Deconjugation of Dehydroamino Acids: Stereoselective Synthesis of (*E*)-Vinylglycines

Paul A. Alexander, Stephen P. Marsden,* Dulce M. Muñoz Subtil
and John C. Reader

School of Chemistry, University of Leeds, Leeds LS2 9JT, U.K

s.p.marsden@leeds.ac.uk

Supporting information and spectra

(Z)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-2-enoate (6a)

mp 40 °C (EtOAc/Petrol); R_F 0.30 (1:1 Petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3346 (w), 3030 (w), 2953 (w), 1722 (s), 1496 (m), 1454 (m), 1435 (m), 1206 (m), 698 (m); δ_H (500 MHz, CDCl₃) 7.36-7.26 (7H, m), 7.21-7.17 (3H, m), 6.66 (1H, t, J = 7.3 Hz), 6.08 (1H, br s), 5.13 (2H, s), 3.74 (3H, s), 2.78 (2H, t, J = 7.7 Hz), 2.53 (2H, dt, J = 7.3, 7.7 Hz); δ_C 165.0, 154.1, 140.9, 136.7, 136.0, 128.5, 128.4, 128.3, 128.2, 128.1, 126.1, 125.6, 67.3, 52.4, 34.2, 30.2; LRMS (ES⁺): m/z = 362 (100 [M+Na]⁺); anal. calc. for C₂₀H₂₁NO₄: C, 70.8; H, 6.24; N, 4.13; found: C, 71.0; H, 6.10; N 4.25%.

(Z)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-2-enoate (6a, Boc-protected)

mp 48 °C (EtOAc/petrol); R_F 0.2 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film): 3335 (w), 2978 (w), 1707 (s), 1657 (w), 1496 (m), 1366 (m), 1269 (m), 1245 (m), 1163 (s), 1048 (m), 700 (w); δ_H (500 MHz, CDCl₃): 7.30-7.25 (2H, m), 7.21-7.19 (3H, m), 6.58 (1H, t, J = 7.7 Hz), 5.86 (1H, br s), 3.76 (3H, s), 2.78 (2H, t, J = 7.7 Hz), 2.52 (2H, q, J = 7.7 Hz), 1.46 (9H, s); δ_C (75 MHz, CDCl₃): 165.3, 153.2, 141.1, 135.5, 128.5, 128.4, 126.1, 126.0, 80.5, 52.3, 34.3, 30.2, 28.2; LRMS (ES⁺): m/z = 306 (80[M+H]⁺), 250 (100[M-^tBu+H]⁺); anal. calc. for C₁₇H₂₃NO₄: C, 66.9; H, 7.59; N, 4.59; found: C, 66.9; H, 7.75; N, 4.60%.

(Z)-Methyl 2-benzyloxycarbonylamino-5-(1-methoxyphen-4-yl)-pent-2-enoate (6b)

mp 53-54 °C (EtOAc/petrol); R_F 0.25 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3319 (w), 2951 (w), 1721 (s), 1657 (w), 1512 (s), 1272 (m), 1246 (s), 1047 (m), 751 (w), 698 (w); δ_H (500

MHz, CDCl₃): 7.36-7.32 (5H, m), 7.07 (2H, d, *J* = 8.5 Hz), 6.81 (2H, d, *J* = 8.5 Hz), 6.65 (1H, t, *J* = 7.3 Hz), 6.10 (1H, br s), 5.13 (2H, s), 3.79 (3H, s), 3.74 (3H, s), 2.72 (2H, t, *J* = 7.7 Hz), 2.50 (2H, dt, *J* = 7.3, 7.7); δ_C (75 MHz CDCl₃): 165.0, 158.0, 154.0, 136.9, 136.0, 133.0, 129.3, 128.6, 128.3, 128.2, 125.5, 113.9, 67.4, 55.3, 52.4, 33.3, 30.5; LRMS (ES⁺): *m/z* = 392 (100 [M+Na]⁺); anal. calc. for C₂₁H₂₃NO₅: C, 68.3; H, 6.28; N, 3.79; found: C, 68.1; H, 6.25; N, 3.65%.

(Z)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-2-enoate (6c)

*R*_F 0.37 (1:1 Et₂O-Petrol); ν_{max}/cm⁻¹ (film) 3320 (s), 2951 (s), 1723 (s), 1660 (s), 1501 (s), 1437 (s), 1279 (s), 1223 (s), 1053 (s), 960 (m), 780 (s), 698 (s); δ_H (500 MHz, CDCl₃): 7.37 – 7.33 (5H, m), 6.63 (1H, t, *J* = 7.3 Hz), 6.15 (1H, br s), 5.86 (1H, d, *J* = 2.6 Hz), 5.84 (1H, d, *J* = 2.6 Hz), 5.14 (2H, s), 3.74 (3H, s), 2.73 (2H, t, *J* = 7.3 Hz), 2.54 (2H, apparent q, *J* = 7.3 Hz), 2.24 (3 H, s); δ_C (75 MHz, CDCl₃): 164.9, 154.0, 152.7, 150.7, 136.2, 135.9, 128.6, 128.3, 128.2, 125.9, 106.2, 106.0, 67.4, 52.4, 27.1, 26.6, 13.5; LRMS (ES⁺): *m/z* = 366 (100 [M+Na]⁺), 344 (95 [M+H]⁺), 300(90) 283(90); HRMS (ES⁺): found M+H⁺, 344.1508; C₁₉H₂₂NO₅⁺ requires 344.1498.

(Z)-Methyl 2-benzyloxycarbonylamino-dodec-2-enoate (6d)

mp 39-40 °C (petrol/EtOAc); *R*_F 0.34 (2:1 petrol-Et₂O); ν_{max}/cm⁻¹ (film) 3317 (w), 2925 (m), 1715 (s), 1501 (m), 1225 (m), 1047 (m); δ_H (500 MHz, CDCl₃): 7.37–7.31 (5H, m), 6.65 (1H, t, *J* = 7.3 Hz), 6.16 (1H, br s), 5.15 (2H, s), 3.75 (3H, s), 2.20 (2H, apparent quartet, *J* = 7.3 Hz), 1.45-1.42 (2H, m), 1.30 – 1.26 (12 H, m), 0.88 (3H, t, *J* = 6.5 Hz); δ_C (75 MHz, CDCl₃): 165.6, 154.6, 139.1, 136.4, 129.0, 128.7, 128.6, 125.5, 67.8, 52.8, 32.3, 29.9, 2 CH₂ signals overlap at 29.8, 29.7, 28.9, 28.7, 23.1, 14.5; LRMS (ES⁺): *m/z* = 384 (80[M+Na]⁺), 362 (90[M+H]⁺) 318 (100[M-43]⁺); anal. calc. for C₂₁H₃₁NO₄: C, 69.8; H, 8.64; N, 3.87; found: C, 69.7; H, 8.75; N, 4.10%.

(Z)-Methyl 2-benzyloxycarbonylamino-4-(N-Boc-piperidin-4-yl)-but-2-enoate (6e)

mp 115-116°C (EtOAc/petrol); R_F 0.1 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3293 (w), 2976 (w), 1725 (s), 1670 (s), 1500 (m), 1434 (m), 1246 (s), 1167 (m), 1050 (m), 772 (w), 698 (w); δ_H (500 MHz, CDCl₃): 7.37-7.32 (5H, m), 6.65 (1H, t, $J = 7.3$ Hz), 6.18 (1H, br s), 5.14 (2H, s), 4.06 (2H, d, $J = 11.5$ Hz), 3.76 (3H, s), 2.66 (2H, t, $J = 12.6$ Hz), 2.16 (2H, t, $J = 7.3$ Hz), 1.64 (2H, br d, $J = 12.8$ Hz), 1.57 (1H, m), 1.45 (9H, s), 1.12 (2H, m); δ_C (75 MHz, CDCl₃): 164.9, 154.8, 154.0, 135.9, 135.8, 128.6, 128.3, 128.2, 126.2, 79.3, 67.4, 52.5, 43.7, 35.6, 35.0, 31.9, 28.5; LRMS (ES⁺): $m/z = 455$ (30[M+Na]⁺), 377 (70[M-^tBu+2H]⁺), 333 (100 [M-Boc+2H]⁺); anal. calc. for C₂₃H₃₂N₂O₆: C, 63.9; H, 7.46; N, 6.5; found: C, 63.8; H, 7.35; N, 6.4%.

(Z)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-2-enoate (6f)

mp 74-75°C (from EtOAc/petrol); R_F 0.34 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3317 (w), 3030 (w), 1715 (s), 1497 (m), 1454 (w), 1299 (m), 1259 (s), 1229 (s), 1046 (m), 698 (m); δ_H (500MHz, CDCl₃): 7.34-7.17 (10H, m), 6.78 (1H, t, $J = 7.3$ Hz), 6.34 (1H, br s), 5.17 (2H, s), 3.75 (3H, s), 3.56 (2H, d, $J = 7.3$ Hz); δ_C (75 MHz, CDCl₃): 165.0, 154.1, 138.6, 135.9, 128.7, 128.6, 128.6, 128.3, 128.2, 126.6, 125.3, 67.5, 52.5, 34.8, one C not visible; LRMS (ES⁺): $m/z = 348$ (100 [M + Na]⁺); anal. calc. for C₁₉H₁₉NO₄: C, 70.1; H, 5.89; N, 4.31; found: C, 70.0; H, 5.95; N, 4.25%.

(Z)-Methyl 2-benzyloxycarbonylaminohept-2,6-dienoate (6g)

R_F 0.35 (1:1 Petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film): 3319 (w), 2952 (w), 1717 (s), 1659 (w), 1504 (m), 1277 (m), 1227 (m), 1050 (m), 698 (w); δ_H (500 MHz, CDCl₃) 7.35-7.30 (5H, m), 6.62 (1H, t, $J = 7.3$ Hz), 6.45 (1H, br s), 5.78 (1H, ddt, $J = 17.1, 10.3, 6.5$ Hz), 5.13 (2H, s), 5.03 (1H, d, $J = 17.1$ Hz), 4.99 (1H, d, $J = 10.3$ Hz), 3.72 (3H, s), 2.30 (2H, apparent q, $J = 7.3$ Hz), 2.21 (2H, dt, $J = 7.3, 6.5$ Hz); δ_C (75 MHz CDCl₃) 165.1, 154.2, 137.2, 136.0, 128.5, 128.2, 128.1, 125.6, 115.6, 67.3, 52.3, 32.1, 27.6; LRMS (ES⁺): $m/z = 312$ (80[M + Na]⁺), 290 (100[M+H]⁺); HRMS (ES⁺): found M+H⁺, 290.1394. C₁₆H₂₀NO₄ requires 290.1392.

(2Z,4E)-Methyl 2-benzyloxycarbonylaminohept-2,4-dienoate (6h)

mp 71-72 °C (EtOAc/petrol); R_F 0.40 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3311 (w), 2952 (m), 1714 (s), 1500 (s), 1436 (s), 1307 (s), 1243 (s), 1050 (m), 973 (m), 698 (m); δ_H (500 MHz, CDCl₃): 7.36-7.31 (5H, m), 7.03 (1H, d, $J = 11.2$ Hz), 6.29 (1H, ddq, $J = 15.0, 11.2, 1.3$ Hz), 6.20 (1H, br s, partly obscured by signal at 6.14), 6.14 (1H, dq, $J = 15.0, 6.8$ Hz), 5.15 (2H, s), 3.74 (3H, s), 1.86 (3H, d, $J = 6.8$ Hz); δ_C (75 MHz CDCl₃): 165.6, 154.3, 139.7, 136.0, 133.8, 128.5, 128.3, 126.5, 121.3, 67.4, 52.4, 19.1; LRMS (ES⁺): $m/z = 276$ (100[M+H]⁺); anal. calc. for C₁₅H₁₇NO₄: C, 65.4; H, 6.22; N 5.09; found: C, 65.3; H, 6.35; N, 4.95%.

(Z)-Methyl 2-benzyloxycarbonylamino-4-methylpent-2-enoate (6i)

mp 68 °C (EtOAc/Petrol), (lit.¹ 66-67 °C); R_F 0.32 (1:1 Petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3320 (w), 2953 (w), 1721 (s), 1661 (w), 1502 (m), 1438 (w), 1279 (m), 1231 (m), 1050 (m), 698 (w); the product was identical by ¹H NMR and ¹³C NMR spectroscopy with the data reported;¹ δ_H (500 MHz, CDCl₃): 7.35-7.32 (5H, m), 6.75 (1H, q, J = 7.3 Hz), 6.17 (1H, br s), 5.15 (2H, s), 3.76 (3H, s), 1.82 (3H, d, J = 7.3 Hz); δ_C (75 MHz, CDCl₃): 165.5, 154.4, 136.4, 133.8, 129.0, 128.7, 128.6, 126.8, 67.8, 52.8, 14.7.

(Z)-Methyl 2-benzyloxycarbonylamino-4-methylpent-2-enoate (6j)

mp 60-62 °C (EtOAc/petrol) (lit.² mp 60-63 °C); R_F 0.31 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3316 (m), 2961 (m), 1719 (s), 1657 (m), 1500 (m), 1315 (m), 1264 (s), 1229 (s), 1049 (m); the product was identical by ¹H NMR spectroscopy with the data reported.³ (500 MHz, CDCl₃): 7.37-7.32 (5H, m), 6.47 (1H, d, J = 10.3 Hz), 6.03 (1H, br s), 5.15 (2H, s), 3.75 (3H, s), 2.71 (1H, m), 1.04 (6H, d, J = 6.4 Hz); δ_C (75 MHz, CDCl₃): 165.8, 154.9, 145.6, 136.4, 128.9, 128.7, 128.6, 123.7, 67.8, 52.8, 28.1, 22.0 ; LRMS (ES⁺): m/z = 300 (100[M+Na]⁺).

(Z)-Methyl 2-benzyloxycarbonylamino-4-ethylhex-2-enoate (6k)

¹ Sai, H.; Ogiku, T.; Ohmizu, H. *Synthesis*, **2003**, 201.

² Shin, C.; Takahashi, N.; Yonezawa, Y. *Chem. Pharm. Bull.*, **1990**, 2020.

³ Schmidt, U.; Griesser, H.; Leitenberger, V.; Lieberknecht, A.; Mangold, R.; Meyer, R.; Riedl, B. *Synthesis* **1992**, 487.

R_F 0.31 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3319 (m), 2961 (m), 2931 (m), 1715 (s), 1657 (m), 1499 (s), 1455 (s), 1326 (s), 1286 (s), 1227 (s), 1050 (m), 775 (m), 698 (m); δ_H (500 MHz, CDCl₃): 7.37-7.32 (5H, m), 6.43 (1H, d, J = 10.7 Hz), 5.90 (1H, br s), 5.15 (2H, s), 3.75 (3H, s), 2.32 (1H, m), 1.50 (2H, m), 1.33 (2H, m), 0.76 (6 H, t, J = 7.7 Hz); δ_C (75 MHz, CDCl₃) 165.6, 155.1, 144.1, 136.5, 128.9, 128.6, 128.5, 126.5, 67.7, 52.7, 41.7, 27.3, 12.1; LRMS (ES⁺): m/z = 633 (60[2M + Na]⁺), 328 (60[M+Na]⁺), 306 (95[M+H]⁺), 262 (100[M-43]); HRMS (ES⁺): found M+H⁺, 306.1710, C₁₇H₂₄NO₄⁺ requires 306.1705.

Standard procedure for deconjugation of dehydroamino acids

6.0 equivalents of LiCl were flame dried in a flask under vacuum and allowed to cool to room temperature. An atmosphere of nitrogen was then introduced. THF (2 ml) and 3.1 equivalents (relative to the dehydroamino acid) of TMP were then added. The solution was cooled to -78°C and *n*BuLi (3.0 equivalents) were added. The mixture was warmed to 0°C and stirred for 15 minutes before cooling to -78°C again. The dehydroamino acid to be deconjugated (typically about 100 mg) was dissolved in THF (5 ml) and added to the solution of base *via* cannula, and then washed in with a further 2ml of THF. The reaction was stirred at -78°C for 20 minutes before being quenched with NH₄Cl_(aq) (5 ml). The reaction was then worked up immediately by addition of NH₄Cl_(aq) (5 ml) and extraction with EtOAc (3 x 15 ml). The combined organic extracts were then dried (MgSO₄), filtered and concentrated under reduced pressure before purification by flash chromatography, typically eluting with a gradient mixture of 4:1 to 1:1 petrol-Et₂O.

(E)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-3-enoate (8a)

R_F 0.32 (1:1 Petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ 3342 (w), 3029 (w), 1723 (s), 1517 (s), 1453 (m), 1214 (s), 1060 (m), 698 (m); δ_H (500 MHz, CDCl₃) 7.35-7.25 (7H, m), 7.21 (1H, d, J = 7.3 Hz), 7.14 (2H, d, J = 7.7 Hz), 5.94 (1H, dt, J = 15.4, 6.4), 5.55 (1H, dd, J = 15.4, 6.0 Hz), 5.39 (1H, d, J = 7.3 Hz), 5.12 (1H, d, J = 12.3 Hz), 5.09 (1H, d, J = 12.3 Hz), 4.91 (1H, apparent t, J = 6.0 Hz), 3.76 (3H, s), 3.39 (2H, d, J = 6.8); a ¹H NMR spectrum was also

run at 57°C to produce sharper signals, δ_{H} (500 MHz, CDCl_3 , 57°C): 7.34-7.26 (7H, m), 7.20 (1H, tt, $J = 7.5, 1.9$ Hz), 7.13 (2H, dd, $J = 7.5, 0.7$ Hz), 5.96 (1H, dtd, $J = 15.4, 6.8, 1.5$ Hz), 5.56 (1H, ddt, $J = 15.4, 6.2, 1.5$ Hz), 5.31 (1H, broad s), 5.14 (1H, d, $J = 12.3$ Hz), 5.11 (1H, d, $J = 12.3$ Hz), 4.89 (1H, br t, $J = 6.7$ Hz), 3.75 (3H, s), 3.39 (2H, d, $J = 6.6$ Hz); δ_{C} (75 MHz, CDCl_3) 171.3, 155.5, 139.2, 136.2, 133.3, 128.6, 128.5, 128.2, 128.1, 126.3, 125.4, 67.0, 55.5, 52.7, 38.4 (one aromatic/alkene signal not visible); LRMS (ES+): $m/z = 362$ (70[M+Na]⁺), 340 (40[M+H]⁺), 296 (100[M-43]⁺); anal. calc. for $\text{C}_{20}\text{H}_{21}\text{NO}_4$: C, 70.8; H, 6.24; N, 4.13; found: C, 70.5; H, 6.30; N, 4.10%.

(E)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-3-enoate (8a, Boc protected)

R_{F} 0.48 (1:1 petrol-Et₂O); $\nu_{\text{max}}/\text{cm}^{-1}$ 3365 (m), 2978 (m), 1747 (s), 1716 (s), 1496 (s), 1367 (s), 1165 (s), 1059 (m), 972 (m), 699 (m); δ_{H} (500 MHz, CDCl_3) 7.28 (2H, apparent t, $J = 7.3$ Hz), 7.20 (1H, apparent t, $J = 7.3$ Hz), 7.15 (2H, d, $J = 7.7$ Hz), 5.93 (1H, dt, $J = 15.0, 6.8$ Hz), 5.55 (1H, dd, $J = 15.0, 5.1$ Hz), 5.13 (1H, br s), 4.84 (1H, m), 3.76 (3H, s), 3.39 (2H, d, $J = 6.8$ Hz), 1.43 (9H, s); δ_{C} (75 MHz CDCl_3): 171.7, 154.9, 139.3, 132.9, 128.6, 128.4, 126.3, 125.8, 80.1, 55.2, 52.6, 38.4, 28.3; LRMS (ES+): $m/z = 328$ (100[M+Na]⁺), 272 (70[M-33]⁺), 247 (40[M-58]⁺), 206 (90[M-99]⁺), 189 (95[M-116]⁺); HRMS (ES+) found M+Na⁺, 328.1521; $\text{C}_{17}\text{H}_{23}\text{NO}_4\text{Na}^+$ requires 328.1525.

(E)-Methyl 2-benzyloxycarbonylamino-5-(1-methoxyphen-4-yl)-pent-3-enoate (8b)

R_{F} 0.25 (1:1 petrol-Et₂O); $\nu_{\text{max}}/\text{cm}^{-1}$ 3346 (m), 2953 (m), 1724 (s), 1512 (s), 1245 (s), 1177 (s), 1036 (s), 972 (m), 739 (w), 698 (w); δ_{H} (500 MHz, CDCl_3): 7.35-7.30 (5H, m), 7.04 (2H, d, $J = 8.6$ Hz), 6.82 (2H, d, $J = 8.6$ Hz), 5.92 (1H, dt, $J = 15.4, 6.4$ Hz), 5.51 (1H, dd, $J = 15.4, 6.0$ Hz), 5.40 (1H, d, $J = 6.9$ Hz), 5.12 (1H, d, $J = 12.4$ Hz), 5.09 (1H, d, $J = 12.4$ Hz), 4.90 (1H, br t, $J = 6.0$ Hz), 3.78 (3H, s), 3.75 (3H, s), 3.32 (2H, d, $J = 6.4$ Hz); δ_{C} (75 MHz, CDCl_3): 171.4, 158.1, 155.5, 136.1, 133.8, 131.2, 129.5, 128.5, 128.2,

128.1, 125.1, 113.9, 67.1, 55.5, 55.3, 52.7, 37.5; LRMS (ES⁺): m/z = 392 (85[M+Na]⁺), 370 (55[M+H]⁺), 326 (200[M-43]⁺), 309 (70[M-60]⁺); HRMS (ES⁺): found M+Na⁺, 392.1474; C₂₁H₂₃NO₅Na⁺ requires 392.1474.

(E)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-3-enoate (8c)

R_F = 0.2 (1:1 Petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film): 3325 (w), 2955 (w), 1713 (s), 1514 (m), 1217 (s), 1058 (m), 699 (w); δ_H (500 MHz, CDCl₃): 7.33-7.30 (5H, m), 5.90 (1H, dt, J = 15.4, 6.4 Hz), 5.85 (2H, br s), 5.60 (1H, dd, J = 15.4, 5.6 Hz), 5.41 (1H, d, J = 6.8), 5.13 (1H, d, J = 12.5 Hz), 5.11 (1H, d, J = 12.5 Hz), 4.92 (1H, m), 3.76 (3H, s), 3.34 (2H, d, J = 6.4), 2.24 (3H, s); δ_C (75 MHz, CDCl₃): 171.2, 155.5, 151.0, 150.9, 136.2, 130.3, 128.5, 128.2, 128.1, 126.1, 106.5, 106.0, 67.1, 55.5, 52.7, 31.0, 13.5; LRMS (ES⁺): m/z = 366 (80[M+Na]⁺), 344 (100[M+H]⁺), 300 (65[M-43]⁺); HRMS (ES⁺): found M+H⁺, 344.1490; C₁₉H₂₂NO₅⁺ requires 344.1498.

(E)-Methyl 2-benzyloxycarbonylamino-dodec-3-enoate (8d)

R_F 0.45 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3342 (m), 3033 (m), 2954 (s), 2926 (s), 2854 (s), 1727 (s), 1515 (s), 1330 (m), 1214 (s), 1050 (m), 970 (m), 697 (m); δ_H (500 MHz, CDCl₃): 7.36-7.32 (5H, m), 5.77 (1H, dt, J = 15.0, 6.9 Hz), 5.45 (1H, dd, J = 15.0, 6.0 Hz), 5.36 (1H, d, J = 7.3 Hz), 5.13 (1H, d, J = 13.0 Hz), 5.10 (1H, d, J = 13.0 Hz), 4.84 (1H, broad t, J = 6.5 Hz), 3.75 (3H, s), 2.01 (2H, q, J = 6.9 Hz), 1.35-1.25 (12H, m), 0.88 (3H, t, J = 6.9 Hz); δ_C (75 MHz, CDCl₃): 172.0, 155.9, 136.2, 135.8, 128.9, 128.6, 128.5, 124.1, 67.5, 56.1, 53.0, 32.6, 32.3, 29.8, 29.7, 29.5, 29.2, 23.1, 14.5; LRMS (ES⁺): m/z = 745 (13[2M + Na]⁺), 425 (62), 384 (93[M+Na]⁺), 362 (20[M+H]⁺), 318 (100); anal. calc. for C₂₁H₃₁NO₄: C, 69.8; H, 8.64; N, 3.87; found: C, 69.5; H, 8.70; N, 3.85%.

(E)-Methyl 2-benzyloxycarbonylamino-4-[4-*N*-(*tert*-butoxycarbonyl)-piperidin-4-yl]-but-3-enoate (8e)

R_F 0.1 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ 3317 (w), 2933 (w), 2852 (w), 1724 (s), 1691 (s), 1572 (m), 1428 (m), 1232 (m), 1170 (m), 1054 (w), 970 (w), 698 (w); δ_H (500 MHz, CDCl₃): 7.36-7.32 (5H, m), 5.71 (1H, dd, J = 15.4, 6.0 Hz), 5.47 (1H, dd, J = 15.4, 5.6 Hz), 5.37 (1H, d, J = 7.7 Hz), 5.12 (2H, s), 4.87 (1H, m), 4.07 (2H, br s), 3.76 (3H, s), 2.71 (2H, t, J = 11.5), 2.12 (1H, m), 1.64 (2H, d, J = 11.5 Hz), 1.45 (9H, s), 1.24 (2H, m); δ_C (75 MHz, CDCl₃): 171.8, 155.9, 155.2, 138.6, 136.6, 128.9, 128.7, 128.6, 123.3, 79.8, 67.5, 56.0, 53.1, 43.9, 38.9, 31.7, 28.9; LRMS (ES⁺): m/z = 455 (95[M+Na]⁺), 333 (100[M-Boc+2H]⁺); HRMS (ES⁺): found M+Na⁺, 455.2155; C₂₃H₃₂N₂O₆Na⁺ requires 455.2158.

(E)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-3-enoate (8f)

6:1 mixture of **8f**/**6f**. R_F 0.34 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ 3334 (w), 3030 (w), 2953 (w), 1722 (s), 1515 (m), 1222 (m), 1053 (m), 967 (m), 738 (m), 696 (m); δ_H (signals for **8f**, 500 MHz, CDCl₃): 7.35-7.66 (10H, m), 6.65 (1H, d, J = 15.8 Hz), 6.18 (1H, dd, J = 15.8, 6.4 Hz), 5.64 (1H, br d, J = 7.3 Hz), 5.13 (2H, s), 5.08 (1H, apparent t, J = 6.4 Hz), 3.76 (3H, s); δ_C (75 MHz, CDCl₃): 171.0, 155.5, 136.1, 135.7, 133.2, 128.6, 128.6, 128.5, 128.2, 128.1, 126.7, 123.4, 67.2, 55.9, 52.8; The signals visible for **6f** were the same as reported earlier; LRMS (ES⁺): m/z = 343 (45[M+NH₄]⁺), 326 (100[M+H]⁺); HRMS (ES⁺): found M+H⁺, 326.1386; C₁₉H₂₀NO₄⁺ requires 326.1392.

(E)-Methyl 2-benzylloxycarbonylaminohept-3-6-dienoate (8g)

R_F 0.61 (1:2 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3341 (s), 3034 (s), 2954 (s), 2898 (s), 2846 (m), 1724 (s), 1638 (s), 1520 (s), 1454 (s), 1435 (s), 1376 (m), 1330 (s), 1211 (s), 1054 (s), 997 (s), 973 (s), 917 (s), 814 (w), 777 (m), 741 (m), 698 (m); δ_H (500 MHz, CDCl₃): 7.36-7.30 (5H, m), 5.84-5.74 (2H, m), 5.51 (1H, dd, J = 15.4, 6.0 Hz), 5.40 (1H, d, J = 6.9 Hz), 5.12 (2H, s), 5.04-5.01 (2H, m), 4.89 (1H, br t, J = 6.7 Hz), 3.76 (3H, s), 2.80 (2H, apparent triplet, J = 6 Hz); δ_C (75 MHz, CDCl₃) 171.4, 155.5, 136.2, 135.5, 132.4, 128.5, 128.2, 128.1, 125.1, 116.2, 67.1, 55.6, 52.7, 36.0; LRMS (ES⁺): m/z = 601 (100[2M+Na]⁺), 353 (95[M+2Na+NH₄]⁺), 290 (100[M+H]⁺); HRMS (ES⁺): found M+H⁺ 290.1404; C₁₆H₂₀NO₄⁺ requires 290.1392.

(E)-Methyl 2-benzylloxycarbonylaminohept-3,5-dienoate and (Z)-methyl 2-benzylloxycarbonylaminohept-2,5-dienoate (8h/9h)

7:1 mixture of **8h/9h**. R_F 0.38 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3335 (w), 2954 (w), 1723 (s), 1516 (m), 1455 (w), 1436 (w), 1217 (m), 1051 (m), 1004 (m), 913 (w), 698 (w); δ_H (signals for **8h**, 500 MHz, CDCl₃): 7.36-7.32 (5H, m), 6.33-6.29 (2H, m), 5.69 (1H, dd, J = 14.1, 6.4 Hz), 5.51 (1H, br s), 5.25 (1H, d, J = 14.9 Hz), 5.16 (1H, d, J = 9.0 Hz), 5.13 (2H, s), 4.97 (1H, apparent t, J = 6.4 Hz), 3.75 (3H, s); signals for minor compound **9h** visible at: 6.65 (1H, t, J = 7.5 Hz), 5.82 (1H, m), 5.26 (1H, d, J = 10.9 Hz), 5.15 (2H, s), 5.06 (1H, d, J = 9.8 Hz), 2.98 (2H, dd, J = 7.5, 6.0 Hz) all other signals are obscured by those of **8h**; δ_C (signals for **8h**, 75 MHz, CDCl₃): 171.4, 155.9, 136.5, 135.8, 134.1, 128.9, 128.7, 128.6, 127.4, 119.8, 67.6, 55.9, 53.2; signals for minor compound **9h** visible at: 165.4, 136.3, 135.0, 134.6, 128.8, 128.6, 117.3, 67.9, 52.9, 33.0, 3 signals unobserved for minor compound **9h**; LRMS (ES⁺): m/z = 298 (40[M + Na]⁺), 276 (90[M+H]⁺), 232 (100[M-43]⁺); HRMS (ES⁺): found M+Na⁺, 298.1069; C₁₅H₁₇NO₄Na⁺ requires 298.1055.

(2Z,3'Z)-2-(3-Benzylloxycarbonylamino-5-ethyl-2-oxo-1-phenylhept-3-enyloxycarbonylamino)-4-ethyl-hex-2-enoic acid methyl ester (12)

R_F 0.2 (1:1 petrol-Et₂O); $\nu_{\max}/\text{cm}^{-1}$ (film) 3312 (w), 2962 (m), 2932 (m), 1714 (s), 1656 (m), 1498 (m), 1456 (m), 1326 (m), 1228 (s), 1058 (m), 698 (w); δ_H (500 MHz, CDCl₃): 7.29-7.23 (10H, m), 6.50 (1H, s), 6.38 (1H, d, J = 10.7 Hz), 6.19 (1H, d, J = 10.7 Hz), 6.06 (1H, br s), 5.97 (1H, br s), 4.98 (2H, br s), 3.66 (3H, s), 2.27 (1H, m), 2.21 (1H, m), 1.46-1.04 (8H, m), 0.77 (6H, t, J = 7.3 Hz), 0.67 (3H, t, J = 7.3 Hz), 0.50 (3H, t, J = 7.3 Hz); δ_C (75 MHz CDCl₃): 191.7, 165.4, 154.7, 154.1, 145.9, 144.7, 136.4, 134.5, 132.4, 130.5, 129.6, 129.3, 129.2, 128.9, 128.6, 128.5, 78.1, 67.7, 52.8, 41.9, 41.7, 27.3, 27.2, 12.1, 11.7; LRMS (ES⁺): m/z = 602 (60[M+Na]⁺), 597 (100[M+NH₄]⁺), 580 (10[M+H]⁺); HRMS (ES⁺) found M+Na⁺, 601.2872; C₃₃H₄₂N₂O₇Na⁺ requires 601.2890.

(E)-2-Benzylloxycarbonylamino-5-phenyl-pent-5-enoic acid (13)

(E)-Methyl 2-benzylloxycarbonylamino-5-phenylpent-3-enoate (**8a**) (100 mg, 0.3 mmol), was added to a mixture of 1 M HCl_(aq) (0.6 ml) and acetic acid (0.6 ml) and refluxed for 3 hours. The mixture was then allowed to cool and water (5 ml) was added and the mixture was extracted with EtOAc (4 x 15 ml). The organic extracts were combined, dried (MgSO₄), filtered and concentrated under reduced pressure to give a colourless powder. This was recrystallised from EtOAc and petrol to give the title compound as colourless crystals (63 mg, 0.19 mmol, 65%), mp 78°-80°C (EtOAc/petrol); R_F 0.14 (EtOAc);

$\nu_{\max}/\text{cm}^{-1}$ 3030 (m), 1721 (s), 1515 (m), 1453 (m), 1414 (w), 1216 (m), 1063 (m), 697 (m); signals in the ^1H NMR spectrum were very broad at room temperature but running the ^1H NMR at 57°C gave rise to sharpened signals, δ_{H} (500 MHz, CDCl_3): 7.32-7.24 (7H, m), 7.17 (1H, tt, $J = 7.5, 1.3$), 7.12 (2H, dd, $J = 7.5, 1.3$), 5.99 (1H, dtd, $J = 15.4, 6.7, 1.3$ Hz), 5.78 (1H, dd, $J = 15.4, 6.2$ Hz), 5.38 (1H, br s), 5.13 (1H, d, $J = 12.3$ Hz), 5.10 (1H, d, $J = 12.3$ Hz), 4.90 (1H, apparent t, $J = 6.2$ Hz), 3.38 (2H, d, $J = 6.7$ Hz); δ_{C} (75 MHz CDCl_3): 175.2, 155.7, 139.0, 136.0, 134.0, 128.6, 128.5, 128.3, 128.2, 126.3, 124.7, 67.3, 55.4, 38.4 (one alkene/aromatic signal not resolved); LRMS (ES⁺): $m/z = 343.2$ (100[$\text{M}+\text{NH}_4$]⁺), 326 (80[$\text{M}+\text{H}$]⁺); anal. calc. for $\text{C}_{19}\text{H}_{19}\text{NO}_4$: C, 70.1; H, 5.89; N, 4.31; found: C, 70.1; H, 5.95; N, 4.30%.

(E)-Methyl 2-amino-5-phenylpent-3-enoate (14)

TMSCl (0.07 ml, 0.3 mmol) was added to a mixture of **8a** (100 mg, 0.3 mmol) and sodium iodide (88 mg, 0.59 mmol), in acetonitrile (2ml) and stirred at room temperature for 5 hours. Water (1 ml) was added and the mixture stirred for 15 minutes. Toluene sulfonic acid monohydrate (67 mg, 0.35 mmol) was then added and the mixture stirred for a further 15 minutes. 1M $\text{HCl}_{(\text{aq})}$ (10 ml) and EtOAc (10 ml) were added and the layers separated. The inorganic layer was basified to pH 10 and extracted with DCM (3 x 15 ml), The combined organic layers were washed with 10% Na_2SO_3 soln (10 ml) and dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the title compound as a yellow oil (40 mg, 0.19 mmol, 65%); $\nu_{\max}/\text{cm}^{-1}$ (film) 3375 (w), 3027 (w), 2952 (w), 1738 (s), 1602 (w), 1453 (w), 1435 (w), 1200 (m), 1172 (m), 972 (m), 700 (m); δ_{H} (500 MHz, CDCl_3): 7.27 (2H, apparent t, $J = 7.3$), 7.21 (1H, t, $J = 7.3$ Hz), 7.17 (2H, d, $J = 7.3$ Hz), 5.92 (1H dt, $J = 15.4, 6.9$ Hz), 5.62 (1H, dd, $J = 15.4, 6.4$ Hz), 4.08 (1H, d, $J = 6.4$ Hz), 3.74 (3H, s), 3.39 (2H, d, $J = 6.9$ Hz); δ_{C} (75 MHz CDCl_3): 174.8, 140.0, 132.4, 129.5, 129.0, 128.9, 126.6, 56.8, 52.7, 39.0; LRMS (ES⁺): $m/z = 247$ (75[$\text{M}+\text{H}+\text{Na}+\text{NH}_4$]⁺) 206 (100[$\text{M}+\text{H}$]⁺); HRMS (ES⁺): found $\text{M}+\text{H}^+$, 206.1185; $\text{C}_{12}\text{H}_{16}\text{NO}_2^+$ requires 206.1181.

(Z)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-2-enoate (6a)

(Z)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-2-enoate (6a)

(Z)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-2-enoate (6a, Boc-protected)

(Z)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-2-enoate (6a, Boc-protected)

(Z)-Methyl 2-benzyloxycarbonylamino-5-(1-methoxyphen-4-yl)-pent-2-enoate (6b)

(Z)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-2-enoate (6c)

(Z)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-2-enoate (6c)

(Z)-Methyl 2-benzyloxycarbonylamino-2-decenoate (6d)

(Z)-Methyl 2-benzyloxycarbonylamino-2-decenoate (6d)

(Z)-Methyl 2-benzyloxycarbonylamino-4-(N-Boc-piperidin-4-yl)-but-2-enoate (6e)

(Z)-Methyl 2-benzyloxycarbonylamino-4-(*N*-Boc-piperidin-4-yl)-but-2-enoate (6e)

(Z)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-2-enoate (6f)

(Z)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-2-enoate (6f)

(Z)-Methyl 2-benzyloxycarbonylaminohept-2,6-dienoate (6g)

(Z)-Methyl 2-benzyloxycarbonylaminohept-2,6-dienoate (6g)

(2Z,4E)-Methyl 2-benzyloxycarbonylamino-2,4-dienoate (6h)

(2*Z*,4*E*)-Methyl 2-benzyloxycarbonylamino-2,4-hexadienoate (6h)

(Z)-Methyl 2-benzyloxycarbonylaminobut-2-enoate (6i)

(Z)-Methyl 2-benzyloxycarbonylaminobut-2-enoate (6i)

(Z)-Methyl 2-benzyloxycarbonylamino-4-methylpent-2-enoate (6j)

(Z)-Methyl 2-benzyloxycarbonylamino-4-methylpent-2-enoate (6j)

(Z)-Methyl 2-benzyloxycarbonylamino-4-ethylhex-2-enoate (6k)

(Z)-Methyl 2-benzyloxycarbonylamino-4-ethylhex-2-enoate (6k)

(E)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-3-enoate (8a)

(E)-Methyl 2-benzyloxycarbonylamino-5-phenylpent-3-enoate (8a)

(E)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-3-enoate (8a, Boc protected)

(E)-Methyl 2-*tert*-butoxycarbonylamino-5-phenylpent-3-enoate (8a, Boc protected)

(E)-Methyl 2-benzyloxycarbonylamino-5-(1-methoxyphen-4-yl)-pent-3-enoate (8b)

(E)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-3-enoate (8c)

(E)-Methyl 2-benzyloxycarbonylamino-5-(5-methylfuran-2-yl)-pent-3-enoate (8c)

(E)-Methyl 2-benzyloxycarbonylaminododec-3-enoate (8d)

(E)-Methyl 2-benzyloxycarbonylaminododec-3-enoate (8d)

(E)-Methyl 2-benzyloxycarbonylamino-4-[4-*N*-(*tert*-butoxycarbonyl)-piperidin-4-yl]-but-3-enoate (8e)

(E)-Methyl 2-benzyloxycarbonylamino-4-[4-*N*-(*tert*-butoxycarbonyl)-piperidin-4-yl]-but-3-enoate (8e)

(E)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-3-enoate (8f)

(E)-Methyl 2-benzyloxycarbonylamino-4-phenylbut-3-enoate (8f)

(E)-Methyl 2-benzoyloxycarbonylaminohept-3-6-dienoate (8g)

(E)-Methyl 2-benzyloxycarbonylaminohept-3-6-dienoate (8g)

(E)-Methyl 2-benzoyloxycarbonylaminohehex-3,5-dienoate and (Z)-methyl 2-benzoyloxycarbonylaminohehex-2,5-dienoate (8h/9h)

(E)-Methyl 2-benzoyloxycarbonylaminohept-3,5-dienoate and (Z)-methyl 2-benzoyloxycarbonylaminohept-2,5-dienoate (8h/9h)

(2Z,3'Z)-2-(3-Benzoyloxycarbonylamino-5-ethyl-2-oxo-1-phenylhept-3-enyloxycarbonylamino)-4-ethyl-hex-2-enoic acid methyl ester (12)

CC(C)C=C(C(=O)NOC(=O)C1=CC=CC=C1)C(=O)OC(=O)C2=CC=CC=C2

(E)-2-Benzylloxycarbonylamino-5-phenyl-pent-5-enoic acid (13)

(E)-2-Benzoyloxycarbonylamino-5-phenyl-pent-5-enoic acid (13)

(E)-Methyl 2-amino-5-phenylpent-3-enoate (14)

(E)-Methyl 2-amino-5-phenylpent-3-enoate (14)