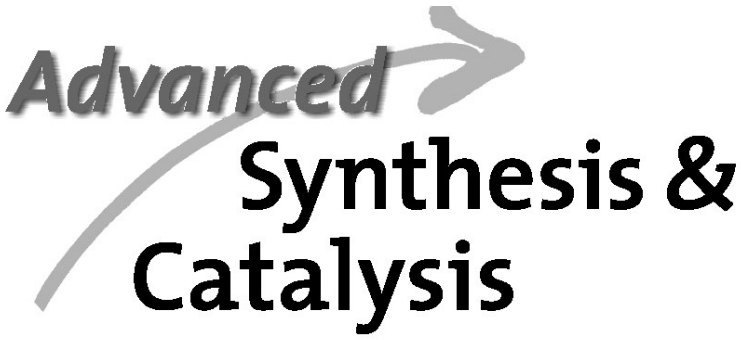

Supporting Information

Imine Additions of Internal Alkynes for the Synthesis of Trisubstituted (*E*)-Alkene and Cyclopropane Peptide Isosteres

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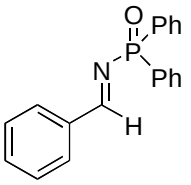
SUPPORTING INFORMATION

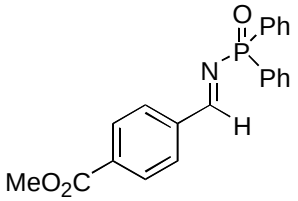
Including experimental procedures and spectral data for all new compounds, including copies of ^{1}H and ^{13}C NMR spectra for **3c**, **6a,b**, **7**, **8**, **9a-j**, **10**, **11**, **12**, **13**, **14**, **15**, **16**, **22**. Crystallographic data for structures **11** and **22** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-270732 for **11** and CCDC-270733 for **22**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.)+ 44 1223/336-033; e-mail: deposit@ccdc.cam.ac.uk]."

Experimental procedures and spectral data for compounds **2**, **3a,b**, **4a,b**, **5a,b**, **17**, **18**, **19**, **20**, and **21** and crystal information files (CIF) for compounds **5a**, **5b** and **21** are in the supplementary information of the preliminary communication of this work, see: P. Wipf, J. Xiao, *Org. Lett.* **2005**, *7*, 103.

General. All moisture-sensitive reactions were performed using syringe-septum cap techniques under an N_2 atmosphere and all glassware was dried in an oven at 150 °C for 2 h prior to use. THF was distilled over sodium/benzophenone ketyl; CH_2Cl_2, toluene and Et_3N were distilled from CaH_2. Me_2Zn (2.0 M solution in toluene) was purchased from Aldrich Company. Reactions were monitored by TLC analysis (EM Science pre-coated silica gel 60 F_{254} plates, 250 μm layer thickness) and visualization was accomplished with a 254 nm UV light and by staining with Vaughn's reagent (4.8 g $(NH_4)_6Mo_7O_{24}\bullet 4H_2O$, 0.2 g $Ce(SO_4)_2\bullet 4H_2O$ in 10 mL conc. H_2SO_4 and 90 mL H_2O). Flash chromatography on SiO_2 (or with 1% Et_3N in mobile phase) was used to purify the crude reaction mixtures. Melting points were determined using a Laboratory Devices Mel-Temp II. Infrared spectra were determined on a Nicolet Avatar 360 FT-IR spectrometer. Microwave reactions were run using an Emrys Optimizer microwave reactor from Personal Chemistry (Biotage). ^{1}H spectra were obtained on Bruker Avance 300, 500 or 600 MHz instruments. ^{19}F NMR spectra were obtained on a Bruker Avance 300 instrument. Chemical shifts were reported in parts per million with the residual solvent peak used as an internal standard. ^{1}H NMR spectra are tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet), number of protons, and coupling constant(s). ^{13}C NMR spectra were obtained at 75 MHz, 125 MHz or 150 MHz using the proton-decoupled pulse sequence with a d_1 of 6 s, 8 s or 12 s for all compounds. Mass spectra were obtained on a Micromass Autospec double focusing instrument (EI) or a Waters Q-Tof mass spectrometer (ESI).

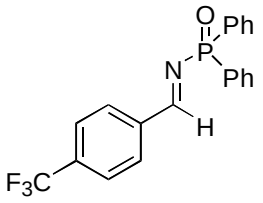


(Diphenylphosphinylimino)methylbenzene (A). Prepared as a white solid according to a literature procedure:[1] ^{1}H NMR δ 9.33 (d, 1 H, *J* = 32.0 Hz), 8.03-8.7.92 (m, 6 H), 7.53-7.45 (m, 9 H).

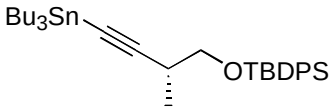


Methyl 4-[(diphenylphosphinylimino)methyl]benzoate (B). Prepared as a yellow solid according to a literature procedure:[1] ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (d, 1 H, *J* = 31.6 Hz), 8.18 (d, 2 H, *J* = 8.4 Hz), 8.08 (d, 2 H, *J* = 8.4 Hz), 7.99-7.92 (m, 4 H), 7.53-7.44 (m, 6 H), 3.97 (s, 3 H).

[1] W. B. Jennings, C. J. Lovely, *Tetrahedron* **1991**, *47*, 5561.

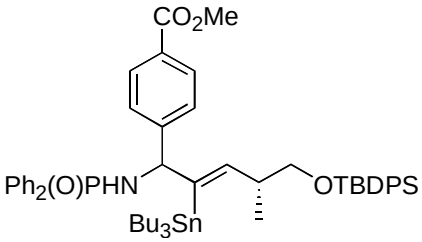


***N*-4-trifluoromethylbenzylidene-*P*,*P*-diphenylphosphinamide (C).** Prepared as a yellow solid according to a literature procedure:[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.39 (d, 1 H, *J* = 31.5 Hz), 8.14 (d, 2 H, *J* = 8.1 Hz), 7.99-7.92 (m, 4 H), 7.78 (d, 2 H, *J* = 8.1 Hz), 7.54-7.47 (m, 6 H).

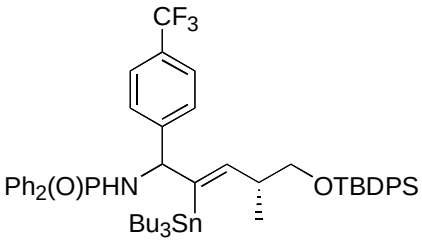


(*R*)-*tert*-Butyl-(2-methyl-4-tributylstannanylbut-3-ynyloxy)diphenylsilane (3c). A solution of 1.32 g (2.74 mmol) of **2** in 50.0 mL of dry THF was treated at -78 °C with 4.80 mL (5.76 mmol) of *n*-BuLi (1.2 M solution in hexanes). The reaction mixture was stirred at -78 °C for 1 h and room temperature for another 1 h, cooled to -78 °C and treated dropwisely with 780 μL (2.88 mmol) of Bu_3SnCl. The resulting mixture was stirred at -78 °C for 30 min, quenched with saturated $NaHCO_3$ at -78 °C, and the solid was extracted with cold ether. The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* (> 5 h) to yield 1.70 g (quant.) of crude **3c** as a colorless oil: $[\alpha]^{25}_D$ +8.3 (*c* 1.41, $CHCl_3$); IR (neat) 3071, 2955, 2930, 2856, 1463, 1428, 1112, 1085, 825, 739, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4 H), 7.46-7.35 (m, 6 H), 3.75 (dd, 1 H, *J* = 9.4, 5.5 Hz), 3.51 (dd, 1 H, *J* = 9.4, 8.0 Hz), 2.77-2.67 (m, 1 H), 1.62-1.51 (m, 6 H), 1.35-1.28 (m, 6 H), 1.24 (d, 3 H, *J* = 6.9 Hz), 1.09 (s, 9 H), 1.00-0.91 (m, 6 H), 0.88 (t, 9 H, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 133.8, 129.6, 127.6, 113.6, 82.2, 67.9, 41.6, 30.3, 28.8, 27.0, 26.8, 26.1, 23.3, 19.3, 18.1, 14.2, 13.7, 10.9; EIMS *m/z* 555 ($[M-C_4H_9]^+$, 1.7), 499 (6), 265 (52), 235 (53), 207 (40), 187 (48), 135 (37), 105 (45), 81 (45), 69 (81); HRMS (EI) *m/z* calcd for $C_{29}H_{43}OSi^{120}Sn$ ($M-C_4H_9$) 555.2105, found 555.2132; FABMS m/*z* calcd for $C_{33}H_{52}OSi^{120}Sn$ 612.281, found 612.282.

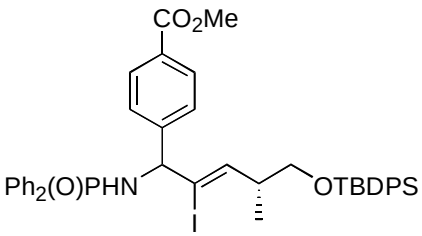
[2] P. Wipf, C. M. Coleman, J. M. Janjic, P. S. Iyer, M. D. Fodor, Y. A. Shafer, C. R. J. Stephenson, C. Kendall, B. W. Day, *J. Comb. Chem.* **2005**, *7*, 322.



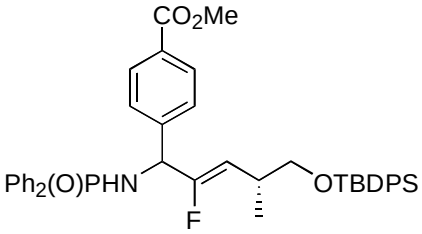
***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-tributyltinyl-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*Z*)-enyl]-*P*,*P*-diphenylphosphinamide (6a).** A suspension of 5.05 g (19.6 mmol) of Cp_2ZrHCl in 50.0 mL of CH_2Cl_2 was treated at room temperature with 6.00 g (9.81 mmol) of **3c**. After 15 min, CH_2Cl_2 was removed via rotavapor and 50.0 mL of toluene was added. The reaction mixture was cooled to –78 °C and treated over a period of 30 min with 4.91 mL (9.82 mmol) of Me_2Zn (2.0 M solution in toluene). The mixture was stirred at –78 °C for 30 min, warmed to room temperature over a period of 5 min and treated in one portion with 2.38 g (6.55 mmol) of imine **B**. The mixture was stirred at room temperature overnight, quenched with saturated NH_4Cl, diluted with EtOAc, filtered through Celite, and washed with H_2O and brine. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on deactivated SiO_2 (1 : 1, hexanes/EtOAc containing 1% Et_3N) to yield 4.18 g (65%) of **6a** as a yellow, oily ~ 2 : 1 mixture of diastereomers: IR (neat) 3380, 3314, 3186, 3071, 2956, 2929, 2856, 1724, 1609, 1463, 1438, 1428, 1279, 1192, 1111, 1078, 1020, 824, 741, 726, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98-7.79 (m, 6 H), 7.72-7.66 (m, 4 H), 7.43 (d, 2 H, J = 9.0 Hz), 7.47-7.28 (m, 12 H), 6.21 (d, 0.35 H, J = 9.9 Hz, dd (^{117}Sn 7.5%, ^{119}Sn 8.6%), $^3J_{H\text{-}Sn}$ = 118 Hz, $^3J_{H\text{-}H}$ = 9.9 Hz), 6.08 (d, 0.65 H, J = 10.0 Hz, dd (^{117}Sn 7.5%, ^{119}Sn 8.6%), $^3J_{H\text{-}Sn}$ = 119 Hz, $^3J_{H\text{-}H}$ = 10.0 Hz), 4.97-4.86 (m, 1 H), 3.91 (s, 3 H), 3.71-3.51 (m, 2 H), 3.15 (dd, 0.65 H, J = 10.6, 6.7 Hz), 3.02 (dd, 0.35 H, J = 10.5, 6.6 Hz), 2.50-2.40 (m, 1 H), 1.26-1.13 (m, 15 H), 1.10 (s, 4 H), 1.08 (s, 5 H), 0.77 (t, 9 H, J = 7.0 Hz), 0.70-0.60 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 166.7, 148.2, 148.0, 144.7, 144.6, 144.4, 144.0, 143.9, 143.2, 135.5, 133.8 (2C), 133.5, 133.4, 133.3, 132.7, 132.6, 132.5, 132.1 (2C), 131.7, 131.5 (2C), 131.4, 130.9, 130.8, 129.6, 129.5, 128.8, 128.7, 128.4, 128.2, 128.0 (2C), 127.6, 127.5, 68.6, 68.3, 62.3, 61.4, 51.8, 42.0, 29.0, 28.8 (2C), 28.6, 27.5, 27.1, 26.8, 26.7, 19.2 (2C), 18.0 (2C), 13.9, 13.6, 13.4, 10.8, 10.6; EIMS *m/z* 976 (M^+, 0.52), 947 (0.44), 920 (87), 630 (30), 552 (6), 450 (24), 336 (100), 201 (57), 135 (39).



***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-tributyltinyl-(4*R*)-methyl-(1*SR*)-(4-trifluoromethylphenyl)pent-(2*Z*)-enyl]-*P,P*-diphenylphosphinamide (6b).** A suspension of 258 mg (1.00 mmol) of Cp_2ZrHCl in 3.00 mL of CH_2Cl_2 was treated at room temperature with 306 mg (500 μmol) of **3c**. After 15 min, CH_2Cl_2 was removed *in vacuo* and 3.00 mL of toluene was added. The reaction mixture was cooled to –78 °C and treated over a period of 30 min with 250 μL (500 μmol) of Me_2Zn (2.0 M solution in toluene). The mixture was stirred at –78 °C for 15 min, warmed to room temperature over a period of 5 min and treated in one portion with 123 mg (333 μmol) of imine **C**. The mixture was stirred at room temperature for 1 h and at 60 °C for 5 h, quenched with saturated NH_4Cl, diluted with EtOAc, filtered through Celite, and washed with H_2O and brine. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on deactivated SiO_2 (1 : 1, hexanes/EtOAc containing 1% Et_3N) to yield 217 mg (67%) of **6b** as a yellow, oily ~ 1 : 1 mixture of diastereomers: IR (neat) 3391, 3173, 3071, 2957, 2929, 2857, 1617, 1461, 1439, 1428, 1325, 1193, 1111, 1069, 1018, 825, 741, 725, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99-7.82 (m, 4 H), 7.78-7.67 (m, 4 H), 7.64-7.30 (m, 16 H), 6.29 (d, 0.5 H, J = 9.9 Hz, dd (^{117}Sn 7.5%, ^{119}Sn 8.6%), $^3J_{H\text{-}Sn}$ = 118 Hz, $^3J_{H\text{-}H}$ = 9.9 Hz), 6.16 (d, 0.5 H, J = 10.0 Hz, dd (^{117}Sn 7.5%, ^{119}Sn 8.6%), $^3J_{H\text{-}Sn}$ = 118 Hz, $^3J_{H\text{-}H}$ = 10.0 Hz), 5.10-4.88 (m, 1 H), 3.77-3.54 (m, 2 H), 3.26 (dd, 0.5 H, J = 10.1, 6.9 Hz), 3.11 (dd, 0.5 H, J = 10.0, 6.8 Hz), 2.64-2.41 (m, 1 H), 1.25-1.17 (m, 15 H), 1.14 (s, 4.5 H), 1.13 (s, 4.5 H), 0.83-0.79 (m, 9 H), 0.76-0.67 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 146.8, 144.6, 143.9, 143.4, 135.6, 133.8, 133.7, 133.6, 133.4, 132.8, 132.7, 132.5, 132.4, 132.1, 132.0, 131.8, 131.6 (2C), 131.4, 130.7, 130.6, 129.6, 128.5, 128.3, 128.2, 128.0, 127.6, 125.2, 123.7 (q, J = 271 Hz), 68.6, 68.4, 62.3, 61.3, 42.0, 28.9, 28.8, 27.2, 26.8, 19.3, 19.2, 18.1, 18.0, 13.4, 10.8, 10.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ -61.16 (s), -61.20 (s); HRMS (ESI) *m/z* calcd for $C_{53}H_{70}F_3NO_2PSi^{120}Sn$ (M+H) 988.3888, found 988.3920.

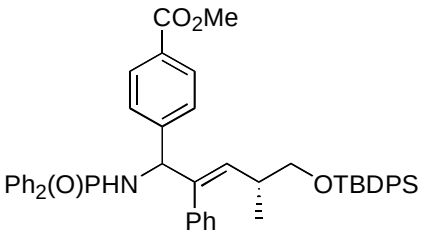


***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-iodo-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*Z*)-enyl]-*P*,*P*-diphenylphosphinamide (7).** A solution of 190 mg (0.194 mmol) of **6a** in 6.00 mL of CH_2Cl_2 was treated at room temperature in one portion with 219 mg (0.973 mmol) of NIS. The reaction mixture was rapidly stirred at room temperature for 4 min, quenched with saturated $Na_2S_2O_3$/$NaHCO_3$ solution, stirred until a clear solution formed, and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc) to yield 100 mg (63%) of **7** as a colorless, solid ~ 1 : 1 mixture of diastereomers: Mp 64-66 °C (ether); IR (neat) 3149, 3071, 2956, 2930, 2894, 2857, 1722, 1610, 1437, 1429, 1281, 1191. 1110, 1019, 910, 728, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00-7.83 (m, 6 H), 7.73-7.69 (m, 2 H), 7.64-7.62 (m, 2 H), 7.55-7.33 (m, 13 H), 7.20-7.15 (m, 1 H), 5.63 (d, 0.5 H, *J* = 8.7 Hz), 5.62 (d, 0.5 H, *J* = 8.7 Hz), 4.81 (d, 0.5 H, *J* = 10.6 Hz), 4.78 (d, 0.5 H, *J* = 10.7 Hz), 3.91 (s, 3 H), 3.70 (dd, 0.5 H, *J* = 11.0, 9.1 Hz), 3.63-3.51 (m, 2 H), 3.37 (dd, 0.5 H, *J* = 9.8, 7.4 Hz), 2.80-2.70 (m, 1 H), 1.08 (s, 4.5 H), 1.04 (s, 4.5 H), 1.00 (d, 1.5 H, *J* = 7.5 Hz), 0.95 (d, 1.5 H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 166.7, 145.9, 145.8 (2C), 145.7, 141.2, 134.0, 135.6, 135.5, 133.6, 133.5 (2C), 133.4 (2C), 132.7, 132.6, 132.4, 132.2, 132.0, 131.8, 131.7, 130.7, 130.4, 129.7 (2C), 129.4, 129.3, 128.7 (2C), 128.6, 128.5, 128.4, 128.3, 128.2, 127.7 (2C), 127.5, 127.1, 127.0, 113.2 (2C), 112.5, 112.4, 67.2, 66.6, 62.7, 62.5, 52.0, 43.4, 43.3, 26.8 (2C), 19.2 (2C), 16.0, 15.5; EIMS *m/z* 756 ([M-C_4H_9]$^+$, 100), 686 (18), 628 (5), 525 (7), 428 (10), 398 (14), 364 (6), 309 (10), 259 (6), 228 (9), 201 (86), 135 (51); HRMS (EI) *m/z* calcd for $C_{38}H_{36}INO_4PSi$ (M-C_4H_9) 756.1196, found 756.1189.



***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-fluoro-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*Z*)-enyl]-*P*,*P*-diphenylphosphinamide (8).** To a solution 1.00 g (1.02 mmol) of **6a** in CH_2Cl_2 (30.0 mL) was added 374 mg (3.06 mmol) of DMAP, 786 mg (3.06 mmol) of AgOTf and 518 mg (3.06 mmol) of XeF_2 at room temperature. The mixture was stirred at room temperature for 5 min, quenched with saturated $NaHCO_3$ solution, and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc) to yield 362 mg (50%) of **8** as a yellowish, foamy ~ 1 : 1 mixture of diastereomers: IR

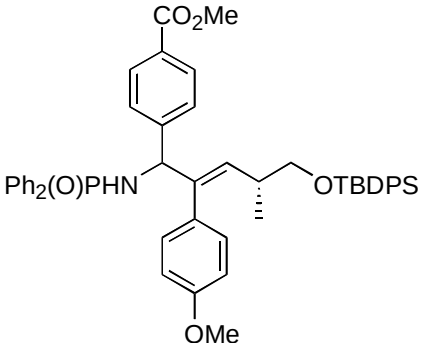
(neat) 3324, 3165, 3071, 2958, 2932, 2859, 1723, 1612, 1436, 1429, 1281, 1189. 1111, 726, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.332 (m, 24 H), 5.02-4.80 (m, 1 H), 4.73 (dd, 0.5 H, *J* = 37.3, 9.5 Hz), 4.69 (dd, 0.5 H, *J* = 37.2, 9.5 Hz), 3.89 (s, 3 H), 3.81-3.70 (m, 0.5 H), 3.60-3.40 (m, 2.5 H), 2.95-2.80 (m, 1 H), 1.07-1.02 (m, 6 H), 1.03 (s, 4.5 H), 0.97 (d, 1.5 H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 166.6, 158.7, 158.6, 158.3, 158.2, 155.3 (2C), 154.9, 154.8, 144.5, 135.5, 135.4, 133.7, 133.6, 133.6 (2C), 133.2, 132.5, 132.4, 132.3 (2C), 132.0, 131.7, 131.6, 129.8, 129.7, 129.6, 129.5, 128.5, 128.4 (2C), 128.3 (2C), 127.5 (2C), 127.2, 127.1, 111.9 (d, *J* = 13.1 Hz), 111.3 (d, *J* = 13.1 Hz), 67.9, 67.8, 55.6 (d, *J* = 28.6 Hz), 55.4 (d, *J* = 30.5 Hz), 51.9, 31.9, 26.8, 26.7, 19.2, 19.1, 17.1, 16.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ -118.17 (dd, *J* = 36.7, 15.5 Hz), -118.17 (dd, *J* = 36.7, 19.7 Hz); HRMS (ESI) *m/z* calcd for $C_{42}H_{45}FNO_4PSiNa$ (M+Na) 728.2737, found 728.2766.



***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-phenyl-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P,P*-diphenylphosphinamide (9a). Stille Coupling, General Protocol A:** In a 10-mL microwave tube, 16.4 mg (387 μmol) of LiCl was flame fused under vacuum. After cooling to room temperature, 7.45 mg (6.44 μmol) of $Pd(PPh_3)_4$ and 25.4 mg (257 μmol) of CuCl were added. The mixture was degassed 3 times under vacuum with an argon purge. Another solution of 47.0 mg (48.1 μmol) of **6a**, 13.1 mg (64.2 μmol) of PhI in DMSO (2.00 mL) was added with stirring. The resulting black mixture was de-gassed by the freeze-thaw process and heated under microwave irradiation at 60 °C for 40 min. The brown solution was quenched with H_2O, and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc) to yield 23.0 mg (63%) of **9a** as a colorless, solid ~1 : 1 mixture of diastereomers: Mp 72-74 °C (ether); IR (neat) 3184, 3054, 2958, 2930, 2858, 1723, 1610, 1437, 1280, 1192, 1111, 1020, 917, 824, 743, 725, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.86 (m, 2 H), 7.84-7.76 (m, 4 H), 7.67-7.63 (m, 2 H), 7.59-7.59 (m, 2 H), 7.48-7.32 (m, 14 H), 7.23-7.17 (m, 3 H), 6.84 (dd, 1 H, *J* = 7.7, 1.9 Hz), 6.78 (dd, 1 H, *J* = 7.7, 1.7 Hz), 5.63 (d, 0.5 H, *J* = 10.1 Hz), 5.51 (d, 0.5 H, *J* = 10.0 Hz), 5.07 (t, 0.5 H, *J* = 10.7 Hz), 5.04 (t, 0.5 H, *J* = 10.7 Hz), 3.91 (s, 1.5 H), 3.90 (s, 1.5 H), 3.58-3.43 (m, 2 H), 3.28-3.21 (m, 1 H), 2.49-2.44 (m, 0.5 H), 2.39-2.33 (m, 0.5 H), 1.07 (s, 4.5 H), 1.00 (s, 4.5 H), 0.98 (d, 1.5 H, *J* = 7.0 Hz), 0.95 (d, 1.5 H, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ

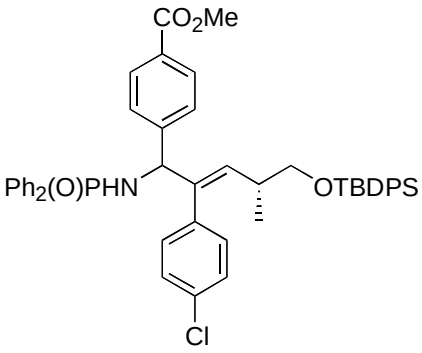
166.9, 166.8, 146.8 (2C), 141.5, 141.4, 137.9, 137.3, 135.5 (2C), 135.4, 134.1, 133.6 (2C), 133.5, 133.4, 133.1, 132.6, 132.7, 132.5, 132.4, 132.3 (2C), 131.9, 131.8 (2C), 129.7, 129.6, 129.5, 129.4, 129.1, 128.9, 128.8, 128.5, 128.4, 128.3 (2C), 128.1, 127.6 (2C), 127.5, 127.3, 127.2 (2C), 68.5, 68.3, 61.3, 60.8, 51.9, 35.9, 26.8 (2C), 19.2 (2C), 17.4, 17.3; EIMS *m/z* 763 (M^+, 0.44), 706 (38), 416 (5), 398 (18), 364 (25), 259 (8), 218 (17), 201 (100), 183 (17), 135 (37), 91 (14), 77 (28); HRMS (EI) *m/z* calcd for $C_{44}H_{41}NO_4PSi$ (M-C_4H_9) 706.2543, found 706.2509.

***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-phenyl-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P,P*-diphenylphosphinamide (9a). Negishi Coupling, General Protocol B:** 1.78 g (13.1 mmol) of $ZnCl_2$ was flame fused under vacuum, dissolved in 40.0 mL of THF, cooled to 0 °C, and treated dropwisely with 4.33 mL (13.0 mmol) of phenyl magnesium bromide (3.0 M solution in Et_2O). The reaction mixture was warmed to room temperature and stirred for 1 h. In a separate flask, a solution of 346 mg (0.425 mmol) of **7** and 113 mg (0.098 mmol) of $Pd(PPh_3)_4$ in 10.0 mL of THF was prepared. The decanted organozinc halide solution was added dropwise to this solution. The reaction mixture was warmed to 55-60 °C, stirred for 4 h, quenched with H_2O, and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc) to yield 277 mg (86%) of **9a** as a colorless, solid ~1 : 1 mixture of diastereomers.



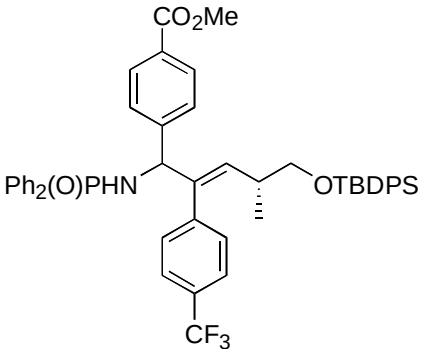
***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(4-methoxyphenyl)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P,P*-diphenylphosphinamide (9b).** According to the General Protocol A, 19.5 mg (460 μmol) of LiCl, 9.0 mg (7.79 μmol) of $Pd(PPh_3)_4$, 39.0 mg (394 μmol) of CuCl, 57.0 mg (58.3 μmol) of **6a**, 22.2 mg (94.9 μmol) of 2-iodoanisole in DMSO (2.00 mL) (microwave irradiation at 60 °C for 20 min, and at 120 °C for an additional 20 min) afforded 29.6 mg (64%) of **9b** as a colorless, foamy ~ 1 : 1 mixture of diastereomers: IR (neat) 3174, 3071, 2956, 2930, 2857, 1721, 1609, 1510, 1437, 1279, 1246, 1187, 1110, 1019, 824, 744, 725, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94-7.92 (m, 2

H), 7.89-7.80 (m, 3 H), 7.73-7.57 (m, 8 H), 7.52-7.30 (m, 12 H), 7.76 (s, 2 H), 6.72 (s, 1 H), 5.63 (d, 0.5 H, *J* = 10.0 Hz), 5.53 (d, 0.5 H, *J* = 9.9 Hz), 5.08 (t, 0.5 H, *J* = 10.7 Hz), 5.04 (t, 0.5 H, *J* = 10.7 Hz), 3.94 (s, 1.5 H), 3.93 (s, 1.5 H), 3.80 (s, 1.5 H), 3.78 (s, 1.5 H), 3.61 (dd, 0.5 H, *J* = 9.8, 6.6 Hz), 3.53 (dd, 0.5 H, *J* = 9.8, 6.4 Hz), 3.50-3.44 (m, 1 H), 3.32-3.26 (m, 1 H), 2.54-2.50 (m, 0.5 H), 2.43-2.37 (m, 0.5 H), 1.10 (s, 4.5 H), 1.03 (s, 4.5 H), 1.01-0.93 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 158.7 (2C), 147.0, 141.0, 135.5, 134.3, 133.7, 133.1, 132.9, 132.4 (2C), 132.1 (2C), 131.9, 130.6, 130.3, 129.8, 129.6, 129.3, 128.8, 128.5 (2C), 127.7, 127.6, 127.5, 127.2, 113.6, 68.5, 68.4, 68.3, 61.5, 61.0, 55.1, 52.0, 35.9, 26.8, 19.2, 17.4; EIMS *m/z* 736 ([M-C_4H_9]$^+$, 37), 706 (42), 630 (100), 537 (42), 398 (23), 364 (27), 218 (18), 201 (63), 183 (12), 135 (25); HRMS (EI) *m/z* calcd for $C_{45}H_{43}NO_5PSi$ (M-C_4H_9) 736.2648, found 736.2684.

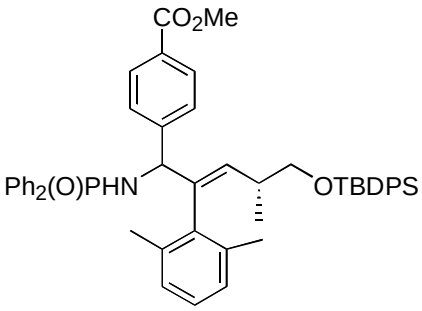


***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(4-chlorophenyl)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P,P*-diphenylphosphinamide (9c).** According to the General Protocol A, 20.8 mg (491 μmol) of LiCl, 9.2 mg (8.0 μmol) of $Pd(PPh_3)_4$, 40.7 mg (411 μmol) of CuCl, 60.0 mg (61.4 μmol) of **6a**, 22.0 mg (92.1 μmol) of 4-chloroiodobenzene in DMSO (2.00 mL) (microwave irradiation at 120 °C for 20 min) afforded 38.7 mg (79%) of **9c** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3309, 3185, 3071, 2957, 2930, 2894, 2857, 1722, 1610, 1489, 1437, 1281, 1192, 1110, 1018, 825, 755, 725, 702 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, 1 H, *J* = 7.5 Hz), 7.89 (d, 1 H, *J* = 7.1 Hz), 7.87-7.75 (m, 4 H), 7.64 (d, 1 H, *J* = 7.9 Hz), 7.63 (d, 1 H, *J* = 7.9 Hz), 7.57 (t, 2 H, *J* = 6.8 Hz), 7.50-7.45 (m, 2 H), 7.44-7.31 (m, 12 H), 7.16 (d, 1 H, *J* = 7.9 Hz), 7.11 (d, 1 H, *J* = 7.6 Hz), 6.75 (d, 1 H, *J* = 8.0 Hz), 6.70 (d, 1 H, *J* = 7.7 Hz), 5.69 (d, 0.5 H, *J* = 10.0 Hz), 5.54 (d, 0.5 H, *J* = 9.8 Hz), 5.05-5.02 (m, 1 H), 3.91 (s, 1.5 H), 3.90 (s, 1.5 H), 3.56 (dd, 0.5 H, *J* = 12.9, 6.7 Hz), 3.52 (dd, 0.5 H, *J* = 9.6, 6.0 Hz), 3.44 (d, 1 H, *J* = 6.1 Hz), 3.25 (b, 1 H), 2.46-2.37 (m, 0.5 H), 2.34-2.26 (m, 0.5 H), 1.07 (s, 4.5 H), 1.00 (s, 4.5 H), 0.97 (d, 1.5 H, *J* = 6.6 Hz), 0.94 (d, 1.5 H, *J* = 6.3 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8 (2C), 146.4, 140.6, 136.4, 135.8, 135.6, 135.5 (3C), 134.7, 133.7, 133.6 (2C), 133.5, 133.3, 133.2, 132.4, 132.3 (2C), 132.2, 132.1, 132.0, 131.9, 130.8, 130.5, 129.8, 129.7 (2C),

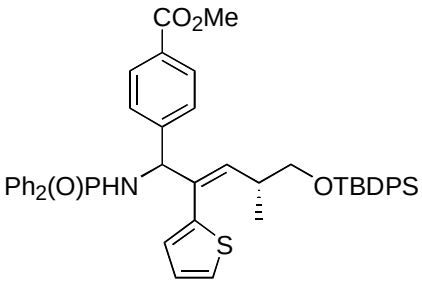
129.6, 129.2, 129.1, 128.6, 128.5 (2C), 128.4 (2C), 127.7, 127.6, 127.5, 127.1, 68.5, 68.3, 61.2, 60.7, 52.0, 36.0, 35.9, 26.9, 26.8, 19.2 (2C), 17.3, 17.2; HRMS (ESI) *m/z* calcd for $C_{48}H_{49}ClNO_4PSiNa$ (M+Na) 820.2755, found 820.2776.



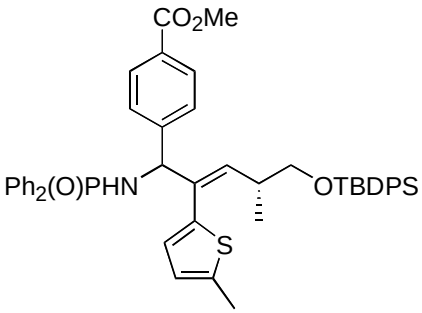
***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(4-trifluoromethylphenyl)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9d).** According to the General Protocol A, 12.6 mg (297 μmol) of LiCl, 5.7 mg (4.9 μmol) of $Pd(PPh_3)_4$, 24.4 mg (246 μmol) of CuCl, 36.0 mg (36.9 μmol) of **6a**, 13.3 mg (48.9 μmol) of 4-trifluoromethyliodobenzene in DMSO (2.00 mL) (microwave irradiation at 60 °C for 20 min and at 120 °C for an additional 40 min) afforded 23.5 mg (77%) of **9d** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3391, 3217, 3072, 2957, 2931, 2895, 2858, 1722, 1612, 1438, 1324, 1282, 1191, 1167, 1110, 1067, 1019, 910, 824, 729, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, 1 H, *J* = 8.3 Hz), 7.90 (d, 1 H, *J* = 8.2 Hz), 7.85-7.76 (m, 4 H), 7.64 (d, 1 H, *J* = 5.9 Hz), 7.63 (d, 1 H, *J* = 6.3 Hz), 7.57 (t, 2 H, *J* = 6.5 Hz), 7.51-7.31 (m, 16 H), 6.96 (d, 1 H, *J* = 8.0 Hz), 6.89 (d, 1 H, *J* = 8.0 Hz), 5.76 (d, 0.5 H, *J* = 10.1 Hz), 5.57 (d, 0.5 H, *J* = 10.2 Hz), 5.10 (t, 0.5 H, *J* = 10.7 Hz), 5.05 (t, 0.5 H, *J* = 11.0 Hz), 3.92 (s, 1.5 H), 3.90 (s, 1.5 H), 3.59-3.53 (m, 1 H), 3.48-3.42 (m, 1 H), 3.28-3.23 (m, 1 H), 2.41-2.36 (m, 0.5 H), 2.30-2.24 (m, 0.5 H), 1.08 (s, 4.5 H), 1.01 (s, 4.5 H), 0.97 (d, 1.5 H, *J* = 6.3 Hz), 0.94 (d, 1.5 H, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 146.2, 142.1, 141.4, 140.6, 135.6, 135.5, 135.0, 134.1, 133.5, 132.7, 132.6, 132.5, 132.4, 132.3, 132.1, 131.9, 131.7, 131.6, 131.5, 131.4, 129.9, 129.8 (2C), 129.7, 129.5, 129.3, 129.2, 128.6, 128.5 (2C), 127.7, 127.6, 127.5, 126.1 (q, *J* = 261 Hz), 68.4, 68.2, 61.1, 60.5, 52.1, 36.0 (2C), 26.9, 19.2, 17.3, 17.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –61.28 (s), –61.29 (s); HRMS (ESI) *m/z* calcd for $C_{49}H_{49}F_3NO_4PSiNa$ (M+Na) 854.2947, found 854.2957.



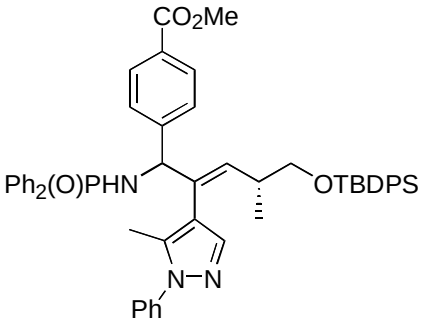
***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(2,6-dimethylphenyl)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9e).** According to the General Protocol A, 22.7 mg (536 μmol) of LiCl, 10.3 mg (8.9 μmol) of $Pd(PPh_3)_4$, 44.0 mg (444 μmol) of CuCl, 65.0 mg (66.5 μmol) of **6a**, 23.0 mg (99.1 μmol) of 2,6-dimethyliodobenzene in DMSO (2.00 mL) (microwave irradiation at 60 °C for 100 min and at 100 °C for an additional 60 min) afforded 26.6 mg (51%) of **9e** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3319, 3195, 3055, 2956, 2929, 2857, 1723, 1610, 1471, 1437, 1280, 1190, 1110, 1021, 824, 754, 725, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04-7.78 (m, 4 H), 7.75-7.08 (m, 22 H), 7.05 (d, 0.5 H, *J* = 7.4 Hz), 6.91 (d, 0.5 H, *J* = 7.2 Hz), 5.61 (d, 0.5 H, *J* = 9.5 Hz), 5.42 (d, 0.5 H, *J* = 9.5 Hz), 5.00-4.80 (bm, 1 H), 3.95 (s, 1.5 H), 3.94 (s, 1.5 H), 3.61-3.35 (m, 3 H), 2.45-2.38 (m, 0.5 H), 2.23 (s, 1.5 H), 2.15-2.08 (m, 0.5 H), 2.12 (s, 1.5 H), 1.92 (s, 1.5 H), 1.59 (s, 1.5 H), 1.05 (s, 1 H), 1.03 (s, 1 H), 1.01 (s, 3.5 H), 0.99 (s, 3.5 H), 0.95 (d, 1.5 H, *J* = 6.5 Hz), 0.88 (d, 1.5 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 147.8, 147.0, 140.3, 140.1, 137.3, 137.2, 136.2, 136.1, 135.5, 135.4, 133.7, 133.6, 133.5, 133.4, 133.3, 132.2, 132.0, 131.8, 129.8, 129.6, 129.0, 128.9, 128.8, 128.4, 127.9, 127.2, 68.2, 67.8, 67.6, 59.9, 59.7, 52.0, 39.0, 38.9, 36.4, 36.3, 29.7, 26.7 (2C), 20.5, 20.4, 19.9, 19.7, 19.1, 16.6, 16.4 (2C); EIMS *m/z* 791 (M^+, 26), 734 (100), 630 (28), 590 (15), 535 (13), 364 (97), 218 (22), 201 (92), 135 (35); HRMS (EI) *m/z* calcd for $C_{50}H_{54}NO_4PSi$ 791.3560, found 791.3500.



***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(2-thiophene)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9f).** According to the General Protocol A, 19.4 mg (458 μmol) of LiCl, 8.8 mg (7.6 μmol) of $Pd(PPh_3)_4$, 37.6 mg (380 μmol) of CuCl, 55.5 mg (56.8 μmol) of **6a**, 18.1 mg (86.2 μmol) of 2-iodothiophene in DMSO (2.00 mL) (microwave irradiation at 60 °C for 20 min, at 100 °C for 20 min and at 120 °C for an additional 40 min) afforded 36.0 mg (82%) of **9f** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3276, 3071, 2956, 2929, 2857, 1722, 1610, 1590, 1437, 1311, 1281, 1191, 1111, 1020, 824, 754, 726, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00-7.78 (m, 6 H), 7.70-7.68 (m, 2 H), 7.65-7.55 (m, 3 H), 7.51-7.31 (m, 13 H), 7.21 (d, 0.5 H, *J* = 5.0 Hz), 7.17 (d, 0.5 H, *J* = 5.0 Hz), 6.91 (dd, 0.5 H, *J* = 4.9, 3.4 Hz), 6.87 (dd, 0.5 H, *J* = 4.9, 3.5 Hz), 6.57 (d, 0.5 H, *J* = 2.9 Hz), 6.51 (d, 0.5 H, *J* = 3.0 Hz), 5.63 (d, 0.5 H, *J* = 10.2 Hz), 5.60 (d, 0.5 H, *J* = 10.1 Hz), 5.12-5.05 (m, 1 H), 3.91 (s, 1.5 H), 3.90 (s, 1.5 H), 3.61 (dd, 0.5 H, *J* = 9.8, 6.0 Hz), 3.52-3.46 (m, 1.5 H), 3.46-3.37 (m, 0.5 H), 3.37-3.30 (m, 0.5 H), 2.82-2.72 (m, 0.5 H), 2.72-2.63 (m, 0.5 H), 1.08 (s, 4.5 H), 1.05 (d, 1.5 H, *J* = 6.5 Hz), 1.04 (d, 1.5 H, *J* = 7.4 Hz), 1.03 (s, 4.5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 146.5, 146.4, 138.1, 137.5, 136.8, 136.6, 135.6, 135.5, 134.1, 133.8, 133.6, 133.5, 133.1, 132.6, 132.5, 132.4, 132.3, 132.0, 131.8 (2C), 131.3, 131.0, 129.6, 129.1, 129.0, 128.5 (2C), 127.7, 127.6, 127.3, 127.1, 126.8, 125.6, 125.5, 68.3, 68.2, 61.5, 61.1, 52.0, 36.3, 27.8, 26.8, 19.2, 17.7, 17.4, 17.3, 13.6; EIMS *m/z* 769 (M^+, 25), 756 (20), 712 (100), 513 (60), 428 (15), 398 (32), 364 (52), 296 (20), 218 (50), 201 (67), 135 (40); HRMS (EI) *m/z* calcd for $C_{42}H_{39}NO_4PSSi$ (M-C_4H_9) 712.2107, found 712.2096.

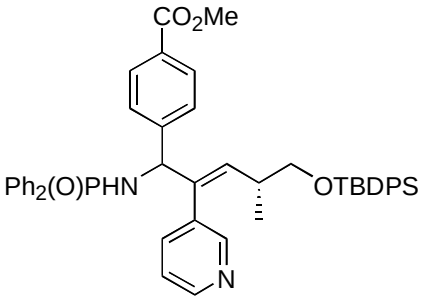


***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(5-methyl-2-thiophene)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9g).** According to the General Protocol A, 20.8 mg (491 μmol) of LiCl, 9.2 mg (8.0 μmol) of $Pd(PPh_3)_4$, 40.7 mg (411 μmol) of CuCl, 60.0 mg (61.4 μmol) of **6a**, 20.6 mg (92.1 μmol) of 5-methyl-2-iodothiophene in DMSO (2.00 mL) (microwave irradiation at 120 °C for 40 min) afforded 27.9 mg (58%) of **9g** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3324, 3185, 3070, 2955, 2930, 2857, 1722, 1610, 1590, 1437, 1311, 1281, 1192, 1111, 1020, 911, 727, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, 2 H, *J* = 8.0 Hz), 7.91 (d, 2 H, *J* = 8.1 Hz), 7.90-7.80 (m, 2 H), 7.76-7.54 (m, 6 H), 7.51-7.31 (m, 12 H), 6.55 (d, 0.5 H, *J* = 2.3 Hz), 6.51 (d, 0.5 H, *J* = 2.3 Hz), 6.37 (d, 0.5 H, *J* = 3.4 Hz), 6.32 (d, 0.5 H, *J* = 3.4 Hz), 5.55 (d, 0.5 H, *J* = 9.7 Hz), 5.54 (d, 0.5 H, *J* = 10.0 Hz), 5.10-5.03 (m, 1 H), 3.90 (s, 3 H), 3.62 (dd, 0.5 H, *J* = 9.7, 5.9 Hz), 3.60-3.40 (m, 2.0 H), 3.40-3.35 (m, 0.5 H), 2.87-2.81 (m, 0.5 H), 2.79-2.72 (m, 0.5 H), 2.39 (s, 1.5 H), 2.37 (s, 1.5 H), 1.09 (s, 4.5 H), 1.07-1.04 (m, 3 H), 1.03 (s, 4.5 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9 (2C), 146.7, 146.6, 140.0, 139.9, 137.5, 136.0, 135.6, 135.6, 135.5 (2C), 135.0, 134.8, 134.5, 134.3, 134.1, 133.7, 133.6 (2C), 133.5, 132.7, 132.6, 132.5, 132.4, 132.1, 132.0, 131.9 (2C), 131.8 (2C), 129.7, 129.6 (2C), 129.5, 129.1, 129.0, 128.5 (3C), 128.4, 128.3, 127.6 (4C), 127.5, 127.4, 127.3, 127.1, 68.4, 68.2, 61.5, 61.1, 51.9, 36.3, 36.2, 26.8 (2C), 19.3, 19.2, 17.5, 17.4, 15.1; HRMS (ESI) *m/z* calcd for $C_{47}H_{50}NO_4PSSiNa$ (M+Na) 806.2865, found 806.2835.



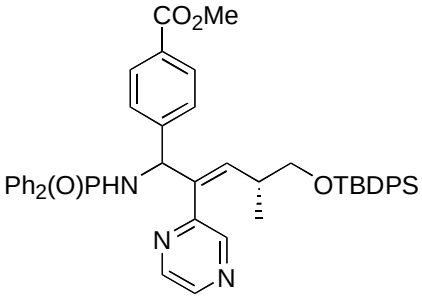
***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(5-methyl-1-phenyl-1*H*-4-pyrazole)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9h).** According to the

General Protocol A, 20.8 mg (491 μmol) of LiCl, 9.2 mg (8.0 μmol) of $Pd(PPh_3)_4$, 40.7 mg (411 μmol) of CuCl, 60.0 mg (61.4 μmol) of **6a**, 26.2 mg (92.1 μmol) of 4-iodo-5-methyl-1-phenyl-1*H*-pyrazole in DMSO (2.00 mL) (microwave irradiation at 120 °C for 20 min) afforded 31.4 mg (61%) of **9h** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3329, 3193, 3070, 2956, 2929, 2857, 1721, 1610, 1501, 1437, 1387, 1280, 1192, 1110, 741, 725, 700 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.93-7.82 (m, 8 H), 7.68-7.58 (m, 5 H), 7.48-7.32 (m, 16 H), 7.05 (s, 0.5 H), 6.97 (s, 0.5 H), 5.81 (d, 0.5 H, *J* = 9.4 Hz), 5.76 (d, 0.5 H, *J* = 9.6 Hz), 5.03 (t, 0.5 H, *J* = 10.1 Hz), 4.95 (t, 0.5 H, *J* = 10.7 Hz), 3.91 (s, 1.5 H), 3.91 (s, 1.5 H), 3.60 (dd, 0.5 H, *J* = 9.7, 5.8 Hz), 3.53 (dd, 0.5 H, *J* = 9.5, 6.6 Hz), 3.47 (d, 1 H, *J* = 5.7 Hz), 3.47-3.40 (m, 0.5 H), 3.40-3.35 (m, 0.5 H), 2.45-2.37 (m, 0.5 H), 2.37-2.30 (m, 0.5 H), 1.75 (s, 1.5 H), 1.73 (s, 1.5 H), 1.07 (s, 4.5 H), 1.06 (d, 1.5 H, *J* = 6.5 Hz), 1.02 (s, 4.5 H), 1.01 (d, 1.5 H, *J* = 5.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8 (2C), 146.8, 139.8, 139.7, 139.5, 137.3, 136.9, 136.5, 135.6, 135.5 (2C), 135.4, 133.6 (2C), 133.5 (2C), 132.4, 132.3, 132.2 (2C), 132.0, 131.9 (2C), 129.7 (2C), 129.6 (3C), 129.1, 129.0, 128.5 (5C), 128.4, 127.7 (2C), 127.6, 127.3, 127.0, 124.6 (2C), 68.2, 61.3, 60.9, 52.0, 36.4 (2C), 26.9, 26.8, 19.3, 19.2, 17.3, 17.1, 10.9, 10.8; HRMS (ESI) *m/z* calcd for $C_{52}H_{55}N_3O_4PSi$ (M+H) 844.3699, found 844.3702.

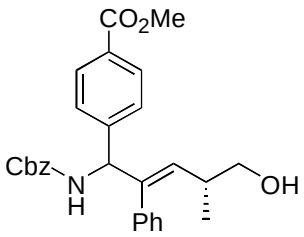


***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-(3-pyridine)-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*E*)-enyl]-*P*,*P*-diphenylphosphinamide (9i).** According to the General Protocol A, 5.0 mg (118 μmol) of LiCl, 2.2 mg (1.9 μmol) of $Pd(PPh_3)_4$, 9.8 mg (99.0 μmol) of CuCl, 14.5 mg (14.8 μmol) of **6a**, 4.6 mg (22.4 μmol) of 3-iodopyridine in DMSO (2.00 mL) (microwave irradiation at 120 °C for 30 min) afforded (from 1 : 1, hexanes/EtOAc to 1 : 20, MeOH/$CHCl_3$) 8.3 mg (72%) of **9i** as a colorless, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3385, 3181, 3055, 2958, 2930, 2857, 1721, 1610, 1437, 1281, 1190, 1111, 753, 724, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, 1 H, *J* = 7.6 Hz), 7.88 (d, 1 H, *J* = 7.7 Hz), 7.85-7.75 (m, 2 H), 7.68-7.53 (m, 8 H), 7.50-7.31 (m, 16 H), 5.83 (d, 0.5 H, *J* = 9.1 Hz), 5.68 (d, 0.5 H, *J* = 9.1 Hz), 5.10 (t, 0.5 H, *J* = 9.1 Hz), 5.00 (t, 0.5 H, *J* = 9.5 Hz), 3.90 (s, 1.5 H), 3.89 (s, 1.5 H), 3.60-3.30 (m, 3 H), 2.40-2.30 (m, 0.5 H), 2.30-2.20 (m, 0.5 H), 1.06 (s, 4.5 H), 1.00 (s, 4.5 H), 1.00-0.96 (m, 1.5 H), 0.95-0.91 (m, 1.5 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6 (2C),

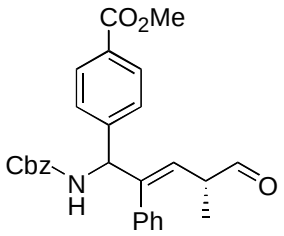
145.9, 145.8, 135.5 (2C), 135.4 (2C), 133.5, 133.4 (3C), 132.8, 132.5, 132.4, 132.3, 132.2, 132.0 (2C), 131.9 (2C), 131.6, 131.5, 129.9, 129.8, 129.7, 129.6, 129.3 (2C), 128.8, 128.7, 128.6, 128.5 (2C), 128.4, 127.7, 127.6 (2C), 127.5, 127.1, 68.4, 68.2, 61.3, 60.7, 52.0, 36.0, 35.9, 26.8 (2C), 19.2 (2C), 17.3; HRMS (ESI) *m/z* calcd for $C_{47}H_{50}N_2O_4PSi$ (M+H) 765.3278, found 765.3264.



***N*-[5-(*tert*-Butyldiphenylsilanyloxy)-2-pyrazine-(4*R*)-methyl-(1*SR*)-(methyl-4-formylbenzoic)pent-(2*Z*)-enyl]-*P*,*P*-diphenylphosphinamide (9j).** According to the General Protocol A, 35.1 mg (828 μmol) of LiCl, 13.5 mg (11.7 μmol) of $Pd(PPh_3)_4$, 60.8 mg (614 μmol) of CuCl, 90.0 mg (92.1 μmol) of **6a**, 28.4 mg (139 μmol) of iodopyrazine in DMSO (3.00 mL) (microwave irradiation at 120 °C for 20 min) afforded (from 1 : 1, hexanes/EtOAc to 1 : 20, MeOH/$CHCl_3$) 67.0 mg (95%) of **9j** as a yellowish, foamy ~1 : 1 mixture of diastereomers: IR (neat) 3367, 3180, 3055, 2961, 2930, 2858, 1721, 1610, 1437, 1280, 1191, 1118, 747, 722, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.92-7.34 (m, 27 H), 5.73 (d, 1 H, *J* = 10.7 Hz), 5.33-5.25 (m, 1 H), 3.83 (s, 1.5 H), 3.82 (s, 1.5 H), 3.63 (dd, 1 H, *J* = 9.9, 5.0 Hz), 3.54-3.45 (m, 2 H), 2.81-2.70 (m, 0.5 H), 2.65-2.56 (m, 0.5 H), 1.06 (s, 4.5 H), 1.04 (m, 1.5 H), 1.01 (s, 4.5 H), 0.85 (d, 1.5 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 152.7, 152.4, 146.8, 146.4, 145.6, 143.4, 143.0, 142.9, 142.7, 139.7, 137.8, 137.0, 136.3, 135.4, 133.6, 133.4, 133.2, 133.1, 133.0, 132.8, 132.6, 132.3 (2C), 132.1, 132.0, 131.9, 131.8, 131.7, 129.7, 129.6, 129.5, 129.3, 128.7, 128.4, 128.3, 127.7, 127.6, 126.9, 126.6, 68.3, 68.2, 61.6, 60.5, 51.8, 36.0, 35.8, 26.7, 19.0, 17.2, 16.9; HRMS (ESI) *m/z* calcd for $C_{46}H_{49}N_3O_4PSi$ (M+H) 766.3230, found 766.3272.

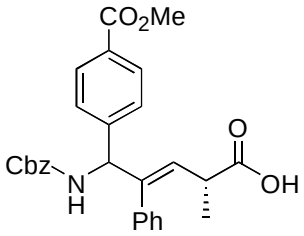


[(1*S*,*R*)-Benzyloxycarbonylamino-5-hydroxy-(4*R*)-methyl-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (10). A solution of 326 mg (0.427 mmol) of **9a** in 22.0 mL of 1 N HCl (g) in MeOH was stirred at room temperature overnight, basified with 5% NaOH to pH > 12, and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*, dissolved in 4.00 mL of EtOAc and 4.00 mL of H_2O, and treated with 179 mg (2.13 mmol) of $NaHCO_3$. After 15 min, the mixture was treated at 0 °C with 73.4 μL (0.512 mmol) of CbzCl. The reaction mixture was stirred at 0 °C for 2 h, diluted with EtOAc and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc) to yield 154 mg (79%) of **10** as a colorless, solid ~ 1 : 1 mixture of diastereomers: Mp 51-53 °C (ether); IR (neat) 3483, 3432, 3343, 3032, 2954, 2925, 2871, 1721, 1611, 1522, 1437, 1282, 1114, 1041, 735, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, 2 H, *J* = 8.3 Hz), 7.35-7.21 (m, 10 H), 6.95-6.84 (m, 2 H), 5.63-5.51 (m, 2 H), 5.25-5.08 (m, 3 H), 3.92 (s, 3 H), 3.48-3.30 (m, 2 H), 2.40-2.31 (m, 1 H), 1.61 (b, 1 H), 0.96 (d, 1.5 H, *J* = 6.7 Hz), 0.88 (d, 1.5 H, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 155.5, 145.1, 141.5, 140.8, 137.9, 137.0, 136.2, 136.1, 133.7, 132.6, 129.7 (2C), 129.2, 129.1, 128.8, 128.4, 128.2, 128.1, 127.3, 127.1, 126.9, 67.3, 66.9, 61.4, 61.2, 52.0, 35.9, 16.8; EIMS *m/z* 428 ($[M\text{-}CH_3O]^+$, 0.5), 306 (2.2), 278 (17), 219 (10), 164 (9), 128 (8), 105 (8), 91 (100), 77 (10), 65 (7); HRMS (EI) *m/z* calcd for $C_{27}H_{26}NO_4$ (M-CH_3O) 428.1862, found 428.1869.

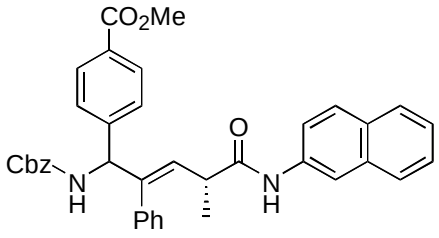


[(1*S*,*R*)-Benzyloxycarbonylamino-(4*R*)-methyl-5-oxo-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (10a). A solution of 140 mg (0.305 mmol) of **10** in 12.0 mL of CH_2Cl_2 was treated at 0 °C with 155 mg (0.365 mmol) of Dess-Martin Periodinane. The reaction mixture was stirred at 0 °C for 1.5 h, quenched with a saturated $Na_2S_2O_3/NaHCO_3$ solution, stirred for 30 min at room temperature, and extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and purified by chromatography on SiO_2 (2 : 1, hexanes/EtOAc) to yield 121 mg (87%) of **10a** as a light yellow, foamy ~ 1 : 1 mixture of diastereomers: IR (neat) 3426, 3345, 3058, 3032, 2952, 2817, 1717, 1521, 1506, 1455, 1436, 1282, 1232, 1191, 1114, 1049, 1020, 913, 735, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.57 (s, 0.5 H), 9.45 (s, 0.5 H), 8.00-7.96 (m, 2 H), 7.35-7.20 (m, 10 H), 6.89 (b, 2 H), 5.70-5.60 (m, 1 H), 5.64 (dd, 1 H, *J* = 12.3, 9.5 Hz) 5.18-5.12 (m, 3 H), 3.92 (s, 1.5 H), 3.91 (s, 1.5 H), 3.08-

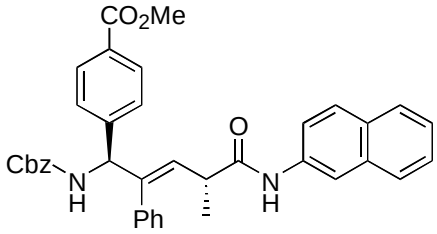
2.95 (m, 1 H), 1.17 (d, 1.5 H, *J* = 7.0 Hz), 1.12 (d, 1.5 H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5, 201.0, 166.7, 166.6, 155.3, 155.2, 144.6, 144.4, 144.3, 136.8, 136.6, 136.1, 129.9 (2C), 129.5 (2C), 128.7, 128.5 (2C), 128.2, 128.1, 127.9, 127.8, 127.3, 127.0, 126.5, 125.6, 67.0, 61.1, 52.1, 46.8, 46.7, 14.2, 14.1; EIMS *m/z* 426 ([M-CH_3O]$^+$, 1), 384 (0.6), 298 (7), 278 (27), 264 (8), 254 (17), 219 (14), 178 (5), 159 (12), 129 (7), 115 (13), 91 (100), 77 (18), 65 (20); HRMS (EI) *m/z* calcd for $C_{27}H_{24}NO_4$ (M-CH_3O) 426.1705, found 426.1685.



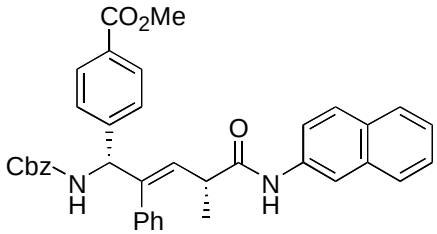
[(1*SR*)-Benzyloxycarbonylamino-(4*R*)-carboxy-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (10b). A solution of 114 mg (0.249 mmol) of **10a** in 6.50 mL of THF was treated at 0 °C with 2.50 mL (5.00 mmol) of 2-methyl-2-butene (2.0 M solution in THF) followed by a solution of 67.4 mg (0.745 mmol) of $NaClO_2$ and 68.4 mg (0.496 mmol) of NaH_2PO_4•H_2O in 6.50 mL of H_2O. The reaction mixture was stirred at 0 °C for 4 h, extracted with EtOAc, and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (from 1 : 1, hexanes/EtOAc to 5 : 95, MeOH/CH_2Cl_2) to yield 106 mg (90%) of **10b** as a colorless, solid ~ 1 : 1 mixture of diastereomers: Mp 63-65 °C (ether); IR (neat) 3337, 3037, 2953, 2894, 1721, 1611, 1518, 1455, 1282, 1252, 1226, 1115, 1047, 842, 761, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (b, 1 H), 8.00-7.94 (m, 2 H), 7.35-7.23 (m, 10 H), 6.93 (b, 2 H), 5.90 (bd, 0.5 H, *J* = 9.2 Hz), 5.79 (bd, 0.5 H, *J* = 9.0 Hz), 5.69 (b, 1 H), 5.30-5.20 (m, 1 H), 5.14 (s, 1 H), 5.09 (s, 1 H), 3.92 (s, 1.5 H), 3.90 (s, 1.5 H), 3.15-3.00 (m, 1 H), 1.30-1.15 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 179.5, 166.8, 155.5, 145.0, 144.7, 142.3, 142.1, 136.8, 136.2, 129.9, 129.5, 129.4, 129.2, 128.9 (2C), 128.5, 128.2, 128.1, 127.8, 127.7, 127.6, 127.4, 127.0, 67.2, 61.0, 52.1, 39.3, 18.0, 17.9; EIMS *m/z* 473 (M$^+$, 0.14), 442 (0.4), 382 (1.2), 254 (9), 219 (7), 191 (18), 176 (6), 147 (17), 129 (11), 108 (14), 91 (100), 77 (19); HRMS (EI) *m/z* calcd for $C_{28}H_{27}NO_6$ 473.1838, found 473.1824.



[(1*S*,*R*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (11+12). A solution of 49.8 mg (0.105 mmol) of **10b** in 1.50 mL of CH_2Cl_2 was treated at room temperature with 12.8 mg (0.105 mmol) of DMAP, 21.1 mg (0.110 mmol) of EDCI and 18.0 mg (0.126 mmol) of 2-aminonaphthalene. The reaction mixture was stirred at room temperature for 5 h, diluted with CH_2Cl_2, and washed with H_2O. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (20 : 1, CH_2Cl_2/Et_2O) to yield 52.9 mg (84%) of **11** (less polar) and **12** (more polar) as colorless solids (**11** : **12** = ~ 1 : 1).

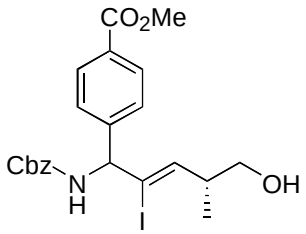


[(1*S*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (11, less polar): colorless solid; Mp 77-79 °C (ether/hexane); $[\alpha]^{25}_D$ -72.9 (*c* 2.2, CH_2Cl_2); IR (neat) 3327, 3053, 3029, 2950, 2929, 2848, 1705, 1534, 1501, 1434, 1282, 1231, 1115, 753, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 8.05 (s, 1 H), 7.99 (d, 2 H, *J* = 8.3 Hz), 7.83-7.71 (m, 4 H), 7.50-7.35 (m, 2 H), 7.34 (d, 2 H, *J* = 8.2 Hz), 7.27 (s, 8 H), 7.10-7.05 (m, 2 H), 5.95 (d, 1 H, *J* = 10.3 Hz), 5.52 (d, 1 H, *J* = 5.3 Hz), 5.36 (bd, 1 H, *J* = 4.8 Hz), 5.15, 5.09 (AB, 2 H, *J* = 12.1 Hz), 3.92 (s, 3 H), 3.30-3.15 (m, 1 H), 1.42 (d, 3 H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 166.5, 155.9, 144.1, 142.9, 137.3, 136.0, 135.9, 133.9, 130.5, 130.2, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 127.7, 127.5, 126.7, 126.3, 124.8, 120.0, 116.2, 67.4, 62.1, 52.2, 41.0, 17.2; EIMS *m/z* 598 (M^+, 1.9), 490 (2.3), 447 (1.9), 300 (6), 278 (8), 219 (12), 169 (10), 143 (30), 129 (12), 115 (21), 91 (100), 69 (22); HRMS (EI) *m/z* calcd for $C_{38}H_{34}N_2O_5$ 598.2468, found 598.2463.

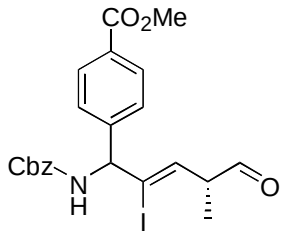


[(1*R*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-phenylpent-(2*E*)-enyl]benzoic acid methyl ester (12, more polar): colorless solid; Mp 83-85 °C (ether); $[\alpha]^{25}_D$ -126.1 (*c* 0.36, CH_2Cl_2); IR (neat) 3326, 3056, 2926, 2850, 1719, 1534, 1501, 1434, 1282, 1231, 1115, 1050, 733, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35 (s, 1 H), 8.02 (s, 1 H), 7.98 (d, 2 H, *J* = 8.4 Hz), 7.82-7.78

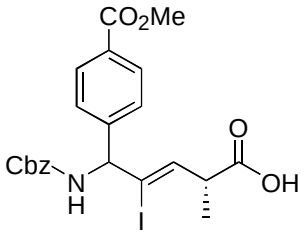
(m, 3 H), 7.65 (bd, 1 H, *J* = 7.4 Hz), 7.50-7.35 (m, 2 H), 7.33 (s, 4 H), 7.28-7.22 (m, 6 H), 6.79 (d, 2 H, *J* = 6.8 Hz), 6.08 (d, 1 H, *J* = 10.1 Hz), 5.62 (d, 1 H, *J* = 6.7 Hz), 5.29 (bd, 1 H, *J* = 5.2 Hz), 5.19 (s, 2 H), 3.92 (s, 3 H), 3.05-2.99 (m, 1 H), 1.32 (d, 3 H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 166.6, 155.9, 143.5, 143.4, 136.1, 135.8, 133.9, 130.9, 130.7, 130.0, 129.9, 129.1, 128.6, 128.4, 128.2, 128.0, 127.7, 127.5, 126.9, 126.4, 124.9, 120.0, 116.7, 67.2, 62.6, 52.2, 41.8, 17.7; EIMS *m/z* 598 (M^+, 1.2), 537 (0.3), 490 (2.7), 459 (8), 305 (9), 278 (6), 245 (4), 210 (25), 169 (15), 143 (50), 108 (31), 91 (100), 79 (35); HRMS (EI) *m/z* calcd for $C_{38}H_{34}N_2O_5$ 598.2468, found 598.2472.



[(1*S*,*R*)-Benzyloxycarbonylamino-5-hydroxy-2-iodo-(4*R*)-methylpent-(2*Z*)-enyl]benzoic acid methyl ester (13). A solution of 347 mg (0.426 mmol) of **7** in 18.0 mL of 1 N HCl (g) in MeOH was stirred overnight at 0 °C, basified with 5% NaOH to pH > 12, and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, dissolved in 8.40 mL of EtOAc and 8.40 mL of H_2O, and treated with 179 mg (2.13 mmol) of $NaHCO_3$. After 15 min, the reaction mixture was treated at 0 °C with 79.6 μL (0.555 mmol) of CbzCl, stirred at 0 °C for 2 h, diluted with EtOAc and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (2 : 1, hexanes/EtOAc) to yield 152 mg (70 %) of **13** as a colorless, foamy ~ 1 : 1 mixture of diastereomers: IR (neat) 3418, 3334, 3033, 2953, 2872, 1708, 1522, 1284, 1239, 1113, 1041, 734, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, 2 H, *J* = 8.4, 2.3 Hz), 7.40-7.36 (m, 7 H), 5.97 (d, 0.5 H, *J* = 8.7 Hz), 5.89 (d, 0.5 H, *J* = 8.7 Hz), 5.54-5.51 (m, 1 H), 5.46 (bd, 0.5 H, *J* = 8.3 Hz), 5.38 (d, 0.5 H, *J* = 8.5 Hz), 5.17, 5.14 (AB, 2 H, *J* = 12.3 Hz), 3.92 (s, 3 H), 3.65-3.50 (m, 2 H), 2.80-2.70 (m, 1 H), 1.74 (b, 1 H), 1.07 (d, 1.5 H, *J* = 6.2 Hz), 1.05 (d, 1.5 H, *J* = 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 155.4, 155.3, 144.2, 144.0, 141.6, 141.2, 136.1, 136.0, 129.9, 129.7 (2C), 128.5, 128.3, 128.2, 128.1, 126.9, 126.7, 109.7, 109.3, 67.3, 67.2, 66.4, 66.3, 63.9, 63.5, 52.1, 43.5, 43.4, 15.5 (2C); EIMS *m/z* 479 ($[M\text{-}CH_2O]^+$, 2.1), 382 (1.3), 338 (13), 261 (10), 231 (5), 201 (6), 157 (5), 142 (8), 128 (7), 115 (8), 91 (100), 77 (6); HRMS (EI) *m/z* calcd for $C_{21}H_{22}INO_4$ (M-CH_2O) 479.0594, found 479.0579.

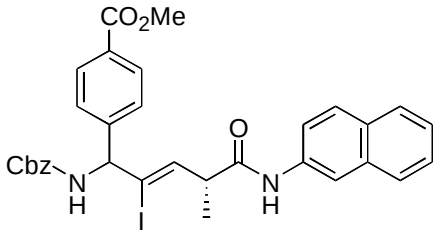


[(1*S*,*R*)-Benzyloxycarbonylamino-2-iodo-(4*R*)-methyl-5-oxopent-(2*Z*)-enyl]benzoic acid methyl ester (13a). A solution of 165 mg (0.324 mmol) of **13** in 7.00 mL of CH_2Cl_2 was treated at 0 °C with 206 mg (0.486 mmol) of Dess-Martin Periodinane. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 6 h, quenched with saturated $Na_2S_2O_3$/$NaHCO_3$ solution, stirred for 30 min at room temperature, and extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo*, and purified by chromatography on SiO_2 (2 : 1, hexanes/EtOAc) to yield 151 mg (92 %) of **13a** as a yellow, foamy ~ 1 : 1 mixture of diastereomers: IR (neat) 3334, 3033, 2952, 1723, 1611, 1519, 1436, 1283, 1233, 1113, 1050, 765, 736, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.63 (s, 1 H), 8.03 (d, 2 H, *J* = 8.4 Hz), 7.41-7.36 (m, 7 H), 6.12-6.08 (m, 1 H), 5.54 (b, 2 H), 5.17, 5.14 (AB, 2 H, *J* = 12.6 Hz), 3.91 (s, 3 H), 3.50-3.40 (m, 1 H), 1.29-1.26 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.4, 166.6, 155.1, 155.0, 143.6, 136.0, 135.2, 134.6, 130.1, 130.0 (2C), 128.6, 128.3, 128.2, 126.9, 126.8, 113.6, 113.3, 67.4, 63.6, 53.5 (2C), 52.1, 13.1; EIMS *m/z* 476 ($[M-CH_3O]^+$, 3), 416 (10), 380 (6), 322 (15), 272 (18), 260 (23), 229 (46), 216 (19), 202 (17), 196 (27), 190 (32), 164 (72), 141 (78), 128 (100), 115 (95); HRMS (EI) *m/z* calcd for $C_{21}H_{19}INO_4$ (M-CH_3O) 476.0359, found 476.0362.

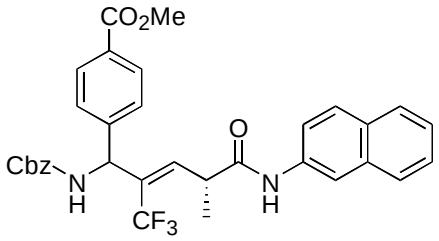


[(1*S*,*R*)-Benzyloxycarbonylamino-(4*R*)-carboxy-2-iodopent-(2*Z*)-enyl]benzoic acid methyl ester (13b). A solution of 150 mg (0.296 mmol) of **13a** in 8.00 mL of THF was treated at 0 °C with 4.00 mL (8.00 mmol) of 2-methyl-2-butene (2.0 M solution in THF) followed by a solution of 80.2 mg (0.887 mmol) of $NaClO_2$ and 81.7 mg (0.592 mmol) of NaH_2PO_4•H_2O in 8.00 mL of H_2O. The reaction mixture was stirred at 0 °C for 3 h and at room temperature for 4 h, extracted with EtOAc, and washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (1 : 1, hexanes/EtOAc to 1 : 10, MeOH/CH_2Cl_2) to yield 147 mg (95%) of **13b** as a colorless, solid ~ 1 : 1 mixture of diastereomers: Mp 55-57 °C (ether); IR (neat) 3323, 3033, 2976, 2952, 1715, 1520, 1284, 1236, 1192, 1050, 912, 733, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)

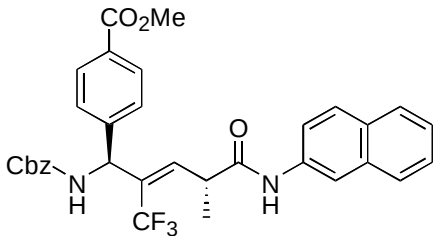
δ 10.31 (b, 1 H), 8.03 (d, 2 H, *J* = 7.4 Hz), 7.41-7.36 (m, 7 H), 6.30-6.23 (m, 1 H), 5.55-5.53 (b, 2 H), 5.22-5.12 (m, 2 H), 3.92 (s, 1.5 H), 3.91 (s, 1.5 H), 3.55-3.45 (m, 1 H), 1.38-1.27 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.6, 166.7, 155.2, 143.8, 137.2, 137.1, 135.9, 130.1, 130.0, 129.9, 129.8, 128.6, 128.4, 128.3, 127.0, 126.7, 67.5, 63.3, 52.2, 46.6, 17.0 (2C); EIMS *m/z* 492 ([M-CH_3O]$^+$, 1.7), 396 (3.3), 352 (5.5), 278 (1.7), 196 (7), 128 (11), 108 (7), 91 (100), 77 (9); HRMS (EI) *m/z* calcd for $C_{21}H_{19}INO_5Si$ (M-CH_3O) 492.0308, found 492.0315.



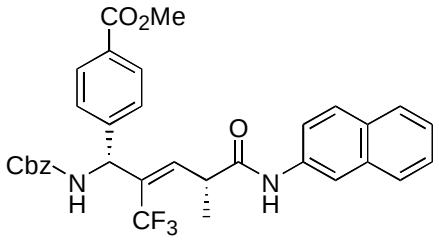
[(1*S*,*R*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-iodopent-(2*Z*)-enyl]benzoic acid methyl ester (14). A solution of 138 mg (0.264 mmol) of **13b** in 4.00 mL of CH_2Cl_2 was treated at room temperature with 32.3 mg (0.264 mmol) of DMAP, 53.1 mg (0.277 mmol) of EDCI and 49.1 mg (0.343 mmol) of 2-aminonaphthalene. The reaction mixture was stirred at room temperature for 6 h, diluted with CH_2Cl_2, and washed with H_2O. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (from 4 : 1, CH_2Cl_2/hexanes to 2 : 1, hexanes/EtOAc) to yield 146 mg (85%) of **14** as a light yellow, solid ~ 1 : 1 mixture of diastereomers: Mp 84-85 °C (ether); IR (neat) 3396, 3323, 3063, 3032, 2951, 1702, 1535, 1501, 1434, 1281, 1230, 1192, 1113, 1050, 731, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 0.5 H), 8.30 (s, 0.5 H), 8.25 (s, 0.5 H), 8.08 (s, 0.5 H), 8.04 (d, 1 H, *J* = 6.3 Hz), 8.02 (d, 1 H, *J* = 6.3 Hz), 7.78 (d, 2 H, *J* = 8.2 Hz), 7.75 (d, 1 H, *J* = 5.8 Hz), 7.67 (d, 0.5 H, *J* = 8.6 Hz), 7.60 (d, 0.5 H, *J* = 7.7 Hz), 7.48-7.38 (m, 5 H), 7.32-7.21 (m, 4 H), 6.38 (d, 0.5 H, *J* = 8.9 Hz), 6.24 (d, 0.5 H, *J* = 8.8 Hz), 5.82 (b, 1 H), 5.53 (bd, 0.5 H, *J* = 6.2 Hz), 5.37 (d, 0.5 H, *J* = 7.2 Hz), 5.25-5.11 (m, 2 H), 3.91 (s, 1.5 H), 3.90 (s, 1.5 H), 3.59-3.51 (m, 1 H), 1.46 (d, 1.5 H, *J* = 7.8 Hz), 1.44 (d, 1.5 H, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 166.5 (2C), 155.7, 155.4, 142.7, 142.4, 138.6, 136.2, 135.8, 135.7, 135.5, 133.7, 130.6, 130.1, 130.0, 128.5 (2C), 128.3, 128.1, 127.9, 127.6 (2C), 127.4, 126.7, 126.3, 124.9, 120.2, 120.0, 117.0, 116.7, 114.7, 111.9, 67.4, 67.3, 64.8, 64.0, 52.2, 48.9 (2C), 16.8, 16.7; EIMS *m/z* 648 (M$^+$, 2.3), 540 (1.8), 199 (15), 169 (9), 143 (23), 128 (48), 105 (25), 97 (37), 91 (63), 69 (49), 57 (100); HRMS (EI) *m/z* calcd for $C_{32}H_{29}IN_2O_5$ 648.1121, found 648.1151.



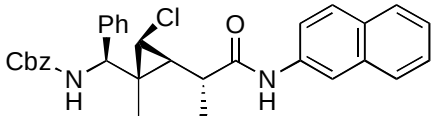
[(1*S*,*R*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-trifluoromethylpent-(2*E*)-enyl]benzoic acid methyl ester (15+16). A solution of 70.0 mg (0.108 mmol) of **14** in 1.00 mL of DMF was treated at room temperature with 20.6 mg (0.108 mmol) of CuTc followed by 137 μL (1.08 mmol) of methyl-2, 2-difluoro-2-(fluorosulfonyl)-acetate. The reaction mixture was warmed to 75-80 °C for 10 h, cooled to room temperature, diluted with Et_2O, and washed with H_2O. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and purified by chromatography on SiO_2 (hexanes/EtOAc) to yield 42.8 mg (67%) of **15** and **16** as a colorless, solid ~1 : 1 mixture of diastereomers. The two diastereomers were separated by chromatography on SiO_2 (50 : 1, CH_2Cl_2/Et_2O).



[(1*S*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-trifluoromethylpent-(2*E*)-enyl]benzoic acid methyl ester (15, less polar): colorless solid; Mp 75-77 °C (ether); $[\alpha]^{25}_D$ +11.1 (*c* 1.0, CH_2Cl_2); IR (neat) 3322, 3034, 2976, 2873, 1704, 1537, 1505, 1283, 1239, 1162, 1121, 747, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 1 H), 8.06 (d, 2 H, *J* = 8.1 Hz), 7.81 (d, 2 H, *J* = 8.9 Hz), 7.79 (d, 2 H, *J* = 8.2 Hz), 7.63 (d, 1 H, *J* = 7.6 Hz), 7.48-7.32 (m, 5 H), 7.28-7.21 (m, 4 H), 6.26 (d, 1 H, *J* = 10.0 Hz), 5.59 (d, 1 H, *J* = 5.8 Hz), 5.29 (bd, 1 H, *J* = 5.3 Hz), 5.10, 5.06 (AB, 2 H, *J* = 12.1 Hz), 3.93 (s, 3 H), 3.80-3.75 (m, 1 H), 1.47 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 166.4, 155.4, 142.0, 137.8, 135.6, 135.4, 133.8, 130.8, 130.7, 130.5, 130.4, 130.3, 128.6 (2C), 128.5, 128.2, 127.8, 127.5, 127.4, 126.5, 125.1, 123.4 (q, *J* = 276.3 Hz), 120.0, 116.8, 67.6, 56.1, 52.3, 41.2, 17.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ 36.54 (s); EIMS *m/z* 590 (M^+, 12), 211 (13), 169 (19), 143 (34), 127 (8), 115 (21), 91 (100), 77 (8); HRMS (EI) *m/z* calcd for $C_{33}H_{29}F_3N_2O_5$ 590.2029, found 590.2009.



[(1*R*)-Benzyloxycarbonylamino-(4*R*)-(naphthalen-2-ylcarbamoyl)-2-trifluoromethylpent-(2*E*)-enyl]benzoic acid methyl ester (16, more polar): colorless solid; Mp 79-81 °C (ether); $[\alpha]_D^{25}$ –58.0 (*c* 1.0, CH_2Cl_2); IR (neat) 3324, 3061, 2953, 1704, 1606, 1532, 1504, 1435, 1283, 1241, 1121, 744, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.27 (s, 1 H), 8.04 (d, 2 H, *J* = 8.3 Hz), 7.79 (d, 3 H, *J* = 8.7 Hz), 7.55 (d, 1 H, *J* = 7.3 Hz), 7.50-7.30 (m, 10 H), 6.41 (d, 1 H, *J* = 11.0 Hz), 5.68 (d, 1 H, *J* = 7.9 Hz), 5.39 (bd, 1 H, *J* = 7.5 Hz), 5.19, 5.15 (AB, 2 H, *J* = 12.2 Hz), 3.92 (s, 3 H), 3.82-3.70 (m, 1 H), 1.48 (d, 3 H, *J* = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 166.4, 155.5, 142.4, 140.3, 135.8, 135.2, 133.8, 130.8, 130.4 (2C), 128.8, 128.6 (2C), 128.4 (2C), 128.1, 127.7, 127.6, 126.6, 126.5, 125.2, 123.5 (q, *J* = 276 Hz), 119.9, 117.1, 67.5, 57.5, 52.2, 41.6, 17.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ -55.02 (s); EIMS *m/z* 590 (M^+, 33), 482 (5), 255 (5), 211 (18), 169 (25), 143 (55), 127 (9), 115 (23), 91 (100), 69 (8); HRMS (EI) *m/z* calcd for $C_{33}H_{29}F_3N_2O_5$ 590.2029, found 590.2006.



(*S*)-({2(*S*)-Chloro-(1*R*)-methyl-(3*S*)-[(1*R*)-(naphthalen-2-ylcarbamoyl)ethyl]cyclopropyl}phenylmethyl)carbamic acid benzyl ester (22). ^1H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 7.95-7.92 (m, 3 H), 7.91 (b, 1 H), 7.64-7.39 (m, 13 H), 5.29 (b, 1 H), 5.28, 5.23 (AB, 2 H, *J* = 12.1 Hz), 4.74 (d, 1 H, *J* = 8.8 Hz), 3.64 (d, 1 H, *J* = 7.9 Hz), 2.60-2.50 (m, 1 H), 1.76 (bt, 1 H, *J* = 9.3 Hz), 1.43 (d, 3 H, *J* = 6.6 Hz), 1.26 (s, 3 H); HRMS (ESI) *m/z* calcd for $C_{32}H_{31}ClN_2O_3Na$ 549.1921, found 549.1942.