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## General Experimental Methods.

Melting points were determined using a hot-stage melting point apparatus and are uncorrected. Infrared spectra were recorded on a FT-IR spectrophotometer as potassium bromide disks of solids ( KBr ) or as thin films of liquids (neat) between sodium chloride plates. Nuclear magnetic resonance spectra $\left({ }^{1} \mathrm{H},{ }^{31} \mathrm{P}\right.$ and ${ }^{13} \mathrm{C}$ NMR) were recorded on either 300 or 400 MHz spectrometers. ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR assignments were confirmed using standard 2D COSY, NOESY, HSQC, and HMBC experiments. Low resolution electrospray ionisation (ESI) were recorded in the positive mode (ESI ${ }^{+}$) on a QMS-quadrupole mass spectrometer. Accurate mass measurements were obtained at high resolution with a FTMS and a 4.7T superconducting magnet. The instrument was externally calibrated with FC5311. Analytical thin-layer chromatography (TLC) was performed on plastic slides coated with silica gel (Polygram SIL g/uv254). Flash chromatography was performed using Merck silica gel 60 (Merck no. 9385), 0.063-0.200 mm (230-400 mesh). Solvents were purified according to standard procedures. Chloroform used for optical rotations was of analytical purity. Degassed methanol and benzene were used in all hydrogenation reactions. Degassed dichloromethane was used in metathesis reactions. Deuterated chloroform was used as supplied. Deuterated dichloromethane was degassed by three freeze-pump-thaw cycles. Grubbs' catalyst refers to bis(tricyclohexylphosphine)benzylidene ruthenium dichloride. ${ }^{18}$ Second generation Grubbs' catalyst refers to tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2ylidene][benzylidene]ruthenium dichloride. ${ }^{19}$ Wilkinson's catalyst refers to chlorotris(triphenylphosphine)rhodium (I). ${ }^{23} \mathrm{Rh}(\mathrm{I})-(S, S)$-Et-DuPHOS refers to (+)-1,2-bis[(2S,5S)-2,5-diethylphospholano]benzene(1,5-cyclooctadiene)rhodium(I) tetrafluoroborate. ${ }^{20} \quad \operatorname{Rh}(\mathrm{I})-(R, R)$-EtDuPHOS refers to (-)-1,2-bis[(2R,5R)-2,5-diethylphospholano]benzene(1,5-cyclooctadiene)rhodium(I) tetrafluoroborate. ${ }^{20}$ All ruthenium-catalysed metathesis reactions were performed using standard Schlenk techniques under an atmosphere of nitrogen or in an argon filled drybox. Solvents were dried and degassed using standard procedures. In all rhodium-phosphine hydrogenations, high purity ( $<10 \mathrm{ppm}$ of
oxygen) hydrogen and argon were used and purified by passage through a series of traps to remove water, oxygen and hydrocarbons. Ethylene and cis-2-butene were used as supplied. The enantiomeric excess of hydrogenation products was determined via analytical gas chromatography (GC) using a chiral column Model C-024 (column: $0.25 \mathrm{~mm} \times 50 \mathrm{~cm}, 50 \mathrm{CP} 2 / X E 60-S V A L S A P E A) ~ u s i n g ~ h e l i u m ~ a s ~$ the carrier gas. Optical rotations were measured with a polarimeter (in a cell length of 1 dm ) at a wavelength of 589 nm (sodium D line) at a temperature of $22^{\circ} \mathrm{C}$.
(2R)-Methyl $2 N$-acetylaminopent-4-enoate (ent-4). ${ }^{16}$ (2Z)-Methyl $2 N$-acetylaminopenta-2,4dienoate $3(40.0 \mathrm{mg}, 0.24 \mathrm{mmol})$, benzene ( 5 ml ), [(COD) $\mathrm{Rh}(R, R)$-Et-DuPHOS]OTf ( 3 mg ), $30 \mathrm{psi} \mathrm{H}_{2}$, $3 \mathrm{~h}, 88 \%$ yield, $96 \%$ ee $(2 R-4), t_{\mathrm{R}}=16.4 \mathrm{~min}(R)\left(\mathrm{GC}\right.$ chiral column Model $\mathrm{C}-024,100^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 5^{\circ} \mathrm{C}$ $\min ^{-1}$ to $280^{\circ} \mathrm{C}$ for 9 min$) .[\alpha]^{22}{ }_{\mathrm{D}}-43.0^{\circ}\left(\mathrm{c}=0.47, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with literature data. ${ }^{16}$
(2S)-Methyl 2 N -benzoylaminopent-4-enoate (6). ${ }^{32}$ (2Z)-Methyl 2 N -benzoylaminopenta-2,4-dienoate (100.0 mg, 0.43 mmol ), benzene ( 8 ml ), [(COD)Rh(S,S)-Et-DuPHOS]OTf ( 3 mg ), $30 \mathrm{psi}_{2}, 3 \mathrm{~h}, 99 \%$ yield, $100 \%$ ee $(2 S-6), t_{\mathrm{R}}=27.0 \mathrm{~min}\left(\mathrm{GC}\right.$ chiral column Model $\mathrm{C}-024,180^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 2^{\circ} \mathrm{C} \mathrm{min}^{-1}$ to $210^{\circ} \mathrm{C}$ for 20 min$) .[\alpha]_{\mathrm{D}}^{22}+49.3^{\circ}\left(\mathrm{c}=1.12, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with literature data. ${ }^{32}$
(2R)-Methyl $2 N$-benzoylaminopent-4-enoate (ent-6). ${ }^{32}$ (2Z)-Methyl $2 N$-benzoylaminopenta-2,4dienoate ( $100.0 \mathrm{mg}, 0.43 \mathrm{mmol}$ ), benzene ( 8 ml ), [(COD)Rh(R,R)-Et-DuPHOS]OTf ( 3 mg ), $30 \mathrm{psi} \mathrm{H}, 3$ $\mathrm{h}, 93 \%$ yield, $100 \%$ ee $(2 R-\mathbf{6}), t_{\mathrm{R}}=26.4 \mathrm{~min}\left(\mathrm{GC}\right.$ chiral column Model $\mathrm{C}-024,180^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 2^{\circ} \mathrm{C}$ $\min ^{-1}$ to $210^{\circ} \mathrm{C}$ for 20 min$) .[\alpha]^{22}-49.7^{\circ}\left(\mathrm{c}=0.64, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with literature data. ${ }^{32}$
(2S)-Methyl $\quad 2 N$-acetylamino-5-phenylpent-4-enoate (13). ${ }^{30} \quad$ (2Z)-Methyl $\quad 2 N$-acetylamino-5-phenylpenta-2,4-dienoate $12(28.0 \mathrm{mg}, 0.11 \mathrm{mmol})$, methanol ( 5 ml ), [(COD)Rh( $S, S$ )-Et-DuPHOS]OTf $(1 \mathrm{mg}), 75 \mathrm{psi} \mathrm{H}_{2}, 2 \mathrm{~h}, 97 \%$ yield, $99 \%$ ee $(2 S-13) .[\alpha]_{\mathrm{D}}^{22}+90.0^{\circ}\left(\mathrm{c}=0.64, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with literature data. ${ }^{30}$
(2R)-Methyl 2N-acetylamino-5-phenylpent-4-enoate (ent-13). ${ }^{30}$ (2Z)-Methyl $2 N$-acetylamino-5-phenylpenta-2,4-dienoate $12(27.4 \mathrm{mg}, 0.11 \mathrm{mmol})$, methanol ( 5 ml ), [(COD) $\mathrm{Rh}(R, R)$-Et-DuPHOS]OTf $(1 \mathrm{mg}), 75 \mathrm{psi}_{2}, 2 \mathrm{~h}, 92 \%$ yield, $99 \%$ ee $(2 R-13) .[\alpha]_{\mathrm{D}}^{22}-89.8^{\circ}\left(\mathrm{c}=1.03, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with literature data. ${ }^{30}$
(2S)-Methyl $2 N$-acetylamino-5-methylhex-4-enoate (15). (2Z)-Methyl $2 N$-acetylamino-5-methylhexa-2,4-dienoate 16 ( $74.0 \mathrm{mg}, 0.38 \mathrm{mmol}$ ), methanol ( 5 ml ), [(COD)Rh(S,S)-Et-DuPHOS]OTf $(2 \mathrm{mg}), 75 \mathrm{psi}_{2}, 2 \mathrm{~h}, 98 \%$ yield, $100 \%$ ee $(2 S-15), t_{\mathrm{R}}=24.2 \mathrm{~min}(\mathrm{GC}$ chiral column Model C-024, $100^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 5^{\circ} \mathrm{C} \min ^{-1}$ to $210^{\circ} \mathrm{C}$ for 7 min$) .[\alpha]_{\mathrm{D}}^{22}+58.2^{\circ}\left(\mathrm{c}=0.79, \mathrm{CHCl}_{3}\right)$, m.p. $46-48^{\circ} \mathrm{C} . v_{\max }$ (neat): $3288 \mathrm{~m}, 2955 \mathrm{w}, 1746 \mathrm{~s}, 1660 \mathrm{~s}, 1538 \mathrm{~m}, 1436 \mathrm{~m}, 1377 \mathrm{~m}, 1274 \mathrm{w}, 1210 \mathrm{w}, 1126 \mathrm{w}, 1030 \mathrm{w}, 736 \mathrm{w} \mathrm{cm}^{-}$ ${ }^{1} .{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 1.59(\mathrm{~s}, 3 \mathrm{H}, \mathrm{H} 6 \mathrm{a}), 1.69(\mathrm{~d}, J 0.9 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{H} 6 \mathrm{~b}), 2.00\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3} \mathrm{CO}\right)$, 2.39-2.60 (m, 2H, H3), $3.72\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{OCH}_{3}\right), 4.63(\mathrm{dt}, J 7.9,5.6 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H} 2), 4.99(\mathrm{t}, J 7.5 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H} 4)$, 6.02 (bs, 1H, NH). ${ }^{13} \mathrm{C}$ NMR. ( $\left.100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 18.0,26.0,\left(\left(\mathrm{CH}_{3}\right)_{2}\right), 23.3\left(\mathrm{CH}_{3} \mathrm{CO}\right), 30.8(\mathrm{C} 3), 52.2$, $52.4\left(\mathrm{C} 2, \mathrm{OCH}_{3}\right), 117.6(\mathrm{C} 4), 136.6(\mathrm{C} 5), 169.8,172.8(\mathrm{C} 1, \mathrm{CONH}) . \mathrm{HRMS}\left(\mathrm{ESI}^{+}, \mathrm{MeOH}\right): \mathrm{m} / \mathrm{z}$ calcd for $\mathrm{C}_{10} \mathrm{H}_{17} \mathrm{NO}_{3} \mathrm{Na}\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$222.1106, found 222.1105.
(2R)-Methyl $2 N$-acetylamino-5-methylhex-4-enoate (ent-15). (2Z)-Methyl $2 N$-acetylamino-5-methylhexa-2,4-dienoate 16 ( $24.5 \mathrm{mg}, 0.12 \mathrm{mmol}$ ), methanol ( 5 ml ), [(COD)Rh( $R, R$ )-Et-DuPHOS]OTf $(1 \mathrm{mg}), 75 \mathrm{psi}_{2}, 2 \mathrm{~h}, 100 \%$ yield, $100 \%$ ee $(2 R-15), t_{\mathrm{R}}=23.9 \mathrm{~min}(\mathrm{GC}$ chiral column Model C-024, $100^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 5^{\circ} \mathrm{C} \mathrm{min}^{-1}$ to $210^{\circ} \mathrm{C}$ for 7 min$) .[\alpha]_{\mathrm{D}}^{22}-58.3^{\circ}\left(\mathrm{c}=0.53, \mathrm{CHCl}_{3}\right)$. Spectral data were consistent with that previously obtained.
(2S,7S)-Dimethyl 2,7-N, $N$ '-dibenzoylamino-oct-4-enedioate (7). (2S)-Methyl $2 N$ -benzoylaminopent-4-enoate $\mathbf{6}(49.0 \mathrm{mg}, 0.21 \mathrm{mmol})$, dichloromethane ( 4 ml$), 2^{\text {nd }}$ generation Grubbs' $\mathbf{S 5}$
catalyst ( $18.0 \mathrm{mg}, 0.02 \mathrm{mmol}, 10 \mathrm{~mol} \%$ ) , $12 \mathrm{~h}, 50^{\circ} \mathrm{C}, 100 \%$ conversion. Purification by flash chromatography $\left(\mathrm{SiO}_{2}\right.$, dichloromethane : light petroleum : ethyl acetate, 1:1:1) gave pure dimer 7 (32.8 $\mathrm{mg}, 36 \%)$ as a pale brown solid, m.p. $140-142^{\circ} \mathrm{C} . t_{\mathrm{R}}(E / Z)=13.5,13.9 \mathrm{~min}(\mathrm{GC}$ column $30 \mathrm{QC} 5 / \mathrm{BPX} 5)$, $150^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 10^{\circ} \mathrm{C} \mathrm{min}^{-1}$ to $280^{\circ} \mathrm{C}$ for 6 min$) .[\alpha]_{\mathrm{D}}^{22}+56.4^{\circ}\left(\mathrm{c}=0.27, \mathrm{CHCl}_{3}\right) . v_{\max }$ (neat): 3322 bm, 2953m, 2358w, 1742s, 1644s, 1603w, 1580w, 1538m, 1488m, 1436m, 1267w, 1218m, 1027w, 973w, $802 \mathrm{w}, 736 \mathrm{~m} \mathrm{~cm}^{-1} .{ }^{1} \mathrm{H}$ NMR (300 MHz, $\mathrm{CDCl}_{3}$ ): $\delta 2.57-2.69(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H} 3,6), 3.67\left(\mathrm{~s}, 6 \mathrm{H}, \mathrm{OCH}_{3}\right), 4.85-$ 4.98 (m, 2H, H2,7), 5.49 (t, J 4.1 Hz, 2H, H4,5), 6.86 (bd, J $7.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{NH}$ ), 7.40-7.44 (m, 4H, H3',5'), 7.48-7.52 (m, 2H, H4'), 7.81-7.83 (m, 4H, H2', $6^{\prime}$ ). ${ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 35.2$ (C3,6), $52.5(\mathrm{C} 2,7), 52.6\left(\mathrm{OCH}_{3}\right), 127.2\left(\mathrm{C}^{\prime}, 6^{\prime}\right), 128.7\left(\mathrm{C}^{\prime}, 5\right.$ ') , $128.8(\mathrm{C} 4,5), 131.9(\mathrm{C} 4$ '), 133.9 $\left(\mathrm{C}^{\prime}\right), 167.1,172.4(\mathrm{C} 1,8, \mathrm{CONH}) . \operatorname{HRMS}\left(\mathrm{ESI}^{+}, \mathrm{MeOH}\right): m / z$ calcd for $\mathrm{C}_{24} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{6} \mathrm{Na}\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$ 461.1689, found 461.1695.

## Attempted dimerisation of (2S)-methyl 2N-acetylamino-5-phenylpent-4-enoate (13). Trial 1: (2S)-

 Methyl $2 N$-acetylamino-5-phenylpent-4-enoate $13(59.3 \mathrm{mg}, 0.24 \mathrm{mmol})$, dichloromethane ( 10 ml ), Grubbs' catalyst ( $19.8 \mathrm{mg}, 0.02 \mathrm{mmol}, 10 \mathrm{~mol} \%$ ), $13 \mathrm{~h}, 50^{\circ} \mathrm{C}, 0 \%$ conversion of $\mathbf{1 3}$ into dimer $\mathbf{5}$. Trial 2: (2S)-Methyl $2 N$-acetylamino-5-phenylpent-4-enoate $\mathbf{1 3}$ ( $59.3 \mathrm{mg}, 0.24 \mathrm{mmol}$ ), dichloromethane ( 7 $\mathrm{ml}), 2^{\text {nd }}$ generation Grubbs' catalyst ( $10.2 \mathrm{mg}, 0.01 \mathrm{mmol}, 5 \mathrm{~mol} \%$ ), $20 \mathrm{~h}, 50^{\circ} \mathrm{C}, 33 \%$ conversion of $\mathbf{1 3}$ into dimer 5.Dimerisation of (2S)-Methyl 2N-acetylaminohex-4-enoate (17). (2S)-Methyl 2 N -acetylaminohex-4enoate $\mathbf{1 7}(17.0 \mathrm{mg}, 0.09 \mathrm{mmol})$, dichloromethane ( 4 ml ), $2^{\text {nd }}$ generation Grubbs' catalyst ( $4.2 \mathrm{mg}, 0.005$ mmol, $5 \mathrm{~mol} \%), 17 \mathrm{~h}, 50^{\circ} \mathrm{C}, 100 \%$ conversion into dimer 5. Spectroscopic data were in agreement with that previously obtained.

Cross metathesis of (2S)-methyl 2 N -acetylaminopent-4-enoate (4) in the presence of (2S)-methyl $\mathbf{2 N}$-acetylaminopenta-2,4-dienoate (3). (2S)-Methyl 2 N -acetylamino-pent-4-enoate 4 ( $34.0 \mathrm{mg}, 0.20$ mmol ), (2Z)-methyl 2 N -acetylamino-penta-2,4-dienoate 3 ( $33.6 \mathrm{mg}, 0.20 \mathrm{mmol}$ ), dichloromethane (4 $\mathrm{ml})$, Grubbs' catalyst ( $16.3 \mathrm{mg}, 0.02 \mathrm{mmol}, 10 \mathrm{~mol} \%$ ), $18 \mathrm{~h}, 50^{\circ} \mathrm{C}$. The ${ }^{1} \mathrm{H}$ NMR spectrum displayed peaks characteristic of the starting allylglycine derivative $\mathbf{4}$ and dienamide $\mathbf{3}$ but no peaks characteristic of expected dimer 5. The mass spectrum displayed peaks attributed to allylglycine derivative 4 and tricyclohexylphosphine-dienamide conjugate addition adduct. Mass Spectrum (ESI ${ }^{+}$, DCM/MeOH): $m / z$ 194.1 $\mathrm{C}_{8} \mathrm{H}_{13} \mathrm{NO}_{3} \mathrm{Na}\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$, 4. $m / z$. $450.4 \mathrm{C}_{26} \mathrm{H}_{45} \mathrm{NO}_{3} \mathrm{P}^{+}\left[\mathrm{M}^{+}\right]$, tricyclohexylphosphine-dienamide adduct.

Cross metathesis of (2S)-methyl 2 N -acetylaminopent-4-enoate (4) in the presence of (2S)-methyl 2N-acetylamino-5-phenylpenta-2,4-dienoate (12). (2S)-Methyl 2 N -acetylaminopent-4-enoate 4 (18.1 $\mathrm{mg}, 0.11 \mathrm{mmol}$ ), (2Z)-methyl 2 N -acetylamino-5-phenylpenta-2,4-dienoate $\mathbf{1 2}$ ( $26.1 \mathrm{mg}, 0.11 \mathrm{mmol}$ ), dichloromethane ( 4 ml ), Grubbs' catalyst ( $8.7 \mathrm{mg}, 0.01 \mathrm{mmol}, 10 \mathrm{~mol} \%$ ), $18 \mathrm{~h}, 50^{\circ} \mathrm{C}, 28 \%$ conversion of $\mathbf{4}$ into dimer $\mathbf{5}$. Dienamide $\mathbf{1 2}$ did not react under these conditions.

Cross metathesis of (2S)-Methyl 2 N -acetylaminopent-4-enoate (4) in the presence of (2S)-Methyl 2N-acetylamino-5-methylhex-4-enoate (15). (2S)-Methyl 2 N -acetylaminopent-4-enoate 4 (12.7 mg, $0.07 \mathrm{mmol})$, (2S)-methyl 2 N -acetylamino-5-methylhex-4-enoate $\mathbf{1 5}$ (12.0 mg, 0.07 mmol ), dichloromethane ( 4 ml ), Grubbs' catalyst $(11.5 \mathrm{mg}, 0.01 \mathrm{mmol}, 20 \mathrm{~mol} \%), 18 \mathrm{~h}, 50^{\circ} \mathrm{C}, 100 \%$ conversion of $\mathbf{4}$ into dimer $\mathbf{5 . 1 5}$ did not react under these conditions.

Wilkinson's hydrogenation of Dimer (7). (2S,7S)-Dimethyl 2,7- $N, N$ '-dibenzoylaminooctanedioate (18). ( $2 S, 7 S$ )-Dimethyl $2,7-N, N$ '-dibenzoylamino-octa-4-enedioate 7 ( $20.0 \mathrm{mg}, 0.05$
mmol ), benzene ( 5 ml ), Wilkinson's catalyst ( 2 mg ), $50 \mathrm{psi}_{2}, 4 \mathrm{~h}, 100 \%$ of $\mathbf{1 8}$ as a brown oil. $t_{\mathrm{R}}=17.2$ $\min \left(\mathrm{GC}\right.$ : Column $30 \mathrm{QC} 5 / \mathrm{BPX5}, 150^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 10^{\circ} \mathrm{C} \mathrm{min}^{-1}$ to $280^{\circ} \mathrm{C}$ for 6 min ). $v_{\max }$ (neat): 3055 m , 2986w, 2955w, 1741s, 1662s, 1603w, 1580w, 1518m, 1486m, 1438s, 1359w, 1286s, 1182m, 1120m, 1028w, 896m cm ${ }^{-1} .{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 1.35-1.53(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H} 4,5), 1.80-2.02(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H} 3,6)$, $3.78\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{OCH}_{3}\right), 4.82(\mathrm{dt}, J 7.4,5.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{H} 2,7), 6.73(\mathrm{bd}, J 7.7 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{NH}), 7.40-7.49(\mathrm{~m}, 6 \mathrm{H}$, H3', $\left.4^{\prime}, 5^{\prime}\right), 7.78-7.82\left(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H}^{\prime}, 5^{\prime}\right) .{ }^{13} \mathrm{C}$ NMR (100 MHz, $\mathrm{CDCl}_{3}$ ): $\delta 24.9(\mathrm{C} 4,5), 32.6(\mathrm{C} 3,6), 52.5,52.7$ $\left(\mathrm{C} 2, \mathrm{OCH}_{3}\right), 127.2\left(\mathrm{C}^{\prime}, 6^{\prime}\right), 128.6\left(\mathrm{C}^{\prime}, 5^{\prime}\right), 131.9\left(\mathrm{C}^{\prime}\right), 134.1\left(\mathrm{C}^{\prime}\right), 167.2,173.2(\mathrm{C} 1,8, \mathrm{CONH})$. HRMS $\left(\mathrm{ESI}^{+}, \mathrm{MeOH}\right): \mathrm{m} / z$ calcd for $\mathrm{C}_{24} \mathrm{H}_{28} \mathrm{~N}_{2} \mathrm{O}_{6} \mathrm{Na}\left[(\mathrm{M}+\mathrm{Na})^{+}\right] 463.1845$, found: 463.1842

## Wilkinson's hydrogenation of (2S)-methyl 2 N -acetylamino-5-phenylpenta-2,4-dienoate (12).

 (2S)-Methyl $2 N$-acetylamino-5-phenylpenta-2,4-dienoate 12 ( $11.5 \mathrm{mg}, 0.05 \mathrm{mmol}$ ), benzene ( 5 ml ), Wilkinson's catalyst ( 1 mg ), $50 \mathrm{psi}_{2}, 4 \mathrm{~h}, 99 \%$ yield of a $1: 4$ mixture of $13: 14$ as a brown oil. This mixture was subjected to the hydrogenation conditions previously described which led to $100 \%$ conversion into $14 . .^{34} . t_{\mathrm{R}}=10.8 \mathrm{~min}\left(\mathrm{GC}\right.$ column $30 \mathrm{QC} 5 / \mathrm{BPX} 5,150^{\circ} \mathrm{C}$ for $1 \mathrm{~min}, 10^{\circ} \mathrm{C} \mathrm{min}{ }^{-1}$ to $280^{\circ} \mathrm{C}$ for 6 min ). $v_{\text {max }}$ (neat): $3054 \mathrm{~m}, 2956 \mathrm{~m}, 1736 \mathrm{~m}, 1676 \mathrm{~m}, 1509 \mathrm{w}, 1438 \mathrm{~m}, 1372 \mathrm{w}, 1265 \mathrm{~s}, 1174 \mathrm{w}, 1120 \mathrm{~m}$, 1028w, $738 \mathrm{~s} \mathrm{~cm}^{-1} .{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 1.53-1.65(\mathrm{~m}, 4 \mathrm{H}, \mathrm{H} 3,4), 1.94\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3} \mathrm{CO}\right), 2.52-$ $2.59(\mathrm{~m}, 2 \mathrm{H}, \mathrm{H} 5), 3.65\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{OCH}_{3}\right), 4.54-4.63(\mathrm{~m}, 1 \mathrm{H}, \mathrm{H} 2), 5.90(\mathrm{bd}, J 7.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{NH}), 7.07-7.29$ (m, 5H, AromCH). ${ }^{13} \mathrm{C}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 23.3\left(\mathrm{CH}_{3} \mathrm{CO}\right), 27.2(\mathrm{C} 4), 32.3(\mathrm{C} 3), 35.5(\mathrm{C} 5), 52.1$, $52.5\left(\mathrm{C} 2, \mathrm{OCH}_{3}\right), 126.1,128.5,132.2($ Arom CH), 141.7, (Arom C), 169.9, $173.2(\mathrm{C} 1, \mathrm{CONH})$. Mass Spectrum ( $\left.\mathrm{ESI}^{+}, \mathrm{MeOH}\right): m / z 272.2 \mathrm{C}_{14} \mathrm{H}_{19} \mathrm{NO}_{3} \mathrm{Na}\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$.
## Linear Pentapeptide: Fmoc-Hag-Pro-Pre-Arg-Hag-OH



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The procedure outlined in the General Section was used to attach the first amino acid, Fmoc-Hag-OH, to Wang resin. Quantities of the resin and coupling reagents are presented in Table 1. The first coupling reaction was shaken for 14 h .

Table 1 Quantities of Reagents used in the Synthesis of Fmoc-Hag-Pro-Pre-Arg-Hag-OH

| Reagent | Mass (mg) or Volume $(\boldsymbol{\mu l})$ | Mole (mmol) |
| :---: | :---: | :---: |
| Wang Resin | 212 mg | 0.19 |
| Fmoc-L-Hag-OH | 195 mg | 0.58 |
| DIC | $90.6 \mu \mathrm{l}$ | 0.58 |
| DMAP | 7.1 mg | 0.06 |

The procedure outlined in the General Section was used for subsequent coupling reactions in the synthesis of pentapeptide Fmoc-Hag-Pro-Pre-Arg-Hag-OH. Quantities of the coupling reagents HATU and NMM are tabulated below (Table 2) and remained constant throughout the synthesis. The quantities of successive amino acids and their reaction durations are detailed in Table 3.

Table 2 Quantities of Coupling Reagents used in the Synthesis of Fmoc-Hag-Pro-Pre-Arg-Hag-OH

| Coupling Reagent | Mass (mg) or Volume (ml) | Mole (mmol) |
| :---: | :---: | :---: |
| HATU | 147 mg | 0.39 |
| NMM | $128 \mu \mathrm{l}$ | 1.16 |

Table 3 Quantities of Amino Acids used in the Synthesis of Fmoc-Hag-Pro-Pre-Arg-Hag-OH

| Amino Acid | Mass (mg) | Mole (mmol) | Reaction Time (h)* |
| :---: | :---: | :---: | :---: |
| Fmoc-L-Arg(Pbf)-OH | 376 | 0.58 | 2 |
| Fmoc-L-Pre-OH | 211 | 0.58 | 3 |
| Fmoc-L-Pro-OH | 196 | 0.58 | 6 |
| Fmoc-L-Hag-OH | 195 | 0.58 | 2 |

* Note: Reaction times have not been optimised.

After the final amino acid coupling, a small aliquot of peptidyl-resin was subjected to the TFA-mediated cleavage procedure described in the General Section. Mass spectral analysis of the isolated residue confirmed formation of the linear pentapeptide (19). Mass spectrum ( $\mathrm{ESI}^{+}, \mathrm{MeCN} / \mathrm{H}_{2} \mathrm{O}$ ): m/z 813.6 $(\mathrm{M}+\mathrm{H})^{+}, \mathrm{C}_{43} \mathrm{H}_{57} \mathrm{~N}_{8} \mathrm{O}_{8}$.requires 813.4; m/z $831.5\left(\mathrm{M}+\mathrm{H}_{2} \mathrm{O}+\mathrm{H}\right)^{+}, \mathrm{C}_{43} \mathrm{H}_{59} \mathrm{~N}_{8} \mathrm{O}_{9}$ requires 831.4; m/z 927.6 $(\mathrm{M}+\mathrm{TFA}+\mathrm{H})^{+}, \mathrm{C}_{45} \mathrm{H}_{58} \mathrm{~F}_{3} \mathrm{~N}_{8} \mathrm{O}_{10}$ requires 927.4.





## S14b





















