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Supporting Information



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# Total Synthesis of Spirastrellolide F Methyl Ester—Part 1: Strategic Considerations and Revised Approach to the Southern Hemisphere**

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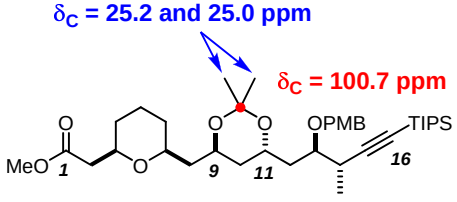
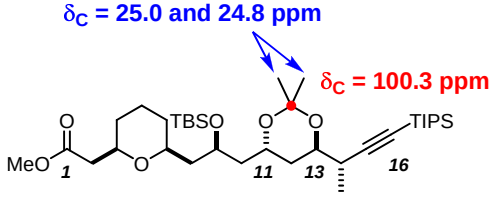
For the assignment of the chiral centers at C.9 and C.11, compound **21** obtained by the Mukaiyama aldol reaction was converted into two different isopropylidene acetal derivatives. The analysis of their $^{13}C$ NMR data established the mutual 1,3-*anti* relationships as shown,[1] which was later confirmed by the X-ray analysis of several advanced intermediates (see the accompanying paper):




The stereochemistry of product **29** generated in the glycolate aldol reaction was deduced from the NMR data of two cyclic acetals and later confirmed by the X-ray structures of more advanced synthetic intermediates (see the accompanying paper):

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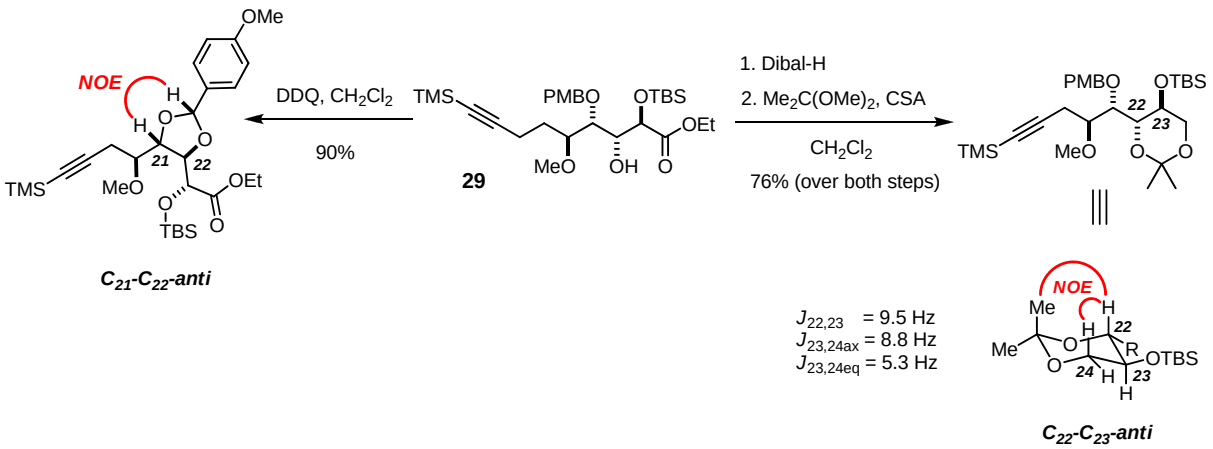
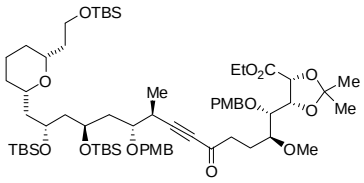
[1] S. D. Rychnovsky, B. Rogers, G. Yang, *J. Org. Chem.* **1993**, *58*, 3511-3515.

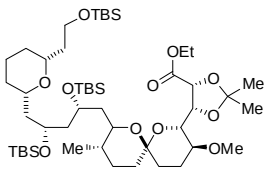



## Characterization Data and NMR Spectra of Key Intermediates

**Alkyne 33:** $[\alpha]_D^{20}$ = +24.8 (c = 0.5, $CH_2Cl_2$). IR (ATR): 2930, 1709, 1612, 1514, 1463, 1380, 1247, 1212, 1171, 1090, 1032, 833 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.31 – 7.24 (m, 4H), 6.88 – 6.80 (m, 4H), 4.67 (d, *J* = 11.1 Hz, 1H), 4.62 (d, *J* = 11.1 Hz, 1H), 4.56 (d, *J* = 6.6 Hz, 1H), 4.49 (d, *J* = 11.3 Hz, 1H), 4.43 (d, *J* = 11.3 Hz, 1H), 4.41 (m, 1H), 4.06 (m, 2H), 3.92 (m, 1H), 3.86 (m, 1H), 3.84 (m, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.70 (*t*, *J* = 6.8 Hz, 2H), 3.61 (m, 1H), 3.44 – 3.27 (m, 3H), 3.26 (s, 3H), 2.97 (m, 1H), 2.66 – 2.51 (m, 2H), 2.05 (m, 1H), 1.90 (m, 1H), 1.83 – 1.36 (m, 13H), 1.60 (s, 3H), 1.40 (s, 3H), 1.25 – 1.09 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 2H), 1.17 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.06 (s, 6H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 ppm (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 187.6, 170.2, 159.3, 159.2, 130.9, 130.7, 129.6 (2C), 129.2 (2C), 113.9 (2C), 113.8 (2C), 110.6, 95.1, 82.2, 80.7, 79.9, 77.8, 76.3, 76.1, 74.7, 73.9, 73.0, 71.2, 67.9, 66.7, 61.1, 60.2, 57.6, 55.4, 55.4, 47.6, 45.1, 41.0, 40.1, 39.6, 32.4, 31.8, 29.7, 26.8, 26.2 (9C), 25.9, 23.9, 23.9, 18.5, 18.2, 18.2, 14.7, 14.2, –3.4, –3.8 (2C), –4.1, –5.1 ppm (2C); HRMS (ESI+): calcd. for $C_{65}H_{114}NO_{14}Si_3$ $[M+NH_4]^+$: 1216.7549; found 1216.7542.

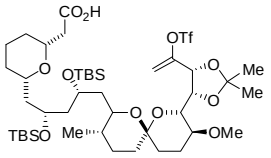



**Spiroketal 34:** $[\alpha]_D^{20}$ = +18.2 (c = 0.5, $CH_2Cl_2$). IR (neat): 2928, 2856, 1735, 1462, 1379, 1254, 1197, 1100, 1018, 937, 807, 773, 662 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_2Cl_2$): δ = 4.61 (d, *J* = 6.9 Hz, 1H), 4.55 (dd, *J* = 6.9, 3.0 Hz, 1H),

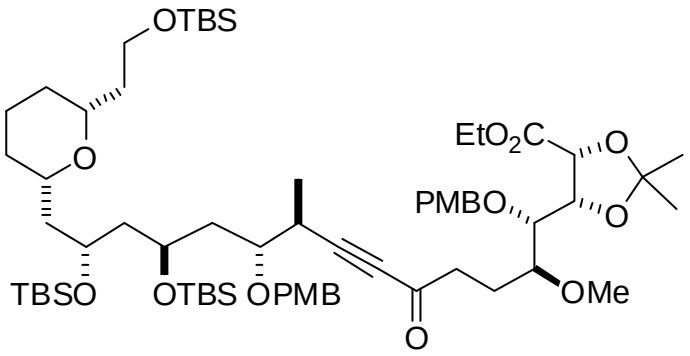


4.24 (qd, *J* = 10.7, 7.1 Hz, 1H), 4.14 – 4.05 (m, 2H), 3.96 (m, 1H), 3.73 – 3.64 (m, 3H), 3.41 – 3.32 (m, 2H), 3.31 (s, 3H), 3.29 – 3.21 (m, 2H), 1.93 (ddd, *J* = 12.6, 8.1, 4.6 Hz, 1H), 1.84 – 1.34 (m, 20H), 1.50 (s, 3H), 1.36 (s, 3H), 1.31 – 1.22 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.21 – 1.07 (m, 2H), 0.95 – 0.80 (m, 2H), 0.89 (s, 27 H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.04 ppm (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.9, 109.9, 95.8, 77.2, 75.9, 75.7, 74.7, 74.4, 73.5, 71.0, 67.7, 67.6, 60.9, 60.5, 56.1, 48.6, 45.9, 41.9, 40.4, 35.7, 35.0, 33.8, 32.5, 32.2, 27.8, 26.6, 26.3 (3C), 26.2 (3C), 26.1 (4C), 24.2, 23.5, 18.6, 18.4, 18.3, 17.9, 14.4, –3.1, –3.7, –3.8, –3.9, –5.2 ppm (2C); HRMS (ESI+): calcd. for $C_{49}H_{96}O_{11}NaSi_3$ $[M+Na]^+$: 967.6164; found 967.6153.

**Enol Triflate 39:** $[\alpha]_D^{20}$ = +33.7° (c = 1.08, $CH_2Cl_2$). IR (neat): 2930, 2857, 1713, 1462, 1424,

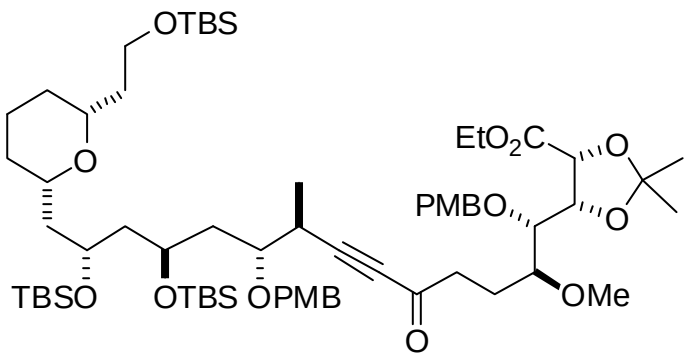



1381, 1250, 1210, 1140, 1098, 1056, 1005, 926, 908, 833, 806, 773, 716 $cm^{-1}$; $^1$H NMR (400 MHz, $CD_2Cl_2$): δ = 10.01 ( br s, 1H), 5.41 (d, *J* = 3.6, 1H), 5.28 (d, *J* = 3.4, 1H), 4.70 (br d, *J* = 6.9, 1H), 4.64 (dd, *J* = 12.2, 7.1 Hz, 1H), 3.98 – 3.85 (m, 2H), 3.78 – 3.66 (m, 1H), 3.58 (dd, *J* = 9.5, 2.3, 1H), 3.53 (br d, *J* = 9.3, 1H), 3.40 – 3.26 (m, 2H), 3.34 (s, 3H), 2.48 (dd, *J* = 15.5, 4.7 Hz, 1H), 2.43 (dd, *J* = 15.5, 7.6, 1H), 2.03 – 1.91 (m, 1H), 1.89 –1.70 (m, 5H), 1.69 – 1.34 (m, 12H), 1.53 (s, 3H), 1.39 (s, 3H), 1.30 – 1.07 (m, 3H), 0.78 (s, 18H), 0.80 (d, *J* = 6.0, 3H), 0.10 (s, 6H), –0.08 (s, 3H), –0.07 ppm (s, 3H); $^{13}$C NMR (100 MHz, $CD_2Cl_2$): δ = 173.0, 153.2, 109.9, 106.5, 96.1, 77.4, 76.3, 75.6, 75.5, 74.3, 74.0, 70.6, 68.1, 67.8, 56.5, 54.4, 47.8, 45.0, 41.9, 41.6, 35.6, 35.0, 34.3, 32.0, 31.4, 28.1, 26.4, 26.2 (4C), 26.2 (3C), 25.5, 23.6, 18.4, 18.3, 18.2, –3.1, –3.7, –3.8, –4.0 ppm; HRMS ($ESI^+$): calcd for $C_{43}H_{77}F_3O_{13}SSi_2Na$ $[M+Na]^+$: 969.4461; found: 969.4468.



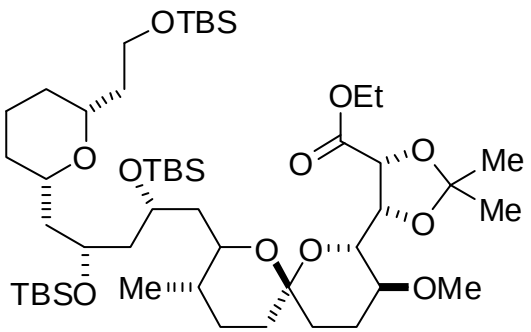

**33**

$^{1}$H NMR (400 MHz, $CDCl_3$)



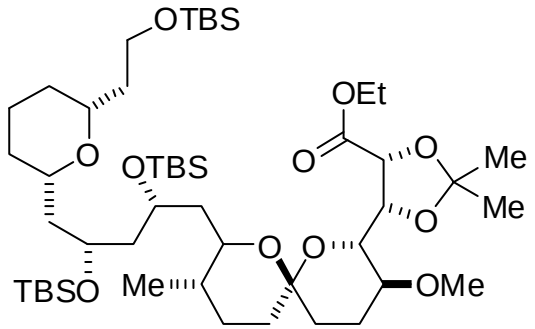

**33**

$^{13}$C NMR (100 MHz, $CDCl_3$)



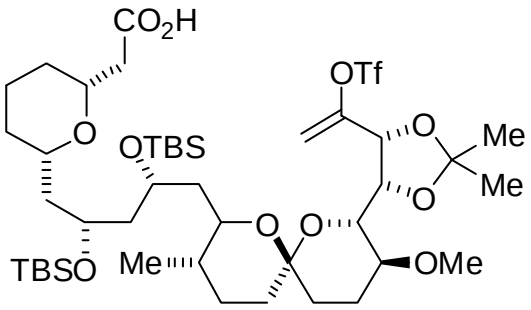

**34**

$^{1}$H NMR (400 MHz, $CD_2Cl_2$)



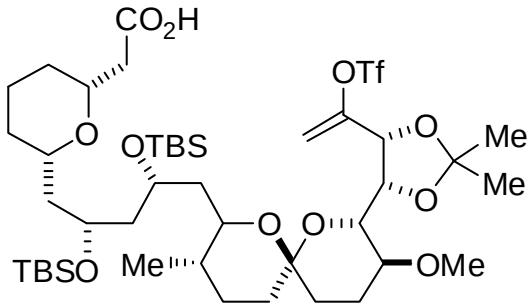

**34**

$^{13}C$ NMR (100 MHz, $CD_2Cl_2$)




**39**

$^{1}$H NMR (400 MHz, $CD_2Cl_2$)




**39**

$^{13}$C NMR (100 MHz, $CD_2Cl_2$)