Supporting Information
Enantioselective Synthesis of β-Fluoro Amines via β-Amino α-Fluoro Nitroalkanes and a Traceless Activating Group Strategy

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SI-I-X

Experimental Section

All reagents and solvents were commercial grade and purified prior to use when necessary. Acetonitrile (MeCN), dichloromethane (CH_2Cl_2), and toluene were dried by passage through a column of activated alumina as described by Grubbs[1] for microscale reactions. Flame-dried (under vacuum) glassware was used for all reactions. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Anhydrous magnesium sulfate ($MgSO_4$) was used as a drying agent after extractions unless otherwise indicated.

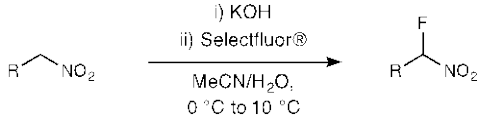
Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μm) plates and flash chromatography utilized 230–400 mesh silica gel from Sorbent Technologies. UV light, and/or the use of *p*-anisaldehyde, potassium permanganate or phosphomolybdic acid solutions were used to visualize products.

IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer and are reported in wavenumbers (cm^{-1}) analyzed as neat films on NaCl plates (transmission). Nuclear magnetic resonance spectra (NMR) were obtained on a Bruker DRX-500 (500 MHz), Bruker AV-400 (400 MHz), or Bruker AV II-600 (600 MHz). Chemical shifts are measured to residual solvent peaks as an internal standard. Mass spectra were recorded on a high resolution Thermo Electron Corporation MAT 95XP-Trap by use of chemical ionization (CI), electron impact ionization (EI), or electro-spray ionization (ESI) by the Indiana University Mass Spectrometry Facility. Optical rotations were measured on a Perkin Elmer-341 polarimeter. Chiral HPLC analysis was conducted on an Agilent 1100 series instrument using the designated ChiralPak column. Absolute configuration was determined by X-ray by the Indiana University Molecular Structure Center.

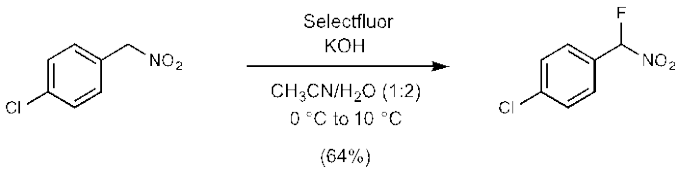
The chiral Brønsted base amidine organocatalysts (mono and bis) and their corresponding acid salts used in this work were prepared according to previous reports from this group.[2]

Preparation of Fluoronitroalkanes and Corresponding Fluoro aza-Henry Products

General Procedure to α-Fluoro Nitroalkanes[3]

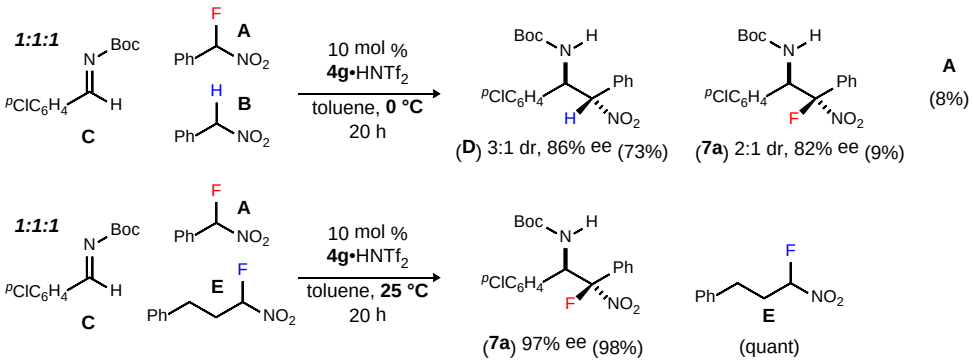


A round bottom flask was charged with the nitroalkane (3.50 mmol) and MeCN/H_2O (2.7 mL/5.4 mL). The solution was cooled to 0 °C, solid KOH (97%) (195 mg, 3.50 mmol) was added, and the reaction was vigorously stirred for 1 h at 0 °C. The reaction mixture was chilled to -20 °C to partially precipitate the nitronate salt and Selectfluor was added as a partially dissolved solution in CH_2Cl_2 which was chilled to -78 °C. This mixture was gradually warmed and vigorously stirred for 30 min or until the reaction exceeded 10 °C. The resulting biphasic mixture was diluted with diethyl ether and stirred for an additional 10 min. The water layer was extracted with diethyl ether, and the combined organics were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (SiO_2) to give the title compound as a colorless oil.



1-Chloro-4-(fluoro(nitro)methyl)benzene (2). This compound was prepared according to the general procedure employing 3.50 mmol of the nitroalkane. The crude oil was purified by flash column chromatography (SiO_2, 1-4% ethyl acetate in hexanes) to give the title compound as a colorless oil (420 mg, 64%). R_f = 0.8 (33% Et_2O/hexanes); IR (film) 3008, 2932, 1579, 1371, 1101 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 6.58 (d, $^2J_{HF}$ = 48.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.4, 129.5 (2C), 128.5 (d, $^2J_{CF}$ = 21.0 Hz), 127.9 (d, $^3J_{CF}$ = 6.0 Hz), 109.2 (d, $^1J_{CF}$ = 239 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) ppm –140.6 (d, J = 48.8 Hz); HRMS (CI): Exact mass calcd for $C_7H_6ClFNO_2$ $[M+H]^+$ 190.0066, found 190.0059.

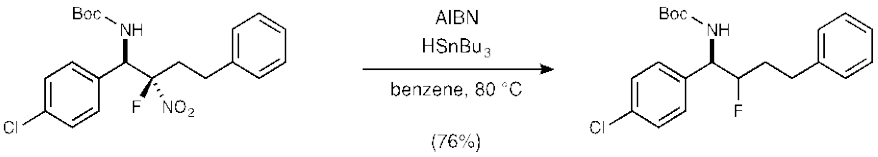
Competition Experiments to Assay Relative Reactivity of Nitroalkane and α-Fluoro Nitroalkanes



SI Scheme 1. Competition Experiments to Assay Relative Reactivity of Nitroalkane and α-Fluoro Nitroalkanes in an Addition Reaction

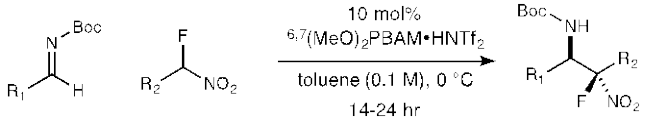
Competition experiments designed to assess relative reactivity of aliphatic and α-fluoro nitroalkanes included the cases summarized in SI Scheme 1, which replicate the trend suggested by relative pK_a (Scheme 1, main text). A competition experiment between α-fluoronitroalkane **A** and its hydrocarbon parent **B** was performed using the optimal catalyst identified in these studies. In the event, formation of the non-fluorinated product (**D**) was observed as the major product. The amount of unreacted **A** and fluorinated product were similar, and a relative rate of 8:1 favors the more reactive hydrocarbon **B**. In a separate experiment, an α-aryl (**A**) and α-alkyl (**E**) fluoronitromethane were compared, but at room temperature due to the lower apparent reactivity for **E** as previously noted [Table 2, entry 10 (main text)]. In this case, sole formation of the benzylic fluoride product **7a** was observed. These behaviors are suggestive of the need for a more Brønsted basic catalyst to activate α-fluoro nitroalkanes, a characteristic that may underpin the lack of prior success.[4] In addition to the thermodynamic effects of fluorine noted above, kinetic effects may also play a role in substrate activation by a bifunctional Brønsted acid/base catalyst. Deprotonation of fluoromethyl acetate compared to methyl acetate, for example, is nearly twice as slow.[5] Reports have also shown that simple fluoronitroalkanes such as fluoronitromethane exhibit decreased C–H acidity, compared to nitromethane, due to destabilizing effects in the carbanion/nitronate via electron-electron repulsion.[6] Collectively, this context and the behaviors outlined here are consistent with rate-limiting nitroalkane deprotonation.

Additional Experiments

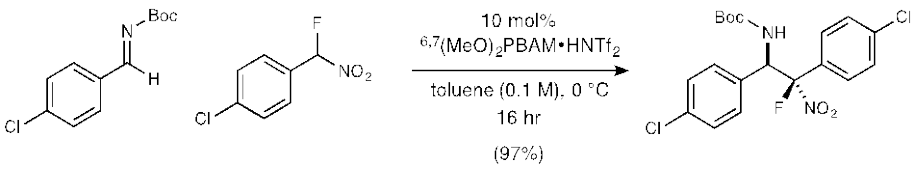


***tert*-Butyl ((1*R*)-1-(4-chlorophenyl)-2-fluoro-4-phenylbutyl)carbamate (S1).** To an oven-dried microwave vial was added the fluoronitroalkane **7h** (5:1 dr, 93% ee; 28 mg, 66 μmol) and benzene (300 μL). In a separate flame-dried vial was added AIBN (4.2 mg, 25 μmol), tributyltin hydride (89 μL, 331 μmol) and benzene (600 μL). Both solutions were subjected to freeze-pump-thaw cycles (-78 °C to RT, 3 cycles) and backfilled with argon. The fluoronitroalkane solution was stirred and heated to 80 °C. The AIBN/tributyltin hydride solution was then added in 4 portions over 60 min by syringe. After 2 h, the reaction mixture was cooled, the volatiles removed by vacuum, and the remaining residue was purified by column chromatography (10% K_2CO_3 in SiO_2 by weight, 2-4-8% ethyl acetate in hexanes) to afford the product as a white foam (19 mg, 76%), which was found to be ~1:1 dr. R_f = 0.9 (25% EtOAc/hexanes); IR (film) 3424, 3320, 3049, 2966, 2918, 2862, 1711, 1496, 1378 cm^{-1}; Mixture of two diastereomers: ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.27 (m, 8H), 7.24-7.17 (m, 8H), 7.11 (d, *J* = 7.2 Hz, 2H), 5.37-5.23 (br m, 2H), 4.80-4.52 (m, 4H), 2.85-2.71 (m, 2H), 2.67-2.62 (m, 1H), 2.16-2.01 (m, 1H), 1.93-1.87 (m, 1H), 1.75-1.60 (m, 3H), 1.44 (br s, 9H), 1.41 (br s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) major diastereomer: ppm 154.9, 140.6, 136.0, 133.5, 128.7, 128.5, 128.4, 128.2, 126.2, 94.7 ($^1J_{CF}$ = 177 Hz), 80.1, 57.0 ($^2J_{CF}$ = 20 Hz), 33.8, 31.3 ($^2J_{CF}$ = 18 Hz), 28.2; minor diastereomer: ppm 155.4, 140.6, 138.4, 133.8, 129.5, 128.8, 128.5, 128.4, 126.2, 94.5 ($^1J_{CF}$ = 178 Hz), 80.1, 56.3 (br), 33.6, 31.2 ($^2J_{CF}$ = 17 Hz), 28.2; ^{19}F NMR (376 Hz, $CDCl_3$) δ −195.8 (minor), –196.5 (major); HRMS (ESI): Exact mass calcd for $C_{21}H_{26}ClFNO_2$ $[M+H]^+$ 378.1631, found 378.1629.

General Procedure to Enantioenriched α-Fluoro β-Amino Nitroalkanes

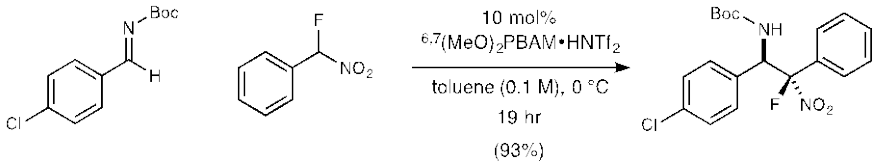


A flame-dried reaction vial was charged with the nitroalkane (55 μmol), toluene (500 μL), and $^{6,7}(MeO)_2$PBAM•$HNTf_2$ (**4g**•$HNTf_2$) (4.5 mg, 5.4 μmol) at room temperature and stirred until homogeneous. The reaction was chilled to 0 °C before the imine (50 μmol) was added. The mixture was stirred at 0 °C for 14-24 h and monitored by TLC. The reaction mixture was quickly flushed through a pad of silica gel and washed through with CH_2Cl_2. The filtrate was concentrated, and the residue was purified by column chromatography (SiO_2, ethyl acetate in hexanes) to afford the title compound.

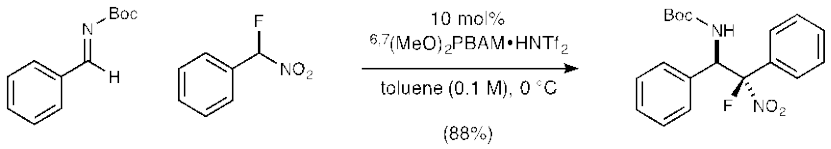


***tert*-Butyl ((1*R*,2*R*)-1,2-bis(4-chlorophenyl)-2-fluoro-2-nitroethyl)carbamate (3).** This compound was prepared according to the general procedure employing 58 μmol of the nitroalkane with a 16 h reaction time. Column chromatography (SiO_2, 2-5% ethyl acetate in hexanes) afforded the adduct as a colorless oil (23 mg,

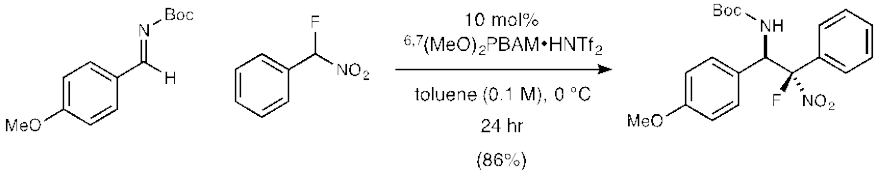
97%), which was found to be 4.8:1 dr and 91% ee for the major diastereomer and 86% ee for the minor diastereomer by chiral HPLC analysis at 230 nm (Chiralpak IA, 7% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 7.15 min, $t_r(d_1e_2$, major/minor) = 8.73 min, $t_r(d_2e_1$, minor/major) = 11.9 min, $t_r(d_2e_2$, minor/minor) = 45.8 min). R_f = 0.85 (25% EtOAc/hexanes); IR (film) 3410, 3313, 2987, 2932, 2869, 1711, 1580, 1502, 1371 cm^{-1}; major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, J = 7.8 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.35-7.31 (m, 4H), 6.15 (dd, J = 28.2, 10.2 Hz, 1H), 5.13 (d, J = 9.6 Hz, 1H), 1.26 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.1, 137.7, 135.4, 131.9, 129.9. 129.5 ($^2J_{CF}$ = 23 Hz), 129.1, 129.0, 127.5 ($^3J_{CF}$ = 9.2 Hz), 118.8 ($^1J_{CF}$ = 243 Hz), 81.1, 57.2 ($^2J_{CF}$ = 18 Hz), 27.9; ^{19}F NMR (376 Hz, $CDCl_3$) δ −139.7 (major), −139.8 (minor); HRMS (ESI): Exact mass calcd for $C_{19}H_{19}Cl_2FN_2NaO_4$ $[M+Na]^+$ 451.0604, found 451.0594.



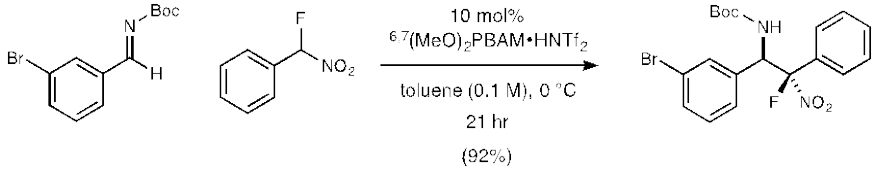
***tert*-Butyl ((1*R*,2*R*)-1-(4-chlorophenyl)-2-fluoro-2-nitro-2-phenylethyl)carbamate (7a).** This compound was prepared according to the general procedure employing 303 μmol of the nitroalkane with a 19 h reaction time. Column chromatography (SiO_2, 3-6% ethyl acetate in hexanes) afforded the adduct as a colorless oil (100 mg, 93%), which was found to be 5.2:1 dr and 95% ee for the major diastereomer by chiral HPLC analysis at 210 nm (Chiralpak IA, 4% EtOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 9.3 min, $t_r(d_1e_2$, major/minor) = 10.3 min, $t_r(d_2e_1$, minor/major) = 12.5 min, $t_r(d_2e_2$, minor/minor) = 24.7 min). R_f = 0.82 (25% EtOAc/hexanes); IR (film) 3425, 3328, 3065, 2982, 2926, 1708, 1583, 1500, 1168 cm^{-1}; major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, J = 7.2 Hz, 2H), 7.50-7.46 (m, 3H), 7.36-7.32 (m, 4H), 6.20 (dd, J = 28.2, 9.6 Hz, 1H), 5.20 (d, J = 9.0 Hz, 1H), 1.24 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.1, 135.2, 132.3, 131.2, 131.0 ($^2J_{CF}$ = 28 Hz), 130.0, 129.0, 128.8, 125.9 ($^3J_{CF}$ = 9.3 Hz), 119.0 ($^1J_{CF}$ = 243 Hz), 80.9, 57.3 ($^2J_{CF}$ = 18 Hz), 27.9; ^{19}F NMR (376 Hz, $CDCl_3$) δ −139.9; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}ClFN_2NaO_4$ $[M+Na]^+$ 417.0993, found 417.0976.



***tert*-Butyl ((1*R*,2*R*)-2-fluoro-2-nitro-1,2-diphenylethyl)carbamate (7b).** This compound was prepared according to the general procedure using the nitroalkane (65.0 mg, 418 μmol) and the imine (78.0 mg, 380 μmol) with a 20 h reaction time. Column chromatography (SiO_2, 15-20% ethyl acetate in hexanes) afforded the product as a colorless oil (120 mg, 88%), which was found to be 3.5:1 dr and 94% ee for the major diastereomer and 84% ee for the minor diastereomer by chiral HPLC analysis at 230 nm (Chiralpak IA, 6% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 7.55 min, $t_r(d_2e_1$, minor/major) = 10.5 min, $t_r(d_1e_2$, major/minor) = 11.3 min, $t_r(d_2e_2$, minor/minor) = 14.5 min). R_f = 0.7 (25% EtOAc/hexanes); IR (film) 3387, 3064, 3034, 2980, 2929, 1697, 1564, 1514, 1163 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 6.4 Hz, 2H), 7.39-7.35 (m, 3H), 7.30-7.22 (m, 4H), 7.10 (m, 1H), 6.14 (dd, J = 28.0, 10.0 Hz, 1H), 5.12 (d, J = 10.0 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.2, 133.7, 131.1, 129.1, 128.8, 128.6 (2C), 128.5, 126.0 ($^2J_{CF}$ = 90 Hz), 118.8 ($^1J_{CF}$ = 241 Hz), 80.9, 57.9 ($^2J_{CF}$ = 20 Hz), 28.0; ^{19}F NMR (376 Hz, $CDCl_3$) δ −139.4 (minor), −139.9 (major); HRMS (CI): Exact mass calcd for $C_{19}H_{22}FN_2O_4$ $[M+H]^+$ 361.1558, found 361.1557.



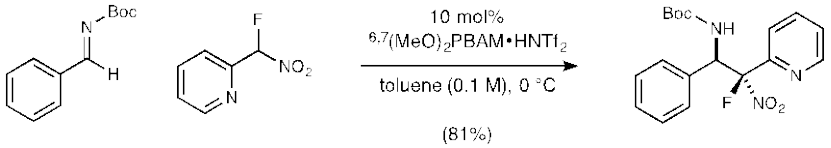
***tert*-Butyl ((1*R*,2*R*)-2-fluoro-1-(4-methoxyphenyl)-2-nitro-2-phenylethyl)carbamate (7c).** This compound was prepared according to the general procedure employing 181 μmol of the nitroalkane with a 24 h reaction time. Column chromatography (SiO_2, 4-7% ethyl acetate in hexanes) afforded the adduct as a colorless oil (60 mg, 86%), which was found to be 5.6:1 dr and 96% ee for the major diastereomer by chiral HPLC analysis at 230 nm (Chiralpak AD-H, 5% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 9.09 min, $t_r(d_2e_1$, minor/major) = 11.2 min, $t_r(d_1e_2$, major/minor) = 12.1 min, $t_r(d_2e_2$, minor/minor) = 18.4 min). R_f = 0.43 (15% EtOAc/hexanes); IR (film) 3416, 3334, 2970, 2935, 1698, 1568, 1513, 1170 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 10.0 Hz, 2H), 7.50-7.43 (m, 3H), 7.36-7.32 (m, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.16 (dd, *J* = 27.6, 12.2 Hz, 1H), 5.15 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 160.0, 154.1. 131.4 ($^2J_{CF}$ = 23.0 Hz), 131.0, 129.8, 128.9 (2C), 126.0 ($^3J_{CF}$ = 10.0 Hz), 119.4 ($^1J_{CF}$ = 243 Hz), 114.2, 80.6, 58.8 ($^2J_{CF}$ = 17.0 Hz), 57.3, 28.0; ^{19}F NMR (376 Hz, $CDCl_3$) δ −140.1; HRMS (ESI): Exact mass calcd for $C_{20}H_{23}FN_2NaO_5$ $[M+Na]^+$ 413.1489, found 413.1479.



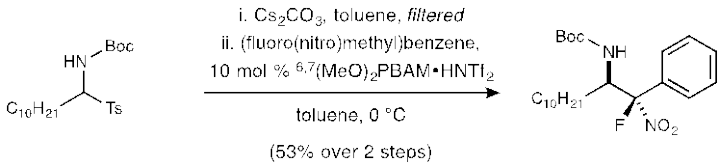
***tert*-Butyl ((1*R*,2*R*)-1-(3-bromophenyl)-2-fluoro-2-nitro-2-phenylethyl)carbamate (7d).** This compound was prepared according to the general procedure employing 119 μmol of the nitroalkane with a 21 h reaction time. Column chromatography (SiO_2, 3-7% ethyl acetate in hexanes) afforded the adduct as a colorless oil (48 mg, 92%), which was found to be 4.8:1 dr and 92% ee for the major diastereomer by chiral HPLC analysis at 210 nm (Chiralpak AD-H, 5% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 9.38 min, $t_r(d_1e_2$, major/minor) = 13.7 min, $t_r(d_2e_1$, minor/major) = 15.3 min, $t_r(d_2e_2$, minor/minor) = 22.8 min). R_f = 0.57 (15% EtOAc/hexanes); IR (film) 3421, 3324, 3069, 2972, 2924, 1710, 1579, 1372, 1165 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 9.8 Hz, 2H), 7.49-7.37 (m, 4H), 7.29-7.22 (m, 2H), 7.12 (m, 1H), 6.20 (dd, *J* = 27.8, 9.2 Hz, 1H), 5.06 (d, *J* = 8.8 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.1, 135.9, 132.3, 131.6, 131.4 ($^2J_{CF}$ = 32.0 Hz), 131.1, 130.3, 128.7 (2C), 125.9 ($^3J_{CF}$ = 10.0 Hz), 122.8, 119.3 ($^1J_{CF}$ = 240 Hz), 81.0, 57.4 ($^2J_{CF}$ = 18.0 Hz), 28.0; ^{19}F NMR (376 Hz, $CDCl_3$) δ −139.8; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}BrFN_2NaO_4$ $[M+Na]^+$ 461.0488, found 461.0479.

***tert*-Butyl ((1*R*,2*R*)-2-fluoro-2-nitro-2-phenyl-1-(pyridin-3-yl)ethyl)carbamate (7e).** This compound was prepared according to the general procedure employing 177 μmol of the nitroalkane with a 23 h reaction time. Column chromatography (SiO_2, 25-55% ethyl acetate in hexanes) afforded the adduct as a colorless oil (50 mg,

86%), which was found to be 6.9:1 dr and 95% ee for the major diastereomer by chiral HPLC analysis at 210 nm (Chiralpak IA, 10% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 11.7 min, $t_r(d_1e_2$, major/minor) = 14.1 min, $t_r(d_2e_2$, minor/minor) = 18.3 min, $t_r(d_2e_1$, minor/major) = 25.4 min). R_f = 0.3 (25% EtOAc/hexanes); IR (film) 3435, 3200, 2979, 2924, 1710, 1572, 1180 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.50 (d, *J* = 4.4 Hz, 1H), 7.73 (d, *J* = 6.8 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.43-7.36 (m, 3H), 7.21-7.17 (m, 1H), 6.20 (dd, *J* = 29.2, 8.4 Hz, 1H), 5.62 (d, *J* = 10.0 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.2, 150.2, 149.8, 136.3, 131.3, 130.6 ($^2J_{CF}$ = 23.0 Hz), 128.8, 125.8 ($^3J_{CF}$ = 9.0 Hz), 123.6, 119.4 ($^1J_{CF}$ = 243 Hz), 81.0, 56.2 ($^2J_{CF}$ = 17.0 Hz), 27.9; ^{19}F NMR (376 Hz, $CDCl_3$) δ −139.6; HRMS (ESI): Exact mass calcd for $C_{18}H_{21}FN_3O_4$ $[M+H]^+$ 362.1519, found 362.1507.

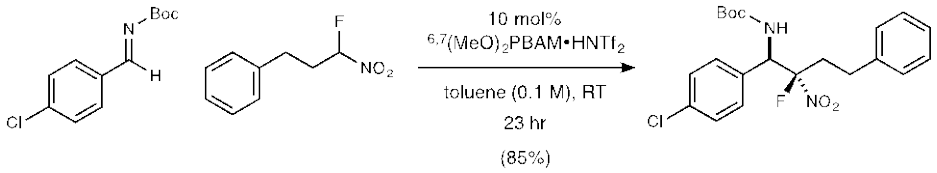


***tert*-Butyl ((1*R*,2*S*)-2-fluoro-2-nitro-1-phenyl-2-(pyridin-2-yl)ethyl)carbamate (7f).** This compound was prepared according to the general procedure using the nitroalkane (46.0 mg, 295 μmol) and imine (58.5 mg, 285 μmol) with a 24 h reaction time. Following filtration, the crude reaction was diluted with DCM and washed with 1.0 M KOH (to remove unreacted nitroalkane). The organics were combined, dried ($MgSO_4$), and filtered. Column chromatography (SiO_2, 15-20% ethyl acetate in hexanes) afforded the product as a colorless oil (83 mg, 81%), which was found to be 2.5:1 dr and 95% ee for the major diastereomer and 94% ee for the minor diastereomer by chiral HPLC analysis at 230 nm (Chiralpak IA, 7% EtOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 12.7 min, $t_r(d_2e_1$, minor/major) = 13.7 min, $t_r(d_1e_2$, major/minor) = 15.9 min, $t_r(d_2e_2$, minor/minor) = 20.8 min). R_f = 0.3 (33% EtOAc/hexanes); IR (film) 3400, 3317, 3061, 2986, 2930, 1705, 1580, 1172 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 1H), 7.78 (ddd, *J* = 9.6, 4.0, 2.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.43-7.41 (m, 1H), 7.40-7.37 (m, 2H), 7.31-7.28 (m, 2H), 7.18-7.14 (m, 1H), 6.22-6-08 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) major diastereomer: ppm 154.2, 150.2 ($^2J_{CF}$ = 28 Hz), 149.2 ($^3J_{CF}$ = 3.0 Hz), 137.4, 134.5, 128.5, 128.5, 128.4, 125.6, 121.5 ($^3J_{CF}$ = 6.0 Hz), 117.5 ($^1J_{CF}$ = 240 Hz), 80.5, 58.0 (br d), 28.1; ^{19}F NMR (376 Hz, $CDCl_3$) δ −134.6 (major), −137.9 (minor); HRMS (ESI): Exact mass calcd for $C_{18}H_{20}FN_3NaO_4$ $[M+Na]^+$ 384.1336, found 384.1325.

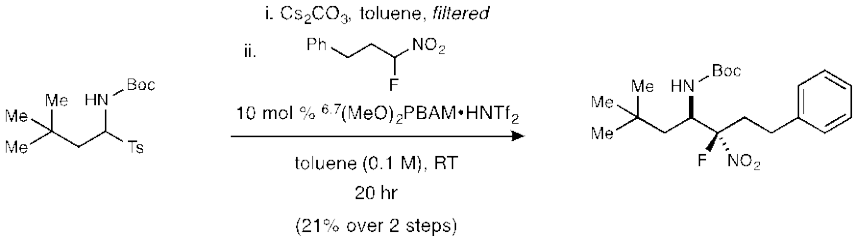


***tert*-Butyl ((1*R*,2*R*)-1-(4-chlorophenyl)-2-fluoro-2-nitro-2-phenylethyl)carbamate (7g).** A vial was charged with the sulfone (85 mg, 200 μmol), Cs_2CO_3 (324 mg, 1.00 mmol), and toluene (1 mL). The heterogeneous mixture was monitored by ^{1}H NMR and stirred at room temperature for 3.5 h. The mixture was carefully loaded onto a plug of Celite and flushed through once with toluene (1 mL) into a separate reaction vial containing (fluoro(nitro)methyl)benzene (37 mg, 240 μmol). The mixture was chilled to 0 °C (or -20 °C) before the catalyst was added (18 mg, 20 μmol) and the reaction stirred for 20 h. The mixture was filtered through a plug of silica gel and concentrated. The residue was purified by column chromatography (SiO_2, 1-3% ethyl acetate in hexanes) to afford the adduct as a colorless oil (45 mg, 53% over 2 steps), which was found to be

6.1:1 dr and 88% ee for the major diastereomer by chiral HPLC analysis at 254 nm (Chiralpak OD-H, 2% ^{i}PrOH/hexanes, 1.0 mL/min: $t_r(d_1e_2$, major/minor) = 5.2 min, $t_r(d_1e_1$, major/major) = 5.5 min, $t_r(d_2e_1$, minor/major) = 6.3 min, $t_r(d_2e_2$, minor/minor) = 8.1 min). R_f = 0.9 (25% EtOAc/hexanes); IR (film) 3425, 3349, 2927, 2858, 1708, 1579, 1175 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.2 Hz, 2H), 7.43-7.38 (m, 3H), 5.18-5.06 (ddd, J = 21.6, 10.8, 10.8 Hz, 1H), 4.39 (d, J = 10.8 Hz, 1H), 1.47-1.33 (m, 4H), 1.31-1.20 (m, 23H), 0.87 (t, J = 8.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.9, 131.5 ($^2J_{CF}$ = 24 Hz), 128.9, 128.4, 125.9 ($^3J_{CF}$ = 10 Hz), 120.1 ($^1J_{CF}$ = 241 Hz), 80.1, 54.4 ($^2J_{CF}$ = 21 Hz), 31.9, 29.5 (2C), 29.4 (2C), 29.3, 29.0, 28.6 ($^4J_{CF}$ = 4 Hz), 28.0, 25.4, 14.1; ^{19}F NMR (376 Hz, $CDCl_3$) δ −141.4 (major), –140.8 (minor); HRMS (ESI): Exact mass calcd for $C_{23}H_{37}FN_2NaO_4$ $[M+Na]^+$ 447.2635, found 447.2635.

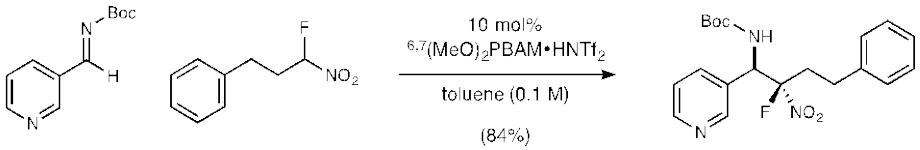


***tert*-Butyl ((1*R*,2*R*)-1-(4-chlorophenyl)-2-fluoro-2-nitro-4-phenylbutyl)carbamate (7h).** This compound was prepared according to the general procedure employing 102 μmol of the nitroalkane with a 23 h reaction time at room temperature. Column chromatography (SiO_2, 2-6% ethyl acetate in hexanes) afforded the adduct as a colorless oil (33 mg, 85%), which was found to be 5.0:1 dr and 93% ee for the major diastereomer by chiral HPLC analysis at 210 nm (Chiralpak IA, 5% EtOH/hexanes, 1.0 mL/min: $t_r(d_2e_1$, minor/major) = 9.2 min, $t_r(d_1e_1$, major/major) = 10.1 min, $t_r(d_1e_2$, major/minor) = 13.9 min, $t_r(d_2e_2$, minor/minor) = 17.7 min). R_f = 0.64 (15% EtOAc/hexanes); IR (film) 3421, 3324, 3027, 2979, 2931, 1710, 1572, 1496 cm^{-1}; major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, J = 8.4 Hz, 2H), 7.32-7.19 (m, 5H), 7.06 (d, J = 7.2 Hz, 2H), 5.57 (d, J = 9.6 Hz, 1H), 5.47 (dd, J = 20.4, 10.2 Hz, 1H), 2.76 (ddd, J = 16.8, 13.2, 4.2 Hz, 1H), 2.61-2.53 (m, 1H), 2.47 (ddd, J = 17.4, 13.8, 4.8 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.3, 138.5, 135.3, 133.0, 129.3, 129.2, 128.7, 128.2, 126.7, 121.5 ($^1J_{CF}$ = 243 Hz), 81.1, 58.1 ($^2J_{CF}$ = 21.0 Hz), 36.7 ($^2J_{CF}$ = 21.0 Hz), 28.1, 28.0; ^{19}F NMR (376 Hz, $CDCl_3$) δ −137.0; HRMS (ESI): Exact mass calcd for $C_{21}H_{24}ClFN_2NaO_4$ $[M+Na]^+$ 445.1306, found 445.1300.

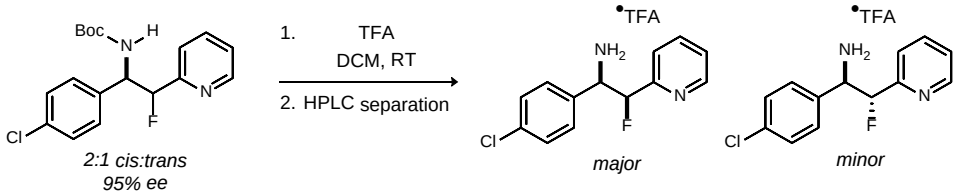


***tert*-Butyl ((3*R*,4*R*)-3-fluoro-6,6-dimethyl-3-nitro-1-phenylheptan-4-yl)carbamate (7i).** A flame-dried vial was charged with the sulfone (36 mg, 100 μmol), Cs_2CO_3 (162 mg, 500 μmol), and toluene (500 μL). The heterogeneous mixture was monitored by ^{1}H NMR and stirred at room temperature for 4.5 h. The mixture was carefully loaded onto a plug of Celite and flushed through once with toluene (500 μL) into a separate reaction vial containing the fluoronitroalkane (20 mg, 110 μmol). The mixture was chilled to 0 °C before the catalyst was added (9.1 mg, 10 μmol) and the reaction stirred for 20 h. The mixture was filtered through a plug of silica gel and concentrated. The residue was purified by column chromatography (SiO_2, 1-4% ethyl acetate in hexanes) to afford the adduct as a colorless oil (8 mg, 21% over 2 steps), which was found to be 10:1 dr and 84% ee for the major diastereomer by chiral HPLC analysis at 210 nm (Chiralpak AD-H, 3% EtOH/hexanes,

1.0 mL/min: $t_r(e_1$, major) = 5.5 min, $t_r(e_2$, minor) = 7.2 min). R_f = 0.8 (15% EtOAc/hexanes); IR (film) 3413, 3346, 2961, 2867, 1707, 1565 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.31-7.27 (m, *J* = 7.2 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 4.61-4.53 (ddd, *J* = 19.8, 14.4, 1.2 Hz, 1H), 4.44 (d, *J* = 10.2 Hz, 1H), 2.76-2.71 (ddd, *J* = 23.5, 12.0, 3.6 Hz, 1H), 2.62 (dddd, *J* = 26.4, 14.4, 12.6, 4.2 Hz, 1H), 2.53-2.48 (ddd, *J* = 25.2, 12.6, 4.8 Hz, 1H), 1.44 (d, *J* = 3.6 Hz, 2H), 1.42 (s, 9H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 155.0, 139.2, 128.6, 128.3, 126.5, 123.1 ($^1J_{CF}$ = 244 Hz), 80.7, 52.4 ($^2J_{CF}$ = 21 Hz), 42.6, 35.5 ($^2J_{CF}$ = 21 Hz), 30.0, 29.4, 28.3, 28.1 ($^3J_{CF}$ = 4 Hz); ^{19}F NMR (376 Hz, $CDCl_3$) δ −140.1 (major), –140.8 (minor); HRMS (ESI): Exact mass calcd for $C_{20}H_{31}FN_2NaO_4$ $[M+Na]^+$ 405.2166, found 405.2158.



***tert*-Butyl ((1*R*,2*R*)-2-fluoro-2-nitro-4-phenyl-1-(pyridin-3-yl)butyl)carbamate (7j).** This compound was prepared according to the general procedure using the nitroalkane (23.0 mg, 126 μmol) and imine (23.5, 114 μmol) with a 22 h reaction time at room temperature. Column chromatography (SiO_2, 40% ethyl acetate in hexanes) afforded the product as a colorless oil (37 mg, 84%), which was found to be 4.4:1 dr and 96% ee for the major diastereomer and 90% ee for the minor diastereomer by chiral HPLC analysis at 210 nm (Chiralpak IA, 10% EtOH/hexanes, 1.0 mL/min: $t_r(d_2e_2$, minor/minor) = 9.6 min, $t_r(d_2e_1$, minor/major) = 10.4 min, $t_r(d_1e_2$, major/minor) = 12.8 min, $t_r(d_1e_1$, major/major) = 14.1 min). R_f = 0.5 (50% EtOAc/hexanes); IR (film) 3421, 3324, 3027, 2979, 2931, 1710, 1496 cm^{-1}; major diastereomer: ^1H NMR (600 MHz, $CDCl_3$) δ 8.62 (m, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.33-7.23 (m, 3H), 7.15-7.08 (m, 1H), 7.06 (d, *J* = 6.6 Hz, 2H), 5.82 (br d, *J* = 9.0 Hz, 1H), 5.54 (dd, *J* = 20.4, 10.2 Hz, 1H), 2.76 (ddd, *J* = 25.2, 12.6, 4.2 Hz, 1H), 2.60 (ddd, *J* = 30.0, 16.2, 3.6 Hz, 1H), 2.47 (ddd, *J* = 15.6, 12.6, 4.2 Hz, 1H), 2.11-2.09 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.7, 150.5, 149.2, 138.3, 135.3, 130.5, 128.7, 128.2, 126.8, 123.8, 121.3 ($^1J_{CF}$ = 244 Hz), 81.5, 56.7 ($^2J_{CF}$ = 21 Hz), 36.8 ($^2J_{CF}$ = 20 Hz), 29.7, 28.1; ^{19}F NMR (376 Hz, $CDCl_3$) δ −137.0 (major), –136.8 (minor); HRMS (ESI): Exact mass calcd for $C_{20}H_{25}FN_3O_4$ $[M+H]^+$ 390.1829, found 390.1823.



***cis*- and *trans*-2-Fluoro-1-phenyl-2-(pyridin-2-yl)ethan-1-amine (8).** To a flask was added the Boc-amine (80 mg, 253 μmol) in dichloromethane (3 mL) under argon. Trifluoroacetic acid (TFA) (580 μL, 7.59 mmol) was added in one portion and the mixture was stirred for 2.5 h. The mixture was diluted with dichloromethane and quenched with satd aq $NaHCO_3$. The organics were combined, dried ($MgSO_4$), filtered and concentrated to a yellow oil that was pure by ^1H NMR (54 mg, 98%). Separation of both diastereomers on reverse phase preparatory HPLC (5-25% aqueous acetonitrile, 210 nm, flow rate: 8 mL/min, R_t = 15.0 min (major), 17.2 min (minor)) afforded the pure diastereomers as their TFA salt.

Major diastereomer ((+)-*cis*-**8**): light yellow oil; $[\alpha]_D^{20}$ +44.6 (*c* 1.25, EtOH, (1*R*,2*S*)-β-fluoroamine); R_f = 0.1

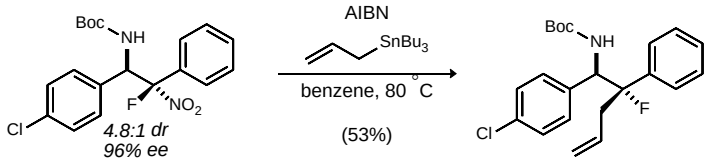
(10% MeOH/CH_2Cl_2); IR (film) 3422, 3048, 2917, 2768, 2681, 1204, 1142 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 8.59 (d, *J* = 5.8 Hz, 1H), 7.82 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.42-7.36 (m, 6H), 5.92 (dd, *J* = 47.2, 7.6 Hz, 1H), 5.09 (dd, *J* = 14.0, 7.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) ppm 161.1 (q, $^2J_{CF}$ = 44.0 Hz), 154.5 (d, $^2J_{CF}$ = 20.0 Hz), 150.6, 139.1, 133.8 (d, $^3J_{CF}$ = 5.0 Hz), 130.9, 130.3, 129.2, 126.2 (d, $^4J_{CF}$ = 2.0 Hz), 124.8 (d, $^3J_{CF}$ = 5.0 Hz), 116.2 (q, $^1J_{CF}$ = 284 Hz), 94.9 ($^1J_{CF}$ = 179 Hz), 58.8 ($^2J_{CF}$ = 21 Hz); ^{19}F NMR (376 Hz, MeOD) δ −181.7; HRMS (ESI): Exact mass calcd for $C_{13}H_{14}FN_2$ $[M+H]^+$ 217.1141, found 217.1137.

Minor diastereomer ((+)-*trans*-**8**): yellow oil; $[\alpha]_D^{20}$ +22 (*c* 0.33, DMSO, (1*R*,2*R*)-β-fluoroamine); R_f = 0.1 (10% MeOH/CH_2Cl_2); IR (film) 3391, 3060, 2922, 2860, 2640, 1675, 1207, 1138 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 8.61 (dd, *J* = 4.2, 0.6 Hz, 1H), 7.69 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.35-7.29 (m, 4H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.06 (dd, *J* = 48.0, 3.6 Hz, 1H), 5.02 (dd, *J* = 24.6, 3.6 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) ppm 161.8 (q, $^2J_{CF}$ = 44.0 Hz), 155.7 (d, $^2J_{CF}$ = 24.0 Hz), 150.2, 138.7, 132.6, 130.6, 129.9, 129.5, 125.3, 122.5 (d, $^3J_{CF}$ = 7.5 Hz), 118.8 (q, $^1J_{CF}$ = 284 Hz), 94.6 ($^1J_{CF}$ = 180 Hz), 59.1 ($^2J_{CF}$ = 21 Hz); ^{19}F NMR (376 Hz, MeOD) δ –197.9; HRMS (ESI): Exact mass calcd for $C_{13}H_{14}FN_2$ $[M+H]^+$ 217.1141, found 217.1137.

The levorotatory diastereomers ((–)-cis/trans-**8**) were prepared using (*S*,*S*)-**4g**·$HNTf_2$ following an identical aza-Henry reaction procedure to access **7f**. The aza-Henry adduct *ent*-**7f** was found to be 2.3:1 dr and 96% ee for the major diastereomer and 94% ee for the minor diastereomer by chiral HPLC analysis (see general entry for **7f** for additional details). Separation of both (–)-cis/trans-**8** diastereomers on reverse phase preparatory HPLC [5-25% aqueous (0.1% TFA) acetonitrile, 210 nm, flow rate: 8 mL/min, R_t = 14.8 min (major), 16.4 min (minor)] afforded the pure diastereomers as their TFA salt, with spectroscopic data identical to their enantiomers.

Major diastereomer ((–)-*cis*-**8**): $[\alpha]_D^{20}$ –53 (*c* 0.45, EtOH, (1*S*,2*R*)-β-fluoroamine).

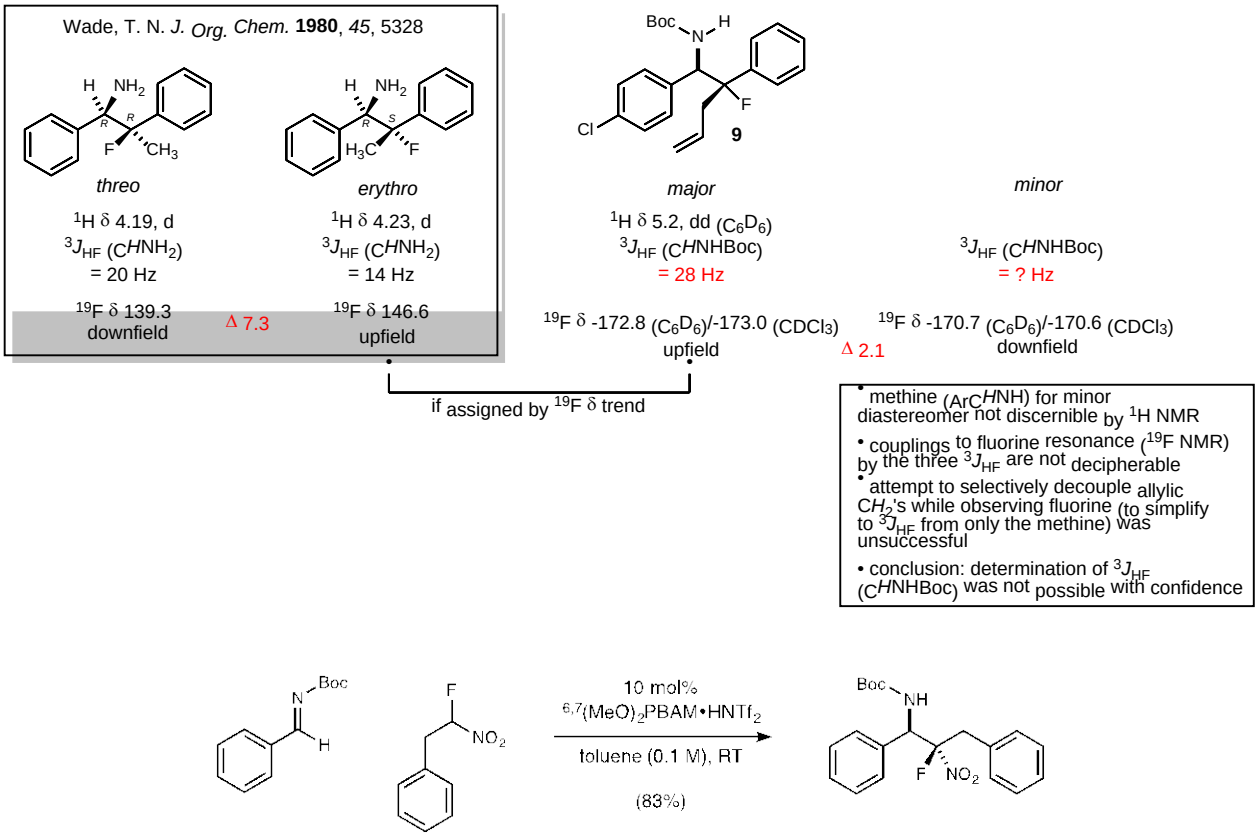
Minor diastereomer ((–)-*trans*-**8**): $[\alpha]_D^{20}$ –54 (*c* 0.35, EtOH, (1*S*,2*S*)-β-fluoroamine).



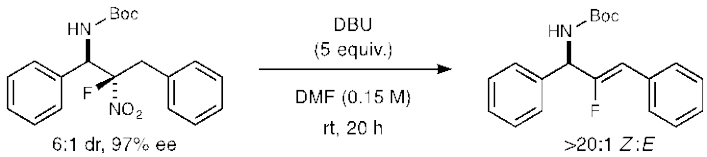
***tert*-Butyl ((1*R*,2*R*)-1-(4-chlorophenyl)-2-fluoro-2-phenylpent-4-en-1-yl)carbamate (9).** To an oven dried vial was added the fluoronitroalkane (25 mg, 63 μmol) and benzene (300 μL). In a separate flame-dried vial was added AIBN (4.2 mg, 25 μmol), allyl tributyltin (196 μL, 634 μmol) and benzene (800 μL). Both solutions were subjected to freeze-pump-thaw cycles (-78 °C to RT, 3 cycles) and backfilled with argon. The fluoronitroalkane solution was heated to 80 °C and stirred. The AIBN/allyl tributyltin solution was then added in 4 portions to the heating stirring solution over 60 min by syringe. After 2 h, the reaction mixture was cooled, the volatiles evaporated, and the remaining residue was purified by column chromatography (10% K_2CO_3 in SiO_2 by weight, 2-7% ethyl acetate in hexanes) to afford the adduct as a white foam (13 mg, 53%), which was found to be >10:1 dr. $[\alpha]_D^{20}$ +123 (*c* 0.35, $CHCl_3$); R_f = 0.9 (25% EtOAc/hexanes); IR (film) 3447, 3378, 2984, 2922, 2362, 1695, 1513, 1493, 1166 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21-7.14 (m, 3H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 7.2 Hz, 2H), 6.90 (d, *J* = 7.8 Hz, 2H), 5.54 (dddd, *J* = 18.6, 13.8, 10.2, 6.6 Hz, 1H), 5.41 (d, *J* = 9.2 Hz, 1H), 5.05 (d, *J* = 16.2 Hz, 1H), 5.04-4.90 (m, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 3.06 (ddd, *J* = 21.0, 14.4, 7.2 Hz, 1H) 2.84 (ddd, *J* = 21.6, 14.4, 6.6 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 155.3, 139.0 ($^2J_{CF}$ = 21 Hz), 136.5, 133.1, 129.7, 128.0, 127.9, 127.4, 124.9 ($^3J_{CF}$ = 12 Hz), 119.0, 100.8 ($^1J_{CF}$ = 243 Hz),

80.2, 60.9 ($^2J_{CF}$ = 20 Hz), 41.8 ($^2J_{CF}$ = 20 Hz), 28.4, 28.0; ^{19}F NMR (376 Hz, $CDCl_3$) δ −173.0; HRMS (ESI): Exact mass calcd for $C_{22}H_{25}ClFNNaO_2$ $[M+Na]^+$ 412.1456, found 412.1458.

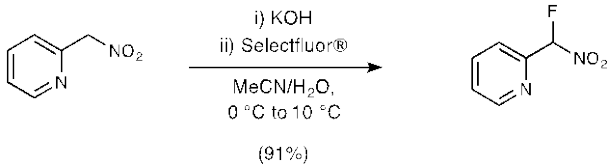
Assignment of relative stereochemistry as shown is based on relative chemical shifts by ^{19}F NMR. Attempts to determine $^3J_{HF}$ of the amine-substituted methine hydrogen were unsuccessful for the minor diastereomer. As a result, the assignment should be considered tentative.



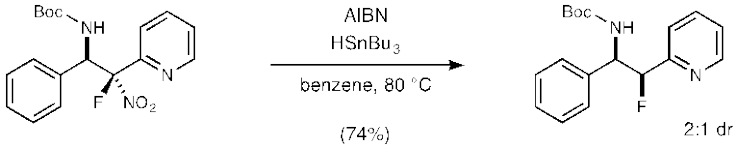
***tert*-Butyl ((1*R*,2*R*)-2-fluoro-2-nitro-1,3-diphenylpropyl)carbamate (10).** This compound was prepared according to the general procedure using the nitroalkane (55.0 mg, 327 μmol) and the imine (61.0 mg, 297 μmol) with a 36 h reaction time. Column chromatography (SiO_2, 5-10% ethyl acetate in hexanes) afforded the product as a colorless oil (92 mg, 83%), which was found to be 6:1 dr and 97% ee for the major diastereomer and 84% ee for the minor diastereomer by chiral HPLC analysis at 210 nm (Chiralpak IB, 3% EtOH/hexanes, 1.0 mL/min: $t_r(d_1e_1$, major/major) = 9.1 min, $t_r(d_2e_2$, minor/minor) = 10.0 min, $t_r(d_1e_2$, major/minor) = 10.8 min, $t_r(d_2e_1$, minor/major) = 14.5 min). R_f = 0.7 (25% EtOAc/hexanes); IR (film) 3424, 3320, 3035, 2980, 2985, 1697, 1572, 1510, 1177 cm^{-1}; major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.38 (m, 5H), 7.27-7.24 (m, 3H), 7.07-7.06 (m, 2H), 5.65 (br d, *J* = 9.8 Hz, 1H), 5.52 (dd, *J* = 20.0, 10.0 Hz, 1H), 3.57-3.44 (m, 1H), 3.06 (dd, *J* = 18.4, 9.8 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 154.3, 130.0, 129.2, 129.1, 128.7 (2C), 128.2, 128.0, 121.2 ($^1J_{CF}$ = 245 Hz), 80.9, 58.9 ($^2J_{CF}$ = 19 Hz), 41.0 ($^2J_{CF}$ = 20 Hz), 28.1; ^{19}F NMR (376 Hz, $CDCl_3$) δ −136.5 (minor), −139.5 (major); HRMS (CI): Exact mass calcd for $C_{20}H_{23}FN_2NaO_4$ $[M]^+$ 397.1540, found 397.1534.



***tert*-Butyl (*R*,*Z*)-(2-fluoro-1,3-diphenylallyl)carbamate (11).** To a vial was added the fluoronitroalkane (22 mg, 59 μmol) in dimethylformamide (392 μL) under argon. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (44 μL, 294 μmol) was added in one portion and the mixture was stirred at room temperature for 20 h. The mixture was quenched with water and the aqueous layer was extracted three times with diethyl ether. The organics were combined, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (SiO_2, 15% diethyl ether in hexanes) to afford the product as a clear oil (10 mg, 53%), which was found to be >20:1 *Z*:*E*. $[\alpha]_D^{20}$ –4.5 (*c* 0.2, $CHCl_3$); R_f = 0.45 (25% Et_2O/hex); IR (film) 3420, 3324, 2979, 2917, 2855, 1697, 1504, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 1H), 7.40-7.31 (m, 9H), 5.84 (d, *J* = 38.8 Hz, 1H), 5.53 (br, 1H), 5.19 (br, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 154.8, 149.7 (d, $^1J_{CF}$ = 261 Hz), 138.1, 132.7, 128.8, 128.7 (d, $^3J_{CF}$ = 7.0 Hz), 128.5, 128.2, 127.5 (d, $^4J_{CF}$ = 2.0 Hz), 126.9, 107.9 (d, $^2J_{CF}$ = 8.0 Hz), 77.2, 70.5, 28.3; ^{19}F NMR (376 Hz, $CDCl_3$) δ −113.9; HRMS (ESI): Exact mass calcd for $C_{20}H_{22}FNNaO_2$ $[M+Na]^+$ 350.1532, found 350.1530.

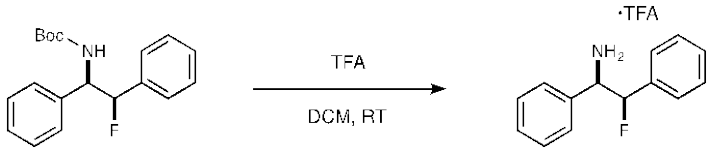


2-(Fluoro(nitro)methyl)pyridine (S2). This compound was prepared according to the general procedure employing 753 μmol of the nitroalkane. The crude oil was purified by flash column chromatography (SiO_2, 30% ethyl acetate in hexanes) to give the title compound as a colorless oil (107 mg, 91%). R_f = 0.55 (33% Et_2O/hexanes); IR (film) 3069, 2934, 2988, 1586, 1377 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.2 Hz, 1H), 7.89-7.85 (m, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.47 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.72 (d, $^2J_{HF}$ = 49.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 150.1, 149.2 (d, $^2J_{CF}$ = 22.5 Hz), 137.7, 126.3, 121.5 (d, $^3J_{CF}$ = 4.5 Hz), 109.1 (d, $^1J_{CF}$ = 239 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) ppm –142.5; HRMS (CI): Exact mass calcd for $C_6H_5FN_2O_2$ $[M]^+$ 157.0408, found 157.0406.



***tert*-Butyl ((1*R*)-2-fluoro-1-phenyl-2-(pyridin-2-yl)ethyl)carbamate (S3).** To an oven-dried microwave vial was added the fluoronitroalkane (20 mg, 55 μmol) and benzene (300 μL). In a separate flame-dried vial was added AIBN (3.6 mg, 22 μmol), tributyltin hydride (75 μL, 277 μmol) and benzene (400 μL). Both solutions were subjected to freeze-pump-thaw cycles (-78 °C to RT, 3 cycles) and backfilled with argon. The fluoronitroalkane solution was stirred and heated to 80 °C. The AIBN/tributyltin hydride solution was then added in 4 portions over 40 minutes by syringe. After 2 hours, the reaction mixture was cooled, the volatiles evaporated, and the remaining residue was purified by column chromatography (10% K_2CO_3 in SiO_2 by weight, 25-30% diethyl ether in hexanes) to afford the product as an off-white foam (14 mg, 74%), which was found to

be ~2:1 dr. R_f = 0.3 (33% Et_2O/hexanes); IR (film) 3428, 3317, 2979, 2924, 1710, 1503, 1179 cm^{-1}; major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 5.6, 0.8 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.29-7.26 (m, 4H), 7.24-7.21 (m, 1H), 7.20-7.16 (m, 1H), 7.07 (br m, 1H), 5.87-5.75 (m, 2H), 5.34 (br m, 1H), 1.33 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 156.7, 154.9, 148.8 (d, $^3J_{CF}$ = 3.0 Hz), 136.4, 128.3, 127.7, 127.6, 127.0, 123.1, 120.4 (d, $^3J_{CF}$ = 5.0 Hz), 94.9 ($^1J_{CF}$ = 180 Hz), 79.6, 57.2 ($^2J_{CF}$ = 21 Hz), 28.2; ^{19}F NMR (376 Hz, $CDCl_3$) δ −194.57 (minor), –197.9 (major); HRMS (ESI): Exact mass calcd for $C_{18}H_{21}FN_2O_2$ $[M+Na]^+$ 339.1485, found 339.1470.



(1*R*,2*R*)-2-Fluoro-1,2-diphenylethan-1-amine trifluoroacetic acid salt (S4). To a flask was added the Boc-amine (6:1 dr, 24 mg, 76 μmol) in dichloromethane (700 μL) under argon. Trifluoroacetic acid (TFA) (115 μL, 1.52 mmol) was added in one portion and the mixture was stirred for 60 min. The mixture was diluted with dichloromethane and quenched with satd aq $NaHCO_3$. The organics were combined, dried ($MgSO_4$), filtered and concentrated to a yellow oil that was pure by ^1H NMR (15 mg, 97%). The mixture was redissolved in dichloromethane (1 mL) and TFA (10 μL) was added and the mixture was stirred for 10 min at room temperature. The volatiles were evaporated to afford the title compound as a tan oil. R_f = 0.2 (EtOAc); IR (film) 3038, 2913, 2858, 2629, 1646, 1529, 1182 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 7.38-7.22 (m, 8H), 7.07-7.05 (d, *J* = 6.4 Hz, 2H), 6.07 (dd, *J* = 47.2, 3.2 Hz, 1H), 4.74 (dd, *J* = 26.8, 3.2 Hz, 1H); ^{13}C NMR (150 MHz, MeOD) ppm 135.8 (d, $^2J_{CF}$ = 20.0 Hz), 132.6, 130.8 (d, $^3J_{CF}$ = 4.0 Hz), 130.3, 129.9, 129.7, 129.4, 126.7 (d, $^3J_{CF}$ = 7.0 Hz), 94.3 ($^1J_{CF}$ = 180 Hz), 60.5 ($^2J_{CF}$ = 21 Hz); ^{19}F NMR (376 Hz, MeOD) δ −196.4. The free base and the TFA salt matched previously reported data.[7]

Chemical Correlation to Determine Relative and Absolute Stereochemistry of Reductive Denitration Products

Compound **S4**: Ph-Ph β-fluoroamine (RNH_2)

R	Ph (lit.)	**d_1 (maj)**	Δ (maj)	Ph (lit.)	**d_2 (min)**	Δ (min)
diastereomer	*eryth*	-	-	*threo*	-	-
δH-β	5.47	**5.51**	0.04	5.41	**5.44**	0.03
δH-α	4.27	**4.36**	0.09	4.26		
δ_F [a]	-18.7	**-16.0**	2.7	-21.4	**-17.66**	3.74
$^3J_{(HH)}$	5.9	**6.0**	0.1	7.0	**6.8**	0.2
$^3J_{(FH)}$	12.9	**13.2**	0.3	14.35		

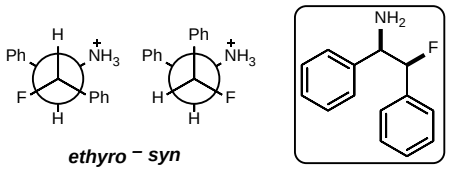
[a] Shift reported as compared to hexafluorobenzene, –164.9 ppm in $CDCl_3$

Compound **S4**:Ph-Ph β-fluoro ammonium (RNH_3^+TFA)

R	Ph (lit.)	Ph (lit.)	**d_1 (maj)**	Δ (maj)
config	*threo*	*eryth*	-	-
δH-β	5.64	6.00	**6.07**	0.07
δH-α	4.43	4.43	**4.74**	0.31
δ_F [a]	-8.7	-32.1	**-31.5**	0.4
$^3J_{(HH)}$	8.0	3.0	**3.2**	0.2
$^3J_{(FH)}$	8.7	26.5	**26.4**	0.1

[a] Shift reported as compared to hexafluorobenzene, –164.9 ppm in $CDCl_3$

Therefore, MAJOR diastereomer from the denitration reaction is erythro (pictured):[7]



ethyro – syn

Determination of the Absolute Configuration of 3 (Single Crystal X-ray)

Crystal data and structure refinement for 15060.

Empirical formula	C19 H19 Cl2 F N2 O4	
Formula weight	429.26	
Crystal color, shape, size	colorless block, 0.31 × 0.29 × 0.24 mm^3	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Monoclinic, $P2_1$	
Unit cell dimensions	a = 9.5907(2) Å	α= 90°.
	b = 17.2393(4) Å	β= 109.6016(11)°.
	c = 13.3259(3) Å	γ = 90°.
Volume	2075.58(8) $Å^3$	
Z	4	
Density (calculated)	1.374 Mg/m^3	
Absorption coefficient	0.348 mm^{-1}	
F(000)	888	

Data collection

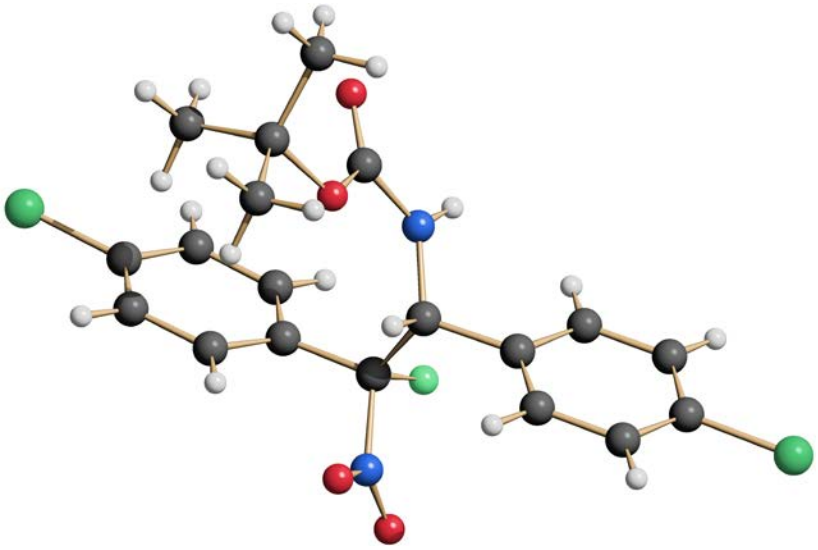
Diffractometer	APEX II Kappa Duo, Bruker
Theta range for data collection	1.62 to 27.52°.
Index ranges	-12<=h<=12, -22<=k<=22, -17<=l<=17
Reflections collected	30851
Independent reflections	9578 [R(int) = 0.0330]
Observed Reflections	9047
Completeness to theta = 27.52°	99.9 %

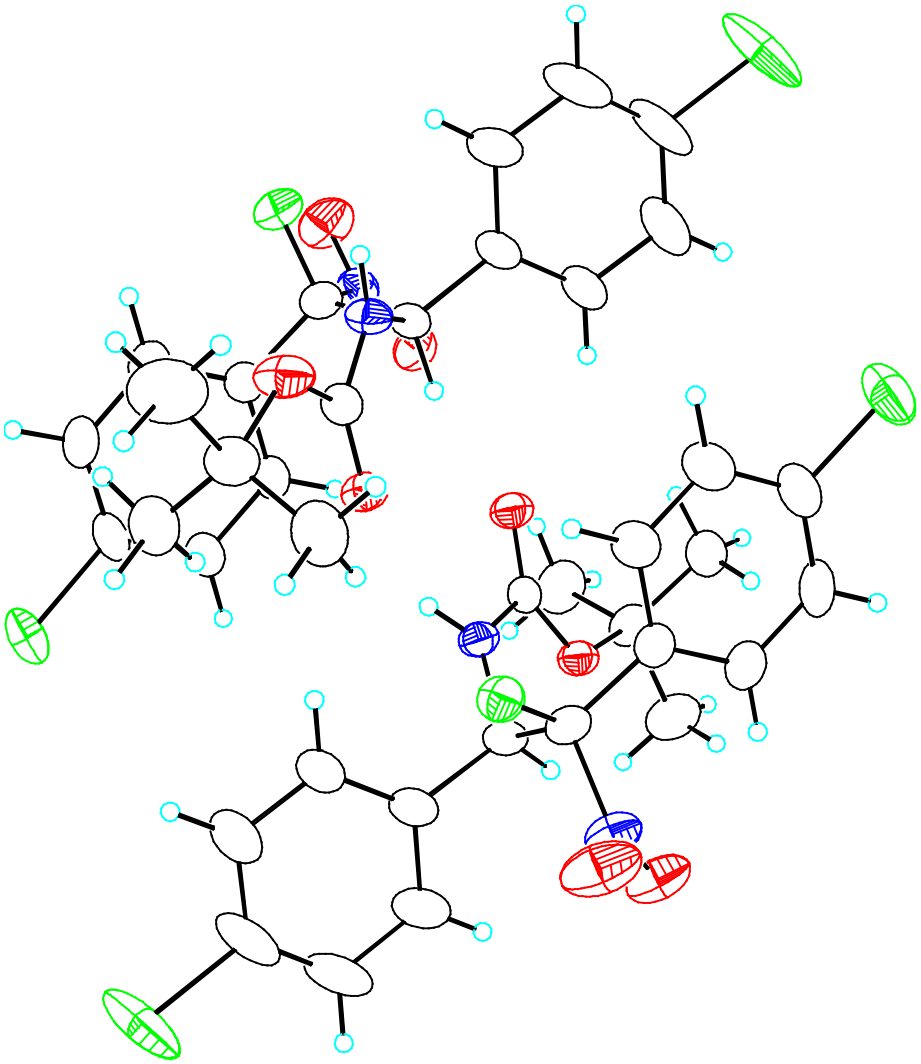
Solution and Refinement

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9211 and 0.8997
Solution	Intrinsic methods
Refinement method	Full-matrix least-squares on F^2
Weighting scheme	$w = [\sigma^2 Fo^2 + AP^2 + BP]^{-1}$, with
	$P = (Fo^2 + 2\,Fc^2)/3$, A = 0.0461, B = 0.4770
Data / restraints / parameters	9578 / 1 / 511
Goodness-of-fit on F^2	1.024
Final R indices [I>2sigma(I)]	R1 = 0.0333, wR2 = 0.0864
R indices (all data)	R1 = 0.0358, wR2 = 0.0888
Absolute structure parameter	-0.01(3)
Largest diff. peak and hole	0.423 and -0.433 $e.Å^{-3}$

Structure solution and refinement

The space group $P2_1$ was determined based on intensity statistics and systematic absences. The structure was solved and refined using the SHELX suite of programs.[8] An intrinsic-methods solution was calculated, which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed, which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final anisotropic full-matrix least-squares refinement on F^2 with 511 variables converged at R1 = 3.32%, for the observed data and wR2 = 8.87% for all data. The goodness-of-fit was 1.023. The largest peak in the final difference electron density synthesis was 0.423 $e^-/Å^3$ and the largest hole was -0.433 $e^-/Å^3$ with an RMS deviation of0.039 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.374 g/cm^3 and F(000), 888 e^-. The remaining electron density is minuscule and located near bonds.





Formula unit (two crystallographically independent molecules).

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