β-, γ- and δ-Lactams as conformational constraints in ring-closing metathesis

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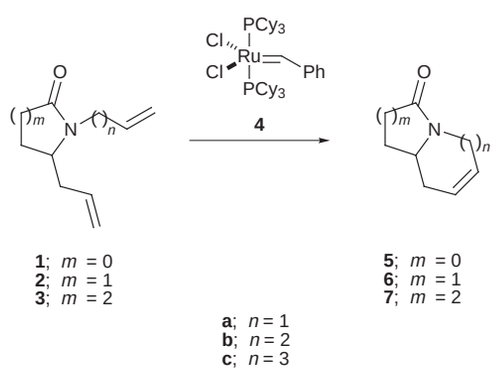
The azabicycloalkenones **5**, **6** and **7** were formed in excellent yields *via* ring-closing metathesis of the bis-alkenyl precursors **1**, **2** and **3**.

Introduction

Ring-closing metathesis (RCM) has recently emerged as a powerful method for the synthesis of a variety of ring systems.[1,2] Ring sizes from five through to complex macrocycles have been synthesised. Here we show how this methodology can be extended to include the synthesis of fused bicyclic systems which contain a nitrogen heteroatom at the angular position. These systems are derived from easily prepared terminal bis-alkenes, and undergo ring-closure with high efficiency. Structures of this type occur in many alkaloid natural products.[3] Of the metathesis catalysts available to date, the most suitable for ring-closure in the presence of heteroatoms is the Grubbs ruthenium alkylidene **4** which is stable and exhibits tolerance to a diverse range of functionality.[4,5] We employ bis-alkenyl substituted lactams (**1**–**3**) of ring size 4–6 and have shown that RCM smoothly affords final products (**5**–**7**) which contain newly formed 6-, 7- and 8-membered rings respectively (Scheme 1).

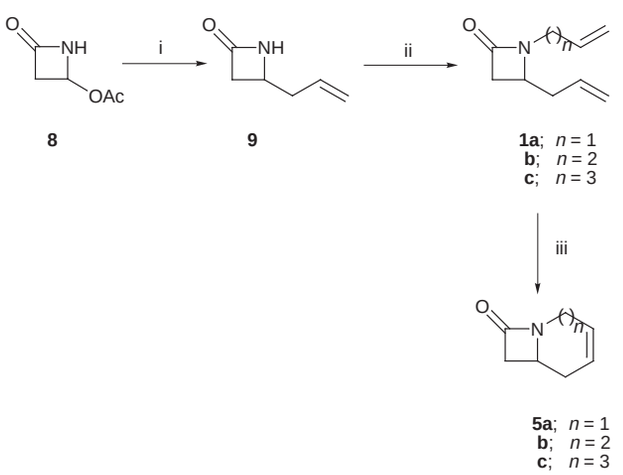


Scheme 1 *Reagents and conditions*: i, 5 mol% **4**, CH_2Cl_2, 25 °C, 2 h.

Results and discussion

Barrett and Gibson have previously reported the use of β-lactams as scaffolds for ring-closing metathesis reactions involving the formation of functionalised 7–9-membered oxygen-, nitrogen- and sulfur-containing heterocycles, together with two 6-membered carbocycles.[6–8] In this work we demonstrate the fusion of 6–8 membered carbocycles onto a β-lactam ring.

Allylation of the iminium species generated *in situ* by treatment of commercially available lactam **8** with $BF_3{\cdot}OEt_2$ followed by allyltrimethylsilane afforded 4-allylazetidin-2-one **9**.[9] Subsequent *N*-alkylation under phase transfer conditions[10] with a series of ω-haloalkenes gave suitable bis-alkenes for RCM. These materials were then subjected to RCM conditions which resulted in the formation of the required bicyclic products **5** in excellent yields (Scheme 2). The yields are summarised in Table 1.



Scheme 2 *Reagents and conditions*: i, $CH_2{=}CHCH_2SiMe_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 67%; ii, $CH_2{=}CH(CH_2)_nBr$, KOH, 18-crown-6, C_6H_6, (**a**, $n = 1$, 47%; **b**, $n = 2$, 35%; **c**, $n = 3$, 37%); iii, 5 mol% **4**, CH_2Cl_2 (see Table 1).

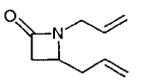
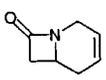
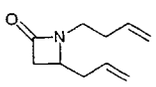
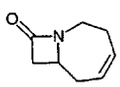
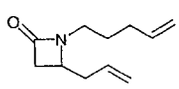
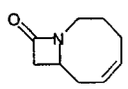
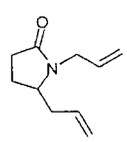
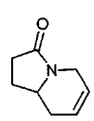
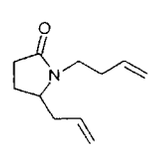
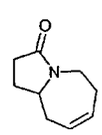
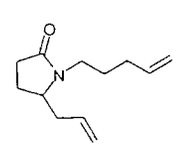
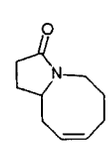
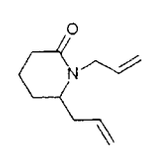
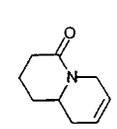
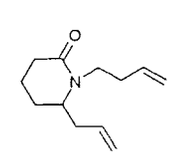
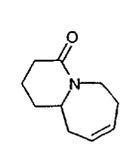
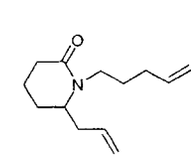
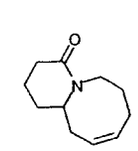
For the synthesis of the bis-alkenes based on γ- and δ-lactams, succinimide **10** and glutarimide **11**, respectively were first *N*-alkylated (Scheme 3). The Mitsunobu reaction[11] was the preferred method for attachment of *N*-propenyl and *N*-butenyl chains, while for the *N*-pentenyl products *N*-alkylation with pentenyl bromide in the presence of sodium hydride was employed.[12]

Partial reduction of the imides **12** and **13** to the corresponding ethoxyamides **14** and **15** (after interception by ethanol) was effected using sodium borohydride and acid following the procedure of Speckamp.[13,14] The pH of the reaction mixture was monitored using bromocresol green indicator, as over acidification can lead to ring-opening of the lactam. Lewis acid mediated formation and allylation of the iminium ions resulted in good yields of the α-allyl products **2** and **3**. The bis-alkenyl 5- and 6-membered lactams **2** and **3** were subjected to efficient ring-closing metathesis using the ruthenium catalyst **4**. Again all the ring-closures took place in high yields and with similar reaction conditions to those used with the corresponding β-lactams **1**. This work is complementary to that of Martin *et al.*, who investigated the ability of Schrock's molybdenum catalyst to effect the ring-closure of ω-vinyl-*N*-alkenyl substituted γ- and δ-lactams.[15]

Conclusions

In conclusion, we have shown that β-, γ- and δ-lactams can be

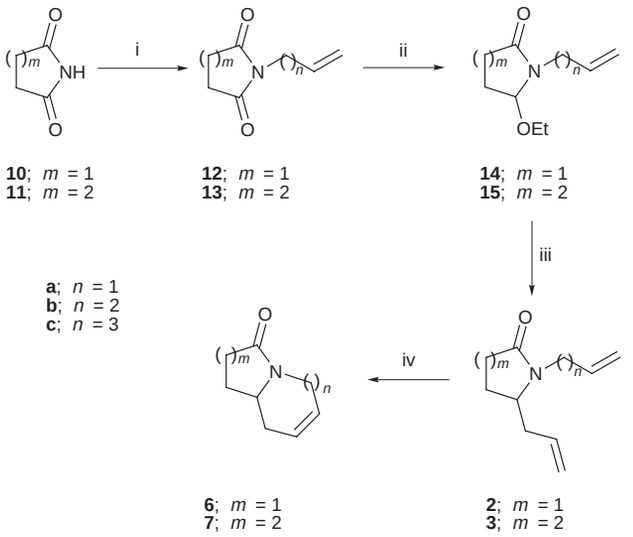
Table 1 Ring-closing methathesis of precursors **1**–**3** to bicyclo lactams **5**–**7**

Bis-alkene	Bicyclic Product	Yield (%)
1a 	**5a** 	80
1b 	**5b** 	95
1c 	**5c** 	92
2a 	**6a** 	84
2b 	**6b** 	94
2c 	**6c** 	82
3a 	**7a** 	84
3b 	**7b** 	80
3c 	**7c** 	91

used as constraints in the formation of 6–8 membered rings (Scheme 1 and Table 1). This methodology gives access to useful nitrogen containing heterocycles in high yields from readily available starting materials. In particular we have successfully formed 8-membered rings in excellent yields, even though many acyclic ring-closures do not proceed efficiently in the 8-membered series.[16] It is envisaged that both the constraining lactam and the alkyl side chains could carry further functionality if desired. It is expected that these types of scaffolds will contain enough inherent rigidity to position the required functionality in space for peptidomimetic applications. Such work is currently under investigation.

Experimental

^{1}H NMR spectra were recorded on Bruker DPX-250 (250 MHz), Bruker DRX-400 (400 MHz) and Bruker DRX-500 (500



10; m = 1
11; m = 2

12; m = 1
13; m = 2

14; m = 1
15; m = 2

a; n = 1
b; n = 2
c; n = 3

6; m = 1
7; m = 2

2; m = 1
3; m = 2

Scheme 3 *Reagents and conditions*: i, CH_2=$CH(CH_2)_n$OH (n = 1 or 2), PPh_3, DEAD, THF, (**12a**, n = 1, 95%; **b**, n = 2, 94%; **13a**, n = 1, 63%; **b**, n = 2, 80%); n = 3, CH_2=$CH(CH_2)_3$Br, NaH, DMF, (**12c**, n = 3, 75%; **13c**, n = 3, 83%); ii, $NaBH_4$, HCl, EtOH, −10 °C, (**14a**, n = 1, 51%; **b**, n = 2, 59%; **c**, n = 3, 71%; **15a**, n = 1, 64%; **b**, n = 2, 64%; **c**, n = 3, 64%; iii, CH_2=$CHCH_2SiMe_3$, BF_3·OEt_2, CH_2Cl_2, (**2a**, n = 1, 81%; **b**, n = 2, 80%; **c**, n = 3, 82%; **3a**, n = 1, 59%; **b**, n = 2, 44%; **c**, n = 3, 53%); iv, 5 mol% **4**, CH_2Cl_2 (see Table 1).

MHz) instruments, using $CDCl_3$ (or other indicated solvent) as reference or internal deuterium lock. The multiplicity of the signal was determined by an attached proton test experiment (APT). Infrared spectra were recorded as solutions in the indicated solvents using a Perkin-Elmer 1600 FTIR series spectrometer. Mass spectra were recorded at the EPSRC Mass Spectrometry Service Centre, University of Swansea (Dr J. Ballantine) or at the University Chemical Laboratory, Cambridge. In Swansea, electron impact (EI) and chemical ionisation (CI) low resolution spectra were carried out on a VG model 12-253 under alternate CI and EI scanning (ACE) conditions. Accurate mass measurements for EI and CI were performed on a +VG ZAB-E instrument. In Cambridge, EI and CI low resolution spectra and accurate mass spectra were performed on a KRATOS MS-890. Electrospray spectra were determined either with an ES Bruker FTICR or a VG-BioQ instrument. All CI measurements were performed with NH_3 as the carrier gas. Analytical TLC was carried out on pre-coated 0.25 mm thick Merck 60 F_{254} silica plates. Visualisation was by absorption of UV light, and spraying with basic potassium permanganate solution followed by thermal development. Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh) under pressure of compressed air.[17] Reagents were purified and dried where necessary by standard techniques.[18] THF was dried from potassium in a recycling still, using benzophenone ketyl as an indicator. Ether refers to diethyl ether. Brine refers to a saturated aqueous solution of sodium chloride. All reactions were performed under an atmosphere of dry nitrogen unless indicated to the contrary. Although all compounds except **5a** and **5b** (which were very volatile) were submitted for combustion analysis only compound **6c** afforded satisfactory elemental analytical data. All the compounds decomposed on attempted distillation, but were judged to be pure by NMR spectroscopy and TLC analysis.

4-Allylazetidin-2-one 9[19]

To a solution of 4-acetoxyazetid-2-one **8** (1.00 g, 7.74 mmol) in dichloromethane (25 cm^3) at room temperature was added allyltrimethylsilane (1.77 g, 15.5 mmol, 2 equiv.) and boron trifluoride–diethyl ether (1.32 g, 9.29 mmol, 1.2 equiv.). The reaction was stirred for 24 h. The solution was washed with

water (2 × 25 cm^3), sodium bicarbonate (25 cm^3) and water (25 cm^3), and dried over magnesium sulfate. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by flash column chromatography (2:1 cyclohexane–ethyl acetate) to yield the title compound **9** as a yellow oil (580 mg, 5.22 mmol, 67%): R_f 0.38 (EtOAc); ν_{max} ($CHCl_3$)/cm^{-1} 3416 (NH), 3014, 1758 (lactam), 1642 (olefin); δ_H (500 MHz; $CDCl_3$) 6.04 (1 H, br, N*H*), 5.85–5.68 (1 H, m, C*H*=CH_2), 5.17–5.08 (2 H, m, CH=C*H*$_2$), 3.73–3.65 (1 H, m, NHC*H*), 3.06 (1 H, ddd, *J* 14.8, 5.0 and 2.1, COC*H*H), 2.61 (1 H, ddd, *J* 14.8, 2.3 and 1.5, COC*H*H), 2.47–2.26 (2 H, m, CHC*H*$_2$CH=CH_2); δ_C (100 MHz; $CDCl_3$) 167.9 (*C*=O), 133.2 (*C*H=CH_2), 118.1 (CH=*C*H$_2$), 47.0, 42.9, 39.5 (*C*H$_2$′s).

Typical procedure for *N*-alkylation of β-lactams 1a–c

1,4-Diallylazetidin-2-one 1a. To a solution of 4-allylazetidin-2-one **9** (350 mg, 3.15 mmol), 18-crown-6 (42 mg, 0.16 mmol, 5 mol%) and crushed potassium hydroxide (389 mg, 6.93 mmol, 2.2 equiv.) in benzene (15 cm^3) was added dropwise a solution of allyl bromide (762 mg, 540 μL, 6.30 mmol, 2 equiv.) in benzene (5 cm^3) over 1 h. The reaction mixture was stirred at room temperature for a further 3 h. The reaction mixture was filtered, and the filtrate was washed with water (10 cm^3). The organic layer was dried over magnesium sulfate and the solvent removed under reduced pressure. The product was purified by flash column chromatography over silica (6:4 EtOAc–hexane) to give the *title compound* **1a** as a colourless liquid (224 mg, 1.48 mmol, 47%): R_f 0.38 (6:4 EtOAc–hexane); ν_{max} ($CDCl_3$)/cm^{-1} 3084, 2925, 1739 (C=O), 1643 (C=C), 1435, 1401, 1360, 1279; δ_H (500 MHz; $CDCl_3$) 5.79–5.71 (2 H, m, 2 × C*H*=CH_2), 5.22–5.09 (4 H, m, 2 × CH=C*H*$_2$), 3.98 (1 H, ddt, *J* 15.7, 5.5 and 1.5, NC*H*H), 3.67–3.60 (2 H, m, NCH*H* and NC*H*), 2.98 (1 H, dd, *J* 14.6 and 5.0, COC*H*H), 2.60 (1 H, dd, *J* 14.6 and 2.4, COCH*H*), 2.52–2.47 (1 H, m, NCHC*H*HCH=CH_2), 2.27–2.15 (1 H, m, NCHCH*H*CH=CH_2); δ_C (62.5 MHz; $CDCl_3$) 166.8 (*C*=O), 132.7, 132.2 (2 × *C*H=CH_2), 118.3, 118.3 (2 × CH=*C*H$_2$), 50.6 (*C*H), 43.4, 41.8, 37.2 (*C*H$_2$′s); *m*/*z* (CI) 169 [(M + NH_4)$^+$, 100%], 152 [(M + H)$^+$, 60], 128 (26), 52 (16) [Found: (M + H)$^+$ 152.1075. $C_9H_{14}NO$ requires *M*, 152.1075].

4-Allyl-1-but-3-enylazetidin-2-one 1b. The product was prepared from 4-allylazetidin-2-one **9** (350 mg, 3.15 mmol) by alkylation with but-3-enyl bromide as described above to give the *title compound* **1b** as a colourless liquid (183 mg, 1.11 mmol, 35%): R_f 0.41 (6:4 EtOAc–hexane); ν_{max} ($CDCl_3$)/cm^{-1} 3082, 2925, 1737 (C=O), 1642 (C=C), 1439, 1406, 1360; δ_H (500 MHz; $CDCl_3$) 5.79–5.71 (2 H, m, 2 × C*H*=CH_2), 5.16–5.05 (4 H, m, 2 × CH=C*H*$_2$) 3.66–3.62 (1 H, m, NC*H*), 3.44 (1 H, dt, 14.1 and 7.4, NC*H*H), 3.06 (1 H, dt, *J* 14.1 and 6.8, NCH*H*), 2.95 (1 H, dd, *J* 14.5 and 5.0, COC*H*H), 2.56 (1 H, dd, *J* 14.5 and 2.4, COCH*H*), 2.53–2.48 (1 H, m, NCHC*H*HCH=CH_2), 2.34–2.23 (3 H, m, NCHCH*H*CH=CH_2 and NCH$_2$C*H*$_2$); δ_C (62.5 MHz; $CDCl_3$) 166.9 (*C*=O), 135.0, 132.7 (2 × *C*H=CH_2), 118.4, 117.1 (2 × CH=*C*H$_2$), 50.7 (*C*H), 41.6, 40.0, 37.2, 32.5 (*C*H$_2$′s); *m*/*z* (CI) 166 [(M + H)$^+$, 100%], 137 (17), 124 (23), 82 (30) [Found: (M + H)$^+$ 166.1216. $C_{10}H_{16}NO$ requires *M*, 166.1231].

4-Allyl-1-pent-4-enylazetidin-2-one 1c. The product was prepared from 4-allylazetidin-2-one **9** (100 mg, 0.90 mmol) by alkylation with pent-4-enyl bromide as described above to give the *title compound* **1c** as a colourless liquid (60 mg, 0.34 mmol, 37%): R_f 0.44 (6:4 EtOAc–hexane); ν_{max} ($CDCl_3$)/cm^{-1} 3019, 2929, 1736 (C=O), 1642 (C=C); δ_H (500 MHz; $CDCl_3$) 5.82–5.72 (2 H, 2 × C*H*=CH_2), 5.16–5.12 (2 H, m, NCHCH$_2$CH=C*H*$_2$), 5.05–4.98 (2 H, m, N(CH$_2$)$_3$CH=C*H*$_2$), 3.65–3.61 (1 H, m, NC*H*), 3.38–3.32 (1 H, m, NC*H*H), 3.05–2.99 (1 H, ddd, *J* 14.1, 7.7 and 6.2, NCH*H*), 2.96 (1 H, dd, *J* 1.45 and 4.9, COC*H*H), 2.58 (1 H, dd, *J* 14.5 and 2.3, COCH*H*), 2.54–2.28 (1 H, m, NCHC*H*HCH), 2.30–2.24 (1 H, m, NCHCH*H*CH), 2.09–2.05 (2 H, m, N(CH$_2$)$_2$C*H*$_2$), 1.70–1.60 (2 H, m, NCH$_2$-C*H*$_2$); δ_C (100 MHz; $CDCl_3$) 166.9 (*C*=O), 137.3, 132.7 (2 × *C*H=CH_2), 118.4, 115.4 (2 × CH=*C*H$_2$), 50.6 (*C*H), 41.6, 40.1, 37.2, 31.1, 27.2 (*C*H$_2$′s); *m*/*z* (ES) 202 [(M + Na)$^+$, 100%] [Found: (M + Na)$^+$ 202.1201. $C_{11}H_{17}NNaO$ requires *M*, 202.1208].

Typical procedure for *N*-alkylation of succinimide 10 and glutarimide 11 using Mitsunobu conditions to prepare 12a,b and 13a,b

***N*-Allylsuccinimide 12a.**[15] To a solution of succinimide **10** (2.00 g, 20.2 mmol), triphenylphosphine (6.88 g, 26.2 mmol, 1.3 equiv.) and allyl alcohol (1.40 g, 1.64 cm^3, 24.2 mmol, 1.2 equiv.) in THF (100 cm^3) at 0 °C was added dropwise diethyl azodicarboxylate (4.56 g, 4.14 cm^3, 26.2 mmol, 1.3 equiv.). The mixture was allowed to warm to room temperature and was stirred for 24 h. The solvent was removed under reduced pressure and ether (100 cm^3) was added. The solution was concentrated under reduced pressure to *ca*. 10 cm^3, and the resulting mixture was filtered. The residue was washed with ether. The filtrate was then concentrated under reduced pressure and purified by flash column chromatography over silica (7:3 hexane–EtOAc) to give the title compound **12a** as a yellow oil (2.67 g, 19.2 mmol, 95%): R_f 0.12 (7:3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3090, 2988, 2940, 1775, 1705 (C=O), 1645 (C=C), 1432, 1394, 1332, 1195, 1176, 1132; δ_H (250 MHz; $CDCl_3$) 5.85–5.69 (1 H, m, C*H*=CH_2), 5.24–5.14 (2 H, m, CH=C*H*$_2$), 4.10 (2 H, dt, *J* 5.9 and 1.3, NC*H*$_2$), 2.71 (4 H, s, 2 × COC*H*$_2$); δ_C (62.5 MHz; $CDCl_3$) 176.7 (2 × *C*=O), 130.7 (*C*H=CH_2), 118.4 (CH=*C*H$_2$), 40.9 (N*C*H$_2$), 28.2 (2 × CO*C*H$_2$).

1-But-3-enylpyrrolidine-2,5-dione 12b.[15] Alkylation of succinimide **10** (100 mg, 1.01 mmol) with but-3-enol as described above gave the title compound **12b** as a pale yellow oil (145 mg, 0.95 mmol, 94%): R_f 0.14 (7:3 hexane–EtOAc); ν_{max}($CDCl_3$)/cm^{-1} 3082, 2982, 2947, 1775, 1702 (C=O), 1641 (C=C), 1436, 1404, 1365, 1346, 1194, 1132; δ_H (250 MHz; $CDCl_3$) 5.78–5.64 (1 H, m, C*H*=CH_2), 5.09–5.00 (2 H, m, CH=C*H*$_2$), 3.59 (2 H, t, *J* 7.1, NC*H*$_2$), 2.68 (4 H, s, 2 × COC*H*$_2$), 2.34 (2 H, qt, *J* 7.1 and 1.2, NCH$_2$C*H*$_2$); δ_C (62.5 MHz; $CDCl_3$) 177.1 (2 × *C*=O), 134.4 (*C*H=CH_2), 117.4 (CH=*C*H$_2$), 37.9 (N*C*H$_2$), 31.9 (NCH$_2$*C*H$_2$), 28.1 (2 × CO*C*H$_2$).

***N*-Allylglutarimide 13a.**[15] Alkylation of glutarimide **11** (2.00 g, 17.7 mmol) with allyl alcohol as described above gave the title compound **13a** as a colourless oil (1.707 g, 11.1 mmol, 63%): R_f 0.16 (7:3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3087, 2966, 2905, 1727, 1675 (C=O), 1430, 1374, 1355, 1335, 1235, 1182, 1124; δ_H (250 MHz; $CDCl_3$) 5.86–5.71 (1 H, m, C*H*=CH_2), 5.19–5.10 (2 H, m, CH=C*H*$_2$), 4.37 (2 H, dt, *J* 5.8 and 1.4, NC*H*$_2$), 2.66 (4 H, t, *J* 6.6, 2 × COC*H*$_2$), 19.4 (2 H, quintet, *J* 6.6, COCH$_2$C*H*$_2$); δ_C (62.5 MHz; $CDCl_3$) 172.1 (2 × *C*=O), 132.2 (*C*H=CH_2), 117.3 (CH=*C*H$_2$), 41.5 (N*C*H$_2$), 32.8 (2 × CO*C*H$_2$), 17.2 (COCH$_2$*C*H$_2$).

1-But-3-enylpiperidine-2,6-dione 13b.[15] Alkylation of glutarimide **11** (2.00 g, 17.7 mmol) with but-3-enol as described above gave the title compound **13b** as a yellow oil (2.368 g, 14.2 mmol, 80%): R_f 0.19 (7:3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3080, 2967, 2906, 1725, 1672 (C=O), 1437, 1404, 1358, 1278, 1180, 1122; δ_H (250 MHz; $CDCl_3$), 5.82–5.66 (1 H, m, C*H*=CH_2), 5.05–4.96 (2 H, m, CH=C*H*$_2$), 3.84 (2 H, t, *J* 7.2, NC*H*$_2$), 2.62 (4 H, t, *J* 6.6, 2 × COC*H*$_2$), 2.27 (2 H, q, *J* 7.2, NCH$_2$C*H*$_2$), 1.90 (2 H, quintet, *J* 6.6, 2 × COCH$_2$C*H*$_2$); δ_C (62.5 MHz; $CDCl_3$) 172.4 (2 × *C*=O), 135.1 (*C*H=CH_2), 116.8 (CH=*C*H$_2$), 38.5 (N*C*H$_2$), 32.9 (2 × CO*C*H$_2$), 32.4 (NCH$_2$*C*H$_2$), 17.1 (COCH$_2$*C*H$_2$).

Typical procedure for *N*-alkylation of succinimide 10 and glutarimide 11 with 5-bromopent-1-ene

1-Pent-4-enylpyrrolidine-2,5-dione 12c.[15] Following the procedure of Mori,[11] a solution of succinimide (5.0 g, 50.5 mmol) in DMF (25 cm^3) was stirred at 0 °C and sodium hydride (60%, 2.22 g, 55.5 mmol, 1.1 equiv.) was added. After the reaction was stirred for 5 minutes the solution was allowed to warm to room temperature and stirred for a further hour. 5-Bromopent-1-ene (7.5 g, 50.5 mmol, 1 equiv.) was added dropwise and the solution stirred for a further 3 h. The reaction was poured into water (50 cm^3) and saturated aqueous ammonium chloride solution (50 cm^3). The reaction mixture was extracted with ether (3 × 25 cm^3) the combined organic layers were washed with water (3 × 50 cm^3) and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the product was purified by flash column chromatography (60 : 40 hexane–ethyl acetate) to give the title compound **12c** as a colourless liquid (6.35 g, 38 mmol, 75%): R_f 0.24 (6 : 4 hexane–EtOAc); ν_{max} ($CHCl_3$)/cm^{-1} 2944, 1774 and 1708 (2 × C=O), 1641 (olefin), 1440, 1403, 1373, 1345; δ_H (250 MHz; $CDCl_3$) 5.81–5.68 (1 H, m, C*H*=CH_2), 5.05–4.92 (2 H, m, CH=CH_2), 3.48 (2 H, t, *J* 6.7, NCH_2), 2.66 (4 H, s, COCH_2), 2.03 (q, *J* 7.3, CH_2CH=CH_2), 1.64 (2 H, quintet, *J* 7.4, NCH_2CH_2); δ_C (63 MHz; $CDCl_3$) 177.2 (2*C*=O), 137.2 (*C*H=CH_2), 115.2 (CH=*C*H_2), 38.4 (N*C*H_2), 30.9, 26.7 (aliphatic *C*H_2′s), 28.1 (2 ring *C*H_2′s).

1-Pent-4-enylpiperidine-2,6-dione 13c.[15] Glutarimide (5.0 g, 44 mmol) was alkylated with pent-4-enyl bromide as described above to give the title compound **13c** as a colourless liquid (6.6 g, 36.5 mmol, 83%): R_f 0.26 (6 : 4 hexane–EtOAc); ν_{max} ($CHCl_3$)/cm^{-1} 2964, 1724 and 1679 (2 × C=O), 1462, 1438, 1389, 1357; δ_H (250 MHz; $CDCl_3$) 5.97–5.70 (1 H, m, C*H*=CH_2), 5.04–4.91 (2 H, m, CH=CH_2), 3.73 (2 H, t, *J* 7.6, NCH_2), 2.62 (4 H, t, *J* 6.5, COCH_2), 2.03 (q, *J* 7.2, CH_2CH=CH_2), 1.90 (2 H, quintet, *J* 6.6, NCH_2CH_2), 1.57 (2 H, quintet, *J* 7.6, $COCH_2CH_2$); δ_C (63 MHz; $CDCl_3$) 172.5 (2*C*=O), 137.8 (*C*H=CH_2), 114.9 (CH=*C*H_2), 39.2 (N*C*H_2), 32.9 (2 ring *C*H_2′s) 31.1, 27.0, 17.2 (aliphatic *C*H_2′s).

Typical procedure for reduction of imides with sodium borohydride in acidic ethanol

5-Ethoxy-1-prop-2-enylpyrrolidin-2-one 14a.[15] To a mixture of *N*-allylsuccinimide **12a** (2.61 g, 18.5 mmol), sodium borohydride (3.00 g, 79 mmol, 4 equiv.) and bromocresol green (6 drops, 0.04 wt%–H_2O) in ethanol (80 cm^3) at −10 °C was added 6 drops 2 M HCl every *ca*. 15 minutes for 2 h. After 2 h, 6 M HCl was added over 30 min to bring the pH to *ca*. 4. Water (30 cm^3) was added and the mixture extracted with dichloromethane (3 × 40 cm^3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ then dried over magnesium sulfate. The solvent was removed under reduced pressure, and the product was purified by flash column chromatography over silica (7 : 3 hexane–EtOAc) to give the title compound **14a** as a colourless oil (1.61 g, 9.5 mmol, 51%): R_f 0.09 (7 : 3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3086, 2981, 2931, 1687 (C=O), 1645 (C=C), 1449, 1416, 1350, 1248, 1172, 1075; δ_H (250 MHz; $CDCl_3$) 5.81–5.66 (1 H, m, C*H*=CH_2), 5.21–5.13 (2 H, m, CH=CH_2), 4.92 (1 H, dd, *J* 6.2 and 1.4, NC*H*), 4.30–4.21 (1 H, m, NC*H*H), 3.57 (1 H, ddd, *J* 15.4, 7.5 and 0.9, NCH*H*), 3.45 (2 H, q, *J* 7.0, OCH_2), 2.62–1.96 (4 H, m, $COCH_2CH_2$), 1.19 (3 H, t, *J* 7.0, OCH_2CH_3); δ_C (62.5 MHz; $CDCl_3$) 174.8 (*C*=O), 132.5 (*C*H=CH_2), 117.9 (CH=*C*H_2), 88.4 (N*C*H), 61.7 (O*C*H_2), 42.8 (N*C*H_2), 29.0, 24.9 (2 × *C*H_2), 15.3 (*C*H_3).

5-Ethoxy-1-but-4-enylpyrrolidin-2-one 14b.[15] Reduction of the imide **12b** (2.62 g, 17.1 mmol) as described above gave the title compound **14b** as a colourless oil (1.84 g, 10.1 mmol, 59%): R_f 0.10 (7 : 3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3081, 2980, 2940, 1686 (C=O), 1641 (C=C), 1456, 1422, 1346, 1249, 1172, 1075; δ_H (250 MHz; $CDCl_3$) 5.85–5.68 (1 H, m, C*H*=CH_2), 5.11–4.99 (2 H, m, CH=CH_2), 4.96 (1 H, dd, *J* 6.2 and 1.5, NC*H*), 3.64–3.53 (1 H, m, NC*H*H), 3.45 (2 H, q, *J* 7.0, OCH_2), 3.19–3.08 (1 H, m, NCH*H*), 2.57–1.95 (6 H, m, $COCH_2CH_2$ and NCH_2CH_2), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3); δ_C (62.5 MHz; $CDCl_3$) 174.9 (*C*=O), 135.3 (*C*H=CH_2), 116.7 (CH=*C*H_2), 89.2 (N*C*H), 61.3 (O*C*H_2), 39.8 (N*C*H_2), 32.1, 29.0, 24.8 (*C*H_2′s), 15.3 (*C*H_3).

5-Ethoxy-1-pent-4-enylpyrrolidin-2-one 14c.[15] Reduction of the imide **12c** (238 mg, 1.42 mmol) as described above gave the title compound **14c** as a colourless liquid (200 mg, 1.01 mmol, 71%): R_f 0.34 (EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3080, 2979, 2932, 1838, 1685 (amide), 1641 (olefin), 1454, 1422, 1376, 1348, 1283, 1218, 1172, 1076; δ_H (250 MHz; $CDCl_3$) 5.88–5.72 (1 H, m, C*H*=CH_2), 5.07–4.94 (3 H, m, CH=CH_2 + C*H*OEt), 3.54–3.41 (1 H, m, NC*H*H), 3.45 (2 H, q, *J* 7.0, OCH_2CH_3), 3.16–3.05 (1 H, m, NCH*H*), 2.59–2.45 (1 H, m, COC*H*H), 2.30–2.24 (1 H, m, COCH*H*), 2.15–2.09 (1 H, m, $COCH_2CHH$), 2.07–2.02 (2 H, m, CH_2CH=CH_2), 1.97–1.92 (1 H, m, $COCH_2CHH$), 1.76–1.55 (2 H, m, NCH_2CH_2), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3); δ_C (63 MHz; $CDCl_3$) 173.2 (*C*=O), 137.7 (*C*H=CH_2), 115.0 (CH=*C*H_2), 89.1 (*C*HOEt), 61.3 (OCH_2CH_3), 40.1 (N*C*H_2), 31.1 (*C*H_2CH=CH_2), 29.0 (CO*C*H_2), 26.8 (NCH_2CH_2), 24.8 ($COCH_2CH_2$), 15.2 (OCH_2CH_3).

6-Ethoxy-1-prop-2-enylpiperidin-2-one 15a. Reduction of the imide **13a** (1.69 g, 11.0 mmol) as described above gave the *title compound* **15a** as a colourless oil (1.28 g, 7.0 mmol, 64%): R_f 0.12 (7 : 3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3084, 2979, 2958, 1638 (C=O), 1467, 1413, 1338, 1269, 1183, 1079; δ_H (250 MHz; $CDCl_3$) 5.85–5.70 (1 H, m, C*H*=CH_2), 5.15–5.07 (2 H, m, CH=CH_2), 4.59–4.50 (2 H, m, NC*H* and NC*H*H), 3.61–3.36 (3 H, m, NCH*H* and OCH_2), 2.46–1.60 (6 H, m, $COCH_2CH_2CH_2CH_2$), 1.21 (3 H, t, *J* 7.0, OCH_2CH_3); δ_C (62.5 MHz; $CDCl_3$) 170.1 (*C*=O), 133.5 (*C*H=CH_2), 117.0 (CH=*C*H_2), 85.2 (N*C*H), 63.4 (O*C*H_2), 46.9 (N*C*H_2), 32.4, 27.0, 15.9, 15.4; *m*/*z* (CI) 184 [(M + H)$^+$, 83%], 157 (42), 140 (100), 115 (18) [Found: (M + H)$^+$ 184.1337. $C_{10}H_{18}NO_2$ requires *M*, 184.1337].

6-Ethoxy-1-but-3-enylpiperidin-2-one 15b.[15] Reduction of the imide **13b** (2.35 g, 14.0 mmol) as described above gave the title compound **15b** as a colourless oil (1.77 g, 9.0 mmol, 64%): R_f 0.13 (7 : 3 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3080, 2978, 2958, 2882, 1638 (C=O), 1472, 1416, 1334, 1184, 1080; δ_H (250 MHz; $CDCl_3$) 5.86–5.69 (1 H, m, C*H*=CH_2), 5.09–4.97 (2 H, m, CH=CH_2), 4.56 (1 H, t, *J* 3.0, NC*H*), 3.81–3.70 (1 H, m, NC*H*H), 3.54–3.40 (2 H, m, OCH_2), 3.16–3.05 (1 H, m, NCH*H*), 2.42–1.59 (8 H, m, $COCH_2CH_2CH_2$ and NCH_2CH_2), 1.21 (3 H, t, *J* 7.0 OCH_2CH_3); δ_C (62.5 MHz; $CDCl_3$) 170.2 (*C*=O), 135.8 (*C*H=CH_2), 116.4 (CH=*C*H_2), 86.9 (N*C*H), 63.3 (O*C*H_2), 45.3 (N*C*H_2), 32.5, 32.3, 27.1, 15.9, 15.4.

6-Ethoxy-1-pent-4-enylpiperidin-2-one 15c.[15] Reduction of the imide **13c** (1.00 g, 5.53 mmol) as described above gave the title compound **15b** as a colourless liquid (747 mg, 3.54 mmol, 64%): R_f 0.42 (EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3079, 2977, 2956, 2882, 1638 (amide), 1473, 1416, 1373, 1336, 1285, 1183, 1080, 1059; δ_H (250 MHz; $CDCl_3$) 5.89–5.73 (1 H, m, C*H*=CH_2), 5.29–4.93 (2 H, m, CH=CH_2), 4.58–4.55 (1 H, m, C*H*OEt), 3.71–3.58 (1 H, m, NC*H*H), 3.55–3.39 (2 H, m, OCH_2CH_3), 3.16–3.04 (1 H, m, NCH*H*), 2.52–2.41 (1 H, m, COC*H*H), 2.35–2.21 (1 H, m, COCH*H*), 2.10–1.97 (4 H, m, CH_2CH_2 and $COCH_2CCHHCHH$), 1.74–1.60 (4 H, m, NCH_2 and $COCH_2CCHHCHH$), 1.22 (3 H, t, *J* 7.0, OCH_2CH_3); δ_C (63 MHz; $CDCl_3$) 170.3 (*C*=O), 138.1 (*C*H=CH_2), 114.8 (CH=*C*H_2), 86.7 (*C*HOEt), 63.3 (OCH_2CH_3), 45.4 (N*C*H_2), 32.3 (CO*C*H_2), 31.2 (*C*HCH=CH_2), 27.2, 27.1, 15.9 (*C*H_2′s), 15.3 (OCH_2CH_3).

Typical procedure for the allylation of ethoxy-lactams 14a–c and 15a–c

1,5-Diallylpyrrolidin-2-one 2a. To a solution of 5-ethoxy-1-prop-2-enylpyrrolidin-2-one **14a** (1.59 g, 9.40 mmol) in dichloromethane (25 cm^3) at room temperature was added allyltrimethylsilane (3.22 g, 4.48 cm^3, 28 mmol, 3 equiv.) and boron trifluoride–diethyl ether (2.67 g, 2.38 cm^3, 18.8 mmol, 2 equiv.). After the reaction mixture was stirred for 24 h, dichloromethane (20 cm^3) was added, and the reaction mixture was washed with water (2 × 25 cm^3). The organic layer was separated and dried over magnesium sulfate and the solvent was then removed under reduced pressure. The crude material was purified by flash column chromatography over silica (10% Et_2O–CH_2Cl_2) to give the *title compound* **2a** as a colourless liquid (1.26 g, 7.6 mmol, 81%): R_f 0.16 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3083, 2928, 1673 (C=O), 1644 (C=C), 1447, 1416, 1363, 1257; δ_H (500 MHz; $CDCl_3$) 5.75–5.64 (2 H, m, 2 × C*H*=CH_2), 5.20–5.10 (4 H, m, 2 × CH=C*H*$_2$), 4.31 (1 H, ddt, *J* 15.5, 4.8 and 1.7, NC*H*H), 3.68–3.63 (1 H, m, NC*H*), 3.51 (1 H, dd, *J* 15.5 and 7.3, NCH*H*), 2.43–2.37 (2 H, m, COC*H*H and NCHC*H*HCH=CH_2), 2.34–2.27 (1 H, m, COCH*H*), 2.19–2.13 (1 H, m, NCHCH*H*CH=CH_2), 2.12–2.05 (1 H, m, $COCH_2$C*H*H), 1.88–1.72 (1 H, m, $COCH_2$CH*H*); δ_C (62.5 MHz; $CDCl_3$) 174.8, 132.8, 132.7 (2 × *C*H=CH_2), 118.7, 117.7 (2 × CH=*C*H$_2$), 56.6 (*C*H), 43.1, 37.3, 30.0, 23.3 (*C*H$_2$′s); *m*/*z* (CI) 166 [(M + H)$^+$, 100%], 124 (9), 52 (15) [Found: (M + NH_4)$^+$ 183.1497. $C_{10}H_{19}N_2O$ requires *M*, 183.1497].

5-Allyl-1-but-3-enylpyrrolidin-2-one 2b. Allylation of 5-ethoxy-1-but-4-enylpyrrolidin-2-one **14b** (1.80 g, 9.85 mmol) as described above gave the *title compound* **2b** as a colourless liquid (1.42 g, 7.9 mmol, 80%): R_f 0.15 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3081, 2932, 1671 (C=O), 1642 (C=C), 1459, 1424, 1367, 1290; δ_H (500 MHz; $CDCl_3$) 5.79–5.65 (2 H, m, 2 × C*H*=CH_2), 5.15–5.01 (4 H, m, 2 × CH=C*H*$_2$), 3.74 (1 H, dt, *J* 13.9 and 7.8, NC*H*H), 3.69–3.64 (1 H, m, NC*H*), 2.98–2.92 (1 H, m, NCH*H*), 2.43–2.15 (6 H, m, NCH_2CH_2, $COCH_2$ and NCHCH_2CH=CH_2), 2.10–2.02 (1 H, m, $COCH_2$C*H*H), 1.75–1.68 (1 H, m, $COCH_2$CH*H*); δ_C (62.5 MHz; $CDCl_3$) 175.0 (*C*=O), 135.2, 132.8 (2 × *C*H=CH_2), 118.7, 116.8 (2 × CH=*C*H$_2$), 56.8 (*C*H), 39.5, 37.5, 31.8, 30.1, 23.4 (*C*H$_2$′s); *m*/*z* (CI) 180 [(M + H)$^+$, 100%], 138 (6) [Found: (M + H)$^+$ 180.1388. $C_{11}H_{18}NO$ requires *M*, 180.1388].

5-Allyl-1-pent-4-enylpyrrolidin-2-one 2c. Allylation of 5-ethoxy-1-pent-4-enylpyrrolidin-2-one **14c** (75 mg, 0.38 mmol) as described above gave the *title compound* **2c** as a colourless liquid (60 mg, 0.31 mmol, 82%): R_f 0.38 (EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3081, 2933, 1670 (C=O), 1642 (C=C), 1460, 1424, 1360, 1288, 1250; δ_H (500 MHz; $CDCl_3$) 5.82–5.73 (1 H, m, $N(CH_2)_3CH$), 5.71–5.63 (1 H, m, $NCHCH_2CH$), 5.14–5.10 (2 H, m, $NCHCH_2CH$=CH_2), 5.02–4.94 (2 H, m, $N(CH_2)_3$-CH=CH_2), 3.67–3.58 (2 H, m, NC*H* and NC*H*H), 2.90 (1 H, ddd, *J* 13.9, 9.0 and 5.0, NCH*H*), 2.41–2.23 (3 H, m, $COCH_2$ and NCHC*H*HCH), 2.19–2.13 (1 H, m, NCHCH*H*CH), 2.10–2.01 (3 H, m, $COCH_2$C*H*H and $N(CH_2)_2CH_2$), 1.75–1.68 (1 H, m, $COCH_2$CH*H*), 1.67–1.50 (2 H, m, NCH_2CH_2); δ_C (62.5 MHz; $CDCl_3$) 175.0 (*C*=O), 137.7, 132.8 (2 × *C*H=CH_2), 118.7, 115.1 (2 × CH=*C*H$_2$), 56.8 (*C*H), 39.9, 37.5, 31.1, 30.1, 26.5, 23.4 (*C*H$_2$′s); *m*/*z* (ES) 216 [(M + Na)$^+$, 100%] [Found: (M + Na)$^+$ 216.1363. $C_{12}H_{19}NNaO$ requires *M*, 216.1364].

1,6-Diallylpiperidin-2-one 3a. Allylation of 6-ethoxy-1-prop-2-enylpiperidin-2-one **15a** (1.26 g, 6.89 mmol) as described above gave the *title compound* **3a** as a colourless liquid (727 mg, 4.06 mmol, 59%): R_f 0.16 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3082, 2954, 1622 (C=O), 1472, 1414, 1345, 1272; δ_H (500 MHz; $CDCl_3$) 5.81–5.73 (1 H, m, NCH_2CH), 5.71–5.63 (1 H, m, $NCHCH_2CH$=CH_2), 5.15–5.08 (4 H, m, 2 × CH=CH_2), 4.55 (1 H, ddt, *J* 15.5, 4.7 and 1.7, NC*H*H), 3.52 (1 H, dd, *J* 15.5 and 6.9, NCH*H*), 3.44–3.39 (1 H, m, NC*H*), 2.47–2.42 (1 H, m, NCHC*H*HCH), 2.40–2.36 (2 H, m, $COCH_2$), 2.26–2.20 (1 H, m, NCHCH*H*CH), 1.91–1.66 (4 H, m, $COCH_2CH_2CH_2$); δ_C (62.5 MHz; $CDCl_3$) 169.9 (*C*=O), 134.1, 133.6 (2 × *C*H=CH_2), 118.1, 116.7 (2 × CH=*C*H$_2$), 55.4 (*C*H), 47.4, 37.0, 31.9, 26.1, 17.1 (*C*H$_2$′s); *m*/*z* (CI) 180 [(M + H)$^+$, 100%], 138 (7) [Found: (M + H)$^+$ 180.1388. $C_{11}H_{18}NO$ requires *M*, 180.1388].

6-Allyl-1-but-3-enylpiperidin-2-one 3b. Allylation of 6-ethoxy-1-but-3-enylpiperidin-2-one **15b** (1.72 g, 8.74 mmol) as described above gave the *title compound* **3b** as a colourless liquid (747 mg, 3.86 mmol, 44%): R_f 0.14 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3080, 2950, 1620 (C=O), 1476, 1447, 1416, 1345, 1265; δ_H (500 MHz; $CDCl_3$) 5.82–5.64 (2 H, m, 2 × C*H*=CH_2), 5.12–5.00 (4 H, m, 2 × CH=C*H*$_2$), 3.96 (1 H, ddd, *J* 13.5, 8.5 and 6.1, NC*H*H), 3.41–3.37 (1 H, m, NC*H*), 2.86 (1 H, ddd, *J* 13.5, 8.3 and 6.2, NCH*H*), 2.45–2.21 (6 H, m, $COCH_2$-$(CH_2)_2CHCH_2$ and NCH_2CH_2), 1.87–1.64 (4 H, m, $COCH_2$-CH_2CH_2); δ_C (62.5 MHz; $CDCl_3$) 170.0 (*C*=O), 135.6, 134.2 (2 × *C*H=CH_2), 118.1, 116.6, (2 × CH=*C*H$_2$), 56.3 (*C*H), 44.9, 37.3, 32.1, 31.9, 26.0 (*C*H$_2$′s); *m*/*z* (CI) 194 [(M + H)$^+$, 100%], 152 (12) [Found: (M + H)$^+$ 194.1545. $C_{12}H_{20}NO$ requires *M*, 194.1545].

6-Allyl-1-pent-4-enylpiperidin-2-one 3c. Allylation of 6-ethoxy-1-pent-4-enylpiperidin-2-one **15c** (594 mg, 2.81 mmol) as described above gave the *title compound* **3c** as a colourless liquid (308 mg, 1.49 mmol, 53%): R_f 0.61 (EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3080, 2948, 1619 (C=O), 1477, 1416, 1345, 1292; δ_H (500 MHz; $CDCl_3$) 5.83–5.75 (1 H, m, $N(CH_2)_3CH$), 5.71–5.63 (1 H, m, $NCHCH_2CH$), 5.11–5.07 (2 H, m, $NCHCH_2$-CH=CH_2), 5.03–4.94 (2 H, m, $N(CH_2)_3CH$=CH_2), 3.82 (1 H, ddd, *J* 13.5, 9.2 and 6.3, NC*H*H), 3.40–3.35 (1 H, m, NC*H*), 2.83 (1 H, ddd, *J* 13.5, 9.2 and 5.8, NCH*H*), 2.44–2.39 (1 H, m, NCHC*H*HCH), 2.35–2.32 (2 H, m, $COCH_2$), 2.26–2.19 (1 H, m, NCHCH*H*CH), 1.85–1.59 (6 H, m, $COCH_2CH_2CH_2$ and NCH_2CH_2); δ_C (62.5 MHz; $CDCl_3$) 170.0 (*C*=O), 138.0, 134.2 (2 × *C*H=CH_2), 118.1, 114.9 (2 × CH=*C*H$_2$), 56.1 (*C*H), 45.1, 37.3, 31.9, 31.2, 26.7, 26.1, 17.0 (*C*H$_2$′s); *m*/*z* (ES) 230 [(M + Na)$^+$, 100%], 208 (15) [Found: (M + H)$^+$ 208.1700. $C_{13}H_{22}NO$ requires *M*, 208.1701].

Typical procedure for ring-closing metathesis reactions

1-Azabicyclo[4.2.0]oct-3-en-8-one 5a.[8] To a solution of the bis-alkenyl lactam **1a** (100 mg, 0.661 mmol) in dichloromethane (20 cm^3) at room temperature was added a solution of **4** (27 mg, 0.033 mmol, 5 mol%) in dichloromethane (10 cm^3) *via* a cannula. The reaction was stirred for 2 h. The solvent was removed under reduced pressure and the product was purified by flash column chromatography (10% Et_2O–CH_2Cl_2) to give the title compound **5a** as a colourless liquid (65 mg, 0.528 mmol, 80%): R_f 0.16 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3042, 2940, 2857, 1740 (C=O), 1648 (C=C), 1450, 1402, 1360, 1264; δ_H (500 MHz; $CDCl_3$) 5.83–5.79 (1 H, m, NCH_2CH=C*H*), 5.70–5.67 (1 H, m, NCH_2CH=CH), 4.06–4.02 (1 H, m, NC*H*H), 3.49–3.42 (2 H, m, NCH*H* and NC*H*), 3.17 (1 H, ddd, *J* 14.5, 4.5 and 2.0, COC*H*H), 2.53 (1 H, dd, *J* 14.5 and 1.7, COCH*H*), 2.46–2.41 (1 H, m, NCH_2CH=CHC*H*H), 2.11–2.03 (1 H, m, NCH_2CH=CHCH*H*); δ_C (62.5 MHz; $CDCl_3$) 166.9 (*C*=O), 123.7, 122.5 (*C*H=*C*H), 43.0 (*C*H), 45.2, 38.4, 28.7 (*C*H$_2$′s); *m*/*z* (CI) 141 [(M + NH_4)$^+$, 100%], 124 (42), 80 (35) (Found: M$^+$ 123.0684. C_7H_9NO requires *M*, 123.0684).

1-Azabicyclo[5.2.0]non-4-en-9-one 5b. Ring-closing metathesis of 4-allyl-1-but-3-enylazetidin-2-one **1b** (100 mg, 0.605 mmol) as described above gave the *title compound* **5b** as a

colourless liquid (79 mg, 0.576 mmol, 95%): R_f 0.14 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3031, 2944, 2919, 1732 (C=O), 1642 (C=C), 1440, 1429, 1413, 1364, 1293; δ_H (500 MHz; $CDCl_3$) 5.95–5.89 (1 H, m, NCH_2CH_2CH), 5.86–5.81 (1 H, m, NCH_2CH_2CH=C*H*), 3.75 (1 H, ddd, *J* 13.4, 5.1 and 3.4, NC*H*H), 3.54–3.50 (1 H, m, NC*H*), 2.99 (1 H, ddd, *J* 14.4, 4.7 and 1.6, COC*H*H), 2.80–2.75 (1 H, m, NCH*H*), 2.55 (1 H, dd, *J* 14.4 and 2.1, COCH*H*), 2.44–2.32 (3 H, m, NCH_2CHHCH=$CHCH_2$), 2.19–2.13 (1 H, m, NCH_2CH*H*); δ_C (62.5 MHz; $CDCl_3$) 165.7 (*C*=O), 131.8, 129.4 (*C*H=*C*H), 50.0 (*C*H), 43.0, 39.6, 34.1, 27.7 (CH_2′s); *m*/*z* (EI) 137 (M^+, 15%), 109 (9), 81 (59), 70 (50), 50 (100) (Found: M^+ 137.0839. $C_8H_{11}NO$ requires *M*, 137.0841).

1-Azabicyclo[6.2.0]dec-5-en-10-one 5c. Ring-closing metathesis of 4-allyl-1-pent-4-enylazetidin-2-one **1c** (293 mg, 1.63 mmol) as described above gave the *title compound* **5c** as a colourless liquid (227 mg, 1.50 mmol, 92%): R_f 0.09 (6:4 hexane–EtOAc); ν_{max} ($CDCl_3$)/cm^{-1} 3022, 2984, 2938, 1728 (C=O), 1444, 1408, 1374, 1249; δ_H (500 MHz; $CDCl_3$) 5.82–5.71 (2 H, m, C*H*=C*H*), 3.79 (1 H, ddd, *J* 14.5, 5.4 and 1.7, NC*H*H), 3.54–3.50 (1 H, m, NC*H*), 2.92 (1 H, dd, *J* 14.4 and 4.9, COC*H*H), 2.66 (1 H, ddd, *J* 14.5, 12.5 and 4.7, NCH*H*), 2.58 (1 H, dd, *J* 14.4 and 2.4, COCH*H*), 2.42–2.29 (3 H, m, $NCHCH_2CH$ and $N(CH_2)_2CH$*H*), 2.05–2.00 (1 H, m, $N(CH_2)_2CH$*H*), 1.95–1.86 (1 H, m, NCH_2CH*H*), 1.56–1.50 (1 H, m, NCH_2CH*H*); δ_C (62.5 MHz; $CDCl_3$) 167.2 (*C*=O), 133.2, 125.5 (*C*H=*C*H), 54.0 (*C*H), 41.2, 40.8, 30.7, 28.1, 24.2 (CH_2′s); *m*/*z* (EI) 202 (M^+, 100%), 122 (28), 109 (100), 96 (25), 81 (75), 67 (62), 54 (88) (Found: M^+ 151.0999. $C_9H_{13}NO$ requires *M*, 151.0997).

1-Azabicyclo[4.3.0]non-3-en-9-one 6a. Ring-closing metathesis of 1,5-diallylpyrrolidin-2-one **2a** (100 mg, 0.60 mmol) as described above gave the *title compound* **6a** as a colourless liquid (69.9 mg, 0.510 mmol, 84%): R_f 0.09 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3043, 2929, 1677 (C=O), 1651 (C=C), 1448, 1425, 1370, 1312, 1267; δ_H (500 MHz; $CDCl_3$) 5.79–5.76 (1 H, m, NCH_2CH), 5.70–5.67 (1 H, m, NCH_2CH=C*H*), 4.26–4.21 (1 H, m, NC*H*H), 3.63–3.57 (1 H, m, NC*H*), 3.54–3.50 (1 H, m, NCH*H*), 2.39–2.36 (2 H, m, $COCH_2$), 2.32–2.25 (2 H, m, NCH(C*H*H)C*H*H), 2.03–1.96 (1 H, m, NCH_2CH=CHCH*H*), 1.69–1.62 (1 H, m, $COCH_2CH$*H*); δ_C (62.5 MHz; $CDCl_3$) 174.2 (*C*=O), 124.1, 123.4 (*C*H=*C*H), 52.9 (*C*H), 40.3, 32.4, 29.9, 25.5 (CH_2′s); *m*/*z* (EI) 137 (M^+, 46%), 108 (11), 82 (33), 54 (100), 41 (27) (Found: M^+ 137.0846. $C_8H_{11}NO$ requires *M*, 137.0841).

1-Azabicyclo[5.3.0]dec-4-en-10-one 6b.[15] Ring-closing metathesis of 5-allyl-1-but-3-enylpyrrolidin-2-one **2b** (100 mg, 0.558 mmol) as described above gave the title compound **6b** as a colourless liquid (79.2 mg, 0.524 mmol, 94%): R_f 0.10 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3027, 2934, 1670 (C=O), 1459, 1439, 1425, 1370, 1294; δ_H (500 MHz; $CDCl_3$) 5.87–5.82 (1 H, m, NCH_2CH_2CH), 5.74–5.70 (1 H, m, NCH_2CH_2CH=C*H*), 3.88 (1 H, ddd, *J* 13.6 and 3.1, NC*H*H), 3.68–3.63 (1 H, m, NC*H*), 3.30–2.98 (1 H, m, NCH*H*), 2.45–2.10 (7 H, m, NCH_2CH_2 and $COCH_2CH$HCHCH_2), 1.60–1.53 (1 H, m, $COCH_2CH$*H*); δ_C (62.5 MHz; $CDCl_3$) 174.3 (*C*=O), 131.7, 128.4 (*C*H=*C*H), 58.6 (*C*H), 41.3, 36.3, 30.4, 27.8, 25.6 (CH_2′s); *m*/*z* (EI) 151 (M^+, 14%), 97 (53), 69 (71), 68 (51), 67 (27) (Found: M^+ 151.0997. $C_9H_{13}NO$ requires *M*, 151.0997).

1-Azabicyclo[6.3.0]undec-5-en-11-one 6c. Ring-closing metathesis of 5-allyl-1-pent-4-enylpyrrolidin-2-one **2c** (100 mg, 0.517 mmol) as described above gave the *title compound* **6c** as a colourless liquid which crystallised on standing (68.7 mg, 0.416 mmol, 80%): mp 43–45 °C: R_f 0.42 (5% MeOH–CH_2Cl_2) (Found: C, 72.6; H, 9.2; N, 8.5. $C_{10}H_{15}NO$ requires C, 72.7; H, 9.15; N, 8.5%); ν_{max} ($CDCl_3$)/cm^{-1} 3022, 2937, 1668 (C=O), 1462, 1422, 1366, 1294; δ_H (500 MHz; $CDCl_3$) 5.81–5.75 (1 H, m, $N(CH_2)_3CH$), 5.70–5.65 (1 H, m, $NCHCH_2CH$), 3.84 (1 H, d, *J* 13.8, NC*H*H), 3.58–3.53 (1 H, m, NC*H*), 2.74–2.69 (1 H, m, NCH*H*), 2.42–2.32 (2 H, m, COC*H*H and NCHC*H*HCH), 2.28–2.22 (2 H, m, COCH*H* and NCHCH*H*CH), 2.10–2.09 (2 H, m, $COCH_2CH$*H* and $N(CH_2)_2CH$*H*), 2.06–1.97 (2 H, m, $COCH_2CH$*H* and NCH_2CH*H*), 1.72–1.66 (1 H, m, $COCH_2CH$*H*), 1.48–1.43 (1 H, m, NCH_2CH*H*); δ_C (62.5 MHz; $CDCl_3$) 175.7 (*C*=O), 133.2, 125.6 (*C*H=*C*H), 61.4 (*C*H), 42.8, 33.0, 30.3, 26.7, 24.4, 24.3 (CH_2′s); *m*/*z* (ES) 188 [$(M + Na)^+$, 100%], 166 (9), 140 (7) [Found: $(M + H)^+$ 166.1235. $C_{10}H_{16}NO$ requires *M*, 166.1232].

1-Azabicyclo[4.4.0]dec-3-en-10-one 7a. Ring-closing metathesis of 1,6-diallylpiperidin-2-one **3a** (51 mg, 0.285 mmol) as described above gave the *title compound* **7a** as a colourless liquid (36 mg, 0.238 mmol, 84%): R_f 0.11 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3042, 2948, 1661 (C=C), 1619 (C=O), 1466, 1447, 1418, 1333, 1248; δ_H (500 MHz; $CDCl_3$) 5.76–5.73 (1 H, m, $NCHCH_2CH$), 5.68–5.65 (1 H, m, NCH_2CH), 4.73–4.68 (1 H, m, NC*H*H), 3.53–3.47 (1 H, m, NC*H*), 3.45–3.42 (1 H, m, NCH*H*), 2.38 (2 H, t, *J* 6.5, $COCH_2$), 2.20–2.13 (1 H, m, NCH_2CH=CHC*H*H), 2.09–1.97 (2 H, m, NCH(CH*H*)C*H*H), 1.85–1.78 (1 H, m, $COCH_2CH$*H*), 1.73–1.65 (1 H, m, $COCH_2CH$*H*), 1.62–1.56 (1 H, m, $COCH_2CH_2CH$*H*); δ_C (62.5 MHz; $CDCl_3$) 169.6 (*C*=O), 124.2, 124.1 (*C*H=*C*H), 52.6 (*C*H), 42.4, 32.9, 32.9, 29.1, 18.4 (CH_2′s); *m*/*z* (EI) 151 (M^+, 79%), 122 (22), 95 (46), 80 (64), 69 (53), 53 (100), 41 (83) (Found: M^+ 151.1002. $C_9H_{13}NO$ requires *M*, 151.0997).

1-Azabicyclo[5.4.0]undec-4-en-11-one 7b. Ring-closing metathesis of 6-allyl-1-but-3-enylpiperidin-2-one **3b** (51 mg, 0.264 mmol) as described above gave the *title compound* **7b** as a colourless liquid (35 mg, 0.212 mmol, 80%): R_f 0.09 (10% Et_2O–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3025, 2950, 1617 (C=O), 1475, 1435, 1416, 1369, 1282; δ_H (500 MHz; $CDCl_3$) 5.74–5.70 (1 H, m, NCH_2CH_2CH), 5.67–5.62 (1 H, m, $NCHCH_2CH$), 4.20 (1 H, ddd, *J* 13.6, 5.7 and 3.8, NC*H*H), 3.66–3.62 (1 H, m, NC*H*), 3.13 (1 H, ddd, *J* 13.6, 10.1 and 2.9, NCH*H*), 2.41–2.25 (6 H, m, $COCH_2$, NCH_2CH_2CH=C*H*CH_2), 1.89–1.82 (2 H, m, $COCH_2CH$HC*H*H), 1.75–1.68 (1 H, m, $COCH_2CH$*H*), 1.65–1.60 (1 H, m, $CO(CH_2)_2CH$*H*); δ_C (62.5 MHz; $CDCl_3$) 169.7 (*C*=O), 130.7, 126.9 (*C*H=*C*H), 57.9 (*C*H), 44.5, 35.6, 31.9, 29.9, 29.1, 18.6 (CH_2′s); *m*/*z* (EI) 165 (M^+, 73%), 111 (86), 83 (85), 55 (100), 41 (86) (Found: M^+ 165.1153. $C_{10}H_{15}NO$ requires *M*, 165.1154).

1-Azabicyclo[6.4.0]dodec-5-en-12-one 7c. Ring-closing metathesis of 6-allyl-1-pent-4-enylpiperidin-2-one **3c** (100 mg, 0.482 mmol) as described above gave the *title compound* **7c** as a colourless liquid (80 mg, 0.446 mmol, 93%): R_f 0.43 (5% MeOH–CH_2Cl_2); ν_{max} ($CDCl_3$)/cm^{-1} 3021, 2948, 1617 (C=O), 1475, 1417, 1366, 1337, 1291; δ_H (500 MHz; $CDCl_3$) 5.79–5.68 (2 H, m, C*H*=C*H*), 4.07 (1 H, ddd, *J* 13.5, 4.1 and 2.9, NC*H*H), 3.39–3.35 (1 H, m, NC*H*), 2.66 (1 H, ddd, *J* 13.5, 12.2 and 3.5, NCH*H*), 2.41–2.18 (5 H, m, $COCH_2(CH_2)_2CHCH_2$ and NCH_2CH*H*), 2.16–2.10 (2 H, m, $N(CH_2)_2CH_2$), 1.90–1.79 (2 H, m, $COCH_2CH$HC*H*H), 1.73–1.64 (2 H, m, $COCH_2CH$HCHC*H*), 1.43–1.38 (1 H, m, NCH_2CH*H*); δ_C (62.5 MHz; $CDCl_3$) 170.6 (*C*=O), 132.7, 126.5 (*C*H=*C*H), 60.4 (*C*H), 48.2, 33.7, 32.4, 30.2, 26.7, 24.2, 18.3 (CH_2′s); *m*/*z* (ES) 202 [$(M + Na)^+$, 100%], 180 (6) [Found: $(M + Na)^+$ 202.1213. $C_{11}H_{17}NNaO$ requires *M*, 202.1208].

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