Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2012

Rhodium-Catalysed Linear-Selective Alkyne Hydroacylation

Sarah-Jane Poingdestre,[a] *Jonathan D. Goodacre,*[b] *Andrew S. Weller*[a] *and Michael C. Willis**[a]

[a]Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford, OX1 3TA, UK.

[b]GlaxoSmithKline, Medicines Research Centre, Gunnels Wood Road, Stevenage, SG1 2NY, UK.

Electronic Supporting Information

Preparation of Aldehydes and Catalytic Procedures

This journal is © The Royal Society of Chemistry 2012

I. General Considerations

Chemicals were purchased from Sigma Aldrich, Alfa Aesar, Acros Organics Ltd., or Strem Chemicals Inc. and used as supplied with the exception of 2-methylthiobenzaldehyde **1a** which was purified by flash column chromatography on silica gel (5% Et_2O/petrol) and distilled (145 °C, 13 mmHg) prior to use. Anhydrous (where stated), HPLC grade solvents were purchased from Sigma Aldrich, Fisher Scientific or Rathburn and used directly without further purification with the exception of Acetone which was distilled from Drierite®. CH_2Cl_2 was obtained dry from an in-house solvent purification system (Innovative Technology Inc. PS-400-7) having passed through anhydrous alumina columns. 'Petrol' refers to the fraction of light petroleum ether boiling in the range 40-60 ^oC.

Reactions were performed with continuous magnetic stirring, under an atmosphere of nitrogen, unless otherwise stated, using standard Schlenk techniques and all glassware was oven-dried overnight (>200 ^oC) and allowed to cool under a flow of nitrogen (passed through a Drierite® filled tube) prior to use. Flash column chromatography was performed using Merck Geduran silica gel 60 (particle size 0.040-0.063 nm) with the indicated eluents. Thin Layer Chromatography (TLC) analysis was carried out on Merck Kieselgel 60 PF254 pre-coated aluminium backed sheets and visualised either by UV fluorescence (254 nm) and/or by staining with vanillin or potassium permanganate ($KMnO_4$).

NMR spectra were recorded at ambient temperature on either Brüker DPX200 (200 MHz), DQX400 (400 MHz) or AVC500 (500 MHz) spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) and referenced relative to the residual solvent peak(s) (as specified). Coupling constants (*J*) are given in Hertz (Hz) and rounded to the nearest 0.5 Hz. Assignments were made on the basis of chemical shifts, coupling constants, DEPT, COSY, HSQC and comparison with spectra of related compounds. Signal multiplicities are denoted as: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br., broad; app., apparent.

Melting points were measured using a Leica Gallen III hot-stage microscope. Low resolution mass spectra were recorded on a Fisons Platform spectrometer (ESI). High resolution mass spectra were measured by the internal service at the University of Oxford using a Bruker Daltronics microTOF spectrometer. *m/z* ratio values are reported in Daltons; high resolution values are calculated to four decimal places from the molecular formula, all found within a tolerance of 5 ppm. Infrared spectra were determined neat using a Bruker Tensor 27 FT spectrometer with an internal range of 600-4000 cm^{-1}.

Ligand **5b**[1] was prepared according to a previously reported procedure. The catalyst $[Rh(nbd)_2]BF_4$ was synthesized according to literature procedure.[2]

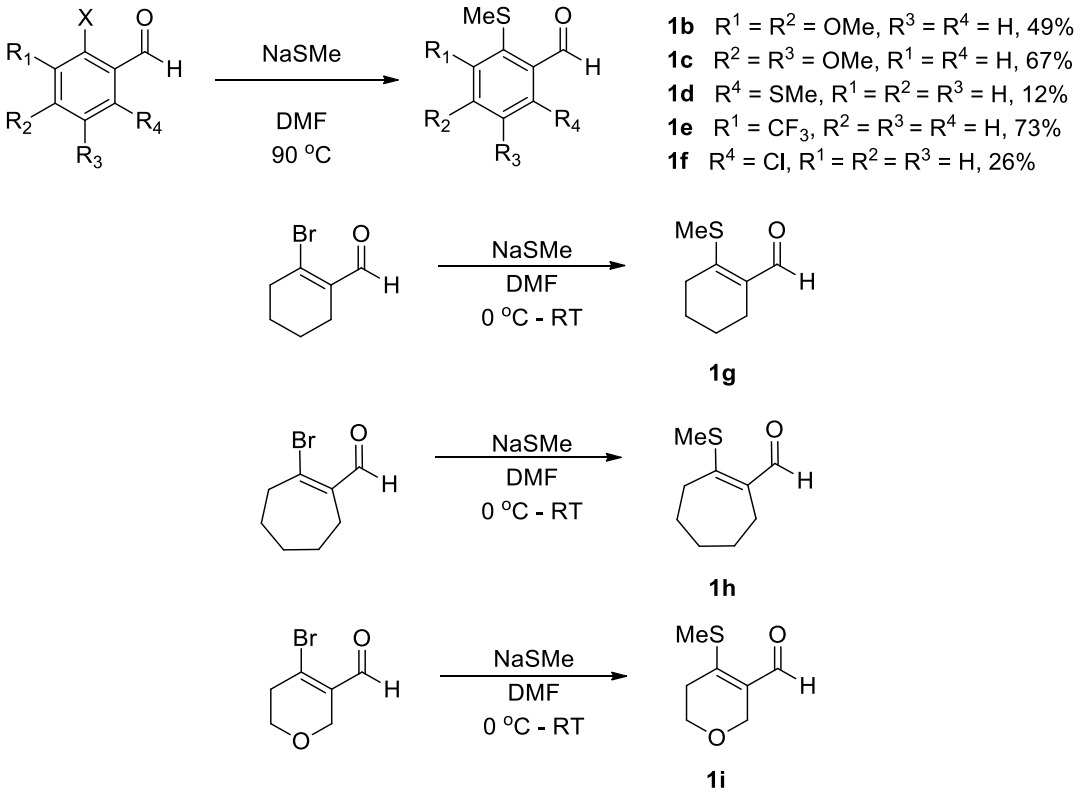
[1] C. Gonzalez-Rodriguez, R. J. Pawley, A. B. Chaplin, A. L. Thompson, A. S. Weller, M. C. Willis, *Angew. Chem. Int. Ed.*, 2011, **50**, 5134.
[2] P. Marce, Y. Díaz, I. Matheu, S. Castillón, *Org. Lett.*, 2008, **10**, 4735.

I. Preparation of Aldehydes

a. The *β*-thio-aldehydes **1b–1i** were prepared from the corresponding 2-haloaldehydes[3] following General Procedure A (Scheme S-1). Data for aldehydes **1b**,[1] **1c**,[4] **1d**,[5] **1e**,[1] **and 1h**[1] was consistent with the literature. *β*-Thio-aldehyde **1d** was obtained as a side product from the synthesis of aldehyde **1f**.

General Procedure A

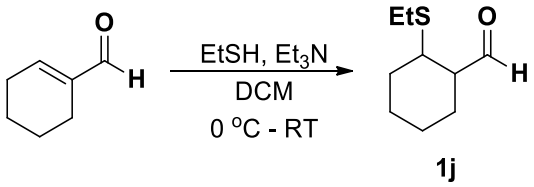
NaSMe (1.2 eq)[6] was added to a DMF solution of the halogenated compound (1.0 eq.) at 0 ºC and the resulting solution stirred at the specified temperature for 18 h. The reaction mixture was allowed to cool to RT, diluted with EtOAc (50 mL), washed with $LiCl_{(aq)}$ (2×50 mL), and brine (1×50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*, and the crude residue purified by flash column chromatography.



Scheme S-1 – General Procedure A for the preparation of aldehydes **1b-1i**

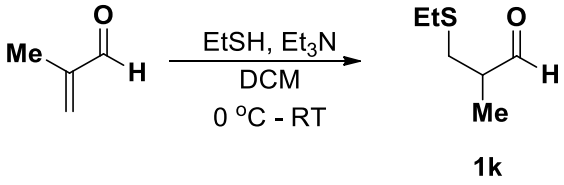
[3] For the synthesis of the 2-bromo aldehydes used in the preparation of **1g**, **1h** and **1i**, see: M-Y. Lin, A. Das, R-S. Liu, *J. Am. Chem. Soc.*, 2006, **128**, 9340.
[4] P. Jacob, G. Anderson, C. K. Meshul; A. T. Shulgin, N. Castagnoli, *J. Med. Chem*., 1977, **20**, 1235.
[5] M. M. Pollard, J. C. Vederas**,** *Tetrahedron*, 2006, **62**, 11908.
[6] 0.8 eq. NaSMe was used in the synthesis of aldehyde **1e.**

b. Et_3N (1.50 mL, 11.0 mmol) was added to a solution of ethanethiol (0.65 mL, 8.9 mmol) and bromo-cyclohex-1-enecarbaldehyde (0.50 mL, 4.4 mmol) in CH_2Cl_2 (2.5 mL) at 0 ºC and the resulting solution stirred for 18 h at RT. Volatiles were removed *in vacuo* and the crude residue purified by flash column chromatography (20% Et_2O/petrol) to afford the title compound **1j**[7] as a colourless oil (467 mg, 62%) as a 9:1 *anti*:*syn* mixture of diastereomers.



Scheme S-2 – Preparation of aldehyde **1j**

c. A solution of ethanethiol (2.70 mL, 36.6 mmol) and methacrolein (2.00 mL, 29.2 mmol) in CH_2Cl_2 (7.0 mL) was added dropwise to Et_3N (5.10 mL, 36.6 mmol) at 0 °C. The resulting reaction mixture was stirred at RT for 48 h before removal of volatiles *in vacuo* and purification by flash column chromatography to afford the title compound **1k**[8] as a yellow oil (1.40 g, 44%).

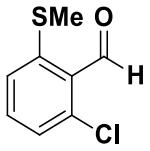


Scheme S-3 – Preparation of aldehyde **1k**

[7] C. González-Rodríguez, S. R. Parsons, A. L. Thompson, M. C. Willis, *Chem Eur. J*., 2010, **16**, 10950.
[8] M. C. Willis, H. Randell-Sly, H, R. L. Woodward, S. J. McNally, G. S. Currie, *J. Org. Chem*., 2006, **71**, 5291.

II. Data for Novel Aldehydes 1f, 1h and 1i

2-Chloro-6-(methylthio)benzaldehyde (1f)



Prepared according to General Procedure A using 2,6-dichlorobenzaldehyde (1.00 g, 5.7 mmol), NaSMe (360 mg, 5.1 mmol) and DMF (10 mL) at 90 °C for 18 h. Flash chromatography (20% Et_2O/petrol) afforded *β*-thio-aldehyde **1f** as a pale yellow solid (279 mg, 26%). m.p. (CH_2Cl_2) 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.65 (1H, s), 7.43-7.38 (1H, m), 7.23-7.17 (2H, m), 2.45 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0, 146.8, 140.3, 133.6, 128.1, 125.6, 123.0, 15.5; LRMS (ESI) *m/z* 241 (60%, $[M+Na+MeOH]^+$), 209 (65%, $[M+Na]^+$); HRMS (ESI) found *m/z* 208.9797 ($[M+Na]^+$), $C_8H_7{}^{35}ClNaOS^+$ requires 208.9797; ν_{max} (neat)/cm^{-1} 3097, 3068, 2924, 2987, 2275, 1668, 1571, 1543.

2-(Methylthio)cyclohept-1-enecarbaldehyde (1h)

Prepared according to General Procedure A using 2-bromocyclohept-1-enecarbaldehyde (700 mg, 3.5 mmol), NaSMe (293 mg, 4.2 mmol) and DMF (15 mL) at RT for 24 h. Flash chromatography (15% Et_2O/petrol) afforded *β*-thio-aldehyde **1h** as a yellow oil (412 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (1H, s), 2.75-2.69 (2H, m), 2.56-2.50 (2H, m), 2.33 (3H, s), 1.83-1.76 (2H, m), 1.65-1.57 (2H, m), 1.46-1.39 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 163.0, 142.5, 34.7, 32.0, 26.0, 25.8, 25.7, 15.4; LRMS (ESI) *m/z* 241 (55%, $[M+K+MeOH]^+$), 209 (50%, $[M+K]^+$), 193 (30%, $[M+Na]^+$); HRMS (ESI) found *m/z* 193.0661 ($[M+Na]^+$), $C_9H_{14}NaOS^+$ requires 193.0658; ν_{max} (film)/cm^{-1} 2922, 2850, 2729, 1654, 1567.

This journal is © The Royal Society of Chemistry 2012

4-(Methylthio)-5,6-dihydro-2H-pyran-3-carbaldehyde (1i)

Prepared according to General Procedure A using 4-bromo-5,6-dihydro-2H-pyran-3-carbaldehyde (2.00 g, 10.6 mmol), NaSMe (890 mg, 12.7 mmol) and DMF (40 mL) at RT for 18 h. Flash chromatography (30% Et_2O/petrol) afforded *β*-thio-aldehyde **1i** as an off-white solid (646 mg, 39%). m.p. (CH_2Cl_2) 48-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (1H, s), 4.33 (2H, t, *J* 2.0), 3.84 (2H, t, *J* 5.5), 2.58 (2H, tt, *J* 5.5, 2.0), 2.36 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.1, 154.4, 132.7, 65.0, 64.1, 29.6, 13.3; LRMS (ESI) *m/z* 213 (65%, $[M+Na+MeOH]^+$), 181 (65%, $[M+Na]^+$); HRMS (ESI) found *m/z* 181.0303 ($[M+Na]^+$), $C_7H_{10}NaO_2S^+$ requires 181.0294; ν_{max} (neat)/cm^{-1} 3004, 2987, 2941, 2904, 2863, 2850, 2827, 2740, 1641, 1572.

This journal is © The Royal Society of Chemistry 2012

III. General Procedures for Rh-Catalysed Hydroacylation

General procedure B (Ligand screen, Table 1)

$[Rh(nbd)_2]BF_4$ and the appropriate ligand were dissolved in acetone (2.0 mL)[9] and stirred at RT for 5 min. H_2(g) was bubbled through the pre-catalyst solution for 2 min, then the solution purged with N_2(g). 2-methylthiobenzaldehyde (39 μL 0.30 mmol) and 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol) were added and the reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with Et_2O, filtered through a short plug of celite and the filtrate concentrated *in vacuo*.

A sample of the crude residue was analysed by ^{1}H NMR in $CDCl_3$, to determine conversion and the regioselectivity of the reaction.

General procedure C (Reaction scope, Tables 2 and 3)

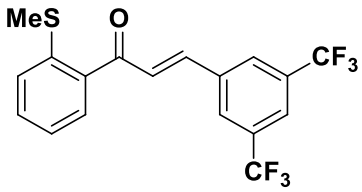
$[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) were dissolved in acetone (1.5 mL) and stirred at RT for 5 min. H_2(g) was bubbled through the pre-catalyst solution for 2 min, then the solution purged with N_2(g). Aldehyde (0.30 mmol) and alkyne (0.45 mmol) were added as a solution in acetone (0.5 mL) and the reaction mixture was stirred at RT for 1-2.5 h. The reaction mixture was diluted with Et_2O, filtered through a short plug of celite and the filtrate concentrated *in vacuo*. The crude residue was purified by flash column chromatography.

A sample of the crude residue was analysed by ^{1}H NMR in $CDCl_3$ to determine the regioselectivity of the reaction.

[9] Table 1, Entry 9, only 1.0 mL of acetone used.

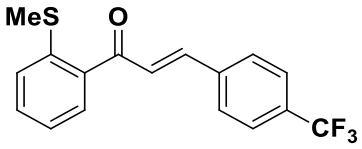
IV. Data for Enones 3a-3u

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3a)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol) and 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3a** as a bright yellow solid (109 mg, 93%). m.p. (CH_2Cl_2) 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (2H, s), 7.89 (1H, s), 7.77 (1H, dd, *J* 8.0, 1.5), 7.68 (1H, d, *J* 16.0), 7.55-7.50 (1H, m), 7.47 (1H, d, *J* 16.0), 7.41(1H, app. d, *J* 8.0), 7.30-7.25 (1H, m), 2.48 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 141.3, 140.85, 137.0, 136.2, 132.5 (2C, q, $J_{C\text{-}F}$ 33.5), 132.2, 129.8, 127.9 (2C, br. s), 127.8, 126.2, 124.2, 123.5-123.2 (m), 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 803 (100%, $[2M+H]^+$), 413 (10%, $[M+Na]^+$); HRMS (ESI) found *m/z* 413.0405 ($[M+Na]^+$), $C_{18}H_{12}F_6NaOS^+$ requires 413.0411; ν_{max} (neat)/cm^{-1} 3099, 2927, 2851, 1653, 1603, 1588.

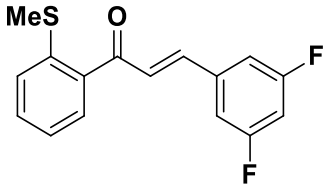
(*E*)-1-(2-(Methylthio)phenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (3b)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol) and 1-ethynyl-4-(trifluoromethyl)benzene (73 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3b** as a yellow solid (80 mg, 83%). m.p. (CH_2Cl_2) 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.62 (6H, m), 7.53-7.47 (1H, m), 7.44-7.37 (1H d, *J* 16.0 overlapping 1H, m), 7.29-7.22 (1H, m), 2.47 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 142.8, 141.1, 138.2, 136.6, 131.9, 131.8 (q, $J_{C\text{-}F}$ 33.0), 129.7, 128.5 (2C), 126.7, 126.2 , 125.9 (2C, q, $J_{C\text{-}F}$ 4.0), 124.2,

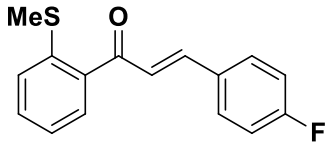
123.8 (q, $J_{C\text{-}F}$ 272.5), 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.8, (3F, s); LRMS (ESI) *m/z* 667 (100%, $[2M+Na]^+$), 345 (70%, $[M+Na]^+$), 323 (25%, $[M+H]^+$); HRMS (ESI) found *m/z* 345.0527 ($[M+Na]^+$), $C_{17}H_{13}F_3NaOS^+$ requires 345.0531; ν_{max} (neat)/cm^{-1} 2961, 2923, 1658, 1599, 1585, 1577, 1556.

(*E*)-3-(3,5-Difluorophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3c)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), 1-ethynyl-4-fluorobenzene (52 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3c** as a yellow solid (74 mg, 91%). m.p. (CH_2Cl_2) 82-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.71 (1H, m), 7.57-7.46 (2H, m), 7.39 (1H, app. d, *J* 8.0), 7.32 (1H, d, *J* 15.5), 7.28-7.22 (1H, m), 7.14-7.07 (2H, m), 6.85 (1H, app. tt, *J* 8.5, 2.0), 2.48 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 163.2 (2C, dd, $J_{C\text{-}F}$ 249.0, 12.8), 142.0 (t, $J_{C\text{-}F}$ 3.0), 141.1, 138.1 (t, $J_{C\text{-}F}$ 9.5), 136.5, 132.0, 129.7, 126.7, 126.2, 124.2, 110.0 (2C, dd, $J_{C\text{-}F}$ 18.5, 7.0), 105.5 (t, $J_{C\text{-}F}$ 25.0), 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.9 (2F, s); LRMS (ESI) *m/z* 603 (100%, $[2M+Na]^+$), 329 (45%, $[M+K]^+$), 313 (60%, $[M+Na]^+$), 291 (20%, $[M+H]^+$); HRMS (ESI) found *m/z* 313.0466 ($[M+Na]^+$), $C_{16}H_{12}F_2NaOS^+$ requires 313.0469; ν_{max} (neat)/cm^{-1} 3083, 2922, 1663, 1620, 1606, 1588.

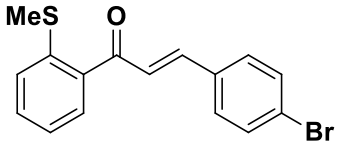
(*E*)-3-(4-Fluorophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3d)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), 1-ethynyl-4-fluorobenzene (52 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) for 2 h at RT. Purification by flash chromatography (30% Et_2O/petrol) afforded the title compound **3d** as a yellow solid (74 mg, 91%). m.p. (CH_2Cl_2) 54-56 °C; ^{1}H NMR (400

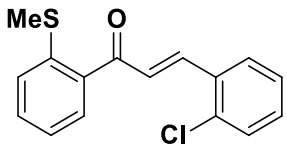
MHz, $CDCl_3$) δ 7.70 (1H, app. d, *J* 7.5), 7.64-7.53 (3H, m), 7.51-7.44 (1H, m), 7.38 (1H, app. d, *J* 8.0), 7.29-7.20 (2H, m), 7.09 (2H, app. t, *J* 8.5), 2.46 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 164.0 (d, $J_{C\text{-}F}$ 252.0), 143.9, 140.6, 137.1, 131.6, 131.0 (d, $J_{C\text{-}F}$ 3.0), 130.4 (2C, d, $J_{C\text{-}F}$ 8.0), 129.4, 126.2, 124.4 (2C), 116.1 (2C, d, $J_{C\text{-}F}$ 22.5), 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.0 (1F, s); LRMS ESI) *m/z* 567 (100%, $[2M+Na]^+$), 295 (65%, $[M+Na]^+$); HRMS (ESI) found *m/z* 295.0561 ($[M+Na]^+$), $C_{16}H_{13}FNaOS^+$ requires 295.0563: ν_{max} (neat)/cm^{-1} 3066, 2977, 2920, 1650, 1595, 1586, 1554, 1504.

(*E*)-3-(4-Bromophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3e)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), 1-ethynyl-4-bromobenzene (81 mg, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3e** as a yellow solid (93 mg, 93%). m.p. (CH_2Cl_2) 77-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (1H, dd, *J* 7.5, 1.5), 7.64-7.44 (1H, d, *J* 16.0 overlapping 5H, m), 7.39 (1H, app. d, *J* 8.0), 7.31 (1H, d, *J* 16.0), 7.28-7.22 (1H, m), 2.46 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 143.7, 140.7, 136.9, 133.7, 132.2 (2C), 131.7, 129.8 (2C), 129.5, 126.2, 125.1, 124.8, 124.1, 16.4; LRMS (ESI) *m/z* 689 (100%, $[2M(^{79}Br)+Na]^+$), 357 (40%, $[M+Na]^+$); HRMS (ESI) found *m/z* 354.9757 ($[M(^{79}Br)+Na]^+$), $C_{16}H_{13}{}^{79}BrNaOS^+$ requires 354.9763; ν_{max} (neat)/cm^{-1} 3096, 2955, 2920, 2853, 1655, 1592, 1562.

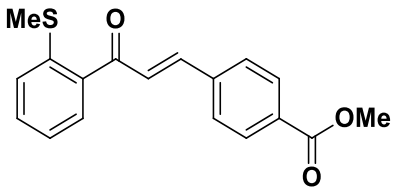
(*E*)-3-(2-Chlorophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3f)



Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), 1-chloro-2-ethynylbenzene (54 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (30% Et_2O/petrol)

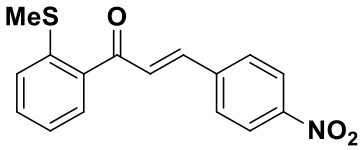
afforded the title compound **3f** as a yellow solid (76 mg, 88%). m.p. (CH_2Cl_2) 59-62 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.01 (1H, d, *J* 16.0), 7.82-7.73 (2H, m), 7.56-7.50 (1H, m), 7.50-7.42 (2H, m), 7.41-7.26 (1H, d, *J* 16.0 overlapping 3H, m), 2.49 (3H, s); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 192.5, 141.3, 140.7, 137.1, 135.6, 133.5, 132.1, 131.7, 130.6, 130.0, 128.2, 127.7, 127.6, 126.6, 124.4, 16.6; LRMS (ESI) *m/z* 599 (100%, $[2M(^{35}Cl)+Na]^+$), 311 (40%, $[M(^{35}Cl)+Na]^+$), 289 (15%, $[M(^{35}Cl)+H]^+$); HRMS (ESI) found *m/z* 311.0265 ($[M(^{35}Cl)+Na]^+$), $C_{16}H_{13}{}^{35}ClNaOS^+$ requires 311.0268; ν_{max} (neat)/cm^{-1} 3065, 2961, 2919, 1650, 1592, 1556.

(*E*)-Methyl 4-(3-(2-(methylthio)phenyl)-3-oxoprop-1-en-1-yl)benzoate (3g)



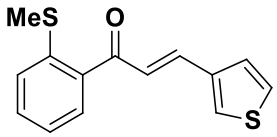
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), methyl 4-ethynylbenzoate (66 mg, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3g** as a bright yellow solid (69 mg, 74%). m.p. (CH_2Cl_2) 119-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (2H, app. d, *J* 8.5), 7.73 (1H, dd, *J* 7.5, 1.5), 7.69-7.62 (3H, m), 7.52-7.46 (1H, m), 7.43-7.37 (2H, m), 7.28-7.22 (1H, m), 3.93 (3H, s), 2.77 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 166.4, 143.3, 140.9, 139.0, 136.7, 131.8, 131.5, 130.1 (2C), 129.6, 128.3 (2C), 126.6, 126.2, 124.1, 52.3 , 16.4; LRMS (ESI) *m/z* 647 (100%, $[2M+Na]^+$), 335 (45%, $[M+Na]^+$), 313 (30%, $[M+H]^+$); HRMS (ESI) found *m/z* 335.0707 ($[M+Na]^+$), $C_{18}H_{16}NaO_3S^+$ requires 335.0712; ν_{max} (neat)/cm^{-1} 3067, 2954, 2913, 1655, 1603, 1564.

(*E*)-1-(2-(Methylthio)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one (3h)



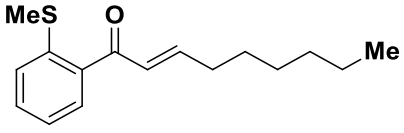
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol), 1-ethynyl-4-nitrobenzene (54 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (100% CH_2Cl_2), followed by recrystallisation from CH_2Cl_2/petrol, afforded the title compound **3h** as a dark yellow crystalline solid (60 mg, 67%). m.p. (CH_2Cl_2) 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (2H, d, *J* 8.5), 7.78-7.75 (3H, m), 7.68 (1H, d, *J* 16.0), 7.54-7.38 (1H, d, *J* 16.0 overlapping 2H, m), 7.30-7.23 (1H, m), 2.48 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 148.5, 141.5, 141.3, 141.0, 136.3, 132.1, 129.8 (2C), 128.9 (2C), 128.1, 126.2, 124.2 (2C), 16.4; LRMS (ESI) *m/z* 354 (20%, $[M+H]^+$), 322 (100%, $[M+Na]^+$); HRMS (ESI) found *m/z* 322.0507 ($[M+Na]^+$), $C_{16}H_{13}NNaO_3S^+$ requires 322.0508; ν_{max} (neat)/cm^{-1} 2917, 2850, 1651, 1604, 1586, 1556, 1513, 1338.

(*E*)-1-(2-(Methylthio)phenyl)-3-(thiophen-3-yl)prop-2-en-1-one (3i)



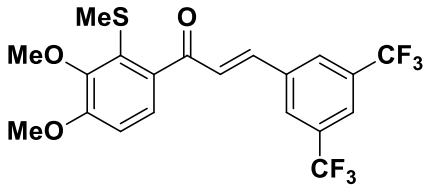
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol) and 3-ethynylthiophene (42 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (35% Et_2O/petrol) afforded the title compound **3i** as a brown oil (75 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (1H, dd, *J* 8.0, 1.5), 7.60 (1H, d, *J* 16.0), 7.57-7.54 (1H, m), 7.49-7.43 (1H, m), 7.40-7.34 (3H, m), 7.23 (1H, m), 7.12 (1H, d, *J* 16.0), 2.46 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 140.3, 138.8, 138.1, 137.3, 131.4, 129.3, 129.1, 127.1, 126.3, 125.3, 124.7, 124.2, 16.5; LRMS (ESI) *m/z* 543 (100%, $[2M+Na]^+$), 299 (35%, $[M+K]^+$), 283 (45%, $[M+Na]^+$), 261 (10%, $[M+H]^+$); HRMS (ESI) found *m/z* 283.0219 ($[M+Na]^+$), $C_{14}H_{12}NaOS_2^+$ requires 283.0222; ν_{max} (neat)/cm^{-1} 2980, 2919, 1650, 1616, 1590, 1558, 1516.

(*E*)-1-(2-(Methylthio)phenyl)non-2-en-1-one (3j)



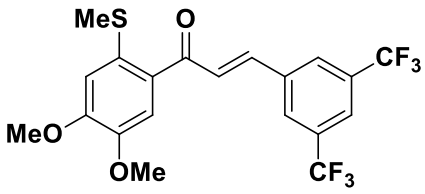
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 μL, 0.30 mmol) and 1-octyne (66 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3j** as a green oil (66 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (1H, dd, *J* 7.5, 1.5), 7.46-7.41 (1H, m), 7.34 (1H, app. d, *J* 7.5), 7.19 (1H, app. td, *J* 7.5, 1.0), 6.87 (1H, dt, *J* 15.5, 7.0), 6.64 (1H, dt, *J* 15.5, 1.5), 2.43 (3H, s), 2.32-2.24 (2H, m), 1.54-1.42 (2H, m), 1.37-1.25 (6H, m), 0.92-0.83 (3H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 151.2, 140.2, 137.1, 131.2, 129.3, 128.6, 126.2, 124.0, 32.8, 31.6, 28.9, 28.0, 22.5, 16.4, 14.0; LRMS (ESI) *m/z* 547 (100%, $[2M+Na]^+$), 285 (50%, $[M+Na]^+$), 263 (20%, $[M+H]^+$); HRMS (ESI) found *m/z* 285.1277 ($[M+Na]^+$), $C_{16}H_{22}NaOS^+$ requires 285.1284; ν_{max} (neat)/cm^{-1} 2924, 2855, 1658, 1614, 1585, 1558.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(3,4-dimethoxy-2-(methylthio)phenyl)prop-2-en-1-one (3k)



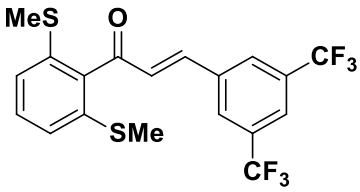
Prepared according to General Procedure C using 3,4-dimethoxy-2-(methylthio)benzaldehyde (64 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (30% Et_2O/petrol), followed by recrystallisation from petrol, afforded the title compound **3k** as a pale yellow solid (82 mg, 61%). m.p. (CH_2Cl_2) 123-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (2H, s), 7.87 (1H, s), 7.50 (1H, d, *J* 16.0), 7.32 (1H, d, *J* 16.0), 7.27 (1H, d, *J* 8.5), 6.96 (1H, d, *J* 8.5), 3.95 (6H, s), 2.43 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.1, 155.3, 150.4, 138.8, 137.2, 136.4, 132.4, (2C, q, $J_{C\text{-}F}$ 33.5), 130.4, 129.8, 127.8 (2C, br. s) 124.8, 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 123.4-123.1 (m), 111.7, 60.5, 58.0, 19.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.3 (6F, s); LRMS (ESI) *m/z* 923 (100%, $[2M+Na]^+$), 473 (20%, $[M+Na]^+$); HRMS (ESI) found *m/z* 473.0601 ($[M+Na]^+$), $C_{20}H_{16}F_6NaO_3S^+$ requires 473.0617; ν_{max} (neat)/cm^{-1} 3013, 2978, 2943, 2923, 1647, 1585.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(4,5-dimethoxy-2-(methylthio)phenyl)prop-2-en-1-one (3l)



Prepared according to General Procedure C using 4,5-dimethoxy-2-(methylthio)benzaldehyde (64 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et_2O/petrol) afforded the title compound **3l** as a yellow solid (93 mg, 73%). m.p. (CH_2Cl_2) 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (2H, s), 7.88 (1H, s), 7.69 (1H, d, *J* 15.5), 7.49 (1H, d, *J* 15.5), 7.26 (1H, s), 6.96 (1H, s), 3.98 (3H, s), 3.94 (3H, s), 3.47 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4, 152.3, 146.5, 139.5, 137.3, 133.7, 132.4 (2C, q, $J_{C\text{-}F}$ 34.5), 130.5, 128.3, 127.8 (2C), 123.2 (app. quin, $J_{C\text{-}F}$ 4.0), 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 112.9, 111.0, 54.4, 56.1, 19.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 923 (100%, $[2M+Na]^+$), 473 (20%, $[M+Na]^+$), 451 (10%, $[M+H]^+$); HRMS (ESI) found *m/z* 473.0613 ($[M+Na]^+$), $C_{20}H_{16}F_6NaO_3S^+$ requires 473.0617; ν_{max} (neat)/cm^{-1} 3025, 2967, 2914, 2853, 1651, 1547.

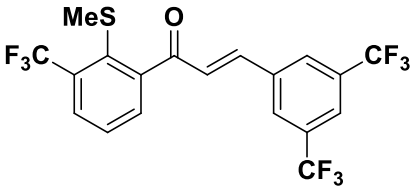
(*E*)-1-(2,6-bis(Methylthio)phenyl)-3-(3,5-bis(trifluoromethyl)phenyl)prop-2-en-1-one (3m)



Prepared according to General Procedure C using 2,6-bis(methylthio)benzaldehyde (59 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (15% Et_2O/petrol) afforded the title compound **3m** as a yellow solid (94 mg, 70%). m.p. (CH_2Cl_2) 116-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, s), 7.87 (1H, s), 7.43-7.37 (1H, m), 7.34 (1H, d, *J* 16.0), 7.27 (2H, d, *J* 8.0), 7.09 (1H, d, *J* 16.0), 2.44 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 141.2,

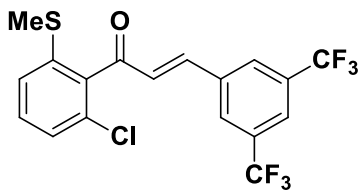
140.3 (2C), 136.8, 135.9, 132.4 (2C, q, $J_{C\text{-}F}$ 33.5), 130.5, 130.2, 128.0 (2C, app. d, $J_{C\text{-}F}$ 3.5), 126.1 (2C), 123.5 (app. quin, $J_{C\text{-}F}$ 4.0) , 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 17.7 (2C); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 895 (100%, $[2M+Na]^+$), 459 (35%, $[M+Na]^+$), 437 (15%, $[M+H]^+$); HRMS (ESI) found 459.0275 ($[M+Na]^+$), $C_{19}H_{14}F_6NaOS_2^+$ requires 459.0282; ν_{max} (neat)/cm^{-1} 3048, 2963, 2924, 1648, 1558.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)-3-(trifluoromethyl)phenyl)prop-2-en-1-one (3n)



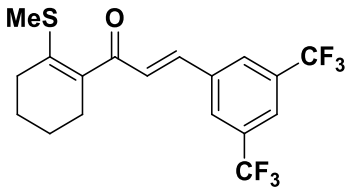
Prepared according to General Procedure C using 2-(methylthio)-3-(trifluoromethyl)benzaldehyde (66 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Purification by flash chromatography (10% Et_2O/petrol) afforded the title compound **3n** as an off-white solid (129 mg, 94%). m.p. (CH_2Cl_2) 97-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, s), 7.92-7.85 (2H, m), 7.63-7.52 (2H, m), 7.43 (1H, d, *J* 16.0), 7.27 (1H, d, *J* 16.0), 2.34 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 148.6, 140.6, 136.5, 135.2 (q, $J_{C\text{-}F}$ 36.5), 132.5 (2C, q, $J_{C\text{-}F}$ 33.5), 132.3, 131.0, 130.0, 129.2, 128.4 (app. q, $J_{C\text{-}F}$ 5.5), 128.0 (2C, br. s), 123.3 (q, $J_{C\text{-}F}$ 74.0), 122.9 (2C, q, $J_{C\text{-}F}$ 273.0), 123.7 (app. quin, $J_{C\text{-}F}$ 4.0), 22.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.7 (3F, s), -63.1 (6F, s); LRMS (ESI) *m/z* 939 (100%, $[2M+Na]^+$), 481 (80%, $[M+Na]^+$); HRMS (ESI) found *m/z* 481.0276 ($[M+Na]^+$), $C_{19}H_{11}F_9NaOS^+$ requires 481.0279; ν_{max} (neat)/cm^{-1} 2961, 2925, 2854, 1649, 1632, 1579.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-chloro-6-(methylthio)phenyl)prop-2-en-1-one (3o)



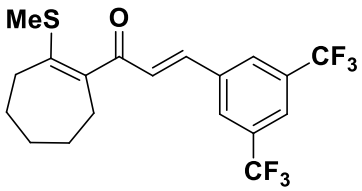
Prepared according to General Procedure C using 2-chloro-6-(methylthio)benzaldehyde (56 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at 50 °C for 18 h. Purification by flash chromatography (25% Et_2O/petrol) afforded the title compound **3o** as a yellow solid (100 mg, 78%). m.p. (CH_2Cl_2) 96-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (2H, s), 7.89 (1H, s), 7.42-7.24 (4H, m), 7.33 (1H, d, *J* 16.5), 2.46 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 142.2, 138.3, 137.8, 136.5, 132.5 (2C, q, $J_{C\text{-}F}$ 33.5), 130.9, 130.7, 129.9, 128.1 (2C, br. s), 127.0, 126.5, 123.9-123.7 (m), 122.9 (2C, q, $J_{C\text{-}F}$ 273.0), 17.5; ^{19}F NMR (376 MHz, $CDCl_3$) -63.0 (6F, s); LRMS (ESI) *m/z* 811 (100%, $[2M(^{35}Cl)+Na]^+$), 417 (50%, $[M(^{35}Cl)+Na]^+$), 395 (80%, $[M+H]^+$); HRMS (ESI) found *m/z* 417.0007 ($[M(^{35}Cl)+Na]^+$), $C_{18}H_{11}{}^{35}ClNaOS^+$ requires 417.0016; ν_{max} (neat)/cm^{-1} 3055, 2960, 2927, 1652, 1632, 1573, 1557.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)cyclohex-1-en-1-yl)prop-2-en-1-one (3p)



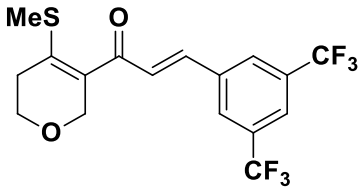
Prepared according to General Procedure C using 2-(methylthio)cyclohex-1-enecarbaldehyde (47 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (10-15% EtOAc/petrol) afforded the title compound **3p** as a bright yellow solid (100 mg, 85%). m.p. (CH_2Cl_2) 96-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (2H, s), 7.85 (1H, s), 7.63 (1H, d, *J* 15.5), 7.31 (1H, d, *J* 15.5), 2.57-2.49 (4H, m), 2.31 (3H, s), 1.83-1.70 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 148.8, 138.4, 137.6, 132.3 (2C, q, $J_{C\text{-}F}$ 33.5), 131.8, 128.0, 127.7 (2C, br. s), 123.1 (2C, q, $J_{C\text{-}F}$ 277.0), 123.0-122.7 (m), 30.1, 28.2, 23.0, 21.9, 15.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 814 (100%, $[2M+Na]^+$), 417 (50%, $[M+Na]^+$), 395 (80%, $[M+H]^+$); HRMS (ESI) found *m/z* 417.0718 ($[M+Na]^+$), $C_{18}H_{16}F_6NaOS^+$ requires 417.0718; ν_{max} (neat)/cm^{-1} 2926, 2848, 1651, 1598, 1515.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)cyclohept-1-en-1-yl)prop-2-en-1-one (3q)



Prepared according to General Procedure C using 2-(methylthio)cyclohept-1-enecarbaldehyde (51 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (15% Et_2O/petrol) afforded the title compound **3q** as a bright yellow solid (77 mg, 63%). m.p. (CH_2Cl_2) 76-78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (2H, s), 7.85 (1H, s), 7.56 (1H, d, *J* 16.0), 7.14 (1H, d, *J* 16.0), 2.71-2.65 (2H, m), 2.60-2.53 (2H, m), 2.28 (3H, s), 1.85-1.80 (2H, m), 1.66 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 149.4 (2C), 141.8, 137.5, 132.3 (2C, q, $J_{C\text{-}F}$ 33.0), 129.6, 127.6 (2C, br. s), 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 122.9-122.7 (m), 33.8, 31.8, 31.1, 26.6, 25.8, 16.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 839 (100%, $[2M+Na]^+$), 447 (50%, $[M+K]^+$), 409 (85%, $[M+H]^+$); HRMS (ESI) found *m/z* 431.0871 ($[M+Na]^+$), $C_{19}H_{18}F_6NaOS^+$ requires 431.0875; ν_{max} (neat)/cm^{-1} 2924, 2855, 1663, 1602.

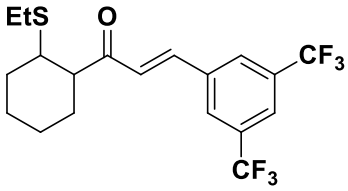
(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(4-(methylthio)-5,6-dihydro-2H-pyran-3-yl)prop-2-en-1-one (3r)



Prepared according to General Procedure C using 4-(methylthio)-5,6-dihydro-2H-pyran-3-carbaldehyde (47 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Recrystallisation from CH_2Cl_2 afforded the title compound **3r** as a bright yellow crystalline solid (100 mg, 84%). m.p. (CH_2Cl_2) 189-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (2H, s), 7.87 (1H, s), 7.69 (1H, d, *J* 15.5), 7.07 (1H, d, *J* 15.5), 4.62 (2H, s), 3.91 (2H, t, *J* 5.5), 2.68-2.61 (2H, m), 2.37 (3H,

s); ^{13}C NMR (126 MHz, d_6-DMSO) δ 185.9, 151.8, 138.7, 137.8, 130.8 (2C), 129.0 (br. s), 127.2, 127.0, 123.2 (2C, q, $J_{C\text{-}F}$ 272.0), 123.0-122.7 (m), 66.5, 63.6, 28.9, 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 815 (100%, $[2M+Na]^+$), 419 (20%, $[M+Na]^+$), 397 (30%, $[M+H]^+$); HRMS (ESI) found *m/z* 419.0513 ($[M+Na]^+$), $C_{17}H_{14}F_6NaOS^+$ requires 419.0511; ν_{max} (neat)/cm^{-1} 3093, 2961, 2921, 2851, 1650, 1597, 1514.

(*E*)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(ethylthio)cyclohexyl)prop-2-en-1-one (3s)

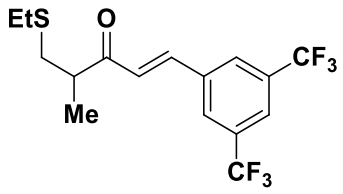


Prepared according to General Procedure C using 2-(ethylthio)cyclohexanecarbaldehyde (77 mg, 0.30 mmol, 9:1 anti:syn), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 μL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Purification by flash chromatography (5% Et_2O/petrol) afforded the title compound **3s** as an off-white solid (95 mg, 80%). This was obtained as an inseparable mixture of diastereomers (9:1 *anti:syn*). m.p. (CH_2Cl_2) 66-68 °C; LRMS (ESI) *m/z* 843 (100%, $[2M+Na]^+$), 433 (40%, $[M+Na]^+$), 411 (30%, $[M+H]^+$); HRMS (ESI) found *m/z* 433.1027 ($[M+Na]^+$), $C_{19}H_{20}F_6NaOS^+$ requires 433.1031; ν_{max} (neat)/cm^{-1} 3049, 2935, 2859, 1689, 1664, 1609.

***Anti* diastereomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, s), 7.87 (1H, s), 7.63 (1H, d, *J* 16.0), 6.93 (1H, d, *J* 16.0), 2.95-2.82 (2H, m), 2.60-2.51 (2H, m), 2.26-2.16 (1H, m), 1.92-1.87 (1H, m) 1.86-1.75 (2H, m), 1.53-1.23 (4H, m), 1.20 (3H, t, *J* 7.5); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.5, 138.8, 136.9, 132.4 (2C, q, $J_{C\text{-}F}$ 33.5), 129.1, 127.9 (2C. app. d, $J_{C\text{-}F}$ 3.0), 123.2 (app. quin, $J_{C\text{-}F}$ 4.0), 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 58.8, 44.1, 34.3, 30.5, 26.0, 25.5, 24.9, 14.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (6F, s,).

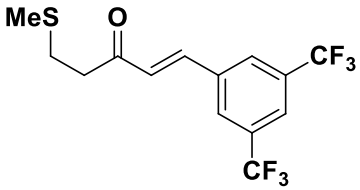
The following NMR signals are consistent with the ***syn* diastereomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, s), 7.64 (1H, d, *J* 16.0), 7.05 (1H, d, *J* 16.0), 2.39-2.32 (1H, m), 2.10-2.03 (1H, m), 1.69-1.64 (1H, m), 1.17 (3H, t, *J* 7.5); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 138.4, 137.0, 127.7 (2C, d, $J_{C\text{-}F}$ 5.0), 126.8, 123.2 (app. quin, $J_{C\text{-}F}$ 4.0), 53.1, 44.6, 31.9, 29.7, 26.4, 24.2, 23.0, 14.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (6F, s).

(*E*)-1-(3,5-bis(Trifluoromethyl)phenyl)-5-(ethylthio)-4-methylpent-1-en-3-one (3t)



Prepared according to General Procedure C using 3-(ethylthio)-2-methylpropanal (33 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 4 h. Purification by flash chromatography (5% Et_2O/petrol) afforded the title compound **3t** as a pale yellow oily solid (60 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, s), 7.89 (1H, s), 7.65 (1H, d, *J* 16.0), 6.94 (1H, d, *J* 16.0), 3.15-3.04 (1H, m), 2.95 (1H, dd, *J* 13.0, 7.5), 2.66-2.53 (3H, m), 1.32-1.23 (6H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2, 139.2, 136.7, 133.5 (2C, q, $J_{C\text{-}F}$ 33.5), 127.9 (2C, br. s), 127.8, 123.5 (app. quin, $J_{C\text{-}F}$ 3.0), 123.0 (2C, q, $J_{C\text{-}F}$ 273.0), 45.6, 34.3, 26.9, 19.6, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (6F, s); LRMS (ESI) *m/z* 763 (95%, $[2M+Na]^+$), 409 (100%, $[M+K]^+$), 393 (40%, $[M+Na]^+$), 371 (25%, $[M+H]^+$); HRMS (ESI) found *m/z* 393.1710 $[M+Na]^+$), $C_{16}H_{16}F_6NaOS^+$ requires 393.0718; ν_{max} (neat)/cm^{-1} 2975, 2931, 1694, 1688, 1614.

(*E*)-1-(3,5-bis(Trifluoromethyl)phenyl)-5-(methylthio)pent-1-en-3-one (3u)

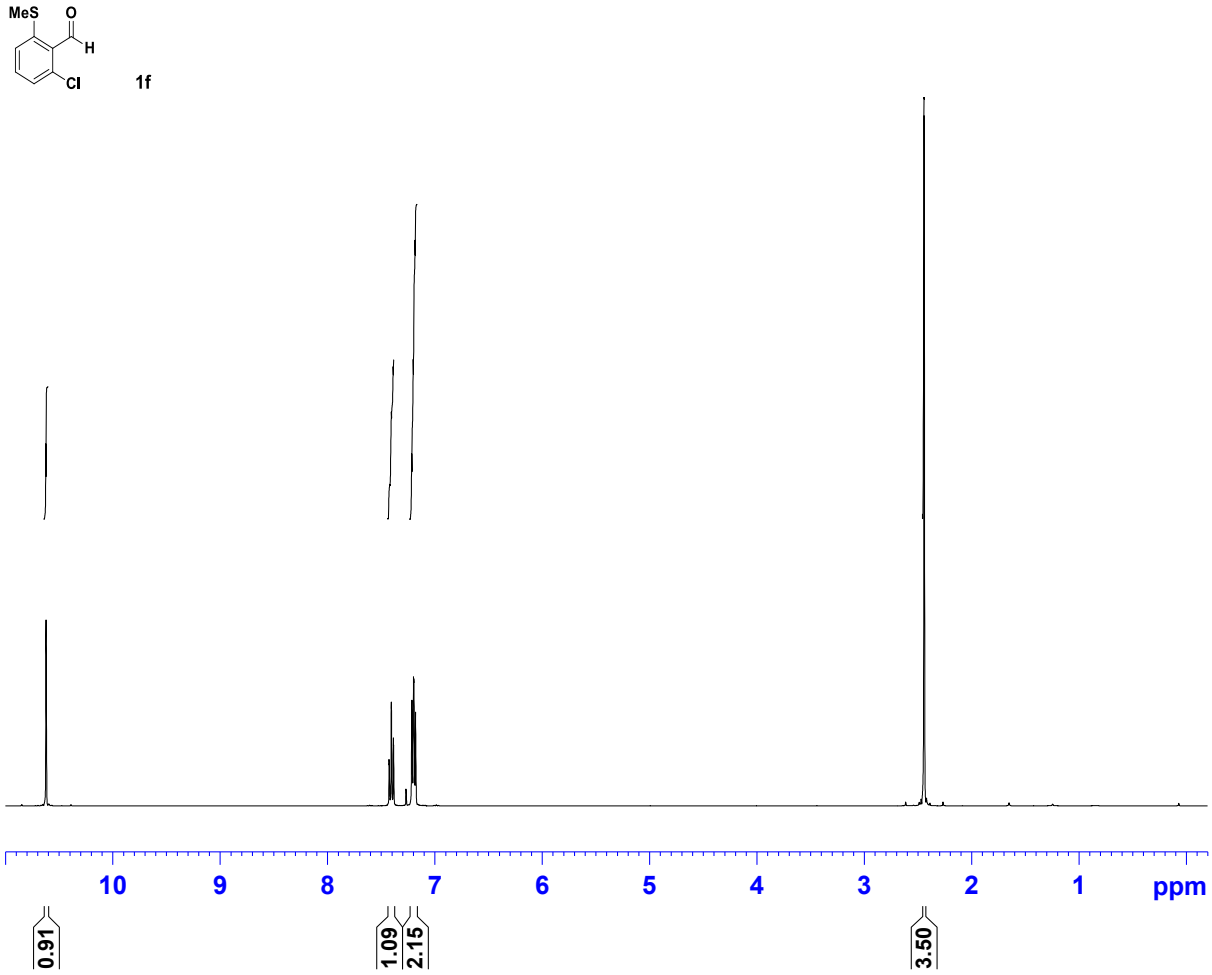


Prepared according to General Procedure C using 3-(methylthio)propionaldehyde (30 µL, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), $[Rh(nbd)_2]BF_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2.5 h. Purification by flash chromatography (5% EtOAc/petrol) afforded the title compound **3u** as an off-white solid (85 mg, 82%). m.p. (CH_2Cl_2) 64-66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (2H, s), 7.89 (1H, s), 7.61 (1H, d, *J* 16.0), 6.88 (1H, d, *J* 16.0), 3.05-2.99 (2H, m), 2.88-2.82 (2H, m), 2.16 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 139.0,

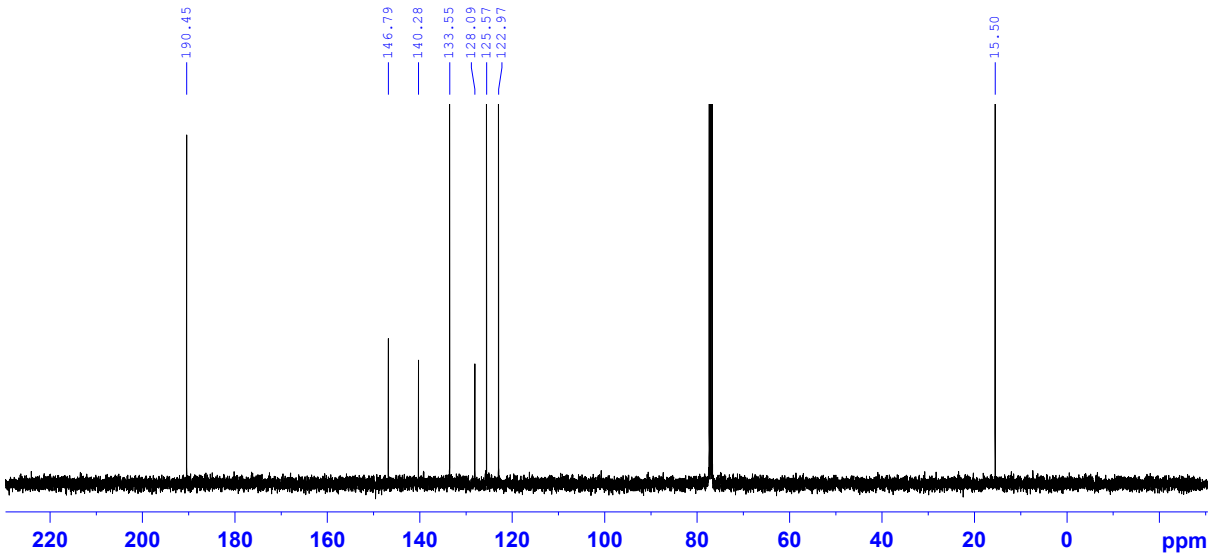
136.6, 132.5 (2C, q, $J_{C\text{-}F}$ 33.5), 128.7, 127.8 (2C, app. d, $J_{C\text{-}F}$ 2.0), 123.5 (app. quin, $J_{C\text{-}F}$ 3.0), 122.8 (2C, q, $J_{C\text{-}F}$ 272.5,), 40.3, 27.5, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (6F, s); LRMS (ESI) *m/z* 365 (100%, $[M+Na]^+$); HRMS (ESI) found *m/z* 365.0401 ($[M+Na]^+$), $C_{14}H_{12}F_6NaOS^+$ requires 365.0405; ν_{max} (neat)/cm^{-1} 3044, 2961, 2934, 2888, 1697, 1612.

V. Spectral Data for Novel Compounds

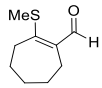
^{1}H NMR (400 MHz, $CDCl_3$)



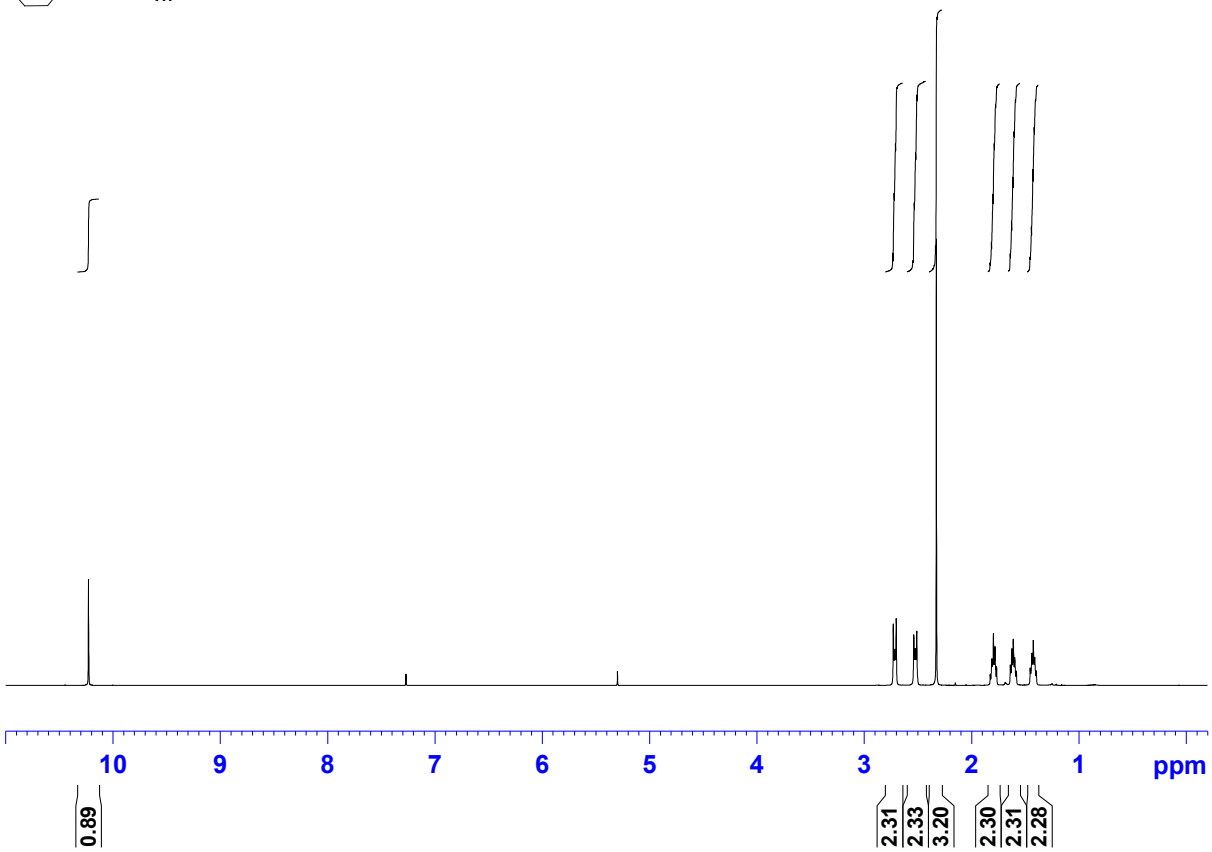
^{13}C NMR (101 MHz, $CDCl_3$)



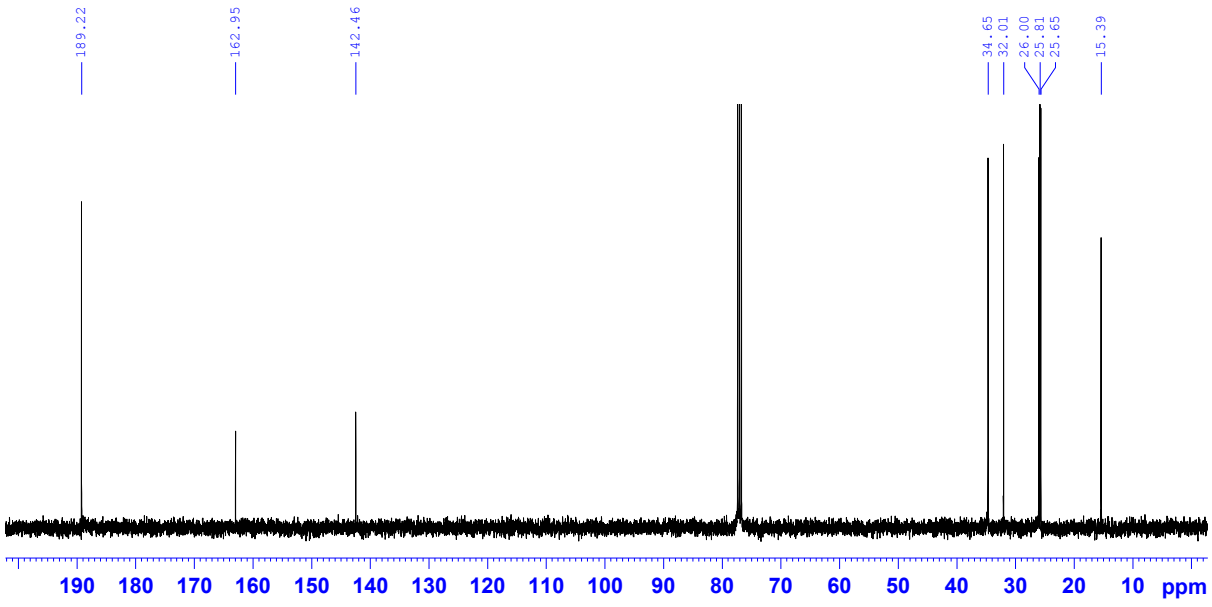
^{1}H NMR (400 MHz, $CDCl_3$)



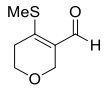
1h



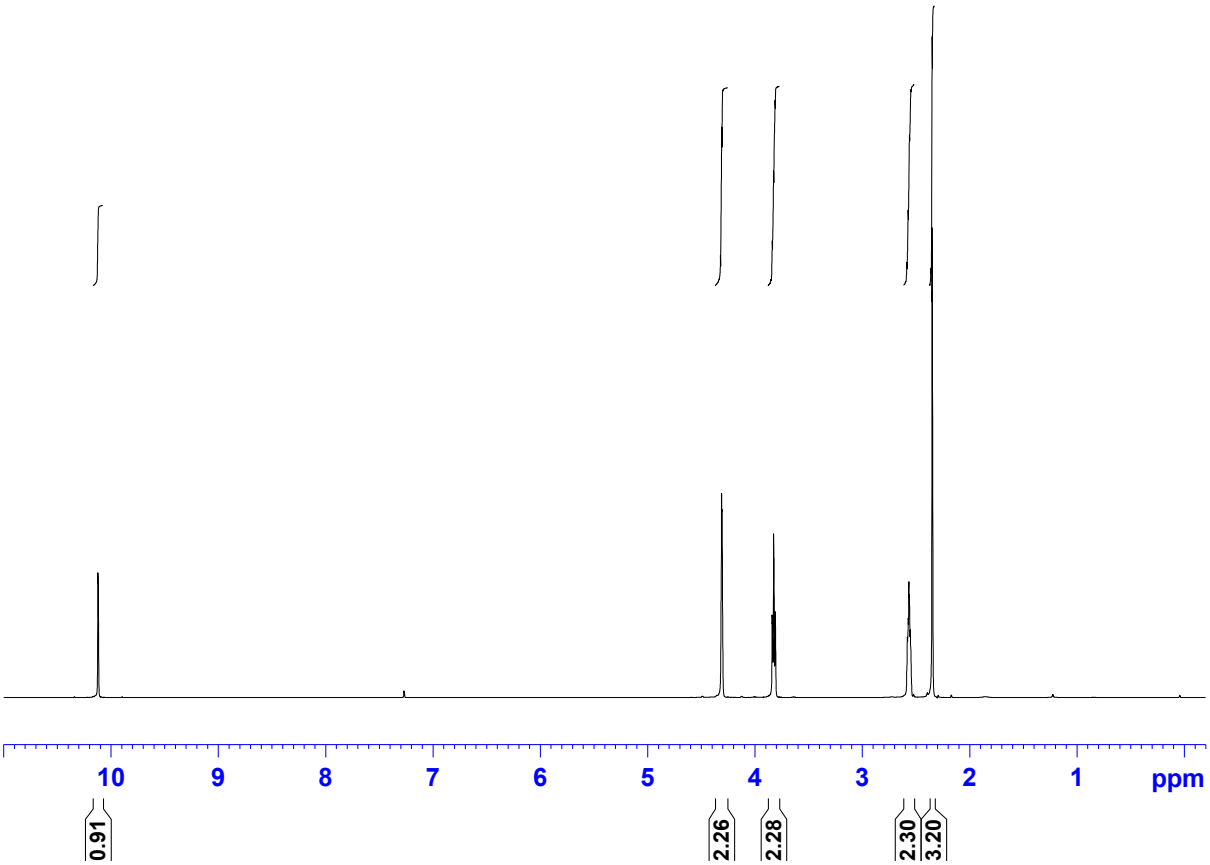
^{13}C NMR (101 MHz, $CDCl_3$)



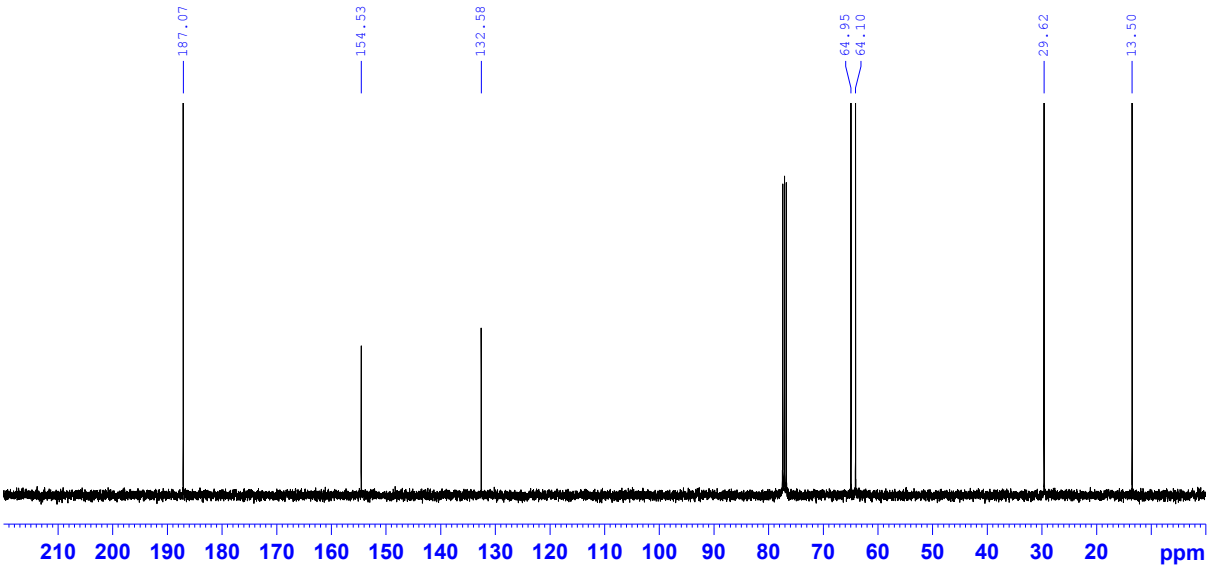
H NMR (400 MHz, $CDCl_3$)



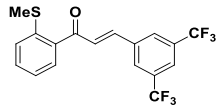
1i



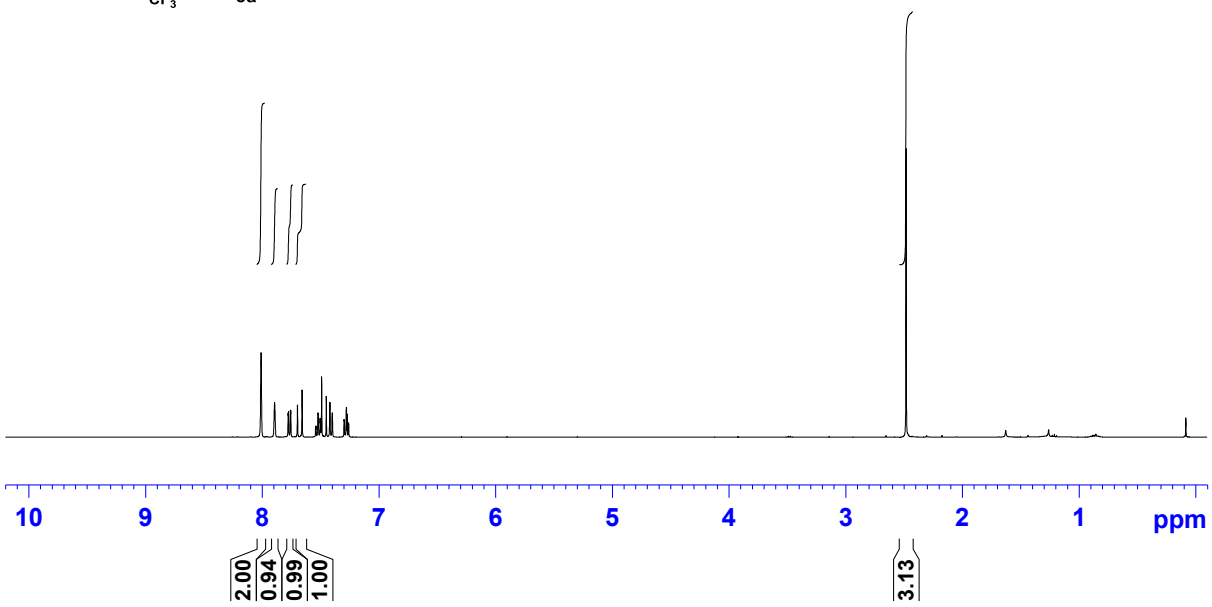
^{13}C NMR (101 MHz, $CDCl_3$)



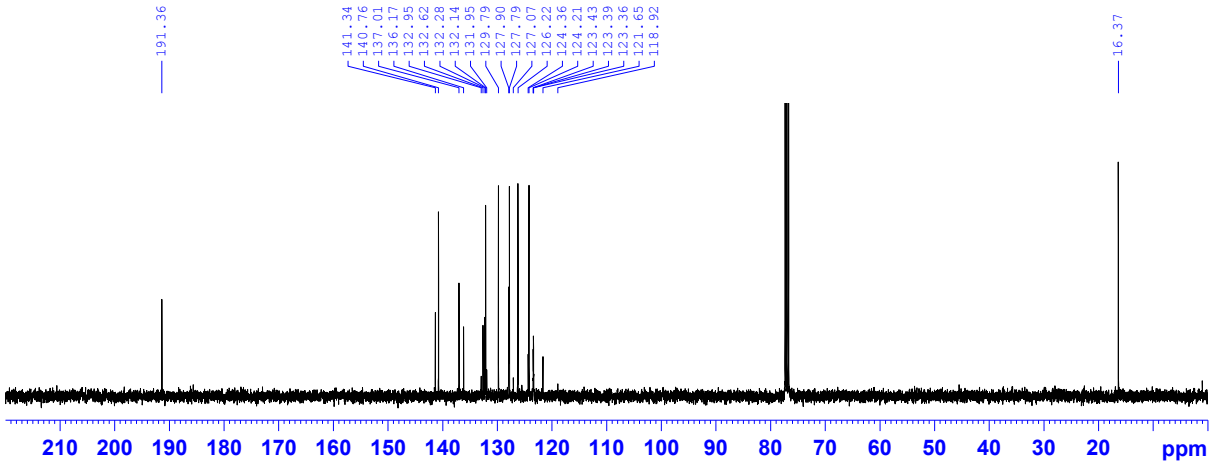
^{1}H NMR (400 MHz, $CDCl_3$)



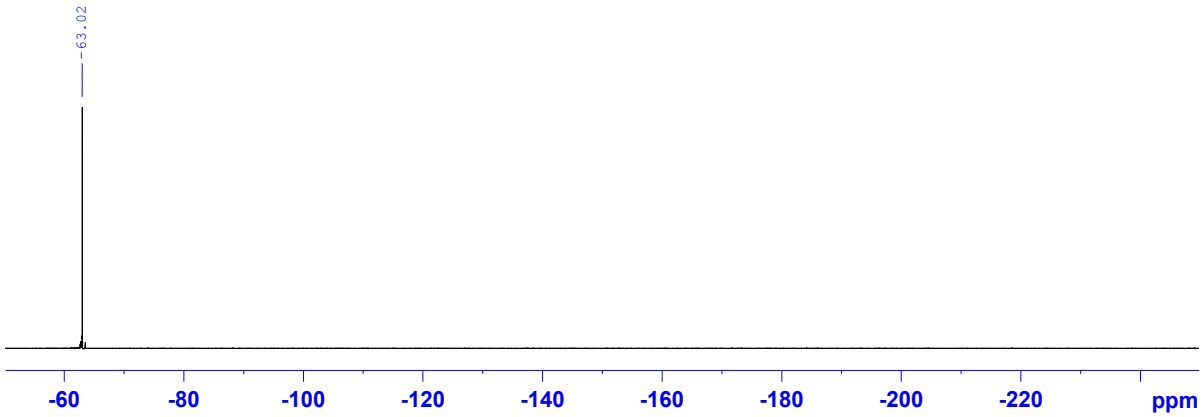
3a



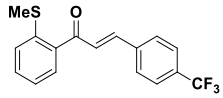
^{13}C NMR (101 MHz, $CDCl_3$)



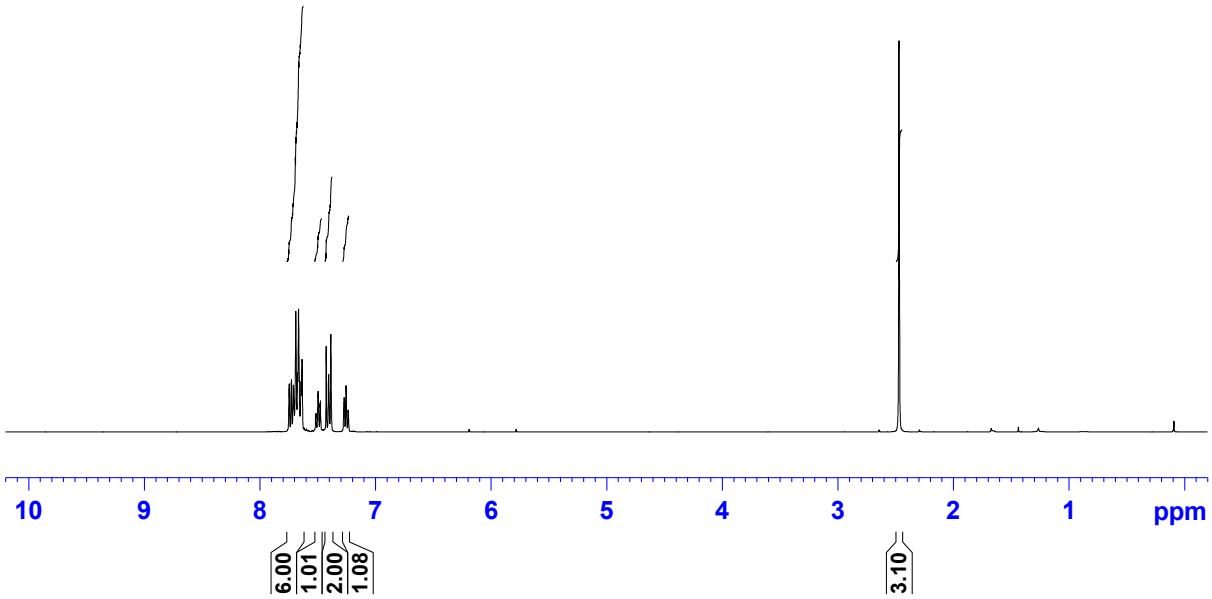
^{19}F NMR (376 MHz, $CDCl_3$)



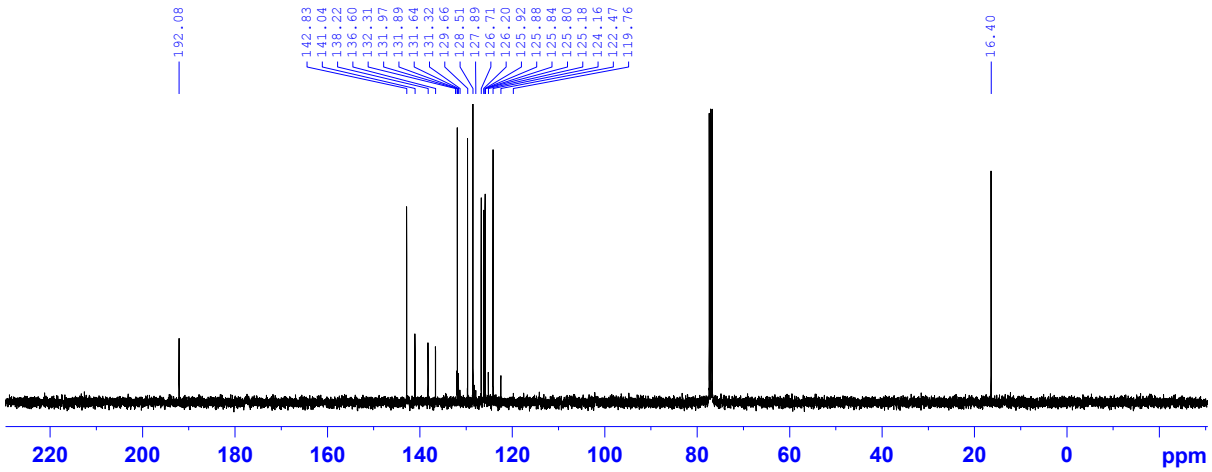
^{1}H NMR (400 MHz, $CDCl_3$)



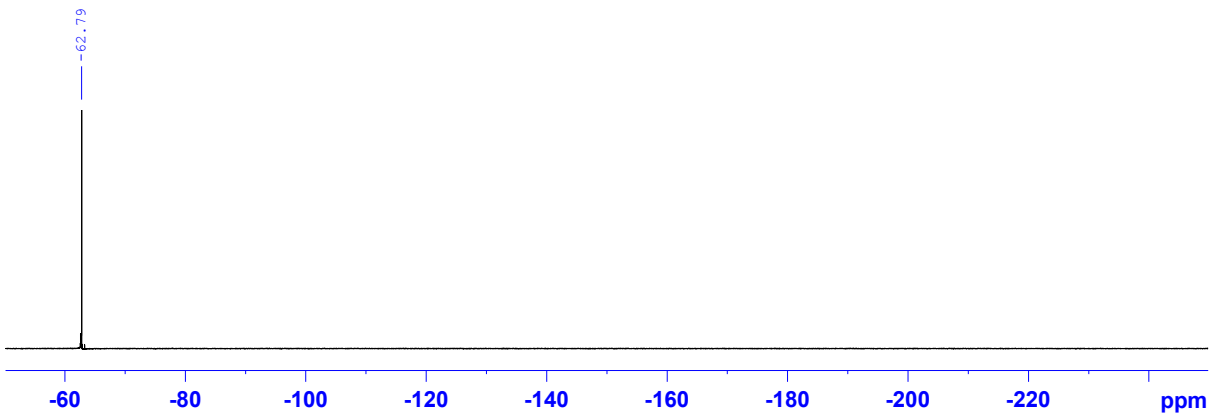
3b



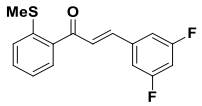
^{13}C NMR (101 MHz, $CDCl_3$)



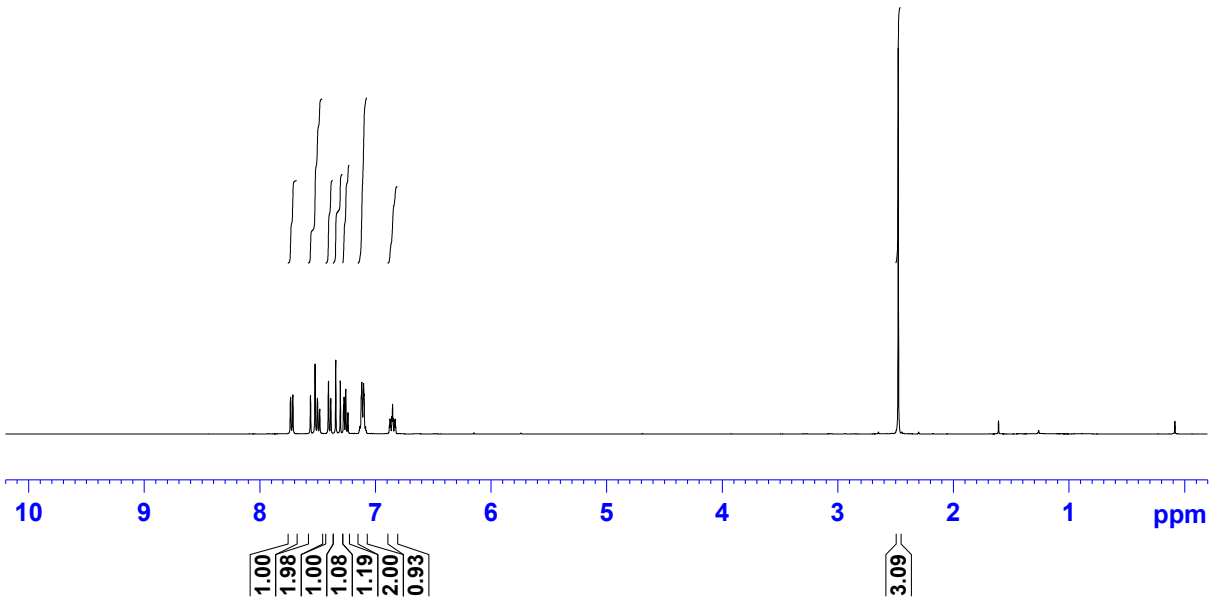
^{19}F NMR (376 MHz, $CDCl_3$)



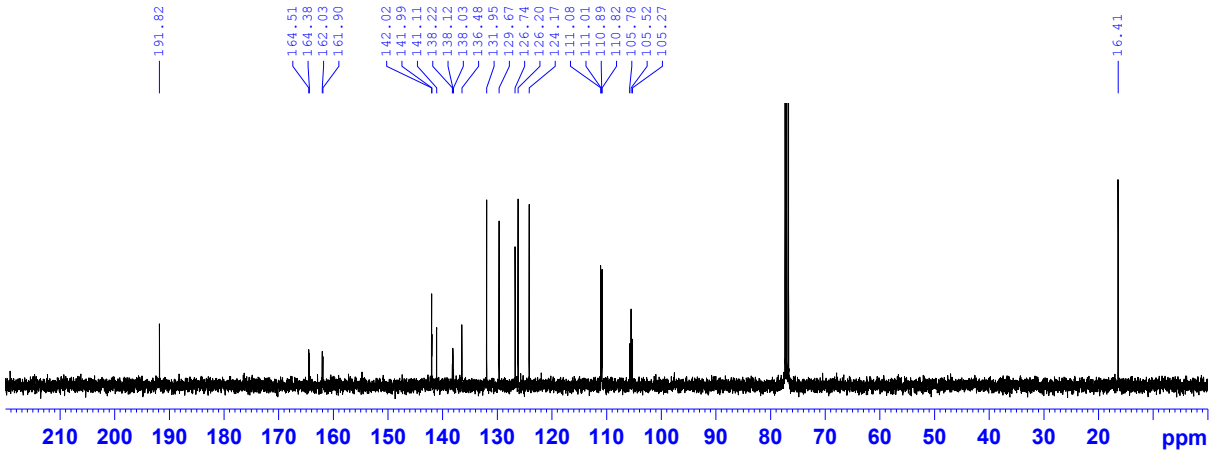
^{1}H NMR (400 MHz, $CDCl_3$)



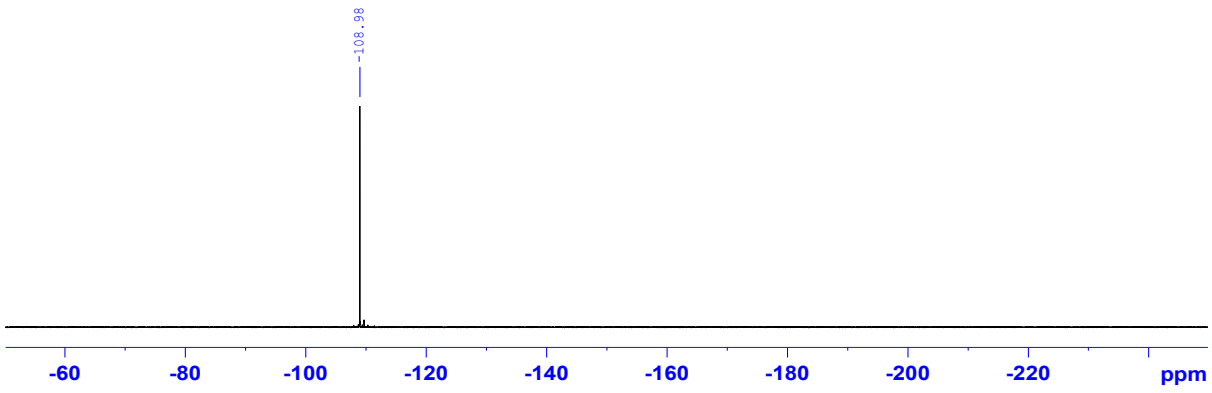
3c



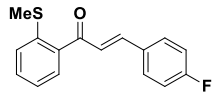
^{13}C NMR (101 MHz, $CDCl_3$)



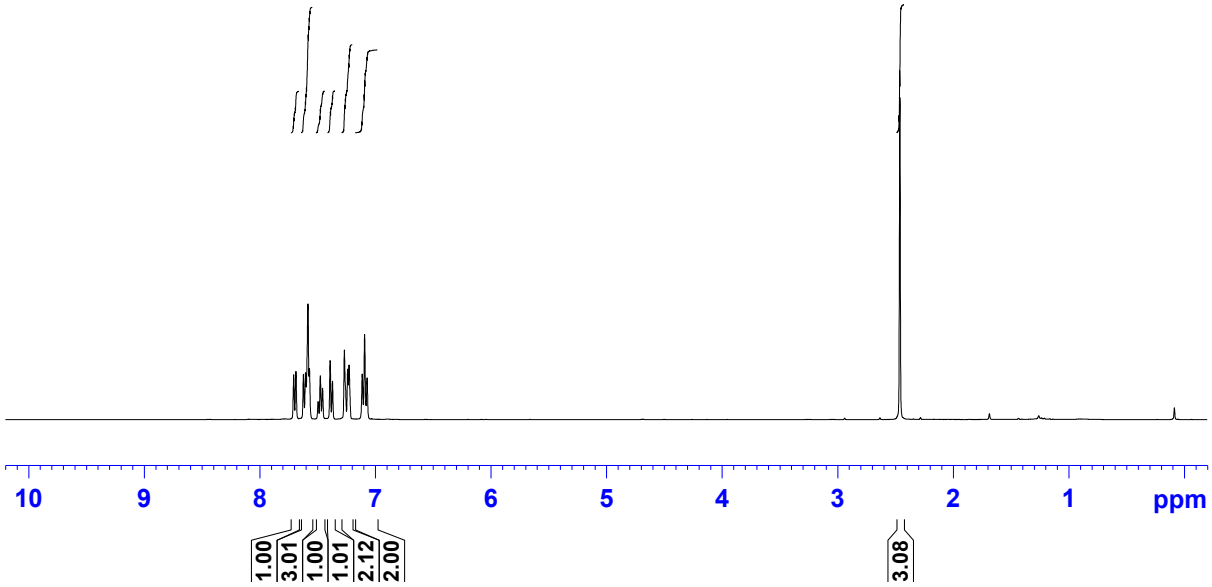
^{19}F NMR (376 MHz, $CDCl_3$)



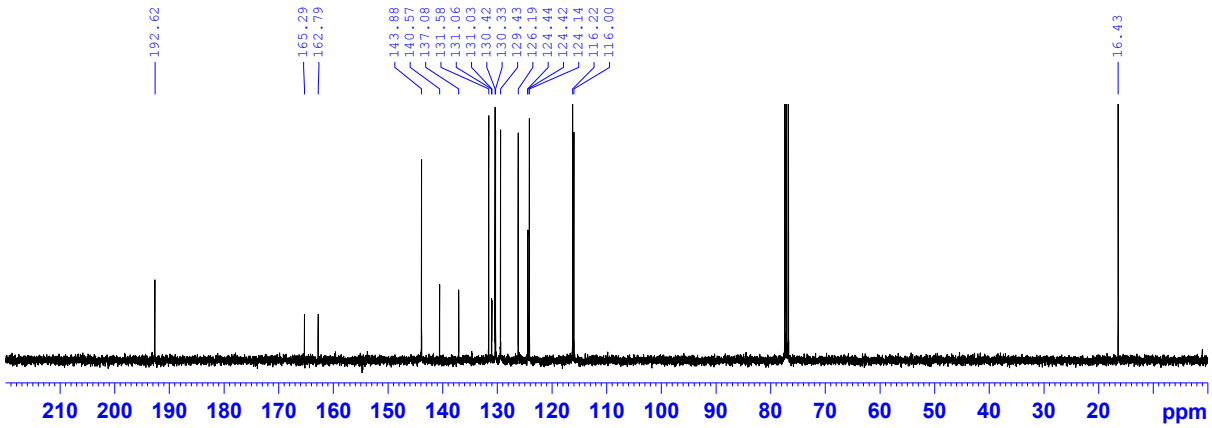
^{1}H NMR (400 MHz, $CDCl_3$)



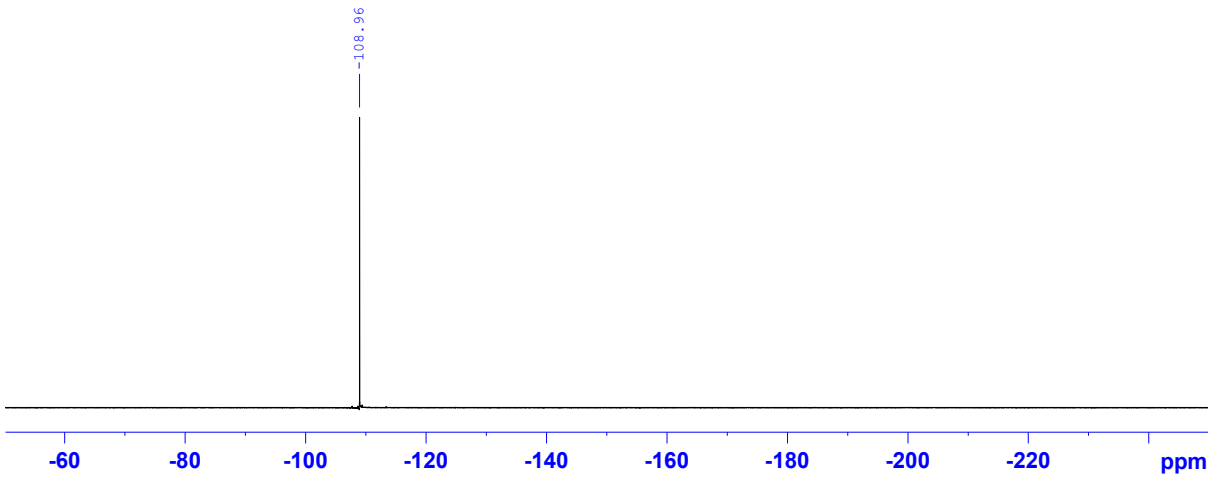
3d



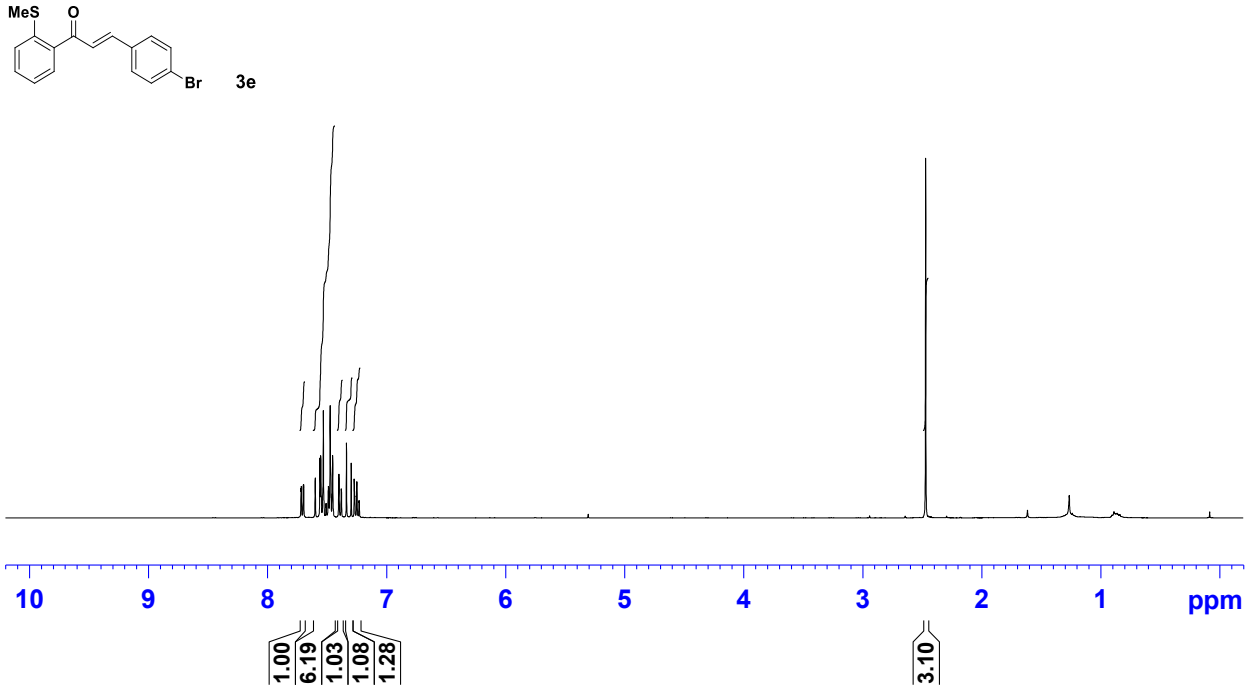
^{13}C NMR (101 MHz, $CDCl_3$)



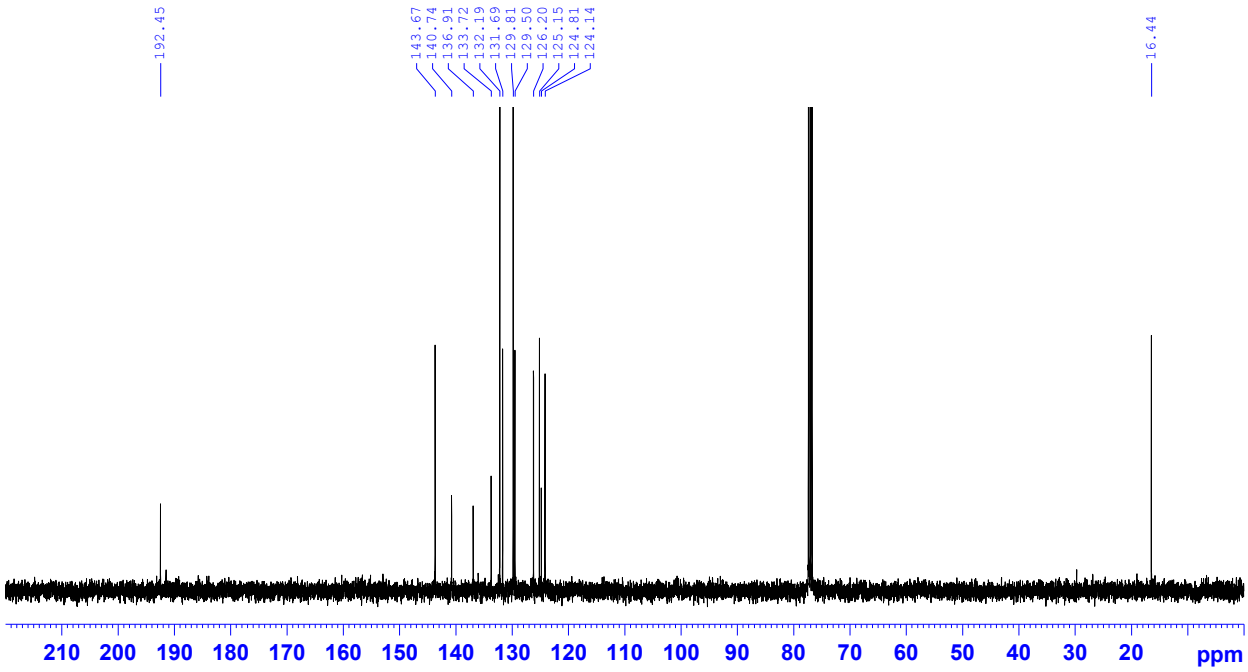
^{19}F NMR (377 MHz, $CDCl_3$)



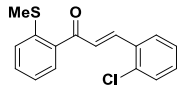
^{1}H NMR (400 MHz, $CDCl_3$)



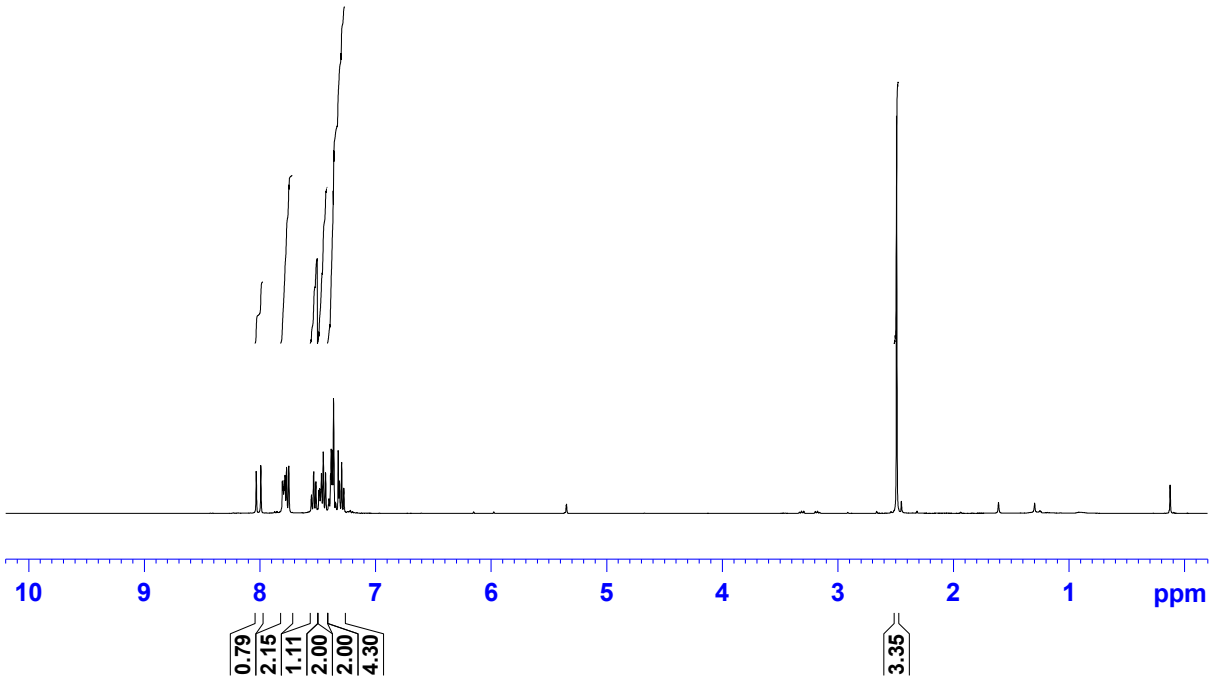
^{13}C NMR (101 MHz, $CDCl_3$)



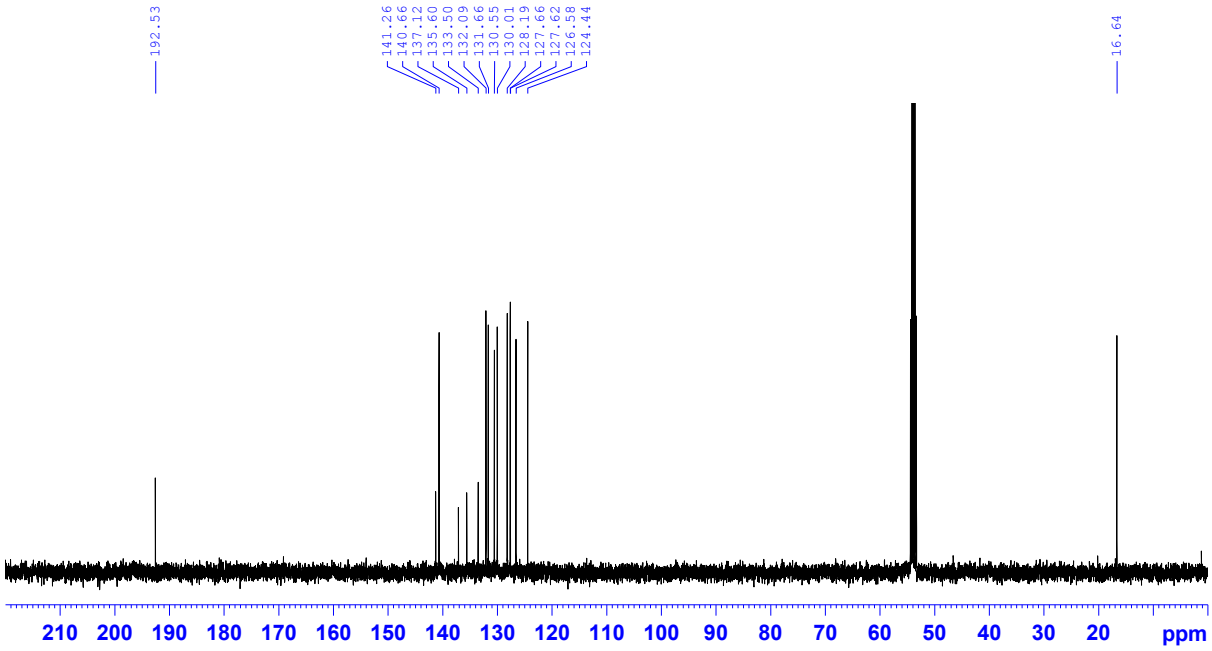
^{1}H NMR (400 MHz, CD_2Cl_2)



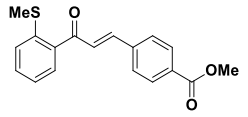
3f



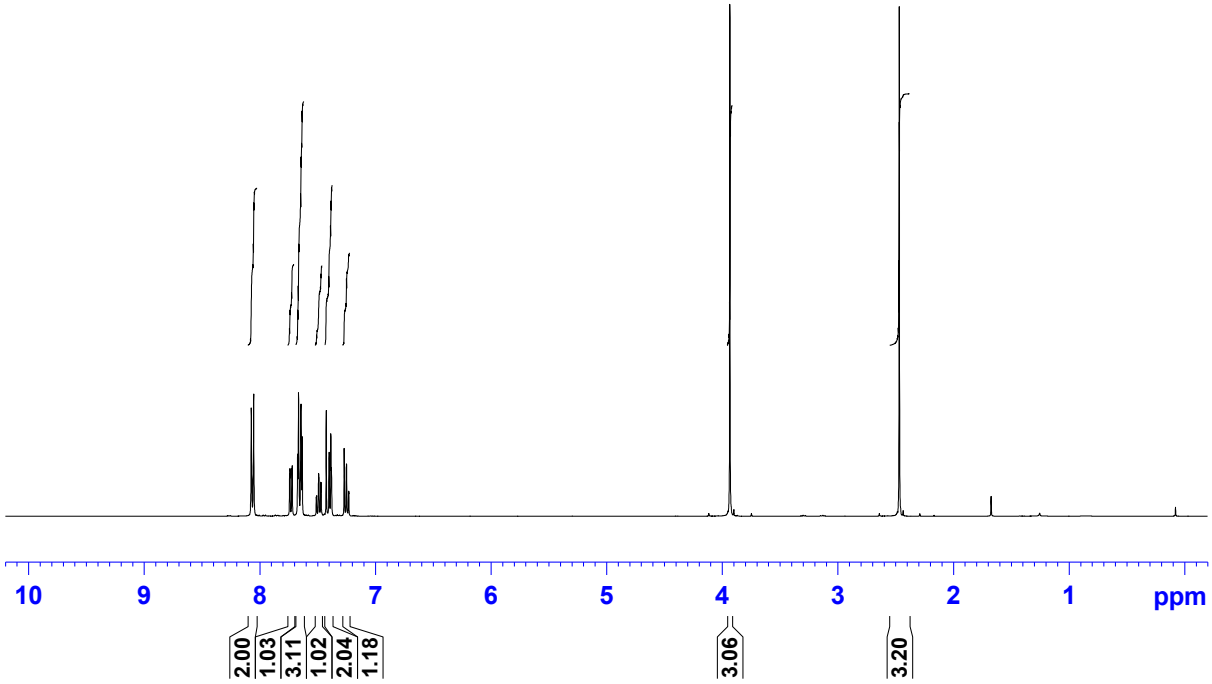
^{13}C NMR (101 MHz, CD_2Cl_2)



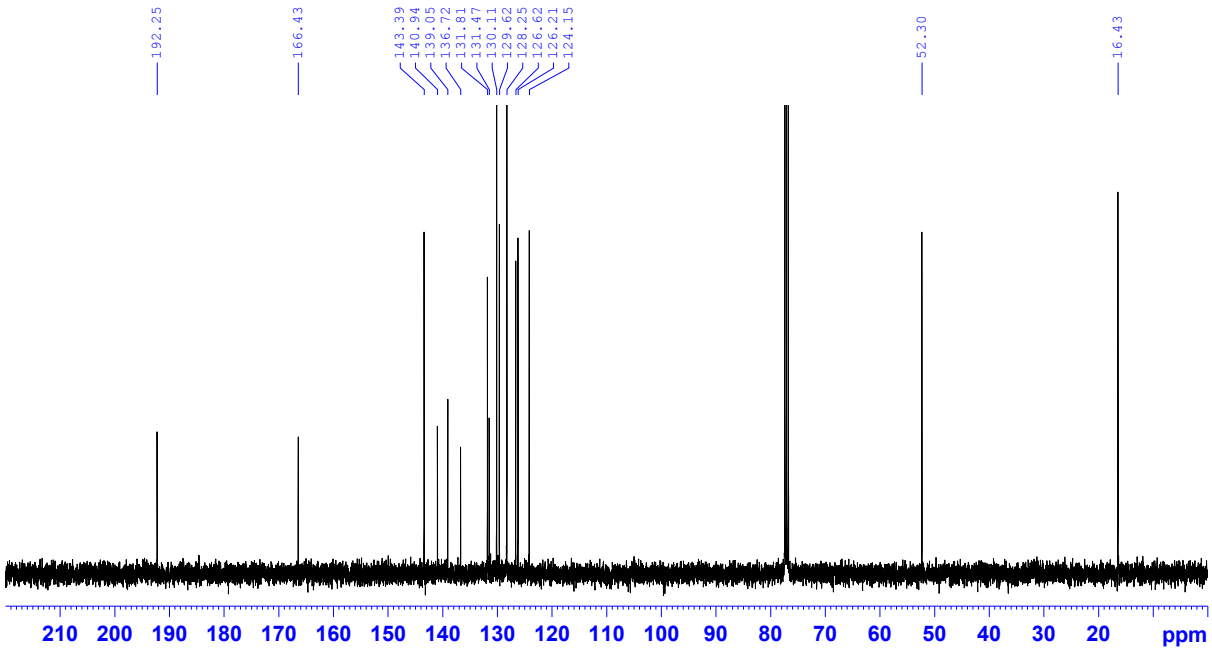
^{1}H NMR (400 MHz, $CDCl_3$)



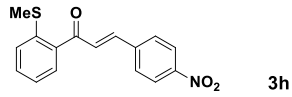
3g



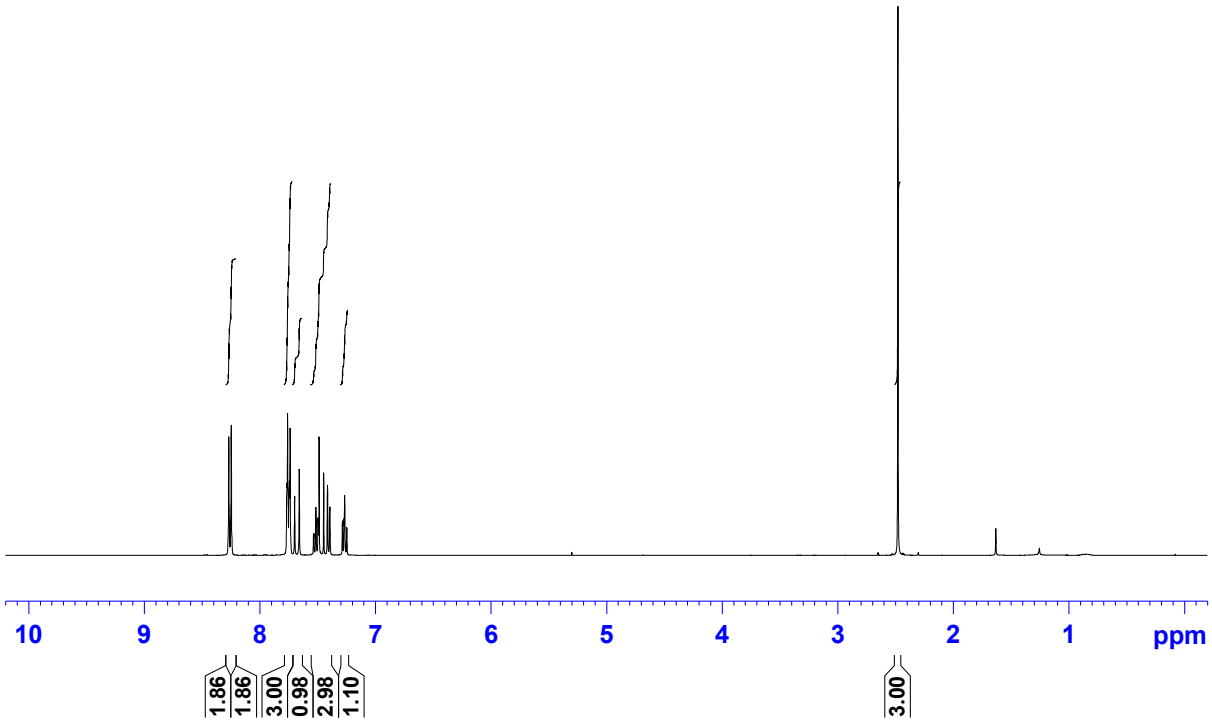
^{13}C NMR (101 MHz, $CDCl_3$)



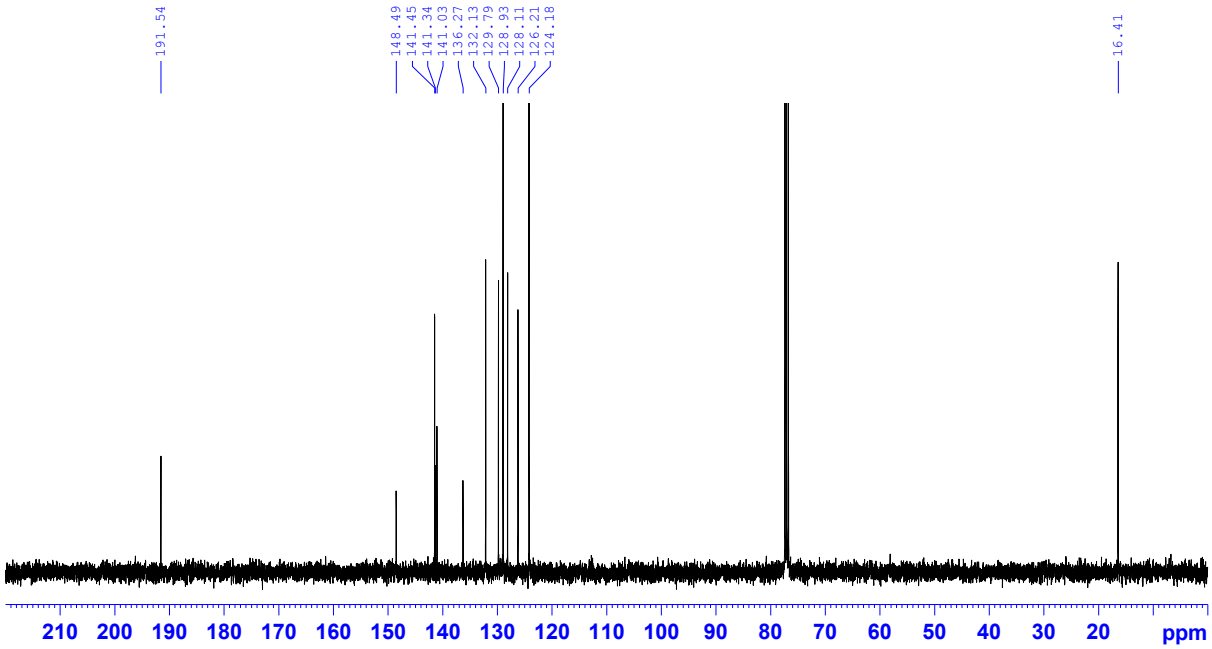
^{1}H NMR (400 MHz, $CDCl_3$)



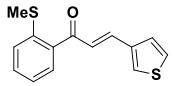
3h



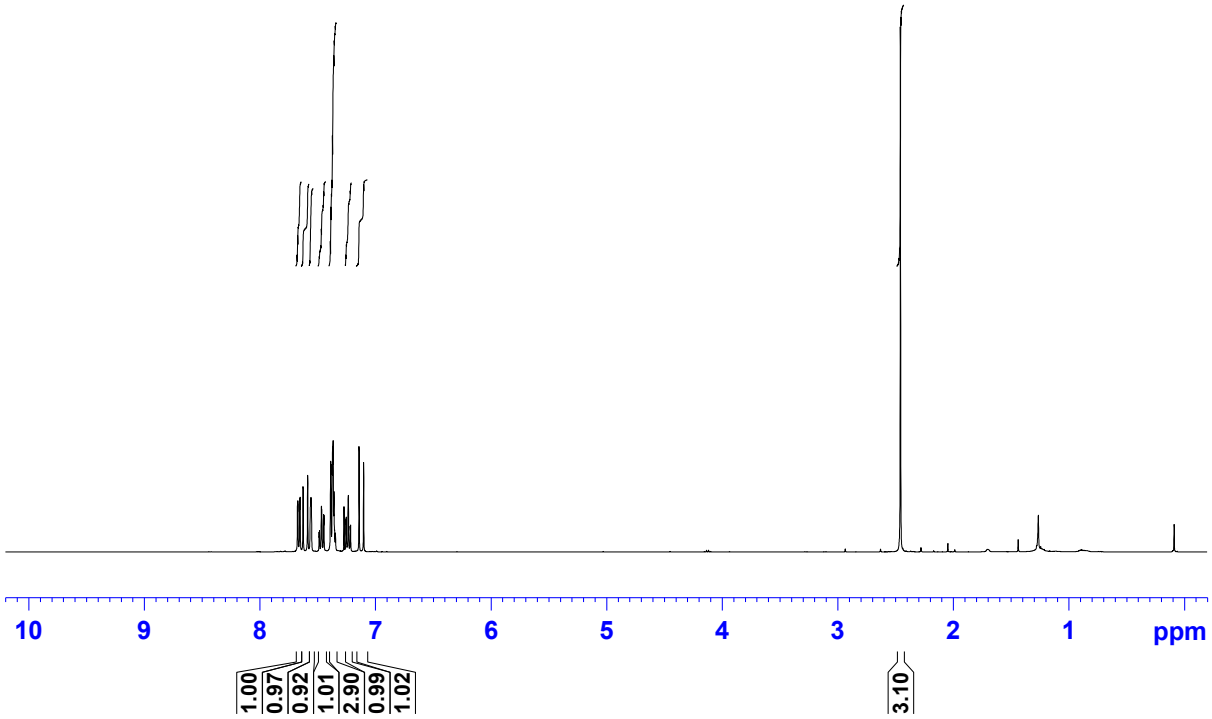
^{13}C NMR (101 MHz, $CDCl_3$)



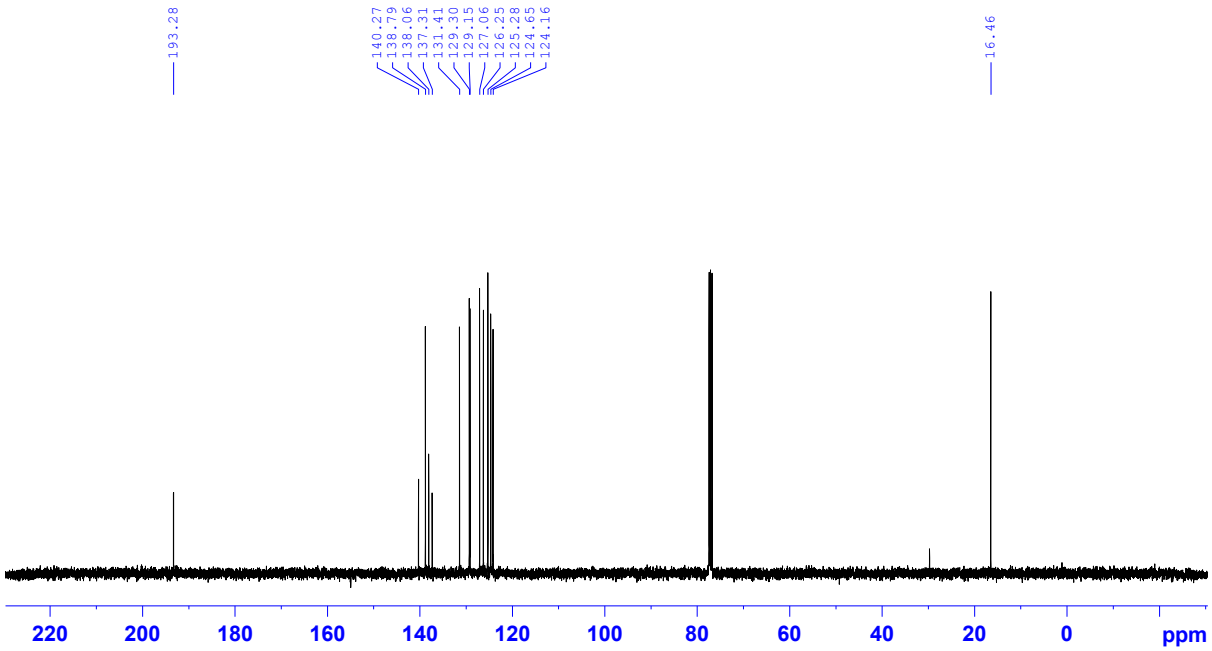
^{1}H NMR (400 MHz, $CDCl_3$)



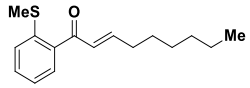
3i



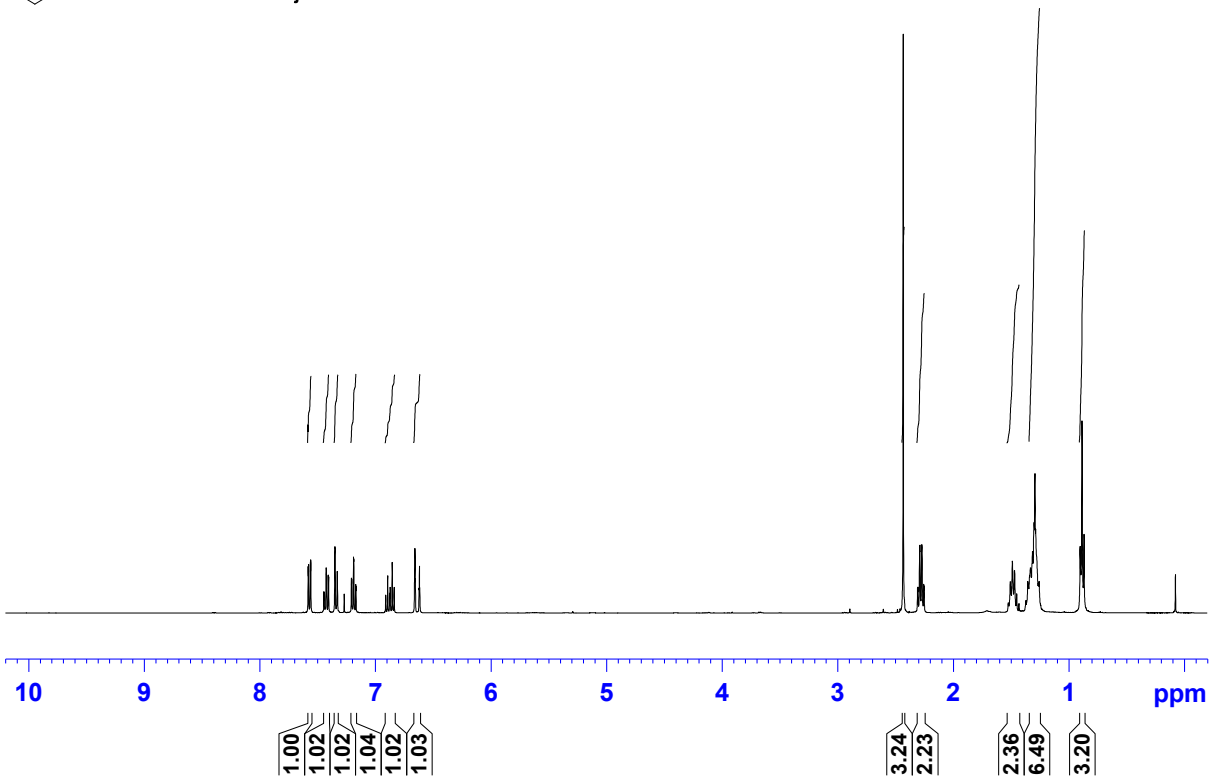
^{13}C NMR (101 MHz, $CDCl_3$)



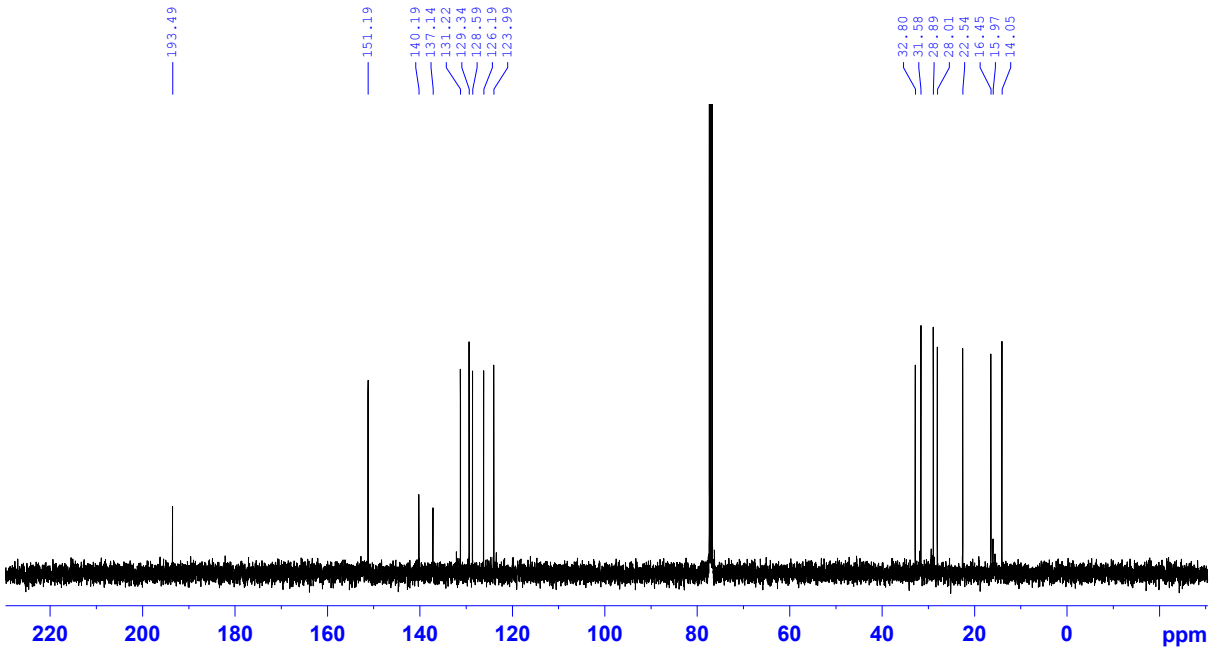
^{1}H NMR (400 MHz, $CDCl_3$)



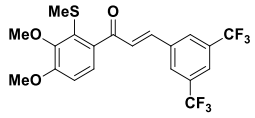
3j



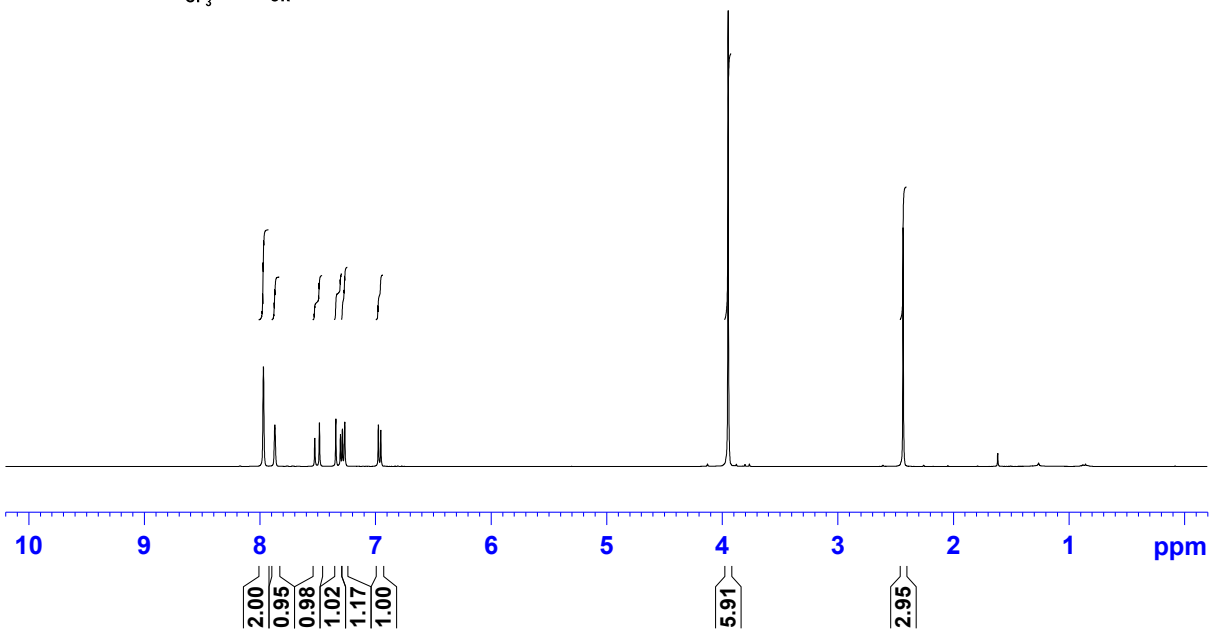
^{13}C NMR (101 MHz, $CDCl_3$)



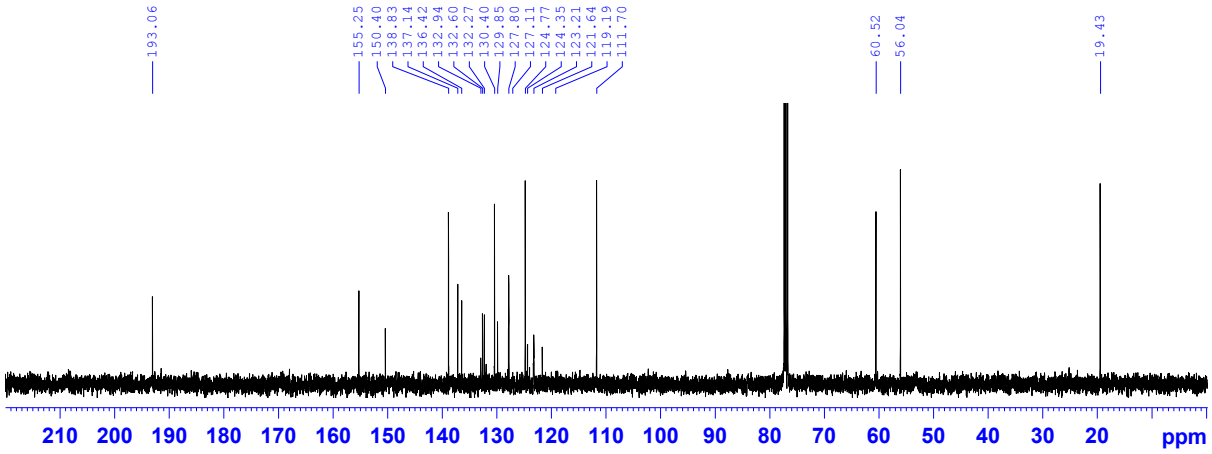
^{1}H NMR (400 MHz, $CDCl_3$)



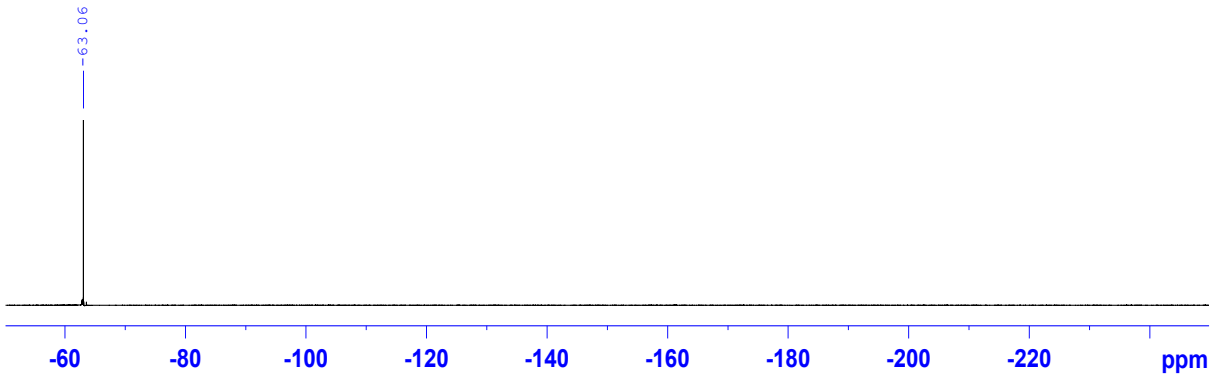
3k



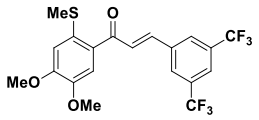
^{13}C NMR (101 MHz, $CDCl_3$)



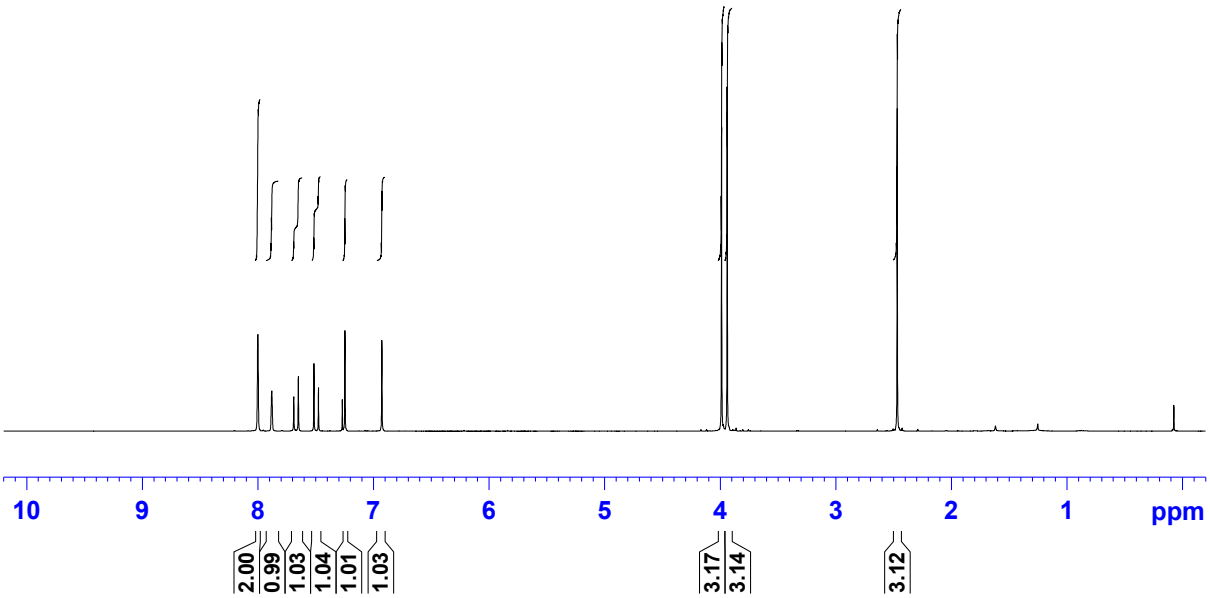
^{19}F NMR (376 MHz, $CDCl_3$



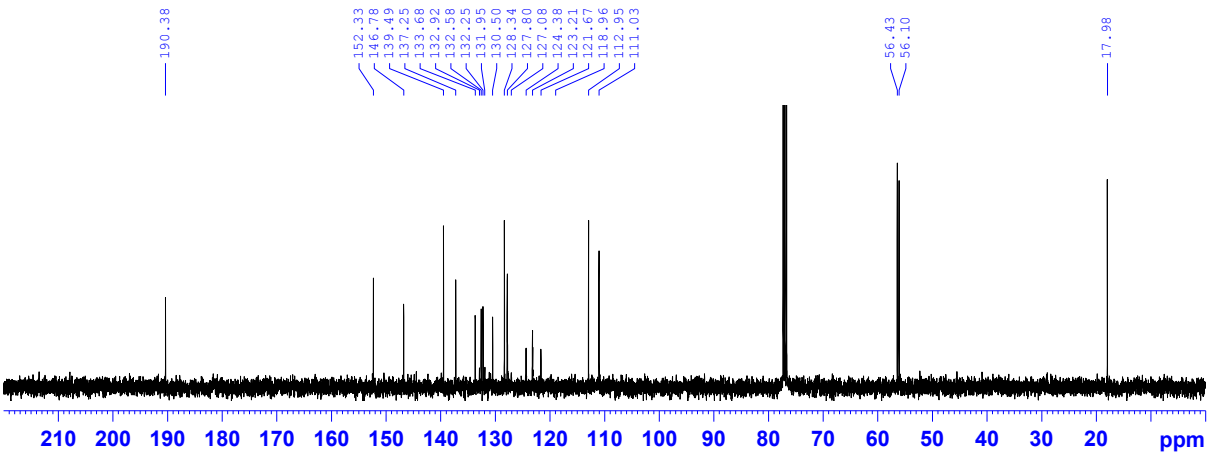
^{1}H NMR (400 MHz, $CDCl_3$)



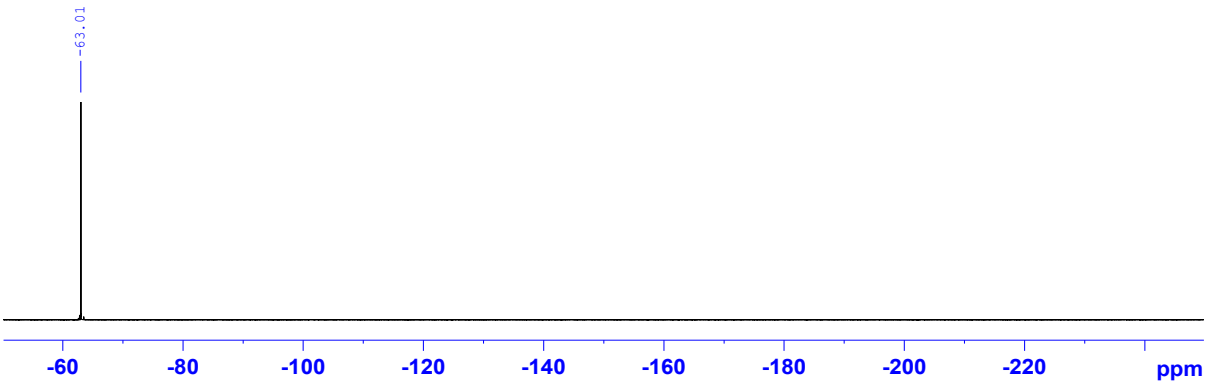
3l



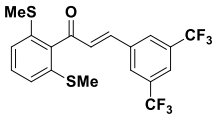
^{13}C NMR (101 MHz, $CDCl_3$)



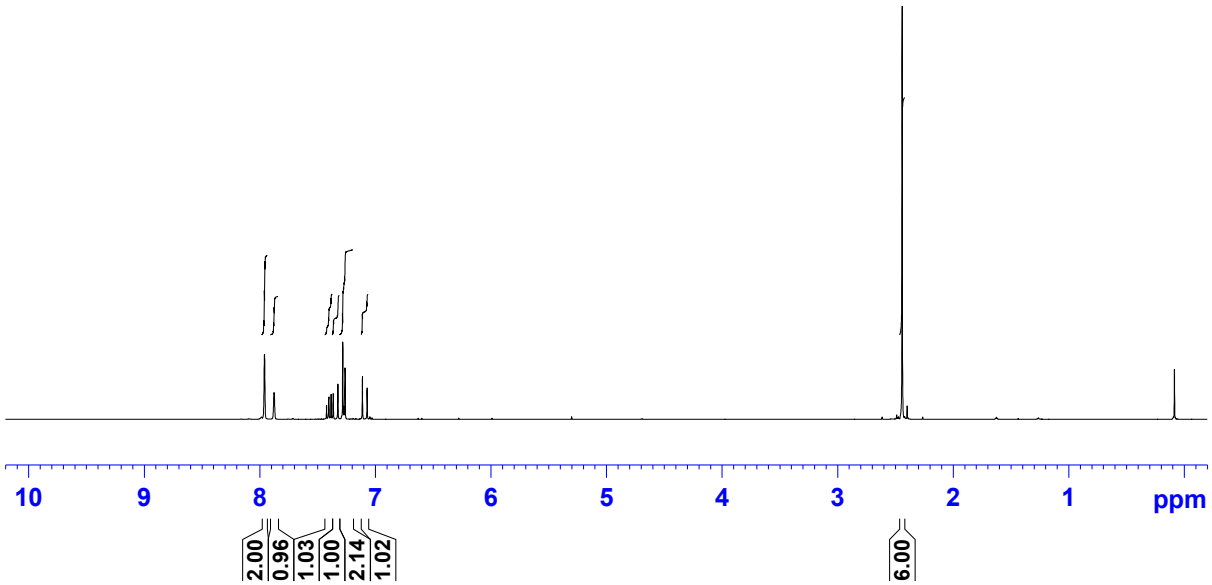
^{19}F NMR (376 MHz, $CDCl_3$)



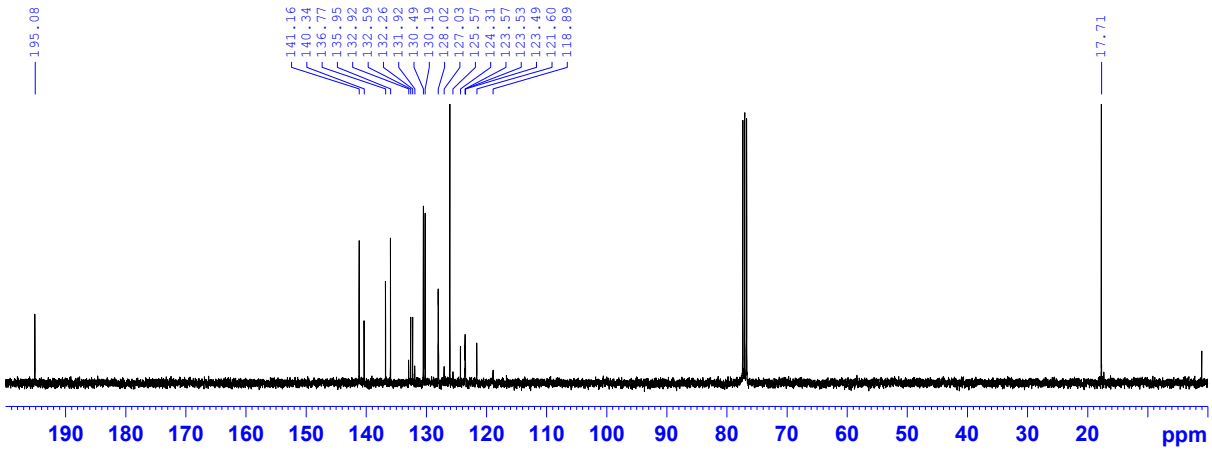
^{1}H NMR (400 MHz, $CDCl_3$)



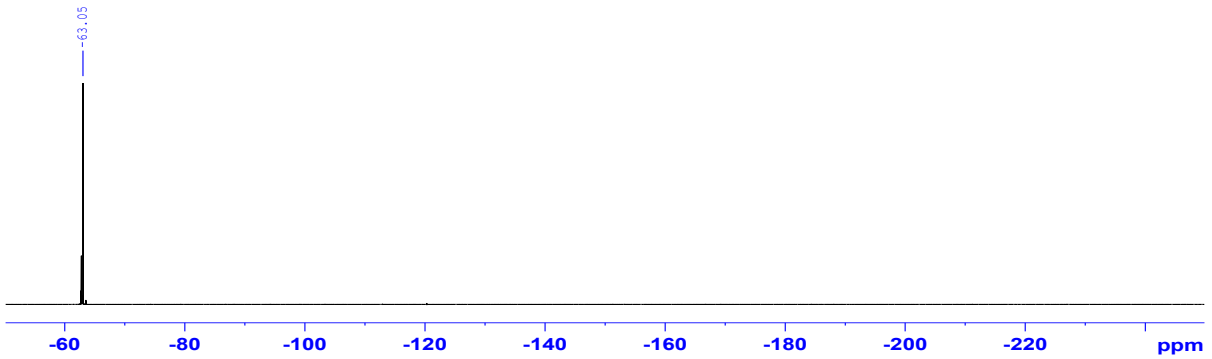
3m



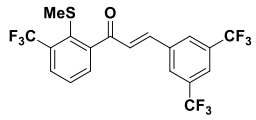
^{13}C NMR (101 MHz, $CDCl_3$)



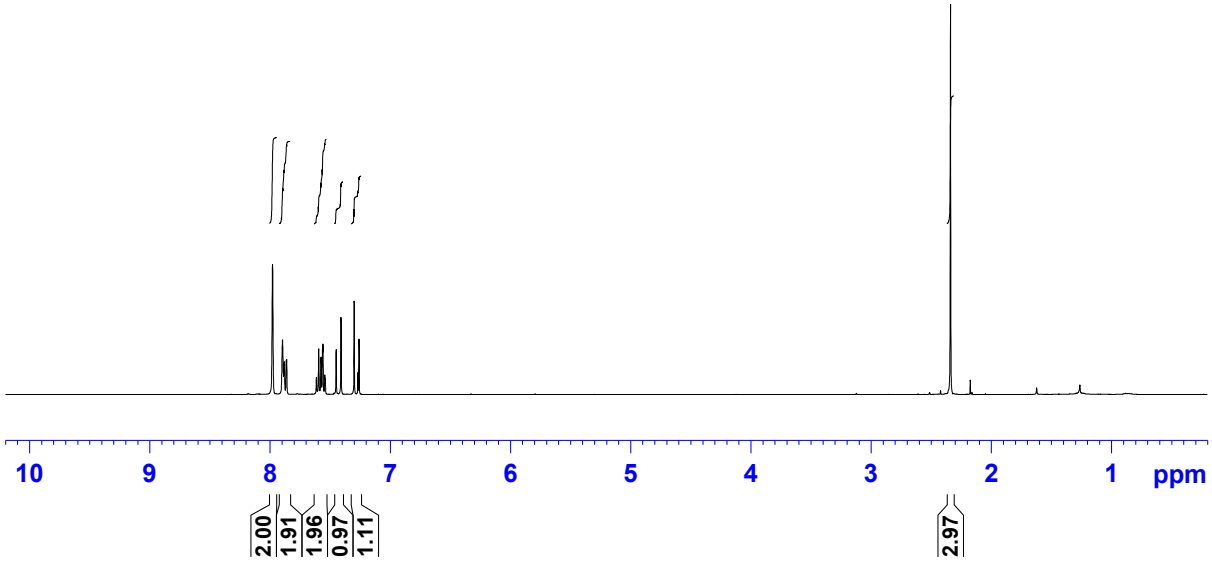
^{19}F NMR (376 MHz, $CDCl_3$)



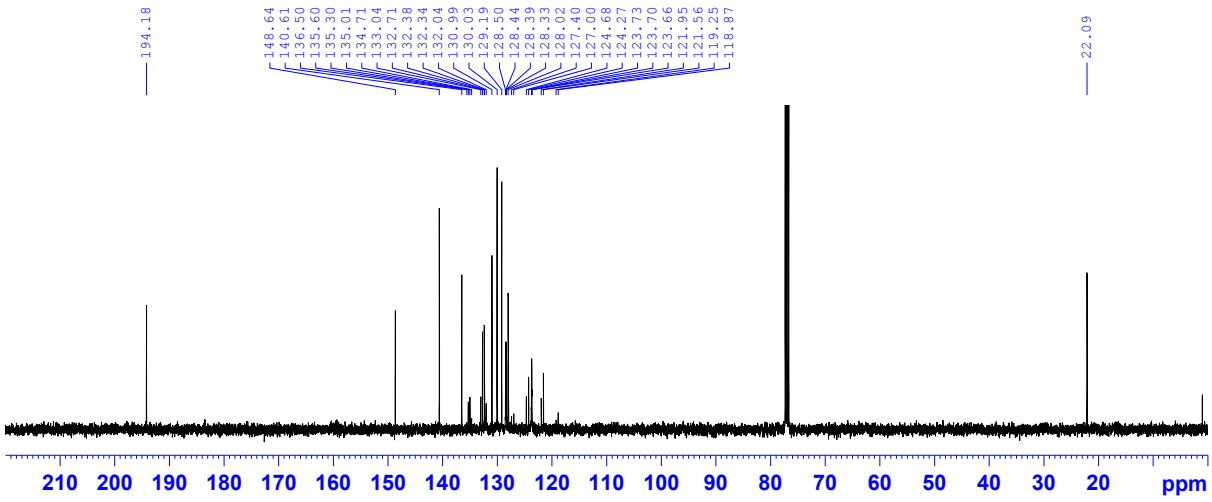
^{1}H NMR (400 MHz, $CDCl_3$)



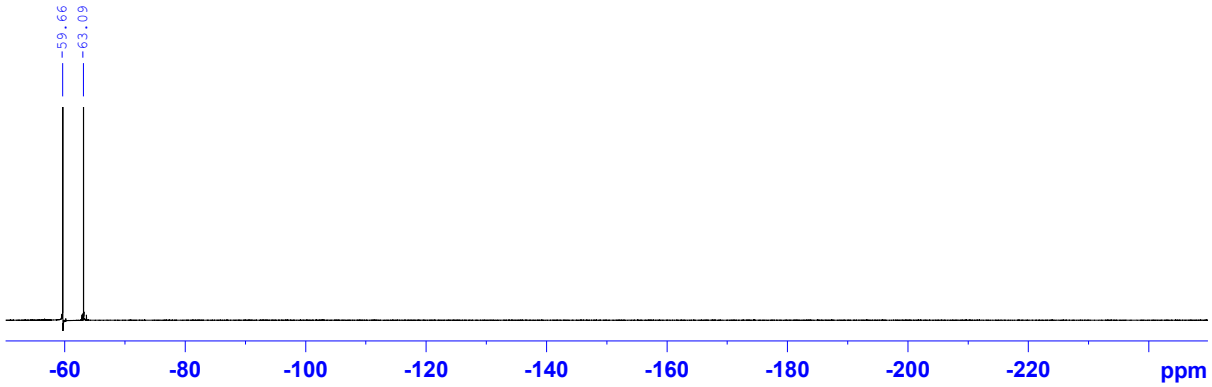
3n



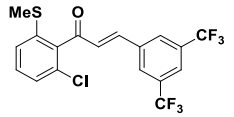
^{13}C NMR (101 MHz, $CDCl_3$)



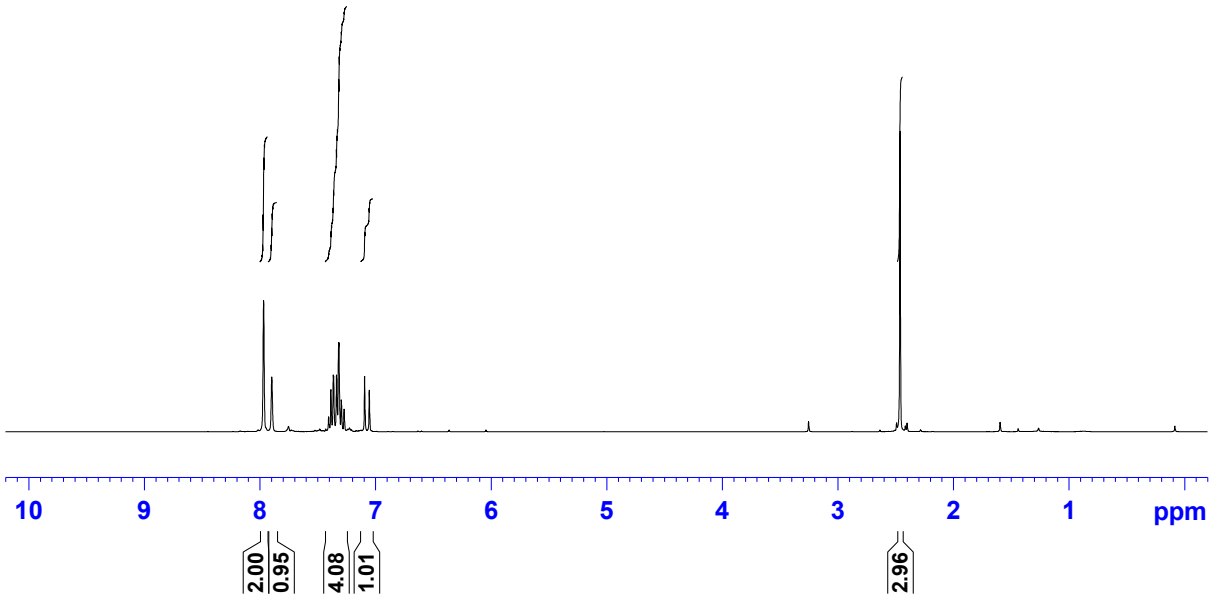
^{19}F NMR (376 MHz, $CDCl_3$)



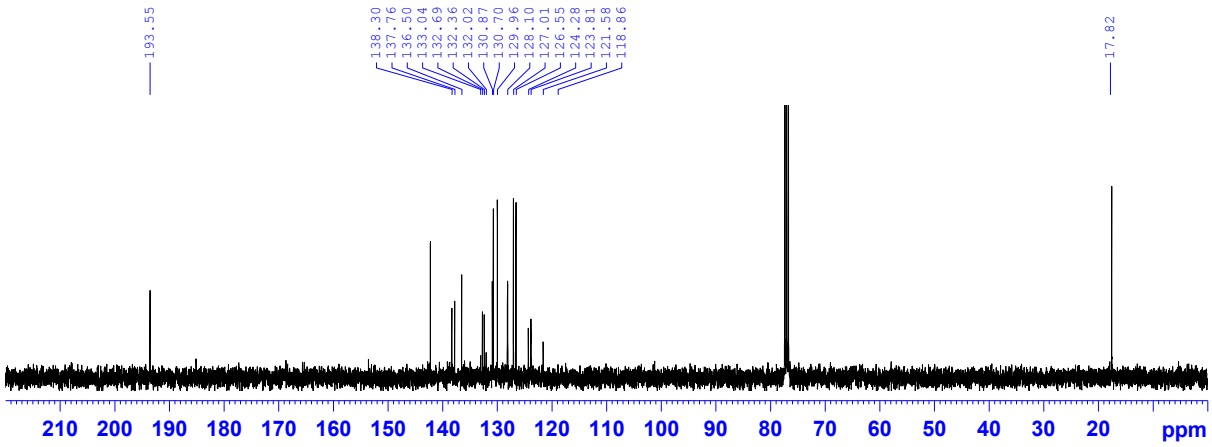
^{1}H NMR (400 MHz, $CDCl_3$)



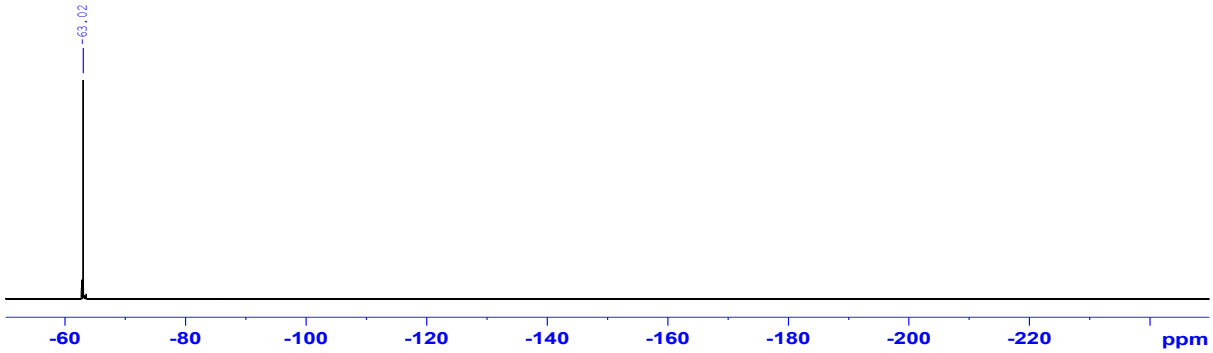
3o



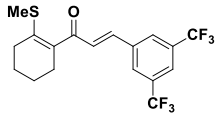
^{13}C NMR (101 MHz, $CDCl_3$)



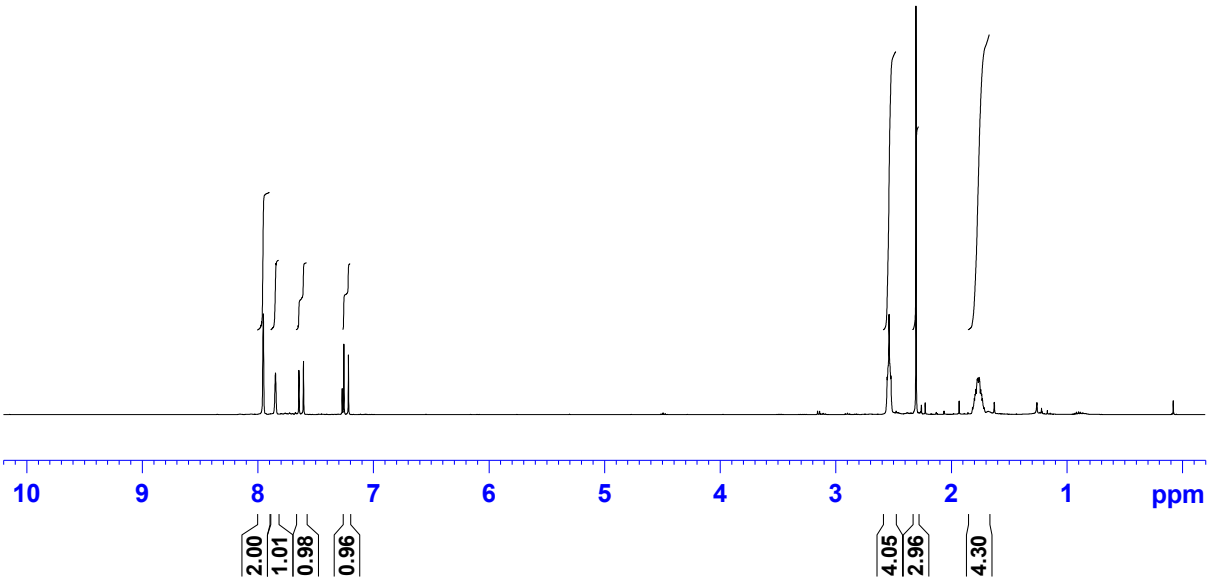
^{19}F NMR (376 MHz, $CDCl_3$)



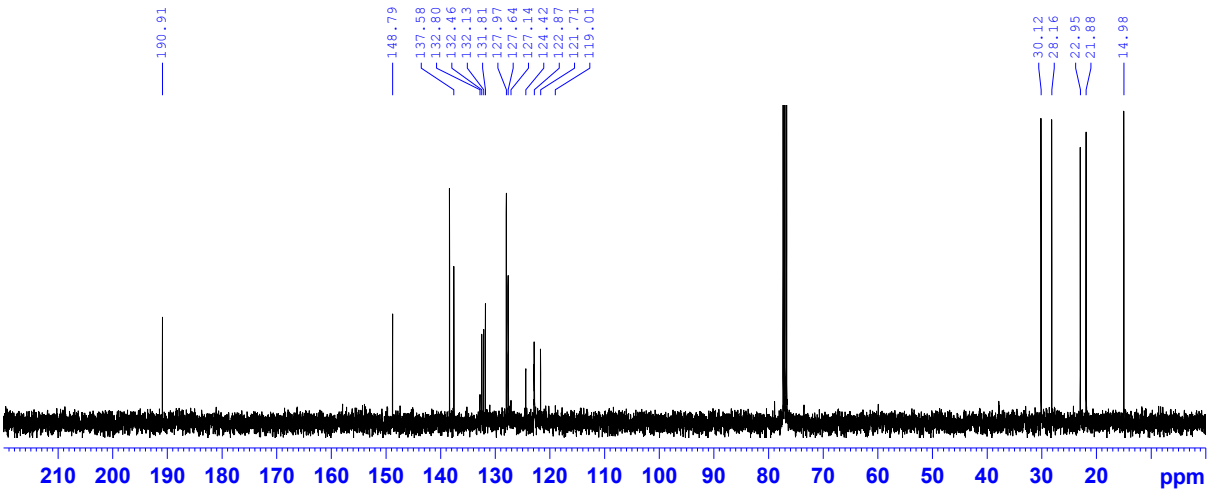
^{1}H NMR (400 MHz, $CDCl_3$)



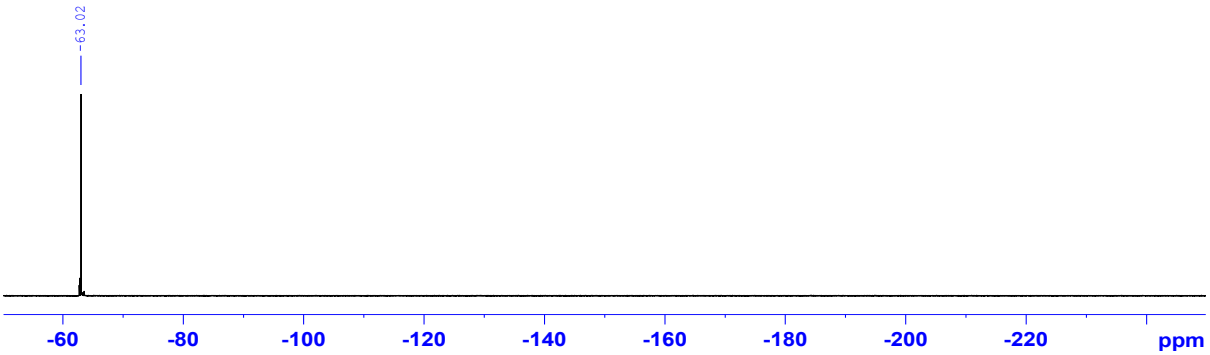
3p



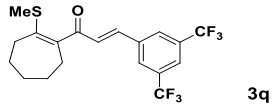
^{13}C NMR (101 MHz, $CDCl_3$)



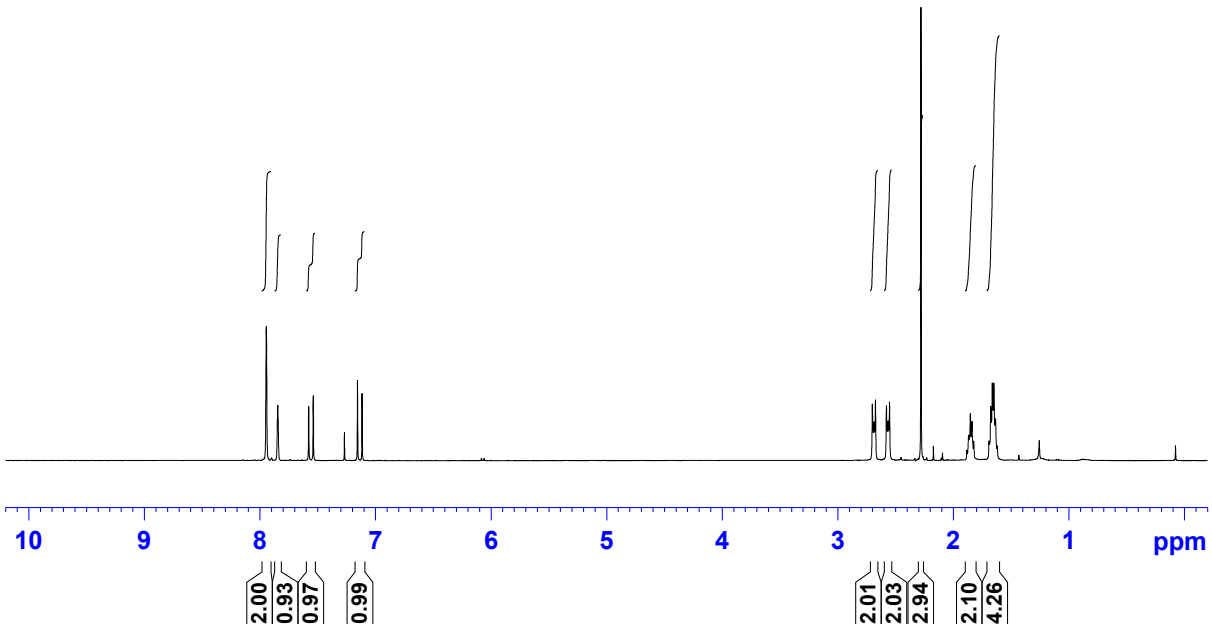
^{19}F NMR (376 MHz, $CDCl_3$)



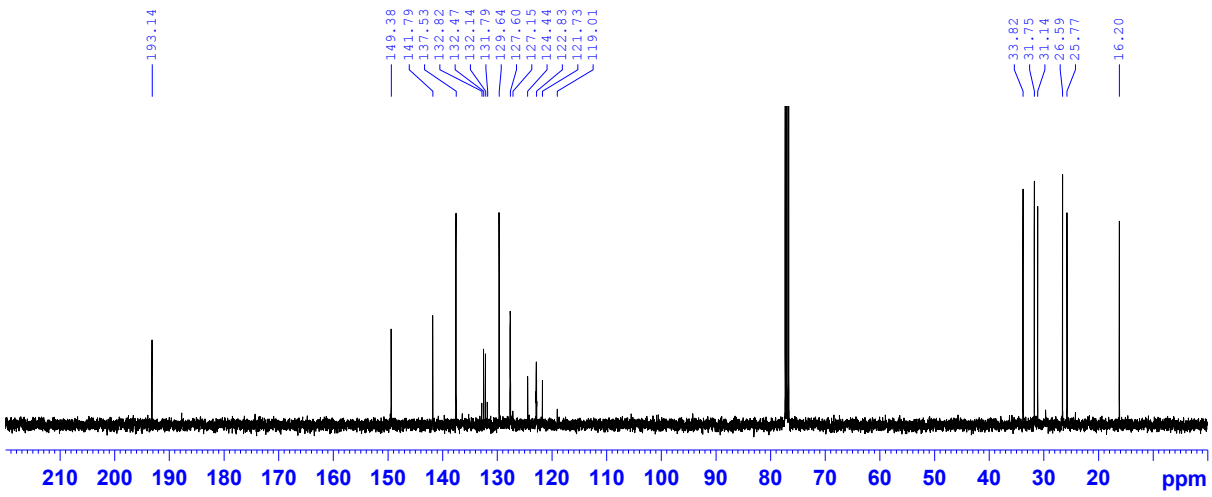
^{1}H NMR (400 MHz, $CDCl_3$)



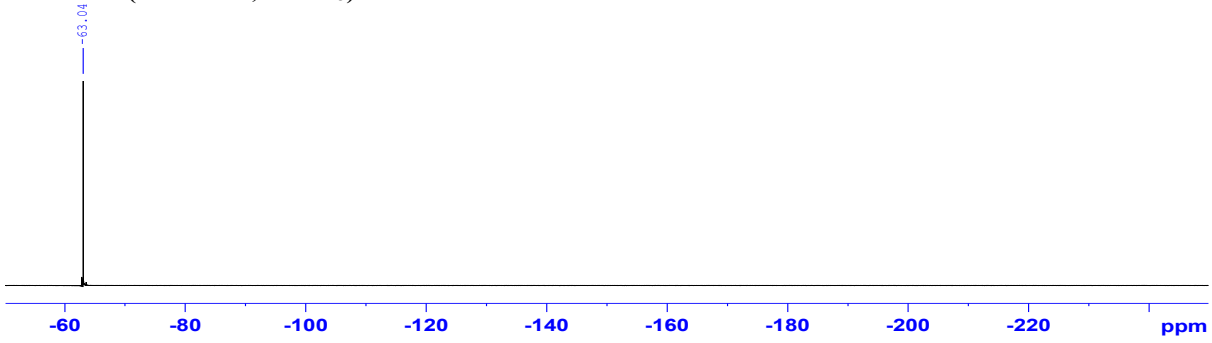
3q



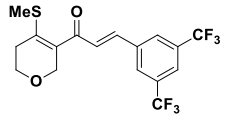
^{13}C NMR (101 MHz, $CDCl_3$)



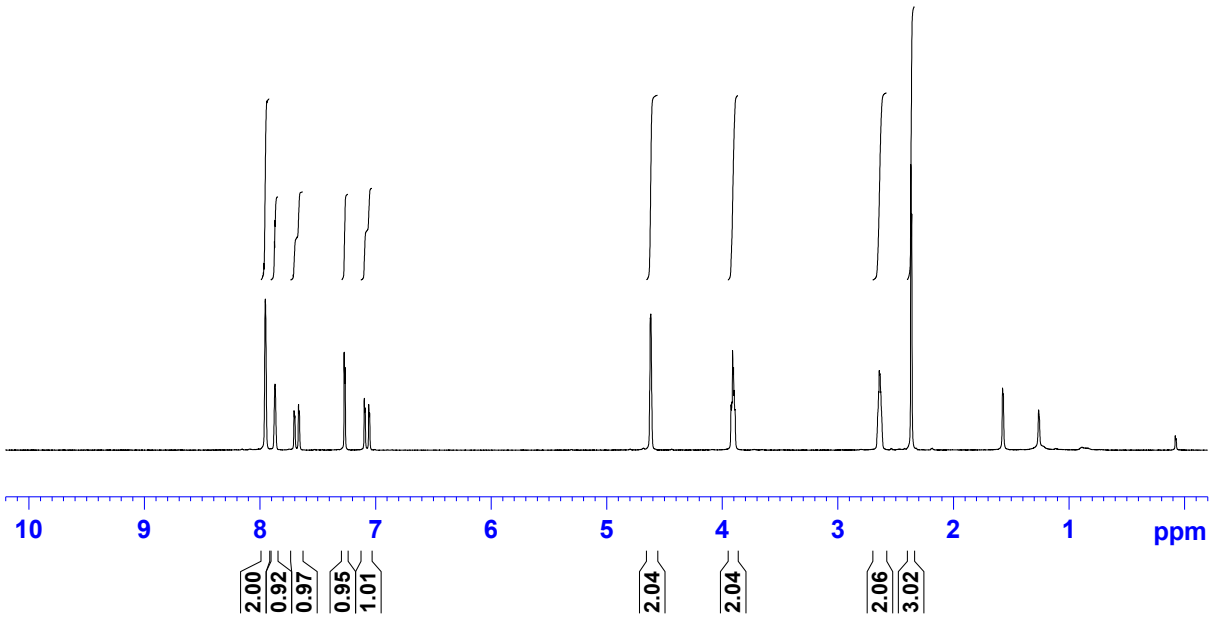
^{19}F NMR (376 MHz, $CDCl_3$)



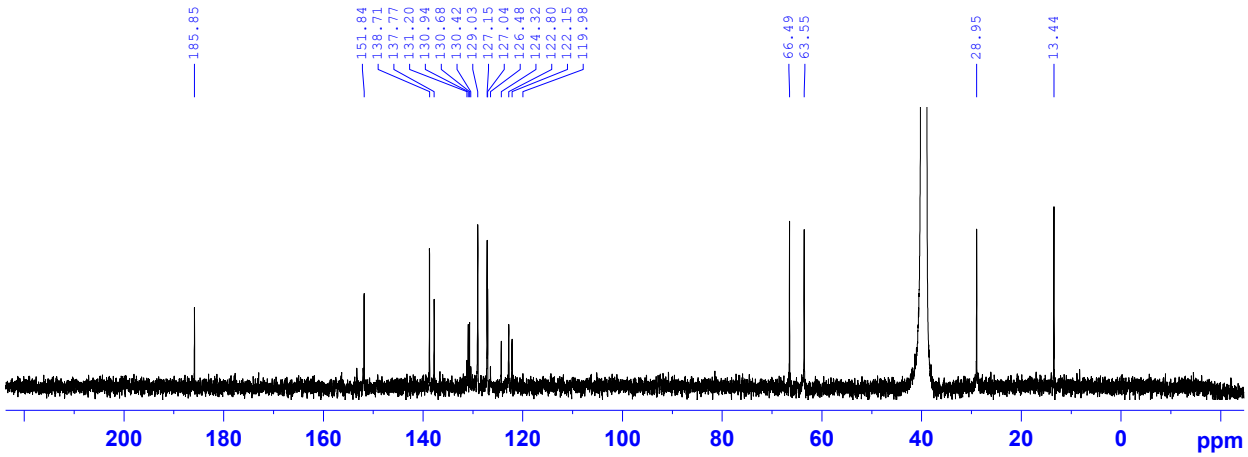
^{1}H NMR (400 MHz, $CDCl_3$)



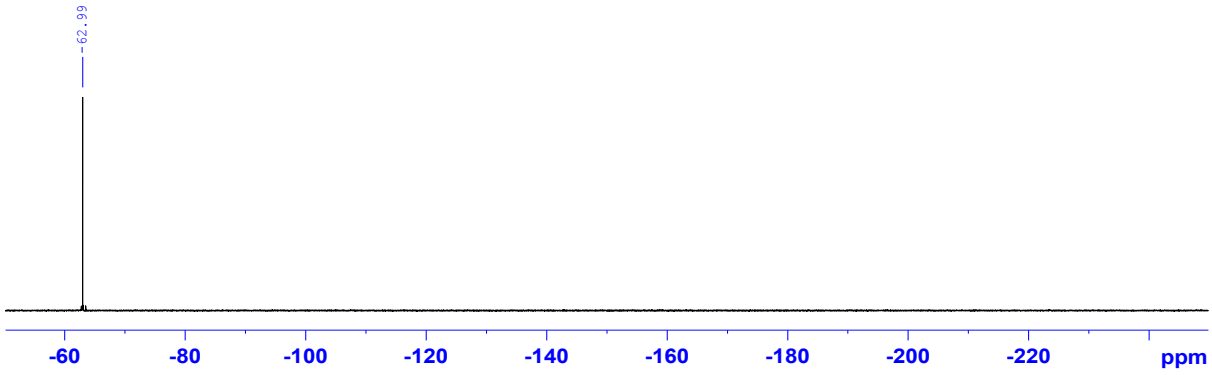
3r



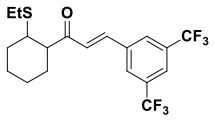
^{13}C NMR (126 MHz, d_6-DMSO)



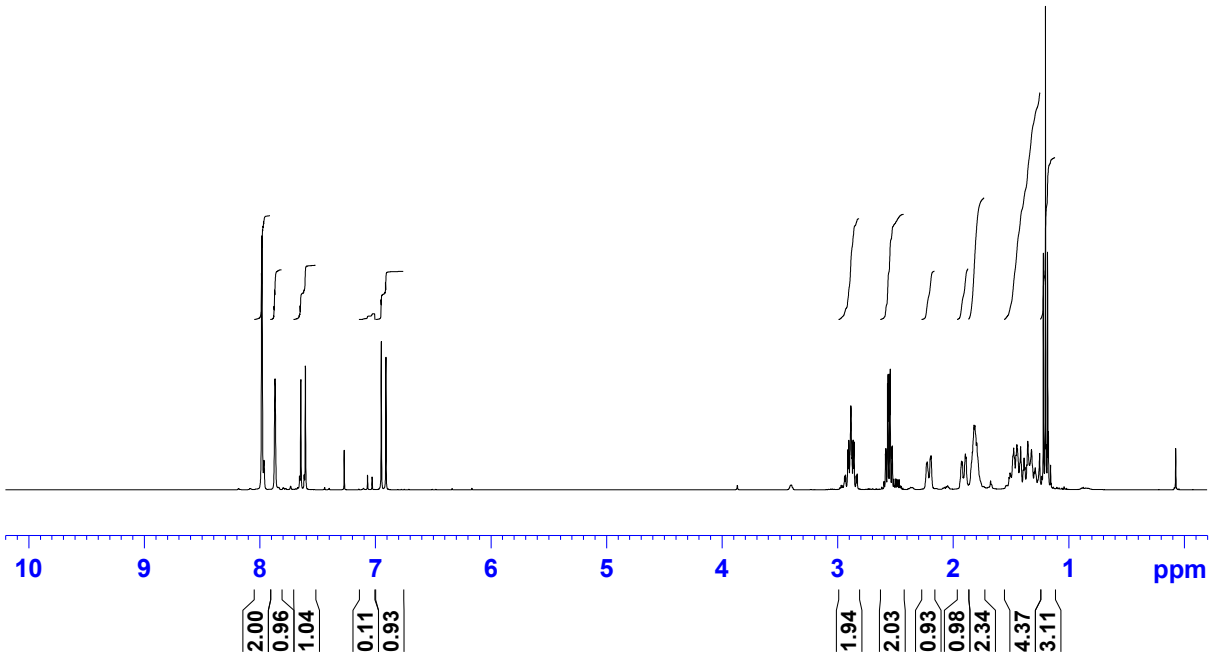
^{19}F NMR (376 MHz, $CDCl_3$)



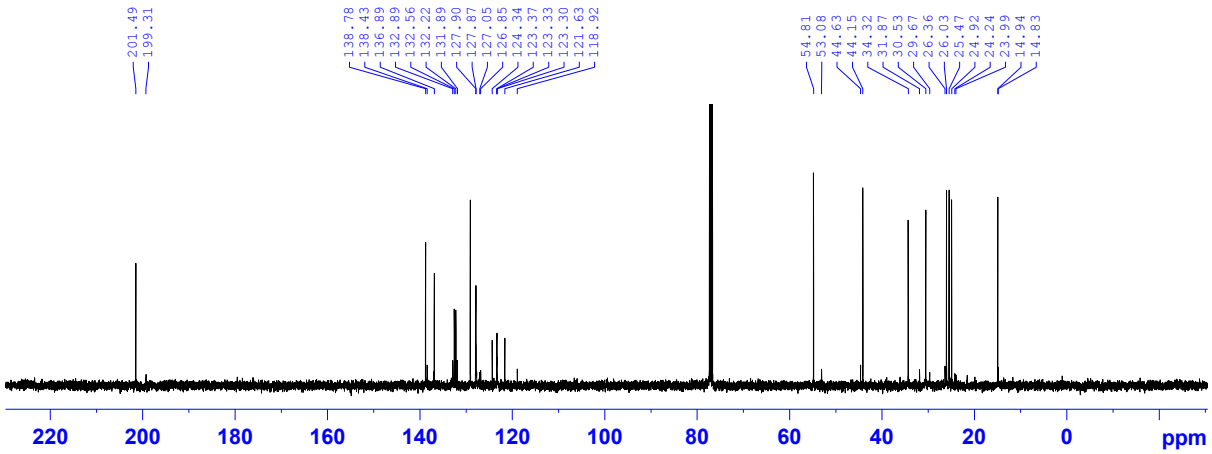
^{1}H NMR (400 MHz, $CDCl_3$)



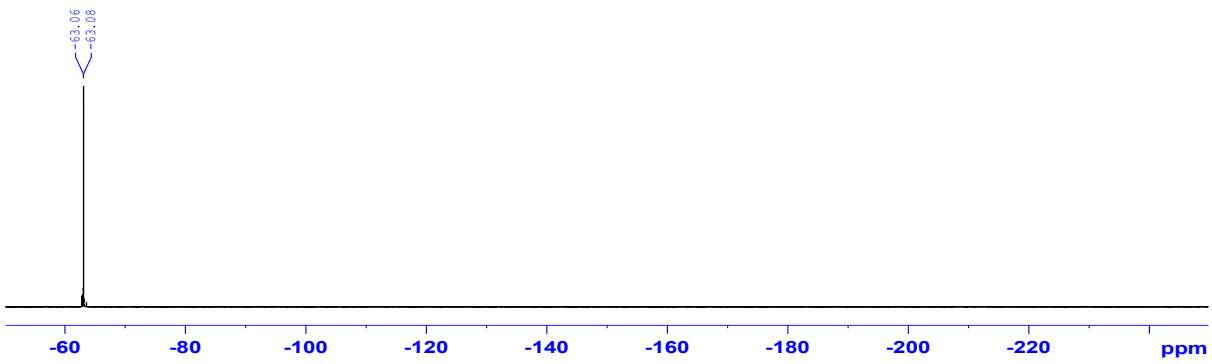
3s



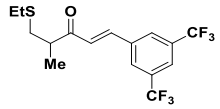
^{13}C NMR (101 MHz, $CDCl_3$)



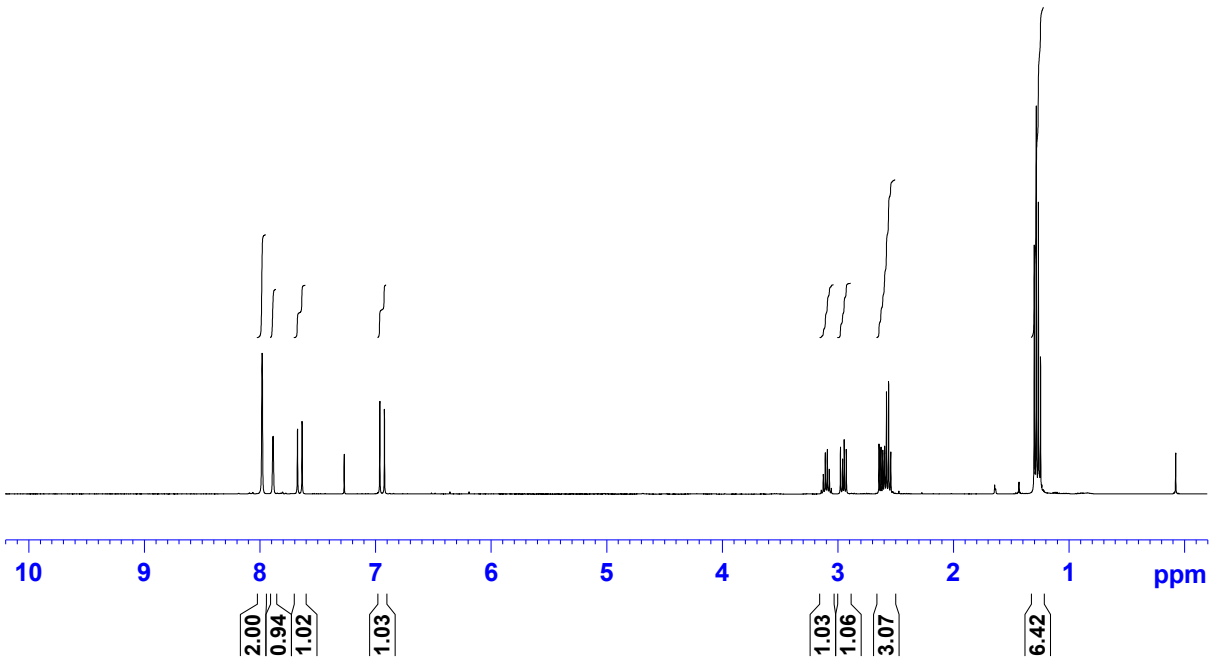
^{19}F NMR (376 MHz, $CDCl_3$)



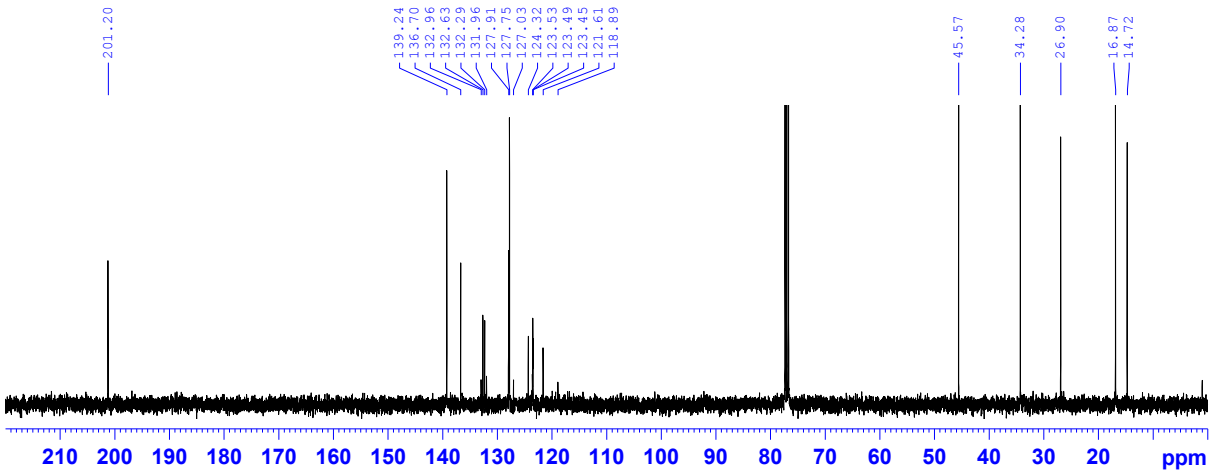
^{1}H NMR (400 MHz, $CDCl_3$)



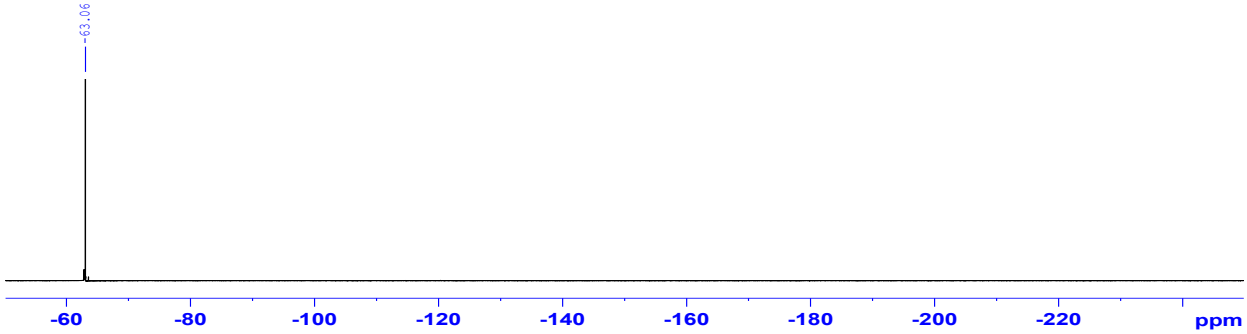
3t



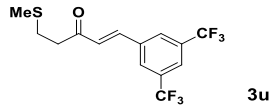
^{13}C NMR (101 MHz, $CDCl_3$)



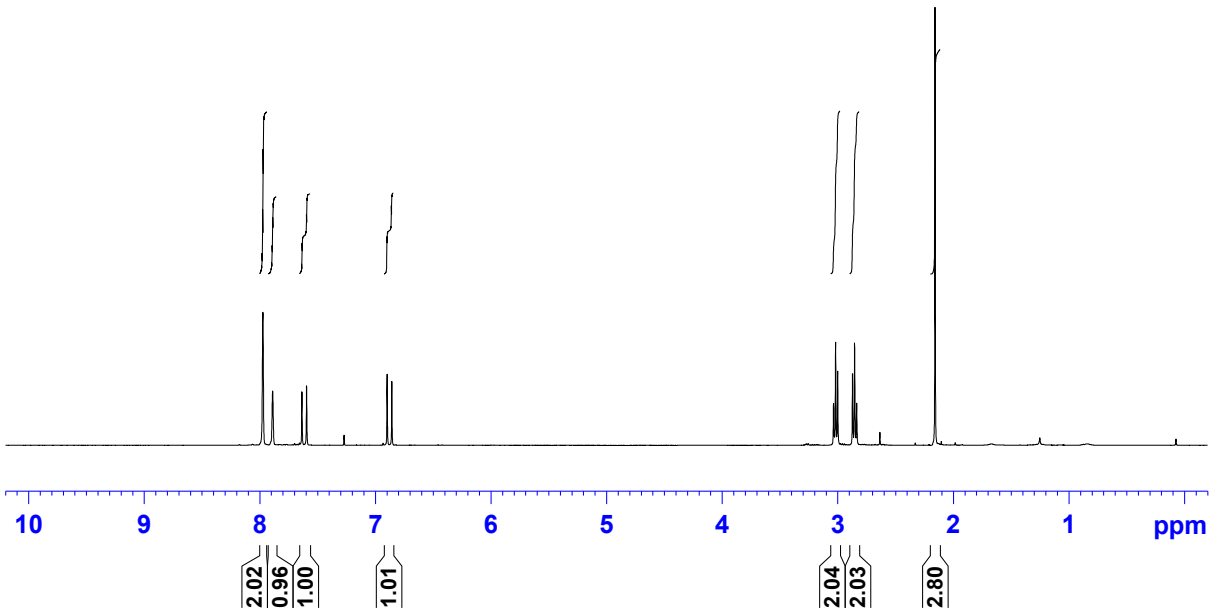
^{19}F NMR (376 MHz, $CDCl_3$)



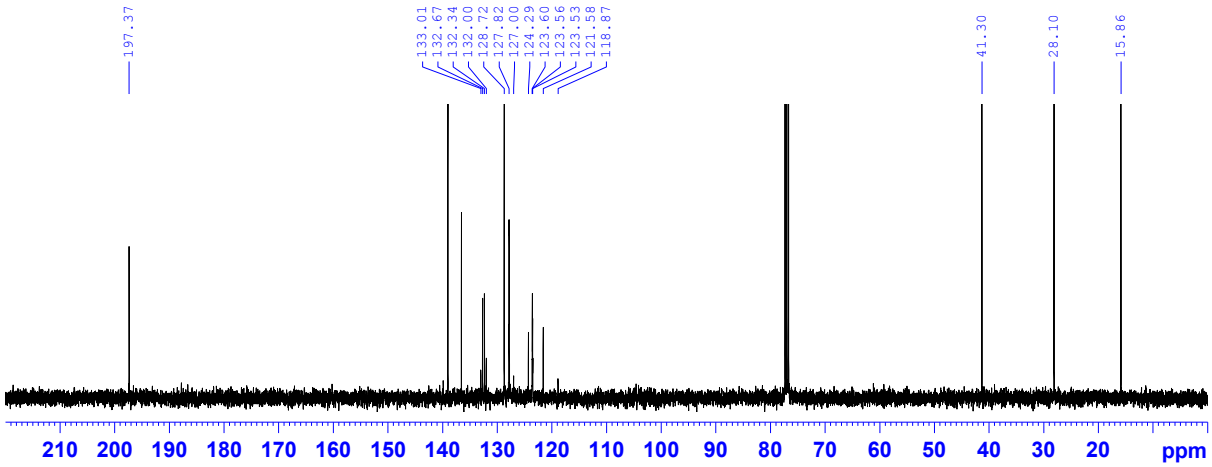
^{1}H NMR (400 MHz, $CDCl_3$)



3u



^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)