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Observations concerning the synthesis of heteroatom-containing 9-membered benzo-fused rings by ring-closing metathesis

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Graphical Abstract

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Observations concerning the synthesis of heteroatom-containing 9-membered benzo-fused rings by ring-closing metathesis

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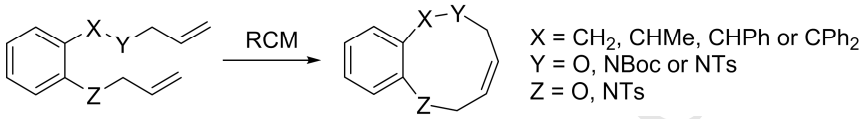

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2,5,6,7-Tetrahydrobenzo[*b*][1,5]oxazonine
2,5,6,7-Tetrahydro-1*H*-benzo[*b*][1,5]diazonine
Isomerization
Benzo-fused

ABSTRACT

A set of benzo-fused dienes with a 1,9-relationship and containing a variety of nitrogen and oxygen heteroatoms were readily synthesized. These dienes were then treated with the Grubbs second generation catalyst with the aim of synthesizing the 9-membered benzannelated heterocycles containing two heteroatoms (either O,O, NR,NR or O,NR where R = Ts or Boc). As previously observed in the literature, many of the dienes did not give the expected ring-closed product. However, a number of the desired products did form, namely with the 1,2-dihydrobenzo[*c*][1,5]oxazonin-7(5*H*)-one, 5,7-dihydrobenzo[*b*][1,5]oxazonine-6(2*H*)-carboxylate and 2,5,6,7-tetrahydrobenzo[*b*][1,5]oxazonine cores, albeit in poor yields. Rather surprisingly, the *N*-allyl-*N*-(2-(N-allyl-4-methylphenylsulfonamido)benzyl)-4-methylbenzenesulfonamide scaffold gave the desired ring-closed 1,6-ditosyl-2,5,6,7-tetrahydro-1*H*-benzo[*b*][1,5]diazonine in a high yield. Furthermore, when treated with the catalyst [RuClH(CO)(PPh_3)$_3$] the alkene isomerized into conjugation only with the benzylic NTs group and not with the phenyl NTs group to afford the 1,6-ditosyl-2,3,6,7-tetrahydro-1*H*-benzo[*b*][1,5]diazonine structure.

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1. Introduction

In the last two decades, ring-closing metathesis (RCM) has become an established synthetic process for the construction of small (5- and 6), medium (7–9) and larger (>9)-membered ring-systems.[1-5] The use of this method has been expanded owing to the compatibility of the process with heteroatoms in the newly created ring systems *viz.*, nitrogen, oxygen and sulfur.[6,7] It should also be noted here that RCM has seen much application in the area of natural products with medium-sized ring systems.[8-10]

The incorporation of two adjacent alkene side chains onto (semi-)rigid motifs has also been employed synthetically, often resulting in the corresponding ring-closed products being formed in good yields.[11] Examples include the incorporation of aromatic rings as part of the diene-containing system, thus resulting in benzo-fused systems with additional rings of various ring-sizes. In addition, benzo-fused systems possessing a variety of heteroatoms have been constructed in this way. In terms of our research group's contribution to this area, the following efforts towards medium-sized benzo-fused heteroatom-containing systems (**1**, figure 1) have been synthesized by RCM, namely 7-[12-14] and 8-membered[12,13,15] benzo-fused ring systems.

It has been shown that 9-membered ring systems are important compounds with rather interesting properties (these characteristics include structural and conformational traits).[16] In addition, (hetero)aromatic ring-fused 9-membered rings represent structural features that have been found in natural products, a typical example being stemmadenine **2**,[17,18] a representative member of the azonino[5,4-*b*]indole family (Figure 1), albeit that apart from the indole portion the ring is fully saturated.

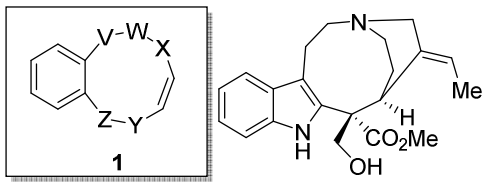

Figure 1: Unsaturated 9-membered benzo-fused rings systems

From a cursory perusal of the literature, it became evident that the synthesis of 9-membered benzo-fused ring systems - a

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generic example **1** shown in figure 1 - had previously been achieved with RCM reactions, albeit with various degrees of success.[11] Examples include the benzoyl-protected 1*H*-benzo[*b*]azonine **3**,[19] biaryl **4**,[20,21] substituted 2,5-dihydro-7*H*-benzo[*b*][1,5]oxathionine **5**,[22] and silyloxy-containing **6**.[23] In terms of indole examples, with respect to compound **2**, substituted 7,10,11,12-tetrahydroazonino[3,2,1-*hi*]indole **7**,[24,25] [1,4]diazonino[1,2-*a*]indole **8**,[26] substituted 6,7-dihydro-5*H*-dibenzo [*c*,*e*]azonine **9**[27] and the hepatitis C virus polymerase enzyme (NS5B) inhibitor **10**[28] (Figure 2) all make up members of this set. It should be noted that generation of 9-membered benzo-fused rings has also been attempted by way of an enyne metathesis strategy, but that this general approach remains challenging.[29,30] In summary, it is evident that the relative paucity of examples of 9-membered rings synthesized by metathesis is reflected in the challenges (including entropic and conformational constraints) associated with the generation of such large ring systems.[31-33]

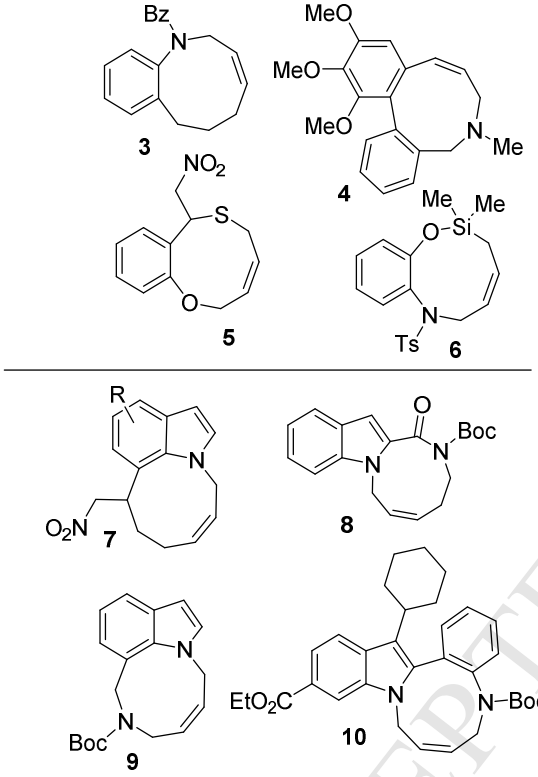
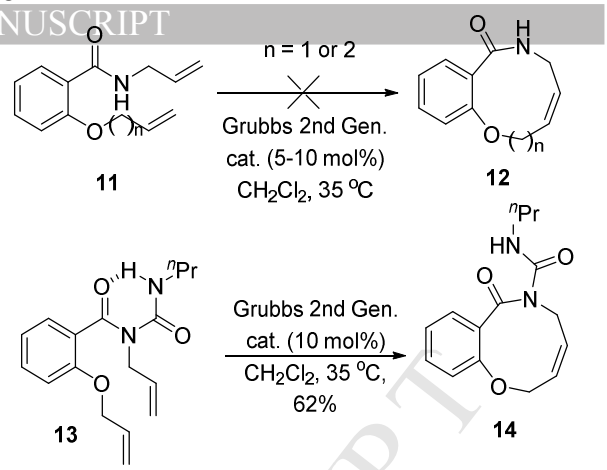


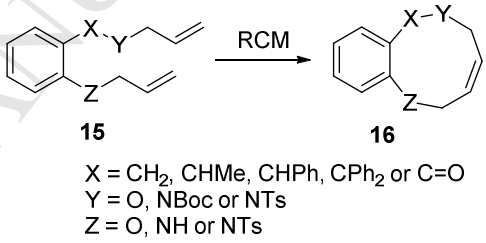
Figure 2: Examples of benzo- and indole-fused 9-membered rings generated by metathetic approaches

In a recent interesting case, Baell and co-workers observed that during the synthesis of peptidomimetic compounds, the attempted ring-closure of benzamide **11** into the anticipated **12** did not occur at all (scheme 1).[34,35] In fact, it was necessary to convert compound **11** into urea **13** in order to effect cyclization to **14**, presumably via intramolecular hydrogen bonding (as shown in **13**) which enhanced the proximity of the two alkene side chains allowing for participation in the RCM process.[34,35]



Scheme 1: Importance of functional groups in metathesis leading to 9-membered ring systems

These reports of the challenges of forming 9-membered rings by RCM have prompted us to disclose results emanating from our laboratory towards the synthesis of benzo-fused systems containing either oxygen or nitrogen and a combination of these two elements in the 9-membered ring. This general approach is illustrated in the general scheme shown below (scheme 2).



Scheme 2: Proposed approach to various benzo-fused 9-membered ring systems

2. Results and discussion

The initial part of the project involved the synthesis of a number of varied diene substrates in which an aromatic ring formed part of the backbone illustrated in Figure 3.

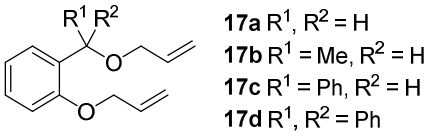


Figure 3: Scaffolds containing an aryl ring and two oxygen atoms in the diene side chains

Therefore, the syntheses commenced with the oxygen containing compounds (**17a-e**). The simplest of these scaffolds viz., 1-(allyloxy)-2-[(allyloxy)methyl]benzene **17a**, was readily generated from 2-(hydroxymethyl)phenol **18** as described in the literature.[36] For the synthesis of compounds with a greater degree of steric hindrance at the benzylic position, scaffolds **17b-d** (figure 3) were generated from 2-allyloxybenzaldehyde **19**[37] and ethyl 2-(allyloxy)benzoate **20**[35] respectively, by making use of an appropriate Grignard addition followed by the allylation of the resultant benzylic alcohol (Scheme 3). Finally, mixed ether-ester scaffold was generated *viz*., allyl 2-allyloxybenzoate **22**, which was synthesized directly from salicylic acid **21** as described in

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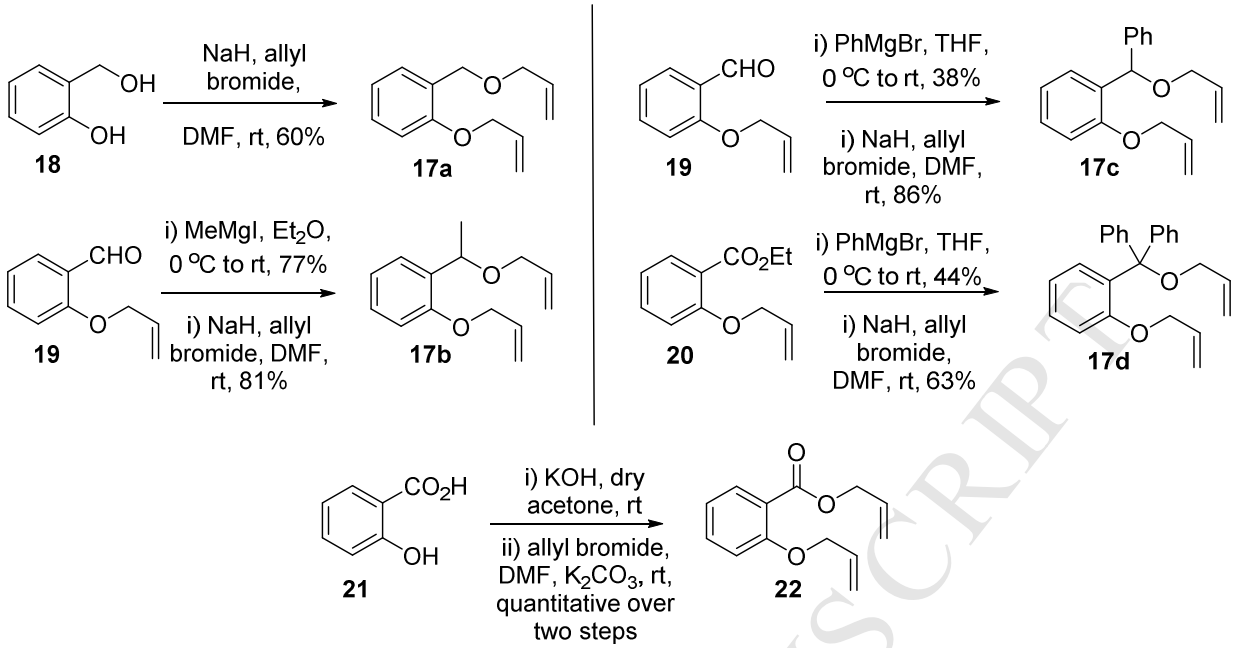
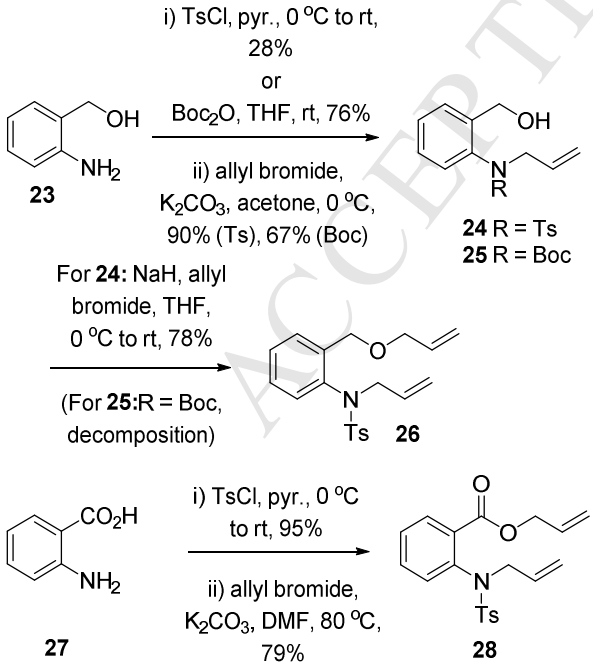
the literature by Brown and Duong,[38] to complete this set of oxygen-containing dienes.



Scheme 3: Synthesis of di-oxygen-containing precursors

The first of the bis-alkene scaffolds involving a mixed set of heteroatoms was synthesized as illustrated in Scheme 4, using 2-aminobenzyl alcohol **23** as the starting material. Transformation of the amine group of **23** into the tosylamide and Boc analogues was followed in both cases by an allylation with allyl bromide mediated by potassium carbonate to yield the mono-allylated analogues **24** and **25** respectively, in reasonable yield (Scheme 4). Failure of the benzylic hydroxyl group to undergo allylation under these conditions necessitated initial deprotonation with a stronger base, *viz.*, sodium hydride, prior to reaction with allyl bromide.



Scheme 4: Scaffolds with nitrogen directly attached to the aryl ring

This afforded the desired di-allyl tosyl-protected compound **26**. Unfortunately, we were unable to obtain the Boc-protected variant in this manner. Of interest here is that the two-step allylation protocol gave better yields of product than an initial NaH-mediated diallylation of the *N*-tosyl protected starting material, since the latter protocol resulted in the formation of multiple products.

In order to maintain as close a structural similarity as possible for this set of scaffolds, the corresponding benzylic oxidized version of **26** *viz.*, allyl 2-[(*N*-allyl-4-methylphenyl)sulfonamide]benzoate **28**, was also synthesized from anthranilic acid **27** via the known *N*-tosylanthranilic acid (Scheme 4).[39]

A second, yet complementary, scaffold containing nitrogen and oxygen atoms, but in different relative positions, were next synthesized (compounds **33** and **34**, Scheme 5). These compounds had the oxygen atom directly linked to the aryl ring and were synthesized from salicylaldehyde **29**. The initial allylation of the phenol group in 2-hydroxybenzaldehyde **29** was achieved in 90% yield and was followed by reductive amination with allylamine and sodium triacetoxyborohydride to give a high yield of the bis-allyl compound **30**. Attempts to convert this material into the Boc-protected analogue **33** or the corresponding tosyl-protected analogue **34**, under a variety of conditions, was unsuccessful in our hands (numerous products by tlc) and thus an alternative one-pot route was developed. In this sequence of reactions, reductive amination of salicylaldehyde **29** was achieved by firstly treating it with allyl amine in the presence of crushed 4 Å molecular sieves. This was followed by reduction of the intermediate imine with sodium borohydride and subsequent reaction of the amine with di-*tert*-butyl dicarbonate to afford the urethane **31** in 72% yield, while tosylation gave the corresponding tosyl-protected analogue **32** in a similar yield. Finally, a regular phenolic allylation protocol gave the desired bis-allylation products **33** and **34** in yields of 86% and 43% respectively. It should be mentioned that it was not necessary to synthesize the related benzamide **11** as Baell and co-workers demonstrated that this compound fails to undergo RCM.[34,35]

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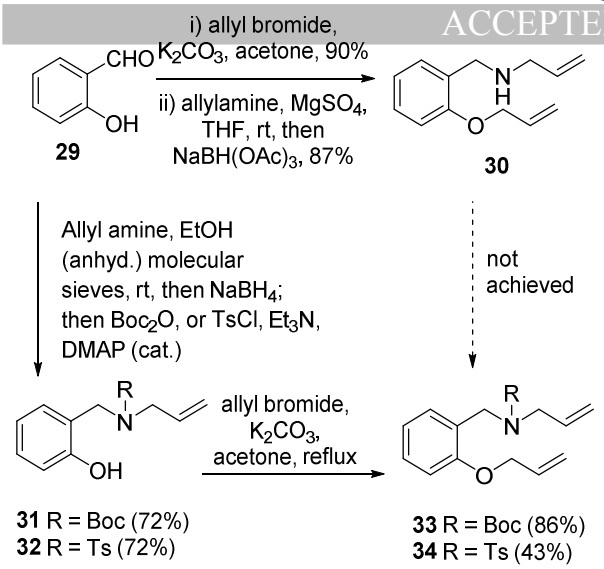
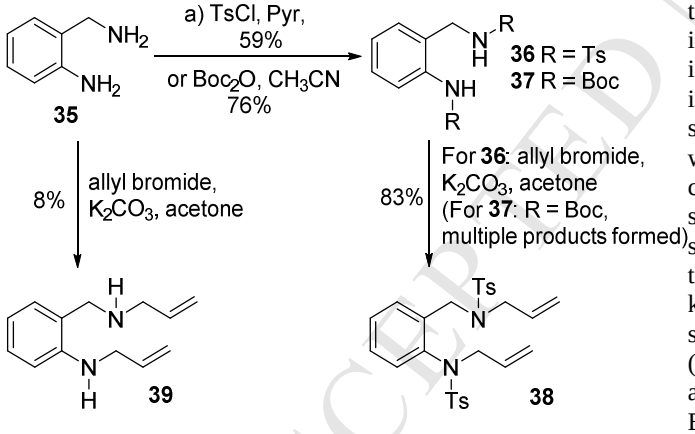


Scheme 5: Scaffolds with oxygen directly attached to aryl ring

Finally, molecules incorporating two nitrogen atoms in the allylic side chains were generated from 2-aminobenzylamine **35** (Scheme 6). Thus, global tosylation of **35** with tosyl chloride in pyridine gave a 59% yield of compound **36.**[40] Similarly, conversion of **35** into the di-Boc[41] analogue **37** was achieved with Boc_2O in acetonitrile in 76% yield. Allylation of **36** then proceeded smoothly to afford the diallyl substrate **38** in 83% yield. However, the synthesis of the corresponding di-Boc derivative proved to be too variable in our hands with most products being typified by loss of the Boc group(s). Finally, allylation of the diamine **35** gave the N-differentiated diallyl analogue **39** in an expected low yield of 8% (Scheme 6)**.**



Scheme 6: Scaffolds with two nitrogen atoms

With the eleven scaffolds in hand, a variety of RCM conditions were applied to facilitate ring-closure. These are discussed in the following section with successes summarized in Table 1.

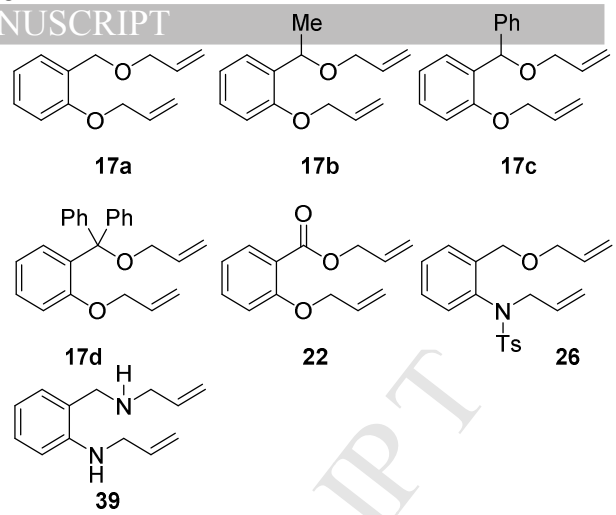


Figure 4: Scaffolds for which the RCM reactions were unsuccessful under the following conditions: Grubbs second generation catalyst, CH_2Cl_2, 30-35 ^oC or toluene, 80 ^oC.

The first attempted metathesis cyclizations for the dioxygen-containing dienes **17a-d** were unfortunately very disappointing (See Figure 4 for structures that were not successfully ring-closed). Initial attempts using the Grubbs second generation catalyst[42] at moderate temperature (reflux, CH_2Cl_2) showed that the starting material was not being consumed (tlc). Subsequent reactions were performed under much more vigorous conditions, in which the same catalyst was used in toluene and the reaction temperature increased from ambient to 80 ^oC. To ensure that the products were not co-eluting with the starting dienes on the TLC plates, column chromatography was performed on all the reaction residues. However, isolation of the same starting materials **17a-d** in each case, as substantiated by NMR spectroscopy, confirmed that cyclization had not occurred. In addition, and of notable interest, was the absence of isomerized by-products, which were identified later in other RCM reactions done in the study (vide infra). It should also be noted that, as concentration has been shown to affect RCM outcomes,[43] the reaction concentrations were kept well below 0.5 M (see experimental section for exact concentrations). In a subsequent attempt to understand whether steric issues might be involved in preventing the RCM process, a single crystal X-ray structure was solved for **17d**, which showed that at least in the solid state, the allyl groups were essentially kept far apart by a "triphenylalkoxy barrier" (see experimental section for the ORTEP diagram of **17d** and its precursor, [2-(allyloxy)phenyl](diphenyl)methanol, a compound in which the allyloxy and alcohol functionalities appear much closer together). Based on our experiences with the synthesis of 8-membered benzo-fused heterocycles by way of RCM reactions,[12,13,15,44] which for the most part provided product in high yields, it would seem that the additional flexibility imparted to the 1,9-diene system by the addition of one extra skeletal atom is a serious enough limiting factor to disfavour the desired reaction. It can be postulated too that the high coordinating abilities of the diallyl ethers could be playing an additional important role in shutting down the metathesis process.

Attempts at cyclizing the allyl 2-(but-3-en-1-yloxy)benzoate **22**, which is essentially an ester version of the Baell benzamide **11**[34,35] shown in Scheme 1, were equally unsuccessful (figure 4), confirming earlier observations concerning the challenges associated with making 9-membered rings from these types of systems by RCM.

The RCM results for the mixed *N,O*-containing dienes proved to be more promising. Although attempted RCM of substrate **26**

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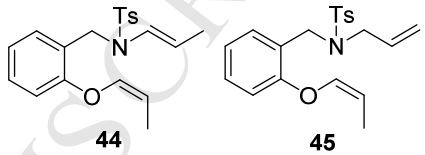
was unsuccessful, RCM of the ester **28** gave product **40** in a poor 15% yield after prolonged heating in toluene (Table 1, entry a), along with 38% of recovered starting material **28**. This result is of some interest since the presence of a carbonyl group over a methylene group essentially allows for some RCM to occur. Of additional interest, RCM involving **33**, in which the amine and oxygen atoms had been interchanged and with the amine being Boc-protected, also resulted in the formation of the 9-membered cyclized product **41** being obtained. In this instance, a slightly better yield of 28% was obtained for the product **41**, although no starting material was recovered (Table 1, entry b).

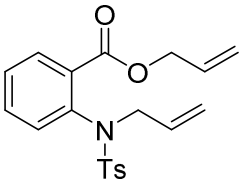
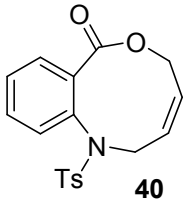
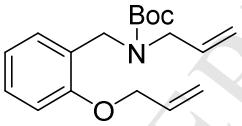
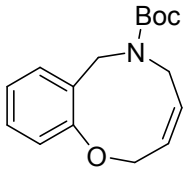
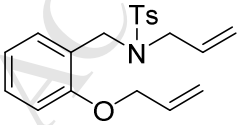
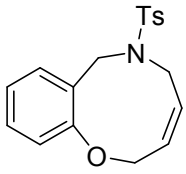
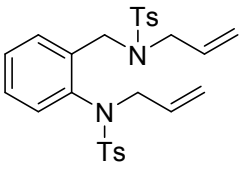
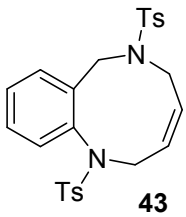
RCM, when applied to the tosylamide **34**, afforded the desired ring closed product **42**, again in a rather poor yield (13%), but nevertheless did provide evidence that formation of such 9-membered rings by RCM was indeed possible (Table 1, entry c). This reaction proved to be quite interesting since apart from the desired 9-membered ring compound **42**, two additional products were isolated during the purification of **42**, in addition to recovered starting material (24%). The products obtained, in which the allyl chain(s) had been isomerized, were **44** (12%) and **45** (23%) (figure 5). It should be noted here that the relationship between metathesis and isomerization has previously been explored and productively exploited.[45-47] It is interesting to note that from the ^{1}H NMR spectra it could be deduced that the allyloxy side chain in both **44** and **45** had isomerized to the intuitively less likely *cis* isomer in both products. This was based on the following analysis of the ^{1}H NMR spectra: both the OCH_2 and the NCH_2CH=CH signals of the starting material, at δ 4.50 and 3.83 respectively, were absent in product **44** and were replaced by new signals typical of the isomerized diene systems. Of particular note was the following: a dq for the OC*H* at δ 6.35 with *J* 8.4 and 1.8 Hz clearly indicated a *cis* double bond, as well as a dq for the NC*H* at δ 6.65 with *J* 14.1 and 1.8 Hz characterizing a *trans* double bond. As to the assignment of the respective *cis* α-H being adjacent to either the N or O atom, this was clarified by comparison with the ^{1}H NMR spectrum of isomer **45**. In the latter spectrum, it was evident that only one of the side chains had undergone isomerization since the methylene signal assigned to the NCH_2CH=CH was still present at δ 3.83, but that the signal for the OCH_2 at δ 4.50 had disappeared. Importantly, the observed dq at δ 6.26 with *J* 7.5 and 1.5 Hz for compound **45** was quite similar to that of **44** and was consequently assigned to the α-H of the O to support the two assigned structures for **44** and **45.**



44 **45**

Figure 5: Side products obtained in the RCM reaction of substrate **34**

Table 1: Summary of successful RCM reactions

Entry no.	Substrate	Conditions	Product A	Yield
a	 **28**	Grubbs II (5 mol%) Toluene, 70 °C, 18 h	 **40**	15% (38% of **28** recovered)
b	 **33**	Grubbs II (5 mol%) Toluene, 70 °C, 12 h	 **41**	28%
c	 **34**	Grubbs II (5 mol%) Toluene, 70 °C, 72 h	 **42**	13% (24% of **34** recovered, also 12% of **44** and 23% of **45**)
d	 **38**	Grubbs II (10 mol%) DCM, 60 °C, 18 h	 **43**	96%

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Lastly, the RCM procedure was applied to the two diamine scaffolds synthesized, namely **38** and **39**. To our satisfaction the ring-closed product **43** was obtained in 96% yield from the diene **38**, while perhaps unsurprisingly, diene **39** failed to cyclize due to the high coordinating affinity of the two secondary amines. It should be stressed that for scaffold **38** only moderate reaction conditions (CH_2Cl_2, 60 °C for 18h) were required (Table 1, entry d). Fortunately, the product **43** proved to be a crystalline solid which allowed for a single crystal X-ray spectroscopic analysis to be performed and confirmed that the desired ring-closure had indeed occurred (See figure 6a). It would thus appear that in this specific case, the presence of the two bulky tosyl groups on the allylamines results in a pre-organized conformation in which the RCM reaction becomes an efficient process.

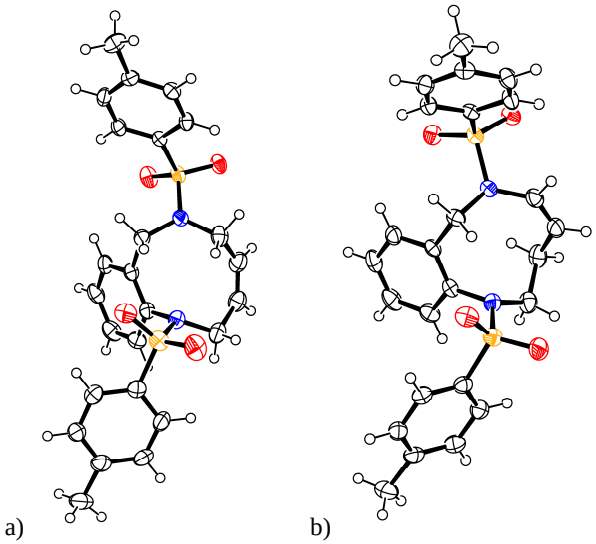
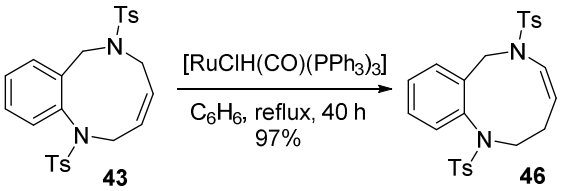


Figure 6: ORTEP diagrams of the X-ray crystal structures of compounds a) **43**, b) **46**, with all thermal ellipsoids at 50% probability, indicating the successful isomerization reaction (**43** → **46**).

With the crystalline 1,6-bis[(4'-methylphenyl)sulfonyl]-2,5,6,7-tetrahydro-1*H*-1,6-benzodiazonine **43** in hand, internal alkene isomerization was investigated with the ruthenium hydride isomerization catalyst, $[RuClH(CO)(PPh_3)_3]$, as illustrated in Scheme 7.[48-50] Isomerization was complete after 18 h (tlc) giving rather surprisingly a single regioisomeric product **46** in a yield of 97%. Careful flash silica gel column chromatography then afforded a clean sample of the crystalline isomer **46** on which a single crystal X-ray analysis was successfully performed after recrystallization (figure 6b). This allowed for the rigorous identification of the regioisomer **46** as the internally isomerized product, with the alkene now in conjugation with the benzyl, rather than that with the phenyl sulfonamide. This result was somewhat unexpected as in previous work involving internal isomerizations in 8-membered benzo-fused systems, mixtures of regioisomers were obtained.[51]



Scheme 7: Isomerization of compound **43** into **46**.

3. Conclusion

From the examples covered in this work, it has been demonstrated that the RCM methodology can indeed be utilized in the formation of several benzannelated bis-heteroatom-containing 9-membered heterocyclic molecules, albeit mostly in unsatisfactory yields. However, predicting which systems will successfully ring-close is still far from being clearly understood. It does appear that spatial pre-organization of the two allyl chains is important, with the bis-tosyl sulfonamide system **38** giving ring-closed product **42** in an excellent yield. In attempting to identify some contributing factors from the small set of bis-alkenes studied, the following was noted: under the conditions used: (a) systems having aryl and benzylic O-allyl side chains did not undergo the RCM in our hands to form the desired 9-membered ring systems; (b) the "benzylic" carbonyl group plays a role when comparing diene systems **26** and **28** (with the latter ester providing some product); (c) the replacement of an aryl O- by an NTs-allyl group generally improved the RCM outcome (for instance, RCM of **22** versus **28**); (d) replacement of a benzylic O- by an NR-allyl improves RCM (compare the unsuccessful results with substrates **17a-d** to those with **33** (R=Boc) and **34** (R= Ts)), and finally, (e) protected N-allyl groups at the aryl and benzylic positions, particularly bearing tosyl groups provided an ideal system for RCM reaction. Furthermore, these observations support results from other groups (for instance Beall and co-workers[34,35]) where it was found that the positioning of functional groups and their spatial characteristics, such as an ability to be involved in intra-molecular bonding interactions, had a significant influence on RCM reaction outcomes. It should further be noted that in select cases, side-products were obtained due to isomerization of the allyl groups. Finally, application of the isomerization catalyst $[RuClH(CO)(PPh_3)_3]$ allowed for the successful isomerization of diazocine **43** into the single regioisomer **46**.

4. Experimental

^1H NMR and ^{13}C NMR spectra were recorded on Bruker 300, Bruker DRX 400, Varian Inova 400 or Varian Inova 300 spectrometers at the frequency indicated. Infra-red spectra were recorded on Bruker IFS 25, Bruker Vector 22 or Thermo Nicolet Nexus 470 fourier transform spectrometers. Mass spectra were recorded on a Kratos MS 9/50, VG 70E MS or VG 70 SEQ mass spectrometer or alternatively a Waters API Q-TOF Ultima, GCT Premier or SYNAPT G2 mass spectrometer. Macherey-Nagel kieselgel 60 (particle size 0.063-0.200 mm) was used for conventional silica gel chromatography. All solvents used for reactions and chromatography were distilled prior to use. Reactions were performed under a blanket of inert gas (Ar or N_2) unless specified.

1-(Allyloxy)-2-[(allyloxy)methyl]benzene 17a: 2-(Hydroxymethyl)phenol **18** (2.00 g, 16.1 mmol) in DMF (20 mL) was cooled to 0 °C and treated with NaH (60% in oil, 1.14 g, 35.4 mmol) and stirred for 15 min. Allyl bromide (8.39 g, 64.4 mmol, 4.0 equiv.) was added and the reaction mixture was stirred at 24 °C for 17 h. H_2O (50 mL) was added and the crude product was extracted with EtOAc (5×100 mL). The combined filtrates were dried ($MgSO_4$) and the solvent removed to give a residue which was purified by column chromatography using EtOAc: hexane (1:9) as eluent to afford the product **17a** as a yellow oil (1.20 g, 60% yield). Spectral data compared well to that published in the literature.[36] ^1H NMR (300 MHz, $CDCl_3$): δ(ppm) = 4.08 (d, 2H, *J* 5.4 Hz, OCH_2), 4.54 (d, 2H, *J* 5.1 Hz, OCH_2), 4.60 (s, 2H, $ArCH_2$), 5.17–5.43 (m, 4H, 2×OCH_2CH=CH_2), 5.91–

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6.10 (m, 2H, 2×OCH_2CH=CH_2), 6.84 (d, 1H, *J* 8.1 Hz, ArH), 6.95 (dd, [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.22 (dd [app. t], 1H, J_1=J_2 8.1 Hz, ArH), 7.41 (d, 1H, *J* 7.5 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 66.8 (CH_2), 68.7 (CH_2), 71.4 (CH_2), 111.4 (CH), 116.7 (CH_2), 116.9 (CH_2), 120.6 (CH), 127.1 (C), 128.3 (CH), 128.7 (CH), 133.3 (CH), 134.9 (CH), 155.9 (C); HRMS: M^+, calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1079.

1-(Allyloxy)-2-[1-(allyloxy)ethyl]benzene 17b: Methyl magnesium iodide was pre-formed by treating Mg turnings (0.11 g, 24 mmol) in Et_2O (30 mL) at 0 °C with methyl iodide (0.23 mL, 0.52 g, 3.7 mmol), followed by vigorous stirring until the turnings had all dissolved. 2-(Allyloxy)benzaldehyde **19**[37] (0.50 g, 3.1 mmol) was then added drop-wise to the solution and the reaction mixture was stirred at 24 °C for a further 18 h after which it was quenched with NH_4Cl (sat.) (20 mL), extracted using EtOAc (3×100 mL) and after drying the solvent ($MgSO_4$) it was removed under vacuum and the residue purified by column chromatography using EtOAc:hexane (1:9) as eluent to afford the product 1-[2-(allyloxy)phenyl]ethanol as a colourless oil (0.42 g, 77% yield). This reaction was repeated and afforded product in similar yields. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 1.52 (d, 3H, *J* 6.5 Hz, CH_3), 2.66 (bs, 1H, OH), 4.59 (dd, 2H, *J* 3.6, 1.5 Hz, OCH_2), 5.14 (m, 1H, CH_3CHOH), 5.30 (d, 1H, *J* 10.5 Hz, *cis* OCH_2CH=CH_2), 5.42 (d, 1H, *J* 17.3 Hz, *trans* OCH_2CH=CH_2), 6.00–6.12 (m, 1H, OCH_2CH=CH_2), 6.86 (d, 1H, *J* 8.2 Hz, ArH), 6.94–6.99 (m, 1H, ArH), 7.19–7.26 (m, 1H, ArH), 7.36 (d, 1H, *J* 7.4 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 22.8 (CH_3), 66.5 (CH_2), 68.7 (CHOH), 111.6 (CH), 117.5 (CH_2), 120.9 (CH), 126.1 (CH), 128.1 (CH), 132.9 (CH), 133.7 (C), 155.4 (C); HRMS; M^+, calcd for $C_{11}H_{14}O_2$ 240.1150, found 240.1160.

1-[2-(Allyloxy)phenyl]ethanol (0.62 g, 3.5 mmol) in DMF (30 mL) was treated with NaH (60% in oil, 280 mg, 6.99 mmol) and stirred at 24 °C for 25 min. Allyl bromide (0.61 mL, 7.0 mmol) was added and the reaction mixture was stirred at 24 °C for 18 h. H_2O (50 mL) was then added and the crude product was extracted with EtOAc (3×100 mL) which produced a residue which was purified by column chromatography using EtOAc:hexane (1:9) as eluent to afford the desired product **17b** as a yellow oil (0.65 g, 81% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 1.42 (d, 3H, *J* 6.3 Hz, CH_3), 3.84–3.92 (m, 2H, OCH_2), 4.54 (d, 2H, *J* 4.8 Hz, OCH_2), 4.96 (q, 1H, *J* 6.3 Hz, $CHCH_3$), 5.15 (dd, 1H, *J* 1.0, 10.5 Hz, *cis* OCH_2CH=CH_2), 5.24–5.28 (m, 2H, OCH_2CH=CH_2), 5.40 (dd, 1H, *J* 1.5, 17.3 Hz, *trans* OCH_2CH=CH_2), 5.87–6.10 (m, 2H, 2×CH_2CH=CH_2), 6.38 (d, 1H, *J* 8.2 Hz, ArH), 6.98 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.20 (dd, 1H, *J* 1.5, 8.1 Hz, ArH), 7.45 (dd, 1H, *J* 1.5, 7.5 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 22.6 (CH_3), 68.6 (OCH_2), 69.5 (OCH_2), 70.9 (CH), 111.5 (CH), 116.3 (CH_2), 116.9 (CH_2), 120.9 (CH), 126.0 (CH), 127.8 (CH), 132.4 (CH), 133.3 (CH), 135.1 (C), 155.5 (C); HRMS; M^+, calcd for $C_{14}H_{18}O_2$ 218.1306, found 218.1306.

1-(Allyloxy)-2-[(allyloxy)(phenyl)methyl]benzene 17c: Phenyl magnesium bromide was pre-formed by treating Mg turnings (0.11 g, 24 mmol) in THF (30 mL) at 0 °C with bromobenzene (0.80 mL, 1.2 g, 7.4 mmol), followed by stirring until the magnesium dissolved. 2-(Allyloxy)benzaldehyde **19**[37] (0.50 g, 3.1 mmol) was then added drop-wise to the solution and the resulting reaction mixture was stirred at 24 °C for a further 18 h after which it was quenched with NH_4Cl (sat.) (50 mL) and extracted with EtOAc (3×100 mL) to afford a residue which was purified by column chromatography using EtOAc:hexane (5:95) as eluent, to provide the product [2-(allyloxy)phenyl](phenyl)methanol as a colourless oil (0.28 g, 38% yield). Repetition of this experiment provided product in similar yields. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 2.97 (d, 1H, *J* 4.5 Hz, OH), 4.42 (d, 2H, *J* 5.1 Hz, OCH_2), 5.12–5.24 (m, 2H, OCH_2CH=CH_2), 5.78–5.91 (m, 1H, OCH_2CH=CH_2), 5.99 (d, 1H, *J* 2.0 Hz, PhC*H*), 6.77 (d, 1H, *J* 8.4 Hz, ArH), 6.86 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.12–7.32 (m, 5H, 5×ArH), 7.31 (d, 2H, *J* 7.2 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 68.8 (CH_2), 72.3 (CHOH), 112.0 (2×CH), 117.5 (CH_2), 117.6 (CH), 120.9 (CH), 126.4 (CH), 127.0 (CH), 127.8 (CH), 128.0 (CH), 128.5 (CH), 132.8 (C), 132.9 (CH), 143.3 (C), 155.6 (C); HRMS; M^+, calcd for $C_{16}H_{16}O_2$ 240.1150, found 240.1160.

[2-(Allyloxy)phenyl](phenyl)methanol (0.41 g, 1.7 mmol) in DMF (20 mL) was treated with NaH (60% in oil, 0.14 g, 3.4 mmol) and stirred for 25 min. Allyl bromide (0.29 mL, 0.41 g, 2.0 mmol) was then added and the reaction mixture was stirred at 24 °C for 18 h after which it was quenched with H_2O (50 mL) and the aqueous solution was extracted with EtOAc (4×100 mL) to afford a residue which was purified by column chromatography using EtOAc:hexane (1:9) as eluent to give the product **17c** as a colourless oil (0.45 g, 86% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 3.94 (d, 2H, *J* 4.2 Hz, OCH_2), 4.43 (s, 2H, OCH_2), 5.07–5.30 (m, 4H, 2×OCH_2CH=CH_2), 5.82 (s, 1H, PhC*H*O), 5.88–5.91 (m, 2H, 2×OCH_2CH=CH_2), 6.74 (d, 1H, *J* 8.1 Hz, ArH), 6.89 (dd [app. t], 1H, J_1=J_2 7.2 Hz, ArH), 7.08–7.22 (m, 4H, 4×ArH), 7.23 (br d, 2H, *J* 7.1 Hz, 2×ArH), 7.46 (dd, 1H, *J* 6.6, 1.2 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 68.8 (OCH_2), 69.8 (OCH_2), 76.2 (CH), 111.7 (CH_2), 116.5 (CH_2), 117.2 (CH), 120.9 (CH), 127.0 (2×CH), 127.1 (2×CH), 128.1 (2×CH), 128.2 (CH), 131.1 (C), 133.1 (CH), 135.0 (CH), 142.1 (C), 155.5 (C); HRMS; M^+, calcd for $C_{19}H_{20}O_2$ 280.1463, found 280.1458.

Ethyl 2-(allyloxy)benzoate 20:[38] To a solution of ethyl 2-hydroxybenzoate (1.3 g, 7.8 mmol) in acetone (50 mL) and K_2CO_3 (3.33 g, 24.1 mmol) was added allyl bromide (2.1 mL, 2.9 g, 24.0 mmol). The reaction mixture was stirred under reflux for 18 h after which H_2O (50 mL) was added and the crude product extracted with EtOAc (4×100 mL). The residue produced was purified by column chromatography using EtOAc:hexane (5:95) as eluent to afford the product **20** as a colourless oil (1.54 g, 96% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 1.38 (t, 3H, *J* 7.1 Hz, CH_3), 4.36 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 4.61 (s, 2H, OCH_2CH), 5.29 (d, 1H, *J* 10.5 Hz, *cis* OCH_2CH=CH_2), 5.51 (dd, 1H, *J* 17.4, 1.5 Hz, *trans* OCH_2CH=CH_2), 6.01–6.07 (m, 1H, OCH_2CH=CH_2), 6.93–7.00 (m, 2H, 2×ArH), 7.43 (dd, 1H, *J* 1.0, 7.5 Hz, ArH), 7.79 (dd, 1H, *J* 1.5, 7.5, Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 14.2 (CH_3), 60.6 CH_2), 69.3 (CH_2), 113.5 (CH), 117.2 (CH_2), 120.2 (CH), 120.9 (C), 131.4 (CH), 132.6 (CH), 133.0 (CH), 157.8 (C), 166.2 (C=O); HRMS; M^+, calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0942.

1-(Allyloxy)-2-[(allyloxy)(diphenyl)methyl]benzene 17d: Magnesium turnings (0.27 g, 11 mmol) in THF (20 mL) at 0 °C were treated with bromobenzene (3.43 g, 2.29 mL, 5.0 mmol) and stirred until the turnings had dissolved to form the phenyl magnesium bromide. Ethyl 2-(allyloxy)benzoate **20** (0.90 g, 4.4 mmol) was then added dropwise to the solution which was stirred at 24 °C for 18 h after which NH_4Cl (sat.) solution (30 mL) was added to quench the reaction. The crude product was extracted with EtOAc (4×50 mL) and the residue purified by column chromatography using EtOAc:hexane (5:95) as eluent to afford the product [2-(allyloxy)phenyl](diphenyl)methanol as a white solid (0.64 g, 44% yield); mp: 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 4.36 (d, 2H, *J* 5.0 Hz, OCH_2), 5.00–5.09 (m, 2H, OCH_2CH=CH_2), 5.25 (s, 1H, OH), 5.51–5.63 (m, 1H, OCH_2CH=CH_2), 6.53 (d, 1H, *J* 6.6 Hz, ArH), 6.82 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 6.93 (d, 1H, *J* 8.1 Hz, ArH), 7.26–7.32 (m, 11H, 11×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 69.3

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(OCH_2), 81.8 (C), 113.3 (CH), 117.1 (CH_2), 120.6 (CH), 126.9 (2×CH), 127.6 (4×CH), 127.7 (4×CH), 128.8 (CH), 130.1 (CH), 132.1 (2×C), 135.9 (C), 146.5 (CH), 156.3 (C); HRMS; M^+, calcd for $C_{22}H_{20}O_2$ 316.1463, found 316.1467.

X-ray crystal structure details of [2-(allyloxy)phenyl](diphenyl)methanol (as shown in figure 7): crystallized from EtOAc-hexane, formula: $C_{22}H_{20}O_2$, M=316.38, crystal size 0.30 × 0.28 × 0.18 mm^3, a = 12.2100(11) Å, b = 14.9811(18) Å, c = 9.4275(10) Å, β = 102.277(5)°, V = 1685.0(3) $Å^3$, ρ_{calc} = 1.247 Mg/m^3, μ = 0.078 mm^{-1}, F(000) = 672, Z = 4, monoclinic, space group P21/c, T = 173(2) K, 13292 reflections collected, 4175 independent reflections, θ_{max} 28.262°, 221 refined parameters, maximum residual electron density 0.314 and -0.296 $e.Å^{-3}$. R_1 = 0.0482, wR_2 = 0.1229. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-1530895.

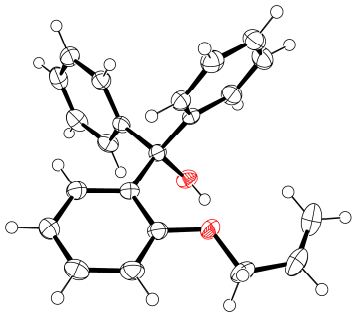

Figure 7: ORTEP diagrams of the X-ray crystal structure of compound [2-(allyloxy)phenyl](diphenyl)methanol, with all thermal ellipsoids at 50% probability.

To a solution of [2-(allyloxy)phenyl](diphenyl)methanol (0.32 g, 0.99 mmol) in DMF (20 mL) at 0 °C was added NaH (60% in oil, 0.08 g, 2 mmol) and the resulting mixture stirred for 30 min. Allyl bromide (0.17 mL, 2.0 mmol) was added to the mixture and stirring continued for 18 h at 24 °C. H_2O (50 mL) was then added and the crude product extracted with EtOAc (4×100 mL) to give a residue which was purified by column chromatography using EtOAc:hexane (5:95) as eluent to afford the product **17d** as a white solid (0.23 g, 63% yield); mp: 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 3.55 (d, 2H, J 3.3 Hz, OCH_2), 4.19 (d, 2H, J 3.9 Hz, OCH_2), 4.84 (dd, 1H, J 17.4, 2.2 Hz, *trans* $OCH_2CH=CH_2$), 4.96 (dd, 1H, J 1.0, 10.5 Hz, *cis* $OCH_2CH=CH_2$), 5.14 (dd, 1H, J 1.0, 10.5 Hz, *cis* $OCH_2CH=CH_2$), 5.36–5.51 (m, 2H, $OCH_2CH=CH_2$ and $OCH_2CH=CH_2$), 5.87–5.93 (m, 1H, $OCH_2CH=CH_2$), 6.77 (d, 1H, J 8.1 Hz, ArH), 7.00 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.21–7.27 (m, 8H, 8×ArH), 7.50 (m, 3H, 3×ArH), 7.87 (d, 1H, J 6.9 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 64.7 (OCH_2), 68.6 (OCH_2), 85.2 (C), 113.3 (CH), 112.9 (CH), 115.1 (CH_2), 116.6 (CH_2), 120.7 (CH), 126.6 (4×CH), 127.2 (CH), 127.8 (CH), 128.5 (4×CH), 128.6 (2×CH), 132.8 (C), 133.0 (C), 135.2 (C), 142.7 (CH), 155.4 (C); HRMS; M^+, calcd for $C_{25}H_{24}O_2$ 356.1776, found 356.1772.

X-ray crystal structure details of compound **17d** (as shown in figure 8): crystallized from EtOAc-hexane, formula: $C_{25}H_{24}O_2$, M = 356.44, crystal size 0.42 × 0.22 × 0.08 mm^3, a = 8.4586(18) Å, b = 9.223(2) Å, c = 13.746(3) Å, α = 77.615(16)°, β = 81.225(16)°, γ = 66.978(14)°, V = 961.2(4) $Å^3$, ρ_{calc} = 1.232 Mg/m^3, μ = 0.076 mm^{-1}, F(000) = 380, Z = 2, triclinic, space group P_{-1}, T = 173(2) K, 7057 reflections collected, 3778 independent reflections, θ_{max} 25.996°, 244 refined parameters, maximum residual electron density 0.742 and -0.363 $e.Å^{-3}$. R_1 = 0.0785, wR_2 = 0.1931. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-1530893.

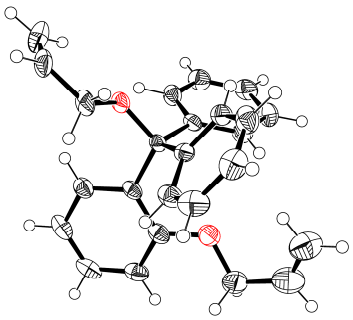

Figure 8: ORTEP diagrams of the X-ray crystal structure of compound **17d**, with all thermal ellipsoids at 50% probability.

Allyl 2-allyloxybenzoate 22[38]: To a solution of salicylic acid **21** (1.50 g, 10.0 mmol) in dry acetone (10 mL) was added pulverised KOH (1.50 g, 22.0 mmol) and the mixture was stirred at 25 °C for 30 min. Removal of the solvent on a rotary evaporator afforded the white di-potassium salt which was dissolved in anhydrous DMF (15 mL) to which allyl bromide (4.0 mL, 45.6 mmol) and anhydrous K_2CO_3 (6.60 g, 47.8 mmol) was added and the reaction mixture stirred for 18 h. H_2O (50 mL) was added and the product extracted with EtOAc (3×50 mL). The combined extracts were dried ($MgSO_4$) to afford the product as an oily residue purified by column chromatography using EtOAc:hexane (5:95) as eluent to yield the diallylated product **22** as a colourless oil (2.28 g, 100% yield). Spectra compared well to that published in the literature.[38] ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 4.65 (dd, 2H, J 5.1, 1.5 Hz, OCH_2), 4.83 (dd, 2H, J 1.2, 5.7, Hz, $COOCH_2$), 5.27–5.56 (m, 4H, 2×CH=CH_2), 5.99–6.15 (m, 2H, 2×CH_2CH=CH_2), 6.97–7.03 (m, 2H, 2×ArH), 7.43–7.49 (m, 1H, ArH), 7.83–7.87 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 65.5 ($COOCH_2$), 69.5 (OCH_2), 113.6 (CH_2), 117.5 (CH), 118.1 (CH), 120.4 (CH_2), 120.6 (C), 131.8 (CH), 132.3 (CH), 132.8 (CH), 133.4 (CH), 158.2 (C), 165.9 (C=O). HRMS: M^+, calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0945.

***N*-Allyl-*N*-[2-(hydroxymethyl)phenyl]-4'-methylbenzenesulfonamide 24**[52]: To a solution of TsCl (8.38 g, 44.7 mmol) in pyridine (25 mL) at 0 °C was added 2-aminobenzyl alcohol **23** (2.50 g, 20.3 mmol) and the reaction mixture was stirred at 24 °C for 18 h. Removal of the solvent under high vacuum gave a residue which was purified by column chromatography using EtOAc:hexane (1:1) as eluent to afford the product *N*-[2-(hydroxymethyl)phenyl]-4'-methylbenzenesulfonamide as a white solid (1.53 g, 28% yield); mp: 142–145 °C. Spectral data of this compound compared well with that published in the literature.[53] ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 2.38 (s, 3H, CH_3), 4.39 (s, 2H, $ArCH_2$), 7.05–7.09 (m, 2H, 2×ArH), 7.20–7.28 (m, 3H, 3×ArH), 7.43 (d, 1H, J 8.0 Hz, ArH), 7.64 (d, 2H, J 7.9 Hz, 2×ArH), 7.88 (bs, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.5 (CH_3), 63.9 (CH_2), 123.4 (CH), 125.3 (CH), 127.0 (2×CH), 129.0 (CH), 129.2 (CH), 129.6 (2×CH), 131.6 (C), 136.3 (C), 136.9 (C), 143.7 (C); HRMS: M^+, calcd for $C_{14}H_{15}NO_3S$ 277.0773, found 277.0765.

To a solution of *N*-[2-(hydroxymethyl)phenyl]-4'-methylbenzenesulfonamide (1.0 g, 3.7 mmol) in acetone (45 mL) was added K_2CO_3 (2.19 g, 15.8 mmol), followed by allyl bromide (1.91 g, 15.8 mmol) and the reaction mixture was then heated

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with vigorous stirring at 60 °C for 22 h. H_2O (20 mL) was added to the cooled reaction mixture and extraction with EtOAc (3×100 mL) produced a residue which was purified by column chromatography using EtOAc:hexane (3:7) as eluent, to afford the desired compound **24** as a brown oil (1.13 g, 97% yield). Spectral data of this compound compared well with that published in the literature.[52] ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 2.46 (s, 3H, CH_3), 3.01–3.09 (m, 1H, NCH_2), 3.70–3.76 (m, 1H, NCH_2), 4.50 (bd, 2H, *J* 10.0 Hz, $ArCH_2$), 4.94–5.03 (m, 3H, $NCH_2CH=CH_2$ and OH), 5.64–5.78 (m, 1H, $NCH_2CH=CH_2$), 6.45 (d, 1H, *J* 7.8 Hz, ArH), 7.14 (dd [app. t], 1H, $J_1=J_2$ 8.0 Hz, ArH), 7.26–7.36 (m, 3H, 3×ArH), 7.54–7.60 (m, 3H, 3×ArH); ^{13}C NMR (75MHz, $CDCl_3$): δ(ppm) = 21.5 (CH_3), 55.0 (CH_2), 61.1 (CH_2), 119.1 (CH_2), 127.5 (CH), 128.0 (2×CH), 128.2 (CH), 129.0 (CH), 129.5 (2×CH), 131.1 (CH), 131.8 (CH), 134.6 (C), 137.0 (C), 142.3 (C), 143.9 (C); HRMS; M^+, calcd for $C_{17}H_{19}NO_3S$ 317.1085, found 317.1098.

***tert*-Butyl allyl[2-(hydroxymethyl)phenyl]carbamate 25**: 2-Aminobenzyl alcohol **23** (0.80 g, 6.5 mmol) was dissolved in THF (30 mL) and Boc_2O (4.5 mL, 19 mmol) was added. The reaction was then stirred at room temperature for 20 h. H_2O (20 mL) was then added and the crude product was then extracted with EtOAc (4 × 100 mL), which was dried with $MgSO_4$. Silica gel column chromatography was then performed using EtOAc:hexane (1:4) as solvent to afford the desired compound, *tert*-butyl-2-(hydroxymethyl)phenylcarbamate as a yellow oil (1.15 g, 76% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 1.50 (s, 9H, 3×CH_3) 2.96 (bs, 1H, NH), 4.56 (s, 2H, $ArCH_2$), 6.96–7.01 (m, 1H, ArH), 7.10 (d, 1H, *J* 7.1 Hz, ArH), 7.24–7.26 (m, 1H, ArH), 7.70 (bs, 1H, OH), 7.82 (d, 1H, *J* 8.1 Hz, ArH); ^{13}C NMR (75MHz, $CDCl_3$): δ(ppm) = 28.2 (3×CH_3), 63.8 (CH_2), 80.3 (C-O), 121.0 (CH), 123.1 (CH), 128.7 (CH), 128.8 (CH), 129.1 (C), 137.7 (C), 153.4 (C=O); HRMS: M^+, calcd for $C_{12}H_{17}NO_3$ 249.1364, found 249.1356.

tert-Butyl-2-(hydroxymethyl)phenylcarbamate (0.994 g, 4.26 mmol) was dissolved in acetone (30 mL) and K_2CO_3 (2.35 g, 17.1 mmol) was added, followed by allyl bromide (1.08 g, 1.46 mL, 8.93 mmol). The reaction was then stirred at 60 °C for 18 h. H_2O (20 mL) was added and the crude product was extracted with EtOAc (4 × 100 mL). The solvent was removed under a vacuum and column chromatography was performed using 10% EtOAc:hexane (1:9) as eluent to afford the desired compound **25** as a yellow oil (0.745 g, 67% yield). ^{1}H NMR (300MHz, $CDCl_3$): δ(ppm) = 1.52 (s, 9H, 3×CH_3), 3.99 (d, 2H, *J* 5.5 Hz, NCH_2), 4.56 (s, 2H, $ArCH_2$), 5.24 (d, 1H, *J* 10.5 Hz, one of $NCH_2CH=CH_2$), 5.32 (d, 1H, *J* 17.2 Hz, one of $NCH_2CH=CH_2$), 5.87–6.00 (m, 1H, $NCH_2CH=$), 6.95–6.99 (m, 1H, ArH), 7.12 (d, 1H, *J* 7.3 Hz, ArH), 7.28–7.33 (m, 1H, ArH), 7.80 (bs, 1H, OH), 8.00 (d, 1H, *J* 8.1 Hz, ArH); ^{13}C NMR (75MHz, $CDCl_3$): δ(ppm) = 28.3 (3×CH_3), 70.4 (CH_2), 71.0 (CH_2), 80.0 (C-O), 117.7 CH_2), 120.1 (CH), 122.4 (CH), 125.3 (C), 129.1 (CH), 129.3 (CH), 138.4 (CH), 138.8 (C), 152.9 (C=O); HRMS: M^+, calcd for $C_{15}H_{21}NO_3$ 263.1521, found 263.1507.

***N*-Allyl-*N*-{2-[(allyloxy)methyl]phenyl}-4'-methylbenzenesulfonamide 26:** To a solution of 4'-methylbenzenesulfonamide **24** (1.07 g, 3.38 mmol) in THF (40 mL) was added NaH (60% in oil, 0.10 g, 4.2 mmol) at 0 °C and the mixture was stirred for 1 h. Allyl bromide (0.37 mL, 0.50 g, 4.2 mmol) was added to the reaction mixture which was stirred at 24 °C for 18 h. H_2O (20 mL) was added to quench any excess NaH and extraction with EtOAc (4×100 mL) gave a crude product purified by column chromatography using EtOAc:hexane (1:4) as eluent, to afford the desired product **26** as a brown oil (0.95 g, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.44 (s, 3H, CH_3), 3.85 (bs, 1H, NCH_2), 4.06 (d, 2H, *J* 5.5 Hz, OCH_2), 4.35 (bs, 1H, NCH_2), 4.69–4.76 (m, 2H, $ArCH_2$), 4.95–5.01 (m, 2H, $NCH_2CH=CH_2$), 5.21 (d, 1H, *J* 10.5 Hz, *cis*-$OCH_2CH=CH_2$), 5.33 (dd, 1H, *J* 1.5, 17.2 Hz, *trans*-$OCH_2CH=CH_2$), 5.67–5.80 (m, 1H, $NCH_2CH=CH_2$), 5.91–6.04 (m, 1H, $OCH_2CH=CH_2$), 6.54 (d, 1H, *J* 7.9 Hz, ArH), 7.12 (dd [app. t], 1H, $J_1=J_2$ 7.5 Hz, ArH), 7.26–7.34 (m, 3H, 3×ArH), 7.54 (d, 2H, *J* 8.2 Hz, 2×ArH), 7.61 (d, 1H, *J* 7.7 Hz); ^{13}C NMR (75MHz, $CDCl_3$): δ (ppm) = 21.5 (CH_3), 54.7 (CH_2), 68.1 (CH_2), 71.5 (CH_2), 116.8 (CH_2), 119.5 (CH_2), 127.4 (CH), 127.7 (CH), 128.0 (2×CH), 128.5 (CH), 128.8 (CH), 129.4 (2×CH), 132.2 (CH), 134.7 (CH), 135.4 (C), 136.8 (C), 140.4 (C), 143.5 (C); HRMS: M^+-Ts, calcd for $C_{13}H_{16}NO$ 202.1223, found 202.1232.

Allyl 2-*N*-allyl-*N*-tosylbenzoate 28: To a mixture of *N*-tosylanthranilic acid (1.0 g, 3.4 mmol) (synthesized from anthranillic acid **27** in 95% yield, as per reference[39]) and anhydrous K_2CO_3 (2.38 g, 17.2 mmol) in anhydrous DMF (20 mL) was added allyl bromide (2.08 g, 17.2 mmol) and the mixture vigorously stirred at 80 °C (oil bath) for 8 h. H_2O (80 mL) was added to the cooled solution which was then extracted with Et_2O (3×50 mL). The extracts were dried ($MgSO_4$) to afford an oily residue which was purified by column chromatography using EtOAc:hexane (3:7) as eluent to give the product **28** as a colourless oil (1.01 g, 79% yield). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 2.43 (s, 3H, $ArCH_3$), 4.29 (d, 2H, *J* 7.2 Hz, NCH_2), 4.71 (d, 2H, *J* 6.0 Hz, OCH_2), 5.00–5.08 (m, 2H, $CH=CH_2$), 5.29–5.45 (m, 2H, $CH=CH_2$), 5.85–6.15 (m, 2H, 2×$CH=CH_2$), 6.92–6.95 (m, 1H, ArH), 7.25 (d, 2H, *J* 8.4 Hz, 2×ArH), 7.38–7.45 (m, 2H, 2×ArH), 7.53 (d, 2H, *J* 8.4 Hz, 2×ArH), 7.88–7.91 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 ($ArCH_3$), 54.6 (NCH_2), 66.1 (OCH_2), 118.7 (CH_2), 119.0 (CH_2), 127.6 (2×CH), 128.2 (C), 129.4 (2×CH), 130.9 (CH), 131.3 (CH), 131.9 (CH), 132.1 (CH), 132.7 (CH), 133.3 (CH), 136.7 (C), 137.9 (C), 143.2 (C), 165.8 (C=O); HRMS: M^+, calcd for $C_{20}H_{21}NO_4S$ 371.1192, found 371.1188.

2-Allyloxy-*N*-allylbenzylamine 30: To a mixture of 2-allyloxybenzaldehyde (1.0 g, 6.3 mmol) (synthesized from salicylaldehyde **29** in 90% yield, as per reference[37]) and anhydrous $MgSO_4$ (2.50 g) in THF (15 mL) was added allylamine (0.34 g, 0.6 mmol) and the resulting yellowish solution stirred for 4 h at 24 °C. $(AcO)_3NaBH$ (2.0 g, 9.4 mmol) was then added at once and the resulting mixture stirred for a further 18 h at 24 °C after which it was treated with HCl (5% v/v, 20 mL) and H_2O (30 mL). EtOAc extraction (3×20 mL) and drying ($MgSO_4$) afforded a residue which was purified by column chromatography using EtOAc:hexane (1:9) as eluent, to yield the product **30** as a mobile oil (1.04 g; 87% yield). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 3.13 (d, 2H, *J* 6.1 Hz, NCH_2), 3.71 (s, 2H, $ArCH_2N$), 4.51 (d, 2H, *J* 5.9 Hz, OCH_2), 5.12–5.43 (m, 4H, $CH=CH_2$), 5.80–6.07 (m, 2H, $CH=CH_2$), 6.80 (d, 1H, *J* 7.6 Hz, ArH), 6.94 (dd [app. t], 1H, $J_1=J_2$ 7.5 Hz, ArH), 7.16 (dd [app. t], 1H, $J_1=J_2$ 7.6 Hz, ArH), 7.57 (d, 1H, *J* 7.5 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 51.9 (NCH_2Ar), 57.3 (NCH_2), 69.0 (OCH_2), 111.7 (CH), 116.9 (CH_2), 117.2 (CH_2), 120.8 (CH), 127.5 (CH), 128.7 (C), 129.9 (CH), 133.8 (CH), 136.8 (CH), 156.9 (C); HRMS: M^+, calcd for $C_{12}H_{17}NO$ 191.1311, found 191.1316.

Allyl-(2-hydroxybenzyl)-carbamic acid *tert*-butyl ester 31[54]: To a solution of salicylaldehyde **29** (1.50 g, 12.3 mmol) in anhydrous EtOH (20 mL) was added allylamine (0.70 g, 12 mmol) and crushed 4A molecular sieves (5.0 g) and the yellow solution was stirred at 24 °C for 18 h after which the solution was

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filtered. To the yellow filtrate was added $NaBH_4$ (0.45 g, 12 mmol) and stirring was continued for a further 24 h. Boc_2O (0.27 g, 13 mmol) was then added and the mixture was stirred for a further 8 h. Saturated aqueous NH_4Cl (20 mL) was added and the solution was further diluted with H_2O (40 mL). The aqueous solution was extracted with EtOAc (3×40 mL) and dried ($MgSO_4$) to afford a residue which was purified by column chromatography using EtOAc:hexane (1:9) as eluent to give the pure product **31** as an oil (2.34 g, 72% yield). The data compared well with the literature.[41] ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 1.47 (s, 9H, 3×CH_3), 3.79 (d, 2H, *J* 6.5 Hz, NCH_2), 4.31 (s, 2H, $ArCH_2N$), 5.10–5.21 (m, 2H, CH=CH_2), 5.72–5.86 (m, 1H, C*H*=CH_2), 6.79 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 6.95 (d, 1H, *J* 7.6 Hz, ArH), 7.04 (d, 1H, *J* 7.5 Hz, ArH), 7.21 (dd [app. t], 1H, J_1=J_2 7.6 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 28.3 (3×CH_3), 46.6 ($ArCH_2N$), 49.0 (NCH_2), 81.7 (C), 117.2 (CH), 117.5 (CH_2), 119.2 (CH), 122.6 (C), 130.0 (CH), 131.4 (CH), 132.9 (CH), 146.5 (C), 156.5 (C=O); HRMS: M^+, calcd for $C_{15}H_{21}NO_3$ 263.1522, found 263.1527.

***N*-allyl-*N*-(2-hydroxybenzyl)-4-methylbenzenesulfonamide 32**: To a solution of salicylaldehyde **29** (1.50 g, 12.3 mmol) in anhydrous EtOH (20 mL) was added allylamine (0.70 g, 12 mmol) and crushed 4A molecular sieves (5.0 g) and the yellow solution was stirred at 24 °C for 18 h after which the solution was filtered. To the yellow filtrate was added $NaBH_4$ (0.45 g, 12 mmol) and stirring was continued for a further 24 h. The resulting mixture was poured into H_2O (200 mL), extracted with EtOAc (4×40 mL) which was dried and evaporated to a thick oil. This material was immediately taken up in DCM (50 mL) to which TsCl (2.58 g, 13.5 mmol), NEt_3 (1.83 g, 18.1 mmol) and DMAP (10 mg) were added. After stirring at 25 °C for 72 h, the solvent was removed and the residue purified by column chromatography using EtOAc:hexane (1:4) as eluent to afford the tosylamide **32** as a white solid (2.81 g; 72%). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 2.47 (s, 3H, $ArCH_3$), 3.70 (br s, 1H, NCH_2CH=CH_2), 3.83 (br s, 1H, NCH_2CH=CH_2), 4.19 (s, 1H, $ArCH_2N$), 4.30 (s, 1H, $ArCH_2N$), 5.08–5.12 (m, 2H, CH=CH_2), 5.43–5.49 (m, 1H, C*H*=CH_2), 6.84–6.86 (m, 1H, ArH), 6.96–6.98 (m, 1H, ArH), 7.10–7.35 (m, 4H, 4×ArH), 7.55–7.80 (m, 2H, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.6 (CH_3), 44.9 ($ArCH_2N$-rotamer), 47.2 ($ArCH_2N$-rotamer), 49.4 (NCH_2CH-rotamer), 50.9 (NCH_2CH-rotamer), 117.3 (CH), 119.5 (CH), 119.9 (CH_2), 122.2 (C), 127.2 (2×CH), 128.5 (2×CH), 129.8 (CH), 130.0 (CH), 130.2 (CH), 143.4 (CH), 144.0(C), 155.9 (C); HRMS: M^+, calcd for $C_{17}H_{20}NO_3S$ 318.1164, found 318.1165.

Allyl-(2-allyloxybenzyl)-carbamic acid *tert*-butyl ester 33: To a mixture of phenol **31** (0.50 g, 1.9 mmol) in dry acetone (20 mL) and anhydrous K_2CO_3 (1.31 g, 9.5 mmol) was added allyl bromide (1.2 g, 9.5 mmol) and the mixture was vigorously stirred under reflux for 18 h, cooled and filtered. The residue obtained by evaporation of the solvent was purified by column chromatography using EtOAc:hexane (1:9) as eluent to afford the product **33** as an oil (0.50 g, 86%). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 1.43 (s, 9H, 3×CH_3), 3.77–3.89 (m, 2H, NCH_2), 4.43–4.55 (m, 4H, $ArCH_2N$ and OCH_2), 5.09–5.42 (m, 4H, 2× CH=CH_2), 5.70–5.86 (m, 1H, NCH_2C*H*=CH_2), 6.01–6.10 (m, 1H, OCH_2C*H*=CH_2), 6.84 (d, 1H, *J* 8.4 Hz, ArH), 6.93 (dd [app. t], 1H, J_1=J_2 8.2 Hz, ArH), 7.18–7.20 (m, 2H, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 28.4 (3×CH_3), 44.6 ($ArCH_2N$), 49.2 (NCH_2), 68.8 (OCH_2), 79.8 (C), 111.4 (CH), 116.4 (C), 117.2 (CH_2), 118.6 (CH_2), 120.6 (C), 128.0 (2×CH), 133.3 (CH), 134.0 (CH), 155.9 (2×C); HRMS: M^+, calcd for $C_{18}H_{25}NO_3$ 303.1836, found 303.1830.

***N*-allyl-*N*-(2-(allyloxy)benzyl)-4-methylbenzenesulfonamide 34**: To a solution of the tosyl phenol **32** (0.14 g, 0.45 mmol) in dry acetone (25 mL) containing anhydrous K_2CO_3 (0.31 g; 2.3 mmol) was added allyl bromide (0.28 g, 2.3 mmol) and the resultant mixture was vigorously stirred and heated under reflux for 24 h. The cooled mixture was filtered and the residue obtained by evaporation of the solvent was chromatographed using EtOAc:hexane (1:4) as eluent to afford the diallyl product **34** (0.70 g, 43% yield). Further elution gave unreacted starting tosyl phenol (0.070 g; 0.23 mmol). The yield based on starting material consumed is thus 87%. ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 2.45 (s, 3H, $ArCH_3$), 3.81 (d, 2H, *J* 6.3 Hz, NCH_2CH), 4.44 (s, 2H, $ArCH_2N$), 4.50 (d, 2H, *J* 5.1 Hz, OCH_2CH), 5.01–5.08 (m, 2H, NCH_2CH=CH_2), 5.28–5.40 (m, 2H, OCH_2CH=CH_2), 5.54–5.58 (m, 1H, NCH_2C*H*=CH_2), 5.96–6.02 (m, 1H, OCH_2C*H*=CH_2), 6.81 (d, 1H, *J* 8.1 Hz, ArH), 6.95 (dd [app. t], 1H, J_1=J_2 8.1 Hz, ArH), 7.22 (dd [app. t], 1H, J_1=J_2 8.1 Hz, ArH), 7.31 (d, 2H, *J* 8.4 Hz, 2×ArH), 7.39 (d, 1H, *J* 8.1 Hz, ArH), 7.72 (d, 2H, *J* 8.4 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 ($ArCH_3$), 45.1 ($ArCH_2N$), 50.5 (NCH_2CH), 68.8 (OCH_2), 111.4 (CH), 117.4 (CH_2), 118.7 (CH_2), 120.8 (CH), 124.8 (C), 127.3 (2×CH), 128.6 (CH),129.5 (2×CH), 130.0 (CH), 132.8 (CH), 133.2 (CH), 137.7 (C), 143.0 (C), 156.3(C); HRMS: M^++1, calcd for $C_{20}H_{24}NO_3S$ 358.1477, found 358.1468.

4-Methyl-*N*-(2-{[(4'-methylphenyl)sulfonyl]amino}benzyl)benzenesulfonamide 36[40]: To a mixture of TsCl (8.6 g, 45 mmol) in pyridine (25 mL) at 0 °C was added 2-aminobenzylamine **35** (2.5 g, 21 mmol) and the resulting reaction mixture stirred for 20 h at 24 °C. Removal of the solvent under vacuum yielded a residue which was purified by column chromatography using EtOAc:hexane (1:1) as eluent to afford the product **36** as a white solid (5.1 g, 59% yield); mp: 127–129 °C. Spectral data of this compound compared well with that published in the literature.[40] ^{1}H NMR (300 MHz,$CDCl_3$): δ(ppm) = 2.39 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 3.81 (d, 2H, *J* 6.6 Hz, $ArCH_2$), 5.10–5.14 (m, 2H, 2×NH), 7.08–7.33 (m, 6H, 6×ArH), 7.34 (d, 2H, *J* 8.2 Hz, 2×ArH), 7.56 (d, 2H, *J* 8.2Hz, 2×ArH), 7.72 (d, 2H, *J* 8.2 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 (2×CH_3), 43.9 (CH_2), 125.8 (CH), 126.7 (CH), 127.1 (2×CH), 127.3 (2×CH), 129.2 (CH), 129.5 (2×CH), 129.8 (2×CH), 130.7 (CH), 130.9 (C), 134.9 (C), 136.0 (C), 136.2 (C), 143.8 (C), 143.8 (C); HRMS: M^+, calcd for $C_{21}H_{22}N_2O_4S_2$ 430.1021, found 430.1023.

***N*-Allyl-*N*-{2-{ally[(4'-methylphenyl)sulfonyl]amino}methyl)phenyl]-4-methylbenzenesulfonamide 38**: To a solution of benzenesulfonamide **36** (4.0 g, 8.8 mmol) in acetone (160 mL) containing K_2CO_3 (4.88 g, 35.4 mmol) was added allyl bromide (4.83 g, 39.9 mmol) and the reaction mixture was vigorously stirred for 18 h at 60 °C. H_2O (100 mL) was added and the crude product was extracted with EtOAc (4×200 mL) to afford a residue purified by column chromatography using EtOAc:hexane (3:7) as eluent to give the product **38** as a white solid (3.8 g, 83% yield); mp: 117–119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.45 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.69–3.79 (m, 2H, $ArCH_2$), 3.89 (dd, 1H, *J* 6.2, 15.2 Hz, NCH_2), 4.39 (dd, 1H, *J* 6.2, 15.6 Hz, NCH_2), 4.51 (d, 1H, *J* 17.0 Hz, NCH_2), 4.76 (d, 1H, *J* 17.0 Hz, NCH_2), 4.94–5.07 (m, 4H, 2×NCH_2CH=CH_2), 5.52–5.73 (m, 2H, 2×NCH_2C*H*=CH_2), 6.41 (d, 1H, *J* 7.9 Hz, ArH), 7.09 (dd [app. t], 1H, J_1=J_2 7.6 Hz, ArH), 7.34–7.36 (m, 5H, 5×ArH), 7.50 (d, 2H, *J* 7.7 Hz, 2×ArH), 7.74 (d, 1H, *J* 7.8 Hz, ArH), 7.77 (d, 2H, *J* 7.7 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.5 (2×CH_3), 47.5 (CH_2), 51.2 (CH_2), 54.8 (CH_2), 118.8 (CH_2), 119.9 (CH_2), 127.2 (4×CH), 128.1 (2×CH), 128.5 (CH), 128.8 (CH),

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129.4 (2×CH), 129.7 (2×CH), 132.0 (CH), 132.5 (CH), 134.6 (C), 137.1 (2×C), 138.9 (C), 143.2 (C), 143.8 (C); HRMS; M^+, calcd for $C_{27}H_{30}N_2O_4S_2$ 511.1647, found 511.1680.

***N*-Allyl-2-(allylamino)methyl)aniline 39**: To a mixture of 2-aminobenzylamine **35** (0.37 g, 3.1 mmol) in anhydrous acetone (20 mL) and potassium carbonate (0.97 g, 7.0 mmol), was added allyl bromide (0.73 g, 6.0 mmol) and the resulting mixture was vigorously stirred under reflux for 4 h. The cooled solution was filtered and evaporation of the solvent afforded a residue which was purified by very careful silica gel column chromatography using EtOAc/hexane (1:4) as eluent, to afford a mixture of products, followed by the desired diallyl compound **39** as a mobile oil (0.050 g, 8% yield). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 3.05 (s, 2H, NCH_2CH=), 3.06 (s, 2H, NCH_2CH=), 3.58 (s, 2H, $ArCH_2N$), 4.50–4.80 (broad signal, 2H, 2×NH), 5.14–5.18 (m, 4H, 2× =CH_2), 5.83–5.90 (m, 2H, 2×=CH), 6.63–6.65 (m, 2H, 2×ArH), 6.97 (d, 1H, *J* 8.2 Hz, H-5), 7.07 (dd [app. t], 1H, J_1=J_2 8.3 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 56.1 (2× NCH_2CH=), 57.4 ($ArCH_2N$), 115.5 (CH), 117.6 (CH), 118.0 (2×=CH_2), 122.8 (C), 128.2 (CH), 130.6 (CH), 135.1 (2×=CH), 147.1 (C); HRMS calcd for $C_{13}H_{18}N_2$ 202.1471, found 202.1468.

Unsuccessful RCM reactions:

As initial RCM experiments with the Grubbs II catalyst (5–10 mol%) in CH_2Cl_2 only returned unreacted starting material, subsequent reactions were performed in dry toluene (0.3–0.7 M) at 80 °C, for a minimum of 18 h. Reactions were monitored by TLC and removal of the solvent afforded residues which were purified by careful column chromatography using EtOAc:hexane mixtures as eluent to give compounds which were evaluated by NMR spectroscopy. Some of the unsuccessful reaction conditions are described in the table 2 below:

Table 2:

Starting material	Reaction concentration (M), toluene	Outcome
17a	0.033	Starting material recovered (30%) and decomposition observed
17b	0.068	Starting material recovered (30%)
17c	0.036	Starting material recovered (44%)
17d	0.042	Decomposition observed
22	0.070	Only starting material observed (by NMR spectroscopy
26	0.035	Decomposition observed
39	0.033	Only starting material observed (by NMR spectroscopy

Successful RCM reactions:

1-Tosyl-2,5-dihydrobenzo[*c*][1,5]oxazonin-7(1*H*)-one 40: Diene **28** (0.21 g, 0.60 mmol) in dry toluene (25 mL) was treated with Grubbs II catalyst (5 mol%, 0.02 g, 0.03 mmol) and the reaction mixture stirred for 18 h at 70 °C. Removal of the solvent afforded a residue which was purified by careful column chromatography using EtOAc:hexane (5-40% gradient) as eluent to give starting material **28** (0.080 g, 38% recovered), followed by the cyclized product **40** as a thick oil (0.050 g, 15%). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 2.40 (s, 3H, $ArCH_3$), 4.18–4.43 (m, 2H, NCH_2), 4.68–4.75 (m, 1H, OCH_2), 5.02–5.05 (m, 1H, OCH_2), 5.80–6.07 (m, 2H, CH=CH), 6.88–6.92 (m, 1H, ArH), 7.27 (d, 2H, *J* 8.2 Hz, 2×ArH), 7.29–7.40 (m, 2H, 2×ArH), 7.52 (d, 2H, *J* 8.2 Hz, 2×ArH), 7.70–7.86 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 (CH_3), 53.4 and 54.6 (NCH_2), 64.8 and 66.1 (OCH_2), 105.0 (C), 118.8 (CH), 119.0 (CH), 127.5 (CH), 127.6 (CH), 128.3 (CH), 128.4 (CH), 129.4 (2×CH), 130.9 (CH), 132.6 (CH), 137.9 (2×C), 143.2 (C), 165.6 (C); HRMS; M^+, calcd for $C_{18}H_{17}NO_3$ 343.0879, found 343.0871.

***Tert*-butyl 2,5-dihydrobenzo[*b*][1,5]oxazonine-6(7*H*)-carboxylate 41**: Diene **33** (0.34 g, 1.1 mmol) in dry toluene (40 mL) was treated with Grubbs II catalyst (5 mol %, 0.05 g, 0.06 mmol) and the reaction mixture stirred for 12 h at 70 °C. Removal of the solvent afforded a residue which was purified by careful column chromatography using EtOAc:hexane (5:95) as eluent to give the desired cyclized product **41** as a thick oil (0.090 g, 28% yield). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 1.51 (s, 9H, 3×CH_3), 3.69–3.78 (m, 2H, N*C*H_2CH=CH), 4.46–4.54 (m, 4H, OCH_2 and $ArCH_2N$), 4.80–4.90 (m, 2H, CH=CH), 6.84 (d, 1H, *J* 8.1 Hz, ArH), 6.95 (dd [app. t], 1H, J_1=J_2 8.4 Hz, ArH), 7.20–7.25 (m, 2H, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 28.6 (3×CH_3), 41.2 and 41.8 (N*C*H_2CH=), 46.1 and 46.8 ($ArCH_2N$), 68.4 and 68.5 (OCH_2), 79.8 and 80.2 (C), 111.4 (2×CH), 121.2 (C), 126.8 (CH), 128.6 (CH), 130.0 (CH), 130.7 (CH), 156.0 (C), 156.8 (C); HRMS; M^+, calcd for $C_{16}H_{21}NO_3$ 275.1522, found 275.1523.

6-Tosyl-2,5,6,7-tetrahydrobenzo[*b*][1,5]oxazonine 42: To a solution of the *O*-allyl-*N*-allyl tosylamide **34** (0.11 g, 0.31 mmol) in dry toluene was added Grubbs II catalyst (0.01 g, 0.01 mmol) and the mixture was heated at 70 °C with stirring for 72 h. The residue obtained upon removal of the solvent was chromatographed and eluted with EtOAc:hexane (1:4) to afford a thick colourless oil (0.05 g) comprising a mixture of compounds. PLC of this mixture with the same solvent to give 4 major bands:

Band 1: A white semi-crystalline solid of the diconjugated isomerized material, **4-methyl-*N*-[(*E*)-prop-1-en-1-yl)-*N*-(2-{[(*Z*)-prop-1-en-1-yl]oxy}benzyl)benzenesulfonamide 44** (0.060 g, 12% yield). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 1.58 (dd, 3H, *J* 1.8, 6.9 Hz, CH=CHCH_3), 1.69 (dd, 3H, *J* 1.8, 6.9 Hz, CH=CHCH_3), 2.46 (s, 3H, $ArCH_3$), 4.54 (s, 1H, $ArCH_2N$ rotamer), 4.59 (s, 1H, $ArCH_2N$ rotamer), 4.73–4.80 (m, 1H, CH=C*H*CH_3), 4.91–4.95 (m, 1H, CH=C*H*CH_3), 6.35 (dq, 1H, *J* 1.8, 8.4 Hz, *cis* OC*H*=CH), 6.65 (dq, 1H, *J* 1.8, 14.1 Hz, *trans* NC*H*=CH), 6.91 (d, 1H, *J* 7.5 Hz, ArH), 7.03 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.22 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.33 (d, 2H, *J* 8.1 Hz, 2×ArH), 7.40 (d, 1H, *J* 7.5 Hz, ArH), 7.73 (d, 2H, *J* 8.1 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 15.3 (2×CH_3), 21.6 ($ArCH_3$), 44.0 ($ArCH_2N$), 107.6 (CH), 114.1 (CH), 122.8 (CH), 124.7 (CH), 126.3 (C), 128.0 (2×CH), 128.2 (CH), 128.3 (CH), 128.3 (2×CH), 136.3 (C), 141.9 (C); HRMS; M^++1, calcd for $C_{20}H_{24}NO_3S$ 358.1477, found 358.1466.

Band 2: Thick oil (0.015 g, 23% yield) for the *cis*-*O*-propenyltosylamide, **(*Z*)-*N*-allyl-4-methyl-*N*-(2-(prop-1-en-1-yloxy)benzyl)benzenesulfonamide 45**. ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 1.67 (dd, 3H, *J* 1.5, 6.9 Hz, CH=CHCH_3), 2.45

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(s, 3H, $ArCH_3$), 3.83 (sharp m, 2H, NCH_2CH=CH), 4.42 (s, 1H, $ArCH_2N$ rotamer), 4.47 (s, 1H, $ArCH_2N$ rotamer), 4.85–4.95 (m, 1H, CH=C*H*CH_3), 5.00–5.10 (m, 2H, CH=CH_2), 5.50–5.63 (m, 1H, NCH_2CH=CH), 6.26 (dq, 1H, *J* 1.5, 6.0 Hz, *cis* OC*H*=CH), 6.88 (d, 1H, *J* 7.5 Hz, ArH), 7.05 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.22 (dd [app. t], 1H, J_1=J_2 7.5 Hz, ArH), 7.31 (d, 2H, *J* 8.4 Hz, 2×ArH), 7.45 (d, 1H, *J* 7.5 Hz, ArH), 7.72 (d, 2H, *J* 8.4 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 9.4 (=CHCH_3), 21.5 ($ArCH_3$), 44.7 ($ArCH_2N$), 50.5 (NCH_2CH=), 107.9 (CH), 114.4 (CH), 118.8 (CH_2), 122.6 (CH), 122.7 (C), 127.0 (2×CH), 127.2 (CH), 128.7 (2×CH), 129.6 (CH), 132.6 (CH), 137.5 (C), 140.7 (CH), 143.1 (C), 155.3 (C); HRMS; M^++1, calcd for $C_{20}H_{24}NO_3S$ 358.1477, found 358.1467.

Band 3: Starting material **34** (0.026 g, 24% recovered).

Band 4: White semisolid crystalline metathesis product, **6-tosyl-2,5,6,7-tetrahydrobenzo[*b*][1,5]oxazonine 42** (0.060 g, 13%). ^{1}H NMR (300 MHz $CDCl_3$): δ(ppm) = 2.46 (s, 3H, $ArCH_3$), 3.89 (d, 2H, *J* 8.4 Hz, NCH_2CH=CH), 4.37 (s, 2H, $ArCH_2N$), 4.73 (dd, 2H, *J* 0.9, 5.7 Hz, OCH_2CH=CH), 5.56–5.82 (m, 2H, C*H*=C*H*), 7.04 (dd [app. t], 2H, J_1=J_2 7.8 Hz, 2×ArH), 7.01–7.40 (m, 4H, 4×ArH), 7.74 (d, 2H, *J* 8.1 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 ($ArCH_3$), 46.1 ($ArCH_2N$), 47.9 (NCH_2CH), 68.3 (OCH_2), 119.5 (CH), 123.9 (CH), 127.1 (2×CH), 128.8 (C), 129.7 (2×CH), 129.8 (CH), 129.9 (CH), 131.4 (CH), 131.6 (CH), 137.7 (C), 143.2 (C), 157.9 (C); HRMS; M^++1, calcd for $C_{18}H_{20}$ NO_3S 330.1164, found 330.1155.

1,6-Bis[(4'-methylphenyl)sulfonyl]-2,5,6,7-tetrahydro-1*H*-1,6-benzodiazonine 43: Diene **38** (0.10 g, 0.19 mmol) in CH_2Cl_2 (10 mL) was treated with the Grubbs II catalyst (10 mol%, 0.017 g, 0.02 mmol) and the reaction mixture was stirred for 18 h under reflux (60 °C, oil bath). Removal of the solvent under high vacuum gave a residue which was purified by column chromatography using EtOAc:hexane (1:4) as eluent to afford the cyclized product **43** as a white solid (0.088 g, 96% yield); mp: 84–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 6H, 2×CH_3), 3.53–3.60 (m, 2H, $ArCH_2$), 4.05–4.12 (m, 1H, NCH_2), 4.29–4.34 (m, 1H, NCH_2), 4.56–4.65 (m, 2H, NCH_2), 5.56–5.59 (m, 2H, CH=CH), 6.47 (d, 1H, *J* 7.9 Hz, ArH), 7.15–7.19 (m, 1H, ArH), 7.26–7.35 (m, 5H, 5×ArH), 7.55–7.61 (m, 3H, 3×ArH), 7.73 (bd, 2H, *J* 8.2 Hz, 2×ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.5 (CH_3), 21.6 (CH_3), 44.7 (CH_2), 47.7 (CH_2), 48.0 (CH_2), 126.8 (2×CH), 126.9 (CH), 127.6 (CH), 127.9 (2×CH), 129.1 (CH), 129.4 (CH), 129.6 (2×CH), 129.8 (2×CH), 130.7 (CH), 132.4 (CH), 135.0 (C), 137.6 (C), 138.3 (C), 139.2 (C), 143.3 (C), 143.9 (C); M^+, calcd for $C_{25}H_{26}N_2O_4S_2$ 482.1334, found 482.1338.

X-ray crystal structure details of compound **43**: crystallized from EtOAc-hexane, formula: $C_{25}H_{26}N_2O_4S_2$, *M* = 482.60, crystal size 0.22 × 0.16 × 0.03 mm^3, *a* = 14.554(7) Å, *b* = 10.454(5) Å, *c* = 15.725(7) Å, b = 107.694(5)°, *V* = 2329.7(18) $Å^3$, ρ_{calc} = 1.376 Mg/m^3, μ = 0.264 mm^{-1}, F(000) = 1016, *Z* = 4, monoclinic, space group P21/c, *T* = 173(2) K, 16606 reflections collected, 5620 independent reflections, θ_{max} 27.997°, 300 refined parameters, maximum residual electron density 0.352 and -0.374 e.$Å^{-3}$. R_1 = 0.0497, wR_2 = 0.1152. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-1530894.

1,6-Bis[(4'-methylphenyl)sulfonyl]-2,3,6,7-tetrahydro-1*H*-1,6-benzodiazonine 46: 2,5,6,7-tetrahydro-1*H*-1,6-benzodiazonine **43** (0.030 g, 0.062 mmol) in benzene-d_6 was treated with the $[RuClH(CO)(PPh_3)_3]$ (10 mol%, 0.010 g, 0.01 mmol) and the reaction mixture was stirred at 90 °C for 40 h. The solvent was removed under high vacuum and the residue purified by column chromatography using EtOAc:hexane (3:7) as eluent, to afford the product **46** as a brown-coloured solid (0.029 g, 97% yield); mp: 192–196 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.76–1.99 (m, 1H, NCH_2CH_2), 2.04–2.17 (m, 1H, NCH_2CH_2), 2.35 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 3.02-3.08 (m, 1H, NCH_2CH_2), 3.91–3.98 (m, 1H, NCH_2CH_2), 4.46–4.59 (m, 2H, $ArCH_2$), 5.61–5.65 (m, 1H, NCH=C*H*), 6.09 (d, 1H, *J* 7.1 Hz, NC*H*=CH), 6.34 (d, 1H, *J* 7.8 Hz, ArH), 7.08–7.13 (m, 1H, ArH), 7.19–7.23 (m, 4H, 4×ArH), 7.29–7.34 (m, 1H, ArH), 7.44 (d, 2H, *J* 7.9 Hz, 2×ArH), 7.62 (d, 2H, *J* 7.9 Hz, 2×ArH), 7.73 (d, 1H, *J* 7.6 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.5 (CH_3), 21.6 (CH_3), 25.2 (CH_2), 51.8 (CH_2), 52.9 (CH_2), 127.3 (CH), 127.4 (2×CH), 127.6 (2×CH), 129.0 (CH), 129.3 (CH), 129.5 (2×CH), 129.6 (2×CH), 130.3 (CH), 132.0 (CH), 132.8 (CH), 135.4 (C), 136.0 (C), 137.9 (C), 140.1 (C), 143.6 (C), 143.6 (C); HRMS; M^+, calcd for $C_{25}H_{26}N_2O_4S_2$ 482.1334, found 482.1341.

X-ray crystal structure details of compound **46**: crystallized from EtOAc-hexane, formula: $C_{25}H_{26}N_2O_4S_2$, *M* = 482.60, crystal size 0.34 × 0.22 × 0.18 mm^3, *a* = 14.600(4) Å, *b* = 10.430(3) Å, *c* = 15.950(4) Å, b = 107.694(5)°, *V* = 2314.0(10) $Å^3$, ρ_{calc} = 1.385 Mg/m^3, μ = 0.266 mm^{-1}, F(000) = 1016, *Z* = 4, monoclinic, space group P21/c, *T* = 173(2) K, 13269 reflections collected, 4538 independent reflections, θ_{max} 25.999°, 300 refined parameters, maximum residual electron density 0.232 and -0.411 e.$Å^{-3}$. R_1 = 0.0357, wR_2 = 0.0903. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-1530896.

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