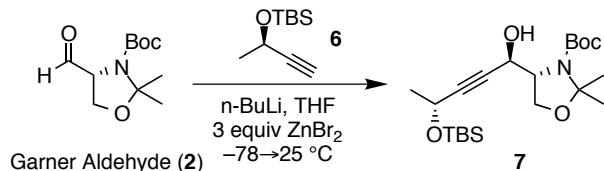


## Experimental Procedures

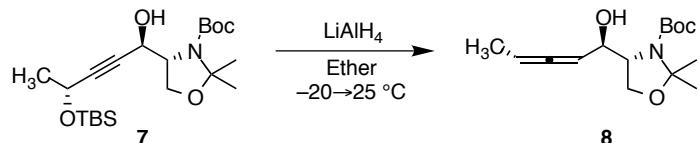
**General.** All reaction solvents were dried over  $\text{CaH}_2$  ( $\text{CH}_2\text{Cl}_2$ ) or  $\text{Na}/\text{benzophenone}$  (ether and THF). TLC was performed on glass-backed silica gel 60 F254 plates (E. Merck) visualized with 254-nm light and *p*-anisaldehyde stain. Chromatography was performed with Merck silica gel 60, 40–63  $\mu\text{m}$  particles. NMR spectra were referenced to solvent peaks ( $\text{CHCl}_3$  = 7.24 ppm;  $\text{C}_6\text{D}_5\text{H}$  = 7.15 ppm;  $\text{CDCl}_3$  = 77.0 ppm;  $\text{C}_6\text{D}_6$  = 128.0 ppm) or internal DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) for spectra recorded in  $\text{D}_2\text{O}$ .

### Addition of (*R*)-3-Butyn-2-ol *t*-Butyldimethylsilyl Ether (**6**) to (*R*)-Garner Aldehyde.



Alkyne **6** (2.08 g, 11.3 mmol, 1.29 equiv) and 40 mL of dry ether were placed in an oven-dried 250-mL round-bottom flask fitted with nitrogen inlet and stir bar. The solution was cooled to  $-78\text{ }^\circ\text{C}$ , and 4.54 mL of *n*-BuLi (2.5 *M* solution in hexanes, 11.3 mmol, 1.30 equiv) was slowly added. The mixture was stirred for 10 minutes at  $-78\text{ }^\circ\text{C}$ , and 5.90 g (26.2 mmol, 3.00 equiv) of  $\text{ZnBr}_2$  (dried *in vacuo* at 100  $^\circ\text{C}$  for 24 h) in 20 mL of ether was added dropwise with stirring. After 15 minutes, 2.0 g (8.73 mmol, 1.0 equiv) of Garner aldehyde in 5 mL of ether was added. The mixture was kept at  $-78\text{ }^\circ\text{C}$  for 2 hours and then allowed to warm to room temperature overnight. The pale yellow reaction mixture was quenched with saturated  $\text{NH}_4\text{Cl}$ , extracted with ether (3  $\times$  75 mL), dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The major diastereomer **7** was isolated by chromatography on silica gel (4:1 hexanes:EtOAc) in 77% yield. TLC:  $R_f$  0.33 (Major), 0.43 (Minor) (4:1 hexanes:EtOAc); IR (Neat) 3440, 2980, 2957, 2933, 2884, 2958, 1692, 1498, 1256, 1170, 1102, 758  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ , 75  $^\circ\text{C}$ ):  $\delta$  0.10 (s, 3H), 0.15 (s, 3H), 0.93 (s, 9H), 1.34 (d,  $J$  = 6.6 Hz, 3H), 1.35 (s, 9H), 1.41 (br s, 3H), 1.62 (br s, 3H), 3.91 (dd,  $J$  = 6.9, 9.5 Hz, 1H), 4.12–4.20 (m, 1H), 4.19 (dd,  $J$  = 2.1, 9.5 Hz, 1H), 4.49 (dq,  $J$  = 1.5, 6.6 Hz, 1H), 4.75 (br d,  $J$  = 6.3 Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ , 75  $^\circ\text{C}$ )  $\delta$  –4.73, –4.22, 18.32, 25.55, 26.02, 27.32, 28.37, 59.47, 62.55, 65.44, 80.74, 83.16, 88.74, 94.92; FAB HRMS Calcd for  $\text{C}_{21}\text{H}_{40}\text{NO}_5\text{Si}$  [M + H] $^+$ : 414.26758. Observed: 414.26795.

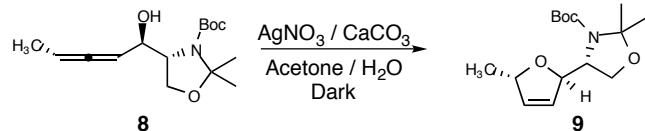
### Allenic Alcohol **8**



An oven-dried, 250-mL flask equipped with a nitrogen inlet and a stir bar was charged with 3.10 g (7.50 mmol) of alcohol **7** and 100 mL of ether. The solution was cooled to  $-20\text{ }^\circ\text{C}$ , 11.25 mL of 1.0 *M*  $\text{LiAlH}_4$  in ether (11.25 mmol, 6.0 hydride equiv) was added, and the solution was stirred for 8 h at  $-20\text{ }^\circ\text{C}$ . The reaction was quenched by the slow addition of cold water, filtered, extracted with ether (3  $\times$  50 mL), dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude product was chromatographed on silica gel (9:1  $\rightarrow$  4:1 hexanes:EtOAc) to afford 608 mg (28%) of NNN. TLC:  $R_f$  0.21 (4:1 hexanes:EtOAc); IR (Neat) 3444, 2978, 2932, 2281, 1968, 1692, 1392, 1366, 1173, 1063, 757;  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ , 75  $^\circ\text{C}$ ):  $\delta$  1.37 (s, 9H), 1.42 (br s, 3H), 1.48 (dd,  $J$  = 3.3, 7.0 Hz, 3H), 1.64 (br s, 3H), 3.72 (dd,  $J$  = 6.3, 9.3 Hz, 1H), 3.93 (dd,  $J$  = 1.8, 9.3 Hz, 1H), 4.01 (dt,  $J$  = 1.5, 6.6 Hz, 1H), 4.49 (dt,  $J$  = 1.5 Hz, 7.1 Hz, 1H), 5.05 (dp,  $J$  =

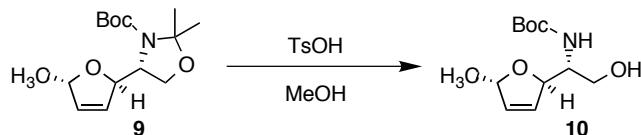
1.8, 7.1 Hz, 1H), 5.24 (o,  $J$  = 3.3 Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ , 75 °C)  $\delta$  14.28, 24.54, 27.56, 28.82, 62.55, 65.10, 72.75, 80.70, 88.01, 93.14, 95.04, 138.5, 205.77; FAB HRMS Calcd for  $\text{C}_{15}\text{H}_{26}\text{NO}_4$  [M + H] $^+$ : 284.18618 Observed: 284.18617.

### **N-Boc-Furanomycinol 1,2-Acetonide (9)**



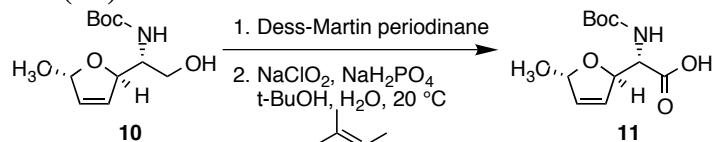
Allenic alcohol NNN (400 mg, 1.41 mmol) was dissolved in 10 mL of acetone plus 3 mL of water in a foil-wrapped, 100-mL round bottom flask. Silver nitrate (240 mg, 1.41 mmol, 1.0 equiv) and  $\text{CaCO}_3$  (282 mg, 2.82 mmol, 2.0 equiv) were added, and the mixture was stirred overnight. The solids were removed by filtration, and after concentration under reduced pressure, the mixture was diluted with water and extracted with ether (3  $\times$  50 mL), dried over  $\text{MgSO}_4$ , concentrated under reduced pressure, and chromatographed on silica gel (9:1 hexanes:EtOAc) to afford 389 mg (97%) of dihydrofuran **9**. TLC:  $R_f$  0.48 (4:1 hexanes:EtOAc); IR (KBr) 2960, 2931, 2910, 1644, 1459, 1382, 1267, 1076, 863  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ , 75 °C):  $\delta$  1.07 (d,  $J$  = 6.3 Hz, 3H), 1.38 (s, 9H), 1.41 (br s, 3H), 1.61 (br s, 3H), 3.69–3.71 (m, 2H), 4.09 (br s, 1H), 4.77 (tp,  $J$  = 1.5, 6.0 Hz, 1H), 5.27 (br s, 1H), 5.58 (dt,  $J$  = 1.5, 6.0 Hz, 1H), 5.75 (dt,  $J$  = 1.5, 6.3 Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ , 75 °C)  $\delta$  21.98, 23.61, 26.95, 28.48, 60.46, 63.76, 79.56, 82.44, 85.64, 94.34, 126.86, 133.30, 152.52; FAB HRMS Calcd for  $\text{C}_{15}\text{H}_{26}\text{NO}_4$  [M + H] $^+$ : 284.18618 Observed: 284.18516.

### **N-Boc-Furanomycinol (10)**



Acetonide **9** (380 mg, 1.34 mmol) and 15 mL of methanol were placed in a 100-mL round bottom flask and 25.4 mg (0.134 mmol, 0.10 equiv) of *p*-toluenesulfonic acid monohydrate was added. The reaction was stirred for 1.5 h, at which point TLC revealed complete consumption of starting material. The mixture was quenched with sat. aq.  $\text{NaHCO}_3$  and concentrated *in vacuo*. The residue was partitioned between water (25 mL) and EtOAc (50 mL). The aqueous layer was extracted with additional portions of EtOAc (2  $\times$  50 mL), and the combined organic layers were dried with  $\text{MgSO}_4$  and concentrated under reduced pressure to afford 315 mg (97%) of **10** as a pale yellow oil. TLC:  $R_f$  0.50 (1:1 hexanes:EtOAc); IR (Neat) 3445, 3391, 2975, 2928, 2871, 1699, 1518, 1505, 1366, 1160, 756;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.16 (d,  $J$  = 6.3 Hz, 3H), 1.34 (s, 9H), 3.21 (br s, 1H), 3.57–3.81 (m, 3H), 4.87–4.99 (m, 2H), 4.99–5.05 (m, 1H), 5.69 (br d,  $J$  = 5.7 Hz, 1H), 5.79 (dt,  $J$  = 1.7 Hz, 5.7 Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ , 75 °C)  $\delta$  21.66, 28.19, 54.11, 64.16, 79.17, 82.89, 86.84, 126.76, 132.49, 156.19; FAB HRMS Calcd for  $\text{C}_{12}\text{H}_{22}\text{NO}_4$  [M + H] $^+$ : 244.15488 Observed: 244.15477.

### **N-Boc Furanomycin (11)**

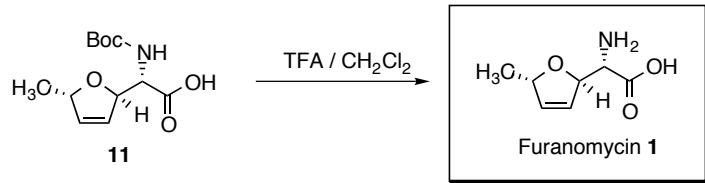


The alcohol (270 mg, 1.11 mmol) was dissolved in 8 mL of dichloromethane in a 50-mL flask, and Dess-Martin periodinane (612 mg, 1.44 mmol, 1.3 equiv) was added. The mixture was stirred

for one hour, diluted with ether (10 mL), and quenched with 10 mL of sat. aq.  $\text{NaHCO}_3$  containing 2.65 g of  $\text{Na}_2\text{S}_2\text{O}_3$ , and diluted with additional 10 mL of ether. The aqueous phase was extracted with ether ( $3 \times 50$  mL), and the combined organic layers were washed with sat. aq.  $\text{NaHCO}_3$  and brine, then dried with  $\text{MgSO}_4$  and concentrated under reduced pressure to afford *N*-Boc furanomycin as a yellow oil which was carried on to the next step without delay.

To the crude aldehyde in a 50-mL round-bottom flask were added *t*-butanol (5 mL), 2-methyl-2-butene (12.5 mL), and 460 mg of  $\text{NaH}_2\text{PO}_4$  in 1 mL of water. The stirred mixture was cooled to 0 °C, and 302 mg (3.33 mmol, 3.0 equiv) of  $\text{NaClO}_2$  in 1 mL of  $\text{H}_2\text{O}$  was slowly added. The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with saturated  $\text{NaHCO}_3$  and extracted with hexanes ( $2 \times 25$  mL). The aqueous layer was acidified to pH 2–3 with 1 *N* HCl and extracted with ether ( $3 \times 50$  mL). The combined ether extracts were dried with  $\text{MgSO}_4$  and concentrated *in vacuo* to afford 219 mg (77%) of **11**. TLC:  $R_f$  0.52 (4:4:1 hexanes:EtOAc:AcOH); IR (Neat) 3440, 3326, 2977, 1714, 1506, 1369  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.21 (d,  $J = 6.0$  Hz, 3H), 1.38 (s, 9H), 4.45 (d,  $J = 9.0$  Hz, 1H), 5.01 (br t,  $J = 5.7$  Hz, 1H), 5.18 (d,  $J = 9.0$  Hz, 1H), 5.34–5.41 (m, 1H), 5.73 (br d,  $J = 6.0$  Hz, 1H), 5.87 (br d,  $J = 6.0$  Hz, 1H), 9.82 (br s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  21.53, 28.16, 56.65, 80.01, 83.48, 86.16, 125.63, 133.58, 155.85, 174.36; FAB MS: *m/z* (relative abundance): 258 (15%,  $[\text{M} + \text{H}]^+$ ), 202 (100%), 158 (23%).

### Furanomycin (1)



*N*-Boc furanomycin (200 mg, 0.78 mmol) and 5 mL of  $\text{CH}_2\text{Cl}_2$  were placed in a 50-mL round-bottom flask and cooled to 0 °C. Trifluoroacetic acid (5 mL) was then added, and the reaction was stirred for 4 hours at room temperature. The reaction mixture was concentrated under reduced pressure, diluted with 2 mL of water, and then loaded onto a 1.5 × 10 cm column of weakly basic Amberlite® IRA 67 ion exchange resin. The column was eluted with 100 mL of water followed by 100 mL of 0.5 *M*  $\text{NH}_4\text{OH}$ . Fractions were spotted on TLC plates, and those giving a positive ninhydrin test were pooled and lyophilized to provide 111 mg (91%) of crude furanomycin. Chromatography of this material on silica gel (9:1 1-propanol: $\text{H}_2\text{O}$ ) followed by recrystallization from acetone/ $\text{H}_2\text{O}$  afforded pure, colorless furanomycin (93 mg, 76%). mp (uncorr) 217–219 °C (dec) [lit<sup>1</sup>: 220–223 °C (dec); lit<sup>2</sup>: 222.5–224.5 °C (dec)];  $[\alpha]_D +139$  (*c* 1,  $\text{H}_2\text{O}$ ) [lit<sup>1</sup>: +136.1 ± 2 (*c* 1,  $\text{H}_2\text{O}$ ); lit<sup>2</sup>: +140 (*c* 1,  $\text{H}_2\text{O}$ )]; TLC:  $R_f$  0.50 (7:3 1-propanol: $\text{H}_2\text{O}$ ); IR (KBr) 3444, 3116, 2944, 2902, 1596, 1542, 1508, 1363, 1099, 752  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ ):  $\delta$  1.25 (d,  $J = 6.5$  Hz, 3H), 3.86 (d,  $J = 2.0$  Hz, 2H), 5.11 (p,  $J = 6.0$  Hz, 1H), 5.45 (dd,  $J = 1.5, 5.5$  Hz, 1H), 5.84 (dt,  $J = 1.5, 6.0$  Hz, 1H), 6.18 (dt,  $J = 1.8, 6.5$  Hz, 1H);  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{D}_2\text{O}$ )  $\delta$  23.25, 59.90, 86.47, 85.51, 126.49, 138.49, 174.33; FAB HRMS Calcd for  $\text{C}_7\text{H}_{12}\text{NO}_3$   $[\text{M} + \text{H}]^+$ : 158.08172 Observed: 158.08182.

(1) Katagiri, K.; Tori, K.; Kimura, Y.; Yoshida, T.; Nagasaki, T.; Minato, H. *J. Med. Chem.* **1967**, *10*, 1149–1154.

(2) Semple, J. E.; Wang, P. C.; Lysenko, Z.; Joullié, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 7505–7510.