Stereoselective (4 + 3) Cycloadditions of Allenyl Ethers-Furans by Chiral Auxiliaries inducing and Evaluation of Anti-Breast Cancer Activity

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**SUPPLEMENTARY INFORMATION**

**Supplementary Methods**

The detailed characterization data of intermediates and target compounds

**Supplementary Results**

Figures. S1. The 1H NMR and 13C NMR spectra of intermediates and target compounds

Table S1. X-ray crystallographic data of compound **3h** (CCDC 2215220).

**Supplementary Methods**

The detailed characterization data of intermediates and target compounds

**6** (1.2 g, 71% yield); 1H NMR (400 MHz, CDCl3) *δ* 4.57 – 4.39 (m, 1H), 4.11 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.20 – 2.04 (m, 2H), 1.97 – 1.66 (m, 3H), 1.18 (s, 3H), 1.10 (s, 3H), 0.98 (s, 3H).

**Aux-6** (1.0 g, 83% yield); 1H NMR (400 MHz, CDCl3) *δ* 4.97 – 4.85 (m, 1H), 4.07 (dt, *J* = 10.9, 1.3 Hz, 1H), 3.52 (dd, *J* = 10.9, 2.5 Hz, 1H), 3.12 – 2.97 (m, 1H), 2.03 – 1.77 (m, 2H), 1.70 – 1.48 (m, 3H), 1.08 (s, 3H), 0.91 (s, 3H), 0.87 (s, 3H).

**7** (1.0 g, 81% yield); 1H NMR (400 MHz, CDCl3) *δ* 4.74 (d, *J* = 0.9 Hz, 1H), 4.33 (dd, *J* = 12.2, 2.4 Hz, 2H), 4.04 (d, *J* = 10.9 Hz, 1H), 3.53 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.40 (d, *J* = 2.4 Hz, 1H), 2.07 (ddd, *J* = 13.2, 9.9, 4.6 Hz, 1H), 1.94 – 1.73 (m, 1H), 1.69 – 1.45 (m, 2H), 1.41 – 1.20 (m, 1H), 1.09 (s, 3H), 0.90 (s, 3H), 0.86 (s, 3H).

**1f** (0.9 g, 90% yield); 1H NMR (400 MHz, CDCl3) *δ* 6.70 (t, *J* = 6.0 Hz, 1H), 5.42 (dd, *J* = 12.9, 6.1 Hz, 2H), 4.82 (s, 1H), 4.06 (d, *J* = 10.9 Hz, 1H), 3.59 (dd, *J* = 10.9, 2.4 Hz, 1H), 2.17 (s, 1H), 1.96 – 1.78 (m, 1H), 1.69 – 1.52 (m, 3H), 1.19 – 0.76 (m, 9H).

**3a**: 26 mg (64%); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.31 (ddd, *J* = 26.9, 6.1, 1.7 Hz, 2H), 5.08 (dd, *J* = 5.2, 1.8 Hz, 1H), 5.00 (d, *J* = 5.0 Hz, 1H), 4.81 (s, 1H), 4.39 (d, *J* = 5.2 Hz, 1H), 3.99 (d, *J* = 10.9 Hz, 1H), 3.50 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.75 (dd, *J* = 15.5, 4.9 Hz, 1H), 2.34 (d, *J* = 15.5 Hz, 1H), 2.06 (td, *J* = 9.8, 5.0 Hz, 1H), 1.91 – 1.76 (m,1H), 1.67 – 1.45 (m, 3H), 1.06 (s, 3H), 0.94 (s, 3H), 0.89 (s, 3H); 13C NMR (100 MHz, CDCl3) *δ* 204.5, 134.2, 132.4, 103.2, 82.5, 80.7, 78.2, 68.4, 47.4, 45.8, 45.4, 42.5, 28.5, 26.0, 24.7, 17.7, 13.6; IR (KBr) cm-1 2962m, 2924m, 2869m, 1725m, 1463w, 1361w, 1322w, 1258w, 1175w, 1095s, 1012s, 964s, 804m, 723s; HRMS (ESI+): C17H24O4 for [M+Na]+, calculated 315.1572, found 315.1566; = + 9.921 (c 1.00, CHCl3).

**3b**: 15 mg (52% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.26 (dd, *J* = 5.9, 1.8 Hz, 1H), 6.07 (d, *J* = 5.9 Hz, 1H), 5.10 – 5.00 (m, 1H), 4.81 (s, 1H), 4.35 (d, *J* = 5.2 Hz, 1H), 3.98 (d, *J* = 10.9 Hz, 1H), 3.49 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.55 (s, 1H), 2.39 (d, *J* = 15.3 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.91 – 1.77 (m, 1H), 1.63 – 1.52 (m, 3H), 1.49 (s, 3H), 1.05 (s, 3H), 0.93 (s, 3H), 0.88 (s, 3H); 13C NMR (100 MHz, CDCl3) *δ* 204.97, 137.38, 132.21, 103.07, 84.80, 81.21, 80.96, 68.40, 51.73, 47.42, 45.44, 42.54, 28.46, 25.95, 24.75, 22.77, 17.68, 13.62; IR (KBr) cm-1 2962m, 2927m, 2866m,1725m, 1460w, 1383w, 1325w, 1178w, 1115s, 1076s, 1006s, 830w, 736m, 727m; HRMS (ESI+): C18H26O4 for [M+Na]+, calculated 329.3918, found 329.17248; = + 17.105, (c 0.67, CHCl3)

**3c:** 21 mg (48% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.27 (d, J = 6.0 Hz, 1H), 6.07 (d, *J* = 5.8 Hz, 1H), 5.07 (d, *J* = 5.2 Hz, 1H), 4.82 (s, 1H), 4.37 (d, *J* = 5.2 Hz, 1H), 3.98 (d, *J* = 11.0 Hz, 1H), 3.49 (d, *J* = 11.0 Hz, 1H), 2.55 (d, *J* = 15.2 Hz, 1H), 2.36 (d, *J* = 15.3 Hz, 1H), 2.07 (ddt, *J* = 14.8, 9.4, 5.3 Hz, 2H), 1.87 – 1.76 (m, 2H), 1.65 – 1.46 (m, 3H), 1.06 (s, 3H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.94 (s, 3H), 0.89 (s, 3H); 13C NMR (100 MHz, CDCl3) *δ* 205.2, 136.0, 132.5, 103.1, 88.1, 81.6, 80.9, 68.4, 50.0, 47.4, 45.4, 42.5, 28.9, 28.5, 26.0, 24.8, 17.7, 13.6, 8.8; IR (KBr) cm-1 2959m, 2924m, 2850m, 1726m, 1470m, 1169w, 1120s, 1069s, 1008s, 967w, 826w, 804w, 733s; HRMS (ESI+): C19H28O4 for [M+Na]+, calculated 343.4188, found 343.18769; = + 16.221, (c 1.00, CHCl3).

**3d:**22 mg (47% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.26 (dd, *J* = 5.9, 1.8 Hz, 1H), 6.08 (d, *J* = 6.0 Hz, 1H), 5.06 (dd, *J* = 5.2, 1.9 Hz, 1H), 4.82 (s, 1H), 4.37 (d, *J* = 5.2 Hz, 1H), 3.99 (d, *J* = 10.9 Hz, 1H), 3.50 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.54 (s, 1H), 2.38 (s, 1H), 2.11 – 2.03 (m, 2H), 1.87 – 1.80 (m, 1H), 1.77 – 1.70 (m, 2H), 1.62 – 1.55 (m, 2H), 1.51 (m, 2H), 1.06 (s, 3H), 0.97 (s, 3H), 0.94 (m, 3H), 0.90 (d, *J* = 2.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) *δ* 205.3, 136.3, 132.2, 103.1, 87.7, 81.6, 80.8, 68.4, 50.3, 47.4, 45.4, 42.5, 38.3, 28.5, 26.0, 24.8, 17.7, 17.4, 14.4, 13.6; IR (KBr) cm-1 2961w, 2930s, 2852w, 1730m, 1604w, 1513w, 1467m, 1393m, 1263m, 1183w, 1085s, 1008s, 962m, 825m, 795m, 764m, 706m, 661m, 559m; HRMS (ESI+): C20H30O4 for [M+Na]+, calculated 357.4458, found 357.20370; = + 140.898, (c 0.20, CHCl3).

**3e:** 22 mg (43% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.27 (dd, *J* = 6.0, 1.8 Hz, 1H), 6.08 (d, *J* = 6.0 Hz, 1H), 5.12 – 5.03 (m, 1H), 4.82 (s, 1H), 4.37 (d, *J* = 5.2 Hz, 1H), 3.99 (dd, *J* = 11.0, 1.3 Hz, 1H), 3.50 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.56 (d, *J* = 15.2 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.08 (ddd, *J* = 12.9, 9.8, 4.7 Hz, 2H), 1.90 – 1.78 (m, 1H), 1.74 – 1.48 (m, 3H), 1.06 (s, 3H), 0.95 (s, 4H), 0.93 – 0.85 (m, 8H); 13C NMR (100 MHz, CDCl3) *δ* 205.2, 136.4, 132.3, 103.1, 87.7, 81.6, 80.8, 68.4, 50.4, 47.4, 45.5, 42.5, 36.1, 32.1, 28.5, 26.0, 24.8, 23.7, 22.6, 17.7, 14.1, 13.6; IR (KBr) cm-1 2957m, 2924m, 2877m, 1731m, 1492m, 1457m, 1396w, 1362w, 1309w,1274m, 1206w, 1184m, 1122m, 1082s, 972s, 893w, 817w, 738w, 708w, 601w; HRMS (ESI+): C22H34O4 for [M+Na]+, calculated 385.4998 found 385.47654; = + 121.312, (c 0.10, CHCl3).

**3f:** 17 mg (35% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.34 (dd, *J* = 6.0, 1.8 Hz, 1H), 6.14 (d, *J* = 6.0 Hz, 1H), 5.12 (d, *J* = 5.3 Hz, 1H), 4.82 (s, 1H), 4.39 (d, *J* = 5.2 Hz, 1H), 3.99 (d, *J* = 10.9 Hz, 1H), 3.66 (s, 2H), 3.61 (dd, *J* = 7.0, 4.4 Hz, 1H), 3.51 (d, *J* = 2.5 Hz, 1H), 2.77 (d, *J* = 15.5 Hz, 1H), 2.38 (d, *J* = 15.4 Hz, 1H), 2.07 (ddd, *J* = 13.9, 9.7, 4.7 Hz, 1H), 1.84 (d, *J* = 6.0 Hz, 1H), 1.65 – 1.49 (m, 3H), 1.06 (s, 3H), 0.94 (s, 3H), 0.92 – 0.85 (m, 9H); 13C NMR (100 MHz, CDCl3) *δ* 204.9, 134.7, 133.1, 103.2, 87.3, 81.4, 81.2, 72.3, 68.4, 67.4, 47.4, 47.3, 45.4, 42.5, 28.5, 25.9, 24.8, 17.7, 15.0, 13.6; IR (KBr) cm-1 2963m, 2959m, 2857m, 1724m, 1467m, 1387w, 1263m, 1078s, 1011m, 965w,829m, 801m, 794m; HRMS (ESI+): C20H30O5 for [M+Na]+, calculated 373.4448, found 373.19847; = + 3.831, (c 0.10, CHCl3).

**3g:** 23 mg (45% yield); yellow oil; 1H NMR (400 MHz, CDCl3) *δ* 6.38 (d, *J* = 1.8 Hz, 1H), 6.20 (d, *J* = 6.0 Hz, 2H), 5.16 (dd, *J* = 5.2, 1.8 Hz, 2H), 5.05 (s, 2H), 4.82 (s, 2H), 4.39 (d, *J* = 5.2 Hz, 2H), 4.10 – 3.94 (m, 6H), 3.49 (dd, *J* = 11.0, 2.5 Hz, 2H), 2.76 (d, *J* = 15.5 Hz, 2H), 2.42 (d, *J* = 15.5 Hz, 2H), 2.12 – 2.00 (m, 3H), 1.83 (dt, *J* = 11.8, 5.8 Hz, 2H), 1.63 – 1.50 (m, 5H), 1.06 (s, 6H), 0.94 (s, 7H), 0.90 (d, *J* = 2.5 Hz, 11H); 13C NMR (100 MHz, CDCl3) *δ* 204.4, 133.7, 133.4, 103.2, 103.1, 88.2, 81.5, 81.3, 68.4, 65.9, 65.63, 5.40, 45.4, 44.8, 42.5, 28.5, 25.9, 24.7, 17.69, 13.6; IR (KBr) cm-1 2953m, 2918m, 2871m, 2853m, 1726m, 1467w, 1373w, 1315w, 1257w, 1176w, 1109s, 1078s, 1014m, 964m, 938m, 838w, 798w, 740m, 613w, 491w; HRMS (ESI+): C20H28O6 for [M+Na]+, calculated 387.4278, found 387.17796; = + 73.604, (c 0.12, CHCl3).

**3h:**21 mg (40% yield); white solid; mp 80.7~81.2°C; 1H NMR (400 MHz, CDCl3) *δ* 6.38 (d, J = 2.0 Hz, 1H), 4.97 (d, J = 5.1 Hz, 1H), 4.95 – 4.93 (m, 1H), 4.84 (s, 1H), 4.52 (d, *J* = 5.1 Hz, 1H), 4.00 (d, *J* = 10.9 Hz, 1H), 3.52 (dd, *J* = 10.9, 2.5 Hz, 1H), 2.77 (d, *J* = 4.8 Hz, 1H), 2.43 (d, *J* = 15.7 Hz, 1H), 2.24 (ddd, *J* = 13.8, 9.9, 4.6 Hz, 1H), 1.97 – 1.78 (m, 1H), 1.69 – 1.42 (m, 3H), 1.06 (s, 3H), 0.97 (s, 3H), 0.90 (s, 3H); 13C NMR (100 MHz, CDCl3) *δ* 203.4, 133.2, 123.1, 103.2, 83.5, 81.9, 79.4, 68.6, 47.5, 45.8, 45.4, 42.4, 28.2, 25.9, 24.7, 17.7, 13.6; IR (KBr) cm-1 2953m, 2927m, 2869m, 2847m, 1736m, 1463w, 1178w, 1111s, 1076s, 1008m, 967s, 829m, 736m, 701m; HRMS (ESI+): C17H23BrO4 for [M+Na]+, calculated 394.2608, found 393.06668; = + 2.450, (c 1.00, CHCl3).

**4** (11 mg, 88% yield) as a white solid. 1H NMR (400 MHz, CDCl3) δ 6.32 (t, *J* = 1.5 Hz, 2H), 5.10 (td, *J* = 3.6, 1.7 Hz, 2H), 4.39 (s, 1H), 2.91 (dd, *J* = 15.0, 4.9 Hz, 1H), 2.55 – 2.45 (m, 1H); = + 103.195, (c 0.10, CHCl3).

**Supplementary Results**

Figures. S1. The 1H NMR and 13C NMR spectra of intermediates and target compounds





























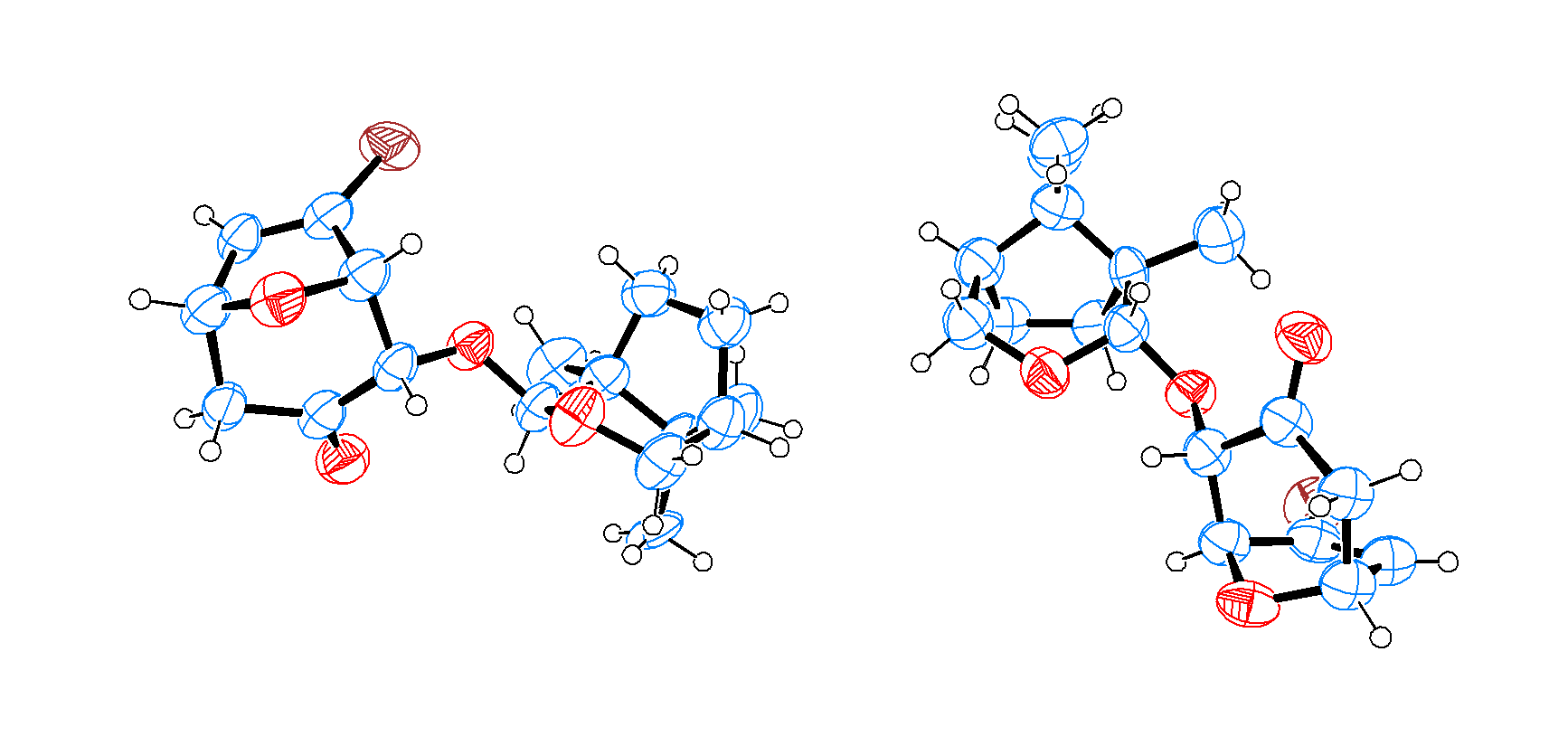








Table S1. X-ray crystallographic data of compound **3h** (CCDC 2215220).



|  |  |
| --- | --- |
| Identification code | 221013a |
| Empirical formula | C17H23BrO4 |
| Formula weight | 371.26 |
| Temperature/K | 298(2) K |
| Crystal system | Monoclinic |
| Space group | P2 (1) |
| Unit cell dimensions | a = 11.1920 (12) Å |
|  | b = 7.1811 (8) Å |
| c = 21.758 (2) Å |
| α/°, β/°, γ/° | 90°, 104.705(4) °, 90° |
| Volume | 1691.4(3) Å3 |
| Z | 4 |
| Density (calculated) | 1.458 mg / m-3 |
| μ / mm‑1 | 2.445 |
| F (000) | 768 |
| Crystal size | 0.27 × 0.07 × 0.04 mm3 |
| 2Θ range for data collection | 1.94° to 28.44° |
| Index ranges | -14 ≤ h ≤ 14, -9 ≤ k ≤ 9, -28 ≤ l ≤ 29 |
| Reflections collected | 7217 |
| Independent reflections | 7230[ R (int) = 0.0000] |
| Data / restraints / parameters | 7230 / 1379 / 406 |
| Goodness-of-fit on F2 | 1.084 |
| Final R indexes [I>2σ (I) i.e.F0>4σ (F0)] | R1 = 0.1030, wR2 = 0.2845 |
| Final R indexes [all data] | R1 = 0.2062, wR2 = 0.3382 |
| Absolute structure parameter | 0.01(3) |
| Extinction coefficient | 0.010(3) |
| Largest diff. peak/hole/ e Å-3 | 0.676/-0.697 |