Enantioselective Imidazole-Directed Allylation of Aldimines and Ketimines

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Supporting Information

General Information. All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen with magnetic stirring unless otherwise indicated. Methylene chloride was obtained from Fisher and purified by degassing with argon followed by passage through an activated neutral alumina column. Benzene was purchased from Fisher and purified by degassing with argon followed by passage through both an activated neutral alumina column and Q5 reactant column. Toluene and triethylamine were purchased from Aldrich and purified by distillation from CaH₂ then stored under nitrogen. Pentane (HPLC grade) was purchased from Fisher and used as received. Anhydrous chloroform (stabilized with amylenes) and methanol were purchased from Aldrich and used as received. The Grubbs second generation and Hoveyda-Grubbs second generation catalysts were obtained from Materia Inc. and used without purification. Allylamine and all ketone reagents were purchased from Aldrich and used as received. ¹H NMR spectra were recorded on Bruker DPX-300 (300 MHz) or DPX-400 (400 MHz) spectrometers. ¹H NMR chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane internal standard (0 ppm) or CD₃OD internal standard (3.31 ppm). Data are reported as follows: (s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, q = quartet, quint = quintet, dd = doublet of doublets, dq = doublet of quartets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, m = multiplet; integration; coupling constant in Hz; assignment). Proton decoupled ¹³C NMR spectra were recorded on Bruker DPX-300 (75 MHz) or DPX-400 (100 MHz) spectrometers and are reported in ppm from CDCl₃ internal standard (77.1 ppm) or CD₃OD internal standard (49.0 ppm). ²⁹Si NMR spectra were recorded on a Bruker DPX-300 (60 MHz) spectrometer and are reported with tetramethylsilane (0 ppm) as an internal standard. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR or Nicolet Avatar 370 DTGS spectrometers. Optical rotations were recorded on a Jasco DIP-1000 digital polarimeter; the concentration c is reported in g/100mL. Low resolution mass spectra were obtained on a JEOL HX100 mass spectrometer in the Columbia University Mass Spectrometry Laboratory.
Preparation of Silane Reagents.

**Preparation of reagent (1S,2R)-4:** A 2-necked round-bottom flask was charged with allyltrichlorosilane (20.4 mL, 141 mmol) and methylene chloride (360 mL). After cooling the solution to 0 °C, triethylamine (34 mL, 244 mmol) was added dropwise via addition funnel over 10 minutes. N-methyl-(1S,2R)-1-amino-2-indanoli (20 g, 122 mmol) was then added portionwise over 15 minutes. The reaction solution was allowed to warm slowly to room temperature while stirring for 12 hours. Following removal of the solvent by distillation, 300 mL of pentane was added to the remaining residue. The heterogeneous mixture was stirred vigorously for 18 hours to ensure complete precipitation of the triethylamine salts. Filtration of the suspension and concentration of the filtrate by distillation afforded the unpurified product as a yellow oil. Purification by distillation under reduced pressure yielded the product as a colorless oil (20.6 g, 64%, b.p. 100 - 106°C @ 0.3 mm Hg, 2.4:1 mixture of diastereomers). ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.34 (m, 1H, Ar-H (both diastereomers)), 7.28-7.20 (m, 3H, Ar-H (both diastereomers)), 5.88-5.74 (m, 1H, SiCH₂CH=CH₂ (minor)), 5.61-5.50 (m, 1H, SiCH₂CH=CH₂ (major)), 5.12-4.83 (m, 3H, SiCH₂CH=CH₂ and OCHCH₂ (both diastereomers)), 4.45 (d, 1H, J = 6.3 Hz, NCHAr (minor)), 4.37 (d, 1H, J = 6.3 Hz, NCHAr (major)), 3.32-3.00 (m, 2H, OCHCH₂Ar (both diastereomers)), 2.75 (s, 3H, NCH₃ (major)), 2.73 (s, 3H, NCH₃ (minor)), 2.04-2.01 (m, 2H, SiCH₂CH=CH₂ (minor)), 1.88-1.85 (m, 2H, SiCH₂CH=CH₂ (minor)); ¹³C NMR (75 MHz, CDCl₃) δ 142.6, 141.6, 141.1, 140.9, 130.8, 130.4, 128.9, 128.8, 127.1, 126.9, 126.0, 125.9, 125.7, 125.7, 117.0, 80.7, 79.5, 68.8, 40.9, 40.7, 31.8, 30.6, 24.6, 24.6, 24.6; ²⁹Si NMR (60 MHz, CDCl₃) δ -5.98, -6.12; IR (neat) 3074, 2942, 2811, 1632, 1477, 1187, 1034, 1007 cm⁻¹; LRMS (FAB⁺) calc'd for C₁₃H₁₆ClNOSi 265.8, found 265.1.

**Preparation of trans-crotylsilane reagent (1S,2R)-11:** A 2-necked round-bottom flask was charged with trans-crotyltrichlorosilaneii (4.1 g, 21.5 mmol) and methylene chloride (50 mL). After cooling the solution to 0 °C, triethylamine (5.0 mL, 35.8 mmol) was added dropwise via syringe over 10 minutes. N-methyl-(1S,2R)-1-amino-2-indanol (2.9 g, 17.7 mmol) was then added portionwise over
15 minutes. The reaction solution was allowed to warm slowly to room temperature while stirring for 12 hours. Following distillation of the solvent under nitrogen, 50 mL of pentane was added to the remaining residue. The heterogeneous mixture was stirred vigorously for 18 hours to ensure complete precipitation of the triethylamine salts. Filtration of the suspension and concentration of the filtrate by distillation afforded the unpurified product as a yellow oil. Purification by distillation under reduced pressure yielded the product 11 as a colorless oil (3.0 g, 60%, b.p. 92-97 °C @ 0.2 mm Hg, 2.8:1 mixture of diastereomers). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.38-7.20 (m, 4H, Ar-H (both diastereomers)), 5.57-5.27 (m, 3H, SiCH$_2$CH=CHMe and OCHCH$_2$ (both diastereomers)), 4.45 (d, 1H, J = 6.6 Hz, NCHAr (minor)), 4.39 (d, 1H, J = 6.3 Hz, NCHAr (major)), 3.34-2.99 (m, 2H, OCHCH$_2$Ar (both diastereomers)), 3.06 (s, 3H, NCH$_3$ (major)), 2.72 (s, 3H, NCH$_3$ (minor)), 1.94-1.91 (m, 2H, SiCH$_2$CH=CHCH$_3$ (minor)), 1.80-1.77 (m, 2H, SiCH$_2$CH=CHCH$_3$ (major)), 1.70-1.67 (m, 3H, CH=CHC$_3$ (minor)), 1.47 (dq, 3H, J = 6.3, 1.2 Hz, CH=CHC$_3$ (major)); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 142.4, 141.3, 140.8, 140.5, 128.5, 128.3, 127.2, 126.7, 126.5, 125.5, 125.4, 125.2, 122.2, 121.9, 80.3, 79.1, 68.5, 40.5, 40.3, 31.4, 30.3, 22.5, 22.4, 18.2, 17.9, 17.9; $^{29}$Si NMR (60 MHz, CDCl$_3$) δ -5.38, 5.38; IR (neat) 3022, 2933, 2810, 1477, 1187, 1169, 1033, 1007 cm$^{-1}$; LRMS (FAB$^+$) calc’d for C$_{14}$H$_{19}$ClNOSi 279.8, found 280.1.

**Preparation of cis-crotylsilane reagent (1S,2R)-13:** A 2-necked round-bottom flask was charged with cis-crotyltrichlorosilane$^\text{iii}$ (5.57 g, 29.4 mmol) and methylene chloride (75 mL). After cooling the solution to 0 °C, triethylamine (6.8 mL, 49 mmol) was added dropwise via syringe over 10 minutes. N-methyl-(1S,2R)-1-amino-2-indanol (4.0 g, 24.5 mmol) was then added portionwise over 15 minutes. The reaction solution was allowed to warm slowly to room temperature while stirring for 12 hours. Following distillation of the solvent under nitrogen, 75 mL of pentane was added to the remaining residue. The heterogeneous mixture was stirred vigorously for 18 hours to ensure complete precipitation of the triethylamine salts. Filtration of the suspension and concentration of the filtrate by distillation afforded the unpurified product as a yellow oil. Purification by distillation under reduced pressure yielded the product 13 as a colorless oil (4.8 g, 70%, b.p. 86-95 °C @ 0.2 mm Hg, 2.7:1 mixture of diastereomers). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.36-7.34 (m, 1H, Ar-H (both
Preparation of Imines

Preparation of allyl-(1H-imidazol-2-ylmethylene)-amine (2): To a solution of 2-formyl imidazole \(^iv\) (3.0 g, 31 mmol) in methanol (50 mL) was added allylamine (2.6 mL, 34 mmol). The solution was stirred for 13 hours, after which the reaction mixture was concentrated. To ensure complete removal of water and methanol from the crude product, benzene (15 mL) was added and removed \(in\ vacuo\) to yield a yellow solid (4.1 g, 98\%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 11.40\) (br s, 1H, NH), 8.30 (s, 1H, N=CH), 7.16 (br d, 2H, \(J = 33.3\) Hz, Ar-H), 5.99 (ddt, 1H, \(J = 17.1, 10.5, 5.7\) Hz, CH=CH\(_2\)), 5.25-5.16 (m, 2H, CH=CH\(_2\)), 4.26 (dq, 2H, \(J = 5.4, 1.2\) Hz, C=NCH\(_2\)); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta 153.8, 144.9, 135.0, 130.8, 118.7, 117.1, 62.5\); IR (neat) 3013, 2982, 2821, 2765, 2687, 1650, 1444, 1387, 1111, 915, 755 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{14}\)H\(_{19}\)ClNOSi 279.8, found 279.1.

Preparation of cyclohexyl-(1H-imidazol-2-ylmethylene)-amine: To a solution of 2-formyl imidazole (300 mg, 3.12 mmol) in methanol (10 mL) was added cyclohexylamine (370 \(\mu\)L, 3.23 mmol). After concentration of the reaction mixture and recrystallization (pentane/methylene chloride)
the product was obtained as a pale yellow solid (440 mg, 80\%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 10.84 (br s, 1H, N-H), 8.31 (s, 1H, HC=N), 7.11 (br d, 2H, J = 54.9 Hz, Ar-H), 3.30-3.24 (m, 1H, C=NCH), 1.77-1.64 (m, 5H, Cy-H), 1.50-1.29 (m, 4H, Cy-H), 1.21-1.14 (m, 1H, Cy-H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 150.7, 145.1, 130.6, 118.3, 69.2, 34.3, 25.4, 24.6; IR (KBr) 3077, 2912, 1634, 1415, 1312, 1275, 745 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{10}\)H\(_{15}\)N\(_3\) 177.2, found (M+H\(^+\)) 178.1.

**Synthesis of 4-[(1H-imidazol-2-ylmethylene)-amino]-butyric acid methyl ester:** To a solution of 2-formyl imidazole (300 mg, 3.12 mmol) in methanol (5 mL) was added triethylamine (450 \(\mu\)L, 3.23 mmol) followed by methyl 4-aminobutyrate hydrochloride (450 mg, 2.92 mmol). After stirring for 7 hours, the reaction solution was concentrated in vacuo. Anhydrous ether (10 mL) was added to the crude product and the solution was stirred for 10 minutes, after which the triethylamine salts were filtered and the filtrate was concentrated. Benzene (5 mL) was added and removed in vacuo to yield a yellow solid (336 mg, 83%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.24 (s, 1H, HC=N), 7.16 (br d, 2H, J=24.6 Hz, Ar-H), 3.68-3.62 (m, 5H, C=NC\(_2\)H\(_2\) and OC\(_3\)H\(_3\) overlapping), 2.40 (t, 2H, J = 7.2 Hz, CH\(_2\)CO\(_2\)Me), 2.01 (quint, 2H, J = 6.9 Hz, C=NCH\(_2\)CH\(_2\)); \(^{13}\)C NMR (75 MHz, CD\(_3\)OD) \(\delta\) 175.5, 152.7, 145.9, 125.0, 60.9, 52.0, 32.3, 27.2; IR (neat) 3117, 2947, 2835, 2691, 1726, 1643, 1439, 1165, 760 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_9\)H\(_{13}\)N\(_3\)O\(_2\) 195.2, found (M+H\(^+\)) 196.2.

**Synthesis of (E)-N-(1-(1H-imidazol-2-yl)ethyldiene)prop-2-en-1-amine:** To a solution of 2-acetylamidazole\(^4\) (300 mg, 2.72 mmol) in chloroform (3 mL) was added allylamine (610 \(\mu\)L, 8.17 mmol). 4 Å molecular sieves were added, and the solution stirred for 14 hours. The reaction mixture was filtered through celite and concentrated in vacuo to give the product as a green oil (375 mg, 93%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 11.36 (br s, N-H), 7.14 (s, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 5.98 (ddt, 1H, J = 17.1, 10.2, 5.4 Hz, CHCH\(_2\)), 5.21-5.09 (m, 2H, CH=CH\(_2\)), 4.18 (d, 2H, 5.4 Hz, C=N-CH\(_2\)), 2.41 (s, 3H, N=C-CH\(_3\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 160.6, 147.4, 134.8, 129.6, 118.6, 115.8, 53.6, 14.6; IR (neat) 3013, 2947, 2835, 2691, 1726, 1643, 1439, 1165, 760 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_8\)H\(_{11}\)N\(_3\) 149.19, found (M+H\(^+\)) 150.1.
Preparation of allyl-[1-(1H-benzoimidazol-2-yl)-ethylidene]-amine (15): To a solution of 2-acetyl benzimidazole\(^4\) (300 mg, 1.87 mmol) in chloroform (6 mL) was added allylamine (420 µL, 5.60 mmol). 4 Å molecular sieves were added, and the solution stirred for 9 hours. After filtering through celite, the filtrate was concentrated in vacuo. Benzene (10 mL) was added and removed in vacuo to yield 15 as a white solid (320 mg, 86%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 10.68 (br s, 1H, NH), 7.84-7.82 (m, 1H, Ar-H), 7.40-7.37 (m, 1H, Ar-H), 7.31-7.23 (m, 2H, Ar-H), 6.06 (ddt, 1H, J = 17.4, 10.5, 5.4 Hz, CH=CH\(_2\)), 5.28-5.15 (m, 2H, CH=CH\(_2\)), 4.24 (d, 2H, 5.1 Hz, C=NC\(_2\)); 13C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 160.2, 151.6, 143.9, 135.0, 133.8, 124.5, 122.5, 120.7, 116.1, 111.2, 54.4, 14.5; IR (neat) 3057, 2980, 2889, 2755, 1647, 1634, 1420, 1312, 916, 743 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{12}\)H\(_{13}\)N\(_3\) 199.3, found (M+H\(^+\)) 200.0.

Preparation of (E)-N-((1H-imidazol-2-yl)(phenyl)methylene)prop-2-en-1-amine (9): To a solution of 2-benzoylimidazole\(^v\) (2.0 g, 11.6 mmol) in methylene chloride (30 mL) was added allylamine (4.3 mL, 58 mmol). 4 Å molecular sieves were added, and the solution refluxed for 40 hours. After filtering through celite, the filtrate was concentrated in vacuo. Recrystallization (toluene/hexanes) provided the product 9 as a grey solid (1.75 g, 71%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.48-7.43 (m, 3H, Ar-H), 7.34-7.31 (m, 2H, Ar-H), 7.17 (s, 1H, Imid-H), 7.09 (s, 1H, Imid-H), 6.01 (ddt, 1H, J = 17.1, 10.5, 5.4 Hz, CH=CH\(_2\)), 5.22-5.09 (m, 2H, CH=CH\(_2\)), 4.09 (dt, 2H, J = 5.4, 1.8 Hz, NCH\(_2\)); 13C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 161.1, 147.1, 136.0, 133.7, 130.8, 129.3, 128.4, 128.0, 118.0, 115.7, 55.3; IR (KBr) 3014, 2900, 2755, 1613, 1437, 1385, 1308, 1107 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{13}\)H\(_{13}\)N\(_3\) 211.3, found (M+H\(^+\)) 212.1.
Preparation of \([1-(1H\text{-}benzimidazol-2-yl})\text{-ethylidene}\]-but-3-enyl-amine (17): To a solution of 2-acetyl benzimidazole\(^\text{iv}\) (437 mg, 2.72 mmol) in anhydrous chloroform (6 mL) was added 3-buten-1-amine\(^\text{vi}\) (386 mg, 5.44 mmol). 4 Å molecular sieves were added, and the solution was stirred for 24 hours. After filtering through celite, the filtrate was concentrated. Benzene (10 mL) was added and then removed \textit{in vacuo} to yield 17 as a tan solid (507 mg, 87%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.83-7.81\) (m, 1H, Ar-H), 7.38-7.36 (m, 1H, Ar-H), 7.27-7.24 (m, 2H, Ar-H), 5.88 (ddt, 1H, \(J = 17.2, 10.4, 6.4\) Hz, \(\mathrm{CH}=\mathrm{CH}_2\)), 5.12-5.02 (m, 2H, \(\mathrm{CH}=\mathrm{CH}_2\)), 3.65 (t, 2H, \(J = 7.2\) Hz, NCH\(_2\)), 2.51-2.45 (m, 5H, \(\mathrm{CH}_2\mathrm{CH}=\mathrm{CH}_2\) and \(\mathrm{N}=\mathrm{CCH}_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 159.6, 151.7, 143.8, 136.3, 133.9, 124.5, 122.5, 120.7, 116.3, 111.2, 51.6, 34.9, 14.6;\) IR (KBr) 3090, 2995, 2893, 1636, 1451, 1312, 1249, 746 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{13}\)H\(_{15}\)N\(_3\) 213.3, found (M+H\(^+\)) 214.2.

Preparation of Allylation Products.

Preparation of (\(R\))-N-allyl-1-(1H-imidazol-2-yl)but-3-en-1-amine (3): To a solution of aldimine 2 (50 mg, 0.37 mmol) in toluene (3.7 mL) was added (1\(S\),2\(R\))-4 (148 mg, 0.55 mmol). The reaction mixture was stirred for 1 hour, after which saturated sodium bicarbonate (2 mL) was added. After 15 minutes, a 30% solution of isopropyl alcohol in chloroform (15 mL) was added along with additional saturated sodium bicarbonate (10 mL). The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (4 x 5 mL). The combined organic layers were dried (MgSO\(_4\)), filtered, and concentrated. The residue was purified by flash chromatography (5% methanol in methylene chloride) to afford amine 3 (53 mg, 80%). \([\alpha]_D = +34.9^\circ\) (c 1.1, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 6.99\) (s, 2H, Ar-H), 5.90-5.68 (m, 2H, \(\mathrm{CH}=\mathrm{CH}_2\times 2\)), 5.17-5.05 (m, 4H, \(\mathrm{CH}=\mathrm{CH}_2\times 2\)), 3.99 (dd, 1H, \(J = 7.8, 5.5\) Hz, ArCH), 3.21-3.09 (m, 2H, NCH\(_2\)CH=CH\(_2\)), 2.66-2.58 (m, 1H, one of CHCH\(_2\)CH=CH\(_2\)), 2.53-2.43 (m, 1H, one of CHCH\(_2\)CH=CH\(_2\)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta 150.4, 136.2, 134.4, 121.6, 118.4, 116.3, 55.8, 50.4, 40.3;\) IR (neat) 2076, 2977, 2913, 2807, 1642, 1451, 1095, 917 cm\(^{-1}\); LRMS (FAB\(^+\)) calc’d for C\(_{10}\)H\(_{15}\)N\(_3\) 177.3, found (M+H\(^+\)) 178.1.
Preparation of [(R)-N-(1-(1H-imidazol-2-yl)but-3-enyl)cyclohexanamine (5): To a solution of the aldimine (50 mg, 0.28 mmol) in toluene (2.8 mL) was added (1S,2R)-4 (112 mg, 0.42 mmol) at room temperature. The reaction mixture was stirred for 12 hours, after which saturated sodium bicarbonate (2 mL) was added. After 15 minutes, a 30% solution of isopropyl alcohol in chloroform (15 mL) was added along with additional saturated sodium bicarbonate (10 mL). The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. The residue was purified by flash chromatography (5% methanol in methylene chloride) to afford amine 5 (52 mg, 85%). [α]D = +32.4° (c 2.1, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 6.98 (s, 2H, Ar-H), 5.80-5.66 (m, 1H, CH=CH₂), 5.11-5.07 (m, 2H, CH=C₂H₅), 4.08 (dd, 1H, J = 7.8, 5.1 Hz, Ar-CH), 2.65-2.57 (m, 1H, one of CH₂CH=CH₂), 2.44-2.31 (m, 2H, overlapping one of CH₂CH=CH₂ and NCH(CH₂)₂), 1.93 (d, 1H, J = 12.6 Hz, Cy-H), 1.70-1.58 (m, 4H, Cy-H), 1.26-0.94 (m, 5H, Cy-H); ¹³C NMR (75 MHz, CDCl₃) δ 151.5, 134.6, 121.1, 118.4, 55.2, 53.6, 40.9, 34.4, 33.3, 26.0, 25.1, 25.0; IR (neat) (3026, 2923, 2853, 1451, 1374, 1096, 992 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₃H₂₁N₃ 219.3, found (M+H)⁺ 220.2.

Preparation of [(R)-1-(1-(1H-imidazol-2-yl)but-3-enyl)pyrrolidin-2-one (6): To a solution of the aldimine (50 mg, 0.26 mmol) in toluene (2.6 mL) was added (1S,2R)-4 (102 mg, 0.38 mmol). The reaction mixture was stirred for one hour, after which the temperature was raised to 45 °C. After stirring the reaction mixture for another hour, the solution was cooled to room temperature and saturated sodium bicarbonate (2 mL) was added. The biphasic solution was stirred for an additional 15 minutes, after which a 30% solution of isopropyl alcohol in chloroform (15 mL) along with saturated sodium bicarbonate (10 mL) was added. The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated in vacuo. Purification by flash chromatography (4% methanol in methylene chloride) gave the product 6 as a white solid (38 mg, 71%). [α]D = +93.0° (c 1.4, CH₂Cl₂);
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.45 (br s, 1H, N-H), 6.99 (s, 2H, Ar-H), 5.79-5.69 (m, 1H, CH=CH\(_2\)), 5.32 (dd, 1H, J = 10.0, 6.4 Hz, Ar-CHN), 5.16-5.06 (m, 2H, CH=CH\(_2\)), 3.51-3.44 (m, 1H, one of NC\(_2\)H\(_2\)), 3.30-3.24 (m, 1H, one of NC\(_2\)H\(_2\)), 2.93-2.80 (m, 2H, C\(_2\)H=CH)\(_2\)), 2.47-2.29 (m, 2H, CH\(_2\)C=O), 2.02-1.93 (m, 2H, NC\(_2\)H\(_2\)); 13C NMR (75 MHz, CD\(_3\)OD) \(\delta\) 177.7, 146.5, 135.1, 122.9, 118.4, 49.9, 44.6, 35.4, 32.0, 18.8; IR (neat) 3152, 2978, 2913, 1656, 1435, 1287, 739 cm\(^{-1}\); LRMS (FAB\(^+\)) calc'd for C\(_{11}\)H\(_{15}\)N\(_3\)O 205.3, found (M+H\(^+\)) 206.3.

Preparation of (S)-N-allyl-2-(1H-imidazol-2-yl)pent-4-en-2-amine (7): To a stirred solution of aldimine (50 mg, 0.34 mmol) in toluene (3.5 mL) was added (1R,2S)-4 (132 mg, 0.5 mmol). After stirring for 30 minutes, aqueous saturated sodium bicarbonate (2 mL) was added to the solution. The resulting biphasic solution was stirred for 15 minutes, after which a 30% solution of isopropanol in chloroform (15 mL) and additional saturated sodium bicarbonate (10 mL) was added. The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO\(_4\)), filtered, and concentrated. After column chromatography (5% methanol in methylene chloride), 7 was obtained as a white solid (55 mg, 85%). \([\alpha]_D^- = -14.2^\circ\) (c 1.0, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 6.98 (s, 2H, Ar-H), 5.88 (ddt, 1H, J = 17.1, 10.2, 5.7 Hz, CH=CH\(_2\)), 5.72 (ddt, 1H, J = 16.5, 10.5, 7.5 Hz, CH=CH\(_2\)), 5.23-5.05 (m, 4H, 2 x CH=CH\(_2\)), 3.13 (ddt, 1H, J = 14.1, 6.0, 1.5 Hz, one of N-C\(_2\)H\(_2\)), 3.02 (ddt, 1H, J = 14.1, 5.7, 1.5 Hz, one of N-C\(_2\)H\(_2\)), 2.61 (d, 2H, J = 7.2 Hz, C\(_2\)H\(_2\)CH=CH\(_2\)), 1.51 (s, 3H, CH\(_3\)); 13C NMR (75 MHz, CD\(_3\)OD) \(\delta\) 153.4, 137.5, 134.4, 122.3, 119.1, 116.5, 57.8, 47.0, 46.8, 23.0; IR (neat) 3028, 2980, 2940, 2859, 2779, 2704, 1645, 1430, 1371, 1096, 916; LRMS (FAB\(^+\)) calc’d for C\(_{11}\)H\(_{17}\)N\(_3\) 191.3, found (M+H\(^+\)) 192.2.

Preparation of (R)-N-allyl-2-(1H-benzo[d]imidazol-2-yl)pent-4-en-2-amine (8): To a solution of ketimine (50 mg, 0.25 mmol) in toluene (2.5 mL) was added (1S,2R)-4. After stirring for 1 hour at room temperature, aqueous saturated sodium bicarbonate (2 mL) was added to the solution. The
resulting biphasic solution was stirred for 15 minutes, after which a 30% solution of isopropanol in chloroform (15 mL) and additional saturated sodium bicarbonate (10 mL) was added. The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. After column chromatography (4% methanol in methylene chloride), 8 was obtained as a white solid (52 mg, 86%). [α]D = +20.3° (c 1.7, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 9.90 (br s, 1H, NH), 7.73 (br s, 1H, Ar-H), 7.40 (br s, 1H, Ar-H), 7.24-7.18 (m, 2H, Ar-H), 5.95-5.70 (m, 2H, CH=CH₂ x 2), 5.25-5.06 (m, 4H, CH=CH₂ x 2), 3.19 (dd, 1H, J = 14.1, 5.7 Hz, one of NCH₂CH=CH₂), 3.09 (dd, 1H, J = 13.8, 5.4 Hz, one of NCH₂CH=CH₂), 2.73 (d, 2H, J = 7.5 Hz, CCH₂C=CH₂), 1.62 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃, 323K) δ 159.6, 136.9, 133.1, 122.3, 119.4, 115.7, 110.8, 57.3, 45.8, 44.9, 24.6, 24.6; IR (KBr) 3076, 2977, 2885, 2843, 1641, 1452, 1411, 1275, 993, 918, 747 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₅H₁₉N₃ 241.3, found (M+H)⁺ 242.1.

Preparation of (S)-N-allyl-1-(1H-imidazol-2-yl)-1-phenylbut-3-en-1-amine (10): To a cooled (10 °C) solution of ketimine 9 (50 mg, 0.24 mmol) in toluene (2.5 mL) was added (1S, 2R)-4. After 38 hours at 10 °C, the reaction mixture was quenched by the addition of aqueous saturated sodium bicarbonate (2 mL). The resulting biphasic mixture was stirred for 15 minutes, after which a 30% solution of isopropanol in chloroform (15 mL) and additional saturated sodium bicarbonate (10 mL) were added. The layers were separated and the aqueous layer was extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. After column chromatography (30% ethyl acetate in hexanes), 10 was obtained as a white solid (41 mg, 69%). [α]D = -25.3° (c 1.2, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 9.34 (br s, 1H, Imid N-H), 7.48-7.45 (m, 2H, Ar-H), 7.35-7.24 (m, 3H, Ar-H), 6.96 (s, 2H, Imid-H), 5.91 (ddt, 1H, J = 15.9, 10.5, 5.7 Hz, one HC=CH₂), 5.55 (ddt, 1H, J = 13.8, 10.2, 6.9 Hz, one HC=CH₂), 5.27-5.07 (m, 4H, 2 x CH=CH₂), 3.32 (dd, 1H, J = 14.4, 7.8 Hz, one CH₂CH=CH₂), 3.19 (dd, 1H, J = 14.4, 6.9 Hz, one CH₂CH=CH₂), 3.11 (dd, 1H, J = 14.1, 6.0 Hz, one CH₂CH=CH₂), 2.90 (dd, 1H, J = 13.8, 5.7 Hz, one CH₂CH=CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 153.6, 145.0, 137.9, 134.4, 129.1, 128.1, 127.9, 122.2, 118.9, 115.9, 63.8, 46.6, 42.1; IR (KBr) 3069, 3026, 2950, 2973, 1641, 1434, 1377, 1099, 994 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₆H₁₉N₃ 253.3, found (M+H)⁺ 254.1.
Preparation of (1R,2S)-N-allyl-1-(1H-imidazol-2-yl)-2-methylbut-3-en-1-amine (12): To a solution of aldimine 2 (50 mg, 0.37 mmol) in toluene (3.7 mL) was added (1S,2R)-11 (155 mg, 0.55 mmol). After stirring for 1 hour at room temperature, aqueous saturated sodium bicarbonate (2 mL) was added to the solution. The resulting biphasic solution was stirred for 15 minutes, after which a 30% solution of isopropanol in chloroform (15 mL) and additional saturated sodium bicarbonate (10 mL) was added. The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. After column chromatography (5% methanol in methylene chloride), 12 was obtained as an oily solid (52 mg, 74%, >95:5 dr). [α]D = +29.9° (c 1.1, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 7.01 (s, 2H, Ar-H), 5.89-5.75 (m, 2H, CH=CH₂ x 2), 5.16-5.03 (m, 4H, CH=CH₂ x 2), 3.91 (d, 1H, J = 4.8 Hz, Ar-CHN), 3.20-3.05 (m, 2H, NCH₂CH=CH₂), 2.76-2.65 (m, 1H, CHCH₃), 0.98 (d, 3H, J = 6.9 Hz, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 149.5, 140.2, 136.4, 121.5, 116.2, 115.8, 60.6, 50.9, 42.7, 14.8; IR (neat) 3148, 3034, 2967, 2886, 2812, 1452, 1095, 917, 737 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₁H₁₇N₃ 191.3, found (M+H)⁺ 192.0.

Preparation of (1R,2R)-N-allyl-1-(1H-imidazol-2-yl)-2-methylbut-3-en-1-amine (14): To a solution of aldimine 2 (50 mg, 0.37 mmol) in toluene (3.7 mL) was added (1S,2R)-13 (155 mg, 0.55 mmol). After stirring for 1 hour at room temperature, aqueous saturated sodium bicarbonate (2 mL) was added to the solution. The resulting biphasic solution was stirred for 15 minutes, after which a 30% solution of isopropanol in chloroform (15 mL) and additional saturated sodium bicarbonate (10 mL) was added. The aqueous layer was separated and extracted with additional 30% isopropanol/chloroform solution (2 x 10 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated. After column chromatography (5% methanol in methylene chloride), 14 was obtained as a clear oil (47 mg, 66%, >95:5 dr). [α]D = +70.9° (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 7.02 (s, 2H, Ar-H), 5.87-5.68 (m, 2H, CH=CH₂ x 2), 5.14-5.02 (m, 4H, CH=CH₂ x 2), 3.72 (d, 1H, J = 8.4 Hz, Ar-CHN), 3.16-3.01 (m, 2H, NCH₂CH=CH₂), 2.59-2.47 (m, 1H, CHCH₃), 0.922
(d, 3H, J = 6.6 Hz, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 149.5, 141.2, 136.3, 121.5, 116.2, 116.0, 61.1, 50.5, 44.3, 17.3; IR (neat) 3076, 2973, 2878, 2810, 1640, 1456, 1097, 919, 736 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₁H₁₇N₃ 191.3, found (M+H)⁺ 192.3.

Preparation of (R)-2-(2-methyl-1,2,3,6-tetrahydropyridin-2-yl)-1H-benzo[d]imidazole (16): To a solution of ketimine 15 (50 mg, 0.25 mmol) in toluene (2.5 mL) was added (1S,2R)-4 (100 mg, 0.38 mmol). After 1 hour, Grubbs second generation catalyst (11 mg, 0.01 mmol) was added. The solution was heated at 45 °C for 14 hours, after which the reaction mixture was cooled to room temperature and quenched with saturated sodium bicarbonate (2 mL). After 15 minutes, the solution was diluted with a 30% isopropanol in chloroform mixture (15 mL). Additional saturated sodium bicarbonate (10 mL) was added, the layers were separated, and the aqueous layer was extracted with 30% isopropanol in chloroform (2 x 10 mL). The combined organic extracts were dried (MgSO₄), filtered and concentrated. The residue was purified by flash chromatography (5 – 7% methanol in methylene chloride) to give 16 as a tan solid (43 mg, 81%). [α]D = -27.5° (c 1.1, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 9.90 (br s, 1H, NH), 7.58 (br s, 2H, Ar-H), 7.26-7.21 (m, 2H, Ar-H), 5.91-5.87 (m, 1H, one CH=CH), 5.71-5.68 (m, 1H, one CH=CH), 3.43 (d, 1H, J = 18.0 Hz, one NCH₂), 3.30 (d, 1H, J = 18.3 Hz, one NCH₂), 3.00 (d, 1H, J = 17.1 Hz, one CCH₂CH=CH), 2.35 (d, 1H, J = 17.7 Hz, one CCH₂CH=CH), 2.00 (br s, 1H, NH), 1.57 (s, 3H, CH₃); ¹³C NMR (75 MHz, CD₃OD, 325 K) δ 159.7, 138.5, 125.3, 123.9, 122.3, 114.7, 52.8, 41.8, 34.7, 27.6; IR (KBr) 3049, 2974, 2920, 1454, 1411, 1274, 1225, 745 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₃H₁₅N₃ 213.3, found (M+H)⁺ 214.2.

Synthesis of (R)-2-(2-methyl-2,3,6,7-tetrahydro-1H-azepin-2-yl)-1H-benzo[d]imidazole (18): To a solution of ketimine 17 (50 mg, 0.23 mmol) in toluene (2.3 mL) was added (1S,2R)-4 (93 mg, 0.35 mmol). After 1 hour, Grubbs second generation catalyst (11 mg, 0.01 mmol) was added. The solution was heated at 45 °C for 14 hours, after which the reaction mixture was cooled to room temperature and quenched with saturated sodium bicarbonate (2 mL). After 15 minutes, the solution was diluted with a
30% isopropanol in chloroform mixture (15 mL). Additional saturated sodium bicarbonate (10 mL) was added, the layers were separated, and the aqueous layer was extracted with 30% isopropanol in chloroform (2 x 10 mL). The combined organic extracts were dried (MgSO₄), filtered and concentrated. The residue was purified by flash chromatography (5 – 6% methanol in methylene chloride) to give 18 as a tan solid (40 mg, 75%). [α]D = +24.8° (c 1.2, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 7.56 (br s, 2H, Ar-H), 7.21-7.19 (m, 2H, Ar-H), 5.74-5.67 (m, 2H, CH=CH), 3.16-3.10 (m, 1H, one of NCH₂), 3.01-2.90 (m, 2H, one NCH₂ and one CH₃CCH₂), 2.84-2.79 (m, 1H, one CH₃CCH₂), 2.38-2.28 (m, 2H, NCH₂CH₂CH=CH), 1.57 (s, 3H, CH₃); ¹³C NMR (75 MHz, CD₃OD) δ 161.8, 139.4, 133.4, 128.2, 123.2, 115.6, 58.8, 43.5, 39.4, 32.6, 30.5; IR (KBr) 3062, 3022, 2967, 2926, 1453, 1411, 1273, 745 cm⁻¹; LRMS (FAB⁺) calc’d for C₁₄H₁₇N₃ 227.3, found (M+H)⁺ 228.2. 

**Determination of Absolute and Relative Configuration.**

To a solution of allylamine 14 (51 mg, 0.27 mmol) in methanol (1 mL) was added p-bromobenzenesulfonylic acid monohydrate (60 mg, 0.24 mmol). After 30 min, the solution was concentrated to a tan solid. A single crystal suitable for X-ray analysis was grown by slow-diffusion of pentane into a THF solution of the salt. The structure was solved and allowed the assignment of absolute and relative stereochemistry for amine 14. The relative stereochemistry of amine 12 could therefore be assigned as syn, and by extension the relative stereochemistry of amines 15 and 16 was assigned as syn as well. The absolute configuration of all other products was assigned by analogy to the crystal structure assignment.

![Structure Image](image)

**Determination of Enantiomeric Excess of Allylation Products.**

The enantiomeric excess (ee) of the products reported in this study was in every case determined by chiral HPLC analysis. In every case the assay was performed on the derived mono- or bis-benzamide derivatives (except 7, which was assayed as its p-NO₂-benzamide, and 8, which was assayed as its bis-ethylcarbamate). Racemic samples were prepared by reacting the appropriate imine with rac-1, which was prepared by mixing equimolar amounts of (S,S)-1 and (R,R)-1. Slight deviations from 50:50 in the racemic traces may therefore be attributed to the error inherent in this procedure.
Carbinamine 3: Chiralpak AD-H column, 45.0% IPA/hexanes, 0.6 mL/min, 254 nm.

Carbinamine 5: Chiralpak AD-H column, 25.0% IPA/hexanes, 1.0 mL/min, 254 nm.
Carbinamine 6: Chiralpak AD-H column, 20% IPA/hexanes, 1.0 mL/min, 254 nm.

Carbinamine 7: Chiralpak AD-H column, 50% IPA/hexanes, 0.6 ml/min, 254 nm.
Carbinamine 8: Chiralpak AD-H column, 1% IPA/hexanes, 1.0 mL/min, 254 nm.

![Racemic](image1)

![Enantioenriched Product](image2)

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Carbinamine 10: Chiralpak AD-H column, 8% EtOH/hexanes, 1.0 mL/min, 254 nm.

![Racemic](image3)

![Enantioenriched Product](image4)

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Carbinamine 12: Chiralpak AD-H column, 12% IPA/hexanes, 1.0 mL/min, 254 nm.

Carbinamine 14: Chiralpak AD-H column, 12% IPA/hexanes, 1.0 mL/min, 254 nm.
Carbinamine 16: Chiralpak OD column, 1% IPA/hexanes, 1.0 mL/min, 254 nm.

![Racemic](Image)

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![Enantioenriched Product](Image)

Carbinamine 18: Chiralpak AD-H column, 10% IPA/hexanes, 1.0 mL/min, 254 nm.

![Racemic](Image)

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![Enantioenriched Product](Image)
$^1$H NMR Spectra.


