Room-Temperature Palladium-Catalyzed Intramolecular Hydroamination of Unactivated Alkenes

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Supporting Information

General Procedures. All reactions were performed under a nitrogen atmosphere using flame-dried glassware. Infrared spectra were measured on a Perkin Elmer Spectrum RX I spectrometer. Mass spectra were collected on an Agilent Gas Chromatograph/Mass Spectrometer 6890 series, a Kratos Profile HV-3 Mass Spectrometer, or a Bruker Esquire Ion-Trap Mass Spectrometer. Column chromatography was performed using silica gel (Whatman, 60 A, 230-400 mesh). NMR spectra were recorded on a Bruker Advance 200 MHz, 300 MHz, or 500 MHz spectrometer. ¹H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual protiated solvent as follows: CHCl₃, 7.26 ppm, CD₃OD, 3.31 ppm. ¹³C NMR chemical shifts (δ) are reported in ppm relative to the carbon resonance of the deuterated solvent as follows: CDCl₃, 77.0 ppm, CD₃OD, 49.0 ppm. ³¹P NMR chemical shifts (δ) are reported in ppm relative to the phosphorus resonance of PPh₃ in CDCl₃, -6.0 ppm.

Materials. Dichloromethane, acetonitrile, diethyl ether, and tetrahydrofuran were degassed with nitrogen and dried by passing through a column of neutral alumina. Toluene was degassed with nitrogen and dried by passing through a column of neutral alumina and a column of Q5 reactant. 3A and 4A molecular sieves were powdered and activated under vacuum at ~ 200 °C for 14 h and stored in a glove box or in an oven at 150 °C. Palladium chloride, copper(II) triflate, and silver tetrafluoroborate were purchased from Strem Chemicals and used without further purification. Anhydrous magnesium sulfate, (1,5-cyclooctadiene)platinum dichloride, benzyl chloroformate, di-*t*-butyldicarboxylate, *p*-toluoyl chloride, acetic anhydride, 3-bromo-2-methylprop-1-ene, and methyl vinyl ketone were purchased from Aldrich and used without further purification. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were used without further purification. (MeCN)₂PdCl₂¹, (dppe)PdCl₂², (BINAP)PdCl₂³, (PPh₃)₂PdCl₂⁴, 2,6-bis(diphenylphosphinomethyl)pyridine dichloropalladium (1)⁵, bis(diphenylphosphinoethyl)phenylphosphine dichloropalladium (6)⁶, 4,4',4''-tri-*t*-butyl-2,2':6',2''-terpyridine dichloropalladium (8)⁷, and 2,6-bis(di-*t*-butylphosphinomethyl)phenyl chloropalladium⁸ were synthesized according to literature procedures.

2,6-Bis(diphenylphosphinomethyl)pyridine dichloroplatinum (7). In a glove box, 2,6-bis(diphenylphosphinomethyl)pyridine⁹ (150 mg, 0.315 mmol) and (COD)PtCl₂ (118 mg, 0.315 mmol) were added to a round-bottomed flask with stir bar. The flask was capped with a septum, removed from the glove box, and placed under N₂. To the flask was added CH₂Cl₂ (2 mL) and the mixture was stirred for 12 h. The resulting white precipitate was collected by vacuum filtration and dried on a high vacuum line for 2 h to afford a white solid (100 mg, 43%). ¹H NMR (300 MHz, CDCl₃): δ 8.24-7.39 (m, 20H),

4.77 (br, 4H). ^{31}P NMR (121 MHz, CDCl_3): δ 21.6 (s with ^{195}Pt satellites, $J_{\text{Pt-P}} = 1264$ Hz).

2,2-Dimethylpent-4-en-1-amine (**22**)¹⁰, 2-phenylpent-4-en-1-amine (**23**)¹¹, 5-amino-3-methylpent-1-en-3-ol (**24**)¹², and 2,2,3-trimethylbut-3-en-1-amine (**27**) were synthesized in a fashion analogous to previously reported methods.

2,2-Dimethylpent-4-en-1-amine (22). Spectral data matches literature values:¹⁰ ^1H NMR (300 MHz, CDCl_3): δ 5.83-5.74 (m, 1H), 5.05-4.99 (m, 2H), 2.45 (s, 2H), 1.97 (d, $J = 7.2$ Hz, 2H), 0.94 (br, 2H), 0.85 (s, 6H).

2-Phenylpent-4-en-1-amine (23). Hygroscopic yellow solid (4.5 g, 76%). ^1H NMR (300 MHz, MeOD): δ 7.38-7.21 (m, 5H), 5.67 (ddt, $J = 10.2, 17.1, 7.2$ Hz, 1H), 5.02-4.90 (m, 2H), 2.94-2.68 (m, 3H), 2.49-2.30 (m, 2H). ^{13}C NMR (75 MHz, MeOD): δ 38.2, 46.5, 48.6, 115.1, 126.3, 127.7, 128.3, 136.4, 142.8. MS (EI, m/z): 162 $[\text{M} + \text{H}]^+$ (75), 146 (25), 130 (75), 103 (70), 91 (100), 77 (85). FTIR (thin film, cm^{-1}): 3370, 2967, 1578, 1482, 1388, 1319, 913, 759, 800.

5-Amino-3-methylpent-1-en-3-ol (24). ^1H NMR (300 MHz, CDCl_3): δ 5.86 (dd, $J = 10.5, 17.1$ Hz, 1H), 5.34 (dd, $J = 2.1, 17.1$ Hz, 1H), 5.08 (dd, $J = 1.8, 10.5$ Hz, 1H), 3.01-2.87 (m, 2H), 1.67-1.49 (m, 3H), 1.25 (s, 3H).

2,2,3-Trimethylbut-3-en-1-amine (27). ^1H NMR (300 MHz, CDCl_3): δ 4.88-4.85 (m, 1H), 4.67-4.66 (m, 1H), 2.48 (s, 2H), 1.97 (s, 2H), 1.80 (s, 3H), 1.24 (br, 2H), 0.89 (s, 6H).

Pent-4-en-1-amine (**25**) and hex-5-en-1-amine (**26**) were synthesized by a slightly modified literature procedure.¹³

To a solution of triphenylphosphine (1 equiv) in THF (0.5 M) at 0 °C was added diisopropylazodicarboxylate (1 equiv) dropwise. After complete addition, the white suspension was stirred for 5 min. To the cold reaction was added 4-penten-1-ol or 5-hexen-1-ol (1 equiv) dropwise and the reaction was stirred for 5 min after complete addition. Phthalimide (1 equiv) was added in one portion to the reaction, the ice bath was removed, and the reaction was stirred at r.t. overnight. The reaction was concentrated and the resulting viscous oil was purified by chromatography (20% EtOAc/Hex) to afford the appropriate phthalimide as a clear oil (75-95%). The resulting phthalimide was dissolved in pentane (1 M) and hydrazine hydrate (2 equiv.) was added. The reaction was stirred for 5-10 min before a white solid started to precipitate out. After 15 min, the solid was collected by vacuum filtration and washed with Et₂O. The solid was placed in an Erlenmeyer flask and a mixture of CH₂Cl₂/6 N HCl (1:1) was added. The mixture was stirred for 15 min and then was vacuum filtered to remove any solid that had not dissolved. The filtrate was transferred to a separatory funnel and the layers were separated. The organic layer was extracted with 6 N HCl and the aqueous layers were combined. The aqueous layer was made basic by the slow addition of KOH pellets at 0 °C and extracted with Et₂O (3x), the organic layers were combined, dried over MgSO₄, filtered, and concentrated to afford the amine as a yellow oil (15-60%). This material was used without further purification.

Pent-4-en-1-amine (25). ¹H NMR (300 MHz, CDCl₃): δ 5.89-5.71 (m, 1H), 5.06-4.91 (m, 2H), 2.71 (t, *J* = 6.9 Hz, 2H), 2.11-2.02 (m, 2H), 1.56-1.41 (m, 2H).

Hex-5-en-1-amine (26). ¹H NMR (300 MHz, CDCl₃): δ 5.80 (ddt, *J* = 9.9, 16.8, 6.6 Hz, 1H), 5.03-4.93 (m, 2H), 2.69 (t, *J* = 6.3 Hz, 2H), 2.05 (q, *J* = 6.9 Hz, 2H), 1.48-1.41 (m, 4H).

Benzyl 2,2-dimethylpent-4-enylcarbamate (2a). To a solution of benzyl chloroformate (0.65 mL, 4.64 mmol) in CH₂Cl₂ (10 mL) was added a solution of amine **22** (500 mg, 4.42 mmol) and diisopropylethylamine (0.85 mL, 4.86 mmol) in CH₂Cl₂ (2 mL) dropwise. The reaction was stirred for 2 days and was concentrated under vacuum. The crude material was purified by chromatography (10% EtOAc/Hex) to afford a colorless

oil (0.92 g, 84%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.37-7.33 (m, 5H), 5.88-5.74 (m, 1H), 5.11 (s, 2H), 5.07-5.00 (m, 2H), 4.78 (br, 1H), 3.04 (d, *J* = 6.6 Hz, 2H), 1.98 (d, *J* = 7.2 Hz, 2H), 0.89 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 24.7, 34.8, 44.31, 50.9, 66.7, 117.5, 128.1, 128.1, 128.5, 134.7, 136.7, 156.8. GC/MS (CI, *m/z*): 247 [M] (1), 232 (2), 173 (3), 108 (10), 91 (100). FTIR (neat, cm⁻¹): 3342, 3071, 2961, 1704, 1532, 1242, 1138, 1040, 999, 915.

tert-Butyl 2,2-dimethylpent-4-enylcarbamate (2b). To a solution of diisopropylethyl amine (0.92 mL, 5.3 mmol) and di-*t*-butyldicarboxylate (0.97 g, 4.42 mmol) in CH₂Cl₂ (10 mL) was added amine **22** (0.5 g, 4.42 mmol) dropwise. The reaction was stirred for 1 h and was then quenched by addition of a saturated aqueous solution of NH₄Cl. The mixture was stirred and the layers were separated. The organic layer was dried over MgSO₄, filtered, and concentrated to afford an oil which was purified by chromatography (10% EtOAc/Hex). A colorless oil was isolated (900 mg, 80%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 5.78 (ddt, *J* = 10.2, 17.7, 7.5 Hz, 1H), 5.01 (d, *J* = 9.0 Hz, 1H), 4.99 (d, *J* = 17.7 Hz, 1H), 4.58 (br, 1H), 2.91 (d, *J* = 6.3 Hz, 2H), 1.92 (d, *J* = 7.5 Hz, 2H), 1.41, (s, 9H), 0.83 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 156.1, 134.8, 117.3, 78.9, 50.3, 44.3, 34.7, 28.4, 24.7. GC/MS (CI, *m/z*): 157 [M - *t*-Bu] (5), 142 (2), 116 (5), 98 (7), 83 (7), 57 (100), 41 (20). FTIR (neat, cm⁻¹): 3356, 2966, 1702, 1514, 1366, 1250, 1173.

4-Methyl-N-(2,2-dimethylpent-4-enyl)benzamide (2c). To a solution of triethylamine (0.124 mL, 0.885 mmol) and amine **22** (0.1 g, 0.885 mmol) in CH₂Cl₂ (2 mL) was added *p*-toluoyl chloride (0.117 mL, 0.885 mmol) dropwise. The reaction was stirred overnight and concentrated under vacuum. The resulting material was purified by chromatography (10% EtOAc/Hex) to afford a colorless oil which solidified to a white solid on standing (185 mg, 90%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 6.16 (br, 1H), 5.89 (ddt, *J* = 11.1, 18.0, 7.2 Hz, 1H), 5.09 (d, *J* = 10.5 Hz, 1H), 5.07 (d, *J* = 6.0 Hz, 1H), 3.31 (d, *J* = 6.3 Hz, 2H), 2.40 (s, 3H), 2.06 (d, *J* = 7.8 Hz, 2H), 0.96 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 21.4, 25.1, 35.1, 44.9, 49.4, 117.5, 126.8, 129.2, 132.2, 135.1, 141.6, 167.5. GC/MS (CI, *m/z*): 231 [M] (2), 148 (25), 119 (100), 91 (20). FTIR (KBr, cm⁻¹): 3368, 2962, 1636, 1548, 1327, 1286, 917.

2d

N-(2,2-dimethylpent-4-en-1-yl)acetamide (2d). To a solution of acetic anhydride (0.25 mL, 2.65 mmol) in CH_2Cl_2 (2 mL) was added amine **22** (0.3 g, 2.65 mmol) dropwise. The reaction was stirred overnight and quenched with 1 M NaOH. The layers were separated and the organic layer was dried over MgSO_4 , filtered, and concentrated. The crude oil was purified by chromatography (70% EtOAc/Hex) to give a clear oil (256 mg, 63%). Spectral data of this material matches literature values.¹⁴ ^1H NMR (300 MHz, CDCl_3): δ 5.82 (ddt, $J = 10.2, 17.7, 7.2$ Hz, 1H), 5.46 (br, 1H), 5.08-5.01 (m, 2H), 3.09 (d, $J = 6.3$ Hz, 2H), 2.0 (s, 3H), 2.0-1.96 (m, 2H), 0.89 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 23.0, 24.6, 34.4, 44.4, 48.9, 117.2, 134.6, 170.2.

2e

2,2-Dimethyl-N-tosylpent-4-en-1-amine (2e). To a solution of 4-methylbenzene-1-sulfonyl chloride (0.51 g, 2.65 mmol) and diisopropylethylamine (0.51 mL, 2.92 mmol) in CH_2Cl_2 (4 mL) at 0 °C was added amine **22** (0.3 g, 2.65 mmol) dropwise. The ice bath was removed and the reaction was stirred for 1 h. The reaction was quenched with 0.1 M aqueous citric acid and the layers were separated. The organic layer was washed with 1 M NaOH, brine, dried over MgSO_4 , filtered, and concentrated. The crude red oil was purified by chromatography (10% EtOAc/Hex) to give a tan oil that solidified on standing to a beige powder (200 mg, 28%). The product was further dried by dissolving in CH_2Cl_2 , stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ^1H NMR (300 MHz, CDCl_3): δ 7.74 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 5.72 (ddt, $J = 10.2, 17.7, 7.2$ Hz, 1H), 5.04-4.97 (m, 2H), 4.41 (br, 1H), 2.68 (d, $J = 6.9$ Hz, 2H), 2.43 (s, 3H), 1.95 (d, $J = 7.2$ Hz, 2H), 0.86 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 21.5, 24.8, 34.1, 44.0, 52.9, 117.8, 127.1, 129.7, 134.3, 143.3. GC/MS (CI, m/z): 267 [M] (1), 184 (70), 155 (100), 112 (20), 98 (25), 91 (70). FTIR (neat, cm^{-1}): 3279, 2965, 1640, 1598, 1466, 1424, 1320, 1160, 1093, 1064, 998, 954, 921, 887, 807, 669.

9a

Benzyl pent-4-enylcarbamate (9a). To a solution of benzyl chloroformate (0.25 mL, 1.78 mmol) in CH_2Cl_2 (5 mL) was added amine **25** (0.2 g, 1.62 mmol) and triethylamine (0.45 mL, 3.56 mmol) in CH_2Cl_2 (5 mL) and the reaction was stirred overnight. The reaction was quenched with 0.1 M aqueous citric acid, the mixture was stirred, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 and the organic layers were combined. These were washed with saturated aqueous NaHCO_3 , dried over MgSO_4 , filtered and concentrated. The crude material was purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (220 mg, 66%). The product was further dried by dissolving in CH_2Cl_2 , stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ^1H NMR (300 MHz, CDCl_3): δ 7.37-7.30 (m,

5H), 5.79 (ddt, $J = 10.2, 17.4, 7.2$ Hz, 1H), 5.10-4.96 (m, 4H), 4.76 (br, 1H), 3.21 (q, $J = 7.2$ Hz, 2H), 2.09 (q, $J = 6.9$ Hz, 2H), 1.61 (quin, $J = 7.2$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 29.1, 30.9, 40.6, 66.6, 115.2, 128.1, 128.5, 136.7, 137.7, 156.4. GC/MS (CI, m/z): 219 [M] (1), 158 (3), 108 (30), 91 (100). FTIR (neat, cm^{-1}): 3336, 2937, 1702, 1538, 1261, 1138, 1003, 913.

tert-Butyl pent-4-enylcarbamate (9b). To a stirring solution of di-*t*-butyldicarbonate (0.39 g, 1.78 mmol) in CH_2Cl_2 (5 mL) was added amine **25** (0.2 g, 1.62 mmol) and triethylamine (0.45 mL, 3.56 mmol) in CH_2Cl_2 (5 mL) and the reaction was stirred overnight. The reaction was quenched with 0.1 M aqueous citric acid, the mixture was stirred, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 and the organic layers were combined. The organic layer was washed with saturated aqueous NaHCO_3 , dried over MgSO_4 , filtered and concentrated. The crude material was purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (190 mg, 64%). The product was further dried by dissolving in CH_2Cl_2 , stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. Spectral data of this material matches literature values.¹⁵ ^1H NMR (300 MHz, CDCl_3): δ 5.80 (ddt, $J = 10.2, 16.8, 6.6$ Hz, 1H), 5.00 (d, $J = 17.1$ Hz, 1H), 4.95 (d, $J = 11.4$ Hz, 1H), 4.56 (br, 1H), 3.10 (q, $J = 6.9$ Hz, 2H), 2.06 (q, $J = 6.9$ Hz, 2H), 1.56 (quin, $J = 6.9$ Hz, 2H), 1.42 (s, 9H).

4-Methyl-N-(pent-4-enyl)benzamide (9c). To a solution of amine **25** (150 mg, 1.76 mmol) and triethylamine (0.30 mL, 2.11 mmol) in CH_2Cl_2 (2 mL) was added *p*-toluoyl chloride (0.26 mL, 1.94 mmol) dropwise and the reaction stirred overnight. The reaction was concentrated and purified by chromatography (20% EtOAc/Hex) to afford a clear oil (194 mg, 54%). The product was further dried by dissolving in CH_2Cl_2 , stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ^1H NMR (500 MHz, CDCl_3): δ 7.66 (d, $J = 8.0$ Hz, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 6.63 (br, 1H), 5.79 (ddt, $J = 10.5, 17.0$ Hz, 7.01H), 5.02 (d, $J = 17.0$ Hz, 1H), 4.96 (d, $J = 10.0$ Hz, 1H), 3.40 (q, $J = 7.0$ Hz, 2H), 2.35 (s, 3H), 2.01 (q, $J = 7.0$ Hz, 2H), 1.68 (quin, $J = 7.5$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 21.3, 28.7, 31.1, 39.5, 115.0, 126.8, 129.0, 131.8, 137.8, 141.5, 167.5. GC/MS (CI, m/z): 203 [M] (5), 161 (5), 148 (50), 119 (100), 91 (40), 65 (10). FTIR (neat, cm^{-1}): 3310, 3076, 2926, 1634, 1548, 1506, 1506, 1437, 1307, 912, 838.

Benzyl hex-5-enylcarbamate (11a). To a stirring solution of amine **26** (0.4 g, 2.91 mmol) and triethylamine (0.89 mL, 6.40 mmol) at 0 °C was added benzyl chloroformate

(0.45 mL, 3.20 mmol) dropwise. The ice bath was removed and the reaction was stirred overnight. The mixture was concentrated and purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (391 mg, 56%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. Spectral data of this material matches literature values.¹⁶ ¹H NMR (300 MHz, CDCl₃): δ 7.36-7.30 (m, 5H), 5.78 (ddt, *J* = 10.2, 16.8, 6.6 Hz, 1H), 5.09 (s, 2H), 4.99 (d, *J* = 16.5 Hz, 1H), 4.95 (d, *J* = 10.2 Hz, 1H), 4.86 (br, 1H), 3.18 (q, *J* = 6.9 Hz, 2H), 2.09-2.02 (m, 2H), 1.55-1.37 (m, 4H).

tert-Butyl hex-5-enylcarbamate (11b). To a stirring solution of amine **26** (0.4 g, 2.91 mmol) and triethylamine (0.89 mL, 6.40 mmol) at 0 °C was added di-*t*-butyldicarbonate (0.7 g, 3.20 mmol) in one portion. The ice bath was removed and the reaction was stirred overnight. The mixture was concentrated and purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (312 mg, 54%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 5.79 (ddt, *J* = 10.2, 17.1, 6.9 Hz, 1H), 5.04-4.92 (m, 2H), 4.49 (br, 1H), 3.19-3.05 (m, 2H), 2.06 (q, *J* = 7.2 Hz, 2H), 1.52-1.41 (m, 13H). ¹³C NMR (75 MHz, CDCl₃): δ 26.0, 28.4, 29.5, 33.3, 78.9, 114.6, 138.4, 156.0. GC/MS (CI, *m/z*): 143 [*M* - *t*-Bu] (10), 99 (5), 57 (100). FTIR (neat, cm⁻¹): 3353, 2978, 2932, 1692, 1526, 1392, 1366, 1251, 1176, 911.

tert-Butyl 2-allylphenylcarbamate (13b). To a solution of di-*t*-butyldicarbonate (859 mg, 4.1 mmol) in CH₂Cl₂ (5 mL) was added a solution of *o*-allylaniline¹⁷ (500 mg, 3.76 mmol) and triethylamine (0.58 mL, 4.1 mmol) in CH₂Cl₂ (2 mL) and the reaction was stirred overnight. The reaction was quenched with 0.1 M citric acid and the layers were separated. The organic layer was washed with saturated aqueous sodium bicarbonate, dried over MgSO₄, filtered and concentrated. The crude material was purified by chromatography (10% EtOAc/Hex) to afford a pale yellow oil (475 mg, 54%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.79 (d, *J* = 8.7 Hz, 1H), 7.25-7.23 (m, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.44 (br, 1H), 6.03-5.90, (m, 1H), 5.16 (dd, *J* = 1.5, 9.0 Hz, 1H), 5.07 (dd, *J* = 1.5, 16.8 Hz, 1H), 3.37 (d, *J* = 5.7 Hz, 1H), 1.53 (s, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 27.3, 36.4, 80.2, 226.4, 121.9, 123.9, 127.2, 129.9, 135.8, 136.4, 146.7, 153.1. GC/MS (CI, *m/z*): 233 [*M*] (5), 177 (75), 132 (75), 118 (50), 77 (10), 57 (100). FTIR (neat, cm⁻¹): 3419, 2981, 2936, 1810, 1732, 1520, 1454, 1372, 1161, 1071, 753.

15a

Benzyl 2-phenylpent-4-enylcarbamate (15a). To a solution of amine **23** (0.5 g, 3.1 mmol) and triethylamine (0.45 mL, 3.26 mmol) in CH₂Cl₂ (5 mL) was added benzyl chloroformate (0.46 mL, 3.26 mmol) dropwise and the reaction stirred overnight. The reaction was quenched with water, the mixture was stirred, and the layers were separated. The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (260 mg, 28%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.33-7.14 (m, 10H), 5.74-5.60 (m, 1H), 5.08-4.95 (m, 4H), 4.58 (br, 1H), 3.68-3.58 (m, 1H), 3.25 (ddd, *J* = 5.1, 9.3, 13.8, 1H), 2.92-2.81 (m, 1H), 2.41-2.36 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 38.1, 45.7, 46.00, 66.6, 115.6, 126.8, 127.7, 128.0, 128.4, 128.6, 135.8, 136.6, 142.0, 156.2. ESI MS (positive mode, *m/z*): 296.3 [M]⁺. FTIR (neat, cm⁻¹): 3337.4, 3064.7, 2927.7, 1702.0, 1521.9, 1454.0, 1252.6, 1141.6, 998.5, 915.7, 699.7.

15b

tert-Butyl 2-phenylpent-4-enylcarbamate (15b). To a solution of amine **23** (0.5 g, 3.1 mmol) in CH₂Cl₂ (5 mL) was added di-*t*-butyldicarbonate (0.68 g, 3.1 mmol) in one portion and the reaction stirred overnight. The reaction was quenched with water, the mixture was stirred, and the layers were separated. The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography (10% EtOAc/Hex) to afford a colorless oil (420 mg, 52%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.23 (m, 5H), 5.70 (ddt, *J* = 9.9, 16.8, 6.9 Hz, 1H), 5.00 (d, *J* = 16.8 Hz, 1H), 4.96 (d, *J* = 9.9 Hz, 1H), 4.13 (br, 1H), 3.59-3.54 (m, 1H), 3.16 (ddd, *J* = 4.5, 8.7, 13.2, 1H), 2.88-2.82 (m, 1H), 2.41-2.36 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 38.0, 45.5, 45.7, 78.9, 116.4, 126.5, 127.7, 128.4, 135.9, 142.2, 155.7. GCMS (CI, *m/z*): 261 [M] (1), 205 (5), 144 (80), 131 (60), 91 (50), 57 (100). FTIR (neat, cm⁻¹): 3360, 2978, 1698, 1505, 1454, 1392, 1366, 1251, 1171, 914, 759, 701.

15c

4-Methyl-*N*-(2-phenylpent-4-enyl)benzamide (15c). To a solution of amine **23** (0.5 g, 3.1 mmol) and triethylamine (0.45 mL, 3.26 mmol) in CH₂Cl₂ (5 mL) was added toluoyl chloride (0.45 mL, 3.26 mmol) dropwise and the reaction stirred overnight. The reaction was quenched with water, the mixture was stirred, and the layers were separated. The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography (10% EtOAc/Hex) to afford a yellow solid which was recrystallized (5% EtOAc/Hex) to give a white solid (260 mg, 30%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.48 (d, *J* = 8.1 Hz, 2H), 7.37-7.15 (m, 5H), 7.16 (d, *J* = 7.8 Hz, 2H), 5.91 (br, 1H), 5.73 (ddt, *J* = 6.9, 9.9, 17.1 Hz, 1H), 5.04 (d, *J* = 17.1 Hz, 2H), 4.98 (d, *J* = 10.5, 2H), 3.96 (ddd, *J* = 5.7, 6.9, 13.2 Hz, 1H), 3.40 (ddd, *J* = 4.8, 9.3, 13.8 Hz, 1H), 3.02 (quin, *J* = 7.2 Hz, 1H), 2.51-2.45 (m, 2H), 2.36 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 21.2, 38.1, 44.8, 45.3, 116.5, 126.7, 127.7, 129.0, 131.7, 135.8, 141.5, 142.1, 167.2. MS (EI, *m/z*): 279 [M] (75), 181 (25), 145 (70), 119 (100), 91 (90). FTIR (thin film, cm⁻¹): 3326, 2923, 1636, 1546, 1506, 1708, 1309, 914, 838, 753, 701.

Benzyl 3-hydroxy-3-methylpent-4-enylcarbamate (17a). To a stirring solution of amine **24** (0.3 g, 2.61 mmol) and triethylamine (0.38 mL, 2.74 mmol) in CH₂Cl₂ (7 mL) at 0 °C was added benzyl chloroformate (0.39 mL, 2.74 mmol) dropwise. The ice bath was removed and the reaction was stirred overnight. The reaction mixture was concentrated and the crude oil was purified by chromatography (20% EtOAc/CH₂Cl₂) to afford a colorless oil (0.45 g, 70%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.40-7.32 (m, 5H), 5.88 (dd, *J* = 10.8, 18.0 Hz, 1H), 5.46 (br, 1H), 5.26 (d, *J* = 17.4 Hz), 5.10-5.06 (m, 3H), 3.33-3.25 (m, 2H), 2.48 (br, 1H), 1.75 (t, *J* = 6.6 Hz, 2H), 1.31 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 28.5, 37.0, 40.8, 66.4, 72.8, 112.0, 127.9, 128.3, 136.6, 144.3, 156.5. GCMS (CI, *m/z*): 172 [M-Ph] (2), 140 (10), 125 (7), 107 (40), 91 (100). FTIR (neat, cm⁻¹): 3413, 2972, 1701, 1522, 1455, 1396, 1258, 1136, 1049, 922, 697.

***tert*-Butyl 3-hydroxy-3-methylpent-4-enylcarbamate (17b).** To a stirring solution of amine **24** (300 mg, 2.61 mmol) in CH₂Cl₂ (7 mL) was added di-*t*-butyldicarbonate (569 mg, 2.61 mmol) in one portion. The reaction was complete by TLC after 2 h and was concentrated. The crude oil was purified by chromatography (20% EtOAc/CH₂Cl₂) to afford a colorless oil (406 mg, 72%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 5.87 (dd, *J* = 11.7, 18.6 Hz, 1H), 5.25 (d, *J* = 17.7 Hz, 1H), 5.08 (d, *J* = 10.8 Hz, 1H), 4.93 (br, 1H), 3.94-3.17 (m, 2H), 1.96 (br, 1H), 1.73 (t, *J* = 6.9 Hz, 2H), 1.44 (s, 9H), 1.31 (s, 3H). ¹³C NMR (75

MHz, CDCl₃): δ 28.3, 28.5, 36.5, 41.2, 72.7, 79.0, 111.9, 144.5, 156.2. GC/MS (CI, *m/z*): 159 [M – *t*-Bu] (1), 141 (30), 126 (10), 98 (5), 89 (15), 82 (25), 57 (100). FTIR (neat, cm⁻¹): 3372, 2978, 2933, 1693, 1515, 1455, 1367, 1252, 1174, 921.

19a

Benzyl 2,2,3-trimethylbut-3-enylcarbamate (19a). To a stirring solution of amine **27** (500 mg, 3.93 mmol) and triethylamine (0.57 mL, 4.34 mmol) in CH₂Cl₂ (2 mL) was added benzyl chloroformate (0.58 mL, 4.13 mmol) dropwise. The reaction stirred overnight and was concentrated. The crude oil was purified by chromatography (10% EtOAc:Hex) to afford a colorless oil (490 mg, 48%). The product was further dried by dissolving in CH₂Cl₂, stirring in 3A molecular sieves for 5 min, filtering to remove the sieves, and concentrating under vacuum. ¹H NMR (300 MHz, CDCl₃): δ 7.38-7.30 (m, 5H), 5.510 (s, 2H), 4.90-4.85 (m, 1H), 4.80 (br, 1H), 4.68-4.64 (m, 1H), 3.06 (d, *J* = 6.9 Hz, 2H), 1.96 (s, 2H), 1.78 (s, 3H), 0.91 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 25.0, 25.1, 35.2, 47.4, 51.4, 66.5, 114.6, 127.8, 127.9, 128.3, 136.6, 142.6, 156.6. GCMS (CI, *m/z*): 261 [M] (1), 205 (5), 108 (5), 97 (15), 91 (100). FTIR (neat, cm⁻¹): 3344, 3071, 2964, 1706, 1538, 1455, 1244, 1134, 1050, 1003, 893, 697.

2a-d

Benzyl *N*-deutero-2,2-dimethylpent-4-enylcarbamate (2a-d). To a solution of substrate **2a** (110 mg, 0.45 mmol) in THF (2 mL) at -78 °C was added *n*-BuLi (2.5 M solution in hexanes, 0.22 mL, 0.53 mmol) dropwise. After complete addition, the cold bath was removed and the reaction was stirred for 15 min. The reaction was quenched with D₂O (4 mL), the mixture was stirred for 5 min, and was transferred to a flame-dried separatory funnel. The layers were separated, the organic layer was dried over 3A sieves, filtered, and concentrated to afford a colorless oil (88 mg, 80%). ¹H NMR (300 MHz, CDCl₃): δ 7.37-7.29 (m, 5H), 5.81 (ddt, *J* = 10.2, 18.0, 7.5 Hz, 1H), 5.19 (s, 2H), 5.07-5.00 (m, 2H), 3.03 (s, 2H), 1.97 (d, *J* = 7.2 Hz, 2H), 0.88 (s, 6H). GCMS (CI, *m/z*): 248 [M] (1), 121 (5), 109 (10), 91 (100).

5

Benzyl 2,2-dimethyl-4-oxopentylcarbamate (5). To a stirring suspension of (MeCN)₂PdCl₂ (20 mol%) and Cu(OTf)₂ (200 mol%) in reagent grade CH₂Cl₂ (0.1 M) was added a solution of substrate **2a** (1 equiv.) in CH₂Cl₂ and the reaction was stirred overnight. The reaction was passed through a pad of SiO₂ eluting with CH₂Cl₂ and the filtrate was concentrated. The crude oil was purified by chromatography (20% EtOAc/Hex) to afford compound **5** as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.37-7.31 (m, 5H), 5.15 (br, 1H), 5.10 (s, 2H), 3.11 (d, *J* = 6.3 Hz, 2H), 2.35 (s, 2H), 2.13 (s, 3H), 0.99 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 25.5, 32.5, 35.2, 50.6, 51.6, 66.7,

120.1, 120.5, 136.6, 156.8, 207.9. GCMS (CI, m/z): 263 [M] (1), 245 (5), 205 (5), 186 (5), 108 (5), 91 (100). FTIR (neat, cm^{-1}): 3344, 2960, 1711, 1538, 1456, 1362, 1242, 1139, 698.

General Hydroamination Conditions

Method A

In a glove box, 2,6-bis(diphenylphosphinomethyl)pyridine dichloropalladium (5 mol%), AgBF_4 (0.1 equiv), $\text{Cu}(\text{OTf})_2$ (0.1 equiv), and MgSO_4 (1 equiv) were added to a round-bottomed flask. The flask was capped with a septum, removed from the glove box, placed under an atmosphere of nitrogen, and CH_2Cl_2 (0.5 – 1.0 mL) was added. To the stirring mixture was added a solution of the substrate (1 equiv) in CH_2Cl_2 (0.5 – 1.0 mL) by syringe. The reaction was stirred for 2 – 16 h while monitoring for the disappearance of olefin by TLC. After complete reaction, the mixture was purified by chromatography (100% CH_2Cl_2) to afford pure product.

Method B

In a glove box, 2,6-bis(diphenylphosphinomethyl)pyridine dichloropalladium (5 mol%), AgBF_4 (0.1 equiv), $\text{Cu}(\text{OTf})_2$ (0.1 equiv), and 3A molecular sieves (25 mg per mL of solvent) were added to a round-bottomed flask. The flask was capped with a septum, removed from the glove box, placed under an atmosphere of nitrogen, and CH_2Cl_2 (0.5 – 1.0 mL) was added. To the stirring mixture was added a solution of the substrate (1 equiv) in CH_2Cl_2 (0.5 – 1.0 mL) by syringe. The reaction was stirred for 2 – 16 h while monitoring for the disappearance of olefin by TLC. After complete reaction, the mixture was purified by chromatography (100% CH_2Cl_2) to afford pure product.

Method C

Same as Method A except 10 mol% 2,6-bis(diphenylphosphinomethyl)pyridine dichloropalladium and 0.2 equiv. of AgBF_4 were used.

Benzyl 2,4,4-trimethylpyrrolidine-1-carboxylate (3a). Method A: Colorless oil (42 mg, 82%), ^1H NMR (300 MHz, CDCl_3): δ 7.37-7.30 (m, 5H), 5.21-5.07 (m, 2H), 3.94 (br, 1H), 3.46-3.34 (m, 2H), 3.07 (d, J = 10.5 Hz, 1H), 1.91 (dd, J = 7.2, 12.6 Hz, 1H), 1.32-1.24 (m, 4H), 1.11 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3 , observed as a mixture of rotamers): δ 20.6, 21.7, 26.3 (major), 26.4 (minor), 37.0 (minor), 37.1 (major), 48.1 (major), 48.8 (minor), 52.8 (minor), 53.4 (major), 59.2, 66.3 (major), 66.7 (minor), 127.7, 127.8, 128.4, 137.1, 154.9, 155.4. GCMS (CI, m/z): 247 [M] (5), 232 (5), 188 (15), 156 (2), 140 (5), 91 (100). FTIR (neat, cm^{-1}): 2959, 2870, 1703, 1455, 1412, 1356, 1200 1173, 1096, 1064.

tert-Butyl 2,4,4-trimethylpyrrolidine-1-carboxylate (3b). Method B: Colorless oil (53 mg, 75%), ^1H NMR (300 MHz, CDCl_3): δ 3.83 (br, 1H), 3.30 (br, 1H), 2.97 (d, $J = 10.8$ Hz, 1H), 1.85 (dd, $J = 7.2, 12.6$ Hz, 1H), 1.46 (s, 9H), 1.34-1.23 (m, 4H), 1.11 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3 , observed as a mixture of rotamers): δ 20.4, 21.3, 25.0, 28.3, 36.5 (major), 36.8 (minor), 47.5 (minor), 48.5 (major), 52.4, 58.3 (major), 59.3 (minor), 78.5, 154.7. GCMS (CI, m/z): 157 [$\text{M} - t\text{-Bu}$] (10), 142 (5), 116 (10), 98 (10), 83 (10), 57 (100). FTIR (neat, cm^{-1}): 2964, 2254, 1678, 1405, 1265, 1167, 1097, 904, 731, 651.

N-p-Toluoyl-2,4,4-trimethylpyrrolidine (3c). Method C: Colorless oil (23 mg, 92%). ^1H NMR (300 MHz, CDCl_3): δ 7.42 (d, $J = 7.8$ Hz, 1H), 7.18 (d, $J = 8.1$ Hz, 1H), 4.34 (br, 1H), 3.29 (d, $J = 10.2$ Hz, 1H), 3.12 (d, $J = 10.2$ Hz, 1H), 2.37 (s, 3H), 1.92 (ddd, $J = 1.5, 7.2, 12.6$ Hz, 1H), 1.44-1.25 (m, 4H), 1.04 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 20.2, 21.4, 25.4, 25.7, 38.2, 47.5, 52.9, 62.7, 127.6, 128.7, 134.3, 140.0, 170.2. GCMS (CI, m/z): 231 [M] (40), 216 (5), 174 (3), 160 (10), 119 (100), 91 (25), 65 (5). FTIR (neat, cm^{-1}): 2958, 2668, 1628, 1415, 1208, 1136, 832, 754.

N-Acetyl-2,4,4-trimethylpyrrolidine (3d). Method C: Colorless oil (17 mg, 68%). Spectral data of this material matches literature values.¹⁸ ^1H NMR (300 MHz, CDCl_3 , observed as a mixture of rotamers): δ = 4.16-3.92 (m, 1H, major), 3.99-3.92 (m, 1H, minor), 3.72 (dd, $J = 1.8, 11.7$ Hz, 1H, minor), 3.19 (s, 2H, major), 2.95 (d, $J = 11.4$ Hz, 1H, minor), 2.06-1.99 (m, 1H, minor), 2.02 (s, 3H, major + minor), 1.92 (dd, $J = 7.5, 12.6$ Hz, 1H, major), 1.46 (dd, $J = 7.8, 12.9$ Hz, 1H, minor), 1.36 (dd, $J = 9.0, 13.2$ Hz, 1H, major), 1.30 (d, $J = 6.0$ Hz, 3H, major), 1.29 (d, $J = 6.3$ Hz, 3H, minor), 1.13 (s, 3H, major + minor), 1.01 (s, 3H, major), 0.98 (s, 3H, minor).

Benzyl 2-methylpyrrolidine-1-carboxylate (10a). Method A: Colorless oil (18 mg, 82%). ^1H NMR (300 MHz, CDCl_3): δ 7.41-7.30 (m, 5H), 5.18-5.10 (m, 2H), 3.97 (br, 1H), 3.44 (br, 2H), 2.07-1.77 (m, 3H), 1.67-1.57 (m, 1H), 1.26-1.15 (m, 3H). ^{13}C NMR

(75 MHz, CDCl₃, observed as a mixture of rotamers): δ 20.0 (major), 20.9 (minor), 22.8 (minor), 22.7 (major), 32.6 (major), 33.3 (minor), 46.3 (major), 46.6 (minor), 52.9 (minor), 53.5 (major), 66.4 (major), 66.6 (minor), 127.8 (major + minor), 128.1 (major + minor), 137.2 (major + minor), 154.7 (major), 155.0 (minor). GCMS (CI, m/z): 219 [M] (5), 204 (5), 160 (10), 112 (5), 91 (100), 65 (5). FTIR (neat, cm⁻¹): 2967, 2876, 1700, 1455, 1411, 1358, 1109, 769.

tert-Butyl 2-methylpyrrolidine-1-carboxylate (10b). Method B: Colorless oil (35 mg, 88%). Spectral data of this material matches literature values.¹⁹ ¹H NMR (300 MHz, CDCl₃): δ 3.85 (br, 1H), 3.34 (br, 2H), 2.01-1.72 (m, 4H), 1.45 (s, 9H), 1.14 (d, J = 6.0 Hz, 3H).

N-p-Toluoyl-2-methylpyrrolidine (10c). Method C: White solid (30 mg, 60%). ¹H NMR (300 MHz, CDCl₃, isolated as a mixture of rotamers 2.6:1): δ 7.41 (br, 2H, major + minor), 7.17 (d, J = 7.8 Hz, 2H, major + minor), 4.32 (br, 1H, major), 4.01 (br, 1H, minor), 3.65 (br, 1H, minor), 3.44 (br, 1H, major), 2.36 (s, 3H, major + minor), 2.12 (br, 1H, major + minor), 1.90 (br, 1H, major + minor), 1.74 (br, 1H, major + minor), 1.65-1.58 (m, 1H, major + minor), 1.34 (br, 3H, major), 0.91 (br, 3H, minor). ¹³C NMR (75 MHz, CDCl₃, 50 °C): δ 20.3, 21.3, 33.1, 53.7, 127.1, 128.8, 135.1, 139.6, 168.9. GCMS (CI, m/z): 203 [M] (5), 161 (5), 148 (40), 119 (100), 91 (25), 65 (5). FTIR (thin film, cm⁻¹): 2966, 2872, 1626, 1413, 1348, 1181, 1021, 830, 754.

Benzyl 2-methylpiperidine-1-carboxylate (12a). Method B: Colorless oil (19 mg, 76%). ¹H NMR (300 MHz, CDCl₃): δ 7.32 (m, 5H), 5.10 (m, 2H), 4.47 (br, 1H), 4.00 (d, J = 12.0 Hz, 1H), 2.89 (dt, J = 2.7, 12.9 Hz, 1H), 1.58 (m, 6H), 1.16 (d, J = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 18.6, 25.6, 30.0, 39.0, 46.4, 66.8, 127.7, 127.8, 128.4, 126.4, 137.1, 155.3. GCMS (CI, m/z): 235 [M] (1), 142 (3), 108 (75), 91 (100). FTIR (neat, cm⁻¹): 2937, 2862, 1698, 1420, 1336, 1260, 1182, 1144, 1063, 751, 697.

***tert*-Butyl 2-methylpiperidine-1-carboxylate (12b).** Method B: Colorless oil (46 mg, 92%). Spectral data of this material matches literature values.¹⁵ ¹H NMR (300 MHz, CDCl₃): δ 4.37 (br, 1H), 3.93-3.88 (m, 1H), 2.79 (dt, *J* = 2.7, 13.2 Hz, 1H), 1.65-1.47 (m, 4H), 1.44 (s, 9H), 1.41-1.31 (m, 2H), 1.11 (d, *J* = 7.2 Hz, 3H).

14b

***tert*-Butyl 2-methylindoline-1-carboxylate (14b).** Method B (32 h): Yellow oil (16 mg, 32%). Spectral data of this material matches literature values.²⁰ ¹H NMR (300 MHz, CDCl₃): δ 7.76-7.64 (br, 1H), 7.19-7.12 (m, 2H), 6.63 (dt, *J* = 0.9, 7.5 Hz, 1H), 4.5 (br, 1H), 3.34 (dd, *J* = 9.6, 15.9 Hz, 1H), 2.60 (dd, *J* = 2.4, 15.9 Hz, 1H), 1.53 (s, 9H), 1.29 (d, *J* = 6.6 Hz, 3H).

16a

Benzyl 2-methyl-4-phenylpyrrolidine-1-carboxylate (16a). Method A: Colorless oil (24 mg, 96%) isolated as a mixture of diastereomers (2.7:1). ¹H NMR (300 MHz, CDCl₃): δ 7.38-7.22 (m, 10H, major + minor), 5.32-5.10 (m, 2H, major + minor), 4.23-3.87 (m, 2H, major + minor), 3.56-3.18 (m, 2H, major + minor), 2.58-2.51 (m, 1H, major), 2.18 (dt, *J* = 4.2, 12.0 Hz, 1H, minor), 2.02-1.94 (m, 1H, minor), 1.71 (q, *J* = 11.1 Hz, 1H, major), 1.50-1.27 (m, 3H, major + minor). ¹³C NMR (75 MHz, CDCl₃, 50 °C): δ 21.0, 42.1, 43.0, 52.9, 54.0, 66.6, 126.8, 127.0, 127.0, 127.8, 128.4, 128.5, 137.2, 140.7, 141.4, 154.9. MS (EI, *m/z*): 295 [M] (70), 218 (60), 204 (60), 188 (65), 160 (25), 91 (100), 77 (60). FTIR (neat, cm⁻¹): 3031, 2964, 1702, 1412, 1356, 1196, 1125, 1096, 756, 698.

16b

***tert*-butyl 2-methyl-4-phenylpyrrolidine-1-carboxylate (16b).** Method A: Colorless oil (21 mg, 84%) isolated as a mixture of diastereomers (2.3:1). ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.21 (m, 5H, major + minor), 4.06-3.80 (m, 2H, major + minor), 3.55-3.42 (m, 1H, minor), 3.28-3.19 (m, 2H, major + minor), 2.50 (dt, *J* = 12.6, 6.3 Hz, 1H, major), 2.16 (dt, *J* = 8.1, 12.0 Hz, 1H, minor), 1.92 (dd, *J* = 5.7, 12.0 Hz, minor), 1.75-1.62 (m, 1H, major), 1.48 (s, 9H, major + minor), 1.34 (d, *J* = 6.0 Hz, 3H, major), 1.27 (d, *J* = 6.3 Hz, 3H, minor). ¹³C NMR (75 MHz, CDCl₃, 50 °C): δ 21.3, 42.3, 43.0, 52.9, 53.1, 53.7, 79.2, 126.7, 127.1, 127.2, 128.6, 141.1, 154.6. MS (EI, *m/z*): 261 [M] (15), 205 (50), 190

(75), 160 (10), 146 (70), 86 (100), 57 (100). FTIR (neat, cm^{-1}): 2972, 2931, 1694, 1396, 1366, 1171, 1126, 757, 699.

***N*-p-tolyl-2-methyl-4-phenylpyrrolidine (16c).** Method C: Colorless oil, which solidified to a white solid on standing (37 mg, 74%) isolated as a mixture of diastereomers (2.7:1). ^1H NMR (300 MHz, CDCl_3): δ 7.48-7.17 (m, 9H, major + minor), 4.58 (br, 1H, minor), 4.40 (br, 1H, major), 3.91-3.76 (m, 1H, major + minor), 3.55 (t, 1H, $J = 10.8$, major + minor), 3.43-3.36 (m, 1H, minor), 3.26-3.14 (m, 1H, major), 2.58 (dt, $J = 12.6, 6.6$ Hz, 1H, major), 2.36 (s, 3H, major + minor), 2.34-2.23 (m, 1H, minor), 2.04-1.99 (m, 1H, minor), 1.82 (q, $J = 12$ Hz, 1H, major), 1.53-1.39 (m, 3H, major + minor). ^{13}C NMR (75 MHz, CDCl_3 , 50 $^\circ\text{C}$): δ 20.7, 21.3, 41.2, 44.0, 126.9, 127.0, 127.1, 127.7, 128.6, 128.7, 128.9, 128.9, 134.5, 135.0, 139.6, 140.2, 141.8, 145.7, 170.0. MS (EI, m/z) 279 [M] (75), 160 (50), 119 (100), 86 (100), 65 (50). FTIR (neat, cm^{-1}): 2965, 2871, 1634, 1416, 1182, 1107, 831, 754, 700.

Benzyl 3-hydroxy-2,3-dimethylpyrrolidine-1-carboxylate (18a). Method A except chromatography was performed using 20%-100% EtOAc/Hex to afford a colorless oil (46 mg, 92%) isolated as a mixture of diastereomers (2.8:1): ^1H NMR (300 MHz, CDCl_3): δ 7.37-7.30 (m, 5H), 5.18-5.08 (m, 2H), 3.76-3.68 (m, 1H, minor diastereomer), 3.60-3.54 (m, 1H, major diastereomer), 3.49 (t, $J = 7.2$ Hz, 2H), 2.04-1.72 (m, 3H), 1.33 (s, 3H), 1.32-1.23 (m, 3H, major diastereomer), 1.14-1.07 (m, 3H, minor diastereomer). ^{13}C NMR (75 MHz, CDCl_3): δ 22.7, 26.2, 37.0, 44.1, 53.4, 61.5, 66.7, 127.8, 127.9, 128.4, 136.9, 155.2. GCMS (CI, m/z): 249 [M] (2), 114 (80), 91 (100), 56 (40). FTIR (neat, cm^{-1}): 3432, 2875, 1679, 1419, 1358, 1215, 1094, 1036, 697.

***tert*-Butyl 3-hydroxy-2,3-dimethylpyrrolidine-1-carboxylate (18b).** Method A except chromatography was performed using 20% EtOAc/Hex to afford pale yellow oil (80 mg, 80%) isolated as a mixture of diastereomers (4:1): ^1H NMR (300 MHz, CDCl_3) δ 3.47-3.40 (m, 1H), 3.36 (t, $J = 7.2$ Hz, 2H), 2.02 (br, 1H), 1.95-1.84 (m, 1H), 1.80-1.69 (m, 1H), 1.43 (s, 9H), 1.30 (s, 3H), 1.17 (d, $J = 6.3$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.7, 28.4, 28.5, 37.1, 43.7, 61.2, 79.1, 154.7. GCMS (CI, m/z): 215 [M] (2), 159 (15),

114 (20), 57 (100). FTIR (neat, cm^{-1}): 3425, 2976, 1671, 1409, 1367, 1170, 1109, 1031, 864.

Benzyl 2-deuteromethyl-4,4-dimethylpyrrolidine-1-carboxylate (3a-d). Method A: Colorless oil (12 mg, 48%): ^1H NMR (300 MHz, CDCl_3) δ 7.37-7.30 (m, 5H), 5.21-5.07 (m, 2H), 3.94 (br, 1H), 3.46-3.34 (m, 2H), 3.07 (d, $J = 10.5$ Hz, 1H), 1.91 (dd, $J = 7.2$, 12.6 Hz, 1H), 1.32-1.24 (m, 3H), 1.11 (s, 3H), 0.98 (s, 3H). ^2H NMR (31 MHz, CHCl_3): δ 1.3 (br). GCMS (CI, m/z): 248 [M]

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