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Synthesis of Substituted 2,3-Dihydro-1*H*-2-benzazepines and 1,2-Dihydroisoquinolines Using an Isomerization-Ring-Closing Metathesis Strategy: Scope and Limitations

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An isomerization-ring-closing metathesis (RCM) approach was used for the synthesis of substituted 2,3-dihydro-1*H*-2-benzazepines and 1,2-dihydroisoquinolines. The 2,3-dihydro-1*H*-2-benzazepines were obtained from *N*-protected *N*-{2-[(1*E*)-prop-1-en-1-yl]benzyl}prop-2-en-1-amines by RCM reaction. A double isomerisation reaction on the *N*-protected *N*-(2-allylbenzyl)prop-2-en-1-amines and a subsequent RCM afforded the substituted 1,2-dihydroisoquinolines. Finally, a selective isomerization of the allylamine group of *N*-protected *N*-(2-allylbenzyl)prop-2-en-1-amines by [RuClH(CO)-$(PPh_3)_3$], followed by RCM, did not afford the expected 2,5-dihydro-1*H*-2-benzazepines but afforded products resulting from deallylation and isomerization of the starting material.

Introduction

Benzazepines **1** as possible pharmaceutical scaffolds have caught the attention of the medicinal chemistry community. Benzazepine examples include compounds such as capsazepine **2**,[1] a commercially available competitive agonist for the vanilloid receptor (VR1) used in the treatment of neuropathic pain (Figure 1), compound **3**, a Gram-positive antibacterial,[2] and compound **4**, a potent histamine H_3 receptor antagonist.[3]

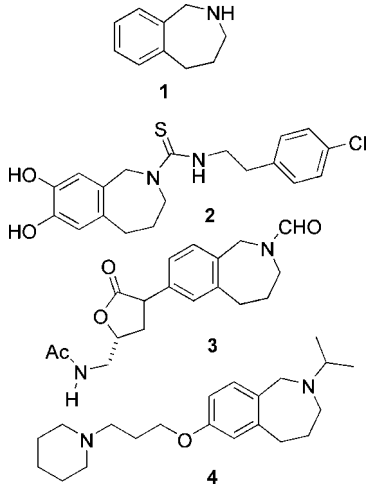

Figure 1. Benzazepine-containing compounds.

Tetrahydroisoquinolines **5** (THIQs) and, of particular interest to us, 1,2-dihydroisoquinolines **6** (DHIQs), have also been incorporated into pharmaceutical compounds. Examples with the latter skeleton include a number of anticancer 1,2-dihydroellipticines **7**,[4] as well as some DHIQ derivatives of KNI-279, a potent HIV protease inhibitor (see **8** in Figure 2).[5]

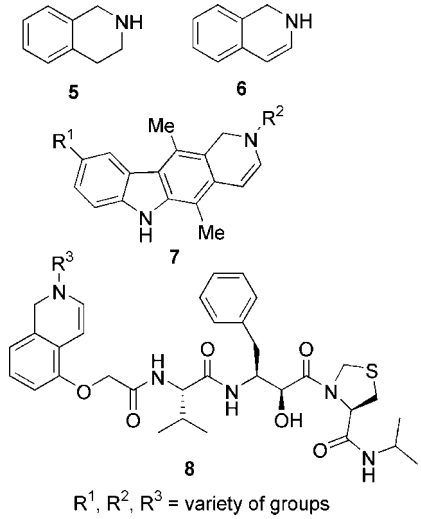

Figure 2. 1,2-DHIQ-containing compounds.

The use of benzazepines with an unsaturation in the heterocyclic ring, such as 2,3-dihydro-1*H*-2-benzazepine (**9**) or 2,5-dihydro-1*H*-2-benzazepine (**10**), have however seen very

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little synthetic application (Figure 3). In addition, compounds such as **9** and **10** have not seen much pharmaceutical investigation, perhaps due to the lack of general synthetic methods for their synthesis. This is surprising as the availability of an alkene in the heterocycle would also offer opportunities for the further functionalization of the benzazepine skeleton. Of the few examples we could find, work by Kogen and co-workers described the synthesis of a small set of substituted 2,3-dihydro-1*H*-benzazepines (Figure 3).[6] This group used a ring closing metathesis (RCM) strategy by reaction of a styrene and an allylamine, as shown in the conversion of compound **11** to afford **12**. Compounds of this type were then tested as acetylcholinesterase (AChE) and serotonin (SERT) dual inhibitors. In addition, Dieltiens and Stevens have recently reported a ring-closing enyne metathesis-cross metathesis approach to afford 1-phosphonylated benzazepines.[7]

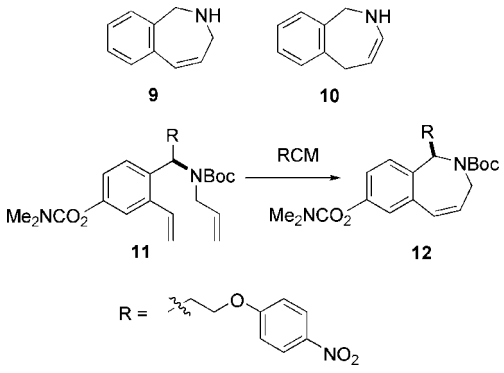


Figure 3. Kogen's RCM approach to 2,3-dihydro-1*H*-benzazepines.

The application of RCM to the synthesis of 1,2-DHIQs has also seen little work reported in the literature. Bennasar and co-workers were however able to synthesize a small library of simple DHIQs by an interesting sequential *N*-acylamide methylenation followed by RCM (**13**→**14**, Figure 4).[8] However, when the same workers attempted to synthesize the 2,5-dihydro-1*H*-2-benzazepine **16** from substrate **15**, using similar conditions, only DHIQ **14c** was isolated, due to the competitive isomerization of the allyl group prior to RCM.

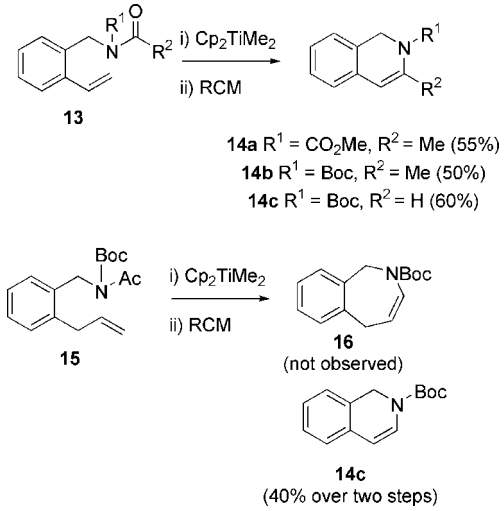


Figure 4. Bennesar's approach to 1,2-DHIQs.

Our research group has been investigating the application of isomerization reactions followed by RCM[9] as a strategy to afford substituted benzannulated heterocycles. In this way we have successfully synthesized a range of benzo-fused heterocycles.[10] Recently we communicated the synthesis of a solitary 2,3-dihydro-1*H*-2-benzazepine and 1,2-dihydroisoquinoline by way of an isomerisation-RCM strategy.[11] In this paper we wish to demonstrate that this strategy, illustrated by the retrosyntheses shown in Figure 5, is firstly amenable to the synthesis of a number of protected 2,3-dihydro-1*H*-2-benzazepines (i.e. **18**→**17**). In addition, the 1,2-dihydroisoquinoline skeleton **19** could also be accessed by the RCM of substrate **20**. Finally, we describe attempts towards the synthesis of a regioisomeric 2,5-dihydro-1*H*-2-benzazepine (i.e. **22**→**21**) by the selective isomerization of the *N*-allyl group prior to RCM. In this paper we will also discuss the scope and limitations of the isomerisation-RCM approach towards the benzannulated compounds of general structure **17**, **19** and **21** (Figure 5). This work was performed using the readily prepared 3-isopropoxy-4-methoxy compound **23** (Scheme 1) as described in some of our previous work.[10]

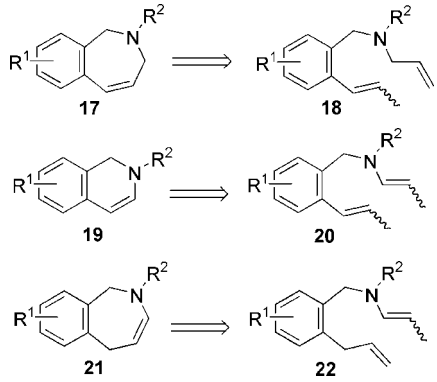
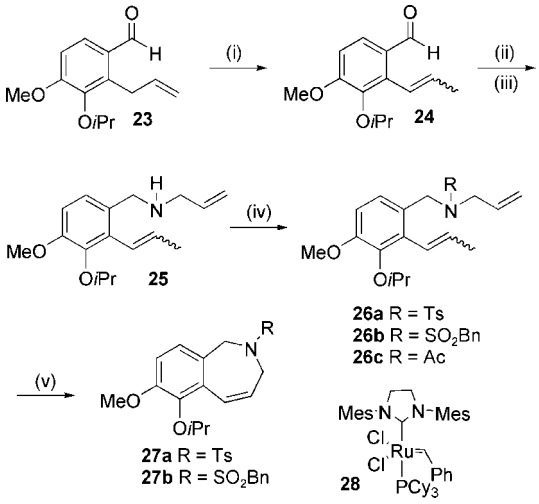


Figure 5. Retrosynthetic analysis of target structures.

Results and Discussion

Synthesis of 2,3-Dihydro-1*H*-2-benzazepines

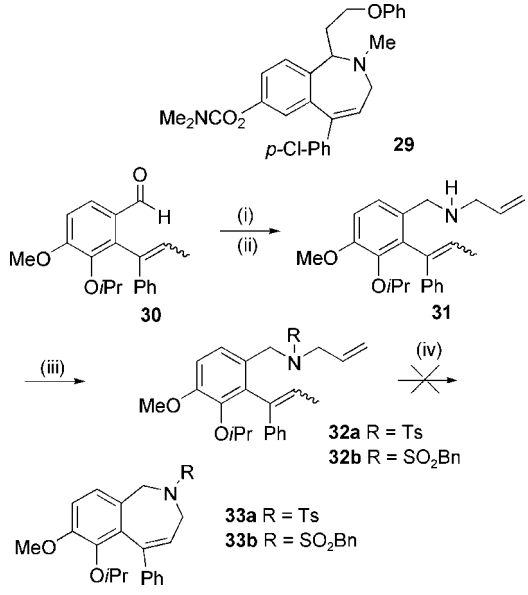
For the synthesis of the 2,3-dihydro-benzazepines we needed to synthesize the general diene substrate **18** which contained a styrene functionality. To this end we isomerized the allyl group of the substituted benzaldehyde **23** to the thermodynamically preferred styrene **24** (mainly *E*) with $[RuClH(CO)(PPh_3)_3]$,[12] as described previously (Scheme 1).[10c] Treatment of benzaldehyde **24** with allylamine, followed by a sodium borohydride reduction, then afforded amine **25** in good yield. At this point the amine was protected with a tosyl- (**26a**), benzylsulfonyl- (**26b**) and acetyl-protecting (**26c**) group to determine if these protecting groups would have an effect on the subsequent RCM reaction.



Scheme 1. (i) $[RuClH(CO)(PPh_3)_3]$ (2%), toluene, 80 °C, quantitative, see ref.[10c]; (ii) allylamine (1.4 equiv.), room temp., 22 h; (iii) $NaBH_4$ (1.2 equiv.), MeOH, 0 °C, 2 h, 89% over two steps; (iv) **26a** R = Ts, NEt_3 (1.4 equiv.), tosyl chloride (1.2 equiv.), CH_2Cl_2, 0 °C to room temp., 3 h, 77%; **26b** R = SO_2Bn, NEt_3 (2.5 equiv.), benzylsulfonyl chloride (1.1 equiv.), CH_2Cl_2, room temp., 18 h, 29%; **26c** R = Ac, acetic anhydride (1.5 equiv.), pyridine (2.5 equiv.), room temp., 3 h, 72%; (v) for **27a**, 5% **28**, 60 °C, 20 h, 82%; for **27b**, 10% **28**, 80 °C, 20 h, 39%; for **27c**, complex mixture.

The RCM reaction was then performed on substrates **26a**–**c** with varying success (Scheme 1).[13] The treatment of **26a** (R = Ts) with 5% Grubbs second-generation catalyst **28** gratifyingly afforded the corresponding tosyl-protected 2,3-dihydro-1*H*-2-benzazepine **27a** in good yield (82%). However, the RCM reactions on substrate **26b** gave less than desirable results. Even doubling the catalyst loading for **26b** resulted in a poor yield of the desired benzazepine **27b** (39%). Finally, the RCM reactions of substrate **26c** only gave a complex mixture of products, which we were unable to purify and identify. This was probably due to competitive isomerizations and deallylation reactions as discussed later in the paper.

We were also interested in using our approach to access structures containing a phenyl ring directly attached to the benzylic position located on the heterocyclic ring (see for instance the AChE and SERT dual inhibitor **29** designed by Kogen and co-workers, Scheme 2).[6b] We thus synthesized compound **30**,[14] in which the styrene was already in place, and subjected this compound to the same reductive amination as described before, to afford allylamine **31** in good yield. The amine group in this compound was then protected with the two sulfonamide protecting groups to afford **32a** and **32b** (Scheme 2). We were now in a position to see if the RCM would tolerate the presence of the sterically hindered, electron-rich styrene functionality. Unfortunately, when substrates **32a** and **32b** were subjected to metathesis with catalyst **28** none of the desired cyclized product **33** was obtained. The ^1H NMR spectra from both substrates indicated the possibility of compounds with two isomerized allyl groups. This would suggest that the allylamine group had been isomerized under the reaction conditions.[15] HRMS on these mixtures provided tentative evidence of the desired ring-closed products but we were unable to obtain pure desired unsaturated benzazepines **33a** and **33b**. A possible reason for these poor results is that the highly hindered and electron-rich diphenyl styrene functionality is not a good alkene partner for this metathesis reaction.[16] Furthermore, the steric crowding at the styrene is likely further exacerbated by *peri* interactions between the isopropyloxy and phenyl groups on substrate **32**.

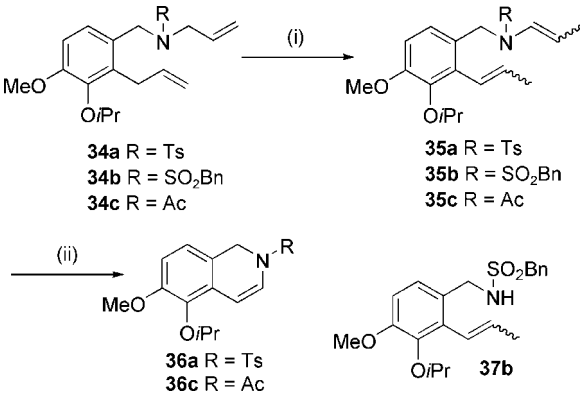


Scheme 2. (i) Allylamine (1.4 equiv.), room temp., 21 h; (ii) $NaBH_4$ (1.2 equiv.), MeOH, 0 °C, 2 h, quantitative over 2 steps; (iii) **32a** R = Ts, NEt_3 (1.4 equiv.), tosyl chloride (1.2 equiv.), CH_2Cl_2, 0 °C to room temp., 3 h, 71%; **32b** R = SO_2Bn, NEt_3 (2.5 equiv.), benzylsulfonyl chloride (1.1 equiv.), CH_2Cl_2, room temp., 4 h, 45%; (iv) 5–8% **28**, 60–80 °C, 22–23 h, complex mixtures.

Synthesis of 1,2-Dihydroisoquinolines

At this point in the project we decided to isomerize both the allyl groups of previously synthesized[10a] compounds **34** with $[RuClH(CO)(PPh_3)_3]$, to afford products **35** as a mixture of *E*/*Z* isomers, and then to see if we could perform the metathesis reaction on these substrates (Scheme 3). Initially **34a** was exposed to $[RuClH(CO)(PPh_3)_3]$ and NMR spectroscopy was used to confirm the success of the isomerisation. However, **35a** was not isolated and catalyst **28** was added directly to the reaction mixture to facilitate the metathesis process. To our satisfaction, 1,2-DHIQ **36a** was obtained in a yield of 76% over the two steps, after chromatographic purification. This methodology proved difficult to repeat when using substrates **34b** and **34c**, and so we decided to isolate the intermediate bis-isomerized compounds **35b** and **35c**. Compound **35c** (R = Ac) was readily obtained in high yield (94%) from **34c**. However, when **34b** (R = SO_2Bn) was treated with $[RuClH(CO)(PPh_3)_3]$, under high temperature conditions (solventless, 135–140 °C), only compound **37b**[17] was obtained, a product from which the *N*-allyl group had been cleaved under the reaction condi-

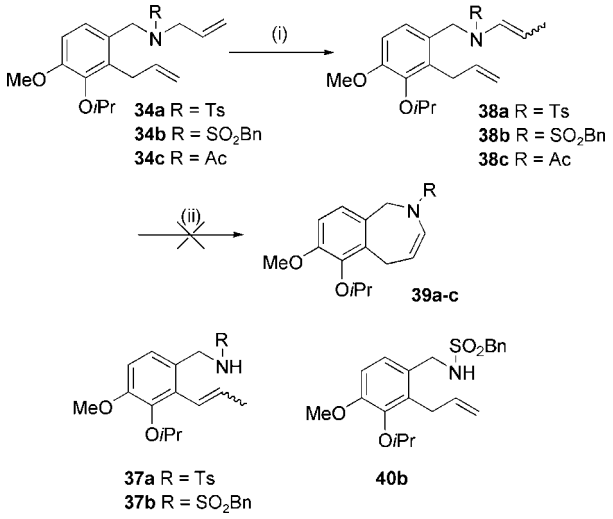
tions.[18] A subsequent reaction at lower temperature (90–100 °C) did afford the bis-isomerized compound **35b**. Unfortunately we were unable to obtain the desired 1,2-DHIQ **36b** by RCM of **35b**, but compound **35c** readily afforded the ring-closed 1,2-DHIQ **36c** in a good yield of 78%, when treated with catalyst **28**.



Scheme 3. (i) [RuClH(CO)(PPh_3)$_3$], 5 mol-%, toluene, Ar, 90–110 °C, ca. 20 h, **35a** not isolated, **35b** 87% (at 135–140 °C only **37b** 56%), **35c** 94%; (ii) catalyst **28**, 5–10 mol-%, toluene, 110 °C, 2–3 h, **36a** 76% (over 2 steps), **36b** complex mixture, **36c** 78%.

Attempted Synthesis of 2,5-Dihydro-1*H*-2-benzazepines

During our investigations into the synthesis of the 1,2-DHIQs it was discovered that the *N*-allyl group of a compounds **34a**–**c** could be isomerized in the presence of the aryl allyl group using the catalyst [RuClH(CO)(PPh_3)$_3$], as long as the reaction temperatures were moderate (ca. 80 °C). This observation thus presented a promising route to the synthesis of the 2,5-dihydro-1*H*-2-benzazepines. Compounds **38a**–**c** were thus synthesized by the treatment of **34a**–**c** with [RuClH(CO)(PPh_3)$_3$] under moderate conditions (1% catalyst, 80 °C in toluene), as depicted in Scheme 4. It was noted that above 80 °C the aryl allyl group also started to isomerize and prolonged heating resulted in other decomposition products. This particular isomerization is of interest as there are very few examples in the literature where a catalyst demonstrates complete selectivity for one allyl group over another.[19] These compounds **38a**–**c**, containing a protected vinylamine group,[20] were then submitted to RCM with catalyst **28** (Scheme 4). Unfortunately the metathesis of substrates **38a**–**c** led to complex product mixtures which were purified with difficulty. In addition we were disappointed to not isolate any of the desired 2,5-dihydro-1*H*-2-benzazepines. For the reaction on **38a** (R = Ts) we were only able to isolate **37a**, indicating that deallylation had occurred, in addition to an isomerization of the aryl allyl group. Furthermore, reaction of **38b** only produced a mixture of **37b** and **40b** (ratio ca. 1:1). These results concur with those obtained by Bennasar and co-workers[8] in which it was found that RCM of protected enamides was in competition with isomerization and, in addition with *N*-devinylation reactions under our reaction conditions.



Scheme 4. (i) [RuClH(CO)(PPh_3)$_3$], 1 mol-%, toluene, Ar, 80 °C, 18–20 h, **38a** 84%, **38b** 90%, **38c** 77%; (ii) Catalyst **28**, 5–10 mol-%, toluene, 60 °C, 19–25 h, for RCM of **38a**, obtained **37a** 47% (note: reaction performed on small scale with 0.5 mol-equiv. of catalyst **28**), for RCM of **38b**, obtained mixture of **37b** and **40b** (ratio ca. 1:1), 58%, for RCM of **38c**, complex mixture.

Conclusions

In this paper we have demonstrated the applicability of an isomerization-RCM approach to the synthesis of 2,3-dihydro-1*H*-2-benzazepines and 1,2-dihydroisoquinolines. Unfortunately the attempt to synthesize the 2,5-dihydro-1*H*-2-benzazepines was foiled due to competitive isomerization and devinylation reactions occurring during the RCM. We intend to use the compounds synthesized as potential scaffolds for biologically active compounds. In addition, we will continue to investigate the isomerization-RCM strategy with other catalysts and conditions to afford potentially interesting benzo-fused heterocycles.

Experimental Section

^{1}H- and ^{13}C-NMR spectra were recorded either on a Bruker AC-200, Bruker 300 or Bruker DRX 400 spectrometer at the frequency indicated. Infrared spectra were recorded on either a Bruker IFS 25 Fourier Transform spectrometer or on a Bruker Vector 22 Fourier Transform spectrometer. Mass spectra were recorded on a Kratos MS 9/50, VG 70E MS or a VG 70 SEQ 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.[21] The Carousel Reaction Station used in this work was manufactured by Radleys Discovery Technologies.

***N*-({3-Isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]phenyl}methylene)prop-2-en-1-amine:** Benzaldehyde **24** (0.436 mmol, 0.102 g) was placed in a flask that was under an Ar atmosphere and to this was added allylamine (0.67 mmol, 0.050 cm^3). The mixture was then stirred at room temp. for 22 h. After this time the excess allylamine was removed in vacuo to yield the desired imine as a yellow-orange oil. The product was essentially pure by ^{1}H NMR spectroscopy and no further purification was required (0.119 g, 100%). A mixture of *E*/*Z* isomers (*E*:*Z* ≈ 6:1) was observed by NMR spec-

troscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1520, 1424, 1216. ^1H NMR (300 MHz, $CDCl_3$, only *E* isomer listed): δ = 1.22–1.28 [6 H, m, $OCH(CH_3)_2$], 1.94 (dd, 3 H, *J* = 5.6 and 1.2 Hz, CH_3), 3.86 (s, 3 H, OCH_3), 4.20 (dd, 2 H, *J* = 5.6 and 1.2 Hz, NCH_2C), 4.38 [1 H, sept, *J* = 6.1 Hz, $OCH(CH_3)_2$], 5.12–5.23 (m, 2 H, $CH=CH_2$), 5.68–5.74 (m, 1 H, $CH=CH_2$), 5.88–6.11 (m, 1 H, $ArCH=CHCH_3$), 6.60 (dd, 1 H, *J* = 16.0 and 1.5 Hz, $ArCH=CHCH_3$), 6.84 (d, 1 H, *J* = 8.6 Hz, 5-H), 7.71 (d, 1 H, *J* = 8.6 Hz, 6-H), 8.41 (s, 1 H, ArCH=N) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.0 (CH_3), 22.5 and 22.6 [$OCH(CH_3)_2$], 55.6 and 55.7 (OCH_3), 63.5 and 63.7 (NCH_2C), 74.7 and 75.1 [$OCH(CH_3)_2$], 110.2 and 110.7 (CH), 115.7 (CH), 123.0 and 123.3 (CH), 124.3 (CH), 127.0 (C), 134.0 (CH), 134.8 (C), 136.3 (CH), 144.2 (C), 154.3 (C), 160.5 and 161.8 (ArCH=N) ppm. MS: *m*/*z* (%) = 273 (4) [M^+], 258 (26), 234 (37), 216 (21), 193 (21), 192 (22), 178 (12), 177 (100), 175 (10), 91 (10), 77 (9), 41 (11). HRMS calculated for $C_{17}H_{23}NO_2$: 273.1729, found: 273.1729.

***N*-{3-Isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}prop-2-en-1-amine (25):** The aforementioned imine (0.402 mmol, 0.110 g) was dissolved in MeOH (1 cm^3) and the solution was cooled to 0 °C in an ice/water bath. To this methanolic solution was added sodium borohydride (0.56 mmol, 0.021 g), and the reaction mixture was left to stir at 0 °C under Ar for 2 h. After this time H_2O was added to destroy the excess sodium borohydride and the pH was neutralised using 1 M HCl and saturated $NaHCO_3$ solutions. The MeOH was removed on the rotary evaporator and the remaining aqueous layer was extracted with EtOAc (3 × 5 cm^3). The combined organics were then dried ($MgSO_4$) and the solvent was removed in vacuo to yield **25** as a yellow oil (0.0985 g, 89%), which was pure by NMR spectroscopy and required no further purification. A mixture of *E*/*Z* isomers (*E*:*Z* ≈ 7:1) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 3010, 2977, 1642, 1598, 1573, 1428, 1439, 1381, 1273. ^1H NMR (300 MHz, $CDCl_3$, only *E* isomer listed): δ = 1.23 [6 H, d, *J* = 6.2 Hz, $OCH(CH_3)_2$], 1.68 (1 H, broad s, NH), 1.90 (dd, 3 H, *J* = 6.5 and 1.5 Hz, CH_3), 3.24 (br. d, 2 H, *J* = 6.0 Hz, NCH_2C), 3.73 (s, 2 H, $ArCH_2NH$), 3.81 (s, 3 H, OCH_3), 4.32 [1 H, sept, *J* = 6.2 Hz, $OCH(CH_3)_2$], 5.10–5.18 (m, 2 H, $CH=CH_2$), 5.90–5.95 (m, 1 H, $CH=CH_2$), 6.10–6.20 (m, 1 H, $ArCH=CHCH_3$), 6.43 (dd, 1 H, *J* = 16.0 and 1.5 Hz, $ArCH=CHCH_3$), 6.73 (d, 1 H, *J* = 8.4 Hz, 5-H), 6.99 (d, 1 H, *J* = 8.4 Hz, 6-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.2 (CH_3), 22.5 [$OCH(CH_3)_2$], 51.0 ($ArCH_2N$),[a] 51.8 (NCH_2C),[a] 55.7 (OCH_3), 75.0 [$OCH(CH_3)_2$], 110.1 (CH), 115.9 (CH), 124.4 (CH), 124.9 (CH), 130.8 (C), 131.7 (CH), 132.8 (C), 136.9 (CH), 145.0 (C), 152.2 (C) ppm. MS: *m*/*z* (%) = 275 (12) [M^+], 232 (100), 218 (31), 216 (44), 192 (41), 178 (28), 177 (55), 176 (58), 175 (55), 161 (51), 41 (52). HRMS calculated for $C_{17}H_{25}NO_2$: 275.1885, found: 275.1875.

***N*-Allyl-*N*-{3-isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}-4-methylbenzenesulfonamide (26a):** The amine **25** (1.68 mmol, 0.463 g) was dissolved in CH_2Cl_2 (5 cm^3) and then cooled to 0 °C in an ice/water bath. To this solution was added NEt_3 (2.5 mmol, 0.35 cm^3) and it was stirred for 5 min before the addition of the tosyl chloride (2.05 mmol, 0.391 g). The reaction mixture was stirred at 0 °C to room temp. for 3 h. After this time, H_2O (5 cm^3) was added and the aqueous layer was extracted with CH_2Cl_2 (5 cm^3). The combined organics were then extracted with H_2O (2 × 5 cm^3) and were dried ($MgSO_4$). The solvent was then removed in vacuo to yield a dark yellow-orange oil that was purified by silica gel column chromatography (5–10% EtOAc/hexane). The desired product **26a** was obtained as a cream-white solid (0.553 g, 77%), with NMR spectroscopy showing a mixture of *E*/*Z* isomers (*E*:*Z* ≈ 8:1), m.p. 62–64 °C. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1522, 1479, 1427, 1339, 1216. ^1H NMR (300 MHz, $CDCl_3$, only *E* isomer listed): δ = 1.23 [6 H, d, *J* = 6.2 Hz, $OCH(CH_3)_2$], 1.86 and rest under 1.23 (br. d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 2.44 (s, 3 H, $ArCH_3$), 3.66 (br. d, 2 H, *J* = 6.4 Hz, NCH_2C), 3.81 (s, 3 H, OCH_3), 4.10–4.32 [3 H, m, $ArCH_2N$ and $OCH(CH_3)_2$], 4.85–4.96 (m, 2 H, $CH=CH_2$), 5.35–5.48 (m, 1 H, $CH=CH_2$), 5.84–5.98 (m, 1 H, $CH=CHCH_3$), 6.36 (1 H, dd, *J* = 16.0 and 1.5 Hz, $ArCH=CH$), 6.73 (d, 1 H, *J* = 8.5 Hz, 5-H), 7.02 (d, 1 H, *J* = 8.5 Hz, 6-H), 7.31 (d, 2 H, *J* = 8.2 Hz, 2 ArH), 7.73 (d, 2 H, *J* = 8.2 Hz, 2 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, only *E* isomer listed, one aromatic C not observed in spectrum): δ = 19.0 (CH_3), 21.5 ($ArCH_3$), 22.4 [$OCH(CH_3)_2$], 48.2 ($ArCH_2N$), 49.5 (NCH_2C), 55.7 (OCH_3), 75.0 [$OCH(CH_3)_2$], 110.1 (CH), 118.5 (CH), 124.5 (CH), 126.7 (CH), 127.3 (2 CH), 129.6 (2 CH), 132.4 (CH), 132.8 (CH), 133.5 (C), 137.3 (C), 143.1 (C), 144.7 (C), 152.5 (C) ppm. MS: *m*/*z* (%) = 429 (3) [M^+], 275 (18), 274 (100), 233 (9), 232 (56), 215 (20), 177 (13), 176 (22), 161 (11), 117 (9), 91 (14). HRMS calculated for $C_{24}H_{31}NO_4S$: 429.1974, found: 429.1978.

***N*-Allyl-*N*-{3-isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}-1-phenylmethanesulfonamide (26b):** The amine **25** (0.744 mmol, 0.205 g) was dissolved in CH_2Cl_2 (2 cm^3); to this was added NEt_3 (1.86 mmol, 0.260 cm^3) and the solution was stirred at room temp. for 15 min. Benzylsulfonyl chloride (0.834 mmol, 0.159 g) was dissolved in CH_2Cl_2 (2 cm^3) and added dropwise to the amine solution and a cloudy white gas evolved during the addition. The reaction mixture was then stirred at room temp. under an Ar atmosphere for 18 h, before the solvent was removed in vacuo to yield a pink-orange oil that solidified on standing. The crude mixture was purified by column chromatography (5–20% EtOAc/hexane) to yield the desired product **26b** as a yellow oil (0.0927 g, 29%). Mixtures of *E*/*Z* isomers were observed in the spectra (*E*:*Z* ≈ 7:1). IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1481, 1439, 1334, 1215. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 [d, *J* = 6.2 Hz, 6 H, $OCH(CH_3)_2$], 1.88 (d, *J* = 6.4 Hz, 3 H, CH_3), 3.55 (d, *J* = 6.5 Hz, 2 H, NCH_2C), 3.81 (s, 3 H, OCH_3), 4.14 (s, 2 H, $ArCH_2N$), 4.23 (s, 2 H, $ArCH_2SO_2$), 4.31 [sept, *J* = 6.2 Hz, 1 H, $OCH(CH_3)_2$], 5.01–5.12 (m, 2 H, $CH=CH_2$), 5.55–5.81 (m, 2 H, $CH=CH_2$ and $ArCH=CH$), 6.34 (d, *J* = 16.1 Hz, 1 H, $ArCH=CH$), 6.76 (d, *J* = 8.5 Hz, 1 H, 5-H), 7.08 (d, *J* = 8.5 Hz, 1 H, 6-H), 7.35–7.36 (m, 5 H, 5 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 1 aromatic C signal not observed in spectrum): δ = 19.1 (CH_3), 22.5 [$OCH(CH_3)_2$], 48.2 ($ArCH_2N$),[a] 49.8 (NCH_2C),[a] 55.7 (OCH_3), 59.4 ($ArCH_2SO_2$), 75.0 [$OCH(CH_3)_2$], 110.3 (CH), 119.0 (CH), 124.5 (CH), 124.8 (CH), 126.3 (C), 128.6 (2 CH), 129.2 (CH), 130.8 (2 CH), 132.4 (CH), 132.9 (CH), 133.2 (C), 144.7 (C), 152.5 (C) ppm. MS: *m*/*z* (%) = 429 (7) [M^+], 275 (20), 274 (100), 233 (10), 232 (70), 216 (17), 177 (13), 176 (13), 91 (49). HRMS calculated for $C_{24}H_{31}NO_4S$: 429.1974, found: 429.1962.

***N*-Allyl-*N*-{3-isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}-acetamide (26c):** A solution was prepared of amine **25** (0.740 mmol, 0.204 g) and pyridine (0.74 mmol, 0.060 cm^3) and was cooled to 0 °C in an ice/water bath. To this was added dropwise a solution of Ac_2O (1.16 mmol, 0.110 cm^3) in pyridine (1.2 mmol, 0.10 cm^3). The reaction mixture was stirred at room temp. under an Ar atmosphere for 3 h, after which time the reaction mixture was diluted with EtOAc (5 cm^3) and stirred for 5 min. The organic layer was subsequently extracted with brine (3 × 10 cm^3) and the combined aqueous layers were extracted with CH_2Cl_2 (3 × 10 cm^3). The organic layers were combined and extracted with saturated NH_4Cl (40 cm^3) that had been basified to pH 11 with a 25% ammonia solution. The combined organics were then dried ($MgSO_4$), filtered and the solvent was removed in vacuo to yield a pale yellow oil. The crude compound was then purified by column chromatography (5–10% EtOAc/hexane) to yield the desired product **26c** as a clear oil (0.168 g, 72%). Significant broadening occurred in the NMR

spectra due to rotamers about the acetyl group (ratio 1:1). IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1630, 1522, 1478, 1424, 1216. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.21–1.25 [m, 6 H, OCH(CH_3)$_2$], 1.86–1.92 (m, 3 H, CHCH_3), 2.08 and 2.13 (2 s, 3 H, COCH_3), 3.69 and 3.96 (2 H, 2 d, J = 4.7 and, J = 5.8 Hz, NCH_2CH), 3.81 and 3.83 (2 s, 3 H, OCH_3), 4.27–4.36 [m, 1 H, OCH(CH$_3$)$_2$], 4.23 and 4.62 (2 s, 2 H, ArCH_2N), 5.04–5.18 (m, 2 H, CH=CH_2), 5.60–6.10 (m, 2 H, CH=CH$_2$CH$_3$ and ArCH=CHCH$_3$), 6.32 (br. d, J = 16.1 Hz, 1 H, ArCH=CHCH$_3$), 6.71–6.87 (m, 2 H, 5-H and 6-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.0 and 19.1 (CH$_3$), 21.4 and 21.5 (COCH_3), 22.4 and 22.5 [OCH(CH_3)$_2$], 45.6 and 47.9 (ArCH_2N),[a] 49.1 and 49.3 (NCH_2C),[a] 55.7 (OCH_3), 75.0 and 75.1 [OCH(CH$_3$)$_2$], 110.2 and 110.4 (CH), 116.5 and 117.2 (CH), 120.8 (CH), 123.6 (CH), 124.2 and 124.6 (CH), 126.7 and 127.4 (C), 132.1 and 132.4 (C), 133.1 and 133.2 (CH), 144.8 and 145.2 (C), 152.2 and 152.3 (C), 170.7 and 171.0 (C=O) ppm. MS: m/z (%) = 317 (72) [M$^+$], 234 (22), 232 (30), 218 (24), 194 (40), 193 (86), 177 (31), 176 (80), 175 (100), 161 (30), 43 (21). HRMS calculated for $C_{19}H_{27}NO_3$: 317.1991, found: 317.1999.

General Procedure for RCM Reactions: The substrate (0.1–0.4 mmol) was dissolved in toluene (5–20 cm^3) and the solution was heated to 60–80 °C under an Ar atmosphere. Grubbs II catalyst **28** (5 mol-%) was added and the reaction mixture was stirred at 60 °C under an Ar atmosphere for 18–24 h. If the reaction mixture still contained starting material (by tlc) a further portion of **28** (5 mol-%) was added and the mixture was heated at 60 °C for a further 18–24 h. The reaction mixture was then cooled to room temp. and the solvent was removed in vacuo to yield a dark brown oil. The crude mixture was subsequently purified by silica gel column chromatography (5–10% EtOAc/hexane) to obtain the desired product.

6-Isopropoxy-7-methoxy-2-[(4-methylphenyl)sulfonyl]-2,3-dihydro-1*H*-2-benzazepine (27a): Compound **26a** (0.473 mmol, 0.203 g) in toluene (20 cm^3) was treated with Grubbs II catalyst **28** (0.025 mmol, 0.021 g) at 60 °C for 19.5 h. After chromatography (5–10% EtOAc/hexane), **27a** was isolated as a pale yellow oil (0.149 g, 82%), that solidified on standing, m.p. 147–149 °C. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1598, 1577, 1490, 1438, 1403, 1382, 1342. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17 [d, J = 6.2 Hz, 6 H, OCH(CH_3)$_2$], 2.32 (s, 3 H, ArCH_3), 3.81 (s, 3 H, OCH_3), 4.09–4.17 [m, 3 H, 3-H and OCH(CH$_3$)$_2$], 4.33 (s, 2 H, 1-H), 5.66–5.73 (m, 1 H, 5-H), 6.72–6.80 (m, 2 H, 4-H and 8-H), 6.93 (d, J = 8.3 Hz, 1 H, 9-H), 7.11 (d, J = 8.3 Hz, 2 H, 2 ArH), 7.45 (d, J = 8.3 Hz, 2 H, 2 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3 (ArCH_3), 22.5 [OCH(CH_3)$_2$], 50.1 (3-C),[a] 51.6 (1-C),[a] 55.8 (OCH_3), 75.8 [OCH(CH$_3$)$_2$], 110.8 (CH), 123.6 (CH), 125.5 (CH), 127.1 (2 CH), 127.2 (CH), 129.1 (2 CH), 129.3 (C), 130.3 (C), 136.5 (C), 142.7 (C), 145.2 (C), 152.6 (C) ppm. MS: m/z (%) = 387 (66) [M$^+$], 295 (18), 232 (23), 190 (83), 189 (100), 175 (38), 163 (55), 161 (40), 103 (33), 91 (91). HRMS calculated for $C_{21}H_{25}NO_4S$: 387.1504, found: 387.1505.

2-(Benzylsulfonyl)-6-isopropoxy-7-methoxy-2,3-dihydro-1*H*-2-benzazepine (27b): Compound **26b** (0.122 mmol, 0.0526 g) in toluene (5 cm^3) was treated with Grubbs II catalyst **28** (0.013 mmol, 0.011 g) at 80 °C for 21 h. After chromatography (5% EtOAc/hexane), **27b** was obtained as a yellow oil (0.0184 g, 39%). IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1666, 1598, 1575, 1490, 1456, 1439, 1354. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 [d, J = 6.2 Hz, 6 H, OCH(CH_3)$_2$], 3.79 (s, 2 H, 3-H), 3.84 (s, 3 H, OCH_3), 4.09–4.11 (m, 2 H, 1-H), 4.33 (s, 2 H, ArCH_2SO$_2$), 4.46 [sept, J = 6.2 Hz, 1 H, OCH(CH$_3$)$_2$], 5.76 (dt, J = 12.6 and 3.9 Hz, 1 H, 5-H), 6.78 (d, J = 8.2 Hz, 1 H, 8-H), 6.92–6.99 (m, 2 H, 4-H and 9-H), 7.16–7.29 (m, 5 H, 5 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.5 [OCH(CH_3)$_2$], 50.7 (3-C),[a] 51.7 (1-C),[a] 55.8 (OCH_3), 58.6 (ArCH_2SO$_2$), 75.5 [OCH(CH$_3$)$_2$], 111.0 (CH), 123.5 (CH), 124.2 (C), 125.3 (CH), 128.3 (CH), 128.4 (CH), 128.5 (2 CH), 128.9 (C), 129.7 (C), 130.6 (2 CH), 145.3 (C), 152.8 (C) ppm. MS: m/z (%) = 387 (28) [M$^+$], 205 (20), 190 (49), 189 (42), 163 (67), 161 (13), 147 (90), 92 (10), 91 (100), 65 (10). HRMS calculated for $C_{21}H_{25}NO_4S$: 387.1504, found: 387.1496.

***N*-{3-Isopropoxy-4-methoxy-2-[(1*E*)-1-phenylprop-1-en-1-yl]benzyl}-prop-2-en-1-amine (31):** Benzaldehyde **30** (1.77 mmol, 0.550 g) was transferred to a flask using Et$_2$O which was then removed under vacuum. To the aldehyde was added allylamine (2.67 mmol, 0.200 cm^3) and the reaction mixture was stirred at room temp. under an Ar atmosphere for 21 h. A small amount of the mixture was removed and analysed by ^1H NMR spectroscopy. It was found that imine formation had occurred and the reaction mixture was subsequently dissolved in MeOH (5.5 cm^3) and cooled to 0 °C in an ice/water bath. Sodium borohydride (2.1 mmol, 0.081 g) was added and the reaction mixture was left to stir under an Ar atmosphere at 0 °C for 2 h. After this time H_2O (10 cm^3) was added and the pH was neutralised using 1 M HCl and saturated $NaHCO_3$ solutions. The reaction mixture was then extracted with CH_2Cl_2 (10 cm^3) and EtOAc (3 × 10 cm^3) and the combined organics were dried ($MgSO_4$). The solution was then filtered and the solvent was removed in vacuo. The desired product **31** was obtained as an essentially pure orange oil and no further purification was deemed necessary (0.620 g, 100%). A mixture of *E*/*Z* isomers (*E*:*Z* ≈ 6:1) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 3494, 1646, 1595, 1479, 1439, 1377, 1340, 1267. ^1H NMR (300 MHz, $CDCl_3$, only *E* isomer listed): δ = 1.04 and 1.13 [6 H, 2 d, J = 6.2 Hz, OCH(CH_3)$_2$], 1.36 and 1.64 (3 H, 2 d, J = 6.1 and 6.9 Hz respectively, CHCH_3), 1.42 (br. s, 1 H, NH), 3.02–3.04 (m, 2 H, NCH_2CH), 3.46 (2 H, distorted AB system, J ≈ 8 Hz, ArCH_2N), 3.84 (s, 3 H, OCH_3), 4.27 [1 H, sept, J = 6.2 Hz, OCH(CH$_3$)$_2$], 4.96–5.06 (m, 2 H, CH=CH_2), 5.69–5.82 (m, 1 H, CH=CH$_2$), 6.41 (q, 1 H, J = 6.9 Hz, C=CHCH$_3$), 6.88 (d, 1 H, J = 8.4 Hz, 5-H), 7.12–7.36 (m, 6 H, 6 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, only peaks for major *E*-isomer listed, 1 aromatic C signal not observed in spectrum): δ = 16.1 (CH$_3$), 22.4 and 22.7 [OCH(CH_3)$_2$], 50.7 (ArCH_2N),[a] 51.7 (NCH_2CH),[a] 55.5 (OCH_3), 74.7 [OCH(CH$_3$)$_2$], 110.8 (CH), 115.6 (CH), 124.1 (CH), 125.3 (CH), 125.9 (2 CH), 126.6 (CH), 128.2 (2 CH), 131.5 (C), 133.4 (C), 136.8 (CH), 141.4 (C), 144.8 (C), 152.3 (C) ppm. MS: m/z (%) = 351 (8) [M$^+$], 310 (9), 253 (7), 252 (17), 219 (30), 131 (18), 69 (100), 32 (14), 28 (88). HRMS calculated for $C_{23}H_{29}NO_2$: 351.2198, found: 351.2197.

***N*-Allyl-*N*-{3-isopropoxy-4-methoxy-2-[(1*E*)-1-phenylprop-1-en-1-yl]benzyl}-4-methylbenzenesulfonamide (32a):** Amine **31** (1.38 mmol, 0.484 g) in CH_2Cl_2 (5 cm^3) and at 0 °C was treated with NEt_3 (1.9 mmol, 0.27 cm^3) and tosyl chloride (1.64 mmol, 0.312 g) as described previously for compound **26a**. After work-up and chromatography (5–15% EtOAc/hexane) **32a** was obtained as a pale pink oil that solidified on standing (0.493 g, 71%). A mixture of *E*/*Z* isomers (*E*:*Z* > ca. 8:1) was observed by NMR spectroscopy, m.p. 110–103 °C. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1601, 1520, 1481, 1430, 1338. ^1H NMR (300 MHz, $CDCl_3$, only major *E* isomer listed): δ = 1.00 and 1.10 [6 H, two d, J = 6.2 Hz, OCH(CH_3)$_2$], 1.60 (d, 3 H, J = 6.8 Hz, CHCH_3), 2.40 (s, 3 H, ArCH_3), 3.68–3.71 (m, 2 H, NCH_2C), 3.85 (s, 3 H, OCH_3), 4.05 (2 H, distorted AB system, J ≈ 8 Hz, ArCH_2N), 4.25 [1 H, sept, J = 6.2 Hz, OCH(CH$_3$)$_2$], 4.79–4.87 (m, 2 H, CH=CH_2), 5.30–5.44 (m, 1 H, CH=CH$_2$), 6.33 (q, 1 H, J = 6.8 Hz, C=CHCH$_3$), 6.92 (d, 1 H, J = 8.6 Hz, 5-H), 7.15–7.30 (m, 8 H, 7 ArH and 6-H), 7.55 (d,

2 H, J = 8.2 Hz, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.0 (CH_3), 21.5 ($ArCH_3$), 22.4 and 22.6 [$OCH(CH_3)_2$], 47.9 ($ArCH_2N$),[a] 50.6 (NCH_2C),[a] 55.5 (OCH_3), 74.7 [$OCH(CH_3)_2$], 111.0 (CH), 118.8 (CH), 122.6 (CH), 125.5 (CH), 125.8 (2 CH), 126.6 (CH), 127.2 (2 CH), 127.6 (CH), 128.2 (2 CH), 129.5 (2 CH), 132.1 (C), 136.1 (C), 132.6 (C), 137.1 (C), 140.7 (C), 143.0 (C), 144.6 (C), 152.4 (C) ppm. MS: m/z (%) = 505 (7) [M^+], 350 (100), 308 (34), 253 (32), 252 (69), 81 (37), 69 (80), 55 (31), 42 (37), 41 (50). HRMS calculated for $C_{30}H_{35}NO_4S$: 505.2287, found: 505.2290.

***N*-Allyl-*N*-{3-isopropoxy-4-methoxy-2-[(1*E*)-1-phenylprop-1-en-1-yl]benzyl}-1-phenylmethanesulfonamide (32b):** Amine **31** (1.34 mmol, 0.470 g) in CH_2Cl_2 (5 cm^3) was treated with NEt_3 (3.6 mmol, 0.50 cm^3) and benzylsulfonyl chloride (1.49 mmol, 0.284 g) in CH_2Cl_2 (2 cm^3), as described for compound **26b**. After work-up and chromatography (5–15% EtOAc/hexane) **32b** was obtained as an orange solid (0.302 g, 45%). A mixture of *E*/*Z* isomers (*E*:*Z* > ca. 8:1) was observed by NMR spectroscopy, m.p. 105–108 °C. IR (NaCl plate): $\tilde{\nu}_{max}$/cm^{-1} = 1482, 1442, 1377, 1337, 1249. ^{1}H NMR (300 MHz, $CDCl_3$, only major *E* isomer listed): δ = 1.00 and 1.08 [6 H, 2 d, J = 6.1 Hz, $OCH(CH_3)_2$], 1.49 (d, 3 H, J = 7.0 Hz, $CHCH_3$), 3.56–3.80 (m, 4 H, NCH_2C and $ArCH_2N$), 3.83 (s, 3 H, OCH_3), 4.11–4.24 [3 H, m, $ArCH_2SO_2$ and $OCH(CH_3)_2$], 4.92–5.01 (m, 2 H, $CH=CH_2$), 5.41–5.55 (m, 1 H, $CH=CH_2$), 6.32 (q, 1 H, J = 7.0 Hz, $C=CHCH_3$), 6.90 (d, 1 H, J = 8.6 Hz, 5-H), 7.14–7.28 (m, 11 H, 10 ArH and 6-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.0 ($CHCH_3$), 22.4 and 22.6 [$OCH(CH_3)_2$], 48.3 ($ArCH_2N$),[a] 50.1 (NCH_2C),[a] 55.5 (OCH_3), 59.1 ($ArCH_2SO_2$), 74.7 and 74.8 [$OCH(CH_3)_2$], 111.2 (CH), 119.2 (CH), 122.7 (CH), 125.6 (CH), 125.7 (2 CH), 126.7 (CH), 127.5 (CH), 128.3 (2 CH), 128.4 (CH), 128.5 (2 CH), 129.0 (C), 130.6 (2 CH), 132.3 (C), 132.7 (C), 136.0 (C), 140.8 (C), 144.5 (C), 152.4 (C) ppm. MS: m/z (%) = 505 (19) [M^+], 350 (100), 308 (49), 256 (76), 254 (62), 91 (55), 70 (35), 69 (76), 60 (53), 56 (66), 53 (63), 42 (78), 41 (79). HRMS calculated for $C_{30}H_{35}NO_4S$: 505.2287, found: 505.2290.

Attempted Synthesis of 6-Isopropoxy-7-methoxy-2-[(4-methylphenyl)sulfonyl]-5-phenyl-2,3-dihydro-1*H*-2-benzazepine 33a and 2-(Benzylsulfonyl)-6-isopropoxy-7-methoxy-5-phenyl-2,3-dihydro-1*H*-2-benzazepine (33b): Compounds **32a** [0.154 g, toluene (15 cm^3), 8% cat **28**, 80 °C, 22 h] and **32b** [0.093 g, toluene (15 cm^3), 5% cat **28**, 60 °C, 23 h] were subjected to RCM as described for compounds **27**. After work-up, column chromatography only afforded complex mixtures which included unreacted starting material (by NMR spectroscopy).

***N*-[3-Isopropoxy-4-methoxy-2-(prop-1-en-1-yl)benzyl]-1-phenyl-*N*-(prop-1-en-1-yl)methanesulfonamide (35b):** Sulfonamide **34b** (0.707 mmol, 0.304 g) was dissolved in distilled toluene (30 cm^3) and the solution was degassed with N_2 for 15 min. [RuClH(CO)(PPh_3)$_3$] (0.0354 mmol, 0.0326 g) was added and the reaction mixture was allowed to stir at 90–100 °C under an Ar atmosphere for 19 h. A ^{1}H NMR spectrum of the crude reaction mixture showed that isomerisation of the double bonds had occurred and the solvent was removed in vacuo to yield a dark brown-black oil. This was then purified by column chromatography (5–10% EtOAc/hexane) to yield the desired product **35b** as a pale yellow oil (0.265 g, 87%). A complex mixture of *E*/*Z* isomers was observed by NMR spectroscopy. [When this reaction was initially attempted under high temperature (135–140 °C), solventless conditions only deallylated compound **37b** was obtained. See reference[31] for experimental details and an X-ray structure of the compound **37b**]. IR (NaCl plate): $\tilde{\nu}_{max}$/cm^{-1} = 1521, 1426, 1354, 1216. ^{1}H NMR (300 MHz, $CDCl_3$, only major isomer listed): δ = 1.19 [6 H, d, J = 6.1 Hz, $OCH(CH_3)_2$], 1.52 (br. d, 3 H, J = 6.6 Hz, $CHCH_3$), 1.85 (br. d, 3 H, J = 6.5 Hz, $CHCH_3$), 3.77 (s, 3 H, OCH_3), 4.07 (s, 2 H, $ArCH_2N$), 4.42–4.44 [4 H, m, $OCH(CH_3)_2$, SO_2CH_2Ar and $NCH=CHCH_3$], 5.45–5.52 (m, 1 H, $CH=CHCH_3$), 6.28 (br. d, 1 H, J = 16.0 Hz, $CH=CHCH_3$), 6.38 (br. d, 1 H, J = 15.5 Hz, $CH=CHCH_3$), 6.72 (d, 1 H, J = 8.6, 5-H), 6.99 (d, 1 H, J = 8.6, 6-H), 7.39 (br. s, 5 H, 5 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, only major isomer listed, 1 CH signal not observed in aromatic portion of spectrum): δ = 15.2 (CH_3), 19.0 (CH_3), 22.4 [$OCH(CH_3)_2$], 48.5 ($ArCH_2N$), 55.5 (OCH_3), 58.5 (SO_2CH_2Ar), 75.0 [$OCH(CH_3)_2$], 106.9 (CH), 110.6 (CH), 121.6 (CH), 124.1 (C), 124.6 (CH), 126.0 (CH), 128.7 (C), 128.8 (2 CH), 131.0 (2 CH), 131.8 (C), 131.9 (CH), 144.3 (C), 151.7 (C) ppm. MS: m/z (%) = 429 (1) [M^+] 373 (30), 274 (17), 219 (38), 216 (13), 178 (12), 177 (100), 175 (10), 145 (20), 117 (18), 91 (49). HRMS calculated for $C_{24}H_{31}NO_4S$; 429.1974, found: 429.1983.

***N*-[3-Isopropoxy-4-methoxy-2-(prop-1-en-1-yl)benzyl]-*N*-(prop-1-en-1-yl)acetamide (35c):** Acetamide **34c** (0.956 mmol, 0.303 g) was dissolved in toluene (30 cm^3) and was treated with [RuClH(CO)(PPh_3)$_3$] (0.0478 mmol, 0.0450 g) at 105 °C as described in the previous procedure. Column chromatography (5–15% EtOAc/hexane) afforded the desired product **35c** as a yellow oil (0.285 g, 94%). The product was found to consist of rotamers (60:40) by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}$/cm^{-1} = 1645, 1481, 1410, 1380, 1216. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22–1.26 [m, 6 H, $OCH(CH_3)_2$], 1.59–1.66 (m, 3 H, $CHCH_3$), 1.90–1.95 and under 2.06 (m, 3 H, $CHCH_3$), 2.06 and 2.30 (2 s, 3 H, $COCH_3$), 3.79 and 3.81 (2 s, 3 H, OCH_3), 4.30–4.39 [m, 1 H, $OCH(CH_3)_2$], 4.65–4.85 (m, 3 H, $ArCH_2N$ and $CH=CHCH_3$), 5.94–5.97 (m, 1 H, $CH=CHCH_3$), 6.41–6.73 and 7.31–7.36 (m, 4 H, 2 ArH and 2 $CH=CHCH_3$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.3 and 15.5 ($CHCH_3$), 19.0 and 19.1 ($CHCH_3$), 22.1 and 22.2 ($COCH_3$), 22.4 and 22.5 [$OCH(CH_3)_2$], 44.8 and 48.2 ($ArCH_2N$), 55.6 (OCH_3), 75.0 and 75.1 [$OCH(CH_3)_2$], 106.9 and 109.0 (CH), 110.5 and 110.6 (CH), 119.9 and 120.8 (CH), 124.3 and 124.7 (CH), 126.3 and 126.9 (C), 128.0 (CH), 131.6 (C), 132.2 and 132.5 (CH), 144.7 and 145.0 (C), 151.6 and 152.0 (C), 169.1 and 169.4 (C=O) ppm. MS: m/z (%) = 317 (29) [M^+] 317 (29), 261 (19), 219 (14), 178 (15), 177 (100), 176 (12), 175 (18), 162 (14), 145 (29), 117 (22), 115 (8), 43 (10). HRMS calculated for $C_{19}H_{27}NO_3$; 317.1991, found: 317.1986.

5-Isopropoxy-6-methoxy-2-[(4-methylphenyl)sulfonyl]-1,2-dihydroisoquinoline (36a): To a degassed solution of methylbenzenesulfonamide **34a** (0.120 g, 0.279 mmol) in toluene (10 cm^3) was added [RuClH(CO)(PPh_3)$_3$] (0.0013 mmol, ca. 0.002 g). The reaction mixture was heated at 110 °C for 2 h under a N_2 atmosphere. Catalyst **28** (0.014 mmol, 0.012 g) was added and the reaction mixture was stirred for another 3 h at 110 °C under N_2. After cooling, the toluene was evaporated under reduced pressure and the organic residue was then subjected to silica gel column chromatography (5–20% EtOAc/hexane) to afford the desired product **36a** as a brown oil (0.079 g, 76%). IR (NaCl plate): $\tilde{\nu}_{max}$/cm^{-1} = 1625, 1597, 1486, 1461, 1439, 1400, 1283. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 [d, J = 6.2 Hz, 6 H, $CH(CH_3)_2$], 2.37 (s, 3 H, $ArCH_3$), 3.77 (s, 3 H, OCH_3), 4.35 [sept, J = 6.2 Hz, 1 H, $CH(CH_3)_2$], 4.48 (s, 2 H, 1-H), 6.22 (d, J = 7.9 Hz, 1 H, 4-H), 6.64 (br. d, 2 Historted AB system, 7-ArH and 8-ArH), 6.74 (d, J = 7.9 Hz, 1 H, 3-H), 7.25 (d, J = 8.1 Hz, 2 H, 2 ArH), 7.67 (d, J = 8.1 Hz, 2 H, 2 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.4 ($ArCH_3$), 22.4 [$CH(CH_3)_2$], 46.8 (NCH_2), 55.7 (OCH_3), 75.2 [$CH(CH_3)_2$], 106.3 (CH), 110.7 (CH), 120.4 (CH), 120.7 (C), 125.3 (C), 126.1 (CH), 126.9 (C), 127.1 (2 CH), 129.2 (C), 129.7 (2 CH), 143.9 (C), 152.4 (C) ppm. MS: m/z (%) = 374 (24), 373 (90) [M^+], 218 (18), 176 (100), 175 (89), 161

(35), 144 (45), 132 (30), 91 (43). HRMS calculated for $C_{20}H_{23}NSO_4$: 373.1348, found: 373.1348.

2-Acetyl-5-isopropoxy-6-methoxy-1,2-dihydroisoquinoline (36c): Acetamide **35c** (0.321 mmol, 0.102 g) was dissolved in toluene (8 cm^3) and degassed using N_2 for 15 min. After this time the solution was heated to 110 °C before the addition of catalyst **28** (0.016 mmol, 0.014 g). The reaction mixture was then left to stir at 110 °C, under Ar for 3 h. The reaction mixture was cooled to room temp. and the solvent was removed in vacuo to yield a brown-black oil. This oil was then purified by column chromatography (5–30% EtOAc/hexane) to yield the desired product **36c** as a clear oil (0.0655 g, 78%). IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1661, 1625, 1575, 1488, 1462, 1440, 1408, 1386, 1351, 1270. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.29 [d, J = 6.2 Hz, 6 H, OCH(CH_3)$_2$], 2.21 (s, 3 H, COCH_3), 3.81 (s, 3 H, OCH_3), 4.23 [sept, J = 6.2 Hz, 1 H, OCH(CH_3)$_2$], 4.84 (s, 2 H, 1-H), 6.17 (d, J = 8.0 Hz, 1 H, 4-H), 6.64- 6.79 (m, 3 H, 3-H, 7-H and 8-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, only major rotamer listed): δ = 21.3 (CH_3), 22.5 [OCH(*C*H_3)$_2$], 43.8 (1-C), 55.8 (OCH_3), 75.4 [O*C*H(CH_3)$_2$], 105.3 (CH), 110.9 (CH), 120.8 (CH), 122.7 (C), 125.0 (C), 125.8 (CH), 141.6 (C), 152.2 (C), 168.4 (C=O) ppm. MS: *m*/*z* (%) = 261 (52) [M^+], 265 (22), 262 (10), 261 (52), 219 (28), 218 (18), 177 (29), 176 (100), 175 (42), 161 (15), 160 (19), 145 (14), 131 (23), 43 (11). HRMS calculated for $C_{15}H_{19}NO_3$; 261.1365, found: 261.1370.

General Procedure for Isomerization Reactions: These reactions were set up in a Carousel Reactor with the reaction tubes being evacuated and placed under Ar three times before the substrates (0.4–0.6 mmol) were added. This was followed by the addition of toluene (20 cm^3) and the solution was degassed using N_2 for 5 min. The solution was heated to 80 °C before the addition of $[RuClH(CO)(PPh_3)_3]$ (1 mol-%), and the reaction mixture was then stirred under Ar for 20 h. The reaction mixture was cooled to room temp. and the solvent was removed in vacuo to yield yellow oils. These oils were purified by column chromatography (5–10% EtOAc/hexane) to afford the desired products **38a**–**c**. The following four compounds were synthesized in this manner.

***N*-(2-Allyl-3-isopropoxy-4-methoxybenzyl)-4-methyl-*N*-[(1*E*)-prop-1-en-1-yl]benzenesulfonamide (38a):** Compound **34a** (0.482 mmol, 0.207 g) was treated with $[RuClH(CO)(PPh_3)_3]$ (0.005 mmol, 0.005 g) as described above. After chromatography (5–10% EtOAc/hexane) **38a** was obtained as a pale yellow oil (0.0532 g, 26%) as well as unreacted starting material (0.120 g, 58% recovery). A mixture of *E*/*Z* isomers (*E*:*Z* ≈ 4:1) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1638, 1599, 1580, 1487, 1439, 1342, 1273. ^1H NMR (300 MHz, $CDCl_3$, only major *E* isomer listed): δ = 1.22–1.26 [9 H, m, OCH(CH_3)$_2$ and CHCH_3], 2.44 (s, 3 H, ArCH_3), 3.38 (br. d, 2 H, J = 4.2 Hz, ArCH_2C), 3.79 (s, 3 H, OCH_3), 4.01 (2 H, distorted AB system, J ≈ 7 Hz, ArCH_2N), 4.47–4.50 [2 H, m, OCH(CH_3)$_2$ and NCH=CHCH_3], 4.74 [1 H, dd, J = 17.2 and 1.7 Hz, CH=C(H)*H*], 4.93 [1 H, dd, J = 10.6 and 1.7 Hz, CH=C(*H*)H], 5.78–5.90 (m, 1 H, NCH=CH_2), 5.95–6.23 (and under d at 7.31, 1 H, m, NCH=CH), 6.69 (d, 1 H, J = 8.4 Hz, 5-H), 6.86 (d, 1 H, J = 8.4 Hz, 6-H), 7.31 (d, 2 H, J = 8.1 Hz, 2 ArH), 7.75 (d, 2 H, J = 8.1 Hz, 2 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, signals for 1 aromatic C and 1 aromatic CH not observed): δ = 14.2 (CHCH_3), 21.5 (ArCH_3), 22.6 [OCH(*C*H_3)$_2$], 30.5 (Ar*C*H_2C), 45.0 (ArCH_2N), 55.5 (OCH_3), 74.6 [O*C*H(CH_3)$_2$], 110.1 (CH), 115.2 (CH), 124.7 (CH), 127.2 (2 CH), 127.3 (CH), 129.6 (2 CH), 132.6 (C), 136.7 (C), 137.1 (CH), 143.4 (C), 145.2 (C), 152.7 (C) ppm. MS: *m*/*z* (%) = 429 (1) [M^+] 389 (38), 192 (50), 191 (17), 177 (22), 176 (100), 175 (18), 161 (26), 144 (18), 91 (24). HRMS calculated for $C_{24}H_{31}NO_4S$: 429.1974, found: 429.1976.

***N*-(2-Allyl-3-isopropoxy-4-methoxybenzyl)-1-phenyl-*N*-[(1*E*)-prop-1-en-1-yl]methanesulfonamide (38b):** Compound **34b** (0.488 mmol, 0.210 g) in toluene (20 cm^3) was treated with $[RuClH(CO)(PPh_3)_3]$ (0.005 mmol, 0.005 g). After chromatography (5% EtOAc/hexane) **38b** was isolated as a pale yellow oil (0.188 g, 90%). A mixture of *E*/*Z* isomers (*E*:*Z* ≈ 3:1) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1663, 1489, 1439, 1355, 1272, 1216. ^1H NMR (300 MHz, $CDCl_3$, only major *E* isomer listed): δ = 1.21 [6 H, d, J = 6.2, OCH(CH_3)$_2$], 1.53 (m, 3 H, CHCH_3), 3.28 (br. d, 2 H, J = 5.8 Hz, ArCH_2C), 3.77 (s, 3 H, OCH_3), 4.07 (br. s, 2 H, ArCH_2N), 4.37–4.46 (m, 2 H, ArCH_2SO_2), 4.35–4.56 [2 H, m, OCH(CH_3)$_2$ and NCH=CH], 4.74 [1 H, dd, J = 17.2 and 1.6 Hz, CH=C(H)*H*], 4.94 [1 H, dd, J = 1.6 and 10.2 Hz, CH=C(*H*)H], 5.65–5.80 (m, 1 H, CH_2CH=CH), 6.30–6.44 (m, 1 H, NCH=CH), 6.72 (d, 1 H, J = 8.6 Hz, 5-H), 6.96 (d, 1 H, J = 8.6 Hz, 6-H), 7.38–7.39 (m, 5 H, 5 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.2 (CH_3), 22.5 [OCH(*C*H_3)$_2$], 30.1 (Ar*C*H_2C), 48.0 (ArCH_2N), 55.5 (OCH_3), 58.5 (ArCH_2SO_2), 74.5 [O*C*H(CH_3)$_2$], 107.0 (CH), 110.2 (CH), 115.2 (CH), 121.0 (CH), 125.9 (C), 124.6 (CH), 126.8 (CH), 128.9 (2 CH), 130.3 (C), 131.9 (2 CH), 133.0 (C), 135.8 (CH), 144.7 (C), 151.6 (C) ppm. MS: *m*/*z* (%) = 429 (1) [M^+] 387 (15), 373 (10), 274 (15), 219 (29), 178 (13), 177 (100), 176 (12), 145 (16), 117 (14), 91 (35). HRMS calculated for $C_{24}H_{31}NO_4S$: 429.1974, found: 429.1981.

***N*-(2-Allyl-3-isopropoxy-4-methoxybenzyl)-*N*-[(1*E*)-prop-1-en-1-yl]-acetamide (38c):** Acetamide **34c** (0.648 mmol, 0.206 g) was treated with $[RuClH(CO)(PPh_3)_3]$ (0.006 mmol, 0.006 g) as described above. After chromatography (5–15% EtOAc/hexane) **38c** was obtained as a pale yellow oil (0.159 g, 77%). A mixture of *E*/*Z* isomers (*E*:*Z* ratio difficult to determine due to the peak broadening because of 1:1 Ac rotamers) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1645, 1522, 1486, 1216. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.24–1.30 [m, 6 H, OCH(CH_3)$_2$], 1.61–1.66 (m, 3 H, CHCH_3), 2.04 and 2.30 (2 s, 3 H, COCH_3), 3.51 (br. s, 2 H, ArCH_2C), 3.79 and 3.82 (2 s, 3 H, OCH_3), 4.42–4.58 [m, 1 H, OCH(CH_3)$_2$], 4.61 and 4.75 (2 s, 2 H, ArCH_2N), 4.80–5.10 (m, 3 H, CH=CH_2 and NCH=CH), 5.85–5.96 (m, 1 H, CH=CH_2), 6.53–6.73 (m, 2 H, 5-H and 6-H), 7.35 (and rest under previous multiplet, NCH=CH, J = 14.5 Hz, 1 H, d) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.3 and 15.5 (CHCH_3), 22.2 (COCH_3), 22.6 [OCH(*C*H_3)$_2$], 30.2 and 30.4 (Ar*C*H_2C), 44.8 and 48.2 (ArCH_2N), 55.5 (OCH_3), 74.5 and 75.0 [O*C*H(CH_3)$_2$], 106.9 and 109.0 (CH), 110.3 and 110.5 (CH), 115.2 (CH), 119.5 and 120.1 (CH), 126.2 and 128.4 (CH), 130.2 and 130.9 (C), 131.2 and 132.5 (C), 135.7 and 136.0 (CH), 145.2 (C), 151.4 and 151.8 (C), 169.0 and 169.6 (C=O) ppm. MS: *m*/*z* (%) = 317 (20) [M^+], 275 (12), 177 (100), 176 (46), 175 (13), 161 (15), 145 (33), 117 (31), 115 (16), 43 (13). HRMS calculated for $C_{19}H_{27}NO_3$: 317.1991, found: 317.1992.

Attempted Synthesis of 6-Isopropoxy-7-methoxy-2-[(4-methylphenyl)sulfonyl]-2,5-dihydro-1*H*-2-benzazepine 39a. Formation of *N*-{3-Isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}-4-methylbenzenesulfonamide (37a): According to the general RCM procedure, benzenesulfonamide **38a** (0.0294 mmol, 0.0126 g) was dissolved in toluene (10 cm^3) and treated with catalyst **28** (0.015 mmol, 0.013 g) at 60 °C for 25 h. After chromatography (5% EtOAc/hexane) **37a** was obtained as a pale yellow oil (0.0053 g, 47%). A mixture of *E*/*Z* isomers (*E*:*Z* = >5:1) was observed by NMR spectroscopy. IR (NaCl plate): $\tilde{\nu}_{max}/cm^{-1}$ = 1599, 1522, 1429, 1334, 1272. ^1H NMR (300 MHz, $CDCl_3$, only major *E* isomer listed): δ = 1.19 [6 H, d, J = 6.2 Hz, OCH(CH_3)$_2$], 1.77 (dd, 3 H, J = 6.5 and 1.4 Hz, CHCHCH_3), 2.43 (s, 3 H, ArCH_3), 3.79 (s, 3 H, OCH_3), 4.08 (2 H, distorted AB system, J ≈ 5.8 Hz, ArCH_2N), 4.27 [1 H, sept, J = 6.2 Hz, OCH(CH_3)$_2$], 4.48 (br. s, 1 H, NH),

5.90–6.02 (m, 1 H, CHC*H*CH_3), 6.21 (dd, 1 H, J = 16.1 and 1.4 Hz, C*H*CHCH_3), 6.65 (d, 1 H, J = 8.4 Hz, 5-H), 6.83 (d, 1 H, J = 8.4 Hz, 6-H), 7.30 (d, 2 H, J = 8.1 Hz, 2 ArH), 7.73 (d, 2 H, J = 8.1 Hz, 2 ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, only major *E* isomer listed): δ = 19.1 (CHCH*C*H_3), 21.5 (ArCH_3), 22.5 [OCH(*C*H_3)$_2$], 45.6 (NCH_2), 55.7 (OCH_3), 75.2 [O*C*H(CH_3)$_2$], 110.3 (CH), 124.2 (CH), 124.9 (CH), 126.2 (C), 127.2 (2 CH), 129.6 (2 CH), 132.6 (CH), 133.0 (C), 136.9 (C), 143.4 (C), 145.1 (C), 153.0 (C) ppm. MS: *m*/*z* (%) = 389 (11) [M$^+$], 264 (31), 218 (90), 192 (61), 176 (27), 131 (61), 91 (47), 117 (31), 69 (100). HRMS calculated for $C_{21}H_{27}NO_4S$: 389.1661, found: 389.1643.

Attempted Synthesis of 2-(Benzylsulfonyl)-6-isopropoxy-7-methoxy-2,5-dihydro-1*H*-2-benzazepine 39b. Formation of Mixture of *N*-{3-Isopropoxy-4-methoxy-2-[(1*E*)-prop-1-en-1-yl]benzyl}-1-phenylmethanesulfonamide 37b and *N*-(2-Allyl-3-isopropoxy-4-methoxybenzyl)-1-phenylmethanesulfonamide 40b: According to the general RCM procedure, benzylsulfonamide **38b** (0.169 mmol, 0.0726 g) in toluene (7 cm^3) was treated with catalyst **28** (0.009 mmol, 0.008 g) at 60 °C for 18.5 h. After chromatography (5–10% EtOAc/hexane), a mixture of **37b** (mainly *E*) and **40b** (ca. 1:1) were obtained as a milky oil which slowly solidified (0.038 g, 58%). The ^{1}H and ^{13}C NMR spectra contained all the signals for **37b** (see ref.[17]). In addition signals at 3.46 (br. d, 2 H, J = 5.5 Hz, ArCH_2CHCH_2), 4.82–4.96 (m, 2 H, ArCH_2CHCH_2) and 6.00–6.05 (m, 1 H, ArCH_2C*H*CH_2) in the ^{1}H NMR spectrum were characteristic for compound **40b**. A signal at 30.6 was also readily identified for the Ar*C*H_2CHCH_2 in the ^{13}C NMR spectrum. Finally, the structures of the compounds were supported by the mass spectra: MS: *m*/*z* (%) = 389 (11) [M$^+$], 264 (31), 234 (19), 218 (90), 192 (100), 176 (27), 130 (61), 91 (60), 69 (100). HRMS calculated for $C_{21}H_{27}NO_4S$: 389.1661, found: 389.1671.

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