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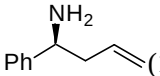
Supporting Information

Highly Diastereoselective and Enantioselective Preparation of Homoallylic Amines. Application for the Synthesis of ß-Amino Acids and γ-Lactams.

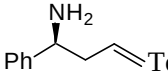
P. Veeraraghavan Ramachandran and Thomas E. Burghardt

Experimental procedures and spectral data

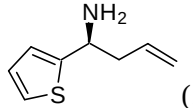
Preparation of *N*-silylimines, *N*-aluminoimines, and all 'allyl'boration reactions were carried out under nitrogen atmosphere. THF was distilled from sodium benzophenone ketyl prior to use; all other chemicals and solvents were purchased commercially and used without further purification; (–)-*B*-allyldiisopinocampheylborane (**I**) was prepared according to Brown's procedure by the treatment of (–)-B-methoxydiisopinocampheylborane with allylmagnesium bromide. The NMR chemical shifts (d) are reported in ppm.



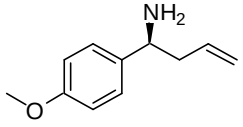
(1*S*)-1-phenylbut-3-en-1-amine (**2a**) from *N*-silyl imine (**1a**). To a stirring solution of (–)-*B*-allyldiisopinocampheylborane (**I**; 1 M in pentane; 6 mL, 6 mmol) diluted with THF (5 mL) and cooled to –78 °C was added **1a** (0.9 g, 5.1 mmol), followed by a slow addition of water (0.09 mL, 5.0 mmol) in THF (0.5 ml). The mixture was stirred for 1 h at –78 °C and it was oxidised with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL) and was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was then extracted with Et_2O (3×50 mL), treated with HCl (30% in H_2O; 3 mL), and stirred for 0.2 h. To the mixture was added water (50 mL) to extract the product. After removal of the organic layer, the aqueous solution of amine hydrochloride was neutralised with NaOH until pH~8. The resulting amine was extracted with Et_2O (3×50 mL), the solvent was removed under reduced pressure, and the material was purified on silica gel (hexanes:ethyl acetate:triethylamine 84.5:15:0.5) to afford 0.66 g (4.5 mmol, 90% yield) of **2a** having 92% ee (HPLC analysis using Chiracel OD-H column and hexanes/isopropanol/triethylamine as the mobile phase). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.69 (br s, 2H), 2.32-2.50 (m, 2H), 4.00 (d, J = 8.0 Hz, 1H), 5.07-5.15 (m, 2H), 5.69-5.82 (m, 1H), 7.22-7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 44.2, 55.4, 117.7, 126.4, 127.0, 128.5, 135.5, 145.8. MS (EI): 128, 106 [Ph-CH^+-NH_2], 79; (CI): 148 [M+H], 131 [M–NH_3]; HRMS: 148.1126 (calc.), 148.1129 (actual). $[a]^{20}_D$ = +43 ($CHCl_3$, c =1.9), lit.:+42, $CHCl_3$, c =0.5).



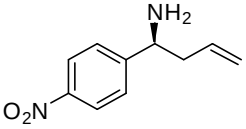
To a solution of benzonitrile (**3a;** 0.52 mL, 5.05 mmol) in Et_2O (5 mL) cooled to 0 ºC was added DIBAL-H (0.89 mL, 5.0 mmol) and the mixture was stirred for 1 h. The obtained *N*-aluminoimine (**4a;** ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.14-0.19 (m, 3H), 0.76-1.07 (m, 12H), 1.79 (m qn, J = 6.6 Hz, 3H), 7.48-7.80 (m, 5H), 9.00 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 22.7, 22.8, 26.3, 26.5, 28.2, 28.3, 28.5, 28.7, 129.4, 129.5, 132.4, 132.8, 133.0, 137.1, 174.5, 175.0) was transferred *via* canula to a solution of **I** (1 M in pentane; 6 mL, 6 mmol) diluted with Et_2O (7 mL) and cooled to –100 °C, followed by a slow addition of methanol (0.20 mL, 5.0 mmol). The mixture was stirred for 3 h, while it was allowed to slowly warm from –100 °C to –78 °C and it was oxidised with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL) and was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was then extracted with Et_2O (3×50 mL), treated with HCl (20% in H_2O; 5 mL), and stirred for 0.2 h. To the mixture was added water (50 mL) to extract the product. After removal of the organic layer, the aqueous solution of amine hydrochloride was neutralised with NaOH until pH~8. The resulting amine was extracted with Et_2O (3×50 mL), the solvent was removed under reduced pressure, and the material was purified on silica gel (hexanes:ethyl acetate:triethylamine 84.5:15:0.5) to afford 0.66 g (4.5 mmol, 90% yield) of **2a** with 88% ee as analysed by the HPLC, having identical spectral data to the reported above. $[a]^{20}_D$ = +39 ($CHCl_3$, c =0.10), lit.: +42 ($CHCl_3$, c =0.5).



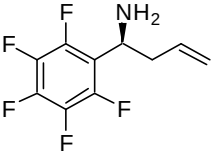
(1*S*)-1-thien-2-ylbut-3-en-1-amine (**2b**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 1.84 (br s, 2H), 2.35-2.75 (m, 2H), 4.29 (t, J = 5.2 Hz, 1H), 5.10-5.19 (m, 1H), 5.68-5.89 (m, 1H), 6.92-6.96 (m, 2H), 7.10-7.20 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 45.3, 51.8, 118.2, 122.8, 123.6, 126.5, 134.5. $[a]^{20}_D$ = –20 ($CDCl_3$, c = 3.75).



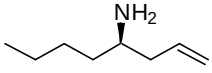
(1*S*)-1-(4-methoxyphenyl)but-3-en-1-amine (**2c**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.71 (br s, 2H), 2.39-2.51 (m, 2H), 3.87 (s, 3H), 4.03 (dd, *J* = 7.6 Hz, 5.8 Hz, 1H), 5.13-5.22 (m, 2H), 5.75-5.89 (m, 1H), 6.95 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 44.6, 55.1, 55.6, 114.1, 117.8, 126.7, 135.9, 138.3, 158.9. $[a]^{20}_{,D}$ = –25 ($CDCl_3$, *c* = 4.90).



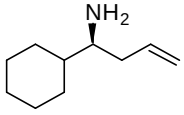
(1*S*)-1-(4-nitrophenyl)but-3-en-1-amine (**2f**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.70 (br s, 2H), 2.37-2.57 (m, 2H), 4.21 (dd, *J* = 7.6 Hz, 5.2 Hz, 1H), 5.17-5.21 (m, 2H), 5.72-5.86 (m, 1H), 7.60 (d, *J* = 8.7 Hz, 2H), 8.25 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 44.0, 54.8, 118.6, 123.6, 127.2, 134.2, 146.9, 153.2. $[a]^{20}_{,D}$ = –24 ($CDCl_3$, *c* = 5.65).



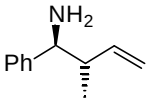
(1*S*)-1-pentafluorophenylbut-3-en-1-amine (**2g**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.85 (br s, 2H), 2.48-2.65 (m, 2H), 4.32 (t, *J* = 7.4 Hz, 1H), 5.03-5.09 (m, 2H), 5.64-5.73 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$, d): –159.80-–160.00 (m, 2F), –154.23 (t, *J* = 22.3 Hz, 1F), –141.70 (t, *J* = 12.1 Hz, 2F); ^{13}C NMR (75 MHz, $CDCl_3$, d): 42.2, 48.0, 118.8, 134.2, 136.0-146.8 (m). MS (EI): 196 [*M*–C_3H_5], 99; (CI): 238 [*M*+H], 196. $[a]^{20}_{,D}$ = +11 ($CHCl_3$, *c* = 5.57).



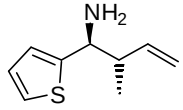
(1*R*)-1-butylbut-3-enylamine (**2h**). To a solution of valeronitrile (**3h**) (0.53 mL, 5.05 mmol) in Et_2O (5 mL) cooled to 0 ºC was added DIBAL-H (0.89 mL, 5.0 mmol) and the mixture was stirred for 1 h. The obtained aluminoimine (**4h**) was transferred *via* canula to a solution of (–)-*B*-allyldiisopinocampheylborane (1 M in pentane; 8 mL, 8 mmol) diluted with Et_2O (8 mL) and cooled to –55 °C, followed by slow addition of methanol (0.20 mL, 5.0 mmol). The mixture was stirred for 3 h at –55 °C, followed by oxidation with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL) and was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was then extracted with Et_2O (3×50 mL), treated with HCl (20% in H_2O, 5 mL), and stirred for 0.2 h. To the mixture was added water (50 mL) to extract the product. After removal of the organic layer, the aqueous solution of amine hydrochloride was neutralised with NaOH until pH~8. The resulting amine was extracted with Et_2O (3×50 mL), the solvent was removed under reduced pressure, and the material was purified on silica gel (hexanes:ethyl acetate:triethylamine 84.5:15:0.5) to afford 0.4 g (3.1 mmol, 65% yield) of **2h**. ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.95 (m, 3H), 1.30-1.48 (m, 8H), 1.87-2.02 (m, 1H), 2.18-2.24 (m, 1H), 2.07-2.08 (m, 1H), 5.01-5.07 (m, 2H), 5.66-5.82 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 15.0, 23.6, 29.2, 38.0, 43.2, 51.1, 117.2, 135.7. MS (EI):126 [M^+], 86 [*M*–C_3H_5], 70; (CI):154 [*M*+H], 136 [M^+], 70. $[a]^{20}_{,D}$ = +4 ($CDCl_3$, *c* = 2.75).



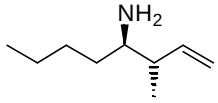
(1*S*)-1-cyclohexylbut-3-en-1-amine (**3i**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.94-1.30 (m, 6H), 1.37 (br s, 2H), 1.67-1.78 (m, 5H), 1.93-2.01 (m, 1H), 2.25-2.31 (m, 1H), 2.56 (q, *J* = 4.2 Hz, 1H), 5.06-5.12 (m, 2H), 5.73-5.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 26.5, 26.6, 26.7, 28.4, 29.8, 39.5, 43.5, 55.4, 117.2, 136.7. MS (EI):152 [*M*–H], 112 [*M*–C_3H_5], 95, 70; (CI):154 [*M*+H], 112; HRMS: 154.1596 (calc.), 154.1599 (actual). $[a]^{20}_{,D}$ = +9 ($CHCl_3$, *c* = 0.37).



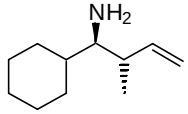
(1*S*,2*S*)-2-methyl-1-phenylbut-3-en-1-amine (**5a**). To potassium *tert*-butoxide (1 M in THF; 6 mL, 6 mmol) diluted with THF (6 mL) and cooled to –78 °C was added *trans*-butene (1 mL, 11 mmol) and butyllithium (2.5 M in hexanes; 2.4 mL, 6.0 mmol). The mixture was stirred for 0.1 h at –78 °C, followed by 0.3 h at –55 °C, and cooled again to –78 °C, when a solution of (–)-*B*-methoxydiisopinocampheylborane (2.28 g, 7.2 mmol) in THF (5 mL) was added and the reaction was stirred for 1 h at –78 °C. To thus generated **V** was added via canula **4a** [prepared as follows: To **3a** (0.52 mL, 5.05 mmol) diluted with THF (5 mL) and cooled to 0 ºC was added DIBAL-H (0.89 mL, 5.0 mmol) and the mixture was stirred for 1 h], followed by methanol (0.20 mL, 5.0 mmol) and the mixture was stirred for 3 h at –78 °C, when it was oxidized with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL) and was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was extracted with Et_2O (3×50 mL) after the acid-base manipulation, the solvent was removed under reduced pressure, and the crude material was purified on silica gel (hexanes:ethyl acetate:triethylamine 84.5:15:0.5) to afford 0.59 g (3.7 mmol, 74% yield) of **5a.** ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.83 (d, *J* = 6.7 Hz, 3H), 1.53 (br s, 2H), 2.37 (q, *J* = 7.4 Hz, 1H), 3.65 (d, *J* = 8.46 Hz, 1H), 5.10-5.204 (m, 2H), 5.69-5.81 (m, 1H), 7.26-7.33 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 17.7, 46.4, 60.7, 115.9, 127.1, 127.3, 128.3, 141.8, 144.7. MS (EI): 160 [*M*–H], 106, 79; (CI): 162, 145, 106. $[a]^{20}_D$ = +76 ($CHCl_3$, *c* =0.92), lit: +1.5 (MeOH, *c* = 1.0).



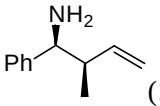
(1*S*,2*S*)-2-methyl-1-thien-2-ylbut-3-en-1-amine (**5b**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.92 (d, *J* = 6.8 Hz, 3H), 1.71 (br s, 2H), 2.38 (q, *J* = 7.3 Hz, 1H), 3.98 (d, *J* = 7.8 Hz, 1H), 5.03-5.21 (m, 2H), 5.45.816 (m 1H), 6.90-6.94 (m, 2H), 7.17-7.20 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 18.2, 47.5, 56.9, 116.3, 123.7, 123.8, 126.0, 140.7, 148.8. $[a]^{20}_D$ = +6 ($CHCl_3$, *c* = 1.55).



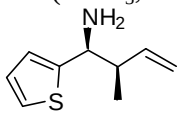
(1*R*,2*S*)-1-butyl-2-methylbut-3-enylamine (**5h**). To potassium *tert*-butoxide (1 M in THF; 6 mL, 6 mmol) diluted with pentane (6 mL) and cooled to –78 °C was added *trans*-butene (1 mL, 11 mmol) and butyllithium (2.5 M in hexanes; 2.4 mL, 6.0 mmol). The mixture was stirred for 0.1 h at –78 °C, followed by 0.3 h at –55 °C, and cooled again to –78 °C, when a solution of (–)-*B*-methoxydiisopinocampheylborane (2.28 g, 7.2 mmol) in pentane (5 mL) was added and the reaction was stirred for 1 h at –78 °C. To thus generated **V** was added via canula a solution of **4h** [prepared as follows: To a solution of valeronitrile (**3h**) (0.55 mL, 5.2 mmol) in pentane (10 mL) cooled to 0 ºC was added DIBAL-H (0.90 mL, 5.0 mmol) and the mixture was stirred for 1 h], followed by methanol (0.20 mL, 5.0 mmol) and the mixture was stirred for 3 h at –78 °C when it was oxidised with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL) and was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was extracted with Et_2O (3×50 mL) after the acid-base manipulations, the solvent was removed under reduced pressure, and the crude material was purified on silica gel (hexanes:ethyl acetate:triethylamine 84.5:15:0.5) to afford 0.4 g (2.8 mmol, 64% yield) of **5h.** ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.95 (t, *J* = 4.5 Hz, 3H), 1.06 (d, *J* = 4.6 Hz, 3H), 1.27-1.40 (m, 8H), 2.16 (q, *J* = 4.5 Hz, 1H), 2.57-2.60 (m, 1H), 5.06-5.09 (m, 2H), 5.72-5.84 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 14.4, 17.0, 23.2, 28.9, 34.9, 44.3, 55.6, 115.4, 141.4. MS (EI): 142 [*M*+H], 86 [*M*–C_4H_7]; (CI): 142 [*M*+H], 86. $[a]^{20}_D$ = +15 ($CDCl_3$, *c* =1.28).



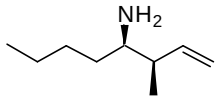
(1*R*,2*S*)-1-cyclohexyl-2-methylbut-3-en-1-amine (**5i**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.99 (d, *J* = 6.4 Hz, 3H), 1.05-1.20 (m, 8H), 1.60-1.68 (m, 5H), 2.24-2.26 (m, 2H), 4,.99-5.06 (m, 2H), 5.66-5.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 18.0, 26.7, 26.9, 27.0, 27.4, 31.2, 40.7, 41.1, 60.3, 115.4, 141.8. MS (EI): 169 [*M*+H], 150 [*M*–NH_3], 112 [*M*–C_4H_7]; (CI): 168 [*M*+H], 151, 112; HRMS: 168.1752 (calc.), 168.1757 (actual). $[a]^{20}_D$ = –18 ($CDCl_3$, *c* = 5.80).



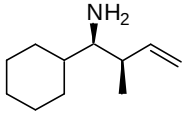
(1*S*,2*R*)-2-methyl-1-phenylbut-3-en-1-amine (**6a**). Amines **6** were obtained like **5**, however *cis*-butene was used in place of *trans*-butene. ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.06 (d, *J* = 7.2 Hz, 3H), 1.65 (br s, 2H), 2.57 (q, *J* = 8.6 Hz, 1H), 3.96 (d, *J* = 5.1 Hz, 1H), 5.08-5.11 (m, 2H), 5.70-5.76 (m, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 15.3, 45.0, 60.2, 115.3, 127.1, 127.4, 128.3, 141.3, 144.5. $[a]^{20}_{,D}$ = –27 ($CDCl_3$, *c* = 2.46).



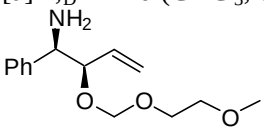
(1*S*,2*R*)-2-methyl-1-thien-2-ylbut-3-en-1-amine (**6b**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.03 (d, *J* = 6.5 Hz, 3H), 1.64 (br s, 2H), 2.56 (q, *J* = 6.4 Hz, 1H), 4.19 (d, *J* = 4.9 Hz, 1H), 5.05-5.08 (m, 2H), 5.73-5.79 (m, 1H), 6.89-6.93 (m, 2H), 7.20 (dd, *J* = 8.2 Hz, 12.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 14.9, 44.9, 56.1, 115.7, 123.6, 123.6, 126.4, 140.4, 149.1. MS (EI): 150, 112, 85; (CI): 168 (*M*+H], 151[*M*+H–NH_3], 112. HRMS: 168.0847 (calc.), 168.0852 (actual). $[a]^{20}_{,D}$ = –53 ($CDCl_3$, *c* = 2.46).



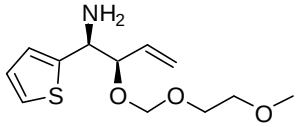
(1*R*,2*R*)-1-butyl-2-methylbut-3-enylamine (**6h**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.96 (t, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.24-1.52 (m, 8H), 2.23 (q, *J* = 6.0 Hz, 1H), 2.68-2.71 (m, 1H), 5.05-5.12 (m, 2H), 5.77-5.88 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 14.3, 14.4, 23.1, 29.2, 34.6, 43.7, 55.4, 114.7, 142.4. MS (EI): 142 [*M*+H], 86 [*M*–C_4H_7], 69, 44; (CI): 142 [*M*+H], 86. $[a]^{20}_{,D}$ = +25 ($CDCl_3$, *c* = 5.25).



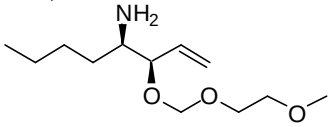
(1*R*,2*R*)-1-cyclohexyl-2-methylbut-3-en-1-amine (**6i**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.03 (d, *J* = 6.6 Hz, 3H), 1.16-1.43 (m, 7H), 1.68-1.92 (m, 6H), 2.37-2.42 (m, 2H), 5.05-5.11 (m, 2H), 5.78-5.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 13.5, 26.6, 26.8, 26.9, 28.5, 30.8, 40.0, 41.0, 60.0, 114.2, 143.5. $[a]^{20}_{,D}$ = +70 ($CDCl_3$, *c* = 1.66).



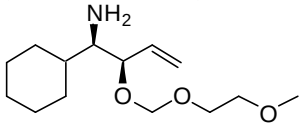
(1*R*,2*R*)-2-[(2-Methoxyethoxy)methoxy]-1-phenylbut-3-en-1-amine (**7a**). To 3-[(2-methoxyethoxy)-methoxy]prop-1-ene (0.91 g, 6.2 mmol) diluted with THF (6 mL) and cooled to –78 °C was added *sec*-butyllithium (1.4 M in cyclohexane; 4.4 mL, 6.1 mmol) and the mixture was stirred for 0.5 h at –78 °C. Then, a solution of (–)-*B*-methoxydiisopinocampheylborane (2.37 g, 7.5 mmol) in THF (5 mL) was added and the mixture was stirred for 1 h. To thus generated **VII** was added via canula a solution of **4a** [prepared as follows: To **3a** (0.52 mL, 5.05 mmol) diluted with THF (5 mL) and cooled to 0 ºC was added DIBAL-H (0.89 mL, 5.0 mmol) and the mixture was stirred for 1 h], followed by methanol (0.20 mL, 5.0 mmol). The reaction was stirred for 3 h at –78 °C and was oxidised with NaOH (3 M in H_2O; 2 mL) and (slowly!) H_2O_2 (30% in H_2O; 1.2 mL). The material was left stirring under positive N_2 pressure while it slowly warmed to RT. The product was extracted with Et_2O (3×50 mL) and the volatiles were removed under reduced pressure. The obtained material was purified on silica gel (hexanes:ethyl acetate:triethylamine 94.5:5:0.5 to 69.5:30:0.5) to furnish **7a** in 65% yield (0.81 g, 3.2 mmol). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.73 (br s, 2H), 3.34 (s, 3H), 3.37-3.49 (m, 4H), 3.96 (d, *J* = 5.8 Hz, 1H), 4.18 (t, *J* = 6.5 Hz, 1H), 4.67 (dd, *J* = 6.9 Hz, 38.7 Hz, 2H), 5.11-5.11 (m, 2H), 5.58-5.69 (m, 1H), 7.21-7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 59.0, 59.8, 67.0, 71.7, 81.7, 93.0, 118.7, 127.2, 127.5, 128.2, 135.5, 142.6. MS (EI):176 [*M*–$OCH_2CH_2OCH_3$], 106, 79, 59; (CI):252 [*M*+H], 176 [*M*+H–$CH_3OCH_2CH_2OH$], 106, 79; HRMS: 252.1600 (calc.), 252.1604 (actual). $[a]^{20}_{,D}$ = +103 ($CHCl_3$, *c* =4.22).



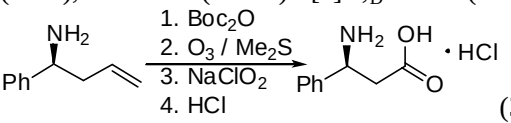
(1*S*,2*R*)-2-[(2-Methoxyethoxy)methoxy]-1-thien-2-ylbut-3-en-1-amine (**7b**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 2.06 (br s, 2H), 3.36 (s, 3H), 3.45-3.63 (m, 4H), 4.18 (t, *J* = 6.6 Hz, 1H), 4.26 (d, *J* = 5.8 Hz, 1H), 4.72 (dd, *J* = 6.9 Hz, 34.5 Hz, 2H), 5.11-5.24 (m, 2H), 5.61-5.73 (m, 1H), 6.86-6.94 (m, 2H), 7.19 (dd, *J* = 1.4 Hz, 4.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 55.8, 59.0, 67.2, 71.7, 81.9, 93.1, 119.4, 124.2, 124.3, 126.4, 135.0, 146.8. MS (EI):205, 112 [2-Thp-CH^+NH_2], 85, 59; (CI): 258 [*M*+H], 182, 165, 112, 89 [$CH_3OCH_2CH_2OCH_2^+$]; HRMS: 258.1164 (calc.), 258.1166 (actual). $[a]^{20}_D$ = +73 ($CHCl_3$, *c* = 9.08).



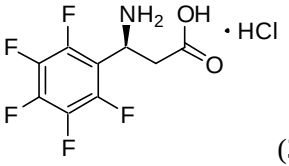
(1*R*,2*R*)-1-Butyl-2-[(2-methoxyethoxy)methoxy]but-3-enylamine (**7h**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.86 (t, *J* = 6.8 Hz, 3H), 1.23-1.45 (m, 5H), 2.65-2.69 (m, 1H), 3.34 (s, 3H), 3.49-3.60 (m, 3H), 3.76-3.83 (m, 2H), 4.69 (dd, *J* = 6.9 Hz, 33.9 Hz, 2H), 5.18-5.26 (m, 2H), 5.58-5.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 14.1, 22.8, 28.4, 33.2, 54.7, 59.0, 67.2, 71.7, 81.6, 92.9, 119.1, 135.9. MS (EI): 156 [*M*–$OCH_2CH_2OCH_3$], 86 [$CH_3CH_2CH_2CH_2CH^+NH_2$], 232 [self-protonating in EI]; (CI): 232 [*M*+H], 156 [*M*+H–$HOCH_2CH_2OCH_3$], 126, 86; HRMS: 232.1913 (calc.), 232.1913 (actual). $[a]^{20}_D$ = +70 ($CHCl_3$, *c* = 2.25).



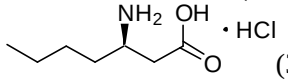
(1*R*,2*R*)-1-Cyclohexyl-2-[(2-methoxyethoxy)methoxy]but-3-en-1-amine (**7i**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.07-1.34 (m, 9H), 1.67-1.76 (m, 5H), 2.47 (t, *J* = 5.2 Hz, 1H), 3.38 (s, 3H), 3.53-3.63 (m, 3H), 3.80-3.86 (m, 1H), 4.07 (t, *J* = 6.6 Hz, 1H), 4.72 (dd, *J* = 7.0 Hz, 36.3 Hz, 2H), 5.22-5.29 (m, 2H), 5.65-5.76 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 25.3, 25.5, 25.6, 26.4, 28.7, 29.7, 38.6, 58.0, 58.6, 66.3, 70.7, 78.1, 91.9, 117.5. MS (EI): 205, 112, 95, 59; (CI): 258 (*M*+H], 182, 112; HRMS: 258.2069 (calc.), 258.2073 (actual). $[a]^{20}_D$ = +18 ($CHCl_3$, *c* = 0.25).



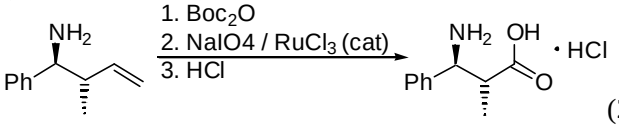
(3*S*)-3-Amino-3-phenylpropanoic acid hydrochloride (**8a**). To **2a** (0.43 g, 2.9 mmol) dissolved in Et_2O (30 mL) was added di-*tert*-butyldicarbonate (0.7 g, 3.55 mmol) and the reaction was stirred for 6 h at RT, after which time the solvent was removed under reduced pressure. The crude material was dissolved in CH_2Cl_2 (150 mL) and methanol (150 mL) and cooled to –78 ºC. Ozone was passed for 1 h (aqueous KI used as an indicator), followed by quenching with Me_2S (2 mL) at –78 °C and stirring for 1 h, while the material warmed to RT. The mixture was washed with H_2O (50 mL) and the organic layer was concentrated under reduced pressure. The crude aldehyde was diluted with 2-methylpropan-2-ol (30 mL) and 2-methylbut-2-ene (5 mL) and to this were added sodium chlorite (2.2 g, 24.3 mmol), sodium phosphate monobasic (2.3 g, 16.9 mmol), and water (6 mL). The mixture was stirred at RT for 1 h and the product was extracted with ethyl acetate (3×60 mL). The solvents were removed under reduced pressure and the obtained acid was filtered through a short plug of silica gel (ether). After evaporation of the solvent, the residue was diluted with Et_2O (10 mL) and treated with HCl (1 M in Et_2O; 3 mL, 3 mmol) for 0.5 h. The obtained solid was filtered and dried to afford **8a** in 84% yield (0.49 g, 2.4 mmol). ^{1}H NMR (200 MHz, D_2O, d): 2.93-3.01 (m, 2H), 4.57 (t, *J* = 7.2 Hz, 1H), 7.24-7.31 (m, 5H); ^{13}C NMR (50 MHz, D_2O, δ): 38.7, 52.4, 127.2, 129.6, 129.8, 135.2, 173.2. $[a]^{20}_D$ = +6 (D_2O, *c* = 0.9), +3.9 (MeOH, *c* = 0.8), (lit.: +3, MeOH, *c* = 2.9).



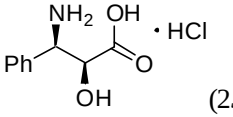
(3*S*)-3-Amino-3-pentafluorophenylpropanoic acid hydrochloride (**8g**). ^{1}H NMR (300 MHz, D_2O, d): 3.06-3.30 (m, 2H), 5.15 (t, *J* = 6.9 Hz, 1H); ^{19}F NMR (282 MHz, D_2O, δ): –161.09-–160.90 (m, 2F), –151.41 (t, *J* = 20.7 Hz, 1F), –141.62-–141.54 (m, 2F); ^{13}C NMR (75 MHz, D_2O, d): 35.8, 42.0, 172.1. $[a]^{20}_{,D}$ = +24 (D_2O, *c* = 2.47).



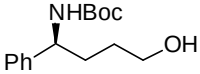
(3*S*)-3-Aminoheptanoic acid hydrochloride (**8h**). ^{1}H NMR (200 MHz, D_2O, d): 0.82 (t, *J* = 4.8 Hz, 3H), 1.29-1.12 (m, 6H), 1.60-1.64 (m, 2H), 2.59-2.82 (m, 2H), 3.51-3.61 (m, 1H); ^{13}C NMR (50 MHz, D_2O, d): 14.2, 22.7, 27.6, 32.6, 36.8, 49.1, 174.1. $[a]^{20}_{,D}$ = +39 (D_2O, *c* = 4.39).



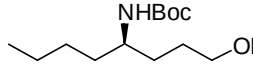
(2*R*,3*S*)-3-Amino-2-methyl-3-phenylpropanoic acid hydrochloride (**8a'**). To **6a** (0.2 g, 1.2 mol) dissolved in Et_2O (12 mL) was added di-*tert*-butyldicarbonate (0.3 g, 1.4 mmol) and the reaction was stirred for 6 h at RT, after which time the solvent was removed under reduced pressure. To the crude material dissolved in CH_3CN (40 mL) was added $RuCl_3 \cdot H_2O$ (0.02 g, 0.1 mmol) and the mixture was cooled to 0 °C. After addition of $NaIO_4$ (0.8 g, 3.7 mmol) dissolved in water (40 mL), the mixture was stirred for 0.5 h, followed by extraction with EtOAc (3×30 mL) and filtration through silica gel (Et_2O). After evaporation of the solvents, the residue was diluted with Et_2O (5 mL) and treated with HCl (1 M in Et_2O; 2 mL, 2 mmol) for 0.5 h. The obtained solid was filtered and dried to afford **8a'** in 77% yield (0.2 g, 0.9 mmol). ^{1}H NMR (200 MHz, D_2O, d): 0.91 (d, *J* = 7.2 Hz, 3H), 2.97-3.09 (m, 1H), 4.36 (d, *J* = 9.4 Hz, 1H), 7.29-7.31 (m, 5H); ^{13}C NMR (50 MHz, D_2O, d):15.4, 43.9, 57.8, 127.4, 127.6, 129.6, 129.8, 134.5, 177.3. $[a]^{20}_{,D}$ = +19 (D_2O, *c* =1.19).



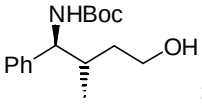
(2*S*,3*R*)-3-Amino-2-hydroxy-3-phenylpropanoic acid hydrochloride (**8a"**): ^{1}H NMR (200 MHz, CD_3OD, d): 3.24-3.29 (m, 1H), 3.86 (t, *J* = 4.5 Hz, 1H), 4.51 (d, *J* = 3.6 Hz, 1H), 7.36-7.40 (m, 5H); $[a]^{20}_{,D}$ = +17 (D_2O, *c* = 0.8).



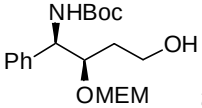
tert-butyl (1*S*)-4-hydroxy-1-phenylbutylcarbamate (**9a**). To **2a** (0.43 g, 2.9 mmol) dissolved in Et_2O (30 mL) was added di-*tert*-butyldicarbonate (0.7 g, 3.5 mmol) and the reaction was stirred for 6 h at RT, after which time the solvent was removed under reduced pressure. The crude material was dissolved in THF (7 mL) and treated with 9-BBN (0.5 M in THF; 13 mL, 6.5 mmol) for 24 h at RT, followed by oxidation with NaOAc (20% in H_2O, 20 mL) and H_2O_2 (30% in H_2O; 6 mL) for 3 h at RT. The product was extracted with Et_2O (3×30 mL), washed with brine, and after evaporation of the solvents purified on silica gel (flash; hexanes:ethyl acetate 2:1) to furnish **9a** in 86% yield (0.66 g, 2.5 mmol). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.45 (s, 9H), 1.53-1.88 (m, 4H), 2.55 (br s, 1H), 3.67 (t, *J* = 5.9 Hz, 2H), 4.67 (br s, 1H), 5.12 (br s, 1H), 7.29-7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 28.3, 29.1, 33.2, 54.6, 62.1, 79.5, 126.3, 127.2, 128.5, 142.7, 155.5.



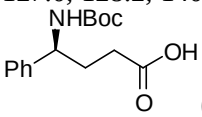
tert-butyl (1*R*)-1-(3-hydroxypropyl)pentylcarbamate (**9h**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.93 (d, *J* = 6.3 Hz, 3H), 1.47 (s, 10H), 1.65-1.69 (m, 1H), 2.12 (br s, 1H), 2.45 (br s, 1H), 3.70-3.76 (m, 2H), 4.73 (br s, 1H), 5.10 (br s, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 14.9, 28.3, 35.4, 36.3, 58.2, 60.7, 79.5, 126.5, 126.8, 128.3, 141.8, 155.7.



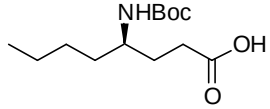
tert-butyl (1*S*,2*R*)-4-hydroxy-2-methyl-1-phenylbutylcarbamate (**9a'**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.93 (d, *J* = 6.3 Hz, 3H), 1.47 (s, 10H), 1.65-1.69 (m, 1H), 2.12 (br s, 1H), 2.45 (br s, 1H), 3.70-3.76 (m, 2H), 4.73 (br s, 1H), 5.10 (br s, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 14.9, 28.3, 35.4, 36.3, 58.2, 60.7, 79.5, 126.5, 126.8, 128.3, 141.8, 155.7.



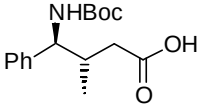
tert-butyl (1*R*,2*R*)-[4-hydroxy-2-(2-methoxy-ethoxymethoxy)-1-phenylbutyl]-carbamate (**9a"**). To **7a** (0.3 g, 1.2 mmol) dissolved in Et_2O (12 mL) was added di-*tert*-butyldicarbonate (0.4 g, 1.3 mmol) and the reaction was stirred for 3 h at RT, after which time the solvent was removed under reduced pressure. The crude material dissolved in THF (6 mL) was added to a slurry of dicyclohexylborane (0.5 g, 2.8 mmol) in THF (6 mL) and stirred for 16 h at RT, cooled to 0 °C and oxidised with NaOH (3 M in H_2O, 0.4 mL) and (slowly!) H_2O_2 (30% in H_2O; 0.7 mL) for 3 h at RT. The product was extracted with Et_2O (3×30 mL), washed with brine, and after evaporation of the solvents purified on silica gel (flash; hexanes:ethyl acetate 1:1) to furnish the desired primary alcohol **9a"** in 68% yield (0.2 g, 0.7 mmol). ^{1}H NMR (200 MHz, $CDCl_3$, d): 1.41 (s, 9H), 1.70-1.90 (m, 2H), 2.75 (br s, 1H), 3.32 (s, 3H), 3.37-3.41 (m, 3H), 3.56-3.77 (m, 3H), 4.06-4.14 (m, 2H), 4.48 (d, *J* = 6.8 Hz, 1H), 4.76 (d, *J* = 7.0 Hz, 1H), 5.51 (d, *J* = 7.8 Hz, 1H), 7.19-7.26 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 29.1, 35.9, 57.7, 58.9, 59.4, 67.7, 71.9, 79.0, 79.8, 95.8, 126.2, 127.0, 128.2, 140.8, 155.3.



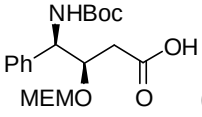
(4*S*)-4-[(*tert*-butoxycarbonyl)amino]-4-phenylbutanoic acid (**10a**). The alcohol **9a** (0.22 g, 0.8 mmol) in DMF (10 mL) was added slowly to a stirring solution of pyridinium dichromate (1.13 g, 3.0 mmol) in DMF (20 mL) and the mixture was stirred for 18 h at RT. The reaction was quenched with H_2O (5 mL), the product was extracted with Et_2O (3×50 mL), the combined ether layers were washed with H_2O (3×50 mL), the solvent was removed and the obtained material was purified on silica gel (flash; hexanes:ethyl acetate 2:1) to afford 0.192 g (0.7 mmol, 86% yield) of **10a**. ^{1}H NMR (200 MHz, $CDCl_3$, d): 1.22 (s, 9H), 1.78-2.01 (m, 1H), 2.35-2.71 (m, 3H), 5.07-5.13 (m, 1H), 7.15-7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 28.0, 28.3, 31.9, 61.9, 82.9, 124.8, 127.3, 128.4, 142.1, 149.0, 174.1.



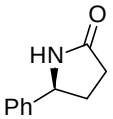
(4*R*)-4-[(*tert*-butoxycarbonyl)amino]octanoic acid (**10h**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.91 (t, *J* = 6.6 Hz, 3H), 1.20-2.67 (m, 11H), 4.04-4.12 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 14.9, 23.2, 28.5, 28.8, 32.1, 34.0, 58.5, 82.9, 149.6, 174.0.



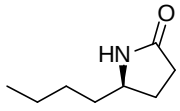
(3*R*,4*S*)-4-[(*tert*-butoxycarbonyl)amino]-3-methyl-4-phenylbutanoic acid (**10a'**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.69 (d, *J* = 6.6 Hz, 3H), 1.25 (s, 9H), 2.28-2.80 (m, 3H), 5.10 (d, *J* = 8.0 Hz, 1H), 7.09-7.12 (m, 2H), 7.30-7.33 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 16.3, 20.0, 31.2, 39.2, 65.7, 82.5, 125.8, 127.2, 127.9, 137.4, 148.7, 173.6.



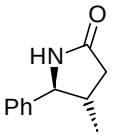
(3*R*,4*R*)-4-[(*tert*-butoxycarbonyl)amino]-3-(2-methoxy-ethoxymethoxy)-4-phenylbutanoic acid (**10a"**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 1.20 (s, 9H), 2.67-2.90 (m, 2H), 3.22-3.71 (m, 8H), 4.38-4.55 (m, 3H), 5.20 (d, *J* = 6.2 Hz, 1H), 7.22-7.30 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 28.3, 29.1, 39.6, 59.4, 65.7, 67.4, 70.2, 71.8, 83.3, 94.3, 126.2, 127.1, 127.7, 128.0, 136.3, 148.7, 171.7.



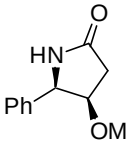
(5*S*)-5-phenylpyrrolidin-2-one (**11a**). The *N*-Boc protected γ-amino acid **10a** (0.13 g, 0.5 mmol) dissolved in CH_2Cl_2 (3 mL) was treated with CF_3COOH (1 mL) for 0.5 h at RT. After concentration under reduced pressure, the obtained material was purified on silica gel (flash; hexanes:ethyl acetate 1:1) to give lactam **11a** (0.074 g, 0.5 mmol, 98%). ^{1}H NMR (300 MHz, $CDCl_3$, d): 1.97-2.11 (m, 1H), 2.41-2.70 (m, 3H), 4.83 (t, *J* = 7.1 Hz, 1H), 6.70 (br s, 1H), 7.34-7.46 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, d): 30.3, 31.3, 58.1, 125.6, 127.8, 128.8, 142.5, 178.7. MS (EI): 161 [M^+], 117, 104, 77; (CI): 162 [*M*+H]. $[a]^{20}_D$ = +25 ($CDCl_3$, *c* = 3.7).



(5*R*)-5-butylpyrrolidin-2-one (**11h**). ^{1}H NMR (200 MHz, $CDCl_3$, d): 0.91 (t, *J* = 6.4 Hz, 3H), 1.25-1.75 (m, 8H), 2.18-2.37 (m, 2H), 3.62 (qn, *J* = 6.4 Hz, 1H), 6.49 (br s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 14.9, 23.4, 28.0, 28.7, 31.0, 37.1, 42.4, 55.2, 177.9. MS (EI): 141 [M^+], 84 [*M*–C_4H_9], 56; (CI): 142 [*M*+H], 126. $[a]^{20}_D$ = +8 ($CDCl_3$, *c* = 2.5), lit.:+8 ($CHCl_3$, *c* = 1.2).



(4*R*,5*S*)-4-methyl-5-phenylpyrrolidin-2-one (**11a'**). ^{1}H NMR (300 MHz, $CDCl_3$, d): 0.72 (d, *J* = 7.2 Hz, 3H), 2.19 (dd, *J* = 8.1 Hz, 16.8 Hz, 1H), 2.59 (dd, *J* = 8.4 Hz, 16.8 Hz, 1H), 2.92 (dt, J = 7.5 Hz, 15.0 Hz, 1H), 4.85 (d, *J* = 7.5 Hz, 1H), 6.13 (br s, 1H), 7.24-7.45 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, d): 16.9, 34.7, 38.0, 61.7, 126.1, 127.4, 128.1, 138.1, 177.4. MS (EI): 175 [M^+], 146 [*M*–C_2H_5], 106; (CI): 176 [*M*+H]. HRMS: 175.0997 (calc.), 175.0998 (actual). $[a]^{20}_D$ = –12 ($CDCl_3$, *c* = 1.4).



(4*R*,5*R*)-4-[(2-methoxyethoxy)methoxy]-5-phenylpyrrolidin-2-one (**11a"**): ^{1}H NMR (300 MHz, $CDCl_3$, δ): 2.60 (dd, *J* = 2.6 Hz, 17.2 Hz, 1H), 2.80 (dd, *J* = 6.3 Hz, 17.4 Hz, 1H), 3.19-3.25 (m, 1H), 3.44 (s, 3H), 3.44-3.53 (m, 3H), 4.29 (d, *J* = 6.9 Hz, 1H), 4.45 (d, *J* = 7.2 Hz, 1H), 4.64-4.68 (m, 1H), 4.98 (d, *J* = 5.4 Hz, 1H), 6.06 (br s, 1H), 7.34-7.49 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 39.4, 59.9, 63.5, 67.6, 72.3, 74.5, 94.6, 127.9, 128.7, 137.4, 177.2. MS (EI): 189 [*M*–CH_3O-CH_2CH_2-OH], 176 [*M*–CH_3O-CH_2CH_2-O-CH_2], 106, 59 [$^+CH_2CH_2OCH_3$]; (CI): 266 [*M*+H], 190 [*M*+H–CH_3-O-CH_2CH_2-OH], 176; HRMS: 266.1392 (calc.), 266.1393 (actual). $[a]^{20}_D$ = –8 ($CHCl_3$, *c* = 0.1).