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Four-component Pd-catalysed cascade/ring closing metathesis. Synthesis of heterocyclic enones☆

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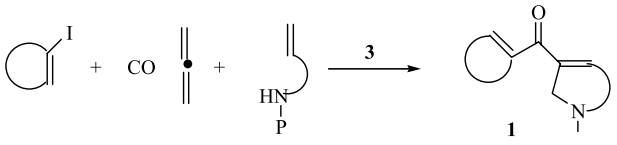
Abstract—A palladium-catalysed four-component process is described involving carbon monoxide, allene and aryl/heteroaryl iodides generating (π-allyl) palladium species, which are intercepted by alkene tethered nitrogen nucleophiles to afford 1,6- and 1,7-dienones. Subsequent ring closing metathesis affords five- and six-membered *N*-heterocyclic enones. The *N*-heterocyclic enones are active dipolarophiles in 1,3-dipolar cycloaddition reactions as exemplified by azomethine ylide and nitrone cycloadditions.

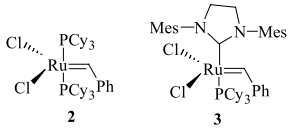
1. Introduction

Previously, we reported the devlopment of a Pd-catalysed three-component cascade/ring closing metathesis (RCM) route for five- and six-membered *N*-heterocycles.[2] In this system the muti-component cascade created the diversity, which is relayed into the final heterocycle by a RCM. Success of this methodology prompted us into investigate a more challenging four-component cascade (4CC)/RCM process accessing versatile heterocylic enones **1** (Scheme 1).

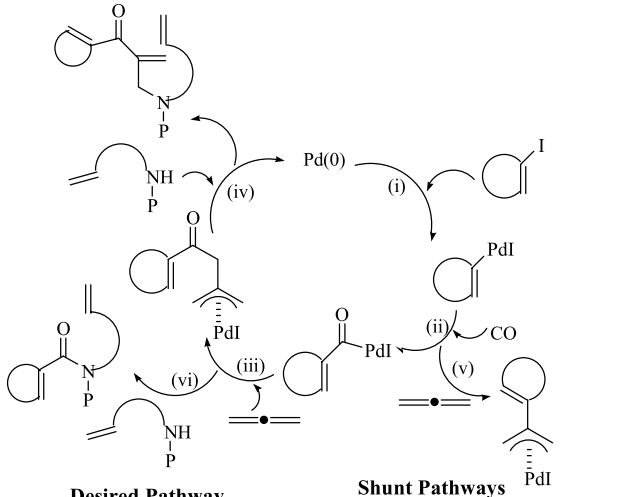


Scheme 1.

The development of new improved metathesis catalysts continues to increase the popularity of this reaction.[3] Whilst RCM reports of acrylates catalysed by **2** can be found in the literature they are not general and often require Lewis acids to achieve synthetically useful yields.[4,5]



Amongst the extended substrate scope second generation Ru catalyst 2 tolerates electron deficient alkenes particularly well. Access via RCM to various cyclic α,β-unsaturated



Scheme 2.

☆ See Ref. 1.

Keywords: Ring closing metathesis; Catalytic cascades; Heterocyclic enones; 1,3-Dipolar cycloadditions.
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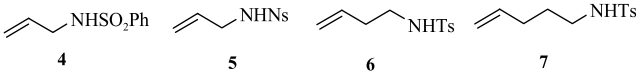
esters, amides and ketones employing **3** is being exploited by a growing number of groups.[6]

In the studies reported herein, we have explored interfacing a 4CC with RCM and RCM with cycloadditions. For the 4CC to be successful carbonylation must occur before allene insertion and allene insertion must in turn be faster than nucleophilic substitution (Scheme 2). An incorrect reactivity order would lead inter alia to shunt pathways (v) and (vi) (Scheme 2). The desired 'molecular queuing' in these 4CC has been reported by the Grigg group for certain nucleophiles[7] and examples employing solid phase combinatorial chemistry reported.[8]

2. Results and discussion

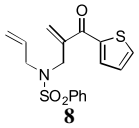
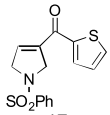
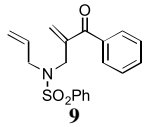
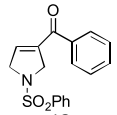
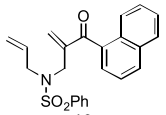
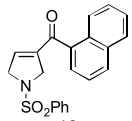
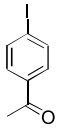
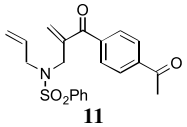
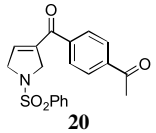
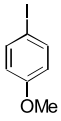
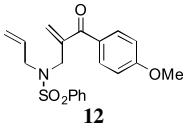
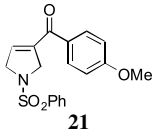
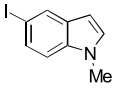
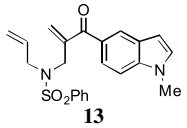
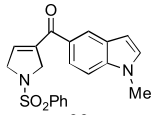
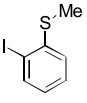
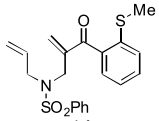
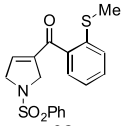
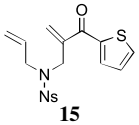
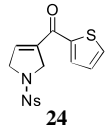
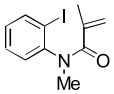
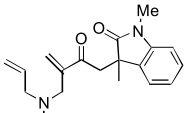
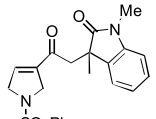
2.1. Four-component cascades employing pronucleophiles 4 and 5



4 **5** **6** **7**

Nitrogen protected alkenyl tethered amine pronucleophiles **4–7** were prepared by literature procedures.[2,8,9] Initial studies employed **4** along with iodothiophene, palladium acetate, triphenylphosphine and potassium carbonate as

Table 1. Sequential four-component cascade-RCM employing nucleophiles **4** and **5**

Entry	Aryl/heteroaryl iodide	Pd-cascade product[a]	Yield (%)[b]	RCM product[c]	Yield (%)[b]
1		 **8**	75	 **17**	94
2		 **9**	75	 **18**	88
3		 **10**	70	 **19**	90
4		 **11**	70	 **20**	93
5		 **12**	55	 **21**	92
6		 **13**	70	 **22**	87
7		 **14**	68	 **23**	25[d]
8		 **15**	65	 **24**	56
9	 **26**	 **16**	65	 **25**	93

[a] $Pd(OAc)_2$ 10 mol%, PPh_3 20 mol%, K_2CO_3 2 mol equiv, toluene, 70 °C, 22–44 h.
[b] Isolated yields.
[c] Compound **3** (5 mol%), toluene 80 °C, 1–14 h.
[d] Compound **3** (12 mol%) employed.

base. The reaction was conducted in toluene at 70 °C under 1 atm of allene and 1 atm of carbon monoxide in a Schlenk tube. To our delight, complete chemoselective conversion to the dienone, **8** was achieved within 38 h (Table 1, entry 1).

Subjecting dienone **8** to **3** (5 mol%) in toluene at 80 °C produced complete conversion to heterocyclic enone **17** (Table 1, entry 1). The scope of the reaction was then explored through variation of the aryl/heteroaryl iodide (Table 1). Electron deficient, electron rich and heteroaryl iodides worked equally well in the tetramolecular cascade, furnishing the dienones **8–15** inside 44 h and with complete conversion in all cases. In each case the ^{1}H NMR spectrum of the crude reaction mixture was devoid of by-products confirming the cascade is chemo- and regioselective. Nucleophile **4** could also be interfaced with the cyclisation-anion capture methodology developed by Grigg et al.,[10] affording dienone **16** from the 'zipper' starting species **26**. Three new carbon–carbon and one carbon–nitrogen bonds are thus formed in this cascade (Table 1, entry 9).

2.2. RCM affording 3-pyrrolines

Catalyst **3** effected complete RCM of **8–16** to the heterocyclic enones, **17–25** within 1–8 h in all cases with the exception of **23**. In this latter case a maximum 40% conversion was achieved with a total catalyst loading of 12 mol%, added in three separate portions of 5, 5 and 2 mol% after 2 and 13 h with a total reaction time of 14 h (Table 1, entry 7). Catalyst poisoning by the nucleophilic sulphur of **14** may be a reason for this. Another possibility could be the formation of an unfavourable and stable chelate. Chelation has been shown in many cases to be detrimental to the ring closing reaction.[11]

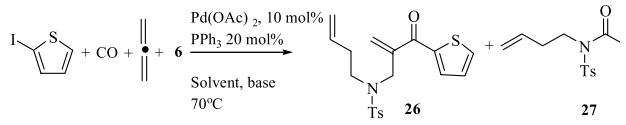
Table 2. Effect of solvent/base on Scheme 3

Entry	Solvent	Base	Yield (%)[a]
1	Toluene	K_2CO_3	33 (20)
2	Toluene	Cs_2CO_3	100 (71)[b]
3	Toluene	NaO^{t}Bu	13
4	CH_3CN	K_2CO_3	60 (41)
5[c]	CH_3CN	K_2CO_3	20
6[d]	CH_3CN	K_2CO_3	57
7	DMF	K_2CO_3	50
8	Toluene	Rb_2CO_3	100 (74)

[a] Conversion calculated from ^{1}H NMR. Isolated yield in parenthesis.
[b] 1:1 mixture of **26** and **27**.
[c] NEt_4Cl (1 mol equiv) added.
[d] $Pd(PPh_3)_4$ used as catalyst.

2.3. Four-component cascades employing nucleophile 6

Initial attempts to employ **6** in the 4CC with iodothiophene resulted in poor conversion to the desired product (Scheme 3, Table 2, entry 1). Optimisation of the reaction conditions was thus investigated. Using cesium carbonate as base



Scheme 3.

resulted in a 1:1 mixture of **26** and **27** (Table 2, entry 2) whilst sodium tertiary butoxide gave poor conversion (Table 2, entry 3). Polar solvents gave greater conversion to product (Table 2, entries 4 and 7) when employing potassium carbonate as the base. However, addition of tetraethylammonium chloride suppressed the reaction (Table 2, entry 5). Preformed Pd(0) catalyst tetrakis triphenylphosphinepalladium did not improve the conversion (Table 2, entry 6). However, rubidium carbonate as base resulted in complete chemoselective conversion to **26** (Table 1, entry 8).

Possible explanations for the unique effect of Rb_2CO_3 include an increased concentration of deprotonated pronucleophile, that is, a low concentration of deprotonated pronucleophile results in poor product conversion (Table 1, entry 1). However, an excess of pronucleophile **6** leads to trapping of the acyl-palladium intermediate (Scheme 2) and the formation of amide **27** (Table 2, entry 2). On moving down group 1 of the periodic table, metal carbonate bonding becomes less covalent in character resulting in a higher concentration of the basic carbonate anion. The concentration of anion follows the trend $K_2CO_3 < Rb_2CO_3 < Cs_2CO_3$. Perhaps rubidium carbonate serendipitously forms the optimum concentration of deprotonated pronucleophile required for total chemoselectivity and conversion to **26** (Table 1, entry 8). Alternatively or additionally it may produce a more active Pd(0) species as a polycarbonate[12] $[Pd(0)(CO_3)_n]^{2n-}$ analogous to the effect of Cl^- ions from $R_4N^+Cl^-$.[13] To our knowledge there is only one other report[14] describing the superiority of Rb_2CO_3 over the more usual K_2CO_3 and Cs_2CO_3.

A comparison of the predicted pK_a's for the protected allylamine, **4** (10.0) and homoallylamine **6** (11.6),[15] shows a difference of over 1.5 units. This suggests, to achieve complete product conversion the necessary concentration of anion is formed from **4** with potassium carbonate (Table 1, entry 1). However, due to its less acidic proton, **6** is only partially deprotonated and poor conversion results (Table 2, entry 1).

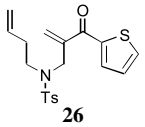
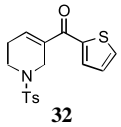
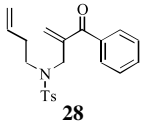
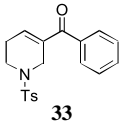
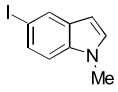
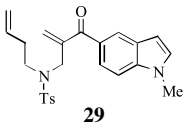
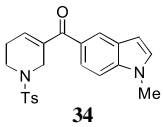
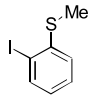
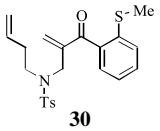
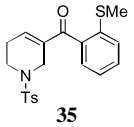
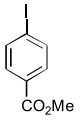
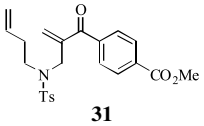
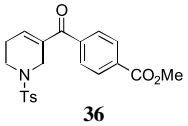
2.4. RCM affording 3-piperideines

With the reaction conditions optimised for **6** the scope of the reaction with respect to the aryl iodide was evaluated (Table 3). The process worked well for a series of iodides yielding acylic dienones **26–31** in 68–75% yield. Subjecting dienones **26–31** to **3** (5 mol%) afforded the six-membered heterocylic enones **32–36** in 73–92% yield (Table 3). Interestingly RCM of thioether analogue **30** afforded 92% conversion and 73% isolated yield of heterocylic enone **35** with 7 mol% of **3** added in two separate portions (Table 3, entry 4). Comparisons with the synthesis of **23** in the analogous five-membered series indicates the formation of a six-membered ring by RCM is more favourable.

2.5. Four-component cascades employing pronucleophile 7

Results achieved from using alkenyl tethered amine **7** in the four-component Pd-cascade parallel those obtained employing **6**. Potassium carbonate was found to give poor

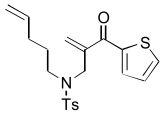
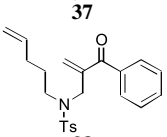
Table 3. Sequential four-component cascade-RCM employing nucleophile **6**

Entry	Aryl/heteroaryl iodide	Pd-cascade product[a]	Yield (%)[b]	RCM product[c]	Yield (%)[b]
1		 **26**	74	 **32**	92
2		 **28**	72	 **33**	90
3		 **29**	68	 **34**	91
4		 **30**	75	 **35**	73[d]
5		 **31**	70	 **36**	86

[a] $Pd(OAc)_2$ 10 mol%, PPh_3 20 mol%, Rb_2CO_3 2 mol equiv, toluene, 70 °C, 18–25 h.
[b] Isolated yields.
[c] Compound **3** (5 mol%), toluene 80 °C, 2–7 h.
[d] Compound **3** (5 mol%) added time zero followed by 2 mol% of **3** after 4 h.

conversions, cesium carbonate gave product mixtures, whilst rubidium carbonate gave near complete conversion to dienone **37**, in 56% isolated yield when using 2-iodothiophene (Table 4, entry 1). This was expected, considering the essential equivalence of the pK_a's of **6** (11.6) and **7** (11.74).[14] Dienone **38** was also formed with complete conversion from iodobenzene in 68% isolated yield employing the same conditions (Table 4, entry 2). Unfortunately subjecting **37** and **38** to RCM using **3** failed to afford any of the seven-membered ring analogues. The acyclic dienone was recovered unchanged after 24 h in both cases.

Table 4. Sequential four-component cascade-RCM employing nucleophile **7**

Entry	Aryl/heteroaryl iodide	Pd-cascade product[a]	Yield (%)[b]
1		 **37**	56
2		 **38**	68

[a] $Pd(OAc)_2$ 10 mol%, PPh_3 20 mol%, Rb_2CO_3 2 mol equiv, toluene, 70 °C, 25 h.
[b] Isolated yields.

2.6. Microwave-accelerated RCM[1]

Microwave irradiation is reported to dramatically accelerate a number of metal catalysed reactions.[16] This encouraged us to evaluate the technique for RCM processes of our acyclic enones. Initially, we studied the microwave-accelerated RCM of **8** using the Smith Creator microwave. DCM was the solvent of choice owing to its microwave transparency[17] allowing the maximum uptake of microwave energy by the substrate and catalyst. A target temperature of 100 °C was set and the catalyst loading and concentration of **8** varied to find the optimum reaction conditions. The results are summarised in Table 5. The best set of conditions (Table 5, entry 3) furnished **17** in 86% yield. Increasing the concentration was found to impede the reaction (Table 5, entries 3 and 4). The temperature profile of the reaction mixture shows rapid heating, which could be ascribed to energy absorption by the ruthenium catalyst **3** or the diene substrate. However, a recent report by Lavastre et al. rules out the former.[18] The pressure of the sealed reaction vessel was monitored and found to stay below 5 bar. Next, we studied the formation of a range of 3-substituted five- and six-membered heterocyclic enones via microwave induced RCM by varying the aryl/heteroaryl group (Table 6).

Table 5. Optimisation of microwave RCM reaction conditions[a]

Entry	Time (min)	Concn (mM)	Catalyst loading (mol%)	Conversion (%)
1	5	1.5	5	100
2	1	1.5	5	100
3	**1**	**1.5**	**2.5**	**100**
4	1	3.0	2.5	90
5	2	3.0	1	88
6	1	3.0	1	88

[a] All reactions performed in CH_2Cl_2. The temperature was set to reach a maximum of 100 °C in all cases.

Table 6. Microwave acclerated RCM[a]

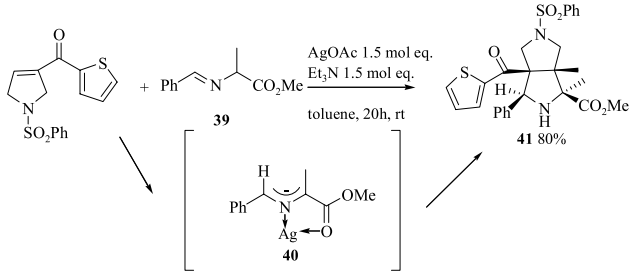
Entry	Starting material	Catalyst loading (mol%)	Product	Conversion (%)[b]	Yield (%)[c]
1	**13**	2.5	**22**	93	80
2	**11**	2.5	**20**	100	87
3	**16**	1	**25**	100	90
4	**8**	2.5	**17**	100	86
5	**29**	5	**34**	92	77
6	**30**	2.5	**35**	92	78

[a] As for Table 6 with a 1 min reaction time and a substrate concentration of 1.5–3.0 mM.
[b] Conversion calculated by ^{1}H NMR.
[c] Isolated yield.

Microwave heating results in shorter reaction times and lower catalyst loadings. Wilson et al. have reported a closely related process.[19]

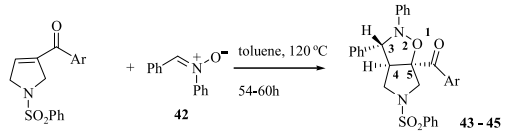
2.7. 1,3-Dipolar cycloaddition reactions

The heterocyclic enones described above were shown to be active dipolarophiles in cycloadditions with azomethine ylides and nitrones. Thus, stiring imine **39** with silver acetate, triethylamine and enone **17** in toluene at room temperature for 20 h afforded a single cycloadduct **41** in 80% isolated yield arising via an *endo*-transition state of the *syn*-metallodipole **40** (Scheme 4). The regio- and stereochemistry of the cycloadduct **41** were established by NOE studies and conform to that expected for Grigg's metal catalysed proline synthesis.[20]



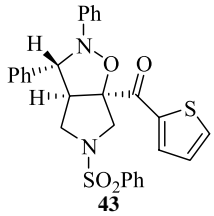
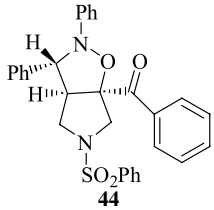
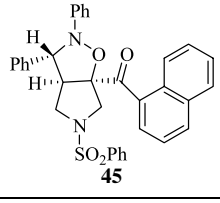
Scheme 4.

Heating the five-membered heterocylic enones **17–19** with diphenyl nitrone **42** in toluene at 120 °C (Schlenk tube) afforded the bicyclic isoxazolidines **43–45** in 58–80% yield as single regio- and diastereoisomers (Scheme 5, Table 7). The nitrone cycloadditions proved to be extremely sensitive towards variation in reaction temperature. Employing enone **17** and decreasing the reaction temperature to 80 °C causes a change in the regioselectivity of the reaction affording a 3.5:1 mixture of diastereoisomers **46** and **47**, respectively, in 70% yield (Scheme 6). Only trace amounts of the thermodynamic regioisomer **43** are formed at this temperature as shown by ^{1}H NMR. Subjecting **46** to reflux in toluene affords the thermodynamic isomer **43** via a retro-cycloaddition/1,3-dipolar cycloaddition along with trace

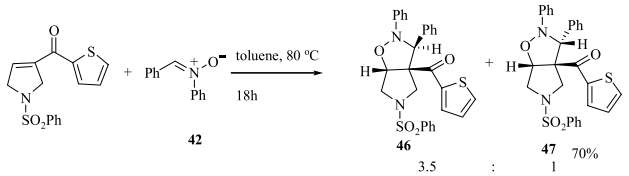


Scheme 5.

Table 7. Cycloadditions of enones **17–19** and nitrone **42**[a]

Entry	Enone	Product	Yield (%)[b]
1	**17**	 **43**	80[c]
2	**18**	 **44**	70
3	**19**	 **45**	58

[a] Toluene 120 °C, sealed tube, 54–60 h.
[b] Isolated yield.
[c] Trace amounts of isomer **45** formed.



Scheme 6.

amounts of enone **17** and diphenyl nitrone **42**. Regioisomer **43** is thought to be favoured under thermodynamic control due to the minimization of steric interactions between the 3-phenyl group of the nitrone and the aryl ketone of the enone.

2.8. Cascade RCM-1,3-dipolar cycloaddition

Finally, a cascade RCM-nitrone cycloaddition was shown to be possible. The ability to create a dipolarophile (dienophile) in situ and interface it with a cycloaddition in a cascade provides valuable synthetic flexibility. Additionally, in this case it results in the formation of three-new bonds and four stereocentres. Heating a mixture of dienone **8**, diphenyl nitrone **42** and catalyst **3** in toluene at 70 °C for

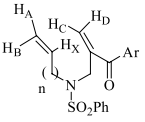
1 h followed by further heating at 90 °C for 17 h afforded a 3:1 mixture of **46** and **47** in 59% isolated yield. Heating to higher temperatures afforded complex mixtures. We have previously reported numerous examples of palladium catalysed multi-component cascades directly interfaced with cycloadditions.[21]

In summary, a novel and diverse route accessing 3-aryl/heteroaryl-acyl substituted heterocyles has been developed via the sequential application of a chemoselective four-component Pd-cascade/RCM sequences. The heterocyclic enones produced via this method can be further elaborated via cycloaddition chemistry. Investigation into the compatibility of other alkene-tethered nucleophiles and substituted allenes in this process is currently underway.

3. 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. Nuclear magnetic resonance spectra were recorded on Bruker DPX250, DPX300 and DPX500 instruments operating at 250, 300 and 500 MHz, respectively. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; q_i, quintet; m, multiplet; dd, doublet of doublets; ddd, double doublet of doublets; ddt, double doublet of triplets; b, broad. Solvents were dried according to established methods, unless purchased dry from Aldrich in sure-seal bottles. Palladium acetate was supplied by Johnson Matthey and ruthenium alkylidene catalysts were 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 version 4.5.

3.1. ^{1}H NMR proton labels:



3.1.1. *N*-Allyl-*N*-[2-(thien-2-ylcarbonyl)prop-2-enyl]benzenesulfonamide (8). Prepared by the general cascade procedure (below) on a 5 mmol scale, using 5.5 mmol of aryl iodide and a reaction time of 38 h. Purification by flash chromatography eluting with 1:20 v/v ether/petrol afforded the product (1.29 g, 75%) as a viscous pale yellow oil; R_f 0.05; (Found: C, 58.80; H, 4.90; N, 4.10. $C_{17}H_{17}NO_3S_2$ requires C, 58.75; H, 4.95; N, 4.05%) υ_{max}/cm^{-1} (film) 1637 (C=O), 1621, 1413, 1342 (S=O_{as}), 1159 (S=O_s), 1091; δ_H (500 MHz, $CDCl_3$) 7.84–7.82 (2H, m, SO_2PhH), 7.68 (1H, dd, $J=5.0$, 1.1 Hz, ArH), 7.63 (1H, dd, $J=3.8$, 1.1 Hz, ArH), 7.58–7.55 (1H, m, SO_2PhH), 7.51–7.48 (2H, m, SO_2PhH), 7.12 (1H, dd, $J=5.0$, 3.8 Hz, ArH), 6.10 (1H, t, $J=1.5$ Hz, =C$H_C$$H_D$), 6.05 (1H, t, $J=1.0$ Hz, =C$H_C$$H_D$), 5.60 (1H, ddt, $J=16.7$, 10.0, 6.6 Hz, CH_X=C$H_A$$H_B$), 5.14 (1H, ddd, $J=16.7$, 2.7, 1.3 Hz, CH_X=CH_A-H_B), 5.11 (1H, ddd, $J=10.0$, 2.3, 1.7 Hz, CH_X=C$H_A$$H_B$), 4.14 (2H, s, NCH_2), 3.86 (2H, d, $J=6.6$ Hz, NCH_2); δ_C (125 MHz, $CDCl_3$) 187.9 (C=O), 143.4, 142.9, 139.8, 134.3, 134.2, 132.7, 132.1, 129.1, 128.0, 127.2, 125.8, 119.9, 51.5 (NCH_2), 47.7 (NCH_2); *m/z* (CI) 365 (60%, M+NH_4^+), 215 (100%).

3.2. General tetramolecular cascade procedure

3.2.1. *N*-Allyl-*N*-(2-benzoylprop-2-enyl)benzenesulfonamide (9). Palladium acetate (112 mg, 0.5 mmol), triphenyl phosphine (262 mg, 1 mmol), potassium carbonate (1.381 g, 10 mmol) and toluene (10 ml) were added to a Schlenk tube, containing a magnetic stirrer bar. A solution of the sulfonamide **4** (985 mg, 5 mmol), and iodobenzene (1.224 g, 6 mmol) in toluene (4 ml) was then added. The tube was sealed and the mixture frozen in liquid nitrogen, and degassed by vacuum pump. The mixture was then allowed to reach room temperature, followed by refreezing and degassing for a second time. Allene (1 bar) was then added to the Schlenk tube and the mixture frozen in a liquid nitrogen bath. Following this CO (1 bar) was added, the tube sealed and the mixture allowed to reach room temperature, before heating in an oil bath at 65–70 °C for 44 h. On completion of the reaction the mixture was allowed to cool to room temperature, the excess gas released and the mixture filtered. Concentration of the filtrate in vacuo gave an orange oil, which was purified by flash chromatography, eluting with 1:4 v/v ether/petrol to afford the product (1.275 mg, 75%) as a viscous, colourless oil; R_f 0.2; (Found: C, 66.55; H, 5.85; N, 4.15. $C_{19}H_{19}NO_3S$ requires C, 66.85; H, 5.60; N, 4.10%); υ_{max}/cm^{-1} (film) 1653 (C=O), 1447, 1344 (S=O_{as}), 1160 (S=O_s), 1092, 983, 932; δ_H (250 MHz, $CDCl_3$) 7.88–7.84 (2H, m, ArH), 7.72–7.60 (2H, m, ArH), 7.60–7.53 (6H, m, ArH), 6.27 (1H, t, $J=1.3$ Hz, =C$H_C$$H_D$), 5.89 (1H, s, =C$H_C$$H_D$), 5.62 (1H, ddt, $J=16.6$, 10.0, 6.6 Hz, CH_X=C$H_A$$H_B$), 5.19–5.10 (2H, m, C$H_X$=C$H_A$$H_B$), 4.15 (2H, t, $J=1.3$ Hz, NCH_2), 3.89 (2H, d, $J=6.6$ Hz, NCH_2); δ_C (63 MHz, $CDCl_3$) 197.3 (C=O), 143.4, 140.0, 137.6, 133.1, 132.9, 132.7, 129.9, 129.6, 129.2, 128.7, 127.6, 120.3, 52.2 (NCH_2), 47.9 (NCH_2); *m/z* (ES) 364 (M^++Na).

3.2.2. *N*-Allyl-*N*-[2-(1-naphthoyl)prop-2-enyl]benzenesulfonamide (10). Prepared by the general cascade procedure on a 5 mmol scale, using 5.5 mmol of aryl iodide and a reaction time of 42 h. Purification by flash chromatography eluting with DCM afforded the product (1.350 g, 70%) as a viscous colourless oil; R_f 0.32; (Found: C, 70.30; H, 5.35; N, 3.60. $C_{23}H_{21}NO_3S$ requires C, 70.55; H, 5.40; N, 3.60%); υ_{max}/cm^{-1} (film) 1652 (C=O), 1446, 1342 (S=O_{as}), 1160 (S=O_s), 1090; δ_H (250 MHz, $CDCl_3$) 8.05–7.87 (5H, m, ArH), 7.62–7.43 (7H, m, ArH), 6.63 (1H, t, $J=1.5$ Hz, =C$H_C$$H_D$), 5.91 (1H, s, =C$H_C$$H_D$), 5.66 (1H, ddt, $J=16.9$, 9.9, 6.8 Hz, CH_X=C$H_A$$H_B$), 5.21 (1H, ddd, $J=16.9$, 2.6, 1.3 Hz, CH_X=C$H_A$$H_B$), 5.18 (1H, dd, $J=9.9$, 1.1 Hz, CH_X=C$H_A$$H_B$), 4.27 (2H, s, NCH_2), 3.93 (2H, d, $J=6.8$ Hz, NCH_2); δ_C (63 MHz, $CDCl_3$), 199.1 (C=O),

145.3, 140.0, 136.1, 134.1, 133.2, 132.9, 132.1, 131.8, 131.1, 129.7, 128.9, 128.1, 127.7, 127.6, 126.9, 125.7, 124.7, 120.03, 52.5 (NCH_2), 47.3 (NCH_2); *m/z* (%) (FAB) 364 (37, $M^+ + H$), 250 (31, $M - SO_2Ph$), 210 (100), 195 (32), 141 (28, SO_2Ph).

3.2.3. *N*-[2-(4-Acetobenzoyl)prop-2-enyl]-*N*-allylbenzenesulfonamide (11). Prepared by the general cascade procedure on a 3 mmol scale, using 3.1 mmol of aryl iodide and a reaction time of 40 h. Purification by flash chromatography eluting with 3:2 v/v ether/petrol afforded the product (800 mg, 70%) as a pale yellow oil; R_f 0.2; (Found: C, 66.05; H, 5.65; N, 3.40. $C_{21}H_{21}NO_4S$ requires C, 65.80; H, 5.50; N, 3.60%); υ_{max}/cm^{-1} (film) 1686 (C=O), 1652 (C=O), 1446, 1343 (S=O_{as}), 1264, 1160 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 8.01 (2H, d, $J=8.3$ Hz, ArH), 7.87–7.84 (2H, m, SO_2PhH), 7.77 (2H, d, $J=8.3$ Hz, ArH), 7.60–7.51 (3H, m, SO_2PhH), 6.35 (H, s, $=CH_CH_D$), 5.90 (1H, s, $=CH_CH_D$), 5.61 (1H, ddt, $J=16.9$, 9.7, 6.5 Hz, $CH_X=CH_AH_B$), 5.15 (1H, d, $J=16.9$ Hz, $CH_X=CH_AH_B$), 5.14 (1H, d, $J=9.7$ Hz, $CH_X=CH_AH_B$), 4.14 (2H, s, NCH_2), 3.89 (2H, d, $J=6.5$ Hz, NCH_2), 2.66 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 197.9 (C=O), 198.6 (C=O), 143.5, 141.3, 140.0, 139.8, 133.2, 132.7, 130.2, 130.0 (=CH_2), 129.7, 128.6, 127.7, 120.4 (=CH_2), 52.4 (NCH_2), 47.7 (NCH_2), 27.3 (CH_3); *m/z* (%) (FAB) 384 (33, $M^+ + H$), 242 (40, $M - SO_2Ph$), 210 (77), 147 (100), 141 (28, SO_2Ph), 115 (47).

3.2.4. *N*-Allyl-*N*-[2-(4-methoxybenzoyl)prop-2-enyl]benzenesulfonamide (12). Prepared by the general cascade procedure on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 44 h. Purification by flash chromatography eluting with 3:7 v/v ethyl acetate/petrol afforded the product (204 mg, 55%) as a colourless oil; R_f 0.25; (Found: C, 64.40; H, 5.75; N, 3.95. $C_{20}H_{21}NO_4S$ requires C, 64.65; H, 5.70; N, 3.75%); υ_{max}/cm^{-1} (film) 1647 (C=O), 1599, 1333 (S=O_{as}), 1308, 1258 (OCH_3), 1160 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$), 7.87–7.83 (2H, m, SO_2PhH), 7.26 (2H, d, $J=8.9$ Hz, ArH), 7.59–7.47 (3H, m, SO_2PhH), 6.92 (2H, d, $J=8.9$ Hz, ArH), 6.14 (1H, s, $=CH_CH_D$), 5.79 (1H, s, $=CH_CH_D$), 5.61 (1H, ddt, $J=16.6$, 10.0, 6.6 Hz, $CH_X=CH_AH_B$), 5.20–5.06 (2H, m, $CH_X=CH_AH_B$), 4.14 (2H, s, NCH_2), 3.88 (2H, d, $J=6.5$ Hz, NCH_2), 3.87 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$), 195.9 (C=O), 163.8, 143.5, 140.1, 133.1, 132.7, 132.4, 130.0, 129.6, 127.6, 126.9, 120.2, 114.0, 55.9 (OMe), 52.0 (NCH_2), 48.3 (NCH_2); *m/z* (ES) 394 ($M^+ + Na$).

3.2.5. *N*-Allyl-*N*-{2-[(1-methyl-1*H*-indol-5-yl)carbonyl]prop-2-en-1-yl}benzenesulfonamide (13). Prepared by the general cascade procedure on a 5 mmol scale, using 5.5 mmol of aryl iodide and a reaction time of 44 h. Purification by flash chromatography eluting with DCM afforded the product (1.320 g, 70%) as a viscous pale yellow oil; R_f 0.15; (Found: C, 67.05; H, 5.65; N, 7.10. $C_{22}H_{22}N_2O_3S$ requires C, 67.00; H, 5.60; N, 7.10%); υ_{max}/cm^{-1} (film) 1652 (C=O), 1605, 1340 (S=O_{as}), 1159 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 8.06 (1H, d, $J=1.6$ Hz, ArH), 7.89–7.84 (2H, m, SO_2PhH), 7.71 (1H, dd, $J=8.7$, 1.6 Hz, ArH), 7.61–7.47 (3H, m, SO_2PhH), 7.34 (d, 1H, $J=8.7$ Hz, ArH) 7.13 (d, 1H, $J=3.2$ Hz, ArH), 6.60 (dd, 1H, $J=3.2$, 0.5 Hz, ArH), 6.15 (1H, s, $=CH_CH_D$), 5.83 (1H, s, $=CH_CH_D$), 5.64 (1H, ddt, $J=16.7$, 10.0, 6.6 Hz, $CH_X=CH_AH_B$), 5.18 (1H, dd, $J=16.7$, 1.3 Hz, $CH_X=CH_AH_B$), 5.13 (1H, dd, $J=10.0$, 1.3 Hz, $CH_X=CH_AH_B$) 4.20 (2H, s, NCH_2), 3.91 (2H, d, $J=6.6$ Hz, NCH_2), 3.84 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$), 197.0 (C=O), 143.4, 139.9, 132.6, 132.3, 130.4, 129.1, 128.7, 127.6, 127.3, 126.3, 124.8, 123.2, 119.8, 109.1, 103.0, 51.5 (NCH_2), 48.0 (NCH_2); 33.0 (CH_3); *m/z* (%) (EI) 394 (4, M^+), 253 (100, M^+), 198, (28), 144, (75), 77 (57).

3.2.6. *N*-Allyl-*N*-{2-[2-(methylthio)benzoyl]prop-2-en-1-yl}benzenesulfonamide(14). Prepared by the general cascade procedure on a 5 mmol scale, using 6 mmol of aryl iodide and a reaction time of 22 h. Purification by flash chromatography eluting with DCM afforded the product (1.320 g, 68%) as a viscous pale yellow oil, which solidified on standing, mp 44–46 °C; R_f 0.15; (Found: C, 61.70; H, 5.50; N, 3.75. $C_{20}H_{21}NO_3S_2$ requires C, 62.00; H, 5.45; N, 3.60%); υ_{max}/cm^{-1} (film) 1655 (C=O), 1446, 1434, 1344 (S=O_{as}), 1161 (S=O_s), 1092; δ_H (250 MHz, $CDCl_3$) 7.88–7.85 (2H, m, SO_2PhH), 7.60–7.53 (3H, m, SO_2PhH), 7.44–7.19 (4H, m, ArH), 6.27 (1H, s, $=CH_CH_D$) 5.80 (1H, s, $=CH_CH_D$), 5.59 (1H, ddt, $J=16.7$, 10.0, 6.6 Hz, $CH_X=CH_AH_B$), 5.15 (1H, d, $J=16.7$ Hz, $CH_X=CH_AH_B$), 5.13 (1H, d, $J=10$ Hz, $CH_X=CH_AH_B$), 4.18 (2H, s, NCH_2), 3.89 (2H, d, $J=6.6$ Hz, NCH_2), 2.42 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$), 197.9 (C=O), 144.3, 140.2, 138.8, 138.1, 133.1, 132.5, 131.5, 130.7, 129.7, 129.6, 127.9, 127.6, 125.0, 120.4, 52.1 (NCH_2), 47.0 (NCH_2), 17.4 (CH_3); *m/z* (ES) 388 ($M^+ + H$).

3.2.7. *N*-Allyl-4-nitro-*N*-[2-(2-thienylcarbonyl)prop-2-en-1-yl]benzenesulfonamide (15). Prepared by the general cascade procedure on a 5 mmol scale, using 5.5 mmol of aryl iodide and a reaction time of 38 h. Purification by flash chromatography eluting with DCM afforded the product (1.260 g, 65%) as colourless viscous oil; R_f 0.18; (Found: C, 52.25; H, 4.15; N, 7.15. $C_{17}H_{16}N_2O_5S_2$ requires C, 52.05; H, 4.10; N, 7.15%); υ_{max}/cm^{-1} (film) 1633 (C=O), 1615, 1527 (NO_2), 1345 (S=O_{as}), 1153 (S=O_s), 1093; δ_H (250 MHz, $CDCl_3$) 8.29 (2H, d, $J=9.0$ Hz, ArH), 7.98 (2H, d, $J=9.0$ Hz, ArH), 7.69 (1H, dd, $J=4.8$, 1.1 Hz, ArH), 7.57 (1H, dd, $J=3.8$, 1.1 Hz, ArH), 7.11 (1H, dd, $J=5.0$, 3.8 Hz, ArH), 6.06 (1H, s, $=CH_CH_D$), 6.05 (1H, s, $=CH_CH_D$), 5.64 (1H, ddt, $J=16.4$, 9.9, 6.5 Hz, $CH_X=H_AH_B$), 5.21 (1H, dd, $J=16.4$, 1.1 Hz, $CH_X=H_AH_B$), 5.20 (1H, dd, $J=9.9$, 1.3 Hz, $CH_X=CH_AH_B$), 4.21 (2H, s, NCH_2), 3.95 (2H, d, $J=6.5$ Hz, NCH_2); δ_C (75 MHz, $CDCl_3$) 187.9 (C=O), 150.3, 146.3, 143.0, 142.9, 135.2, 134.6, 131.9, 128.8, 128.5, 126.8, 124.7, 120.9, 51.6 (NCH_2), 48.2 (NCH_2); *m/z* (%) (EI) 206 (100, $M - SO_2PhNO_2$), 111 (69).

3.2.8. *N*-Allyl-*N*-{[2-[1,3-dimethyl-2-oxo-2,3-dihydro-1*H*-indol-3-yl]acetyl]prop-2-enyl}benzenesulfonamide (16). Prepared by the general cascade procedure on a 1 mmol scale, using 1 mmol of aryl iodide and a reaction time of 28 h. Purification by flash column chromatography eluting with 4:1 v/v ether/petrol afforded the product (282 mg, 65%) as a viscous colourless oil; R_f 0.17; (Found: C, 65.50; H, 6.15; N, 6.50. $C_{24}H_{26}N_2O_4S$ requires C, 65.75; H, 6.00; N, 6.80%); υ_{max}/cm^{-1} (film) 1711 (C=O), 1679 (N–C=O), 1614, 1348 (S=O_{as}), 1159 (S=O_s), 1092; δ_H

(250 MHz, $CDCl_3$) 7.74–7.71 (2H, m, SO_2PhH), 7.56–7.46 (3H, m, SO_2PhH), 7.24 (1H, td, $J=7.7$, 1.3 Hz, ArH), 7.09 (1H, dd, $J=7.5$, 1.0 Hz, ArH), 7.02 (1H, td, $J=7.5$, 0.9 Hz, ArH), 6.88 (1H, d, $J=7.5$ Hz, ArH), 6.25 (1H, s, $=CH_CH_D$), 6.14 (1H, s, $=CH_CH_D$), 5.39 (1H, ddt, $J=$ 16.8, 10.1, 6.6 Hz, $CH_X=CH_AH_B$), 4.97 (1H, d, $J=$ 10.1 Hz, $CH_X=CH_AH_B$), 4.93 (1H, d, $J=16.8$ Hz, $CH_X=CH_AH_B$), 3.73 (2H, d, $J=1.3$ Hz, NCH_2), 3.66 (2H, d, $J=6.6$ Hz, $=CHCH_2$), 3.49 (1H, d, $J=17.8$ Hz, O=CCHH), 3.37 (1H, d, $J=17.8$ Hz, COCHH), 3.27 (3H, s, NCH_3), 1.36 (3H, s, CCH_3); δ_C (63 MHz, $CDCl_3$) 197.3 (C=O), 180.4 (C=O), 143.7, 142.9, 139.5, 133.4, 132.6, 131.8, 129.1, 127.9, 127.1, 126.5 ($=CH_2$), 122.2, 121.8, 119.7 ($=CH_2$), 108.1, 51.5 (CH_2), 46.4 (CH_2), 45.3 (CH_2), 45.1 (CCH_3), 26.4 (CH_3), 24.9 (CH_3); *m/z* (ES) 461 ($M^+ + Na$).

3.3. General RCM procedure

Grubb's second generation catalyst **3** (5.5 mg, 6.5 μmol) was added to a magnetically stirred solution of acyclic enone (0.13 mmol), in anhydrous toluene (50 ml) and the mixture stirred under argon atmosphere at 80 °C for 1–14 h. Concentration in vacuo yielded the crude product, which was purified by flash chromatography.

3.3.1. [1-(Phenysulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl] (thien-2-yl)methanone (17). Prepared by the general RCM procedure on a 0.33 mmol scale and a reaction time of 3 h. Purification by flash chromatography eluting with DCM afforded the product (99 mg, 94%), which crystallised from petrol/DCM as colourless needles, mp 152–154 °C; R_f 0.1; (Found: C, 56.15; H, 4.20; N, 4.50; $C_{15}H_{13}NO_3S_2$ requires C, 56.40; H, 4.10; N, 4.30%); υ_{max}/cm^{-1} (film); δ_H (500 MHz, $CDCl_3$) 7.90–7.86 (2H, m, SO_2PhH), 7.67 (1H, dd, $J=4.9$, 1.1 Hz, ArH), 7.65 (1H, dd, $J=3.8$, 1.1 Hz, ArH) 7.63–7.60 (1H, m, SO_2PhH), 7.57–7.54 (2H, m, SO_2PhH), 7.12 (1H, dd, $J=4.9$, 3.8 Hz, ArH), 6.58 (1H, q_i, $J=2.1$ Hz, =CH), 4.48 (2H, 2×ddd, $J=4.9$, 2.1, 1.0 Hz, NCH_2), 4.44 (2H, 2×ddd, $J=4.9$, 2.1, 1.0 Hz, NCH_2); δ_C (125 MHz, $CDCl_3$) 181.2 (C=O), 142.3, 138.9, 136.8, 134.8, 134.2, 133.1, 133.0, 129.4, 128.1, 127.5, 57.0 (NCH_2), 54.5 (NCH_2); *m/z* (%) (FAB) 320 (100, $M^+ + H$), 178 (23, $M-SO_2Ph$), 111 (60).

3.3.2. Phenyl[1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]methanone (18). Prepared by the general RCM procedure on a 0.12 mmol scale and a reaction time of 3 h. Purification by flash chromatography eluting with 7:3 v/v petrol/ethyl acetate afforded the product (34 mg, 88%), which crystallised from petrol/ether as colourless needles, mp 102–104 °C; R_f 0.19; (Found: C, 65.05; H, 4.90; N, 4.60. $C_{17}H_{15}NO_3S$ requires C, 65.15; H, 4.80; N, 4.45%); υ_{max}/cm^{-1} (film) 1644 (C=O), 1446, 1346 ($S=O_{as}$), 1291, 1165 ($S=O_s$), 1103; δ_H (500 MHz, $CDCl_3$) 7.90–7.88 (2H, m, ArH), 7.68–7.61 (3H, m, ArH), 7.59–7.54 (3H, m, ArH), 7.46–7.42 (m, 2H, ArH), 6.36 (1H, q, $J=2.1$ Hz, =CH), 4.48 (2H, 2×ddd, $J=4.7$, 2.1, 1.0 Hz, NCH_2), 4.43 (2H, 2×ddd, $J=4.7$, 2.1, 1.0 Hz, NCH_2); δ_C (125 MHz, $CDCl_3$) 190.6 (C=O), 138.9, 137.2, 137.1, 136.9, 133.0, 132.8, 129.4, 128.8, 128.6, 127.5, 56.1 (NCH_2), 54.4 (NCH_2); *m/z* (%) (CI), 331 (100, $M+NH_4^+$), 172 (100, $M-SO_2Ph$).

3.3.3. 1-Naphthyl[1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]methanone (19). Prepared by the general RCM procedure on a 0.2 mmol scale and a reaction time of 5 h. Purification by flash chromatography eluting with DCM afforded the product (63 mg, 90%) as an off white amorphous solid, mp 61–63 °C; R_f 0.05; (Found: C, 68.85; H, 4.85; N, 4.00. $C_{21}H_{17}NO_3S$ requires C, 69.40; H, 4.70; N, 3.85%); υ_{max}/cm^{-1} (film) 1644 (C=O), 1446, 1347 ($S=O_{as}$), 1290, 1166 ($S=O_s$), 1102; δ_H ($CDCl_3$, 250 MHz) 8.00–7.90 (5H, m, ArH), 7.62–7.45 (7H, m, ArH), 6.26 (1H, q, $J=2.1$ Hz, =CH), 4.56 (2H, 2×dd, $J=$ 4.2, 2.1 Hz, NCH_2), 4.39 (2H, 2×dd, $J=4.4$, 2.1 Hz, NCH_2); δ_C ($CDCl_3$, 63 MHz), 199.5 (C=O), 145.3, 139.9, 136.1, 134.1, 133.2, 132.9, 132.1, 131.8, 131.1, 129.7, 128.1, 127.7, 127.6, 126.9, 125.7, 124.7, 120.3, 52.4 (NCH_2), 47.3 (NCH_2); *m/z* (%) (EI) 363 (11, M^+), 155 (55), 127 (72), 77 (100); HRMS found 364.1000. $C_{21}H_{18}NO_3S$ requires 364.1007.

3.3.4. 1-{(4-[(1-Phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]carbonyl)phenyl}ethanone (20). Prepared by the general RCM procedure on a 0.15 mmol scale and a reaction time of 2 h. Purification by flash chromatography eluting with ether afforded the product (50 mg, 93%) as colourless needles, mp 167–169 °C; R_f 0.27; (Found: C, 64.30; H, 4.75; N, 3.90. $C_{17}H_{19}NO_4S$ requires C, 64.20; H, 4.80; N, 3.95%); υ_{max}/cm^{-1} (film) 1685 (C=O), 1652 (C=O), 1350 ($S=O_{as}$), 1167 ($S=O_s$), 1092; δ_H (250 MHz, $CDCl_3$) 8.01 (2H, d, $J=8.6$ Hz, ArH), 7.91–7.88 (2H, m, SO_2PhH), 7.73 (2H, d, $J=8.6$ Hz, ArH), 7.65–7.53 (3H, m, SO_2PhH), 6.40–6.39 (1H, br m, =CH), 4.49–4.34 (4H, m, 2×NCH_2), 2.64 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 197.3 (C=O), 189.9 (C=O), 141.1, 140.3, 139.3, 138.8, 136.6, 133.6, 129.8, 129.3, 128.8, 127.9, 56.6 (NCH_2), 54.6 (NCH_2), 27.3 (CH_3); *m/z* (%) (EI) 355 (6, M^+), 214 (67, $M-SO_2Ph$), 147 (100), 77 (78).

3.3.5. (4-Methoxyphenyl)[1-(phenylsulfonyl)-2, 5-dihydro-1*H*-pyrrol-3-yl]methanone (21). Prepared by the general RCM procedure on a 0.3 mmol scale and a reaction time of 4 h. Purification by flash chromatography eluting with 3:2 v/v ether/petrol afforded the product (89 mg, 92%) as colourless needles, mp 162–164 °C; R_f 0.17; (Found: C, 62.70; H, 5.00; N, 4.05. $C_{18}H_{17}NO_4S$ requires C, 62.95; H, 5.00; N, 4.10%); υ_{max}/cm^{-1} (film) 1633 (C=O), 1568, 1334 ($S=O_{as}$), 1153 ($S=O_s$), 1099, 1023; δ_H (250 MHz, $CDCl_3$) 7.91–7.87 (2H, m, SO_2PhH), 7.71 (2H, d, $J=$ 9.0 Hz, ArH), 7.63–7.57 (3H, m, SO_2PhH), 6.92 (2H, d, $J=$ 9.0 Hz, ArH), 6.30 (1H, q, $J=2.0$ Hz, =CH), 3.87 (3H, s, CH_3) 4.50–4.39 (4H, m, 2×NCH_2); δ_C (63 MHz, $CDCl_3$) 189.5 (C=O), 163.9, 139.3, 137.1, 135.9, 133.4, 131.6, 130.1, 129.8, 127.9, 114.2, 56.4, 55.9, 55.0; *m/z* (ES) 344 ($M+H^+$).

3.3.6. (1-Methyl-1*H*-indol-5-yl)[1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]methanone (22). Prepared by the general RCM procedure on a 0.4 mmol scale and a reaction time of 2 h. Purification by flash chromatography eluting with 3:2 v/v ether/petrol afforded the product (129 mg, 87%) as colourless needles, mp 139–141 °C; R_f 0.2; (Found: C, 65.45; H, 5.15; N, 7.60. $C_{20}H_{18}N_2O_3S$ requires C, 65.55; H, 4.95; N, 7.65%); υ_{max}/cm^{-1} (film) 1652 (C=O), 1344 ($S=O_{as}$), 1166 ($S=O_s$); δ_H (250 MHz,

$CDCl_3$) 8.03 (s, 1H, ArH), 7.92–7.90 (2H, m, SO_2PhH), 7.70–7.54 (4H, m, SO_2PhH and ArH), 7.34 (1H, d, J= 8.8 Hz, ArH), 7.13 (1H, d, J=3.1 Hz, ArH), 6.58 (1H, d, J=3.1 Hz, ArH), 6.32 (1H, br s, =CH), 4.53–4.51 (2H, br m, NCH_2), 4.45–4.44 (2H, br m, NCH_2); δ_C (63 MHz, $CDCl_3$) 190.8 (C=O), 139.3, 139.1, 136.9, 135.0, 133.0, 130.6, 129.3, 128.8, 127.7, 127.5, 123.8, 122.5, 109.4, 103.0, 56.0 (NCH_2), 54.8 (NCH_2), 33.1 (CH_3); *m/z* (ES) 344 ($M^+ + Na$).

3.3.7. [2-(Methylthio)phenyl][1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]methanone (23). Prepared by the general RCM procedure on a 0.18 mmol scale and a reaction time of 14 h. Purification by flash chromatography eluting with DCM afforded the product (16 mg, 25%), which crystallised from DCM/hexane as colourless needles, mp 135–137 °C; R_f 0.1; (Found: C, 59.95; H, 4.50; N, 3.70. $C_{18}H_{17}NO_3S_2$ requires C, 60.15; H, 4.75; N, 3.90%); υ_{max}/cm^{-1} 1625 (C=O), 1460, 1332 ($S=O_{as}$), 1159 ($S=O_s$), 1073; δ_H (300 MHz, $CDCl_3$) 7.88 (2H, m, SO_2PhH), 7.66–7.54 (3H, m, SO_2PhH), 7.43 (1H, t, J=7.5 Hz, ArH), 7.33 (2H, d, J=7.5 Hz, ArH), 7.16 (1H, t, J=7.5 Hz, ArH), 6.20 (1H, br s, =CH), 4.48–4.47 (2H, br m, NCH_2), 4.38–4.37 (2H, br m, NCH_2), 2.40 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 191.5 (C=O), 140.4, 139.5, 138.6, 137.1, 137.0, 133.4, 131.9, 129.7, 129.4, 127.9, 127.5, 124.8, 56.4 (NCH_2), 54.18 (NCH_2), 17.0 (CH_3); *m/z* (ES) 360 ($M+H^+$).

3.3.8. {1-[(4-Nitrophenyl)sulfonyl]-2, 5-dihydro-1*H*-pyrrol-3-yl}(2-thienyl)methanone (24). Prepared by the general RCM procedure on a 1.45 mmol scale and a reaction time of 6 h. The product precipitated as an off white solid (295 mg, 56%), mp 216–218 °C; R_f 0.1; (Found: C, 49.50; H, 3.50; N, 7.90. $C_{15}H_{12}N_2O_5S_2$ requires C, 49.45; H, 3.30; N, 7.7%); υ_{max}/cm^{-1} 1633 (C=O), 1596, 1527 (NO_2), 1345 ($S=O_{as}$), 1157 ($S=O_s$), 1108, 1062; δ_H (250 MHz, $CDCl_3$) 8.41 (2H, d, J=8.9 Hz, ArH), 8.07 (2H, d, J=8.9 Hz, ArH), 7.71–7.68 (2H, m, ArH and ArH), 7.14 (1H, dd, J=4.8, 3.9 Hz, ArH), 6.60 (1H, q_i, J=1.9 Hz, =CH), 4.52–4.46 (br m, 1H, 2×NCH_2); *m/z* (%) (EI) 178 (49, $M-SO_2PhNO_2$), 111 (100).

3.3.9. 1,3-Dimethyl-3-{2-oxo-2-[(1-phenylsulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl]ethyl}-1,3-dihydro-2*H*-indol-2-one (25). Prepared by the general RCM procedure on a 0.08 mmol scale and a reaction time of 1 h. Purification by flash chromatography eluting with ether yielded the product (33 mg, 93%) as a colourless solid, mp 69–71 °C; R_f 0.1; (Found: C, 64.30; H, 5.45; N, 6.55. $C_{22}H_{22}N_2O_4S$ requires C, 64.35; H, 5.40; N, 6.80%); υ_{max}/cm^{-1} (film) 1709 (C=O), 1677 (N–C=O), 1614, 1348 ($S=O_{as}$), 1167 ($S=O_s$), 1104; δ_H (250 MHz, $CDCl_3$) 7.79 (2H, m, SO_2PhH), 7.61–7.48 (3H, m, SO_2PhH), 7.25 (1H, td, J= 7.5, 1.4 Hz, ArH), 7.06 (1H, dd, J=7.5, 1.4 Hz, ArH), 6.98 (1H, td, J=7.5, 0.9 Hz, ArH), 6.86 (1H, d, J=7.5 Hz, ArH), 6.50 (1H, q_i, J=2.0 Hz, =CH), 4.43–4.29 (2H, m, NCH_2), 4.09–4.05 (2H, m, NCH_2), 3.26 (2H, s, CCH_2), 3.24 (3H, s, CH_3), 1.33 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 192.5 (C=O), 180.5 (C=O), 143.9, 139.8, 136.9, 135.1, 133.5, 133.4, 129.8, 128.5, 127.8, 122.7, 122.2, 108.7, 56.2, 53.6, 46.3, 45.4, 26.8, 25.0; *m/z* (FAB) 411 (28%, $M^+ + H$), 215 (48%, $M-SO_2Ph$), 174 (49%), 160 (100%), 108 (90%).

3.3.10. *N*-But-3-en-1-yl-4-methyl-*N*-[2-(2-thienylcarbonyl)prop-2-en-1-yl]benzenesulfonamide (26). Prepared by the general cascade procedure employing rubidium carbonate base on a 2 mmol scale, using 2.4 mmol of aryl iodide and a reaction time of 18 h. Purification by flash chromatography eluting with petrol/ether 7:3 v/v afforded the product (540 mg, 72%) as a pale yellow oil; R_f 0.2; (Found: C, 60.55; H, 5.65; N, 3.65. $C_{19}H_{21}NO_3S_2$ requires C, 60.75; H, 5.65; N, 3.75%); υ_{max}/cm^{-1} (film) 1641 (C=O), 1432, 1342 ($S=O_{as}$), 1298, 1166 ($S=O_s$), 1093; δ_H (250 MHz, $CDCl_3$) 7.71 (2H, d, J=8.2 Hz, ArH), 7.79 (1H, dd, J=4.9, 1.1 Hz, ArH), 7.64 (1H, dd, J=3.8, 1.1 Hz, ArH), 7.29 (2H, d, J=8.2 Hz, ArH), 7.13 (1H, dd, J=4.9, 3.8 Hz, ArH), 6.15 (1H, t, J=1.5 Hz, =C$H_C$$H_D$), 6.07 (1H, s, =C$H_C$$H_D$), 5.66 (1H, ddt, J=17.0, 10.5, 6.7 Hz, CH_X=C$H_A$$H_B$), 5.06–4.97 (2H, m, C$H_X$=C$H_A$$H_B$), 4.14 (2H, s, NCH_2), 3.25 (2H, t, J=7.5 Hz, NCH_2), 2.43 (3H, s, CH_3), 2.26 (2H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 188.4 (C=O), 143.8, 143.2, 136.9, 134.9, 134.8, 134.8, 130.2, 128.4, 127.6, 126.5, 117.7, 49.4 (NCH_2), 49.3 (NCH_2), 33.1 (=CHCH_2), 21.9 (CH_3); *m/z* (ES) 348 ($M+H^+$).

3.3.11. *N*-(2-Benzoylprop-2-en-1-yl)-*N*-but-3-en-1-yl-4-methylbenzenesulfonamide (28). Prepared by the general cascade procedure employing rubidium carbonate base on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 19 h. Purification by flash chromatography eluting with petrol/ether 4:1 v/v afforded the product (265 mg, 72%) as a viscous colourless oil; R_f 0.12; υ_{max}/cm^{-1} (film) 1652 (C=O), 1340 ($S=O_{as}$), 1157 ($S=O_s$), 1091; δ_H (250 MHz, $CDCl_3$) 7.74–7.70 (3H, m, ArH), 7.73 (2H, d, J=8.0 Hz, ArH) 7.61–7.53 (1H, m, ArH), 7.48–7.41 (2H, m, ArH), 7.32 (2H, d, J=8.0 Hz, ArH), 6.31 (1H, t, J= 1.5 Hz, =C$H_C$$H_D$), 5.91 (1H, s, =C$H_C$$H_D$), 5.68 (1H, ddt, J=17, 10.4, 6.7 Hz, CH_X=C$H_A$$H_B$), 5.07–4.99 (2H, m, C$H_X$=C$H_A$$H_B$), 4.16 (2H, s, NCH_2), 3.29–3.23 (2H, m, NCH_2), 2.44 (3H, s, CH_3), 2.31–2.22 (2H, m, CH_2); δ_C (63 MHz, $CDCl_3$) 197.3 (C=O), 143.9, 143.6, 137.6, 136.9, 134.8, 133.0, 130.2, 130.0, 129.3, 128.7, 127.7, 117.7, 49.5 (NCH_2), 49.2 (NCH_2), 33.1 (=CHCH_2), 21.9 (CH_3); *m/z* (EI) 370 ($M+H^+$); HRMS found 370.1472, $C_{21}H_{24}NO_3S$ requires 370.1471.

3.3.12. *N*-But-3-en-1-yl-4-methyl-*N*-{2-[(1-methyl-1*H*-indol-5-yl)carbonyl]prop-2-en-1-yl}benzenesulfonamide (29). Prepared by the general cascade procedure employing rubidium carbonate on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 25 h. Purification by flash chromatography eluting with DCM afforded the product (282 mg, 68%), which crystallised from DCM/petrol as colourless prisms, mp 103–105 °C; R_f 0.26; (Found: C, 67.90; H, 6.10; N, 6.60. $C_{24}H_{26}N_2O_3S$ requires C, 68.20; H, 6.20; N, 6.65%); υ_{max}/cm^{-1} (film) 1645 (C=O), 1339 ($S=O_{as}$), 1157 ($S=O_s$), 1091; δ_H (250 MHz, $CDCl_3$) 8.09 (1H, d, J=1.5 Hz, ArH), 7.73 (2H, d, J=8.2 Hz, ArH), 7.72 (1H, dd, J=8.7, 1.5 Hz, ArH), 7.33 (1H, d, J=8.7 Hz, ArH), 7.28 (2H, d, J=8.2 Hz, ArH), 7.12 (1H, d, J=3.2 Hz, ArH), 6.58 (1H, d, J=3.2 Hz, ArH), 6.17 (1H, s, =C$H_C$$H_D$), 5.83 (1H, s, =CH$H_D$), 5.69 (1H, ddt, J= 17.0, 10.2, 6.7 Hz, CH_X=C$H_A$$H_B$), 5.07–4.99 (2H, m, C$H_X$=C$H_A$$H_B$), 4.22 (2H, s, NCH_2), 3.81 (3H, s, CH_3), 3.32–3.26 (2H, m, NCH_2), 2.40 (3H, s, CH_3), 2.40–2.26 (2H, m, CH_2); δ_C (63 MHz, $CDCl_3$) 198.5 (C=O), 144.1,

143.8, 139.5, 137.1, 135.0, 131.0, 130.1, 129.0, 128.0, 127.7, 126.9 (=CH_2), 125.2, 123.6, 117.6 (=CH_2), 109.6, 103.4, 49.7 (NCH_2), 49.3 (NCH_2), 33.5 (=$CHCH_2$), 33.1 (NCH_3), 21.9 (CH_3); *m/z* (%) (EI) 422 (1, M^+), 267 (43, M−Ts), 144 (51), 91 (49).

3.3.13. *N*-But-3-en-1-yl-4-methyl-*N*-{2-[2(methylthio) benzoyl]prop-2-en-1-yl}benzenesulfonamide (30). Prepared by the general cascade procedure employing rubidium carbonate on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 22 h. Purification by flash chromatography eluting with petrol/ether 4:1 v/v afforded the product (310 mg, 75%), which crystallised from DCM/petrol as pale yellow needles, mp 97–99 °C; R_f 0.1; (Found: C, 63.30; H, 5.95; N, 3.60. $C_{22}H_{25}NO_3S_2$ requires C, 63.60; H, 6.05; N, 3.35%); υ_{max}/cm^{-1} (film) 1653 (C=O), 1340 (S=O_{as}), 1157 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 7.74 (2H, d, J=8.0 Hz, ArH), 7.47–7.16 (4H, m, ArH), 7.33 (2H, d, J=8.0 Hz, ArH), 6.32 (1H, s, =C$H_C$$H_D$), 5.81 (1H, s, =C$H_C$$H_D$), 5.67 (1H, ddt, J=17.0, 10.4, 6.8 Hz, CH_X=C$H_A$$H_B$), 5.07–4.99 (2H, m, C$H_X$=C$H_A$$H_B$), 4.18 (2H, s, NCH_2), 3.27 (2H, m, NCH_2), 2.44 (3H, s, CH_3), 2.43 (3H, s, CH_3), 2.33–2.22 (2H, m, CH_2); δ_C (63 MHz, $CDCl_3$) 198.5 (C=O), 144.6, 143.9, 138.7, 138.2, 136.9, 134.9, 131.5, 130.9, 130.2, 129.6, 128.0, 127.6, 125.1, 117.7, 49.5 (NCH_2), 48.3 (NCH_2), 33.1 (=CCH_2), 21.9 (CH_3), 17.5 (CH_3); *m/z* (%) (EI) 260 (22, M−Ts), 191 (75), 137 (63), 91 (100).

3.3.14. Methyl 4-[2-({but-3-en-1-yl[(4-methylphenyl)sulfonyl]amino}methyl)acryloyl]benzenesulfonamide (31). Prepared by the general cascade procedure employing rubidium carbonate on a 1 mmol scale, using 1.2 mmol of aryl iodide and a reaction time of 21 h. Purification by flash chromatography eluting with petrol/ether 1:1 v/v afforded the product (300 mg, 70%), which crystallised from ether/hexane as colourless needles, mp 79–80 °C; R_f 0.2; (Found: C, 64.60; H, 6.00; N, 3.25. $C_{23}H_{25}NO_5S$ requires C, 64.60; H, 5.90; N, 3.30%); υ_{max}/cm^{-1} (film) 1723 (MeOC=O), 1653 (C=O), 1340 (S=O_{as}), 1158 (S=O_s), 1109, 1092; δ_H (250 MHz, $CDCl_3$) 8.11 (2H, d, J=8.2 Hz, ArH), 7.75 (2H, d, J=8.2 Hz, ArH), 7.72 (2H, d, J=8.2 Hz, ArH), 7.32 (2H, d, J=8.2 Hz, ArH), 6.38 (1H, s, =C$H_C$$H_D$), 5.91 (1H, s, =C$H_C$$H_D$), 5.68 (1H, ddt, J=17.3, 10.7, 6.7 Hz, CH_X=C$H_A$$H_B$), 5.07–5.00 (2H, m, C$H_X$=C$H_A$$H_B$), 4.15 (2H, s, NCH_2), 3.96 (3H, s, CH_3), 3.30–3.29 (2H, m, NCH_2), 2.44 (3H, s, CH_3), 2.31–2.22 (2H, m, CH_2); δ_C (63 MHz, $CDCl_3$) 196.7 (C=O), 166.6 (C=O), 144.0, 143.6, 141.3, 136.8, 134.8, 133.7, 130.4, 130.2, 129.9, 129.7, 127.7, 117.7, 52.9 (OCH_3), 49.7 (NCH_2), 49.1 (NCH_2), 33.2 (=CHCH_2), 21.9 (CH_3); *m/z* (ES) 428 ($M+H^+$).

3.3.15. {1-[(4-Methylphenyl)sulfonyl]-1,2,5,6-tetrahydropyridin-3-yl}(2-thienyl)methanone (32). Prepared by the general RCM procedure on a 0.26 mmol scale and a reaction time of 3 h. Purification by flash chromatography eluting with 3:2 v/v petrol/ether afforded the product (83 mg, 92%) as colourless needles, mp 119–120 °C; R_f 0.06; (Found: C, 58.65; H, 5.20; N, 4.30. $C_{17}H_{17}NO_3S_2$ requires C, 58.75; H, 4.95; N, 4.05%); υ_{max}/cm^{-1} (film) 1642 (C=O), 1343 (S=O_{as}), 1273, 1166 (S=O_s), 1093; δ_H (400 MHz, $CDCl_3$) 7.72 (2H, d, J=8.1 Hz, ArH), 7.65 (1H, d, J=4.9 Hz, ArH), 7.56 (1H, d, J=3.7 Hz, ArH), 7.34 (2H, d, J=8.1 Hz, ArH), 7.11 (1H, dd, J=4.9, 3.7 Hz, ArH), 6.83 (1H, br s, =CH), 3.95 (2H, s, NCH_2), 3.26 (2H, t, J=5.6 Hz, NCH_2), 2.51–2.50 (2H, br m, CH_2), 2.43 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 186.2 (C=O), 143.8, 142.2, 137.3, 135.3, 133.6, 133.4, 133.2, 129.8, 127.8, 44.5 (NCH_2), 42.0 (NCH_2), 25.9 (=CHCH_2), 21.5 (CH_3); *m/z* (%) (EI) 347 (3, M^+), 192 (80, M−Ts), 124.1 (49), 111 (92), 91 (100).

3.3.16. {1-[(4-Methylphenyl)sulfonyl]-1,2,5,6-tetrahydropyridin-3-yl}(phenyl)methanone (33). Prepared by the general RCM procedure on a 0.2 mmol scale and a reaction time of 2 h. Purification by flash chromatography eluting with 7:3 v/v petrol/ether afforded the product (60 mg, 90%) as colourless needles, mp 134–135 °C; R_f 0.05; (Found: C, 67.05; H, 5.65; N, 4.10. $C_{19}H_{19}NO_3S$ requires C, 66.85; H, 5.60; N, 4.15%); υ_{max}/cm^{-1} (film) 1642 (C=O), 1343 (S=O_{as}), 1166 (S=O_s), 1092; δ_H (250 MHz, $CDCl_3$) 7.74 (2H, d, J=8.2 Hz, ArH), 7.59–7.50 (3H, m, ArH), 7.44–7.27 (2H, m, ArH), 7.34 (2H, d, J=8.2 Hz, ArH), 6.2 (1H, q, J=2.1 Hz, =CH), 3.96 (2H, br d, J=2.1 Hz, NCH_2), 3.23 (2H, t, J=5.7 Hz, NCH_2), 2.53–2.46 (2H, m, CH_2), 2.44 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 198.0 (C=O), 144.3, 141.4, 137.7, 135.4, 133.4, 132.4, 130.2, 129.5, 128.7, 128.2, 44.7 (NCH_2), 42.4 (NCH_2), 26.5 (=CHCH_2), 22.0 (CH_3); *m/z* (ES) 342 (M^++H).

3.3.17. (1-Methyl-2,3-dihydro-1*H*-indol-5-yl){1-[(4-methylphenyl)sulfonyl]-1,2,5,6-tetrahydropyridin-3-yl}methanone (34). Prepared by the general RCM procedure on a 0.15 mmol scale and a reaction time of 5 h. Purification by flash chromatography eluting with 2:3 v/v petrol/ether afforded the product (54 mg, 91%) as colourless needles, mp 116–118 °C; R_f 0.16; υ_{max}/cm^{-1} (film) 1635 (C=O), 1340 (S=O_{as}), 1164 (S=O_s), 1098; δ_H (250 MHz, $CDCl_3$) 7.95 (1H, d, J=1.5 Hz, ArH), 7.74 (2H, d, J=8.2 Hz, ArH), 7.59 (1H, dd, J=8.6, 1.5 Hz, ArH), 7.34 (2H, d, J=8.2 Hz, ArH) 7.33 (1H, d, J=8.6 Hz, ArH), 7.13 (1H, d, J=3.5 Hz, ArH), 6.57 (1H, d, J=3.5 Hz, ArH), 6.57–6.54 (H, m, =CH), 4.01 (2H, br d, J=2.1 Hz, NCH_2), 3.82 (3H, s, CH_3), 3.26 (2H, t, J=5.7 Hz, NCH_2), 2.52–2.47 (2H, m, CH_2), 2.44 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 198.0 (C=O), 144.1, 139.2, 138.6, 135.7, 133.6, 130.9, 130.2, 129.1, 128.2, 128.0, 124.5, 123.4, 109.6, 103.1, 45.2 (NCH_2), 42.6 (NCH_2), 33.5, 26.2, 22.0; *m/z* (%) (CI) 395 (100, M^++H), 241 (90) 189 (31); HRMS found 395.1426, $C_{22}H_{23}N_2O_3S$ requires 384.1424.

3.3.18. {1-[(4-Methylphenyl)sulfonyl]-1,2,5,6-tetrahydropyridin-3-yl}[2-(methylthio)phenyl]methanone (35). Prepared by the general RCM procedure employing 5 mol% of **3**, followed by an extra 2 mol% of **3** after 4 h on a 0.32 mmol scale and a reaction time of 7 h. Purification by flash chromatography eluting with 3:2 v/v petrol/ether afforded the product (90 mg, 73%), which crystallised from DCM/petrol as colourless needles, mp 139–141 °C; R_f 0.11; (Found: C, 62.00; H, 5.50; N, 3.60. $C_{20}H_{21}NO_3S_2$ requires C, 62.00; H, 5.45; N, 3.60%); υ_{max}/cm^{-1} (film) 1644 (C=O), 1340 (S=O_{as}), 1162 (S=O_s), 1091; δ_H (250 MHz, $CDCl_3$) 7.74 (2H, d, J=8.1 Hz, ArH), 7.43–7.32 (2H, m, ArH), 7.36 (2H, d, J=8.1 Hz, ArH), 7.19–7.17 (2H, m, ArH), 6.49 (1H, br s, =CH), 3.97 (2H, br d, J=1.8 Hz, NCH_2), 3.21 (2H, t, J=5.7 Hz, NCH_2), 2.44 (5H, s, CH_3

and CH_2), 2.40 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 195.9 (C=O), 144.2, 142.9, 138.3, 138.0, 136.4, 133.4, 131.1, 130.2, 128.8, 128.2, 128.0, 125.1, 44.2 (NCH_2), 42.3 (NCH_2), 26.7, 22.0, 17.4; *m/z* (ES) 388 ($M^+ + H$).

3.3.19. Methyl 4-({1-[(4-methylphenyl)sulfonyl]-1,2,5,6-tetrahydropyridin-3-yl}carbonyl)benzoate (36). Prepared by the general ring closing metathesis procedure on a 0.12 mmol scale and a reaction time of 3 h. Purification by flash chromatography eluting with 7:3 v/v petrol/ether afforded the product (41 mg, 86%) as colourless needles, mp 157–159 °C; R_f 0.15; (Found: C, 62.70; H, 5.50; N, 3.20. $C_{21}H_{21}NO_5S$ requires C, 63.15; H, 5.30; N, 3.50%); υ_{max}/cm^{-1} (film) 1723 (MeOC=O) 1645 (C=O), 1344 ($S{=}O_{as}$), 1280, 1166 ($S{=}O_s$), 1093; δ_H (250 MHz, $CDCl_3$) 8.09 (2H, d, $J=8.3$ Hz, ArH), 7.74 (2H, d, $J=8.2$ Hz, ArH), 7.61 (2H, d, $J=8.3$ Hz, ArH), 7.36 (2H, d, $J=8.2$ Hz, ArH), 6.62 (1H, q, $J=2.0$ Hz, =CH), 3.96–3.94 (2H, m, NCH_2), 3.94 (3H, s, OCH_3), 3.25 (2H, t, $J=5.7$ Hz, NCH_2), 2.52–2.50 (2H, m, CH_2), 2.45 (3H, s, CH_3); δ_C (63 MHz, $CDCl_3$) 197.7 (C=O), 166.6 (C=O), 144.3, 142.5, 141.6, 135.5, 133.4, 133.3, 130.2, 129.9, 129.2, 128.2, 52.9 (OCH_3), 44.5 (NCH_2), 42.3 (NCH_2), 26.6 (=CH*C*H_2), 22.0 (CH_3); *m/z* (ES) 400 ($M^+ + H$); HRMS found 417.1476, $C_{21}H_{25}N_2O_5S$ requires 417.1479.

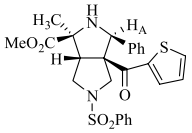
3.3.20. *N*-Pent-4-en-1-yl-*N*-[2-(2-(thienyl)prop-2-en-1-yl (37). Prepared by the general cascade procedure on a 2 mmol scale, using 2.5 mmol of aryl iodide and a reaction time of 25 h. Purification by flash chromatography eluting with 4:1 v/v petrol/ether afforded the product (440 mg, 56%) as a viscous pale yellow oil; R_f 0.12; υ_{max}/cm^{-1} (film) 1636 (C=O), 1622, 1413, 1340 ($S{=}O_{as}$), 1158 ($S{=}O_s$), 1091; δ_H (250 MHz, $CDCl_3$) 7.70 (2H, d, $J=8.2$ Hz, ArH), 7.69 (1H, d, $J=5.1$ Hz, ArH), 7.64 (1H, d, $J=3.6$ Hz, ArH) 7.33 (2H, d, $J=8.2$ Hz, ArH), 7.12 (1H, dd, $J=5.1$, 3.6 Hz, ArH), 6.16 (1H, s, =CH_CH$_D$), 6.06 (1H, s, =CH$_C$$H_D$), 5.71 (1H, ddt, $J=16.9$, 10.3, 6.6 Hz, CH_X=CH$_A$H$_B$), 4.99 (1H, d, $J=10.3$ Hz, CHX=CH_AH$_B$), 4.97 (1H, d, $J=16.9$ Hz, CH$_X$=CH$_A$$H_B$), 4.11 (2H, s, NCH_2), 3.17 (2H, t, $J=7.7$ Hz, NCH_2), 2.43 (3H, s, CH_3), 2.04–1.96 (2H, m, =CHCH_2), 1.59 (2H, q_i, $J=7.7$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 188.5 (C=O), 144.1, 143.8, 143.3, 137.7, 136.9, 134.9, 134.8, 130.1, 128.4, 127.6, 126.4 (=CH_2), 115.8 (=CH_2), 49.6 (NCH_2), 49.4 (NCH_2), 31.2 (=CH*C*H_2), 27.7 (CH_2), 21.9 (CH_3); *m/z* (%) (CI) 390 (5, $M^+ + H$), 170 (48), 99 (100), 86 (100); HRMS found 390.1192, $C_{20}H_{24}NO_3S_2$ requires 390.1192.

3.3.21. *N*-Pent-4-en-1-yl-*N*-(2-phenyl)prop-2-en-1-yl] benzenesulfonamide (38). Prepared by the general cascade procedure on a 2 mmol scale, using 2.5 mmol of aryl iodide and a reaction time of 25 h. Purification by flash chromatography eluting with DCM afforded the product (520 mg, 68%) as a viscous pale yellow oil; R_f 0.27; υ_{max}/cm^{-1} (film) 1654 (C=O), 1448, 1339 ($S{=}O_{as}$), 1159 ($S{=}O_s$), 1091; δ_H (250 MHz, $CDCl_3$) 7.72 (2H, d, $J=8.2$ Hz, ArH), 7.71 (2H, d, $J=7.5$ Hz, ArH), 7.57 (1H, t, $J=7.5$ Hz, ArH), 7.44 (2H, t, $J=7.5$ Hz, ArH), 7.31 (2H, d, $J=8.2$ Hz, ArH), 6.31 (1H, s, =CH_CH$_D$), 5.90 (1H, s, =CH$_C$$H_D$), 5.73 (1H, ddt, $J=16.9$, 10.2, 6.6 Hz, CH_X=CH$_A$H$_B$), 5.00 (1H, d, $J=10.2$ Hz, CH$_X$=CH_AH$_B$), 4.97 (1H, d, $J=16.9$ Hz, CH$_X$=CH$_A$$H_B$), 4.13 (2H, s, NCH_2), 3.18 (2H, t, $J=7.7$ Hz, NCH_2), 2.44 (3H, s, CH_3), 2.06–1.97 (2H, m, =CHCH_2), 1.60 (2H, q_i, $J=7.7$ Hz, CH_2); δ_C (63 MHz, $CDCl_3$) 197.1 (C=O), 143.8, 143.7, 137.7, 137.6, 136.9, 133.0, 130.2, 130.0, 129.2, 128.7, 127.7, 115.8, 49.8 (NCH_2), 49.2 (NCH_2), 31.2 (=CH*C*H_2), 27.8 (CH_2), 21.9 (CH_3); *m/z* (%) (CI) 384 (10, $M^+ + H$), 164 (90), 86 (100); HRMS found 384.1632, $C_{22}H_{26}NO_3S$ requires 384.1628.

3.4. General procedure for microwave RCM

Substrate and CH_2Cl_2 (4 ml) were combined in a microwave pressure vial, containing a small magnetic stirrer bar, to afford solutions of either 1.5 or 3.0 mM. Catalyst **3** (1–5 mol%) was then added to this solution and the pressure vial immediately sealed and subjected to microwave irradiation (Smith Creator model). The solvent was then removed and the product conversion measured by 500 MHz NMR analysis. Passing the crude product through a small pad of silica, eluting with ether/petrol, afforded the product.

3.4.1. Methyl 1-methyl-2,3-diphenyl-5-(phenylsulfonyl)-3a-(thien-2-yl carbonyl)octahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (41). Triethylamine (57 µl, 0.4 mmol), and silver acetate (66 mg, 0.4 mmol) were added to a stirred solution of enone **17** (84 mg, 0.26 mmol) in toluene (10 ml). A solution of imine (60 mg, 0.29 mmol) in toluene (1 ml) was then added and reaction mixture stirred at room temperature for 20 h. Filtration and concentration in vacuo afforded the crude product as a single isomer. Purification by flash column chromatography eluting with 1:2 v/v ethyl acetate/petrol afforded the product as a colourless amorphous solid, mp 75–77 °C; R_f 0.15; υ_{max} /cm^{-1} (film) 3334 (NH), 1733 (C=O), 1637 (MeOC=O), 1412, 1350 (S=Oas), 1246, 1169 (S=Os), δ_H (500 MHz, CDCl3) 7.83–7.81 (2H, m, SO_2PhH), 7.62–7.60 (1H, m, SO_2PhH), 7.55–7.52 (2H, m, SO_2PhH), 7.37 (1H, dd, $J=5.0$, 1.0 Hz, ArH), 7.14–7.12 (2H, m, ArH), 7.09–7.07 (3H, m, ArH), 6.84 (1H, dd, $J=4.0$, 1.0 Hz, ArH), 6.75 (1H, dd, $J=5.0$, 4.0 Hz, ArH), 4.48 (1H, s, NCH_APh), 4.03 (1H, d, $J=10.0$ Hz, NCHH), 3.82 (3H, s, OCH3), 3.77–3.71 (2H, m, NCH_2), 3.27 (1H, d, $J=10.0$ Hz, NCHH), 3.14 (1H, br s, NH), 2.93 (1H, dd, $J=10.2$, 8.1 Hz, CH), 1.61 (3H, s, CH3); *m/z* (ES) 533 ($M^+ + Na$); HRMS found 533.6284, $C_{26}H_{26}N_2O_5S_2 + Na$ requires 533.6280.



NOE data:

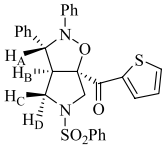
Signal irradiated	Enhancement (%)
	H_A
CH_3	2.1

3.5. General thermodynamic controlled nitrone cycloaddition procedure (A)

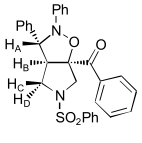
Diphenyl nitrone (183 mg, 0.93 mmol) was added to a solution of **17** (145 mg, 0.46 mmol) in toluene (20 ml) in

a Schlenk tube. The reaction mixture was immersed in a pre-heated oil bath at 120 °C and stirred under a nitrogen atmosphere for 54 h. Concentration in vacuo afforded the crude product comprising of a 9:1 mixture of **43** and **46**. Flash chromatograph eluting with DCM afforded the pure isomers in a 80% combined yield.

3.5.1. 2,3-Diphenyl-5-(phenylsulfonyl)hexahydro-6a*H*-pyrrolo[3,4-*a*]isoxazol-6a-yl(thien-2-yl)methanone (43). Crystallisation from DCM/petrol afforded colourless needles; mp 157–159 °C; R_f 0.3; (Found: C, 65.25; H, 4.80; N, 5.60. $C_{28}H_{24}N_2O_4S_2$ requires C, 65.10; H, 4.70; N, 5.40%); υ_{max}/cm^{-1} (film) 1657 (C=O), 1490, 1446, 1353 (S=O_{as}), 1170 (S=O_s), 1091; δ_H (500 MHz, $CDCl_3$) 8.22 (1H, dd, J=3.2, 1.2 Hz, ArH), 7.80–7.88 (2H, m, SO_2PhH), 7.71 (1H, dd, J=3.2, 1.2 Hz, ArH), 7.61 (1H, tt, J=6.7, 1.2 Hz, SO_2PhH), 7.54–7.50 (2H, m, SO_2PhH), 7.36–7.28 (4H, m, ArH), 7.18–7.15 (3H, m, ArH) 7.06 (1H, tt, J=6.7, 1.2 Hz, ArH), 7.00–6.96 (3H, m, ArH), 4.11 (1H, d, J=11 Hz, NCH), 4.10 (1H, d, J=8.0 Hz, NCH_A), 3.78 (1H, td, J=8.0, 1.3 Hz, CH_B), 3.73 (1H, br d, J=10.4 Hz, NCH_D), 3.03 (1H, dd, J=10.4, 8 Hz, NCH_C), 3.02 (1H, d, J=11 Hz, NCH); δ_C (125 MHz, $CDCl_3$) 191.7 (C=O), 147.8, 139.4, 137.5, 136.0, 135.8, 135.0, 133.3, 129.3, 129.0, 128.6, 128.5, 128.3, 128.0, 127.9, 125.1, 119.9, 94.1, 77.9, 61.1, 57.0, 51.7; *m/z* (ES) 517 (M^++H).



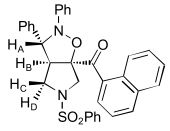
3.5.2. 2,3-Diphenyl-5-(phenylsulfonyl)hexahydro-6a*H*-pyrrolo[3,4-*a*]isoxazol-6a-yl(phenyl)methanone (44). Following procedure A (0.47 mmol scale, 60 h) using enone **18** a single isomer was obtained. Purification by flash column chromatography eluting with DCM afforded the product (140 mg, 70%), which crystallised from DCM/petrol as colourless needles, mp 161–163 °C; R_f 0.4; (Found: C, 70.40; H, 5.05; N, 5.50. $C_{30}H_{26}N_2O_4S$ requires C, 70.55; H, 5.15; N, 5.50%); υ_{max}/cm^{-1} (film) 1681 (C=O), 1490, 1446, 1351 (S=O_{as}), 1170 (S=O_s), 1091; δ_H (500 MHz, $CDCl_3$) 8.18 (2H, d, J=7.9 Hz, ArH), 7.79 (2H, d, J=7.9 Hz, ArH), 7.63–7.57 (2H, m, ArH), 7.51–7.48 (4H, m, ArH), 7.31–7.30 (5H, m, ArH), 7.12 (2H, t, J=7.9 Hz, ArH), 6.99 (1H, t, J=7.2 Hz, ArH), 6.84 (2H, d, J=7.9 Hz, ArH), 4.19 (1H, d, J=11.2 Hz, NCH), 4.10 (1H, d, J=7.3 Hz, NCH_APh), 3.96 (1H, dd, J=7.3, 7.2 Hz, CH_B), 3.72 (1H, d, J=10.3 Hz, NCH_D), 3.04 (1H, dd, J=10.3, 7.2 Hz, NCH_C), 3.02 (1H, d, J=11.2 Hz, NCH); δ_C (125 MHz, $CDCl_3$) 198.2 (C=O), 147.6, 137.9, 135.0, 134.2, 133.8, 133.3, 130.0, 129.9, 129.1, 128.6, 128.5 128.4, 127.9, 127.7, 124.7, 119.6, 94.2, 76.7, 60.8, 56.6, 51.3; *m/z* (ES) 511 (M^++H).



NOE data:

Signal irradiated	Enhancement (%)		
	H_A	H_B	H_C
H_A		0	4.8
H_C	11.2		

3.5.3. 2,3-Diphenyl-5-(phenylsulfonyl)hexahydro-6a*H*-pyrrolo [3,4-*a*]isoxazol-6a-yl(1-napththyl)methanone (45). Following proceedure A (0.43 mmol scale, 58 h) using enone **19** a single isomer was obtained. Purification by flash column chromatograph eluting with DCM afforded the product (140 mg, 58%), which crystallised from DCM/petrol as colourless needles, mp 165–167 °C; R_f 0.35; (Found: C, 72.60; H, 5.05; N, 5.15. $C_{34}H_{28}N_2O_4S$ requires C, 72.85; H, 5.05; N, 5.00%); υ_{max}/cm^{-1} (film) 1641 (C=O), 1490, 1446, 1350 (S=O_{as}), 1170 (S=O_s), 1091; δ_H (500 MHz, $CDCl_3$) 8.21 (1H, d, J=8.2 Hz, ArH), 8.07 (1H, d, J=7.3 Hz, ArH), 8.02 (1H, d, J=8.3 Hz, ArH), 7.90 (1H, d, J=7.3 Hz, ArH), 7.84 (2H, d, J=7.3 Hz, ArH), 7.60–7.50 (6H, m, ArH), 7.29–7.23 (5H, m, ArH), 7.02 (2H, t, J=7.5 Hz, ArH), 6.92 (1H, t, J=7.5 Hz, ArH), 6.60 (2H, d, J=7.5 Hz, ArH), 4.20 (1H, d, J=11.0 Hz, NCH), 4.09 (1H, d, J=7.3 Hz, NCH_A), 3.80 (1H, d, J=10.3 Hz, NCH_D), 3.81–3.76 (1H, m, CH_B), 3.32 (1H, d, J=11.0 Hz, NCH), 3.20 (1H, dd, J=10.3, 7.3 Hz, NCH_C); δ_C (125 MHz, $CDCl_3$) 205.05 (C=O), 147.1, 138.1, 135.3, 133.9, 133.3, 133.0, 132.6, 130.7, 129.3, 129.2, 128.7, 28.4, 128.3, 128.1, 127.9, 127.8, 127.2, 126.4, 125.2, 124.5, 124.1, 119.5, 94.7, 75.6, 63.5, 56.9, 51.7; *m/z* (%) (EI) 560 (16, M^+), 155 (100), 127 (68), 77 (78).



NOE data:

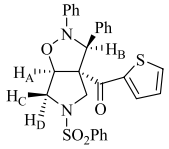
Signal irradiated	Enhancement (%)		
	H_A	H_B	H_C
H_A		0	11.1
H_C	5.1		

3.6. General kinetic controlled nitrone cycloaddition procedure (B)

Diphenyl nitrone (125 mg, 0.63 mmol) was added to a solution of **17** (180 mg, 0.57 mmol) in toluene (20 ml). The reaction mixture was immersed in a pre-heated oil bath at 80 °C and stirred under a nitrogen atmosphere for 32 h. Concentration in vacuo afforded the crude product comprising of a 3.5:1 mixture of **45** and **46**, respectively. Flash chromatography eluting with DCM afforded the pure isomers in a 70% combined yield. The data for **45** is collected above.

3.6.1. *exo*-[2,3-Diphenyl-(5-(phenylsulfonyl)hexahydro-3a*H*-pyrrolo[3,4-*a*]isoxazol-3a-yl]thien-2-yl)methanone (46). Crystallisation from DCM/petrol afforded colourless needles, mp 149–151 °C; R_f 0.2; (Found: C, 65.30; H, 4.95; N, 5.55. $C_{28}H_{24}N_2O_4S_2$ requires C, 65.10; H, 4.70; N, 5.40%); υ_{max}/cm^{-1} (film) 1652 (C=O), 1352 (S=O_{as}),

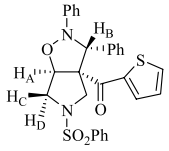
1167 (S=O_s), δ_H (500 MHz, $CDCl_3$) 7.81–7.79 (2H, m, SO_2PhH), 7.66 (1H, dd, $J=3.7$, 0.8 Hz, ArH_C), 7.61–7.57 (1H, m, SO_2PhH), 7.53 (1H, dd, $J=4.9$, 0.8 Hz, ArH), 7.50–7.48 (2H, m, SO_2PhH), 7.18–6.88 (11H, m, 10×ArH), 5.57 (1H, dd, $J=5.1$, 1.2 Hz, OCH_A), 4.74 (1H, s, $PhCH_B$), 3.94 (1H, d, $J=10.5$ Hz, NCH), 3.82 (1H, d, $J=10.5$ Hz, NCH), 3.76 (1H, dd, $J=11.3$, 1.2 Hz, NCH_C), 3.38 (1H, dd, $J=11.3$, 5.1 Hz, NCH_D); δ_C (125 MHz, $CDCl_3$) 188.0 (C=O), 147.5, 143.6, 135.0, 134.6, 134.5, 133.3, 133.2, 129.3, 128.7, 128.6, 128.5, 128.3, 127.9, 127.8, 123.9, 118.3, 81.8, 77.6, 74.9, 56.1, 53.4; *m/z* (ES) 539 ($M^+ + Na$).



NOE data:

Signal irradiated	Enhancement (%)
	H_C
H_A	5.9
H_B	4.0

3.6.2. [*endo*-2,3-Diphenyl-(5-(phenylsulfonyl)hexahydro-3a*H*-pyrrolo[3,4-*a*]isoxazol-3a-yl]thien-2-yl)methanone (47). The product is isolated as a pale yellow froth. R_f 0.15; (Found: C, 64.95; H, 4.70; N, 5.40. $C_{28}H_{24}N_2O_4S_2$ requires C, 65.10; H, 4.70; N, 5.40%); υ_{max}/cm^{-1} (film) 1644 (C=O), 1490, 1353 (S=O_{as}), 1169 (S=O_s), δ_H (250 MHz, $CDCl_3$) 7.84 (1H, dd, $J=3.92$, 0.9 Hz, ArH), 7.76–7.53 (5H, m, ArH), 7.67 (1H, dd, $J=4.9$, 0.9 Hz, ArH) 7.08 1H, dd, $J=4.9$, 3.9 Hz, ArH) 7.34–6.99 (10H, m, ArH), 5.35 (1H, dd, $J=6.8$, 3.0 Hz, OCH_A), 5.07 (1H, s, NCH_B), 3.79 (1H, dd, $J=10.0$, 3.0 Hz, NCH_C), 3.47 (1H, dd, $J=10.6$, 6.8 Hz, NCH_D), 3.25 (1H, d, $J=11.2$ Hz, NCH), 3.19 (1H, d, $J=11.2$ Hz, NCH); *m/z* (ES) 539 ($M^+ + Na$).



Acknowledgements

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References and notes

1. Preliminary communications: Grigg, R.; Hodgson, A.; Morris, J.; Sridharan, V. *Tetrahedron Lett.* **2003**, *44*, 1023–1026. Grigg, R.; Martin, W.; Morris, J.; Sridharan, V. *Tetrahedron Lett.* **2003**, *44*, 4899–4901.
2. Preliminary communication: Dondas, H. A.; Blame, G.; Clique, B.; Grigg, R.; Hodgson, A.; Morris, J.; Sridharan, V. *Tetrahedron Lett.* **2001**, *42*, 8673–8675. Dondas, H. A; Clique, B.; Cetinkaya, B.; Grigg. R.; Kilner, C.; Morris, J.; Sridharan, V. *Tetrahedron*. *61*, see doi: 10.1016/j.tet.2005.08.078.
3. (a) Furstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043. (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (c) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592–4633.
4. (a) Nicolaou, K. C.; Rodriguez, R. M.; Mitchell, H. J.; van Delft, F. L. *Angew. Chem., Int. Ed.* **1998**, *37*, 1874–1876 and references cited therein. (b) Wipf, P.; Weiner, W. S. *J. Org. Chem.* **1999**, *64*, 5321–5324 and references cited therein.
5. For a classic paper evaluating, categorising and exemplifying the application of **2** and **3** to alkene cross-metathesis see: Chatterjee, A. K.; Choi, T. L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.
6. Furstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem.* **2000**, *65*, 2204–2207. Davis, F. A.; Deng, J. *Org. Lett.* **2005**, *6*, 3719–3722. Davis, F. A.; Wu, Y. *Org. Lett.* **2004**, *6*, 1269–1272.
7. Grigg, R.; Brown, S.; Sridharan, V.; Uttley, M. D. *Tetrahedron Lett.* **1997**, *38*, 5031–5034.
8. Grigg, R.; Machachlan, W.; Rasparini, M. *Chem. Commun.* **2000**, 2241–2242.
9. Henry, J. R.; Marcin, L. R.; McIntosh, M. C.; Scola, P. M.; Harris, G. D., Jr.; Weinreb, S. M. *Tetrahedron Lett.* **1989**, *30*, 5709–5712.
10. Brown, S.; Clarkson, S.; Grigg, R.; Thomas, W. A.; Sridharan, V.; Wilson, D. M. *Tetrahedron* **2001**, *57*, 1347–1359. Anwar, U.; Casaschi, A.; Grigg, R.; Sansano, J. M. *Tetrahedron* **2001**, *57*, 1361–1367. Grigg, R.; Sridharan, V. *J. Organomet. Chem.* **1999**, *576*, 65–87.
11. (a) Furstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130–9136. (b) Furstner, A. *Synlett* **1999**, 1523–1533.
12. Gai, X.; Grigg, R.; Collard, S.; Muir, J. E. *Chem. Commun.* **2000**, 1765–1766.
13. (a) Jeffrey, T. *Tetrahedron Lett.* **1985**, *26*, 2667–2670. (b) Jeffrey, T. *Synthesis* **1987**, 70–71. Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314–321.
14. Furstner, A.; Dierkes, T.; Thiel, O. R.; Blanda, G. *Chem. Eur. J.* **2001**, *7*, 5286–5298.
15. pK_a's calculated using the ACD/I-Lab service, version 4.5.
16. Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717–727.
17. Nayo, K. G.; Hearhoof, E. H.; Leiddle, J. *Org. Lett.* **2002**, *4*, 1567–1570.
18. Gabacia, S.; Desai, B.; Lavastre, O.; Kappe, C. O. *J. Org. Chem.* **2003**, *68*, 9136–9139.
19. Yang, C.; Murray, W.; Wilson, L. J. *Tetrahedron Lett.* **2003**, *44*, 1783–1786.
20. Barr, D. A.; Grigg, R.; Gunaratne, H. Q. N.; Kemp, J.; McMeekin, P.; Sridharan, V. *Tetrahedron* **1988**, *44*, 557–570.
21. Grigg, R.; Liu, A.; Shaw, D.; Suganthan, S.; Washington, M. L.; Woodall, D. E.; Yoganathan, G. *Tetrahedron Lett.* **2000**, *41*, 7129–7133.Aftab, T.; Grigg, R.; Ladlow, M.; Sridharan, V.; Thornton-Pett, M. *Chem. Commun.*, 1754–1755. Grigg, R.; Millington, E. L.; Thornton-Pett, M. *Tetrahedron Lett.* **2002**, *43*, 2685–2688. Fielding, M. R.; Grigg, R.; Sridharan, V.; Thornton-Pett, M.; Urch, C. J. *Tetrahedron* **2003**, *57*, 7737–7748.