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A ring closing metathesis-manganese dioxide oxidation sequence for the synthesis of substituted pyrroles

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ABSTRACT

The combination of ring closing, or enyne metathesis with oxidation in order to prepare *N*-sulfonyl pyrroles is described. Reasonable to good yields were obtained for a variety of substituents and the procedure may also be conducted in one-pot. 2-Bromo *N*-sulfonyl adducts prepared in this manner were subjected to an intramolecular Heck-type cyclisation, forming cyclic sulfonamides.

1. Introduction

The synthesis of aromatic heterocycles is of interest, in part due to their many applications. Several well-developed, classical methods – such as the Paal-Knorr reaction and its variants for example – are available to chemists for the construction of this compound class.[1] More recently, the advent of structurally well-defined ruthenium metathesis catalysts (see Fig. 1, **1**–**3**) for inter and intramolecular carbon-carbon bond formation has opened up alternative strategies for the assembly of aromatic heterocycles.[2] As shown in Scheme 1, post metathesis, elimination[3] and oxidation reactions[4] have been used to convert the intermediate non-aromatic compounds into the aromatic products.

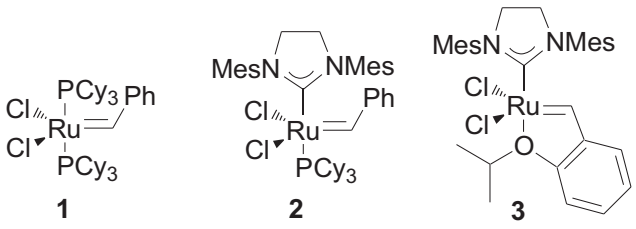
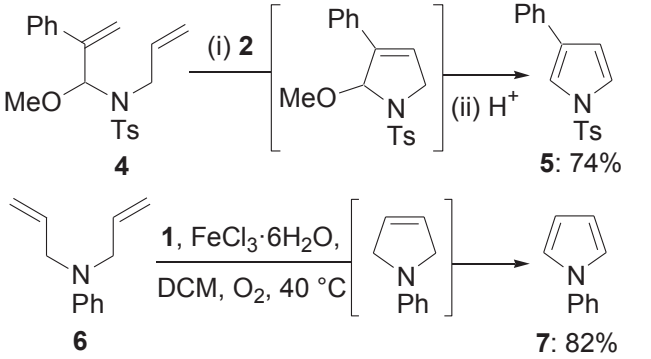


Fig. 1. Ruthenium-based catalysts for ring closing metathesis (RCM).



Scheme 1. Selected examples of metathesis followed by elimination,[3c] or oxidation[4g] for the synthesis of pyrroles.

For several years we have investigated the synthesis and chemistry of a range of benzo-fused cyclic sulfonamides (e.g., **10**)[5] and as an extension of this work also considered methods for the synthesis of *N*-sulfonyl pyrroles (Scheme 2). *N*-Sulfonyl pyrroles represent useful compounds,[6] methods exist for their regioselective functionalisation, for example and they participate in Diels–Alder cycloaddition reactions.[7] This paper describes a robust metathesis-oxidation strategy to prepare a range of *N*-

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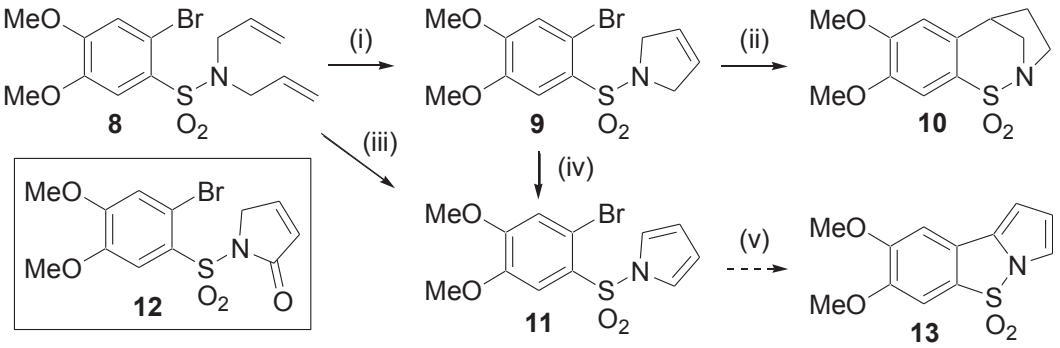


(i) **1** (5 mol%), DCM, rt, 95%; (ii) $Pd(OAc)_2$, PPh_3, K_2CO_3, DMF, 110 °C, 15 h; then H_2, rt, 12 h, 52%; (iii) **1** (5 mol%), PhH, rt, 0.75 h; then TBHP (2 equiv.) rt, 18 h, 38% **11** and 22% **12**; (iv) MnO_2 (20 equiv.), PhH, 80 °C, 1 h, quant.; (v) Intramolecular Heck-type reaction.

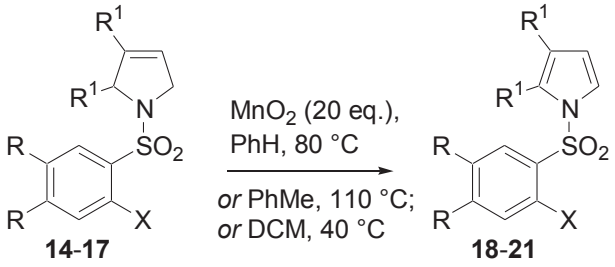
Scheme 2. An RCM-oxidation-based route to *N*-sulfonyl pyrrole **11**.

functionalised pyrroles and includes some preliminary Pd-mediated cyclisation reactions as a means to prepare more elaborate fused scaffolds (e.g., **13**).

2. Results and discussion

As outlined in Scheme 2, we have previously reported how an intramolecular Heck reaction (IHR) of *N*-sulfonyl dihydropyrrole **9**, followed by alkene reduction, generates cyclic sulfonamide **10** whose behaviour in the presence of reductants has been studied.[5a,d] In relation to this study we became interested in the analogous chemistry of the *N*-sulfonyl pyrrole family of compounds; exemplified by the sulfonyl tethered 2-aryl pyrrole **13**. Thus, a means to access functionalised *N*-sulfonyl pyrroles (of the type **11**) was considered. As depicted in Scheme 2, one attractive method utilises RCM whereupon, in the same reaction vessel, the initially formed dihydropyrrole (e.g., **9**) is oxidised into the corresponding pyrrole (e.g., **11**).[4f] This method relies on the addition of *tert*-butyl hydroperoxide (TBHP) to the initially formed dihydropyrrole which may act as an oxidant directly, or may convert the low-oxidation state ruthenium into a more aggressive oxidant. Our initial exploration of this method provided interesting results. Treatment of **8** with Grubbs catalyst **1**, under the recommended conditions[4f] resulted in a rapid RCM to generate **9**. At this stage TBHP was added and the mixture was stirred overnight (for approximately 18 h). Purification by flash column chromatography provided the expected *N*-sulfonyl pyrrole **11** as the main product (38%). However, the oxidation did not proceed to completion and dihydropyrrole **9** (22%) was isolated. Additionally, unsaturated lactam **12** (22%) was also detected. Based on this finding we sought an alternative method that might avoid side product formation. Since it is well-appreciated that manganese(IV) dioxide can oxidise non-aromatic precursors[8] the use of this reagent was considered. As shown in Scheme 2, treatment of dihydropyrrole **9** with an excess of MnO_2, in benzene at reflux, efficiently led to the formation of pyrrole **11**.

Based on the success and efficiency of this heterogeneous reaction its similar use was studied for a range of *N*-sulfonyl dihydropyrroles. As shown in Scheme 3 efficient conversion was observed for several different aryl substitution patterns. Benzene (Entries 1 and 2) could be replaced with toluene also at reflux (Entry 3). In these examples, presumably due to the temperature, reaction periods of 1–3 h were typically required to achieve complete oxidation. The use of less than 20 equiv of MnO_2 was studied. In these cases the reactions do proceed, however, with smaller amounts of the heterogeneous oxidant the reactions were found to afford the product in lower yields than those reported in Scheme 3 and did not reach completion in the same reaction period.



Entry	Substrate	Product	R	X	R^1	Yield[a]
1	**14**	**18**	H	Br	H	90%[b]
2	**15**	**19**	OCH_2O	Br	H	89%[b]
3	**16**	**20**	OMe	Br	$(CH_2)_4$	58%[c] 69%[d]
4	**17**	**21**	H	NO_2	H	98%[d]

[a]Isolated yields following chromatographic purification; [b]PhH; [c]PhMe; [d]DCM

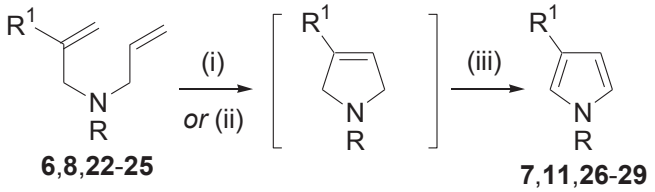
Scheme 3. Manganese(IV) dioxide mediated oxidation of *N*-sulfonyl dihydropyrroles.

In terms of purification; simple filtration, in order to remove the manganese-based material was performed through Celite®. In the case of benzene, NMR spectroscopy typically indicated no further purification was necessary and it may be the case that the spent Grubbs catalyst is converted into an insoluble species at this stage. However, when toluene was used small amounts of benzaldehyde were produced and therefore, chromatographic purification became necessary.

In an attempt to move away from benzene and to obviate the formation of PhCHO as a side product when toluene was used, dichloromethane was considered. As Entries 3 and 4 indicate similar yields may be achieved using this solvent. However, longer reaction periods were required in order to achieve these comparable yields. The preparation of pyrrole **21** demonstrated compatibility with the nitro-containing nosyl protecting group (Entry 4).[9]

Based on the optimisation study described above the possibility of telescoping the RCM and the Mn-mediated oxidation was considered. As shown in Scheme 4 this proved to be feasible and the different phases could be performed sequentially in the same

reaction vessel. Entries 1 to 4 show that a range of different *N*-substituted diallyl compounds were subjected to RCM in DCM at room temperature with Grubbs catalyst **1**. On completion of metathesis, MnO_2 was added and the mixture was heated to reflux overnight. Good to excellent yields of the *N*-sulfonyl (**11**, **26**), amido (**27**) and phenyl (**7**) pyrrole products (Entries 1–4) were observed demonstrating the compatibility of this sequence with alternative *N*-substutents.

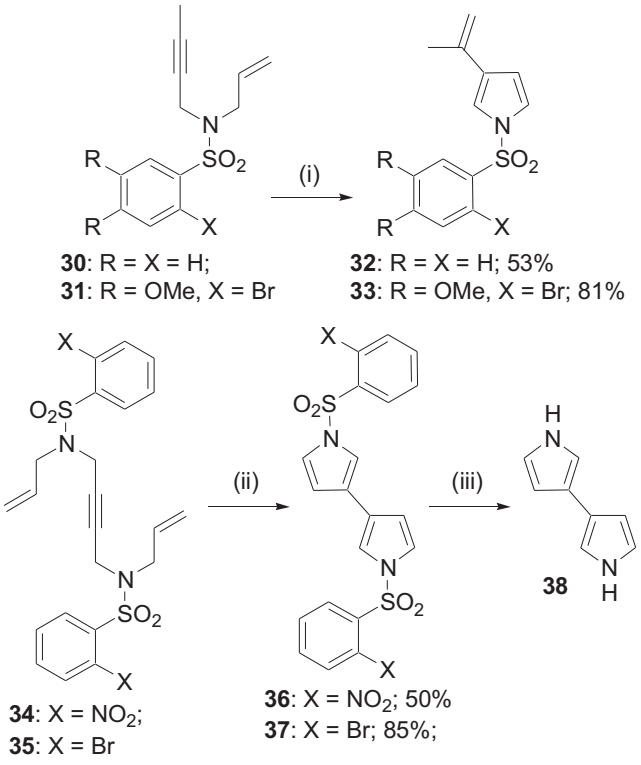


(i) **1** (3 mol%), DCM, rt, 1 h to 18 h; (ii) **3** (3 mol%), DCM, 40 °C, 3 - 15 h (or PhMe 80 °C); (iii) MnO_2 (20 equiv.), 40 °C, 18 h (or PhMe 110 °C).

Entry	Substrate	Product	R	R^1	Yield[a]
1	**8**	**11**	$ArSO_2$[b]	H	95%
2	**22**	**26**	$PhSO_2$	H	74%
3	**23**	**27**	Bz	H	91%
4	**6**	**7**	Ph	H	84%
5[c]	**24**	**28**	Ph	Me	68%
6[d]	**25**	**29**	$PhSO_2$	Ph	71%

[a]Isolated yields; [b]For structure see Scheme 2; [c]**3**, DCM, 40 °C, 15 h; [c]**3**, PhMe, 80 °C, 3 h.

Scheme 4. One-pot RCM-oxidation for the synthesis of substituted pyrroles.



(i) **1** (3 mol%), DCM, rt, 3 h; then MnO_2 (20 equiv.), 40 °C, 18-24 h;
(ii) **1** (3-5 mol%), DCM, rt, 1 h; then MnO_2 (30-42 equiv.), 40 °C, 24 h;
(iii) **36**, PhSH, K_2CO_3, DMF, rt, 24 h, 75%.

Scheme 5. One-pot enyne metathesis-oxidation for the synthesis of substituted pyrroles.

In order to prepare more densely substituted pyrroles the second generation Hoveyda Grubbs catalyst **3** was used at elevated temperature for the RCM reaction phase. Thus, in either DCM (Entry 5) or toluene (Entry 6) the 3-methyl and 3-phenyl substituted pyrroles **28** and **29** were ultimately accessed in acceptable yield.

Following the success of the alkene metathesis approach a conceptually similar enyne metathesis-oxidation sequence was investigated. As described in Scheme 5, alkynes **30** and **31** were initially treated with **1** in order to affect enyne metathesis, whereupon the in situ formed 3-substituted pyrrolines were then treated with MnO_2. In this manner, pyrroles **32** and **33** were synthesised in reasonable to good yield.[10] In an extension of this idea, alkynes **34** and **35**, synthesised by double propargylation using 1,4-dichlorobut-2-yne with the corresponding *N*-allyl sulfonamides,[11] were converted into bis-pyrroles **36** and **37**. To demonstrate the potential utility of this method, under standard conditions[9] the nosyl groups in compound **36** were cleaved in order to prepare bis-pyrrole **38**.[12]

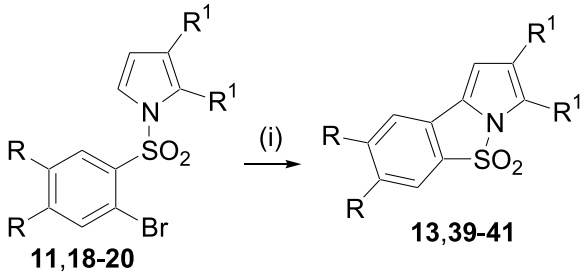
There are reports concerning the use of pyrroles in intramolecular Heck-type processes,[13] however, as a substrate class these systems have not been as widely studied as typical alkenes.[14,15] Mechanistically, it is likely that this type of substrate undergoes reaction via a pathway involving a C–H activation in the ring forming step as opposed to π-bond insertion (termed concerted metallation deprotonation pathway).[14] The IHR of several of the previously discussed 2-bromo-functionalised *N*-sulfonyl pyrroles was considered. In all cases, as shown in Scheme 6, under standard Heck-type conditions using $Pd(OAc)_2$ as a pre-catalyst, triphenylphosphine and potassium carbonate in DMF at elevated temperatures, average to good yields of the corresponding cyclic sulfonamides were obtained. In the case of the tetrasubstituted pyrrole **41**, a single crystal X-ray structure provided unequivocal structural confirmation.[16]

It is interesting to note that compound **18** has been reported to undergo a Suzuki-type reaction, demonstrating that, under the specified reaction conditions at least, this type of cross coupling proceeds at a faster rate than the intramolecular processes reported here.[17]

Following these positive results, bis-pyrrole **37** was subjected to identical conditions in the hope that a double, regioselective, intramolecular Heck-type process might occur. Unfortunately, this proved too ambitious and a complex reaction mixture was produced, which could not be simplified chromatographically.

3. Conclusion

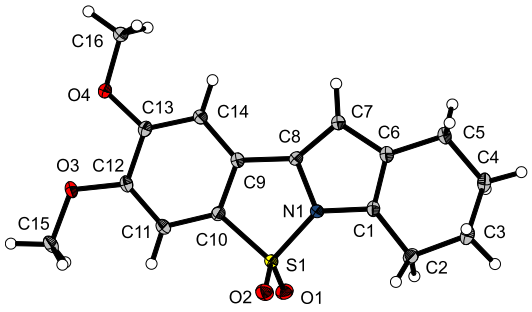
In summary, a protocol has been reported for the conversion of a range of dihydropyrroles into the corresponding pyrroles which relies on MnO_2 as the heterogeneous oxidant. In turn the dihydropyrroles were accessed by ring closing or enyne metathesis and the two processes can be performed in one reaction vessel if desired. In optimised cases yields obtained were good and the reactions cleanly proceeded to completion. Indeed in certain instances microanalytically pure material can be obtained by simple filtration suggesting that the remaining ruthenium catalyst may be absorbed by the heterogeneous manganese. Appropriately substituted *N*-sulfonyl pyrroles were converted into their parent pyrrole (e.g., **38**) and subjected to intramolecular Heck-type cyclisations demonstrating their potential further use.[7]



(i) $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), K_2CO_3, DMF, 110 °C.

Entry	Substrate	Product	R	R^1	Yield[a]
1	**11**	**13**	OMe	H	65%
2	**18**	**39**	H	H	79%
3	**19**	**40**	OCH_2O	H	38%
4	**20**	**41**	OMe	$(CH_2)_4$	75%

[a]Isolated yield following chromatographic purification



Scheme 6. Intramolecular Heck reaction of pyrrole-based sulfonamides **11**, **18**–**20** and single crystal X-ray crystallographic structure of **41** (Ortep plots to 50% probability).

4. Experimental

4.1. General directions

Reagents from commercial suppliers were used without further purification and anhydrous DMF, toluene (PhMe), cyclohexane (*c*-Hex) and DCM were purchased and used as such. Thin layer chromatography (TLC) was carried out on Merck silica gel aluminium sheets (60 F254). Merck silica gel (60, 0.040–0.063 mm) was used for the flash column chromatography. NMR spectra were recorded on Varian 300 MHz, 400 MHz, or 500 MHz spectrometers and calibrated using trimethylsilane (TMS). All values are reported in ppm. IR spectra were recorded on a Bruker Alpha FTIR spectrometer. High Resolution Mass Spectra (HRMS) were recorded using a Waters Crop, Micromass LCT, Electrospray Ionisation (ESI) spectrometer. Elemental analysis was performed at UCD. Melting Points were determined in an open capillary on a Gallenkamp melting point apparatus and are uncorrected. 2-Bromo-4,5-dimethoxybenzene-1-sulfonyl chloride,[5a] *N*-allyl-2-bromobenzenesulfonamide,[5e] *N*-allyl-2-bromo-4,5-dimethoxybenzenesulfonamide,[5e] *N*-allylaniline,[4f,18] *N*,*N*-diallylbenzene sulfonamide **22**,[19] *N*,*N*-diallylbenzamide **23**,[20] *N*,*N*-diallylaniline **6**,[4f] *N*-allyl-*N*-(2-methylallyl)aniline **24**,[4g] *N*-allylbenzenesulfonamide,[21] 6-bromobenzo[d]-[1,3]-dioxole-5-sulfonyl chloride,[22] 1-((2-nitrophenyl)sulfonyl)dihydropyrrole **17**,[23] 3-bromo-2-phenylprop-1-ene[5e] and *N*-allyl-2-nitrobenzene sulfonamide[5e] were all prepared according to literature.

4.2. General method for pyrrole formation

All one-pot reactions were carried out in the same solvent and consisted of two phases. Part one: The substrate was treated with either Grubbs first generation **1** (3–5 mol %), or Hoveyda-Grubbs second generation catalyst **3** (3–5 mol %) and monitored using TLC (and/or ^{1}H NMR spectroscopy) to ensure reactions were complete. Part two: MnO_2 (20 equiv) was added and the mixture heated to reflux. Commercial MnO_2 was stored at temperatures over 100 °C prior to use and was weighed and briefly cooled in air before addition. Following oxidation the mixture was cooled and filtered under vacuum through Celite®, washing with an appropriate solvent. Solvent removal under reduced pressure afforded the crude material which was purified by flash column chromatography where necessary.

4.2.1. 1-((2-Bromo-4,5-dimethoxyphenyl)sulfonyl)-1H-pyrrole 11 (MnO_2 method). 1-((2-Bromo-4,5-dimethoxyphenyl)sulfonyl)dihydropyrrole **9**[5a] (74 mg, 0.21 mmol, 1 equiv) was dissolved in PhH (5 mL). To this reaction mixture MnO_2 (370 mg, 4.25 mmol, 20 equiv) was added. Stirring was continued at reflux for 1 h. The reaction mixture was allowed to cool to room temperature and the insoluble MnO_2 was filtered under vacuum through Celite® and washed with DCM (2×10 mL). Following solvent removal under reduced pressure and purification by flash column chromatography (*c*-Hex-EtOAc; 4:1), **11** (73 mg, quant.) was isolated as a colourless crystalline solid. Mp 129–131 °C; R_f=0.30 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=2366, 2341, 1506, 1429, 1220, 1167, 1054, 755, 673, 615, 571 cm^{-1}; HRMS (ESI): calcd for $[(C_{12}H_{12}NO_4S^{79}Br+H)]^+$ 345.9749, found 345.9760; ^{1}H NMR (400 MHz, $CDCl_3$) 7.37 (1H, s, CH), 7.24–7.21 (2H, m, CH), 7.08 (1H, s, CH), 6.31–6.29 (2H, m, CH), 3.89 (3H, s, CH_3), 3.80 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ=153.2, 148.2, 129.9, 121.5, 117.7, 112.9, 112.7, 112.5, 56.6, 56.4 ppm; Anal. found (Calcd) for $C_{12}H_{12}BrNO_4S$: C, 41.71% (41.63%); H, 3.31% (3.49%); N, 3.88% (4.05%).

4.2.2. 1-((2-Bromo-4,5-dimethoxyphenyl)sulfonyl)-1H-pyrrole 11 (TBHP method). Under N_2 a solution of **8** (58 mg, 0.15 mmol, 1 equiv) in degassed benzene (1 mL) was treated at room temperature with **1** (6 mg, 0.07 mmol, 5 mol %). Stirring was continued for 45 min at which point TBHP, a 5.5 M solution in decane (60 μL, 0.33 mmol, 2 equiv) was added. Stirring was continued at room temperature for 18 h whereupon the mixture was purified by flash column chromatography (*c*-Hex-EtOAc; 3:1) which gave **11** (20 mg, 38%) as a colourless solid with data as above. Further elution gave the dihydropyrrole **9**[5a] (12 mg, 22%) and unsaturated lactam **12** (12 mg, 22%) as a viscous oil. Data for **12**: R_f=0.10 (*c*-Hex-EtOAc; 3:1) $\bar{\nu}_{max}$=3061, 2930, 2846, 1722, 1585, 1502, 1438, 1363, 1335, 1262, 1154, 1019, 732 cm^{-1}; HRMS (ESI): calcd for $[(C_{12}H_{12}NO_5S^{79}Br+Na)]^+$ 383.9517, found 383.9533; ^{1}H NMR (400 MHz, $CDCl_3$) 7.82 (1H, s, CH), 7.34 (1H, dt, *J*=6.0, 2.0 Hz, CH), 7.06 (1H, s, CH), 6.05 (1H, dt, *J*=6.0, 2.0 Hz, CH), 4.79 (2H, t, *J*=2.0 Hz, CH_2), 3.97 (3H, s, CH_3), 3.86 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 169.9, 153.4, 147.9, 147.1, 129.0, 126.6, 116.9, 115.9, 111.8, 56.6, 56.55, 53.1 ppm.

4.2.3. 1-((2-Bromophenyl)sulfonyl)-1H-pyrrole 18. [13b]Dihydropyrrole **14**[5a] (25 mg, 0.087 mmol, 1 equiv) was dissolved in PhH (5 mL). To this reaction mixture MnO_2 (153 mg, 1.76 mmol, 20 equiv) was added. Stirring was continued at reflux for 18 h and as described above the reaction mixture was allowed to cool to room temperature, filtered and washed with DCM (2×20 mL). Solvent removal under reduced pressure gave **18** (22 mg, 90%) as colourless crystalline solid. Mp 90–93 °C (lit.[13b] mp 83–85 °C); R_f=0.45 (*c*-Hex-EtOAc, 12:1); ^{1}H NMR (400 MHz, $CDCl_3$) 7.76–7.71 (2H, m, CH), 7.47–7.40 (2H, m, CH), 7.24–7.23 (2H, m, CH), 6.34–6.33 (2H, m, CH) ppm; ^{13}C

NMR (100 MHz, $CDCl_3$) 138.9, 136.9, 134.6, 130.3, 127.9, 121.7, 120.3, 113.0 ppm.

4.2.4. 1-[(6-Bromobenzo[d]-[1,3]-dioxol-5-yl)sulfonyl]-2,5-dihydro-1H-pyrrole 15. At 0 °C a solution of 6-bromobenzo[d]-[1,3]-dioxole-5-sulfonyl chloride[22] (1.232 g, 4.114 mmol, 1 equiv) in DCM (40 mL) was treated sequentially with Et_3N (0.86 mL, 6.17 mmol, 1.5 equiv) and then diallylamine (0.61 mL, 4.94 mmol, 1.25 equiv). The mixture was stirred for 18 h during which time room temperature was reached. H_2O (25 mL) was added followed by 1 M HCl (25 mL). The resultant aqueous layer was further extracted with DCM (2×20 mL) and the combined organic layers were dried over $MgSO_4$. Filtration, solvent removal under reduced pressure and purification by flash column chromatography (*c*-Hex-EtOAc; 5:1) gave *N,N*-diallyl-6-bromobenzo[d]-[1,3]-dioxole-5-sulfonamide (1.09 g, 74%) as a viscous oil [R_f=0.40 (*c*-Hex-EtOAc; 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) 7.61 (1H, s, CH), 7.12 (1H, s, CH), 6.10 (2H, s, CH_2), 5.72–5.63 (2H, m, CH), 5.20–5.14 (4H, m, CH_2), 4.21 (4H, s, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 151.9, 147.2, 132.6, 119.1, 114.9, 113.2, 112.1, 106.1, 102.9, 49.0 ppm]. *N,N*-Diallyl-6-bromobenzo[d]-[1,3]-dioxole-5-sulfonamide (510 mg, 1.42 mmol, 1 equiv) in degassed DCM (15 mL) was treated with **1** (58 mg, 0.070 mmol, 5 mol %). Stirring was continued at rt for 15 h. Silica gel (ca. 1 g) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (*c*-Hex-EtOAc; 6:1 to 4:1) gave **15** (470 mg, quant.) as a colourless solid. Mp=111 °C; R_f=0.35 (*c*-Hex-EtOAc; 2:1); $\bar{\nu}_{max}$=3101, 3054, 2915, 2868, 1611, 1504, 1489, 1327, 1243, 1165, 1149, 1094, 1034, 922 cm^{-1}; HRMS (ESI): calcd for $[(C_{11}H_{10}NO_4S^{79}Br+H)]^+$ 331.9592, found 331.9580; ^{1}H NMR (400 MHz, $CDCl_3$) 7.59 (1H, s, CH), 7.12 (1H, s, CH), 6.06 (2H, s, CH_2), 5.77 (2H, s(br), CH), 4.21 (4H, s, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 151.3, 147.0, 131.8, 125.1, 115.0, 113.1, 111.6, 102.9, 54.8 ppm; Anal. found (Calcd) for $C_{11}H_{10}BrNO_4S$: C, 39.73% (39.76%); H, 2.94% (3.01%); N, 4.09% (4.22%).

4.2.5. 1-((3,4-Dioxolophenyl)sulfonyl)-1H-pyrrole 19. A solution of **15** (77 mg, 0.23 mmol, 1 equiv) in benzene (5 mL) was treated with MnO_2 (405 mg, 4.66 mmol, 20 equiv). The mixture was heated to reflux with stirring for 3 h. On cooling the mixture was filtered through Celite® and the residue washed with DCM (2×10 mL). The solvent was removed under reduced pressure to give **19** (68 mg, 89%) as a colourless crystalline solid. Mp=154–156 °C; R_f=0.30 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=3152, 3112, 3009, 2959, 2918, 2853, 1608, 1503, 1479, 1371, 1353, 1249, 1189, 1145, 1057, 1026, 734 cm^{-1}; HRMS (EI): calcd for $[(C_{11}H_8NO_4S^{79}Br)]^+$ 328.9357, found 328.9371; ^{1}H NMR (400 MHz, $CDCl_3$) 7.34 (1H, s, CH), 7.19 (2H, t, *J*=2.5 Hz, CH), 7.09 (1H, s, CH), 6.27 (2H, t, *J*=2.5 Hz, CH), 6.07 (2H, s, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 152.4, 147.5, 131.6, 121.4, 115.4, 113.9, 112.8, 110.4, 103.2 ppm.

4.2.6. 1-((2-Bromo-4,5-dimethoxyphenyl)sulfonyl)-4,5,6,7-tetrahydro-1H-indole 20. According to the procedure described above, a solution of **16**[5c] (195 mg, 0.485 mmol, 1 equiv) in DCM (15 mL) was treated with MnO_2 (854 mg, 9.82 mmol, 20 equiv) at reflux for 18 h. On cooling the mixture was filtered through Celite®, washing with DCM (2×10 mL). Following solvent removal the crude product was purified by gradient elution flash column chromatography (*c*-Hex-EtOAc; 9:1 to 3:1) to afford **20** (134 mg, 69%) as a colourless viscous oil. R_f=0.25 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=3090, 3061, 3011, 2934, 2845, 1585, 1503, 1437, 1364, 1261, 1215, 1164, 1117, 1020 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{18}NO_4S^{79}Br+H)]^+$ 400.0218, found 400.0226; ^{1}H NMR (400 MHz, $CDCl_3$) 7.31 (1H, d, *J*=Hz, CH), 7.17 (1H, s, CH), 7.10 (1H, s, CH), 6.04 (1H, d, *J*=Hz, CH), 3.95 (3H, s, CH_3), 3.82 (3H, s, CH_3), 2.49–2.46 (2H, m, CH_2), 2.44–2.41 (2H, m, CH_2), 1.75–1.57 (4H, m, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 152.9, 147.9, 130.7, 129.3, 123.2, 122.5, 117.6, 112.7, 112.3, 110.9, 56.6, 56.4, 23.1, 22.9, 22.85, 22.6 ppm.

4.2.7. 1-((2-Nitrophenyl)sulfonyl)-1H-pyrrole 21.[24] The requisite dihydropyrrole **17**[23] (0.55 g, 1.9 mmol, 1 equiv) in DCM (20 mL) was treated with MnO_2 (5.60 g, 64.9 mmol, 30 equiv) and stirring was continued at reflux for 24 h. The reaction mixture was allowed to cool to room temperature and the insoluble MnO_2 was filtered through Celite®, washed with DCM (2×20 mL) and the product **21** (0.48 g, 98%) was isolated as a colourless solid following solvent removal under reduced pressure. Mp 85 °C; R_f=0.30 (*c*-Hex-EtOAc, 3:1); $\bar{\nu}_{max}$=3142, 3088, 2917, 2849, 1541, 1376, 1173, 1061, 751, 585 cm^{-1}; HRMS (EI): calcd for $[(C_{10}H_8N_2O_4S)]^+$ 252.0205, found 252.0211; ^{1}H NMR (400 MHz, $CDCl_3$) 7.61–7.26 (4H, m, CH), 7.23 (2H, dd, *J*=5.0, 2.5 Hz, CH), 6.38–6.37 (2H, m, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 147.6, 134.9, 134.8, 132.5, 129.5, 124.8, 121.7, 113.8 ppm.

4.2.8. 1-Benzenesulfonyl-1H-pyrrole 26.[25] Under a nitrogen atmosphere, *N,N*-diallylbenzene sulfonamide **22**[21] (660 mg, 2.78 mmol, 1 equiv) was dissolved in DCM (30 mL). Grubbs catalyst **1** (69.5 mg, 0.084 mmol, 3.0 mol %) was added and the reaction was stirred at room temperature for 3 h. MnO_2 (6.09 g, 70.0 mmol, 25 equiv) was then added to the reaction flask and heated to reflux with stirring for 18 h. On cooling the contents of the reaction were filtered through Celite® and washed with DCM (2×20 mL). The filtrate was concentrated under reduced pressure and purified by flash column chromatography (*c*-Hex-EtOAc; 6:1) which gave **26** (426 mg, 74%) as a pale yellow solid. Mp=86–88 °C (lit.[25] mp=87–88 °C); R_f=0.50 (*c*-Hex-EtOAc; 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) 7.87–7.84 (2H, m, CH) 7.61–7.57 (1H, m, CH), 7.52–7.48 (2H, m, CH), 7.17–7.16 (2H, m, CH), 6.31–629 (2H, m, CH), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 139.1, 133.7, 129.3, 126.7, 120.8, 113.6 ppm; Anal. found (Calcd) for $C_{10}H_9NO_2S$: C, 57.76% (57.95%); H, 4.07% (4.38%); N, 6.91% (6.76%).

4.2.9. Phenylpyrrol-1-yl-methanone 27.[4g] As described above, under a nitrogen atmosphere, *N,N*-diallylbenzamide **22**[20] (315 mg, 1.57 mmol, 1 equiv) was dissolved in DCM (15 mL). Grubbs catalyst **1** (38.5 mg, 0.047 mmol, 3.0 mol %) was added to the reaction vessel. The reaction flask was stirred at room temperature for 2.5 h before MnO_2 (3.80 g, 43.7 mmol, 28 equiv) was added and the reaction mixture was heated to reflux for 18 h. The contents of the reaction vessel were filtered through Celite®, concentrated under reduced pressure and purified using column chromatography (*c*-Hex-EtOAc; 6:1) to yield **27** (244 mg, 91%) as a yellow oil. R_f=0.45 (*c*-Hex-EtOAc; 6:1); HRMS (EI): calcd for $C_{11}H_9NO$ 171.0684, found 171.0683; ^{1}H NMR (400 MHz, $CDCl_3$) 7.76–7.74 (2H, m, CH) 7.62–7.58 (1H, m, CH), 7.53–7.49 (2H, m, CH), 7.28 (2H, s, CH), 6.35 (2H, s, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 167.7, 133.2, 132.2, 129.5, 128.4, 121.3, 113.1 ppm.

4.2.10. 1-Phenyl-1H-pyrrole 7.[4g] Under a nitrogen atmosphere *N,N*-diallylaniline **6**[4f] (120 mg, 0.694 mmol, 1 equiv) was dissolved in DCM (15 mL). Grubbs catalyst **1** (17.3 mg, 0.021 mmol, 3.0 mol %) was added to the reaction flask. The mixture was stirred at room temperature for 3 h before MnO_2 (1.22 g, 14.0 mol, 20 equiv) was added. The reaction was heated to reflux and stirred for 18 h. On cooling the resultant mixture was filtered through Celite® and washed with DCM (2×10 mL). The crude product, obtained after solvent removal under reduced pressure, was purified by flash column chromatography (*c*-Hex-EtOAc; 6:1) which gave **7** (83 mg, 84%) as a yellow solid. Mp=59–60 °C (lit.[4g] mp=59–60 °C); R_f=0.65 (*c*-Hex-EtOAc; 6:1); HRMS (EI): calcd for $C_{10}H_9N$ 143.0735, found 143.0728; ^{1}H NMR (400 MHz, $CDCl_3$) 7.45–7.39 (4H, m, CH)

7.27–7.23 (1H, m, CH), 7.10 (2H, s, CH), 6.35 (2H, s, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 140.8, 129.5, 125.6, 120.5, 119.3, 110.3 ppm.

4.2.11. 3-Methyl-1-phenyl-1H-pyrrole 28. [4g]As above, under N_2 a degassed solution of compound **24** (75 mg, 0.41 mmol, 1 equiv) in anhydrous DCM (8 mL) was treated with Hoveyda-Grubbs catalyst **3** (12.5 mg, 0.02 mmol, 5.0 mol %). Stirring was continued at reflux for 15 h. On cooling MnO_2 (695 mg, 7.99 mmol, 20 equiv) was added and stirring was continued at reflux for 18 h. The reaction mixture was allowed to cool to room temperature, filtered through Celite® and washed with DCM (2×20 mL). Following solvent removal under reduced pressure purification was performed by flash column chromatography (*c*-Hex-EtOAc; 19:1) which gave **28** (44 mg, 68%) as a colourless solid. Mp 50–52 °C (lit.[4g] mp 46–49 °C); R_f=0.60 (*c*-Hex-EtOAc; 12:1); ^{1}H NMR (400 MHz, $CDCl_3$) 7.42–7.35 (4H, m, CH), 7.21 (1H, t, *J*=7.0 Hz, CH), 7.00 (1H, s, CH), 6.88 (1H, s, CH), 6.19 (1H, s, CH), 2.18 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 140.7, 129.4, 125.1, 121.1, 119.9, 118.9, 117.1, 111.9, 12.0 ppm.

4.2.12. N-Allyl-N-(2-phenylallyl)benzene sulfonamide 25. [26]*N*-Allylbenzene sulfonamide[21] (500 mg, 2.53 mmol, 1 equiv) was dissolved in DMF (25 mL) and cooled to 0 °C. Sodium hydride, 60% w/w in mineral oil (130 mg, 3.25 mmol, 1.3 equiv), was added and the mixture was stirred for 0.5 h. 3-Bromo-2-phenylprop-1-ene[5e] (820 mg, 4.16 mmol, 1.65 equiv) was added in a dropwise fashion and the reaction mixture was stirred for 3 h during which period room temperature was reached. Et_2O (30 mL) and H_2O (30 mL) were added and the phases were separated. The resultant aqueous phase was further extracted with Et_2O (2×30 mL) and the combined ethereal extracts were dried over $MgSO_4$. The crude product, obtained after filtration and solvent removal, was purified by column chromatography (*c*-Hex-EtOAc; 6:1) which gave **25** (0.45 g, 57%) as a viscous yellow oil. R_f=0.40 (*c*-Hex-EtOAc; 6:1); ^{1}H NMR (300 MHz; $CDCl_3$) 7.75 (2H, dd, 2H, *J*=8.5, 1.25 Hz, CH), 7.25–7.47 (8H, m, CH), 5.52–5.38 (1H, m, CH), 5.43 (1H, s, CH_2), 5.21 (1H, s, CH_2), 5.06 (1H, d, *J*=10.0 Hz, CH_2), 5.04 (1H, d, *J*=16.0 Hz, CH_2), 4.24 (2H, s, CH_2), 3.73 (2H, d, *J*=6.5 Hz, CH_2) ppm; ^{13}C NMR (100 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.

4.2.13. 3-Phenyl-1-(phenylsulfonyl)-1H-pyrrole 29. [6c]Under N_2 a degassed solution of compound **25** (330 mg, 1.05 mmol, 1 equiv) in anhydrous toluene (25 mL) was treated with Hoveyda-Grubbs catalyst **3** (33 mg, 0.053 mmol, 5.0 mol %). Stirring was continued at 80 °C for 3 h after which time MnO_2 (520 mg, 5.98 mmol, 5 equiv) was added and stirring was continued at reflux for 15 h. The reaction mixture was allowed to cool to room temperature and filtered through Celite®. The residue was washed with PhMe (2×20 mL). Solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (*c*-Hex-EtOAc; 4:1) to afford **25** (210 mg, 71%) as a waxy solid. R_f=0.30 (*c*-Hex-EtOAc; 4:1); $\bar{\nu}_{max}$=3063, 2923, 2853, 1729, 1447, 1364, 1364, 1170, 1129, 1061, 753, 724, 683, 586 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.92 (2H, dd, *J*=8.5, 1.25 Hz, CH), 7.65–7.35 (8H, m, CH), 7.25–7.23 (2H, m, CH), 6.64 (1H, dd, *J*=3.0, 1.75 Hz, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 139.1, 134.1, 134.0, 130.0, 129.6, 128.9, 127.5, 127.0, 125.7, 121.8, 116.5, 112.5 ppm.

4.2.14. N-Allyl-N-(but-2-yn-1-yl)benzene sulfonamide 30. N-Allylbenzene sulfonamide[21] (690 mg, 3.50 mmol, 1 equiv) was dissolved in DMF (40 mL) and cooled to 0 °C. Sodium hydride 60% w/w in mineral oil (180 mg, 4.50 mmol, 1.3 equiv) was added and the mixture was stirred for 0.5 h. 1-Bromobut-2-yne (0.5 mL, 5.6 mmol, 1.6 equiv) was added in a dropwise fashion. Stirring was continued for 2 h during which period room temperature was reached. Et_2O (30 mL) and H_2O (30 mL) were added and the phases were separated. The resultant aqueous phase was further extracted with Et_2O (3×15 mL). The combined ethereal extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Further purification by flash column chromatography (*c*-Hex-EtOAc; 3:1) gave **30** (0.835 g, 96%) as a waxy solid. R_f=0.55 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=3067, 2920, 2296, 2227, 1703, 1479, 1329, 1157, 1090, 996, 720, 552 cm^{-1}; HRMS (EI): calcd for $[(C_{13}H_{15}NO_2S)]^+$ 248.0745, found 248.0742; ^{1}H NMR (300 MHz, $CDCl_3$) 7.87–7.84 (2H, m, CH), 7.60–7.47 (3H, m, CH), 5.78–5.69 (1H, m, CH), 5.30–5.23 (2H, m, CH_2), 4.04 (2H, q, *J*=2.5 Hz, CH_2), 3.80 (2H, d, *J*=6.5 Hz, CH_2), 1.52 (3H, t, *J*=2.5 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=139.2, 132.4, 132.1, 128.6, 127.8, 119.6, 81.9, 77.3, 49.0, 36.3, 3.2 ppm.

4.2.15. 1-(Phenylsulfonyl)-3-(prop-1-en-2-yl)-1H-pyrrole 32. [27]Under N_2 a degassed solution of compound **30** (700 mg, 2.81 mmol, 1 equiv) in anhydrous DCM (35 mL) was treated with **1** (76 mg, 0.092 mmol, 3.0 mol %). Stirring was continued at room temperature for 3 h. To this reaction mixture MnO_2 (8.03 g, 92.3 mmol, 33 equiv) was added. Stirring was continued at reflux for 24 h. The reaction mixture was allowed to cool to room temperature and filtered through Celite® and washed with DCM (2×30 mL). The crude material was purified by flash column chromatography (*c*-Hex-EtOAc; 3:1) which gave **32** (370 mg, 53%) as a waxy pale yellow solid. R_f=0.55 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=3140, 3067, 2922, 1584, 1447, 1365, 1171, 1059, 754, 724, 624 cm^{-1}; HRMS (EI): calcd for $[(C_{13}H_{13}NO_2S)]^+$ 247.0667, found 247.0663; ^{1}H NMR (300 MHz, $CDCl_3$) 7.85 (2H, d, *J*=8.0 Hz, CH), 7.59–7.47 (3H, m, CH), 7.13–7.11 (2H, m, CH), 6.47–6.45 (1H, m, CH), 5.22 (1H, s, CH_2), 4.91 (1H, s, CH_2), 1.99 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 138.9, 135.8, 133.8, 129.7, 129.3, 126.7, 121.4, 116.9, 111.4, 110.9, 27.3 ppm.

4.2.16. N-Allyl-2-bromo-N-(but-2-yn-1-yl)-4,5-dimethoxybenzene sulfonamide 31. N-Allyl-2-bromo-4,5-dimethoxybenzene sulfonamide[5e] (300 mg, 0.89 mmol, 1 equiv) was dissolved in DMF (15 mL) and cooled to 0 °C. Sodium hydride, 60% w/w in mineral oil (46 mg, 1.2 mmol, 1.3 equiv) was added and the mixture was stirred for 0.5 h. 1-Bromobut-2-yne (0.13 mL, 1.5 mmol, 1.65 equiv) was added in a dropwise fashion and stirring was continued for 2 h. Over this period room temperature was reached and Et_2O (25 mL) and H_2O (25 mL) were added. The resultant aqueous phase was further extracted with Et_2O (3×10 mL) and the combined ethereal extracts were dried over $MgSO_4$. The crude product, obtained after filtration and solvent removal, was purified by column chromatography (*c*-Hex-EtOAc; 5:1) which gave **31** (327 mg, 94%) as a colourless oil. R_f=0.20 (*c*-Hex/EtOAc; 2:1); $\bar{\nu}_{max}$=3087, 3008, 2921, 2845,1585, 1503, 1462, 1439, 1361, 1262, 1023, 597; HRMS (ESI): calcd for $[(C_{15}H_{18}NO_4S^{79}Br+Na)]^+$ 410.0042 found 410.0038; ^{1}H NMR (500 MHz, $CDCl_3$): 7.61 (1H, s, CH), 7.13 (1H, s, CH), 5.68–5.73 (1H, m, CH), 5.28 (1H, dd, *J*=17.0, 1.5 Hz, CH_2), 5.22 (1H, dd, *J*=10.5, 1.5 Hz, CH_2), 4.04 (2H, q, *J*=2.5 Hz, CH_2), 4.00 (2H, d, *J*=6.5 Hz, CH_2), 3.87 (3H, s, CH_3), 3.85 (3H, s, CH_3), 1.71 (3H, t, *J*=2.5 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 152.2, 147.7, 132.3, 130.8, 119.5, 117.4, 114.6, 112.2, 81.0, 72.5, 56.5, 56.4, 49.2, 36.2, 3.5 ppm.

4.2.17. 1-((2-Bromo-4,5-dimethoxyphenyl)sulfonyl)-3-(prop-1-en-2-yl)-1H-pyrrole 33. Under N_2 a degassed solution of **31** (300 mg, 0.772 mmol, 1 equiv) in anhydrous DCM (15 mL) was treated with **1** (19 mg, 0.023 mmol, 3 mol %). Stirring was continued at room temperature for 3 h. To this reaction mixture MnO_2 (1.16 g, 13.1 mmol, 20 equiv) was added and stirring was continued at reflux for 18 h. The reaction mixture was allowed to cool to room temperature and filtered through Celite® washing with DCM (2×20 mL). The crude material obtained following solvent removal under reduced pressure was purified by flash column chromatography (*c*-Hex-EtOAc; 4:1) and recrystallization dissolving in DCM followed by layering with *c*-Hex which gave **33** (240 mg, 81%) as a colourless crystalline solid. Mp 93–95 °C (DCM); R_f=0.35 (*c*-Hex-

EtOAc; 2:1); $\bar{\nu}_{max}$=2987, 2968, 2921, 1505, 1369, 1256, 1165, 1065, 795, 673, 603 cm^{-1}; HRMS (ESI): calcd for $[(C_{15}H_{16}NO_4S^{79}Br+Na)]^+$ 407.9881, found 407.9900; ^1H NMR (500 MHz, $CDCl_3$) 7.45 (1H, s, CH), 7.15–7.19 (2H, m, CH), 7.13 (1H, s, CH), 6.47 (1H, d, *J*=3.5 Hz, CH), 5.23 (1H, s(br), CH_2), 4.94–4.91 (1H, m, CH_2), 3.87 (3H, s, CH_3), 3.85 (3H, s, CH_3), 2.00 (3H, d, *J*=1.0 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 153.3, 148.2, 136.0, 129.8, 129.6, 122.2, 117.7, 117.5, 113.0, 112.5, 110.8, 110.4, 56.6, 56.4, 21.0 ppm.

4.2.18. N,N′-(but-2-yn-1,4-diyl)-bis-(N-allyl-2-nitrobenzenesulfonamide) 34. *N*-Allyl-2-nitrobenzene sulfonamide[5e] (700 mg, 2.89 mmol, 2.5 equiv) was dissolved in MeCN (30 mL) before K_2CO_3 (600 mg, 4.34 mmol, 4 equiv) and 1,4-dichlorobutyne (0.11 mL, 1.1 mmol, 1 equiv) were added. The reaction mixture was heated to reflux for 48 h. On cooling to room temperature EtOAc (40 mL) and H_2O (40 mL) were added. The resultant aqueous phase was further extracted with EtOAc (3×15 mL) and the combined organic phases were dried over $MgSO_4$. After filtration and solvent removal the crude product was purified by flash column chromatography (*c*-Hex-EtOAc; 3:1) which gave **34** (580 mg, 97%) as a yellow oil. R_f=0.40 (*c*-Hex-EtOAc; 1:1); $\bar{\nu}_{max}$=3142, 3086, 2979, 2921, 1739, 1575, 1423, 1329, 1156, 1057, 930, 897, 755, 565 cm^{-1}; HRMS (EI): calcd for $[(C_{22}H_{22}N_4O_8S_2)]^+$ 534.0879, found 534.0880; ^1H NMR (400 MHz, $CDCl_3$) 8.00–7.97 (2H, m, CH), 7.71–7.67 (4H, m, CH), 7.64–7.61 (2H, m, CH), 5.61 (2H, ddt, *J*=16.5, 10.0, 6.5 Hz, CH), 5.22–5.17 (4H, m, CH_2), 4.01 (4H, s, CH_2), 3.86 (4H, d, *J*=6.5 Hz, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 148.0, 133.9, 132.8, 131.9, 131.4, 130.8, 124.0, 119.7, 78.5, 49.4, 35.8 ppm.

4.2.19. 1,1′-Bis-((2-nitrophenyl)sulfonyl)-1H,1′H-3,3′-bipyrrole 36. Under N_2 a degassed solution of compound **34** (400 mg, 0.749 mmol, 1 equiv) in anhydrous DCM (8 mL) was treated with **1** (18 mg, 0.022 mmol, 3 mol %). Stirring was continued at room temperature for 1 h before MnO_2 (1.40 g, 16.1 mmol, 20 equiv) was added and the reaction mixture was heated to reflux for 12 h. An additional portion of MnO_2 (0.70 g, 8.1 mmol, 10 equiv) was added and stirring at reflux was continued for 12 h. The reaction mixture was allowed to cool to room temperature and filtered through Celite®. The residue was washed with DCM (2×20 mL) and solvent removal under reduced pressure gave the crude product. Purification by flash column chromatography (*c*-Hex-EtOAc; 1:1) gave **36** (188 mg, 50%) as a pale brown solid. R_f=0.30 (*c*-Hex-EtOAc; 1:1); $\bar{\nu}_{max}$=3131, 2852, 1733, 1592, 1439, 1370, 1352, 1230, 1155, 1040, 851, 656 cm^{-1}; HRMS (EI): calcd for $[(C_{20}H_{14}N_4O_8S_2)]^+$ 502.0253, found 502.0301; ^1H NMR (400 MHz, $CDCl_3$): 7.77–7.66 (8H, m, CH), 7.34 (2H, t, *J*=1.5 Hz, CH), 7.25–7.23 (2H, m, CH), 6.51 (2H, dd, *J*=3.5, 1.5 Hz, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 148.0, 135.2, 132.8, 132.6, 129.9, 124.9, 122.7, 119.6, 117.3, 112.3 ppm.

4.2.20. 1H,1′H-3,3′-bis-pyrrole 38. [12a]At room temperature a mixture of compound **36** (56 mg, 0.11 mmol, 1 equiv) and K_2CO_3 (50 mg, 0.36 mmol, 3.3 equiv) in DMF (5 mL) was treated with PhSH (14 μL, 0.14 mmol, 1.3 equiv). Stirring was continued at room temperature for 24 h whereupon EtOAc (8 mL) and water (10 mL) were added. The resultant aqueous layer was further extracted with EtOAc (5×8 mL) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal and column chromatography (*c*-Hex-EtOAc; 2:1) afforded **38** (11 mg, 75%) as an amorphous yellow solid with data matching literature.[12a] R_f=0.45 (*c*-Hex/EtOAc; 2:1); $\bar{\nu}_{max}$=3344, 3281, 2923, 1672, 1637, 1075, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.12 (2H, s, NH), 6.93–6.92 (2H, m, CH), 6.81–6.79 (2H, m, CH) 6.41–6.39 (2H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) 119.6, 118, 113.2, 106.7 ppm.

4.2.21. N,N′-(but-2-yn-1,4-diyl)-bis-(N-allyl-2-bromobenzenesulfonamide) 35. *N*-Allyl-2-bromobenzene sulfonamide[5e] (1.00 g, 3.62 mmol, 2.5 equiv) was dissolved in MeCN (40 mL), and 1,4-dichlorobutyne (0.14 mL, 1.4 mmol, 1 equiv) was added in a dropwise fashion along with K_2CO_3 (2.00 g, 14.5 mmol, 4 equiv). The reaction mixture was heated to reflux for 48 h, cooled to room temperature and EtOAc (40 mL) and H_2O (40 mL) were added. The resultant aqueous phase was further extracted with EtOAc (3×15 mL). The combined organic phases were dried over $MgSO_4$. The crude product, obtained after filtration and solvent removal, was purified by flash column chromatography (*c*-Hex-EtOAc; 4:1) which gave **35** (0.80 g, 93%) as a yellow oil. R_f=0.40 (*c*-Hex-EtOAc; 4:1); $\bar{\nu}_{max}$=3086, 2980, 2921, 1739, 1574, 1423, 1329, 1156, 1057, 930, 897, 755, 565 cm^{-1}; HRMS (ESI): calcd for $[(C_{22}H_{22}N_2O_4S_2^{79}Br_2+Na)]^+$ 622.9285, found 622.9282; ^1H NMR (300 MHz, $CDCl_3$) 8.12 (2H, d, *J*=8.5, Hz, CH), 7.73 (2H, d, *J*=8.5 Hz, CH), 7.47–7.37 (4H, m, CH), 5.69–5.61 (2H, m, CH), 5.28–5.20 (4H, m, CH_2), 4.06 (4H, s, CH_2), 3.93 (4H, dd, *J*=1.5, 6.5 Hz, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 138.9, 135.6, 133.7, 132.2, 131.8, 127.6, 120.5, 120.0, 78.7, 49.3, 35.9.

4.2.22. 1,1′-Bis-((2-bromophenyl)sulfonyl)-1H,1′H-3,3′-bipyrrole 37. Under N_2, a degassed solution of compound **35** (100 mg, 0.166 mmol, 1 equiv) in anhydrous DCM (5 mL) was treated with **1** (6.8 mg, 0.008 mmol, 5 mol %). Stirring was continued at room temperature for 1 h before MnO_2 (300 mg, 3.45 mmol, 21 equiv) was added. The reaction mixture was stirred and heated to reflux for 12 h. At this stage a further portion of MnO_2 (300 mg, 3.45 mmol, 21 equiv) was added and the mixture was further heated to reflux for 12 h. The reaction mixture was allowed to cool to room temperature filtered through Celite® and washed with DCM (2×20 mL). Solvent removal under reduced pressure and purification by flash column chromatography (*c*-Hex-EtOAc; 3:1) gave **37** (81 mg, 85%) as a colourless crystalline solid. Mp 227–230 °C; R_f=0.30 (*c*-Hex-EtOAc; 2:1); $\bar{\nu}_{max}$=1178, 1155, 1070, 1043, 766, 738, 699, 651, 606, 585 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 7.86 (2H, dd, *J*=7.5, 2.0 Hz, CH), 7.74–7.71 (2H, m, CH), 7.48–7.42 (4H, m, CH), 7.29 (2H, s, CH), 7.25 (2H, d, *J*=2.5, Hz, CH), 6.43 (2H, dd, *J*=3.0, 1.5 Hz, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 138.6, 136.0, 134.8, 130.6, 128.1, 122.8, 121.9, 120.4, 117.0, 115.0 ppm; Anal. found (Calcd) for $C_{20}H_{14}Br_2N_2O_4S_2$: C, 41.40 (42.12); H, 2.47 (2.47); N, 4.88 (4.91).

4.2.23. 7,8-Dimethoxybenzo-[d]-pyrrolo-[1,2-b]-isothiazole 5,5-dioxide 13. Under N_2 a mixture of **11** (200 mg, 0.578 mmol, 1 equiv), $Pd(OAc)_2$ (13 mg, 0.058 mmol, 10 mol %), PPh_3 (30.3 mg, 0.116 mmol, 20 mol %) and K_2CO_3 (160 mg, 1.16 mmol, 2 equiv) in anhydrous DMF (8 mL) was heated to 110 °C for 15 h. The reaction mixture was cooled and EtOAc (10 mL) and H_2O (10 mL) were added. The resultant aqueous layer was further extracted with EtOAc (5×10 mL) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (*c*-Hex-EtOAc; 2:1) which afforded **13** (100 mg, 65%) as a colourless crystalline solid. Mp=170–173 °C; R_f=0.30 (*c*-Hex-EtOAc; 2:1); $\bar{\nu}_{max}$=3108, 2962, 2849, 1606, 1495, 1441, 1321, 1240, 1159, 1038, 844, 714, 621, 584 cm^{-1}; HRMS (ESI): calcd for $[(C_{12}H_{11}NO_4S+H)]^+$ 266.0487, found 266.0495; ^1H NMR (400 MHz, $CDCl_3$) 7.18 (1H, s, CH), 7.10 (1H, dd, *J*=3.0, 1.0 Hz, CH), 6.96 (1H, s, CH), 6.38–6.35 (2H, m, CH), 3.99 (3H, s, CH_3), 3.94 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 154.1, 149.1, 129.3, 128.2, 122.4, 116.8, 116.1, 104.6, 104.0, 102.9, 56.5, 56.4 ppm.

4.2.24. Benzo-[d]-pyrrolo-[1,2-b]-isothiazole 5,5-dioxide 39. [13b]Following the procedure described above: Under N_2, **18** (144 mg, 0.503 mmol, 1 equiv), $Pd(OAc)_2$ (11.6 mg, 0.052 mmol, 10 mol %), PPh_3 (27.2 mg, 0.104 mmol, 20 mol %) and K_2CO_3 (143 mg, 1.04 mmol, 2 equiv) in anhydrous DMF (8 mL) were heated at 110 °C for 15 h. On cooling EtOAc (10 mL) and H_2O (10 mL) were added. The resultant aqueous layer was further extracted with EtOAc

(5×10 mL) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (*c*-Hex-EtOAc; 6:1) afforded **37** (82 mg, 79%) as a colourless solid. Mp 133–135 °C (lit.[13b] mp=98–100 °C). R_f=0.30 (*c*-Hex-EtOAc, 6:1); $\bar{\nu}_{max}$=2961, 2922, 2141, 2118, 1457, 1322, 1160, 1063, 746, 706, 586, 466, 420 cm^{-1}; HRMS (ESI): calcd for $[(C_{10}H_7NO_2S+Na)]^+$ 228.0094, found 228.0099; ^1H NMR (500 MHz, $CDCl_3$) 7.73 (1H, d, *J*=8.0 Hz, CH), 7.61–7.53 (2H, m, CH), 7.37 (1H, dt, *J*=8.0, 1.0 Hz, CH), 7.14 (1H, d, *J*=3.5 Hz, CH), 6.48 (1H, d, *J*=3.5 Hz, CH), 6.42 (1H, t, *J*=3.5 Hz, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 136.8, 134.3, 129.3, 128.1, 127.7, 122.5, 120.9, 117.2, 116.3, 105.4 ppm.

4.2.25. [1,3]-dioxolo-[4′,5′:4,5]-benzo-[1,2-d]-pyrrolo-[1,2-b]-isothiazole 5,5-dioxide 40. As described above: Under N_2, **19** (55 mg, 0.16 mmol, 1 equiv), $Pd(OAc)_2$ (3.7 mg, 0.017 mmol, 10 mol %), PPh_3 (8.7 mg, 0.033 mmol, 20 mol %) and K_2CO_3 (46 mg, 0.33 mmol, 2 equiv) in anhydrous DMF (5 mL) was heated at 110 °C for 18 h. After cooling EtOAc (8 mL) and H_2O (8 mL) were added. The resultant aqueous layer was further extracted with EtOAc (5×10 mL) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (*c*-Hex-EtOAc; 3:1) gave **40** (15 mg, 38%) as a pale yellow crystalline solid. Mp=215–218 °C; R_f=0.40 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=3442, 3144, 3057, 2920, 2851, 1602, 1475, 1322, 1102, 996, 817, 699, 546 cm^{-1}; HRMS (EI): calcd for $[(C_{11}H_7NO_4S)]^+$ 249.0096, found 249.0101; ^1H NMR (400 MHz, $CDCl_3$) 7.14 (1H, s, CH), 7.12–7.11 (1H, m, CH), 6.95 (1H, s, CH), 6.40–6.35 (2H, m, CH), 6.13 (2H, s, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 154.1, 149.1, 129.3, 128.2, 122.4, 116.8, 116.1, 104.6, 104.0, 102.9, 102.5 ppm.

4.2.26. 2,3-Dimethoxy-7,8,9,10-tetrahydrobenzo[4,5]isothiazolo[2,3-a]indole 5,5-dioxide 41. As described above a mixture of **20** (93 mg, 0.23 mmol, 1 equiv), $Pd(OAc)_2$ (6 mg, 0.03 mmol, 10 mol %), PPh_3 (14 mg, 0.053 mmol, 20 mol %) and K_2CO_3 (76 mg, 0.55 mmol, 2 equiv) in anhydrous DMF (5 mL) was heated to 110 °C under N_2 for 15 h. The reaction mixture was cooled and EtOAc (10 mL) and H_2O (10 mL) were added. The resultant aqueous layer was further extracted with EtOAc (3×5 mL) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (*c*-Hex-EtOAc; 3:1) which afforded **41** (55 mg, 75%) as a colourless crystalline solid. Mp=208–210 °C (EtOAc); R_f=0.30 (*c*-Hex-EtOAc; 3:1); $\bar{\nu}_{max}$=2924, 2851, 1582, 1539, 1489, 1459, 1416, 1315, 1284, 1153,1045, 844 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{17}NO_4S+Na)]^+$ 342.0776, found 342.0781; ^1H NMR (400 MHz, $CDCl_3$) 7.11 (1H, s, CH), 6.84 (1H, s, CH), 6.06 (1H, s, CH), 3.98 (3H, s, CH_3), 3.91 (3H, s, CH_3), 2.83–2.89 (2H, m, CH_2), 2.39–2.44 (2H, m, CH_2), 1.71–1.86 (4H, m, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 154.0, 148.5, 129.4, 127.9, 127.6, 125.5, 123.0, 104.5, 104.1, 102.3, 56.4, 56.35, 23.1, 22.7, 22.3, 21.3 ppm; Anal. found (Calcd) for $C_{16}H_{17}NO_4S$: C, 60.11% (59.98%); H, 5.37% (5.35%); N, 4.10% (4.37%). Recrystallisation from EtOAc gave crystals suitable for X-ray crystallography.

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