Electronic Supplementary Information

A Convenient Approach to Acyclic Unsaturated Amino Acids via Ring-Closing Metathesis

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General Experimental.

Unless otherwise noted, all air and moisture sensitive reactions were carried out under a positive pressure of nitrogen atmosphere in oven-dried glassware using anhydrous solvents. Reagents were purchased from commercial sources and used without further purification. Reactions were magnetically stirred and examined by thin layer chromatography (TLC) using ultraviolet light (254 nm) and/or aqueous potassium permanganate solution for visualization. All lactams, macrolactam, unsaturated amino acids, and unsaturated amino esters were treated as light sensitive.

$^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded on Bruker DPX-300 or 400 instruments. Chemical shifts are reported in parts per million (ppm) relative to chloroform ($\delta$ 7.26) or methanol ($\delta$ 3.31) for $^1$H NMR and chloroform ($\delta$ 77.0) for $^{13}$C NMR. Multiplicities and other abbreviations are expressed as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (qu), multiplet (m), broad (br), and apparent (app). Coupling constants are recorded in Hertz (Hz). High resolution mass spectrometry fast atom bombardment (HRMS FAB) was conducted using a Kratos MS50TC instrument. All microwave-based reactions were carried out using CEM Discover Microwave Synthesizer with Explorer Carousel.
Experimental.

*N*-allylpent-4-enamide (3a):\textsuperscript{1}

To a MW reaction tube was added allylamine 1 (732 µL, 9.78 mmol) and 4-pentenoic acid 2a (1 mL, 9.78 mmol). The tube was sealed and placed in the MW reactor (300 W, 150 °C, 250 psi pressure, 30 min with continuous stirring while cooling the vessel) in solvent-free conditions. Purification by silica gel column chromatography (25% EtOAc in CH\textsubscript{2}Cl\textsubscript{2}) afforded 1.30 g (96%) of 3a as a yellow oil (TLC: \(R_f\) = 0.49): \(\textsuperscript{1}H\) NMR (300 MHz, CDCl\textsubscript{3}, ppm) \(\delta\) 6.62 (br s, 1H), 5.75–5.67 (m, 2H), 5.11–4.89 (m, 4H), 3.79–3.75 (m, 2H), 2.31–2.20 (m, 4H); \(\textsuperscript{13}C\) NMR (75 MHz, CDCl\textsubscript{3}, ppm) \(\delta\) 172.3, 136.9, 134.1, 115.8, 115.2, 41.6, 35.4, 29.4; HRMS (FAB) calcd for C\textsubscript{8}H\textsubscript{13}NO (MNa\textsuperscript{+}) 162.0889, found 162.0887.

*N*-allyl-3-methylpent-4-enamide (3b):

Experimental procedure for 3a was followed, with allylamine 1 (925 µL, 12.36 mmol) and 3-methyl-4-pentenoic acid 2b (1 mL, 8.24 mmol). Purification by silica gel column chromatography (10% EtOAc in CH\textsubscript{2}Cl\textsubscript{2}) afforded 1.25 g (99%) of 3b (TLC: \(R_f\) = 0.42) as a pale yellow oil: \(\textsuperscript{1}H\) NMR (300 MHz, CDCl\textsubscript{3}, ppm) \(\delta\) 6.57 (br s, 1H), 5.75–5.64 (m, 2H), 5.12–4.86 (m, 4H), 3.78 (m, 2H), 2.66–2.58 (m, 1H), 2.19 (dd, \(J = 15.0, 9.0\) Hz, 1H), 2.08 (dd, \(J = 15.0, 9.0\) Hz, 1H), 0.97 (d, \(J = 6.6\) Hz, 3H); \(\textsuperscript{13}C\) NMR (75 MHz, CDCl\textsubscript{3}, ppm) \(\delta\) 171.9, 142.6, 134.2, 115.8, 113.1, 43.3, 41.6, 34.5, 19.4; HRMS (FAB) calcd for C\textsubscript{9}H\textsubscript{15}NO (MNa\textsuperscript{+}) 176.1045, found 176.1040.
**N-allyl-3,3-dimethylpent-4-enamide (3c):**

Experimental procedure for 3a was followed, with allylamine 1 (1.12 mL, 15.0 mmol) and 3,3-methyl-4-pentenoic acid 2c (960 mg, 7.5 mmol). Purification by silica gel column chromatography (10% EtOAc in CH₂Cl₂) afforded 784 mg (63%) of 3c as a yellow oil (TLC: R₆ = 0.27): ¹H NMR (400 MHz, CDCl₃, ppm) δ 5.91 (dd, J = 17.2, 10.8 Hz, 1H), 5.85–5.76 (m, 1H), 5.61 (br s, 1H), 5.16 (dd, J = 17.2, 1.2 Hz, 1H), 5.10 (dd, J = 10.8, 1.2 Hz, 1H), 5.01 (dd, A₂X system, J = 17.2, 10.8 Hz, 2H), 3.84 (t, J = 5.6 Hz, 2H), 2.20 (s, 2H), 1.13 (s, 6H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 170.8, 147.2, 134.3, 116.1, 111.4, 49.3, 41.7, 36.2, 26.9 (2 C); HRMS (FAB) calcd for C₉H₁₅NO (MNa⁺) 190.1202, found 190.1201.

**N-allyl-4-methylpent-4-enamide (3d):**

Experimental procedure for 3a was followed, with allylamine 1 (329 µL, 4.39 mmol) and ethyl-4-methyl-4-pentenoate 2d (700 µL, 4.39 mmol). Purification by silica gel column chromatography (10% EtOAc in CH₂Cl₂) afforded 391 mg of 3d (58%) as a yellow oil (TLC: R₆ = 0.23): ¹H NMR (400 MHz, CDCl₃, ppm) δ 6.69 (br s, 1H), 5.77–5.68 (m, 1H), 5.07 (d, J = 17.2 Hz, 1H), 5.00 (d, J = 10.0, 1H), 4.65 (s, 1H), 4.60 (s, 1H), 3.76 (m, 2H), 2.31–2.22 (m, 4H), 1.64 (s, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 172.6, 144.2, 134.1, 115.7, 110.1, 41.6, 34.4, 33.1, 22.2; HRMS (FAB) calcd for C₉H₁₅NO (MNa⁺) 176.1045, found 176.1047.
**N-allylhex-5-enamide (3e):**

Experimental procedure for 3a was followed, with allylamine 1 (315 µL, 4.21 mmol) and 5-hexenoic acid 2e (500 µL, 4.21 mmol). Purification by silica gel column chromatography (8% EtOAc in CH₂Cl₂) afforded 586 mg (91%) of 3e as a pale yellow oil (TLC: Rf = 0.32): ¹H NMR (300 MHz, CDCl₃, ppm) δ 6.52 (br s, 1H), 5.77–5.63 (m, 2H), 5.11–4.87 (m, 4H), 3.79–3.75 (m, 2H), 2.15 (t, J = 7.8 Hz, 2H), 2.04–1.97 (m, 2H), 1.66 (qu, J = 7.8 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃, ppm) δ 172.9, 137.7, 134.1, 115.8, 114.9, 41.6, 35.5, 32.9, 24.6; HRMS (FAB) calcd for C₉H₁₅NO (MNa⁺) 176.1045, found 176.1045.

**Tert-butyl-allylpent-4-enoylcarbamate (4a):**

To an oven-dried round-bottomed flask was added N-allylpent-4-enamide 3a (1.23 g, 8.85 mmol), Boc₂O (3.858 g, 17.7 mmol; added as liquid), DMAP (432 mg, 3.54 mmol), and CH₃CN (8 mL). The 1 M reaction mixture was stirred at rt for 2 h, under nitrogen atmosphere. The resulting deep red reaction mixture was concentrated *in vacuo* to give a deep red oil. Purification by silica gel column chromatography (3:10:87, Et₃N/EtOAc/hexane) afforded 2.11 g of 4a (100%) as a yellow oil (TLC: Rf = 0.76): ¹H NMR (300 MHz, CDCl₃, ppm) δ 5.81–5.67 (m, 2H), 5.09–4.90 (m, 4H), 4.23 (d, J = 5.7 Hz, 2H), 2.92 (t, J = 7.8 Hz, 2H), 2.37–2.30 (m, 2H), 1.45 (s, 9H); ¹³C NMR (75 MHz, CDCl₃, ppm) δ 174.7, 152.8, 137.3, 133.4, 116.2, 114.9, 82.7, 46.3, 37.4, 28.9, 27.8 (3 C); HRMS (FAB) calcd for C₁₃H₂₁NO₃ (MNa⁺) 262.1413, found 262.1408.
**Tert-butyl-3-methylpent-4-enoylallylcarbamate (4b).**

Experimental procedure for 4a was followed, with N-allyl-3-methylpent-4-enamide 3b (200 mg, 1.31 mmol), Boc₂O (685 mg, 3.14 mmol), DMAP (64 mg, 0.524 mmol), and CH₃CN (1 mL). Purification by silica gel column chromatography (3:10:87, Et₃N/EtOAc/hexane) afforded 320 mg of 4b (97%) as a yellow oil (TLC: Rf = 0.70): ¹H NMR (300 MHz, CDCl₃, ppm) δ 5.84–5.70 (m, 2H), 5.12–4.89 (m, 4H), 4.25 (d, J = 5.7 Hz, 2H), 2.95–2.69 (m, 3H), 1.48 (s, 9H), 1.03 (d, J = 6.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm) δ 174.3, 152.9, 143.1, 133.5, 116.3, 112.9, 82.8, 46.4, 44.7, 34.1, 27.9 (3 C), 19.7; HRMS (FAB) calcd for C₁₄H₂₃NO₃ (MNa⁺) 276.1570, found 276.1568.

**Tert-butyl-3,3-dimethylpent-4-enoylallylcarbamate (4c):**

Experimental procedure for 4a was followed, with N-allyl-3,3-dimethylpent-4-enamide 3c (714 mg, 4.27 mmol), Boc₂O (2.33 g, 10.67 mmol), DMAP (260 mg, 2.13 mmol), and CH₃CN (4 mL). Purification by silica gel column chromatography (3:10:87, Et₃N/EtOAc/hexane) afforded 915 mg of 4c (80%) as a yellow oil (TLC: Rf = 0.76): ¹H NMR (400 MHz, CDCl₃, ppm) δ 5.94 (dd, J = 17.2, 10.8 Hz, 1H), 5.82–5.75 (m, 1H), 5.14–5.07 (m, 2H), 4.95–4.89 (m, 2H), 4.23 (d, J = 5.6 Hz, 2H), 2.97 (s, 2H), 1.49 (s, 9H), 1.12 (s, 6H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 173.6, 153.2, 147.3, 133.6, 116.4, 110.4, 82.7, 48.5, 46.5, 36.8, 27.9 (3 C), 27.1 (2 C); HRMS (FAB) calcd for C₁₅H₂₅NO₃ (MNa⁺) 290.1726, found 290.1725.
**Tert-butyl-4-methylpent-4-enoylallylcarbamate (4d):**

Experimental procedure for 4a was followed, with N-allyl-4-methylpent-4-enamide 3d (198 mg, 1.29 mmol), Boc₂O (676 mg, 3.10 mmol), DMAP (63 mg, 0.516 mmol), and CH₃CN (1 mL). Purification by silica gel column chromatography (3:8:89, Et₃N/EtOAc/hexane) afforded 311 mg of 4d (95%) as a yellow oil (TLC: $R_f = 0.71$): ¹H NMR (400 MHz, CDCl₃, ppm) δ 5.81–5.72 (m, 1H), 5.11–5.06 (m, 2H), 4.70 (s, 1H), 4.66 (s, 1H), 4.25 (d, $J = 5.6$ Hz, 2H), 2.98 (t, $J = 8.0$ Hz, 2H), 2.31 (t, $J = 8.0$ Hz, 2H), 1.72 (s, 3H), 1.48 (s, 9H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 175.1, 152.8, 144.6, 133.4, 116.3, 109.9, 82.8, 46.4, 36.5, 32.7, 27.9 (3 C), 22.6; HRMS (FAB) calecd for C₁₄H₂₃NO₃ (MNa⁺) 276.1570, found 276.1564.

**Tert-butyl-allylhex-5-enoylcarbamate (4e):**

Experimental procedure for 4a was followed, with N-allylhex-5-enaminde 3e (360 mg, 2.35 mmol), Boc₂O (1.229 g, 5.64 mmol), DMAP (115 mg, 0.94 mmol), and CH₃CN (2 mL). Purification by silica gel column chromatography (3:10:87, Et₃N/EtOAc/hexane) afforded 565 mg of 4e (95%) as a yellow oil (TLC: $R_f = 0.71$): ¹H NMR (300 MHz, CDCl₃, ppm) δ 5.82–5.71 (m, 2H), 5.06–4.92 (m, 4H), 4.25 (d, $J = 5.7$ Hz, 2H), 2.84 (t, $J = 7.5$ Hz, 2H), 2.11–2.04 (m, 2H), 1.72 (qu, $J = 7.5$, 2H), 1.48 (s, 9H); ¹³C NMR (75 MHz, CDCl₃, ppm) δ 175.4, 152.9, 138.1, 133.4, 116.2, 114.9, 82.8, 46.4, 37.5, 33.1, 27.9 (3 C), 24.2; HRMS (FAB) calecd for C₁₄H₂₃NO₃ (MNa⁺) 276.1570, found 276.1567.
(Z)-tert-butyl-3,4-dihydro-2-oxo-2H-azepine-1(7H)-carboxylate (5a).\(^2\)

To an oven-dried round-bottomed flask fitted with a condenser was added tert-butylallylpent-4-enoylcarbamate 4a (100 mg, 4.18 mmol) and deoxygenated CH\(_2\)Cl\(_2\) (418 mL). Grubbs’ second-generation ruthenium catalyst A (18 mg, 2.09 mmol, 5 mol %) was then added in one aliquot. The 1 mM reaction mixture was heated to reflux (50 °C) with stirring for 24 h in the absence of light, under a stream of nitrogen atmosphere. Following removal of the solvent, Ru scavenger (SiO\(_2\)-Si(CH\(_2\))\(_3\)NH\(_2\),\(^3\) 10 equiv w/w relative to catalyst) and hexane (10 mL) were added and the resulting mixture was stirred vigorously at rt for 2 h. The crude product was passed through a pad of silica gel (100 mg per approximately 100 mg crude product) using a fritted filtration column, eluting with 3% Et\(_3\)N in hexane (20 mL) and further with 3:10:87 Et\(_3\)N/EtOAc/hexane (10 mL). The filtrate was then concentrated to dryness to obtain 85 mg (97%) of 5a as a yellow oil without the need for further purification: \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta 5.85–5.74 (m, 2H), 4.34–4.32 (m, 2H), 2.87 (t, J = 6.4 Hz, 2H), 2.48 (m, 2H), 1.52 (s, 9H); \(^13\)C NMR (100 MHz, CDCl\(_3\), ppm) \(\delta 174.2, 152.2, 131.7, 124.3, 82.8, 41.9, 36.1, 27.9 (3 C), 25.6;\) HRMS (FAB) calcd for C\(_{11}\)H\(_{17}\)NO\(_3\) (MNa\(^+\)) 234.1101, found 234.1102.

(Z)-tert-butyl-3,4-dihydro-4-methyl-2-oxo-2H-azepine-1(7H)-carboxylate (5b):

Experimental procedure for 5a was followed, with tert-butyl-3-methylpent-4-enoylallylcarbamate 4b (108 mg, 0.426 mmol), Grubbs’ second-generation ruthenium catalyst A (18 mg, 0.0213 mmol, 5 mol %), and deoxygenated CH\(_2\)Cl\(_2\) (427 mL). The crude product 5b was obtained as a yellow oil (87 mg, 91%)
without the need for further purification: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 5.75 (ddd, $J$ = 11.2, 6.0, 1.6 Hz, 1H), 5.64 (ddd, $J$ = 11.2, 3.2 Hz, 1H), 4.29 (m, 2H), 2.83–2.73 (m, 2H), 2.67 (m, 1H), 1.51 (s, 9H), 1.12 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 173.1, 152.1, 137.8, 123.0, 82.9, 43.3, 41.9, 31.5, 27.9 (3 C), 21.5; HRMS (FAB) calcd for C$_{12}$H$_{19}$NO$_3$ (MNa$^+$) 248.1257, found 248.1257.

(Z)-tert-butyl-3,4-dihydro-4,4-dimethyl-2-oxo-2$H$-azepine-1(7$H$)-carboxylate (5c):

Experimental procedure for 5a was followed, with tert-butyl 3,3-dimethylpent-4-enoylallylcarbamate 4c (107 mg, 0.40 mmol), Grubbs’ second-generation ruthenium catalyst A (17 mg, 0.02 mmol, 5 mol %), and deoxygenated CH$_2$Cl$_2$ (400 mL). The crude product 5c was obtained as a yellow oil (94 mg, 98%) without the need for further purification: $^1$H NMR (400 MHz, CDCl$_3$, ppm): 5.65 (dt, $J$ = 11.2, 6.0 Hz, 1H), 5.50 (d, $J$ = 11.2 Hz, 1H), 4.26 (d, $J$ = 6.0 Hz, 2H), 2.72 (s, 2H), 1.49 (s, 9H), 1.09 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm): 172.4, 152.1, 142.4, 121.1, 82.9, 49.1, 41.9, 35.2, 29.7 (2 C), 27.9 (3 C); HRMS (FAB) calcd for C$_{13}$H$_{21}$NO$_3$ (MNa$^+$) 262.1413, found 262.1411.

Macrolactam 6a:

Experimental procedure for 5a was followed, with tert-butyl-allylpent-4-enoylcarbamate 4a (200 mg, 0.836 mmol), Grubbs’ second-generation ruthenium catalyst A (35 mg, 0.0418 mmol, 5 mol %), and deoxygenated CH$_2$Cl$_2$ (21 mL). Reaction mixture concentration
= 40 mM. Ru scavenger (SiO₂-Si(CH₂)₃NH₂, 20 equiv w/w relative to catalyst) was used for catalyst byproducts removal and a pad of silica gel (200 mg per approximately 100 mg crude product) was used to pass the crude product through, eluting with 3% Et₃N in hexane (40 mL) and further with 3:10:87 Et₃N/EtOAc/hexane (20 mL). Purification by silica gel column chromatography (3% Et₃N in hexane) afforded 94 mg of 6a (53%) as a colourless oil, which crystallized over time to give a white solid (TLC: \( R_f = 0.15 \)): \(^1\)H NMR (400 MHz, CDCl₃, ppm) \( \delta \) 5.53–5.29 (m, 4H, 2 CH=C=CH), 4.22 (m, 4H), 2.86–2.82 (m, 4H), 2.33 (m, 4H), 1.52 (s, 18H); \(^{13}\)C NMR (100 MHz, CDCl₃, ppm; presence of rotamers) \( \delta \) 174.4, 174.2, 153.3, 153.1, 131.3, 129.2, 127.8, 125.8, 82.9, 82.8, 45.8, 45.5, 37.4, 37.2, 28.0 (6 C), 27.6, 27.4; HRMS (FAB) calcd for C₂₂H₃₄N₂O₆ (MNa⁺) 445.2309, found 445.2305.

(Z)-6-(tert-butoxycarbonyl)-hex-4-enoic acid (7a):
2 M 1:1 LiOH in THF/H₂O (220 µL × 2) were independently added to lactam 5a (33 mg, 0.156 mmol). The 0.35 M biphasic reaction mixture was stirred at 30 ºC for 2 h in the absence of light. Water (2 mL) was added and the crude product was extracted with EtOAc (5 mL). The pH of the aqueous phase was acidified by a dropwise addition of 1 M HCl. The crude product was extracted three times with EtOAc (10 mL) and further with CH₂Cl₂ (10 mL). The combined organic layers were dried (MgSO₄), filtered, and the solvent was evaporated \textit{in vacuo} to give a yellow oil. Purification by silica gel column chromatography (6% CH₃OH in CH₂Cl₂) afforded 35 mg of 7a (97%) as a yellow oil (TLC: \( R_f = 0.17 \)): \(^1\)H NMR (400 MHz, CD₃OD, ppm) \( \delta \) 5.49–5.39 (m, 2H), 3.70 (d, \( J \) =
6.0 Hz, 2H), 2.37 (m, 4H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 178.1, 155.9, 130.3, 127.5, 79.4, 37.4, 33.7, 28.3 (3 C), 22.4; HRMS (FAB) calcd for C$_{11}$H$_{19}$NO$_4$ (MH$^+$) 230.1387, found 230.1392.

(Z)-6-(tert-butoxycarbonyl)-3-methylhex-4-enoic acid (7b).

Experimental procedure for 7a was followed, with lactam 5b (55 mg, 0.244 mmol) and 2 M 1:1 LiOH in THF/H$_2$O (350 $\mu$L $\times$ 2). Purification by silica gel column chromatography (6% CH$_3$OH in CH$_2$Cl$_2$) afforded 55 mg of 7b (93%) as a colourless oil (TLC: $R_f$ = 0.24): $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 5.39 (dt, $J = 10.8$, 6.8 Hz, 1H), 5.28 (app t, $J = 10.4$ Hz, 1H), 4.75 (br s, 1H), 3.76 (m, 2H), 3.03–2.94 (m, 1H), 2.36 (dd, $J = 15.2$, 6.0 Hz, 1H), 2.25 (dd, $J = 15.2$, 8.8 Hz, 1H), 1.43 (s, 9H), 1.02 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 177.3, 155.9, 136.4, 125.9, 79.4, 41.6, 37.6, 28.8, 28.4 (3 C), 20.9; HRMS (FAB) calcd for C$_{12}$H$_{21}$NO$_4$ (MH$^+$) 244.1543, found 244.1554.

(Z)-6-(tert-butoxycarbonyl)-3,3-dimethylhex-4-enoic acid (7c):

Experimental procedure for 7a was followed, with lactam 5c (50 mg, 0.209 mmol) and 2 M 1:1 LiOH in THF/H$_2$O (300 $\mu$L $\times$ 2). The crude product 7c was obtained as a yellow oil (50 mg, 93%) without the need for further purification: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 5.47 (d, $J = 12.0$ Hz, 1H), 5.27 (dt, 12.0, 6.8 Hz, 1H), 4.75 (br s, 1H), 3.89 (m, 2H), 2.43 (s, 2H), 1.02 (d, 6.8 Hz, 3H), 1.36 (s, 9H), 0.89 (d, 6.8 Hz, 3H), 1.86 (dt, 12.0, 6.8 Hz, 1H), 2.36 (dd, 15.2, 6.0 Hz, 1H), 1.43 (s, 9H), 1.02 (d, 6.8 Hz, 3H), $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 177.3, 155.9, 136.4, 125.9, 79.4, 41.6, 37.6, 28.8, 28.4 (3 C), 20.9; HRMS (FAB) calcd for C$_{12}$H$_{21}$NO$_4$ (MH$^+$) 244.1543, found 244.1554.
1.44 (s, 9H), 1.26 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 176.5, 155.9, 138.9, 126.8, 79.5, 47.4, 38.5, 35.5, 29.2 (2 C), 28.4 (3 C); HRMS (FAB) calcd for C$_{13}$H$_{23}$NO$_4$(MH$^+$) 258.1699, found 258.1692.

**(E)-6-(tert-butoxycarbonyl)hex-4-enoic acid (8a):**

Experimental procedure for 7a was followed, with macrolactam 6a (20 mg, 0.047 mmol) and 2 M 1:1 LiOH in THF/H$_2$O (700 µL × 2). The product 8a was obtained as a yellow oil (20 mg, 93%): $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 5.64–5.57 (m, 1H), 5.54–5.49 (m, 1H), 4.61 (br s, 1H), 3.69 (m, 2H), 2.44–2.32 (m, 4H), 1.44 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 178.1, 155.9, 130.3, 127.5, 79.4, 42.4, 33.7, 28.3 (3 C), 27.1; HRMS (FAB) calcd for C$_{11}$H$_{19}$NO$_4$(MH$^+$) 230.1387, found 230.1383.

**(Z)-tert-butyl-5-(ethoxycarbonyl)pent-2-enylcarbamate (9a):**

To lactam 5a (47 mg, 0.222 mmol) in absolute EtOH (634 µL) at 0 ºC, was added Cs$_2$CO$_3$ (108 mg, 0.333 mmol). The 0.35 M reaction mixture was stirred at 30 ºC for 2 h in the absence of light. EtOH was removed in vacuo and the resulting residue was filtered through a short plug of Celite, eluting with Et$_2$O. The filtrate was concentrated to dryness to give 57 mg of 9a (100%) as a yellow oil without the need for further purification: $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 5.52–5.43 (m, 2H), 4.62 (br s, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 3.76 (m, 2H), 2.37 (m, 4H), 1.44 (s, 9H), 1.25 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100
MHZ, CDCl₃, ppm) δ 172.9, 155.8, 130.6, 127.4, 79.3, 60.4, 37.4, 33.9, 28.4 (3 C), 22.7, 14.2; HRMS (FAB) calcd for C₁₃H₂₃NO₄ (MNa⁺) 280.1519, found 280.1523.

(Z)-tert-butyl-5-(ethoxycarbonyl)-4-methylpent-2-enylcarbamate (9b):

Experimental procedure for 9a was followed, with lactam 5b (63 mg, 0.28 mmol), Cs₂CO₃ (136 mg, 0.42 mmol), and EtOH (800 µL). The crude product 9b was obtained as a yellow oil (100%, 76 mg) without the need for further purification: ¹H NMR (400 MHz, CDCl₃, ppm) δ 5.39 (dt, J = 10.8, 6.8 Hz, 1H), 5.27 (app t, J = 10.4 Hz, 1H), 4.69 (br s, 1H), 4.16–4.04 (m, 2H), 3.86–3.68 (m, 2H), 3.06–2.95 (m, 1H), 2.31 (dd, J = 15.2, 6.0 Hz, 1H), 2.21 (dd, J = 15.2, 8.8 Hz, 1H), 1.43 (s, 9H), 1.22 (t, J = 7.2 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 172.4, 155.8, 136.7, 125.7, 79.2, 60.3, 41.8, 37.5, 28.9, 28.4 (3 C), 20.9, 14.2; HRMS (FAB) calcd for C₁₄H₂₅NO₄ (MNa⁺) 294.1675, found 294.1682.

(Z)-tert-butyl-5-(ethoxycarbonyl)-4,4-dimethylpent-2-enylcarbamate (9c):

Experimental procedure for 9a was followed, with lactam 5c (30 mg, 0.125 mmol), Cs₂CO₃ (61 mg, 0.187 mmol), and 1:1 EtOH/CH₂Cl₂ (180 µL × 2). Purification by silica gel column chromatography (2% EtOAc in CH₂Cl₂) afforded 31 mg of 9c (86%) as a yellow oil (TLC: Rf = 0.19): ¹H NMR (400 MHz, CDCl₃, ppm) δ 5.46 (d, J = 12.0 Hz, 1H), 5.27 (dt, J = 12.0, 6.8 Hz, 1H), 4.68 (br s, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.89 (m, 2H), 2.37 (s, 2H), 1.44 (s, 9H), 1.26–1.23 (m, 9H); ¹³C NMR (100 MHz, CDCl₃, ppm) δ 171.7, 155.7,
139.3, 126.3, 79.3, 60.1, 47.6, 38.4, 35.8, 29.2 (2 C), 28.4 (3 C), 14.3; HRMS (FAB) calcd for C_{15}H_{27}NO_{4} (MNa^+) 308.1832, found 308.1829.

**(E)-tert-butyl-5-(ethoxycarbonyl)pent-2-enylcarbamate (10a):**

Experimental procedure for 9a was followed, with macrolactam 6a (21 mg, 0.0497 mmol), Cs_{2}CO_{3} (24 mg, 0.0745 mmol), and EtOH (142 µL). The crude product 10a was obtained as a yellow oil (25 mg, 98%) without the need for further purification: ^1H NMR (400 MHz, CDCl₃, ppm) δ 5.58 (dt, J = 15.2, 6.0 Hz, 1H), 5.49 (dt, J = 15.2, 5.6 Hz, 1H), 4.52 (br s, 1H), 4.15–4.09 (m, 2H), 3.67 (m, 2H), 2.39–2.28 (m, 4H), 1.43 (s, 9H), 1.24 (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl₃, ppm) δ 173.1, 155.7, 130.5, 127.7, 79.3, 60.3, 42.4, 33.8, 28.4 (3 C), 27.4, 14.2; HRMS (FAB) calcd for C_{13}H_{23}NO_{4} (MNa^+) 280.1519, found 280.1526.
$^1$H and $^{13}$C NMR Spectra
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References for Supplementary Information

