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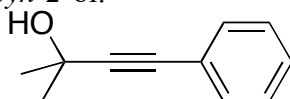
**α,β -Unsaturated Imines from Titanium Hydroamination and
Functionalization by Rhodium C–H Activation**

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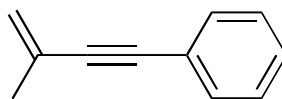
Synthesis of enyne starting materials

Synthesis of 2-Methyl-4-phenyl-3-butyne-2-ol.



A 500 mL roundbottom flask was charged with dry THF (200 mL) and a stir bar. The flask was cooled with a dry ice-acetone bath, and phenylacetylene (11.24 g, 110 mmol) was added. Dropwise, n-butyllithium (68.8 mL, 1.6 M in hexanes, 110 mmol) was added over about 15 min. The solution was stirred for 10 min after the addition was complete. Dry acetone (5.808 g, 7.343 mL, 100 mmol) was added over 5 min, and the resulting solution was stirred 20 min at $-78\text{ }^{\circ}\text{C}$. The solution was then allowed to warm slowly to room temperature. Cautiously, water (40 mL) was added, followed by anhydrous potassium carbonate until the aqueous phase became pasty. The organic phase was decanted, and the aqueous layer was washed with 2×30 mL of ether. The combined organic solutions were dried (MgSO_4) and distilled under reduce pressure, which afforded the alcohol as a colorless oil (95%, 15.22 g). b.p $80\text{--}81\text{ }^{\circ}\text{C}$ (~ 0.2 mmHg). Spectroscopic data were consistent with those reported in the literature.¹

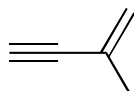
Synthesis of (3-Methyl-3-buten-1-ynyl)-benzene



A 150 mL Schlenck tube was charged with a stir bar, activated HY-12 zeolite (2.60 g), PhCl (60 mL), and 2-Methyl-4-phenyl-3-butyne-2-ol (7.267 g). The suspension was heated for 2 h at $130\text{ }^{\circ}\text{C}$ under stirring. After cooling to room temperature, the zeolite was removed by filtration. The product was distilled under reduced pressure (b.p. $35\text{ }^{\circ}\text{C}$, ~ 0.2 mmHg), which afforded the product as a colorless oil (58.1%, 3.744 g). $^1\text{H NMR}$ (300 MHz, CDCl_3): $\delta = 7.326$ (2 H, m),

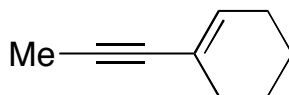
7.181 (3 H, m), 5.290 (1 H, d, $J = 1.1$ Hz), 5.185 (1 H, s), 1.879 (3 H, d, $J = 1.7$ Hz). Spectroscopic data were consistent with those reported in the literature.²

Synthesis of 2-Methyl-1-buten-3-yne



The preparation of 2-methyl-1-buten-3-yne was done similar to the literature³ description. In a 1 L 3-neck flask was loaded acetic anhydride (240 g, 2.35 mol) and *p*-toluenesulfonic acid monohydrate (16 g, 84.1 mmol). After cooling the solution in an ice bath, 2-methyl-3-butyn-2-ol (120.2 g, 1.40 mol, Aldrich) and 20 g of boiling chips were added. After addition, the mixture was gradually warmed and then stirred for 2 h at room temperature. The highly volatile enyne product was distilled from the reaction mixture. The distillation was stopped when the active distillate temperature indicated over 100 °C. The distilled compound was shaken with 20 mL of an ice-cold KOH solution. The organic layer was collected and dried over MgSO₄. Distillation through a short column afforded 2-methyl-1-buten-3-yne in a 51.4% yield (47.6 g), b.p. 35 °C (~760 mmHg). ¹H NMR (300 MHz, CDCl₃): $\delta = 5.339$ (1 H, m), 5.247 (1 H, m), 2.827 (1 H, s), 1.857 (3 H, m). ¹³C{¹H} NMR (CDCl₃): $\delta = 125.9, 123.2, 84.8, 76.1, 23.1$.

Synthesis of 1-Prop-1-ynyl-cyclohexene

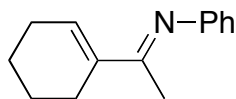


In a 250 mL Schlenk flask with a 24/40 joint was loaded a stir bar, 1-ethynylcyclohexene (10 g, 94.29 mmol), and THF 100 mL. The flask was cooled in a dry ice-acetone bath, and 2.0 M *n*-BuLi in hexanes (48 mL, 96 mmol) was added via syringe. After the reaction stirred for 1 h at -78 °C, iodomethane (5.98 mL, 96 mmol) was added dropwise. The reaction was allowed to warm to room temperature and stir an additional 30 min. The THF was removed by rotary evaporation. An ether solution of the product was washed with water then dried with MgSO₄. Distillation under reduced pressure afforded the product as a colorless oil (8.36 g, 74% yield). b.p. 33 °C (0.2 mmHg). ¹H NMR (300 MHz, CDCl₃): $\delta = 5.951$ (1 H, t, $J = 1.4$ Hz), 2.047 (4 H, m), 1.888 (3 H, s), 1.560 (4 H, m). ¹³C{¹H} NMR (CDCl₃): $\delta = 133.0, 120.9, 82.5, 81.4, 29.4$,

25.4, 22.3, 21.5, 3.98. MS (EI) $m/z = 120$ (M^+). Spectroscopic data were consistent with those reported in the literature.⁴

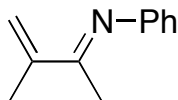
Synthesis of products in Table 1

Entry 1



In a 40 mL pressure tube was loaded a stir bar, 1-ethynylcyclohexene (1.180 mL, 10 mmol), aniline (0.911 mL, 10 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.3824 g, 1 mmol), and toluene (5 mL). The tube was sealed with a threaded Teflon cap and removed from the glove box. The reaction was heated at 50 °C in an oil bath for 16 h. The reaction was filtered through a plug of Al_2O_3 on a fritted funnel using CH_2Cl_2 as eluent. The volatiles were removed by rotary evaporation. The product was distilled under reduced pressure to afford the imine as a pale yellow oil (1.75 g, 88%). b.p. 100 °C, ~0.2 mmHg. ^1H NMR (300 MHz, CDCl_3): $\delta = 7.294$ (2 H, m), 7.002 (1 H, m), 6.702 (2 H, m), 6.531 (1 H, m), 2.457 (2 H, m), 2.279 (2 H, m), 1.931 (3 H, s), 1.689 (4 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): $\delta = 166.4, 152.1, 139.3, 133.6, 128.6, 122.6, 119.3, 26.1, 24.6, 22.5, 21.95, 15.7$. Elemental Analysis: Calc. For $\text{C}_{14}\text{H}_{17}\text{N}$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.10; H, 8.44; N, 7.03. MS (EI) $m/z = 199$ (M^+). A similar reaction has been done to form the same product using HgCl_2 as catalyst.⁵

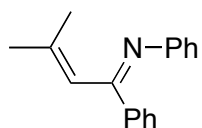
Entry 2



In a 40 mL pressure tube was loaded a stir bar, 2-methyl-1-buten-3-yne (0.951 mL, 10 mmol), aniline (0.911 mL, 10 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.3824 g, 1 mmol), and toluene (5 mL). The tube was fitted with a threaded Teflon cap and removed from the glove box. The reaction was heated in a 50 °C oil bath for 44 h. The reaction was filtered through a plug of Al_2O_3 on a fritted funnel using CH_2Cl_2 as eluent. The volatiles were removed by rotary evaporation and distilled under reduced pressure to afford the product as a pale yellow oil (1.023 g, 64%). b.p. 33 °C, ~0.2 mmHg. ^1H NMR (300 MHz, CDCl_3): $\delta = 7.320$ (2 H, t, $J = 7.3$ Hz), 7.056 (1 H, t, $J = 7.3$ Hz), 6.726 (2 H, d, $J = 7.1$ Hz), 5.665 (1 H, d, $J = 0.7$ Hz), 5.581 (1 H, d, $J = 1.0$ Hz), 2.097

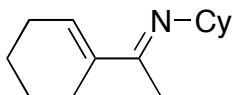
(3 H, s), 1.982 (3 H, s). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): $\delta = 166.4, 151.7, 145.6, 128.7, 122.9, 119.9, 118.96, 19.3, 15.8$. Elemental Analysis: Calc. For $\text{C}_{11}\text{H}_{13}\text{N}$: C, 82.97; H, 8.23; N, 8.80. Found: C, 82.89; H, 7.99; N, 8.88. MS (EI) $m/z = 159$ (M^+). A similar reaction has been done to form the same product using HgCl_2 as catalyst.⁵

Entry 3



In a 40 mL of pressure tube was loaded a stir bar, (3-methyl-3-buten-1-ynyl)benzene (1.422 g, 10 mmol), aniline (0.911 mL, 5 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.3824 g, 1 mmol), and toluene (5 mL). The tube was sealed with a threaded Teflon cap and removed from the dry box. The reaction was heated at 130 °C in an oil bath for 19 h. The reaction was filtered through Al_2O_3 on a fritted filter with CH_2Cl_2 as an eluent. Volatiles were removed in vacuo and the product was distilled under reduced pressure (115 – 116 °C, ~0.2 mmHg). Finally, the product was purified on an alumina column using pentane:ether (40:1) as eluent. The product was obtained as a yellow oil (1.647 g, 70%). ^1H NMR (300 MHz, CDCl_3): $\delta = 7.918$ (2 H, m), 7.473 (3 H, m), 7.339 (2 H, m), 7.059 (1 H, m), 6.944 (2 H, m), 5.847 (1 H, d, $J = 1.2$ Hz), 1.783 (3 H, s), 1.430 (3 H, d, $J = 1.7$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): $\delta = 166.8, 151.6, 141.8, 139.6, 130.2, 128.4, 128.3, 128.2, 123.3, 120.8, 120.5, 25.4, 21.3$. Elemental Analysis: Calc. For $\text{C}_{17}\text{H}_{17}\text{N}$: C, 86.77; H, 7.28; N, 5.95. Found: C, 86.28; H, 7.04; N, 5.66. MS (EI) $m/z = 253$ (M^+).

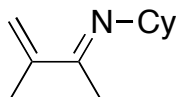
Entry 4



A 40 mL pressure tube was loaded with a stir bar, 1-ethynylcyclohexene (1.180 mL, 10 mmol), cyclohexylamine (1.15 mL, 10 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.3824 g, 1 mmol), and toluene 5 mL. The tube was sealed with a Teflon cap and removed from the glove box. The reaction was heated in a 50 °C oil bath for 24 h. The solution was filtered through Al_2O_3 on a fritted glass funnel and washed through with CH_2Cl_2 . Volatiles were removed by rotary evaporation, and the product was distilled under reduced pressure (71 °C, ~0.2 mmHg). The product was collected as

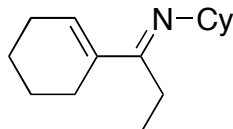
a pale yellow oil (1.60 g, 78%). ^1H NMR (300 MHz, CDCl_3): δ = 6.189 (1 H, m), 3.313 (1 H, m), 2.255 (2 H, m), 2.114 (2 H, m), 1.891 (3 H, s), 1.723 (2 H, m), 1.566 (7 H, m), 1.43 ~ 1.10 (5 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (300 MHz, CDCl_3): δ = 163.2, 140.4, 129.2, 59.1, 33.6, 25.9, 25.7, 25.1, 24.8, 22.6, 22.1, 13.1. Elemental Analysis: Calc. For $\text{C}_{14}\text{H}_{23}\text{N}$: C, 82.69; H, 11.40; N, 6.89. Found: C, 81.99; H, 11.46; N, 6.97. MS (EI) m/z = 205 (M^+).

Entry 5



A 40 mL pressure tube was loaded with a stir bar, 2-methyl-1-buten-3-yne (0.951 mL, 10 mmol), cyclohexylamine (1.444 mL, 10 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.3824 g, 1 mmol), and toluene (5 mL). The tube was sealed with a Teflon cap and removed from the dry box. The reaction was heated in a 50 °C oil bath for 43 h. The solution was filtered through Al_2O_3 on a fritted glass funnel and washed through with CH_2Cl_2 . Volatiles were removed by rotary evaporation. The product was distilled under reduced pressure (27 °C, ~0.2 mmHg) and collected as a colorless oil (1.20 g, 73%). ^1H NMR (300 MHz, CDCl_3): δ = 5.357 (1 H, m), 5.272 (1 H, m), 3.328 (1 H, m), 1.939 (3 H, s), 1.899 (3 H, t, J = 0.7 Hz), 1.72 ~ 1.12 (10 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (300 MHz, CDCl_3): δ = 162.8, 147.1, 116.3, 59.5, 33.5, 25.8, 24.7, 19.8, 13.2. Elemental Analysis: Calc. For $\text{C}_{11}\text{H}_{19}\text{N}$: C, 79.94; H, 11.59; N, 8.48. Found: C, 79.74; H, 11.23; N, 8.68. MS (EI) m/z = 165 (M^+).

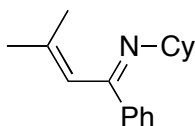
Entry 6



A 40 mL pressure tube was loaded with a stir bar, 1-(prop-1-ynyl)cyclohexene (0.9616 g, 8 mmol), aniline (0.73 mL, 8 mmol), $\text{Ti}(\text{dmpm})(\text{NMe}_2)_2$ (0.2466 g, 0.8 mmol), and chlorobenzene (4 mL). The tube was sealed with a Teflon stopper and removed from the dry box. The reaction was heated in a 100 °C oil bath for 5 h. The solution was filtered through Al_2O_3 on a fritted glass funnel and washed through with CH_2Cl_2 . Volatiles were removed by rotary evaporation. The product was distilled under reduced pressure (110 °C, ~0.2 mmHg) and collected as a pale

yellow oil (1.20 g, 73%). ^1H NMR (300 MHz, DMSO- d_6 at +150 °C): δ = 7.268 (2 H, m), 6.992 (1 H, m), 6.629 (2 H, m), 5.563 (1 H, bs), 2.990 (1 H, d), 2.744 (1 H, s), 2.15 – 1.70 (7 H, m), 1.70 ~ 1.42 (4 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (300 MHz, DMSO- d_6 at +150 °C): δ = 170.4, 163.1, 152.1, 134.5, 129.5, 129.4, 125.7, 125.2, 124.96, 123.4, 123.3, 119.8, 119.7, 119.2, 114.6, 52.99, 50.8, 42.7, 28.9, 28.8, 28.4, 25.9, 25.6, 25.5, 23.2, 23.0, 22.6, 22.3, 18.8. ^1H NMR (300 MHz, C_6D_6 at room temperature): δ = 7.103 (2 H, m), 6.859 (1 H, m), 6.667 (2 H, m), 5.416 (0.7 H, s), 5.264 (0.3 H, s), 2.894 (1.5 H, s), 2.560 (0.5 H, s), 2.05 – 1.65 (4 H, m), 1.56 ~ 1.22 (7 H, m). Elemental Analysis: Calc. For $\text{C}_{15}\text{H}_{19}\text{N}$: C, 84.46; H, 8.98; N, 6.57. Found: C, 84.0; H, 8.59; N, 6.77. MS (EI) m/z = 213 (M^+).

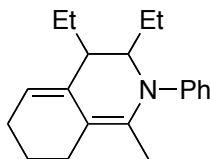
Entry 7



A 40 mL pressure tube was loaded with a stir bar, (3-methyl-3-buten-1-ynyl)benzene (1.1376 g, 8 mmol), cyclohexylamine (0.930 mL, 8 mmol), $\text{Ti}(\text{dmpm})(\text{NMe}_2)_2$ (0.2466 g, 0.8 mmol), and chlorobenzene (4 mL). The tube was sealed with a Teflon stopper and removed from the dry box. The reaction was heated in a 100 °C oil bath for 5 h. The solution was filtered through Al_2O_3 on a fritted glass funnel and washed through with CH_2Cl_2 . Volatiles were removed by rotary evaporation. The product was distilled under reduced pressure (85 °C, ~0.2 mmHg). The final purification was accomplished using column chromatography on alumina with pentane: ether (volume rate is 8:1) as eluent. The product was obtained as a yellow oil (1.40 g, 73%). ^1H NMR (300 MHz, CDCl_3): δ = 7.776 (2 H, m), 7.345 (3 H, m), 5.884 (1 H, d, J = 1.2 Hz), 3.528 (1 H, m), 1.925 (3 H, s), 1.86 ~ 1.20 (13 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (300 MHz, CDCl_3): δ = 163.6, 140.3, 139.2, 129.2, 128.0, 127.6, 120.3, 60.9, 33.4, 25.8, 25.0, 24.8, 20.5. Elemental Analysis: Calc. For $\text{C}_{17}\text{H}_{23}\text{N}$: C, 84.59; H, 9.60; N, 5.80. Found: C, 83.75; H, 9.29; N, 5.70. MS (EI) m/z = 241 (M^+).

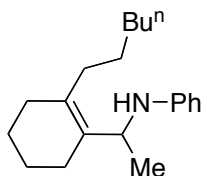
Synthesis of products in Scheme 1

3-hexyne insertion product



A 40 mL pressure tube was loaded with a stir bar, 1-ethynylcyclohexene (1.060 g, 10 mmol), aniline (0.930 g, 10 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (0.382 g, 1 mmol), and toluene (5 mL). The tube was sealed with a threaded Teflon cap and removed from the glove box. After the reaction was heated at 50 °C in an oil bath for 16 h, H_2O (90 mg, 5 mmol), $\text{RhCl}(\text{PPh}_3)_3$ (185 mg, 0.2 mmol), and 3-hexyne (4.100 g, 50 mmol) were added (in that order) to the pressure tube. The reaction was heated at 150 °C for 16 h. The reaction mixture was filtered through a plug of Al_2O_3 on a fritted funnel using CH_2Cl_2 as eluent. The volatiles were removed by rotary evaporation and distilled under reduced pressure to afford the product as yellow oil. (1.86 g, 66%). ^1H NMR (500 MHz, C_6D_6): δ = 7.10 (2 H, m), 6.84 (2 H, m), 6.79 (1 H, m), 5.20 (1 H, m), 3.40 (1 H, m), 2.61 (1 H, m), 2.36 (1 H, m), 2.09 (2 H, m), 1.70 (7 H, m), 1.39 (2 H, m), 1.12 (2 H, m), 0.98 (3 H, m), 0.72 (3 H, m). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6): δ = 149.6, 137.9, 134.3, 128.9, 121.1, 121.0, 120.9, 120.8, 113.1, 65.3, 49.3, 27.4, 26.1, 25.8, 25.3, 23.6, 17.1, 12.0, 11.5. Elemental Analysis: Calc. For $\text{C}_{20}\text{H}_{27}\text{N}$: C, 85.40; H, 9.60; N, 4.98. Found: C, 84.88; H, 9.68; N, 4.99. MS (EI) m/z = 281 (M^+).

1-hexene insertion product



A 40 mL pressure tube was loaded with a stir bar, 1-ethynylcyclohexene (324 mg, 3.06 mmol), aniline (285 mg, 3.06 mmol), $\text{Ti}(\text{dap})_2(\text{NMe}_2)_2$ (116.9 mg, 0.31 mmol), and toluene (5 mL). The tube was sealed with a threaded Teflon cap and removed from the glove box. After the reaction was heated at 50 °C in an oil bath for 16 h, H_2O (28 mg, 1.6 mmol), $\text{RhCl}(\text{PPh}_3)_3$ (57 mg, 0.06 mmol), and 1-hexene (1.28 g, 15.30 mmol) were added (in that order) to the pressure tube. The reaction was heated at 150 °C for 16 h. The reaction mixture was filtered through a plug of Al_2O_3 on a fritted funnel using CH_2Cl_2 as eluent. The volatiles were removed by rotary

evaporation to get crude yellow oil. The oil was dissolved in toluene (2 mL) and added to a suspension of NaB(CN)H₃ (385 mg, 6.12 mmol) and ZnCl₂ (416 mg, 3.06 mmol) in MeOH (5 mL). After stirring for 20 h at room temperature, the mixture was filtered. The solid residue was washed with CH₂Cl₂ (30 mL). Then saturated Na₂CO₃ solution was added to the filtrate. After extraction with CH₂Cl₂ (6 × 30 mL) the organic layer was dried over MgSO₄. Evaporation of the organic solvent under vacuum and column chromatography on silica gel (pentane:Et₂O = 1:1) afforded the pure amine product. 500 mg (58%). The compound is also readily purified by recrystallization from CH₂Cl₂/pentane as the HCl adduct. The hydrochloride was prepared by addition of excess 1.0 M HCl in ether to an ethereal solution of the amine. ¹H NMR (500 MHz, C₆D₆): δ = 7.13 (2 H, m), 6.69 (1 H, m), 6.55 (2 H, m), 4.33 (1 H, m), 3.25 (1 H, s), 1.88 (8 H, m), 1.24 (10 H, m), 1.02 (3 H, m), 0.88 (3 H, m). ¹³C{¹H} NMR (C₆D₆), δ = 148.5, 133.1, 131.9, 129.6, 129.4, 117.3, 113.2, 49.2, 33.2, 32.2, 30.1, 28.7, 23.5, 23.3, 23.1, 23.0, 22.9, 21.1, 14.3. Elemental Analysis (on HCl adduct): Calc. For C₂₀H₃₁N•HCl: C, 74.66; H, 9.64; N, 4.36. Found: C, 74.09; H, 9.46; N, 4.36. MS (EI) *m/z* = 285 (M⁺).

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1. T. Ishikawa, T. Mizuta, K. Hagiwara, T. Aikawa, T. Kudo, S. Saito, *J. Org. Chem.* **2003**, *68*, 3702.
 2. G. Sartori, A. Pastorio, R. Maggi, F. Bigi *Tetrahedron* 1996, **52**, 8287-8296.
 3. L. Brandsma, *Preparative Acetylenic Chemistry*, Elsevier Publishing Co.: Amsterdam, 1971.
 4. Z.-X. Wang, G.-A. Cao, Y. Shi, *J. Org. Chem.* 1999, **64**, 7646-50.
 5. J. Barluenga, F. Aznar, C. Valdés, M.-P. Cabal *J. Org. Chem.* 1991, **56**, 6166-71.