Formation of seven-membered rings by RCM of vinyl bromides


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DOI: 10.1055/a-1845-4195

Please cite this article as: Ajavakom V, Pandokrak P, Salim S S et al. Formation of seven-membered rings by RCM of vinyl bromides. Synlett 2022. doi: 10.1055/a-1845-4195

Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:
Grubbs II catalyst mediated ring-closing metathesis (RCM) of mono-brominated dienes is reported to proceed in moderate to good yields (40–80%) where the linking chain contains five atoms, leading to carbocyclic and heterocyclic 7-membered bromo-olefins. Notably, RCM to form 5-, 6- or 8-membered bromo-olefins was unsuccessful, with the exception of one example where RCM afforded diethyl 3-bromocyclohex-3-ene-1,1-dicarboxylate. In this case a bromomethyl-substituted cyclohexene was obtained as a byproduct. The utility of selected bromo-olefin RCM products was demonstrated through their participation in Suzuki-Miyaura reactions. Vinyl halide exchange (Br→Cl) was noted as a side reaction under RCM conditions.

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Richard Brown, University of Southampton, School of Chemistry, Southampton, United Kingdom of Great Britain and Northern Ireland
Formation of seven-membered rings by RCM of vinyl bromides

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Received: The date will be inserted once the manuscript is accepted.

Abstract: Grubbs II catalyst mediated ring-closing metathesis (RCM) of mono-brominated dienes is reported to proceed in moderate to good yields (40–80%) where the linking chain contains five atoms, leading to carbocyclic and heterocyclic 7-membered bromo-olefins. Notably, RCM to form 5-, 6- or 8-membered bromo-olefins was unsuccessful, with the exception of one example where RCM afforded diethyl 3-bromocyclohex-3-ene-1,1-dicarboxylate. In this case a bromomethyl-substituted cyclohexene was obtained as a byproduct. The utility of selected bromo-olefin RCM products was demonstrated through their participation in Suzuki-Miyaura reactions. Vinyl halide exchange (Br →Cl) was noted as a side reaction under RCM conditions.

Key words: Ring-closing metathesis, Grubbs catalyst, vinyl bromides, carbocycles, heterocycles

Diene ring-closing metathesis (RCM) is well-established as a powerful tool for the synthesis of structurally diverse carbocycles and heterocycles since the advent of well-defined ruthenium-based carbene catalysts that are compatible with a wide variety of functionality. 1 Despite the tremendous advances that have been made in the development of practically useful metathesis catalysts, and applications, 1 there still remain limitations to RCM of some substrate classes. Regio-defined cyclic vinyl bromides are valuable synthetic intermediates, particularly as substrates for transition metal catalysed cross-coupling reactions, 2 and as precursors to reactive intermediates. However, accessing vinyl bromides by alkene metathesis is not without challenges. Cross-metathesis (CM) of vinyl bromides with Grubbs’ catalysts is hindered by the undesirable formation of unstable Fischer carbene intermediates, which rapidly decompose to form terminal carbide and phosphoniomethylidene complexes that are inactive in promoting metathesis. 3 In independent studies the groups of Grubbs and Weinreb both reported that they were unsuccessful in attempts to form cyclic vinyl bromides by RCM, 4,5 whereas Weinreb and co-workers were able to demonstrate the efficient cyclisation of the corresponding chlorinated substrates. 4a In more extensive studies, Gatti et al. demonstrated that when mono-brominated dienes are treated with Grubbs II (GII), metathesis initially proceeds at the unhalogenated olefin and the alkyl bromide subsequently reacts irreversibly when forced into close proximity with the metal centre. 6 This problem was elegantly overcome through modulation of the reactivity of the bromo-olefin moiety with respect to the ruthenium centre by introduction of a “protecting” phenyl substituent in the terminal position cis to the bromo group. Coordination of the bromo substituent to the ruthenium centre was thus prevented, permitting efficient RCM of a series of alkenyl bromides (Scheme 1).

Scheme 1 RCM of vinyl bromides

In 2003 we reported the synthesis of carbocyclic and heterocyclic fluoro-olefins by RCM of mono-fluorodienes, 7 where the interest lay in the fluorine-containing products themselves. We also became interested in RCM of bromo-dienes, as a route to cyclic vinyl bromides as potentially useful synthetic intermediates for C–C bond formation. Here we
describe the RCM of bromo-dienes, showing that the reaction may proceed without the introduction of a “protecting” substituent in certain cases.

As our preliminary results preceded the reports of Gatti et al., and the mechanistic insight detailed therein, the bromo-diene substrates described here contained simple 3-bromobut-3-en-1-yl, and 2-bromoprop-2-en-1-yl chains. Initial investigations were carried out using a sulfamide-linked diene substrate 1a, analogous to the fluorinated dienes reported previously. Hanson has previously utilised RCM strategies to access cyclic sulfamide scaffolds for the synthesis of HIV protease inhibitor analogues, whilst we have reported the synthesis of a range of cyclic sulfonamides and sulfamides via diene and enyne RCM. The sulfamide-linked RCM substrate 1a was synthesised in four steps from chlorosulfonyl isocyanate, in a similar manner to the previously reported fluorinated dienes. As our preliminary results preceded the reports of Gatti et al., we have reported the synthesis of a range of cyclic sulfonamides and sulfamides via diene and enyne RCM. The sulfamide-linked RCM substrate 1a was synthesised in four steps from chlorosulfonyl isocyanate, in a similar manner to the previously reported fluorinated dienes.7,9a,12,13

Pleasingly, on treatment with Grubbs II catalyst, giving trisubstituted alkene 2a in excellent yield (Scheme 2). Greatly encouraged by this result, several unsymmetrical N-substituted sulfamides (1b–d) were synthesised, and subjected to metathesis conditions to yield the 7-membered bromo-alkenes 2b–d in 60–80% yields. Interestingly, an inseparable byproduct was clearly evident in the NMR spectra of the N-Boc sulphonamide 2d, which was subsequently identified to be the vinyl chloride 3d (2d:3d ~83:17, 1H NMR). The structure of the chlorinated by-product 3d was confirmed by independent synthesis by RCM of the chloro-analogue of 1d (90%, see SI for details). Close inspection of the 1H NMR spectra of the RCM products 2a–c also revealed minor amounts of the chloro-alkenes 3b (19:1) and 3c (15:1) to be present.

To investigate the chemoselectivity of the reaction, a sulfamide derivative 1e bearing methallyl and 2-bromoallyl appendages was treated with Grubbs II catalyst, giving trisubstituted alkene 4 as the major product in 66% isolated yield, along with the cyclised vinyl bromide 3e (8%). It is notable that the non-cyclised 2-bromoallyl chain in 4 had undergone partial chloride exchange (Br:Cl ~ 14:1). By contrast, Br/Cl exchange was not evident in the spectrum of 2e.

In addition to highlighting the lower metathesis reactivity of the vinyl bromide compared to the methallyl group, the competition experiment indicates that Cl/Br exchange most likely occurs in the acyclic bromoalkene. The origin of the chloride in 3e and 4 is the GII complex, or a degradation product, as it is the only chlorinated species present in the reaction.

It was of interest to explore the generality of RCM of vinyl bromides with a series of carbon and heteroatom linked diene substrates (Table 1). Towards this goal, a variety of mono-bromo dienes were prepared, including a series of sulfonamide-linked dienes 5–7 and an analogous series of malonate derived dienes 8–12.

Table 1 RCM of sulfonamide- and carbon linked mono-brominated dienes.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Method</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>A</td>
<td></td>
<td>ND*</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>A</td>
<td></td>
<td>ND*</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>A</td>
<td></td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>A</td>
<td></td>
<td>ND*</td>
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<tr>
<td>5</td>
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<tr>
<td>6</td>
<td></td>
<td>C</td>
<td></td>
<td>60</td>
</tr>
</tbody>
</table>

Scheme 2 RCM of sulfamide-linked brominated dienes

In addition to highlighting the lower metathesis reactivity of the vinyl bromide compared to the methallyl group, the competition experiment indicates that Cl/Br exchange most likely occurs in the acyclic bromoalkene. The origin of the chloride in 3e and 4 is the GII complex, or a degradation product, as it is the only chlorinated species present in the reaction.

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<tr>
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<td>ND*</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>A</td>
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<td>4</td>
<td></td>
<td>A</td>
<td></td>
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<tr>
<td>6</td>
<td></td>
<td>C</td>
<td></td>
<td>60</td>
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</tbody>
</table>

Scheme 3 Competition experiment

To investigate the chemoselectivity of the reaction, a sulfamide derivative 1e bearing methallyl and 2-bromoallyl appendages was treated with Grubbs II catalyst, giving trisubstituted alkene 4 as the major product in 66% isolated yield, along with the cyclised vinyl bromide 3e (8%). It is notable that the non-cyclised 2-bromoallyl chain in 4 had undergone partial chloride exchange (Br:Cl ~ 14:1). By contrast, Br/Cl exchange was not evident in the spectrum of 2e.
An interesting trend was observed in treatment of sulfonamide-linked dienes 5–7 with Grubbs II. Attempted RCM of dienes 5 and 6 did not yield the corresponding 5- and 6-membered cyclic bromo-olefins 13 and 14, respectively (Table 1, Entries 1 and 2). By contrast, exposure of diene 7 to the same conditions delivered 7-membered heterocycle 15 with an isolated yield of 44% (Entry 3). As observed in the sulfamide series, the cyclised product contained a small amount of the vinyl chloride (Br:Cl ~ 15:1, 1H NMR). Similarly, RCM of carbon linked diene 8 did not proceed to the 6-membered bromo-olefin 16 using Grubbs II catalyst (Entry 4), but the 7-membered cyclic bromo-olefin 17 was isolated in good yield of 80% from homologous diene 9 (Br:Cl ~ 17:1, Entry 5). With the objective of suppressing initial reaction of the halo-olefin with the catalyst, cyclisation of trisubstituted Z bromo-olefin 10 was investigated, giving bromohexene 17 in moderately reduced yield (60%, Entry 6) compared to 9. The formation of 8-membered rings via RCM is more challenging, and consequently, failure of Grubbs II to effect cyclisation of diene 11 is perhaps not surprising, with only styrene CM product 18 (21%) and recovered 11 (39%) obtained (Entry 7).

The results thus far suggested an interesting selectivity for the RCM of mono-brominated dienes leading to 7-membered rings. In an effort to probe the reaction towards 6-membered rings further, the position of the bromo-olefin relative to the carbon linker group was extended by one methylene in 12. Curiously, treatment of diene 12 with Grubbs II in refluxing benzene for 12 h afforded four different compounds; an inseparable mixture 6-membered cyclic vinyl bromide 19 and the chloro-analogue 20 (19:20 ~ 8.6:1) in 36% yield along with 21% of an inseparable mixture of carbocycles 21 and 22 (21:22 = 5:1, Entry 8).

The origin of carbocycles 21 and 22 was not immediately apparent to us. Consequently, in an effort to gain further insight into the reaction, an isotopic labelling study was conducted. Thus, treatment of partially deuterated malonate 12-d3 with Grubbs II afforded halogenated carbocycles 19-d3/20-d3 and 21-d3/22-d3 in 48% and 44% yield, respectively, again with significant Br/Cl exchange (Table 2, Entry 1).

As anticipated, cyclic vinyl halides 19-d3 and 20-d3 exhibit deuterium incorporation at the 2- and 3-positions (1H NMR), which is consistent with a typical RCM catalytic cycle. More interestingly, this study enables determination of the origin of the additional CH2 unit at C-5 in halomethylcyclohexenes 21-d3 and 22-d3. The lack of deuterium incorporation at C-5 in 21-d3/22-d3 (1H NMR) suggests that the methylene is derived from the bromo-olefin moiety of malonate 12-d3. Homologation reactions with ruthenium alkylidene species have been previously described, proceeding through ruthenacyclobutane intermediates. However, for such processes, a non-carbene ruthenium catalyst is employed with the ruthenium alkylidene complex being generated through in-situ reaction with a diazo compound.

To investigate whether a cooperative non-carbene catalytic pathway could operating in this case, malonate 12-d3 was exposed to ruthenium catalyst (Catalyst A) formed in-situ from [RuCl2(p-cymene)], tricyclohexylphosphine, 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride and Cs2CO3 (Table 2, Entry 2). Interestingly, the outcome was almost identical to that using Grubbs II catalyst. Although the reaction did not proceed to completion in this case, carbocycles 19-d3/20-d3 and 21-d3/22-d3 were obtained in 33% and 29% yields, respectively. It is noteworthy that an increased amount of allylic chloride 22-d3, was isolated (21-d3:22-d3 ~ 72:28, 1H NMR) when using catalyst A instead of Grubbs II (~9:1, 1H NMR).

### Table 2 Ru-catalysed cyclisations of partially deuterated malonate 12-d3.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield 19-d3 and 20-d3</th>
<th>Yield 21-d3 and 22-d3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Grubbs II</td>
<td>48% (7:3)²</td>
<td>44% (9:1)²</td>
</tr>
<tr>
<td>2</td>
<td>Catalyst A*</td>
<td>33% (8:2)²</td>
<td>29% (7:3)²</td>
</tr>
</tbody>
</table>

* Catalyst A formed in situ from [RuCl2(p-cymene)], tricyclohexylphosphine, 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride and Cs2CO3. ** Ratio determined by 1H NMR. * Yield based on recovered 12-d3.
These results suggest that both carbene and non-carbene complexes may be involved in catalysis, and proposed catalytic cycles are presented to account for catalytic turnover in both reaction manifolds (Scheme 4).

Scheme 4 Proposed reaction pathways leading to RCM and demethylenative cyclisation of 12-ds with Cl/Br exchange.

Formation of six-membered vinyl halides 21-ds/22-ds can be accounted for by a typical RCM catalytic cycle, initiated at the non-halogenated olefin of malonate 12-ds, and proceeding by way of intermediates 23 and 24 (Scheme 4, red cycle). As noted in the formation of 4 (see Scheme 3), vinylic Br/Cl exchange does not require involvement of the haloalkene in RCM, and halide exchange in 12-ds may be mediated via a ruthenium carbene or a Ru species formed through degradation of the Grubbs II catalyst (Scheme 4, top left). The Ru complex also provides a source of chloride ion.

It is proposed that halogenated ruthenacyclobutane intermediate 24 sits at a junction with a second cycle, where an alternate fragmentation gives 26, leading to allylic halides 21-ds/22-ds following substitution with Br/Cl (blue cycle). The resulting non-carbene ruthenium species 27 may participate in a cooperative catalytic cycle via cyclometallation of 12-ds to give ruthenacyclopentane 28, which following fragmentation gives intermediate 29. Finally, substitution with Br/Cl yields carbycycles 21-ds/22-ds, with regeneration of a metal carbene catalyst 25. Peppers et al. have proposed similar interplay of synergistic reaction mechanisms during the cyclopropanation/RCM of enynes proceeding through concurrent metal carbene and π-Lewis acid mediated catalytic cycles.

Having established that several 7-membered cyclic bromo-olefins could be effectively accessed via RCM, we endeavored to demonstrate the utility of these scaffolds with a series of cross-coupling reactions. To this end, vinyl bromides 2a and 17 were submitted to Suzuki-Miyaura reaction conditions (Scheme 5). Vinyl bromide 2a was treated with Pd(PPh₃)₄ and 2-formylphenyl boronic acid, under basic bi-phasic conditions, and after just 10 min heating at reflux, afforded the cross-coupled olefin 30 in 71% yield. By comparison, Suzuki-Miyaura coupling of bromo-olefin 17 and 3-methoxyphenyl boronic acid under reflux conditions afforded olefin 31 in excellent high yield (92%).

Scheme 5 Suzuki-Miyaura reactions of RCM products.

To conclude, this study has demonstrated RCM of certain mono-brominated dienes without the need for ‘protecting’ the bromo-olefin unit from the ruthenium catalyst centre, providing access to several carbocyclic and heterocyclic seven-membered bromo-olefins. Br/Cl exchange was noted as a side reaction during the study, where the source of the chloride is the ruthenium catalyst. In accord with previous reports, 5-, 6- and 8-membered rings were unattainable, with the exception of one case in which the 6-membered carbocycle was obtained along with a non-metathesis halomethylated side-product. The utility of the vinyl bromide RCM products was demonstrated by palladium catalysed cross-coupling reactions.


Primary Data for this article are available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083 and can be cited using the following DOI: (number will be inserted prior to online publication).
Acknowledgment

The authors acknowledge EPSRC and GlaxoSmithKline for a CASE award (S. S. S.), the Royal Society for a University Research Fellowship (R. C. D. B.), and the European Regional Development Fund (ERDF) for funding the AI-Chem project through the INTERREG IVa program 4061. This work was also supported by the Center of Excellence for Innovation in Chemistry (PERCH-CIC). In the commemoration of Professor Robert Grubbs for his discovery on this field.

References


(13) See supporting information for full details of the synthesis of RCM substrates 2 and 5-12.


(18) Halide exchange has previously been observed in reactions of ruthenium alkylidene catalysts with vinyl bromides. See ref. 3.
**Supporting Information**

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<td>Figure S45, S46. 1H- and 13C-NMR spectra of compound 15 in CDCl3</td>
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General procedures: All chemicals were used as received from standard chemical suppliers unless otherwise stated. All reactions were monitored by thin layer chromatography (TLC) on aluminum sheets coated with silica gel containing a fluorescent indicator (Merck) and were visualized under UV light with wavelength 254 nm, iodine or potassium permanganate solution. Flash column chromatography was carried out on Silica 60 (Fisher Matrix). Evaporation refers to rotary evaporation of solvent. IR spectra were recorded on a Perkin-Elmer Spectrum GX 60237 and Perkin-Elmer FT-IR spectrum 400 spectrometers. Spectra of solid samples were recorded as ATR. $^1$H-NMR and $^{13}$C-NMR were recorded in CDCl$_3$ solution using Bruker AC300 or AM300 (300 and 75MHz respectively), or Bruker DPX400, ADVANCE 400 or ASCEND 400 (400 and 100 MHz respectively) spectrometers. Chemical shift ($\delta$) are reported in ppm referenced to residual solvent signal, CDCl$_3$ ($\delta$H 7.27, $\delta$C 77.0), and coupling constants ($J$) are in Hertz (Hz) and were recorded in ppm High resolution mass spectra (HRMS) were recorded on a Bruker Daltomics microOTOF-QII mass spectrometer with an electrospray ionization (ESI) source.
To a solution of N,N'-dibenzyl-N-(2-bromoprop-2-en-1-yl)sulfuric diamide (100 mg, 0.25 mmol) in CH$_3$CN (5 mL) were added NaH (6 mg, 0.25 mmol) (CAUTION! Liberation of explosive gas) and n-Bu$_4$NBr (16 mg, 0.05 mmol) at 0 °C. After stirring for 10 min, allyl bromide (22 µL, 0.25 mmol) was added. The reaction mixture was stirred for 15 h at rt and before quenching by careful addition of water (10 mL). The solution was extracted with EtOAc (3×15 mL). The combined organic phases were dried over MgSO$_4$ and concentrated under reduced pressure to afford the crude product as a yellow oil. Purification was accomplished by column chromatography eluting with EtOAc/hexane (4:96) to give compound 1a (97 mg, 89%) as a colourless oil.

$^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 7.35-7.25 (10H, m), 5.87-5.79 (1H, m), 5.78 (1H, s), 5.62 (1H, s), 5.20 (1H, d, $J$ = 10.1 Hz), 5.11 (1H, d, $J$ = 17.1 Hz), 4.45 (2H, s), 4.40 (2H, s), 3.95 (2H, s), 3.72 (2H, d, $J$ = 6.6 Hz). $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 136.1 (C), 135.3 (C), 132.8 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH$_2$), 127.8 (CH), 120.4 (C), 119.6 (CH$_2$), 54.5 (CH$_2$), 51.3 (CH$_2$), 50.7 (CH$_2$), 49.9 (CH$_2$). IR $\nu_{max}$ (cm$^{-1}$): 2921, 1639, 1629, 1496, 1456. LRMS (ES$^+$): m/z (% rel. intensity) 437 (100) and 435 (95) [M+H]$^+$. HRMS (ES$^+$): Calcd. for C$_{20}$H$_{23}$BrN$_2$O$_2$SNa: 459.0536, found 459.0530.
To a solution of N-benzyl-N’-methyl-N’-(prop-2-en-1-yl)sulfuric diamide (102 mg, 0.42 mmol) in CH₃CN (5 mL) were added NaH (10.3 mg, 0.42 mmol) (CAUTION! Liberation of explosive gas) and n-Bu₄NBr (27.1 mg, 0.05 mmol) at 0 °C. After stirring for 10 min, 2,3-dibromopropene (41 µL, 0.42 mmol) was added. The reaction mixture was stirred for 15 h at rt and before quenching by careful addition of water (10 mL). The solution was extracted with EtOAc (3x15 mL). The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure to afford the crude product as a yellow oil. Purification by column chromatography eluting with EtOAc/hexane (2:98) afforded compound 1b (111 mg, 73%) as a colourless oil.

¹H NMR (CDCl₃, 400 MHz) δ 7.38-7.25 (5H, m), 5.91 (1H, d, J = 1.1 Hz), 5.82 (1H, ddt, J = 17.0, 10.3, 6.6 Hz), 5.64 (1H, d, J = 1.1 Hz), 5.22 (1H, d, J = 10.1 Hz), 5.13 (1H, d, J = 17.1 Hz), 4.37 (2H, s), 3.97 (2H, s), 3.71 (2H, d, J = 6.6 Hz), 2.76 (3H, s).

¹³C NMR (CDCl₃, 100 MHz) δ 136.1 (C), 132.7 (CH), 128.6 (CH), 128.3 (CH), 127.8 (C) 119.6 (CH₂), 58.4 (CH₂), 51.3 (CH₂), 50.6 (CH₂), 49.7 (CH₂), 34.6 (CH₃).

LRMS (ES⁺): m/z (% rel. intensity) 361 (100) and 359 (90) [M+H]⁺. HRMS (ES⁺): Calcd. For Calcd. for C₁₄H₂₀⁷⁹BrN₂O₂S: 359.0351, found 359.0345.
**N-Benzyl-N-(2-bromoprop-2-en-1-yl)-N'-methyl-N'-{(prop-2-en-1-yl)sulfuric diamide (1c)**

![Chemical Structure](image)

To a solution of *N*-benzyl-*N*-(2-bromoprop-2-en-1-yl)-*N*'methyl-*N*'methylsulfuric diamide (170 mg, 0.53 mmol) in CH₃CN (5 mL) were added NaH (12.7 mg, 0.53 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu₄NBr (34 mg, 0.11 mmol) at 0 °C. After stirring for 10 min, allyl bromide (46 µL, 0.53 mmol) was added. The reaction mixture was stirred for 15 h at rt and before careful addition of water (10 mL). The solution was extracted with EtOAc (3x15 mL). The combined organic solution was dried (MgSO₄) and concentrated under reduced pressure to afford the crude product as a yellow oil.

Purification by column chromatography eluting with EtOAc/hexane (2:98) afforded compound 1c (100 mg, 53%) as a colourless oil.

**1H NMR (CDCl₃, 400 MHz)** δ 7.34-7.25 (5H, m), 5.80 (1H, ddt, J = 17.0, 10.2, 6.4 Hz), 5.79 (1H, d, J = 2.0 Hz), 5.63 (1H, d, J = 2.0 Hz), 5.25 (1H, dd, J = 13.1, 1.4 Hz), 5.20 (1H, dd, J = 5.1, 1.4 Hz), 4.42 (2H, s), 3.92 (2H, s), 3.75 (2H, d, J = 6.3 Hz), 2.74 (3H, s).

**13C NMR (CDCl₃, 100 MHz)** δ 135.9 (C), 132.9 (CH), 128.9 (CH), 128.6 (CH), 128.0 (C), 120.4 (CH₂) 118.9 (CH₂), 54.7 (CH₂), 53.5 (CH₂), 51.4 (CH₂), 34.5 (CH₃).

**LRMS (ES⁺): m/z (% rel. intensity) 361 (100) and 359 (100) [M+H]⁺. HRMS (ES⁺):**

Calcd. for C₁₄H₂₀BrN₂O₂S: 359.0351, found 359.0363.
Following the procedure of Dewynter et al., \(^1\) to a solution of chlorosulfonylisocyanate (0.290 mL, 3.40 mmol) in CH\(_2\)Cl\(_2\) (8 mL) at 0 °C was added \(t\)-BuOH (0.35 mL, 3.40 mmol). The mixture was stirred for 10 min at 0 °C, and then Et\(_3\)N (0.46 mL, 3.40 mmol) was added followed by a solution of \(N\)-benzyl-\(N\)-allyl amine (0.50 g, 3.40 mmol) in CH\(_2\)Cl\(_2\) (2 mL). The mixture was stirred for 12 h at rt. CH\(_2\)Cl\(_2\) (5 mL) was added and the solution was washed with 1 N HCl (3 x 5 mL) and H\(_2\)O (2 x 5 m), dried (MgSO\(_4\)) and concentrated under reduced pressure. Purification by flash chromatography eluting with hexane/Et\(_2\)O (1:1)) yielded tert-butyl (\(N\)-allyl-\(N\)-benzylsulfamoyl)carbamate as a colourless oil (1.0 g, 3.0 mmol, 90 %). Data are consistent with those previously reported.\(^2\)

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.30-7.33 (5H, m), 5.77 (1H, ddt, \(J = 16.7, 10.1, 6.4\) Hz), 5.23 (1H, dd, \(J = 10.1, 1.0\) Hz), 5.17 (1H, dd, \(J = 16.7, 1.0\) Hz), 4.56 (2H, s), 3.88 (2H, d, \(J = 6.4\) Hz), 1.50 (9H, s). \(^1\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 150.2 (C), 135.9 (C), 132.0 (HC), 128.8 (CH), 128.5 (CH), 128.0 (CH\(_2\)), 119.8 (CH\(_2\)), 83.7 (C), 51.6 (CH\(_2\)), 50.2 (CH\(_2\)), 28.6 (CH\(_3\)). IR \(\nu_{\text{max}}\) / cm\(^{-1}\): 3285, 2973, 2931, 1734, 1441, 1360, 1147, 1148, 925, 821. LRMS (ES\(^+\), CH\(_3\)CN) \(m/z\): 349 (50) [M+Na\(^+\)].


**tert-Butyl (N-allyl-N-benzylsulfamoyl)(2-bromoallyl)carbamate (1d)**

To a stirring solution of *tert*-butyl (N-allyl-N-benzylsulfamoyl)carbamate (100 mg, 0.30 mmol) in DMF (10 mL) was added NaHMDS (0.30 mL of 1.0 M solution in THF, 0.30 mmol), 2,3-dibromo-1-propene (37.0 µL, 0.30 mmol) and NaI (2.3 mg, 0.015 mmol). The mixture was stirred for 12 h at 60 °C, then H₂O (5 mL) was added and the mixture was extracted with EtOAc (3 x 5 mL). The combined organic solution was washed with water (3 x 5 mL) and brine (3 x 5 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography eluting with Et₂O/hexane (4:2) to provide the title compound **1d** as a colourless oil (117 mg, 0.26 mmol, 88 %).

**¹H NMR** (400 MHz, CDCl₃) δ 7.28-7.36 (5H, m), 5.93 (1H, d, J = 2.5 Hz), 5.75 (1H, ddt, J = 17.1, 10.2, 6.5 Hz), 5.62 (1H, d, J = 2.5 Hz), 5.21 (1H, dd, J = 10.2, 1.3 Hz), 5.15 (1H, dd, J = 17.1, 1.3 Hz), 4.53 (2H, s), 4.47 (2H, s), 3.88 (2H, d, J = 6.5 Hz), 1.50 (9H, s). **¹³C NMR** (100 MHz, CDCl₃) δ 151.3 (C), 136.2 (C), 128.9 (CH), 132.3 (CH), 128.6 (CH), 128.3 (C), 128.2 (CH), 119.8 (CH₂), 117.9 (CH₂), 84.5 (C), 55.5 (CH₂), 52.3 (CH₂), 50.7 (CH₂), 28.3 (CH₃). **IR νmax/cm⁻¹**: 2981, 1729, 1369, 1321, 1248, 1055, 911, 800. **LRMS (ES⁺, CH₃CN) m/z (relative intensity %)** 469 (100) and 467 (98) [M+Na]⁺. **HRMS (ES⁺)**: Calcd. for C₁₈H₂₅⁷⁹BrN₂O₄Na: 467.0610, found 467.0612.
To a stirred solution of N-(2-methyl-2-propenyl)-N’-phenylmethyl-N’-(2-propenyl)sulfamide (160 mg, 0.46 mmol) in THF (10 mL) was added t-BuOK (52 mg, 0.46 mmol) and 18-crown-6 (122 mg, 0.46 mmol). After 30 min 3-bromo-2-methyl propene (60 μL, 0.59 mmol) was added and the reaction mixture was stirred at rt for 10 h. Water (10 mL) was added, and the organic phase was separated, re-extracting with Et₂O (3 x 15 mL). The combined organic extract was washed with brine (10 mL), dried (MgSO₄) and concentrated under reduced pressure to yield the crude product as a yellow oil. Purification by flash chromatography on silica gel (10 g) eluting with Et₂O/hexane (5:95) afford triene 1e as a pale yellow oil (178 mg, 0.45 mmol, 97%).

¹H NMR (300 MHz, CDCl₃) δ 7.39-7.27 (5H, m), 5.94 (1H, dt, J = 2.2, 1.1 Hz), 5.86 (1H, ddt, J = 17.2, 10.3, 6.6 Hz), 5.66 (1H, dt, J = 2.2, 0.7 Hz), 5.23 (1H, dq, J = 9.9, 1.5 Hz), 5.14 (1H, dq, J = 17.2, 1.5 Hz), 5.04-5.01 (1H, m), 5.00-4.97 (1H, m), 4.41 (2H, s), 4.07 (2H, s), 3.75 (2H, s, J = 6.6 Hz), 1.78 (3H, s). ¹³C NMR (75 MHz, CDCl₃) δ 139.6 (C), 136.2 (C), 133.0 (CH), 128.9 (CH), 128.6 (CH), 127.6 (CH), 127.8 (C), 120.1 (CH₂), 119.6 (CH₂), 115.3 (CH₂), 54.5 (CH₂), 53.7 (CH₂), 50.8 (CH₂Ph), 50.0 (CH₂), 20.3 (CH₃). IR νₘₐₓ neat (cm⁻¹): 3079, 2980, 2917, 1329, 1146, 891. LRMS (ES⁺, CH₃CN) m/z (relative intensity %): 423 (100) and 421 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C₁₇H₂₃⁷⁹BrN₂O₂S: 399.0737, found 399.0742.
To a solution of compound 1a (31.2 mg, 0.07 mmol) in benzene (5 mL) was added a solution of the Grubbs II catalyst (6.0 mg, 7.0 µmol) in benzene (2 mL). The reaction mixture was stirred and degassed for 30 seconds, then heated at reflux for 18 h. At this time, a second portion of the Grubbs II catalyst (3.0 mg, 3.5 µmol) was added as a solution in benzene (1 mL) and heating was continued for 18 h. The solution was concentrated under reduced pressure to afford the crude product as a black oil. Purification by column chromatography eluting with EtOAc/hexane (2:98) afforded the cyclised product 2a (26 mg, 90%) as a white solid.

Data for 2a: M.p. 106–108 °C. $^{1}$H NMR (CDCl$_3$, 400 MHz) δ 7.40-7.24 (10H, m), 6.24 (1H, t, $J = 5.7$ Hz), 4.52 (2H, s), 4.45 (2H, s), 4.03 (2H, s), 3.60 (2H, d, $J = 5.7$ Hz). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 135.6 (C), 135.3 (C), 130.5 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 122.7 (C), 52.4 (CH$_2$), 52.1 (CH$_2$), 44.1 (CH$_2$). IR $\nu_{max}$ (cm$^{-1}$) 3030, 2919, 1507, 1456, 1359. LRMS (ES$^+$, CH$_3$CN) m/z (relative intensity %): 431 (100) and 429 (100) [M+Na]$^+$. HRMS (ES$^+$): Calcd. for C$_{18}$H$_{19}$BrN$_2$NaO$_2$S: 429.0242, found 429.0239.
7-Benzy1-4-bromo-2-methyl-2,3,6,7-tetrahydro-1H-1,4,2,7-thiadiazepine-1,1-dione (2b) and 7-benzy1-4-chloro-2-methyl-2,3,6,7-tetrahydro-1H-1,4,2,7-thiadiazepine-1,1-dione (3b)

To a solution of compound 2b (29.0 mg, 0.08 mmol) in benzene (6 mL) was added a solution of Grubbs II catalyst (6.8 mg, 8.0 µmol) in benzene (2 mL). The reaction mixture was stirred and degassed for 30 s, then heated at reflux for 18 h. The solution was concentrated under reduced pressure to afford the crude product as a black oil. Purification by column chromatography eluting with EtOAc/hexane (2:98) afforded an inseparable mixture (>19:1, 1H NMR) of vinyl bromide 2b and vinyl chloride 3b (20 mg, 75%) as a white solid.

NMR data are recorded on a mixture of 2b and 3b reporting major peaks for 2b and selected peaks for 3b. 1H NMR (CDCl3, 400 MHz) δ 7.39-7.26 (5H, m), 6.29 (1H, t, J = 5.9 Hz), 4.43 (2H, s), 4.21 (2H, s), 3.55 (2H, d, J = 5.8 Hz), 3.03 (3H, s). {minor signals for vinyl chloride 3b: δ 6.06 (1H, t, J = 6.00 Hz), 4.43 (2H, s), 4.15 (2H, s), 3.64 (2H, d, J = 6.0 Hz), 3.02 (3H, s)}. 13C NMR (CDCl3, 100 MHz) δ 135.7 (C), 130.5 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 122.7 (C), 56.7 (CH2), 52.8 (CH2), 43.9 (CH2), 36.5 (CH3). {minor signals for vinyl chloride 3b: δ 55.4 (CH2), 53.1 (CH2), 43.1 (CH2), 36.8 (CH3)}. LRMS (ES+, CH3CN) m/z (relative intensity %): 333 (100), 331 (100) [M+H]⁺. HRMS (ES⁺): Calcd. for C12H15BrN2NaO2S: 354.9909, found 354.9912.
2-Benzyl-4-bromo-7-methyl-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-1,1-dione (2c) and 2-benzyl-4-bromo-7-methyl-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-1,1-dione (3c)

To a solution of compound 1c (28.8 mg, 0.08 mmol) in benzene (6 mL) was added a solution of Grubbs II catalyst (6.8 mg, 8.0 µmol) in benzene (2 mL). The reaction mixture was stirred and degassed for 30 seconds, then heated at reflux for 18 h. The solution was concentrated under reduced pressure to afford the crude product as a black oil. Purification by column chromatography eluting with EtOAc/hexane (2:98) afforded an inseparable mixture (15:1, ¹H NMR) of vinyl bromide 2c and vinyl chloride 3c (15.3 mg, 60%) as a white solid.

NMR data are recorded on a mixture of 2c and 3c reporting major peaks for 2c and selected peaks for 3c. ¹H NMR (CDCl₃, 400 MHz) δ 7.39-7.26 (5H), 6.39 (1H, t, J = 5.9 Hz), 4.44 (2H, s), 4.00 (2H, s), 3.75 (2H, d, J = 5.8 Hz), 2.95 (3H, s). {minor signals for vinyl chloride 3c: δ 6.13 (1H, t, J = 6.0 Hz), 4.30 (2H, s), 4.17 (2H, s), 3.60 (2H, d, J = 6.0 Hz), 3.11 (3H, s).} ¹³C NMR (CDCl₃, 100 MHz) δ 135.4 (C), 130.7 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 122.8 (C), 52.6 (CH₂), 52.1 (CH₂), 48.2 (CH₂), 36.8 (CH₃). {minor signals for vinyl chloride 3c are undetectable because they are too small.}. HRMS (ES⁺): Calcd. for C₁₂H₁₅BrN₂Na₂O₂S: 354.9909, found 354.9908.
tert-butyl 7-benzyl-4-bromo-1,1-dioxo-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-2-carboxylate (2d) and tert-butyl 7-benzyl-4-chloro-1,1-dioxo-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-2-carboxylate (3d)

To a stirring solution of bromo-olefin 1d (60.0 mg, 0.14 mmol) in benzene (15 mL) was added Grubbs II catalyst (12.0 mg, 14 μmol). The mixture was heated under reflux for 12 h, after which time a second portion of catalyst (12.0 mg, 14 μmol) was added and the mixture was stirred for a further 12 h under reflux. The mixture was cooled to room temperature and concentrated under reduced pressure. The resulting brown oil was purified by column chromatography eluting with Et2O/hexane (2:8) to provide the vinyl bromide 2d and the vinyl chloride 3d as an 83:17 (1H NMR) inseparable mixture (54.0 mg, 0.12 mmol, 70 % yield).

1H NMR (83:17 mixture of vinyl bromide 2d and vinyl chloride 3d, 400 MHz, CDCl3), major signals for vinyl bromide 2d: δ 7.32-7.39 (5H, m), 6.06 (1H, t, J = 4.6 Hz), 4.60 (2H, s), 4.50 (2H, s), 3.78 (2H, d, J = 4.6 Hz), 1.57 (9H, s). {minor signals for vinyl chloride 3d: δ 5.83 (1H, t, J = 4.8 Hz), 4.52 (2H, s), 4.48 (2H, s), 3.81 (2H, d, J = 4.8 Hz}}. 13C NMR (83:17 mixture of vinyl bromide 2d and vinyl chloride 3d, 100 MHz, CDCl3), major signals for vinyl bromide 2d: δ 151.3, 135.3 (C), 129.3 (C), 128.8 (CH), 128.7 (CH), 128.3 (CH), 122.1 (CH), 85.3 (C), 52.9 (CH2), 51.8 (CH2), 45.7 (CH2), 28.4 (CH3). {minor signals for vinyl chloride 3d: δ 52.4 (CH2), 49.8 (CH2), 43.9 (CH2), 28.0 (CH3)}. IR νmax / cm⁻¹: 2890, 1727, 1369, 1323, 1258, 1176, 1146, 1094, 943. LRMS (ES⁺, CH3CN) m/z (relative intensity %) 441 (100), 439 (100) [M+Na]⁺. {selected peaks for 3d: 395 (30) [M⁺{35Cl}⁺Na]⁺.}
2-(2-Bromo-2-propenyl)-4-methyl-7-(phenylmethyl)-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-1,1-dione (4) and 4-bromo-2-(2-methyl-2-propenyl)-7-(phenylmethyl)-2,3,6,7-tetrahydro-1H-1λ6,2,7-thiadiazepine-1,1-dione (2e)

To a stirred solution of sulfamide 1e (85 mg, 0.21 mmol) in benzene (10 mL) was added a solution of Grubbs II catalyst (17.8 mg, 21 μmol) in benzene (10 mL). The mixture was stirred and degassed for 1 h. The reaction mixture was heated at reflux for 10 h before concentration under reduced pressure yielded the crude product as a black oil. Purification by flash chromatography on silica gel (4 g) eluting with Et2O/hexane (4:96) afforded the cyclised product 4 as a white solid (50.4 mg, 0.14 mmol, 66%), and the cyclized vinyl bromide 2e also as a white solid (6 mg, 16 μmol, 8%).

Data for compound 4 (isolated as a mixture containing a small amount of the chloro analogue (Br:Cl ~ 14:1, 1H NMR). Mpt. = 115–116 °C. 1H NMR (300 MHz, CDCl3) δ 7.30-7.20 (5H, m), 5.90 (1H, dt, J = 2.2, 1.5 Hz), 5.60 (1H, dt, J = 2.2, 1.1 Hz), 5.38 (1H, dt, J = 1.8, 5.1 Hz), 4.33 (2H, s), 4.04 (2H, br s), 3.71 (2H, s), 3.52 (2H, dd, J = 4.8, 1.5 Hz), 1.72 (3H, d, J = 2.5 Hz). 13C NMR (75 MHz, CDCl3) δ 137.3 (C), 135.6 (C), 128.9 (C), 128.6 (CH), 128.3 (C), 128.2 (CH), 127.9 (CH), 121.9 (CH), 118.8 (CH2), 56.7 (CH2), 52.1 (CH2), 48.7 (CH2), 43.2 (CH2), 24.0 (CH3). IR νmax neat (cm⁻¹): 3051, 2934, 1600, 1330, 898. LRMS (ES⁺, CH3CN) m/z (relative intensity %): 395 (100), 393 (100) [M+Na]+. HRMS (ES⁺): Calcd. for C15H19BrN2O2S: 371.0423, found 371.0427.

Data for compound 2e: Mpt. = 116 °C. 1H NMR (300 MHz, CDCl3) δ 7.31-7.23 (5H, m), 6.15 (1H, t, J = 5.9 Hz), 4.99-4.96 (2H, m), 4.35 (2H, s), 4.07 (2H, s), 3.84 (2H, s), 3.70 (2H, s), 3.45 (2H, s), 3.30 (2H, s), 2.95 (2H, s), 2.75 (2H, s), 2.50 (2H, s), 2.25 (2H, s), 2.00 (2H, s), 1.75 (2H, s), 1.50 (2H, s), 1.25 (2H, s), 1.00 (2H, s), 0.80 (2H, s), 0.60 (2H, s).
3.52 (2H, d, $J = 5.9$ Hz), 1.73 (3H, d, $J = 1.1$ Hz). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 139.4 (C), 135.6 (C), 130.2 (HC=CBr), 128.7 (CH), 128.2 (CH), 128.0 (CH), 122.6 (C), 115.6 (CH$_2$), 54.8 (CH$_2$), 52.3 (CH$_2$), 51.7 (CH$_2$), 44.0 (CH$_2$), 19.5 (CH$_3$). IR $\nu_{\text{max}}$ neat (cm$^{-1}$): 3079, 2975, 1363, 1160, 726. LRMS (ES$^+$, CH$_3$CN) $m/z$ (relative intensity %): 395 (100), 393 (100) [M+Na]$^+$. HRMS (ES$^+$): Calcd. for C$_{15}$H$_{19}$BrN$_2$O$_2$S: 371.0423, found 371.0424.
A sample of pure vinyl chloride 3d was prepared by RCM of tert-butyl (N-allyl-N-benzylsulfamoyl)(2-chloroallyl)carbamate (Scheme SI 1).

**Scheme SI 1.** Synthesis of vinyl chloride 3d by chloro-olefin RCM

*tert-Butyl (N-allyl-N-benzylsulfamoyl)(2-chloroallyl)carbamate*

To a stirring solution of *tert*-butyl (N-allyl-N-benzylsulfamoyl)carbamate (500 mg, 1.53 mmol) in DMF (50 mL) was added NaHMDS (1.53 mL of a 1.0 M solution in THF, 1.53 mmol), followed by 2,3 dichloro-1-propene (115 µL, 1.53 mmol) and NaI (11.5 mg, 0.075 mmol). The mixture was stirred for 12 h at 60 °C then H₂O (50 mL) was added and the mixture was extracted with EtOAc (3 x 50 mL). The combined EtOAc solution was washed with water (3 x 50 mL) and brine (3 x 50 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography, eluting with Et₂O/hexane (4:2) to provide the *tert*-Butyl (N-allyl-N-benzylsulfamoyl)(2-chloroallyl)carbamate as a colourless oil (542 mg, 1.35 mmol, 89%).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.23-7.33 (5H, m), 5.74 (1H, dtd, $J$ = 17.1, 10.1, 6.5), 5.45 (1H, d, $J$ = 1.5 Hz), 5.43 (1H, d, $J$ = 1.5 Hz), 5.18 (1H, d, $J$ = 10.3 Hz), 5.13 (1H, d, $J$ = 17.1 Hz), 4.25 (2H, s), 4.38 (2H, s), 3.84 (2H, d, $J$ = 6.5 Hz), 1.50 (9H, s).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.9 (C), 137.2 (C), 135.9 (C), 132.0 (CH), 128.6 (CH), 128.2 (CH), 127.8 (CH), 119.4 (CH$_2$), 113.4 (CH$_2$), 84.2 (C), 52.3 (CH$_2$), 51.4 (CH$_2$), 50.3 (CH$_2$), 28.0 (CH$_3$).

IR $\nu_{\text{max}}$/cm$^{-1}$: 3008, 1727, 1366, 1321, 1247, 1141, 1055, 923, 892, 799.

LRMS (ES$^+$, CH$_3$CN) $m/z$ (relative intensity %) 425 (30), 423 (100) [M+Na]$^+$. HRMS (ES$^+$) C$_{18}$H$_{25}$ClN$_2$O$_4$SNa = calculated 423.1112, found 423.1112

**tert-butyl 7-benzyl-4-chloro-1,1-dioxo-2,3,6,7-tetrahydro-1H-1,6,2,7-thiadiazepine-2-carboxylate (3d)** – using chloro-olefin RCM

![Chemical structure](image)

Following the procedure of Weinreb and Chao,$^3$ to a stirring solution of tert-butyl (N-allyl-N-benzylsulfamoyl)(2-chloroallyl)carbamate (100 mg, 0.26 mmol) in benzene (40 mL) was added Grubbs II catalyst (83 mg, 26 $\mu$mol). The mixture was heated under reflux for 24 h, then cooled and concentrated under reduced pressure. The resulting brown oil was purified by column chromatography, eluting with Et$_2$O/hexane (2:8) to provide the title vinyl chloride 3d as a colourless oil (87 mg, 0.23 mmol, 90 %).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32-7.38 (5H, m), 5.83 (1H, t, $J$ = 4.8 Hz), 4.52 (2H, s), 4.48 (2H, s), 3.81 (2H, d, $J$ = 4.8 Hz), 1.57 (9H, s). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 151.6 (C), 134.8 (C), 133.1(C), 128.9 (CH), 128.4 (CH), 128.3 (CH), 123.5 (CH), 84.8 (C), 52.4 (CH$_2$), 49.8 (CH$_2$), 43.9 (CH$_2$), 28.0 (CH$_3$). IR $\nu_{\text{max}}$/cm$^{-1}$: 2981, 1719, 1369, 1322, 1271, 1176, 1147, 1096. LRMS (ES$^+$, CH$_3$CN) $m/z$ (relative intensity %) 397

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To a solution of \( N - (2\text{-bromoallyl}) - 4\text{-methylbenzenesulfonamide} \) (100 mg, 0.34 mmol) in \( \text{CH}_3\text{CN} \) (5 mL) was added \( \text{NaH} \) (8.3 mg, 0.34 mmol) (CAUTION! Liberation of explosive gas) and \( n\text{-Bu}_4\text{NBr} \) (22.2 mg, 0.07 mmol) at 0 °C. After stirring for 10 min, allyl bromide (30 µL, 0.34 mmol) was added. The reaction mixture was stirred for 15 h at rt and before quenching by careful addition of water (15 mL). The solution was extracted with \( \text{EtOAc} \) (3x15 mL) and water (10 mL). The combined organic solution was dried (MgSO\(_4\)) and concentrated under reduced pressure to afford the crude product as a yellow oil. Purification by column chromatography eluting with \( \text{EtOAc/hexane (6:94)} \) to give compound 5 (84.3 mg, 75 %) as a colourless oil. Data are consistent with those previously reported.

\( ^1\text{H NMR} \) (CDCl\(_3\), 400 MHz) \( \delta \) 7.71 (2H, d, \( J = 8.1 \) Hz), 7.28 (2H, d, \( J = 8.1 \) Hz), 5.82 (1H, dt, \( J = 2.2, 1.5 \) Hz), 5.58 (1H, m), 5.56 (1H, ddt, \( J = 16.9, 10.1, 6.6 \) Hz), 5.17 (1H, d, \( J = 10.1 \) Hz), 5.12 (1H, d, \( J = 16.9 \) Hz), 4.00 (2H, s), 3.82 (2H, d, \( J = 6.6 \) Hz), 2.41 (3H, s). \( ^{13}\text{C NMR} \) (CDCl\(_3\), 100 MHz) \( \delta \) 143.5 (C), 137.2 (C), 132.0 (CH), 129.8 (CH), 127.9 (CH\(_2\)), 127.3 (CH), 119.9 (C), 119.3 (CH\(_2\)), 53.8 (CH\(_2\)), 50.0 (CH\(_2\)), 21.5 (CH\(_3\)).

\( \text{IR} \) \( \nu_{\text{max}} \) (cm\(^{-1}\)) 3083, 2922, 1692, 1598, 1494, 1441. LRMS (ES\(^+\)): \( \text{m/z} \) (% rel. intensity) 353 (100), 355 (100) [M+Na\(^+\)]. HRMS (ES\(^+\)): \( \text{C}_{16}\text{H}_{16}^{35}\text{BrNO}_2\text{SNa} = \text{calculated} \) 351.9977, found 351.9975.

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N-(2-Bromoallyl)-N-(but-3-enyl)-4-methylbenzenesulfonamide (6)

To a solution of N-(2-bromoallyl)-4-methylbenzenesulfonamide (127 mg, 0.44 mmol) in CH$_3$CN (10 mL) was added NaH (10.5 mg, 0.44 mmol) (CAUTION! Liberation of explosive gas) and n-Bu$_4$NBr (14.1 mg, 0.044 mmol) at 0 °C. After stirring for 10 min, 4-bromobutene (45 µL, 0.44 mmol) was added. The reaction mixture was stirred for 15 h at rt and before quenching by careful addition of water (15 mL). The solution was extracted with EtOAc (3x15 mL) and washed with water (10 mL). The combined organic phases were dried (MgSO$_4$) and concentrated under reduced pressure to afford the crude product as a yellow oil. Purification by column chromatography eluting with EtOAc/hexane (1:9) afforded compound 6 (85 mg, 56%) as a colourless oil. Data are consistent with those previously reported.$^4$

$^1$H NMR (CDCl$_3$, 400 MHz) δ 7.69 (2H, d, $J = 8.2$ Hz), 7.28 (2H, d, $J = 8.0$ Hz), 5.85 (1H, br s), 5.64 (1H, ddt, $J = 17.1$, 10.2, 6.8 Hz), 5.59 (1H, br s), 5.01 (1H, d, $J = 10.2$ Hz), 5.00 (1H, br s), 4.02 (2H, s), 3.21(2H, t, $J = 7.6$ Hz), 2.40 (3H, s), 2.20 (2H, m).

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ 143.5 (C), 136.9 (C), 134.4 (CH), 129.7 (CH), 128.2 (CH$_2$), 127.3 (CH), 119.2 (C), 117.3 (CH$_2$), 55.5 (CH$_2$), 47.6 (CH$_2$), 32.7 (CH$_2$), 21.5 (CH$_3$). IR $\nu_{max}$ (cm$^{-1}$) 2922, 1635, 1597, 1350 (m). LRMS (ES$^+$): $m/z$ (% rel. intensity) 368 (100), 366 (100) [M+Na]$^+$. HRMS (ES$^+$): Calcd. for C$_{14}$H$_{18}^{79}$BrN$_2$SNa: 366.0134, found 366.0135.
N-(2-Bromoallyl)-4-methyl-N-(pent-4-enyl)benzenesulfonamide (7)

To a solution of N-(2-bromoallyl)-4-methylbenzenesulfonamide (150 mg, 0.52 mmol) in CH$_3$CN (5 mL) was added NaH (12 mg, 0.52 mmol) (CAUTION! Liberation of explosive gas) and n-Bu$_4$NBr (33 mg, 0.10 mmol) at 0 °C. After stirring for 10 min, 5-bromo-1-pentene (60 µL, 0.52 mmol) was added. The reaction mixture was stirred for 15 h at rt before quenching by careful addition of water (15 mL). The solution was extracted with EtOAc (3x15 mL) and washed with water (10 mL). The combined organic phases were dried (MgSO$_4$) and concentrated under reduced pressure to afford the crude product as a yellow oil. Purification by column chromatography on silica eluting with EtOAc/hexane (4:96) afforded compound 7 (164 mg, 88%) as a colourless oil.

$^1$H NMR (CDCl$_3$, 400 MHz) δ 7.69 (2H, d, $J = 8.2$ Hz), 7.28 (2H, d, $J = 8.0$ Hz), 5.85 (1H, br s), 5.71 (1H, ddt, $J = 17.0$, 10.3, 6.6 Hz), 5.58 (1H, br s), 5.01-4.91 (2H, m), 3.99 (2H, s), 3.14 (2H, t, $J = 7.8$ Hz), 2.40 (3H, s), 1.99 (2H, q, $J = 7.1$ Hz), 1.64-1.55 (2H, m). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 143.4 (C), 137.2 (C), 137.2 (CH), 129.6 (CH), 128.3 (CH$_2$), 127.2 (CH), 119.1 (C), 115.3 (CH$_2$), 55.5 (CH$_2$), 47.9 (CH$_2$), 30.7 (CH$_2$), 27.2 (CH$_2$), 21.4 (CH$_3$). IR $\nu_{\text{max}}$ (cm$^{-1}$) 3077, 2924, 1641, 1573, 1443, 1341. LRMS (ES$^+$): $m/z$ (% rel. intensity) 382 (100), 380 [M+Na]$^+$. HRMS (ES$+$): Calcd. for C$_{18}$H$_{19}$BrN$_2$NaO$_2$S [M+CH$_3$CN+Na]$^+$: 429.0242, found 429.0239.
To a stirred solution of diethyl-2-(2-bromoallyl)malonate (400 mg, 1.43 mmol) in THF (10 mL) was added t-BuOK (160 g, 1.43 mmol) and 18-crown-6 (378 mg, 1.43 mmol). After stirring for 10 min, 4-bromo-1-butene (145 μL, 1.43 mmol) was added. The reaction mixture was stirred 3 h before quenching with water (10 mL). The organic phase was separated and the aqueous phase was extracted with Et₂O (3 x 15 mL). The combined organic phases were washed with brine (10 mL), dried (MgSO₄) and concentrated under reduced pressure to yield the crude product as a brown oil. Purification by flash chromatography on silica gel (6 g) eluting with EtOAc/hexane (1:99) afforded 8 as a colourless oil (300 mg, 63%).

¹H NMR (300 MHz, CDCl₃) δ 5.71 (1H, ddt, J = 16.8, 10.2, 6.2 Hz), 5.58 (1H, d, J = 1.5 Hz), 5.51 (1H, d, J = 1.5 Hz), 5.01-4.86 (2H, m), 4.16-4.09 (4H, m), 3.10 (2H, s), 2.10-2.00 (2H, m), 1.95-1.84 (2H, m), 1.20 (6H, t, J = 7.3 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 170.4 (C), 137.2 (CH), 132.2 (C), 122.6 (CH₂), 115.1 (CH₂), 61.5 (CH₂), 56.8 (C), 42.9 (CH₂), 30.6 (CH₂), 28.3 (CH₂), 14.0 (CH₃). IR νmax neat (cm⁻¹): 2980, 1729, 1189, 1146, 908. LRMS (ES⁺, CH₃CN) m/z (relative intensity %): 357 (100), 355 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C₁₄H₂₁⁷⁹BrO₄Na: 355.0515 found 355.0513.
2-(2-Bromo-allyl)-2-pent-4-enyl-malic acid diethyl ester (9)

To a stirred solution of diethyl-2-(2-bromoallyl)malonate (300 mg, 1.08 mmol) in THF (10 mL) was added t-BuOK (121 g, 1.08 mmol) and 18-crown-6 (285 mg, 1.08 mmol). After stirring for 10 min, 5-bromo-1-pentene (128 μL, 1.08 mmol) was added. The reaction mixture was stirred 3 h, then water (10 mL) was added. The organic phase was separated re-extracting the aqueous phase with Et₂O (3 x 15 mL). The combined organic solution was washed with brine (10 mL), dried (MgSO₄) and concentrated under reduced pressure to yield the crude product as a brown oil. Purification by flash chromatography on silica gel (6 g) eluting with EtOAc/hexane (1:99) afforded 9 as a colourless oil (180 mg, 48%).

¹H NMR (300 MHz, CDCl₃) δ 5.70 (1H, ddt, J = 17.2, 10.3, 6.6 Hz), 5.58-5.55 (1H, m), 5.49 (1H, d, J = 1.8 Hz), 5.00-4.80 (2H, m), 4.19-4.04 (4H, m), 3.09 (2H, d, J = 0.7 Hz), 2.05-1.90 (4H, m), 1.27-1.20 (2H, m), 1.85 (6H, t, J = 6.9 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 170.6 (C), 137.9 (CH), 127.5 (C), 121.5 (CH₂), 115.0 (CH₂), 61.5 (CH₂), 57.2 (C), 42.9 (CH₂), 33.7 (CH), 30.9 (CH₂), 23.4 (CH₂), 14.0 (CH₃). IR νmax neat (cm⁻¹): 2980, 1729, 1187, 1146, 1023, 907. LRMS (ES⁺, CH₃CN) m/z (relative intensity %): 369 (100), 371 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C₁₅H₂₃BrO₄Na: 369.0672 found 369.0672.
To a stirred solution of diethyl 2-(pent-4-en-1-yl)malonate (319 mg, 1.40 mmol) in THF (10 mL) was added \( \text{t-BuOK} \) (157 mg, 1.40 mmol) and 18-crown-6 (370 mg, 1.40 mmol). The reaction mixture was stirred for 30 min. A solution of 2-bromobut-2-en-1-ol\(^5\) (300 mg, 1.40 mmol) was added. The reaction mixture was stirred for 15 h before addition of water (15 mL). The organic phase was separated, re-extracting the aqueous phase with Et\(_2\)O (3 x 20 mL). The combined organic solution was washed with brine (15 mL), dried (MgSO\(_4\)) and concentrated under reduced pressure to yield the crude product as a yellow oil. Purification by flash chromatography on silica gel (10 g) eluting with Et\(_2\)O/hexane (4:96) afforded \( \text{10} \) as a colourless oil (455 mg, 90%).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 5.78 (1H, ddt, \( J = 17.2, 10.3, 6.6 \) Hz), 5.80 (1H, q, \( J = 6.6 \) Hz), 5.02 (1H, dq, \( J = 17.2, 1.5 \) Hz), 4.97 (1H, dq, \( J = 10.2, 1.5 \) Hz), 4.21-4.04 (4H, m), 3.18 (2H, br s), 2.12-2.03 (2H, m), 2.02-1.94 (2H, m), 1.73 (2H, quin, \( J = 6.6 \) Hz), 1.27 (6H, t, \( J = 7.3 \) Hz).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 170.9 (C), 138.0 (CH), 128.4 (C), 122.1 (CH), 114.9 (CH\(_2\)), 61.3 (CH\(_2\)), 57.3 (C), 43.0 (CH\(_2\)), 33.7 (CH\(_2\)), 30.8 (CH\(_2\)), 23.4 (CH\(_2\)), 17.1 (CH\(_3\)), 14.0 (CH\(_3\)).

IR \( \nu_{\text{max}} \) (cm\(^{-1}\)): 2979, 1730, 1181, 1130.

LRMS (ES\(^+\), CH\(_3\)CN) \( m/z \) (relative intensity %): 385 (100), 383 (100) [M+Na]\(^+\).

HRMS (ES\(^+\)): Calcd. for C\(_{16}\)H\(_{25}\)\(^{79}\)BrO\(_3\)Na: 383.0828, found 383.0825.

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2-(2-Bromo-allyl)-2-hex-5-enyl-malonic acid diethyl ester (11)

![Structural formula of 11]

To a stirred solution of diethyl 2-(2-bromo-allyl)malonate (200 mg, 0.72 mmol) in THF (10 mL) was added t-BuOK (81 mg, 0.72 mmol) and 18-crown-6 (190 mg, 0.72 mmol). After stirring for 10 min, 6-bromo-1-pentene (106 μL, 0.79 mmol) was added. The reaction mixture was stirred for 3 h before addition of water (10 mL). The organic phase was separated, re-extracting the aqueous phase with Et₂O (3 x 15 mL). The combined organic solution was washed with brine (10 mL), dried (MgSO₄) and concentrated under reduced pressure to yield the crude product as a brown oil. Purification by flash chromatography on silica gel (8 g) eluting Et₂O/hexane (1:99) afforded 11 as a colourless oil (196 mg, 76%).

**¹H NMR** (300 MHz, CDCl₃) δ 5.70 (1H, ddt, J = 17.2, 10.3, 6.6 Hz), 5.58-5.55 (1H, m), 5.49 (1H, d, J = 1.8 Hz), 4.96-4.84 (2H, m), 4.19-4.04 (4H, m), 3.08 (2H, d, J = 0.7 Hz), 2.03-1.89 (4H, m), 1.40-1.29 (2H, m), 1.20-1.08 (2H, m), 1.19 (6H, t, J = 7.3 Hz).

**¹³C NMR** (75 MHz, CDCl₃) δ 170.6 (C), 138.5 (CH), 127.5 (C), 121.5 (CH₂), 115.0 (CH₂), 61.5 (CH₂), 57.1 (C), 42.8 (CH₂), 33.3 (CH₂), 31.1 (CH₂), 28.4 (CH₂), 23.4 (CH₂), 14.0 (CH₃).

**IR** νmax neat (cm⁻¹): 2979, 2933, 1730, 1226, 1226, 1181, 1028, 906.

**LRMS** (ES⁺, MeOH) m/z (relative intensity %): 385 (100), 383 (100) [M+Na]⁺. **HRMS** (ES⁺): Calcd. for C₁₆H₂₅BrO₄Na: 383.0828, found 383.0834.
To a stirred solution of diethyl 2-allylmalonate (101 mg, 0.51 mmol) in THF (10 mL) was added t-BuOK (58 mg, 0.51 mmol) and 18-crown-6 (135 mg, 0.51 mmol). After stirring for 20 min, a solution of 3-bromobut-3-en-1-yl trifluoromethanesulfonate (145 μL, 0.51 mmol) in THF (5 mL) was added. The reaction mixture was stirred for 3 h before addition of water (10 mL). The organic phase was separated, re-extracting the aqueous phase with Et₂O (3 x 10 mL). The combined organic solution was washed with brine (10 mL), dried (MgSO₄) and concentrated under reduced pressure to yield the crude product as a brown oil. Purification by flash chromatography on silica gel (8 g) eluting with Et₂O/hexane (2:98) afforded 12 as a colourless oil (120 mg, 0.36 mmol, 70%).

¹H NMR (300 MHz, CDCl₃) δ 5.70 (1H, ddt, J = 16.8, 9.2, 7.7 Hz), 5.62-5.58 (1H, m), 5.41 (1H, d, J = 1.8 Hz), 5.20-5.10 (2H, m), 4.20-4.05 (4H, m), 2.68 (2H, dd, J = 7.3, 1.1 Hz), 2.43-2.34 (2H, m, CH₂C(CO₂Et)₂), 2.20-2.10 (2H, m, H₂C=CBrCH₂), 1.28 (6H, t, J = 7.3 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 170.8 (C), 133.2 (CH), 132.1 (C), 119.3 (CH₂), 117.0 (CH₂), 61.3 (CH₂), 56.7 (C), 37.3 (CH₂), 36.4 (CH₂), 31.1 (CH₂), 14.0 (CH₃). IR νmax neat (cm⁻¹): 2981, 1729, 1192. LRMS (ES⁺, CH₃CN) m/z (relative intensity %): 357 (100), 355 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C₁₄H₂₁O₄⁷⁹BrNa: 355.0515, found 355.0514.

6-Bromo-1-tosyl-2,3,4,7-tetrahydro-1H-azepine (15)

To a solution of sulphonamide 7 (20 mg, 0.054 mmol) in CH₂Cl₂ (3 mL) was added a solution of Grubbs II catalyst (4.7 mg, 5.6 µmol) in CH₂Cl₂ (3 mL). The reaction mixture was stirred and degassed for 2 min, then heated at reflux for 10 h. The solution was concentrated under reduced pressure to afford the crude product as a black oil. Purification by column chromatography on silica gel (4 g) eluting with Et₂O/hexane (4:96) afforded cyclized product 15 (8 mg, 44%) as a colourless oil. The purified product contained a small amount of the chloro analogue (Br:Cl = 15:1, ¹H NMR).

¹H NMR (CDCl₃, 400 MHz) δ 7.63 (2H, d, J = 8.0 Hz), 7.23 (2H, d, J = 8.0 Hz), 6.01 (1H, tt, J = 5.8, 1.1 Hz), 4.11 (2H, br s), 3.34 (2H, t, J = 6.4 Hz), 2.38 (3H, s), 2.06-1.96 (2H, m), 1.82-1.72 (2H, m). {minor signals for vinyl chloride 15Cl: δ 5.86 (1H, t, J = 5.8, 1.1 Hz).} ¹³C NMR (CDCl₃, 100 MHz) δ 143.1 (C), 136.3 (C), 133.1 (CH), 129.3 (CH), 126.8 (CH), 119.0 (C), 53.9 (CH₂), 48.1 (CH₂), 26.5 (CH₂), 26.2 (CH₂), 21.2 (CH₃). {minor signals for vinyl chloride 15Cl are undetectable.} IR νmax (cm⁻¹) 2924, 1335, 841. ESMS (+ve): m/z (% rel. intensity) 354 (100), 352 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C₁₃H₁₆⁷⁹BrNO₂SNa: 351.9977, found 351.9977.
To a stirred solution of 2-(2-bromo-allyl)-2-pent-4-enyl-malonic acid diethyl ester (9, 30 mg, 0.090 mmol) in benzene (3 mL) was added a solution of Grubbs II catalyst (7.6 mg, 5.6 µmol) in benzene (6 mL). The mixture was stirred and degassed for 1 hour, then heated at reflux for 18 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel (4 g) eluting with Et2O/hexane (2:98) afforded bromocycloheptene 17 as a colourless oil (23 mg, 72 µmol, 80%). The purified product contained a small amount of the chloro analogue (Br:Cl = 17:1, 1H NMR).

To a stirred solution of diene 10 (71 mg, 0.19 mmol) in benzene (15 mL) was added a solution of Grubbs II catalyst (20 mg, 23 µmol) in benzene (5 mL). The mixture was stirred and degassed for 1 h, then heated at reflux for 10 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel (4 g) eluting with Et2O/hexane (2:98) afforded bromocycloheptene 17 as a colourless oil (37 mg, 0.11 mmol, 60%).

1H NMR (300 MHz, CDCl3) δ 6.17 (1H, t, J = 6.2 Hz), 4.14 (4H, q, J = 7.3 Hz), 3.15 (2H, br s), 2.17-2.12 (2H, m), 2.08-2.01 (2H, m), 1.69-1.60 (2H, m), 1.20 (6H, t, J = 7.3 Hz). {minor signals for vinyl chloride 17Cl δ 6.01 (1H, t, J = 6.2 Hz), 3.12 (2H, br s).} 13C NMR (75 MHz, CDCl3) δ 171.2 (C), 135.5 (CH), 120.2 (C), 62.0 (CH2), 56.1 (C), 43.2 (CH2), 36.0 (CH2), 29.6 (CH2), 22.2 (CH2), 14.0 (CH3). {minor signals for vinyl chloride 17Cl are undetectable.} IR νmax neat (cm⁻¹): 2980, 1729, 1251, 1217, 1092, 1030. LRMS (ES⁺, CH3CN) m/z (relative intensity %): 343 (100), 341 [M+Na]⁺. HRMS (ES⁺): Calcd. for C13H2079BrO4: 319.0540, found 319.0536.
Diethyl (E)-2-(2-bromoallyl)-2-(6-phenylhex-5-en-1-yl)malonate (18)

To a stirred solution of 11 (50.0 mg, 0.138 mmol) in benzene (7 mL) was added a solution of Grubbs II catalyst (23.5 mg, 28 µmol) in benzene (7 mL). The reaction mixture was stirred and degassed for 1 h, then heated at reflux for 18 h. Concentration under reduced pressure afforded the crude product as black oil. Purification by flash chromatography on silica gel (6 g) eluting with Et₂O/hexane (2:98) afforded the cross-metathesis product 18 as a colourless oil (12.5 mg, 28.8 µmol, 21%). Starting diene 11 (20.0 mg, 55.3 µmol, 40%) was also recovered.

¹H NMR (300 MHz, CDCl₃) δ 7.25-7.18 (5H, m), 6.30 (1H, dt, J = 15.8, 1.6 Hz), 6.10 (1H, dt, J = 15.8, 7.0 Hz), 5.55 (1H, d, J = 1.5 Hz), 5.48 (1H, d, J = 1.8 Hz), 4.11 (4H, q, J = 7.3 Hz), 3.09 (2H, br s), 2.21-2.10 (2H, m), 2.00-1.93 (2H, m), 1.52 (2H, s), 1.43 (2H, quint, J = 7.7 Hz), 1.17 (6H, t, J = 7.0 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 170.7 (C), 137.5 (C), 130.5 (CH), 130.1 (CH), 128.5 (CH), 127.0 (C), 126.8 (CH), 125.9 (CH), 121.6 (CH₂), 61.5 (CH₂), 57.1 (C), 42.8 (CH₂), 32.6 (CH₂), 31.1 (CH₂), 29.3 (CH₂), 23.4 (CH₂), 14.0 (CH₃). IR νmax neat (cm⁻¹): 2932, 1731, 1233, 1197, 1152.

LRMS (ES⁺, CH₃CN) m/z (relative intensity %): 461 (100), 459 (100) [M+Na]⁺.

HRMS (ES⁺): Calcd. for C₂₂H₂₀⁷⁹BrO₄: 437.1322, found 437.1324.
Reaction of bromodiene 12 with Grubbs II catalyst

To a stirred solution of 12 (80 mg, 0.24 mmol) in benzene (20 mL) was added a solution of Grubbs II catalyst (25 mg, 29 µmol) in benzene (4 mL). The mixture was stirred and degassed for 1 hour, then heated at reflux for 12 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel (10 g) eluting with Et2O/hexane (4:96) to afford and inseparable mixture cyclic vinyl bromide 19 and chloride 20 a colourless oil (8.6:1, 26 mg, 0.09 mmol, 36%) and cyclic allylic halides 21/22 (5:1, 16 mg, 0.05 mmol, 21%) also as a colourless oil.

Data for the mixture of 4-bromo-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester (19) and 4-chloro-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester (20)

Data recorded from a mixture of vinyl bromide 19 and vinyl chloride 20 (ratio ~8.6:1, 1H NMR). Major peaks reported for vinyl bromide 19. 1H NMR (300 MHz, CDCl3) δ 6.02 (1H, tt, J = 4.0, 1.8 Hz), 4.22 (4H, q, J = 6.9 Hz), 2.65 (2H, dt, J = 4.0, 2.2 Hz), 2.56-2.49 (2H, m), 2.26 (2H, t, J = 6.6 Hz), 1.27 (6H, t, J = 7.3 Hz). 13C NMR (75 MHz, CDCl3) δ 170.8 (C), 125.6 (CH), 120.6 (C), 61.6 (CH2), 52.0 (C), 32.5 (CH2), 32.1 (CH2), 29.2 (CH2), 14.0 (CH3). IR νmax neat (cm⁻¹): 2978, 1726, 1246, 1174, 1084, 1042. LRMS (ES+, CH3CN) m/z (relative intensity %): 329 (100), 327 (100) [M+Na]⁺. HRMS (ES⁺): Calcd. for C12H17BrO4Na: 327.0202, found 327.0199.
Data for mixture of 4-bromomethyl-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester (21) and 4-chloromethyl-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester (22)

\[ \begin{align*}
X = \text{Br} \quad (21) \quad X = \text{Cl} \quad (22) \\
(21 + 22) = 21\% \\
(21:22 \sim 5:1, \quad \text{\textsuperscript{1}H NMR})
\end{align*} \]

Data recorded from a mixture of allylic bromide 21 and allylic chloride 22 (ratio ~5:1, \textsuperscript{1}H NMR). Major peaks reported for allylic bromide 21. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \)

- 5.78 (1H, t, \( J = 4.0 \text{ Hz} \)),
- 4.16-4.07 (4H, m),
- 3.83 (2H, s),
- 2.56-2.51 (2H, m),
- 2.18-2.10 (4H, m),
- 1.18 (6H, t, \( J = 7.3 \text{ Hz} \)).

}\{\text{minor signals for allylic chloride 22: 5.72 (1H, t, \( J = 4.0 \text{ Hz} \)), 3.90 (2H, d, \( J = 1.1 \text{ Hz} \))}\}\}

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \( \delta \)

- 171.2 (C),
- 133.8 (C),
- 124.8 (CH),
- 61.4 (CH\textsubscript{2}),
- 52.7 (C),
- 37.9 (CH\textsubscript{2}),
- 30.8 (CH\textsubscript{2}),
- 27.4 (CH\textsubscript{2}),
- 23.5 (CH\textsubscript{2}),
- 14.0 (CH\textsubscript{3}).

}\{\text{minor signals for allylic chloride 22 are undetectable, because they are too small.}\}\}

IR \( v_{\text{max}} \) neat (cm\textsuperscript{-1}): 2979, 1727, 1240, 1176, 1083, 1034. LRMS (ES\textsuperscript{+}, CH\textsubscript{3}CN) m/z (relative intensity %): 343 (100), 342 (100) [M+Na]\textsuperscript{+}. \{\text{for 22: 297 (16) and 299 (5) [M+Na]\textsuperscript{+}}\}\}

HRMS (ES\textsuperscript{+}): Calcd. for C\textsubscript{13}H\textsubscript{19}BrO\textsubscript{4}Na: 341.0359, found 341.0365.
Reaction of deuterated diene 12-d_5 with Grubbs II catalyst

To a stirred solution of deuterated diene 12-d_5 (63 mg, 0.19 mmol) in benzene (9 mL) was degassed for 10 min, then Grubbs II catalyst (16 mg, 19 μmol, 10 mol %) was added. The mixture was heated at reflux for 16 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel eluting with Et_2O/hexane (3:97) afforded the cyclic vinyl halides 19-d_3/20-d_3 as a colourless oil (28 mg, ~48%) and cyclised allylic halides 21-d_3/22-d_3 (27 mg, ~44%) also as a colourless oil.

Selected data recorded from mixture of vinyl bromide 19-d_3 and vinyl chloride 20-d_3 (ratio ~7:3, ^1H NMR). Major peaks reported for vinyl bromide 19-d_3: ^1H NMR (300 MHz, CDCl_3) δ 4.11 (4H, q, J = 7.1 Hz), 2.41 (2H, dd, J = 8.9, 7.7 Hz), 2.17-2.12 (2H, m), 1.16 (6H, t, J = 7.1 Hz) {minor signals for vinyl chloride 20-d_3: ^1H NMR: 2.29 (2H, dd, J = 8.9, 7.7 Hz)}. ^13C NMR (75 MHz, CDCl_3) δ 170.8, 120.6, 61.6, 51.8, 32.1, 29.8, 29.2, 28.5, 14.0. {minor signals for vinyl chloride 20-d_3 are undetectable, because they are too small.}

Selected data recorded from mixture of allylic bromide and chloride 21-d_3/22-d_3: ^1H NMR (300 MHz, CDCl_3) δ 4.22-4.16 (4H, m), 3.91 (2H, s), 2.26-2.19 (4H, m), 1.25 (6H, t, J = 7.3 Hz). {minor signals for allylic chloride 22-d_3: ^1H NMR: 3.97 (2H, s)}. ^13C NMR (75 MHz, CDCl_3) δ 171.2, 133.8, 61.4, 52.5, 37.8, 27.4, 23.5, 14.0. {minor signals for allylic chloride 22-d_3 are undetectable, because they are too small.}
Reaction of $d_5$-bromodiene 12-$d_5$ with $[\text{RuCl}_2(\text{p-cymene})]_2$/cy$_3$P/1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride/Cs$_2$CO$_3$.

Benzene (3.5 mL) was degassed for 10 min, then $[\text{RuCl}_2(\text{p-cymene})]_2$ (3 mg, 4.8 µmol, 5 mol %), Cs$_2$CO$_3$ (6 mg, 19.5 µmol, 20 mol %), cy$_3$P (3 mg, 9.7 µmol, 10 mol %), 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (3 mg, 9.7 µmol, 10 mol %) were added. The mixture was heated at 40 °C for 10 min, giving an orange solution, to which, a degassed solution of deuterated diene 12-$d_5$ (33 mg, 0.10 mmol) in benzene (1.5 mL) was added. The reaction mixture was heated at reflux for 16 h. Concentration under reduced pressure afforded the crude product, which was purified by flash chromatography on silica gel eluting with Et$_2$O/hexane (3:97) to afford the cyclic vinyl halides 19-$d_3$/20-$d_3$ as a colourless oil (10 mg, ~33%) and cyclized allylic halides 21-$d_3$/22-$d_3$ (9 mg, ~29%) also as a colourless oil, and recovered starting material 22 (10 mg, 30%). Selected characterisation data for 19-$d_3$–22-$d_3$ are reported above.
**2,7-Dibenzyl-4-(o-formylphenyl)-2,3,6,7-tetrahydro-1,2,7-thiadiazepine 1,1-dioxide (30)**

![Chemical Structure](image)

To a solution of vinyl bromide **2a** (25 mg, 0.06 mmol) in THF (2 mL) was added a solution of 2M Na₂CO₃ (1 mL) and 2-formylphenyl boronic acid (11 mg, 0.075 mmol). Pd(PPh₃)₄ (5 mg, 4 µmol) was added. The reaction mixture was heated at reflux for 2 h. After cooling to rt water (5 mL) was added, and the mixture was extracted with EtOAc (3 x 15 mL). The combined organic solution was dried (MgSO₄) and concentrated under reduced pressure to afford the crude product as a brown oil. Purification by column chromatography on silica gel eluting with 14% EtOAc/hexane (14:86) afforded cross-coupling product **30** (19 mg, 71%) as a yellow oil.

**¹H NMR** (CDCl₃, 400 MHz) δ 9.83 (1H, s), 7.78 (1H, d, J = 7.4 Hz), 7.57-7.20 (12 H, m), 6.93 (1H, d, J = 7.4 Hz), 5.57 (1H, t, J = 4.8 Hz), 4.60 (2H, s), 4.57 (2H, s), 4.01 (2H, s), 3.88 (2H, d, J = 6.5 Hz). **¹³C NMR** (CDCl₃, 100 MHz) δ 191.3 (CH), 143.7 (C), 136.3 (C), 136.2 (C), 133.8 (CH), 133.7 (C), 131.0 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 52.7 (CH₂), 48.6 (CH₂), 43.9 (CH₂). **IR** νmax (cm⁻¹) 3031, 2923, 1698, 1595, 1496, 1456. **LRMS** (ES⁺): m/z (% rel. intensity) 433.0 (100) [M+H]⁺. **HRMS** (ES⁺): Calcd. for C₂₅H₂₅N₂O₃S: 432.1508, found 433.1580.
3-(3-Methoxy-phenyl)-cyclohept-3-en-1,1-dicarboxylic acid diethyl ester (31)

Following the procedure of Banwell et al.,\textsuperscript{7} to a stirred solution of 17 (20 mg, 63 µmol) in THF (2 mL) was added a solution of Na\textsubscript{2}CO\textsubscript{3} (200 mg) in H\textsubscript{2}O (1 mL) and 3-methoxyphenylboronic acid (14 mg, 94 µmol). Pd(PPh\textsubscript{3})\textsubscript{4} (3.5 mg, 3 µmol) was added. The reaction mixture was heated at reflux for 2 h, cooled to rt, then water (5 mL) was added. The mixture was extracted with Et\textsubscript{2}O (3 x 5 mL). The combined organic solutions were washed with brine and concentrated under reduced pressure to yield the crude product as a black oil. Purification by flash chromatography on silica gel (4 g) eluting with Et\textsubscript{2}O/hexane (1:9) afforded the cross-coupling product 31 as a pale-yellow oil (20 mg, 57 µmol, 92%).

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.11 (1H, t, \( J = 8.1 \) Hz), 6.87-6.82 (1H, m), 6.81-6.78 (1H, m), 6.68 (1H, ddd, \( J = 8.4, 2.6, 1.1 \) Hz), 6.07 (1H, t, \( J = 6.6 \) Hz.), 4.06-3.80 (4H, m), 3.73 (3H, s), 3.14 (2H, br s), 2.29-2.15 (4H, m), 1.77-1.68 (2H, m), 0.97 (6H, t, \( J = 7.0 \) Hz). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \( \delta \) 171.7 (C), 160.0 (C), 146.1 (CH), 139.0 (C), 131.9 (CH), 129.0 (CH), 118.7 (CH), 111.8 (CH), 61.1 (CH\textsubscript{2}), 55.3 (CH\textsubscript{3}), 55.0 (C), 36.7 (CH\textsubscript{2}), 36.1 (CH\textsubscript{2}), 28.2 (CH\textsubscript{2}), 22.1 (CH\textsubscript{3}), 13.7 (CH\textsubscript{3}). IR \( \nu_{\max} \) neat (cm\textsuperscript{-1}): 2956, 1730, 1218, 1185, 1051. LRMS (ES\textsuperscript{+}, CH\textsubscript{3}CN) \( m/z \) (relative intensity %): 369 (100) [M+Na]\textsuperscript{+}. HRMS (ES\textsuperscript{+}): Calcd. for C\textsubscript{20}H\textsubscript{26}O\textsubscript{5}Na: 369.1672, found 369.1666.

Figure S1. $^1$H-NMR spectrum of compound 1a in CDCl$_3$

Figure S2. $^1$H-NMR expanded spectrum of compound 1a in CDCl$_3$
Figure S3. $^1$H-NMR expanded spectrum of compound 1a in CDCl$_3$

Figure S4. $^{13}$C-NMR spectrum of compound 1a in CDCl$_3$
Figure S5. $^1$H-NMR spectrum of compound 1b in CDCl$_3$

Figure S6. $^1$H-NMR expanded spectrum of compound 1b in CDCl$_3$
Figure S7. $^1$H-NMR expanded spectrum of compound 1b in CDCl$_3$

Figure S8. $^{13}$C-NMR spectrum of compound 1b in CDCl$_3$
Figure S9. $^1$H-NMR spectrum of compound 1c in CDCl$_3$.

Figure S10. $^1$H-NMR expanded spectrum of compound 1c in CDCl$_3$. 
Figure S11. $^1$H-NMR expanded spectrum of compound 1c in CDCl$_3$

Figure S12. $^{13}$C-NMR spectrum of compound 1c in CDCl$_3$
Figure S13. $^1$H-NMR spectrum of 1d in CDCl$_3$

Figure S14. $^1$H-NMR spectrum of 1d in CDCl$_3$
Figure S15. $^1$H-NMR spectrum of 1e in CDCl$_3$

Figure S16. $^{13}$C-NMR spectrum of 1e in CDCl$_3$
Figure S17. $^1$H-NMR spectrum of compound 2a in CDCl$_3$.

Figure S18. $^{13}$C-NMR spectrum of compound 2a in CDCl$_3$. 
Figure S19. $^1$H-NMR spectrum of compound 2b/3b in CDCl$_3$

Figure S20. $^{13}$C-NMR spectrum of compound 2b/3b in CDCl$_3$
Figure S21. $^1$H-NMR spectrum of compound 2c/3c in CDCl$_3$

Figure S22. $^{13}$C-NMR spectrum of compound 2c/3c in CDCl$_3$
Figure S23. $^1$H-NMR spectrum of 4 in CDCl$_3$

Figure S24. $^{13}$C-NMR spectrum of 4 in CDCl$_3$
Figure S25. $^1$H-NMR spectrum of 2e in CDCl$_3$

Figure S26. $^{13}$C-NMR spectrum of 2e in CDCl$_3$
Figure S27. $^1$H-NMR spectrum of compound 5 in CDCl$_3$

Figure S28. $^{13}$C-NMR spectrum of compound 5 in CDCl$_3$
Figure S29. $^1$H-NMR spectrum of compound 6 in CDCl$_3$

Figure S30. $^{13}$C-NMR spectrum of 6 in CDCl$_3$
Figure S31. $^1$H-NMR spectrum of 7 in CDCl$_3$.

Figure S32. $^{13}$C-NMR spectrum of 7 in CDCl$_3$.
Figure S33. $^1$H-NMR spectrum of compound 8 in CDCl$_3$

Figure S34. $^{13}$C-NMR spectrum of compound 8 in CDCl$_3$
Figure S35. $^1$H-NMR spectrum of compound 9 in CDCl$_3$.

Figure S36. $^1$H-NMR expanded spectrum of compound 9 in CDCl$_3$. 
Figure S37. $^1$H-NMR expanded spectrum of compound 9 in CDCl$_3$

Figure S38. $^{13}$C-NMR spectrum of compound 9 in CDCl$_3$
Figure S39. $^1$H-NMR spectrum of compound 10 in CDCl$_3$

Figure S40. $^{13}$C-NMR spectrum of compound 10 in CDCl$_3$
Figure S41. $^1$H-NMR spectrum of compound 11 in CDCl$_3$

Figure S42. $^{13}$C-NMR spectrum of compound 11 in CDCl$_3$
Figure S43. $^1$H-NMR spectrum of compound 12 in CDCl$_3$

Figure S44. $^{13}$C-NMR spectrum of compound 12 in CDCl$_3$
Figure S45. $^1$H-NMR spectrum of compound 15 in CDCl$_3$

Figure S46. $^{13}$C-NMR spectrum of compound 15 in CDCl$_3$
Figure S47. $^1$H-NMR spectrum of compound 17 in CDCl$_3$

Figure S48. $^{13}$C-NMR spectrum of compound 17 in CDCl$_3$
Figure S49. $^1$H-NMR spectrum of compound 18 in CDCl$_3$.

Figure S50. $^{13}$C-NMR spectrum of compound 18 in CDCl$_3$. 
Figure S51. $^1$H-NMR spectrum of compound 19/20 in CDCl$_3$

Figure S52. $^{13}$C-NMR spectrum of compound 19/20 in CDCl$_3$
Figure S53. $^1$H-NMR spectrum of compound 21/22 in CDCl$_3$

Figure S54. $^{13}$C-NMR spectrum of compound 21/22 in CDCl$_3$
Figure S55. $^1$H-NMR spectrum of compound 19-d$_3$/20-d$_3$ in CDCl$_3$

Figure S56. $^{13}$C-NMR spectrum of compound 19-d$_3$/20-d$_3$ in CDCl$_3$
Figure S57. $^1$H-NMR spectrum of compound 21-d$_3$/22-d$_3$ in CDCl$_3$.

Figure S58. $^{13}$C-NMR spectrum of compound 21-d$_3$/22-d$_3$ in CDCl$_3$. 

$X =$ Br (21-d$_3$)  
$X =$ Cl (22-d$_3$)  
21-d$_3$:22-d$_3$ $\sim$ 9:1
Figure S59. $^1$H-NMR spectrum of compound 30 in CDCl$_3$

Figure S60. $^{13}$C-NMR spectrum of compound 30 in CDCl$_3$
Figure S61. $^1$H-NMR spectrum of compound 31 in CDCl₃

Figure S62. $^{13}$C-NMR spectrum of compound 31 in CDCl₃