Supporting Information for:

Asymmetric Carbon-Carbon Bond Formations in Conjugate Additions of Lithiated *N*-Boc Allylic and Benzylic Amines to Nitroalkenes: Enantioselective Synthesis of Substituted Piperidines, Pyrrolidines and Pyrimidinones

Timothy A. Johnson[†], Doo Ok Jang[‡], Brian W. Slafer[†], Michael D. Curtis[†] and Peter Beak^{†*}

[†]Department of Chemistry, Roger Adams Laboratory, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801

[‡]Department of Chemistry, Yonsei University, Wonju 220-710, Korea

General. All lithiation reactions were performed in oven dried or flame dried glassware under a positive pressure of nitrogen with freshly distilled solvents. Tetrahydrofuran (THF) and diethyl ether was distilled from sodium and benzophenone. Toluene and dichloromethane were distilled from CaH₂. (–)-Sparteine was distilled from the commercially available (Aldrich) compound and stored under nitrogen. Commercial *tert*-BuLi (solution in pentane), *sec*-BuLi (solution in cyclohexane), and *n*-BuLi (solution in hexanes) were titrated prior to use against *N*-pivaloyl-*o*-toluidine according to literature procedure.¹ Nitroalkenes were either obtained from Aldrich or synthesized according to literature procedure.²

Column chromatography was performed on silica gel (230-400 mesh). Preparative high pressure liquid chromatography (HPLC) was performed using Waters Delta 600 pump system equipped with Nova-Pak@ 6fJ.m silica column (Waters, 19 x 300 mm). Analytical HPLC was performed using Rainin HPXL pump systems. Melting points (mp) were obtained using a Thomas-Hoover melting point apparatus and are uncorrected. The University of Illinois George L. Clark X-ray Facility performed all X-ray crystallography. The University of Illinois Mass Spectrometry Center performed all Mass spectrometry. The ZAB-SE mass spectrometer was purchased in part with grants from the Division of Research Resources, National Institutes of Health (RR 01575), the National Science Foundation (PCM 8121494), and the National Institute of General Medical Sciences (GM 27029). The 70-VSE mass spectrometer was purchased in part with a grant from the Division of Research Resources, National Institutes of Health (RR 04648). The University of Illinois Microanalytical Service Laboratory performed all elemental analysis.

When an elemental analysis was not obtained, purity was established based on ^1H NMR, ^{13}C NMR spectra and HRMS. When CSP-HPLC was used for enantiomeric purity analyses, authentic racemic materials for determining enantiomeric excess were prepared under the same reaction conditions for the chiral compounds except using achiral dibutylbispidine³ instead of (–)-sparteine. Analytical chiral stationary phase (CSP) HPLC was performed on either Whelk-O (Regis Chemical Co., 25 cm x 4.6 mm i.d.) or Chiral-Pak Ad chiral column (Chiral Technologies INC, 25 cm x 4.6 mm i.d.) using mixtures of isopropanol (IPA) and hexane. Diastereomeric ratios were determined by ^1H NMR integration.

Allyl-(4-methoxy-phenyl)-carbamic Acid *tert*-Butyl Ester (5). To a stirred solution of allyl bromide (1.07 mL, 12.3 mmol) in THF (30 mL) was added NaH (0.377 g, 15.7 mmol). The reaction mixture was cooled to 0 °C and a solution of *N*-Boc anisidine (2.50 g, 11.20 mmol) in THF (20 mL) was added dropwise. After complete addition, the reaction was warmed to, stirred overnight, and carefully quenched with H₂O (40 mL). The aqueous was extracted with ether (3 x 50 mL) and the combined organics were dried over MgSO₄ and concentrated. Purification by silica gel column chromatography (8:1 hexanes/EtOAc) provided **5** (2.82 g, 96 %) as an oil. ^1H NMR (CDCl₃, 500 MHz) δ 1.45 (s, 9H, (CH₃)₃CO), 3.79 (s, 3H, CH₃O), 4.18 (d, J = 5.7 Hz, 1H, NCH₂), 5.13 (m, 2H, CH=CH₂), 3.90 (m, 1H, CH=CH₂), 6.83 (m, 2H, PhH), 7.12 (br m, 2H, PhH); ^{13}C NMR (CDCl₃, 125.6 MHz) δ 28.2 (CH₃), 53.0 (CH₂), 55.3 (CH₃), 78.0 (C), 113.7 (CH), 116.6 (CH₂), 127.8 (CH), 134.3 (CH), 135.6 (C), 154.7 (C), 157.4 (C). Anal. Calcd for C₁₅H₂₁NO₃: C, 68.42; H, 8.04; N, 5.32. Found C, 68.25; H, 8.04; N, 5.45.

(4-Methoxy-phenyl)-(5-nitro-3-phenyl-pent-1-enyl)-carbamic Acid *tert*-Butyl Ester (23). The general lithiation procedure was followed using **2** (3.0 g, 8.84 mmol) and nitroethylene^{2b} **16** (0.645 g, 8.84 mmol) premixed with TMSCl (1.12 mL, 8.84 mmol). Purification by column chromatography (4:1 pet ether/EtOAc) gave **23** (3.06 g, 82 %) as a colorless oil. ^1H NMR (acetone-*d*₆, 500 MHz) δ 1.42 (s, 9H, *Or*-Bu), 2.12 (m, 1H, NO₂CH₂CH₂), 2.18 (m, 1H, NO₂CH₂CH₂), 3.11 (m, 1H, CHPh), 3.82 (s, 3H, OMe), 4.26 (m, 2H, CH₂NO₂), 5.06 (t, J = 9.7 Hz, 1H, CH=CHN), 6.70 (d, J = 9.0 Hz, 1H, CH=CHN), 6.88 (m, 4H, PhH), 7.11-7.22 (m, 5H, PhH); ^{13}C NMR (acetone-*d*₆, 125.6 MHz) δ 28.0 (CH₃), 34.5 (CH₂), 39.4 (CH), 55.6 (CH₃), 74.0 (CH₂), 81.1 (C), 114.6 (CH), 127.1 (CH),

127.7 (CH), 128.9 (CH), 129.0 (CH), 129.4 (CH), 135.5 (C), 143.3 (C), 153.7 (C), 158.8 (C). Anal. Calcd for C₂₃H₂₈N₂O₅: C, 66.97; H, 6.84; N, 6.79. Found C, 66.85; H, 6.94; N, 6.70. $[\alpha]_D^{20}$: +175.1 ° (*c* = 1.4, MeOH).

(3,6-Dimethyl-4-nitromethyl-hept-1-enyl)-(4-methoxy-phenyl)-carbamic Acid *tert*-Butyl Ester (26). The general lithiation procedure was followed using **4** (0.256 g, 0.922 mmol) and **12** (0.155 g, 1.19 mmol). Purification by column chromatography (10:1 pet ether/EtOAc) gave **26** (0.277 g, 74 %, 84:16 dr) as a colorless oil. **Major diastereomer:** ¹H NMR (acetone-*d*₆, 500 MHz) δ 0.61 (d, *J* = 6.6 Hz, 3H, CHCH₃), 0.73 (d, *J* = 6.6 Hz, 3H, CHCH₃), 0.79 (d, *J* = 6.6 Hz, 3H, CHCH₃), 0.94 (quint, *J* = 6.9 Hz, 1H, CHCH₂CH), 1.15 (quint, *J* = 6.9 Hz, 1H, CHCH₂CH), 1.36 (s, 9H, *Ot*-Bu), 1.44 (nonet, *J* = 6.6 Hz, 1H, CH₂CH(CH₃)₂), 1.97 (m, 1H, CHCH₃), 2.05 (m, 1H, CHCH₂NO₂), 3.73 (s, 3H, OMe), 4.17 (dd, *J* = 12.6, 7.9 Hz, 1H, CH₂NO₂), 4.36 (dd, *J* = 12.4, 5.3 Hz, 1H, CH₂NO₂), 4.64 (t, *J* = 9.0 Hz, 1H, CH=CHN), 6.52 (d, *J* = 8.9 Hz, 1H, CH=CHN), 6.85 (m, 2H, PhH), 7.13 (m, 2H, PhH); ¹³C NMR (acetone-*d*₆, 125.6 MHz) δ 16.8 (CH₃), 22.7 (CH₃), 23.0 (CH₃), 25.8 (CH), 28.3 (CH₃), 32.4 (CH), 39.4 (CH₂), 41.1 (CH), 55.6 (CH₃), 78.6 (CH₂), 81.1 (C), 114.5 (CH), 128.6 (CH), 130.0 (CH), 136.0 (C), 153.9 (C), 158.6 (C). Anal. Calcd for C₂₂H₃₄N₂O₅: C, 65.00; H, 8.43; N, 6.89. Found C, 64.95; H, 8.44; N, 6.98.

(4-Methoxy-phenyl)-(5-nitro-4-phenyl-pent-1-enyl)-carbamic Acid *tert*-Butyl Ester (27). The general lithiation procedure was followed using **5** (3.37 g, 12.8 mmol) and **10** (2.67 g, 17.89 mmol). Purification by column chromatography (4:1 pet ether/EtOAc) gave **27** (3.92 g, 74 %) as a colorless oil. ¹H NMR (acetone-*d*₆, 500 MHz) δ 1.41 (s, 9H, *Ot*-Bu), 1.97 (m, 2H, CH₂CH=CH), 3.30 (quint, *J* = 6.6 Hz, 1H, CHPh), 3.81 (s, 3H, OMe), 4.59 (m, 2H, CH₂NO₂), 4.72 (q, *J* = 8.1 Hz, 1H, CH=CHN), 6.52 (d, *J* = 9.0 Hz, 1H, CH=CHN), 6.93 (m, 2H, PhH), 7.15 (m, 4H, PhH), 7.23 (m, 1H, PhH), 7.29 (m, 2H, PhH); ¹³C NMR (acetone-*d*₆, 125.6 MHz) δ 28.1 (CH₃), 30.8 (CH₂), 44.5 (CH), 55.6 (CH₃), 80.3 (CH₂), 81.0 (C), 114.6 (CH), 128.0 (CH), 128.3 (CH), 129.1 (CH), 129.2 (CH), 130.4 (CH), 135.4 (C), 140.7 (C), 153.6 (C), 158.7 (C). Anal. Calcd for C₂₃H₂₈N₂O₅: C, 66.97; H, 6.84; N, 6.79. Found C, 66.86; H, 6.81; N, 6.74.

(4-Methoxy-phenyl)-(3-nitro-1,2-diphenyl-propyl)-carbamic Acid *tert*-Butyl Ester (37). The general lithiation procedure was followed using **28** (0.100 g, 0.32 mmol) and **30** (0.070 g, 0.48 mmol). Purification by column chromatography (9:1 hexanes/EtOAc) gave the **37** (0.120 g, 81%, 68:32 dr). The diastereomers were separated by recrystallization from CH₂Cl₂/EtOH. **Major diastereomer:** mp 140-142 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.36 (s, 9H), 3.81 (s, 3H), 4.24 (s, 1H), 4.97 (t, *J* = 11.0 Hz, 1H), 6.00 (s, 1H), 6.76 (d, *J* = 6.5 Hz, 2H), 6.86 (d, *J* = 6.5 Hz, 2H), 6.98-7.22 (m, 8H); ¹³C NMR (125.7 MHz, CDCl₃) δ 28.2, 46.6, 55.2, 61.8, 80.3, 80.7, 113.6, 127.5, 127.6, 127.7, 128.2, 128.7, 129.6, 130.8, 136.3, 137.0, 156.1, 158.5. Anal. Calcd for C₂₇H₃₀N₂O₅: C, 70.11; H, 6.54; N, 6.06. Found: C, 70.02; H, 6.52; N, 6.12. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 2.5 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: rt = 12.3 min (>99 %), 13.4 min (<1 %). **Minor diastereomer:** ¹H NMR (400 MHz, CDCl₃) δ 1.18 (s, 9H), 3.77 (s, 3H), 4.38 (s, 3H), 5.77 (s, 1H), 6.16 (s, 2H), 6.64 (d, *J* = 6.4 Hz, 2H), 7.34-7.54 (m, 10H); ¹³C NMR (125.7 MHz, CDCl₃) δ 28.1, 45.5, 55.2, 61.9, 80.0, 113.2, 128.1, 128.6, 128.7, 128.8, 128.9, 129.0, 137.2, 137.7, 155.1, 158.3. HRMS Calcd for C₂₇H₃₀N₂O₅: 462.2155; Found: 462.2154.

(4-Methoxy-phenyl)-(3-methyl-2-nitromethyl-1-phenyl-butyl)-carbamic Acid *tert*-Butyl Ester (38). The general lithiation procedure was followed using **28** (0.5 g, 1.60 mmol) and **31** (0.086 g, 0.75 mmol). Purification by column chromatography (95:5 hexanes/EtOAc) gave **38** (0.190 g, 90%, >99:1 dr). **Major diastereomer:** mp 106-106 °C; ¹H NMR (400 MHz, CDCl₃) δ 0.80 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 7.2 Hz, 3H), 1.31 (s, 9H), 1.60-1.70 (m, 1H), 3.19 (s, 1H), 3.78 (s, 3H), 4.68-4.86 (m, 2H), 5.45 (s, 1H), 6.55 (s, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 7.2 Hz, 2H), 7.14-7.27 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 15.3, 20.9, 27.5, 28.4, 44.4, 55.5, 61.9, 74.1, 80.7, 113.6, 128.1, 128.3, 129.6, 131.2, 136.9, 156.4, 158.6. Anal. Calcd for C₂₄H₃₂N₂O₅: C, 67.27; H, 7.53; N, 6.54. Found: C, 67.23; H, 7.58; N, 6.58. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Chiral Pak-AD column with 2 % IPA/hexanes mobile phase and a flow rate of 0.4 mL/min: rt = 19.5 min (3 %), 20.7 min (97 %).

(4-Methoxy-phenyl)-(2-methyl-3-nitro-1-phenyl-propyl)-carbamic Acid *tert*-Butyl Ester (39). The general lithiation procedure was followed using **28** (0.310 g, 1.0 mmol) and **32** (0.13 g, 1.5 mmol). Purification by column chromatography (9:1 hexanes/EtOAc) gave **39** (0.38 g, 95%, 90:10 dr). The diastereomers were separated by flash column chromatography. Suitable crystals for X-ray diffraction of the title compound were obtained by slow evaporation from Et₂O/pet ether. **Major diastereomer:** mp 125-126 °C; ¹H NMR (500 MHz, CDCl₃) δ 0.86 (d, *J* = 6.5 Hz, 3H), 1.33 (s, 9H), 3.76 (s, 3H), 4.52 (t, *J* = 11.0 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 5.26 (s, 1H), 6.58 (s, 2H), 6.71 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 6.5 Hz, 2H), 7.14-7.28 (m, 3H); ¹³C NMR (125.7 MHz, CDCl₃) δ 15.7, 28.1, 34.9, 55.1, 63.3, 80.1, 80.3, 113.5, 127.9, 128.1, 129.2, 130.7, 131.0, 136.7, 155.6, 158.4, 158.5. Anal. Calcd for C₂₂H₂₈N₂O₅: C, 65.98; H, 7.05; N, 7.00. Found: C, 65.63; H, 7.00; N, 7.00. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 1 % IPA/hexanes mobile phase and a flow rate of 0.2 mL/min: rt = 49.3 min (<1 %), 51.3 min (>99 %). **Minor diastereomer:** ¹H NMR (500 MHz, CDCl₃) δ 1.37 (s, 9H), 1.44 (d, *J* = 6.0 Hz, 3H), 3.06-3.18 (m, 1H), 3.80 (s, 3H), 4.00-4.07 (m, 1H), 4.18 (dd, *J* = 4.0, 12.3 Hz, 1H), 5.27 (d, *J* = 11.5 Hz, 1H), 6.57 (d, *J* = 7.0 Hz, 2H), 6.74 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 7.0 Hz, 2H), 7.20-7.30 (m, 3H); ¹³C NMR (125.7 MHz, CDCl₃) δ 15.4, 28.2, 34.4, 55.3, 63.4, 79.6, 113.6, 128.3, 128.6, 129.1, 130.8, 131.5, 137.0, 155.5, 158.5. HRMS Calcd for C₂₂H₂₈N₂O₅: 400.1998; Found: 400.1998.

(2-Cyclohexyl-3-nitro-1-phenyl-propyl)-(4-methoxy-phenyl)-carbamic Acid *tert*-Butyl Ester (40). The general lithiation procedure was followed using **28** (0.500 g, 1.60 mmol) and **11** (0.372 g, 2.40 mmol). Purification by column chromatography (8.5:1.5 hexanes/EtOAc) gave **40** (0.69 g, 92%, 92:8 dr). The diastereomers were separated by preparative HPLC (9.7:0.3 hexanes/EtOAc). The major diastereomer was less retained. **Major diastereomer:** mp 144-146 °C; ¹H NMR (400 MHz, CDCl₃) δ 0.80-1.75 (m, 20H), 3.17 (s, 1H), 3.79 (s, 3H), 4.67-4.86 (m, 2H), 5.50 (s, 1H), 6.56 (s, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 6.8 Hz, 2H), 7.10-7.28 (m, 3H); ¹³C NMR (125.7 MHz, CDCl₃) δ 26.0, 26.1, 26.1, 26.6, 28.1, 31.1, 38.1, 44.1, 53.4, 55.2, 61.1, 74.7, 113.3, 127.9, 128.1, 129.3, 130.9, 136.7, 156.1, 158.3. Anal. Calcd for C₂₇H₃₆N₂O₅: C, 69.21; H, 7.74; N, 5.98. Found: C, 68.30; H, 7.70; N, 5.99. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Chiral Pak AD column with 3 % IPA/hexanes mobile phase and a flow rate of 0.3 mL/min: rt = 13.0 min (96 %), 14.6 min (4 %).

Minor diastereomer: ^1H NMR (500 MHz, CDCl_3) δ 1.00-2.30 (m, 20H), 3.08 (s, 1H), 3.80 (s, 3H), 3.96 (dd, $J = 3.5, 13.8$ Hz, 1H), 4.33 (dd, $J = 7.5, 14.0$ Hz, 1H), 5.50 (s, 1H), 6.56 (s, 2H), 6.70-7.30 (m, 7H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 26.4, 26.6, 26.7, 27.4, 28.2, 31.8, 37.7, 43.4, 55.3, 60.4, 74.5, 80.3, 113.6, 128.3, 128.5, 129.4, 130.9, 137.1, 155.4, 158.5. Anal. Calcd for $\text{C}_{27}\text{H}_{36}\text{N}_2\text{O}_5$: C, 69.21; H, 7.74; N, 5.98. Found: C, 68.26; H, 7.86; N, 5.92.

(4-Methoxy-phenyl)-(3-nitro-1-phenyl-2-triisopropylsilyloxy-propyl)-carbamic Acid *tert*-Butyl Ester (41). The general lithiation procedure was followed using **28** (0.310 g, 1.00 mmol) and **15** (0.300 g, 1.50 mmol). Purification by column chromatography (9:1 hexanes/EtOAc) gave **41** (0.420 g, 82%, 77:23 dr). The diastereomers were separated by preparative HPLC (93:7 hexanes/EtOAc). The major diastereomer was less retained. **Major diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 0.65-0.75 (m, 3H), 0.83 (d, $J = 7.5$ Hz, 9H), 0.90 (d, $J = 7.5$ Hz, 9H), 1.36 (s, 9H), 3.79 (s, 3H), 4.73 (s, 1H), 4.92 (dd, $J = 2.5, 13.3$ Hz, 1H), 5.04 (s, 1H), 5.48-5.60 (m, 1H), 6.75 (s, 4H), 7.20-7.30 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 12.9, 18.0, 18.0, 28.2, 55.3, 67.2, 71.8, 113.7, 128.1, 128.1, 129.5, 129.9, 137.9, 158.3. HRMS FAB ($M+1$) Calcd for $\text{C}_{30}\text{H}_{46}\text{N}_2\text{O}_6\text{Si}$: 559.3203; Found: 559.3204. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 1 % IPA/hexanes mobile phase and a flow rate of 0.2 mL/min: rt = 46.2 min (88 %), 48.7 min (12 %). **Minor diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.04-1.16 (m, 21H), 1.35 (s, 9H), 3.81 (s, 3H), 4.34 (dd, $J = 7.0, 13.5$ Hz, 1H), 4.50 (d, $J = 12.5$ Hz, 1H), 5.23 (d, $J = 5.0$ Hz, 1H), 5.45 (s, 1H), 6.82 (d, $J = 8.5$ Hz, 2H), 7.03 (d, $J = 8.5$ Hz, 2H), 7.28-7.36 (m, 3H), 7.38-7.44 (m, 2H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 12.8, 18.1, 28.1, 55.4, 68.4, 72.0, 79.6, 113.9, 127.8, 128.1, 128.5, 129.5, 137.0, 154.9, 158.2. HRMS Calcd for $\text{C}_{30}\text{H}_{46}\text{N}_2\text{O}_6\text{Si}$: 558.3125; Found: 558.3125. The enantiomeric ratio of the minor diastereomer was determined by CSP-HPLC on a Whelk-O column with 1 % IPA/hexanes mobile phase and a flow rate of 0.2 mL/min: rt = 52.9 min (27 %), 57.1 min (73 %).

(4-Methoxy-phenyl)-(3-nitro-1-phenyl-propyl)-carbamic Acid *tert*-Butyl Ester (42). The general lithiation procedure was followed using **28** (0.310 g, 1.00 mmol) and **16** (0.110 g, 1.50 mmol). Purification by column chromatography (9:1 hexanes/EtOAc) gave **42** (0.270 g, 71 %). ^1H NMR (400 MHz, CDCl_3) δ 1.40 (s, 9H), 2.52-2.76 (m, 2H), 3.78 (s, 3H), 4.46-4.58 (m,

2H), 5.59 (t, $J = 6.8$ Hz, 1H), 6.59 (d, $J = 8.4$ Hz, 2H), 6.73 (d, $J = 9.2$ Hz, 2H), 7.10-7.18 (m, 2H), 7.24-7.34 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 28.2, 29.5, 55.2, 57.0, 72.9, 80.3, 113.7, 125.3, 128.1, 128.2, 128.4, 129.0, 130.7, 130.8, 138.7, 155.5, 158.5. HRMS Calcd for $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_5$: 386.1842; Found: 386.1842. The enantiomeric ratio was determined by CSP-HPLC on a Chiral Pak AD column with 4 % IPA/hexanes mobile phase and a flow rate of 0.5 mL/min: rt = 31.3 min (4 %), 36.0 min (96 %).

(2-Furan-2-yl-3-nitro-1-phenyl-propyl)-(4-methoxy-phenyl)-carbamic Acid *tert*-Butyl Ester (43). The general lithiation procedure was followed using **28** (0.300 g, 0.960 mmol) and **14** (0.200 g, 1.44 mmol). Purification by column chromatography (85:15 hexanes/EtOAc) gave the title compound (0.610 g, 84 %, 63:37 dr). The diastereomers were separated by preparative HPLC (85:15 hexanes/EtOAc). The major diastereomer was less retained. **Major diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.36 (s, 9H), 3.80 (s, 3H), 4.40- 4.50 (m, 1H), 4.96-5.14 (m, 2H), 5.86 (s, 1H), 5.95 (d, $J = 3.0$ Hz, 1H), 6.03-6.10 (m, 1H), 6.61 (s, 2H), 6.76 (d, $J = 8.0$ Hz, 2H), 6.94 (d, $J = 7.5$ Hz, 2H), 7.06-7.22 (m, 4H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 28.2, 40.9, 55.3, 61.0, 80.8, 109.3, 110.2, 113.7, 127.8, 129.0, 130.6, 136.6, 142.3, 149.7, 158.6. HRMS Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_6$: 452.1947; Found: 452.1947. The enantiomers of the major diastereomer were inseparable by CSP-HPLC. **Minor diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.28 (s, 9H), 3.79 (s, 3H), 4.27 (dd, $J = 3.5, 12.7$ Hz, 1H), 4.50 (dd, $J = 10.5, 12.8$ Hz, 1H), 4.71 (s, 1H), 5.53 (s, 1H), 6.30-6.47 (m, 3H), 6.50 (d, $J = 2.5$ Hz, 1H), 6.72 (d, $J = 8.0$ Hz, 2H), 7.26-7.44 (m, 5H), 7.47-7.54 (m, 1H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 28.2, 39.9, 55.3, 62.6, 77.0, 109.5, 110.7, 113.5, 128.7, 128.9, 129.0, 130.4, 136.9, 142.4, 150.8, 154.7, 158.4. HRMS Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_6$: 452.1947; Found: 452.1948. The enantiomeric ratio of the minor diastereomer was determined by CSP-HPLC on a Whelk-O column with 2 % IPA/hexanes mobile phase and a flow rate of 0.4 mL/min: rt = 42.3 min (4 %), 45.1 min (96 %).

(4-Methoxy-phenyl)-(3-nitro-1-phenyl-2-thiophen-2-yl-propyl)-carbamic Acid *tert*-Butyl Ester (44). The general lithiation procedure was followed using **28** (0.500 g, 1.60 mmol) and **33** (0.370 g, 2.40 mmol). Purification by column chromatography (85:15 hexanes/EtOAc) gave **44** (0.664 g, 89%, 89:11 dr). The diastereomers were separated by preparative HPLC (9:1

hexanes/EtOAc). The major diastereomer was less retained. **Major diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.36 (s, 9H), 3.80 (s, 3H), 4.63 (m, 1H), 4.94 (t, J = 11.5 Hz, 1H), 5.18 (d, J = 10 Hz, 1H), 5.88 (s, 1H), 6.60 (s, 2H), 6.63-6.80 (m, 4H), 6.70-7.20 (m, 6H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 28.2, 42.3, 55.3, 62.8, 80.7, 113.7, 125.1, 126.6, 126.9, 127.8, 129.4, 130.7, 136.2, 139.7, 158.6. HRMS Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$: 468.1719; Found: 468.1719. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Chiral Pak AD column with 1 % IPA/hexanes mobile phase and a flow rate of 0.5 mL/min: rt = 41.0 min (3 %), 52.8 min (97 %). **Minor diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.28 (s, 9H), 3.79 (s, 3H), 4.36 (d, J = 7.0 Hz, 2H), 4.56 (s, 1H), 5.52 (s, 1H), 6.31 (s, 2H), 6.68 (d, J = 6.5 Hz, 2H), 7.06 (dd, J = 3.5, 5.0 Hz, 1H), 7.17 (s, 1H), 7.30-7.44 (m, 6H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 28.2, 41.1, 55.3, 63.8, 80.2, 113.4, 125.2, 127.0, 127.2, 128.8, 128.9, 129.0, 137.4, 140.1, 158.5. HRMS Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_5\text{S}$: 468.1719; Found: 468.1718.

Furan-2-yl-3-nitro-2-phenyl-propyl)-(4-methoxy-phenyl)-carbamic Acid *tert*-Butyl Ester (45). The general lithiation procedure was followed using **29** (0.303 g, 1.0 mmol) and **10** (0.220 g, 1.50 mmol). Purification by column chromatography (85:15 hexanes/EtOAc) gave **45** (0.440 g, 98 %, >99:1 dr). **Major diastereomer:** ^1H NMR (500 MHz, CDCl_3) δ 1.48 (s, 3H), 3.64-3.74 (m, 1H), 3.81 (s, 3H), 3.89-3.96 (m, 1H), 4.70-4.78 (m, 2H), 5.07 (t, J = 2.5 Hz, 1H), 5.97 (s, 1H), 6.34 (s, 1H), 6.84-6.88 (m, 2H), 7.15-7.40 (m, 9H); ^{13}C NMR (125.7 MHz, CDCl_3) δ 28.1, 48.5, 49.5, 55.3, 75.7, 81.1, 102.6, 106.5, 113.5, 127.5, 127.6, 128.0, 128.9, 134.6, 136.9, 145.6, 153.4, 157.4. HRMS Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_6$: 451.1869; Found: 451.1868. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 6 % IPA/hexanes mobile phase and a flow rate of 1.5 mL/min: rt = 35.9 min (>99 %), 38.3 min (<1 %).

(4-Methoxy-phenyl)-[3-(2-nitro-cyclohexyl)-3-phenyl-propenyl]-carbamic Acid *tert*-Butyl Ester (48). The general lithiation procedure was followed using **2** (0.200 g, 0.588 mmol) and **46** (0.093 mL, 0.823 mmol) except for the reaction was quenched at -78°C with saturated NH_4Cl and the workup involved washing with saturated NH_4Cl rather than brine/ H_2O . Purification by column chromatography (5:1 pet ether/EtOAc) gave **48** (0.179 g, 65 %, 84:16 dr).

Major diastereomer: ^1H NMR (acetone- d_6 , 400 MHz) δ 0.89 (m, 2H, ring CH_2), 1.10 (m, 1H, ring CH), 1.26-1.62 (m, 3H, ring CH_2 , CH), 1.44 (s, 9H, *Ot*-Bu), 1.89 (m, 2H, ring CH_2), 2.29 (br d, $J = 14.6$ Hz, 1H, ring- CHCHPh), 3.24 (br m, 1H, CHPh), 3.84 (s, 3H, *OMe*), 5.07 (br m, 1H, O_2NCH), 5.15 (t, $J = 9.8$ Hz, 1H, CH=CHN), 6.51 (m, 1H, PhH), 6.65 (d, $J = 9.8$ Hz, 1H, CH=CHN), 6.82 (m, 2H, PhH), 6.99 (m, 1H, PhH), 7.10 (m, 3H, PhH); ^{13}C NMR (acetone- d_6 , 125.6 MHz) δ 20.5 (CH_2), 24.2 (CH_2), 24.9 (CH_2), 27.6 (CH), 31.2 (CH_2), 44.4 (CH), 45.5 (CH), 55.2 (CH_3), 80.5 (C), 83.6 (CH), 114.0 (CH), 126.3 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 129.6 (CH), 135.7 (C), 141.8 (C), 153.2 (CH), 158.0 (C). Anal. Calcd for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_5$: C, 69.50; H, 7.35; N, 6.00. Found C, 69.50; H, 7.39; N, 5.99. $[\alpha]_{\text{D}}^{20}$: +193.7° ($c = 1.60$, EtOAc). The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 10 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: rt = 9.10 min (>99 %), 11.5 min (<1 %). **Minor diastereomer:** ^1H NMR (acetone- d_6 , 500 MHz) δ 0.71 (m, 1H, ring CH), 1.22 (m, 2H, ring CH), 1.39 (m, 1H, ring CH), 1.39 (s, 9H, *Ot*-Bu), 1.51 (m, 1H, ring CH), 1.66 (m, 2H, ring CH), 1.86 (m, 1H, ring CH), 2.28 (m, 1H, ring- CHCHPh), 3.12 (dd, $J = 9.2$, 6.7 Hz, 1H, CHPh), 3.81 (s, 3H, *OMe*), 4.21 (td, $J = 9.6$, 4.3 Hz, 1H, O_2NCH), 5.26 (t, $J = 9.9$ Hz, 1H, CH=CHN), 6.61 (d, $J = 9.8$ Hz, 1H, CH=CHN), 6.80 (m, 4H, PhH), 6.99 (m, 2H, PhH), 7.17 (m, 3H, PhH); ^{13}C NMR (acetone- d_6 , 125.6 MHz) δ 23.5 (CH_2), 25.5 (CH_2), 27.6 (CH), 31.45 (CH_2), 43.0 (CH), 44.7 (CH), 55.1 (CH_3), 80.6 (C), 87.7 (CH), 114.1 (CH), 126.5 (CH), 128.0 (CH), 128.4 (CH), 128.7 (CH), 134.9 (C), 140.3 (C), 153.2 (CH), 160.9 (C).

(4-Methoxy-phenyl)-(5-nitro-3,4-diphenyl-hex-1-enyl)-carbamic Acid *tert*-Butyl Ester (49). The general lithiation procedure was followed using **2** (0.150 g, 0.441 mmol) and **47** (0.094 g, 0.573 mmol) except for the reaction was quenched at -78 °C with saturated NH_4Cl and the workup involved washing with saturated NH_4Cl rather than brine/ H_2O . Purification by column chromatography (4:1 pet ether/EtOAc) gave **49** (0.179 g, 65 %, 55:45 dr). **Major diastereomer:** mp 183-184 °C; ^1H NMR (acetone- d_6 , 500 MHz) δ 1.43 (s, 9H, *Ot*-Bu), 1.54 (d, $J = 6.6$ Hz, 3H, CHCH_3), 3.38 (dd, $J = 9.0$, 5.8 Hz, 1H, CHPh), 3.85 (s, 3H, *OMe*), 4.0 (br m, 1H, CHPh), 5.06 (quint, $J = 6.6$ Hz, 1H, O_2NCH), 5.25 (t, $J = 9.3$ Hz, 1H, CH=CHN), 6.47 (m, 2H, PhH), 6.73 (d, $J = 8.9$ Hz, 1H, CH=CHN), 6.83 (m, 2H, PhH), 6.94 (m, 5H, PhH), 7.05 (m, 3H, PhH), 7.24 (m, 2H, PhH); ^{13}C NMR (acetone- d_6 , 125.6 MHz) δ 18.1 (CH_3), 27.7 (CH_3), 43.6

(CH), 55.2 (CH), 55.4 (CH₃), 80.6 (C), 84.6 (CH), 114.2 (CH), 126.2 (CH), 127.3 (CH), 127.8 (CH), 127.8 (CH), 128.4 (CH), 129.7 (CH), 135.9 (C), 136.7 (C), 140.8 (C), 153.4 (CH), 158.2 (C). Anal. Calcd for C₃₀H₃₄N₂O₅: C, 71.69; H, 6.82; N, 5.57. Found C, 71.42; H, 6.83; N, 5.33. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 10 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: rt = 11.7 min (>99 %), 17.5 min (<1 %). **Minor diastereomer:** ¹H NMR (acetone-*d*₆, 500 MHz) δ 1.31 (d, *J* = 6.6 Hz, 3H, CHCH₃), 1.44 (s, 9H, *Ot*-Bu), 3.66 (t, *J* = 10.5 Hz, 1H, CHPh), 3.79 (dd, *J* = 10.3, 5.8 Hz 1H, CHPh), 3.86 (s, 3H, OMe), 5.06 (quint, *J* = 6.6 Hz, 1H, O₂NCH), 5.31 (t, *J* = 9.3 Hz, 1H, CH=CHN), 6.57 (m, 2H, PhH), 6.72 (d, *J* = 9.7 Hz, 1H, CH=CHN), 6.77 (m, 2H, PhH), 6.95 (m, 5H, PhH), 7.06 (m, 3H, PhH), 7.22 (m, 2H, PhH); ¹³C NMR (acetone-*d*₆, 125.6 MHz) δ 14.7 (CH₃), 27.6 (CH₃), 44.0 (CH), 54.7 (CH), 55.3 (CH₃), 80.9 (C), 84.9 (CH), 114.4 (CH), 126.2 (CH), 127.3 (CH), 127.8 (CH), 128.0 (CH), 128.3 (CH), 129.81 (CH), 135.6 (C), 136.0 (C), 140.8 (C), 153.4 (CH), 158.4 (C). Anal. Calcd for C₃₀H₃₄N₂O₅: C, 71.69; H, 6.82; N, 5.57. Found C, 71.36; H, 6.87; N, 5.52.

(4-Methoxy-phenyl)-[(2-nitro-cyclohexyl)-phenyl-methyl]-carbamic Acid *tert*-Butyl Ester (50) The general lithiation procedure was followed using **28** (0.310 g, 1.00 mmol) and **46** (0.190 g, 1.50 mmol). Purification by column chromatography (95:5 hexanes/EtOAc) gave **50** (0.440 g, 77 %, 68:32 dr). The diastereomers were separated by flash column chromatography. The major diastereomer was less retained. **Major diastereomer:** ¹H NMR (400 MHz, CDCl₃) δ 1.34, (s, 9H), 1.15-1.58 (m, 4H), 2.32-2.52 (m, 2H), 3.12- 3.22 (m, 1H), 3.79 (s, 3H), 4.95 (d, *J* = 3.2 Hz, 1H), 5.77 (d, *J* = 12.0 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 6.8 Hz, 2H), 7.16-7.27 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 20.0, 21.2, 23.6, 25.3, 25.9, 28.2, 38.1, 55.2, 60.9, 80.5, 84.2, 113.4, 127.5, 127.9, 128.1, 129.4, 131.0, 131.1, 136.8, 156.0, 158.4. HRMS Calcd for C₂₅H₃₂N₂O₅: 440.2311; Found: 440.2311. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 2.5 % IPA/hexanes mobile phase and a flow rate of 0.5 mL/min: rt = 18.9 min (2 %), 20.5 min (98 %). **Minor diastereomer:** ¹H NMR (400 MHz, CDCl₃) δ 1.05-2.05 (m, 16H), 4.03 (d, *J* = 14.0 Hz, 1H), 3.12 (s, 1H), 3.77 (s, 3H), 4.43 (s, 1H), 5.29 (s, 1H), 6.54 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 7.24-7.40 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 20.3, 24.5, 25.0, 28.2, 31.6, 41.6, 55.3, 68.4, 80.1, 83.2, 113.6, 127.8, 128.1, 128.3, 129.2, 140.1, 155.6, 131.1, 136.8, 156.0,

158.4. HRMS Calcd for $C_{25}H_{32}N_2O_5$: 440.2311; Found: 440.2312. The enantiomeric ratio of the minor diastereomer was determined by CSP-HPLC on a Whelk-O column with 2.5 % IPA/hexanes mobile phase and a flow rate of 0.5 mL/min: $rt = 17.2$ min (95 %), 57.1 min (5 %).

(4-Methoxy-phenyl)-(3-nitro-1,2-diphenyl-butyl)-carbamic Acid *tert*-Butyl Ester (51).

The general lithiation procedure was followed using **28** (0.500 g, 1.60 mmol) and **47** (0.390 g, 2.40 mmol). Purification by column chromatography (9:1 hexanes/EtOAc) gave the **51** (0.550 g, 72 %, 60:40 dr). The diastereomers were separated by preparative HPLC (93:7 hexanes/EtOAc). The major diastereomer was less retained. **Major diastereomer:** 1H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 9H), 1.61 (d, $J = 6.5$ Hz, 3H), 3.80 (s, 3H), 4.35 (d, $J = 11.0$ Hz, 1H), 5.38 (s, 1H), 6.31 (d, $J = 11.0$ Hz, 1H), 6.52-7.04 (m, 14H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.0, 28.1, 50.0, 55.2, 59.8, 80.6, 84.0, 113.4, 127.4, 127.9, 128.1, 129.6, 129.6, 130.4, 131.1, 134.1, 137.1, 156.2, 158.5. Anal. Calcd for $C_{28}H_{32}N_2O_5$: C, 70.57; H, 6.77; N, 5.88. Found: C, 70.57; H, 6.77; N, 5.88. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 2 % IPA/hexanes mobile phase and a flow rate of 0.4 mL/min: $rt = 24.5$ min (12 %), 27.3 min (88 %). **Minor diastereomer:** 1H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.63 (d, $J = 7.0$ Hz, 3H), 3.81 (s, 3H), 4.20-4.80 (m, 1H), 5.50 (s, 2H), 6.75-7.45 (m, 14H). Anal. Calcd for $C_{28}H_{32}N_2O_5$: C, 70.57; H, 6.77; N, 5.88. Found: C, 69.13; H, 5.99; N, 5.93.

Conversion of 23 to 58.

Part 1: 5-Nitro-3-phenyl-pentanoic Acid Methyl Ester. The general procedure for conversion to 5-nitro-pentanoic acid methyl esters was followed using **23** (2.95 g, 7.16 mmol) except esterification was achieved by stirring the crude acid in methanol (100 mL) with HCl (17.8 mL of a 2N solution in Et_2O , 35.6 mmol). Concentration and purification by column chromatography (4:1 pet ether/EtOAc) gave the title compound (1.40 g, 82 %) as an oil. **Major diastereomer:** 1H NMR ($CDCl_3$, 500 MHz) δ 2.23 (m, 1H, CH_2CH_2CHPh), 2.50 (dq, $J = 13.9$, 4.3 Hz, 1H, CH_2CH_2CHPh), 2.68 (d, $J = 7.3$ Hz, 1H, CH_2CO_2Me), 3.19 (m, 1H, $CHPh$), 3.61 (s, 3H, OCH_3), 4.19 (m, 2H, CH_2NO_2), 7.18 (m, 2H, PhH), 7.26 (m, 1H, PhH), 7.33 (m, 2H, PhH); ^{13}C NMR ($CDCl_3$, 125.6 MHz) δ 33.0 (CH), 39.1 (CH), 41.1 (CH_2), 51.7 (CH_3), 73.4 (CH_2), 127.3 (CH), 127.5 (CH), 129.0 (CH), 141.0 (C), 171.8 (C). HRMS-FAB ($M+1$) Calcd for $C_{12}H_{16}NO_4$: 238.1079; Found: 238.1078.

Part 2: 4-Phenylpiperidin-2-one (58). The general hydrogenation-cyclization procedure was followed using 5-nitro-3-phenyl-pentanoic acid methyl ester (1.35 g, 5.69 mmol). Filtration of the catalyst followed by concentration gave **58** (0.960 g, 96 %) as a white solid: mp 154-155 °C. ¹H NMR (CDCl₃, 500 MHz) δ 1.92 (m, 1 H, CH₂CHPh), 2.08 (m, 1 H, CH₂CHPh), 2.48 (dd, *J* = 17.6, 11.2 Hz, 1H, CHCH₂CO), 2.68 (ddd, *J* = 17.8, 5.3, 1.7 Hz, 1H, CHCH₂CO), 3.10 (tdd, *J* = 11.2, 5.2, 3.2 Hz, 1H, CHPh), 3.39 (dd, *J* = 7.7, 3.4 Hz, 2H, CHCH₂N), 7.10 (br s, 1H, NH); 7.23 (m, 3H, PhH), 7.34 (m, 2H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 29.4 (CH₂), 38.3 (CH), 41.2 (CH₂), 126.5 (CH), 126.8 (CH), 128.7 (CH), 143.5 (C), 172.4 (C). HRMS-FAB (M+1) Calcd for C₁₁H₁₄NO: 176.1075; Found: 176.1075.

Conversion of 17 to 62.

Part 2: 3,4-Diphenylpyrrolidin-2-one (62). The general hydrogenation-cyclization procedure was followed using 4-nitro-2,3-diphenyl-butyric acid methyl ester (0.095 g, 0.317 mmol). Purification by column chromatography gave **62** (0.063 g, 85 %) as an oil. The ¹H NMR spectrum was consistent with reported literature values.⁴ [α]_D²⁰: -243.8 ° (*c* = 0.64, CHCl₃)

Conversion of 25 to 63.

Part 1: 2-Methyl-4-nitro-3-phenyl-butyric Acid Methyl Ester. The general procedure for conversion to 4-nitro-butyric acid methyl esters was followed using **25** (3.00 g, 7.03 mmol). Purification by column chromatography (5:1 pet ether/EtOAc) gave the title compound (1.19 g, 71 %, >99:1 dr) a white solid: mp 53-55 °C. ¹H NMR (CDCl₃, 500 MHz) δ 1.03 (d, *J* = 7.1 Hz, 3H, CHCH₃), 2.78 (dq, *J* = 9.8, 7.1 Hz, 1H, CHCH₃), 3.71 (m, 1H, CHPh), 3.72 (s, 3H, OCH₃), 4.70 (d, *J* = 7.3 Hz, 2H, NO₂CH₂), 7.17 (m, 4H, PhH), 7.31 (m, 6H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 15.9 (CH₃), 42.6 (CH), 46.7 (CH), 52.1 (CH₃), 78.5 (CH₂), 127.9 (CH), 128.0 (CH), 129.0 (CH), 137.0 (C), 175.0 (C). Anal. Calcd for C₁₂H₁₅NO₄: C, 60.75; H, 6.37; N, 5.90. Found C, 60.81; H, 6.27; N, 5.99. [α]_D²⁰: +28.5 ° (*c* = 1.0, CHCl₃).

Part 2: 3-Methyl-4-phenyl-pyrrolidin-2-one (63). The general hydrogenation-cyclization procedure was followed using 2-methyl-4-nitro-3-phenyl-butyric acid methyl ester (0.095 g, 0.317 mmol). Recrystallization from hexanes/EtOAc gave **62** (0.499 g, 68 %) as white

crystals: mp 100-101 °C. lit.⁵ mp 100-101 °C. The ¹H NMR and ¹³C NMR spectra were consistent with reported literature values.⁵ [α]_D²⁰: -68.3 ° (*c* = 1.0, CHCl₃). lit.⁵ (enantiomer) [α]_D²⁰: +73.5 ° (*c* = 0.95, CHCl₃).

Conversion of 26 to 64.

Part 1: 2,5-Dimethyl-3-nitromethyl-hexanoic Acid Methyl Ester. The general procedure for conversion to 4-nitro-butyric acid methyl esters was followed using **26** (2.86 g, 7.03 mmol). Purification by column chromatography (9:1 pet ether/EtOAc) gave the title compound (1.14 g, 75 %, 84:16 dr) as an oil. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 0.86 (d, *J* = 6.5 Hz, 3H, CH₂CHMe₂), 0.87 (d, *J* = 6.6 Hz, 3H, CH₂CHMe₂), 0.88 (m, 1H, CH₂CHMe₂), 1.14 (m, 1H, CH₂CHMe₂), 1.16 (d, *J* = 7.0 Hz, 3H, CHMe), 1.59 (nonet, *J* = 6.6 Hz, 1H, CHMe₂), 2.61 (m, 1H, NO₂CH₂CH), 2.67 (m, 1H, CHMe), 3.66 (s, 3H, OMe), 4.35 (dd, *J* = 12.4, 6.4 Hz, 1H, NO₂CH₂), 4.45 (dd, *J* = 12.5, 6.7 Hz, 1H, NO₂CH₂), ¹³C NMR (CDCl₃, 125.6 MHz) δ 13.0 (CH₃), 22.1 (CH₃), 22.5 (CH₃), 25.1 (CH), 37.7 (CH), 38.3 (CH₂), 40.0 (CH), 51.7 (CH₃), 77.2 (CH₂), 174.8 (C). HRMS-FAB (*M*+1) Calcd for C₁₀H₂₀NO₄: 218.1392; Found: 218.1391.

Part 2: 4-iso-Butyl-3-methyl-pyrrolidin-2-one (64). The general hydrogenation-cyclization procedure was followed using 2,5-dimethyl-3-nitromethyl-hexanoic acid methyl ester (1.09 g, 5.02 mmol). Purification by column chromatography (19:1 EtOAc/MeOH) gave **64** (0.670 g, 86 %, 84:16 dr) as an oil. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 0.86 (d, *J* = 6.7 Hz, 3H, CH₂CHMe₂), 0.88 (d, *J* = 6.4 Hz, 3H, CH₂CHMe₂), 1.14 (d, *J* = 6.9 Hz, 3H, CHMe), 1.28 (ddd, *J* = 13.3 9.3, 5.6 Hz, 1H, CH₂CHMe₂), 1.40 (ddd, *J* = 13.5 8.5, 4.7 Hz, 1H, CH₂CHMe₂), 1.55 (m, 1H, CH₂CHMe₂), 1.94-2.07 (m, 2H, CHMe, NCH₂CH), 2.87 (t, *J* = 9.2 Hz, 1H, NCH₂), 3.40 (dd, *J* = 9.5, 7.5 Hz, 1H, NCH₂), 7.08 (br m, 1H, NH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 14.4 (CH₃), 21.9 (CH₃), 23.3 (CH₃), 25.8 (CH), 41.4 (CH), 42.5 (CH), 42.8 (CH₂), 46.6 (CH₂), 181.1 (C). Anal. Calcd for C₉H₁₇NO: C, 69.63; H, 11.04; N, 9.02. Found C, 69.33; H, 11.30; N, 8.97.

Conversion of **27** to **65**.

Part 1: 4-Nitro-3-phenyl-butyric Acid Methyl Ester.⁶ The general procedure for conversion to 4-nitro-butyric acid methyl esters was followed using **27** (2.90 g, 7.03 mmol). Purification by column chromatography (4:1 pet ether/EtOAc) gave the title compound (1.32 g, 84 %) as an oil. ¹H NMR (CDCl₃, 500 MHz) δ 2.78 (dd, *J* = 7.3, 1.5 Hz, 2H, CH₂CO₂Me), 3.63 (s, 3H, OCH₃), 3.99 (quint. *J* = 7.5 Hz, 1H, CHPh), 4.64 (dd, *J* = 12.6, 7.9 Hz, 1H, NO₂CH₂), 4.74 (dd, *J* = 12.9, 7.1 Hz, 1H, NO₂CH₂), 7.20-7.37 (m, 5H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 37.4 (CH₂), 40.1 (CH), 51.9 (CH₃), 79.3 (CH₂), 127.3 (CH), 128.0 (CH), 129.1 (CH), 138.2 (C), 171.1 (C). Anal. Calcd for C₁₁H₁₃NO₄: C, 59.19; H, 5.87; N, 6.27. Found C, 59.03; H, 5.59; N, 6.30.

Part 2: 4-Phenyl-pyrrolidin-2-one (65). The general hydrogenation-cyclization procedure was followed using 4-nitro-3-phenyl-butyric acid methyl ester (1.28 g, 5.73 mmol). Purification by column chromatography (19:1 CH₂Cl₂/MeOH) gave **65** (0.828 g, 90 %,) as a white solid: mp 74-77 °C. lit.⁶ mp 91-93 °C (enantiomer). The ¹H NMR and ¹³C NMR spectra were consistent with reported literature values. [α]_D²⁰: -15.9 ° (*c* = 1.2, MeOH), 75:25 er. lit.⁶ (enantiomer) [α]_D²⁰: -33.8 ° (*c* = 0.89, MeOH).

3,4-Diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (66). The general reduction and protection procedure was followed using **62** (0.055 g, 0.234 mmol). Purification by column chromatography (10:1 pet ether/EtOAc) gave **66** (0.044 g, 58 %,) as a white solid: mp 117-119 °C. ¹H NMR (CDCl₃, 500 MHz) δ 1.50 (s, 9H, C(CH₃)₃), 3.50 (m, 4H, CHPh, NCH₂), 3.95 (m, 1H, NCH₂), 4.04 (m, 1H, NCH₂), 7.13-7.30 (m, 10H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 28.5 (CH₃), 50.4 (CH), 51.5 (CH), 52.8 (CH₂), 53.5 (CH₂), 79.4 (C), 126.9 (CH), 127.0 (CH), 127.5 (CH), 128.5 (CH), 139.3 (C), 154.3 (C). Anal. Calcd for C₂₁H₂₅NO₂: C, 77.98; H, 7.79; N, 4.33. Found C, 77.70; H, 7.91; N, 4.38. [α]_D²⁰: -91.8° (*c* = 1.0, CHCl₃).

3-Methyl-4-phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (67). The general reduction and protection procedure was followed using **63** (0.230 g, 1.31 mmol). Purification by column chromatography (8:1 pet ether/EtOAc) gave **67** (0.280 g, 82 %,) as an oil. ¹H NMR

(CDCl₃, rotational isomers, 500 MHz) δ 0.95 (d, J = 8.1 Hz, 3H, CHCH₃), 1.47 (s, 9H, *tert*-Bu), 2.29 (m, 1H, CHCH₃), 2.79 (m, 1H, CHPh), 2.99 (m, 1H, CH₂N), 3.35 (m, 1H, CH₂N), 3.78 (m, 2H, CH₂N), 7.23 (m, 3H, PhH), 7.32 (m, 2H, PhH); ¹³C NMR (CDCl₃, rotational isomers, 125.6 MHz) δ 15.4 (CH₃), 27.4 (CH₃), 39.8 (CH), 40.8 (CH), 51.6 (CH), 52.4 (CH), 52.8 (CH₂), 52.9 (CH₂), 53.4 (CH₂), 53.7 (CH₂), 79.0 (C), 126.8 (CH), 126.9 (CH), 127.6 (CH), 128.5 (CH), 139.8 (C), 139.9 (C), 154.2 (C), 154.3 (C). Anal. Calcd for C₁₆H₂₃NO₂: C, 73.53; H, 8.87; N, 5.36. Found C, 73.56; H, 9.06; N, 5.05. $[\alpha]_D^{20}$: -26.4 ° (c = 1.1, CHCl₃).

3-*iso*-Butyl-4-methyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (68). The general reduction and protection procedure was followed using **64** (0.120 g, 0.773 mmol). Purification by column chromatography (10:1 pet ether/EtOAc) gave **68** (0.148 g, 79 %), as an oil. ¹H NMR (CDCl₃, 500 MHz) δ 0.86 (d, J = 6.6 Hz, 3H, CH₂CHMe₂), 0.88 (d, J = 6.4 Hz, 3H, CH₂CHMe₂), 0.97 (d, J = 6.2 Hz, 3H, CHMe), 1.09 (ddd, J = 13.5, 10.0, 4.7 Hz, 1H, CH₂CHMe₂), 1.33 (ddd, J = 13.3, 9.4, 3.7 Hz, 1H, CH₂CHMe₂), 1.43 (s, 9H, C(CH₃)₃), 1.52 (m, 1H, CH₂CHMe₂), 1.67 (m, 2H, NCH₂CH, CHMe), 2.81 (m, 2H, NCH₂), 3.53 (dd, J = 10.8, 7.5 Hz, 1H, NCH₂), 3.58 (dd, J = 10.8, 7.3 Hz, 1H, NCH₂); ¹³C NMR (CDCl₃, 125.6 MHz) δ 15.8 (CH₃), 21.7 (CH₃), 23.9 (CH₃), 26.7 (CH), 28.5 (CH₃), 39.1 (CH), 41.4 (CH₂), 43.4 (CH), 51.9 (CH₂), 53.1 (CH₂), 78.8 (C), 154.4 (C). HRMS-FAB (M+1) Calcd for C₁₄H₂₈NO₂: 242.2120; Found: 242.2120. $[\alpha]_D^{20}$: -87.5 ° (c = 0.80, CHCl₃).

3-Phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (69). The general reduction and protection procedure was followed using **65** (0.150 g, 0.930 mmol). Purification by column chromatography (10:1 pet ether/EtOAc) gave **69** (0.181 g, 79 %), as an oil. The ¹H NMR and ¹³C NMR spectra were consistent with reported literature values.⁷ $[\alpha]_D^{20}$: +5.5 ° (c = 1.6, CHCl₃).

{3-[*tert*-Butoxycarbonyl-(4-methoxy-phenyl)-amino]-2,3-diphenyl-propyl}-carbamic Acid *tert*-Butyl Ester (70). A mixture of **36** (0.200 g, 0.430 mmol) and Raney nickel (1 mL) in MeOH (10 mL) was stirred under 200 psi of H₂. After 48 h, the solution was filtered through celite pad and extracted with ether and CH₂Cl₂. After evaporation of the solvent, the residue was dissolved in CH₂Cl₂ (10 mL) and treated with Boc₂O (0.090 g, 0.430 mmol) for 6 h at room

temperature. After evaporation of the solvent, the residue was separated with flash chromatography on silica gel (9:1 hexanes/EtOAc) affording **70** (0.170 g, 74%): mp 114-115 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.35 (s, 9H), 1.42 (s, 9H), 3.30-3.56 (m, 2H), 3.78 (s, 3H), 4.36-4.28 (m, 1H), 4.78 (s, 1H), 6.05 (s, 1H), 6.71 (s, 3H), 6.86 (d, *J* = 6.0 Hz, 2H), 6.72-7.20 (m, 9H); ¹³C NMR (125.7 MHz, CDCl₃) δ 28.2, 28.4, 44.3, 47.0, 55.2, 61.5, 78.8, 80.1, 126.4, 127.0, 127.5, 128.3, 128.7, 129.2, 129.8, 131.2, 137.9, 139.9, 155.8, 156.3, 158.2. Anal. Calcd for C₃₂H₄₀N₂O₅: C, 72.15; H, 7.57; N, 5.26. Found: C, 71.43; H, 7.53; N, 5.31.

1-(4-Methoxy-phenyl)-4,5-diphenyl-tetrahydro-pyrimidin-2-one (71). A solution of **70** (0.100 g, 0.186 mmol) and KO^tBu (0.040 g, 0.372 mmol) in THF (5 mL) was heated at reflux for 1 h. The reaction mixture was diluted with ether, washed with H₂O, and dried over anhydrous MgSO₄. After evaporation of the solvent, the residue was separated by flash column chromatography (EtOAc) affording **71** (0.060 g, 90 %): mp 228-229 °C; ¹H NMR (500 MHz, CDCl₃) δ 3.25-3.33 (m, 1H), 3.55-3.63 (m, 2H), 3.66 (s, 3H), 4.92 (d, *J* = 3.5 Hz, 1H), 5.37 (s, 1H), 6.68 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 7.15-7.50 (m, 10H); ¹³C NMR (125.7 MHz, CDCl₃) δ 41.7, 44.3, 55.2, 69.3, 113.8, 126.5, 127.3, 127.5, 127.7, 128.2, 128.7, 128.9, 135.6, 141.3, 141.4, 156.0, 157.6. HRMS Calcd for C₂₃H₂₂N₂O₂: 358.1681; Found: 358.1681.

1-Benzyl-4-phenyl-5-triisopropylsilanyloxy-piperidin-2-one (74). The general benzylation procedure was followed using **57** (0.400 g, 1.15 mmol). Purification by column chromatography (3:1 pet ether/EtOAc) gave (0.451 g, 90 %) as a colorless oil: ¹H NMR (CDCl₃, 500 MHz) δ 0.98 (m, 21 H, ((CH₃)₂CH)₃Si), 2.75 (dd, *J* = 17.6, 3.6 Hz, 1H, CHCH₂CON), 3.06 (m, 2H, NCH₂), 3.14 (dd, *J* = 17.8, 6.6 Hz, 1H, CHCH₂CON), 3.32 (q, *J* = 5.4 Hz, 1H, CHPh), 4.13 (q, *J* = 3.4 Hz, 1H, CHOTIPS), 4.51 (d, *J* = 14.7 Hz, 1H, NCH₂Ph), 4.71 (d, *J* = 15.0 Hz, 1H, NCH₂Ph), 7.17 (m, 2H, PhH), 7.26 (m, 8H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 12.1 (CH), 17.9 (CH₃), 32.6 (CH₂), 45.3 (CH), 49.8 (CH₂), 50.8 (CH₂), 69.9 (CH), 127.0 (CH), 127.2 (CH), 127.3 (CH), 128.1 (CH), 128.4 (CH), 128.7 (CH), 136.6 (C), 140.8 (C), 169.0 (C). HRMS-FAB (M+1) Calcd for C₂₇H₄₀NO₂Si: 438.2828; Found: 438.2826.

Conversion of **74** to **78**.

Part 1: 3-Allyl-1-benzyl-4-phenyl-5-triisopropylsilanyloxy-piperidin-2-one. The general procedure for *t*-BuLi enolization was followed using **74** (0.235 g, 0.537 mmol) and allyl bromide (0.185 mL, 2.14 mmol). Purification by column chromatography (5:1 pet ether/EtOAc) gave the title compound (0.227 g, 89 %, >97:3 dr) as a colorless oil. ¹H NMR (CDCl₃, 400 MHz) δ 0.67 (m, 3H, CH₃CHSi), 0.75 (d, *J* = 6.8 Hz, 9H, CH₃CHSi), 0.79 (d, *J* = 6.8 Hz, 9H, CH₃CHSi), 2.12 (quint, *J* = 6.1 Hz, 1H, CH₂=CHCH₂CH), 2.82 (m, 2H, CH₂=CHCH₂CH), 2.98 (t, *J* = 9.3 Hz, 1H, CHPh), 3.17 (dd, *J* = 11.9, 8.5 Hz, 1H, NCH₂), 3.32 (dd, *J* = 11.9, 4.6 Hz, 1H, NCH₂), 4.09 (td, *J* = 8.8, 4.6 Hz, 1H, CHOTIPS), 4.50 (d, *J* = 14.4 Hz, 1H, NCH₂Ph), 4.80 (d, *J* = 14.4 Hz, 1H, PhCH₂N), 5.05 (m, 2H, CH₂=CH), 5.74 (m, 1H, CH₂=CHCH₂), 7.15-7.23 (m, 3H, PhH), 7.30 (m, 7H, PhH); ¹³C NMR (CDCl₃, 100.6 MHz) δ 12.3 (CH), 17.7 (CH₃), 17.7 (CH₃), 34.1 (CH₂), 45.9 (CH), 50.3 (CH₂), 51.2 (CH), 52.9 (CH₂), 70.5 (CH), 117.8 (CH₂), 126.9 (CH), 127.5 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 128.6 (CH), 135.1 (CH), 136.9 (C), 141.0 (C), 170.7 (C). HRMS-FAB (M+1) Calcd for C₃₀H₄₄NO₂Si: 478.3141; Found: 478.3140. [α]_D²⁰: -56.3° (*c* = 2.2, CHCl₃).

Part 2: 3-Allyl-1-benzyl-4-phenyl-5-triisopropylsilanyloxy-piperidine (78). The general reduction procedure for benzyl lactams was followed using 3-allyl-1-benzyl-4-phenyl-5-triisopropylsilanyloxy-piperidin-2-one (0.112 g, 0.236 mmol) and lithium aluminum hydride (0.708 mL of a 1 M solution in THF, 0.708 mmol) with a 6 h reflux period. Purification by column chromatography (15:1 pet ether/EtOAc) provided **78** (0.094 g, 86 %) as a colorless oil. ¹H NMR (CDCl₃, 500 MHz) δ 0.67 (m, 3H, CH₃CHSi), 0.75 (d, *J* = 6.8 Hz, 9H, CH₃CHSi), 0.79 (d, *J* = 6.8 Hz, 9H, CH₃CHSi), 1.68 (dt, *J* = 14.4, 8.8 Hz, 1H, CH₂N), 1.90 (m, 3H, CH₂=CHCH₂CH, CH₂N), 2.07 (m, 1H, CH₂=CHCH₂CH), 2.18 (dd, *J* = 11.6, 9.6 Hz, 1H, CHPh), 3.06 (ddd, *J* = 11.2, 3.9, 1.3 Hz, 1H, NCH₂), 3.11 (ddd, *J* = 11.7, 4.5, 1.5 Hz, 1H, NCH₂), 3.48 (d, *J* = 13.1 Hz, 1H, NCH₂Ph), 3.76 (d, *J* = 12.9 Hz, 1H, PhCH₂N), 3.97 (td, *J* = 9.6, 4.5 Hz, 1H, CHOTIPS), 4.90 (m, 2H, CH₂=CH), 5.65 (m, 1H, CH₂=CHCH₂), 7.18-7.31 (m, 6H, PhH), 7.36 (m, 4H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 12.4 (CH), 17.8 (CH₃), 17.8 (CH₃), 35.9 (CH₂), 39.8 (CH), 57.2 (CH), 58.9 (CH₂), 61.2 (CH₂), 62.8 (CH₂), 73.7 (CH), 116.0 (CH₂), 126.3 (CH), 127.0 (CH), 128.0 (CH), 128.1 (CH), 129.2 (CH), 136.4 (CH), 137.9 (C),

142.1 (C). HRMS-FAB (M-1) Calcd for C₃₀H₄₄NOSi: 462.3192; Found: 462.3192. [α]_D²⁰: -32.7 ° (*c* = 1.3, CHCl₃).

2-Oxo-3,4-diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (79). The general procedure for the protection of pyrrolidinones was followed using **62** (0.100 g, 0.421 mmol). Purification by column chromatography (4:1 pet ether/EtOAc) provided **79** (0.110 g, 77 %) as a colorless oil. ¹H NMR (CDCl₃, 500 MHz) δ 1.59 (s, 9H, *Or*-Bu), 3.63 (td, *J* = 11.0, 8.1 Hz, 1H, CHPh), 3.79 (t, *J* = 11.3 Hz, 1H, CH₂N), 3.94 (d, *J* = 11.8 Hz, 1H, COCHPh), 4.26 (dd, *J* = 10.7, 8.1 Hz, 1H, CH₂N), 7.15-7.36 (m, 10H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 27.9 (CH₃), 45.7 (CH), 50.9 (CH₂), 57.0 (CH), 83.1 (C), 127.2 (CH), 127.4 (CH), 127.5 (CH), 128.5 (CH), 128.5 (CH), 128.8 (CH), 136.0 (C), 138.4 (C), 150.0 (C), 172.7 (C). HRMS-EI (M⁺) Calcd for C₂₁H₂₃NO₃: 337.1678; Found: 337.1684. [α]_D²⁰: -87.0 ° (*c* = 1.1, CHCl₃)

3-Methyl-2-oxo-4-phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (80). The general procedure for the protection of pyrrolidinones was followed using **64** (0.098 g, 0.559 mmol). Purification by column chromatography (4:1 pet ether/EtOAc) provided **80** (0.148 g, 90 %) as a white solid: mp 107-108 °C ¹H NMR (CDCl₃, 500 MHz) δ 1.20 (d, *J* = 6.8 Hz, 3H, CHCH₃), 1.55 (s, 9H, *Or*-Bu), 2.71 (dq, *J* = 13.5, 6.9 Hz, 3H, CHCH₃), 3.02 (q, *J* = 10.7 Hz, 1H, CHPh), 3.60 (t, *J* = 10.9 Hz, 1H, CH₂N), 4.07 (dd, *J* = 10.9, 8.4 Hz, 1H, CH₂N), 7.24-7.42 (m, 5H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 13.3 (CH₃), 27.9 (CH₃), 45.6 (CH), 45.9 (CH), 51.2 (CH₂), 82.8 (C), 127.3 (CH), 127.5 (CH), 128.9 (CH), 138.8 (C), 150.0 (C), 175.1 (C). Anal. Calcd for C₁₆H₂₁NO₃: C, 69.79; H, 7.69; N, 5.09. Found C, 69.40; H, 7.91; N, 5.19. [α]_D²⁰: -44.5 ° (*c* = 0.33, CHCl₃).

3-Allyl-3-methyl-2-oxo-4-phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (82). The general procedure for LDA enolization was followed using **80** (0.075 g, 0.272 mmol) and allyl bromide (0.071 mL, 0.816 mmol). Purification by column chromatography (9:1 pet ether/EtOAc) gave **82** (0.071 g, 83 %, >97:3 dr) as a colorless oil. ¹H NMR (CDCl₃, 400 MHz) δ 0.87 (s, 3H, CCH₃), 1.57 (s, 9H, *Or*-Bu), 2.13 (dd, *J* = 14.1, 9.0 Hz, 1H, CH₂CH=CH₂), 2.54 (dd, *J* = 14.1, 4.9 Hz, 1H, CH₂CH=CH₂), 3.45 (t, *J* = 10.7 Hz, 1H, CHPh), 3.94 (m, 2H, CH₂N),

5.21 (d, $J = 5.6$ Hz, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.24 (s, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.84 (m, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 7.21 (m, 2H, PhH), 7.33 (m, 3H, PhH); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ 19.4 (CH_3), 28.0 (CH_3), 40.5 (CH_2), 43.1 (CH), 47.5 (CH_2), 49.9 (C), 83.0 (C), 119.2 (CH_2), 127.4 (CH), 128.4 (CH), 128.6 (CH), 134.0 (CH), 136.7 (C), 150.1 (C), 177.0 (C). HRMS-EI (M^+) Calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_3$: 315.1834; Found: 315.1825.

3-Allyl-1,3-dimethyl-4-phenyl-pyrrolidine (83). The general reduction procedure for benzyl lactams was followed using **82** (0.035 g, 0.111 mmol) and lithium aluminum hydride (0.665 mL of a 1 M solution in THF, 0.665 mmol) with a 6 h reflux period. Purification by column chromatography on basic alumina (25:1 pet ether/EtOAc) provided **83** (0.017 g, 72 %) as a colorless oil. ^1H NMR (CDCl_3 , 500 MHz) δ 0.65 (s, 3H, CCH_3), 2.25 (dd, $J = 7.5, 1.1$ Hz, 1H, CHPh), 2.27 (dd, $J = 12.4, 9.3$ Hz, 2H, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.40 (s, 3H, NCH_3), 2.80 (d, $J = 9.5$ Hz, 1H, CH_2N), 2.87 (t, $J = 9.2$ Hz, 1H, CH_2N), 3.00 (t, $J = 7.4$ Hz, 1H, CH_2N), 3.19 (t, $J = 8.6$ Hz, 1H, CH_2N), 5.08 (m, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.11 (m, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.24 (s, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.85 (m, 1H, $\text{CH}_2\text{CH}=\text{CH}_2$), 7.18-7.31 (m, 5H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 23.5 (CH_3), 29.6 (CH_2), 42.8 (CH), 45.0 (C), 46.7 (CH_2), 53.3 (CH_3), 61.7 (CH_2), 69.1 (CH_2), 117.5 (CH_2), 119.2 (CH_2), 126.2 (CH), 127.9 (CH), 128.9 (CH), 135.6 (CH), 140.6 (C). HRMS-FAB ($\text{M}+1$) Calcd for $\text{C}_{15}\text{H}_{22}\text{N}$: 216.1752; Found: 216.1751.

2-Formyl-4,5-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (85). The general lithiation procedure was followed using **59** (0.100 g, 0.296 mmol) and DMF (0.073 mL, 0.946 mmol) as the electrophile. Purification by column chromatography (4:1 pet ether/EtOAc) gave **85** (0.079 g, 73 %, 81:19 dr) as an oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 1.50 (s, 9H, *Or*-Bu), 1.83 (q, $J = 12.2$ Hz, 1H, CHCH_2CH), 2.13 (m 1H, CHCH_2CH), 3.05 (m, 3H, CHPh , NCH_2), 3.77 (dt, $J = 11.7, 2.8$ Hz, 1H, CHPh), 4.18 (m 1H, CHPh , NCH), 6.97-7.20 (m, 10H, PhH), 9.56 (d, $J = 2.9$ Hz, 1H, CHO); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 28.2 (CH_3), 33.4 (CH_2), 46.5 (CH), 47.8 (CH), 51.8 (CH_2), 64.4 (CH), 80.8 (C), 126.4 (CH), 126.5 (CH), 126.7 (CH), 127.3 (CH), 127.4 (CH), 127.8 (CH), 128.2 (CH), 128.3 (CH), 128.3 (CH), 140.5 (C), 142.4 (C), 195.0 (CH). Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_3$: C, 75.59; H, 7.45; N, 3.83. Found C, 75.51; H, 7.50; N, 3.78.

4,5-Diphenyl-2-trimethylsilylanyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (**86**).

The general lithiation procedure was followed using **59** (0.100 g, 0.296 mmol) and TMSCl (0.120 mL, 0.946 mmol) as the electrophile. Purification by column chromatography (25:1 pet ether/EtOAc) gave **86** (0.083 g, 69 %, >97:3 dr) as a white solid. Crystals suitable for X-ray crystallographic analysis were obtained by vapor diffusion with Et₂O/pentane: mp 151-153 °C. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 0.15 (s, 9H, (CH₃)₃Si), 1.53 (s, 9H, Ot-Bu), 1.79 (q, *J* = 12.5 Hz, 1H, CHCH₂CH), 1.95 (ddd, *J* = 12.6, 3.5, 2.4 Hz, 1H, CHCH₂CH), 2.58 (d, *J* = 12.4 Hz, 1H, NCH), 2.93 (td, *J* = 11.0, 4.1 Hz, 1H, CHPh), 3.04 (m 2H, CHPh, NCH₂), 4.22 (dd, *J* = 13.3, 3.9 Hz, 1H, NCH₂), 7.05-7.22 (m, 10H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ -0.7 (CH₃), 28.5 (CH₃), 35.3 (CH₂), 49.3 (CH), 50.7 (CH), 51.3 (CH), 54.6 (CH₂), 79.3 (C), 126.1 (CH), 126.3 (CH), 127.5 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 141.7 (C), 144.0 (C), 155.1 (C). HRMS-FAB (M+1) Calcd for C₂₅H₃₆NO₂Si: 410.2515; Found: 410.2513. [α]_D²⁰: -7.2 ° (*c* = 1.1, CHCl₃).

4,5-Diphenyl-piperidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (88**).** The general lithiation procedure was followed using **59** (0.210 g, 0.622 mmol) and excess CO₂ gas as the electrophile. The reaction mixture was acidified with 10 % HCl during work up. The crude acid was esterified with an ethereal solution of CH₂N₂ (10 eq.). Purification by column chromatography (4:1 pet ether/EtOAc) gave **88** (0.186 g, 76 %, >97:3 dr) as a white solid: mp 94-96 °C. **Major diastereomer:** ¹H NMR (CDCl₃, 400 MHz) δ 1.47 (s, 9H, Ot-Bu), 2.11 (q, *J* = 12.5 Hz, 1H, CHCH₂CH), 2.31 (ddd, *J* = 13.6, 5.3, 3.6 Hz, 1H, CHCH₂CH), 2.93 (td, *J* = 12.3, 3.4 Hz, 1H, CHPh), 3.08 (dt, *J* = 11.9, 6.3 Hz, 1H, CHPh), 3.64 (dd, *J* = 13.0, 6.4 Hz, 1H, NCH₂), 3.75 (s, 3H, OCH₃), 4.02 (dd, *J* = 13.9, 5.7 Hz, 1H, NCH₂), 4.30 (dd, *J* = 11.5, 5.3 Hz, 1H, NCH), 6.98-7.24 (m, 10H, PhH); ¹³C NMR (CDCl₃, 100.6 MHz) δ 28.2 (CH₃), 34.1 (CH₂), 46.3 (CH), 47.8 (CH), 52.0 (CH), 47.3 (CH₃), 80.8 (C), 126.5 (CH), 126.5 (CH), 127.3 (CH), 127.5 (CH), 128.2 (CH), 128.3 (CH), 142.7 (C), 143.0 (C), 155.6 (C), 172.5 (C). Anal. Calcd for C₂₄H₂₉NO₄: C, 72.89; H, 7.39; N, 3.54. Found C, 72.61; H, 7.35; N, 3.73. [α]_D²⁰: -8.5 ° (*c* = 0.20, CHCl₃).

2,6-Dimethyl-3,4-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (89). The general lithiation procedure was followed using **59** (0.050 g, 0.147 mmol) and MeOTf (0.051 mL, 0.454 mmol) as the electrophile. Purification by column chromatography (25:1 pet ether/EtOAc) gave **89** (0.021 g, 41 %, 93:7 dr) as an oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 1.05 (d, J = 7.0 Hz, 3 H, CH_3CH), 1.46 (d, J = 6.7 Hz, 3 H, CH_3CH), 1.51 (s, 9H, *Ot*-Bu), 1.71 (dt, J = 13.9, 9.4 Hz, 1H, CHCH_2CH), 2.10 (dt, J = 13.5, 4.0 Hz, 1H, CHCH_2CH), 3.47 (m, 2H, CHPh), 2.89 (m, 2H, CHPh), 3.76 (dq, J = 10.1, 5.8, 3.9 Hz 1H, NCHCH_2), 4.50 (qd, J = 6.8, 6.1 Hz, 1H, NCHCH), 7.06 (m, 2H, PhH), 7.15 (m, 8H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 13.4 (CH_3), 22.1 (CH_3), 28.5 (CH_3), 39.4 (CH), 41.9 (CH_2), 47.8 (CH), 49.2 (CH), 54.55 (CH), 79.5 (C), 125.9 (CH), 126.1 (CH), 127.5 (CH), 128.0 (CH), 128.3 (CH), 128.9 (CH), 140.7 (C), 144.5 (C), 155.9 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_2$: 366.2433; Found: 366.2432.

2-Formyl-4,5-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (92). The general lithiation procedure was followed using **59** (0.400 g, 1.18 mmol) and DMF (0.294 mL, 3.79 mmol) as the electrophile. Purification by column chromatography (5:1 pet ether/EtOAc with 2.5 % Et_3N) gave **92** (0.321 g, 74 %, 91:9 dr) as an oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 1.52 (s, 9H, *Ot*-Bu), 2.03 (td, J = 13.3, 7.1 Hz, 1H, CHCH_2CH), 2.54 (m 1H, CHCH_2CH), 2.81 (td, J = 12.2, 3.2 Hz, 1H, CHPh), 2.96 (m 1H, CHPh), 3.11 (t, J = 12.1 Hz, 1H, NCH_2), 4.30 (dd rotational isomers, J = 13.5, 3.6 Hz, 1H, NCH_2), 4.94 (d rotational isomers, J = 6.2 Hz, 1H, NCH_2), 6.98-7.20 (m, 10H, PhH), 9.78 (s rotational isomers, 1H, CHO); ^{13}C NMR (rotational isomers, CDCl_3 , 125.6 MHz) δ 28.3 (CH_3), 31.3 (CH_2), 32.0 (CH_2), 33.4 (CH_2), 44.3 (CH), 44.6 (CH), 46.5 (CH), 46.5 (CH), 47.5 (CH_2), 48.0 (CH_2), 49.0 (CH_2), 60.2 (CH), 61.4 (CH), 80.8 (C), 126.4 (CH), 126.6 (CH), 127.4 (CH), 127.8 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 140.4 (C), 140.6 (C), 142.6 (C), 155.4 (C), 201.5 (CH).

Conversion of **92** to **93**.

Part 1: 4,5-Diphenyl-2-vinyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester. To a solution of methyl triphenylphosphonium bromide (0.340 g, 0.95 2mmol) in THF (3 mL) was at -78°C was added *n*-BuLi (0.581 mL of a 1.5 M solution in hexanes, 0.872 mmol). The solution was warmed to rt for 1h and cooled back to -78°C . A solution of **92** (0.290 g, 0.793 mmol) in

THF (3 mL) was added via cannula and the reaction was stirred for 1 h at $-78\text{ }^{\circ}\text{C}$, warmed to rt and quenched with H_2O (5 mL). The aqueous was extracted with ether (3 x 15 mL) and the combined organics were dried over MgSO_4 and concentrated. The residue was filtered through a plug of silica gel (Et_2O) and concentrated. Purification by column chromatography (19:1 pet ether/ EtOAc) gave the title compound (0.199 g, 69 %, >99:1 dr) as a white solid: mp $98\text{--}100\text{ }^{\circ}\text{C}$

Major diastereomer: ^1H NMR (CDCl_3 , 400 MHz) δ 1.51 (s, 9H, *Ot-Bu*), 2.07 (m, 2H, CHCH_2CH), 2.86-3.22 (m 3H, CHPh , NCH_2), 4.18 (dd rotational isomers, $J = 13.4, 3.9\text{ Hz}$, 1H, NCH_2), 5.04 (br m rotational isomers, 1H, CHN), 5.2 (d, $J = 17.6\text{ Hz}$, 1H, CH=CH), 5.36 (t, $J = 9.8\text{ Hz}$, 1H, CH=CH), 5.93 (ddd, $J = 17.1, 10.5, 3.1\text{ Hz}$, 1H, CH=CH), 7.00-7.20 (m, 10H, PhH); ^{13}C NMR (rotational isomers, CDCl_3 , 100.6 MHz) δ 28.4 (CH_3), 37.1 (CH_2), 37.8 (CH_2), 42.9 (CH), 43.3 (CH), 45.7 (CH_2), 46.7 (CH_2), 48.4 (CH), 49.0 (CH), 51.9 (CH), 53.1 (CH), 79.7 (C), 79.8 (C), 116.0 (CH_2), 116.1 (CH_2), 126.1 (CH), 126.4 (CH), 126.4 (CH), 127.5 (CH), 127.9 (CH), 128.1 (CH), 128.2 (CH), 136.6 (CH), 136.7 (CH), 141.2 (C), 141.5 (C), 143.6 (C), 143.6 (C), 155.2 (C), 155.2 (C). Anal. Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_2$: C, 79.30; H, 8.04; N, 3.85. Found C, 79.34; H, 8.15; N, 4.04. $[\alpha]_{\text{D}}^{20}$: -33.3° ($c = 1.1$, CHCl_3).

Part 2: 2-Ethyl-4,5-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (93). A solution of 4,5-diphenyl-2-vinyl-piperidine-1-carboxylic acid *tert*-butyl ester (0.135 g, 0.371 mmol) in EtOAc (8 mL) was hydrogenated at 50 psi for 17 h with Pd/C (0.040g). Filtration through a silica plug (EtOAc) and concentration provided **93** (0.128 g, 94 %) as a white solid: mp $99\text{--}102\text{ }^{\circ}\text{C}$

Major diastereomer: ^1H NMR (rotational isomers, CDCl_3 , 500 MHz) δ 0.98 (t, $J = 7.5\text{ Hz}$, 3H, CH_2CH_3), 1.51 (s, 9H, *Ot-Bu*), 1.70 (m, 1H, CHCH_2CH), 1.84-2.04 (m 3H, CH_2CH_3 , CHCH_2CH), 2.83-3.20 (m, 3H, CHPh , NCH_2), 4.10 (dd, $J = 13.3, 4.3\text{ Hz}$, 1H, CHN), 4.29 (m, 1H, CHN), 7.01-7.20 (m, 10H, PhH); ^{13}C NMR (rotational isomers, CDCl_3 , 100.6 MHz) δ 10.7 (CH_3), 10.9 (CH_3), 22.8 (CH_2), 23.2 (CH_2), 28.4 (CH_3), 36.4 (CH_2), 37.5 (CH_2), 42.6 (CH), 42.9 (CH), 44.4 (CH_2), 45.7 (CH_2), 48.5 (CH), 49.0 (CH), 51.4 (CH), 52.6 (CH), 79.4 (C), 126.0 (CH), 126.3 (CH), 126.4 (CH), 127.5 (CH), 127.8 (CH), 127.8 (CH), 128.0 (CH), 128.1 (CH), 128.2 (CH), 141.3 (C), 141.6 (C), 143.6 (C), 143.7 (C), 154.9 (C), 155.1 (C). HRMS-FAB ($\text{M}+1$) Calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_2$: 366.2433; Found: 366.2432.

6-Ethyl-2-methyl-3,4-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (**94**).

The general lithiation procedure was followed using **93** (0.093 g, 0.255 mmol) and MeOTf (0.092 mL, 0.815 mmol) as the electrophile. Purification by column chromatography (20:1 pet ether/EtOAc) gave **94** (0.055 g, 57 %, >99:1 dr) as an oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 0.99 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.21 (d, J = 6.9 Hz, 3H, CHCH_3), 1.54 (s, 9H, *Or*-Bu), 1.73 (dq, J = 14.5, 7.3 Hz, 1H, CHCH_2CH_3), 1.88 (dt, J = 13.7, 4.7 Hz, 1H, CHCH_2CH), 2.0 (td, J = 12.5, 5.9 Hz, 1H, CHCH_2CH), 2.05 (dq, J = 15.2, 7.6 Hz, 1H, CHCH_2CH_3), 2.83 (t, J = 11.0 Hz, 1H, CHPh), 3.14 (td, J = 12.0, 5.0 Hz, 1H, CHPh), 3.78 (dq, J = 9.5, 6.8 Hz, 1H, CHCH_3), 4.2 (qd, J = 7.6, 3.7 Hz, 1H, CH_2CHCH_2), 6.95-7.15 (m, 10H, PhH); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ 11.1 (CH_3), 19.7 (CH_3), 23.8 (CH_2), 28.6 (CH_3), 36.4 (CH_2), 45.4 (CH), 53.0 (CH), 54.3 (CH), 55.3 (CH), 79.4 (C), 125.9 (CH), 126.1 (CH), 127.6 (CH), 128.0 (CH), 128.1 (CH), 142.4 (C), 144.1 (C), 156.6 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{25}\text{H}_{34}\text{NO}_2$: 380.2590; Found: 380.2591. $[\alpha]_D^{20}$: -54.0 $^\circ$ (c = 0.80, CHCl_3).

Conversion of **72** to **95**.

Part 1: 1-Benzyl-4,5-diphenyl-3-phenylselanyl-piperidin-2-one. The general procedure for *t*-BuLi enolization was followed using **72** (0.900 g, 2.64 mmol) and phenylselanyl chloride (0.607 mL, 3.17 mmol). Purification by column chromatography (7:3 pet ether/EtOAc) gave the title compound (0.972 g, 74 %, 88:12 dr) as a colorless oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 3.12 (td, J = 11.6, 4.3 Hz, 1H, PhCH), 3.20 (dd, J = 12.7, 4.3 Hz, 1H, PhCH), 3.28 (t, J = 11.5 Hz, 1H, NCH_2), 3.39 (dd, J = 11.6, 8.2 Hz, 1H, NCH_2), 3.32 (dd, J = 11.9, 4.6 Hz, 1H, NCH_2), 4.07 (d, J = 8.1 Hz, 1H, CHSePh), 4.61 (d, J = 14.4 Hz, 1H, NCH_2Ph), 4.78 (d, J = 14.3 Hz, 1H, PhCH_2N), 6.83 (m, 2H, PhH), 6.99-7.38 (m, 16H, PhH), 7.61 (m, 2H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 48.2 (CH), 49.3 (CH), 51.2 (CH_2), 52.3 (CH_2), 53.3 (CH), 126.7 (CH), 127.0 (CH), 127.5 (CH), 127.8 (CH), 128.0 (C), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.6 (CH), 128.9 (CH), 136.2 (CH), 136.5 (C), 139.4 (C), 141.9 (C), 169.4 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{30}\text{H}_{28}\text{NOSe}$: 498.1336; Found: 498.1335.

Part 2: 1-Benzyl-4,5-diphenyl-5,6-dihydro-1H-pyridin-2-one (95**).** To a solution of 1-benzyl-4,5-diphenyl-3-phenylselanyl-piperidin-2-one (0.768 g, 1.55 mmol) in EtOAc (30 mL)

was added 30 % H₂O₂ (3.57 mL) and the mixture was stirred vigorously for 30 min. The organics were separated, washed with sat. NaHCO₃ (2 x 30 mL), dried over Na₂SO₄ and concentrated. Purification by column chromatography (1:1 pet ether/EtOAc) gave **95** (0.474 g, 90 %) as a white solid: mp 103-104 °C ¹H NMR (CDCl₃, 500 MHz) δ 3.34 (dd, *J* = 12.4, 1.9 Hz, 1H, PhCH), 3.96 (dd, *J* = 12.4, 5.1 Hz, 1H, NCH₂), 4.06 (dd, *J* = 4.9, 1.7 Hz, 1H, NCH₂), 4.46 (d, *J* = 15.0 Hz, 1H, NCH₂Ph), 4.67 (d, *J* = 15.0 Hz, 1H, PhCH₂N), 6.74 (s, 1H, CH=CPh), 6.96 (m, 2H, PhH), 7.12-7.34 (m, 11H, PhH), 7.46 (m, 2H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 42.3 (CH), 49.3 (CH₂), 52.6 (CH₂), 121.3 (CH), 126.2 (CH), 127.0 (CH), 127.3 (CH), 127.6 (CH), 127.8 (CH), 128.3 (C), 128.7 (CH), 128.8 (CH), 129.4 (CH), 136.3 (C), 136.6 (C), 138.9 (C), 149.8 (C), 165.0 (C). HRMS-FAB (M+1) Calcd for C₂₄H₂₂NO: 340.1701; Found: 340.1701.

1-Benzyl-4,5-diphenyl-piperidin-2-one (96). A solution of **95** (0.410 g, 1.21 mmol) in EtOAc (25 mL) was hydrogenated at 250 psi for 17 h with Pd(OH)₂ (0.410 g). Filtration of the catalyst and concentration provided the crude product which was purified by column chromatography (1:1 pet ether/EtOAc) to provide **96** (0.358 g, 87 %, >95:5 dr) as a white solid: mp 105-107. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 2.83 (dd, *J* = 17.8, 5.8 Hz, 1H, COCH₂), 2.96 (dd, *J* = 17.8, 5.8 Hz, 1H, COCH₂), 3.45-3.52 (m, 4H, PhCH, NCH₂), 4.72 (d, *J* = 14.4 Hz, 1H, NCH₂Ph) 4.81 (d, *J* = 14.1 Hz, 1H, PhCH₂N), 6.67 (m, 4H, PhH), 7.15 (m, 6H, PhH), 7.28-7.42 (m, 5H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 36.0 (CH₂), 43.4 (CH), 43.8 (CH), 48.6 (CH₂), 50.4 (CH₂), 126.9 (CH), 127.0 (CH), 127.6 (CH), 127.9 (CH), 127.9 (CH), 128.1 (C), 128.3 (CH), 128.6 (CH), 136.7 (C), 139.0 (C), 139.4 (C), 169.3 (C). Anal. Calcd for C₂₄H₂₃NO: C, 84.42; H, 6.79; N, 4.10. Found C, 84.34; H, 6.80; N, 4.27. [α]_D²⁰: +60.0° (*c* = 1.1, CHCl₃).

Conversion of **96** to **97**.

Part 1: 3-Allyl-1-benzyl-4,5-diphenyl-piperidin-2-one. The general procedure for *t*-BuLi enolization was followed using **96** (0.090 g, 0.263 mmol) and allyl bromide (0.091 mL, 1.05 mmol). Purification by column chromatography (3:1 pet ether/EtOAc) gave the title compound (0.093 g, 93 %, >95:5 dr) as a colorless oil. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 2.75 (m, 2H, CH₂CH=CH₂), 2.90 (dt, *J* = 8.5, 4.5 Hz, 1H, CHCO), 3.35 (t, *J* = 3.4

Hz, 1H, NCH₂), 3.44 (m, 3H, CHPh, NCH₂), 4.62 (d, *J* = 14.1 Hz, 1H, NCH₂Ph), 4.93 (d, *J* = 14.3 Hz, 1H, NCH₂Ph), 5.14 (m, 1H, CH=CH₂), 5.17 (d, *J* = 1.1 Hz, 1H, CH=CH₂), 5.88 (m, 1H, CH=CH₂), 6.64 (m, 4H, PhH), 7.14 (m, 6H, PhH), 7.35 (m, 5H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 36.7 (CH₂), 40.6 (CH), 44.6 (CH), 46.8 (CH), 48.1 (CH₂), 50.7 (CH₂), 117.6 (CH₂), 126.7 (CH), 126.8 (CH), 127.6 (CH), 127.8 (CH), 127.9 (C), 128.1 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 135.9 (CH), 136.8 (C), 139.3 (C), 139.4 (C), 171.8 (C). HRMS-FAB (M+1) Calcd for C₂₇H₂₈NO: 382.2171; Found: 382.2171.

Part 2: 3-Allyl-1-benzyl-4,5-diphenyl-piperidine (97). The general reduction procedure for benzyl lactams was followed using 3-allyl-1-benzyl-4,5-diphenyl-piperidin-2-one (0.085 g, 0.222 mmol) and lithium aluminum hydride (0.666 mL of a 1 M solution in THF, 0.666 mmol). Purification by column chromatography (20:1 pet ether/EtOAc) provided **97** (0.069 g, 85 %) as a colorless oil. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 1.69 (dt, *J* = 14.4, 8.4 Hz, 1H, CH₂CH=CH₂), 1.96 (t, *J* = 10.9 Hz, 1H, CHPh), 2.04 (m, 1H, CHCH₂CH=CH₂), 2.41 (m, 1H, CH₂CH=CH₂), 2.59 (dd, *J* = 11.3, 3.8 Hz, 1H, CHPh), 2.81 (dd, *J* = 12.0, 5.4 Hz, 1H, CH₂N), 3.03 (m, 1H, NCH₂), 3.28 (d, *J* = 11.5 Hz, 1H, NCH₂), 3.33 (dd, *J* = 12.0, 3.5 Hz, 1H, NCH₂), 3.56 (d, *J* = 13.1 Hz, 1H, NCH₂Ph), 3.70 (d, *J* = 13.2 Hz, 1H, NCH₂Ph), 4.89 (d, *J* = 16.9 Hz, 1H, CH=CH₂), 4.95 (dd, *J* = 10.0, 1.0 Hz, 1H, CH=CH₂), 5.71 (m, 1H, CH=CH₂), 7.14 (m, 6H, PhH), 7.29 (m, 2H, PhH), 7.39 (m, 4H, PhH), 7.47 (m, 3H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 33.8 (CH), 36.3 (CH₂), 47.3 (CH), 52.7 (CH), 58.9 (CH₂), 59.6 (CH₂), 63.8 (CH₂), 116.1 (CH₂), 125.8 (CH), 125.9 (CH), 126.9 (CH), 126.9 (CH), 127.5 (C), 128.2 (CH), 128.9 (CH), 129.1 (CH), 130.8 (CH), 136.3 (CH), 138.6 (C), 141.8 (C), 142.3 (C). HRMS-FAB (M+1) Calcd for C₂₇H₃₀N: 369.2378; Found: 368.2377. [α]_D²⁰: -106.6 ° (*c* = 0.50, CHCl₃).

Conversion of 96 to 98.

Part 1: 1-Benzyl-3,4-diphenyl-piperidine. The general reduction procedure for benzyl lactams was followed using **96** (0.400 g, 1.17 mmol) and lithium aluminum hydride (3.51 mL of a 1 M solution in THF, 3.51 mmol) with a 6 h reflux period. Purification by column chromatography (8:1 pet ether/EtOAc) provided the title compound (0.332 g, 87 %) as a colorless oil. ¹H NMR (CDCl₃, 500 MHz) δ 1.65 (m, 1H, CH₂CH₂CH), 2.26 (m, 2H,

CH₂CH₂CH, PhCH), 2.70 (dd, $J = 11.5, 3.8$ Hz, 1H, CHPh), 3.12 (m, 1H, CH₂N), 3.15 (m, 1H, CH₂N), 3.24 (m, 1H, CH₂N), 3.15 (dt, $J = 11.1, 1.4$ Hz, 1H, CH₂N), 3.59 (d, $J = 12.9$ Hz, 1H, NCH₂Ph), 3.66 (d, $J = 13.1$ Hz, 1H, PhCH₂N), 6.83 (m, 2H, PhH), 7.15-7.50 (m, 13H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 25.8 (CH₂), 46.6 (CH), 46.7 (CH), 54.2 (CH₂), 59.0 (CH₂), 63.7 (CH₂), 125.7 (CH), 125.9 (CH), 126.9 (CH), 126.9 (CH), 127.6 (CH), 127.9 (C), 128.2 (CH), 129.1 (CH), 130.7 (CH), 138.8 (C), 141.8 (C), 143.9 (C). HRMS-FAB (M+1) Calcd for C₂₄H₂₆N: 328.2065; Found: 328.2066.

Part 2: 3,4-Diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (98). A solution of 1-benzyl-3,4-diphenyl-piperidine (0.300 g, 0.916 mmol) and Boc₂O (0.420 mL, 1.83 mmol) in EtOAc (21 mL) was hydrogenated at atmospheric pressure for 18 h with Pd(OH)₂ (0.156 g). Filtration of the catalyst and concentration provided the crude product which was purified by column chromatography (10:1 pet ether/EtOAc) to provide **98** (0.241 g, 78 %) as a white solid: mp 126-127 °C. ¹H NMR (CDCl₃, 500 MHz) δ 1.52 (s, 9H, Ot-Bu), 1.69 (m, 1H, CH₂CH₂CH), 2.19 (qd, $J = 12.7, 4.3$ Hz, 1H, CH₂CH₂CH), 3.08 (m, 2H, CHPh), 3.21 (dt, $J = 9.2, 3.5$ Hz, 1H, CH₂N), 3.41 (d, $J = 11.0$ Hz, 1H, CH₂N), 4.50 (m, 2H, CH₂N), 6.84 (m, 4H, PhH), 7.04-7.18 (m, 6H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 24.9 (CH₂), 28.3 (CH₃), 43.8 (CH₂), 45.3 (CH), 46.2 (CH), 48.8 (CH₂), 79.6 (C), 126.0 (CH), 126.1 (CH), 127.2 (CH), 127.7 (CH), 129.4 (CH), 140.5 (C), 143.1 (C), 154.9 (C). HRMS-FAB (M+1) Calcd for C₂₂H₂₈NO₂: 338.2120; Found: 338.2120. [α]_D²⁰: -136.5 ° ($c = 1.0$, CHCl₃).

2-Methyl-4,5-diphenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (99). The general lithiation procedure was followed using **98** (0.100 g, 0.296 mmol) and MeOTf (0.107 mL, 0.947 mmol) as the electrophile. Purification by column chromatography (20:1 pet ether/EtOAc) gave **99** (0.068 g, 66 %, 92:8 dr) as a white solid. Crystals suitable for X-ray crystallographic analysis were obtained by slow evaporation from pet ether: mp 112-114 °C. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 1.34 (d, $J = 6.2$ Hz, 3H, CHCH₃), 1.54 (s, 9H, Ot-Bu), 2.03 (ddd, $J = 13.5, 7.3, 3.0$ Hz, 1H, CH₂CH₂CH), 2.08 (td, $J = 13.3, 10.7$ Hz, 1H, CH₂CH₂CH), 3.27 (ddd, $J = 12.4, 9.0, 2.7$ Hz, 1H, CHPh), 3.34 (dd, $J = 14.1, 10.9$ Hz, 1H, CH₂N), 3.61 (dt, $J = 10.9, 8.3$ Hz, 1H, CHPh), 4.19 (dq, $J = 13.1, 6.6$ Hz, 1H, CH₃CHN),

4.26 (dd, $J = 14.1, 7.5$ Hz, 1H, CH_2N), 6.83 (m, 2H, PhH), 6.95 (m, 3H, PhH), 7.03 (m, 5H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 19.4 (CH_3), 28.5 (CH_3), 32.4 (CH_2), 42.0 (CH), 42.2 (CH_2), 45.3 (CH), 50.1 (CH), 79.3 (C), 125.5 (CH), 126.3 (CH), 127.5 (CH), 127.7 (CH), 127.9 (CH), 128.8 (CH), 140.0 (C), 142.1 (C), 155.3 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{23}\text{H}_{30}\text{NO}_2$: 352.2277; Found: 352.2276.

Representative Procedure for Lithiation of Boc-3,4-disubstituted Pyrrolidines: 2,3-Dimethyl-4-phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (100) and 2,4-Dimethyl-3-phenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (101). To a stirring solution of **67** (0.103 g, 0.394 mmol) in ether (4.0 mL) under N_2 was added **1** (0.117 mL, 0.512 mmol). The solution was cooled to -78°C and *sec*-BuLi (0.355 mL of a 1.44 M solution in cyclohexane, 0.512 mmol) was added. The solution was stirred for 4 h at -78°C and MeOTf (0.147 mL, 1.30 mmol) was added and the solution was stirred for an addition 15 min at -78°C , warmed to rt and quenched with H_2O (10 mL). The aqueous was extracted with ether (3 x 10 mL) and the combined organics were dried over MgSO_4 . Purification by column chromatography (12:1 pet ether/EtOAc) gave a 58:42 mixture of **100** and **101** (0.074 g, 69 %, >95:5 dr) as a colorless oil. **Major diastereomer:** ^1H NMR ($\text{DMSO}-d_6$, 100°C , 500 MHz) δ 0.83 (d, $J = 6.5$ Hz, 3H, CH_3CH), 0.91 (d, $J = 6.6$ Hz, 3H, CH_3CH), 1.20 (d, $J = 6.0$ Hz, 3H, CH_3CH), 1.33 (d, $J = 6.1$ Hz, 3H, CH_3CH), 1.43 (s, 18H, *Ot*-Bu), 1.88 (m, 1H, CH_3CH), 2.21 (m, 1H, CH_3CH), 2.38 (t, $J = 7.0$ Hz, 1H, NCH), 2.74 (dt, $J = 11.1, 7.9$ Hz, 1H, PhCH), 2.90 (t, $J = 10.5$ Hz, 1H, PhCH), 3.21 (t, $J = 10.8$ Hz, 1H, NCH₂), 3.31 (m, 1H, CH_3CHN), 3.64 (m, 1H, CH_3CHN), 3.83 (m, 2H, NCH), 7.20-7.35 (m, 20H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 14.9 (CH_3), 15.0 (CH_3), 18.8 (CH), 19.8 (CH), 28.5 (CH_3), 19.8 (CH), 19.8 (CH), 39.5 (CH), 39.7 (CH), 49.1 (CH), 49.7 (CH), 50.8 (CH), 51.2 (CH), 53.2 (CH_2), 53.4 (CH_2), 53.9 (CH_2), 60.4 (CH), 61.3 (CH), 62.4 (CH), 78.9 (C), 79.1 (C), 126.8 (CH), 126.9 (CH), 127.6 (CH), 128.1 (CH), 128.5 (CH), 139.6 (C), 139.9 (C), 154.4 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{17}\text{H}_{26}\text{NO}_2$: 276.1964; Found: 276.1964.

2-Methyl-3,4-diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (102). The general lithiation procedure was followed using **66** (0.100g, 0.309 mmol) and MeOTf (0.115 mL, 1.02 mmol) as the electrophile. Purification by column chromatography (12:1 pet ether/EtOAc)

gave **102** (0.085 g, 82 %, >95:5 dr) as an oil. **Major diastereomer:** ^1H NMR (DMSO- d_6 , 100 °C, 500 MHz) δ 1.30 (d, J = 6.0 Hz, 3H, CH_3CH), 1.45 (s, 9H, *Ot*-Bu), 3.09 (dd, J = 11.8, 9.2 Hz, 1H, PhCH), 3.36 (t, J = 10.9 Hz, 1H, NCH_2), 3.52 (td, J = 11.4, 7.3 Hz, 1H, PhCH), 4.75 (dq, J = 9.2, 5.9 Hz, 1H, NCHCH_3), 4.03 (dd, J = 10.6, 7.4 Hz, 1H, NCH_2), 7.10-7.27 (m, 10H, PhH); ^{13}C NMR (DMSO- d_6 , 100 °C, 125.6 MHz) δ 18.2 (CH_3), 27.7 (CH_3), 48.7 (CH), 52.8 (CH_2), 59.3 (CH), 60.3 (CH), 77.9 (C), 126.0 (CH), 126.1 (CH), 126.9 (CH), 127.3 (CH), 127.6 (CH), 127.8 (CH), 138.6 (C), 138.7 (C), 153.0 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_2$: 338.2120; Found: 338.2120.

3,4-Diphenyl-2-trimethylsilanyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (103).

The general lithiation procedure was followed using **66** (0.100g, 0.309 mmol) and TMSCl (0.129 mL, 1.02 mmol) as the electrophile. Purification by column chromatography (15:1 pet ether/EtOAc) gave **103** (0.095 g, 78 %, >95:5 dr) as an oil. **Major diastereomer:** ^1H NMR (DMSO- d_6 , 100 °C, 500 MHz) δ 0.14 (s, 9H, $(\text{CH}_3)_3\text{Si}$), 1.47 (s, 9H, *Ot*-Bu), 3.18 (td, J = 10.9, 6.4 Hz, 1H, PhCH), 3.25 (t, J = 10.7 Hz, 1H, NCH_2), 3.35 (t, J = 10.3 Hz, 1H, PhCH), 4.14 (dd, J = 8.5, 7.3 Hz, 1H, NCH_2), 7.08-7.24 (m, 10H, PhH); ^{13}C NMR (CDCl_3 , rotational isomers, 25 °C, 125.6 MHz) δ -1.8 (CH_3), 28.5 (CH_3), 54.1 (CH), 54.5 (CH_2), 54.8 (CH), 55.2 (CH), 56.1 (CH), 126.6 (CH), 126.8 (CH), 127.5 (CH), 128.0 (CH), 128.3 (CH), 128.4 (CH), 139.0 (C), 141.0 (C), 155.1 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{24}\text{H}_{34}\text{NO}_2\text{Si}$: 396.2359; Found: 396.2357.

2-Formyl-3,4-diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (104). The general lithiation procedure was followed using **66** (0.100g, 0.309 mmol) and DMF (0.079 mL, 1.02 mmol) as the electrophile. Purification by column chromatography (4:1 pet ether/EtOAc) gave **104** (0.084 g, 77 %, >95:5 dr) as an oil. **Major diastereomer:** ^1H NMR (DMSO- d_6 , 100 °C, 400 MHz) δ 1.42 (s, 9H, *Ot*-Bu), 3.53 (t, J = 10.5 Hz, 1H, PhCH), 3.63 (t, J = 10.7 Hz, 1H, NCH_2), 3.75 (q, J = 8.3 Hz, 1H, PhCH), 4.02 (m, 1H, NCH_2), 4.14 (dd, J = 10.7, 3.4 Hz, 1H, NCH), 7.12-7.28 (m, 10H, PhH), 9.49 (d, J = 3.7 Hz, 1H, CHO); ^{13}C NMR (DMSO- d_6 , rotational isomers, 25 °C, 100.6 MHz) δ 28.5 (CH_3), 28.7 (CH_3), 49.9 (CH), 50.9 (CH), 51.8 (CH), 52.7 (CH), 54.1 (CH_2), 72.1 (CH), 72.4 (CH), 80.5 (C), 80.6 (C), 127.7 (CH), 127.9 (CH), 128.5 (CH), 129.0 (CH), 129.1 (CH), 137.4 (C), 138.6 (C), 138.7 (C), 153.3 (C), 154.5 (C), 199.6 (CH). HRMS-FAB ($M+1$) Calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_3$: 352.1913; Found: 352.1914.

3,4-Diphenyl-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (106). The general lithiation procedure was followed using **66** (0.100 g, 0.309 mmol) and excess CO₂ gas as the electrophile. The reaction mixture was acidified with 10 % HCl during work up. The crude acid was esterified with an ethereal solution of CH₂N₂ (10 eq.). Purification by column chromatography (4:1 pet ether/EtOAc) gave **106** (0.090 g, 76 %, >95:5 dr) as an oil. **Major diastereomer:** ¹H NMR (DMSO-*d*₆, 100 °C, 500 MHz) δ 1.41 (s, 9H, Ot-Bu), 3.49 (t, *J* = 10.7 Hz, 1H, PhCH), 3.50 (t, *J* = 9.4 Hz, 1H, NCH₂), 3.61 (s, 3H, OCH₃), 3.72 (td, *J* = 11.2, 7.4 Hz, 1H, NCH₂), 4.05 (dd, *J* = 10.4, 7.7 Hz, 1H, PhCH), 4.29 (d, *J* = 9.2 Hz, 1H, NCH), 7.13-7.26 (m, 10H, PhH); ¹³C NMR (CDCl₃, rotational isomers, 25 °C, 125.6 MHz) δ 28.2 (CH₃), 28.3 (CH₃), 50.6 (CH), 51.8 (CH), 51.9 (CH), 52.1 (CH), 52.9 (CH₂), 53.7 (CH₂), 56.7 (CH), 57.4 (CH), 66.1 (CH₃), 66.7 (CH₃), 80.2 (C), 80.4 (C), 127.2 (CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 137.5 (C), 137.6 (C), 137.7 (C), 153.2 (C), 153.9 (C), 172.9 (C), 173.0 (C). HRMS-FAB (M+1) Calcd for C₂₃H₂₈NO₄: 382.2018; Found: 382.2016.

2,5-Dimethyl-3,4-diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (107). The general lithiation procedure was followed using **102** (0.055 g, 0.163 mmol) and MeOTf (0.061 mL, 0.539 mmol) as the electrophile. Purification by column chromatography (20:1 pet ether/EtOAc) gave **107** (0.025 g, 43 %, >95:5 dr) as an oil. **Major diastereomer:** ¹H NMR (CDCl₃, 500 MHz) δ 1.37 (d, *J* = 5.1 Hz, 6H, CH₃CH), 1.50 (s, 9H, Ot-Bu), 2.88 (m, 2H, PhCH), 3.90 (br m, 2H, NCH), 7.06-7.24 (m, 10H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 28.5 (CH₃), 60.2 (CH), 60.8 (CH), 79.2 (C), 126.8 (CH), 128.0 (CH), 128.4 (CH), 139.2 (C), 154.0 (C). HRMS-FAB (M+1) Calcd for C₂₃H₃₀NO₂: 352.2277; Found: 352.2278.

Representative Procedure for Boc-deprotection and Tosylation of Pyrrolidines: 2-Methyl-3,4-diphenyl-1-(toluene-4-sulfonyl)-pyrrolidine. To a solution of **102** (0.095 g, 0.282 mmol) in CH₂Cl₂ (7.8 mL) was added TFA (0.78 mL) dropwise. The solution was stirred for 1 h at rt, carefully treated with sat. NaHCO₃ (20 mL) and stirred vigorously until gas evolution ceased. The aqueous was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organics were dried over Na₂SO₄ and concentrated. The residue was redissolved in CH₂Cl₂ (2 mL) and Et₃N

(0.098 mL, 0.705 mmol) was added followed by tosyl chloride (0.065 g, 0.338 mmol). The solution was stirred for 1 h, diluted with CH₂Cl₂ (10 mL) and washed with 0.1 N HCl. The aqueous was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organics were dried over MgSO₄ and concentrated. Purification by column chromatography (5:1 pet ether/EtOAc) gave the title compound (0.088 g, 80 %) as an oil. Crystals suitable for X-ray crystallographic analysis were obtained by addition of pentane: mp 100-101 °C. ¹H NMR (CDCl₃, 500 MHz) δ 1.47 (d, *J* = 6.0 Hz, 3H, CHMe), 2.52 (s, 3H, CH₃Ph), 2.86 (td, *J* = 11.4, 7.5 Hz, 1H, CHPh), 2.99 (dd, *J* = 11.8, 9.2 Hz, 1H, CHPh), 3.59 (t, *J* = 11.8 Hz, 1H, CH₂N), 3.73 (dq, *J* = 9.1, 6.2 Hz, 1H, CHMe), 4.04 (dd, *J* = 12.0, 7.5 Hz, 1H, CH₂N), 6.86 (m, 2H, PhH), 6.97 (m, 2H, PhH), 7.11-7.21 (m, 6 H, PhH), 7.44 (d, *J* = 10.6 Hz, 2H, PhH), 7.77 (d, *J* = 8.2 Hz, 2H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 20.6 (CH₃), 21.5 (CH₃), 50.2 (CH), 55.2 (CH₂), 60.9 (CH), 64.0 (CH), 127.0 (CH), 127.1 (CH), 127.2 (CH), 127.5 (CH), 127.7 (CH), 128.4 (CH), 128.6 (CH), 129.8 (CH), 135.2 (C), 137.8 (C), 138.3 (C), 143.6 (C). Anal. Calcd for C₂₄H₂₅NO₂S: C, 73.62; H, 6.44; N, 3.58. Found C, 73.59; H, 6.45; N, 3.74.

Octahydro-isoindole-2-carboxylic Acid *tert*-Butyl Ester (108). A solution of **109** (5.93 g, 26.6 mmol) in EtOAc (150 mL) was hydrogenated at atmospheric pressure for 6 h with Pd/C (0.900 g). Filtration of the catalyst and concentration provided **108** (5.98 g, 99 %) as an oil. ¹H NMR (CDCl₃, 500 MHz) δ 1.44 (s, 9H, Ot-Bu), 1.28-1.60 (m, 8H, ring-CH₂), 2.14 (m, 2H, CH₂CHCH₂), 3.17 (dd, *J* = 10.4, 5.4 Hz, 2H, NCH₂), 3.28 (dd, *J* = 10.7, 7.0 Hz, 2H, NCH₂); ¹³C NMR (CDCl₃, 125.6 MHz) δ 22.7 (CH₂), 25.8 (CH₂), 28.5 (CH₃), 36.9 (CH), 49.7 (CH₂), 78.8 (C), 155.2 (C). HRMS-FAB (*M*+1) Calcd for C₁₃H₂₄NO₂: 226.1807; Found: 226.1808.

1,3,3a,4,7,7a-Hexahydro-isoindole-2-carboxylic Acid *tert*-Butyl Ester (109). To a mixture of LAH (6.27 g, 165 mmol) in THF (50 mL) was added a solution of 1,2,3,6-tetrahydrophtalamide (10.0 g, 66.1 mmol) in THF (150 mL) carefully dropwise. The green mixture was refluxed for 24 h after complete addition, cooled to rt and quenched carefully with sat. Na₂SO₄. Excess Na₂SO₄ solid was added and the mixture filtered and concentrated to an orange oil. The oil was redissolved in CH₂Cl₂ (150 mL) and a solution of Boc₂O (15.2 mL, 66.1 mmol) in CH₂Cl₂ (20 mL) was added dropwise. The resulting red solution was stirred for 1 h and concentrated. Purification by column chromatography (9:1 pet ether/EtOAc) and short-path

distillation provided **109** (10.8 g, 73 %) as an oil. **¹H NMR** (CDCl₃, 500 MHz) δ 1.42 (s, 9H, *Ot*-Bu), 1.87 (dd, *J* = 6.3, 3.7 Hz, 2H, CH₂CHCH₂), 2.22 (m, 4H, CH=CHCH₂), 3.09 (dd, *J* = 10.3, 5.2 Hz, 2H, NCH₂), 3.37 (dd, *J* = 10.5, 6.5 Hz, 2H, NCH₂), 5.60 (s, 2H, CH=CH); **¹³C NMR** (CDCl₃, 125.6 MHz) δ 24.6 (CH₂), 28.4 (CH₃), 33.7 (CH), 50.8 (CH₂), 78.8 (C), 124.3 (CH), 155.2 (C). Anal. Calcd for C₁₃H₂₁NO₂: C, 69.92; H, 9.48; N, 6.27. Found C, 69.73; H, 9.51; N, 6.41.

3,4-Diphenyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (110). A solution of *cis*-1-benzyl-3,4-diphenyl-pyrrolidine (1.75 g, 5.58 mmol) and Boc₂O (2.56 mL, 11.2 mmol) in EtOAc (62 mL) was hydrogenated at 100 psi for 14 h with Pd(OH)₂ (0.600 g). Filtration of the catalyst and concentration provided the crude product which was purified by column chromatography (9:1 pet ether/EtOAc) to provide **110** (1.51 g, 78 %) as a white solid: mp 97-98 °C. **¹H NMR** (CDCl₃, 500 MHz) δ 1.56 (s, 9H, C(CH₃)₃), 3.66 (m, 2H, CHPh), 3.82 (m, 4H, NCH₂), 6.77 (m, 4H, PhH), 7.12 (m, 6H, PhH); **¹³C NMR** (CDCl₃, 125.6 MHz) δ 28.5 (CH₃), 48.4 (CH), 49.2 (CH), 49.8 (CH₂), 50.3 (CH₂), 79.5 (C), 126.5 (CH), 127.9 (CH), 128.2 (CH), 138.6 (C), 154.6 (C). Anal. Calcd for C₂₁H₂₅NO₂: C, 77.98; H, 7.79; N, 4.33. Found C, 78.05; H, 8.04; N, 4.56.

Representative Procedure for Asymmetric Deprotonation of *meso*-Boc-3,4-disubstituted Pyrrolidines: 1-Trimethylsilanyl-octahydro-isoindole-2-carboxylic Acid *tert*-Butyl Ester (111). To a stirring solution of **108** (0.267 g, 1.18 mmol) in ether (7.5 mL) –78 °C under N₂ was added a precooled solution of **1** (0.708 mL, 3.08 mmol) and *sec*-BuLi (2.42 mL of a 1.27 M solution in cyclohexane, 0.512 mmol) in ether (7.5 mL) at –78 °C via a cold transfer flask. The solution was stirred for 3.5 h at –78 °C and TMSCl (0.494 mL, 3.89 mmol) was added and the solution was stirred for an additional 1 h at –78 °C, warmed to rt and quenched with H₂O (20 mL). The aqueous was extracted with ether (3 x 20 mL) and dried over MgSO₄. Purification by column chromatography (10:1 pet ether/EtOAc) gave **111** (0.176 g, 50 %, >95:5 dr) as a colorless oil. **Major diastereomer:** **¹H NMR** (CDCl₃, 500 MHz) δ 0.18 (s, 9H, (CH₃)₃Si), 1.20-1.60 (m, 8H, ring-CH₂), 1.44 (s, 9H, *Ot*-Bu), 2.0 (m, 1H, ring-CH), 2.15 (m, 1H, ring-CH), 3.00 (br m, 1H, NCH₂), 3.13 (dd, *J* = 10.7, 7.7 Hz, 2H, NCH₂), 3.34 (br m, 1H, NCH₂); **¹³C NMR** (CDCl₃, 125.6 MHz) δ -1.9 (CH₃), 21.6 (CH₂), 23.6 (CH₂), 25.3 (CH₂), 28.5

(CH₃), 39.5 (CH). Anal. Calcd for C₁₆H₃₁NO₂Si: C, 64.59; H, 10.50; N, 4.71. Found C, 64.40; H, 10.37; N, 4.71. [α]_D²⁰: -0.5 ° (*c* = 0.35, CHCl₃).

1-Trimethylsilyl-1,3,3a,4,7,7a-hexahydro-isoindole-2-carboxylic Acid *tert*-Butyl Ester (112). The general asymmetric deprotonation procedure was followed using **109** (0.589 g, 2.64 mmol) and TMSCl (1.10 mL, 8.70 mmol) as the electrophile. Purification by column chromatography (20:1 pet ether/EtOAc) gave **112** (0.375 g, 48 %, >95:5 dr) as an oil. **Major diastereomer:** ¹H NMR (CDCl₃, rotational isomers, 500 MHz) δ 0.04 (s, 9H, (CH₃)₃Si), 1.43 (s, 9H, *Ot*-Bu), 1.84 (m, 2H, CH=CHCH₂), 2.15 (m, 4H, CH=CHCH₂, CH=CHCH₂CH), 2.98 (d, *J* = 2.8 Hz, 1H, NCH), 3.13 (dd, *J* = 10.7, 7.7 Hz, 2H, NCH₂), 3.20 (br m, 2H, NCH₂), 3.20 (s, 2H, CH=CHCH₂); ¹³C NMR (CDCl₃, rotational isomers, 125.6 MHz) δ -1.8 (CH₃), 24.3 (CH₂), 24.5 (CH₂), 26.9 (CH₂), 27.1 (CH₂), 28.5 (CH₃), 28.6 (CH₃), 33.6 (CH), 34.4 (CH), 35.8 (CH), 36.5 (CH), 50.6 (CH₂), 51.0 (CH₂), 54.4 (CH), 55.5 (CH), 78.4 (C), 79.1 (C), 78.4 (C), 124.1 (CH), 124.2 (CH), 124.5 (CH), 124.7 (CH), 155.2 (C), 155.8 (C). Anal. Calcd for C₁₆H₂₉NO₂Si: C, 65.03; H, 9.89; N, 4.74. Found C, 64.73; H, 10.01; N, 4.86.

3,4-Diphenyl-2-trimethylsilyl-pyrrolidine-1-carboxylic Acid *tert*-Butyl Ester (113). The general asymmetric deprotonation procedure was followed using **110** (0.100 g, 0.309 mmol) and TMSCl (0.129 mL, 1.02 mmol) as the electrophile. Purification by column chromatography (19:1 pet ether/EtOAc) gave **113** (0.056 g, 46 %, 85:15 dr) as a white solid: mp 72-74 °C. **Major diastereomer:** ¹H NMR (CDCl₃, rotational isomers, 500 MHz) δ 0.15 (s, 9H, (CH₃)₃Si), 1.57 (s, 9H, *Ot*-Bu), 3.60 (m, 3H, PhCH, NCH₂), 3.79 (d, *J* = 4.3 Hz, 1H, NCH), 3.90 (m, 1H, NCH₂), 6.74 (m, 4H, PhH), 7.09 (m, 6H, PhH); ¹³C NMR (CDCl₃, rotational isomers, 125.6 MHz) δ -1.8 (CH₃), 28.6 (CH₃), 48.7 (CH), 49.3 (CH₂), 49.8 (CH), 50.9 (CH₂), 51.8 (CH), 52.1 (CH), 55.0 (CH), 126.3 (CH), 126.5 (CH), 127.8 (CH), 128.0 (CH), 128.1 (CH), 128.2 (CH), 138.0 (C), 138.8 (C), 140.2 (C), 141.5 (C), 151.9 (C). Anal. Calcd for C₂₄H₃₃NO₂Si: C, 72.86; H, 8.41; N, 3.54. Found C, 72.67; H, 8.47; N, 3.76. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 7.5 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: rt = 4.20 min (58 %), 5.40 min (42 %).

2-(Toluene-4-sulfonyl)-1-trimethylsilanyl-octahydro-isoindole. The general procedure for Boc-deprotection and tosylation of pyrrolidines was followed using **111** (0.170 g, 0.571 mmol). Purification by column chromatography (5:1 pet ether/EtOAc) gave the title compound (0.164 g, 82 %) as a white solid. ¹H NMR (CDCl₃, 500 MHz) δ 0.11 (s, 9H, (CH₃)₃Si), 0.96 (m, 2H, ring-CH₂), 1.07 (m, 1H, ring-CH₂), 1.26 (m, 3H, ring-CH₂), 1.38 (m, 2H, ring-CH₂), 1.88 (dtd, *J* = 11.1, 5.6, 1.5 Hz, 1H, ring-CH), 2.28 (m, 1H, ring-CH), 2.41 (s, 3H, CH₃Ph), 2.78 (d, *J* = 1.8 Hz, 1H, NCH), 3.06 (t, *J* = 9.9 Hz, 1H, NCH₂), 3.26 (t, *J* = 8.6 Hz, 1H, NCH₂), 7.29 (d, *J* = 8.2 Hz, 2H, PhH), 7.71 (d, *J* = 8.2 Hz, 2H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ -2.1 (CH₃), 20.8 (CH₂), 21.4 (CH), 24.3 (CH₂), 24.5 (CH₂), 28.4 (CH₂), 36.9 (CH), 40.3 (CH₃), 50.1 (CH₂), 58.5 (CH), 127.8 (CH), 129.3 (CH), 133.9 (C), 143.0 (C). Anal. Calcd for C₁₈H₂₉NO₂SSi: C, 61.49; H, 8.31; N, 3.98. Found C, 61.42; H, 8.37; N, 4.05. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 5 % IPA/hexanes mobile phase and a flow rate of 2.0 mL/min: rt = 6.26 min (87 %), 8.57 min (13 %). Recrystallization from pet ether provided the title compound (0.065 g, 33 %, 97:3 er). Crystals suitable for X-ray crystallographic analysis were obtained by vapor diffusion with pentane/ether: mp 120-121 °C.

2-(Toluene-4-sulfonyl)-1-trimethylsilanyl-octahydro-isoindole (from 112). A solution of **112** (0.109 g, 0.368 mmol) in EtOAc (5 mL) was hydrogenated at atmospheric pressure for 2 h with Pd/C (0.025 g). Filtration of the catalyst and concentration provided the crude in which the general procedure for Boc-deprotection and tosylation of pyrrolidines was followed. Purification by column chromatography (5:1 pet ether/EtOAc) gave the title compound (0.101 g, 82 %) which was spectroscopically identical to the compound derived from **111**. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 5 % IPA/hexanes mobile phase and a flow rate of 2.0 mL/min: rt = 7.34 min (73 %), 10.60 min (27 %).

Representative Procedure for Transmetalation of Enantioenriched Stannanes and Conjugate Addition to Nitroalkenes: (4-Methoxy-phenyl)-(5-nitro-3,4-diphenyl-pent-1-enyl)-carbamic Acid *tert*-Butyl Ester (*ent*-17). To a stirring solution of **114**⁸ (0.310 g, 0.617 mmol) in toluene (13 mL) under N₂ was added **1** (0.170 mL, 0.741 mmol). The solution was

cooled to $-78\text{ }^{\circ}\text{C}$ and *n*-BuLi (0.511 mL of a 1.45 M solution in hexanes, 0.741 mmol) was added. The yellow solution was stirred for 1 h at $-78\text{ }^{\circ}\text{C}$ and **10** (0.120 g, 0.802 mmol) in toluene (3 mL) was added dropwise over 1 h by syringe pump. After complete addition, the solution was stirred for an additional 10 min at $-78\text{ }^{\circ}\text{C}$, quenched with MeOH (1 mL) and warmed to rt. The solution was poured into water (10 mL) and brine (5 mL) and extracted with ether (3 x 15 mL). The combined organics were dried over MgSO_4 and concentrated to an orange oil. Purification by silica gel column chromatography (3:1 pet ether/EtOAc) gave **ent-17** (0.178 g, 59 %, 85:15 dr) as a colorless oil. The ^1H NMR and ^{13}C NMR spectra were consistent with reported literature values.⁹ The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 10 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: $t_{\text{r}} = 23.3$ min (88 %), 29.6 min (12 %).

Transmetalation of 115. The general transmetalation procedure was followed using **115**⁹ (0.600 g, 1.19 mmol) and **10** (0.235 g, 0.155 mmol). Purification by silica gel column chromatography (3:1 pet ether/EtOAc) gave **ent-17** (0.489 g, 84 %, 85:15 dr) as a colorless oil. The enantiomeric ratio of the major diastereomer was determined by CSP-HPLC on a Whelk-O column with 10 % IPA/hexanes mobile phase and a flow rate of 1.0 mL/min: $t_{\text{r}} = 23.3$ min (85 %), 29.6 min (15 %).

Representative Procedure for Enantiomeric Purity Determination of 2-Piperidones by Reduction and Acylation: 3-Hydroxy-4-phenyl-piperidine-1-carboxylic Acid (–)-Menthyl Ester (116). To a solution of **57** (0.275 g, 0.792 mmol) in THF (14 mL) was added lithium aluminum hydride (2.38 mL of a 1M solution in THF, 2.38 mmol) and the solution was refluxed for 4h. The solution was cooled to rt and saturated Na_2SO_4 (1 mL) was added cautiously. Excess Na_2SO_4 solid was added and the solid was filtered off, washed with ether (2 x 25 mL) and the filtrate was concentrated. The residue was redissolved in CH_2Cl_2 (7 mL) and Et_3N (0.164 mL, 1.18 mmol) and (–)-menthylchloroformate (0.170 mL, 0.792 mmol) were added. The solution was stirred for 14 h and then poured into H_2O (10 mL), extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over MgSO_4 and concentrated. Purification by column chromatography (3:1 pet ether/EtOAc) gave **116** (0.236 g, 83%, >97:3 dr) as a colorless oil. GC: ($t_{\text{i}} = 100\text{ }^{\circ}\text{C}$ $t_{\text{f}} = 200\text{ }^{\circ}\text{C}$, $20\text{ }^{\circ}\text{C}/\text{min}$) $t_{\text{Rmajor}} = 37.23\text{ min.}$, $t_{\text{Rminor}} = 36.4\text{ min}$ **Major diastereomer:** ^1H NMR (CDCl_3 , 500 MHz) δ 0.83 (d, $J = 6.6\text{ Hz}$, 3H, CH_3CH), 0.93 (m, 1H, $(\text{CH}_3)_2\text{CH}$), 0.93

(d, $J = 6.8$ Hz, 6H, $(\text{CH}_3)_2\text{CH}$), 1.10 (m, 1H, ring-CH), 1.41 (m, 1H, NCHCH_2), 1.55 (m, 1H, ring-CH), 1.70 (m, 2H, ring- CH_2), 1.83 (m, 2H, NCHCH_2 , ring-CH), 1.95 (quintd, $J = 6.7$, 4.5 Hz, 1H, ring-CH), 2.11 (m, 1H, ring-CH), 2.55 (td, $J = 10.2$, 3.9 Hz, 1H, CHPh), 2.68 (br t, $J = 11.1$ Hz, 1H, NCH_2), 2.68 (br t, $J = 12.0$ Hz, 1H, NCH_2), 3.69 (br m, 1H, NCH_2), 4.25 (br m, 1H, NCH_2), 4.45 (br m, 1H, HOCH), 4.60 (td, $J = 10.7$, 4.3 Hz, 1H, CHO), 7.27 (m, 3H, PhH), 7.36 (m, 2H, PhH); ^{13}C NMR (CDCl_3 , 125.6 MHz) δ 16.6 (CH_3), 20.7 (CH), 22.0 (CH_3), 23.6 (CH_2), 26.4 (CH), 31.3 (CH), 34.3 (CH_2), 41.5 (CH_2), 43.9 (CH_2), 47.3 (CH), 49.6 (CH_2), 51.4 (CH), 70.8 (CH), 75.4 (CH), 127.2 (CH), 127.8 (CH), 128.9 (CH), 141.4 (C), 155.2 (C). HRMS-FAB ($M+1$): Calcd for $\text{C}_{22}\text{H}_{34}\text{NO}_3$: 360.2539; Found: 360.2538.

1-Benzyl-3-hydroxy-4-phenyl-piperidine (118). To a solution of 72 (0.20 g, 0.753 mmol) in dry THF (15 mL) under a N_2 atmosphere at -78°C was added $t\text{-BuLi}$ (0.53 mL of a 1.7 M solution in pentane, 0.90 mmol). The yellow solution was stirred for 30 min at -78°C , and added to **117** (0.28 g, 0.90 mmol) in THF (5 mL) through inverse addition. The solution was stirred for 2.5 h at -78°C , warmed to rt, and quenched with sat. $\text{Na}_2\text{S}_2\text{O}_3$ solution (10 mL). The aqueous layer was extracted with Et_2O (3×20 mL), dried over MgSO_4 , and concentrated. Filtration through a plug of silica (2:1 pet ether/ EtOAc) and concentration gave a residue which was dissolved in dry THF (12 mL). LAH was added (2.36 mL of a 1M solution in THF, 2.15 mmol) in one portion. The mixture was heated to reflux for 18 h, cooled to rt, and quenched with sat. Na_2SO_4 solution (5 mL). The organic layer was dried over Na_2SO_4 and concentrated. Purification by column chromatography (5:1 pet ether/ EtOAc) gave **118** (0.123 g, 61%) as a white solid: mp $90.5\text{--}92^\circ\text{C}$. ^1H NMR (CDCl_3 , 500 MHz) δ 1.71-1.81 (m, 2H, $\text{CH}_2\text{CH}_2\text{N}$), 1.88 (t, $J = 10.8$ Hz, 1H, $\text{CH}_2\text{CH}_2\text{N}$), 1.99 (td, $J = 11.4$, 3.2 Hz, 1H, $\text{CH}_2\text{CH}_2\text{N}$), 2.30 (td, $J = 10.5$, 4.7 Hz, 1H, $\text{CH}_2\text{CH}(\text{Ph})$), 2.84 (d, $J = 11.2$ Hz, 1H, $\text{CH}(\text{OH})\text{CH}_2\text{N}$), 3.08 (dd, $J = 10.3$, 3.9 Hz, 1H, $\text{CH}(\text{OH})\text{CH}_2\text{N}$), 3.53 (q, $J = 24.7$, 13.1 Hz, 2H, $\text{CH}(\text{Ph})$), 3.73 (td, $J = 9.9$, 4.3 Hz, 1H, $\text{CH}(\text{OH})$), 7.14-7.25 (m, 10H, PhH); ^{13}C NMR (CDCl_3 , 125.7 MHz) δ 32.1 (CH_2), 51.5 (CH), 53.6 (CH_2), 60.1 (CH_2), 63.1 (CH_2), 71.9 (CH), 127.1 (CH), 127.3 (CH), 128.2 (CH), 128.4 (CH), 1328.9 (CH), 129.5 (CH), 138.1 (C), 142.5 (C). Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{NO}$: C, 80.86; H, 7.92; N, 5.24. Found C, 80.85; H, 7.96; N, 5.29.

1-Benzyl-2-oxo-4-phenyl-piperidine-3-carboxylic Acid Methyl Ester (119). The general procedure for *t*-BuLi enolization was followed using **72** (0.378 g, 0.142 mmol) and methyl chloroformate (0.143 mL, 1.85 mmol). Purification by column chromatography (2:1 pet ether/EtOAc) gave the **119** (0.416 g, 90 %, >95:5 dr) as a colorless oil. **Major diastereomer:** ^1H NMR (acetone- d_6 , 500 MHz) δ 2.01 (m, 1 H, CH_2CHPh), 2.17 (qd, J = 11.8, 5.6 Hz, 1H, CH_2CHPh), 3.35 (m, 1H, CHCH_2N), 3.40 (m, 1H, CHPh), 3.46 (m, 1H, CHCH_2N), 3.50 (s, 3H, OCH_3), 3.71 (d, J = 11.6 Hz, 1H, CHCO_2Me), 4.58 (d, J = 14.5 Hz, 1H, PhCH_2N), 4.70 (d, J = 14.5 Hz, 1H, PhCH_2N), 7.26-7.38 (m, 10 H, PhH); ^{13}C NMR (acetone- d_6 , 125.6 MHz) δ 29.8 (CH_2), 43.5 (CH), 47.0 (CH_2), 50.1 (CH_2), 51.7 (CH), 57.1 (CH_3), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.5 (CH), 129.2 (CH), 129.3 (CH), 138.1 (C), 143.0 (C), 166.0 (C), 170.9 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{20}\text{H}_{22}\text{NO}$: 324.1600; Found: 324.1600.

Conversion of 119 to 120.

Part 1: (1-Benzyl-4-phenyl-piperidin-3-yl)-methanol. The general reduction procedure for benzyl lactams was followed using **119** (0.260 g, 0.804 mmol) and lithium aluminum hydride (8.03 mL of a 1 M solution in THF, 8.03 mmol) with a 6 h reflux period. Purification by column chromatography (EtOAc) provided the title compound (0.168 g, 74 %) as a colorless oil. **Major diastereomer:** ^1H NMR (CDCl_3 , 400 MHz) δ 1.86 (m, 2H, CHCH_2O , CH_2CHPh), 2.05 (m, 3H, CHCH_2N , CH_2CHPh), 2.36 (td, J = 11.2, 3.4 Hz, 2H, CHCH_2N), 2.99 (d, J = 10.8 Hz, 1H, CHCH_2N), 3.23 (m, 2H, OH, CHCH_2O), 3.38 (d, J = 10.3 Hz, 1H, CHCH_2O), 3.57 (d, J = 12.9 Hz, 1H, PhCH_2N), 3.66 (d, J = 12.9 Hz, 1H, PhCH_2N), 7.20-7.43 (m, 10 H, PhH); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ 34.1 (CH_2), 43.8 (CH), 44.9 (CH), 53.7 (CH_2), 57.3 (CH_2), 63.4 (CH_2), 64.8 (CH_2), 126.3 (CH), 127.0 (CH), 127.4 (CH), 128.1 (CH), 128.4 (CH), 129.3 (CH), 137.7 (C), 144.4 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{19}\text{H}_{24}\text{NO}$: 282.1858; Found: 282.1859.

Part 2: 3-Hydroxymethyl-4-phenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester (120). A solution of (1-benzyl-4-phenyl-piperidin-3-yl)-methanol (0.165 g, 0.586 mmol) and Boc_2O (0.269 mL, 1.17 mmol) in EtOAc (15 mL) was hydrogenated at atmospheric pressure overnight with $\text{Pd}(\text{OH})_2$ (0.100 g). Filtration of the catalyst and concentration provided the crude product which was purified by column chromatography (3:1 pet ether/EtOAc) to provide **120** (0.149 g, 87 %) as a white solid: mp 133-134 °C. lit.¹⁰ mp 132-133 °C The ^1H NMR and ^{13}C

NMR spectra were consistent with reported literature values.¹⁰ Ref $[\alpha]_{\text{D}}^{20}$: +8.09 ° ($c = 1.1$, MeOH). lit.¹⁰ $[\alpha]_{\text{D}}^{20}$: +6.4 ° ($c = 0.4$, MeOH).

Conversion of 120 to 121.

Part 1: 3-(4-Methoxy-phenoxy-methyl)-4-phenyl-piperidine-1-carboxylic Acid *tert*-Butyl Ester. To a solution of **120** (0.075 g, 0.257 mmol) in CH₂Cl₂ (3.5 mL) was added Et₃N (0.054 mL, 0.386 mmol) followed by methanesulfonyl chloride (0.030 mL, 0.386 mmol) at rt. The solution was stirred for 10 min and poured into H₂O (10 mL). The aqueous was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organics were dried over MgSO₄ and concentrated to give the crude mesylate. To a solution of *p*-methoxyphenol (0.064 g, 0.514 mmol) in DMF (1.0 mL) was added NaH (0.019 g, 0.771 mmol) and the mixture was stirred for 10 min. To the mixture was added a solution of the mesylate in DMF (2 mL) and the reaction was stirred at 60 °C for 2 h. The reaction was then heated to reflux for 10 min, cooled to rt and quenched carefully with H₂O (1 mL). The reaction was poured into H₂O (10 mL) and the aqueous was extracted with ether (3 x 15 mL). The combined organics were dried over MgSO₄ and concentrated. Purification by column chromatography (6:1 pet ether/EtOAc) provided the title compound (0.074 g, 73 %) as a colorless oil. The ¹H NMR and ¹³C NMR spectra were consistent with reported literature values.¹⁰ $[\alpha]_{\text{D}}^{20}$: +26.3 ° ($c = 0.51$, MeOH). lit.¹⁰ $[\alpha]_{\text{D}}^{20}$: +22.9 ° ($c = 0.26$, MeOH).

Part 2: (+)-Femoxetine (121). The general reduction procedure for benzyl lactams was followed using 3-(4-methoxy-phenoxy-methyl)-4-phenyl-piperidine-1-carboxylic acid *tert*-butyl ester (0.045 g, 0.113 mmol) and lithium aluminum hydride (0.565 mL of a 1 M solution in THF, 0.565 mmol) stirring the reaction 4 h at rt. Purification by column chromatography on basic alumina (3:1 pet ether/EtOAc) provided **83** (0.024 g, 67 %) as a colorless oil. The ¹H NMR and ¹³C NMR spectra were consistent with reported literature values.¹⁰ $[\alpha]_{\text{D}}^{20}$: +73.0 ° ($c = 0.55$, MeOH). lit.¹⁰ $[\alpha]_{\text{D}}^{20}$: +75.7 ° ($c = 0.6$, MeOH).

3-*iso*-Butyl-4-methyl-pyrrolidine-1-carboxylic Acid (–)-Menthyl Ester. The general reduction and acylation procedure was followed using **64** (0.120 g, 0.77 mmol). Purification by column chromatography (11:1 pet ether/EtOAc) gave the title compound (0.212 g, 85 %, >97:3

dr) as an oil. GC: ($t_i = 100\text{ }^{\circ}\text{C}$ $t_f = 200\text{ }^{\circ}\text{C}$, $20\text{ }^{\circ}\text{C/min}$) $t_{R\text{major}} = 14.867\text{ min}$. **Major diastereomer:** $^1\text{H NMR}$ (CDCl_3 , 500 MHz) δ 0.78 (d, $J = 6.9\text{ Hz}$, 3H, CH_3CH), 0.88 (m, 12H, $(\text{CH}_3)_2\text{CHCH}_2$), 0.99 (d, $J = 6.4\text{ Hz}$, 3H, CH_3CH), 1.04 (dd, $J = 12.9, 3.4\text{ Hz}$, 1H, ring-CH), 1.11 (ddd, $J = 13.6, 10.3, 4.7\text{ Hz}$, 2H, $(\text{CH}_3)_2\text{CHCH}_2$), 1.34 (m, 2H, ring-CH, CH_3CH), 1.47 (m, 1H, $(\text{CH}_3)_2\text{CHCH}_2$), 1.54 (m, 1H, $(\text{CH}_3)_2\text{CHCH}_2$), 1.70 (m, 4H, $\text{CH}_2\text{CHCH}_2\text{N}$, ring-CH), 1.93 (septet, $J = 13.9, 2.8\text{ Hz}$, 1H, CH_3CH), 2.06 (m 1H, ring-CH), 2.84 (m, 2H, NCH_2), 3.61 (m, 2H, NCH_2), 4.52 (td, $J = 11.0, 4.5\text{ Hz}$, 1H, CHO); $^{13}\text{C NMR}$ (CDCl_3 , 125.6 MHz) δ 15.8 (CH_3), 16.5 (CH_3), 20.8 (CH), 21.6 (CH_3), 23.5 (CH_2), 23.9 (CH), 26.2 (CH_3), 26.7 (CH_3), 31.3 (CH), 34.3 (CH_2), 41.3 (CH_2), 41.8 (CH_2), 47.3 (CH), 51.9 (CH_2), 53.1 (CH_2), 74.4 (CH), 154.7 (C). HRMS-FAB ($M+1$) Calcd for $\text{C}_{20}\text{H}_{38}\text{NO}_2$: 324.2903; Found: 324.2902. $[\alpha]_D^{20}$: -128.1° ($c = 1.6$, CHCl_3).

3-Phenyl-pyrrolidine-1-carboxylic Acid (–)-Menthyl Ester. The general reduction and acylation procedure was followed using **65** (0.150 g, 0.93 mmol). Purification by column chromatography (10:1 pet ether/EtOAc) gave the title compound (0.230 g, 75 %, 75:25 dr) as an oil. **Major diastereomer:** $^1\text{H NMR}$ (CDCl_3 , 500 MHz) δ 0.82 (d, $J = 6.0\text{ Hz}$, 3H, CH_3CH), 0.91 (d, $J = 6.8\text{ Hz}$, 6H, $(\text{CH}_3)_2\text{CH}$), 0.97 (m, 1H, ring-CH), 1.08 (m, 1H, ring-CH), 1.36 (m, 1H, ring-CH), 1.51 (m, 2H, $(\text{CH}_3)_2\text{CH}$), 1.68 (m, 2H, NCHCH_2 , ring-CH), 1.97 (m 2H, NCHCH_2 , ring-CH), 2.12 (m, 1H, ring-CH), 2.26 (m, 1H, ring-CH), 3.37 (m, 3H, PhCH , NCH_2), 3.64 (m, 1H, NCH_2), 3.87 (m, 1H, NCH_2), 4.58 (td, $J = 10.7, 4.3\text{ Hz}$, 1H, CHO), 7.23 (m, 3H, PhH), 7.34 (m, 2H, PhH); $^{13}\text{C NMR}$ (CDCl_3 , 125.6 MHz) δ 16.4 (CH_3), 20.7 (CH), 20.8 (CH), 22.0 (CH_3), 23.5 (CH_2), 26.2 (CH), 31.2 (CH), 32.1 (CH_2), 32.4 (CH_2), 33.1 (CH_2), 33.2 (CH_2), 34.3 (CH_2), 41.7 (CH_2), 43.2 (CH), 44.0 (CH), 44.1 (CH), 45.5 (CH_2), 45.8 (CH_2), 45.9 (CH_2), 47.2 (CH), 47.3 (CH_2), 52.1 (CH_2), 74.6 (CH), 74.6 (CH), 126.7 (CH), 126.9 (CH), 128.5 (CH), 141.2 (C), 141.2 (C), 141.2 (C), 154.7 (C), 154.8 (C). Anal. Calcd for $\text{C}_{21}\text{H}_{31}\text{NO}_2$: C, 76.55; H, 9.48; N, 4.25. Found C, 76.63; H, 9.74; N, 4.42.

3-(4-Methoxy-phenoxyethyl)-4-phenyl-piperidine-1-carboxylic Acid (–)-Menthyl Ester. To a solution of 3-(4-Methoxy-phenoxyethyl)-4-phenyl-piperidine-1-carboxylic acid *tert*-butyl ester (0.074 g, 0.186 mmol) in CH_2Cl_2 (5 mL) was added TFA (0.500 mL). TLC indicated no remaining starting material after 45 min of stirring. The reaction was washed with

sat NaHCO₃ (15 mL) and the organics separated. The aqueous was extracted with CH₂Cl₂ (3 x 15 mL) and the combined organics were dried over Na₂SO₄ and concentrated. The residue was dissolved in dry CH₂Cl₂ (3.5 mL) under N₂ atmosphere. Et₃N (0.028 mL, 0.203 mmol) was added followed by (–)-menthylchloroformate (0.044 mL, 0.203 mmol) and the reaction was stirred for 16 h. Concentration and purification of the residue by column chromatography (4:1 pet ether/EtOAc) of the residue gave the title compound (0.017 g, 80 %, >97:3 dr) as a colorless oil.

Major diastereomer: ¹H NMR (CDCl₃, 500 MHz) δ 0.85 (d, *J* = 6.6 Hz, 3H, CH₃CH), 0.90 (m, 1H, ring-CH₂), 0.93 (d, *J* = 6.4 Hz, 6H, (CH₃)₂CH), 0.94 (d, *J* = 6.4 Hz, 6H, (CH₃)₂CH), 1.0 (m, 1H, ring-CH), 1.11 (qd, *J* = 12.8, 3.2 Hz, 1H, NCHCH₂), 1.42 (t, *J* = 11.2 Hz, 1H, ring-CH), 1.53 (m, 1H, (CH₃)₂CH), 1.70 (m, 2H, ring-CH₂), 1.80 (m, 2H, NCHCH₂, ring-CH), 1.98 (m, 1H, ring-CH), 2.12 (m, 2H, CHCH₂O, ring-CH), 2.68 (m, 1H, NCH₂), 2.85 (dd, *J* = 13.5, 11.3 Hz, 1H, NCH₂), 2.88 (m, 1H, CHPh), 3.50 (dd, *J* = 9.5, 7.1 Hz, 1H, OCH₂), 3.65 (dd, *J* = 9.5, 2.8 Hz, 1H, OCH₂), 3.73 (s, 3H, OCH₃), 4.32 (br m, 1H, NCH₂), 4.55 (br m, 1H, NCH₂), 4.60 (td, *J* = 10.9, 4.0 Hz, 1H, CHO), 6.68 (m, 2H, PhH), 6.76 (m, 2H, PhH), 7.20 (m 3H, PhH), 7.29 (m, 2H, PhH); ¹³C NMR (CDCl₃, 125.6 MHz) δ 16.8 (CH₃), 20.2 (CH), 22.0 (CH₃), 23.8 (CH₂), 26.5 (CH), 31.3 (CH), 33.7 (CH₂), 34.3 (CH₂), 41.5 (CH₂), 44.3 (CH₂), 44.8 (CH), 47.3 (CH), 47.4 (CH₂), 55.6 (CH₃), 68.5 (CH₂), 75.2 (CH), 114.4 (CH), 115.3 (CH), 126.7 (CH), 127.4 (CH), 128.7 (CH), 143.4 (C), 152.9 (C), 153.7 (C), 155.3 (C). HRMS-FAB (*M*+1): Calcd for C₃₀H₄₂NO₄: 480.3114; Found: 480.3115. [α]_D²⁰: -18.8 ° (*c* = 0.85, CHCl₃).

3-(4-Bromo-phenyl)-1-(4-methoxy-phenyl)-1-(3-nitro-1,2-diphenyl-propyl)-urea.

To a solution **36** (0.200 g) in CH₂Cl₂ (5 mL) was added trifluoroacetic acid (1 mL) at room temperature. The reaction mixture was stirred for 2h. After evaporation of volatile materials under reduced pressure, the residue was dissolved in ether, washed with sat. NaHCO₃, dried over MgSO₄, filtered and concentrated *in vacuo* affording 0.148 g (84%) of the crude amine. The product was used for the next step without further purification: ¹H NMR (400 MHz, CDCl₃) δ 3.73 (s, 3H), 3.96 (s, 1H), 4.03 (ddd, *J* = 6.0, 8.2, 8.3 Hz, 1H), 4.61 (d, *J* = 8.0 Hz, 1H), 4.83 (dd, *J* = 8.8, 13.6 Hz, 1H), 5.08 (dd, *J* = 6.0, 13.2 Hz, 1H), 6.54-6.60 (m, 2H), 6.70-6.77 (m, 2H), 7.00-7.08 (m, 4H), 7.14-7.30 (m, 6H). The crude amine and *p*- bromophenyl isocyanate (0.185 g, 0.51 mmol) in ether (10 mL) were stirred for 48 h at room temperature. After evaporation of the

solvent, the residue was separated with flash column chromatography (9:1 hexanes/EtOAc) affording 0.167 g (59%) of the title compound: mp 144-145 °C; ¹H NMR (500 MHz, CDCl₃) δ 3.87 (s, 3H), 4.14-4.24 (m, 1H), 4.98 (t, *J* = 11.5 Hz, 1H), 5.22 (dd, *J* = 3.0, 12.5 Hz, 1H), 6.00-6.12 (m, 2H), 6.40 (s, 1H), 6.67 (s, 1H), 6.87 (d, *J* = 7.0 Hz, 2H), 6.88-7.60 (m, 14H); ¹³C NMR (125.7 MHz, CDCl₃) δ 46.7, 55.5, 60.0, 80.7, 115.1, 121.1, 127.6, 127.8, 127.9, 128.2, 128.8, 129.7, 131.4, 131.7, 133.1, 136.1, 137.0, 137.5, 154.9, 169.1. HRMS Calcd for C₂₉H₂₆BrN₃O₄: 559.1107; Found: 559.1101. Suitable crystals for X-ray diffraction of the title compound were obtained by recrystallization from 2-propanol/CH₂Cl₂.

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