SUPPLEMENTARY MATERIAL

Diversity-Oriented Synthesis of Cyclopropyl 5-Azaspiroalkanes

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Experimental procedures and spectral data for all new compounds, including copies of ^1H and ^{13}C NMR spectra.

General Methods. All moisture-sensitive reactions were performed under an atmosphere of N₂ and glassware was flame dried under vacuum prior to use. DME and THF were dried by distillation over Na/Benzophenone and Et₃N and Cl(CH₂)₂Cl were dried by distillation over CaH₂. Toluene and CH₂Cl₂ were purified by filtration through activated alumina. Me₂Zn was purchased from the Aldrich Chemical Company and Cp₂ZrHCl was prepared according to a modification of a literature protocol (Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B. *Org. Synth.* **1993**, *71*, 77). 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 (NH₄)₆Mo₇O₂₄•4H₂O and 0.20 g of Ce(SO₄)₂ in 100 mL of 3.5 N H₂SO₄ solution). NMR spectra were recorded at 300 MHz/75 MHz (¹H NMR/¹³C NMR) using a Bruker AVANCE 300 MHz spectrometer at 21 °C unless stated otherwise. Chemical shifts (□) 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.

N-{[(*S*^{*})-(1*S*^{*},2*R*^{*})-2-[2-(*tert*-Butyldiphenylsilyloxy)ethyl]cyclopropyl]-[1-(2-phenylallyl)cyclopropyl]methyl}-*P,P*-diphenylphosphinamide (**3b**). To a suspension of Cp₂ZrHCl (0.35 g, 1.4 mmol) in dry CH₂Cl₂ (4.0 mL) was added a solution of *tert*-butyl(but-3-ynyloxy)diphenylsilane (0.42 g, 1.4 mmol) in dry CH₂Cl₂ (2.0 mL). The reaction mixture was stirred for 5 min, solvent was removed *in vacuo* and the residue was dissolved in (CH₂Cl)₂ (4.0 mL), cooled to -30 °C, treated with Me₂Zn (0.69 mL, 1.4 mmol, 2.0 M in toluene) and warmed to 0 °C. After addition of **2** (Ar = C₆H₅) (0.30 g, 0.91 mmol), the mixture was stirred at 0 °C for

2 h, cooled to $-30\text{ }^{\circ}\text{C}$ and treated with a solution of $\text{Zn}(\text{CH}_2\text{I})_2\cdot\text{DME}$ (3.6 mmol) in $(\text{CH}_2\text{Cl})_2$ (3.0 mL). $\text{Zn}(\text{CH}_2\text{I})_2\cdot\text{DME}$ was prepared by dropwise addition of CH_2I_2 (0.59 mL, 7.3 mmol) to a freshly prepared solution of Et_2Zn (0.45 g, 3.6 mmol) and DME (0.39 mL, 3.6 mmol) in $(\text{CH}_2\text{Cl})_2$ (3.0 mL) at $-30\text{ }^{\circ}\text{C}$ and used after stirring for 10 min. The reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$, stirred for 3 h, quenched with saturated NH_4Cl , diluted with EtOAc, and filtered through Celite/Florisil (1:1). The aqueous layer was extracted with EtOAc (2x) and the combined organic layers were washed with brine, dried (MgSO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (3:2, hexanes/EtOAc containing 1% Et_3N) to yield **3b** (0.36 g, 55%) as a colorless foam: IR (neat) 3208, 3054, 2929, 2857, 1437, 1428, 1185, 1109 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.09-7.99 (m, 4 H), 7.83-7.79 (m, 4 H), 7.41-7.38 (m, 2 H), 7.27-7.22 (m, 8 H), 7.10-7.00 (m, 7 H), 5.26 (d, $J = 1.5\text{ Hz}$, 1 H), 5.08 (bs, 1 H), 3.90-3.76 (m, 2 H), 3.09 (d, $J = 14.9\text{ Hz}$, 1 H), 2.88 (dd, $J = 9.6, 6.1\text{ Hz}$, 1 H), 2.48 (d, $J = 14.8\text{ Hz}$, 1 H), 2.37 (app. q, $J = 9.2\text{ Hz}$, 1 H), 1.89-1.78 (m, 1 H), 1.29-1.13 (m, 1 H), 1.20 (s, 9 H), 0.80-0.72 (m, 1 H), 0.53-0.43 (m, 2 H), 0.39-0.31 (m, 2 H), 0.29-0.20 (m, 2 H), 0.16-0.10 (m, 1 H); ^{13}C NMR (C_6D_6) δ 146.30, 142.51, 136.01, 135.85, 135.52, 134.16, 132.78, 132.66, 132.61, 132.48, 131.37, 129.88, 126.70, 115.06, 64.51, 61.33, 38.02, 37.36, 27.18, 24.53, 23.40, 23.34, 19.43, 14.75, 11.54, 10.78, 10.08; MS (ESI) m/z (rel. intensity) 710 ($[\text{M}+1]^+$, 100); HRMS (ESI) m/z calculated for $\text{C}_{46}\text{H}_{53}\text{NO}_2\text{PSi}$ ($\text{M}+1$) 710.3583, found 710.3563.

Methyl 3-((1*S,2*S**)-2-((*S**)-(*N*-diphenylphosphinoamino)(1-(2-phenylallyl)cyclopropyl)methyl)cyclopropyl)propanoate (3c).** To a solution of 3-(2-{*P,P*-diphenylphosphinoamino-[1-(2-phenylallyl)cyclopropyl]methyl}cyclopropyl)propionic acid

triisopropylsilyl ester¹ (90 mg, 0.14 mmol) in dry THF (2.0 mL) was added TBAF (0.21 mL, 0.21 mmol, 1.0 M in THF). The reaction mixture was stirred for 1 h, diluted with water and 10% HCl and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na₂SO₄) and concentrated. The residue was dissolved in MeOH (2.0 mL) and treated with TMSCHN₂ (0.14 mL, 0.27 mmol, 2.0 M in hexanes). The mixture was stirred for 1 h, quenched with sat. NH₄Cl and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na₂SO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (2:3, hexanes/EtOAc containing 1% v/v Et₃N) to afford **3c** (61 mg, 87%) as a colorless oil: IR (neat) 3209, 3057, 2997, 2949, 2925, 2861, 1736, 1437, 1187, 1123, 1109 cm⁻¹; ¹H NMR (C₆D₆) δ 8.11-7.98 (m, 4 H), 7.41-7.37 (m, 2 H), 7.18-7.04 (m, 9 H), 5.26 (d, *J* = 1.5 Hz, 1 H), 5.04 (bs, 1 H), 3.41 (dd, *J* = 9.6, 6.0 Hz, 1 H), 3.30 (s, 3 H), 3.01 (d, *J* = 14.8 Hz, 1 H), 2.59 (d, *J* = 14.8 Hz, 1 H), 2.41-2.28 (m, 3 H), 1.64-1.52 (m, 1 H), 1.47-1.33 (m, 1 H), 0.93-0.83 (m, 1 H), 0.66-0.57 (m, 1 H), 0.47-0.43 (m, 1 H), 0.39-0.25 (m, 4 H), 0.14 (dt, *J* = 8.3, 5.0 Hz, 1 H); ¹³C NMR (C₆D₆) δ 173.89, 146.05, 142.51, 136.16, 135.63, 134.48, 133.93, 132.92, 132.79, 132.64, 132.52, 131.44, 131.40, 131.35, 128.52, 128.47, 127.59, 126.66, 115.00, 61.30, 50.92, 37.97, 34.08, 29.53, 24.35, 24.27, 24.09, 24.04, 17.59, 12.26, 10.43, 10.00; MS (EI) *m/z* (rel. intensity) 513 (M⁺, 32), 356 (29), 296 (34), 218 (100), 201 (75); HRMS (EI) *m/z* calculated for C₃₂H₃₆NO₃P 513.2433, found 513.2438.

***N*-[1-(2-Phenylallyl)cyclopropylmethyl]-*P,P*-diphenylphosphinamide (6).** To a solution of **4²** (65 mg, 0.20 mmol) at 0 °C in (CH₂Cl)₂ (1.0 mL) was added Me₂Zn (98 μ L, 0.20 mmol, 2.0 M in toluene). The reaction mixture was warmed to r.t., stirred for 1 h, cooled to -20 °C,

¹ Wipf, P.; Stephenson, C. R. J.; Okumura, K. *J. Am. Chem. Soc.* **2003**, *125*, 14694-14695.

transferred via canula to a mixture of $\text{Zn}(\text{CH}_2\text{I})_2$ (0.59 mmol) in $(\text{CH}_2\text{Cl})_2$ (1.0 mL), warmed to r.t. and stirred for 4 h. The solution was quenched with saturated NH_4Cl , diluted with EtOAc and filtered through Celite/Florisil (1:1). The aqueous layer was extracted with EtOAc (2x) and the combined organic layers were washed with brine, dried (MgSO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (2:3, hexanes/EtOAc containing 1% Et_3N) to yield **6** (45 mg, 61%) as a colorless oil: IR (neat) 3203, 2955, 2924, 2854, 1437, 1186, 1162, 1123, 1108 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.04-7.96 (m, 4 H), 7.35-7.28 (m, 2 H), 7.13-7.04 (m, 9 H), 5.21 (d, $J = 1.6$ Hz, 1 H), 5.06 (d, $J = 1.3$ Hz, 1 H), 2.88-2.74 (m, 3 H), 2.58 (s, 2 H), 0.21-0.13 (m, 4 H); ^{13}C NMR (C_6D_6) δ 146.61, 142.69, 135.21, 133.52, 132.69, 132.57, 131.50, 131.46, 126.72, 114.66, 47.75, 39.16, 20.44, 20.33, 10.90; MS (EI) m/z (intensity) 387 (M^+ , 4), 359 (5), 318 (5), 230 (43), 218 (93), 201 (100), 170 (63), 155 (27); HRMS (EI) m/z calculated for $\text{C}_{25}\text{H}_{26}\text{NOP}$ 387.1752, found 387.1741.

***N*-{1-[1-(2-Phenylallyl)cyclopropyl]ethyl}-*P,P*-diphenylphosphinamide (7).** To a cooled (0 °C) solution of **5**³ (0.30 g, 0.87 mmol) in dry CH_2Cl_2 (5.0 mL) was added Me_2Zn (0.43 mL, 0.87 mmol, 2.0 M in toluene). The reaction mixture was stirred for 1 h, cooled to -30 °C, transferred via cannula to a solution of $\text{Zn}(\text{CH}_2\text{I})_2$ (2.16 mmol) in CH_2Cl_2 (10 mL), warmed to r.t., stirred for 4 h, quenched with saturated NH_4Cl , and diluted with CH_2Cl_2 . The aqueous layer was extracted with CH_2Cl_2 (3x), and the combined organic layers were washed with water and brine, dried (MgSO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:4, hexanes/EtOAc containing 1% v/v Et_3N) to give **7** (0.30 g, 85%) as a colorless foam: IR (neat) 3196, 3077, 3056, 2971, 2930, 2870, 1623, 1591, 1573, 1494, 1483, 1453, 1438, 1337,

³ Phosphinamide **4** was prepared by *N*-phosphinoylation of propargyl amine followed by Sonagashira coupling with iodobenzene.

1306, 1188, 1123, 1108 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.23-7.97 (m, 5 H), 7.60-7.39 (m, 10 H), 5.40 (s, 1 H), 5.23 (s, 1 H), 3.11-2.97 (m, 2 H), 2.66 (d, $J = 14.7$ Hz, 1 H), 2.38 (b, 1 H), 1.41 (d, $J = 6.4$ Hz, 3 H), 0.52-0.43 (m, 4 H); ^{13}C NMR (CDCl_3) δ 145.94, 141.93, 134.46, 133.71, 132.76, 132.55, 132.43, 132.11, 131.99, 131.79, 128.61, 128.45, 128.38, 127.53, 126.35, 115, 47, 53.44, 37.44, 24.24, 24.14, 21.39, 11.20, 9.97; MS (EI) m/z (intensity) 401 (M^+ , 19), 383 (70), 283 (9), 244 (20), 218 (100), 201 (94), 184 (40); HRMS (EI) m/z calculated for $\text{C}_{26}\text{H}_{28}\text{NOP}$ 401.1909, found 401.1902.

***N*-Allyl-*N*-((*S*^{*})-((1*S*^{*},2*S*^{*})-2-butylcyclopropyl)(1-(2-phenylallyl)cyclopropyl)methyl)-*P,P*-diphenylphosphinamide (**8a**). **General Protocol A.** To a suspension of NaH (50 mg, 2.1 mmol) in dry THF (3.0 mL) was added **3a**¹ (0.20 g, 0.41 mmol). The reaction mixture was stirred for 20 min, treated with HMPA (0.36 mL, 2.1 mmol) and allyl iodide (0.38 mL, 4.1 mmol), heated at 70 °C for 1 h, cooled to r.t., quenched with sat. NH_4Cl and extracted with EtOAc (3x). The combined organic layers were washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (3:1, hexanes/EtOAc containing 1% v/v Et_3N) to afford **8a** (0.21 g, 95%) as a colorless foam: IR (neat) 3057, 2955, 2924, 2854, 1438, 1203, 1118, 1104 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.05-7.98 (m, 4 H), 7.56-7.52 (m, 2 H), 7.21-7.15 (m, 2 H), 7.12-7.02 (m, 7 H), 6.19-6.05 (m, 1 H), 5.37 (d, $J = 1.4$ Hz, 1 H), 5.10 (d, $J = 1.2$ Hz, 1 H), 4.81-4.75 (m, 2 H), 4.01-3.78 (m, 2 H), 3.53-3.46 (m, 1 H), 3.38 (d, $J = 15.5$ Hz, 1 H), 2.54 (d, $J = 15.6$ Hz, 1 H), 1.84-1.76 (m, 1 H), 1.43-1.29 (m, 4 H), 1.09-0.88 (m, 3 H), 0.95 (t, $J = 6.9$ Hz, 3 H), 0.70-0.51 (m, 2 H), 0.45-0.36 (m, 2 H), 0.22-0.16 (m, 1 H), 0.14-0.08 (m, 1 H); ^{13}C NMR (C_6D_6) δ 145.86, 142.79, 139.72, 139.68, 135.59, 135.02, 133.95, 133.36, 133.17, 133.10, 133.05, 132.98, 131.31, 131.27, 128.58, 126.61, 115.11, 114.43, 63.38, 47.45, 47.39,**

³ Phosphinamide **5** was prepared by addition of MeMgBr to imine **2** ($\text{Ar} = \text{C}_6\text{H}_5$).

39.78, 33.71, 31.95, 23.01, 19.98, 19.91, 17.61, 15.14, 14.43, 10.03, 7.61; MS (EI) m/z (rel. intensity) 523 (M^+ , 3), 366 (75), 201 (100); HRMS (ESI) m/z calculated for $C_{35}H_{42}NOP$ 523.3004, found 523.3016.

***N*-Allyl-*N*-{((*S*^{*})-(1*S*^{*},2*R*^{*})-2-[2-(*tert*-butyldiphenylsilyloxy)ethyl]cyclopropyl}-[1-(2-phenylallyl)cyclopropyl)methyl]-*P,P*-diphenylphosphinamide (**8b**).** According to the General Protocol A, **3b** (0.15 g, 0.21 mmol), NaH (25 mg, 1.1 mmol), and HMPA (0.19 mL, 1.1 mmol), allyl iodide (0.18 mL, 2.1 mmol) in dry THF (2.0 mL) afforded **8b** (0.14 g, 88%) as a colorless foam: IR (neat) 3055, 3013, 2929, 2857, 1625, 1472, 1438, 1428, 1204, 1112 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.07-7.97 (m, 4 H), 7.87-7.84 (m, 4 H), 7.57-7.54 (m, 2 H), 7.29-7.18 (m, 8 H), 7.11-6.99 (m, 7 H), 6.15-6.02 (m, 1 H), 5.35 (d, $J = 1.1$ Hz, 1 H), 5.06 (s, 1 H), 4.79-4.74 (m, 2 H), 3.97-3.75 (m, 4 H), 3.42-3.33 (m, 2 H), 2.56 (d, $J = 15.7$ Hz, 1 H), 2.29-2.18 (m, 1 H), 1.22 (s, 9 H), 1.14-1.08 (m, 1 H), 1.02-0.87 (m, 3 H), 0.60-0.51 (m, 1 H), 0.42-0.34 (m, 2 H), 0.16-0.07 (m, 2 H); ^{13}C NMR (C_6D_6) δ 145.87, 142.75, 139.54, 136.02, 135.33, 135.00, 134.51, 134.46, 133.68, 133.34, 133.22, 133.11, 132.99, 131.29, 129.91, 128.55, 126.61, 115.26, 114.38, 64.34, 63.49, 47.43, 39.69, 37.25, 27.18, 19.99, 19.92, 19.48, 14.89, 14.58, 10.03, 7.58; MS (ESI) m/z (rel. intensity) 750 ($[M+1]^+$, 100), 672 (58); HRMS (ESI) m/z calculated for $\text{C}_{49}\text{H}_{57}\text{NO}_2\text{PSi}$ ($M+1$) 750.3896, found 750.3871.

Methyl 3-((1*S*^{*},2*S*^{*})-2-((*S*^{*})-(N-allyldiphenylphosphinoylamino)(1-(2-phenylallyl)cyclopropyl)methyl)cyclopropyl)propanoate (8c**).** To a suspension of NaH (23

mg, 0.58 mmol) in dry THF (1.0 mL) was added a solution of **3c** (60 mg, 0.12 mmol) in dry THF (0.50 mL). The reaction mixture was stirred for 20 min, treated with HMPA (0.36 mL, 2.1 mmol) and allyl iodide (0.38 mL, 4.1 mmol), heated at 70 °C for 1 h, cooled to r.t., quenched with sat. NH₄Cl and extracted with EtOAc (3x). The combined organic layers were washed with H₂O and brine, dried (Na₂SO₄) and concentrated. The residue was dissolved in MeOH (2.0 mL) and treated with TMSCHN₂ (0.12 mL, 0.23 mmol, 2.0 M in hexanes) and the mixture was stirred for 1 h, quenched with sat. NH₄Cl and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na₂SO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (3:2, hexanes/EtOAc containing 1% v/v Et₃N) to afford **8c** (42 mg, 65%) as a colorless oil: IR (neat) 3057, 2994, 2923, 1736, 1438, 1199, 1118 cm⁻¹; ¹H NMR (C₆D₆) δ 8.07-7.98 (m, 4 H), 7.54-7.51 (m, 2 H), 7.21-7.03 (m, 9 H), 6.14-6.01 (m, 1 H), 5.35 (s, 1 H), 5.05 (d, *J* = 1.1 Hz, 1 H), 4.78-4.73 (m, 2 H), 3.98-3.73 (m, 2 H), 3.40 (s, 3 H), 3.40-3.31 (m, 2 H), 2.49 (d, *J* = 15.7 Hz, 1 H), 2.37-2.31 (m, 2 H), 2.12-2.02 (m, 1 H), 1.15-0.91 (m, 2 H), 0.87-0.84 (m, 2 H), 0.57-0.48 (m, 1 H), 0.38-0.35 (m, 2 H), 0.11--0.01 (m, 2 H); ¹³C NMR (C₆D₆) δ 173.54, 139.50, 135.35, 134.72, 133.70, 133.25, 133.14, 133.06, 133.02, 131.38, 131.34, 131.31, 128.60, 126.56, 115.33, 114.35, 105.50, 63.28, 50.98, 47.33, 47.27, 39.70, 33.87, 29.37, 20.28, 19.85, 19.78, 17.08, 14.80, 10.00, 7.57; MS (ESI) *m/z* (rel. intensity) 576 ([M+Na]⁺, 92), 554 ([M+1]⁺, 100), 258 (57); HRMS (ESI) *m/z* calculated for C₃₅H₄₁NO₃P (M+1) 554.2824, found 554.2819.

***N*-Allyl-*N*-((*S*^{*})-((*1S*^{*},*2S*^{*})-2-butylcyclopropyl)(1-(2-(4-chlorophenyl)allyl)cyclopropyl)methyl)-*P,P*-diphenylphosphinamide (**8d**).** According to the General Protocol A, **3d**¹ (0.10 g, 0.19 mmol), NaH (23 mg, 0.97 mmol), HMPA (0.17 mL, 0.97 mmol), and allyl iodide (0.18 mL, 1.9 mmol) in dry THF (2.0 mL) afforded **8d** (81 mg, 75%) as a colorless oil: IR (neat) 3058, 2991, 2955, 2924, 2854, 1493, 1437, 1202, 1118, 1102 cm⁻¹; ¹H

NMR (C_6D_6) δ 7.99-7.92 (m, 4 H), 7.28 (d, J = 8.6 Hz, 2 H), 7.15-7.12 (m, 2 H), 7.05-7.03 (m, 6 H), 6.10-5.97 (m, 1 H), 5.23 (s, 1 H), 5.06 (s, 1 H), 4.80-4.75 (m, 2 H), 3.96-3.74 (m, 2 H), 3.49 (t, J = 9.8 Hz, 1 H), 3.29 (d, J = 15.7 Hz, 1 H), 2.36 (d, J = 15.7 Hz, 1 H), 1.77-1.72 (m, 1 H), 1.36-1.34 (m, 4 H), 1.04-0.87 (m, 6 H), 0.67-0.59 (m, 1 H), 0.56-0.47 (m, 1 H), 0.37-0.31 (m, 2 H), 0.22-0.17 (m, 1 H), 0.14-0.08 (m, 1 H); ^{13}C NMR (C_6D_6) δ 144.69, 141.20, 139.50, 133.38, 133.30, 133.03, 132.91, 131.40, 131.36, 131.32, 128.67, 115.21, 114.76, 62.94, 62.91, 47.39, 47.33, 39.69, 33.71, 31.96, 23.02, 19.97, 19.77, 19.71, 17.57, 15.18, 14.42, 10.03, 7.70; MS (EI) m/z (rel. intensity) 557 (M^+ , 7), 366 (90), 300 (34), 258 (45), 201 (100); HRMS (EI) m/z calculated for $C_{35}H_{41}NOPCl$ 557.2614, found 557.2622.

***N*-Allyl-*N*-((*S*^{*})-((*1S*^{*},*2S*^{*})-2-butylcyclopropyl)(1-(2-(4-methoxyphenyl)allyl)cyclopropyl)methyl)-*P,P*-diphenylphosphinamide (**8e**).** According to the General Protocol A, **3e**¹ (0.10 g, 0.19 mmol), NaH (23 mg, 0.19 mmol), HMPA (0.17 mL, 0.97 mmol), and allyl iodide (0.18 mL, 2.0 mmol) in dry THF (3.0 mL) afforded **8e** (75 mg, 69%) as a colorless foam: IR (neat) 3058, 2955, 2924, 2854, 1606, 1512, 1437, 1248, 1201, 1118 cm^{-1} ; 1H NMR (C_6D_6) δ 8.07-8.00 (m, 4 H), 7.55-7.50 (m, 2 H), 7.09-7.03 (m, 6 H), 6.84-6.79 (m, 2 H), 6.20-6.08 (m, 1 H), 5.36 (d, J = 1.4 Hz, 1 H), 5.04 (d, J = 1.0 Hz, 1 H), 4.83-4.77 (m, 2 H), 4.04-3.80 (m, 2 H), 3.48 (app. t, J = 9.6 Hz, 1 H), 3.40 (d, J = 15.4 Hz, 1 H), 3.32 (s, 3 H), 2.60 (d, J = 15.4 Hz, 1 H), 1.85-1.77 (m, 1 H), 1.43-1.29 (m, 4 H), 1.08-0.89 (m, 6 H), 0.71-0.52 (m, 2 H), 0.49-0.42 (m, 2 H), 0.23-0.18 (m, 1 H), 0.15-0.09 (m, 1 H); ^{13}C NMR (C_6D_6) δ 159.70, 145.16, 139.74, 139.70, 135.53, 135.06, 135.00, 133.89, 133.34, 133.23, 133.14, 133.02, 131.32, 131.28, 115.14, 114.06, 112.77, 63.73, 54.77, 47.46, 47.40, 39.79, 33.71, 31.96, 23.02, 20.05, 19.98, 19.92, 17.64, 15.17, 14.42, 9.97, 7.61; MS (EI) m/z (rel. intensity) 553 (M^+ , 1), 366 (26), 201 (100); HRMS (EI) m/z calculated for $C_{36}H_{44}NO_2P$ 553.3110, found 553.3094.

***N*-Allyl-*N*-((*S*^{*})-((*1S*^{*},*2S*^{*})-2-butylcyclopropyl)(1-(2-(3-methoxyphenyl)allyl)cyclopropyl)methyl)-*P,P*-diphenylphosphinamide (**8f**).** According to the General Protocol A, **3f**¹ (0.14 g, 0.26 mmol), NaH (52 mg, 1.3 mmol), HMPA (0.23 mL, 1.3 mmol), and allyl iodide (0.24 mL, 2.6 mmol) in dry THF (3.0 mL) afforded **8f** (0.14 g, 96%) as a colorless foam: IR (neat) 3058, 2954, 2923, 2854, 1597, 1576, 1437, 1202, 1118 cm⁻¹; ¹H NMR (C₆D₆) δ 8.07-7.99 (m, 5 H), 7.37-7.36 (m, 1 H), 7.22-7.12 (m, 1 H), 7.08-7.06 (m, 6 H), 6.80-6.77 (m, 1 H), 6.19-6.06 (m, 1 H), 5.43 (d, *J* = 1.2 Hz, 1 H), 5.11 (d, *J* = 0.9 Hz, 1 H), 4.83-4.77 (m, 2 H), 4.03-3.80 (m, 2 H), 3.51-3.45 (m, 1 H), 3.48 (s, 3 H), 3.40 (d, *J* = 15.6 Hz, 1 H), 2.61 (d, *J* = 15.5 Hz, 1 H), 1.83-1.75 (m, 1 H), 1.38-1.31 (m, 4 H), 1.06-0.89 (m, 3 H), 0.96 (t, *J* = 6.9 Hz, 3 H), 0.71-0.52 (m, 2 H), 0.49-0.39 (m, 2 H), 0.22-0.10 (m, 2 H); ¹³C NMR (C₆D₆) δ 160.39, 146.05, 144.48, 139.68, 139.64, 135.58, 135.07, 133.94, 133.40, 133.20, 133.14, 133.08, 133.02, 131.36, 131.32, 131.26, 131.23, 129.53, 119.13, 115.12, 114.61, 113.41, 112.56, 63.66, 63.63, 54.96, 47.50, 47.44, 39.72, 33.73, 31.92, 23.00, 20.11, 20.05, 17.65, 15.15, 14.37, 10.04, 7.62; MS (EI) *m/z* (rel. intensity) 553 (M⁺, 2), 366 (67), 296, 35, 201 (100); HRMS (EI) *m/z* calculated for C₃₆H₄₄NO₂P 553.3110, found 553.3121.

***N*-Allyl-*N*-((*S*^{*})-((*1S*^{*},*2S*^{*})-2-butylcyclopropyl)(1-(2-(2-methoxyphenyl)allyl)cyclopropyl)methyl)-*P,P*-diphenylphosphinamide (**8g**).** According to the General Protocol A, **3g**¹ (57 mg, 0.11 mmol), NaH (22 mg, 0.56 mmol), HMPA (97 μ L, 0.56 mmol), and allyl iodide (0.10 mL, 1.1 mmol) in dry THF (2.0 mL) afforded **8g** (54 mg, 89%) as a colorless foam: IR (neat) 3046, 2950, 2923, 1489, 1436, 1204, 1117 cm⁻¹; ¹H NMR (C₆D₆) δ 8.07-7.99 (m, 4 H), 7.42 (dd, *J* = 7.4, 1.7 Hz, 1 H), 7.11-7.05 (m, 7 H), 6.86 (td, *J* = 7.4, 0.7

Hz, 1 H), 6.55 (d, $J = 8.1$ Hz, 1 H), 6.02-5.89 (m, 1 H), 5.24 (s, 1 H), 5.22 (s, 1 H), 4.81-4.72 (m, 2 H), 4.04-3.79 (m, 2 H), 3.61 (dd, $J = 10.1, 9.1$ Hz, 1 H), 3.39 (d, $J = 15.6$ Hz, 1 H), 3.34 (s, 3 H), 2.66 (d, $J = 15.3$ Hz, 1 H), 1.79-1.73 (m, 1 H), 1.36-1.31 (m, 4 H), 1.19-1.05 (m, 1 H), 0.95-0.91 (m, 5 H), 0.58-0.40 (m, 4 H), 0.24-0.18 (m, 1 H), 0.10-0.04 (m, 1 H); ^{13}C NMR (C_6D_6) δ 157.09, 146.30, 139.84, 136.56, 135.55, 134.93, 133.90, 133.69, 133.23, 133.10, 133.06, 132.93, 131.25, 131.10, 130.77, 120.97, 117.42, 114.84, 111.05, 63.03, 55.04, 47.62, 41.74, 33.70, 31.94, 23.03, 20.79, 20.72, 20.23, 17.82, 15.14, 14.39, 10.63, 8.12; MS (EI) m/z (rel. intensity) 553 (M^+ , 1), 366 (55), 296 (30), 257 (31), 201 (100); HRMS (EI) m/z calculated for $\text{C}_{36}\text{H}_{44}\text{NO}_2\text{P}$ 553.3110, found 553.3101.

(4*S)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-5-(diphenylphosphinoyl)-8-phenyl-5-azaspiro[2.6]non-7-ene (9a).** General Protocol B. To a solution of **8a** (0.15 g, 0.29 mmol) in

dry CH_2Cl_2 (57 mL) was added 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (24 mg, 0.029 mmol). The reaction mixture was heated at reflux for 7 h, cooled to r.t., filtered through Celite and concentrated. The residue was purified by chromatography on deactivated SiO_2 (3:2, hexanes/EtOAc containing 1% v/v Et_3N) to afford **9a** (0.11 g, 75%) as a colorless foam: IR (neat) 3057, 2998, 2954, 2924, 2870, 2853, 1635, 1592, 1492, 1437, 1205, 1120, 1107 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.06-7.92 (m, 4 H), 7.20-7.03 (m, 11 H), 5.49 (dd, $J = 6.4, 3.5$ Hz, 1 H), 3.98-3.88 (m, 1 H), 3.61 (ddd, $J = 17.4, 9.9, 6.9$ Hz, 1 H), 3.03 (t, $J = 8.9$ Hz, 1 H), 2.78 (d, $J = 16.5$ Hz, 1 H), 2.48 (d, $J = 16.5$ Hz, 1 H), 1.65-1.56 (m, 1 H), 1.40-1.35 (m, 4 H), 1.03-0.85 (m, 3 H), 0.94 (t, $J = 6.3$ Hz, 3 H), 0.81-0.78 (m, 1 H), 0.67-0.63 (m, 1 H), 0.39-0.26 (m, 4 H); ^{13}C NMR (C_6D_6) δ 144.86, 144.22, 135.39, 135.34, 133.71, 133.06, 132.93, 132.80, 131.42, 131.38, 131.33, 131.30, 127.13, 127.08, 126.22, 65.18, 65.14, 41.85, 41.78, 40.30, 34.22, 32.02, 23.98, 23.91, 23.09, 22.99, 19.55, 17.21, 14.42, 13.56, 13.16, 12.30; MS (EI) m/z (rel. intensity) 495 (M^+ , 12),

398 (9), 294 (45), 201 (100); HRMS (EI) m/z calculated for $C_{33}H_{38}NOP$ 495.2691, found 495.2686.

(4*S*^{*})-4-{2-[(1*S*^{*},2*R*^{*})-2-(*tert*-Butyldiphenylsilanyloxy)ethyl]cyclopropyl}-5-

(diphenylphosphinoyl)-8-phenyl-5-azaspiro[2.6]non-7-ene (9b). According to the General Protocol B, **8b** (0.13 g, 0.17 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (15 mg, 0.017 mmol) in CH_2Cl_2 (35 mL) afforded **9b** (89 mg, 71%) as a colorless foam: IR (neat) 3070, 2998, 2929, 2856, 1437, 1428, 1206, 1108 cm^{-1} ; 1H NMR (C_6D_6) δ 8.02-7.93 (m, 5 H), 7.85-7.80 (m, 4 H), 7.28-7.22 (m, 8 H), 7.18-7.12 (m, 2 H), 7.10-7.07 (m, 3 H), 7.03-7.00 (m, 3 H), 5.48 (dd, $J = 6.6, 3.7$ Hz, 1 H), 3.88-3.71 (m, 3 H), 3.53 (ddd, $J = 17.3, 10.2, 7.2$ Hz, 1 H), 2.91 (app t, $J = 8.8$ Hz, 1 H), 2.74 (d, $J = 16.4$ Hz, 1 H), 2.44 (d, $J = 16.5$ Hz, 1 H), 2.02-1.91 (m, 1 H), 1.34-1.25 (m, 1 H), 1.21 (s, 9 H), 1.01-0.82 (2 H), 0.75-0.71 (m, 1 H), 0.59-0.55 (m, 1 H), 0.32-0.23 (m, 4 H); ^{13}C NMR (C_6D_6) δ 144.85, 144.17, 136.06, 135.34, 135.26, 134.56, 133.67, 133.62, 132.98, 132.85, 131.43, 131.29, 129.87, 127.25, 127.20, 127.08, 126.21, 65.17, 64.48, 41.72, 41.66, 40.20, 37.61, 27.17, 23.93, 23.85, 19.45, 19.33, 13.96, 13.21, 13.17, 12.27; MS (ESI) m/z (rel. intensity) 744 ($[M+Na]^+$, 100), 722 ($[M+1]^+$, 27); HRMS (ESI) m/z calculated for $C_{47}H_{53}NO_2PSi$ ($M+1$) 722.3583, found 722.3618.

3-{[(1*S*^{*},2*S*^{*})-2-[(4*S*^{*})-5-(Diphenylphosphinoyl)-8-phenyl-5-azaspiro[2.6]non-7-en-4-yl]cyclopropyl}propionic acid methyl ester (9c). According to the General Protocol B, **8c** (16

mg, 0.029 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (2.5 mg, 2.9 μ mol) in CH_2Cl_2 (6.0 mL) afforded **9c** (9.6 mg, 63%) as a colorless oil: IR (neat) 3048, 2999, 2925, 1734, 1437, 1195, 1120, 1107 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.08-7.92 (m, 4 H), 7.20-7.09 (m, 7 H), 7.04-7.01 (m, 3 H), 5.49 (dd, $J = 6.7, 3.9$ Hz, 1 H), 3.92-3.79 (m, 1 H), 3.58 (ddd, $J = 17.5, 10.3, 7.1$ Hz, 1 H), 3.40 (s, 1 H), 2.83 (app t, $J = 8.8$ Hz, 1 H), 2.71 (d, $J = 16.6$ Hz, 1 H), 2.47-2.26 (m, 3 H), 1.87-1.75 (m, 1 H), 1.40-1.28 (m, 1 H), 1.02-0.95 (m, 1 H), 0.93-0.84 (m, 1 H), 0.69-0.62 (m, 1 H), 0.60-0.52 (m, 1 H), 0.30-0.18 (m, 4 H); ^{13}C NMR (C_6D_6) δ 173.61, 144.77, 144.24, 135.36, 135.01, 133.67, 133.37, 133.12, 133.00, 132.87, 131.50, 131.46, 131.33, 131.30, 128.51, 127.23, 127.18, 127.10, 126.21, 65.28, 50.93, 41.62, 41.56, 40.17, 33.98, 29.73, 23.92, 23.83, 19.67, 16.78, 13.21, 13.12, 12.16; MS (EI) m/z (rel. intensity) 525 (M^+ , 16), 324 (38), 201 (100); HRMS (EI) m/z calculated for $\text{C}_{33}\text{H}_{36}\text{NO}_3\text{P}$ 525.2433, found 525.2452.

(4S*)-4-((1S*,2S*)-2-Butylcyclopropyl)-8-(4-chlorophenyl)-5-(diphenylphosphinoyl)-5-azaspiro[2.6]non-7-ene (9d). According to the General Protocol B, **8d** (80 mg, 0.14 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (12 mg, 0.014 mmol) in CH_2Cl_2 (29 mL) afforded **9d** (55 mg, 72%) as a colorless foam: IR (neat) 3058, 2955, 2924, 2854, 1490, 1437, 1204, 1120, 1107 cm^{-1} ; ^1H NMR (C_6D_6) δ 8.00-7.88 (m, 4 H), 7.15-7.02 (m, 8 H), 6.83-6.78 (m, 2 H), 5.31 (dd, $J = 6.5, 3.6$ Hz, 1 H), 3.89 (b app t, $J = 14.7$ Hz, 1 H), 3.62-3.50 (m, 1 H), 3.05 (t, $J = 8.4$ Hz, 1 H), 2.58 (d, $J = 16.6$ Hz, 1 H), 2.37 (d, $J = 16.7$ Hz, 1 H), 1.64-1.54 (m, 1 H), 1.40-1.30 (m, 5 H), 0.96-0.91 (m, 4 H), 0.88-0.78 (m, 2 H), 0.67-0.63 (m, 1 H), 0.38-0.33 (m, 1 H), 0.31-0.22 (m, 3 H); ^{13}C NMR (C_6D_6) δ 143.12, 142.86, 135.32, 135.27, 133.69, 133.59, 133.03, 132.90, 132.87, 132.74, 131.47, 131.44, 131.35, 128.54,

127.50, 64.93, 41.82, 41.76, 40.26, 34.24, 32.01, 23.88, 23.81, 23.09, 19.49, 17.15, 14.40, 13.54, 12.89, 12.27; MS (EI) m/z (rel. intensity) 529 (M^+ , 11), 328 (33), 201 (100); HRMS (EI) m/z calculated for $C_{33}H_{37}NOPCl$ 529.2301, found 529.2298.

(4*S)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-8-(4-methoxyphenyl)-5-(diphenylphosphinoyl)-5-azaspiro[2.6]non-7-ene (9e).** According to the General Protocol B, **8e** (70 mg, 0.13 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (11 mg, 0.013 mmol) in CH_2Cl_2 (25 mL) afforded **9e** (53 mg, 80%) as a colorless foam: IR (neat) 3057, 2998, 2954, 2926, 2853, 1606, 1510, 1437, 1284, 1247, 1204, 1181, 1120 cm^{-1} ; 1H NMR (C_6D_6) δ 8.07-7.92 (m, 4 H), 7.15-7.03 (m, 8 H), 6.82-6.77 (m, 2 H), 5.51-5.47 (m, 1 H), 4.03-3.91 (m, 1 H), 3.63 (ddd, $J = 17.1, 9.9, 7.1$ Hz, 1 H), 3.35 (s, 3 H), 3.01 (t, $J = 8.8$ Hz, 1 H), 2.84 (d, $J = 16.4$ Hz, 1 H), 2.46 (d, $J = 16.4$ Hz, 1 H), 1.62-1.53 (m, 1 H), 1.44-1.30 (m, 4 H), 1.04-0.88 (m, 3 H), 0.94 (t, $J = 6.5$ Hz, 3 H), 0.82-0.79 (m, 1 H), 0.67-0.63 (m, 1 H), 0.40-0.27 (m, 4 H); ^{13}C NMR (C_6D_6) δ 159.34, 143.77, 135.55, 135.51, 133.88, 133.10, 132.98, 132.85, 131.33, 131.27, 128.42, 128.10, 127.31, 125.64, 125.59, 113.97, 65.31, 65.28, 54.84, 41.81, 41.75, 40.26, 34.27, 32.05, 23.93, 23.86, 23.11, 19.68, 17.25, 14.43, 13.61, 13.37, 12.28; MS (EI) m/z (rel. intensity) 525 (M^+ , 17), 324 (51), 201 (100); HRMS (EI) m/z calculated for $C_{34}H_{40}NO_2P$ 525.2797, found 525.2794.

(4*S*^{*})-4-((1*S*^{*},2*S*^{*})-2-Butylcyclopropyl)-8-(3-methoxyphenyl)-5-(diphenylphosphinoyl)-5-azaspiro[2.6]non-7-ene (9f). According to the General Protocol B, **8f** (80 mg, 0.14 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (12 mg, 0.014 mmol) in CH₂Cl₂ (29 mL) afforded **9f** (57 mg, 75%) as a colorless foam: IR (neat) 3059, 2998, 2955, 2924, 2853, 1597, 1437, 1203, 1121, 1107 cm⁻¹; ¹H NMR (C₆D₆) δ 8.04-7.94 (m, 4 H), 7.15-7.03 (m, 7 H), 6.87-6.85 (m, 1 H), 6.81-6.79 (m, 1 H), 6.71-6.68 (m, 1 H), 5.53 (dd, *J* = 6.3, 3.8 Hz, 1 H), 3.99-3.87 (m, 1 H), 3.59 (ddd, *J* = 17.1, 10.0, 7.1 Hz, 1 H), 3.38 (s, 3 H), 3.00 (t, *J* = 8.7 Hz, 1 H), 2.81 (d, *J* = 16.4 Hz, 1 H), 2.48 (d, *J* = 16.5 Hz, 1 H), 1.61-1.52 (m, 1 H), 1.43-1.30 (m, 4 H), 1.01-0.81 (m, 3 H), 0.93 (t, *J* = 6.6 Hz, 3 H), 0.80-0.73 (m, 1 H), 0.65-0.62 (m, 1 H), 0.38-0.25 (m, 4 H); ¹³C NMR (C₆D₆) δ 160.32, 146.57, 144.39, 135.62, 135.55, 133.92, 133.12, 133.00, 132.88, 131.35, 131.30, 129.48, 128.45, 128.14, 127.23, 127.19, 118.78, 112.71, 112.35, 65.34, 54.89, 41.94, 41.87, 40.46, 34.27, 34.10, 32.03, 24.06, 23.98, 23.10, 22.98, 19.74, 17.30, 14.37, 13.65, 13.34, 12.37; MS (EI) *m/z* (rel. intensity) 525 (M⁺, 10), 324 (40), 201 (100); HRMS (EI) *m/z* calculated for C₃₄H₄₀NO₂P 525.2797, found 525.2823.

(4*S*^{*})-4-((1*S*^{*},2*S*^{*})-2-Butylcyclopropyl)-8-(2-methoxyphenyl)-5-(diphenylphosphinoyl)-5-azaspiro[2.6]non-7-ene (9g). According to the General Protocol B, **8g** (50 g, 0.090 mmol) and 1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)tricyclohexylphosphine)ruthenium (8.0 mg, 9.0

[mol] in CH₂Cl₂ (18 mL) afforded **9g** (40 mg, 84%) as a colorless foam: IR (neat) 3058, 2997, 2954, 2925, 2853, 1488, 1437, 1249, 1204, 1119 cm⁻¹; ¹H NMR (C₆D₆) δ 8.08-8.05 (m, 4 H), 7.15-7.06 (m, 8 H), 6.92-6.88 (m, 1 H), 6.50 (d, *J* = 8.3 Hz, 1 H), 5.42 (dd, *J* = 5.7, 3.5 Hz, 1 H), 4.05-3.96 (m, 1 H), 3.65-3.53 (m, 1 H), 3.29 (s, 3 H), 3.15-2.99 (m, 1 H), 3.09 (d, *J* = 16.7 Hz, 1 H), 2.45 (d, *J* = 16.6 Hz, 1 H), 1.57-1.46 (m, 1 H), 1.50-1.25 (m, 5 H), 1.06-0.83 (m, 3 H), 0.93 (t, *J* = 6.7 Hz, 1 H), 0.68-0.63 (m, 1 H), 0.50-0.42 (m, 2 H), 0.41-0.35 (m, 1 H), 0.33-0.29 (m, 1 H); ¹³C NMR (C₆D₆) δ 156.71, 144.62, 135.78, 135.67, 135.49, 134.14, 134.00, 133.10, 132.97, 131.28, 131.24, 131.19, 129.57, 120.84, 110.79, 65.59, 65.56, 54.72, 41.77, 41.70, 40.87, 34.25, 32.07, 24.32, 24.25, 23.11, 19.56, 17.23, 14.42, 13.60, 13.05, 11.83; MS (EI) *m/z* (rel. intensity) 525 (M⁺, 12), 523 (22), 324 (36), 201 (100); HRMS (ESI) *m/z* calculated for C₃₄H₄₀NO₂P 525.2797, found 525.2808.

***N*-{(*S*^{*})-((*1S*^{*},*2S*^{*})-2-Butylcyclopropyl)-[1-(2-oxo-2-phenylethyl)cyclopropyl]methyl}-*P,P*-diphenylphosphinamide (**10**).** To a solution of **3a** (0.15 g, 0.31 mmol) in THF (2.0 mL) and water (1.0 mL) was added NaIO₄ (0.33 g, 1.6 mmol) and OsO₄ (8.0 mg, 0.031 mmol). The reaction mixture was stirred for 3 h, diluted with water and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na₂SO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (3:2 then 2:3, hexanes/EtOAc containing 1% v/v Et₃N) to afford **10** (0.12 g, 77%) as a colorless foam: IR (neat) 3220, 3064, 2999, 2953, 2923, 2848, 1677, 1435, 1184, 1124 cm⁻¹; ¹H NMR (C₆D₆) δ 8.18-8.08 (m, 4 H), 7.88-7.86 (m, 2 H), 7.12-7.03 (m, 9 H), 4.64 (t, *J* = 8.7 Hz, 1 H), 3.86 (d, *J* = 17.6 Hz, 1 H), 2.49 (app q, *J* = 9.0 Hz, 1 H), 2.31 (d, *J* = 17.6 Hz, 1 H), 1.39-1.27 (m, 5 H), 1.18-1.09 (m, 1 H), 0.90-0.86 (m, 3 H), 0.78-0.71 (m, 1 H), 0.61-0.47 (m, 3 H), 0.42-0.35 (m, 2 H), 0.26-0.19 (m, 1 H), 0.16-0.12 (m, 1 H); ¹³C NMR (C₆D₆) δ 200.57, 137.82, 136.50, 136.32, 134.84, 134.62, 132.96, 132.81, 132.69, 132.38, 132.25, 131.31, 131.27, 131.19, 131.15, 128.62, 128.56, 128.21, 61.42, 44.37, 33.89,

32.05, 23.64, 23.57, 23.01, 22.69, 22.63, 18.19, 14.39, 13.24, 11.52, 11.05; MS (EI) m/z (rel. intensity) 485 (M^+ , 10), 326 (42), 268 (34), 218 (64), 201 (100); HRMS (EI) m/z calculated for $C_{31}H_{36}NO_2P$ 485.2484, found 485.2498.

***N*-{(*S**)-((*1S**,*2S**)-2-Butylcyclopropyl)-{1-[2-(3-methoxyphenyl)-2-oxoethyl]cyclopropyl}methyl}-*P,P*-diphenylphosphinamide (11).** To a solution of **3f** (0.18 g, 0.35 mmol) in THF (3.0 mL) and water (1.5 mL) was added NaIO₄ (0.38 g, 1.8 mmol) and OsO₄ (10 mg, 0.035 mmol). The reaction mixture was stirred for 3 h, diluted with water and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na₂SO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (1:1, hexanes/EtOAc containing 1% v/v Et₃N) to afford **11** (0.10 g, 56%) as a colorless oil: IR (neat) 3228, 3059, 2998, 2955, 2924, 2854, 1676, 1596, 1582, 1464, 1437, 1258, 1191, 1123 cm⁻¹; ¹H NMR (C₆D₆) δ 8.18-8.08 (m, 4 H), 7.66 (bs, 1 H), 7.50-7.47 (m, 1 H), 7.10-7.00 (m, 7 H), 6.90-6.86 (m, 1 H), 4.55 (t, J = 8.4 Hz, 1 H), 3.89 (d, J = 17.4 Hz, 1 H), 3.27 (s, 3 H), 2.49 (app q, J = 9.4 Hz, 1 H), 2.36 (d, J = 17.5 Hz, 1 H), 1.46-1.28 (m, 6 H), 1.16-1.10 (m, 1 H), 0.88 (t, J = 6.8 Hz, 3 H), 0.78-0.76 (m, 1 H), 0.61-0.50 (m, 2 H), 0.45-0.35 (m, 2 H), 0.26-0.13 (m, 2 H); ¹³C NMR (C₆D₆) δ 200.10, 159.98, 139.00, 136.15, 135.99, 134.49, 134.29, 132.42, 132.30, 132.03, 131.91, 130.91, 130.81, 129.35, 120.90, 119.36, 112.50, 61.15, 54.57, 44.03, 33.53, 31.68, 23.31, 22.63, 22.48, 17.83, 13.99, 12.74, 11.20, 10.79; MS (EI) m/z (rel. intensity) 515 (M^+ , 0.4), 449 (10), 223 (55), 199 (48), 135 (56); HRMS (EI) m/z calculated for C₃₂H₃₈NO₃P 515.2589, found 515.2589.

1-[(4*S,6*S**)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-6-phenyl-5-azaspiro[2.4]hept-5-yl]ethanone (12a) and 1-[(4*S**,6*R**)-4-((1*S**,2*S**)-2-butylcyclopropyl)-6-phenyl-5-azaspiro[2.4]hept-5-yl]ethanone (12b).** A solution of **10** (0.14 g, 0.29 mmol) in MeOH (2.0 mL) was treated at 0 °C with a solution of HCl (2.0 mL, 2.0 M in MeOH). The reaction mixture was stirred for 1 h and concentrated. The residue was dissolved in MeOH (2.0 mL), treated with NaBH₃CN (91 mg, 1.44 mmol), stirred for 4 h and concentrated. The residue was suspended in dry CH₂Cl₂ (4.0 mL), cooled to 0 °C, and treated with DIPEA (0.50 mL, 2.9 mmol) and AcCl (0.20 mL, 2.9 mmol). The reaction mixture was stirred for 4 h, quenched with sat. NH₄Cl and extracted with EtOAc (3x). The combined organic layers were washed with water, 10% HCl and brine, dried (Na₂SO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (9:1 then 4:1 then 3:2, hexanes/EtOAc containing 1% v/v Et₃N) to afford the desired pyrrolidines **12a** (43 mg, 48%) and **12b** (20 mg, 22%) as a mixture of colorless oils.

12a (major isomer): IR (neat) 3062, 2994, 2956, 2925, 2871, 1650, 1398, 1346 cm⁻¹; ¹H NMR (5.7:1 mixture of amide bond rotamers) major rotamer (CDCl₃) δ 7.38-7.27 (m, 5 H), 4.94 (t, *J* = 8.4 Hz, 1 H), 3.29 (d, *J* = 9.6 Hz, 1 H), 2.41 (dd, *J* = 11.8, 8.4 Hz, 1 H), 1.92 (dd, *J* = 12.8, 7.6 Hz, 1 H), 1.78 (s, 3 H), 1.42-1.15 (m, 7 H), 0.93-0.79 (m, 5 H), 0.90 (t, *J* = 7.1 Hz, 3 H), 0.56-0.39 (m, 4 H), 0.34-0.28 (m, 1 H); minor rotamer (representative signals) δ 5.24 (bt, 1 H), 2.86 (bd, 1 H); ¹³C NMR (CDCl₃) δ 171.05, 144.08, 128.85, 127.12, 125.53, 68.50, 63.18, 44.99, 33.83, 31.68, 25.71, 23.07, 22.87, 22.61, 16.06, 14.16, 13.99, 10.99, 5.27; MS (EI) *m/z* (rel. intensity) 311 (M⁺, 100), 255 (49), 214 (70), 172 (57); HRMS (EI) *m/z* calculated for C₂₁H₂₉NO 311.2249, found 311.2244.

12b (minor isomer): IR (neat) 3061, 2994, 2957, 2923, 2855, 1650, 1397 cm⁻¹; ¹H NMR (6.9:1 mixture of amide bond rotamers) major rotamer (CDCl₃) δ 7.34-7.21 (m, 5 H), 5.02 (d, *J* = 8.6 Hz, 1 H), 3.54 (d, *J* = 8.2 Hz, 1 H), 3.06 (dd, *J* = 12.5, 8.8 Hz, 1 H), 1.74 (s, 3 H), 1.35-1.22 (m,

5 H), 1.24-1.18 (m, 1 H), 1.13-1.09 (m, 1 H), 0.90 (t, $J = 6.9$ Hz, 3 H), 0.86-0.79 (m, 1 H), 0.73-0.68 (m, 1 H), 0.66-0.59 (m, 1 H), 0.44-0.35 (m, 2 H), 0.26-0.17 (m, 2 H); minor rotamer (representative signals) δ 5.18 (d, $J = 9.2$ Hz, 1 H), 3.27 (d, $J = 6.0$ Hz, 1 H), 2.90 (dd, $J = 12.8, 9.4$ Hz, 1 H), 2.16 (s, 3 H); ^{13}C NMR major rotamer (CDCl_3) δ 170.78, 144.57, 128.51, 126.93, 125.59, 67.48, 62.90, 42.57, 34.01, 31.67, 23.99, 23.53, 23.45, 22.60, 16.75, 16.17, 14.17, 9.78, 3.39; MS (EI) m/z (rel. intensity) 311 (M^+ , 30), 214 (70), 172 (100); HRMS (EI) m/z calculated for $\text{C}_{21}\text{H}_{29}\text{NO}$ 311.2249, found 311.2250.

1-[(4*S,6*S**)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-6-(3-methoxyphenyl)-5-azaspiro[2.4]hept-5-yl]ethanone (13a) and 1-[(4*S**,6*R**)-4-((1*S**,2*S**)-2-butylcyclopropyl)-6-(3-methoxyphenyl)-5-azaspiro[2.4]hept-5-yl]ethanone (13b).** A solution of **11** (60 mg, 0.12 mmol) in MeOH (1.5 mL) was treated at 0 °C with a solution of HCl (1.5 mL, 2.0M in MeOH). The reaction mixture was stirred for 1 h and concentrated. The residue was dissolved in MeOH (1.0 mL), treated with NaBH_3CN (37 mg, 0.58 mmol), stirred for 4 h and concentrated. The residue was suspended in dry CH_2Cl_2 (2.0 mL), cooled to 0 °C, and treated with DIPEA (0.20 mL, 1.2 mmol) and AcCl (82 μL , 1.2 mmol). The reaction mixture was stirred for 4 h, quenched with sat. NH_4Cl and extracted with EtOAc (3x). The combined organic layers were washed with water, 10% HCl and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (9:1 then 4:1 then 3:2, hexanes/EtOAc containing 1% v/v Et_3N) to afford a mixture of **13a** and **13b** (27 mg, 68%) as a colorless oil. The diastereoisomers were separated by chromatography on SiO_2 (4:1, hexanes/EtOAc) to afford **13a** (16 mg) and **13b** (9.0 mg).

13a (major isomer): IR (neat) 2995, 2956, 2925, 1648, 1601, 1397, 1262 cm^{-1} ; ^1H NMR (5.9:1 mixture of amide bond rotamers) major rotamer (CDCl_3) δ 7.28 (t, $J = 7.8$ Hz, 1 H), 6.97 (d, $J =$

7.6 Hz, 1 H), 6.93 (s, 1 H), 6.81 (dd, $J = 8.2, 2.2$ Hz, 1 H), 4.91 (t, $J = 8.3$ Hz, 1 H), 3.81 (s, 3 H), 3.27 (d, $J = 9.6$ Hz, 1 H), 2.41 (dd, $J = 12.8, 9.3$ Hz, 1 H), 1.90 (dd, $J = 12.8, 7.5$ Hz, 1 H), 1.81 (s, 3 H), 1.52-1.22 (m, 6 H), 1.12-1.10 (m, 1 H), 0.92-0.79 (m, 2 H), 0.90 (t, $J = 7.1$ Hz, 3 H), 0.56-0.39 (m, 4 H), 0.34-0.30 (m, 1 H); minor rotamer (representative signals) δ 5.20 (bt, 1 H), 2.86 (bd, 1 H); ^{13}C NMR (CDCl_3) δ 171.15, 160.15, 145.85, 121.95, 117.84, 112.22, 111.42, 68.52, 63.20, 55.18, 44.96, 33.88, 31.62, 25.67, 23.07, 22.84, 22.64, 16.19, 14.07, 13.96, 10.86, 5.33; MS (EI) m/z (rel. intensity) 341 (M^+ , 70), 244 (48), 202 (100); HRMS (EI) m/z calculated for $\text{C}_{22}\text{H}_{31}\text{NO}_2$ 341.2355, found 341.2355.

13b (minor isomer): IR (neat) 2995, 2956, 2923, 2854, 1651, 1601, 1397, 1261 cm^{-1} ; ^1H NMR (8.1:1 mixture of amide bond rotamers) major rotamer (CDCl_3) δ 7.25-7.19 (m, 1 H), 6.85-6.76 (m, 3 H), 4.98 (d, $J = 8.8$ Hz, 1 H), 3.79 (s, 3 H), 3.53 (d, $J = 8.3$ Hz, 1 H), 3.06 (dd, $J = 12.5, 9.1$ Hz, 1 H), 1.76 (s, 3 H), 1.33-1.23 (m, 6 H), 1.27-1.19 (m, 1 H), 1.13-1.07 (m, 1 H), 0.89 (t, $J = 6.8$ Hz, 3 H), 0.85-0.80 (m, 1 H), 0.74-0.61 (m, 2 H), 0.45-0.35 (m, 1 H), 0.30-0.20 (m, 2 H); minor rotamer (representative signals) δ 5.15 (d, $J = 9.5$ Hz, 1 H), 3.26 (d, $J = 5.7$ Hz, 1 H), 2.89 (dd, $J = 13.3, 9.6$ Hz, 1 H), 2.16 (s, 3 H); ^{13}C NMR (CDCl_3) δ 170.80, 1159.82, 146.38, 129.60, 118.07, 112.28, 111.38, 67.54, 62.87, 55.20, 42.56, 34.03, 31.69, 24.14, 23.49, 22.62, 16.78, 16.32, 14.18, 9.82, 3.54; MS (EI) m/z (rel. intensity) 341 (M^+ , 38), 244 (58), 202 (100); HRMS (EI) m/z calculated for $\text{C}_{22}\text{H}_{31}\text{NO}_2$ 341.2355, found 341.2356.

***N*-[1-(2-Oxo-2-phenylethyl)cyclopropylmethyl]-*P,P*-diphenylphosphinamide (14).** To a solution of **6** (0.16 g, 0.42 mmol) in dry THF (10 mL) was added OsO_4 (12 mg, 0.047 mmol) and NaIO_4 (0.45 g, 2.1 mmol). The reaction mixture was stirred for 4 h at r.t., quenched with sat. NH_4Cl and extracted with EtOAc (3x). The combined organic layers were washed with H_2O and brine, dried (MgSO_4), and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:4, hexanes/EtOAc containing 1% v/v Et_3N) to afford **14** (0.13 g, 77%) as a colorless foam: IR

(neat) 3201, 3058, 3003, 2922, 1686, 1596, 1580, 1438, 1448, 1353, 1310, 1277, 1211, 1186, 1123, 1110 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.94-7.79 (m, 6 H), 7.49-7.26 (m, 9 H), 3.50 (b, 1 H), 3.20-1.8 (m, 2 H), 2.98-2.93 (m, 2 H), 0.58-0.50 (m, 4 H); ^{13}C NMR (CDCl_3) δ 199.66, 137.23, 133.41, 133.17, 132.09, 131.97, 131.71, 128.64, 128.54, 128.37, 128.10, 48.57, 43.62, 18.02, 11.45; MS (EI) m/z (intensity) 389 (M^+ , 28), 371 (24), 284 (54), 218 (12), 201 (100), 172 (32); HRMS (EI) m/z calculated for $\text{C}_{24}\text{H}_{24}\text{NO}_2$ 389.1545, found 389.1539.

1-(6-Phenyl-5-aza-spiro[2.4]hept-5-yl)-ethanone (15). To a cooled (0 °C) solution of HCl (11 mL, 2.0 M in MeOH) was added a solution of **14** (99 mg, 0.26 mmol) in MeOH (1.0 mL). The reaction mixture was stirred for 1.5 h at 0 °C and concentrated. The residue was dissolved in MeOH (20 mL), treated with NaBH_3CN (80 mg, 1.3 mmol), stirred for 48 h at r.t. and concentrated. The residue was dissolved in THF (5.0 mL) and DIPEA (5.0 mL) and treated with AcCl (0.10 g, 1.3 mmol). The reaction mixture was stirred for 4 h, quenched with sat. NH_4Cl and extracted with EtOAc (2x). The combined organic layers were washed with H_2O and brine, dried (MgSO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (EtOAc containing 1% v/v Et_3N) to afford **15** (48 mg, 87%) as a colorless oil: IR (neat) 3059, 3027, 2997, 2947, 2863, 1644, 1592, 1494, 1393, 1418, 1377, 1355, 1306, 1226, 1182, 1131, 1114 cm^{-1} ; ^1H NMR (3.0:1 mixture of amide bond rotamers) major rotamer (CDCl_3) δ 7.37-7.17 (m, 6 H), 5.01 (dd, $J = 8.0, 2.7$ Hz, 1 H), 3.79 (d, $J = 11.8$ Hz, 1 H), 3.51 (d, $J = 11.8$ Hz, 1 H), 2.61 (dd, $J = 12.4, 8.1$ Hz, 1 H), 1.84 (s, 3 H), 1.66 (dd, $J = 12.3, 2.6$ Hz, 1 H), 0.66-0.32 (m, 4 H); minor rotamer (representative signals) d 5.31 (dd, $J = 8.2, 2.4$ Hz, 1 H), 3.71 (d, $J = 9.8$ Hz, 1 H), 3.46 (d, $J = 9.8$ Hz, 1 H), 2.50 (dd, $J = 12.5, 8.3$ Hz, 1 H), 2.10 (s, 3 H); ^{13}C NMR major rotamer (CDCl_3) δ 170.34, 143.58, 128.77, 127.30, 125.69, 63.18, 54.89, 44.66, 22.43, 18.98, 14.05, 7.12; MS (EI) m/z (intensity) 215 (M^+ , 100), 172 (55), 158 (32), 145 (60), 129 (21).

5-(Diphenylphosphinoyl)-7-phenyl-5-azaspiro[2.5]octan-7-ol (18). To a cooled (0 °C) solution of **6** (0.12 g, 0.31 mmol) in CH₂Cl₂ (5.0 mL) was added *m*-CPBA (0.23 g, 0.94 mmol, ~70 wt%). The reaction mixture was stirred for 3 h at r.t., quenched with sat. NH₄Cl, and extracted with CH₂Cl₂ (3x). The combined organic layers were dried (MgSO₄) and concentrated. The residue was dissolved in THF (5.0 mL), treated with HMPA (0.20 mL, 1.1 mmol) and NaH (26 mg, 1.1 mmol) and heated at 70 °C for 4 h, cooled to 0 °C and quenched with sat. NH₄Cl solution. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were washed with H₂O and brine, dried (MgSO₄), and concentrated. The residue was purified by chromatography on deactivated SiO₂ (1:4, hexanes/EtOAc containing 1% v/v Et₃N) to give **18** (69 mg, 47%) as a colorless oil: IR (neat) 3357, 3057, 3027, 2995, 2914, 2847, 1601, 1591, 1495, 1488, 1439, 1391, 1377, 1349, 1315, 1286, 1244, 1220, 1198, 1177, 1121, 1105 cm⁻¹; ¹H NMR (CDCl₃) δ 8.10-8.02 (m, 4 H), 7.67-7.32 (m, 11 H), 5.59 (s, 1 H), 3.54 (dd, *J* = 19.2, 13.7 Hz, 1 H), 3.41 (d, *J* = 14.7 Hz, 1 H), 3.48-3.34 (m, 1 H), 2.67 (d, *J* = 13.6 Hz, 1 H), 2.59 (dd, *J* = 13.4, 7.6 Hz, 1 H), 1.39 (d, *J* = 13.4 Hz, 1 H), 0.97-0.96 (m, 1 H), 0.82-0.75 (m, 1 H), 0.40-0.30 (m, 2 H); ¹³C NMR (CDCl₃) δ 144.89, 132.74, 132.09, 131.40, 130.34, 129.68, 128.98, 128.90, 128.81, 128.73, 128.19, 127.01, 125.19, 71.38, 57.51, 54.11, 46.07, 15.88, 13.83, 8.30; MS (ESI) *m/z* (intensity) 426 ([M+Na]⁺, 100), 412 (12), 386 (3), 218 (10), 201 (2); HRMS (ESI) *m/z* calculated for C₂₅H₂₆NO₂PNa (M+Na) 426.1599, found 426.1595.

5-(Diphenylphosphinoyl)-4-methyl-7-phenyl-5-azaspiro[2.5]octan-7-ol (19). To a cooled (0 °C) solution of **7** (0.15 g, 0.37 mmol) in CH₂Cl₂ (5.0 mL) was added *m*-CPBA (97 mg, 0.56

mmol, ~70 wt%). The reaction mixture was warmed to r.t., stirred for 6.5 h and quenched with sat. NH_4Cl . The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were washed with H_2O and brine, dried (MgSO_4), and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:4, hexanes/ EtOAc containing 1% v/v Et_3N) to give **17** (0.10 g, 64%) as an inseparable 1:1 mixture of distereoisomers. The mixture of epoxides **17** (91 mg, 0.22 mmol) was dissolved in dry THF (5.0 mL), treated with HMPA (0.19 mL, 1.1 mmol) and NaH (26 mg, 1.1 mmol), heated at 70 °C for 2.5 h, cooled to 0 °C and quenched with sat. NH_4Cl solution. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were washed with H_2O and brine, dried (MgSO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:4, hexanes/ EtOAc containing 1% v/v Et_3N) to afford **19a** and **19b** (55 mg, 57%) as a separable 1.3:1 mixture of diastereomers.

19a (major isomer): IR (neat) 3288, 3059, 2974, 2920, 2851, 1738, 1591, 1495, 1483, 1463, 1338, 1374, 1337, 1310, 1253, 1183, 1121 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.86-7.83 (m, 2 H), 7.87-7.68 (m, 2 H), 7.56-7.27 (m, 11 H), 3.66 (dd, $J = 13.1, 9.6$ Hz, 1 H), 3.38 (dd, $J = 13.2, 3.9$ Hz, 1 H), 2.94 (app. quintet $J = 7.1$ Hz, 1 H), 2.88 (b, 1 H), 2.24 (d, $J = 13.7$ Hz, 1 H), 1.82 (d, $J = 13.7$ Hz, 1 H), 1.25 (d, $J = 7.2$ Hz, 3 H), 0.40-0.31 (m, 3 H), 0.18-0.08 (m, 1 H); ^{13}C NMR (CDCl_3) δ 145.47, 132.91, 132.79, 132.59, 132.46, 131.92, 131.76, 131.08, 128.63, 128.48, 128.32, 128.03, 127.36, 126.39, 72.03, 71.93, 56.87, 51.37, 43.94, 20.69, 20.58, 15.57, 14.54, 9.64; MS (EI) m/z (intensity) 417 (24), 399 (43), 384 (30), 230 (7), 201 (100); HRMS (EI) m/z calculated for $\text{C}_{26}\text{H}_{28}\text{NO}_2\text{P}$ 417.1872, found 417.1858.

19b (minor isomer): IR (neat) 3364, 3058, 3026, 2974, 2935, 1493, 1488, 1439, 1446, 1427, 1380, 1362, 1325, 1311, 1255, 1202, 1179, 1163, 1135, 1121, 1103 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.94-7.90 (m, 4 H), 7.56-7.28 (m, 11 H), 5.72 (s, 1 H), 3.49 (dd, $J = 21.0, 14.5$ Hz, 1 H), 3.10 (ddd, $J = 14.4, 8.8, 1.7$ Hz, 1 H), 2.68 (d, $J = 14.0$ Hz, 1 H), 2.59-2.49 (m, 1 H), 1.41 (d, $J = 6.8$ Hz, 3 H), 1.05 (bd, $J = 14.0$ Hz, 1 H), 0.91-0.84 (m, 1 H), 0.73-0.66 (m, 1 H), 0.25-0.10 (m, 2 H); ^{13}C NMR (CDCl_3) δ 145.20, 132.81, 132.69, 132.41, 132.29, 132.12, 131.98, 131.77, 130.53, 128.97, 128.81, 128.16, 126.96, 125.27, 71.34, 56.00, 51.33, 41.48, 18.93, 15.83, 15.45,

9.14; MS (EI) m/z (intensity) 417 (72), 399 (44), 334 (5), 298 (10), 258 (21), 230 (76), 201 (100), 186 (25); HRMS (EI) m/z calculated for $C_{26}H_{28}NO_2P$ 417.1872, found 417.1856.

***N*-(*S*^{*})-{[(*IS*^{*},*2S*^{*})-2-Butylcyclopropyl](1-{[(*S*^{*})-2-phenyloxiran-2-yl]methyl}cyclopropyl)methyl}-*P,P*-diphenylphosphinamide (20) and *N*-(*S*^{*})-{[(*IS*^{*},*2S*^{*})-2-butylcyclopropyl](1-{[(*R*^{*})-2-phenyloxiran-2-yl]methyl}cyclopropyl)methyl}-*P,P*-diphenylphosphinamide (21).** To a solution of **3a** (0.15 g, 0.30 mmol) in dry CH_2Cl_2 (3.0 mL) was added *m*-CPBA (0.34 g, 1.2 mmol, ~60 wt%) in two portions (over 2 h). The reaction mixture was stirred for 4 h at r.t., filtered through basic alumina and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:1 hexanes/EtOAc containing 1% v/v Et_3N) to afford a 1:1 mixture of **20** and **21** (0.12 g, 77%) as a colorless oil. The diastereoisomers were separated by chromatography on deactivated SiO_2 (2:3 then 1:1, hexanes/EtOAc containing 1% v/v Et_3N) to afford diastereomerically pure epoxides **20** and **21**.

20: IR (neat) 3225, 3058, 2995, 2955, 2923, 2854, 1437, 1188, 1123 cm^{-1} ; 1H NMR (C_6D_6) δ 8.18-8.11 (m, 2 H), 8.04-7.97 (m, 2 H), 7.26-7.23 (m, 2 H), 7.13-7.04 (m, 9 H), 4.25 (t, J = 10.5 Hz, 1 H), 2.60 (d, J = 5.7 Hz, 1 H), 2.33 (d, J = 15.6 Hz, 1 H), 2.28-2.21 (m, 1 H), 2.22 (d, J = 5.7 Hz, 1 H), 1.81 (d, J = 15.4 Hz, 1 H), 1.49-1.29 (m, 5 H), 1.01-0.89 (m, 1 H), 0.93 (t, J = 6.9 Hz, 3 H), 0.87-0.73 (m, 2 H), 0.61-0.51 (m, 2 H), 0.29 (dt, J = 9.2, 5.5 Hz, 1 H), 0.24-0.17 (m, 2 H), 0.10-0.07 (m, 1 H); ^{13}C NMR (C_6D_6) δ 140.96, 136.82, 136.38, 135.14, 134.70, 132.86, 132.74, 132.56, 132.43, 131.21, 128.23, 127.40, 126.35, 61.76, 60.17, 57.69, 39.68, 34.32, 32.22, 23.91, 23.85, 23.77, 23.11, 18.11, 14.43, 13.76, 11.45, 11.33; MS (EI) m/z (rel. intensity) 499 (M^+ , 8), 481 (27), 326 (46), 218 (43), 201 (100); HRMS (EI) m/z calculated for $C_{32}H_{38}NO_2P$ 499.2640, found 499.2628.

21: IR (neat) 3226, 3058, 2995, 2955, 2923, 2854, 1438, 1188, 1123 cm^{-1} ; 1H NMR (C_6D_6) δ 8.19-8.11 (m, 4 H), 7.29-7.26 (m, 2 H), 7.14-7.01 (m, 9 H), 4.56 (dd, J = 10.2, 7.9 Hz, 1 H),

3.26 (d, $J = 5.2$ Hz, 1 H), 2.98 (d, $J = 15.9$ Hz, 1 H), 2.28 (d, $J = 5.2$ Hz, 1 H), 2.09 (app q, $J = 10.1$ Hz, 1 H), 1.60 (d, $J = 15.9$ Hz, 1 H), 1.41-1.26 (m, 6 H), 1.16-1.10 (m, 1 H), 0.91 (t, $J = 6.8$ Hz, 3 H), 0.73-0.66 (m, 1 H), 0.65-0.57 (m, 1 H), 0.55-0.48 (m, 1 H), 0.31-0.19 (m, 3 H), 0.05 (dt, $J = 8.3, 4.9$ Hz, 1 H); ^{13}C NMR (C_6D_6) δ 141.70, 136.62, 135.99, 134.94, 134.29, 135.06, 132.94, 132.35, 132.23, 131.39, 131.35, 131.28, 131.25, 128.62, 128.45, 128.40, 127.51, 126.28, 61.80, 60.67, 54.10, 39.57, 34.13, 32.24, 24.05, 23.95, 23.40, 23.36, 23.07, 18.15, 14.44, 14.41, 12.04, 11.14; MS (EI) m/z (rel. intensity) 499 (M^+ , 4), 481 (53), 326 (28), 218 (33), 201 (100); HRMS (EI) m/z calculated for $\text{C}_{32}\text{H}_{38}\text{NO}_2\text{P}$ 499.2640, found 499.2635.

(4*S,7*S**)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-5-(diphenylphosphinoyl)-7-phenyl-5-azaspiro[2.5]octan-7-ol (22).** To a suspension of NaH (14 mg, 0.35 mmol) in dry THF (1.0 mL) was added a solution of **20** (35 mg, 0.070 mmol) in dry THF (0.40 mL) and HMPA (61 μL , 0.35 mmol). The reaction mixture was heated at 70 °C for 30 min, cooled to 0 °C, quenched with sat. NH_4Cl solution and extracted with EtOAc (3x). The combined organic layers were washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (7:3, hexanes/EtOAc containing 1% v/v Et_3N) to afford **22** (25 mg, 71%) as a colorless oil: IR (neat) 3331, 3059, 3003, 2954, 2923, 2852, 1439, 1179, 1120, 1105 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.01-7.94 (m, 2 H), 7.91-7.84 (m, 2 H), 7.60-7.56 (m, 2 H), 7.49-7.40 (m, 6 H), 7.35-7.32 (m, 2 H), 7.25-7.19 (m, 1 H), 6.21 (s, 1 H), 3.66 (dd, $J = 22.1, 14.5$ Hz, 1 H), 3.28-3.20 (m, 1 H), 2.86 (d, $J = 14.0$ Hz, 1 H), 1.67-1.39 (m, 6 H), 1.32-1.23 (m, 2 H), 1.11 (d, $J = 14.0$ Hz, 1 H), 1.01 (t, $J = 7.0$ Hz, 3 H), 0.86 (dt, $J = 8.8, 5.6$ Hz, 1 H), 0.61-0.52 (m, 2 H), 0.49-0.43 (m, 1 H), 0.35-0.28 (m, 1 H), 0.27-0.22 (m, 1 H), 0.20-0.14 (m, 1 H); ^{13}C NMR (CDCl_3) δ 145.42, 133.00, 132.88, 132.74, 132.62, 132.18, 132.06, 132.02, 131.94, 131.91, 131.02, 130.39, 129.32, 128.82, 128.65, 128.51, 128.34, 128.01, 126.78, 125.28, 71.18, 64.53, 52.99, 42.63, 34.20, 32.53, 22.77, 19.49, 19.37, 19.07, 16.98, 14.22, 13.89, 13.12, 8.93; MS (EI) m/z

(rel. intensity) 499 (M^+ , 15), 481 (23), 230 (32), 201 (100); HRMS (EI) m/z calculated for $C_{32}H_{38}NO_2P$ 499.2640, found 499.2637.

[(4*S, 6*S**)-4-((1*S**,2*S**)-2-Butylcyclopropyl)-5-(diphenylphosphinoyl)-6-phenyl-5-azaspiro[2.4]hept-6-yl]methanol (**23**).** To a suspension of NaH (18 mg, 0.45 mmol) in dry THF (1.3 mL) was added a solution of **21** (45 mg, 0.090 mmol) in dry THF (0.50 mL) and HMPA (78 μ L, 0.45 mmol). The reaction mixture was heated at 70 °C for 30 min, cooled to 0 °C, quenched with sat. NH_4Cl solution and extracted with EtOAc (3x). The combined organic layers were washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on deactivated SiO_2 (1:1, hexanes/EtOAc containing 1% v/v Et_3N) to afford **23** (34 mg, 75%) as a colorless oil: IR (neat) 3289, 3058, 3000, 2954, 2925, 2855, 1438, 1184, 1119, 1105 cm^{-1} ; 1H NMR ($CDCl_3$) δ 7.83-7.74 (m, 4 H), 7.50-7.35 (m, 9 H), 7.26-7.19 (m, 2 H), 3.50 (d, $J = 7.3$ Hz, 2 H), 3.02 (b, 1 H), 2.36 (dd, $J = 9.3, 8.1$ Hz, 1 H), 2.13-1.96 (m, 2 H), 1.45-1.34 (m, 1 H), 1.26-1.12 (m, 4 H), 0.96-0.90 (m, 1 H), 0.85 (t, $J = 6.7$ Hz, 3 H), 0.80-0.74 (m, 1 H), 0.62-0.55 (m, 2 H), 0.53-0.45 (m, 2 H), 0.28 (app t, $J = 6.4$ Hz, 2 H), 0.14-0.07 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 145.30, 134.27, 133.89, 132.82, 132.70, 132.58, 132.46, 132.20, 131.51, 131.48, 131.40, 131.37, 128.32, 128.24, 128.15, 128.07, 128.03, 127.20, 125.70, 72.24, 72.16, 67.01, 55.23, 45.73, 32.83, 31.30, 22.50, 20.60, 20.52, 18.73, 18.13, 14.07, 13.30, 11.96, 9.64; MS (EI) m/z (rel. intensity) 499 (M^+ , 13), 481 (19), 230 (31), 201 (100); HRMS (EI) m/z calculated for $C_{32}H_{36}NOP$ ($M-H_2O$) 481.2535, found 481.2525.

ppm

ppm

46

ppm

160.424

160.393

146.048

144.475

139.678

139.637

133.136

129.528

128.315

127.997

127.675

119.134

115.123

114.610

113.413

112.556

m-OMe N-allyl

63.660

63.628

54.956

54.916

47.503

47.441

39.917

33.730

33.698

31.987

31.923

22.996

20.107

20.050

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15.150

14.371

10.040

7.618

ppm

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140

120

100

80

60

40

20

0

60

Current Data Parameters
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EXPNO 3
PROCNO 1

F2 - Acquisition Parameters

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DE 6.00 usec
TE 300.0 K
D1 3.00000000 sec
D3 0.00100000 sec

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PL1 0.00 dB
SFO1 75.5007908 MHz

===== CHANNEL f2 =====
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NUC2 1H
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PL2 120.00 dB
PL12 12.00 dB
SFO2 300.2318014 MHz

F2 - Processing parameters
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GB 0
PC 1.40

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F2P -10.000 ppm
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ppm

cfs-6-153b

ppm

ppm

ppm

ppm