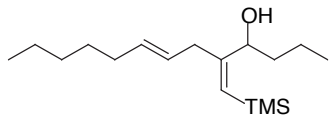
APPENDIX

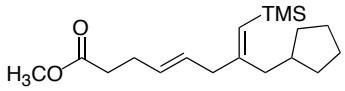
A Regioselective Ru Catalyzed Alkene-Alkyne Coupling

Barry M. Trost*, Michelle Machacek and Matthew J. Schnaderbeck

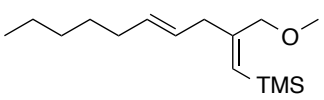
Department of Chemistry
Stanford University
Stanford, California 94305-5080



Compound 7. Colorless oil. Flash chromatography in 0-6% ether/ petroleum ether. R_f = 0.38 in 10% ether:pet ether. IR (neat): 3387, 2958, 2929, 2874, 1613, 1466, 1249, 971, 838 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.42 (m, 2H), 5.37 (s, 1H), 4.39 (m, 1H), 2.90 (dd, J = 4.8, 15.8 Hz, 1H), 2.72 (dd, J = 4.9, 15.7 Hz, 1H), 2.03 (m, 2H), 1.624 (m., 2H), 1.5-1.2 (m, 9H), 0.94 (t, J = 7.2Hz, 3H), 0.88 (t, J = 6.9Hz, 3H), 0.12 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.4, 132.7, 128.4, 127.0, 75.0, 37.7, 35.7, 32.5, 31.3, 29.1, 22.5, 19.3, 14.1, 14.0, 0.7. HRMS calcd. for $C_{17}H_{34}OSi$: 282.2380, found: 282.2380.

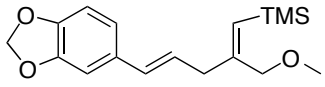


Compound 10. Colorless oil. Flash chromatography in 0-2% ether/ petroleum ether. R_f = 0.60 in 10% ether:pet ether. IR (neat): 2952, 2869, 1744, 1609, 1437, 1248, 1169, 838 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.44 (m, 2H), 5.17 (s, 1H), 3.67 (s, 3H), 2.75 (d, J = 4.8 Hz, 2H), 2.43-2.32 (m, 4H), 2.13 (d, J = 7.5 Hz, 2H), 2.03 (septet, J = 7.5 Hz, 1H), 1.70-1.47 (m, 8H), 0.08 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.8, 157.7, 129.7 (2C), 124.6, 51.5, 42.1, 41.6, 38.4, 34.0, 32.3, 27.8, 25.1, 0.47. Anal. calcd. for $C_{18}H_{32}O_2Si$: C, 70.07%; H, 10.45%. Found: C, 69.87%; H, 10.52%.

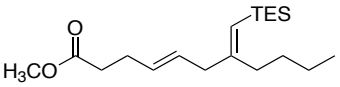


Compound 12. Colorless oil. Flash chromatography in petroleum ether. IR (film): 2956, 2926, 2850, 1620, 1452, 1248, 1102, 970, 838 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.50

(s, 1H), 5.40-5.50 (m, 2H), 3.93 (s, 2H), 3.32 (s, 3H), 2.83 (d, J = 5.5 Hz, 2H), 2.03 (m, 2H), 1.4-1.2 (m, 6H), 0.90 (t, J = 6.5 Hz, 3H), 0.13 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.2, 132.9, 128.2, 127.2, 74.0, 57.7, 40.3, 32.5, 31.4, 29.2, 22.5, 14.1, 0.5. HRMS calcd. for $C_{15}H_{30}OSi$: 254.2067. Found: 239.1892 (M^+ - CH_3); Anal. calcd. for $C_{15}H_{30}OSi$: C, 70.79%; H, 11.88%. Found: C, 70.61%; H, 11.74%.

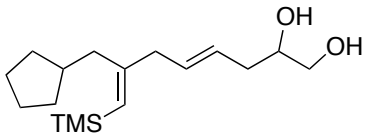


Compound 14. colorless oil. flash chromatography in petroleum ether. R_f = 0.6 in 10% ether/pet ether. IR (film): 2952, 2894, 1617, 1503, 1490, 1446, 1249, 1041, 840 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.95 (s, 1H), 6.95-6.75 (m, 2H), 6.30 (d, J = 15.6 Hz, 1H), 6.06 (dt, J = 15.7 , 7.2 Hz, 1H), 5.96 (s, 2H), 5.55 (s, 1H), 3.97 (s, 2H), 3.34 (s, 3H), 3.03 (d, J = 7.1 Hz, 2H), 0.13 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.6, 148.0, 146.8, 132.3, 131.3, 129.1, 126.3, 120.5, 108.2, 105.5, 100.9, 73.9, 57.7, 40.4, 0.30; HRMS calcd. for $C_{17}H_{24}O_3Si$: 304.1495. Found: 304.1492. Anal. calcd. for $C_{17}H_{24}O_3Si$: C, 67.06%; H; 7.95%. Found: C, 66.83%; H, 8.10%.

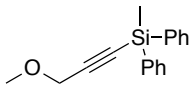


Compound 16. Colorless oil. Flash chromatography in 0-2% ether/petroleum ether. R_f = 0.64 in 10% ether/pet ether. IR (film): 2954, 2874, 1744, 1609, 1458, 1436, 1237, 1154, 1015, 970, 714 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.5-5.4 (m, 2H), 5.08 (s, 1H), 3.67 (s, 3H), 2.77 (d, J = 4.5 Hz, 2H), 2.4-2.3 (m, 4H), 2.1-2.05 (m, 2H), 1.4-1.2 (m, 4H), 0.93 (m, 12H), 0.58 (q, J = 7.9 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.7, 159.4,

129.9, 129.6, 120.4, 51.4, 42.1, 36.1, 34.0, 31.0, 27.7, 22.9, 13.9, 7.5, 4.7. HRMS calcd. for $C_{19}H_{36}O_2Si$: 324.2486. Found: 324.2476.

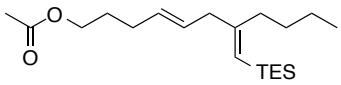


Compound 18. Colorless oil. Flash chromatography in 0-20% ether/petroleum ether. IR (film): 3372, 2951, 2869, 1609, 1431, 1247, 1072, 972, 836, 668 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.55 (dt, *J* = 6.7, 15.3 Hz, 1H), 5.43 (dt, *J* = 6.9, 15.4 Hz, 1H), 5.18 (s, 1H), 3.8-3.65 (m, 2H), 3.48 (dd, *J* = 7.2, 11.0 Hz, 1H), 2.80 (d, *J* = 6.6 Hz, 2H), 2.00 (m, 1H), 2.3-2.1 (m, 4H), 1.8-1.4 (m, 8H), 1.2-1.0 (m, 2H), 0.09 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.5, 132.7, 126.8, 124.9, 71.5, 66.2, 42.2, 41.7, 38.4, 36.6, 32.3, 25.0, 0.4; HRMS calcd. for $C_{17}H_{32}O_2Si$: 296.2173. Found: 296.2172. Anal. calcd. for $C_{17}H_{32}O_2Si$: C, 68.86%; H, 10.88%. Found: C, 68.90%; H, 10.91%.

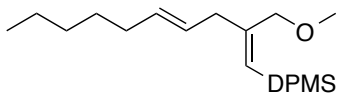


Compound 19. To a solution of methyl propargyl ether (1.0 mL, 11.8 mmol) in THF (12 mL) at -78ºC was added a 1.5 M solution of n-butyllithium in hexanes (7.8 mL, 11.8 mmol). The solution was stirred for 30 min. at -78ºC, then a solution of diphenylmethylsilyl chloride (2.7 mL, 13.0 mmol) in THF (5 mL) was added. The reaction was allowed to warm to room temperature. The mixture was then quenched with water and extracted twice with ether. The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated by rotary evaporation. Purification by kugelrohr distillation (175 ºC @ 1 mm Hg) afforded 2.7 g (86%) of **19** as a colorless oil.

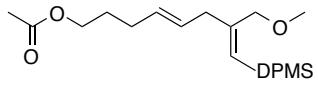
IR (film): 3069, 3000, 2933, 2821, 2174, 1589, 1429, 1353, 1253, 1187, 1107, 1007, 903, 792, 728, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.65-7.6 (m, 4H), 7.4-7.25 (m, 6H), 4.16 (s, 2H), 3.38 (s, 3H), 0.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 134.9, 134.5, 129.7, 127.9, 104.7, 87.8, 60.4, 57.5, -2.3.



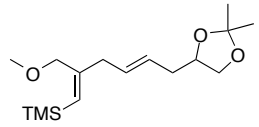
Compound 21. colorless oil. flash chromatography in 0-3% ether/petroleum ether. R_f = 0.57 in 5% ether/ pet ether. IR (neat): 2954.7, 2874, 1744, 1610, 1459, 1365, 1241, 1043, 1017, 907, 715 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.43 (m, 2H), 5.08 (s, 1H), 4.06 (t, J = 6.7 Hz, 2H), 2.77 (d, J = 3.6 Hz, 2H), 2.07 (m, 7H), 1.67 (m, 2H), 1.32 (m, 4H), 0.93 (m, 12H), 0.58 (q, J=7.8 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.18, 159.4, 130.39, 129.45, 120.25, 63.98, 42.26, 36.23, 31.08, 28.84, 28.43, 23.06, 21.00, 14.10, 7.62, 4.79. Anal calcd for $C_{20}H_{38}O_2Si$: C, 70.94%; H, 11.31%. Found: C, 70.74%; H, 11.47%.



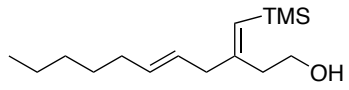
Compound 22. Colorless oil. Flash chromatography in 0-3% ether/petroleum ether. IR(neat): 3048, 2956, 2925, 2855, 1617, 1466, 1428, 1250, 1110, 970, 793, 732, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.53 (m, 4H), 7.34 (m, 6H), 5.80 (s, 1H), 5.47 (m, 2H), 3.75 (s, 2H), 2.92 (m, 5H), 2.04 (m, 2H), 1.42-1.28 (m, 6H), 0.88 (t, J=6.6Hz, 2H), 0.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.90, 138.00, 134.50, 133.27, 128.94, 127.75, 126.93, 123.39, 73.81, 57.50, 40.39, 32.52, 31.33, 29.16, 22.51, 14.06, -1.62. Anal calcd for $C_{25}H_{34}OSi$: C, 79.31%; H, 9.05%. Found: C, 79.10%; H, 8.89%.



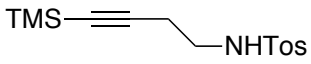
Compound 23. colorless oil. flash chromatography in 5-10% ether/petroleum ether. Rf=0.57 in 20% ether/ pet ether. IR (neat): 3068, 2925, 2814, 1740, 1616, 1428, 1366, 1242, 1109, 1042, 971, 792, 733, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.52 (m, 4H), 7.34 (m, 6H), 5.79 (s, 1H), 5.50 (m, 2H), 4.07 (t, J=6.6Hz, 2H), 3.74 (s, 2H), 2.91 (m, 5H), 2.11 (m, 2H), 2.04 (s, 3H), 1.71 (m, 2H), 0.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.13, 157.51, 137.87, 134.49, 131.44, 128.95, 128.11, 127.75, 123.62, 73.76, 63.91, 57.50, 40.30, 28.85, 28.38, 20.97, -1.66. Anal calcd for $C_{25}H_{32}O_3Si$: C, 73.49%; H, 7.89%. Found: C, 73.54%; H, 7.70%.



Compound 24. Colorless oil. Flash chromatography in 0-10% ether/petroleum ether. R_f = 0.54 in 20% ether/pet ether. IR (neat): 2985, 2953, 2896, 3819, 1619, 1378, 1370, 1249, 1215, 1101, 1064, 839 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.55-5.39 (m, 3H), 4.12 (m, 1H), 4.00 (m, 1H), 3.90 (s, 2H), 3.57 (m, 1H), 3.28 (s, 3H), 2.83 (d, J = 6.3Hz, 2H), 2.45-2.36 (m,1H), 2.29-2.20 (m, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 0.10 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.59, 130.78, 128.56, 127.04, 108.86, 75.52, 73.85, 68.86, 57.71, 40.19, 36.83, 26.88, 25.65, 0.44. Anal calcd for $C_{16}H_{30}O_3Si$: C, 64.38%; H, 10.13%. Found: C, 64.12%; H, 10.07%.

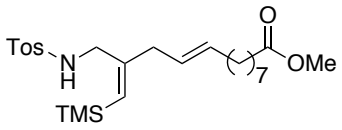


Compound 26. Colorless oil. Flash chromatography in 0-12% ether/petroleum ether. IR (neat): 3333, 2956, 2928, 2874, 1612, 1435, 1248, 1042, 971, 839cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.49-5.31 (m, 3H), 3.69 (t, J = 6.9 Hz, 2H), 2.77 (d, J = 5.4 Hz, 2H), 2.42 (t, J=6.6Hz, 2H), 2.04-1.98 (m, 2H), 1.53-1.28 (m, 7H), 0.88 (t, J=6.6Hz, 3H), 0.12 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.77, 132.95, 128.00, 127.54, 61.02, 42.52, 38.77, 32.48, 31.34, 29.11, 22.51, 14.06, 0.41. Anal calcd for $C_{15}H_{30}OSi$: C, 70.80%; H, 11.88%. Found: C, 70.69%; H, 11.74%.

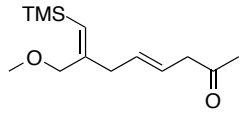


Compound 27. To a solution of alkynyl alcohol (1 equiv), NHBocTos (1.2 equiv), triphenylphosphine (1.2 equiv), in THF (0.3M) at 0ºC is added diethylazodicarboxylate or diisopropylazodicarboxylate (1.2 equiv). Let warm slowly to room temperature and stir overnight. Concentrate reaction mixture and purify directly by flash chromatography in ether/pet ether. To a solution of the boc-tosyl-protected alkynyl amine (1 equiv) in methylene chloride (0.35M) is added triflouroacetic acid (5 equivalents). Let stir at room temperature for 24 h. Concentrate *in vacuo* and purify directly by flash chromatography in ether/pet ether. To a solution of tosyl-protected alkynyl amine (1.1 equiv) in THF (0.5M) at -78ºC is added nBuLi (2 equiv) in hexanes. Solid appears, warm to 0ºC and stir for 45ºC, then add trimethylsilyl chloride (2.2 equiv). Let warm slowly to room temperature. A white ppt forms. Quench with water, extract aqueous layer with ether. Combined organics are washed with with water and brine, dried over magnesium sulfate, and concentrated *in vacuo*. Flash chromatography in ether/pet ether yields a white solid.

mp 91-93 °C. R_f = 0.53 in 50% ether/pet ether. IR (film): 3285, 2959, 2177, 1599, 1421, 1329, 1250, 1161, 1094, 1038, 844, 663 cm^{-1}. ^1H NMR (300MHz, $CDCl_3$): δ 7.75 (d, J = 8.4Hz, 2H), 7.31 (d, J = 8.1Hz, 2H), 4.71 (m, 1H), 3.08 (m, 2H), 2.43 (s, 3H), 2.37 (m, 2H), 0.13 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 143.55, 136.85, 129.73, 127.01, 102.39, 87.50, 41.62, 21.49, 20.96, -0.08. Anal calcd for $C_{14}H_{21}NO_2SSi$: C, 56.91%; H, 7.16%; S, 10.85%. Found: C, 56.74%; H, 7.30%; S, 11.02%.



Compound 29. light yellow oil. flash chromatography in ether/petroleum ether. R_f = 0.21 in 20% ether/pet ether. IR (neat): 3277, 2928, 2655, 1740, 1436, 1330, 1249, 1163, 840. ^1H NMR (300MHz $CDCl_3$): δ 7.76 (d, J = 6.6Hz, 2H), 7.30 (d, J = 6.9Hz, 2H), 5.40 (s, 1H), 5.26 (m, 2H), 4.54 (m, 1H), 3.65 (s, 3H) 3.59 (d, J = 6Hz, 2H), 2.71 (d, J = 6Hz, 2H), 2.42 (s, 3H), 2.29 (t, 7.5Hz, 2H), 1.94 (m, 2H), 1.61 (m, 2H), 1.27 (m, 8H), -0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.27, 151.28, 143.40, 136.49, 133.35, 130.34, 129.60, 127.16, 126.67, 51.39, 46.65, 40.55, 34.01, 32.40, 29.17, 29.01(2C), 28.85, 24.86, 21.44, -0.01. Anal calcd for $C_{25}H_{41}NO_4SSi$: C, 62.85%; H, 8.23%; N, 2.93%; S, 7.79%. Found: C, 62.89%; H, 8.17%; N, 2.89%, S, 7.56%.



Compound 31. Colorless oil. Flash chromatography in 0-15% ether/petroleum ether. R_f = 0.35 in 20% ether/pet ether. IR (neat): 2954, 2922, 2886, 1719, 1619, 13578, 1249, 1101, 970, 840 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.58-5.55 (m, 2H), 5.47 (s, 1H),

3.91 (s, 2H), 3.30 (s, 3H), 3.16 (d, J = 4.2H z, 2H), 2.88 (d, J = 3.9Hz, 2H), 2.15 (s, 3H), 0.11 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 207.31, 153.24, 132.32, 128.89, 123.97, 73.83, 57.76, 47.64, 40.18, 29.35, 0.42. Anal calcd for $C_{13}H_{24}O_2Si$: C, 64.95%; H, 10.06%. Found: C, 64.78%; H, 10.16%.