Three-Component Aldimine Addition — Cyclopropanation.  
An Efficient New Methodology for Amino Cyclopropane Synthesis

Peter Wipf,* Christopher Kendall, and Corey R. J. Stephenson
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Experimental: In a typical protocol, a suspension of 390 mg (1.51 mmol) of Cp₂ZrHCl in 2 mL of CH₂Cl₂ was treated at room temperature with 190 mL (1.65 mmol) of 1-hexyne. After 2 min, the yellow solution was cooled to −78 °C and treated with 750 mL (1.50 mmol) of a 2.0 M solution of dimethylzinc in toluene. The resulting yellow solution was warmed to room temperature over a period of 5 min, and a solution of 153 mg (0.501 mmol) of imine 2 in 2 mL of CH₂Cl₂ was added. The reaction mixture was heated at reflux for 1 h, cooled to room temperature, treated with 200 mL (2.48 mmol) of CH₂I₂ and heated at reflux for an additional 2 h. The solution was quenched with saturated NH₄Cl, poured into EtOAc, filtered through Celite, washed with H₂O, saturated NaHCO₃ and brine, dried (MgSO₄), filtered through a pad of florisil, and concentrated in vacuo. The residue was chromatographed on deactivated SiO₂ (1:9, hexanes/EtOAc containing 1% Et₃N) to yield 149 mg (74%) of 3 as a colorless solid.

Experimental part. ¹H and ¹³C NMR spectra for all new compounds. X-ray structure of the para-nitrobenzoyl derivative of 25.
General. All moisture sensitive reactions were performed using syringe-septum cap techniques under an N\textsubscript{2} atmosphere and all glassware was dried in an oven at 140°C for 2 h prior to use. Reactions carried out at -78°C employed a CO\textsubscript{2}-acetone bath. THF was distilled over sodium / benzophenone ketyl, and CH\textsubscript{3}Cl and toluene were distilled from CaH\textsubscript{2}. Dimethylzinc was purchased from Aldrich Company. Zirconocene hydrochloride\textsuperscript{1} and all imines\textsuperscript{2} were prepared according to literature procedures.

Reactions were monitored by TLC, and visualization was accomplished with a 254 nm UV light and by staining with a PMA solution (5 g of phosphomolybdic acid in 100 mL of 95% EtOH) or a p-anisaldehyde solution (2.5 mL of p-anisaldehyde, 2 mL of AcOH, and 3.5 mL of conc. H\textsubscript{2}SO\textsubscript{4} in 100 mL of 95% EtOH). Flash chromatography on SiO\textsubscript{2} or deactivated SiO\textsubscript{2} (1% Et\textsubscript{3}N 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. \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were obtained on a Bruker Avance 300 instrument in CDCl\textsubscript{3}. Chemical shifts were reported in parts per million with the residual solvent peak used as an internal standard. \textsuperscript{1}H NMR spectra were run at 300 MHz and 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). \textsuperscript{13}C NMR spectra were run at 76 MHz using the proton decoupled pulse sequence with a delay of 5 seconds. Mass spectra were obtained on a Micromass Autospec double focusing instrument.

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\begin{align*}
&\text{C}_4\text{H}_9\text{NHP(O)Ph}_2 \\
&\text{(4)}
\end{align*}
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\(N-(1-\text{Phenyl-hept-2- enyl})-\text{P,P-diphenylphosphinam ide (4)}\). A suspension of 264 mg (1.02 mmol) of zirconocene hydrochloride in 2 mL of dry THF was treated at room temperature with 125 \(\mu\)L (1.09 mmol) of 1-hexyne. After 5 min, the green solution was cooled to -78 °C and treated with 500 \(\mu\)L (1.00 mmol) of dimethylzinc (2.0 M solution in toluene). The resulting orange solution was warmed to room temperature over a period of 5 min, and a solution of 152 mg (0.498 mmol) of imine 2 in 2 mL of dry THF was added in one portion. The reaction mixture was heated to 40 °C for 3 h, cooled to room temperature, quenched with AcOH, poured into EtOAc, filtered through a pad of florisoris, washed with saturated NaHCO\textsubscript{3} and brine, dried (MgSO\textsubscript{4}), and concentrated in vacuo. The residue was chromatographed on deactivated SiO\textsubscript{2} (1:9, hexanes/EtOAc containing 1% Et\textsubscript{3}N) to yield 127 mg (65%) of 4 as a colorless solid; mp 139-140 °C (EtOAc/hexane); IR (KBr) 3127, 2952, 2922, 2859, 1456, 1437, 1194, 1182, 1121, 1109, 722, 695 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 8.00-7.93 (m, 2 H), 7.89-7.82 (m, 2 H), 7.55-7.23 (m, 11 H), 5.69 (ddt, 1 H, \(J = 15.3, 6.2, 1.2\) Hz), 5.53 (dt, 1 H, \(J = 15.3, 6.6, 1.1\) Hz), 4.83 (td, 1 H, \(J = 9.4, 6.4\) Hz), 3.34 (dd, 1 H, \(J = 9.4, 6.2\) Hz), 2.01 (q, 2 H, \(J = 6.4\) Hz), 1.34-1.26 (m, 4 H), 0.90 (t, 3 H, \(J = 7.0\) Hz); \textsuperscript{13}C NMR \(\delta\) 143.03, 142.96, 133.73, 133.39, 132.45, 132.29, 132.17, 132.06, 132.01, 131.67, 128.44, 128.37, 128.21, 127.10, 126.92, 56.87, 31.77, 31.12, 22.19, 13.88; EIMS m/z 389 (M\textsuperscript{+}, 15), 332 (19), 306 (25), 216 (98), 201 (92), 188 (100), 172 (35), 143 (55), 129 (87), 115 (35), 91 (33), 77 (60); HRMS (EI) m/z calcd for C\textsubscript{25}H\textsubscript{28}NOP 389.1909, found 389.1906.

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\textsuperscript{1} S. L. Buchwald, S. J. LaMaire, R. B. Nielsen, B. T. Watson, S. M. King \textit{Org. Synth.} \textbf{1993}, \textit{71}, 77

\textsuperscript{2} W. B. Jennings, C. J. Lovely \textit{Tetrahedron} \textbf{1991}, \textit{47}, 5561
N-{(R*)-[(1R*,2R*)-2-Butylocyclopropyl](phenyl)methyl}-P,P-diphenylphosphinamide (3). General Protocol.
A suspension of 390 mg (1.51 mmol) of zirconocene hydrochloride in 2 mL of dry CH₂Cl₂ was treated at room temperature with 190 μL (1.65 mmol) of 1-hexyne. After 2 min, the yellow solution was cooled to −78 °C and treated with 750 μL (1.50 mmol) of dimethylzinc (2.0 M solution in toluene). The resulting yellow solution was warmed to room temperature over a period of 5 min, and a solution of 153 mg (0.501 mmol) of imine 2 in 2 mL of dry CH₂Cl₂ was added in one portion. The reaction mixture was heated to reflux for 1 h, cooled to room temperature, treated with 200 μL (2.48 mmol) of diiodomethane and heated at reflux for a further 2 h. The solution was quenched with saturated NH₄Cl, poured into EtOAc, filtered through celite, washed with H₂O, saturated NaHCO₃ and brine, dried (MgSO₄), filtered through a pad of florisil, and concentrated in vacuo. The residue was chromatographed on deactivated SiO₂ (1:9, hexanes/EtOAc containing 1% Et₃N) to yield 149 mg (74%) of 3 as a colorless solid: mp 150-151 °C (EtOAc/hexane); IR (KBr) 3185, 3059, 2957, 2923, 2856, 1456, 1437, 1183, 1123, 1110, 1086, 1065, 724, 698 cm⁻¹; ¹H NMR δ 7.97-7.90 (m, 2 H), 7.80-7.73 (m, 2 H), 7.53-7.40 (m, 4 H), 7.36-7.22 (m, 7 H), 3.80 (q, 1 H, J = 8.9 Hz), 3.33 (t, 1 H, J = 6.6 Hz), 1.36-1.29 (m, 5 H), 1.10-0.98 (m, 2 H), 0.89 (t, 3 H, J = 7.0 Hz), 0.78-0.72 (m, 1 H), 0.41 (dt, 1 H, J = 8.6, 4.8 Hz), 0.26 (dt, 1 H, J = 8.3, 5.0 Hz); ¹³C NMR δ 143.37, 143.30, 134.30, 133.15, 132.60, 132.42, 132.29, 131.96, 131.84, 131.71, 131.67, 131.57, 131.54, 131.43, 128.42, 128.29, 128.23, 128.09, 127.74, 127.62, 126.96, 126.77, 58.84, 33.22, 31.69, 26.85, 26.79, 22.52, 18.92, 14.10, 10.61; EIMS m/z 403 (M⁺, 7), 360 (3), 319 (17), 306 (81), 256 (27), 201 (100), 91 (36), 77 (37); HRMS (EI) m/z calcld for C₂₄H₂₅NOP 403.2065, found 403.2066.

N-{(R*)-[(1R*,2R*)-1,2-Dietylocyclopropyl](phenyl)methyl}-P,P-diphenylphosphinamide (9). According to the General Protocol, 390 mg (1.51 mmol) of zirconocene hydrochloride, 190 μL (1.67 mmol) of 3-hexyne, 750 μL (1.50 mmol) of dimethylzinc (2.0 M solution in toluene), 153 mg (0.501 mmol) of imine 2 (3 h reaction time), and 200 μL (2.48 mmol) of diiodomethane (12 h reaction time) afforded 93 mg (46%) of 9 as a colorless solid: mp 136-137 °C (EtOAc/hexane); IR (KBr) 3188, 3058, 2961, 2930, 2870, 1453, 1426, 1185, 1123, 1109, 1094, 1063, 752, 720, 699 cm⁻¹; ¹H NMR δ 7.91-7.84 (m, 2 H), 7.76-7.68 (m, 2 H), 7.55-7.40 (m, 4 H), 7.34-7.21 (m, 5 H), 7.19-7.16 (m, 2 H), 4.24 (t, 1 H, J = 10.7 Hz), 3.23 (dd, 1 H, J = 10.0, 7.0 Hz), 1.69 (dq, 1 H, J = 14.8, 7.4 Hz), 1.50 (dq, 1 H, J = 13.9, 6.9 Hz), 1.31-1.16 (m, 2 H), 0.97-0.84 (m, 1 H), 0.94 (t, 3 H, J = 7.3 Hz), 0.87 (t, 3 H, J = 7.3 Hz), 0.66 (tt, 1 H, J = 8.5, 6.1 Hz), -0.03 (dd, 1 H, J = 5.5, 4.8 Hz); ¹³C NMR δ 142.31, 142.25, 134.18, 132.79, 132.60, 132.47, 131.92, 131.79, 131.72, 131.69, 131.57, 131.53, 131.06, 128.47, 128.31, 128.15, 127.99, 127.20, 126.81, 58.08, 30.69, 30.62, 23.69, 22.92, 21.95, 14.36, 14.07, 11.57; EIMS m/z 403 (M⁺, 7), 306 (46), 284 (59), 218 (45), 201 (100), 157 (17), 146 (15), 129 (19), 91 (10), 77 (16); HRMS (EI) m/z calcld for C₂₄H₂₅NOP 403.2065, found 403.2075.
N-\{(R\*)-[(1R*,2R*)-2-2-[(tert-Butyldiphenylsilyl)oxy]ethyl)cyclopropyl](phenyl)methyl\}-P,P-
diphenylphosphinamide (11). According to the General Protocol, 390 mg (1.51 mmol) of zirconocene hydrochloride, 531 mg (1.72 mmol) of alkyne 10,\(^3\) 750 μL (1.50 mmol) of dimethylzinc (2.0 M solution in toluene), 153 mg (0.501 mmol) of imine 2 (2 h reaction time), and 200 μL (2.48 mmol) of diiodomethane (12 h reaction time) afforded 216 mg (68%) of 11 as a colorless oil: IR (neat) 3189, 3070, 2930, 2857, 1456, 1437, 1428, 1390, 1191, 1123, 1068, 1028, 823, 722, 694 cm\(^{-1}\); \(^1\)H NMR δ 7.95-7.87 (m, 2 H), 7.81-7.66 (m, 6 H), 7.49-7.37 (m, 10 H), 7.34-7.26 (m, 7 H), 3.87-3.70 (m, 3 H), 3.43 (dd, 1 H, J = 8.7, 5.7 Hz), 1.59 (dq, 1 H, J = 13.5, 6.8 Hz), 1.39 (dq, 1 H, J = 13.7, 6.8 Hz), 1.08 (s, 9 H), 1.08-1.01 (m, 1 H), 0.87-0.76 (m, 1 H), 0.44 (dt, 1 H, J = 8.6, 4.9 Hz), 0.30 (dt, 1 H, J = 8.4, 5.1 Hz); \(^13\)C NMR δ 143.22, 143.15, 135.50, 135.47, 134.11, 133.93, 133.89, 133.05, 132.38, 132.25, 131.88, 131.75, 131.65, 131.62, 131.52, 131.49, 131.33, 129.45, 128.40, 128.20, 127.53, 127.50, 126.94, 126.70, 63.98, 58.54, 36.40, 26.83, 26.57, 26.51, 19.07, 15.53, 10.20; EIMS m/z 629 (M\(^+\), 3), 573 (100), 398 (28), 319 (17), 306 (92), 256 (17), 218 (18), 201 (94), 183 (20); HRMS (EI) m/z calcd for C\(_{60}\)H\(_{44}\)NO\(_{3}\)PSi 629.2879, found 629.2887.

O-Triisopropylsilyl-4-\{(1R*,2R*)-2-\{(R\*)-
[(diphenylphosphoryl)amino](phenyl)methyl\}cyclopropyl\}butanamide (13). According to the General Protocol, 390 mg (1.51 mmol) of zirconocene hydrochloride, 405 mg (1.51 mmol) of alkyne 12, 750 μL (1.50 mmol) of dimethylzinc (2.0 M solution in toluene), 153 mg (0.501 mmol) of imine 2 (1 h reaction time), and 160 μL (1.99 mmol) of diiodomethane (1.5 h reaction time) afforded 217 mg (73%) of 13 as a colorless oil: IR (neat) 3185, 3059, 2945, 2867, 1717, 1457, 1437, 1257, 1186, 1123, 1110, 1067, 1018, 884, 748, 723, 697 cm\(^{-1}\); \(^1\)H NMR δ 7.97-7.90 (m, 2 H), 7.80-7.72 (m, 2 H), 7.51-7.40 (m, 4 H), 7.35-7.24 (m, 7 H), 3.78 (q, 1 H, J = 9.0 Hz), 3.49 (dd, 1 H, J = 8.8, 6.0 Hz), 2.36 (t, 2 H, J = 7.4 Hz), 1.70 (qn, 2 H, J = 7.4 Hz), 1.46-1.24 (m, 4 H), 1.17-1.00 (m, 2 H), 1.09 (d, 18 H, J = 7.3 Hz), 0.80-0.69 (m, 1 H), 0.43 (dt, 1 H, J = 8.5, 4.9 Hz), 0.28 (dt, 1 H, J = 8.4, 5.0 Hz); \(^13\)C NMR δ 173.82, 143.28, 143.20, 134.24, 133.03, 132.54, 132.26, 131.92, 131.80, 131.68, 131.64, 131.56, 131.52, 131.31, 128.43, 128.25, 128.08, 126.98, 126.67, 58.76, 35.48, 32.84, 26.65, 25.94, 24.97, 18.49, 17.73, 11.81, 10.58; EIMS m/z 589 (M\(^+\), 9), 546 (53), 388 (17), 329 (100), 319 (20), 306 (56), 256 (20), 216 (76), 201 (73), 131 (30), 99 (38), 91 (23), 77 (40); HRMS (EI) m/z calcd for C\(_{53}\)H\(_{44}\)NO\(_{3}\)PSi 589.3141, found 589.3131.

O-Ethyl-N-2-\{(1R*,2R*)-2-\{(R\*)-\[(diphenylphosphoryl)amino](phenyl)methyl\}cyclopropyl\}ethyl-N-(4-
methylphenyl)sulfonylcarbamate (15). According to the General Protocol, 390 mg (1.51 mmol) of zirconocene hydrochloride, 495 mg (1.68 mmol) of alkyne 14,\(^4\) 750 μL (1.50 mmol) of dimethylzinc (2.0 M solution in

\(^3\) P. Wipf, W. Xu *Org. Synth.* 1997, 74, 205

toluene), 153 mg (0.501 mmol) of imine 2 (2 h reaction time), and 200 µL (2.48 mmol) of diiodomethane (12 h reaction time) afforded 138 mg (45%) of 15 as a colorless oil: IR (neat) 3344, 3187, 3060, 2990, 1731, 1438, 1370, 1353, 1274, 1187, 1170, 1123, 1089, 728, 700, 675 cm⁻¹; ¹H NMR δ 7.98-7.91 (m, 2 H), 7.83-7.74 (m, 4 H), 7.53-7.42 (m, 4 H), 7.38-7.25 (m, 9 H), 4.11 (q, 2 H, J = 7.1 Hz), 3.90 (t, 2 H, J = 7.7 Hz), 3.85-3.72 (m, 1 H), 3.51 (dd, 1 H, J = 8.5, 6.3 Hz), 2.46 (s, 3 H), 1.77 (dq, 1 H, J = 13.7, 6.9 Hz), 1.53 (dq, 1 H, J = 13.7, 7.7 Hz), 1.20-1.11 (m, 1 H), 1.17 (t, 3 H, J = 7.1 Hz), 0.82-0.71 (m, 1 H), 0.47 (dt, 1 H, J = 8.6, 5.2 Hz), 0.39 (dt, 1 H, J = 8.4, 5.1 Hz); ¹³C NMR δ 152.22, 144.31, 143.05, 142.98, 136.75, 134.18, 133.01, 132.39, 132.27, 131.93, 131.80, 131.63, 131.60, 131.29, 129.21, 128.51, 128.32, 128.22, 128.15, 127.97, 127.46, 127.09, 126.75, 63.15, 58.61, 46.96, 34.06, 26.53, 26.47, 21.58, 16.11, 13.96, 10.39; EIMS m/z 616 (M⁺, 2), 461 (8), 415 (10), 360 (9), 319 (17), 306 (100), 256 (15), 243 (24), 216 (23), 201 (89), 155 (39), 91 (52), 77 (28); HRMS (EI) m/z calcd for C₃₅H₃₇N₂O₃PS 616.2161, found 616.2154.

N-((R*)-((1R*,2R*)-2-Butylecyclopropyl)[4-carboxymethylphenyl]methyl)-P,P-diphenylphosphinamide (17). According to the General Protocol, 0.21 g (0.81 mmol) of zirconocene hydrochloride, 95 µL (0.83 mmol) of 1-hexyne, 0.41 mL (0.82 mmol) of Me₂Zn (2.0 M solution in toluene), 0.10 g (0.28 mmol) of imine 16 (1 h reaction time), and 0.11 mL (1.4 mmol) of diiodomethane (1 h reaction time) afforded 88 mg (69%) of 17 as a colorless solid: mp 141-143 °C (EtOAc/hexanes); IR (KBr) 3172, 2954, 2921, 1720, 1437, 1275, 1181, 1107 cm⁻¹; ¹H NMR δ 7.98-7.88 (m, 4 H), 7.76-7.69 (m, 2 H), 7.69-7.56 (m, 4 H), 7.34-7.28 (m, 4 H), 3.93 (s, 3 H), 3.83 (q, 1 H, J = 8.8 Hz), 3.46 (dd, 1 H, J = 8.4, 5.7 Hz), 1.4-1.2 (m, 5 H), 1.17-1.09 (m, 1 H), 1.04-0.95 (m, 1 H), 0.91-0.86 (m, 3 H), 0.80-0.76 (m, 1 H), 0.42 (dt, 1 H, J = 8.5, 4.8 Hz), 0.28 (dt, 1 H, J = 8.3, 5.0 Hz); ¹³C NMR δ 167.14, 148.81, 148.75, 134.15, 133.12, 132.60, 132.47, 132.17, 132.12, 132.09, 132.04, 131.97, 131.93, 131.39, 129.85, 129.03, 128.78, 128.61, 128.55, 128.38, 127.01, 58.78, 52.28, 33.46, 31.96, 27.11, 27.04, 22.75, 19.20, 14.33, 10.98; EIMS m/z 461 (M⁺, 13), 364 (100), 256 (37), 218 (17), 201 (91), 164 (9); HRMS (EI) m/z calcd for C₃₅H₃₇N₂O₃PS 461.2120, found 461.2134.

N-((R*)-((1R*,2R*)-2-2-[[(tert-Butyldiphenylsilyl)oxy]ethyl]cyclopropyl)[4-carboxymethylphenyl]methyl)-P,P-diphenylphosphinamide (18). According to the General Protocol, 213 mg (0.826 mmol) of zirconocene hydrochloride, 255 mg (0.827 mmol) of alkylene 10, 410 µL (0.820 mmol) of Me₂Zn (2.0 M solution in toluene), 100 mg (0.275 mmol) of imine 16 (1 h reaction time), and 110 µL (1.37 mmol) of diiodomethane (1 h reaction time) afforded 155 mg (84%) of 18 as a colorless foam: IR (neat) 3179, 2930, 2858, 1721, 1435, 1280, 1187, 1109 cm⁻¹; ¹H NMR δ 7.94 (d, 2 H, J = 8.3 Hz), 7.87-7.80 (m, 2 H), 7.71-7.67 (m, 1 H), 7.65-7.59 (m, 5 H), 7.44-7.32 (m, 11 H), 7.29-7.23 (m, 4 H), 3.92 (s, 3 H), 3.84-3.68 (m, 3 H), 3.43 (dd, 1 H, J = 8.6, 5.3 Hz), 1.49-1.40 (m, 2 H), 1.02 (s, 9 H), 1.02-0.94 (m, 1 H), 0.84-0.78 (m, 1 H), 0.42 (dt, 1 H, J = 8.6, 5.0 Hz), 0.28 (dt, 1 H, J = 8.3, 5.2 Hz); ¹³C
N-{[(R*)-[(1R*,2R*)-2-Butylcyclopropyl](4-chlorophenyl)methyl]}-P,P-diphenylphosphinamide (20). According to the General Protocol, 228 mg (0.884 mmol) of zirconocene hydrochloride, 101 μL (0.879 mmol) of 1-hexyne, 440 μL (0.880 mmol) of Me₂Zn (2.0 M solution in toluene), 100 mg (0.294 mmol) of imine 19 (1 h reaction time), and 120 μL (1.49 mmol) of diiodomethane (12 h reaction time) afforded 84 mg (65%) of 20 as a colorless solid: mp 148-149 °C (EtOAc/hexanes); IR (KBr) 3434, 3179, 2920, 1490, 1460, 1436, 1184 cm⁻¹; ¹H NMR δ 7.96-8.79 (m, 2 H), 7.78-7.71 (m, 2 H), 7.57-7.43 (m, 4 H), 7.38-7.19 (m, 6 H), 3.81-3.72 (m, 1 H), 3.34 (dd, 1 H, J = 8.3, 5.6 Hz), 1.4-1.25 (m, 5 H), 1.15-1.08 (m, 1 H), 1.02-0.95 (m, 1 H), 0.92-0.87 (m, 3 H), 0.79-0.71 (m, 1 H), 0.39 (dt, 1 H, J = 8.5, 4.8 Hz), 0.28 (dt, 1 H, J = 8.3, 5.1 Hz); ¹³C NMR δ 142.09, 142.03, 134.09, 133.24, 132.72, 132.44, 132.31, 132.09, 131.96, 131.90, 131.78, 131.75, 131.52, 128.62, 128.43, 128.38, 128.26, 58.39, 33.36, 31.86, 26.90, 26.82, 22.65, 19.09, 14.24, 10.86; EIMS m/z 437 (M⁺, 4), 340 (54), 256 (17), 201 (100), 77 (21); HRMS (EI) m/z calcd for C₂₉H₂₃NO₄PSi (M-C₆H₅) 630.2230, found 630.2225.

N-{[(R*)-[(1R*,2R*)-2-Butylcyclopropyl](3-methoxyphenyl)methyl]}-P,P-diphenylphosphonamide (22). According to the General Protocol, 346 mg (1.34 mmol) of zirconocene hydrochloride, 154 μL (1.34 mmol) of 1-hexyne, 670 μL (1.34 mmol) of Me₂Zn (2.0 M solution in toluene), 150 mg (0.447 mmol) of imine 21 (2 h reaction time), and 180 μL (2.24 mmol) of diiodomethane (4 h reaction time) afforded 99 mg (51%) of 22 as a colorless solid: mp 115-117 °C (EtOAc/hexanes); IR (KBr) 3433, 3164, 2922, 1599, 1461, 1435, 1184 cm⁻¹; ¹H NMR δ 7.91 (ddd, 2 H, J = 11.9, 7.9, 1.4 Hz), 7.78-7.71 (m, 2 H), 7.51-7.40 (m, 4 H), 7.35-7.27 (m, 2 H), 7.21 (t, 1 H, J = 7.9 Hz), 6.86 (d, 1 H, J = 7.7 Hz), 6.79-6.75 (m, 2 H), 3.78 (s, 3 H), 3.78-3.69 (m, 1 H), 3.30 (dd, 1 H, J = 8.6, 5.9 Hz), 1.35-1.25 (m, 5 H), 1.07-0.94 (m, 2 H), 0.89-0.84 (m, 3 H), 0.78-0.72 (m, 1 H), 0.40 (dt, 1 H, J = 9.4, 4.8 Hz), 0.24 (dt, 1 H, J = 10.9, 5.9 Hz); ¹³C NMR δ 159.62, 145.32, 145.24, 134.50, 133.38, 132.80, 132.64, 132.58, 132.51, 132.16, 132.04, 131.94, 131.90, 131.78, 131.75, 131.66, 129.47, 128.67, 128.60, 128.54, 128.50, 128.47, 128.40, 128.37, 128.30, 59.10, 55.35, 33.44, 31.91, 26.97, 26.91, 22.74, 19.17, 14.32, 10.96; EIMS m/z 433 (M⁺, 5), 390 (3), 376 (5), 349 (27), 336 (69), 256 (20), 232 (28), 201 (72), 86 (100), 69 (57); HRMS (EI) m/z calcd for C₂₂H₂₉NO₂P 433.2171, found 433.2165.
N-{1-(R*)-[(1R*,2R*)-2-Butylcyclopropyl]-3-phenylprop-2-ynyl]-P,P-diphenylphosphonamide (24). According to the General Protocol, 392 mg (1.51 mmol) of zirconocene hydrochloride, 190 µL (1.65 mmol) of 1-hexyne, 750 µL (1.50 mmol) of Me₂Zn (2.0 M solution in toluene), 168 mg (0.510 mmol) of imine 23 (3 h reaction time), and 200 µL (2.48 mmol) of diiodomethane (12 h reaction time) afforded 96 mg (44%) of 24 as a colorless oil: ¹H NMR δ 8.08-8.01 (m, 2 H), 7.95-7.88 (m, 2 H), 7.54-7.28 (m, 11 H), 4.27 (td, 1 H, J = 9.5, 5.5 Hz), 3.32 (dd, 1 H, J = 10.0, 7.7 Hz), 1.38-1.09 (m, 8 H), 0.87 (t, 3 H, J = 7.0), 0.71 (dt, 1 H, J = 9.0, 4.5 Hz), 0.33 (dt, 1 H, J = 8.2, 4.9 Hz).

N-[(R*)-[(1R*,2R*)-2-Butylcyclopropyl][phenyl]methyl]-4-benzamide (25). A solution of 91.0 mg (0.226 mmol) of 3 in 5 mL of a 1 N solution of HCl (g) in MeOH was stirred at room temperature for 3 h, basified with 5% NaOH, and extracted with CH₂Cl₂. The organic layer was dried (MgSO₄), concentrated in vacuo, dissolved in 3 mL of CH₂Cl₂, and treated with 205 mg (0.906 mmol) of benzoic anhydride, 10.0 mg (0.0819 mmol) of dimethylaminopyridine, and 240 µL (1.38 mmol) of diisopropylethylamine. The reaction mixture was stirred at room temperature for 1 h, poured into EtOAc, washed with H₂O and brine, dried (MgSO₄), and concentrated in vacuo. The residue was purified on SiO₂ (4:1, hexanes/EtOAc) to yield 69 mg (99%) of 25 as a colorless solid: mp 115-116 °C (hexane); IR (KBr) 3354, 2955, 2921, 2954, 1632, 1524, 1490, 701 cm⁻¹; ¹H NMR δ 7.85-7.81 (m, 2 H), 7.57-7.28 (m, 8 H), 6.54 (d, 1 H, J = 7.9 Hz), 4.72 (t, 1 H, J = 8.3 Hz), 1.44-1.32 (m, 5 H), 1.25-1.20 (m, 1 H), 1.05-0.98 (m, 2 H), 0.88 (t, 3 H, J = 7.1 Hz), 0.65 (dt, 1 H, J = 8.2, 4.9 Hz), 0.49 (dt, 1 H, J = 8.0, 5.3 Hz); ¹³C NMR δ 166.60, 141.99, 134.67, 131.41, 128.54, 128.47, 127.24, 126.88, 126.67, 57.15, 33.42, 31.86, 24.31, 22.42, 17.87, 14.05, 11.38; EIMS m/z 307 (M⁺, 19), 292 (4), 264 (6) 250 (14), 236 (16), 222 (31), 210 (40), 160 (15), 152 (22), 105 (100), 77 (53); HRMS (EI) m/z calcd for C₂₁H₂₅NO 307.1936, found 307.1935.