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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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Formation of seven-membered rings by RCM of vinyl bromides

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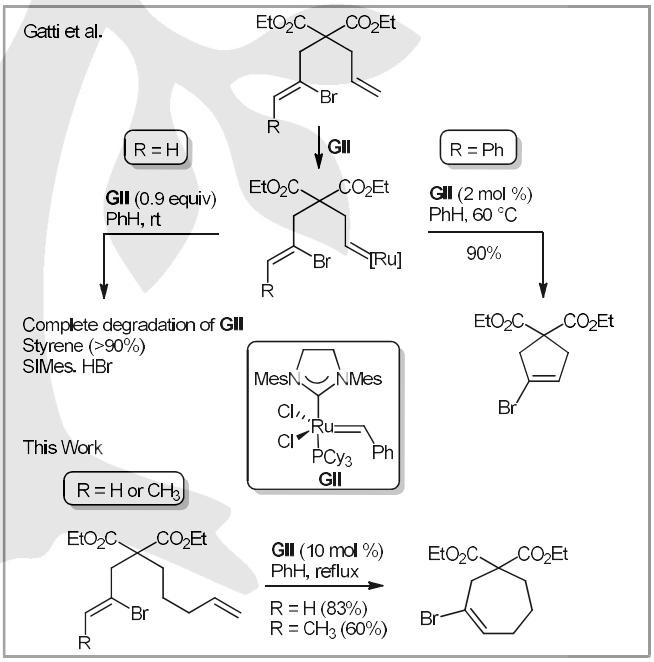
Abstract: Grubbs II catalyst mediated ring-closing metathesis (RCM) of mono-brominated dienes is reported to proceed in moderate to good yields (40–80%) where the linking chain contains five atoms, leading to carbocyclic and heterocyclic 7-membered bromo-olefins. Notably, RCM to form 5-, 6- or 8-membered 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 alkenyl 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).

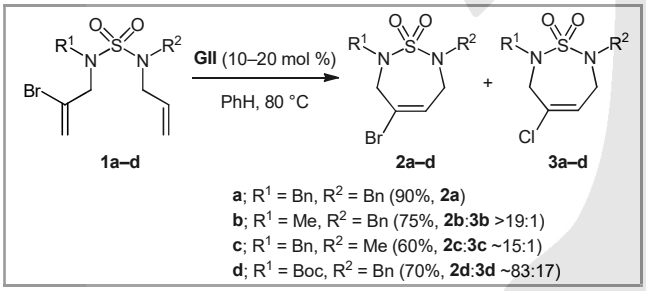


Scheme 1 RCM of vinyl bromides

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

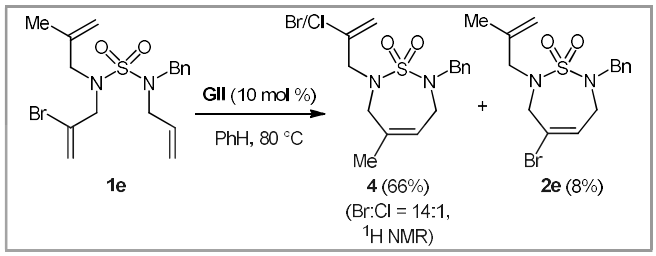
describe the RCM of bromo-dienes, showing that the reaction may proceed without the introduction of a "protecting" substituent in certain cases.

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.[8] Hanson has previously utilised RCM strategies to access cyclic sulfamide scaffolds for the synthesis of HIV protease inhibitor analogues,[9] whilst we have reported the synthesis of a range of cyclic sulfonamides[10] and sulfamides[7,11] *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 in refluxing benzene for 10 h, sulfamide **1a** underwent successful RCM affording 7-membered cyclic vinyl bromide **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, ^{1}H 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 ^{1}H NMR spectra of the RCM products **2a–2c** also revealed minor amounts of the chloro-alkenes **3b** (19:1) and **3c** (15:1) to be present.



Scheme 2 RCM of sulfamide-linked brominated dienes

To investigate the chemoselectivity of the reaction, a sufamide 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**.

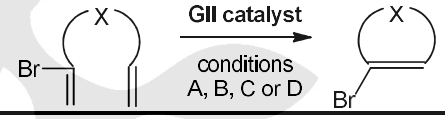


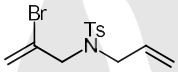
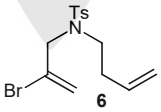
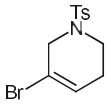
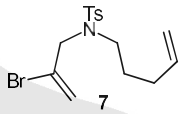
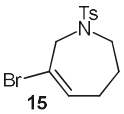
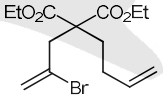
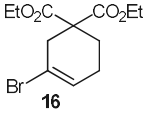
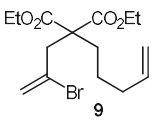
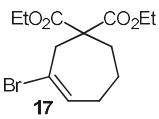
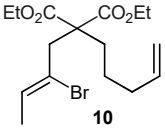
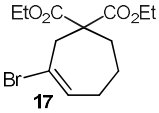
Scheme 3 Competition experiment

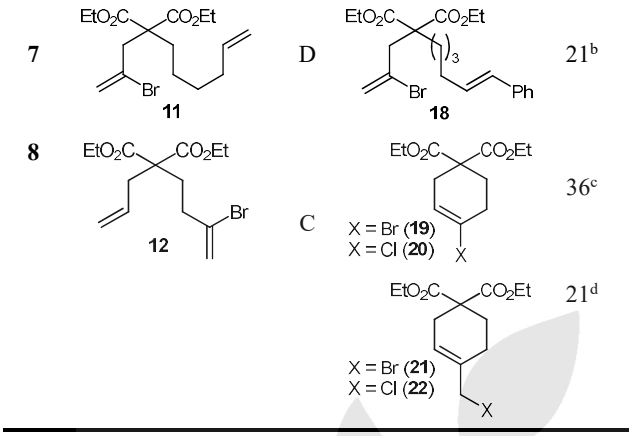
In addition to highlighting the lower metathesis reactivity of the vinyl bromide compared to the methallyl group, the competition experiment indicates that Cl/Br exchange most likely occurs in the acyclic bromoalkene. The origin of the chloride in **3e** and **4** is the **GII** complex, or a degradation 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**.[13]

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



Entry	Diene	Method	Product	Yield
1	 **5**	A	 **13**	ND[a]
2	 **6**	A	 **14**	ND[a]
3	 **7**	A	 **15**	44
4	 **8**	A	 **16**	ND[a]
5	 **9**	B	 **17**	80
6	 **10**	C	 **17**	60



Reagents and Conditions: A) **GII** (10 mol %), PhH, reflux, 10 h; B) **GII** (6 mol %), PhH, reflux, 18 h; C) **GII** (12 mol %), PhH, reflux, 10–12 h; D) **GII** (20 mol %), PhH, reflux, 18 h. [a] Not detected (ND) with majority of starting material recovered. [b] 39% recovery of starting material. [c] Ratio of **19**:**20** = 8.6:1. [d] Ratio of **21**:**22** = 5:1.

An interesting trend was observed on 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, ^{1}H 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).[14] With the objective of suppressing initial reaction of the halo-olefin with the catalyst, cyclisation of trisubstituted *Z* bromo-olefin **10** was investigated, giving bromoheptene **17** in moderately reduced yield (60%, Entry 6) compared to **9**. The formation of 8-membered rings *via* RCM is more challenging,[4,14] 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).

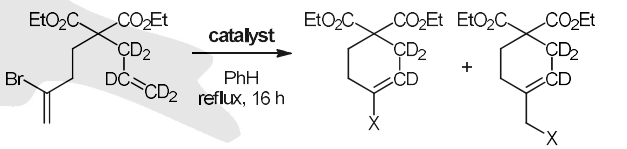
The results thus far suggested an interesting selectivity for the RCM of mono-brominated dienes leading to 7-membered rings. In an effort to probe the reaction towards 6-membered rings further, the position of the bromo-olefin relative to the carbon linker group was extended by one methylene in **12**. 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-d$_5$** with Grubbs II afforded halogenated carbocycles **19-d$_3$**/**20-d$_3$** and **21-d$_3$**/**22-d$_3$** in 48% and 44% yield, respectively, again with significant Br/Cl exchange (Table 2, Entry 1).

As anticipated, cyclic vinyl halides **19-d$_3$** and **20-d$_3$** exhibit deuterium incorporation at the 2- and 3-positions (^{1}H NMR), which is consistent with a typical RCM catalytic cycle. More interestingly, this study enables determination of the origin of the additional CH_2 unit at C-5 in halomethylcyclohexenes **21-d$_3$** and **22-d$_3$**. The lack of deuterium incorporation at C-5 in **21-d$_3$**/**22-d$_3$** (^{1}H NMR) suggests that the methylene is derived from the bromo-olefin moiety of malonate **12-d$_5$**. Homologation reactions with ruthenium alkylidene species have been previously described, proceeding through ruthenacyclobutane intermediates.[15] 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-d$_5$** was exposed to ruthenium catalyst (Catalyst A) formed *in-situ* from [RuCl$_2$(*p*-cymene)]$_2$, tricyclohexylphosphine, 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride and Cs_2CO_3 (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-d$_3$**/**20-d$_3$** and **21-d$_3$**/**22-d$_3$** were obtained in 33% and 29% yields, respectively. It is noteworthy that an increased amount of allylic chloride **22-d$_3$** was isolated (**21-d$_3$**:**22-d$_3$** ~ 72:28, ^{1}H-NMR) when using catalyst A instead of Grubbs II (~ 9:1, ^{1}H- NMR).

Table 2 Ru-catalysed cyclisations of partially deuterated malonate **12-d$_5$**.

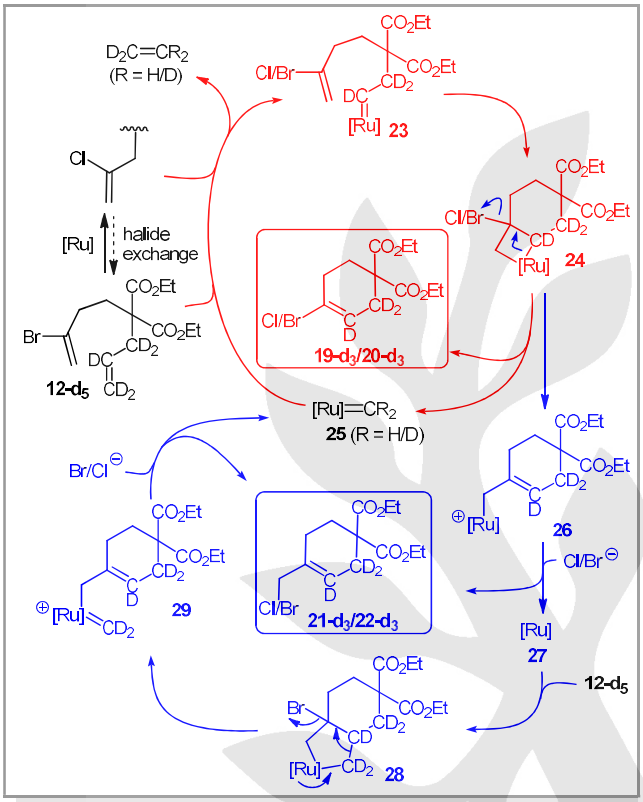


12-d$_5$ **19-d$_3$**; X = Br **20-d$_3$**; X = Cl **21-d$_3$**; X = Br **22-d$_3$**; X = Cl

Entry	Catalyst	Yield **19-d$_3$** and **20-d$_3$**	Yield **21-d$_3$** and **22-d$_3$**
1	Grubbs II	48% (7:3)[b]	44% (9:1)[b]
2	Catalyst A[a]	33% (8:2)[b] (48%)[c]	29% (7:3)[b] (41%)[c]

[a] Catalyst A formed *in situ* from [RuCl$_2$(*p*-cymene)]$_2$, tricyclohexylphosphine, 1,3-bis(2,4,6-trimethylphenyl) imidazolinium chloride and Cs_2CO_3. [b] Ratio determined by ^{1}H NMR. [c] Yield based on recovered **12-d$_5$**.

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).

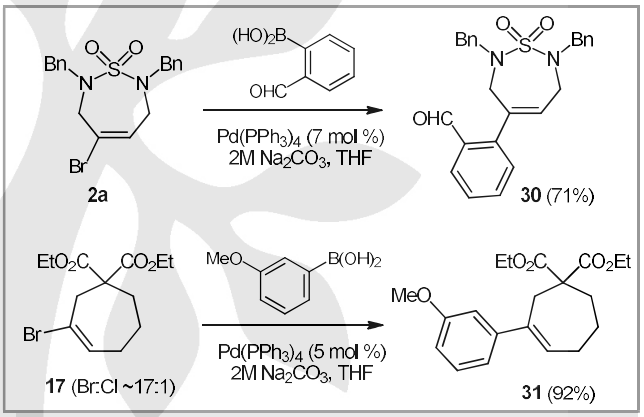


Scheme 4 Proposed reaction pathways leading to RCM and demethylenative cyclisation of **12-d$_5$** with Cl/Br exchange.

Formation of six-membered vinyl halides **21-d$_3$/22-d$_3$** can be accounted for by a typical RCM catalytic cycle, initiated at the non-halogenated olefin of malonate **12-d$_5$**, 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-d$_5$** may be mediated via a ruthenium carbene or a Ru species formed through degradation of the Grubbs II catalyst (Scheme 4, top left).[18] 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-d$_3$/22-d$_3$** 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-d$_5$** to give ruthenacyclopentane **28**,[16] which following fragmentation gives intermediate **29**. Finally, substitution with Br$^-$/Cl$^-$ yields carbocycles **21-d$_3$/22-d$_3$** 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[17] 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 $Pd(PPh_3)_4$ 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.

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Supporting Information

Formation of seven-membered rings by RCM of vinyl bromides

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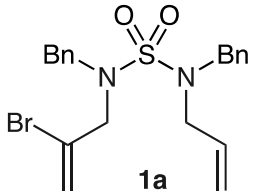
General procedures: All chemicals were used as received from standard chemical suppliers unless otherwise stated. All reactions were monitored by thin layer chromatography (TLC) on aluminum sheets coated with silica gel containing a fluorescent indicator (Merck) and were visualized under UV light with 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 (δ) are reported in ppm referenced to residual solvent signal, $CDCl_3$ (δ_H 7.27, δ_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.

N,N'-Dibenzyl-N-(2-bromoprop-2-en-1-yl)-N'-prop-2-en-1-ylsulfuric diamide **(1a)**

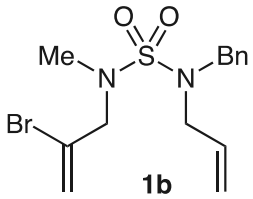


1a

To a solution of *N,N'*-dibenzyl-*N*-(2-bromoprop-2-en-1-yl)sulfuric diamide (100 mg, 0.25 mmol) in CH_3CN (5 mL) were added NaH (6 mg, 0.25 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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 (3x15 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) δ 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) δ 136.1 (C), 135.3 (C), 132.8 (CH), 128.9 (CH), 128.7 (CH), 128.6 (**C**H), 128.5 (**C**H), 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** ν_{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 $C_{20}H_{23}{}^{81}BrN_2O_2SNa$: 459.0536, found 459.0530.

***N-Benzyl-N'-(2-bromoprop-2-en-1-yl)-N'-methyl-N-(prop-2-en-1-yl)sulfuric diamide* (1b)**

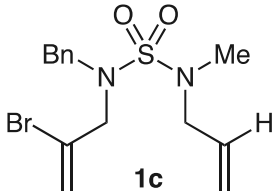


1b

To a solution of *N-benzyl-N'-methyl-N-(prop-2-en-1-yl)sulfuric diamide* (102 mg, 0.42 mmol) in CH_3CN (5 mL) were added NaH (10.3 mg, 0.42 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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 $MgSO_4$ 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.

^{1}H NMR ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 136.1 (C), 132.7 (CH), 128.6 (CH), 128.3 (CH), 127.8 (C) 119.6 (CH_2), 58.4 (CH_2), 51.3 (CH_2), 50.6 (CH_2), 49.7 (CH_2), 34.6 (CH_3). **LRMS** (ES^+): *m/z* (% rel. intensity) 361 (100) and 359 (90) $[M+H]^+$. **HRMS** (ES^+): Calcd. For Calcd. for $C_{14}H_{20}{}^{79}BrN_2O_2S$: 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)**

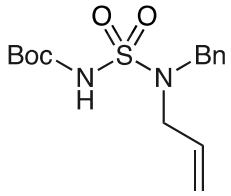


1c

To a solution of *N-benzyl-N-(2-bromoprop-2-en-1-yl)-N'-methylsulfuric diamide* (170 mg, 0.53 mmol) in CH_3CN (5 mL) were added NaH (12.7 mg, 0.53 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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 ($MgSO_4$) 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.

^{1}H NMR ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 135.9 (C), 132.9 (CH), 128.9 (CH), 128.6 (CH), 128.0 (C), 120.4 (CH_2) 118.9 (CH_2), 54.7 (CH_2), 53.5 (CH_2), 51.4 (CH_2), 34.5 (CH_3). **LRMS** (ES^+): *m/z* (% rel. intensity) 361 (100) and 359 (100) $[M+H]^+$. **HRMS** (ES^+): Calcd. For Calcd. for $C_{14}H_{20}{}^{79}BrN_2O_2S$: 359.0351, found 359.0363.

tert-Butyl (N-allyl-N-benzylsulfamoyl)carbamate



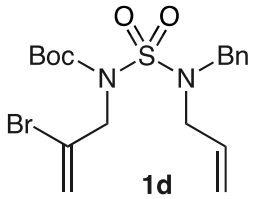
Following the procedure of Dewynter *et al*,[1] to a solution of chlorosulfonylisocyanate (0.290 mL, 3.40 mmol) in CH_2Cl_2 (8 mL) at 0 °C was added *t*-BuOH (0.35 mL, 3.40 mmol). The mixture was stirred for 10 min at 0 °C, and then Et_3N (0.46 mL, 3.40 mmol) was added followed by a solution of *N*-benzyl-*N*-allyl amine (0.500 g, 3.40 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred for 12 h at rt. CH_2Cl_2 (5 mL) was added and the solution was washed with 1 N HCl (3 x 5 mL) and H_2O (2 x 5 m), dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography eluting with hexane/Et_2O (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, $CDCl_3$) δ 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.2 (C), 135.9 (C), 132.0 (HC), 128.8 (CH), 128.5 (CH), 128.0 (CH), 119.8 (CH_2), 83.7 (C), 51.6 (CH_2), 50.2 (CH_2), 28.6 (CH_3). **IR** ν_{max} / cm^{-1}: 3285, 2973, 2931, 1734, 1441, 1360, 1147, 1148, 925, 821. LRMS (ES^+, CH_3CN) *m/z*: 349 (50) $[M+Na]^+$.

[1] Dewynter, G.; Aouf, N.; Criton, M.; Montero, J. L. *Tetrahedron* **1993**, *49*, 65–76.

[2] Hill-Cousins, J. T.; Salim, S. S.; Bakar, Y. M.; Bellingham, R. K.; Light, M. E.; Brown, R. C. D., *Tetrahedron* **2014**, *70*, 3700-3706.

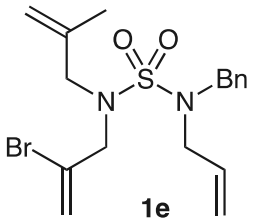
tert-Butyl (N-allyl-N-benzylsulfamoyl)(2-bromoallyl)carbamate (1d)



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 H_2O (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 (Na_2SO_4) and concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography eluting with Et_2O/hexane (4:2) to provide the title compound **1d** as a colourless oil (117 mg, 0.26 mmol, 88 %).

^{1}H NMR (400 MHz, $CDCl_3$) 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). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.3 (C), 136.2 (C), 128.9 (CH), 132.3 (CH), 128.6 (CH), 128.3 (C), 128.2 (CH), 119.8 (CH_2), 117.9 (CH_2), 84.5 (C), 55.5 (CH_2), 52.3 (CH_2), 50.7 (CH_2), 28.3 (CH_3). **IR** ν_{max} / cm^{-1}: 2981, 1729, 1369, 1321, 1248, 1144, 1055, 911, 800. LRMS (ES^+, CH_3CN) *m/z* (relative intensity %) 469 (100) and 467 (98) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{18}H_{25}{}^{79}BrN_2O_4SNa$: 467.0610, found 467.0612.

N-(2-Bromo-2-propenyl)-N-(2-methyl-2-propenyl)-N'-phenylmethyl-N'-(2-propenyl)sulfamide **(1e)**

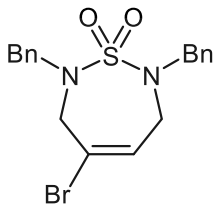


1e

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 Et_2O (3 x 15 mL). The combined organic extract was washed with brine (10 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_2O/hexane (5:95) afford triene **1e** as a pale yellow oil (178 mg, 0.45 mmol, 97%).

^{1}H NMR (300 MHz, $CDCl_3$) 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), 3.87 (2H, s), 3.75 (2H, d, *J* = 6.6 Hz), 1.78 (3H, s). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 139.6 (C), 136.2 (C), 133.0 (CH), 128.9 (CH), 128.6 (CH), 127.6 (CH), 127.8 (C), 120.1 (CH_2), 119.6 (CH_2), 115.3 (CH_2), 54.5 (CH_2), 53.7 (CH_2), 50.8 (CH_2Ph), 50.0 (CH_2), 20.3 (CH_3). **IR** ν_{max} neat (cm^{-1}): 3079, 2980, 2917, 1329, 1146, 891. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 423 (100) and 421 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{17}H_{23}{}^{79}BrN_2O_2S$: 399.0737, found 399.0742.

2,7-Dibenzyl-4-bromo-2,3,6,7-tetrahydro-1,2,7-thiadiazepine 1,1-dioxide **(2a)**

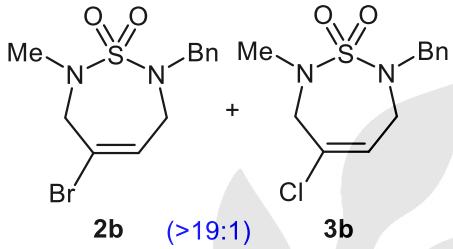


2a

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 (**C**H), 128.7 (**C**H), 128.6 (**C**H), 128.3 (**C**H), 128.2 (**C**H), 122.7 (**C**), 52.4 (**C**H_2), 52.1 (CH_2), 44.1 (**C**H_2). **IR** ν_{max} (cm^{-1}) 3030, 2919, 1507, 1456, 1359. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 431 (100) and 429 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{18}H_{19}{}^{79}BrN_2NaO_2S$: 429.0242, found 429.0239.

7-Benzyl-4-bromo-2-methyl-2,3,6,7-tetrahydro-1H-1λ⁶,2,7-thiadiazepine-1,1-dione **(2b) and** ***7-benzyl-4-chloro-2-methyl-2,3,6,7-tetrahydro-1H-1λ⁶,2,7-thiadiazepine-1,1-dione*** **(3b)**

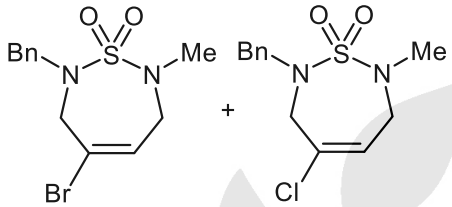


2b (>19:1) **3b**

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, ^{1}H 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**. **^{1}H NMR** ($CDCl_3$, 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)}. **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 135.7 (C), 130.5 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 122.7 (C), 56.7 (CH_2), 52.8 (CH_2), 43.9 (CH_2), 36.5 (CH_3). {minor signals for vinyl chloride **3b**: δ 55.4 (CH_2), 53.1 (CH_2), 43.1 (CH_2), 36.8 (CH_3)}. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 333 (100), 331 (100) $[M+H]^+$. HRMS (ES^+): Calcd. for $C_{12}H_{15}{}^{81}BrN_2NaO_2S$: 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)**

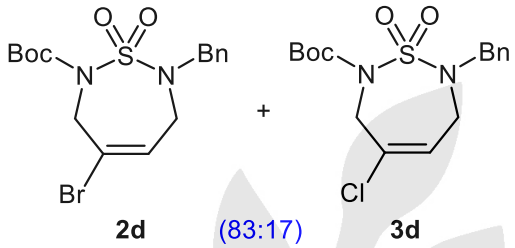


2c (15:1) **3c**

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, ^{1}H 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**. **^{1}H NMR** ($CDCl_3$, 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)}. **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 135.4 (C), 130.7 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 122.8 (C), 52.6 (CH_2), 52.1 (CH_2), 48.2 (CH_2), 36.8 (CH_3). {minor signals for vinyl chloride **3c** are undetectable because they are too small.}. HRMS (ES^+): Calcd. for $C_{12}H_{15}{}^{81}BrN_2NaO_2S$: 354.9909, found 354.9908.

***tert*-butyl 7-benzyl-4-bromo-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6,2,7-thiadiazepine-2-carboxylate (2d) and *tert*-butyl 7-benzyl-4-chloro-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6,2,7-thiadiazepine-2-carboxylate (3d)**

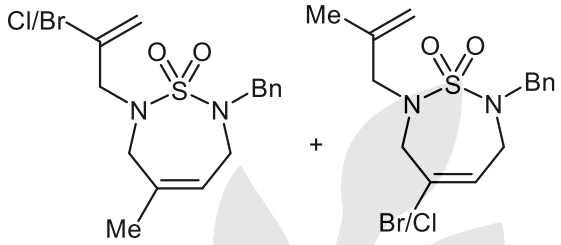


2d (83:17) **3d**

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 Et_2O/hexane (2:8) to provide the vinyl bromide **2d** and the vinyl chloride **3d** as an 83:17 (^{1}H NMR) inseparable mixture (54.0 mg, 0.12 mmol, 70 % yield).

^{1}H NMR (83:17 mixture of vinyl bromide **2d** and vinyl chloride **3d**, 400 MHz, $CDCl_3$), 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)}. **^{13}C NMR** (83:17 mixture of vinyl bromide **2d** and vinyl chloride **3d**, 100 MHz, $CDCl_3$), 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 (CH_2), 51.8 (CH_2), 45.7 (CH_2), 28.4 (CH_3). {minor signals for vinyl chloride **3d**: δ 52.4 (CH_2), 49.8 (CH_2), 43.9 (CH_2), 28.0 (CH_3)}. **IR** ν_{max} / cm^{-1}: 2890, 1727, 1369, 1323, 1258, 1176, 1146, 1094, 943. LRMS (ES^+, CH_3CN) *m/z* (relative intensity %) 441 (100), 439 (100) $[M+Na]^+$. {selected peaks for **3d**: 395 (30) $[M\{^{35}Cl\}+Na]^+$.}

***2-(2-Bromo-2-propenyl)-4-methyl-7-(phenylmethyl)-2,3,6,7-tetrahydro-1H-1λ⁶,2,7-thiadizepine-1,1-dione* (4) and *4-bromo-2-(2-methyl-2-propenyl)-7-(phenylmethyl)-2,3,6,7-tetrahydro-1H-1λ⁶,2,7-thiadizepine-1,1-dione* (2e)**



4 (66%)
(Br:Cl = 14:1, ^{1}H NMR)

2e (8%)

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 Et_2O/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%).

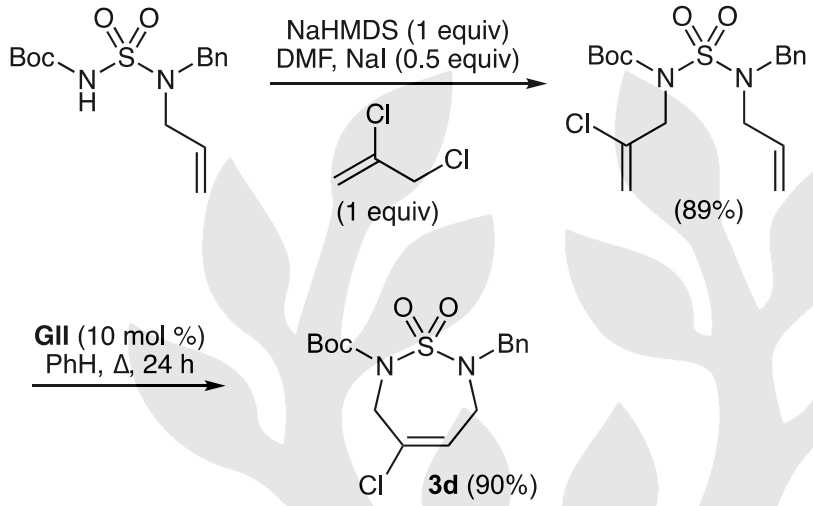
Data for compound **4** (isolated as a mixture containing a small amount of the chloro analogue (Br:Cl ~ 14:1, ^{1}H NMR). **Mpt.** = 115–116 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30-7.20 (5H, m), 5.90 (1H, dt, *J* = 2.2, 1.5 Hz), 5.60 (1H, dt, *J* = 2.2, 1.1 Hz), 5.38 (1H, dt, *J* = 1.8, 5.1 Hz), 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 137.3 (C), 136.2 (C), 128.6 (CH), 128.3 (C), 128.2 (CH), 127.9 (CH), 121.9 (CH), 118.8 (CH_2), 56.7 (CH_2), 52.1 (CH_2), 48.7 (CH_2), 43.2 (CH_2), 24.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 3051, 2934, 1360, 1330, 1156, 898. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 395 (100), 393 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{15}H_{19}{}^{79}BrN_2O_2S$: 371.0423, found 371.0427.

Data for compound **2e**: **Mpt.** = 116 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) 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),

3.52 (2H, d, J = 5.9 Hz), 1.73 (3H, d, J = 1.1 Hz). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 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** ν_{max} neat (cm^{-1}): 3079, 2975, 1363, 1160, 726. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 395 (100), 393 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{15}H_{19}{}^{79}BrN_2O_2S$: 371.0423, found 371.0424.

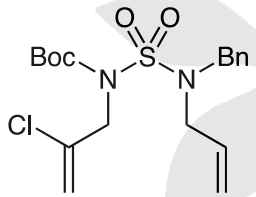
Chloro-olefin RCM

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

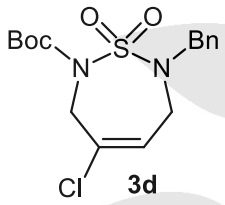
tert-Butyl (N-allyl-N-benzylsulfamoyl)(2-chloroallyl)carbamate



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 H_2O (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 (Na_2SO_4) and concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography, eluting with Et_2O/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, $CDCl_3$) δ 7.23-7.33 (5H, m), 5.74 (1H, ddt, *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, $CDCl_3$) δ 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** ν_{max} / cm^{-1}: 3008, 1727, 1366, 1321, 1247, 1141, 1055, 923, 892, 799. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %) 425 (30), 423 (100) $[M+Na]^+$. **HRMS** (ES^+) $C_{18}H_{25}{}^{35}ClN_2O_4SNa$ = calculated 423.1112, found 423.1112

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



3d

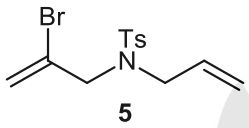
Following the procedure of Weinreb and Chao,[3] to a stirring solution of *tert*-butyl (*N*-allyl-*N*-benzylsulfamoyl)(2-chloroallyl)carbamate (100 mg, 0.26 mmol) in benzene (40 mL) was added Grubbs II catalyst (83 mg, 26 μmol). The mixture was heated under reflux for 24 h, then cooled and concentrated under reduced pressure. The resulting brown oil was purified by column chromatography, eluting with Et_2O/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, $CDCl_3$) δ 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, $CDCl_3$) δ 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** ν_{max} / cm^{-1}: 2981, 1719, 1369, 1322, 1271, 1176, 1147, 1096. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %) 397

[3] Chao, W.; Weinreb, S. M. *Org. Lett.* **2003**, *5*, 2505–2507.

(33), 395 (100) $[M+Na]^+$. **HRMS** (ES^+): $C_{16}H_{21}{}^{35}ClN_2O_4SNa$ = calculated 395.0803, found 395.0805

***N-Allyl-N-(2-bromoallyl)-4-methylbenzenesulfonamide* (5)**



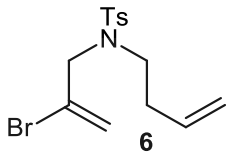
5

To a solution of *N*-(2-bromoally)-4-methylbenzenesulfonamide (100 mg, 0.34 mmol) in CH_3CN (5 mL) was added NaH (8.3 mg, 0.34 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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 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 EtOAc/hexane (6:94) to give compound **5** (84.3 mg, 75 %) as a colourless oil. Data are consistent with those previously reported.[4]

^{1}H NMR ($CDCl_3$, 400 MHz) δ 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}C NMR** ($CDCl_3$, 100 MHz) δ 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). **IR** ν_{max} (cm^{-1}) 3083, 2922, 1692, 1598, 1494, 1441. **LRMS** (ES^+): *m/z* (% rel. intensity) 353 (100), 355 (100) $[M+Na]^+$. **HRMS** (ES^+): $C_{16}H_{16}{}^{79}BrNO_2SNa$ = calculated 351.9977, found 351.9975.

[4] Lee, C.-W.; Oh, K. S.; Kim, K. S.; Ahn, K. H., *Org Lett* **2000**, *2*, 1213–1216.

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

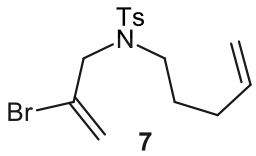


6

To a solution of *N*-(2-bromoally)-4-methylbenzenesulfonamide (127 mg, 0.44 mmol) in CH_3CN (10 mL) was added NaH (10.5 mg, 0.44 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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** ν_{max} (cm^{-1}) 2922, 1635, 1597, 1350 (m). LRMS (ES^+): *m/z* (% rel. intensity) 368 (100), 366 (100) $[M+Na]^+$. HRMS (ES+): Calcd. for $C_{14}H_{18}{}^{79}BrNO_2SNa$: 366.0134, found 366.0135.

***N-(2-Bromoallyl)-4-methyl-N-(pent-4-enyl)benzenesulfonamide* (7)**

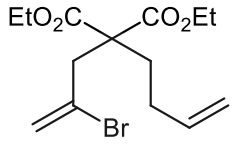


7

To a solution of *N*-(2-bromoally)-4-methylbenzenesulfonamide (150 mg, 0.52 mmol) in CH_3CN (5 mL) was added NaH (12 mg, 0.52 mmol) (CAUTION! Liberation of explosive gas) and *n*-Bu_4NBr (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** ν_{max} (cm^{-1}) 3077, 2924, 1641, 1573, 1443, 1341. LRMS (ES^+): *m/z* (% rel. intensity) 382 (100), 380 $[M+Na]^+$. HRMS (ES+): Calcd. for $C_{18}H_{19}{}^{79}BrN_2NaO_2S$ $[M+CH_3CN+Na]^+$: 429.0242, found 429.0239.

***2-(2-Bromo-allyl)-2-but-3-enyl-malonic acid diethyl ester* (8)**

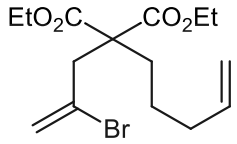


8

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 Et_2O (3 x 15 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) 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%).

^{1}H NMR (300 MHz, $CDCl_3$) 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.4 (C), 137.2 (CH), 132.2 (C), 122.6 (CH_2), 115.1 (CH_2), 61.5 (CH_2), 56.8 (C), 42.9 (CH_2), 30.6 (CH_2), 28.3 (CH_2), 14.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2980, 1729, 1189, 1146, 908. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 357 (100), 355 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{14}H_{21}{}^{79}BrO_4Na$: 355.0515 found 355.0513.

***2-(2-Bromo-allyl)-2-pent-4-enyl-malonic acid diethyl ester* (9)**

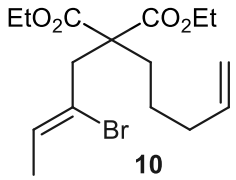


9

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 Et_2O (3 x 15 mL). The combined organic solution was washed with brine (10 mL), dried ($MgSO_4$) 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%).

^{1}H NMR (300 MHz, $CDCl_3$) 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.6 (C), 137.9 (CH), 127.5 (C), 121.5 (CH_2), 115.0 (CH_2), 61.5 (CH_2), 57.2 (C), 42.9 (CH_2), 33.7 (CH), 30.9 (CH_2), 23.4 (CH_2), 14.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2980, 1729, 1187, 1146, 1023, 907. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 369 (100), 371 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{15}H_{23}{}^{79}BrO_4Na$: 369.0672 found 369.0672.

***(Z)-2-(2-Bromo-but-2-enyl)-2-pent-4-enyl-malonic acid diethyl ester* (10)**



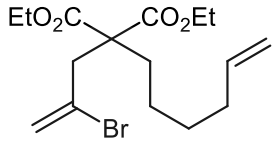
10

To a stirred solution of diethyl 2-(pent-4-en-1-yl)malonate (319 mg, 1.40 mmol) in THF (10 mL) was added *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_2O (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_2O/hexane (4:96) afforded **10** as a colourless oil (455 mg, 90%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 ν_{max}** neat (cm^{-1}): 2979, 1730, 1181, 1130. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 385 (100), 383 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{16}H_{25}{}^{79}BrO_4Na$: 383.0828, found 383.0825.

[5] Prepared according to the method described by Loh *et al.*: Loh, T. P.; Cao, G. Q.; Pei, J. *Tetrahedron Lett.* **1998**, *39*, 1453–1456.

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

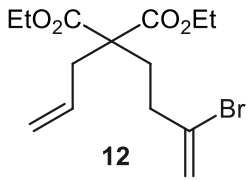


11

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 Et_2O (3 x 15 mL). The combined organic solution was washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure to yield the crude product as a brown oil. Purification by flash chromatography on silica gel (8 g) eluting Et_2O/hexane (1:99) afforded **11** as a colourless oil (196 mg, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.6 (C), 138.5 (CH), 127.5 (C), 121.5 (CH_2), 115.0 (CH_2), 61.5 (CH_2), 57.1 (C), 42.8 (CH_2), 33.3 (CH_2), 31.1 (CH_2), 28.4 (CH_2), 23.4 (CH_2), 14.0 (CH_3). **IR** ν_{max} 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 $C_{16}H_{25}{}^{79}BrO_4Na$: 383.0828, found 383.0834.

2-(3-Bromo-but-3-enyl)-2-but-3-enyl-malonic acid diethyl ester (12)



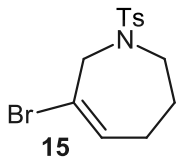
12

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[6] (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 Et_2O (3 x 10 mL). The combined organic solution was washed with brine (10 mL), dried ($MgSO_4$) 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 Et_2O/hexane (2:98) afforded **12** as a colourless oil (120 mg, 0.36 mmol, 70%).

^{1}H NMR (300 MHz, $CDCl_3$) 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, C**H**$_2$C$(CO_2Et)_2$), 2.20-2.10 (2H, m, H_2C=CBrC**H**$_2$), 1.28 (6H, t, *J* = 7.3 Hz). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.8 (C), 133.2 (CH), 132.1 (C), 119.3 (CH_2), 117.0 (CH_2), 61.3 (CH_2), 56.7 (C), 37.3 (CH_2), 36.4 (CH_2), 31.1 (CH_2), 14.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2981, 1729, 1192. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 357 (100), 355 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{14}H_{21}O_4{}^{79}BrNa$: 355.0515, found 355.0514.

[6] Prepared according to the method described by Nuñez *et al.*: Nuñez, A.; Abarca, B.; Cuadro, A. M.; Alvarez-Builla, J.; Vaquero, J. J. *J. Org. Chem.* **2009**, *74*, 4166–4176.

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



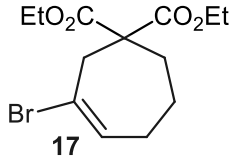
15

(Br:Cl = 15:1, ^{1}H NMR)

To a solution of sulphonamide **7** (20 mg, 0.054 mmol) in CH_2Cl_2 (3 mL) was added a solution of Grubbs II catalyst (4.7 mg, 5.6 μmol) in CH_2Cl_2 (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 Et_2O/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, ^{1}H NMR).

^{1}H NMR ($CDCl_3$, 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.}. **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.1 (C), 136.3 (C),133.1 (CH), 129.3 (CH), 126.8 (CH), 119.0 (C), 53.9 (CH_2), 48.1 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 21.2 (CH_3). {minor signals for vinyl chloride **15Cl** are undetectable}. **IR** ν_{max} (cm^{-1}) 2924, 1335, 841. **ESMS** (+ve): *m/z* (% rel. intensity) 354 (100), 352 (100) $[M+Na]^+$. **HRMS (ES$^+$):** Calcd. for $C_{13}H_{16}{}^{79}BrNO_2SNa$: 351.9977, found 351.9977.

Diethyl 3-bromocyclohept-3-ene-1,1-dicarboxylate **(17) (from 9)**



17

(Br:Cl = 17:1, ^{1}H NMR)

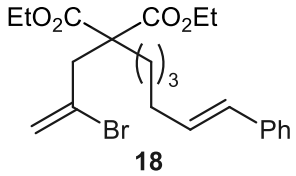
To a stirred solution of 2-(2-bromo-allyl)-2-pent-4-enyl-malonic acid diethyl ester (**9**, 30 mg, 0.090 mmol) in benzene (3 mL) was added a solution of Grubbs II catalyst (7.6 mg, 5.6 μmol) in benzene (6 mL). The mixture was stirred and degassed for 1 hour, then heated at reflux for 18 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel (4 g) eluting with Et_2O/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, ^{1}H NMR).

Diethyl 3-bromocyclohept-3-ene-1,1-dicarboxylate **(17) (from 10)**

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 Et_2O/hexane (2:98) afforded bromocycloheptene **17** as a colourless oil (37 mg, 0.11 mmol, 60%).

^{1}H NMR (300 MHz, $CDCl_3$) 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).}. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.2 (C), 135.5 (CH), 120.2 (C), 62.0 (CH_2), 56.1 (C), 43.2 (CH_2), 36.0 (CH_2), 29.6 (CH_2), 22.2 (CH_2), 14.0 (CH_3). {minor signals for vinyl chloride **17Cl** are undetectable.}. **IR** ν_{max} neat (cm^{-1}): 2980, 1729, 1251, 1217, 1092, 1030. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 343 (100), 341 $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{13}H_{20}{}^{79}BrO_4$: 319.0540, found 319.0536.

***Diethyl (E)-2-(2-bromoallyl)-2-(6-phenylhex-5-en-1-yl)malonate* (18)**

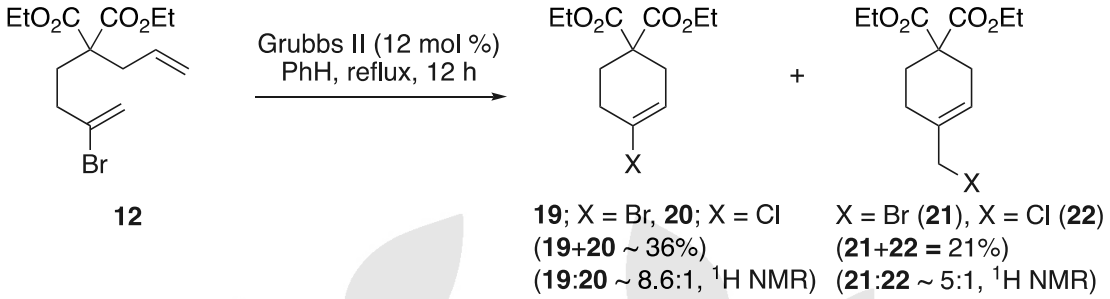


18

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 Et_2O/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.

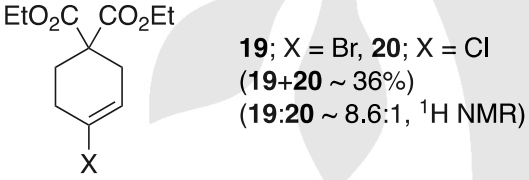
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.18 (5H, m), 6.30 (1H, dt, *J* = 15.8, 1.6 Hz), 6.10 (1H, dt, *J* = 15.8, 7.0 Hz), 5.55 (1H, d, *J* = 1.5 Hz), 5.48 (1H, d, *J* = 1.8 Hz), 4.11 (4H, q, *J* = 7.3 Hz), 3.09 (2H, br s), 2.21-2.10 (2H, m), 2.00-1.93 (2H, m), 1.52 (2H, s), 1.43 (2H, quint, *J* = 7.7 Hz), 1.17 (6H, t, *J* = 7.0 Hz). **^{13}C NMR** (75 MHz, $CDCl_3$) 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 (CH_2), 61.5 (CH_2), 57.1 (C), 42.8 (CH_2), 32.6 (CH_2), 31.1 (CH_2), 29.3 (CH_2), 23.4 (CH_2), 14.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2932, 1731, 1233, 1197, 1152. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 461 (100), 459 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{22}H_{30}{}^{79}BrO_4$: 437.1322, found 437.1324.

Reaction of bromodiene 12 with Grubbs II catalyst



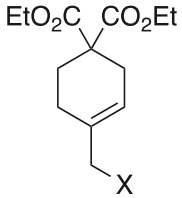
To a stirred solution of **12** (80 mg, 0.24 mmol) in benzene (20 mL) was added a solution of Grubbs II catalyst (25 mg, 29 μmol) in benzene (4 mL). The mixture was stirred and degassed for 1 hour, then heated at reflux for 12 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification by flash chromatography on silica gel (10 g) eluting with Et_2O/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, ^{1}H NMR). Major peaks reported for vinyl bromide **19**. **^{1}H NMR** (300 MHz, $CDCl_3$) 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.8 (C), 125.6 (CH), 120.6 (C), 61.6 (CH_2), 52.0 (C), 32.5 (CH_2), 32.1 (CH_2), 29.2 (CH_2), 14.0 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2978, 1726, 1246, 1174, 1084, 1042. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 329 (100), 327 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{12}H_{17}{}^{79}BrO_4Na$: 327.0202, found 327.0199.

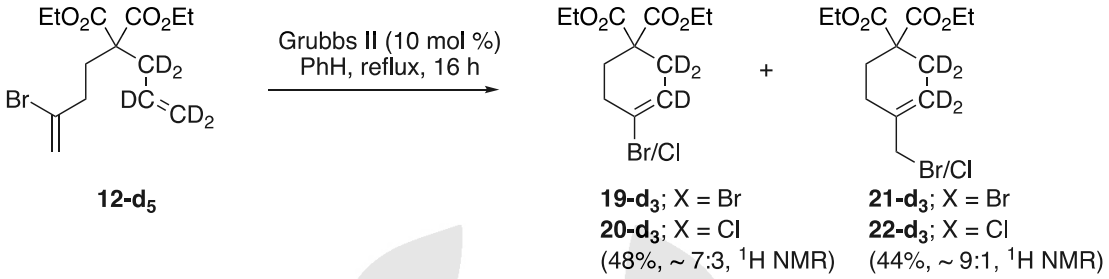
Data for mixture of ***4-bromomethyl-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester*** (**21**) and ***4-chloromethyl-cyclohex-3-ene-1,1-dicarboxylic acid diethyl ester*** (**22**)



X = Br (**21**), X = Cl (**22**)
(**21**+**22** = 21%)
(**21**:**22** ~ 5:1, ^{1}H NMR)

Data recorded from a mixture of allylic bromide **21** and allylic chloride **22** (ratio ~5:1, ^{1}H NMR). Major peaks reported for allylic bromide **21**. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.78 (1H, t, *J* = 4.0 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 Hz). {minor signals for allylic chloride **22**: 5.72 (1H, t, *J* = 4.0 Hz), 3.90 (2H, d, *J* = 1.1 Hz)}. **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.2 (C), 133.8 (C), 124.8 (CH), 61.4 (CH_2), 52.7 (C), 37.9 (CH_2), 30.8 (CH_2), 27.4 (CH_2), 23.5 (CH_2), 14.0 (CH_3). {minor signals for allylic chloride **22** are undetectable, because they are too small.} **IR** ν_{max} neat (cm^{-1}): 2979, 1727, 1240, 1176, 1083, 1034. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 343 (100), 342 (100) $[M+Na]^+$. {for **22**: 297 (16) and 299 (5) $[M+Na]^+$}. **HRMS** (ES^+): Calcd. for $C_{13}H_{19}{}^{79}BrO_4Na$: 341.0359, found 341.0365.

Reaction of d_5-bromodiene 12-d5 with Grubbs II catalyst

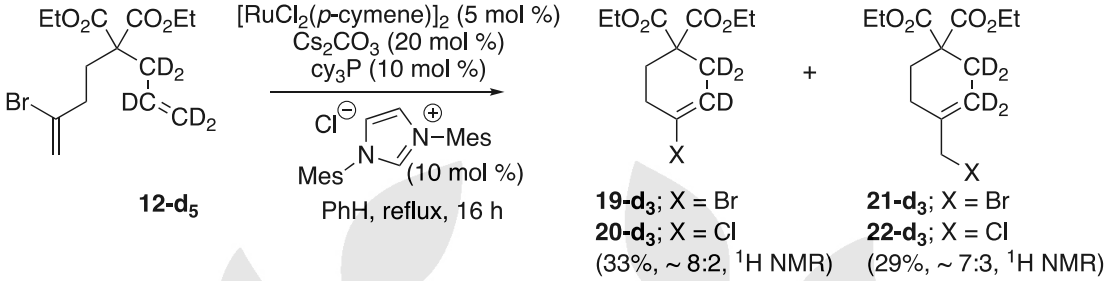


To a stirred solution of deuterated diene **12-d_5** (63 mg, 0.19 mmol) in benzene (9 mL) was degassed for 10 min, then Grubbs II catalyst (16 mg, 19 μmol, 10 mol %) was added. The mixture was heated at reflux for 16 h. Concentration under reduced pressure afforded the crude product as a black oil. Purification 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, ^{1}H NMR). Major peaks reported for vinyl bromide **19-d_3**: **^{1}H 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**: **^{1}H NMR**: 2.29 (2H, dd, *J* = 8.9, 7.7 Hz)}. **^{13}C 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.}

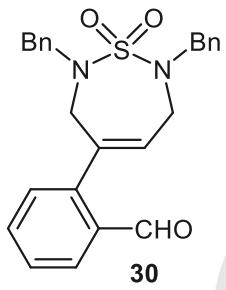
Selected data recorded from mixture of allylic bromide and chloride **21-d_3/22-d_3**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.22-4.16 (4H, m), 3.91 (2H, s), 2.26-2.19 (4H, m), 1.25 (6H, t, *J* = 7.3 Hz). {minor signals for allylic chloride **22-d_3**: **^{1}H NMR**: 3.97 (2H, s)}. **^{13}C NMR** (75 MHz, $CDCl_3$) 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 [$RuCl_2$(*p*-cymene)]$_2$/cy_3P/1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride/Cs_2CO_3.



Benzene (3.5 mL) was degassed for 10 min, then [$RuCl_2$(*p*-cymene)]$_2$ (3 mg, 4.8 μmol, 5 mol %), Cs_2CO_3 (6 mg, 19.5 μmol, 20 mol %), cy_3P (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_2O/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)**

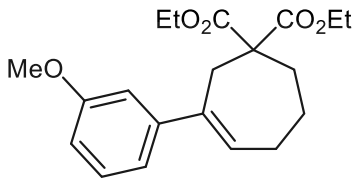


30

To a solution of vinyl bromide **2a** (25 mg, 0.06 mmol) in THF (2 mL) was added a solution of 2M Na_2CO_3 (1 mL) and 2-formylphenyl boronic acid (11 mg, 0.075 mmol). $Pd(PPh_3)_4$ (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 ($MgSO_4$) 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.

^{1}H NMR ($CDCl_3$, 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). ^{13}C NMR ($CDCl_3$, 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 (CH_2), 48.6 (CH_2), 43.9 (CH_2). **IR** ν_{max} (cm^{-1}) 3031, 2923, 1698, 1595, 1496, 1456. **LRMS** (ES^+): *m/z* (% rel. intensity) 433.0 (100) $[M+H]^+$. **HRMS** (ES^+): Calcd. for $C_{25}H_{24}N_2O_3S$: 432.1508, found 433.1580.

***3-(3-Methoxy-phenyl)-cyclohept-3-ene-1,1-dicarboxylic acid diethyl ester* (31)**



31

Following the procedure of Banwell *et al*.,[7] to a stirred solution of **17** (20 mg, 63 μmol) in THF (2 mL) was added a solution of Na_2CO_3 (200 mg) in H_2O (1 mL) and 3-methoxyphenylboronic acid (14 mg, 94 μmol). $Pd(PPh_3)_4$ (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_2O (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_2O/hexane (1:9) afforded the cross-coupling product **31** as a pale-yellow oil (20 mg, 57 μmol, 92%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 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). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 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_2), 55.3 (CH_3), 55.0 (C), 36.7 (CH_2), 36.1 (**C**H_2), 28.2 (CH_2), 22.1 (CH_2), 13.7 (CH_3). **IR** ν_{max} neat (cm^{-1}): 2956, 1730, 1218, 1185, 1051. **LRMS** (ES^+, CH_3CN) *m/z* (relative intensity %): 369 (100) $[M+Na]^+$. **HRMS** (ES^+): Calcd. for $C_{20}H_{26}O_5Na$: 369.1672, found 369.1666.

[7] Banwell, M. G.; Wu, A. W. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2671-2672.

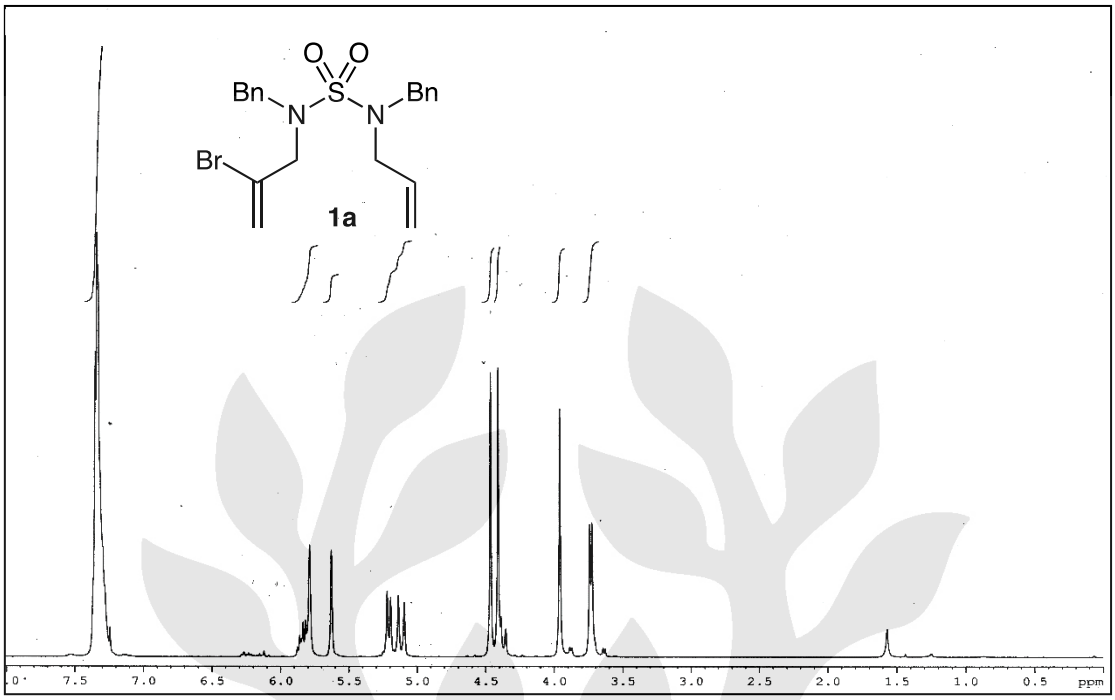


Figure S1. ^{1}H-NMR spectrum of compound **1a** in $CDCl_3$

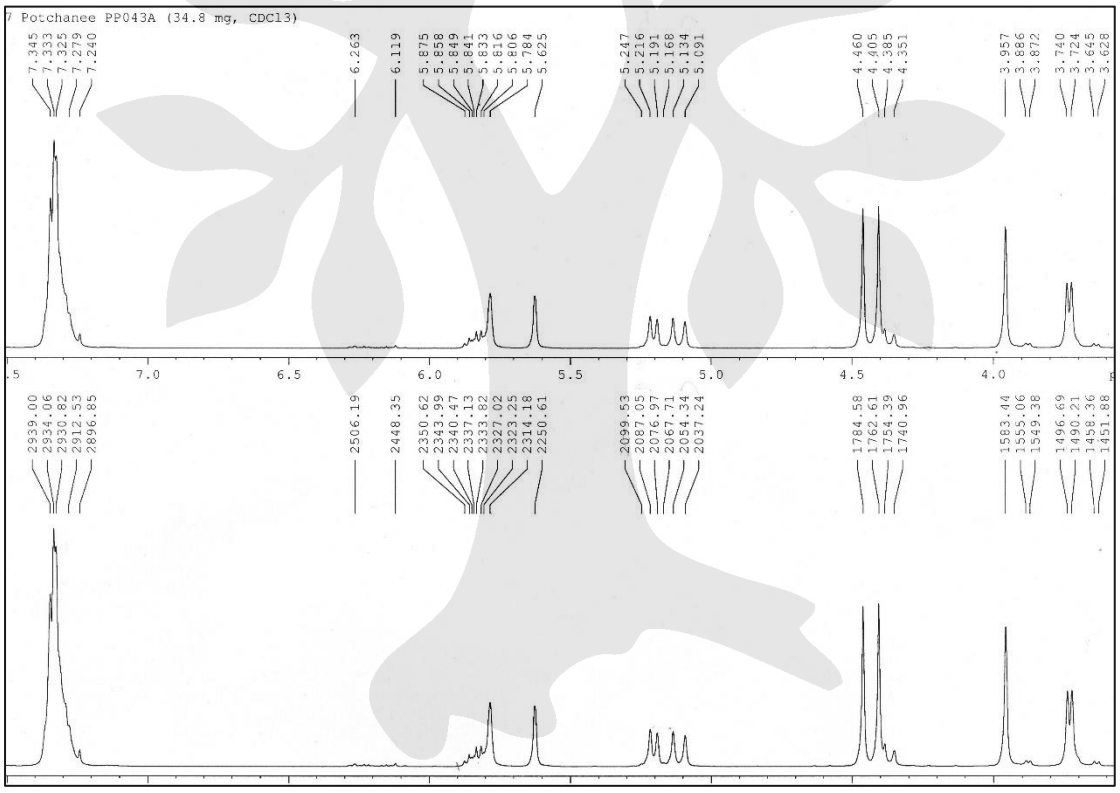


Figure S2. ^{1}H-NMR expanded spectrum of compound **1a** in $CDCl_3$

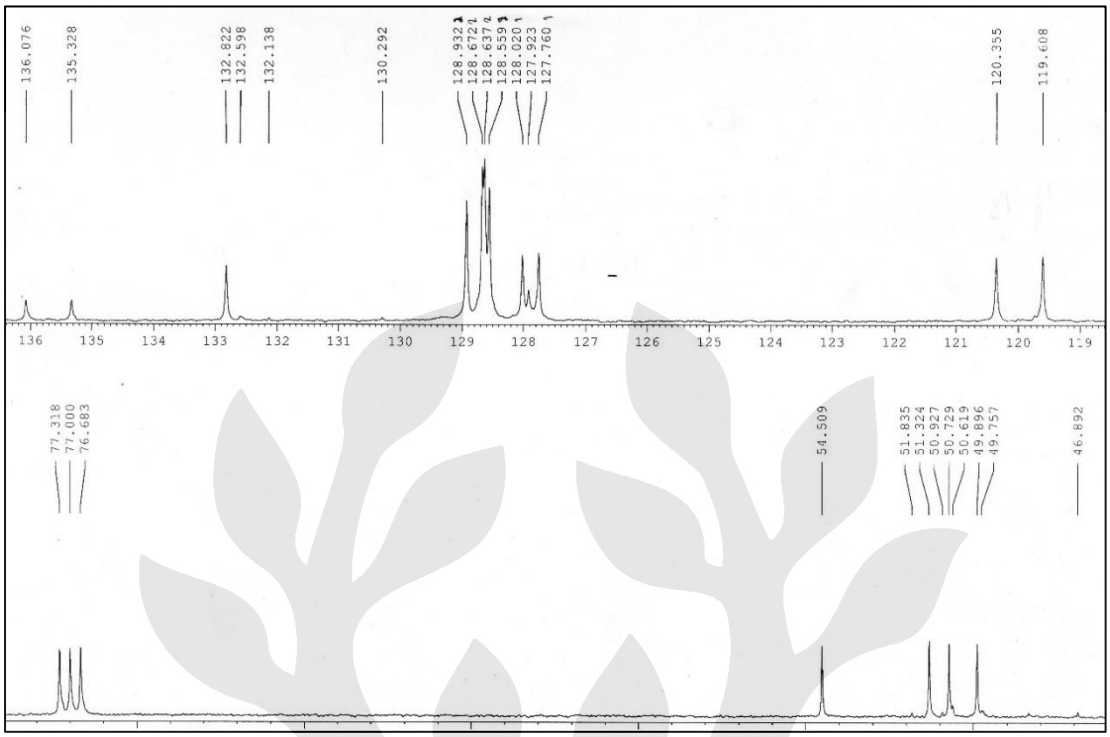


Figure S3. ^{1}H-NMR expanded spectrum of compound **1a** in $CDCl_3$

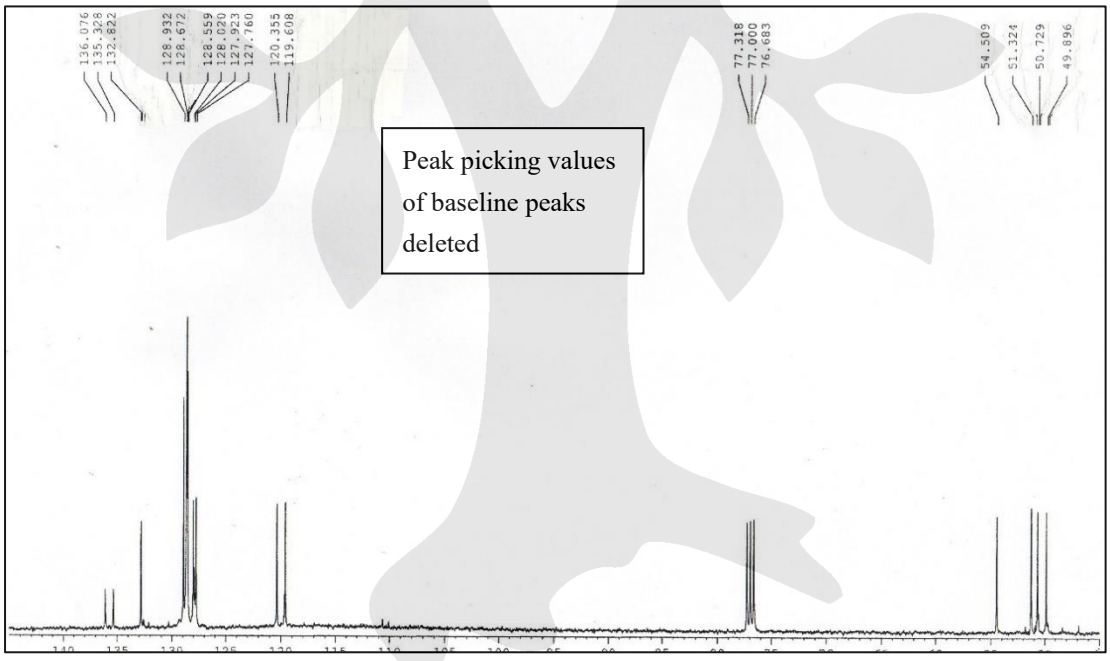


Figure S4. ^{13}C-NMR spectrum of compound **1a** in $CDCl_3$

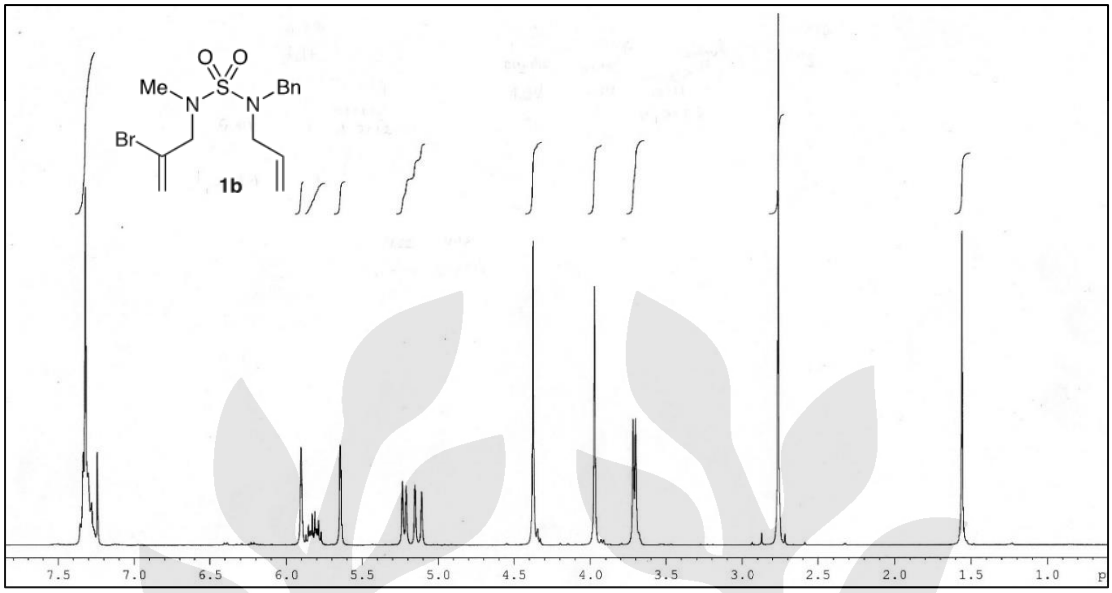


Figure S5. ^{1}H-NMR spectrum of compound **1b** in $CDCl_3$

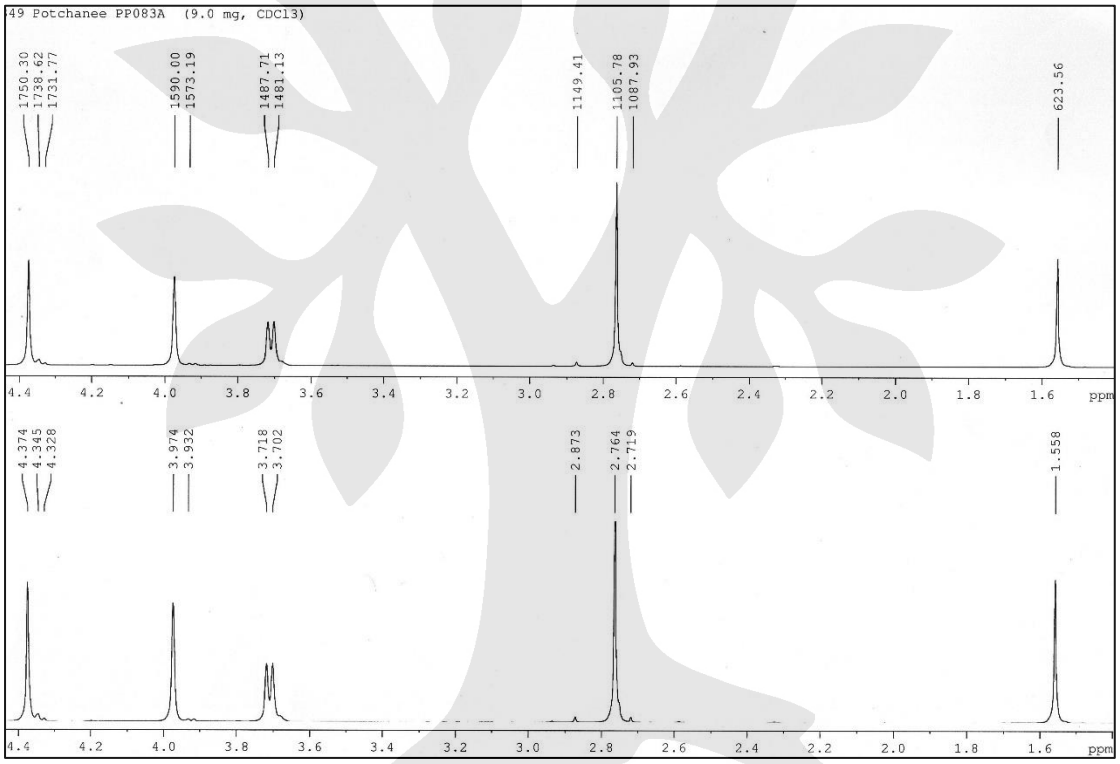


Figure S6. ^{1}H-NMR expanded spectrum of compound **1b** in $CDCl_3$

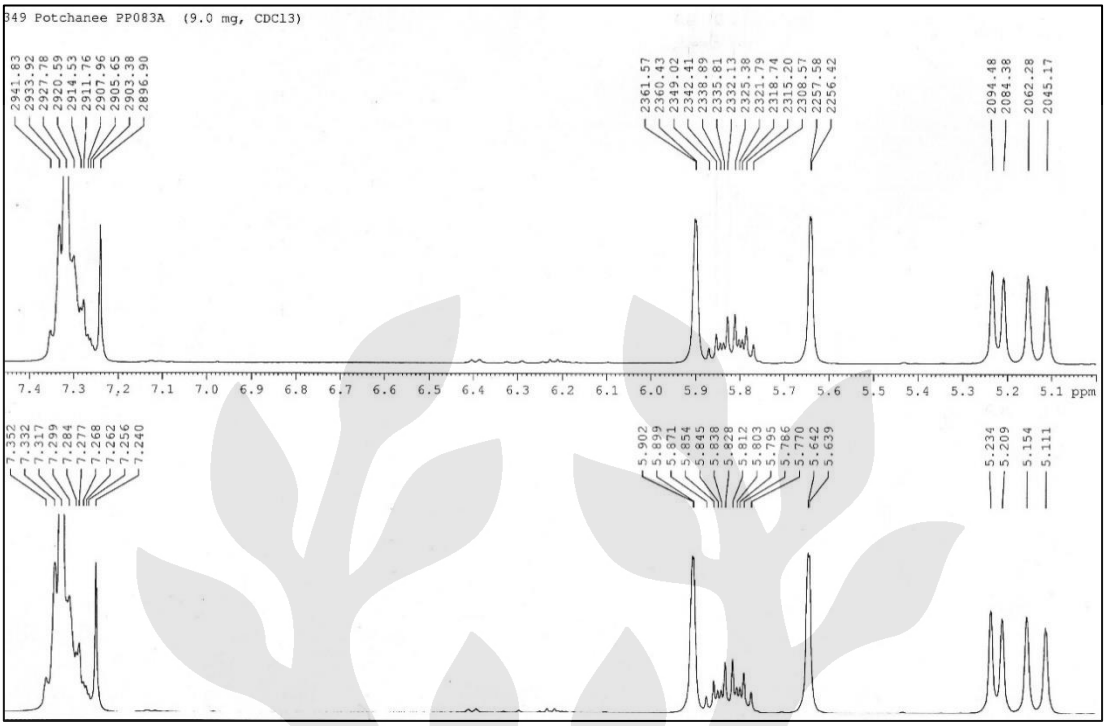


Figure S7. ^{1}H-NMR expanded spectrum of compound **1b** in $CDCl_3$

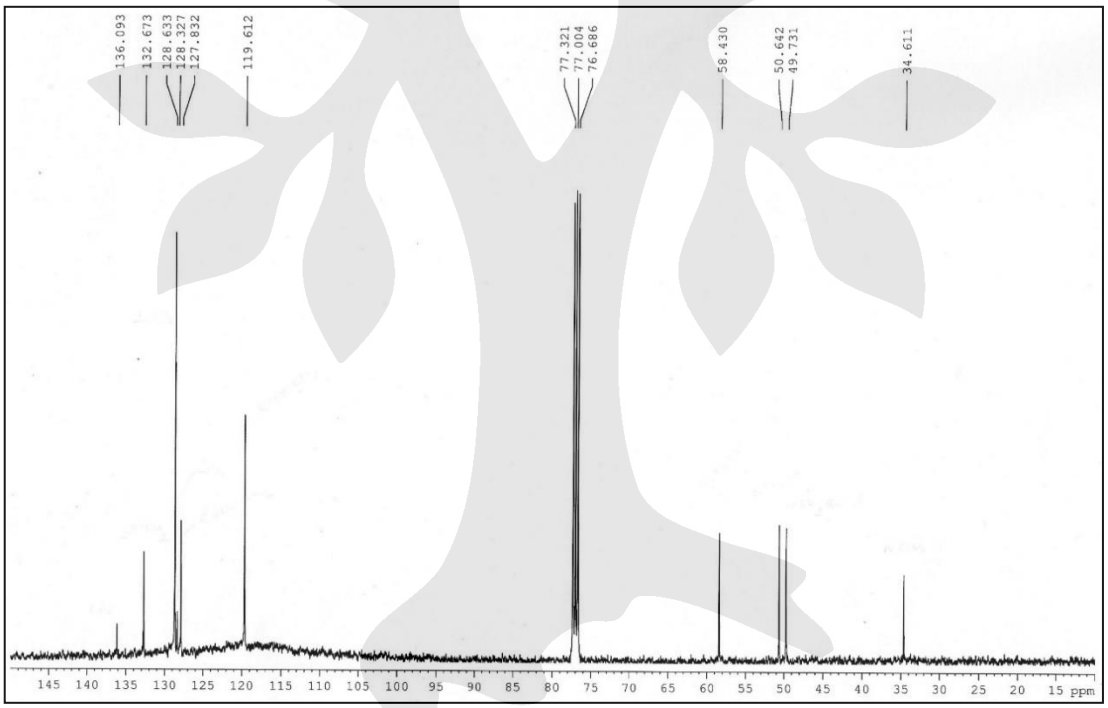


Figure S8. ^{13}C-NMR spectrum of compound **1b** in $CDCl_3$

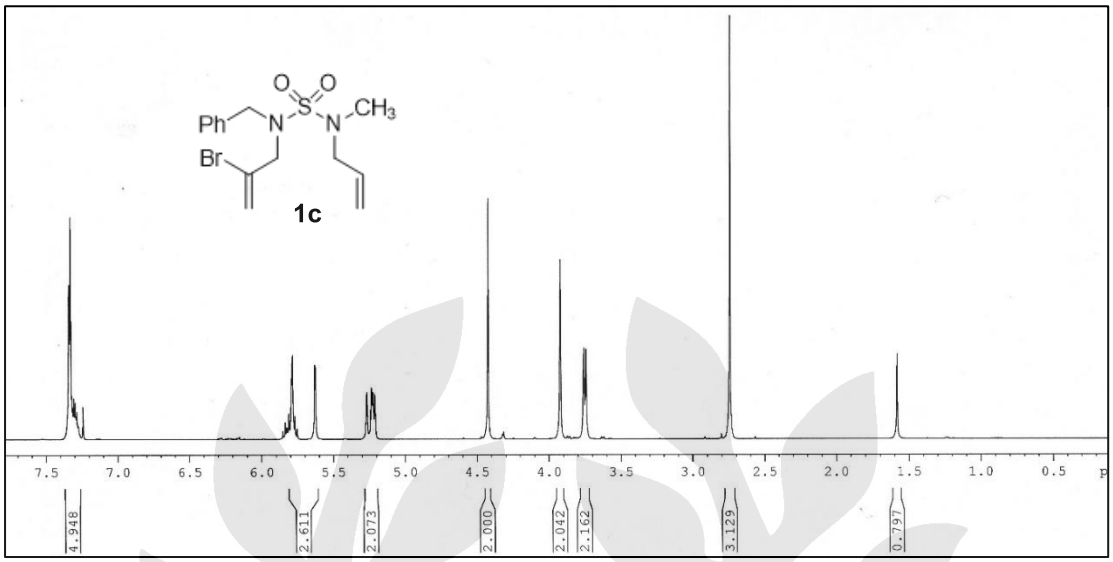


Figure S9. ^{1}H-NMR spectrum of compound **1c** in $CDCl_3$

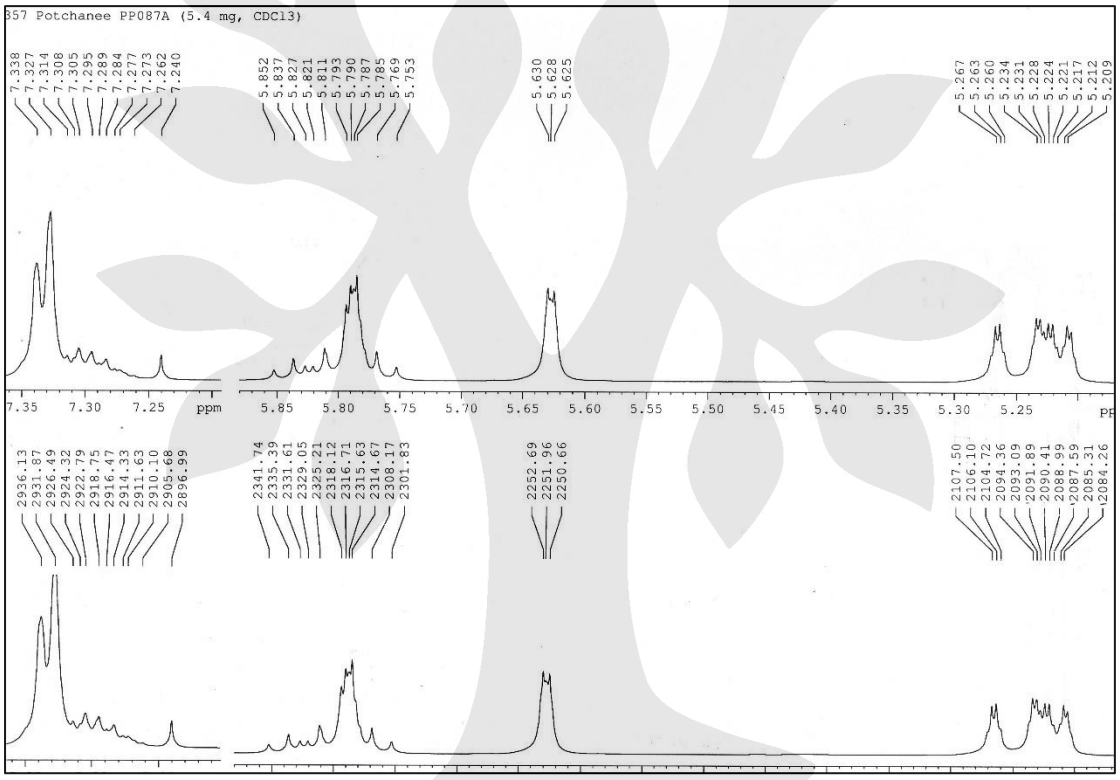


Figure S10. ^{1}H-NMR expanded spectrum of compound **1c** in $CDCl_3$

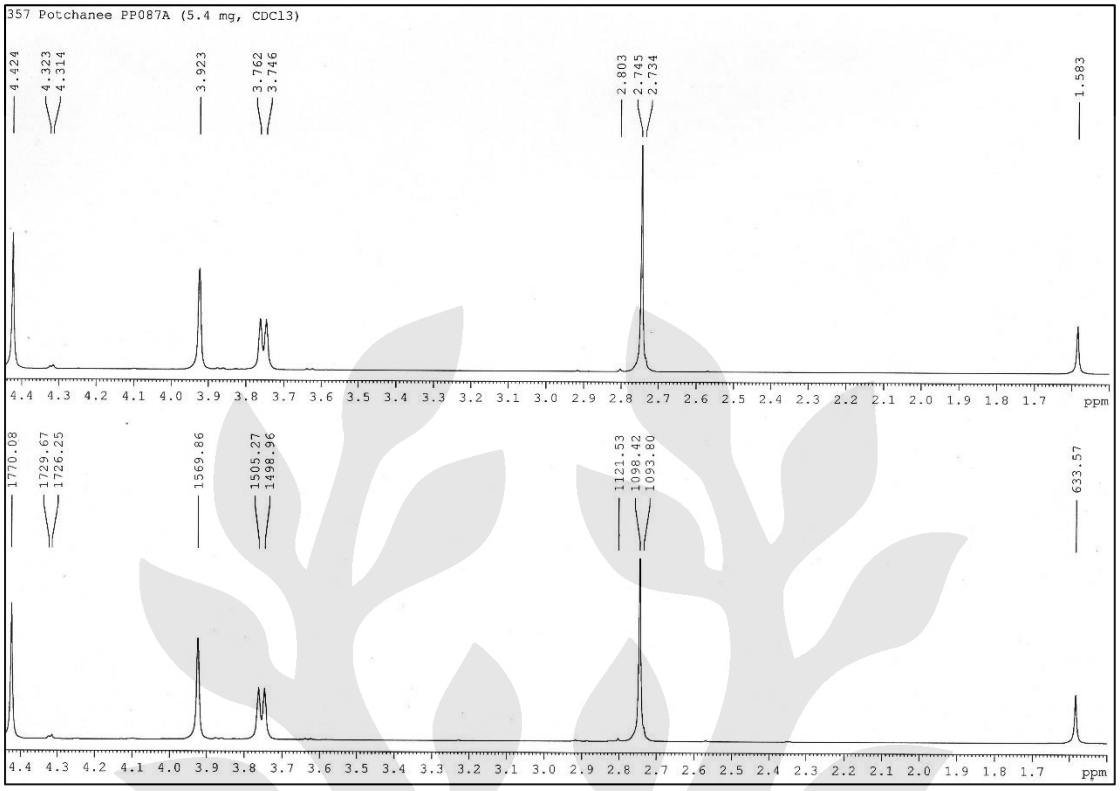


Figure S11. ^{1}H-NMR expanded spectrum of compound **1c** in $CDCl_3$

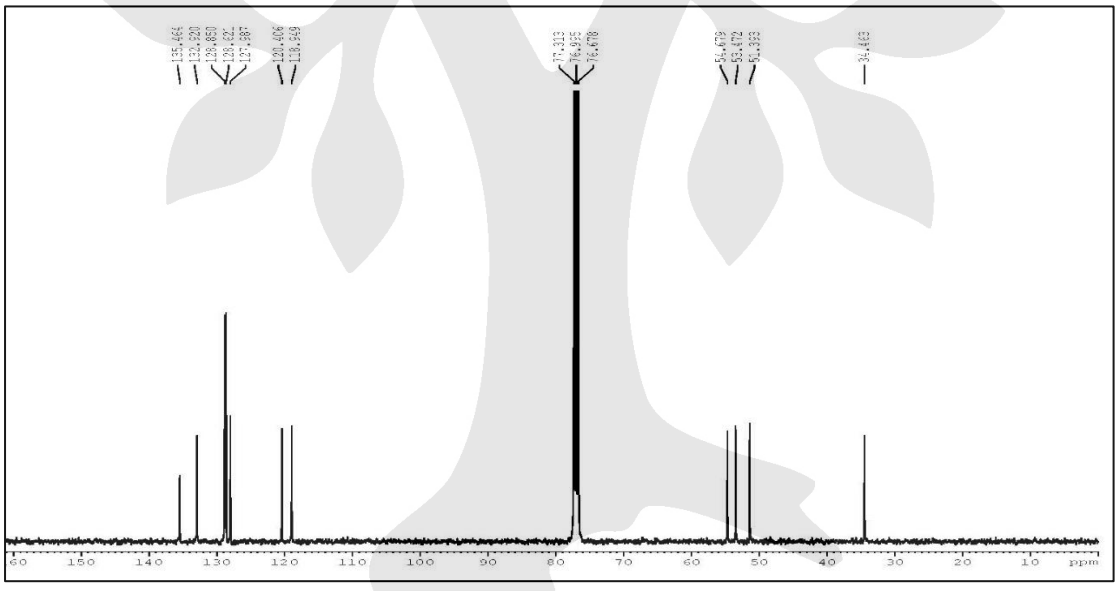


Figure S12. ^{13}C-NMR spectrum of compound **1c** in $CDCl_3$

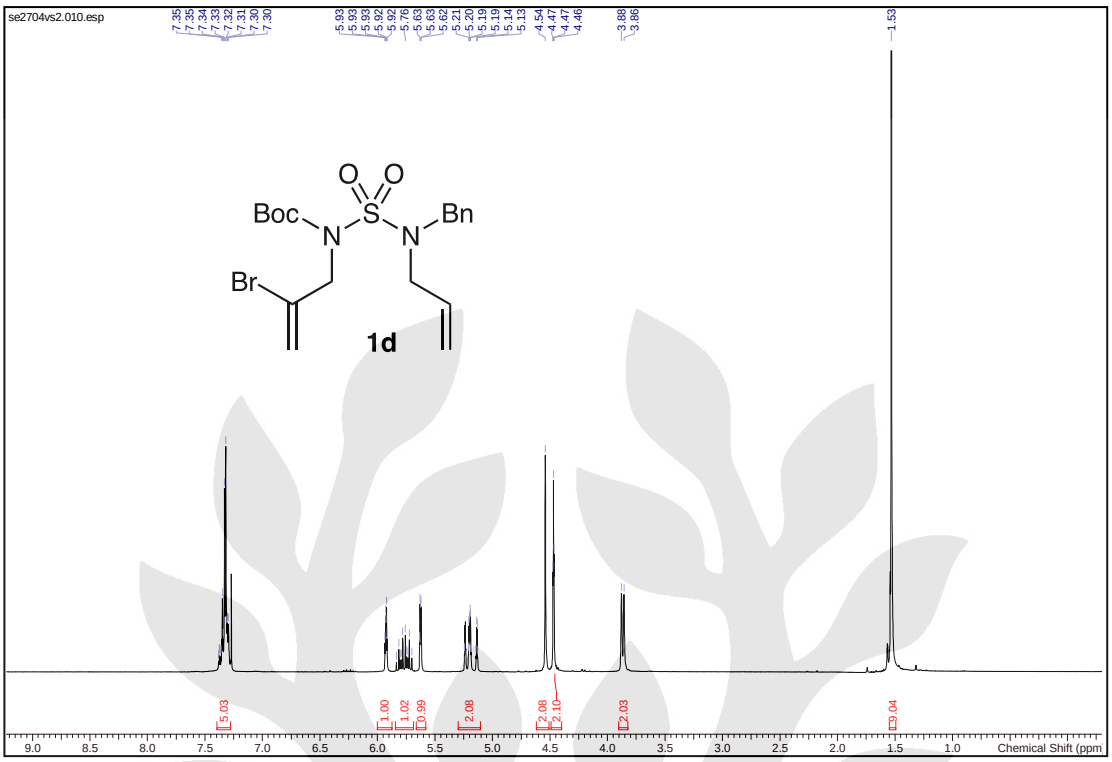


Figure S13. ^{1}H-NMR spectrum of **1d** in $CDCl_3$

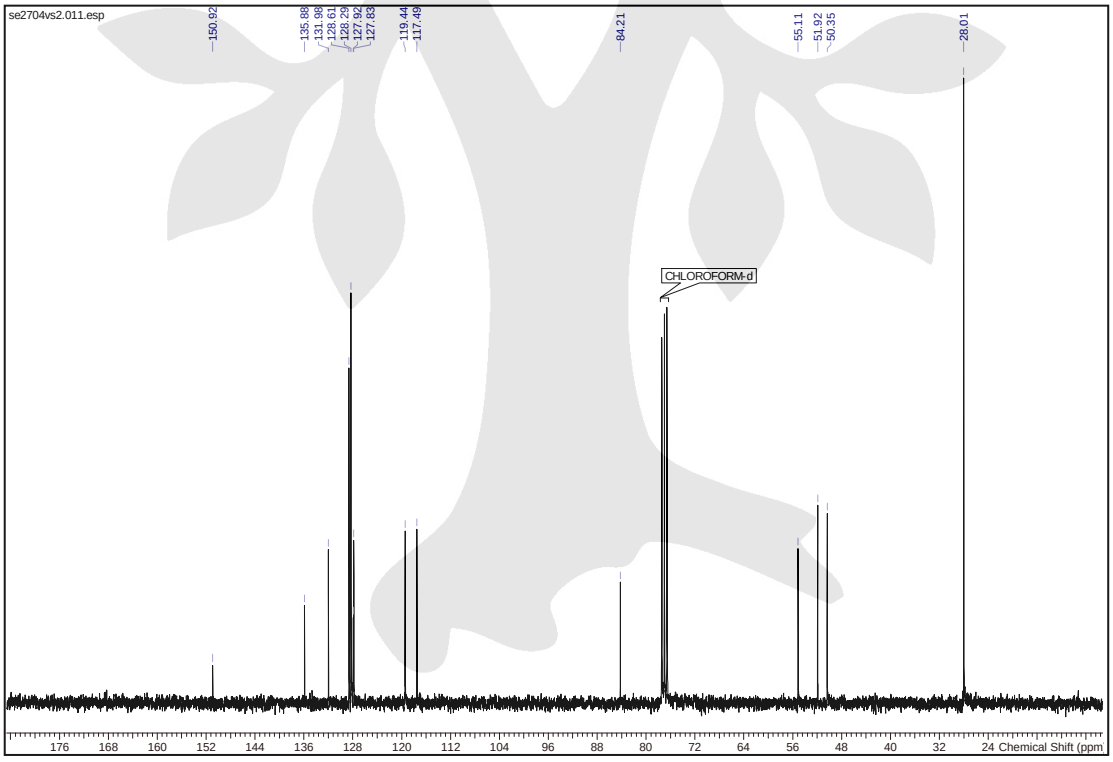


Figure S14. ^{1}H-NMR spectrum of **1d** in $CDCl_3$

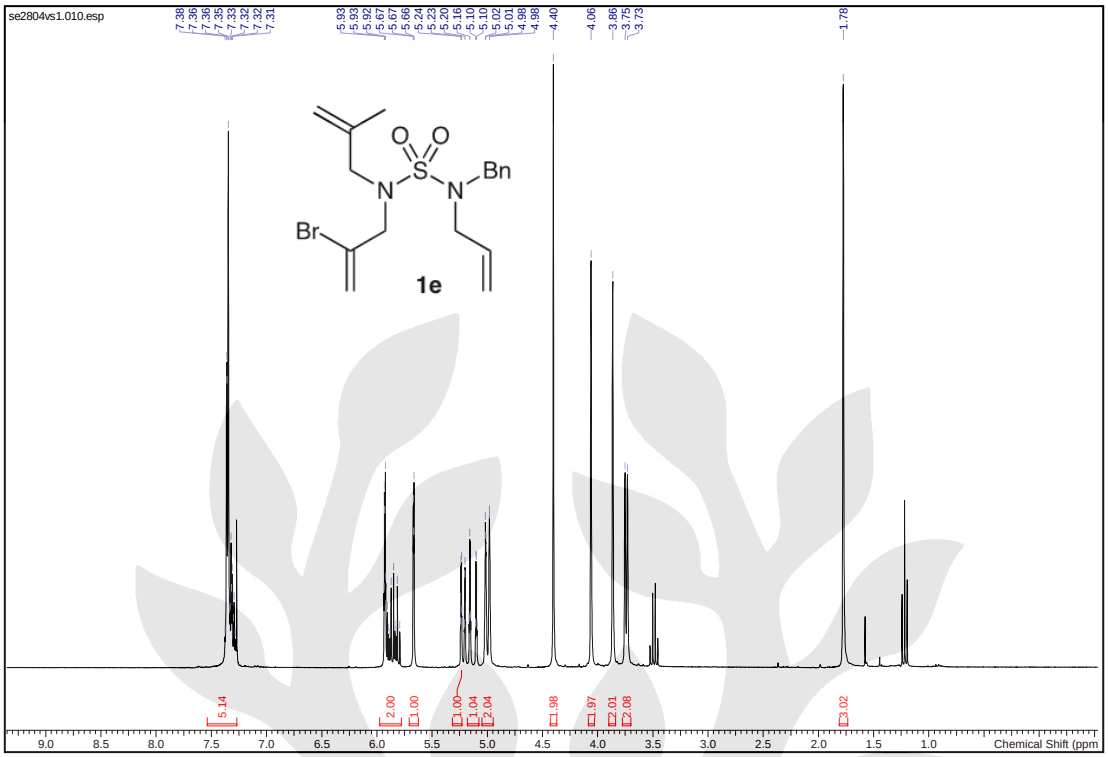


Figure S15. ^{1}H-NMR spectrum of **1e** in $CDCl_3$

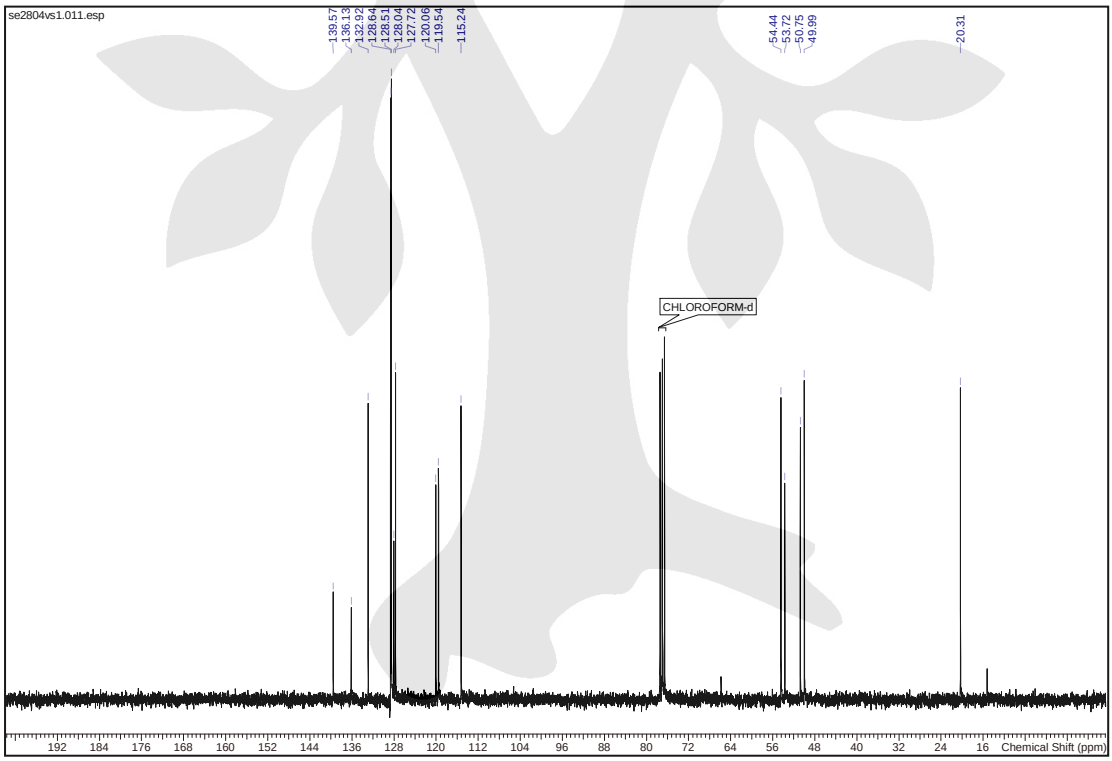


Figure S16. ^{13}C-NMR spectrum of **1e** in $CDCl_3$

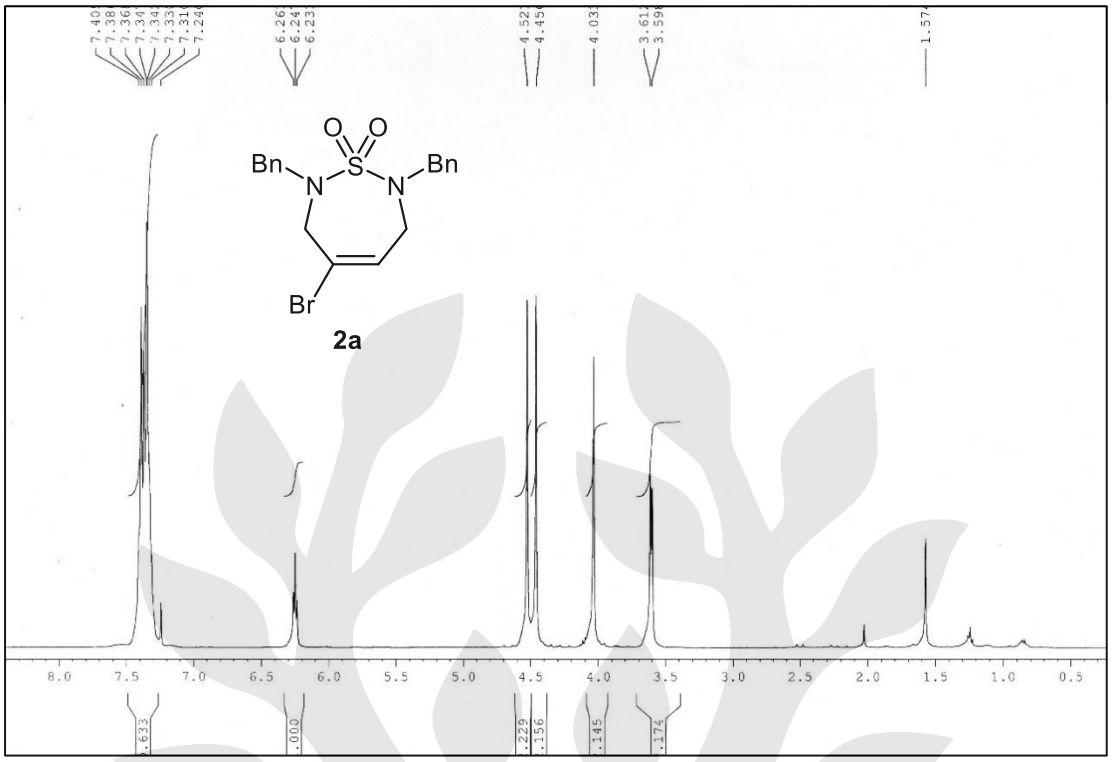


Figure S17. ^{1}H-NMR spectrum of compound **2a** in $CDCl_3$

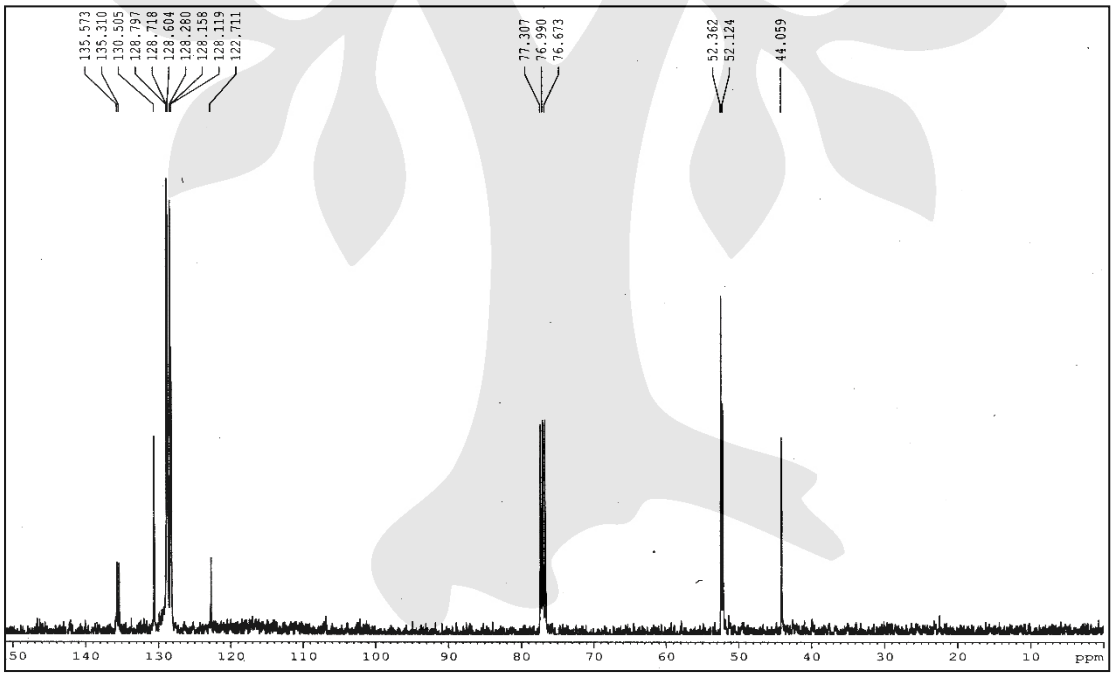


Figure S18. ^{13}C-NMR spectrum of compound **2a** in $CDCl_3$

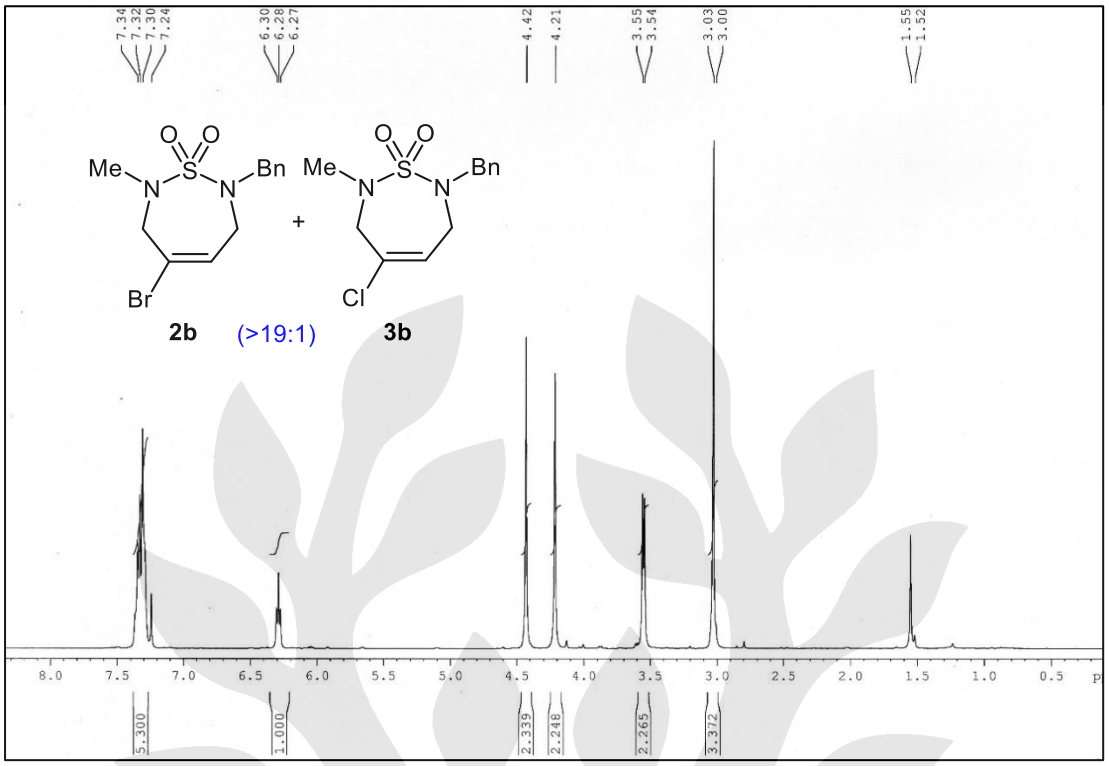


Figure S19. ^{1}H-NMR spectrum of compound **2b/3b** in $CDCl_3$

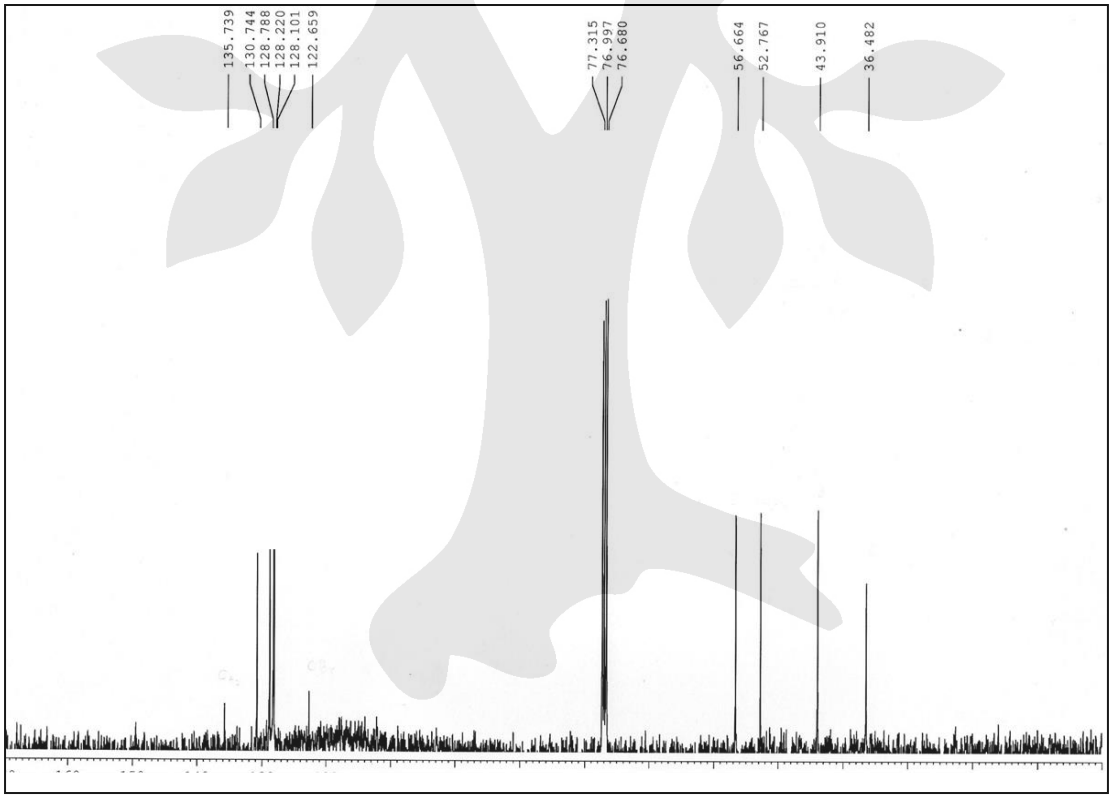


Figure S20. ^{13}C-NMR spectrum of compound **2b/3b** in $CDCl_3$

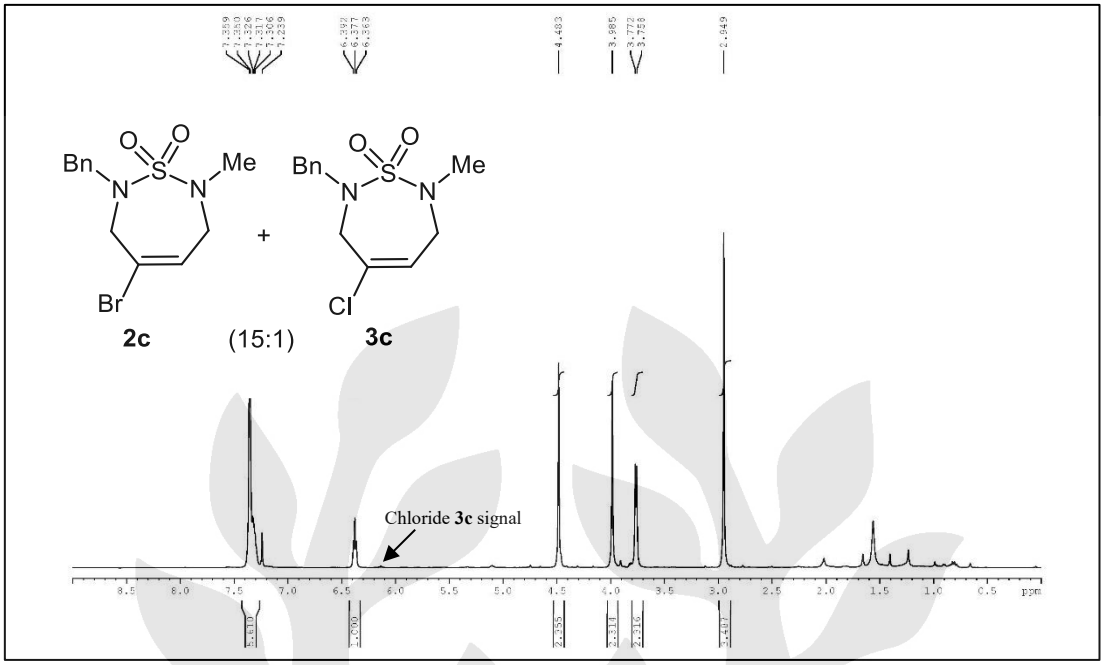


Figure S21. ^{1}H-NMR spectrum of compound **2c/3c** in $CDCl_3$

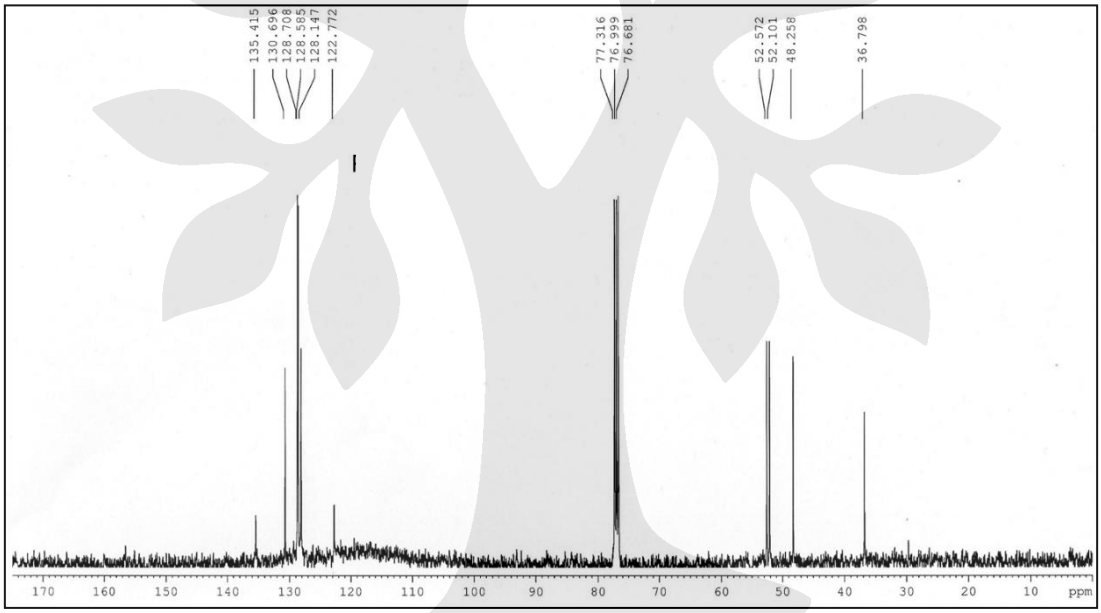


Figure S22. ^{13}C-NMR spectrum of compound **2c/3c** in $CDCl_3$

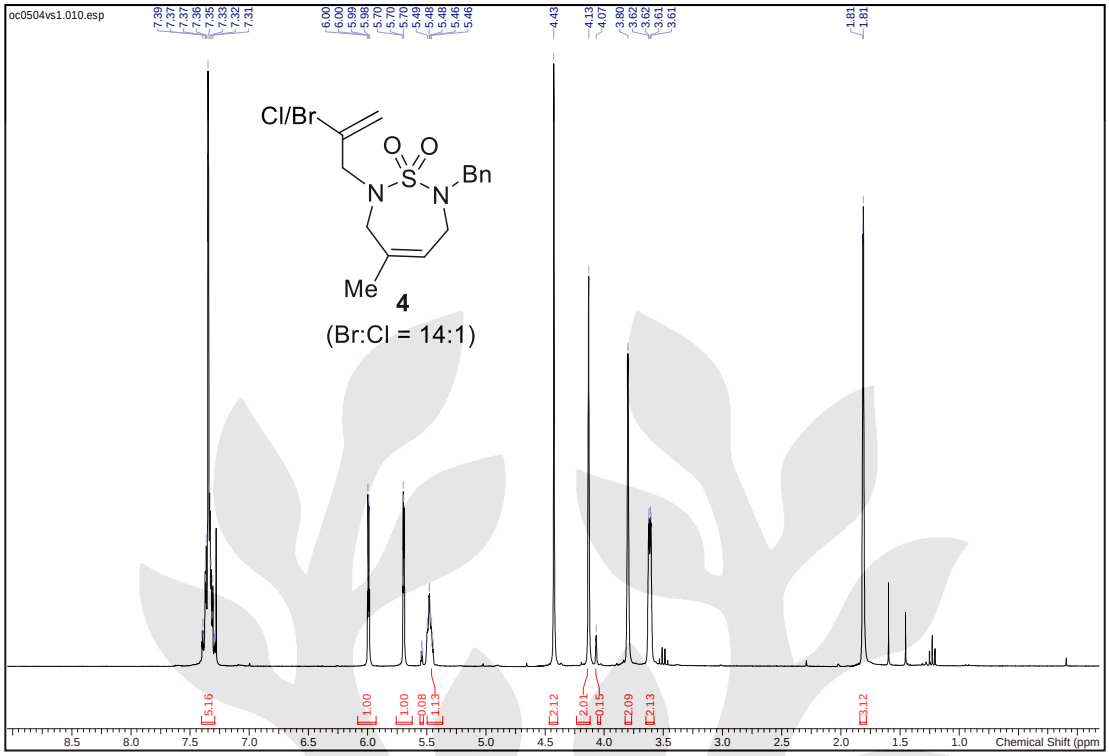


Figure S23. ^{1}H-NMR spectrum of **4** in $CDCl_3$

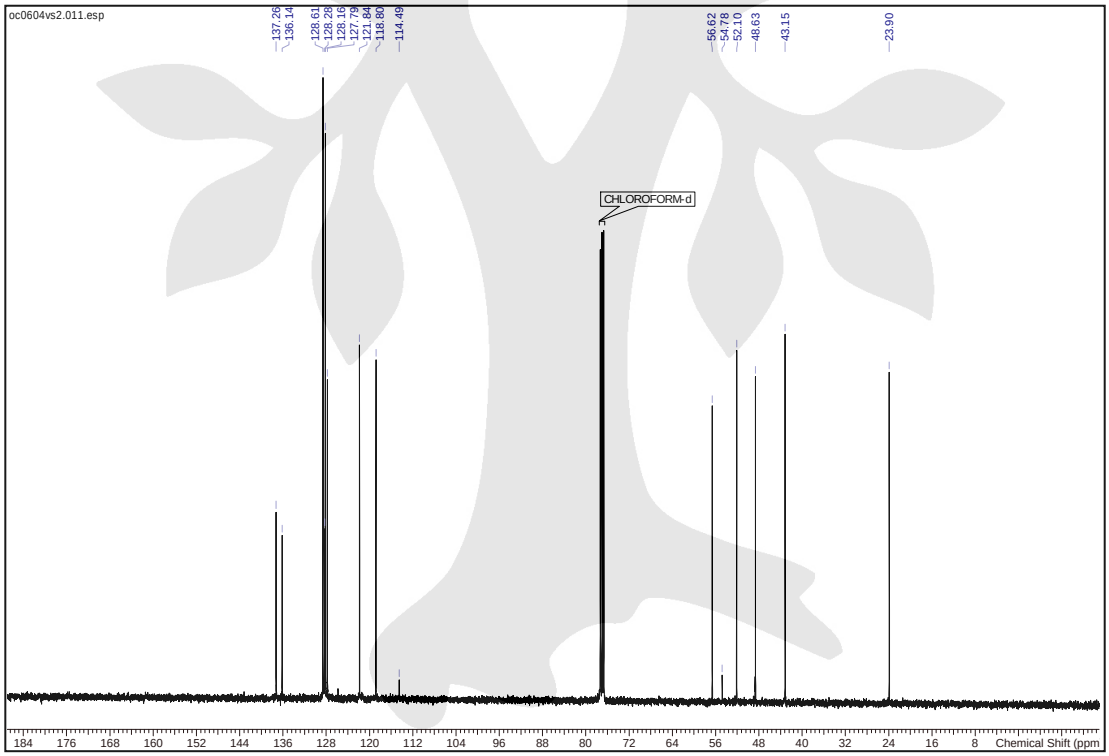


Figure S24. ^{13}C-NMR spectrum of **4** in $CDCl_3$

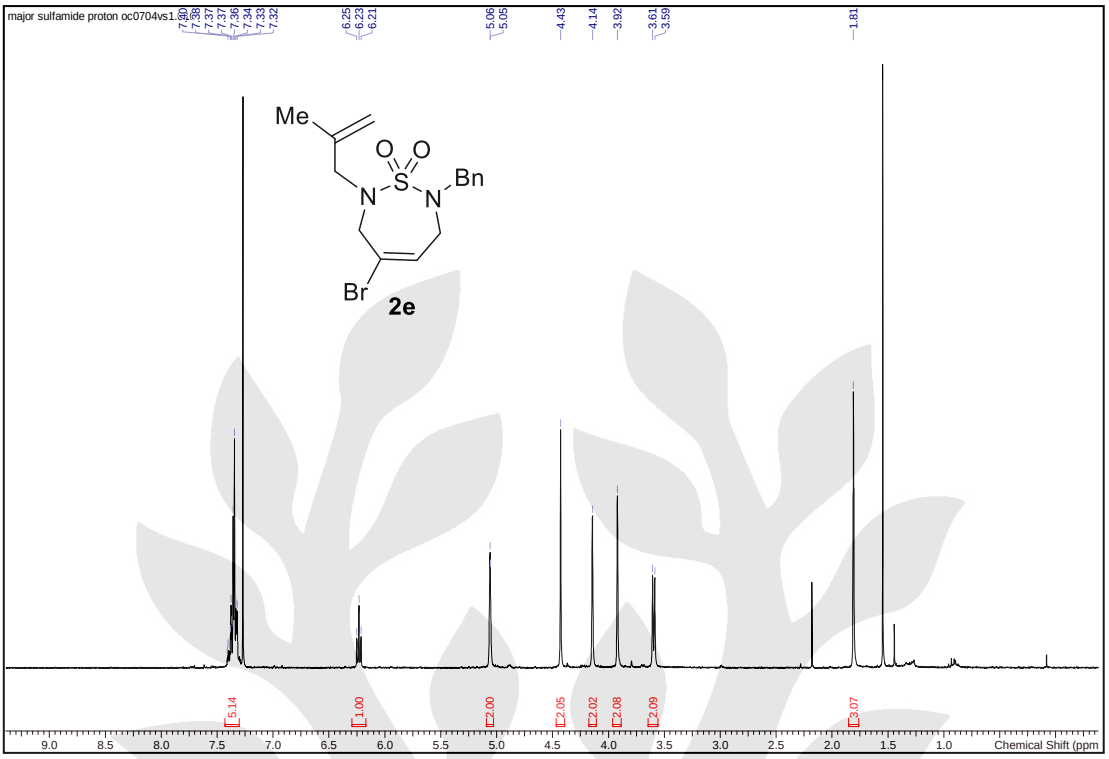


Figure S25. ^{1}H-NMR spectrum of **2e** in $CDCl_3$

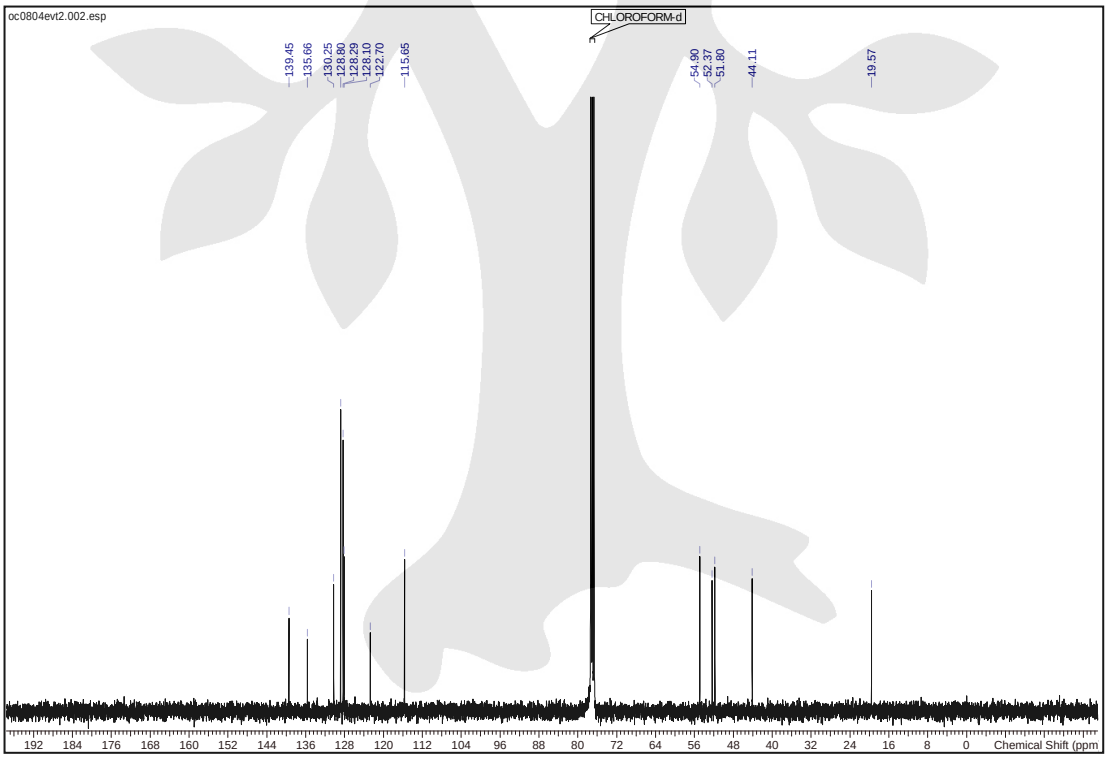


Figure S26. ^{13}C-NMR spectrum of **2e** in $CDCl_3$

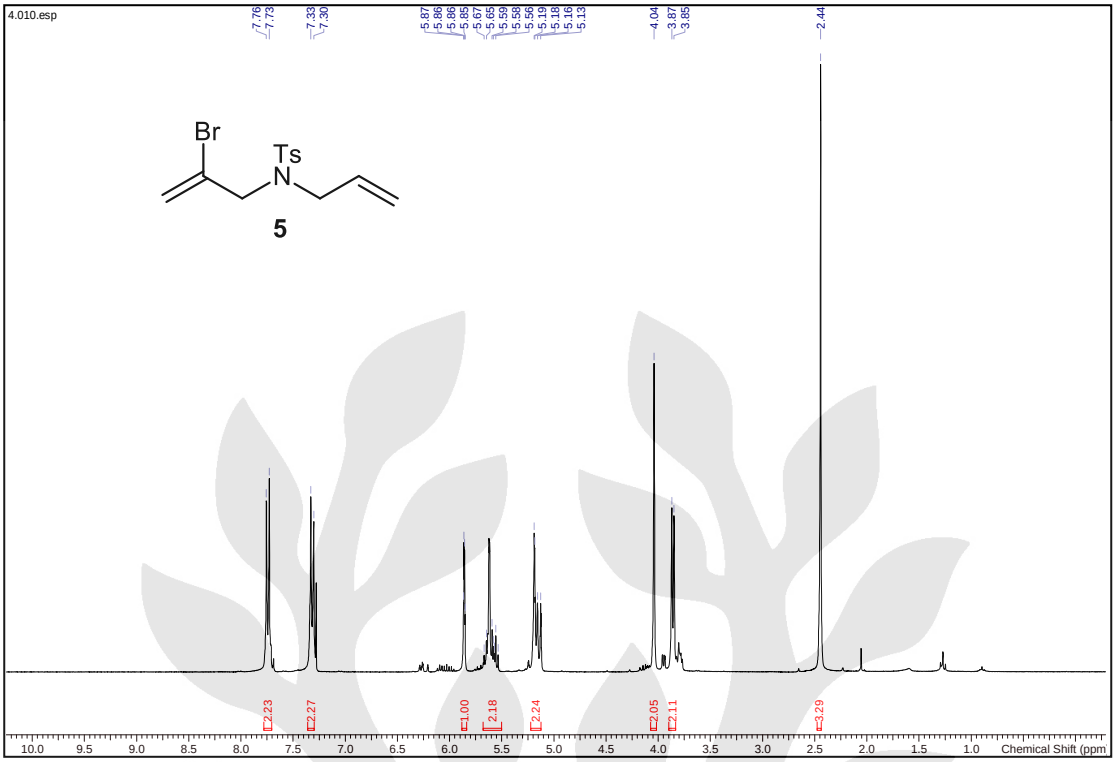


Figure S27. ^{1}H-NMR spectrum of compound **5** in $CDCl_3$

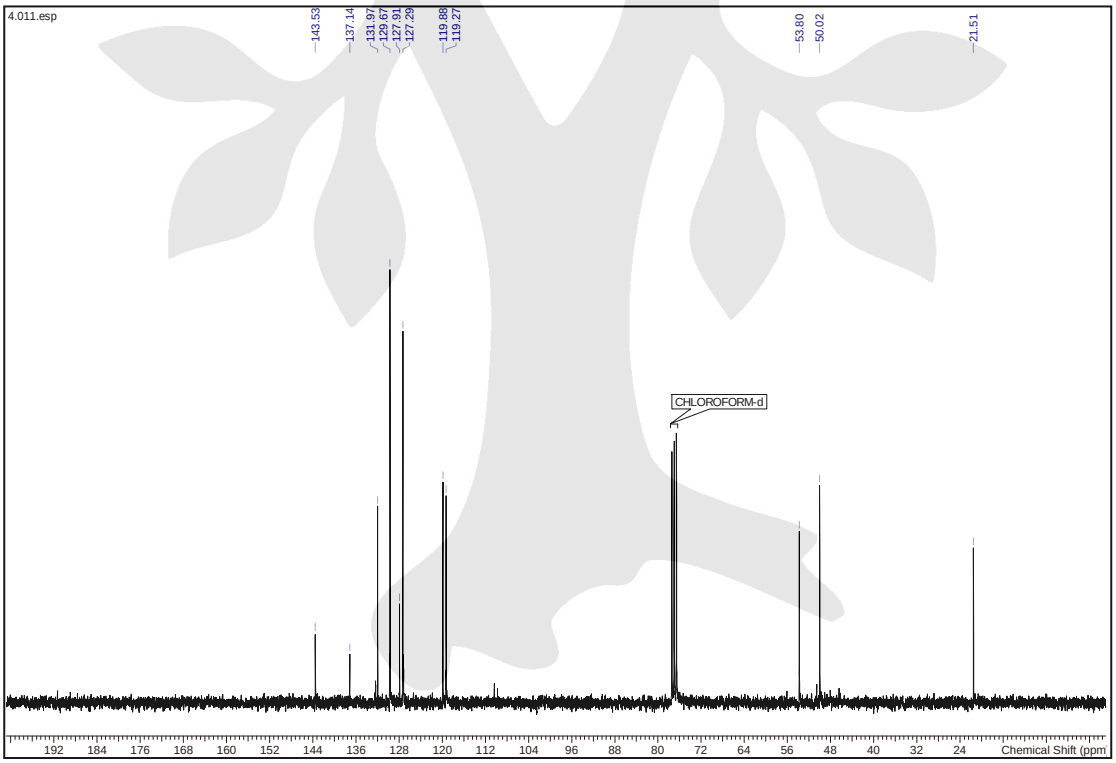


Figure S28. ^{13}C-NMR spectrum of compound **5** in $CDCl_3$

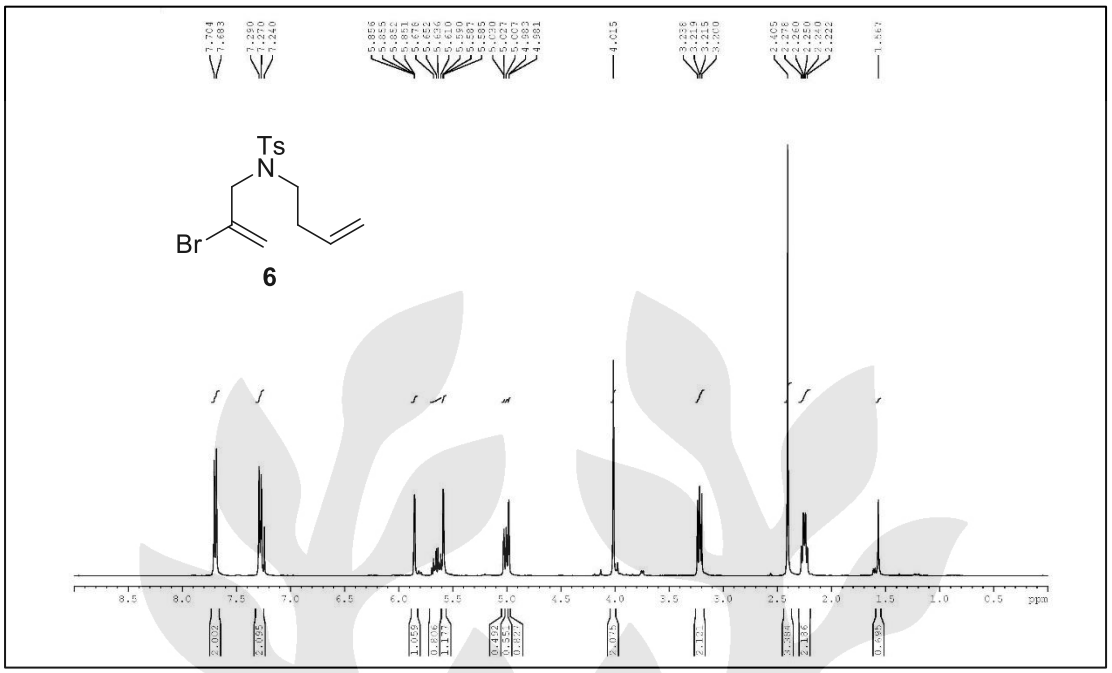


Figure S29. ^{1}H-NMR spectrum of compound **6** in $CDCl_3$

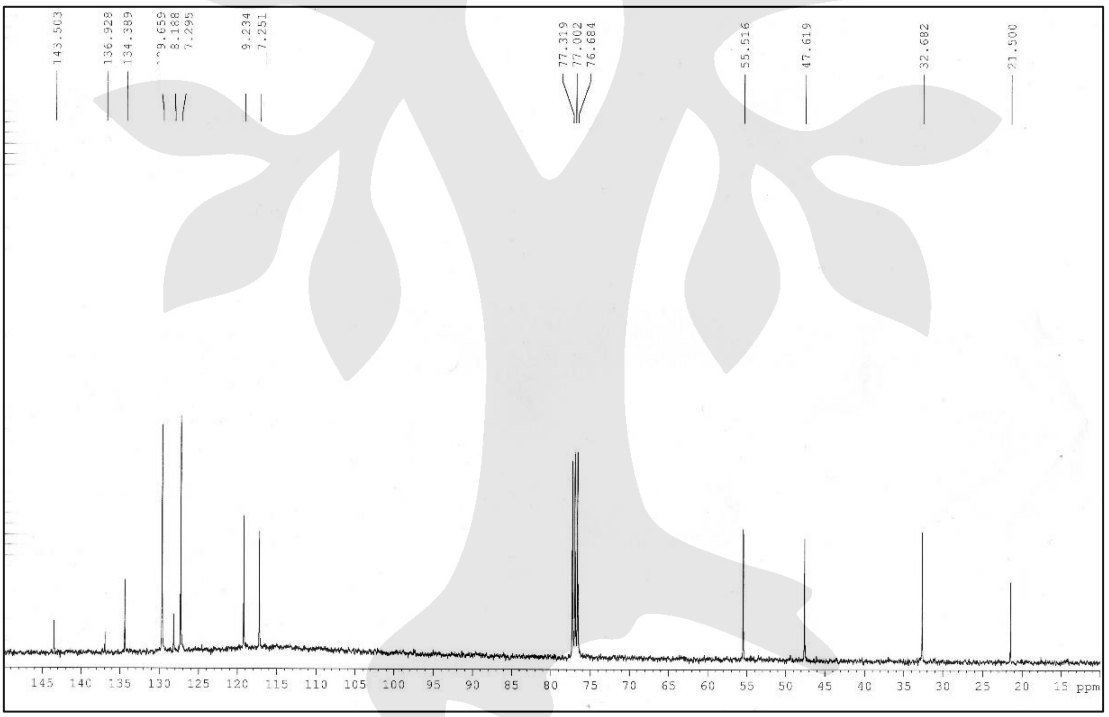


Figure S30. ^{13}C-NMR spectrum of **6** in $CDCl_3$

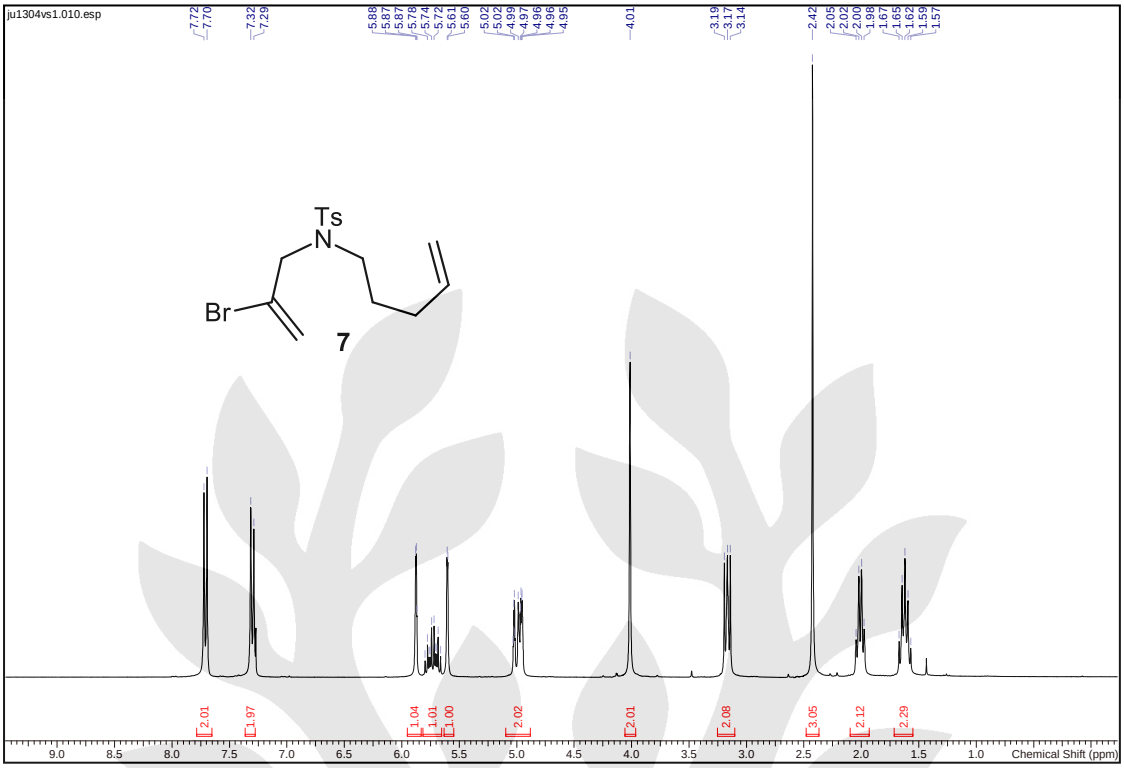


Figure S31. ^{1}H-NMR spectrum of **7** in $CDCl_3$

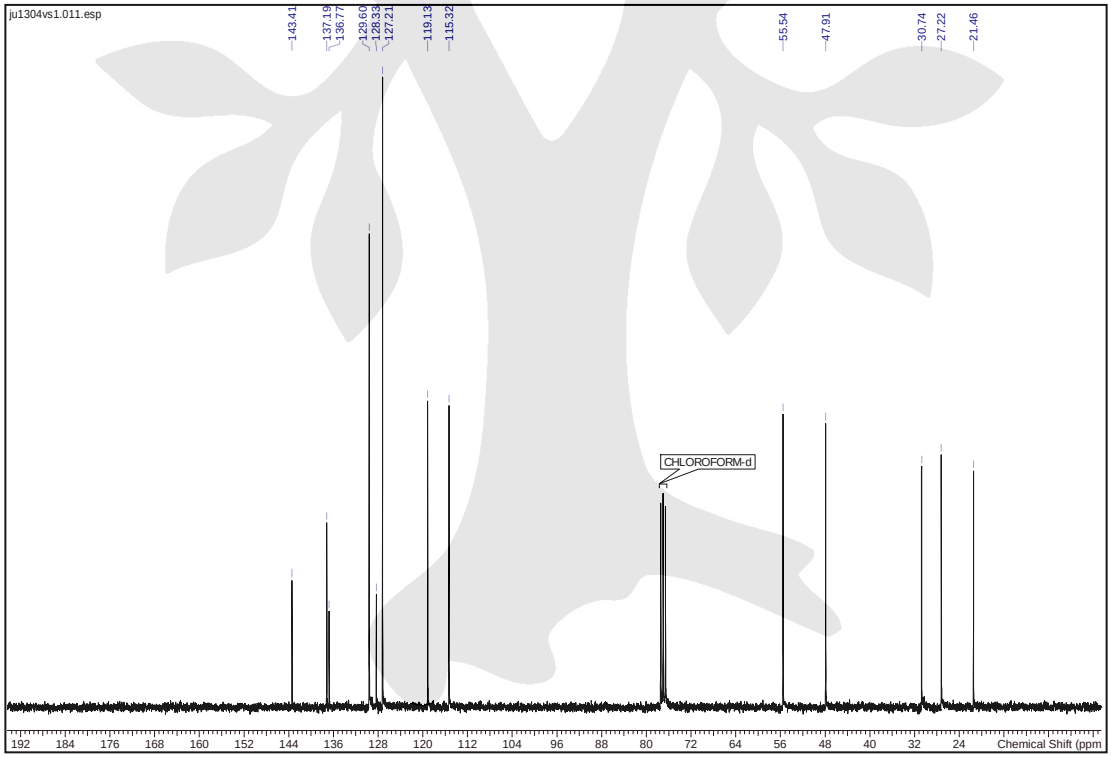


Figure S32. ^{13}C-NMR spectrum of **7** in $CDCl_3$

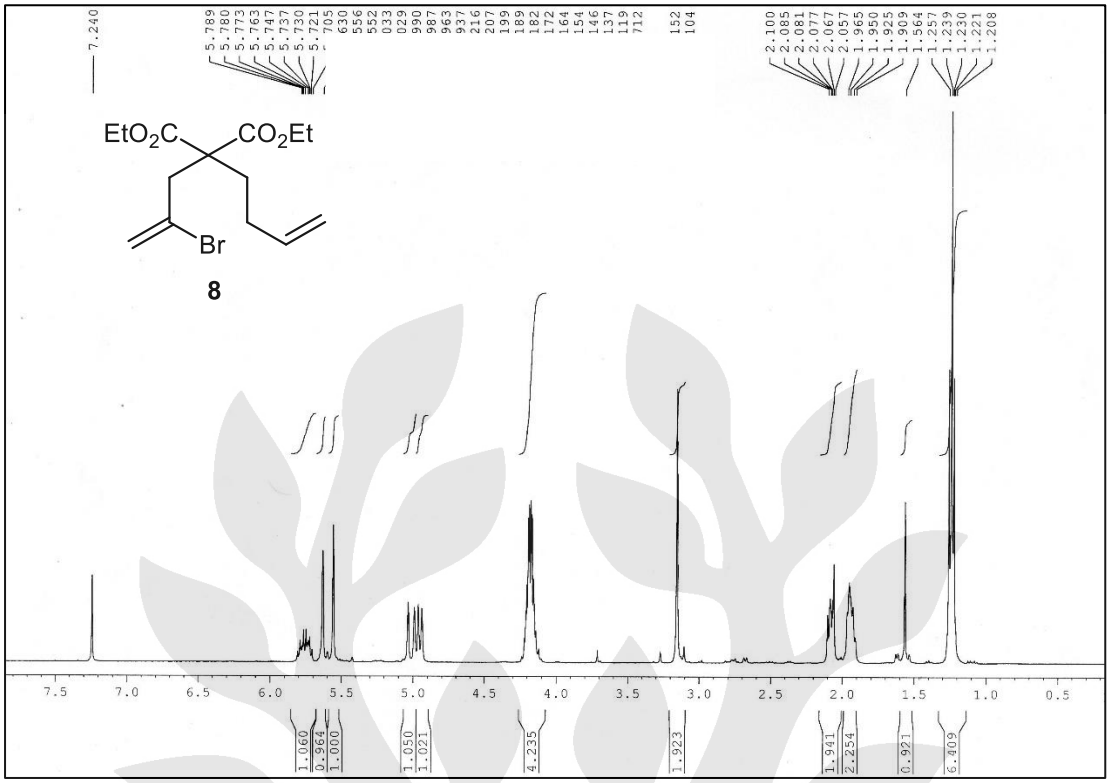


Figure S33. ^{1}H-NMR spectrum of compound **8** in $CDCl_3$

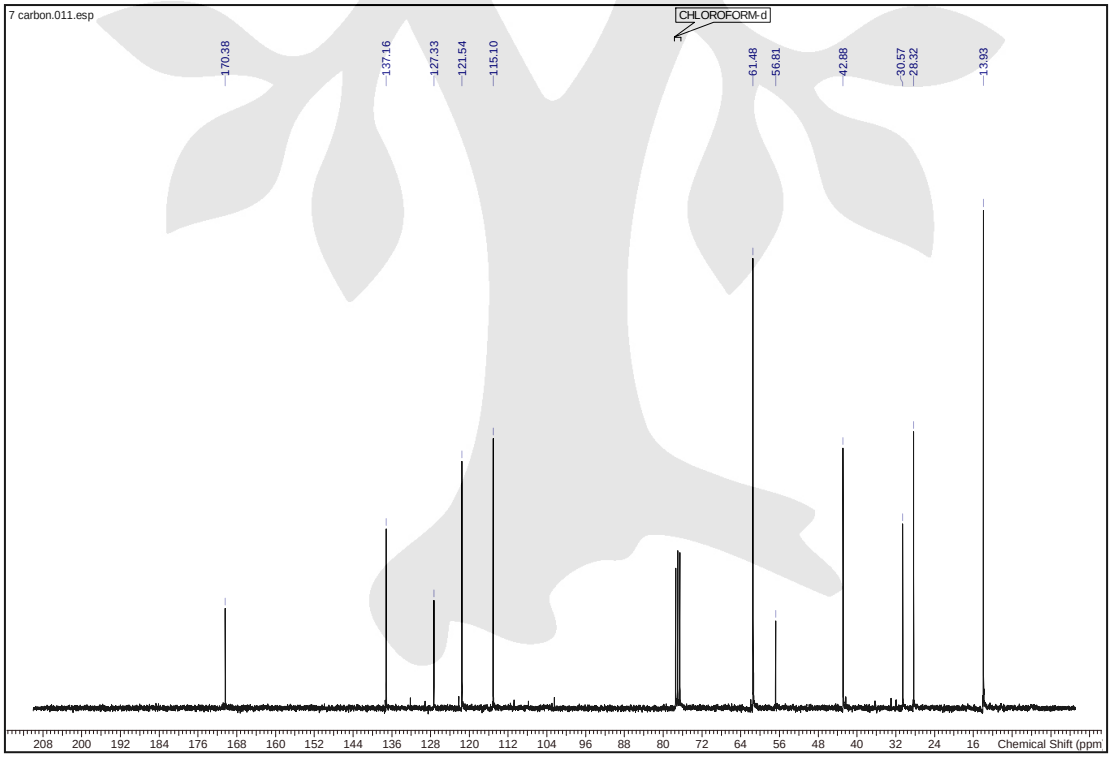


Figure S34. ^{13}C-NMR spectrum of compound **8** in $CDCl_3$

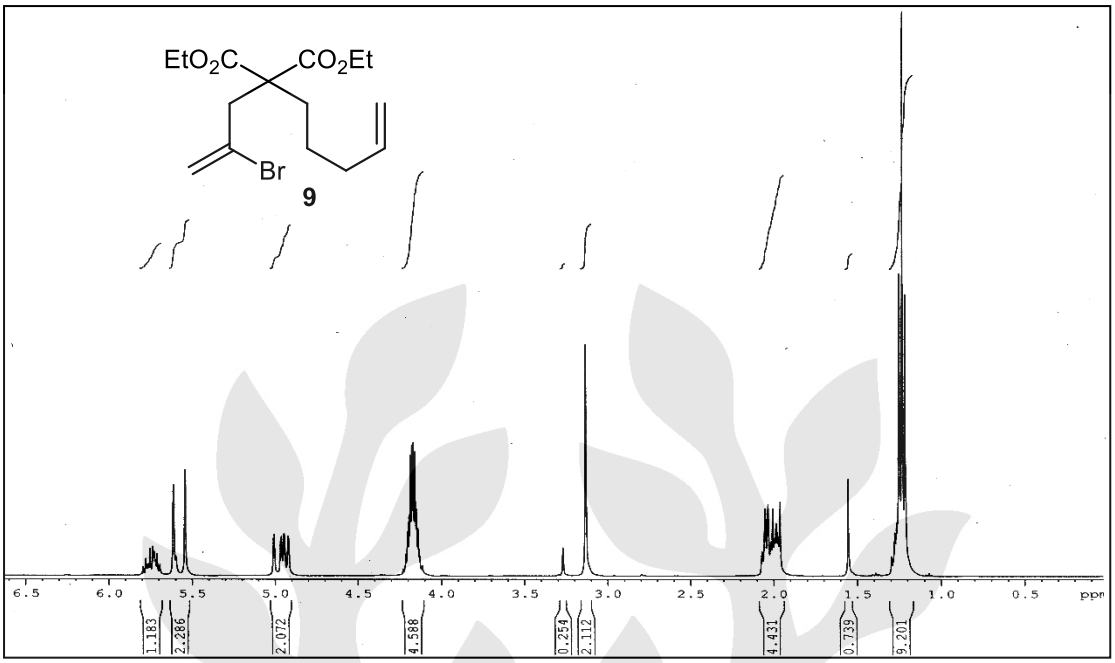


Figure S35. ^{1}H-NMR spectrum of compound **9** in $CDCl_3$

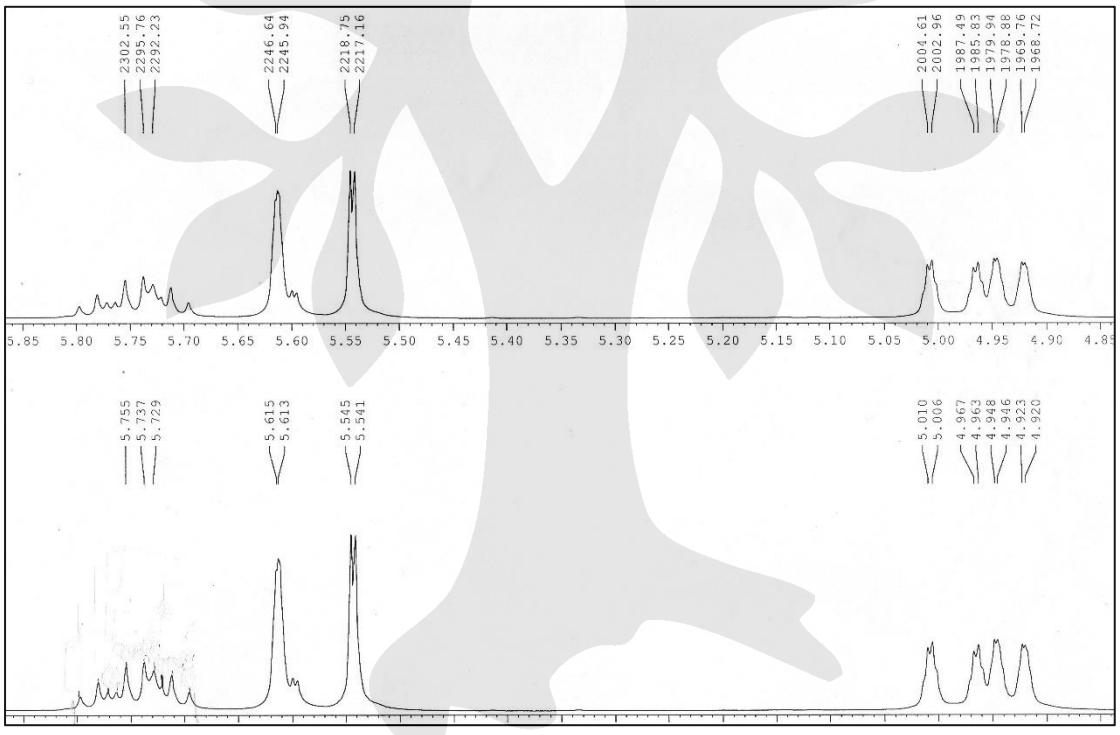


Figure S36. ^{1}H-NMR expanded spectrum of compound **9** in $CDCl_3$

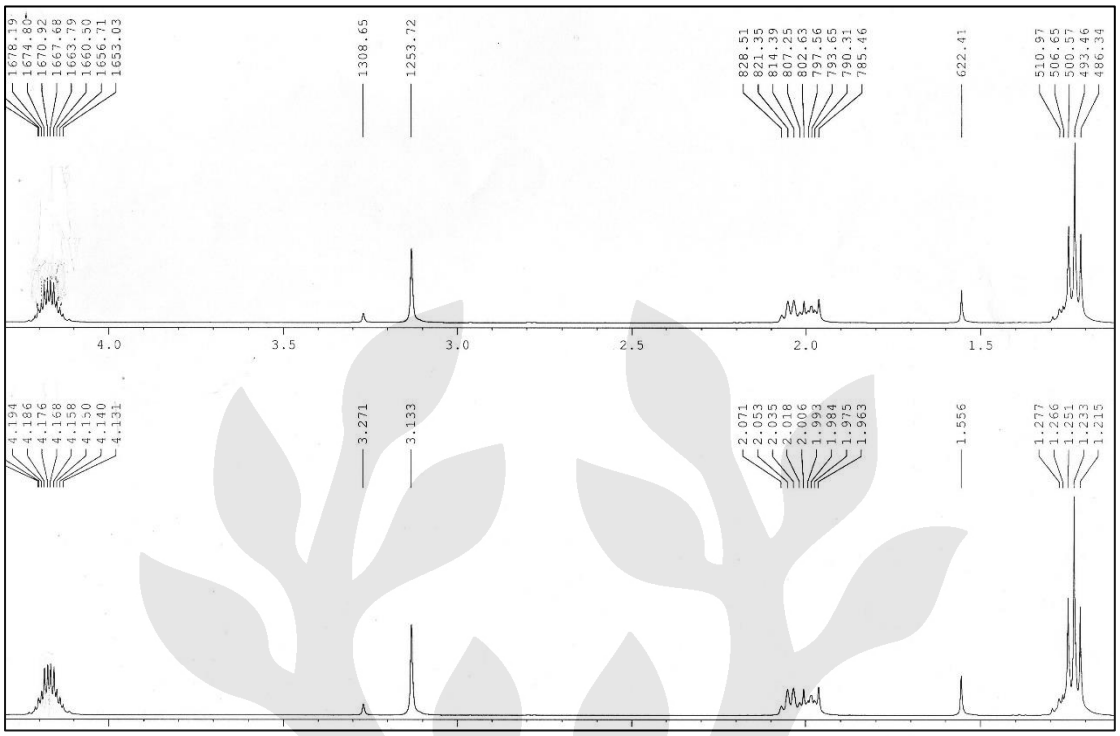


Figure S37. ^{1}H-NMR expanded spectrum of compound **9** in $CDCl_3$

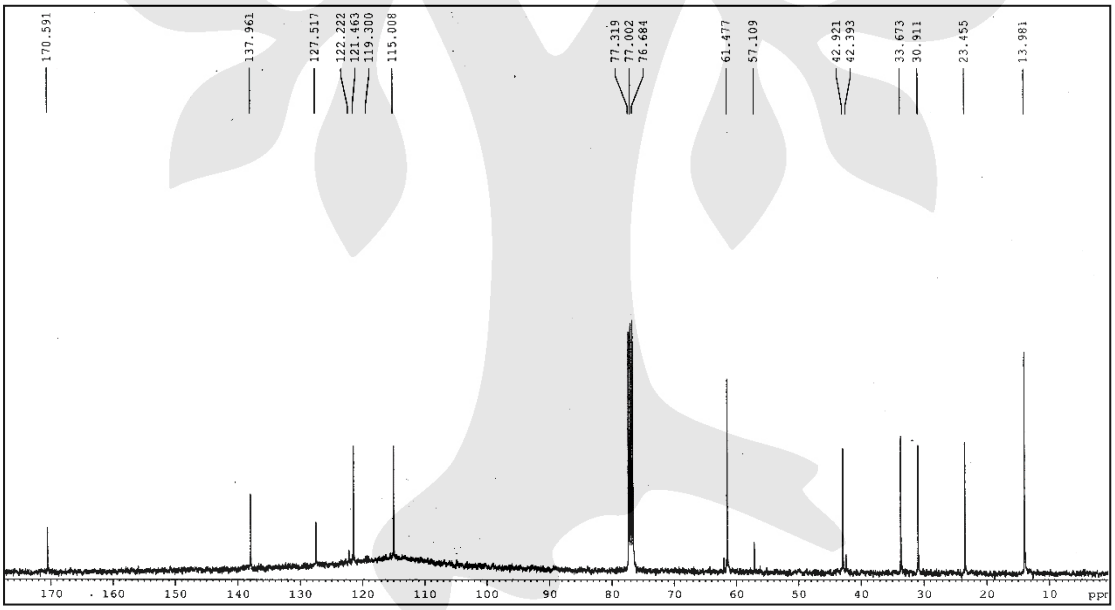


Figure S38. ^{13}C-NMR spectrum of compound **9** in $CDCl_3$

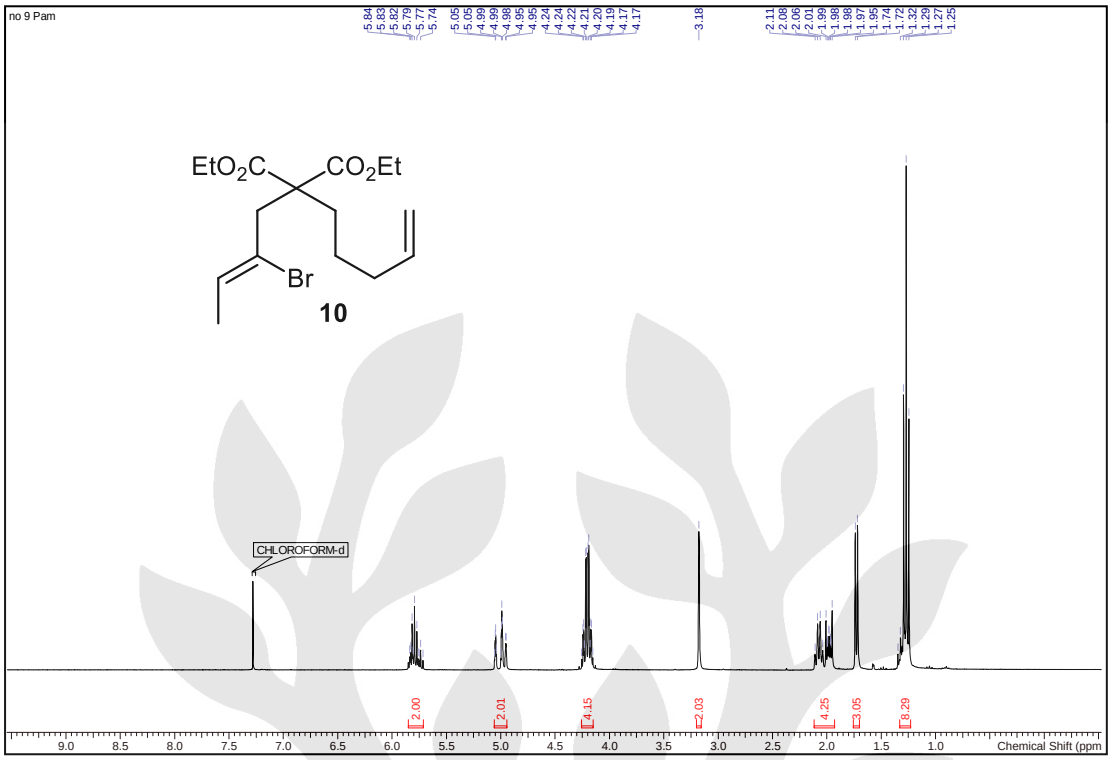


Figure S39. ^{1}H-NMR spectrum of compound **10** in $CDCl_3$

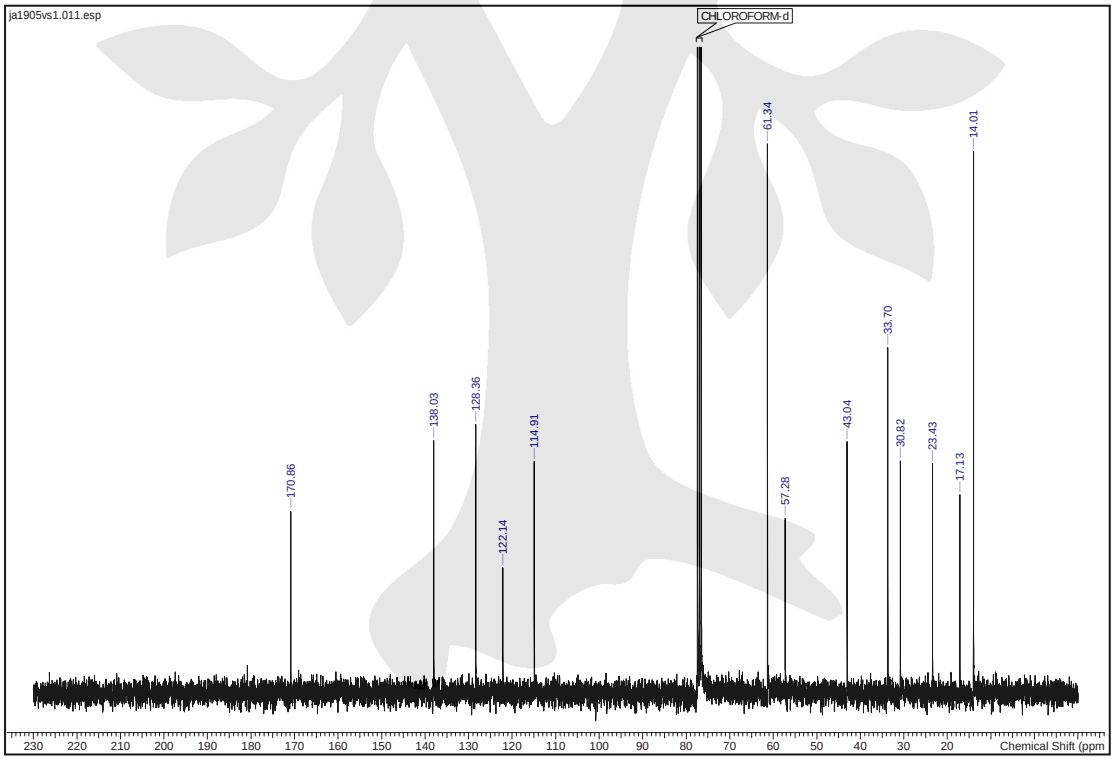


Figure S40. ^{13}C-NMR spectrum of compound **10** in $CDCl_3$

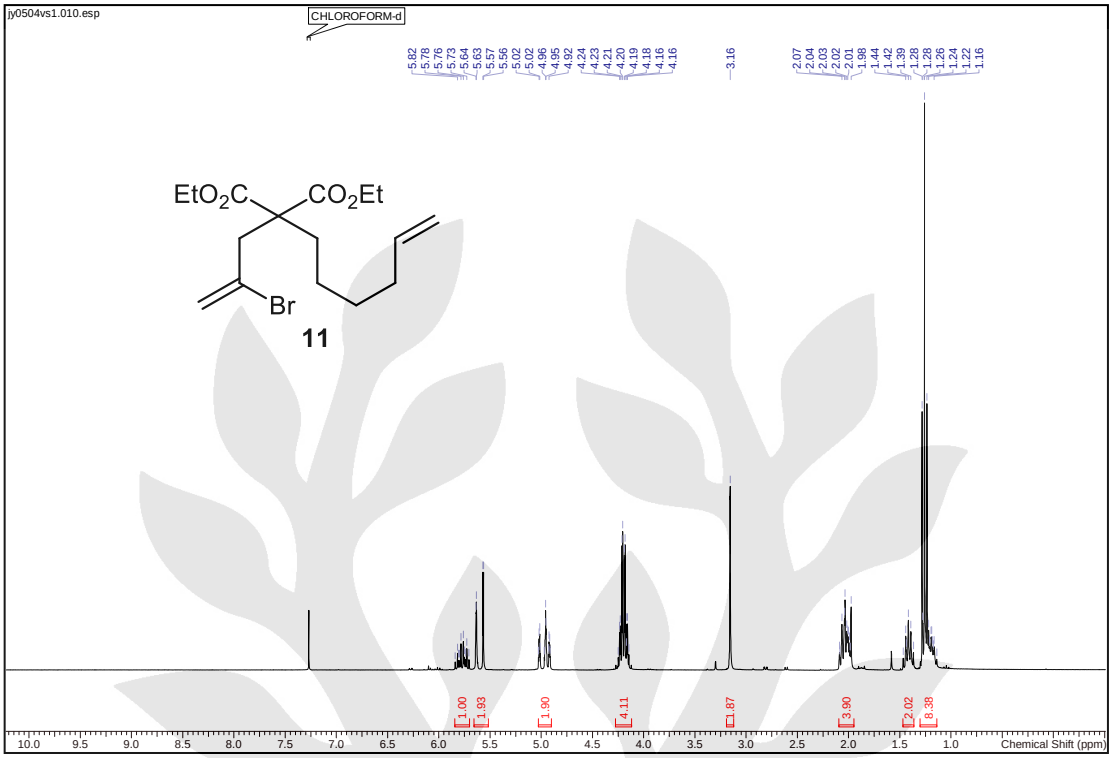


Figure S41. ^{1}H-NMR spectrum of compound **11** in $CDCl_3$

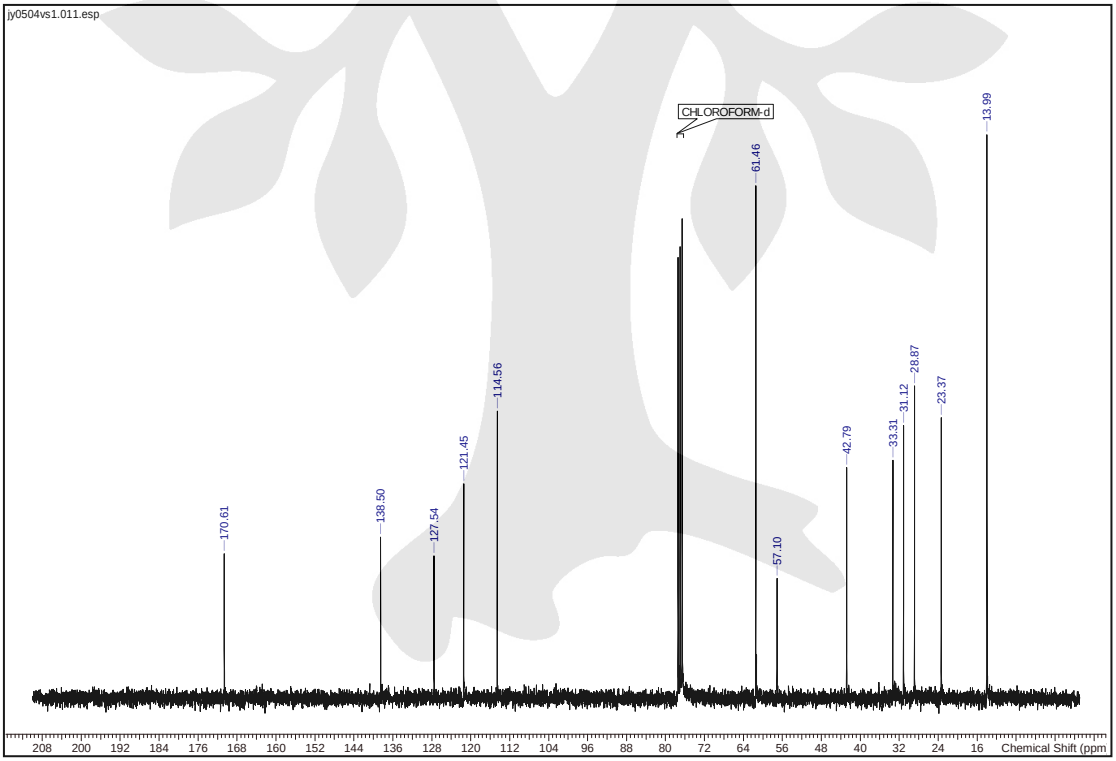


Figure S42. ^{13}C-NMR spectrum of compound **11** in $CDCl_3$

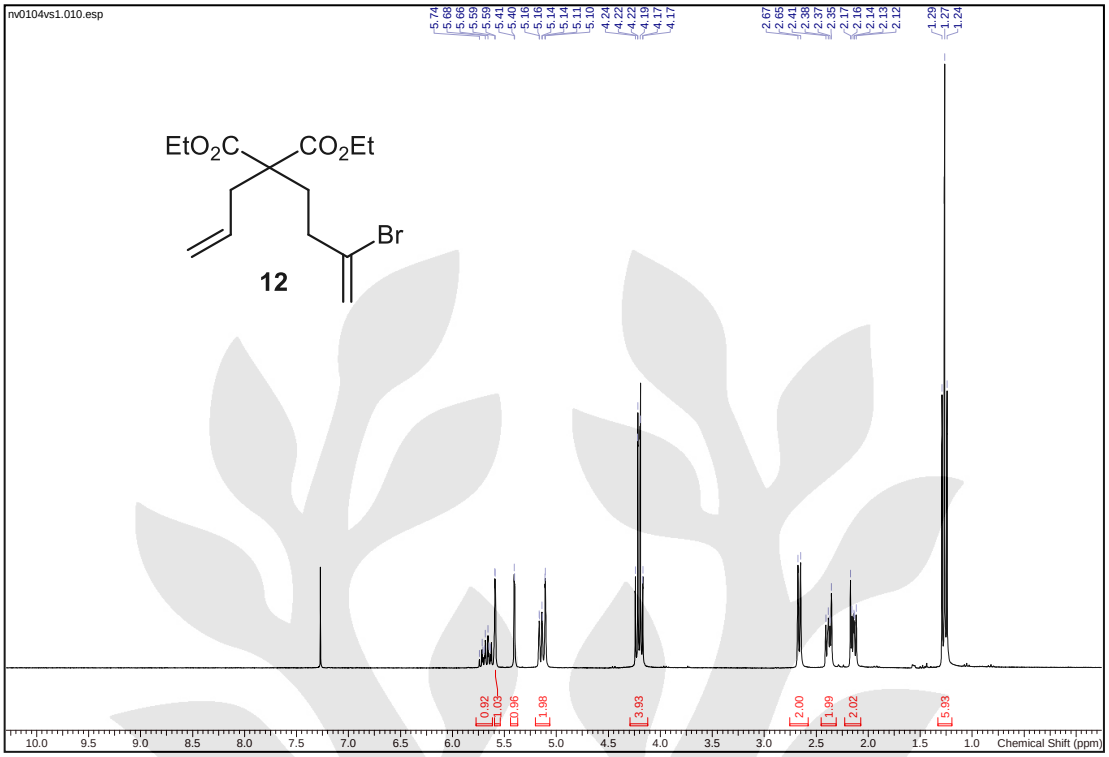


Figure S43. ^{1}H-NMR spectrum of compound **12** in $CDCl_3$

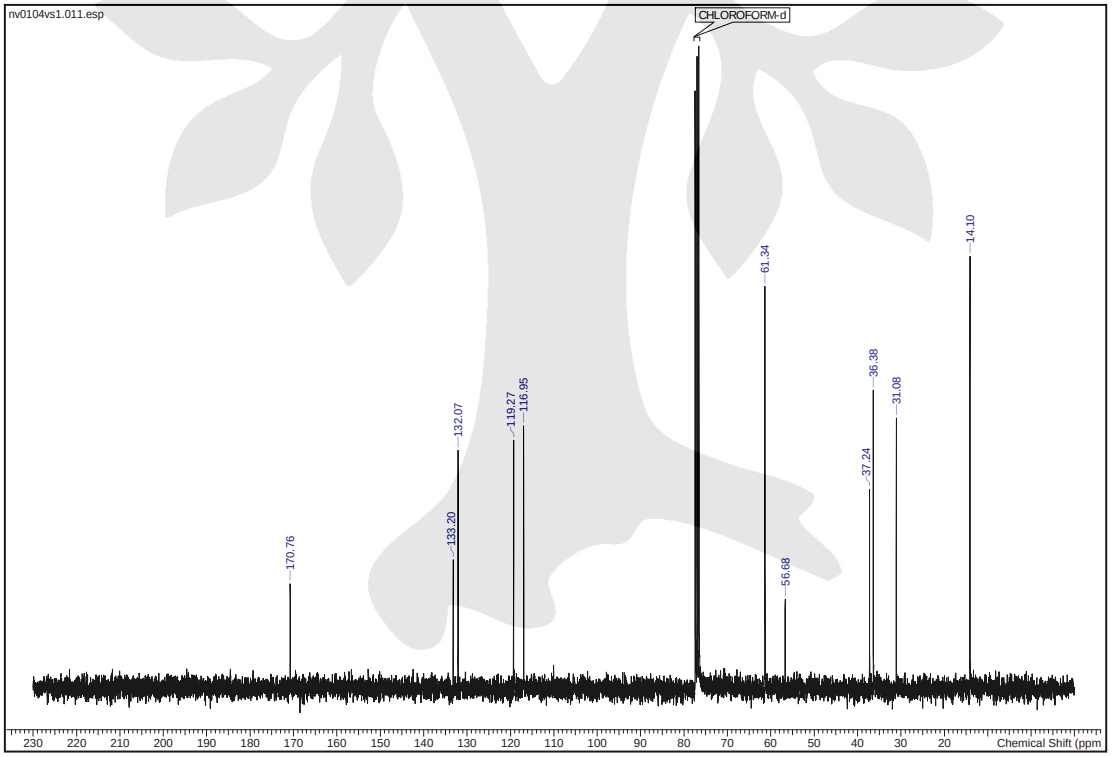


Figure S44. ^{13}C-NMR spectrum of compound **12** in $CDCl_3$

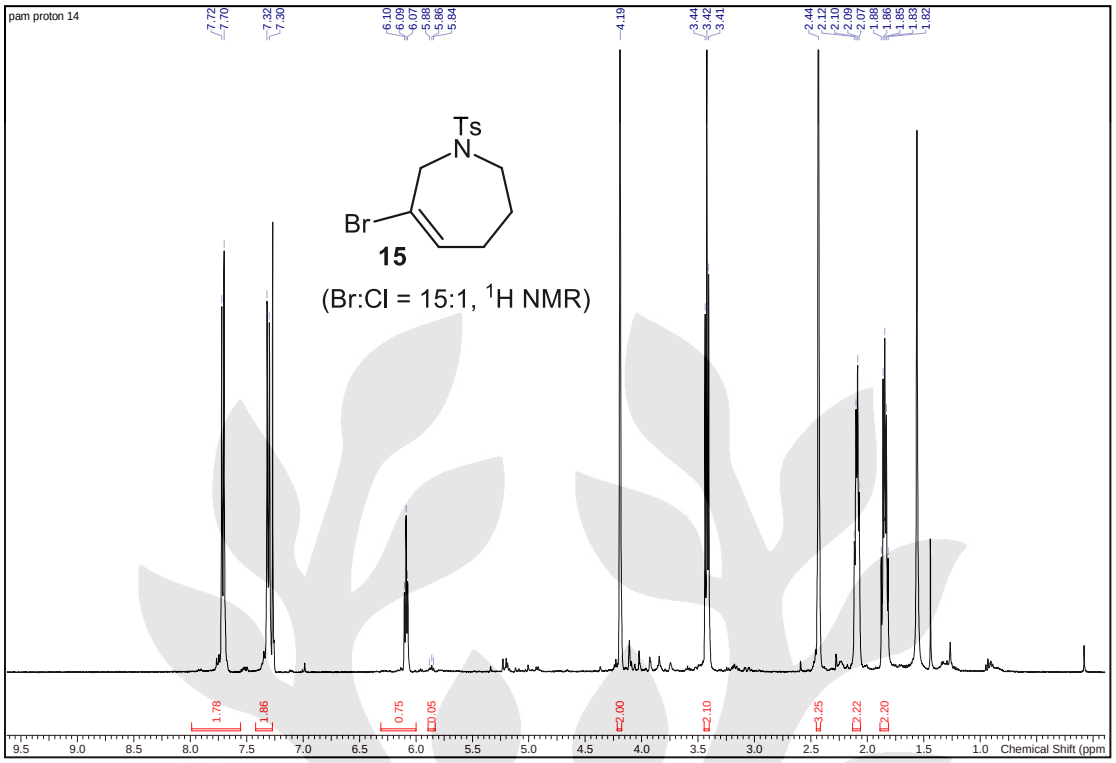


Figure S45. ^{1}H-NMR spectrum of compound **15** in $CDCl_3$

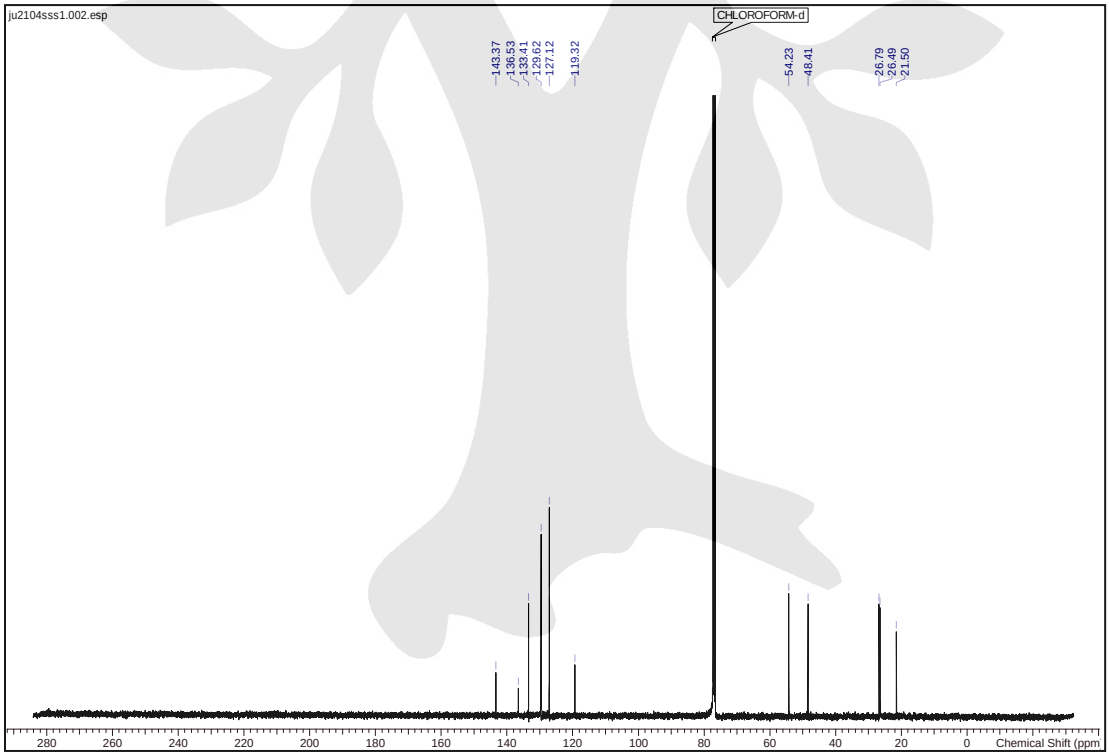


Figure S46. ^{13}C-NMR spectrum of compound **15** in $CDCl_3$

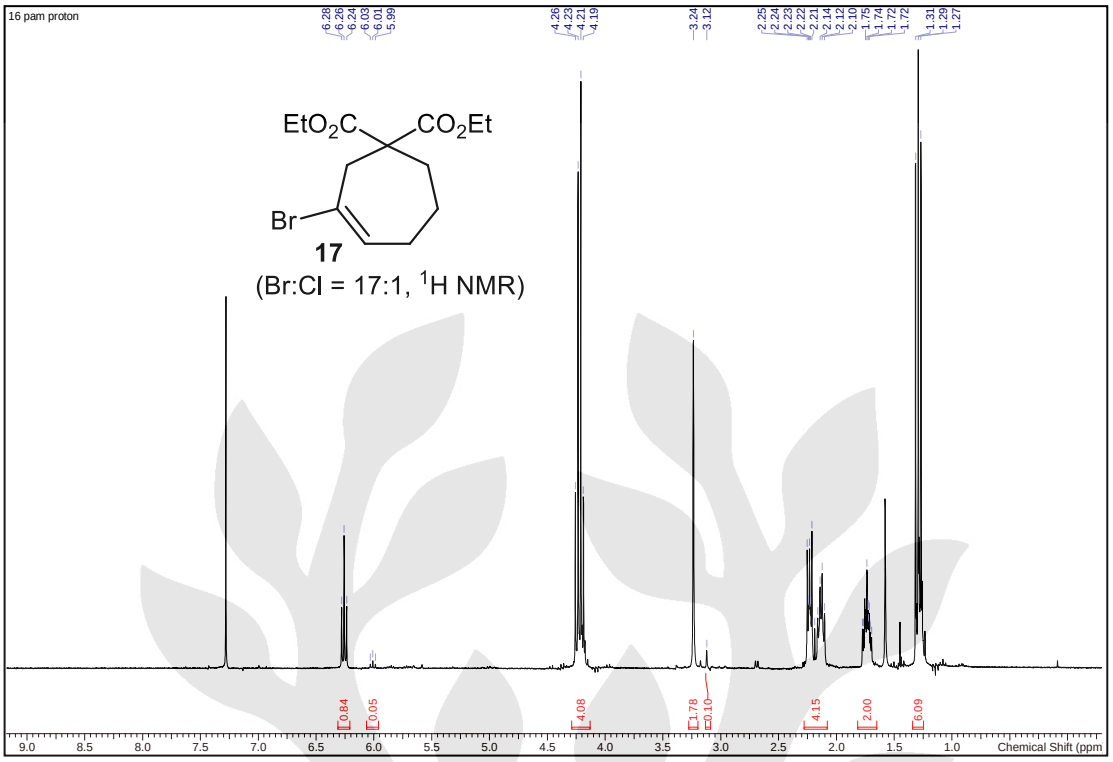


Figure S47. ^{1}H-NMR spectrum of compound **17** in $CDCl_3$

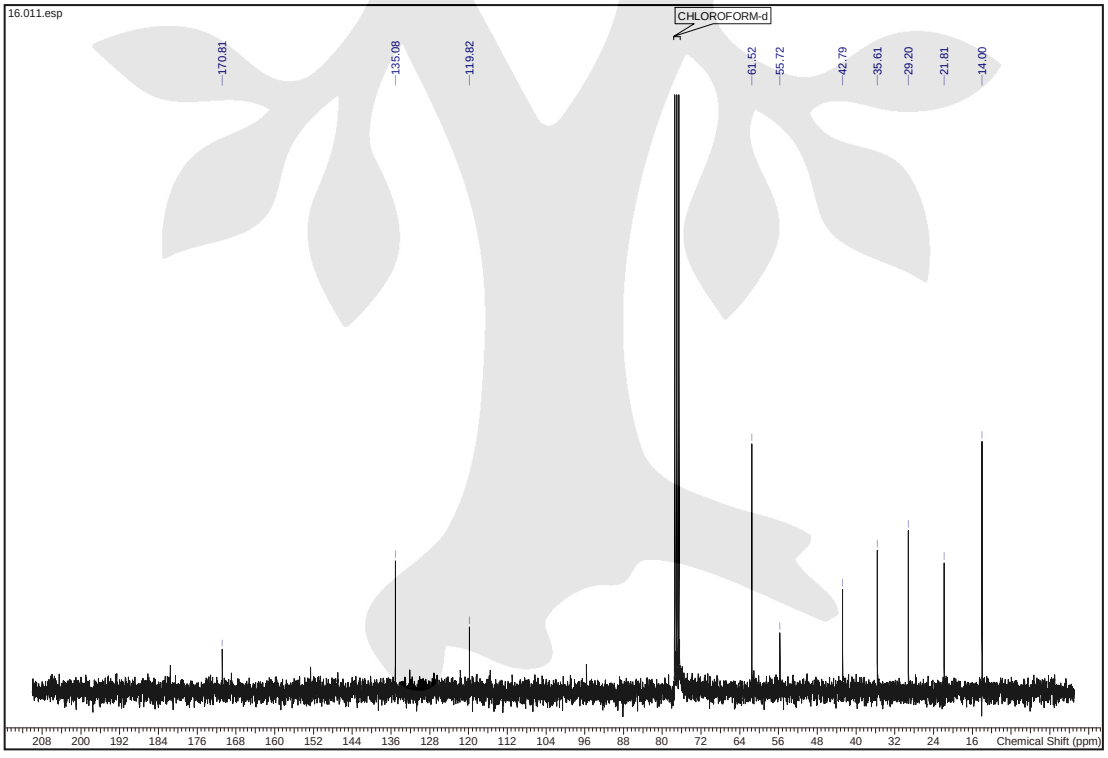


Figure S48. ^{13}C-NMR spectrum of compound **17** in $CDCl_3$

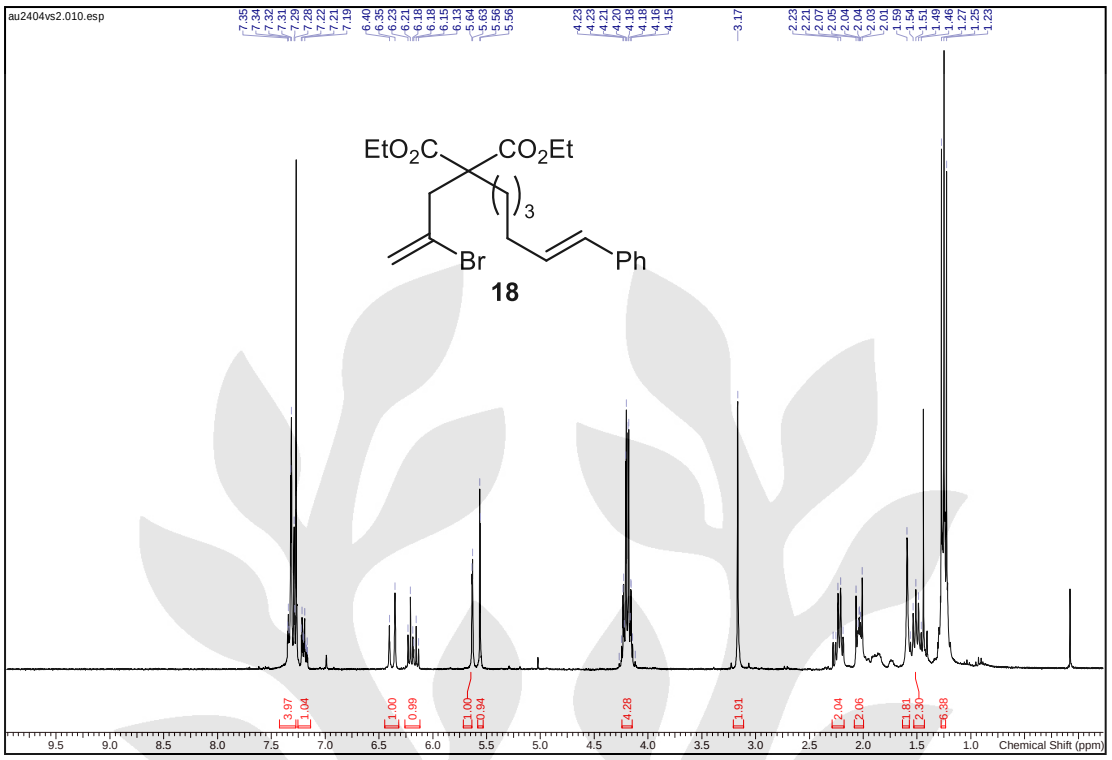


Figure S49. ^{1}H-NMR spectrum of compound **18** in $CDCl_3$

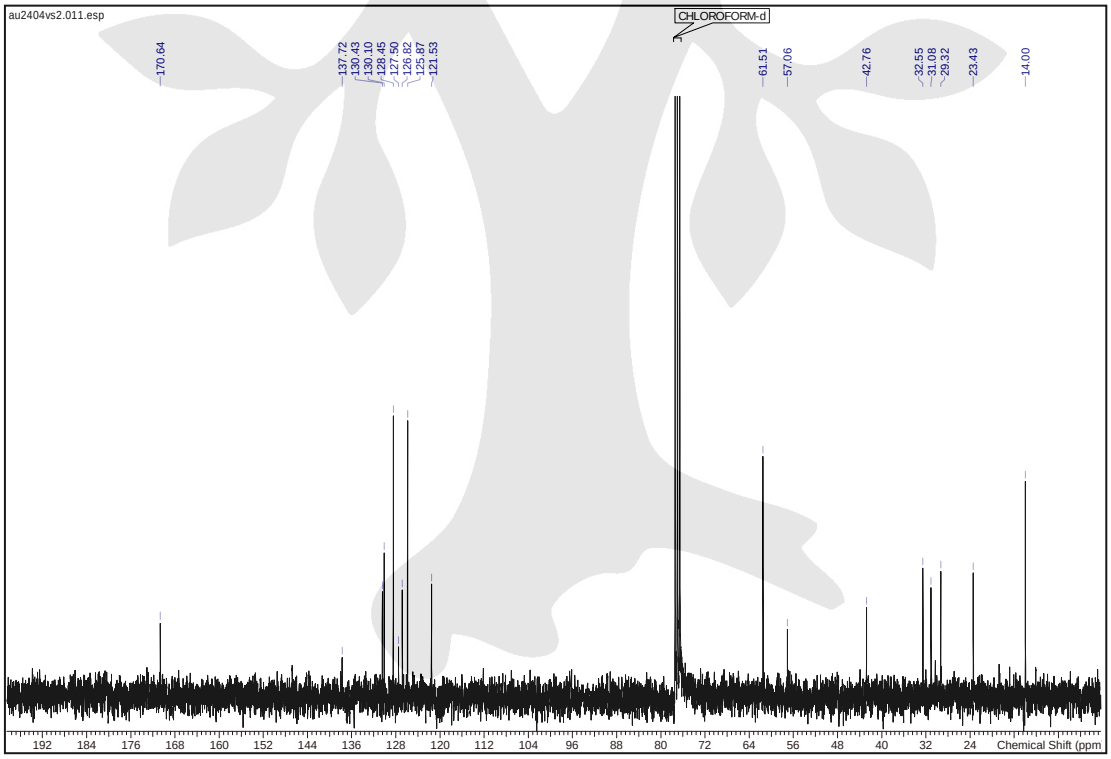


Figure S50. ^{13}C-NMR spectrum of compound **18** in $CDCl_3$

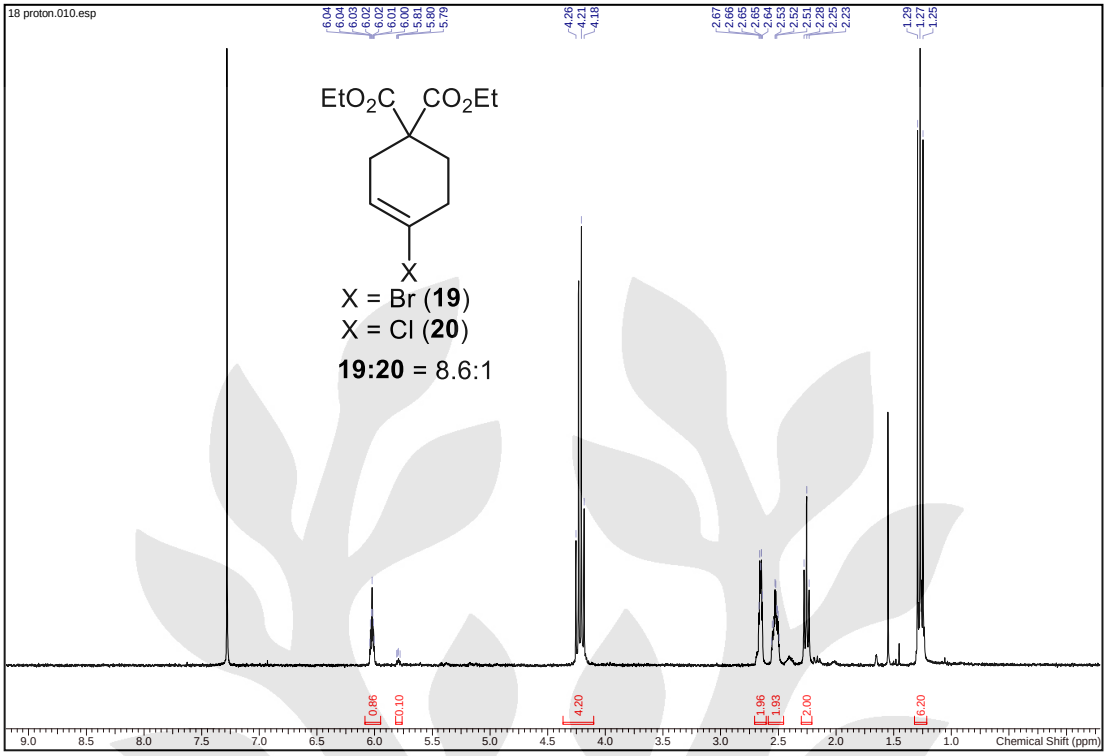


Figure S51. ^{1}H-NMR spectrum of compound **19/20** in $CDCl_3$

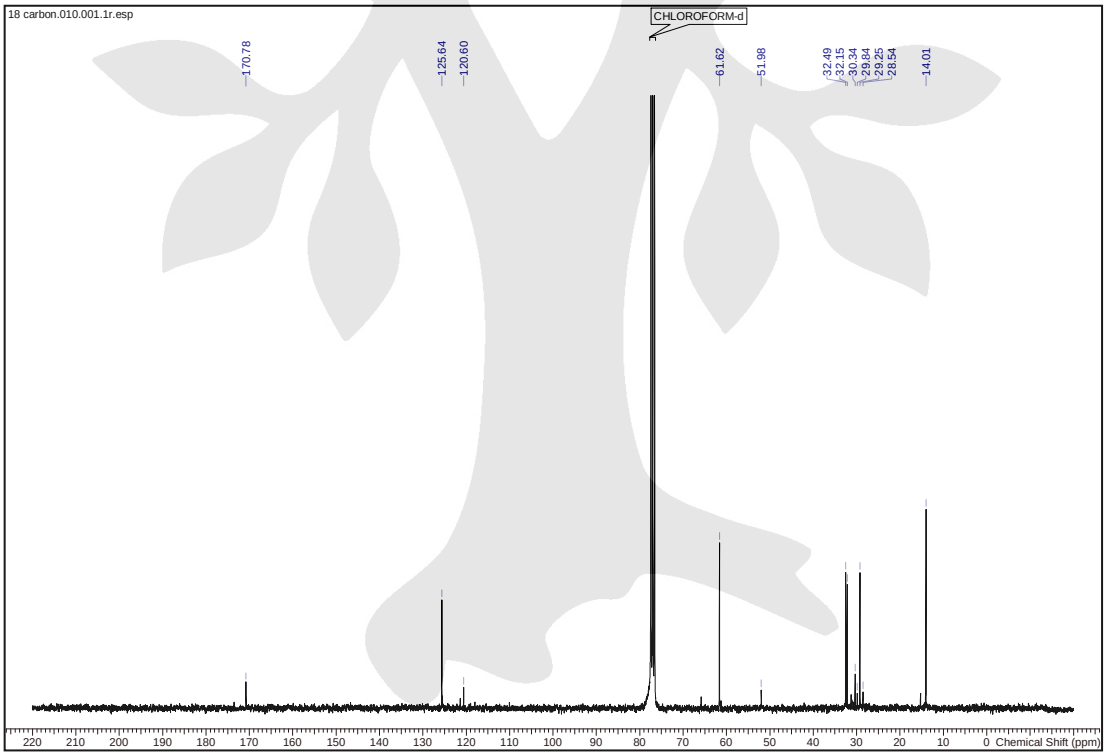


Figure S52. ^{13}C-NMR spectrum of compound **19/20** in $CDCl_3$

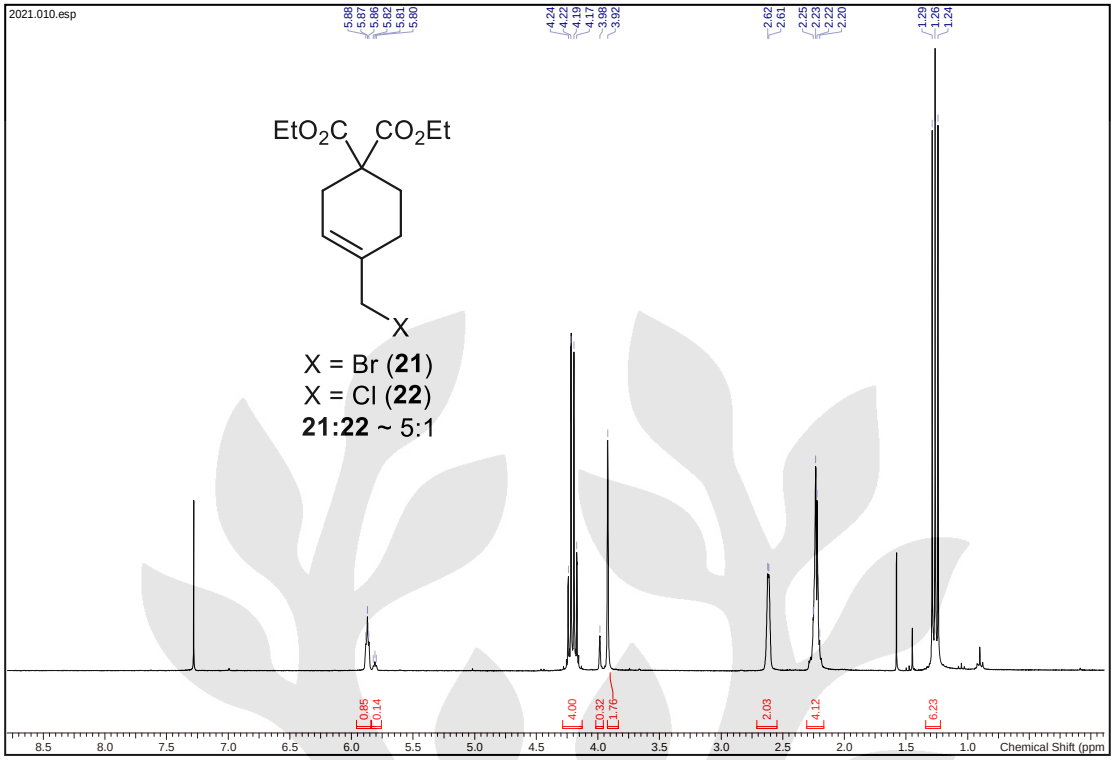


Figure S53. ^{1}H-NMR spectrum of compound **21/22** in $CDCl_3$

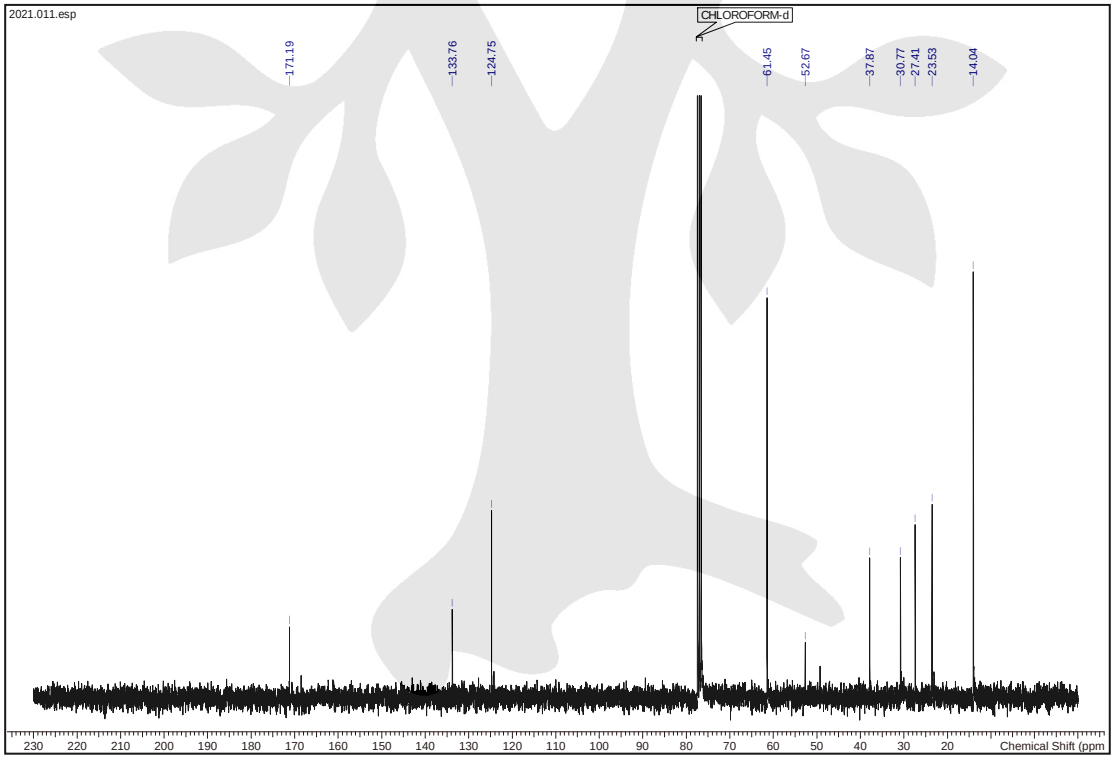


Figure S54. ^{13}C-NMR spectrum of compound **21/22** in $CDCl_3$

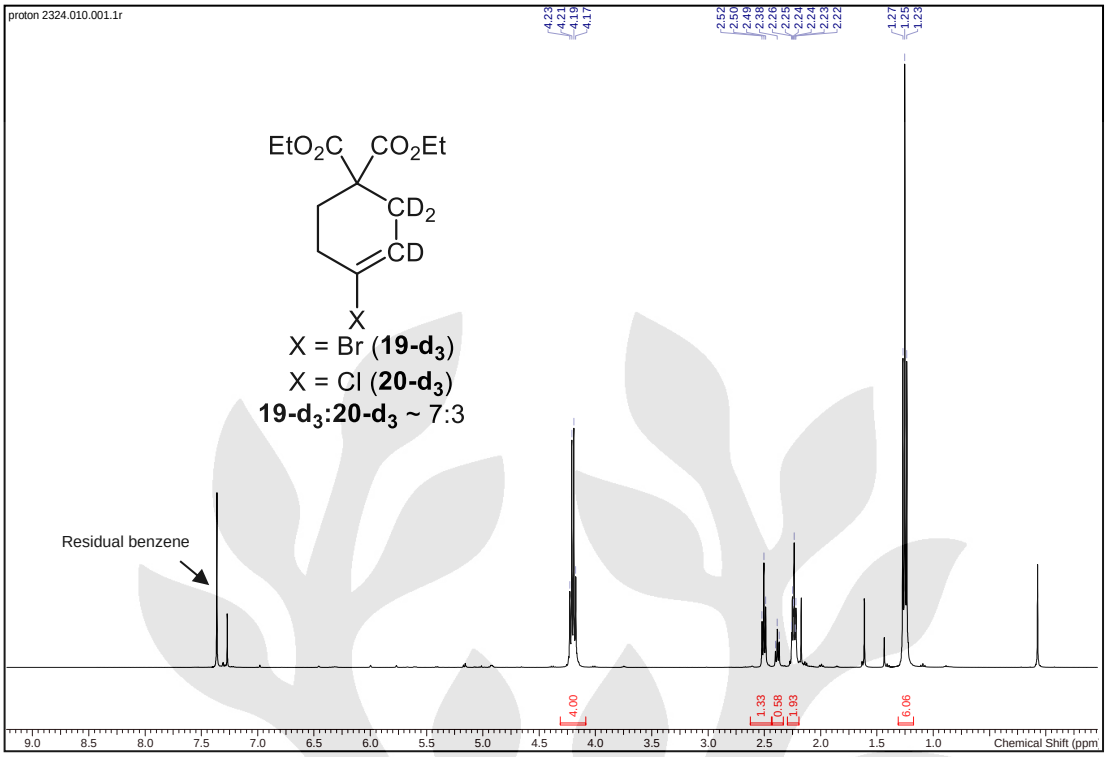


Figure S55. ^{1}H-NMR spectrum of compound **19-d$_3$/20-d$_3$** in $CDCl_3$

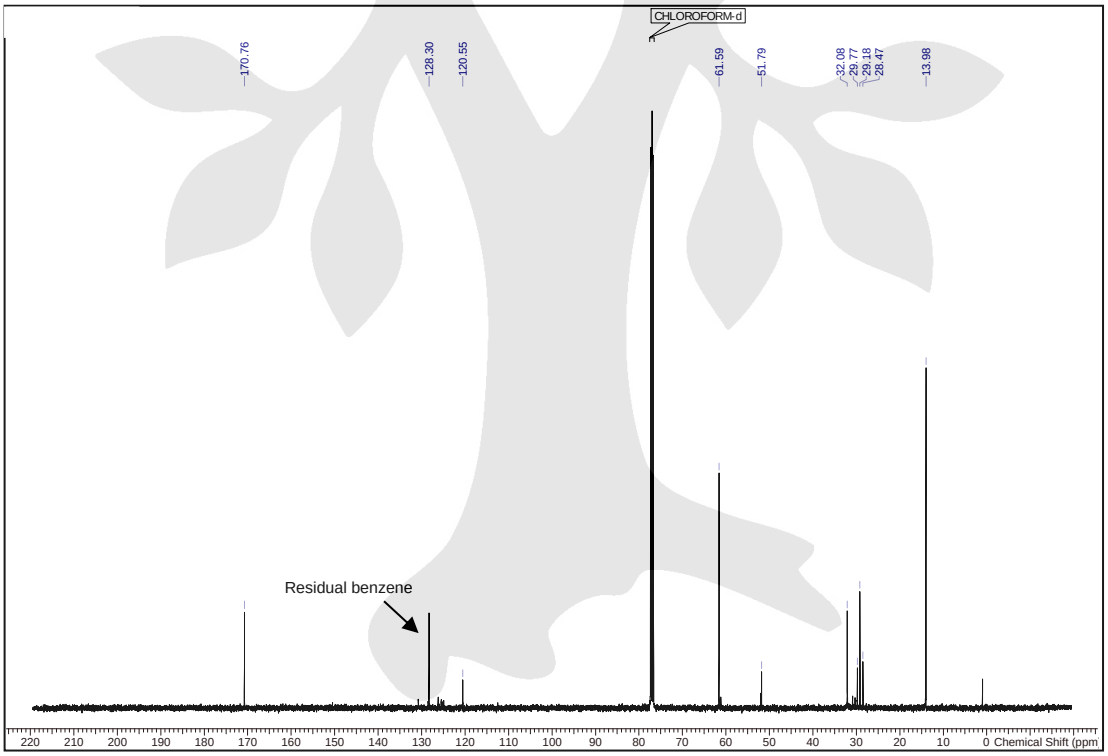


Figure S56. ^{13}C-NMR spectrum of compound **19-d$_3$/20-d$_3$** in $CDCl_3$

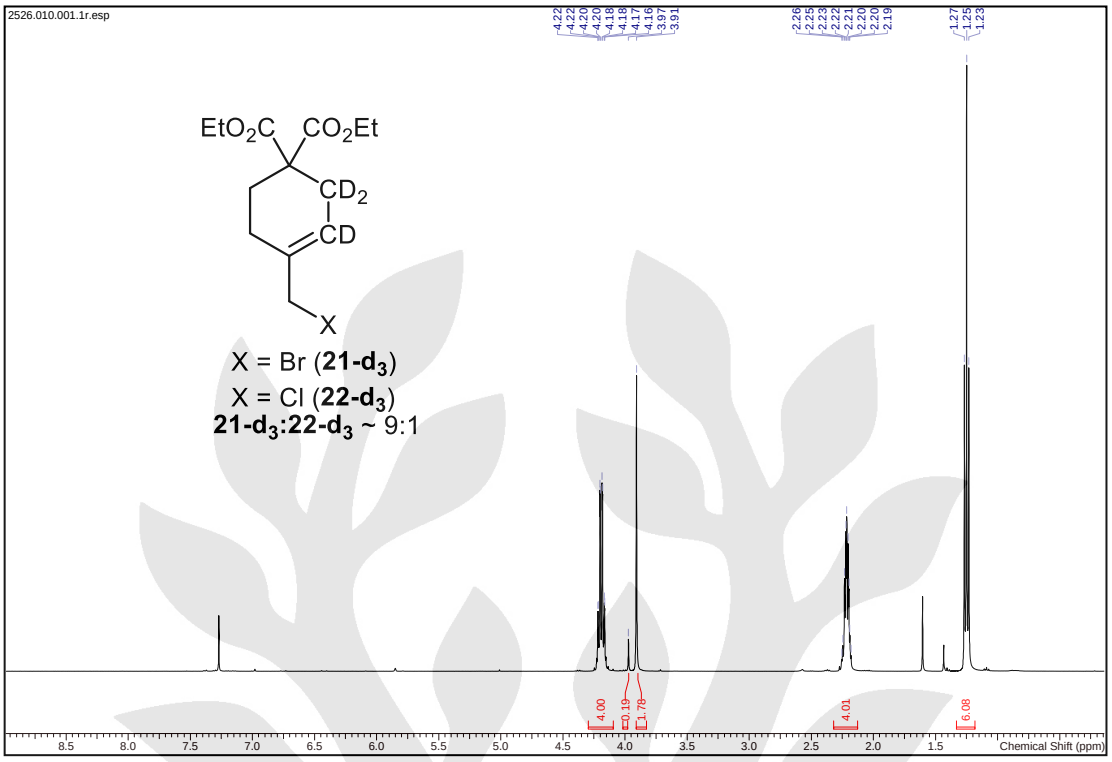


Figure S57. ^{1}H-NMR spectrum of compound **21-d$_3$/22-d$_3$** in $CDCl_3$

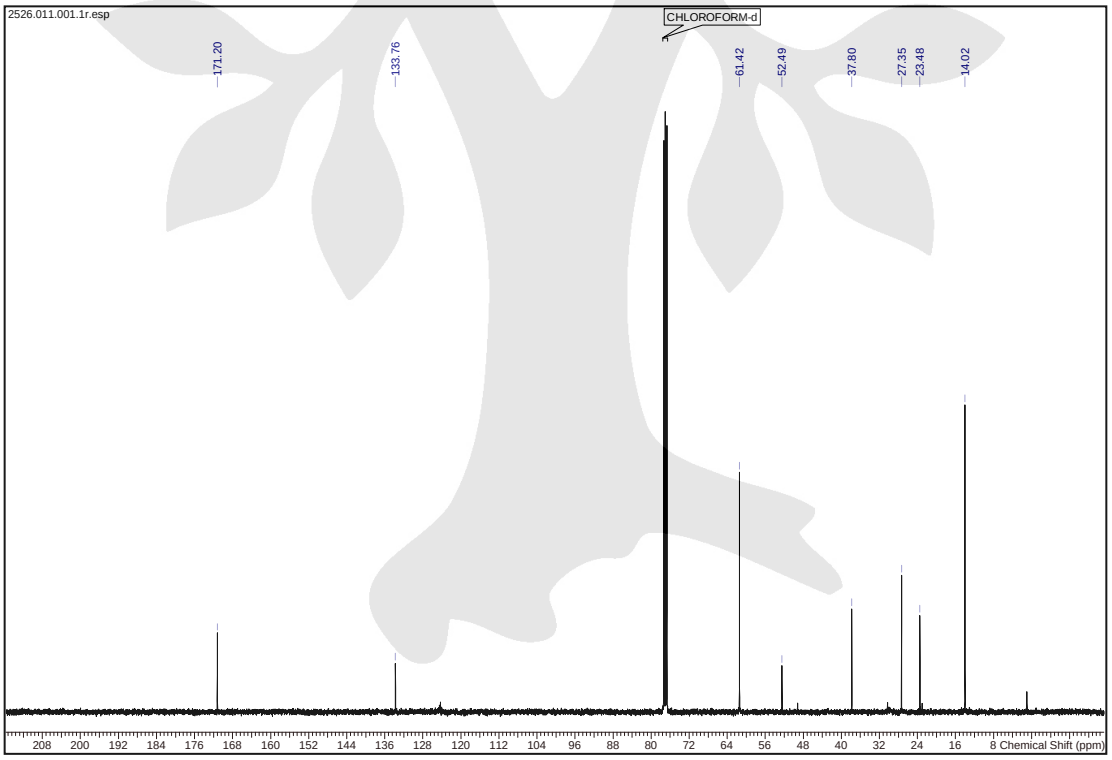


Figure S58. ^{13}C-NMR spectrum of compound **21-d$_3$/22-d$_3$** in $CDCl_3$

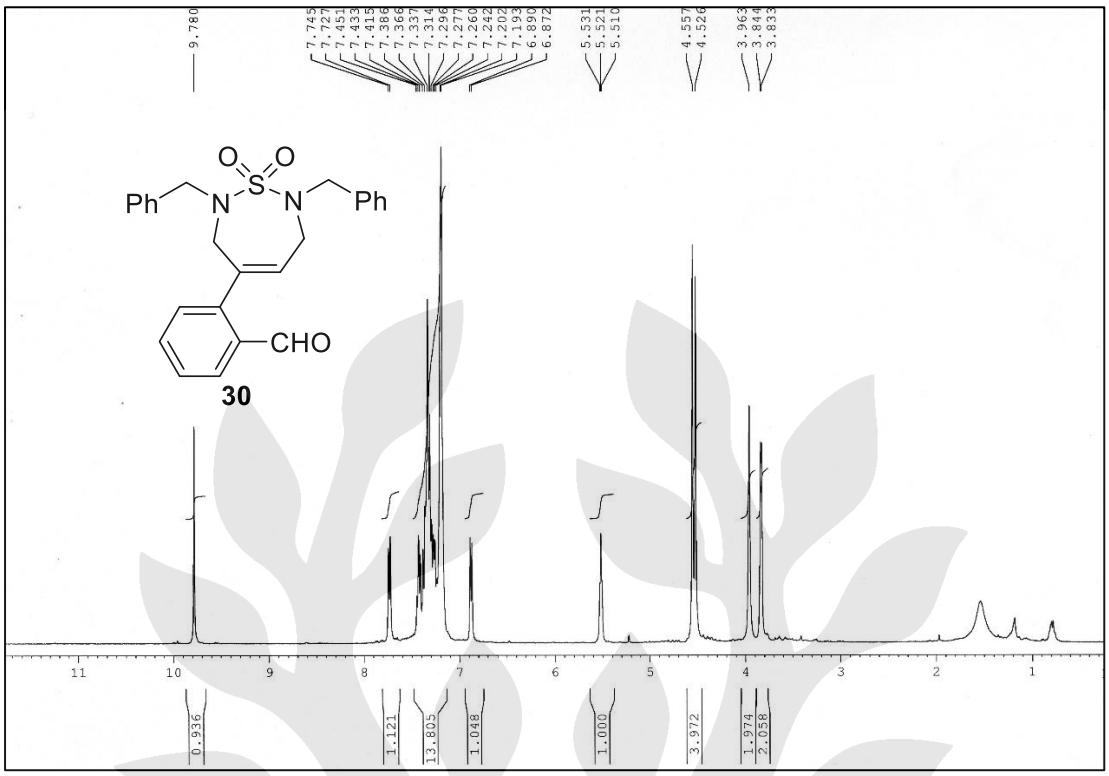


Figure S59. ^{1}H-NMR spectrum of compound **30** in $CDCl_3$

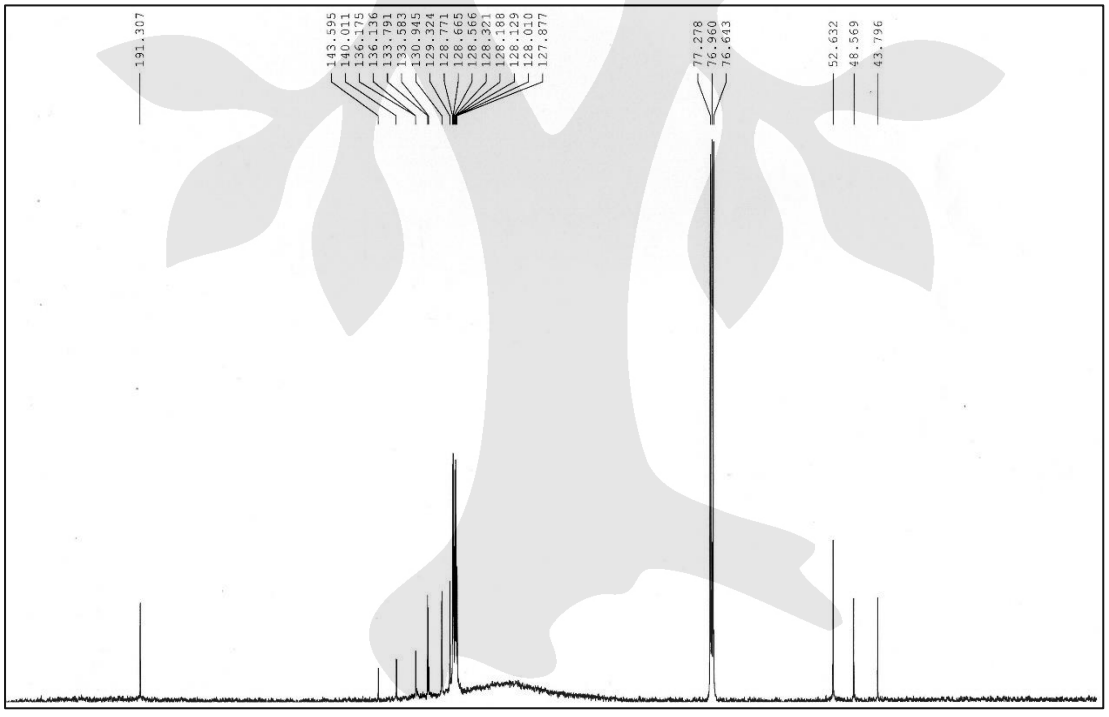


Figure S60. ^{13}C-NMR spectrum of compound **30** in $CDCl_3$

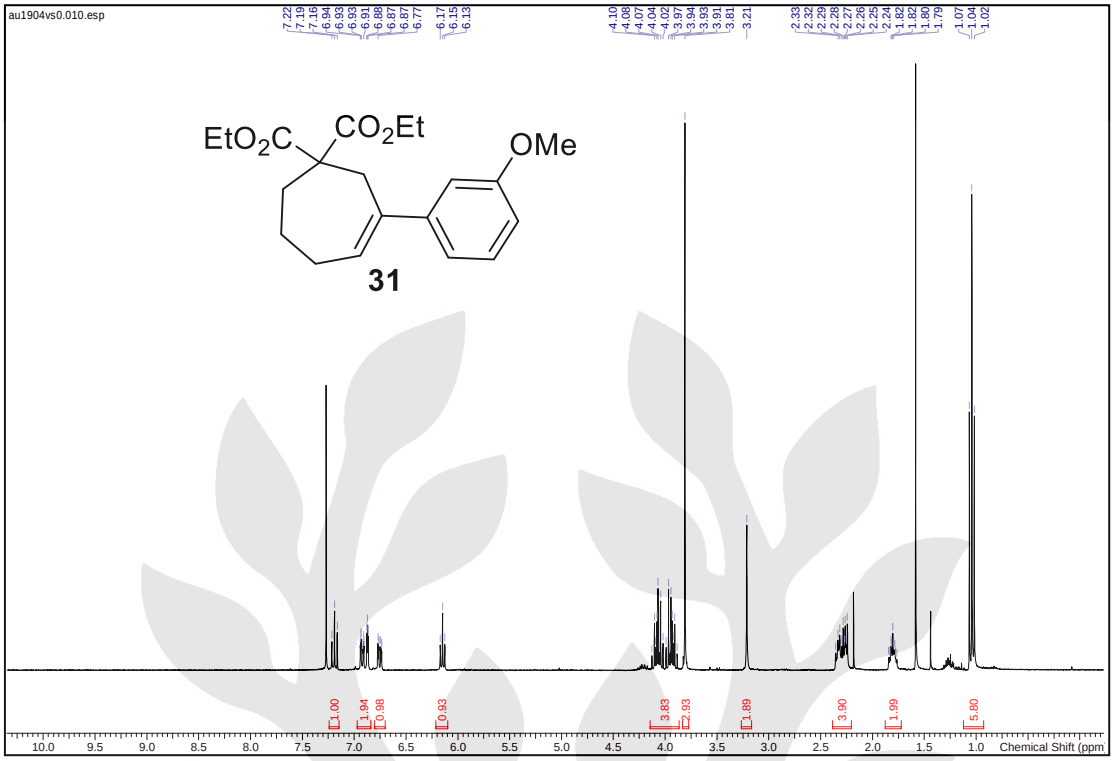


Figure S61. ^{1}H-NMR spectrum of compound **31** in $CDCl_3$

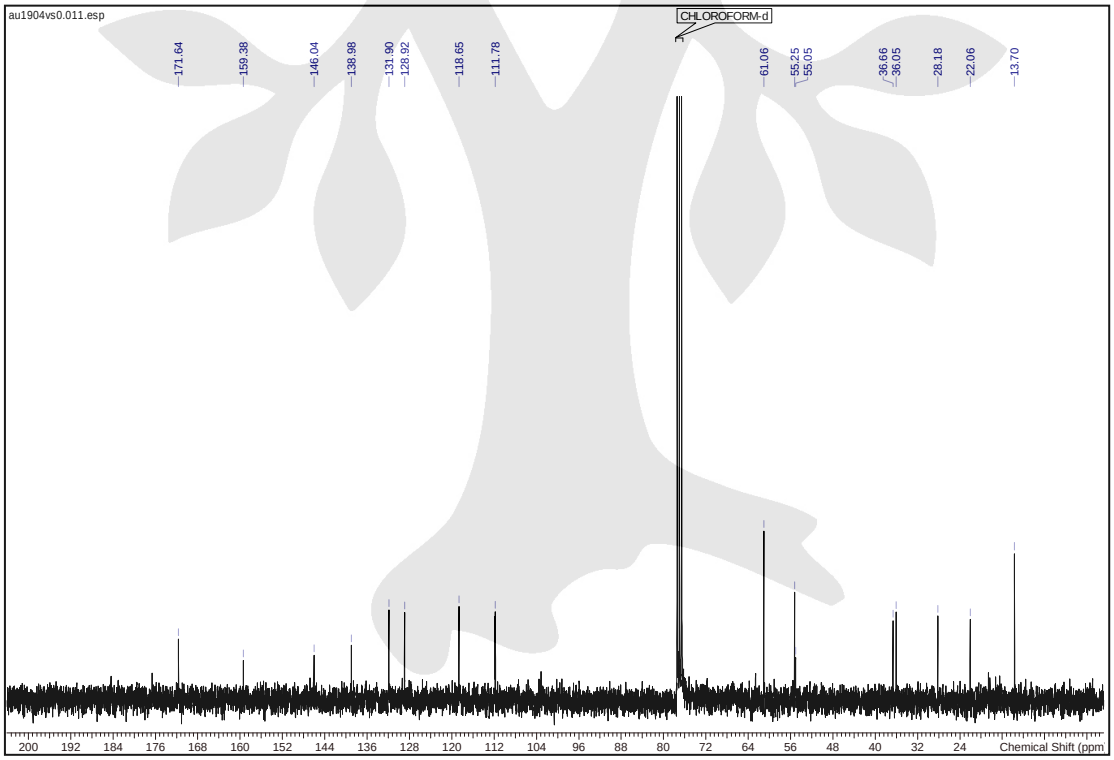


Figure S62. ^{13}C-NMR spectrum of compound **31** in $CDCl_3$