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Supporting Information

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Pyridine-*N*-Oxide as a Mild Reoxidant which Transforms Osmium Catalysed Oxidative Cyclisation

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Contents

1. Experimental Details

Tetrahydrofuran, acetonitrile and toluene were purified prior to use by filtration through two activated alumina columns (activated basic aluminium oxide, Brockmann I, standard grade, ~ 150 mesh, 58 Å). Reagents obtained from Acros, Aldrich, Avocado, Fluka and Lancaster fine chemicals suppliers were used directly.

Flash column chromatography was carried out using silica gel 60 (0.040-0.063 mm) (Merck) using head pressure by means of head bellows. Thin layer chromatography was performed on commercially available pre-coated aluminium-backed plates (0.25 mm silica gel with fluorescent indicator UV_{254}). Visualisation was achieved by either the quenching of UV fluorescence, $KMnO_4$ or vanillin stain.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE AV400 (400 MHz and 100.6 MHz), Bruker DPX400 (400 MHz and 100.6 MHz) or a Bruker AVANCE AV500 (500 MHz and 125.7 MHz) spectrometer. Signal positions were recorded in δ ppm with the abbreviations s, d, t, q, quin., sx, br and m denoting singlet, doublet, triplet, quartet, quintet, sextet, broad and multiplet respectively. All NMR chemical shifts were referenced to residual solvent peaks or to $SiMe_4$ as an internal standard. All coupling constants, *J*, are quoted in Hz.

Infra-red spectra were recorded on a Bruker Tensor 27 FTIR spectrometer. Spectra were analysed either as thin films between NaCl plates, KBr disks or in a chloroform solution cell. Mass spectra (*m/z*) and HRMS were recorded under the conditions of electrospray (ESI), chemical (CI) and field (FI) ionisation. Melting points were obtained using a Leica VMTG heated-stage microscope and are uncorrected. "Petrol" refers to the fraction of petroleum ether boiling in the range 40-60 ºC unless otherwise stated and "ether" refers to diethyl ether.

1.1 General Procedures

General Procedure 1: Deprotection of phthalimide and subsequent nitrogen protection

A solution of substrate in methanolic methylamine (5 mL per mmol substrate) was heated to 40 °C until TLC indicated complete consumption of starting material. The reaction mixture was concentrated and the residue taken up in CH_2Cl_2 (2 mL per mmol substrate). CbzCl or NsCl (1.10 eq.) and DMAP (2.00 eq.) were added and the reaction stirred for 16 h. H_2O (20 mL) and ether (20 mL) were added and the layers separated. The aqueous layer was extrated with ether (3 × 20 mL) and the combined extracts washed with aqueous HCl (1 M, 20 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography as indicated.

General Procedure 2: Tetrahydropyran deprotection

The substrate (1.00 eq.) and PPTS (0.10 eq.) were dissolved in EtOH (8 mL per mmol starting material) and heated to 55 ˚C for 4 h. The reaction mixture was then concentrated onto silica gel and purified by flash column chromatography as indicated.

General Procedure 3: Organic oxidative cyclisation

Potassium osmate dihydrate (5 mol%) was added to a solution of substrate (1.00 eq.), pyridine-*N*-oxide (2.00 eq.), CSA (6.00 eq.) and citric acid (0.75 eq.) in CH_2Cl_2 (25 mL per mmol substrate) and the reaction stirred until TLC indicated complete consumption of starting material. Na_2SO_3 (0.10 eq.) was added and the mixture stirred for 30 minutes. Aqueous NaOH (2 M, 20 mL) and EtOAc (20 mL) were added and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organics were washed sequentially with

aqueous HCl (1 M, 20 mL) and aqueous NaOH (2 M, 20 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography as indicated.

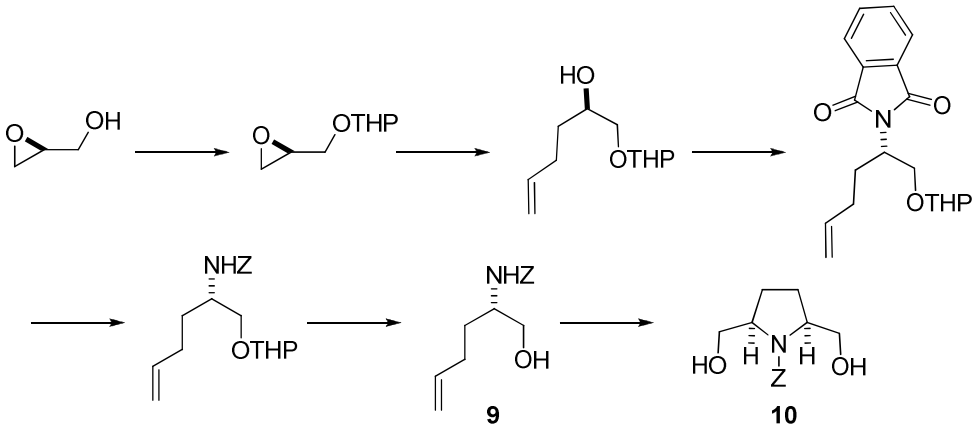
General Procedure 4: One-pot oxidation of primary alcohol to carboxylic acid

The alcohol substrate (1.00 eq.) and TEMPO (0.07 eq.) were dissolved in MeCN (5 mL per mmol substrate) and pH 6.7 buffer (3.75 mL per mmol substrate) and stirred at 35 °C. NaOCl (0.025 mL commercial bleach) in H_2O (0.5 mL per mmol substrate) and $NaClO_2$ (2.00 eq.) in H_2O (1 mL per mmol substrate) were added simultaneously and the reaction mixture stirred at 35 ^oC for 16 h. The heat was removed and the pH was adjusted to 3 with solid citric acid before extracting with EtOAc (3 × 20 mL). The combined organic phases were concentrated and the residue dissolved in saturated aqueous Na_2CO_3 and washed with EtOAc (2 × 20 mL). The aqueous phase was acidified to pH 3 with aqueous H_3PO_4 (1 M), saturated with NaCl and extracted with EtOAc (3 × 20 mL). The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated to give the crude acid which was purified by flash column chromatography as indicated.

General Procedure 5: Aqueous oxidative cyclisation

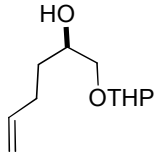
Potassium osmate dihydrate (5 mol%) was added to a solution of substrate (1.00 eq.), pyridine-*N*-oxide (2.00 eq.), citric acid (0.75 eq.) and TFA (1 mL per mmol substrate) in 9:1 acetone:H_2O (20 mL per mmol substrate) and the reaction stirred at 40 °C until TLC indicated complete consumption of starting material. Na_2SO_3 (0.10 eq.) was added and the mixture stirred for 30 minutes. H_2O (20 mL) and EtOAc (20 mL) were added and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organics were washed with aqueous HCl (1 M, 20 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography as indicated.

2. Data for starting materials and Pyrrolidines 10-32



Scheme 1: Synthesis of amino-alcohol **9** and pyrrolidine **10**

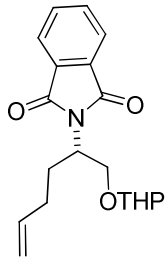
(2*R*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)hex-5-en-2-ol



Allylmagnesium bromide (1.0 M in ether, 40.1 mL, 40.1 mmol) was added to copper(I) bromide dimethyl sulfide complex (274 mg, 1.34 mmol) at −78 °C and the mixture stirred for 30 minutes. A solution of 2-((*R*)-oxiran-2-ylmethoxy)tetrahydro-2*H*-pyran[1] (4.23 g, 26.7 mmol) in THF (8.0 mL) was added dropwise and the reaction mixture stirred at −78 °C for 30 minutes, then at 0 °C for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (40 mL) and the mixture extracted with ether (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated to give the crude product. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:ether, R_f 0.15) gave the *alcohol* (4.41 g, 22.0 mmol, 82%) as an oil.

ν_{max}(thin film)/cm^{-1} 3444, 3076, 2942, 1641, 1442, 1353, 1262, 1201, 1123, 1075, 1033; δ_H (400 MHz, $CDCl_3$) 5.81 (1 H, ddt, *J* 17.1, 10.3, 6.6), 5.02 (1 H, dd, *J* 17.1, 1.5), 4.94 (1 H, dd, *J* 10.3, 1.5), 4.56-4.53 (1 H, m), 3.91-3.83 (1 H, m), 3.77-3.72 (1.5 H, m), 3.60 (0.5 H, dd, *J* 10.9, 2.8), 3.54-3.47 (1.5 H, m), 3.34 (0.5 H, m), 3.21 (0.5 H, s), 2.79 (0.5 H, s), 2.26-2.07 (2 H, m), 1.84-1.46 (8 H, m); δ_C (100.6 MHz, $CDCl_3$) 138.3, 114.8, 100.1, 100.0, 73.8, 72.9, 70.1, 69.9, 63.1, 63.0, 32.3, 32.2, 30.7, 30.6, 29.8, 25.2, 25.2, 19.9, 19.8; ***m/z*** (ESI$^+$) 223 (100%, [M+Na])$^+$; **HMRS** (ESI$^+$) $C_{11}H_{20}O_3Na$ requires *MNa* 223.1305, found 223.1307 (□0.95 ppm).

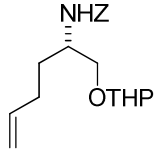
2-((2*S*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)hex-5-en-2-yl)isoindoline-1,3-dione



Di-*iso*propyl azodicarboxylate (6.06 g, 30.0 mmol) was added dropwise to a solution of the alcohol (3.00 g, 15.0 mmol), phthalimide (4.41 g, 30.0 mmol) and triphenylphosphine (7.86 g, 30.0 mmol) in THF (207 mL) at 0 °C and the reaction stirred at room temperature for 12 h, whereupon TLC analysis indicated complete consumption of starting material. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO_2, eluting with 9:1 ether:petrol then 8:2 ether:petrol, R_f 0.26) to afford the *protected amino alcohol* (4.67 g, 14.2 mmol, 95%) as an oil.

ν_{max}(thin film)/cm^{-1} 2943, 1775, 1712, 1641, 1468, 1375, 1201, 1125, 1075, 1035; **δ_H** (400 MHz, C_6D_6) 7.60-7.58 (2 H, m), 7.01-6.99 (2 H, m), 5.75 (1 H, ddt, *J* 16.9, 10.1, 6.7), 5.05-5.01 (1 H, m), 5.00-4.96 (1 H, m), 4.88-4.78 (1 H, m), 4.77-4.75 (0.5 H, m), 4.63 (0.5 H, t, *J* 3.4), 4.48 (0.5 H, t, *J* 9.8), 4.20-4.11 (1 H, m), 3.89 (0.5 H, ddd, *J* 11.2, 9.1, 3.3), 3.76 (0.5 H, dd, *J* 10.5, 5.5), 3.73 (0.5 H, ddd, *J* 12.1, 9.3, 3.0), 3.48-3.37 (1 H, m), 2.41-2.29 (1 H, m), 2.10-2.02 (2 H, m), 1.83-1.65 (2 H, m), 1.60-1.55 (1 H, m), 1.48-1.44, (1 H, m), 1.41-1.22 (3 H, m); **δ_C** (100.6 MHz, C_6D_6) 168.5, 168.4, 137.6, 133.5, 133.4, 132.5, 132.4, 123.0, 122.9, 115.4, 115.3, 98.8, 98.0, 67.1, 66.8, 61.7, 61.6, 52.1, 52.0, 30.9, 30.9, 30.7, 28.6, 28.2, 25.7, 25.6, 22.7, 19.6, 19.3; ***m/z*** (ESI^+) 352 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{19}H_{23}NNaO_4$ requires *MNa* 352.1519, found 352.1525 (□1.74 ppm).

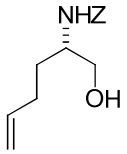
Benzyl (2*S*)-1-(tetrahydro-2*H*-pyran-2-yloxy)hex-5-en-2-ylcarbamate



The protected amino alcohol (136 mg, 0.68 mmol) was subjected to General Procedure 1 using CbzCl as the electrophile. Purification by flash column chromatography (SiO_2, eluting with 9:1 petrol:acetone, R_f 0.21) furnished the *carbamate* (205 mg, 0.615 mmol, 90%) as an oil.

ν_{max}(thin film)/cm^{-1} 3329, 2943, 1719, 1531, 1453, 1243, 1124, 1068, 1033; δ_H (400 MHz, C_6D_6) 7.36-7.14 (5 H, m), 5.90-5.79 (1 H, m), 5.22 (2 H, s), 5.13-5.04 (2.5 H, m), 4.92 (0.5 H, d, *J* 8.6), 4.50 (0.5 H, t, *J* 3.4), 4.45-4.44 (0.5 H, m), 4.10-4.00 (1 H, m), 3.81-3.71 (2 H, m), 3.44-3.40 (2 H, m), 2.16-2.10 (2 H, m), 1.71-1.53 (4 H, m), 1.43-1.26 (4 H, m); δ_C (100.6 MHz, C_6D_6) 156.2, 156.1, 138.4, 138.3, 137.6, 137.5, 133.3, 132.7, 128.6, 128.5, 122.8, 115.0, 114.9, 99.4, 98.6, 70.0, 69.2, 66.6, 66.5, 62.3, 61.8, 51.0, 50.7, 31.7, 30.8, 30.7, 30.6, 25.7, 25.6, 23.3, 19.9, 19.7, 19.6; ***m/z*** (ESI$^+$) 356 (100%, [M+Na]$^+$); **HRMS** (ESI$^+$) $C_{19}H_{27}NNaO_4$ requires *MNa* 356.1832, found 356.1833 (□0.11 ppm).

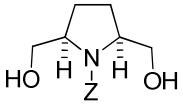
(*S*)-Benzyl 1-hydroxyhex-5-en-2-ylcarbamate 9



The carbamate (0.290 g, 0.87 mmol) was subjected to General Procedure 2. Purification by flash chromatography (SiO_2, eluting with 7:3 petrol:acetone, R_f 0.28) yielded *amino alcohol* **9** (0.192 g, 0.77 mmol, 88%) as plates.

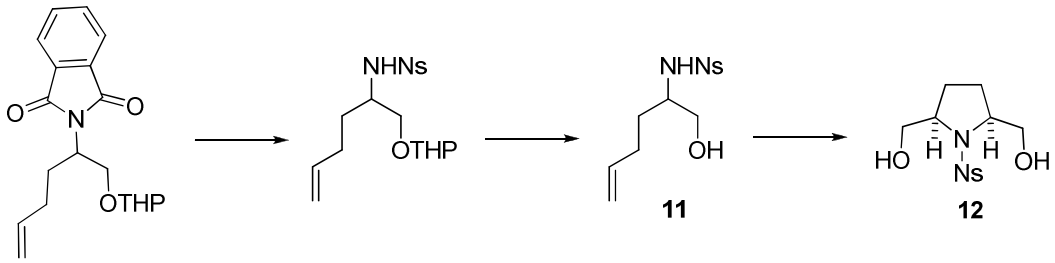
m.p. 49-50 °C; ν_{max}(KBr disk)/cm^{-1} 3317, 2945, 1687, 1540, 1452, 1251, 1020; δ_H (400 MHz, $CDCl_3$) 7.39-7.25 (5 H, m), 5.80 (1 H, ddd, *J* 17.0, 10.1, 6.8), 5.10 (2 H, s), 5.04 (1 H, d, *J* 17.0), 5.01-5.00 (1 H, br. s), 4.99 (1 H, d, *J* 10.1), 3.75-3.68 (2 H, m), 3.60-3.56 (1 H, m), 2.46 (1 H, br. s), 2.17-2.07 (2 H, m), 1.69-1.51 (2 H, m); δ_C (100.6 MHz, $CDCl_3$) 156.7, 137.6, 136.4, 128.6, 128.2, 128.1, 115.3, 66.9, 65.3, 52.7, 30.5, 30.1; ***m/z*** (ESI$^+$) 272 (100%, [M+Na]$^+$); **HRMS** (ESI$^+$) $C_{14}H_{19}NNaO_3$ requires *Mna* 272.1257, found 272.1258 (□0.16 ppm); $[\alpha]_D^{18}$ □17.3 (*c* 1.0, CH_2Cl_2).

***cis*-Benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate 10**



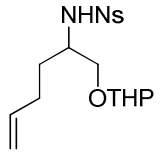
Amino alcohol **9** (48 mg, 0.19 mmol) was subjected to General Procedure 3, reaction time 4 h. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.26) gave *pyrrolidine* **10** (48 mg, 0.18 mmol, 94%) as an oil.

ν_{max}(thin film)/cm^{-1} 3377, 2957, 1785, 1674, 1418, 1358, 1173, 1043; δ_H (500 MHz, d_6-DMSO, 373K) 7.38-7.30 (5 H, m), 5.11 (2 H, s), 4.36 (2 H, t, *J* 5.6), 3.89-3.86 (2 H, m), 3.56-3.52 (2 H, m), 3.46-3.42 (2 H, m), 1.94-1.84 (4 H, m); δ_C (125 MHz, d_6-DMSO, 373K) 155.4, 137.7, 128.8, 128.1, 127.8, 66.4, 63.3, 60.6, 26.8; ***m/z*** (ESI$^+$) 288 (100%, [M+Na]); **HRMS** (ESI$^+$) $C_{14}H_{19}NNaO_4$ requires *MNa* 288.1206, found 288.1205 (+0.31 ppm).



Scheme 2: Synthesis of amino-alcohol **11** and pyrrolidine **12**

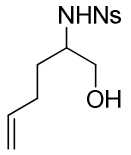
(±)-2-Nitro-*N*-(1-(tetrahydro-2*H*-pyran-2-yloxy)hex-5-en-2-yl)benzenesulfonamide



The protected amino alcohol (225 mg, 0.689 mmol) was subjected to General Procedure 1 using NsCl as the electrophile. Purification by flash column chromatography (SiO_2, eluting with 4:1 petrol:acetone, R_f 0.22) furnished the *sulfonamide* (211 mg, 0.558 mmol, 81%) as an oil.

ν_{max}(thin film)/cm^{-1} 3330, 2944, 1543, 1416, 1357, 1169, 1034; δ_H (400 MHz, C_6D_6) 7.99 (0.5 H, dd, *J* 7.8, 1.3), 7.96 (0.5 H, dd, *J* 7.8, 1.5), 7.20-7.14 (1 H, m), 6.93-9.88 (1 H, m), 6.80-6.75 (1 H, m), 6.12 (0.5 H, d, *J* 5.8), 5.91 (0.5 H, d, *J* 7.3), 5.76 (1 H, ddt, *J* 16.9, 10.1, 6.6), 5.08-5.00 (2 H, m), 4.33 (0.5 H, dd, *J* 4.5, 2.8), 4.28 (0.5 H, t, *J* 3.4), 3.71-3.63 (2 H, m), 3.60 (0.5 H, dd, *J* 7.1, 4.0), 3.58 (0.5 H, dd, *J* 7.8, 4.3), 3.37-3.28 (1 H, m), 3.22 (0.5 H, dd, *J* 10.6, 5.1), 3.10 (0.5 H, ddd, *J* 10.1, 5.3), 2.22-2.02 (2 H, m), 1.65-1.22 (8 H, m); δ_C (100.6 MHz, C_6D_6) 148.1, 137.9, 137.8, 135.8, 135.4, 132.9, 132.7, 132.3, 130.4, 128.3, 124.9, 115.3, 115.2, 99.5, 99.0, 69.8, 68.9, 62.4, 61.9, 54.7, 54.5, 32.2, 32.0, 30.6, 30.4, 30.1, 30.0, 25.5, 25.4, 19.8, 19.4; ***m/z*** (ESI$^+$) 407 (100%, [M+Na]$^+$); **HRMS** (ESI$^+$) $C_{17}H_{24}N_2NaO_6S$ requires *MNa* 407.1247, found 407.1247 (0.00 ppm).

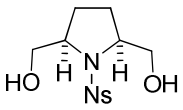
(±)-*N*-(1-Hydroxyhex-5-en-2-yl)-2-nitrobenzenesulfonamide 11



The sulfonamide (180 mg, 0.468 mmol) was subjected to General Procedure 2. Purification by flash chromatography (SiO_2, eluting with 7:3 petrol:acetone, R_f 0.26) yielded *amino alcohol* **11** (141 mg, 0.426 mmol, 91%) as an orange oil.

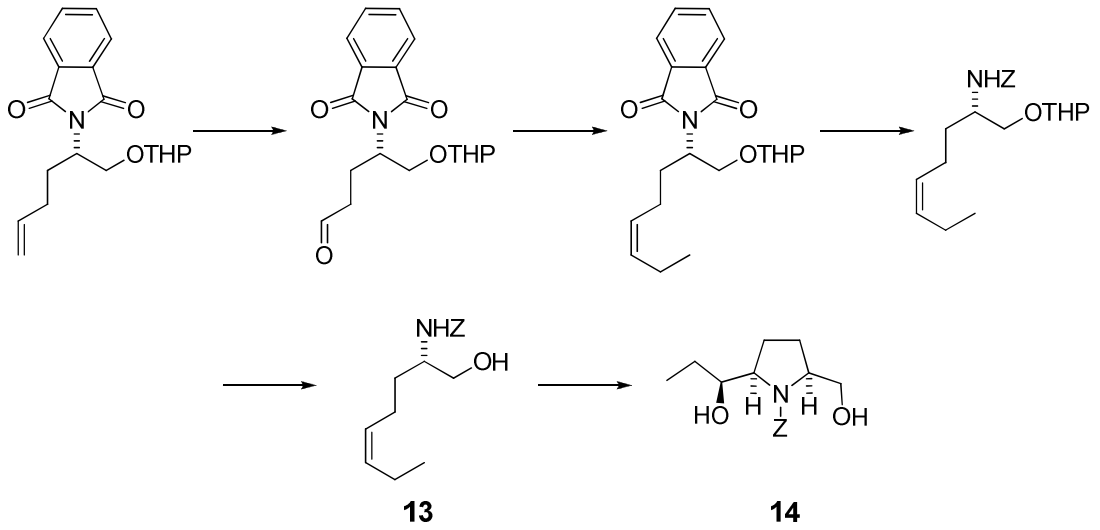
ν_{max}(thin film)/cm^{-1} 3345, 2397, 1641, 1594, 1540, 1417, 1363, 1167, 1126, 1061; **δ_H** (400 MHz, $CDCl_3$) 8.17-8.14 (1 H, m), 7.90-7.87 (1 H, m), 7.76-7.74 (2 H, m), 5.76 (1 H, ddd, *J* 16.9, 10.4, 6.6), 5.55 (1 H, d, *J* 7.6), 4.94-4.87 (2 H, m), 3.63-3.45 (3 H, m), 2.13-1.96 (2 H, m), 1.94 (1 H, br. s), 1.70-1.53 (2 H, m); **δ_C** (100.6 MHz, $CDCl_3$) 148.6, 137.0, 134.7, 133.6, 132.9, 130.7, 125.4, 115.6, 64.7, 56.1, 30.9, 29.6; ***m/z*** (ESI□) 299 (100%, [M□H]□); **HRMS** (ESI□) $C_{12}H_{15}N_2O_5S$ requires *M□H* 299.0696, found 299.0697 (□0.15 ppm).

***cis*-1-(2-Nitrophenylsulfonyl)pyrrolidine-2,5-diyl)dimethanol 12**



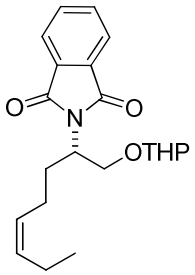
Amino alcohol **11** (60 mg, 0.20 mmol) was subjected to General Procedure 3. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.23) gave *pyrrolidine* **12** (58 mg, 0.18 mmol, 92%) as orange needles.

m.p. 104-106 °C; **ν_{max}**(KBr disk)/cm^{-1} 3375, 2940, 1544, 1374, 1165; **δ_H** (400 MHz, $CDCl_3$) 8.06 (1 H, dd, *J* 7.3, 1.3), 7.78-7.70 (2 H, m), 7.62 (1 H, dd, 7.5, 1.6), 4.01-3.99 (2 H, m), 3.91 (2 H, dd, *J* 11.6, 3.8), 3.65 (2 H, dd, *J* 11.6, 3.8), 2.93 (2 H, br. s), 2.10-2.02 (2 H, m), 1.93-1.86 (2 H, m); **δ_C** (100.6 MHz, $CDCl_3$) 148.9, 134.1, 132.0, 131.6, 131.4, 124.1, 65.1, 63.1, 27.5; ***m/z*** (ESI^+) 339 (100%, [M+Na]); **HRMS** (ESI^+) $C_{12}H_{16}N_2NaO_6S$ requires *MNa* 339.0621, found 339.0622 (□0.14 ppm).



Scheme 3: Synthesis of amino-alcohol **13** and pyrrolidine **14**

2-((2*S*,*Z*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)oct-5-en-2-yl)isoindoline-1,3-dione



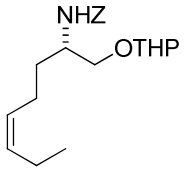
Osmium tetroxide (51 mg, 0.20 mmol) was added to a solution of 4-methyl morpholine *N*-oxide (937 mg, 8.00 mmol) and protected amino alcohol (1.320g, 4.00 mmol) in 1:10:8 H_2O:THF:^{t}BuOH (38 mL) and allowed to stir for 16 h, after which TLC analysis indicated complete consumption of starting material. Sodium sulfite (0.050g) was added and the mixture stirred for 30 minutes before adding H_2O (50 mL) and extracting with EtOAc (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield the diol as a pale yellow oil which was then dissolved in CH_2Cl_2 (40 mL). Silica-supported sodium periodate (0.96 mmol $NaIO_4$/g, 8.33 g, 8.00 mmol) was added and the reaction stirred for 4 h. Filtration through cotton wool and concentration of the filtrate *in vacuo* gave the corresponding aldehyde as an oil.

n-Propyl triphenylphosphonium bromide (3.10 g, 8.04 mmol) was dried overnight at 55 ˚C under vacuum. Toluene (67 mL) was added and the suspension cooled to 0 ˚C prior to dropwise addition of KHMDS (0.5 M solution in toluene, 15.6 mL, 7.80 mmol). The resulting bright

orange solution was warmed to room temperature and stirred for 20 minutes before cooling to –78 ˚C. A solution of the crude aldehyde in THF (20 mL) was added dropwise and the reaction stirred for 3 h. Saturated aqueous ammonium chloride (50 mL) and ether (50 mL) were added and the layers separated. The aqueous phase was extracted with ether (3 × 50 mL) and the combined organic layers washed with brine (25 mL), dried (Na_2SO_4), filtered and concentrated. Flash column chromatography (SiO_2, eluting with 9:1 petrol:acetone, R_f 0.27) afforded the *protected amino alcohol* (1.160 g, 3.24 mmol, 81%) as an oil.

ν_{max}(thin film)/cm^{-1} 2942, 1774, 1711, 1613, 1467, 1375, 1201, 1125, 1076, 1035; δ_H (400 MHz, C_6D_6) 7.60-7.58 (2 H, m), 6.98-6.95 (2 H, m), 5,45-5.42 (2 H, m), 4.93-4.82 (1 H, m), 4.77 (0.5 H, t, *J* 3.1), 4.64 (0.5 H, t, *J* 3.4), 4.51 (0.5 H, t, *J* 10.0), 4.22-4.15 (1 H, m), 3.90 (0.5 H, ddd, *J* 11.4, 9.1, 3.0), 3.79 (0.5 H, dd, *J* 10.6, 5.3), 3.74 (0.5 H, ddd, *J* 11.4, 9.3, 2.8), 3.48-3.38 (1 H, m), 2.45-2.34 (1 H, m), 2.19-2.11 (2 H, m), 2.02-1.96 (2 H, m), 1.88-1.63 (2 H, m), 1.60-1.56 (1 H, m), 1.49-1.45 (1 H, m), 1.42-1.11 (3 H, m), 0.94 (1.5 H, t, *J* 7.6), 0.93 (1.5 H, t, *J* 7.6); δ_C (100.6 MHz, C_6D_6) 168.6, 168.6, 133.5, 133.4, 132.7, 132.5, 132.4, 123.0, 122.9, 98.8, 98.0, 67.2, 66.9, 61.7, 61.6, 52.0, 51.2, 29.4, 29.0, 25.7, 25.6, 24.4, 20.8, 19.3, 14.4; ***m/z*** (ESI$^+$) 380 (100%, [M+Na]$^+$); **HRMS** (ESI$^+$) $C_{21}H_{27}NNaO_4$ requires *MNa* 380.1832, found 384.1831 (+0.28 ppm).

Benzyl (2*S*,*Z*)-1-(tetrahydro-2*H*-pyran-2-yloxy)oct-5-en-2-ylcarbamate

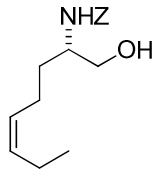


The protected amino alcohol (1.145 g, 3.20 mmol) was subjected to General Procedure 1 using CbzCl as the electrophile. Purification by flash column chromatography (SiO_2, eluting with 9:1 petrol:acetone, R_f 0.25) furnished the *carbamate* (940 mg, 2.59 mmol, 81%) as an oil.

ν_{max}(thin film)/cm^{-1} 3330, 2944, 1720, 1531, 1454, 1241, 1124, 1067, 1033; δ_H (400 MHz, C_6D_6) 7.37-7.14 (5 H, m), 5.55-5.44 (2 H, m), 5.23-5.22 (2 H, m), 5.05 (0.5 H, d, *J* 9.6), 4.84 (0.5 H, d, *J* 8.6), 4.51 (0.5 H, t, *J* 3.4), 4.46 (0.5 H, t, *J* 3.3), 4.12-4.05 (1 H, m), 3.82-3.74 (2 H, m), 3.44-3.37 (2 H, m), 2.21-2.20 (2 H, m), 2.12-2.05 (2 H, m), 1.72-1.54 (5 H, m), 1.42-1.26 (3 H, m), 1.01 (3 H, t, *J* 7.5); δ_C (100.6 MHz, C_6D_6) 156.4, 136.4, 133.5, 132.4, 132.3, 128.6, 128.4, 128.2, 99.4, 98.6, 70.0, 69.2, 66.5, 66.5, 62.3, 61.8, 51.2, 50.9, 32.5, 30.9, 30.7, 25.7, 25.6, 24.1, 20.8,

19.9, 19.6, 14.5; ***m/z*** (ESI^+) 384 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{21}H_{31}NNaO_4$ requires *MNa* 384.2145, found 384.2147 (□0.45 ppm).

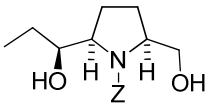
(*S*,*Z*)-Benzyl 1-hydroxyoct-5-en-2-ylcarbamate 13



The carbamate (870 mg, 2.41 mmol) was subjected to General Procedure 2. Purification by flash chromatography (SiO_2, eluting with 4:1 petrol:acetone, R_f 0.19) yielded *amino alcohol* **13** (531 mg, 1.90 mmol, 79%) as plates.

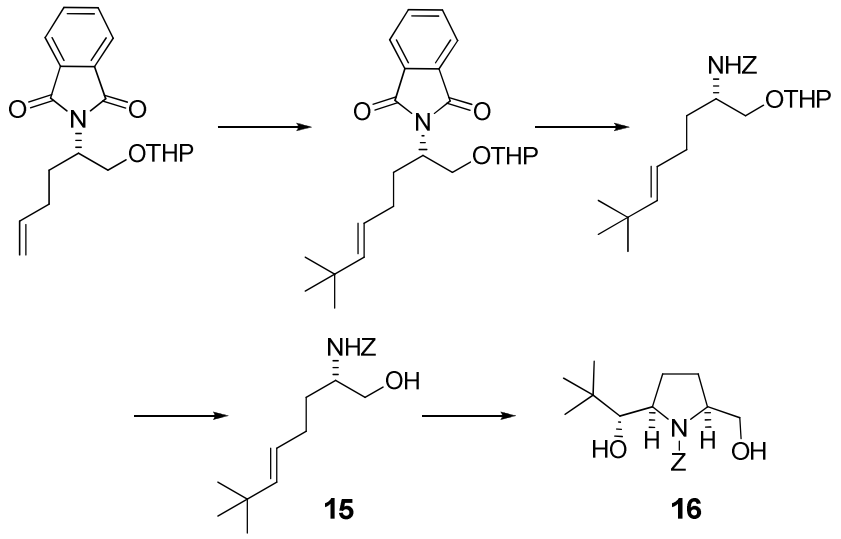
m.p. 51-52 °C; ν_{max}(KBr disk)/cm^{-1} 3327, 3006, 2961, 1698, 1537, 1455, 1243, 1062; δ_H (400 MHz, $CDCl_3$) 7.37-7.31 (5 H, m), 5.44-5.38 (1 H, m), 5.33-5.27 (1 H, m), 5.11 (2 H, s), 4.93 (1 H, br. s), 3.72-3.69 (2 H, m), 3.60-3.56 (1 H, m), 2.31 (1 H, br. s), 2.11 (2 H, q, *J* 7.3), 2.02 (2 H, qu, *J* 7.3), 1.65-1.47 (2 H, m), 0.95 (3 H, t, *J* 7.5); δ_C (100.6 MHz, $CDCl_3$) 158.6, 136.4, 133.9, 132.8, 128.6, 128.2, 127.6, 66.9, 65.5, 52.9, 31.3, 23.6, 20.5, 14.3; ***m/z*** (ESI^+) 300 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{16}H_{23}NNaO_3$ requires *MNa* 300.1570, found 300.1570 (0.00 ppm); $[\alpha]_D^{18}$ □26.4 (*c* 1.0, CH_2Cl_2).

(2*S*,5*R*)-Benzyl 2-(hydroxymethyl)-5-((*S*)-1-hydroxypropyl)pyrrolidine-1-carboxylate 14



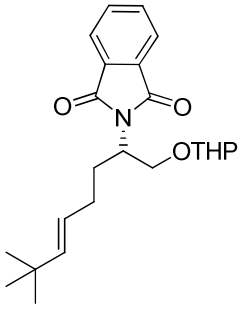
Amino alcohol **13** (97 mg, 0.35 mmol) was subjected to General Procedure 3. Purification by flash column chromatography (SiO_2, eluting with 3:1 petrol:acetone, R_f 0.22) gave *pyrrolidine* **14** (99 mg, 0.34 mmol, 96%) as an oil.

ν_{max}(thin film)/cm^{-1} 3383, 3034, 2963, 1681, 1587, 1498, 1413, 1354, 1202, 1163, 1109; δ_H (500 MHz, d_6-DMSO, 373K) 7.39-7.30 (5 H, m), 5.10 (2 H, s), 4.47 (1 H, t, *J* 5.5), 4.37 (1 H, d, *J* 4.7), 3.93-3.89 (1 H, m), 3.81-3.73 (2 H, m), 3.58-3.51 (2 H, m), 2.05-1.99 (1 H, m), 1.96-1.82 (2 H, m), 1.76-1.69 (1 H, m), 1.40-1.27 (2 H, m), 0.89 (3 H, t, *J* 7.4); δ_C (125 MHz, d_6-DMSO, 373K) 155.4, 137.7, 128.7, 127.9, 127.8, 72.2, 66.8, 63.5, 63.3, 60.5, 27.2, 27.1, 23.7, 10.6; ***m/z*** (ESI^+) 316 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{16}H_{24}NO_4$ requires *MH* 294.1700, found 294.1702 (□0.61 ppm); $[\alpha]_D^{18}$ +8.0 (*c* 1.0, CH_2Cl_2).



Scheme 4: Synthesis of amino-alcohol **15** and pyrrolidine **16**

2-((2*S*,*E*)-7,7-Dimethyl-1-(tetrahydro-2*H*-pyran-2-yloxy)oct-5-en-2-yl)isoindoline-1,3-dione

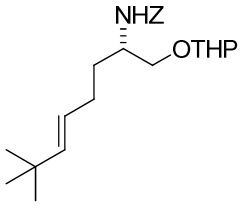


Grubbs-Hoveyda second generation catalyst (87 mg, 0.139 mmol) was added to a solution of the protected amino alcohol (917 mg, 2.78 mmol) in 3,3-dimethyl-1-butene (17 mL) and stirred at 40 ˚C for 12 h. The reaction mixture was concentrated and purified by flash column chromatography (SiO_2, eluting with 9:1 petrol:acetone, R_f 0.35) to give the *protected amino alcohol* (968 mg, 2.50 mmol, 90%) as a pale brown oil.

ν_{max}(thin film)/cm^{-1} 2951, 1775, 1712, 1468, 1376, 1201, 1125, 1066, 1035; δ_H (400 MHz, C_6D_6) 7.61-7.59 (2 H, m), 6.98-6.96 (2 H, m), 5.53-5.49 (1 H, m), 5.41-5.33 (1 H, m), 4.92-4.82 (1 H, m), 4.78-4.77 (0.5 H, m), 4.64 (0.5 H, t, *J* 3.3), 4.52 (0.5 H, t, *J* 10.0), 4.24-4.15 (1 H, m), 3.94-3.88 (0.5 H, m), 3.81 (0.5 H, dd, *J* 10.4, 5.3), 3.77-3.72 (0.5 H, m), 3.49-3.38 (1 H, m), 2.46-2.34 (1 H, m), 2.14-2.08 (2 H, m), 1.87-1.56 (3 H, m), 1.49-1.45 (1 H, m), 1.42-1.12 (3 H, m), 1.06 (4.5 H, s), 1.05 (4.5 H, s); δ_C (100.6 MHz, C_6D_6) 168.5, 142.7, 142.6, 133.5, 133.4, 132.5, 132.5, 123.7, 123.7, 123.0, 122.9, 98.8, 97.9, 67.3, 66.9, 61.7, 61.6, 51.9, 51.1, 32.8, 30.7, 30.0, 29.9,

29.8, 29.3, 28.9, 25.7, 25.6, 19.3; ***m/z*** (ESI^+) 408 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{23}H_{31}NNaO_4$ requires *MNa* 408.2145, found 408.2151 (□1.48 ppm).

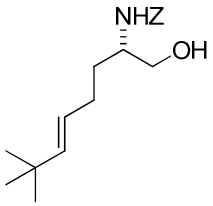
Benzyl (2*S*,*E*)-7,7-dimethyl-1-(tetrahydro-2*H*-pyran-2-yloxy)oct-5-en-2-ylcarbamate



The protected amino alcohol (890 mg, 2.31 mmol) was subjected to General Procedure 1 using CbzCl as the electrophile. Purification by flash column chromatography (SiO_2, eluting with 92:8 petrol:acetone, R_f 0.34) furnished the *carbamate* (890 mg, 2.06 mmol, 89%) as an oil.

ν_{max}(thin film)/cm^{-1} 3331, 2951, 2867, 1720, 1530, 1454, 1382, 1362, 1242, 1124, 1068, 1033; δ_H (400 MHz, C_6D_6) 7.37-7.14 (5 H, m), 5.61-5.57 (1 H, m), 5.48-5.41 (1 H, m), 5.23 (2 H, s), 5.07 (0.5 H, d, *J* 8.6), 4.83 (0.5 H, d, *J* 9.1), 4.50 (0.5 H, t, *J* 3.4), 4.45 (0.5 H, t, *J* 3.5), 4.15-4.06 (1 H, m), 3.82-3.75 (2 H, m), 3.43-3.37 (2 H, m), 2.18-2.13 (2 H, m), 1.74-1.60 (3 H, m), 1.59-1.55 (2 H, m), 1.39-1.22 (3 H, m), 1.12 (9 H, s); δ_C (100.6 MHz, C_6D_6) 156.1, 142.3, 142.2, 133.2, 128.6, 128.6, 128.5, 124.4, 124.3, 122.7, 99.5, 98.7, 70.1, 69.5, 66.5, 66.5, 62.3, 61.8, 51.1, 50.1, 32.9, 32.5, 30.9, 30.7, 29.9, 29.6, 25.7, 25.6, 19.9, 19.6; ***m/z*** (ESI^+) 412 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{23}H_{35}NNaO_4$ requires *MNa* 412.2458, found 412.2460 (□0.49 ppm).

(*S*,*E*)-Benzyl 1-hydroxy-7,7-dimethyloct-5-en-2-ylcarbamate 15

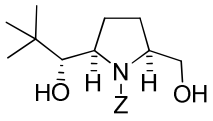


The carbamate (720 mg, 1.85 mmol) was subjected to General Procedure 2. Purification by flash chromatography (SiO_2, eluting with 85:15 petrol:acetone, R_f 0.29) yielded *amino alcohol* **15** (457 mg, 1.50 mmol, 81%) as an oil.

ν_{max}(thin film)/cm^{-1} 3330, 3033, 2956, 1704, 1533, 1455, 1361, 1251, 1064; δ_H (400 MHz, $CDCl_3$) 7.39-7.30 (5 H, m), 5.47 (1 H, d, *J* 15.7), 5.33-5.25 (1 H, m), 5.10 (2 H, s), 4.96 (1 H, br. s), 3.70-3.69 (2 H, m), 3.59-3.58 (1 H, m), 2.45 (1 H, br. s), 2.09-2.03 (2 H, m), 1.65-1.49 (2 H,

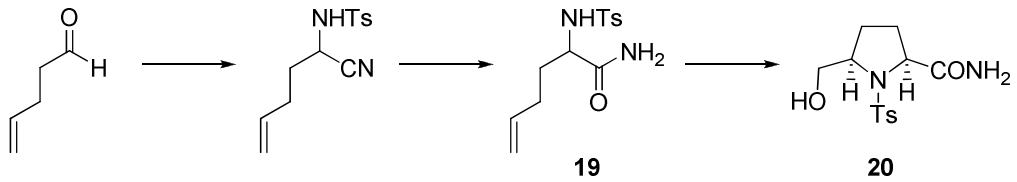
m), 0.98 (9 H, s); δ_C (100.6 MHz, $CDCl_3$) 156.7, 142.6, 136.4, 128.5, 128.2, 128.1, 123.3, 66.9, 65.5, 53.0, 32.8, 31.3, 29.7, 29.1; ***m/z*** (ESI^+) 328 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{18}H_{28}NO_3$ requires *MH* 306.2064, found 306.2062 (+0.61 ppm); $[\alpha]_D^{18}$ □10.7 (*c* 1.0, CH_2Cl_2).

(2*R*,5*S*)-Benzyl-2-((*R*)-1-hydroxy-2,2-dimethylpropyl)-5-(hydroxymethyl)pyrrolidine-1-carboxylate 16



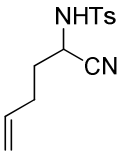
Amino alcohol **15** (59 mg, 0.19 mmol) was subjected to General Procedure 3. Purification by flash column chromatography (SiO_2, eluting with 4:1 petrol:acetone, R_f 0.26) gave *pyrrolidine* **16** (57 mg, 0.17 mmol, 92%) as an oil.

ν_{max}(thin film)/cm^{-1} 3402, 3034, 2956, 1682, 1498, 1416, 1361, 1213, 1157, 1099, 1014; δ_H (500 MHz, d_6-DMSO, 373K) 7.39-7.29 (5 H, m), 5.12-5.05 (2 H, m), 4.87 (1 H, t, *J* 4.7), 4.23 (1 H, d, *J* 4.6), 4.07 (1 H, t, *J* 7.3), 3.90-3.82 (2 H, m), 3.51-3.48 (1 H, m), 2.91 (1 H, dd, *J* 7.3, 4.4), 2.05-2.00 (1 H, m), 1.92-1.87 (2 H, m), 1.63-1.59 (1 H, m), 0.90 (9 H, s); δ_C (125 MHz, d_6-DMSO, 373K) 156.1, 137.7, 128.7, 128.0, 127.9, 80.3, 66.5, 62.0, 60.2, 59.4, 35.1, 31.4, 26.6, 25.9; ***m/z*** (ESI^+) 344 (100%, $[M+Na]^+$); **HRMS** (ESI^+) $C_{18}H_{28}NO_4$ requires *MH* 322.2012, found 322.2012 (0.00 ppm); $[\alpha]_D^{18}$ □19.3 (*c* 1.0, CH_2Cl_2).



Scheme 5: Synthesis of amino-amide **19** and pyrrolidine **20**

(±)-*N*-(1-Cyanopent-4-enyl)-4-methylbenzenesulfonamide

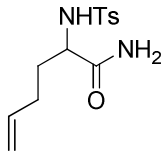


Potassium cyanide (1.19 g, 18.2 mmol) was added to a solution of 4-pentenal (1.50 g, 17.8 mmol) and ammonium acetate (4.12 g, 53.4 mmol) in EtOH (36 mL) and the reaction was stirred at room temperature for 72 h. The reaction mixture was concentrated and the residue taken up in

ether (20 mL). Aqueous HCl (6 M, 10 mL) was added and the layers were separated before washing the aqueous layer with two further portions of ether (2 × 20 mL). The pH was adjusted to 12 with aqueous NaOH (40% by weight, saturated with NaCl) and the product amine was extracted with ether (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield the crude amino nitrile which was dissolved in CH_2Cl_2 (20 mL). *p*-Toluenesulfonyl chloride (3.73 g, 19.6 mmol) and DMAP (4.35 g, 35.6 mmol) were added and the reaction stirred at room temperature for 16 h. Aqueous HCl (1 M, 20 mL) and ether (20 mL) were added and the layers separated. The aqueous phase was extracted with ether (3 × 20 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated to give the crude product. Flash column chromatography (SiO_2, eluting with 85:15 petrol:acetone, R_f 0.27) afforded the *amino nitrile* (2.09 g, 7.91 mmol, 44%) as plates.

m.p. 85-86 °C; $\boldsymbol{\nu_{max}}$(KBr disk)/cm^{-1} 3584, 3266, 3080, 2930, 2247, 1643, 1598, 1495, 1443, 1340, 1162, 1091, 1019; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.80 (2 H, d, *J* 8.3), 7.36 (2 H, d, *J* 8.3), 5.70 (1 H, ddt, *J* 17.4, 9.9, 6.8), 5.59 (1 H, d, *J* 7.3), 5.09-5.04 (2 H, m), 4.22 (1 H, q, *J* 7.3), 2.45 (3 H, s), 2.52-2.20 (2 H, m), 1.89 (2 H, q, *J* 7.3); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 144.7, 135.9, 135.1, 134.1 130.1, 127.3, 117.4, 43.7, 32.9, 29.0, 21.7; ***m/z*** (ESI$^-$) 263 (100%, $[M-H]^-$); **HRMS** (ESI$^+$) $C_{13}H_{16}N_2NaO_2S$ requires *MNa* 287.0825, found 287.0825 (+0.1 ppm).

(±)-2-(4-Methylphenylsulfonamido)hex-5-enamide 19

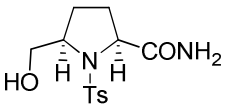


Concentrated HCl (6 mL) was added to a solution of the amino nitrile (440 mg, 1.66 mmol) in ether (3 mL) and the reaction mixture stirred at room temperature for 16 h, then H_2O (10 mL) and EtOAc (20 mL) were added and the layers separated. The aqueous phase was extracted with EtOAc (4 × 20 mL) and the combined organic extracts washed with saturated aqueous NaCl (20 mL), dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.27) afforded *amino amide* **19** (323 mg, 1.14 mmol, 69%) as plates.

m.p. 146-147 °C; $\boldsymbol{\nu_{max}}$(KBr disk)/cm^{-1} 3408, 2949, 1683, 1452, 1365, 1161, 1032; $\boldsymbol{\delta_H}$ (400 MHz, d_4-MeOH) 7.75 (2 H, d, *J* 8.2), 7.37 (2 H, d, *J* 8.2), 5.69 (1 H, ddt, *J* 16.7, 10.6, 6.6), 4.92-4.87 (2 H, m), 3.71 (1 H, dd, *J* 8.6, 5.1), 2.43 (3 H, s), 2.08-1.99 (1 H, m), 1.97-1.87 (1 H, m), 1.76-1.67

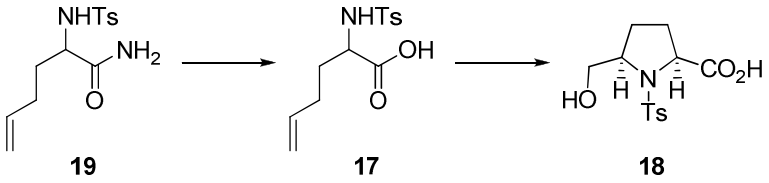
(1 H, m), 1.63-1.55 (1 H, m); δ_C (100 MHz, d_4-MeOH) 175.6, 143.9, 138.0, 137.2, 129.7, 127.3, 114.9, 56.3, 32.7, 29.7, 20.5; ***m/z*** (ESI$^-$) 281 (100%, [M–H]$^-$); **HRMS** (ESI$^+$) $C_{13}H_{18}N_2NaO_3S$ requires *MNa* 305.0930, found 305.0931 (–0.3 ppm).

(±)-*cis*-5-(Hydroxymethyl)-1-tosylpyrrolidine-2-carboxamide 20



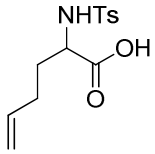
Amino amide **19** (100 mg, 0.350 mmol) was subjected to General Procedure 5, reaction time 26 h. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.25) gave *pyrrolidine* **20** (78 mg, 0.260 mmol, 75%) as plates.

m.p. 183-185 °C; ν_{max}(KBr disk)/cm^{-1} 3260, 1652, 1343, 1157, 1074; δ_H (400 MHz, d_4-MeOH) 7.79 (2 H, d, *J* 8.2), 7.47 (2 H, d, *J* 8.2), 4.11 (1 H, br. s), 3.97-3.94 (1 H, m), 3.73-3.67 (2 H, m), 2.47 (3 H, s), 1.96-1.94 (2 H, m), 1.70-1.62 (2 H, m); δ_C (100 MHz, d_4-MeOH) 172.0, 144.6, 134.5, 130.1, 127.9, 64.0, 63.7, 63.4, 29.7, 29.1, 20.5; ***m/z*** (ESI$^+$) 321 (100%, [M+Na]$^+$); **HRMS** (ESI$^+$) $C_{13}H_{19}N_2O_4S$ requires *MH* 299.1060, found 299.1060 (+0.1 ppm).



Scheme 6: Synthesis of amino-acid **17** and pyrrolidine **18**

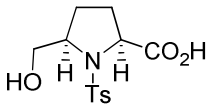
(±)-2-(4-Methylphenylsulfonamido)hex-5-enoic acid 17



The amino amide **19** (150 mg, 0.530 mmol) was dissolved in MeOH (3 mL) and aqueous KOH (6 M, 1 mL) and heated at reflux for 24 h. The reaction mixture was cooled to room temperature and acidified to pH 3 with aqueous HCl (6 M), the MeOH was evaporated and the aqueous layer extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography (SiO_2, eluting with 70:29:1 petrol:acetone:AcOH, R_f 0.43) gave *amino acid* **17** (113 mg, 0.40 mmol, 75%) as plates.

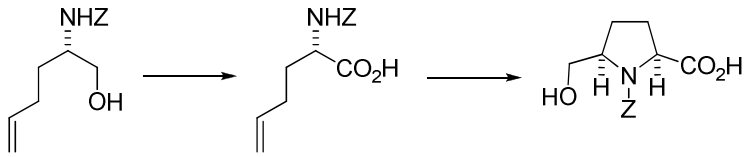
m.p. 82-83 °C; ν_{max}(KBr disk)/cm^{-1} 3386, 2948, 2836, 1724, 1598, 1495, 1444, 1332, 1161, 1094, 1022; δ_H (400 MHz, $CDCl_3$) 8.29 (1 H, br. s), 7.73 (2 H, d, *J* 8.2), 7.29 (2 H, d, *J* 8.2), 5.70 (1 H, ddt, *J* 17.4, 10.6, 6.7), 5.42 (1 H, d, *J* 6.5), 4.99-4.94 (2 H, m), 3.93 (1 H, td, *J* 8.3, 4.8), 2.41 (3 H, s), 1.91-1.82 (2 H, m), 1.77-1.68 (2 H, m); δ_C (100 MHz, $CDCl_3$) 176.7, 143.9, 136.5, 136.3, 129.7, 127.2, 116.2, 54.9, 32.2, 29.0, 21.5; ***m/z*** (ESI$^-$) 282 (100%, [M−H]$^-$); **HRMS** (ESI$^-$) $C_{13}H_{16}NO_4S$ requires *M*−*H* 282.0795, found 282.0792 (+0.8 ppm).

(±)-*cis*-5-(Hydroxymethyl)-1-tosylpyrrolidine-2-carboxylic acid 18



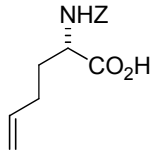
Amino acid **17** (70 mg, 0.25 mmol) was subjected to General Procedure 5, reaction time 24 h. Purification by flash column chromatography (SiO_2, eluting with 60:39:1 petrol:acetone:AcOH, R_f 0.27) gave *pyrrolidine* **18** (59 mg, 0.20 mmol, 79%) as needles.

m.p. 169-170 °C; ν_{max}(KBr disk)/cm^{-1} 3490, 3249, 2953, 1732, 1598, 1494, 1345, 1161, 1006; δ_H (400 MHz, $CDCl_3$) 8.62 (1 H, br. s), 7.55 (2 H, d, *J* 8.1), 7.35 (2 H, d, *J* 8.1), 4.32 (1 H, dd, *J* 8.6, 4.8), 4.02 (1 H, dd, *J* 11.6, 3.3), 3.86-3.81 (1 H, m), 3.64 (1 H, dd, *J* 11.6, 3.0), 2.69 (1 H, br. s), 2.44 (3 H, s), 2.16-2.11 (1 H, m), 2.00-1.92 (1 H, m), 1.88-1.83 (1 H, m), 1.78-1.70 (1 H, m); δ_C (100 MHz, $CDCl_3$) 177.4, 144.4, 134.2, 130.1, 127.3, 64.6, 62.9, 61.8, 29.9, 27.5, 21.6; ***m/z*** (ESI$^-$) 298 (100%, [M−H]$^-$); **HRMS** (ESI$^-$) $C_{13}H_{16}NO_5S$ requires *M*−*H* 298.0744, found 298.0740 (+1.3 ppm).



Scheme 7: Synthesis of amino-acid **21** and pyrrolidine **22**

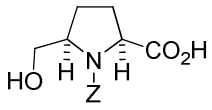
(*S*)-2-(Benzyloxycarbonylamino)hex-5-enoic acid 21



Amino alcohol **9** (280 mg, 1.12 mmol) was subjected to General Procedure 4. Purification by flash column chromatography (SiO_2, eluting with 79:20:1 petrol:acetone:AcOH, R_f 0.27) gave amino acid **21**[2] (221 mg, 0.84 mmol, 75%) as an oil.

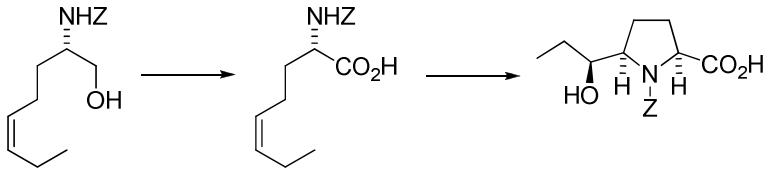
ν_{max}(thin film)/cm^{-1} 3404, 2962, 1715, 1531, 1454, 1260, 1054; δ_H (400 MHz, d_4-MeOH) 7.38-7.27 (5 H, m), 5.82 (1 H, ddd, *J* 16.9, 10.4, 6.7), 5.10 (2 H, s), 5.07-4.98 (2 H, m), 4.18 (1 H, dd, *J* 9.3, 4.5), 2.19-2.10 (2 H, m), 1.97-1.88 (1 H, m), 1.81-1.72 (1 H, m); δ_C (100.6 MHz, d_4-MeOH) 175.1, 157.7, 137.4, 137.2, 128.5, 128.0, 127.8, 115.2, 66.5, 53.7, 31.1, 30.1; ***m/z*** (ESI$^+$) 525 (100%, [2M+H]$^+$), 262 (62%, [M+H]$^+$); **HRMS** (ESI$^+$) $C_{14}H_{17}NNaO_4$ requires *MNa* 286.1050, found 286.1042 (+2.83 ppm); $[\alpha]_D^{18}$ +5.8 (*c* 1.0, CH_2Cl_2).

(2*S*,5*R*)-1-(Benzyloxycarbonyl)-5-(hydroxymethyl)pyrrolidine-2-carboxylic acid 22



Amino acid **21** (70 mg, 0.27 mmol) was subjected to General Procedure 5, reaction time 25 h. Purification by flash column chromatography (SiO_2, eluting with 69:30:1 petrol:acetone:AcOH, R_f 0.35) gave *pyrrolidine* **22** (56 mg, 0.20 mmol, 75%) as an oil.

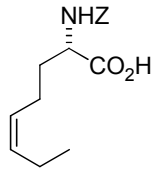
ν_{max}(thin film)/cm^{-1} 3490, 2956, 1705, 1499, 1418, 1357, 1209, 1123; δ_H (500 MHz, d_6-DMSO, 373K) 7.38-7.29 (5 H, m), 5.10 (2 H, br. s), 4.30-4.27 (1 H, m), 3.97-3.93 (1 H, m), 3.66 (1 H, dd, *J* 10.6, 3.8), 3.47 (1 H, dd, *J* 10.6, 7.6), 2.25-2.19 (1 H, m), 1.99-1.92 (3 H, m); δ_C (125 MHz, d_6-DMSO, 373K) 174.4, 154.7, 137.4, 128.7, 128.1, 127.7, 66.5, 62.6, 60.5, 28.7, 27.4; ***m/z*** (ESI$^+$) 557 (55%, [2M+H]$^+$), 279 (100%, [M+H]$^+$); **HRMS** (ESI$^+$) $C_{14}H_{17}NNaO_5$ requires *MNa* 302.0999, found 302.0996 (+1.10 ppm); $[\alpha]_D^{18}$ +6.6 (*c* 1.0, CH_2Cl_2).



13 **23** **24**

Scheme 8: Synthesis of amino-acid **23** and pyrrolidine **24**

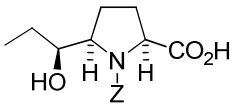
(*S*,*Z*)-2-(Benzyloxycarbonylamino)oct-5-enoic acid 23



Amino alcohol **13** (280 mg, 1.01 mmol) was subjected to General Procedure 4. Purification by flash column chromatography (SiO_2, eluting with 79:20:1 petrol:acetone:AcOH, R_f 0.32) gave *amino acid* **23** (165 mg, 0.57 mmol, 56%) as an oil.

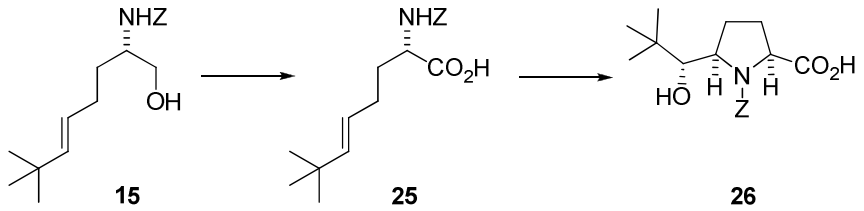
ν_{max}(thin film)/cm^{-1} 3408, 2964, 1714, 1531, 1455, 1260, 1056; δ_H (400 MHz, d_4-MeOH) 7.38-7.28 (5 H, m), 5.46-5.40 (1 H, m), 5.35-5.28 (1 H, m), 5.14-5.06 (2 H, m), 5.15 (1 H, dd, *J* 9.6, 4.5), 2.23-2.07 (2 H, m), 2.02 (2 H, qu, *J* 7.6), 1.92-1.83 (1 H, m), 1.78-1.68 (1 H, m), 0.93 (3 H, t, J 7.6); δ_C (100.6 MHz, d_4-MeOH) 175.3, 157.7, 137.3, 133.2, 128.5, 128.0, 127.8, 127.3, 66.5, 53.8, 31.7, 23.4, 20.4, 13.7; ***m/z*** (ESI□) 581 (100%, [2M□H]□), 290 (65%, [M□H]□); **HRMS** (ESI$^+$) $C_{16}H_{21}NNaO_4$ requires *MNa* 314.1363, found 314.1358 (+1.47 ppm); $[\alpha]_D^{18}$ +4.9 (*c* 1.0, CH_2Cl_2).

(2*S*,5*R*)-1-(Benzyloxycarbonyl)-5-((*S*)-1-hydroxypropyl)pyrrolidine-2-carboxylic acid 24



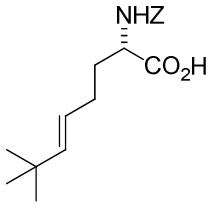
Amino acid **23** (110 mg, 0.378 mmol) was subjected to General Procedure 5, reaction time 26 h. Purification by flash column chromatography (SiO_2, eluting with 74:25:1 petrol:acetone:AcOH, R_f 0.23) gave *pyrrolidine* **24** (105 mg, 3.40 mmol, 90%) as an oil.

ν_{max}(thin film)/cm^{-1} 3480, 2967, 1649, 1499, 1416, 1119; δ_H (500 MHz, d_6-DMSO, 373K) 7.39-7.30 (5 H, m), 5.11 (2 H, s), 4.37-4.33 (1 H, m), 3.91-3.88 (1 H, m), 3.81-3.78 (1 H, m), 2.26-2.19 (1 H, m), 2.07-1.94 (2 H, m), 1.88-1.83 (1 H, m), 1.49-1.43 (1 H, m), 1.39-1.31 (1 H, m), 0.91 (3 H, t, J 7.4); δ_C (125 MHz, d_6-DMSO, 373K) 175.2, 154.8, 137.3, 128.7, 128.1, 127.9, 127.8, 127.7, 72.3, 66.8, 63.6, 60.6, 29.1, 26.7, 24.6, 10.7; ***m/z*** (ESI□) 613 (40%, [2M□H]□), 307 (100%, [M□H]□); **HRMS** (ESI$^+$) $C_{16}H_{21}NNaO_5$ requires *MNa* 330.1312, found 330.1312 (+0.09 ppm); $[\alpha]_D^{18}$ □13.5 (*c* 1.0, CH_2Cl_2).



Scheme 9: Synthesis of amino-acid **25** and pyrrolidine **26**

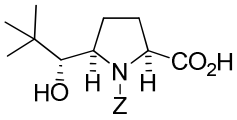
(*S*,*E*)-2-(Benzyloxycarbonylamino)-7,7-dimethyloct-5-enoic acid 25



Amino alcohol **15** (125 mg, 0.41 mmol) was subjected to General Procedure 4. Purification by flash column chromatography (SiO_2, eluting with 79:20:1 petrol:acetone:AcOH, R_f 0.26) gave *amino acid* **25** (93 mg, 0.29 mmol, 71%) as an oil.

ν_{max}(thin film)/cm^{-1} 3403, 2959, 1715, 1520, 1455, 1239, 1058; δ_H (400 MHz, d$_4$-MeOH) 7.39-7.30 (5 H, m), 5.50 (1 H, d, *J* 15.6), 5.34 (1 H, dt, *J* 15.6, 6.8), 5.14-5.07 (2 H, m), 5.15 (1 H, dd, *J* 9.3, 4.3), 2.17-2.02 (2 H, m), 1.93-1.84 (1 H, m), 1.77-1.68 (1 H, m), 1.00 (9 H, s); δ_C (100.6 MHz, d$_4$-MeOH) 175.2, 158.2, 143.2, 137.3, 128.5, 128.0, 127.8, 123.1, 66.5, 53.7, 32.6, 31.7, 29.1, 29.0; ***m/z*** (ESI□) 637 (100%, [2M□H]□), 318 (70%, [M□H]□); **HRMS** (ESI$^+$) $C_{18}H_{25}NNaO_4$ requires *MNa* 342.1676, found 342.1669 (+1.98 ppm); $[\alpha]_D^{18}$ +4.9 (*c* 1.0, CH_2Cl_2).

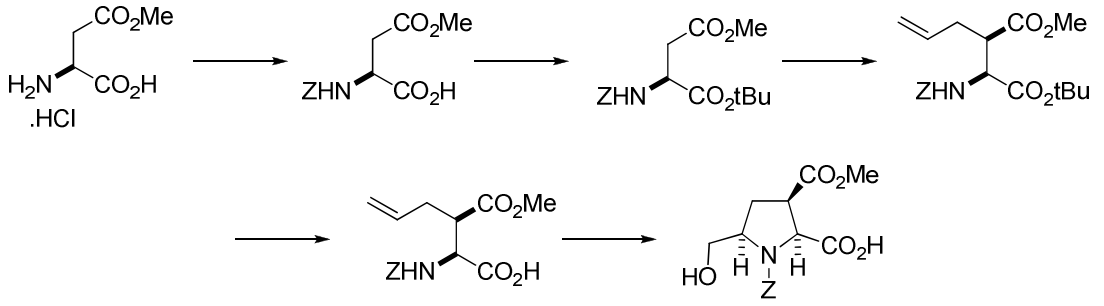
(2*S*,5*R*)-1-(Benzyloxycarbonyl)-5-((*R*)-1-hydroxy-2,2-dimethylpropyl)pyrrolidine-2-carboxylic acid 26



Amino acid **25** (68 mg, 0.213 mmol) was subjected to General Procedure 5, reaction time 28 h. Purification by flash column chromatography (SiO_2, eluting with 79:20:1 petrol:acetone:AcOH, R_f 0.26) gave *pyrrolidine* **26** (62 mg, 0.185 mmol, 87%) as an oil.

ν_{max}(thin film)/cm^{-1} 3480, 2958, 1694, 1212, 1118; δ_H (500 MHz, d$_6$-DMSO, 373K) 7.36-7.30 (5 H, m), 5.10-5.08 (2 H, m), 4.35 (1 H, t, *J* 8.5 H), 4.15 (1 H, t, *J* 6.9), 2.98 (1 H, d, *J* 7.3), 2.38-2.32 (1 H, m), 2.13-1.91 (2 H, m), 1.74-1.68 (1 H, m), 0.92 (9 H, s); δ_C (125 MHz, d$_6$-DMSO,

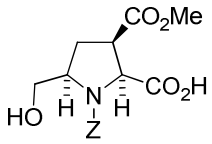
373K) 176.5, 155.4, 137.3, 128.6, 128.1, 127.9, 79.7, 66.9, 60.2, 59.4, 34.9, 31.2, 26.5, 26.3; ***m/z*** (ESI□) 670 (45%, [2M□H]□), 335 (100%, [M□H]□); **HRMS** (ESI+) $C_{18}H_{25}NNaO_5$ requires *MNa* 358.1625, found 358.1624 (+0.30 ppm); $[\alpha]_D^{18}$ +18.4 (*c* 1.0, CH_2Cl_2).



27 **28**

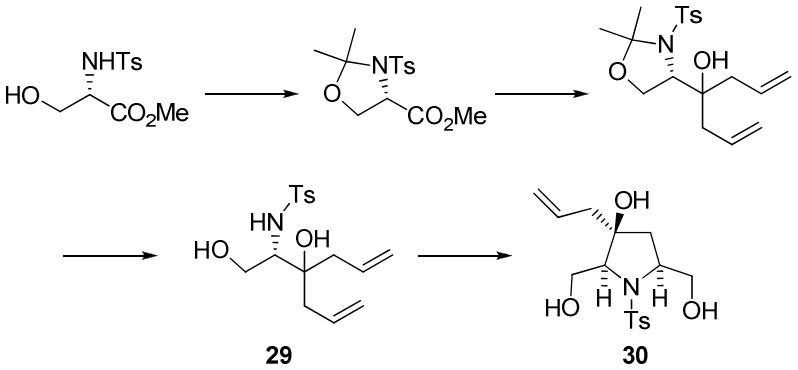
Scheme 10: Synthesis of amino-acid **27** and pyrrolidine **28**

(2*S*,3*R*,5*R*)-1-(Benzyloxycarbonyl)-5-(hydroxymethyl)-3-(methoxycarbonyl)pyrrolidine-2-carboxylic acid 28



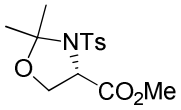
Amino acid **27**[3] (140 mg, 0.436 mmol) was subjected to General Procedure 5, reaction time 26 h. Purification by flash column chromatography (SiO_2, eluting with 64:35:1 petrol:acetone:AcOH, R_f 0.24) gave *pyrrolidine* **28** (115 m, 0.340 mmol, 78%) as an oil.

ν_{max}(thin film)/cm^{-1} 3452, 2955, 1739, 1417, 1320, 1124; δ_H (500 MHz, d_6-DMSO, 373K) 7.39-7.31 (5 H, m), 5.12 (2 H, s), 4.65 (1 H, d, *J* 8.8), 3.95-3.93 (1 H, m), 3.83 (1 H, dd, *J* 10.4, 3.9), 3.64 (3 H, s), 3.58 (1 H, dd, *J* 10.4, 7.3), 3.43 (1 H, dt, *J* 11.2, 7.9), 2.33-2.19 (2 H, m); δ_C (125 MHz, d_6-DMSO, 373K) 171.8, 170.8, 154.6, 137.2, 128.8, 128.2, 127.8, 67.0, 63.3, 62.2, 59.9, 52.0, 45.4, 31.0; ***m/z*** (ESI□) 673 (40%, [2M□H]□), 337 (100%, [M□H]□); **HRMS** (ESI+) $C_{16}H_{19}NNaO_7$ requires *MNa* 360.1054, found 360.1053 (+0.30 ppm); $[\alpha]_D^{18}$ +1.1 (*c* 1.0, CH_2Cl_2).



Scheme 11: Synthesis of amino-alcohol **29** and pyrrolidine **30**

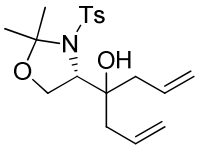
(*S*)-Methyl 2,2-dimethyl-3-tosyloxazolidine-4-carboxylate



2,2-Dimethoxypropane (3.14 g, 30.2 mmol) was added to a solution of (*S*)-methyl 3-hydroxy-2-(4-methylphenylsulfonamido)propanoate (550 mg, 2.01 mmol) and PPTS (142 mg, 0.563 mmol) in toluene (20 mL) and the reaction stirred at 80 ^{o}C for 6 h. The mixture was cooled to room temperature and concentrated to give the crude product. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.63) gave the *ester* (622 mg, 1.98 mmol, 98%) as pale yellow plates.

m.p. 95-97 ^{o}C; ν_{max}(KBr disk)/cm^{-1} 2991, 2953, 2889, 1760, 1738, 1599, 1496, 1437, 1370, 1347, 1290, 1203, 1160, 1100, 1037, 833; δ_H (400 MHz, $CDCl_3$) 7.77 (2 H, d, *J* 8.2), 7.30 (2 H, d, *J* 8.2), 4.44 (1 H, dd, *J* 6.8, 2.7), 4.14 (1 H, dd, *J* 9.2, 6.8), 4.06 (1 H, dd, *J* 9.2, 2.7), 3.61 (3 H, s), 2.42 (3 H, s), 1.71 (3 H, s) and 1.58 (3 H, s); δ_C (100.6 MHz, $CDCl_3$) 170.9, 143.8, 137.6, 129.5, 127.7, 98.9, 67.2, 60.0, 52.6, 27.6, 25.5, 21.6; ***m/z*** (ESI$^+$) 314 (100%, [M+H]$^+$), 336 (50%, [M+Na]$^+$); **HRMS** (ESI$^+$). $C_{14}H_{19}NO_5SNa$ requires *MNa* 336.0876, found 336.0877 (□0.27 ppm)]; $[\alpha]_D^{19}$ □80.2 (*c* 1.0, CH_2Cl_2).

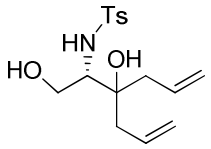
(*S*)-4-(2,2-Dimethyl-3-tosyloxazolidin-4-yl)hepta-1,6-dien-4-ol



Allylmagnesium bromide (1.0 M in ether, 4.18 mL, 4.18 mmol) was added dropwise to a solution of the ester (596 mg, 1.90 mmol) in THF (19 mL) at 0 °C and the mixture stirred at 0 °C for 2.5 h. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate (20 mL) and the mixture extracted with ether (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated to give the crude product. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:ether, R_f 0.43) gave the *alcohol* (555 mg, 1.52 mmol, 80%) as needles.

m.p. 113-115 °C; $\boldsymbol{\nu_{max}}$(KBr disk)/cm^{-1} 3474, 3074, 2983, 2941, 1639, 1598, 1439, 1370, 1333, 1236, 1145, 1091, 1005, 919, 838, 816; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.80 (2 H, d, *J* 8.3), 7.34 (2 H, d, *J* 8.3), 6.08-5.93 (2 H, m), 5.17-4.97 (4 H, m), 4.57 (1 H, d, *J* 2.3), 3.89 (1 H, dd, *J* 9.8, 1.5), 3.81 (1 H, dd, *J* 7.1, 1.5), 3.69 (1 H, dd, *J* 9.8, 7.1), 2.66 (1 H, ddt, *J* 14.2, 5.6, 1.5), 2.56-2.51 (1 H, m), 2.45 (3 H, s), 2.20 (1 H, dd, *J* 14.2, 9.0), 2.05 (1 H, ddd, *J* 14.8, 9.6, 2.3), 1.75 (3 H, s), 1.49 (3 H, s); $\boldsymbol{\delta_C}$ (100.6 MHz, $CDCl_3$) 144.1, 135.7, 134.1, 133.9, 129.6, 128.3, 118.2, 117.8, 99.7, 74.8, 66.2, 65.9, 42.5, 41.3, 28.8, 23.9, 21.6; ***m/z*** (ESI$^+$) 366 (65%, $[M+H]^+$), 388 (50%, $[M+Na]^+$); **HRMS** (ESI$^+$). $C_{19}H_{27}NO_4SNa$ requires *MNa* 388.1553, found 388.1553 (+0.10 ppm)]; $\boldsymbol{[\alpha]_D^{19}}$ +55.8 (*c* 1.0, CH_2Cl_2).

(*S*)-*N*-(3-Allyl-1,3-dihydroxyhex-5-en-2-yl)-4-methylbenzenesulfonamide 29

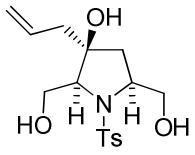


The alcohol (543 mg, 1.49 mmol) was dissolved in 12:4:5 AcOH:H_2O:CH_2Cl_2 (2.0 mL) and stirred at room temperature for 16 h, then concentrated to give the crude product. Purification by flash column chromatography (SiO_2, eluting with 1:1 petrol:ethyl acetate, R_f 0.33) gave *amino alcohol* **29** (483 mg, 1.48 mmol, 99%) as needles.

m.p. 93-95 °C; $\boldsymbol{\nu_{max}}$(KBr disk)/cm^{-1} 3474, 3300, 3075, 2979, 2923, 1640, 1599, 1439, 1328, 1158, 1092, 1048, 998, 921, 882, 815; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.77 (2 H, d, *J* 8.3), 7.30 (2 H, d, *J* 8.3), 5.80 (1 H, d, *J* 9.1), 5.77-5.63 (2 H, m), 5.15-4.95 (4 H, m), 3.91 (1 H, d, *J* 11.8), 3.53-3.50 (1 H, m), 3.20 (1 H, dt, *J* 9.1, 2.8), 3.13 (1 H, br. s), 3.04 (1 H, s), 2.45-2.39 (4 H, m), 2.30 (1 H, dd, 14.4, 6.9), 2.26 (1 H, dd, 14.4, 8.2) and 2.15 (1 H, dd, 14.4, 7.6); $\boldsymbol{\delta_C}$ (100.6 MHz, $CDCl_3$) 143.6, 137.8, 132.4, 132.3, 129.8, 127.0, 119.5, 119.4, 76.8, 62.3, 57.9, 40.9, 40.0, 21.5; ***m/z*** (ESI$^+$) 326

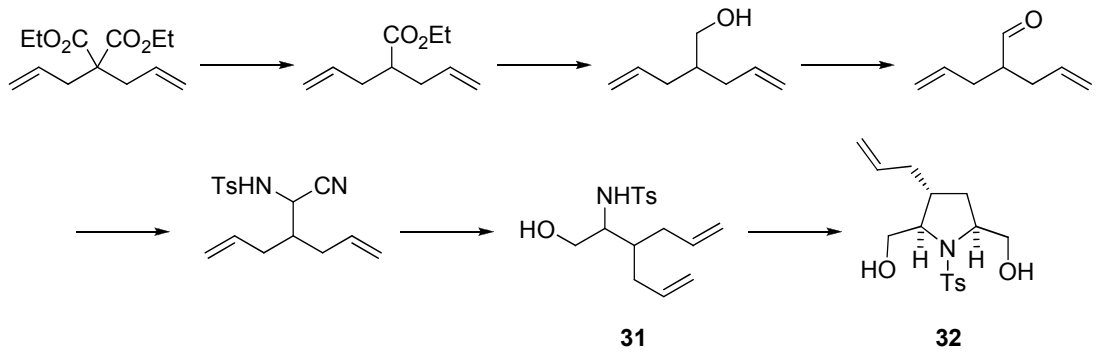
(55%, $[M+H]^+$), 348 (40%, $[M+Na]^+$); **HRMS** (ESI^+). $C_{16}H_{23}NO_4SNa$ requires *MNa* 348.1240, found 348.1235 (+1.57 ppm)]; $[\alpha]_D^{18}$ □4.5 (*c* 1.0, CH_2Cl_2).

((2*S*,3*S*,5*S*)-3-Allyl-3-hydroxy-1-tosylpyrrolidine-2,5-diyl)dimethanol 30



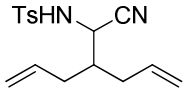
Potassium osmate dihydrate (3.8 mg, 0.010 mmol) was added to a solution of amino alcohol **29** (68 mg, 0.209 mmol), pyridine-*N*-oxide (40 mg, 0.418 mmol), citric acid (30 mg, 0.157 mmol) and TFA (0.2 mL) in 9:1 acetone:H_2O (4.2 mL) and the reaction stirred at 40 °C for 16 h. Na_2SO_3 (10 mg) was added and the mixture stirred for 30 minutes. Aqueous NaOH (2 M, 10 mL) and EtOAc (10 mL) were added and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organics were washed sequentially with aqueous HCl (1 M, 20 mL) and aqueous NaOH (2 M, 20 mL), dried over Na_2SO_4, filtered and concentrated to give the crude product. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol:acetone, R_f 0.20) gave *pyrrolidine* **30** (62 mg, 0.182 mmol, 87%, 15:1 mixture of diastereomers) as prisms.

m.p. 100-102 ^oC; ν_{max}(KBr disk)/cm^{-1} 3374, 2930, 1641, 1598, 1433, 1340, 1162, 1092, 1038, 1002, 922, 817; δ_H (400 MHz, $CDCl_3$) 7.73 (2 H, d, *J* 8.2), 7.36 (2 H, d, *J* 8.2), 5.61 (1 H, ddt, *J* 17.1, 10.1, 7.3), 5.02-4.99 (1 H, m), 4.83 (1 H, dd, *J* 17.1, 1.6), 4.35 (1 H, br. s), 4.12 (1 H, dd, *J* 11.3, 2.8), 4.06 (1 H, dd, *J* 11.6, 3.6), 4.00-3.86 (3 H, m), 3.74-3.70 (1 H, m), 3.66 (1 H, dd, *J* 11.3, 2.3), 3.31 (1 H, t, *J* 3.6), 2.46 (3 H, s), 1.99-1.94 (2 H, m), 1.81 (1 H, dd, *J* 13.6, 9.0), 1.72 (1 H, dd, *J* 14.1, 7.3); δ_C (100.6 MHz, $CDCl_3$) 144.4, 133.4, 132.6, 130.0, 127.7, 119.1, 79.2, 67.8, 65.1, 63.6, 60.3, 43.4, 40.1, 21.6; ***m/z*** (ESI^+) 342 (85%, $[M+H]^+$), 364 (75%, $[M+Na]^+$); **HRMS** (ESI^+). $C_{16}H_{23}NO_5SNa$ requires *MNa* 364.1189, found 364.1190 (□0.34 ppm)]; $[\alpha]_D^{19}$ +14.3 (*c* 1.0, CH_2Cl_2).



Scheme 12: Synthesis of amino-alcohol **31** and pyrrolidine **32**

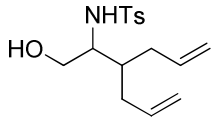
(±)-*N*-(2-Allyl-1-cyanopent-4-enyl)-4-methylbenzenesulfonamide



Potassium cyanide (246 mg, 3.78 mmol) was added to a solution of the aldehyde[4] (460 mg, 3.70 mmol) and ammonium acetate (857 mg, 11.1 mmol) in EtOH (7.5 mL) and the reaction was stirred at room temperature for 72 h. The reaction mixture was concentrated and the residue taken up in ether (20 mL). Aqueous HCl (6 M, 10 mL) was added and the layers were separated before washing the aqueous layer with two further portions of ether (2 × 20 mL). The pH was adjusted to 12 with aqueous NaOH (40% by weight, saturated with NaCl) and the product amine was extracted with ether (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield the crude amino nitrile which was dissolved in CH_2Cl_2 (3.7 mL). *p*-Toluenesulfonyl chloride (320 mg, 1.68 mmol) and DMAP (559 mg, 4.57 mmol) were added and the reaction stirred at room temperature for 16 h. Aqueous HCl (1 M, 20 mL) and ether (20 mL) were added and the layers separated. The aqueous phase was extracted with ether (3 × 20 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated to give the crude product. Flash column chromatography (SiO_2, eluting with 9:1 petrol:acetone, R_f 0.28) furnished the *amino nitrile* (332 mg, 1.09 mmol, 30%) as plates.

m.p. 65-66 °C; ν_{max}(KBr disk)/cm^{-1} 3264, 2964, 2252, 1642, 1598, 1443, 1338, 1165, 1091; δ_H (400 MHz, $CDCl_3$) 7.77 (2 H, d, *J* 8.3), 7.37 (2 H, d, *J* 8.3), 5.81-5.67 (2 H, m), 5.36 (1 H, d, *J* 7.3), 5.20-5.12 (4 H, m), 4.33 (1 H, br. s), 2.45 (3 H, s), 2.33-2.12 (4 H, m), 1.99-1.94 (1 H, m); δ_C (100.6 MHz, $CDCl_3$) 144.6, 136.0, 134.7, 134.2, 130.1, 127.2, 119.2, 119.0, 116.4, 47.3, 41.5, 34.8, 34.3, 21.7; ***m/z*** (ESI$^+$) 363 (100%, $[M+MeCN+NH_4]^+$); **HRMS** (ESI$^+$) $C_{16}H_{24}N_3O_2S$ requires *MNH4* 322.1584, found 322.1584 (□0.16 ppm).

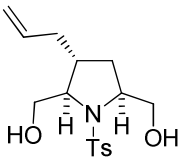
(±)-*N*-(3-Allyl-1-hydroxyhex-5-en-2-yl)-4-methylbenzenesulfonamide 31



DIBAL-H (1.5 M in toluene, 1.81 mL, 2.71 mmol) was added to a solution of the amino nitrile (330 mg, 1.08 mmol) in CH_2Cl_2 (4 mL) at □20 °C and stirred for 6 h, whereupon TLC indicated complete consumption of starting material. MeOH (5 mL) was added, followed by ether (20 mL) and aqueous HCl (1 M, 20mL). The layers were separated and the aqueous phase extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. This crude product was dissolved in MeOH (10 mL) and cooled to 0 °C prior to addition of $NaBH_4$ (90 mg, 2.39 mmol). TLC indicated complete consumption of substrate after 2 h and the reaction was quenched with saturated aqueous NH_4Cl (20 mL) and extracted with ether (4 × 20 mL). The combined extracts were dried over Na_2SO_4, filtered and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, eluting with 4:1 petrol:acetone, R_f 0.24) to yield *amino alcohol* **31** (173 mg, 0.47 mmol, 43%) as an oil.

$\boldsymbol{\nu_{max}}$(thin film)/cm^{-1} 3283, 3076, 2924, 1640, 1599, 1442, 1327, 1159, 1327, 1159, 1092; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.78 (2 H, d, *J* 8.3), 7.32 (2 H, d, *J* 8.3), 5.63 (2 H, ddd, *J* 16.9, 10.1, 7.1), 5.07 (1 H, d, *J* 8.6), 5.03-4.91 (4 H, m), 3.59 (1 H, dd, *J* 11.4, 5.8), 3.52 (1 H, dd, *J* 11.4, 4.3), 3.35-3.29 (1 H, m), 2.44 (3 H, s), 2.10-1.92 (4 H, m), 1.73-1.65 (1 H, m); $\boldsymbol{\delta_C}$ (100.6 MHz, $CDCl_3$) 143.6, 137.5, 136.4, 136.2, 129.7, 127.2, 117.2, 117.1, 62.5, 57.3, 39.5, 34.4, 34.2, 21.5; ***m/z*** (ESI□) 308 (100%, [M□H]□); **HRMS** (ESI□) $C_{16}H_{22}NO_3S$ requires *M*□*H* 308.1315, found 308.1314 (+0.45 ppm).

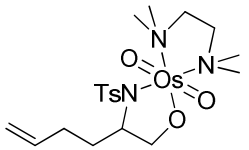
(±)-((2*R*,3*R*,5*S*)-3-Allyl-1-tosylpyrrolidine-2,5-diyl)dimethanol 32



Amino alcohol **31** (36 mg, 0.116 mmol) was subjected to General Procedure 5, reaction time 14 h. Purification by flash column chromatography (SiO_2, eluting with 7:3 petrol:acetone, R_f 0.26) gave *pyrrolidine* **32** (34 mg, 0.104 mmol, 90%, 20:1 mixture of diastereomers) as yellow prisms.

m.p. 101-103 °C; ν_{max}(KBr disk)/cm^{-1} 3384, 2927, 1598, 1339, 1160; δ_H (400 MHz, $CDCl_3$) 7.75 (2 H, d, *J* 8.3), 7.36 (2 H, d, *J* 8.3), 5.50 (1 H, ddd, *J* 17.2, 10.4, 6.8), 4.94 (1 H, ddt, *J* 10.4, 1.8, 1.0), 4.82 (1 H, ddt, *J* 17.2, 3.3, 1.3), 3.94 (1 H, dd, *J* 11.6, 3.5), 3.85 (1 H, dd, *J* 11.1, 3.8), 3.81-3.77 (1 H, m), 3.68-3.61 (2 H, m), 3.35-3.31 (1 H, m), 3.03 (2 H, br. s), 2.47 (3 H, s), 2.27-2.20 (1 H, m), 1.94 (1 H, ddd, J 12.6, 7.1, 5.1), 1.78-1.71 (1 H, m), 1.57-1.50 (1 H, m), 1.30-1.23 (1 H, m); δ_C (100.6 MHz, $CDCl_3$) 144.2, 135.3, 133.9, 129.9, 127.7, 117.0, 67.9, 65.7, 65.0, 62.3, 39.3, 37.2, 32.9, 21.6; ***m/z*** (ESI$^+$) 384 (100%, M+MeCN+NH_4^+), 348 (70%, $[M+Na]^+$); **HRMS** (ESI$^+$) $C_{16}H_{23}NNaO_4S$ requires *MNa* 348.1240, found 328.1241 (□0.33 ppm).

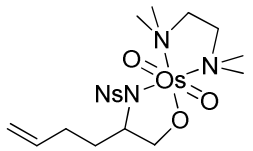
(±)-Osmate Ester 39



Potassium osmate dihydrate (74 mg, 0.200 mmol) dissolved in water (4.5 mL) was added dropwise to a solution of the amino alcohol **3** (49 mg, 0.182 mmol) and *N*,*N*,*N*□,*N*□-tetramethylethylenediamine (23 mg, 0.200 mmol) in acetone (18 mL) at room temperature. Aqueous HCl (1 M) was added dropwise until the mixture reached pH 7 and the resulting brown solution stirred at room temperature for 2 h, then concentrated. Purification by flash column chromatography (SiO_2, eluting with 3:2 petrol-acetone, R_f 0.20) furnished the *osmate ester* **39** (93 mg, 0.154 mmol, 84%) as a brown waxy solid.

ν_{max} (thin film) 2927, 1639, 1461, 1299, 1149, 1092, 1004, 913, 878, 845, 802, 731; δ_H (400 MHz; $CDCl_3$) 7.82 (2 H, d, *J* 8.1), 7.21 (2 H, d, *J* 8.1), 5.85 (1 H, ddt, *J* 17.0, 10.3, 6.6), 5.03 (1 H, dd, *J* 17.0, 1.7), 4.94-4.91 (1 H, m), 3.93 (1 H, d, *J* 9.9), 3.77 (1 H, dd, *J* 9.9, 4.2), 3.41-3.27 (5 H, m), 3.19 (1 H, ddd, *J* 10.5, 6.8, 4.2), 2.94 (3 H, s), 2.88 (3 H, s), 2.87-2.83 (1 H, m), 2.75 (3 H, s), 2.68-2.64 (1 H, m), 2.37 (3 H, s), 2.21-2.06 (2 H, m), 1.88-1.83 (2 H, m); δ_C (100 MHz; $CDCl_3$) 141.7, 140.1, 138.9, 129.0, 127.4, 114.3, 81.3, 67.4, 65.2, 63.2, 53.3, 52.7, 50.1, 46.7, 31.5, 31.0, 21.5; ***m/z*** (ESI$^+$) 607 (25%, $[M+H]^+$), 666 (100%, $[M+NH_4+MeCN]^+$); **HRMS** (ESI$^+$) $C_{19}H_{33}N_3SO_5OsNa$ requires *MNa* 630.1648, found 630.1646. (+0.05 ppm).

(±)-Osmate Ester 40



Potassium osmate dihydrate (47 mg, 0.128 mmol) dissolved in water (2.9 mL) was added dropwise to a solution of the amino alcohol **11** (35 mg, 0.116 mmol) and *N*,*N*,*N*□,*N*□-tetramethylethylenediamine (15 mg, 0.200 mmol) in acetone (11.7 mL) at room temperature. Aqueous HCl (1 M) was added dropwise until the mixture reached pH 7 and the resulting brown solution stirred at room temperature for 2 h, then concentrated. Purification by flash column chromatography (SiO_2, eluting with 1:1 petrol-acetone, R_f 0.30) furnished the *osmate ester* **40** (42 mg, 0.0660 mmol, 57%) as a brown waxy solid.

$\boldsymbol{\nu_{max}}$ (thin film) 2931, 1639, 1542, 1463, 1374, 1314, 1158, 1127, 1066, 1014, 958, 913, 881, 845, 803, 779, 732; $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$) 8.12-8.09 (1 H, m), 7.56-7.53 (3 H, m), 5.81 (1 H, ddt, *J* 17.0, 10.3, 6.6), 5.00 (1 H, dd, *J* 17.0, 1.7), 4.92-4.89 (1 H, m), 4.17 (1 H, d, *J* 10.2), 4.12 (1 H, dd, *J* 10.2, 3.6), 3.35-3.30 (1 H, m), 3.24-3.08 (5 H, m), 3.05-3.00 (1 H, m), 2.93 (3 H, s), 2.85 (3 H, s), 2.81-2.77 (1 H, m), 2.75 (3 H, s), 2.16-2.06 (2 H, m), 1.98-1.79 (2 H, m); $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 149.3, 138.6, 136.4, 132.0, 131.3, 129.4, 123.4, 114.5, 81.4, 67.5, 65.1, 63.4, 52.7, 51.4, 51.4, 47.7, 31.9, 31.0; ***m/z*** (ESI^+) 660 (15%, $[M+Na]^+$), 696 (100%, $[M+NH_4+MeCN]^+$); **HRMS** (ESI^+) $C_{18}H_{30}N_4SO_7OsNa$ requires *MNa* 661.1342, found 661.1345. (–0.49 ppm).

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