

## [Supporting Information]

# The C2 Selective Nucleophilic Substitution Reactions of 2,3-Epoxy Alcohols Mediated by Trialkyl Borates: The First Endo-Mode Epoxide-Opening Reaction through an Intramolecular Metal Chelate

Minoru Sasaki, Keiji Tanino, Atsushi Hirai, and Masaaki Miyashita\*

Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060-0810, Japan

## Experimental

General. All reactions were carried out under a dry nitrogen atmosphere. Routine flash column chromatography was achieved with Merck silica gel 60 for purification of products.

Material. Anhydrous DMF was dried by distillation from P<sub>2</sub>O<sub>5</sub>.

Epoxy alcohols **1**<sup>1</sup>, **2**<sup>2</sup>, **3**<sup>2</sup>, **4**<sup>2</sup>, **5**<sup>1</sup>, *syn*-**6**<sup>2</sup> and *anti*-**6**<sup>2</sup> were prepared according to the previously described procedures, respectively. Diol (**2S, 3R, 4S**)-1-Benzyloxy-3-methyl-2,4-pentanediol was also previously reported<sup>1</sup>.

## Typical Procedure for the Azide Substitution Reaction of 2,3-Epoxy Alcohols.

**(2S\*,3S\*)-2-Azide-4-benzyloxy-1,3-butanediol:** A mixture of epoxy alcohol **2** (2.10 g, 10.8 mmol), (MeO)<sub>3</sub>B (2.4 mL, 21.6 mmol), and NaN<sub>3</sub> (1.4 g, 21.6 mmol) in DMF (30 mL) was stirred at 50 °C for 3 h. After cooling to 0 °C, a saturated aqueous solution of NaHCO<sub>3</sub> was added, and the mixture was stirred for 30 min. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was successively washed with water, a saturated aqueous solution of NaHCO<sub>3</sub>, brine, and dried over MgSO<sub>4</sub>. Concentration under reduced pressure followed by flash column chromatography afforded 2.47 g (96%) of the title compound as a 92:8 mixture of regio isomers. Treatment of the mixture with sodium periodate followed by column chromatography afforded the 1,3-diol in pure form. IR (neat) 3398, 2100, 1497, 1094, 1028, 914, 700 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 2.18 (t, *J*= 6.3 Hz, 1 H), 2.62 (d, *J*= 5.8 Hz, 1 H), 3.55-3.60 (m, 1 H), 3.59 (dd, *J*= 5.4, 9.7 Hz, 1 H), 3.68 (dd, *J*= 3.6, 9.7 Hz, 1 H), 3.73-3.97 (m, 3 H), 4.58 (s, 2 H), 7.29-7.41 (m, 5 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ 62.39, 63.79, 70.33, 70.94, 73.47, 127.75 (2 C), 127.84, 128.35 (2 C), 137.19; HRMS Calcd for C<sub>11</sub>H<sub>16</sub>N<sub>3</sub>O<sub>3</sub> ([M+H]); 238.1191. Found: 238.1217.

**(2S\*,3S\*)-2-Azide-4-(*tert*-butyldimethylsiloxy)-1,3-butanediol:** IR (neat) 3400, 2102, 1256, 1123, 1086 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 0.11 (s, 3 H), 0.11 (s, 3 H), 0.92 (s, 9 H), 2.23 (t, *J*= 6.1 Hz,

1 H), 2.62 (d,  $J = 5.9$  Hz, 1 H), 3.52 (ddd,  $J = 4.6, 5.3, 7.6$  Hz, 1 H), 3.64-3.83 (m, 3 H), 3.87 (dd,  $J = 5.4, 6.5$  Hz, 1 H), 3.97 (ddd,  $J = 4.6, 5.9, 11.7$  Hz, 1 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  5.33 (2 C), 18.34, 25.91 (3 C), 63.01, 63.64, 63.70, 71.71; HRMS Calcd for  $\text{C}_{10}\text{H}_{24}\text{N}_3\text{O}_3\text{Si}$  ([M+H]); 262.1587. Found: 265.1587.

**(2S\*,3R\*)-2-Azide-1,3-hexanediol:** IR (neat) 3380, 2102, 1072  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.97 (t,  $J = 6.6$  Hz, 3 H), 1.20-1.64 (m, 4 H), 2.11 (d,  $J = 5.3$  Hz, 1 H), 2.18 (t,  $J = 5.8$  Hz, 1 H), 3.43 (dt,  $J = 4.9, 5.1$  Hz, 1 H), 3.75-3.84 (m, 1 H), 3.90 (dd,  $J = 5.1, 5.3$  Hz, 2 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  13.99, 18.86, 35.85, 62.41, 66.82, 72.19; HRMS Calcd for  $\text{C}_6\text{H}_{14}\text{N}_3\text{O}_2$  ([M+H]); 160.1086. Found: 160.1070.

**(2S\*,3R\*)-2-Azide-4-benzyloxy-1,3-butanediol:** IR (neat) 3400, 2104, 1454, 1096, 1028, 698  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  2.15 (t,  $J = 6.3$  Hz, 1 H), 2.51 (d,  $J = 5.3$  Hz, 1 H), 3.55-3.62 (m, 3 H), 3.80-3.88 (m, 2 H), 3.95-4.03 (m, 1 H), 4.57 (s, 2 H), 7.28-7.40 (m, 5 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  62.97, 64.17, 70.99 (2 C), 73.64, 127.80 (2 C), 127.94, 128.45 (2 C), 137.23; HRMS Calcd for  $\text{C}_{11}\text{H}_{16}\text{N}_3\text{O}_3$  ([M+H]); 238.1191. Found: 238.1200.

**(2S\*,3R\*)-2-Azide-1,3-hexanediol:** IR (neat) 3380, 2104, 1049  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.96 (t,  $J = 7.1$  Hz, 3 H), 1.35-1.62 (m, 4 H), 1.94 (d,  $J = 5.9$  Hz, 1 H), 2.07-2.16 (br, 1 H), 3.41-3.46 (m, 1 H), 3.70-3.98 (m, 3 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  14.11, 18.81, 36.54, 63.61, 66.89, 72.04; HRMS Calcd for  $\text{C}_6\text{H}_{14}\text{N}_3\text{O}_2$  ([M+H]); 160.1086. Found: 160.1082.

**(2R\*,3R\*,4R\*)-3-Azide-1-benzyloxy-2,4-pentanediol:** IR (neat) 3400, 2104, 1454, 1096, 1028, 698  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.30 (d,  $J = 6.3$  Hz, 3 H), 2.63-2.68 (br, 1 H), 2.73 (d,  $J = 5.3$  Hz, 1 H), 3.45 (dd,  $J = 6.3, 8.1$  Hz, 1 H), 3.62 (dd,  $J = 5.3, 9.6$  Hz, 1 H), 3.71 (dd,  $J = 3.3, 9.6$  Hz, 1 H), 3.75-3.85 (m, 1 H), 3.99-4.10 (m, 1 H), 4.59 (s, 2 H), 7.28-7.40 (m, 5 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  19.23, 67.79, 69.04, 71.10, 71.71, 73.59, 127.83 (2 C), 127.96, 128.46 (2 C), 137.19; HRMS Calcd for  $\text{C}_{12}\text{H}_{18}\text{N}_3\text{O}_3$  ([M+H]); 252.1348. Found: 252.1358.

#### Typical Procedure for the Phenylthio Substitution Reaction of 2,3-Epoxy Alcohols.

**(2S\*,3R\*)-4-Benzylxy-2-(phenylthio)-1,3-butanediol:** A mixture of epoxy alcohol **2** (58.3 mg, 0.3 mmol),  $(\text{MeO})_3\text{B}$  (44  $\mu\text{L}$ , 0.39 mmol), and NaSPh (60.0 mg 0.45 mmol) in DMF (1.5 mL) was stirred at rt for 3 h. After cooling to 0 °C, a saturated aqueous solution of  $\text{NaHCO}_3$  was added, and the mixture was stirred for 30 min. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was successively washed with water, a saturated aqueous solution of  $\text{NaHCO}_3$ , brine, and dried over  $\text{MgSO}_4$ . Concentration under reduced pressure followed by flash column chromatography afforded 89.0

mg (97%) of the title compound as a 95:5 mixture of regio isomers. Treatment of the mixture with sodium periodate followed by column chromatography afforded The 1,3-diol in pure form was obtained by preparative TLC separation. IR (neat) 3420, 1583, 1497, 1105, 1072, 1026, 910, 696 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 2.83-2.88 (m, 2 H), 3.33 (ddd, J= 4.9, 6.1, 7.9 Hz, 1 H), 3.70 (dd, J= 5.8, 9.6 Hz, 1 H), 3.80 (dd, J= 3.6, 9.6 Hz, 1 H), 3.86-3.91 (m, 2 H), 3.93-4.02 (m, 1 H), 4.49 (d, J=11.9 Hz, 1 H), 4.54 (d, J=11.9 Hz, 1 H), 7.22-7.44 (m, 10 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ 52.82, 63.14, 71.93, 72.15, 73.37, 127.25, 127.67 (2 C), 127.74, 128.31 (2 C), 128.97 (2 C), 131.82 (2 C), 133.59, 137.36; HRMS Calcd for C<sub>17</sub>H<sub>20</sub>O<sub>3</sub>S; 304.1133. Found: 304.1119.

**(2S\*,3R\*)-2-(Phenylthio)-1,3-hexanediol:** IR (neat) 3380, 1583, 1479, 1124, 1067, 1026, 692 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 0.94 (t, J= 7.1 Hz, 3 H), 1.24-1.76 (m, 4 H), 2.44 (bd, J= 5.1 Hz, 1 H), 2.54 (bt, J= 5.8 Hz, 1 H), 3.23 (dt, J= 5.1, 5.3 Hz, 1 H), 3.83-4.00 (m, 3 H), 7.23-7.47 (m, 5 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ 14.04, 19.13, 37.03, 57.06, 62.57, 73.03, 127.39, 129.08 (2 C), 132.04 (2 C), 133.75; HRMS Calcd for C<sub>12</sub>H<sub>18</sub>O<sub>2</sub>S; 226.1027. Found: 226.1045.

**(2S\*,3R\*)-4-(tert-Butyldimethylsiloxy)-2-(phenylthio)-1,3-butanediol:** IR (neat) 3410, 1585, 1472, 1256, 1119, 1026, 1005, 908, 691 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 0.06 (s, 3 H), 0.08 (s, 3 H), 0.89 (s, 9 H), 2.89 (d, J= 4.9 Hz, 1 H), 2.99 (dd, J= 5.9, 7.3 Hz, 1 H), 3.26-3.32 (m, 1 H), 3.72-3.97 (m, 5 H), 7.22-7.45 (m, 5 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ -5.36 (2 C), 18.27, 25.87 (3 C), 52.52, 63.27, 64.79, 73.26, 127.21, 128.97 (2 C), 131.75 (2 C), 133.61; HRMS Calcd for C<sub>16</sub>H<sub>28</sub>O<sub>3</sub>SSi; 328.1528. Found: 328.1514.

**(2R\*,3R\*)-2-(Phenylthio)-1,3-hexanediol:** IR (neat) 3327, 1560, 1508, 1124, 1084, 914, 689 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 0.92 (t, J= 7.1 Hz, 3 H), 1.23-1.74 (m, 4 H), 2.37 (dt, J= 1.5, 6.1 Hz, 1 H), 2.47 (dd, J= 1.0, 4.9 Hz, 1 H), 3.25 (dt, J= 4.0, 5.4 Hz, 1 H), 3.75-3.96 (m, 3 H), 7.23-7.49 (m, 5 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ 14.06, 19.09, 36.77, 58.58, 63.61, 72.44, 127.35, 129.07 (2 C), 132.14 (2 C), 134.02; HRMS Calcd for C<sub>12</sub>H<sub>18</sub>O<sub>2</sub>S; 226.1027. Found: 226.1032.

**(2R\*,3R\*)-4-Benzylxy-2-(phenylthio)-1,3-butanediol:** IR (neat) 3420, 1655, 1508, 1090, 1024, 698 cm<sup>-1</sup>; <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 2.56 (t, J= 6.4 Hz, 1 H), 2.82 (d, J= 3.6 Hz, 1 H), 3.44 (dt, J= 4.1, 5.4 Hz, 1 H), 3.66 (dd, J= 5.3, 9.5 Hz, 1 H), 3.77-3.92 (m, 2 H), 4.10-4.17 (m, 1 H), 4.52 (s, 2 H), 7.22-7.47 (m, 10 H); <sup>13</sup>C NMR (67.8 MHz, CDCl<sub>3</sub>) δ 55.14, 63.22, 71.19, 71.47, 73.56, 127.30, 127.76 (2 C), 127.81, 128.38 (2 C), 129.06 (2 C), 131.91 (2 C), 133.93, 137.42; HRMS Calcd for C<sub>17</sub>H<sub>20</sub>O<sub>3</sub>S; 304.1133. Found: 304.1119.

### Typical Procedure for the Cyanide Substitution Reaction of 2,3-Epoxy Alcohols.

**(2S\*, 3S\*)-4-Benzyl-2-cyano-1,3-butanediol:** A mixture of epoxy alcohol **2** (58.3 mg, 0.3 mmol),  $(\text{EtO})_3\text{B}$  (0.15 mL, 0.9 mmol), and NaCN (58.8 mg 1.2 mmol) in DMF (1.5 mL) was stirred at 70 °C for 15 h. After cooling to 0 °C, a saturated aqueous solution of  $\text{NaHCO}_3$  was added, and the mixture was stirred for 30 min. The mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was successively washed with water, a saturated aqueous solution of  $\text{NaHCO}_3$ , brine, and dried over  $\text{MgSO}_4$ . Concentration under reduced pressure followed by flash column chromatography afforded 63.9 mg (96%) of the title compound as a 92:8 mixture of regio isomers. Treatment of the mixture with sodium periodate followed by column chromatography afforded the 1,3-diol in pure form. IR (neat) 3410, 2247, 1508, 1074, 1028, 916, 700  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  2.50-2.58 (br, 1 H), 2.82 (bd,  $J= 6.1$  Hz, 1 H), 2.97 (dt,  $J= 4.8, 8.6$  Hz, 1 H), 3.67 (dd,  $J= 5.1, 9.8$  Hz, 1 H), 3.76 (dd,  $J= 3.5, 9.8$  Hz, 1 H), 3.98 (d,  $J= 4.8$  Hz, 2 H), 4.10-4.13 (m, 1 H), 4.60 (s, 2 H), 7.28-7.41 (m, 5 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  37.41, 60.50, 69.04, 71.32, 73.78, 118.26, 127.85 (2 C), 128.12, 128.53 (2 C), 136.91; HRMS Calcd for  $\text{C}_{12}\text{H}_{15}\text{NO}_3$ ; 221.1052. Found: 222.1051.

**(2S\*, 3R\*)-2-Cyano-1,3-hexanediol:** IR (neat) 3410, 2245, 1070  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.98 (t,  $J= 7.1$  Hz, 3 H), 1.35-1.80 (m, 4 H), 2.25-2.32 (br, 1 H), 2.34-2.45 (br, 1 H), 2.78 (dt,  $J= 4.9, 7.4$  Hz, 1 H), 3.92-4.08 (m, 3 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  13.85, 18.63, 37.31, 40.75, 60.45, 70.06, 119.14; HRMS Calcd for  $\text{C}_7\text{H}_{14}\text{NO}_2$  ([M+H]); 144.1024. Found: 144.1047.

**(2S\*, 3S\*)-4-(tert-Butyldimethylsiloxy)-2-cyano-1,3-butanediol:** IR (neat) 3420, 2249, 1256, 1076  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.12 (s, 3 H), 0.13 (s, 3 H), 0.92 (s, 9 H), 2.43 (t,  $J= 6.3$  Hz, 1 H), 2.71 (d,  $J= 6.8$  Hz, 1 H), 2.91 (dt,  $J= 4.9, 8.7$  Hz, 1 H), 3.78 (dd,  $J= 4.5, 10.5$  Hz, 1 H), 3.88 (dd,  $J= 3.6, 10.5$  Hz, 1 H), 3.94-4.04 (m, 3 H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  -5.39, -5.36, 18.32, 25.87 (3 C), 37.23, 60.25, 64.44, 69.87, 118.54; HRMS Calcd for  $\text{C}_{11}\text{H}_{24}\text{NO}_3\text{Si}$  ([M+H]); 246.1525. Found: 246.1507.

### References

- 1) Palombi, L.; Bonadies, F.; Scettri. *Tetrahedron*. **1997**, 53, 15867-15876.
- 2) Sasaki, M.: Tanino, K.: Miyashita, M. *Org. Lett.* **2001**, 3, 1765-1767.

## **Quantum mechanic calculations of transition structures.**

Calculations were performed with GAUSSIAN 98 program. GAUSSIAN 98, Revision A.1, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. GAUSSIAN Inc.; Pittsburgh, PA (1998).

### **Transition Structure A**

E(B3LYP/6-31G\*//HF/3-21G) = -647.901959475 hartrees

Center Number	Atomic Number	Coordinates (Angstroms)		
		X	Y	Z
1	6	0.000000	0.000000	0.000000
2	6	0.000000	0.000000	1.442044
3	7	2.421730	0.000000	1.594597
4	8	-1.403929	-0.111457	0.493413
5	6	0.331652	-1.331889	-0.645826
6	8	-0.611340	-2.251006	-0.086565
7	5	-1.898200	-1.598569	0.191439
8	8	-2.760249	-1.479568	-0.971398
9	8	-2.517330	-2.142924	1.367583
10	1	0.095775	-0.945680	1.921656
11	6	-0.084949	1.268911	2.239645
12	1	0.229768	0.908777	-0.515591
13	1	1.338003	-1.613125	-0.376748
14	1	0.235278	-1.262556	-1.724249
15	1	-2.696869	-2.265524	-1.529701
16	1	-3.456221	-1.927837	1.415517
17	7	2.595147	1.061408	1.098430
18	7	2.698595	2.115362	0.614376
19	1	-1.114511	1.597512	2.254655
20	1	0.534539	2.032825	1.785744
21	1	0.256843	1.093832	3.249127

### **Transition Structure B**

E(B3LYP/6-31G\*//HF/3-21G) = - 647.881981482 hartrees

Center Number	Atomic Number	Coordinates (Angstroms)		
		X	Y	Z
1	6	0.000000	0.000000	0.000000
2	6	0.000000	0.000000	1.465989

3	7	1.737793	0.000000	2.206895
4	8	-1.409578	0.102112	0.130163
5	6	-0.360945	1.302693	2.176259
6	8	0.326096	1.461308	3.414676
7	5	1.466151	0.596766	3.714605
8	8	2.571084	1.359581	4.253886
9	8	1.207664	-0.590781	4.506200
10	7	2.438451	-1.012029	2.092613
11	7	3.079857	-1.908708	1.933874
12	6	0.465579	-1.281788	-0.688880
13	1	0.515018	0.864855	-0.417334
14	1	-0.324034	-0.906257	1.930753
15	1	-1.423226	1.295456	2.346008
16	1	-0.126492	2.121793	1.506152
17	1	2.519887	2.282342	3.978935
18	1	1.248678	-0.408171	5.451662
19	1	-0.007959	-2.132335	-0.211050
20	1	0.139775	-1.262025	-1.724238
21	1	1.543992	-1.405956	-0.661105

---

#### Transition Structure c

E(B3LYP/6-31G\*//HF/3-21G) = -647.907529984 hartrees

Center Number	Atomic Number	Coordinates (Angstroms)		
		X	Y	Z
1	6	0.000000	0.000000	0.000000
2	6	0.000000	0.000000	1.450882
3	7	2.205721	0.000000	2.101362
4	6	-0.289594	1.327412	2.137773
5	8	-1.402219	-0.144301	0.476243
6	8	-1.188270	2.050056	1.301464
7	5	-2.219484	1.209894	0.677071
8	8	-3.318174	0.890811	1.545560
9	8	-2.590870	1.738349	-0.615044
10	1	0.169849	0.947406	-0.472109
11	6	0.472273	-1.206424	-0.764051
12	1	0.072060	-0.916659	1.978330
13	1	0.636739	1.861012	2.240980
14	1	-0.716512	1.135900	3.113806
15	1	-4.109580	0.637817	1.057306
16	1	-2.183366	2.600261	-0.761774
17	7	2.934233	-0.274971	1.204579
18	7	3.640994	-0.544734	0.326061
19	1	0.165547	-2.109126	-0.251028
20	1	0.032954	-1.208518	-1.755215
21	1	1.552148	-1.186288	-0.836789

---