-1,5-diphenylpenta-2,4-dien-1-one (234 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazo-acetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 344 mg (76%; 76% de, 93% ee); run 2, 344 mg (76%; 74% de, 92% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 0.7 mL/min) with t_r(major) 16.8 min, t_r(minor) 22.4 min.

$[\alpha]^{20}_D$ = –176 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.76-7.73 (m, 2H), 7.22-7.20 (m, 2H), 7.16-7.04 (m, 9H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.19 (dd, *J* = 15.7, 8.3 Hz, 1H), 5.25 (d, *J* = 2.8 Hz, 1H), 5.15 (d, *J* = 5.5 Hz, 1H), 4.43 (ddd, *J* = 8.0, 5.4, 2.6 Hz, 1H), 3.18 (septet, *J* = 6.7 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 12H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.4, 157.2, 146.4, 141.0, 137.4, 132.3, 130.8, 130.2, 129.6, 129.2, 129.0, 128.3, 127.5, 127.2, 126.3, 124.7, 98.4, 84.4, 52.4, 28.3, 23.8;

IR (film) 3061, 3027, 2965, 2930, 2870, 1774, 1752, 1645, 1448, 1163, 1061 cm^{-1};

HRMS (ESI) calcd for $C_{31}H_{32}O_3Na$ (M + Na^+) 475.2243, found 475.2258.

(2*R*,3*R*)-2,6-Diisopropylphenyl 3-butyl-2,3-dihydro-5-phenylfuran-2-carboxylate (Table 3, entry 10). General Procedure A was followed, with (–)-bpy*, (*E*)-1-phenyl-2-hepten-1-one (188 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 370 mg (91%; 96% de, 79% ee); run 2, 378 mg (93%; 97% de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 4.1 min, t_r(minor) 4.9 min.

$[\alpha]^{20}_D$ = –53.6 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.74-7.72 (m, 2H), 7.14-7.03 (m, 6H), 5.27 (d, *J* = 2.8 Hz, 1H), 5.29 (d, *J* = 5.3 Hz, 1H), 3.61-3.52 (m, 1H), 3.23-3.06 (m, 2H), 1.58-1.38 (m, 2H), 1.34-1.10 (m, 16H), 0.85 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.9, 156.4, 146.5, 141.1, 131.2, 129.3, 128.9, 127.7, 127.4, 126.2, 124.7, 99.4, 84.2, 49.3, 36.1, 29.8, 28.3, 23.8, 23.3, 14.6;

IR (film) 3066, 3029, 2963, 2930, 2871, 1776, 1751, 1650, 1602, 1578, 1466, 1448 cm^{-1};

HRMS (ESI) calcd for $C_{27}H_{34}O_3Na$ (M + Na^+) 429.2400, found 429.2390.

(2*R*,3*S*)-2,6-Diisopropylphenyl 5-hexyl-2,3-dihydro-3-phenylfuran-2-carboxylate (Table 3, entry 11). General Procedure B was followed, with (–)-bpy*, (*E*)-1-phenyl-1-nonen-3-one (216 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (345 mg, 1.4 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 300 mg (69%; 84% de, 77% ee); run 2, 300 mg (69%; 88% de, 73% ee). The ee was determined after reduction by LAH on an OD-H column (hexanes/*iso*-propanol 98:2, flow 1.0 mL/min) with t_r(major) 17.1 min, t_r(minor) 12.3 min.

$[\alpha]^{20}_{D}$ = –174 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.38-7.36 (m, 2H), 7.21-7.18 (m, 2H), 7.13-7.04 (m, 4H), 5.16 (d, *J* = 4.9 Hz, 1H), 4.71 (d, *J* = 2.3 Hz, 1H), 4.68 (dd, *J* = 4.6, 2.4 Hz, 1H), 3.13 (septet, *J* = 6.7 Hz, 2H), 2.25 (t, *J* = 7.5 Hz, 2H), 1.60 (quintet, *J* = 7.5 Hz, 2H), 1.33-1.10 (m, 18H), 0.86 (t, *J* = 6.9 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 170.8, 161.1, 146.4, 144.2, 141.1, 129.5, 128.0, 127.4, 124.7, 98.6, 86.6, 54.3, 32.3, 29.6, 28.6, 28.3, 27.3, 23.9, 23.3, 14.7;

IR (film) 3065, 3029, 2962, 2930, 2871, 1776, 1754, 1673, 1602, 1493, 1456, 1248, 1144, 1096 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{38}O_3Na$ ($M + Na^+$) 457.2713, found 457.2733.

(2*R*,3*R*)-2,6-Diisopropylphenyl 5-hexyl-2,3-dihydro-3-methylfuran-2-carboxylate (Table 3, entry 12). General Procedure B was followed, with (–)-bpy*, (*E*)-2-decen-4-one (154 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (345 mg, 1.4 mmol). After chromatography on silica gel (hexanes/ethyl ether 100:1), the title compound was isolated as a colorless oil: run 1, 291 mg (78%; >90% de, 72% ee); run 2, 305 mg (82%; >90% de, 69% ee). The ee was determined, after reduction by LAH, on an OD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 7.4 min, t_r(minor) 8.8 min.

$[\alpha]^{20}_{D}$ = –70.8 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.11-7.04 (m, 3H), 4.77 (d, *J* = 5.7 Hz, 1H), 4.52-4.50 (m, 1H), 3.48-3.45 (m, 1H), 3.13 (septet, *J* = 6.8 Hz, 2H), 2.17 (t, *J* = 7.4 Hz, 2H), 1.55 (quintet, *J* = 7.4 Hz, 2H), 1.33-1.14 (m, 18H), 1.13-1.10 (d, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 6.7 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 171.0, 159.5, 146.4, 141.1, 127.3, 124.7, 100.1, 85.6, 43.8, 32.3, 29.5, 28.6, 28.3, 27.2, 23.8, 23.3, 22.0, 14.6;

IR (film) 3067, 2963, 2930, 2871, 1778, 1751, 1674, 1459, 1245, 1161, 1095 cm^{-1};

HRMS (ESI) calcd for $C_{24}H_{36}O_3Na$ ($M + Na^+$) 395.2557, found 395.2562.

4. Derivatization of Dihydrofurans (eq 2 and eq 3)

((2*R*,3*S*)-2,3-Dihydro-5-hexyl-3-phenylfuran-2-yl)methanol (eq 2). A solution of $LiAlH_4$ (1.0 M in Et_2O; 0.23 mL, 0.23 mmol) was added dropwise to a stirred solution of the ester (run 1, >90% de and 77% ee; run 2, >90% de and 73% ee; 100 mg, 0.23 mmol) in Et_2O (5.0 mL). The reaction mixture was stirred for 10 min, and then the reaction was quenched with 1.0 N NaOH (0.2 mL). The mixture was stirred for 5 min, and then it was filtered and concentrated. After chromatography on silica gel (hexanes/ethyl ether 15:1), the title compound was isolated as a colorless oil: run 1, 57 mg (95%; 77% ee); run 2, 58 mg (97%; 73% ee). The ee was determined on an OD-H column (hexanes/*iso*-propanol 98:2, flow 1.0 mL/min) with t_r(major) 17.1 min, t_r(minor) 12.3 min.

$[\alpha]^{20}_D$ = –74.9 (c = 1.00, CH_2Cl_2);

^{1}H NMR (C_6D_6, 400 MHz) δ 7.18-7.12 (m, 4H), 7.07-7.04 (m, 1H), 4.56 (dt, *J* = 2.2, 1.1 Hz, 1H), 4.34 (dt, *J* = 6.7, 5.0 Hz, 1H), 3.83 (dq, *J* = 6.7, 1.9 Hz, 1H), 3.53 (t, *J* = 5.0 Hz, 2H), 2.12 (t, *J* = 7.8 Hz, 2H), 1.71 (t, *J* = 5.6 Hz, 1H), 1.51 (quintet, *J* = 7.5 Hz, 2H), 1.31-1.17 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 159.9, 145.4, 129.2, 128.2, 127.3, 99.4, 90.8, 64.9, 51.6, 32.3, 29.7, 28.7, 27.4, 23.3, 14.6;

IR (film) 3424, 3062, 3028, 2954, 2929, 2859, 1669, 1602, 1493, 1455, 1159 cm^{-1};

HRMS (ESI) calcd for $C_{17}H_{24}O_2Na$ ($M + Na^+$) 283.1669, found 283.1676.

(2*R*,3*R*)-2,6-Diisopropylphenyl 2-acetoxy-3-butyl-5-oxo-5-phenylpentanoate (eq 3). The procedure for entry 4 of Table 3 was followed, with the ester (run 1, >90% de and 79% ee; run 2, >90% de and 76% ee; 50 mg, 0.12 mmol), 10% aq HBF_4 (1.0 mL), NEt_3 (0.10 mL, 0.74 mmol), DMAP (3.0 mg, 0.025 mmol), and Ac_2O (0.060 mL, 0.64 mmol). Purification by column chromatography on silica gel (hexanes/ethyl ether 20:1) furnished the title compound as a colorless oil: run 1, 50 mg (87%; >90% de, 78% ee); run 2, 53 mg (92%; >90% de, 76% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 99:1, flow 1.0 mL/min) with t_r(major) 5.0 min, t_r(minor) 6.3 min.

$[\alpha]^{20}_D$ = –11.4 (c = 1.00, CH_2Cl_2);

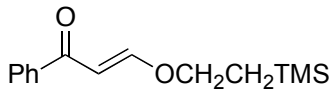
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03-8.00 (m, 2H), 7.60-7.57 (m, 1H), 7.50-7.47 (m, 2H), 7.23-7.13 (m, 3H), 5.54 (d, *J* = 2.3 Hz, 1H), 3.24-3.22 (m, 2H), 3.17-3.08 (m, 1H), 3.08-2.90 (m, 1H), 2.90-2.60 (m, 1H), 2.22 (s, 3H), 1.62-1.52 (m, 2H), 1.50-1.33 (m, 4H), 1.17 (d, *J* = 6.3 Hz, 12H), 0.94 (t, *J* = 6.9 Hz, 3H);

^{13}C NMR (C_6D_6, 100 MHz) δ 198.0, 170.6, 169.1, 145.1, 140.6, 137.2, 133.4, 128.9, 128.2, 127.0, 124.1, 73.5, 39.3, 35.4, 31.8, 29.5, 27.4, 23.7, 22.8, 20.8, 14.1;

IR (film) 3065, 2965, 2932, 2871, 1769, 1751, 1689, 1598, 1449, 1366, 1229, 1174 cm^{-1};

HRMS (ESI) calcd for $C_{29}H_{38}O_5Na$ ($M + Na^+$) 489.2611, found 489.2636.

5. Application to Deoxy-C-nucleoside Synthesis (Figure 1)



(*E*)-3-(2-(Trimethylsilyl)ethoxy)-1-phenylprop-2-en-1-one. 1-Phenylprop-2-yn-1-one (650 mg, 5.0 mmol) was added dropwise to a solution of trimethylsilylethanol (650 mg; 5.5 mmol) and *N*-methylmorpholine (657 mg, 6.5 mmol) in CH_2Cl_2 (5.0 mL) at r.t. The reaction mixture was stirred for 2 days, and then a saturated solution of NH_4Cl (10 mL) was added. The mixture was extracted with CH_2Cl_2 (10 mL x 3), and the combined organic layers were dried over $MgSO_4$ and concentrated. The resulting dark-brown oil was purified by column chromatography (hexanes/Et_2O 8:1), which furnished the title compound (820 mg, 66%). This reaction was not optimized.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91-7.89 (m, 2H), 7.77 (d, *J* = 12.2 Hz, 1H), 7.54-7.52 (m, 1H), 7.50-7.44 (m, 2H), 6.35 (d, *J* = 12.2 Hz, 1H), 4.13-4.09 (m, 2H), 1.15-1.11 (m, 2H), 0.09 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 218.2, 191.0, 164.4, 132.4, 128.6, 128.2, 102.3, 70.5, 18.1, –1.2;

IR (film) 3064, 2953, 2896, 1664, 1601, 1586, 1575, 1447, 1381, 1250, 1192, 1172, 858, 838 cm^{-1};

LCMS (ES+APCI) calcd for $C_{14}H_{20}O_2SiNa$ ($M + Na^+$) 271.1125, found 271.2.

((2*S*,3*R*,5*S*)-3-(2-(Trimethylsilyl)ethoxy)-tetrahydro-5-phenylfuran-2-yl)methanol. General Procedure A was followed, with (–)-bpy*, (*E*)-3-(2-(trimethylsilyl)ethoxy)-1-phenylprop-2-en-1-one (248 mg, 1.0 mmol), and 2,6-diisopropylphenyldiazoacetate (271 mg, 1.1 mmol). ^{1}H NMR analysis of the unpurified dihydrofuran product revealed only one diastereomer.

The unpurified product was subjected to hydrogenation (1 atm) with Pd on activated carbon (10% w/w; 5 mg) and NEt_3 (70 μL, 0.5 mmol) in MeOH (3.0 mL) for 1 h. The reaction mixture was filtered through a plug of silica gel (Et_2O as the eluant) and concentrated. A solution of LAH (1.0 M in Et_2O; 1.0 mL, 1.0 mmol) was added to a solution of the tetrahydrofuran in Et_2O (4.0 mL). The mixture was stirred for 5 min, and then the reaction was quenched by adding water (0.1 mL) and stirring for 10 min. The reaction mixture was dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (hexanes/Et_2O 5:1), which furnished the title compound as a colorless oil: run 1, 216 mg (73%); run 2, 236 mg (80%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.28 (m, 5H), 5.12 (dd, *J* = 10.5, 5.4 Hz, 1H), 4.09 (dt, *J* = 4.8, 3.4 Hz, 1H), 4.02 (ddd, *J* = 6.3, 2.8, 1.4 Hz, 1H), 3.88 (dd, *J* = 11.7, 3.6 Hz, 1H), 3.72 (dd, *J* = 11.7, 4.9 Hz, 1H), 3.60-3.53 (m, 2H), 2.35 (ddd, *J* = 13.3, 5.4, 1.5 Hz, 1H), 1.97 (br s, 1H), 1.91 (ddd, *J* = 13.3, 10.5, 6.4 Hz, 1H), 1.00-0.96 (m, 2H), 0.05 (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.6, 128.9, 128.2, 126.4, 85.6, 81.1, 80.8, 67.0, 64.2, 41.7, 18.8, –0.9;

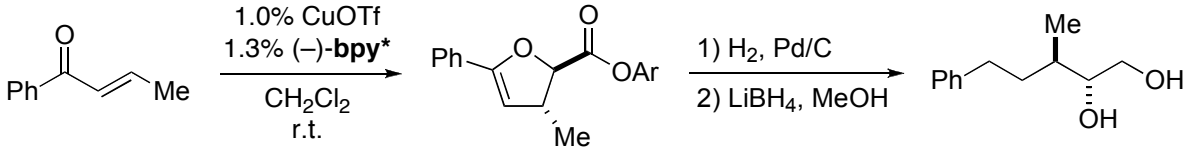
IR (film) 3414, 2952, 2893, 1715, 1362, 1222, 1098, 1057 cm^{-1};
LCMS (ES+APCI) calcd for $C_{16}H_{26}O_3SiNa$ ($M + Na^+$) 317.1543, found 317.2.

(2*S*,3*R*,5*S*)-Tetrahydro-2-(hydroxymethyl)-5-phenylfuran-3-ol. To a solution of ((2*S*,3*R*,5*S*)-3-(2-(trimethylsilyl)ethoxy)-tetrahydro-5-phenylfuran-2-yl)methanol (50.0 mg, 0.17 mmol) in toluene (2.5 mL) was added $BF_3{\cdot}OEt_2$ (23.5 μL, 0.19 mmol). The reaction mixture was stirred for 1 h, and then the reaction was quenched by the addition of a saturated solution of $NaHCO_3$ (2.0 mL). The mixture was extracted with Et_2O (5 mL x 3), dried over $MgSO_4$, and concentrated. Purification by column chromatography (CH_2Cl_2/MeOH 50:1) furnished the title compound as a white solid: run 1, 30 mg (87%; 93% ee); run 2, 28 mg (85%; 94% ee). The ee was determined on an AD-H column (hexanes/*iso*-propanol 95:5, flow 1.0 mL/min) with t_r(major) 32.1 min, t_r(minor) 28.9 min.

The spectral data matched the values reported previously.[3]
$[\alpha]^{20}_D$ = –44.9 (c = 1.00, $CHCl_3$);
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.28 (m, 5H), 5.18 (dd, *J* = 10.2, 5.6 Hz, 1H), 4.41 (dt, *J* = 6.0, 2.4 Hz, 1H), 4.03-3.99 (m, 1H), 3.81 (dd, *J* = 11.6, 4.3 Hz, 1H), 3.73 (dd, *J* = 11.6, 5.0 Hz, 1H), 2.37 (br s, 2H), 2.25 (ddd, *J* = 13.3, 5.7, 1.9 Hz, 1H), 2.25 (ddd, *J* = 13.3, 10.2, 6.3 Hz, 1H);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.2, 128.7, 128.1, 126.3, 87.5, 80.4, 73.9, 63.6, 44.0;
IR (film) 3274, 2940, 2832, 1490, 1452, 1358, 1102, 1054, 1028 cm^{-1};
LCMS (ES+APCI) calcd for $C_{11}H_{14}O_3Na$ ($M + Na^+$) 217.0835, found 217.1.

6. Determination of Stereochemistry

The stereochemistry of the dihydrofurans was assigned on the basis of the synthesis described in Section 5 (above) and by correlation with (2*R*,3*R*)-3-methyl-5-phenylpentane-1,2-diol.



$[\alpha]^{20}_{D} = 17.3$ (c = 0.83, $CHCl_3$).[4]

7. References

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