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Δ^3-Aryl/heteroaryl substituted heterocycles via sequential Pd-catalysed termolecular cascade/ring closing metathesis (RCM)

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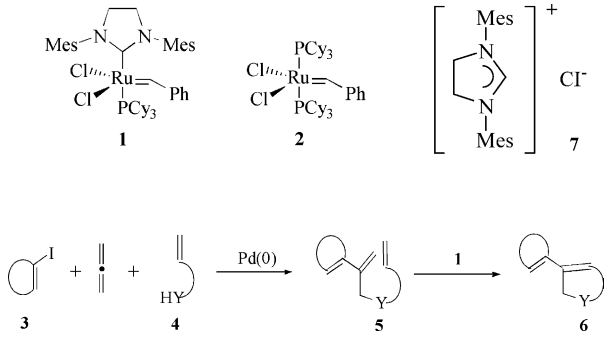
Abstract—A novel sequential Pd-catalysed termolecular allenylation cascade/Ru catalysed RCM process affords a diverse range of Δ^3-aryl/heteroaryl substituted five–seven membered nitrogen and oxygen heterocycles. Further elaboration, via 1,3-dipolar cycloaddition, in selected cases, afforded fused heterocyclic ring systems.

1. Introduction

Multicomponent cascade reactions are highly attractive from a drug discovery point of view.[1,2] Products of high complexity and diversity, which are often difficult to synthesize in a stepwise linear fashion, can be quickly accessed in a single reaction vessel. Our own efforts in this area have recently focused on employing allenes as 3-carbon building blocks in Pd-catalysed molecular queuing processes, which, combined with core organic reactions, afford products, which are of high synthetic value. Recent examples include termolecular Pd-catalysed allenylation/1,3-dipolar cycloadditions,[3,4] Pd/In Barbier type allylation,[5] and Petasis/Pd termolecular queuing processes.[6] Ring closing metathesis continues to be a highly popular reaction for the formation of carbo- and heterocyclic ring systems.[7,8] This is largely to the discovery of air-stable, second generation Ru catalysts, such as **1**, which exhibit higher thermal stability and wider functional group tolerance than parent complex **2**.[9–11] The formation of previously unattainable tri-and tetrasubstituted double bonds by **1** has also extended the scope of this excellent reaction.[12,13] Our previous work in this area has involved combination of RCM with a subsequent Heck reaction affording fused, spiro and bridged ring heterocycles.[14] Examples of strategies involving a fluorous biphasic solvent system and polymer support palladium catalyst were developed, which afforded good yields of bridged tricyclic heterocycles.[15] In other studies, we combined our palladium-catalysed cyclisation-anion capture methodology with subsequent RCM as an additional strategy for the synthesis of fused, spiro and bridged ring heterocycles.[16] Further studies showed *N*-allyl-anilines,[17] and isoquinoline and β-carboline enamines[18] were viable RCM substrates with the first generation catalyst **2**. We now report in full a 3-component Pd-catalysed cascade process employing an aryl/heteroaryl/vinyl iodide **3**, allene gas and an alkene tethered nucleophile **4**, which when coupled with RCM affords a novel and diverse strategy for the synthesis of heterocycles **6** (Scheme 1).[19–21]



Scheme 1.

Our initial studies employed *N*-allylbenzene sulphonamide as the nucleophile in the 3-component cascade and $Pd(OAc)_2$ (10 mol%) and PPh_3 (20 mol%) as the catalyst system. 1,6-Dienes **8–11** were obtained in 79–88% yield

Keywords: Ruthenium; Allene; Dipolar cycloaddition; Azomethine ylides.
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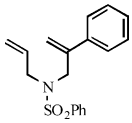
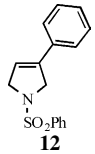
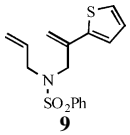
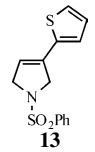
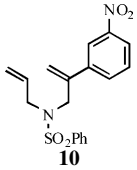
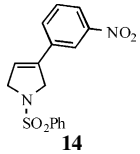
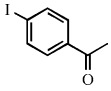
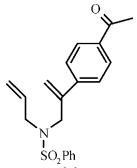
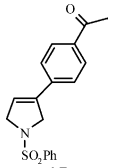
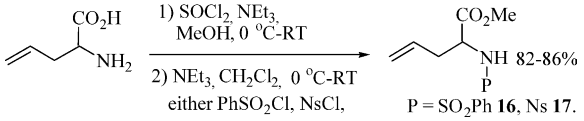
Table 1. 3-Pyrrolines via sequential pd catalysed cascade synthesis of *N*,*N*-diallylsulphonamides/RCM

Entry	Aryl/heteroaryl/vinyl iodide	Pd-cascade product[a]	Yield (%)	RCM product[b]	Yield (%)[c]
1		 **8**	86[a]/(86)[d]	 **12**	74
2		 **9**	79[a]/(72)[d]	 **13**	73
3		 **10**	85[a]/(68)[d]	 **14**	85
4		 **11**	88[a]/(70)[d]	 **15**	75

[a] Reactions carried out in toluene at 80 °C for 18 h and employed 1 mmol aryl/heteroaryl/vinyl iodide, 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, 2 mol equiv K_2CO_3, allene (1 bar) and 1 mol equiv of *N*-allylbenzene sulphonamide.
[b] Reactions carried out in toluene at 80 °C for 2–4 h and employed 5 mol% of catalyst **1**.
[c] Isolated yield.
[d] Reactions carried out in toluene at 80 °C for 16 h and employed 1 mmol aryl/heteroaryl/vinyl iodide, 2 mol% $Pd(OAc)_2$, 4 mol% of salt **7**, 3 mol equiv Cs_2CO_3, allene (0.5 bar) and 1 mol equiv of *N*-allylbenzene sulphonamide.

(Table 1).[22] We have also utilized a low loading (2 mol%) palladium/dihydroimidazol-2-ylidine catalyst system for the synthesis of the 1,6-dienes.[5,15] In this latter case, aryl/heteroaryl/vinyl iodides (1 mmol) reacted with allene (0.5 atm), $Pd(OAc)_2$ (2 mol%), salt **7** (4 mol%), Cs_2CO_3 (3 mol equiv) and *N*-allylbenzene sulphonamide in toluene at 70–80 °C over 16 h to give **8–11** (Table 1, entries 1–4) in 68–86% yield

Subjecting dienes **8–11** to **1** in toluene at 80 °C afforded Δ^3-pyrrolidines **12–15** in 73–94% yield (Table 1). With the process successfully established variation of the nucleophile tether was investigated. Nucleophile **16** was readily prepared in 86% yield from commercially available racemic allyl glycinate (Scheme 2). Employing the above conditions in the multi-component Pd-cascade afforded the α,ω-dienes **18–26** in yields of 41–81% (Table 2). The addition of tetraalkylammonium salt NEt_4Cl was found to be beneficial in this case.[23] Subjecting **18–26** to **1** in toluene at 80 °C afforded Δ^3- tetrahydropyridines **27–35** in 75–96% yield. Electron rich, deficient or sterically encumbered aryl groups

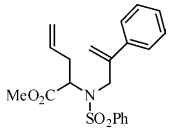
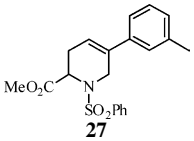
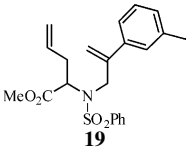
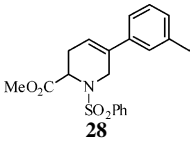
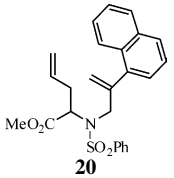
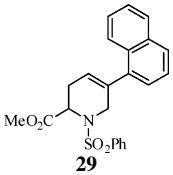
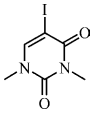
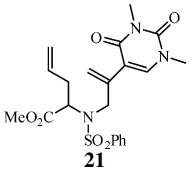
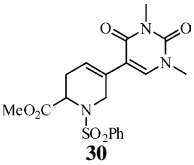
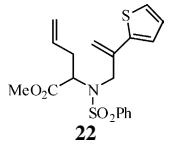
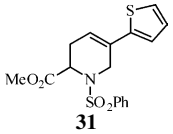
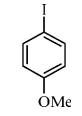
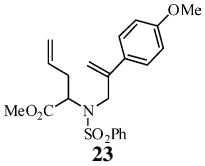
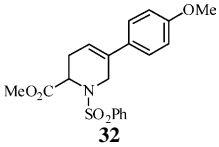
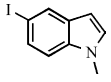
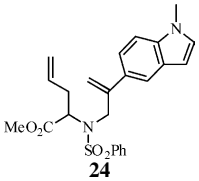
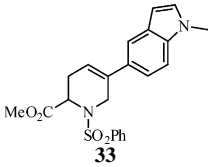
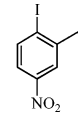
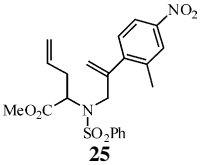
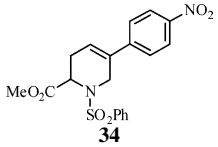
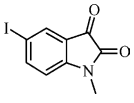
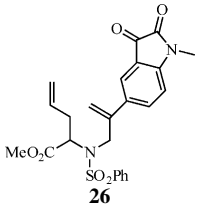
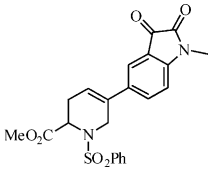


Scheme 2.

can thus be incorporated into this process with equal success. The poor yield in the Pd-cascade for entry 9 may be the result of nucleophilic attack of **16** on the activated carbonyl of the isatin. A limited investigation into nitrogen protecting groups for methyl allylglycinate (Scheme 2) showed the 2,4-dinitrobenzenesulfonyl (DNs) and Boc groups to be incompatible with the Pd-cascade conditions. However, the 4-nitrobenzenesulfonyl (Ns)[24] group proved to be suitable and nucleophile **17** was employed in the 3-component Pd-cascade process to afford **36–38** in 43–71% yield (Table 3). On subjecting **36–38** to **1** tetrahydropyridines **39–41** were formed in 76–98% yield (Table 3). Facile removal of the Ns group afforded the pipecolinic acid derivatives **42** and **43** in 83 and 70% yield, respectively, (Scheme 3).

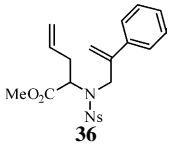
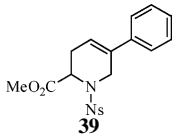
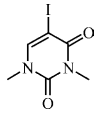
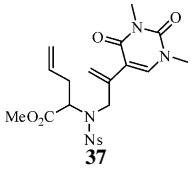
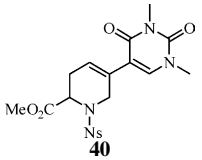
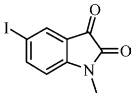
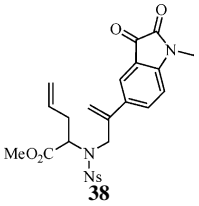
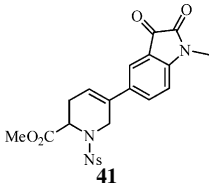
The free amino esters allowed further structural elaboration through cycloaddition chemistry. Refluxing **42**, benzaldehyde and *N*-methyl maleimide (NMM) in toluene afforded a 3.5:1 mixture of *endo* and *exo* cycloadducts **44** and **45** (Scheme 4) arising from the *syn*-dipole formed from the iminium ion generated in situ from **42** and benzaldehyde.[25] The structure of the major isomer **44** was established by X-ray crystallography (Fig. 1) and that of the minor isomer **45** by NOE studies and coupling constants. These structures are in agreement with previous related work.[26] Refluxing **42** and **43** with salicylaldehyde **46** afforded cycloadducts **47** and **48** in 56 and 54% yield, respectively.[27] The relative stereochemistry of **47** and **48** was assigned from chemical

Table 2. 3-Piperideines via sequential cascade synthesis of *N*-allyl-*N*-homoallylsulphonamides/RCM

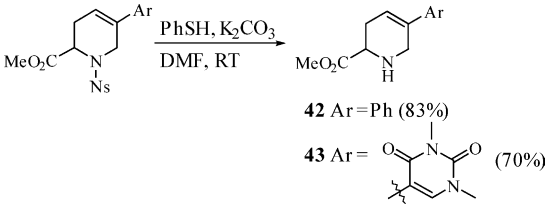
Entry	Aryl/heteroaryl/vinyl iodide	Pd-cascade product[a]	Yield (%)	RCM product[b]	Yield (%)[c]
1		 **18**	81	 **27**	77
2		 **19**	80	 **28**	75
3		 **20**	70	 **29**	75
4		 **21**	70	 **30**	84
5		 **22**	71	 **31**	71
6		 **23**	68	 **32**	96
7		 **24**	80	 **33**	83
8		 **25**	72	 **34**	74
9		 **26**	41	 **35**	83

[a] Reactions were carried out in toluene at 80 °C for 18 h and employed 1 mmol aryl/heteroaryl/vinyl iodide, 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, 2 mol equiv K_2CO_3, allene (1 bar), 1 mol equiv NEt_4Cl and 1 mol equiv **7**.
[b] Reactions were carried out in toluene at 80 °C for 2–4 h and employed 5 mol% of catalyst **1**.
[c] Isolated yield.

Table 3. Sequential Pd/Ru processes employing 4-nitrobenzenesulphonyl protection

Entry	Aryl/heteroaryl/vinyl iodide	Pd-cascade product[a]	Yield (%)	RCM product[b]	Yield (%)[c]
1		 **36**	71	 **39**	98
2		 **37**	67	 **40**	93
3		 **38**	43	 **41**	76

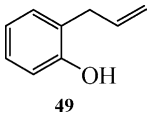
[a] Reactions carried out in toluene at 80 °C for 18 h and employed 1 mmol aryl/heteroaryl/vinyl iodide, 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, 2 mol equiv K_2CO_3, allene (1 bar), 1 mol equiv NEt_4Cl and 1 mol equiv **7**.
[b] Reactions carried out in toluene at 80 °C for 2–4 h and employed 5 mol% of catalyst **1**.
[c] Isolated yield.



Scheme 3.

shift values, coupling constants and NOE studies and is in agreement with related work previously reported by our group (Scheme 5).[28]

There has been comparatively little exploration of RCM routes to benzoxepines although there are examples involving both α,ω-diene and ene-yne precursors.[14,29] This lack of examples encouraged us to explore the alkene tethered oxygen nucleophile **49** in our Pd cascade/RCM process with three representative aryl iodides. The Pd-cascade afforded dienes **53–55** in 78–80% yield (Table 4). The RCM reaction of these dienes, utilizing **1**, proved to be more sluggish than for the formation of the five- and six-membered *N*-heterocycles and reaction times of 18 h were required to afford moderate yields of **56–58** (Table 4, 56–62%).


49

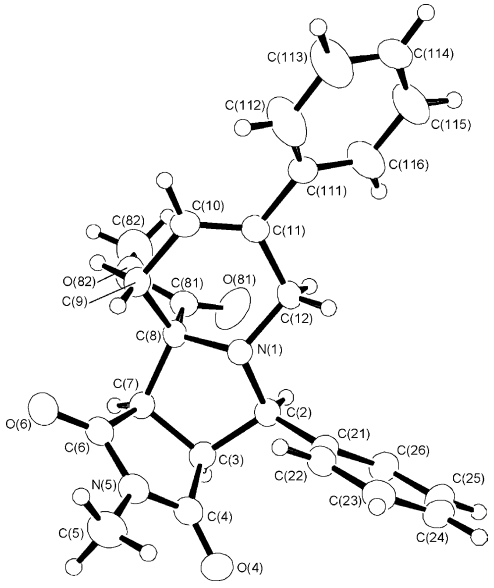
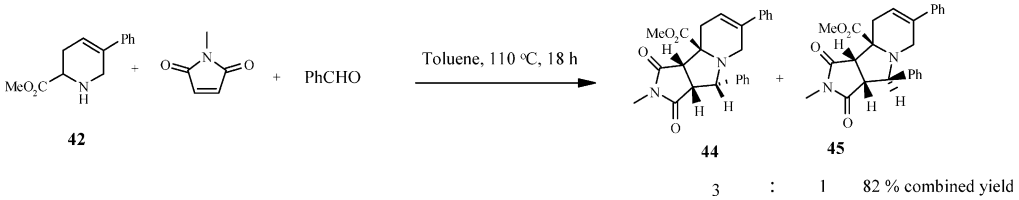
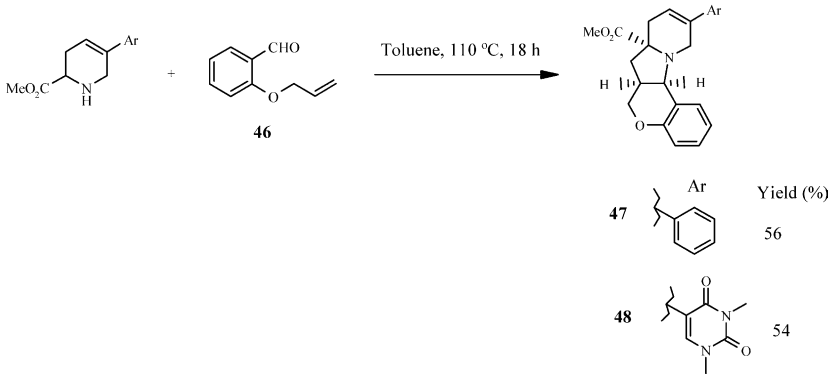


Figure 1. X-ray structure of **44**.

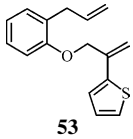
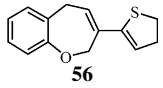
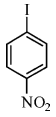
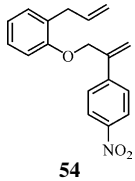
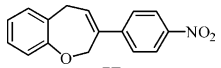
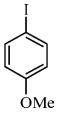
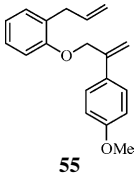
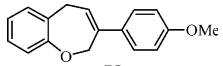


Scheme 4.



Scheme 5.

Table 4. Benzoxapines via sequential pd catalysed cascade synthesis/RCM

Entry	Aryl/heteroaryl/vinyl iodide	Pd-cascade product[a]	Yield (%)	RCM product[b]	Yield (%)[c]
1		 **53**	78	 **56**	69
2		 **54**	78	 **57**	62
3		 **55**	80	 **58**	56

[a] Reactions were carried out in toluene at 80 °C for 18 h and employed 1 mmol aryl/heteroaryl iodide, 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, 2 mol equiv K_2CO_3, allene (1 bar), and 1 mol equiv **7**.
[b] Reactions were carried out in toluene at 80 °C for 18 h and employed 5 mol% of catalyst **1**.
[c] Isolated yield.

In summary, a novel and diverse route accessing 3-aryl/heteroaryl/vinyl substituted heterocycles has been developed via the sequential employment of a chemoselective 3-component Pd-cascade/RCM sequence. An investigation into the compatibility of other alkene-tethered nucleophiles in this process is currently underway.

2. Experimental

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Mass spectral data were obtained from a VG Autospec instrument operating at 70 eV (EI and FAB) or ZD 2000 electrospray instrument (ES). Accurate molecular masses were obtained from the EPSRC Swansea Mass Spectroscopy service using perfluorotributylamine or polyethylenimine as an internal standard. Microanalyses were obtained using a Carbo Erba MOD11016 instrument. IR spectra were determined on a Nicolet Magna FT-IR 560 spectrometer. The IR samples were prepared as thin films by evaporation of a solution of the compound in DCM onto a germanium plate. X-ray structural data were collected on a Stadi 4-circle diffractometer. Column chromatography was performed using silica gel 60 (Merck, 230–400 mesh). Nuclear magnetic resonance spectra were recorded on Bruker DPX250, DPX300 and DPX500 instruments operating at 250, 300 and 500 MHz, respectively. Solvents were dried according to established methods,[30] unless purchased dry from Aldrich in sure-seal bottles. Palladium acetate was supplied by Johnson Matthey and ruthenium alkylidene catalysts were purchased from Strem and Aldrich and used as received. The term ether refers to diethyl ether and the term petrol refers to the 40–60 °C boiling point fraction of petroleum ether. All the compounds are named according to the IUPAC system and names were obtained using the ACD/*i*-Lab software.

2.1. General termolecular cascade procedure

With PPh_3 ligands. Palladium acetate (23 mg, 0.1 mmol), triphenylphosphine (53 mg, 0.2 mmol), potassium carbonate (276 mg, 2 mmol), tetraethylammonium chloride

(166 mg, 1 mmol) for **18–26** and toluene (8 ml) were added to a Schlenk tube, containing a magnetic stirrer bar. A solution of the nucleophile (1 mmol), and aryl iodide (1–1.2 mmol) in toluene (2 ml) was then added. The tube was then sealed and the mixture frozen in liquid nitrogen, and degassed by vacuum pump. The solid mixture was then allowed to reach room temperature, resulting in a liquid mixture, followed by re-freezing and degassing for a second time. Allene (1 bar) was then added to the Schlenk tube, and the mixture heated in an oil bath at 80 °C for 40 h. On completion of the reaction the excess gas was released and the mixture filtered. Concentration of the filtrate in vacuo afforded the crude product, which was purified by flash chromatography.

With in situ generated carbene ligands. *N*-Sulfonylpropargylamine (1 mol equiv), aryl iodide (1.1 mol equiv), palladium acetate (2 mol%), 1,3-dimesityl-4,5-dihydroimidazol-2-ylidine (4 mol%) and cesium carbonate (3 mol equiv) were dissolved in toluene (10 ml) in a Schlenk tube. The mixture was subjected to two freeze, pump, thaw cycles, charged with allene (0.5 atm), stirred for 16–18 h at 70–80 °C, cooled, excess allene vented and the solvent evaporated under reduced pressure. The crude product was purified by flash chromatography.

2.1.1. *N*-Allyl-*N*-(2-phenyl-allyl)-benzenesulfonamide (8). The product was isolated as a pale yellow oil (86%); (Found: C, 69.20; H, 5.90; N, 4.30; S, 10.20; $C_{18}H_{19}NO_2S$ requires C, 69.00; H, 6.11; N, 4.50; S, 10.20%); ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1635 (C=C), 1344 (S=O_{as}), 1161 (S=O_s), 991 (CH), 911; δ_H (250 MHz; $CDCl_3$) 7.75 (2H, dd, $J=8.5$, 1.2 Hz, $PhSO_2$), 7.25–7.47 (8H, m, Ph and $PhSO_2$), 5.52–5.38 (1H, m, CH=), 5.43 (1H, s, CH_2=), 5.21 (1H, s, CH_2=), 5.06 (1H, d, $J=10.1$ Hz, CH_{cis}H=CH), 5.04 (1H, d, $J=16.2$ Hz, CHH_{trans}=CH), 4.24 (2H, s, CH_2–C=), 3.73 (2H, d, $J=6.5$ Hz, CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 142.9, 140.4, 138.9, 133.1 132.6, 129.6, 128.9, 128.5, 127.7, 126.9, 119.9, 116.9, 50.9, 49.9; *m/z* (%) 313 (10, M^+), 210 (70, M−$PhCCH_2$), 172 (41, M−$PhSO_2$), 141 (74, $PhSO_2$), 118 (79, PhC=CH_2CH_3), 77 (100, Ph).

2.1.2. *N*-Allyl-*N*-(2-thiophen-2-yl-allyl)benzenesulfonamide (9). The product was isolated as a pale yellow oil (79%); (Found: C, 59.90; H, 5.20; N, 4.10; S, 20.00; $C_{16}H_{17}NO_2S_2$ requires C, 60.20; H, 5.36; N, 4.40; S, 20.10%); ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1653 (C=C), 1341 (S=O_{as}), 1163 (S=O_s), 998 (CH), 900 (CH); δ_H (250 MHz; $CDCl_3$) 7.83 (2H, dd, $J=8.4$, 1.5 Hz, $PhSO_2$), 7.46–7.55 (3H, m, $PhSO_2$), 6.94 (1H, dd, $J=5.1$, 3.7 Hz, thienyl-H), 7.14 (1H, d, $J=5.1$ Hz, thienyl-H), 7.22 (1H, d, $J=3.5$ Hz, thienyl-H), 5.52 (1H, s, CH_2=), 5.47–5.38 (1H, m, CH=), 5.09 (1H, s, CH_2=), 5.07 (1H, d, $J=10.0$ Hz, CHH_{cis}=CH), 5.03 (1H, dd, $J=16.2$, 1.1 Hz, CH_{trans}H=CH), 4.19 (2H, s, CH_2–C=), 3.82 (2H, d, $J=6.5$ Hz, CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 142.2, 140.4, 136.2, 133.1, 132.3, 129.6, 128.1, 127.7, 125.2, 120.0, 115.1, 50.8, 50.1; *m/z* (%) 319 (6, M^+), 210 (50, M−$PhCCH_2$), 178 (52, M−$PhSO_2$), 141 (66, $PhSO_2$), 124 (100, thiophen-C=CH_2CH_3), 109 (56, thiophen-C=CH_2), 77 (95, Ph).

2.1.3. *N*-Allyl-*N*-[2-(3nitrophenyl)allyl]benzenesulfonamide (10). The product was isolated as a pale yellow solid (85%); mp 75–77 °C; (Found: C, 60.10; H, 5.15; N, 7.80; S, 8.80; $C_{18}H_{18}N_2O_4S$ requires C, 60.30; H, 5.10; N, 7.80; S, 8.90%); ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1653 (C=C), 1636 (C=C), 1528 (NO_2), 1347 (S=O_{as}), 1161 (S=O_s), 998; δ_H (250 MHz; $CDCl_3$) 8.23 (1H, d, $J=1.9$ Hz, $PhNO_2$), 8.15 (1H, d, $J=8.4$ Hz, $PhNO_2$), 7.78–7.81 (3H, m, $PhNO_2$ and $PhSO_2$), 7.47–7.60 (4H, m, $PhNO_2$ and $PhSO_2$), 5.60 (1H, s, CH_2=), 5.36–5.50 (1H, m, CH=), 5.38 (1H, s, CH_2=), 5.12 (1H, dd, $J=10.1$, 0.8 Hz, CH_{cis}H=CH), 5.07 (1H, dd, $J=16.1$, 1.1 Hz, CH_{trans}H=CH), 4.27 (2H, s, CH_2–C=), 3.76 (2H, d, $J=6.5$ Hz, CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 148.7, 141.3, 140.4, 140.1, 133.2, 133.1, 132.2, 129.9, 129.6, 127.6, 123.2, 121.9, 120.3, 119.4, 50.8, 50.2; *m/z* (%) 358 (1, M^+), 210 (21, M−$PhCCH_2$), 141 (29, $PhSO_2$), 77 (100, Ph).

2.1.4. *N*-[2-(4-Acetyl-phenyl)-allyl]-*N*-allyl-benzenesulfonamide (11). The product was isolated as a pale orange solid. (88%); mp 100–102 °C; ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1682 (C=O), 1345 (S=O_{as}), 1162 (S=O_s), 998 (CH), 925 (CH), 847 (PhCOMe); δ_H (250 MHz; $CDCl_3$) 7.92 (2H, d, $J=8.5$ Hz, PhCOMe), 7.79 (2H, dd, $J=8.5$, 1.3 Hz, $PhSO_2$), 7.44–7.53 (5H, m, PhCOMe and $PhSO_2$), 5.57 (1H, s, CH_2=), 5.30–5.50 (1H, m, CH=), 5.34–5.04 (2H, m, C$H_{cis}H_{trans}$=C), 5.09 (1H, s, CH_2=), 4.27 (2H, s, CH_2–C=), 3.74 (2H, d, $J=6.5$ Hz, CH_2–CH=), 2.62 (3H, s, CH_3); δ_C (50 MHz; $CDCl_3$) 198.2 (C=O), 143.4, 142.2, 140.2, 136.9, 133.1, 132.3, 129.6, 128.9, 127.6, 127.1, 120.0, 118.8, 50.8, 49.9, 27.1; *m/z* (%) 355 (9, M^+), 210 (77, M−$PhCCH_2$), 141 (72, M−$PhSO_2$), 77 (100, Ph), 43 (58, allyl); HRMS Found: 355.1242, $C_{20}H_{21}NO_3S$ requires 355.1245.

2.2. General ring closing metathesis procedure

Grubbs' second generation catalyst (5 mol%) was added to a magnetically stirred solution of the diene (0.13 mmol), in anhydrous toluene (40 ml) and the mixture stirred under an argon atmosphere at 80 °C for 2–4 h. Concentration in vacuo afforded the crude product as a brown oil, which was purified by flash chromatography.

2.2.1. 1-Benzenesulfonyl-3-phenyl-2,5-dihydro-1*H*-pyrrole (12). The product was isolated as a pale yellow solid (34 mg, 74%); mp 120–122 °C; ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1446 (Ph C=C), 1339 (S=O_{as}), 1167 (S=O_s), 830 (CH); δ_H (250 MHz; $CDCl_3$) 7.89 (2H, dd, $J=8.2$, 1.5 Hz, $PhSO_2$), 7.53–7.58 (3H, m, $PhSO_2$), 7.29–7.33 (5H, m, Ph), 6.01 (1H, qi, $J=2.1$ Hz, CH=), 4.29–4.34 and 4.48–4.53 (4H, m, CH_2–C= and CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 137.7, 137.4, 133.3, 132.8, 129.7, 129.1, 128.9, 127.8, 125.8, 119.3, 56.1, 55.3; *m/z* (%) 285 (8, M^+), 144 (54, M−$PhSO_2$), 77 (93, Ph), 41 (100, allyl).

2.2.2. 1-Benzenesulfonyl-3-thiophen-2-yl-2,5-dihydro-1*H*-pyrrole (13). The product was isolated as a colourless solid (38 mg, 82%); mp 105–107 °C; Found: C, 57.50; H, 4.35; N, 4.60; S, 21.90; $C_{16}H_{15}NO_2S$ requires C, 57.70; H, 4.50; N, 4.80; S, 22.00%; ν_{max}/cm^{-1} (CH_2Cl_2 solution) 1339 (S=O_{as}), 1166 (S=O_s), 830 (CH); δ_H (250 MHz; $CDCl_3$) 7.88 (2H, dd, $J=7.8$, 1.4 Hz, $PhSO_2$), 7.54–7.59

(3H, m, $PhSO_2$), 7.22 (1H, d, $J=5.3$ Hz, thienyl-H), 6.96 (1H, dd, $J=5.3$, 3.5 Hz, thienyl-H), 6.88 (1H, m, thienyl-H), 6.01 (1H, qi, $J=2.0$ Hz, CH=), 4.25–4.34 and 4.43–4.45 (4H, m, CH_2–C= and CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 137.3, 136.4, 133.3, 132.2, 129.7, 128.0, 127.8, 125.9, 125.2, 118.6, 55.8, 55.7; *m/z* (%) 291 (9, M^+), 150 (100, $M-PhSO_2$), 77 (56, Ph).

2.2.3. 1-Benzenesulfonyl-3-(3-nitro-phenyl)-2,5-dihydro-1*H*-pyrrole (14). The product was isolated as a colourless solid (49 mg, 93%); mp 130–132 °C; Found: C, 58.50; H, 4.50; N, 8.20; S, 9.90; $C_{16}H_{15}NO_2S$ requires C, 58.20; H, 4.27; N, 8.50; S, 9.70; ν_{max}/cm^{-1} (CH_2Cl_2 solution) 3088, 2918, 1530 (NO_2), 1348 (S=O_{as}), 1166 (S=O_s), 830 (CH); δ_H (250 MHz; $CDCl_3$) 8.12–8.22 (2H, m, $PhNO_2$), 7.91 (2H, dd, $J=8.2$, 1.5 Hz, $PhSO_2$), 7.55–7.64 (5H, m, $PhSO_2$ and $PhNO_2$), 6.01 (1H, t, $J=2.1$ Hz, CH=), 4.37–4.40 and 4.51–4.55 (4H, m, CH_2–C= and CH_2–CH=); δ_C (50 MHz; $CDCl_3$) 148.9, 137.2, 135.9, 134.4, 133.5, 131.6, 130.2, 129.8, 127.8, 123.4, 122.8, 120.6, 56.1, 55.1; *m/z* (%) 330 (34, M^+), 189 (100, $M-PhSO_2$), 143 (54, $M-PhSO_2$ and NO_2), 115 (68, $M-PhNO_2$ and OPh), 77 (86, Ph).

2.2.4. 1-[4-(1-Benzenesulfonyl-2,5-dihydro-1*H*-pyrrol-3-yl)-phenyl]-ethanone (15). The product was isolated as a colourless solid (32 mg, 75%); mp 145–147 °C; Found: C, 66.20; H, 5.30; N, 4.10; S, 9.60; $C_{18}H_{17}NO_3S$ requires C, 66.00; H, 5.23; N, 4.30; S, 9.80; ν_{max}/cm^{-1} (CH_2Cl_2 solution) 2919, 1680 (C=O), 1339 (S=O_{as}), 1166 (S=O_s), 828 (CH); δ_H (250 MHz; $CDCl_3$) 7.94 (4H, m, $PhSO_2$ and PhCOMe), 7.55–7.60 (3H, m, $PhSO_2$), 7.37 (2H, d, $J=$ 8.5 Hz, PhCOMe), 6.18 (1H, t, $J=2.1$ Hz, CH=), 4.33–4.37 and 4.50–4.55 (4H, m, CH_2–C= and CH_2–CH=), 2.60 (3H, s, CH_3); δ_C (50 MHz; $CDCl_3$) 197.3 (C=O), 137.1, 137.0, 136.9, 133.4, 129.8, 129.2, 127.7, 125.9, 122.3, 56.1, 55.1, 27.0; *m/z* (%) 327 (23, M^+), 186 (100, $M-PhSO_2$), 170 (57, $M-PhSO_2$ and O), 144 (42, $M-PhSO_2N(CH_2)_2$), 115 (43, M−PhCOMe and OPh), 77 (57, Ph), 43 (63, COMe).

2.3. General allyl glycinate ester formation and *N*-sulfonyl protection

2.3.1. Methyl 2-[(phenylsulfonyl)amino]-4-pentenoate (16). Thionyl chloride (1.35 ml, 0.0181 mol) was added dropwise to a stirred solution of allyl glycinate (2.09 g, 0.0181 mol) in methanol (150 ml) at 0 °C and the solution was allowed to warm to ambient temperature. After 1 h the methanol was removed and the residue dissolved in DCM (100 ml). Benzenesulfonyl chloride (2.35 ml, 0.0181 mol) dissolved in DCM (20 ml) was added to the reaction mixture followed by triethylamine (5.7 ml, 0.056 mol). After 16 h the mixture was washed with water (2×20 ml), dried ($MgSO_4$), filtered and the filtrate concentrated. Purification of the residue by flash chromatography eluting with DCM afforded the product (3.8 g, 78%), which crystallised from DCM/petrol as colourless needles, mp 75–76 °C; R_f 0.13; (Found: C, 53.40; H, 5.45; N, 4.95. $C_{12}H_{15}NO_4S$ requires C, 53.50; H, 5.60; N, 5.20%); ν_{max}/cm^{-1} (Nujol) 3291 (NH), 1741 (C=O), 1331 (S=O_{as}), 1163 (S=O_s), 1092; δ_H (250 MHz, $CDCl_3$) 7.88–7.83 (2H, m, ArH), 7.62–7.47 (3H, m, ArH), 5.62 (1H, ddt, $J=18.0$, 14.3, 6.8 Hz, C*H*=CH_2), 5.27 (1H, d, $J=9.0$ Hz, NH), 5.13–5.04 (2H, m, CH=CH_2), 4.10–4.02 (1H, dt, $J=9.0$, 6.8 Hz NCH), 3.5 (3H, s, CH_3), 2.47 (2H, t, $J=6.8$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 171.6 (C=O), 140.1, 133.3, 131.6, 129.5, 127.6, 120.3, 55.6, 52.9, 37.9; *m/z* (ES) 292 (M^+ + Na).

2.3.2. Methyl 2-{[(4-nitrophenyl)sulfonyl]amino}pent-4-enoate (17).[31] Prepared by the above *N*-sulfonyl protection procedure on a 0.05 mol scale. Purification by flash chromatograpy eluting with DCM afforded the product (8.65 g, 55%) as a pale yellow solid. Crystallisation from DCM/petrol afforded colourless needles, mp 134–136 °C; R_f 0.15; (Found: C, 45.80; H, 4.40; N, 8.75. $C_{12}H_{14}N_2O_6S$ requires C, 45.85; H, 4.50; N, 8.90%); ν_{max}/cm^{-1} (film) 1741 (C=O), 1539 (NO_2), 1350 (S=O_{as}), 1171 (S=O_s); δ_H (250 MHz, $CDCl_3$) 8.35 (2H, d, $J=9.0$ Hz, ArH), 8.04 (2H, d, $J=9.0$ Hz, ArH), 5.61 (1H, ddt, $J=16.9$, 10.4, 7.2 Hz, C*H*=CH_2), 5.32 (1H, d, $J=8.6$ Hz, NH), 5.18–5.08 (2H, m, CH=CH_2), 4.13 (1H, dt, $J=8.6$, 5.9 Hz, NCH), 2.55–2.49 (2H, m, CH_2); *m/z* (ES) 337 (M^+ + Na).

2.3.3. Methyl 2-[(2-phenyl-2-propenyl)(phenylsulfonyl) amino]-4-pentenoate (18). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of the aryl iodide and a reaction time of 40 h. Purification by flash chromatograpy eluting with DCM afforded the product (312 mg, 81%) as a colourless oil; R_f 0.34; (Found: C, 65.15; H, 6.15; N, 3.90. $C_{21}H_{23}NO_4S$ requires C, 65.45; H, 6.00; N, 3.65%); ν_{max}/cm^{-1} (film) 1741 (C=O), 1447, 1345 (S=O_{as}), 1158 (S=O_s) 1091, 916; δ_H (250 MHz, $CDCl_3$) 7.85–7.81 (2H, m, SO_2PhH), 7.61–7.46 (3H, m, SO_2PhH), 7.38–7.28 (5H, m, PhH), 5.78 (1H, ddt, $J=16.7$, 9.8, 6.8 Hz, C*H*=CHH), 5.85 (1H, d, $J=$ 0.9 Hz, =CH*H*), 5.41 (1H, d, $J=0.9$ Hz, =C*H*H), 5.00 (1H, d, $J=16.7$ Hz, CH=CH_{trans}), 4.98 (1H, d, $J=$ 9.8 Hz, CH=CH_{cis}H), 4.48 (1H, dd, $J=8.0$, 6.9 Hz, NCH), 4.42 (1H, d, $J=16.0$ Hz, NC*H*H), 4.36 (1H, d, $J=16.0$ Hz, NCH*H*), 3.89 (s, 3H, CH_3), 2.64–2.58 (1H, m, =CHC*H*H), 2.43–2.35 (m, 1H, =CH*H*); δ_C (63 MHz, $CDCl_3$) 170.8 (C=O), 144.0, 139.9, 139.2, 133.7, 133.2, 129.3, 128.8, 128.4, 128.1, 126.8, 118.7, 116.5, 59.8 (NCH), 52.2 (OCH_3), 50.2 (NCH_2), 35.2 (=CH*C*H_2); *m/z* (%) (EI) 385 (4, M^+), 326, (43, $M-CO_2Me$), 284 (78), 244 (34, $M-SO_2Ph$), 144 (45), 117 (95), 77 (100, Ph).

2.3.4. Methyl 2-{[2-(3-methylphenyl)-2-propenyl]-(phenylsulfonyl)amino}-4-pentenoate (19). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of the aryl iodide and a reaction time of 34 h. Purification by flash chromatograpy eluting with DCM afforded the product (318 mg, 80%) as a colourless oil; R_f 0.24; (Found: C, 66.25; H, 6.40; N, 3.50. $C_{22}H_{25}NO_4S$ requires C, 66.15; H, 6.30; N, 3.50%); ν_{max}/cm^{-1} (film) 1742 (C=O), 1447, 1437, 1345 (S=O_{as}), 1159 (S=O_s), 1091, 919; δ_H (250 MHz, $CDCl_3$) 7.85–7.81 (2H, m, SO_2PhH), 7.59–7.49 (3H, m, SO_2PhH), 7.26–7.12 (4H, m, ArH), 5.63 (1H, ddt, $J=16.8$, 9.7, 6.9 Hz, C*H*=CHH), 5.46 (1H, d, $J=0.8$ Hz, =CH*H*), 5.39 (1H, d, $J=0.8$ Hz, =C*H*H), 5.01 (1H, d, $J=16.8$ Hz, CH=CH_{trans}), 5.00 (1H, d, $J=9.7$ Hz, CH=CH_{cis}H), 4.48 (1H, dd, $J=8.0$, 6.8 Hz, NCH), 4.48 (1H, d, $J=17.5$ Hz, NC*H*H), 4.38 (1H, d, $J=17.5$ Hz, NCH*H*), 3.40 (3H, s, OCH_3), 2.64–2.60 (1H, m, =CHC*H*H), 2.43–2.34 (1H, m, =CHCH*H*), 2.34 (3H, s, $ArCH_3$); δ_C (63 MHz, $CDCl_3$) 170.9 (C=O), 144.1, 138.3,

133.7, 133.1, 129.3, 129.1, 128.7, 127.5, 123.8, 118.7, 116.2, 59.9 (NCH), 52.2 (OCH_3), 50.2 (NCH_2), 35.2 (=CHCH_2), 21.9 (ArCH_3); *m/z* (%) (FAB) 400 (69, M^++H), 399 (19, M^+), 340 (27, M−CO_2Me), 259 (100), 258 (34, M−SO_2Ph), 158 (20), 131 (47), 77 (13, C_6H_5).

2.3.5. Methyl 2-{[2-(2-naphthyl)-2-propenyl](phenylsulfonyl)amino}-4-pentenoate (20). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.1 mmol of aryl iodide, $Pd_2(dba)_3$ (0.05 mmol) and a reaction time of 44 h. Purification by flash column chromatography eluting with 4:1 v/v petrol/ethyl acetate afforded the product (295 mg, 69%) as a viscous, pale yellow oil; R_f 0.22; (Found: C, 68.75; H, 5.95; N, 3.20. $C_{23}H_{25}NO_4S$ requires C, 68.95; H, 5.80; N, 3.20%); ν_{max}/cm^{-1} (film) 1742 (C=O), 1447, 1347 (S=O_{as}), 1158 (S=O_s), 1091, 921; δ_H (250 MHz, $CDCl_3$) 8.11–8.08 (1H, m, ArH), 7.83–7.79 (4H, m, ArH), 7.54–7.43 (6H, m, ArH), 7.28 (1H, dd, *J*=7.5, 1.2 Hz, ArH), 5.82 (1H, d, *J*=1.4 Hz, =CH_CH_D), 5.72 (1H, ddt, *J*=16.9, 10.2, 6.8 Hz, C*H*=CHH), 5.32, (1H, d, *J*=1.4 Hz, =C*H*H), 5.12 (1H, d, *J*=10.2 Hz, CH=CH_{cis}H), 5.09 (1H, d, *J*=16.9 Hz, CH=CHH_{trans}), 4.59 (1H, dd, *J*=8.2, 5.5 Hz, NCH), 4.32 (1H, d, *J*=18.5 Hz, NC*H*H), 4.19 (1H, d, *J*=18.5 Hz, NCH*H*), 3.39 (3H, s, CH_3), 2.67–2.58 (1H, m, =CHC*H*H), 2.49–2.38 (1H, m, =CHCH*H*); δ_C (63 MHz, $CDCl_3$) 170.9 (C=O), 144.6, 139.7, 138.8, 134.0, 133.3, 133.2, 131.8, 129.3, 128.7, 128.3, 128.0, 126.8, 126.3, 126.1, 125.8, 125.6, 119.0, 117.5, 60.2 (NCH), 52.3 (OCH_3), 52.0 (NCH_2), 35.4 (=CHCH_2); *m/z* (ES) 458 (M^++Na).

2.3.6. Methyl 2-{[2-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinyl)-2-propenyl](phenylsulfonyl)amino}-4-pentenoate (21). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 40 h. Purification by flash chromatography eluting with 9:1 v/v ether/ethyl acetate afforded the product (314 mg, 70%) as a colourless oil; R_f 0.27; (Found: C, 56.30; H, 5.75; N, 9.45. $C_{21}H_{26}N_2O_6S$ requires C, 56.35; H, 5.65; N, 9.40%), ν_{max}/cm^{-1} (film) 1741 (MeOC=O), 1702 (N–C=O), 1655 (N(N)C=O), 1448, 1340 (S=O_{as}), 1266, 1159 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 7.82 (2H, m, SO_2PhH), 7.60–7.48 (3H, m, SO_2PhH), 7.27 (1H, d, *J*=0.8 Hz, =CH), 5.73 (1H, ddt, *J*=16.9, 10.1, 6.8 Hz, C*H*=CHH), 5.49 (1H, d, *J*=0.8 Hz, =CH*H*), 5.39 (1H, s, =C*H*H), 5.05 (1H, ddd, *J*=16.9, 2.9, 1.4 Hz, CH=CHH_{trans}), 5.01 (1H, dd, *J*=10.1, 1.4 Hz, CH=CH_{cis}H), 4.50 (1H, dd, *J*=8.3, 6.8 Hz, NCH), 4.28 (1H, d, *J*=16.3 Hz, NC*H*H), 4.19 (1H, d, *J*=16.3 Hz, NCH*H*), 3.46 (3H, s, CH_3), 3.44 (3H, s, CH_3), 3.42 (3H, s, CH_3), 2.75–2.66 (1H, m, =CHC*H*H), 2.57–2.45 (1H, m, =CHCH*H*); δ_C (63 MHz, $CDCl_3$), 170.8 (C=O), 162.7 (C=O), 151.8 (C=O), 142.0, 139.6, 138.5, 134.1, 133.2, 129.2, 128.2, 120.0, 118.4, 112.5, 60.4 (NCH), 52.4 (OCH_3), 50.6 (NCH_2), 37.5 (NCH_3), 34.8 (NCH_3), 28.4 (=CHCH_2); *m/z* (ES) 470 (M^++Na).

2.3.7. Methyl 2-{(phenylsulfonyl)[2-(2-thienyl)-2-propenyl]amino}-4-pentenoate (22). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 38 h. Purification by flash chromatography afforded the product (278 mg, 71%), as a viscous, pale yellow oil, R_f 0.15; (Found: C, 58.30; H, 5.35; N, 3.80. $C_{19}H_{21}NO_4S$ requires C, 58.30; H, 5.40; N, 3.60%); ν_{max}/cm^{-1} (film) 1740 (C=O), 1447, 1437, 1343 (S=O_{as}), 1160 (S=O_s), 1191, 1091, 923; δ_H (250 MHz, $CDCl_3$) 7.87–7.83 (2H, m, SO_2PhH), 7.64–7.49 (3H, m, SO_2PhH), 7.20 (1H, dd, *J*=5.1, 1.0 Hz, ArH), 7.13 (1H, dd, *J*=3.7, 1.0 Hz, ArH), 6.98 (1H, dd, *J*=5.1, 3.7 Hz, ArH), 5.65 (1H, ddt, *J*=16.9, 9.9, 6.9 Hz, C*H*=CHH), 5.58 (1H, s, =CH*H*), 5.30 (1H, s, =C*H*H), 4.99–5.04 (2H, m, CH=C$H_{cis}H_{trans}$), 4.53 (1H, t, *J*=7.4 Hz, NCH), 4.42 (1H, d, *J*=17 Hz, NC*H*H), 4.35 (1H, d, *J*=17 Hz, NCH*H*), 3.40 (3H, s, CH_3), 2.64–2.56 (1H, m, =CHC*H*H), 2.49–2.40 (1H, m, =CHCH*H*); δ_C (63 MHz, $CDCl_3$), 170.8 (C=O), 142.5, 139.8, 137.5, 133.6, 133.3, 129.4, 128.0, 127.9, 125.1, 124.5, 118.8, 114.7, 59.9 (NCH), 52.3 (OCH_3), 49.7 (NCH_2), 35.3 (=CHCH_2); *m/z* (ES) 414 (M^+ + Na).

2.3.8. Methyl 2-{[2-(-methoxyphenyl)-2-propenyl]-(phenylsulfonyl)amino}-4-pentenoate (23). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 42 h. Purification by flash chromatography eluting with DCM afforded the product (259 mg, 63%), as a colourless oil, R_f 0.11; (Found: C, 63.50; H, 6.20; N, 3.40. $C_{22}H_{25}NO_5S$ requires C, 63.60; H, 6.05; N, 3.35%); ν_{max}/cm^{-1} (film) 1741 (C=O), 1514, 1342 (S=O_{as}), 1249 (O–Me), 1159 (S=O_s), 1090, 1030, 836; δ_H (500 MHz, $CDCl_3$) 7.84–7.82 (2H, m, SO_2PhH), 7.58–7.56 (1H, m, SO_2PhH), 7.51–7.48 (2H, m, SO_2PhH), 7.31 (2H, d, *J*=8.9 Hz, ArH), 6.84 (2H, d, *J*=8.9 Hz, ArH), 5.61 (1H, ddt, *J*=16.5, 9.7, 6.9 Hz, C*H*=CHH), 5.39 (1H, d, *J*=0.8 Hz, =CH*H*), 5.29 (1H, d, *J*=0.8 Hz, =C*H*H), 4.99 (1H, d, *J*=9.7 Hz, CH=CH_{cis}H), 4.98 (1H, d, *J*=16.5 Hz, CH=CHH_{trans}), 4.45 (1H, dd, *J*=8.1, 6.7 Hz, NCH), 4.38 (1H, d, *J*=16.6 Hz, NC*H*H), 4.34 (1H, d, *J*=16.6 Hz, NCH*H*), 3.81 (3H, s, CH_3), 3.39 (3H, s, CH_3), 2.66–2.61 (1H, m, =CHC*H*H), 2.40–2.35 (1H, m, =CHCH*H*); δ_C (125 MHz, $CDCl_3$), 170.4 (C=O), 159.5, 142.9, 139.7, 133.5, 132.7, 131.2, 128.9, 127.7, 127.6, 118.2, 114.8, 113.8, 59.5 (CH_3), 55.3 (NCH), 51.8 (CH_3), 50.0 (NCH_2), 34.8 (=CHCH_2); *m/z* (%) (EI) 415 (17, M^+), 356 (20, M−CO_2Me), 274 (100, M−SO_2Ph), 174 (88), 147 (86), 133 (78).

2.3.9. Methyl 2-{[2-(1-methyl-1*H*-indol-5-yl)-2-propenyl](phenylsulfonyl)amino}-4-pentanoate (24). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 40 h. Purification by flash chromatography, eluting with DCM yielded the product (353 mg, 80%) as a viscous colourless oil, R_f 0.1; (Found: C, 66.00; H, 5.95; N, 6.25. $C_{24}H_{26}N_2O_4S$ requires C, 65.75; H, 5.95; N, 6.25%); ν_{max}/cm^{-1} (film) 1741 (C=O), 1446, 1336 (S=O_{as}), 1159 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 7.87–7.82 (2H, m, SO_2PhH), 7.58–7.45 (4H, m, ArH), 7.26 (2H, br s, ArH), 7.05 (1H, d, *J*=3.1 Hz, ArH), 6.44 (1H, d, *J*=3.1 Hz, ArH), 5.63 (1H, ddt, *J*=17.0, 10.3, 6.9 Hz, C*H*=CHH), 5.46 (1H, d, *J*=1.0 Hz, =CH*H*), 5.35 (1H, d, *J*=1.0 Hz, =C*H*H), 5.03–4.95 (2H, m, CH=C$H_{cis}H_{trans}$), 4.49 (1H, dd, *J*=8.2, 6.6 Hz, NCH), 4.46 (2H, br s, NCH_2), 3.79 (3H, s, CH_3), 3.39 (3H, s, CH_3), 2.70–2.64 (1H, m, =CHC*H*H), 2.45–2.38 (1H, m, =CHCH*H*); δ_C (63 MHz, $CDCl_3$), 171.0

(C=O), 144.7, 140.1, 136.9, 133.9, 133.0, 130.6, 129.8, 129.2, 128.7, 128.1, 120.9, 119.1, 118.6 (=CH_2), 114.8 (=CH_2), 109.4, 101.8, 59.3 (NCH), 52.2 (OCH_3), 50.8 (NCH_2), 35.3 (=CHCH_2), 33.3 (NCH_3); *m/z* (ES) 461 (M^+ + Na).

2.3.10. Methyl 2-{[2-(2-methyl-4-nitrophenyl)-2-propenyl](phenylsulfonyl)amino}-4-pentenoate (25). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.1 mmol aryl iodide and $Pd_2(dba)_3$ (0.05 mmol, 92 mg) in place of $Pd(OAc)_2$ and a reaction time of 40 h. Purification by flash column chromatography eluting with 4:1 v/v petrol/ethyl acetate afforded the product (322 mg, 72%) as a viscous pale yellow oil, which solidified on standing. Crystallisation from DCM/petrol afforded colourless needles, mp 67–69 °C; R_f 0.18; (Found: C, 59.35; H, 5.60; N, 6.20; $C_{22}H_{24}N_2O_6S$ requires C, 59.45; H, 5.45; N, 6.30%); ν_{max}/cm^{-1} (film) 1742 (C=O), 1519 (C–NO_2), 1447, 1346 (S=O_{as}), 1311, 1158 (S=O_s), 1091, 926; δ_H (500 MHz; $CDCl_3$) 8.04 (1H, d, J=2.4 Hz, ArH_E), 7.98 (1H, dd, J=8.4, 2.4 Hz, ArH), 7.81–7.79 (2H, m, SO_2Ph), 7.58–7.58 (1H, m, SO_2PhH), 7.50–7.47 (2H, m, SO_2PhH), 7.24 (1H, d, J=8.4 Hz, ArH), 5.69 (1H, ddt, J=17.0, 10.2, 6.8 Hz, C*H*=CHH), 5.66 (1H, d, J=0.8 Hz, =CH*H*), 5.14 (1H, d, J=0.8 Hz, =C*H*H), 5.11 (1H, ddd, J=10.2, 2.9, 1.4 Hz, CH=CH_{cis}H), 5.08 (1H, d, J=17.0 Hz, CH=CHH_{trans}), 4.53 (1H, dd, J=8.4, 6.5 Hz, NCH), 4.14 (1H, dt, J=18.3, 1.6 Hz, NC*H*H), 4.09 (1H, dt, J=18.3, 6 Hz, NCH*H*), 3.43 (1H, s, OCH_3), 2.65–2.59 (1H, m, =CHC*H*H), 2.42 (1H, s, $ArCH_3$), 2.42–2.38 (1H, m, =CHCH*H*); δ_C (125 MHz, $CDCl_3$) 170.4 (C=O), 147.2, 146.9, 143.9, 139.3, 137.5, 133.0, 132.7, 129.9, 129.0, 127.6, 125.0, 120.8, 118.8, 117.4, 59.6 (NCH), 51.9 (OCH_3), 50.32 (NCH_2), 35.0 (=CHCH_2), 19.8 ($ArCH_3$); *m/z* (ES) 467 (M^+ + Na).

2.3.11. Methyl 2-{[2-(1-methyl-2,3-dioxo)-2,3-dihydro-1*H*-indole-5-yl]prop-2-enyl(phenylsulfonyl)amino}pent-4-enoate (26). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 48 h. Purification by flash chromatography eluting with 2:3 v/v ethyl acetate/petrol affords the product (193 mg, 41%), as red solid, which crystallised from DCM/petrol as red needles, mp 116–118 °C; R_f 0.2; (Found: C, 61.35; H, 5.25; N, 5.85. $C_{24}H_{24}N_2O_6S$ requires C, 61.55; H, 5.15; N, 6.0%); ν_{max}/cm^{-1} (film) 1740 (MeOC=O), 1619, 1593, 1331 (S=O_{as}), 1267, 1160 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 7.84–7.81 (2H, m, SO_2PhH), 7.72 (1H, dd, J=8.3, 2.0 Hz, ArH), 7.65–7.49 (4H, m, SO_2PhH and ArH), 6.89 (1H, d, J=8.3 Hz, ArH), 5.60 (1H, ddt, J=16.9, 9.8, 6.9 Hz, C*H*=CHH), 5.49 (1H, s, =CH*H*), 5.45 (1H, s, =C*H*H), 5.02 (1H, d, J=16.9 Hz CH=CHH_{trans}), 5.02 (1H, d, J=9.8 Hz CH=CH_{cis}H), 4.48 (1H, t, J=7.4 Hz, NCH), 4.41 (1H, d, J=16.9 Hz, NC*H*H), 4.30 (1H, d, J=16.9 Hz, NCH*H*), 3.41 (3H, s, CH_3), 3.27 (3H, s, CH_3), 2.67–2.55 (1H, m, =CHC*H*H), 2.42–2.30 (m, 1H, =CHCH*H*); δ_C (63 MHz, $CDCl_3$) 183.7 (C=O), 170.6 (C=O), 158.7 (C=O), 151.2, 142.4, 139.6, 136.9, 135.2, 133.4, 129.4, 128.0, 123.5, 118.9, 117.7, 117.3, 110.3, 59.7 (NCH), 52.4 (OCH_3), 50.0 (NCH_2), 35.2 (=CHCH_2), 26.8 (N–CH_3); *m/z* (%) (EI); 468 (57, M^+), 409 (72, M−CO_2Me), 327 (82, M−SO_2Ph), 200 (55), 144 (70), 77 (100).

2.3.12. Methyl 5-phenyl-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (27). Prepared by the general ring closing metathesis procedure on a 0.13 mmol scale and a reaction time of 3 h. Purification by flash column chromatography eluting with 1:1 v/v petrol/ether to afforded the product (36 mg, 77%) as a viscous, colourless oil. R_f 0.25; (Found: C, 63.65; H, 5.40; N, 4.00; $C_{19}H_{19}NO_4S$ requires C, 63.85; H, 5.35; N, 3.90%); ν_{max}/cm^{-1} (film) 1744 (C=O), 1447, 1342 (S=O_{as}), 1202, 1164 (S=O_s), 1097; δ_H (500 MHz, $CDCl_3$) 7.78–7.76 (2H, m, SO_2PhH), 7.51–7.49 (1H, m, SO_2PhH), 7.45–7.41 (2H, m, SO_2PhH), 7.25–7.18 (5H, m, PhH), 5.94–5.96 (1H, br m, =CH), 4.86 (1H, dd, J=5.5, 3.0 Hz, NCH), 4.50 (1H, ddd, J=16.4, 3.9, 1.9 Hz, NC*H*H), 4.09 (1H, ddd, J=16.4, 5.3, 3.0 Hz, NCH*H*), 3.40 (3H, s, CH_3), 2.66–2.64 (2H, br m, =CHCH_2); δ_C (75 MHz, $CDCl_3$) 171.2 (C=O), 139.5, 138.6, 134.1, 133.1, 129.3, 128.9, 128.3, 127.6, 125.6, 119.7, 52.7 (NCH), 52.6 (OCH_3), 43.9 (NCH_2), 28.5 (=CHCH_2); *m/z* (%) (EI) 357 (11, M^+), 298 (40, M−CO_2Me), 216 (48, M−SO_2Ph), 156 (100), 129 (44), 77 (70, Ph).

2.3.13. Methyl 5-(3-methylphenyl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (28). Prepared by the general ring closing metathesis procedure on a 0.14 mmol scale and reaction time of 2 h. Purification by flash chromatography eluting with 4:1 v/v petrol/ethyl acetate afforded the product (38 mg, 75%) as a colourless oil, which crystallised on standing to afford colourless needles, mp 59–61 °C; R_f 0.23; (Found: C, 64.80; H, 5.95; N, 3.85. $C_{20}H_{21}NO_4S$ requires C, 64.65; H, 5.70; N, 3.75%); ν_{max}/cm^{-1} (film) 1744 (C=O), 1447, 1340 (S=O_{as}), 1202, 1163 (S=O_s), 1098, 1032, 971; δ_H (250 MHz, $CDCl_3$), 7.86–7.82 (2H, m, SO_2PhH), 7.62–7.48 (3H, m, SO_2PhH), 7.25–7.22 (4H, m, ArH), 6.03–6.00 (1H, br m, =CH), 4.93 (1H, t, J=4.3 Hz, NCH), 4.51 (1H, dd, J=16.4, 2.0 Hz, NC*H*H), 4.14 (1H, ddd, J=16.4, 5.0, 2.8 Hz, NCHC*H*), 3.46 (3H, s, OCH_3), 2.73–2.72 (2H, br m, =CHCH_2), 2.35 (3H, s, $ArCH_3$); δ_c (63 MHz, $CDCl_3$) 171.2 (C=O), 139.5, 138.6, 134.2, 133.1, 129.4, 129.1, 128.8, 128.5 127.6, 126.3, 122.7, 119.5, 52.7 (NCH), 52.6 (OCH_3), 44.0 (NCH_2), 28.6 (=CHCH_2), 21.9 ($PhCH_3$); *m/z* (%) (EI) 371 (27, M^+), 312 (54, M−CO_2Me), 230 (86, M−SO_2Ph), 170 (10), 77 (60, Ph).

2.3.14. Methyl 5-(2-naphthyl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (29). Prepared by the general ring closing metathesis procedure on a 0.14 mmol scale and a reaction time of 5 h. Purification by flash chromatography eluting with 4:1 v/v petrol/ethyl acetate afforded the product (43 mg, 75%), which crystallised from petrol/DCM as colourless needles, mp 144–146 °C; R_f 0.21; (Found: C, 67.65; H, 5.20; N, 3.70. $C_{23}H_{21}NO_4S$ requires C, 67.80; H, 5.20; N, 3.45%); ν_{max}/cm^{-1} (film) 1742 (C=O), 1447, 1341 (S=O_{as}), 1201, 1164 (S=O_s), 1095; δ_H (250 MHz, $CDCl_3$) 7.86–7.76 (5H, m, ArH), 7.62–7.41 (6H, m, ArH), 7.23 (1H, dd, J=7.0, 1.6 Hz, ArH), 5.78 (1H, bdd, J=5.5, 2.3 Hz, =CH), 5.06 (1H, dd, J=6.3, 2.0 Hz, NCH), 4.39 (1H, br d, J=16.5 Hz, NC*H*H), 4.08 (1H, dd, J=16.5, 2.2 Hz, NCH*H*), 3.56 (3H, s, CH_3), 2.93–2.73 (2H, br m, =CHCH_2); δ_C (63 MHz, $CDCl_3$), 171.4 (C=O), 139.2, 137.9, 134.8, 134.0, 133.1, 131.8, 129.3, 128.8, 128.5, 127.7, 126.7, 126.3, 125.6, 125.4, 122.8, 122.4, 52.7

(NCH), 52.6, (OCH_3), 46.4 (NCH_2), 28.7 (=CH*C*H_2); *m*/*z* (%) (EI) 407 (44, M^+), 348 (25, $M-CO_2Me$), 266 (100, $M-SO_2Ph$), 206 (73), 179 (76), 165 (50), 141 (42), 77 (80).

2.3.15. Methyl 5-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinyl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (30). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 3 h. Purification by flash column chromatography eluting with 3:2 v/v petrol/ethyl acetate afforded the product (48 mg, 84%), which crystallised from DCM/petrol as colourless needles, mp 196–198 °C; R_f 0.1; (Found: C, 54.40; H, 5.05; N, 9.85. $C_{19}H_{21}N_3O_6S$ requires C, 54.40; H, 5.05; N, 10.0%); ν_{max}/cm^{-1} (film) 1742 (MeOC=O), 1702 (NC=O), 1652 (N(N)C=O), 1448, 1339 (S=O_{as}), 1164 (S=O_s), 1095; δ_H (250 MHz, $CDCl_3$) 7.88–7.83 (2H, m, SO_2PhH), 7.62–7.47 (3H, m, SO_2PhH), 7.06 (1H, s, ArH), 6.10–6.07 (1H, br m, =CH_B), 4.88 (1H, dd, $J=5.6$, 2.9 Hz, NCH), 4.43 (1H, d, $J=16.3$ Hz, NC*H*H), 4.05 (1H, ddd, $J=16.3$, 4.9, 3.2 Hz, NCH*H*), 3.51 (3H, s, CH_3), 3.41 (3H, s, CH_3), 3.34 (3H, s, CH_3), 2.65–2.63 (2H, br m, =CHCH_2); δ_C (63 MHz, $CDCl_3$) 171.1 (C=O), 162.3 (C=O), 151.6 (C=O), 140.0, 139.6, 133.1, 129.4, 128.6, 127.6, 122.7, 112.8, 52.7 (NCH), 52.5 (OCH_3), 43.7 (NCH_2), 37.5 (CH_3), 28.5 (CH_3), 28.1 (=CH*C*H_2) *m*/*z* (%) (EI) 419 (9, M^+), 278 (68, $M-SO_2Ph$), 218 (100), 77 (25, Ph).

2.3.16. Methyl 1-(phenylsulfonyl)-5-(2-thienyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (31). Prepared by the general ring closing metathesis procedure on a 0.13 mmol scale and a reaction time of 3 h. Purification by flash column chromatography eluting with DCM affords the product (33 mg, 71%) as a viscous colourless oil; R_f 0.15; (Found: C, 55.90; H, 4.90; N, 3.60; $C_{17}H_{17}NO_4S_2$ requires C, 56.20; H, 4.7; N, 3.85%); ν_{max}/cm^{-1} (film) 1743 (C=O), 1447, 1339 (S=O_{as}), 1202, 1164 (S=O_s), 1098. δ_H (250 MHz, $CDCl_3$), 7.86–7.82 (2H, m, SO_2PhH), 7.63–7.49 (3H, m, SO_2PhH), 7.16 (1H, dd, $J=5.0$, 0.8 Hz, ArH), 7.05–6.93 (2H, m, ArH and ArH), 6.09–6.06 (1H, br m, =CH), 4.25 (1H, t, $J=$ 4.5 Hz, NCH), 4.71 (1H, dd, $J=16.1$, 1.9 Hz, NC*H*H), 4.17 (dd, 1H, $J=16.1$, 1.9 Hz, NCH*H*), 3.40 (3H, s, CH_3), 2.71–7.76 (2H, br m, =CHCH_2). δ_C (63 MHz, $CDCl_3$) 171.0 (C=O), 142.1, 139.5, 133.2, 129.4, 128.5, 127.8, 127.5, 124.4, 122.6, 118.8, 52.8 (NCH), 52.7 (OCH_3), 43.6 (NCH_2), 28.2 (=CH*C*H_2); *m*/*z* (%) (EI) 363 (6, M^+), 304 (18, $M-CO_2Me$,), 222 (72, $M-SO_2$ Ph,), 162 (100), 77 (59, Ph).

2.3.17. Methyl 5-(4 methoxyphenyl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (32). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 2 h. Purification by flash column chromatography eluting with 4:1 v/v ether/ petrol afforded the product (43 mg, 96%) as a viscous, colourless oil; R_f 0.35; (Found: C, 61.85; H, 5.75, N, 3.55. $C_{20}H_{21}NO_5S$ requires C, 62.00; H, 5.46; N, 3.62%); ν_{max}/cm^{-1} (film) 1744 (C=O), 1514, 1341 (S=O_{as}), 1248 (OCH_3), 1163 (S=O_s), 1097, 1024; δ_H (250 MHz, $CDCl_3$), 7.86–7.82 (2H, m, SO_2PhH), 7.58–7.51 (3H, m, SO_2PhH), 7.23 (2H, d, $J=8.9$ Hz, ArH), 6.85 (2H, d, $J=8.9$ Hz, ArH), 5.96–5.93 (1H, br m, =CH), 4.92 (1H, t, $J=4.2$ Hz, NCH), 4.48 (1H, dd, $J=16.3$, 1.9 Hz, NC*H*H), 4.11 (1H, dd, $J=$ 16.3, 1.9 Hz, NCH*H*), 3.80 (3H, s, CH_3), 3.46 (3H, s, CH_3), 2.74–2.71 (2H, br m, =CHCH_2); δ_C (63 MHz, $CDCl_3$) 171.2 (C=O), 159.8, 139.5, 133.4, 133.1, 131.1, 129.3, 127.6, 126.6, 118.1, 114.3, 55.7 (OCH_3), 52.8 (NCH), 52.6 (OCH_3), 44.0 (NCH_2), 28.5 (=CH*C*H_2); *m*/*z* (ES) 410 ($M^+ + Na$).

2.3.18. Methyl 5-(1-methyl-1*H*-indole-5-yl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (33). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 5 h. Purification by flash column chromatography eluting with 4:1 v/v ether/ petrol affords the product (41 mg, 85%) as a colourless oil, which solidified on standing, mp 138–140 °C; R_f 0.35; (Found: C, 64.25; H, 5.55; N, 6.90; $C_{22}H_{22}N_2O_4S$ requires C, 64.35; H, 5.40; N, 6.80%); ν_{max}/cm^{-1} (film) 1743 (C=O), 1446, 1339 (S=O_{as}), 1201, 1161 (S=O_s), 1097; δ_H (250 MHz, $CDCl_3$) 7.87–7.83 (2H, m, SO_2PhH), 7.57–7.46 (4H, m, 3×SO_2PhH and ArH), 7.26 (1H, d, $J=8.6$ Hz, ArH_E) 7.19 (1H, dd, $J=8.6$, 1.7 Hz, ArH), 7.05 (1H, d, $J=3.1$ Hz, ArH), 6.46 (1H, d, $J=3.1$ Hz, ArH), 6.00–5.97 (1H, m, =CH), 4.95 (1H, t, $J=4.2$ Hz, NCH), 4.60 (1H, dd, $J=16.3$, 1.9 Hz, NC*H*H), 4.21 (1H, ddd, $J=$ 16.3, 5.0, 2.8 Hz, NCH*H*), 4.17 (3H, s, CH_3), 3.45 (3H, s, CH_3), 2.76–2.73 (2H, br m, =CHCH_2); *m*/*z* (ES) 433 ($M^+ + Na$).

2.3.19. Methyl 5-(2-methyl-4-nitrophenyl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (34). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 5 h. Purification by flash chromatography eluting with 1:4 v/v ethyl acetate/ petrol afforded the product (35 mg, 74%), which crystallised from petrol/DCM as colourless needles, mp 154–156 °C; R_f 0.1; (Found: C, 57.90; H, 4.90; N, 6.50. $C_{22}H_{24}N_2O_6S$ requires C, 57.70; H, 4.85; N, 6.75%); ν_{max}/cm^{-1} (film) 1743 (C=O), 1518 (NO_2), 1447, 1344 (S=O_{as}), 1289, 1021, 1166 (S=O_s), 1095; δ_H (500 MHz, $CDCl_3$) 8.04 (1H, d, $J=2.4$ Hz, ArH), 7.99 (1H, dd, $J=8.4$, 2.4 Hz, ArH), 7.81–7.79 (2H, m, SO_2PhH), 7.60–7.58 (1H, m, SO_2PhH) 7.53–7.50 (2H, m, SO_2PhH), 7.17 (1H, d, $J=8.4$ Hz, ArH), 5.65–5.62 (1H, m, =CH), 4.97 (1H, dd, $J=6.7$, 1.8 Hz, NCH), 4.22–4.18 (1H, m, NC*H*H), 3.96–3.92 (1H, m, NCH*H*), 3.52 (3H, s, OCH_3), 2.78–2.72 (2H, m, =CHCH_2), 2.28 (3H, s, $ArCH_3$); δ_C (125 MHz, $CDCl_3$) 170.6 (C=O), 147.4, 145.9, 138.7, 137.8, 134.1, 132.9, 129.8, 129.0, 127.2, 125.1, 122.5, 120.9, 52.3 (NCH), 52.0 (OCH_3), 44.8 (NCH_2), 28.0 (=CH*C*H_2), 19.6 ($ArCH_3$); *m*/*z* (%) (EI) 416 (2, M^+), 357 (75, $M-CO_2Me$), 275 (93, $M-SO_2Ph$), 215 (61), 141 (53, SO_2Ph), 77 (100, C_6H_5).

2.3.20. Methyl 5-(1-methyl-2,3,dioxo-2,3-dihydro-1*H*-indol-5-yl)-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (35). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 3 h. Purification by flash column chromatography eluting with 3:2 v/v ethyl acetate/petrol afforded the product (39 mg, 83%) as red needles, mp 175–177 °C; R_f 0.2; (Found: C, 57.85; H, 5.05; N, 5.75. $C_{22}H_{20}N_2O_6S$ with 1 equiv of H_2O requires C, 57.65; H, 4.85; N, 6.36%); ν_{max}/cm^{-1} (film) 1739 (MeO–C=O), 1620, 1338 (S=O_{as}), 1164 (S=O_s), 1098; δ_H (250 MHz, $CDCl_3$) 7.86–7.83 (2H, m, SO_2PhH), 7.65–7.50 (5H, m, 3×

SO_2PhH and ArH), 6.87 (1H, d, $J=8.4$ Hz, ArH), 6.09–6.01 (1H, br m, =CH), 4.94 (1H, t, $J=4.2$ Hz, NCH), 4.44 (1H, dd, $J=16.3$, 1.9 Hz, NC*H*H), 4.11 (1H, dd, $J=16.3$, 1.9 Hz, NCH*H*), 3.47 (3H, s, CH_3), 3.26 (3H, s, CH_3), 2.76 (2H, br s, =CHCH_2). δ_C (63 MHz, $CDCl_3$) 183.1 (C=O), 170.2 (C=O), 157.9 (C=O), 150.5, 138.5, 134.6, 134.0, 132.6, 131.6, 128.8, 126.9, 121.6, 119.9, 117.2, 109.8, 52.0 (NCH), 52.8 (OCH_3), 43.0 (NCH_2), 27.5 (=CCH_2), 26.1 (CH_3); *m/z* (ES) 463 ($M^+ + Na$); HRMS found 463.0940, [$C_{22}H_{20}N_2O_6S + Na$] requires 463.0961.

2.3.21. Methyl 2-{[(4-nitrophenyl)sulfonyl](2-phenylprop-2-enyl)amino}pent-4-enoate (36). Prepared by the general termolecular cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 42 h. Purification by flash chromatography eluting with 4:1 v/v petrol/ether afforded the product (611 mg, 71%), which crystallised from DCM/petrol as colourless needles, mp 81–83 °C. R_f 0.2; (Found: C, 58.70; H, 5.15; N, 6.40; $C_{21}H_{22}N_2O_6S$ requires C, 58.60; H, 5.15; N, 6.50%); ν_{max}/cm^{-1} (film) 1742 (C=O), 1530 (NO_2), 1350 ($S=O_{as}$), 1163 ($S=O_{as}$), 1090; δ_H (500 MHz, $CDCl_3$) 8.27 (2H, d, $J=8.9$ Hz, ArH), 7.97 (2H, d, $J=8.9$ Hz, ArH_E), 7.30–7.26 (5H, m, ArH), 5.69–5.61 (1H, ddt, $J=16.8$, 9.8, 6.8 Hz, C*H*=CHH), 5.44 (1H, s, =C*H*H), 5.34 (1H, s, =CH*H*), 5.07–5.03 (2H, m, CH=C$H_{cis}H_{trans}$), 4.54 (1H, t, $J=$ 7.4 Hz, NCH), 4.43 (1H, d, $J=16.6$ Hz, NC*H*H), 4.35 (1H, d, $J=16.6$ Hz, NCH*H*), 3.50 (3H, s, CH_3), 2.74–2.68 (1H, m, =CH–C*H*H), 2.52–2.46 (1H, m,=CH*H*); δ_C (125 MHz, $CDCl_3$) 170.1 (C=O), 150.0, 145.5, 143.1, 138.6, 133.0, 129.0, 128.5, 128.2, 126.4, 124.0, 118.7, 117.0, 60.1 (NCH), 52.1 (OCH_3), 50.3 (N–CH_2), 34.8 (=CHCH_2); *m/z* (ES) 453 ($M^+ + Na$).

2.3.22. Methyl 2-{[2-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)prop-2-enyl][(4-nitrophenyl sufonyl)]amino}pent-4-enoate (37). Prepared by the general termolecular cascade procedure on a 2.9 mmol scale, using 3.3 mmol of aryl iodide and a reaction time of 46 h. Purification by flash chromatography eluting with 1:1 v/v ethyl acetate/ether afforded the product (960 mg, 67%), which crystallised from DCM/petrol as colourless needles, mp 140–142 °C. R_f 0.17; (Found: C, 51.25; H, 5.00; N, 11.45. $C_{21}H_{24}N_4O_8S$ requires C, 51.20; H, 4.90; N, 11.40%); ν_{max}/cm^{-1} (film) 1742 (MeO–C=O), 1702 (N–C=O), 1653 (N(N)C=O), 1531 (NO_2), 1350 ($S=O_2$), 1161 ($S=O_3$); δ_H ($CDCl_3$ 250 MHz) 8.35 (2H, d, $J=9.0$ Hz, ArH), 8.02 (2H, d, $J=9.0$ Hz, ArH), 7.27 (1H, s, ArH), 5.71 (1H, ddt, $J=16.9$, 10.2, 6.6 Hz, C*H*=CHH), 5.43 (1H, d, $J=1.0$ Hz, =C*H*H), 5.38 (1H, d, $J=1.0$ Hz, =CH*H*), 5.11 (1H, ddd, $J=16.9$, 3.1, 1.5 Hz, CH=CHH_{trans}), 5.05 (1H, ddd, $J=10.2$, 2.6, 1.7 Hz, CH=CH_{cis}) 4.58 (1H, dd, $J=8.7$, 6.4 Hz, NCH), 4.24 (2H, s, NCH_2), 3.51 (3H, s, CH_3), 3.43 (3H, s, CH_3), 3.33 (3H, s, CH_3), 2.81–2.69 (1H, m, =CHC*H*H); 2.64–2.52 (1H, m, =CHCH*H*); δ_C (63 MHz, $CDCl_3$) 170.5 (C=O), 162.7 (C=O), 152.5 (C=O), 150.2, 145.1, 141.8, 138.7, 133.7, 129.5, 124.3, 119.8 (=CH_2), 118.8 (=CH_2), 112.7, 61.0 (NCH), 52.6 (OCH_3), 50.4 (NCH_2), 37.5 (NCH_3), 34.8 (=CHCH_2), 28.4 NCH_3; *m/z* (EI) 492 (4, M^+), 433 (21, $M-CO_2Me$), 387 (100), 369 (47), 306 (100, $M-SO_2PhNO_2$).

2.3.23. Methyl 2-{[(4-nitrophenyl)sulfonyl][2-(1-methyl-2,3,-dioxo-2,3,-dihydro-1*H*-indol-5-yl)prop-2-enyl]amino}-pent-4-enoate (38). Prepared by the general termolecular cascade procedure on a 2.0 mmol scale, using 2.0 mmol of aryl iodide and a reaction time of 48 h. $Pd_2(dba)_3$ (0.05 mmol) was used in place of $Pd(OAc)_2$. Purification by flash column chromatography eluting with 7:3 v/v petrol/ethyl acetate afforded the product (380 mg, 43%) as red needles, mp 141–143 °C; R_f 0.21; (Found: C, 55.90; H, 4.45; N, 8.05. $C_{24}H_{23}N_3O_8S$ requires C, 56.15; H, 4.50; N, 8.20%); ν_{max}/cm^{-1} (film) 1741 (MeO–C=O), 1620, 1529 (NO_2), 1349 ($S=O_{as}$), 1165 ($S=O_s$) 1092; δ_H (250 MHz, $CDCl_3$) 8.35 (2H, d, $J=8.9$ Hz, ArH), 8.01 (2H, d, $J=8.9$ Hz, ArH), 7.68 (1H, dd, $J=8.2$, 1.9 Hz, ArH_I), 7.58 (1H, d, $J=1.9$ Hz, ArH), 6.88 (1H, d, $J=8.2$ Hz, ArH), 5.63 (1H, ddt, $J=16.7$, 9.8, 6.9 Hz, C*H*=CHH), 5.5 (1H, s, =C*H*H), 5.4 (1H, s, =CH*H*), 5.02–5.09 (2H, m, CH=C$H_{cis}H_{trans}$), 4.54 (1H, t, $J=7.4$ Hz, NCH), 4.44 (1H, d, $J=16.8$ Hz, NC*H*H), 4.26 (1H, d, $J=16.8$ Hz, NCH*H*), 3.49 (3H, s, CH_3), 3.28 (3H, s, CH_3), 2.61–2.73 (1H, m, =CHC*H*H), 2.36–2.50 (1H, m, =CHCH*H*); δ_C (75 MHz, $CDCl_3$) 183.6 (C=O), 170.3 (C=O), 158.6 (C=O), 151.4, 150.6, 145.3, 141.8, 136.7, 134.8, 133.1, 129.3, 124.5, 123.4, 119.4, 117.8, 110.4, 60.4 (NCH), 52.7 (OCH_3), 50.4 (NCH_2), 35.3 (=CHCH_2), 23.0 (NCH_3); *m/z* (ES) 536 ($M^+ + Na$).

2.3.24. Methyl 1-[(4-nitrophenyl)sulfonyl]-5-phenyl-1,2,3,6-tetrahydropyridine-2-yl(propan-1-one) (39). Prepared by the general ring closing metathesis procedure on a 0.05 mmol scale and a reaction time of 1 h. Purification by flash column chromatography eluting with 3:2 v/v petrol/ether afforded the product (206 mg, 98%) as colourless needles, mp 112–114 °C. R_f 0.19; (Found: C, 56.65; H, 4.75; N, 6.95. $C_{19}H_{18}N_2O_6S$ requires C, 56.71; H, 4.50; N, 6.95%); ν_{max}/cm^{-1} (film) 1743 (C=O), 1530 (NO_2), 1349 ($S=O_{as}$), 1167 ($S=O_{as}$), 1097; δ_H (250 MHz, $CDCl_3$), 8.37 (2H, d, $J=8.6$ Hz, ArH), 8.03 (2H, d, $J=8.6$ Hz, ArH), 7.38–7.26 (5H, m, ArH), 6.10–6.06 (1H, br m, =CH), 4.98 (1H, dd, $J=5.5$, 2.8 Hz, NCH), 4.57 (1H, dd, $J=16.1$, 1.7 Hz, NC*H*H), 4.13 (1H, ddd, $J=16.1$, 5.3, 3.2 Hz, NCH*H*) 3.54 (3H, s, CH_3), 2.81–2.77 (2H, br m, =CHCH_2); δ_C (63 MHz, $CDCl_3$) 170.6 (C=O), 150.4, 145.1, 138.2, 133.8, 129.1, 128.9, 128.6, 125.5, 124.6, 119.9, 53.1, 52.9, 44.0, 28.6; *m/z* (%) (EI) 402 (3, M^+), 343 (6, $M-CO_2Me$), 216 (40), 156 (100, SO_2PhNO_2), 129 (32).

2.3.25. Methyl 5-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1-[(4-nitorphenyl)sulfonyl]-1,2,3,6-tetrahydropyridine-2-carboxylate (40). Prepared by the general ring closing metathesis procedure on a 0.16 mmol scale and a reaction time of 1 h. Purification by flash chromatography eluting with 3:2 v/v ethyl acetate/petrol afforded the product (702 mg, 93%) as colourless needles, mp 221–223 °C; R_f 0.14; (Found: C, 49.05; H, 4.40; N, 12.20. $C_{19}H_{20}N_4O_8S$ requires C, 49.15; H, 4.35; N, 12.05%); ν_{max}/cm^{-1} (film) 1742 (MeO–C=O), 1702 (N–C=O), 1653 (N(N)C=O), 1530 (NO_2), 1350 ($S=O_{as}$), 1167 ($S=O_s$); δ_H ($CDCl_3$, 250 MHz) 8.36 (2H, d, $J=$ 8.9 Hz, ArH), 8.06 (2H, d, $J=8.9$ Hz, ArH), 7.08 (1H, s, ArH), 5.98–5.94 (1H, br m, =CH), 4.91 (1H, dd, $J=6.6$, 1.65 Hz, NCH), 4.61 (1H, d, $J=16.6$ Hz, NC*H*H), 4.06–3.99 (1H, m, NCH*H*), 3.58 (3H, s, CH_3), 3.41 (3H, s, CH_3), 3.34 (3H, s, CH_3), 2.70–2.61 (2H, br m, =CHCH_2); δ_C (63 MHz, $CDCl_3$) 170.6 (C=O), 162.4 (C=O), 151.6

(C=O), 150.4, 145.4, 140.4, 128.9, 124.6, 122.6, 112.6, 53.0 (NCH), 52.9 (OMe), 43.8 (NCH_2), 37.5 (NCH_3), 28.5 (=CHCH_2), 27.9 (NCH_3); *m/z* (%) (FAB) 465 (100, M+ H^+), 279 (31, M−SO_2PhNO_2), 218 (24).

2.3.26. Methyl 5-(1,3-dimethyl-2,4,-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1-[(4-nitrophenyl)sulfonyl]-1,2,3,6-tetrahydropyridine-2-carboxylate (41). Prepared by the general ring closing metathesis procedure on a 0.058 mmol scale and a reaction time of 1 h. Purification by flash column chromatography eluting with 1:1 v/v ethyl acetate/petrol afforded the product (216 mg, 76%) as red needles, mp 224–226 °C; R_f 0.16; (Found: C, 54.40; H, 3.90; N, 8.45. $C_{22}H_{19}N_3O_8S$ requires C, 54.45; H, 3.95; 8.65%); ν_{max}/cm^{-1} (film) 1740 (MeO–C=O), 1621, 1530 (NO_2), 1349 ($S{=}O_{as}$) 1168 ($S{=}O_s$); δ_H (250 MHz, $CDCl_3$), 8.39 (2H, d, J=9.0 Hz, ArH), 8.03 (2H, d, J=9.0 Hz, ArH), 7.56 (2H, dd, J=7.3, 1.8 Hz, ArH), 7.54 (1H, s, ArH), 6.88 (1H, dd, J=7.3, 1.8 Hz, ArH), 6.11–6.09 (1H, br m, =CH), 4.98 (1H, t, J=4.2 Hz, NCH), 4.48 (1H, dd, J=16.2, 1.9 Hz, NC*H*H), 4.08 (m, 1H, NCH*H*), 3.54 (3H, s, CH_3), 3.27 (3H, s, CH_3), 2.83 (2H, br s, =CHCH_2); *m/z* (ES) 508 (M^+ + Na).

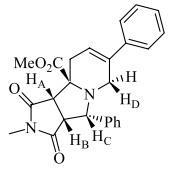
2.3.27. Methyl 5-phenyl-1,2,3,6-tetrahydropyridine-2-carboxylate (42). A solution of 39 (215 mg, 0.5 mmol) and benzene thiol (62 μl, 0.6 mmol) in DMF (4 ml) was added to a suspension of K_2CO_2 (0.208 g, 1.5 mmol) in DMF (3 ml) and the mixture stirred for 3 h at room temperature, quenched with 10% $NaHCO_3$ solution (6 ml) and extracted with ether (3×5 ml). The combined organic extracts were washed with water (5 ml), dried ($MgSO_4$), filtered and the filtrate concentrated in vacuo. Purification of the residue by flash chromatography eluting with ether afforded the product (88 mg, 83%) as pale yellow needles, mp 46–48 °C; R_f 0.1; (Found: C, 71.60; H, 7.20; N, 6.35. $C_{13}H_{15}NO_2$ requires C, 71.85; H, 6.95; N, 6.45%); ν_{max}/cm^{-1} (film) 3342 (NH), 1738 (C=O), 1435, 1202, 1174; δ_H (300 MHz, $CDCl_3$) 7.33–7.23 (5H, m, ArH), 6.16–6.13 (1H, br m, =CH), 3.90–3.80 (2H, m, NCH_2), 3.77 (3H, s, CH_3), 3.65 (1H, dd, J=9.1, 5.0 Hz, NCH), 2.55–2.45 (2H, m, =CHCH_2); δ_C (75 MHz, $CDCl_3$) 174.2 (C=O), 139.9, 136.8, 128.8, 127.7, 125.3, 121.5, 55.0 (OCH_3), 52.6 (NCH), 46.5 (NCH_2), 29.0 (=CHCH_2); *m/z* (EI) 217 (21, M^+), 158 (100, M−CO_2Me), 91 (38).

2.3.28. Methyl 5-(1,3,-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1,2,3,6-tetrahydropyridine-2-carboxylate (43). Prepared by the above method, on a 1.4 mmol scale and a reaction time of 18 h. Purification by flash chromatography eluting with 9:1 v/v DCM/MeOH afforded the product (266 mg, 70%) as a pale yellow solid, mp 76–78 °C; R_f 0.28; (Found: C, 55.75; H, 5.80; N, 15.20. $C_{13}H_{15}NO_2$ requires C, 55.25; H, 6.10; N, 15.05%); ν_{max}/cm^{-1} (film) 1701 (C=O), 1653, 1437, 1293; δ_H (250 MHz, $CDCl_3$), 7.08 (1H, s, ArH), 6.15–6.14 (1H, br m, =CH), 3.76 (3H, s, CH_3), 3.69 (2H, br s, NCH_2), 3.64 (1H, dd, J= 9.2, 5.2 Hz, NCH), 3.42 (3H, s, CH_3), 3.35 (3H, s, CH_3), 2.50–2.32 (2H, m, =CHCH_2); *m/z* (%) (FAB) 280 (100, M^+), 220 (10, M−CO_2Me,), 193 (6).

2.4. Intermolecular cycloaddition

Benzaldehyde (22 μl, 0.2 mmol), and *N*-methyl maleimide (25 mg, 0.23 mmol) were added to a stirred solution of **42** (45 mg, 0.2 mmol) in toluene (6 ml). The reaction mixture was immersed in a pre-heated oil bath at 110 °C and stirred under a nitrogen atmosphere for 54 h. Concentration in vacuo gave the crude product, which comprised 3.5:1 mixture of **44** and **45**. Preparative HPLC (Luna C18/7:3 v/v MeCN/H_2O, 0.6 ml/min, detection at 254 nm) afforded pure **44** and **45** in 80% combined yield.

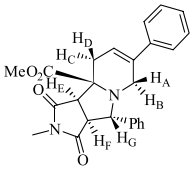
2.4.1. *endo*-Methyl 2-methyl-1,3-dioxo-4,7-diphenyl 1,2,3,3a,4,6,9,9b-octahydro-9a*H*-pyrrolo[3,4-*a*]indolizine-9a-carboxylate (44). Crystallisation from DCM/petrol afforded colourless needles, mp 105–107 °C; R_f 0.17; (Found: C, 72.15; H, 5.65; N, 6.50. $C_{25}H_{24}N_2O_4$ requires C, 72.10; H, 5.80; N, 6.75%); ν_{max}/cm^{-1} (film) 1750 (MeOC=O), 1702 (N–C=O), 1435, 1286; δ_H (500 MHz, C_6D_6), 7.16–7.03 (7H, m, ArH), 6.97–6.96 (3H, m, ArH), 6.02 (1H, m, =CH), 4.80 (1H, d, J=9.7 Hz, NCH_C), 3.82–3.80 (1H, m, NC*H*H|), 3.79–3.77 (1H, m, NCH*H*) 3.38 (1H, ddd, J=17.5, 6.5, 2.9 Hz, =CHC*H*H), 3.25 (3H, s, Me), 3.22 (1H, ddd, J=17.5, 6.4, 1.7 Hz, =CHCH*H*), 3.07 (1H, dd, J=9.7, 7.9 Hz, PhCHCH_B), 2.84 (1H, d, J=7.9 Hz, $NCCH_A$), 2.56 (3H, s, Me); δ_C (63 MHz, $CDCl_3$) 175.5 (C=O), 175.4 (C=O), 173.7 (C=O), 139.2, 137.4, 135.1, 131.0, 129.0, 128.7, 128.3, 127.8, 125.3, 120.6, 68.5, 68.3, 52.6, 51.1, 49.7, 48.7 (NCH_2), 31.8 (=CHCH_2), 25.3; *m/z* (%) (EI) 416 (1, M^+), 357 (100, M−CO_2Me);



NOE data:

Signal irradiated	Enhancement (%)			
	H_A	H_B	H_C	H_D
H_A		8.5		
H_B	12.1		9.5	
H_C		17.7		5.6

2.4.2. *exo*-Methyl 2-methyl-1,3-dioxo-4,7-diphenyl 1,2,3,3a,4,6,9,9b-octahydro-9a*H*-pyrrolo[3,4-*a*]indolizine-9a-carboxylate (45). Crystallisation from CH_3CN/H_2O afforded colourless needles, mp 212–214 °C, R_f 0.27; (Found: C, 71.90; H, 5.55; N, 6.50. $C_{25}H_{24}N_2O_4$ requires C, 72.10; H, 5.80; N, 6.75%); ν_{max}/cm^{-1} (film) 1769 (MeOC=O), 1693 (N–C=O), 1496, 1443, 1380, 1076; δ_H (500 MHz, C_6D_6), 7.58–7.57 (2H, m, ArH), 7.23–7.20 (2H, m, ArH), 7.14–7.12 (1H, m, ArH), 7.03–6.97 (5H, m, ArH), 6.10–6.09 (1H, m, =CH), 4.88 (1H, d, J=5.2 Hz, NCH_G), 3.63–3.60 (1H, m, NCH_AH_B), 3.43–3.34 (2H, m, NCH_AH_B and =CHCH_CH_D), 3.20 (3H, s, CO_2Me), 2.80 (1H, d, J= 9.8 Hz, CH_E), 2.77 (1H, dd, J=9.8, 5.2 Hz, CH_F), 2.73 (3H, s, NMe), 2.45–2.40 (1H, m, $CHCH_CH_D$); δ_C (75 MHz, $CDCl_3$) 175 (C=O), 174.4 (C=O), 171.3 (C=O), 139.7, 137.7, 133.4, 128.0, 127.3, 127.1, 126.4, 126.3, 123.8, 120.5, 68.4 (*C*CO_2Me), 66.5 (NCH), 53.2, 52.4, 50.9, 46.1 (NCH_2), 35.2 (=CHCH_2), 23.9 (NCH_3); *m/z* (ES) 416 (M);



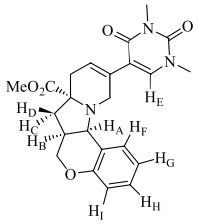
NOE data:

Signal irradiated	Enhancement (%)					
	H_A	H_B	H_C	H_D	H_E	H_G
H_A		25.0				6.9
H_C				31.7	15.2	
H_E			3.3			
H_G	5.7					

2.5. Intramolecular cycloaddition

2.5.1. Methyl-10-phenyl-6a,8,11,12a,tetrahydro-6*H*-chromeno[3,4-β]indolizine-7a(7*H*)-carboxylate (47). Salicylic aldehyde **46** (92 mg, 0.57 mmol) in toluene (2 ml) was added to a solution of **42** (112 mg, 0.52 mmol) in toluene (8 ml). The reaction mixture was immersed in a pre-heated oil bath at 110 °C and stirred under a nitrogen atmosphere for 26 h. Concentration in vacuo afforded a yellow gum, which was purified by flash column chromatography eluting with DCM to afford **47** (101 mg, 56%), which crystallised from DCM/petrol as colourless plates, mp 157–159 °C; R_f 0.34; ν_{max}/cm^{-1} (film) 1727 (C=O), 1488, 1224, 1192, 1172; δ_H (500 MHz, C_6D_6), 7.31–7.29 (2H, m, ArH), 7.26 (1H, dd, J=7.5, 1.6 Hz, ArH), 7.18–7.04 (m, 5H, ArH), 6.81 (1H, td, J=7.5, 1.5 Hz, ArH), 5.98 (1H, ddd, J=6.4, 4.0, 1.8 Hz =CH), 4.45 (1H, d, J=6.7 Hz, NCH), 4.28 (1H, br d, J=15.7 Hz, NC*H*H), 4.06 (1H, br d, J=15.7 Hz, NCH*H*), 3.77 (1H, dd, J=10.7, 8.5 Hz, OC*H*H) 3.67 (1H, dd, J=10.7, 4.4 Hz, OCH*H*), 3.33 (3H, s, CH_3), 2.98 (1H, ddd, J=16.4, 6.4, 1.8 Hz, =CC*H*H), 2.28–2.23 (1H, m, CH_2CH), 2.14–2.07 (2H, m, =CCH*H* and CHC*H*H), 1.43 (1H, dd, J=13.3, 5.0 Hz, CHCH*H*); δ_C (75 MHz, $CDCl_3$) 176.0 (C=O), 156.3, 140.1, 136.8, 131.6, 129.0, 128.7, 127.6, 125.6, 123.1, 121.7, 120.9, 117.8, 68.6 (OCH_2), 65.3 (NC), 58.3 (NCH), 51.9, 47.8 (CH_2), 38.3 (CH_2), 37.2 (CH_2), 34.9; *m/z* (%) (EI) 361 (1, M^+), 302 (100, $M-CO_2Me$). HRMS found 362.1747. $C_{23}H_{24}NO_3$ requires 362.1756.

2.5.2. Methyl 10-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-6a,8,11,12a-tetrahydro-6*H*-chromeno[3,4-β]indolizine-7a (7*H*)-carboxylate (48). Salicylic aldehyde **46** (70 mg, 0.43 mmol) in toluene (2 ml) was added to a solution of **43** (100 mg, 0.36 mmol) in toluene (8 ml). The reaction mixture was immersed in a pre-heated oil bath at 110 °C and stirred under a nitrogen atmosphere for 34 h. Work up (as above) followed by flash column chromatography eluting with 3:2 v/v ethyl acetate/petrol afforded **48** (82 mg, 54%), which crystallised from DCM/petrol as colourless plates, mp 238–240 °C; R_f 0.25; (Found: C, 65.40; H, 6.00; N, 9.70. $C_{23}H_{25}N_3O_5$ requires C, 65.25; H, 5.95; N, 9.90%) ν_{max}/cm^{-1} (film) 1725 (MeO–C=O), 1701 (N–C=O), 1652 (N(N)C=O), 1488, 1453, 1224, 1174, 1196; δ_H (500 MHz, $CDCl_3$) 7.22 (1H, dd, J=7.5, 1.7 Hz, ArH_F) 7.18 (1H, td, J=7.5, 1.7 Hz, ArH_G), 6.98 (1H, s, ArH_E), 6.94–6.90 (2H, m, ArH_H and ArH_I), 6.12–6.11 (1H, m, =CH), 4.25 (1H, d, J=7.1 Hz, NCH), 3.96 (1H, dd, J=10.6, 4.7 Hz, OC*H*H), 3.93 (1H, d, J=15.4 Hz, NC*H*H), 3.90 (1H, dd, J=10.6, 8.1 Hz, OCH*H*), 3.74 (3H, s, CH_3), 3.57 (d, 1H, J=15.4 Hz, NCH*H*) 3.38 (3H, s, CH_3), 3.33 (3H, s, CH_3), 2.97 (1H, ddd, J=16.6, 6.3, 2.0 Hz, =CHC*H*H), 2.60–2.56 (1H, m, OCH_2CH), 2.41 (1H, dd, J=13.3, 8.5 Hz, NCC*H*H), 2.21 (1H, d, J=16.6 Hz, =CHCH*H*), 1.71 (1H, dd, J=13.3, 5.3 Hz, NCCH*H*); *m/z* (%) (FAB) 424 (49, M^++H), 464 (55, $M-CO_2Me$);



NOE data:

Signal irradiated	Enhancement (%)		
	H_A	H_B	H_C
H_A		9.6	
H_B	6.8		3.4

2.5.3. 2-Allylphenyl-2-(thienyl)prop-2-en-1yl ether (53). Prepared by the general termolecular cascade procedure employing 2-allyphenol as the nucleophile on a 2 mmol scale, using 2.5 mmol of aryl iodide and a reaction time of 16 h. Purification by flash chromatograpy eluting with 19:1 v/v petrol/ether afforded the product (398 mg, 78%) as a colourless liquid; R_f 0.05; (Found: C, 74.90; H, 6.15; $C_{16}H_{16}OS$. requires C, 74.95; H, 6.30%); ν_{max}/cm^{-1} (film) 1638, 1600, 1586, 1488, 1231, 1090; δ_H (250 MHz, $CDCl_3$) 7.25 (1H, d, J=4.0 Hz, ArH), 7.18 (2H, d, J=7.7 Hz, ArH and ArH), 7.13 (1H, d, J=3.7 Hz, ArH) 7.02 (1H, dd, J=4.0, 3.7 Hz, ArH) 6.93 (2H, t, J=7.7 Hz, ArH and ArH), 5.98 (1H, ddt, J=16.9, 10.2, 6.7 Hz, C*H*=CHH), 5.62 (1H, s, =CH*H*), 5.38 (1H, s, =C*H*H), 5.03 (1H, d, J=16.9 Hz, CH=CHH_{trans}), 5.02 (1H, d, J=10.2 Hz, CH=CH_{cis}H), 4.87 (2H, s, OCH_2), 3.42 (2H, d, J=6.7 Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 156.5, 142.4, 137.5, 137.4, 130.4, 129.5, 127.8, 127.7, 125.0, 124.3, 121.4, 115.9, 113.3, 112.1, 70.0 (OCH_2), 34.8 (CH_2); *m/z* (%) (EI) 256 (14, M^+), 215 (39), 123 (100), 79 (50).

2.5.4. 2-Allylphenyl-2-(4-nitrophenyl)prop-2-en-1-yl ether (54). Prepared by the general termolecular cascade procedure employing 2-allyphenol as the nucleophile on a 2 mmol scale, using 2.5 mmol of aryl iodide and a reaction time of 21 h. Purification by flash chromatography eluting with 9:1 v/v petrol/ether afforded the product (460 mg, 78%), which crystallised from DCM/petrol as colourless needles, mp 51–53 °C; R_f 0.16; (Found: C, 73.05; H, 6.00; N, 4.50. $C_{18}H_{17}NO_3$ requires C, 73.20; H, 5.80; N, 4.75%); ν_{max}/cm^{-1} (film) 1597, 1505 (NO_2), 1492, 1343 (NO_2), 1243; δ_H (250 MHz, $CDCl_3$) 8.20 (2H, d, J=8.9 Hz, ArH), 8.14 (2H, d, J=8.9 Hz, ArH), 7.22 (1H, d, J=8.0 Hz, ArH), 7.16 (1H, d, J=8.0 Hz, ArH), 6.94 (2H, t, J=8.0 Hz, ArH), 5.87 (1H, ddt, J=17.2, 10.7, 6.6 Hz, C*H*=CHH), 5.76 (1H, s, =CH*H*), 5.68 (1H, s, =C*H*H), 4.95 (1H, d, J=10.7 Hz, CH=CH_{cis}H), 4.94 (1H, d, J=17.2 Hz, CH=CHH_{trans})

4.92 (2H, s, OCH_3), 3.29 (2H, d, $J=6.6$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 156.2, 147.8, 145.3, 142.3, 137.1, 130.6, 129.4, 127.8, 127.4, 124.1, 121.7, 118.9, 115.9, 111.9, 69.9 (OCH_2), 34.7 (CH_2); *m/z* (%) (EI) 295 (18, M^+), 131 (42), 115 (100), 77 (35).

2.5.5. 1-Allyl-2{[2-(4-methoxyphenyl)prop-2-en-1-yl] oxy}benzene (55). Prepared by the general termolecular cascade procedure employing 2-allyphenol as the nucleophile on a 3 mmol scale, using 3.5 mmol of aryl iodide and a reaction time of 30 h. Purification by flash chromatograpy eluting with 19:1 v/v petrol/ether afforded the product (680 mg, 80%) as a colourless liquid; R_f 0.4; (Found: C, 81.10; H, 7.10; $C_{19}H_{20}O_2$ requires C, 81.40; H, 7.19%); ν_{max}/cm^{-1} (film) 1635, 1607, 1513, 1491, 1243, 1031; δ_H (250 MHz, $CDCl_3$) 7.42 (2H, d, $J=8.7$ Hz, ArH), 7.23–7.14 (2H, m, ArH), 6.95–6.83 (2H, m, ArH), 6.86 (2H, d, $J=$ 8.7 Hz, ArH), 5.98 (1H, ddt, $J=17.0$, 10.3, 6.7 Hz, C*H*=CHH), 5.51 (1H, s, =CH*H*), 5.39 (1H, s, =C*H*H), 5.04–4.97 (2H, m, C_X=$H_{cis}H_{trans}$), 4.87 (2H, s, OCH_2), 3.36 (2H, d, $J=6.7$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 159.8, 156.6, 143.0, 137.4, 131.4, 130.3, 129.5, 127.7, 127.6, 121.2, 115.8, 114.2, 113.2, 112.1, 70.3 (OCH_2), 55.7 (OCH_3), 34.8 (CH_2); *m/z* (ES) 281 ($M^+ + H$).

2.6. Modified ring closing metathesis procedure

2.6.1. 3-(2-Thienyl)-2,5-dihydro-1-benzoxepine (56). Catalyst **1** (22 mg, 2.5 μm) was added to a magnetically stirred solution of 53 (130 mg, 0.5 mmol), in anhydrous toluene (120 ml). The mixture then stirred under an argon atmosphere at 80 °C for 16 h. Concentration in vacuo afforded a brown oil, which was purified by flash chromatography eluting with 7:3 v/v petrol/DCM to afford the product (68 mg, 59%), which crystallised from DCM/hexane as colourless needles, mp 84–86 °C; R_f 0.35; (Found: C, 73.35; H, 5.40. $C_{14}H_{12}OS$ requires C, 73.65; H, 5.30%); ν_{max}/cm^{-1} (film) 1614, 1440, 1254, 1234; δ_H (250 MHz, $CDCl_3$) 7.26–7.02 (5H, m, ArH), 6.94 (1H, dd, $J=5.1$, 3.5 Hz, ArH), 6.84 (1H, d, $J=3.5$ Hz, ArH), 6.34 (1H, br t, $J=5.7$ Hz, =CH), 4.93 (2H, d, $J=1.8$ Hz, OCH_2), 3.62 (2H, d, $J=5.7$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 129.1, 128.5, 127.7, 124.7, 124.0, 123.9, 122.2, 121.5, 72.6 (OCH_2), 31.6 (CH_2); *m/z* (%) (EI) 228 (100, M^+), 165 (27), 131 (47), 97 (44).

2.6.2. 3-(4-Nitrophenyl)-2,5-dihydro-1-benzoxepine (57). Prepared by the modified general RCM procedure on a 0.46 mmol scale and a reaction time of 23 h. Purification by flash chromatography eluting with 1:1 v/v DCM/petrol afforded the product (76 mg, 62%), which crystallized from petrol/DCM as pale yellow needles, mp 94–96 °C; R_f 0.3; (Found: C, 71.65; H, 5.05. N, 5.10; $C_{16}H_{13}NO_3$ requires C, 71.90; H, 4.90; N, 5.25%); ν_{max}/cm^{-1} (film) 1652, 1516 (NO_2), 1343 (NO_2), 1229; δ_H (250 MHz, $CDCl_3$) 8.17 (2H, d, $J=8.8$ Hz, ArH), 7.37 (2H, d, $J=8.8$ Hz, ArH), 7.27–7.05 (4H, m, ArH), 6.31 (1H, br t, $J=5.7$ Hz, =CH), 4.95 (2H, d, $J=1.7$ Hz, OCH_2), 3.70 (2H, d, $J=5.7$ Hz, CH_2), δ_C (63 MHz, $CDCl_3$) 158.8, 147.3, 147.0, 137.3, 134.2, 129.4, 128.9, 128.8, 127.0, 124.7, 124.2, 121.5, 72.3 (OCH_2), 32.1 (CH_2); *m/z* (%) (EI) 267 (100, M^+), 252 (47), 220 (36), 131 (71), 91 (49).

2.6.3. 3-(4-Methoxyphenyl)-2,5-dihydro-1-benzoxepine (58). Prepared by the modified general RCM procedure on a 0.46 mmol scale and a reaction time of 22 h. Purification by flash chromatography eluting with 1:1 v/v DCM/petrol afforded the product (68 mg, 56%), which crystallised from hexane as colourless needles, mp 72–74 °C; R_f 0.35; ν_{max}/cm^{-1} (film) 1603, 1491, 1254, 1229, 1030; δ_H (300 MHz, $CDCl_3$) 7.24–7.02 (4H, m, ArH), 7.18 (2H, d, $J=8.7$ Hz, ArH), 6.83 (2H, d, $J=8.7$ Hz, ArH), 6.05 (1H, br t, $J=$ 5.5 Hz, =CH), 4.90 (2H, d, $J=2.1$ Hz, OCH_2), 3.62 (2H, d, $J=5.5$ Hz, CH_2); δ_C (75 MHz, $CDCl_3$) 159.5, 158.9, 138.3, 135.4, 133.1, 129.2, 128.4, 127.6, 124.4, 123.8, 121.5, 114.2, 73.2 (OCH_2), 55.7 (OCH_3), 31.9 (CH_2); *m/z* (%) (EI) 252 (100, M^+), 237 (82, $M-CH_3$) 131 (45); HRMS found 252.1143, $C_{17}H_{16}O_2$ requires 252.1145.

2.7. Single-crystal X-ray analysis for 44

Crystallographic data for **44** was measured on a Nonius Kappa CCD area-detector diffractometer using ϕ and ω-scans and graphite monochromated Mo Kα radiation ($\lambda=0.71073$ Å). The structure was solved by direct methods using SHELXS-86[32] and were refined by full-matrix least-squares (based on F^2) using SHELXL-97.[33] The weighting scheme used was $w=[\sigma^2(F_o^2)+(0.1235P)^2+0.0127P]^{-1}$ where $P=(F_o^2+2F_c^2)/3$. All non-hydrogen atoms were refined with anisotropic displacement parameters whilst hydrogen atoms were constrained to predicted positions using a riding model. The residuals wR_2 and R_1, given below, are defined as $wR_2=(\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[wF_o^2]^2)^{1/2}$ and $R_1=\Sigma||F_o|-|F_c||/\Sigma|F_o|$.

Crystal data for **44**. $C_{25}H_{24}N_2O_4$, $0.33\times0.20\times0.10$ mm, $M=416.46$, monoclinic, space group $P2_1/n$, $a=6.4754(1)$, $b=12.1259(2)$, $c=30.0988(6)$ Å, $\beta=93.3630(10)°$, $U=$ 2359.29(7) Å^3, $Z=2$, $D_c=1.172$ Mg m^{-3}, $\mu=0.08$ mm^{-1}, $F(000)=880$, $T=150(2)$ K.

Data collection. $1.36 \leq\theta\leq 26°$; 4602 independent reflections were collected [$R_{int}=0.082$]; 3209 reflections with $I>2\sigma(I)$.

Structure refinement. Number of parameters=283, goodness of fit, $s=1.084$; $wR_2=0.1980$, $R_1=0.0611$.

Full supplementary crystallographic data, which include hydrogen co-ordinates, thermal parameters and complete bond lengths and angles, have been deposited at the Cambridge Crystallographic Data Centre (CCDC 275316) and are available on request.

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