Supplementary data

Microwave-Assisted Synthesis of Allylic Amines: Considerable Rate Acceleration in the Hydrozirconation-Transmetalation-Aldimine Addition Sequence

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General:

All moisture-sensitive reactions were performed under an atmosphere of N₂ and glassware was flame dried under vacuum prior to use. Toluene was 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)₂Mo₇O₂₄·4H₂O and 0.20 g of Ce(SO₄)₂ in 100 mL of 3.5 N H₂SO₄). NMR spectra were recorded in CDCl₃ at 300 MHz/75 MHz (¹H NMR/¹³C NMR) at 21 °C unless stated otherwise. 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. Mass spectra were obtained on a double focusing instrument. Microwave reactions were run using a CEM Discover microwave reactor.

(E)-N-(1-Phenylhept-2-enyl)-P,P-diphenylphosphinamide (3).¹a General Protocol A. To a suspension of Cp₂ZrHCl (0.13 g, 0.49 mmol) in dry toluene (2.0 mL) was added 1 (60 mL, 0.52 mmol). The reaction mixture was heated in the microwave reactor (60 °C, 150 W) for 5 min, cooled to -78 °C, treated with Me₂Zn (0.16 mL, 0.33 mmol, 2.0 M in toluene), and warmed to 0 °C. After addition of 2 (0.10 g, 0.33 mmol), the mixture was heated in the microwave reactor (100 °C, 150 W) for 5 min, cooled to 0 °C, quenched with MeOH (0.25-0.50 mL), diluted with EtOAc, filtered through SiO₂ and concentrated. The residue was purified by chromatography on deactivated SiO₂ (3:7, hexanes/EtOAc containing 1% v/v Et₃N) to afford 3 (93 mg, 73%) as a colorless solid: ¹H NMR δ 7.97-7.90 (m, 2 H), 7.87-7.80 (m, 2 H), 7.53-7.21 (m, 11 H), 5.66 (ddt, J = 15.3, 6.2, 1.3 Hz, 1 H), 5.51 (ddt, J = 15.3, 6.4, 0.9 Hz, 1 H), 4.81 (td, J = 9.4, 6.4 Hz, 1 H), 3.25 (dd, J = 9.2, 6.1 Hz, 1 H), 1.99 (q, J = 6.2 Hz, 2 H), 1.31-1.26 (m, 4 H), 0.88 (t, J = 6.9 Hz, 3 H).

(E)-N-{5-[(tert-Butyldiphenylsilyl)oxy]-1-phenylpent-2-enyl}-P,P-diphenylphosphinamide (10).¹b According to the General Protocol A, Cp₂ZrHCl (0.13 g, 0.49 mmol), 9 (0.16 g, 0.52 mmol), Me₂Zn (0.16 mL, 0.33 mmol, 2.0 M in toluene) and 2 (0.10 g, 0.33 mmol) afforded 10 (0.12 g, 62%) as a colorless foam: ¹H NMR δ 7.94-7.79 (m, 4 H), 7.63 (d, J = 6.4 Hz, 4 H), 7.45-7.23 (m, 17 H), 5.74 (dd, J = 15.4, 6.0 Hz, 1 H),
5.52 (dt, \( J = 15.5, 6.5 \) Hz, 1 H), 4.85-4.76 (m, 1 H), 3.63 (t, \( J = 6.5 \) Hz, 2 H), 3.25-3.20 (m, 1 H), 2.26 (q, \( J = 6.5 \) Hz, 2 H), 1.01 (s, 9 H).

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\text{(CH}_2\text{)}_2\text{N(Ts)CO}_2\text{Pr}
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**O-Isopropyl-N-but-3-ynyl-N-(4-methylphenyl)sulfonyl carbamate (11).** A solution of 4-methylbenzenesulfonyl isocyanate (2.6 g, 10 mmol) in dry THF (20 mL) was treated under nitrogen with Ph_3P (2.6 g, 10 mmol) and 3-butyn-1-ol (0.51 mL, 6.7 mmol), cooled to 0 °C, and treated dropwise with DIAD (1.6 mL, 10 mmol). The reaction mixture was warmed to r.t., stirred for 2 h, concentrated and purified by chromatography on SiO_2 (9:1, hexanes/EtOAc) to afford 11 (1.3 g, 65%) as a colorless solid: Mp 71.6-73.4 °C (hexanes/EtOAc); IR (KBr) 3308, 2988, 2934, 1731, 1597, 1357, 1170, 1089, 1102, 899, 811, 735 cm\(^{-1}\); \(^1\)H NMR (7.83 (d, \( J = 8.3 \) Hz, 2 H), 7.30 (d, \( J = 8.4 \) Hz, 2 H), 4.89 (septet, \( J = 6.3 \) Hz, 1 H), 4.01 (app t, \( J = 7.3 \) Hz, 2 H), 2.65 (td, \( J = 7.6, 2.7 \) Hz, 2 H), 2.43 (s, 3 H), 2.02 (t, \( J = 2.6 \) Hz, 1 H), 1.15 (d, \( J = 6.3 \) Hz, 6 H); \(^{13}\)C NMR (151.93, 144.81, 137.21, 129.56, 129.30, 128.63, 80.60, 72.26, 70.79, 45.49, 21.85, 20.25; MS (EI) \( m/z \) (intensity) 309 (M\(^+\), 27), 287 (12), 270 (34), 245 (28), 206 (37), 184 (100), 155 (74), 91 (46); HRMS (EI) \( m/z \) calculated for C\(_{15}\)H\(_{19}\)NO\(_4\)S 309.1035, found 309.1041.

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\text{(E)-Methyl 4-\{1-diphenylphosphinoylamino-5-(isopropoxycarbonyltosylamino)pent-2-ynyl\}benzoate (13). General Protocol B.} \quad \text{To a suspension of Cp}_2\text{ZrHCl (0.10 g, 0.40 mmol) in dry toluene (1.6 mL) was added 11 (0.14 g, 0.46 mmol). The reaction mixture was heated in the microwave reactor in the flash heat mode (80 °C, 75 W) for 40 sec, cooled to -78 °C, treated with Me}_2\text{Zn (0.19 mL, 0.38 mmol, 2.0 M in toluene), and warmed to 0 °C. After addition of 12 (94 mg, 0.26 mmol), the solution was heated in the microwave reactor in the flash heat mode (100 °C, 150 W) for 40 sec, cooled to r.t, quenched with 1.0 M NH}_4\text{Cl, and diluted with EtOAc and 1.0 M NaHCO}_3. \quad \text{The aqueous layer was extracted with of EtOAc (2x) and the combined organic layers were washed with water (2x) and brine (2x), dried (MgSO}_4\) and purified by chromatography on deactivated SiO}_2 (1:9, hexanes/EtOAc containing 1% v/v Et}_3\text{N) to afford 13 (0.14 g, 80%)}
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as a colorless solid: Mp 62.8-64.8 °C (hexanes/EtOAc); IR (KBr) 3167, 3057, 2982, 2952, 1723, 1609, 1437, 1362, 1280, 1186, 1167, 1107, 1122, 1087 cm⁻¹; ¹H NMR 7.97-7.89 (m, 4 H), 7.83-7.74 (m, 4 H), 7.51-7.26 (m, 10 H), 5.82 (dd, J = 15.4, 5.5 Hz, 1 H), 5.51 (td, J = 14.2, 6.4 Hz, 1 H), 4.85-4.79 (m, 2 H), 3.91 (s, 3 H), 3.84 (t, J = 7.0 Hz, 2 H), 3.63 (bt, J = 7.1 Hz, 1 H), 2.42 (s, 3 H), 1.27 (bs, 1 H), 1.09 (d, J = 6.2 Hz, 6 H), 0.97-0.86 (m, 1 H); ¹³C NMR 167.18, 151.96, 147.85, 147.79, 144.67, 137.43, 135.00, 134.94, 132.60, 132.51, 132.38, 132.18, 132.10, 131.73, 130.11, 129.53, 129.39, 128.87, 128.76, 128.70, 128.58, 128.48, 127.538, 127.54, 72.05, 56.53, 52.70, 46.67, 33.09, 21.85; MS (EI) m/z (intensity) 674 (M⁺, 45), 473 (48), 416 (28), 404 (52), 216 (87), 201 (100), 155 (40), 91 (65); HRMS (EI) m/z calculated for C₃₆H₃₉N₂O₆PS: 674.2216, found 674.2224.

(E)-Methyl 4-{1-[(diphenylphosphinoyl)amino]hept-2-enyl}benzoate (14). Aaccording to the General Protocol B, Cp₂ZrHCl (0.10 g, 0.40 mmol), 1 (51 µL, 0.44 mmol), Me₂Zn (0.19 mL, 0.38 mmol, 2.0 M in toluene) and 12 (94 mg, 0.26 mmol) afforded 14 (0.11 g, 95%) as a colourless solid: ¹H NMR 7.99-7.81 (m, 4 H), 7.48-7.36 (m, 8 H), 5.65 (dd, J = 15.3, 6.1 Hz, 1 H), 5.54-5.44 (m, 1 H), 4.84 (td, J = 9.7, 6.1 Hz, 1 H), 3.92 (s, 3 H), 3.28 (td, J = 9.7, 6.1 Hz, 1 H), 1.98 (q, J = 6.6 Hz, 2 H), 1.31-1.24 (m, 4 H), 0.87 (t, J = 6.9 Hz, 3 H).

(E)-N-(2-Ethyl-1-phenylpent-2-enyl)-P,P-diphenylphosphinamide (16). General Protocol C: To a suspension of Cp₂ZrHCl (0.10 g, 0.40 mmol) in dry toluene (2.0 mL) was added 15 (50 µL, 0.44 mmol). The reaction mixture was heated in the microwave reactor in the flash heat mode (100 °C, 100 W) for 40 sec, cooled to -78 °C, treated with Me₂Zn (0.19 mL, 0.38 mmol, 2.0 M in toluene), and warmed to 0 °C. After addition of 2 (79 mg, 0.26 mmol), the solution was heated in the microwave reactor in the flash heat.
mode (100 °C, 150 W) for 40 sec, cooled to r.t., quenched with 1.0 M NH₄Cl, vigorously stirred, and diluted with EtOAc and 1.0 M NaHCO₃. The aqueous layer was extracted with EtOAc (2x), and the combined organic layers were washed with water (2x) and brine (2x), dried (MgSO₄) and concentrated. The residue was purified by chromatography on deactivated SiO₂ (1:9, hexanes/EtOAc containing 1% v/v Et₃N) to afford 16 (75 mg, 77%) as a colorless solid: ¹H NMR δ 7.95-7.85 (m, 4 H), 7.45-7.29 (m, 11 H), 5.53 (t, J = 14.3 Hz, 1 H), 4.73 (t, J = 10.7 Hz, 1 H), 3.24 (td, J = 10.0, 6.1 Hz, 1 H), 2.16-2.04 (m, 3 H), 1.78-1.68 (m, 1 H), 1.63 (s, 1 H), 1.03 (t, J = 7.5 Hz, 3 H), 0.70 (t, J = 7.6 Hz, 3 H).

(E)-Methyl 4-(1-diphenylphosphinoxylamino-2-propylhex-2-enyl)benzoate (18). According to the General Protocol C, Cp₂ZrHCl (0.21 g, 0.80 mmol), 17 (0.13 mL, 0.87 mmol), Me₂Zn (0.40 mL, 0.80 mmol, 2.0 M in toluene) and 12 (0.19 g, 0.52 mmol) afforded 18 (0.18 g, 74%) as a colorless solid: Mp 91.9-92.3 °C (hexanes/EtOAc); IR (KBr) 3181, 2957, 2930, 2869, 1722, 1610, 1436, 1281, 1107, 1123, 1019 cm⁻¹; ¹H NMR δ 7.97-7.77 (m, 6 H), 7.50-7.35 (m, 8 H), 5.50 (t, J = 7.2 Hz, 1 H), 4.76 (t, J = 10.6 Hz, 1 H), 3.90 (s, 3 H), 3.28 (dd, J = 10.3, 6.3 Hz, 1 H), 2.14-2.02 (m, 3 H), 1.74-1.71 (dq, J = 14.5, 7.3 Hz, 1 H), 1.45-1.37 (m, 2 H), 1.17-1.09 (m, 2 H), 0.93 (t, J = 7.3 Hz, 3 H), 0.74 (t, J = 7.3 Hz, 3 H); ¹³C NMR δ 167.21, 148.28, 140.24, 140.18, 133.71, 133.61, 132.72, 132.59, 132.41, 132.28, 132.16, 131.89, 130.02, 129.29, 128.77, 128.61, 128.78, 59.51, 52.29, 31.40, 30.15, 23.23, 22.34, 14.46, 14.23; MS (EI) m/z (intensity) 475 (M⁺, 59), 446 (16), 432 (14), 364 (63), 274 (45), 218 (53), 201 (100), 77 (48); HRMS (EI) m/z calculated for C₂₀H₃₄NO₃P 475.2276, found 475.2283.
(E)-Methyl 4-(1-diphenylphosphinoylamino-3-cyclohexyl-2-methylallyl)benzoate (19). General Protocol D. To a suspension of Cp₂ZrHCl (0.14 g, 0.55 mmol) in dry toluene (1.5 mL) was added a freshly prepared solution of 5 (0.25 mL, 0.28 mmol, 1.1 M in toluene). The reaction mixture was heated in the microwave reactor (60 °C, 150 W) for 30 min, treated with 5 (0.25 mL, 0.28 mmol, 1.1 M in toluene), heated in the microwave reactor (60 °C) for 15 min, cooled to −78 °C, treated with Me₂Zn (0.14 mL, 0.28 mmol, 2.0 M in toluene), and warmed to 0 °C. After addition of 12 (0.10 g, 0.28 mmol), the solution was heated in the microwave reactor (100 °C, 150 W) for 5 min, cooled to 0 °C, quenched with MeOH (0.25-0.50 mL), diluted with EtOAc, filtered through SiO₂ and concentrated. The residue was purified by chromatography on deactivated SiO₂ (3:7, hexanes/EtOAc containing 1% v/v Et₃N) to afford 19 (81 mg, 60%) as a colorless foam: Mp 147.0-148.6 °C (hexanes/EtOAc); IR (KBr) 3165, 3057, 2926, 2849, 1721, 1609, 1438, 1273, 1199, 1183, 1108 cm⁻¹; ¹H NMR [d] 7.96-7.87 (m, 4 H), 7.85-7.77 (m, 2 H), 7.50-7.31 (m, 8 H), 5.24 (d, J = 9.1 Hz, 1 H), 4.71 (t, J = 10.7 Hz, 1 H), 3.88 (s, 3 H), 3.43 (dd, J = 10.5, 6.8 Hz, 1 H), 2.27-2.14 (m, 1 H), 1.73-1.62 (m, 5 H), 1.51 (d, J = 1.0 Hz, 3 H), 1.35-1.19 (m, 3 H), 1.15-0.98 (m, 2 H); ¹³C NMR [d] 166.83, 147.46, 147.40, 134.47, 133.38, 132.98, 132.61, 132.55, 132.47, 132.34, 131.94, 131.82, 131.68, 131.25, 129.61, 128.76, 128.42, 128.38, 128.26, 128.21, 127.02, 61.23, 51.95, 36.75, 32.83, 32.74, 25.91, 25.81, 13.30; MS (EI) m/z (intensity) 487 (M⁺, 27), 404 (50), 364 (22), 286 (100), 218 (81), 201 (100); HRMS (EI) m/z calculated for C₃₀H₃₄NO₃P 487.2276, found 487.2266.

(E)-N-(3-Cyclohexyl-2-ethyl-1-phenylallyl)-P,P-diphenylphosphinamide (20). According to the General Protocol D, Cp₂ZrHCl (0.17 g, 0.66 mmol), 6 (89 mg, 0.66 mmol), Me₂Zn (0.16 mL, 0.33 mmol, 2.0 M in toluene) and 2 (0.10 g, 0.33 mmol) afforded 20 (91 mg, 63%) as a colorless foam: Mp 135.5-137.2 °C (hexanes/EtOAc); IR
(KBr) 3207, 3056, 2962, 2849, 1491, 1447, 1437, 1185, 1123, 1108 cm$^{-1}$; $^1$H NMR: 7.99-7.92 (m, 2 H), 7.89-7.82 (m, 2 H), 7.51-7.33 (m, 8 H), 7.31-7.18 (m, 3 H), 5.44 (d, $J$ = 9.5 Hz, 1 H), 4.72 (t, $J$ = 11.0 Hz, 1 H), 3.23 (dd, $J$ = 10.2, 6.1 Hz, 1 H), 2.34-2.23 (m, 1 H), 2.17-2.05 (m, 1 H), 1.74-1.62 (m, 6 H), 1.37-1.07 (m, 5 H), 0.68 (t, $J$ = 7.5 Hz, 3 H); $^{13}$C NMR: 142.57, 142.52, 139.39, 139.33, 133.70, 133.19, 132.82, 132.66, 132.53, 131.99, 131.86, 131.73, 131.69, 131.65, 131.45, 128.37, 128.30, 128.22, 128.13, 127.79, 127.53, 127.04, 58.74, 36.77, 33.44, 26.01, 25.95, 22.16, 13.92; MS (El) $m/z$ (intensity) 443 (M$^+$, 23), 360 (28), 306 (28), 242 (94), 218 (78), 201 (100); HRMS (El) $m/z$ calculated for C$_{29}$H$_{34}$NOP 443.2378, found 443.2387.

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