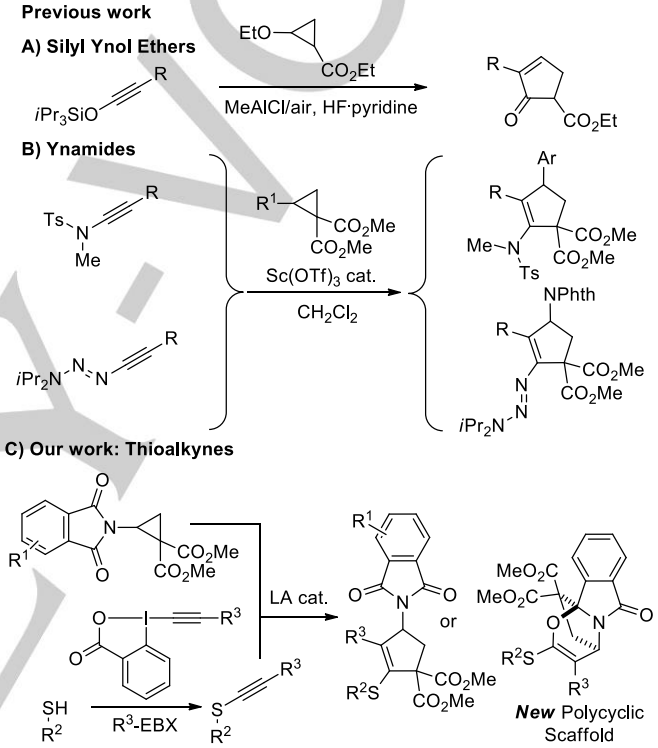
Divergent Reactivity of Thioalkynes in Lewis Acid-Catalyzed Annulations with Donor-Acceptor Cyclopropanes**

Sophie Racine, Bence Hegedüs, Rosario Scopelliti and Jérôme Waser*

Abstract: Efficient methods for the convergent synthesis of (poly)cyclic scaffolds are urgently needed in synthetic and medicinal chemistry. Herein, we describe new annulation reactions of thioalkynes with phthalimide-substituted donor-acceptor cyclopropanes, which gave access to highly substituted cyclopentenes and polcyclic ring systems. With silyl-thioalkynes, Lewis acid catalysed (3+2) annulation reaction with DA-cyclopropanes took place affording 1-thio-cyclopenten-3-amines. On the other hand, an unprecedented polycyclic compound was formed with alkyl-thioalkynes through a reaction pathway directly involving the phthalimide group. The two transformations proceeded in good yield and tolerated a large variety of functional groups.

Synthetic methods giving access to broad chemical diversity in only few steps are of great interest. There is a strong need in the pharmaceutical and agro-chemical industries for new molecular scaffolds with a rigid structure and multiple heteroatom substitutions allowing more specific binding to biological targets.[1] In this context, annulation reactions of Donor-Acceptor cyclopropanes (DA-cyclopropanes) have been highly successful for the synthesis of saturated carbo- and hetero-cycles.[2] In particular, (3+2) and (4+2) annulations of nitrogen-based DA-cyclopropanes with aldehydes, ketones and enol-ethers have been extensively explored in our group and give highly substituted tetrahydrofuryl- and cyclopentyl-amines.[3] Later an enantioselective version of the (3+2) annulation was developed,[4] as well as a synthesis of nucleoside analogs using nucleobase-substituted DA-cyclopropanes.[5]

Carbonyl compounds, imines and enol ethers are privileged partners in the Lewis acid catalyzed (3+2) annulation with DA-cyclopropanes.[2] In contrast, alkynes remain poorly investigated in (3+2) annulations,[6] although cyclopentenes are of great interest as building blocks in organic chemistry. In particular, alkynes bearing adjacent heteroatoms exhibit improved reactivity and selectivity in annulation reactions and give access to heteroatom-substituted ring systems. The first report of a (3+2) annulation between DA-cyclopropanes and ynol ethers to form cyclopentenones was described by Ready and co-workers in 2008 (Scheme 1, **A**).[7a] In 2014, Johnson and co-workers reported the first use of ynamides to give highly substituted cyclic enamides (Scheme 1, **B**). [7b] Finally, Severin and co-workers reported in collaboration with our group the only example of (3+2) annulation of nitrogen-based DA-cyclopropanes and triazene-substituted alkynes (Scheme 1, **B**).[7c]



Scheme 1. Annulations of DA-cyclopropanes with electron-rich alkynes.

So far, the use of thioalkynes in (3+2) annulations has not been reported, although they have been successfully applied in [4+2],[8a-f] [3+2][8g] and [2+2][8h-i] cycloadditions as well as in the Pauson-Khand reaction.[8j] Only three examples of (3+2) annulations of thioalkynes were reported, but none of them were based on the use of DA cyclopropanes.[9] The development of a (3+2) annulation between DA-cyclopropanes and thioalkynes would provide a novel easy access to 1-thio-cyclopenten-3-amines. Thio-substituted five membered rings exhibit bioactivity against diabetes, HIV, psychological, neurological and proliferative disorders.[10] Furthermore, the sulfur atom allows numerous unique chemical transformations in addition to the hydrolysis to ketones possible with enamides and enolethers.[11a] For example, vinyl sulfides are easily turned into electron deficient vinyl sulfones by oxidation,[11b-c] which gives access to reductive desulfonylation,[12a-b] and Michael addition.[12c-d] Recently, we developed a new chemoselective alkynylation of thiols with cyclic hypervalent iodine reagents,[13]

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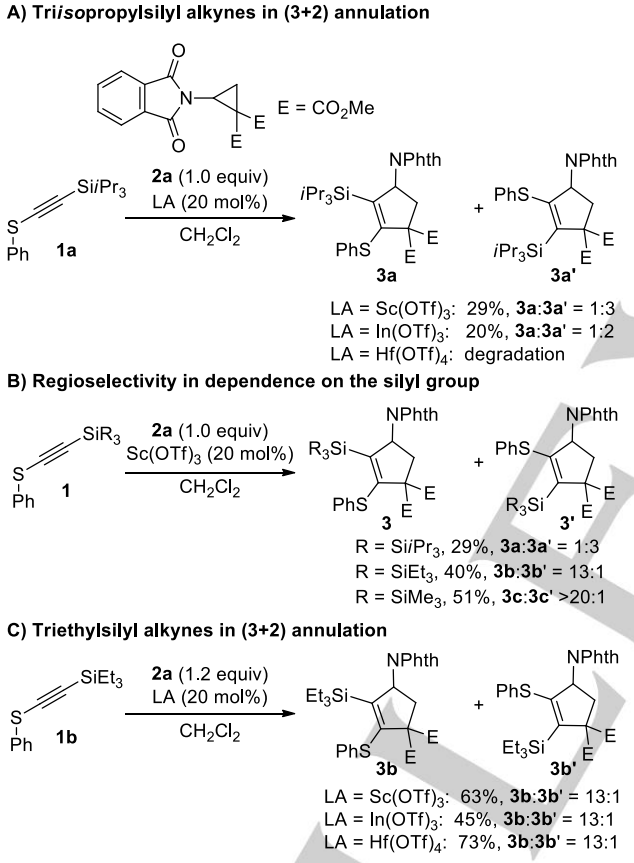
making thioalkynes easily accessible starting materials, and therefore even more attractive partners for (3+2) annulations.

Herein, we present new Lewis acid catalyzed annulations between DA-cyclopropanes and thiolalkynes, giving access either to cyclopentenes or complex polycyclic ring systems in dependence on the alkyne substituent (Scheme 1, **C**). The (3+2) annulation of silyl-substituted thioalkynes with phthalimide and aryl-substituted DA cyclopropanes provided a fast access to cyclopentenes in high yield and regioselectivity. In contrast, alkyl-substituted thioalkynes underwent an unprecedented annulation process with phthalimide-substituted DA-cyclopropanes to give access to new polycyclic ring systems, highlighting the unique reactivity of thioalkynes.

We first investigated the (3+2) annulation of tri*iso*propylsilyl- (TIPS) thioalkynes **1a** and phthalimide DA-cyclopropane **2a**, which has been highly successful in annulations with enol ethers and aldehydes (Scheme 2).[3] Thioalkynes **1a** was synthesized from the corresponding thiol using commercially available

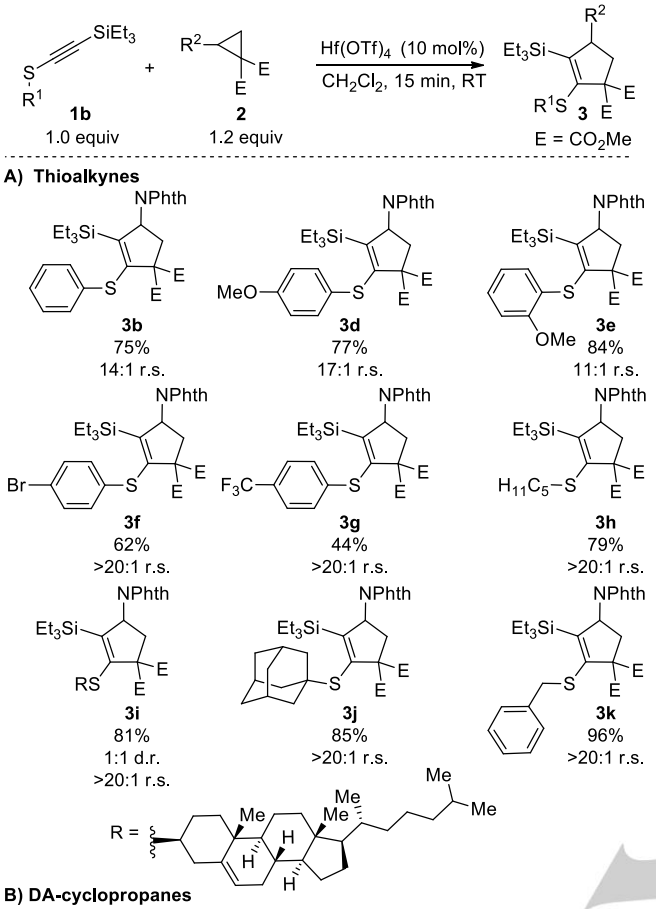


Scheme 2. First attempts with TIPS thioalkyne **1a** in the (3+2) annulation with DA cyclopropane **2a** (**A**), regioselectivity in dependence on the silyl group (**B**) and (3+2) annulation with TES thioalkyne **1b** (**C**). Reactions in **A** and **B** with 0.07 mmol alkyne **1**, in **C** with 0.23 mmol. Isolated yields after column chromatography are reported.

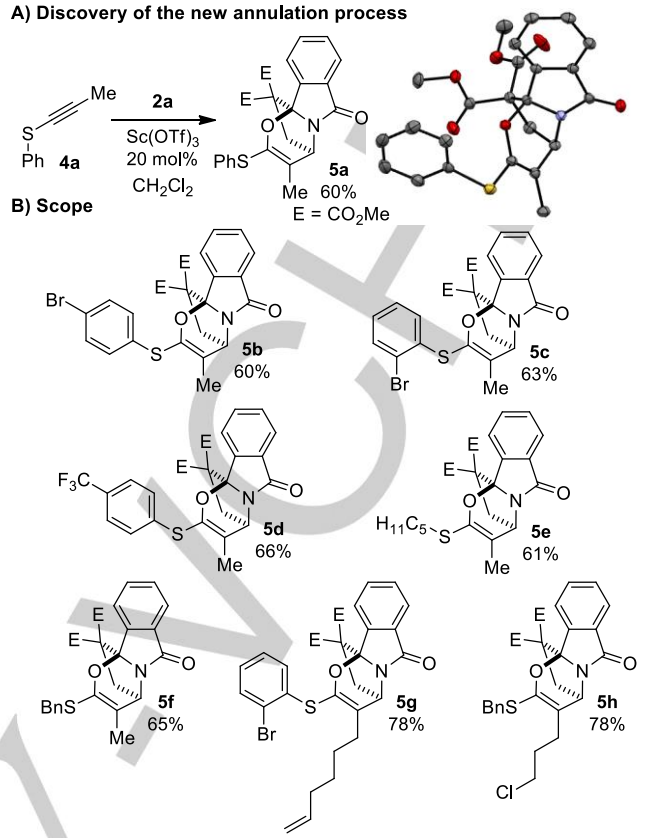
tri*iso*propylsilyl-ethynyl-benziodoxolone (TIPS-EBX) as previously reported by our group.[12a] A preliminary screening of Lewis acids showed that the desired product could be obtained as a mixture of two regioisomers (1:3 ratio) in low yield with scandium triflate as catalyst (Scheme 2 **A**). Low yield and regioselectivity were also observed with indium triflate, and hafnium triflate led to complete degradation of cyclopropane **2a**. Zinc triflate, copper triflate, indium chloride and iron chloride did not give conversion to the desired cyclopentenamine. A comparison between TIPS, TES (triethylsilyl) and TMS (trimethylsilyl) thioalkynes **1a-c** was then performed (Scheme 2, **B**). The outcome of the (3+2) reaction was strongly dependent on the hindrance of the silane functional group. The yield increased from 29% with TIPS to 40% with TES and finally reached 51% with TMS. The main regioisomer switched from 1-thio-cyclopenten-5-amine **3a'** with TIPS-thioalkyne **1a** to 1-thio-cyclopenten-3-amines **3b** and **3c** with TES and TMS-thioalkynes **1b** and **1c**. Complete regioselectivity was observed with TMS-thioalkyne **1c**. Although the yield of **3c** could be improved to 79% when using 5 mol% of indium triflate, the yield were low to moderate when other thioalkynes were tested.[14] This was due to substantial removal of the TMS group under the reaction conditions. We therefore turned our attention to more stable TES thioalkynes, which still provided good regioselectivity in the (3+2) annulation reaction. With scandium triflate as catalyst, the yield could be increased to 63% by using a slight excess of cyclopropane **2a** (Scheme 2, **C**). With indium and hafnium triflate, product **3b** was obtained in 45% and 73% yield respectively, with 13:1 regioselectivity.

With hafnium triflate, the catalyst loading could be lowered to 10 mol% to provide compound **3b** in 75% yield in 15 min at room temperature (Scheme 3, **A**). Products **3d** and **3e** bearing an electron-donating group on the aromatic ring were obtained in better yields than in the case of electron-withdrawing substituents (products **3f** and **3g**). A shorter reaction time (few minutes instead of 15 minutes) was also observed in the case of more electron-rich benzene rings. Primary, secondary and tertiary alkyl thioalkynes gave also good results. Compounds **3h-j** were isolated in 79%, 81% and 85% yield respectively. Finally, compound **3k** was obtained in 96% yield from TES benzyl thioalkynes **1k**. The electronic properties of the phthalimide cyclopropane played also an important role in the reaction (Scheme 3, **B**). When the (3+2) reaction was conducted with electron rich methoxy-substituted phthalimide **2b** the yield dropped to 36% (product **3l**). In contrast, the yield increased to 96% with nitro-substituted phthalimide **2c** (product **3m**). With a maleimide substituent, similar yield and regioselectivity were obtained as with phthalimide (product **3n**).[15] The reaction was also successful with methoxy phenyl-substituted DA-cyclopropane **2e** under the same reaction conditions, affording the (3+2) annulation product **3o** in 70% yield and high regioselectivity.

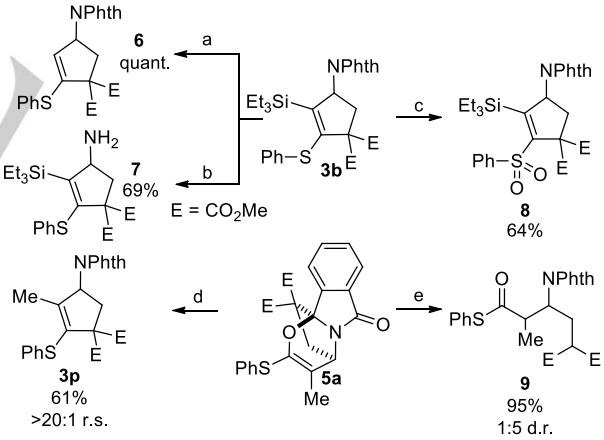
Next, alkyl-thioalkynes were examined. Surprisingly, when the (3+2) reaction catalyzed by scandium triflate was conducted with methyl-thioalkyne **4a**, a new compound **5a** was isolated in 60% yield and only traces of the (3+2) product were detected (Scheme 4, **A**). The polycyclic structure of compound **5a** could be established by X-ray analysis.[16] Such participation of the phthalimide group is unprecedented with DA aminocyclopropanes, highlighting the unique reactivity of thioalkynes. The scope of the cascade reaction was investigated with various alkyl-thioalkynes (Scheme 4, **B**). The desired polycyclic products were isolated in good yields with thiophenol derivatives (products **5a-d**). When the sulfur was substituted with a pentyl or a benzyl group, the corresponding products **5e** and **5f** were obtained in 61% and 65% yield, respectively. The cascade reaction also tolerated other alkyl groups on the alkyne, leading to compounds **5g** and **5h** in 78% yield. Unfortunately, when the reaction was conducted with phenyl-thioalkynes, complete degradation was observed.



Scheme 3. Scope of the (3+2) reaction between TES-thioalkynes and donor-acceptor cyclopropanes. Reactions in **A** with 0.23 mmol alkyne **1**, in **B** with 0.10 mmol. Isolated yields after column chromatography are reported.



Scheme 4. Discovery and scope of the new annulation process.

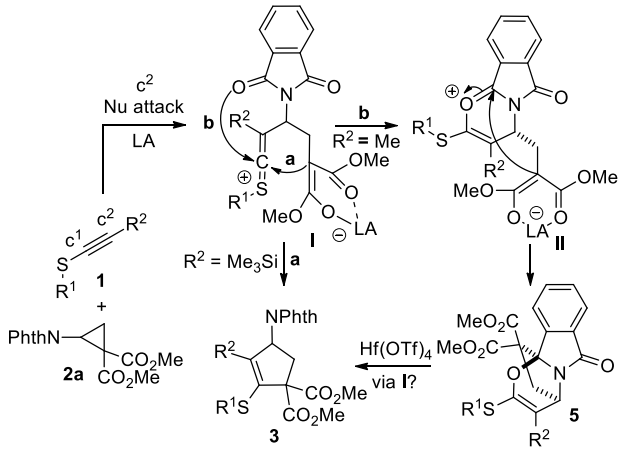


Scheme 5. Further derivatizations of 1-thio-cyclopenten-3-amine **3b** and polycyclic compound **5a**. Reaction conditions: a) TFA, 0°C; b) 5 equiv ethylene-diamine, *iso*propanol, reflux; c) 2.2 equiv *m*CPBA, CH_2Cl_2; d) 20 mol% $Hf(OTf)_4$ CH_2Cl_2; e) 1 equiv *p*TsOH, CH_2Cl_2.

Several transformations of compounds **3b** and **5a** were then performed (Scheme 5). Our attempts to remove the TES group with TBAF failed. Fortunately, the TES group was easily removed in TFA at 0 °C. The phthalimide protecting group was cleaved using ethylene diamine at reflux in 69% yield.[2a] Vinyl sulfide **3b** was easily oxidized to the corresponding sulfone **8** in 64% yield.[11b-c] Interestingly, when compound **5a** was treated with catalytic hafnium triflate, the (3+2) product **3p** was isolated in 61% yield.[17] Finally, product **5a** was cleanly converted to the corresponding thioester **9** in presence of *para*-toluene sulfonic acid.

We propose a speculative mechanism to explain the outcome of the developed annulation reactions (Scheme 6). Attack of the more nucleophilic C2 position of alkyne **1** proceeds to give sulfonium intermediate **I**. In the case of the very bulky TIPS group, steric effects dominate and favor C1 attack. From intermediate **I**, two different cyclizations can occur: via attack of the malonate anion onto the thioketene to give (3+2) annulation product **3** (path **a**); or via attack of the phthalimide carbonyl oxygen to give oxonium **II** (path **b**).

From **II**, attack of the malonate finally leads to the observed polycyclic product **5**. To rationalize the divergent reactivity of silyl and alkyl alkynes, one may speculate that the silyl group stabilizes further the carbocation via a β-silyl effect, making the attack of the hard oxygen nucleophile less favorable. Conversion of polycyclic compound **5** back to the (3+2) product **3** most probably proceeds via intermediate **I**.



Scheme 6. Proposed mechanism for the developed annulation reactions.

Thanks to the unique reactivity of thioalkynes, we have successfully developed two new annulation processes with DA-cyclopropanes using Lewis acid catalysts. The first (3+2) annulation between phthalimide DA-cyclopropanes and silyl thioalkynes gave access to 1-thio-cyclopenten-3-amines in high yield and regioselectivity. The cascade annulation between DA-cyclopropanes and alkyl thioalkynes on the other hand allowed the synthesis of polycyclic compounds with unprecedented rigid scaffolds. The results obtained further demonstrate the unique reactivity of both DA aminocyclopropanes and thioalkynes, and set the basis for further applications in annulation reactions and other transformations in the future.

Keywords: Alkynes • Donor-Acceptor cyclopropanes • Lewis acid • Catalysis • Annulation

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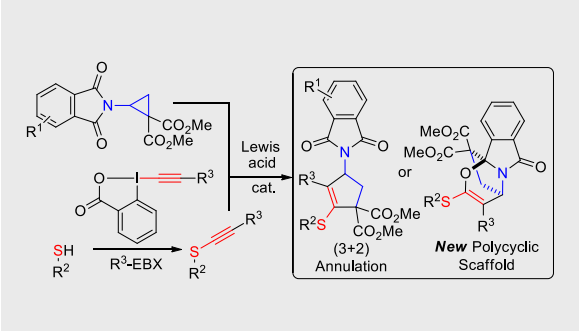
[14] 29 to 53%, see Supporting Information for further details.

[15] No product was obtained when using nucleobase-substituted DA cyclopropanes.
[16] The X-Ray data for compound **5a** has been deposited at the Cambridge Crystallographic Data Centre: CCDC 1453960.
[17] Under the same reaction conditions, product **9** could not be obtained directly from the alkyne **4a** and DA cyclopropane **2a**. Speculatively, the presence of the coordinating cyclopropane **2a** could change the properties of the hafnium catalyst.

COMMUNICATION

Divergent reactivity: We describe new annulation reactions of thioalkynes with donor-acceptor aminocyclopropanes. With silyl-thioalkynes, Lewis acid catalysed (3+2) annulation reaction took place affording 1-thio-cyclopenten-3-amines. In contrast, an unprecedented polycyclic compound was formed with alkyl-thioalkynes.



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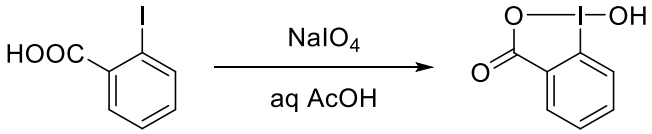
1. General methods

HPLC grade solvents purchased from Sigma-Aldrich or freshly distilled solvents were used for flash chromatography. Reaction solvents were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 30 ppm, Karl-Fischer titration). Commercially available reagents were purchased from Acros, Aldrich, Fluka, VWR, Aplichem, Merck or TCI and used without any further purification. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plates and visualized with UV light and permanganate stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H NMR spectra were measured on a Brucker DPX-400, 400 MHz spectrometer, all signals are reported in ppm with the corresponding internal solvent peak or TMS as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration; interpretation). ^{13}C NMR spectra were carried out with ^{1}H-decoupling on a Brucker DPX-400 101 MHz. All signals are reported in ppm with the corresponding internal solvent signal or TMS as standard. Infrared spectra were obtained on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, sh = shoulder). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. The following compounds dicarboxylate dimethyl 2-(5-methoxy-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**2b**), dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**2c**), dimethyl 2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)cyclopropane-1,1-dicarboxylate (**2d**), dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (**2e**), (2-bromophenyl)(prop-1-yn-1-yl)sulfane (**4c**), (2-bromophenyl)(oct-7-en-1-yn-1-yl)sulfane (**4g**), (TMS-EBX) **15**, ($(CH_2)_3$Cl-EBX) **19**, ($(CH_2)_4CHCH_2$-EBX) **22**, were prepared in previous work. However, all experimental procedures for the synthesis of the products described in the article are copied here from the indicated publications to facilitate the reproduction of the results. Only the spectra of new compounds are provided.

2. Synthesis of starting materials

2.1 Hypervalent iodine reagents

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (11).



10 **11**

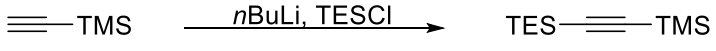
Following a reported procedure of Skulski and co-workers,[1] $NaIO_4$ (9.06 g, 42.3 mmol, 1.05 equiv) and 2-iodobenzoic acid (**10**) (10.0 g, 40.3 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. acetic acid (60 mL). The reaction mixture was protected from light with aluminum foil and refluxed for 4 hours. The reaction mixture was then diluted with cold water (200 mL) and allowed to cool to room temperature. After 1 h, the crude product was collected by filtration, washed with ice cold water (3 x 20 mL) and acetone (3 x 20 mL). The pure product **11** (10.4 g, 39.4 mmol, 98 %) was obtained as a colorless solid.

^{1}H NMR (400 MHz, Dimethyl-sulfoxide-d_6) δ 8.02 (dd, 1 H, *J* = 7.7, 1.4 Hz, ArH), 7.97 (m, 1 H, ArH), 7.85 (dd, 1 H, *J* = 8.2, 0.7 Hz, ArH), 7.71 (td, 1 H, *J* = 7.6, 1.2 Hz, ArH).

^{13}C NMR (101 MHz, Dimethyl-sulfoxide-d_6) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4.

NMR values correspond to the literature.[1]

Triethylsilyl trimethylsilylacetylene (13).



12 **13**

Following a reported procedure of Corey and co-workers,[2] a flame-dried round-bottom flask was put under nitrogen, ethynyltrimethylsilane (**12**) (1.36 g, 13.8 mmol, 1.0 equiv) and dry THF (21 mL) were added and cooled down to -78 °C. Then *n*-butyllithium (2.5 M in hexanes, 5.5 mL, 14 mmol, 0.98 equiv) was added dropwise. The mixture was warmed to 0 °C and stirred for 5 minutes. The mixture was then cooled back to -78 °C and chlorotri*iso*propylsilane (2.32 mL, 13.8 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (20 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 30 mL). The organic layer was washed with water (30 mL), then brine (30 mL) and dried over $MgSO_4$. It was filtered and concentrated under reduced pressure to obtain a colorless liquid **13** (3.0 g, 14 mmol, quantitative yield) which was pure enough without further purification.

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[1] L. Kraszkiewicz, L. Skulski, *Arkivoc*. **2003**, *6*, 120.

[2] C. J. Helal, P. A. Magriotis, E. J. Corey, *J. Am. Chem. Soc.* **1996**, *118*, 10938–10939.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 0.99 (t, *J* = 7.9 Hz, 9H, TES), 0.59 (q, *J* = 7.9 Hz, 6H, TES), 0.17 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 115.38, 111.19, 7.38, 4.29, 0.00.

NMR values correspond to the literature.[3]

Tri*iso*propylsilyl trimethylsilylacetylene (14).

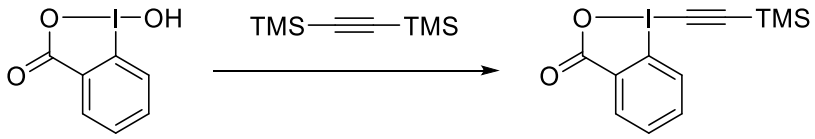
12 **14**

Following a reported procedure of Corey and co-workers, a flame-dried round-bottom flask was put under nitrogen, ethynyltrimethylsilane (**12**) (3.0 g, 31 mmol, 1.0 equiv) and dry THF (48 mL) were added and cooled down to -78 °C. Then *n*-butyllithium (2.5 M in hexanes, 12 mL, 30 mmol, 0.98 equiv) was added dropwise. The mixture was warmed to 0 °C and stirred for 5 minutes. The mixture was then cooled back to -78 °C and chlorotri*iso*propylsilane (6.55 mL, 30.6 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water (60 mL), then brine (60 mL) and dried over $MgSO_4$. It was filtered and concentrated under reduced pressure to obtain a colorless liquid **14** (7.79 g, 30.6 mmol, 99% yield) which was pure enough without further purification.

^{1}H NMR (400 MHz, Chloroform-*d*) *δ* 1.06 (m, 21 H, TIPS), 0.17 (s, 9 H, TMS).

^{1}H NMR values correspond to the literature.[3]

1-[(Trimethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TMS-EBX, 15).



11 **15**

Following a reported procedure,[4] trimethylsiyltriflate (2.8 mL, 15 mmol, 1.4 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**11**) (3.00 g, 11.4 mmol, 1.00 equiv) in acetonitrile (85 mL) until the mixture turned colorless. Bis(trimethylsilyl)acetylene (2.14 g, 12.5 mmol, 1.10 equiv) was then added dropwise, followed, after 20 min, by the addition of pyridine (1.2 mL, 15 mmol, 1.4 equiv). The mixture was stirred 30 min. The solvent was then removed under reduced pressure and the yellow crude oil was

[3] S. Nicolai, S. Erard, D. F. González, J. Waser, *Org. Lett.* **2010**, *12*, 384–387.

[4] Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Simonsen, A. J. *J. Org. Chem.* **1996**, *61*, 6547.

dissolved in dichloromethane (80 mL). The organic layer was washed with a large amount of water (130 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 65 mL). The organic layer was washed with brine (130 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (2.3 mL) afforded **15** (2.35 g, 6.84 mmol, 60% yield) as a colorless solid.

Mp: 143-145°C (dec).

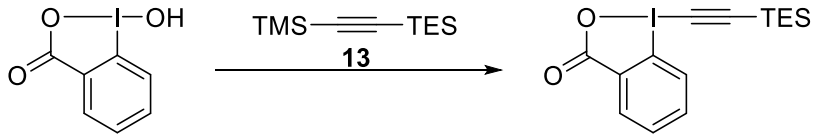
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 6.4, 1.9 Hz, 1 H, ArH), 8.19 (m, 1 H, ArH), 7.78 (m, 2 H, ArH), 0.32 (s, 9 H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) 166.4, 134.9, 132.6, 131.7, 131.4, 126.1, 117.2, 115.4, 64.2, -0.5.

IR ν 3389 (w), 2967 (w), 1617 (s), 1609 (s), 1562 (m), 1440 (w), 1350 (m), 1304 (w), 1254 (w), 1246 (w), 1112 (w), 1008 (w), 852 (s), 746 (m), 698 (m), 639 (m).

The characterization data corresponded to the reported values.[4]

1-[(Triethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TES-EBX, 16).



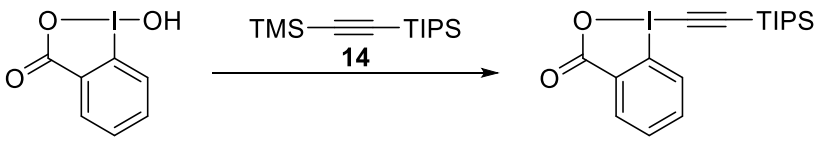
11 **16**

Following a reported procedure,[4] trimethylsilyltriflate (2.6 mL, 14 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**11**) (3.4 g, 12.8 mmol, 1.0 equiv) in acetonitrile (50 mL) until the mixture turned colorless. The mixture was cooled to 0°C and (trimethylsilyl)(triethylsilyl)acetylene (**13**) (3.0 g, 14 mmol, 1.1 equiv) was then added dropwise. The reaction mixture was stirred at 0°C for 1 h and then allowed to warm to room temperature. After 20 min pyridine (1.14 mL, 14.1 mmol, 1.1 equiv) was added and the mixture was stirred for an additional 30 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (150 mL). The organic layer was washed with a large amount of water (240 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 120 mL). The organic layer was washed with brine (240 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (20 mL) afforded **16** (2.56 g, 6.63 mmol, 52% yield) as golden needles

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (m, 1 H, ArH), 8.24 (m, 1 H, ArH), 7.75 (m, 2 H, ArH), 1.06 (t, *J* = 8.0 Hz, 9 H, TES), 0.73 (q, *J* = 8.0 Hz; 6H, TES).

NMR values correspond to the literature.[2]

1-((Tri*iso*-propylsilyl)ethynyl)-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, 17).



11 **17**

Following a reported procedure,[4] 2-iodosylbenzoic acid (**11**) (6.9 g, 26 mmol, 1.0 equiv) was added to a flame-dried two-neck round-bottom flask. Dry acetonitrile (160 mL) was added and cooled to 0 °C under nitrogen. Trimethylsilyltriflate (5.16 mL, 28.7 mmol, 1.1 equiv) was added dropwise over 30 minutes. (Trimethylsilyl)(tri*iso*propylsilyl)acetylene (**14**) (7.32 g, 28.7 mmol, 1.1 equiv) was added dropwise over 15 minutes. The mixture was stirred for 40 minutes, then pyridine (2.30 mL) was added. The solvent was evaporated under vacuum. The crude product was dissolved in DCM (60 mL) and washed with 1 M HCl (60 mL) and the aqueous layer was extracted with DCM (60 mL). The organic layers were combined, washed with a saturated solution of sodium bicarbonate (2 x 60 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca.* 40 mL) afforded **17** (9.43 g, 22.0 mmol, 84%) as colorless crystals.

Mp 170.0 – 176.0 °C (decomposition).

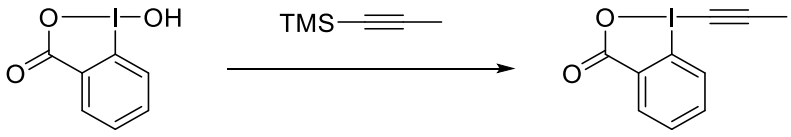
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (m, 1 H, ArH), 8.29 (m, 1 H, ArH), 7.76 (m, 2 H, ArH), 1.16 (m, 21 H, TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1.

NMR values correspond to the literature.[2]

Propynyl-1,2-benziodoxol-3(1*H*)-one (Me-EBX, 18).

a) From **11**:



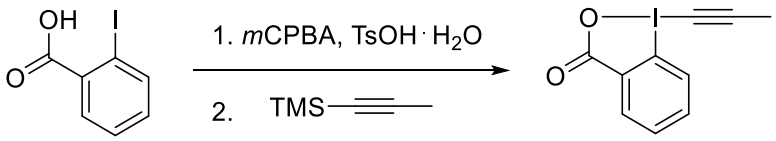
11 **18**

Following a modified reported procedure of Waser and co-workers[5] 2-iodosylbenzoic acid (**11**) (1.0 g, 3.8 mmol, 1.0 equiv) was added to a flame-dried round-bottom flask. Dry DCM (10 mL) was added. Distilled trimethylsilyltriflate (0.755 mL, 4.17 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred for 1 hour and 1-(trimethylsilyl)propyne (0.623 mL, 4.17 mmol, 1.1) was added dropwise. The reaction mixture was stirred for 5 hours, quenched with saturated sodium bicarbonate (20 mL) and stirred for 5 minutes vigorously. The layers were

[5] J. P. Brand, J. Waser, *Angew. Chem. Int. Ed.* **2010**, *49*, 7304–7307.

separated in a separatory funnel. The aqueous layer was washed with DCM (2 x 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude white solid was purified by column chromatography using AcOEt as the eluting solvent to afford **18** (454 mg, 1.59 mmol, 42 %) as a white solid.

b) One-pot synthesis:



10 **18**

Following a slightly modified reported procedure of Olofsson and co-workers,[6] 2-iodobenzoic acid (**10**) (3.00 g, 12.1 mmol. 1.0 equiv), *para*-toluenesulfonic acid monohydrate (TsOH•H_2O, 2.32 g, 12.1 mmol, 1.0 equiv) and *meta*-chloroperoxybenzoic acid (*m*CPBA-77%, 2.98 g, 13.3 mmol, 1.1 equiv) were added to a flame dried round-bottom flask. The flask was put under nitrogen and dry DCM (25 mL) and TFE (25 mL) were added. The reaction mixture was stirred for 1 hour at 40 °C, then 1-(trimethylsilyl)propyne (2.53 mL, 16.9 mmol, 1.4 equiv) was added. The reaction was stirred overnight at 40 °C, then was stopped and was let to cool to room temperature. The solvent was evaporated under vacuum. To the crude solid DCM (45 mL) and saturated sodium bicarbonate (45 mL) were added and the mixture was shaken in a separatory funnel until no gas formation was observed. The organic layer was collected and the aqueous layer was washed with DCM (2x50 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude mixture was purified by column chromatography using AcOEt as the eluting solvent to afford **18** (974 mg, 3.40 mmol, 28 %) as a white solid.

RF = 0.1 ethyl acetate.

Mp 124.0 – 150.0 °C (decomposition).

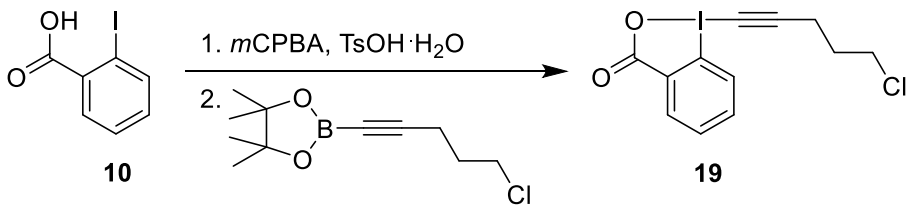
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (m, 1 H, ArH), 8.18 (m, 1 H, ArH), 7.76 (m, 2 H, ArH), 2.28 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.7, 134.8, 132.5, 131.6, 126.4, 117.4, 115.6, 105.1, 39.0, 5.7.

NMR values correspond to the literature.[7]

(5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1*H*)-one (19).

[6] M. J. Bouma, B. Olofsson, *Chem. – Eur. J.* **2012**, *18*, 14242–14245.
[7] R. Frei, J. Waser, *J. Am. Chem. Soc.* **2013**, *135*, 9620–9623.



Following a slightly modified procedure,[6] 2-iodobenzoic acid (**10**) (3.76 g, 15.2 mmol, 1.00 eq.), *para*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$, 2.88 g, 15.2 mmol, 1.00 eq.) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 4.11 g, 16.7 mmol, 1.10 eq.) were dissolved in dichloromethane (30 mL) and 2,2,2-trifluoroethanol (30 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which 5-chloro-1-pentynyl-1-boronic acid pinacol ester (4.85 g, 21.2 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 90 minutes at room temperature, filtered and concentrated *in vacuo*. The resulting oil was dissolved in dichloromethane (15 mL) and under vigorous stirring, saturated aq. $NaHCO_3$ (15 mL) was added. The mixture was stirred for 10 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (ethyl acetate) to afford **19** (3.76 g, 10.8 mmol, 71%) as a white solid.

RF = 0.15 ethyl acetate

Mp 138.5-141.7 °C.

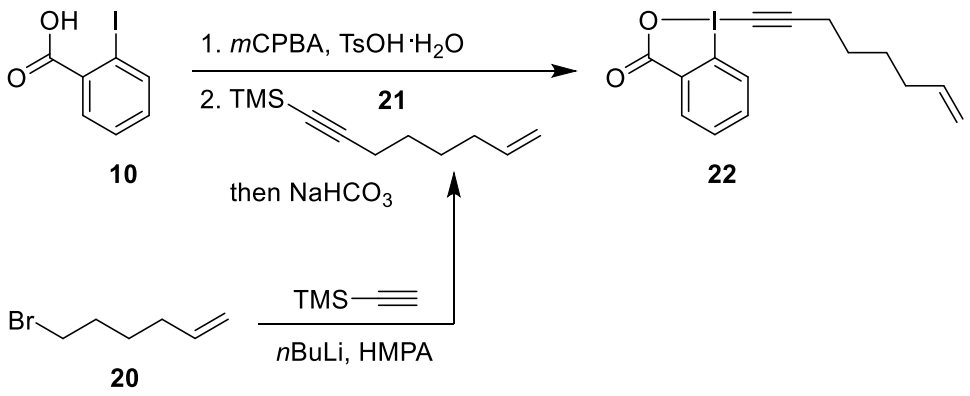
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.41-8.34 (m, 1 H, Ar*H*), 8.22-8.13 (m, 1 H, Ar*H*), 7.82-7.68 (m, 2 H, Ar*H*), 3.71 (t, 2 H, *J* = 6.1 Hz, $ClCH_2CH_2$), 2.82 (t, 2 H, *J* = 6.9 Hz, $CCCH_2CH_2$), 2.18-2.05 (m, 2 H, $ClCH_2CH_2$).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 166.8, 134.9, 132.5, 131.6, 131.6, 126.4, 115.8, 107.1, 43.4, 41.2, 30.7, 18.0.

IR ν 2942 (w), 2866 (w), 2171 (w), 2091 (w), 1727 (w), 1617 (s), 1556 (w), 1441 (w), 1339 (m), 1213 (w), 1023 (w), 846 (w), 742 (s).

HRMS (ESI) $C_{12}H_{11}ClIO_2^+$ $[M+H]^+$ calc. = 348.9487; $[M+H]^+$ obs. = 348.9484.

Oct-6-en-1-ynyl)-1,2-benziodoxol-3(1*H*)-one (20).



To a mixture of trimethylsilylacetylene (7.23 g, 73.6 mmol, 1.20 eq.) and dry THF (40 mL) was added at -78 °C under nitrogen 2.5 M *n*BuLi in hexanes (31.9 mL, 80.0 mmol, 1.30 eq.) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 60 minutes, after which a mixture consisting of 6-bromohexene (**20**) (10.0 g, 61.3 mmol, 1.00 eq.), hexamethylphosphoramide (HMPA, 12.0 mL, 67.5 mmol, 1.10 eq.) and dry THF (20 mL) was slowly added *via* cannula over a 20 minute time period. The reaction mixture was stirred for 60 minutes at -78 °C, followed by 24 hours of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH_4Cl (50 mL) and diluted with water (5 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure trimethyl(oct-7-en-1-yn-1-yl)silane (**21**, 10.6 g, 58.8 mmol, 95.9% yield) as a colorless liquid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.79 (ddt, 1 H, J = 16.9, 10.2, 6.7 Hz, CH_2CHCH_2), 5.04-4.91 (m, 2 H, CH_2CHCH_2), 2.22 (t, 2 H, J = 6.9 Hz, CH_2), 2.11-2.01 (m, 2 H, CH_2), 1.58-1.43 (m, 4 H, CH_2), 0.14 (s, 9 H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 138.8, 114.7, 107.6, 84.5, 33.3, 28.2, 28.1, 19.9, 0.3.

The values of the NMR spectra are in accordance with reported literature data.[8]

Following a slightly modified procedure,[6] 2-iodobenzoic acid (**10**) (9.82 g, 39.6 mmol, 1.00 eq.), *para*-toluenesulfonic acid monohydrate (7.53 g, 39.6 mmol, 1.00 eq.) and *meta*-chloroperoxybenzoic acid (10.7 g, 43.6 mmol, 1.10 eq.) were dissolved in dichloromethane (73 mL) and 2,2,2-trifluoroethanol (73 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which trimethyl(oct-7-en-1-yn-1-yl)silane (**21**) (10.0 g, 55.4 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 hours at room temperature, filtered and concentrated *in vacuo*. The resulting oil was dissolved in

[8] Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 1245.

dichloromethane (700 mL) and under vigorous stirring, saturated aq. $NaHCO_3$ (700 mL) was added. The mixture was stirred for 1 hour, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (ethyl acetate) to afford **22** (2.60 g, 7.34 mmol, 19%) as a white solid. In addition, starting trimethyl(oct-7-en-1-yn-1-yl)silane (**21**) (3.20 g, 17.7 mmol) was recovered and re-submitted to the above described conditions to afford additional **22** (1.18 g, 3.33 mmol, 28%) as a white solid, giving an overall yield of 27% brsm.

RF = 0.34 ethyl acetate.

Mp 48-58 °C.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.43-8.36 (m, 1 H, Ar*H*), 8.21-8.13 (m, 1 H, Ar*H*), 7.80-7.69 (m, 2 H, Ar*H*), 5.81 (ddt, 1 H, *J* = 17.0, 10.2, 6.7 Hz, CH_2CHCH_2), 5.10-4.95 (m, 2 H, CH_2CHCH_2), 2.61 (t, 2 H, *J* = 7.0 Hz), 2.17-2.07 (m, 2 H), 1.73-1.51 (m, 4 H).

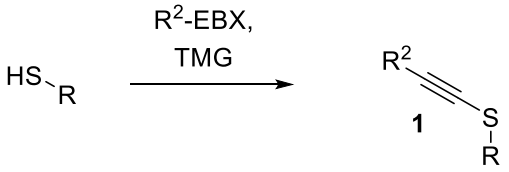
^{13}C NMR (101 MHz, Chloroform-*d*): δ 166.7, 138.1, 134.8, 132.5, 131.6, 131.6, 126.2, 115.7, 115.2, 109.5, 39.7, 33.2, 28.1, 27.7, 20.4.

IR ν 3294 (w), 2912 (w), 2869 (w), 1731 (w), 1650 (w), 1625 (w), 1447 (m), 1250 (w), 1101 (s), 1018 (m), 747 (s).

HRMS (ESI) $C_{15}H_{16}IO_2^+$ $[M+H]^+$ calc. = 355.0189; $[M+H]^+$ obs. = 355.0182.

2.2 Preparation of thioalkynes

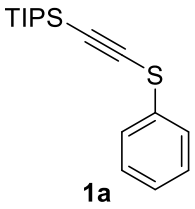
General procedure for thioalkynylation, GP1.



The thiol (1 equiv) was stirred in a flame dried flask under nitrogen in dry THF (0.073 M) with TMG (1.1 equiv). After five minutes of stirring, the corresponding EBX reagent (1.1 equiv) was added in one portion. The reaction was quenched with water and extracted two times with diethyl ether. The organics were dried over anhydrous $MgSO_4$ and concentrated under pressure with silica and triethylamine. The product was purified by column chromatography using pentane with 1% triethylamine as eluting solvent.

2.2.1 TIPS-Thioalkynes

((Phenylthio)ethynyl)triisopropylsilane (1a).



1a

Following the **GP1**, with benzene-thiol (0.38 mL, 3.6 mmol, 1 eq), TMG (0.56 mL, 4.4 mmol, 1.1 eq) and TIPS-EBX (**17**) (1.7 g, 4.4 mmol, 1.1 eq). The desired thiol **1a** (1.04 g, 3.59 mmol, 99 %) was obtained as a colorless oil.

RF = 0.67 pentane.

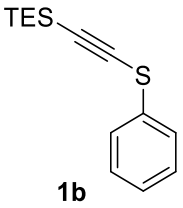
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.44 (m, 2 H, ArH), 7.34 (m, 2 H, ArH), 7.22 (m, 1 H, ArH), 1.12 (m, 21 H, TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 132.9, 129.3, 126.5, 126.1, 103.4, 91.1, 18.8, 11.5.

NMR values correspond to the literature.[7]

2.2.2 TES-Thioalkynes

Triethyl((phenylthio)ethynyl)silane (1b).



1b

Following the **GP1**, with thiophenol (0.28 mL, 2.7 mmol, 1 equiv), TMG (3.8 mL, 3.0 mmol, 1.1 equiv) and TES-EBX (**16**) (1.2 g, 3.0 mmol 1.1 equiv), the desired thiol **1b** (0.67 g, 2.7 mmol, 100%) was obtained as a colorless oil.

RF = 0.36 pentane.

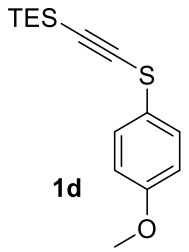
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.32 (m, 2H, Ar-H), 7.30 – 7.23 (m, 2H, Ar-H), 7.17 – 7.11 (m, 1H, Ar-H), 0.97 (t, *J* = 7.9 Hz, 9H, TES), 0.61 (q, *J* = 7.7 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 132.4, 129.0, 126.2, 125.9, 104.1, 90.6, 7.3, 4.2.

IR 3066 (w), 2955 (m), 2880 (m), 2093 (m), 1583 (w), 1478 (w), 1013 (s), 860 (s).

HRMS (ESI) calcd for $C_{14}H_{20}AgSSi^{+}$ $[M+Ag]^{+}$ 355.0100; found 355.0105.

Triethyl(((4-methoxyphenyl)thio)ethynyl)silane (1d).



1d

Following the **GP1**, with 4-methoxy benzenethiophenol (0.49 mL, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M) (5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX **16** (0.17 g, 0.44 mmol 1.1 equiv), the desired thiol **1d** (0.10 g, 0.37 mmol, 91%) was obtained as a colorless liquid.

RF = 0.24 pentane.

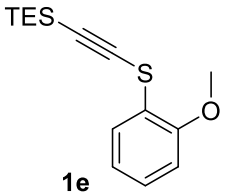
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 8.9 Hz, 2H, Ar-H), 6.89 (d, *J* = 8.9 Hz, 2H, Ar-H), 3.80 (s, 3H, OMe), 1.02 (t, *J* = 7.9 Hz, 9H, TES), 0.66 (q, *J* = 7.9 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.7, 128.2, 122.5, 114.8, 102.3, 92.1, 55.2, 7.3, 4.2.

IR 2954 (w), 2880 (w), 2091 (w), 1594 (w), 1493 (m), 1292 (w), 1245 (s), 1027 (m), 858 (s).

HRMS (ESI) calcd for $C_{15}H_{23}OSSi^+$ $[M+H]^+$ 279.1233; found 279.1236.

Triethyl(((2-methoxyphenyl)thio)ethynyl)silane (1e).



1e

Following the **GP1**, with 2-methoxy benzenethiophenol (0.49 mL, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol **1e** (0.11 g, 0.40 mmol, 100%) was obtained as a colorless liquid.

RF = 0.34 pentane.

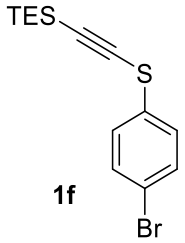
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar-H), 7.11 (ddd, *J* = 8.1, 7.4, 1.6 Hz, 1H, Ar-H), 6.93 (td, *J* = 7.6, 1.2 Hz, 1H, Ar-H), 6.75 (dd, *J* = 8.1, 1.1 Hz, 1H, Ar-H), 3.78 (s, 3H, OMe), 0.96 (t, *J* = 7.9 Hz, 9H, TES), 0.66 – 0.41 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.0, 127.0, 126.3, 121.5, 121.0, 110.2, 104.4, 90.6, 55.7, 7.3, 4.2.

IR 2954 (w), 2880 (w), 2093 (w), 1582 (w), 1471 (s), 1270 (w), 1243 (s), 1016 (s), 856 (s).

HRMS (ESI) calcd for $C_{15}H_{23}OSSi^+$ $[M+H]^+$ 279.1233; found 279.1234.

Triethyl(((4-bromo)thio)ethynyl)silane (1f).



1f

Following the **GP1**, with 4-bromo benzenethiophenol (76 mg, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol **1f** (0.13 g, 0.40 mmol, 100%) was obtained as a colorless liquid.

RF = 0.75 pentane.

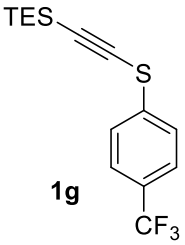
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.29 (d, *J* = 8.6 Hz, 2H, Ar-H), 1.03 (t, *J* = 7.9 Hz, 9H, TES), 0.78 – 0.54 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 132.2, 131.9, 127.6, 120.2, 105.1, 89.9, 7.5, 4.4.

IR 2957 (m), 2880 (w), 2095 (m), 1466 (m), 1391 (w), 1234 (w), 1079 (m), 1010 (s), 860 (s).

HRMS (ESI) calcd for $C_{14}H_{19}Ag^{79}BrSSi^{+}$ $[M+Ag]^{+}$ 432.9206; found 432.9202.

Triethyl(((4-(trifluoromethyl)phenyl)thio)ethynyl)silane (1g).



1g

Following the **GP1**, with 4-trifluoro benzenethiophenol (0.055 mL, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol **1g** (0.11 g, 0.36 mmol, 89%) was obtained as a colorless liquid.

RF = 0.9 pentane.

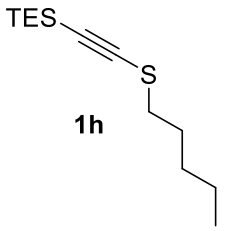
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.45 (d, *J* = 8.3 Hz, 2H, Ar-H), 0.97 (t, *J* = 7.9 Hz, 9H, TES), 0.62 (q, *J* = 7.9 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.0, 128.6 (q, *J* = 32.8 Hz), 126.0 (q, *J* = 3.9 Hz), 125.7, 124.0 (q, *J* = 271.9 Hz), 106.3, 88.9, 7.5, 4.3.

IR 2956 (w), 2877 (w), 2098 (w), 1608 (w), 1325 (s), 1167 (m), 1127 (s), 1064 (m), 1014 (m), 860 (s), 828 (m).

HRMS (ESI) calcd for $C_{15}H_{19}AgF_3SSi^{+}$ $[M+Ag]^{+}$ 422.9974; found 422.9977.

Triethyl((pentylthio)ethynyl)silane (1h).



1h

Following the **GP1**, with 1-pentane-thiol (0.050 mL, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol **1h** (0.088 g, 0.37 mmol, 91%) was obtained as a colorless liquid.

RF = 0.92 pentane.

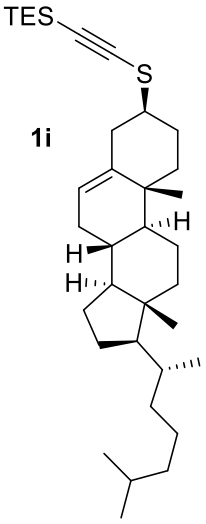
^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.55 (t, *J* = 7.3 Hz, 2H, CH_2), 1.59 (p, *J* = 7.3 Hz, 2H, CH_2), 1.30 – 1.11 (m, 4H, CH_2), 0.82 (t, *J* = 7.9 Hz, 9H, TES), 0.74 (t, *J* = 7.1 Hz, 3H, CH_3), 0.52 – 0.34 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 97.9, 95.6, 35.7, 30.3, 28.7, 22.2, 13.9, 7.5, 4.5.

IR 2957 (m), 2866 (w), 2091 (m), 1460 (w), 1380 (w), 1237 (w), 1017 (m), 862 (s).

HRMS (ESI) calcd for $C_{13}H_{27}SSi^+$ $[M+H]^+$ 243.1597; found 243.1602.

((((3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)thio)ethynyl)triethylsilane (1i).



1i

Following the **GP1**, with cholesteryl thiol (0.16 mg, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol **1i** (0.199 g, 0.368 mmol, 92%) was obtained as a colorless oil.

RF = 0.64 pentane.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.18 (dd, *J* = 4.8, 2.5 Hz, 1H, C=CH), 2.55 (tt, *J* = 12.3, 4.0 Hz, 1H, CHS), 2.35 (td, *J* = 12.8, 12.3, 2.6 Hz, 1H), 2.19 (ddd, *J* = 13.8, 4.5, 2.0 Hz, 1H), 1.89 – 1.71 (m, 4H), 1.70 – 1.53 (m, 1H), 1.50 – 0.86 (m, 21H), 0.84 – 0.78 (m, 12H, TES and CH_3), 0.73 (d, *J* = 6.5 Hz, 3H, CH_3), 0.68 (dd, *J* = 6.6, 1.8 Hz, 6H, CH_3), 0.43 (q, *J* = 7.9 Hz, 6H, TES).

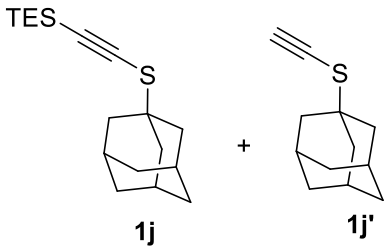
^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.5, 121.6, 100.1, 93.6, 56.7, 56.2, 50.2, 47.5, 42.3, 39.7, 39.5, 38.9, 36.7, 36.2, 35.8, 31.9, 31.8, 28.9, 28.2, 28.0, 24.3, 23.8, 22.8, 22.6, 21.0, 19.2, 18.7, 11.9, 7.5, 4.5.

One carbon not resolved.

IR 2943 (s), 2089 (m), 2068 (w), 1464 (m), 1377 (w), 1239 (w), 1064 (w), 1013 (m), 967 (w), 909 (w), 862 (m).

HRMS (ESI) calcd for $C_{35}H_{60}AgSSi^+$ $[M+Ag]^+$ 647.3230; found 647.3243.

((Adamantan-1-ylthio)ethynyl)triethylsilane (1j).



Following the **GP1**, with 1-adamantane-thiol (0.067 mg, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol, 1.1 equiv), the desired thiol was obtained as an inseparable mixture of alkyne **1j** and unprotected thio alkyne **1j'** (ratio 1:0.4) (0.084 g, **1j** 0.20 mmol, **1j'** 0.07 mmol, 67%).

RF = 0.74 pentane.

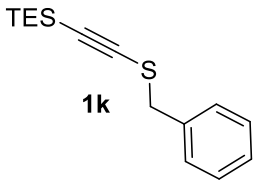
^{1}H NMR (400 MHz, Chloroform-*d*) δ 1.91 (s, 3H, CH), 1.78 (d, *J* = 2.9 Hz, 6H, CH_2), 1.60 – 1.40 (m, 6H, CH_2), 0.82 (t, *J* = 7.9 Hz, 9H, TES), 0.43 (q, *J* = 7.9 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 101.2, 93.2, 49.3, 46.3, 42.8, 36.1, 30.1, 7.6, 4.6.

IR 3300 (w), 2910 (s), 2856 (m), 2361 (w), 2082 (m), 1449 (m), 1303 (w), 1230 (w), 1032 (m), 1026 (m), 864 (m).

HRMS (ESI) calcd for $C_{18}H_{31}SSi^+$ $[M+H]^+$ 307.1910; found 307.1910.

Triethyl((benzylthio)ethynyl)silane (1k).



1k

Following the **GP1**, with benzylthiol (0.047 mL, 0.40 mmol, 1 equiv), TMG solution in THF (0.079 M, 5.6 mL, 0.44 mmol, 1.1 equiv) and TES-EBX (**16**) (0.17 g, 0.44 mmol 1.1 equiv), the desired thiol **1k** (0.080 g, 0.31 mmol, 76%) was obtained as a colorless liquid.

RF = 0.8 pentane.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 – 7.13 (m, 5H, Ar-H), 3.79 (s, 2H, CH_2), 0.80 (t, *J* = 7.9 Hz, 9H, TES), 0.42 (q, *J* = 7.9 Hz, 6H, TES).

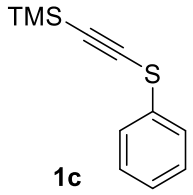
^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.7, 129.2, 128.6, 127.8, 100.0, 95.0, 40.5, 7.5, 4.5.

IR 3297 (w), 2955 (m), 2873 (m), 2085 (m), 1456 (m), 1416 (w), 1236 (m), 1006 (m), 859 (s).

HRMS (ESI) calcd for $C_{15}H_{23}SSi^+$ $[M+H]^+$ 263.1284; found 263.1288.

2.2.3 TMS-Thioalkynes

Trimethyl((phenylthio)ethynyl)silane (1c).



1c

Following the **GP1**, with benzenethiophenol (0.93 mL, 9.1 mmol, 1 equiv), TMG (1.25 mL, 10.0 mmol, 1.1 equiv) and TMS-EBX (**15**) (3.4 g, 10 mol 1.1 equiv), the desired thiol **1c** (1.37 g, 6.61 mmol, 73%) was obtained as a colorless oil.

RF = 0.48 pentane.

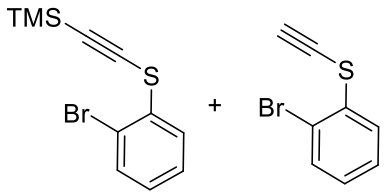
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.29 (m, 2H, Ar-H), 7.27 – 7.21 (m, 2H, Ar-H), 7.16 – 7.08 (m, 1H, Ar-H), 0.15 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 132.7, 129.4, 126.6, 126.2, 106.5, 90.2, 0.1.

IR 3283 (w), 3066 (w), 2943 (w), 2095 (m), 1584 (w), 1255 (m), 1029 (m), 879 (s).

HRMS (ESI) calcd for $C_{11}H_{14}AgSSi^+$ $[M+Ag]^+$ 312.9631; found 312.9627.

(((2-Bromophenyl)thio)ethynyl)trimethylsilane (1l).



1l **1l'**

Following the **GP1**, with 2-bromo benzenethiophenol (0.077 mL, 0.64 mmol, 1 equiv), TMG (0.081 mL, 0.71 mmol, 1.1 equiv) and TMS-EBX (**15**) (0.26 g, 0.71 mmol 1.1 equiv), the desired thiol was obtained as mixture of **1l** and **1l'** with a ratio of 5:1 (0.163 g, 2.7 mmol, 94%) as a colorless oil.

RF = 0.42 pentane.

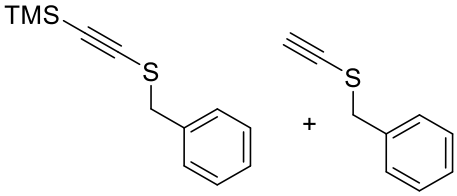
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar-H), 7.37 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar-H), 7.28 – 7.20 (m, 1H, Ar-H), 6.97 (td, *J* = 7.7, 1.5 Hz, 1H, Ar-H), 0.15 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.3, 132.8, 128.3, 127.6, 127.1, 119.7, 108.4, 89.0, -0.0.

IR 3646 (w), 3272 (w), 2961 (w), 2097 (m), 1439 (m), 1253 (m), 1019 (m), 875 (s), 839 (s).

HRMS (ESI) calcd for $C_{11}H_{13}{}^{79}BrSSi$ [M+] 283.9691; found.

((Benzylthio)ethynyl)trimethylsilane (1m).



1m **1m'**

Following the **GP1**, with phenylmethanethiol (0.076 mL, 0.64 mmol, 1 equiv), TMG (0.081 mL, 0.71 mmol, 1.1 equiv) and TMS-EBX (**15**) (0.26 g, 0.71 mmol 1.1 equiv), the desired thiol was obtained as a mixture of **1m** and **1m'** with a ratio of 9:1 (0.054 g, 0.26 mmol, 40%) as a colorless oil.

RF = 0.46 pentane.

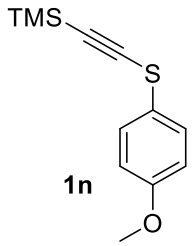
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (m, 5H, Ar-H), 3.94 (s, 2H, CH_2), 0.14 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.5, 129.2, 128.6, 127.8, 102.4, 94.3, 40.3, -0.0.

IR 3063 (w), 3022 (w), 2960 (w), 2089 (m), 1623 (w), 1496 (w), 1458 (w), 1249 (m), 882 (s), 842 (s).

HRMS (ESI) calcd for $C_{12}H_{17}SSi^{+}$ $[M+H]^{+}$ 221.0815; found 221.0815.

(((4-Methoxyphenyl)thio)ethynyl)trimethylsilane (1n).



1n

Following the **GP1**, with phenylmethanthiol (0.175 mL, 1.43 mmol, 1 equiv), TMG (0.20 mL, 1.6 mmol, 1.1 equiv) and TMS-EBX (**15**) (0.54 g, 1.6 mmol 1.1 equiv), the desired product **1n** (0.23 g, 0.96 mmol, 67 %) was obtained as a colorless oil.

RF = 0.59 pentane.

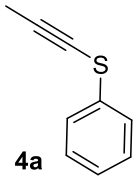
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 8.9 Hz, 2H, Ar-H), 6.93 (d, *J* = 8.9 Hz, 2H, Ar-H), 3.83 (s, 3H, OMe), 0.25 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.0, 128.8, 122.5, 115.1, 104.6, 91.7, 55.5, -0.0.

HRMS (ESI) calcd for $C_{12}H_{17}OSSi^{+}$ $[M+H]^{+}$ 237.0764; found 237.0760.

2.2.4 Alkyl-Thioalkynes

Prop-1-ynylsulfanyl-benzene (4a).



4a

Following the **GP1**, with benzenethiol (0.22 mL, 2.2 mmol, 1 equiv), TMG (0.33 mL, 2.6 mmol, 1.1 equiv) and Me-EBX (**18**) (0.680 g, 2.38 mmol, 1.1 equiv). The crude product was purified by distillation (0.1 mbar, 80 – 90 °C) to afford **4a** (0.250 g, 1.69 mmol, 78 %) as a colorless oil.

RF = 0.86 pentane.

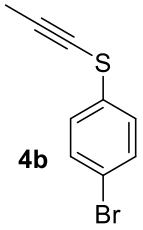
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.41 (m, 2 H, ArH), 7.32 (m, 2 H, ArH), 7.20 (m, 1 H, ArH) 2.11 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 133.7, 129.2, 126.3, 126.0, 95.5, 64.0, 5.4.

NMR values correspond to the literature.[9]

(4-Bromophenyl)(prop-1-yn-1-yl)sulfane (4b).

[9] E. P. Levanova, V. A. Grabel'nykh, A. V. Elaev, N. V. Russavskaya, L. V. Klyba, A. I. Albanov, O. A. Tarasova, N. A. Korchevin, *Russ. J. Gen. Chem.* **2013**, *83*, 1341–1344.



4b

Following the **GP1**, with 4-bromothiophenol (0.22 g, 1.1 mmol, 1 equiv), TMG (0.17 mL, 1.3 mmol, 1.1 equiv) and Me-EBX (**18**) (0.35 mg, 1.3 mmol, 1.1 equiv). The crude product was purified by distillation (0.8 mbar, 180 °C) to afford **4b** (149 mg, 0.646 mmol, 59 %) as a colorless oil.

RF = 0.87 pentane.

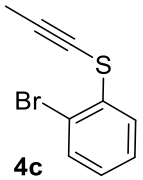
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.46 - 7.41 (m, 2 H, ArH), 7.30 - 7.25 (m, 2 H, ArH), 2.10 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 133.1, 132.2, 127.5, 119.9, 96.3, 63.3, 5.4.

IR 2909 (s), 1722 (s), 1689 (s), 1466 (s), 1382 (s), 1084 (s), 1000 (s), 975 (s), 807 (s).

HRMS (ESI) calcd for $C_9H_8{}^{79}BrS^+$ $[M+H]^+$ 226.9525; found 226.9516.

(2-Bromophenyl)(prop-1-yn-1-yl)sulfane (4c).



4c

Following the **GP1**, with 2-bromothiophenol (0.12 g, 0.60 mmol, 1 equiv) TMG (0.086 mL, 0.66 mmol, 1.1 equiv) and Me-EBX (**18**) (0.19 g, 1.3 mmol, 1.1 equiv). The desired thiol **4c** (0.13 g, 0.56 mmol, 93%) was obtained as a clear colorless oil.[7]

RF = 0.61 pentane.

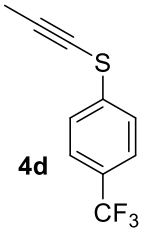
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70 (dd, 1 H, *J* = 8.0, 1.6 Hz, ArH), 7.47 (dd, 1 H, *J* = 7.9, 1.3 Hz, ArH), 7.34 (ddd, 1 H, *J* = 8.0, 7.4, 1.3 Hz, ArH), 7.06 (ddd, 1 H, *J* = 7.9, 7.4, 1.6 Hz, ArH), 2.14 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.4, 132.6, 128.1, 127.1, 126.8, 119.2, 97.5, 63.7, 5.4.

IR ν 3059 (w), 2913 (w), 1563 (w), 1447 (s), 1430 (s), 1104 (w), 1019 (s).

HRMS (ESI) $C_9H_8{}^{79}BrS^+$ $[M+H]^+$ calc. = 226.9525; $[M+H]^+$ obs. = 226.9519.

Prop-1-yn-1-yl(4-(trifluoromethyl)phenyl)sulfane (4d).



Following the **GP1**, with 4-(trifluoromethyl)benzenethiol (0.11 mL, 0.79 mmol, 1 equiv), TMG (0.12 mL, 0.95 mmol, 1.1 equiv) and Me-EBX (**18**) (250 mg, 0.874 mmol, 1.1 equiv). The crude product was purified by distillation (0.5 mbar, 150 °C) to afford **4d** (103 mg, 0.477 mmol, 60%) as a colorless oil.

RF = 0.71 pentane.

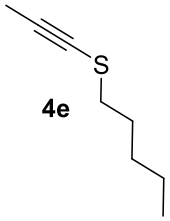
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.56 (m, 2 H, ArH), 7.50 (m, 2 H, ArH), 2.14 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 139.3, 128.4 (q, *J* = 32.8 Hz), 126.0 (q, *J* = 3.7 Hz), 125.6, 124.2 (q, *J* = 271.8 Hz), 97.3, 62.5, 5.4.

IR 1601 (s), 1316 (s), 1117 (m), 1011 (s), 826 (s).

HRMS (ESI) calcd for $C_{10}H_8F_3S^+$ $[M+H]^+$ 217.0293; found 217.0286.

Pentyl(prop-1-yn-1-yl)sulfane (4e).



Following the **GP1**, with pentane-1-thiol (0.42 mL, 1.1 mmol, 1 equiv), TMG (0.17 mL, 1.3 mmol, 1.1 equiv) and Me-EBX (**18**) (350 mg, 1.22 mmol, 1.1 equiv). The desired thiol **4e** (100 mg, 0.703 mmol, 63%) was obtained as a colorless oil.

RF = 0.78 pentane, $KMnO_4$ staining.

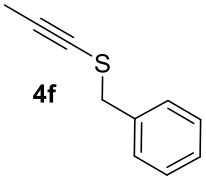
^{1}H NMR (400 MHz, Choloroform-*d*): δ 2.66 (t, 2 H, *J* = 7.3 Hz, SCH_2), 1.95 (s, 3 H, CH_3), 1.72 (quint, 2 H, *J* = 7.3 Hz, CH_2), 1.43 - 1.28 (m, 4 H, CH_2), 0.91 (t, 3H, *J* = 7.1 Hz, CH_2CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 89.6, 67.6, 35.5, 30.6, 29.2, 22.4, 14.1, 5.2.

IR 2928 (m), 2861 (s), 1677 (s), 1510 (s), 1466 (s), 1365 (s), 1268 (m), 912 (s).

HRMS (ESI) calcd for $C_8H_{15}S^+$ $[M+H]^+$ 143.0889; found 143.0883.

Benzyl(prop-1-yn-1-yl)sulfane (4f).



4f

Following the **GP1**, with benzylthiol (0.20 mL, 1.7 mmol, 1 equiv), TMG (0.26 mL, 2.0 mmol, 1.1 equiv) and Me-EBX (**18**) (0.534 g, 1.87 mmol, 1.1 equiv). The desired thiol **4f** (0.126 g, 0.777 mmol, 46 %) was obtained as a colorless oil.

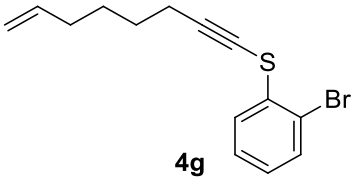
RF = 0.47 pentane.

^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.37 - 7.727 (m, 5 H, ArH), 3.90 (s, 2 H, CH_2), 2.11 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 137.1, 129.1, 128.6, 127.7, 91.4, 67.4, 40.2, 5.1.

NMR values correspond to the literature.[7]

(2-Bromophenyl)(oct-7-en-1-yn-1-yl)sulfane (4g).



4g

Following the **GP1**, with 2-bromothiophenol (0.10 g, 0.50 mmol, 1 equiv) TMG (0.072 mL, 0.55 mmol, 1.1 equiv) and $CH_2CH(CH_2)_4$-EBX (**22**) (0.099 g, 0.55 mmol, 1.1 equiv). The desired thiol **4g** (137 mg, 0.465 mmol, 93%) was obtained as a clear colorless oil.[7]

RF = 0.69 pentane.

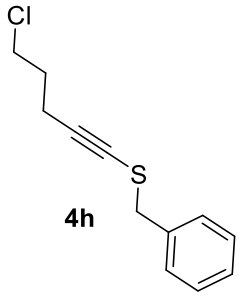
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68 (dd, 1 H, *J* = 8.0, 1.6 Hz, Ar*H*), 7.48 (dd, 1 H, *J* = 7.9, 1.3 Hz, Ar*H*), 7.34 (ddd, 1 H, *J* = 8.0, 7.4, 1.3 Hz, Ar*H*), 7.06 (ddd, 1 H, *J* = 7.7, 7.6, 1.6 Hz, Ar*H*), 5.83 (ddt, 1 H, *J* = 16.9, 10.2, 6.7 Hz, C*H*CH_2), 5.09-4.95 (m, 2 H, CHCH_2), 2.50 (t, 2 H, *J* = 6.8 Hz, CCC$H_2$$CH_2$), 2.16-2.06 (m, 2 H, CH_2), 1.72-1.50 (m, 4 H, CH_2).

^{3}C NMR ($CDCl_3$, 100 MHz): δ 138.5, 135.6, 132.6, 128.1, 127.1, 126.8, 119.3, 114.9, 101.8, 64.7, 33.3, 28.2, 28.1, 20.3.

IR ν 3062 (w), 2859 (w), 1736 (w), 1706 (m), 1447 (m), 1430 (m), 1174 (w), 1019 (m), 912 (m), 745 (s).

HRMS (ESI) $C_{14}H_{16}{}^{79}BrS^+$ $[M+H]^+$ calc. = 295.0151; $[M+H]^+$ obs. = 295.0152.

Benzyl(5-chloropent-1-yn-1-yl)sulfane (4h).



4h

Following the **GP1**, with benzylthiol (0.040 mL, 0.40 mmol, 1 equiv), TMG solution in THF THF (0.079 M) (5.6 mL, 0.44 mmol, 1.1 equiv) and $Cl(CH_2)_3$-EBX (**19**) (0.15 g, 0.44 mmol, 1.1 equiv), the desired thiol **4h** (0.085 g, 0.38 mmol, 95%) was obtained as a colorless liquid.

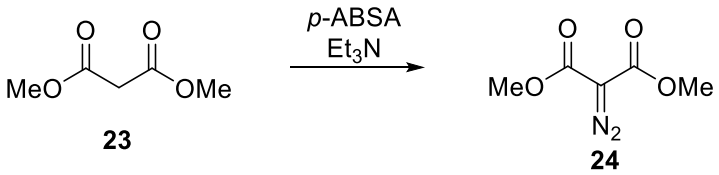
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.31 (m, 5H, Ar-H), 3.92 (s, 2H, benzylic CH_2), 3.55 (t, *J* = 6.4 Hz, 2H, CH_2Cl), 2.49 (t, *J* = 6.7 Hz, 2H, CH_2), 1.91 (p, *J* = 6.5 Hz, 2H, CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.8, 129.0, 128.5, 127.6, 93.8, 69.4, 43.5, 39.9, 31.3, 17.5.

IR 3036 (w), 2958 (m), 2928 (m), 2189 (w), 1949 (w), 1494 (s), 1453 (s), 1428 (m), 1353 (w), 1290 (s), 1238 (m), 1202 (w), 1072 (m), 1030 (m).

HRMS (ESI) calcd for $C_{12}H_{14}ClS^+$ $[M+H]^+$ 225.0499; found 225.0496.

2.3 Synthesis of donor-acceptor cyclopropanes
Dimethyl-2-diazomalonate (24).



23 **24**

Following a slightly modified reported procedure of Waser and co-workers, [10] 4-acetamidobenzenesulfonyl azide (6.85 g, 28.5 mmol, 1.5 equiv) was added in a flame-dried round bottom flask. The flask was put under nitrogen and dry acetonitrile (80 mL), triethylamine (6.36 mL, 45.6 mmol, 2.4 equiv) and dimethyl malonate **23** (2.2 mL, 19 mmol, 1 equiv) were added. The reaction mixture was stirred at room temperature for 24 hours. The solvent was evaporated and the crude product was filtered on cotton, washing with acetonitrile (30 mL). The crude mixture was concentrated under reduced pressure and filtered on cotton one more time, washing with DCM (30 mL). The crude product was purified by column chromatography using a

[10] F. de Nanteuil, J. Waser, *Angew. Chem., Int. Ed.* **2011**, *50*, 12075.

mixture of pentane/AcOEt (8:2, 1 % Et_3N) as eluting solvent. The pure diazo-compound **24** (3.0 g, 19 mmol, 99 %) was obtained as a slightly yellow oil (solid at 4 °C).

RF = 0.32 PET/Et_2O (1:1).

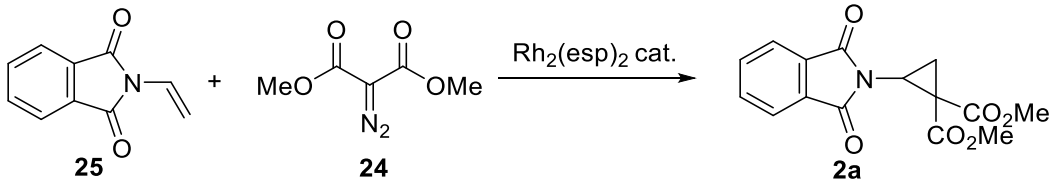
^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.85 (s, 6 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.2, 52.4.

The carbon-diazo signal cannot be detected.

NMR values correspond to the literature[10]

Dimethyl-2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (2a).



Following a reported procedure of Waser and co-workers,[10] N-vinyl-phthalimide **25** (2.0 g, 11 mmol 1.0 equiv) and bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (8.8 mg, 0.012 mmol, 0.1 mol%) were added in a flame-dried round-bottom flask and the flask was put under nitrogen. Then dry DCM (28 mL) was added and the solution was cooled down to 0 °C with an ice/water bath. A solution of dimethyldiazomalonate (**24**) (2.2 g, 14 mmol, 1.2 equiv) in dry DCM (6 mL) was added dropwise over 5 minutes. After the addition, the mixture was allowed to warm to room temperature and stirred overnight. The solvent was then removed under reduced pressure and the crude product was directly purified by column chromatography using a mixture of pentane/AcOEt (from 8:2 to 6:4) as eluting solvent. The pure product **2a** (3.2 g, 11 mmol, 91% yield) was obtained as a colorless solid.

RF = 0.34 hexane/AcOEt (6:4).

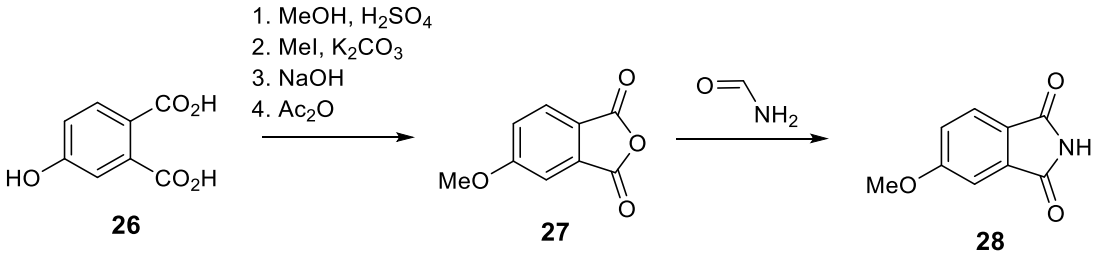
Mp 131.8 – 133.9 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (m, 2 H, Phthalimide-ArH), 7.71 (m, 2 H, Phthalimide-ArH), 3.81 (s, 3 H, OCH_3), 3.68 (dd, 1 H, *J* = 8.5, 6.6 Hz, NCH), 3.59 (s, 3 H, OCH_3), 2.69 (dd, 1 H, *J* = 6.5, 6.5 Hz, CH_2), 2.02 (dd, 1 H, *J* = 8.5, 6.4 Hz, CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.5, 167.8, 166.9, 134.3, 131.4, 123.5, 53.1, 53.0, 34.9, 33.1, 19.6.

NMR values correspond to the literature.[10]

5-Methoxyisoindoline-1,3-dione (28).



Following a modified procedure,[11] a solution of 4-hydroxyphthalic acid **26** (2.00 g, 11.0 mmol, 1.00 eq), catalytic sulfuric acid (0.10 mL, 1.9 mmol, 0.17 eq) and MeOH (20.0 mL), was stirred at reflux for 7 hours. under air. The solvent was removed under reduced pressure to afford crude dimethyl 4-hydroxyphthalate. The crude diester was dissolved in acetone (70 mL) and reacted with potassium carbonate (7.40 g, 53.5 mmol, 5.00 eq) at 50 °C for 20 min. Iodomethane (1.47 mL, 23.6 mmol, 2.20 eq) was added, and the mixture was stirred at reflux overnight. K_2CO_3 was removed by filtration and the solvent was removed under reduced pressure to afford a colorless oil.

The crude was dissolved in acetone (16.0 mL) and a 11 M solution of sodium hydroxide, (6.00 mL, 66.0 mmol, 6.20 eq) was added, and the solution was stirred for 6 hours under air at rt. The solution was then acidified with 2 M HCl to pH 3, and concentrated under reduced pressure. Then, the crude 4-methoxyphthalic acid was dissolved into acetone (50 mL) and dried over $MgSO_4$, filtered through a plug of cotton wool, and the solvent was removed in vacuo. The crude diacid was partitioned between 2 M NaOH (50 mL) and DCM (50 mL). The organic layer was extracted with NaOH 2 M (50 mL). The combined aqueous phase was cooled down to 0 °C and acidified with 37% HCl % to pH 3. The aqueous layer was then extracted five times with AcOEt (50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford the crude diacid as a light brown solid (1.82 g).

A solution of crude 4-methoxyphthalic acid **27** (1.82 g, 9.28 mmol, 1.00 eq) in acetic anhydride (25.0 mL, 266 mmol, 28.7 eq) was stirred at reflux for 21 hours. Volatiles were removed in vacuo to afford a dark brown solid. The crude was dissolved in DCM (50 mL) and filtered through fritted glass to remove solid impurities. The solution was concentrated under reduced pressure and dried in vacuo to afford the anhydride **27** as a light brown solid (1.62 g, 9.08 mmol, 83% yield over 4 steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, 1 H, J = 8.5, 0.4 Hz, Ar), 7.41 (d, 1 H, J = 2.2 Hz, Ar), 7.35 (dd, 1 H, J = 8.5, 2.3 Hz, Ar), 3.98 (s, 3 H, OMe).

[11] P. H. Mazzocchi, P. Wilson, F. Khachik, L. Klingler, S. Minamikawa, *J. Org. Chem.* **1983**, *48*, 2981.

HRMS (ESI) calcd for $C_9H_7O_4^+$ $[M+H]^+$ 179.0339; found 179.0349.

The ^{1}H NMR data for **27** corresponded to the reported values.[12]

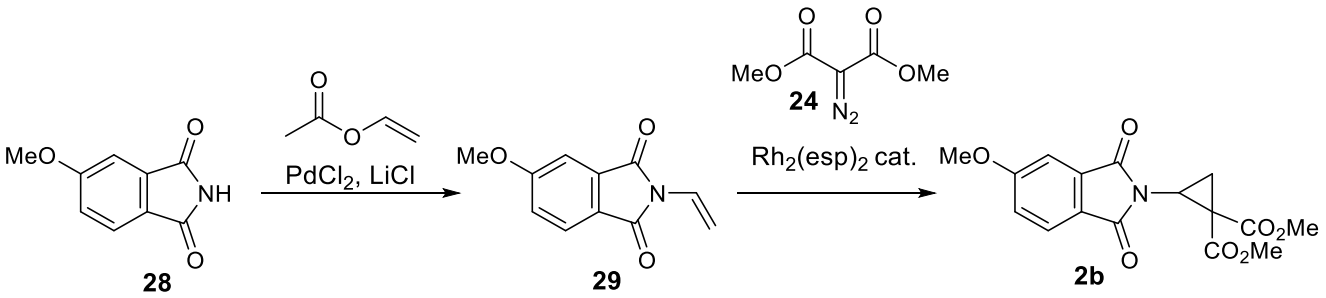
Following a modified procedure,[13] 5-methoxyisobenzofuran-1,3-dione (**27**) (1.58 g, 8.84 mmol, 1.00 eq) and formamide (35.0 mL, 880 mmol, 100 eq) were divided between four 20 mL microwave vials sealed with a microwave cap. The mixture was stirred at rt until the product was completely dissolved, then heated 2 times at 200 °C for 30 sec with 10 sec pre-stirring, using Biotage Initiator 2.0 microwave reactor. The mixture was cooled to 0 °C to induce crystallization and cold water (10 mL) was added into each vial. The obtained solid was filtrated over filter paper, washed with water (15 mL) and hexanes (20 mL) and dried under reduced pressure to afford 5-methoxyisoindoline-1,3-dione (**28**) as a beige solid (982 mg, 5.54 mmol, 63% yield) which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, 1 H, J = 8.3, 0.4 Hz, Ar), 7.59 (br s, 1 H, NH), 7.33 (d, 1 H, J = 2.2 Hz, Ar), 7.20 (dd, 1 H, J = 8.3, 2.3 Hz, Ar), 3.94 (s, 3 H, OMe).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.7, 165.0, 135.2, 125.4, 124.5, 120.4, 108.1, 56.2.

HRMS (ESI) calcd for $C_9H_8NO_3^+$ $[M+H]^+$ 178.0499; found 178.0497.

Dicarboxylate dimethyl 2-(5-methoxy-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (2b).



Following a modified procedure,[14] 5-methoxyisoindoline-1,3-dione (**28**) (980 mg, 5.53 mmol, 1.00 eq), $PdCl_2$ (98.0 mg, 0.553 mmol, 0.100 eq), LiCl (235 mg, 5.53 mmol, 1.00 eq, weighted in a glovebox) and vinyl acetate (13.7 mL, 148 mmol, 26.8 eq) were heated under reflux for 24 hours. The mixture was cooled down to room temperature and diluted with DCM/MeOH 4:1 (20 mL). Activated charcoal was added and the resulting suspension was filtered through a pad of Celite (DCM/MeOH 4:1 100 mL) and concentrated under reduced pressure. Purification by silica

[12] N. J. Hinde, C. D. Hall, *J. Chem. Soc., Perkin Trans. 2.* **1998**, 1249.

[13] K. Kacprzak, Synth. Commun. **2003**, *33*, 1499.

[14] E. Bayer, K. Geckeler, Angew. Chem. Int. Ed. Engl. 1979, *18*, 533.

gel chromatography (pentane/AcOEt 90:10 to 75:25) afforded 5-methoxy-2-vinylisoindoline-1,3-dione (**29**) as a colorless solid (828 mg, 4.08 mmol, 74% yield).

RF = 0.56 hexane/AcOEt (6:4).

Mp 102.2 – 105.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, 1 H, J = 8.3 Hz, Ar), 7.32 (d, 1 H, J = 2.2 Hz, Ar), 7.17 (dd, 1 H, J = 8.3, 2.2 Hz, Ar), 6.83 (dd, 1 H, J = 16.4, 9.9 Hz, =CH), 6.03 (d, 1 H, J = 16.4 Hz, =CH), 4.99 (d, 1 H, J = 9.9 Hz, =CH), 3.93 (s, 3 H, OMe).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.3, 165.1, 134.4, 125.5, 124.0, 123.5, 120.6, 108.2, 104.0, 56.3.

IR 1779 (w), 1720 (s), 1639 (w), 1619 (w), 1493 (w), 1386 (s), 1307 (w), 1295 (w), 1021 (w).

HRMS (ESI) calcd for $C_{11}H_{10}NO_3^+$ $[M+H]^+$ 204.0655; found 204.0662.

Following a modified procedure,[15] the corresponding 5-methoxy-2-vinylisoindoline-1,3-dione (**29**) (0.130 g, 0.640 mmol, 1.00 eq) was dissolved in dry dichloromethane (10.0 mL) and the solution was cooled down to 0 °C with an ice/water bath. Then, bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (0.5 mg, 0.6 µmol, 0.1 mol%) was added in one portion. A solution in dichloromethane (2.0 mL) of dimethyldiazomalonate (**24**) (0.121 g, 0.768 mmol, 1.20 eq) was added dropwise over 5 min. After the addition, the mixture was allowed to warm to room temperature and stirred overnight. The solvent was then removed under reduced pressure and the crude was purified by Biotage (SNAP Cartridge KP-Sil 10 g, 6:4 Hexane/AcOEt), to obtain dicarboxylate dimethyl 2-(5-methoxy-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**2b**) as a colorless solid (176 mg, 0.528 mmol, 83% yield).

RF = 0.15 pent/AcOEt (6:4).

Mp 113.5 – 117.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 1 H, J = 8.3 Hz, Phth), 7.27 (d, 1 H, J = 2.2 Hz, Phth), 7.14 (dd, 1 H, J = 8.3, 2.3 Hz, Phth), 3.90 (s, 3 H, OMe), 3.80 (s, 3 H, OMe-C=O), 3.66 (dd, 1 H, J = 8.5, 6.6 Hz, N-CH), 3.59 (s, 3 H, OMe-C=O), 2.68 (t, 1 H, J = 6.5 Hz, CH_2), 1.99 (dd, 1 H, J = 8.5, 6.4 Hz, CH_2).

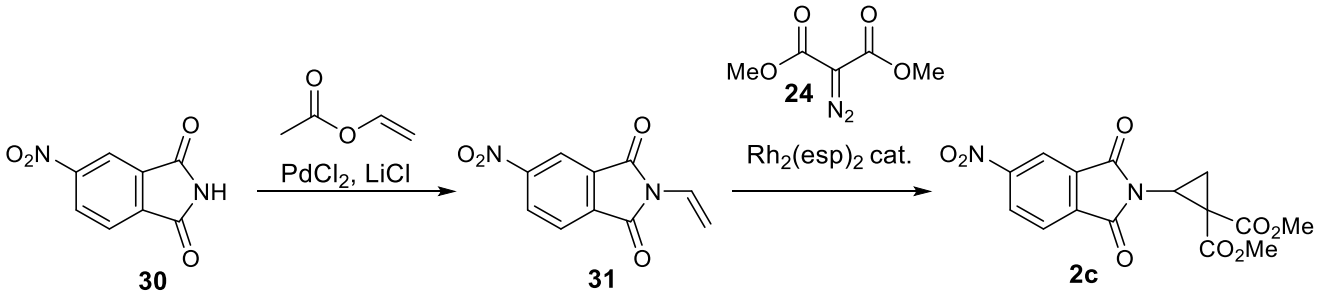
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 167.8, 167.6, 167.0, 165.0, 134.1, 125.3, 123.4, 120.4, 108.1, 56.2, 53.2, 53.0, 35.0, 33.2, 19.7.

IR 2955 (w), 1720 (s), 1492 (m), 1437 (m), 1397 (s), 1288 (s), 1133 (m), 1018 (w).

HRMS (ESI) calcd for $C_{16}H_{16}NO_7^+$ $[M+H]^+$ 334.0921; found 334.0915.

[15] F. Gonzalez-Bobes, M. D. B. Fenster, S. Kiau, L. Kolla, S. Kolotuchin, M. Soumeillant, *Adv. Synth. Catal.* **2008**, *350*, 813.

Dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (2c).



Following a modified procedure,[14] 5-nitrosoindoline-1,3-dione (**30**) (1.00 g, 5.20 mmol, 1.00 eq), $PdCl_2$ (92.0 mg, 0.520 mmol, 0.100 eq), LiCl (0.221 mg, 5.20 mmol, 1.00 eq, weighted in a glovebox) and vinyl acetate (12.9 mL, 139 mmol, 26.8 eq) were heated under reflux for 20 hours. The mixture was cooled down to room temperature and the solvent was evaporated under reduced pressure. The crude was purified by column chromatography using silica gel (Hexane/AcOEt 8:2 to 5:5) to afford 5-nitro-2-vinylisoindoline-1,3-dione (**31**) as a bright yellow solid (1.14 g, 5.23 mmol, quantitative yield).

RF = 0.32 pent/AcOEt (9:1).

Mp 144.3 – 148.6°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (dd, 1 H, J = 2.0, 0.5 Hz, Ar), 8.63 (dd, 1 H, J = 8.1, 2.0 Hz, Ar), 8.08 (m, 1 H, Ar), 6.88 (dd, 1 H, J = 16.4, 9.8 Hz, CH-N), 6.14 (dd, 1 H, J = 16.4, 0.5 Hz, $=CH_2$), 5.16 (dd, 1 H, J = 9.8, 0.4 Hz, $=CH_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 164.2, 152.1, 136.1, 133.1, 129.8, 125.0, 123.6, 119.2, 106.3.

IR 3101 (w), 3074 (w), 2924 (w), 1709 (s), 1533 (s), 1383 (s), 1341 (s), 1307 (s), 1062 (m), 1024 (s), 915 (s).

HRMS (ESI) calcd for $C_{10}H_6N_2O_4$ [M^+] 218.0328; found 218.0355.

Following a modified procedure,[15] the corresponding 5-nitro-2-vinylisoindoline-1,3-dione (**31**) (0.500 g, 2.29 mmol, 1.00 eq) was dissolved in dry dichloromethane (10.0 mL) and the solution was cooled down to 0 °C with an ice/water bath. Then, bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (1.7 mg, 2.3 µmol, 0.10 mol%). was added in one portion. A solution in dichloromethane (2.0 mL) of dimethyldiazomalonate (**24**) (0.544 g, 2.75 mmol, 1.20 eq)was added dropwise over 5 min. After the addition, the mixture was allowed to warm to room temperature and stirred overnight. The solvent is then removed under reduced pressure and the crude was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 7:3 Hexane/AcOEt), to obtain Dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**2c**) as a colorless solid (712 mg, 2.04 mmol, 89% yield).

RF = 0.19 pent/AcOEt (8:2).

Mp 113.0 – 115.8 °C.

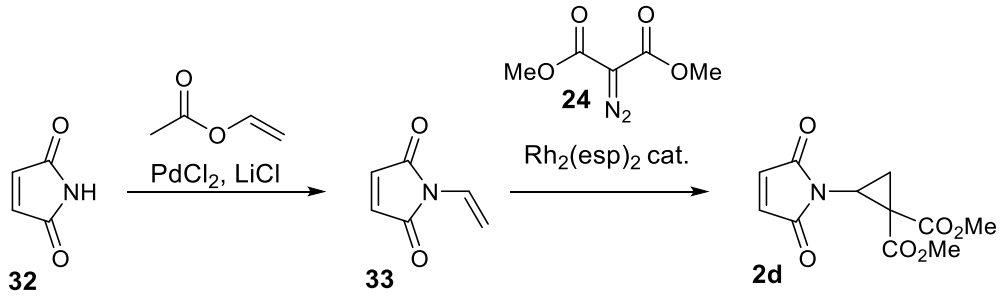
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (m, 2 H, Ar), 8.03 (d, 1 H, J = 8.1 Hz, Ar), 3.83 (s, 3 H, OMe), 3.70 (m, 1 H, CH-N), 3.62 (s, 3 H, OMe), 2.63 (m, 1 H, CH_2), 2.07 (m, 1 H, CH_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.1, 165.9, 165.6, 152.0, 135.9, 132.9, 129.6, 124.9, 119.0, 53.3, 53.2, 35.0, 33.1, 19.7.

IR 3110 (w), 2956 (w), 2926 (w), 2853 (w), 1726 (s), 1541 (m), 1400 (m), 1344 (s), 1222 (s), 1130 (m).

HRMS (ESI) calcd for $C_{15}H_{13}N_2O_8^+$ $[M+H]^+$ 349.0666; found 349.0664.

Dimethyl 2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)cyclopropane-1,1-dicarboxylate (2d).



Following a modified procedure,[14] maleimide (**32**) (1.30 g, 13.4 mmol, 1 equiv), palladium (II) chloride (0.237 g, 1.34 mmol, 0.1 equiv), lithium chloride (57.0 mg, 1.34 mmol, 0.1 equiv) and vinyl acetate (33.2 mL, 359 mmol, 27 equiv) were added in a microwave tube sealed with a microwave cap. After stirring at 80 °C for 23 h, the resulting mixture was cooled down to room temperature. Purification by Biotage (SNAP cartridge KP-Sil 50 g, hexane/AcOEt 93/7 to 40/60) afforded 1-vinyl-1*H*-pyrrole-2,5-dione (**33**) (1.74 g, 14.1 mmol, quantitative) as a bright yellow oil.

RF = 0.54 hexane/AcOEt (7:3).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (s, 2 H, CH-C=O), 6.67 (dd, 1 H, J = 16.4, 9.8 Hz, CH-N), 5.87 (d, 1 H, J = 16.3 Hz, $=CH_2$), 4.94 (d, 1 H, J = 9.8 Hz, $=CH_2$);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 134.5, 123.1, 103.4;

IR 3087 (w), 2359 (w), 2113 (w), 1716 (s), 1641 (m), 1384 (s), 1307 (w), 1221 (w), 1130 (w), 896 (w), 845 (m);

HRMS (APPI) calcd for $C_6H_5NO_2$ $[M^+]$ 123.0320; found 123.0323.

Following a modified procedure,[15] a solution of dimethyl 2-diazomalonate (**24**) (96 mg, 0.61 mmol, 1.5 equiv) in dichloromethane (1.0 mL) was added dropwise over 5 minutes to a solution

of 1-vinyl-1*H*-pyrrole-2,5-dione (**33**) (50. mg, 0.41 mmol, 1 equiv) and bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] (0.7 mg, 0.9 µmol, 0.2 mol %) in dichloromethane (2.0 mL) at 0 °C. The resulting mixture was stirred for 5 hours at room temperature and finally concentrated under reduced pressure. Purification by Biotage (SNAP cartridge KP-Sil 10 g, hexane/AcOEt 95/5 to 70/30) afforded dimethyl 2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)cyclopropane-1,1-dicarboxylate (**2d**) (66.9 mg, 0.264 mmol, 65% yield) as a colorless oil.

RF = 0.38 hexane/AcOEt (6:4).

Mp 78.4-80.7 °C ;

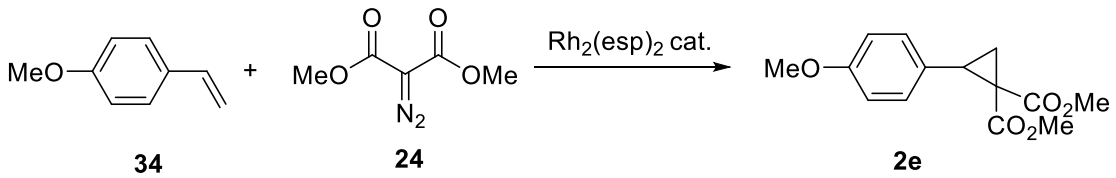
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 2 H, CH-C=O), 3.79 (s, 3 H, Me-O), 3.66 (s, 3 H, Me-O), 3.56-3.51 (m, 1 H, CH-N), 2.56 (dd, 1 H, J = 6.4, 6.5 Hz, CH_2), 1.96-1.91 (m, 1 H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 168.4, 167.0, 134.1, 53.1, 53.0, 34.3, 32.9, 19.3;

IR 2363 (w), 1727 (s), 1437 (w), 1332 (w), 1296 (w), 1220 (w), 1135 (w);

HRMS (ESI) calcd for $C_{11}H_{11}NNaO_6^+$ $[M+Na]^+$ 276.0479; found 276.0485.

Dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (2e).



34 **24** **2e**

Following a reported procedure,[15] $Rh_2(esp)_2$ (4.8 mg, 6.3 µmol, 0.1 mol%) was loaded in a flask in the glovebox. A solution of styrene (**34**) (0.85 mL, 6.3 mmol, 1 equiv, 1.2 M in DCM) (freshly filtered over a pad of aluminum oxide) was then added and the reaction mixture was stirred at 0°C. After 5 min, a solution of diazomalonate **24** (1.0 g, 6.3 mmol, 1.0 equiv, 1.2 M in DCM) was added. The resulting mixture was stirred at 0 °C for 10 min and then stirred overnight at 23 °C. The reaction mixture was then concentrated under reduced pressure and purified directly by column chromatography (PET/Et_2O 5:1 to 3:1) afforded cyclopropane **2e** (1.58 g, 5.98 mmol, 95%).

RF = 0.24 PET/ Et_2O (3:1).

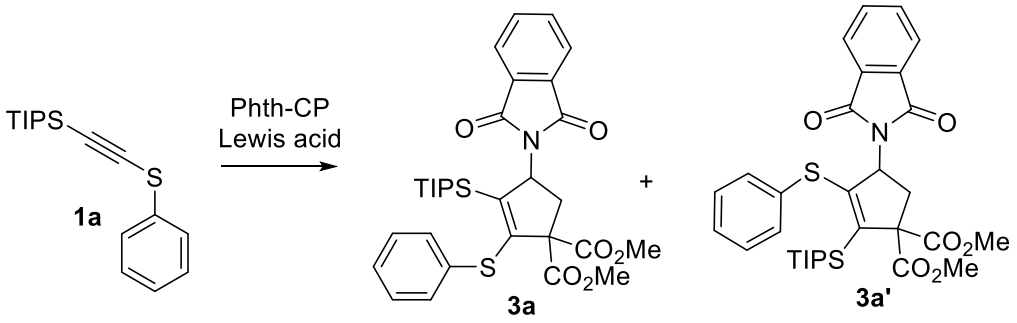
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.17-7.11 (m, 2H; ArH), 6.86-6.79 (m, 2H; ArH), 3.81 (s, 3H; CH_3), 3.80 (s, 3H; CH_3), 3.41 (s, 3H; CH_3), 3.20 (t, *J* = 8.2 Hz, 1H; CHPh), 2.18 (dd, *J* = 8.1, 5.2 Hz, 1H; CH_2), 1.74 (dd, *J* = 9.3, 5.2 Hz, 1H; CH_2).

The characterization data for **2e** corresponded to the reported values.[16]

3. Lewis acid catalysed reactions

3.1 [3+2] reaction with TIPS alkyne 1a

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(phenylthio)-2-(triisopropylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3a')



Thioalkyne **1a** (19 mg, 0.066 mmol, 1 equiv) was added with 0.3 mL of DCM to the phthalimide cyclopropane **2a** (20 mg, 0.066 mmol, 1 equiv) and scandium triflate (6.5 mg, 0.013 mmol, 0.2 equiv) in a flame dried flask under nitrogen and stirred for 1 hour. Then 0.1 mL of triethylamine was added as well as silica and the solvent was removed under reduced pressure. The product was purified through column chromatography with a mixture of pentane and ethylacetate (9:1 to 8:2) as eluting solvent. The desired compound was obtained as a mixture of two inseparable regio-isomers (1:3) **3a** and **3a'** (11 mg, 0.019 mmol, 29%) as a colorless oil. When the same reaction was performed with indium triflate (7.4 mg, 0.013 mmol, 0.2 equiv), the desired compound was obtained as a mixture of two inseparable regio-isomers (2:1) **3a** and **3a'** (7.6 mg, 0.019 mmol, 20%).

The ratio of regioisomers were determined by NMR through the integration of the NCH protons (minor at 5.37 ppm and major at 5.41 ppm) and the major regioisomer was assigned by correlation with the results obtained with TES-1-thiocyclopenten-3-amines.

RF = 0.67 pent/AcOEt (8:2).

^{1}H NMR (400 MHz, Chloroform-d, major isomer **3a'**) δ 7.81 (dd, *J* = 5.2, 3.2 Hz, 2H, Ar-H), 7.75 – 7.56 (m, 2H, Ar-H), 7.39 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.22 (q, *J* = 7.6 Hz, 2H, Ar-H), 7.05 (t, *J* = 7.4 Hz, 1H, Ar-H), 5.45 (t, *J* = 8.0 Hz, 1H, NCH), 3.59 (s, 3H, ester), 3.22 (dd, *J* = 13.8, 7.7 Hz, 1H, CH_2), 3.00 (d, *J* = 2.0 Hz, 3H, ester), 2.73 (dd, *J* = 13.9, 8.6 Hz, 1H, CH_2), 1.37 (m, 3H, TIPS), 1.07 – 0.72 (m, 18H, TIPS).

^{13}C NMR (101 MHz, Chloroform-d, major isomer **3a'**) δ 171.1, 168.3, 158.8, 143.8, 136.6, 134.2, 128.7, 128.7, 127.8, 127.4, 125.4, 123.4, 69.3, 58.9, 52.9, 52.3, 38.8, 19.0, 13.1.

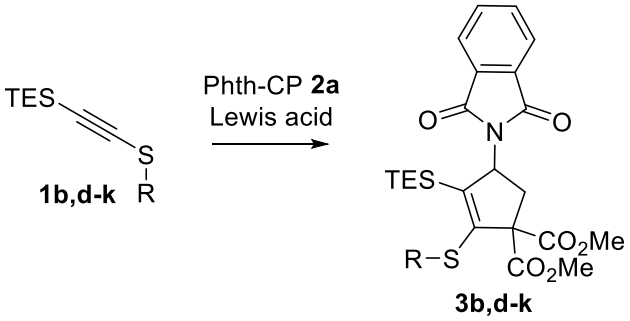
[16] F. De Simone, T. Saget, F. Benfatti, S. Almeida, J. Waser, *Chem. - Eur. J.* **2011**, *17*, 14527–14538.

IR 2950 (m), 2867 (w), 2265 (w), 1722 (s), 1713 (s), 1583 (w), 1472 (w), 1384 (m), 1354 (m), 1270 (m), 1199 (m), 1176 (m), 1116 (m), 973 (w), 910 (m), 883 (m).

HRMS (ESI) calcd for $C_{32}H_{40}NO_6SSi^+$ $[M+H]^+$ 594.2340; found 594.2364.

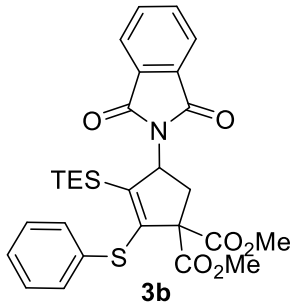
3.2 [3+2] reaction with TES alkyne

General procedure for TES scope of the 3+2 reaction (GP2).



Phthalimide cyclopropane **2a** (84 mg, 0.28 mmol, 1.2 equiv) and hafnium triflate (16 mg, 0.023 mmol, 0.1 equiv) were solubilized in dry DCM (2 mL) in a flame dried flask under nitrogen at room temperature. Then the thioalkyne (0.23 mmol, 1 equiv) was added with 0.3 mL of DCM to the reaction. After completion (between a few seconds and maximum 15 minutes), 0.5 mL of triethylamine was added as well as silica and the solvent was removed under reduced pressure. The product was purified through column chromatography with a mixture of pentane and ethylacetate (8:2 to 7:3) as eluting solvent. The ratio of regioisomers were determined by NMR through the integration of the NCH protons (major typically at 5.37 ppm and minor typically at 5.41 ppm). NMR studies as well as X-ray measurement were performed to assign the major regioisomer.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(phenylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3b).



Following the general procedure **GP2**, with the thioalkyne **1b** (57 mg, 0.23 mmol, 1 equiv), the desired product was obtained as a mixture of two inseparable regio-isomers (13:1) **3b** (95 mg, 0.17 mmol, 75%) as a white solid.

When the reaction was performed with 20 mol% hafnium triflate (33 mg, 0.046 mmol, 0.2 equiv), the desired compound was obtained as a mixture of two inseparable regio-isomers (13:1) **3b** (93 mg, 0.17 mmol, 73%).

When the same reaction was performed with scandium triflate (23 mg, 0.046 mmol, 0.2 equiv), the desired compound was obtained as a mixture of two inseparable regio-isomers (13:1) **3b** (80 mg, 0.15 mmol, 63%).

When the same reaction was performed with indium triflate (26 mg, 0.046 mmol, 0.2 equiv), the desired compound was obtained as a mixture of two inseparable regio-isomers (13:1) **3b** (58 mg, 0.10 mmol, 45%).

Mp 167.0-169.1 °C.

RF = 0.42 pent/AcOEt (8:2).

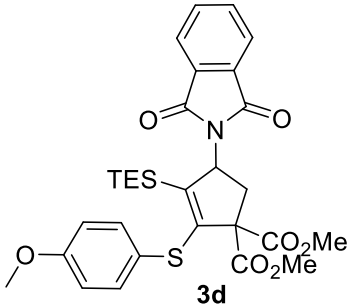
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.79 (m, 2H, ArH), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H, ArH), 7.38 – 7.33 (m, 2H, ArH), 7.24 (t, *J* = 7.7 Hz, 2H, ArH), 7.10 – 7.00 (m, 1H, ArH), 5.36 (t, *J* = 8.2 Hz, 1H, NCH), 3.63 (s, 3H, ester), 3.18 – 3.09 (m, 1H, CH_2), 3.08 (s, 3H, ester), 2.78 (dd, *J* = 13.5, 8.3 Hz, 1H, CH_2), 0.77 (m, 9H, TES), 0.71 – 0.46 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.7, 169.5, 168.6, 161.3, 142.8, 137.9, 135.2, 132.8, 129.8, 128.2, 126.3, 124.4, 70.3, 59.2, 53.9, 53.4, 40.0, 8.3, 4.2.

IR 3460 (w), 3065 (w), 2955 (w), 1720 (s), 1608 (w), 1441 (w), 1362 (m), 1284 (m), 1120 (m), 1049 (w).

HRMS (ESI) calcd for $C_{29}H_{33}NNaO_6SSi^+$ $[M+Na]^+$ 574.1690; found 574.1702.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-((4-methoxyphenyl)thio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3d).



3d

Following the general procedure **GP2**, with the thioalkyne **1d** (64 mg, 0.23 mmol, 1 equiv), the desired product **3d** was obtained as a mixture of two inseparable regio-isomers (17:1) (103 mg, 0.177 mmol, 77%) as a white solid.

RF = 0.45 pent/AcOEt (7:3).

Mp 163.9-166.4 °C.

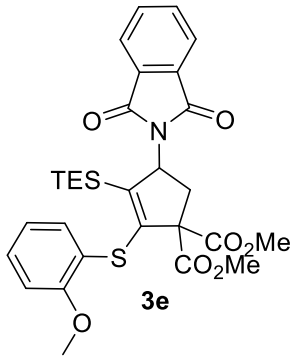
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H, Ar-H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.29 (d, *J* = 8.9 Hz, 2H, Ar-H), 6.81 (d, *J* = 8.9 Hz, 2H, Ar-H), 5.33 (t, *J* = 8.2 Hz, 1H, NCH), 3.72 (s, 3H, MeO), 3.61 (s, 3H, ester), 3.15 (s, 3H, ester), 3.07 (dd, *J* = 13.4, 8.1 Hz, 1H, CH_2), 2.75 (dd, *J* = 13.4, 8.2 Hz, 1H, CH_2), 0.83 – 0.70 (m, 9H, TES), 0.65 – 0.40 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 168.7, 167.7, 158.4, 158.1, 143.0, 134.3, 131.9, 129.6, 126.9, 123.5, 114.5, 69.3, 58.3, 55.4, 52.9, 52.6, 39.4, 7.4, 3.3.

IR 2954 (w), 2881 (w), 1721 (s), 1578 (w), 1470 (w), 1385 (m), 1271 (m), 1122 (m), 1017 (w).

HRMS (ESI) calcd for $C_{30}H_{35}NNaO_7SSi^+$ $[M+Na]^+$ 604.1796; found 604.1803.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-((2-methoxyphenyl)thio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3e).



3e

Following the general procedure **GP2**, with the thioalkyne **1e** (64 mg, 0.23 mmol, 1 equiv), the desired product **3e** was obtained as a mixture of two inseparable regio-isomers (11:1) (113 mg, 0.194 mmol, 84%) as a crystalizing oil.

RF = 0.48 pent/AcOEt (7:3).

Mp 112.2-112.7 °C.

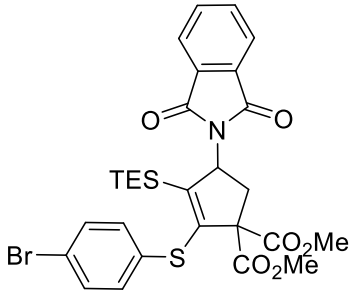
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (dd, *J* = 5.4, 3.0 Hz, 2H, Ar-H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.46 (dd, *J* = 7.7, 1.6 Hz, 1H, Ar-H), 7.06 (td, *J* = 7.7, 1.7 Hz, 1H, Ar-H), 6.97 (td, *J* = 7.5, 1.3 Hz, 1H, Ar-H), 6.78 (dd, *J* = 8.1, 1.3 Hz, 1H, Ar-H), 5.39 (t, *J* = 8.3 Hz, 1H, NCH), 3.86 (s, 3H, MeO), 3.67 (s, 3H, ester), 3.29 – 3.14 (m, 1H, CH_2), 3.11 (s, 3H, ester), 2.77 (dd, *J* = 13.5, 8.2 Hz, 1H, CH_2), 0.86 – 0.71 (m, 9H, TES), 0.60 (qd, *J* = 7.7, 1.3 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 168.5, 167.7, 161.1, 155.4, 141.7, 134.2, 132.0, 127.8, 126.0, 126.0, 123.5, 121.5, 110.1, 69.5, 58.4, 55.9, 53.0, 52.3, 39.0, 7.3, 3.2.

IR 2954 (w), 2881 (w), 1720 (s), 1599 (w), 1460 (w), 1385 (m), 1275 (s), 1183 (m), 1120 (m), 1015 (w), 954 (w), 833 (w).

HRMS (ESI) calcd for $C_{30}H_{35}NNaO_7SSi^+$ $[M+Na]^+$ 604.1796; found 604.1805.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-((4-bromophenyl)thio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3f).



3f

Following the general procedure **GP2**, with the thioalkyne **1f** (75 mg, 0.23 mmol, 1 equiv), the desired product **3f** was obtained as a mixture of two inseparable regio-isomers (20:1) (90 mg, 0.14 mmol, 62%) as a white solid.

RF = 0.81 pent/AcOEt (7:3).

Mp 177.1-180.2 °C.

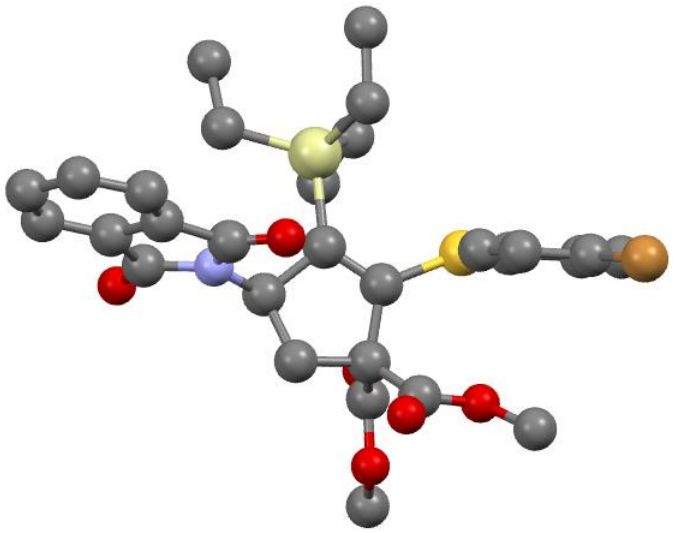
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.46 – 7.31 (m, 2H, Ar-H), 7.38 – 7.25 (m, 2H, Ar-H), 5.38 (t, *J* = 8.2 Hz, 1H, NCH), 3.67 (s, 3H, ester), 3.18 (s, 3H, ester), 3.12 (dd, *J* = 13.5, 8.2 Hz, 1H, CH_2), 2.82 (dd, *J* = 13.5, 8.2 Hz, 1H, CH_2), 0.78 (t, *J* = 7.8 Hz, 9H, TES), 0.67 – 0.40 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.6, 168.5, 167.6, 161.4, 141.3, 136.5, 134.3, 131.8, 128.7, 123.6, 119.1, 69.4, 58.4, 53.1, 52.6, 39.0, 7.3, 3.2. One carbon is not resolved.

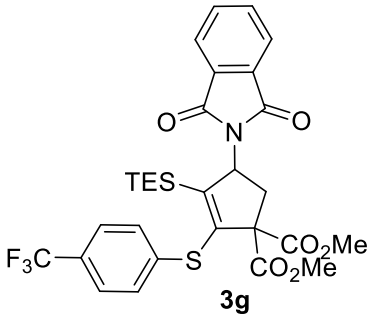
IR 2938 (w), 2880 (w), 1721 (s), 1467 (w), 1386 (m), 1273 (m), 1121 (w), 1011 (w).

HRMS (ESI) calcd for $C_{29}H_{32}{}^{79}BrNNaO_6SSi^+$ $[M+Na]^+$ 652.0795; found 652.0796.

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: **CCDC 1470377**



Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-((4-trifluoromethylphenyl)thio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3g).



3g

Following the general procedure **GP2**, with the thioalkyne **1g** (73 mg, 0.23 mmol, 1 equiv), the desired product **3g** was obtained as a mixture of two inseparable regio-isomers >20:1) (63 mg, 0.10 mmol, 44%) as a white solid.

RF = 0.73 pent/AcOEt (7:3).

Mp 152.1-153.2 °C.

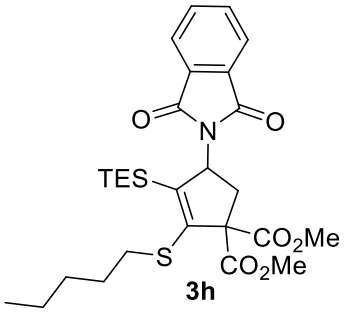
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (dd, *J* = 5.4, 3.0 Hz, 2H, Ar-H), 7.74 (dt, *J* = 5.3, 2.2 Hz, 2H, Ar-H), 7.52 (m, 4H, Ar-H), 5.41 (td, *J* = 8.2, 1.4 Hz, 1H, NCH), 3.69 (d, *J* = 1.5 Hz, 3H, ester), 3.14 (m, 4H, ester and CH_2), 2.85 (ddd, *J* = 13.6, 8.3, 1.5 Hz, 1H, CH_2), 0.88 – 0.67 (m, 9H, TES), 0.68 – 0.44 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.6, 168.4, 167.7, 162.4, 142.8, 140.6, 134.4, 131.8, 127.3 (q, *J* = 32.7 Hz), 126.7, 125.6 (d, *J* = 3.8 Hz), 124.2 (q, *J* = 271.7 Hz), 123.6, 69.5, 58.4, 53.1, 52.5, 38.9, 7.3, 3.1.

IR 2953 (w), 2882 (w), 1723 (s), 1617 (w), 1389 (m), 1329 (s), 1274 (m), 1170 (m), 1131 (s), 1012 (w), 845 (w).

HRMS (ESI) calcd for $C_{30}H_{32}F_3NNaO_6SSi^+$ $[M+Na]^+$ 642.1564; found 642.1589.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(pentylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3h).



3h

Following the general procedure **GP2**, with the thioalkyne **1h** (56 mg, 0.23 mmol, 1 equiv), the desired product **3h** was obtained as a mixture of two inseparable regio-isomers (33:1) (99 mg, 0.18 mmol, 79%) as a colorless oil.

RF = 0.71 pent/AcOEt (7:3).

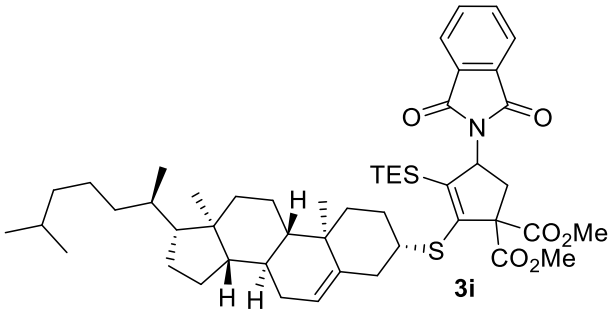
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.60 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 5.29 (dd, *J* = 8.1, 7.0 Hz, 1H, NCH), 2.87 (dd, *J* = 13.4, 7.0 Hz, 1H, CH_2), 2.77 (dd, *J* = 13.4, 8.1 Hz, 1H, CH_2), 2.76 – 2.67 (m, 2H, CH_2 chain), 1.48 (p, *J* = 7.4 Hz, 2H, CH_2 chain), 1.32-1.23 (m br., 4H, CH_2 chain), 0.83 – 0.74 (m, 3H, CH_3 chain), 0.74 (t, *J* = 7.8 Hz, 9H, TES), 0.60 – 0.52 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 170.5, 168.3, 150.3, 148.4, 134.8, 132.5, 124.0, 71.7, 59.2, 53.6, 53.5, 41.2, 35.7, 31.8, 29.7, 23.0, 14.6, 8.1, 4.0.

IR 2953 (w), 2879 (w), 1718 (s), 1460 (w), 1383 (m), 1265 (m), 1116 (m), 1009 (w), 913 (w).

HRMS (ESI) calcd for $C_{28}H_{40}NO_6SSi^+$ $[M+H]^+$ 546.2340; found 546.2338.

Dimethyl 3-(((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)thio)-4-(1,3-dioxoisoindolin-2-yl)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3i).



3i

Following the general procedure **GP2**, with the thioalkyne **1i** (124 mg, 0.230 mmol, 1 equiv), the desired product **3i** was obtained as a mixture of two inseparable diastereo-isomers (158 mg, 0.187 mmol, 81%, 1:1 d.r.) as a white foam.

RF = 0.82 pent/AcOEt (7:3).

Mp 84.1-87.3 °C.

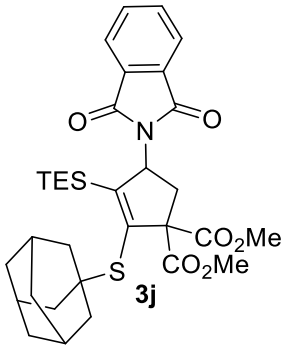
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar-H), 7.60 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 5.27 (m, 2H, C=CH and NCH), 3.70 (s, 3H, ester), 3.65 (s, 3H, ester), 3.00 – 2.83 (m, 2H, CH_2 cyclopentyl and CHS), 2.75 (ddd, *J* = 16.2, 13.3, 8.1 Hz, 1H, CH_2 cyclopentyl), 2.33 – 2.22 (m, 1H), 2.11 (dd, *J* = 26.9, 13.7 Hz, 1H), 1.94 – 1.65 (m, 5H), 1.49 – 1.11 (m, 13H), 1.10-0.97 (m, 7H), 0.93-0.84 (m, 5H), 0.82-0.69 (m, 19H, TES and CH_3 and other protons), 0.62 – 0.51 (m, 9H, TES and CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.3, 171.2, 169.8, 169.7, 167.6, 148.7, 146.6, 146.4, 141.9, 141.9, 134.1, 131.9, 123.4, 121.1, 121.1, 71.1, 58.6, 58.6, 56.8, 56.2, 53.1, 53.0, 52.9, 50.3, 50.2, 47.4, 47.3, 42.3, 40.5, 40.5, 40.3, 40.0, 39.9, 39.8, 39.7, 39.5, 36.7, 36.7, 36.2, 35.8, 31.9, 31.9, 30.6, 30.0, 28.3, 28.0, 24.3, 23.9, 22.8, 22.6, 21.0, 19.4, 18.7, 11.9, 7.4, 3.3. Some carbon are not resolved.

IR 2946 (s), 2875 (m), 2092 (w), 1465 (w), 1382 (w), 1015 (w), 917 (w), 869 (w).

HRMS (ESI) calcd for $C_{50}H_{73}NNaO_6SSi^+$ $[M+Na]^+$ 866.4820; found 866.4810.

Dimethyl 3-(adamantan-1-ylthio)-4-(1,3-dioxoisoindolin-2-yl)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3j).



3j

Following the general procedure **GP2**, with the inseparable mixture of alkyne **1j** and unprotected thio alkyne **1i'** (ratio 1:0.4) (0.071 g, **1j** 0.17 mmol, **1j'** 0.06 mmol), the desired product was obtained as a single regio-isomer **3j** (86 mg, 0.14 mmol, 85%) as a white foam.

RF = 0.69 pent/AcOEt (7:3).

Mp 165.6-168.9 °C.

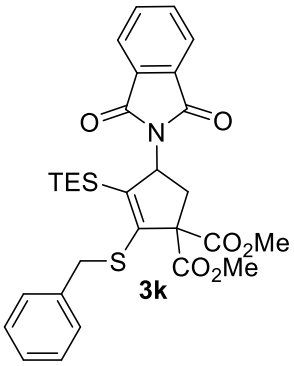
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.59 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 5.21 – 5.02 (m, 1H, NCH), 3.68 (s, 3H, ester), 3.61 (s, 3H, ester), 2.97 (dd, *J* = 12.6, 9.1 Hz, 1H, CH_2), 2.66 (dd, *J* = 12.7, 7.4 Hz, 1H, CH_2), 1.98 – 1.90 (m, 3H, CH), 1.82 (t, *J* = 3.5 Hz, 6H, CH_2), 1.64 – 1.44 (m, 6H, CH_2), 0.81 – 0.67 (m, 9H, TES), 0.67 – 0.57 (m, 2H, TES), 0.53 (m, 4H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.2, 169.6, 167.6, 156.7, 145.0, 134.1, 131.9, 123.4, 71.9, 58.3, 52.9, 52.9, 51.2, 44.4, 39.2, 36.2, 30.6, 7.4, 4.1.

IR 2902 (m), 2858 (w), 1720 (s), 1613 (w), 1444 (w), 1387 (m), 1267 (s), 1199 (m), 1118 (m), 1030 (w), 898 (w).

HRMS (ESI) calcd for $C_{33}H_{44}NO_6SSi^+$ $[M+H]^+$ 610.2653; found 610.2678.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(benzylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3k).



Following the general procedure **GP2**, with the thioalkyne **1k** (60 mg, 0.23 mmol, 1 equiv), the desired product **3k** was obtained as a mixture of two inseparable regio-isomers (33:1) (125 mg, 0.221 mmol, 96%) as a colorless oil.

RF = 0.63 pent/AcOEt (7:3).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.60 (dd, *J* = 5.4, 3.0 Hz, 2H, Ar-H), 7.24 – 7.15 (m, 5H, Ar-H), 5.31 (dd, *J* = 8.1, 7.1 Hz, 1H, NCH), 4.02 (d, *J* = 11.1 Hz, 1H, CH_2 benzylic), 3.94 (d, *J* = 11.1 Hz, 1H, CH_2 benzylic), 3.74 (s, 3H, ester), 3.67 (s, 3H, ester), 2.92 (dd, *J* = 13.4, 7.1 Hz, 1H, CH_2), 2.79 (dd, *J* = 13.4, 8.1 Hz, 1H, CH_2), 0.86 – 0.69 (m, 9H, TES), 0.63 – 0.45 (m, 6H, TES).

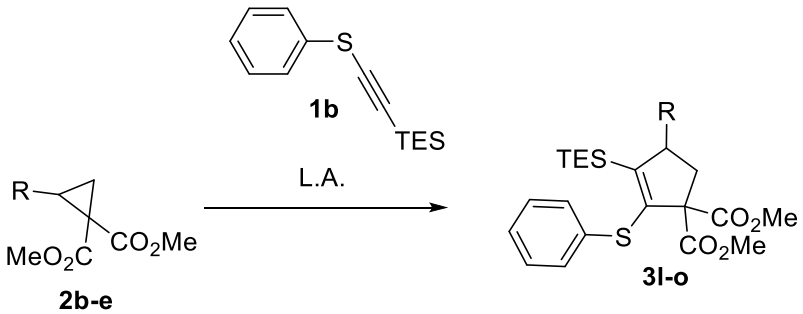
^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 170.5, 168.3, 151.2, 147.9, 137.6, 134.8, 132.5, 129.9, 129.2, 127.9, 124.0, 71.8, 59.1, 53.7, 53.6, 41.2, 40.3, 8.1, 4.0.

IR 3072 (w), 2942 (w), 1718 (s), 1441 (w), 1341 (w), 1258 (m), 1202 (w), 1118 (m), 911 (s).

HRMS (ESI) calcd for $C_{30}H_{36}NO_6SSi^+$ $[M+H]^+$ 566.2027; found 566.2032.

3.3 [3+2] reaction with TES thioalkyne and different DA-cyclopropanes

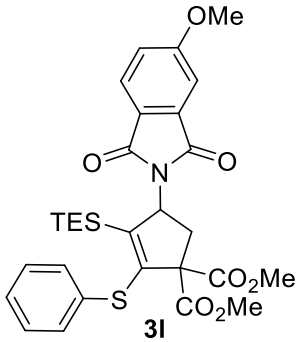
General procedure for the cyclopropane scope. (GP3)



Phthalimide cyclopropane **2b-e** (0.10 mmol, 1.2 eq) and hafnium triflate (6.0 mg, 0.0083 mmol, 0.1 eq) were solubilized in dry DCM (0.8 mL) in a flame dried flask under nitrogen. Then the

triethyl((phenylthio)ethynyl)silane (**1b**) (21 mg, 0.083 mmol, 1 eq) was added with 0.3 mL of DCM to the reaction. After completion, 0.2 mL of triethylamine was added as well as silica and the solvent was removed under reduced pressure. The product was purified through column chromatography with a mixture of pentane and ethylacetate (8:2 to 7:3) as eluting solvent.

Dimethyl 4-(5-methoxy-1,3-dioxoisoindolin-2-yl)-3-(phenylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3l).



3l

Following the general procedure **GP3**, with the cyclopropane **2b** (34 mg, 0.10 mmol, 1.2 equiv), the desired product **3l** was obtained as a mixture of two inseparable regio-isomers (ratio 20:1) (18 mg, 0.031 mmol, 36%) as a colorless oil.

RF = 0.30 pent/AcOEt (8:2).

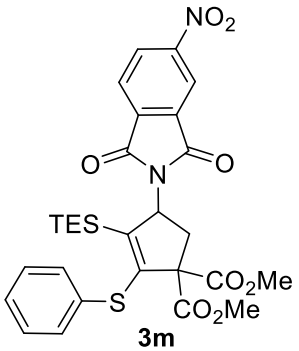
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.3 Hz, 1H, ArH), 7.33 (m, 2H, ArH), 7.30 (d, *J* = 2.3 Hz, 1H, ArH), 7.24 (t, *J* = 7.8 Hz, 2H, ArH), 7.13 (dd, *J* = 8.3, 2.4 Hz, 1H, ArH), 7.05 (t, *J* = 7.4 Hz, 1H, ArH), 5.33 (t, *J* = 8.2 Hz, 1H, NCH), 3.88 (s, 3H, ester), 3.63 (s, 3H, MeO), 3.12 (d, *J* = 13.5 Hz, 1H, CH_2), 3.07 (s, 3H, ester), 2.76 (dd, *J* = 13.5, 8.1 Hz, 1H, CH_2), 0.77 (t, *J* = 7.8 Hz, 9H, TES), 0.59 (q, *J* = 7.5 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 169.4, 166.5, 166.2, 160.0, 152.9, 144.0, 137.5, 137.0, 134.1, 130.5, 129.8, 128.3, 126.5, 125.7, 119.9, 70.4, 59.3, 57.1, 54.0, 53.5, 40.0, 8.3, 4.2.

IR 3062 (w), 2953 (m), 1715 (s), 1606 (w), 1486 (m), 1444 (m), 1377 (s), 1278 (s), 1196 (m), 1111 (m), 1015 (m), 913 (w).

HRMS (ESI) calcd for $C_{30}H_{36}NO_7SSi^+$ $[M+H]^+$ 582.1976; found 582.1982.

Dimethyl 4-(5-nitro-1,3-dioxoisoindolin-2-yl)-3-(phenylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3m).



3m

Following the general procedure **GP3**, with cyclopropane **2c** (35 mg, 0.10 mmol, 1.2 equiv), the desired product **3m** was obtained as a mixture of two inseparable regio-isomers (ratio 20:1) (47 mg, 0.078 mmol, 94%) as a white foam.

RF = 0.50 pent/AcOEt (8:2).

Mp 64.9-69.1 °C.

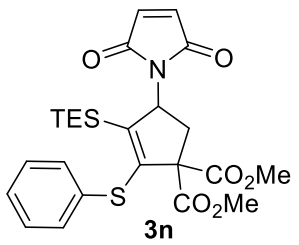
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 1.9 Hz, 1H, Ar-H), 8.60 (dd, *J* = 8.2, 2.0 Hz, 1H, Ar-H), 8.04 (d, *J* = 8.1 Hz, 1H, Ar-H), 7.35 (d, *J* = 7.7 Hz, 2H, Ar-H), 7.26 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.09 (t, *J* = 7.3 Hz, 1H, Ar-H), 5.40 (t, *J* = 8.1 Hz, 1H, NCH), 3.64 (s, 3H, ester), 3.19 (m, 1H, CH_2), 3.18 – 3.05 (s,3H, ester), 2.83 (dd, *J* = 13.6, 8.3 Hz, 1H, CH_2), 0.78 (t, *J* = 7.8 Hz, 9H, TES), 0.58 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 169.4, 166.5, 166.2, 160.1, 152.9, 144.0, 137.5, 137.0, 134.1, 130.3, 129.8, 128.3, 126.5, 125.7, 119.9, 70.4, 59.9, 54.0, 53.5, 40.0, 8.2, 4.2.

IR 3071 (w), 2957 (w), 2881 (w), 1722 (s), 1568 (w), 1442 (w), 1383 (m), 1346 (s), 1264 (m), 1116 (m), 973 (w), 913 (m).

HRMS (ESI) calcd for $C_{29}H_{33}N_2O_8SSi^+$ $[M+H]^+$ 597.1721; found 597.1727.

Dimethyl 4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-3-(phenylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3n).



3n

Following the general procedure **GP3**, with the cyclopropane **2d** (25 mg, 0.10 mmol, 1.2 equiv), the desired product **3n** was obtained as a mixture of two inseparable regio-isomers (ratio 17:1) (26 mg, 0.052 mmol, 62%) as a colorless oil.

RF = 0.71 pent/AcOEt (7:3).

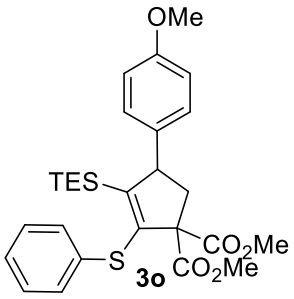
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.25 (m, 2H, Ar-H), 7.25 – 7.14 (m, 4H, Ar-H and C=CH), 7.04 (t, *J* = 7.3 Hz, 1H, Ar-H), 5.17 (t, *J* = 8.1 Hz, 1H, NCH), 3.60 (s, 3H, ester), 3.08 (s, 3H, ester), 2.97 (dd, *J* = 13.5, 8.1 Hz, 1H, CH_2), 2.72 (dd, *J* = 13.5, 8.2 Hz, 1H, CH_2), 0.79 (t, *J* = 7.9 Hz, 9H, TES), 0.57 (q, *J* = 7.7 Hz, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.6, 170.0, 168.5, 159.8, 142.4, 136.8, 134.5, 128.8, 127.3, 125.5, 69.3, 58.1, 53.0, 52.5, 39.1, 7.4, 3.2.

IR 2978 (w), 2881 (w), 1712 (s), 1579 (w), 1442 (w), 1394 (m), 1270 (m), 1161 (m), 1090 (w), 1011 (w), 912 (m), 832 (m).

HRMS (ESI) calcd for $C_{25}H_{32}NO_6SSi^+$ $[M+H]^+$ 502.1714; found 502.1716.

Dimethyl 4-(4-methoxyphenyl)-2-(phenylthio)-3-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3o).



3o

Following the general procedure **GP3**, with the cyclopropane **2e** (25 mg, 0.10 mmol, 1.2 eq), the desired product **3o** was obtained as a mixture of two inseparable regio-isomers (ratio >20:1) (30 mg, 0.058 mmol, 70%) as a colorless oil.

RF = 0.9 pent/AcOEt (8:2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.26 (m, 4H, Ar-H), 7.16 (m, 3H, Ar-H), 6.91 (d, *J* = 8.6 Hz, 2H, Ar-H), 4.10 (dd, *J* = 8.6, 6.2 Hz, 1H, ArCH), 3.86 (s, 3H, MeO), 3.50 (s, 3H, ester), 3.37 (s, 3H, ester), 3.18 (dd, *J* = 13.8, 8.5 Hz, 1H, CH_2), 2.58 (dd, *J* = 13.9, 6.2 Hz, 1H, CH_2), 0.87 (t, *J* = 7.9 Hz, 9H, TES), 0.72 – 0.40 (m, 6H, TES).

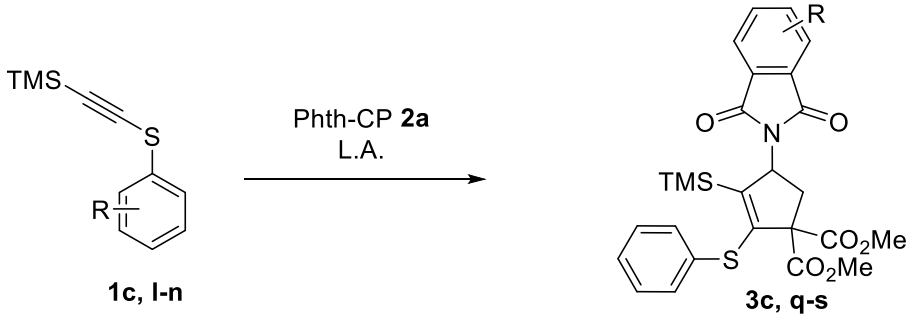
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 171.1, 165.8, 158.9, 141.0, 137.3, 136.6, 129.4, 129.1, 127.8, 125.9, 114.3, 70.9, 55.8, 55.7, 53.0, 52.9, 45.2, 7.9, 4.0.

IR 2998 (w), 2953 (m), 2879 (w), 2834 (w), 1733 (s), 1612 (w), 1583 (w), 1512 (m), 1442 (w), 1249 (s), 1173 (m), 1089 (w), 1039 (m), 913 (w), 836 (w).

HRMS (ESI) calcd for $C_{28}H_{37}O_5SSi^+$ $[M+H]^+$ 513.2125; found 513.2144.

3.4 [3+2] reaction with TMS thioalkynes

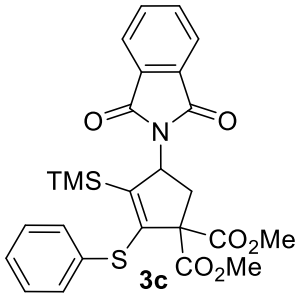
General procedure for TMS scope of the 3+2 reaction. (GP4)



1c, l-n **3c, q-s**

Phthalimide cyclopropane **2a** (70 mg, 0.23 mmol, 1.2 equiv) and indium triflate (6.5 mg, 0.012, 0.05 equiv) were solubilized in dry DCM (2 mL) in a flame dried flask under nitrogen. Then thioalkyne **1** (0.19 mmol, 1.0 equiv) was added with 0.3 mL of DCM to the reaction. After completion, 0.5 mL of triethylamine was added as well as silica and the solvent was removed under reduced pressure. The product was purified through column chromatography with a mixture of pentane and ethylacetate (8:2) as eluting solvent.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(phenylthio)-2-(trimethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3c).



3c

Following the general procedure **GP4** with the thioalkyne **1c** (57 mg, 0.19 mmol, 1.0 equiv), the desired product **3c** (78 mg, 0.15 mmol, 79%) was obtained as a colorless oil.

RF = 0.39 pent/AcOEt (8:2).

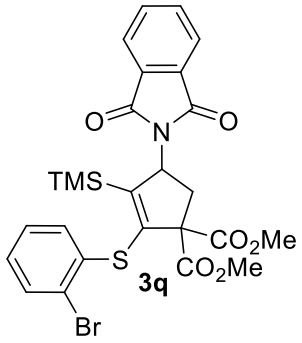
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.45 – 7.33 (m, 2H, Ar-H), 7.29 (dd, *J* = 15.2, 7.3 Hz, 2H, Ar-H), 7.18 – 7.04 (m, 1H, Ar-H), 5.49 (t, *J* = 8.2 Hz, 1H, NCH), 3.68 (s, 3H, ester), 3.21 (s, 3H, ester), 3.13 (dd, *J* = 13.4, 8.3 Hz, 1H, CH_2), 2.89 (dd, *J* = 13.4, 8.2 Hz, 1H, CH_2), 0.06 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 170.0, 168.6, 162.1, 142.2, 137.8, 135.2, 132.8, 129.8, 128.1, 126.3, 124.5, 70.3, 58.5, 54.0, 53.5, 40.1, 0.0.

IR 3051 (w), 2957 (w), 2257 (w), 1718 (s), 1472 (w), 1385 (m), 1270 (m), 1120 (m), 910 (s), 850 (s).

HRMS (ESI) calcd for $C_{26}H_{27}NNaO_6SSi^+$ $[M+Na]^+$ 532.1221; found 532.1216.

Dimethyl 3-((2-bromophenyl)thio)-4-(1,3-dioxoisoindolin-2-yl)-2-(trimethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3q).



Following the general procedure **GP4** with the thioalkyne **1l** (55 mg, 0.19 mmol, 1.0 equiv), the desired product **3q** (33 mg, 0.055 mmol, 29%) was obtained as a colorless oil.

RF = 0.63 pent/AcOEt (7:3).

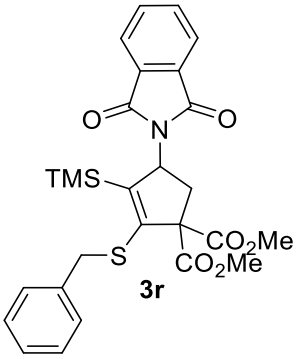
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar-H), 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar-H), 7.58 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar-H), 7.45 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar-H), 7.31 (td, *J* = 7.7, 1.4 Hz, 1H, Ar-H), 6.96 (td, *J* = 7.6, 1.5 Hz, 1H, Ar-H), 5.47 (t, *J* = 8.3 Hz, 1H, NCH), 3.72 (s, 3H, ester), 3.24 (s, 3H, ester), 3.13 (dd, *J* = 13.4, 8.4 Hz, 1H, CH_2), 2.85 (dd, *J* = 13.4, 8.1 Hz, 1H, CH_2), 0.00 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 169.6, 168.8, 163.7, 142.4, 140.0, 135.4, 133.5, 132.9, 129.4, 129.0, 127.4, 124.6, 121.6, 70.6, 58.7, 54.3, 53.7, 40.1, 0.0.

IR 2956 (w), 1719 (s), 1566 (w), 1385 (m), 1261 (m), 1109 (m), 970 (w), 912 (w), 848 (m).

HRMS (ESI) calcd for $C_{26}H_{26}{}^{79}BrNNaO_6SSi^+$ $[M+Na]^+$ 610.0326; found 610.0320.

Dimethyl 3-(benzylthio)-4-(1,3-dioxoisoindolin-2-yl)-2-(trimethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3r).



3r

Following the general procedure **GP4**, with the thioalkyne **1m** (42 mg, 0.19 mmol, 1.0 equiv), the desired product **3r** (42 mg, 0.081 mmol, 43%) was obtained as a colorless oil.

RF = 0.54 pent/AcOEt (7:3).

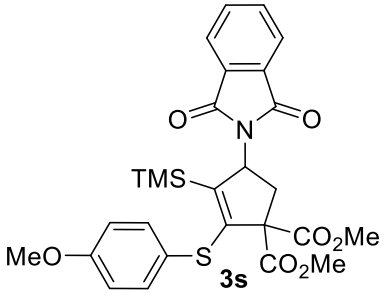
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar-H), 7.60 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.24 – 7.09 (m, 5H, Ar-H), 5.35 (t, *J* = 7.6 Hz, 1H, NCH), 3.98 (d, *J* = 11.3 Hz, 1H, benzylic CH_2), 3.90 (d, *J* = 11.2 Hz, 1H, benzylic CH_2), 3.72 (s, 3H, ester), 3.67 (s, 3H, ester), 2.89 (dd, *J* = 13.2, 7.4 Hz, 1H, CH_2), 2.81 (dd, *J* = 13.2, 7.9 Hz, 1H, CH_2), -0.00 (s, 9H, TMS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 170.3, 168.1, 153.5, 146.8, 137.5, 134.6, 132.3, 129.6, 129.0, 127.7, 123.8, 71.5, 58.2, 56.2, 53.5, 53.4, 40.6, -0.2.

IR 3027 (w), 2957 (w), 1723 (s), 1443 (w), 1388 (m), 1270 (m), 1203 (w), 1123 (m), 911 (w), 849 (m).

HRMS (ESI) calcd for $C_{27}H_{29}NNaO_6SSi^+$ $[M+Na]^+$ 546.1377; found 546.1388.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-((4-methoxyphenyl)thio)-2-(trimethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (3s).



3s

Following the general procedure **GP4**, with the thioalkyne **1n** (54 mg, 0.19 mmol, 1.0 equiv), the desired product **3s** was obtained (49 mg, 0.10 mmol, 53%) as a slightly yellow oil.

RF = 0.45 pent/AcOEt (7:3).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.28 (d, *J* = 8.8 Hz, 2H, Ar-H), 6.80 (d, *J* = 8.9 Hz, 2H, Ar-H), 5.39 (t, *J* = 8.2 Hz, 1H, NCH),

3.76 (s, 3H, ester), 3.54 (s, 3H, ester), 3.03 (dd, *J* = 13.4, 8.3 Hz, 1H, CH_2), 2.86 – 2.78 (m, 1H, CH_2), 0.00 (s, 9H, TMS).

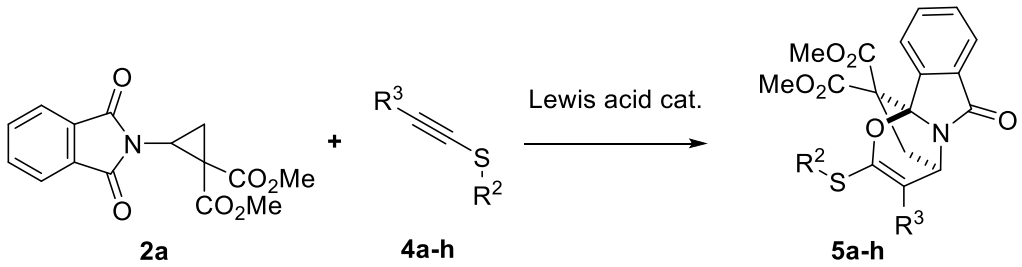
^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 169.7, 168.6, 160.4, 158.9, 143.2, 135.1, 132.7, 130.2, 127.8, 124.3, 115.3, 70.1, 58.3, 56.2, 53.8, 53.5, 40.2, 0.0.

IR 3664 (w), 3471 (w), 2957 (w), 1721 (s), 1451 (w), 1393 (m), 1247 (m), 1128 (m), 910 (s), 845 (m).

HRMS (ESI) calcd for $C_{27}H_{30}NO_7SSi^+$ $[M+H]^+$ 540.1507; found 540.1509.

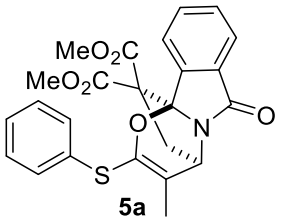
3.5 Cascade reaction with alkylethynylthiols

General procedure for the cascade reactions (GP5).



To a flame-dried microwave vial dimethyl-2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**2a**) (1.0 equiv) was added. Then the vial was put under nitrogen and scandium triflate (0.2 equiv) was added to it in the glove box. The vial was removed and put under nitrogen. DCM (3/4 portion) was added, then the thioalkyne (1.2 equiv) in DCM (1/4 portion) was added. After completion, the reaction was quenched with Et_3N (*ca*. 0.1 mL) and purified as indicated.

Dimethyl-3-methyl-6-oxo-2-(phenylthio)-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5a).



Following the **GP5**, with phthalimide cyclopropane **2a** (100 mg, 0.330 mmol, 1 equiv), scandium triflate (33 mg, 0.066 mmol, 0.2 equiv), thioalkyne **4a** (59 mg, 0.36 mmol, 1.2 equiv) and DCM (1.1 mL, 0.30 M). The reaction was quenched after 6 hours and purified by column chromatography using a mixture of pentane/AcOEt (9:1, 1 % Et_3N) as eluting solvent. The product fractions were collected and evaporated under vacuum. Then the product was dissolved in DCM (0.1 mL) and precipitated with pentane (2 mL). The obtained product was dried under vacuum to afford **5a** (88 mg, 0.20 mmol, 60 %) as a colorless solid.

RF = 0.32 pentane/AcOEt (6:4).

Mp 154.0 - 157.0 °C

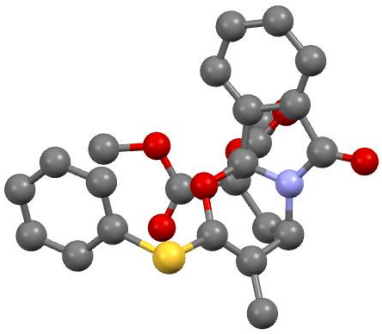
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.78 (m, 1 H, Phthalimide-ArH), 7.68 (m, 1 H, Phthalimide-ArH), 7.54 (m, 1 H, Phthalimide-ArH), 7.52 (m, 1 H, Phthalimide-ArH), 7.30 – 7.15 (m, 5 H, PhH), 4.61 (d, 1 H, *J* = 6.0 Hz, NCH), 3.58 (s, 3 H, OCH_3), 3.46 (d, 1 H, *J* = 12.8 Hz, CH_2), 3.22 (s, 3 H, OCH_3), 2.89 (dd, 1 H, *J* = 12.8, 6.2 Hz, CH_2), 2.08 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 168.7, 167.5, 162.0, 141.6, 139.5, 134.7, 133.0, 132.2, 130.7, 130.0, 129.1, 127.1, 123.8, 123.7, 123.1, 97.9, 67.6, 53.1, 52.9, 52.1, 47.6, 17.6.

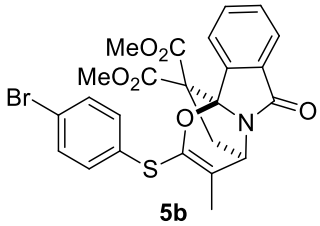
IR 2978 (w). 1722 (s). 1602 (m). 1393 (m). 1257 (s). 1171 (m). 1053 (s). 975 (s). 882 (s).

HRMS (ESI) calcd for $C_{24}H_{22}NO_6S^+$ $[M+H]^+$ 452.1162; found 452.1164.

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: **CCDC 1453960**.



Dimethyl-2-((4-bromophenyl)thio)-3-methyl-6-oxo-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5b).



5b

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4b** (68 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 24 hours and purified by column chromatography using a mixture of pentane/AcOEt (6:4, 1 % Et_3N) as eluting solvent to afford **5b** (97 mg, 0.18 mmol, 60 %) as a colorless oil.

RF = 0.58 pentane/AcOEt (1:1).

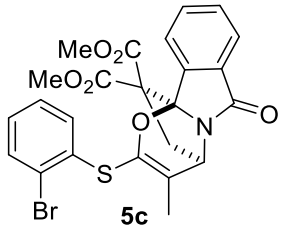
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.78 (m, 1 H, Phthalimide-ArH), 7.67 (m, 1 H, Phthalimide-ArH), 7.55 (m, 1 H, Phthalimide-ArH), 7.51 (m, 1 H, Phthalimide-ArH), 7.38 (m, 2 H, ArH), 7.11 (m, 2 H, ArH), 4.60 (d, 1 H, *J* = 6.1 Hz, NCH), 3.65 (s, 3 H, OCH_3), 3.44 (d, 1 H, *J* = 12.9 Hz, CH_2), 3.23 (s, 3 H, OCH_3), 2.88 (dd, 1 H, *J* = 12.9, 6.2 Hz, CH_2), 2.05 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 168.6, 167.5, 162.0, 141.1, 139.3, 134.6, 132.3, 132.2, 132.2, 131.5, 130.8, 123.8, 123.7, 123.6, 121.1, 98.0, 67.6, 53.2, 52.9, 52.1, 47.6, 17.5.

IR 2950 (m). 1725 (s). 1391 (m). 1253 (s). 1167 (w). 1054 (w). 976 (m).

HRMS (ESI) calcd for $C_{24}H_{20}{}^{79}BrNNaO_6S^+$ $[M+Na]^+$ 552.0087; found 552.0088.

Dimethyl-2-((2-bromophenyl)thio)-3-methyl-6-oxo-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5c).



5c

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4c** (68 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 24 hours and purified by column chromatography using a mixture of pentane/AcOEt (6:4, 1 % Et_3N) as eluting solvent to afford **5c** (103 mg, 0.190 mmol, 63 %) as a colorless foam.

RF = 0.49 pentane/AcOEt (1:1).

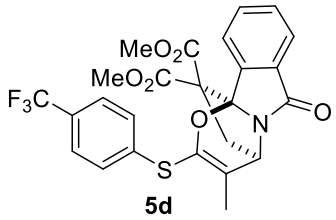
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.79 (m, 1 H, Phthalimide-ArH), 7.70 (m, 1 H, Phthalimide-ArH), 7.55 (m, 1 H, Phthalimide-ArH), 7.51 (m, 1 H, Phthalimide-ArH), 7.47 (dd, 1 H, *J* = 7.9, 1.4 Hz, ArH), 7.15 (td, 1 H, *J* = 7.6, 1.4 Hz, ArH), 7.06 (dd, 1 H, *J* = 8.0, 1.6 Hz, ArH), 6.98 (td, 1 H, *J* = 7.6, 1.6 Hz, ArH), 4.63 (d, 1 H, *J* = 6.1 Hz, NCH), 3.82 (s, 3 H, OCH_3), 3.49 (d, 1 H, *J* = 12.9 Hz, CH_2), 3.24 (s, 3 H, OCH_3), 2.92 (dd, 1 H, *J* = 12.9, 6.2 Hz, CH_2), 2.04 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 168.6, 167.7, 162.1, 140.4, 139.3, 135.2, 134.5, 133.0, 132.3, 130.8, 128.4, 128.1, 127.4, 126.1, 123.9, 123.7, 122.1, 98.1, 67.7, 53.5, 52.9, 52.3, 47.7, 17.6.

IR 2950 (m). 1731 (s). 1438 (m). 1391 (m). 1256 (s). 1167 (m). 1054 (s). 973 (s).

HRMS (ESI) calcd for $C_{24}H_{20}{}^{79}BrNNaO_6S^+$ $[M+Na]^+$ 552.0087; found 552.0070.

Dimethyl-3-methyl-6-oxo-2-((4-(trifluoromethyl)phenyl)thio)-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5d).



5d

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4d** (78 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 6 hours and purified by column chromatography using a mixture of pentane/AcOEt (8:2 to 7:3, 1 % Et_3N) as eluting solvent to afford **5d** (0.10 g, 0.20 mmol, 66 %) as a colorless foam.

RF = 0.43 pentane/AcOEt (6:4).

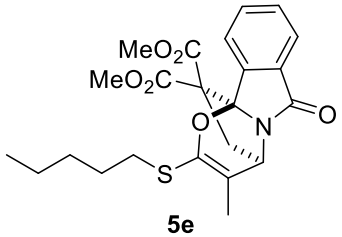
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.79 (m, 1 H, Phthalimide-ArH), 7.67 (m, 1 H, Phthalimide-ArH), 7.56 (m, 1 H, Phthalimide-ArH), 7.52 (m, 1 H, Phthalimide-ArH), 7.48 (m, 2 H, ArH), 7.29 (m, 2 H, ArH), 4.63 (d, 1 H, *J* = 6.1 Hz, NCH), 3.70 (s, 3 H, OCH_3), 3.48 (d, 1 H, *J* = 12.9 Hz, CH_2), 3.25 (s, 3 H, OCH_3), 2.91 (dd, 1 H, *J* = 12.9, 6.1 Hz, CH_2), 2.06 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 168.5, 167.6, 162.0, 140.3, 139.2, 138.6, 134.6, 132.4, 130.8, 128.8 (q, *J* = 32.7 Hz), 128.5, 126.0 (q, *J* = 3.8 Hz), 125.4, 124.1 (q, *J* = 266.1 Hz), 123.8, 123.8, 98.1, 67.6, 53.3, 53.0, 52.1, 47.6, 17.6.

IR 2950 (m). 1720 (s). 1601 (s). 1391 (s). 1319 (s). 1250 (m). 1160 (s). 1114 (s). 1054 (s). 971 (s).

HRMS (ESI) calcd for $C_{25}H_{20}F_3NO_6S^+$ $[M+Na]^+$ 520.1036; found 520.1033.

Dimethyl-3-methyl-6-oxo-2-(pentylthio)-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5e).



5e

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4e** (51 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 4.5 hours and purified by column chromatography using a mixture of pentane/AcOEt (8:2, 1 % Et_3N) as eluting solvent to afford **5e** (81 mg, 0.18 mmol, 61 %) as a colorless oil.

RF = 0.32 pent/AcOEt (6:4).

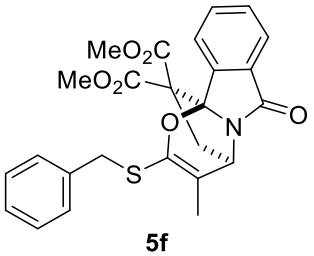
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (dt, *J* = 6.2, 3.5 Hz, 2H, Ar-H), 7.47 (qd, *J* = 7.9, 3.8 Hz, 2H, Ar-H), 4.44 (d, *J* = 5.9 Hz, 1H, NCH), 3.90 (s, 3H, ester), 3.32 (d, *J* = 12.7 Hz, 1H, CH_2), 3.17 (s, 3H, ester), 2.77 (dd, *J* = 12.7, 6.1 Hz, 1H, CH_2), 2.53 (td, *J* = 7.3, 3.0 Hz, 2H, chain CH_2), 1.87 (s, 3H, Me), 1.44 (q, *J* = 6.9 Hz, 2H, chain CH_2), 1.29 – 1.14 (m, 4H, chain CH_2), 0.78 (t, *J* = 7.0 Hz, 3H, chain CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) 168.6, 167.7, 161.8, 142.4, 139.5, 134.7, 132.0, 130.5, 123.5, 123.4, 118.7, 97.5, 67.3, 53.3, 52.7, 51.8, 47.6, 32.0, 30.7, 29.3, 22.2, 17.1, 13.9.

IR 2953 (w), 2860 (w), 1723 (s), 1444 (w), 1392 (m), 1249 (s), 1174 (m), 1052 (m), 976 (m), 880 (w).

HRMS (ESI) calcd for $C_{23}H_{28}NO_6S^+$ $[M+H]^+$ 446.1632; found 446.1641.

Dimethyl-2-(benzylthio)-3-methyl-6-oxo-4H,6H-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5f).



5f

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4f** (59 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 4.5 hours and purified by column chromatography using a mixture of pentane/AcOEt (6:4, 1 % Et_3N) as eluting solvent to afford **5f** (90 mg, 0.19 mmol, 65 %) as a yellowish oil.

RF = 0.23 pentane/AcOEt (6:4).

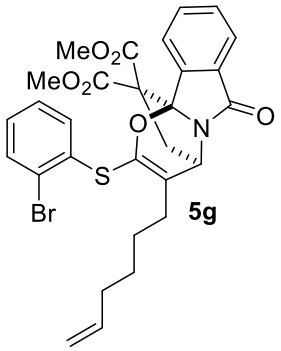
^{1}H NMR (400 MHz, Choloroform-*d*): δ 7.87 (m, 2 H, Phthalimide-ArH), 7.65 (m, 2 H, Phthalimide-ArH), 7.39 – 7.14 (m, 5 H, PhH), 4.51 (d, 1 H, *J* = 6.0 Hz, NCH), 4.02 (s, 3 H, OCH_3), 3.91 (d, 1 H, *J* = 12.6 Hz, SCH_2), 3.77 (d, 1 H, *J* = 12.6 Hz, SCH_2), 3.47 (d, 1 H, *J* = 12.7 Hz, CH_2), 3.33 (s, 3 H, OCH_3), 2.89 (dd, 1 H, *J* = 12.7, 6.1 Hz, CH_2), 1.82 (s, 3 H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 168.7, 168.0, 161.7, 142.1, 139.7, 137.4, 134.9, 132.2, 130.7, 129.0, 128.5, 127.3, 123.8, 123.7, 120.4, 97.8, 67.6, 53.5, 52.9, 51.9, 47.8, 36.7, 17.0.

IR 2950 (w). 1720 (s). 1391 (m). 1253 (s). 1167 (m). 1051 (s). 971 (s). 881 (s).

HRMS (ESI) calcd for $C_{25}H_{24}NO_6S^+$ $[M+H]^+$ 466.1319; found 466.1329.

Dimethyl 2-((2-bromophenyl)thio)-6-oxo-3-(pent-4-en-1-yl)-4,6-dihydro-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5g).



Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4g** (106 mg, 0.360 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 4.5 hours and purified by column chromatography using a mixture of pentane/AcOEt (8:2, 1 % Et_3N) as eluting solvent to afford **5g** (0.14 g, 0.24 mmol, 78 %) as a colorless oil.

RF = 0.5 pent/AcOEt (7:3).

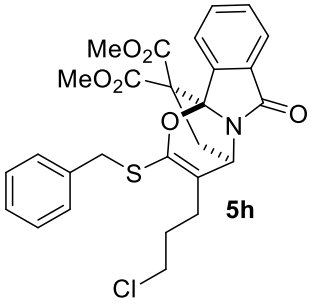
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 – 7.68 (m, 1H, Ar-H), 7.69 – 7.59 (m, 1H, Ar-H), 7.48 – 7.43 (m, 2H, Ar-H), 7.39 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar-H), 7.07 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H, Ar-H), 6.98 (dd, *J* = 8.0, 1.6 Hz, 1H, Ar-H), 6.91 (td, *J* = 7.6, 1.7 Hz, 1H, Ar-H), 5.70 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, CH=C), 4.99 – 4.80 (m, 2H, C=CH_2), 4.64 (d, *J* = 6.2 Hz, 1H, NCH), 3.74 (s, 3H, ester), 3.39 (d, *J* = 13.0 Hz, 1H, CH_2), 3.19 (s, 3H, ester), 2.86 (dd, *J* = 12.9, 6.4 Hz, 1H, CH_2), 2.40 (ddd, *J* = 14.7, 9.1, 6.0 Hz, 1H, chain CH_2), 2.30 (ddd, *J* = 14.3, 8.7, 6.1 Hz, 1H, chain CH_2), 1.99 (q, *J* = 7.0 Hz, 2H, chain CH_2), 1.23-1.56 (m,4H, chain CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 167.6, 161.7, 140.7, 139.1, 138.5, 135.3, 134.4, 132.8, 132.2, 130.6, 129.9, 128.4, 127.9, 127.2, 123.8, 123.6, 121.9, 114.7, 97.9, 67.7, 53.4, 52.8, 50.5, 47.9, 33.3, 31.6, 28.3, 27.5.

IR 3076 (w), 3001 (w), 2952 (w), 2928 (w), 2855 (w), 1720 (s), 1618 (w), 1435 (m), 1390 (m), 1279 (m), 1251 (m), 1089 (m), 1019 (m), 972 (w), 914 (w).

HRMS (ESI) calcd for $C_{29}H_{29}BrNO_6S^+$ $[M+H]^+$ 598.0893; found 598.0899.

Dimethyl 2-(benzylthio)-3-(3-chloropropyl)-6-oxo-4,6-dihydro-4,10b-ethano[1,3]oxazino[2,3-a]isoindole-11,11-dicarboxylate (5h).



5h

Following the **GP5**, with phthalimide cyclopropane **2a** (91 mg, 0.30 mmol, 1 equiv), scandium triflate (30 mg, 0.060 mmol, 0.2 equiv), thioalkyne **4h** (81 mg, 0.36 mmol, 1.2 equiv) and DCM (1 mL, 0.3 M). The reaction was quenched after 4.5 hours and purified by column chromatography using a mixture of pentane/AcOEt (8:2, 1 % Et_3N) as eluting solvent to afford **5h** (123 mg, 0.230 mmol, 78 %) as a colorless oil.

RF = 0.43 pent/AcOEt (7:3).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.69 (m, 2H, Ar-H), 7.58 – 7.48 (m, 2H, Ar-H), 7.12 (dd, *J* = 5.1, 1.9 Hz, 3H, Ar-H), 7.04 – 6.92 (m, 2H, Ar-H), 4.45 (d, *J* = 6.1 Hz, 1H, NCH), 3.90 (s, 3H, ester), 3.80 (d, *J* = 12.7 Hz, 1H, CH_2 benzylic), 3.58 (d, *J* = 12.7 Hz, 1H, CH_2 benzylic), 3.40 – 3.25 (m, 3H, CH_2Cl and CH_2), 3.22 (s, 3H, ester), 2.76 (dd, *J* = 12.8, 6.2 Hz, 1H, CH_2), 2.32 – 2.10 (m, 2H, chain CH_2), 1.73 – 1.47 (m, 2H, chain CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 167.7, 161.2, 143.6, 139.4, 137.2, 134.6, 132.1, 130.6, 128.8, 128.4, 127.3, 123.7, 123.4, 122.5, 97.6, 67.5, 53.5, 52.8, 50.3, 48.2, 44.0, 36.2, 31.0, 28.4.

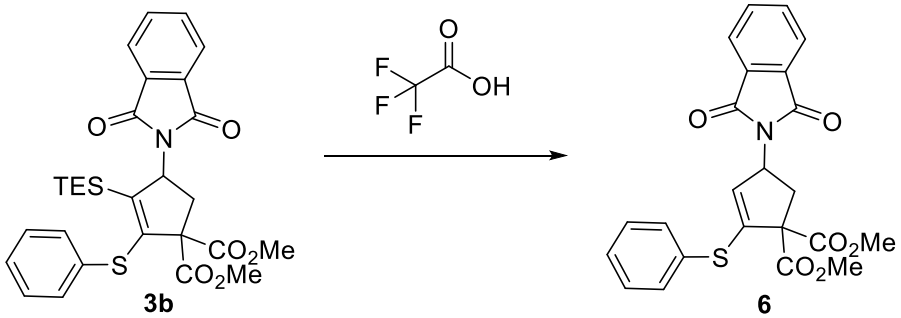
IR 3063 (w), 3029 (w), 2954 (w), 2843 (w), 1719 (s), 1620 (w), 1436 (m), 1395 (m), 1277 (m), 1254 (m), 1197 (w), 1095 (m), 1055 (m), 975 (m), 913 (w), 884 (w).

HRMS (ESI) calcd for $C_{27}H_{27}ClNO_6S^+$ $[M+H]^+$ 528.1242; found 528.1249.

4 Derivatization

4.1 From 1-thiopenten-3-amine 3b

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(phenylthio)cyclopent-2-ene-1,1-dicarboxylate (6).



3b **6**

Compound **3b** (48 mg, 0.087 mmol, 1 equiv) was stirred in a flame dried flask under nitrogen in TFA (0.2 mL) at 0 °C for 18 hours. At 0 °C water (0.4 mL) was added and the mixture was extracted three times with AcOEt (1 mL). The combined organics were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography with a mixture of pentane/AcOEt (8:2), affording the pure product **6** (38 mg, 0.087 mmol, quantitative) as a colorless oil.

RF = 0.53 pent/AcOEt (7:3).

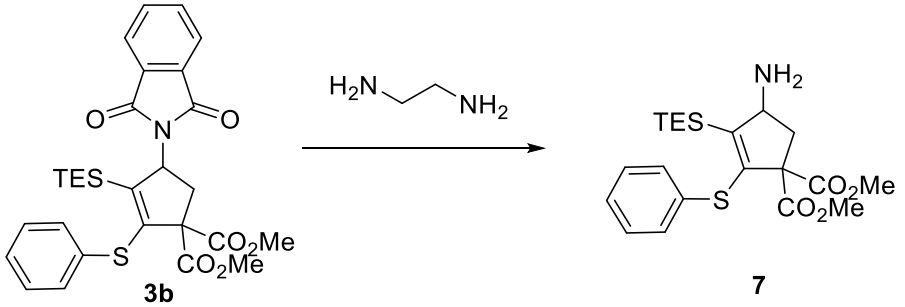
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.63 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.52 – 7.43 (m, 2H, Ar-H), 7.26 (t, *J* = 7.2 Hz, 2H, Ar-H), 7.20 (t, *J* = 7.2 Hz, 1H, Ar-H), 5.41 (d, *J* = 2.4 Hz, 1H, C=CH), 5.34 (ddd, *J* = 8.6, 5.9, 2.4 Hz, 1H, NCH), 3.79 – 3.72 (m, 6H, esters), 3.07 (dd, *J* = 13.9, 8.8 Hz, 1H, CH_2), 2.96 (dd, *J* = 13.9, 5.9 Hz, 1H, CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.6, 169.7, 167.6, 141.2, 134.0, 133.8, 132.9, 131.8, 131.5, 129.3, 128.1, 123.3, 68.1, 53.3, 53.0, 53.0, 38.1.

IR 3056 (w), 2959 (w), 1718 (s), 1609 (w), 1464 (w), 1440 (w), 1388 (m), 1365 (m), 1272 (m), 1124 (m), 968 (w), 863 (w).

HRMS (ESI) calcd for $C_{23}H_{19}NNaO_6S^+$ $[M+Na]^+$ 460.0825; found 460.0828.

Dimethyl 4-amino-3-(phenylthio)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (7).



3b **7**

From an adapted procedure of Crawley et al.[17] compound **3b** (25 mg, 0.045 mmol, 1 equiv) and ethylene diamine (15µL, 0.22 mmol, 5 equiv) were stirred in a sealed vial under nitrogen at reflux in *iso*-propanol (1 mL) for 18 hours. The reaction mixture was concentrated under reduced pressure with silica. The crude powder was purified by column chromatography using a mixture of pentane AcOEt (7:3). The pure product was washed with saturated solution of $NaHCO_3$ and dried over dry Na_2CO_3 affording the amine **7** (13.2 mg, 0.031 mmol, 69%) as a yellow oil.

RF = 0.27 pent/AcOEt (7:3).

[17] O. Kanie, S. C. Crawley, M. M. Palcic, O. Hindsgaul, *Carbohydrate Research*, **1993**, *243*, 139.

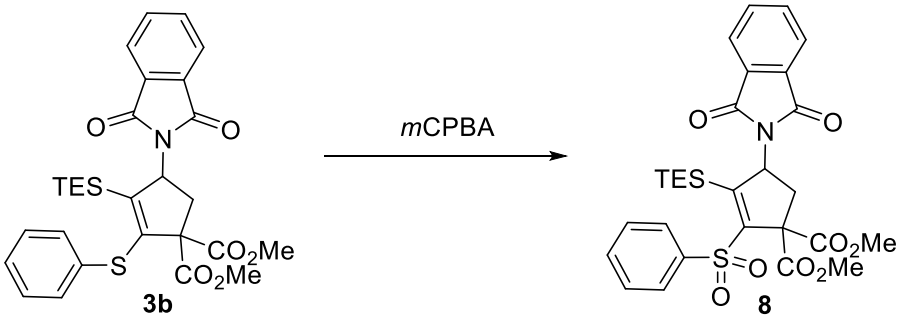
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.15 (t, *J* = 7.7 Hz, 2H, Ar-H), 7.10 – 7.05 (m, 2H, Ar-H), 7.06 – 6.99 (m, 1H, Ar-H), 4.02 (dd, *J* = 7.6, 2.6 Hz, 1H, NCH), 3.41 (s, 3H, ester), 3.23 (s, 3H, ester), 2.89 (dd, *J* = 13.9, 7.6 Hz, 1H, CH_2), 2.28 (dd, *J* = 13.9, 2.6 Hz, 1H, CH_2), 1.36 (br.s, 2H, NH_2), 0.89 (t, *J* = 7.8 Hz, 9H, TES), 0.77 – 0.67 (m, 6H, TES).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 170.2, 166.0, 140.0, 136.7, 128.7, 127.1, 125.4, 69.7, 60.9, 52.7, 52.4, 44.6, 7.6, 3.4.

IR 2954 (w), 2879 (w), 1733 (s), 1595 (w), 1549 (w), 1456 (w), 1441 (w), 1273 (s), 1159 (w), 1086 (w), 1014 (w), 906 (w).

HRMS (ESI) calcd for $C_{21}H_{31}NNaO_4SSi^+$ $[M+Na]^+$ 444.1635; found 444.1631.

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-(phenylsulfonyl)-2-(triethylsilyl)cyclopent-2-ene-1,1-dicarboxylate (8).



From an adapted procedure of Crowley et al.[18] compound **3b** (15 mg, 0.027 mmol, 1 equiv) and *m*CPBA (10 mg, 0.060 mmol, 2.2 equiv) were stirred in a flamed dried flask under nitrogen in dry DCM (1 mL) at 0 °C for 1 hour followed by 4 hours at room temperature. The reaction mixture was purified by column chromatography with DCM, affording the pure sulfone **8** (10 mg, 0.017 mmol, 64%) as a white solid.

Mp 187.2-187.9 °C.

RF = 0.17 pent/AcOEt (8:2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.67 – 7.62 (m, 2H, Ar-H), 7.60 (dd, *J* = 5.6, 3.1 Hz, 2H, Ar-H), 7.40 (t, *J* = 7.7 Hz, 2H, Ar-H), 7.27 (t, *J* = 7.3 Hz, 1H, Ar-H), 5.38 (t, *J* = 8.1 Hz, 1H, NCH), 3.62 (s, 3H, ester), 2.95 (dd, *J* = 13.6, 8.2 Hz, 1H, CH_2), 2.80 (s, 3H, ester), 2.58 (dd, *J* = 13.6, 8.1 Hz, 1H, CH_2), 0.74 (t, *J* = 7.8 Hz, 9H, TES), 0.54 (q, *J* = 7.8 Hz, 6H, TES).

[18] P. J. Crowley, J. M. Percy, K. Stansfield, *Tetrahedron Lett.* **1996**, *37*, 8237–8240.

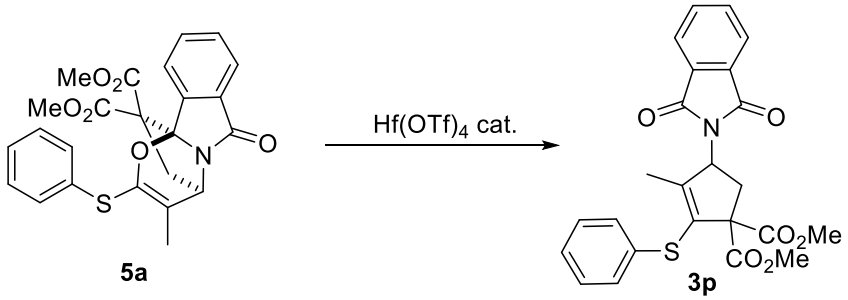
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.0, 167.6, 167.5, 160.9, 151.8, 142.9, 134.4, 131.7, 129.8, 129.0, 125.2, 123.6, 65.8, 58.7, 53.2, 52.2, 40.6, 7.2, 4.1.

IR 2955 (w), 2871 (w), 1739 (m), 1717 (s), 1659 (w), 1467 (w), 1442 (w), 1383 (m), 1355 (w), 1276 (m), 1196 (w), 1117 (w), 1053 (w), 974 (w), 894 (w).

HRMS (ESI) calcd for $C_{29}H_{34}NO_7SSi^+$ $[M+H]^+$ 568.1820; found 568.1830.

4.2 From polycyclic compound 5a

Dimethyl 4-(1,3-dioxoisoindolin-2-yl)-3-methyl-2-(phenylthio)cyclopent-2-ene-1,1-dicarboxylate (3p).



Compound **5a** (15 mg, 0.033 mmol, 1 eq) was stirred in a flame dried flask under nitrogen in dry DCM (1 mL) with hafnium triflate (4.7 mg, 0.0066 mmol, 0.2 equiv) at room temperature for 10 minutes. Triethylamine (0.2 mL) and silica were added to the reaction mixture and concentrated under reduced pressure. The crude mixture was purified by column chromatography with a mixture of pentane/AcOEt (8:2), affording the pure product **3p** (9.2 mg, 0.020 mmol, 61%) as a colorless oil.

RF = 0.61 pent/AcOEt (7:3).

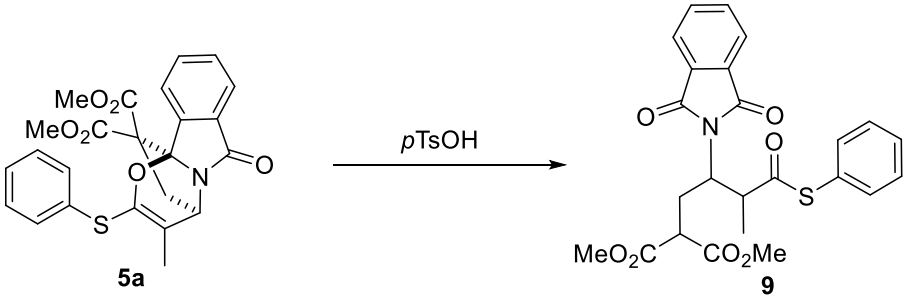
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar-H), 7.67 (d, *J* = 3.1 Hz, 2H, Ar-H), 7.37 – 7.14 (m, 4H, Ar-H), 7.04 (tt, *J* = 6.5, 1.9 Hz, 1H, Ar-H), 5.37 (ddd, *J* = 8.8, 7.4, 1.4 Hz, 1H, NCH), 3.60 (s, 3H, ester), 3.53 (s, 3H, ester), 3.05 (dd, *J* = 13.4, 8.7 Hz, 1H, CH_2), 2.99 (dd, *J* = 13.4, 7.4 Hz, 1H, CH_2), 1.60 (d, *J* = 1.3 Hz, 3H, methyl).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 170.0, 167.6, 151.6, 136.0, 134.2, 131.7, 128.8, 128.0, 126.9, 125.3, 123.5, 67.6, 56.2, 53.0, 52.8, 36.5, 13.9.

IR 3059 (w), 3007 (w), 2942 (w), 1721 (s), 1584 (w), 1401 (w), 1385 (m), 1363 (m), 1273 (m), 1124 (m), 1020 (w), 982 (w), 913 (w).

HRMS (ESI) calcd for $C_{24}H_{21}NNaO_6S^+$ $[M+Na]^+$ 474.0982; found 474.0992.

Dimethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-3-methyl-4-oxo-4-(phenylthio)butyl)malonate (9).



Compound **5a** (15 mg, 0.033 mmol, 1 eq) was stirred in a flame dried flask under nitrogen in dry DCM (1 mL) with *p*TsOH (5.2 mg, 0.033 mmol, 1 equiv) at room temperature for 10 minutes. The reaction mixture was filtered through a silica pad with a mixture of pentane/AcOEt (8:2), affording the pure product **9** as a mixture of two diastereoisomers (5:1) (15 mg, 0.032 mmol, 95%) as a colorless oil. The ratio of diastereoisomers was obtained by integration of the NCH proton at 4.48 and 4.38 ppm.

RF = 0.46 pent/AcOEt (7:3).

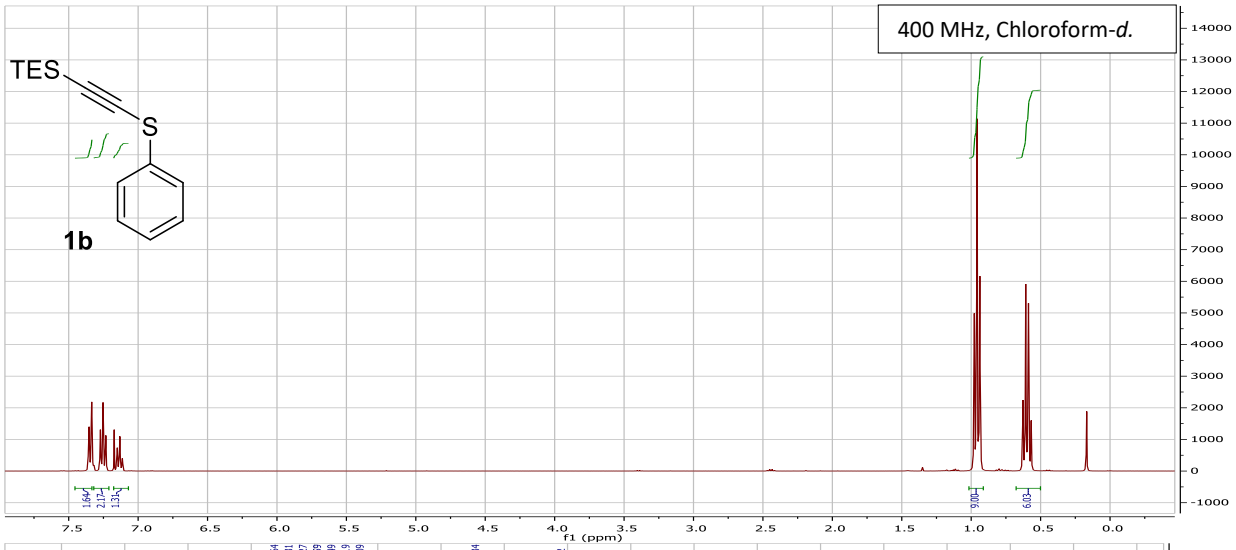
^{1}H NMR (400 MHz, Chloroform-*d,* major diastereoisomer) δ 7.80 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar-H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 7.44 – 7.29 (m, 5H, Ar-H), 4.48 (ddd, *J* = 11.4, 10.2, 3.3 Hz, 1H, NCH), 3.65 (s, 3H, ester), 3.59 (dq, *J* = 10.3, 7.0 Hz, 1H, CH), 3.43 (s, 3H, ester), 3.23 (dd, *J* = 8.4, 6.1 Hz, 1H, $(CO_2Me)_2CH$), 2.79 (ddd, *J* = 14.6, 11.5, 6.3 Hz, 1H, CH_2), 2.37 (ddd, *J* = 14.6, 8.5, 3.4 Hz, 1H, CH_2), 1.09 (d, *J* = 6.9 Hz, 3H, methyl).

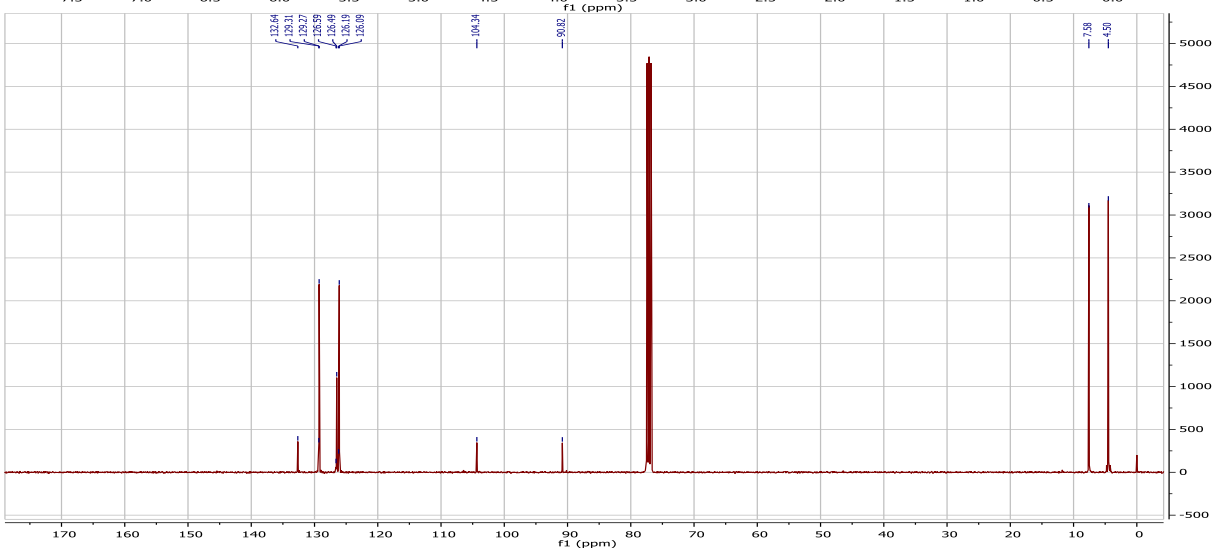
^{13}C NMR (101 MHz, Chloroform-*d,* major diastereoisomer) δ 193.6, 163.7, 163.2, 162.8, 129.2, 129.1, 126.1, 124.3, 124.0, 121.9, 118.3, 47.6, 47.4, 46.4, 44.9, 44.2, 24.3, 10.8.

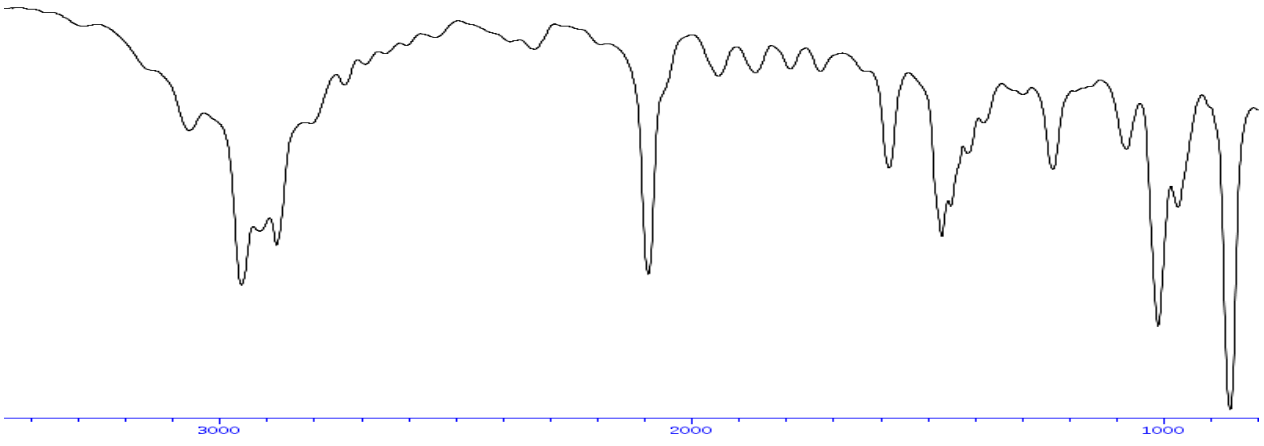
IR 3063 (w), 2955 (w), 1754 (m), 1740 (m), 1713 (s), 1468 (w), 1440 (m), 1377 (m), 1364 (m), 1274 (w), 1201 (w), 1158 (m), 956 (m), 915 (w).

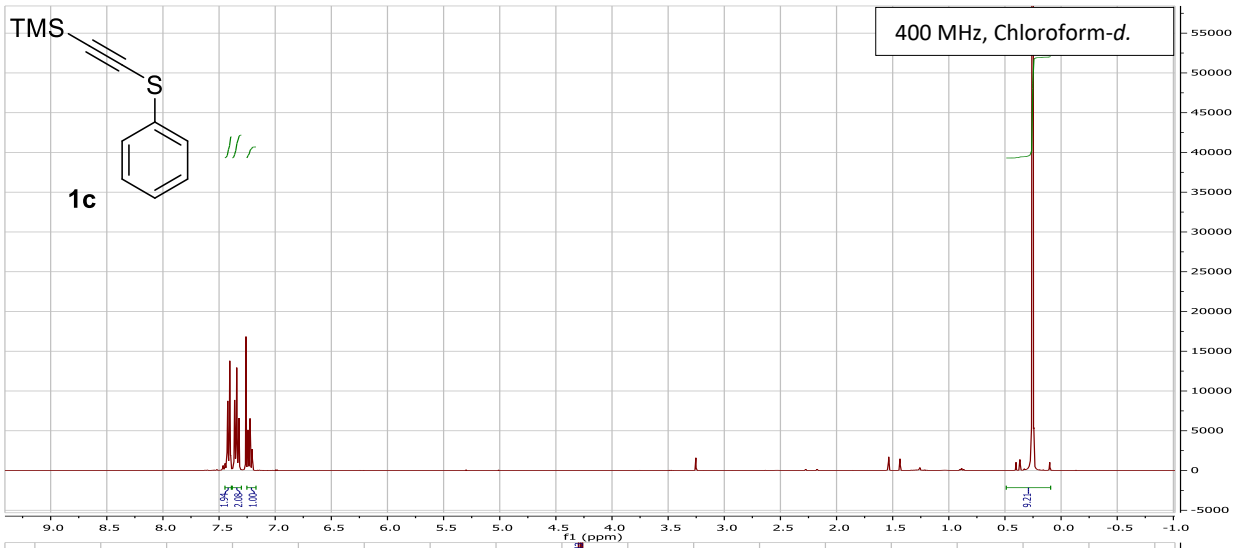
HRMS (ESI) calcd for $C_{24}H_{23}NNaO_7S$ [M+Na] 492.1093; found 492.1101.

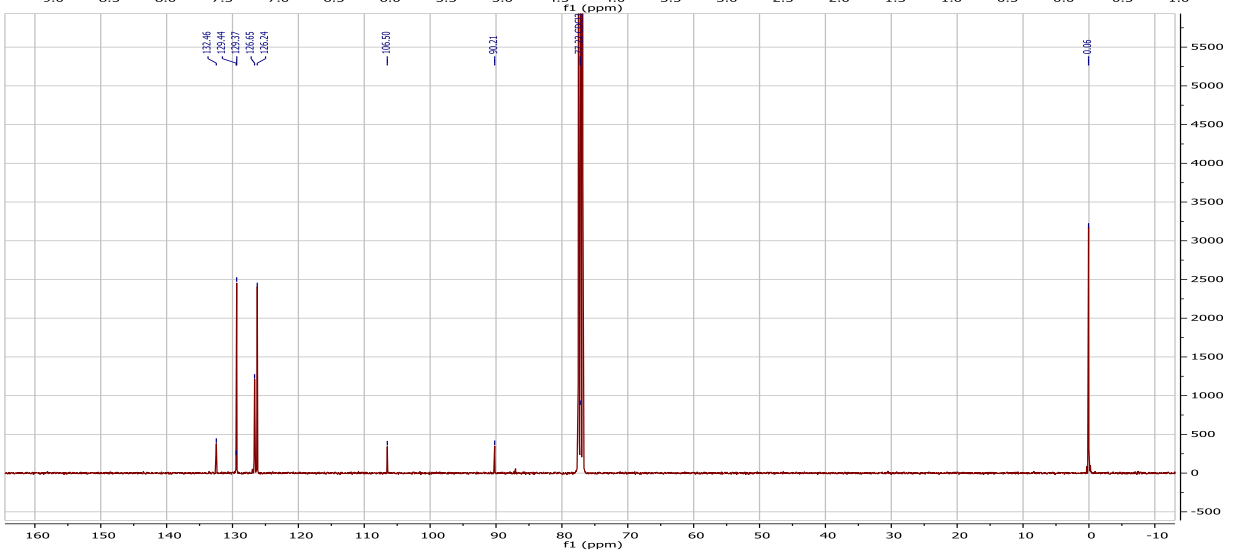
5 Spectra of new compounds

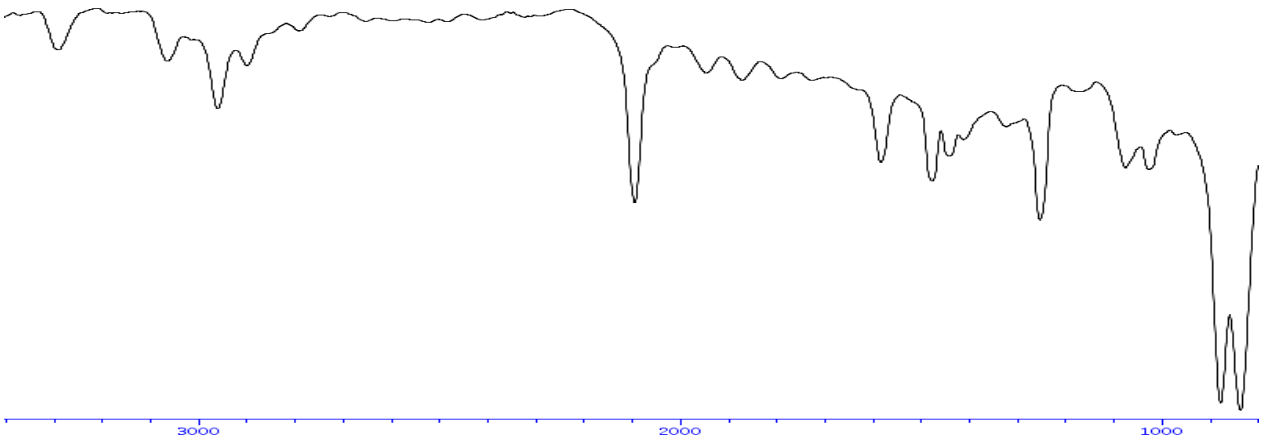

400 MHz, Chloroform-*d*.
TES
S
1b
f1 (ppm)

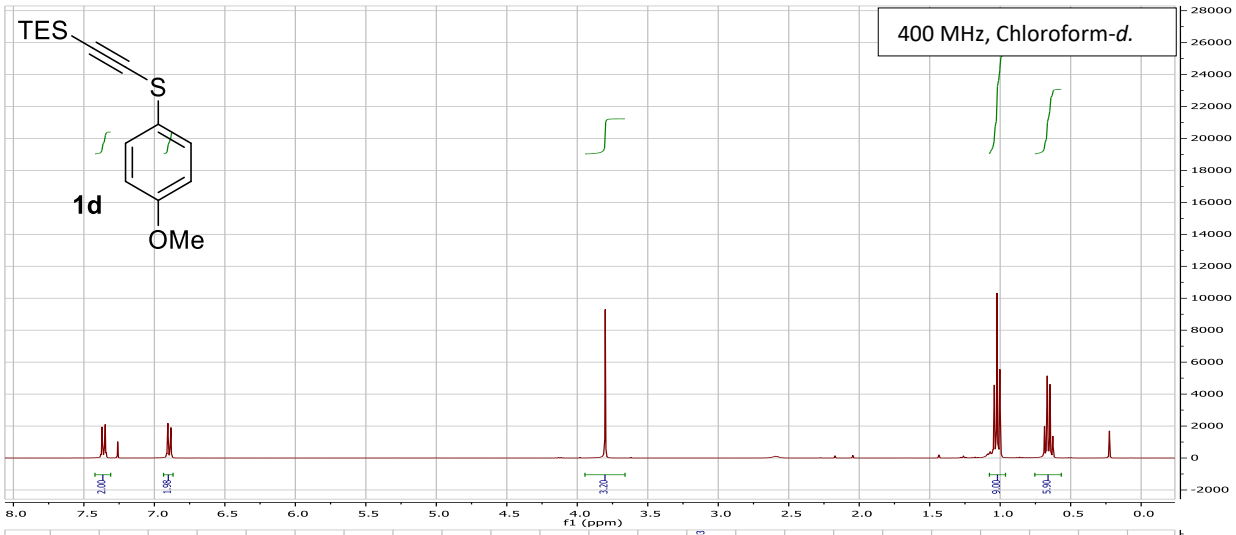

f1 (ppm)

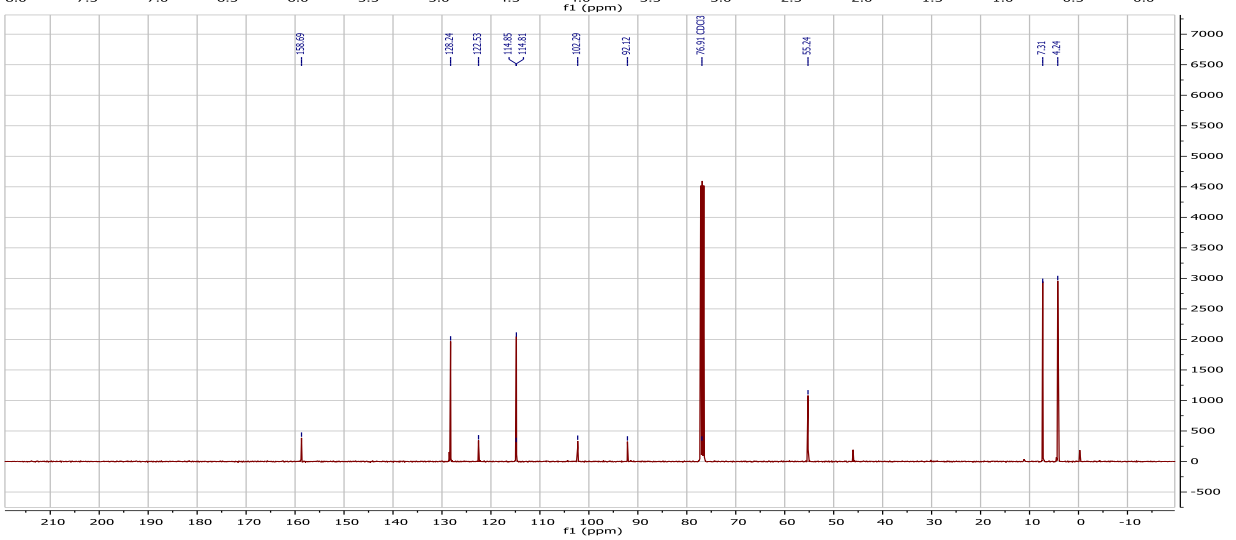

3000
2000
1000

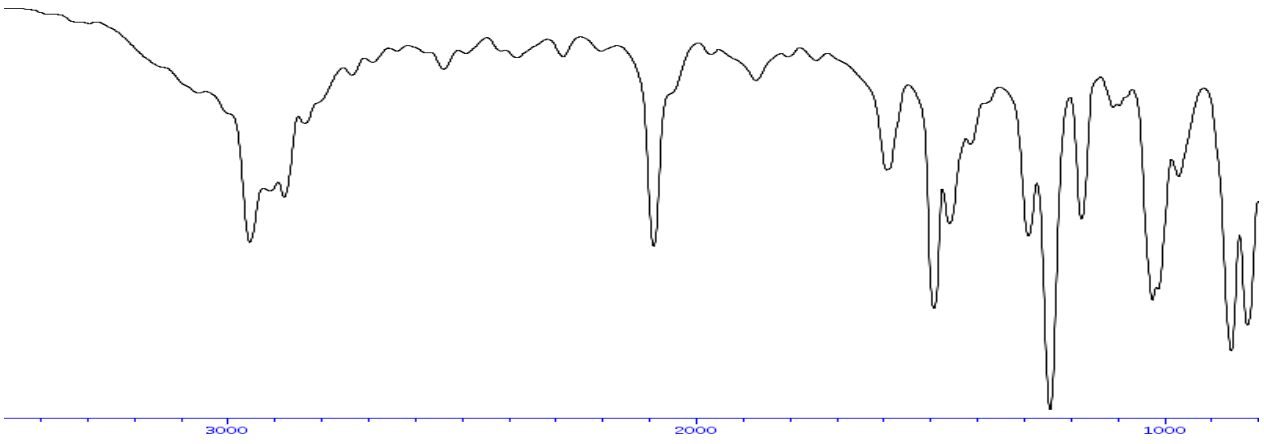

TMS
S
1c
400 MHz, Chloroform-d.
f1 (ppm)

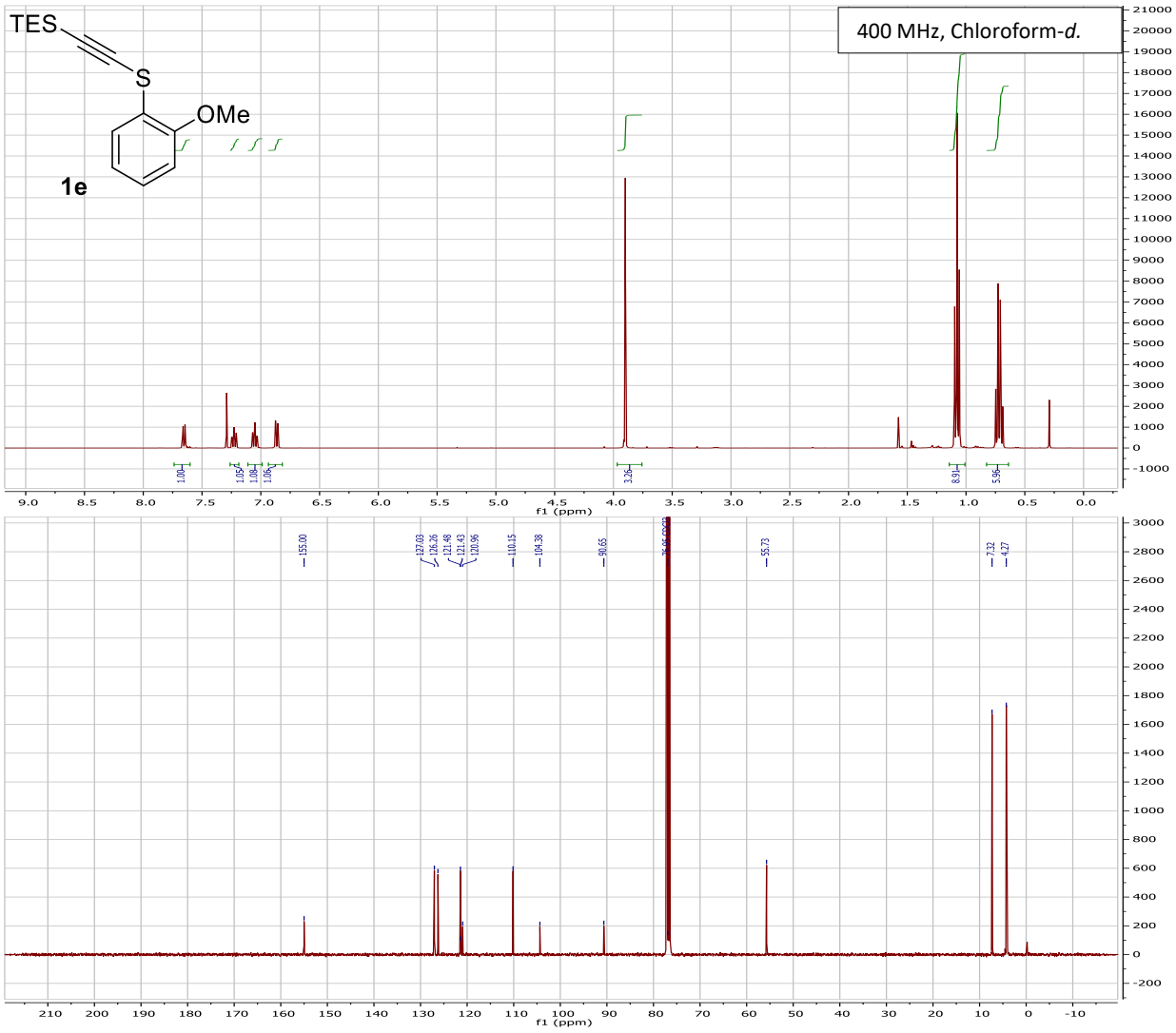

132.46
128.44
129.37
126.65
126.24
106.50
90.21
77.33
77.00
76.66
0.06
f1 (ppm)

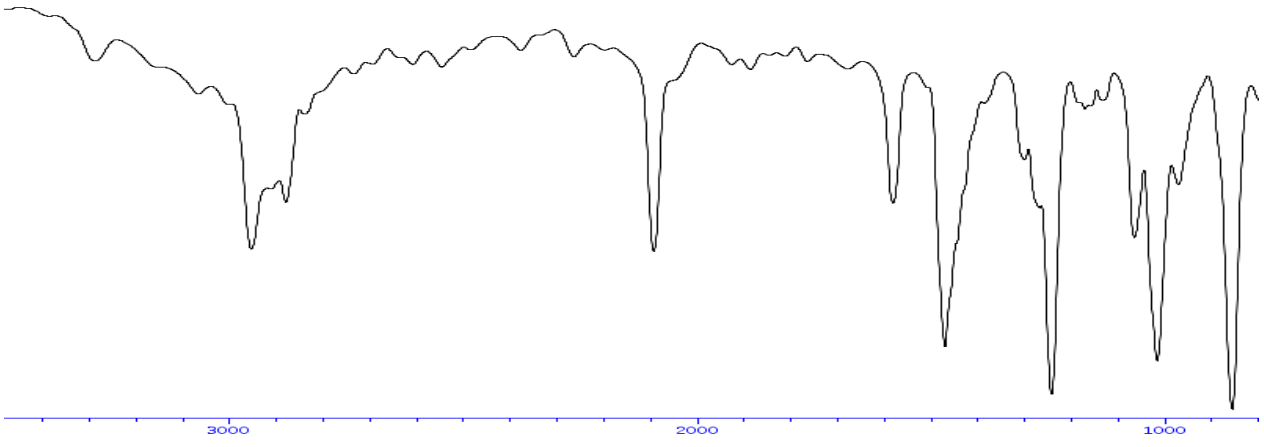

3000
2000
1000

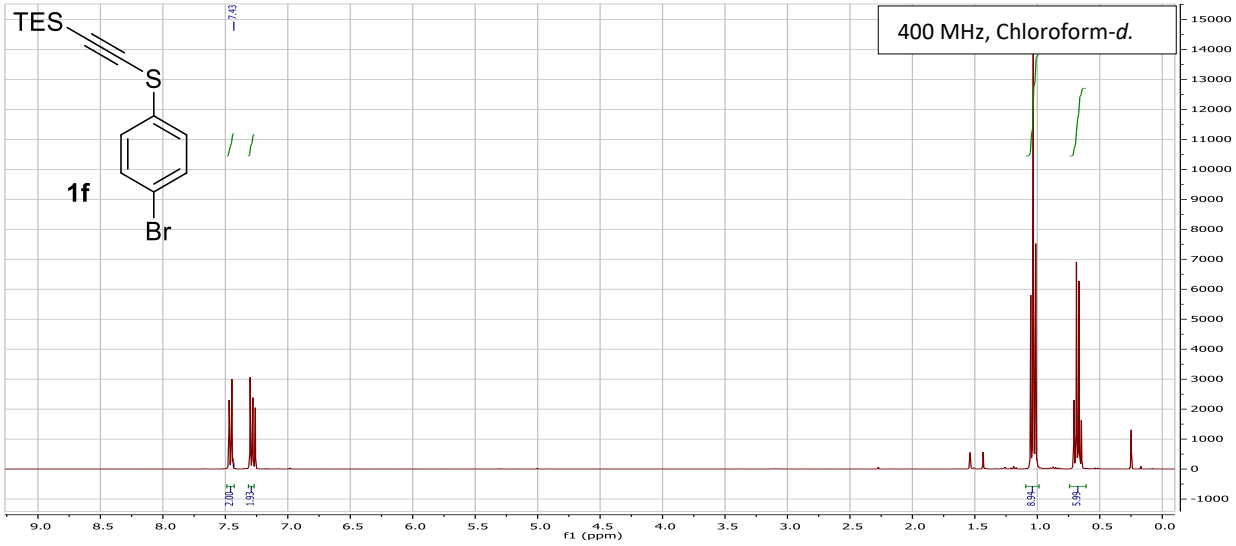

TES
S
1d
OMe
400 MHz, Chloroform-d.

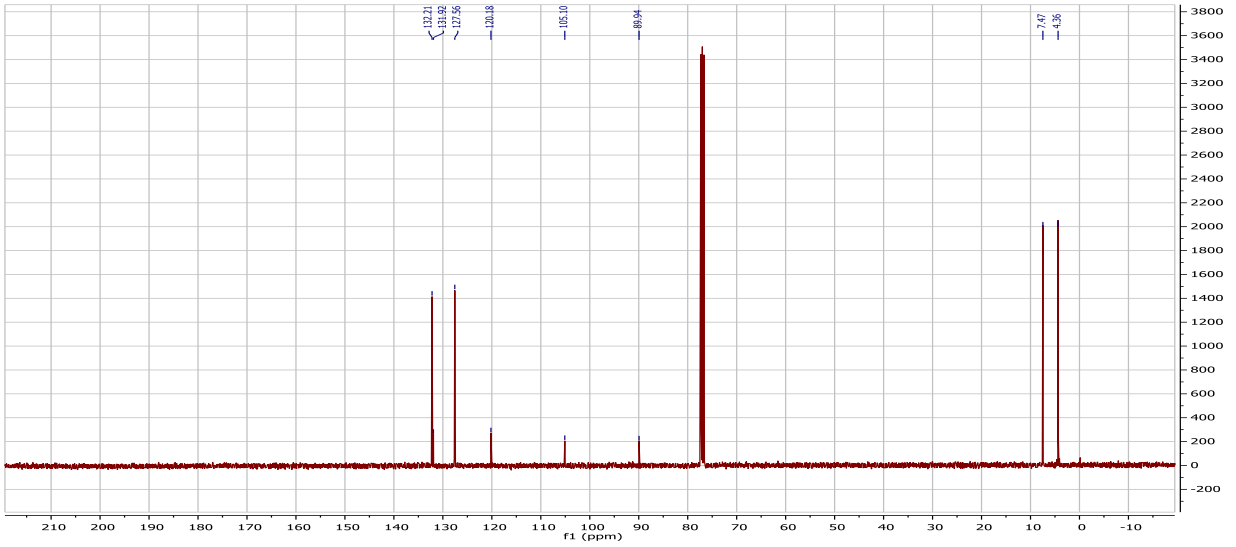

158.69
128.24
122.53
114.85
114.81
102.29
91.12
76.91 CDCl3
55.24
7.31
4.24
f1 (ppm)

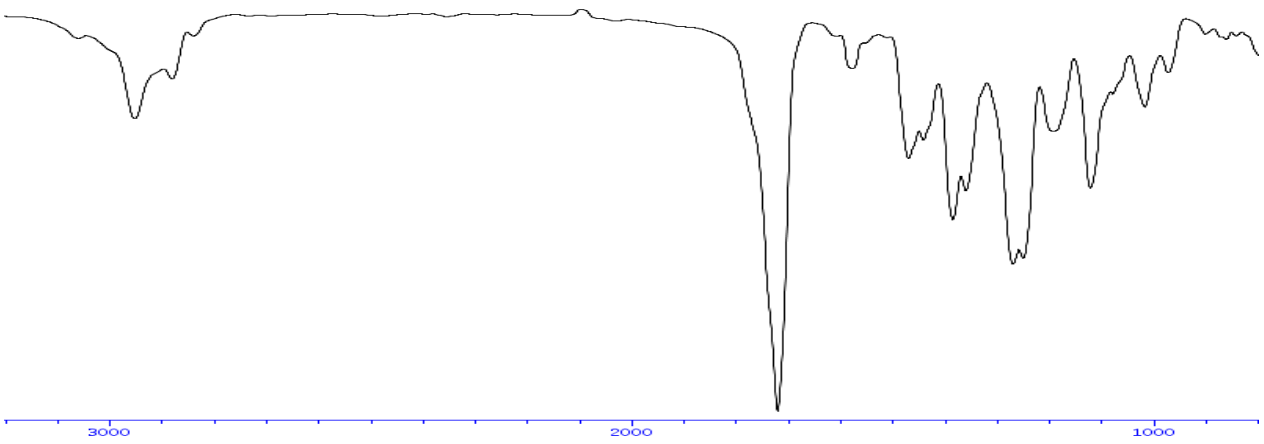

3000
2000
1000

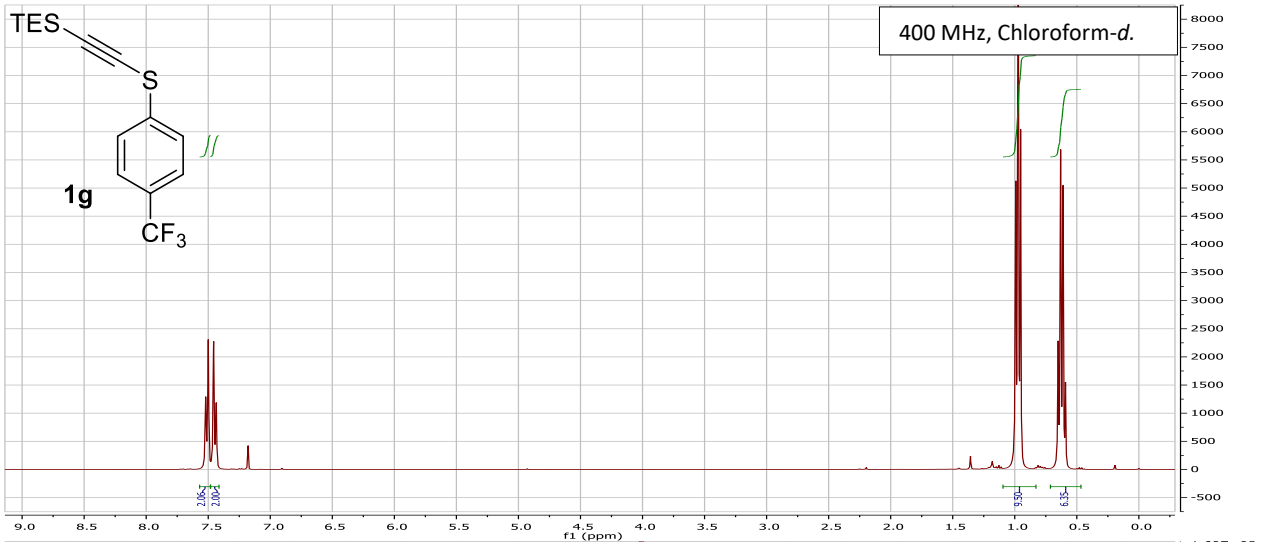

TES
S
OMe
1e
400 MHz, Chloroform-d.
f1 (ppm)
155.00
127.03
126.26
121.48
121.43
120.96
110.15
104.38
90.65
55.73
7.32
4.27

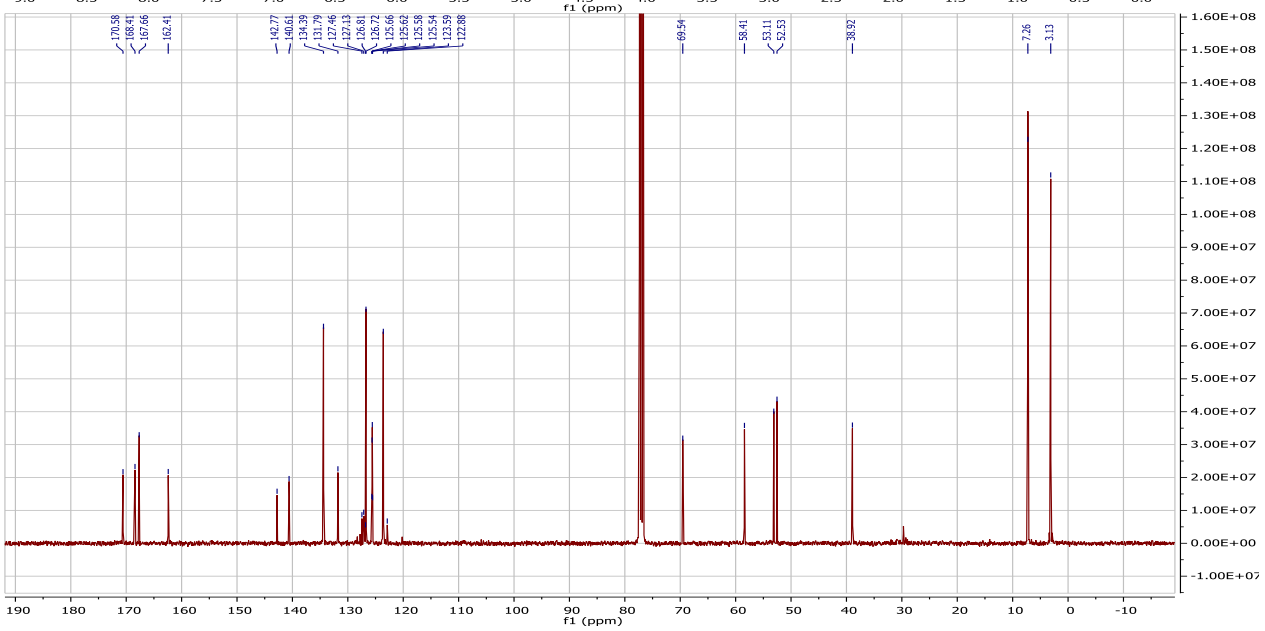

3000
2000
1000

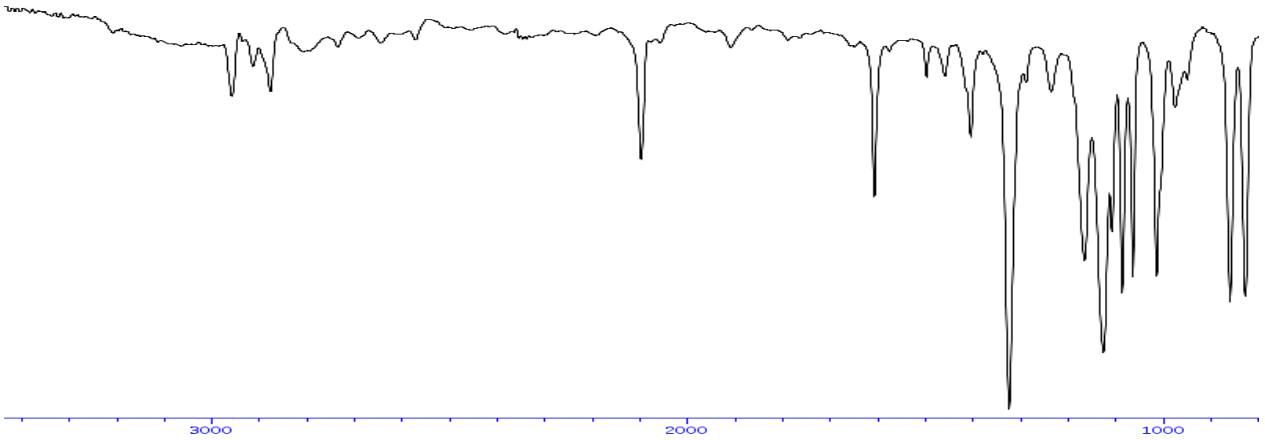

TES
S
Br
1f
400 MHz, Chloroform-d.
7.43
2.00
1.93
8.94
5.99
f1 (ppm)

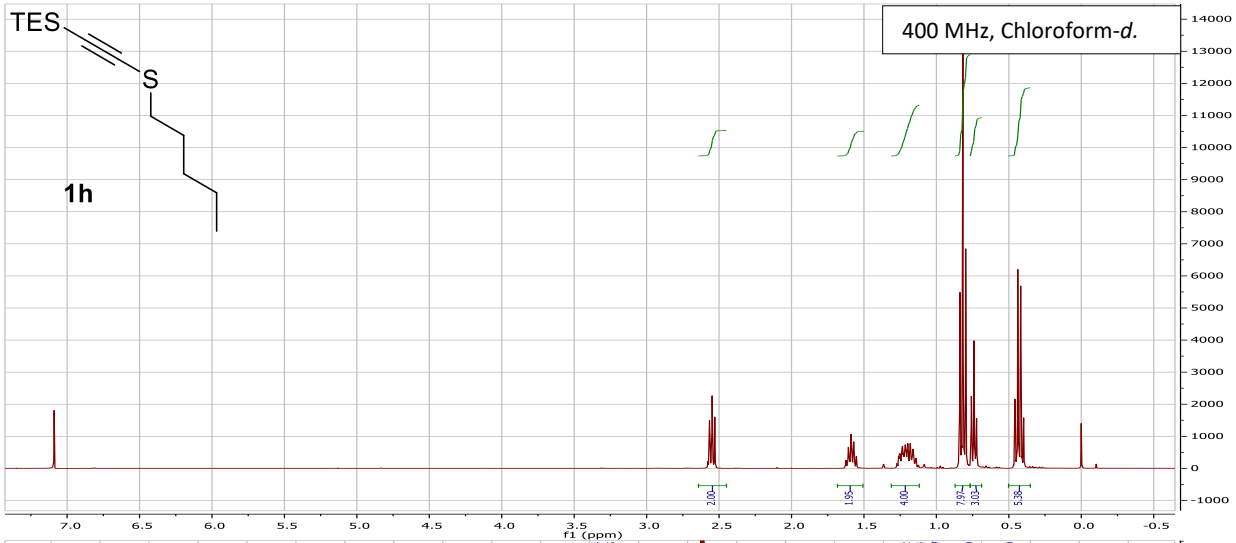

132.21
131.92
127.56
120.18
105.10
80.94
7.47
4.36
f1 (ppm)

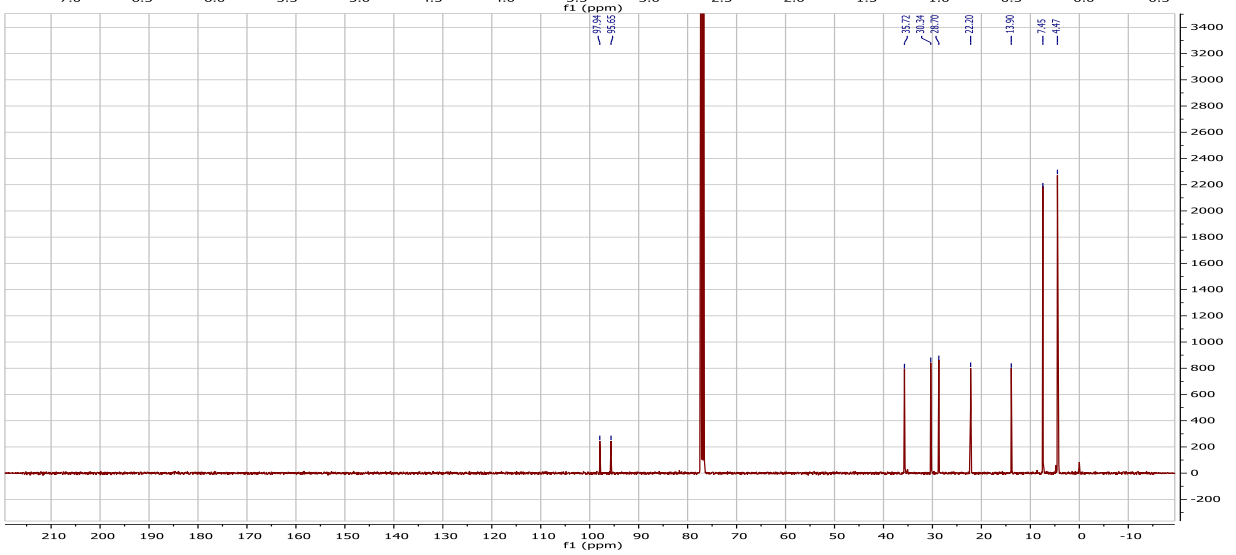

3000
2000
1000

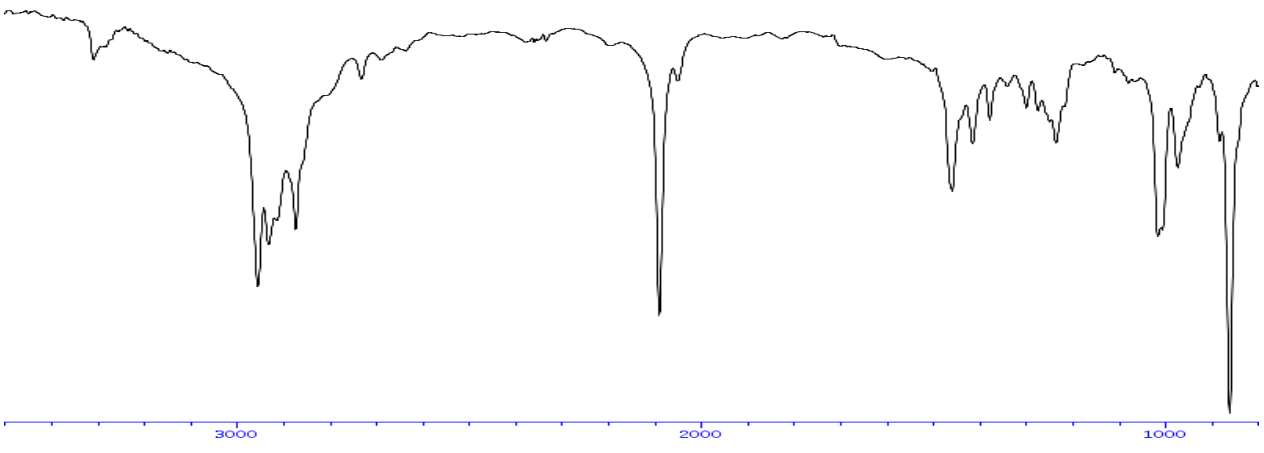

TES
S
1g
CF3
400 MHz, Chloroform-d.
f1 (ppm)

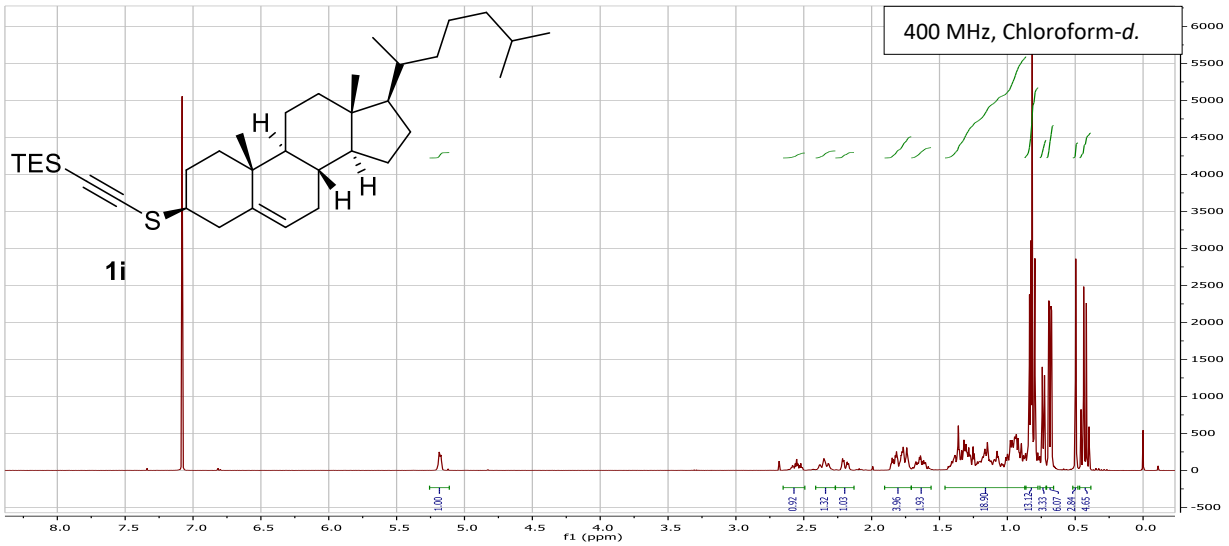

170.58
168.41
167.66
162.41
142.77
140.61
134.39
131.79
127.46
127.13
126.81
126.72
125.66
125.62
125.58
125.54
123.59
122.88
69.54
58.41
53.11
52.53
38.92
7.26
3.13
f1 (ppm)

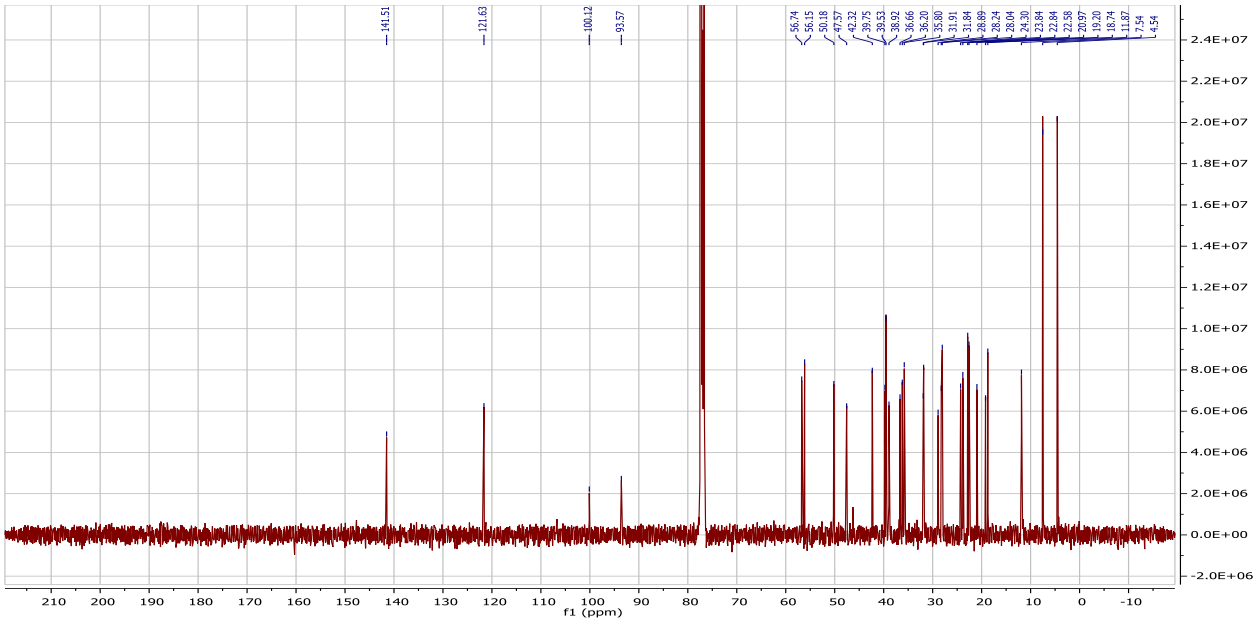

3000
2000
1000

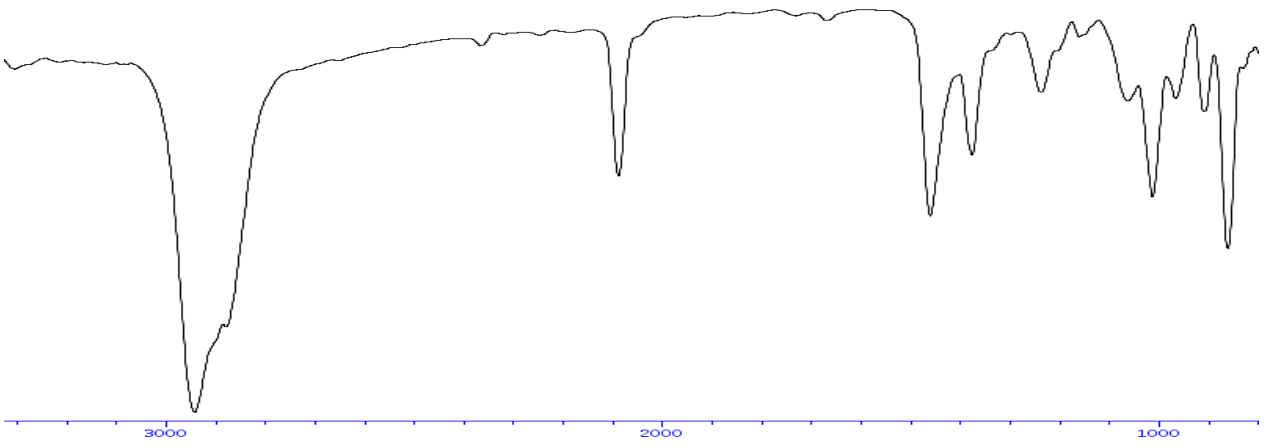

TES
S
1h
400 MHz, Chloroform-d.
f1 (ppm)

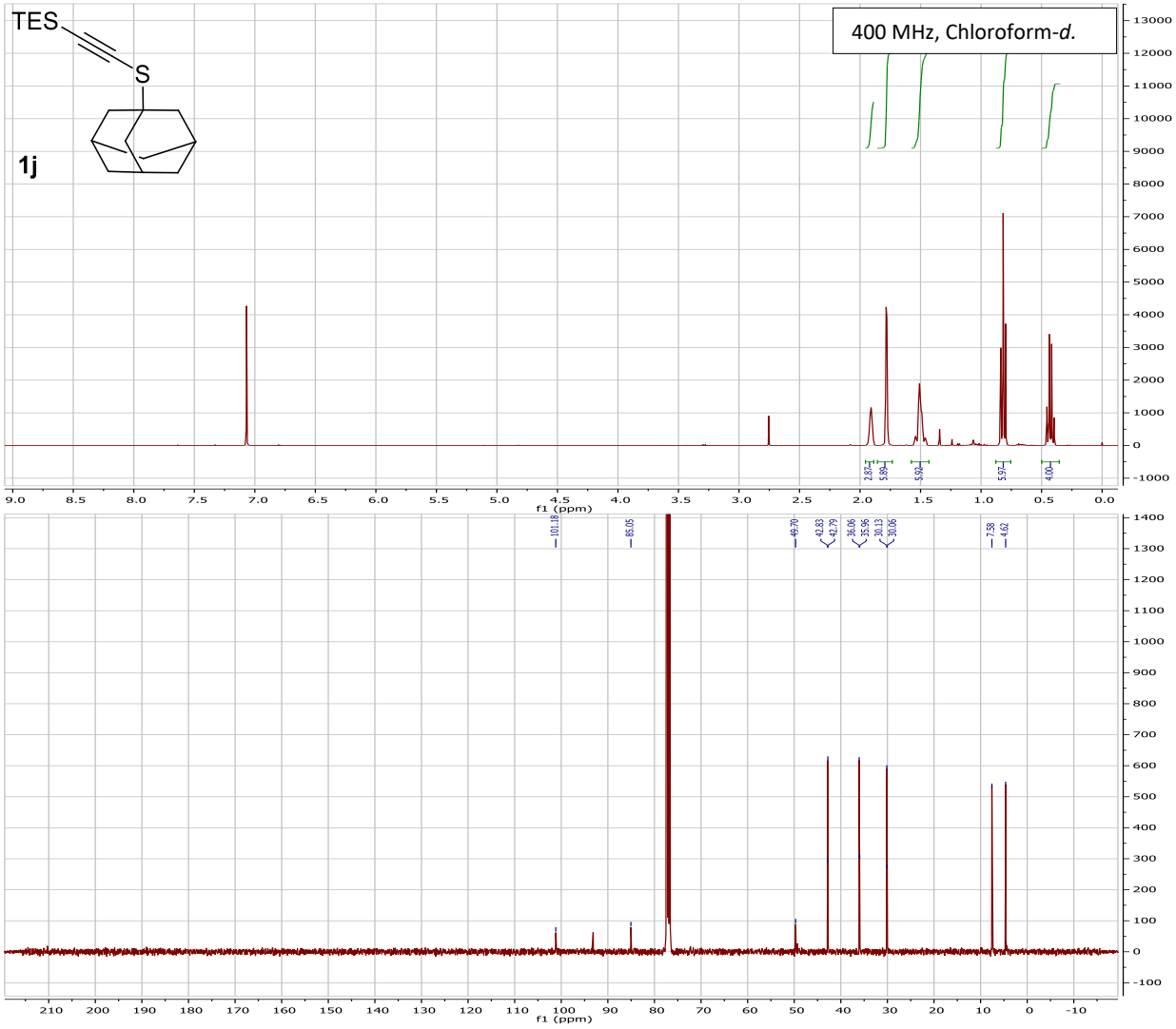

97.94
95.65
35.72
30.24
28.70
22.20
13.90
7.45
4.47
f1 (ppm)

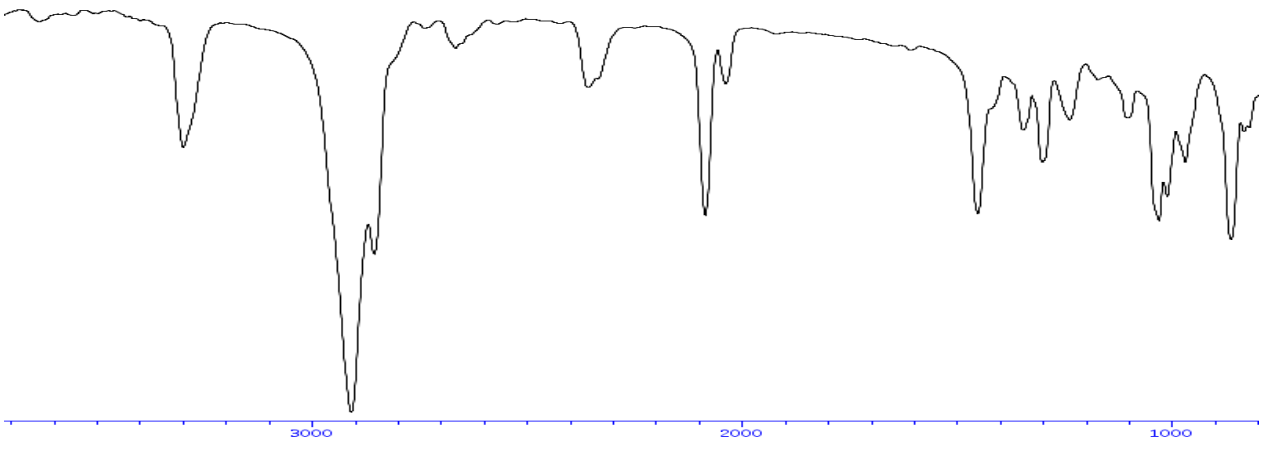

3000
2000
1000

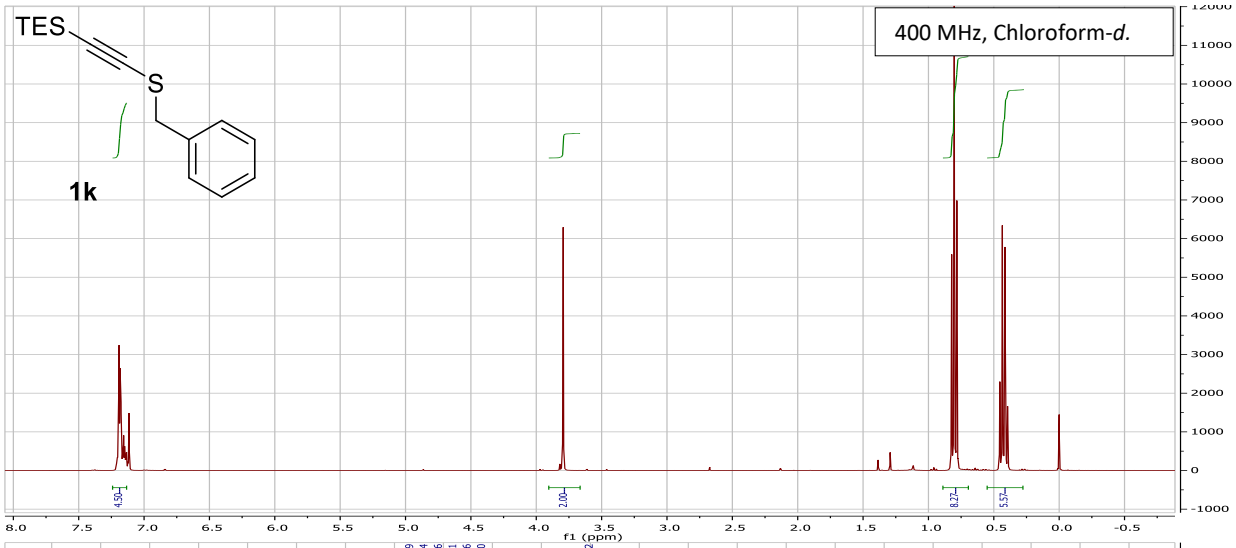

400 MHz, Chloroform-d.
TES
S
H
H
H
1i
f1 (ppm)

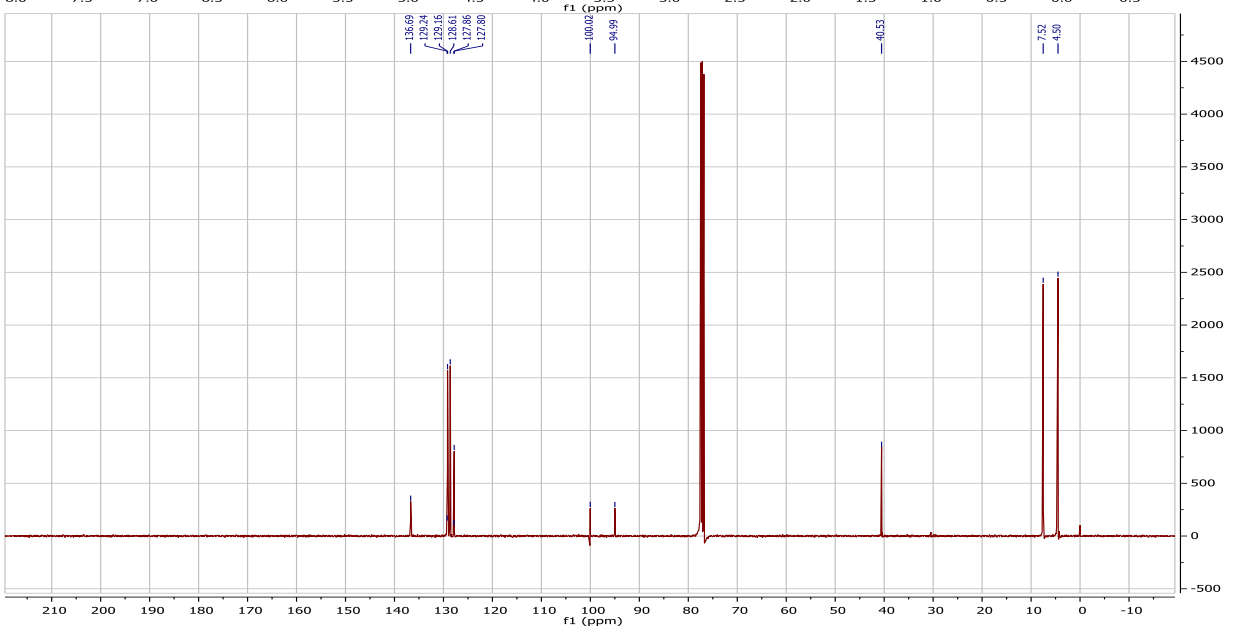

141.51
121.63
100.12
93.57
56.74
56.15
50.18
47.57
42.32
39.75
39.53
38.92
36.66
36.20
35.80
31.91
31.84
28.89
28.24
28.04
24.30
23.84
22.84
22.58
20.97
19.20
18.74
11.87
7.54
4.54
f1 (ppm)

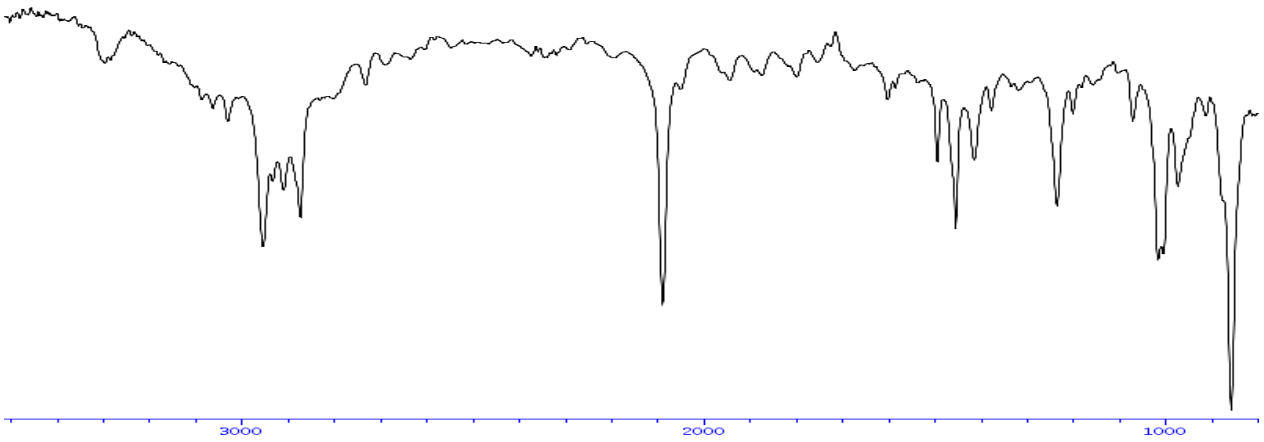

3000
2000
1000

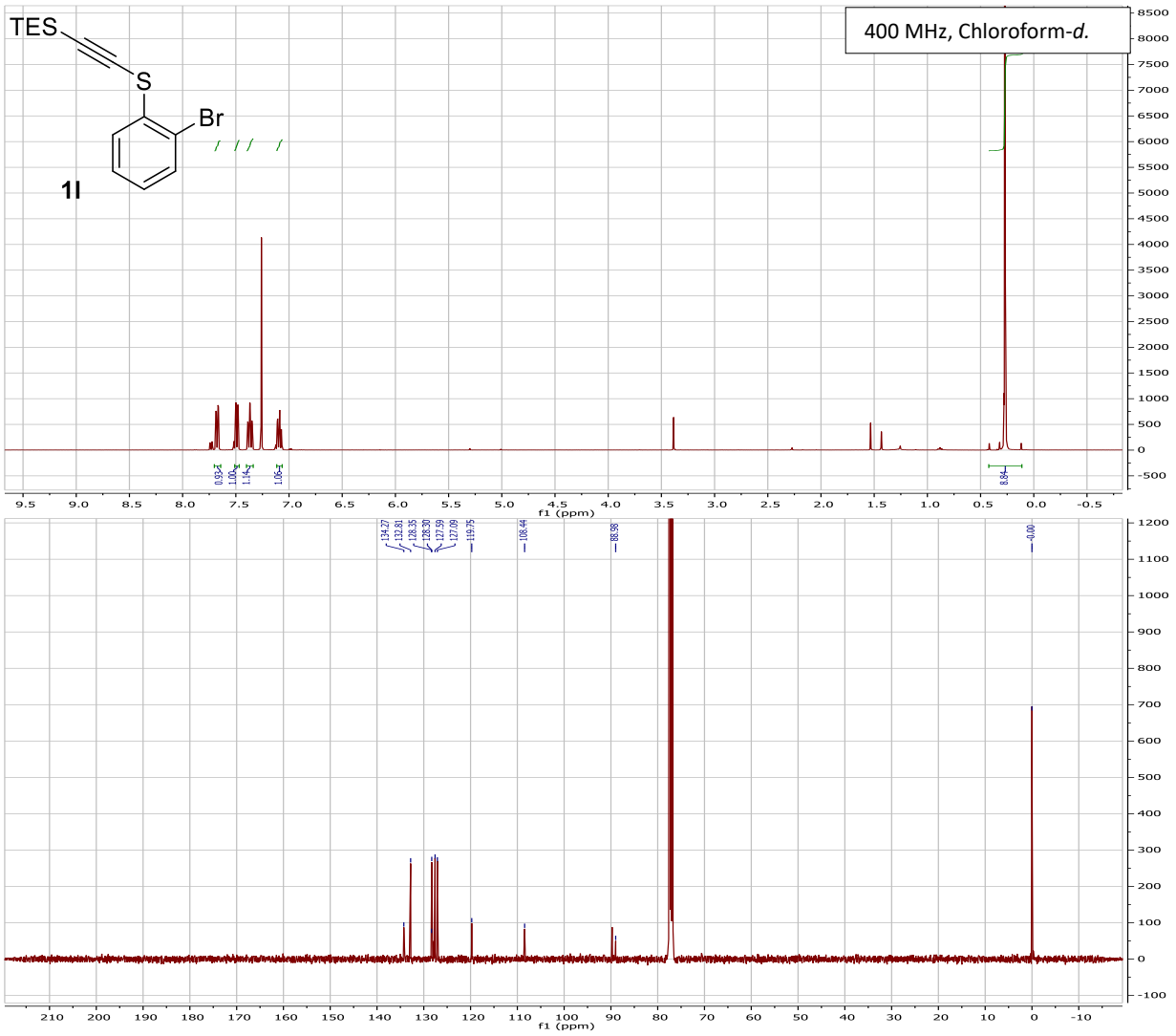

TES
S
1j
400 MHz, Chloroform-d.
f1 (ppm)
101.18
85.05
49.70
42.83
42.79
26.06
25.96
20.13
20.06
7.58
4.62

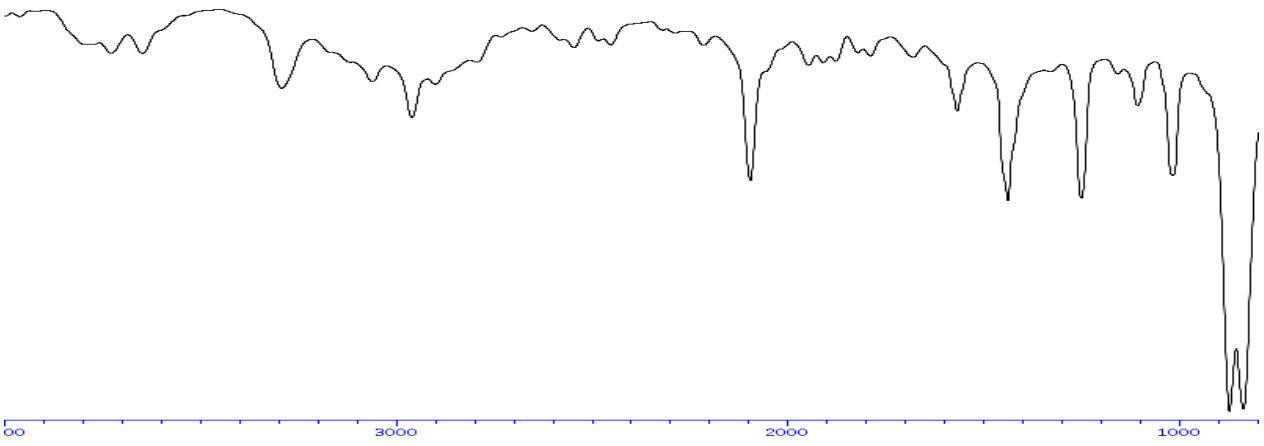

3000
2000
1000

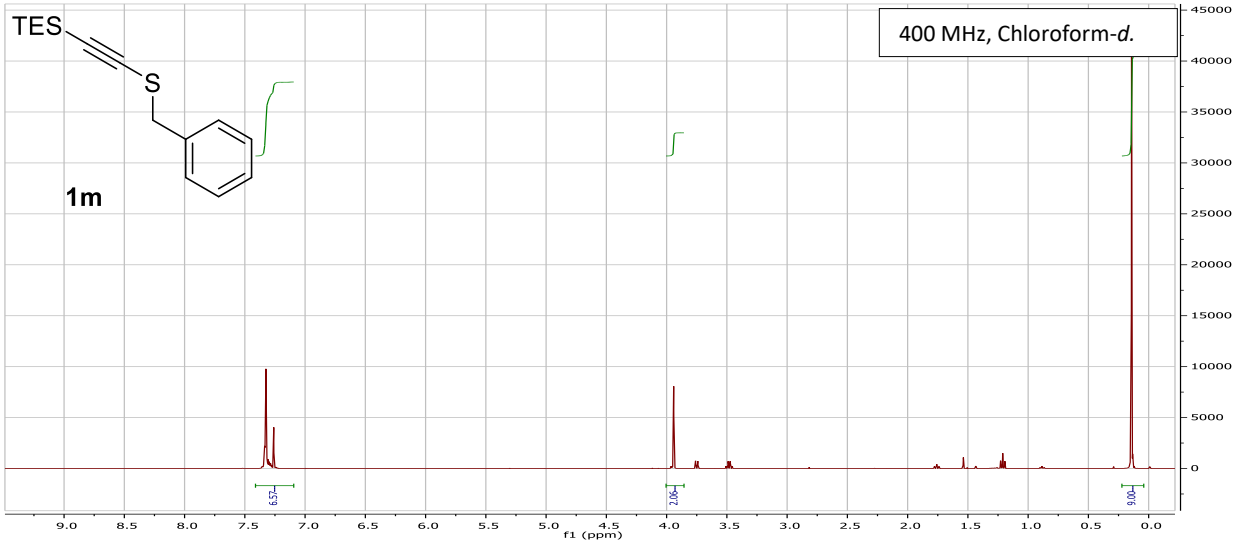

TES
S
1k
400 MHz, Chloroform-d.
f1 (ppm)

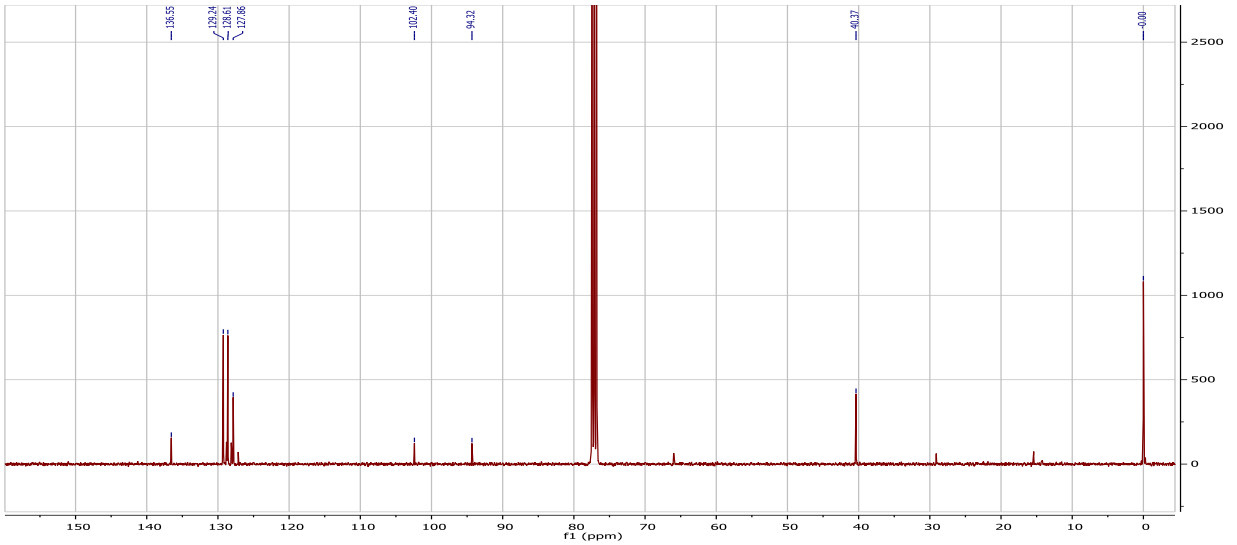

136.69
129.24
129.16
128.61
127.86
127.80
100.02
94.99
40.53
7.52
4.50
f1 (ppm)

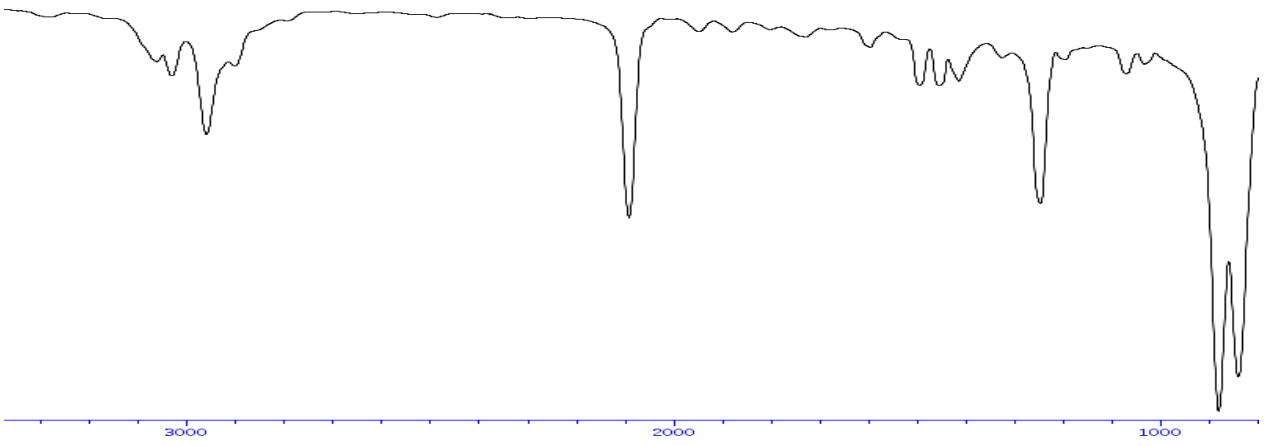

3000
2000
1000

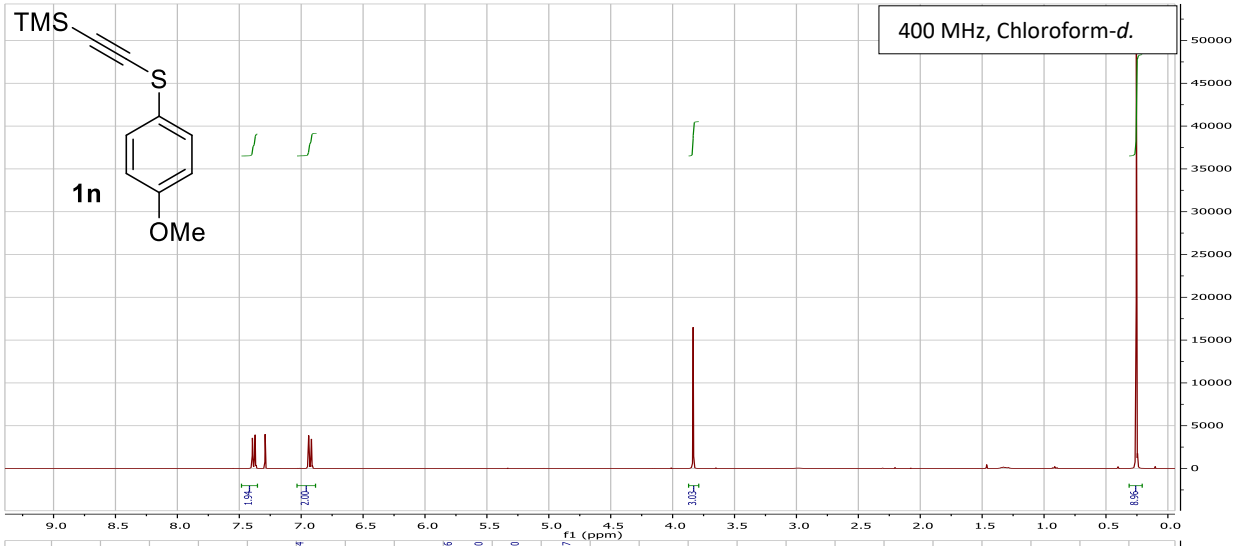

TES
S
Br
1l
400 MHz, Chloroform-d.
f1 (ppm)
f1 (ppm)

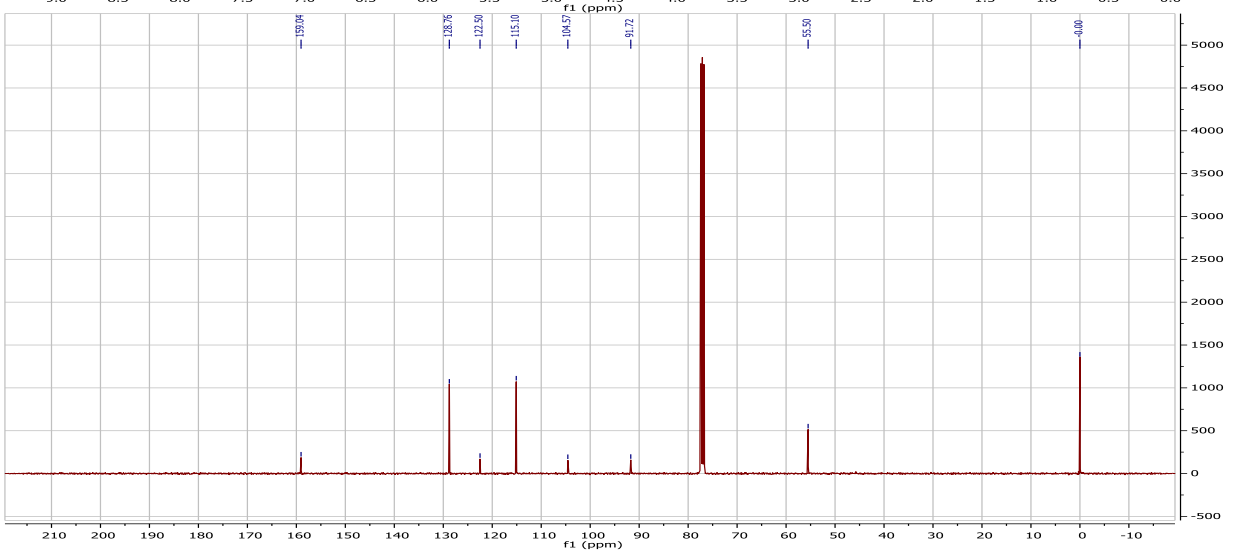


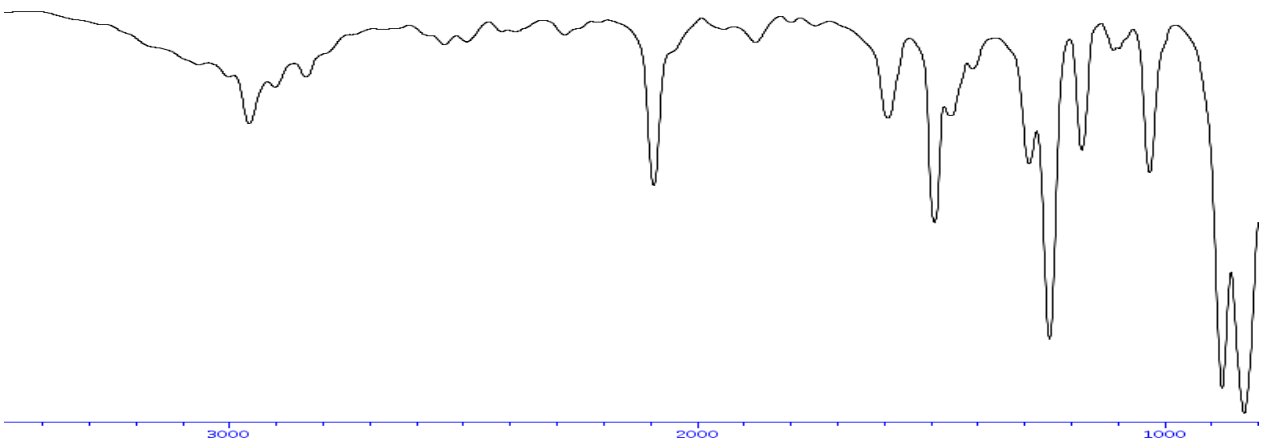

TES
S
1m
400 MHz, Chloroform-d.
f1 (ppm)

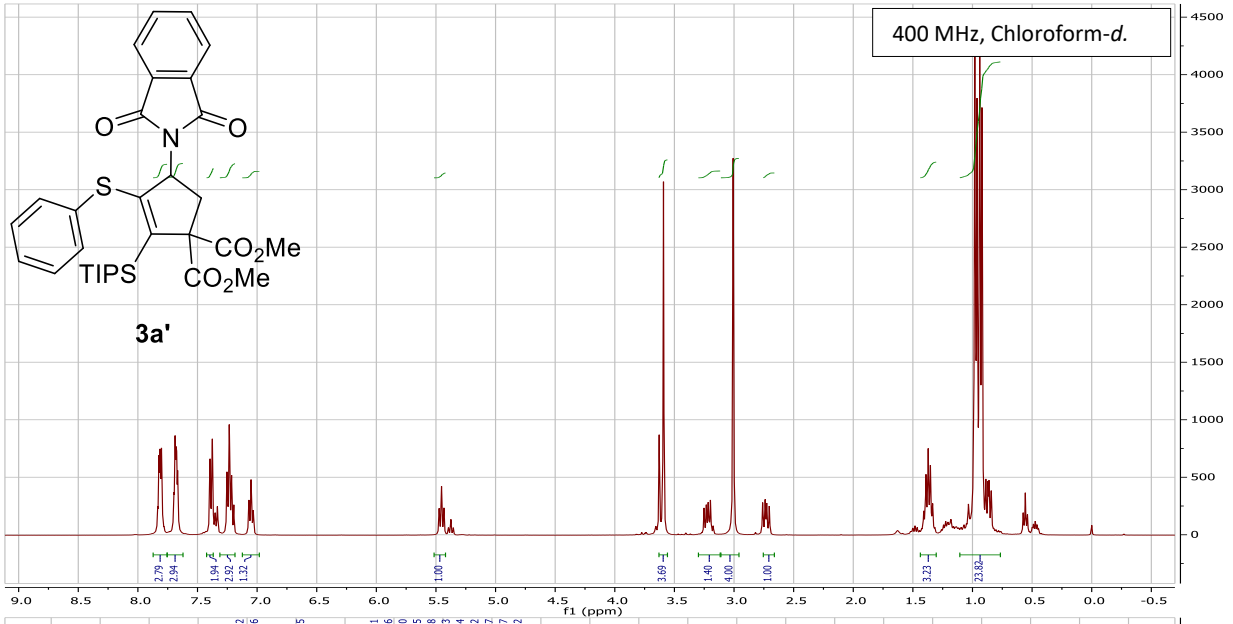

136.55
129.24
128.61
127.86
102.40
94.22
40.37
0.00
f1 (ppm)

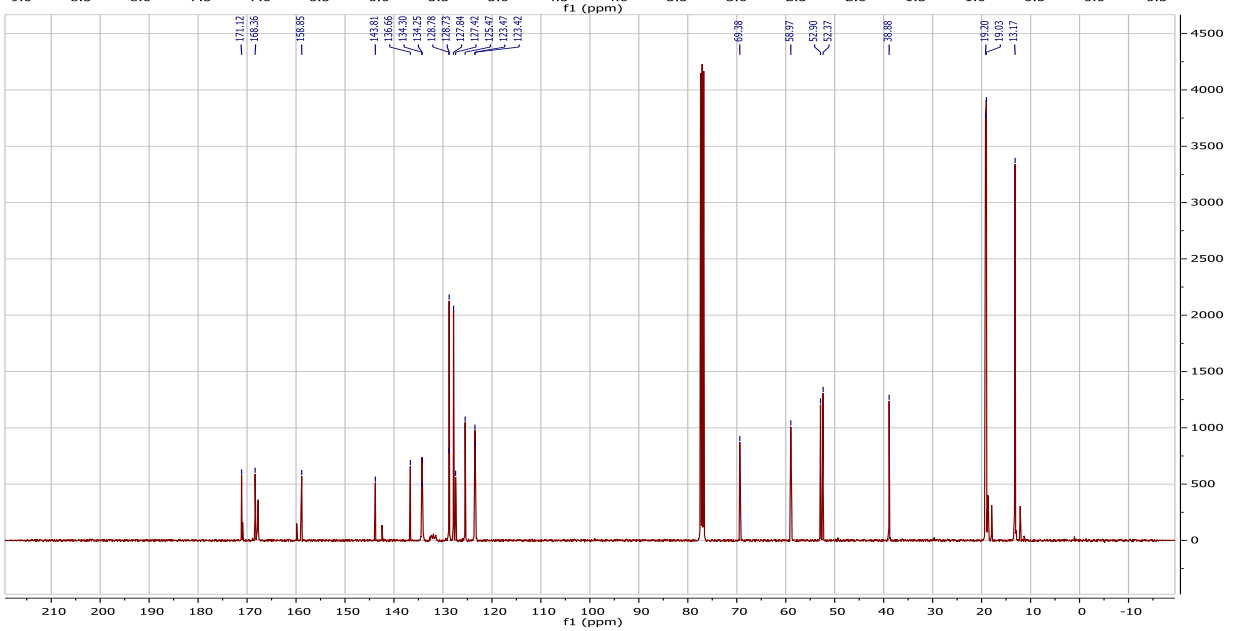

3000
2000
1000

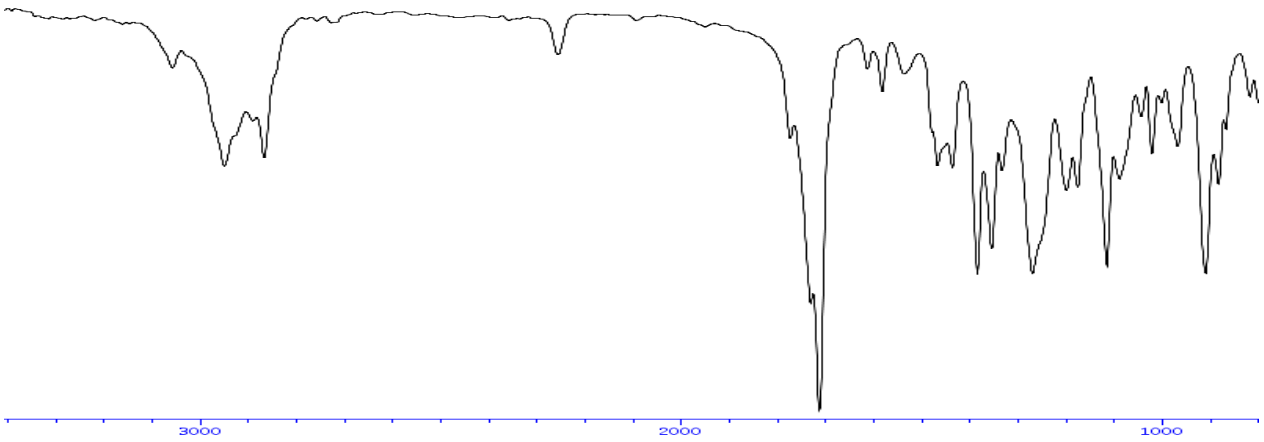

TMS
S
1n
OMe
400 MHz, Chloroform-d.
f1 (ppm)

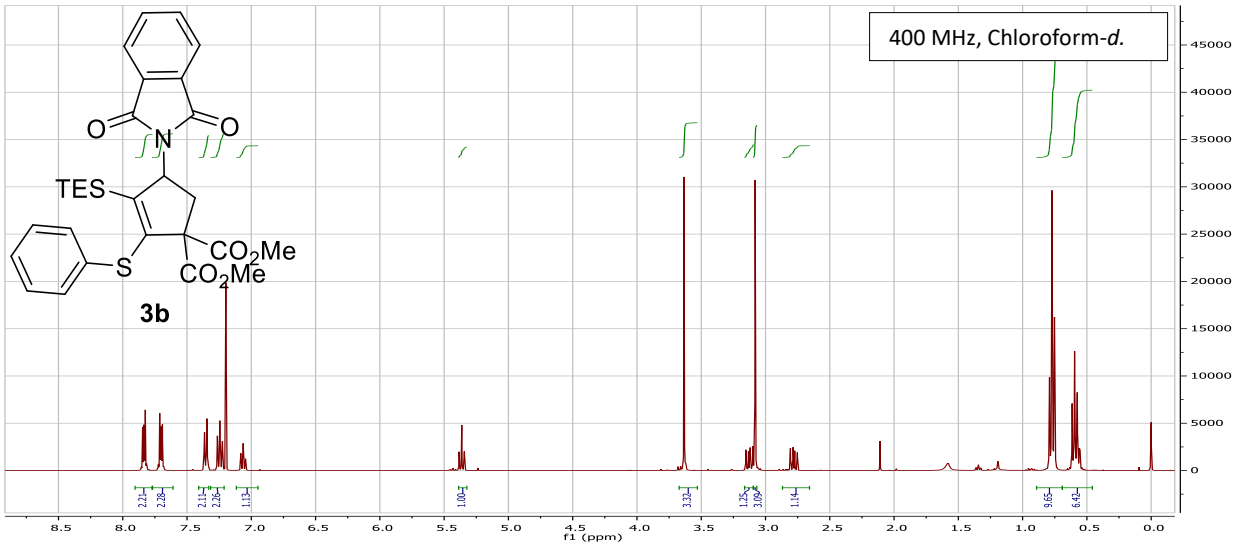

159.04
128.76
122.50
115.10
104.57
91.72
55.50
0.00
f1 (ppm)

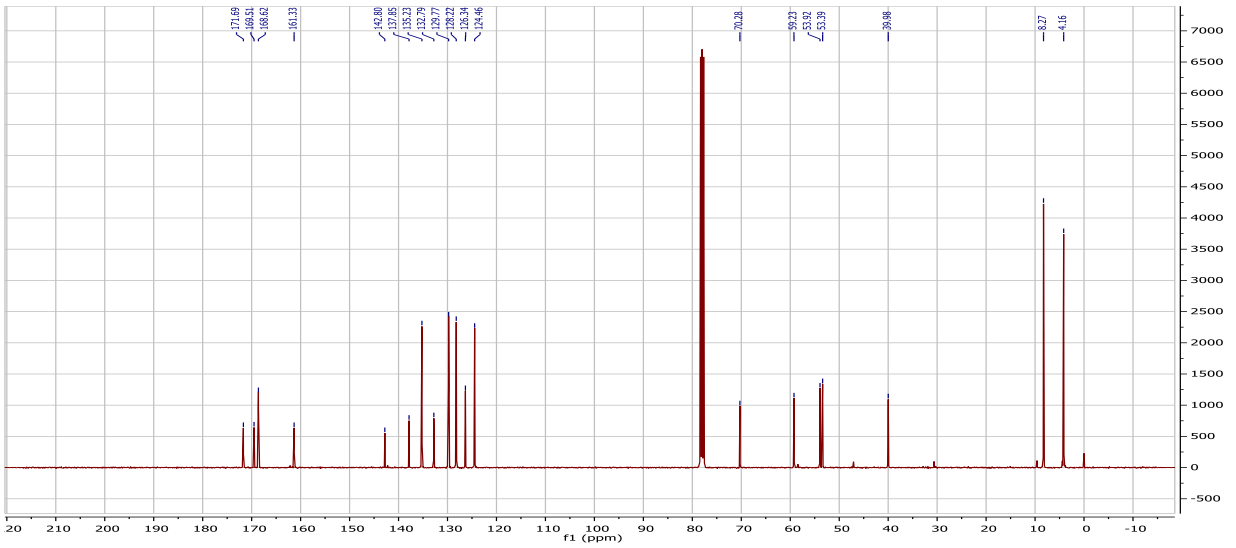

3000
2000
1000

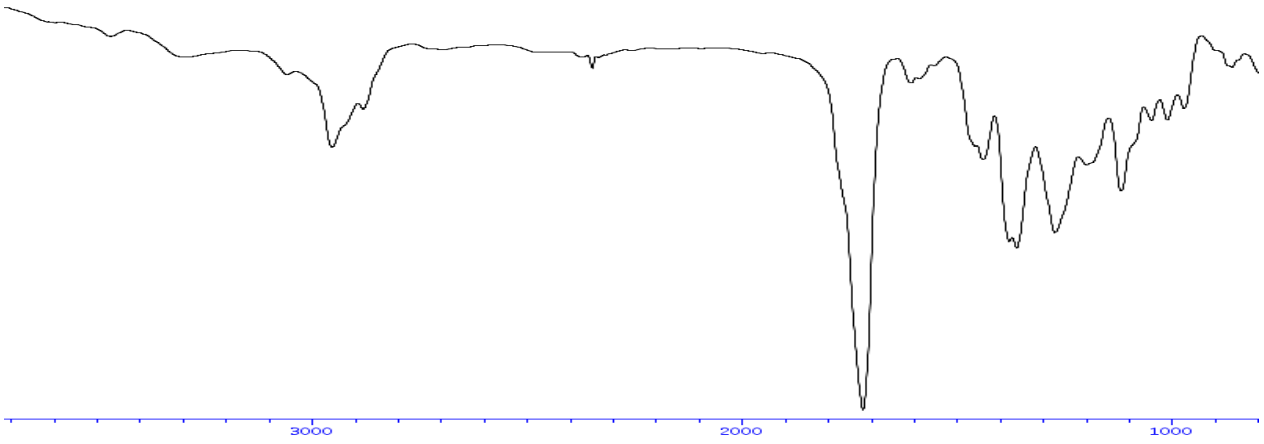

400 MHz, Chloroform-*d*.
O
N
O
S
TIPS
CO_2Me
CO_2Me
3a'
f1 (ppm)

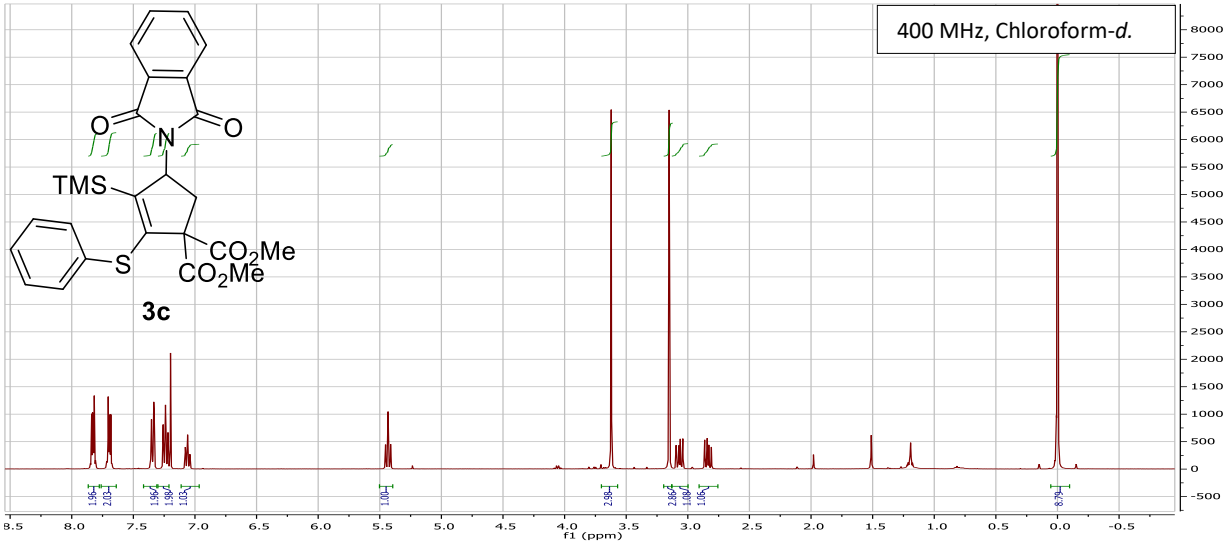

171.12
168.36
158.85
143.81
136.66
134.30
134.25
128.78
128.73
127.84
127.42
125.47
123.47
123.42
69.38
58.97
52.90
52.37
38.88
19.20
19.03
13.17
f1 (ppm)

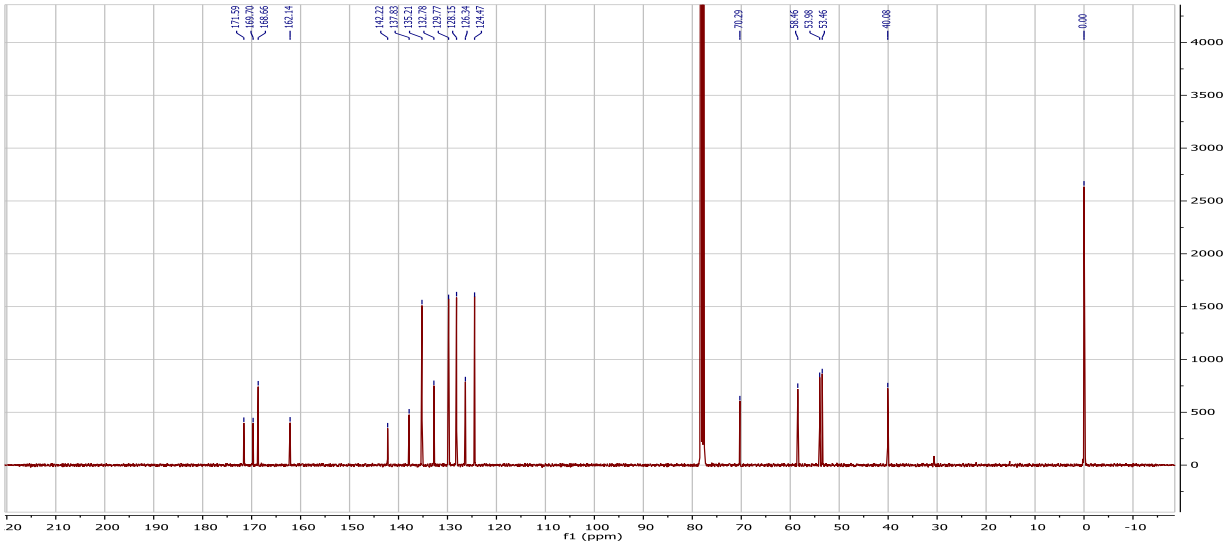

3000
2000
1000


400 MHz, Chloroform-d.
O
N
O
TES
S
CO2Me
CO2Me
3b
f1 (ppm)


171.69
169.51
168.62
161.33
142.80
137.05
135.23
132.79
129.77
128.22
126.34
124.46
70.28
59.23
53.92
53.39
39.88
8.27
4.16
f1 (ppm)


3000
2000
1000


400 MHz, Chloroform-d.
TMS
CO2Me
CO2Me
3c
f1 (ppm)


171.59
168.70
168.66
162.14
142.22
137.83
135.21
132.78
129.77
128.15
126.34
124.47
70.29
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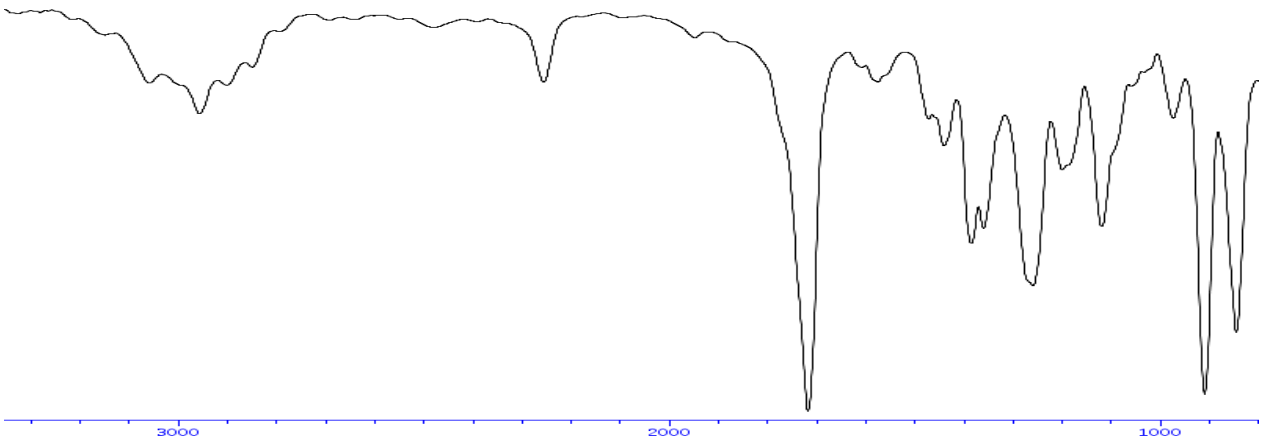
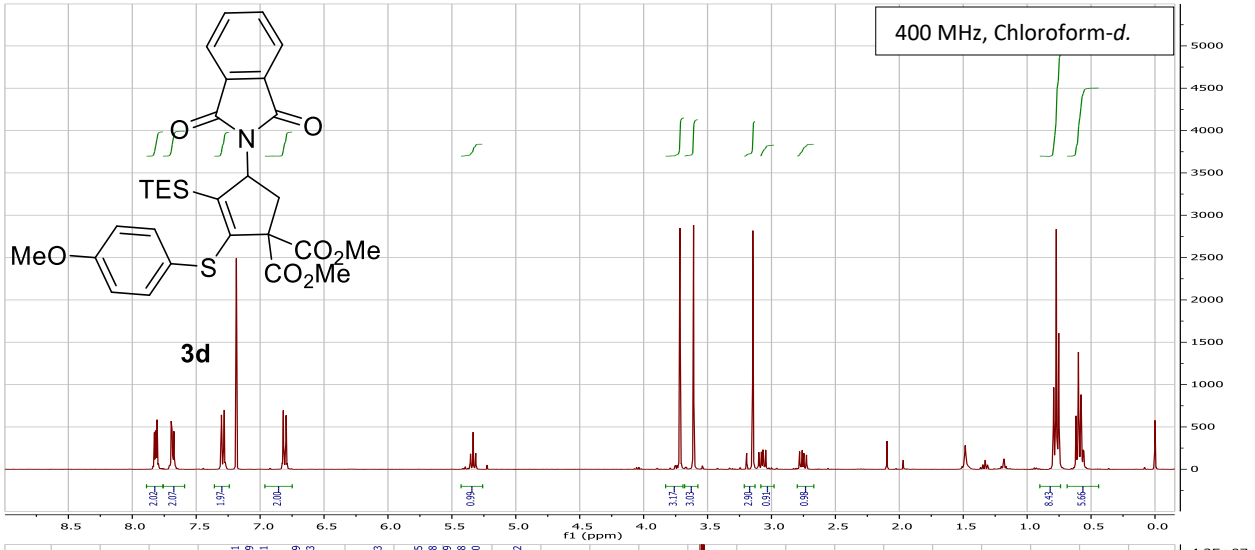
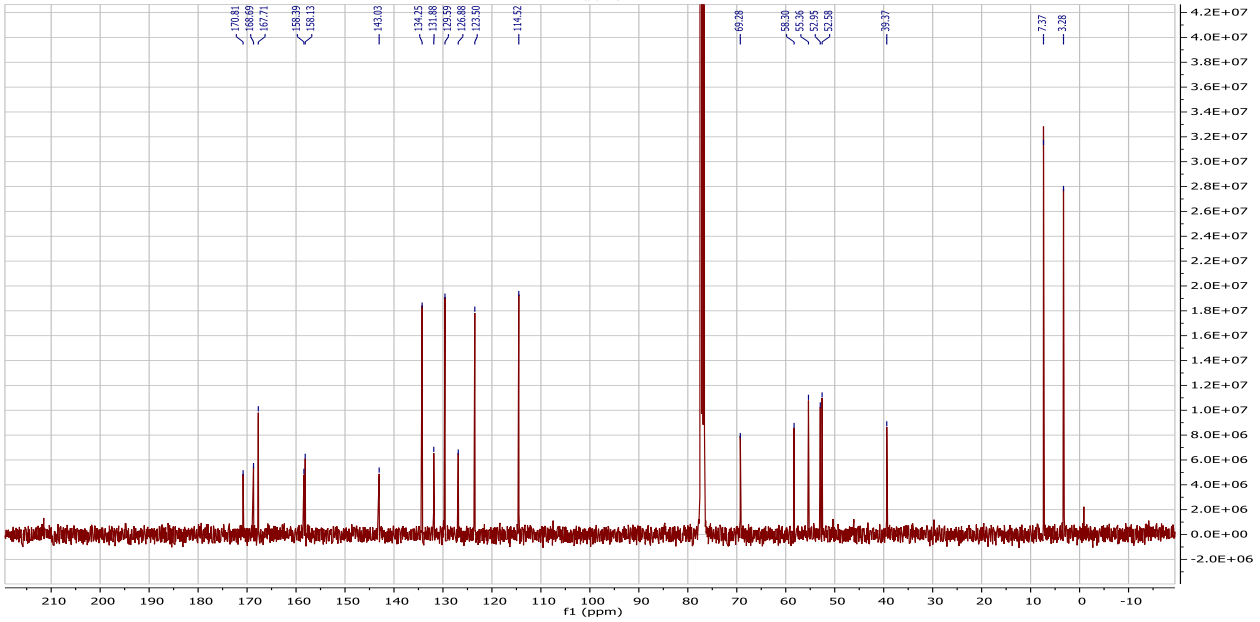
53.98
53.46
40.08
0.00
f1 (ppm)


3000
2000
1000


400 MHz, Chloroform-d.
O
N
O
TES
MeO
S
CO2Me
CO2Me
3d
f1 (ppm)


170.81
168.69
167.71
158.39
158.13
143.03
134.25
131.88
129.59
126.88
123.50
114.52
69.28
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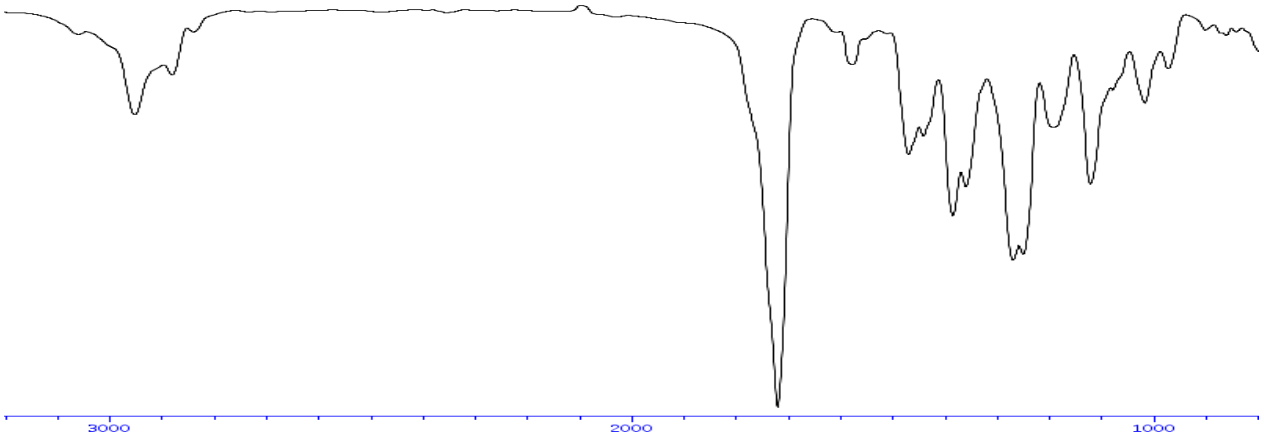
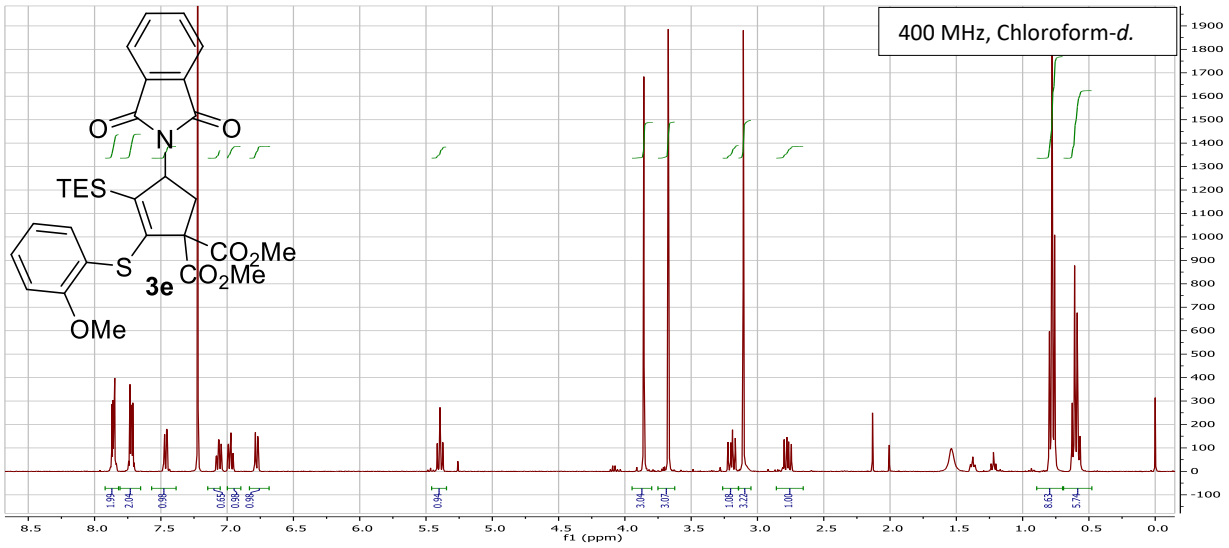
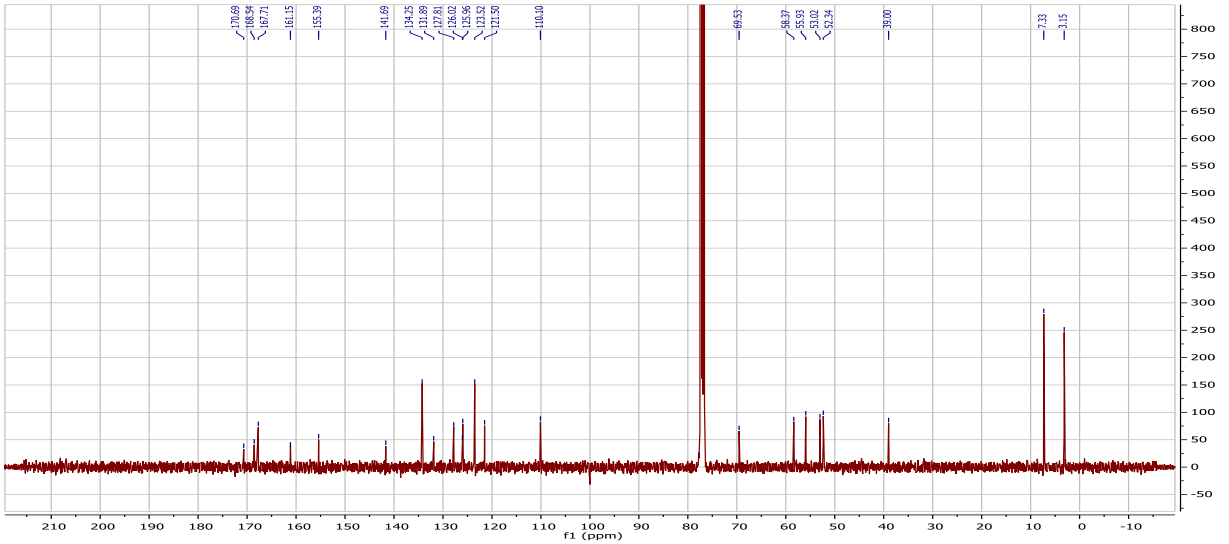
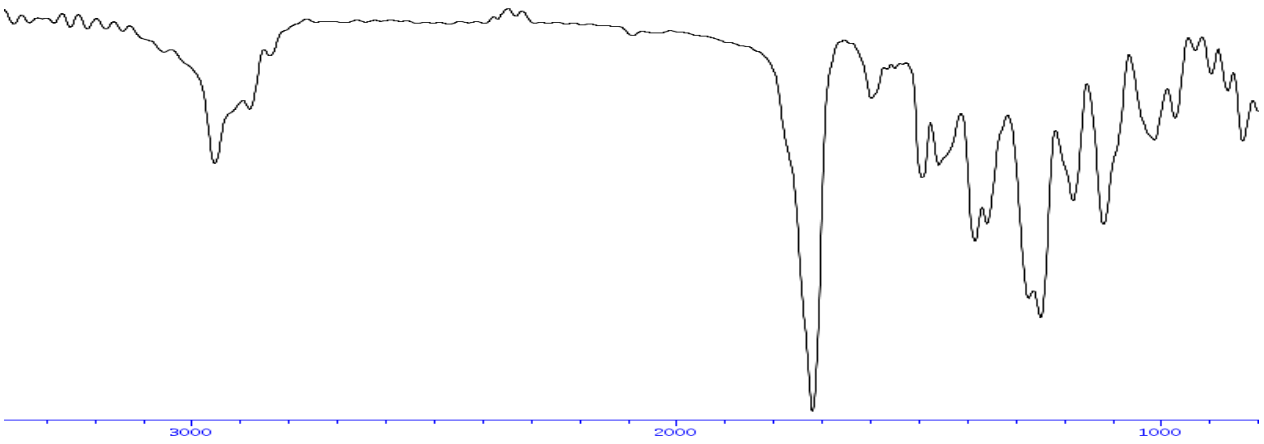
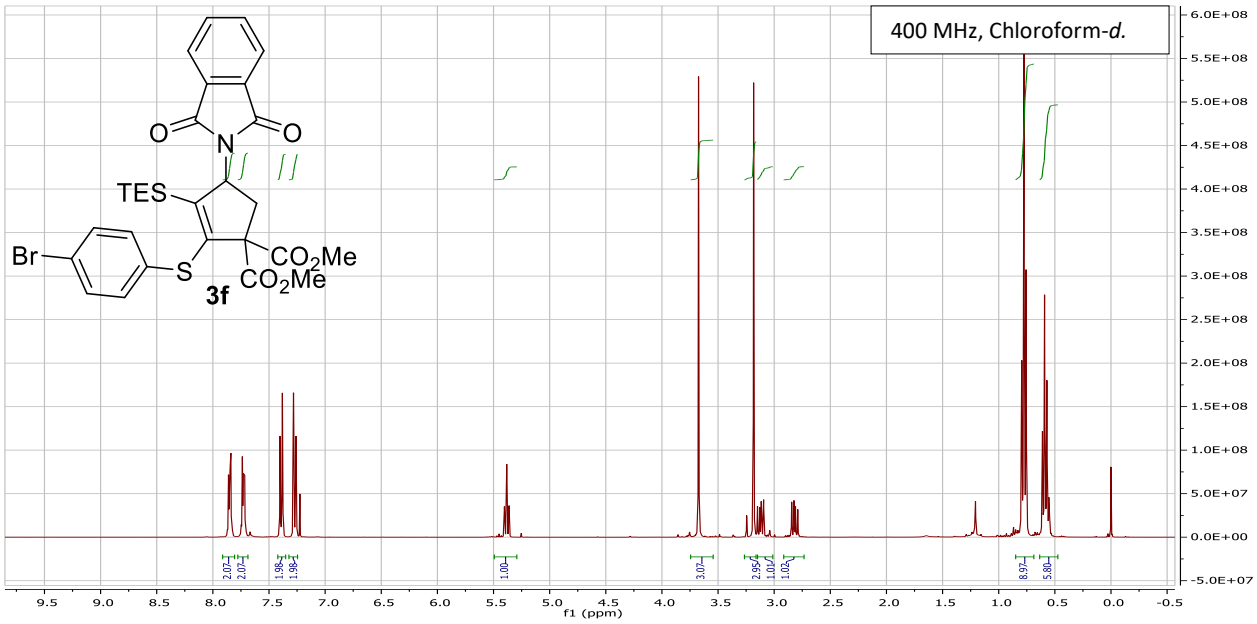
52.95
52.58
39.37
7.37
3.28
f1 (ppm)

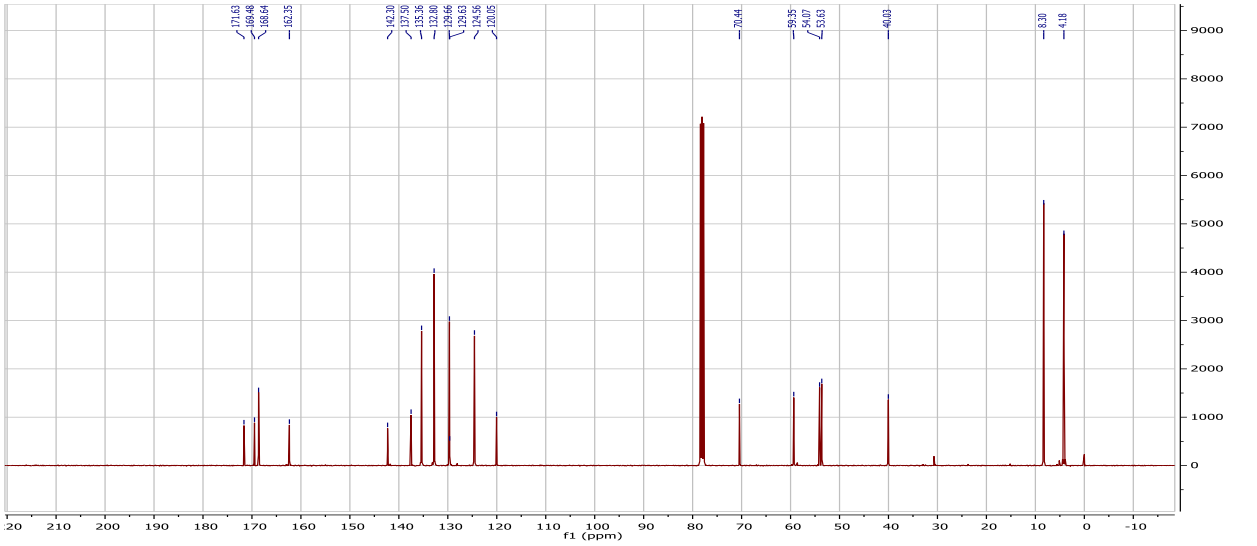

3000
2000
1000

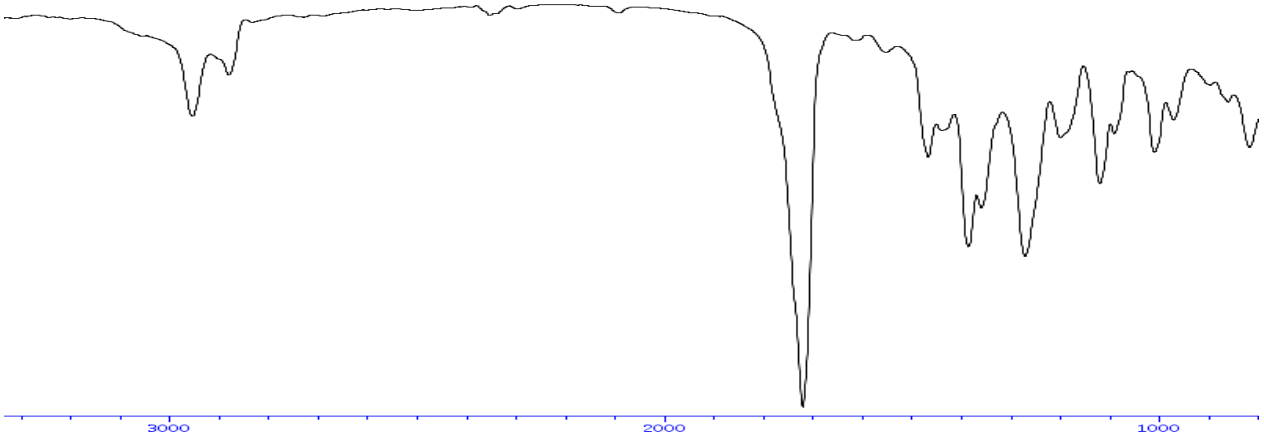

400 MHz, Chloroform-d.
TES
CO2Me
CO2Me
S
OMe
3e
f1 (ppm)

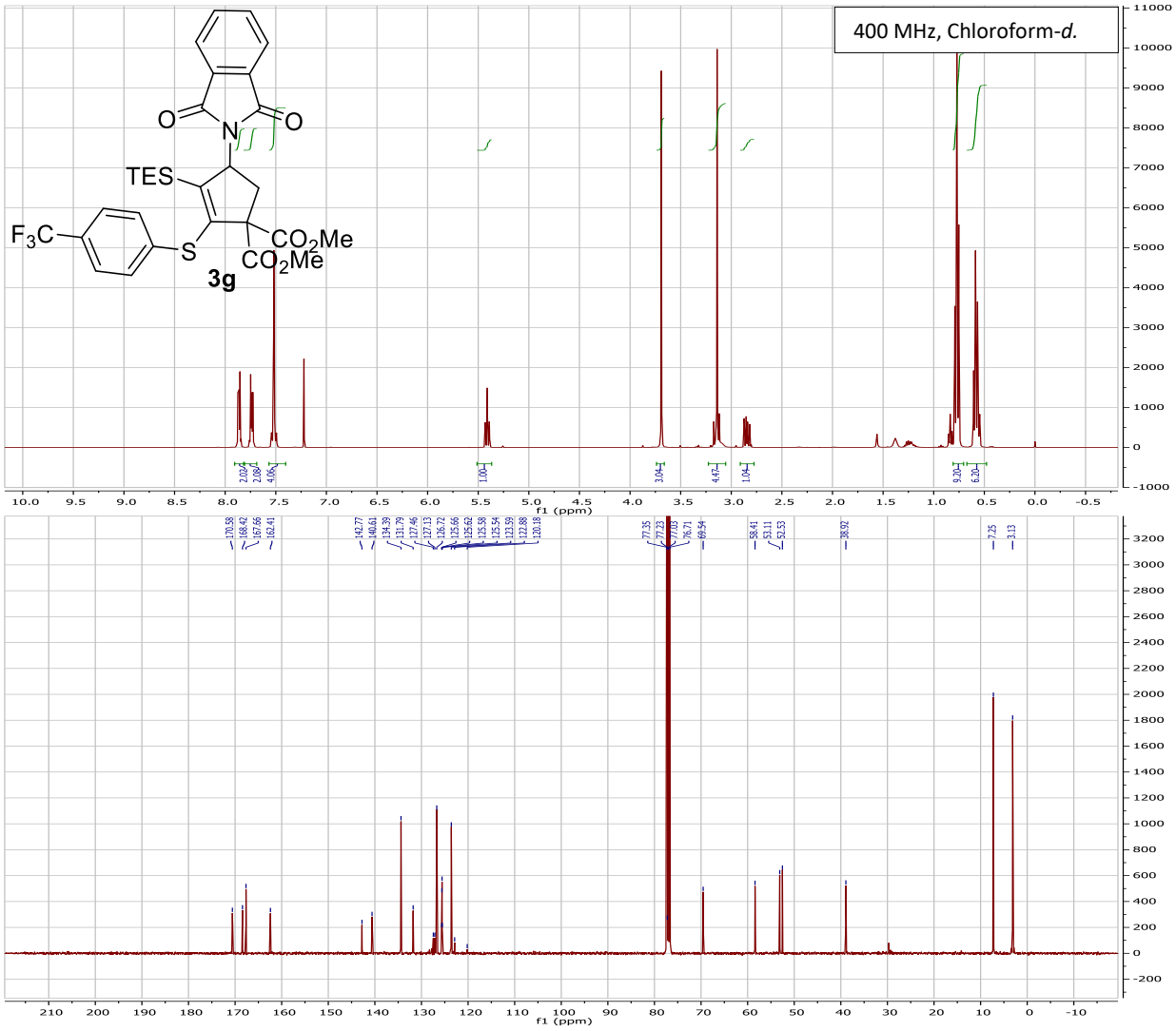

f1 (ppm)

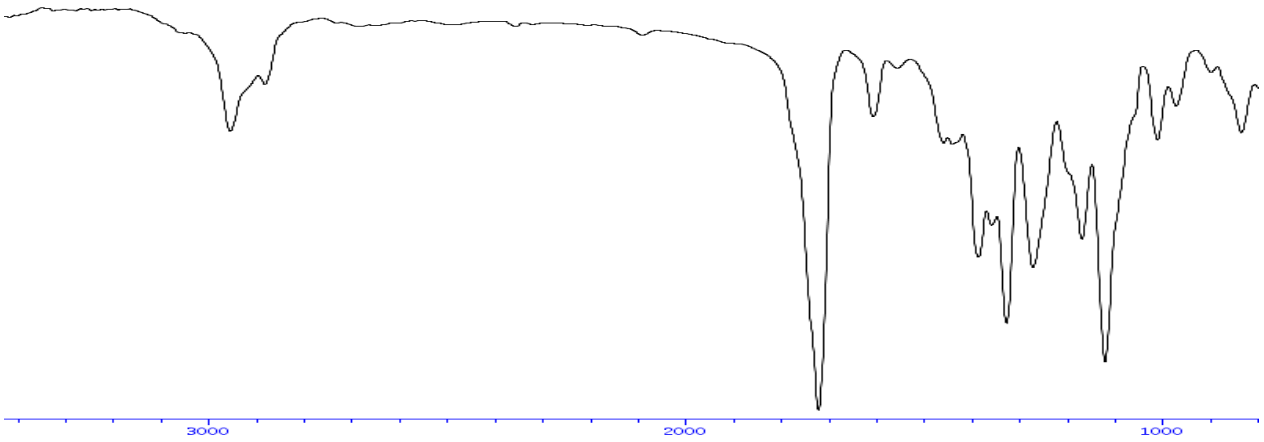

3000
2000
1000

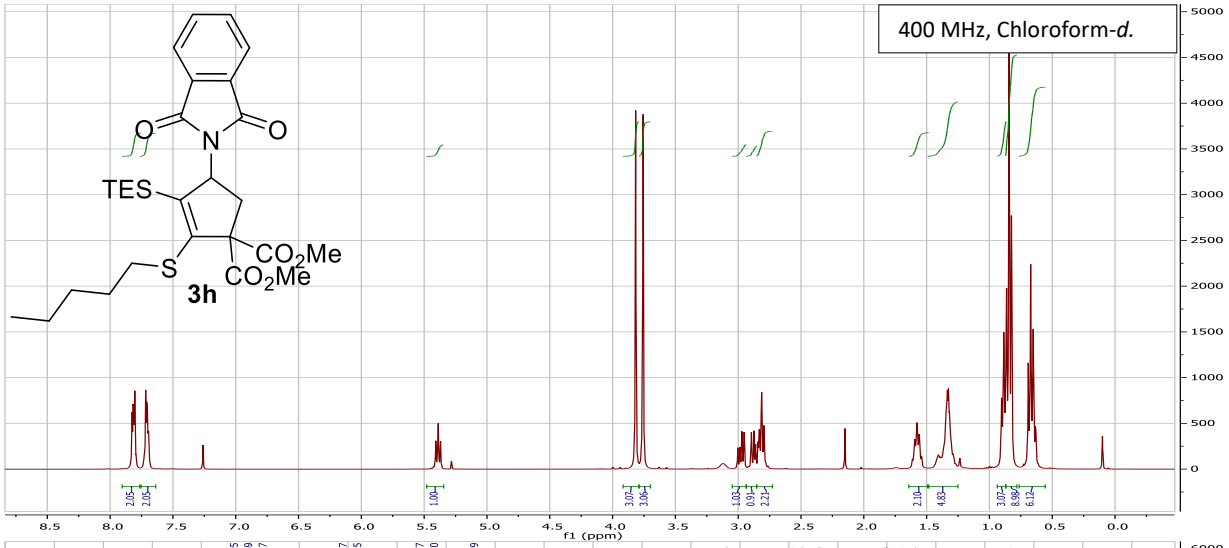

400 MHz, Chloroform-d.
O
N
O
TES
Br
S
CO2Me
CO2Me
3f
f1 (ppm)

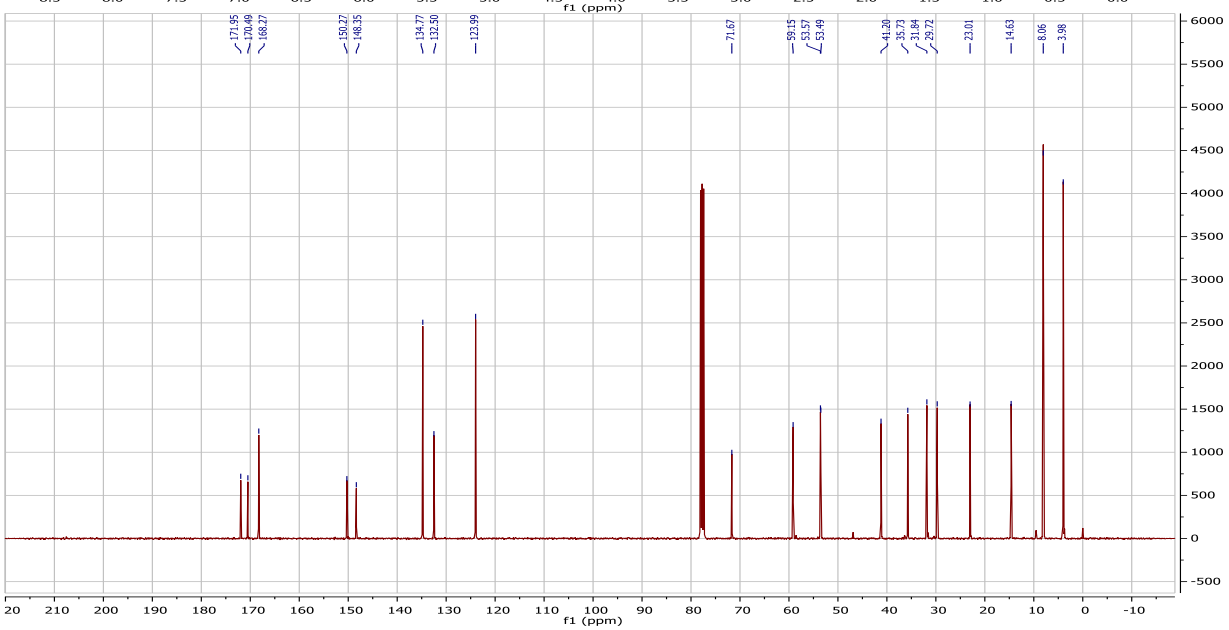

171.63
169.48
168.64
162.35
142.30
137.50
135.36
132.80
129.66
129.63
124.56
120.05
70.44
59.35
54.07
53.63
40.03
8.30
4.18
f1 (ppm)

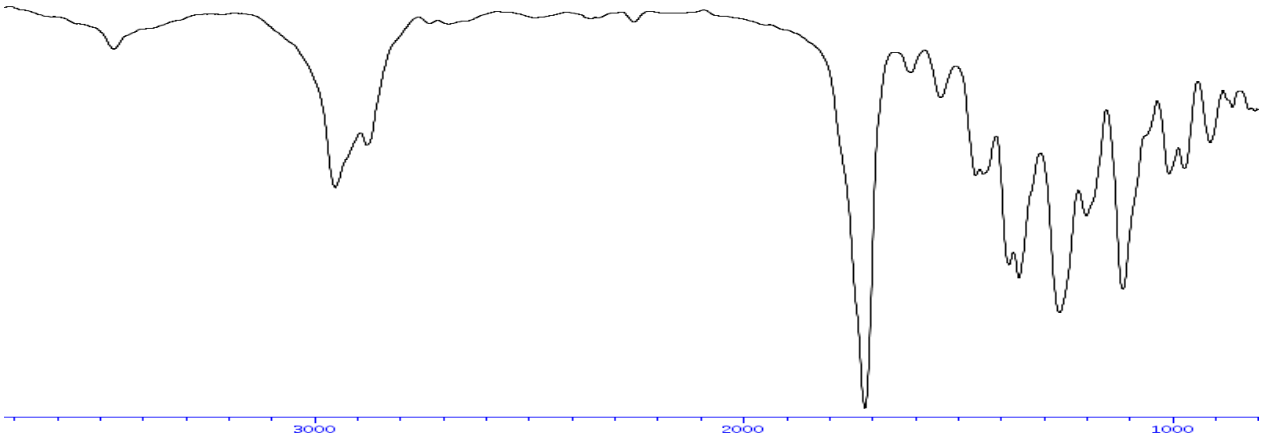

3000
2000
1000

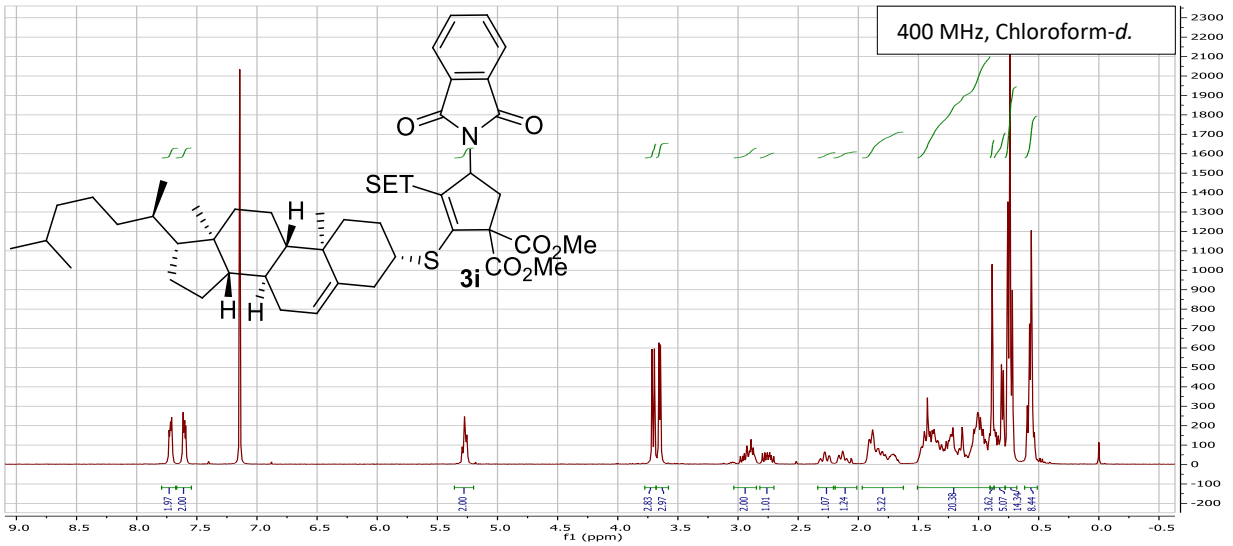

400 MHz, Chloroform-d.
O
N
O
TES
F3C
S
CO2Me
CO2Me
3g
f1 (ppm)

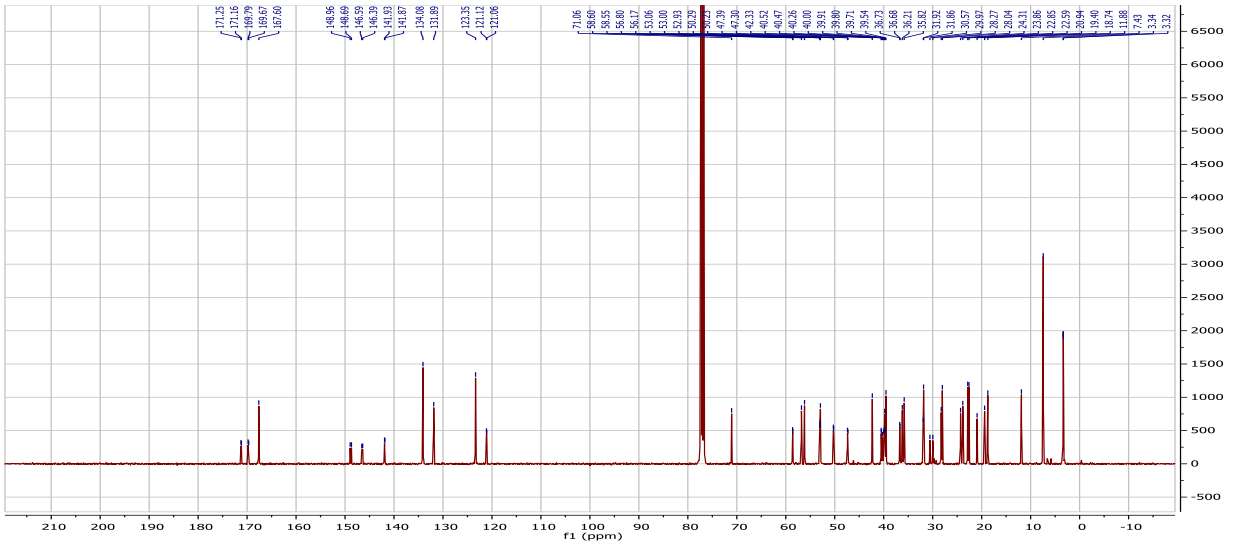

3000
2000
1000

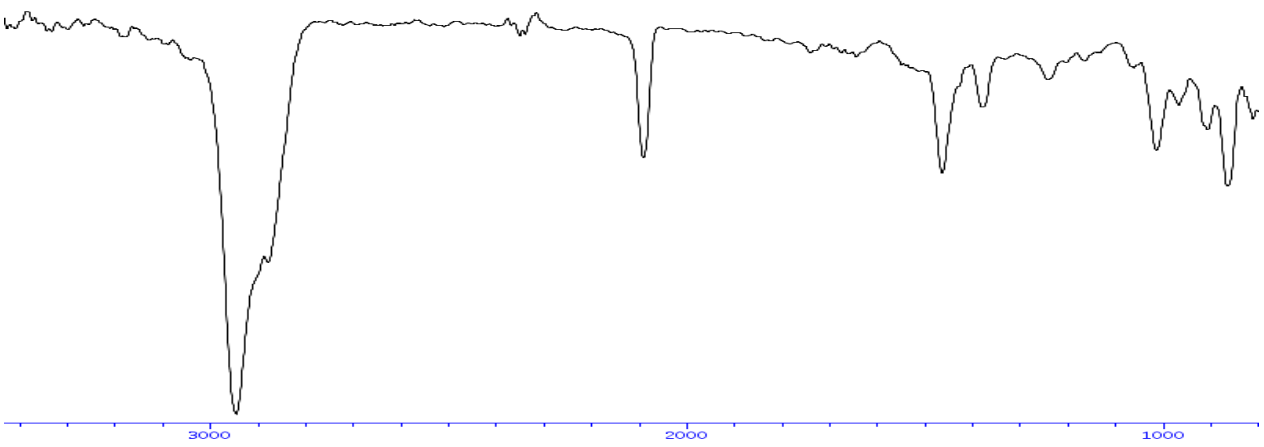

400 MHz, Chloroform-d.
O
N
O
TES
S
CO2Me
CO2Me
3h
f1 (ppm)

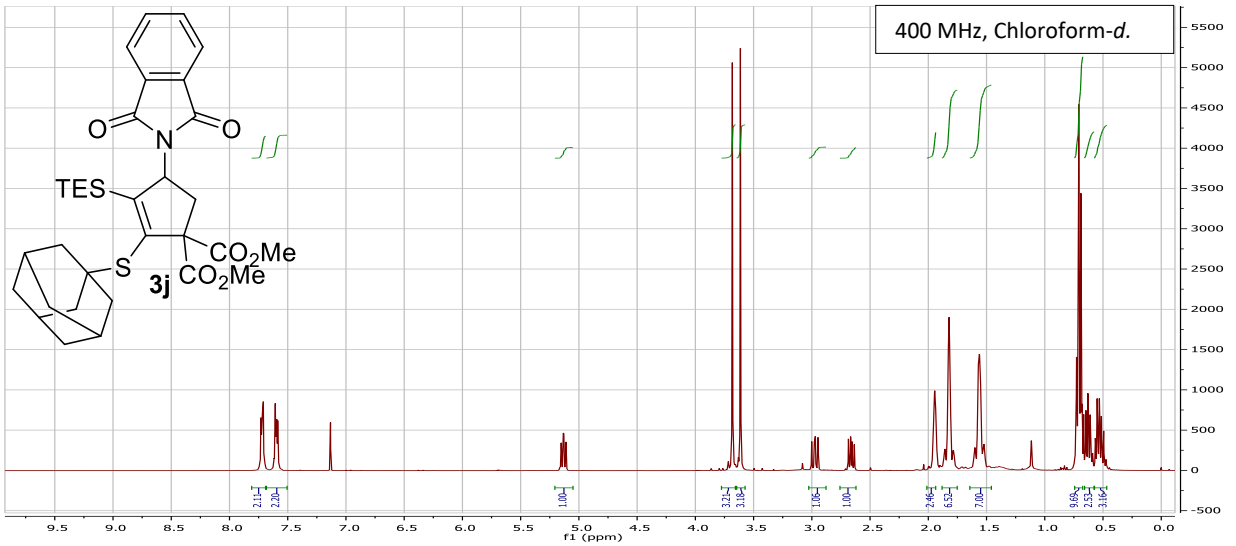

171.95
170.40
168.27
150.27
148.35
134.77
132.50
123.99
71.67
59.15
53.57
53.49
41.20
35.73
31.84
29.72
23.01
14.63
8.06
3.98
f1 (ppm)

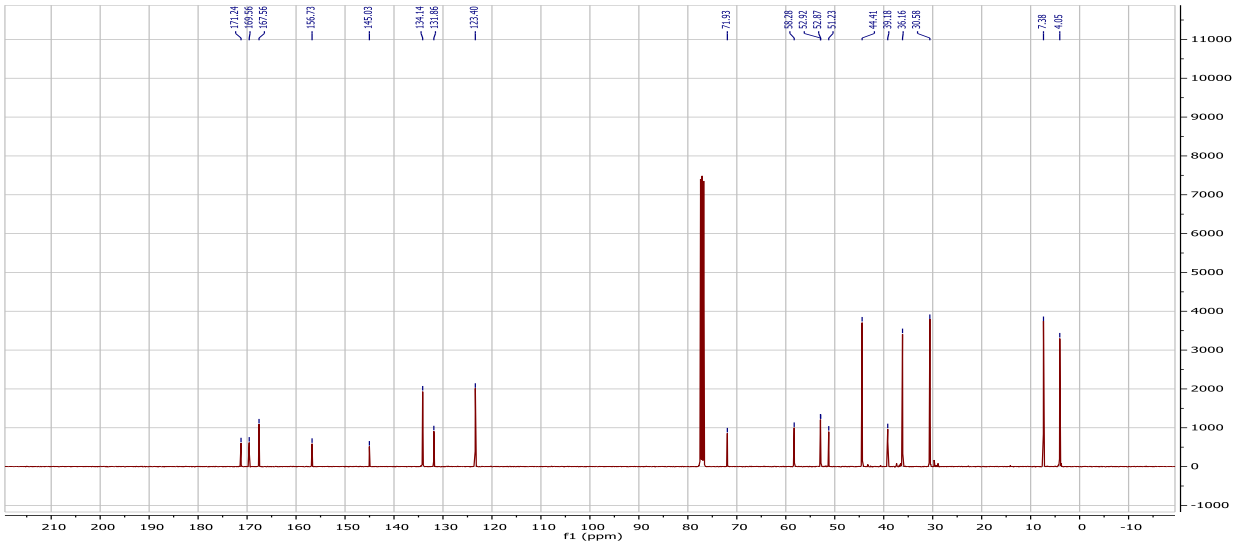

3000
2000
1000

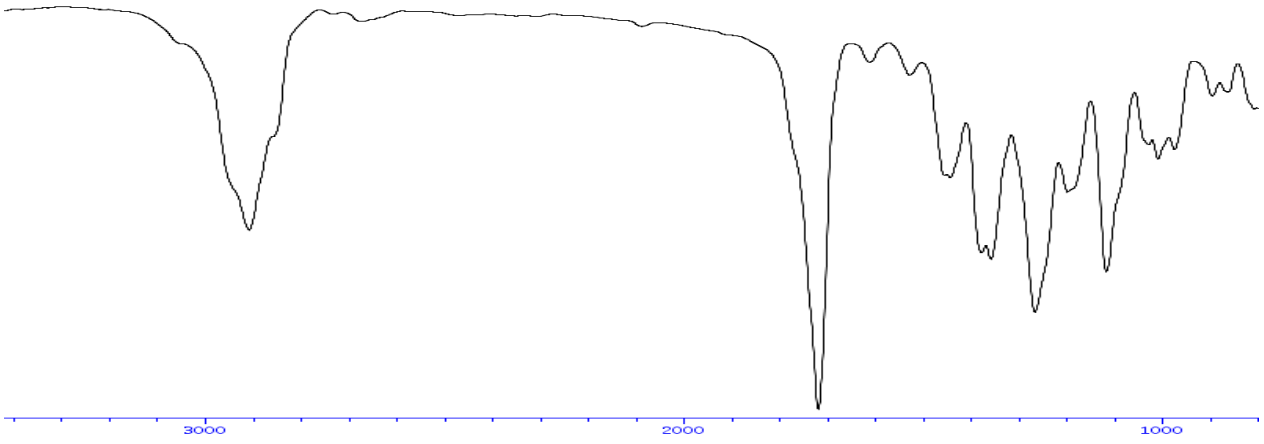

400 MHz, Chloroform-*d*.
O
N
O
SET
CO2Me
CO2Me
S
H
H
H
3i
f1 (ppm)

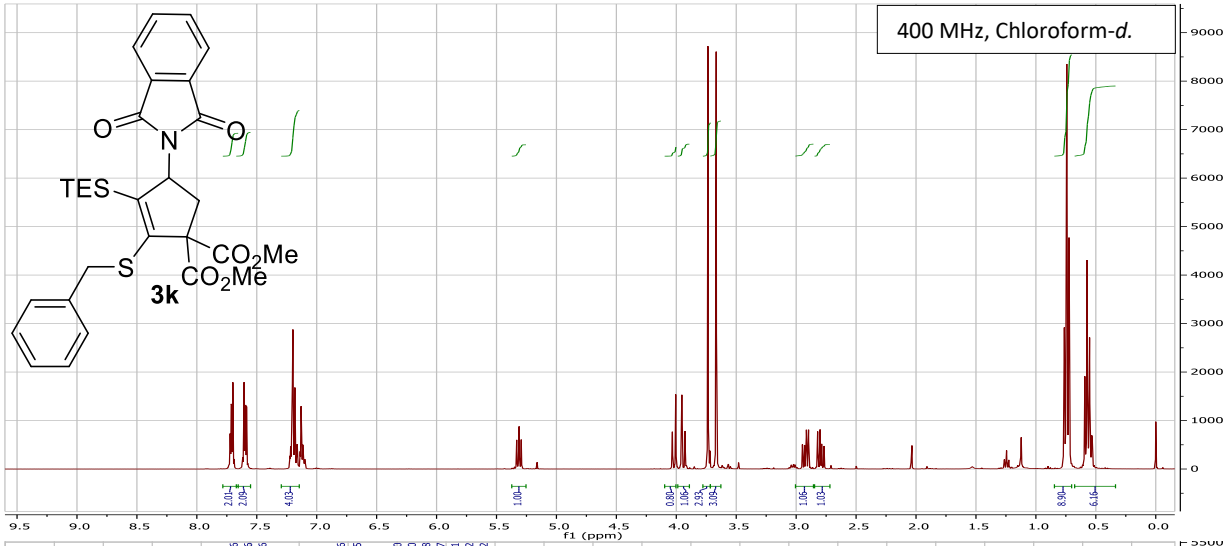

f1 (ppm)

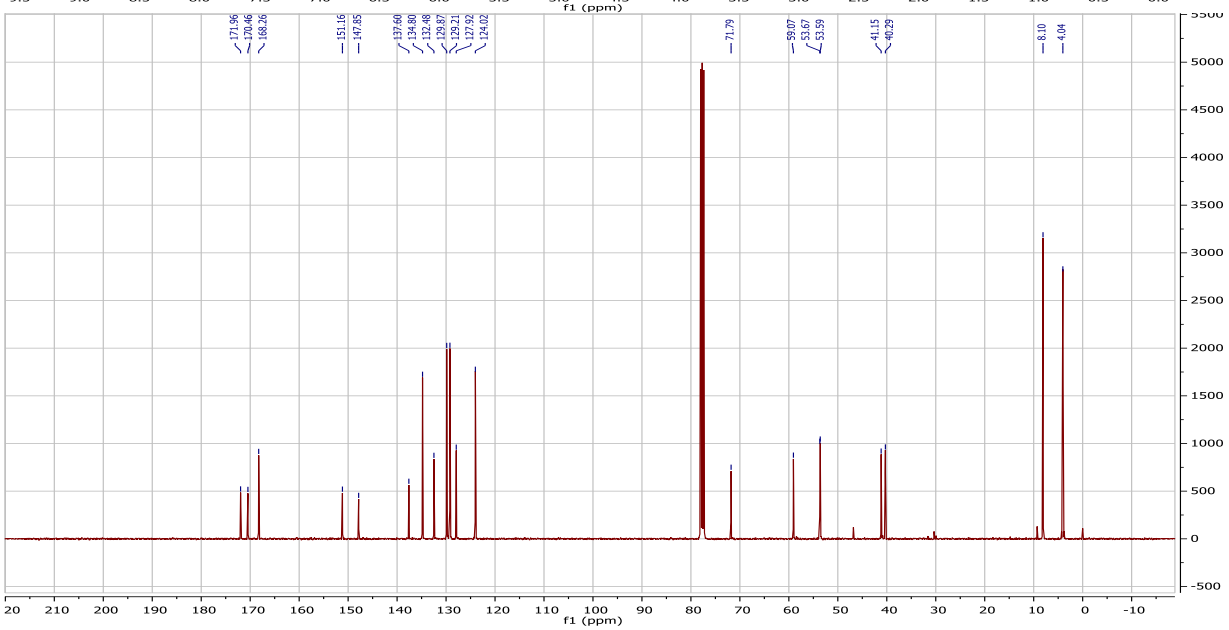

3000
2000
1000

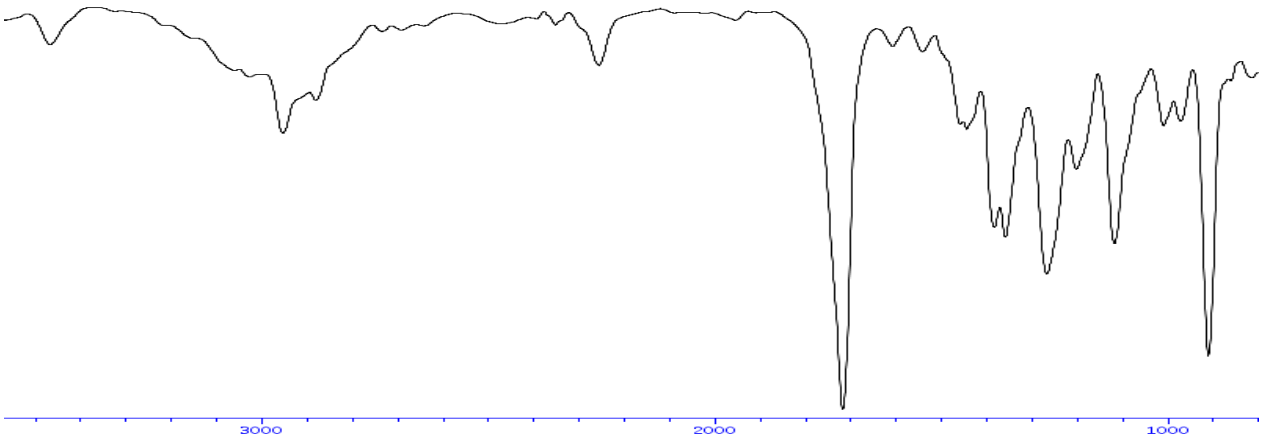

400 MHz, Chloroform-*d*.
O
N
O
TES
S
CO2Me
CO2Me
3j
f1 (ppm)

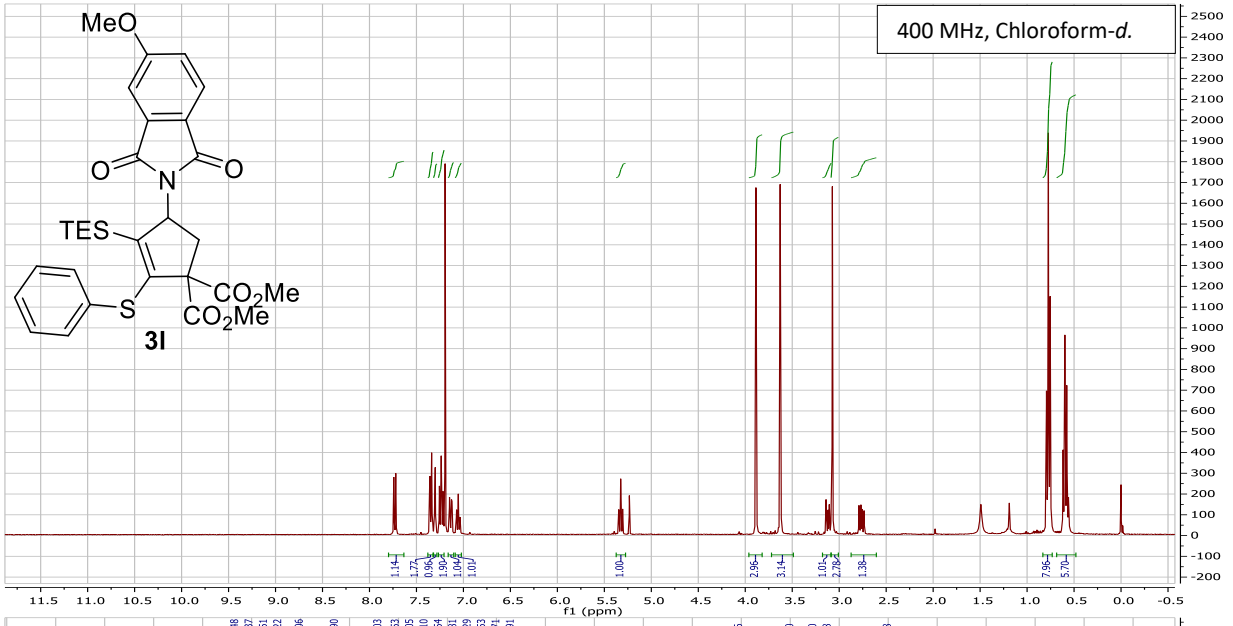

171.24
169.56
167.56
156.73
145.03
134.14
131.86
123.40
71.93
58.28
52.92
52.87
51.23
44.41
39.18
36.16
30.58
7.38
4.05
f1 (ppm)

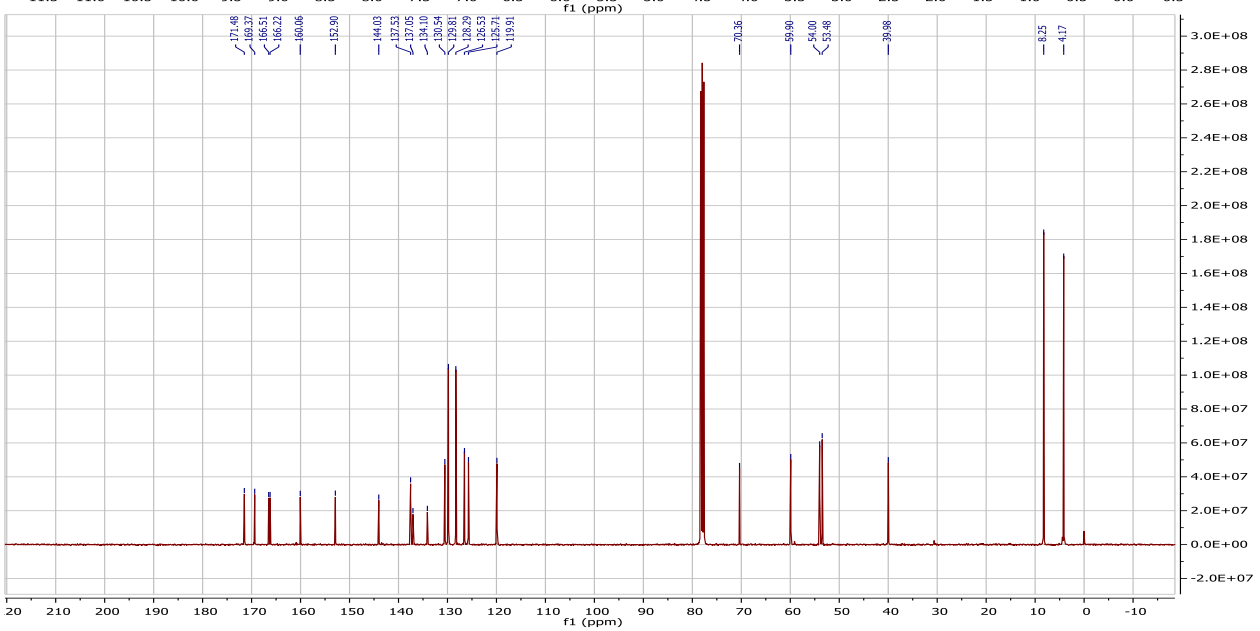

3000
2000
1000

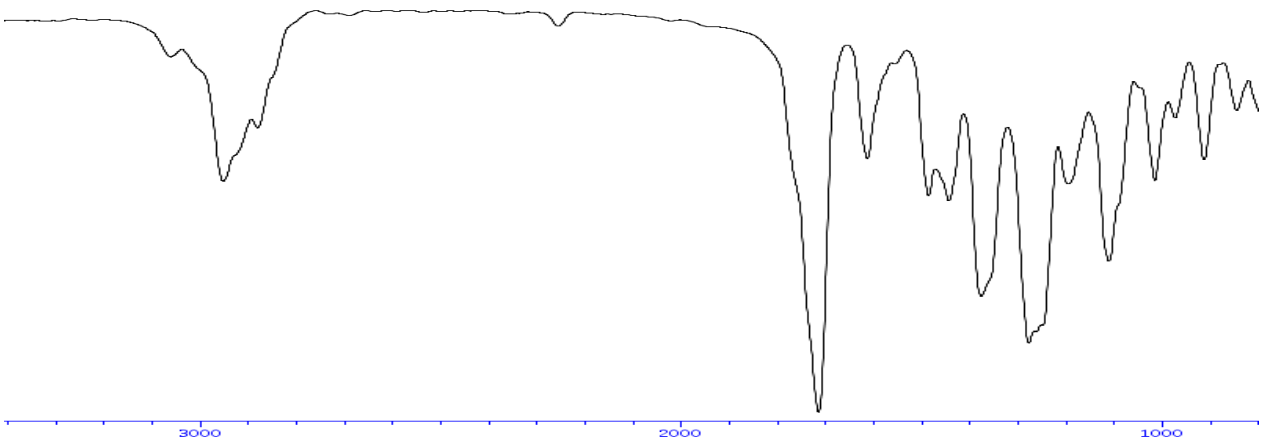

400 MHz, Chloroform-d.
TES
CO2Me
CO2Me
S
N
O
O
3k
f1 (ppm)


f1 (ppm)

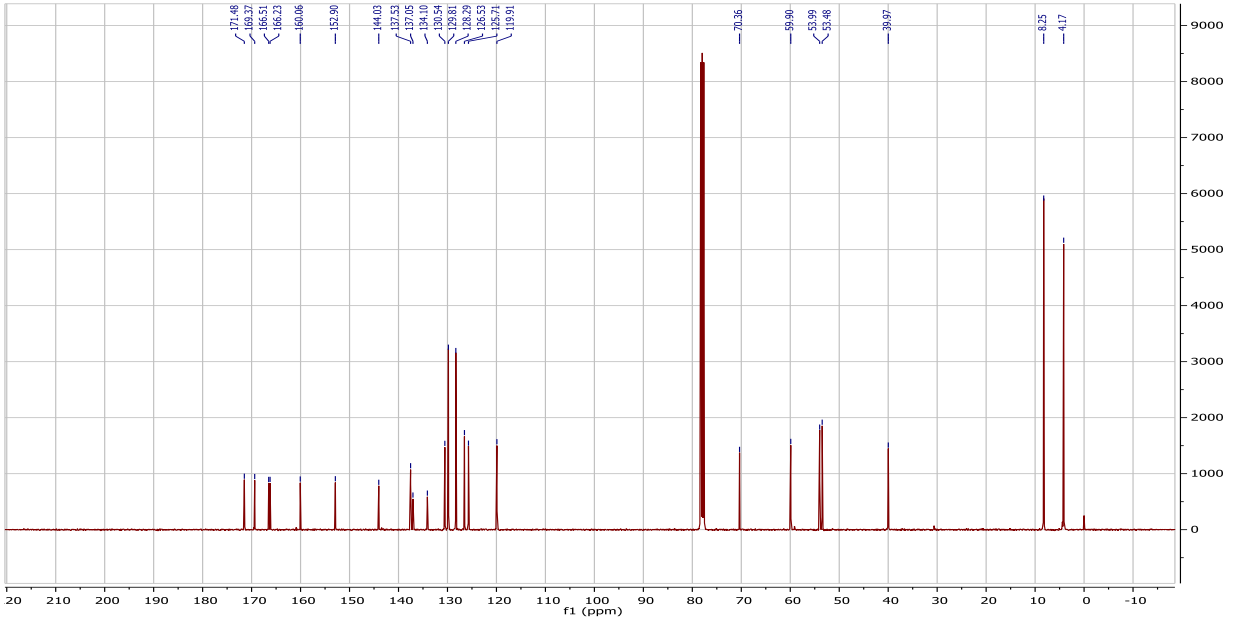

3000
2000
1000

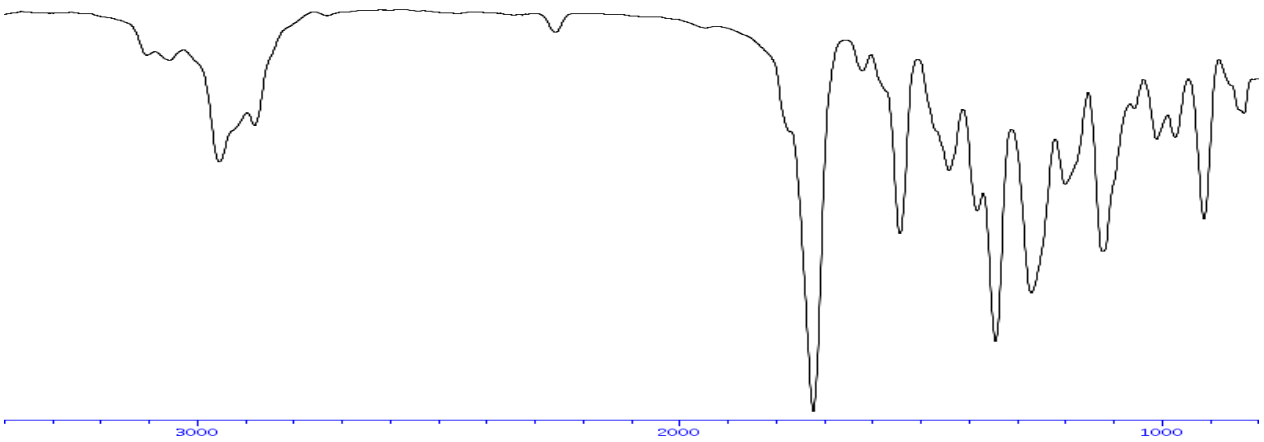

MeO
O
N
O
TES
S
CO2Me
CO2Me
3l
400 MHz, Chloroform-d.
f1 (ppm)

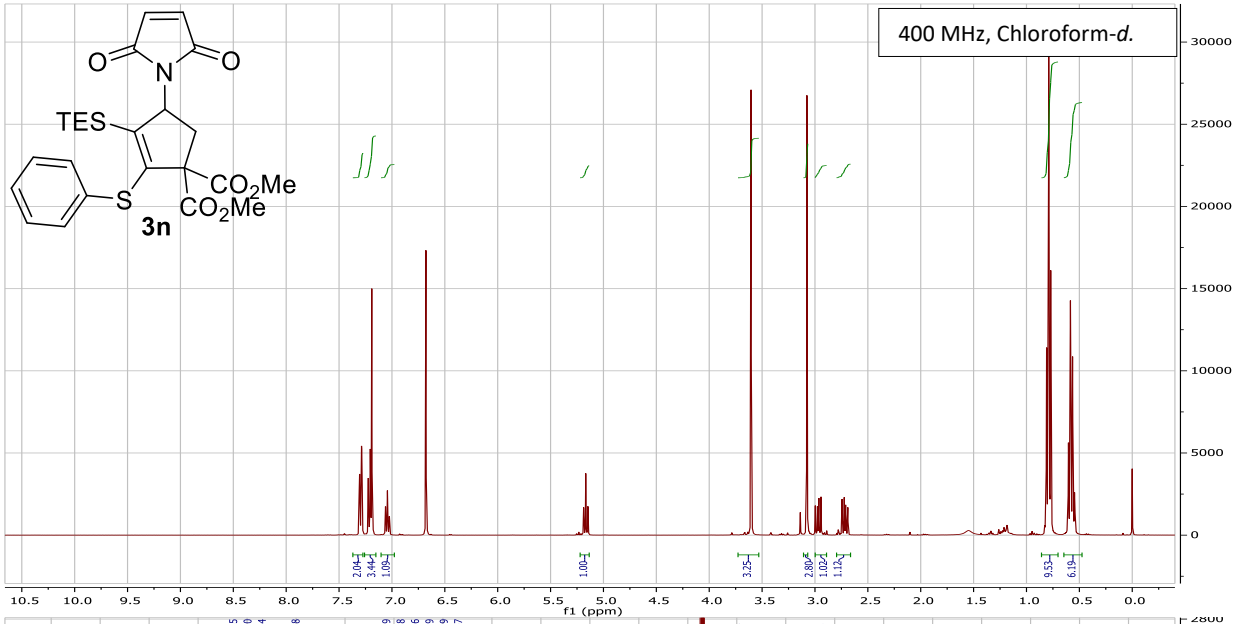

171.48
169.37
166.51
166.22
160.06
152.90
144.03
137.53
137.05
134.10
130.54
129.81
128.29
126.53
125.74
119.91
70.36
59.90
54.00
53.48
39.98
8.25
41.17
f1 (ppm)

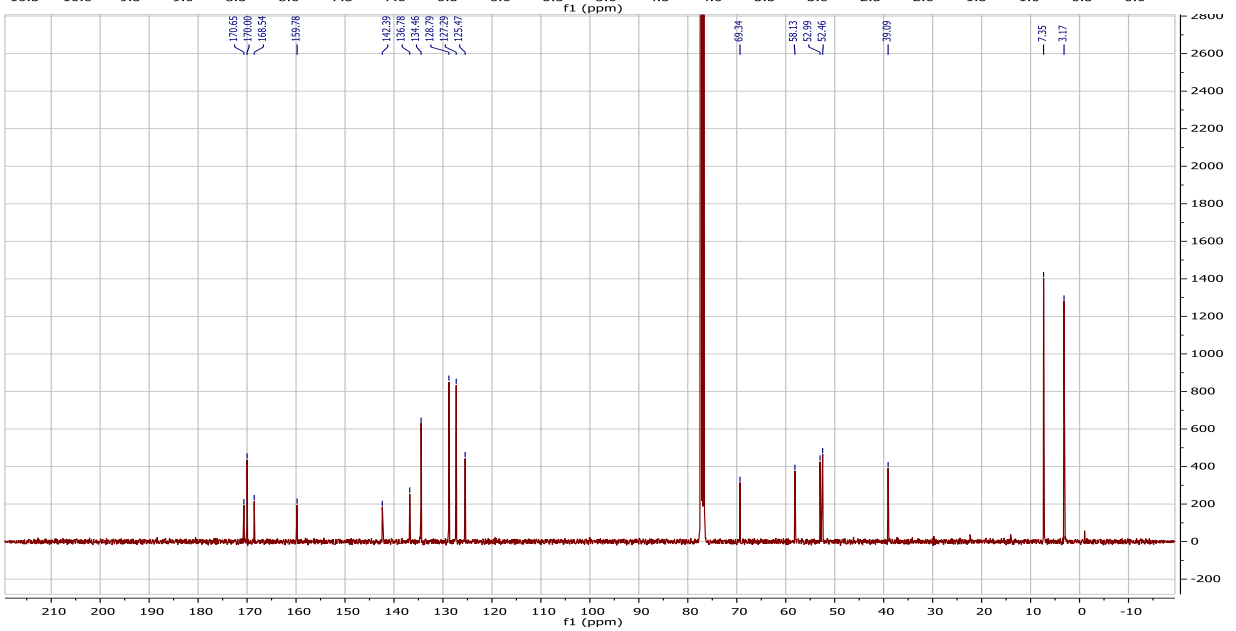

3000
2000
1000

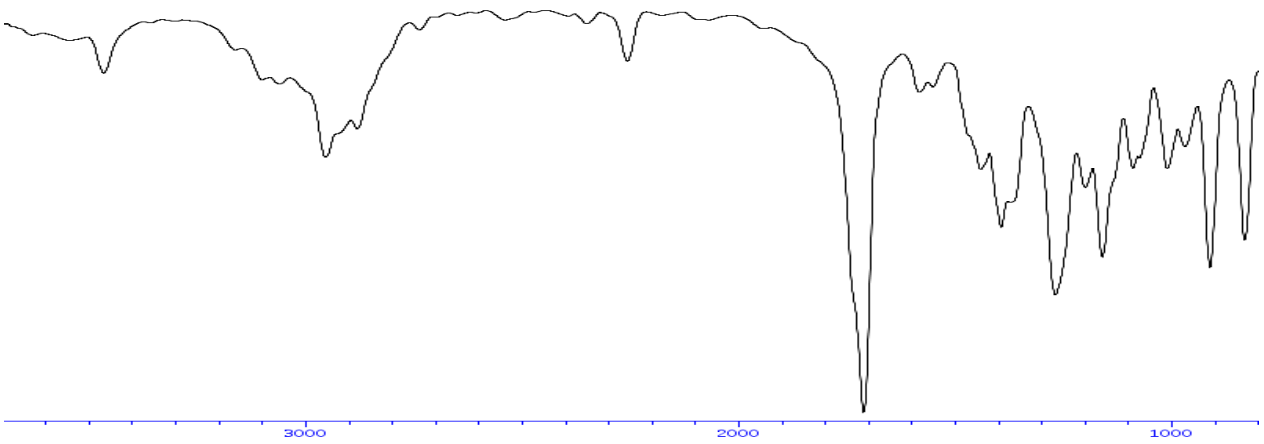

400 MHz, Chloroform-d.
O2N
O
N
O
TES
S
CO2Me
CO2Me
3m
f1 (ppm)

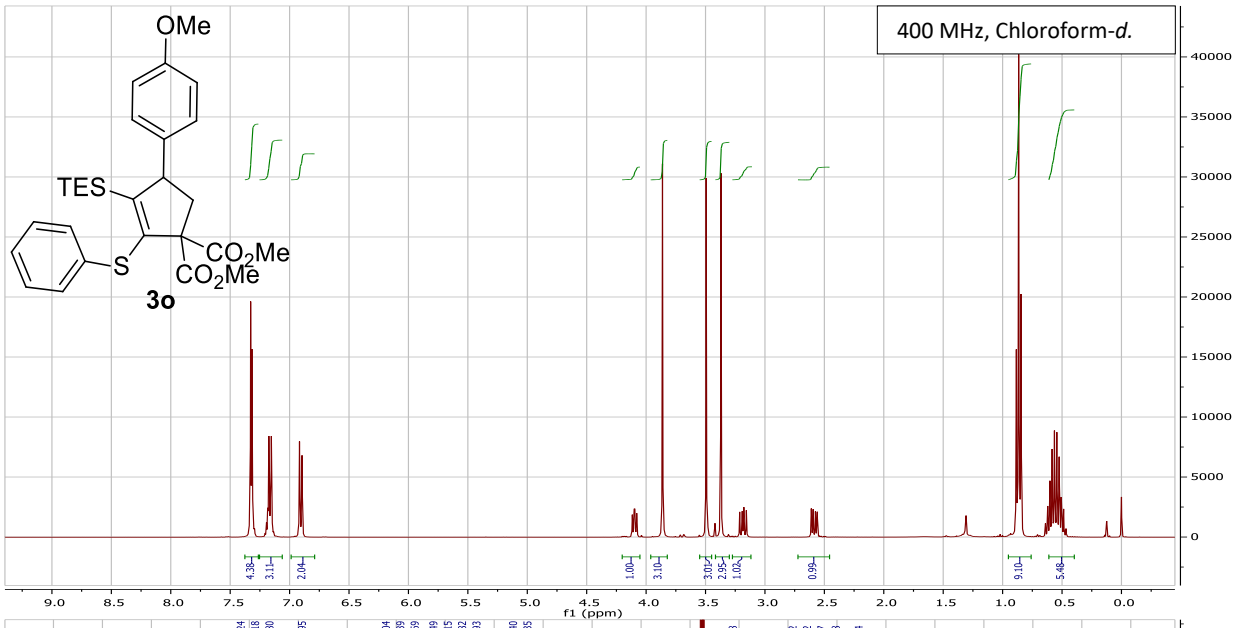

171.48
169.37
166.51
166.23
160.06
152.90
144.03
137.53
137.05
134.10
130.54
129.81
128.29
126.53
125.71
119.91
70.36
59.90
53.99
53.48
39.97
8.25
4.17
f1 (ppm)

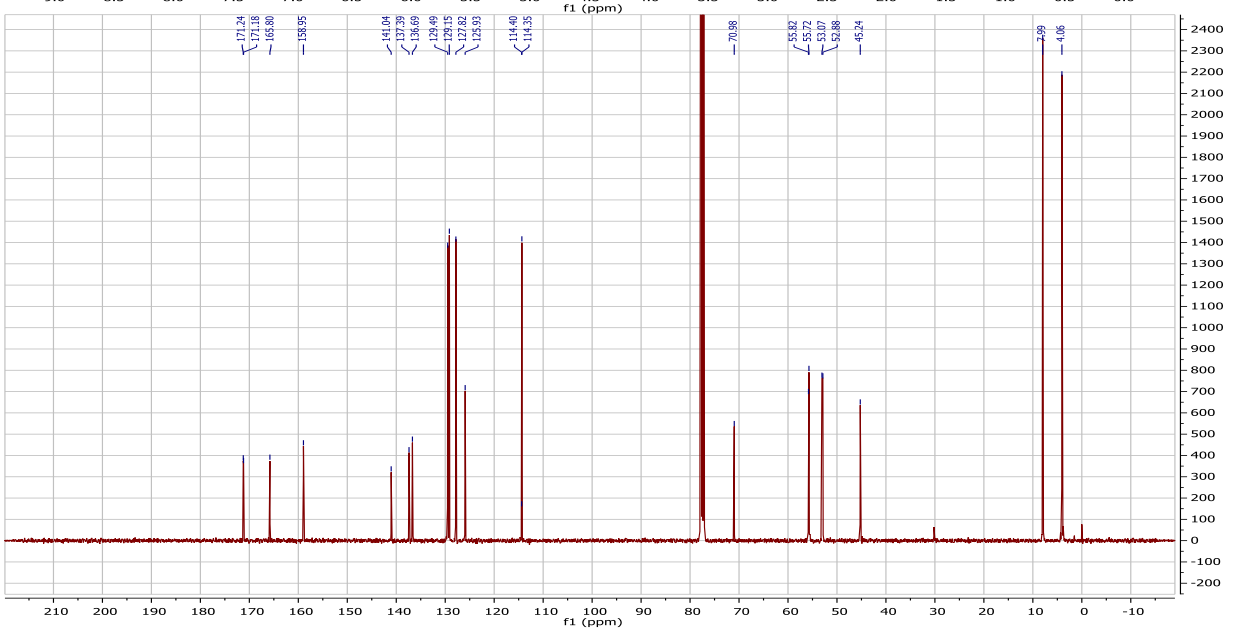

3000
2000
1000

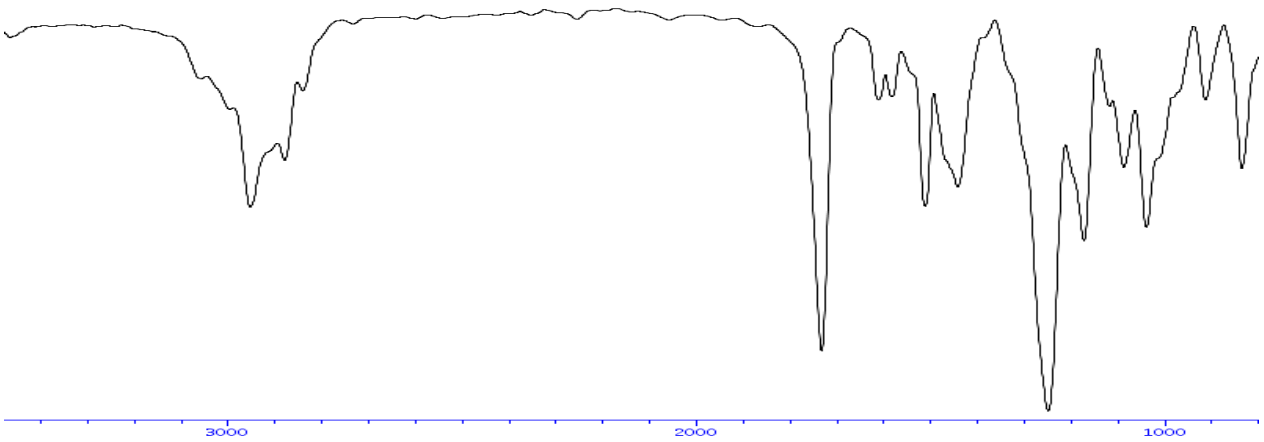

400 MHz, Chloroform-d.
TES
CO2Me
CO2Me
3n
f1 (ppm)

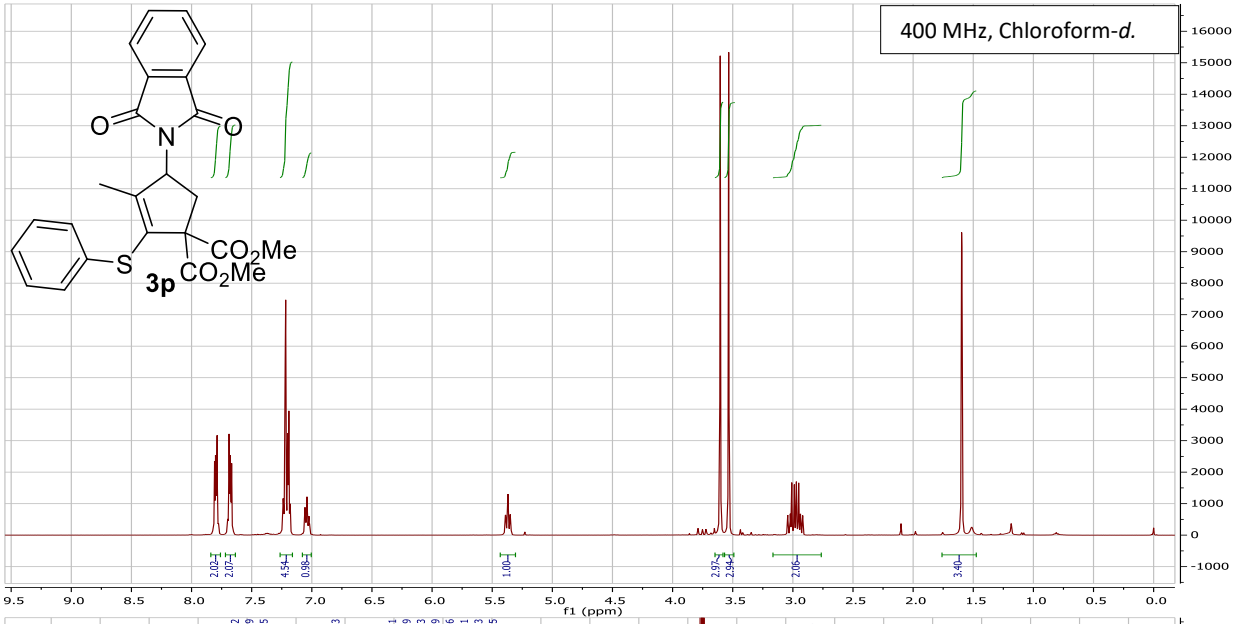

170.65
170.00
168.54
159.78
142.39
136.78
134.46
128.79
127.29
125.47
69.34
58.13
52.99
52.46
39.09
7.35
3.17
f1 (ppm)

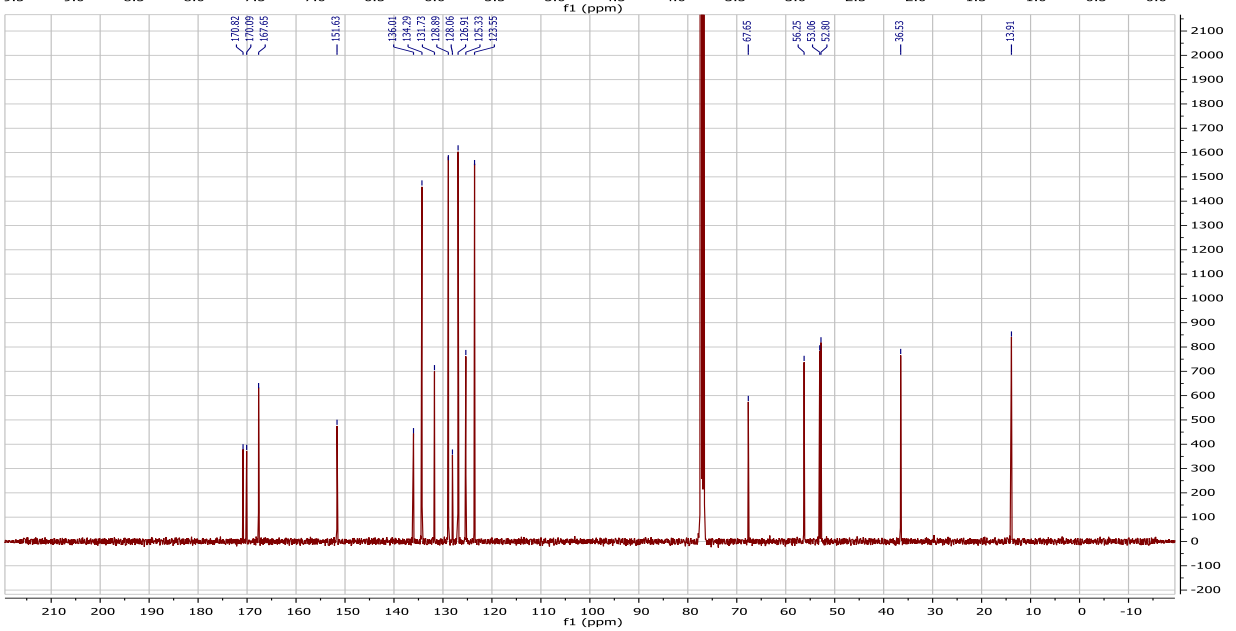

3000
2000
1000

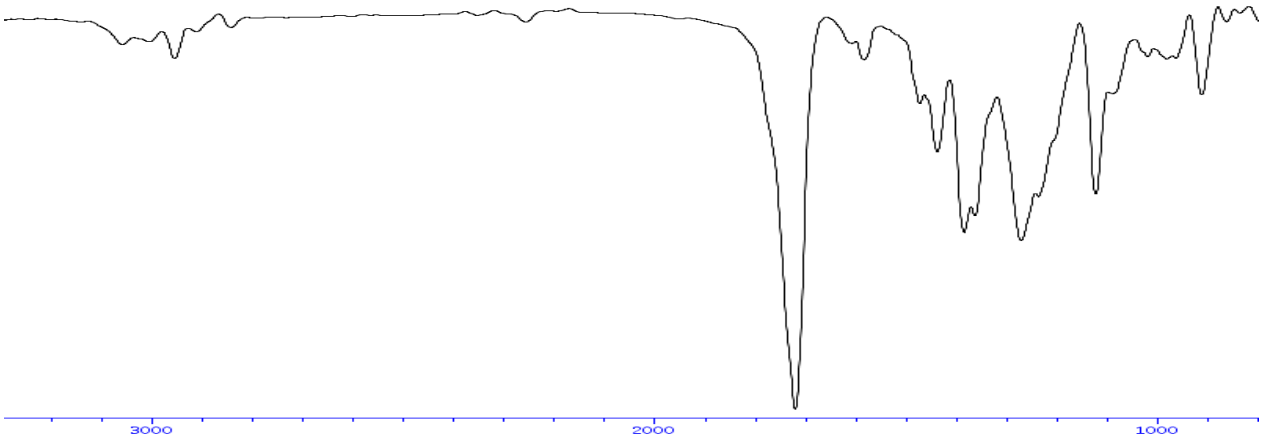

OMe
TES
S
CO2Me
CO2Me
3o
400 MHz, Chloroform-d.
f1 (ppm)

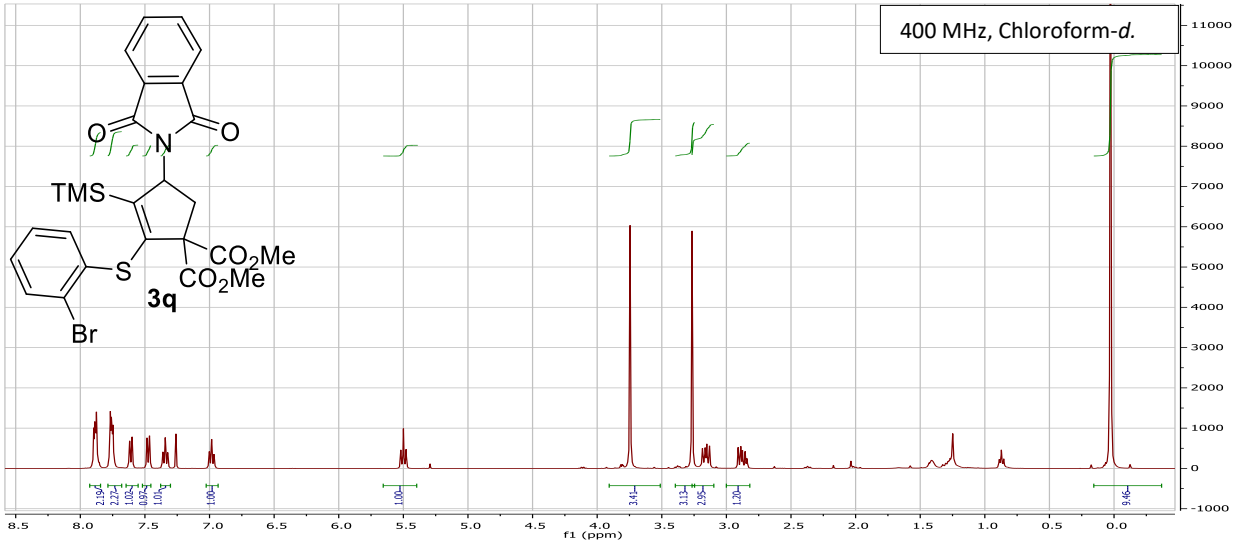

f1 (ppm)

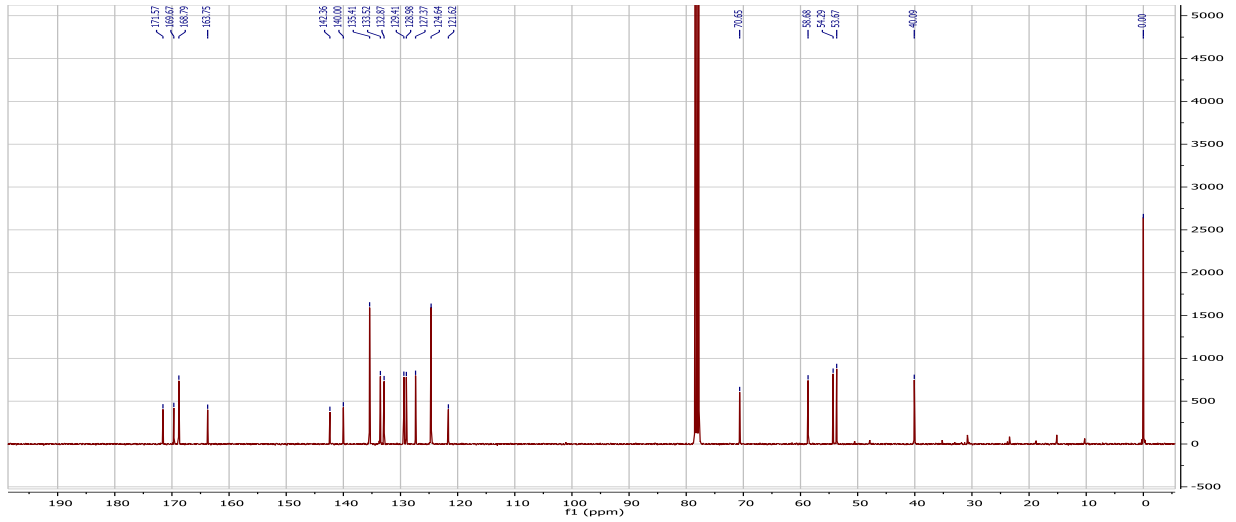

3000
2000
1000

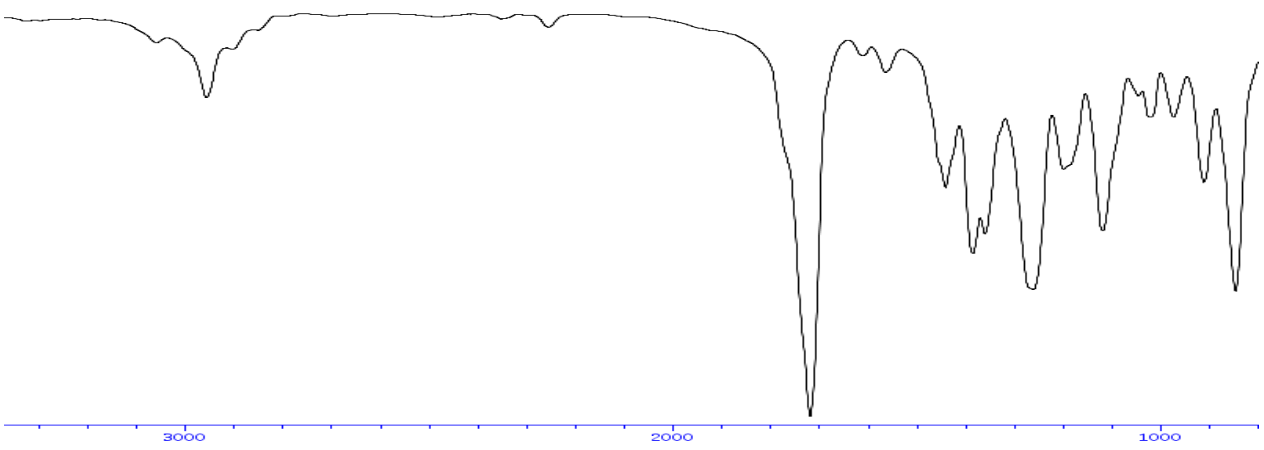

400 MHz, Chloroform-d.
O
N
O
S
CO2Me
CO2Me
3p
f1 (ppm)

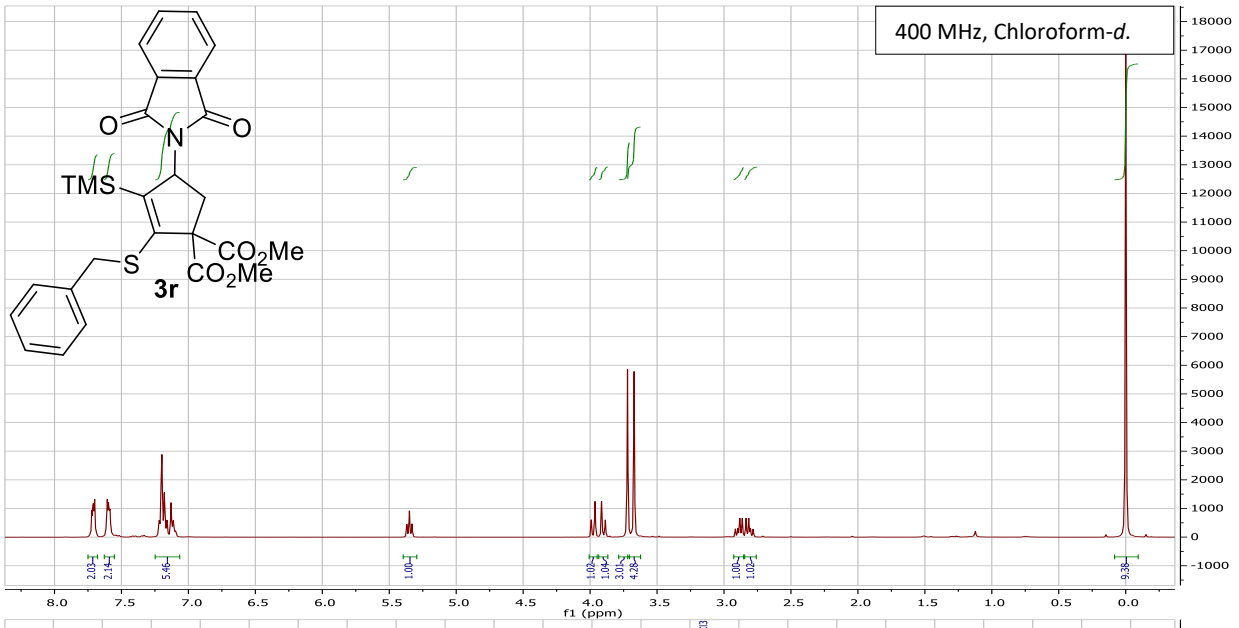

170.82
170.09
167.65
151.63
136.01
134.29
131.73
128.89
128.06
126.91
125.33
123.55
67.65
56.25
53.06
52.80
36.53
13.91
f1 (ppm)

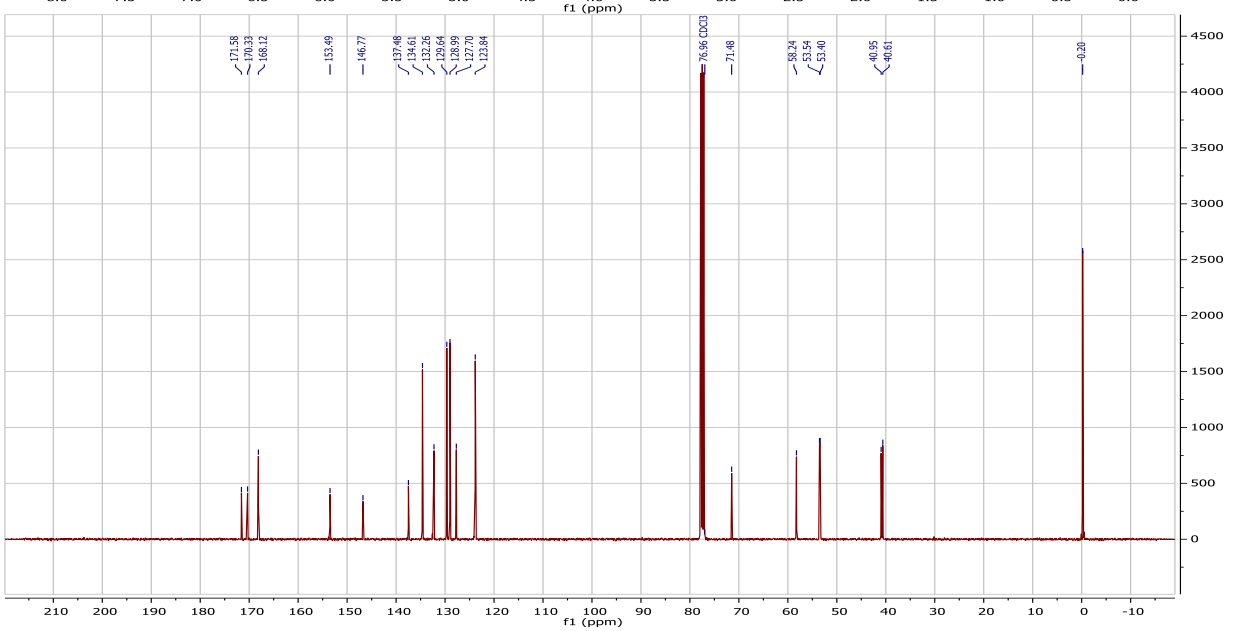

3000
2000
1000

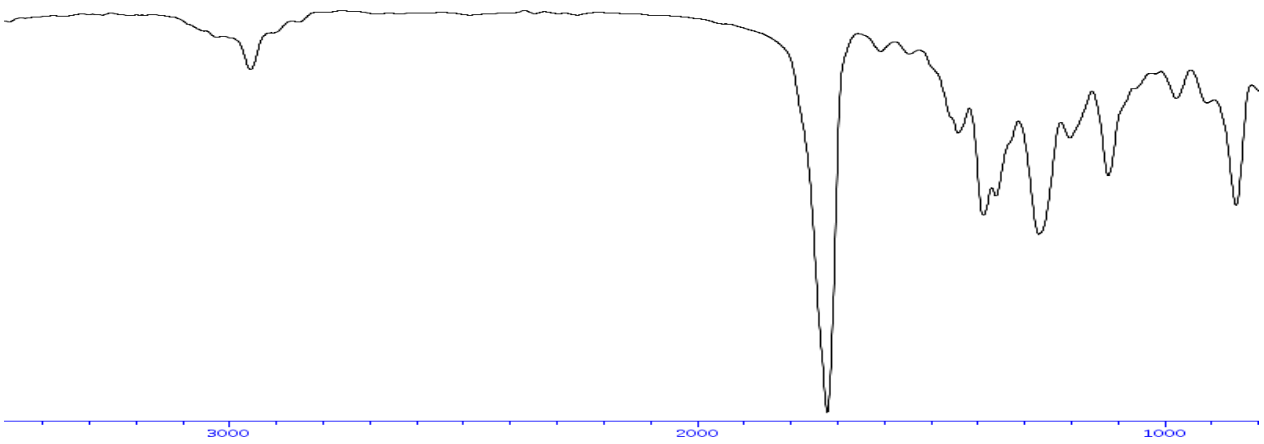

400 MHz, Chloroform-*d*.
O
N
O
TMS
S
CO_2Me
CO_2Me
3q
Br
f1 (ppm)

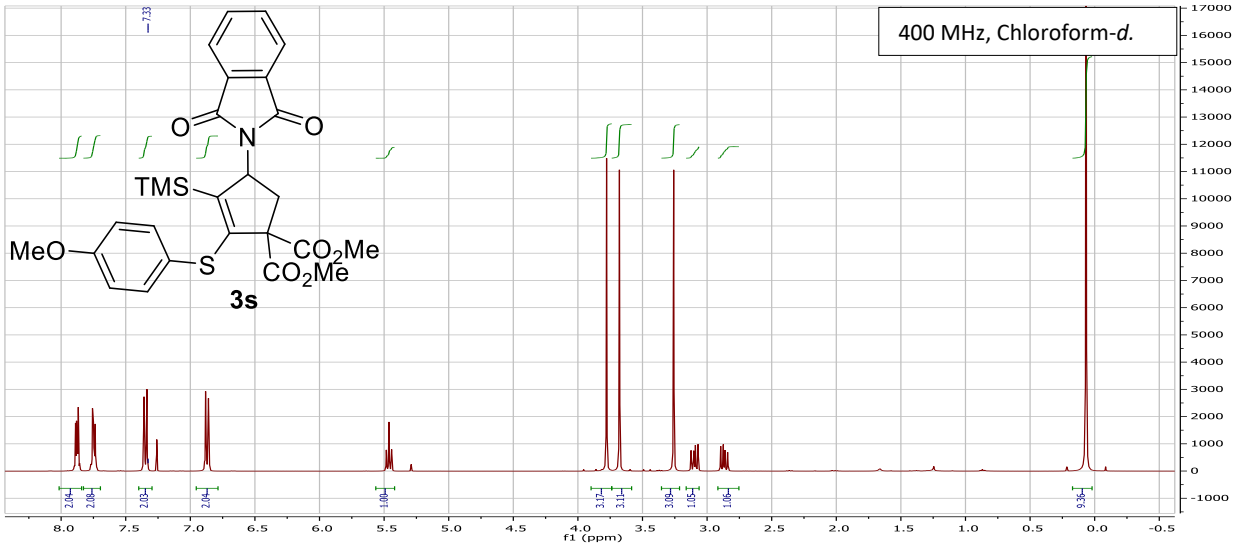

f1 (ppm)

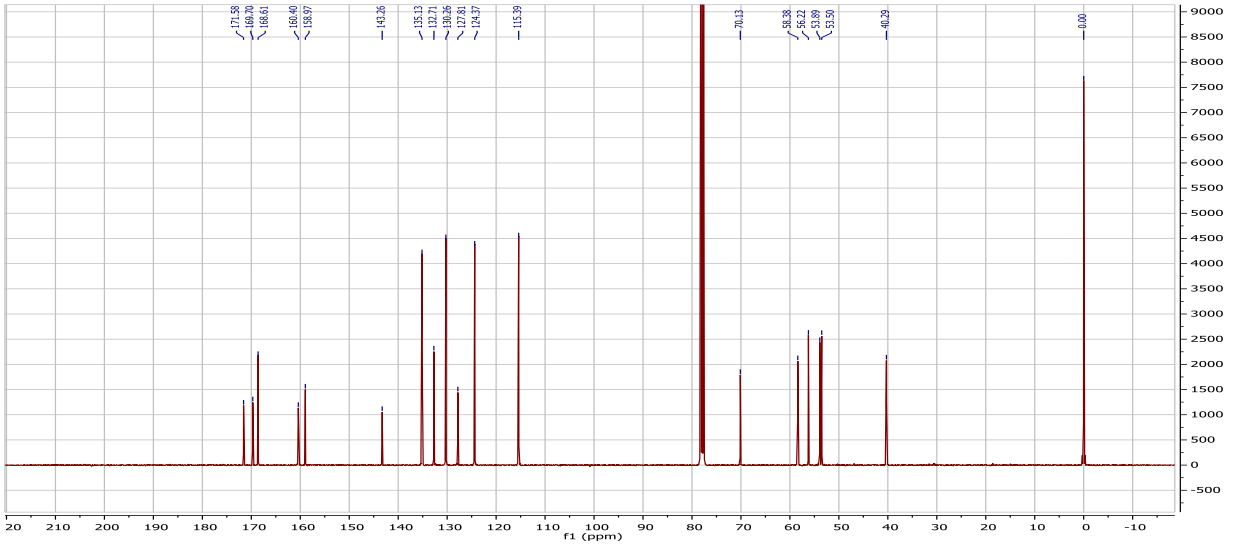

3000
2000
1000

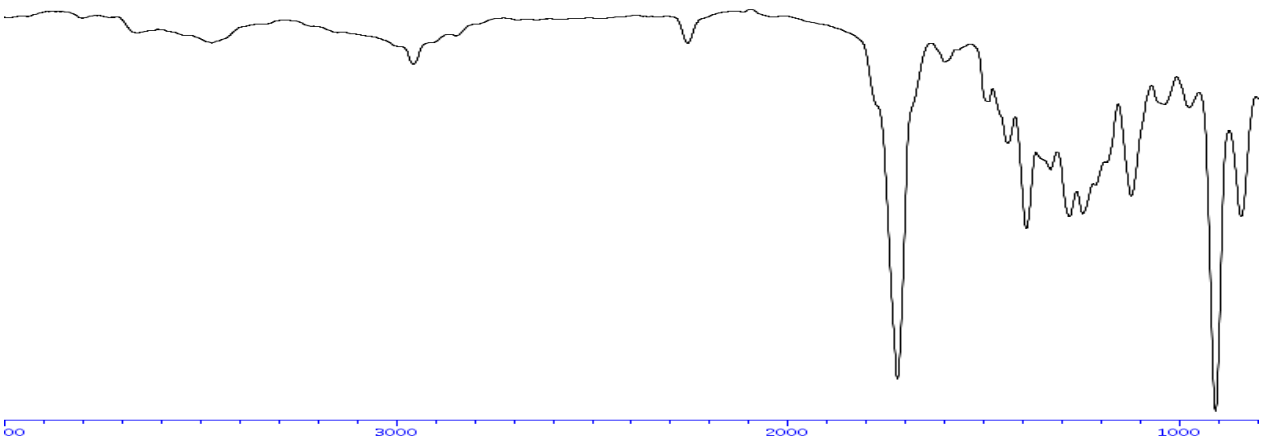

400 MHz, Chloroform-d.
O
N
O
TMS
S
CO2Me
CO2Me
3r
f1 (ppm)

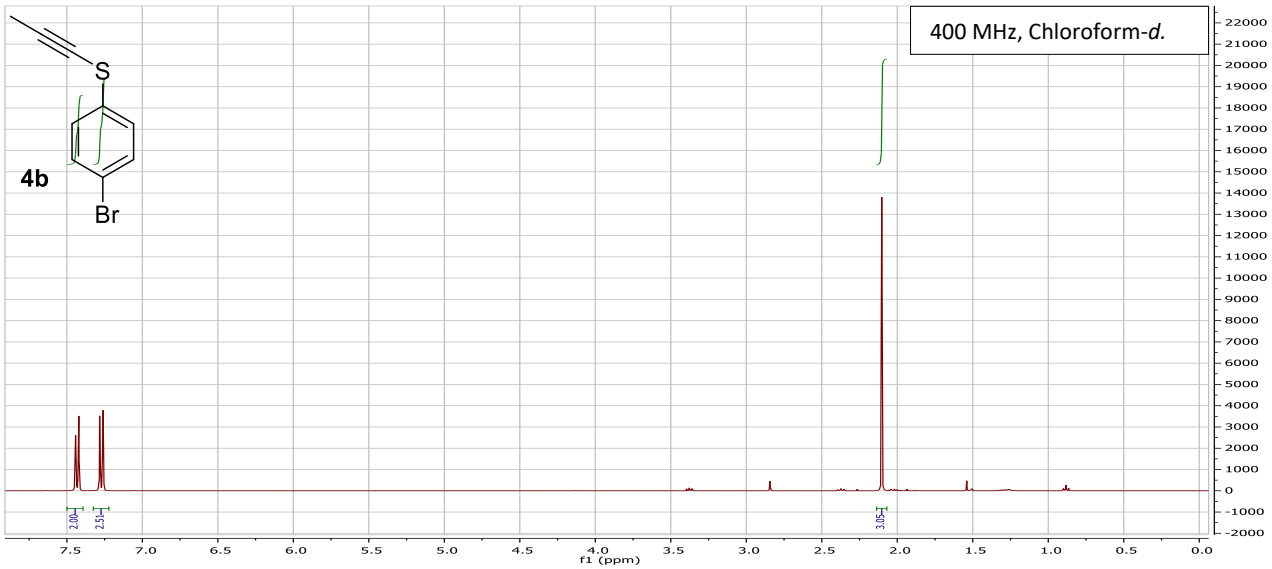

171.58
170.33
168.12
153.49
146.77
137.48
134.61
132.26
129.64
128.99
127.70
123.84
76.96 CDCl3
71.48
58.24
53.54
53.40
40.95
40.61
-0.20
f1 (ppm)

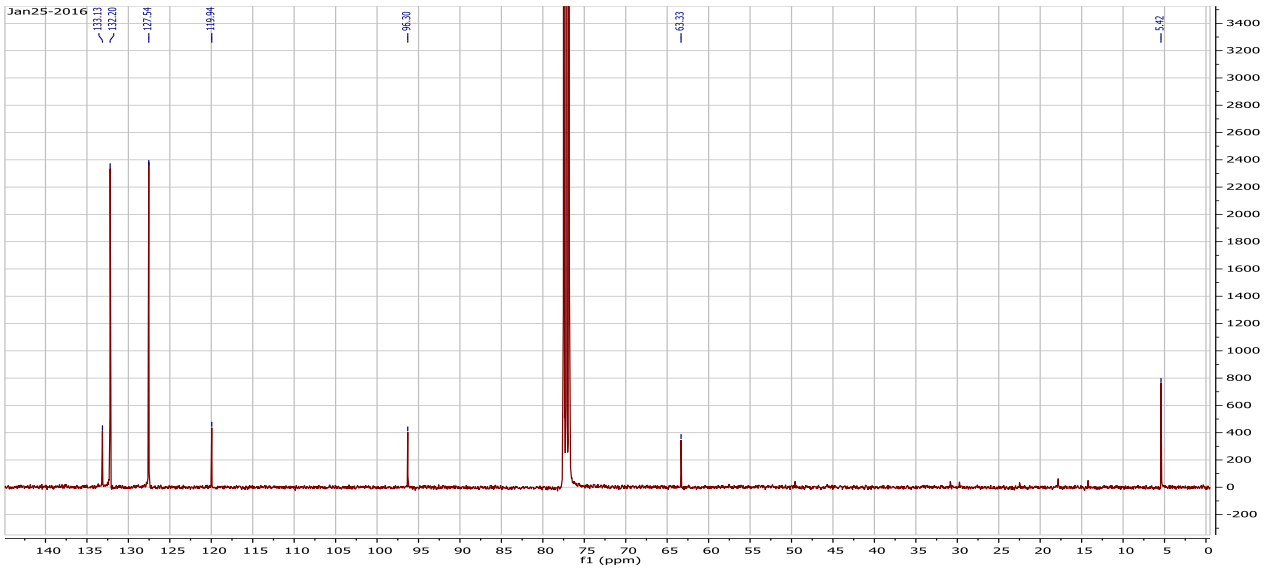

3000
2000
1000

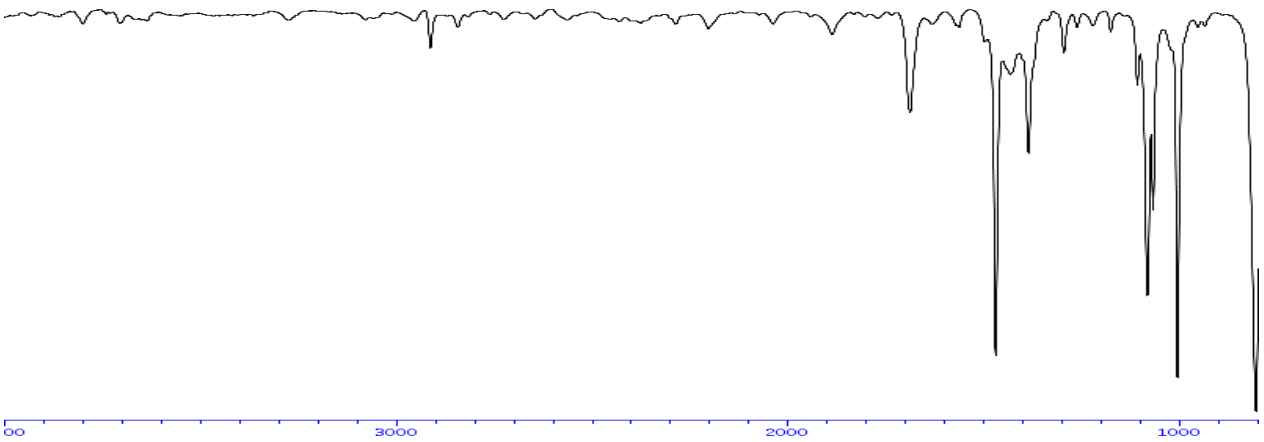

400 MHz, Chloroform-d.
TMS
MeO
S
CO2Me
CO2Me
3s
f1 (ppm)

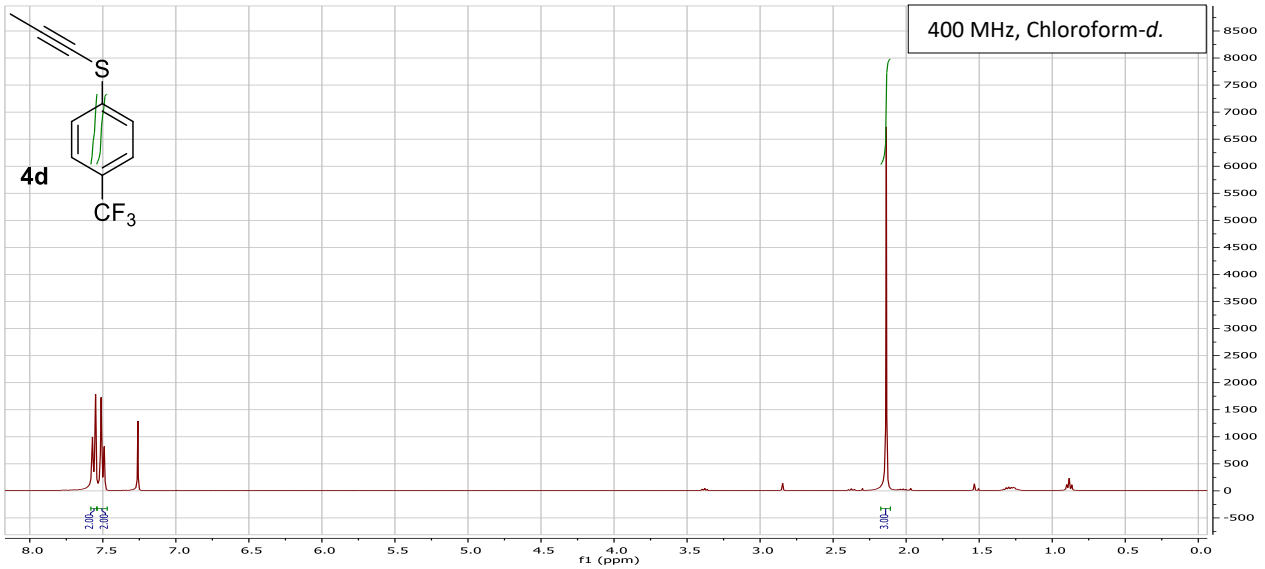

f1 (ppm)

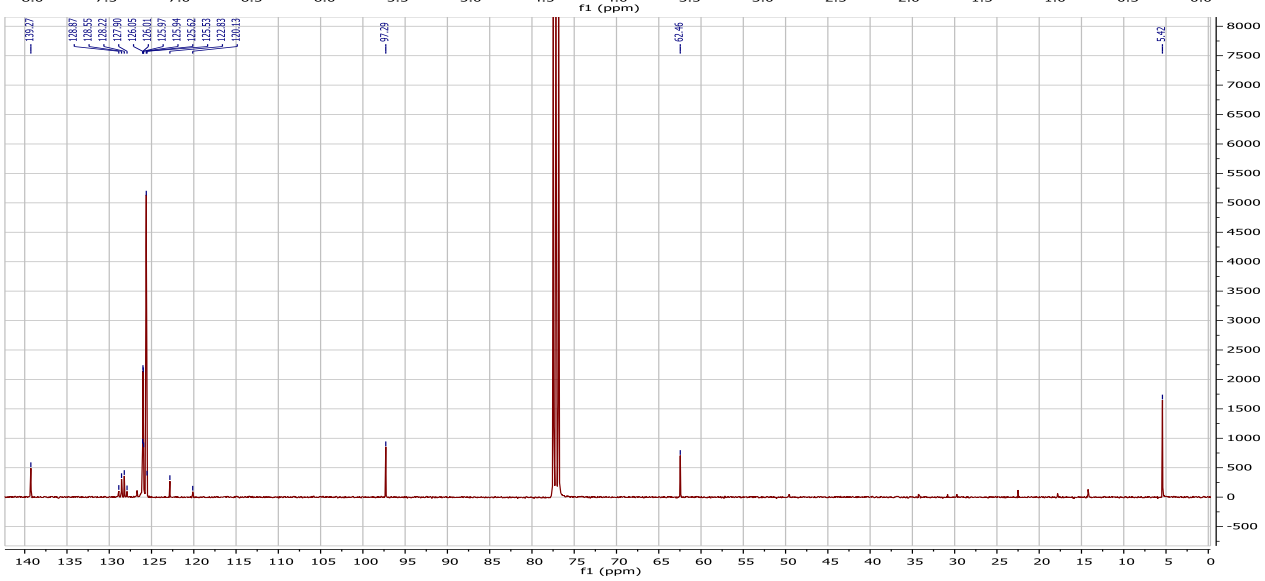


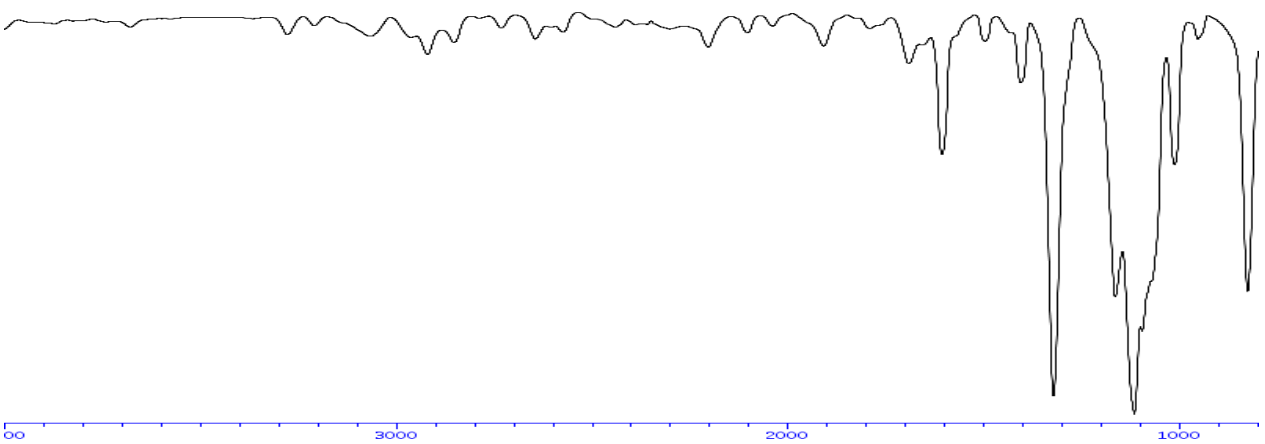

400 MHz, Chloroform-d.
S
4b
Br
f1 (ppm)

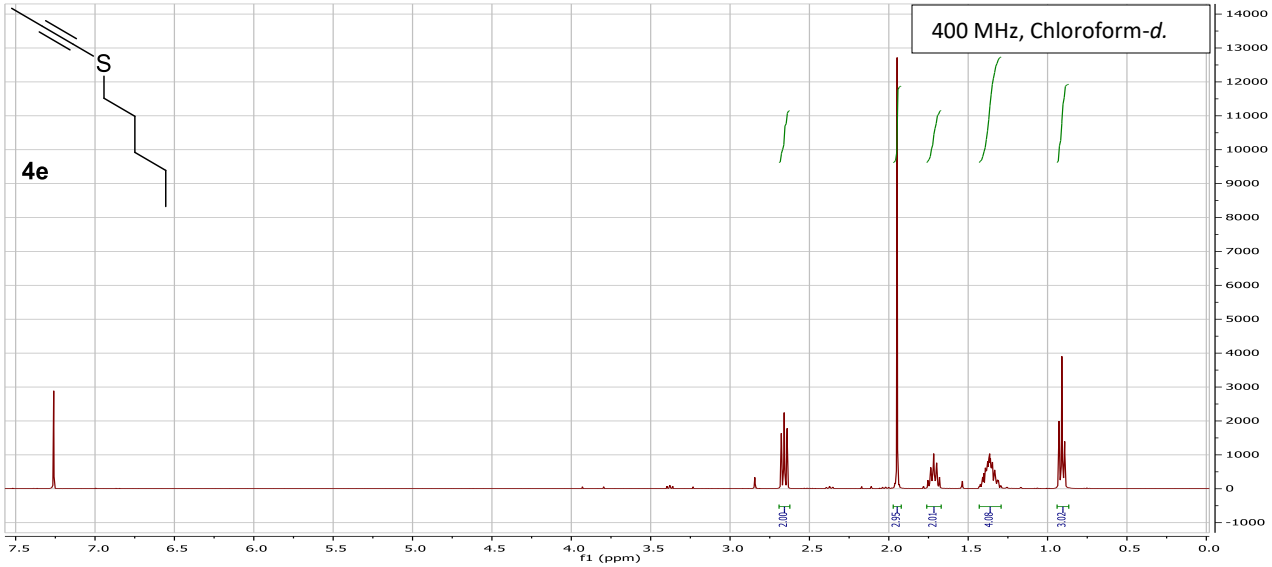

Jan25-2016
133.13
132.20
127.54
119.94
96.30
63.33
5.42
f1 (ppm)

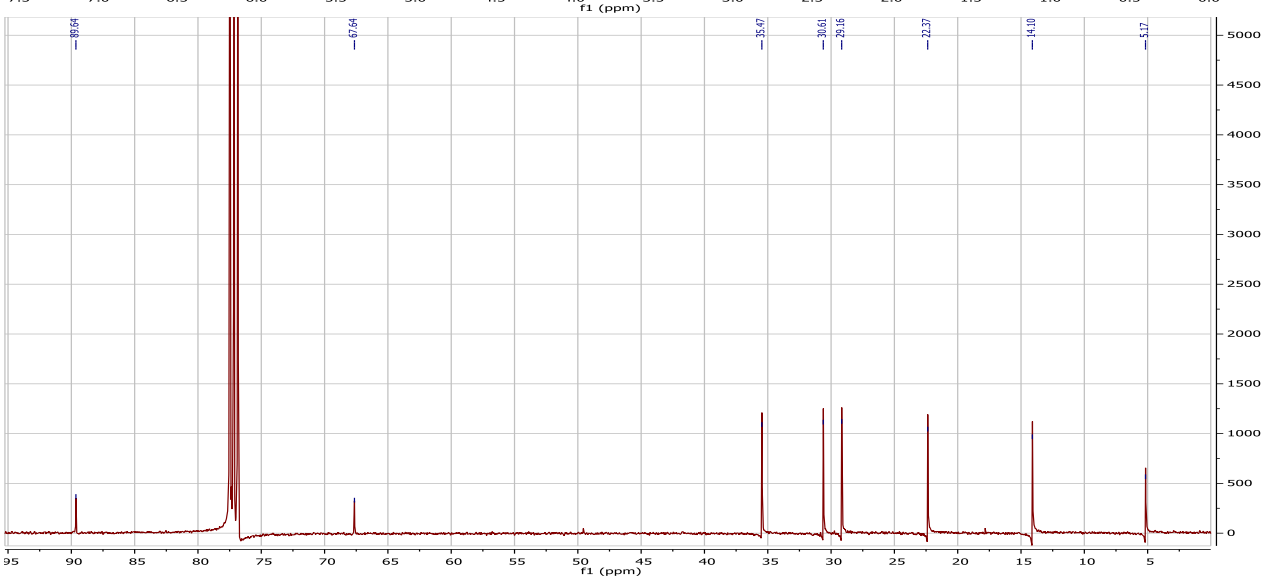


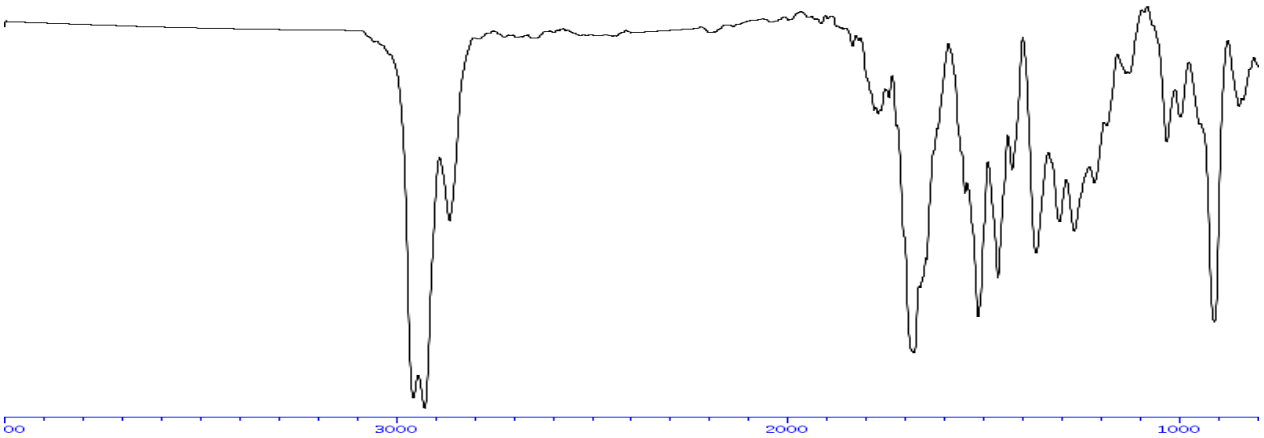

400 MHz, Chloroform-*d*.
S
4d
CF3
f1 (ppm)

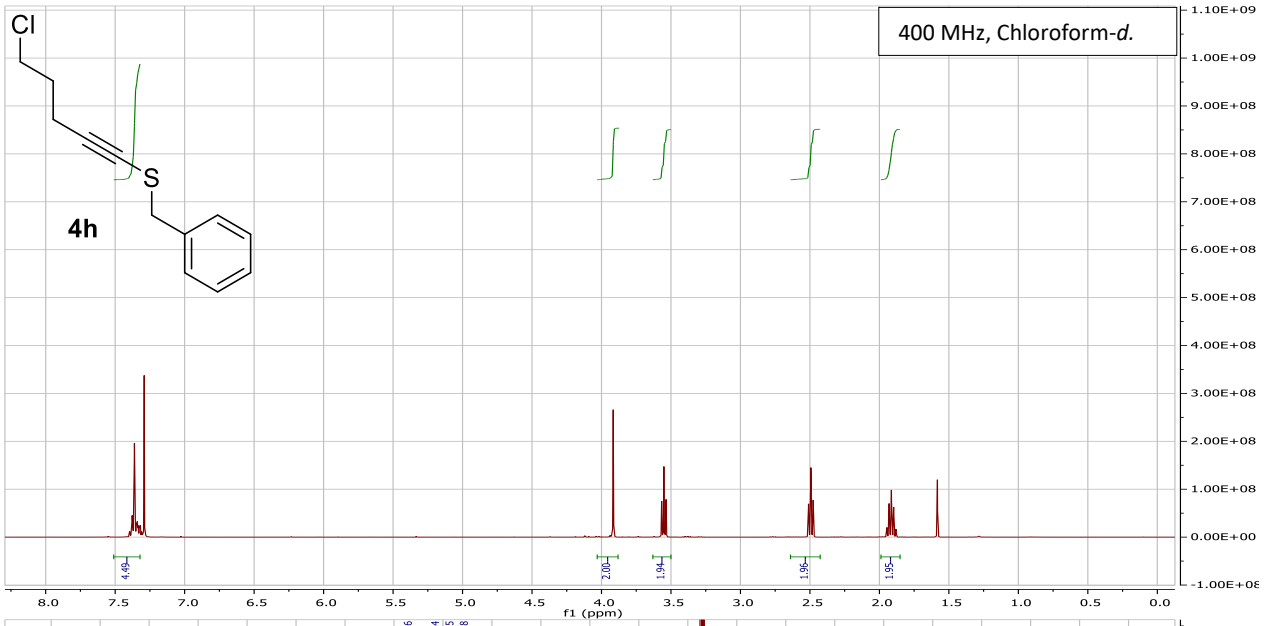

139.27
128.87
128.55
128.22
127.90
126.05
126.01
125.97
125.94
125.62
125.53
123.83
120.13
97.29
62.46
5.42
f1 (ppm)

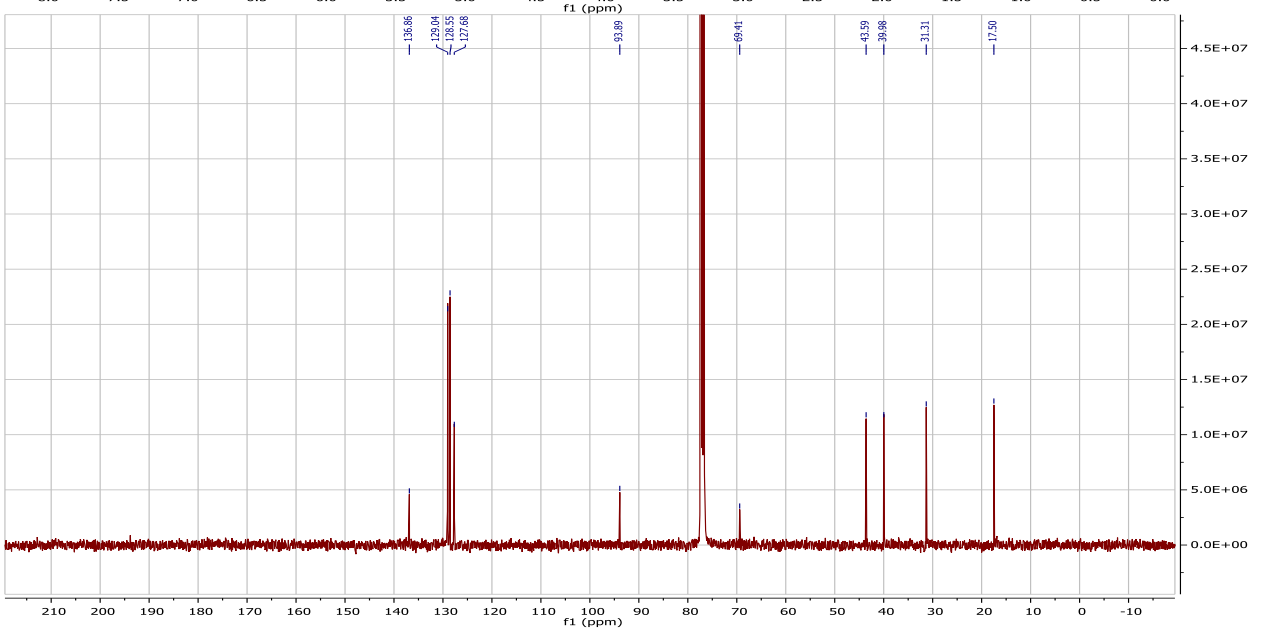

3000
2000
1000

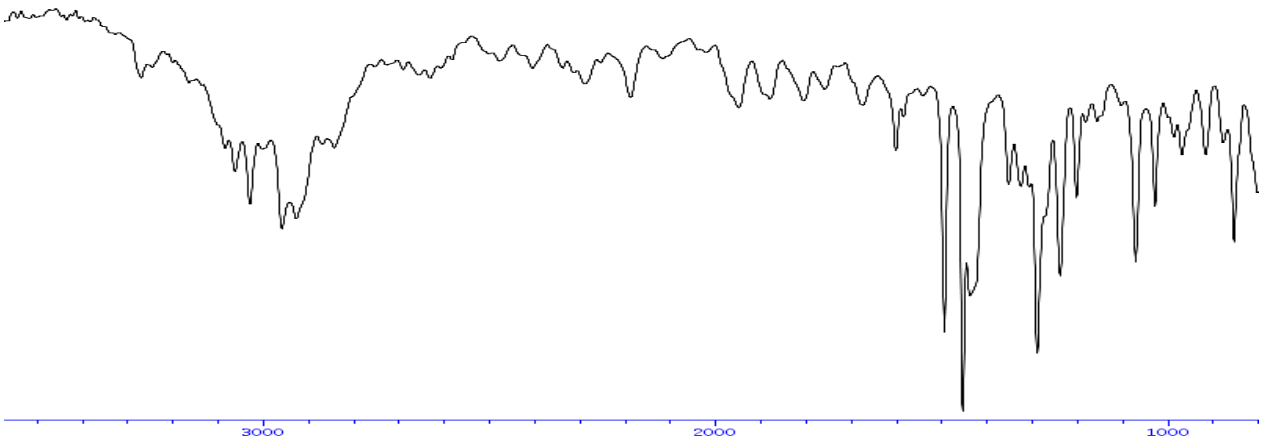

400 MHz, Chloroform-d.
S
4e
f1 (ppm)

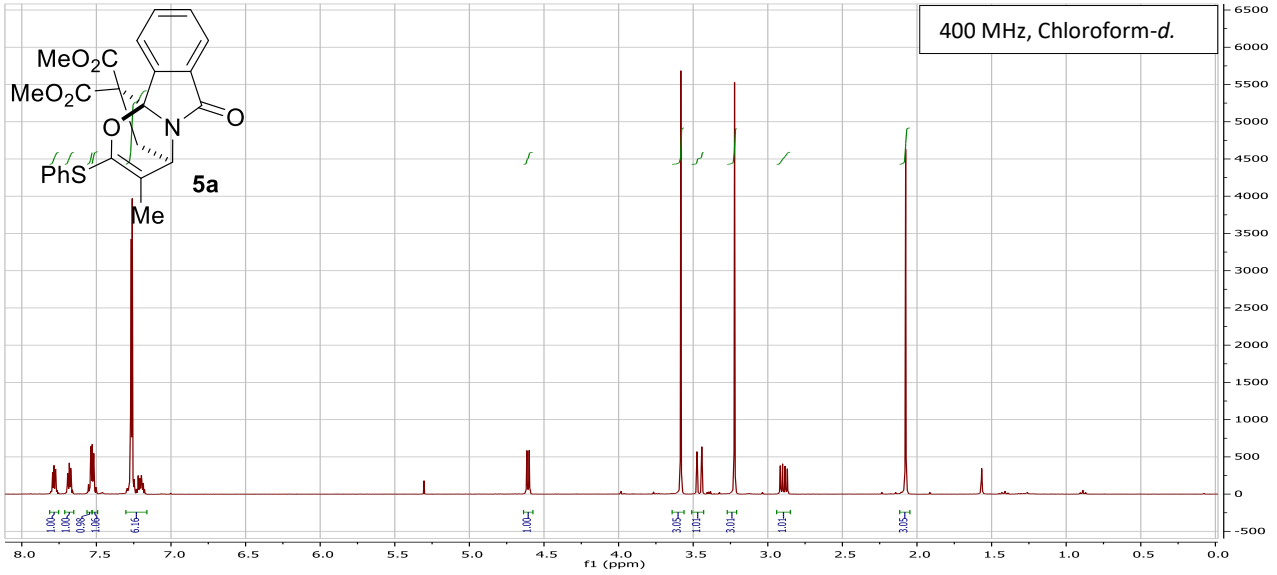

89.64
67.64
35.47
30.61
29.16
22.37
14.10
5.17
f1 (ppm)

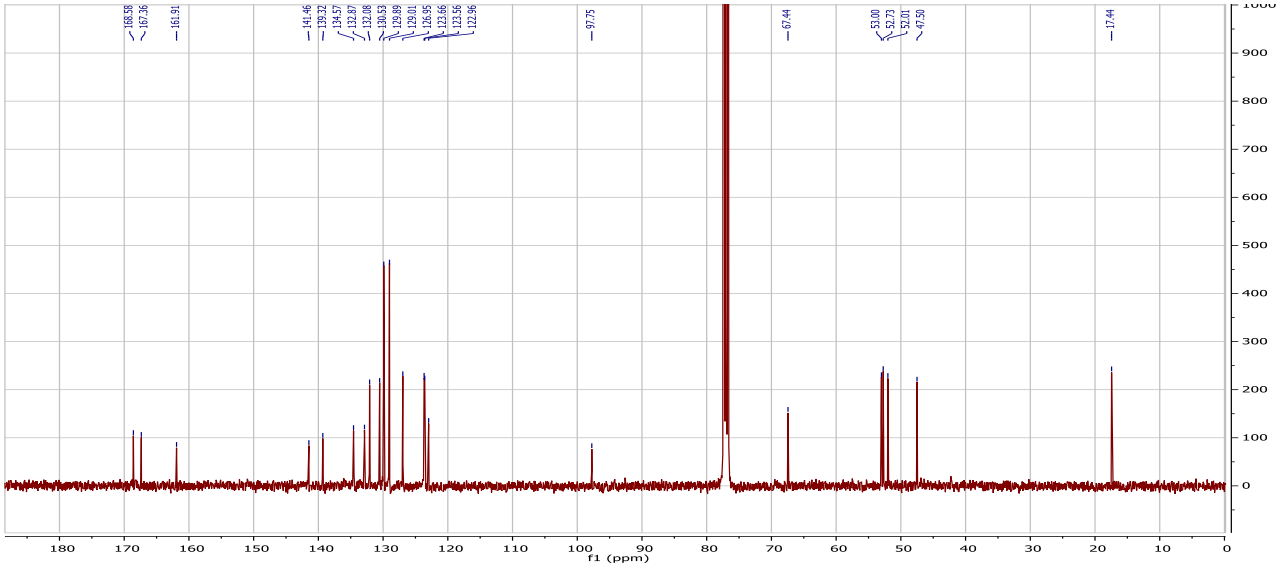


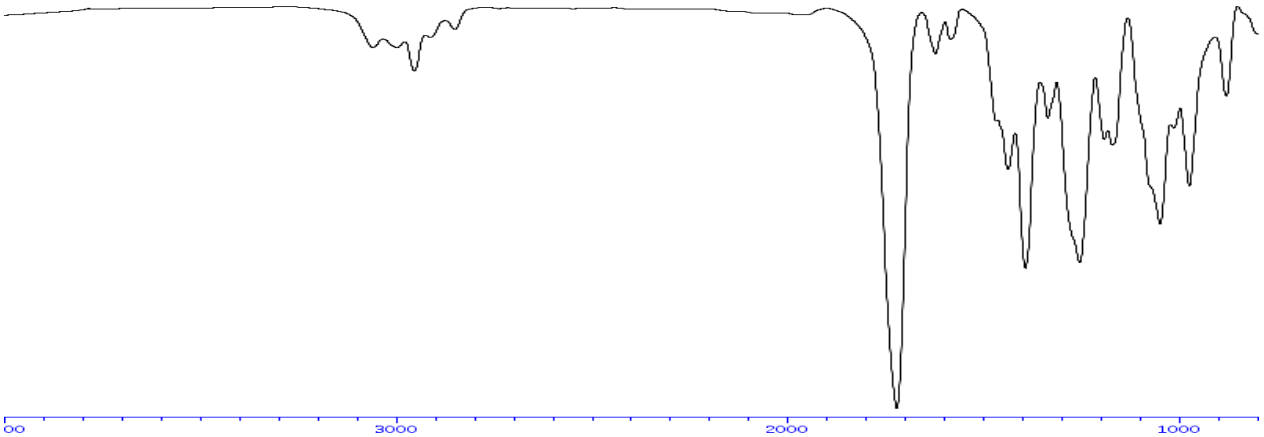

Cl
S
4h
400 MHz, Chloroform-d.
4.49
2.00
1.94
1.96
1.95
f1 (ppm)

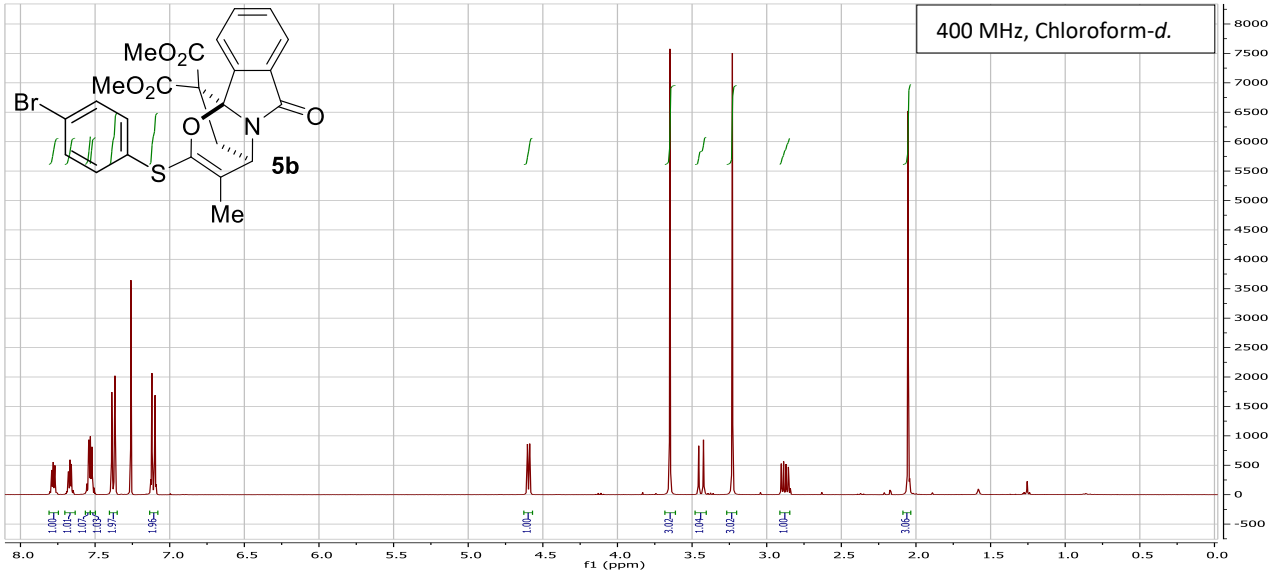

136.86
129.04
128.55
127.68
93.89
69.41
43.59
39.98
31.31
17.50
f1 (ppm)

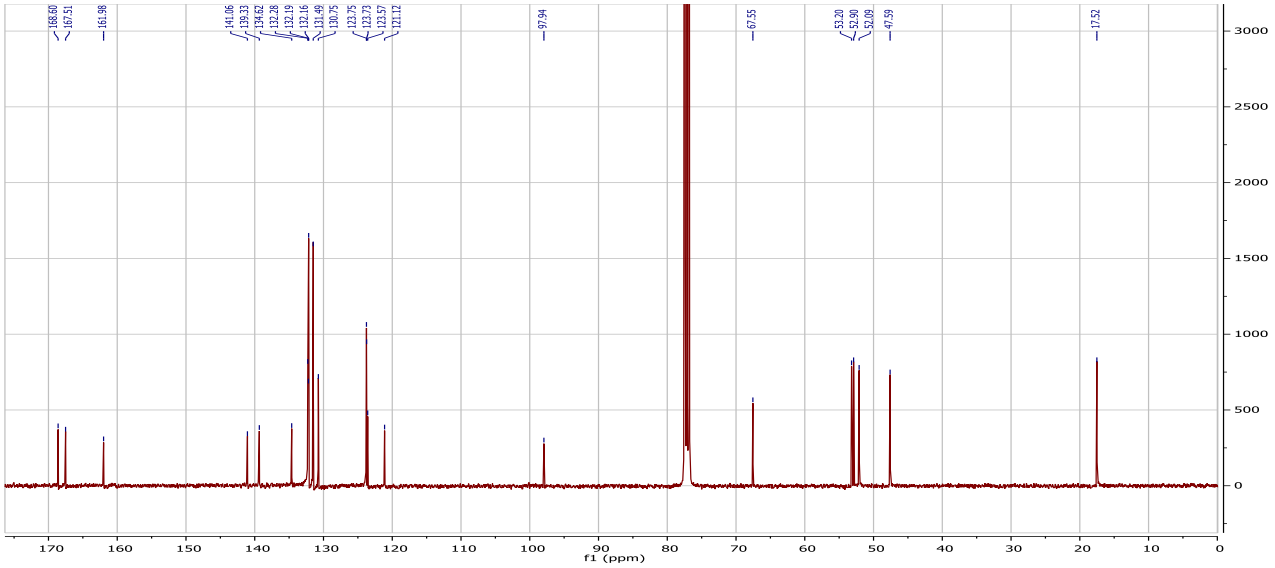

3000
2000
1000

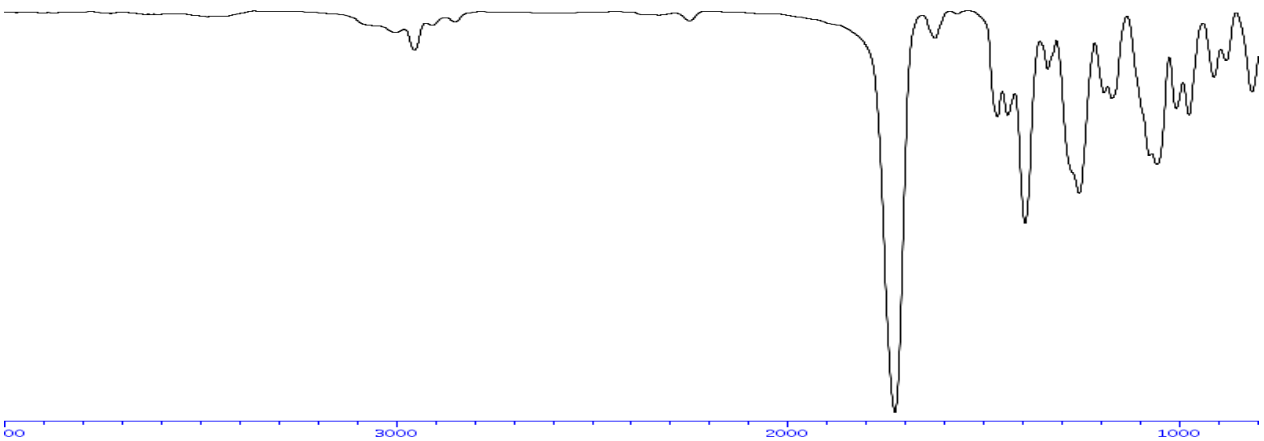

400 MHz, Chloroform-d.
MeO2C
MeO2C
O
N
O
PhS
Me
5a
f1 (ppm)

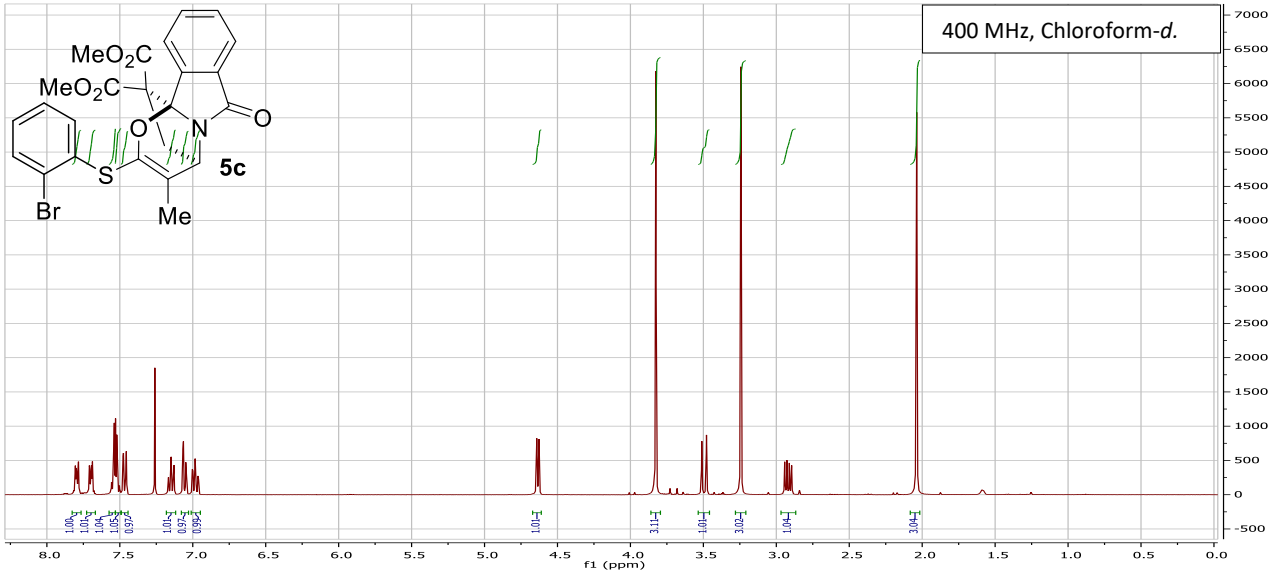

168.58
167.36
161.91
141.46
139.32
134.57
132.87
132.08
130.53
129.89
129.01
126.95
123.66
123.56
122.96
97.75
67.44
53.00
52.73
52.01
47.50
17.44
f1 (ppm)

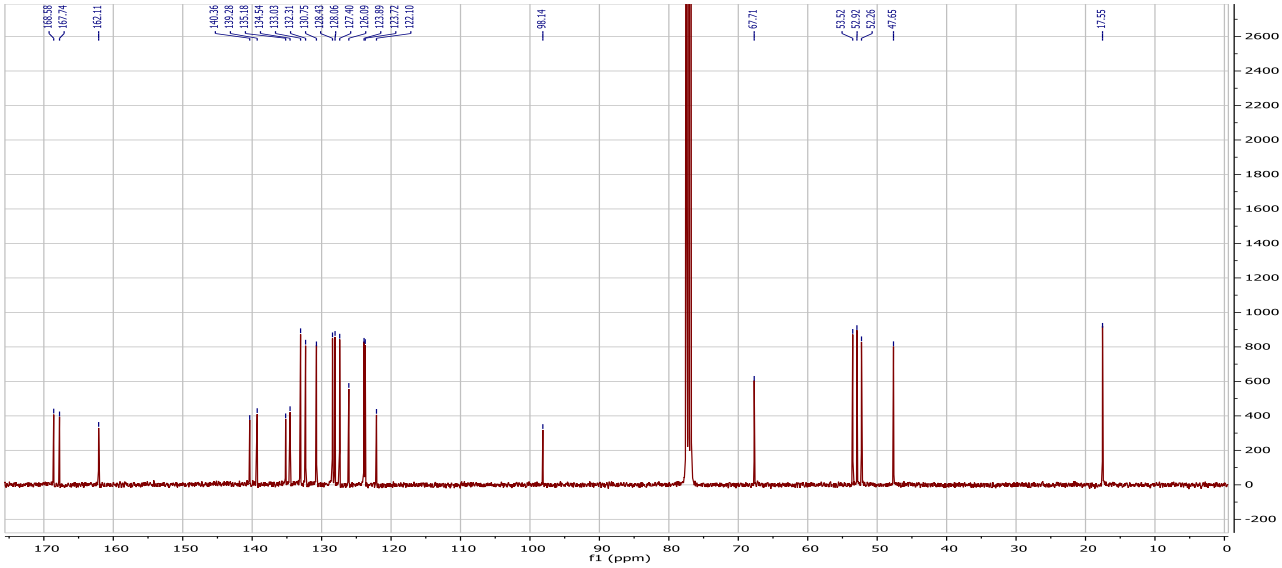

3000
2000
1000


400 MHz, Chloroform-*d*.
MeO_2C
MeO_2C
Br
O
N
O
S
Me
5b
f1 (ppm)


168.60
167.51
161.98
141.06
139.33
134.62
132.28
132.19
132.16
131.49
130.75
123.75
123.73
123.57
121.12
97.94
67.55
53.20
52.90
52.09
47.59
17.52
f1 (ppm)


3000
2000
1000


MeO2C
MeO2C
O
N
O
S
Br
Me
5c
400 MHz, Chloroform-d.
f1 (ppm)


168.58
167.74
162.11
140.36
139.28
135.18
134.54
133.03
132.31
130.75
128.43
128.06
127.40
126.09
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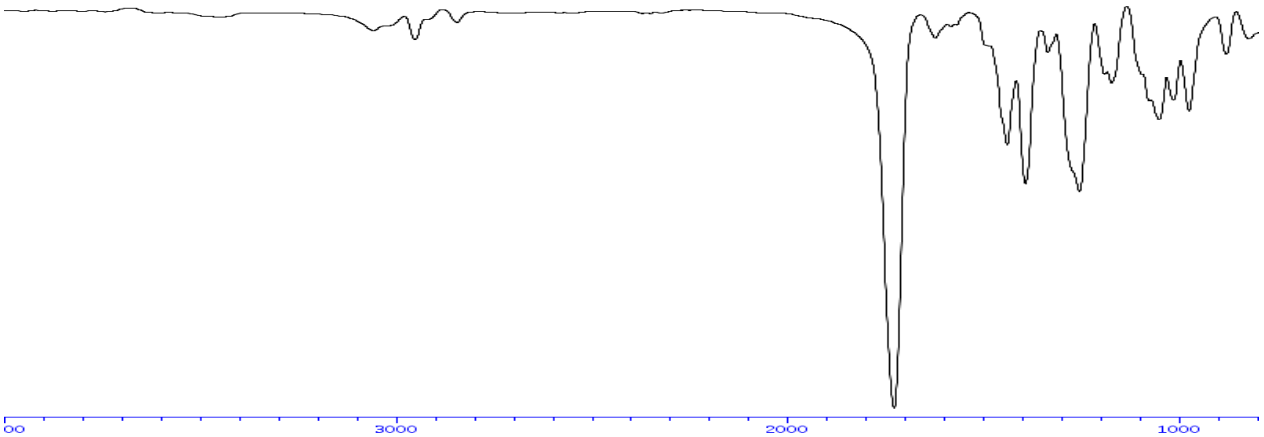
53.52
52.92
52.26
47.65
17.55
f1 (ppm)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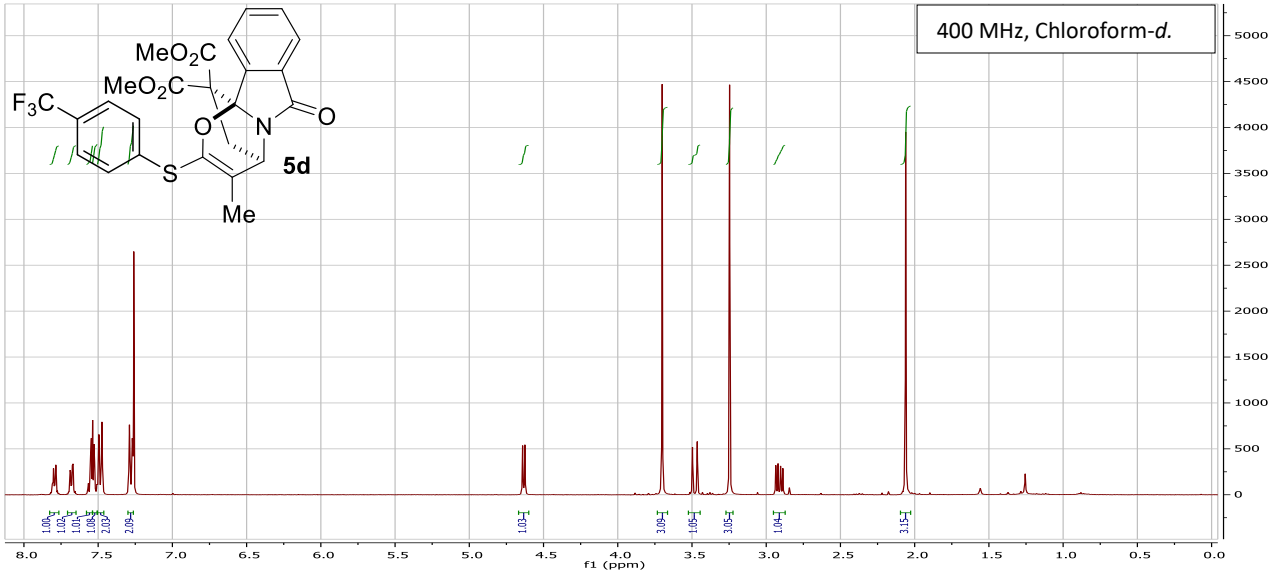
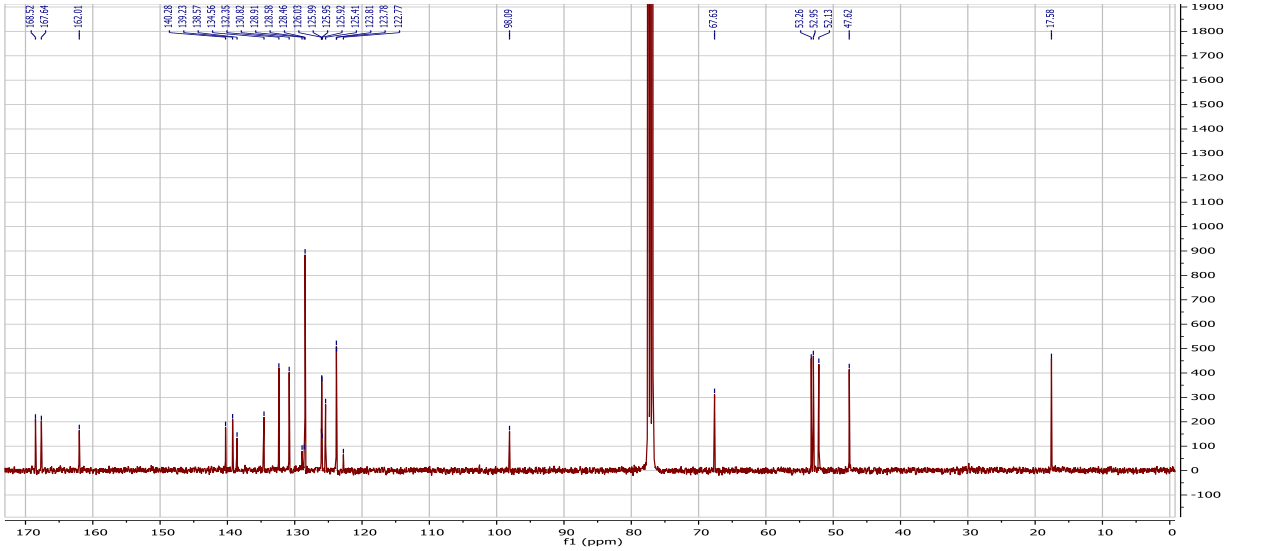
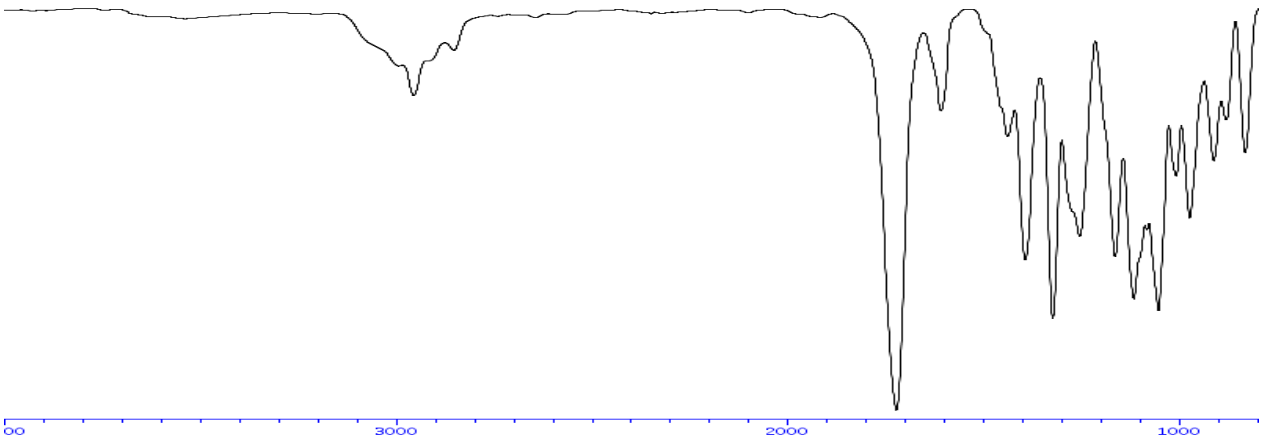
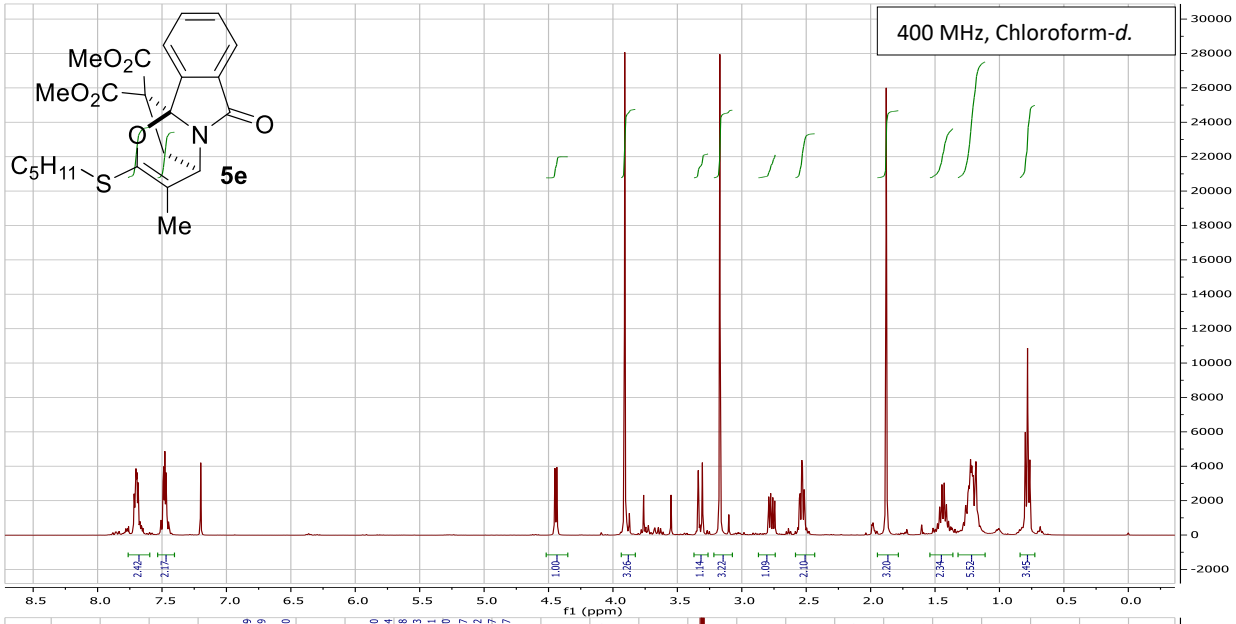
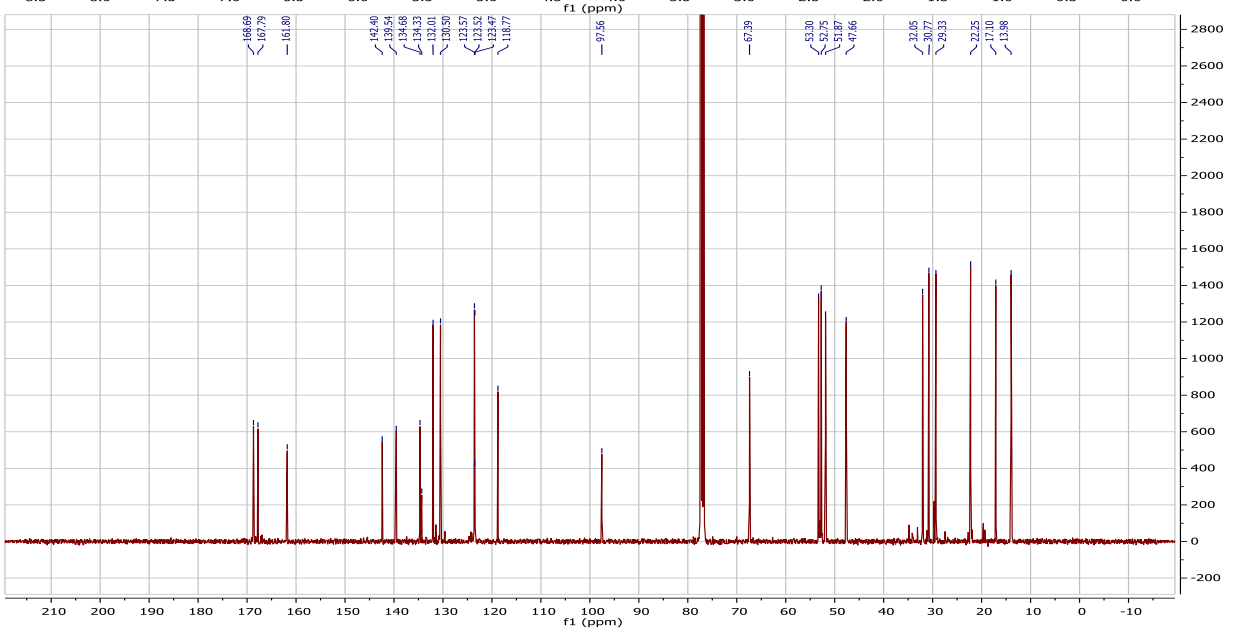
2000
1000

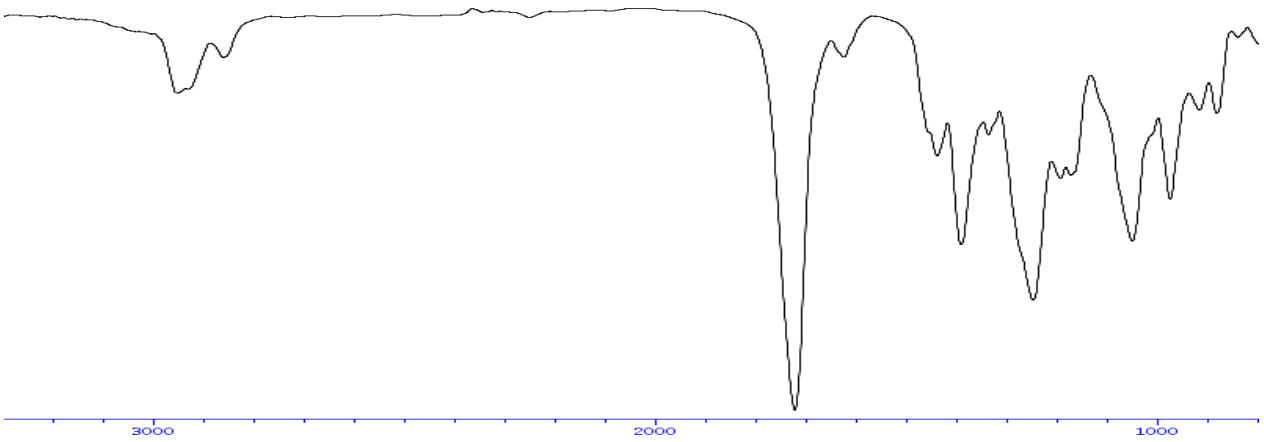

400 MHz, Chloroform-d.
MeO2C
MeO2C
F3C
O
N
O
S
Me
5d
f1 (ppm)

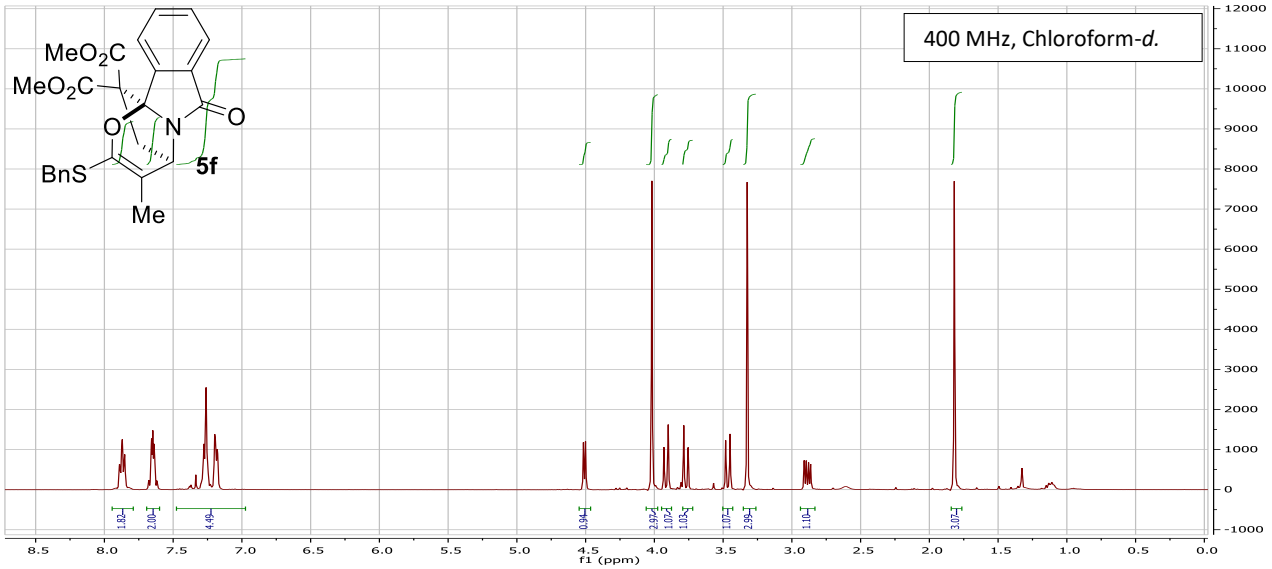

f1 (ppm)

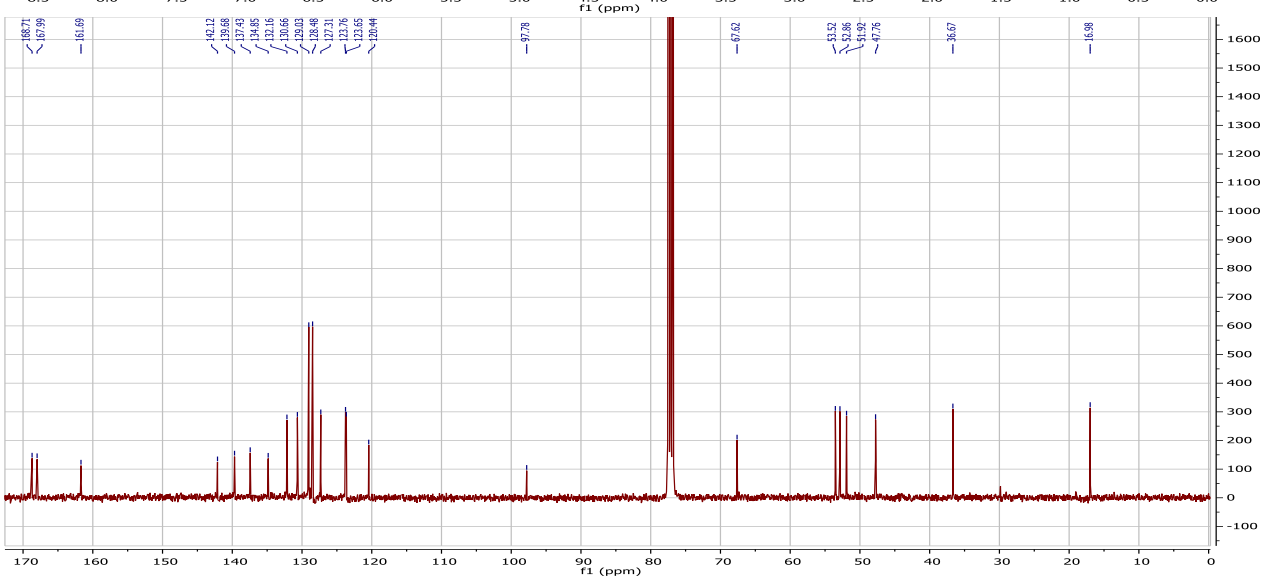


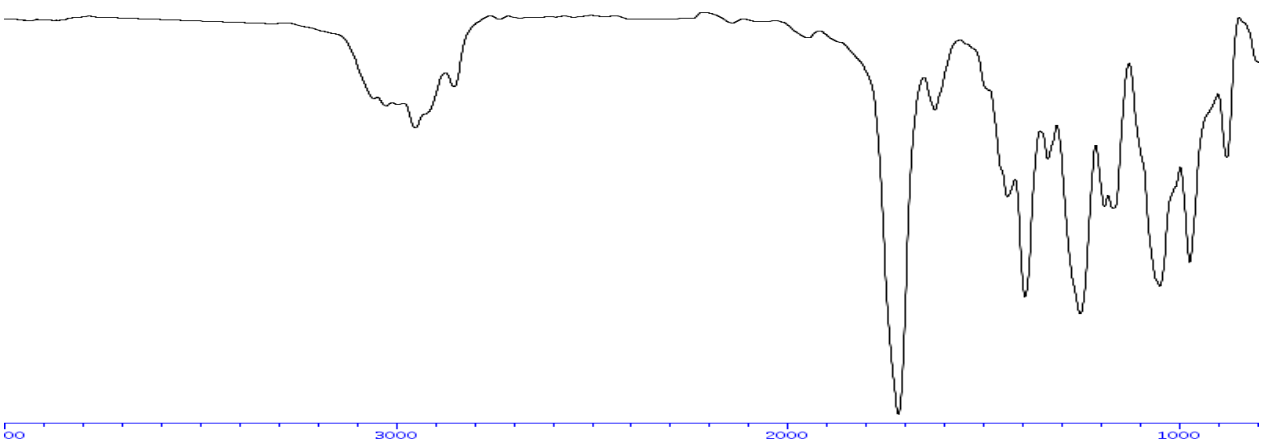

MeO2C
MeO2C
O
N
O
C5H11
S
Me
5e
400 MHz, Chloroform-d.
f1 (ppm)

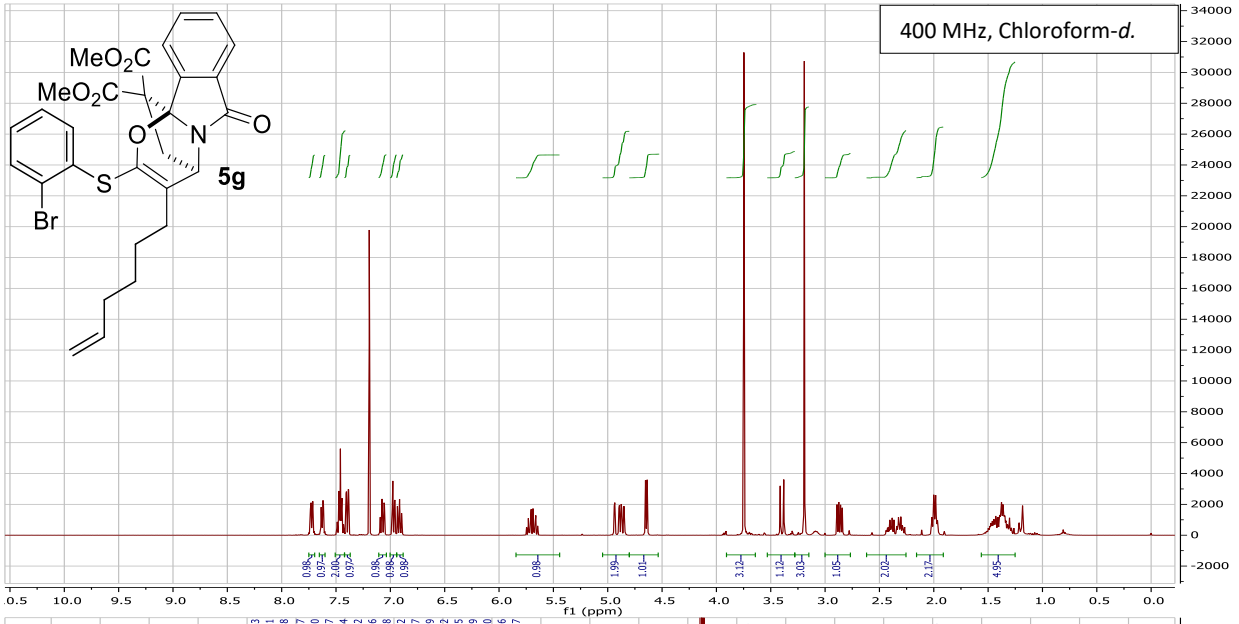

168.69
167.79
161.80
142.40
139.54
134.68
134.33
132.01
130.50
123.57
123.52
123.47
118.77
97.56
67.39
53.30
52.75
51.87
47.66
32.05
30.77
29.33
22.25
17.10
13.98
f1 (ppm)

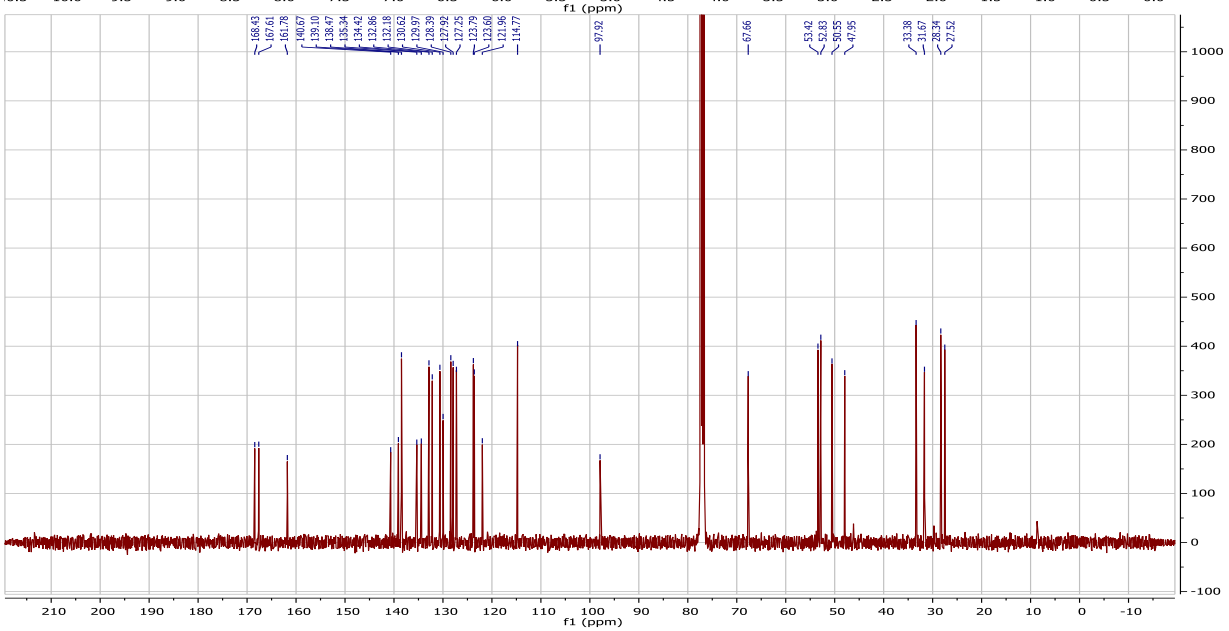

3000
2000
1000

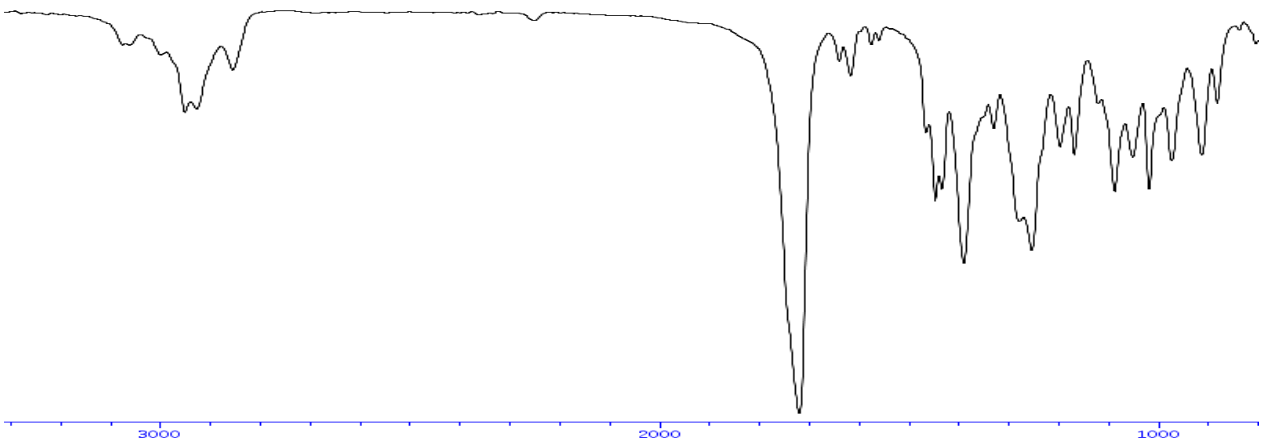

MeO2C
MeO2C
O
N
O
BnS
Me
5f
400 MHz, Chloroform-d.
f1 (ppm)

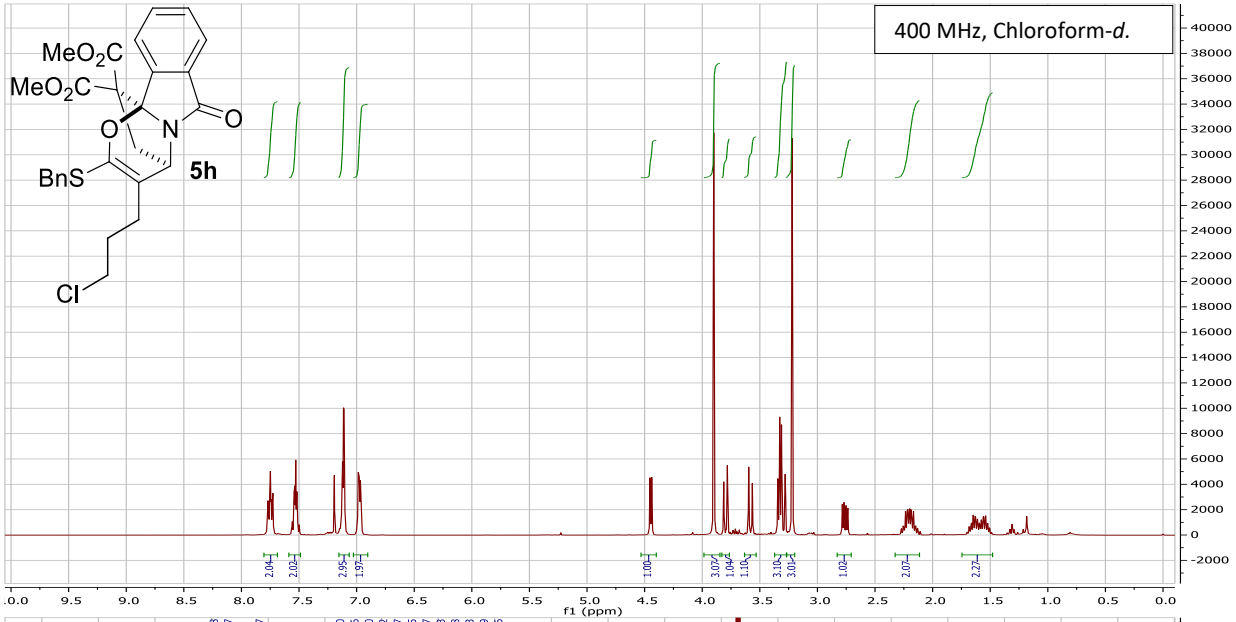

168.71
167.99
161.69
142.12
139.68
137.43
134.85
132.16
130.66
129.03
128.48
127.31
123.76
123.65
120.44
97.78
67.62
53.52
52.86
51.92
47.76
36.67
16.98
f1 (ppm)

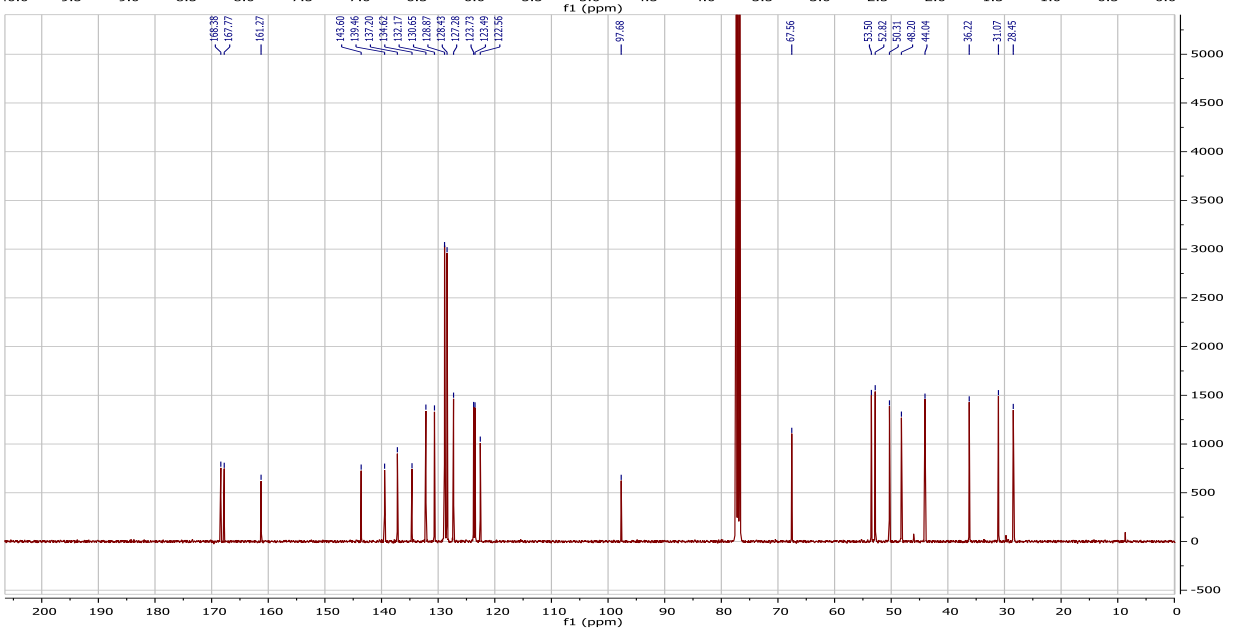

3000
2000
1000

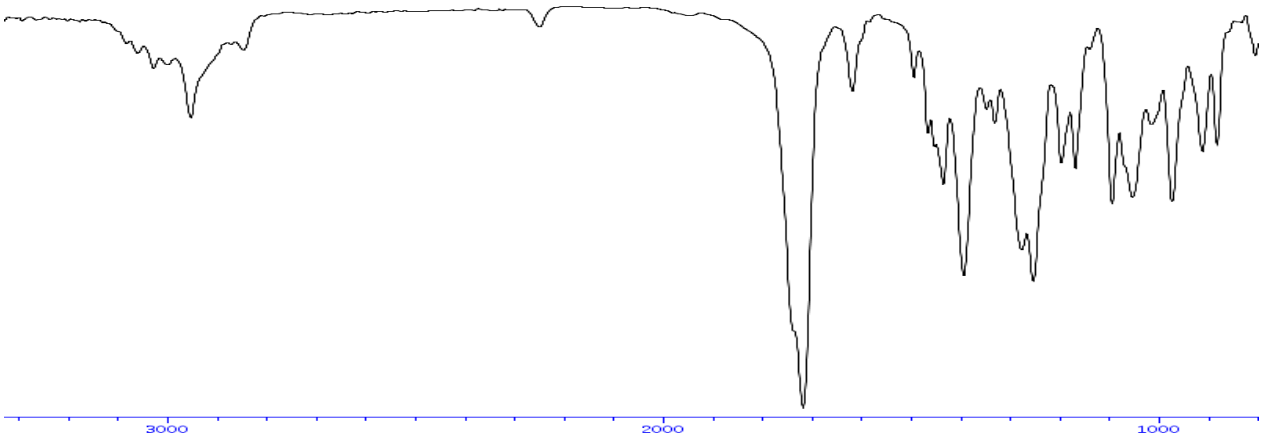

400 MHz, Chloroform-*d*.
MeO2C
MeO2C
O
N
O
S
Br
5g
f1 (ppm)

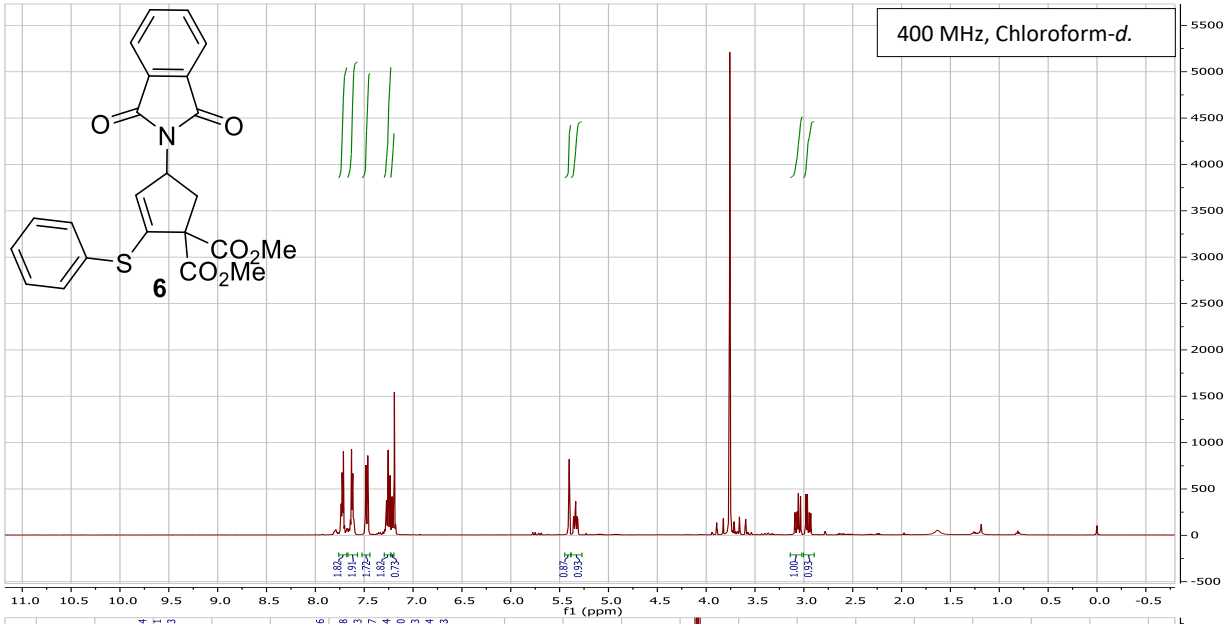

168.43
167.61
161.78
140.67
139.10
138.47
135.34
134.42
132.86
132.18
130.62
129.97
128.39
127.92
127.25
123.79
123.60
121.96
114.77
97.92
67.66
53.42
53.83
50.55
47.95
33.38
31.67
28.34
27.52
f1 (ppm)

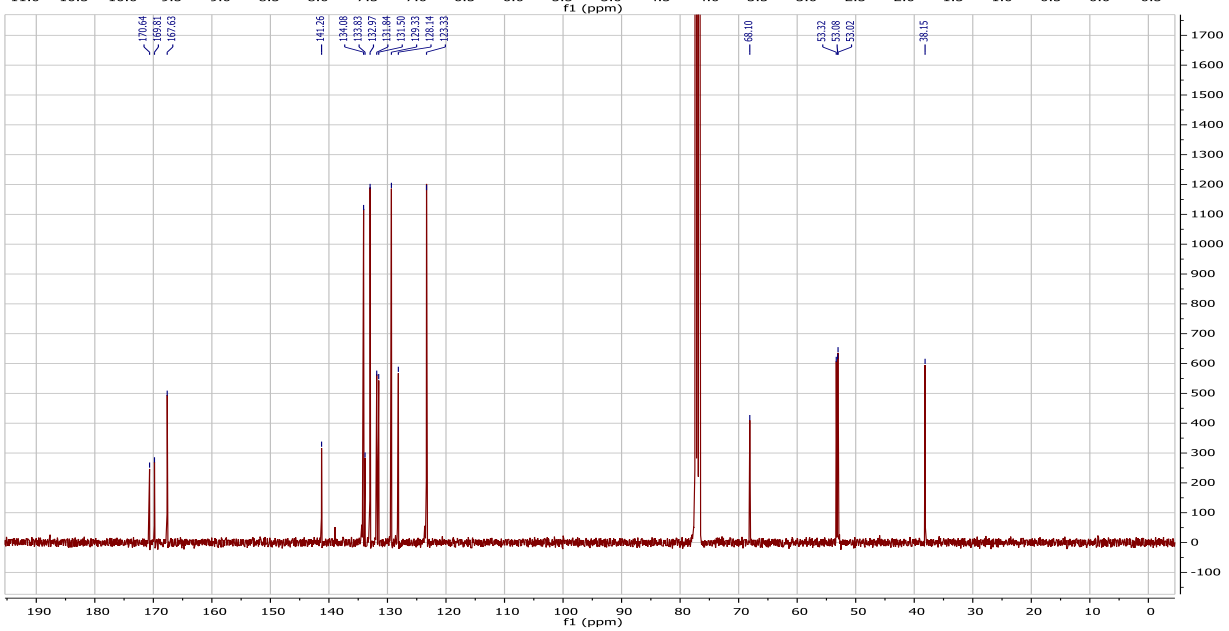

3000
2000
1000

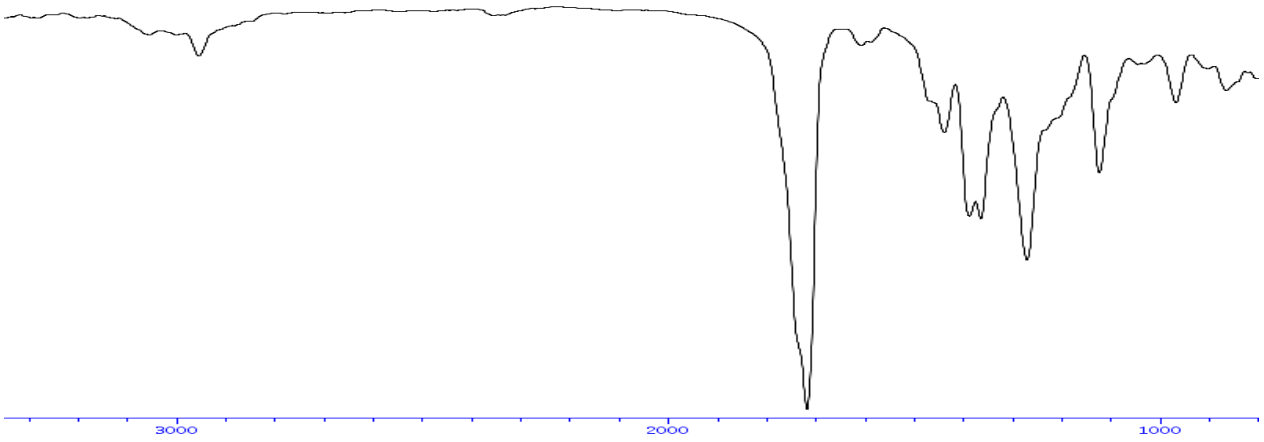

400 MHz, Chloroform-d.
MeO2C
MeO2C
O
N
O
BnS
5h
Cl
f1 (ppm)

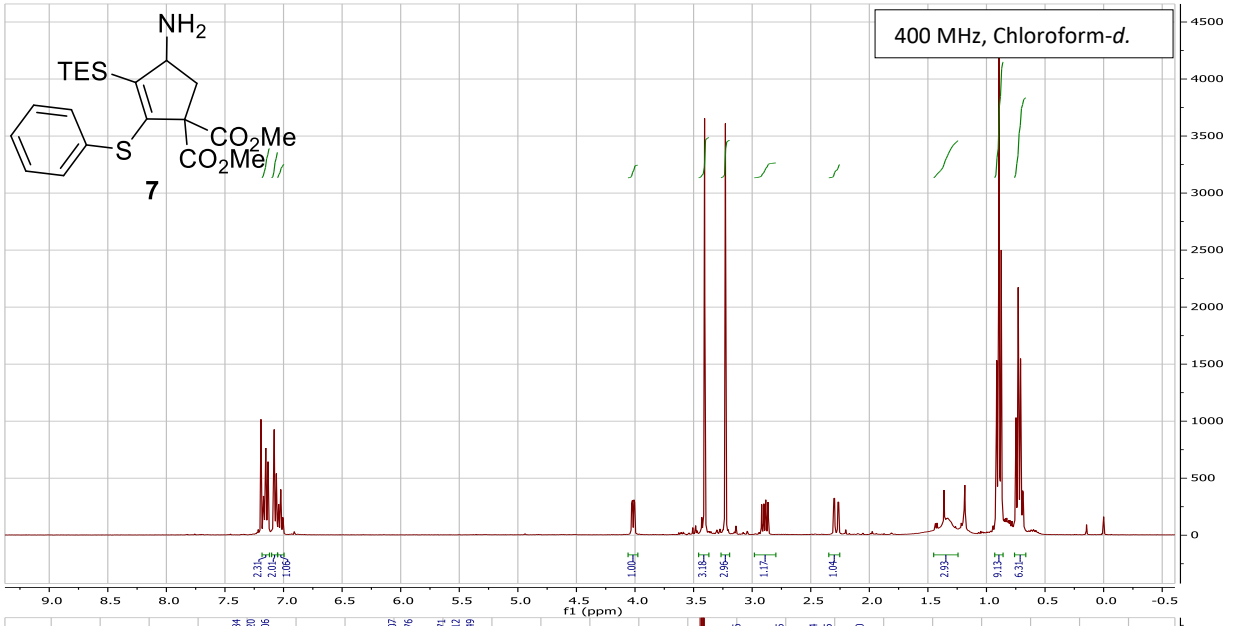

168.38
167.77
161.27
143.60
139.46
137.20
134.62
132.17
130.65
128.87
128.43
127.28
123.73
123.49
122.56
97.68
67.56
53.50
52.82
50.31
48.20
44.04
36.22
31.07
28.45
f1 (ppm)

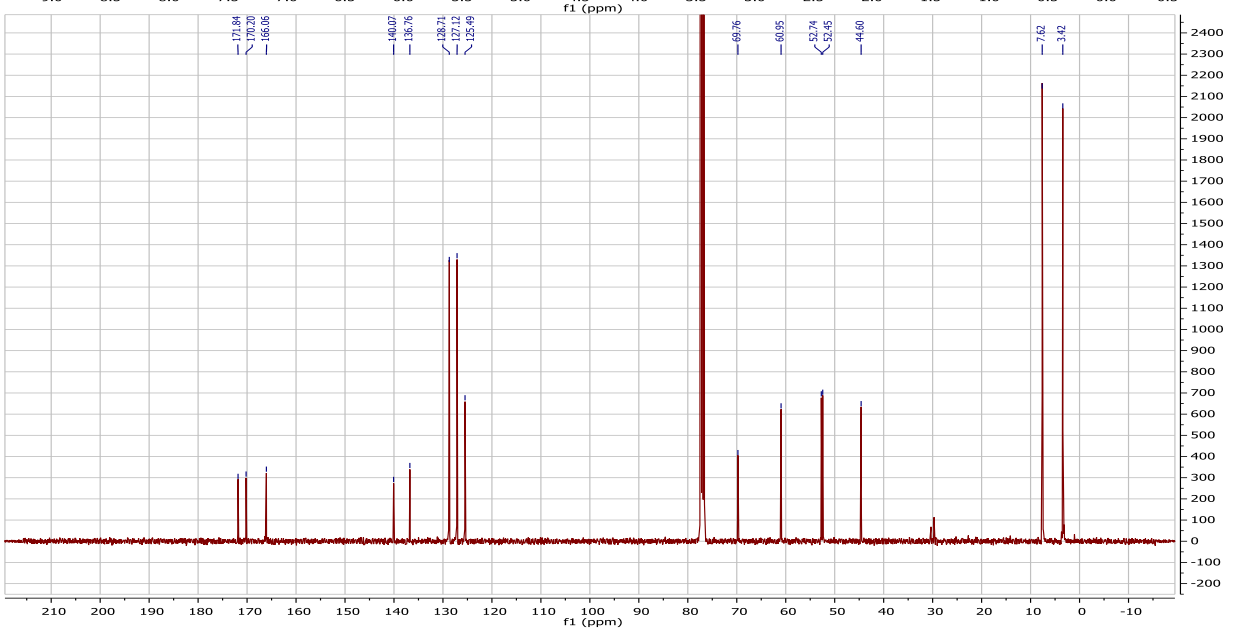

3000
2000
1000

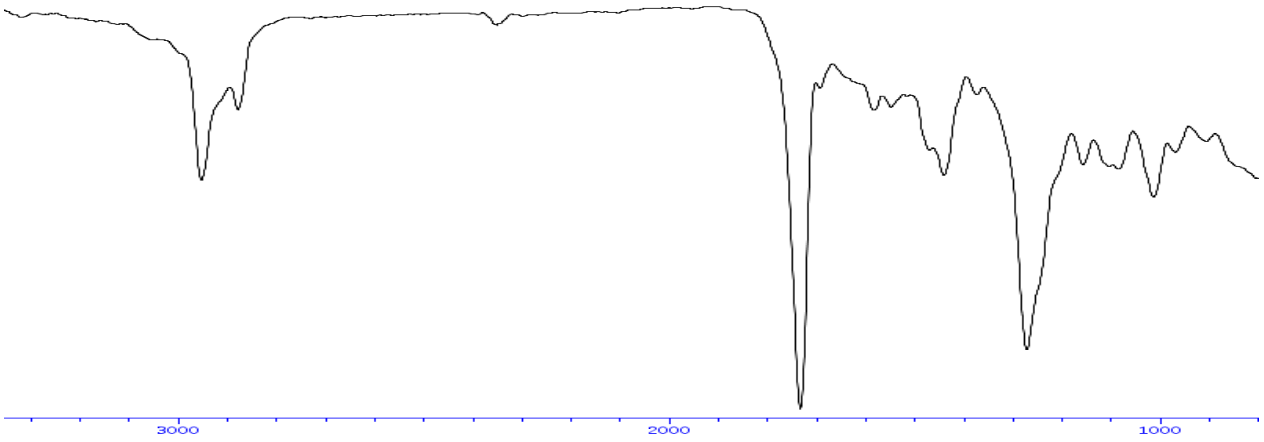

400 MHz, Chloroform-d.
O
N
O
S
CO2Me
CO2Me
6
f1 (ppm)

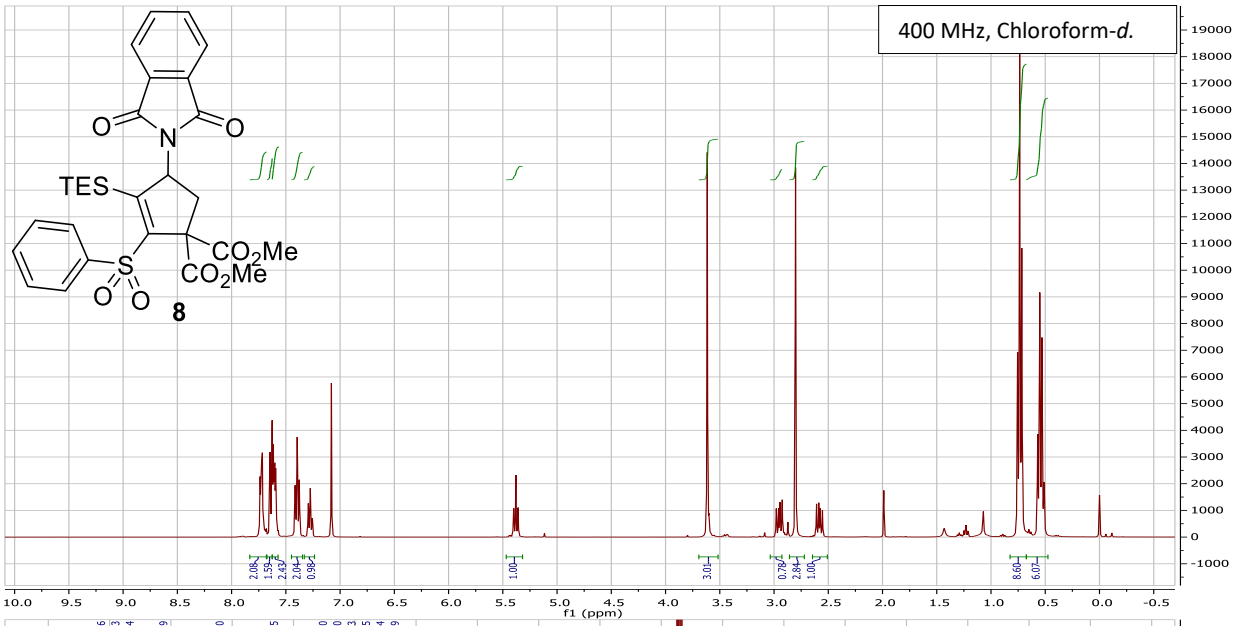

170.64
169.81
167.63
141.26
134.08
133.83
132.97
131.84
131.50
129.33
128.14
123.33
68.10
53.32
53.08
53.02
38.15
f1 (ppm)

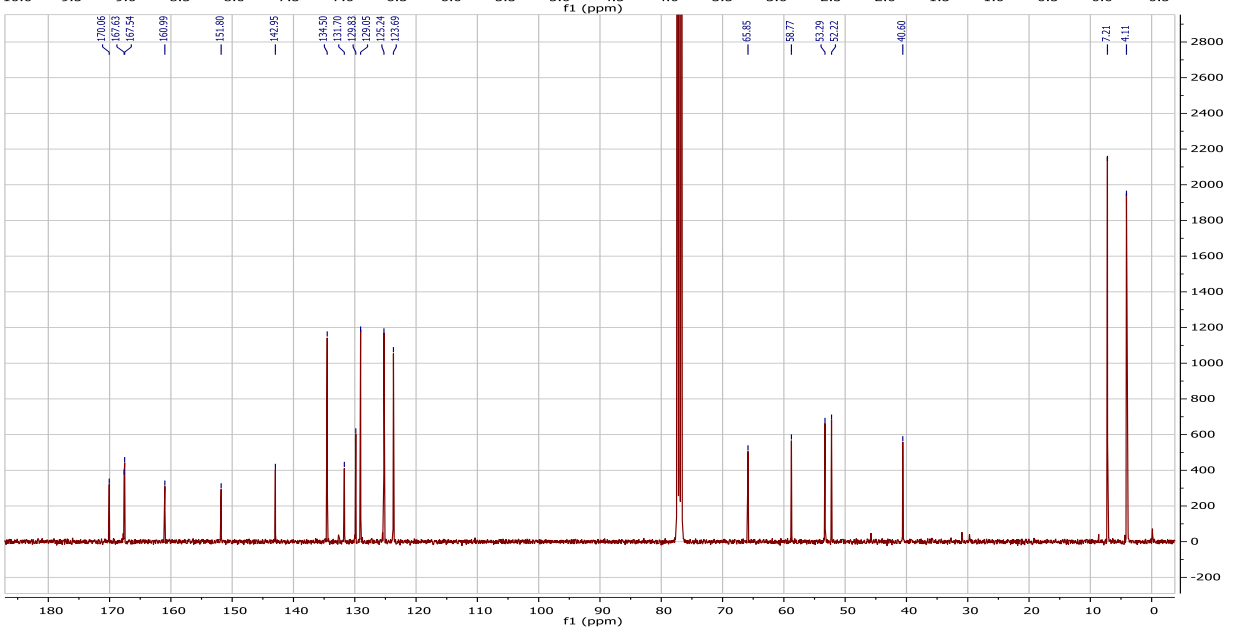

3000
2000
1000


NH2
TES
S
CO2Me
CO2Me
7
400 MHz, Chloroform-d.
f1 (ppm)


171.84
170.20
166.06
140.07
136.76
128.71
127.12
125.49
69.76
60.95
52.74
52.45
44.60
7.62
3.42
f1 (ppm)


3000
2000
1000


400 MHz, Chloroform-d.
TES
CO2Me
CO2Me
8
f1 (ppm)


170.06
167.63
167.54
160.99
151.80
142.95
134.50
131.70
129.83
129.05
125.24
123.69
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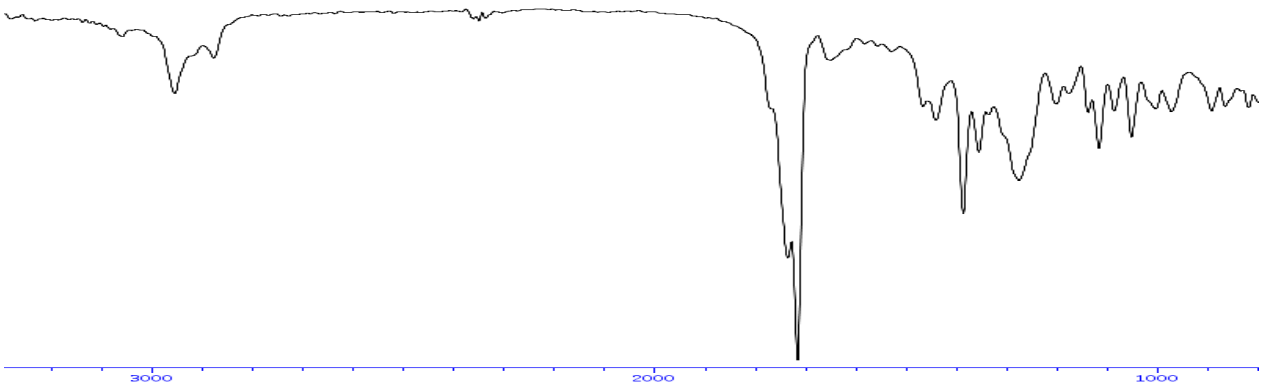
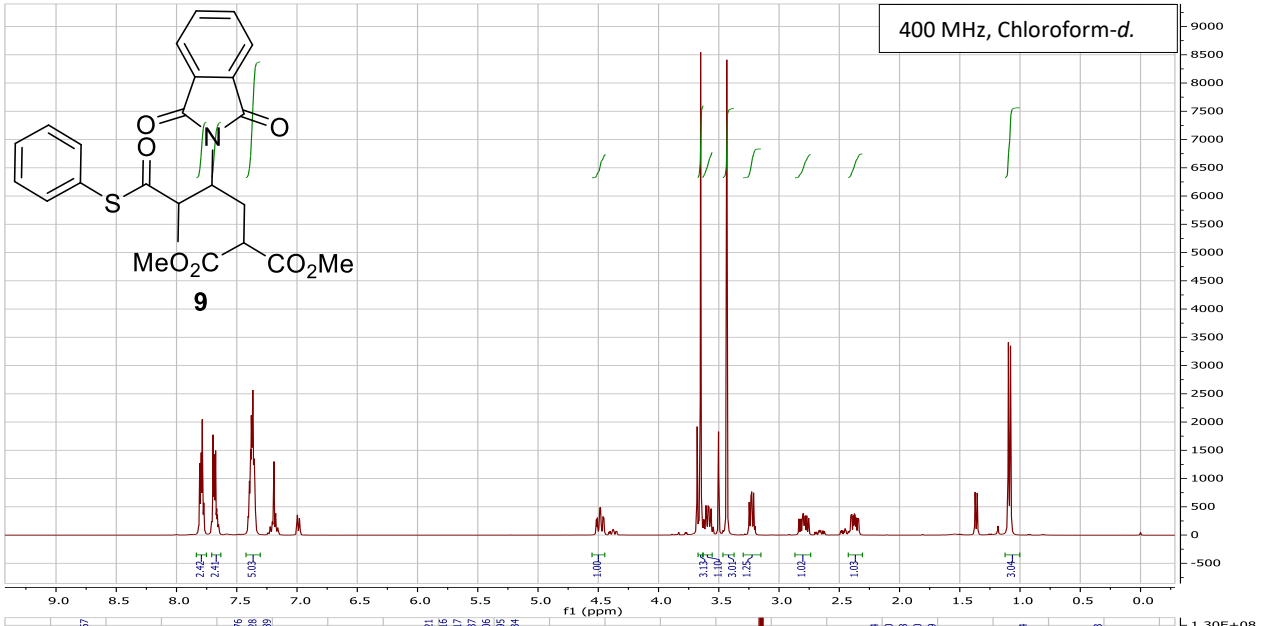
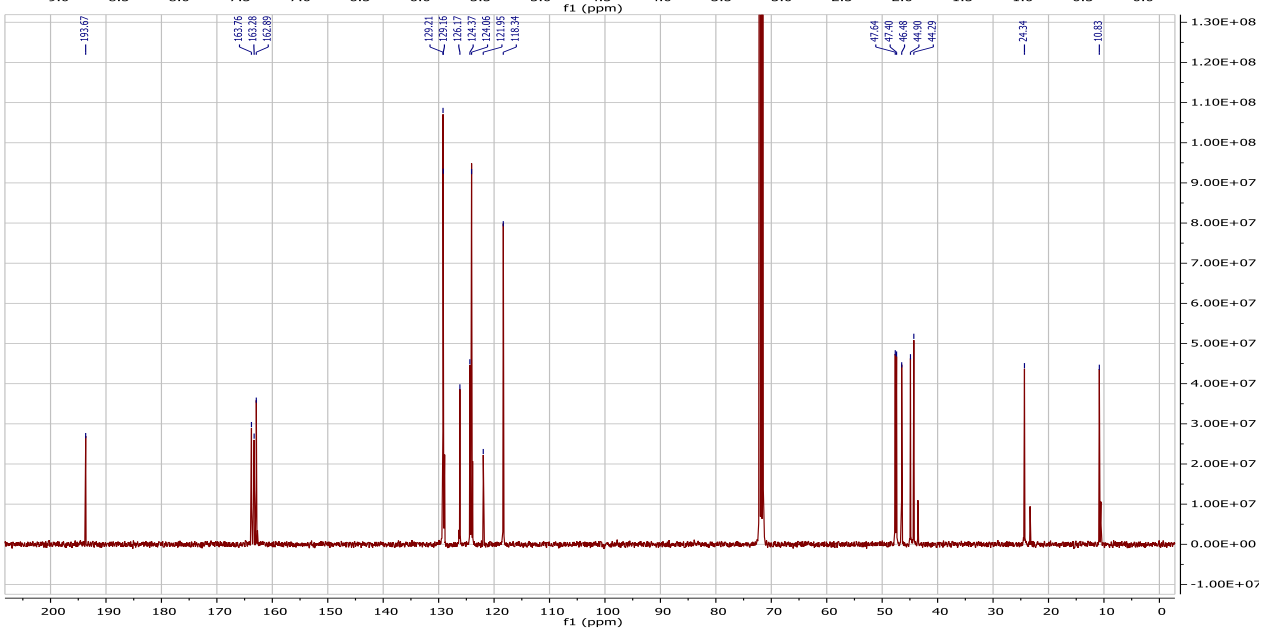
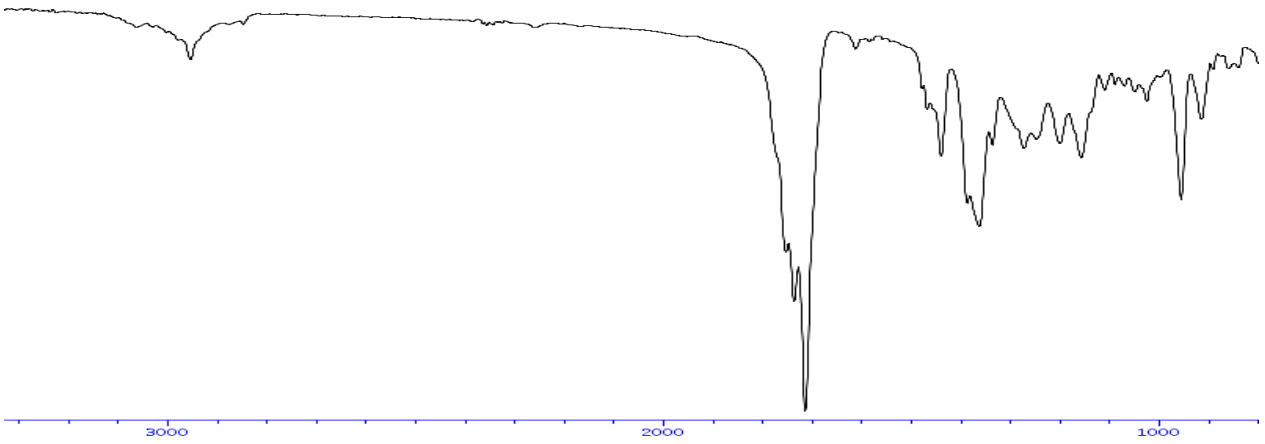
52.22
40.60
7.21
4.11
f1 (ppm)


3000
2000
1000


400 MHz, Chloroform-d.
O
O
N
O
S
MeO2C
CO2Me
9
f1 (ppm)


193.67
163.76
163.28
162.89
129.21
129.16
126.17
124.37
124.06
121.95
118.34
47.64
47.40
46.48
44.90
44.29
24.34
10.83
f1 (ppm)


3000
2000
1000