Dihydrothiophenes containing quaternary stereogenic centres by sequential stereospecific rearrangements and ring-closing metathesis

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Supporting information

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General information

NMR spectra were recorded on a Bruker Ultrashield 300 MHz, 400 MHz or 500 MHz spectrometer. The chemical shifts (δ) are reported in ppm downfield of trimethylsilane and coupling constants (J) reported in hertz and rounded to 0.1 Hz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (qn), sextuplet (sext), octuplet (oct), multiplet (m), broad (b) or a combination of these. Where this combination involves abbreviations containing more than one letter, the abbreviations are separated by spaces and x for clarity purposes (for example: quintet of triplet reads qn x t). Other abbreviations include C_q (quaternary carbon), H_{Ar}, CH_{Ar} and C_{qAr} (aromatic protons and carbons). Two geminal protons with different shifts are assigned the same number XX but noted H-XX and H-XX'. Solvents were used as internal standards when assigning NMR spectra (δ_H: $CDCl_3$ 7.26 ppm; δ_C: $CDCl_3$ 77.0 ppm). Coupling constants were calculated automatically by ChemDraw Ultra 11.0 software.

Low and high resolution mass spectra were recorded by staff at the University of Manchester. Electrospray spectra were recorded on a Micromass Platform II, and high resolution mass spectra were recorded either on a Waters QTOF or a Thermo Finnigan MAT95XP mass spectrometer, and are accurate to ±0.001 Da. For compounds containing chlorine, only the ^{35}Cl isotope is reported. GC-MS was performed on a Agilent 7890 (GC)/5975C (MS) spectrometer using the following parameters, unless otherwise stated:

Oven temperature: 50 °C (3min hold) then 25 °C/min to 300 °C (5min hold), total 18 min

Injector temperature : 300 °C (back injector)

Split injection : split ratio 20:1

Aux Heater: 300 °C

MS source: 230 °C

MS quad: 150 °C

Ionisation mode: EI

Column : Agilent H5-5ms, 30 m x 0.25 mm x 0.25 µm (film thickness)

Carrier gas : helium, column flow 1 mL/min.

Infrared spectra were recorded on a PerkinElmer FT-IR Spectrum BX spectrometer. Absorptions reported are the most intense, and quoted as wavenumbers in cm^{-1}.

Melting points (mp) were determined on a Bibby Stuart Scientific Melting Point SMP10 apparatus and are uncorrected.

Optical rotation measurements $[\alpha]_D$ were taken on a AA-100 polarimeter in a cell with a 0.25 dm path length. The temperature T, solvent S and concentration *c* (in grams per 100 mL) are as stated: $[\alpha]_D^T$: x (*c*, S).

Thin layer chromatography (TLC) was performed using commercially available pre-coated plates (Macherey-Nagel Polygram® Sil G/UV_{254} for TLC, 0.20 mm) and visualised with UV light at 254 nm, phosphomolybdic acid dip or Seebach's dip (2.5 g of phosphomolybdic acid hydrate, 1.0 g of cerium(IV) sulfate tetrahydrate, 3.2 mL of conc. sulfuric acid and 90.5 mL of water).

Flash chromatography was carried out using Fluorochem Davisil 40-63 µÅ silica gel by means of compressed air.

Chiral HPLC measurements were carried out using a Hewlett Packard instrument fitted with a Daicel Chiralcel OD-H, a Daicel Chiralcel AD-H, or a (*R*,*R*)-Whelk-01 stationary phase with a mixture of hexane and isopropyl alcohol as eluent, at. Absorptions were measured both at 214 and 254 nm. When the internal temperature of the apparatus could be set, it has been specified in the individual experimental procedure. Otherwise, the measurement was carried out at room temperature.

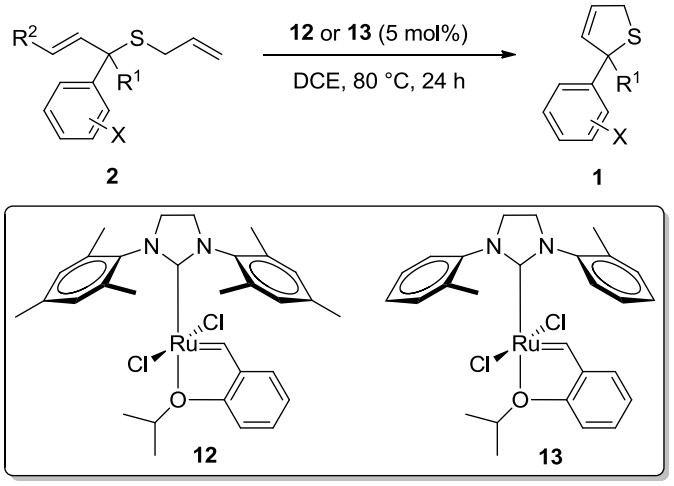
All reactions were conducted under a nitrogen atmosphere unless otherwise stated. Glassware was oven or flame dried. The temperatures stated are those for an external bath. An acetone/dry ice bath was used for -78°C. For all other temperatures, a cryo-cooler apparatus Haake EK 90 was used.

All solvents and reagents requiring purification were done so following standard laboratory techniques.[1] Tetrahydrofuran was distilled under nitrogen from sodium using benzophenone indicator. Dichloromethane and diisopropylamine were obtained by distillation from calcium hydride under nitrogen. Triethylamine and pyridine were stored over KOH. Dry diethyl ether and toluene were provided by the SPS (Solvent Purification System) Pure Solv model PS-MD-5, serial PS-08-150 apparatus from Innovative Technology *Inc*. Petrol refers to the fraction of light petroleum ether boiling between 40 and 65 °C. *n*-Butyllithium was generally purchased from Sigma-Aldrich as a 1.6 M solution in hexanes, or occasionally from Acros as a 2.5 M solution in hexanes, and was titrated prior to use against

a solution of *N*-benzylbenzamide.[2] All other solvents and commercially available reagents were used as received.

General procedures

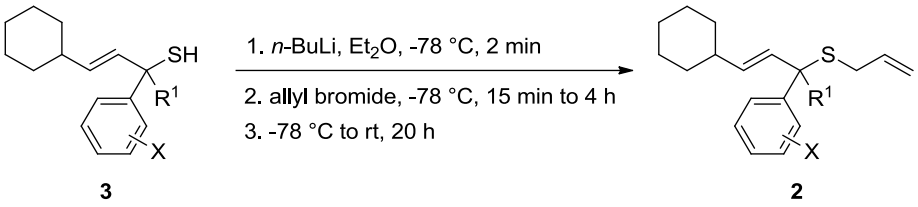
General procedure A – *Ring-closing metathesis of allyl sulfides **2** to 2,5-dihydrothiophenes **1**.*



Based on a modification of the method reported by Grubbs and co-workers.[3]

Dichloroethane was degassed by bubbling nitrogen through it for 30 min and kept under argon. In a flame-dried flask, cooled in a dessicator under vaccum and purged with argon, was added a solution of **2** (1.0 eq) in degassed DCE (10 mL/mmol of **2**), followed by either catalyst **12** or **13.** The flask was purged with argon after each addition. The reaction was heated to 80 °C for 24 h and cooled to room temperature. Ethyl vinyl ether (10 mL/mmol of **2**) was added, the reaction was stirred for 10 min and concentrated under reduced pressure. Further purification by column chromatography (Pentane 100%, Pentane/Et_2O 100:1 to 98:2) afforded the pure 2,5-dihydrothiophenes **1**.

General procedure B – *Allylation of tertiary thiols **3** to sulfides **2**.*

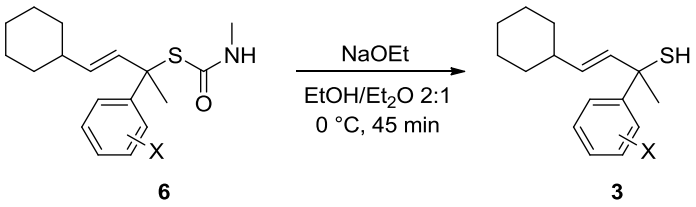


3 **2**

By the method developed within the Clayden group.[4]

To a solution of thiol **3** (1.0 eq) in Et_2O (10 mL/mmol of **3**) at -78 °C *n*-BuLi (1.1 eq) was added dropwise. The reaction was stirred at -78 °C for 2 min before allyl bromide (1.2 eq) was added. The reaction was stirred at -78 °C for 15 min to 4 h (generally 2 to 4 h) before it was slowly warmed to room temperature and allowed to stir for 20 h. A few drops of water were carefully added, the reaction was stirred at for 1 min before more water and Et_2O were added. The layers were separated and the aqueous layer was extracted with Et_2O (x3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Further purification by column chromatography (Pentane 100%, Pentane/Et_2O 100:1 to 98:2) and careful evaporation of the solvents on the rotary evaporator without vaccum afforded the pure tertiary sulfides **2**.

General procedure C – *Deprotection of methylcarbamothioates **6** to tertiary thiols **3**.*



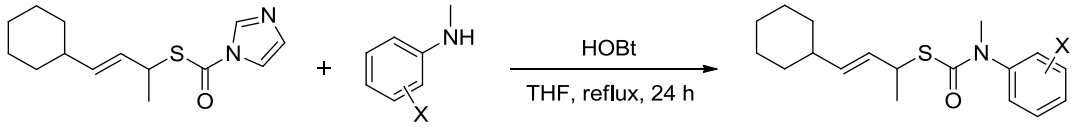
6 **3**

By the method developed within the Clayden group.[5,6]

To a solution of methylcarbamothioate **6** (1.0 eq) in EtOH/Et_2O 2:1 (10 mL/mmol of **6**) at 0 °C was added NaOEt (21% w/w in EtOH, 2.0 eq) dropwise. The reaction was stirred at 0 °C for 45 min before saturated aqueous NH_4Cl (2 mL/mmol of **6**) was added. The reaction was warmed to room temperature, water and Et_2O were added and the layers were separated. The aqueous layer was extracted with pentane/Et_2O 1:1 (x3). The combined organic layers

were washed with plenty of water, dried over $MgSO_4$, filtered and concentrated. Further purification by column chromatography (Pentane 100%, Pentane/Et_2O 99:1 to 97:3) and careful evaporation of the solvents on the rotary evaporator without vaccum afforded the pure tertiary thiols **3**.

General procedure D – *Preparation of phenyl(methyl)carbamothioates **4**.*

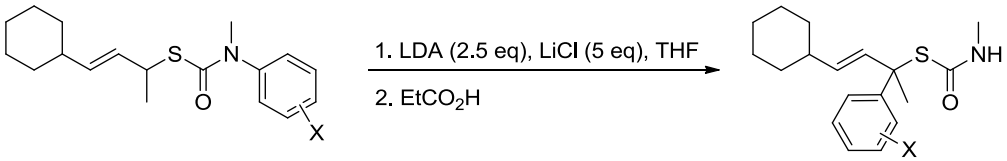


10 **11** **4**

By the method developed within the Clayden group,[7] based on a modification of the method reported by Vaidyanathan and co-workers.[8]

To a solution of 1*H*-imidazole-1-carbamathioate **10** (1.0 eq) in THF (1.0 mL/50 mg of **10**) at room temperature were added HOBt (0.5 to 1.5 eq) and *N*-methylaniline **11** (1.2 eq). The reaction was heated to reflux for 24 h. Once cooled to room temperature, EtOAc was added and the organic mixture was washed with aqueous HCl (1.0 mL/50 mg of **10**) for 20 min. The organic layer was separated, dried over $MgSO_4$, filtered and concentrated. Further purification by column chromatography afforded the pure phenyl(methyl)carbamothioates **4**.

General procedure E – *Lithiation of phenyl(methyl)carbamothioates **4** with LDA·LiCl.*



4 **6**

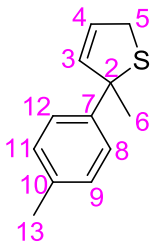
By the method developed within the Clayden group.[5,6]

To a solution of DIPA (3.0 eq) in THF (1.0 mL) at -78 °C *n*-BuLi (2.5 eq) was added dropwise. The mixture was stirred at -78 °C for 5 min then warmed to approximately -40 °C by allowing only the bottom of the flask to be in contact with the cooling bath and stirred at this

temperature for 15 min, then cooled down to -78 °C for 5-10 min. Oven-dried LiCl (5.0 eq) was added to a solution of phenyl(methyl)carbamothioate **4** (50 mg, 1.0 eq) in THF (1.5 mL) which was cooled to -78 °C before the dropwise addition of LDA. The reaction was either allowed to stir at -78 °C for the stated time or warmed slowly to the desired temperature by addition of room temperature acetone in the cool bath and stirred at this temperature for the stated time. In this last case, the reaction was cooled back to -78 °C before being quenched. Propionic acid (3.0 eq) was added dropwise, the reaction was allowed to stir at -78 °C for 10 min and warmed to room temperature. Water and Et_2O were added and the layers were separated. The aqueous layer was extracted with Et_2O (x3). The combined organic layers were washed with plenty of water and brine, dried over $MgSO_4$, filtered and concentrated. Further purification by column chromatography afforded the pure rearranged methylcarbamothioates **6**.

Experimental procedures and characterisation data

1e: 2-Methyl-2-(*p*-tolyl)-2,5-dihydrothiophene.

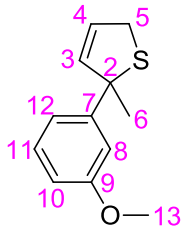


General procedure A was followed using (*E*)-allyl(4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl)sulfane **2e** (100 mg, 0.33 mmol) and **13** to afford the title compound as a pale yellow oil (55 mg, 87%).

R_f: 0.57 (Pet/EtOAc 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.31 (d, *J* = 8.1 Hz, 2H, H-9, H-11), 7.12 (d, *J* = 8.1 Hz, 2H, H-8, H-12), 5.89 (dt, *J* = 6.2, 2.3 Hz, 1H, H-4), 5.84 (dt, *J* = 6.2, 2.2 Hz, 1H, H-3), 3.91 (t, *J* = 2.3 Hz, 2H, H-5), 2.32 (s, 3H, H-13), 1.90 (s, 3H, H-6); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 144.6 (C-10), 138.8 (C-3), 136.2 (C-7), 128.9 (C-8, C-12), 126.2 (C-4), 125.8 (C-9, C-11), 64.8 (C-2), 39.6 (C-5), 31.0 (C-6), 20.9 (C-13); **IR**: ν_{max}(film)/cm^{-1} 1510 (C=C), 1449 (C=C_{Ar}), 814, 750, 719; **GC-MS**: 190.1 (M) 11.3 min; **HRMS**: found 190.0816, $[M]^+$ requires 190.0811.

The equivalent enantioenriched 2,5-dihydrothiophene (*R*)-2-methyl-2-(*p*-tolyl)-2,5-dihydrothiophene (*R*)-**1e** (86:14 *e.r.*, 54 mg, 91%) was prepared from (*R*)-allyl(4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl)sulfane (*R*)-**2e** (93 mg, 0.31 mmol) following general procedure A (**12**). **$[\alpha]_D^{24}$**: +9.6 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 99:1, 0.5 mL/min, 28 °C, minor 9.7 min, major 10.3 min (214.4 nm).

1h: 2-(3-Methoxyphenyl)-2-methyl-2,5-dihydrothiophene.



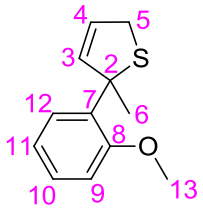
General procedure A was followed using (*E*)-allyl(4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl)sulfane **2h** (100 mg, 0.32 mmol) and **13** to afford the title compound as a pale yellow oil (53 mg, 82%).

R_f: 0.72 (Pent/Et_2O 95:5); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 7.24 (t, *J* = 8.0 Hz, 1H, H-11), 7.01 (ddd, *J* = 8.0, 1.6, 0.8 Hz, 1H, H-12), 6.98 (t, *J* = 2.2 Hz, 1H, H-8), 6.75 (ddd, *J* = 8.0, 2.2, 0.8 Hz, 1H, H-10), 5.90 (dt, *J* = 6.2, 2.5 Hz, 1H, H-3), 5.86 (dt, *J* = 6.2, 2.2 Hz, 1H, H-4), 3.91 (t, *J* = 2.2 Hz, 2H, H-5), 3.81 (s, 3H, H-13), 1.90 (s, 3H, H-6); **^{13}C NMR**: (125 MHz, $CDCl_3$) δ (ppm) 159.5 (C-9), 149.2 (C-7), 138.5 (C-4), 129.3 (C-11), 126.6 (C-3), 118.3 (C-12), 112.3 (C-8), 111.5 (C-10), 64.9 (C-2), 55.2 (C-13), 39.6 (C-5), 31.0 (C-6); **IR**: ν_{max}(film)/cm^{-1} 1581 (C=C), 1485 (C=C_{Ar}), 1431 (C=C_{Ar}), 1256 (C_{Ar}-O), 1040, 694; **GC-MS**: 206.1 (M), 12.0 min; **HRMS**: found 206.0753, $[M]^+$ requires 206.0760.

The equivalent enantioenriched 2,5-dihydrothiophene (*S*)-2-methyl-2-(3-methoxyphenyl)-2,5-dihydrothiophene (*S*)-**1h** (6:94 *e.r.*, 66 mg, 94%) was prepared from (*S*)-allyl(4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl)sulfane (*S*)-**2h** (108 mg, 0.34 mmol) following general procedure A (**12**).

$[\alpha]_D^{24}$: +9.8 (*c* 1.00, $CDCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 99:1, 0.5 mL/min, 28 °C, major 14.8 min, minor 16.1 min (214.4 nm).

1i: 2-(2-Methoxyphenyl)-2-methyl-2,5-dihydrothiophene.



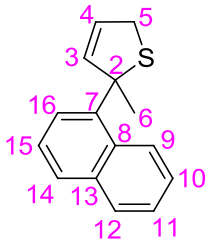
General procedure A was followed using (*E*)-allyl(4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl)sulfane **2i** (100 mg, 0.31 mmol) and **13** to afford the title compound as a pale yellow oil (59 mg, 91%).

R_f: 0.51 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.25-7.18 (m, 2H, H-9, H-11), 6.91 (dd, *J* = 8.2, 1.0 Hz, 1H, H-12), 6.87 (td, *J* = 7.5, 1.2 Hz, 1H, H-10), 6.16 (dt, *J* = 6.4, 2.3 Hz, 1H, H-3), 5.90 (dt, *J* = 6.4, 2.6 Hz, 1H, H-4), 3.91 (s, 3H, H-13), 3.81 (ddd, *J* = 14.8, 2.6, 2.3 Hz, 1H, H-5), 3.73 (dt, *J* = 14.8, 2.4 Hz, 1H, H-5), 1.88 (s, 3H, H-6); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 156.8 (C-8), 137.2 (C-3), 136.4 (C-7), 127.8 (C-9 or C-11), 126.4 (C-4), 125.1 (C-11 or C-9), 120.2 (C-10), 111.8 (C-12), 64.2 (C-2), 55.4 (C-13), 38.7 (C-5), 31.4 (C-6); **IR**: ν_{max}(film)/cm^{-1} 1488 ($C{=}C_{Ar}$), 1434 ($C{=}C_{Ar}$), 1236 (C_{Ar}-O), 1025, 751; **GC-MS**: 206.1 (M), 11.8 min; **HRMS**: found 206.0759, $[M]^+$ requires 206.0760.

The equivalent enantioenriched 2,5-dihydrothiophene (*S*)-2-methyl-2-(2-methoxyphenyl)-2,5-dihydrothiophene (*S*)-**1i** (8:92 *e.r.*, 55 mg, 90%) was prepared from (*S*)-allyl(4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl)sulfane (*S*)-**2i** (93 mg, 0.29 mmol) following general procedure A (**13**).

$[\alpha]_D^{24}$: +173.2 (*c* 1.00, $CDCl_3$); **HPLC**: Chiralpak IB, Hexane/*i*-PrOH 99:1, 0.5 mL/min, 28 °C, minor 9.5 min, major 10.0 min (214.4 nm, 254.4 nm).

1j: 2-Methyl-2-(naphthalen-1-yl)-2,5-dihydrothiophene.



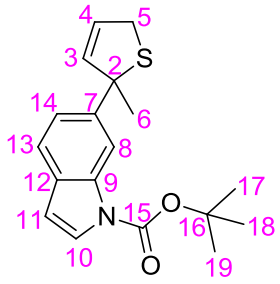
General procedure A was followed using (*E*)-allyl(4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl)sulfane **2j** (200 mg, 0.59 mmol, as a 1:0.7 mixture with by-product **2j'**) and **12** to afford the title compound as a mixture with **2j'** (**1j**/**2j'** 1:0.6).

R_f: 0.41/0.62 (Pent/Et_2O 95:5); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 8.36 (d, *J* = 8.4 Hz, 1H, H-9), 7.87 (bdd, *J* = 8.1, 1.4 Hz, 1H, H-12), 7.74 (d, *J* = 8.1 Hz, 1H, H-14), 7.56 (td, *J* = 7.0, 1.4 Hz, 1 H, H_{Ar}), 7.51-7.41 (m, 6H, H-10, H-11, H-15, $H_{Ar\text{-}2j'}$), 7.37 (d, *J* = 7.9 Hz, 1H, H-16), 6.28 (dt, *J* = 6.4, 2.2 Hz, 1H, H-3), 6.03 (dt, *J* = 6.4, 2.6 Hz, 1H, H-4), 3.94 (dt, *J* = 14.9, 2.4 Hz, 1H, H-5), 3.90 (dt, *J* = 14.9, 2.4 Hz, 1H, H-5), 2.10 (s, 3H, H-6).

The equivalent enantioenriched 2,5-dihydrothiophene (*R*)-2-Methyl-2-(naphthalen-1-yl)-2,5-dihydrothiophene (*R*)-**1j** (78:22 *e.r.*, a mixture with (*R*)-**2j** and **2j'** (**1j**/**2j**/**2j'** 1:0.6:1) was tentatively prepared from (*R*)-allyl(4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl)sulfane (*R*)-**2j'** (200 mg, 0.59 mmol, as a 1:0.5 mixture with by-product **2j'**) following general procedure A (**12**).

HPLC: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 99:1, 0.5 mL/min, 28 °C, minor 18.4 min, major 19.5 min (214 nm).

1l: *tert*-Butyl 6-(2-methyl-2,5-dihydrothiophen-2-yl)-1*H*-indole-1-carboxylate.



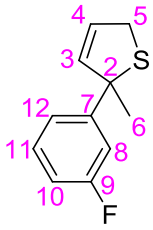
General procedure A was followed using (*E*)-*tert*-butyl 6-(2-(allylthio)-4-cyclohexylbut-3-en-2-yl)-1*H*-indole-1-carboxylate **2l** (70 mg, 0.16 mmol) and **13** to afford the title compound as a colourless oil (33 mg, 63%).

R_f: 0.56 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.24 (s, 1H, H-11), 7.59 (d, *J* = 3.5 Hz, 1H, H-8), 7.50 (d, *J* = 8.3 Hz, 1H, H-14), 7.34 (dd, *J* = 8.3, 1.7 Hz, 1H, H-13), 6.52 (d, *J* = 3.5 Hz, 1H, H-12), 5.94 (s, 2H, H-3, H-4), 3.95 (2H, H-5), 2.00 (s, 3H, H-6), 1.69 (s, 9H, H-17, H-18, H-19); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 149.8 (C-15), 143.8 (C-9), 139.0 (C-3 or C-4), 135.0 (C-7), 129.1 (C-10), 126.3 (C-8), 126.2 (C-4 or C-3), 121.5 (C-13), 120.7 (C-14), 112.3 (C-11), 107.2 (C-12), 83.5 (C-16), 65.6 (C-2), 39.6 (C-5), 31.4 (C-6), 28.2 (C-17, C-18, C-19); **IR**: ν_{max}(film)/cm^{-1} 1729 (C=O), 1333 (C_{Ar}=N), 1151 (C-O_{ester}), 1129, 721; **GC-MS**: *m/z* 215.0 $[M-C_5H_9O_2+H]^+$ 13.7 min; **HRMS**: found 315.1288, $[M]^+$ requires 315.1288.

The equivalent enantioenriched 2,5-dihydrothiophene (*R*)-*tert*-Butyl 6-(2-methyl-2,5-dihydrothiophen-2-yl)-1*H*-indole-1-carboxylate (*R*)-**1l** (77:23 *e.r.*) was prepared from (*R*)-*tert*-butyl 6-(2-(allylthio)-4-cyclohexylbut-3-en-2-yl)-1*H*-indole-1-carboxylate (*R*)-**2l** (33 mg, 0.08 mmol) following general procedure A (**13**).

$[\alpha]_D^{25}$: -14.4 (*c* 0.125, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 99:1, 0.5 mL/min, 28 °C, minor 30.9 min, major 39.9 min (214.4 nm, 254.4 nm).

1m: 2-(3-Fluorophenyl)-2-methyl-2,5-dihydrothiophene.



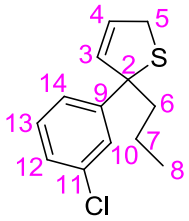
General procedure A (CH_2Cl_2, reflux, 24 h then DCE, 80 °C, 42 h) was followed using allyl(2-(3-fluorophenyl)but-3-en-2-yl)sulfane **2m** (80 mg, 0.36 mmol) and **13** (2x5 mol%) to afford the title compound as a yellow oil (49 mg, 70%).

R_f: 0.71 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.26 (t, J = 8.1 Hz, 1H, H-11), 7.19 (ddd, J = 8.1, 1.7, 1.1 Hz, 1H, H-12), 7.12 (dt, J = 10.7, 2.1 Hz, 1H, H-10), 6.89 (tdd, J = 8.1, 2.5, 1.0 Hz, 1H, H-8), 5.93 (dt, J = 6.2, 2.5 Hz, 1H, H-3), 5.83 (dt, J = 6.2, 2.3 Hz, 1H, H-4), 3.92 (t, J = 2.3 Hz, 2H, H-5), 1.90 (s, 3H, H-6); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 164.0/161.5 (C-9), 150.3/150.2 (C-7), 138.1 (C-4), 129.7/129.6 (C-11), 127.0 (C-3), 121.5 (C-12), 113.5/113.4 (C-8), 113.3/113.1 (C-10), 64.6/64.5 (C-2), 39.7 (C-5), 30.8 (C-6); **IR**: ν_{max}(film)/cm^{-1} 1587 (C=C), 1485 (C=C_{Ar}), 1436 (C=C_{Ar}), 1251 (C-F), 691; **GC-MS**: *m/z* 194.1 $[M]^+$ 10.8 min; **HRMS**: found 194.0552, $[M]^+$ requires 194.0560.

The equivalent enantioenriched 2,5-dihydrothiophene (*R*)-2-methyl-2-(3-fluorophenyl)-2,5-dihydrothiophene (*R*)-**1m** (86:14 *e.r.*, 20 mg, 57%) was prepared from (*R*)-allyl(2-(3-fluorophenyl)but-3-en-2-yl)sulfane (*R*)-**2m** (40 mg, 0.18 mmol) following general procedure A (**12**).

$[\alpha]_D^{24}$: -13.4 (*c* 1.00, $CDCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 99:1, 0.2 mL/min, 28 °C, minor 23.9 min, major 24.9 min (214.4 nm, 254.4 nm).

1n: 2-(3-Chlorophenyl)-2-propyl-2,5-dihydrothiophene.



General procedure R was followed using allyl(3-(3-chlorophenyl)hex-1-en-3-yl)sulfane **2n** (39 mg, 0.15 mmol) and **13** to afford the title compound as a yellow oil (27 mg, 77%).

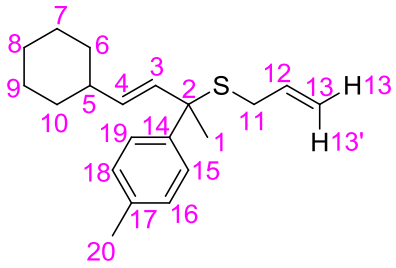
R_f: 0.81 (Pent/Et_2O 95:5); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 7.38 (t, *J* = 1.9 Hz, 1H, H-10), 7.28 (dt, *J* = 7.8, 1.4 Hz, 1H, H-12), 7.24 (t, *J* = 7.8 Hz, 1H, H-13), 7.17 (ddd, *J* = 7.8, 1.9, 1.4 Hz, 1H, H-14), 5.94 (dt, *J* = 6.3, 2.5 Hz, 1H, H-4), 5.87 (dt, *J* = 6.3, 2.2 Hz, 1H, H-3), 3.82 (q, *J* = 2.5 Hz, 2H, H-5), 2.07 (sym. m, 2H, H-6), 1.28-1.20 (m, 1H, H-7), 0.92 (t, *J* = 7.3 Hz, 3H, H-8), 1.49-1.41 (m, 1H, H-7'); **^{13}C NMR**: (125 MHz, $CDCl_3$) δ (ppm) 149.3 (C-9), 135.7 (C-3), 134.2 (C-11), 129.5 (C-13), 127.9 (C-4), 126.6 (C-14), 126.5 (C-10), 124.3 (C-12), 69.9 (C-2), 45.7 (C-6), 39.3 (C-5), 19.0 (C-7), 14.2 (C-8); **IR**: ν_{max}(film)/cm^{-1} 1592 (C=C), 1568 (C=C_{Ar}), 1464 (C=C_{Ar}), 1236, 1081, 871, 782, 742, 689 (C-Cl); **GC-MS**: *m/z* 238.1 $[M]^+$, 12.6 min; **HRMS**: found 238.0582, $[M]^+$ requires 238.0578.

The equivalent enantioenriched 2,5-dihydrothiophene (*R*)-2-(3-chlorophenyl)-2-propyl-2,5-dihydrothiophene (*R*)-**1n** (92:8 *e.r.*, 5 mg, 31%) was prepared from (*R*)-allyl(3-(3-chlorophenyl)hex-1-en-3-yl)sulfane (*R*)-**2n** (18 mg, 0.07 mmol) following general procedure A (**13**).

$[\alpha]_D^{24}$: -43.2 (*c* 0.50, $CDCl_3$); **HPLC**: Chiralcel OD-H, Hexane/*i*-PrOH 99:1, 0.2 mL/min, 28 °C, major 22.3 min, minor 23.7 min (214.4 nm, 254.4 nm).

Note: *no conditions could be found to separate the enantiomers of thiols **3** and sulfides **2**. Only enantiomeric ratios for the derivatised 2,5-dihydrothiophenes **1** are reported.*

2e: (*E*)-Allyl(4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl)sulfane.

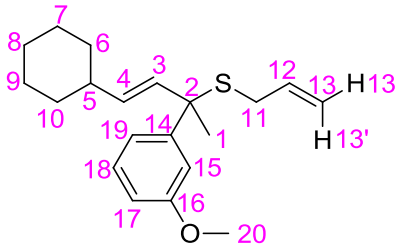


General procedure B was followed using (*E*)-4-cyclohexyl-2-(*p*-tolyl)but-3-ene-2-thiol **3e** (546 mg, 2.10 mmol) to afford the title compound as a colourless oil (479 mg, 76%).

R_f: 0.69 (Pent/Et_2O 98:2); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 7.41 (d, *J* = 8.2 Hz, 2H, H-15, H-19), 7.12 (d, *J* = 8.2 Hz, 2H, H-16, H-18), 5.79 (ddt, *J* = 17.0 Hz, 10.0, 7.2 Hz, 1H, H-12), 5.76 (dd, *J* = 15.7, 1.1, Hz, 1H, H-3), 5.51 (dd, *J* = 15.7, 6.9 Hz, 1H, H-4), 5.11 (dq, *J* = 17.0, 1.0 Hz, 1H, H-13'), 5.00 (bdd, *J* = 10.0, 1.0 Hz, 1H, H-13), 3.02 (ddt, *J* = 12.9, 7.2, 1.0 Hz, 1H, H-11), 2.960 (ddt, *J* = 12.9, 7.2, 1.0 Hz, 1H, H-11'), 2.32 (s, 3H, H-20), 2.10-2.03 (m, 1H, H-5), 1.78-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.71 (s, 3H, H-1), 1.33-1.08 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (125 MHz, $CDCl_3$) δ (ppm) 142.3 (C-17), 136.3 (C-14), 135.5 (C-4), 134.8 (C-12), 132.6 (C-3), 128.8 (C-16, C-18), 126.9 (C-15, C-19), 116.8 (C-13), 53.3 (C-2), 40.7 (C-5), 33.4 (C-11), 33.3/33.2 (C-6, C-10), 27.7 (C-1), 26.1/26.0 (C-7, C-8, C-9), 20.9 (C-20); **IR**: ν_{max}(film)/cm^{-1} 1510 (C=C_{Ar}), 1447 (C=C_{Ar}), 983, 913, 815; **GC-MS**: 227.2 (M-SC_3H_5), 14.7 min; **HRMS**: found 300.1897, $[M]^+$ requires 300.1906.

The equivalent enantiopure (*R*)-(*E*)-allyl(4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl)sulfane (*R*)-**2e** (137 mg, 98%, 60% over 3 steps from (*R*)-**4e**) was prepared from (*R*)-(*E*)-4-cyclohexyl-2-(*p*-tolyl)but-3-ene-2-thiol (*R*)-**3e** (121 mg, 0.46 mg) following general procedure B.
$[\alpha]_D^{24}$: +36.6 (*c* 1.00, $CDCl_3$).

2h: (*E*)-Allyl(4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl)sulfane.

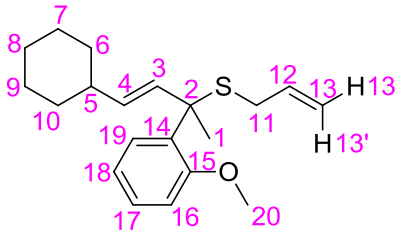


General procedure B was followed using (*E*)-4-cyclohexyl-2-(3-methoxyphenyl)but-3-ene-2-thiol **3h** (228 mg, 0.82 mmol) to afford the title compound as a pale yellow oil (170 mg, 65%).

R_f: 0.62 (Pent/Et_2O 96:4); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.23 (t, *J* = 8.0 Hz, 1H, H-18), 7.12 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1H, H-19), 7.10 (t, *J* = 2.0 Hz, 1H, H-15), 6.76 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1H, H-17), 5.80 (ddt, *J* = 17.0, 10.0, 7.1 Hz, 1H, H-12), 5.76 (dd, *J* = 15.7, 1.1 Hz, 1H, H-3), 5.52 (dd, *J* = 15.7, 6.9 Hz, 1H, H-4), 5.11 (dq, *J* = 17.0, 1.5 Hz, 1H, H-13'), 5.01 (dd, *J* = 10.0, 1.5 Hz, 1H, H-13), 3.81 (s, 3H, H-20), 3.04 (ddt, *J* = 12.9, 7.1, 1.0 Hz, 1H, H-11), 2.90 (ddt, *J* = 12.9, 7.1, 1.0 Hz, 1H, H-11'), 2.09-2.02 (m, 1H, H-5), 1.78-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.72 (s, 3H, H-1), 1.35-1.07 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 159.4 (C-16), 147.1 (C-14), 135.8 (C-4), 134.6 (C-12), 132.3 (C-3), 129.1 (C-18), 119.5 (C-19), 116.9 (C-13), 113.3 (C-15), 111.8 (C-17), 55.2 (C-20), 53.5 (C-2), 40.8 (C-5), 33.4 (C-11), 33.3/33.2 (C-6, C-10), 27.7 (C-1), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1599 (C=C), 1580 (C=C), 1483 (C=C_{Ar}), 1448 (C=C_{Ar}), 1289, 1254 (C_{Ar}-O), 1046, 915, 776; **MS**: *m/z* (ES-) 243 [M-SC_3H_5]$^-$ (30%); **HRMS**: found 243.1733, [M-SC_3H_5]$^-$ requires 243.1743.

The equivalent enantioenriched sulfide (*S*)-(*E*)-allyl(4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl)sulfane (*S*)-**2h** (114 mg, 100%) was prepared from (*S*)-(*E*)-4-cyclohexyl-2-(3-methoxyphenyl)but-3-ene-2-thiol (*S*)-**3h** (100 mg, 0.36 mmol) following general procedure B. **$[\alpha]_D^{24}$**: -14.8 (*c* 1.00, $CHCl_3$).

2i: (*E*)-Allyl(4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl)sulfane.



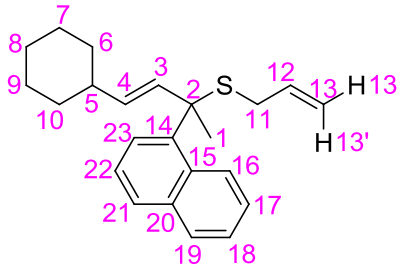
General procedure B was followed using (*E*)-4-cyclohexyl-2-(2-methoxyphenyl)but-3-ene-2-thiol **3i** (208 mg, 0.75 mmol) to afford the title compound as a pale yellow oil (234 mg, 98%).

R_f: 0.31 (Pent/Et_2O 98:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.58 (dd, *J* = 7.7, 1.7 Hz, 1H, H-19), 7.24 (ddd, *J* = 8.1, 7.4, 1.7 Hz, 1H, H-17), 6.92 (td, *J* = 7.7, 1.2 Hz, 1H, H-18), 6.88 (dd, *J* = 8.1, 1.1 Hz, 1H, H-16), 5.80 (ddt, *J* = 17.0, 10.0, 7.1 Hz, 1H, H-12), 5.73 (dd, *J* = 15.7, 1.2 Hz, 1H, H-3), 5.22 (dd, *J* = 15.7, 7.1 Hz, 1H, H-4), 5.12 (dq, *J* = 17.0, 1.6 Hz, 1H, H-13'), 5.00 (dd, *J* = 10.0, 1.6 Hz, 1H, H-13), 3.79 (s, 3H, H-20), 3.01 (bd, *J* = 7.1 Hz, 2H, H-11), 2.06-1.99 (m, 1H, H-5), 1.77 (s, 3H, H-1), 1.73-1.61 (m, 4H, H-6, H-7, H-9, H-10), 1.32-1.03 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 157.9 (C-15), 134.8 (C-12), 134.8 (C-4), 132.4 (C-14), 132.3 (C-3), 129.1 (C-19), 128.3 (C-17), 120.2 (C-18), 116.7 (C-13), 112.3 (C-16), 55.2 (C-20), 54.1 (C-2), 40.8 (C-5), 33.7 (C-11), 33.5/33.4 (C-6, C-10), 26.6 (C-1), 26.2/26.1 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1486 ($C{=}C_{Ar}$), 1448 ($C{=}C_{Ar}$), 1243 (C_{Ar}-O), 1029, 914, 752; **GC-MS**: *m/z* 243.2 $[M\text{-}SC_3H_5]^+$ 14.3 min; **HRMS**: found 243.1734, $[M\text{-}SC_3H_5]^+$ requires 243.1743.

The equivalent enantioenriched sulfide (*S*)-(*E*)-allyl(4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl)sulfane (*S*)-**2i** (97 mg, 100%) was prepared from (*S*)-(*E*)-4-cyclohexyl-2-(2-methoxyphenyl)but-3-ene-2-thiol (*S*)-**3i** (85 mg, 0.31 mmol) following general procedure B.

$[\alpha]_D^{24}$: -10.0 (*c* 1.00, $CHCl_3$).

2j: (*E*)-Allyl(4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl)sulfane.

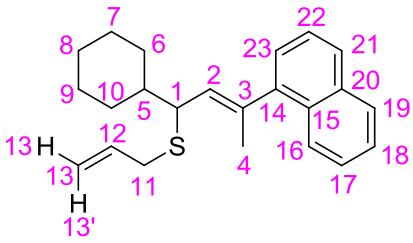


General procedure B was followed using (*E*)-4-cyclohexyl-2-(naphthalen-1-yl)but-3-ene-2-thiol **3j** (380 mg, 1.28 mmol) to afford the title compound as a mixture with by-product **2j'** (350 mg, **2j**/**2j'** 1:0.7).

R_f: 0.63 (Pent/Et_2O 95:5); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 8.69-8.67 (m, 1H, H-16), 7.87-7.85 (m, 1H, H-19), 7.78-7.73 (m, 2H, H_{Ar}), 7.49-7.40 (m, 3 H, H_{Ar}), 5.89 (dd, *J* = 15.9, 1.2 Hz, 1H, H-3), 5.70 (ddt, *J* = 17.0, 10.0, 7.1 Hz, 1H, H-12), 5.33 (dd, *J* = 15.9, 7.1 Hz, 1H, H-4), 5.03 (dq, *J* = 17.0, 1.2 Hz, 1H, H-13'), 4.95 (dq, *J* = 10.0, 1.2 Hz, 1H, H-13), 2.98 (ddt, *J* = 12.9, 7.4, 1.2 Hz, 1 H, H-11), 2.84 (ddt, *J* = 12.9, 7.1, 1.2 Hz, 1H, H-11), 2.06-2.01 (m, 1H, H-5), 1.97 (s, 3H, H-1), 1.83-1.57 (m, 12H, $H_{Cy\text{-}\mathbf{2j+2j'}}$), 1.31-0.87 (m, 16H, $H_{Cy\text{-}\mathbf{2j+2j'}}$, H_{Et2O}); **^{13}C NMR**: (100 MHz, $CDCl_3$, *-C_{Ar} and C_{Cy} for both **2j** and **2j'** reported, could not be all assigned, some may be superimposed-*) δ (ppm) 143.5 (C-15), 139.3 (C_{Ar}), 136.1 (C-4), 134.4 (C-12), 133.7 (C-3), 133.5 (C_{Ar}), 131.4 (C_{Ar}), 128.8/128.7 (C-19), 128.5/128.4 (C-16), 127.1 (C_{Ar}), 125.7/125.6/125.5/125.1/124.6/124.1 (C_{Ar}), 116.9 (C-13), 54.9 (C-2), 42.6 (C_{Cy}), 40.8 (C-5), 33.4 (C-11), 33.0 (C_{Cy}), 30.2 (C-1), 26.5/26.4/26.3/26.1/26.0 (C_{Cy}).

The equivalent enantioenriched sulfide (*R*)-(*E*)-allyl(4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl)sulfane (*R*)-**2j** (**2j**/**2j'** 1:0.5) was tentatively prepared from (*R*)-(*E*)-4-cyclohexyl-2-(naphthalen-1-yl)but-3-ene-2-thiol (*R*)-**3j** (294 mg, 0.99 mmol) following general procedure B (warming to 0 °C).

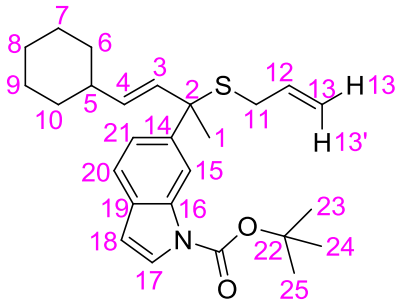
2j': (*E*)-Allyl(1-cyclohexyl-3-(naphthalen-1-yl)but-2-en-1-yl)sulfane.



General procedure B was followed using (*E*)-4-cyclohexyl-2-(naphthalen-1-yl)but-3-ene-2-thiol **3j** (380 mg, 1.28 mmol) to afford the title compound as a mixture with the expected product **2j** (350 mg, **2j**/**2j'** 1:0.7).

R_f: 0.63 (Pent/Et_2O 95:5); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 7.95-7.93 (m, 1H, H-16), 7.85-7.83 (m, 1H, H-19), 7.78-7.73/7.49-7.40 (m, 4H, H_{Ar}), 7.30 (dd, *J* = 7.0, 1.2 Hz, 1H, H-22), 5.95 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H, H-12), 5.49 (dq, *J* = 10.8, 1.4 Hz, 1 H, H-2), 5.25 (dq, *J* = 17.0, 1.4 Hz, 1H, H-13'), 5.14 (dq, *J* = 10.0, 1.4 Hz, 1H, H-13), 3.67 (dd, *J* = 10.8, 6.7 Hz, 1H, H-1), 3.31 (ddt, *J* = 13.8, 7.0, 1.4 Hz, 1H, H-11), 3.23 (ddt, *J* = 13.8, 7.0, 1.4 Hz, 1H, H-11'), 2.10 (d, *J* = 1.4 Hz, 3H, H-4), 2.06-2.01 (m, 1H, H-5), 1.83-1.57 (m, 12H, $H_{Cy\text{-}\mathbf{2j}+\mathbf{2j'}}$), 1.31-0.87 (m, 16H, $H_{Cy\text{-}\mathbf{2j}+\mathbf{2j'}}$); **^{13}C NMR**: (100 MHz, $CDCl_3$, *-C_{Ar} and C_{Cy} for both **2j** and **2j'** reported, could not be all assigned, some may be superimposed-*) δ (ppm) 143.2 (C-15), 139.3 (C_{Ar}), 135.2/134.9 (C-12), 133.5 (C_{Ar}), 131.4 (C_{Ar}), 131.0/130.9 (C-2), 127.1 (C_{Ar}), 126.0/125.8 (C-16), 125.7/125.6/125.5/125.1/124.6/124.1 (C_{Ar}), 116.7 (C-13), 48.5 (C-1), 42.6 (C_{Cy}), 33.6 (C-11), 33.0 (C_{Cy}), 26.5/26.4/26.3/26.1/26.0 (C_{Cy}).

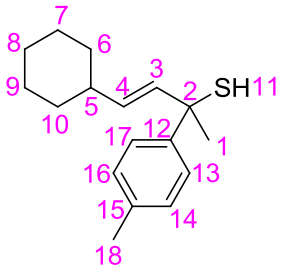
2l: (*E*)-*tert*-Butyl 6-(2-(allylthio)-4-cyclohexylbut-3-en-2-yl)-1*H*-indole-1-carboxylate.



General procedure B was followed using (*E*)-*tert*-butyl 6-(4-cyclohexyl-2-mercaptobut-3-en-2-yl)-1*H*-indole-1-carboxylate **3l** (138 mg, 0.36 mmol) to afford the title compound as a colourless oil (81 mg, 53%).

R_f: 0.72 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.33 (bs, 1H, H-15), 7.60 (bd, *J* = 3.6 Hz, 1H, H-17), 7.49 (d, *J* = 8.3 Hz, 1H, H-20), 7.45 (dd, *J* = 8.3, 1.6 Hz, 1H, H-21), 6.53 (dd, *J* = 3.6, 0.6 Hz, 1H, H-18), 5.86 (dd, *J* = 15.7, 1.1 Hz, 1H, H-3, 5.79 (ddt, *J* = 17.0, 10.0, 7.1 Hz, 1H, H-12), 5.54 (dd, *J* = 15.7, 7.0 Hz, 1H, H-4), 5.10 (dq, *J* = 17.0, 1.5 Hz, 1H, H-13'), 5.00 (bdd, *J* = 10.0, 1.5 Hz, 1H, H-13), 3.02 (d, *J* = 7.1 Hz, 2H, H-11), 2.11-2.03 (m, 1H, H-5), 1.82 (s, 3H, H-1), 1.79-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.69 (s, 9H, H-24, H-25, H-26), 1.35-1.08 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 149.8 (C-22), 141.6 (C-16), 135.5 (C-4), 134.8 (C-12), 132.9 (C-3), 129.2 (C-19), 126.4 (C-17), 122.4 (C-21), 120.4 (C-20), 116.8 (C-13), 113.7 (C-15), 106.9 (C-18), 83.6 (C-23), 54.1 (C-2), 40.8 (C-5), 33.6 (C-11), 33.4/33.2 (C-6, C-10), 28.2 (C-1), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1734 (C=O), 1369 (C=N-$_{Ar}$), 1341, 1155 (C-O_{ester}), 1129; **GC-MS**: 253.2 (M-SC_3H_5-(CO)OC_4H_9), 27.1 min; **HRMS**: found 253.1837, $[M]^+$ requires 253.1825.

3e: (*E*)-4-Cyclohexyl-2-(*p*-tolyl)but-3-ene-2-thiol.



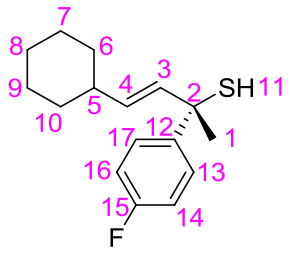
General procedure C was followed using (*E*)-*S*-4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl methylcarbamothioate **6e** (666 mg, 2.10 mmol) to afford the title compound as a colourless oil (546 mg, 100%).

R_f: 0.68 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.40 (d, *J* = 8.2 Hz, 2H, H-13, H-17), 7.11 (d, *J* = 8.2 Hz, 2H, H-14, H-16), 5.83 (dd, *J* = 15.5, 1.1 Hz, 1H, H-3), 5.56 (dd, *J* = 15.5, 6.8 Hz, 1H, H-4), 2.33 (s, 3H, H-18), 2.17 (s, 1H, H-11), 2.06-1.98 (m, 1H, H-5), 1.84 (s, 3H, H-1), 1.77-1.63 (m, 4H, H-6, H-7, H-9, H-10), 1.34-1.06 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 143.9 (C-15), 136.3 (C-12), 135.8 (C-3), 133.7 (C-4), 128.8 (C-14, C-16), 126.2 (C-13, C-17), 50.4 (C-2), 40.4 (C-5), 33.1/33.0 (C-6, C-10), 32.1 (C-1), 26.1/26.0 (C-7, C-8, C-9), 20.9 (C-18); **IR**: ν_{max}(film)/cm^{-1} 1510 (C=C_{Ar}), 1447

($C=C_{Ar}$), 968, 815, 772; **GC-MS**: 227.2 (M-SH), 12.3 min; **HRMS**: found 260.1583, $[M]^+$ requires 260.1593.

The equivalent enantioenriched thiol (*R*)-(*E*)-4-cyclohexyl-2-(*p*-tolyl)but-3-ene-2-thiol (*R*)-**3e** (153 mg, 91%) was prepared from (*R*)-(*E*)-*S*-4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl methylcarbamothioate (*R*)-**6e** (205 mg, 0.65 mmol) following general procedure C.
$[\alpha]_D^{24}$: +21.0 (*c* 1.00, $CHCl_3$).

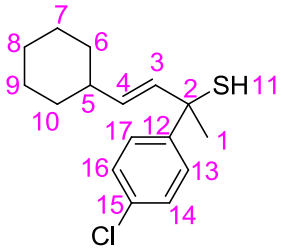
(*S*)-**3f**: (*S*,*E*)-4-Cyclohexyl-2-(4-fluorophenyl)but-3-ene-2-thiol.



General procedure C was followed using (*S*,*E*)-*S*-4-cyclohexyl-2-(4-fluorophenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6f** (41 mg, 0.13 mmol) to afford the title compound as a colourless oil (19 mg, 56%).

$[\alpha]_D^{25}$: -4.2 (*c* 1.00, $CDCl_3$); **R_f**: 0.83 (Pent/Et_2O 98:2); **^{1}H NMR**: (500 MHz; $CDCl_3$) δ (ppm) 7.48 (dd, *J* = 8.8, 5.3 Hz, 2H, H-11, H-16), 6.98 (t, *J* = 8.8 Hz, 2H, H-13, H-17), 5.81 (dd, *J* = 15.5, 1.2 Hz, 1H, H-3), 5.55 (dd, *J* = 15.5, 6.9 Hz, 1H, H-4), 2.19 (s, 1H, H-11), 2.04-1.99 (m, 1H, H-5), 1.84 (s, 3H, H-1), 1.75-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.32-1.06 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (125 MHz, $CDCl_3$) δ (ppm) 161.5 (d, $^1J_{C,F}$ = 244.3 Hz, C-15), 142.6 (d, $^4J_{C,F}$ = 2.7 Hz, C-12), 135.5 (C-3), 134.1 (C-4), 128.2 (d, $^3J_{C,F}$ = 7.9 Hz, C-13, C-17), 114.9/114.7 (d, $^2J_{C,F}$ = 21.2 Hz, C-14, C-16), 50.1 (C-2), 40.3 (C-5), 33.0/32.9 (C-6, C-10), 32.3 (C-1), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1603 (C=C), 1506 ($C=C_{Ar}$), 1448 ($C=C_{Ar}$), 1231 (C-F), 1161, 969, 832; **GC-MS**: 231.2 (M-SH), 12.9 min; **HRMS**: found 231.1535, $[M]^+$ requires 231.1544.

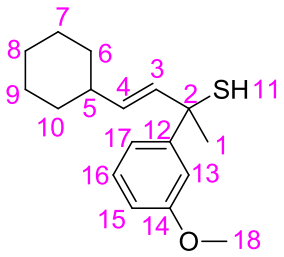
3g: (*E*)-2-(4-Chlorophenyl)-4-cyclohexylbut-3-ene-2-thiol.



General procedure C was followed using (*E*)-*S*-4-cyclohexyl-2-(4-chlorophenyl)but-3-en-2-yl methylcarbamothioate **6g** (214 mg, 0.63 mmol) to afford the title compound as a colourless oil (99 mg, 56%).

R_f: 0.58 (Pent/Et_2O 98:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.45 (d, *J* = 8.7 Hz, 2H, H-14, H-16), 7.27 (d, *J* = 8.7 Hz, 2H, H-13, H-17), 5.80 (dd, *J* = 15.5, 1.2 Hz, 1H, H-3), 5.55 (dd, *J* = 15.5, 6.8 Hz, 1H, H-4), 2.19 (s, 1H, H-11), 2.06-1.98 (m, 1H, H-5), 1.83 (s, 3H, H-1), 1.75-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.33-1.05 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 145.4 (C-12), 135.2 (C-3), 134.3 (C-4), 132.5 (C-15), 128.2 (C-13, C-17), 127.9 (C-14, C-16), 50.2 (C-2), 40.4 (C-5), 33.0/32.9 (C-6, C-10), 32.1 (C-1), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1490 ($C{=}C_{Ar}$), 1448 ($C{=}C_{Ar}$), 1095, 969, 828 (C-Cl); **GC-MS**: 246.1 (M-SH_2), 13.5 min; **HRMS**: found 246.1160, $[M]^+$ requires 246.1170.

3h: (*E*)-4-Cyclohexyl-2-(3-methoxyphenyl)but-3-ene-2-thiol.



General procedure C was followed using (*E*)-*S*-4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl methylcarbamothioate **6h** (128 mg, 0.38 mmol) to afford the title compound as a colourless oil (86 mg, 81%).

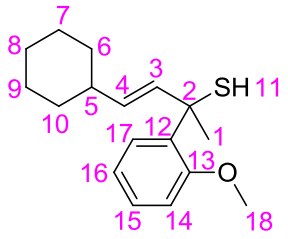
R_f: 0.43 (Pent/Et_2O 98:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.24 (t, *J* = 8.0 Hz, 1H, H-10), 7.11 (ddd, *J* = 8.0, 2.1, 0.8 Hz, 1H, H-17), 7.09 (t, *J* = 2.1 Hz, 1H, H-13), 6.77 (ddd, *J* = 8.0, 2.1, 0.8 Hz, 1H, H-15), 5.83 (dd, *J* = 15.5, 1.2 Hz, 1H, H-3), 5.59 (dd, *J* = 15.5, 6.9 Hz, 1H,

H-4), 3.82 (s, 3H, H-18), 2.20 (s, 1H, H-11), 2.08-1.99 (m, 1H, H-5), 1.85 (s, 3H, H-1), 1.77-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.35-1.07 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 159.3 (C-14), 148.6 (C-12), 135.5 (C-3), 133.9 (C-4), 129.1 (C-10), 118.7 (C-17), 112.7 (C-13), 111.6 (C-15), 55.2 (C-18), 50.5 (C-2), 40.4 (C-5), 33.0/32.9 (C-6, C-10), 32.0 (C-1), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1653 (C=O), 1598 (C=C), 1486 (C=C_{Ar}), 1255 (C_{Ar}-O), 1043, 697; **GC-MS**: 242.2 (M-SH_2), 13.60 min; **HRMS**: found 276.1533, $[M]^+$ requires 276.1542.

The equivalent enantioenriched thiol (*S*)-(*E*)-4-cyclohexyl-2-(3-methoxyphenyl)but-3-ene-2-thiol (*S*)-**3h** (108 mg, 72%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6h** (180 mg, 0.54 mmol) following general procedure C.

$[\alpha]_D^{25}$: +2.4 (*c* 1.00, $CDCl_3$).

3i: (*E*)-4-Cyclohexyl-2-(2-methoxyphenyl)but-3-ene-2-thiol.



General procedure C was followed using (*E*)-*S*-4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl methylcarbamothioate **6i** (450 mg, 1.35 mmol) to afford the title compound as a colourless oil (313 mg, 84%).

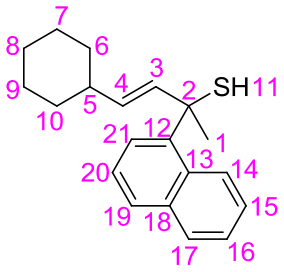
R_f: 0.43 (Pent/Et_2O 98:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.36 (dd, *J* = 8.1, 1.7 Hz, 1H, H-17), 7.24 (ddd, 8.1, 7.3, 1.7, 1H, H-15), 6.91 (dd, *J* = 8.1, 1.2 Hz, 1H, H-16), 6.89 (dd, *J* = 8.1, 1.2 Hz, 1H, H-14), 5.90 (dd, *J* = 15.6, 1.2 Hz, 1H, H-3), 5.40 (dd, *J* = 15.6, 7.0 Hz, 1H, H-4), 3.86 (s, 3H, H-18), 3.07 (s, 1H, H-11), 2.03-1.95 (m, 1H, H-5), 1.86 (s, 3H, H-1), 1.73-1.62 (m, 4H, H-6, H-7, H-9, H-10), 1.32-1.03 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 157.4 (C-13), 135.2 (C-12), 134.9 (C-3), 133.1 (C-4), 128.3 (C-15), 126.5 (C-17), 120.2 (C-16), 111.8 (C-14), 55.1 (C-18), 48.6 (C-2), 40.5 (C-5), 33.1 (C-6, C-10), 29.8 (C-1), 26.2/26.1 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1487 (C=C_{Ar}), 1447 (C=C_{Ar}),

1242 (C_{Ar}-O), 1027, 750, 544; **GC-MS**: *m/z* 243.1 $[M\text{-}SH]^+$, 12.6 min; **HRMS**: found 243.1737, $[M\text{-}SH]^+$ requires 243.1743.

The equivalent enantioenriched thiol (*S*)-(*E*)-4-cyclohexyl-2-(2-methoxyphenyl)but-3-ene-2-thiol (*S*)-**3i** (93 mg, 61%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6i** (185 mg, 0.55 mmol) following general procedure C.

$[\alpha]_D^{25}$: -13.2 (*c* 1.00, $CDCl_3$).

3j: (*E*)-4-Cyclohexyl-2-(naphthalen-1-yl)but-3-ene-2-thiol.

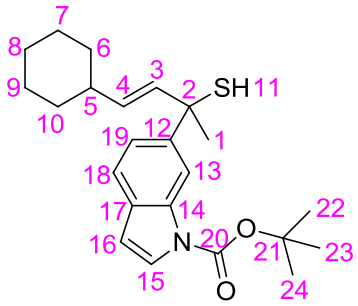


General procedure C was followed using (*E*)-*S*-4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl methylcarbamothioate **6j** (540 mg, 1.53 mmol) to afford the title compound as a colourless oil (427 mg, 94%).

R_f: 0.57 (Pent/Et_2O 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.50-8.47 (m, 1H, H-14), 7.86-7.84 (m, 1H, H-17), 7.78 (d, *J* = 8.1 Hz, 1H, H-19), 7.68 (dd, *J* = 7.4, 1.0 Hz, 1H, H-20), 7.49-7.42 (m, 3H, H-15, H-16, H-21), 5.96 (dd, *J* = 15.6, 1.2 Hz, 1H, H-3), 5.47 (d, *J* = 15.6, 7.0 Hz, 1H, H-4), 2.50 (s, 1H, H-11), 2.07 (s, 3H, H-1), 2.02-1.94 (m, 1H, H-5), 1.82-1.63 (m, 4H, H-6, H-7, H-9, H-10), 1.29-0.98 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 141.6 (C-13), 136.4 (C-3), 135.0 (C-4), 134.9 (C-18), 130.7 (C-12), 128.9 (C-17), 128.7 (C-19), 128.3 (C-14), 125.1/124.8/124.5 (C-15, C-16, C-21), 123.8 (C-20), 51.0 (C-2), 40.4 (C-5), 34.6 (C-1), 32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1447 (C=C_{Ar}), 967, 800, 775; **GC-MS**: 263.1 (M-SH), 13.9 min; **HRMS**: found 296.1582, $[M]^+$ requires 296.1593.

The equivalent enantioenriched thiol (*R*)-(*E*)-4-cyclohexyl-2-(naphthalen-1-yl)but-3-ene-2-thiol (*R*)-**3j** (302 mg, 90%) was prepared from (*R*)-(*E*)-*S*-4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl methylcarbamothioate (*R*)-**6j** (400 mg, 1.13 mmol) following general procedure C. **$[\alpha]_D^{25}$**: +67.6 (*c* 1.00, $CDCl_3$).

3l: (*E*)-*tert*-Butyl 6-(4-cyclohexyl-2-mercaptobut-3-en-2-yl)-1*H*-indole-1-carboxylate.



General procedure C was followed using (*E*)-*tert*-butyl 6-(4-cyclohexyl-2-((methylcarbamoyl)thio)but-3-en-2-yl)-1*H*-indole-1-carboxylate **6l** (290 mg, 0.66 mmol) to afford the title compound as a colourless oil (148 mg, 58%).

R_f: 0.68 (Pent/Et_2O 95:5); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.36 (bs, 1H, H-13), 7.60 (bd, *J* = 3.7 Hz, 1H, H-15), 7.48 (dd, *J* = 8.3, 0.5 Hz, 1H, H-18), 7.39 (dd, *J* = 8.3, 1.8 Hz, 1H, H-19), 6.53 (dd, *J* = 3.7, 0.5 Hz, 1H, H-16), 5.92 (dd, *J* = 15.5, 1.2 Hz, 1H, H-3), 5.59 (dd, *J* = 15.5, 6.9 Hz, 1H, H-4), 2.27 (s, 1H, H-11), 2.07-1.99 (m, 1H, H-5), 1.94 (s, 3H, H-1), 1.77-1.63 (m, 4H, H-6, H-7, H-9, H-10), 1.69 (s, 9H, H-22, H-23, H-24), 1.34-1.07 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 149.8 (C-20), 143.2 (C-14), 136.2 (C-3), 134.9 (C-12), 133.6 (C-4), 129.2 (C-17), 126.4 (C-15), 121.8 (C-19), 120.4 (C-18), 113.0 (C-13), 106.9 (C-16), 83.6 (C-21), 51.2 (C-2), 40.4 (C-5), 33.0/32.9 (C-6, C-10), 32.5 (C-1), 28.2 (C-22, C-23, C-24), 26.2/26.0 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 1732 (C=O), 1433 (C=C_{Ar}), 1369 (C_{Ar}=N), 1334, 1251 (C-O_{ester}), 1154, 1129; **GC-MS**: *m/z* 251.2 $[M\text{-}SH\text{-}C_5H_9O_2]^+$, 14.7 min; **HRMS**: found 352.2258, $[M\text{-}SH]^+$ requires 352.2271.

The equivalent enantioenriched thiol (*R*)-(*E*)-*tert*-butyl 6-(4-cyclohexyl-2-mercaptobut-3-en-2-yl)-1*H*-indole-1-carboxylate (*R*)-**3l** (30 mg, 39%) was prepared from (*R*)-(*E*)-*tert*-butyl 6-(4-cyclohexyl-2-((methylcarbamoyl)thio)but-3-en-2-yl)-1*H*-indole-1-carboxylate (*R*)-**6l** (88 mg, 0.20 mmol) following general procedure C.

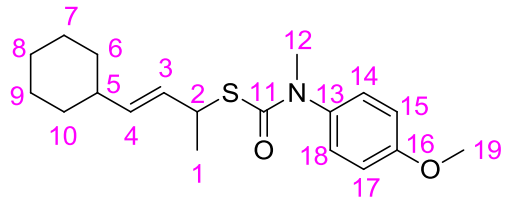
$[\alpha]_D^{25}$: +2.0 (*c* 1.00, $CHCl_3$).

For experimental procedures and characterisation data of **4a**, **4b** and **4c**, please see:

- G. Mingat, J. Clayden, *Synthesis*, 2012, **44**, 2723

- G. Mingat, P. MacLellan, M. Laars, J. Clayden, *Org. Lett.*, 2014, **16**, 1252.

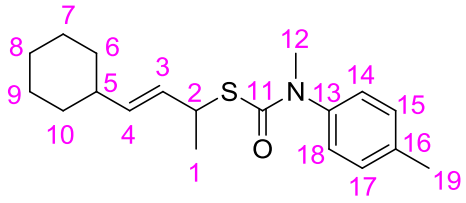
4d: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 4-methoxyphenyl(methyl)carbamothioate.



General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (150 mg, 0.57 mmol), HOBt (1.0 eq), and 4-methoxy-*N*-methylaniline. Purification by column chromatography (Pet 100%, Pet/EtOAc 95:5, 9:1) afforded the title compound as a yellow oil (181 mg, 96%).

R_f: 0.60 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.17 (d, *J* = 8.9 Hz, 2H, H-14, H-18), 6.90 (d, *J* = 8.9 Hz, H-15, H-17), 6.52 (dd, *J* = 15.6, 6.5 Hz, 1H, H-4), 5.40 (dd, *J* = 15.6, 6.8 Hz, 1H, H-3), 4.06 (qn, *J* = 6.8 Hz, 1H, H-2), 3.82 (s, 3H, H-19), 3.27 (s, 3H, H-12), 1.92-1.83 (m, 1H, H-5), 1.70-1.59 (m, 4H, H-6, H-7, H-9, H-10), 1.35 (d, *J* = 6.8 Hz, 3H, H-1), 1.27-0.96 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.8 (C-11), 159.3 (C-16), 136.8 (C-4), 134.7 (C-13), 129.6 (C-14, C-18), 128.4 (C-3), 114.6 (C-15, C-17), 55.4 (C-19), 42.5 (C-2), 40.3 (C-5), 38.3 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1648 (C=O), 1509 (C=C_{Ar}), 1244 (C_{Ar}-O), 834; **MS**: *m/z* (ES^+) 334 $[M+H]^+$ (50%), 356 $[M+Na]^+$ (100%); **HRMS**: found 334.1838, $[M+Na]^+$ requires 334.1836.

4e: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate.



General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (180 mg, 0.68 mmol), HOBt (0.5 eq) and 4-methyl-*N*-methylaniline. Purification by filtration over silica (Pet/EtOAc 9:1) afforded the title compound as a yellow oil (185 mg, 86%).

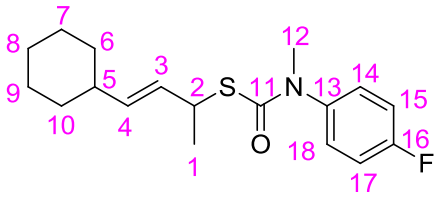
R_f: 0.76 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.20 (d, *J* = 8.2 Hz, 2H, H-14, H-18), 7.14 (d, *J* = 8.2 Hz, 2H, H-15, H-17), 5.52 (dd, *J* = 15.6, 6.2 Hz, 1H, H-4), 5.40 (ddd, *J* = 15.6, 6.8, 1.0 Hz, 1H, H-3), 4.07 (qn, *J* = 6.8 Hz, 1H, H-2), 3.28 (s, 3H, H-12), 2.37, (s, 3H, H-19), 1.91-1.83 (m, 1H, H-5), 1.69-1.60 (m, 4H, H-6, H-7, H-9, H-10), 1.36 (d, *J* = 6.8 Hz, 3H, H-1), 1.27-0.95 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.6 (C-11), 139.5 (C-16), 138.3 (C-13), 136.9 (C-4), 130.1 (C-14, C-18), 128.3 (C-3), 128.0 (C-15, C-17), 42.6 (C-2), 40.3 (C-5), 38.2 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.2 (C-19), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1651 (C=O), 1513 (C=C_{Ar}), 1268 (C_{Ar}-N), 1107; **MS**: *m/z* (ES$^+$) 318 $[M+H]^+$ (100%), 340 $[M+Na]^+$ (60%); **HRMS**: found 318.1892, $[M+H]^+$ requires 338.1887.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate (*S*)-**4e** (94:6 *e.r.*, 101 mg, 83%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 100 mg, 0.38 mmol) following the same procedure.
$[\alpha]_D^{22}$: -5.3 (*c* 1.10, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, major 5.8 min, minor 6.7 min (214.4 nm, 254.4 nm).

The other enantiomer (*R*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate (*R*)-**4e** (13:87 *e.r.*, 210 mg, 87%) was prepared from (*R*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*R*)-**10a** (88:12 *e.r.*, 200 mg, 0.76 mmol) following the same procedure.

HPLC: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, minor 8.9 min, major 11.0 min (214.4 nm).

4f: (*E*)-S-4-Cyclohexylbut-3-en-2-yl 4-fluorophenyl(methyl)carbamothioate.



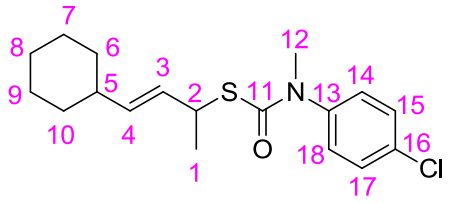
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (190 mg, 0.72 mmol), HOBt (0.5 eq) and 4-fluoro-*N*-methylaniline. Purification by column chromatography (Pet 100%, Pet/EtOAc 98:2 to 96:4) afforded the title compound as a yellow oil (182 mg, 79%).

R_f: 0.45 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.24 (dd, *J* = 9.0, 4.9 Hz, 2H, H-14, H-18), 7.08 (t, *J* = 9.0 Hz, 2H, H-15, H-17), 5.54 (dd, *J* = 15.5, 6.0 Hz, 1H, H-4), 5.40 (ddd, *J* = 15.5, 6.9, 1.0 Hz, 1H, H-3), 4.07 (qn, *J* = 6.9 Hz, 1H, H-2), 3.28 (s, 3H, H-12), 1.93-1.84 (m, 1H, H-5), 1.71-1.59 (m, 4H, H-6, H-7, H-9, H-10), 1.36 (d, *J* = 6.9 Hz, 3H, H-1), 1.28-0.96 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 175.9 (d, $^1J_{C,F}$ = 254.5 Hz, C-16), 168.7 (C-11), 138.1 (C-13), 137.1 (C-4), 130.2 (m, C-14, C-18), 128.2 (C-3), 116.4 ($^2J_{C,F}$ = 22.4 Hz, C-15, C-17), 42.7 (C-2), 40.3 (C-5), 38.2 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0/25.9 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1650 (C=O), 1507 (C=C_{Ar}), 1220 (C-F), 839; **MS**: *m/z* (ES$^+$) 322 $[M+H]^+$ (100%); **HRMS**: found 322.1628, $[M+H]^+$ requires 322.1636.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 4-fluorophenyl(methyl)carbamothioate (*S*)-**4f** (94:6 *e.r.*, 170 mg, 93%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 150 mg, 0.57 mmol) following the same procedure.

$[\alpha]_D^{26}$: -15.4 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/i-PrOH 95:5, 1.0 mL/min, 28 °C, major 8.2 min, minor 10.0 min (214.4 nm, 254.4 nm).

4g: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 4-chlorophenyl(methyl)carbamothioate.



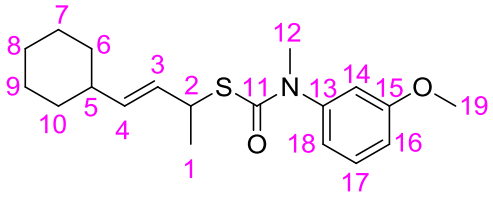
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (180 mg, 0.68 mmol), HOBt (0.5 eq) and 4-chloro-*N*-methylaniline. Purification by filtration over silica (Pet/EtOAc 9:1) afforded the title compound as a yellow oil (169 mg, 73%).

R_f: 0.77 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.36 (d, *J* = 8.8 Hz, 2H, H-14, H-18), 7.20 (d, *J* = 8.8 Hz, 2H, H-15, H-17), 5.54 (dd, *J* = 15.4, 6.4 Hz, 1H, H-4), 5.41 (ddd, *J* = 15.4, 6.8, 1.2 Hz, 1H, H-3), 4.08 (qn, *J* = 6.8 Hz, 1H, H-2), 3.28 (s, 3H, H-12), 1.93-1.84 (m, 1H, H-5), 1.71-1.58 (m, 4H, H-6, H-7, H-9, H-10), 1.37 (d, *J* = 6.8 Hz, 3H, H-1), 1.28-0.96 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.4 (C-11), 140.7 (C-13), 137.2 (C-4), 133.9 (C-16), 129.6 (C-14, C-18), 129.5 (C-15, C-17), 128.1 (C-3), 42.7 (C-2), 40.3 (C-5), 38.1 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1651 (C=O), 1486 (C=C_{Ar}), 1280 (C_{Ar}-N), 964; **MS**: *m/z* (ES^+) 338 $[M+H]^+$ (70%), 360 $[M+Na]^+$ (100%); **HRMS**: found 338.1346, $[M+H]^+$ requires 338.1340.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 4-chlorophenyl(methyl)carbamothioate (*S*)-**4g** (95:5 *e.r.*, 86 mg, 67%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 100 mg, 0.38 mmol) following the same procedure.

$[\alpha]_D^{25}$: -11.6 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, major 5.7 min, minor 6.5 min (214.4 nm).

4h: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 3-methoxyphenyl(methyl)carbamothioate.



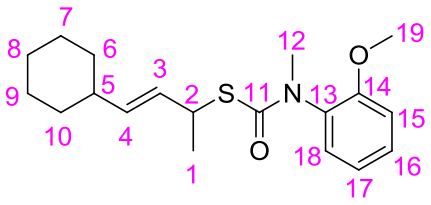
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (400 mg, 1.51 mmol), HOBt (1.5 eq) and 3-methoxy-*N*-methylaniline. Purification by column chromatography (Pet 100%, Pet/EtOAc 97:3 to 92:8) afforded the title compound as a yellow oil (444 mg, 86%).

R_f: 0.48 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.30 (t, *J* = 8.2 Hz, 1H, H-17), 6.89 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H, H-16 or H-18), 6.86 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H, H-18 or H-16), 6.80 (t, *J* = 2.4 Hz, 1H, H-14), 5.53 (ddd, *J* = 15.6, 6.6, 0.8 Hz, 1H, H-4), 5.41 (ddd, *J* = 15.6, 6.8, 1.0 Hz, 1H, H-3), 4.08 (qn, *J* = 6.8 Hz, 1H, H-2), 3.82 (s, 3H, H-19), 3.30 (s, 3H, H-12), 1.93-1.84 (m, 1H, H-5), 1.71-1.58 (m, 4H, H-6, H-7, H-9, H-10), 1.37 (d, *J* = 6.8 Hz, 3H, H-1), 1.28-0.96 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.4 (C-11), 160.2 (C-15), 143.3 (C-13), 137.0 (C-4), 130.0 (C-17), 128.3 (C-3), 120.3 (C-18 or C-16), 113.9 (C-14), 113.7 (C-16 or C-18), 55.4 (C-19), 42.6 (C-2), 40.4 (C-5), 38.1 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1651 (C=O), 1599 (C=C_{Ar}), 1283 (C_{Ar}-N), 1217 (C_{Ar}-O), 1042; **MS**: *m/z* (ES$^+$) 334 $[M+H]^+$ (100%), 356 $[M+Na]^+$ (40%); **HRMS**: found 356.1649, $[M+Na]^+$ requires 356.1655.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 3-methoxyphenyl(methyl)carbamothioate (*S*)-**4h** (95:5 *e.r.*, 169 mg, 89%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 150 mg, 0.57 mmol) following the same procedure.

$[\alpha]_D^{20}$: -10.8 (*c* 1.60, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, major 8.9 min, minor 11.2 min (254.4 nm).

4i: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 2-methoxyphenyl(methyl)carbamothioate.



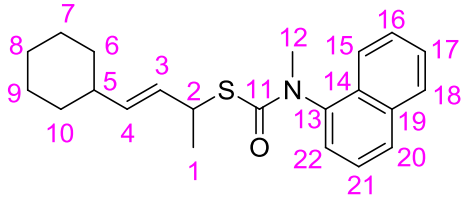
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (400 mg, 1.51 mmol), HOBt (1.5 eq) and 2-methoxy-*N*-methylaniline. Purification by column chromatography (Pet 100%, Pet/EtOAc 97:3 to 92:8) afforded the title compound as a colourless sticky oil (444 mg, 88%).

R_f: 0.48 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.36 (td, *J* = 8.0, 1.4 Hz, 1H, H-18), 7.21 (bd, *J* = 8.0 Hz, 1H, H-15), 6.96, (m, 2H, H-16, H-17), 5.50 (m, 1H, H-4), 5.40 (m, 1H, H-3), 4.07 (m, H-2), 3.85 (s, 3H, H-19), 3.21 (s, 3H, H-12), 1.91-1.84 (m, 1H, H-5), 1.69-1.60 (m, 4H, H-6, H-7, H-9, H-10), 1.35 (d, *J* = 6.8 Hz, 3H, H-1)/1.32 (d, *J* = 6.8 Hz, 3H, H-1) *-rotamers-*, 1.25-0.95 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 156.2/156.1 (C-11) *-rotamers-*, 136.7/136.6 (C-4) *-rotamers-*, 130.8 (C-15), 130.2 (C-18), 128.6/128.5 (C-3), 120.8 (C-16 or C-17), 112.2/112.1 (C-17 or C-16), 55.6 (C-19), 42.3/42.2 (C-2) *-rotamers-*, 40.4 (C-5), 36.7 (C-12), 32.8/32.7 (C-6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1651 (C=O), 1499 (C=C_{Ar}), 1271 (C_{Ar}-N), 747; **MS**: *m/z* (ES^+) 334 $[M+H]^+$ (100%); **HRMS**: found 356.1659, $[M+Na]^+$ requires 356.1655.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 2-methoxyphenyl(methyl)carbamothioate (*S*)-**4i** (94:6 *e.r.*, 208 mg, 82%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 200 mg, 0.76 mmol) following the same procedure.

$[\alpha]_D^{24}$: -16.0 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, major 10.7 min, minor 13.7 min (214.4 nm, 254.4 nm).

4j: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl methyl(naphthalen-1-yl)carbamothioate.



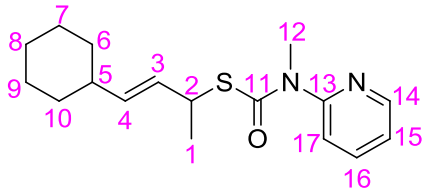
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1H-imidazole-1-carbothioate **10a** (200 mg, 0.76 mmol), HOBt (1.5 eq) and *N*-methylnaphthalen-1-amine **11j**.[6] Purification by column chromatography (Pet/EtOAc 95:5, 9:1) afforded the title compound as a brown solid (110 mg, 41%).

R_f: 0.36 (Pet/EtOAc 8:2); **mp**: 83-85 °C; **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.80-7.76 (m, 2H, H_{Ar}), 7.70-7.67 (m, 1H, H_{Ar}), 7.47-7.31 (m, 4H, H_{Ar}), 5.40 (bdd, *J* = 15.5, 5.6 Hz, 1H, H-4)/5.36 (bdd, *J* = 15.5, 5.6 Hz, 1H, H-4) *-rotamers-*, 5.26 (dd, *J* = 15.5, 6.8 Hz, 1H, H-3)/5.17 (dd, *J* = 15.5, 6.8 Hz, 1H, H-3) *-rotamers-*, 4.01-3.96 (bq, *J* = 6.8 Hz, 1H, H-2), 3.30 (s, 3H, H-12)/3.29 (s, 3H, H-12) *-rotamers-*, 1.75-1.68 (m, 1H, H-5), 1.57-1.48 (m, 4H, H-6, H-7, H-9, H-10), 1.21 (d, *J* = 6.8 Hz, 3H, H-1)/1.19 (d, *J* = 6.8 Hz, 3H, H-1), 1.12-0.81 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 169.4/169.3 (C-11) *-rotamers-*, 138.1/138.0 (C_{qAr}), 136.9/136.6 (C-4), 134.6 (C_{qAr}), 130.5 (C_{qAr}), 129.3 (CH_{Ar}), 128.5 (C-3), 128.4 (CH_{Ar}), 128.2 (CH_{Ar}), 127.5/127.4 (CH_{Ar}) *-rotamers-*, 127.2/127.2 (CH_{Ar}) *-rotamers-*, 126.5 (CH_{Ar}), 125.6/125.6 (CH_{Ar}) *-rotamers-*, 122.6 /122.4 (CH_{Ar}) *-rotamers-*, 42.4 (C-2), 40.3/40.2 (C-5) *-rotamers-*, 40.0 (C-12), 32.8/32.6 (C-6, C-10), 26.0/25.9 (C-7, C-8, C-9), 20.9/20.7 (C-1) *-rotamers-*; **IR**: ν_{max}(film)/cm^{-1} 1643 (C=O), 1338, 1279 (C_{Ar}-N), 777; **MS**: *m/z* (ES^+) 354 $[M+H]^+$ (100%), 376 $[M+Na]^+$ (80%); **HRMS**: found 354.1889, $[M+H]^+$ requires 354.1887.

The equivalent enantioenriched thiocarbamate (*R*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(naphthalen-1-yl)carbamothioate (*R*)-**4j** (14:86 *e.r.*, 645 mg, 62%) was prepared from (*R*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*R*)-**10a** (88:12 *e.r.*, 780 mg, 2.95 mmol) following the same procedure.

$[\alpha]_D^{22}$: -4.2 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, minor 12.2 min, major 15.1 min (214.4 nm, 254.4 nm).

4k: (*E*)-*S*-4-Cyclohexylbut-3-en-2-yl methyl(pyridin-2-yl)carbamothioate.



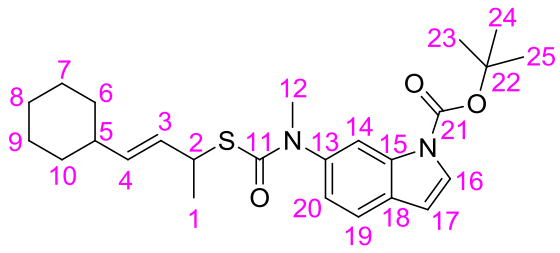
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (400 mg, 1.51 mmol), HOBt (1.5 eq) and 2-(methylamino)pyridine. Purification by column chromatography (Pet 100%, Pet/EtOAc 98:2 to 85:15) afforded the title compound as a colourless oil (108 mg, 23%).

R_f: 0.67 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.45 (ddd, *J* = 4.8, 1.9, 0.8 Hz, 1H, H-14), 7.69 (ddd, *J* = 8.2, 7.3, 1.9 Hz, 1H, H-16), 7.61 (d, *J* = 8.2 Hz, 1H, H-17), 7.12 (ddd, *J* = 7.3, 4.8, 1.0 Hz, 1H, H-15), 5.61 (ddd, *J* = 15.5, 6.6, 0.9 Hz, 1H, H-4), 5.47 (ddd, *J* = 15.5, 6.9, 1.1 Hz, 1H, H-3), 4.16 (qn, *J* = 6.9 Hz, 1H, H-2), 3.46 (s, 3H, H-12), 1.97-1.88 (m, 1H, H-5), 1.72-1.60 (m, 4H, H-6, H-7, H-9, H-10), 1.43 (d, *J* = 6.9 Hz, 1H, H-1), 1.30-1.00 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.9 (C-11), 154.3 (C-13), 148.2 (C-14), 137.5 (C4, C-16), 127.9 (C-3), 121.0 (C-15), 120.4 (C-17), 42.5 (C-2), 40.3 (C-5), 34.9 (C-12), 32.8/32.7 (C-6, C-10), 26.1/25.9 (C-7, C-8, C-9), 20.9 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1663 (C=O), 1467 (C=C_{Ar}), 1329 (C_{Ar}=N), 1294 (C_{Ar}-N), 1040, 964, 778; **MS**: *m/z* (ES$^+$) 305 $[M+H]^+$ (100%), 327 $[M+Na]^+$ (30%); **HRMS**: found 305.1681, $[M+H]^+$ requires 305.1683.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(pyridin-2-yl)carbamothioate (*S*)-**4k** (94:6 *e.r.*, 93 mg, 47%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 170 mg, 0.64 mmol) following the same procedure.

$[\alpha]_D^{22}$: -66.6 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, major 6.7 min, minor 7.7 min (214.4 nm, 254.4 nm).

4l: (*E*)-*tert*-Butyl 6-((((4-cyclohexylbut-3-en-2-yl)thio)carbonyl)(methyl)amino)-1*H*-indole-1-carboxylate.



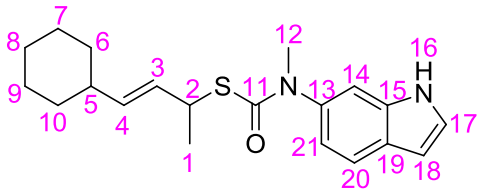
To a solution of **4l'** (100 mg, 0.29 mmol, 1.0 eq) in CH_2Cl_2 (1.0 mL) were sequentially added di-*tert*-butyl dicarbonate (1.2 eq), triethylamine (1.0 eq) and DMAP (0.2 eq). The reaction was stirred at room temperature for 20 h. Water was added. The organic layer was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (Pet 100%, Pet/EtOAc 98:2 to 95:5) afforded the title compound as a colourless sticky oil (128 mg, 100%).

R_f: 0.77 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.08 (bs, 1H, H-14), 7.62 (d, *J* = 3.6 Hz, 1H, H-16), 7.56 (d, *J* = 8.2 Hz, 1H, H-19), 7.12 (dd, *J* = 8.2, 1.9 Hz, 1H, H-20), 6.57 (dd, *J* = 3.6, 0.4 Hz, 1H, H-17), 5.52 (dd, *J* = 15.9, 6.8 Hz, 1H, H-4), 5.40 (dd, *J* = 15.9, 6.8 Hz, 1H, H-3), 4.09 (qn, *J* = 6.8 Hz, 1H, H-2), 1.91-1.82 (m, 1H, H-5), 1.67 (s, 9H, H-23, H-24, H-25), 1.67-1.59 (m, 4H, H-6, H-7, H-9, H-10), 1.36 (d, *J* = 6.8 Hz, 3H, H-1), 1.26-0.95 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.8 (C-11), 149.4 (C-13), 138.5 (C-15), 136.8 (C-4), 128.4 (C-3), 127.3 (C-16), 125.6 (C-18), 123.1 (C-20), 121.4 (C-19), 115.5 (C-14), 107.1 (C-17), 84.1 (C-22), 42.6 (C-2), 40.4 (C-5), 38.6 (C-12), 32.8/32.7 (C-6, C-10), 28.2 (C-23, C-24, C-25), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1736 (C=O), 1612 (C=O), 1441 (C=C_{Ar}), 1333 (C-O_{ester}), 1239 (C_{Ar}-N), 1154, 1040; **MS**: *m/z* (ES$^+$) 443 $[M+H]^+$ (100%), 465 $[M+Na]^+$ (80%); **HRMS**: found 465.2192, $[M+Na]^+$ requires 465.2182.

The equivalent enantioenriched thiocarbamate (*S*)-*tert*-butyl 6-((((4-cyclohexylbut-3-en-2-yl)thio)carbonyl)(methyl)amino)-1*H*-indole-1-carboxylate (*S*)-**4l** (95:5 *e.r.*, 168 mg, 100%, 88% over 2 steps from (*S*)-**10a**) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-indol-6-yl(methyl)carbamothioate (*S*)-**4l'** (95:5 *e.r.*, 130 mg, 0.38 mmol) following the same procedure.

[α]$_D^{23}$: +14.8 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, major 19.0 min, minor 27.2 min (214.4 nm, 254.4 nm).

4l': (*E*)-S-4-Cyclohexylbut-3-en-2-yl 1*H*-indol-6-yl(methyl)carbamothioate.



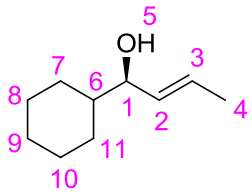
General procedure D was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate **10a** (125 mg, 0.47 mmol), HOBt (1.1 eq) and *N*-methyl-1*H*-indol-6-amine **11l**. Purification by column chromatography (Pet 100%, Pet/EtOAc 9:1, 85:15) afforded the title compound as a white solid (159 mg, 99%).

R_f: 0.48 (Pet/EtOAc 8:2); **mp**: 133-135 °C; **^{1}H NMR**: (400 MHz; $CDCl_3$) *δ* (ppm) 8.27 (bs, 1H, H-16), 7.65 (d, *J* = 8.3 Hz, 1H, H-20), 7.31 (bt, *J* = 1.3 Hz, 1H, H-14), 7.28 (dd, *J* = 3.0, 2.7 Hz, 1H, H-17), 6.99 (dd, *J* = 8.3, 1.3 Hz, 1H, H-21), 6.58 (ddd, *J* = 3.0, 2.0, 0.8 Hz, 1H, H-18), 5.51 (dd, *J* = 15.8, 6.5 Hz, 1H, H-4), 5.39 (dd, *J* = 15.8, 6.8 Hz, 1H, H-3), 4.07 (qn, *J* = 6.8 Hz, 1H, H-2), 3.35 (s, 3H, H-12), 1.90-1.81 (m, 1H, H-5), 1.68-1.58 (m, 4H, H-6, H-7, H-9, H-10), 1.35 (d, *J* = 6.8 Hz, 3H, H-1), 1.26-0.93 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) *δ* (ppm) 160.9 (C-11), 149.8 (C-13), 136.7 (C-4), 135.5 (C-15), 128.5 (C-3), 125.8 (C-17), 124.6 (C-18), 121.4 (C-20), 120.1 (C-21), 111.6 (C-14), 102.9 (C-18), 42.5 (C-2), 40.3 (C-5), 38.7 (C-12), 32.8/32.7 (C6, C-10), 26.1/26.0 (C-7, C-8, C-9), 21.1 (C-1); **IR**: ν_{max}(film)/cm^{-1} 3317 (NH), 1633 (C=O), 1450 (C=C_{Ar}), 1347 (C_{Ar}-N), 1295 (C_{Ar}-N), 1093, 655; **MS**: *m/z* (ES$^+$) 343 [M+H]$^+$ (50%), 365 [M+Na]$^+$ (60%); **HRMS**: found 343.1841, [M+H]$^+$ requires 343.1839.

The equivalent enantioenriched thiocarbamate (*S*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(pyridin-2-yl)carbamothioate (*S*)-**4l'** (95:5 *e.r.*, 154 mg, 88%) was prepared from (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (95:5 *e.r.*, 135 mg, 0.51 mmol) following the same procedure.

[α]$_D^{24}$: -3.2 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 95:5, 1.0 mL/min, 28 °C, major 32.5 min, minor 51.1 min (214.4 nm, 254.4 nm).

(*R*)-**5a**: (*R*,*E*)-1-Cyclohexylbut-2-en-1-ol**.**[9]



By the method reported by Sharpless and co-workers.[9]

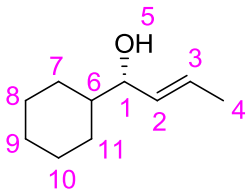
To a solution of 1-cyclohexyl-2-buten-1-ol (±)-**5a** (2.0 g, 13.0 mmol, 1.0 eq) in CH_2Cl_2 (50.0 mL) at rt, was added (+)-diisopropyl tartrate ((+)-DIPT) (0.15 eq) followed by powdered 4 Å molecular sieves (500 mg, 20-30%w/w based on **5a**, previously dried under reduced pressure at 160 °C overnight). The reaction was cooled to -20 °C (internal temperature monitored). Titanium(IV) isopropoxide (Ti(O*i*-Pr)$_4$) (0.10 eq) was added and the reaction was stirred at -20 °C for 20 to 30 min. Anhydrous *tert*-butyl hydroperoxide (TBHP) (5.5 M in decane, 0.6 eq) was added dropwise, maintaining the internal temperature between -22 and -20 °C. The reaction was stirred at -20 °C for 15 h before an aliquot (0.1 mL) was removed and quenched with 2.0 mL of an aqueous solution of $FeSO_4{\cdot}7H_2O$ and citric acid monohydrate (33 g of $FeSO_4.7H_2O$, 11 g of citric acid monohydrate, 100 mL of distilled water). ^{1}H NMR spectrum of the aliquot showed an allylic alcohol/epoxide ratio of 1:1.3. The reaction was quenched at -20 °C by adding the aforementioned ferrous aqueous solution (40 mL), warming the reaction to rt and stirring vigorously until two clear phases appeared (30 min). The reaction mixture was extracted with CH_2Cl_2 (x2). The combined organic layers were concentrated to the original volume and washed with 30% NaOH in brine (13 mL, 1.0 mL/mmol of substrate). The mixture was extracted with CH_2Cl_2 (x3), the combined organic layers were washed with brine (x2), dried over anhydrous $MgSO_4$, filtered and concentrated. Purification by column chromatography (Pet 100%, Pet/EtOAc 95:5 to 85:15) afforded the title compound as a colourless oil (1:99 *e.r.*, 645 mg, 65% conversion based on alcohol/epoxide ratio, 92% isolated yield based on conversion).

$[\alpha]_D^{20}$: -1.0 (*c* 1.20, $CHCl_3$), lit[9] **$[\alpha]_D^{25}$**: -13.33, (*c* 2.76, EtOH); **GC**: Astec Chiraldex™ G-TA, method: 50-80 °C (5 °C/min), 80-102 °C (1 °C/min), 102 °C (5 min hold), 102-110 °C (1 °C/min), 110-180 °C (5 °C/min), major 43.91 min, minor 44.67 min [(±)-**5a**: 43.94/44.56 min].

R_f: 0.58 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 5.62 (dq, *J* = 15.3, 6.4 Hz, 1H, H-3), 5.47 (ddq, *J* = 15.3, 7.2, 1.4 Hz, 1H, H-2), 3.75 (t, *J* = 7.2 Hz, 1H, H-1), 1.87-1.83 (m, 1H, H-6), 1.77-1.63 (m, 4H, H-7, H-8, H-10, H-11), 1.70 (dd, *J* = 6.4, 1.4 Hz, 3H, H-4), 1.43-0.86 (m, 7H, H-7', H-8', H-9, H-10', H-11', H-5).

Matches published data.[9]

(*S*)-**5a**: (*E*,*S*)-1-Cyclohexylbut-2-en-1-ol**.**



By the method reported by Noyori and co-workers.[10]

i-PrOH was degassed by bubbling nitrogen through it for 30 min and kept under argon. A test tube was carefully flame-dried and cooled to room temperature in a dessicator under vaccum, then under argon and kept under an argon atmosphere. A solution of (*E*)-**7** (1.21 g, 7.97 mmol, 1.0 eq) in degassed *i*-PrOH (16.0 mL), followed by (*R*,*R*)-**8** (0.05 mol%) and K_2CO_3 (0.02 eq) were added to the testing tube, which was purged with argon before it was put in the autoclave. The reaction was stirred under 40 bar of hydrogen at 30 °C (the autoclave was placed in a sand bath) for 7 days. The crude mixture was concentrated under vaccum. Purification by column chromatography (Pet 100%, Pet/EtOAc 98:2 to 95:5) afforded the title compound as a pale yellow oil (88:12 *e.r.*, 763 mg, 62%).

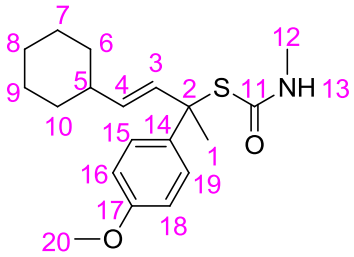
GC: Astec Chiraldex^{TM} G-TA, method: 50-80 °C (5 °C/min), 80-102 °C (1 °C/min), 102 °C (5 min hold), 102-110 °C (1 °C/min), 110-180 °C (5 °C/min), minor 44.03 min, major 44.53 min [(±)-**5a**: 43.94/44.56 min].

For other data, see (*R*)-**5a**.

For experimental procedures and characterisation data of **6b** and **6c**, please see:

G. Mingat, P. MacLellan, M. Laars, J. Clayden, *Org. Lett.*, 2014, **16**, 1252.

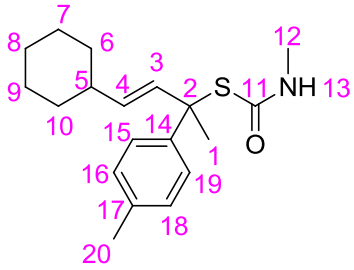
6d: (*E*)-*S*-4-Cyclohexyl-2-(4-methoxyphenyl)but-3-en-2-yl methylcarbamothioate.



General procedure E (-40 °C, 1 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 4-methoxyphenyl(methyl)carbamothioate **4d** (50 mg, 0.15 mmol). Purification by column chromatography (Pet+1%Et_3N, Pet+1%Et_3N/EtOAc 98:2 to 85:15) afforded the title compound as a pale yellow oil (12 mg, 24%).

R_f: 0.41 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.45 (d, *J* = 8.8 Hz, 2H, H-15, H-19), 6.85 (d, *J* = 8.8 Hz, 2H, H-16, H-18), 6.00 (d, *J* = 15.8 Hz, 1H, H-3), 5.53 (dd, *J* = 15.8, 7.2 Hz, 1H, H-4), 5.29 (bs, 1H, H-13), 3.80 (s, 3H, H-20), 2.74 (d, *J* = 4.8 Hz, 3H, H-12), 2.10-1.98 (m, 1H, H-5), 1.92 (s, 3H, H-1), 1.74-1.63 (m, 4H H-6, H-7, H-9, H-10), 1.33-1.05 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) *compound too unstable, degraded on the NMR timescale*.

6e: (*E*)-*S*-4-Cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl methylcarbamothioate.



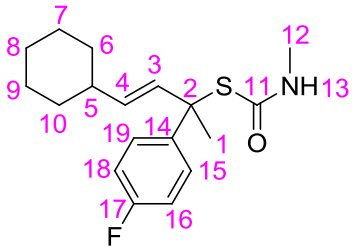
General procedure E (-60 °C for 3 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate **4e** (666 mg, 2.10 mmol). The title compound was obtained as a pale yellow oil without purification (717 mg, 99%).

R_f: 0.45 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.42 (d, *J* = 8.2 Hz, 2H, H-15, H-19), 7.13 (d, *J* = 8.2 Hz, 2H, H-16, H-18), 6.02 (d, *J* = 15.7 Hz, 1H, H-3), 5.55 (dd, *J* = 15.7, 7.0 Hz, 1H, H-4), 5.30 (bs, 1H, H-13), 2.74 (d, *J* = 4.8 Hz, 3H, H-12), 2.32 (s, 3H, H-20), 2.09-2.01 (m, 1H, H-5), 1.92 (s, 3H, H-1), 1.75-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.33-1.05 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 166.7 (C-11), 141.6 (C-17), 136.6 (C-14), 136.3 (C-4), 132.3 (C-3), 128.9 (C-16, C-18), 126.8 (C-15, C-19), 56.3 (C-2), 40.7 (C-5), 33.0/32.9 (C-6, C-10), 27.6 (C-1), 27.3 (C-12), 26.0/25.9 (C-7, C-8, C-9), 21.0 (C-20); **IR**: ν_{max}(film)/cm^{-1} 3316 (NH), 1652 (C=O), 1510 (C=C_{Ar}), 1448, 1210, 814; **MS**: *m/z* (ES$^+$) 340 $[M+Na]^+$ (100%); **HRMS**: found 318.1888, $[M+H]^+$ requires 318.1887.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-*S*-4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6e** (91:9 *e.r.*, 38 mg, 76%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate (*S*)-**4e** (94:6 *e.r.*, 50 mg, 0.16 mmol) following general procedure E (-60 °C, 1 h).
$[\alpha]_D^{22}$: -16.9 (*c* 2.83, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/*i*-PrOH 96:4, 1.0 mL/min, major 12.0 min, minor 17.5 min (214.4 nm, 254.4 nm).

The other enantiomer (*R*)-(*E*)-*S*-4-cyclohexyl-2-(*p*-tolyl)but-3-en-2-yl methylcarbamothioate (*R*)-**6e** (13:87 *e.r.*, 210 mg, 100%) was prepared from (*R*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(*p*-tolyl)carbamothioate (*R*)-**4e** (13:87 *e.r.*, 50 mg, 0.16 mmol) following general procedure E (-60 °C, 3 h).
HPLC: Chiralpak AD-H, Hexane/*i*-PrOH 96:4, 1 mL/min, 28 °C, minor 13.1 min, major 16.4 min (214.4 nm).

6f: (*E*)-S-4-Cyclohexyl-2-(4-fluorophenyl)but-3-en-2-yl methylcarbamothioate.



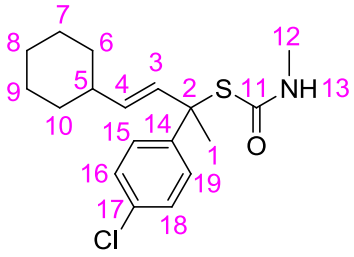
General procedure E (-60 °C, 2.5 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 4-fluorophenyl(methyl)carbamothioate **4f** (45 mg, 0.14 mmol). Purification by column

chromatography (Pet 100%, Pet/EtOAc 98:2 to 9:1) afforded the title compound as a colourless oil (32 mg, 71%).

R_f: 0.48 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.50 (dd, *J* = 8.9, 5.3 Hz, 2H, H-15, H-19), 6.99 (t, *J* = 8.9 Hz, 2H, H-16, H-18), 6.00 (d, *J* = 15.8 Hz, 1H, H-3), 5.52, (dd, *J* = 15.8, 7.0 Hz, 1H, H-4), 5.27 (bs, 1H, H-13), 2.74 (d, *J* = 4.9 Hz, 3H, H-12), 2.09-2.00 (m, 1H, H-5), 1.90 (s, 3H, H-1), 1.74 (m, 4H, H-6, H-7, H-9, H-10), 1.33-1.05 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 166.3 (C-11), 161.5 (d, $^1J_{C,F}$ = 244.2 Hz, C-17), 140.7 (d, $^4J_{C,F}$ = 2.8 Hz, C-14), 136.5 (C-4), 132.1 (C-3), 128.8 (d, $^3J_{C,F}$ = 7.7 Hz, C-15, C-19), 114.8 (d, $^2J_{C,F}$ = 21.3 Hz, C-16, C-18), 55.9 (C-2), 40.6 (C-5), 33.0/32.9 (C-6, C-10), 27.7 (C-1), 26.0/25.9 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 3310 (NH), 1650 (C=O), 1504 (C=C_{Ar}), 1220 (C-F), 831; **MS**: *m/z* (ES$^+$) 322 $[M+H]^+$ (50%); **HRMS**: found 344.1458, $[M+Na]^+$ requires 344.1455.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-S-4-cyclohexyl-2-(4-fluorophenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6f** (94:6 *e.r.*, 41 mg, 82%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl 4-fluorophenyl(methyl)carbamothioate (*S*)-**4f** (94:6 *e.r.*, 50 mg, 0.16 mmol) following general procedure E (-60 °C, 3 h).
$[\alpha]_D^{26}$: -16.0 (*c* 1.00, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/i-PrOH 96:4, 1.0 mL/min, 28 °C, major 11.4 min, minor 13.3 min (214.4 nm, 254.4 nm).

6g: (*E*)-*S*-4-Cyclohexyl-2-(4-chlorophenyl)but-3-en-2-yl methylcarbamothioate.

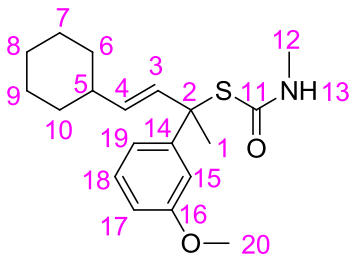


General procedure E (-50 °C, 1.5 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 4-chlorophenyl(methyl)carbamothioate **4g** (45 mg, 0.13 mmol). Purification by column chromatography (Pet/EtOAc 95:5) afforded the title compound as a pale yellow oil (35 mg, 77%).

R_f: 0.45 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.47 (d, *J* = 8.7 Hz, 2H, H-16, H-18), 7.26 (d, *J* = 8.7 Hz, 2H, H-15, H-19), 5.99 (d, *J* = 15.7 Hz, 1H, H-3), 5.51 (dd, *J* = 15.7, 7.0 Hz, 1H, H-4), 5.26 (bs, 1H, H-13), 2.74 (d, *J* = 4.8 Hz, 3H, H-12), 2.09-2.00 (m, 1H, H-5), 1.89 (s, 3H, H-1), 1.74-1.63 (m, 4H, H-6, H-7, H-9, H-10), 1.32-1.05 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 166.1 (C-11), 143.7 (C-14), 136.6 (C-4), 132.5 (C-17), 131.8 (C-3), 128.5 (C-16, C-18), 128.1 (C-15, C-19), 55.9 (C-2), 40.6 (C-5), 32.9/32.8 (C-6, C-10), 29.7 (C-8), 27.5 (C-1), 27.4 (C-12), 26.0/25.9 (C-7, C-9); **IR**: ν_{max}(film)/cm^{-1} 3313 (NH), 1651 (C=O), 1489 ($C=C_{Ar}$), 1209, 1011, 821 (C-Cl); **MS**: *m/z* (ES^+) 360 $[M+Na]^+$ (100%); **HRMS**: found 360.1159, $[M+Na]^+$ requires 360.1160.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-*S*-4-cyclohexyl-2-(4-chlorophenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6g** (94:6 *e.r.*, 29 mg, 63%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl 4-chlorophenyl(methyl)carbamothioate (*S*)-**4g** (95:5 *e.r.*, 46 mg, 0.14 mmol) following general procedure E (-50 °C, 2 h).
$[\alpha]_D^{22}$: -18.3 (*c* 2.74, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/*i*-PrOH 96:4, 1.0 mL/min, major 22.7 min, minor 28.2 min (214.4 nm, 254.4 nm).

6h: (*E*)-*S*-4-Cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl methylcarbamothioate.



General procedure E (-60 °C, 3 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 3-methoxyphenyl(methyl)carbamothioate **4h** (130 mg, 0.39 mmol). The title compound was obtained as a beige solid without purification (128 mg, 98%).

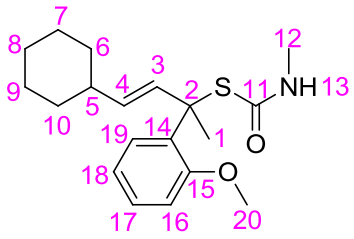
R_f: 0.39 (Pet/EtOAc 8:2); **mp**: 73-75 °C; **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.24 (t, *J* = 8.0 Hz, 1H, H-18), 7.13 (ddd, *J* = 8.0, 1.6, 0.7 Hz, 1H, H-17), 7.10 (t, *J* = 2.4 Hz, 1H, H-15), 6.78 (ddd, *J* = 8.0, 2.4, 0.7 Hz, 1H, H-19), 6.01 (d, *J* = 15.7 Hz, 1H, H-3), 5.56 (dd, *J* = 15.7, 7.1 Hz, 1H, H-4), 5.27 (bs, 1H, H-13), 3.80 (s, 3H, H-20), 2.74 (d, *J* = 4.8 Hz, 3H, H-12), 2.10-2.02 (m, 1H, H-5), 1.91 (s, 3H, H-1), 1.74-1.64 (m, 4H, H-6, H-7, H-9, H-10), 1.34-1.06 (m, 6H, H-6', H-7', H-8, H-

8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 166.5 (C-11), 159.3 (C-16), 146.5 (C-14), 136.4 (C-4), 132.1 (C-3), 129.1 (C-18), 119.3 (C-17), 113.3 (C-15), 112.0 (C-19), 56.4 (C-2), 55.2 (C-20), 40.7 (C-5), 33.0/32.9 (C-6, C-10), 27.6 (C-1, C-12), 26.1/25.9 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 3262 (NH), 1648 (C=O), 1530 (C=C_{Ar}), 1227 (C_{Ar}-O), 1043, 975, 704, 627; **MS**: *m/z* (ES^+) 334 $[M+H]^+$ (50%), 356 $[M+Na]^+$ (100%); **HRMS**: found 334.1837, $[M+H]^+$ requires 334.1836.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-*S*-4-cyclohexyl-2-(3-methoxyphenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6h** (95:5 *e.r.*, 120 mg, 100%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl 3-methoxyphenyl(methyl)carbamothioate (*S*)-**4h** (95:5 *e.r.*, 120 mg, 0.36 mmol) following the same procedure.

$[\alpha]_D^{22}$: -9.8 (*c* 0.82, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/*i*-PrOH 96:4, 1.0 mL/min, major 27.3 min, minor 29.2 min (254.4 nm).

6i: (*E*)-S-4-Cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl methylcarbamothioate.



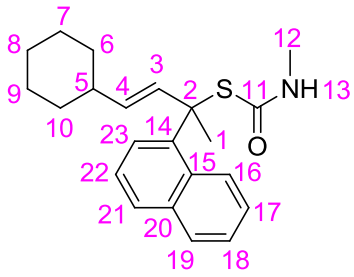
General procedure E (-60 °C, 3.5 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 2-methoxyphenyl(methyl)carbamothioate **4i** (50 mg, 0.15 mmol). The title compound was obtained as a dark yellow/orange oil without purification (50 mg, 99%).

R_f: 0.38 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.52 (dd, *J* = 8.0, 1.6 Hz, 1H, H-19), 7.26 (dd, *J* = 8.0, 1.6 Hz, 1H, H-17), 6.95-6.89 (m, 2H, H-16, H-18), 6.03 (dd, *J* = 15.8, 0.8 Hz, 1H, H-3), 5.42 (dd, *J* = 15.8, 7.2 Hz, 1H, H-4), 5.36 (bs, 1H, H-13), 3.81 (s, 3H, H-20), 2.73 (d, *J* = 4.8 Hz, 3H, H-12), 2.06-2.00 (m, 1H, H-5), 2.00 (s, 3H, H-1), 1.72-1.62 (m, 4H, H-6, H-7, H-9, H-10); 1.31-1.02 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 167.6 (C-11), 157.6 (C-15), 135.4 (C-4), 132.1 (C-3), 131.4 (C-14), 129.0 (C-19), 128.8 (C-17), 120.2 (C-18), 112.3 (C-16), 56.0 (C-2), 55.3 (C-20), 40.7 (C-5), 33.0

(C-6, C-10), 27.2 (C-12), 26.3 (C-1), 26.1/25.9 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 3305 (NH), 1641 (C=O), 1219 (C_{Ar}-O), 749; **MS**: *m/z* (ES$^+$) 334 $[M+H]^+$ (50%), 356 $[M+Na]^+$ (50%); **HRMS**: found 334.1838, $[M+H]^+$ requires 334.1835.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-S-4-cyclohexyl-2-(2-methoxyphenyl)but-3-en-2-yl methylcarbamothioate (*S*)-**6i** (94:6 *e.r.*, 142 mg, 100%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl 2-methoxyphenyl(methyl)carbamothioate (*S*)-**4i** (94:6 *e.r.*, 142 mg, 0.43 mmol) following general procedure E (-60 °C, 3 h).
$[\alpha]_D^{23}$: -16.4 (*c* 1.00, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/*i*-PrOH 90:10, 1.0 mL/min, major 7.6 min, minor 10.4 min (214.4 nm, 254.4 nm).

6j: (*E*)-*S*-4-Cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl methylcarbamothioate.



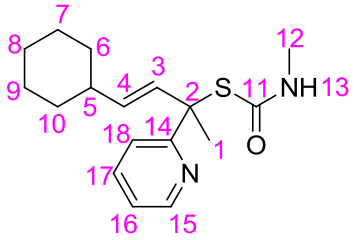
General procedure E (-60 °C, 2.5 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(naphthalen-1-yl)carbamothioate **4j** (50 mg, 0.14 mmol). Purification by column chromatography (Pet 100%, Pet/EtOAc 95:5, 9:1) afforded the title compound as a pale yellow oil (45 mg, 90%).

R_f: 0.38 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.55 (m, 1H, H-16), 7.84 (m, 1H, H-19), 7.80 (d, *J* = 8.2 Hz, 1H, H-21), 7.76 (dd, *J* = 7.4, 0.9 Hz, 1H, H_{Ar}), 7.47-7.41 (m, 3H, H_{Ar}), 6.17 (d, *J* = 15.8 Hz, 1H, H-3), 5.32 (dd, *J* = 15.8, 7.1 Hz, 1H, H-4), 5.15 (bs, 1H, H-13), 2.66 (d, *J* = 4.8 Hz, 3H, H-12), 2.25 (s, 3H, H-1), 2.02-1.94 (m, 1H, H-5), 1.67-1.59 (m, 4H, H-6, H-7, H-9, H-10), 1.26-0.94 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 166.7 (C-11), 138.5 (C_{qAr}), 137.0 (C-4), 134.9 (C_{qAr}), 133.1 (C-3), 130.6 (C_{qAr}), 129.1/129.0 (C19, C-21), 128.6 (C-16), 126.2 (CH_{Ar}), 125.0 (CH_{Ar}), 124.7 (CH_{Ar}), 124.1 (CH_{Ar}), 57.2 (C-2), 40.7 (C-5), 32.6 (C-6, C-10), 30.1 (C-1), 27.3 (C-12), 26.0/25.9 (C-7, C-8, C-

9); **IR**: ν_{max}(film)/cm^{-1} 3268 (NH), 1650 (C=O), 1507 (C=C$_{Ar}$), 1211, 802, 775; **MS**: *m/z* (ES$^+$) 376 [M+Na]$^+$ (95%); **HRMS**: found 354.1888, [M+Na]$^+$ requires 354.1887.

The equivalent enantioenriched thiocarbamate (*R*)-(*E*)-*S*-4-cyclohexyl-2-(naphthalen-1-yl)but-3-en-2-yl methylcarbamothioate (*R*)-**6j** (15:85 *e.r.*, 438 mg, 71%) was prepared from (*R*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl 2-(naphthalen-1-yl)(methyl)carbamothioate (*R*)-**4j** (14:86 *e.r.*, 618 mg, 1.75 mmol) following general procedure E (-60 °C, 3 h).
[α]$_D^{25}$: +72.6 (*c* 1.00, $CHCl_3$); **HPLC**: Chiralcel OD-H, Hexane/*i*-PrOH 98:2, 0.5 mL/min, 28 °C, minor 64.7 min, major 68.2 min (214.4 nm, 254.4 nm).

6k: (*E*)-*S*-4-Cyclohexyl-2-(pyridin-2-yl)but-3-en-2-yl methylcarbamothioate.



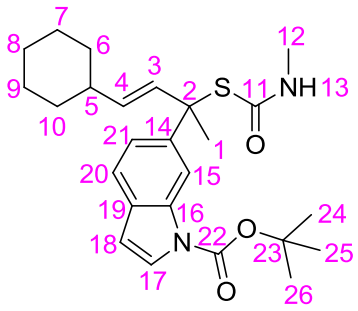
General procedure E (-78 °C, 2 h) was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(pyridin-2-yl)carbamothioate **4k** (50 mg, 0.16 mmol). Purification by column chromatography (Pet 100%, Pet/EtOAc 9:1 to 6:4) afforded the title compound as a colourless oil (21 mg, 42%).

R$_f$: 0.29 (Pet/EtOAc 1:1); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.56 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H, H-15), 7.66 (td, *J* = 7.7, 1.6 Hz, 1H, H-17), 7.47 (d, *J* = 7.7 Hz, 1H, H-18), 7.16 (ddd, *J* = 7.7, 4.8, 0.6 Hz, 1H, H-16), 6.76 (bs, 1H, H-13), 6.04 (d, *J* = 15.7 Hz, 1H, H-3), 5.57 (dd, *J* = 15.7, 7.0 Hz, 1H, H-4), 2.76 (d, *J* = 4.7 Hz, 3H, H-12), 2.08-2.00 (m, 1H, H-5), 1.93 (s, 3H, H-1), 1.73-1.62 (m, 4H, H-6, H-7, H-9, H-10), 1.31-1.04 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 168.7 (C-11), 163.7 (C-14), 148.3 (C-15), 137.2 (C-4), 136.7 (C-17), 131.3 (C-3), 121.9 (C-16), 121.2 (C-18), 57.3 (C-2), 40.7 (C-5), 32.9 (C6, C-10), 27.3 (C-12), 26.1 (C-1), 25.9 (C-7, C-8, C-9); **IR**: ν_{max}(film)/cm^{-1} 3305 (NH), 1655 (C=O), 1466 (C=C$_{Ar}$), 1429 (C=C$_{Ar}$), 967, 782, 745; **MS**: *m/z* (ES$^+$) 305 [M+H]$^+$ (100%), 327 [M+Na]$^+$ (20%); **HRMS**: found 327.1503, [M+Na]$^+$ requires 327.1502.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-*S*-4-cyclohexyl-2-(pyridin-2-yl)but-3-en-2-yl methylcarbamothioate (*S*)-**6k** (93:7 *e.r.*, 15 mg, 30%) was prepared from (*S*)-(*E*)-*S*-4-cyclohexylbut-3-en-2-yl methyl(pyridin-2-yl)carbamothioate (*S*)-**4k** (94:6 *e.r.*, 50 mg, 0.16 mmol) following the same procedure.

$[\alpha]_D^{22}$: -68.0 (*c* 1.00, $CHCl_3$); **HPLC**: (*R*,*R*)-Whelk-01, Hexane/*i*-PrOH 90:10, 1.0 mL/min, 28 °C, major 15.4 min, minor 19.3 min (214.4 nm).

6l: (*E*)-*tert*-Butyl 6-(4-cyclohexyl-2-((methylcarbamoyl)thio)but-3-en-2-yl)-1*H*-indole-1-carboxylate.



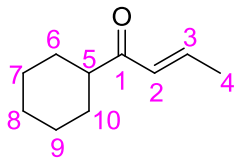
General procedure E (-60 °C, 2.5 h) was followed using (*E*)-*tert*-butyl 6-((((4-cyclohexylbut-3-en-2-yl)thio)carbonyl)(methyl)amino)-1*H*-indole-1-carboxylate **4l** (60 mg, 0.14 mmol). Purification by column chromatography (Pet 100%, Pet/EtOAc 95:5 to 9:1) afforded the title compound as a pale yellow oil (26 mg, 43%).

R_f: 0.40 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.36 (bs, 1H, H-15), 7.60 (bd, *J* = 3.6 Hz, 1H, H-17), 7.48 (t, *J* = 8.2 Hz, 1H, H-20), 7.44 (dd, *J* = 8.2, 1.7 Hz, 1H, H-21), 6.52 (d, *J* = 3.6 Hz, 1H, H-18), 6.08 (d, *J* = 15.8 Hz, 1H, H-3), 5.56 (dd, *J* = 15.8, 7.1 Hz, 1H, H-4), 5.32 (bs, 1H, H-13), 2.73 (bd, *J* = 4.8 Hz, 3H, H-12), 2.11-2.01 (m, 1H, H-5), 2.03 (s, 3H, H-1), 1.74-1.63 (m, 4H, H-6, H-7, H-9, H-10), 1.68 (s, 6H, H-24, H-25, H-26), 1.32-1.06 (m, 6H, H-6', H-7', H-8, H-8', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 167.8 (C-11), 151.5 (C-22), 136.3 (C-4), 132.6 (C-3), 126.2 (C-17), 122.2 (C-21), 120.4/120.3 (C-20) *-rotamers-*, 113.8 (C-15), 107.1/106.9 (C-18) *-rotamers-*, 83.6 (C-23), 57.2 (C-2), 40.8/40.7 (C-5) *-rotamers-*, 32.9 (C-6, C-10), 28.2 (C-24, C-25, C-26), 27.9 (C-1), 27.3 (C-12), 26.3/25.9 (C-7, C-8, C-9), *C-14/C-16/C-19 not visible-*; **IR**: ν_{max}(film)/cm^{-1} 3338 (NH), 1732 (C=O), 1655 (C=C), 1335(C_{Ar}=N), 1153 (C-O_{ester}), 766; **MS**: *m/z* (ES^+) 465 $[M+Na]^+$ (30%); **HRMS**: found 465.2176, $[M+Na]^+$ requires 465.2182.

The equivalent enantioenriched thiocarbamate (*S*)-(*E*)-*tert*-butyl 6-(4-cyclohexyl-2-((methylcarbamoyl)thio)but-3-en-2-yl)-1*H*-indole-1-carboxylate (*S*)-**6l** (90:10 *e.r.*, 24 mg, 41%) was prepared from (*S*)-(*E*)-*tert*-butyl 6-((((4-cyclohexylbut-3-en-2-yl)thio)carbonyl)(methyl)amino)-1*H*-indole-1-carboxylate (*S*)-**4l** (95:5 *e.r.*, 58 mg, 0.13 mmol) following the same procedure.

[α]$_D^{23}$: -1.2 (*c* 1.00, $CHCl_3$); **HPLC**: Chiralcel OD-H, Hexane/*i*-PrOH 90:10, 1.0 mL/min, 28 °C, major 5.1 min, minor 5.8 min (214.4 nm, 254.4 nm).

(*E*)-**7**: (*E*)-1-Cyclohexylbut-2-en-1-one.



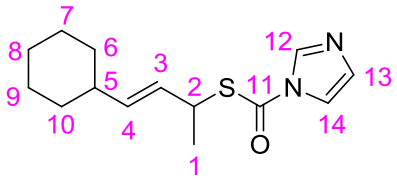
By a modification of the methods reported by Kobayashi,[11a] Nau[11b] and co-workers.

To a solution of 1-cyclohexylbut-2-en-1-ol (1.0 g, 6.5 mmol, 1.0 eq) in $CHCl_3$ (65.0 mL) was added oven-dried manganese dioxide (20 eq). The reaction was heated to 40 °C for 5.5 days. The crude mixture was filtered through celite and washed with warm $CHCl_3$ (55 °C). The filtrate was concentrated under low vaccum, on the rotary evaporator. Purification by column chromatography (Pet 100%, Pet/EtOAc 99:1, 98:2) afforded the title compound as a colourless liquid (501 mg, 51%).

R$_f$: 0.66 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 6.94-6.82 (dq, *J* = 15.6, 6.8 Hz, 1H, H-3), 6.21-6.15 (dd, *J* = 15.6, 1.6 Hz, 1H, H-2), 2.57-2.49 (m, 1H, H-5), 1.90-1.87 (dd, *J* = 6.8, 1.6 Hz, 3H, H-4), 1.81-1.66 (m, 6H, H-6, H-7, H-8, H-9, H-10), 1.43-1.14 (m, 4H, H-6', H-7', H-9', H-10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 203.3 (C-1), 142.1 (C-3), 130.2 (C-2), 48.5 (C-5), 28.7/25.9/25.7 (C-6, C-7, C-8, C-9, C-10), 18.2 (C-4) ; **IR**: ν_{max}(film)/cm^{-1} 1691 (C=O), 1663 (C=C), 1627 (C=C), 1444, 968, 730; **MS**: *m/z* (ES$^+$) 153 [M+H]$^+$ (100%), 175 [M+Na]$^+$ (40%); **HRMS**: found 153.1277, [M+H]$^+$ requires 153.1274.

Matches published data.[12]

10a: *S*-4-Cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate.



By the method developed within the Clayden group.[7]

To a stirred solution of 1-cyclohexylbut-2-en-1-ol (1.0 g, 6.48 mmol, 1.0 eq) in DCE (40.0 mL) at room temperature were added thiocarbonydiimidazole (2.0 eq) and DMAP (0.1 eq). The reaction was heated to 40 °C for 26 h. Once at room temperature, EtOAc was added and the crude mixture was washed with brine (x2). The organic layer was separated, dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (Pet/EtOAc 9:1 to 8:2) afforded the title compound as a yellow oil (1.55 g, 90%).

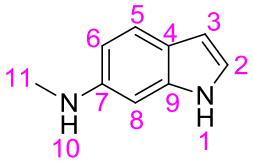
R_f: 0.51 (Pet/EtOAc 8:2); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.16 (s, 1H, H-12), 7.43 (d, *J* = 1.2 Hz, 1H, H-14), 7.07 (s, 1H, H-13), 5.73 (dd, *J* = 15.6, 6.8 Hz, 1H, H-4), 5.47 (ddd, *J* = 15.6, 7.2, 1.2 Hz, 1H, H-3), 4.34 (qn, *J* = 7.2 Hz, 1H, H-2), 1.99-1.91 (m, 1H, H-5), 1.74-1.62 (m, 4H, H-6, 7, 9, 10), 1.52 (d, *J* = 7.2 Hz, 3H, H-1), 1.31-1.01 (m, 6H, H-6', 7', 8, 9', 10'); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 165.6 (C-11), 139.6 (C-4), 135.4 (C-12), 130.7 (C-13), 126.2 (C-3), 115.8 (C-14), 43.6 (C-2), 40.3 (C-5), 32.6/32.6 (C-6, C-10), 26.0/25.9 (C-7, C-8, C-9), 20.6 (C-1); **IR**: ν_{max}(film)/cm^{-1} 1689 (C=O), 1212, 882; **MS**: *m/z* (ES+) 265 $[M+H]^+$ (100%), 287 $[M+Na]^+$ (55%); **HRMS**: found 265.1369, $[M+H]^+$ requires 265.1370.

The equivalent enantioenriched (*S*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*S*)-**10a** (5:95 *e.r.*, 318 mg, 89%) was prepared from (*R*)-1-cyclohexylbut-2-en-1-ol (*R*)-**5a** (1:99 *e.r.*, 208 mg, 1.35 mmol).

$[\alpha]_D^{20}$: -48.0 (*c* 0.70, $CHCl_3$); **HPLC**: Chiralpak AD-H, Hexane/*i*-PrOH 97:3, 1.0 mL/min, minor 15.3 min, major 20.3 min (214.4 nm, 254.4 nm).

The other enantiomer (*R*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (*R*)-**10a** (88:12 *e.r.*, 1.18 g, 90%) was prepared from (*S*)-1-cyclohexylbut-2-en-1-ol (*S*)-**5a** (88:12 *e.r.*, 763 mg, 4.95 mmol).

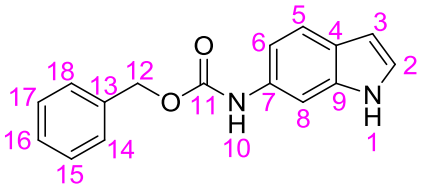
11l: *N*-Methyl-1*H*-indol-6-amine.[6]



To a solution of benzyl 1*H*-indol-6-ylcarbamate **11l'** (1.19 g, 4.47 mmol, 1.0 eq) in THF (18.0 mL) at 0 °C was added $LiAlH_4$ (1.0 M in Et_2O, 1.5 eq) dropwise. The reaction was warmed to rt and heated to reflux for 4 h. At rt, water (0.5 mL) was carefully added followed by NaOH 15% (20.0 mL) and a solution of Rochelle's salt (10.0 mL). The layers were separated and the aqueous layer was extracted with EtOAc (x3). The combined organic fractions were washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (Pet/EtOAc 9:1 to 2:8) afforded the title compound as a brown oil (499 mg, 76%).

R_f: 0.16 (Pet/EtOAc 1:1); **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 7.89 (bs, 1H, H-1), 7.42 (d, J = 8.4 Hz, 1H, H-5), 7.00 (dd, J = 3.1, 2.4 Hz, 1H, H-2), 6.58 (bs, 1H, H-8), 6.54 (dd, J = 8.4, 2.1 Hz, 1H, H-6), 6.43 (ddd, J = 3.0, 2.1, 0.8 Hz, 1H, H-3), 3.67 (bs, 1H, H-10), 2.88 (s, 3H, H-11); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 145.9 (C-7), 137.4 (C-9), 121.5 (C-2), 121.1 (C-5), 120.2 (C-4), 109.9 (C-6), 102.4 (C-3), 92.5 (C-8), 31.5 (C-11); **IR**: ν_{max}(film)/cm^{-1} 3403 (NH), 1629 (C=C), 1516 (C=C_{Ar}), 801, 717; **MS**: *m/z* (ES$^+$) 147 $[M+H]^+$ (90%); **HRMS**: found 147.0922, $[M+H]^+$ requires 147.0917.

11l': Benzyl 1*H*-indol-6-ylcarbamate.[6]

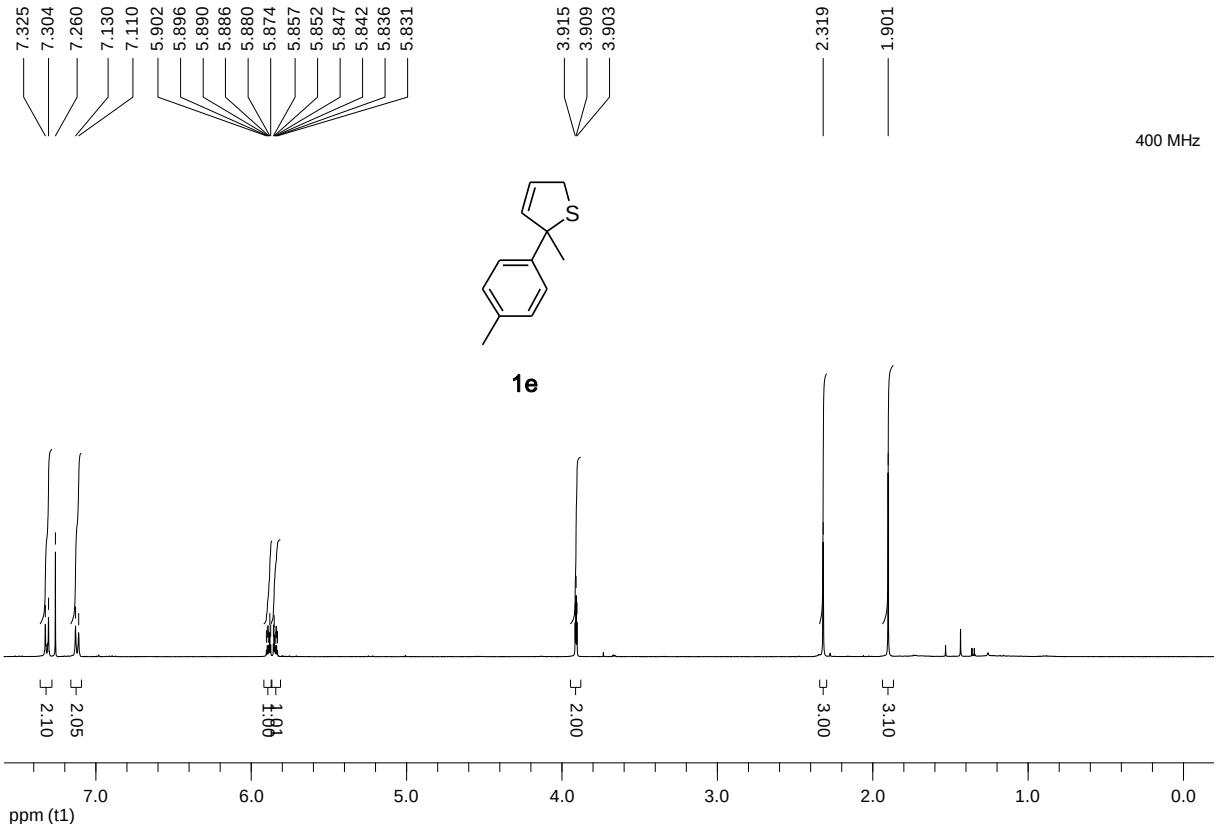


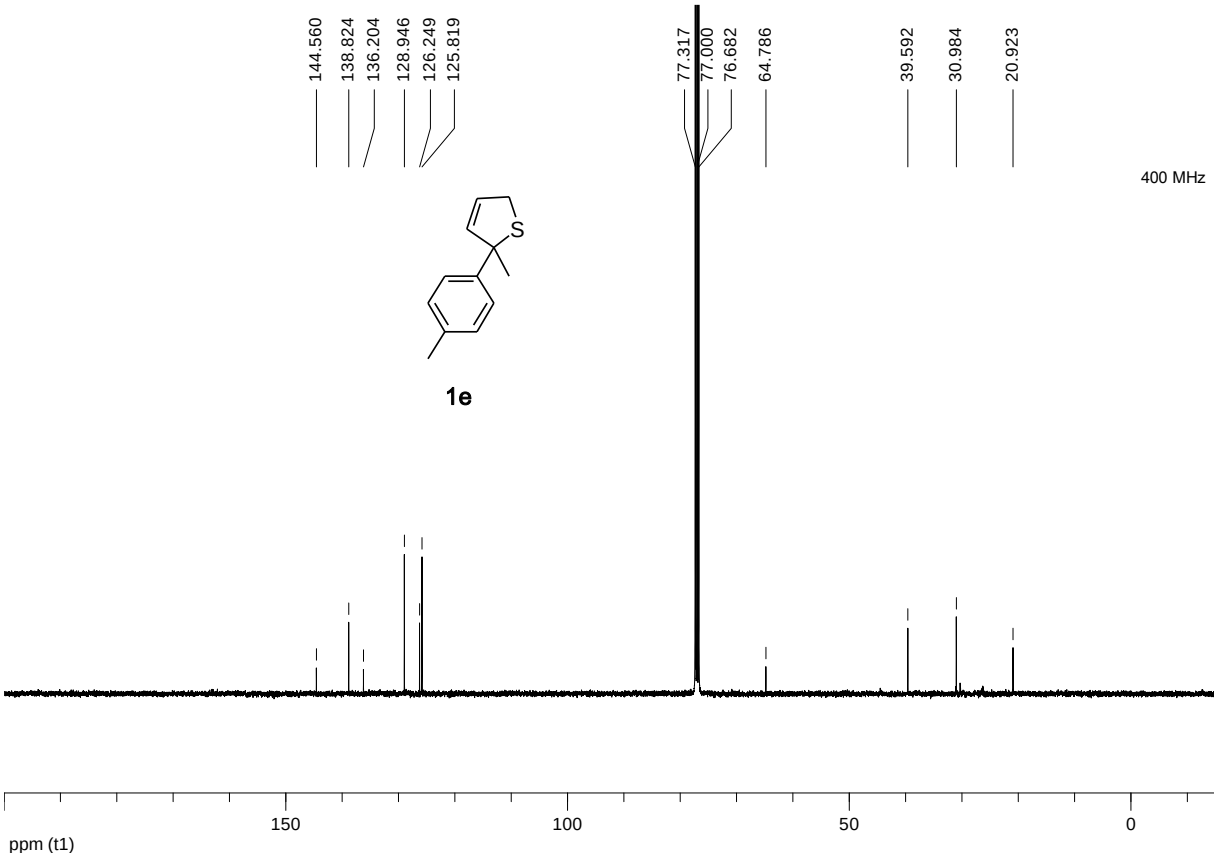
To a solution of 1*H*-indol-6-amine (500 mg, 3.78 mmol, 1.0 eq) and pyridine (2.6 eq) in CH_2Cl_2 (4.0 mL) at 0 °C was added benzyl chloroformate (2.4 eq) dropwise. The reaction was warmed to rt and stirred for 24 h. Saturated aqueous $NaHCO_3$ (10 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification by column

chromatography (Pet/EtOAc 95:5 to 7:3) afforded the title compound as a beige/yellow solid (968 mg, 96%).

R_f: 0.28 (Pet/EtOAc 8:2); **mp**: 133-135 °C; **^{1}H NMR**: (400 MHz; $CDCl_3$) δ (ppm) 8.13 (bs, 1H, H-1), 7.84 (bs, 1H, H-8), 7.52 (d, J = 8.4 Hz, 1H, H-5), 7.44-7.32 (m, 5H, H-14, H-15, H-16, H-17, H-18), 7.16 (dd, J = 3.2, 2.4 Hz, 1H, H-2), 6.81 (dd, J = 8.4, 1.9 Hz, 1H, H-6), 6.72 (bs, 1H, H-10), 6.49 (ddd, J = 3.2, 2.0, 0.9 Hz, 1H, H-3), 5.22 (s, 1H, H-12); **^{13}C NMR**: (100 MHz, $CDCl_3$) δ (ppm) 153.6 (C-11), 136.2/136.1 (C-9, C-13), 132.6 (C7), 128.6/128.3 (C-14, C-15, C-16, C-17, C-18), 124.3 (C-4), 124.1 (C-2), 120.8 (C-5), 112.6 (C-6), 102.4 (C-3), 101.5 (C-8), 66.9 (C-12); **IR**: ν_{max}(film)/cm^{-1} 3384 (NH), 3331 (NH), 1700 (C=O), 1527 (C=C_{Ar}), 1235, 1053, 720, 696; **MS**: *m/z* (ES^+) 289 $[M+Na]^+$ (100%); **HRMS**: found 267.1120, $[M+H]^+$ requires 267.1128.

^{1}H and ^{13}C NMR spectra

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30.984
20.923
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1e
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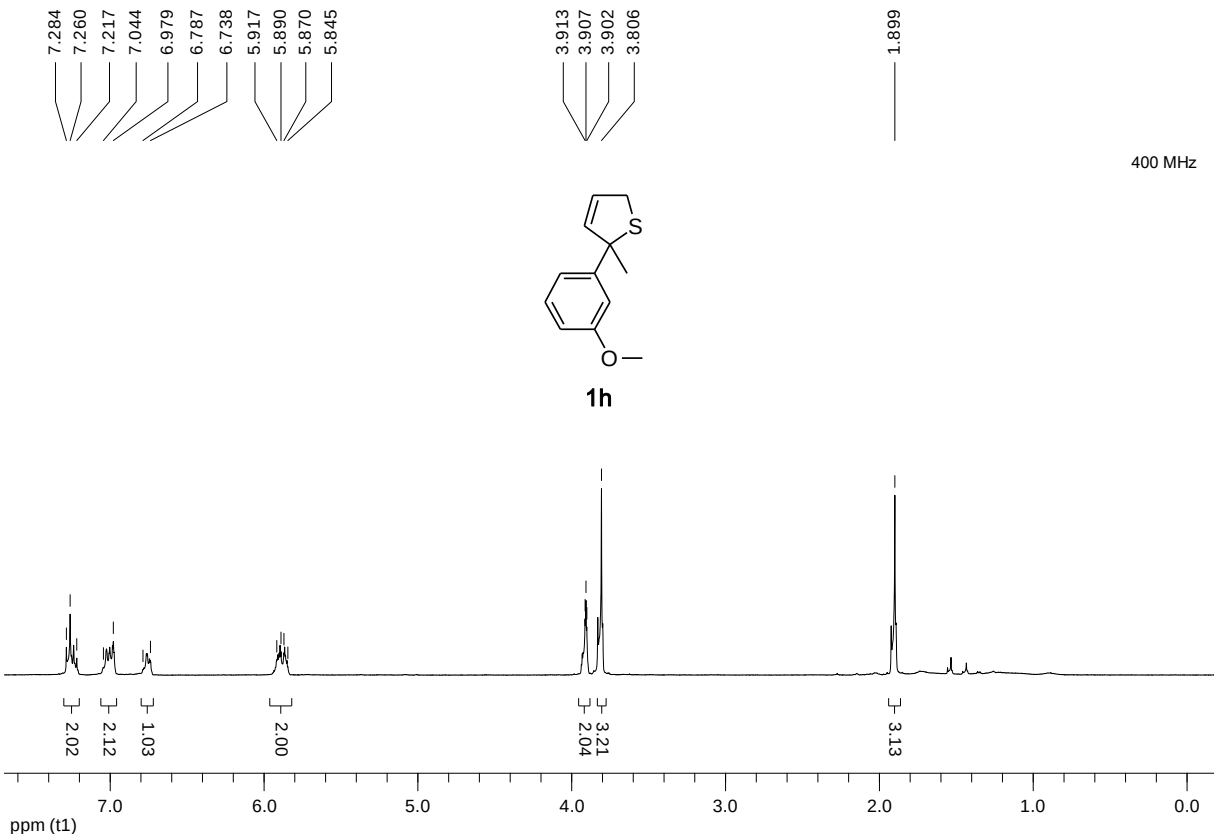
100
50
0
ppm (t1)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3.913
3.907
3.902
3.806
1.899
400 MHz
S
O
1h
2.02
2.12
1.03
2.00
2.04
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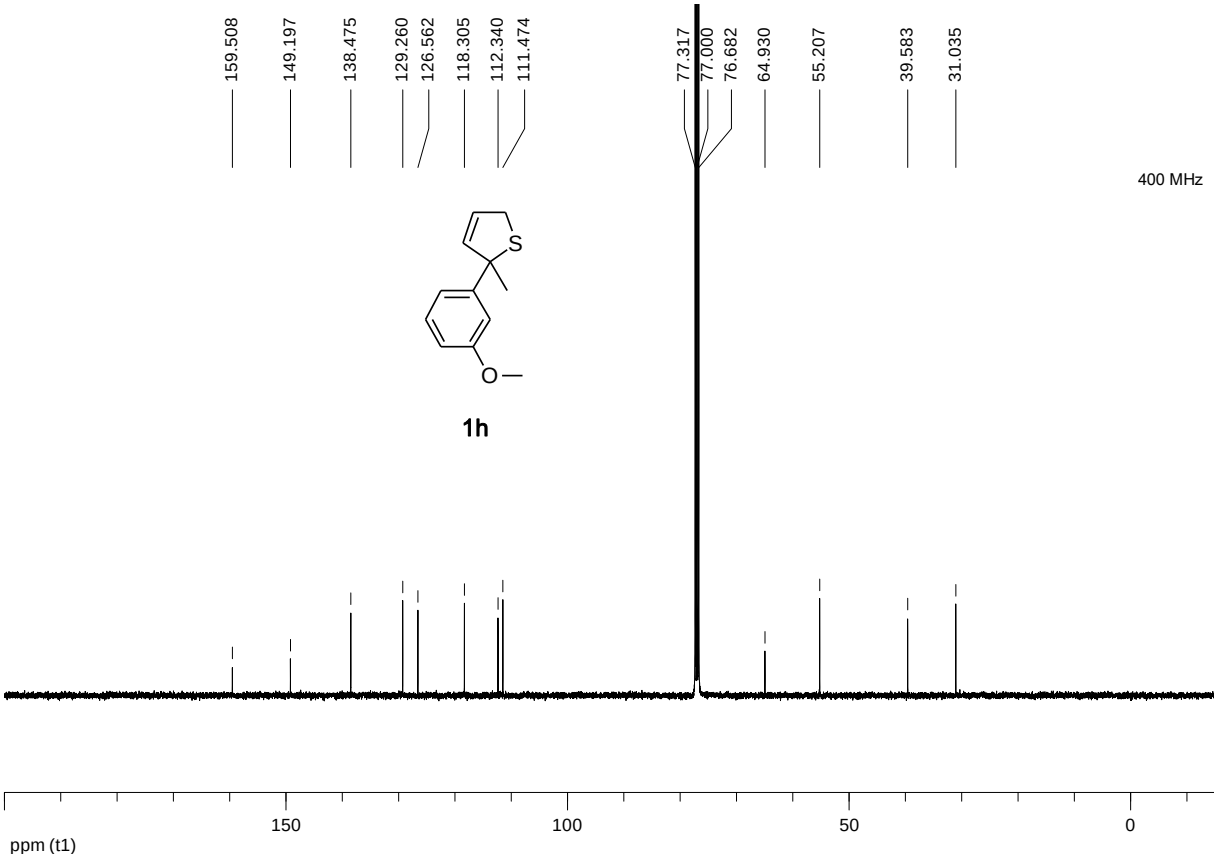
ppm (t1)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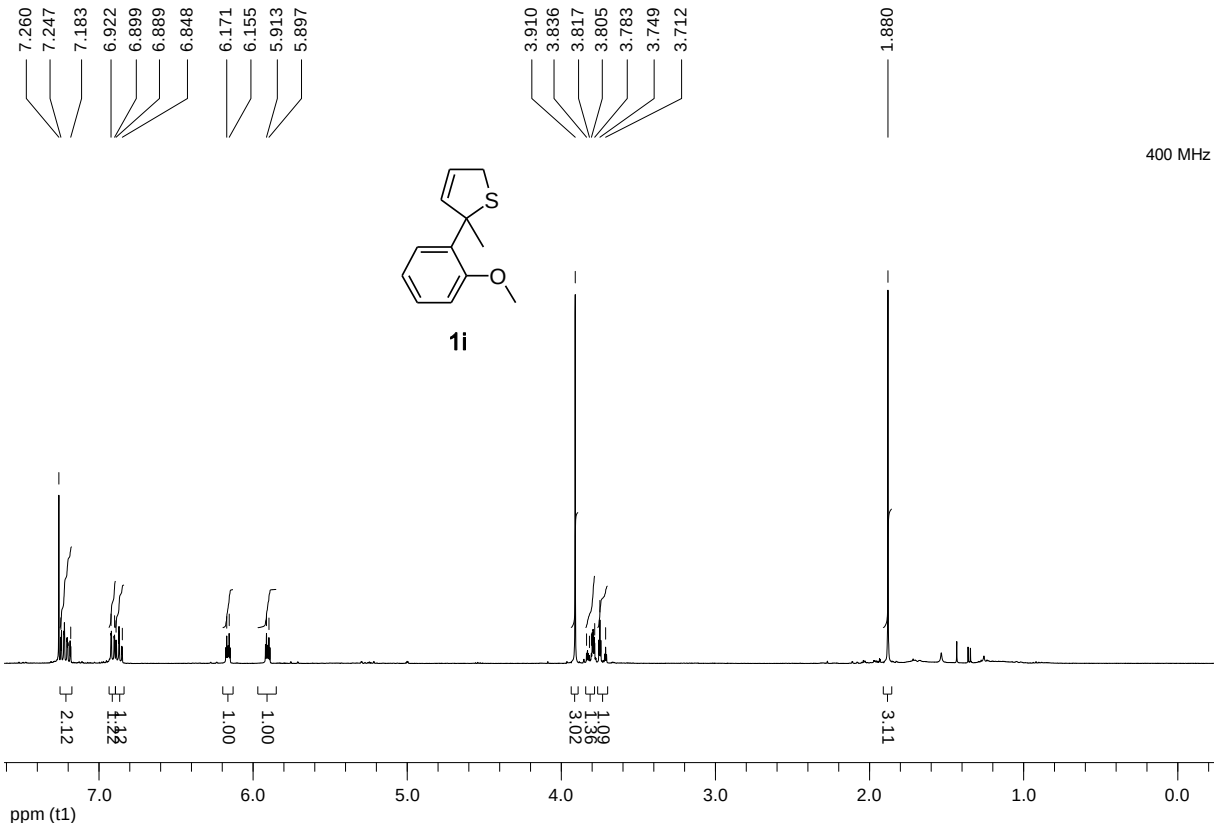
ppm (t1)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6.171
6.155
5.913
5.897
3.910
3.836
3.817
3.805
3.783
3.749
3.712
1.880
400 MHz
S
O
1i
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1.22
1.00
1.00
3.02
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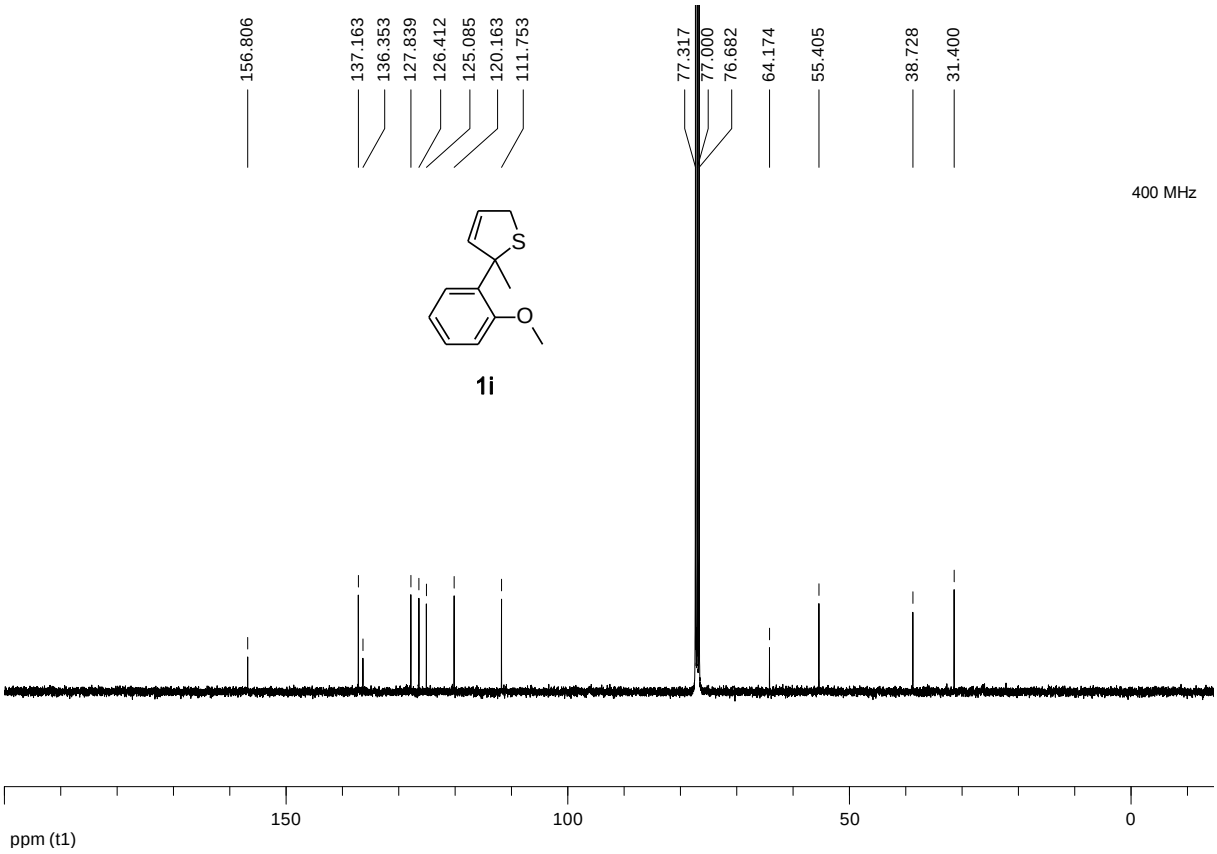
ppm (t1)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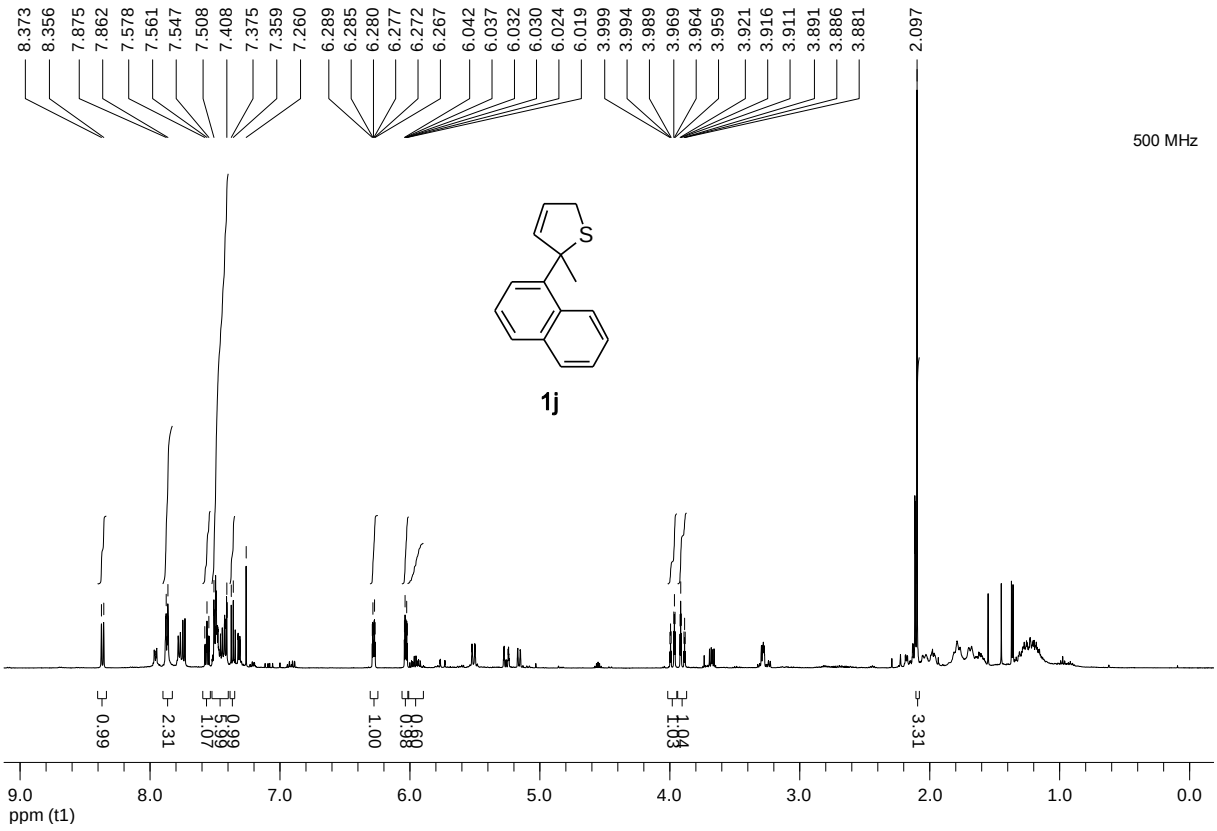
50
0
ppm (t1)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7.561
7.547
7.508
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6.285
6.280
6.277
6.272
6.267
6.042
6.037
6.032
6.030
6.024
6.019
3.999
3.994
3.989
3.969
3.964
3.959
3.921
3.916
3.911
3.891
3.886
3.881
2.097
500 MHz
S
1j
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2.31
1.07
0.89
1.00
0.88
1.08
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6.0
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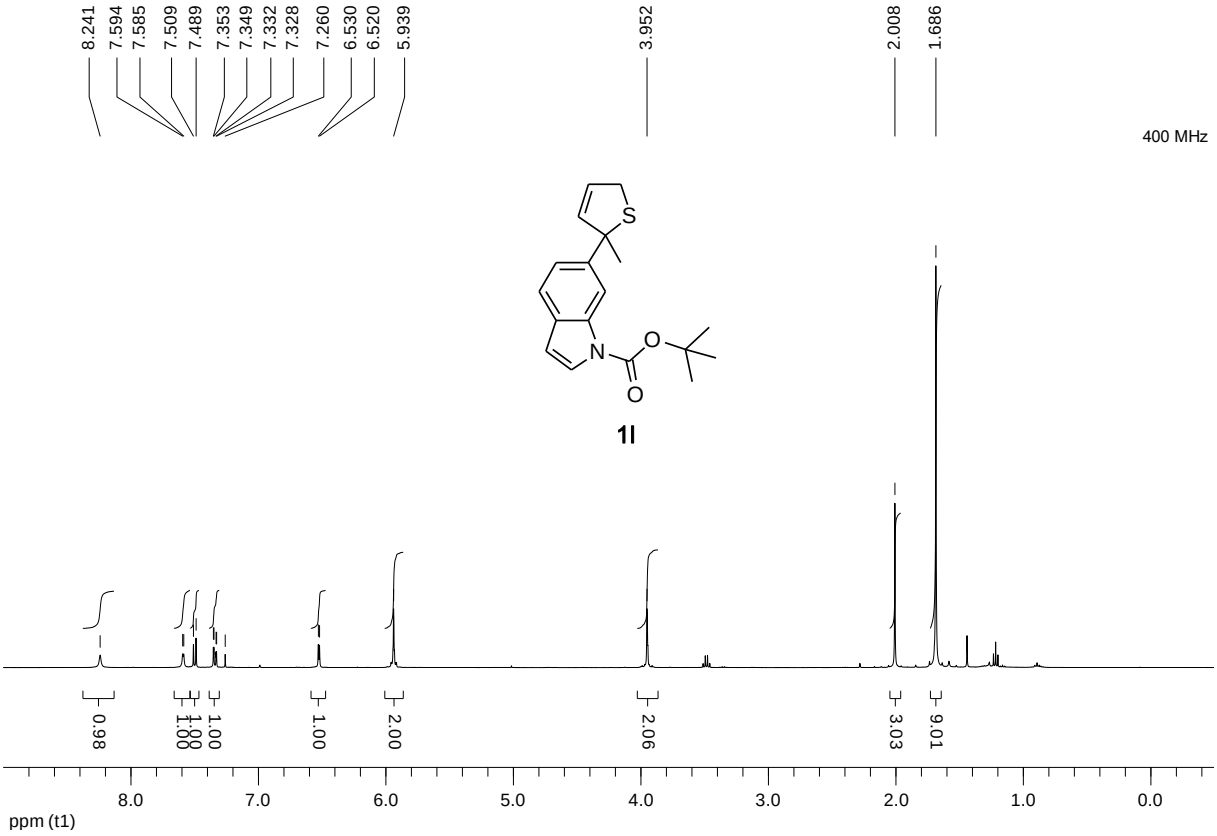
ppm (t1)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7.509
7.489
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7.332
7.328
7.260
6.530
6.520
5.939
3.952
2.008
1.686
400 MHz
S
N
O
O
1l
0.98
1.00
1.00
1.00
1.00
2.00
2.06
3.03
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6.0
5.0
4.0
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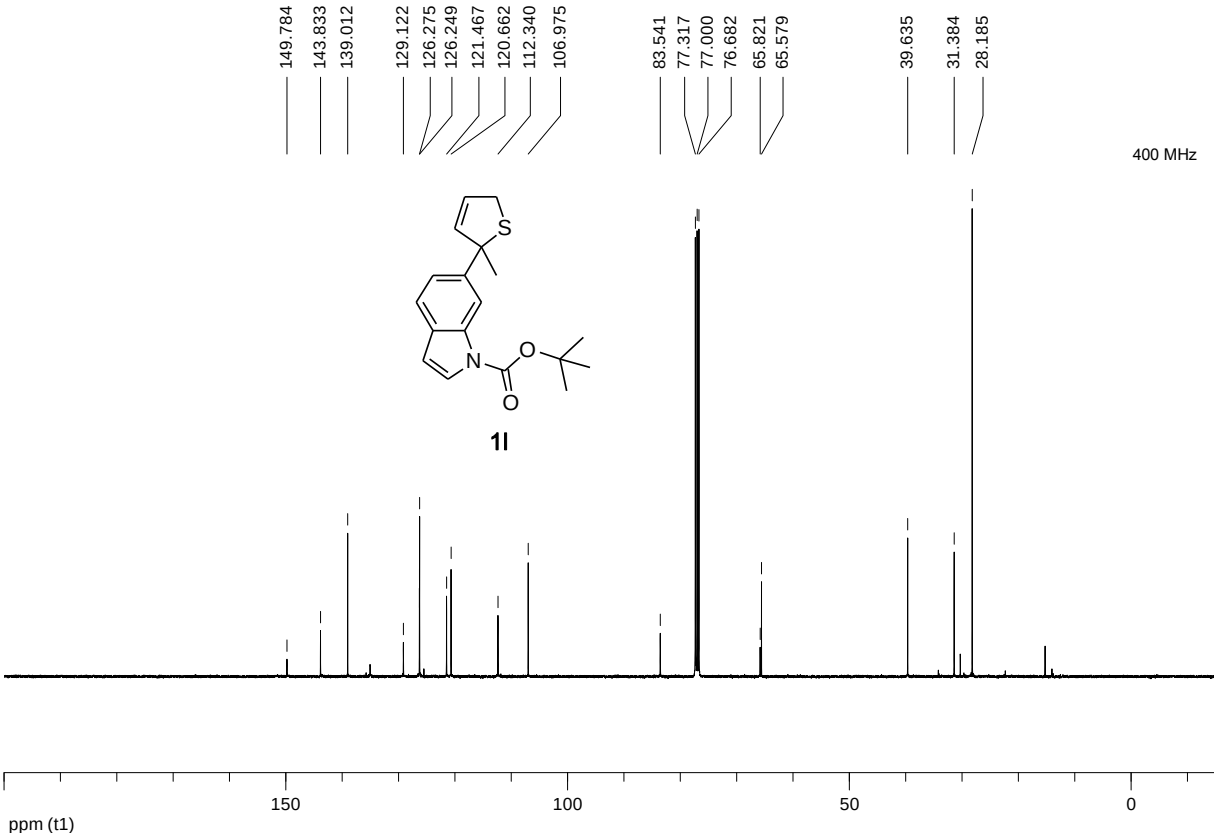
2.0
1.0
0.0
ppm (t1)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120.662
112.340
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76.682
65.821
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28.185
400 MHz
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N
O
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1l
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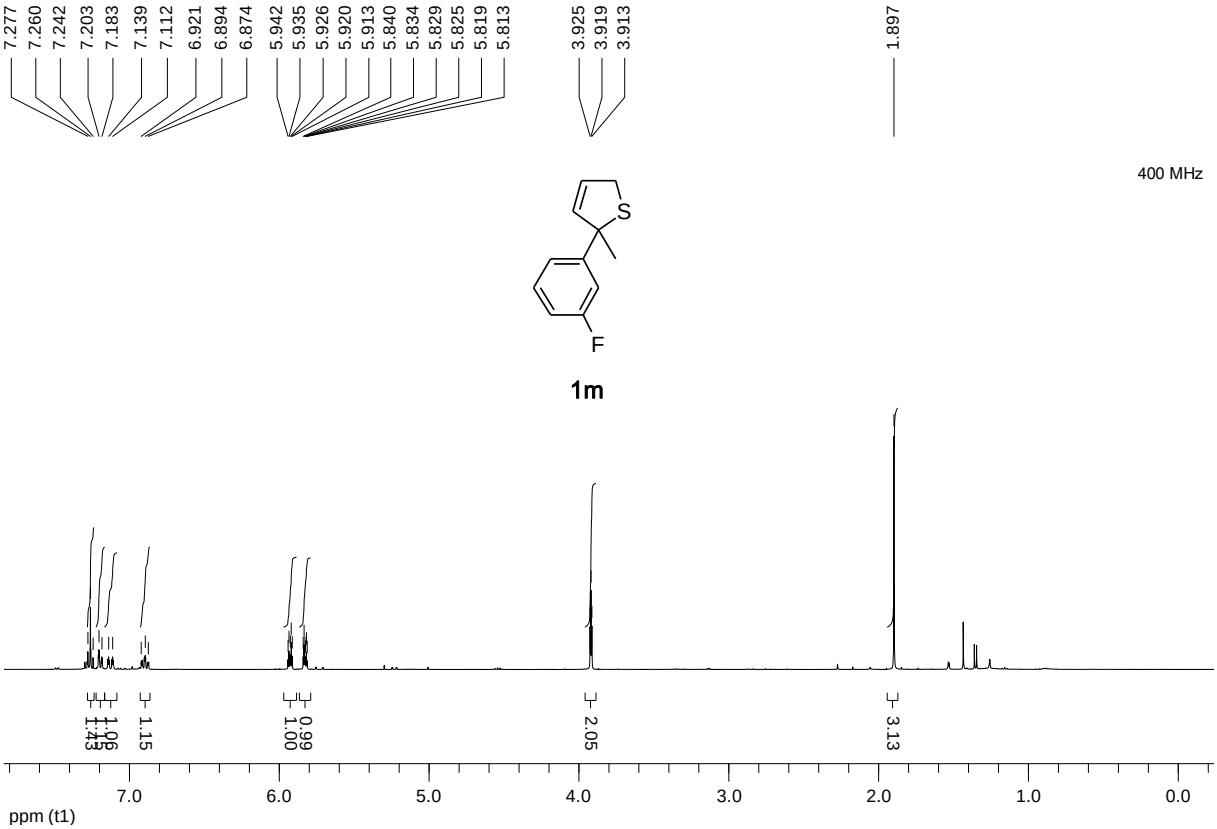
100
50
0
ppm (t1)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5.819
5.813
3.925
3.919
3.913
1.897
400 MHz
S
F
1m
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1.06
1.15
1.00
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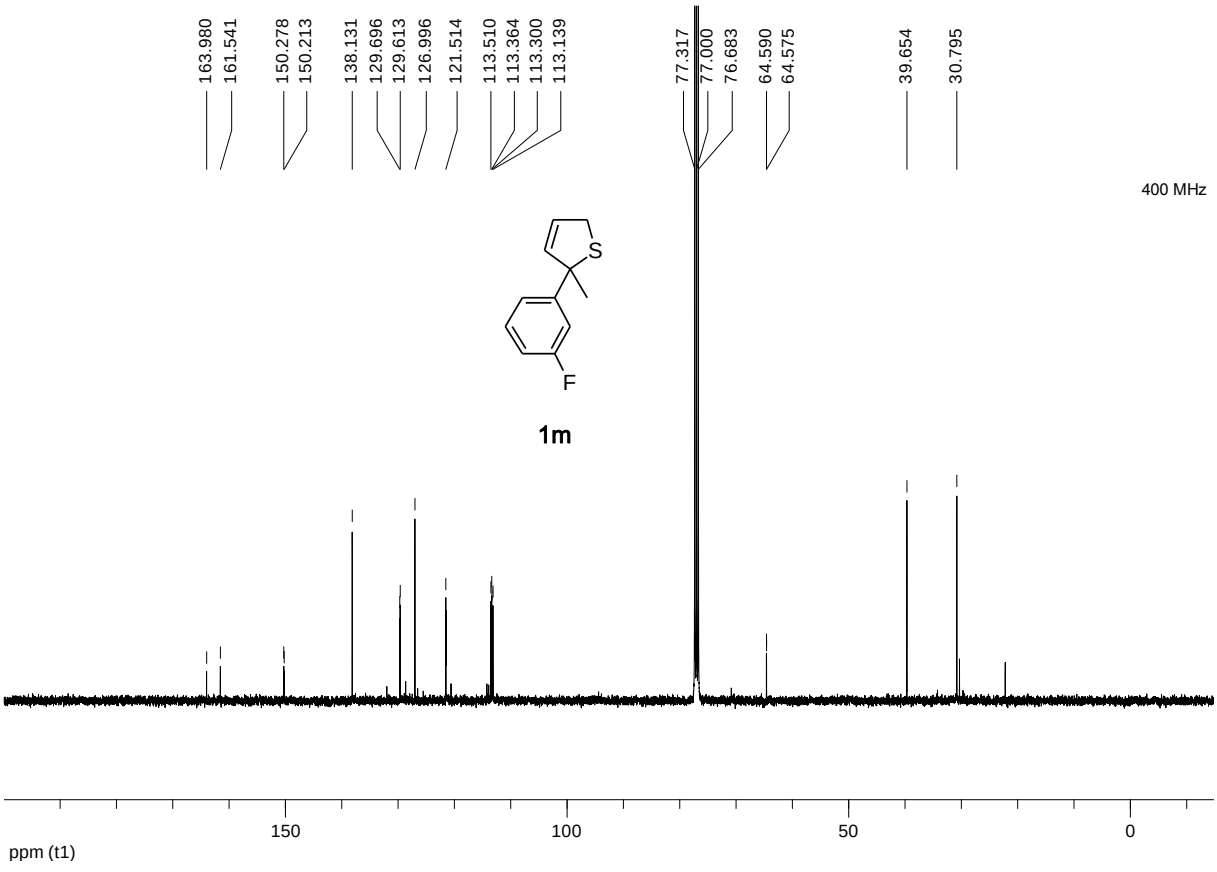
ppm (t1)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77.317
77.000
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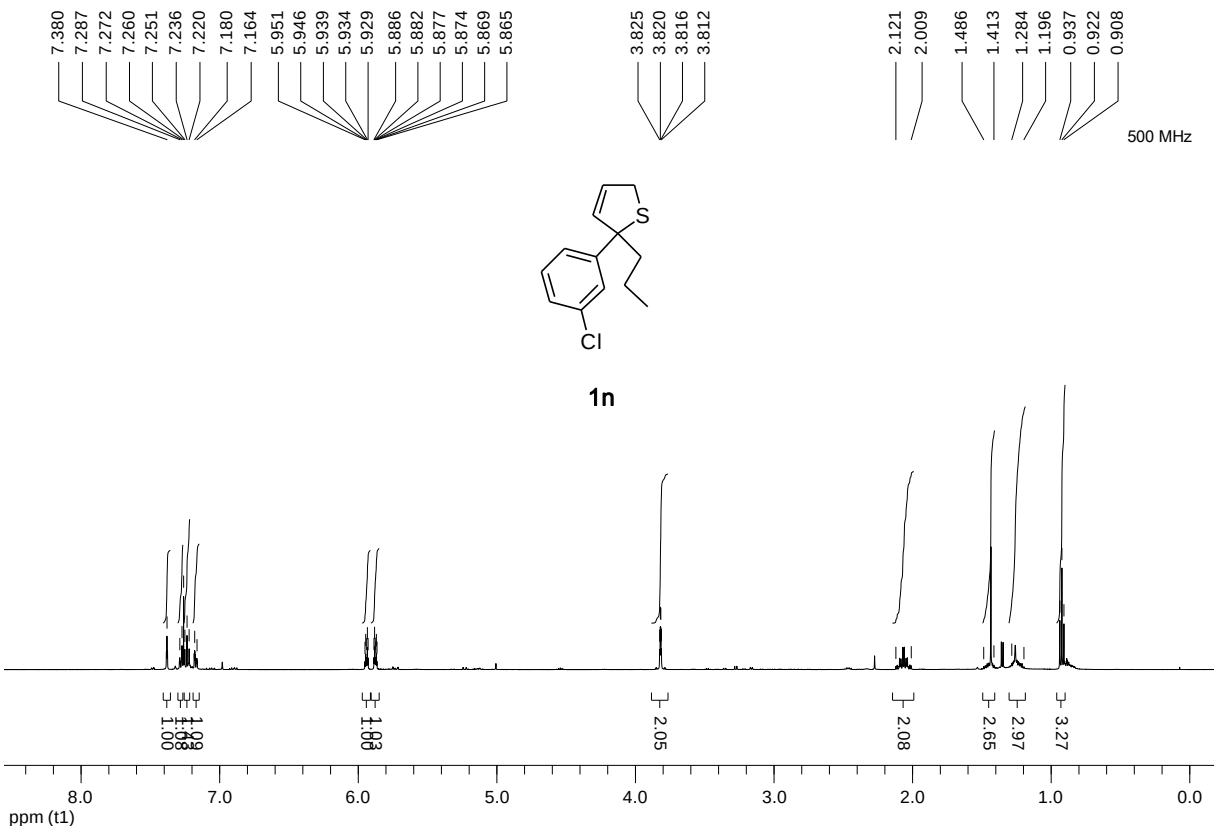
ppm (t1)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5.929
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5.882
5.877
5.874
5.869
5.865
3.825
3.820
3.816
3.812
2.121
2.009
1.486
1.413
1.284
1.196
0.937
0.922
0.908
500 MHz
S
Cl
1n
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1.09
1.03
2.05
2.08
2.65
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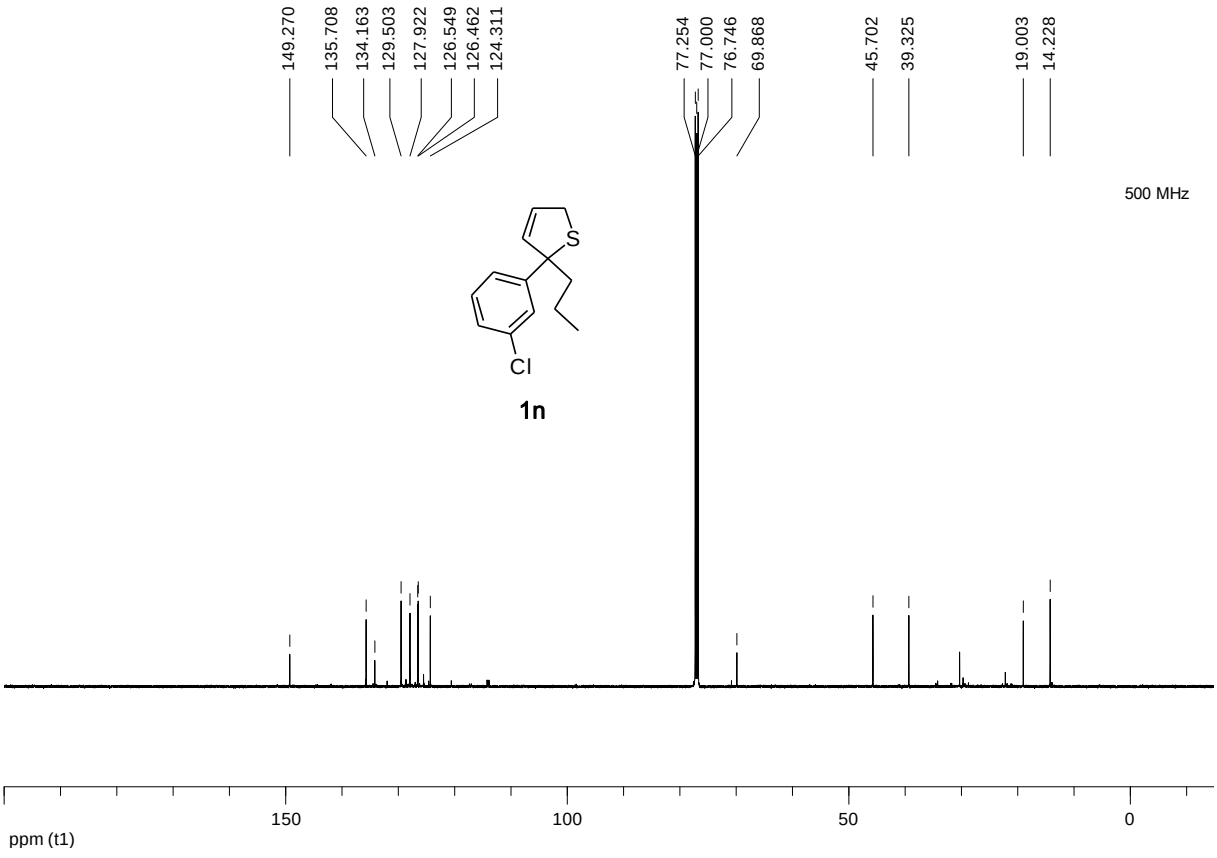
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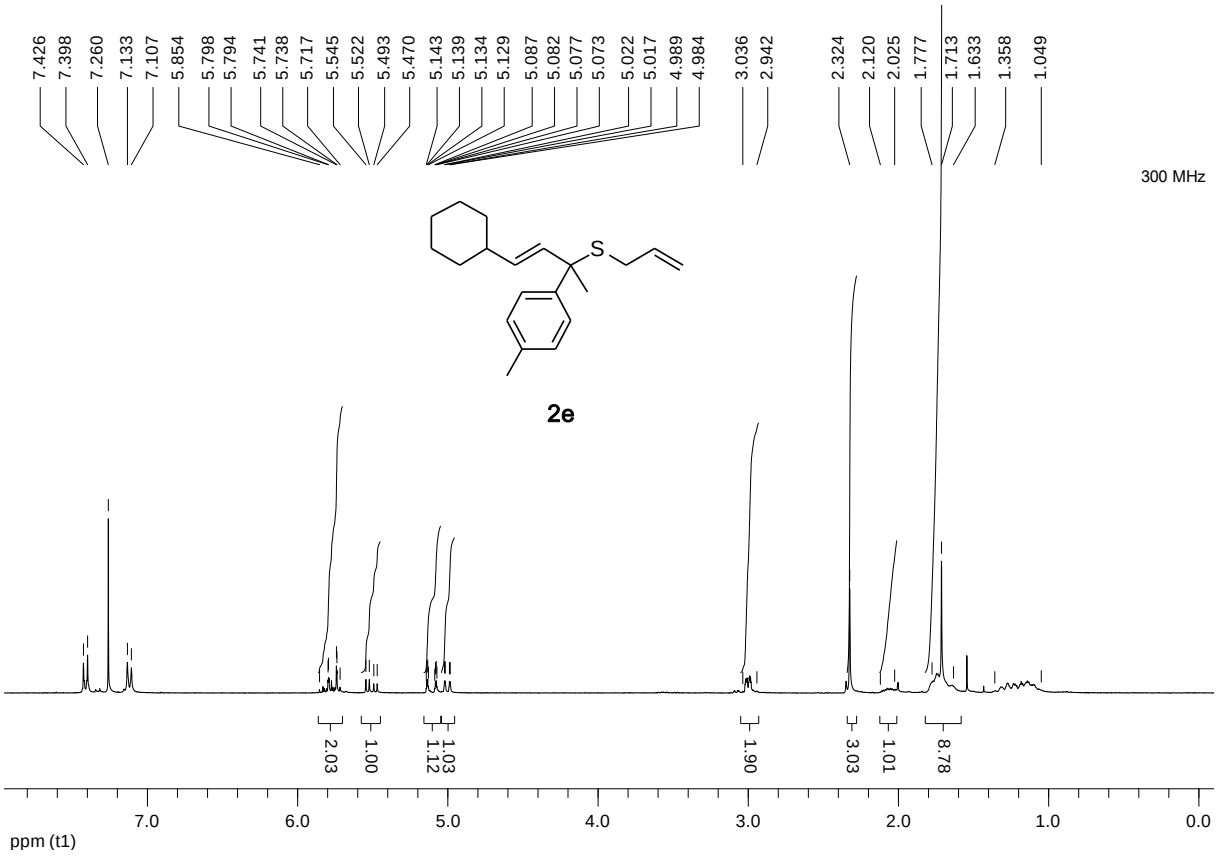
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5.077
5.073
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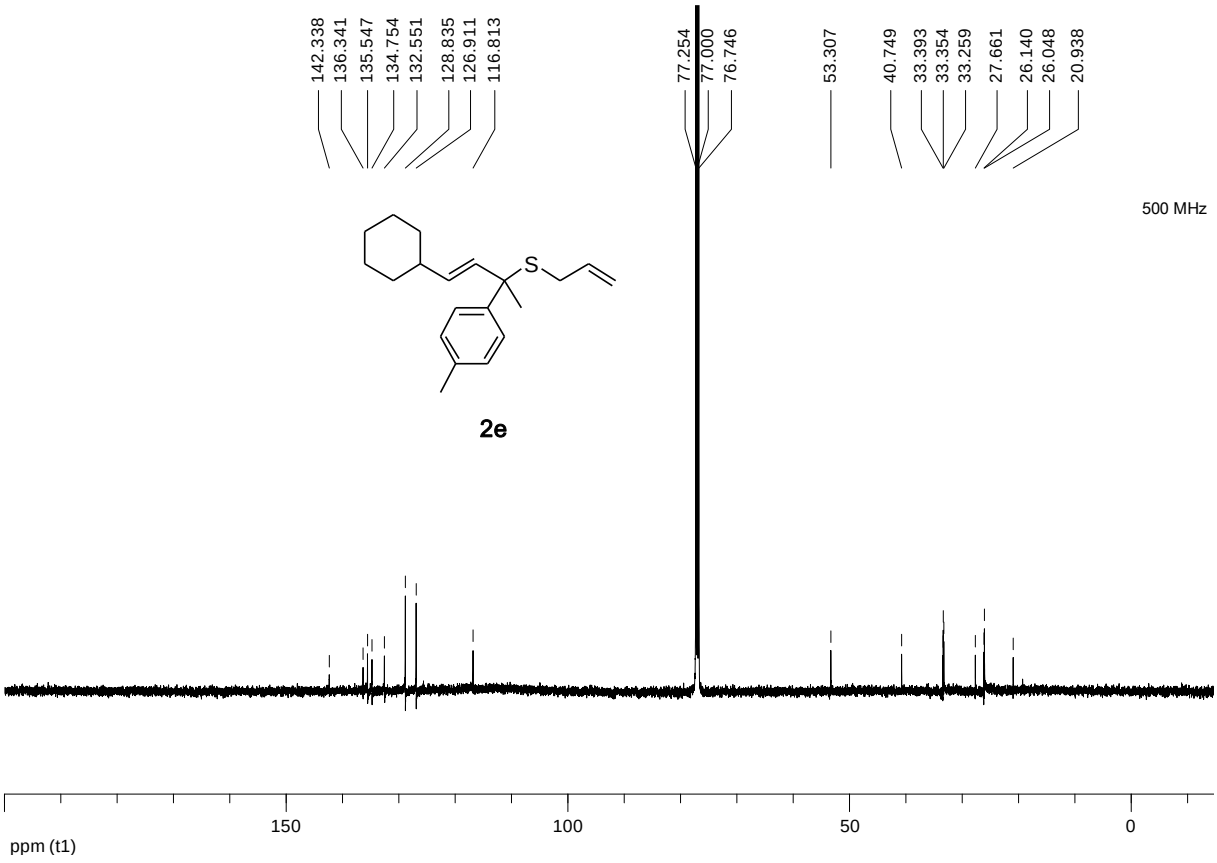
ppm (t1)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40.749
33.393
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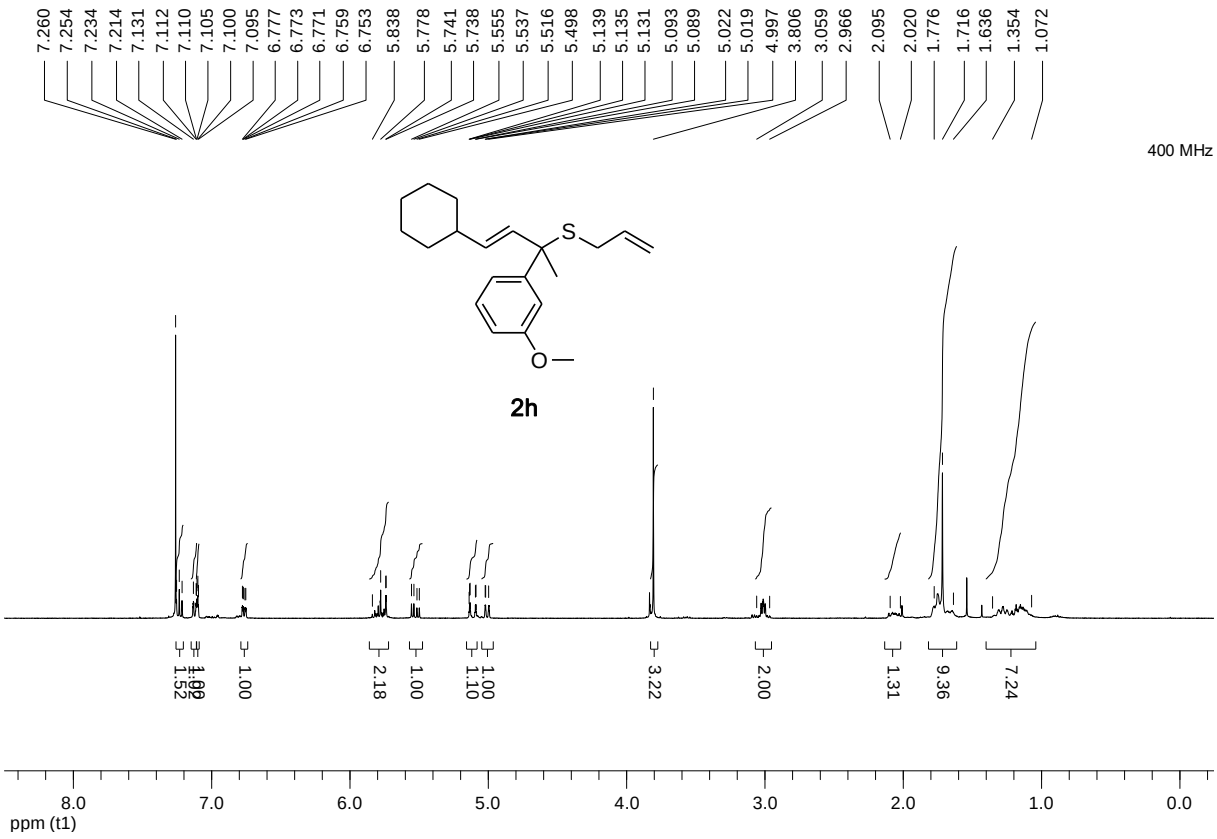
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5.838
5.778
5.741
5.738
5.555
5.537
5.516
5.498
5.139
5.135
5.131
5.093
5.089
5.022
5.019
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3.806
3.059
2.966
2.095
2.020
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1.716
1.636
1.354
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O
2h
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1.00
1.10
3.22
2.00
1.31
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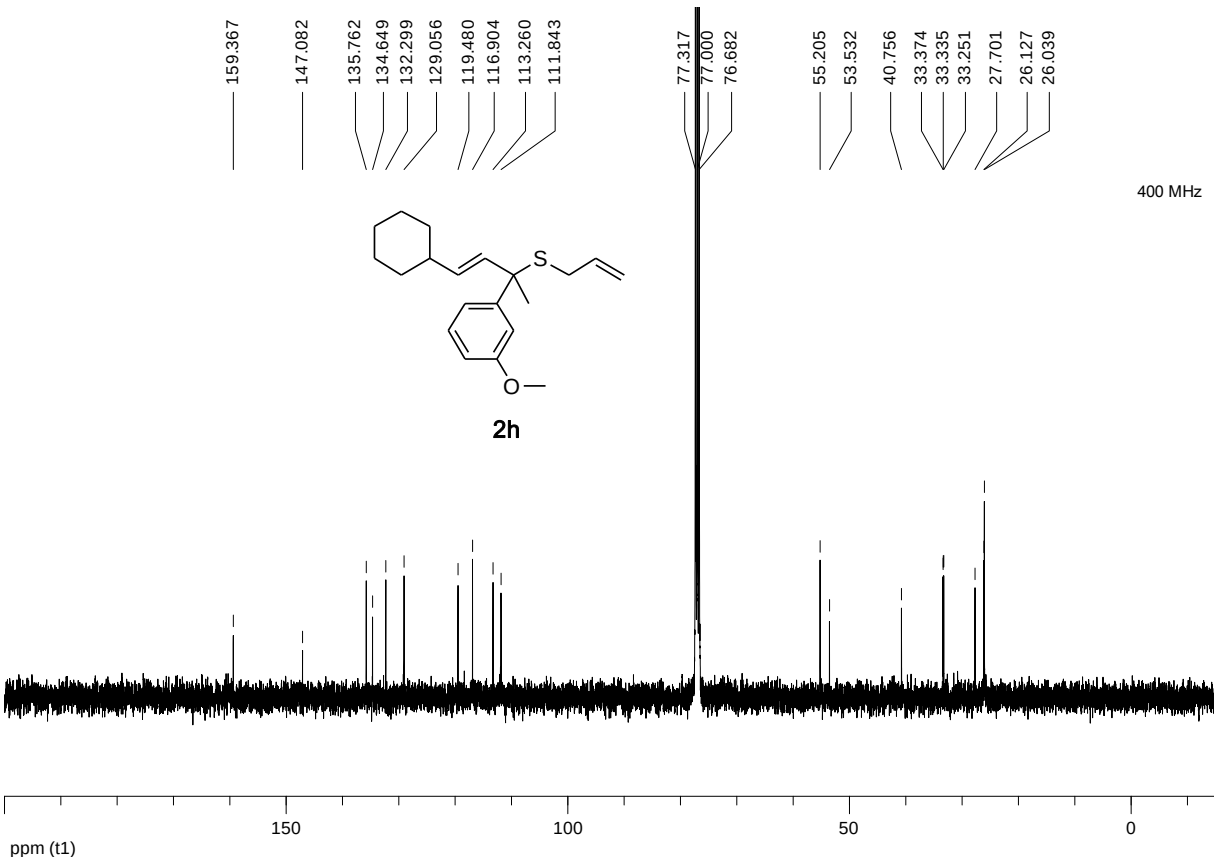
ppm (t1)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40.756
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33.335
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2h
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100
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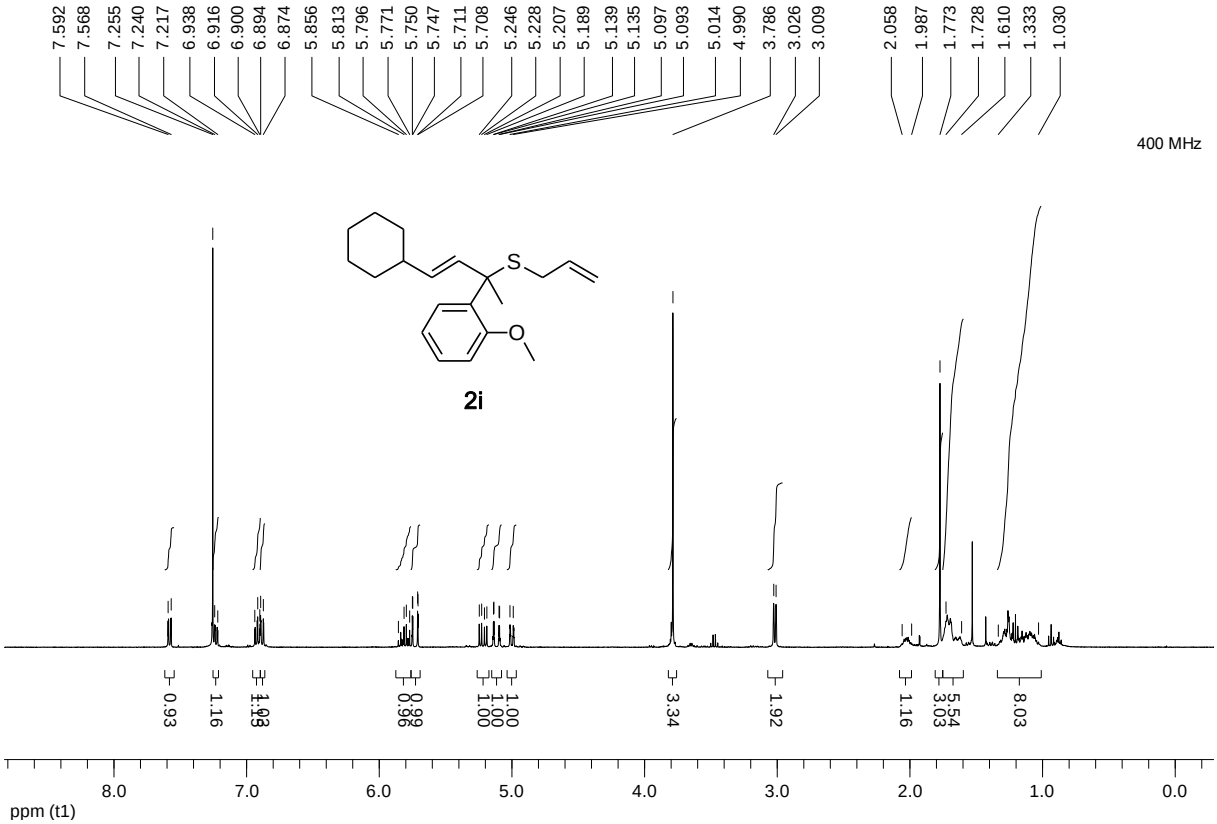
ppm (t1)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5.097
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1.773
1.728
1.610
1.333
1.030
400 MHz
S
O
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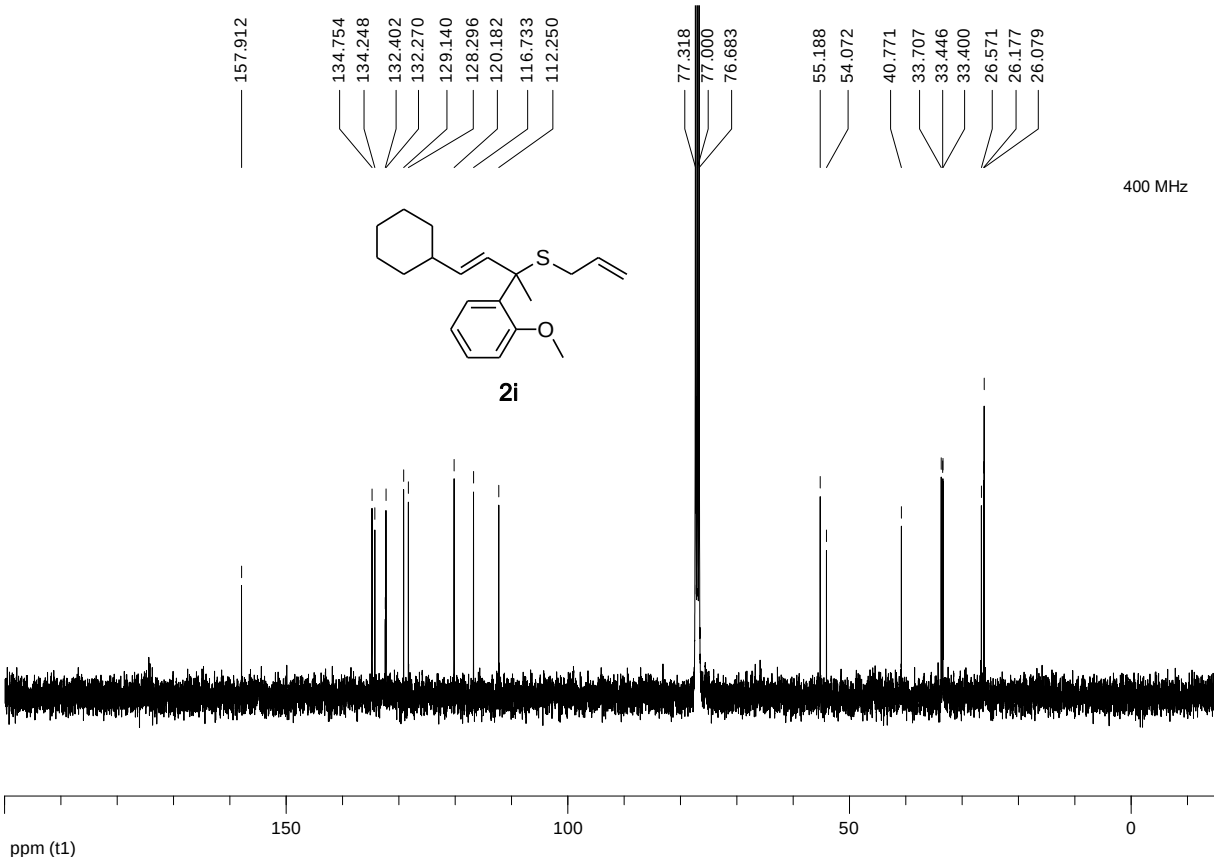
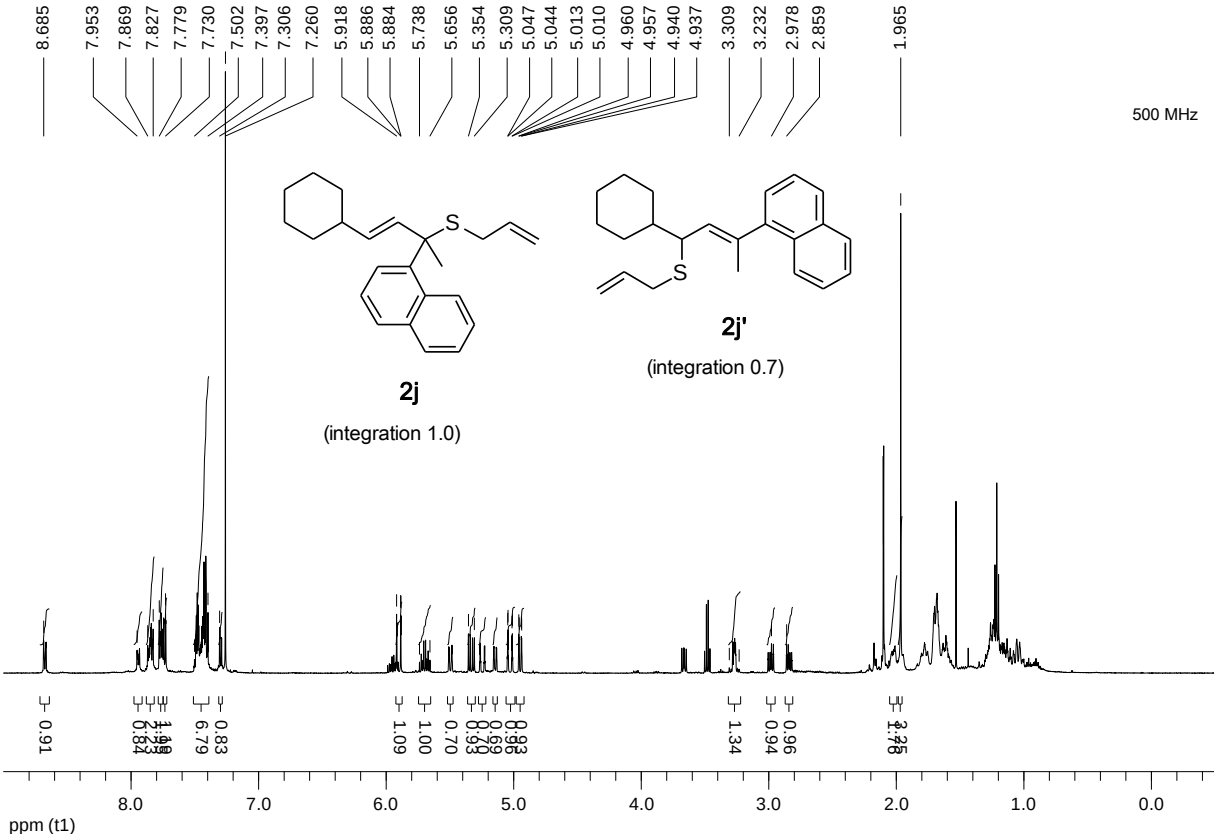
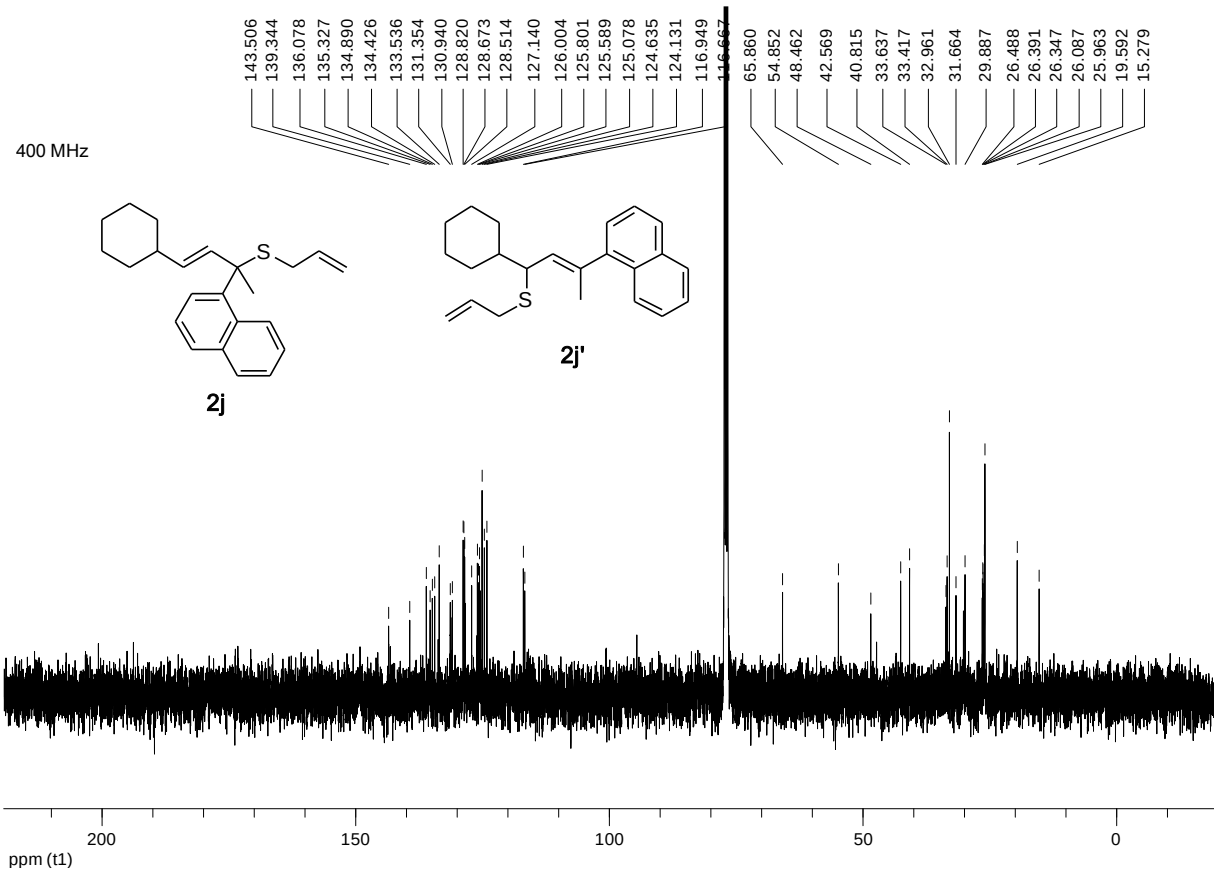
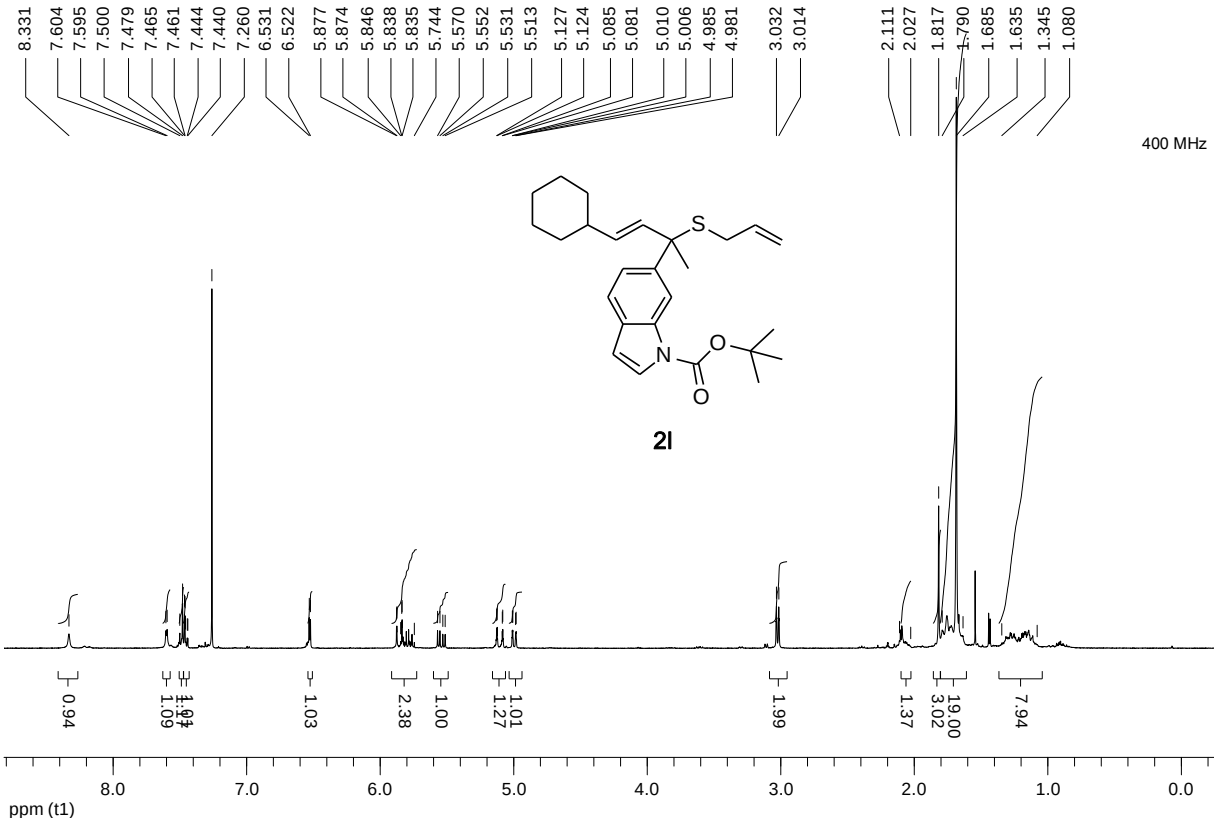
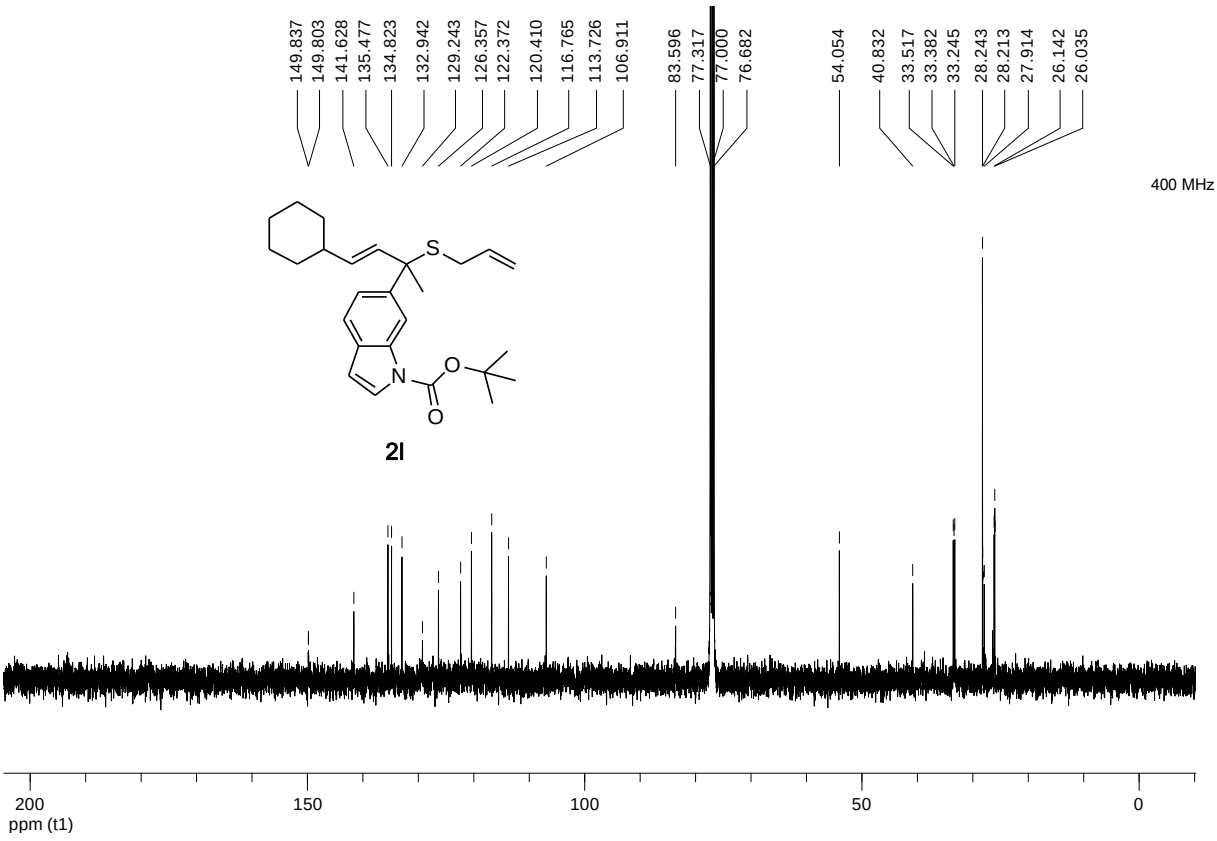
1.98
0.98
0.98
1.00
1.00
1.00
3.34
1.92
1.16
3.03
5.54
8.03
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

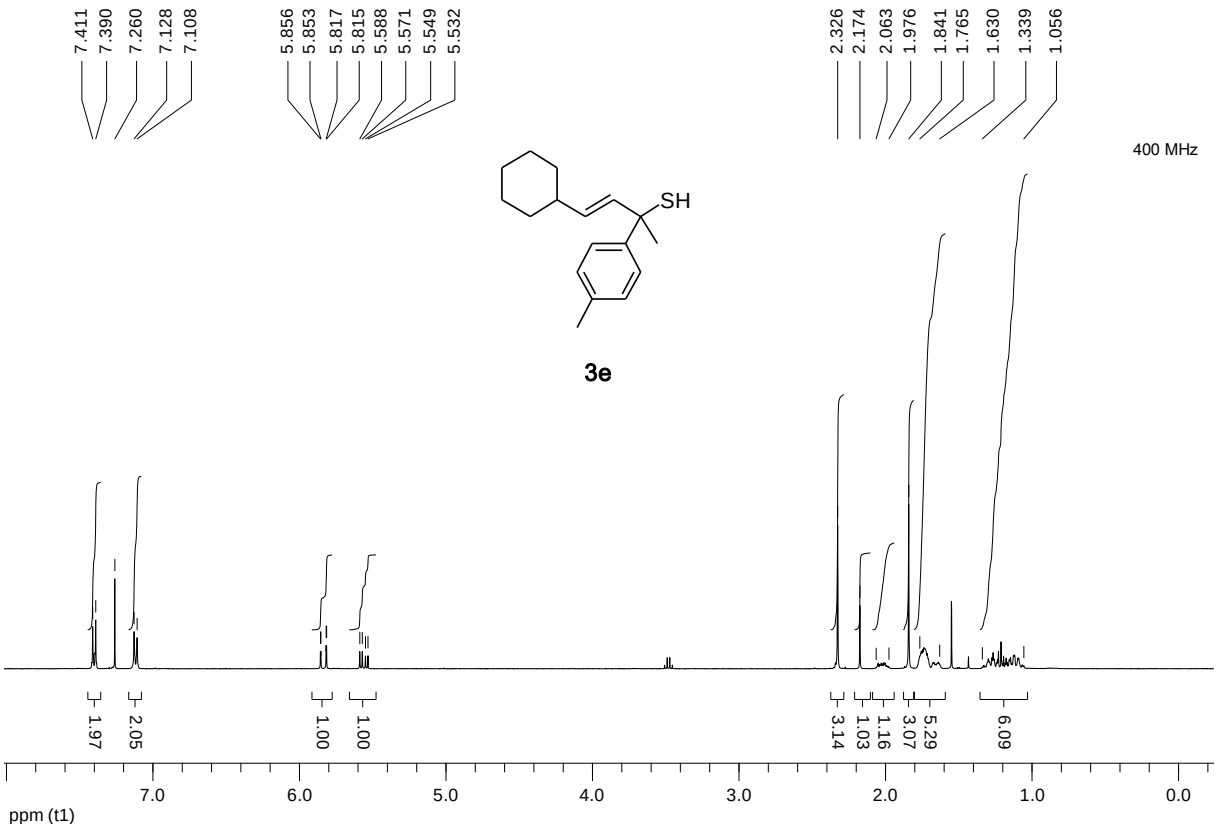

157.912
134.754
134.248
132.402
132.270
129.140
128.296
120.182
116.733
112.250
77.318
77.000
76.683
55.188
54.072
40.771
33.707
33.446
33.400
26.571
26.177
26.079
400 MHz
S
O
2i
150
100
50
0
ppm (t1)

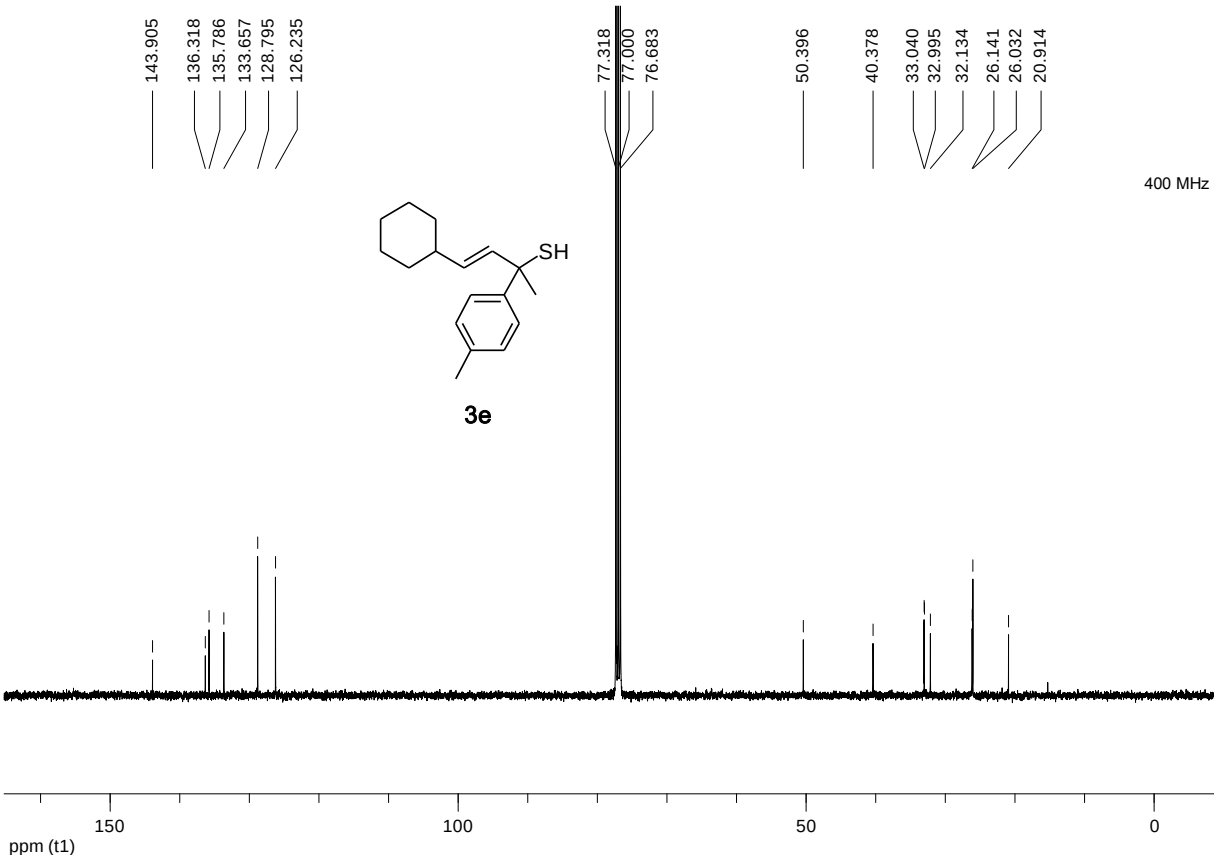

8.685
7.953
7.869
7.827
7.779
7.730
7.502
7.397
7.306
7.260
5.918
5.886
5.884
5.738
5.656
5.354
5.309
5.047
5.044
5.013
5.010
4.960
4.957
4.940
4.937
3.309
3.232
2.978
2.859
1.965
500 MHz
2j
(integration 1.0)
2j'
(integration 0.7)
0.91
6.79
0.83
1.09
1.00
0.70
1.34
0.94
0.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

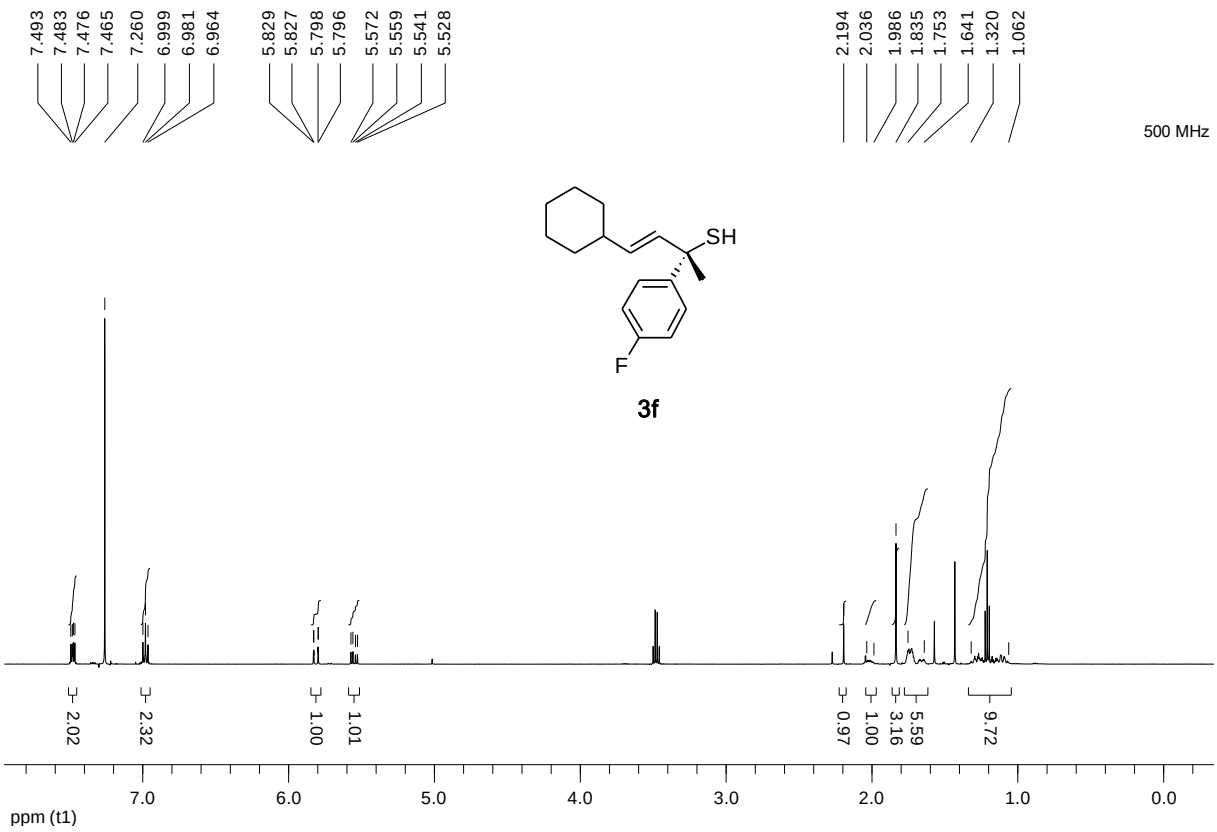

143.506
139.344
136.078
135.327
134.890
134.426
133.536
131.354
130.940
128.820
128.673
128.514
127.140
126.004
125.801
125.589
125.078
124.635
124.131
116.949
65.860
54.852
48.462
42.569
40.815
33.637
33.417
32.961
31.664
29.887
26.488
26.391
26.347
26.087
25.963
19.592
15.279
400 MHz
2j
2j'
200
150
100
50
0
ppm (t1)

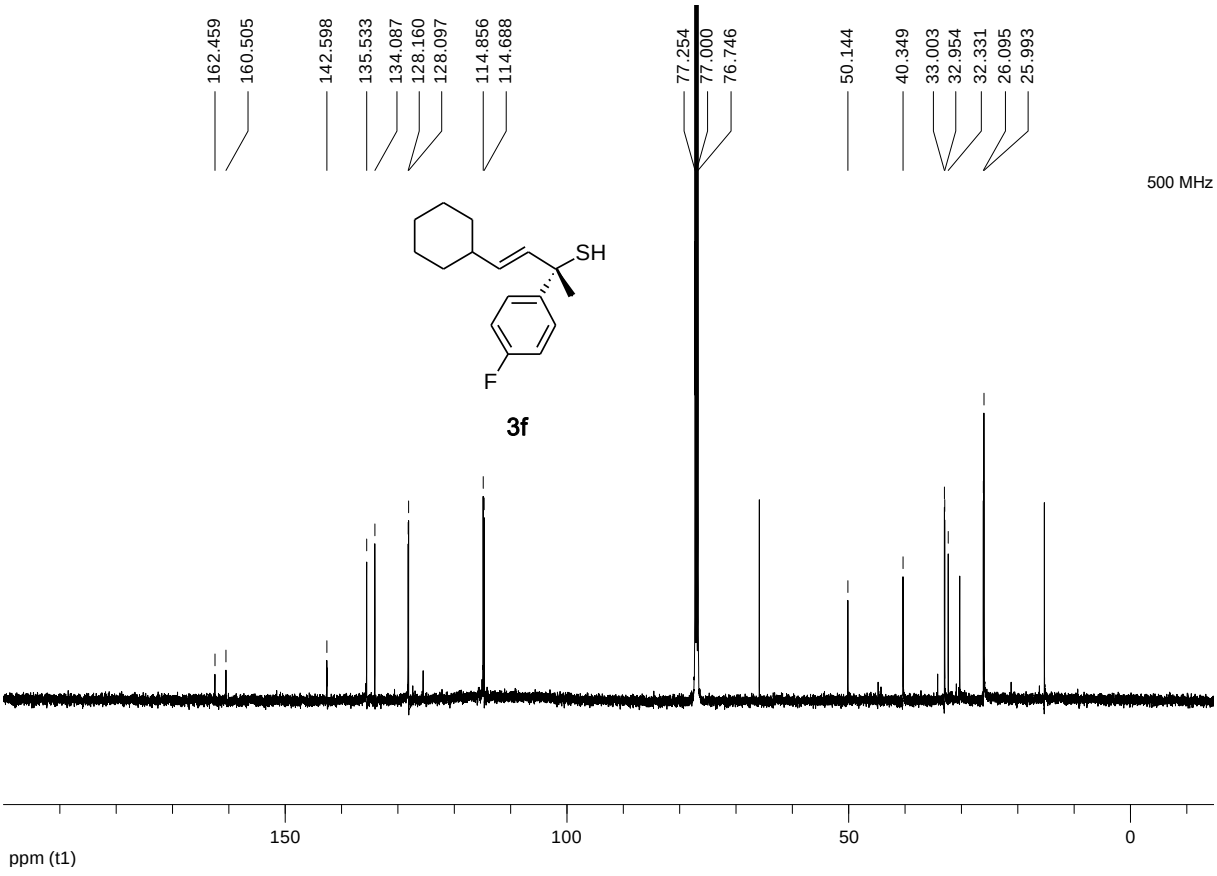

8.331
7.604
7.595
7.500
7.479
7.465
7.461
7.444
7.440
7.260
6.531
6.522
5.877
5.874
5.846
5.838
5.835
5.744
5.570
5.552
5.531
5.513
5.127
5.124
5.085
5.081
5.010
5.006
4.985
4.981
3.032
3.014
2.111
2.027
1.817
1.790
1.685
1.635
1.345
1.080
400 MHz
S
N
O
O
2l
0.94
1.09
1.03
2.38
1.00
1.27
1.01
1.99
1.37
19.00
3.02
7.94
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

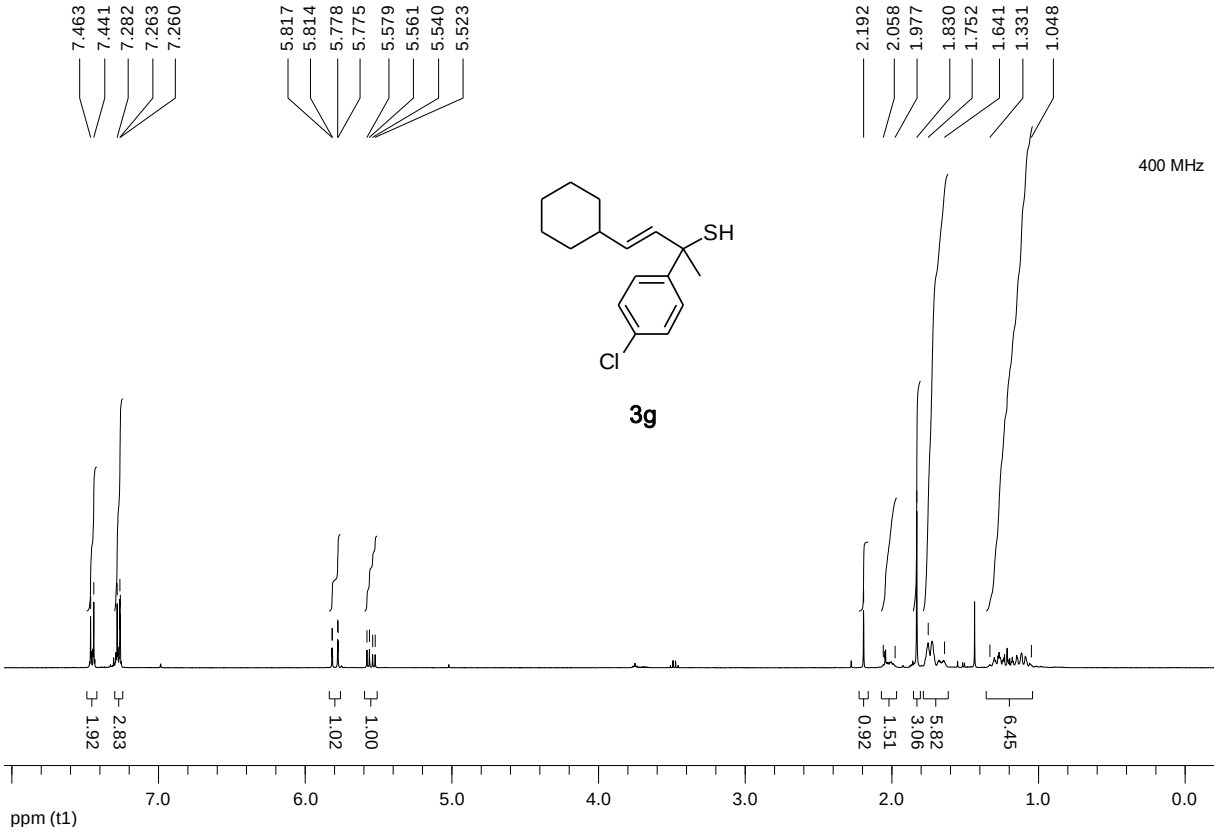

149.837
149.803
141.628
135.477
134.823
132.942
129.243
126.357
122.372
120.410
116.765
113.726
106.911
83.596
77.317
77.000
76.682
54.054
40.832
33.517
33.382
33.245
28.243
28.213
27.914
26.142
26.035
400 MHz
S
N
O
O
2l
200
150
100
50
0
ppm (t1)

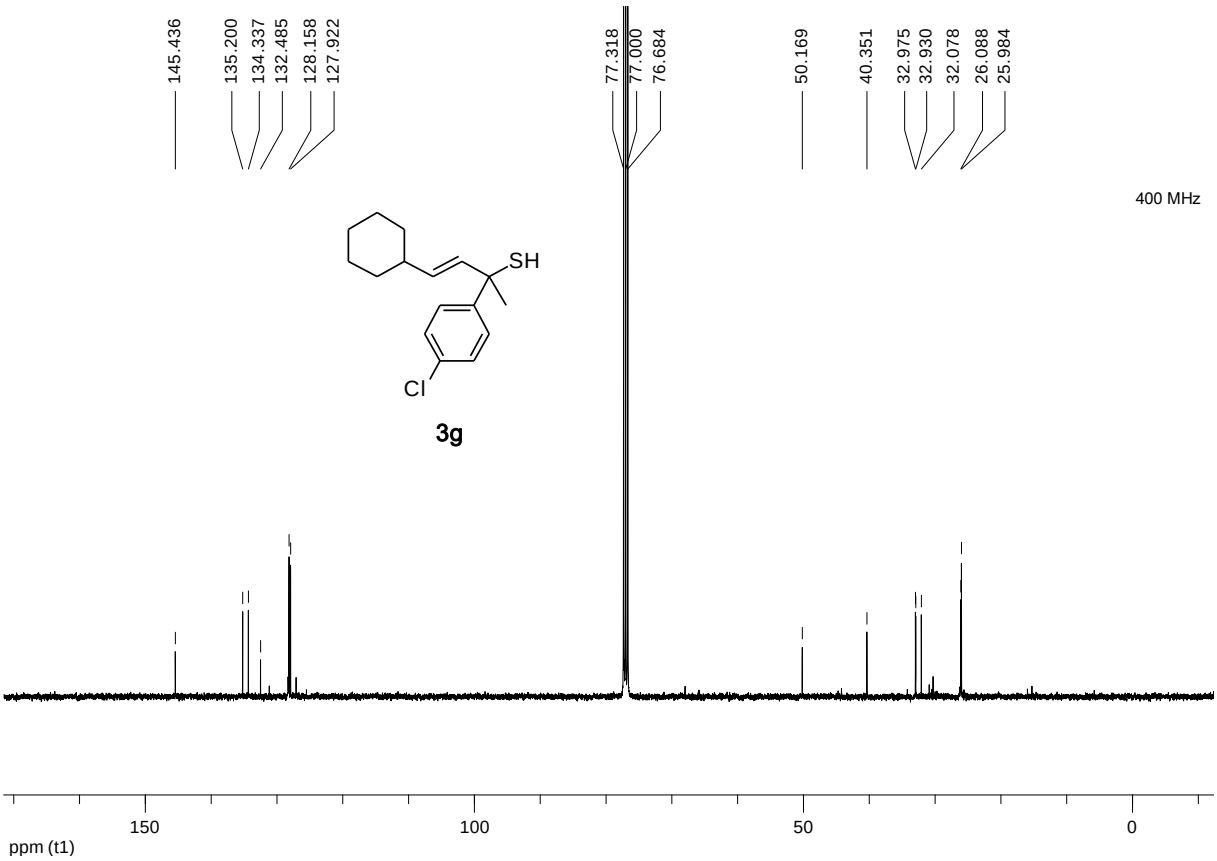

7.411
7.390
7.260
7.128
7.108
5.856
5.853
5.817
5.815
5.588
5.571
5.549
5.532
2.326
2.174
2.063
1.976
1.841
1.765
1.630
1.339
1.056
400 MHz
SH
3e
1.97
2.05
1.00
1.00
3.14
1.03
1.19
3.07
5.29
6.09
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

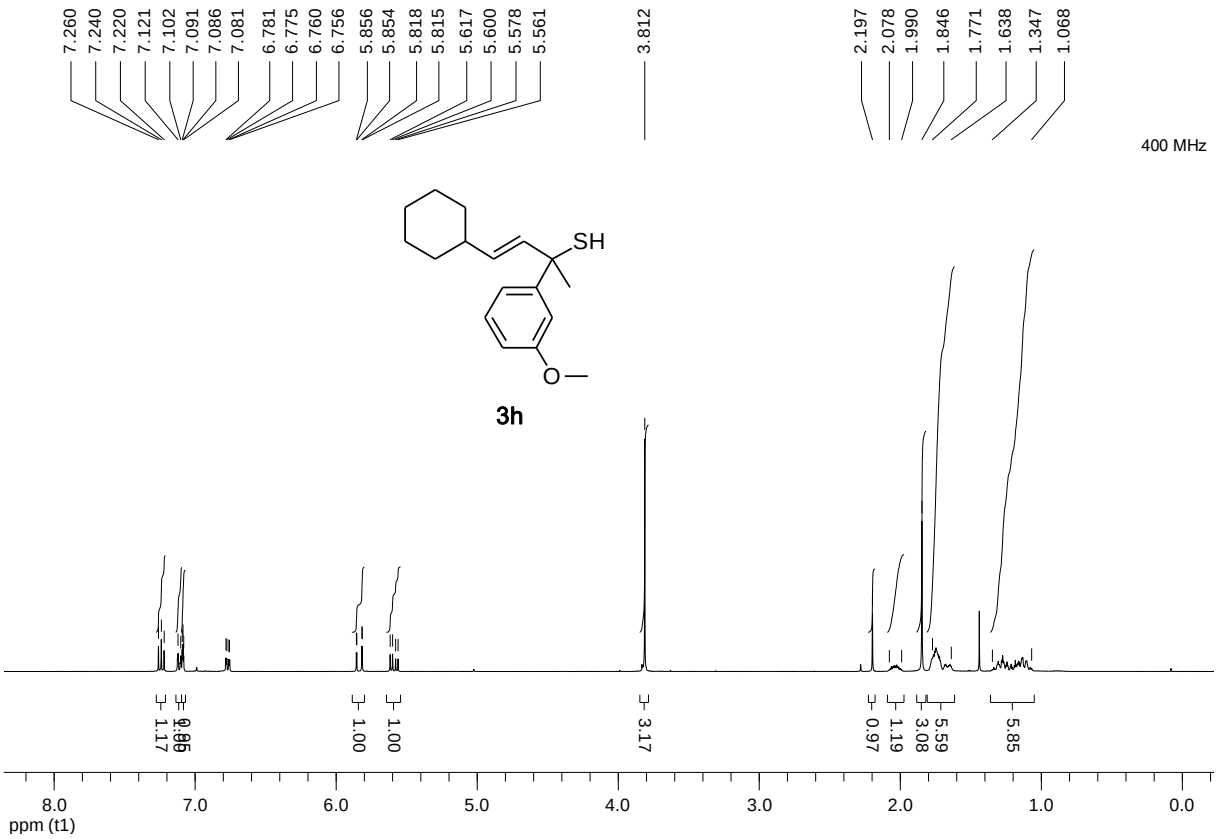

143.905
136.318
135.786
133.657
128.795
126.235
77.318
77.000
76.683
50.396
40.378
33.040
32.995
32.134
26.141
26.032
20.914
400 MHz
SH
3e
150
100
50
0
ppm (t1)

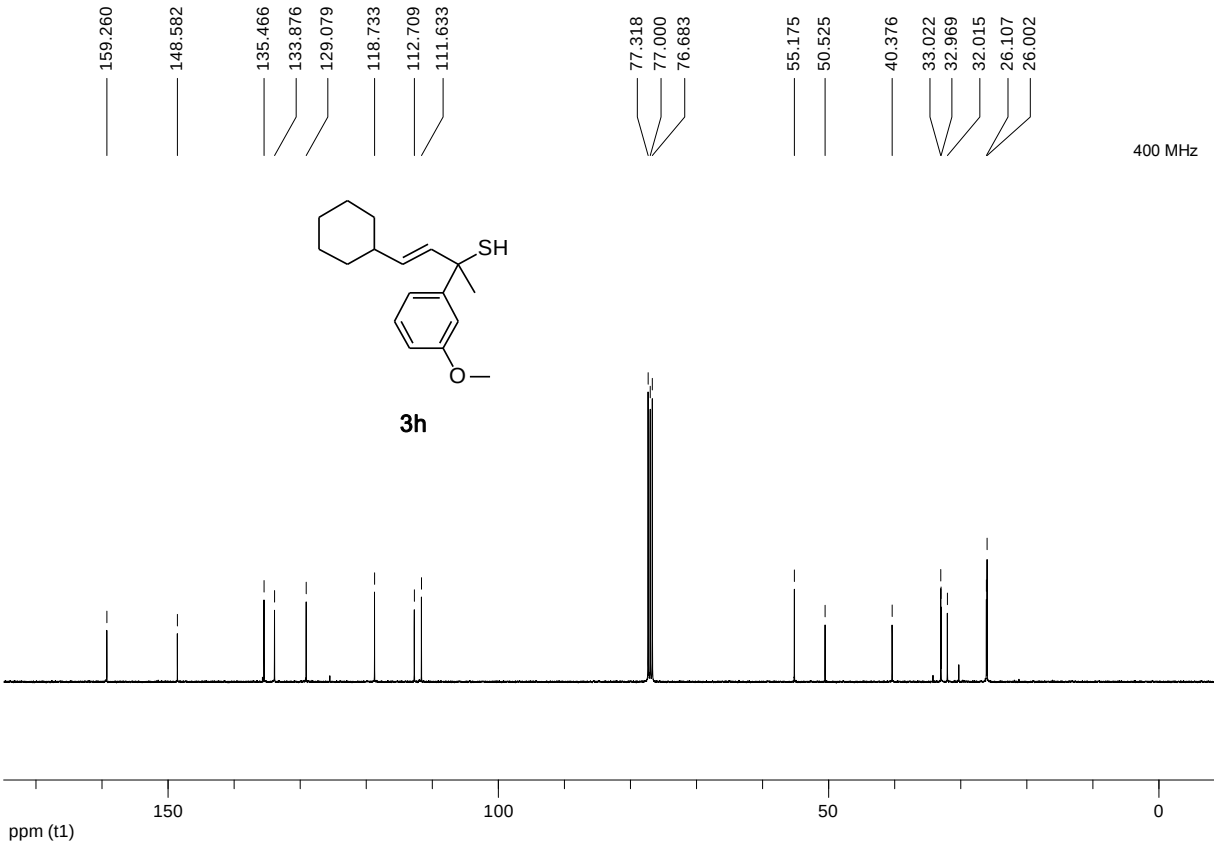

7.493
7.483
7.476
7.465
7.260
6.999
6.981
6.964
5.829
5.827
5.798
5.796
5.572
5.559
5.541
5.528
2.194
2.036
1.986
1.835
1.753
1.641
1.320
1.062
500 MHz
SH
F
3f
2.02
2.32
1.00
1.01
0.97
1.00
3.16
5.59
9.72
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

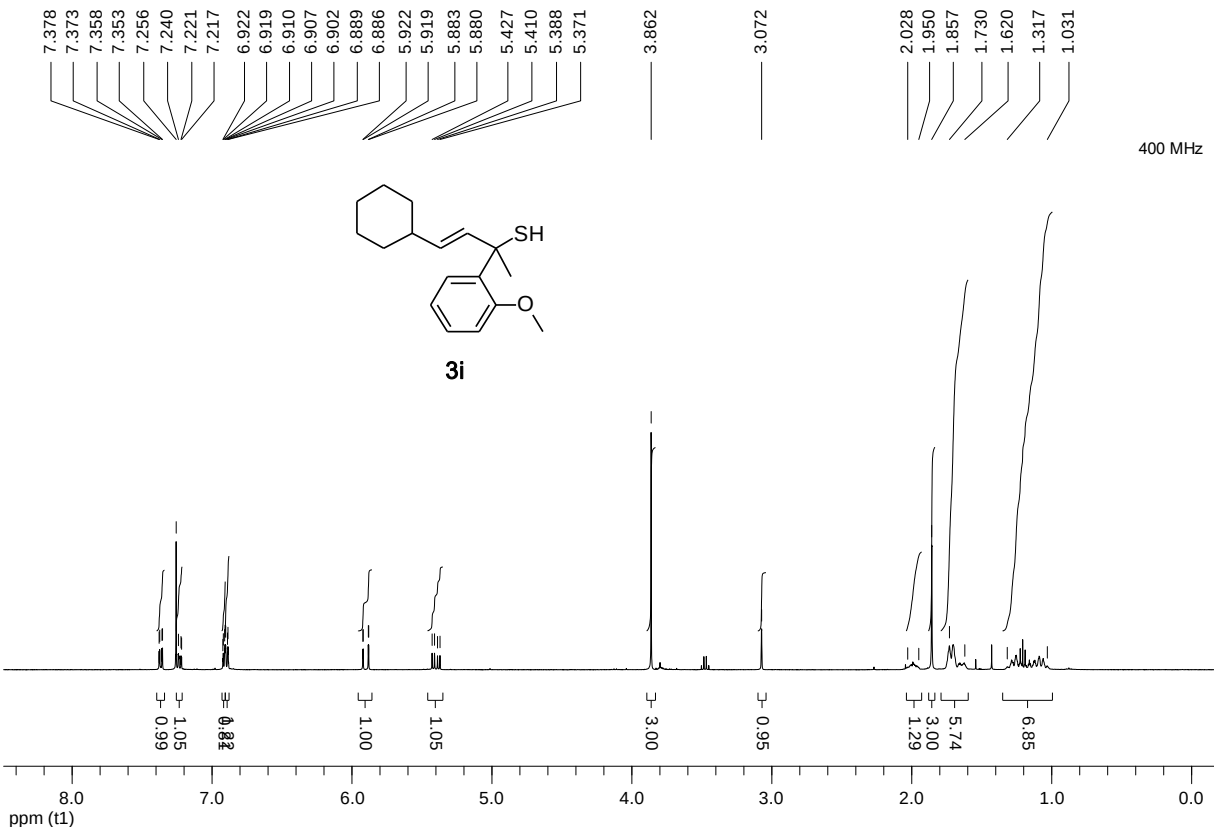

162.459
160.505
142.598
135.533
134.087
128.160
128.097
114.856
114.688
77.254
77.000
76.746
50.144
40.349
33.003
32.954
32.331
26.095
25.993
500 MHz
SH
F
3f
150
100
50
0
ppm (t1)

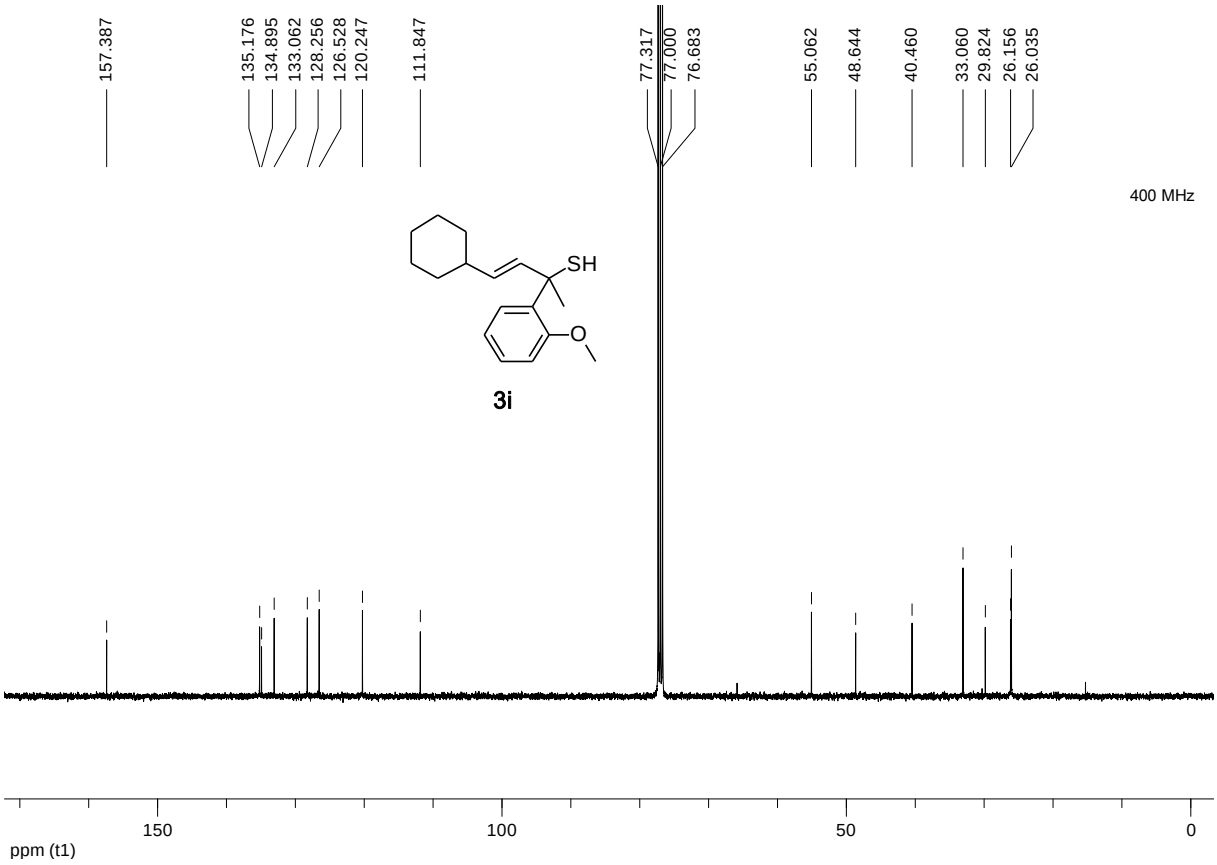

7.463
7.441
7.282
7.263
7.260
5.817
5.814
5.778
5.775
5.579
5.561
5.540
5.523
2.192
2.058
1.977
1.830
1.752
1.641
1.331
1.048
400 MHz
SH
Cl
3g
1.92
2.83
1.02
1.00
0.92
1.51
3.06
5.82
9.45
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

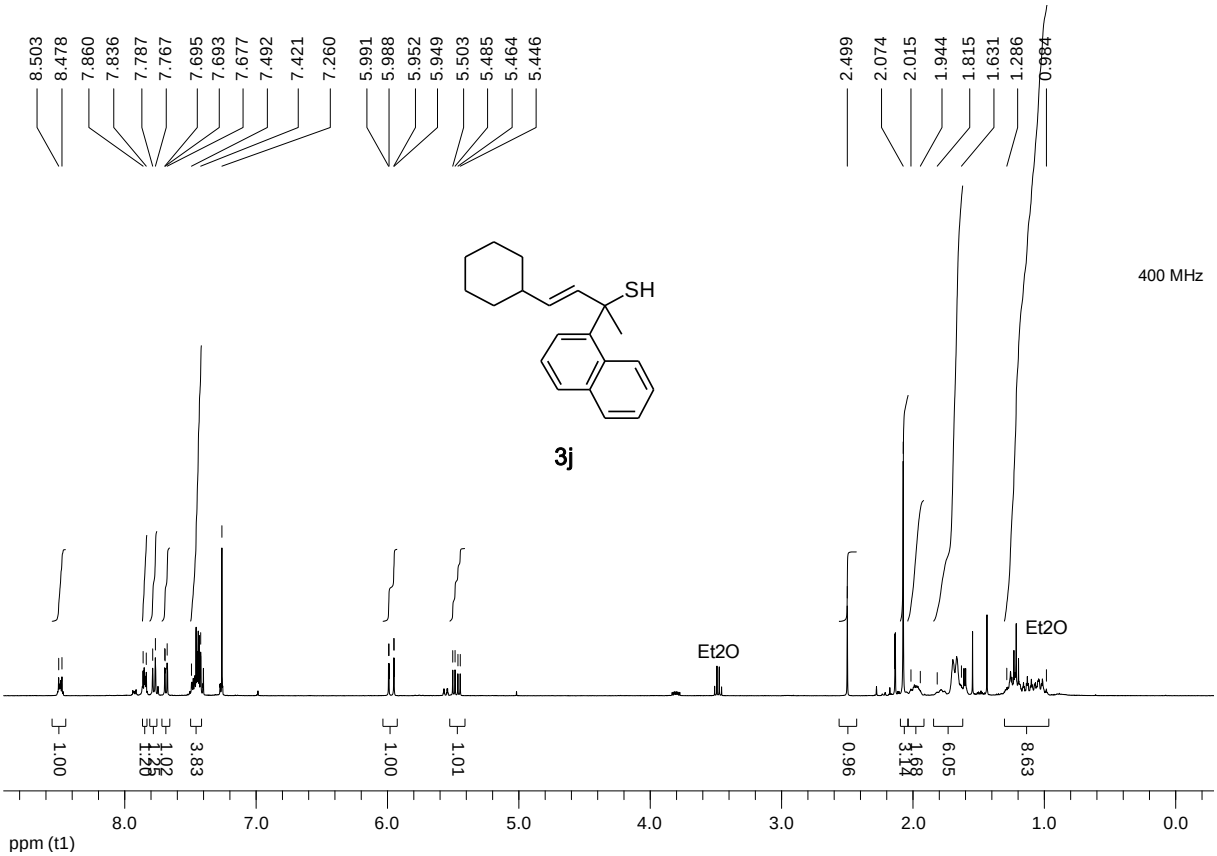

145.436
135.200
134.337
132.485
128.158
127.922
77.318
77.000
76.684
50.169
40.351
32.975
32.930
32.078
26.088
25.984
400 MHz
SH
Cl
3g
150
100
50
0
ppm (t1)

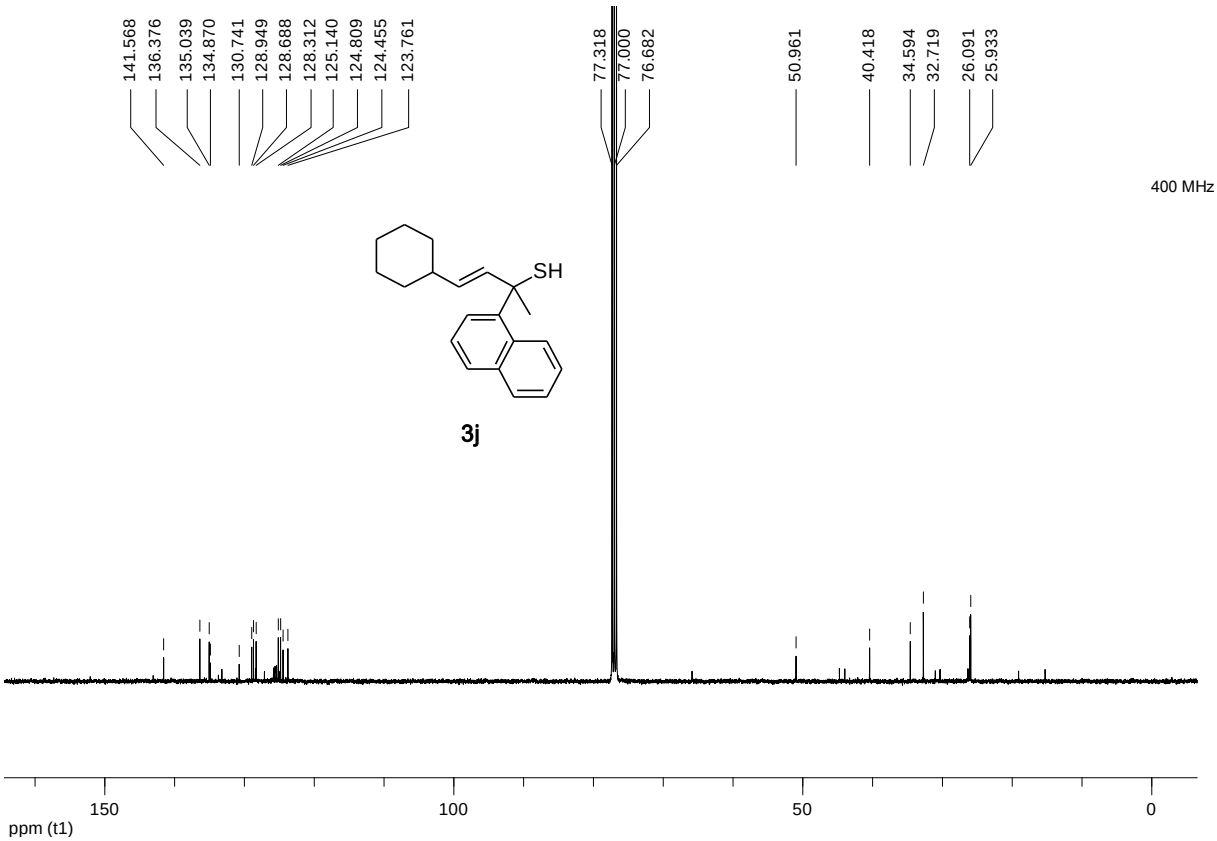

7.260
7.240
7.220
7.121
7.102
7.091
7.086
7.081
6.781
6.775
6.760
6.756
5.856
5.854
5.818
5.815
5.617
5.600
5.578
5.561
3.812
2.197
2.078
1.990
1.846
1.771
1.638
1.347
1.068
400 MHz
SH
O
3h
1.17
0.98
1.00
1.00
3.17
0.97
1.19
3.08
5.59
5.85
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

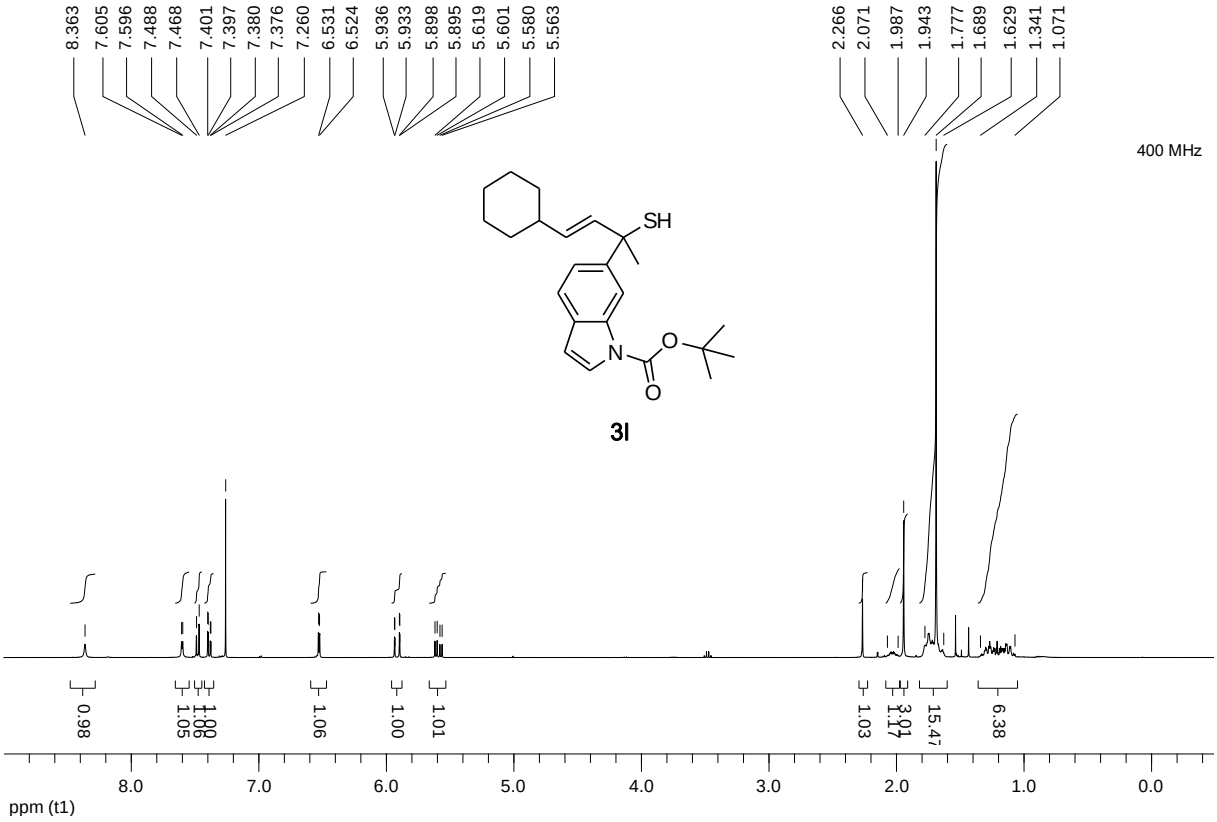

159.260
148.582
135.466
133.876
129.079
118.733
112.709
111.633
77.318
77.000
76.683
55.175
50.525
40.376
33.022
32.969
32.015
26.107
26.002
400 MHz
SH
O
3h
150
100
50
0
ppm (t1)

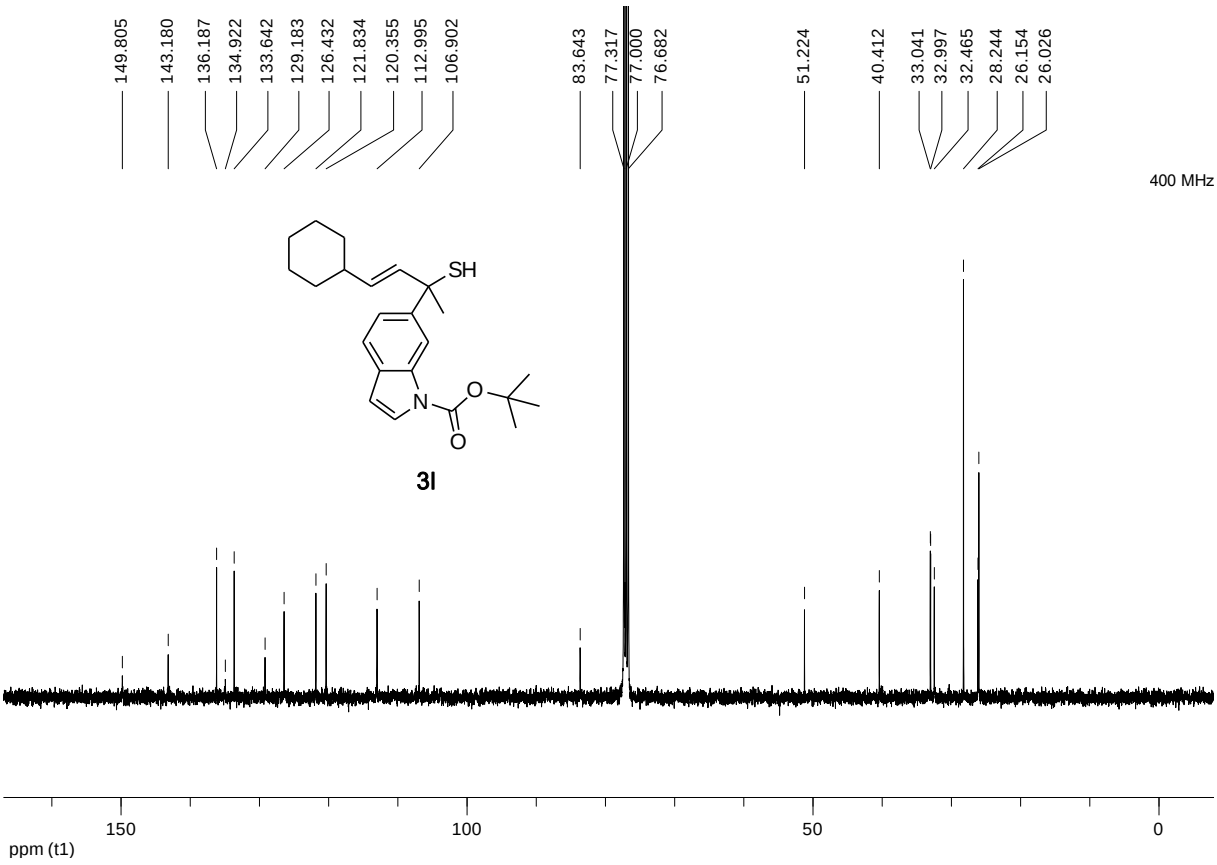

7.378
7.373
7.358
7.353
7.256
7.240
7.221
7.217
6.922
6.919
6.910
6.907
6.902
6.889
6.886
5.922
5.919
5.883
5.880
5.427
5.410
5.388
5.371
3.862
3.072
2.028
1.950
1.857
1.730
1.620
1.317
1.031
400 MHz
SH
O
3i
0.99
1.05
1.00
1.05
3.00
0.95
1.29
3.00
5.74
6.85
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

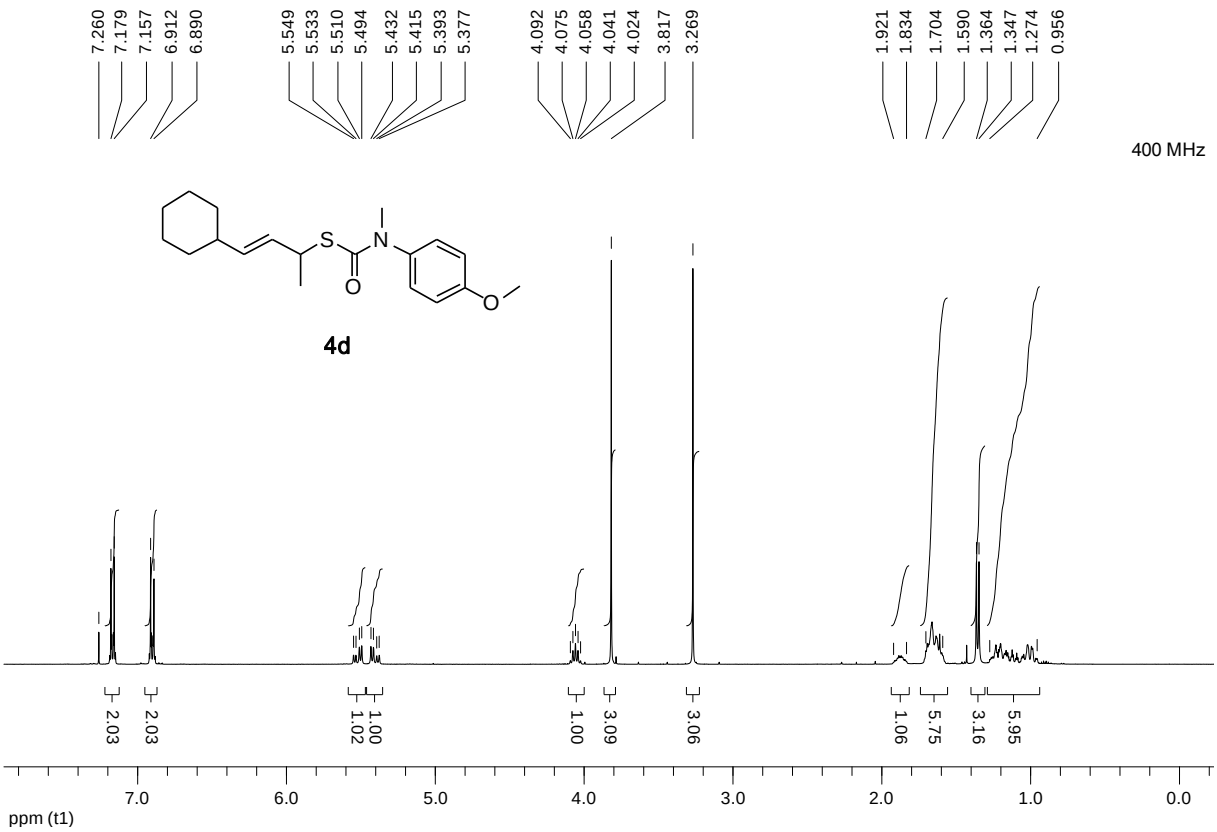

157.387
135.176
134.895
133.062
128.256
126.528
120.247
111.847
77.317
77.000
76.683
55.062
48.644
40.460
33.060
29.824
26.156
26.035
400 MHz
SH
O
3i
150
100
50
0
ppm (t1)

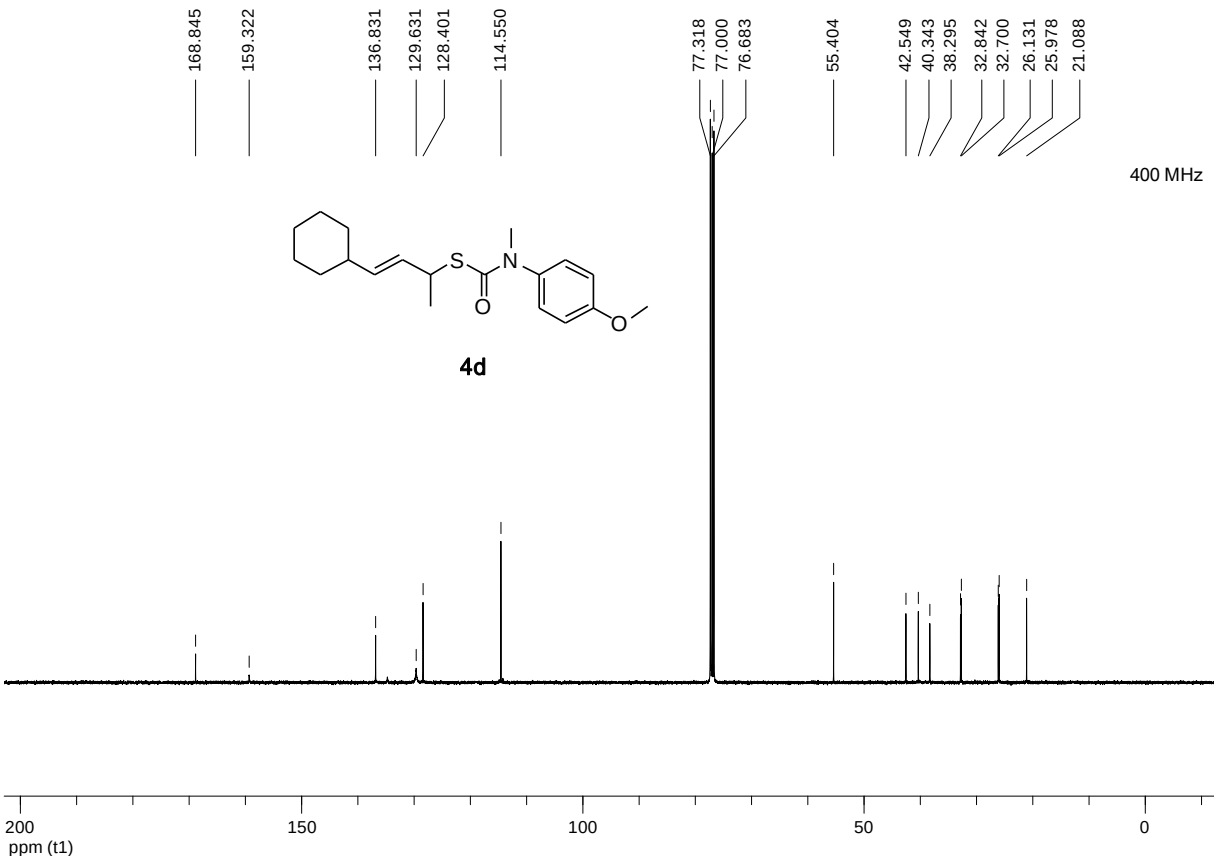

8.503
8.478
7.860
7.836
7.787
7.767
7.695
7.693
7.677
7.492
7.421
7.260
5.991
5.988
5.952
5.949
5.503
5.485
5.464
5.446
2.499
2.074
2.015
1.944
1.815
1.631
1.286
0.984
SH
3j
400 MHz
Et2O
Et2O
1.00
1.25
1.12
3.83
1.00
1.01
0.96
3.14
1.68
6.05
8.63
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

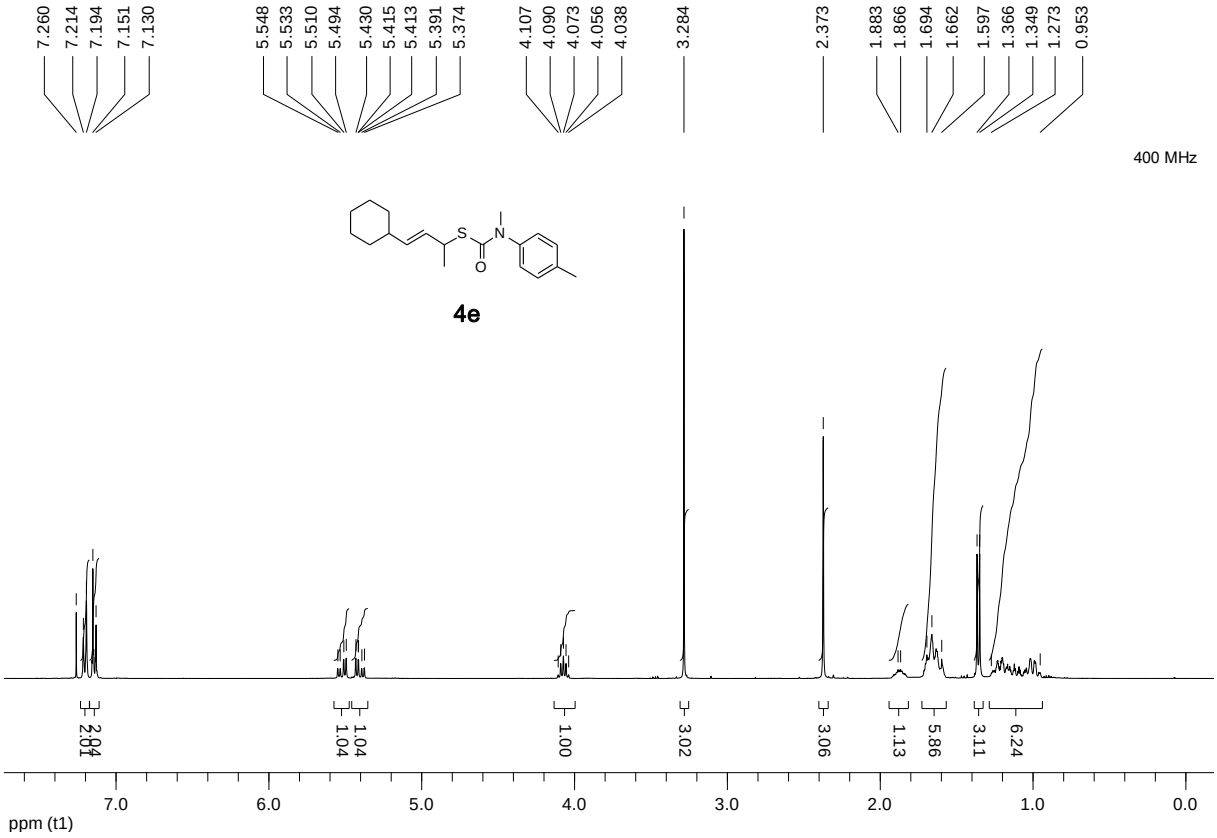

141.568
136.376
135.039
134.870
130.741
128.949
128.688
128.312
125.140
124.809
124.455
123.761
77.318
77.000
76.682
50.961
40.418
34.594
32.719
26.091
25.933
SH
3j
400 MHz
150
100
50
0
ppm (t1)

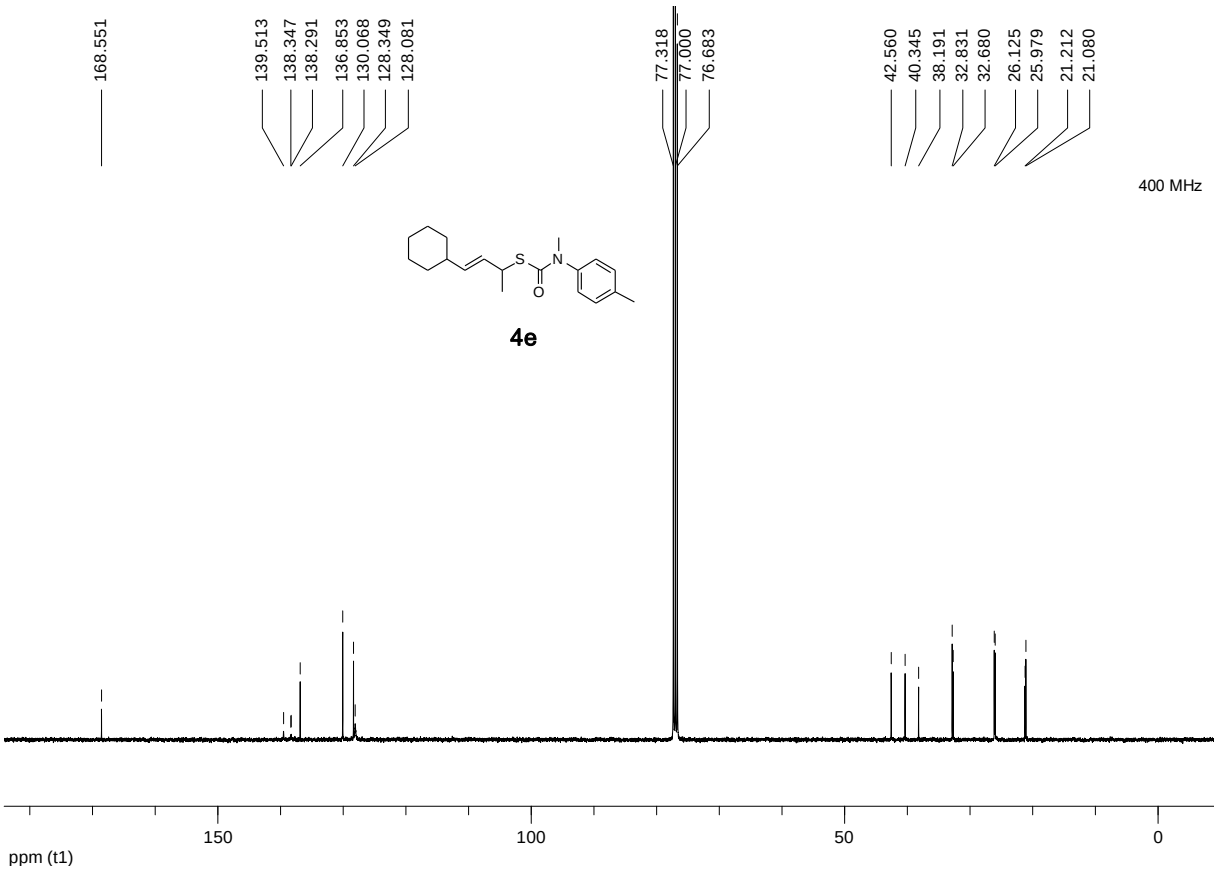

8.363
7.605
7.596
7.488
7.468
7.401
7.397
7.380
7.376
7.260
6.531
6.524
5.936
5.933
5.898
5.895
5.619
5.601
5.580
5.563
2.266
2.071
1.987
1.943
1.777
1.689
1.629
1.341
1.071
400 MHz
SH
O
N
O
3l
0.98
1.05
1.08
1.00
1.06
1.00
1.01
1.03
3.01
3.17
15.47
6.38
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

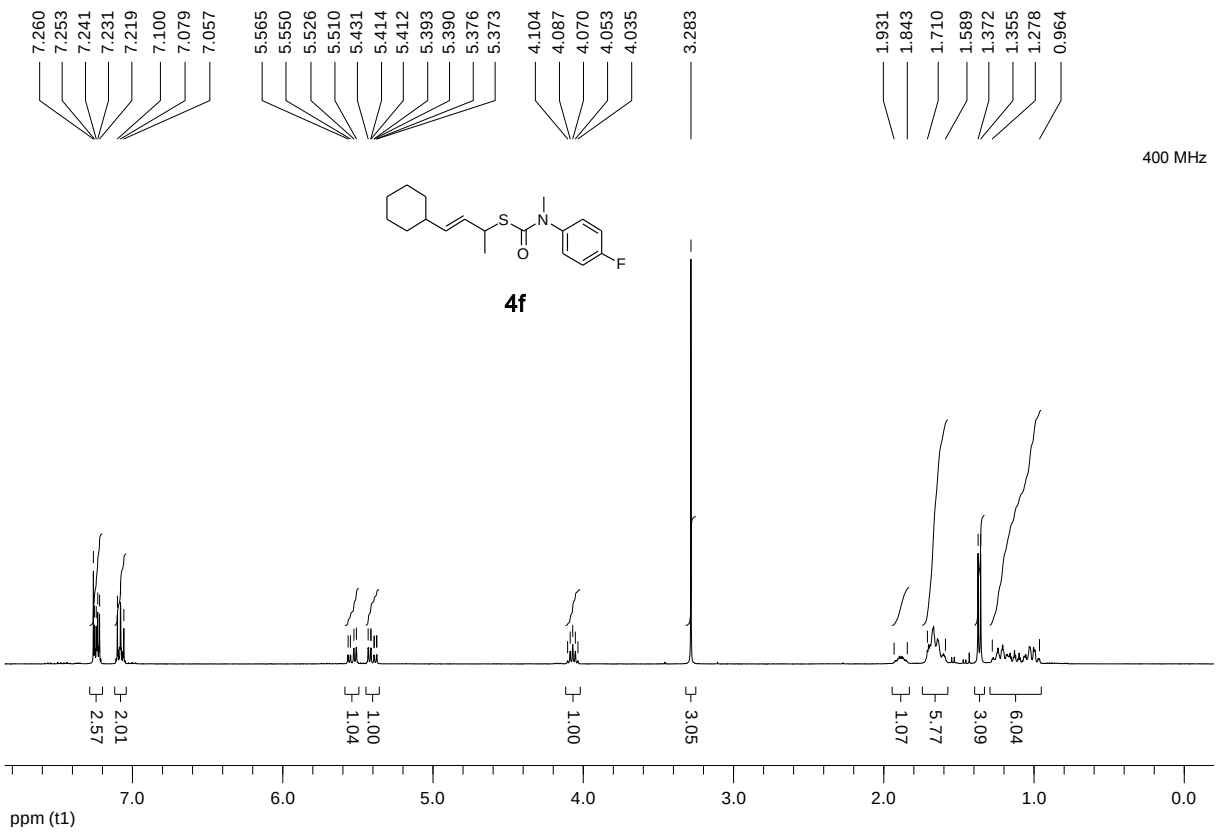

149.805
143.180
136.187
134.922
133.642
129.183
126.432
121.834
120.355
112.995
106.902
83.643
77.317
77.000
76.682
51.224
40.412
33.041
32.997
32.465
28.244
26.154
26.026
400 MHz
SH
O
N
O
3l
150
100
50
0
ppm (t1)

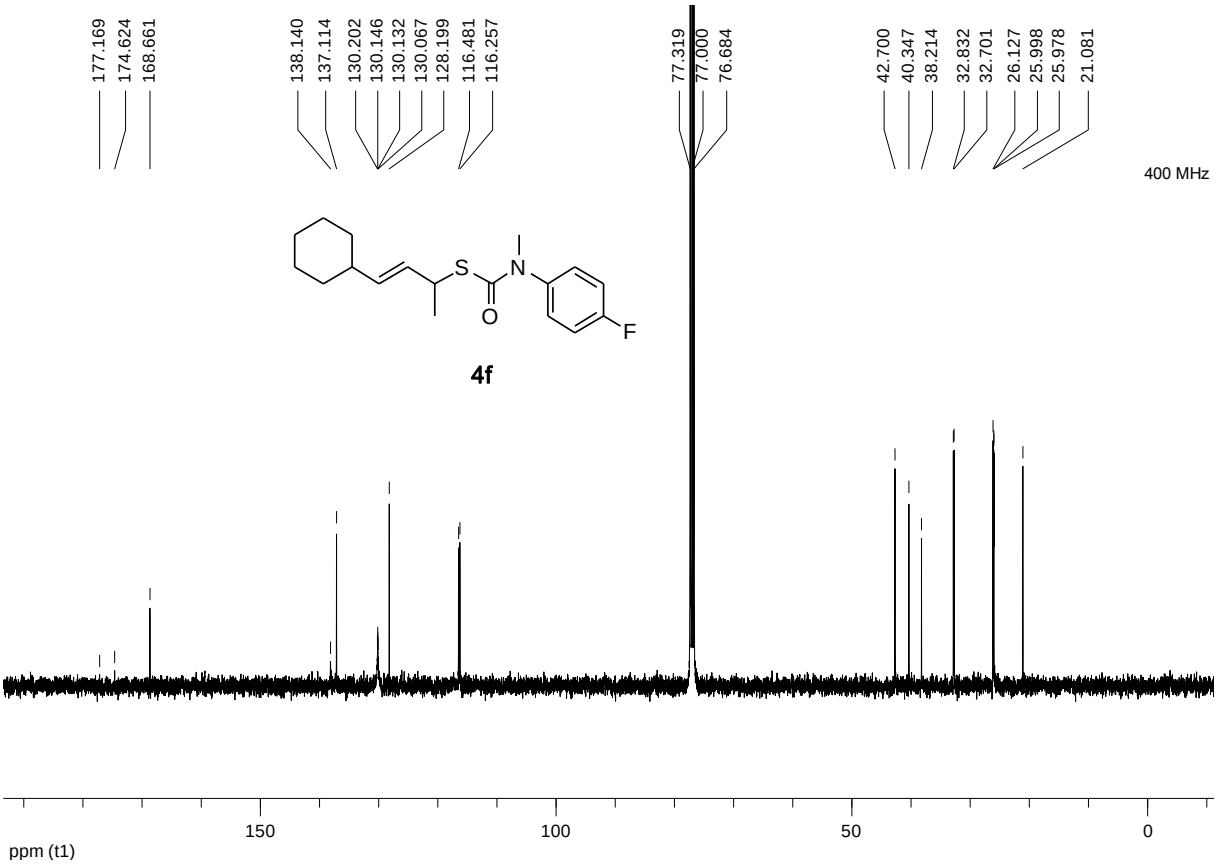

7.260
7.179
7.157
6.912
6.890
5.549
5.533
5.510
5.494
5.432
5.415
5.393
5.377
4.092
4.075
4.058
4.041
4.024
3.817
3.269
1.921
1.834
1.704
1.590
1.364
1.347
1.274
0.956
400 MHz
S
N
O
O
4d
2.03
2.03
1.02
1.00
1.00
3.09
3.06
1.06
5.75
3.16
5.95
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

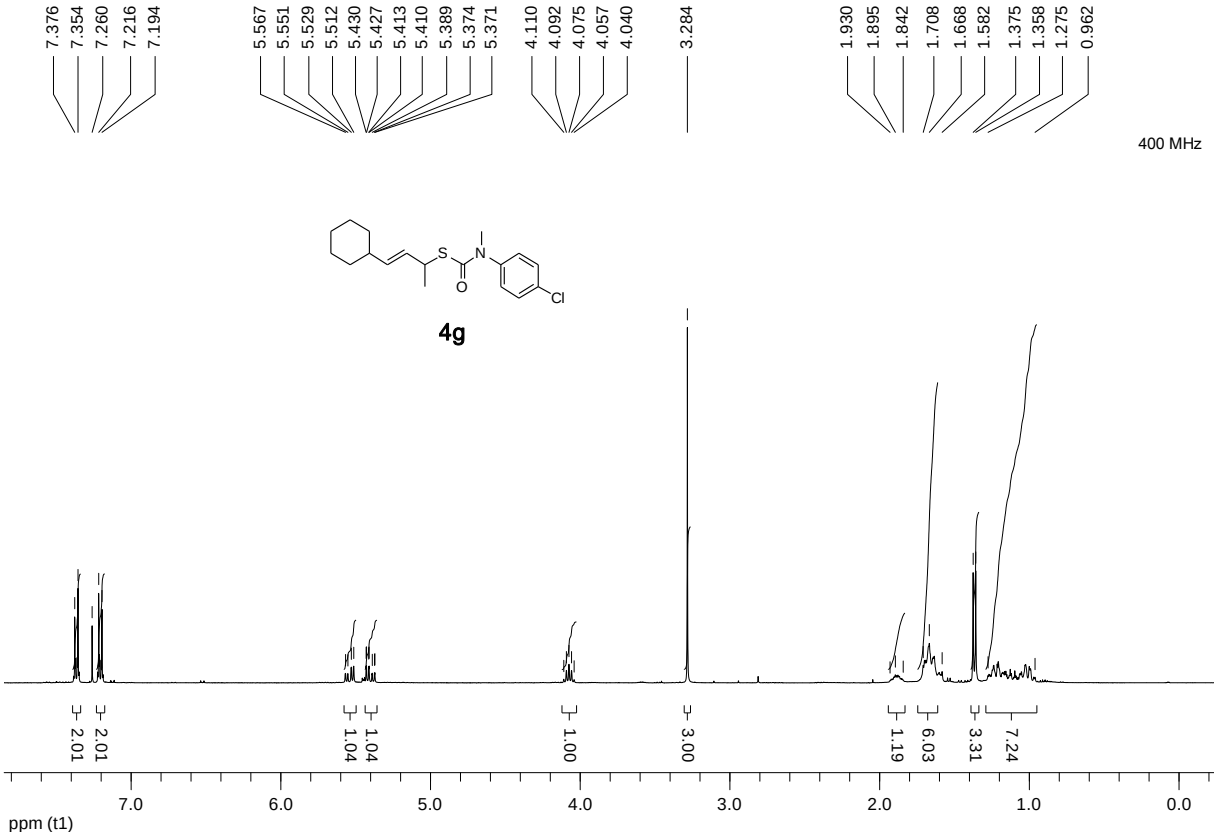

168.845
159.322
136.831
129.631
128.401
114.550
77.318
77.000
76.683
55.404
42.549
40.343
38.295
32.842
32.700
26.131
25.978
21.088
400 MHz
S
N
O
O
4d
200
150
100
50
0
ppm (t1)

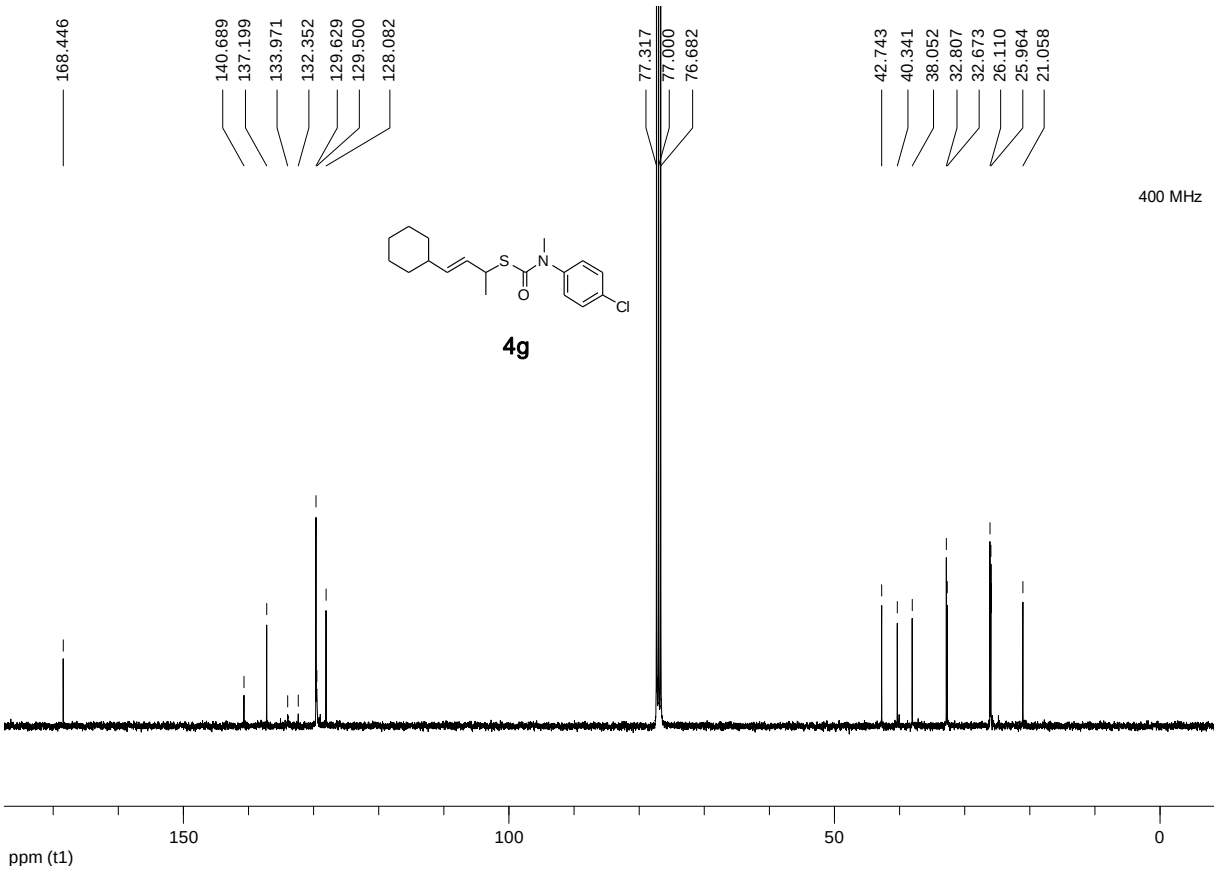

7.260
7.214
7.194
7.151
7.130
5.548
5.533
5.510
5.494
5.430
5.415
5.413
5.391
5.374
4.107
4.090
4.073
4.056
4.038
3.284
2.373
1.883
1.866
1.694
1.662
1.597
1.366
1.349
1.273
0.953
400 MHz
4e
2.04
1.04
1.04
1.00
3.02
3.06
1.13
5.86
3.11
9.24
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

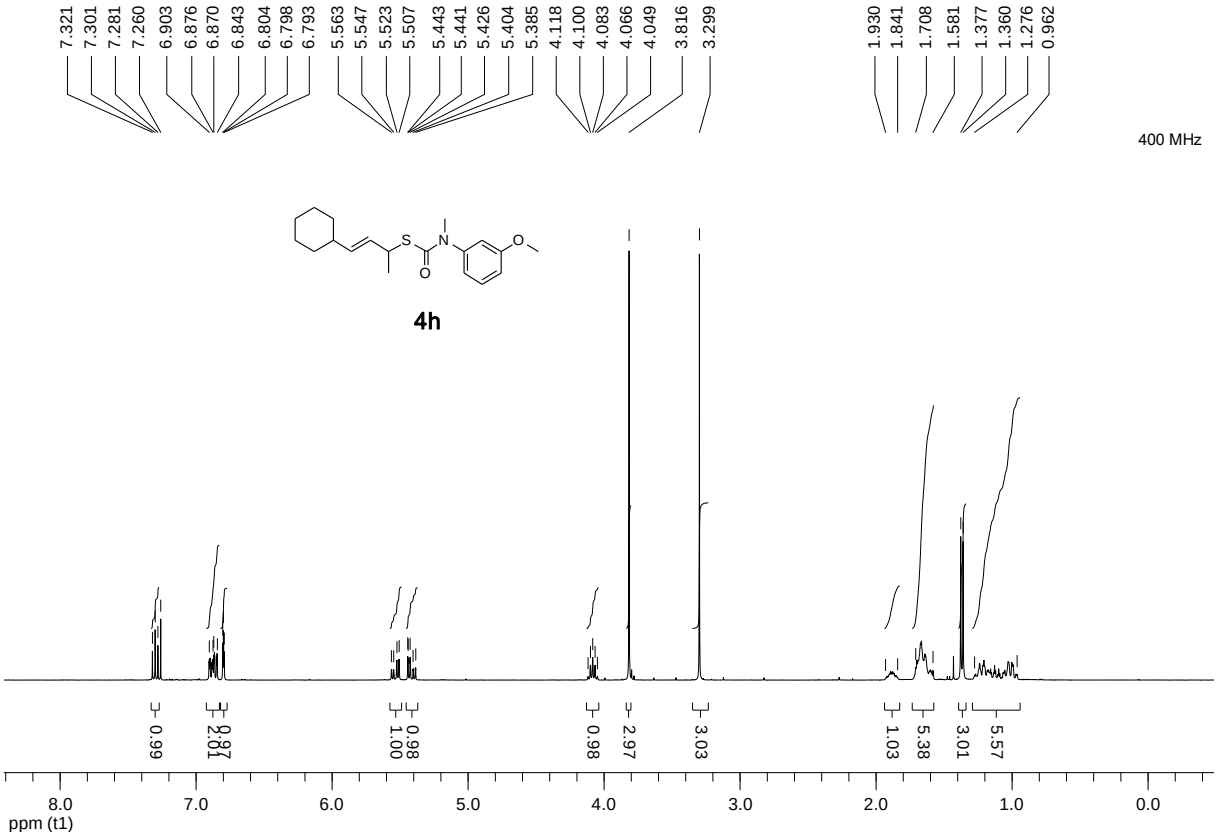

168.551
139.513
138.347
138.291
136.853
130.068
128.349
128.081
77.318
77.000
76.683
42.560
40.345
38.191
32.831
32.680
26.125
25.979
21.212
21.080
400 MHz
4e
150
100
50
0
ppm (t1)

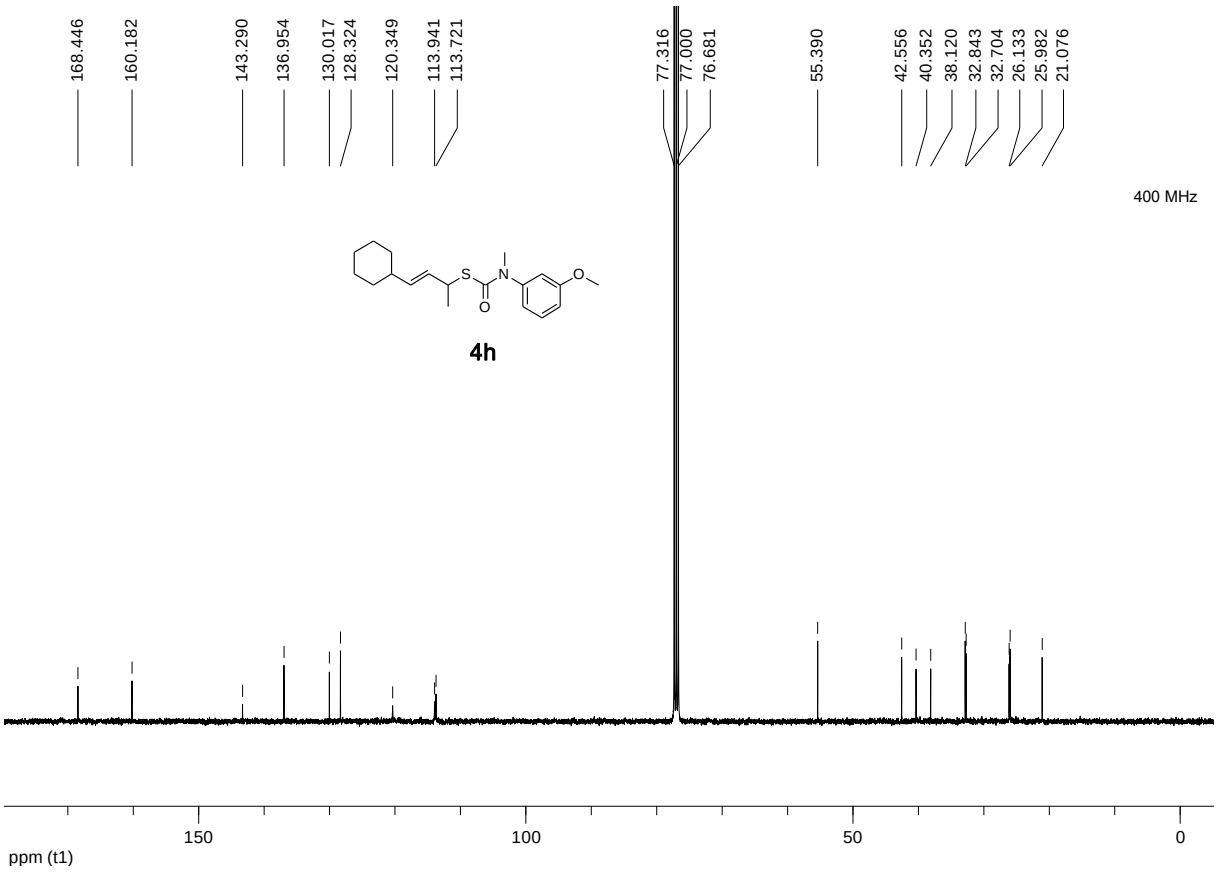

7.260
7.253
7.241
7.231
7.219
7.100
7.079
7.057
5.565
5.550
5.526
5.510
5.431
5.414
5.412
5.393
5.390
5.376
5.373
4.104
4.087
4.070
4.053
4.035
3.283
1.931
1.843
1.710
1.589
1.372
1.355
1.278
0.964
400 MHz
4f
2.57
2.01
1.04
1.00
1.00
3.05
1.07
5.77
3.09
6.04
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

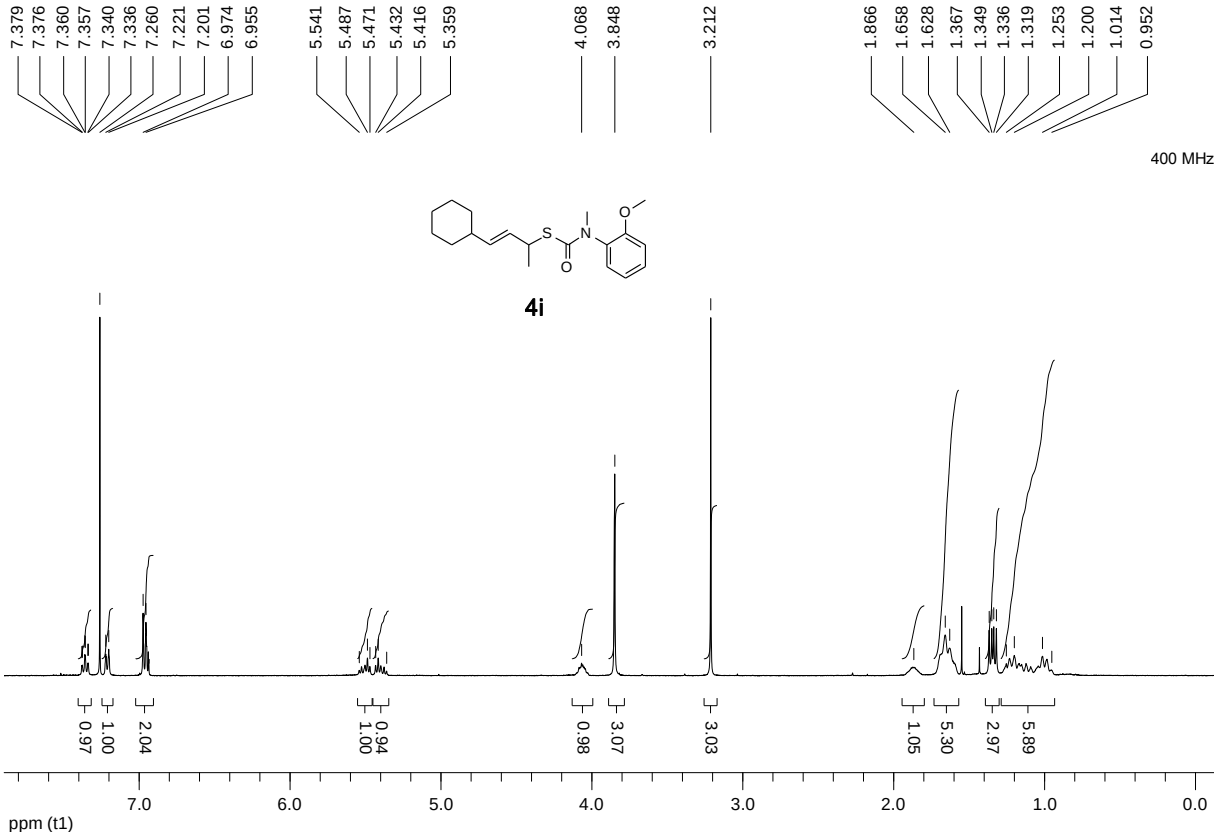

177.169
174.624
168.661
138.140
137.114
130.202
130.146
130.132
130.067
128.199
116.481
116.257
77.319
77.000
76.684
42.700
40.347
38.214
32.832
32.701
26.127
25.998
25.978
21.081
400 MHz
4f
150
100
50
0
ppm (t1)

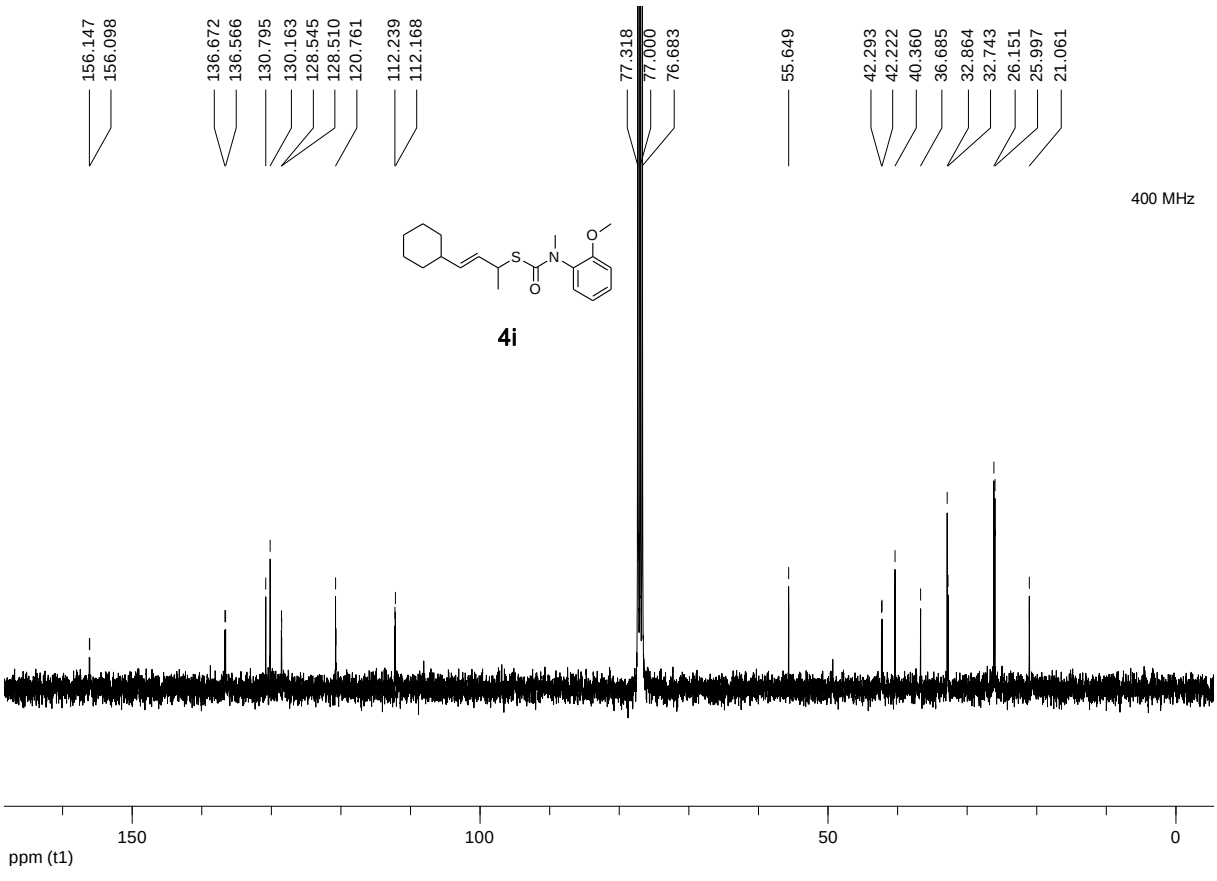

7.376
7.354
7.260
7.216
7.194
5.567
5.551
5.529
5.512
5.430
5.427
5.413
5.410
5.389
5.374
5.371
4.110
4.092
4.075
4.057
4.040
3.284
1.930
1.895
1.842
1.708
1.668
1.582
1.375
1.358
1.275
0.962
400 MHz
4g
2.01
2.01
1.04
1.04
1.00
3.00
1.19
6.03
3.31
7.24
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

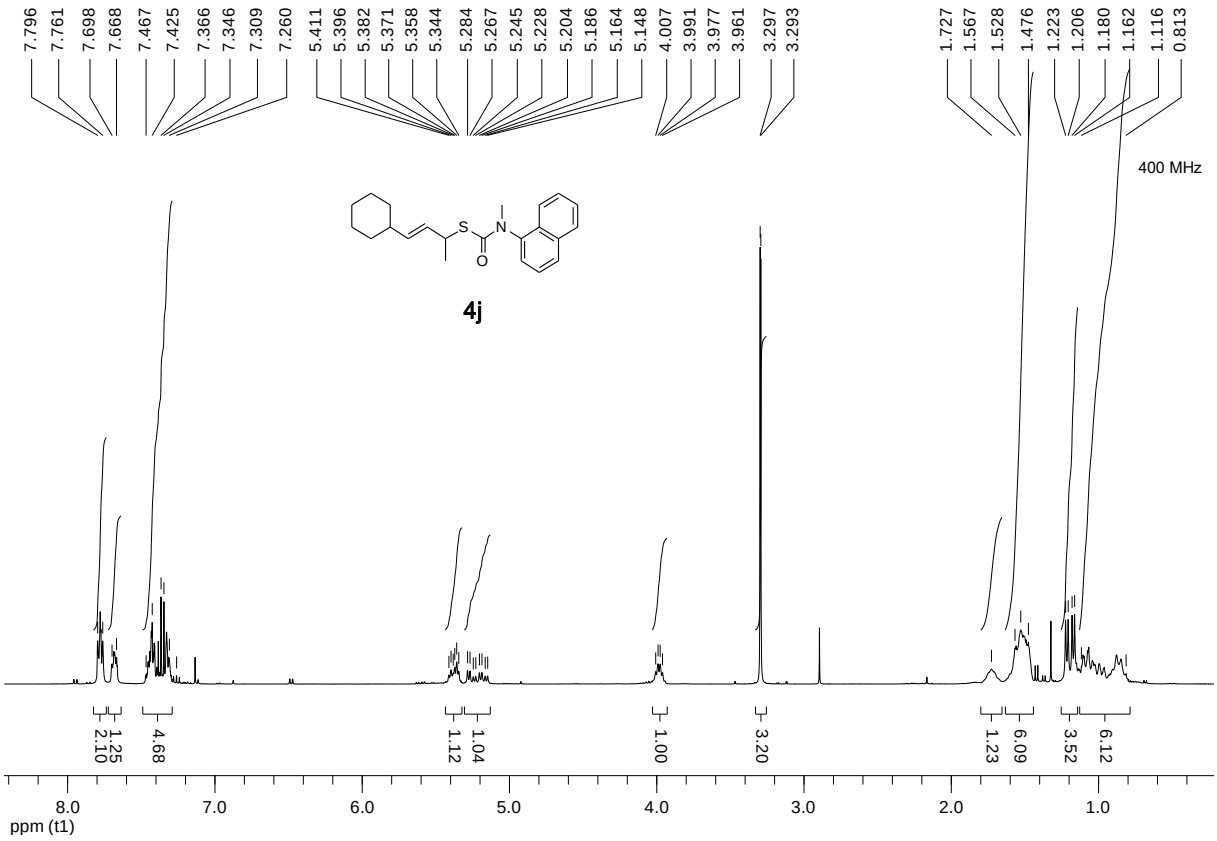

168.446
140.689
137.199
133.971
132.352
129.629
129.500
128.082
77.317
77.000
76.682
42.743
40.341
38.052
32.807
32.673
26.110
25.964
21.058
400 MHz
4g
150
100
50
0
ppm (t1)

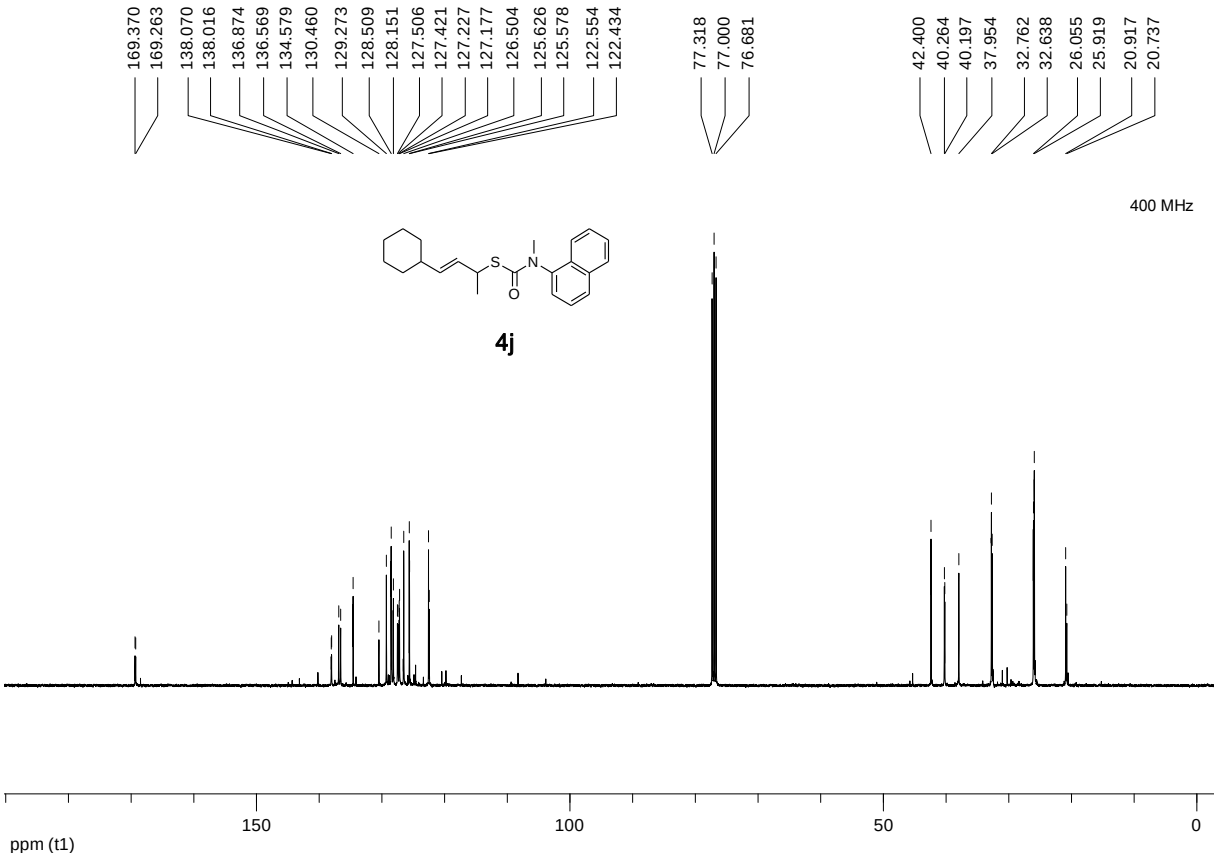

7.321
7.301
7.281
7.260
6.903
6.876
6.870
6.843
6.804
6.798
6.793
5.563
5.547
5.523
5.507
5.443
5.441
5.426
5.404
5.385
4.118
4.100
4.083
4.066
4.049
3.816
3.299
1.930
1.841
1.708
1.581
1.377
1.360
1.276
0.962
400 MHz
4h
0.99
2.01
1.00
0.98
2.97
3.03
1.03
5.38
3.01
5.57
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

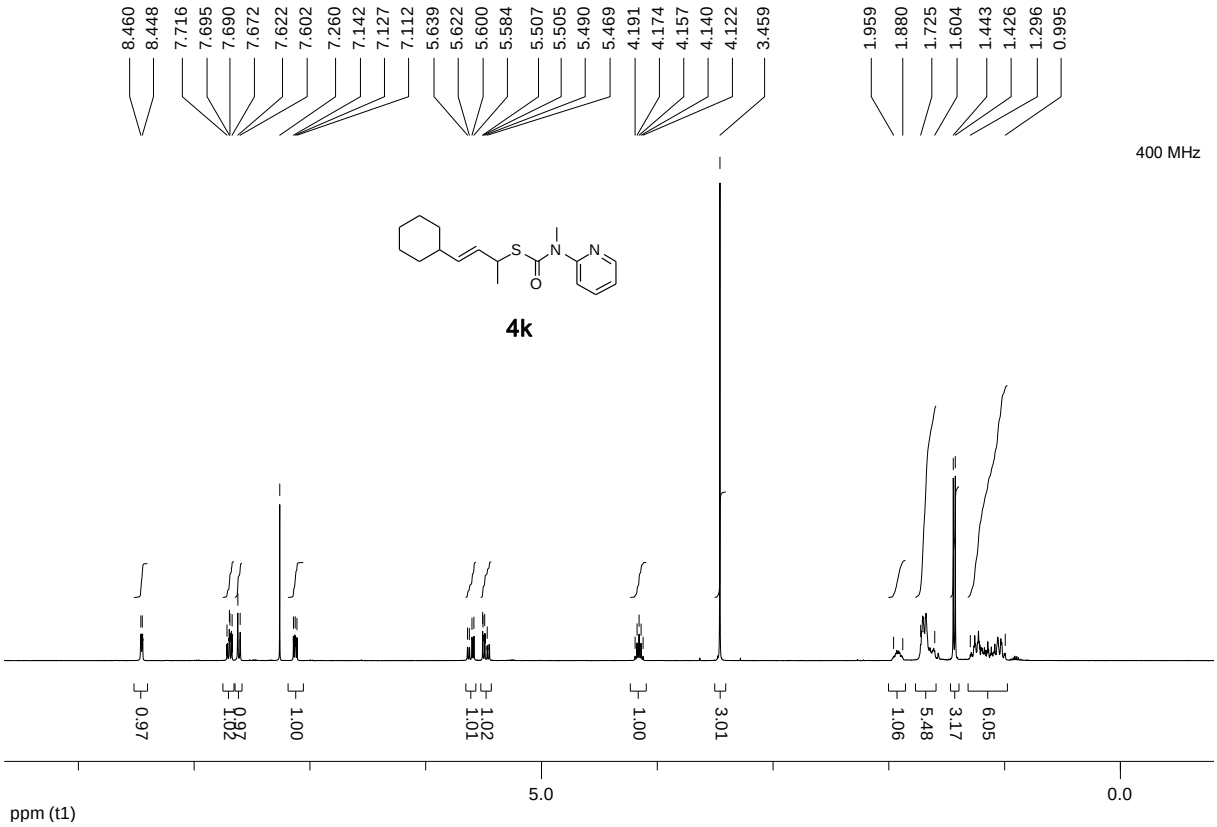

168.446
160.182
143.290
136.954
130.017
128.324
120.349
113.941
113.721
77.316
77.000
76.681
55.390
42.556
40.352
38.120
32.843
32.704
26.133
25.982
21.076
400 MHz
4h
150
100
50
0
ppm (t1)

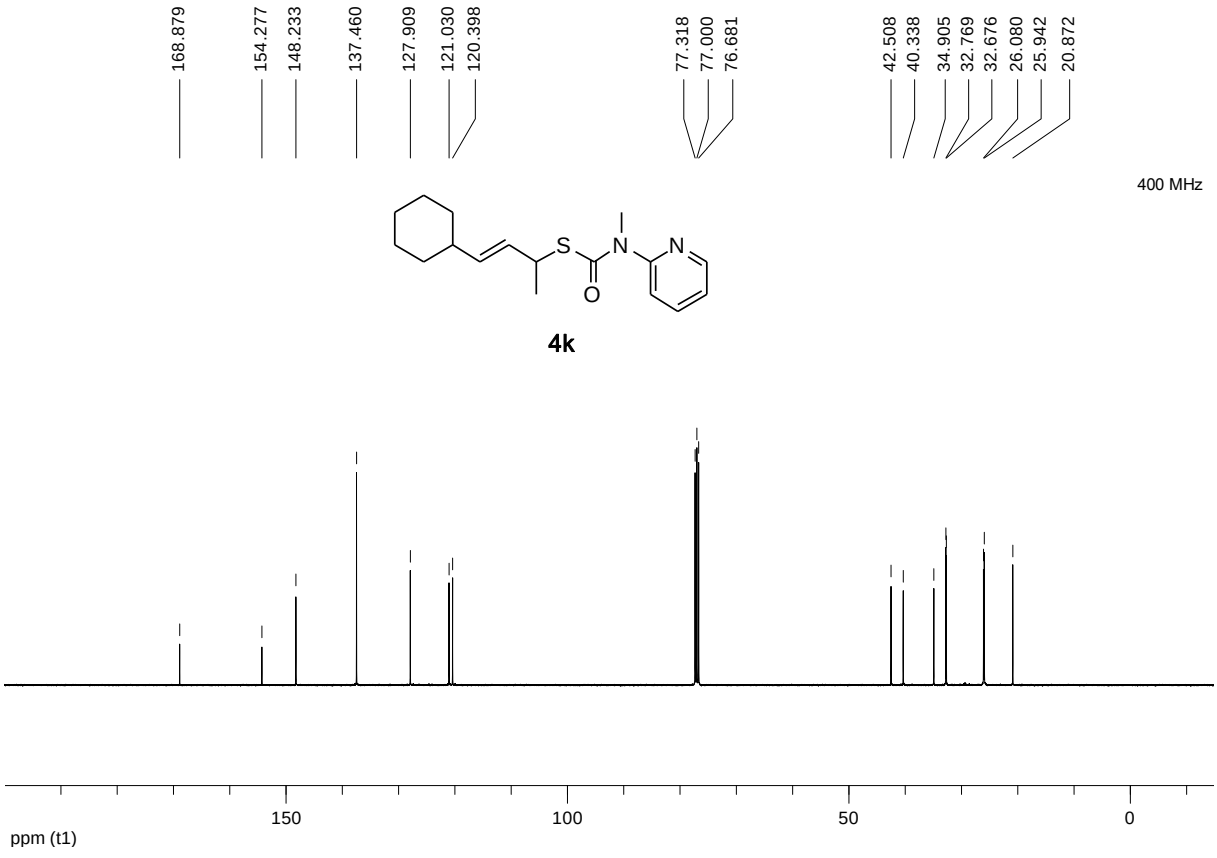

7.379
7.376
7.360
7.357
7.340
7.336
7.260
7.221
7.201
6.974
6.955
5.541
5.487
5.471
5.432
5.416
5.359
4.068
3.848
3.212
1.866
1.658
1.628
1.367
1.349
1.336
1.319
1.253
1.200
1.014
0.952
400 MHz
4i
0.97
1.00
2.04
0.94
1.00
0.98
3.07
3.03
1.05
5.30
2.97
5.89
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

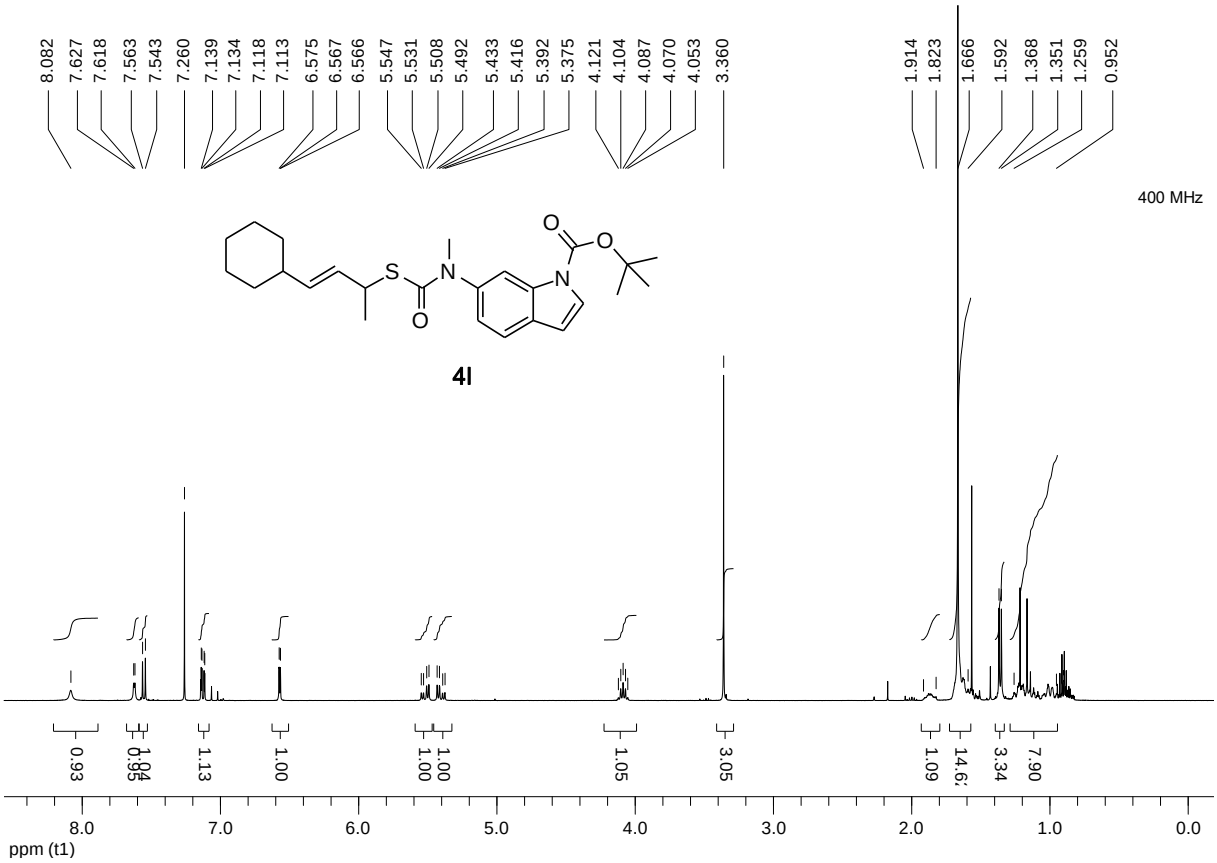

156.147
156.098
136.672
136.566
130.795
130.163
128.545
128.510
120.761
112.239
112.168
77.318
77.000
76.683
55.649
42.293
42.222
40.360
36.685
32.864
32.743
26.151
25.997
21.061
400 MHz
4i
150
100
50
0
ppm (t1)

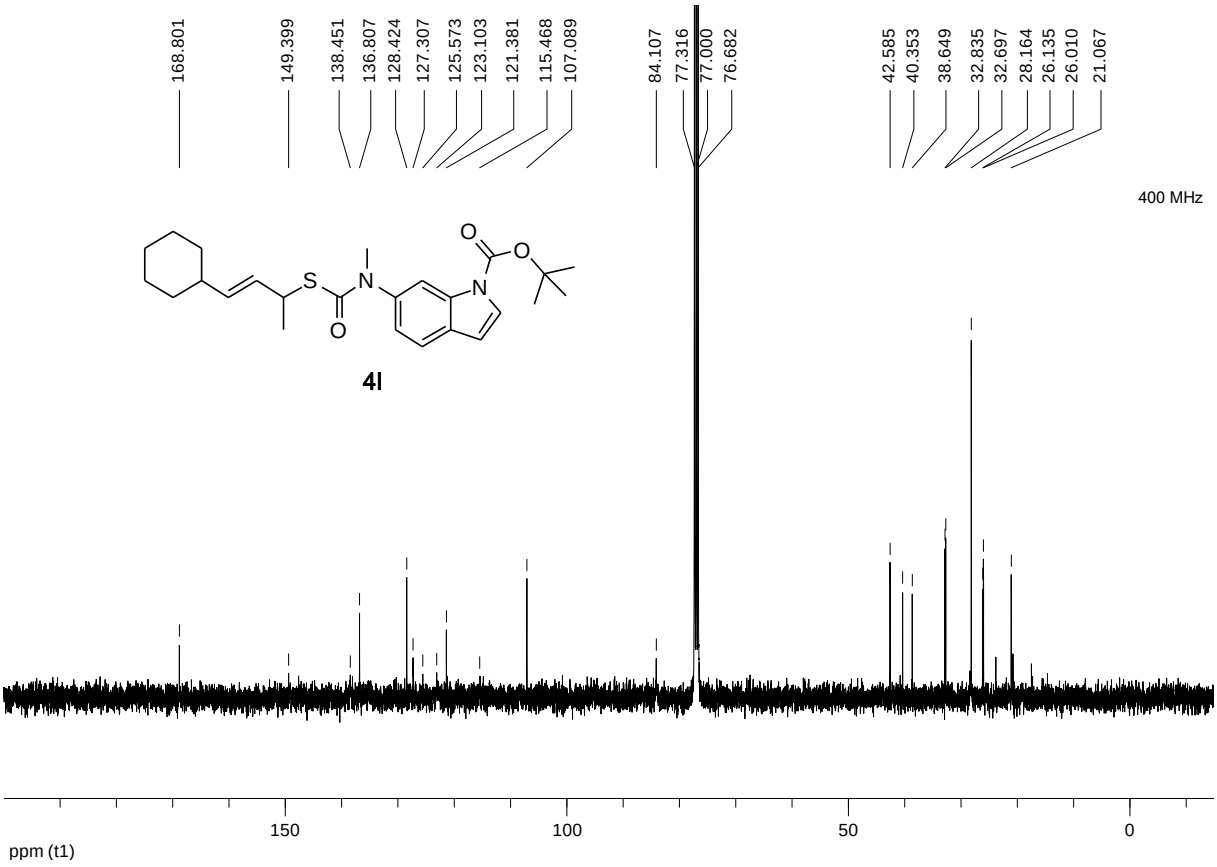

7.796
7.761
7.698
7.668
7.467
7.425
7.366
7.346
7.309
7.260
5.411
5.396
5.382
5.371
5.358
5.344
5.284
5.267
5.245
5.228
5.204
5.186
5.164
5.148
4.007
3.991
3.977
3.961
3.297
3.293
1.727
1.567
1.528
1.476
1.223
1.206
1.180
1.162
1.116
0.813
400 MHz
4j
2.10
1.25
4.88
1.12
1.04
1.00
3.20
1.23
6.09
3.52
6.12
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

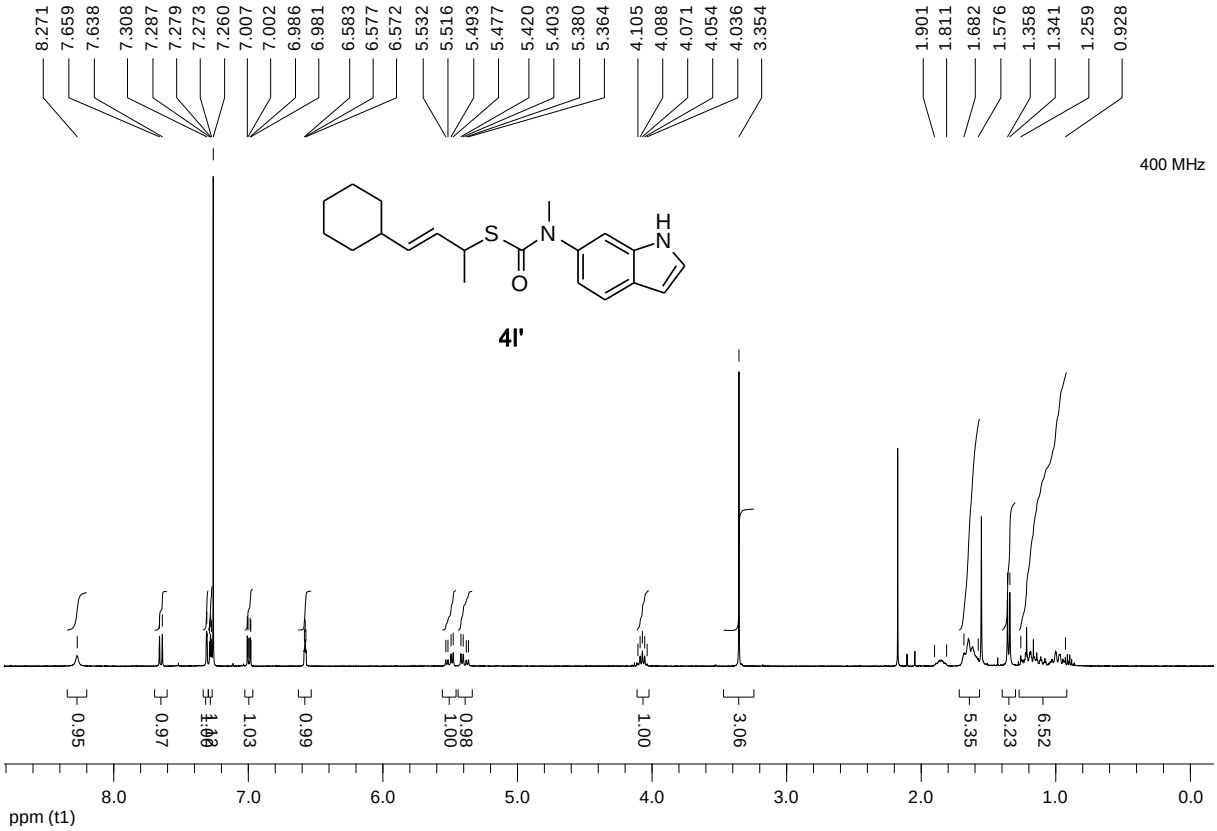

169.370
169.263
138.070
138.016
136.874
136.569
134.579
130.460
129.273
128.509
128.151
127.506
127.421
127.227
127.177
126.504
125.626
125.578
122.554
122.434
77.318
77.000
76.681
42.400
40.264
40.197
37.954
32.762
32.638
26.055
25.919
20.917
20.737
400 MHz
4j
150
100
50
0
ppm (t1)

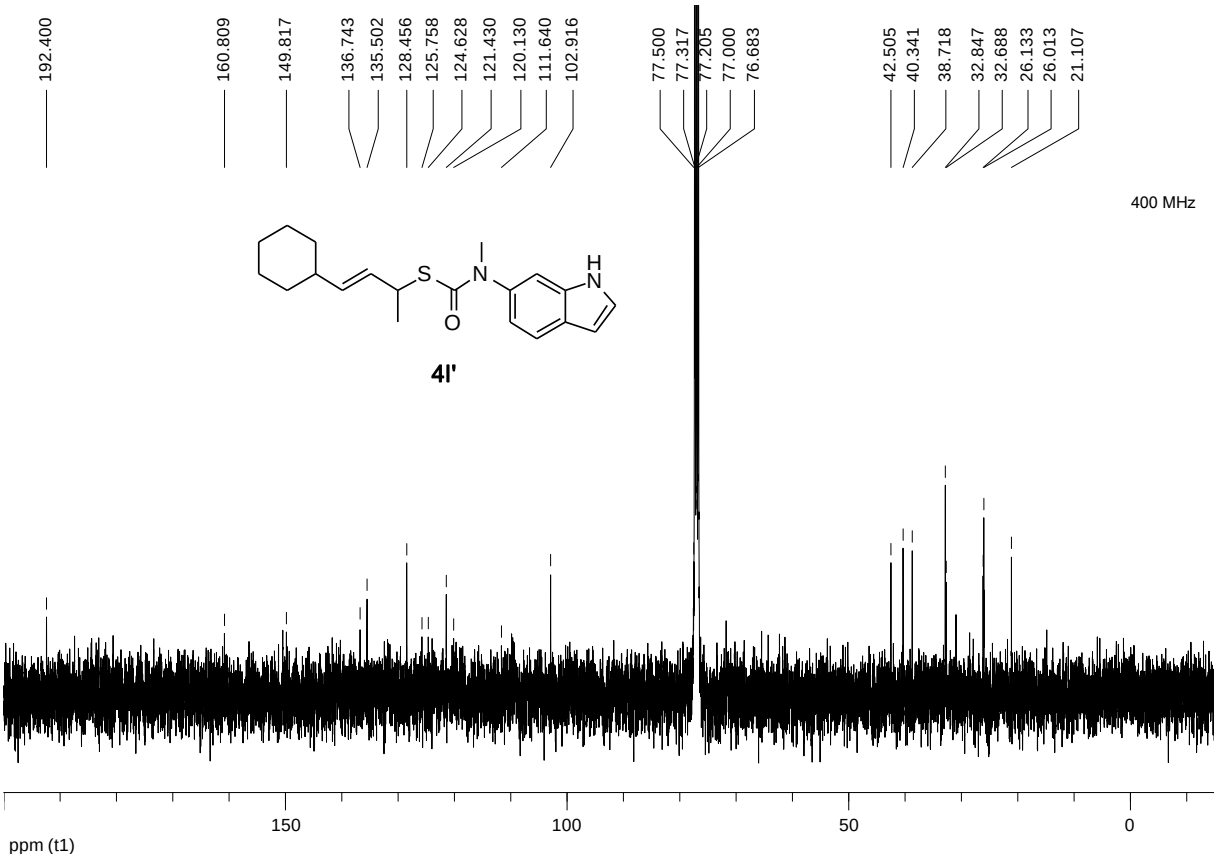

8.460
8.448
7.716
7.695
7.690
7.672
7.622
7.602
7.260
7.142
7.127
7.112
5.639
5.622
5.600
5.584
5.507
5.505
5.490
5.469
4.191
4.174
4.157
4.140
4.122
3.459
1.959
1.880
1.725
1.604
1.443
1.426
1.296
0.995
400 MHz
4k
0.97
1.02
1.00
1.01
1.02
1.00
3.01
1.06
5.48
3.17
6.05
5.0
0.0
ppm (t1)

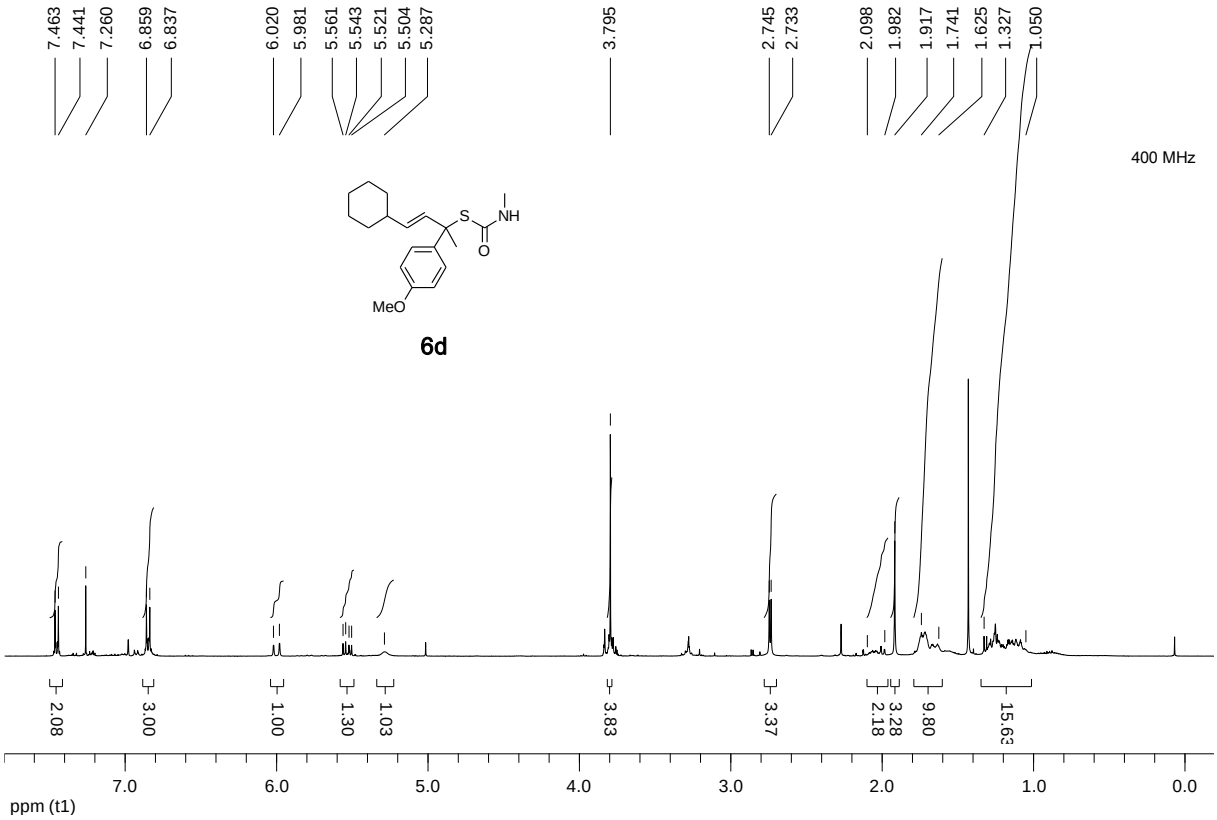

168.879
154.277
148.233
137.460
127.909
121.030
120.398
77.318
77.000
76.681
42.508
40.338
34.905
32.769
32.676
26.080
25.942
20.872
400 MHz
4k
150
100
50
0
ppm (t1)


8.082
7.627
7.618
7.563
7.543
7.260
7.139
7.134
7.118
7.113
6.575
6.567
6.566
5.547
5.531
5.508
5.492
5.433
5.416
5.392
5.375
4.121
4.104
4.087
4.070
4.053
3.360
1.914
1.823
1.666
1.592
1.368
1.351
1.259
0.952
400 MHz
4l
0.93
0.95
1.04
1.13
1.00
1.00
1.00
1.05
3.05
1.09
14.6
3.34
7.90
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

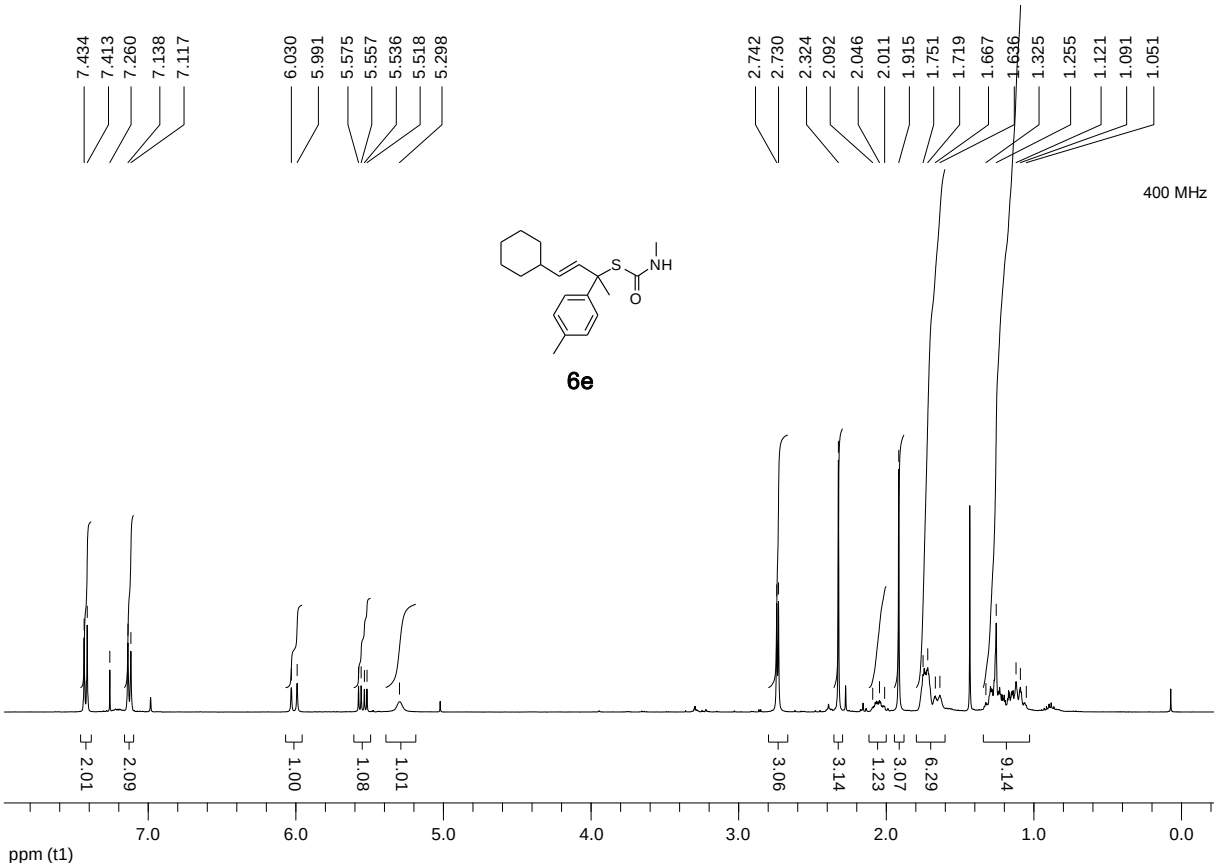

168.801
149.399
138.451
136.807
128.424
127.307
125.573
123.103
121.381
115.468
107.089
84.107
77.316
77.000
76.682
42.585
40.353
38.649
32.835
32.697
28.164
26.135
26.010
21.067
400 MHz
4l
150
100
50
0
ppm (t1)


8.271
7.659
7.638
7.308
7.287
7.279
7.273
7.260
7.007
7.002
6.986
6.981
6.583
6.577
6.572
5.532
5.516
5.493
5.477
5.420
5.403
5.380
5.364
4.105
4.088
4.071
4.054
4.036
3.354
1.901
1.811
1.682
1.576
1.358
1.341
1.259
0.928
400 MHz
S
N
H
N
O
4l'
0.95
0.97
1.00
1.03
0.99
1.00
0.98
1.00
3.06
5.35
2.23
6.52
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

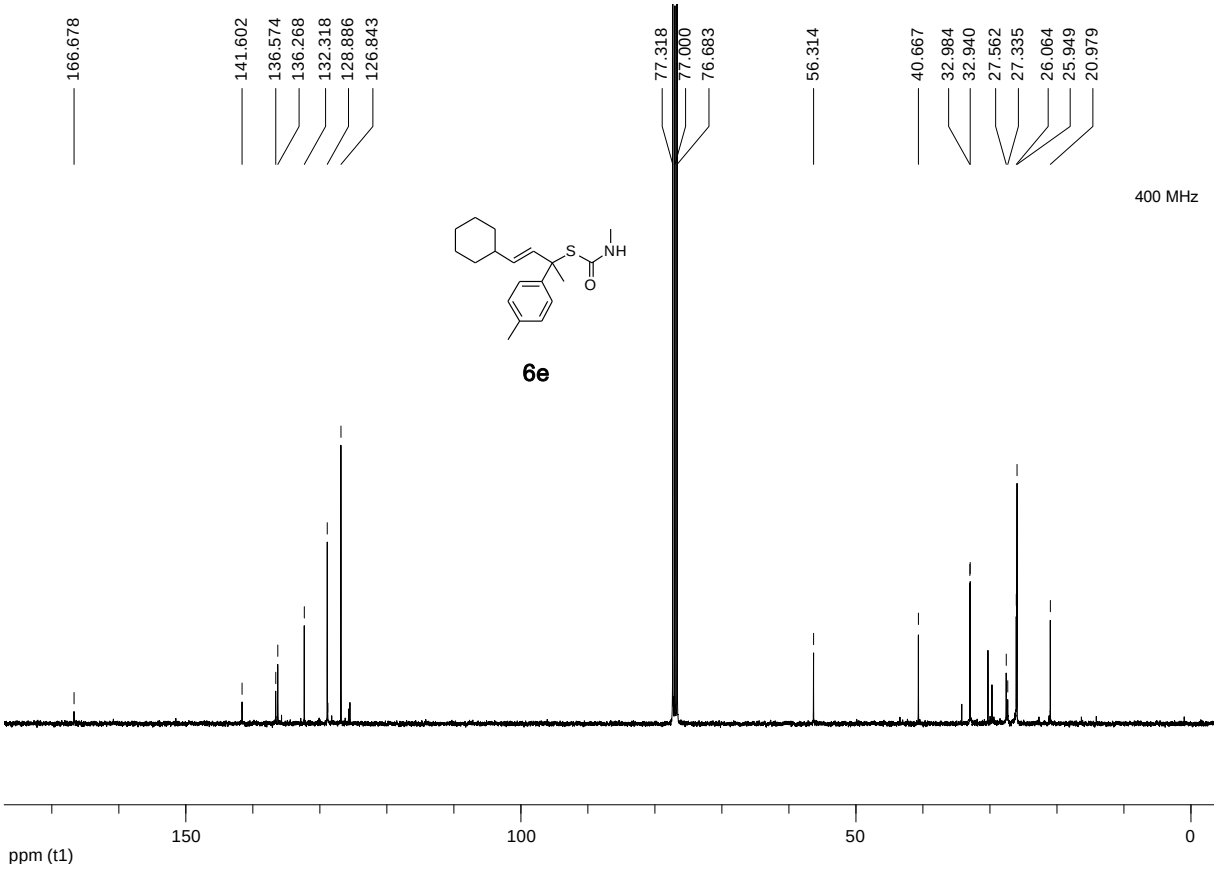

192.400
160.809
149.817
136.743
135.502
128.456
125.758
124.628
121.430
120.130
111.640
102.916
77.500
77.317
77.205
77.000
76.683
42.505
40.341
38.718
32.847
32.688
26.133
26.013
21.107
400 MHz
S
N
H
N
O
4l'
150
100
50
0
ppm (t1)


7.463
7.441
7.260
6.859
6.837
6.020
5.981
5.561
5.543
5.521
5.504
5.287
3.795
2.745
2.733
2.098
1.982
1.917
1.741
1.625
1.327
1.050
400 MHz
S
NH
O
MeO
2.08
3.00
1.00
1.30
1.03
3.83
3.47
2.18
3.28
6.80
15.93
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

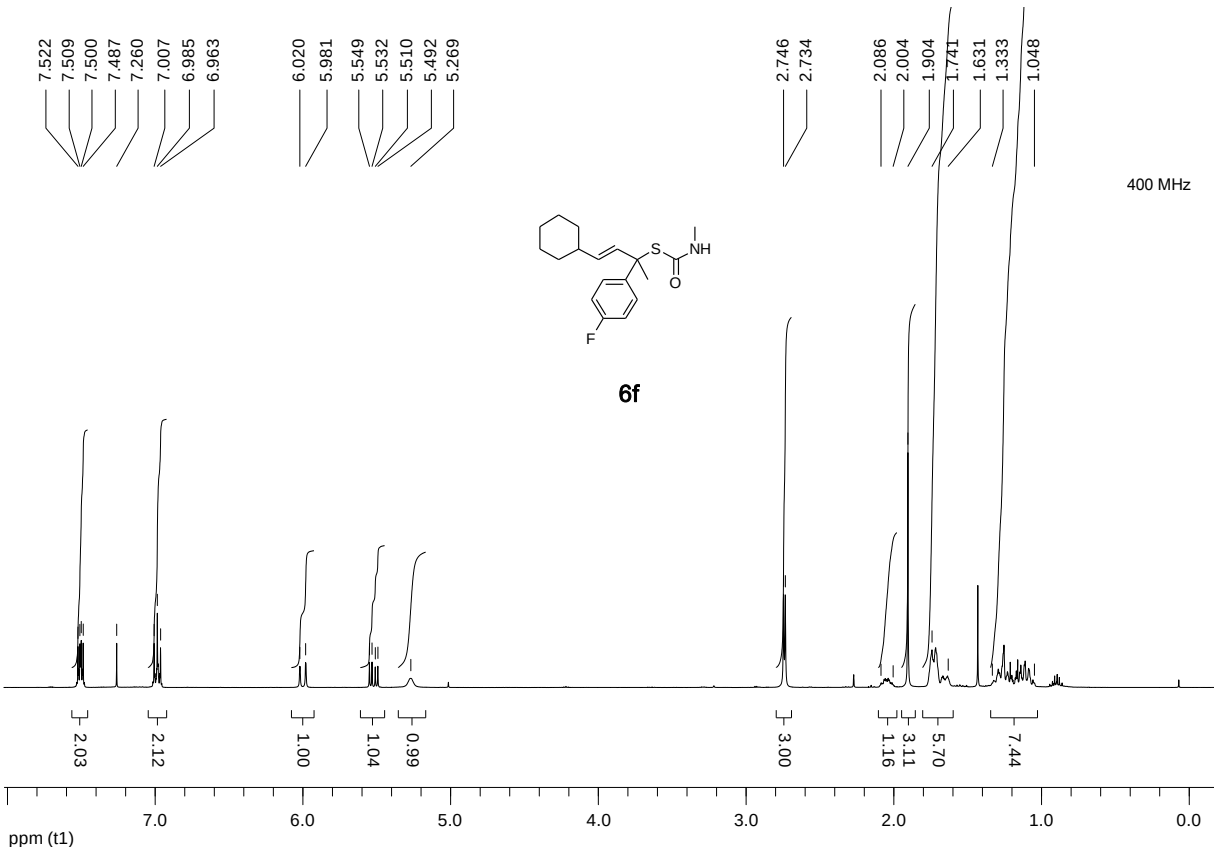
6d


7.434
7.413
7.260
7.138
7.117
6.030
5.991
5.575
5.557
5.536
5.518
5.298
2.742
2.730
2.324
2.092
2.046
2.011
1.915
1.751
1.719
1.667
1.636
1.325
1.255
1.121
1.091
1.051
400 MHz
S
NH
O
2.01
2.09
1.00
1.08
1.01
3.06
3.14
1.23
3.07
6.29
9.14
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

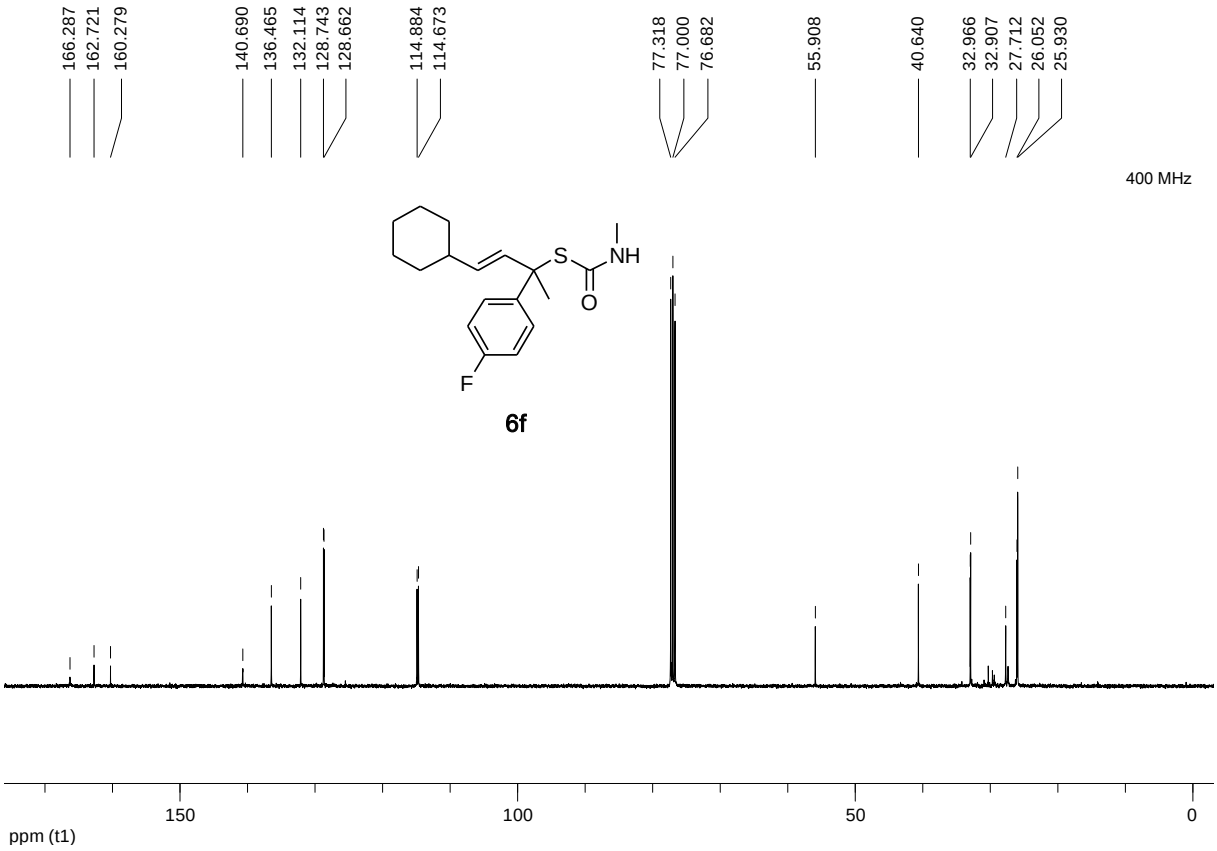
6e


166.678
141.602
136.574
136.268
132.318
128.886
126.843
77.318
77.000
76.683
56.314
40.667
32.984
32.940
27.562
27.335
26.064
25.949
20.979
400 MHz
S
NH
O
150
100
50
0
ppm (t1)

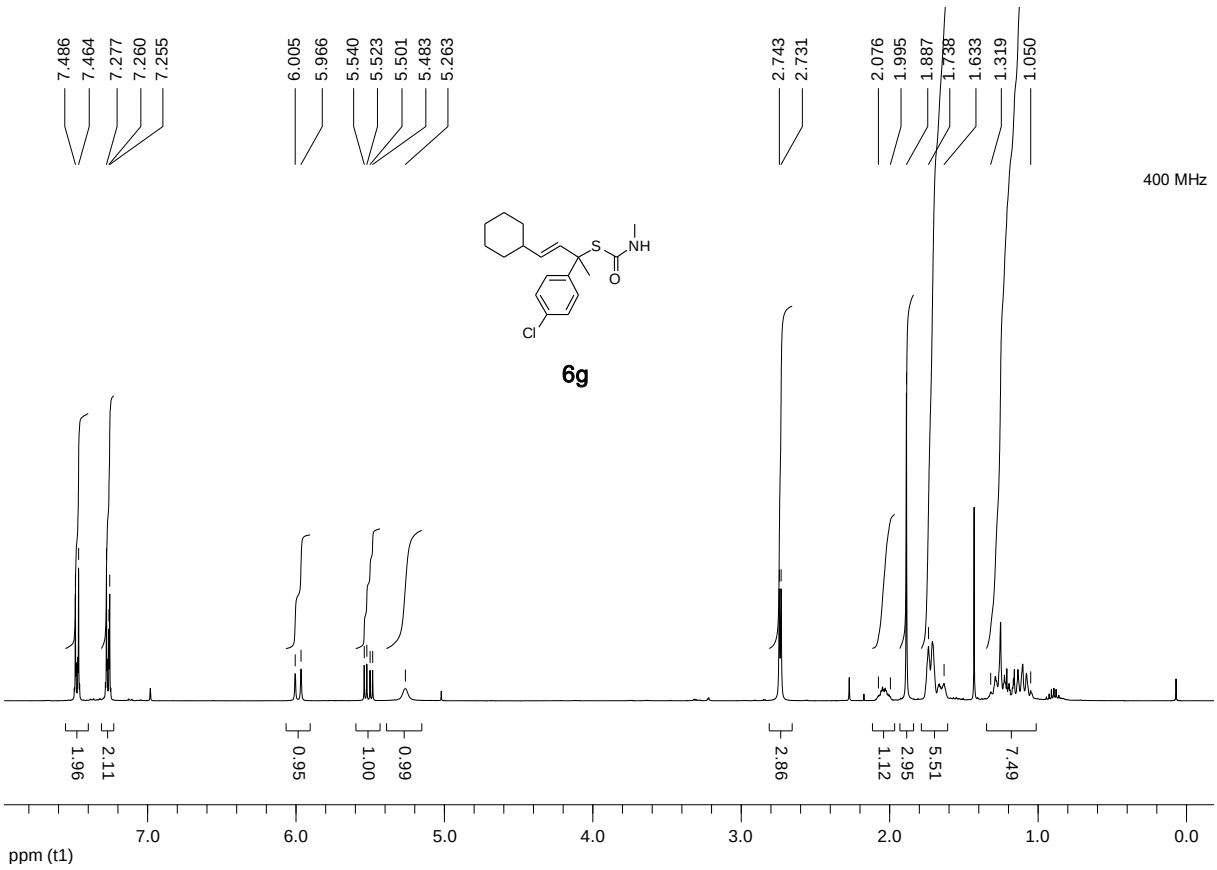
6e


7.522
7.509
7.500
7.487
7.260
7.007
6.985
6.963
6.020
5.981
5.549
5.532
5.510
5.492
5.269
2.746
2.734
2.086
2.004
1.904
1.741
1.631
1.333
1.048
400 MHz
S
NH
O
F
2.03
2.12
1.00
1.04
0.99
3.00
1.16
3.11
5.70
7.44
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

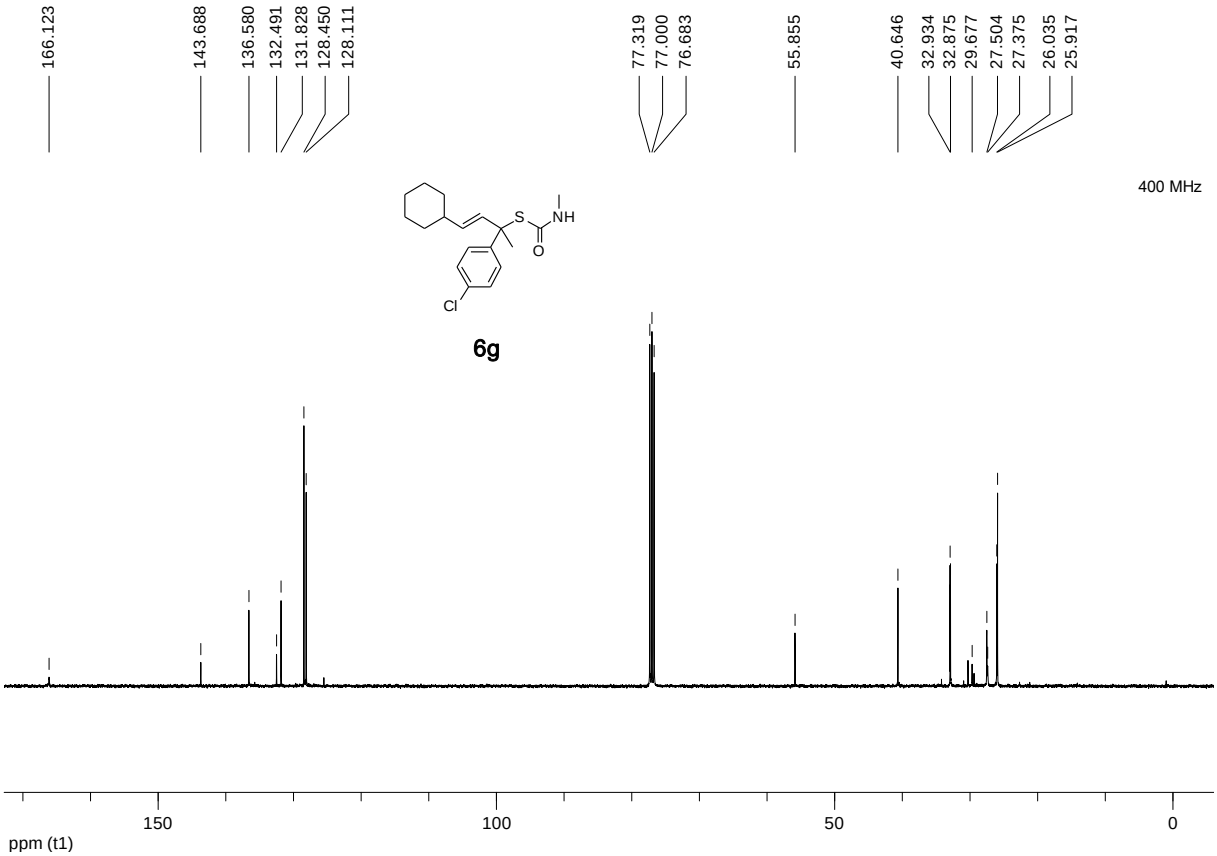
6f


166.287
162.721
160.279
140.690
136.465
132.114
128.743
128.662
114.884
114.673
77.318
77.000
76.682
55.908
40.640
32.966
32.907
27.712
26.052
25.930
400 MHz
S
NH
O
F
150
100
50
0
ppm (t1)

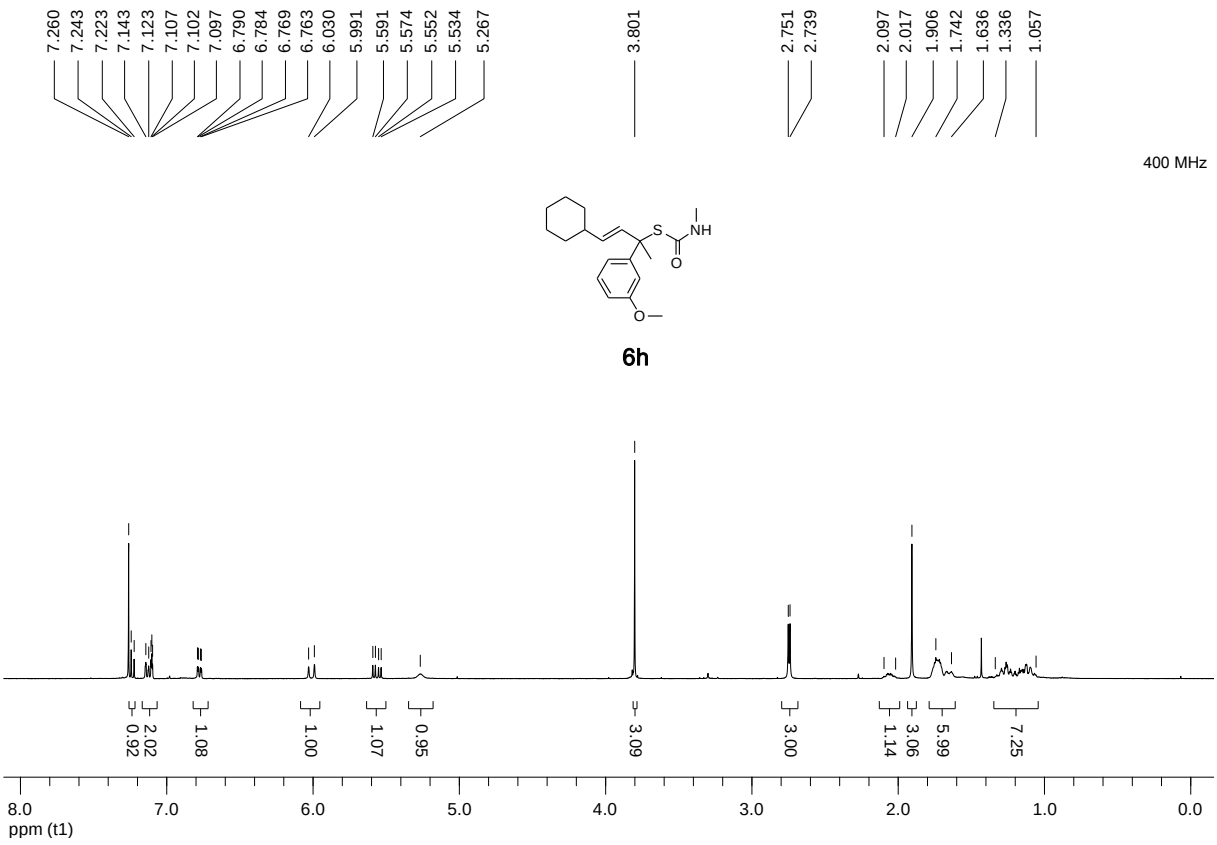
6f


7.486
7.464
7.277
7.260
7.255
6.005
5.966
5.540
5.523
5.501
5.483
5.263
2.743
2.731
2.076
1.995
1.887
1.738
1.633
1.319
1.050
400 MHz
S
NH
O
Cl
1.96
2.11
0.95
1.00
0.99
2.86
1.12
2.95
5.51
7.49
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

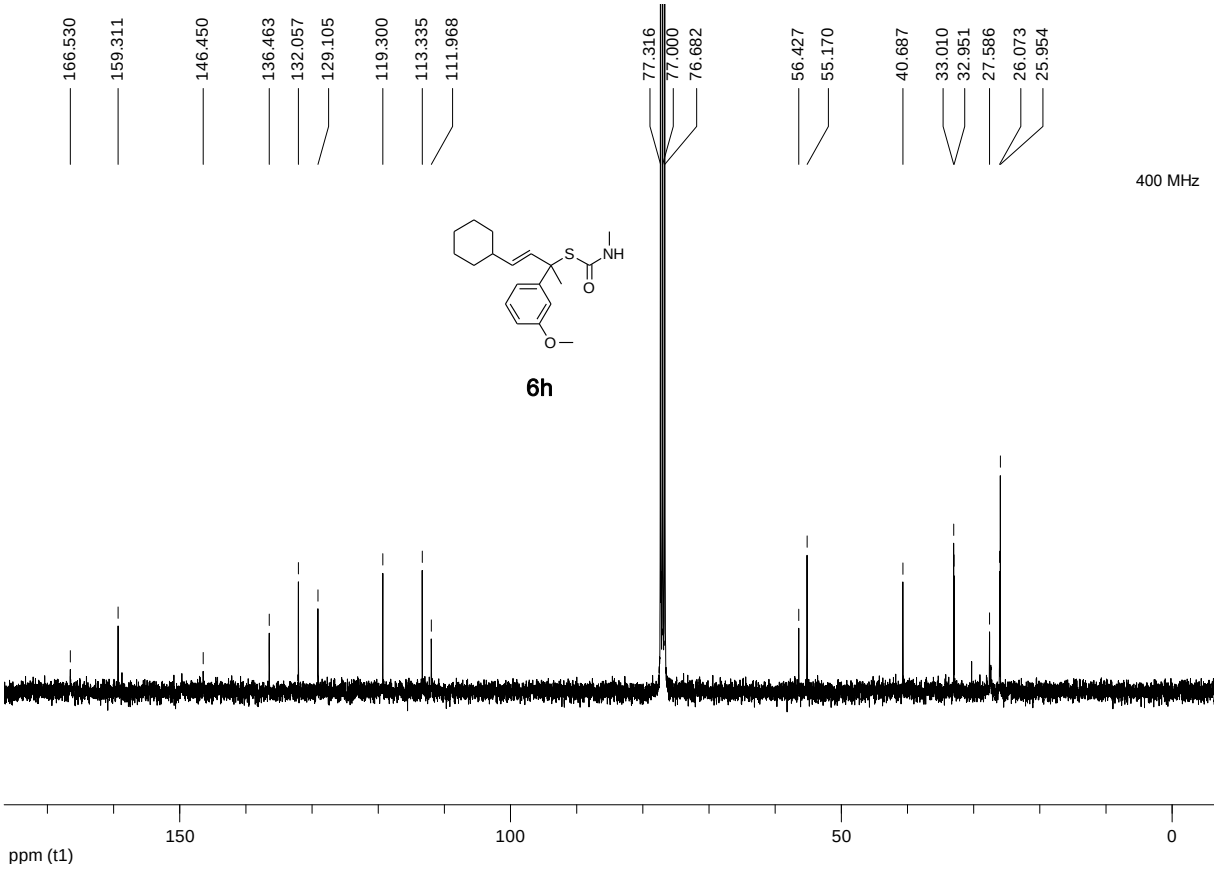
6g


166.123
143.688
136.580
132.491
131.828
128.450
128.111
77.319
77.000
76.683
55.855
40.646
32.934
32.875
29.677
27.504
27.375
26.035
25.917
400 MHz
S
NH
O
Cl
150
100
50
0
ppm (t1)

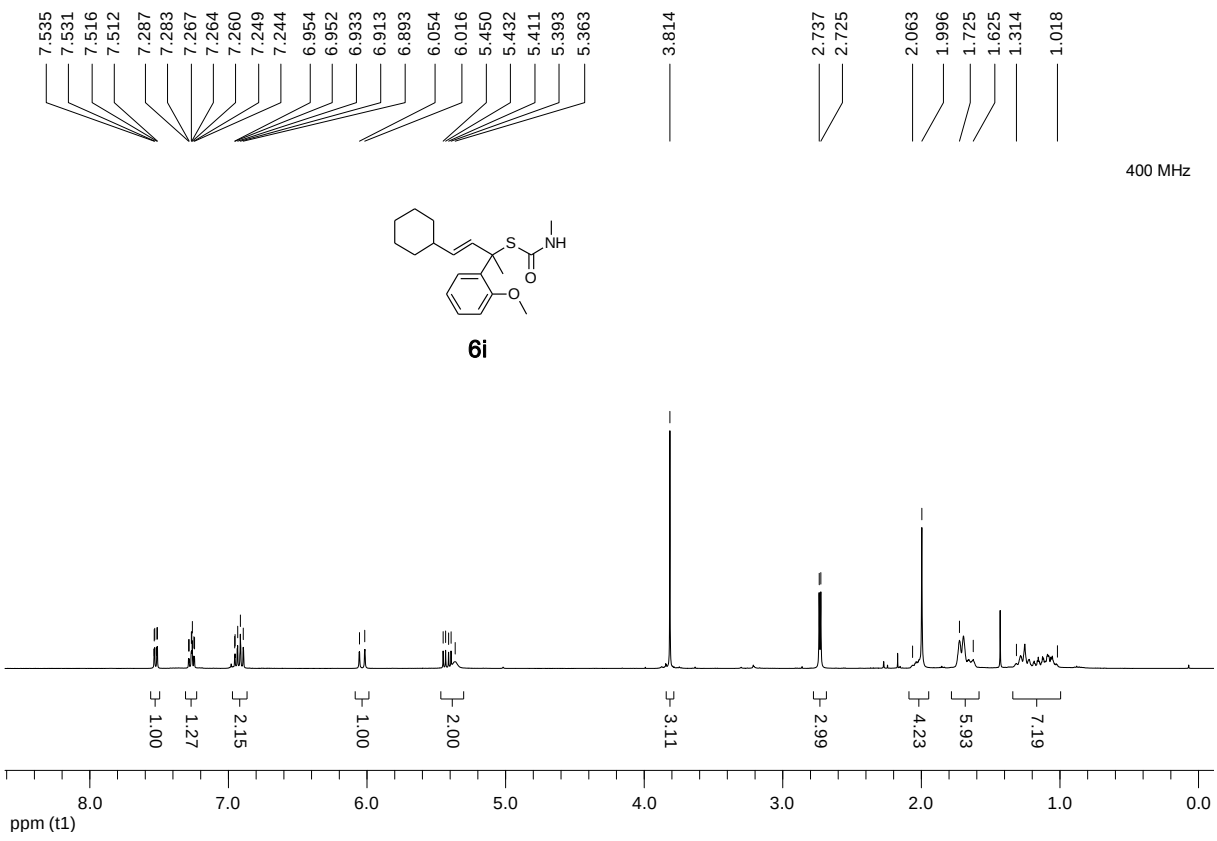
6g


7.260
7.243
7.223
7.143
7.123
7.107
7.102
7.097
6.790
6.784
6.769
6.763
6.030
5.991
5.591
5.574
5.552
5.534
5.267
3.801
2.751
2.739
2.097
2.017
1.906
1.742
1.636
1.336
1.057
400 MHz
S
NH
O
O
0.92
2.02
1.08
1.00
1.07
0.95
3.09
3.00
1.14
3.06
5.99
7.25
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

6h


166.530
159.311
146.450
136.463
132.057
129.105
119.300
113.335
111.968
77.316
77.000
76.682
56.427
55.170
40.687
33.010
32.951
27.586
26.073
25.954
400 MHz
S
NH
O
O
150
100
50
0
ppm (t1)

6h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NH
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O
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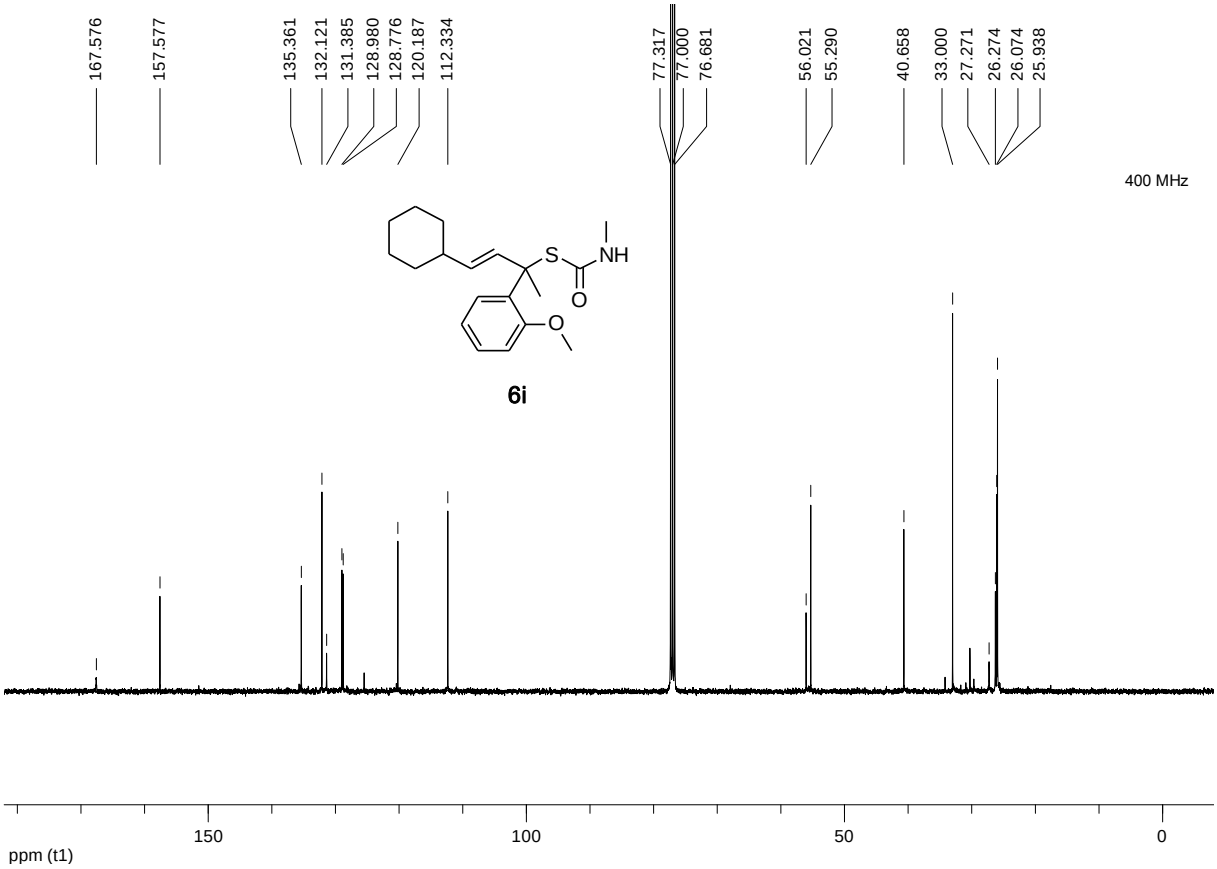
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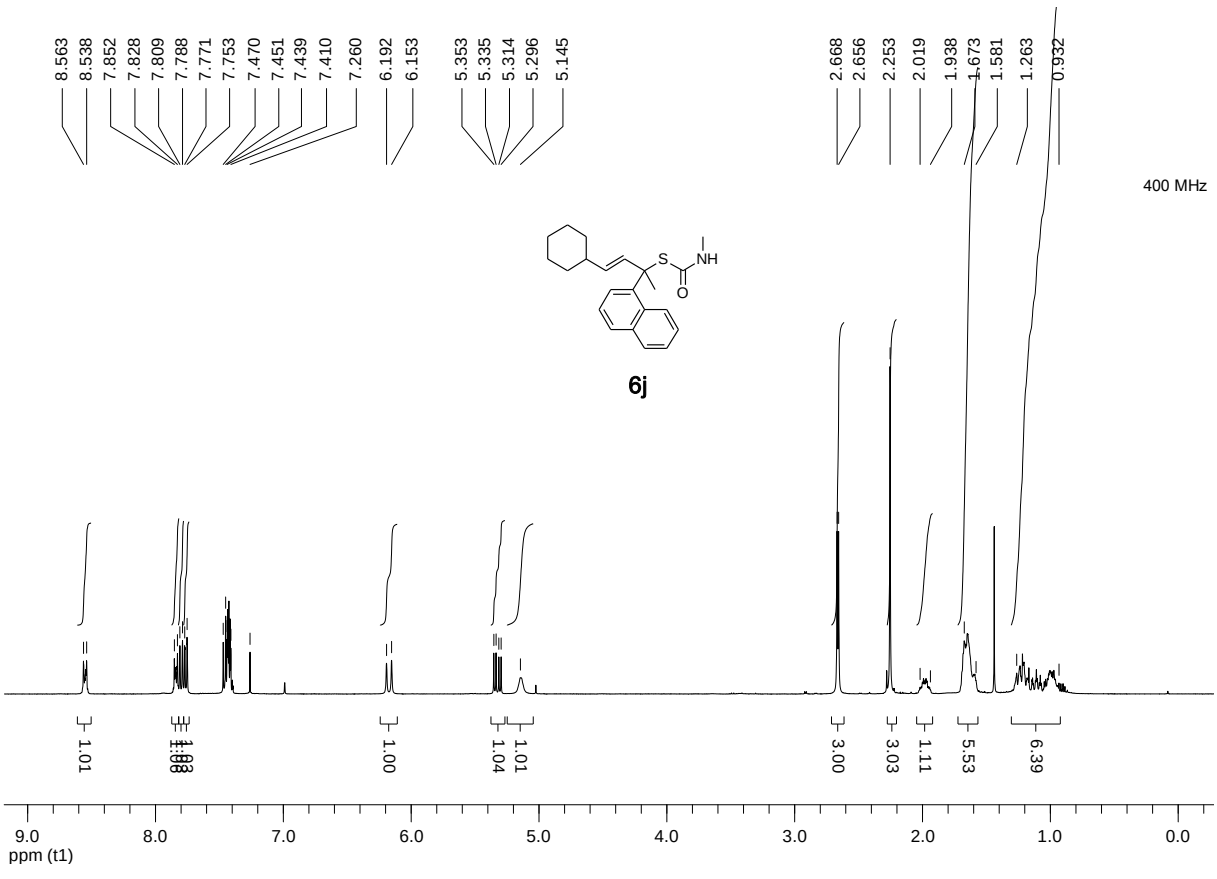
ppm (t1)

6i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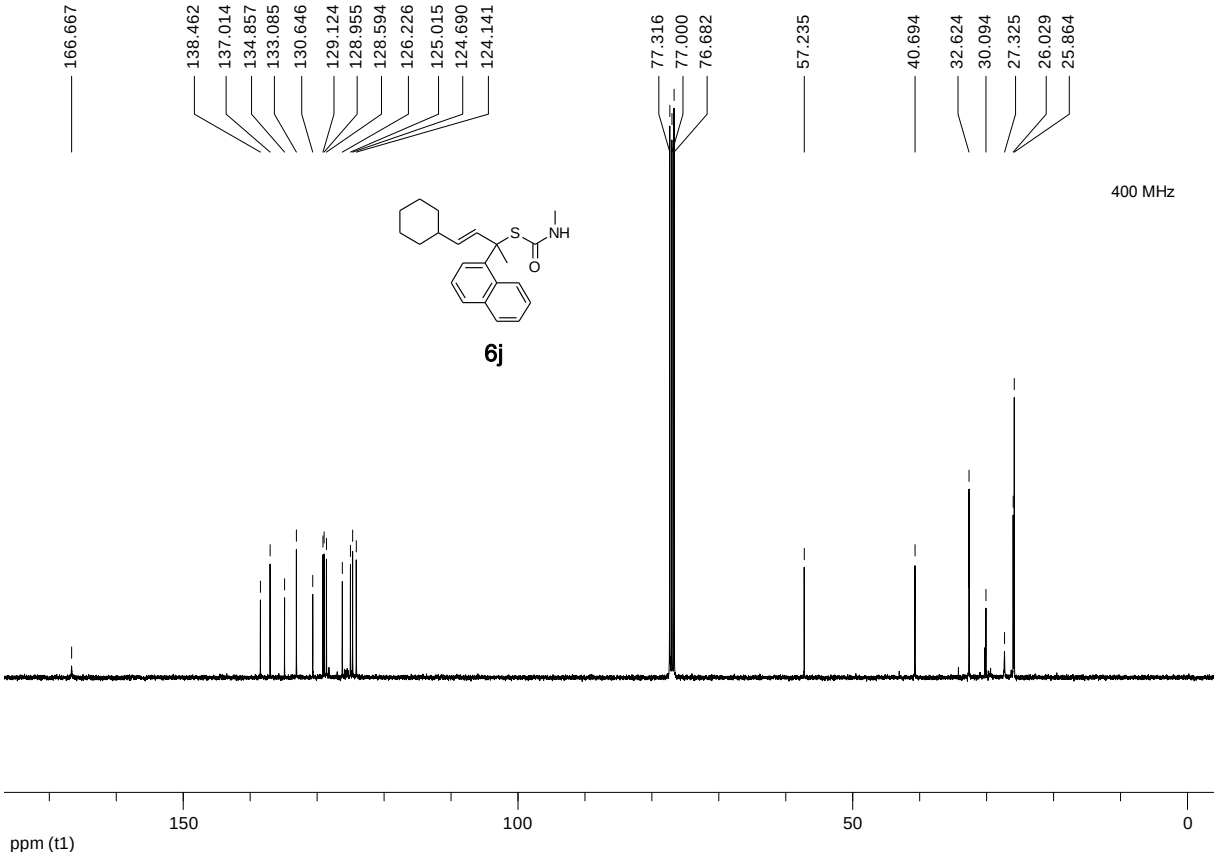
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O
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ppm (t1)

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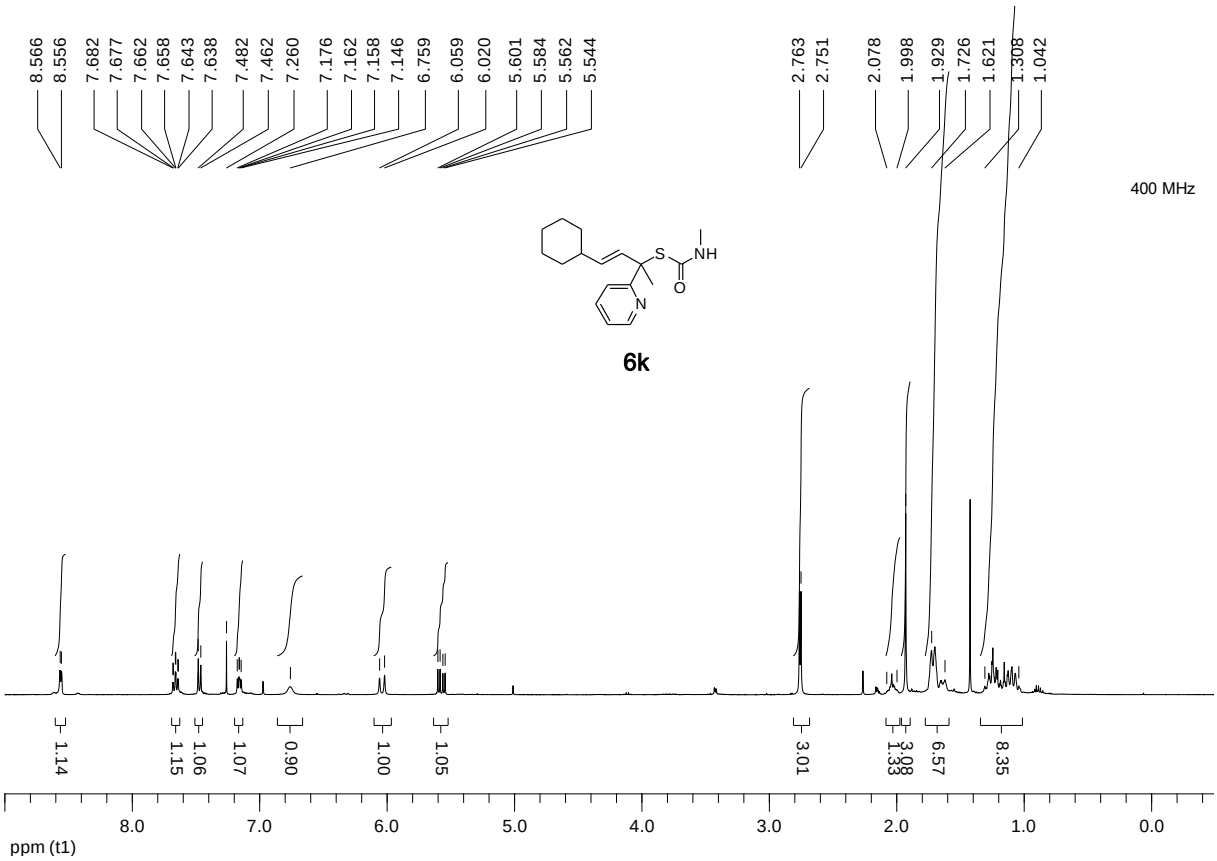
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7.158
7.146
6.759
6.059
6.020
5.601
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O
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1.07
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1.33
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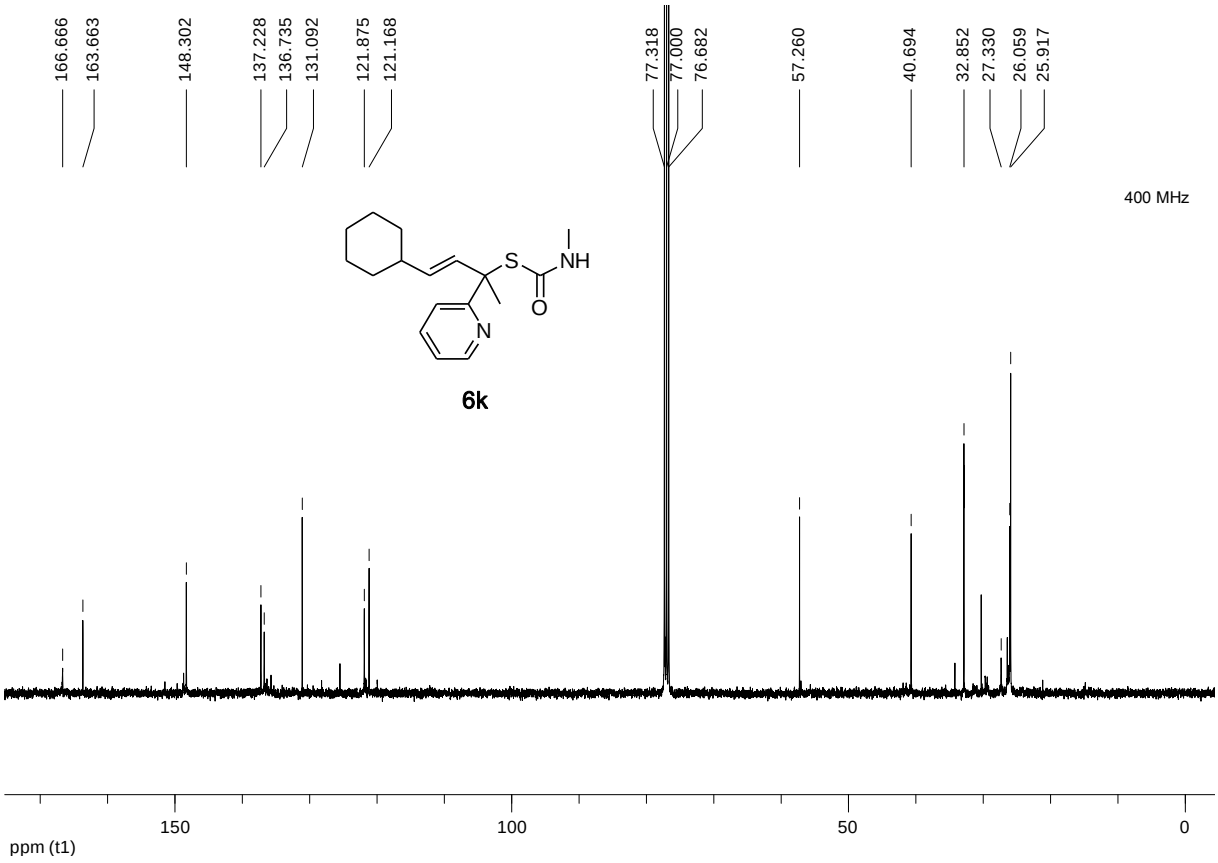
ppm (t1)

6k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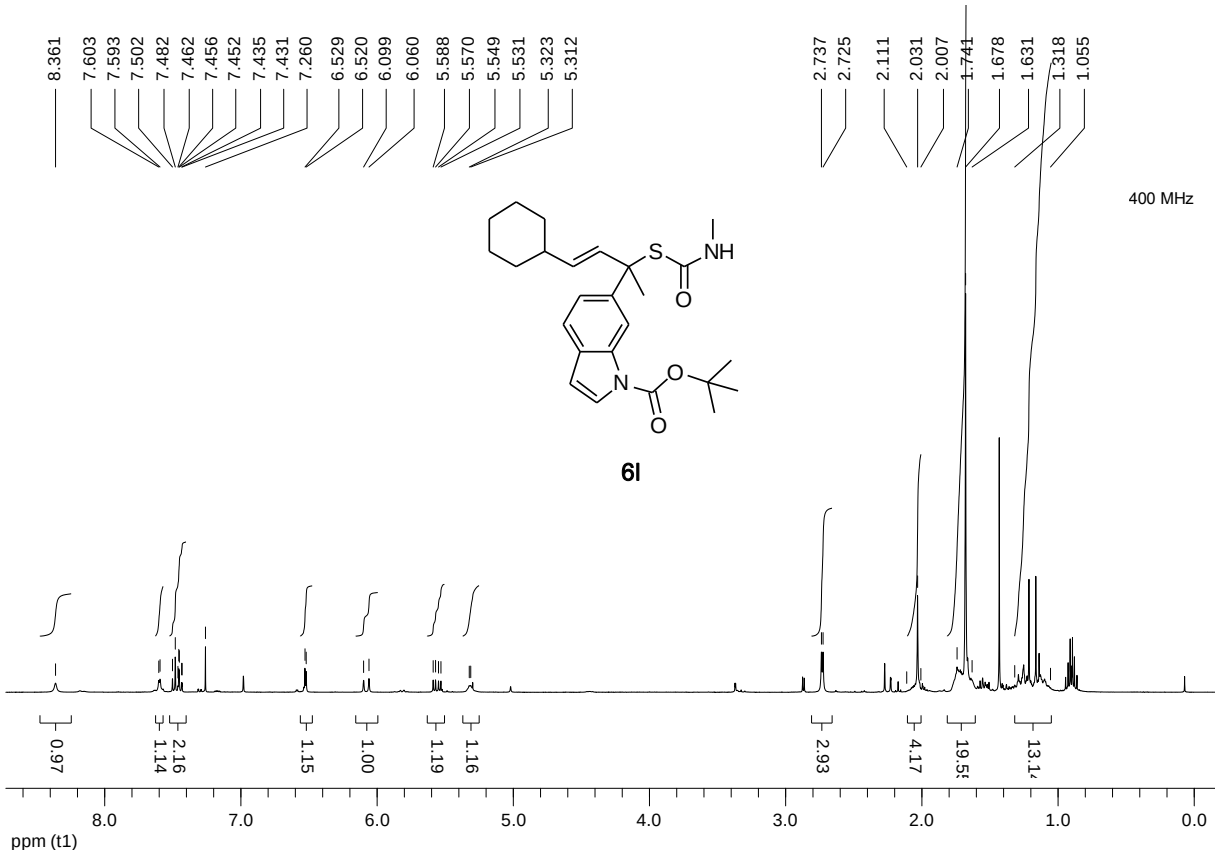
6k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5.570
5.549
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1.678
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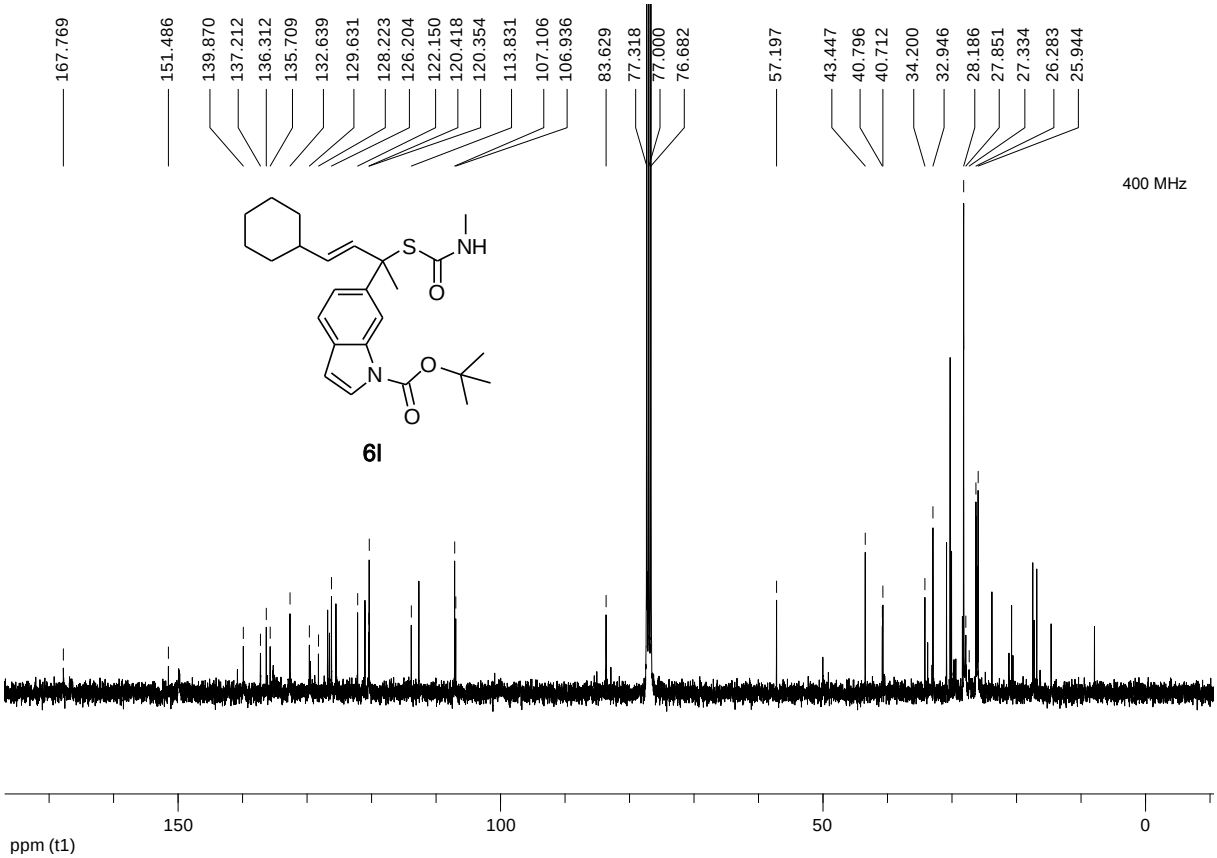
ppm (t1)

6l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107.106
106.936
83.629
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77.000
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57.197
43.447
40.796
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32.946
28.186
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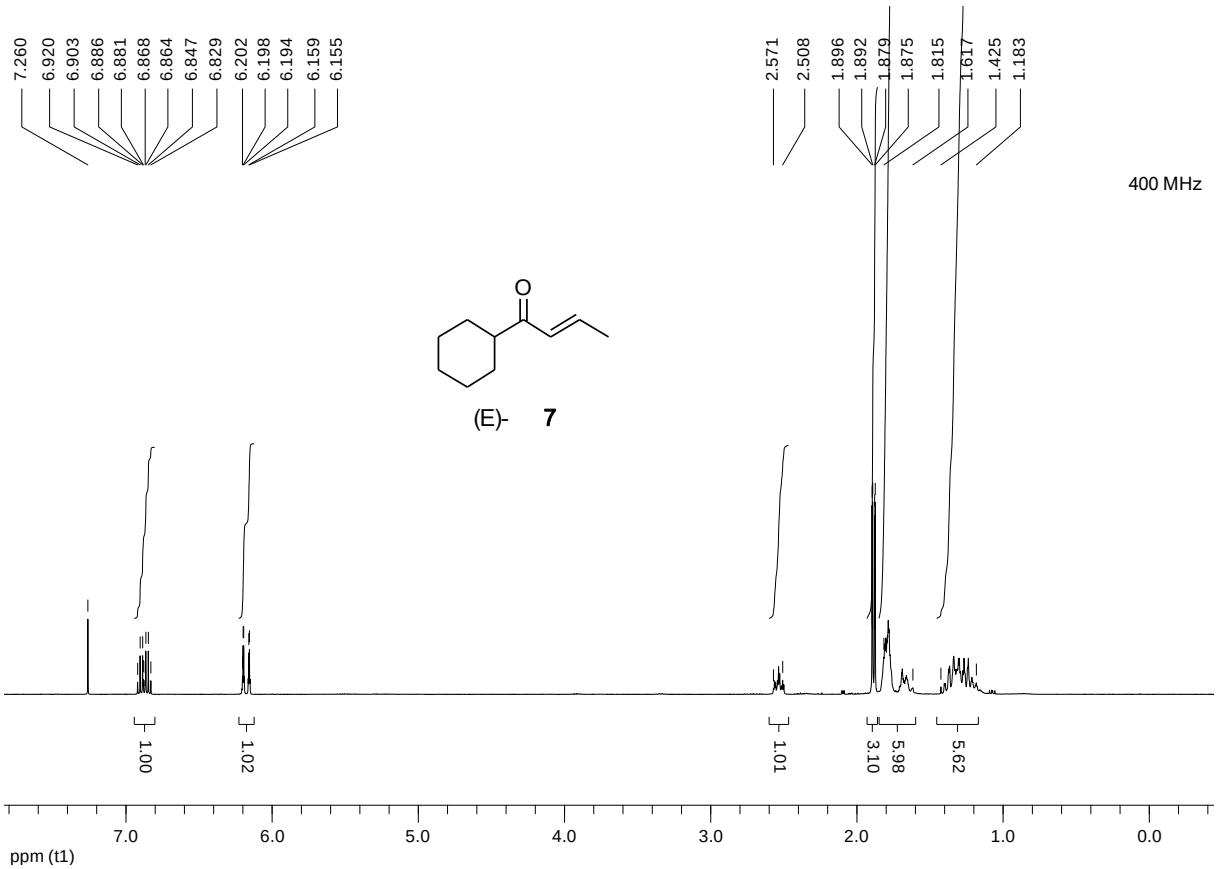
0
ppm (t1)

6l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2.571
2.508
1.896
1.892
1.879
1.875
1.815
1.617
1.425
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400 MHz
O
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1.02
1.01
3.10
5.98
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1.0
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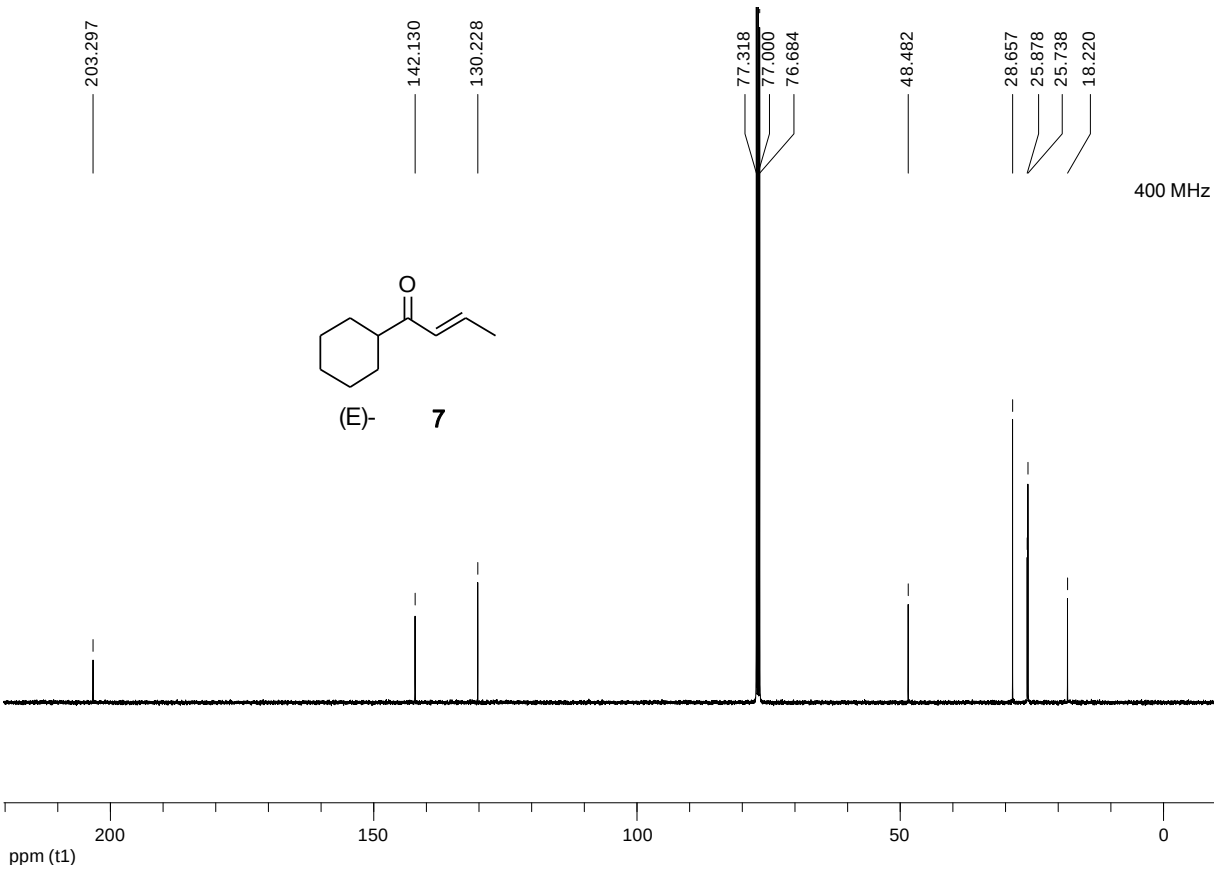
ppm (t1)

(E)- **7**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(E)- 7
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50
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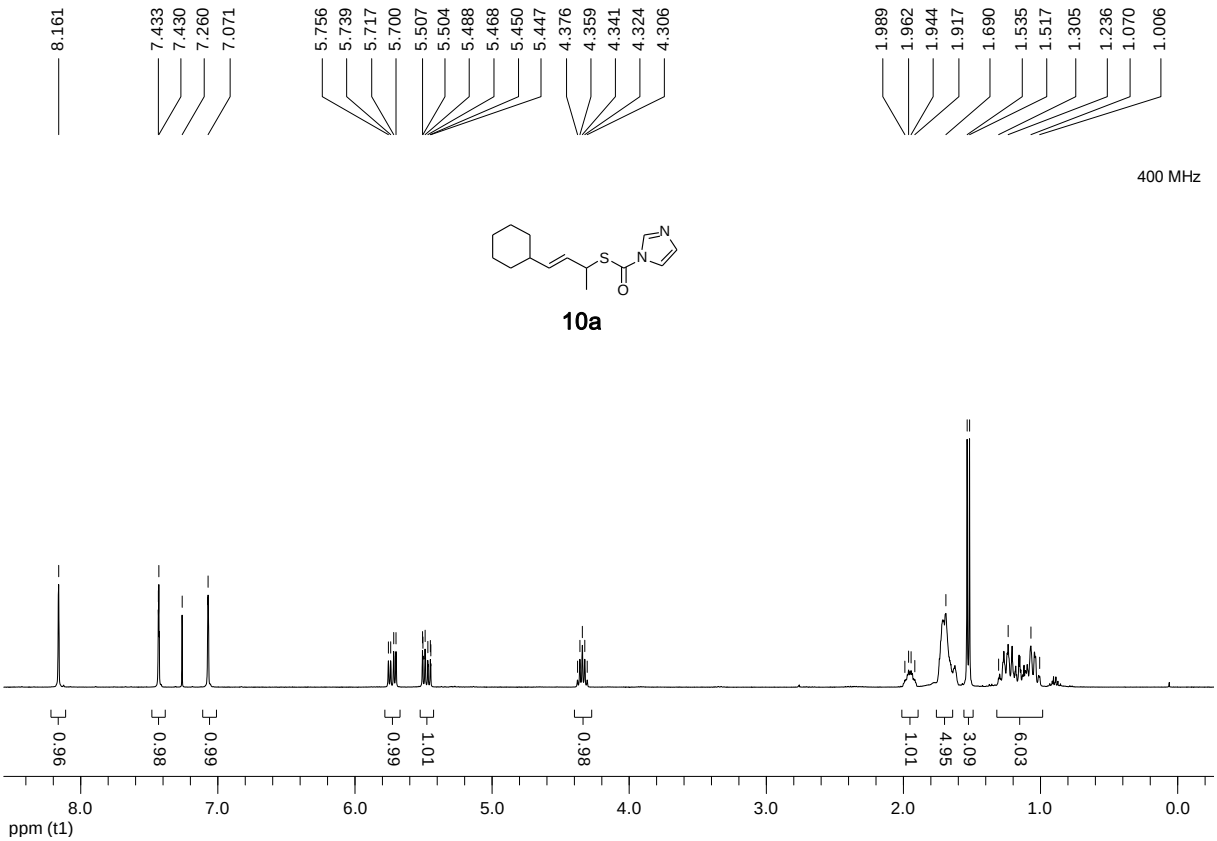
ppm (t1)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N
S
N
O
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1.01
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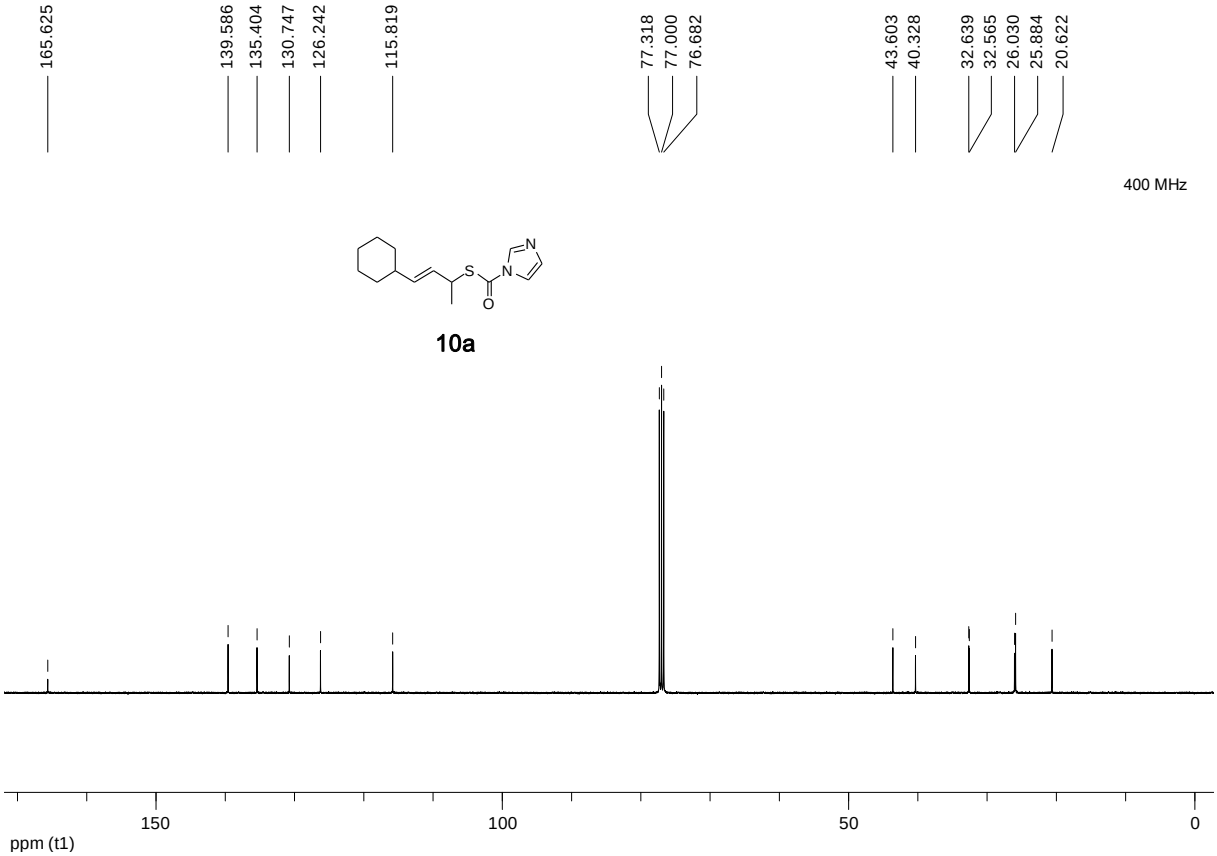
ppm (t1)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50
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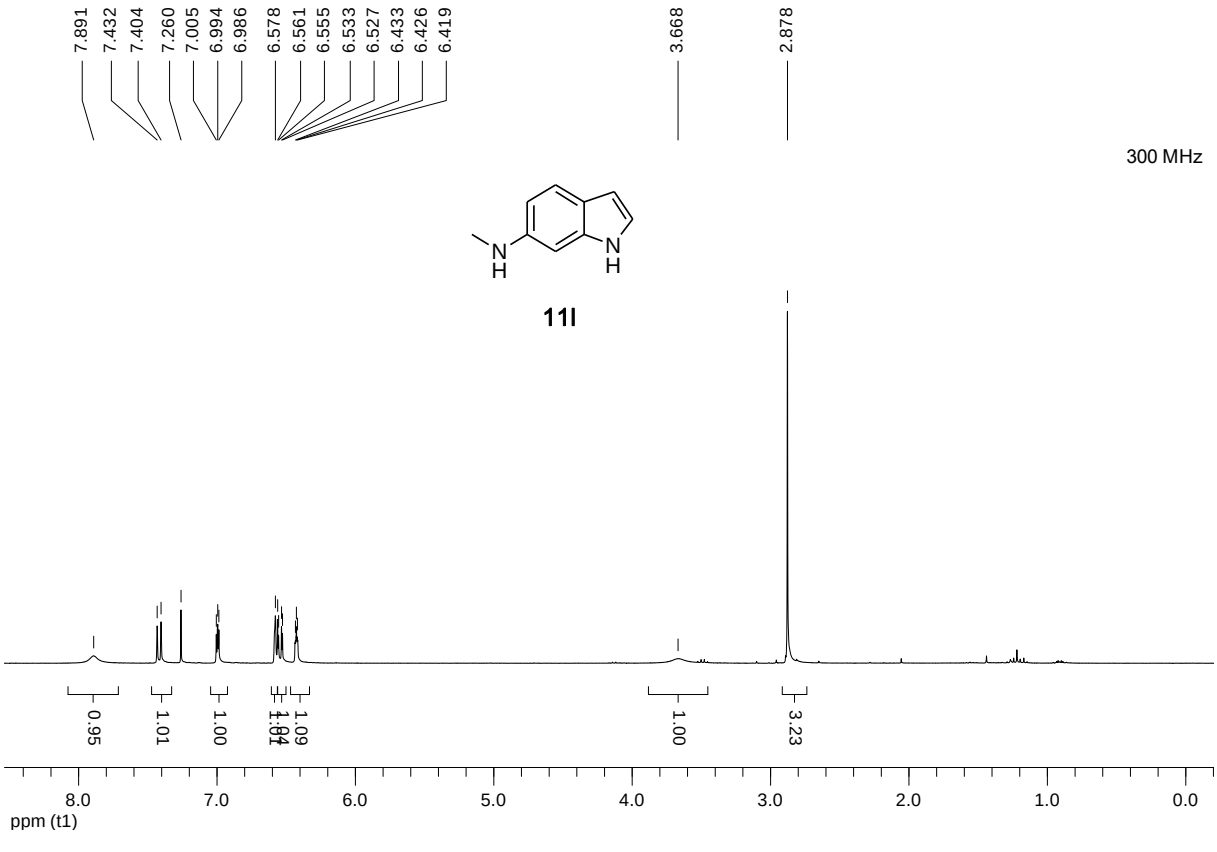
ppm (t1)

10a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6.433
6.426
6.419
3.668
2.878
300 MHz
N
H
N
H
0.95
1.01
1.00
1.04
1.09
1.00
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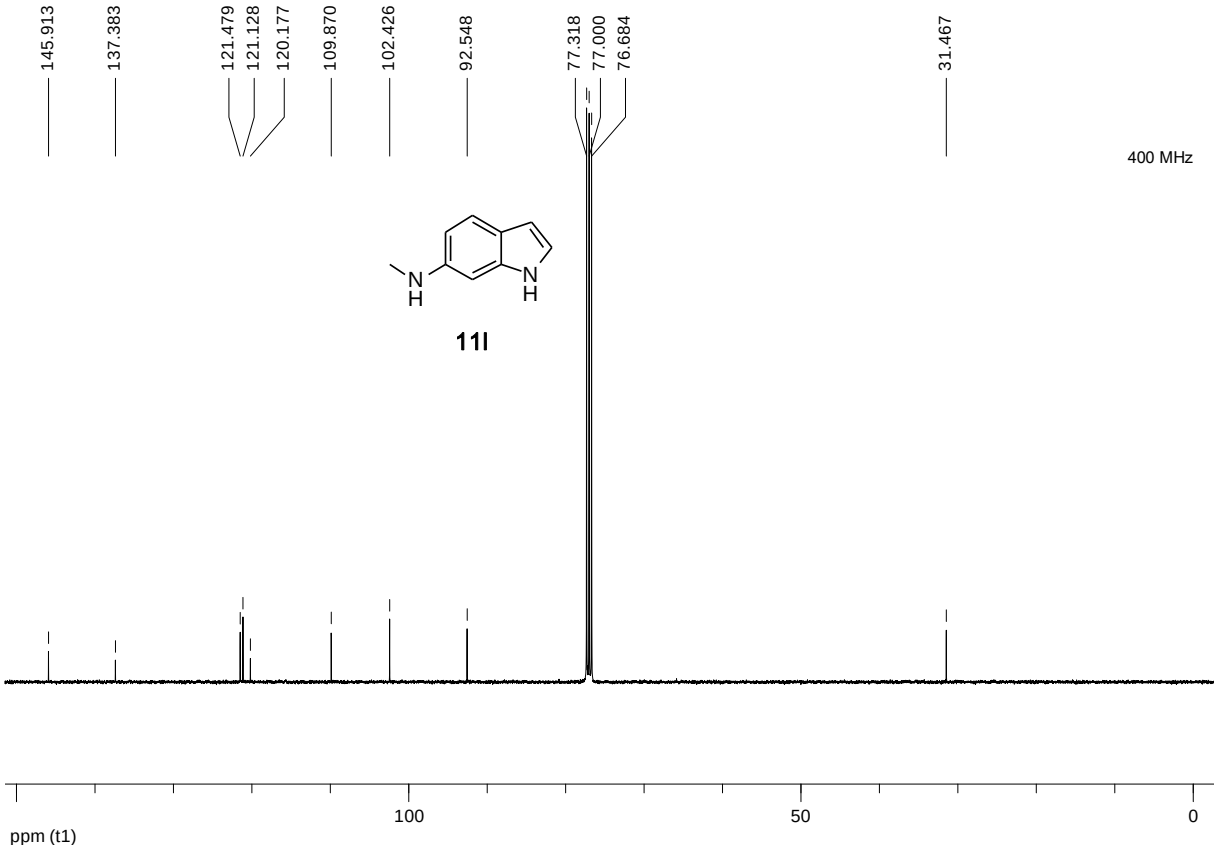
ppm (t1)

11l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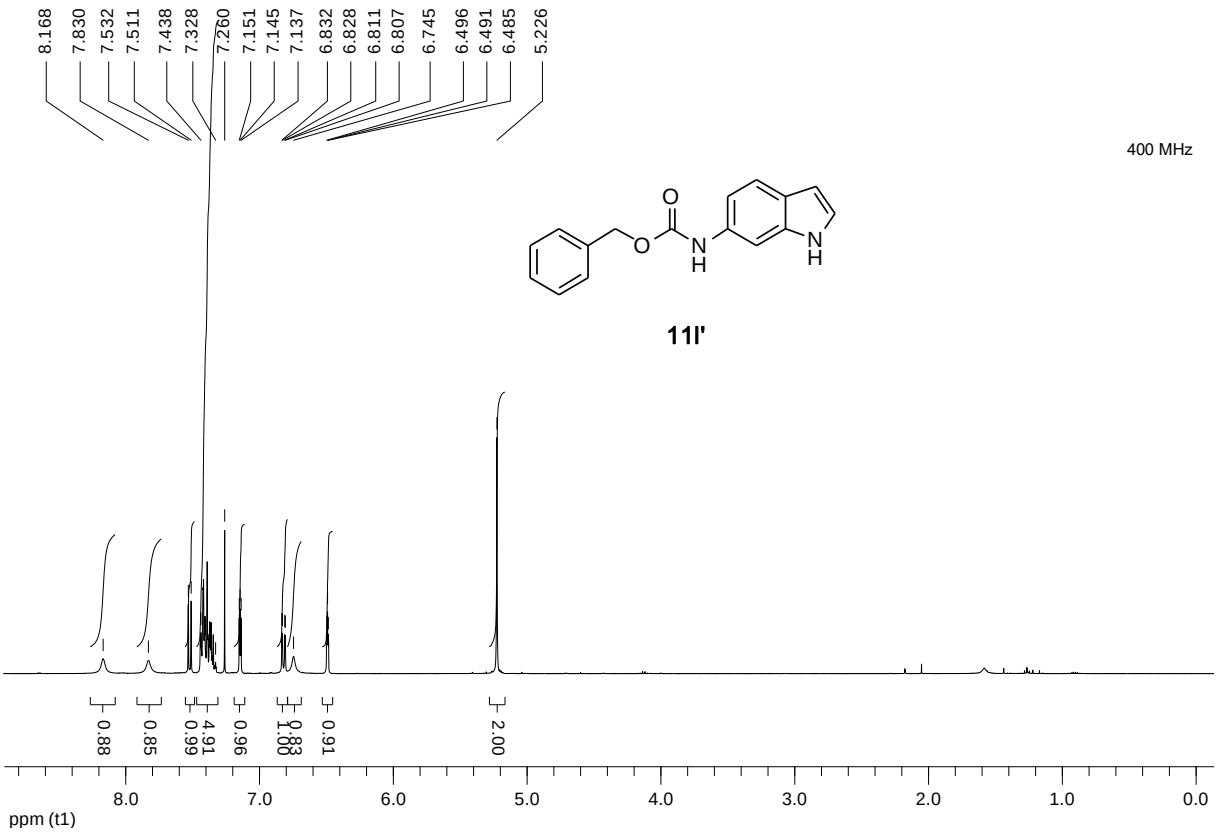
400 MHz
11l
100
50
0
ppm (t1)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6.807
6.745
6.496
6.491
6.485
5.226
400 MHz
11l'
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0.85
0.99
4.91
0.96
1.00
0.83
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2.0
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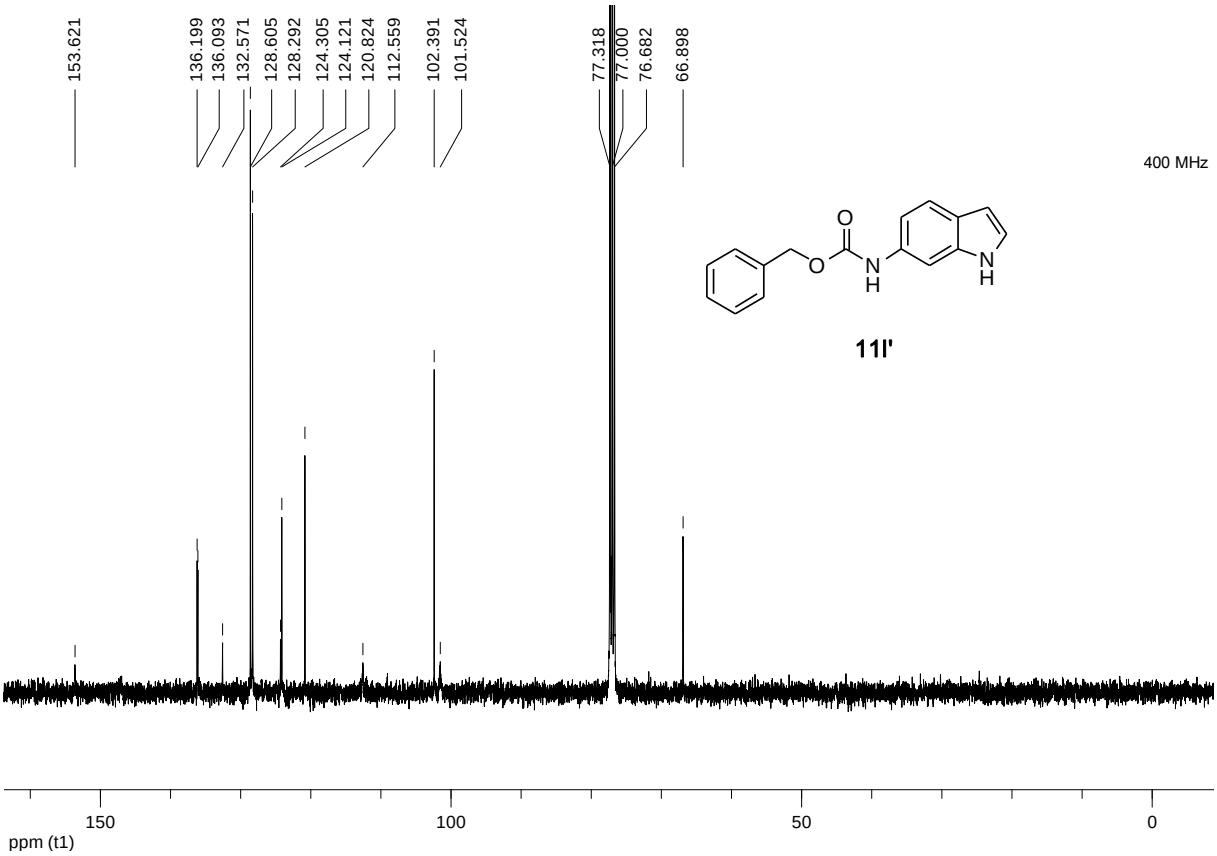
0.0
ppm (t1)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77.000
76.682
66.898
400 MHz
O
O
N
H
N
H
11l'
150
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50
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ppm (t1)

NMR studies of 4aLi:

(1-(((4-methoxyphenyl)(methyl)carbamoyl)thio)allyl)lithium

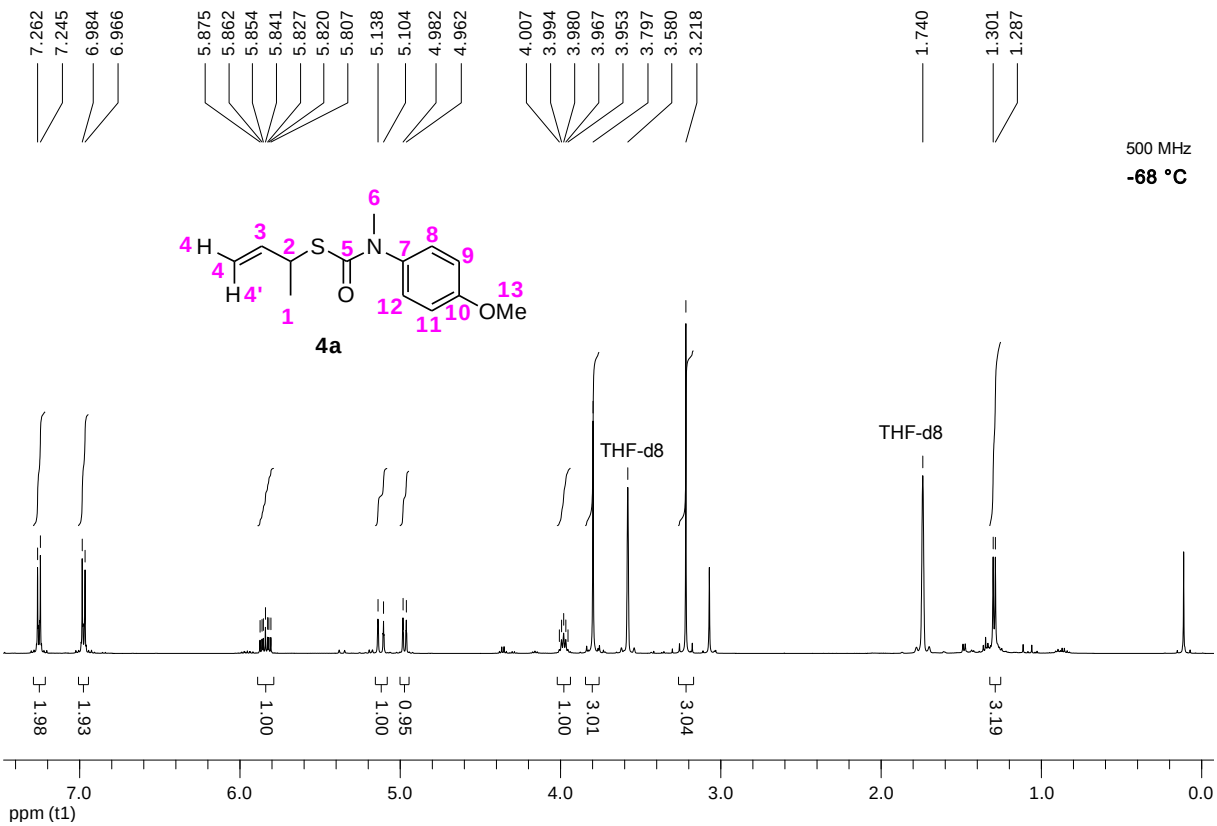


Figure 1: *^{1}H NMR spectrum of allylic thiocarbamate **4a** in d8-THF at -68 °C.*

Entry	^{1}H shift (ppm)	Multiplicity (integration)	*J* (Hz)	H
1	7.25	d (2)	8.8	8, 12
2	6.98	d (2)	8.8	9, 11
3	5.84	ddd (1)	17.0, 10.3, 6.7	3
4	5.12	dd (1)	17.0, 1.3	4’
5	4.97	dd (1)	10.3, 1.0	4
6	3.98	qn (1)	6.7	2
7	3.80	s (3)	-	13
8	3.22	s (3)	-	6
9	1.29	d (3)	6.7	1

Table 1: *Data for ^{1}H NMR spectrum of allylic thiocarbamate **4a** at -68 °C.*

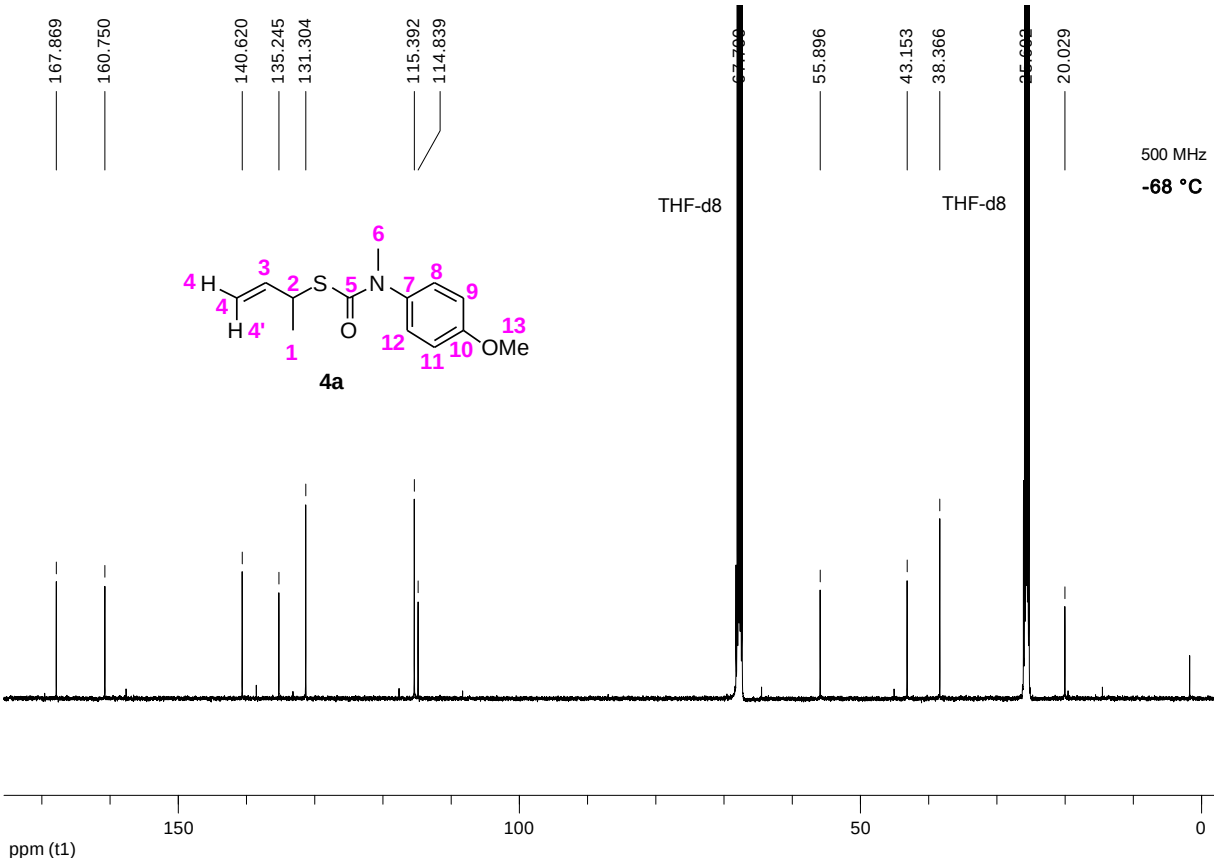


Figure 2: *^{13}C NMR spectrum of allylic thiocarbamate **4a** in d8-THF at -68 °C.*

Entry	^{13}C shift (ppm)	C
1	167.9	5
2	160.8	10
3	140.6	3
4	135.2	7
5	131.3	8, 12
6	115.4	9, 11
7	114.8	4
8	55.9	13
9	43.2	2
10	38.4	6
11	20.0	1

Table 2: *Data for ^{13}C NMR spectrum of allylic thiocarbamate **4a** at -68 °C.*

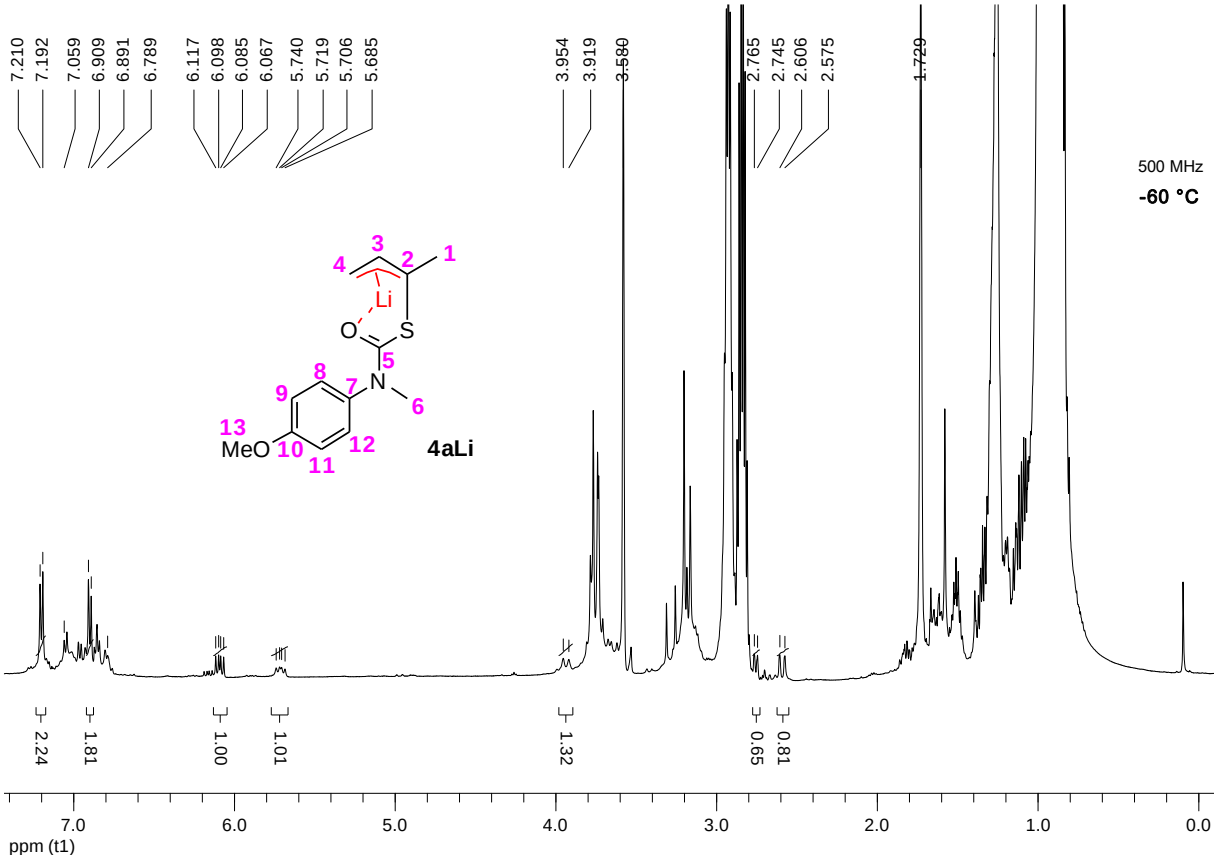


Figure 3: *^{1}H NMR spectrum of lithiated allylic thiocarbamate **4aLi** in d8-THF at -60 °C.*

The main evidence for formation of the allylithium **4aLi** was disappearance of the quartet at 3.98 ppm in **4aLi**, confirming deprotonation of H-2 (Figure 1, Figure 3).

Secondly, the signal for H-3 turned from a ddd in **4a** to a dd in **4aLi**, indicating it was then coupling with only two protons, rather than three, protons (Figure 1, Figure 3). Moreover, its chemical shift had not changed significantly (from 5.84 ppm to 6.09 ppm), in agreement with the literature,[13] which reports ^{1}H chemical shifts around 6 ppm for the middle hydrogen of alkylallyl carbanions.

Finally, signals for both terminal allylic hydrogens had considerably shifted upfield, from 5.12 and 4.97 ppm in **4a** to 2.75 and 2.59 ppm in **4aLi**. This was consistent with the formation of a delocalised anion resulting in a considerably increased negative charge on the terminal allylic carbon.

The coupling constants measured for these three signals in **4aLi** are consistent with them coupling together (Table 3). Similar values have been reported for alkylallyl carbanions.[13]

Entry	Shift (ppm)	Multiplicity	Integration	Coupling constant (Hz)	H
1	6.09	dd	1	16.0, 9.5	3
2	2.75	bd	0.65	10.0	4
3	2.59	bd	0.81	15.5	4’

Table 3: *^{1}H NMR data for lithiated allylic thiocarbamate **4aLi** in d8-THF at -60 °C.*

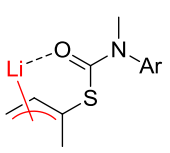
The signals for the allylic system in **4aLi** were accompanied by two sharp doublets in the aromatic region, with similar chemical shifts (7.20/6.90 ppm, Figure 3) compared with **4a** (7.25/6.98 ppm, Figure 1).

In the ^{1}H NMR spectrum for **4aLi**, we also observed another set of broader signals (Table 4), in a 1:1 ratio (Figure 3).

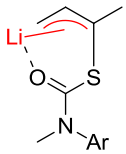
Entry	Shift (ppm)	Multiplicity	Integration	Coupling constant (Hz)	H
1	7.06-6.79	m	-	-	H_{Ar}
2	5.71	dd	1	17.0, 10.5	
3	3.94	bd	1.3	17.4	

Table 4: *^{1}H NMR data for lithiated allylic thiocarbamate **4aLi** in d8-THF at -60 °C.*

We initially thought that this resulted from formation of allyllithium **4aLi** as an *E*/*Z* mixture (Figure 4), but this was not in accordance with the ^{13}C NMR spectrum, showing no similar double set of peaks (Figure 5).



(*E*)-**4aLi**



(*Z*)-**4aLi**

Figure 4: *E- and Z-isomers of allyllithium **4aLi**.*

Furthermore, it seems more likely that the allyllithium possesses the *Z* geometry, as revealed by (carbo)lithiation/reprotonation experiments in allylic thiocarbamates[14] and *N*-allyl-*N*’-ureas[15] previously reported within the group. Moreover, the broader aspect of this set of peaks, in particular in the aromatic region, suggests a rather different – and more

complicated – structure, possibly including metalation of the phenyl ring. Due to large solvent and base peaks, we were unable to identify further this second compound.

Comparison of the ^{13}C NMR spectra for non-lithiated **4a** and lithiated **4aLi** brought additional information (Figure 2, Figure 5, Table 4).

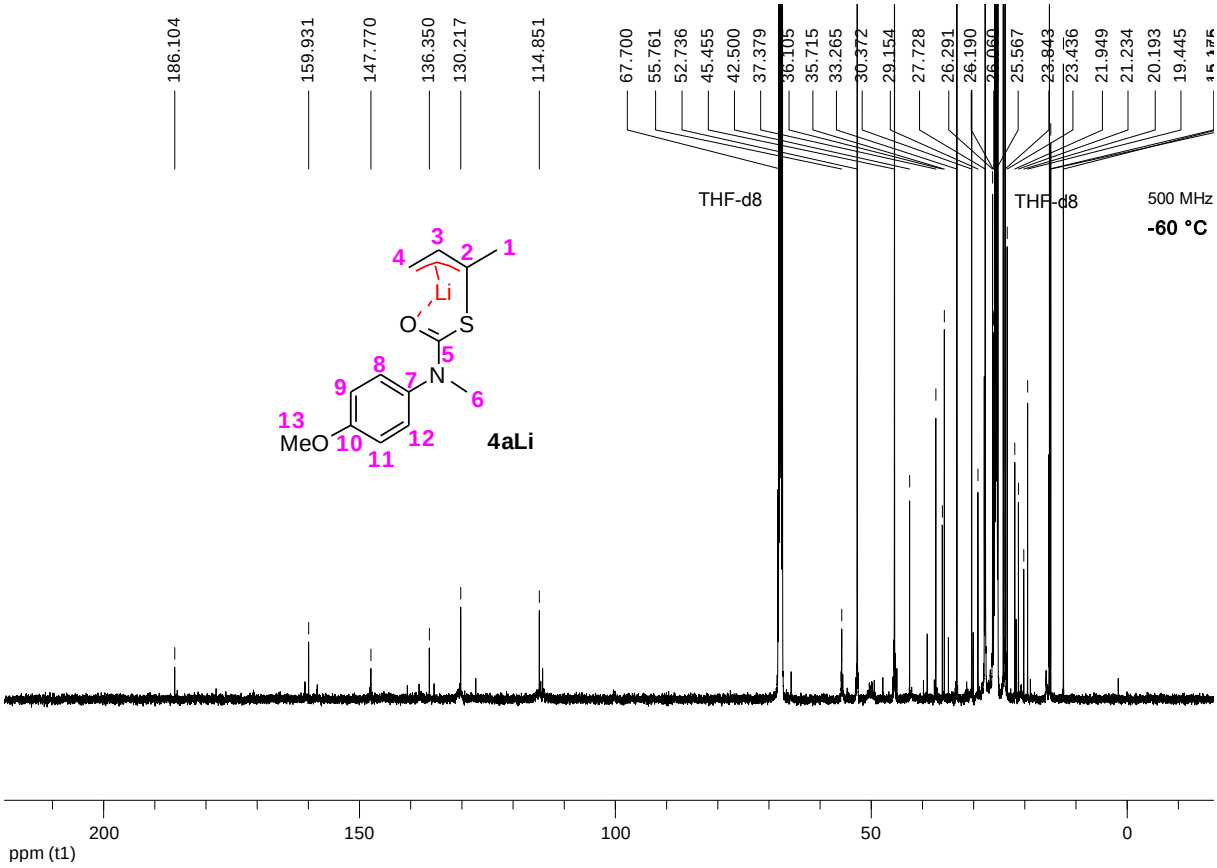


Figure 5: *^{13}C NMR spectrum for lithiated allylic thiocarbamate **4aLi** in d8-THF at -60 °C.*

Entry	4a: ^{13}C shift (ppm)	4aLi: ^{13}C shift (ppm)	C
1	167.9	186.1	5
2	160.8	159.9	10
3	140.6	147.8	3
4	135.2	136.4	7
5	131.3	130.2	8, 12
6	115.4	114.9	9, 11
7	114.8	55.8	4

Table 4: *Comparison of ^{13}C NMR data in allylic thiocarbamate **4a** and lithiated allylic thiocarbamate **4aLi**.*

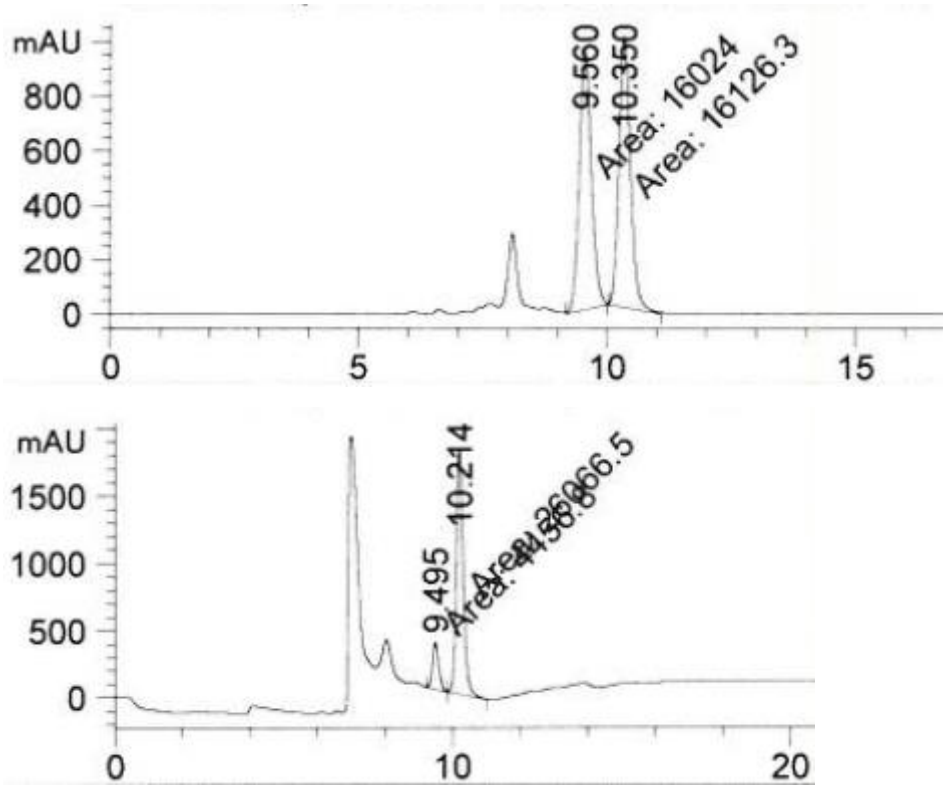
The carbonyl peak had significantly shifted from 167.9 ppm in **4a** to 186.1 ppm in **4aLi** (Table 4), confirming coordination of the carbonyl oxygen with the lithium atom, which rendered the carbon more deshielded.

The chemical shift of C-3 did not vary significantly, slightly increasing to 147.8 ppm in **4aLi** (Table 4), a similar value to those reported in the literature for the middle carbon of the allyllithium system.[13,16]

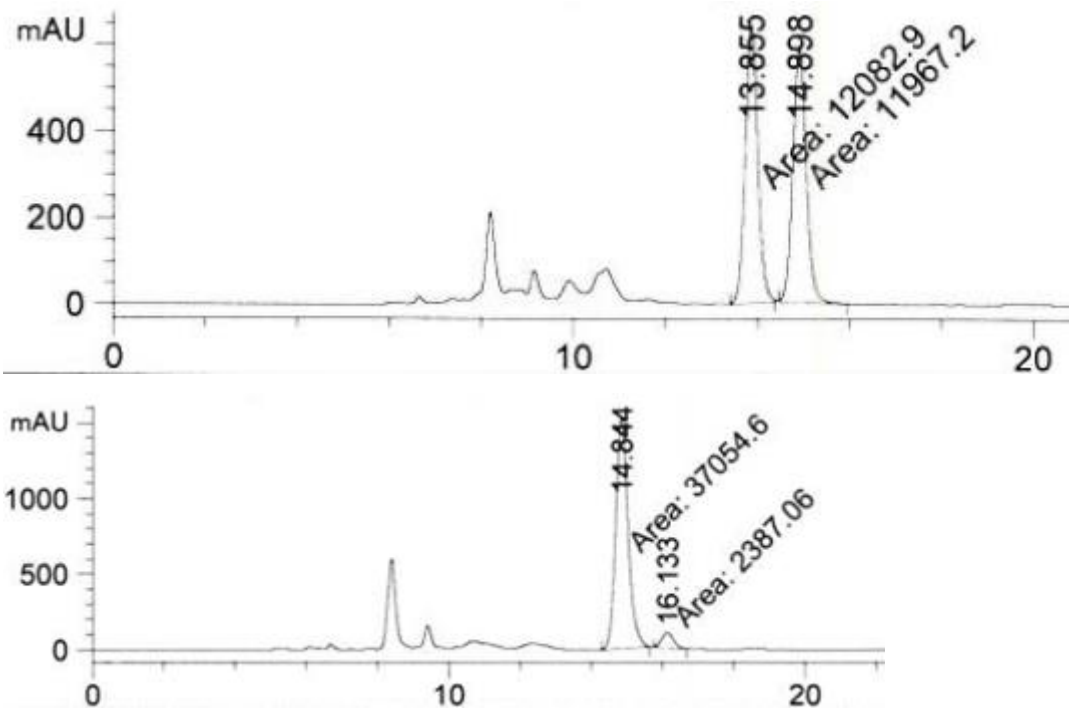
Moreover, comparing the spectra before and after lithiation clearly showed that one carbon had considerably shifted upfield from the 110-160 ppm region (Table 4). We assumed the "missing carbon" was C-4, due to the disappearance of the localised double bond between C-3 and C-4. Based on literature precedent,[16a,b,d,e,17] this carbon was then expected to give a peak around 50-65 ppm, which is very likely to be that observed at 55.8 ppm, given its similar height as those in the 110-190 ppm region.

HPLC scans

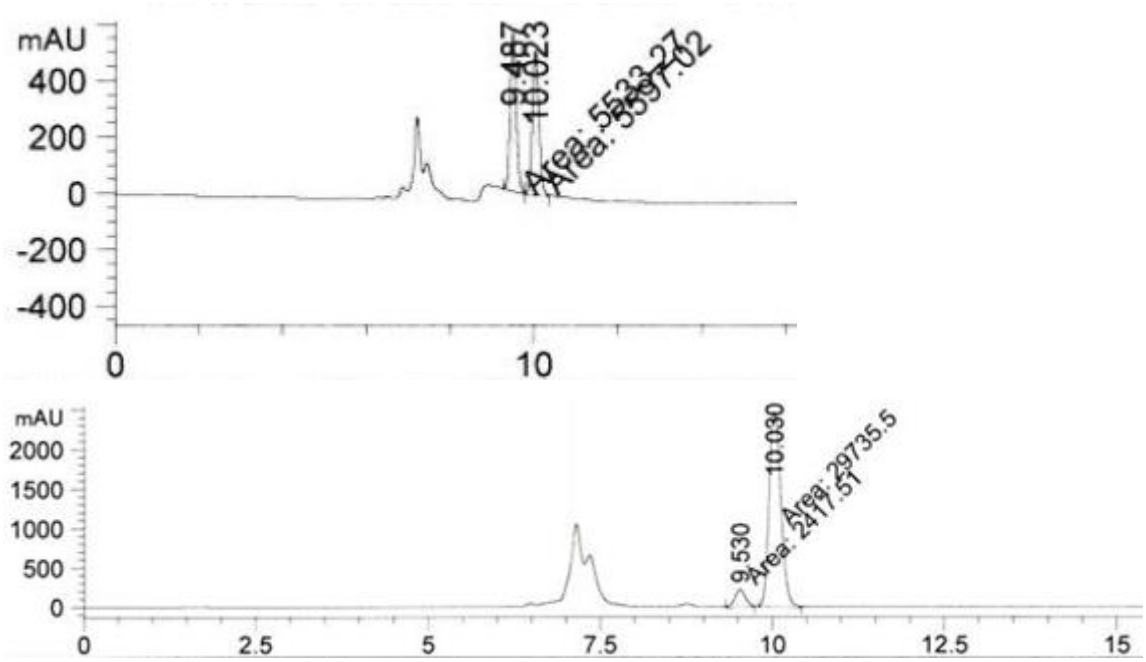
(*R*)-**1e**



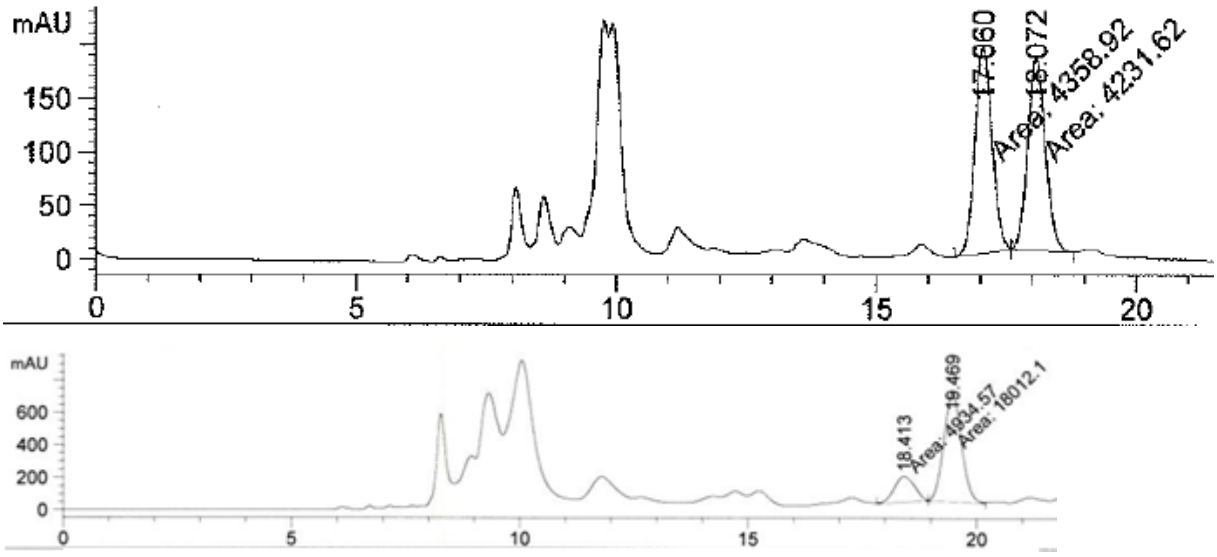
(*S*)-**1h**



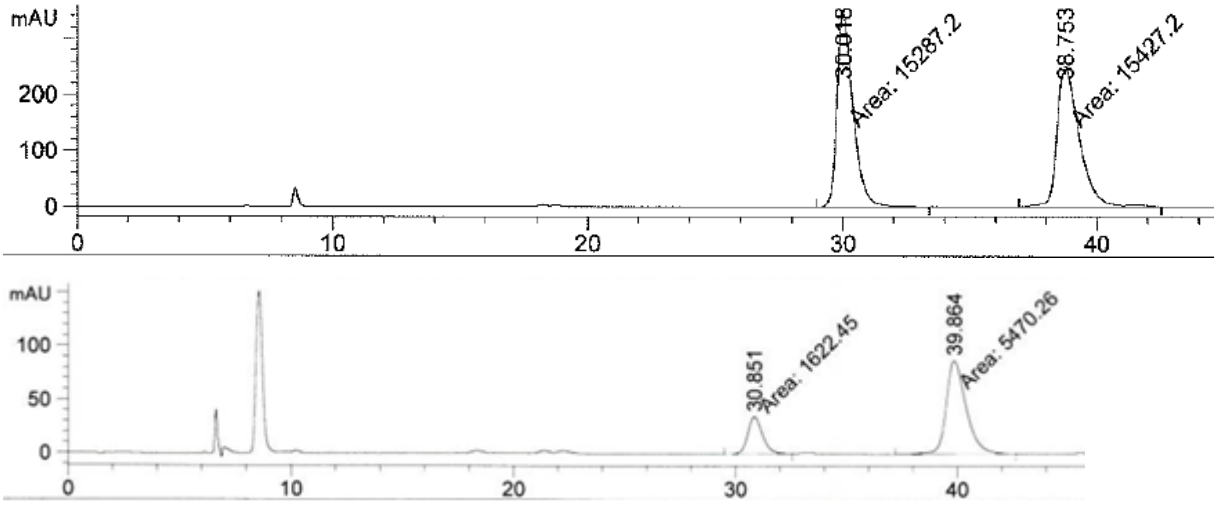
(*S*)-**1i**


mAU
400
200
0
-200
-400
0
10
9.487
10.023
mAU
2000
1500
1000
500
0
0
2.5
5
7.5
10
12.5
15
9.530
10.030
Area: 29735.5
Area: 2417.51

(*R*)-**1j**

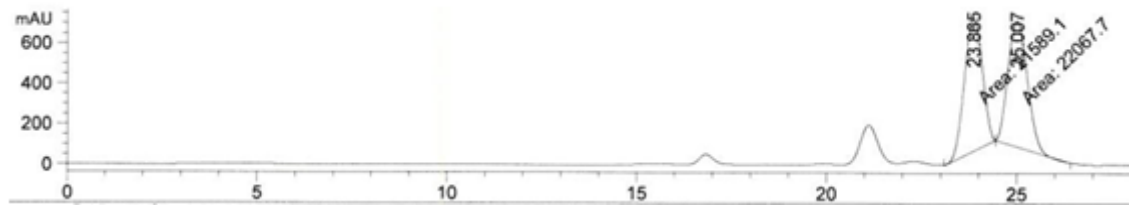

mAU
150
100
50
0
0
5
10
15
20
Area: 4358.92
Area: 4231.62
mAU
600
400
200
0
0
5
10
15
20
18.413
19.469
Area: 4934.57
Area: 18012.1

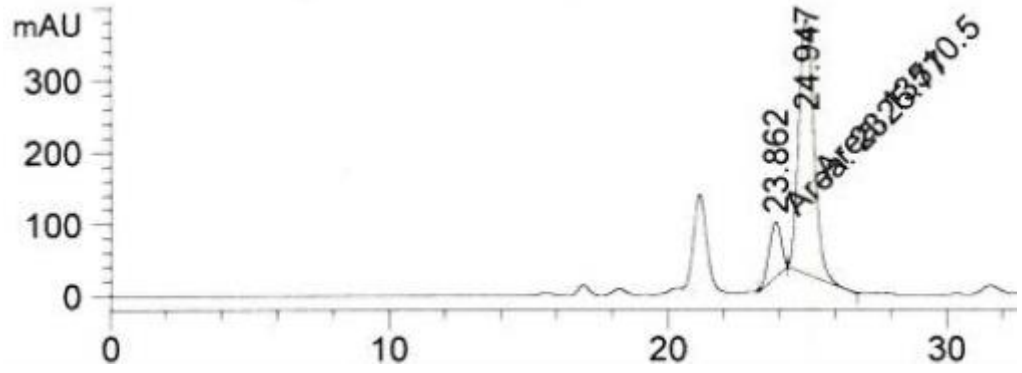
(*R*)-**1l**


mAU
200
100
0
0
10
20
30
40
Area: 15287.2
Area: 15427.2

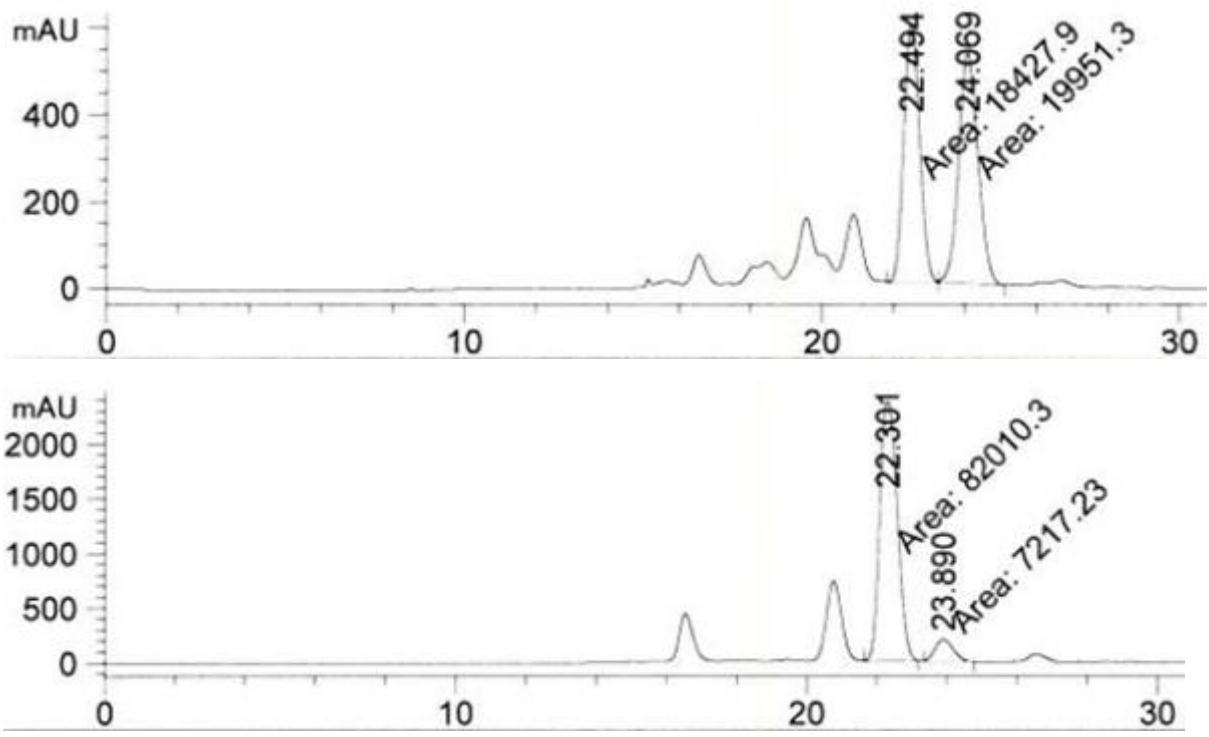
mAU
100
50
0
0
10
20
30
40
30.851
Area: 1622.45
39.864
Area: 5470.26

(*R*)-**1m**

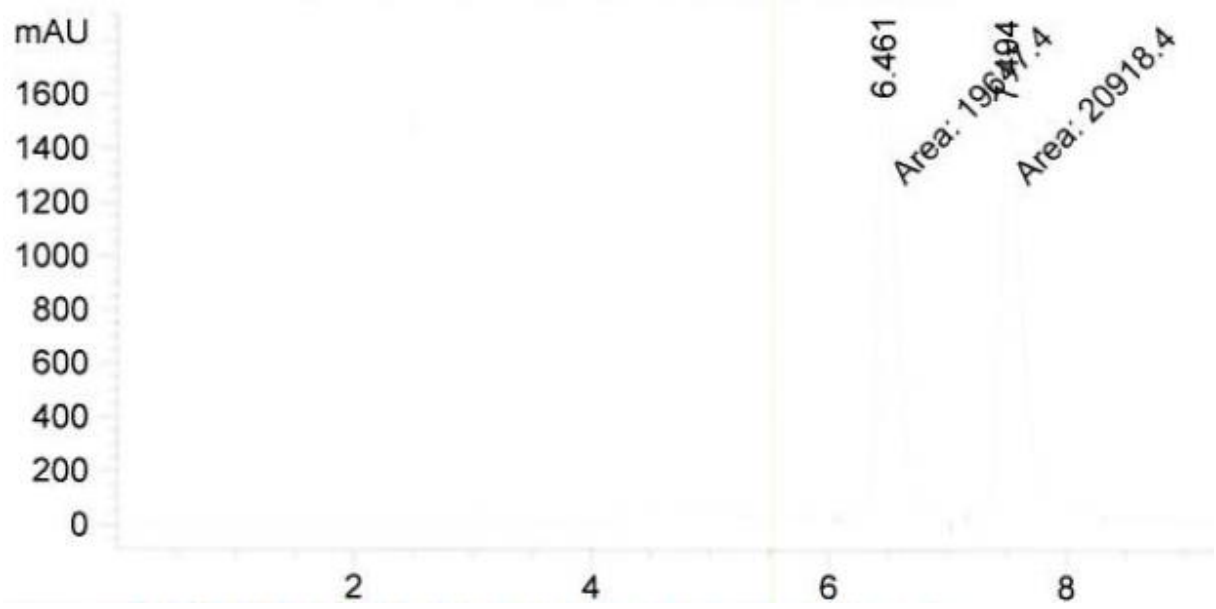

mAU
600
400
200
0
0
5
10
15
20
25
23.865
Area: 22067.7

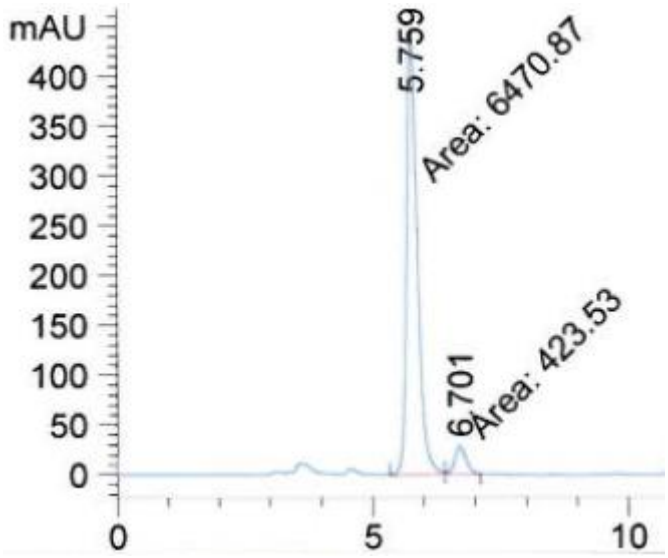

mAU
300
200
100
0
0
10
20
30
23.862
24.947

(*R*)-**1n**

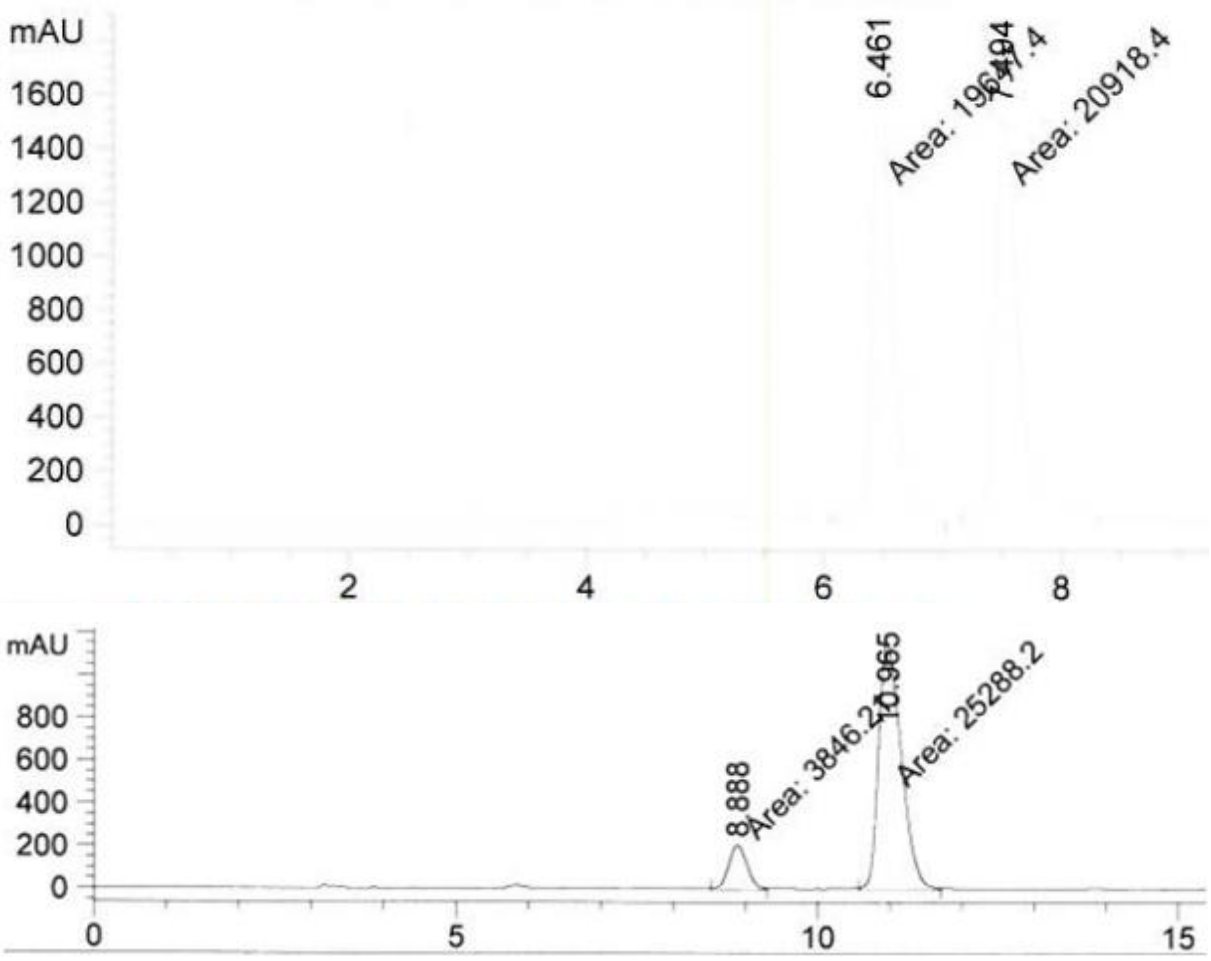

mAU
400
200
0
0
10
20
30
22.494
Area: 18427.9
24.069
Area: 19951.3
mAU
2000
1500
1000
500
0
0
10
20
30
22.301
Area: 82010.3
23.890
Area: 7217.23

(*S*)-**4e**


mAU
1600
1400
1200
1000
800
600
400
200
0
2
4
6
8
6.461
Area: 20918.4


mAU
400
350
300
250
200
150
100
50
0
0
5
10
5.759
Area: 6470.87
6.701
Area: 423.53

(*R*)-**4e**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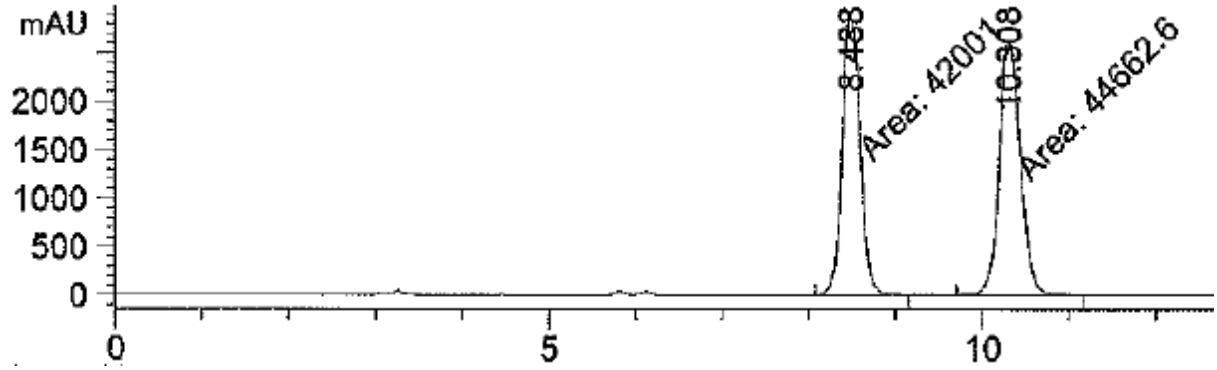
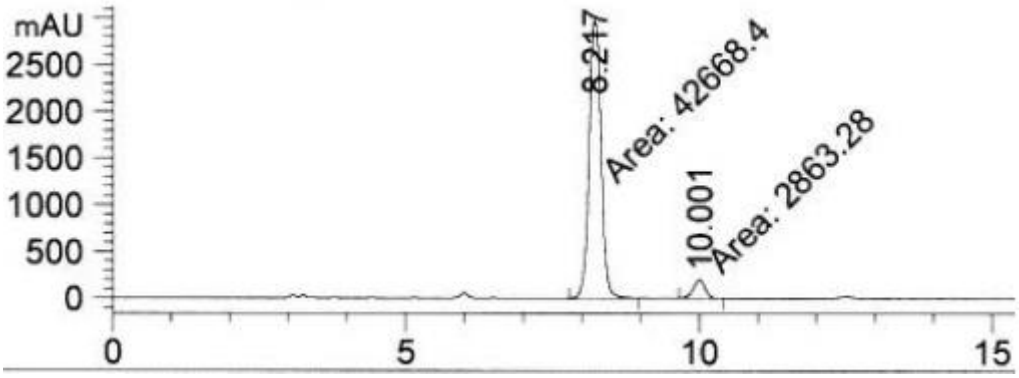
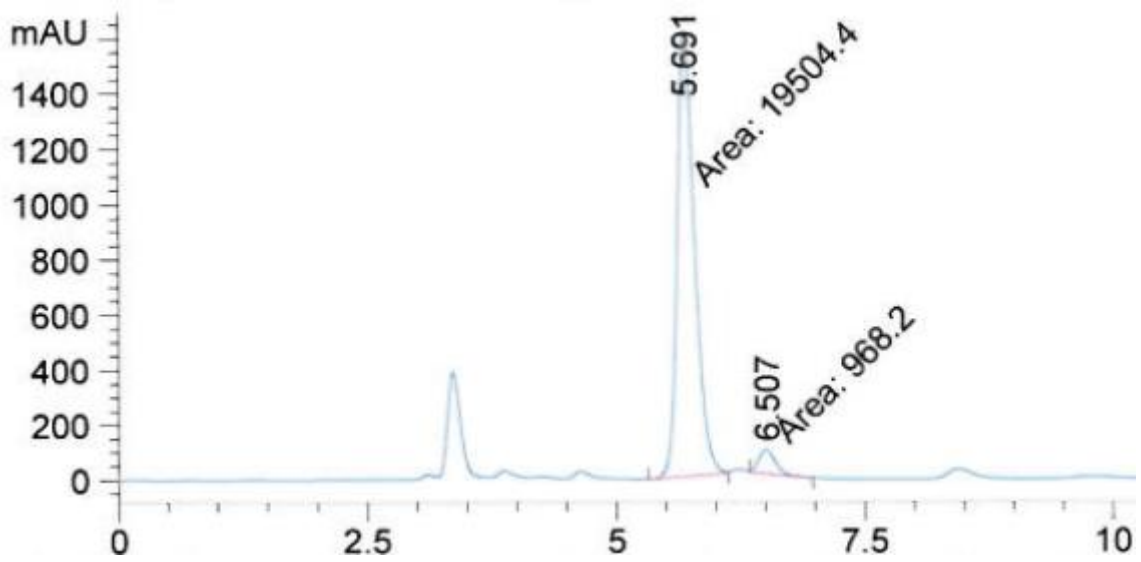
1600
1400
1200
1000
800
600
400
200
0
2
4
6
8
6.461
Area: 20918.4
mAU
800
600
400
200
0
0
5
10
15
8.888
Area: 25288.2

(*S*)-**4f**

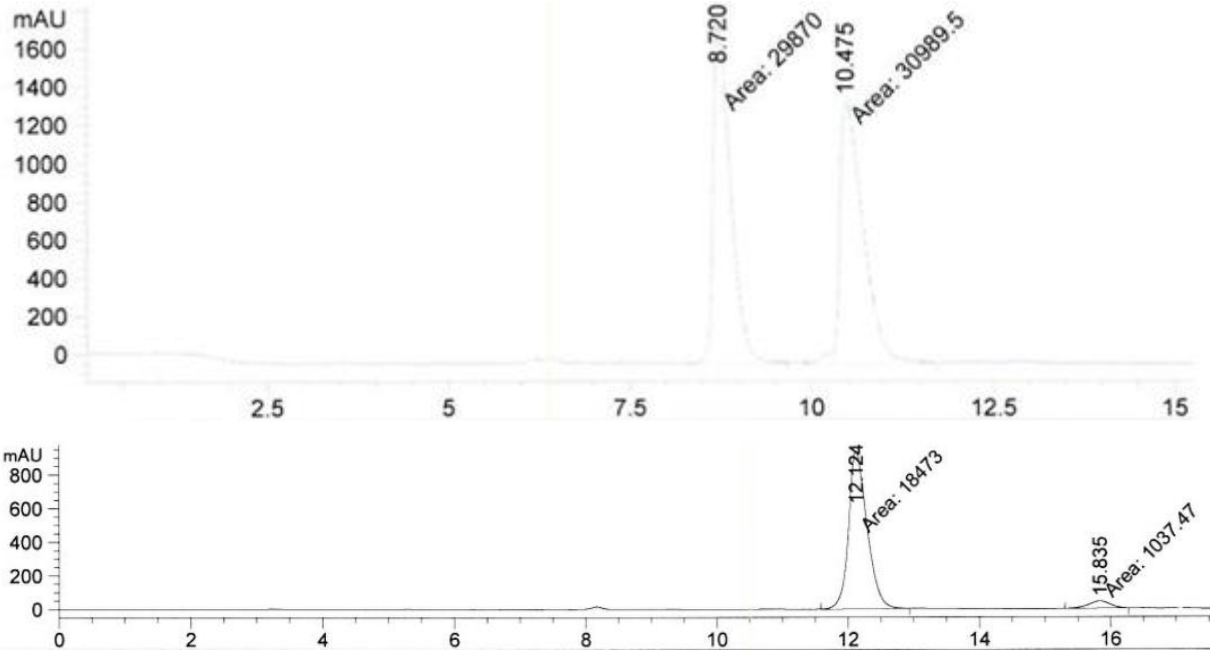

mAU
2000
1500
1000
500
0
0
5
10
8.433
Area: 42001
10.308
Area: 44662.6


mAU
2500
2000
1500
1000
500
0
0
5
10
15
8.247
Area: 42668.4
10.001
Area: 2863.28

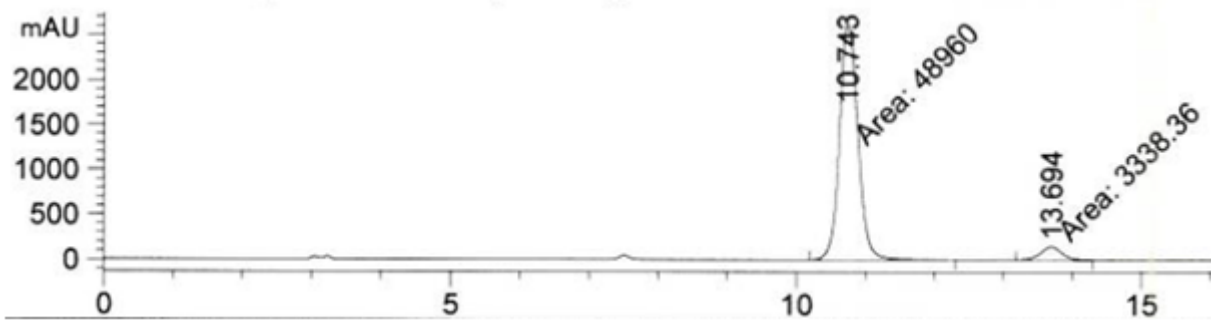
(*S*)-**4g**


mAU
1400
1200
1000
800
600
400
200
0
0
2.5
5
7.5
10
5.691
Area: 19504.4
6.507
Area: 968.2

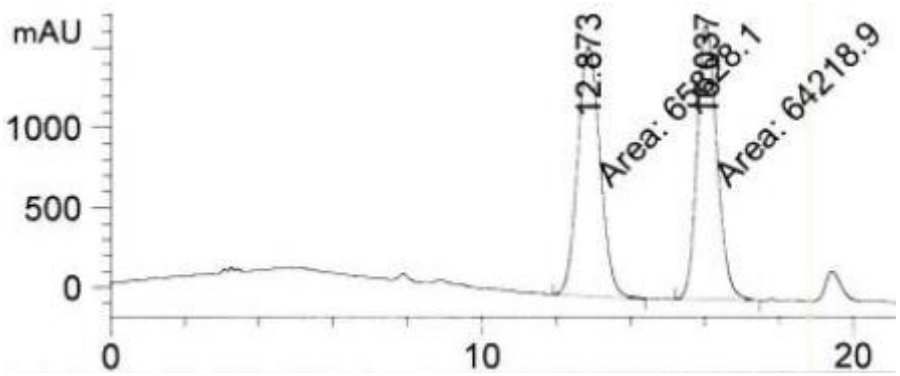
(*S*)-**4h**

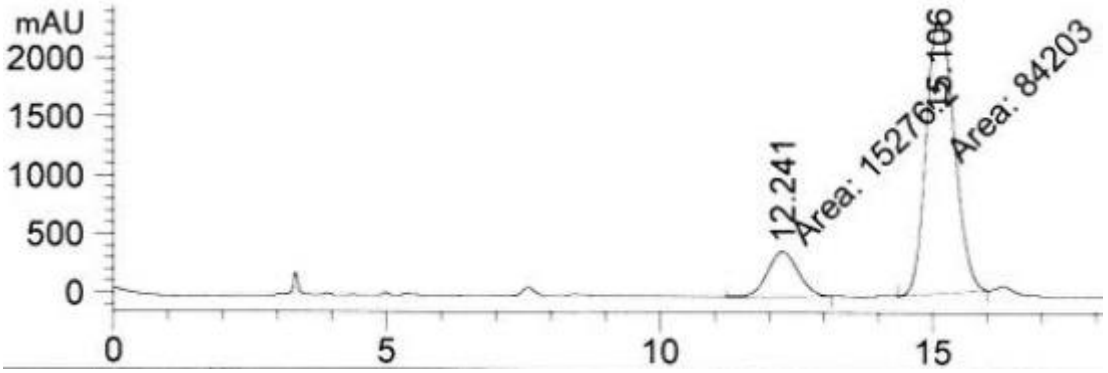

mAU
1600
1400
1200
1000
800
600
400
200
0
2.5
5
7.5
10
12.5
15
8.720
Area: 29870
10.475
Area: 30989.5
mAU
800
600
400
200
0
0
2
4
6
8
10
12
14
16
12.124
Area: 18473
15.835
Area: 1037.47

(*S*)-**4i**

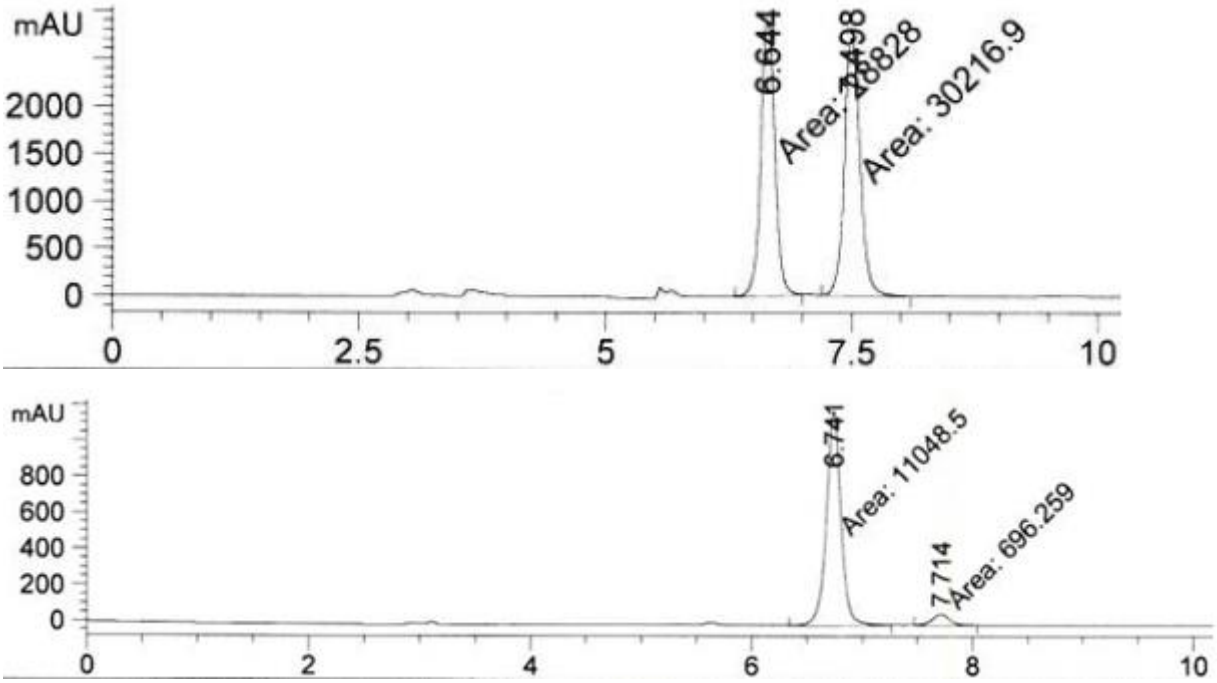

mAU
2000
1500
1000
500
0
0
5
10
15
10.743
Area: 48960
13.694
Area: 3338.36

(*R*)-**4j**

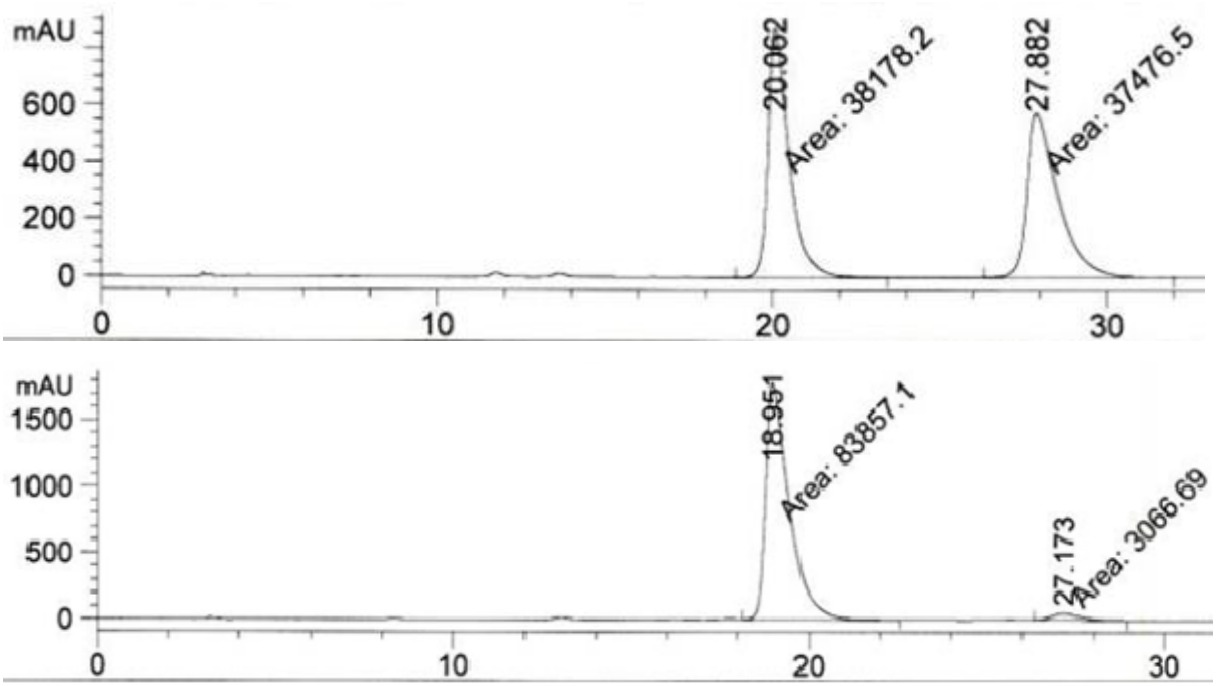

mAU
1000
500
0
0
10
20
12.873
Area: 64218.9


mAU
2000
1500
1000
500
0
0
5
10
15
12.241
15.106
Area: 84203

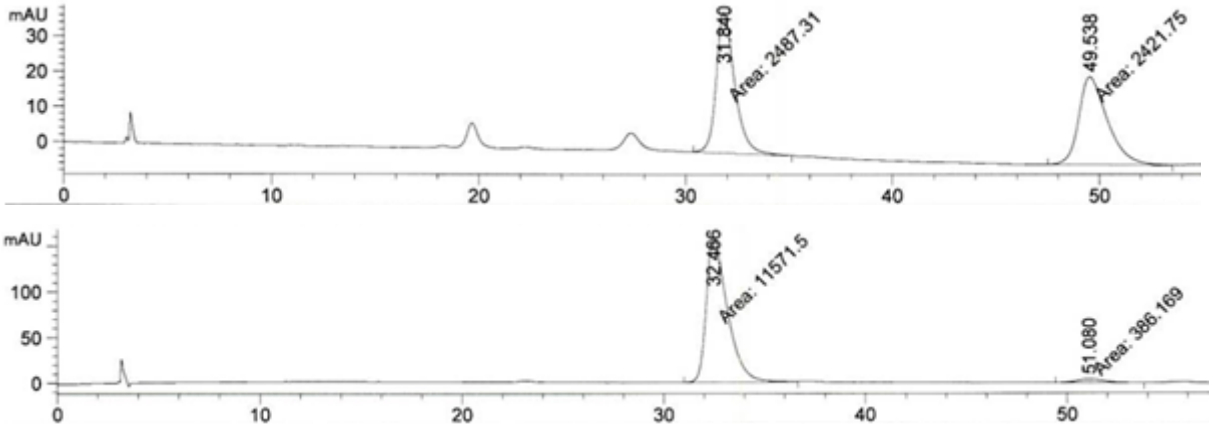
(*S*)-**4k**


mAU
2000
1500
1000
500
0
6.644
Area: 28828
Area: 30216.9
0
2.5
5
7.5
10
mAU
800
600
400
200
0
6.741
Area: 11048.5
7.714
Area: 696.259
0
2
4
6
8
10

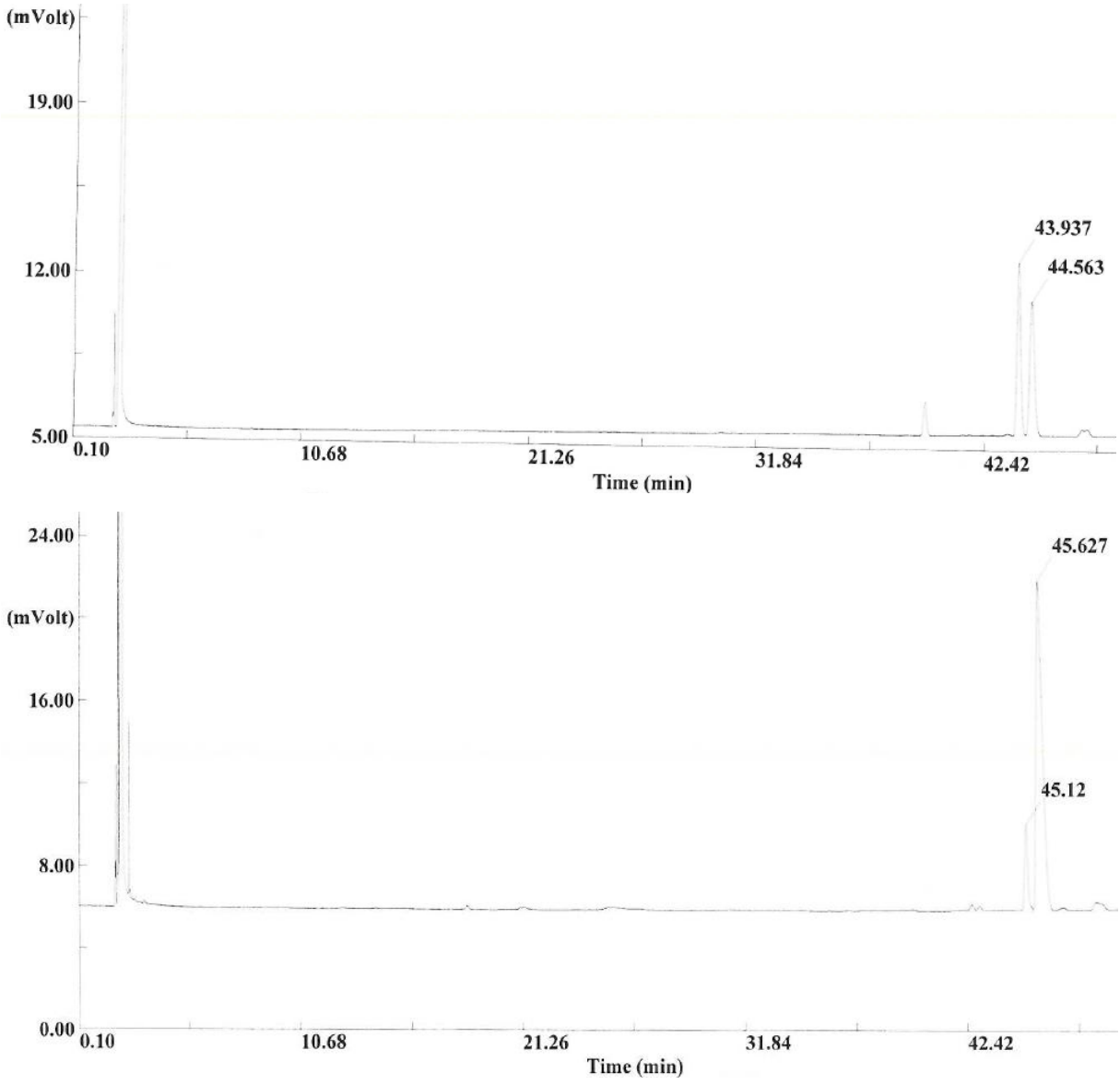
(*S*)-**4l**


mAU
600
400
200
0
20.062
Area: 38178.2
27.882
Area: 37476.5
0
10
20
30
mAU
1500
1000
500
0
18.951
Area: 83857.1
27.173
Area: 3066.69
0
10
20
30

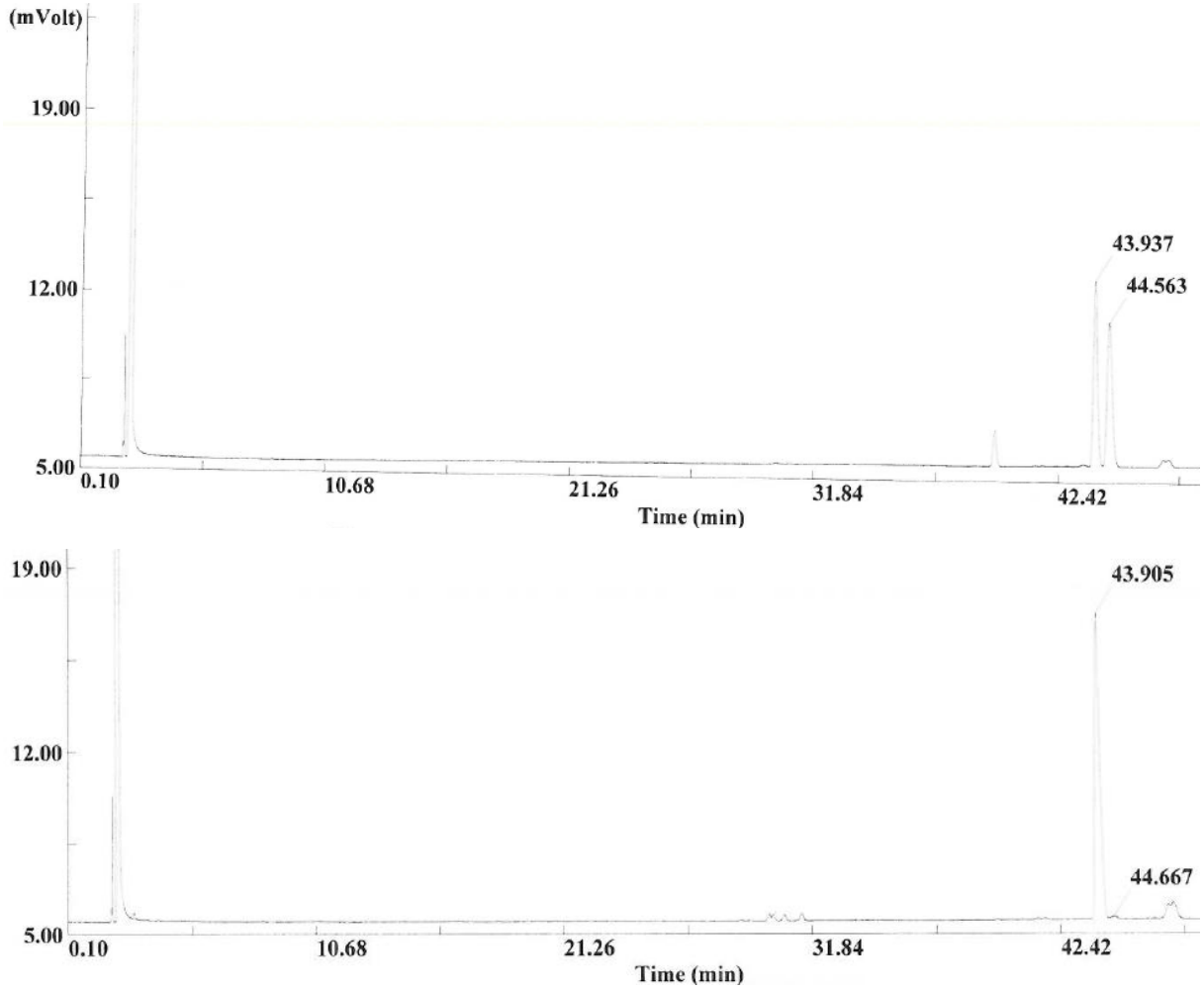
(*S*)-**4l'**


mAU
31.840
Area: 2487.31
49.538
Area: 2421.75
mAU
32.466
Area: 11571.5
51.080
Area: 386.169

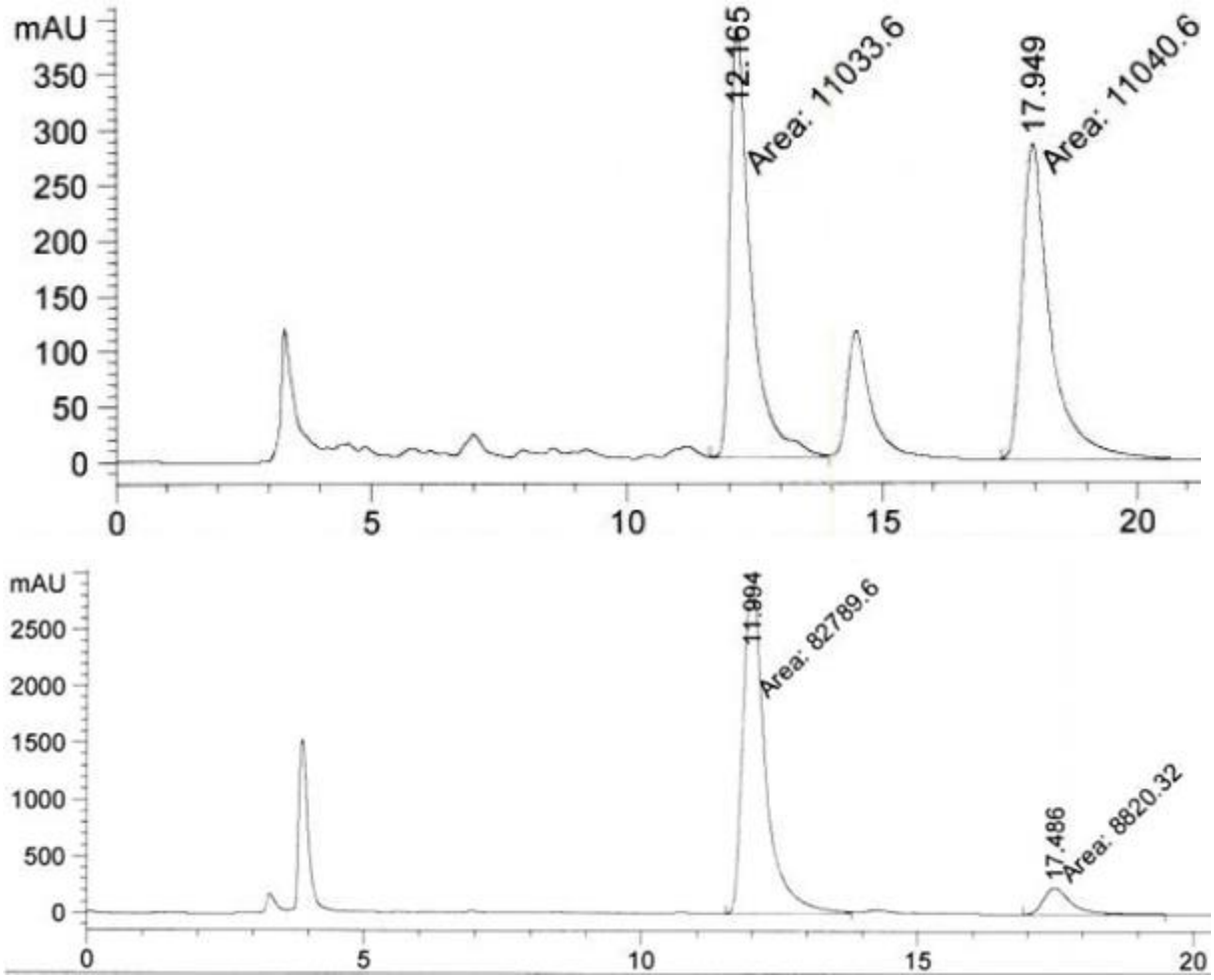
(*E*,*S*)-**5a**


(mVolt)
43.937
44.563
Time (min)
45.627
45.12
Time (min)

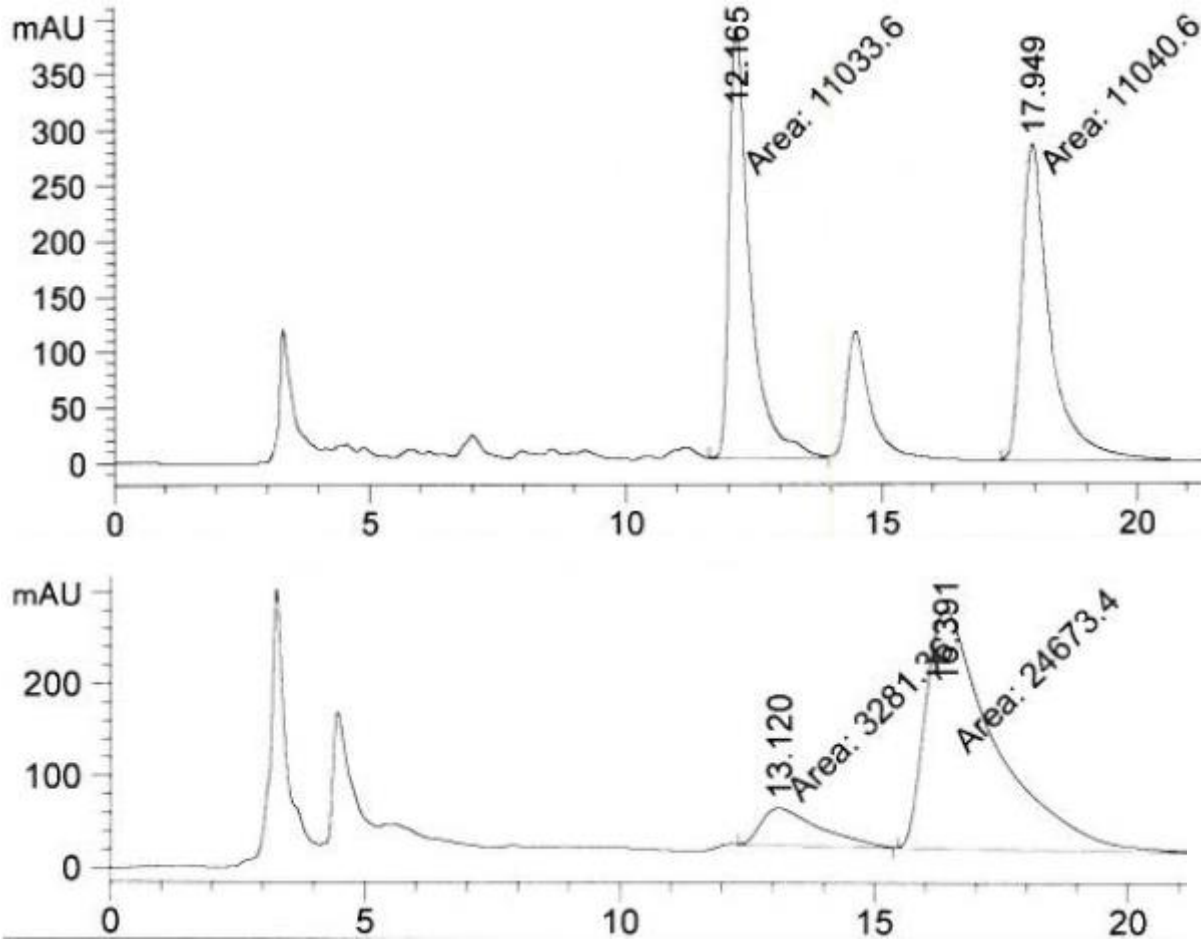
(*E*,*R*)-**5a**


(mVolt)
19.00
12.00
5.00
43.937
44.563
0.10
10.68
21.26
31.84
42.42
Time (min)
19.00
12.00
5.00
43.905
44.667
0.10
10.68
21.26
31.84
42.42
Time (min)

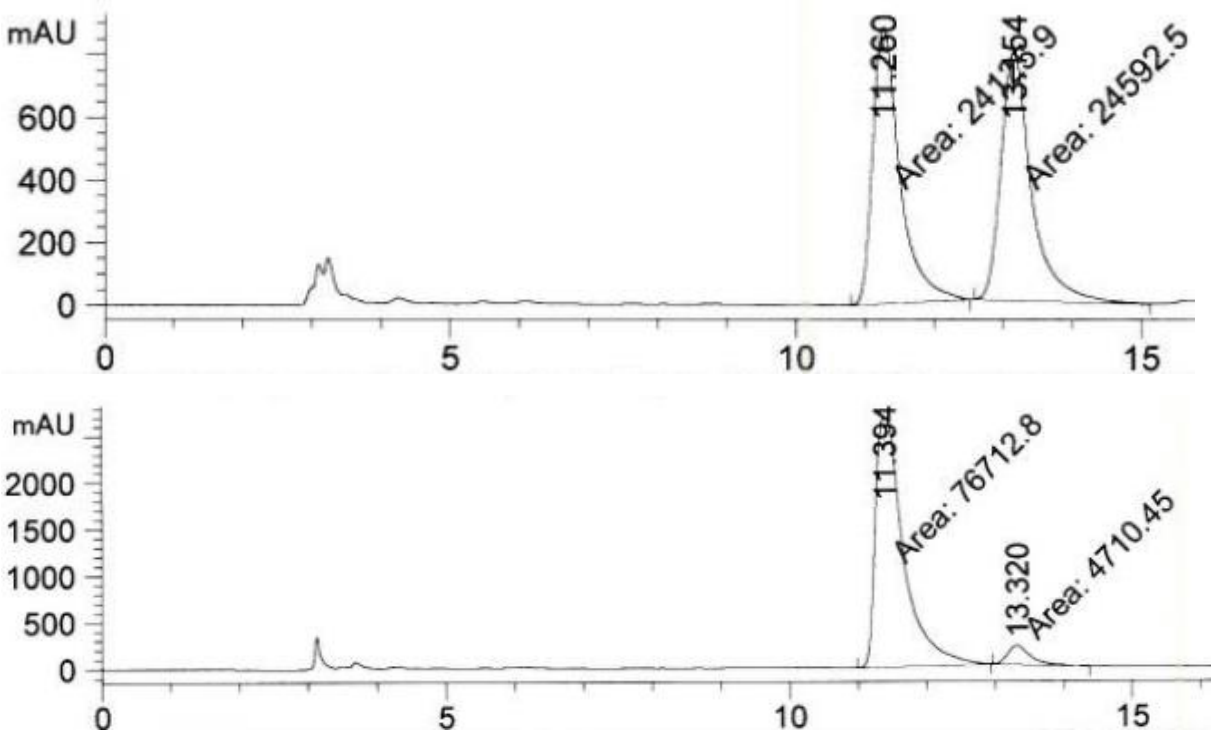
(*S*)-**6e**


mAU
350
300
250
200
150
100
50
0
12.165
Area: 11033.6
17.949
Area: 11040.6
0
5
10
15
20
mAU
2500
2000
1500
1000
500
0
11.994
Area: 82789.6
17.486
Area: 8820.32
0
5
10
15
20

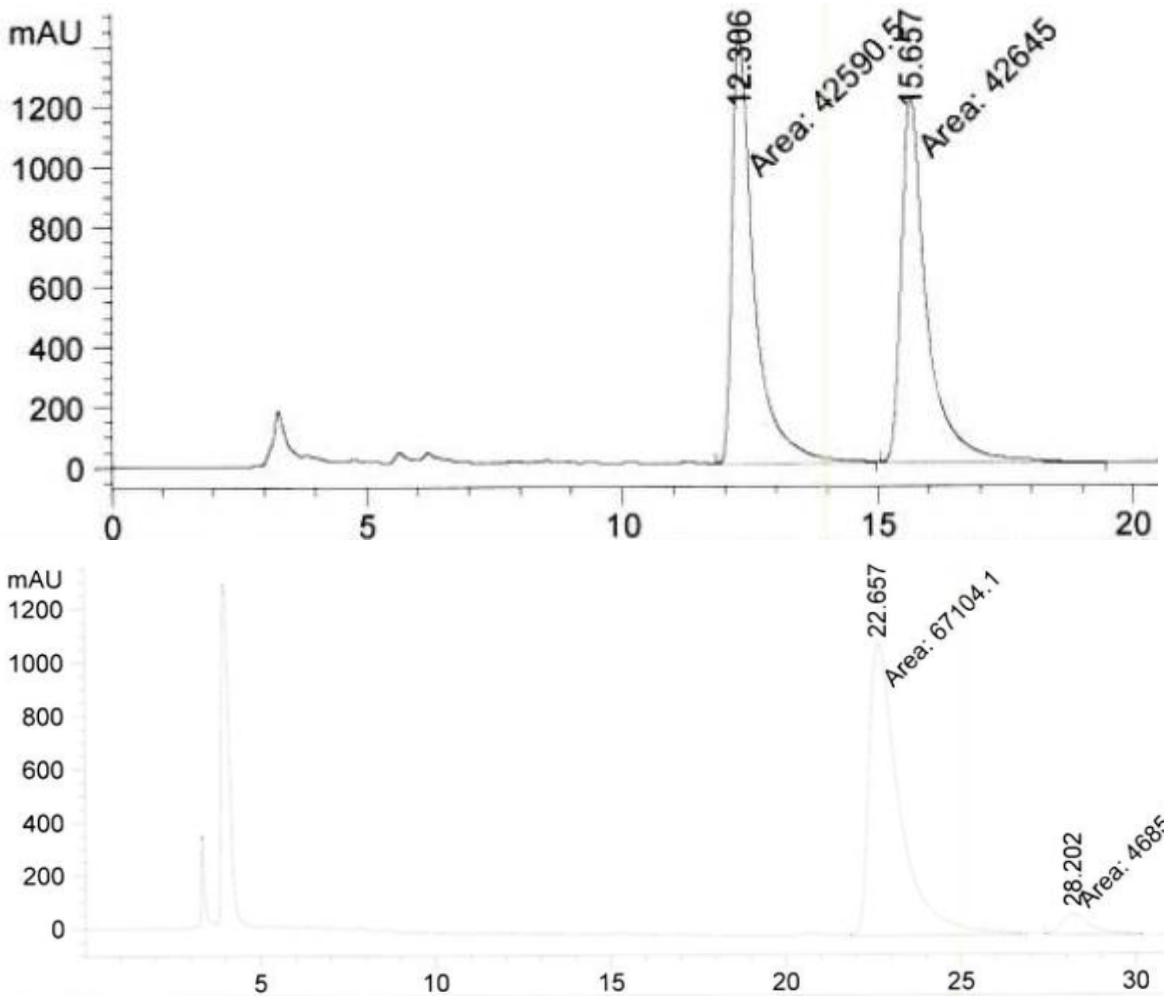
(*R*)-**6e**


mAU
350
300
250
200
150
100
50
0
12.165
Area: 11033.6
17.949
Area: 11040.6
0
5
10
15
20
mAU
200
100
0
13.120
Area: 3281.3
Area: 24673.4
0
5
10
15
20

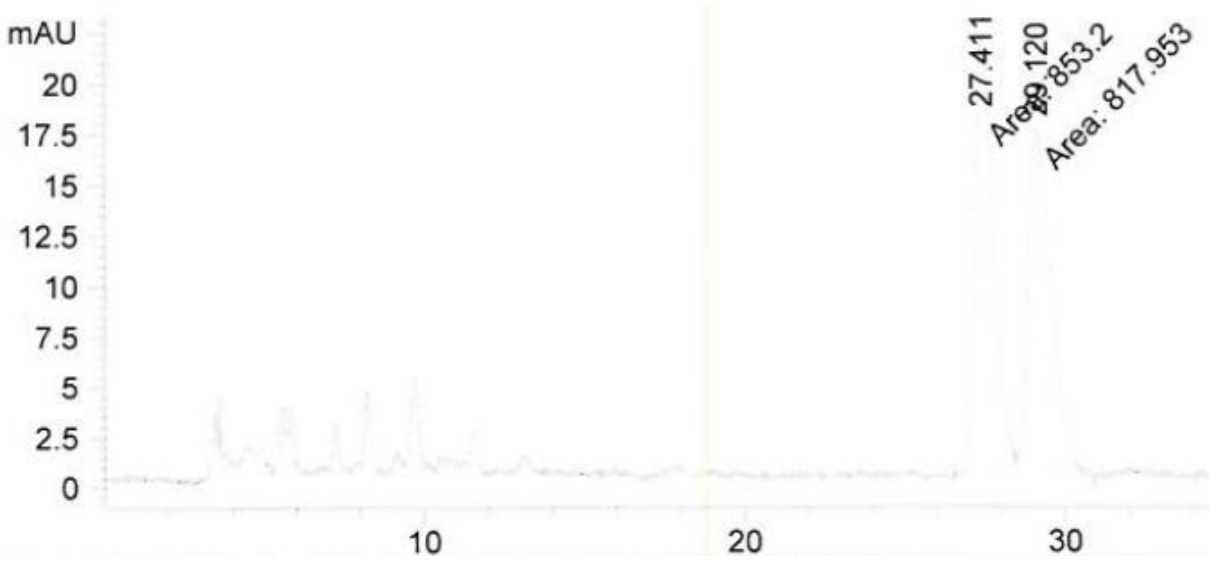
(*S*)-**6f**

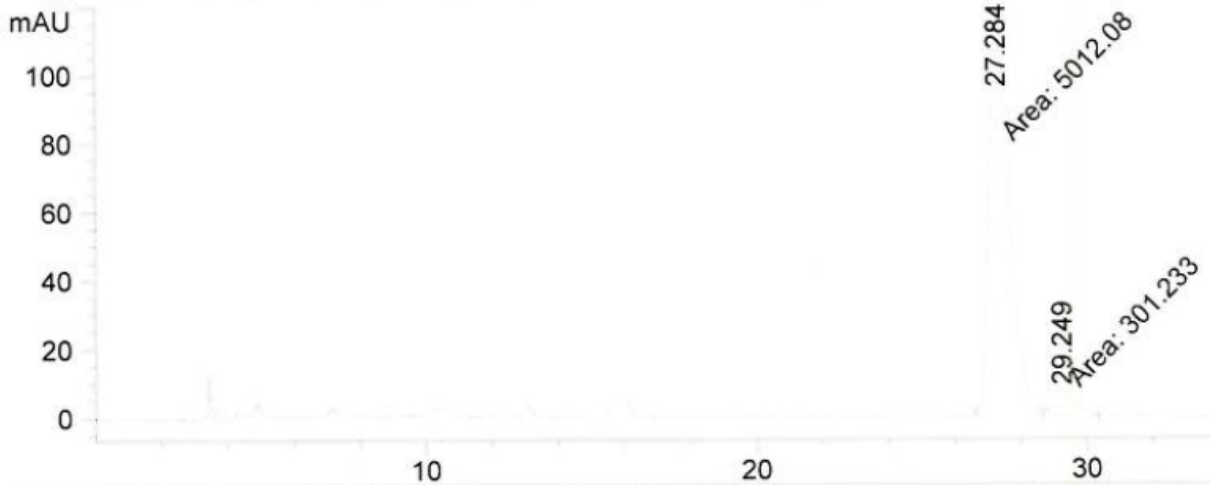

mAU
600
400
200
0
11.260
Area: 24
Area: 24592.5
0
5
10
15
mAU
2000
1500
1000
500
0
11.394
Area: 76712.8
13.320
Area: 4710.45
0
5
10
15

(*S*)-**6g**

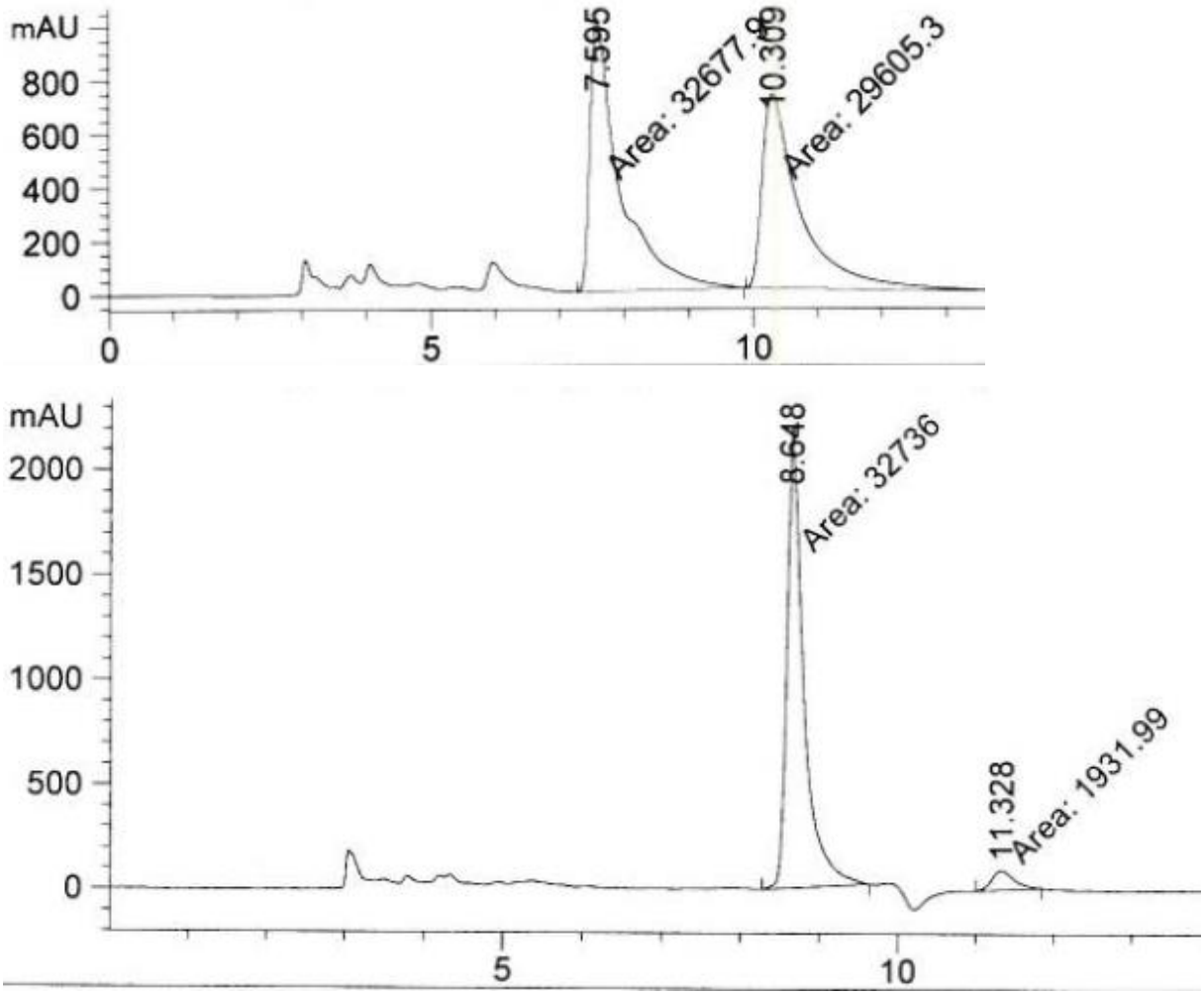

mAU
1200
1000
800
600
400
200
0
12.306
Area: 42590.57
15.657
Area: 42645
0
5
10
15
20
mAU
1200
1000
800
600
400
200
0
22.657
Area: 67104.1
28.202
Area: 4685.64
5
10
15
20
25
30

(*S*)-**6h**

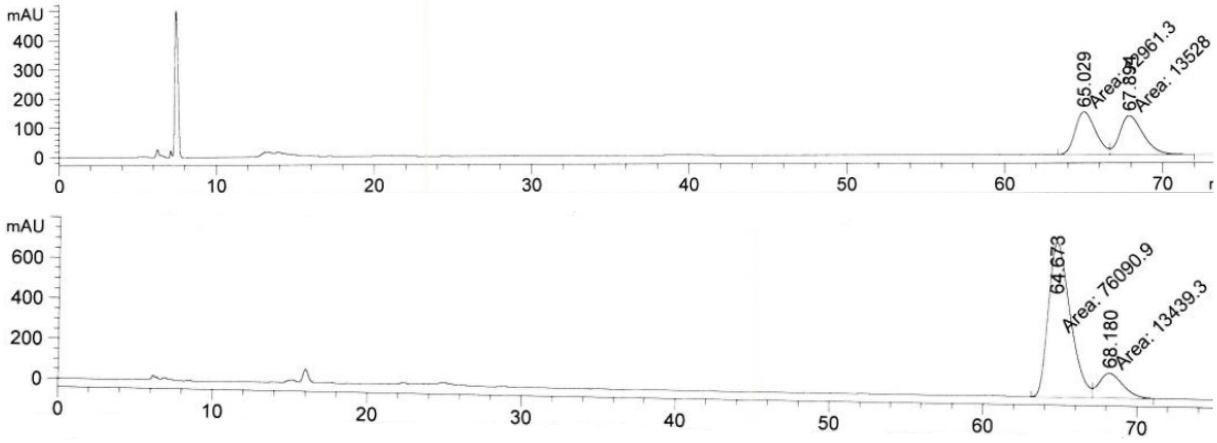

mAU
20
17.5
15
12.5
10
7.5
5
2.5
0
10
20
30
27.411
Area: 853.2
29.120
Area: 817.953


mAU
100
80
60
40
20
0
10
20
30
27.284
Area: 5012.08
29.249
Area: 301.233

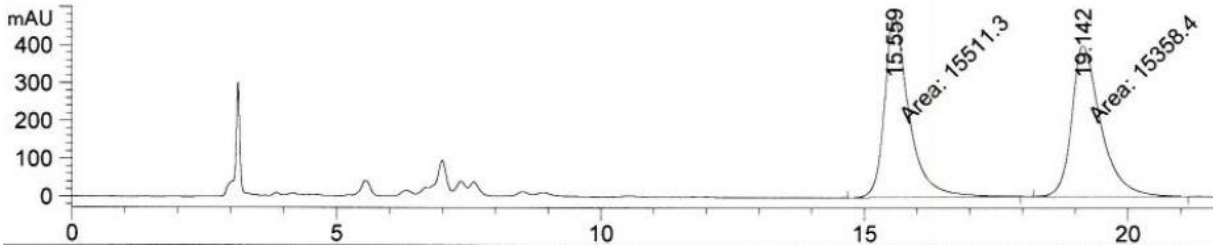
(*S*)-**6i**

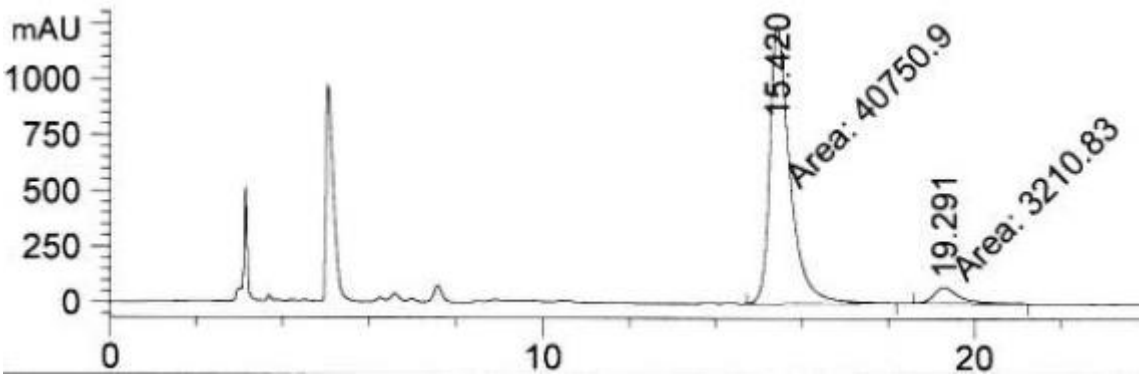

mAU
800
600
400
200
0
0
5
10
7.595
Area: 32677.8
10.309
Area: 29605.3
mAU
2000
1500
1000
500
0
5
10
8.648
Area: 32736
11.328
Area: 1931.99

(*R*)-**6j**

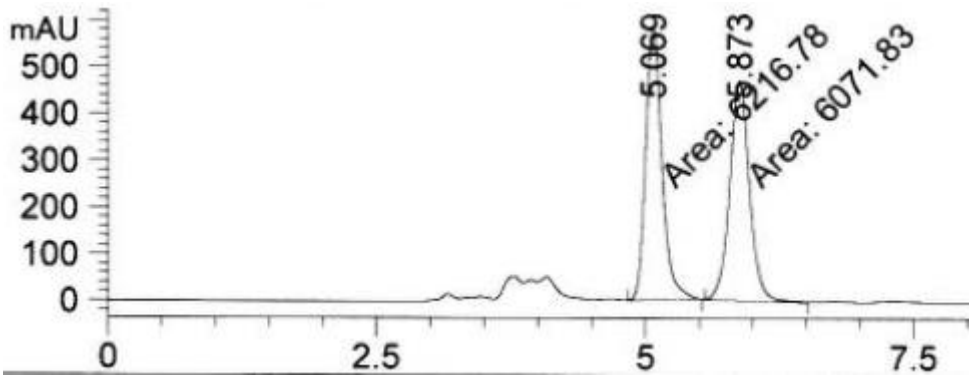

mAU
400
300
200
100
0
0
10
20
30
40
50
60
70
65.029
Area: 12961.3
Area: 13528
mAU
600
400
200
0
0
10
20
30
40
50
60
70
64.673
Area: 76090.9
68.180
Area: 13439.3

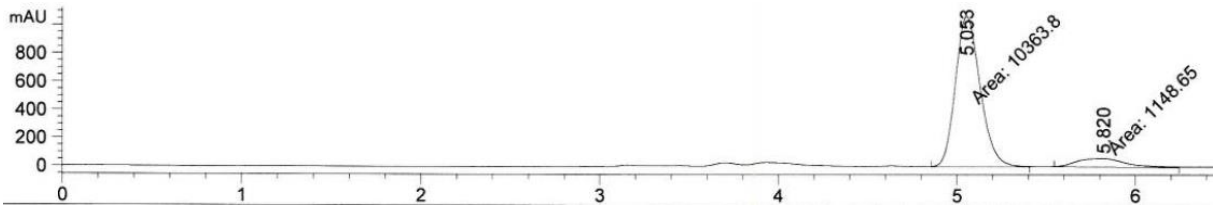
(*S*)-**6k**


mAU
400
300
200
100
0
0
5
10
15
20
15.559
Area: 15511.3
19.142
Area: 15358.4

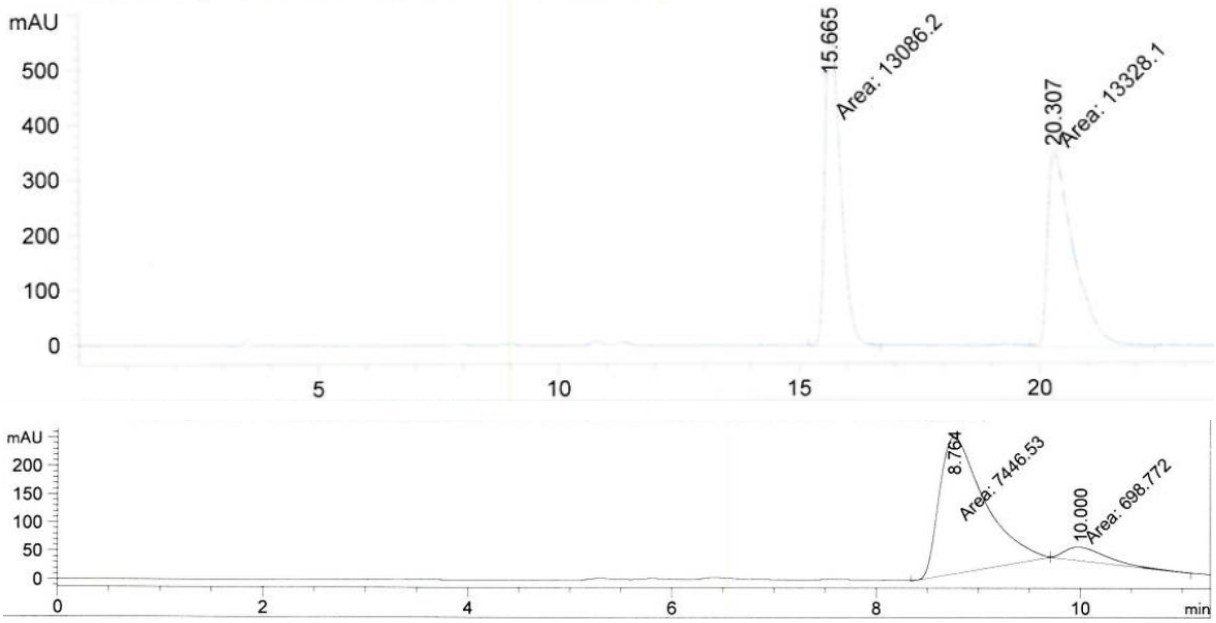

mAU
1000
750
500
250
0
0
10
20
15.420
Area: 40750.9
19.291
Area: 3210.83

(*S*)-**6l**

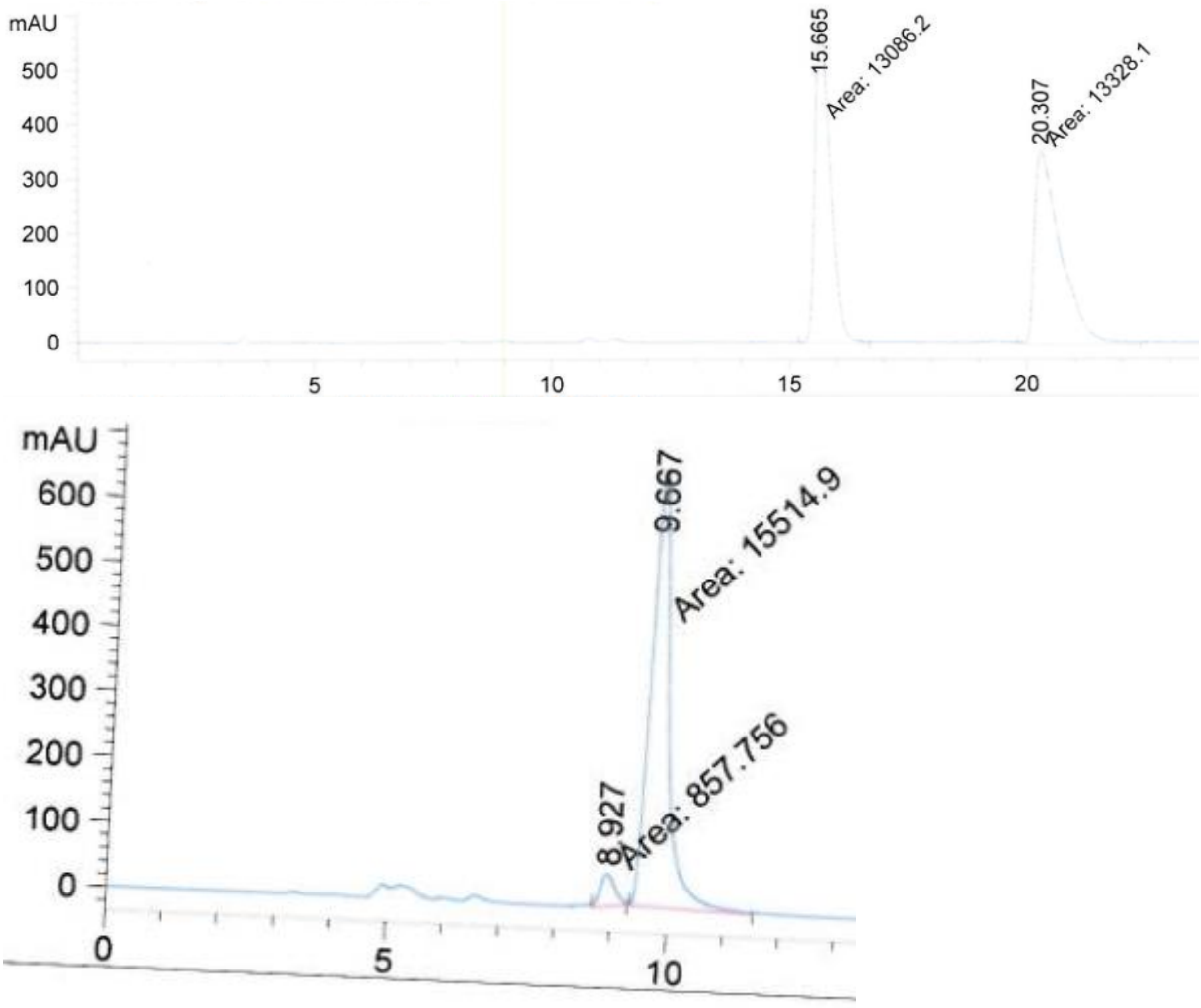

mAU
500
400
300
200
100
0
0
2.5
5
7.5
5.069
Area: 6216.78
Area: 6071.83


mAU
800
600
400
200
0
0
1
2
3
4
5
6
5.053
Area: 10363.8
5.820
Area: 1148.65

(*R*)-**10a**


mAU
500
400
300
200
100
0
15.665
Area: 13086.2
20.307
Area: 13328.1
5
10
15
20
mAU
200
150
100
50
0
8.764
Area: 7446.53
10.000
Area: 698.772
0
2
4
6
8
10
min

(*S*)-**10a**


mAU
500
400
300
200
100
0
15.665
Area: 13086.2
20.307
Area: 13328.1
5
10
15
20
mAU
600
500
400
300
200
100
0
9.667
Area: 15514.9
8.927
Area: 857.756
0
5
10

References

1. Perrin, D. D.; Armarego, W. L. F., *Purification of Laboratory Chemicals 3rd Ed.*; Pergamon press, **1988**.
2. Burchat A. F.; Michael Cong J.; Nielsen N. *J. Organomet. Chem.* **1997**, *542*, 281.
3. Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589.
4. Mingat, G.; MacLellan, P.; Laars, M.; Clayden J. *Org. Lett.* **2014**, *16*, 1252.
5. Clayden, J.; Dufour, J.; Grainger, D. M.; Helliwell, M. *J. Am. Chem. Soc.* **2007**, *129*, 7488.
6. MacLellan, P.; Clayden, J. *Chem. Commun.* **2011**, *47*, 3395.
7. Mingat, G.; Clayden, J. *Synthesis* **2012**, *44*, 2723.
8. Larrivée-Aboussafy, C.; Jones, B. P.; Price, K. E.; Hardink, M. A.; McLaughlin, R. W.; Lillie, B. M.; Hawkins, J. M.; Vaidyanathan, R. *Org. Lett.* **2010**, *12*, 324.
9. Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
10. Ohkuma, T.; Koizumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 13529.
11. (a) Mugishima, T.; Tsuda, M.; Kasai, Y.; Ishiyama, H.; Fukushi, E.; Kawabata, J.; Watanabe, M.; Akao, K.; Kobayashi, J. i. *J. Org. Chem.* **2005**, *70*, 9430; (b) Moorthy, J. N.; Samanta, S.; Koner, A. L.; Saha, S.; Nau, W. M. *J. Am. Chem. Soc.* **2008**, *130*, 13608.
12. (a) For NMR data of (*E*)-**7** and *Z*/*E* isomerisation during oxidation of allylic alcohols, see: Liu, J.; Ma, S. *Org. Lett.* **2013**, *15*, 5150 and references therein; (b) for NMR data of (*E*)-**7**, see: Ochiai, M.; Yoshimura, A.; Takeshi, M.; Nishi, Y.; Hirobe, M. *J. Am. Chem. Soc.* **2008**, *130*, 3742.
13. Buncel, E.; Durst, T. (Ed.), *Comprehensive carbanion chemistry, Studies in Organic Chemistry Volume 5, Part A Structure and Reactivity*, Chapter 6, II, page 274, Elsevier Scientific Publishing Company: Amsterdam-Oxford-New York, **1980**.
14. Castagnolo, D.; Foley, D. J.; Berber, H.; Luisi, R.; Clayden, J. *Organic Letters* **2013**, *15*, 2116.

15. Tetlow, D. J.; Hennecke, U.; Raftery, J.; Waring, M. J.; Clarke, D. S.; Clayden, J. *Org. Lett.* **2010**, *12*, 5442.

16. (a) Neugebauer, W.; von Rague Schleyer, P. *J. Organomet. Chem.* **1980**, *198*, C1; (b) Schlosser, M.; Stähle, M. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 145; (c) Fraenkel, G.; Halasa, A. F.; Mochel, V.; Stumpe, R.; Tate, D. *J. Org. Chem.* **1985**, *50*, 4563; (d) Winchester, W. R.; Bauer, W.; von Ragué Schleyer, P. *J. Chem. Soc., Chem. Commun.* **1987**, 177 and references therein; (e) Piffl, M.; Weston, J.; Günther, W.; Anders, E. *J. Org. Chem.* **2000**, *65*, 5942 and references therein.

17. Balzer, H.; Berger, S. *Chem. Ber.* **1992**, *125*, 733.