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Supporting Information

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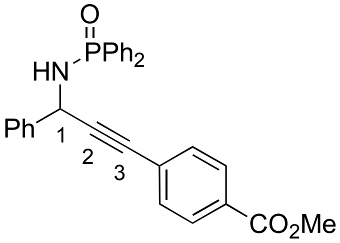
SUPPLEMENTARY MATERIAL

Pericyclic Cascade Reactions of *C*-Bicyclo[1.1.0]butylbenzylamines

Peter Wipf,* and Maciej A. A. Walczak
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260
pwipf@pitt.edu

Experimental procedures and spectral data for new compounds. NOESY spectrum for **12**.

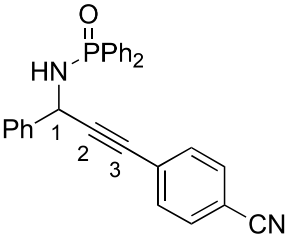
General Methods. All moisture-sensitive reactions were performed under an atmosphere of N_2 and glassware was flame dried under vacuum prior to use. THF was dried by distillation over Na/benzophenone and *i*-Pr_2NH was dried by distillation over CaH_2. Toluene and CH_2Cl_2 were purified by filtration through activated alumina. Me_2Zn (2.0 M in toluene) and Et_2Zn (neat) were purchased from the Aldrich Chemical Company. 3-bromo-1-phenylpropyne, cyclopropylallyl bromide and (*Z*)-cinnamyl bromide were obtained from 1-phenyl-1-propyn-3-ol,[1] cyclopropylallyl alcohol[2] and (*Z*)-cinnamyl alcohol,[3] respectively, via reaction with $Ph_3P{\cdot}Br_2$/imidazole in CH_2Cl_2 at 0 ºC. 2,2-Dibromo-1-(chloromethyl)-1-phenylcyclopropane **3**,[4] PhCH=NP(O)Ph_2,[5] *t*-BuCH=NP(O)Ph_2,[6] and *c*-C_6H_{11}CH=NTs[7] were prepared according to literature protocols. Unless otherwise stated, solvents or reagents were used as received. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F-254 plates (particle size 0.040-0.055 mm, 230-400 mesh) and visualization was accomplished with a 254 nm UV light and/or by staining with Vaughn's reagent (4.8 g of $(NH_4)_6Mo_7O_{24}{\bullet}4H_2O$ and 0.20 g of $Ce(SO_4)_2$ in 100 mL of 3.5 N H_2SO_4 solution). NMR spectra were recorded at 300 MHz/75 MHz (^{1}H NMR/^{13}C NMR) or 500 MHz/125 MHz (^{1}H NMR/^{13}C NMR) using Bruker AVANCE 300 MHz or Bruker AVANCE 500 MHz spectrometers at 21 °C. Chemical shifts (δ) are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constants, and integration. IR spectra were obtained on a Nicolet AVATAR 360 FT-IR E.S.P. spectrometer. Mass spectra were obtained on a Micromass Autospec double focusing instrument. Melting points were recorded on Mel-Temp II apparatus and are uncorrected. Microwave reactions were run on a Personal Chemistry workstation.



1a

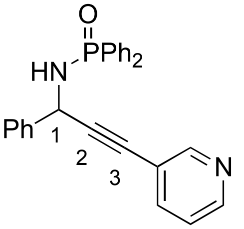
***N*-(3-(4-Methoxycarbonylphenyl)-1-phenylprop-2-ynyl)-*P,P*-diphenylphosphinamide (1a). General Protocol A.** A suspension of CuI (0.17 g, 0.91 mmol) and $Pd(PPh_3)_4$ (0.52 g, 0.45 mmol) in degassed *i*-Pr_2NH (100 mL) was cooled to 0 °C and treated with methyl 4-iodobenzoate (2.4 g, 9.1 mmol). A solution of alkyne **20** (3.0 g, 9.1 mmol) in THF (25 mL) was added via syringe and the reaction mixture was vigorously stirred at 0 °C for 1.5 h, quenched with sat. NH_4Cl, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **1a** (2.5 g, 59%) as a colorless solid: Mp 188.2-191.0 °C (hexanes/CH_2Cl_2); IR (KBr) 2951, 2847, 1721, 1604, 1493, 1451, 1437, 1404, 1308, 1276, 1186, 1126, 1109 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11-8.04 (m, 2

H), 7.98 (d, *J* = 8.3 Hz, 2 H), 7.90-7.83 (m, 2 H), 7.68 (d, *J* = 7.2 Hz, 2 H), 7.57-7.30 (m, 11 H), 5.44 (app t, *J* = 9.7 Hz, 1 H, NH), 3.94 (s, 3 H, CH_3), 3.54 (b t, *J* = 7.9 Hz, 1 H, H_1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.40 (CO), 139.90, 133.21, 132.67, 132.54, 131.97, 131.84, 131.71, 131.53, 131.09, 129.61, 129.30, 128.67, 128.52, 128.35, 128.04, 127.31, 127.19, 91.90 (d, *J* = 5.7 Hz, C_2), 84.73 (C_3), 52.14 (OCH_3), 47.00 (C_1); MS (EI) *m/z* (rel intensity) 465 (M^+, 72), 388 (15), 330 (8), 264 (84), 201 (100); HRMS (EI) calc for $C_{29}H_{24}NO_3P$ 465.1494, found 465.1480.



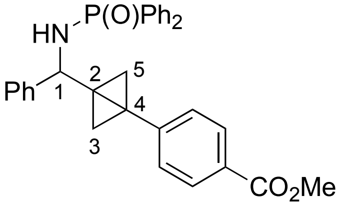
1b

***N*-(3-(4-Cyanophenyl)-1-phenylprop-2-ynyl)-*P,P*-diphenylphosphinamide (1b).** According to the General Protocol A, alkyne **20** (0.50 g, 1.5 mmol), 4-iodobenzonitrile (0.33 g, 1.5 mmol), CuI (0.028 g, 0.15 mmol) and $Pd(PPh_3)_4$ (0.087 g, 0.075 mmol) in *i*-Pr_2NH (25 mL) and THF (10 mL) afforded **1b** (0.40 g, 62%) as a colorless solid: Mp 213.3-214.8 °C (hexanes/EtOAc); IR (KBr) 3434, 3148, 2227, 1603, 1438, 1187, 1126, 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 12.1, 7.9 Hz, 2 H), 7.91 (dd, *J* = 12.0, 8.0 Hz, 2 H), 7.71 (d, *J* = 7.3 Hz, 2 H), 7.62-7.35 (m, 13 H), 5.48 (app t, *J* = 9.6 Hz, 1 H, NH), 4.07 (app t, *J* = 9.0 Hz, 1 H, H_1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.64, 139.57, 132.95, 132.49, 132.35, 132.04, 131.91, 131.81, 131.74, 131.68, 131.25, 131.12, 128.65, 128.45, 128.28, 128.06, 127.45, 127.08, 118.27 (CN), 111.49, 93.46 (d, *J* = 5.0 Hz, C_2), 83.74 (C_3), 46.82 (C_1); MS *m/z* (rel. intensity) 432 (M^+, 67), 355 (4), 328 (14), 307 (3), 277 (7), 231 (92), 201 (100), 185 (17); HRMS (EI) calc for $C_{28}H_{21}N_2OP$ 432.1389, found 432.1392.



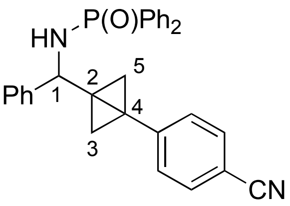
1c

***N*-(1-Phenyl-3-(pyridin-3-yl)prop-2-ynyl)-*P,P*-diphenylphosphinamide (1c).** According to the General Protocol A, alkyne **20** (2.0 g, 6.0 mmol), 3-iodopyridine (1.2 g, 6.0 mmol), CuI (0.11 g, 0.60 mmol) and $Pd(PPh_3)_4$ (0.35 g, 0.030 mmol) in *i*-Pr_2NH (100 mL) and THF (20 mL) were stirred at 0 ºC for 2.5 h. The reaction mixture was quenched with sat. NH_4Cl and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4) and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:10) afforded **1c** (1.9 g, 77%) as a colorless oil that solidified upon standing: IR (neat) 3151, 3058, 1620, 1592, 1566, 1476, 1438, 1412, 1307, 1276, 1188, 1123, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.64-8.55 (m, 2 H), 8.14 (dd, *J* = 12.1, 7.7 Hz, 2 H), 7.93 (dd, *J* = 12.1, 8.0, 2 H), 7.75-7.71 (m, 2 H), 7.61-7.36 (m, 9 H), 7.31-7.27 (m, 2 H), 5.52 (app t, *J* = 9.6 Hz, 1 H, H_1), 4.01 (app t, *J* = 8.9 Hz, 1 H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.86, 148.30, 139.86, 139.79, 138.41, 133.09, 132.79, 132.48, 132.38, 131.79, 131.73, 131.60, 131.39, 131.08, 128.49, 128.32, 128.22, 128.15, 127.84, 127.03, 122.70, 119.64, 92.47 (d, *J* = 5.2 Hz, C_2), 81.82 (C_3), 46.69 (C_1); MS (EI) *m/z* (rel. intensity) 408 (M^+, 77), 331 (7), 305 (13), 283 (12), 207 (100), 201 (59), 192 (14); HRMS (EI) calc for $C_{26}H_{21}N_2OP$ 408.1392, found 408.1373.



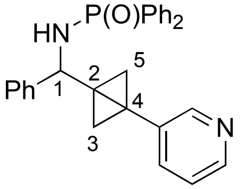
2a

***N*-((3-(4-Methoxycarbonylphenyl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*P,P*-diphenylphosphinamide (2a). General Protocol B.** Amide **1a** (1.0 g, 2.2 mmol) was dissolved in dry CH_2Cl_2 (80 mL), cooled to 0 °C and treated with Me_2Zn (1.1 mL, 2.2 mmol, 2.0 M in PhMe). After 1 h at 0 oC, the reaction mixture was cooled to –50 °C and transferred via cannula into a cold (-50 °C) solution of $(CH_2I)_2Zn$ prepared by the addition of CH_2I_2 (0.69 mL, 8.6 mmol) to a solution of Et_2Zn (0.53 g, 4.3 mmol) in CH_2Cl_2 (80 mL) at -50 °C. The reaction mixture was warmed to 0 °C, stirred for 30 min, and quenched with sat. NH_4Cl. Extraction with EtOAc followed by purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4 to 1:6) afforded **2a** (0.45 g, 42%) as a colorless solid: Mp 158.3-160.1 ºC (hexanes/CH_2Cl_2); IR (KBr) 3423, 3262, 3058, 2931, 1728, 1720, 1606, 1438, 1279, 1189, 1117 cm^{-1}; ^1H (300 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 11.9, 8.0 Hz, 2 H), 7.78 (d, *J* = 8.4 Hz, 2 H), 7.68 (dd, *J* = 11.3, 7.2 Hz, 2 H), 7.47-7.34 (m, 3 H), 7.28-7.23 (m, 3 H), 7.15-7.06 (m, 4 H), 6.90 (d, *J* = 8.3 Hz, 2 H), 6.76 (d, *J* = 7.0 Hz, 2 H), 4.60 (app t, *J* = 8.6 Hz, 1 H, H_1), 3.86 (s, 3 H, OCH_3), 3.68 (dd, *J* = 7.8, 5.6 Hz, 1 H. NH), 2.23 (d, *J* = 6.6 Hz, 1 H, H_{3exo} or H_{5exo}), 1.98 (d, *J* = 6.6 Hz, 1 H, H_{5exo} or H_{3exo}), 1.00 (s, 1 H, H_{3endo} or H_{5endo}), 0.93 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.85 (CO), 142.12, 139.91, 139.83, 132.02, 131.89, 131.82, 131.70, 131.53, 131.22, 129.13, 128.28, 128.18, 128.12, 128.02, 127.94, 127.25, 126.80, 126.50, 125.24, 54.88 (C_1), 51.69 (OCH_3), 34.08 (C_3 or C_5), 31.61 (C_5 or C_3), 30.75 (d, *J* = 5.1 Hz, C_2), 20.58 (C_4); MS (ES) *m/z* (rel. intensity) 516 ($[M+Na]^+$, 100), 413 (45), 371 (10), 301 (12), 227 (17), 221 (7), 201 (5); HRMS (ES) calc for $C_{31}H_{28}NNaO_3P$ (M+Na) 516.1705, found 516.1722.



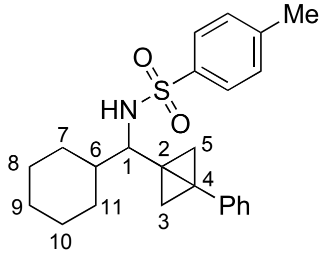
2b

***N*-((3-(4-Cyanophenyl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*P,P*-diphenylphosphinamide (2b).** According to General Protocol B, amide **1b** (1.1 g, 2.6 mmol) and Me_2Zn (1.3 mL, 2.6 mmol, 2.0 in PhMe) in CH_2Cl_2 (85 mL) were reacted with $(CH_2I)_2Zn$ prepared by the addition of CH_2I_2 (0.83 mL, 10 mmol) to the solution of Et_2Zn (0.64 g, 5.2 mmol) in CH_2Cl_2 (85 mL) at -50 ^{o}C. The reaction mixture was stirred at 0 ^{o}C for 1 h, quenched with sat. NH_4Cl, and extracted (3x) with CH_2Cl_2. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **2b** (0.41 g, 35%) as a colorless foam: IR (KBr) 3500, 3057, 2930, 2223, 1605, 1438, 1189, 1123 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (ddt, *J* = 12.0, 6.7, 1.6 Hz, 2 H), 7.61 (ddt, *J* = 12.1, 6.9, 1.4 Hz, 2 H), 7.48-7.20 (m, 7 H), 7.12-7.03 (m, 4 H), 6.80 (dd, *J* = 6.7, 1.8 Hz, 2 H), 6.65 (dd, *J* = 6.9, 1.5 Hz, 2 H), 4.50 (app. t, *J* = 8.4 Hz, 1 H, H_1), 3.46 (dd, *J* = 7.5, 5.2 Hz, 1 H, NH), 2.17 (dd, *J* = 6.8, 1.1 Hz, 1 H, H_{3exo} or H_{5exo}), 1.88 (dd, *J* = 6.6, 0.6 Hz, 1 H, H_{5exo} or H_{3exo}), 0.96 (s, 1 H, H_{3endo} or H_{5endo}), 0.88 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.65, 139.58, 139.50, 133.77, 132.80, 132.08, 131.92, 131.80, 131.52, 131.09, 128.43, 128.37, 128.24, 128.20, 128.13, 127.56, 126.82, 125.89, 119.22 (CN), 107.91, 54.99 (C_1), 34.69 (C_3 or C_5), 31.80 (C_5 or C_3), 31.58 (d, *J* = 4.7 Hz, C_2), 20.85 (C_4); MS (EI) *m/z* (rel. intensity) 460 (M^{+}, 44), 346 (7), 306 (17), 259 (100), 243 (38), 201 (82); HRMS (EI) calc for $C_{30}H_{25}N_2OP$ 460.1705, found 460.1703.



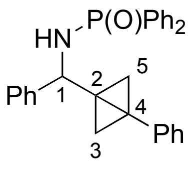
2c

***N*-((3-(Pyridin-3-yl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*P,P*-diphenylphosphinamide (2c).** According to General Protocol B, amide **1c** (0.50 g, 1.2 mmol) and Me_2Zn (0.61 mL, 1.2 mmol, 2.0 in PhMe) in CH_2Cl_2 (40 mL) were reacted with $(CH_2I)_2Zn$ prepared by the addition of CH_2I_2 (0.40 mL, 4.9 mmol) to a solution of Et_2Zn (0.30 g, 2.5 mmol) in CH_2Cl_2 (40.0 mL) at -50 ºC. The reaction mixture was stirred at 0 ºC for 14 h, quenched with sat. NH_4Cl, and extracted (3x) with CH_2Cl_2. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc/MeOH, 1:8:1) afforded **2c** (0.21 g, 40%) as a colorless foam: IR (neat) 3058, 2926, 1591, 1570, 1477, 1454, 1438, 1420, 1311, 1191, 1123, 1110 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, *J* = 3.9 Hz, 1 H), 7.97 (bs, 1 H), 7.80 (ddd, *J* = 11.9, 8.0, 1.4 Hz, 2 H), 7.66 (dd, *J* = 12.0, 7.1 Hz, 2 H), 7.42-7.20 (m, 8 H), 7.12-7.01 (m, 3 H), 6.92 (dd, *J* = 7.8, 4.7 Hz, 1 H), 6.70 (d, *J* = 6.9 Hz, 1 H), 4.52 (t, *J* = 8.3 Hz, 1 H, H_1), 3.66 (app t, *J* = 5.6 Hz, 1 H, NH), 2.14 (d, *J* = 6.6 Hz, 1 H, H_{3exo} or H_{5exo}), 1.80 (d, *J* = 6.6 Hz, 1 H, H_{5exo} or H_{3exo}), 0.90 (s, 1 H, H_{3endo} or H_{5endo}), 0.80 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.95, 146.07, 139.87, 139.79, 133.90, 132.65, 132.19, 132.07, 131.95, 131.83, 131.61, 131.39, 128.35, 128.29, 128.25, 128.19, 128.11, 128.09, 127.47, 126.83, 122.48, 55.01 (C_1), 33.65 (C_3 or C_5), 30.99 (C_5 or C_3), 28.69 (d, *J* = 5.2 Hz, C_2), 18.07 (C_4); MS (EI) *m/z* (rel. intensity) 436 (M^+, 36), 332 (16), 306 (7), 235 (15), 218 (19), 201 (60), 77 (100); HRMS (EI) calc for $C_{28}H_{25}N_2OP$ 436.1705, found 436.1692.



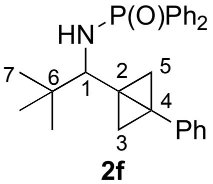
2d

Cyclohexyl(3-phenylbicyclo[1.1.0]but-1-yl)-*N*-tosylmethanamine (2d). General Protocol C. 2,2-Dibromo-1-(bromomethyl)-1-phenylcyclopropane **3** (0.50 g, 1.4 mmol) was dissolved in Et_2O (10.0 mL), cooled to –78 °C and treated with MeLi (0.84 mL, 1.4 mmol, c = 1.6 M in Et_2O). The reaction mixture was allowed to warm up to –50 °C over 1 h, cooled to –78 °C and treated with *t*-BuLi (0.81 mL, 2.2 mmol, c = 1.7 M in pentane). After 1 h at –78 °C, a solution of *c*-$C_6H_{11}CH=NTs$ (0.15 g, 0.54 mmol) in THF (5.0 mL) was added, the reaction mixture was stirred for 10 min, warmed up to rt, quenched with sat. NH_4Cl, and extracted (3x) with EtOAc. The combined organic layers were washed with water, brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 4:1) afforded **2d** (0.16 g, 75%) as a light yellow oil: IR (neat) 3286, 2925, 2853, 1601, 1447, 1325, 1159 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.48 (m, 2 H), 7.31-7.27 (m, 2 H), 7.22-7.10 (m, 5 H), 4.40 (d, *J* = 8.0 Hz, 1 H, NH), 3.43 (dd, *J* = 8.0, 3.9 Hz, 1 H, H_1), 2.41 (s, 3 H, CH_3), 1.94 (d, *J* = 6.7 Hz, 1 H, H_{3exo} or H_{5exo}), 1.87 (d, *J* = 6.7 Hz, 1 H, H_{5exo} or H_{3exo}), 1.67-1.53 (m, 6 H), 1.09-1.01 (m, 5 H), 0.97 (s, 1 H, H_{3endo} or H_{5endo}), 0.84 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 138.0, 135.8, 129.4, 128.4, 126.9, 125.6, 125.2, 56.9 (C_1), 42.5 (C_6), 32.3 (C_3 or C_5), 30.7 (C_5 or C_3), 28.9, 28.8, 26.2, 26.1, 26.0, 25.0 (CH_3), 21.4, 18.4 (C_4); MS (EI) *m/z* (rel. intensity) 395 (M^+, 15), 312 (14), 266 (40), 240 (19), 91 (100); HRMS (EI) calc for $C_{24}H_{29}NO_2S$ 395.1919, found 395.1919.



2e

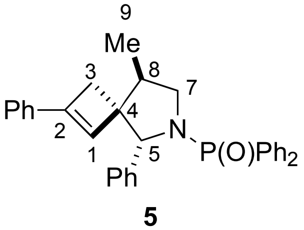
***N*-(Phenyl-(3-phenylbicyclo[1.1.0]but-1-yl)methyl)-*P,P*-diphenylphosphinamide (2e).** According to the General Protocol C, 2,2-dibromo-1-bromomethyl-phenylcyclopropane **3** (0.30 g, 0.81 mmol) in Et_2O (5.0 mL) was treated with MeLi (0.59 mL, 0.81 mmol, c = 1.4 M in Et_2O), followed by *t*-BuLi (0.56 mL, 0.81 mmol, c = 1.5 M in pentane) and a solution of $PhCH{=}NP(O)Ph_2$ (0.11 g, 0.32 mmol) in THF (5.0 mL). The reaction mixture was warmed up to rt, quenched with sat. NH_4Cl and extracted (3x) with EtOAc. The combined organic layers were washed with water, brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **2f** (0.10 g, 73%) as a colorless oil: IR (neat) 3059, 1680, 1597, 1438, 1191 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (ddd, J = 10.5, 6.8, 1.5 Hz, 2 H), 7.70 (ddd, J = 12.1, 5.1, 1.4 Hz, 2 H), 7.56-7.38 (m, 4 H), 7.31-7.27 (m, 4 H), 7.18-7.10 (m, 4 H), 6.93 (dd, J = 7.8, 1.6 Hz, 2 H), 6.81 (dd, J = 7.7, 1.4 Hz, 2 H), 4.68 (app t, J = 8.5 Hz, 1 H, H_1), 4.45 (dd, J = 7.8, 5.3 Hz, 1 H, NH), 2.13 (d, J = 6.7 Hz, 1 H, H_{3exo} or H_{5exo}), 1.99 (d, J = 6.7 Hz, 1 H, H_{5exo} or H_{3exo}), 0.94 (s, 1 H, H_{3endo} or H_{5endo}), 0.89 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.44, 140.36, 135.76, 132.16, 132.04, 131.99, 131.86, 131.59, 131.44, 128.38, 128.26, 128.22, 128.11, 128.02, 127.96, 127.16, 127.01, 125.56, 125.03, 55.02 (C_1), 33.18 (C_3 or C_5), 30.91 (C_5 or C_3), 28.30 (d, J = 5.2 Hz, C_2), 20.15 (C_4); MS (EI) *m/z* (rel. intensity) 435 (M^+, 14), 306 (50), 218 (43), 201 (100); HRMS (EI) calc for $C_{29}H_{26}NOP$ 435.1752, found 435.1749.



2f

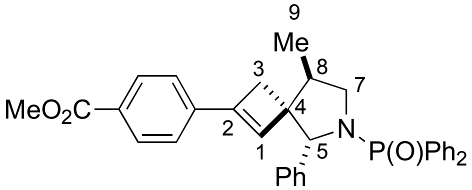
***N*-(2,2-Dimethyl-1-(3-phenylbicyclo[1.1.0]but-1-yl)propyl)-*P,P*-diphenylphosphinamide (2f).** According to the General Protocol C, 2,2-dibromo-1-bromomethyl-phenylcyclopropane **3** (0.30 g, 0.81 mmol) in Et_2O (5.0 mL) was treated with MeLi (0.59 mL, 0.81 mmol, c = 1.4 M in Et_2O), followed by *t*-BuLi (0.56 mL, 0.81 mmol, c = 1.5 M in pentane) and a solution of *t*-$BuCH{=}NP(O)Ph_2$ (0.093 g, 0.32 mmol) in THF (5.0 mL). The reaction mixture was warmed up to rt, quenched with sat. NH_4Cl and extracted (3x) with EtOAc. The combined organic layers were washed with water, brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **2f** (0.094 g, 71%) as a colorless oil: IR (neat) 2957, 1438, 1188, 1123, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57-7.51 (m, 2 H), 7.45-7.21 (m, 13 H), 3.12 (dd, J = 11.0, 7.6 Hz, 1 H, H_1), 2.69 (dd, J = 11.0, 4.4 Hz, 1 H, NH), 2.15 (d, J = 6.6 Hz, 1 H, H_{3exo} or H_{5exo}), 2.03 (d, J = 6.6, 1 H, H_{5exo} or H_{3exo}), 1.06

(s, 10 H, H_{3endo} or H_{5endo}, H_7), 0.92 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.94, 134.60, 132.84, 132.70, 132.57, 132.28, 132.16, 131.71, 131.31, 131.27, 130.00, 128.28, 128.23, 128.20, 128.07, 128.03, 127.91, 126.68, 125.51, 59.22 (C_1), 37.56 (C_3 or C_5), 33.79 (C_5 or C_3), 30.16 (d, J = 9.9 Hz, C_2), 27.98 (C_6), 27.17 (C_7), 18.23 (C_4); MS (EI) *m/z* (rel. intensity) 415 (M^+, 66), 414 (46), 357 (52), 284 (11), 199 (100), 181 (26), 154 (16); HRMS (EI) calc for $C_{27}H_{30}NOP$ 415.2065, found 415.2051.



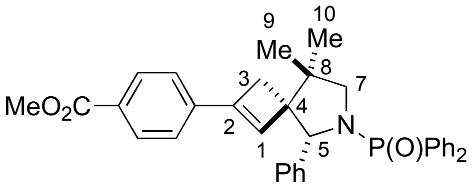
5

(*4S*,5R*,8R)-6-(*N*-(*P,P*-Diphenylphosphinyl))-8-methyl-2,5-diphenyl-6-azaspiro[3.4]oct-1-ene (5). General Protocol D.** Bicyclobutane **4a** (0.049 g, 0.11 mmol), allyl bromide (0.068 g, 0.56 mmol) and Bu_4NHSO_4 (0.020 g, 0.056 mmol) were dissolved in PhMe (5.0 mL), and treated with 50% aq NaOH (5.0 mL). The reaction mixture was vigorously stirred at rt for 36 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The product was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to give **5** (0.033 g, 63%) as a colorless oil: IR (neat) 2922, 1489, 1438, 1200, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (ddd, J = 11.7, 4.8, 1.6 Hz, 3 H), 7.61 (ddd, J = 11.8, 8.3, 1.3 Hz, 3 H), 7.49-7.44 (m, 5 H), 7.35-7.20 (m, 4 H), 7.15-7.06 (m, 5 H), 6.77 (s, 1 H, H_1), 4.54 (d, J = 11.3 Hz, 1 H, H_5), 3.59-3.49 (m, 1 H, H_7), 3.27-3.17 (m, 1 H, H_7), 2.81-2.69 (m, 1 H, H_8), 2.39 (d, J = 13.4 Hz, 1 H, H_3), 2.25 (d, J = 13.4 Hz, 1 H, H_3), 0.94 (d, J = 6.6 Hz, 3 H, H_9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.08, 144.04, 134.02, 132.56, 132.43, 132.32, 132.20, 131.67, 131.29, 128.54, 128.43, 128.37, 128.26, 127.85, 127.79, 127.67, 127.26, 126.67, 124.67, 69.25 (C_5), 56.66 (d, J = 3.8 Hz, C_4), 52.66 (C_7), 36.69 (C_8), 32.37 (C_3), 11.89 (C_9); MS (EI) *m/z* (rel. intensity) 475 (M^+, 29), 318 (9), 306 (52), 274 (28), 230 (20), 201 (100); HRMS (EI) calc for $C_{32}H_{30}NOP$ 475.2065, found 475.2095.



6

(*4S*,5R*,8R)-6-(*N*-(*P,P*-Diphenylphosphinyl))-2-((4-methoxycarbonyl)phenyl)-8-methyl-5-phenyl-6-azaspiro[3.4]oct-1-ene (6).** According to General Protocol D, bicyclobutane **2a** (0.10 g, 0.20 mmol), allyl bromide (0.12 g, 1.0 mmol) and Bu_4NHSO_4 (0.034 g, 0.10 mmol) were dissolved in PhMe (10.0 mL) and treated with 50% aq NaOH (10.0 mL). The reaction mixture was vigorously stirred at rt for 36 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford **6** as a colorless oil (0.090 g, 83%): IR (neat) 3058, 2954, 2925, 2871, 1719, 1617, 1428, 1453, 1438, 1410, 1359, 1280, 1193, 1121, 1109 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05-7.97 (m, 4 H), 7.63 (dd, *J* = 11.1, 8.1 Hz, 2 H), 7.52-7.48 (m, 3 H), 7.40 (d, *J* = 8.2 Hz, 2 H), 7.31-7.24 (m, 4 H), 7.15-7.11 (m, 4 H), 6.96 (s, 1 H, H_1), 4.58 (d, *J* = 11.5 Hz, 1 H, H_5), 3.94 (s, 3 H, OCH_3), 3.59 (app t, *J* = 7.3 Hz, 1 H, H_7), 3.26 (q, *J* = 10.3 Hz, 1 H, H_7), 2.82-2.79 (m, 1 H, H_8), 2.45 (d, *J* = 13.3 Hz, 1 H, H_3), 2.30 (d, *J* = 13.3 Hz, 1 H, H_3), 0.97 (d, *J* = 6.5 Hz, 3 H, H_9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.77 (CO), 148.03, 143.84, 143.35, 138.09, 134.75, 132.53, 132.41, 132.32, 132.20, 131.57, 131.33, 129.66, 129.16, 128.55, 128.39, 127.86, 127.68, 127.26, 126.79, 124.56, 68.93 (C_5), 57.03 (d, *J* = 3.5 Hz, C_4), 52.72 (C_7), 51.99 (OCH_3), 36.80 (d, *J* = 5.4 Hz, C_8), 32.41 (C_3), 11.91 (C_9); MS (EI) *m/z* (rel. intensity) 533 (M$^+$, 15), 332 (24), 306 (43), 230 (11), 215 (14), 201 (80), 118 (100); HRMS (EI) calc for $C_{34}H_{32}NO_3P$ 533.2120, found 533.2129.

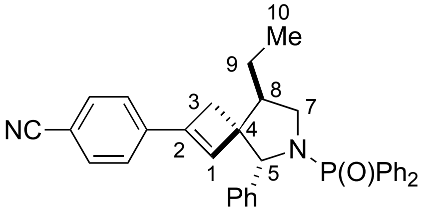


7

(*4S*,5R)-6-(*N*-(*P,P*-Diphenylphosphinyl))-2-((4-methoxycarbonyl)phenyl)-8,8-dimethyl-5-phenyl-6-azaspiro[3.4]oct-1-ene (7) from 4c.** A mixture of bicyclobutane **2a** (0.030 g, 0.061 mmol), 3-bromo-2-methylpropene (0.030 mL, 0.030 mmol), Bu_4NHSO_4 (0.010 g, 0.030 mmol), powdered NaOH (0.012 g, 0.61 mmol) and K_2CO_3 (0.042 g, 0.30 mmol) in PhMe (3.0 mL) was vigorously stirred at rt for 2.5 h and at 110 ºC for an additional 12 h. The reaction mixture was diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford a mixture (2.3:1) of diastereoisomers of **7** (0.022 g, 66%) as a colorless oil. Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03-7.84 (m, 3 H), 7.53-7.46 (m, 5 H), 7.20-7.11 (m, 5 H), 7.04-6.92 (m, 6 H), 6.32 (s, 1 H, H_1), 4.74 (d, *J* = 11.0 Hz, 1 H, H_5), 3.86 (s, 3 H, OCH_3), 3.53-3.30 (m, 2 H, H_7), 2.75 (d, *J* = 12.9 Hz, 1 H, H_3), 2.36 (d, *J* = 12.9 Hz, 1 H, H_3), 1.38 (s, 3 H, H_9 or H_{10}), 0.94 (s, 3 H, H_{10} or H_9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.70 (CO), 145.97, 141.48, 141.30, 133.46, 132.59, 132.47, 132.30, 132.18, 131.87, 131.59, 129.49, 128.55, 128.39, 128.30, 127.53, 127.36, 127.22, 127.17, 126.36, 124.28, 68.21 (C_5), 60.52 (C_4), 59.89 (C_7), 51.98 (OCH_3), 42.48 (C_8), 31.60 (C_3), 23.15 (C_9 or C_{10}), 21.78 (C_{10} or C_9); IR(neat) 2955, 1720, 1605, 1438, 1280, 1193, 1122, 1109 cm^{-1}; MS (EI) *m/z* (rel. intensity) 547 (M$^+$, 52), 532 (9), 500

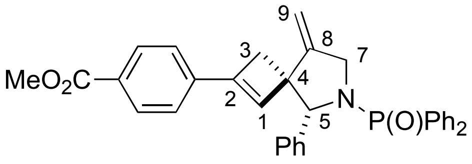
(10), 470 (8), 346 (53), 230 (15), 201 (100); HRMS (EI) calc for $C_{35}H_{34}NO_3P$ 547.2276, found 547.2251. Minor isomer (representative signals): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (s, 1 H, H_1), 4.81 (d, *J* = 11.5 Hz, 1 H, H_5), 3.87 (s, 3 H, OCH_3), 3.31 (app d, *J* = 10.8 Hz, 1 H, H_7), 2.50 (d, *J* = 13.2 Hz, 1 H, H_3), 1.36 (s, 3 H, H_9 or H_{10}), 1.07 (s, 3 H, H_{10} or H_9); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.87 (C_5), 43.49 (C_8), 32.24 (C_3), 23.98 (C_9 or C_{10}), 21.51 (C_{10} or C_9),.

Synthesis of **7** from *N*-((3-(4-methoxycarbonylphenyl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*N*-(2-methylallyl)-*P,P*-diphenylphosphinamide (**21**). A solution of bicyclobutane **19** (0.025 g, 0.047 mmol) in PhMe (1.5 mL) was heated at reflux (110 ºC) for 6.5 h. The solvent was evaporated, and purification of the residue by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded a diastereomeric mixture (2.5:1) of **7** (0.020 g, 80%).



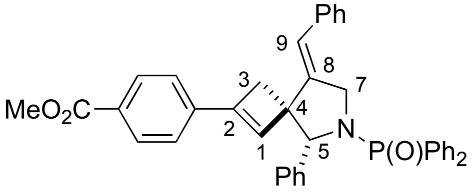
8

(*4S*,5R*,8R)-2-(4-Cyanophenyl)-6-(*N*-(*P,P*-diphenylphosphinyl))-8-ethyl-5-phenyl-6-azaspiro[3.4]oct-1-ene (8).** A suspension of bicyclobutane **2b** (0.11 g, 0.24 mmol), crotyl bromide (0.12 mL, 1.2 mmol), Bu_4NHSO_4 (0.041 g, 0.12 mmol), powdered NaOH (0.10 g, 2.4 mmol) and K_2CO_3 (0.17 g, 1.2 mmol) in PhMe (10 mL) was vigorously stirred at rt for 4 h, and at 50 °C for an additional 14 h. The reaction mixture was diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **8** (0.063 g, 51%) as a colorless oil: IR (neat) 3060, 2960, 2925, 2873, 2225, 1612, 1558, 1497, 1454, 1439, 1299, 1194, 1109 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (ddd, *J* = 11.8, 7.7, 1.9 Hz, 2 H), 7.62-7.56 (m, 4 H), 7.50-7.44 (m, 4 H), 7.39-7.36 (m, 2 H), 7.31-7.23 (m, 3 H), 7.15-7.06 (m, 4 H), 7.00 (s, 1 H, H_1), 4.51 (d, *J* = 11.6 Hz, 1 H, H_5), 3.64 (ddd, *J* = 11.0, 8.0, 3.0 Hz, 1 H, H_7), 3.26 (td, *J* = 12.3, 10.0 Hz, 1 H, H_7), 2.57 (ddd, *J* = 18.2, 10.4, 3.8 Hz, 1 H, H_8), 2.42 (d, *J* = 13.4 Hz, 1 H, H_3), 2.30 (d, *J* = 13.4 Hz, 1 H, H_3), 1.49-1.35 (m, 1 H, H_9), 1.30-1.18 (m, 1 H, H_9), 0.86 (t, *J* = 7.4 Hz, 3 H, H_{10}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.68, 142.22, 138.00, 136.82, 133.28, 132.54, 132.41, 132.31, 132.20, 131.65, 131.44, 131.41, 128.66, 128.49, 127.94, 127.77, 127.27, 126.94, 125.18, 118.92 (CN), 110.98, 69.33 (C_5), 56.94 (d, *J* = 3.0 Hz, C_4), 51.49 (C_7), 44.14 (d, *J* = 5.3 Hz, C_8), 32.67 (C_3), 21.92 (C_9), 13.09 (C_{10}); MS (ES) *m/z* (rel. intensity) 1051 ($[2M+Na]^+$, 15), 537 ($[M+Na]^+$, 72), 515 ($[M+1]^+$, 100); HRMS (ES) calc for $C_{34}H_{32}N_2OP$ (M+H) 515.2252, found 515.2251.



9

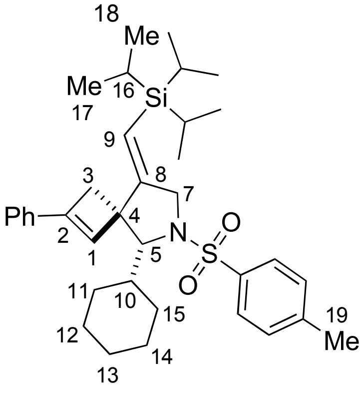
(*4S*,5R*,*)-6-(*N*-(*P,P*-Diphenylphosphinyl))-2-((4-methoxycarbonyl)phenyl)-8-methylene-5-phenyl-6-azaspiro[3.4]oct-1-ene (9). According to General Protocol D, a solution of bicyclobutane **2a** (0.32 g, 0.62 mmol), propargyl bromide (0.50 mL, 3.1 mmol, 80% in PhMe), and Bu_4NHSO_4 (0.11 g, 0.32 mmol) in PhMe (30 mL) was treated with 50% aq NaOH (30 mL). The reaction mixture was vigorously stirred at rt for 24 h, diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The residual oil was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford **9** (0.29 g, 87%) as a colorless oil: IR (neat) 3058, 2959, 1721, 1603, 1438, 1280, 1195, 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 6.8, 1.7 Hz, 2 H), 7.92 (ddd, *J* = 11.7, 7.9, 1.7 Hz, 2 H), 7.71 (ddd, *J* = 11.8, 8.3, 1.4 Hz, 2 H), 7.52-7.44 (m, 4 H), 7.40-7.34 (m, 4 H), 7.30-7.20 (m, 3 H), 7.03-7.00 (m, 2 H), 5.77 (s, 1 H, H_1), 4.93 (d, *J* = 1.4 Hz, 2 H, H_9), 4.58 (d, *J* = 10.3 Hz, 1 H, H_5), 4.34 (ddt, *J* = 14.4, 12.1, 2.4 Hz, 1 H, H_7), 4.04 (dd, *J* = 14.3, 5.5 Hz, 1 H, H_7), 3.91 (s, 3 H, OCH_3), 3.28 (d, *J* = 12.6 Hz, 1 H, H_3), 2.92 (d, *J* = 12.6 Hz, 1 H, H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.71 (CO), 150.76, 146.39, 142.72, 142.66, 137.88, 132.53, 132.49, 132.40, 132.37, 131.67, 130.82, 129.73, 129.57, 128.65, 128.49, 128.30, 128.21, 128.05, 128.00, 127.02, 126.56, 124.85, 105.56 (C_9), 69.91 (C_5), 57.59 (C_4), 52.03 (OCH_3), 50.71 (C_7), 46.42 (C_3); MS (EI) *m/z* (rel. intensity) 531 (M^+, 27), 417 (6), 330 (65), 217 (21), 201 (100); HRMS (EI) calc for $C_{30}H_{34}NO_3P$ 531.1963, found 531.1941.



10

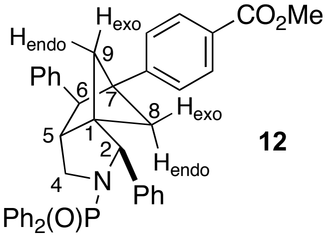
(*4S*,5R*,8Z*)-6-(*N*-(*P,P*-Diphenylphosphinyl))-2-((4-methoxycarbonyl)phenyl)-5-phenyl–8-phenylmethylene-6-azaspiro[3.4]oct-1-ene (10). According to General Protocol D, a solution of bicyclobutane **2a** (0.050 g, 0.10 mmol), Bu_4NHSO_4 (0.017 g, 0.051 mmol), and 1-phenyl-3-bromopropyne (0.099 g, 0.51 mmol) in PhMe (5.0 mL) was treated with 50% aq NaOH (5.0 mL). The reaction mixture was vigorously stirred at rt for 36 h, diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The residual oil was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford **10** (0.030 g, 49%) as a colorless oil: IR (neat) 3059, 2950, 1720, 1666, 1603, 1494, 1455, 1438, 1410, 1310, 1281, 1194, 1111 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2 H), 7.89 (ddd, *J* = 11.8, 8.2, 1.5 Hz, 2 H), 7.73 (ddd, *J* = 11.8, 8.3, 1.3 Hz, 2 H), 7.54-7.38 (m, 7 H), 7.32-7.18 (m, 7

H), 7.11 (d, $J = 7.8$ Hz, 2 H), 6.95 (dd, $J = 6.7$, 2.8 Hz, 2 H), 6.33 (s, 1 H, H_1), 5.88 (s, 1 H, H_9), 4.65 (ddd, $J = 14.7$, 11.1, 2.7 Hz, 1 H, H_7), 4.55 (d, $J = 9.8$ Hz, 1 H, H_5), 4.39 (ddd, $J = 15.1$, 5.1, 1.9 Hz, 1 H, H_7), 3.92 (s, 3 H, OCH_3), 3.32 (d, $J = 12.6$ Hz, 1 H, H_3), 3.02 (d, $J = 12.5$ Hz, 1 H, H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.73 (CO), 146.54, 143.57, 142.56, 137.82, 136.73, 133.10, 132.48, 132.35, 131.78, 131.38, 130.79, 129.78, 129.66, 128.73, 128.41, 128.32, 128.09, 127.07, 126.84, 126.56, 124.94, 121.32, 69.09 (C_5), 58.89 (C_4), 52.10 (OCH_3), 49.00 (C_7), 46.89 (C_3); MS (EI) *m/z* (rel. intensity) 607 (M^+, 40), 407 (70), 307 (9), 217 (18), 201 (100); HRMS (EI) calc for $C_{28}H_{24}NO_2$ ($M-C_{12}H_{10}OP$) 406.1807, found 406.1814.



11

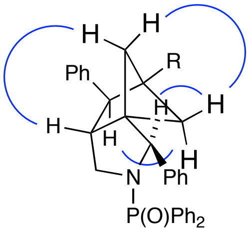
(*4S*,5R*,8Z*)-5-Cyclohexyl-6-(*N*-tosyl)-2-phenyl-8-(triisopropylsilyl)methylene-6-azaspiro[3.4]oct-1-ene (11). According to the General Protocol D, a solution of bicylobutane **2d** (0.068 g, 0.17 mmol), (3-bromoprop-1-ynyl)triisopropylsilane (0.24 g, 0.86 mmol) and Bu_4NHSO_4 (0.029 g, 0.086 mmol) in PhMe (5.0 mL) was treated with 50 % aq NaOH (5.0 mL). The reaction mixture was vigorously stirred at rt for 24 h, diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 4:1) afforded **11** (0.062 g, 62%) as a colorless foam: IR (neat), 1626, 1449, 1349, 1162 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, $J = 8.2$ Hz, 2 H), 7.36-7.30 (m, 5 H), 7.29 (m, 2 H), 6.12 (s, 1 H, H_1), 5.45 (app. t, $J = 2.1$ Hz, 1 H, H_9), 4.29 (dd, $J = 16.0$, 2.0 Hz, 1 H, H_7), 4.13 (dd, $J = 16.0$, 1.9 Hz, 1 H, H_7), 3.77 (d, $J = 3.2$ Hz, 1 H, H_5), 2.49 (s, 3 H, H_{18}), 1.96 (d, $J = 12.2$ Hz, 1 H, H_3), 1.83 (d, $J = 12.2$ Hz, 1 H, H_3), 1.77-1.68 (m, 7 H, H_{10}, H_{11}, H_{15}, H_{12} or H_{14}), 1.85-0.91 (m, 25 H, H_{14} or H_{12}, H_{13}, H_{16}, H_{17}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 146.9, 143.4, 136.1, 133.6, 129.6, 128.4, 127.7, 125.3, 124.7, 112.7, 71.1 (C_5), 57.2 (C_4), 52.8 (C_7), 47.3 (C_3), 43.6 (C_{10}), 31.1, 28.2, 26.5 (x2), 26.2, 21.5 (C_{19}), 19.0 (C_{17} or C_{18}), 18.8 (C_{18} or C_{17}), 11.8 (C_{16}); MS (EI) *m/z* (rel. intensity) 589 (M^+, 30), 506 (100), 434 (17); HRMS (EI) calc for $C_{36}H_{51}NO_2SSi$ 589.3410, found 589.3397.



12

(*2S*,5R*,6S)-3-(*N*-(*P,P*-Diphenylphosphinyl))-7-((4-methoxycarbonyl)phenyl)-2,6-diphenyl-3-azatricyclo[5.1.1.0^{1,5}]nonane (12) from (*E*)-cinnamyl bromide.** According to General Protocol C, a solution of bicyclobutane **1a** (0.030 g, 0.061 mmol), (*E*)-cinnamyl bromide (0.069 g, 0.30 mmol) and Bu_4NHSO_4 (0.010 g, 0.030 mmol) in PhMe (3.0 mL) was treated with 50% aq NaOH (3.0 mL). The reaction mixture was vigorously stirred at rt for 2 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **12** (0.034 g, 93%) as a colorless oil: IR (neat) 3059, 3027, 2949, 1720, 1611, 1495, 1451, 1438, 1310, 1280, 1196, 1111 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 10.5, 7.6 Hz, 2 H), 7.69 (d, *J* = 8.5 Hz, 2 H), 7.64 (dd, *J* = 11.5, 7.5 Hz, 2 H), 7.40-7.35 (m, 3 H), 7.21 (t, *J* = 7.7 Hz, 3 H), 7.16 (d, *J* = 8.0 Hz, 1 H), 7.11 (dd, *J* = 7.6, 2.8 Hz, 4 H), 6.95-6.94 (m, 3 H), 6.81 (d, *J* = 8.2 Hz, 2 H), 6.71 (s, 2 H), 4.50 (d, *J* = 9.8 Hz, 1 H, H_2), 3.75 (s, 3 H, OCH_3), 3.55 (t, *J* = 8.5 Hz, 1 H, H_4), 3.38 (q, *J* = 9.9 Hz, 1 H, H_4), 3.23 (d, *J* = 4.1 Hz, 1 H, H_6), 2.96 (bs, 1 H, H_5), 2.42 (dd, *J* = 9.3, 7.2 Hz, 1 H, H_{8endo}), 1.87 (d, *J* = 6.4 Hz, 1 H, H_{8exo}), 1.80 (d, *J* = 6.9 Hz, 1 H H_{9exo}), 1.68 (dd, *J* = 9.2, 7.4 Hz, 1 H, H_{9endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.14 (CO), 146.65, 141.60, 141.54, 140.93, 132.60, 132.48, 132.40, 132.28, 131.70, 129.41, 128.76, 128.60, 128.45, 128.23, 128.12, 128.04, 126.92, 126.47, 126.28, 126.06, 62.66 (C_2), 59.40 (C_7), 59.29 (d, *J* = 4.4 Hz, C_1), 54.21 (C_6), 52.07 (OCH_3), 51.34 (d, *J* = 6.0 Hz, C_5), 49.24 (C_4), 48.78 (C_8), 39.42 (C_9); MS (EI) *m/z* (rel. intensity) 609 (M^+, 61), 532 (3), 408 (33), 344 (19), 333 (21), 320 (21), 306 (27), 230 (41), 201 (100); HRMS (EI) calc for $C_{40}H_{36}NO_3P$ 609.2433, found 609.2432.

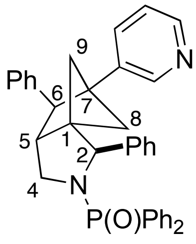
The relative configuration of **12** was assigned based on NOESY experiment, showing following nOe enhancements (copy of NOESY spectra of **12** is given at the end of Supporting Material):



12, R = *p*-$C_6H_4CO_2Me$

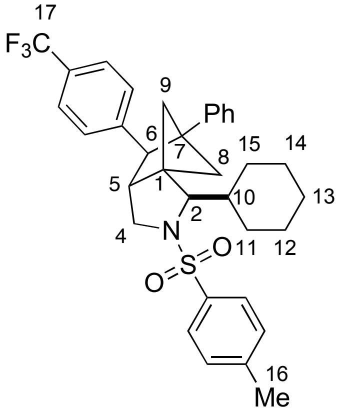
Synthesis of 12 from (*Z*)-cinnamyl bromide. According to General Protocol C, a solution of bicyclobutane **2a** (0.036 g, 0.073 mmol), freshly prepared (*Z*)-cinnamyl bromide (0.071 g, 0.36 mmol) and Bu_4NHSO_4, (0.012 g, 0.036 mmol) in PhMe (3.0 mL) and 50% aq NaOH (3.0 mL) was vigorously stirred at rt for

1 h. The reaction mixture was diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification of the residue by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **12** (0.023 g, 52%).



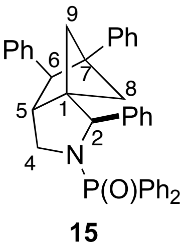
13

(2*S,5*R**,6*S**)-3-(*N*-(*P,P*-Diphenylphosphinyl))-2,6-diphenyl-7-(pyridin-3-yl)-3-azatricyclo[5.1.1.0^{1,5}]nonane (13)**. According to General Protocol C, a solution of bicyclobutane **2c** (0.051 g, 0.12 mmol), (*E*)-cinnamyl bromide (0.012 g, 0.59 mmol) and Bu_4NHSO_4 (0.020 g, 0.058 mmol) in PhMe (5.0 mL) and 50 % aq NaOH (5.0 mL) was vigorously stirred at rt for 1 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification of the residue by chromatography on SiO_2 (hexanes/EtOAc/MeOH, 1:8:1) afforded **13** (0.021 g, 32%) as a colorless oil: IR (neat) 3057, 3028, 2974, 2880, 1601, 1495, 1481, 1451, 1439, 1416, 1350, 1300, 1264, 1234, 1197, 1121 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (bs, 1 H), 8.03 (bs 1 H), 7.93-7.86 (m, 2 H), 7.67-7.60 (m, 2 H), 7.37-7.33 (m, 3 H), 7.24-7.16 (m, 4 H), 7.13-7.06 (m, 4 H), 6.97-6.90 (m, 5 H), 6.46 (dd, J = 6.1, 3.1 Hz, 2 H), 4.51 (d, J = 9.9 Hz, 1 H, H_2), 3.55 (app t, J = 8.6 Hz, 1 H, H_4), 3.38 (q, J = 9.9 Hz, 1 H, H_4), 3.21 (d, J = 4.0 Hz, 1 H, H_6), 2.97 (bs, 1 H, H_5), 2.42 (t, J = 7.0 Hz, 1 H, H_{8endo}), 1.89 (d, J = 6.9 Hz, 1 H H_{8exo}), 1.80 (d, J = 7.0 Hz, 1 H, H_{9exo}), 1.70 (t, J = 7.1 Hz, 1 H, H_{9endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.89, 147.56, 141.38, 140.59, 133.66, 132.48, 132.36, 132.28, 132.16, 131.66, 131.56, 128.61, 128.45, 128.30, 128.12, 128.05, 127.98, 127.89, 126.83, 126.54, 125.96, 122.75, 62.53 (C_2), 59.54 (d, J = 4.4 Hz, C_1), 59.51, 57.25 (C_7), 54.03 (C_6), 51.23 (d, J = 6.2 Hz, C_5), 49.07 (C_4), 48.33 (C_8), 39.41 (C_9); MS (EI) *m/z* (rel. intensity) 552 (M^+, 31), 461 (6), 434 (7), 351 (46), 320 (21), 232 (25), 201 (61), 91 (100); HRMS (EI) calc for $C_{37}H_{33}N_2OP$ 552.2331, found 552.2309.



14

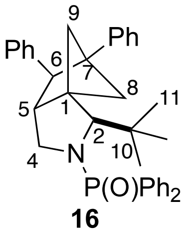
(*2R*,*5R*,*6S)-3-(*N*-Tosyl)-2-cyclohexyl-7-phenyl-6-(4-trifluoromethylphenyl)-3-azatricyclo[5.1.1.0^{1,5}]nonane (14).** According to the General Protocol D, bicyclobutane **2e** (0.038 g, 0.088 mmol), (*E*)-1-(3-bromoprop-1-enyl)-4-(trifluoromethyl)benzene (0.0.087 g, 0.44 mol) and Bu_4NHSO_4 (0.015 g, 0.044 mmol) were dissolved in PhMe (4.0 mL) and treated with 50% aq NaOH (4.0 mL). The reaction mixture was vigorously stirred at rt for 2 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc 1:4) afforded **15** (0.029 g, 59%) as a colorless oil: IR (neat) 2928, 2854, 1618, 1326, 1164 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 7.95 (d, *J* = 8.0 Hz, 2 H), 7.22-7.17 (m, 2 H), 6.98-6-94 (m, 5 H), 6.76 (d, *J* = 8.0 Hz, 2 H), 6.61-6.58 (m, 2 H), 3.79 (t, *J* = 8.0 Hz, 1 H, H_4), 3.69 (d, *J* = 5.4 Hz, 1 H, H_2), 3.07 (t, *J* = 9.7 Hz, 1 H, H_4), 2.91 (d, *J* = 4.0 Hz, 1 H, H_6), 2.76-2.73 (m, 1 H, H_5), 2.1-1.7 (m, 4 H, H_8, H_9), 1.99 (s, 3 H, CH_3), 1.46-1.25 (m, 7 H, H_{10}, H_{11}, H_{15}, H_{13}), 1.06-1.04 (m, 4 H, H_{12}, H_{14}); ^{13}C NMR (75 MHz, C_6D_6) δ 145.6, 143.0, 140.5, 135.9, 130.2, 129.5, 128.6, 128.5, 127.9, 126.7, 126.2, 125.2, 66.4 (C_2), 59.8 (C_7), 55.7, 53.2, 52.6, 51.1, 49.1, 42.9, 40.6, 30.9, 30.0, 27.0, 26.8, 21.1; MS (EI) *m/z* (rel. intensity) 579 (M$^+$, 2), 496 (100), 424 (7); HRMS (EI) calc for $C_{34}H_{36}NO_2FS$ 579.2419, found 579.2418.



15

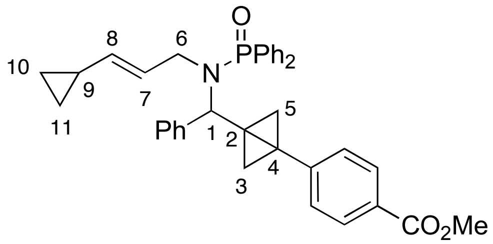
(2*S,*5R**,*6S**)-3-(*N*-(*P,P*-Diphenylphosphinyl))-2,6,7-triphenyl-3-azatricyclo[5.1.1.0^{1,5}]nonane (15).** According to the General Protocol D, bicyclobutane **2e** (0.038 g, 0.088 mmol), (*E*)-cinnamyl bromide (0.0.087 g, 0.44 mol), Bu_4NHSO_4 (0.015 g, 0.044 mmol) were dissolved in PhMe (4.0 mL) and treated with 50% aq NaOH (4.0 mL). The reaction mixture was vigorously stirred at rt for 2 h, diluted with water, and extracted (3x) with

EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc 1:4) afforded **15** (0.029 g, 59%) as a colorless oil: IR (neat) 1601, 1496, 1439, 1202, 1120, 1111 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04-7.99 (m, 2 H), 7.81-7.75 (m, 2 H), 7.52-7.48 (m, 2 H), 7.39-7.22 (m, 9 H), 7.15-7.06 (m, 6 H), 6.90-6.89 (m, 4 H), 4.63 (d, J = 9.6 Hz, 1 H, H_2), 3.68 (app. t, J = 8.4 Hz, 1 H, H_4), 3.51 (app. q, J = 9.2 Hz, 1 H, H_4), 3.34 (bs, 1 H, H_6), 3.06 (bs, 1 H, H_5), 2.52 (dd, J = 8.9, 6.9 Hz, 1 H, H_{8endo}), 1.98 (d, J = 6.3 Hz, 1 H, H_{8exo}), 1.92 (d, J = 6.7 Hz, 1 H, H_{9exo}), 1.78 (dd, J = 9.2, 7.0 Hz, 1 H, H_{9endo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.61, 141.57, 141.29, 141.09, 132.43, 132.31, 132.25, 132.12, 131.60, 128.52, 128.36, 128.29, 128.26, 127.97, 127.78, 126.62, 126.05, 125.98, 125.92, 62.60 (C_2), 59.26 (C_7), 58.91 (d, J = 4.3 Hz, C_1), 53.79 (C_6), 51.30 (d, J = 6.4 Hz, C_5), 49.09 (C_4), 48.59 (C_8), 39.22 (C_9); MS (EI) *m/z* (rel. intensity) 551 (M^+, 59), 434 (7), 350 (30), 306 (25), 230 (28), 201 (100); HRMS (EI) calc for $C_{38}H_{34}NOP$ 551.2378, found 551.2360.



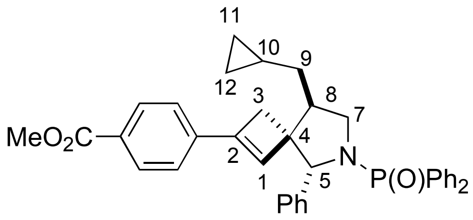
16

(*2R*,5R*,6S)-3-(*N*-(*P,P*-Diphenylphosphinyl))-2-*tert*-butyl-6,7-diphenyl-3-azatricyclo[5.1.1.0^{1,5}]nonane (16)**. Bicyclobutane **2f** (0.027 g, 0.065 mmol), (*E*)-cinnamyl bromide (0.064 g, 0.32 mmol) and Bu_4NHSO_4 (0.016 g, 0.032 mmol) were dissolved in PhMe (3.0 mL), followed by addition of 50% aq NaOH (3.0 mL). The reaction mixture was stirred at rt for 2 h, diluted with water, extracted (3x) with EtOAc and the combined organic layers were washed with water, brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexane/EtOAc, 1:4) afforded **16** (0.019 g, 54%) as a colorless oil: IR (neat) 1479, 1437, 1201, 1121, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85-7.79 (m, 4 H), 7.57-7.46 (m, 6 H), 7.12-7.05 (m, 6 H), 6.95-6.93 (m, 2 H), 6.84-6.82 (m, 2 H), 3.81 (d, J = 8.6 Hz, 1 H, H_2), 3.46-3.42 (m, 1 H, H_4), 3.23-3.22 (m, 1 H, H_5), 3.08 (d, J = 4.1 Hz, 1 H, H_6), 3.04-2.94 (m, 1 H, H_4), 2.48 (dd, J = 9.3, 7.2 Hz, 1 H, H_{8endo}), 2.24 (d, J = 6.9 Hz, 1 H, H_{8exo}), 1.81 (dd, J = 9.5, 6.8 Hz, 1 H, H_{9endo}), 1.70 (d, J = 6.5 Hz, 1 H, H_{9exo}), 0.97 (s, 9 H, H_{11}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.71, 141.22, 133.73, 132.60, 132.48, 132.34, 132.21, 131.51, 128.31, 128.27, 128.24, 128.14, 128.08, 127.95, 127.83, 127.70, 126.02, 125.97, 125.90, 67.69 (C_2), 59.36 (C_7), 56.38 (d, J = 4.3 Hz, C_1), 55.60 (C_6), 53.70 (d, J = 6.4 Hz, C_5), 51.05 (C_4), 50.11 (C_8), 41.15 (C_9), 36.57 (C_{10}), 28.41 (C_{11}); MS (EI) 475 (65), 280 (32), 201 (100); HRMS (EI) calc for $C_{32}H_{29}NOP$ (M-C_4H_9) 474.1987, found 474.2001.

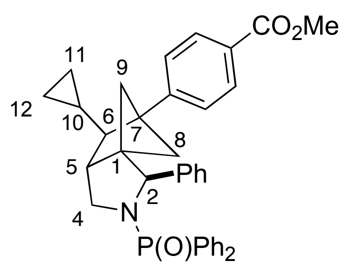


18

***N*-((3-(4-Methoxycarbonylphenyl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*N*-(3-cyclopropylallyl)-*P,P*-diphenylphosphinamide (18).** According to General Protocol C, a solution of bicyclobutane **2a** (0.078 g, 0.15 mmol), freshly prepared cyclopropylallyl bromide (0.130 g, 0.79 mmol) and Bu_4NHSO_4 (0.027 g, 0.080 mmol) in PhMe (7.0 mL) was treated with 50% aq NaOH (7.0 mL), and vigorously stirred at rt for 1 h. The reaction mixture was diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. The resulting oil was purified by chromatography on a short pad of SiO_2 (hexanes/EtOAc, 1:4) to afford crude, unstable amide **18** (0.062 g, 68%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08-7.93 (m, 6 H), 7.87-7.84 (m, 7 H), 7.54-7.53 (m, 3 H), 6.89-6.86 (m, 3 H), 5.63 (dd, *J* = 14.4, 6.7 Hz, 1 H, H_1), 4.69 (dd, *J* = 15.9, 8.9 Hz, 1 H, H_8), 4.61 (d, *J* = 9.0 Hz, 1 H, H_9), 4.02 (s, 3 H, OCH_3), 3.75-3.90 (m, 1 H, H_6), 3.57-3.50 (m, 1 H, H_6), 2.55 (d, *J* = 6.5 Hz, 1 H, H_{3exo} or H_{5exo}), 1.87 (d, *J* = 6.5 Hz, 1 H, H_{5exo} or H_{3exo}), 1.00 (s, 1 H, H_{3endo} or H_{5endo}), 0.78-0.75 (m, 4 H, H_{10}, H_{11}), 0.72 (s, 1 H, H_{5endo} or H_{3endo}), 0.31-0.30 (m, 1 H, H_9); ^{13}C NMR (75 MHz, C_6D_6) δ 166.75 (CO), 142.55, 138.99, 137.76, 134.16, 133.00, 132.89, 132.71, 132.59, 131.05, 129.49, 128.87, 128.32, 128.19, 128.00, 127.68, 127.51, 127.24, 125.84, 125.41, 62.02 (C_1), 51.40 (OCH_3), 49.79 (C_6), 37.60 (C_1 or C_5), 34.06 (C_5 or C_3), 29.66 (d, *J* = 3.8 Hz, C_1), 23.59 (C_4), 13.68 (C_9), 6.80 (C_{10} or C_{11}), 6.74 (C_{11} or C_{10}).



19a

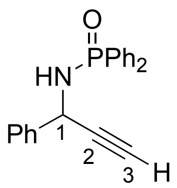


19b

(*4S*,5R*,8R)-8-Cyclopropyl-6-(*N*-(*P,P*-diphenylphosphinamido))-2-((4-methoxycarbonyl)phenyl)-5-phenyl-6-azaspiro[3.4]oct-1-ene (19a) and (*2S*,5R*,8R*)*-6-Cyclopropyl-3-(*N*-(*P,P*-diphenylphosphinamido))-7-((4-methoxycarbonyl)phenyl)-2-phenyl-3-azatricyclo[5.1.1.0^{1,5}]nonane (19b)**. A solution of amide **18** (0.054 g, 0.094 mmol) in PhMe (5.0 mL) was stirred at rt for 12 h. The solvent was removed in vacuo and the residual oil was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford **19a** (0.018 g, 33%) and **19b** (0.017 g, 31%).

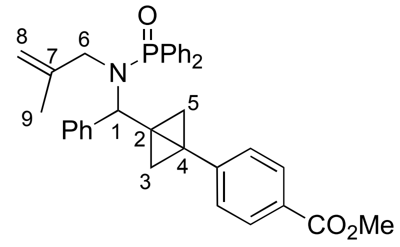
19a. Obtained as a colorless oil: IR (neat) 2919, 1720, 1604, 1438, 1279, 1196, 1109 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.99-7.91 (m, 3 H), 7.64-7.57 (m, 2 H), 7.51-7.42 (m, 4 H), 7.36-7.23 (m, 6 H), 7.16-7.08 (m, 4 H), 6.92 (s, 1 H, H$_1$), 4.51 (d, J = 11.3 Hz, 1 H, H$_5$), 3.91 (s, 3 H, OCH$_3$), 3.78-3-71 (m, 1 H, H$_7$), 3.33 (app q, J = 10.1 Hz, 1 H, H$_7$), 2.82-2.71 (m, 1 H, H$_8$), 2.42 (d, J = 13.4 Hz, 1 H, H$_3$), 2.30 (d, J = 13.5 Hz, 1 H, H$_3$), 1.22-1.19 (m, 2 H H$_9$), 0.57-0.53 (m, 1 H, H$_{10}$), 0.38-0.33 (m, 2 H, H$_{11}$ or H$_{12}$), -0.06- -0.09 (m, 2 H, H$_{12}$ or H$_{11}$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 166.81 (CO), 143.94, 143.88, 143.04, 138.02, 135.12, 133.15, 132.53, 132.40, 132.29, 132.17, 131.62, 131.42, 130.54, 129.68, 129.10, 128.60, 128.43, 127.92, 127.75, 127.30, 126.82, 124.57, 69.27 (C$_5$), 56.62 (d, J = 3.3 Hz, C$_4$), 52.08 (OCH$_3$), 51.61 (C$_7$), 42.85 (d, J = 5.6 Hz, C$_8$), 33.75 (C$_3$), 32.62 (C$_9$), 9.95 (C$_{10}$), 4.95 (C$_{11}$ or C$_{12}$), 4.22 (C$_{12}$ or C$_{11}$); MS (EI) *m/z* (rel. intensity) 573 (M$^+$, 52), 486 (27), 372 (73), 319 (19), 306 (56), 230 (31), 212 (48), 201 (100); HRMS (EI) calc for $C_{37}H_{36}NO_3P$ 573.2433, found 573.2393.

19b. Obtained as a colorless oil: IR (neat) 2949, 1721, 1610, 1438, 1278, 1179 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.03-7.96 (m, 2 H), 7.94-7.91 (m, 2 H), 7.75-7.44 (m, 3 H), 7.35-7.13 (m, 12 H), 4.50 (d, J = 9.7 Hz, 1 H, H$_2$), 3.90 (s, 3 H, OCH$_3$), 3.57 (td, J = 9.8, 2.0 Hz, 1 H, H$_4$), 3.24 (app q, J = 10.0 Hz, 1 H, H$_4$), 2.53-2.46 (m, 1 H, H$_5$), 2.27 (dd, J = 9.4, 6.8 Hz, 1 H, H$_{8endo}$), 1.82 (dd, J = 6.9, 1.5 Hz, 1 H, H$_{8exo}$), 1.79 (d, J = 6.9 Hz, H$_{9exo}$), 1.56 (dd, J = 9.5, 6.9 Hz, 1 H, H$_{9endo}$), 1.27 (dd, J = 9.6, 3.4 Hz, 1 H, H$_6$), 0.49-0.37 (m, 1 H, H$_{10}$), 0.28-0.19 (m, 1 H, H$_{11}$ or H$_{12}$), 0.06--0.05 (m, 1 H, H$_{12}$ or H$_{11}$), -0.14--0.22 (m, 1 H, H$_{11}$ or H$_{12}$), -0.49--0.57 (m, 1 H, H$_{12}$ or H$_{11}$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 167.15 (CO), 147.83, 141.60, 141.54, 133.48, 132.47, 132.34, 132.27, 132.15, 131.58, 130.84, 129.25, 128.57, 128.40, 128.02, 127.94, 127.86, 127.81, 126.64, 126.12, 125.96, 62.58 (C$_2$), 59.24 (d, J = 4.4 Hz, C$_1$), 57.71 (C$_7$), 55.34 (C$_6$), 51.97 (OCH$_3$), 50.76 (C$_5$), 48.81 (C$_4$), 46.68 (C$_8$), 39.77 (C$_9$), 12.46 (C$_{10}$), 5.53 (C$_{11}$ or C$_{12}$), 2.09 (C$_{12}$ or C$_{11}$); MS (EI) *m/z* (rel. intensity) 573 (M$^+$, 6), 436 (9), 372 (34), 320 (8), 306 (19), 218 (22), 201 (100); HRMS (EI) calc for $C_{37}H_{36}NO_3P$ 573.2433, found 573.2463



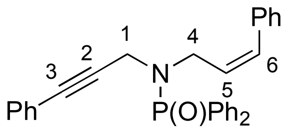
20

***N*-(1-Phenylprop-2-ynyl)-*P,P*-diphenylphosphinamide (20).** A solution of *N*-benzylidene-*P,P*-diphenylphosphinamide (12 g, 39 mmol) in dry THF (100 mL) was cooled to 0 °C and treated with HCCMgBr (160 mL, 77 mmol, 0.5 M in THF). The reaction mixture was stirred at 0 °C for 30 min, slowly quenched with sat. NH$_4$Cl, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na$_2$SO$_4$), and evaporated. The resulting solid was purified by chromatography on SiO$_2$ (hexanes/EtOAc, 1:4) to afford **20** (12 g, 90%) as a colorless solid: Mp 152.0-153.1 °C (hexanes/CH$_2$Cl$_2$); IR (KBr) 3292, 3159, 3056, 2858, 1625, 1491, 1452, 1436, 1186, 1125, 1109 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15-8.09 (m, 2 H), 7.99-7.92 (m, 2 H), 7.72-7.72 (m, 2 H), 7.66-7.35 (m, 9 H), 5.22 (td *J* = 10.1, 2.2 Hz, 1 H, H_1), 3.61 (app t, *J* = 8.9 Hz, 1 H, NH), 2.64 (d, *J* = 2.4 Hz, 1 H, H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.84, 139.78, 133.10, 132.80, 132.72, 132.67, 132.30, 132.22, 132.18, 132.05, 131.40, 131.00, 128.80, 128.76, 128.56, 128.19, 127.26, 83.53 (d, *J* = 6.0 Hz, C_2), 73.85 (C_3), 46.58 (C_1); MS (EI) 331 (M^+, 93), 305 (50), 277 (8), 254 (12), 201 (100), 183 (19), 155 (21), 130 (67); HRMS (EI) calc for $C_{21}H_{18}NOP$ 331.1126, found 331.1129.



21

***N*-((3-(4-Methoxycarbonylphenyl)bicyclo[1.1.0]but-1-yl)(phenyl)methyl)-*N*-(2-methylallyl)-*P,P*-diphenylphosphinamide (21).** According to General Protocol C, a solution of bicyclobutane **2a** (0.10 g, 0.20 mmol), 3-bromo-2-methylpropene (0.10 mL, 1.0 mmol) and Bu_4NHSO_4 (0.013 g, 0.10 mmol) in PhMe (10 mL) and 50% aq NaOH (10 mL) was vigorously stirred at rt for 1 h. The reaction mixture was diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated. Purification by chromatography on SiO_2 (hexanes/EtOAc, 1:4) afforded **19** (0.10 g, 90%) as a colorless oil: IR (neat) 3059, 2948, 1718, 1607, 1437, 1311, 1280, 1181, 1117 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99-7.89 (m, 6 H), 7.67 (d, *J* = 8.3 Hz, 2 H), 7.43-7.42 (m, 3 H), 7.10 (d, *J* = 7.2 Hz, 2 H), 7.01 (t, *J* = 7.6 Hz, 2 H), 6.89 (d, *J* = 7.2 Hz, 2 H), 6.63 (d, *J* = 7.2 Hz, 2 H), 4.87 (d, *J* = 6.2 Hz, 2 H, H_8), 4.38 (d, *J* = 11.7 Hz, 1 H, H_1), 3.88 (s, 3 H, OCH_3), 3.53 (dd, *J* = 16.1, 10.8 Hz, 1 H, H_6), 3.27 (dd, *J* = 16.3, 10.5 Hz, 1 H, H_6), 2.27 (d, *J* = 6.0 Hz, 1 H, H_{3exo} or H_{5exo}), 1.86 (d, *J* = 6.3 Hz, 1 H, H_{5exo} or H_{3exo}), 1.57 (s, 3 H, H_9), 0.58 (s, 1 H, H_{3endo} or H_{5endo}), 0.51 (s, 1 H, H_{5endo} or H_{3endo}); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 167.32 (CO), 142.20, 141.87, 141.82, 137.19, 137.15, 134.66, 133.67, 132.81, 132.69, 132.42, 132.30, 129.12, 128.99, 128.38, 128.17, 127.86, 127.38, 126.49, 125.25, 113.54 (C_8), 63.10 (C_1), 53.12 (C_6), 52.02 (OCH_3), 37.47 (C_3 or C_5), 34.31 (C_5 or C_3), 28.86 (d, *J* = 4.8 Hz, C_2), 23.18 (C_9), 20.60 (C_4); MS (EI) *m/z* (rel. intensity) 547 (M^+, 19), 346 (27), 319 (14), 306 (10), 272 (9), 230 (23), 215 (18), 201 (96), 183 (6), 118 (100); HRMS (EI) calc for $C_{35}H_{34}NO_3P$ 547.2276, found 547.2277.



22

***N*-Cinnamyl-*N*-(3-phenylprop-2-ynyl)-*P,P*-diphenylphosphinamide (22).** To a solution of *N*-(3-phenylprop-2-ynyl)-*N*-diphenylphosphinamide[8] (0.050 g, 0.15 mmol) in PhMe (5.0 mL) was added freshly prepared (*Z*)-cinnamyl bromide (0.15 g, 0.76 mmol) followed by Bu_4NHSO_4 (0.025 g, 0.076 mmol) and 50% aq NaOH (5.0 mL). The reaction mixture was vigorously stirred at rt for 1 h, diluted with water and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4) and evaporated. The crude oil was purified by chromatography on SiO_2 (hexanes/EtOAc, 1:4) to afford **21** (0.046 g, 67%) as a colorless oil: IR (neat) 3056, 1598, 1490, 1439, 1357, 1203, 1122, 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.7, 4.2 Hz, 6 H), 7.61-7.51 (m, 9 H), 7.40-7.25 (m, 5 H), 6.74 (d, *J* = 11.6 Hz, 1 H, H_6), 5.94 (td, *J* = 12.1, 5.9 Hz, 1 H, H_5), 4.18 (dd, *J* = 9.0, 7.7 Hz, 2 H, H_1), 4.08 (d, *J* = 9.7 Hz, 2 H, H_4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.30, 132.68, 132.44, 132.31, 132.11, 131.97, 131.93, 131.64, 130.40, 128.72, 128.65, 128.48, 128.14, 128.10, 128.06, 128.03, 126.92, 122.67, 85.06 (d, *J* = 6.7 Hz, C_2), 84.39 (C_3), 43.93 (d, *J* = 3.0 Hz, C_4), 36.30 (d, *J* = 5.3 Hz, C_1); MS (EI) *m/z* (rel. intensity) 447 (M^+, 12), 446 (29), 332 (29), 246 (21), 230 (10), 217 (7), 210 (100); HRMS (EI) calc for $C_{30}H_{25}NOP$ (M-H) 446.1674, found 446.1661.

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8. Prepared by the reaction of $Ph_2P(O)Cl$ with propargyl amine, followed by Sonogashira coupling with iodobenzene.

NOESY spectrum of cpd 12

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F2HI               95.68 Hz
F1PLO              5.089 ppm
F1LO             2545.37 Hz
F1PHI              1.100 ppm
F1HI              549.98 Hz
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F2HZCM         154.41373 Hz/cm
F1PPMCM          0.26598 ppm/cm
F1HZCM         133.02550 Hz/cm
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