Silyl Imine Electrophiles in Enantioselective Catalysis: A Rosetta Stone for Peptide Homologation, Enabling Diverse N-Protected Aryl Glycines from Aldehydes in Three Steps

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Experimental Section

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General Procedure B: Bromonitromethane Addition to N-TMS-Protected Imines- Acetyl Bromide Quench

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(1E)-1,1,1-Trimethyl-N-(4-iodophenyl)silanamine (11e)

Fluorenylmethyl (1R)-2-bromo-1-(4-iodophenyl)-2-nitroethylcarbamate (12e)

Fluorenylmethyl (1R)-2-bromo-1-(4-(trifluoromethyl)phenyl)-2-nitroethylcarbamate (12f)

Fluorenylmethyl (1R)-2-bromo-1-phenyl-2-nitroethylcarbamate (12g)

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(1E)-1,1,1-Trimethyl-N-(naphthalen-2-ylmethylene)silanamine (11i)

Fluorenylmethyl (1R)-2-bromo-1-(2-naphthalenyl)-2-nitroethylcarbamate (12i)

Fluorenylmethyl (1R)-2-bromo-1-(4-methoxyphenyl)-2-nitroethylcarbamate (12j)

N-Fmoc-4-Cl-Phenylglycine-Nα-MeBn (13)

N-Fmoc-4-Cl-Phenylglycine-Leu-O’Bu (14)

N-Cbz-4-Cl-Phenylglycine-Leu-O’Bu (15)

N-Alloc-4-Cl-Phenylglycine-Leu-O’Bu (16)

N-N3Ac-4-Cl-Phenylglycine-Ala-OMe (17)
Experimental Section

Glassware was oven-dried overnight at 120 °C for all non-aqueous reactions. All reagents and solvents were commercial grade and purified prior to use when necessary. Tetrahydrofuran (THF) was dried by passage through a column of activated alumina as described by Grubbs.¹ This was done to accurately quantitate the amount of water in each reaction. NIS was recrystallized from dioxane/CCl₄.

Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 µm) plates, and flash chromatography utilized 230-400 mesh silica gel from Scientific Adsorbents. Products were visualized by UV light, iodine, and/or the use of ninhydrin, potassium permanganate, p-anisaldehyde, ceric ammonium molybdate, and potassium iodoplatinate solutions.

Melting points were measured on a Meltemp melting point apparatus and were not corrected. IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer and are reported in wavenumbers (cm⁻¹). Liquids and oils were analyzed as neat films on a NaCl plate (transmission), whereas solids were applied to a diamond plate (ATR). Nuclear magnetic resonance spectra (NMR) were acquired on a Bruker DRX-400 (400 MHz) or a Bruker AVIII-600 (600 MHz) spectrometer. Chemical shifts are measured relative to residual solvent peaks as an internal standard set to 7.26 and 77.1 for CDCl₃. Mass spectra were recorded on a Thermo Electron Corporation MAT 95XP-Trap mass spectrometer by use of chemical ionization (CI), electron impact ionization (EI) or electrospray ionization (ESI) by the Indiana University Mass Spectrometry Facility. A post-acquisition gain correction was applied using sodium formate or sodium iodide as the lock mass. Optical rotations were measured on a Perkin Elmer-341 polarimeter.

**General Procedure A: Synthesis of N-TMS-Protected Imines**

According to the procedure of Collet and coworkers,² in a flame-dried round bottom flask under argon, n-butyl lithium (1 equiv.) was added to hexamethyldisilazane (1.1 equiv) at 0 °C. After stirring for 10 m, the aldehyde (1 equiv.), in THF (10 M), was added via cannula. The reaction was allowed to stir at rt for 1 h before the solvent was removed. The crude material was treated with TMSCl (1 equiv.), and allowed to stir for 1 h at rt. The reaction was then diluted with hexanes and filtered under argon. The solvent was removed, giving the crude imine which was then purified via distillation.

**General Procedure B: Bromonitromethane Addition to N-TMS-Protected Imines- Acetyl Bromide Quench**

A solution of the imine (1 equiv) and PBAM³ (0.05 equiv) in toluene (0.3 M) was cooled to -78 °C. Bromonitromethane was added to the reaction mixture in aliquots (0.2 equiv every 2 h) over 10 h. The reaction

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¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Organometallics 1996, 15, 1518-1520.
² Vidal, J.; Damestoy, S.; Guy, L.; Hannachi, J. C.; Aubry, A.; Collet, A. Chemistry-a European Journal 1997, 3, 1691-1709.
³ Davis, T. A.; Wilt, J. C.; Johnston, J. N. J. Am. Chem. Soc. 2010, 132, 2880-+
was then stirred at -78 °C for an additional 16 h before addition of acetyl bromide at -78 °C (1 equiv). The reaction was then stirred at -78 °C for 3 h and subsequently quenched at -78 °C by the addition of water. The reaction mixture was diluted with CH2Cl2 and dried (MgSO4). The solvent was removed in vacuo, and the crude reaction mixture was purified by column chromatography to give the α-bromonitro adduct as a mixture of inseparable diastereomers.

**General Procedure C: Bromonitromethane Addition to N-TMS-Protected Imines**

A solution of the imine (1 equiv) and PBAM (0.10 equiv) in toluene (0.3 M) was cooled to -78 °C. Bromonitromethane was added to the reaction mixture in aliquots (0.2 equiv every 2 h) over 10 h. The reaction was then stirred at -78 °C for an additional 16 h before its quench at -78 °C with an acylating reagent (1 equiv). The reaction was then warmed to 0 °C and stirred for 20 h. The solvent was removed in vacuo, and the crude reaction mixture was purified by column chromatography to give the α-bromonitro adduct as a mixture of inseparable diastereomers.

**General Procedure D: Amide Synthesis Using an Amine (Free Base)**

The amine (1.2 equiv) was added dropwise to a solution of α-bromo nitroalkane (1.0 equiv, 0.2 M) and NIS (1.0 equiv) in THF and H2O (5.0 equiv) at 0 °C, followed by K2CO3 (2.0 equiv). The reaction mixture was stirred at 0 °C for 2 d. The resulting mixture was diluted with dichloromethane, dried with MgSO4 and then filtered through Celite. The filtrate was concentrated and subjected to purification by flash column chromatography on silica gel.

**General Procedure E: Amide Synthesis Using an Ammonium Salt**

K2CO3 (5.0 equiv) was added to the suspension of the ammonium salt (2.0 equiv) and the α-bromo nitroalkane (1.0 equiv, 0.2 M) in DME and H2O (5.0 equiv) at 0 °C, followed by NIS (100 mol%). The reaction mixture was placed under an atmosphere of O2 and stirred at 0 °C for 24 h. The resulting mixture was diluted with dichloromethane and then filtered. The filtrate was concentrated and subjected to purification by flash column chromatography on silica gel.

**N-(2-Bromo-1-(4-chlorophenyl)-2-nitroethyl)-1,1,1-trimethylsilanamine (S1)**

The N-TMS-imine\(^4\) (40.0 mg, 189 µmol) and bromonitromethane (16.0 µl, 227 µmol) were stirred at rt in CDCl3 for 1 h and then analyzed directly by NMR. \(^1\)H NMR indicated 81% conversion to the N-TMS-protected α-bromo nitroalkane (1.6:1 dr), with some N-TMS-imine and bromonitromethane remaining. Notably, the peaks

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\(^4\) Commercially available.
seen at 1.43 and 1.22 ppm, corresponding to the NH protons of each diastereomer, appear as doublets which integrate to a single proton. The coupling constants for each peak (12.6 and 13.2 Hz, respectively) suggest the protons couple only to the neighboring benzylic methyne proton. These details indicate that the compound observed is the suggested N-TMS-protected adduct, and not the free amine which would result from deprotection of the TMS group.

N-TMS-protected α-bromo nitroalkane $^1$H NMR$^5$ (600 MHz, CDCl$_3$) δ 7.35 (m, 4H), 7.28 (d, $J = 8.4$ Hz, 2H), 7.20 (d, $J = 8.4$ Hz, 2H), 6.22 (d, $J = 3.6$ Hz, 1H), 5.82 (d, $J = 9.0$ Hz, 1H), 4.85 (dd, $J = 12.6$, 3.6 Hz, 1H), 4.49 (dd, $J = 13.2$, 9.0 Hz, 1H), 1.43 (d, $J = 12.6$ Hz, 1H), 1.22 (d, $J = 13.2$ Hz, 1H), 0.00 (s, 9H), -0.02 (s, 9H); 13C NMR$^5$ (150 MHz, CDCl$_3$) ppm 138.6, 138.3, 134.3, 134.1, 129.1, 128.9, 128.2, 127.8, 91.1, 83.5, 61.1, 59.8, 0.0, -0.1.

N-((1R)-2-Bromo-1-(4-chlorophenyl)-2-nitroethyl)acetamide (10a)

Following General Procedure B, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with acetyl bromide (11.6 µl, 94 µmol), provided the α-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO$_2$, 30% ethyl acetate in hexanes), as a viscous yellow oil (23.4 mg, 78%). The enantiomeric excess of the major and minor diastereomers were determined to be 93 and 91% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 10% iPrOH/hexanes, 1.0 mL/min, $t_d$(d$_1$e$_1$, minor) = 10.2 min, $t_d$(d$_1$e$_2$, major) = 18.6 min, $t_d$(d$_2$e$_1$, minor) = 13.9 min, $t_d$(d$_2$e$_2$, major) = 16.0 min). $R_f$ = 0.18 (30% EtOAc/hexanes); IR (film) 3266, 2925, 1661, 1566, 1538, 1094 cm$^{-1}$; $^1$H NMR$^5$ (600 MHz, CDCl$_3$) δ 7.39 (d, $J = 6.4$ Hz, 2H), 7.37 (d, $J = 6.4$ Hz, 2H), 7.30 (d, $J = 8.5$ Hz, 2H), 7.27 (d, $J = 8.8$ Hz, 2H), 6.87 (br d, $J = 8.5$ Hz, 1H), 6.49 (br d, $J = 8.0$ Hz, 1H), 6.37 (d, $J = 4.5$ Hz, 1H), 6.35 (d, $J = 5.6$ Hz, 1H), 5.91 (dd, $J = 8.6$, 4.4 Hz, 1H), 5.78 (dd, $J = 8.9$, 5.6 Hz, 1H), 2.14 (s, 3H), 2.11 (s, 3H); 13C NMR$^5$ (150 MHz, CDCl$_3$) ppm 169.9, 169.7, 135.5, 135.4, 133.1, 132.7, 129.5, 129.4, 128.4 (2C), 83.9, 80.3, 56.0, 55.8, 23.1 (2C); HRMS (CI): Exact mass calcd for C$_{10}$H$_{11}$BrClN$_2$O$_3$ [M+H]$^+$ 320.9636, found 320.9628.

Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with acetyl chloride (6.7 µl, 94 µmol), provided the α-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO$_2$, 30% ethyl acetate in hexanes), as a viscous yellow oil.

$^5$ Spectra of an inseparable mixture of diastereomers.
The enantiomeric excess of the major and minor diastereomers were determined to be 92 and 91% ee, respectively.

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N-((1R)-2-Bromo-1-(4-chlorophenyl)-2-nitroethyl)benzamidine (10b)
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Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with benzoyl chloride (11 µl, 94 µmol), provided the α-bromo nitroalkane (1:4:1 mixture of diastereomers), after flash column chromatography (SiO\textsubscript{2}, 15% ethyl acetate in hexanes), as a white solid (25.2 mg, 70%). The enantiomeric excess of the major and minor diastereomers were determined to be 94 and 95% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 20% iPrOH/hexanes, 1.0 mL/min, \(t\text{r}(d_1e_1, \text{minor}) = 8.6\) min, \(t\text{r}(d_1e_2, \text{major}) = 19.5\) min, \(t\text{r}(d_2e_1, \text{minor}) = 6.7\) min, \(t\text{r}(d_2e_2, \text{major}) = 14.1\) min). \(R_f = 0.15\) (15% EtOAc/hexanes); mp = 147-150 °C (dec); IR (film) 3299, 2923, 1641, 1564, 1521, 1343 cm\textsuperscript{-1}; \(^1\)H NMR\textsuperscript{5} (600 MHz, CDCl\textsubscript{3}) \(\delta 7.87\) (d, \(J = 7.3\) Hz, 2H), 7.82 (d, \(J = 7.3\) Hz, 2H), 7.59 (m, 2H), 7.56 (br d, \(J = 8.9\) Hz, 1H), 7.50 (m, 4H), 7.38 (m, 6H), 7.32 (d, \(J = 8.5\) Hz, 2H), 7.03 (br d, \(J = 8.4\) Hz, 1H), 6.48 (d, \(J = 4.3\) Hz, 1H), 6.45 (d, \(J = 5.1\) Hz, 1H), 6.10 (dd, \(J = 8.5, 4.2\) Hz, 1H), 5.97 (dd, \(J = 8.9, 5.1\) Hz, 1H); \(^1^3\)C NMR\textsuperscript{5} (150 MHz, CDCl\textsubscript{3}) ppm 167.1, 166.9, 135.5, 135.4, 133.2, 133.0 (2C), 132.8, 132.4 (2C), 129.6, 129.4, 128.9, 128.4, 128.2, 127.2, 127.1, 84.2, 80.3, 56.3, 56.1; HRMS (ESI): Exact mass calcd for C\textsubscript{15}H\textsubscript{12}BrClN\textsubscript{2}NaO\textsubscript{3} [M+Na\textsuperscript{+}] \(404.9612\), found 404.9638.

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N-((1R)-2-Bromo-1-(4-chlorophenyl)-2-nitroethyl)pivalamide (10c)
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Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with pivaloyl chloride (11.5 µl, 94 µmol), provided the α-bromo nitroalkane (1:4:1 mixture of diastereomers), after flash column chromatography (SiO\textsubscript{2}, 10% ethyl acetate in hexanes), as a white solid (22.7 mg, 67%). The enantiomeric excess of the major and minor diastereomers were determined to be 96 and 97% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 20% iPrOH/hexanes, 1.0 mL/min, \(t\text{r}(d_1e_1, \text{minor}) = 5.5\) min, \(t\text{r}(d_1e_2, \text{major}) = 9.5\) min, \(t\text{r}(d_2e_1, \text{minor}) = 4.8\) min, \(t\text{r}(d_2e_2, \text{major}) = 18.7\) min). \(R_f = 0.21\) (15% EtOAc/hexanes); mp = 142-146 °C (decomposition); IR (film) 3319, 2969, 1643, 1560, 1543, 1350, 1213 cm\textsuperscript{-1}; \(^1\)H NMR\textsuperscript{5} (600 MHz, CDCl\textsubscript{3}) \(\delta 7.39\) (d, \(J = 8.5\) Hz, 2H), 7.37 (d, \(J = 8.5\) Hz, 2H), 7.28 (d, \(J = 8.4\) Hz, 2H), 7.24 (d, \(J = 8.4\) Hz, 2H), 7.03 (br d, \(J = 8.5\) Hz, 1H), 6.50 (br d, \(J = 8.0\) Hz, 1H), 6.39 (d, \(J = 3.9\) Hz, 1H), 6.37 (d, \(J = 4.9\) Hz, 1H), 5.88 (dd, \(J = 8.4, 3.9\) Hz, 1H), 5.74 (dd, \(J = 8.8, 5.0\) Hz, 1H), 1.30 (s, 9H), 1.27 (s, 9H); \(^1^3\)C
2-Azido-N-((1R)-2-bromo-1-(4-chlorophenyl)-2-nitroethyl)acetamide (10d)

Following General Procedure C, the N-TMS-imine (50 mg, 236 µmol) and bromonitromethane (18.0 µl, 236 µmol), when quenched with azidoacetyl chloride (28.2 µl, 236 µmol), provided the α-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO₂, 15% ethyl acetate in hexanes), as a white solid (70.0 mg, 82%). The enantiomeric excess of both the major and minor diastereomers was determined to be 91% ee by chiral HPLC analysis (Chiralcel AD-H, 20% tPrOH/hexanes, 0.6 mL/min, tᵣ(d₁e₁, minor) = 10.5 min, tᵣ(d₁e₂, major) = 17.2 min, tᵣ(d₂e₁, minor) = 15.3 min, tᵣ(d₂e₂, major) = 18.5 min). Rᶠ = 0.27 (30% EtOAc/hexanes); mp = 154-156 °C (dec); IR (film) 3290, 3026, 2116, 1662, 1553, 1537, 1317, 1287 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.61 (br d, J = 8.9 Hz, 1H), 7.41 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.22 (br d, J = 8.6 Hz, 1H), 6.35 (d, J = 4.1 Hz, 1H), 6.34 (d, J = 5.1 Hz, 1H), 5.91 (dd, J = 8.9, 4.4 Hz, 1H), 5.76 (dd, J = 9.1, 5.3 Hz, 1H), 4.18 (d, J = 16.9 Hz, 1H), 4.15 (d, J = 17.0 Hz, 1H), 4.10 (d, J = 16.8 Hz, 1H), 4.09 (d, J = 16.9 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) ppm 166.5, 166.2, 135.8, 135.7, 132.6, 132.1, 129.6, 129.5, 128.3 (2C), 83.6, 79.9, 55.7, 55.6, 52.4 (2C); HRMS (CI): Exact mass calcd for C₁₀H₁₀BrClN₅O₃ [M+H]+ 363.9635, found 363.9638.

Fluorenylmethyl (1R)-2-bromo-1-(4-chlorophenyl)-2-nitroethylcarbamate (10e)

Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 ml, 94 µmol), when quenched with fluorenylmethyl chloroformate (24.3 mg, 94 µmol), provided the α-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a white solid (35.8 mg, 76%). The enantiomeric excess of both the major and minor diastereomers was determined to be 91% ee by chiral HPLC analysis (Chiralcel AD-H, 20% tPrOH/hexanes, 1.0 mL/min, tᵣ(d₁e₁, minor) = 12.0 min, tᵣ(d₁e₂, major) = 38.8 min, tᵣ(d₂e₁, minor) = 13.3 min, tᵣ(d₂e₂, major) = 22.4 min). Rᶠ = 0.29 (20% EtOAc/hexanes); mp = 154-156 °C (dec); IR (film) 3307, 1701, 1566, 1508, 1493, 1246 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 7.6 Hz, 4H), 7.58 (br s, 4H), 7.37 (m, 12H), 7.23 (br s, 4H), 6.30 (br s,
Benzyl (1R)-2-bromo-1-(4-chlorophenyl)-2-nitroethylcarbamate (10f)

Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with benzyl chloroformate (13.2 µl, 94 µmol), provided the α-bromo nitroalkane (1.3:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a white solid (28.1 mg, 72%). The enantiomeric excess of the major and minor diastereomers were determined to be 91 and 90% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 15% t-PrOH/hexanes, 0.7 mL/min, \( t_{d1e1, \text{minor}} \) = 17.9 min, \( t_{d1e2, \text{major}} \) = 31.3 min, \( t_{d2e1, \text{minor}} \) = 19.3 min, \( t_{d2e2, \text{major}} \) = 29.7 min). \( R_f \) = 0.19 (10% EtOAc/hexanes); mp = 112-115 °C; IR (film) 3308, 2924, 1699, 1567, 1532, 1494, 1350, 1249, 1093, 1015 cm⁻¹; \(^1^H\) NMR (600 MHz, CDCl₃) δ 7.38 (m, 14H), 7.28 (d, \( J = 7.8 \) Hz, 2H), 7.25 (d, \( J = 8.2 \) Hz, 2H), 6.31 (br s, 2H), 6.01 (br d, \( J = 6.8 \) Hz, 1H), 5.70 (br s, 1H), 5.65 (br s, 1H), 5.52 (br s, 1H), 5.16 (s, 2H), 5.14 (s, 2H); \(^1^C\) NMR (150 MHz, CDCl₃) ppm 155.4, 155.1, 135.5 (2C), 135.4 (2C), 133.4, 132.8, 129.4 (3C), 128.6 (2C), 128.5, 128.3 (2C), 128.2 (2C), 84.3, 80.7, 67.8 (2C), 57.9 (2C); HRMS (ESI): Exact mass calcd for C₁₆H₁₄BrClN₂NaO₄ [M+Na]⁺ 434.9718, found 434.9708.

Allyl (1R)-2-bromo-1-(4-chlorophenyl)-2-nitroethylcarbamate (10g)

Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with allyl chloroformate (10 µl, 94 µmol), provided the α-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a viscous white paste (27.8 mg, 85%). The enantiomeric excess of both the major and minor diastereomers was determined to be 91% ee by chiral HPLC analysis (Chiralcel AD-H, 8% t-PrOH/hexanes, 1.0 mL/min, \( t_{d1e1, \text{minor}} \) = 17.1 min, \( t_{d1e2, \text{major}} \) = 30.8 min, \( t_{d2e1, \text{minor}} \) = 16.2 min, \( t_{d2e2, \text{major}} \) = 33.4 min). \( R_f \) = 0.13 (10% EtOAc/hexanes); IR (film) 3307, 2925, 1699, 1568, 1532, 1494, 1352, 1278, 1250, 1093 cm⁻¹; \(^1^H\) NMR (600 MHz, CDCl₃) δ 7.40 (d, \( J = 8.4 \) Hz, 2H), 7.39 (d, \( J = 9.0 \) Hz, 2H), 7.30 (d, \( J = 8.4 \) Hz, 2H), 7.26 (d, \( J = 9.0 \) Hz, 2H), 6.32 (br s, 2H), 6.00 (br d, \( J = 9.7 \) Hz, 1H), 5.93 (m, 2H), 5.69 (dd, \( J = 9.1, 4.3 \) Hz, 1H), 5.63 (br d, \( J = 8.8 \) Hz, 2H), 5.48 (br s, 1H), 4.57 (m, 2H), 4.46 (br s, 2H), 4.34 (m, 2H); \(^1^C\) NMR (100 MHz, CDCl₃) ppm 155.5, 155.3, 143.4 (2C), 141.3 (2C), 135.4, 135.3, 133.3, 132.8, 129.3 (2C), 128.3, 128.2, 127.8 (2C), 127.1 (2C), 124.9 (2C), 120.1 (2C), 83.9, 80.5, 67.3 (2C), 57.9 (2C), 47.0 (2C); HRMS (ESI): Exact mass calcd for C₂₃H₁₈BrClN₂NaO₄ [M+Na]⁺ 523.0031, found 523.0057.
Hz, 1H), 5.50 (br dd, \( J = 8.0, 5.9 \) Hz, 1H), 5.34 (d, \( J = 16.5 \) Hz, 2H), 5.27 (d, \( J = 10.5 \) Hz, 2H), 4.62 (m, 4H); \( ^{13} \)C NMR \( ^{5} \) (150 MHz, CDCl\( _3 \)) ppm 155.2, 155.0, 135.5, 135.4, 132.8, 132.0, 131.9, 129.5, 129.4, 128.3, 128.1, 118.6, 118.5, 84.3, 80.6, 66.6 (2C), 57.8 (2C); HRMS (ESI): Exact mass calcd for C\(_{12}\)H\(_{12}\)BrClN\(_2\)NaO\(_4\) [M+Na]\(^+\) 384.9561, found 384.9581.

Assignment of Absolute Configuration for N-TMS Imine Adducts by Chemical Correlation

\((R)-\text{tert-Butyl 2-bromo-1-(4-chlorophenyl)-2-nitroethylcarbamate (S2)}\)

As reported previously, \(^7\) a solution of the imine (81.0 mg, 338 \( \mu \)mol) and H,Quin\( ^{6}(\text{Anth})^{2}\text{Pyr})\cdot\text{BAM}\cdot\text{HOTf}^{6}\) (10.9 mg, 16.9 \( \mu \)mol) in toluene (1.1 mL) was cooled to -20 °C and treated with bromonitromethane (63.0 mg, 406 \( \mu \)mol). The reaction mixture was stirred at -20 °C for 2 d, and then concentrated and directly subjected to purification by flash column chromatography on silica gel (10% ethyl acetate in hexanes) to give the \( \alpha \)-bromo nitroalkane as a white solid (111 mg, 87%), which was determined to be 98% ee (each diastereomer) and 1:1 dr by chiral HPLC analysis (Chiralcel AD-H, 10% \( \text{iPrOH} \)/hexanes, 1 mL/min, \( t_r(d_1e_1, \text{minor}) = 14.5 \) min, \( t_r(d_1e_2, \text{major}) = 19.3 \) min, \( t_r(d_2e_1, \text{minor}) = 15.7 \) min, \( t_r(d_2e_2, \text{major}) = 25.5 \) min \( t_r(\text{major}) = 14.5, 19.3 \) min, \( t_r(\text{major}) = 15.7, 25.5 \) min. Figure 1).

Figure 1: HPLC trace of S2 prepared via known method.

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\(^6\) Singh, A.; Yoder, R. A.; Shen, B.; Johnston, J. N. \( \text{J. Am. Chem. Soc.} \) \textbf{2007}, 129, 3466-3467Shen, B.; Johnston, J. N. \( \text{Org. Lett.} \) \textbf{2008}, 10, 4397-4400.
Following General Procedure C, the N-TMS-imine (20 mg, 94 µmol) and bromonitromethane (7.3 µl, 94 µmol), when quenched with Boc anhydride (20.5 mg, 94 µmol), provided the α-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a white solid (12.9 mg, 36%). The enantiomeric excess of both the major and minor diastereomers was determined to be 80 and 81% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 10% iPrOH/hexanes, 1 mL/min, \( t_r(d_1e_1, \text{minor}) = 14.5 \text{ min}, t_r(d_1e_2, \text{major}) = 19.5 \text{ min}, t_r(d_2e_1, \text{minor}) = 15.8 \text{ min}, t_r(d_2e_2, \text{major}) = 26.2 \text{ min}. \) Figure 2). \( R_f = 0.49 \) (20% EtOAc/hexanes); spectroscopic data (¹H NMR) was in complete accord with that previously reported.⁷ The absolute configuration at the benzylic carbon was therefore determined by chemical correlation.

**Figure 2.** HPLC trace of S₂ prepared from N-TMS imine, bromonitromethane and Boc₂O, in the presence of PBAM. \( \lambda_{210} \)

| Peak RetTime Type | Width | Area | Height | Area % |
|-------------------|-------|------|--------|--------|
| 1 14.473 MM       | 0.4915| 405.68488 | 13.75372 | 4.1881 |
| 2 15.837 MM       | 0.5064| 461.33539 | 15.18413 | 4.7626 |
| 3 19.487 MM       | 0.5862| 3880.64160 | 108.11904 | 40.0618 |
| 4 26.232 MM       | 0.8118| 4938.96484 | 101.39876 | 50.9875 |

**Fluorenylmethyl (1R)-2-bromo-1-(3-chlorophenyl)-2-nitroethylcarbamate (12a)**

Following General Procedure C, the N-TMS-imine⁵ (40.0 mg, 190 µmol) and bromonitromethane (15.0 µl, 190 µmol), when quenched with fluorenylmethyl chloroformate (49.0 mg, 190 µmol), provided the α-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a white foam (59.8 mg, 63%). The enantiomeric excess of the major and minor diastereomers were

⁷ Shen, B.; Makley, D. M.; Johnston, J. N. *Nature* **2010**, *465*, 1027-1032.
Fluorenylmethyl (1R)-2-bromo-1-(2,4-dichlorophenyl)-2-nitroethylcarbamate (12b)

Following General Procedure C, the N-TMS-imine² (20 mg, 81 µmol) and bromonitromethane (6.3 µl, 81 µmol), when quenched with fluorenylmethyl chloroformate (21 mg, 81 µmol), provided the α-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a yellow viscous oil (30.2 mg, 70%). The enantiomeric excess of the major and minor diastereomers were determined to be 90 and 91% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 8% 1PrOH/hexanes, 0.7 mL/min, \( t_r(d_{1e1}, \text{minor}) = 41.2 \text{ min} \), \( t_r(d_{1e2}, \text{major}) = 44.4 \text{ min} \), \( t_r(d_{2e1}, \text{minor}) = 43.3 \text{ min} \), \( t_r(d_{2e2}, \text{major}) = 54.0 \text{ min} \)). \( R_f = 0.42 \) (30% EtOAc/hexanes); IR (film) 3316, 2925, 1713, 1568, 1515, 1477, 1451, 1256, 1248 cm⁻¹; \(^1\)H NMR\(^5\) (600 MHz, CDCl₃) δ 7.79 (br d, \( J = 7.0 \text{ Hz} \), 4H), 7.55 (br m, 4H), 7.47 (br s, 2H), 7.42 (br t, \( J = 7.2 \text{ Hz} \), 6H), 7.30 (br m, 6H), 6.51 (br s, 1H), 6.47 (br d, \( J = 4.7 \text{ Hz} \), 1H), 6.25 (br d, \( J = 8.8 \text{ Hz} \), 1H), 6.04 (br s, 1H), 5.76 (br s, 1H), 5.72 (br s, 1H), 4.56 (br m, 2H), 4.45 (br s, 2H), 4.25 (br m, 2H); \(^1^3\)C NMR\(^5\) (150 MHz, CDCl₃) ppm 154.5 (2C), 143.4, 143.3, 141.3 (2C), 130.7, 130.2, 129.7, 128.1, 127.9, 127.8 (4C), 127.1 (4C), 124.9, 124.8, 124.7, 120.0 (4C), 82.3, 77.5, 67.5 (2C), 56.0, 55.6, 47.1 (2C); HRMS (ESI): Exact mass caled for C₂₃H₁₇BrCl₂N₂NaO₄ [M+Na]⁺ 556.9641, found 556.9644.

Fluorenylmethyl (1R)-2-bromo-1-(4-bromophenyl)-2-nitroethylcarbamate (12c)

Following General Procedure C, the N-TMS-imine⁸ (40 mg, 160 µmol) and bromonitromethane (12.0 µl, 160 µmol), when quenched with fluorenylmethyl chloroformate (41 mg, 160 µmol), provided the α-bromo

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⁸ Betschart, C.; Schmidt, B.; Seebach, D. Helv. Chim. Acta 1988, 71, 1999-2021.
nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a yellow solid (55.5 mg, 64%). The enantiomeric excess of the major and minor diastereomers were determined to be 86 and 85% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 20% ⁴PrOH/hexanes, 1.0 mL/min, \( t_r(d_{1e1}, \text{minor}) = 13.6 \) min, \( t_r(d_{1e2}, \text{major}) = 25.0 \) min, \( t_r(d_{2e1}, \text{minor}) = 12.7 \) min, \( t_r(d_{2e2}, \text{major}) = 44.9 \) min). \( R_f = 0.38 \) (30% EtOAc/hexanes); mp = 103-105 °C; IR (film) 3310, 3065, 1704, 1567, 1511, 1491, 1335, 1249, 1075, 739 cm⁻¹; ¹H NMR (CDCl₃) \( \delta \) 7.79 (d, \( J = 7.2 \) Hz, 4H), 7.56 (br m, 6H), 7.43 (t, \( J = 7.8 \) Hz, 6H), 7.34 (br m, 4H), 7.17 (br m, 4H), 6.31 (br d, \( J = 5.4 \) Hz, 2H), 6.00 (br d, \( J = 9.0 \) Hz, 1H), 5.66 (br s, 1H), 5.61 (br s, 1H), 5.48 (br dd, \( J = 6.0 \) Hz, 1H), 4.58 (br m, 2H), 4.46 (br s, 2H), 4.24 (br m, 2H); ¹³C NMR (CDCl₃) ppm 155.5, 155.1, 143.3 (2C), 141.2 (2C), 132.4, 132.3, 128.5, 128.4 127.8 (2C), 127.6, 127.1 (3C), 124.9 (2C), 123.7, 123.5, 120.1 (2C), 84.0, 80.4, 67.3 (2C), 57.8 (2C), 47.1 (2C); HRMS (ESI): Exact mass calcd for C₂₃H₁₈Br₂N₂NaO₄ [M+Na]⁺ 566.9526, found 566.9528.

Fluorenylmethyl (1R)-2-bromo-1-(4-fluorophenyl)-2-nitroethylcarbamate (12d)

Following General Procedure C, the N-TMS-imine² (40 mg, 205 µmol) and bromonitromethane (16.0 µl, 205 µmol), when quenched with fluorenylmethyl chloroformate (53 mg, 205 µmol), provided the \( \alpha \)-bromo nitroalkane (1.3:1 mixture of diastereomers), after flash column chromatography (SiO₂, 10% ethyl acetate in hexanes), as a yellow solid (74.0 mg, 74%). The enantiomeric excess of both the major and minor diastereomers was determined to be 86% ee by chiral HPLC analysis (Chiralcel IA, 20% ⁴PrOH/hexanes, 1.0 mL/min, \( t_r(d_{1e1}, \text{minor}) = 13.2 \) min, \( t_r(d_{1e2}, \text{major}) = 20.0 \) min, \( t_r(d_{2e1}, \text{minor}) = 11.4 \) min, \( t_r(d_{2e2}, \text{major}) = 33.7 \) min). \( R_f = 0.35 \) (40% EtOAc/hexanes); mp = 98-101 °C; IR (film) 3315, 2925, 1713, 1607, 1568, 1511, 1352, 1230, 759, 740 cm⁻¹; ¹H NMR (CDCl₃) \( \delta \) 7.79 (d, \( J = 7.8 \) Hz, 4H), 7.59 (br s, 4H), 7.43 (t, \( J = 7.5 \) Hz, 6H), 7.31 (m, 6H), 7.09 (br s, 4H), 6.32 (br s, 2H), 6.02 (br d, \( J = 8.8 \) Hz, 1H), 5.66 (br s, 2H), 5.52 (br s, 1H), 4.58 (br dd, \( J = 17.0 \), 10.1 Hz, 2H), 4.46 (br s, 2H), 4.24 (br m, 2H); ¹³C NMR (CDCl₃) ppm 163.0 (d, \( J_{CF} = 249.2 \) Hz, 2C), 155.5, 155.2, 143.4 (2C), 141.3 (2C), 130.1 (2C), 128.8 (2C), 127.8 (2C), 127.1 (d, \( J_{CF} = 4.8 \) Hz, 2C), 124.9, 124.8, 120.1 (2C), 116.3 (d, \( J_{CF} = 22.1 \) Hz), 116.2 (d, \( J_{CF} = 22.9 \) Hz), 84.1, 80.8, 67.3 (2C), 57.9, 57.8, 47.1 (2C); HRMS (Cl): Exact mass calcd for C₂₃H₁₉BrFN₂O₄ [M+H⁺]⁺ 485.0507, found 485.0518.

(E)-1,1,1-Trimethyl-N-(4-iodophenyl)silanamine (11e)

Following the General Procedure A, the aldehyde (2.0 g, 8.62 mmol) provided the imine (0.7 g, 27%) as a pale
yellow oil. \( R_f = 0.27 \) (10% EtOAc/hexanes); bp = 85 °C/0.5 mm Hg; IR (film) 2952, 1642, 1585, 1481, 1394, 1250, 1094, 1006, 836 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 8.90 (s, 1H), 7.80 (d, \( J = 8.4 \) Hz, 2H), 7.54 (d, \( J = 7.8 \) Hz, 2H), 0.27 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) ppm 167.2, 137.7, 137.4, 98.2, -1.23.\(^9\)

**Fluorenylmethyl (1R)-2-bromo-1-(4-iodophenyl)-2-nitroethylcarbamate (12c)**

Following General Procedure C, the \( N \)-TMS-imine (40.0 mg, 132 \( \mu \)mol) and bromonitromethane (10.0 \( \mu \)l, 132 \( \mu \)mol), provided the \( \alpha \)-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO\(_2\), 10% ethyl acetate in hexanes), as a yellow solid (65.0 mg, 83%). The enantiomeric excess of both the major and minor diastereomers was determined to be 88% ee by chiral HPLC analysis (Chiralcel AD-H, 15% \( i \)PrOH/hexanes, 1.0 mL/min, \( t_d(d_1e_1, \text{minor}) = 21.6 \) min, \( t_d(d_1e_2, \text{major}) = 80.5 \) min, \( t_d(d_2e_1, \text{minor}) = 20.5 \) min, \( t_d(d_2e_2, \text{major}) = 45.1 \) min). \( R_f = 0.29 \) (20% EtOAc/hexanes); mp = 175-177 °C; IR (film) 3309, 1703, 1566, 1512, 1246 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 7.77 (d, \( J = 7.2 \) Hz, 4H), 7.12 (br s, 4H), 7.57 (br s, 4H), 7.41 (dd, \( J = 7.8, 7.8 \) Hz, 4H), 7.31 (br m, 4H), 7.02 (br s, 4H), 6.28 (br s, 2H), 5.96 (br s, 1H), 5.62 (br s, 1H), 5.58 (br s, 1H), 5.44 (br s, 1H), 4.55 (br s, 2H), 4.44 (br s, 2H), 4.22 (br m, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) ppm 155.4, 155.2, 143.4, 143.3, 141.3 (2C), 138.3 (2C), 133.9 (2C), 128.6, 128.5, 127.8 (2C), 127.1 (2C), 124.8 (2C), 120.1 (2C), 95.4, 95.3, 83.9, 80.3, 67.3 (2C), 58.0 (2C), 47.1 (2C); HRMS (ESI): Exact mass calcd for C\(_{23}\)H\(_{18}\)BrI\(_2\)N\(_2\)O\(_4\) [M+Na]\(^+\) 614.9387, found 614.9395.

**Fluorenylmethyl (1R)-2-bromo-1-(4-(trifluoromethyl)phenyl)-2-nitroethylcarbamate (12f)**

Following General Procedure C, the \( N \)-TMS-imine (40 mg, 163 \( \mu \)mol) and bromonitromethane (13.0 \( \mu \)l, 163 \( \mu \)mol), provided the \( \alpha \)-bromo nitroalkane (1.3:1 mixture of diastereomers), after flash column chromatography (SiO\(_2\), 10% ethyl acetate in hexanes), as a white solid (57.9 mg, 66%). The enantiomeric excess of the major and minor diastereomers were determined to be 80 and 76% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 20% \( i \)PrOH/hexanes, 1.0 mL/min, \( t_d(d_1e_1, \text{minor}) = 8.9 \) min, \( t_d(d_1e_2, \text{major}) = 30.7 \) min, \( t_d(d_2e_1, \text{minor}) = 9.8 \) min, \( t_d(d_2e_2, \text{major}) = 19.3 \) min). \( R_f = 0.37 \) (30% EtOAc/hexanes); mp = 180-182 °C (decomposition); IR (film) 3310, 2925, 1704, 1568, 1515, 1326, 1251, 1170, 1129, 1069, 740 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 7.89 (d, \( J = 6.6 \) Hz, 4H), 7.66

\(^9\) HRMS was attempted, but the desired mass was not able to be detected. This is most likely due to the instability of the compound.
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(1R)-2-bromo-1-phenyl-2-nitroethylcarbamate (12g)

Following General Procedure C, the \( N \)-TMS-imine \(^{10} \) (40.0 mg, 226 \( \mu \)mol) and bromonitromethane (17.5 \( \mu \)l, 226 \( \mu \)mol), when quenched with fluorenylmethyl chloroformate (58.0 mg, 226 \( \mu \)mol), provided the \( \alpha \)-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO\(_2\), 10% ethyl acetate in hexanes), as a white solid (67.3 mg, 63%). The enantiomeric excess of both the major and minor diastereomers was determined to be 65 and 66% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 20% \( \text{i-PrOH/hexanes} \), 1.0 mL/min, \( t_{R}(d_{1}e_{1}, \text{minor}) = 14.9 \) min, \( t_{R}(d_{1}e_{2}, \text{major}) = 22.2 \) min, \( t_{R}(d_{2}e_{1}, \text{minor}) = 13.3 \) min, \( t_{R}(d_{2}e_{2}, \text{major}) = 32.6 \) min). \( R_{f} = 0.24 \) (20% EtOAc/hexanes); mp = 174-177 °C; IR (film) 3322, 1694, 1563, 1530, 1449, 1252, 738 cm\(^{-1}\); \(^{1}H\) NMR (600 MHz, CDCl\(_3\)) \( \delta \) 7.77 (d, \( J = 7.2 \) Hz, 4H), 7.59 (br s, 4H), 7.41 (m, 10H), 7.30 (m, 8H), 6.33 (br s, 2H), 5.99 (br d, \( J = 6.6 \) Hz, 1H), 5.70 (br s, 1H), 5.57 (br s, 1H), 5.52 (br s, 1H), 4.55 (m, 2H), 4.42 (br m, 2H), 4.24 (br m, 2H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) ppm 155.6, 155.3, 143.6, 143.5 (2C), 141.3 (2C), 134.7, 129.3, 129.2, 127.8 (2C), 127.2, 127.1, 126.8 (2C), 125.0, 124.9, 120.1 (4C), 84.6, 80.9, 67.4 (2C), 58.4 (2C), 47.1 (2C); HRMS (ESI): Exact mass calcd for C\(_{23}H_{19}BrN_{2}O_{4}\) [M+Na]+ 466.0528, found 466.0515.

Fluorenylmethyl (1R)-2-bromo-2-nitro-1-(\( p \)-tolyl)ethylcarbamate (12h)

Following General Procedure C, the \( N \)-TMS-imine \(^{8} \) (40.0 mg, 209 \( \mu \)mol) and bromonitromethane (16.3 \( \mu \)l, 209 \( \mu \)mol), when quenched with fluorenylmethyl chloroformate (54.0 mg, 209 \( \mu \)mol), provided the \( \alpha \)-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO\(_2\), 10% ethyl acetate in hexanes), as a yellow solid (63.2 mg, 63%). The enantiomeric excess of both the major and minor diastereomers was determined to be 70 and 71% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 20% \( \text{i-PrOH/hexanes} \), 1.0 mL/min, \( t_{R}(d_{1}e_{1}, \text{minor}) = 13.4 \) min, \( t_{R}(d_{1}e_{2}, \text{major}) = 38.4 \) min, \( t_{R}(d_{2}e_{1}, \text{minor}) = 15.6 \) min, \( t_{R}(d_{2}e_{2}, \text{major}) =

\(^{10}\) Commercially available.
21.3 min). Rf = 0.24 (20% EtOAc/hexanes); mp = 105-108 °C; IR (film) 3311, 3021, 1705, 1565, 1512, 1450, 1349, 1249, 738 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.77 (d, J = 7.2 Hz, 4H), 7.58 (br s, 4H), 7.41 (dd, J = 7.8, 7.8 Hz, 4H), 7.30 (br m, 4H), 7.12 (br s, 8H), 6.31 (br s, 2H), 6.00 (br d, J = 7.8 Hz, 1H), 5.65 (br s, 1H), 5.59 (br d, J = 7.8 Hz, 1H), 5.49 (br s, 1H), 4.54 (dd, J = 10.7, 6.7 Hz, 1H), 4.53 (dd, J = 11.2, 6.8 Hz, 1H), 4.41 (br m, 2H), 4.23 (dd, J = 13.3, 6.7 Hz, 2H), 2.36 (s, 3H), 2.35 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) ppm 155.5, 155.2, 143.6, 143.5 (2C), 141.3, 139.4 (2C), 131.2, 129.9 (2C), 127.8 (2C), 127.1 (2C), 126.7, 126.6, 125.0, 124.9, 120.0 (2C), 84.5, 81.1, 67.4 (2C), 58.3, 58.2, 47.1 (2C), 21.1 (2C); HRMS (ESI): Exact mass calcd for C₂₄H₂₁BrN₂O₄ [M⁺] 480.0685, found 480.0675.

(E)-1,1,1-Trimethyl-Ν-(naphthalen-2-ylmethylene)silanamine (11i)

Following the General Procedure A, the aldehyde (2.7 g, 17.3 mmol) provided the imine (2.9 g, 73%) as a pale yellow solid. Rf = 0.23 (5% EtOAc/hexanes); bp = 168 °C/1.1 mm Hg; mp = 39-41 °C; IR (film) 2954, 1643, 1248, 859 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.18 (s, 1H), 8.18 (s, 1H), 8.07 (dd, J = 8.5, 1.5 Hz, 1H), 7.95 (dd, J = 6.6, 2.4 Hz, 1H), 7.90 (m, 2H), 7.57 (dd, J = 6.9, 6.9, 1.8 Hz, 1H), 7.54 (dd, J = 6.9, 6.9, 1.7 Hz, 1H), 0.34 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) ppm 168.6, 136.4, 135.2, 133.1, 130.9, 128.9, 128.4, 127.9, 127.3, 126.4, 123.7, -1.09; HRMS (ESI): Exact mass calcd for C₁₁H₉N [M+H-C₃H₉Si]⁺ 155.0735, found 155.0696.

Fluorenylmethyl (1R)-2-bromo-1-(2-naphthalenyl)-2-nitroethylcarbamate (12i)

Following General Procedure C, the N-TMS-imine (40.0 mg, 176 µmol) and bromonitromethane (13.7 µl, 176 µmol), when quenched with fluorenylmethyl chloroformate (46 mg, 176 µmol), provided the α-bromo nitroalkane (1:1 mixture of diastereomers), after flash column chromatography (SiO₂, 15% ethyl acetate in hexanes), as a yellow solid (57.0 mg, 63%). The enantiomeric excess of both the major and minor diastereomers was determined to be 83 and 84% ee, respectively, by chiral HPLC analysis (Chiralcel IA, 10% iPrOH/hexanes, 1.0 mL/min, tₐ(d₁e₁, minor) = 24.9 min, tₐ(d₁e₂, major) = 57.7 min, tₐ(d₂e₁, minor) = 23.7 min, tₐ(d₂e₂, major) = 38.9 min). Rf = 0.19 (20% EtOAc/hexanes); mp = 176-179 °C (dec); IR (film) 3297, 2921, 2358, 1705, 1563, 1512, 1325, 1241, 1040 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.89 (m, 8H), 7.80 (m, 6H), 7.62 (br m, 2H), 7.56 (m, 4H), 7.43 (m, 6H), 7.33 (m, 4H), 6.45 (br s, 2H), 6.12 (br d, J = 7.2 Hz, 1H), 5.90 (br s, 1H), 5.71 (br s, 1H), 4.60 (dd, J = 10.8, 6.7 Hz, 1H), 4.57 (br m, 1H), 4.46 (br m, 2H), 4.27 (br s, 2H); ¹³C NMR (150 MHz, CDCl₃) ppm 155.6, 155.3, 143.5, 143.4, 141.3 (3C), 133.4 (2C), 133.1, 133.0, 131.5, 129.3 (2C), 128.1, 127.8 (4C), 127.7 (2C), 126.7 (2C), 126.6 (2C), 125.0, 124.9, 120.0 (2C), 84.5, 81.1, 67.4 (2C), 58.3, 58.2, 47.1 (2C), 21.1 (2C); HRMS (ESI): Exact mass calcd for C₂₅H₂₂BrN₂O₄Fmoc [M+C₄H₄N⁺] 584.0735, found 584.0735.
Fluorenylmethyl $(1R)$-2-bromo-1-(4-methoxyphenyl)-2-nitroethylcarbamate (12j)

Following General Procedure C, the $N$-TMS-imine\(^8\) (40 mg, 193 µmol) and bromonitromethane (15.0 µl, 193 µmol), when quenched with fluorenylmethyl chloroformate (50 mg, 193 mmol), provided the $\alpha$-bromo nitroalkane (1.2:1 mixture of diastereomers), after flash column chromatography (SiO\(_2\), 15% ethyl acetate in hexanes), as a yellow solid (73.2 mg, 76%). The enantiomeric excess of the major and minor diastereomers were determined to be 59 and 62% ee, respectively, by chiral HPLC analysis (Chiralcel AD-H, 20% $i$-PrOH/hexanes, 1.0 mL/min, $t_d$($d_1$e\(_1\), minor) = 16.9 min, $t_d$($d_1$e\(_2\), major) = 52.2 min, $t_d$($d_2$e\(_1\), minor) = 18.3 min, $t_d$($d_2$e\(_2\), major) = 27.3 min) = 18.3, 27.3 min). $R_f$ = 0.22 30% EtOAc/hexanes); mp = 109-112°C; IR (film) 3309, 2927, 1704, 1566, 1514, 1251, 740 cm\(^{-1}\); \(^1\)H NMR\(^5\) (600 MHz, CDCl\(_3\)) $\delta$ 7.79 (d, $J$ = 7.2 Hz, 4H), 7.60 (br s, 4H), 7.42 (t, $J$ = 7.2 Hz, 6H), 7.32 (br s, 4H), 7.23 (br s, 2H), 6.91 (br d, $J$ = 7.4 Hz, 4H), 6.31 (br s, 2H), 6.01 (br s, 1H), 5.62 (br s, 2H), 5.49 (br s, 1H), 5.56 (br s, 2H), 4.43 (br s, 2H), 4.25 (dd, $J$ = 13.2, 6.7 Hz, 2H); \(^1\)C NMR\(^5\) (150 MHz, CDCl\(_3\)) ppm 160.2 (2C), 155.5, 155.3, 143.5 (2C), 141.3 (4C), 128.1 (2C), 127.8, (2C), 127.1 (2C), 125.0, 124.9, 120.0 (2C), 114.6, 114.5, 84.3, 81.3, 67.4 (2C), 58.1, 57.9, 55.3 (2C), 47.1 (2C); HRMS (ESI): Exact mass calcd for C\(_{24}\)H\(_{21}\)BrN\(_2\)O\(_5\) [M+Na]\(^+\) 519.0526, found 519.0540.

$N$-Fmoc-4-Cl-Phenylglycine-$N$-$\alpha$-MeBn (13)

Following General Procedure D, the $\alpha$-bromo nitroalkane (10 mg, 20 µmol) and $\alpha$-methyl benzyl amine (97% ee, 3.0 µl, 20 µmol) provided the amide (single diastereomer), after column chromatography (SiO\(_2\), 20% ethyl acetate in hexanes), as a white solid (6.7 mg, 66% yield). [\(\alpha\)]\(_{D}\)^20 -20.0 (c 0.04, CHCl\(_3\)); $R_f$ = 0.10 (20% EtOAc/hexanes); mp = 224-226°C; IR (film) 3298, 2923, 1684, 1647, 1540 cm\(^{-1}\); \(^1\)H NMR (600 MHz) $\delta$ 7.76 (d, $J$ = 7.2 Hz, 2H), 7.55 (br s, 2H), 7.40 (t, $J$ = 7.8 Hz, 3H), 7.35 (m, 6H), 7.30 (m, 4H), 6.22 (br s, 1H), 5.84 (br s, 1H), 5.15 (br s, 1H), 5.10 (br s, 1H), 4.35 (br s, 2H), 4.18 (br s, 1H), 1.39 (d, $J$ = 6.0 Hz, 3H); \(^1\)C NMR (150 MHz) ppm 168.2, 155.5, 143.7, 143.6, 142.1, 141.2, 136.7, 129.3, 128.8, 128.6, 127.7 (2C), 127.0, 126.1, 125.0, 119.9, 67.1, 58.1, 49.4, 47.1, 21.1; HRMS (ESI): Exact mass calcd for C\(_{31}\)H\(_{28}\)ClN\(_2\)O\(_3\) [M+H]\(^+\) 511.1783, found 511.1807.
**N-Fmoc-4-Cl-Phenylglycine-Leu-O'Bu (14)**

Following General Procedure E, the α-bromo nitroalkane (30 mg, 60 μmol) and the ammonium salt of leucine (27 mg, 120 μmol) provided the dipeptide (single diastereomer) after flash column chromatography (15% ethyl acetate in hexanes) as a white solid (21.3 mg, 62%). \([\alpha]^{20}_D\) -34.2 (c 0.78, CHCl₃); Rf = 0.14 (20% EtOAc/hexanes); mp 146-149 °C; IR (film) 3312, 2958, 2925, 1727, 1662, 1531, 1367, 1245, 1149, 762 cm⁻¹; \(^1\)H NMR (600 MHz, CDCl₃) δ 7.75 (d, \(J = 7.8\) Hz, 2H), 7.56 (br s, 2H), 7.39 (t, \(J = 7.2\) Hz, 2H), 7.33 (br s, 4H), 7.29 (br s, 2H), 6.22 (br s, 1H), 6.09 (br d, \(J = 5.4\) Hz, 1H), 5.20 (br d, \(J = 3.6\) Hz, 1H), 4.47 (br s, 1H), 4.34 (br s, 2H), 4.18 (br s, 1H), 1.51 (br m, 2H), 1.46 (s, 9H), 1.30 (br m, 1H), 0.79 (br s, 6H); \(^{13}\)C NMR (150 MHz, CDCl₃) ppm 171.6, 168.6, 155.4, 143.7, 141.2, 136.8, 134.4, 129.2, 128.6, 127.7, 127.0, 125.0, 119.9, 82.4, 67.1, 58.2, 51.6, 47.1, 41.5, 27.9, 24.8, 22.6, 21.9; HRMS (ESI): Exact mass calcd for C₃₃H₃₈ClN₂O₅ [M+H]^+ 577.2464, found 577.1032.

**N-Cbz-4-Cl-Phenylglycine-Leu-O'Bu (15)**

Following General Procedure E, the α-bromo nitroalkane (25 mg, 60 μmol) and the ammonium salt of leucine (27 mg, 120 μmol) provided the dipeptide (single diastereomer) after flash column chromatography (15% ethyl acetate in hexanes) as a white solid (18.4 mg, 63%). \([\alpha]^{20}_D\) -39.2 (c 0.77, CHCl₃); Rf = 0.19 (20% EtOAc/hexanes); mp 92-95 °C; IR (film) 3315, 2957, 2927, 1727, 1662, 1529, 1493, 1241, 1149 cm⁻¹; \(^1\)H NMR (600 MHz, CDCl₃) δ 7.32 (br s, 9H), 6.16 (br s, 1H), 6.07 (br s, 1H), 5.19 (br s, 1H), 5.10 (d, \(J = 12.0\) Hz, 1H), 5.02 (d, \(J = 12.6\) Hz, 1H), 4.46 (ddd, \(J = 8.4, 8.4, 6.0\) Hz, 1H), 1.49 (br m, 2H), 1.45 (s, 9H), 1.29 (br m, 1H), 0.79 (d, \(J = 6.6\) Hz, 3H), 0.77 (d, \(J = 6.6\) Hz, 3H); \(^{13}\)C NMR (150 MHz, CDCl₃) ppm 171.6, 168.6, 155.4, 136.8, 136.1, 134.4, 129.2, 128.8, 128.5, 128.1, 128.0, 82.4, 67.1, 58.2, 51.6, 41.5, 27.9, 24.7, 22.6, 21.9; HRMS (ESI): Exact mass calcd for C₂₆H₃₃ClN₂NaO₅ [M+Na]^+ 511.1970, found 511.1951.
**N-Alloc-4-Cl-Phenylglycine-Leu-O′Bu (16)**

Following General Procedure E, the α-bromo nitroalkane (22 mg, 60 μmol) and the ammonium salt of leucine (27 mg, 120 μmol) provided the dipeptide (single diastereomer) after flash column chromatography (15% ethyl acetate in hexanes) as a white solid (17.9 mg, 68%). [$\alpha$]$_{D}^{20}$ -47.6 (c 0.86, CHCl$_3$); $R_f$ = 0.14 (20% EtOAc/hexanes); mp 84-86 °C; IR (film) 3314, 2956, 2922, 1728, 1663, 1531, 1368, 1242, 1150 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$) δ 7.32 (s, 4H), 6.15 (d, $J$ = 7.8 Hz, 2H), 5.87 (br s, 1H), 5.28 (br d, $J$ = 15.0 Hz, 1H), 5.19 (br d, $J$ = 9.6 Hz, 2H), 4.55 (dd, $J$ = 13.2, 5.4 Hz, 1H), 4.50 (dd, $J$ = 13.8, 6.0 Hz, 1H), 4.46 (ddd, $J$ = 8.4, 8.4, 5.4 Hz, 1H), 1.53 (dd, $J$ = 8.2, 5.6 Hz, 1H), 1.50 (ddd, $J$ = 8.2, 5.5 Hz, 1H), 1.45 (s, 9H), 1.31 (m, 1H), 0.80 (d, $J$ = 6.6 Hz, 3H), 0.77 (d, $J$ = 6.5 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) ppm 171.7, 168.7, 155.3, 136.8, 134.4, 132.4, 129.1, 128.6, 117.9, 82.4, 65.9, 58.1, 51.6, 41.5, 27.9, 24.7, 22.6, 21.8; HRMS (ESI): Exact mass calcd for C$_{22}$H$_{31}$ClN$_2$NaO$_5$ [M+Na]$^+$ 461.1814, found 461.1797.

**N$_3$Ac-4-Cl-Phenylglycine-Ala-OMe (17)**

Following a modified General Procedure E, the α-bromo nitroalkane (40 mg, 110 μmol) and the ammonium salt of alanine (18.5 mg, 130 μmol), when stirred at 0 °C for 4 h, provided the dipeptide (single diastereomer), after column chromatography (SiO$_2$, 50% ethyl acetate in hexanes), as a white solid (19.3 mg, 50% yield). [$\alpha$]$_{D}^{20}$ -86.7 (c 0.03, CHCl$_3$); $R_f$ = 0.06 (30% EtOAc/hexanes); mp = 165-168 °C (dec); IR (film) 3293, 2923, 2105, 1738, 1645, 1544, 1492, 1222 cm$^{-1}$; $^1$H NMR (600 MHz) δ 7.70 (d, $J$ = 6.9 Hz, 1H), 7.36 (d, $J$ = 8.5 Hz, 2H), 7.32 (d, $J$ = 8.5 Hz, 2H), 6.83 (d, $J$ = 7.3 Hz, 1H), 5.61 (d, $J$ = 7.0 Hz, 1H), 4.56 (dq, $J$ = 7.2, 7.2 Hz, 1H), 4.06 (d, $J$ = 16.6 Hz, 1H), 4.01 (d, $J$ = 16.6 Hz, 1H), 3.77 (s, 3H), 1.31 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (150 MHz) ppm 173.0, 168.6, 166.5, 135.8, 134.6, 129.2, 128.6, 55.9, 52.6, 52.4, 48.3, 17.9; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{16}$ClN$_5$NaO$_4$ [M+Na]$^+$ 376.0783, found 376.0784.