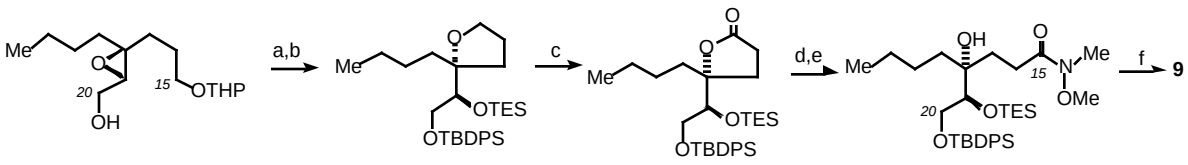
Supporting Information:

Total Synthesis of Reveromycin A

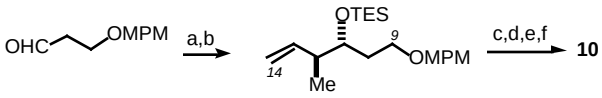
Takeshi Shimizu,* Tsutomu Masuda, Katsuya Hiramoto, and Tadashi Nakata*
RIKENThe (The Institute of Physical and Chemical Research), Wako-shi, Saitama 351-0198, Japan

Synthesis of Weinreb Amide **9**[a]



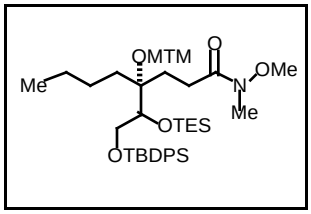
[a]Reagents and conditions: (a) aq AcOH, THF, room temperature; TsOH, MeOH, room temperature (88%); (b) TBDPSCl, imidazole, DMAP, DMF, 0 °C to room temperature; TESCl, 0 °C to room temperature (80%); (c) $RuCl_3$, $NaIO_4$, CH_3CN, CCl_4, phosphate buffer (pH 8), room temperature (92%); (d) Me_2AlCl, MeNHOMe•HCl, CH_2Cl_2, 0 °C to room temperature (e) TESCl, imidazole, DMAP, DMF, 0 °C to room temperature; (f) DMSO, Ac_2O, room temperature (67%, 3 steps).

Synthesis of Alkyne **10**[a]

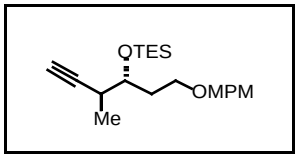


[a]Reagents and conditions: (a) (-)-*E*-crotyldiisopinocampheylborane, BF_3•Et_2O, THF, Et_2O, -78 °C; 30% H_2O_2, NaOH, reflux (95% ee); (b) TESCl, imidazole, DMAP, DMF, 0 °C (88%, 2 steps); (c) OsO_4, NMO, acetone, H_2O, room temperature (77%); (d) $Pb(OAc)_4$, toluene, room temperature (86%); (e) CBr_4, Ph_3P, Et_3N, CH_2Cl_2, 0 °C (92%); (f) *n*-BuLi, THF, -78 °C to room temperature (84%).

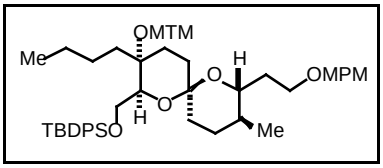
Supplementary material



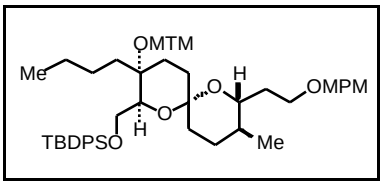
Compound 9: ^{1}H-NMR (270 MHz, $CDCl_3$) δ 0.65 (q, *J* = 7.6 Hz, 2H), 0.65 (q, *J* = 7.6 Hz, 2H), 0.66 (q, *J* = 7.6 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.6 Hz, 9H), 1.06 (s, 9H), 2.02 (s, 3H), 3.15 (s, 3H), 3.58 (dd, *J* = 10.7, 5.9 Hz, 1H), 3.63 (s, 3H), 3.84 (dd, *J* = 5.9, 3.1 Hz, 1H), 3.94 (dd, *J* = 10.7, 3.1 Hz, 1H), 4.48 (d, *J* = 10.5 Hz, 1H), 4.51 (d, *J* = 10.5 Hz, 1H); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ 5.2, 7.1, 14.1, 14.6, 19.1, 23.5, 25.9, 26.5, 27.0, 28.5, 32.2, 32.3, 61.1, 66.6, 67.0, 78.5, 81.2, 127.5, 127.5, 129.5, 129.5, 133.0, 133.2,135.6, 135.6, 174.3.



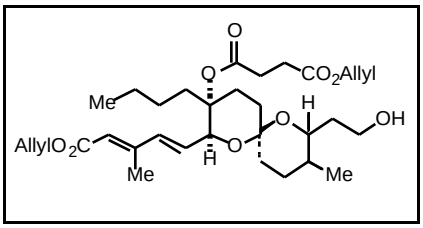
Compound 10: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.59 (q, *J* = 7.6 Hz, 6H), 0.95 (t, *J* = 7.6 HH), 1.16 (d, *J* = 6.9 Hz, 3H), 1.72 (ddt, *J* = 13.9, 8.6, 6.9 Hz, 1H), 2.00 (ddt, *J* = 13.9, 6.9, 4.0 Hz, 1H), 2.05 (d, *J* = 2.3 Hz, 1H), 2.60 (m, 1H), 3.53 (t, *J* = 6.9 Hz, 2 H), 3.80 (s, 3H), 3.91 (dt, *J* = 8.6, 4.0 Hz, 1H), 4.43 (s, 2 H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 5.0, 6.9, 14.3, 32.3, 33.2, 55.3, 66.9, 69.9, 72.5, 86.2, 113.7, 129.3, 130.0, 159.1.



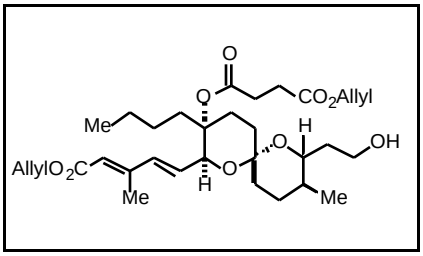
Compound 12: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.80 (t, *J* = 6.4 Hz, 3H), 0.80 (t, *J* = 6.4 Hz, 3H), 1.05 (s, 9H), 2.15 (s, 3H), 3..47 (dd, *J* = 9.2, 6.2 Hz, 1H), 3.62 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.79 (m, 2H), 4.37 (s, 2H), 4.37 (d, *J* = 10.5 Hz, 1H), 4.43 (d, *J* = 10.5 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.3-7.7 (m, 10H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1, 14.6, 17.9, 19.2, 23.2, 24.6, 25.3, 26.9, 27.5, 31.7, 32.4, 33.0, 33.4, 34.9, 55.3, 63.8, 66.3, 67.3, 72.6, 73.5, 76.8, 78.1, 96.0, 113.6, 127.6, 129.5, 129.5, 129.7, 130.8, 133.4, 133.7, 135.5, 135.6, 158.9, 159.2.



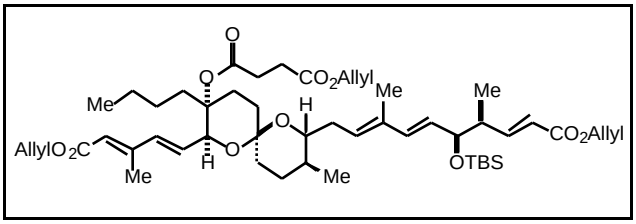
Compound 13: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 1.05 (s, 9H), 1.48 (m, 1H), 2.06 (s, 3H), 3.27 (ddd, *J* = 9.6, 9.6, 2.3 Hz, 1H), 3.75 (dd, *J* = 11.0, 7.8 Hz, 1H), 3.80 (s, 3H), 3.95 (dd, *J* = 11.0, 2.3 Hz, 1H), 4.18 (d, *J* = 11.5 Hz, 1H), 4.31 (dd, *J* = 7.8, 2.3 Hz, 1H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 10.5 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.3-7.7 (m, 10H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3, 17.6, 19.4, 23.3, 24.0, 25.3, 27.0, 27.6, 29.3, 30.7, 34.1, 34.9, 35.3, 55.4, 62.9, 66.6, 67.2, 72.8, 74.6, 75.3, 77.2, 96.5, 113.9, 127.5, 127.6, 129.2, 129.5, 129.5, 134.2, 134.3, 135.9, 135.9, 158.9.



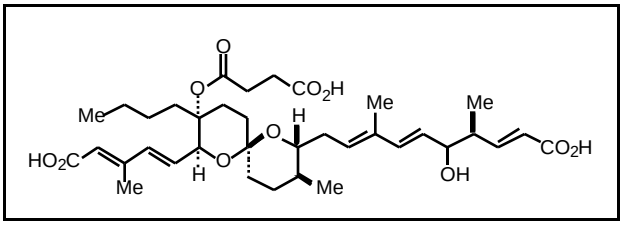
Compound 19: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.81 (d, *J* = 6.0 Hz, 3H), 0.83 (t, *J* = 6.9 Hz, 3H), 2.33 (d, *J* = 0.9 Hz, 3H), 2.64 (m, 4H), 3.64 (ddd, *J* = 12.5, 5.1, 4.1 Hz, 1H), 3.68 (m, 1H), 3.86 (m, 1H), 4.60 (dd, *J* = 5.5, 1.4 Hz, 2H), 4.64 (ddt, *J* = 5.5, 1.4, 1.4 Hz, 2H), 4.67 (brd, *J* = 6.4, 1H), 5.24 ((ddt, *J* = 10.5, 1.4, 1.4 Hz, 1H), 5.25 (ddt, *J* = 10.5, 1.4, 1.4 Hz, 1H), 5.32 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1H), 5.34 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1 H), 5.87 (brq, *J* = 0.9 Hz, 1H), 5.91 (ddt, *J* = 17.0, 10.5, 5.5 Hz, 1H), 5.96 (ddt, *J* = 17.0, 10.5, 5.5 Hz, 1H), 6.34 (dd, *J* = 15.6, 6.4 Hz, 1H), 6.35 (d, *J* = 15.6, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.9, 14.4, 17.7, 22.7, 24.2, 24.6, 27.2, 29.1, 30.0, 32.1, 33.0, 33.5, 35.3, 60.2, 64.7, 65.4, 77.0, 77.6, 83.0, 95.9, 118.1, 118.4, 120.0, 132.0, 132.4, 132.4, 137.9, 151.7, 166.4, 171.3, 171.9.



Compound 21: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.4 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H), 2.29 (d, *J* = 0.9 Hz, 3H), 2.64 (m, 4H), 3.38 (ddd, *J* = 9.6, 9.6, 2.3 Hz, 1H), 3.77 (ddd, *J* = 10.1, 4.6, 4.6 Hz, 1H), 4.06 (ddd, *J* = 10.1, 10.1, 3.7 Hz, 1H), 4.59 (ddd, *J* = 6.0, 1.4, 1.4 Hz, 2H), 4.62 (ddd, *J* = 6.0, 1.4, 1.4 Hz, 2H), 5.23 ((ddt, *J* = 10.5, 1.4, 1.4 Hz, 1H), 5.23 (ddt, *J* = 10.5, 1.4, 1.4 Hz, 1H), 5.32 (ddt, *J* = 17.4, 1.4, 1.4 Hz, 1H), 5.33 (ddd, *J* = 17.4, 1.4, 1.4 Hz, 1 H), 5.40 (dd, *J* = 5.5, 0.9 Hz, 2H), 5.84 (brs, 1H), 5.90 (ddt, *J* = 17.4, 10.5, 1.4 Hz, 1H), 5.95 (ddt, *J* = 17.4, 10.5, 1.4 Hz, 1H), 6.11 (dd, *J* = 16.0, 5.5 Hz, 1H), 6.35 (dd, *J* = 16.0, 0.9, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.8, 14.1, 17.2, 23.0, 25.3, 25.5, 26.3, 29.1, 29.7, 30.3, 30.5, 35.4, 35.4, 35.6, 59.0, 64.5, 65.4, 72.1, 75.8, 84.1, 97.4, 117.8, 118.4, 119.1, 131.5, 131.9, 132.5, 134.6, 152.3, 166.7, 171.7, 172.0.



Compound 27: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.76 (d, *J* = 6.4 Hz, 3H), 0.82 (t, *J* = 7.3 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.70 (s, 3H), 2.24 (m, 1H), 2.28 (s, 3H), 2.46 (m, 1H), 2.64 (m, 4H), 3.41 (ddd, *J* = 10.1, 6.4, 6.4 Hz, 1H), 4.09 (dd, *J* = 7.3, 5.0 Hz, 1H), 4.59 (br d, *J* = 6.0 Hz, 1H), 4.61 (d, *J* = 8.7 Hz, 1H), 4.63 (br d, *J* = 6.0 Hz, 2H), 5.23 (brd *J* = 10.5 Hz, 3H), 5.32 (brd, *J* = 17.4 Hz, 2H), 5.34 (dd, *J* = 17.4, 1.4 Hz, 1H), 5.42 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.53 (dd, *J* = 7.3, 7.3 Hz, 1H), 5.82 (dd, *J* = 16.0, 1.4 Hz, 1H), 5.86 (brs, 1H), 5.86-6.00 (m, 3H), 6.13 (d, *J* = 15.6 Hz, 1 H), 6.32 (d, *J* = 15.6 Hz, 1H), 6.37 (dd, *J* = 15.6, 8.7 Hz, 1H), 7.04 (dd, *J* = 16.0, 7.3 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ –4.9, –4.1, 12.6, 13.9, 14.1, 14.3, 17.6, 18.2, 17.6, 18.2, 22.7, 24.0, 24.5, 25.8, 27.5, 29.2, 30.0, 31.5, 31.7, 33.3, 34.0, 35.7, 43.8, 64.6, 64.8, 65.4, 74.6, 76.8, 78.2, 83.1, 95.7, 117.8, 118.1, 118.3, 119.8, 120.6, 127.3, 127.8, 132.0, 132.4, 132.4, 133.1, 134.2, 135.9, 137.7, 151.8, 152.2, 166.3, 166.4, 171.3, 171.9.



Reveromycin A (1): ^{1}H-NMR (500 MHz, CD_3OD) δ 0.82 (d, *J* = 6.4 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.79 (s, 3 H), 2.30 (s, 3 H), 2.63 (m, 4H), 3.49 (ddd, *J* = 10.1, 3.7. 3.7 Hz, 1H), 4.10 (dd, *J* = 7.3, 6.4 Hz, 1H), 4.66 (d, *J* = 8.2 Hz, 1H), 5.57 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.63 (dd, *J* = 7.3, 6.9 Hz, 1H), 5.85 (dd, *J* = 15.6, 0.9 Hz, 1H) , 5.92 (brs, 1H), 6.28 (d, *J* = 15.6 Hz, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.50 (dd, *J* = 15.6, 8.2 Hz, 1H), 7.01 (dd, *J* = 15.6, 7.3 Hz, 1H); ^{1}H-NMR (500 MHz, DMSO) δ 0.72 (d, *J* = 6.0 Hz, 3H), 0.77 (t, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 1.67 (s, 3 H), 2.18 (s, 3 H), 2.45 (m, 2H), 3.98 (dd, *J* = 6.4, 5.5 Hz, 1H), 4.49 (d, *J* =9.6 Hz, 1H), 5.46 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.53 (dd, *J* = 6.9, 6.4 Hz, 1H), 5.71 (d, *J* = 15.6 Hz, 1H) , 5.85 (brs, 1H), 6.17 (d, *J* = 15.6 Hz, 1H), 6.34 (dd, *J* = 15.6, 9.6 Hz, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 6.84 (dd, *J* = 15.6, 7.3 Hz, 1H); ^{13}C-NMR (125 MHz, CD_3OD) δ 13.0, 14.2, 14.7, 15.4, 18.2, 23.8, 25.1, 25.3, 28.6, 29.9, 31.2, 32.9, 33.0, 34.8, 35.3, 36.9,

44.1, 76.2, 76.9, 79.8, 84.2, 97.0, 121.5, 122.5, 128.1, 129.2, 134.2, 135.3, 137.9, 139.3, 152.5, 152.9, 170.1, 170.1, 173.2, 176.1.