Efficient Asymmetric Synthesis of Quaternary (*E*)-Vinylglycines by Deconjugative Alkylation of Dehydroamino Acids

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Supporting Information

Benzyloxycarbonylamino(diethoxyphosphoryl)acetic acid (–)-8-phenylmenthyl ester **8**

EDC (20.4 g, 70.9 mmol) was added to a stirred solution of *N*-Cbz-diethylphosphonoglycine¹ (24.5 g, 70.9 mmol), (–)-8-phenylmenthol (17.8 g, 76.8 mmol) and DMAP (1.7 g, 14 mmol) in DCM (100 ml) at room temperature under nitrogen. The reaction mixture was stirred for 4 days. The reaction mixture was diluted with DCM (200 ml) and washed successively with a 1M aqueous hydrogen chloride solution (100 ml), a saturated aqueous sodium hydrogen carbonate solution (100 ml) and brine (50 ml). The organic extracts were dried (Na₂SO₄), filtered and evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, eluting with 1:1 petrol-ethyl acetate, to give recovered (–)-8-phenylmenthol (4.88 g) as a colourless oil and phosphonate **8** (27.76 g, 70 %, 88:12 mixture of diastereoisomers) as a colourless oil; *R*_F 0.4 (50% EtOAc in petrol); [*α*]_D²⁴ +20.68 (c. 9.6 in CHCl₃); (Found: C, 64.1; H, 7.75; N, 2.60; P, 5.45; C₃₀H₄₂NPO₇ requires: C, 64.39; H, 7.56; N, 2.50; P, 5.53 %); *ν*_{max} / cm^{–1} (CHCl₃ solution) 3246, 1725, 1536, 1497, 1306, 1266, 1213, 1047 and 1027; *δ*_H (300 MHz, CDCl₃) 7.45–7.05 (10H, m, Ph), 5.31 (1H, brd, *J* 8.5, NH), 5.15 (2H, s, CH₂Ph(Cbz)), 4.89 (1H, td, *J* 10.8 and 4.1, CHOCO), 3.85–4.23 (5H, m, OCH₂CH₃ × 2 and P-CH) and 2.10–0.80 (23H, m, aliphatic H); peak visible for minor isomer at 4.68 (1H, dd, ²*J*_{P-H} 22.0 and *J* 9.2, P-CH); *δ*_H (500 MHz, d₆-DMSO, 300K) 7.96 (1H, brd, *J* 8.9, NH), 7.43–7.07 (10H, m, Ph), 5.13 (1H, d, *J* 12.5, CH_AH_BPh(Cbz)), 5.09 (1H, d, *J* 12.5, CH_AH_BPh(Cbz)), 4.71 (1H, td, *J* 10.6 and 4.2, CHOCO), 4.19 (1H, dd, ²*J*_{P-H} 23.5 and *J* 9.2, P-CH), 4.07 (1H, apparent q, *J* 7.7, OCH_AH_BCH₃), 3.98–3.80 (3H, m, OCH_AH_BCH₃ and OCH₂CH₃) and 2.02–0.77 (23H, m, aliphatic H); peaks visible for minor isomer at 8.16 (1H, brd, *J* 8.6, NH), 5.04 (1H, d, *J* 12.5, CH_AH_BPh(Cbz)), and 4.59 (1H, dd, ²*J*_{P-H} 23.3 and *J* 9.4, P-CH); *δ*_C (75 MHz, CDCl₃) 166.3, 155.6 (³*J*_{P-C} 5.7), 151.8, 136.5, 128.9, 128.7, 128.6, 128.4, 126.0, 125.9, 77.3, 67.7, 63.9 (²*J*_{P-C} 6.8), 63.7 (²*J*_{P-C} 6.7), 52.7 (¹*J*_{P-C} 146.9), 51.0, 41.3, 39.9, 34.8, 31.7, 29.2, 26.8, 24.2, 22.2, 16.7 and 16.7; peaks visible for minor isomer at 165.6, 150.8, 136.3, 128.8, 128.1, 78.2, 67.9, 64.1 (²*J*_{P-C} 9.1), 53.7 (¹*J*_{P-C} 148.0), 50.7, 41.3, 39.9, 34.7, 31.8, 28.8, 27.5, and 25.3; *δ*_P (³¹P, 202 MHz, d₆-DMSO) 17.80 and 17.48; *m/z* (low resolution, ES) 560.1 (100%, M⁺+H).

¹ R. Shankar and A. I. Scott, *Tetrahedron Lett.* **1993**, 34, 231–234.

General procedure for formation of dehydroamino acid esters 5

DBU or tetramethylguanidine (1.0 equivalent) was added to a stirred solution of phosphonate **8** (1.0 equivalent) in DCM (0.5 M, typical concentration) at room temperature under nitrogen. The reaction mixture was stirred for 30 minutes. The aldehyde was then added (as a solution in DCM when required) and stirring continued for 24 hours. The reaction mixture was absorbed directly onto silica and purified by flash chromatography, typically eluting with petrol-diethyl ether, to give the (Z)-dehydroamino acid esters **5**.

(Z)-2-Benzyloxycarbonylamino-12-phenylundec-2-enoic acid (–)-8-phenylmenthyl ester **5a**

Using tetramethylguanidine. Colourless oil; R_F 0.15 (5 % EtOAc in petrol); $[\alpha]_D^{23} +31.8$ (c. 4.65 in CHCl_3); (Found: C, 76.9; H, 9.3; N, 2.4; $\text{C}_{36}\text{H}_{51}\text{NO}_4$ requires: C, 76.97; H, 9.15; N, 2.49 %); $\nu_{\text{max}} / \text{cm}^{-1}$ (CHCl_3 solution) 3390, 1716, 1658, 1497, 1455, 1257 and 1219; δ_{H} (300 MHz, CDCl_3) 7.45-7.05 (10H, m, Ph), 6.24 (1H, t, J 7.4, H-3), 5.12 (1H, d, J 12.5, $\text{CH}_A\text{H}_B\text{Ph}(\text{Cbz})$), 5.03 (1H, d, J 12.5, $\text{CH}_A\text{H}_B\text{Ph}(\text{Cbz})$), 5.18-4.98 (1H, brs, NH), 4.87 (1H, td, J 10.8 and 4.4, CHOCO) and 2.18-0.83 (36H, m, aliphatic H); δ_{C} (75 MHz, CDCl_3) 163.8, 154.4, 152.7, 139.8, 136.8, 128.9, 128.5, 128.5, 128.5, 128.4, 125.8, 125.3, 75.6, 67.3, 50.7, 41.8, 39.8, 34.9, 32.3, 31.7, 29.9, 29.8, 29.8, 29.7, 29.7, 28.7, 28.5, 26.8, 23.7, 23.1, 22.2 and 14.6; m/z (low resolution, ES) 579.5 (31%, $\text{M}^+ + \text{NH}_4^+$) and 562.5 (100%, $\text{M}^+ + \text{H}$).

(Z)-2-Benzyloxycarbonylamino-4-phenylbut-2-enoic acid (–)-8-phenylmenthyl ester **5b**

Using DBU. Colourless oil (^1H -NMR analysis revealed the product to be a 7:3 mixture of the dehydroamino ester **5b** and its deconjugated isomer **5b*** as a 3:1 mixture of diastereoisomers); R_F 0.26 (20 % Et_2O in petrol); $[\alpha]_D^{25} +5.3$ (c. 6.5 in CHCl_3); $\nu_{\text{max}} / \text{cm}^{-1}$ (CHCl_3 solution) 3383, 1715, 1657, 1600, 1496, 1455, 1296, 1256, 1221; δ_{H} (300 MHz, CDCl_3) 7.5-7.2 (15H, m, Ph), 6.36 (1H, t, J 7.4, H-3), 5.14 (1H, d, J 12.3, $\text{CH}_A\text{H}_B\text{Ph}(\text{Cbz})$), 5.07 (1H, d, J 12.7, $\text{CH}_A\text{H}_B\text{Ph}(\text{Cbz})$), 4.79 (1H, td, J 10.8 and 4.3, CHOCO), 3.38 (2H, d, J 7.7, H-4) and 2.15-0.79 (18H, m, aliphatic H); signals visible for minor isomers at 6.63 (1H, d, J 16.7, H-4), 6.12 (1H, dd, J 16.2 and 7.0, H-3), 5.87 (1H, dd, J 15.4 and 4.8, H-3) and 4.27 (1H, apparent t, J 7.2, H-2); δ_{C} (75 MHz, CDCl_3) 163.2, 152.2, 136.3, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 126.6, 126.6, 126.4, 125.6, 125.3, 124.9, 75.4, 67.1, 50.3, 41.4, 39.4, 34.5, 34.5, 31.3, 29.4, 26.3, 23.1 and 21.7; m/z (low resolution, ES) 526.0 (100%, $\text{M}^+ + \text{H}$); m/z (accurate mass, ES) Found: $\text{M}^+ + ^{23}\text{Na}$, 548.2772. $\text{C}_{34}\text{H}_{39}\text{NO}_4\text{Na}$ requires M, 548.2777.

(Z)-2-Benzyloxycarbonylamino-5-phenylpent-2-enoic acid (–)-8-phenylmenthyl ester 5c

Using DBU. Colourless oil; R_F 0.23 (15 % Et₂O in petrol); $[\alpha]_D^{25} +2.4$ (c. 9.5 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3386, 3323, 1738, 1714, 1659, 1601, 1496, 1454, 1265 and 1221; δ_H (300 MHz, CDCl₃) 7.01-7.50 (15H, m, Ph), 6.22 (1H, t, J 7.4, H-3), 5.11 (1H, d, J 12.4, CH_AH_B Ph(Cbz)), 5.03 (1H, d, J 12.4, CH_AH_B Ph(Cbz)), 4.86 (1H, td, J 10.8 and 4.3, $CHOCO$), 2.68 (2H, m, H-5), 2.37 (2H, q, J 7.6, H-4), 2.07 (1H, td, J 11.4 and 3.5, $CHC(CH_3)_2$ Ph), 1.80 (2H, m, CH_2CHCH_3), 1.67 (1H, m, aliphatic H), 1.45 (1H, m, aliphatic H), 1.25 (3H, s, CH_3CCH_3 Ph), 1.16 (3H, s, CH_3CCH_3 Ph), 0.85 (3H, s, CH_3CH) and 0.8-1.35 (3H, m, aliphatic H), NH not visible; δ_C (75 MHz, CDCl₃) 163.3, 153.9, 152.2, 141.2, 137.2, 136.3, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 126.1, 125.7, 125.3, 124.9, 75.4, 67.0, 50.3, 41.4, 39.4, 34.5, 34.2, 31.3, 30.2, 29.2, 26.4, 23.5 and 21.8; m/z (low resolution, ES) 562.0 (22%, $M^+ + ^{23}Na$), 557.0 (35%, $M^+ + NH_4^+$) and 540.0 (100%, $M^+ + H$); m/z (accurate mass, ES) Found: $M^+ + Na$, 562.2929. C₃₅H₄₁NO₄Na requires M, 562.2933.

General method for asymmetric deconjugative alkylation of dehydroamino acid esters 5

A flask charged with lithium chloride (6.0 equivalents) was flame dried under vacuum, allowed to cool to room temperature and transferred to a nitrogen atmosphere. THF and diisopropylamine (3.0 equivalents, 0.6 M typical concentration) were added and the mixture cooled to –78 °C before a solution of *n*-butyllithium (3.0 equivalents, ~1.6 M in hexanes) was added. The reaction mixture was stirred for 20 minutes at 0 °C, recooled to –78 °C and a solution of the (Z)-dehydroamino acid **5** (1.0 equivalent) in THF (0.2 M, typical concentration) was added dropwise. The reaction mixture was stirred for 20 minutes before alkyl halide (4.0 equivalents unless otherwise stated) was added. The reaction mixture was stirred for a further 7 hours (or until reaction was shown to be complete by TLC) at –78 °C under nitrogen. The reaction mixture was quenched with a saturated aqueous ammonium chloride solution, diluted with water and the mixture extracted with ethyl acetate (3×). The combined organic extracts were dried (Na₂SO₄), filtered and evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, typically eluting with petrol-diethyl ether, to give α,α -disubstituted amino acid **4**.

(2R,3E)-2-Benzyloxycarbonylamino-2-methyldodec-3-enoic acid (–)-8-phenylmenthyl ester 4a

Colourless oil; R_F 0.44 (20 % Et₂O in petrol); $[\alpha]_D^{20} -2.7$ (c. 0.70 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3418, 3360, 1724, 1496, 1455, 1264 and 1241; δ_H (300 MHz, CDCl₃) 7.43-7.20 (9H, m, Ph), 7.17-7.09 (1H, m, Ph), 5.67 (1H, dt, J 15.6 and 6.7, H-4), 5.52 (1H, d, J 15.6, H-3), 5.32 (1H, brs, NH), 5.11 (1H, d, J 12.3, CH_AH_B Ph(Cbz)), 5.02 (1H, d, J 12.3, CH_AH_B Ph(Cbz)), 4.82 (1H, td, J 10.5 and 4.4, $CHOCO$), 2.08-1.87 (4H, m, H-5 and CH_2CHOCO), 1.50 (3H, s, Me), 1.45-1.15 (20H, m, aliphatic H) and 1.10-0.70 (10H, m, aliphatic H); δ_C (75 MHz, CDCl₃) 172.5, 154.8, 151.1, 137.0, 132.8, 129.7, 128.9, 128.6, 128.5, 128.5, 126.0, 125.8, 77.7, 66.8, 60.4, 50.6, 41.6, 40.5, 34.9, 32.6, 32.3, 31.7, 29.9, 29.7, 29.7, 29.4, 29.3, 27.6, 25.5, 23.1, 23.1, 22.2 and 14.5; m/z (low resolution, ES) 593.2 (25%,

$M^+ + NH_4$), 577.2 (42%, $M^+ + H + ^{13}C$), 576.2 (100%, $M^+ + H$) and 362.0 (29%); m/z (accurate mass, ES) Found: $M^+ + ^{23}Na$, 598.3890. $C_{37}H_{53}NO_4Na$ requires M , 598.3872.

(2*R*,3*E*)-2-Benzylloxycarbonylamino-2-ethyldodec-3-enoic acid (–)-8-phenylmenthyl ester 4b

Colourless oil; R_F 0.57 (20 % Et_2O in petrol); $[\alpha]_D^{26} -4.65$ (c. 0.71 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3420, 3369, 1718, 1495, 1455, 1244 and 1068; δ_H (300 MHz, $CDCl_3$) 7.42-7.21 (9H, m, Ph), 7.19-7.10 (1H, m, Ph), 5.70-5.57 (2H, m, H-4 and NH), 5.45 (1H, d, J 15.4, H-3), 5.13 (1H, d, J 12.3, $CH_AH_BPh(Cbz)$), 5.03 (1H, d, J 12.3, $CH_AH_BPh(Cbz)$), 4.82 (1H, td, J 10.2 and 4.1, $CHOCO$), 2.25 (1H, m, $CH_AH_BCH_3$), 2.07-1.87 (5H, m, H-5, $CH_AH_BCH_3$, CH_2CHOCO) and 1.48-0.70 (33H, m, aliphatics); δ_C (75 MHz, $CDCl_3$) 172.2, 154.3, 150.9, 137.2, 132.4, 128.9, 128.5, 128.5, 128.5, 126.1, 126.1, 125.8, 77.8, 66.7, 64.5, 50.5, 41.7, 40.6, 34.8, 32.6, 32.3, 31.7, 30.1, 29.9, 29.7, 29.7, 29.4, 28.3, 27.7, 25.0, 23.1, 22.2, 14.5 and 8.5; m/z (low resolution, ES) 1197.5 (25%, $2M^+ + NH_4^+ + ^{13}C$), 1196.6 (30%, $2M^+ + NH_4^+$), 1179.6 (18%, $2M^+ + H$), 607.3 (25%, $M^+ + NH_4^+$), 591.2 (42%, $M^+ + H + ^{13}C$) and 590.1 (100%, $M^+ + H$); m/z (accurate mass, ES) Found: $M^+ + H$, 590.4200. $C_{38}H_{56}NO_4$ requires M , 590.4209.

(2*R*,3*E*)-2-Benzyl-2-benzylloxycarbonylamino-dodec-3-enoic acid (–)-8-phenylmenthyl ester 4c

Colourless oil; R_F 0.43 (15 % Et_2O in petrol); $[\alpha]_D^{22} +15.04$ (c. 0.645 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3415, 1725, 1496, 1455, 1206, 1073 and 1022; δ_H (300 MHz, $CDCl_3$) 7.46-7.27 (5H, m, Ph), 7.23-7.01 (10H, m, Ph), 5.60 (1H, dt, J 15.4 and 6.7, H-4), 5.47 (1H, d, J 15.4, H-3), 5.22 (1H, brs, NH), 5.11 (2H, s, $CH_2Ph(Cbz)$), 4.80 (1H, td, J 10.8 and 4.1, $CHOCO$), 3.36 (1H, d, J 13.8, CH_AH_BPh), 3.23 (1H, d, J 13.8, CH_AH_BPh), 2.03 (3H, m, H-5 and CH_2CHOCO), 1.89 (1H, brd, J 11.3, CH_2CHOCO) and 1.60-0.71 (30H, m, aliphatics); δ_C (75 MHz, $CDCl_3$) 171.1, 154.7, 151.3, 137.2, 136.7, 133.0, 131.1, 129.4, 128.9, 128.7, 128.5, 128.5, 128.4, 127.1, 125.9, 125.4, 78.3, 66.7, 64.9, 50.4, 41.6, 40.3, 40.1, 34.9, 32.6, 32.3, 31.8, 29.9, 29.7, 29.7, 29.4, 28.2, 27.7, 26.1, 23.1, 22.1 and 14.6; m/z (low resolution, ES) 669.2 (15%, $M^+ + NH_4^+$), 653.3 (42%, $M^+ + H + ^{13}C$), 652.2 (87%, $M^+ + H$), 144.7 (78%) and 114.8 (100%); m/z (accurate mass, ES) Found: $M^+ + H$, 652.4359. $C_{43}H_{58}NO_4$ requires M , 652.4366.

(2*R*,3*E*)-2-Allyl-2-benzylloxycarbonylamino-dodec-3-enoic acid (–)-8-phenylmenthyl ester 4d

Colourless oil; R_F 0.39 (15 % Et_2O in petrol); $[\alpha]_D^{20} +3.74$ (c. 0.695 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3420, 1719, 1495, 1467, 1221, 1086 and 1071; δ_H (300 MHz, $CDCl_3$) 7.40-7.23 (9H, m, Ph), 7.15 (1H, m, Ph), 5.65 (1H, dt, J 15.4 and 6.7, H-4), 5.62-5.50 (2H, m, $CH_2CH=CH_2$ and NH), 5.46 (1H, d, J 15.4, H-3), 5.15-5.00 (4H, m, $CH_2Ph(Cbz)$ and $CH_2CH=CH_2$), 4.82 (1H, td, J 10.8 and 4.1, $CHOCO$), 2.93 (1H, dd, J 13.8 and 6.7, $CH_AH_BCH=CH_2$), 2.60 (1H, dd, J 13.8 and 7.2, $CH_AH_BCH=CH_2$), 1.98 (4H, m, H-5 and CH_2CHOCO), 1.59-1.15 (21H, m, aliphatic H) and 1.13-0.68 (9H, m, aliphatic H); δ_C (75 MHz, $CDCl_3$) 171.8, 154.4, 151.0, 137.2, 132.9, 132.5, 128.9, 128.5, 128.4, 128.3, 126.1, 125.9, 125.8, 119.8, 78.0, 66.7, 63.3, 50.5, 41.9, 40.6, 39.6, 34.8, 32.6, 32.3, 31.7, 30.0, 29.9, 29.7, 29.7, 29.4, 27.7, 25.0, 23.1, 22.2 and 14.5; m/z (low resolution, ES) 619.3 (18%,

$M^+ + NH_4^+$), 603.2 (43%, $M^+ + H + ^{13}C$), 602.3 (100%, $M^+ + H$) and 388.1 (53%); m/z (accurate mass, ES) Found: $M^+ + H$, 602.4211. $C_{39}H_{56}NO_4$ requires M , 602.4209.

(2*S*,3*E*)-2-Benzylloxycarbonylamino-2-benzylloxymethyldodec-3-enoic acid (–)-8-phenylmenthyl ester 4e

(NB - The product was further purified by preparative HPLC to give an analytical sample, for which the overall yield is 35%) Colourless oil; R_F 0.29 (15% Et_2O in petrol); $[\alpha]_D^{21} -19.5$ (c. 0.2 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3421, 1724, 1496, 1454, 1241, 1093 and 1056; δ_H (300 MHz, $CDCl_3$) 7.43–7.08 (15H, m, Ph), 5.90 (1H, s, NH), 5.73 (1H, dt, J 15.9 and 6.7, H-4), 5.40 (1H, d, J 15.9, H-3), 5.12 (1H, d, J 12.8, $CH_AH_BPh(Cbz)$), 5.05 (1H, d, J 12.3, $CH_AH_BPh(Cbz)$), 4.84 (1H, td, J 10.8 and 4.1, $CHOCO$), 4.52 (1H, d, J 12.3, CH_AH_BPh), 4.44 (1H, d, J 12.3, CH_AH_BPh), 4.00 (1H, d, J 9.2, CH_AH_BOBn), 3.80 (1H, d, J 9.2, CH_AH_BOBn), 2.10–1.78 (4H, m, aliphatic H), 1.55–1.15 (21H, m, aliphatic H) and 0.98–0.67 (9H, m, aliphatic H); δ_C (75 MHz, $CDCl_3$) 169.4, 153.3, 149.4, 136.8, 135.8, 132.6, 127.4, 127.2, 127.0, 127.0, 126.9, 126.7, 126.6, 124.7, 124.4, 123.7, 76.6, 72.4, 70.5, 65.3, 63.3, 49.2, 40.2, 39.2, 33.4, 31.2, 30.8, 30.2, 29.0, 28.4, 28.2, 27.8, 26.3, 26.2, 22.9, 21.6, 20.6 and 13.1; m/z (low resolution, ES); 683.0 (22%, $M^+ + H + ^{13}C$) and 682.1 (39%, $M^+ + H$); m/z (accurate mass, ES) Found: $M^+ + H$, 682.4469. $C_{44}H_{60}NO_5$ requires M , 682.4471.

(2*R*,1'*E*)-2-Benzylloxycarbonylamino-2-dec-1'-enylsuccinic acid 4-*t*-butyl, 1-[(–)-8-phenylmenthyl] diester 4f

Colourless oil; R_F 0.55 (20 % Et_2O in petrol); $[\alpha]_D^{26} -9.88$ (c. 4.23 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3422, 1738, 1496, 1455, 1368, 1155 and 1027; δ_H (300 MHz, $CDCl_3$) 7.40–7.15 (10H, m, Ph), 6.26 (1H, s, NH), 5.74 (1H, dt, J 15.6 and 6.7, H-2'), 5.37 (1H, d, J 15.6, H-1'), 5.10 (2H, s, $CH_2Ph(Cbz)$), 4.90 (1H, td, J 10.8 and 4.1, $CHOCO$), 3.39 (1H, d, J 16.9, H-3_A), 2.85 (1H, d, J 16.6, H-3_B), 2.20–1.90 (4H, m, aliphatic H) and 1.65–0.70 (39H, m, aliphatic H); δ_C (75 MHz, $CDCl_3$) 171.3, 169.8, 154.4, 151.0, 137.2, 133.7, 128.8, 128.5, 128.3, 128.2, 127.5, 126.1, 125.8, 81.5, 78.3, 66.6, 61.2, 50.6, 41.5, 40.6, 40.2, 34.9, 32.5, 32.3, 31.7, 30.2, 29.8, 29.7, 29.2, 28.5, 28.1, 27.8, 24.8, 23.1, 22.1 and 14.5; m/z (low resolution, ES) 698.4 (82%, $M^+ + ^{23}Na$) and 699.4 (42%, $M^+ + ^{23}Na + ^{13}C$); m/z (accurate mass, ES) Found: $M^+ + ^{23}Na$, 698.4389. $C_{42}H_{61}NO_6^{23}Na$ requires M , 698.4397.

(2*R*,3*E*)-2-Benzylloxycarbonylamino-2-methyl-4-phenylbut-3-enoic acid (–)-8-phenylmenthyl ester 4g

Colourless oil; R_F 0.42 (30 % Et_2O in petrol); $[\alpha]_D^{22} +6.88$ (c. 0.48 in $CHCl_3$); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3414, 3367, 1721, 1496, 1454, 1260 and 1058; δ_H (300 MHz, $CDCl_3$) 7.45–7.07 (15H, m, Ph), 6.54 (1H, d, J 16.4, H-4), 6.34 (1H, d, J 16.4, H-3), 5.43 (1H, brs, NH), 5.14 (1H, d, J 12.3, $CH_AH_BPh(Cbz)$), 5.04 (1H, d, J 12.3, $CH_AH_BPh(Cbz)$), 4.84 (1H, td, J 10.8 and 4.1, $CHOCO$), 1.88 (2H, m, CH_2CHOCO) and 1.70–0.70 (18H, m, aliphatic H), signal visible for minor diastereoisomer at 6.10 (1H, d, J 15.9, H-3); δ_C (75 MHz, $CDCl_3$) 172.3, 154.8, 151.1, 137.0, 136.6, 130.9, 129.5, 128.9, 128.9, 128.7, 128.5, 128.2, 127.1, 126.0, 125.8, 125.7, 77.8, 67.0, 60.7, 50.5, 41.6, 40.5, 34.9, 31.7, 28.8, 27.5, 25.9, 23.7 and 22.2; m/z (low resolution, ES) 562.2 (25%, $M^+ + Na$), 557.2 (55%, $M^+ + NH_4^+$), 540.2 (70%,

M⁺+H) and 389.1 (100%); m/z (accurate mass, ES) Found: M⁺+²³Na, 562.2927. C₃₅H₄₁NO₄²³Na requires M, 562.2933.

(2S,3E)-2-Benzyloxycarbonylamino-2-benzyloxymethyl-4-phenylbut-3-enoic (–)-8-phenylmenthyl ester 4h

Colourless oil; *R*_F 0.46 (30 % Et₂O in petrol); [α]_D²⁶ –26.02 (c. 0.42 in CHCl₃); $\nu_{\max}$ / cm^{–1} (CHCl₃ solution) 3418, 1721, 1599, 1495, 1453, 1241, 1053 and 697; δ_{H} (300 MHz, CDCl₃) 7.47–7.07 (20H, m, Ph), 6.62 (1H, d, *J* 15.9, H-4), 6.22 (1H, d, *J* 16.4, H-3), 6.02 (1H, brs, NH), 5.16 (1H, d, *J* 12.8, CH_AH_BPh(Cbz)), 5.06 (1H, d, *J* 12.3, CH_AH_BPh(Cbz)), 4.86 (1H, td, *J* 10.8 and 4.6, CHOCO), 4.55 (1H, d, *J* 11.8, CH_AH_BPh), 4.48 (1H, d, *J* 11.8, CH_AH_BPh), 4.06 (1H, brd, *J* 9.2, CH_AH_BOBn), 3.89 (1H, brd, *J* 9.2, CH_AH_BOBn), 2.04 (1H, brd, *J* 10.2, aliphatic H), 1.84 (1H, dt, *J* 11.8 and 3.1, aliphatic H) and 1.52–0.60 (15H, m, aliphatic H); δ_{C} (75 MHz, CDCl₃) 170.6, 154.9, 150.7, 138.0, 137.2, 136.5, 132.2, 128.9, 128.9, 128.8, 128.6, 128.5, 128.4, 128.4, 128.2, 128.2, 127.1, 126.1, 125.8, 125.1, 78.4, 74.0, 72.2, 66.9, 65.1, 50.8, 41.7, 40.7, 34.8, 31.7, 30.7, 27.8, 24.1, 22.1; m/z (low resolution, ES) 669.1 (33%, M⁺+²³Na+¹³C), 668.1 (71%, M⁺+²³Na) and 646.1 (69%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 646.3553. C₄₂H₄₈NO₅ requires M, 646.3532.

(2R,3E)-2-Benzyloxycarbonylamino-2-methyl-5-phenylpent-3-enoic acid (–)-8-phenylmenthyl ester 4i

Colourless oil; *R*_F 0.46 (30 % Et₂O in petrol); [α]_D²² +6.74 (c. 0.445 in CHCl₃); $\nu_{\max}$ / cm^{–1} (CHCl₃ solution) 3414, 3368, 1722, 1495, 1453, 1258, 1241 and 1050; δ_{H} (300 MHz, CDCl₃) 7.42–7.08 (15H, m, Ph), 5.81 (1H, dt, *J* 15.4 and 6.7, H-4), 5.62 (1H, d, *J* 15.8, H-3), 5.28 (1H, brs, NH), 5.11 (1H, d, *J* 11.8, CH_AH_BPh(Cbz)), 5.01 (1H, d, *J* 11.8, CH_AH_BPh(Cbz)), 4.83 (1H, td, *J* 10.8 and 4.6, CHOCO), 3.36 (2H, d, *J* 6.2, H-5), 1.92 (2H, m, CH₂CHOCO) and 1.60–0.69 (18H, m, aliphatic H); δ_{C} (75 MHz, CDCl₃) 172.3, 154.8, 151.2, 140.0, 136.9, 131.4, 130.9, 129.0, 128.9, 128.8, 128.6, 128.5, 128.2, 126.6, 126.0, 125.8, 77.5, 66.9, 60.4, 50.4, 41.6, 40.5, 38.8, 34.9, 31.7, 28.7, 27.5, 25.9, 23.4 and 22.2; m/z (low resolution, ES) 576.1 (10%, M⁺+Na), 571.2 (57%, M⁺+NH₄⁺), 554.1 (100%, M⁺+H) and 340.0 (47%); m/z (accurate mass, ES) Found: M⁺+²³Na, 576.3105. C₃₆H₄₃NO₄²³Na requires M, 576.3090.

(2S,3E)-2-Benzyloxycarbonylamino-2-benzyloxymethyl-5-phenylpent-3-enoic (–)-8-phenylmenthyl ester 4j

Colourless oil isolated in >95% purity determined by ¹H-NMR analysis; *R*_F 0.5 (30 % Et₂O in petrol); [α]_D²⁶ –4.83 (c. 0.12 in CHCl₃); $\nu_{\max}$ / cm^{–1} (CHCl₃ solution) 3414, 1722, 1628, 1601, 1241, 1084 and 1062; δ_{H} (300 MHz, CDCl₃) 7.45–7.05 (20H, m, Ph), 5.90 (1H, dt, *J* 15.4 and 6.7, H-4), 5.87 (1H, brs, NH), 5.49 (1H, d, *J* 15.4, H-3), 5.12 (1H, d, *J* 12.3, CH_AH_BPh(Cbz)), 5.04 (1H, d, *J* 12.3, CH_AH_BPh(Cbz)), 4.84 (1H, td, *J* 10.8 and 4.1, CHOCO), 4.50 (1H, d, *J* 12.3, OCH_AH_BPh), 4.43 (1H, d, *J* 11.8, OCH_AH_BPh), 3.97 (1H, d, *J* 8.7, CH_AH_BOBn), 3.78 (1H, d, *J* 8.7, CH_AH_BOBn), 3.36 (2H, d, *J* 6.1, H-5), 1.99 (1H, brd, *J* 11.8, CH_AH_BCHOCO), 1.85 (1H, dt, *J* 3.1 and 11.8, CH_AH_BCHOCO) and 1.60–0.60 (15H, m, aliphatic H); δ_{C} (75 MHz, CDCl₃) 170.2, 154.4, 150.5, 139.4, 137.7, 136.7, 131.8, 128.6, 128.4,

128.4, 128.3, 128.0, 128.0, 127.7, 127.6, 126.6, 126.1, 125.7, 125.5, 125.4, 77.7, 73.4, 71.5, 66.3, 64.4, 50.1, 41.1, 40.2, 38.4, 34.4, 31.2, 29.7, 27.2, 24.2 and 21.7; m/z (low resolution, ES) 660.0 (25%, $M^+ + H$); m/z (accurate mass, ES) Found: $M^+ + H$, 660.3707. $C_{43}H_{50}NO_5$ requires M , 660.3689.

Reduction of amino acid esters 4 to oxazolidinones 12

Method 1: Lithium aluminium hydride (1M solution in THF, 4 equivalents) was added to a stirred solution of α, α -disubstituted amino acid (1 equivalent) in THF at 0 °C under nitrogen. The reaction mixture was stirred for 1 hour at 0 °C. The mixture was quenched cautiously with methanol and warmed to room temperature. Sodium borohydride (8 equivalents) was added and the reaction mixture stirred for 1 hour at room temperature. The reaction mixture was quenched with 1M aqueous sodium hydroxide solution and stirring continued for 24 hours. The mixture was diluted with water and extracted with ethyl acetate (3 $\times$). The combined organic extracts were dried ($NaSO_4$), filtered and evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, eluting with petrol-diethyl ether, to give the oxazolidinone.

Method 2: Powdered lithium borohydride (16 equivalents) was cautiously added to a stirred solution of α, α -disubstituted amino acid (1 equivalent) in diethyl ether at room temperature under nitrogen. The reaction mixture was heated at reflux for 1 hour. The reaction mixture was cooled to room temperature and quenched with a 1M aqueous sodium hydroxide solution. The mixture was heated at reflux for 30 minutes. The reaction mixture was cooled to room temperature and excess diethyl ether was removed under reduced pressure. THF was added and the reaction mixture stirred for 24 hours at room temperature. The remaining THF was removed under reduced pressure and the residue diluted with water. The aqueous mixture was extracted with ethyl acetate (3 $\times$). The combined organic extracts were dried ($NaSO_4$), filtered and evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, eluting with petrol-diethyl ether, to give the oxazolidinone.

(1'*E*,4*R*)-4-Methyl-4-dec-1'-enyloxazolidin-2-one 12a

Colourless oil; R_F 0.45 (60 % Et_2O in petrol); $[\alpha]_D^{24}$ -14.38 (c. 1.05 in $CHCl_3$); (Found: C, 69.95; H, 10.7; N, 5.9; $C_{14}H_{25}NO_2$ requires: C, 70.25; H, 10.53; N, 5.85%); ν_{max} / cm^{-1} ($CHCl_3$ solution) 3270, 1756, 1466, 1389, 1284 and 1041; δ_H (300 MHz, $CDCl_3$) 5.73 (1H, dt, J 15.6 and 6.7, H-2'), 5.61 (1H, s, NH), 5.53 (1H, d, J 15.6, H-1'), 4.17 (1H, d, J 8.2, H-5_A), 4.11 (1H, d, J 8.2, H-5_B), 2.07 (2H, q, H-3'), 1.47 (3H, s, Me), 1.45-1.23 (12H, m, $CH_2 \times 6$) and 0.92 (3H, t, J 6.7, H-10'); δ_C (75 MHz, $CDCl_3$) 159.4, 132.2, 132.0, 58.6, 32.5, 32.3, 30.7, 29.8, 29.7, 29.6, 29.4, 25.9, 23.1 and 14.5; m/z (low resolution, ES) 281.1 (100%, $M^+ + CH_4^+CN$) and 257.1 (93%, $M^+ + NH_4^+$). An enantiomeric excess of 95% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak AS (250 $\times$ 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 26 and 36 minutes.

Representative HPLC chromatograms of racemic and enantiopure 12a:

Racemic:

Enantioenriched:

(1'*E*,4*R*)-4-Ethyl-4-dec-1'-enyloxazolidin-2-one 12b

Colourless oil; R_F 0.47 (60 % Et₂O in petrol); $[\alpha]_D^{24}$ -26.84 (c. 0.97 in CHCl₃); (Found: C, 70.85; H, 10.75; N, 5.65; C₁₅H₂₇NO₂ requires: C, 71.10; H, 10.74; N, 5.53%); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3245, 1755, 1462, 1393, 1380 and 1270; δ_H (300 MHz, CDCl₃) 6.01 (1H, s, NH), 5.69 (1H, dt, J 15.6 and 6.9, H-2'), 5.41 (1H, dd, J 15.6 and 1.3, H-1'), 4.16 (1H, d, J 8.7, H-5_A), 4.12 (1H, d, J 8.7, H-5_B), 2.05 (2H, q, J 6.9, H-3'), 1.70 (1H, dq, J 14.6 and 7.4, CH_AH_BCH₃), 1.66 (1H, dq, J 14.6 and 7.4, CH_AH_BCH₃), 1.43–1.20 (12H, m, CH₂ × 6) and 0.90 (6H, m, CH₃ × 2); δ_C (75 MHz, CDCl₃) 159.8, 132.1, 131.3, 75.8, 62.0, 32.6, 32.5, 32.3, 29.8, 29.7, 29.5, 29.5, 23.1, 14.5 and 8.4; m/z (low resolution, ES) 295.2 (35%, M⁺+CH₄⁺CN) and 271.2 (100%, M⁺+NH₄⁺). An enantiomeric excess of 94% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak AS (250 × 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 19 and 29 minutes.

(4*R*,1'*E*)-4-Benzyl-4-dec-1'-enyloxazolidin-2-one 12c

Colourless oil; R_F 0.24 (50 % Et₂O in petrol); $[\alpha]_D^{24}$ -43.8 (c. 0.32 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3255, 1753, 1392 and 1035; δ_H (300 MHz, CDCl₃) 7.35-7.22 (3H, m, Ph), 7.18-7.11 (2H, m, Ph), 5.56 (1H, dt, J 15.9 and 5.6, H-2'), 5.48 (1H, d, J 15.9, H-1'), 5.23 (1H, brs, NH), 4.31 (1H, d, J 8.2, H-5_A), 4.16 (1H, d, J 8.2, H-5_B), 2.97 (1H, d, J 13.3, CH_AH_BPh), 2.91 (1H, d, J 13.3, CH_AH_BPh), 2.03 (2H, q, J 6.7, H-3'), 1.39-1.16 (12H, m, CH₂ × 6) and 0.88 (3H, t, J 6.7, H-10'); δ_C (75 MHz, CDCl₃) 158.5, 134.8, 132.1, 130.4, 130.3, 128.5, 127.3, 75.4, 61.6, 45.5, 32.1, 31.9, 29.4, 29.2, 29.1, 29.0, 22.7 and 14.1; m/z (low resolution, ES) 654.6 (75%, 2M⁺+²³Na+¹³C), 653.6 (100%, 2M⁺+²³Na), 338.3 (89%, M⁺+²³Na) and 316.3 (65%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 316.2282. C₂₀H₃₀NO₂ requires M, 316.2277. An enantiomeric excess of 96% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak AD (250 × 4.6 mm) HPLC column, eluting with 3% IPA in hexane at a rate of 1 ml/min with retention times of 15 and 25 minutes.

(1'*E*,4*R*)-4-Allyl-4-dec-1'-enyloxazolidin-2-one 12d

Colourless oil; R_F 0.23 (50 % Et₂O in petrol); $[\alpha]_D^{24}$ -2.47 (c. 0.85 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3350, 1754, 1478, 1423, 1380, 1346, 1130 and 1000; δ_H (300 MHz, CDCl₃) 5.80-5.65 (3H, m, H-2', CH₂CH=CH₂ and NH), 5.45 (1H, d, J 15.6 and 1.3, H-1'), 5.25-5.15 (2H, m, CH₂CH=CH₂), 4.20 (1H, d, J 8.5, H-5_A), 4.11 (1H, d, J 8.2, H-5_B), 2.42 (2H, m, CH₂CH=CH₂), 2.05 (2H, q, J 6.7, H-3'), 1.43-1.20 (12H, m, CH₂ × 6) and 0.88 (3H, t, J 6.7, H-10'); δ_C (75 MHz, CDCl₃) 159.4, 132.5, 131.7, 131.0, 120.9, 75.4, 61.0, 44.1, 32.6, 32.3, 29.8, 29.7, 29.5, 29.4, 23.1 and 14.5; m/z (low resolution, ES) 307.2 (52%, M⁺+CH₄⁺CN), 304.1 (100%) and 266.2 (57%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 266.2113. C₁₆H₂₈NO₂ requires M, 266.2120. An enantiomeric excess of 93% was

determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak AS (250 × 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 21 and 36 minutes.

(1'*E*,4*S*)-4-Benzoyloxymethyl-4-dec-1'-enyloxazolidin-2-one 12e

Colourless oil; R_F 0.30 (60 % Et₂O in petrol); $[\alpha]_D^{24}$ -45.48 (c. 0.73 in CHCl₃); (Found: C, 72.85; H, 9.0; N, 4.3; C₂₁H₃₁NO₃ requires: C, 73.01; H, 9.04; N, 4.05%); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3270, 1754, 1454, 1097 and 1044; δ_H (300 MHz, CDCl₃) 7.40-7.25 (5H, m, Ph), 5.76 (1H, dt, J 15.9 and 6.7, H-2'), 5.68 (1H, s, NH), 5.48 (1H, d, J 15.9, H-1'), 4.56 (2H, s, CH₂Ph), 4.30 (1H, d, J 8.5, H-5_A), 4.07 (1H, d, J 8.5, H-5_B), 3.45 (2H, s, CH₂OBn), 2.04 (2H, apparent q, J 6.7, H-3'), 1.42-1.18 (12H, m, CH₂ × 6) and 0.88 (3H, t, J 6.4, H-10'); δ_C (75 MHz, CDCl₃) 159.5, 137.8, 133.4, 128.9, 128.4, 128.1, 125.9, 74.4, 74.0, 73.6, 61.5, 32.7, 32.3, 29.8, 29.7, 29.5, 29.3, 23.1 and 14.5; m/z (low resolution, ES) 387.1 (77%, M⁺+CH₄⁺CN), 363.2 (100%, M⁺+NH₄⁺) and 346.1 (17%, M⁺+H). An enantiomeric excess of 93% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OJ (250 × 4.6 mm) HPLC column, eluting with 5% IPA in hexane at a rate of 1 ml/min with retention times of 13 and 21 minutes.

(1'*E*,4*R*)-4-Dec-1'-enyl-4-(2''-hydroxyethyl)oxazolidin-2-one 12f and (1'*E*,4*R*)-4-dec-1'-enyl-4-hydroxymethyl-(1,3)-oxazinan-2-one 12f'

12f, colourless oil; R_F 0.33 (80 % EtOAc in petrol); $[\alpha]_D^{24}$ -28.03 (c. 0.79 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3305, 1748, 1467, 1394, 1276, 1037 and 972; δ_H (300 MHz, CDCl₃) 6.47 (1H, s, NH), 5.68 (1H, dt, J 15.4 and 6.9, H-2'), 5.35 (1H, d, J 15.6, H-1'), 4.12 (1H, d, J 8.2, H-5_A), 4.07 (1H, d, J 8.5, H-5_B), 3.71 (2H, m, H-2''), 2.69 (1H, s, OH), 2.08-1.86 (3H, m, H-3' and H-1''_A), 1.72 (1H, dt, J 14.1 and 4.1, H-1''_B), 1.36-1.12 (12H, m, CH₂ × 6) and 0.81 (3H, t, J 6.9, H-10'); δ_C (75 MHz, CDCl₃) 160.0, 132.4, 130.6, 76.7, 61.4, 59.1, 41.0, 32.6, 32.3, 29.8, 29.7, 29.6, 29.5, 23.1 and 14.5; m/z (low resolution, ES) 270.2 (90%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 270.2067. C₁₅H₂₈NO₃ requires M, 270.2069. An enantiomeric excess of 95% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OD-H (250 × 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 10 and 14 minutes.

12f', colourless oil; R_F 0.12 (80 % EtOAc in petrol); $[\alpha]_D^{24}$ +20.03 (c. 0.28 in CHCl₃); (Found: C, 66.7; H, 10.25; N, 5.0; C₁₅H₂₇NO₃ requires: C, 66.88; H, 10.10; N, 5.20%); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3271, 1698, 1478, 1427, 1315, 1112 and 1079; δ_H (300 MHz, CDCl₃) 6.78 (1H, s, NH), 5.70 (1H, dt, J 15.4 and 6.7, H-2'), 5.22 (1H, d, J 15.4, H-1'), 4.14 (2H, m, H-6), 3.52 (1H, d, J 11.5, CH_AH_BOH), 3.40 (1H, d, J 11.5, CH_AH_BOH), 2.60 (1H, brs, OH), 2.02 (3H, m, H-3' and H-5_A), 1.55 (1H, brd, J 13.8, H-5_B), 1.36-1.13 (12H, m, CH₂ × 6) and 0.81 (3H, t, J 6.7, H-10'); δ_C (75 MHz, CDCl₃) 155.7, 135.3, 130.8, 68.9, 63.7, 59.9, 32.7, 32.3, 29.8, 29.7, 29.6, 29.6, 28.5, 23.1 and 14.5; m/z (low resolution, ES) 561.1 (20%, 2M⁺+²³Na), 539.2 (100%, 2M⁺+H), 311.0 (52%, M⁺+CH₄⁺CN) and 270.0 (60%, M⁺+H).

An enantiomeric excess of 95% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OD-H (250 × 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 9 and 18 minutes.

(4*R*,1'*E*)-4-Methyl-4-styryloxazolidin-2-one 12g

Colourless solid, mp 76.7-77.5 °C; R_F 0.27 (80 % Et₂O in petrol); $[\alpha]_D^{24}$ -24.87 (c. 1.34 in CHCl₃); (Found: C, 71.0; H, 6.65; N, 6.7; C₁₂H₁₃NO₂ requires: C, 70.92; H, 6.45; N, 6.89%); ν_{max} / cm⁻¹ (CHCl₃ solution) 3271, 1748, 1391, 1288, 1038 and 969; δ_H (300 MHz, CDCl₃) 7.40-7.23 (5H, m, Ph), 6.61 (1H, d, J 16.1, PhCHCH), 6.27 (1H, s, NH), 6.22 (1H, d, J 16.1, PhCHCH), 4.25 (1H, d, J 8.4, H-5_A), 4.17 (1H, d, J 8.4, H-5_B) and 1.58 (3H, s, Me); δ_C (75 MHz, CDCl₃) 159.6, 136.1, 131.6, 130.4, 129.1, 128.7, 127.1, 76.9, 59.0 and 26.0; m/z (low resolution, ES) 244.9 (100%, M⁺+CH₄⁺CN). An enantiomeric excess of 93% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OJ (250 × 4.6 mm) HPLC column, eluting with 5% IPA in hexane at a rate of 1 ml/min with retention times of 51 and 81 minutes.

(4*S*,1'*E*)-4-Benzoyloxymethyl-4-styryloxazolidin-2-one 12h

Colourless oil; R_F 0.39 (80 % Et₂O in petrol); $[\alpha]_D^{23}$ -58.24 (c. 1.48 in CHCl₃); (Found: C, 73.5; H, 6.4; N, 4.65; C₁₉H₁₉NO₃ requires: C, 73.77; H, 6.19; N, 4.53%); ν_{max} / cm⁻¹ (CHCl₃ solution) 3271, 1750, 1496, 1452, 1391, 1096 and 1043; δ_H (300 MHz, CDCl₃) 7.40-7.22 (10H, m, Ph), 6.68 (1H, d, J 16.1, PhCHCH), 6.27 (1H, s, NH), 6.21 (1H, d, J 16.1, PhCHCH), 4.57 (2H, s, CH₂Ph), 4.40 (1H, d, J 8.5, H-5_A), 4.17 (1H, d, J 8.5, H-5_B) and 3.56 (2H, s, CH₂OBn); δ_C (75 MHz, CDCl₃) 159.7, 137.7, 136.1, 131.7, 129.1, 129.0, 128.7, 128.5, 128.3, 128.2, 127.1, 74.3, 74.0, 73.5 and 62.0; m/z (low resolution, ES) 350.9 (100%, M⁺+CH₄⁺CN), 326.9 (42%, M⁺+NH₄⁺) and 309.9 (22%, M⁺+H). An enantiomeric excess of 95% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OJ (250 × 4.6 mm) HPLC column, eluting with 20% IPA in hexane at a rate of 1 ml/min with retention times of 53 and 68 minutes.

(4*R*,1'*E*)-4-Methyl-4-(3'-phenylpropenyl)oxazolidin-2-one 12i

Colourless oil; R_F 0.42 (80 % Et₂O in petrol); $[\alpha]_D^{24}$ -20.74 (c. 0.68 in CHCl₃); (Found: C, 71.6; H, 7.2; N, 6.7; C₁₃H₁₅NO₂ requires: C, 71.87; H, 6.96; N, 6.45%); ν_{max} / cm⁻¹ (CHCl₃ solution) 3270, 1749, 1495, 1476, 1453, 1391, 1287 and 1038; δ_H (300 MHz, CDCl₃) 7.35-7.10 (5H, m, Ph), 6.34 (1H, s, NH), 5.86 (1H, dt, J 15.6 and 6.7, H-2'), 5.56 (1H, d, J 15.6, H-1'), 4.14 (1H, d, J 8.5, H-5_A), 4.08 (1H, d, J 8.2, H-5_B), 3.38 (2H, d, J 6.7, H-3') and 1.44 (3H, s, Me); δ_C (75 MHz, CDCl₃) 159.7, 139.7, 133.8, 130.4, 129.0, 129.0, 126.8, 76.9, 58.7, 38.8 and 25.9; m/z (low resolution, ES) 258.9 (100%, M⁺+CH₄⁺CN), 234.9 (38%, M⁺+NH₄⁺) and 217.9 (5%, M⁺+H). An enantiomeric excess

of 95% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak OJ (250 × 4.6 mm) HPLC column, eluting with 10% IPA in hexane at a rate of 1 ml/min with retention times of 19 and 43 minutes.

(4*S*,1'*E*)-4-Benzoyloxymethyl-4-(3'-phenylpropenyl)oxazolidin-2-one 12j

Colourless oil; R_F 0.48 (80 % Et₂O in petrol); $[\alpha]_D^{24}$ -60.39 (c. 0.52 in CHCl₃); $\nu_{\max}$ / cm⁻¹ (CHCl₃ solution) 3270, 1748, 1495, 1472, 1453, 1393, 1266 and 1044; δ_H (300 MHz, CDCl₃) 7.38-7.10 (10H, m, Ph), 6.07 (1H, s, NH), 5.92 (1H, dt, J 15.6 and 6.7, H-2'), 5.53 (1H, dt, J 15.6 and 1.3, H-1'), 4.53 (2H, s, OCH₂Ph), 4.30 (1H, d, J 8.4, H-5_A), 4.07 (1H, d, J 8.4, H-5_B), 3.45 (2H, s, CH₂OBn), 3.38 (2H, d, J 6.7, H-3'); δ_C (75 MHz, CDCl₃) 159.6, 139.6, 137.8, 131.8, 130.5, 129.0, 129.0, 129.0, 128.4, 128.1, 126.8, 74.3, 74.0, 73.4, 61.6 and 38.9; m/z (low resolution, ES) 364.7 (74%, M⁺+CH₄⁺CN), 345.7 (38%, M⁺+²³Na) and 323.8 (100%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 324.1605. C₂₀H₂₂NO₃ requires M, 324.1600. An enantiomeric excess of 92% was determined by chiral HPLC using a Daicel Chemical Industries Ltd. Chiralpak AS (250 × 4.6 mm) HPLC column, eluting with 20% IPA in hexane at a rate of 1 ml/min with retention times of 95 and 106 minutes.

(2*R*,3*E*)-2-Amino-2-methyldodec-3-enoic acid 13

Water (8.1 μl, 0.45 mmol) was added to a stirred suspension of α,α -disubstituted amino acid **4a** (89 mg, 0.15 mmol) and potassium *tert*-butoxide (173 mg, 1.55 mmol) in 1,4-dioxane (2 ml) under nitrogen at room temperature. The reaction mixture was refluxed for 17 hours. The reaction mixture was cooled to room temperature, quenched with water (2 ml) and the solution was neutralised with Amberlite IRC-50 (H⁺ form). The solution was filtered and the resin washed with methanol (10 ml). The filtrate was evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, eluting with 95:5 chloroform-methanol, to give (-)-8-phenylmenthol (29 mg, 82 %) as a colourless oil and then 10:3:1 chloroform-methanol-water (the lower phase of this mixture was used), to give amino acid **13** (30 mg, 88%) as a colourless powder, mp 216.3-218.9 °C; R_F 0.30 (10:3:1 CHCl₃-MeOH-H₂O {lower phase}); $[\alpha]_D^{24}$ -1.17 (c. 0.98 in MeOH); $\nu_{\max}$ / cm⁻¹ (diamond transition cell) 3308-2108, 1655, 1611, 1496, 1455, 1389 and 1358; δ_H (300 MHz, CD₃OD) 5.72 (1H, dt, J 15.9 and 6.4, H-4), 5.60 (1H, d, J 15.9, H-3), 2.00 (2H, dt, J 6.9 and 6.7, H-5), 1.45 (3H, s, Me), 1.40-1.13 (12H, m, CH₂ × 6) and 0.81 (3H, t, J 6.9, H-12); δ_C (75 MHz, CD₃OD) 175.9, 133.6, 130.7, 62.8, 33.9, 33.4, 30.9, 30.7, 30.6, 30.4, 24.1, 23.6 and 14.8; m/z (low resolution, ES) 269.1 (100%, M⁺+CH₄⁺CN) and 228.1 (100%, M⁺+H); m/z (accurate mass, ES) Found: M⁺+H, 228.1955. C₁₃H₂₆NO₂ requires M, 228.1964.

Details of X-ray crystallographic assignment of stereochemistry in alkylation reactions

As part of a subsequent application to natural product synthesis, the following alkylation was undertaken, and the crystalline derivative **14** then obtained. Full details of the synthesis of **14** along with the X-ray crystal data will be disclosed in a future publication.