# Reductive Umpolung for Asymmetric Synthesis of Chiral α-Allenic Alcohols

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#### ■ Instrumentation and Chemicals■

NMR spectra were recorded on a JNM-ECS400, operating at 400 MHz for <sup>1</sup>H NMR and 100.5 MHz for <sup>13</sup>C NMR, and JNM-ECA600, operating at 600 MHz for <sup>1</sup>H NMR and 150.9 MHz for <sup>13</sup>C NMR. Chemical shift values for <sup>1</sup>H and <sup>13</sup>C are referenced to Me<sub>4</sub>Si and the residual solvent resonances, respectively. Chemical shifts are reported in  $\delta$  ppm. Mass spectra were obtained with JMS-T100TD (DART). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F<sub>254</sub>. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) and aluminum oxide (Nacalai Tesuque, Alumina Activated 200) were used for column chromatography. IR spectra were measured with a Thermo Scientific iD7 ATR Accessory for the Thermo Scientific Nicolet iS5 FT-IR Spectrometer. HPLC analyses were measured on a Yanaco MP-500D apparatus.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. CuCl was purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. PhMe<sub>2</sub>SiB(pin) was purchased from Wako Pure Chemical Industries, stored under nitrogen, and used as received. NaOtBu, LiOtBu and KOtBu were purchased from Tokyo Chemical Industry Co., stored under nitrogen, and used as received. LiOMe and LiOSiMe<sub>3</sub> were purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. Toluene was purchased from Kanto Chemical Co., and purified by passage through activated alumina under positive argon pressure as described by Grubbs *et al.* c-Octane was purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. Aldehydes **1a–1g** were purchased from TCI Chemical Co., stored under nitrogen, and used as received as received. Propargylic phosphates **2a–g**, were prepared by the reported procedure.<sup>1</sup>(*S*,*S*)-L1·HBF<sub>4</sub> was prepared according to our previous report.<sup>2</sup>

# Characterization Data for Propargylic Phosphates Diethyl {3-[4-(Trifluoromethyl)phenyl]-2-propyn-1-yl} Phosphate (2b)



Brown oil. **IR (neat)** 1168, 1267, 1372, 1405, 1616, 2108, 2987 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.37 (td, J = 7.2, 0.92 Hz, 6H), 4.14–4.22 (m, 4H), 4.91 (d, J = 10.0 Hz, 2H), 7.53–7.60 (m, 4H). <sup>13</sup>C NMR (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  16.2 (d, J = 6.0 Hz), 55.5 (d, J = 4.5 Hz), 64.2 (d, J = 6.0 Hz), 85.4 (d, J = 7.5 Hz), 85.8, 124.0 (q, J = 270 Hz), 125.3 (q, J = 4.4 Hz), 125.8, 130.5, 132.0 (q, J = 21.0 Hz). HRMS–DART (m/z): [M]<sup>+</sup> calcd for C<sub>14</sub>H<sub>16</sub>F<sub>3</sub>O<sub>4</sub>P, 336.0733; found, 336.0731.

#### Diethyl [3-(2-Naphthalenyl)-2-propyn-1-yl] Phosphate (2e)



Yellow oil. **IR** (neat) 1264, 1371, 1444, 1500, 1596, 2234, 2983 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.37 (t, J = 7.2 Hz, 6H), 4.17–4.22 (m, 4H), 4.95 (d, J = 9.6 Hz, 2H), 7.48–7.51 (m, 3H), 7.78–7.83 (m, 3H), 7.99 (s, 1H). <sup>13</sup>**C NMR** (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  16.1 (d, J = 6.7 Hz), 55.8(d, J = 4.8 Hz), 64.1 (d, J = 6.7 Hz), 83.3(d, J = 6.7 Hz), 87.6, 119.2, 126.6, 127.0, 127.7, 127.8, 128.0, 128.2, 132.0, 132.8, 133.0. **HRMS–DART** (m/z): [M]<sup>+</sup> calcd for C<sub>17</sub>H<sub>19</sub>O<sub>4</sub>P, 318.1015; found, 318.1012.

### Diethyl 2-Heptyn-1-yl Phosphate (2f)



Yellow oil. **IR** (neat) 986, 1148, 1265, 1375, 1457, 2237, 2934 cm<sup>-1</sup>. <sup>1</sup>**H** NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.91 (t, J = 7.2 Hz, 3H), 1.33–1.38 (m, 6H), 1.40–1.53 (m, 4H), 2.21–2.25 (m, 2H), 4.11–4.18 (m, 4H), 4.64–4.67 (m, 2H). <sup>13</sup>**C** NMR (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  13.5, 16.1 (d, J = 7.2 Hz), 18.4, 21.9, 30.3, 55.8 (d, J = 4.8 Hz), 63.9 (d, J = 7.2 Hz), 74.1 (d, J = 8.6 Hz), 88.6. **HRMS–DART** (m/z): [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>21</sub>O<sub>4</sub>P, 248.1172; found, 248.1169.

# Diethyl (5-Phenyl-2-pentyn-1-yl) Phosphate (2g)



Yellow oil. **IR** (neat) 1372, 1454, 1496, 1604, 2234, 2933, 2983 cm<sup>-1</sup>. <sup>1</sup>**H** NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.34 (t, J = 7.2 Hz, 6H), 2.52–2.54 (m, 2H), 2.84 (t, J = 7.8 Hz, 2H), 4.09–4.15 (m, 4H), 4.63–4.66 (m, 2H), 7.20–7.22 (m, 3H), 7.28–7.31 (m, 2H). <sup>13</sup>**C** NMR (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  16.0 (d, J = 6.2 Hz), 20.9, 34.6, 55.6 (d, J = 4.8 Hz), 63.5 (d, J = 6.2 Hz), 74.9 (d, J = 7.7 Hz), 87.6, 126.3, 128.3, 128.4, 140.3. **HRMS–DART** (m/z): [M]<sup>+</sup> calcd for C<sub>15</sub>H<sub>21</sub>O<sub>4</sub>P, 296.1172; found, 296.1169.

# Procedure for Asymmetric Reductive Coupling between Aldehydes and Propargylic Phosphates

The reaction in Table 1, entry 8 is representative. CuCl (2.0 mg, 0.02 mmol), (*S*,*S*)-L1·HBF<sub>4</sub> (13.4 mg, 0.02 mmol) and LiO*t*Bu (3.2 mg, 0.04 mmol) were placed in a vial containing a magnetic stirring bar. The vial was sealed with a Teflon<sup>®</sup>-coated silicon rubber septum, and then the vial was evacuated and filled with argon. Toluene (1.0 mL) was added to the vial, and then the mixture was stirred at room temperature for 30 min. Next, (dimethylphenylsilyl)boronic acid pinacol ester [PhMe<sub>2</sub>SiB(pin)] (81.8  $\mu$ L, 0.3 mmol) and *p*-tolualdhyde (1a) (35.3  $\mu$ L, 0.3 mmol) were added and stirred for 10 min. Then, LiO*t*Bu (16.0 mg, 0.2 mmol) and propargylic phosphate 2a (53.7 mg, 0.2 mmol) was added successively added. After 12 h stirring at 40 °C, the reaction mixture was diluted with THF (2.5 mL) and treated with TBAF (450  $\mu$ L, 1.0 M THF solution). After 30 min stirring at 25 °C, the reaction mixture was quenthced with water and extracted with ethyl acetate (3 times), washed with brine and dried over sodium sulfate. After filtration, the resulting solution was evaporated under reduced pressure. After volatiles were removed under reduced pressure, flash column chromatography on silica gel (5–40% EtOAc/hexane) gave **3aa** (26.9 mg, 0.114 mmol) in 57% yield.

# Characterization Data for Chiral α-Allenic Alcohols (S)-2-Phenyl-1-(p-tolyl)buta-2,3-dien-1-ol (3aa)



The product **3aa** was purified by flash chromatography on silica gel (5–40% EtOAc/Hexane) (Table 1 entry 8; 26.9 mg, 0.114 mmol, 57% yield). Yellow oil. **IR** (neat) 1512, 1598, 1683, 1939, 2920, 3028, 3405 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.23 (d, *J* = 6.0 Hz, 1H), 2.32 (s, 3H), 5.29 (qd, *J* = 12.0, 2.8 Hz, 2H), 5.68 (m, 1H), 7.13–7.19 (m, 3H), 7.24–7.28 (m, 2H), 7.33–7.37 (m, 4H). <sup>13</sup>**C NMR** (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  21.1, 72.1, 81.4, 110.0, 126.8, 126.9, 127.0, 128.4, 129.1, 134.0, 137.6, 139.0, 207.6. **HRMS–DART** (*m*/*z*): [M-OH]<sup>+</sup> calcd for C<sub>17</sub>H<sub>15</sub>, 219.1168; found, 219.1171. [ $\alpha$ ]<sub>D</sub><sup>24</sup> +61.3 (*c* 0.72, CHCl<sub>3</sub>). The ee value 88% ee) of **3aa** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 29.1 min (*S* isomer) and 33.1 min (*R* isomer)]. The absolute configuration of **3aa** was assigned by consideration of the stereochemical pathway.



rac-3aa				
No	rt (min)	area	area (%)	
1	28.13	5646432	51.266	
2	32.50	5367464	48.734	

(S)- <b>3</b> aa				
No	rt (min)	area	area (%)	
1	29.06	1698044	94.109	
2	33.12	106285	5.891	

# (S)-1-(p-Tolyl)-2-[4-(trifluoromethyl)phenyl]buta-2,3-dien-1-ol (3ab)



The product **3ab** was purified by flash chromatography on silica gel (5–30% EtOAc/Hexane) (Table 2; 32.3 mg, 0.106 mmol, 53% yield). Due to the contamination of inseparable impurites, **3ab** was converted to the *p*-nitrobenzoate derivative **5ab** by benzoylation. The experimental data of **5ab**; Yellow solid. **M.p.** 94–95 °C. **IR** (neat) 1409, 1433, 1528, 1610, 1725, 2855, 2924 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.35 (s, 3H), 5.33 (qd, J = 13.2, 2.4 Hz, 2H), 6.99 (m, 1H), 7.17–7.19 (m, 2H), 7.26–7.42 (m, 2H), 7.47–7.54 (m, 4H), 8.21–8.29 (m, 4H). <sup>13</sup>**C NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  21.2, 74.5, 81.6, 105.9, 123.6, 124.0 (q, J = 273.5 Hz), 125.5 (q, J = 4.3 Hz,), 126.9, 127.6, 129.2 (q, J = 33.2 Hz), 129.5, 130.9, 134.2 (q, J = 57.0 Hz), 135.4, 137.3, 138.9, 150.6, 163.7, 209.3. **HRMS–DART** (m/z): [M]<sup>+</sup> calcd for C<sub>25</sub>H<sub>18</sub>FNO<sub>4</sub>, 453.1182; found, 453.1188. [ $\alpha$ ]<sub>D</sub><sup>26</sup> +59.3 (c 0.41, CHCl<sub>3</sub>). The evalue (84% ee) of **5ab** (or **3ab**) was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 20.8 min (S isomer) and 23.6 min (R isomer)]. The absolute configuration of **5ab** (or **3ab**) was assigned by consideration of the stereochemical pathway.



rac-5ab				
No	rt (min)	area	area (%)	
1	20.57	1626388	50.518	
2	23.32	1593008	49.482	

(S)-5ab				
rt (min)	area	area (%)		
20.84	4237245	92.121		
23.56	362426	7.879		
	ab rt (min) 20.84 23.56	ab         rt (min)       area         20.84       4237245         23.56       362426		

#### (S)-2-(4-Methoxyphenyl)-1-(p-tolyl)buta-2,3-dien-1-ol (3ac)



The product **3ac** was purified by flash chromatography on silica gel (5–30% EtOAc/Hexane) (Table 2; 24.5 mg, 0.092 mmol, 46% yield). Due to the contamination of inseparable impurites, **3ac** was converted to the *p*-nitrobenzoate derivative **5ac** by benzoylation. The experimental data of **5ac**; Yellow oil. **IR** (neat) 1511, 1527, 1607, 1725, 1942, 2837, 2933 cm<sup>-1</sup>. <sup>1</sup>H **NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  2.34 (s, 3H), 3.76 (s, 3H), 5.22 (qd, J = 12.0, 2.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.95 (s, 1H), 7.16 (d, J = 7.8 Hz, 2H), 7.30 (d, J = 9.0 Hz, 2H), 7.41 (d, J = 7.8 Hz, 2H), 8.21–8.27 (m, 4H). <sup>13</sup>C **NMR** (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  21.2, 55.2, 75.0, 80.8, 106.1, 114.0, 123.5, 125.6, 127.7, 127.8, 129.3, 130.9, 134.8, 135.7, 138.5, 150.5, 158.8, 163.7, 208.4. **HRMS–DART** (m/z): [M]<sup>+</sup> calcd for C<sub>25</sub>H<sub>21</sub>NO<sub>5</sub>, 415.1414; found, 415.1421. [ $\alpha$ ]D<sup>24</sup> +41.2 (c 0.78, CHCl<sub>3</sub>). The ee value (71% ee) of **5ac** (or **3ac**) was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> IC-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 44.6 min (major) and 52.9 min (minor)]. The absolute configuration of **5ac** (or **3ac**) was assigned by consideration of the stereochemical pathway.





The product **3ad** was purified by flash chromatography on silica gel (5–40% EtOAc/Hexane) (Table 2; 11.5 mg, 0.046 mmol, 23% yield). Yellow oil. **IR** (neat) 1512, 1952, 2866, 2922, 2952, 3019, 3056, 3402 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  2.17 (s, 3H), 2.28 (brs, 1H), 2.31 (s, 3H), 5.01-5.06 (m, 2H), 5.40 (brs, 1H), 7.07–7.09 (m, 4H), 7.10–7.17 (m, 2H), 7.25–7.26 (m, 2H). <sup>13</sup>**C NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  19.9, 21.2, 74.5, 79.0, 108.6, 125.6, 126.5, 127.5, 128.8 (×2C), 130.4, 134.0, 136.8, 137.4, 138.8, 204.7. **HRMS–DART** (*m/z*): [M-OH]<sup>+</sup> calcd for C<sub>18</sub>H<sub>17</sub>, 233.1325; found, 233.1325. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +56.2 (*c* 0.91, CHCl<sub>3</sub>). The ee value (80% ee) of **3ad** was determined by chiral HPLC analysis [CHIRALCEL®OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 15.3 min (*S* isomer) and 18.0 min (*R* isomer)]. The absolute configuration of **3ad** was assigned by consideration of the stereochemical pathway.



rac-3ad				
rt (min)	area	area (%)		
17.20	2862854	51.054		
20.07	2744656	48.946		
	ad rt (min) 17.20 20.07	ad rt (min) area 17.20 2862854 20.07 2744656		

(S)-3ad				
No	rt (min)	area	area (%)	
1	15.35	2992328	89.775	
2	18.05	340827	10.225	

(S)-2-(Naphthalen-2-yl)-1-(p-tolyl)buta-2,3-dien-1-ol (3ae)



The product **3ae** was purified by flash chromatography on silica gel (5–40% EtOAc/Hexane) (Table 2; 22.3 mg, 0.078 mmol, 39% yield). Yellow oil. **IR** (neat) 1625, 1684, 1701, 1935, 2920, 3054, 3418 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.29 (m, 1H), 2.32 (s, 3H), 5.37 (qd, J = 12.0, 2.8 Hz, 2H), 5.83 (m, 1H), 7.13–7.15 (m, 2H), 7.39–7.44 (m, 4H), 7.56 (m, 1H), 7.71–7.77 (m, 4H). <sup>13</sup>**C NMR** (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  21.1, 72.1, 81.8, 110.3, 125.1, 125.5, 125.9, 126.1, 126.9, 127.5, 127.9, 128.1, 129.2, 131.3, 132.4, 133.4, 137.6, 139.0, 208.2. **HRMS–DART** (*m*/*z*): [M-OH]<sup>+</sup> calcd for C<sub>21</sub>H<sub>17</sub>, 269.1325; found, 269.1322. [ $\alpha$ ]<sub>D</sub><sup>26</sup> +37.3 (*c* 0.92, CHCl<sub>3</sub>). The ee value (85% ee) of **3ae** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 35.3 min (major) and 41.2 min (minor)]. The absolute configuration of **3ae** was assigned by consideration of the stereochemical pathway.



rac-3ae				
No	rt (min)	area	area (%)	
1	37.35	3850859	53.472	
2	42.17	3350717	46.528	

( <i>S</i> )- <b>3ae</b>				
No	rt (min)	area	area (%)	
1	35.33	19875567	92.282	
2	41.16	1662322	7.718	

### (S)-1-(p-Tolyl)-2-vinylidenehexan-1-ol (3af)





The product **3af** was purified by flash chromatography on silica gel (5-40% EtOAc/hexane) (Table 2; 20.8 mg, 0.096 mmol, 48% yield). Yellow oil. The spectrum data of product **3af** was consistent with the literature.<sup>3</sup> **HRMS–DART** (*m/z*): [M-OH]<sup>+</sup> calcd for C<sub>15</sub>H<sub>19</sub>, 199.1481; found, 199.1482.  $[\alpha]_D^{25}$  +82.3 (*c* 0.91, CHCl<sub>3</sub>). The ee value (79% ee) of **3af** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 95:5, 0.4 mL/min, 40 °C, 220 nm UV detector, retention time = 12.7 min (*S* isomer) and 13.9 min (*R* isomer)]. The absolute configuration of **3af** was assigned by the Mosher's NMR spectroscopic method. Comparison of <sup>1</sup>H NMR chemical shifts of Mosher's ester derivatives was illustrated below.



# (S)-2-Phenethyl-1-(p-tolyl)buta-2,3-dien-1-ol (3ag)



The product **3ag** was purified by flash chromatography on silica gel (5–40% EtOAc/Hexane) (Table 2; 20.6 mg, 0.078 mmol, 39% yield). Yellow oil. **IR** (neat) 1496, 1512, 1603, 1955, 2921, 3025, 3382 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  2.06–2.17 (m, 2H), 2.11 (d, *J* = 4.8 Hz, 1H), 2.34 (s, 3H), 2.67–2.70 (m, 2H), 5.02–5.03 (m, 2H), 5.08 (m, 1H), 7.10–7.11 (m, 2H), 7.13–7.17 (m, 3H), 7.22–7.26 (m, 4H). <sup>13</sup>C **NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  21.2, 29.6, 33.8, 74.0, 80.3, 107.8, 125.8, 126.6, 128.2, 128.4, 129.1, 137.5, 138.9, 141.8, 204.2. **HRMS–DART** (*m*/*z*): [M-OH]<sup>+</sup> calcd for C<sub>19</sub>H<sub>19</sub>, 247.1481; found, 247.1480. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +60.7 (*c* 1.39, CHCl<sub>3</sub>). The ee value (87% ee) of **3ag** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 18.4 min (*S* isomer) and 20.7 min (*R* isomer)]. The absolute configuration of **3ag** was assigned by consideration of the stereochemical pathway.



rac-3ag				
No	rt (min)	area	area (%)	
1	20.31	6103614	48.355	
2	23.01	6518840	51.645	

No	rt (min)	area	area (%)
1	18.38	9623109	93.355
2	20.73	685021	6.645

# (S)-1-[4-(Tert-butyl)phenyl]-2-phenylbuta-2,3-dien-1-ol (3ba)



The product **3ba** was purified by flash chromatography on silica gel (5–40% EtOAc/Hexane) (Table 2; 23.9 mg, 0.086 mmol, 43% yield). Yellow oil. **IR** (neat) 1606, 1689, 1939, 2867, 2903, 2960, 3416 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.30 (s, 9H), 2.23 (d, J = 5.6 Hz, 1H), 5.31 (qd, J = 12.4, 2.4 Hz, 2H), 5.68 (m, 1H), 7.19 (m, 1H), 7.25–7.29 (m, 2H), 7.34–7.40 (m, 6H). <sup>13</sup>C NMR (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  31.3, 34.5, 72.0, 81.5, 109.9, 125.4, 126.7, 126.8, 127.0, 128.4, 134.1, 138.9, 150.8, 207.6. **HRMS–DART** (*m/z*): [M-OH]<sup>+</sup> calcd for C<sub>20</sub>H<sub>21</sub>, 261.1638; found ,261.1642. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +9.5 (*c* 0.93, CHCl<sub>3</sub>). The ee value (79% ee) of **3ba** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 20.9 min (*S* isomer) and 28.8 min (*R* isomer)]. The absolute configuration of **3ba** was assigned by consideration of the stereochemical pathway.



### (S)-1-(3,5-Dimethylphenyl)-2-phenylbuta-2,3-dien-1-ol (3ca)



The product **3ca** was purified by flash chromatography on silica gel (5-40% EtOAc/Hexane) (Table 2; 17.5 mg, 0.07 mmol, 35% yield). Yellow oil. **IR** (neat) 1494, 1599, 1675, 1939, 2915, 3013, 3375 cm<sup>-1</sup>. <sup>1</sup>H **NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.29 (s, 6H), 5.34 (qd, J = 12.0, 3.2 Hz 2H), 5.62 (m, 1H), 6.91 (s, 1H), 6.99–7.07 (m, 3H), 7.17 (m, 1H), 7.26 (m, 1H), 7.34–7.40 (m, 2H). <sup>13</sup>C **NMR** (100.5 MHz, CDCl<sub>3</sub>)  $\delta$  21.3, 72.3, 81.5, 110.0, 124.7, 126.8, 127.0, 128.4, 130.0, 134.0, 138.0, 141.8, 207.6. **HRMS–DART** (m/z): [M-OH]<sup>+</sup> calcd for C<sub>18</sub>H<sub>17</sub>, 233.1325; found, 233.1329. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +55.6 (*c* 0.87, CHCl<sub>3</sub>). The ee value (78% ee) of **3ca** was determined by chiral HPLC analysis [CHIRALCEL® AD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 31.3 min (*R* isomer) and 39.7 min (*S* isomer)]. The absolute configuration of **3ca** was assigned by consideration of the stereochemical pathway.



# (S)-2-Phenyl-1-[4-(trifluoromethoxy)phenyl]buta-2,3-dien-1-ol (3da)



The product **3da** was purified by flash chromatography on silica gel (5–30% EtOAc/Hexane) (Table 2; 28.8 mg, 0.094 mmol, 47% yield). Due to the contamination of inseparable impurites, **3da** was converted to the *p*-nitrobenzoate derivative **5da** by benzoylation. The experimental data of **5da**; Yellow solid. **M.p.** 85–87°C. **IR** (neat) 1221, 1346, 1508, 1529, 1607, 1727, 2924 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.22–5.28 (m, 2H), 7.04 (m, 1H), 7.20–7.26 (m, 3H), 7.29–7.32 (m, 2H), 7.37–7.38 (m, 2H), 7.54–7.56 (m, 2H), 8.21–8.23 (m, 2H), 8.27–8.29 (m, 2H). <sup>13</sup>**C NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  74.1, 81.2, 106.4, 120.4 (q, *J* = 258.6 Hz), 121.0, 123.6, 126.6, 127.5, 128.7, 129.1, 130.9, 133.1, 135.2, 136.5, 149.3, 150.7, 163.7, 209.1. **HRMS–DART** (*m*/*z*): [M]<sup>+</sup> calcd for C<sub>24</sub>H<sub>16</sub>F<sub>3</sub>NO<sub>5</sub>, 455.0975; found, 455.0982. [*a*]<sub>D</sub><sup>25</sup> +7.3 (*c* 0.38, CHCl<sub>3</sub>). The ee value (69% ee) of **5da** (or **3da**) was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> AD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 26.8 min (*S* isomer) and 32.0 min (*R* isomer)]. The absolute configuration of **5da** (or **3da**) was assigned by consideration of the stereochemical pathway.



rac-5da			
No	rt (min)	area	area (%)
1	26.93	1536540	49.893
2	32.07	1543107	50.107

(S)-5da

No	rt (min)	area	area (%)
1	26.80	2522452	84.743
2	32.02	454142	15.257

# (S)-1-(4-Fluorophenyl)-2-phenylbuta-2,3-dien-1-ol (3ea)



The product **3ea** was purified by flash chromatography on silica gel (5-40% EtOAc/Hexane) (Table 2; 22.6 mg, 0.094 mmol, 47% yield). Yellow oil. **IR** (neat) 1449, 1599, 1682, 1939, 2924, 3060, 3411 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  2.28 (m, 1H), 5.27 (qd, J = 12.6, 2.4 Hz, 2H), 5.72 (m, 1H), 7.00–7.04 (m, 2H), 7.20 (m, 1H), 7.26–7.29 (m, 2H), 7.34–7.36 (m, 2H), 7.41–7.43 (m, 2H). <sup>13</sup>**C NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  71.7, 81.5, 110.0, 115.2 (d, J = 21.0 Hz), 126.4, 126.9, 127.2, 128.6 (d, J = 9.0 Hz), 133.7, 137.7 (d, J = 3.0 Hz), 162.3 (d, J = 246.0 Hz), 207.6. **HRMS–DART** (*m/z*): [M-OH]<sup>+</sup> calcd for C<sub>16</sub>H<sub>12</sub>F, 223.0918; found, 223.0917. [ $\alpha$ ]<sub>D</sub><sup>24</sup> +26.3 (*c* 1.08, CHCl<sub>3</sub>). The ee value (76% ee) of **3ea** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> AD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 40.9 min (*S* isomer) and 43.2 min (*R* isomer)]. The absolute configuration of **3ea** was assigned by consideration of the stereochemical pathway.



rac-3ea				
No	rt (min)	area	area (%)	
1	40.19	4491228	54.793	
2	42.36	3705552	45.207	

(S)-**3ea** 

No	rt (min)	area	area (%)
1	40.86	889497	88.129
2	43.21	119819	11.871

#### (S)-1-(3-Methoxyphenyl)-2-phenylbuta-2,3-dien-1-ol (3fa)



The product **3fa** was purified by flash chromatography on silica gel (3–30% EtOAc/Hexane) (Table 2; 27.2 mg, 0.108 mmol, 54% yield). Due to the contamination of inseparable impurites, **3fa** was converted to the acetate derivative **5fa** by acetylation. The experimental data of **5fa**;Yellow oil. **IR** (neat) 1452, 1491, 1587, 1600, 1740, 1941, 2934 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  2.11 (s, 3H), 3.79 (s, 3H), 5.18–5.21 (m, 2H), 6.76 (m, 1H), 6.82–7.02 (m, 3H), 7.17 (m, 1H), 7.23–7.28 (m, 3H), 7.33–7.36 (m, 2H). <sup>13</sup>**C NMR** (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  21.2, 55.2, 73.4, 80.5, 106.7, 113.3, 113.5, 119.8, 126.7, 127.1, 128.4, 129.4, 133.7, 139.9, 159.6, 170.0, 209.1. **HRMS–DART** (*m/z*): [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>19</sub>O<sub>3</sub>, 295.1329; found, 295.1331. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +45.0 (*c* 0.86, CHCl<sub>3</sub>). The ee value (71% ee) of **5fa** (or **3fa**) was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> AD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 75.4 min (*R* isomer) and 88.7 min (*S* isomer)]. The absolute configuration of **5fa** (or **3fa**) was assigned by consideration of the stereochemical pathway.



rac-5fa				
No	rt (min)	area	area (%)	
1	71.98	3181688	50.350	
2	87.61	3137471	49.650	

 (S)-5fa

 No
 rt (min)
 area
 area (%)

 1
 75.37
 269870
 14.343

 2
 88.71
 1611664
 85.657

(S)-1-(Benzo[d][1,3]dioxol-5-yl)-2-phenylbuta-2,3-dien-1-ol (3ga)



The product **3ga** was purified by flash chromatography on silica gel (5–30% EtOAc/Hexane) (Table 2; 20.8 mg, 0.078 mmol, 39% yield). Due to the contamination of inseparable impurites, **3ga** was converted to the *p*-nitrobenzoate derivative **5ga** by benzoylation. The experimental data of **5ga**; Yellow oil. **IR** (neat) 1346, 1444, 1489, 1503, 1607, 1725, 2922 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.23–5.32 (m, 2H), 5.96 (s, 2H), 6.78 (m, 1H), 6.93 (d, J = 2.4 Hz, 1H), 7.02–7.04 (m, 2H), 7.19–7.22 (m, 1H), 7.26–7.31 (m, 2H), 7.34–7.38 (m, 2H), 8.20–8.28 (m, 4H). <sup>13</sup>C NMR (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  74.6, 81.8, 101.3, 106.6, 108.1, 108.2, 121.9, 123.6, 126.6, 127.4, 128.6, 130.9, 131.5, 133.3, 135.6, 147.9, 148.0, 150.6, 163.7, 208,6. HRMS–DART (*m/z*): [M]<sup>+</sup> calcd for C<sub>24</sub>H<sub>17</sub>NO<sub>6</sub>, 415.1050; found, 45.1061. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +27.2 (*c* 0.12, CHCl<sub>3</sub>). The ee value (72% ee) of **5ga** (or **3ga**) was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> AD-3 column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 98:2, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time = 91.0 min (*S* isomer) and 113.6 min (*R* isomer)]. The absolute configuration of (*S*)-**5ga** (or **3ga**) was assigned by consideration of the stereochemical pathway.



rac-5ga				
No	rt (min)	area	area (%)	
1	93.02	1068696	48.722	
2	113.02	1124773	51.278	

(S)-5ga

No	rt (min)	area	area (%)
1	90.97	1104087	85.781
2	113.63	183019	14.219

# ■ Unsuccessful Examples in Asymmentric Reductive Coupling ■



#### ■ Procedure for Derivatization to Chiral Butenolide ■

**Scheme 1. 4aa** was synthesized according to the Ma's report.<sup>4</sup> To an oven-dried 20 mL Schlenk flask were added CuCl (83.2 mg, 0.84 mmol), (*S*)-**3aa** (99.3 mg, 0.42 mmol, 90% ee), and Et<sub>2</sub>O (2.5 mL) under N<sub>2</sub> atmosphere. The flask was sealed using a rubber stopper. "BuMgCl (1.05 mL, 2 M in Et2O, 2.1 mmol) was then added dropwisely to the reaction mixture at -78 °C over 20 min, which was followed by warming up to room temperature naturally. After 15 h, the rubber stopper was removed, followed by installation of a CO<sub>2</sub> balloon over the flask neck immediately. The reaction mixture was stirred at room temperature for 1.5 h, followed by quenching with 10 mL of saturated NH<sub>4</sub>Cl aq. After being stirred at room temperature for 15 min, the reaction mixture became homogenous. Then HCl (3 M) were added. The resulting mixture was extracted with Et<sub>2</sub>O. The combined organic layer was washed with brine, dried over MgSO4, filtrated and concentrated. The crude product was purified by column chromatography.

### (S)-3-Pentyl-4-phenyl-5-(p-tolyl)furan-2(5H)-one (4aa)



The product **4aa** was purified by flash chromatography on silica gel (2–20% EtOAc/Hexane) (0.42 mmol scale, Scheme 1; 60.5 mg, 0.19 mmol, 45% yield). Yellow oil. **IR** (neat) 1182, 1309, 1445, 1515, 1752, 2859, 2926 cm<sup>-1</sup>. <sup>1</sup>**H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  0.88 (t, J = 7.2 Hz, 3H), 1.29–1.37 (m, 4H), 1.58–1.72 (m, 2H), 2.29 (s, 3H), 2.45–2.54 (m, 2H), 6.11 (m, 1H), 7.06–7.09 (m, 4H), 7.18–7.21 (m, 2H) 7.32–7.48 (m, 3H). <sup>13</sup>C NMR (150.9 MHz, CDCl<sub>3</sub>)  $\delta$  14.0, 21.2, 22.3, 24.4, 27.9, 31.8, 83.6, 127.3, 127.8, 128.7, 128.7, 129.4, 129.5, 131.6, 132.0, 139.0, 158.7, 174.2. **HRMS–DART** (*m*/*z*): [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>25</sub>O<sub>2</sub>, 321.1849; found, 321.1840. [ $\alpha$ ]<sub>D</sub><sup>18</sup> +6.7 (*c* 0.50, CHCl<sub>3</sub>). The ee value (89% ee) of **4aa** was determined by chiral HPLC analysis [CHIRALCEL<sup>®</sup> OD-3 column, 4.6 mm × S18

250 mm, Daicel Chemical Industries, hexane/2-propanol = 95:5, 0.8 mL/min, 40 °C, 220 nm UV detector, retention time = 8.8 min (*S* isomer) and 10.5 min (*R* isomer)]. The absolute configuration of **4aa** was assigned by consideration of the stereochemical pathway.



### ■ References■

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<sup>1</sup>H NMR spectrum of (S)-**5ac** 



 $^{13}$ C NMR spectrum of (S)-5ac



<sup>1</sup>H NMR spectrum of (S)-3ad



<sup>13</sup>C NMR spectrum of (S)-3ad



<sup>1</sup>H NMR spectrum of (S)-3ae







<sup>13</sup>C NMR spectrum of (S)-**3af** 



<sup>1</sup>H NMR spectrum of (*S*)-Mosher's ester of (*S*)-**3af** 



<sup>1</sup>H NMR spectrum of (*R*)-Mosher's ester of (*S*)-**3af** 





<sup>13</sup>C NMR spectrum of (*S*)-**3ag** 



<sup>1</sup>H NMR spectrum of (S)-**3ba** 









<sup>1</sup>H NMR spectrum of (S)-5da











 $^{13}$ C NMR spectrum of (S)-5fa







<sup>1</sup>H NMR spectrum of (S)-4aa

