Supplementary Material for Organic & Biomolecular Chemistry
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Supplementary data

A highly stereoselective ether directed palladium catalysed aza-Claisen rearrangement

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Experimental Data and Characterisation of Compounds

General Experimental

All reactions were performed under a nitrogen atmosphere unless otherwise noted. Reagents and starting materials were obtained from commercial sources and used as received. THF and diethyl ether were distilled from sodium and benzophenone. Lithium chloride was oven dried (100 °C) for at least 12 h before use. Brine refers to a saturated solution of sodium chloride. Flash column chromatography was carried out using Fisher Matrex silica 60. Macherey-Nagel aluminium backed plates pre-coated with silica gel 60 (UV 254) were used for thin layer chromatography and were visualised by staining with KMnO4.

1H NMR and 13C NMR spectra were recorded on a Bruker DPX 400 spectrometer with chemical shift values in ppm relative to residual chloroform (δH 7.28 & δC 77.2) as standard. Infrared spectra were recorded using Golden Gate apparatus on a JASCO FTIR 410 spectrometer and mass spectra were obtained using a JEOL JMS-700 spectrometer. Melting points were determined on a Reichert platform melting point apparatus. Optical rotations were determined as solutions irradiating with the sodium D line (λ= 589 nm) using a AA series Automatic polarimeter. [α]D values are given in units 10⁻¹deg cm² g⁻¹.

General Procedures

General procedure 1: Williamson ether protection of (S)-ethyl lactate

\[ \text{CO}_2\text{Et} \quad \text{OH} \quad \rightarrow \quad \text{OR} \quad \text{CO}_2\text{Et} \]

Sodium Hydride (60% in mineral oil) (1.1 eq) was washed with petroleum ether (3 x 3 mL). The grey powder was then suspended in THF and cooled to 0 °C. Ethyl (S)-lactate (1 eq) was then added, dropwise, and the solution was allowed to stir for 0.5 h. The alkyl halide (1.4 eq) was added and, after 0.75 h, the reaction mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was concentrated, acidified with 2 M hydrochloric acid (20 mL) and extracted with ethyl acetate (2 x 40 mL). The organic layers were combined, dried (MgSO₄) and concentrated in vacuo. Purification was carried out by flash column chromatography using ethyl acetate / petroleum ether.
General procedure 2: DIBAL-H reduction to the aldehyde

\[ \text{CO}_2\text{Et} \rightarrow \text{CHO} \]

The ester (1.0 eq) was dissolved in diethyl ether (30 mL) and cooled to -78 °C. DIBAL-H (1 M in hexane) (1.05 eq) was added dropwise and the reaction mixture was allowed to stir at -78 °C for 1.5 h. The reaction was quenched by the addition of a saturated solution of ammonium chloride (20 mL) and warmed to room temperature producing a white precipitate. The precipitate was filtered through a pad of Celite® and washed with diethyl ether (3 x 100 mL). The filtrate was then dried (MgSO₄) and concentrated \textit{in vacuo}. The aldehyde was used without further purification.

General procedure 3: Horner-Wadsworth-Emmons reaction

\[ \text{CHO} \rightarrow \text{CO}_2\text{Et} \]

Lithium chloride (1.2 eq) was suspended in acetonitrile (20 mL). A solution of triethylphosphonoacetate (1.2 eq) in acetonitrile (30 mL) was added along with 1,8-diazabicyclo(5,4,0)undec-7-ene (1.2 eq). The aldehyde (1.0 eq) in acetonitrile (40 mL) was then added and the reaction mixture was allowed to stir for 2 h at room temperature. The reaction mixture was concentrated \textit{in vacuo}. The resulting residue was dissolved in ethyl acetate (100 mL), washed with water (2 x 70 mL), dried (MgSO₄) and concentrated \textit{in vacuo}. Purification was carried out by flash column chromatography using ethyl acetate / petroleum ether.

General procedure 4: DIBAL-H reduction to allylic alcohol

\[ \text{CO}_2\text{Et} \rightarrow \text{OH} \]

The unsaturated ester (1.0 eq) was dissolved in diethyl ether (20 mL) and cooled to -78 °C. DIBAL-H (1 M in hexane) (2.2 eq) was added dropwise and the reaction mixture was allowed to stir at -78 °C for 4 h. The reaction was quenched by the addition of a saturated solution of ammonium chloride (20 mL) and warmed to room temperature producing a white precipitate. The precipitate was filtered through a pad of Celite® and washed with diethyl ether (3 x 100 mL). The filtrate was then dried (MgSO₄) and concentrated \textit{in vacuo}. Purification was carried out by flash column chromatography eluting with ethyl acetate / petroleum ether.

General procedure 5: Trichloroacetimidate synthesis

\[ \text{OH} \rightarrow \text{HNCCl}_3 \]

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Sodium Hydride (60% in mineral oil) (1.2 eq) was washed with petroleum ether (3 x 5 mL), suspended in THF (20 mL) and cooled to 0 °C. A solution of the allylic alcohol (1.0 eq) in THF (6 mL) was then added slowly. After 0.5 h, trichloroacetonitrile (1.2 eq) was added causing the formation of a light yellow colour. After 1 h the reaction mixture was warmed to room temperature and filtered through a short pad of aluminium oxide. This was washed with diethyl ether (20 mL) and the combined filtrate was concentrated in vacuo to give the desired allylic trichloroacetimidate. The product was used without further purification.

**General Procedure 6: Bis(acetonitrile)palladium(II) chloride catalysed rearrangement**

![Chemical structure](image)

The trichloroacetimidate was dissolved in THF (10 mL). Bis(acetonitrile)palladium(II) chloride (10 mol%) was then added and the reaction mixture stirred for 24 h. Concentration in vacuo followed by purification by flash column chromatography eluting with ethyl acetate / petroleum ether gave the target compounds.

**Ethyl (S)-2-(tert-Butyldimethylsilyloxy)propanoate**

A mixture of ethyl (S)-lactate (6.2 mL, 55.1 mmol), tert-butyldimethylsilyl chloride (TBDMSCl) (9.98 g, 66.1 mmol) and imidazole (5.61 g, 82.6 mmol) in THF (65 mL) were stirred for 12 h at room temperature. The white precipitate was filtered and washed with ethyl acetate (20 mL). The combined filtrate was concentrated and purified by flash column chromatography (5% ethyl acetate / petroleum ether) giving the title compound as a white liquid in quantitative yield. $[\alpha]_D$ - 31.1 (c 1.0, CHCl$_3$); $\delta$ (400 MHz, CDCl$_3$) 0.06 (3H, s, Si(CH$_3$)$_2$), 0.09 (3H, s, Si(CH$_3$)$_2$), 0.83 (9H, s, tBuSi), 1.20 (3H, t, $J$ 7.1 Hz, OCH$_2$CH$_3$), 1.32 (3H, d, $J$ 6.7 Hz, 3-H$_3$), 4.10 (2H, m, OCH$_2$CH$_3$), 4.24 (1H, q, $J$ 6.7 Hz, 2-H); $\delta$ (100 MHz, CDCl$_3$) -4.9 (CH$_3$), -4.6 (CH$_3$), 14.4 (CH$_3$), 18.5 (C), 21.5 (CH$_3$), 26.0 (CH$_3$), 60.9 (CH$_2$), 68.7 (CH), 174.3 (C); $m/z$ (CI) 233 (MH$^+$, 100%), 217 (7), 192 (5), 175 (6), 134 (5).

**Ethyl (S)-2-(Trityloxy)propionate**

Ethyl (S)-lactate (3.5 g, 29.7 mmol) was added to a solution of triphenylmethyl chloride (9.9 g, 35.6 mmol) and 1,8-diazabicyclo(5,4,0)undec-7-ene (6.2 mL, 41.5 mmol) in dichloromethane (130 mL). The reaction mixture was allowed to stir for 48 h before being quenched with water (100 mL). The organic layer was separated and the aqueous layer extracted with dichloromethane (3 x 50 mL). The combined organic layers were then dried (MgSO$_4$) and concentrated. Purification by flash column chromatography (50% ethyl acetate / petroleum ether) gave the title compound.
compound as a white solid in quantitative yield. $\nu_{\text{max}}$/cm$^{-1}$ (neat) 2982 (CH), 1749 (CO); $[\alpha]_D^{22}$ 32.4 (c 1.4, CHCl$_3$); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 1.07 (3H, t, $J$ 7.1 Hz, OCH$_2$CH$_3$), 1.38 (3H, d, $J$ 6.7 Hz, 3-H$_3$), 3.70 (2H, m, OCH$_2$CH$_3$), 4.19 (1H, q, $J$ 6.7 Hz, 2-H), 7.23-7.51 (15H, m, 3 x Ph); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 14.2 (CH$_3$), 20.4 (CH$_3$), 60.6 (CH$_2$), 70.0 (CH), 127.5 (CH), 128.1 (CH), 129.4 (CH), 144.3 (C), 173.9 (C); (Found (CI): 360.1725. C$_{24}$H$_{24}$O$_3$ requires 360.1725).

Ethyl (S)-2-Benzylxopropionate$^3$

The reaction was carried out according to general procedure 1 using (S)-ethyl lactate (5.0 mL, 44.5 mmol) giving the title compound as a colourless oil (8.77 g, 95%). $[\alpha]_D^{22}$ -69.3 (c 1.0, CHCl$_3$); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 1.26 (3H, t, $J$ 7.1 Hz, CH$_3$), 1.42 (3H, d, $J$ 6.8 Hz, 3-H$_3$), 4.04 (1H, q, $J$ 6.8, 2-H), 4.19 (2H, m, OCH$_2$), 4.42 (1H, d, $J$ 11.6, PhCH), 4.68 (1H, d, $J$ 11.6, PhCH), 7.21-7.49 (5H, m, Ph); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 14.6 (CH$_3$), 19.1 (CH$_3$), 61.0 (CH$_3$), 72.3 (CH$_3$), 74.4 (CH), 128.2 (CH), 128.3 (CH), 128.8 (CH), 137.9 (C), 173.6 (C); (Found (CI) 209.1178. C$_{12}$H$_{16}$O$_3$ requires 209.1178).

Ethyl (S)-2-Methoxypropionate$^4$

The reaction was carried out according to general procedure 1 using (S)-ethyl lactate (7.7 mL, 67.8 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / petroleum ether) to give the title ester as pale liquid (4.29 g, 48%). $\nu_{\text{max}}$/cm$^{-1}$ (neat) 2985 (CH), 1745 (CO); $[\alpha]_D^{22}$ -115.3 (c 1.0, CHCl$_3$); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 1.23 (3H, t, $J$ 7.1 Hz, OCH$_2$CH$_3$), 1.33 (3H, d, $J$ 6.8 Hz, 3-H$_3$), 3.33 (3H, s, OMe), 3.80 (1H, q, $J$ 6.8 Hz, 2-H), 4.14 (2H, q, $J$ 7.1 Hz, OCH$_2$CH$_3$); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 14.6 (CH$_3$), 18.7 (CH$_3$), 57.8 (CH$_3$), 61.2 (CH$_2$), 76.6 (CH), 173.3 (C); m/z (CI): 133 (MH$^+$, 100%), 97 (27), 85 (56).

Ethyl (S)-2-Methoxyethoxymethoxypropionate$^5$

The reaction was carried out according to general procedure 1 using (S)-ethyl lactate (4.8 mL, 42.4 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / petroleum ether) to give the title compound (8.73 g, quantitative yield) as a colourless oil. $\nu_{\text{max}}$/cm$^{-1}$ (neat) 2895 (CH), 1746 (CO); $[\alpha]_D^{23}$ -62.7 (c 2.0, CHCl$_3$); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 1.29 (3H, t, $J$ 7.1 Hz, OCH$_2$CH$_3$), 1.43 (3H, d, $J$ 6.8 Hz, 3-H$_3$), 3.40 (3H, s, OMe), 3.54 (2H, m, OCH$_2$CH$_2$O), 3.75 (2H, m, OCH$_2$CH$_2$O), 4.18 (2H, q, $J$ 7.1 Hz, OCH$_2$CH$_3$), 4.25 (1H, q, $J$ 6.8 Hz, 2-H), 4.80 (2H, s, OCH$_2$O); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 14.5 (CH$_3$), 18.9 (CH$_3$), 59.3 (CH$_3$), 61.2 (CH$_2$), 67.7 (CH$_2$), 71.8 (CH), 72.0 (CH), 95.1 (CH$_2$), 173.4 (C). (Found (CI): 207.1232. C$_{12}$H$_{16}$O$_5$ requires 207.1232).
The reaction was carried out according to general procedure 2 using ethyl-(S)-2-(tert-butyldimethylsilyloxy)propanoate (13.8 g, 59.5 mmol) giving the title compound (6.82 g, 61%).

\[
\begin{align*}
\delta_H (400 MHz, CDCl_3) & 0.13 (3H, s, Si(CH_3)_2), 0.15 (3H, s, Si(CH_3)_2), 0.82 (9H, s, 'BuSi), 1.19 (3H, d, J 6.8 Hz, 3-H_3), 3.99 (1H, q, J 6.7 Hz, 2-H), 9.51 (1H, m, CHO).
\end{align*}
\]

\[(S)-2-Trityloxypropanal\]

The reaction was carried out according to general procedure 2 using ethyl-(S)-2-trityloxypropionate (10.67 g, 29.7 mmol) giving the title compound (7.66 g, 82%) as a white solid.

\[
\begin{align*}
\delta_H (400 MHz, CDCl_3) & 1.33 (3H, d, J 6.9 Hz, 3-H_3), 4.03 (1H, qd, J 6.9, 3.1 Hz, 2-H), 7.21-7.54 (15H, m, 3 x Ph), 8.71 (1H, d, J 3.1 Hz, CHO).
\end{align*}
\]

\[(S)-2-Benzylloxypropanal\]

The reaction was carried out according to general procedure 2 using ethyl (S)-2-benzyloxypropionate (3.0 g, 14.4 mmol) giving the title compound (2.37 g, quantitative yield) as a yellow oil.

\[
\begin{align*}
\delta_H (400 MHz, CDCl_3) & 1.35 (3H, d, J 6.9, 3-H_3), 3.89 (1H, qd, J 6.9, 3.2, 2-H), 4.10 (1H, d, J 11.7, PhCH/H), 4.62 (1H, d, J 11.7, PhCH/H), 7.24 (5H, m, Ph), 9.61 (1H, d, J 3.2, CHO).
\end{align*}
\]

\[(S)-2-(Methoxyethoxymethoxy)propanal\]

The reaction was carried out according to general procedure 2 using ethyl (S)-2-methoxyethoxymethoxypropionate (5.0 g, 24.3 mmol) giving the title aldehyde (3.93 g, quantitative yield) as a yellow oil.

\[
\begin{align*}
\delta_H (400 MHz, CDCl_3) & 1.32 (3H, d, J 7.1 Hz, 3-H), 3.38 (3H, s, OMe), 3.48-3.90 (4H, m, OCH_2CH_2O), 4.1 (1H, qd, J 7.1, 1.9 Hz, 2-H), 4.81 (2H, s, OCH_2O), 9.62 (1H, d, J 1.9 Hz, 1-CHO).
\end{align*}
\]

Ethyl (2E,4S)-4-(tert-Butyldimethylsilyloxy)pent-2-enoate
The reaction was carried out according to general procedure 3 using the (S)-2-tert-
butyldimethylsilyloxypropanal (6.82 g, 36.3 mmol). Purification was carried out by flash column
chromatography (5% ethyl acetate / petroleum ether) giving the title compound (7.59 g, 81%) as
a colourless oil. \( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 2929 (CH), 1719 (CO), 1660 (C=C); \([\alpha]_D^{21} +4.4 \) (c 1.0, CHCl$_3$); 
\( \delta_H \) (400 MHz, CDCl$_3$) 0.10 (3H, s, Si(CH$_3$)$_2$), 0.12 (3H, s, Si(CH$_3$)$_2$), 0.95 (9H, s, 'BuSi), 1.29
(3H, d, J 6.4 Hz, 5-H$_3$), 1.33 (3H, t, J 7.2 Hz, OCH$_2$CH$_3$), 4.23 (2H, m, OCH$_2$CH$_3$), 4.48 (1H, m, 4-H), 6.01 (1H, dd, J 15.6, 1.8 Hz, 2-H), 6.95 (1H, dd, J 15.6, 4.1 Hz, 3-H); \( \delta_C \) (100 MHz, CDCl$_3$) -4.5 (CH$_3$), 14.6 (CH$_3$), 23.8 (CH$_3$), 26.0 (CH$_3$), 60.6 (CH$_2$), 68.0 (CH), 119.3 (CH), 128.5 (CH), 129.3 (CH), 152.2 (CH), 167.1 (C); (Found (CI): 258.1652. C$_{13}$H$_{26}$O$_3$Si requires 258.1651).

Ethyl (2E,4S)-4-(Trityloxy)pent-2-enoate

The reaction was carried out according to general procedure 3 using (S)-2-trityloxypropanal (8.99
g, 28.4 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / petroleum ether) giving the title compound (8.51 g, 78%) as white solid. Mp 112-114 \degree C; \( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 2978 (CH), 1714 (CO), 1664 (C=C); \( \delta_H \) (400 MHz, CDCl$_3$) 1.10 (3H, d, J 6.4 Hz, 5-H$_3$), 1.27 (3H, t, J 7.1 Hz, OCH$_2$CH$_3$), 4.12 (2H, q, J 7.1 Hz, OCH$_2$CH$_3$), 4.25 (1H, quin, J 6.4 Hz, 4-H), 5.48 (1H, dd, J 15.7, 1.1 Hz, 2-H), 6.54 (1H, dd, J 15.7, 6.1 Hz, 3-H), 7.21-7.53 (15H, m, 3 x Ph); \( \delta_C \) (100 MHz, CDCl$_3$) 14.6 (CH$_3$), 22.5 (CH$_3$), 60.4 (CH$_2$), 70.0 (CH), 87.7 (C), 118.3 (CH), 127.5 (CH), 128.2 (CH), 129.2 (CH), 145.0 (C), 150.8 (CH), 166.8 (C); (Found (Cl): 386.1882. C$_{26}$H$_{26}$O$_3$ requires 386.1882).

Ethyl (2E, 4S)-4-Benzoxypent-2-enoate

The reaction was carried out according to general procedure 3 using (S)-2-benzyloxypropanal (2.37 g, 14.4 mmol). Purification by flash column chromatography (40% ethyl acetate / petroleum ether) gave the title compound (3.14 g, 93%) as an oil. \( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 2979 (CH), 1717 (C=C); \([\alpha]_D^{23} -50.4 \) (c 1.0, CHCl$_3$); \( \delta_H \) (400 MHz, CDCl$_3$) 1.2 (6H, m, OCH$_2$CH$_3$ and 5-H$_3$), 4.10 (1H, m, 4-H), 4.20 (2H, q, J 6.3, OCH$_2$CH$_3$), 4.42 (1H, d, J 11.8, PhCH$_2$), 4.56 (1H, d, J 11.8, PhCH$_2$), 6.04 (1H, dd, J 15.7, 1.3, 2-H), 6.91 (1H, dd, J 15.7, 6.0, 3-H), 7.29-7.46 (5H, m, Ph); \( \delta_C \) (100 MHz, CDCl$_3$) 14.6 (CH$_3$), 21.0 (CH$_3$), 60.8 (CH$_2$), 71.0 (CH$_2$), 74.2 (CH), 121.7 (CH), 127.9 (CH), 128.0 (CH), 129.2 (CH), 138.6 (C), 149.5 (CH), 166.6 (C); \( m/z \) (Cl) 235 (MH$^+$, 100%), 189 (10), 145 (5), 107 (12), 91 (31).

Ethyl (2E,4S)-4-Methoxypent-2-enoate

The reaction was carried out according to general procedure 3 using (S)-2-benzyloxypropanal (2.37 g, 14.4 mmol). Purification by flash column chromatography (40% ethyl acetate / petroleum ether) gave the title compound (3.14 g, 93%) as an oil. \( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 2979 (CH), 1717 (C=C); \([\alpha]_D^{23} -50.4 \) (c 1.0, CHCl$_3$); \( \delta_H \) (400 MHz, CDCl$_3$) 1.2 (6H, m, OCH$_2$CH$_3$ and 5-H$_3$), 4.10 (1H, m, 4-H), 4.20 (2H, q, J 6.3, OCH$_2$CH$_3$), 4.42 (1H, d, J 11.8, PhCH$_2$), 4.56 (1H, d, J 11.8, PhCH$_2$), 6.04 (1H, dd, J 15.7, 1.3, 2-H), 6.91 (1H, dd, J 15.7, 6.0, 3-H), 7.29-7.46 (5H, m, Ph); \( \delta_C \) (100 MHz, CDCl$_3$) 14.6 (CH$_3$), 21.0 (CH$_3$), 60.8 (CH$_2$), 71.0 (CH$_2$), 74.2 (CH), 121.7 (CH), 127.9 (CH), 128.0 (CH), 129.2 (CH), 138.6 (C), 149.5 (CH), 166.6 (C); \( m/z \) (Cl) 235 (MH$^+$, 100%), 189 (10), 145 (5), 107 (12), 91 (31).
Ethyl (S)-2-methoxypropanoate (1.5 g, 12.9 mmol) was dissolved in diethyl ether (20 mL) and cooled to -78 °C. DIBAL-H (1 M in hexane) (2.2 eq) was added dropwise and the reaction mixture was allowed to stir at -78 °C for 3 h. The reaction was quenched by the addition of a saturated solution of ammonium chloride (30 mL) and warmed to room temperature producing a white precipitate. The precipitate was filtered through a pad of Celite®, which was washed with diethyl ether (3 x 100 mL). The filtrate was then dried (MgSO₄) and concentrated in vacuo to give the corresponding alcohol (0.88 g, 67%). Dimethyl sulfoxide (2.4 eq) was added to a solution of oxalyl chloride (1.2 eq) in dichloromethane (10 mL) at -78 °C. The resulting solution was allowed to stir for 0.25 h before (S)-2-methoxypropanol (0.88 g, 8.7 mmol) in dichloromethane (10 mL) was added. This solution was allowed to stir for a further 0.25 h. Triethylamine (5 eq) was then added and the reaction brought to room temperature with stirring, over 2 h. A solution of lithium chloride (1.2 eq) in dichloromethane (5 mL) was prepared and stirred for 0.25 h before triethyl phosphonoacetate (1.2 eq) and 1,8-diazabicycloundec-7-ene (1.2 eq) were added and the mixture was allowed to stir for 0.5 h. The phosphonoacetate solution was then added slowly to the aldehyde solution and the reaction mixture was allowed to stir for 12 h. The reaction mixture was then diluted with diethyl ether (50 mL) and quenched with brine solution. The organic phase was separated, dried (MgSO₄) and concentrated under vacuum. Purification by flash column chromatography (30% ethyl acetate / petroleum ether) gave the title compound (0.33 g, 58% over two steps) as a brown oil. 

\[\nu_{\text{max/cm}^{-1}} (\text{neat}) 2980 (\text{CH}), 1716 (\text{CO}), 1658 (\text{C} = \text{C}); [\alpha]_D^{22} -34.1 \text{ (c } 1.0, \text{ CHCl}_3); \delta_H (400 \text{ MHz, CDCl}_3) 1.28 \text{ (3H, d, J } 6.4 \text{ Hz, 5-H)}; 1.32 \text{ (3H, t, J } 7.2 \text{ Hz, OCH}_2\text{C}_3); 3.34 \text{ (3H, s, OMe)}, 3.91 \text{ (1H, quin x d, J } 6.4, 1.8 \text{ Hz, 4-H)}; 4.22 \text{ (2H, q, J } 7.1 \text{ Hz, OCH}_2\text{C}_3), 5.98 \text{ (1H, dd, J } 15.7, 1.3 \text{ Hz, 2-H)}, 6.84 \text{ (1H, dd, J } 15.7, 6.2 \text{ Hz, 3-H)}; \delta_C (100 \text{ MHz, CDCl}_3) 14.6 \text{ (CH)}; 20.7 \text{ (CH)}; 57.0 \text{ (CH)}; 60.8 \text{ (CH)}; 76.5 \text{ (CH)}; 121.7 \text{ (CH)}; 149.3 \text{ (CH)}; 166.7 \text{ (C)}; \text{ (Found (CI): 159.1021. C}_8\text{H}_{14}\text{O}_3 \text{ requires 159.1021).}

(S)-2-Methoxymethoxypropanol

The first reaction was carried out according to general procedure 1 using ethyl (S)-lactate (2.0 g, 16.9 mmol) to give ethyl (S)-2-methoxymethoxypropanoate. Ethyl (S)-2-methoxymethoxypropanoate was dissolved in diethyl ether (20 mL) and cooled to -78 °C. DIBAL-H (1 M in hexane) (2.2 eq) was added dropwise and the reaction mixture was allowed to stir at -78 °C for 3 h. The reaction was quenched by the addition of a saturated solution of ammonium chloride (30 mL) and warmed to room temperature producing a white precipitate. The precipitate was filtered through a pad of Celite®, which was washed with diethyl ether (3 x 100 mL). The filtrate was then dried (MgSO₄) and concentrated in vacuo. Purification by flash column chromatography (50% ethyl acetate / petroleum ether) gave the title compound (1.67 g, 71%) as a yellow liquid. 

\[\nu_{\text{max/cm}^{-1}} (\text{neat}) 3408 (\text{OH}), 2930 (\text{CH}); [\alpha]_D^{25} -80.0 \text{ (c } 1.0, \text{ CHCl}_3); \delta_H (400 \text{ MHz, CDCl}_3) 1.17 \text{ (3H, d, J } 6.4 \text{ Hz, 3-H)}; 2.60 \text{ (1H, br s, OH)}, 3.43 \text{ (3H, s, OMe)}, 3.46 \text{ (1H, dd, J } 11.8, 7.0 \text{ Hz, 1-H/H)}, 3.53 \text{ (1H, dd, J } 11.8, 2.9 \text{ Hz, 1-H/H}), 3.70 \text{ (1H, quin x d, J } 6.4, 2.8 \text{ Hz, 2-H)}, 4.71 \text{ (1H, d, J } 14.7 \text{ Hz, OCH/HO)}, 4.76 \text{ (1H, d, J } 14.7 \text{ Hz, OCH/OH}); \delta_C (100 \text{ MHz,
Ethyl (2E,4S)-4-Methoxymethoxypent-2-enoate9

Dimethyl sulfoxide (2.4 eq) was added to a solution of oxalyl chloride (1.2 eq) in dichloromethane (50 mL) at -78 °C. The resulting solution was allowed to stir for 0.25 h before (S)-2-methoxymethoxypropanol (1.65 g, 13.9 mmol) in dichloromethane (10 mL) was added. This solution was allowed to stir for a further 0.25 h. Triethylamine (5.0 eq) was then added and the reaction brought to room temperature with stirring over 2 h. A solution of lithium chloride (1.2 eq) in dichloromethane (50 mL) was prepared and stirred for 0.25 h before triethyl phosphonoacetate (1.2 eq) and 1,8-diazabicyclo(5,4,0)undec-7-ene (1.2 eq) were added and the mixture was allowed to stir for 0.5 h. The phosphonoacetate solution was then added slowly to the aldehyde solution and the reaction mixture was allowed to stir for 12 h. The reaction mixture was then diluted with diethyl ether (50 mL) and quenched with brine solution. The organic layer was separated, dried (MgSO4) and concentrated under vacuum. Purification by flash column chromatography (30% ethyl acetate / petroleum ether) gave the title compound (1.50 g, 58% over two steps) as a brown oil.

υmax/cm-1 (neat) 2981 (CH), 1720 (CO), 1660 (C=C); [α]D21 -80.0 (c 1.0, CHCl3); δH (400 MHz, CDCl3) 1.27 (6H, m, OCH2CH3, 5-H3), 3.37 (3H, s, OMe), 4.20 (2H, q, J 7.1 Hz, OCH2CH3), 4.35 (1H, quin x d, J 6.6, 1.3 Hz, 4-H), 4.6 (2H, s, OCH2O), 6.8 (1H, dd, J 14.8, 2.1 Hz, 2-H), 6.8 (1H, dd, J 14.8, 6.3 Hz, 3-H); δC (100 MHz, CDCl3) 14.5 (CH3), 20.9 (CH3), 55.8 (CH3), 60.8 (CH2), 71.4 (CH), 94.8 (CH), 121.3 (CH), 149.1 (CH), 166.7 (C); (Found (Cl): 189.1125. C9H16O4 requires 189.1127).

Ethyl (2E,4S)-4-Methoxyethoxymethoxypent-2-enoate

The reaction was carried out according to general procedure 3 using (S)-2-methoxyethoxymethoxypropanal (4.20 g, 25.9 mmol). Purification was carried out by flash column chromatography (30% ethyl acetate / petroleum ether) giving the title compound (1.69 g, 28%) as a yellow liquid. υmax/cm-1 (neat) 2983 (CH), 1748 (CO), 1656 (C=C); [α]D21 -53.5 (c 1.0, CHCl3); δH (400 MHz, CDCl3) 1.28 (6H, m, OCH2CH3, 5-H3), 3.39 (3H, s, OMe), 3.54-3.78 (4H, m, OCH2CH2O), 4.15 (2H, q, J 7.2 Hz, OCH2CH3), 4.42 (1H, quin x d, J 6.8, 1.6 Hz, 4-H), 4.70 (1H, d, J 6.8 Hz, OC/HOH), 4.73 (1H, d, J 6.8 Hz, OCH/HOH), 5.99 (1H, dd, J 15.6, 1.6 Hz, 2-H), 6.8 (1H, dd, J 15.6, 5.6 Hz, 3-H); (Found (Cl) 233.1390. C11H21O5 requires 233.1389).

(2E,4S)-4-(tert-Butyldimethylsilyloxy)pent-2-en-1-ol6
The reaction was carried out according to general procedure 4 using ethyl (2E,4S)-4-(tert-butylidimethylsilyloxy)pent-2-enoate (0.10 g, 0.4 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / hexane) to give the desired compound (0.05 g, 52%) as a clear oil. 

υmax/cm⁻¹ (neat) 3343 (OH), 2928 (CH); [α]D²⁹ +3.7 (c 3.0, CHCl₃); δH (400 MHz, CDCl₃) 0.08 (3H, s, Si(CH₃)₂), 0.09 (3H, s, Si(CH₃)₂), 0.84 (9H, s, tBuSi), 1.16 (3H, d, J 6.3 Hz, 5-H), 1.34 (H, br s, OH), 4.08 (2H, d, J 6.0 Hz, 1-H₂), 4.27 (1H, quin, J 6.1 Hz, 4-H), 5.63-5.74 (2H, m, 2-H and 3-H); δC (100 MHz, CDCl₃) -4.3 (CH₃), -4.2 (CH₃), 18.6 (C), 24.6 (CH₃), 26.2 (CH₃), 63.5 (CH₂), 68.8 (CH), 127.6 (CH), 136.7 (CH); (Found (Cl): 217.1626. C₁₁H₂₅O₂Si requires 217.1624).

(2E,4S)-4-Trityloxypent-2-en-1-ol

The reaction was carried out according to general procedure 4 using ethyl (2E,4S)-4-(trityloxy)pent-2-enoate (3.0 g, 7.8 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / hexane) to give the desired compound (2.59g, 97%) as a viscous oil. υmax/cm⁻¹ (neat) 3347 (OH), 2925 (CH), 1595 (C=C); δH (400 MHz, CDCl₃) 0.69 (1H, t, J 6.0 Hz, OH, (D₂O exchange)), 1.15 (3H, t, J 6.4 Hz, 5-H₃), 3.77 (2H, m, 1-H₂), 4.16 (1H, quin, J 6.4 Hz, 4-H), 5.24 (1H, dt, J 16.0, 6.0 Hz 2-H), 5.34 (1H, dd, J 15.6, 6.8 Hz, 3-H) 7.22-7.54 (15H, m, 3 x Ph); δC (100 MHz, CDCl₃) 23.6 (CH₃), 63.3 (CH₂), 70.8 (CH₂), 70.8 (CH), 87.4 (C), 126.8 (CH), 127.2 (CH), 128.1 (CH), 129.4 (CH), 136.2 (CH), 145.5 (C); m/z (Cl) 327 ((MH⁺)-OH, 8%), 243 (100), 183 (80), 145 (35).

(2E,4S)-4-Benzoxypent-2-en-1-ol

The reaction was carried out according to general procedure 4 using ethyl (2E,4S)-4-benzyloxypent-2-enoate (1.99 g, 8.5 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / hexane) to give the desired allylic alcohol (0.85 g, 52%). υmax/cm⁻¹ (neat) 3419 (OH), 2868 (CH), 1697 (C=C); [α]D²₂ -38.1 (c 1.0, CHCl₃); δH (400 MHz, CDCl₃) 1.32 (3H, d, J 6.4, 5-H₃), 1.39 (1H, br t, J 6.4 Hz, OH), 4.00 (1H, quin, J 6.4, 4-H), 4.20 (2H, t, J 5.2 Hz, 1-H₂), 4.42 (1H, d, J 12.0 Hz, PhCH/H), 4.57 (1H, d, J 12.0 Hz, PhCH/H), 5.6 (1H, dd, J 15.6, 7.2 Hz, 3-H), 5.7 (1H, dt, J 15.6, 5.2 Hz, 2-H), 7.15-7.56 (5H, m, Ph); δC (100 MHz, CDCl₃) 21.8 (CH₃), 63.1 (CH₂), 70.4 (CH₂), 75.3 (CH), 127.7 (CH), 128.0 (CH), 128.7 (CH), 131.5 (CH), 133.5 (CH), 139.0 (C); m/z (EI) 192 (M⁺, 2%), 150 (15), 134 (15), 107 (55), 91 (100).

(2E,4S)-4-Methoxypent-2-en-1-ol

The reaction was carried out according to general procedure 4 using ethyl (2E,4S)-4-methoxypent-2-enoate (1.99 g, 8.5 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / hexane) to give the desired allylic alcohol (0.85 g, 52%). υmax/cm⁻¹ (neat) 3347 (OH), 2925 (CH), 1697 (C=C); [α]D²⁹ -38.1 (c 1.0, CHCl₃); δH (400 MHz, CDCl₃) 1.32 (3H, d, J 6.4, 5-H₃), 1.39 (1H, br t, J 6.4 Hz, OH), 4.00 (1H, quin, J 6.4, 4-H), 4.20 (2H, t, J 5.2 Hz, 1-H₂), 4.42 (1H, d, J 12.0 Hz, PhCH/H), 4.57 (1H, d, J 12.0 Hz, PhCH/H), 5.6 (1H, dd, J 15.6, 7.2 Hz, 3-H), 5.7 (1H, dt, J 15.6, 5.2 Hz, 2-H), 7.15-7.56 (5H, m, Ph); δC (100 MHz, CDCl₃) 21.8 (CH₃), 63.1 (CH₂), 70.4 (CH₂), 75.3 (CH), 127.7 (CH), 128.0 (CH), 128.7 (CH), 131.5 (CH), 133.5 (CH), 139.0 (C); m/z (EI) 192 (M⁺, 2%), 150 (15), 134 (15), 107 (55), 91 (100).
The reaction was carried out according to general procedure 4 using ethyl (2\(E\),4\(S\))-4-methoxypent-2-enoate (880 mg, 5.57 mmol). Purification was carried out by flash column chromatography (50% ethyl acetate / petroleum ether) to give the title compound as yellow liquid (563 mg, 87%). \(\nu\)max/cm\(^{-1}\) (neat) 3363 (OH), 2872 (CH), 1673 (C=C); \([\alpha]_D\)\(^{21}\) -35.6 (c 1.0, CHCl\(_3\)); \(\delta\)H (400 MHz, CDCl\(_3\)) 1.18 (3H, d, \(J\) 6.3 Hz, 5-H\(_3\)), 1.50 (1H, br s, OH), 3.30 (3H, s, OMe), 3.78 (1H, quin, \(J\) 6.4 Hz, 4-H), 4.19 (2H, d, \(J\) 5.3 Hz, 1-H\(_2\)), 5.63 (1H, dd, \(J\) 15.5, 7.5 Hz, 3-H), 5.84 (1H, dt, \(J\) 15.5 and 5.3 Hz, 2-H); \(\delta\)C (100 MHz, CDCl\(_3\)) 21.4 (CH\(_3\)), 56.3 (CH\(_3\)), 63.3 (CH\(_2\)), 77.6 (CH), 131.3 (CH), 133.5 (CH); (Found (CI): 117.0918. C\(_{6}\)H\(_{12}\)O\(_2\) requires 117.0916).

\((2\(E\),4\(S\))-4-Methoxymethoxypent-2-en-1-ol\)

\begin{align*}
\text{OMOM} & \xrightarrow{\text{CO}_2\text{Et}} \text{OMOM} & \text{OH}
\end{align*}

The reaction was carried out according to general procedure 4 using ethyl (2\(E\),4\(S\))-4-methoxymethoxypent-2-enoate (0.39 g, 2.07 mmol). Purification was carried out by flash column chromatography (80% ethyl acetate / petroleum ether) to give the title compound (0.21 g, 84%). \(\nu\)max/cm\(^{-1}\) (neat) 3403 (OH), 2931 (CH); \([\alpha]_D\)\(^{23}\) -117.9 (c 1.0, CHCl\(_3\)); \(\delta\)H (400 MHz, CDCl\(_3\)) 1.23 (3H, d, \(J\) 6.2 Hz, 5-H\(_3\)), 2.21 (H, br s, OH), 3.34 (3H, s, OMe), 4.09 (2H, dd, \(J\) 5.1, 1.6 Hz, 1-H\(_2\)), 4.16 (1H, quin, \(J\) 7.0 Hz, 4-H), 4.51 (1H, d, \(J\) 6.7 Hz OCH\(_2\)O), 4.62 (1H, d, \(J\) 6.7 Hz, OCH\(_2\)O), 5.53 (1H, ddt, \(J\) 15.0, 7.0, 1.6 Hz, 3-H), 5.74 (1H, dt, \(J\) 15.0, 5.1 Hz, 2-H); \(\delta\)C (100 MHz, CDCl\(_3\)) 21.3 (CH\(_3\)), 55.3 (CH\(_3\)), 63.0 (CH\(_2\)), 72.0 (CH), 93.8 (CH\(_2\)), 130.9 (CH), 132.8 (CH); (Found (CI): 121.0866. C\(_{5}\)H\(_{12}\)O\(_3\) requires 121.0865).

\((2\(E\),4\(S\))-4-Methoxyethoxymethoxypent-2-en-1-ol\)

\begin{align*}
\text{OMEM} & \xrightarrow{\text{CO}_2\text{Et}} \text{OMEM} & \text{OH}
\end{align*}

The reaction was carried out according to general procedure 4 using ethyl (2\(E\),4\(S\))-4-methoxyethoxymethoxypent-2-enoate (1.04 g, 4.48 mmol). Purification was carried out by flash column chromatography (90% ethyl acetate / petroleum ether) giving the title compound (0.76 g, 89%) as a yellow liquid. \(\nu\)max/cm\(^{-1}\) (neat) 3418 (OH), 2928 (CH); \([\alpha]_D\)\(^{21}\) -73.0 (c 1.0, CHCl\(_3\)); \(\delta\)H (400 MHz, CDCl\(_3\)) 1.21 (3H, d, \(J\) 6.4 Hz, 5-H\(_3\)), 1.63 (1H, br s, OH), 3.44 (3H, s, OMe), 3.51 (2H, m, OCH\(_2\)CH\(_2\)O), 3.60 (2H, m, OCH\(_2\)CH\(_2\)O), 4.16 (2H, dd, \(J\) 6.5, 1.2 Hz, 1-H\(_2\)), 4.23 (1H, q, \(J\) 6.4 Hz, 4-H), 4.70 (1H, d, \(J\) 7.0 Hz, OCH\(_2\)O), 4.77 (1H, d, \(J\) 7.0 Hz, OCH\(_2\)O), 5.61 (1H, m, 3-H), 5.85 (1H, m, 2-H); \(\delta\)C (100 MHz, CDCl\(_3\)) 21.6 (CH\(_2\)), 59.4 (CH\(_3\)), 63.2 (CH\(_2\)), 67.1 (CH\(_2\)), 72.2 (CH\(_2\)), 73.0 (CH), 93.6 (CH\(_2\)), 131.1 (CH), 133.3 (CH); m/z (CI) 143 (MH\(^+\) - CH\(_3\)O and OH, 100%), 129 (12), 123 (7), 89 (100).

\((3\(R\),4\(S\))-3-(Trichloromethylcarbonylamino)-4-(tert-butyldimethylsilyloxy)penta-1-ene and (3\(S\),4\(S\))-3-(Trichloromethylcarbonylamino)-4-(tert-butyldimethylsilyloxy)penta-1-ene\)

\begin{align*}
\text{OMEM} & \xrightarrow{\text{CO}_2\text{Et}} \text{OMEM} & \text{OH}
\end{align*}
The reactions were carried out according to general procedures 5 and 6 using $(2E,4S)$-4-(tert-butylidimethylsilyloxy)pent-2-en-1-ol (0.48 g, 2.21 mmol). Purification was carried out by flash column chromatography (30% ethyl acetate / petroleum ether) giving the title compounds (0.54 g, 68% over two steps) as a yellow oil. $\nu_{\text{max}}$ (neat) 3426 (NH), 2929 (CH), 1721 (CO); $(3R,4S)$-3-(trichloromethylcarbonylamino)-4-(tert-butylidimethylsilyloxy)penta-1-ene (major compound): $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 0.12 (3H, s, Si(CH$_3$)$_2$), 0.14 (3H, s, Si(CH$_3$)$_2$), 0.93 (9H, s, tBuSi), 1.19 (3H, d, J 6.4 Hz, 5-H$_3$), 4.06 (1H, m, 4-H), 4.29 (1H, m, 3-H), 5.33 (2H, m, 1-H), 5.86 (1H, m, 2-H), 7.13 (1H, br s, NH); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) -4.5 (CH$_3$), -3.9 (C), -3.5 (CH$_3$), 18.2 (C), 20.6 (CH$_3$), 26.1 (CH$_3$), 59.7 (CH), 69.8 (CH), 119.8 (CH$_2$), 132.0 (CH), 161.2 (C); (Found (CI): 360.0722. C$_{13}$H$_{25}$O$_2$NSiCl$_3$ requires 360.0720).

$(3R,4S)$-3-(Trichloromethylcarbonylamino)-4-(trityloxy)penta-1-ene and $(3S,4S)$-3-(Trichloromethylcarbonylamino)-4-(trityloxy)penta-1-ene

The reactions were carried out according to general procedures 5 and 6 using $(2E,4S)$-4-trityloxy pent-2-en-1-ol (1.22 g, 3.6 mmol). Purification was carried out by flash column chromatography (30% diethyl ether / petroleum ether) giving the title compounds (1.22 g, 70% over two steps) as a yellow oil. $\nu_{\text{max}}$ (neat) 3411 (NH), 3021 (CH), 1713 (CO), 1597 (C=C); $(3R,4S)$-3-(trichloromethylcarbonylamino)-4-(trityloxy)penta-1-ene (major compound): $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 0.97 (3H, d, J 6.4 Hz, 5-H$_3$), 3.41 (1H, qd, J 6.3 and 3.1 Hz, 4-H), 4.06 (1H, m, 3-H), 5.34 (2H, m, 1-H$_2$), 6.06 (1H, m, 2-H), 7.12-7.76 (15H, m, 3 x Ph); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 18.3 (CH$_3$), 58.8 (CH), 71.8 (CH), 87.4 (C), 119.1 (CH$_2$), 127.7 (CH), 127.8 (CH), 128.0 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 129.0 (CH), 129.2 (CH), 129.4 (C), 133.0 (CH), 144.9 (C), 147.2 (C), 161.2 (C); $(3S,4S)$-3-(trichloromethylcarbonylamino)-4-(trityloxy)penta-1-ene (minor compound): $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 0.95 (3H, d, J 6.4 Hz, 5-H$_2$), 3.61 (1H, m, 4-H), 3.94 (1H, m, 3-H), 5.16 (2H, m, 1-H$_2$), 6.25 (1H, m, 2-H), 7.12-7.76 (15H, m, 3 x Ph); $m/z$ (CI) 490 (MH$^+$, 1%), 452 (1), 387 (1), 285 (3), 243 (100).

$(3R,4S)$-3-(Trichloromethanecarbonylamino)-4-(benzyloxy)penta-1-ene and $(3S,4S)$-3-(Trichloromethanecarbonylamino)-4-(benzyloxy)penta-1-ene
The reactions were carried out according to general procedures 5 and 6 using \((2E,4S)-4\)benzyloxypent-2-en-1-ol \((0.15 \text{ g}, 0.8 \text{ mmol})\). Purification was carried out by flash column chromatography \((20\% \text{ ethyl acetate / hexane})\) to give a brown oil \((0.16 \text{ g}, 62\% \text{ over two steps})\).

\[ \text{υ}_{\max}/\text{cm}^{-1} \text{ (neat)} 3415 \text{ (NH)}, 2869 \text{ (CH)}, 1714 \text{ (CO)}, 1598 \text{ (C=C)}; (3R,4S)-3-(trichloromethanecarbonylamino)-4-(benzyloxy)penta-1-ene \text{(major compound)}: \delta_{H} \text{ (400 MHz, CDCl}_{3} \text{)} 1.22 \text{ (3H, d, } J_{6.4} \text{ Hz, 5-H)}, 3.74 \text{ (1H, m, 4-H)}, 4.36 \text{ (1H, m, 3-H)}, 4.67 \text{ (2H, s, PhCH}_{2} \text{)}, 5.29 \text{ (2H, m, 1-H)}, 5.87 \text{ (1H, m, 2-H)}, 7.24-7.39 \text{ (5H, m, Ph)}; \delta_{C} \text{ (100 MHz, CDCl}_{3} \text{)} 15.8 \text{ (CH)}, 57.8 \text{ (CH)}, 70.8 \text{ (CH)}, 75.0 \text{ (CH)}, 92.7 \text{ (C)}, 116.9 \text{ (CH)}, 127.7 \text{ (CH)}, 128.0 \text{ (CH)}, 128.6 \text{ (CH)}, 131.7 \text{ (CH)}, 137.8 \text{ (C)}, 161.0 \text{ (C)}; \text{m/z } \text{(CI) 338 (MH}^{+}, 25\%), 302 (22), 218 (15), 181 (70), 105 (100).\]

\((3R,4S)-3-(Trichloromethylcarbonylamino)-4-(methoxy)penta-1-ene \text{ and } (3S,4S)-3-(Trichloromethylcarbonylamino)-4-(methoxy)penta-1-ene\)

The reactions were carried out according to general procedures 5 and 6 using \((2E,4S)-4\)methoxypent-2-en-1-ol \((0.29 \text{ g}, 2.50 \text{ mmol})\). Purification was carried out by flash column chromatography \((30\% \text{ ethyl acetate / petroleum ether})\) to give the title compounds \((0.33 \text{ g}, 49\% \text{ over two steps})\) as a brown oil. \[ \text{υ}_{\max}/\text{cm}^{-1} \text{ (neat) 3339 (NH), 1705 (CO), 1598 (C=C)}; (3R,4S)-3-(trichloromethylcarbonylamino)-4-(methoxy)penta-1-ene \text{(major compound)}: \delta_{H} \text{ (400 MHz, CDCl}_{3} \text{)} 1.18 \text{ (3H, d, } J_{6.4} \text{ Hz, 5-H}), 3.38 \text{ (3H, s, OMe)}, 3.55 \text{ (1H, m, 4-H)}, 4.38 \text{ (1H, m, 3-H)}, 5.28 \text{ (2H, m, 1-H)}, 5.77-5.94 \text{ (1H, m, 2-H)}, 7.10 \text{ (1H, br s, NH)}; \delta_{C} \text{ (100 MHz, CDCl}_{3} \text{)} 15.6 \text{ (CH)}, 57.2 \text{ (CH)}, 58.0 \text{ (CH)}, 77.9 \text{ (CH)}, 93.2 \text{ (C)}, 119.5 \text{ (CH)}, 132.0 \text{ (CH)}, 161.4 \text{ (C)}; \text{m/z } \text{(CI) 274 (MH}^{+}, 4\%), 260 (75), 226 (17), 190 (100).\]

\((3R,4S)-3-(Trichloromethylcarbonylamino)-4-(methoxymethoxy)penta-1-ene \text{ and } (3S,4S)-3-(Trichloromethylcarbonylamino)-4-(methoxymethoxy)penta-1-ene\)
The reactions were carried out according to general procedures 5 and 6 using \((2E,4S)-4\text{-methoxymethoxypent-2-en-1-ol}\) (0.44 g, 3.7 mmol). Purification was carried out by flash column chromatography (30% ethyl acetate / petroleum ether) to give the title compounds (0.68 g, 64% over two steps) as an orange oil. \(\nu_{\text{max}}/\text{cm}^{-1}\) (neat): \(3302\) (NH), \(2935\) (CH), \(1712\) (CO), \(1643\) (C=C); \((3R,4S)-3\text{-}(trichloromethylcarbonylamino)-4\text{-}(methoxymethoxy)penta-1-ene\) (major compound): \(\delta H\) (400 MHz, \(\text{CDCl}_3\)) 1.26 (3H, d, \(J 6.4\) Hz, 5-H3), 3.43 (3H, s, OMe), 3.88 (1H, qd, \(J 6.4\) and \(3.0\) Hz, 4-H), 4.35 (1H, m, 3-H), 4.69 (1H, d, \(J 6.8\), O\(\text{CH}_2\)O) 4.71 (1H, d, \(J 6.8\) Hz, O\(\text{CH}_2\)O), 5.36 (2H, m, 1-H2), 7.89 (1H, br s, NH); \(\delta C\) (100 MHz, \(\text{CDCl}_3\)) 18.4 (CH3), 56.2 (CH), 58.1 (CH3), 77.7 (CH), 92.1 (C), 97.0 (CH2), 119.6 (CH2), 131.8 (CH), 161.7 (C); \((3S,4S)-3\text{-}(trichloromethylcarbonylamino)-4\text{-}(methoxymethoxy)penta-1-ene\) (minor compound): \(\delta H\) (400 MHz, \(\text{CDCl}_3\)) 1.24 (3H, d, \(J 6.4\) Hz, 5-H3), 3.39 (3H, s, OMe), 3.93 (1H, qd, \(J 6.4\), 2.8 Hz, 4-H), 4.43 (1H, m, 3-H), 4.63 (1H, d, \(J 6.8\), O\(\text{CH}_2\)O) 4.79 (1H, d, \(J 6.8\) Hz, O\(\text{CH}_2\)O), 5.27 (2H, m, 1-H2), 7.10 (1H, br s, NH); \(\delta C\) (100 MHz, \(\text{CDCl}_3\)) 17.8 (CH3), 56.1 (CH), 58.2 (CH3), 74.1 (CH), 94.3 (C), 95.3 (CH2), 117.3 (CH2), 135.3 (CH), 161.7 (C); (Found (CI): 290.0127. \(\text{C}_9\text{H}_{14}\text{O}_3\text{NCl}_3\) requires 290.0118).

\((3R,4S)-3\text{-}(Trichloromethylcarbonylamino)-4\text{-}(methoxyethoxymethoxy)penta-1-ene\) and \((3S,4S)-3\text{-}(Trichloromethylcarbonylamino)-4\text{-}(methoxyethoxymethoxy)penta-1-ene\)

The reactions were carried out according to general procedures 5 and 6 using \((2E,4S)-4\text{-methoxyethoxymethoxypent-2-en-1-ol}\) (0.52 g, 2.7 mmol). Purification was carried out by flash column chromatography (30% ethyl acetate / petroleum ether) giving the title compounds (0.54 g, 60% over two steps) as a yellow oil. \(\nu_{\text{max}}/\text{cm}^{-1}\) (neat): \(3289\) (NH), \(2930\) (CH), \(1708\) (C=O), \(1601\) (C=C); \((3R,4S)-3\text{-}(trichloromethylcarbonylamino)-4\text{-}(methoxyethoxymethoxy)penta-1-ene\) (major compound): \(\delta H\) (400 MHz, \(\text{CDCl}_3\)) 1.27 (3H, d, \(J 6.8\) Hz, 5-H3), 3.39 (3H, s, OMe), 3.56-3.78 (4H, m, O\(\text{CH}_2\)CH2O), 3.91 (1H, qd, \(J 6.4\), 2.8 Hz, 4-H), 4.41 (1H, t, \(J 8.4\) Hz, 3-H), 4.80 (1H, d, \(J 6.0\) Hz, O\(\text{CH}_2\)O), 4.82 (1H, d, \(J 6.0\) Hz, O\(\text{CH}_2\)O), 5.35 (2H, m, 1-H2), 5.90 (1H, m, 2-H), 7.73 (1H, br s, NH); \(\delta C\) (100 MHz, \(\text{CDCl}_3\)) 18.0 (CH3), 58.3 (CH), 59.4 (CH), 68.0 (CH2), 72.0 (CH2), 77.4 (CH3), 93.8 (C), 95.7 (CH2), 119.6 (CH2), 131.9 (CH), 162.2 (C); \((3S,4S)-3\text{-}(trichloromethylcarbonylamino)-4\text{-}(methoxyethoxymethoxy)penta-1-ene\) (minor compound): \(\delta H\) (400 MHz, \(\text{CDCl}_3\)) 1.29 (3H, d, \(J 6.4\) Hz, 5-H3), 3.41 (3H, s, OMe), 3.56-3.78 (4H, m, O\(\text{CH}_2\)CH2O), 4.03 (1H, qd, \(J 6.4\), 2.4 Hz, 4-H), 4.27 (1H, t, \(J 8.4\) Hz, 3-H), 4.72 (1H, d, \(J 6.0\) Hz, O\(\text{CH}_2\)O), 4.74 (1H, d, \(J 6.0\) Hz, O\(\text{CH}_2\)O), 5.26 (2H, m, 1-H2), 5.70 (1H, m, 2-H), 7.15 (1H, br s, NH); \(m/z\) (CI) 334 (MH+, 5%), 306 (6), 260 (95), 258 (100), 214 (22), 162 (40).
Synthesis of Oxazolidinones for Assignment of Relative Configuration of the Rearrangement Products: (4\textit{R},5\textit{S})-4-Vinyl-5-methyl-oxazolidin-2-one and (4\textit{S},5\textit{S})-4-Vinyl-5-methyl-oxazolidin-2-one

A mixture of (3\textit{R},4\textit{S})-3-(trichloromethylcarbonylamino)-4-(tert-butyldimethylsilyloxy)penta-1-ene and (3\textit{S},4\textit{S})-3-(trichloromethylcarbonylamino)-4-(tert-butyldimethylsilyloxy)penta-1-ene (0.11 g, 0.3 mmol) and tetra-n-butylammonium fluoride (1.0 M solution in THF, 0.32 mL, 0.32 mmol) in THF (5 mL) was allowed to stir at room temperature for 0.5 h. The reaction mixture was concentrated and the resulting residue was taken up in ethyl acetate (20 mL), washed with water (10 mL), dried (MgSO₄) and concentrated in vacuo. Purification by flash column chromatography (70% ethyl acetate / petroleum ether) gave a yellow oil. The oil was added to a solution of potassium hydroxide (0.12 g, 2.22 mmol) in isopropanol (5 mL) and the reaction mixture was allowed to stir at room temperature for 12 h. The mixture was then concentrated and the resulting residue was dissolved in water (10 mL) and extracted with ethyl acetate (5 x 10 mL). The organic layers were combined, dried (MgSO₄) and concentrated in vacuo to give the title compounds (16 mg, 41% over two steps) as a colourless oil.  

\( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 3279 (NH), 2984 (CH), 1732 (CO), 1644 (C=C); (4\textit{R},5\textit{S})-4-vinyl-5-methyl-oxazolidin-2-one:  \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 1.34 (3H, d, \( J = 6.5 \text{ Hz} \), 5-CH₃), 4.33 (1H, t, \( J = 6.1 \text{ Hz} \), 4-H), 4.82 (1H, dq, \( J = 7.9, 6.5 \text{ Hz} \), 5-H), 5.30 (2H, m, 4-CH=CH₃), 5.78 (1H, m, 4-C≡CH₂);  \( \delta_{\text{C}} \) (100 MHz, CDCl₃) 16.4 (CH₃), 58.8 (CH), 76.7 (CH), 133.4 (CH), 160.1 (C); (4\textit{S},5\textit{S})-4-vinyl-5-methyl-oxazolidin-2-one:  \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 1.40 (3H, d, \( J = 6.2 \text{ Hz} \), 5-CH₃), 3.90 (1H, m, 4-CH=CH₂), 4.33 (1H, qd, \( J = 7.9, 6.1 \text{ Hz} \), 5-H), 5.24 (2H, m, 4-CH=CH₂), 5.78 (1H, m, 4-C≡CH₂);  \( \delta_{\text{C}} \) (100 MHz, CDCl₃) 19.3 (CH₃), 63.3 (CH), 79.2 (CH), 119.3 (CH₂), 135.7 (CH), 160.0 (C); (Found (Cl): 128.0711. C₆H₁₀O₂N requires 128.0712);  

(1\textit{R},2\textit{R})-Hexanoic acid (2-hydroxy-1-methyl-2-phenyl-ethyl)-N-methylamide

Hexanoic anhydride (0.3 mL, 1.3 mmol) was added dropwise over several minutes to a solution of (-)-pseudoephedrine (0.2 g, 1.2 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 0.5 h before the excess anhydride was quenched by the addition of a saturated solution of aqueous sodium bicarbonate solution (10 mL). The reaction mixture was then extracted with ethyl acetate (3 x 20 mL), the organic layers were then combined, dried (MgSO₄) and concentrated in vacuo. Purification by flash column chromatography (50% ethyl acetate / petroleum ether) gave the title compound (0.31 g, 97%).  

\( [\alpha]_{D}^{21} = -87.2 \) (c 1.0, CHCl₃);  \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 0.81 (3H, t, \( J = 7.0 \text{ Hz} \), 6'-H₃), 0.91 (1H, d, \( J = 6.7 \text{ Hz} \), OH), 1.01 (2H, d, \( J = 7.0 \text{ Hz} \), 1-CH₃), 1.24 (4H, m, 4'-H₂, 5'-H₂), 1.43 (2H, m, 3'-H₂), 2.14 (2H, q, \( J = 15.4, 7.8 \text{ Hz} \), 2'-H₂), 2.71 (3H, s, NCH₃), 4.31 (1H, m, 1-H), 4.41 (1H, q, \( J = 14.5, 8.1 \text{ Hz} \), 2-H), 7.08-7.35 (5H, m, Ph);
δC (100 MHz, CDCl3) 13.9 (CH3), 14.5 (CH3), 15.3 (CH3), 22.5 (CH2), 24.7 (CH2), 31.5 (CH2), 34.4 (CH2), 58.3 (CH), 75.5 (CH), 126.3 (CH), 127.6 (CH), 128.3 (CH), 142.5 (C), 175.7 (C); (Found (CI): 264.1965. C16H23NO2 requires 264.1964).

(1R,2R,2'R)-2'-Methylhexanoic acid (2-hydroxy-1-methyl-2-phenyl-ethyl)-N-methylamide12

\[
\begin{align*}
\text{Ph} & \quad \text{Me} \\
\text{O} & \quad \text{O} \\
\text{N} & \quad \text{N}
\end{align*}
\]

A solution of lithium chloride (0.28 g, 6.6 mmol) and di-isopropylamine (0.34 mL, 2.5 mmol) in THF (5 mL) was cooled to -78 °C before n-butyllithium (2.4 M in hexane, 0.91 mL, 2.3 mmol) was added. The solution was warmed briefly to 0 °C, then was cooled to -78 °C and stirred for 0.5 h. A solution of (1R,2R)-hexanoic acid (2-hydroxy-1-methyl-2-phenyl-ethyl)-N-methylamide (0.29 g, 1.1 mmol) in THF (5 mL), cooled to 0 °C, was transferred to the reaction flask and the resulting solution was stirred at -78 °C for 1 h, 0 °C for 0.25 h and at room temperature for 5 min. The reaction mixture was then cooled to 0 °C and methyl iodide (0.25 mL, 1.6 mmol) was added. After 1 h, the reaction was quenched with a saturated solution of aqueous ammonium chloride solution (20 mL). The two phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The organic layers were combined, dried (MgSO4) and concentrated. Purification by flash column chromatography (50% ethyl acetate / petroleum ether) gave the title compound (0.14 g, 45%).

υmax/cm^-1 (neat) 3377 (OH), 2931 (CH), 1613 (CO), 1454, 1407, 1109, 1050; [α]D21 -122.6 (c 1.0, CHCl3); δH (3:1 rotamer ratio, * denotes minor rotamer peaks, 400 MHz, CDCl3) 0.91 (3H, t, J 7.2 Hz, 6'-H3), 1.04 (3H, d, J 6.8 Hz, CH3), 1.16-1.42 (8H, m, 3'-H, 4'-H2, 5'-H2, CH3), 1.68 (1H, m, 3'-H), 2.59 (1H, sex, J 6.8 Hz, 2'-H), 2.81 (3H, s, CH3), 2.95* (3H, s, N-CH3), 4.04* (1H, br m, 1-H), 4.31 (1H, br m, 1-H), 4.58* (1H, m, 2-H), 4.67 (1H, t, J 7.2 Hz, 2-H), 7.25-7.57 (5H, m, Ph); δC (3:1 rotamer ratio, * denotes minor rotamer peaks, 100 MHz, CDCl3) 14.0 (CH3), 14.4 (CH3), 15.5* (CH3), 17.4 (CH2), 17.7 (CH2), 22.7 (CH2), 26.9* (CH), 29.6 (CH2), 33.7 (CH2), 34.0* (CH2), 35.7* (CH), 36 (CH), 58.1 (CH), 60.0* (CH), 75.4* (CH), 76.5 (CH2), 126.2 (CH), 126.9* (CH), 127.4 (CH), 128.2 (CH), 128.4* (CH), 128.7* (CH), 141.2* (C), 142.6 (C), 178.0* (C), 179.1 (C); (Found (CI): 278.2119. C17H27NO2 requires 278.2120).

(2R)-2-Methylhexan-1-ol13

\[
\begin{align*}
\text{Ph} & \quad \text{Me} \\
\text{O} & \quad \text{OH}
\end{align*}
\]

n-Butyllithium (2.4 M in hexane, 20 mL, 47.3 mmol) was added to a solution of diisopropylamine (7.2 mL, 50.9 mmol) in THF at -78 °C. The resulting solution was stirred at -78 °C for 10 min, then warmed to 0 °C, and held at this temperature of 10 min. Borane-ammonia complex (90%, 1.67 g, 48.51 mmol) was added in one portion and the suspension was cooled to 0 °C before a solution of (1R,2R,2'R)-2'-methylhexanoic acid (2-hydroxy-1-methyl-2-phenyl-ethyl)-N-methylamide (3.36 g, 48.5 mmol) in THF (35 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was then cooled to 0 °C before 2 M hydrochloric acid (120 mL) was carefully added and allowed to stir for
0.5 h. The organic layer was then separated followed by extraction of the aqueous layer with ether (4 x 45 mL). The combined organic layers were washed sequentially with 2 M hydrochloric acid (20 mL), 1 M sodium hydroxide solution (20 mL) and brine (20 mL). The ether extracts were dried (MgSO₄) and concentrated. Purification by flash column chromatography (40% diethyl ether / petroleum ether) gave the title compound (0.86 g, 62%) as a colourless liquid. [α]D^21 +12.8 (c 1.0, CHCl₃); δH (400 MHz, CDCl₃) 0.89-0.99 (6H, m, 2-CH₃, 6-H₃), 1.09-1.48 (7H, m, 3-H₂, 4-H₂, 5-H₂, OH), 1.63 (1H, m, 2-H), 3.44 (1H, dd, J 10.4, 6.4 Hz, 1-H), 3.54 (1H, dd, J 10.4, 6.4 Hz, 1-H); δC (100 MHz, CDCl₃) 14.1 (CH₃), 16.6 (CH₃), 23.0 (CH₂), 29.2 (CH₂), 32.9 (CH₂), 35.8 (CH), 68.5 (CH₂).

**Ethyl (2E,4R)-4-Methyloctan-2-enoate**

Dimethyl sulfoxide (0.15 mL, 2.1 mmol) was added to a solution of oxalyl chloride (0.1 mL, 1.03 mmol) in dichloromethane (5 mL) at -78 °C. The resulting solution was allowed to stir for 15 min before (2R)-2-methylhexan-1-ol (0.1 g, 0.9 mmol) in dichloromethane (7 mL) was added. This solution was then allowed to stir for 15 min. Triethylamine (0.6 mL, 4.3 mmol) was then added and the reaction mixture was brought to room temperature and stirred for 2 h. A solution of lithium chloride (45 mg, 1.0 mmol) in dichloromethane (5 mL) was prepared and stirred for 15 min. Triethyl phosphonoacetate (0.2 mL, 1.0 mmol) was then added followed by 1,8-diazabicyclo(5,4,0)undec-7-ene (0.16 mL, 1.0 mmol) and the mixture was allowed to stir for 30 min. The aldehyde solution was then added to the phosphonoacetate solution and the reaction mixture was stirred for 12 h. The reaction was quenched with brine (15 mL), concentrated and then extracted with diethyl ether (3 x 10 mL), dried (MgSO₄) and concentrated in vacuo. Purification by flash column chromatography (30% ether / petroleum ether) gave the title compound (0.05 g, 34%) as a colourless oil. ʋmax/cm⁻¹ (neat) 2959 (CH), 2924 (CH), 1717 (CO), 1651 (C=C), 1263, 1177; [α]D^23 +30.8 (c 1.0, CHCl₃); δH (400 MHz, CDCl₃) 0.81 (3H, t, J 6.8 Hz, OCH₂C₃H₃), 0.97 (3H, d, J 6.8 Hz, 5-H₃), 1.16-1.38 (9H, m, 5-H₂, 6-H₂, 7-H₂, 8-H₃), 2.21 (1H, sept, J 6.8 Hz, 4-H), 4.11 (2H, q, J 7.2 Hz, OCH₂CH₃), 5.70 (1H, dd, J 16.0, 1.2 Hz, 2-H), 6.79 (1H, dd, J 16.0, 7.6 Hz, 3-H); δC (100 MHz, CDCl₃) 13.0 (CH₃), 13.3 (CH₃), 18.4 (CH₃), 21.7 (CH₂), 28.4 (CH₂), 34.7 (CH₂), 35.5 (CH), 59.1 (CH), 118.5 (CH), 153.8 (CH), 166.0 (C); (Found (CI): 184.1464. C₁₁H₂₀NO₂ requires 184.1463).

**(2E,4R)-4-Methylbutan-2-ene-1-ol**

The reaction was carried out according to general procedure 4 using ethyl (2E,4R)-4-methyloctan-2-enoate (0.4 g, 2.2 mmol) in diethyl ether (5 mL) at -78 °C. Purification by flash column chromatography (30% diethyl ether / petroleum ether) gave the title compound as a clear liquid (0.14 g, 45%). δH (400 MHz, CDCl₃) 0.84-0.95 (5H, m, 7-H₂, 8-H₃), 0.99 (3H, d, J 6.8 Hz, 4-
CH₃), 1.22-1.56 (4H, m, 5-H₂, 6-H₂), 2.14 (1H, quin, J 6.4 Hz, 4-H), 3.49 (1H, m, OH), 4.12 (2H, t, J 4.8 Hz, 1-H₂), 5.60 (2H, m, 2-H, 3-H); m/z (CI): 141 (MH⁺, 5%), 125 (100), 99 (100), 83 (11).

(3S,4R)-3-(Trichloromethylcarbonylamino)-4-methylocta-1-ene and (3R,4R)-3-(Trichloromethylcarbonylamino)-4-methylocta-1-ene

The reactions were carried out according to general procedures 5 and 6 using (2E,4R)-4-methyloctan-2-en-1-ol (0.16 g, 1.1 mmol). Purification by chromatography (50% diethyl ether / petroleum ether (40-60)) gave the target compounds (0.19 g, 59%) as a colourless oil. νmax/cm⁻¹ (neat) 3330 (NH), 2958 (CH), 2928, 2857, 1694 (CO), 1513, 817; major isomer: δH (400 MHz, CDCl₃) 0.81-1.02 (6H, m, 4-CH₃, 8-H₃), 1.21-1.46 (6H, m, 5-H₂, 6-H₂, 7-H₂), 2.05 (1H, m, 4-H), 4.42 (1H, m, 3-H), 5.26 (2H, m, 1-H₂), 5.82 (1H, m, 2-H), 6.63 (1H, br s, NH); minor isomer: δH (400 MHz, CDCl₃) 0.81-1.02 (6H, m, 4-CH₃, 8-H₃), 1.21-1.46 (6H, m, 5-H₂, 6-H₂, 7-H₂), 1.91 (1H, m, 4-H), 4.48 (1H, m, 3-H), 5.18 (2H, m, 1-H₂), 5.82 (1H, m, 2-H), 6.48 (1H, br s, NH); m/z (CI) 286 (MH⁺, 26%), 216 (12), 167 (6), 125 (12), 104 (5).

References