Electronic Supplementary Material (ESI) for ChemComm.

Pd(II)-catalyzed cyclization of 2-methyl aromatic ketones with maleimides through weak chelation assisted dual C–H activation

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Electronic Supporting Information (ESI)

Contents

1. General Information

All reactions were carried out in oven-dried glassware. Solvents were purchased from Thermo Fisher Scientific and Spectrochem. Pvt. Ltd., India, and used directly without further purification. Commercially available aromatic acids, maleimides, and metal salts were obtained from Sigma-Aldrich Co., Alfa Aesar, Tokyo Chemical Industry Co. Ltd., BLD Pharmatech Ltd., and Spectrochem. Pvt. Ltd., India. Analytical thin-layer chromatography (TLC) was represented on silica gel 60 F_{254} aluminium plates. Visualization was achieved by UV light. Products were purified by column chromatography using 100-200 mesh and 60-100 mesh silica gel. ^{1}H and ^{13}C NMR spectra were recorded on the Bruker instrument (400 MHz and 500 MHz). Chemical shifts (d) were reported in parts per million (ppm) reference to residual solvent peaks ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). The following abbreviations were used to show the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sext, sextet; sep, septet; m, multiplet; br, broad; dd, double-doublet; td, triple-doublet; tt, triple-triplet; etc. Coupling constants (*J*) were reported in the Hertz unit (Hz). High-resolution mass spectra (HRMS) were recorded on Bruker Mass spectrometer using electrospray ionization-time of flight (ESI-TOF).

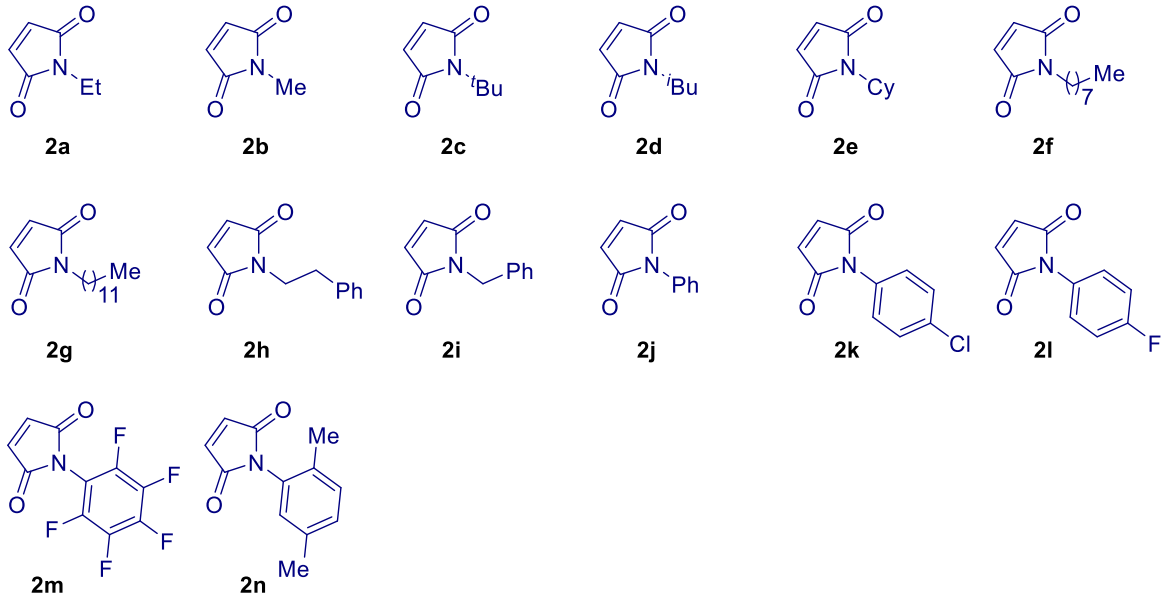
2. Experimental Section

2.a Preparation of Ligands, Aromatic Ketones, Esters, and Maleimides

Monoprotected amino acid ligands **L1-10** were prepared from the commercially available amino acids followed by literature reports[1-3] and **L11-12** were purchased.

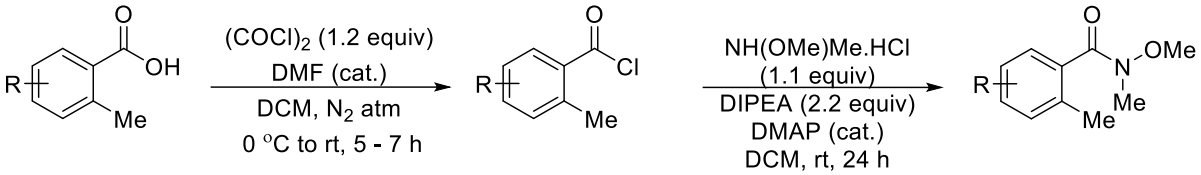
Maleimides **2a-b**, **2e**, and **2i-j** were purchased and maleimides **2c-d**, **2f-h**, and **2k-n** were synthesized from commercially available maleic anhydride and amines followed by literature reports.[4-5]

-List of substrates



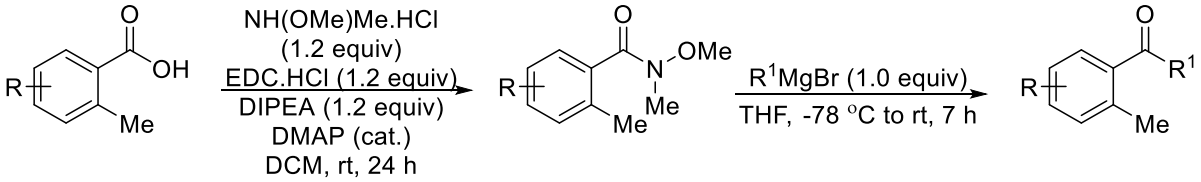
Aromatic ketones and ester were synthesized from commercially available carboxylic acids and *p*-xylene followed by literature reports.[6-10]

Reaction Procedure 1:



A clean and dry Schlenk round-bottom flask with a magnetic stir bar was charged with corresponding carboxylic acid (1.0-2.0 g) in dry DCM (25-50 mL) and oxalyl chloride (1.2 equiv) followed by 2-3 drops of *N*,*N*-dimethylformamide was added at 0 °C in the nitrogen atmosphere. The reaction is allowed to reach slowly at room temperature and stir for 5-7 hours at the same temperature. Upon completion, the excess oxalyl chloride and solvent were removed in vacuo and the acid chloride was used for the next step without further purification.

To a stirring solution of *N*,*O*-dimethylhydroxylamine hydrochloride (1.1 equiv) and *N*,*N*-diisopropylethylamine (2.2 equiv) in DCM (25-50 mL) were added corresponding carboxylic acid chloride and a small amount of 4-(dimethylamino)pyridine. The reaction allowed to stir for 24 hours at room temperature. Upon completion, the organic layer was washed with 0.2 M HCl (aq) and sat. $NaHCO_3$ (aq). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the aromatic weinreb amides.

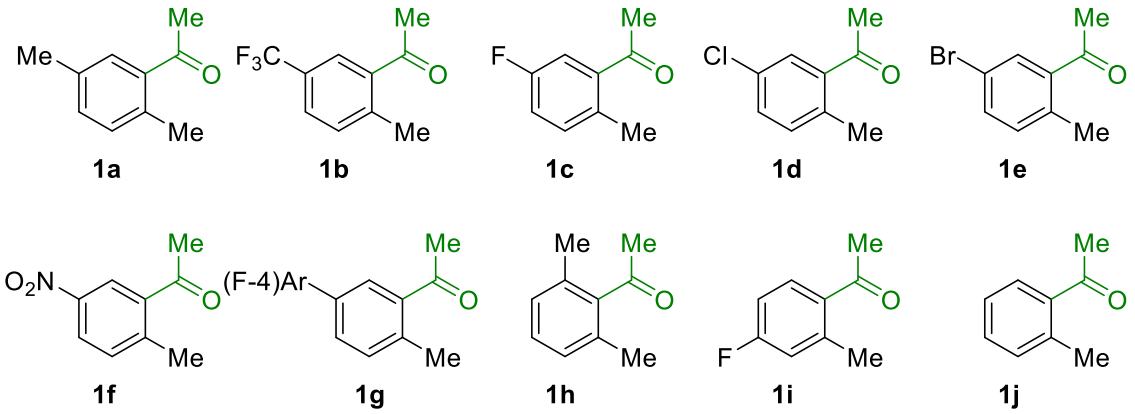


To a stirring solution of corresponding carboxylic acid (1.0 g), N-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (1.2 equiv) and *N*,*N*-diisopropylethylamine (1.2 equiv) in DCM (25 mL) were added *N*,*O*-dimethylhydroxylamine hydrochloride (1.2 equiv) and a small amount of 4-(dimethylamino)pyridine. The reaction allowed to stir for 24 hours at room temperature. Upon completion, the organic layer was washed with 0.2 M HCl (aq) and sat. $NaHCO_3$ (aq). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the aromatic weinreb amides.

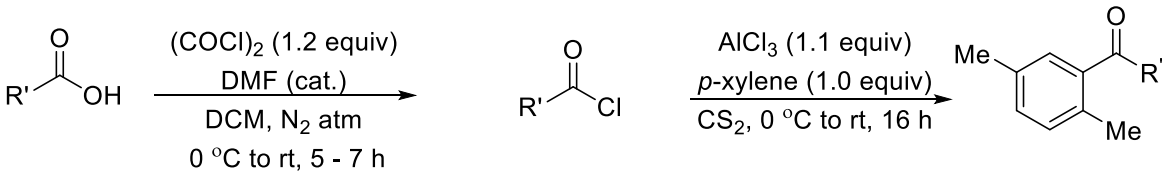
A clean and dry Schlenk round-bottom flask with a magnetic stirrer bar was capped with a rubber septum, evacuated, and refilled with nitrogen three times. The corresponding aromatic weinreb amide (0.5-1.0 g) in freshly distilled dry THF (20-40 mL) was added by syringes and cooled to -78 °C. The 1.5 M THF solution of Grignard reagent (1.0 equiv) was added dropwise by syringe after being stirred at room temperature for 5 hours sat. NH_4Cl (aq) was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3 times), washed with water, sat. NaCl (aq) and the organic layer were separated, dried over anhydrous Na_2SO_4. The filtered was concentrated under reduced pressure and the crude residue was purified by silica-gel flash chromatography (hexane/EtOAc; 20/1) to afford the aromatic ketones.

Aromatic ketones **1a-g** and **1i-j** were synthesized from aromatic weinreb amides and methylmagnesium bromide followed by Reaction Procedure 1. Aromatic ketone **1h** was purchased from BLD Pharma. Pvt. Ltd.

-List of substrates



Reaction Procedure 2:



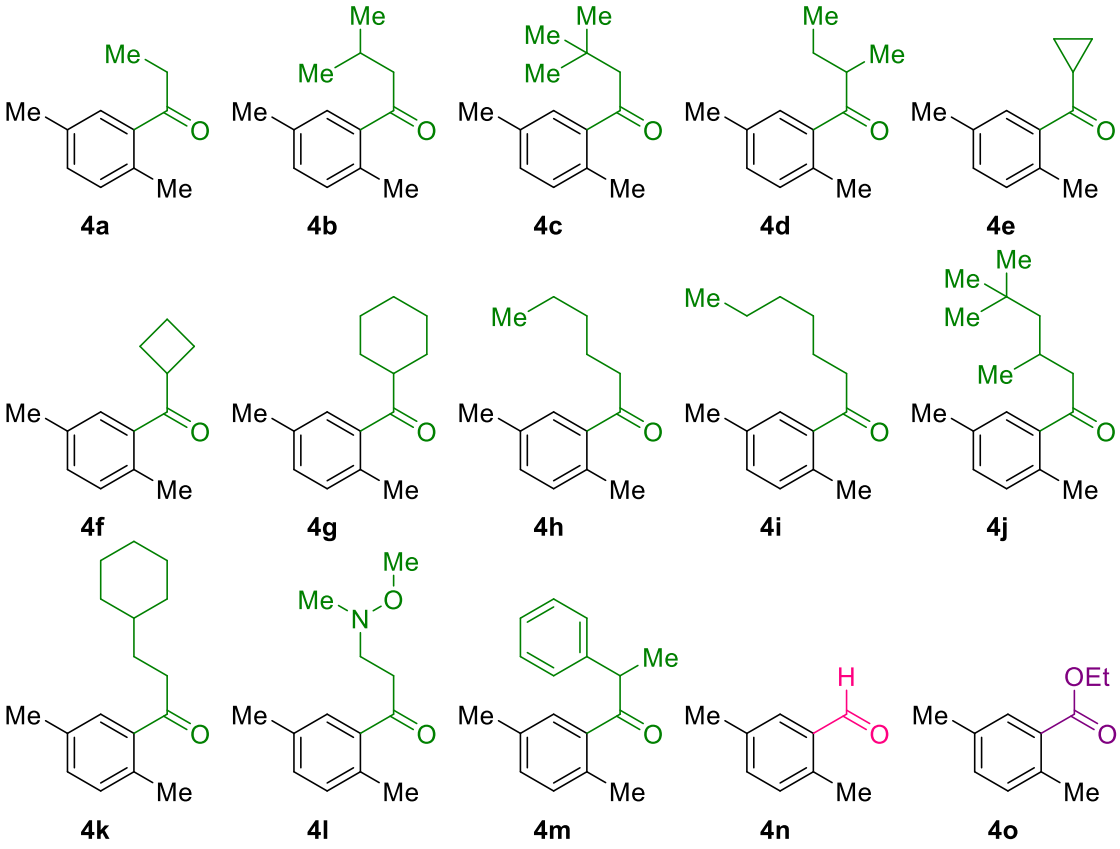
A clean and dry Schlenk round-bottom flask with a magnetic stir bar was charged with corresponding carboxylic acid (1.0 g) in dry DCM (25 mL) and oxalyl chloride (1.2 equiv) followed by 2-3 drops of *N*,*N*-dimethylformamide was added at 0 °C in nitrogen atmosphere. The reaction is allowed to reach slowly at room temperature and stir for 5-7 hours at the same temperature. Upon completion, the excess oxalyl chloride and solvent were removed in vacuo and the carboxylic acid chloride was used for the next step without further purification.

Aluminum chloride (1.1 equiv) was taken in a clean and dry Schlenk round-bottom flask in nitrogen atmosphere followed by carbon disulfide (15 mL) and *p*-Xylene (1.0 equiv) was added. The stir reaction mixture cooled to 0 °C and the corresponding acid chloride was added drop by drop. The reaction was stirred at 0 °C for 1 hour then allowed to reach slowly at room temperature and stirred for 16 hours at room temperature. Upon completion, the reaction mixture was poured into ice and diluted with DCM. The aqueous layer was washed with DCM (3 times) and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to get the aromatic ketones.

Aromatic Ketones **4a** and **4l** were synthesized from commercially available ethylmagnesium bromide and vinylmagnesium bromide followed by Reaction Procedure 1. Substrate **4i** was synthesized from freshly prepared hexylmagnesium bromide followed by Reaction Procedure 1. Aromatic Ketones **4b-h**, **4j-k** and **4m** were synthesized from *p*-xylene and corresponding carboxylic acid chloride followed by Reaction Procedure 2. The aromatic ester **4o** was prepared

from the corresponding carboxylic acid in ethanol solvent in the presence of a catalytic amount of H_2SO_4 at reflux condition followed by the literature procedure.

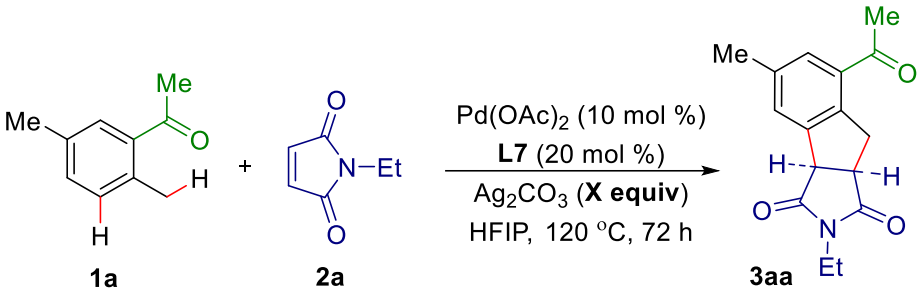
-List of substrates



2.b Optimization of Reaction Conditions

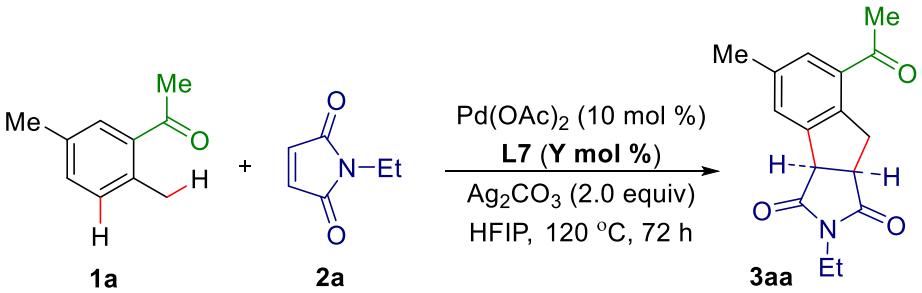
A clean and oven-dry pressure tube with a magnetic stir bar was charged with $Pd(OAc)_2$ (10-15 mol %), **L7** (10-30 mol %), Ag_2CO_3 (2.0-3.0 equiv), and the model aromatic ketone **1a** (20.0 mg, 0.135 mmol) and maleimide **2a** (34.0 mg, 2.0 equiv) were added followed by the addition of HFIP (0.8 mL, 0.17 M). Afterward, the pressure tube was tightly sealed by a screwcap and stirred at room temperature for 5 minutes then the sealed tube was placed in a preheated oil bath at 120-110 °C and stirred for 72 hours. After completing the reaction, the reaction mixture was cooled to room temperature and diluted by EtOAc. Then the reaction mixture was filtered by a celite/silica plug and concentrated in vacuo. The crude reaction mixture was used to check ^1H NMR for calculating the yield of the resulting product **3aa** and mesitylene was taken as an internal standard.

Table S1: Screening of Quantity of Ag_2CO_3



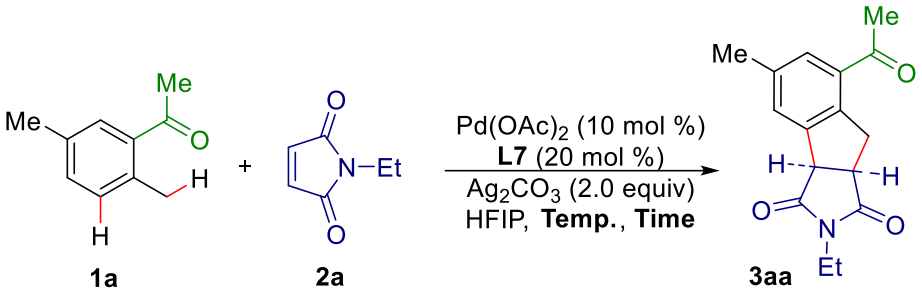
Entry	Oxidant	(Z equiv)	Yield of 3aa (%)
1.	Ag_2CO_3	2.0	42
2.	Ag_2CO_3	2.5	50
3.	Ag_2CO_3	3.0	41

Table S2: Screening of Quantity of **L7**



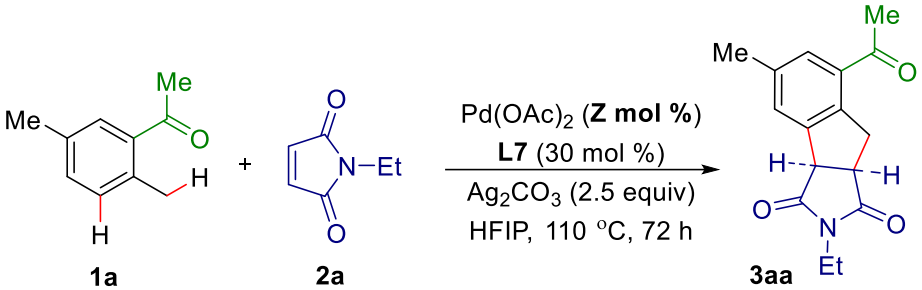
Entry	L7 (Y mol%)	Yield of 3aa (%)
1.	20	42
2.	10	43
3.	15	45
4.	30	59

Table S4: Screening of Reaction Temperature and Time



Entry	Time (hour)	Temp. (°C)	Yield of 3aa (%)
1.	72	120	42
2.	72	110	58
3.	90	110	60

Table S4: Screening of Quantity of $Pd(OAc)_2$



Entry	$Pd(OAc)_2$ (Z mol %)	Yield of 3aa (%)
1.	10	73
2.	15	92

2.c Synthetic of [3+2] Annulation Products

A clean and oven-dry pressure tube with a magnetic stir bar was charged with $Pd(OAc)_2$ (15 mol %), **L7** (30 mol %), Ag_2CO_3 (2.5 equiv), and respective aromatic ketone and ester substrate (40.0 mg) and maleimide (2.0 equiv) were added followed by the addition of HFIP (0.17 M). Afterward, the pressure tube was tightly sealed by a screwcap and stirred at room temperature for 5 minutes. Then the sealed tube was placed in a preheated oil bath at 110 °C and stirred for 72 hours. After completing the reaction, the reaction mixture was cooled to room temperature and diluted by EtOAc. Then the reaction mixture was filtered by a celite/silica plug and concentrated in vacuo. The residual reaction mixture was purified by silica gel column chromatography using hexane, and EtOAc as eluents to obtain the pure [3+2] annulation products.

2.d 1.0 mmol Scale Reaction Procedure

A clean and oven-dry pressure tube with a magnetic stir bar was charged with $Pd(OAc)_2$ (33.7 mg, 15 mol %), **L7** (52.0 mg, 30 mol %), Ag_2CO_3 (687.5 mg, 2.5 equiv), and respective aromatic ketone **4e** (174.0 mg, 1.0 mmol) and maleimide **2b** (222.0 mg, 2.0 equiv) were added followed by the addition of HFIP (5.9 mL, 0.17 M). After that, the pressure tube was tightly sealed by a screwcap and stirred at room temperature for 5 minutes. Then the sealed tube was placed in a preheated oil bath at 110 ^oC and stirred for 72 hours. After completing the reaction, the reaction mixture was cooled to room temperature and diluted by EtOAc. Then the reaction mixture was filtered by a celite/silica plug and concentrated in vacuo. The residual reaction mixture was purified by silica gel column chromatography using hexane, and EtOAc as eluents to obtain the pure [3+2] annulation products. The annulation product **5eb** isolated 209.0 mg as a yellow solid in 74% yield.

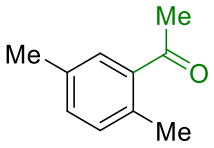
2.e Application Reactions[11]

$NaBH_4$ (5.0 equiv) was slowly added portion wise onto a solution of ketone **5ob** (1.0 equiv) in MeOH (c = 0.2 M) at 0 °C. The resulting solution was stirred for 1 hour at the same temperature (monitored by TLC). After completion water was added and the aqueous layer was washed by EtOAc (3 times), the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum to afford the desired product **6** was purified by flash column chromatography.[11]

3. References

1. R. M. Herbst, D. Shemin, *Organic Synthesis*, 2003, **19**, 4-4.
2. G. Naturale, M. Lamblin, C. Commandeur, F. X. Felpin, J. Dessolin, *Eur. J. Org. Chem.*, 2012, **29**, 5774-5788.
3. Y. Wang, K. M. Lazor, K. E. DeMeester, H. Liang, T. K. Heiss, C. L. Grimes, *J. Am. Chem. Soc.*, 2017, **139**, 13596-13599.
4. J. Zhou, X. Cai, X. Huang, Y. Dai, L. Sun, B. Zhang, H. Qian, *Eur. J. Med. Chem.*, 2017, **138**, 1158-1169.
5. J. Han, X. Huang, L. Sun, Z. Li, H. Qian, W. Huang, *Biochem. Pharmacol*., 2013, **86**, 297-308.
6. H. Park, Y. Li, J.-Q. Yu, *Angew. Chem., Int. Ed*., 2019, **58**, 11424-11428.
7. T. Solomek, P. Stacko, A. T. Veetil, T. Pospısil, P. Klan, *J. Org. Chem*. **2010**, *75*, 7300–7309.
8. T. Pospısil, A. T. Veetil, L. A. P. Antony, P. Klan, *Photochem. Photobiol. Sci*. **2008**, *7*, 625–632.
9. D. Wu, S.-S. Cui, F. Bian, W. Yu, *Org. Lett.* **2021**, *23*, 6057−6061.
10. Y. Masuda, N. Ishida, M. Murakami, *J. Am. Chem. Soc*. **2015**, *137*, 14063−14066.
11. M. Lanzi, J. Merad, D. Boyarskaya, G. Maestri, C. Allain, G. Masson, *Org. Lett*. **2018**, *20*, 5247–5250.

4. Spectral Data of Synthesized Compounds:

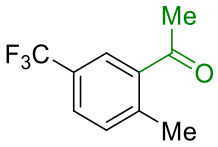


1-(2,5-Dimethylphenyl)ethan-1-one (1a)

Colourless liquid, prepared followed by reaction procedure 1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (s, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 2.56 (s, 3H), 2.48 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 202.0, 137.6, 135.2, 135.2, 132.3, 132.0, 123.0, 29.6, 21.1, 20.9.

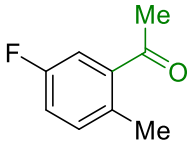


1-(2-Methyl-5-(trifluoromethyl)phenyl)ethan-1-one (1b)

Colourless liquid, prepared followed by reaction procedure 1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (s, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 2.61 (s, 3H), 2.56 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.6, 142.5, 138.2, 132.7, 128.6 (q, *J* = 31.3 Hz), 127.9 (q, *J* = 4.0 Hz), 125.9 (q, *J* = 4.0 Hz), 123.9 (d, *J* = 272.7 0 Hz), 29.6, 21.6.

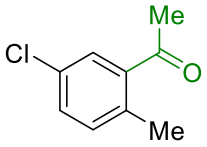


1-(5-Fluoro-2-methylphenyl)ethan-1-one (1c)

Colourless liquid, prepared followed by reaction procedure 1

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.19 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.07 (td, *J* = 8.2, 2.8 Hz, 1H), 2.55 (s, 3H), 2.46 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.5 (d, *J* = 2.0 Hz), 160.7 (d, *J* = 246.4 Hz), 138.9 (d, *J* = 5.0 Hz), 133.9 (d, *J* = 3.0 Hz), 133.5 (d, *J* = 7.1 Hz), 118.4 (d, *J* = 21.2 Hz), 116.0 (d, *J* = 23.2 Hz), 29.5, 20.8.

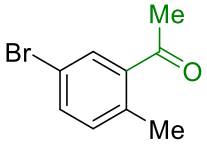


1-(5-Chloro-2-methylphenyl)ethan-1-one (1d)

Colourless liquid, prepared followed by reaction procedure 1

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 2.3 Hz, 1H), 7.32 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 2.55 (s, 3H), 2.46 (s, 3H).

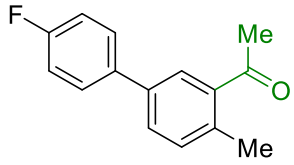
^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.5, 139.0, 136.8, 133.4, 131.5, 131.4, 129.2, 29.6, 21.0.



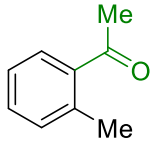
1-(5-Bromo-2-methylphenyl)ethan-1-one (1e)

Colourless liquid, prepared followed by reaction procedure 1

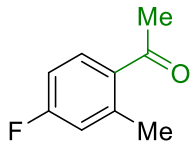
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.1 Hz, 1H), 7.46 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 2.55 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.3, 139.4, 137.2, 134.3, 133.7, 132.1, 119.2, 29.6, 21.1.



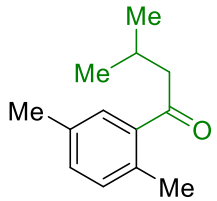
1-(4'-Fluoro-4-methyl-[1,1'-biphenyl]-3-yl)ethan-1-one (1g)
Colourless liquid, prepared followed by reaction procedure 1
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (s, 1H), 7.53 (d, *J* = 7.4 Hz, 3H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 8.3 Hz, 2H), 2.62 (s, 3H), 2.55 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.8, 162.6 (d, *J* = 247.4 Hz), 138.3, 137.9, 137.3, 136.4 (d, *J* = 3.0 Hz), 132.6, 129.9, 128.6 (d, *J* = 8.1 Hz), 127.8, 115.9 (d, *J* = 22.2 Hz), 29.7, 21.2.



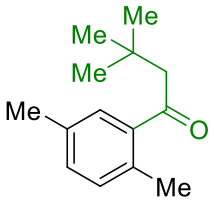
1-(*o*-Tolyl)ethan-1-one (1i)
Colourless liquid, prepared followed by reaction procedure 1
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.23 (q, *J* = 7.7 Hz, 2H), 2.55 (s, 3H), 2.52 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.7, 138.4, 137.5, 132.0, 131.5, 129.4, 125.7, 29.5, 21.6.



1-(4-Fluoro-2-methylphenyl)ethan-1-one (1j)
Colourless liquid, prepared followed by reaction procedure 1
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (dd, *J* = 9.4, 5.8 Hz, 1H), 6.95 – 6.88 (m, 2H), 2.54 (s, 3H), 2.52 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 165.44, 162.92 (d, *J* = 254.5 Hz), 142.6 (d, *J* = 9.1 Hz) 133.7 (d, *J* = 3.0 Hz), 132.2 (d, *J* = 10.0 Hz), 118.9 (d, *J* = 21.2 Hz), 112.6 (d, *J* = 21.2 Hz), 29.5, 22.0 (d, *J* = 1.0 Hz).



1-(2,5-Dimethylphenyl)-3-methylbutan-1-one (4b)
Colourless liquid, prepared followed by reaction procedure 2.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (s, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 2.75 (d, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 2.35 (s, 3H), 2.25 (dp, *J* = 13.6, 6.8 Hz, 1H), 0.98 (s, 3H), 0.97 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.0, 138.7, 135.1, 134.5, 131.8, 131.7, 129.0, 50.7, 25.2, 22.8, 21.0, 20.7.

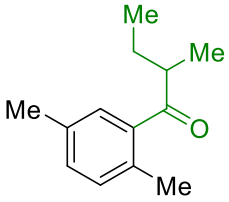


1-(2,5-Dimethylphenyl)-3,3-dimethylbutan-1-one (4c)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (s, 1H), 7.14 (d, *J* = 7.9 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 2.78 (s, 2H), 2.42 (s, 3H), 2.35 (s, 3H), 1.04 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.7, 140.3, 135.0, 133.9, 131.8, 131.5, 128.8, 53.9, 31.8, 30.1, 21.0, 20.5.

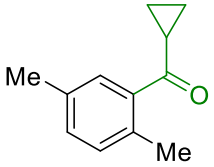


1-(2,5-Dimethylphenyl)-2-methylbutan-1-one (4d)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (s, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 3.18 (p, *J* = 6.7 Hz, 1H), 2.38 (s, 3H), 2.35 (s, 3H), 1.79 (dt, *J* = 12.9, 6.2 Hz, 1H), 1.42 (dq, *J* = 14.2, 7.1 Hz, 1H), 1.15 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.4, 139.1, 135.1, 134.4, 131.6, 131.4, 128.2, 45.6, 26.3, 21.0, 20.3, 16.2, 11.9.

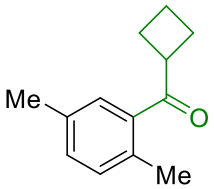


Cyclopropyl(2,5-dimethylphenyl)methanone (4e)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (s, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 2.45 (s, 1H), 2.43 (s, 3H), 2.37 (s, 3H), 1.24 (h, *J* = 3.7 Hz, 2H), 1.03 (dp, *J* = 7.3, 3.8, 3.2 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.4, 139.8, 135.2, 133.7, 131.6, 131.4, 128.9, 21.0, 20.8, 20.3, 12.0.

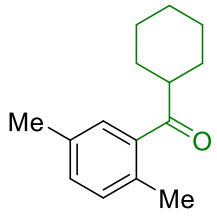


Cyclobutyl(2,5-dimethylphenyl)methanone (4f)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (s, 1H), 7.13 (q, *J* = 7.9 Hz, 2H), 3.91 (p, *J* = 8.4 Hz, 1H), 2.47 (s, 3H), 2.42 – 2.35 (m, 2H), 2.34 (s, 3H), 2.22 (q, *J* = 10.6 Hz, 2H), 2.03 (h, *J* = 9.2 Hz, 1H), 1.88 (dh, *J* = 10.4, 5.6, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.4, 136.7, 135.4, 135.1, 131.9, 129.2, 44.3, 25.3, 21.0, 21.0, 18.0.

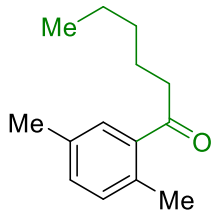


Cyclohexyl(2,5-dimethylphenyl)methanone (4g)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (s, 1H), 7.11 (q, *J* = 8.0 Hz, 2H), 3.08 – 2.97 (m, 1H), 2.34 (s, 6H), 1.83 (dd, *J* = 23.4, 12.7 Hz, 4H), 1.69 (d, *J* = 12.1 Hz, 1H), 1.49 – 1.18 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.1, 139.1, 135.0, 133.9, 131.4, 131.2, 127.7, 49.0, 28.8, 26.0, 25.8, 21.0, 20.1.

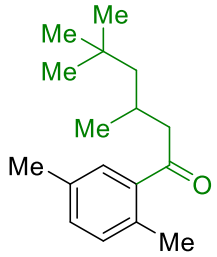


1-(2,5-Dimethylphenyl)hexan-1-one (4h)

Colourless liquid, prepared followed by reaction procedure 2.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 2.86 (t, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 2.35 (s, 3H), 1.71 (q, *J* = 6.4, 5.9 Hz, 2H), 1.34 (td, *J* = 7.0, 3.0 Hz, 4H), 0.91 (t, *J* = 6.0 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.2, 138.4, 135.1, 134.6, 131.8, 131.8, 128.9, 41.7, 31.6, 24.2, 22.6, 21.0, 20.7, 14.0.

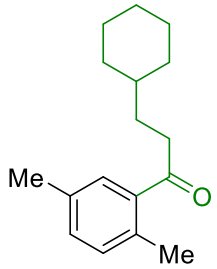


1-(2,5-Dimethylphenyl)-3,5,5-trimethylhexan-1-one (4j)

Colourless liquid, prepared followed by reaction procedure 2.

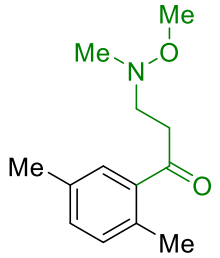
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (s, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 2.87 (dd, *J* = 16.1, 5.4 Hz, 1H), 2.70 (dd, *J* = 16.1, 8.4 Hz, 1H), 2.43 (s, 3H), 2.35 (s, 3H), 2.23 (td, *J* = 12.4, 5.9 Hz, 1H), 1.28 (dd, *J* = 13.9, 4.3 Hz, 1H), 1.16 (dd, *J* = 14.1, 6.5 Hz, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.1, 138.7, 135.1, 134.6, 131.9, 131.8, 129.0, 51.5, 51.2, 31.3, 30.1, 26.5, 23.0, 21.0, 20.7.

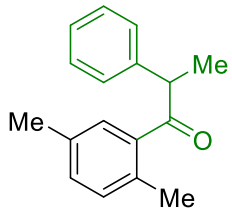


3-Cyclohexyl-1-(2,5-dimethylphenyl)propan-1-one (4k)

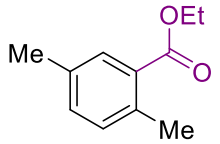
Colourless liquid, prepared followed by reaction procedure 2.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.43 (s, 3H), 2.35 (s, 3H), 1.79 – 1.63 (m, 5H), 1.59 (q, *J* = 7.5 Hz, 2H), 1.33 – 1.10 (m, 4H), 0.93 (q, *J* = 11.3, 10.7 Hz, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.5, 138.4, 135.1, 134.6, 131.8, 131.7, 128.8, 39.3, 37.5, 33.3, 31.8, 26.6, 26.4, 21.0, 20.8.



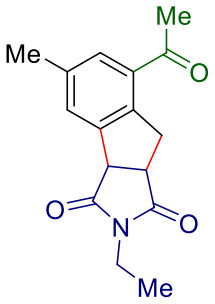
1-(2,5-Dimethylphenyl)-3-(methoxy(methyl)amino)propan-1-one (4l)
Colourless liquid, prepared followed by reaction procedure 2.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (s, 1H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 3.45 (s, 3H), 3.15 (t, *J* = 6.7 Hz, 2H), 3.02 (t, *J* = 6.7 Hz, 2H), 2.59 (s, 3H), 2.43 (s, 3H), 2.35 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 203.5, 138.1, 135.2, 134.9, 132.0, 131.9, 129.0, 60.0, 55.8, 45.2, 39.3, 21.0, 20.7.



1-(2,5-Dimethylphenyl)-2-phenylpropan-1-one (4m)
Colourless liquid, prepared followed by reaction procedure 2.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (s, 1H), 7.23 (d, *J* = 6.4 Hz, 4H), 7.16 (t, *J* = 6.4 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 4.50 (q, *J* = 6.8 Hz, 1H), 2.26 (s, 3H), 2.25 (s, 3H), 1.52 (d, *J* = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 204.9, 140.5, 138.6, 134.8, 134.6, 131.5, 128.8, 128.4, 128.0, 127.0, 50.7, 21.0, 20.3, 18.6.



Ethyl 2,5-dimethylbenzoate (4o)
Colourless liquid.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 4.36 (q, *J* = 6.6 Hz, 2H), 2.55 (s, 3H), 2.34 (s, 3H), 1.40 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.0, 136.9, 135.2, 132.6, 131.6, 131.0, 129.7, 60.7, 21.3, 20.8, 14.4.



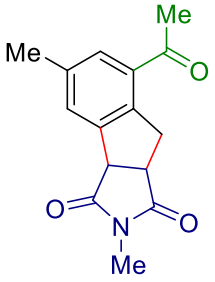
7-Acetyl-2-ethyl-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3aa)

3aa was prepared from **1a** (0.27 mmol) and **2a** according to general procedure 2.c; eluent is 15% EtOAc in hexane; yellow solid (61 mg); yield is 84%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.58 (s, 1H), 4.24 (d, *J* = 7.0 Hz, 1H), 3.74-3.60 (m, 3H), 3.47 (q, *J* = 7.0, 6.0 Hz, 2H), 2.56 (s, 3H), 2.42 (s, 3H), 1.09 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 179.7, 177.3, 139.8, 139.5, 138.0, 134.0, 131.2, 130.1, 51.1, 44.2, 36.0, 34.0, 28.0, 21.3, 13.1.

HRMS (ESI-TOF): m/z was calculated for $C_{16}H_{21}N_2O_3^+$ $[M+H]^+$ 289.1547, found 289.1524.



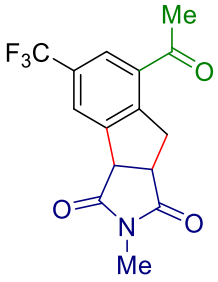
7-Acetyl-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ab)

3ab was prepared from **1a** (0.27 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; colourless crystal (56 mg); yield is 81%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.58 (s, 1H), 4.27 (d, *J* = 6.6 Hz, 1H), 3.77 – 3.59 (m, 3H), 2.90 (s, 3H), 2.55 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.9, 179.9, 177.5, 139.8, 139.4, 138.0, 134.0, 131.2, 130.1, 51.1, 44.2, 36.0, 28.0, 25.1, 21.2.

HRMS (ESI-TOF): m/z was calculated for $C_{15}H_{16}NO_3^+$ $[M+H]^+$ 258.1125, found 258.1113.

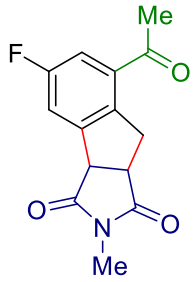


7-Acetyl-2-methyl-5-(trifluoromethyl)-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3bb)

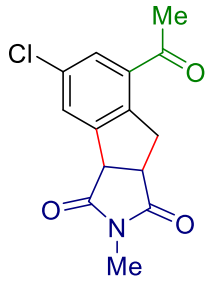
3bb was prepared from **1b** (0.20 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light brown solid (31 mg); yield is 50%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (s, 2H), 4.38 (d, *J* = 7.0 Hz, 1H), 3.90 – 3.70 (m, 3H), 2.95 (s, 3H), 2.63 (s, 3H).

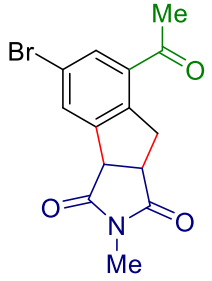
^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.6, 179.2, 176.5, 146.9, 140.6, 134.5, 127.1 (q, *J* = 3.0 Hz), 126.1 (q, *J* = 3.0 Hz), 51.0, 44.0, 36.5, 28.0, 25.4.
HRMS (ESI-TOF): m/z was calculated for $C_{15}H_{16}F_3N_2O_3^+$ $[M+NH_4]^+$ 329.1108, found 329.1100.



7-Acetyl-5-fluoro-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3cb)
3cb was prepared from **1c** (0.26 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light brown solid (36 mg); yield is 52%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.46 (m, 2H), 4.30 (d, *J* = 7.1 Hz, 1H), 3.77 – 3.62 (m, 3H), 2.93 (s, 3H), 2.55 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.6 (d, *J* = 2.0 Hz), 179.5, 176.8, 162.2 (d, *J* = 248.5 Hz), 141.3 (d, *J* = 8.1 Hz), 138.2 (d, *J* = 3.0 Hz), 134.9 (d, *J* = 6.1 Hz), 117.4 (d, *J* = 23.2 Hz), 116.7 (d, *J* = 23.2 Hz), 51.1, 51.0, 44.2, 35.7, 27.9, 25.3.
HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{12}FNNaO_3^+$ $[M+Na]^+$ 284.0693, found 284.0675.



7-Acetyl-5-chloro-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3db)
3db was prepared from **1d** (0.24 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; yellow solid (41 mg); yield is 63%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (s, 1H), 7.75 (s, 1H), 4.30 (d, *J* = 5.1 Hz, 1H), 3.77 – 3.63 (m, 3H), 2.93 (s, 3H), 2.56 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.6, 179.4, 176.7, 141.2, 141.1, 135.0, 133.8, 130.4, 129.5, 51.0, 44.1, 35.9, 28.0, 25.3.
HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{13}ClNO_3^+$ $[M+H]^+$ 278.0578, found 278.0533.



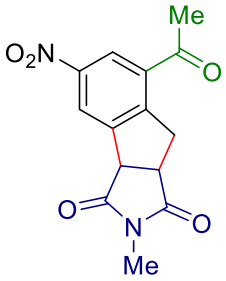
7-Acetyl-5-bromo-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3eb)

3eb was prepared from **1e** (0.19 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light brown solid (12 mg); yield is 20%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 (s, 2H), 4.31 (d, *J* = 6.5 Hz, 1H), 3.78 – 3.61 (m, 3H), 2.94 (s, 3H), 2.57 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.5, 179.4, 176.7, 141.8, 141.4, 135.3, 133.3, 132.5, 121.5, 50.9, 44.0, 36.0, 28.0, 25.3.

HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{12}BrNNaO_3^+$ $[M+Na]^+$ 343.9893, found 343.9910.



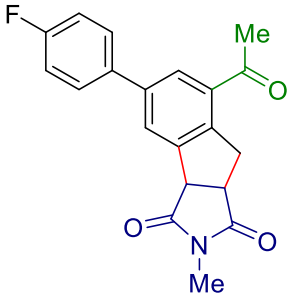
7-Acetyl-2-methyl-5-nitro-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3fb)

3fb was prepared from **1f** (0.22 mmol) and **2b** according to general procedure 2.c; eluent is 25% EtOAc in hexane; white solid (10 mg); yield is 16%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 (s, 1H), 8.31 (s, 1H), 4.44 (d, *J* = 8.2 Hz, 1H), 3.77 (t, *J* = 8.3 Hz, 1H), 3.63 (dd, *J* = 18.6, 10.6 Hz, 2H), 3.51 (s, 3H), 2.97 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.7, 178.7, 175.9, 147.8, 147.5, 140.1, 132.9, 123.1, 121.7, 61.9, 51.4, 43.7, 34.0, 25.5.

HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{12}N_2NaO_5^+$ $[M+Na]^+$ 311.0638, found 311.0663.



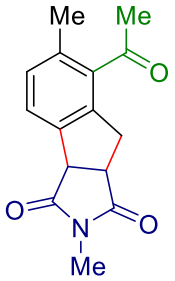
7-Acetyl-5-(4-fluorophenyl)-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3gb)

3gb was prepared from **1g** (0.17 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; yellow liquid (24 mg); yield is 41%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 9.2 Hz, 2H), 7.60 – 7.49 (m, 2H), 7.15 (t, *J* = 8.6 Hz, 2H), 4.37 (d, *J* = 7.1 Hz, 1H), 3.87 – 3.67 (m, 3H), 2.94 (s, 3H), 2.63 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.7, 179.8, 177.3, 162.9 (d, *J* = 248.5 Hz), 141.6, 140.7, 140.3, 135.9 (d, *J* = 4.0 Hz), 134.6, 129.2, 129.0 (d, *J* = 9.1 Hz), 127.8, 116.0 (d, *J* = 21.2 Hz), 51.2, 44.2, 36.1, 28.1, 25.2.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{16}FNNaO_3^+$ $[M+Na]^+$ 360.1006, found 360.0999.



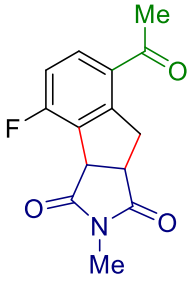
7-Acetyl-2,6-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3hb)

3hb was prepared from **1h** (0.27 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; brown solid (17 mg); yield is 25%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 4.30 (d, *J* = 8.0 Hz, 1H), 3.64 (ddd, *J* = 10.6, 7.9, 3.0 Hz, 1H), 3.45 – 3.29 (m, 2H), 2.93 (s, 3H), 2.48 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.2, 179.7, 177.2, 139.3, 137.6, 135.8, 134.6, 130.7, 126.3, 51.3, 44.0, 33.9, 31.6, 25.2, 19.7.

HRMS (ESI-TOF): m/z was calculated for $C_{15}H_{16}NO_3^+$ $[M+H]^+$ 258.1125, found 258.1104.



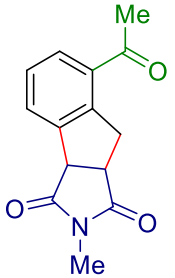
7-Acetyl-4-fluoro-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ib)

3ib was prepared from **1i** (0.26 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; brown solid (38 mg); yield is 55%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 8.6, 4.8 Hz, 1H), 7.08 (t, *J* = 8.5 Hz, 1H), 4.55 (d, *J* = 7.4 Hz, 1H), 3.85 – 3.67 (m, 3H), 2.95 (s, 3H), 2.56 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.3, 179.0, 175.2, 162.4 (d, *J* = 260.6 Hz), 147.6 (d, *J* = 6.1 Hz), 133.2 (d, *J* = 9.1 Hz), 130.6 (d, *J* = 4.0 Hz), 125.9 (d, *J* = 17.2 Hz), 115.1 (d, *J* = 21.1 Hz), 49.5, 49.4, 44.3, 37.3, 27.9, 25.3.

HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{13}FNO_3^+$ $[M+H]^+$ 262.0874, found 262.0874.



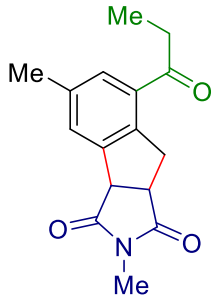
7-Acetyl-2-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3jb)

3jb was prepared from **1j** (0.30 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light yellow solid (47 mg); yield is 65%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 4.32 (d, *J* = 7.0 Hz, 1H), 3.83 – 3.63 (m, 3H), 2.91 (s, 3H), 2.57 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.8, 179.8, 177.4, 142.8, 139.4, 134.2, 130.3, 129.6, 128.0, 51.2, 44.0, 36.4, 28.0, 25.2.

HRMS (ESI-TOF): m/z was calculated for $C_{14}H_{14}NO_3^+$ $[M+H]^+$ 244.0968, found 244.0985.



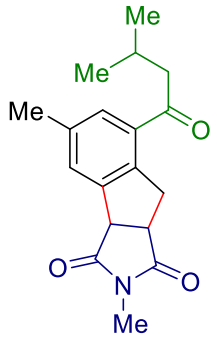
2,5-Dimethyl-7-propionyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5ab)

5ab was prepared from **4a** (0.25 mmol) and **2b** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light brown solid (41 mg); yield is 62%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (s, 1H), 7.57 (s, 1H), 4.27 (d, *J* = 7.0 Hz, 1H), 3.76 – 3.63 (m, 3H), 3.03 – 2.92 (m, 2H), 2.91 (s, 3H), 2.41 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.7, 180.0, 177.6, 139.7, 139.4, 138.0, 133.9, 130.3, 129.8, 51.1, 44.2, 36.0, 32.9, 25.2, 21.3, 8.3.

HRMS (ESI-TOF): m/z was calculated for $C_{16}H_{18}NO_3^+$ $[M+H]^+$ 272.1281, found 272.1277.



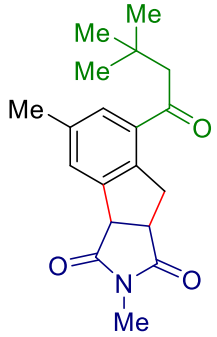
2,5-Dimethyl-7-(3-methylbutanoyl)-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5bb)

5bb was prepared from **4b** (0.21 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light yellow solid (53 mg); yield is 85%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (s, 1H), 7.56 (s, 1H), 4.26 (d, *J* = 6.9 Hz, 1H), 3.74 – 3.63 (m, 3H), 2.91 (s, 3H), 2.77 (d, *J* = 7.0 Hz, 2H), 2.41 (s, 3H), 2.24 (tt, *J* = 13.0, 5.8 Hz, 1H), 0.96 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.2, 180.0, 177.6, 139.7, 139.4, 137.9, 134.4, 130.4, 129.7, 51.1, 48.7, 44.2, 35.9, 25.2, 25.1, 22.9, 22.8, 21.3.

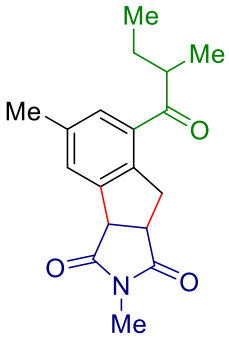
HRMS (ESI-TOF): m/z was calculated for $C_{18}H_{22}NO_3^+$ $[M+H]^+$ 300.1594, found 300.1594.



7-(3,3-Dimethylbutanoyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5cb)

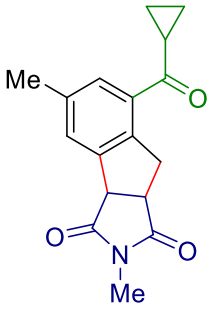
5cb was prepared from **4c** (0.20 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; yellow solid (44 mg); yield is 72%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (s, 1H), 7.54 (s, 1H), 4.26 (d, *J* = 6.6 Hz, 1H), 3.70 – 3.61 (m, 3H), 2.91 (s, 3H), 2.78 (s, 2H), 2.40 (s, 3H), 1.02 (s, 9H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.6, 180.0, 177.5, 139.40, 139.36, 137.8, 135.6, 130.6, 129.5, 51.2, 51.1, 44.2, 35.8, 31.6, 30.1, 25.1, 21.3.
HRMS (ESI-TOF): m/z was calculated for $C_{19}H_{24}NO_3^+$ $[M+H]^+$ 314.1751, found 314.1730.



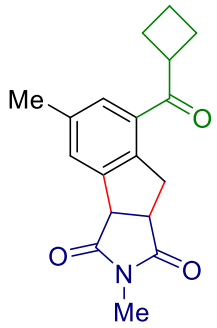
2,5-Dimethyl-7-(2-methylbutanoyl)-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5db)

5db was prepared from **4d** (0.21 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; yellow oil (45 mg); yield is 72% (dr 1:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (s, 2H), 7.56 (s, 2H), 4.26 (d, *J* = 6.2 Hz, 2H), 3.65 (s, 6H), 3.31 (h, *J* = 5.9 Hz, 2H), 2.91 (s, 6H), 2.41 (s, 6H), 1.76 (ddt, *J* = 20.3, 13.8, 7.1 Hz, 2H), 1.42 (ddt, *J* = 14.9, 10.7, 7.9 Hz, 2H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.87 (dt, *J* = 15.5, 7.4 Hz, 6H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.63, 205.61, 180.0, 177.5, 140.03, 139.99, 139.5, 137.9, 133.9, 130.0, 129.6, 51.2, 44.1, 43.01, 42.97, 35.8, 26.7, 26.5, 25.1, 21.3, 17.0, 16.6, 11.9, 11.8.
HRMS (ESI-TOF): m/z was calculated for $C_{18}H_{22}NO_3^+$ $[M+H]^+$ 300.1594, found 300.1573.



7-(Cyclopropanecarbonyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5eb)

5eb was prepared from **4e** (0.23 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; brown solid (53 mg); yield is 82%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (s, 1H), 7.56 (s, 1H), 4.35 – 4.25 (m, 1H), 3.63 (s, 3H), 2.91 (s, 3H), 2.55 (tt, *J* = 8.0, 3.8 Hz, 1H), 2.42 (s, 3H), 1.24 – 1.15 (m, 2H), 1.06 – 0.94 (m, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.6, 180.0, 177.5, 139.2, 138.9, 138.0, 135.3, 130.3, 129.5, 51.2, 44.2, 35.5, 25.1, 21.3, 18.5, 12.0, 11.6.
HRMS (ESI-TOF): m/z was calculated for $C_{17}H_{18}NO_3^+$ $[M+H]^+$ 284.1281, found 284.1259.



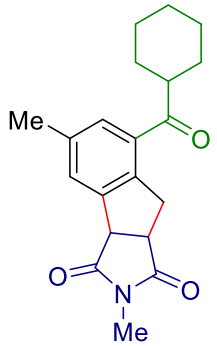
7-(Cyclobutanecarbonyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5fb)

5fb was prepared from **4f** (0.21 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; yellow solid (51 mg); yield is 81%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (s, 1H), 7.45 (s, 1H), 4.26 (d, *J* = 7.2 Hz, 1H), 3.93 (p, *J* = 8.6 Hz, 1H), 3.78 – 3.63 (m, 3H), 2.90 (s, 3H), 2.38 (s, 3H), 2.36 – 2.19 (m, 4H), 2.10 – 2.00 (m, 1H), 1.91 – 1.83 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.9, 180.0, 177.6, 140.2, 139.5, 137.8, 132.5, 130.5, 129.7, 51.1, 44.2, 42.9, 35.9, 25.2, 25.12, 25.06, 21.3, 18.1.

HRMS (ESI-TOF): m/z was calculated for $C_{18}H_{20}NO_3^+$ $[M+H]^+$ 298.1438, found 298.1421.



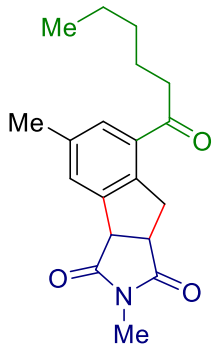
7-(Cyclohexanecarbonyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5gb)

5gb was prepared from **4g** (0.18 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light yellow solid (56 mg); yield is 93%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (s, 2H), 4.26 (d, *J* = 5.4 Hz, 1H), 3.76 – 3.60 (m, 3H), 3.17 (dt, *J* = 10.8, 5.3 Hz, 1H), 2.90 (s, 3H), 2.40 (s, 3H), 1.85 – 1.67 (m, 4H), 1.52 – 1.16 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.0, 180.0, 177.5, 140.0, 139.5, 137.9, 133.5, 129.9, 129.5, 51.1, 46.5, 44.1, 35.7, 29.5, 29.2, 26.0, 25.9, 25.8, 25.1, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{24}NO_3^+$ $[M+H]^+$ 326.1751, found 326.1734.



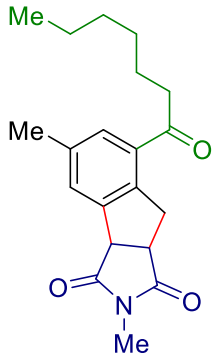
7-Hexanoyl-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5hb)

5hb was prepared from **4h** (0.20 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; white solid (37 mg); yield is 60%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.56 (s, 1H), 4.26 (d, *J* = 6.9 Hz, 1H), 3.73 – 3.61 (m, 3H), 2.96 – 2.83 (m, 5H), 2.40 (s, 3H), 1.68 (q, *J* = 7.0, 6.0 Hz, 2H), 1.39 – 1.30 (m, 4H), 0.89 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.5, 180.0, 177.6, 139.7, 139.4, 137.9, 134.0, 130.4, 129.8, 51.1, 44.2, 39.7, 35.9, 31.6, 25.1, 24.0, 22.6, 21.3, 14.0.

HRMS (ESI-TOF): m/z was calculated for $C_{19}H_{24}NO_3^+$ $[M+H]^+$ 314.1751, found 314.1751.



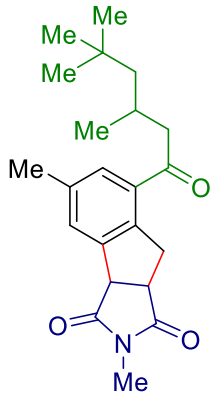
7-Heptanoyl-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5ib)

5ib was prepared from **4i** (0.18 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light yellow solid (39 mg); yield is 65%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.57 (s, 1H), 4.27 (d, *J* = 7.0 Hz, 1H), 3.75 – 3.62 (m, 3H), 2.92 (s, 3H), 2.89 (t, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 1.68 (p, *J* = 7.1 Hz, 2H), 1.38 – 1.28 (m, 6H), 0.88 (t, *J* = 8.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.5, 180.0, 177.6, 139.7, 139.5, 138.0, 134.1, 130.4, 129.8, 51.2, 44.2, 39.8, 36.0, 31.8, 29.1, 25.2, 24.3, 22.6, 21.3, 14.2.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{26}NO_3^+$ $[M+H]^+$ 328.1907, found 328.1899.



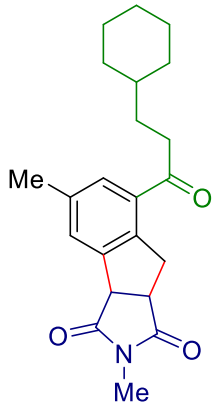
2,5-Dimethyl-7-(3,5,5-trimethylhexanoyl)-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5jb)

5jb was prepared from **4j** (0.16 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; yellow solid (39 mg); yield is 67% (dr 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (s, 2H), 7.56 (s, 2H), 4.27 (d, *J* = 6.9 Hz, 2H), 3.67 (q, *J* = 9.0, 7.6 Hz, 6H), 2.91 (d, *J* = 2.2 Hz, 6H), 2.89 – 2.82 (m, 2H), 2.79 – 2.70 (m, 2H), 2.41 (s, 6H), 2.21 (dt, *J* = 12.7, 6.8 Hz, 2H), 1.30 – 1.24 (m, 2H), 1.15 (dd, *J* = 14.1, 6.4 Hz, 2H), 0.96 (d, *J* = 2.7 Hz, 3H), 0.94 (d, *J* = 2.4 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.32, 201.27, 180.01, 179.97, 177.6, 139.7, 139.6, 139.4, 137.9, 134.5, 134.4, 130.4, 130.3, 129.7, 51.3, 51.2, 51.1, 50.6, 49.42, 49.40, 44.2, 35.91, 35.89, 31.29, 31.27, 30.12, 30.09, 26.4, 26.3, 25.2, 25.1, 23.1, 23.0, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{22}H_{30}NO_3^+$ $[M+H]^+$ 356.2220, found 356.2194.



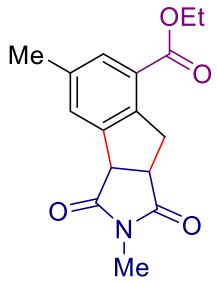
7-(3-Cyclohexylpropanoyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (5kb)

5kb was prepared from **4k** (0.16 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; brown oil (44 mg); yield is 76%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.55 (s, 1H), 4.26 (d, *J* = 6.6 Hz, 1H), 3.72 – 3.61 (m, 3H), 2.95 – 2.87 (m, 5H), 2.40 (s, 3H), 1.70 (t, *J* = 13.1 Hz, 5H), 1.56 (q, *J* = 7.3 Hz, 2H), 1.26 – 1.15 (m, 4H), 0.96 – 0.88 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.7, 180.0, 177.5, 139.7, 139.4, 137.9, 134.0, 130.3, 129.7, 51.1, 44.2, 37.4, 37.3, 35.9, 33.3, 31.7, 26.6, 26.3, 25.1, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{22}H_{28}NO_3^+$ $[M+H]^+$ 354.2064, found 354.2054.



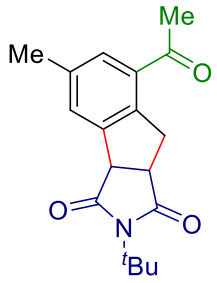
Ethyl 2,5-dimethyl-1,3-dioxo-1,2,3,3a,8,8a-hexahydroindeno[1,2-c]pyrrole-7-carboxylate (5ob)

5ob was prepared from **4o** (0.22 mmol) and **2b** according to general procedure 2.c; eluent is 10% EtOAc in hexane; off white solid (24 mg); yield is 37%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (s, 1H), 7.56 (s, 1H), 4.34 (q, *J* = 7.3 Hz, 2H), 4.29 (d, *J* = 7.0 Hz, 1H), 3.79 – 3.60 (m, 3H), 2.92 (s, 3H), 2.38 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 180.0, 177.5, 166.4, 140.6, 138.9, 138.0, 131.5, 130.1, 127.3, 61.1, 51.4, 43.9, 35.9, 25.2, 21.1, 14.5.

HRMS (ESI-TOF): m/z was calculated for $C_{16}H_{17}NNaO_4^+$ $[M+Na]^+$ 310.1050, found 310.1052.



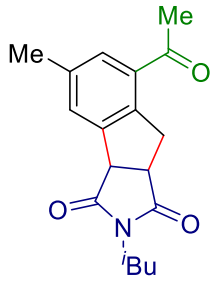
7-Acetyl-2-(*tert*-butyl)-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ac)

3ac was prepared from **1a** (0.27 mmol) and **2c** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light brown solid (49 mg); yield is 61%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.55 (s, 1H), 4.08 (d, *J* = 8.4 Hz, 1H), 3.72 – 3.45 (m, 3H), 2.57 (s, 3H), 2.41 (s, 3H), 1.50 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.1, 181.0, 178.4, 140.2, 139.9, 137.9, 134.0, 131.1, 130.1, 58.5, 50.9, 44.1, 36.5, 28.4, 28.1, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{18}H_{22}NO_3^+$ $[M+H]^+$ 300.1594, found 300.1585.



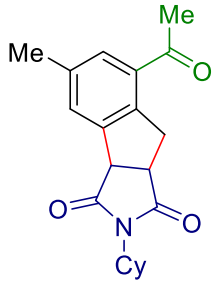
7-Acetyl-2-isobutyl-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ad)

3ad was prepared from **1a** (0.27 mmol) and **2d** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light brown solid (56 mg); yield is 69%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (s, 1H), 7.59 (s, 1H), 4.27 (d, *J* = 7.0 Hz, 1H), 3.79 – 3.64 (m, 3H), 3.25 (dd, *J* = 7.4, 2.3 Hz, 2H), 2.58 (s, 3H), 2.43 (s, 3H), 2.00 – 1.91 (m, 1H), 0.77 (dd, *J* = 9.9, 6.7 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 180.1, 177.7, 139.7, 138.0, 134.0, 131.2, 130.0, 50.9, 46.2, 44.1, 36.2, 28.0, 27.1, 21.3, 20.1, 20.0.

HRMS (ESI-TOF): m/z was calculated for $C_{18}H_{22}NO_3^+$ $[M+H]^+$ 300.1594, found 300.1586.



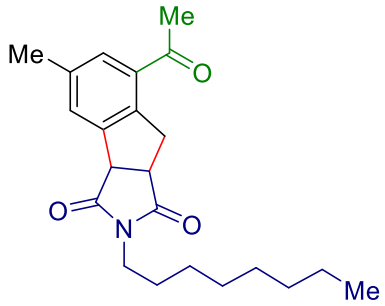
7-Acetyl-2-cyclohexyl-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ae)

3ae was prepared from **1a** (0.27 mmol) and **2e** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light brown solid (53 mg); yield is 60%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.56 (s, 1H), 4.16 (d, *J* = 7.7 Hz, 1H), 3.87 (tt, *J* = 12.3, 4.0 Hz, 1H), 3.72 – 3.53 (m, 3H), 2.56 (s, 3H), 2.41 (s, 3H), 2.11 – 1.98 (m, 2H), 1.75 (d, *J* = 11.2 Hz, 2H), 1.60 (d, *J* = 11.4 Hz, 1H), 1.51 – 1.42 (m, 2H), 1.28 – 1.14 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 180.0, 177.6, 139.8, 137.9, 134.0, 131.1, 130.0, 51.9, 50.8, 43.9, 36.3, 28.9, 28.7, 28.0, 25.9, 25.8, 25.1, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{23}NNaO_3^+$ $[M+Na]^+$ 348.1570, found 348.1581.



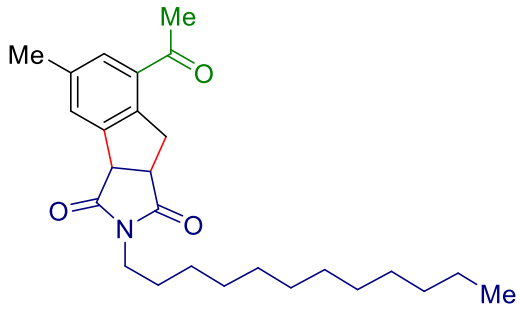
7-Acetyl-5-methyl-2-octyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3af)

3af was prepared from **1a** (0.27 mmol) and **2f** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light brown solid (60 mg); yield is 63%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.57 (s, 1H), 4.23 (d, *J* = 7.1 Hz, 1H), 3.75 – 3.59 (m, 3H), 3.38 (t, *J* = 7.5 Hz, 2H), 2.55 (s, 3H), 2.40 (s, 3H), 1.45 (p, *J* = 7.3 Hz, 2H), 1.24 – 1.14 (m, 10H), 0.83 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 179.9, 177.5, 139.7, 139.6, 138.0, 134.0, 131.1, 130.0, 51.0, 44.1, 39.1, 36.1, 31.7, 29.1, 29.1, 28.0, 27.6, 26.7, 22.7, 21.2, 14.1.

HRMS (ESI-TOF): m/z was calculated for $C_{22}H_{30}NO_3^+$ $[M+H]^+$ 356.2220, found 356.2189.



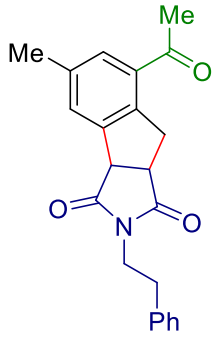
7-Acetyl-2-dodecyl-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ag)

3ag was prepared from **1a** (0.27 mmol) and **2g** according to general procedure 2.c; eluent is 10% EtOAc in hexane; light brown solid (67 mg); yield is 60%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.58 (s, 1H), 4.24 (d, *J* = 7.1 Hz, 1H), 3.77 – 3.59 (m, 3H), 3.39 (t, *J* = 7.4 Hz, 2H), 2.56 (s, 3H), 2.41 (s, 3H), 1.46 (p, *J* = 6.9 Hz, 2H), 1.28 – 1.15 (m, 18H), 0.86 (t, *J* = 6.7 Hz, 3H).

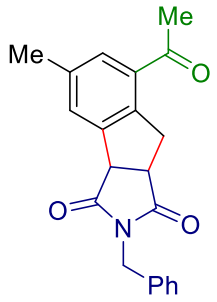
^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.9, 179.9, 177.5, 139.8, 139.7, 138.0, 134.0, 131.2, 130.1, 51.0, 44.2, 39.1, 36.1, 32.0, 29.7, 29.6, 29.5, 29.4, 29.2, 28.0, 27.7, 26.8, 22.8, 21.3, 14.2.

HRMS (ESI-TOF): m/z was calculated for $C_{26}H_{41}N_2O_3^+$ $[M+NH_4]^+$ 429.3112, found 429.3137.

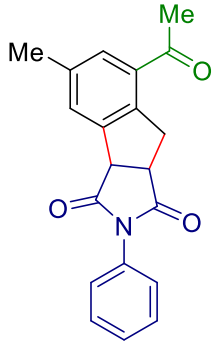


7-Acetyl-5-methyl-2-phenethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ah)

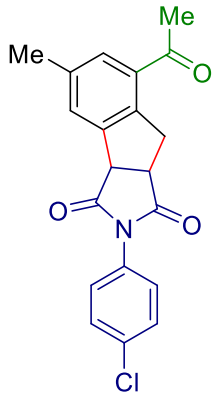
3ah was prepared from **1a** (0.27 mmol) and **2h** according to general procedure 2.c; eluent is 10% EtOAc in hexane; yellow liquid (43 mg); yield is 46%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (s, 1H), 7.51 (s, 1H), 7.08 – 7.02 (m, 3H), 6.95 (d, *J* = 5.9 Hz, 2H), 4.17 (d, *J* = 7.3 Hz, 1H), 3.68 (t, *J* = 7.4 Hz, 2H), 3.61 – 3.52 (m, 3H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.58 (s, 3H), 2.42 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.9, 179.6, 177.2, 139.7, 139.5, 137.9, 137.4, 133.9, 131.1, 130.0, 128.8, 128.3, 126.5, 50.9, 43.9, 39.9, 36.1, 33.2, 28.0, 21.3.
HRMS (ESI-TOF): m/z was calculated for $C_{22}H_{22}NO_3^+$ $[M+H]^+$ 348.1594, found 348.1601.



7-Acetyl-2-benzyl-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ai)
3ai was prepared from **1a** (0.27 mmol) and **2i** according to general procedure 2.c; eluent is 15% EtOAc in hexane; light yellow solid (42 mg); yield is 47%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (s, 1H), 7.59 (s, 1H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.28 – 7.22 (m, 3H), 4.62 – 4.51 (m, 2H), 4.27 (d, *J* = 7.1 Hz, 1H), 3.79 – 3.61 (m, 3H), 2.57 (s, 3H), 2.42 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 179.5, 177.1, 139.8, 139.4, 138.0, 135.7, 133.9, 131.2, 130.1, 128.7, 128.7, 128.0, 51.1, 44.2, 42.6, 36.0, 28.0, 21.2.
HRMS (ESI-TOF): m/z was calculated for $C_{21}H_{20}NO_3^+$ $[M+H]^+$ 334.1438, found 334.1431.



7-Acetyl-5-methyl-2-phenyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3aj)
3aj was prepared from **1a** (0.27 mmol) and **2j** according to general procedure 2.c; eluent is 20% EtOAc in hexane; light brown solid (28 mg); yield is 33%.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (s, 1H), 7.64 (s, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 2H), 4.42 (d, *J* = 8.8 Hz, 1H), 3.90 – 3.69 (m, 3H), 2.59 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.0, 178.9, 176.4, 139.9, 139.4, 138.2, 134.1, 131.9, 131.4, 130.2, 129.2, 128.7, 126.5, 51.1, 44.4, 36.4, 28.0, 21.3.
HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{18}NO_3^+$ $[M+H]^+$ 320.1281, found 320.1258.



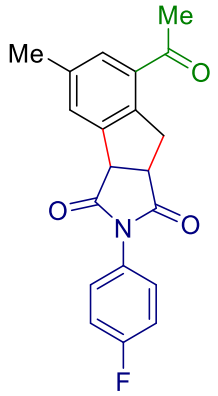
7-Acetyl-2-(4-chlorophenyl)-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3ak)

3ak was prepared from **1a** (0.27 mmol) and **2k** according to general procedure 2.c; eluent is 20% EtOAc in hexane; light brown solid (39 mg); yield is 41%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (s, 1H), 7.63 (s, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 4.42 (d, *J* = 7.9 Hz, 1H), 3.89 – 3.69 (m, 3H), 2.59 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 178.7, 176.1, 139.8, 139.2, 138.3, 134.4, 134.0, 131.5, 130.3, 130.1, 129.3, 127.7, 51.0, 44.3, 36.4, 28.0, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{16}ClNNaO_3^+$ $[M+Na]^+$ 376.0711, found 376.0715.



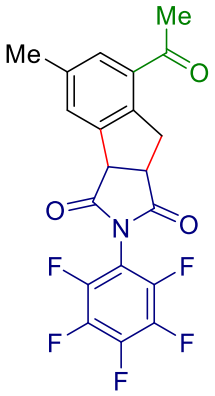
7-Acetyl-2-(4-fluorophenyl)-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3al)

3al was prepared from **1a** (0.27 mmol) and **2l** according to general procedure 2.c; eluent is 20% EtOAc in hexane; yellow solid (30 mg); yield is 33%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (s, 1H), 7.63 (s, 1H), 7.21 (dd, *J* = 8.2, 4.9 Hz, 2H), 7.10 (t, *J* = 8.2 Hz, 2H), 4.43 (d, *J* = 7.9 Hz, 1H), 3.89 – 3.69 (m, 3H), 2.59 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 178.9, 176.3, 162.2 (d, *J* = 249.5 Hz), 139.8, 139.2, 138.3, 134.1, 131.4, 130.2, 128.3 (d, *J* = 9.1 Hz), 127.7 (d, *J* = 3.0 Hz), 116.2 (d, *J* = 23.2 Hz), 51.0, 44.3, 36.4, 28.0, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{17}FNO_3^+$ $[M+H]^+$ 338.1187, found 338.1174.



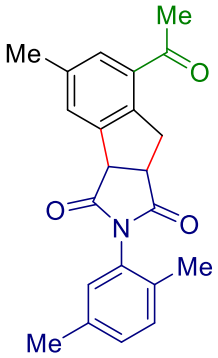
7-Acetyl-5-methyl-2-(perfluorophenyl)-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3am)

3am was prepared from **1a** (0.27 mmol) and **2m** according to general procedure 2.c; eluent is 20% EtOAc in hexane; brown solid (50 mg); yield is 45%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (s, 1H), 7.60 (s, 1H), 4.52 (d, *J* = 8.2 Hz, 1H), 3.99 – 3.72 (m, 3H), 2.60 (s, 3H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.9, 176.5, 174.1, 139.5, 138.6, 138.5, 134.1, 131.8, 123.0, 51.6, 45.1, 36.4, 27.9, 21.3.

HRMS (ESI-TOF): m/z was calculated for $C_{20}H_{12}F_5NNaO_3^+$ $[M+Na]^+$ 432.0630, found 432.0642.



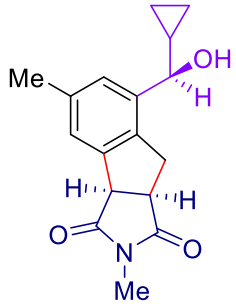
7-Acetyl-2-(2,5-dimethylphenyl)-5-methyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (3an)

3an was prepared from **1a** (0.27 mmol) and **2n** according to general procedure 2.c; eluent is 20% EtOAc in hexane; brown solid (60 mg); yield is 64% (dr 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (s, 2H), 7.64 (s, 2H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 3H), 6.93 (s, 1H), 6.61 (s, 1H), 4.45 (d, *J* = 8.0 Hz, 1H), 4.40 (d, *J* = 7.5 Hz, 1H), 3.91 – 3.68 (m, 6H), 2.59 (s, 6H), 2.44 (s, 3H), 2.43 (s, 3H), 2.32 (s, 3H), 2.22 (s, 3H), 2.14 (s, 3H), 1.58 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.94, 198.89, 179.0, 178.9, 176.5, 176.4, 139.8, 139.7, 139.6, 139.4, 138.2, 138.1, 136.9, 136.8, 134.1, 134.0, 132.4, 132.3, 131.4, 131.3, 131.0, 130.9, 130.7, 130.6, 130.4, 130.2, 130.0, 128.5, 128.2, 51.35, 51.30, 44.7, 44.5, 36.5, 36.2, 28.0, 21.25, 21.23, 20.9, 20.7, 17.4, 16.6.

HRMS (ESI-TOF): m/z was calculated for $C_{22}H_{22}NO_3^+$ $[M+H]^+$ 348.1594, found 348.1611.



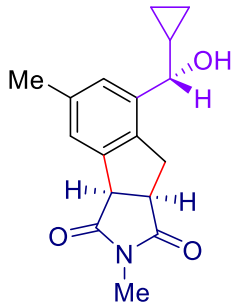
(3aR,8aR)-7-((R)-cyclopropyl(hydroxy)methyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (6R)

Eluent is 30% EtOAc in hexane; light brown liquid; yield is 23%.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (s, 1H), 7.23 (s, 1H), 4.29 (d, *J* = 7.9 Hz, 1H), 4.07 (d, *J* = 8.4 Hz, 1H), 3.62 (ddd, *J* = 10.5, 7.9, 2.6 Hz, 1H), 3.51 – 3.30 (m, 2H), 2.92 (s, 3H), 2.36 (s, 3H), 1.68 (s, 1H), 1.24 – 1.19 (m, 1H), 0.62 (td, *J* = 8.3, 3.9 Hz, 1H), 0.53 (tt, *J* = 9.1, 4.3 Hz, 1H), 0.44 – 0.33 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.2, 177.7, 140.1, 138.2, 137.9, 135.8, 127.3, 125.0, 76.6, 51.7, 44.2, 33.4, 25.2, 21.4, 18.4, 3.5, 3.0.

HRMS (ESI-TOF): m/z was calculated for $C_{17}H_{19}NNaO_3^+$ $[M+H]^+$ 308.1257, found 308.1235.



(3aR,8aR)-7-((S)-cyclopropyl(hydroxy)methyl)-2,5-dimethyl-8,8a-dihydroindeno[1,2-c]pyrrole-1,3(2H,3aH)-dione (6S)

Eluent is 30% EtOAc in hexane; light brown liquid; yield is 23%.

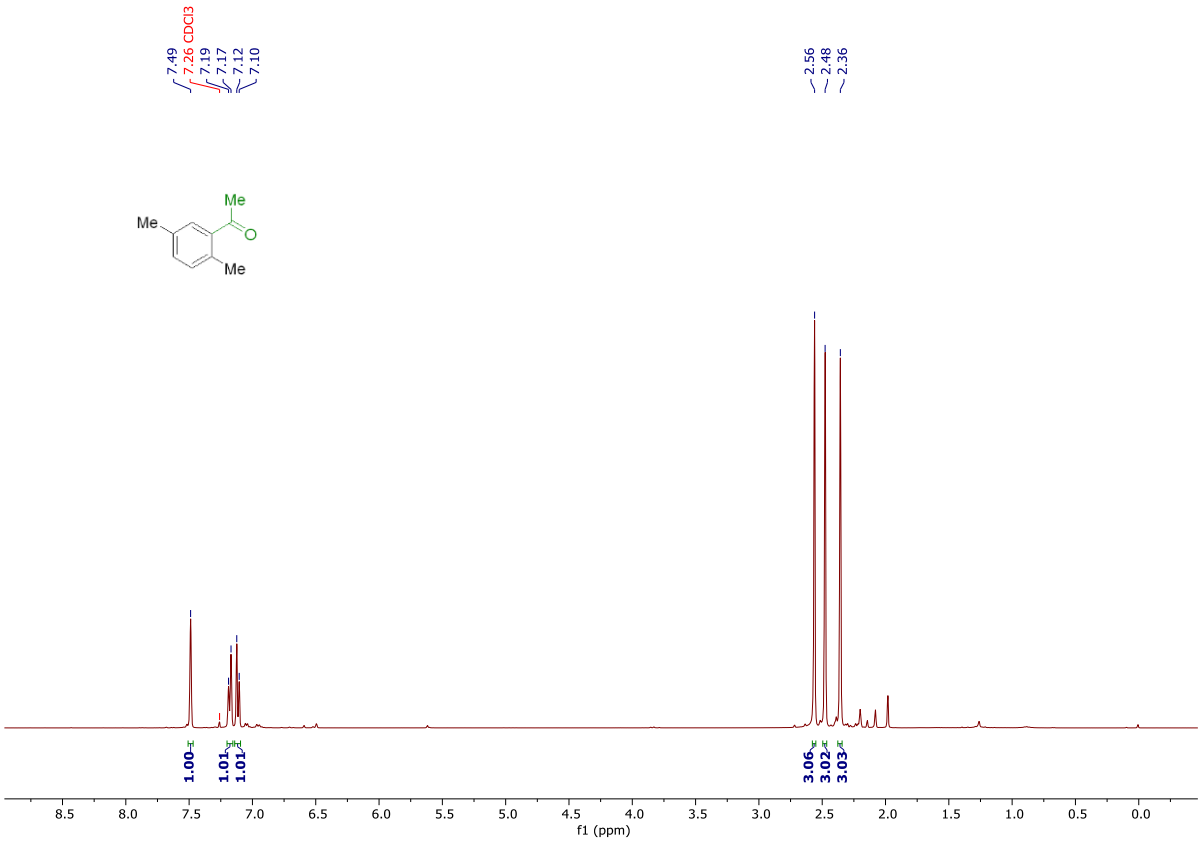
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (s, 1H), 7.23 (s, 1H), 4.28 (d, *J* = 8.0 Hz, 1H), 4.07 (d, *J* = 8.2 Hz, 1H), 3.63 (td, *J* = 8.0, 5.3 Hz, 1H), 3.43 (d, *J* = 7.8 Hz, 2H), 2.93 (s, 3H), 2.36 (s, 3H), 1.65 (s, 1H), 1.29 (dd, *J* = 5.2, 2.8 Hz, 1H), 0.64 (td, *J* = 8.4, 4.0 Hz, 1H), 0.54 (tt, *J* = 8.9, 4.9 Hz, 1H), 0.41 (dq, *J* = 9.7, 4.8 Hz, 1H), 0.33 (dq, *J* = 9.9, 5.0 Hz, 1H).

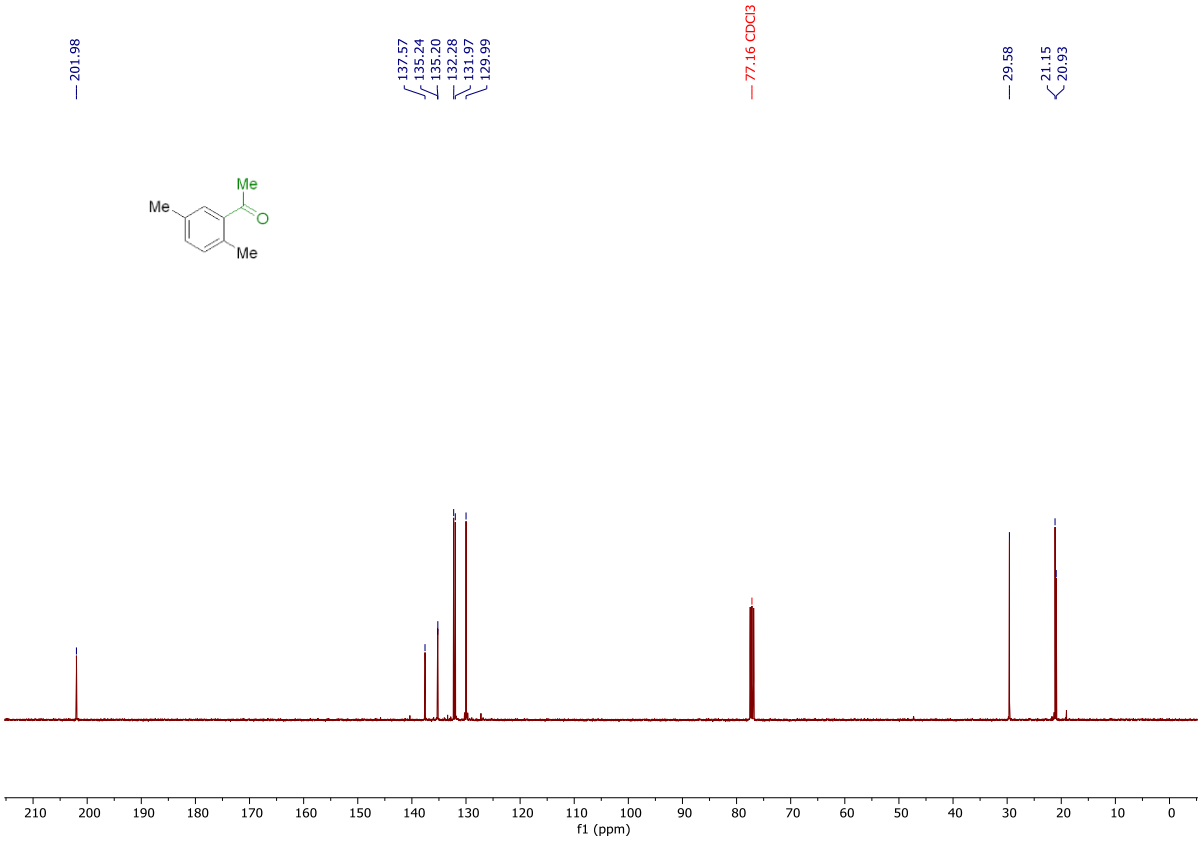
^{13}C NMR (101 MHz, $CDCl_3$) δ 180.3, 177.6, 139.8, 138.2, 138.0, 136.2, 127.4, 125.1, 76.5, 51.7, 44.2, 33.3, 25.2, 21.4, 17.8, 3.6, 2.9.

HRMS (ESI-TOF): m/z was calculated for $C_{17}H_{19}NNaO_3^+$ $[M+H]^+$ 308.1257, found 308.1233.

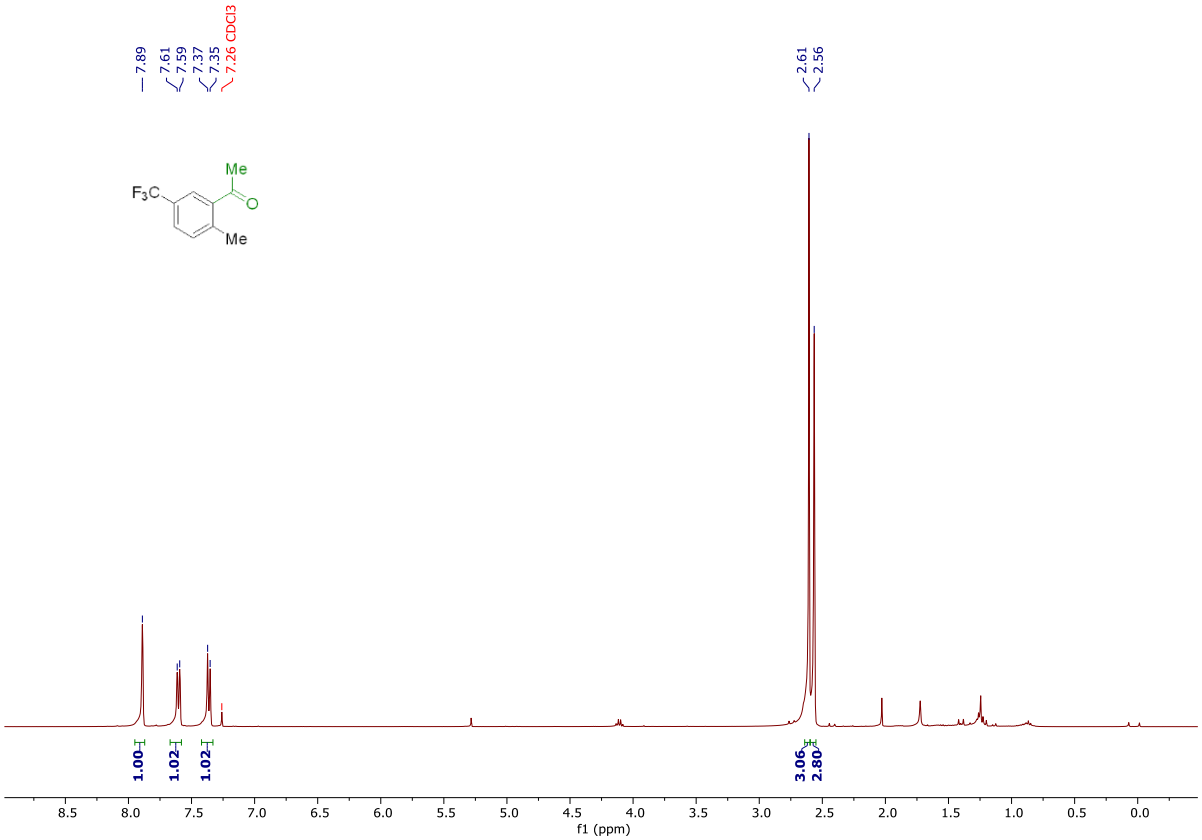
5. ^{1}H and ^{13}C NMR Spectra

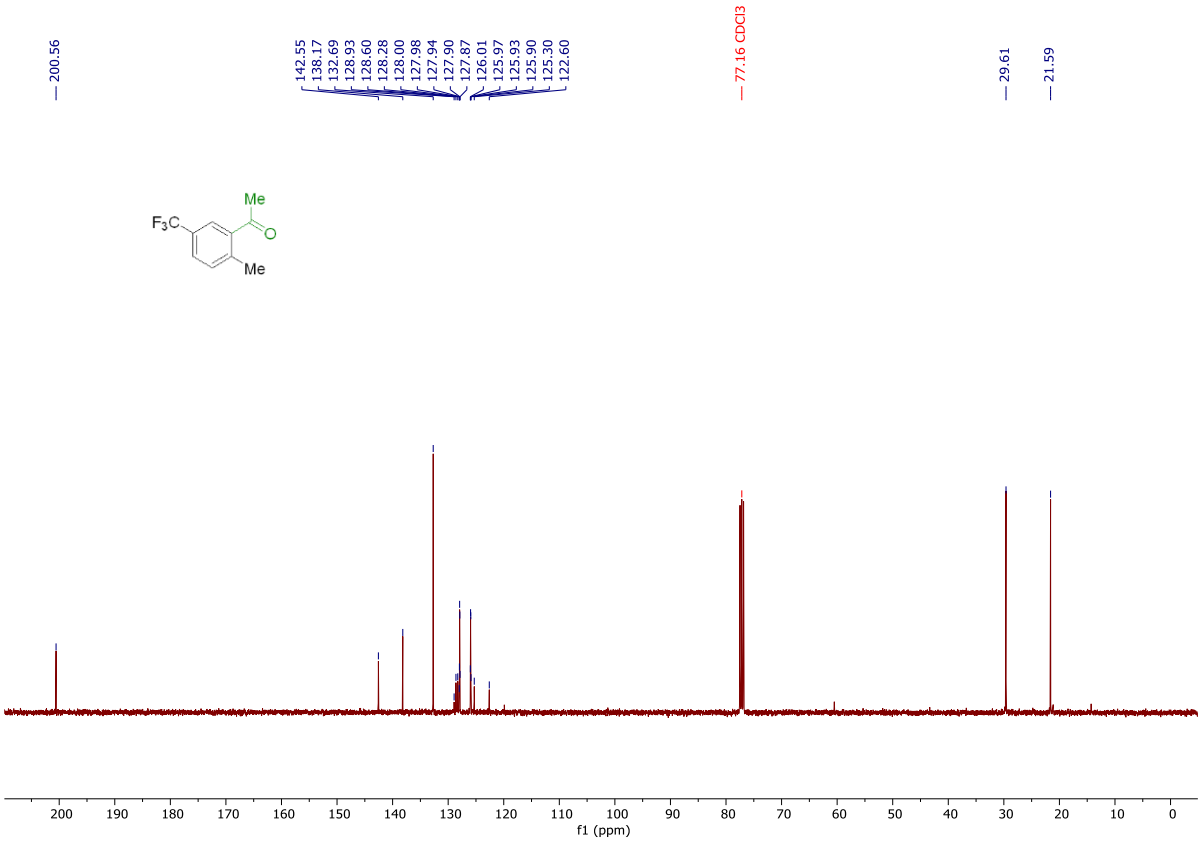
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1a



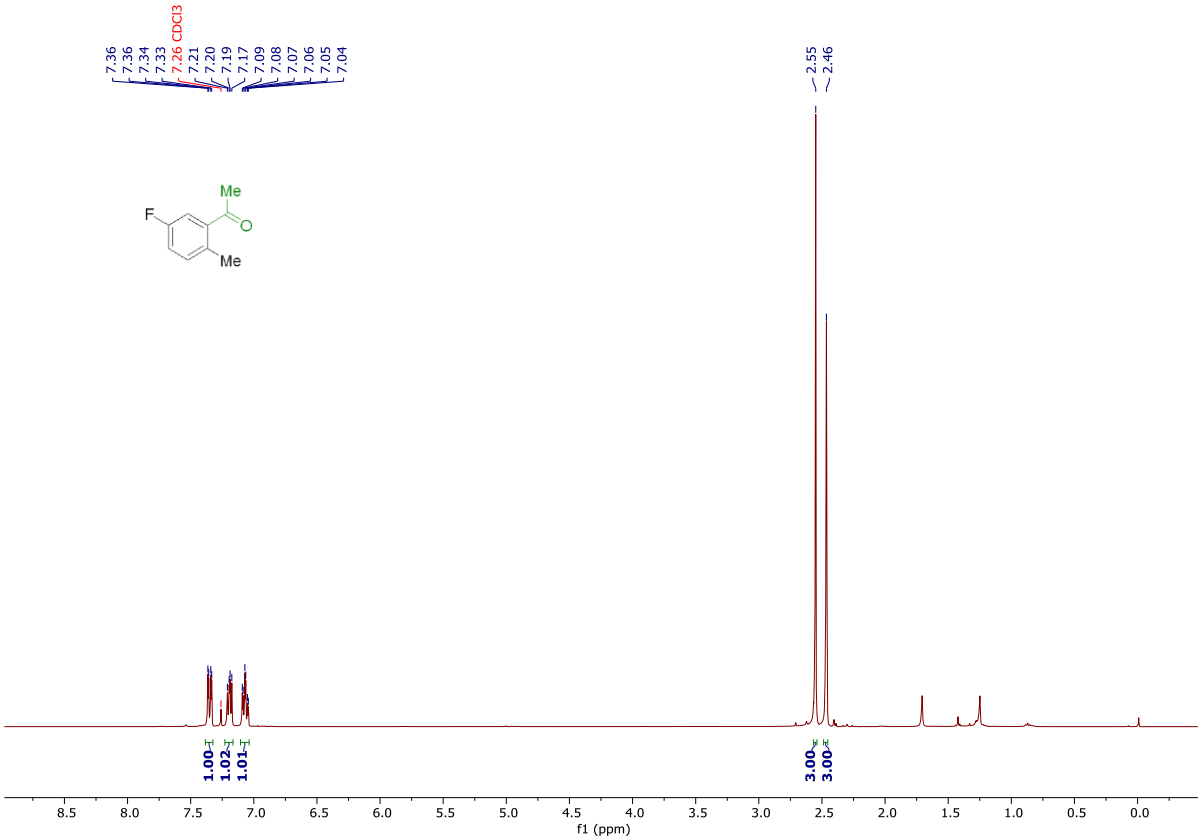


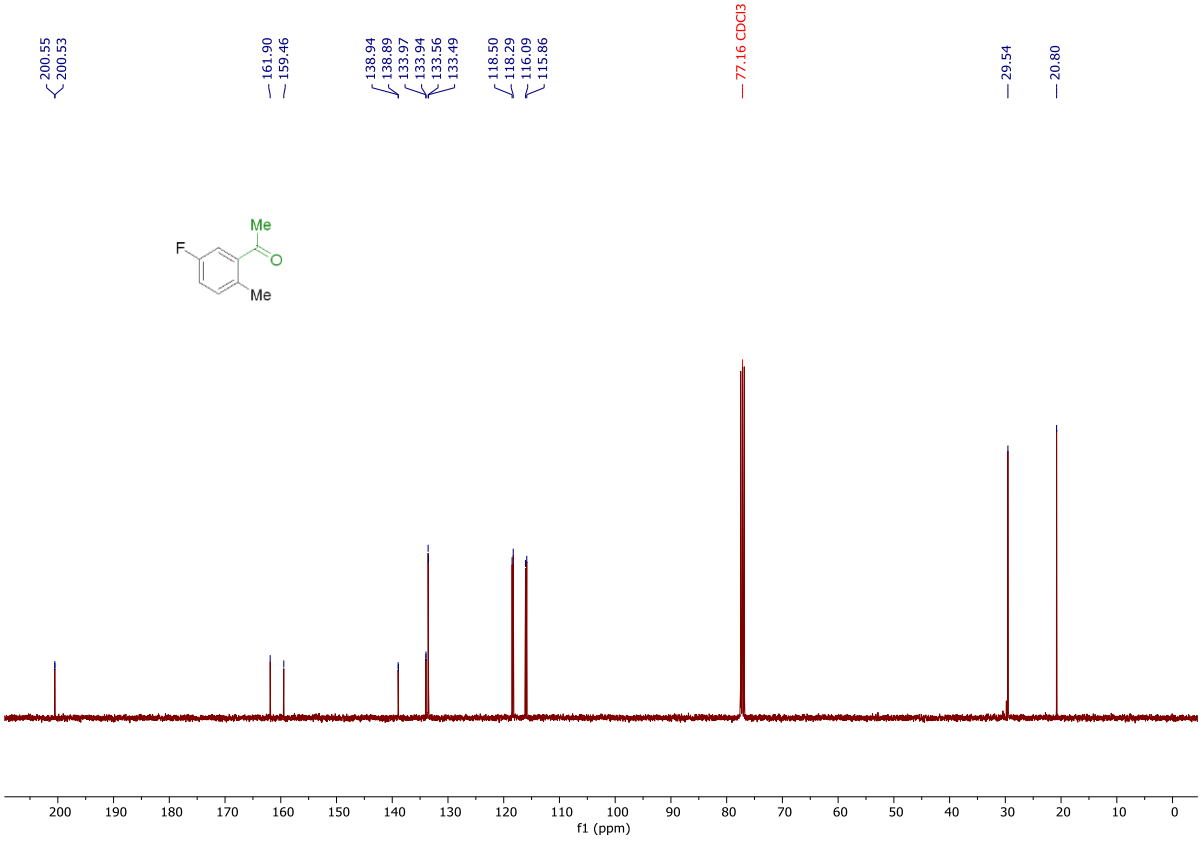
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1b



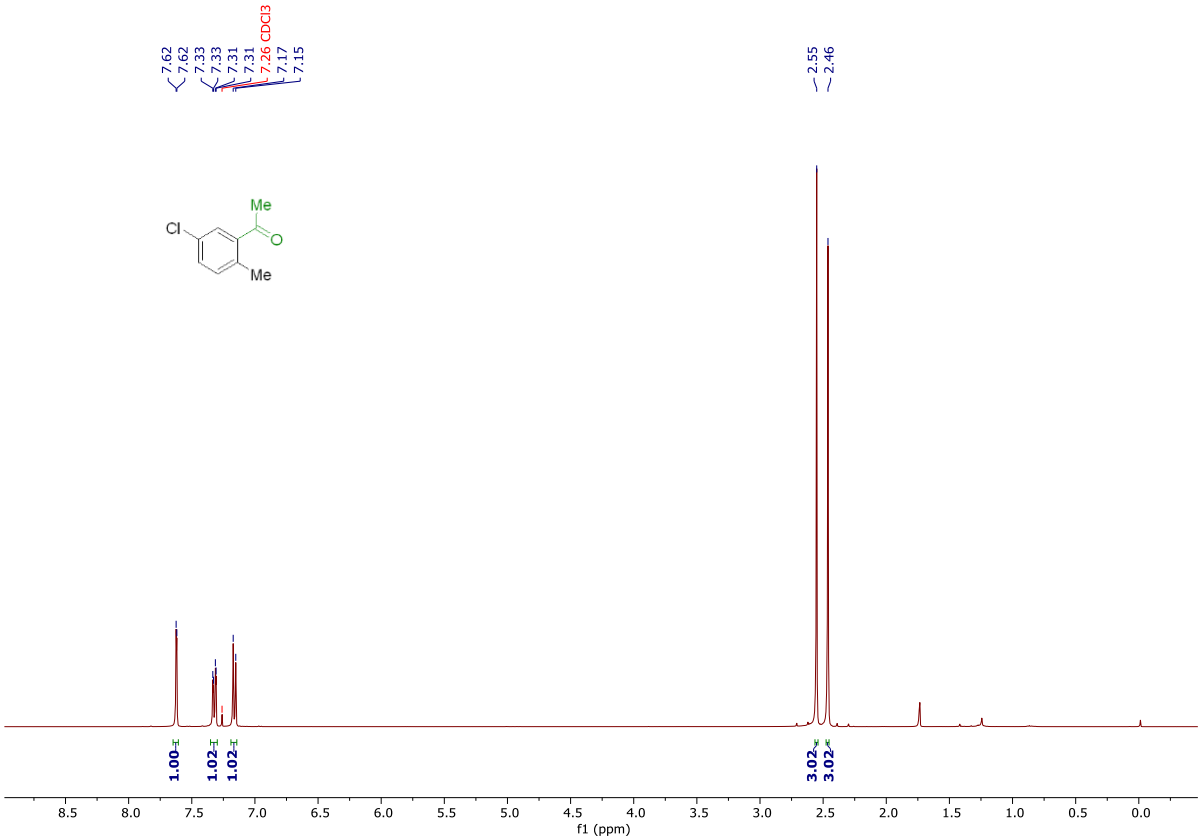


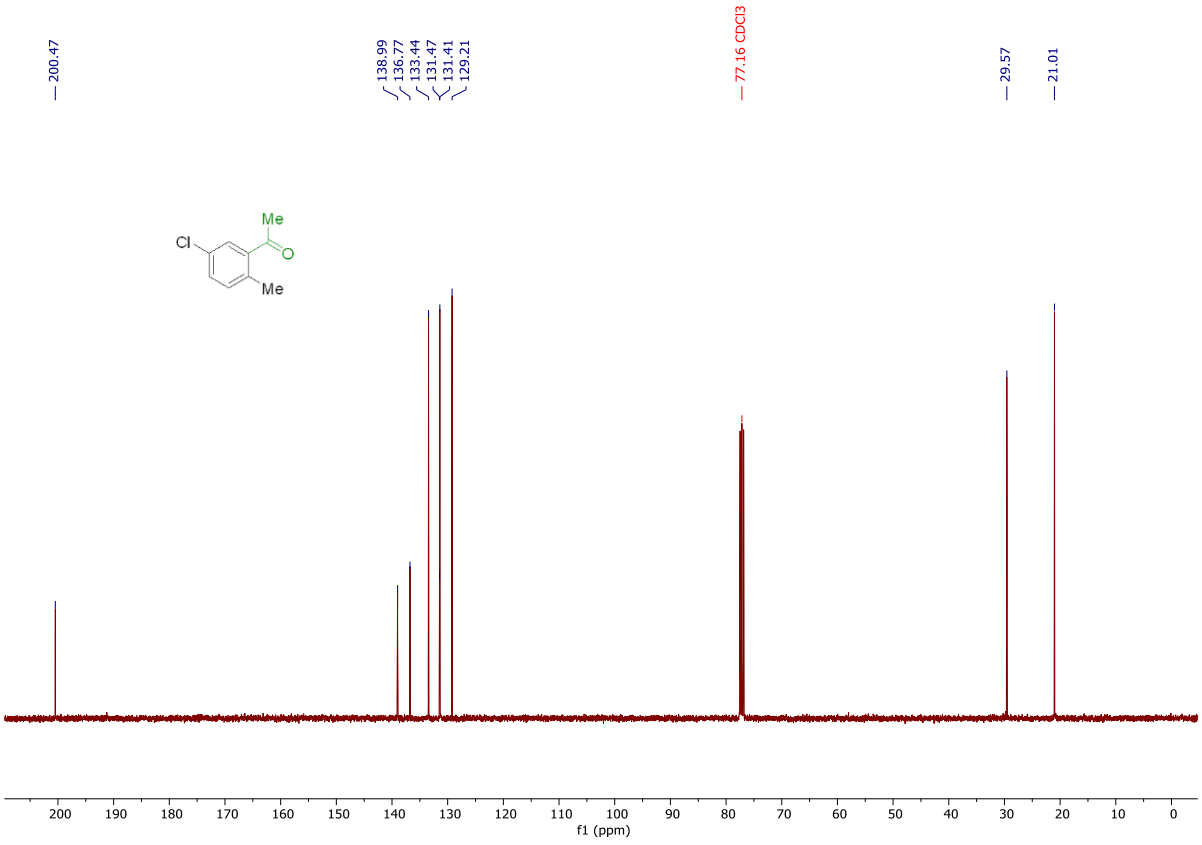
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1c



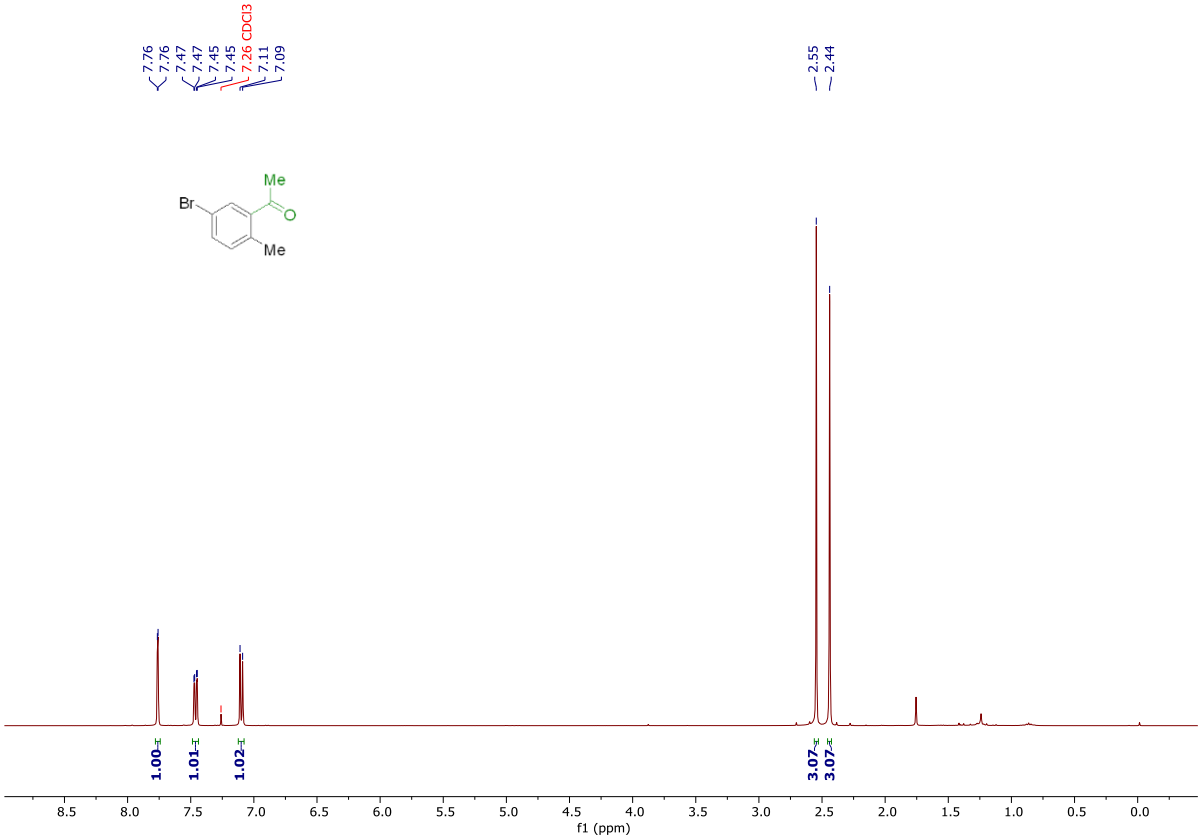


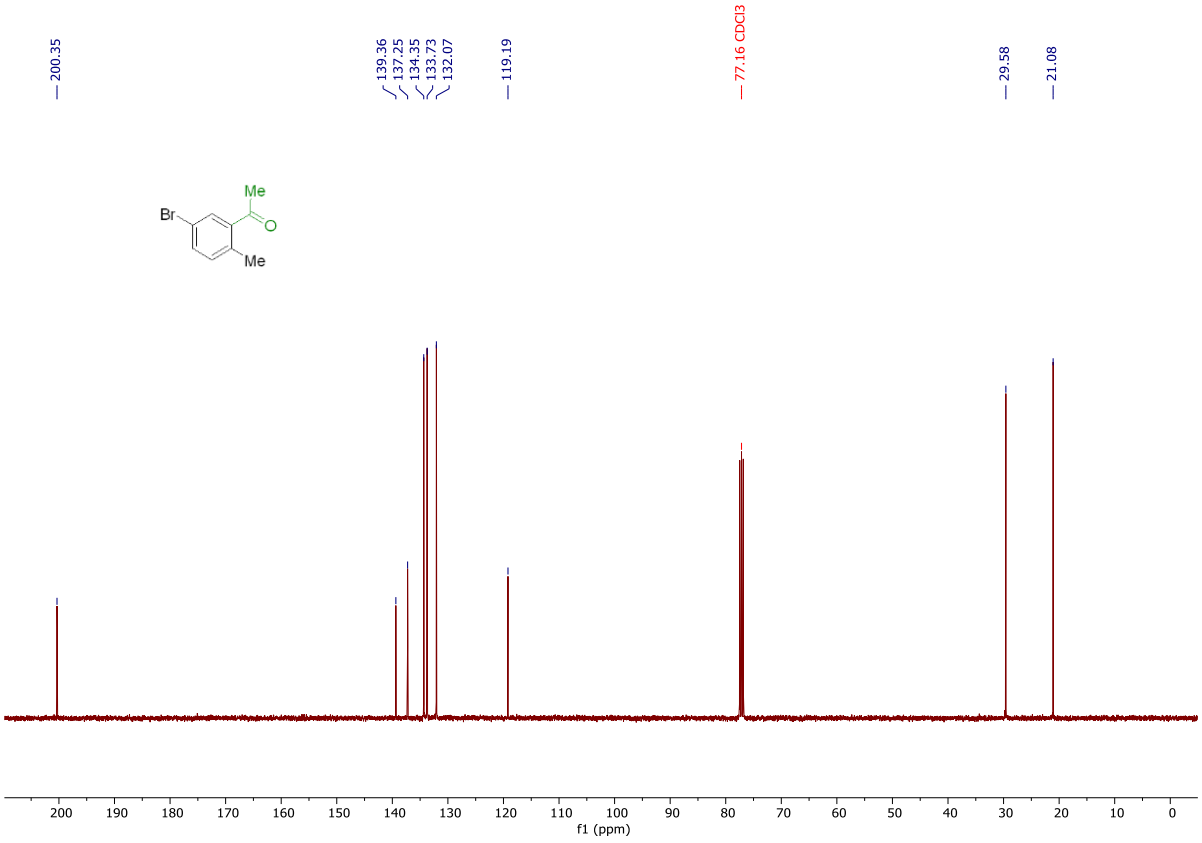
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1d



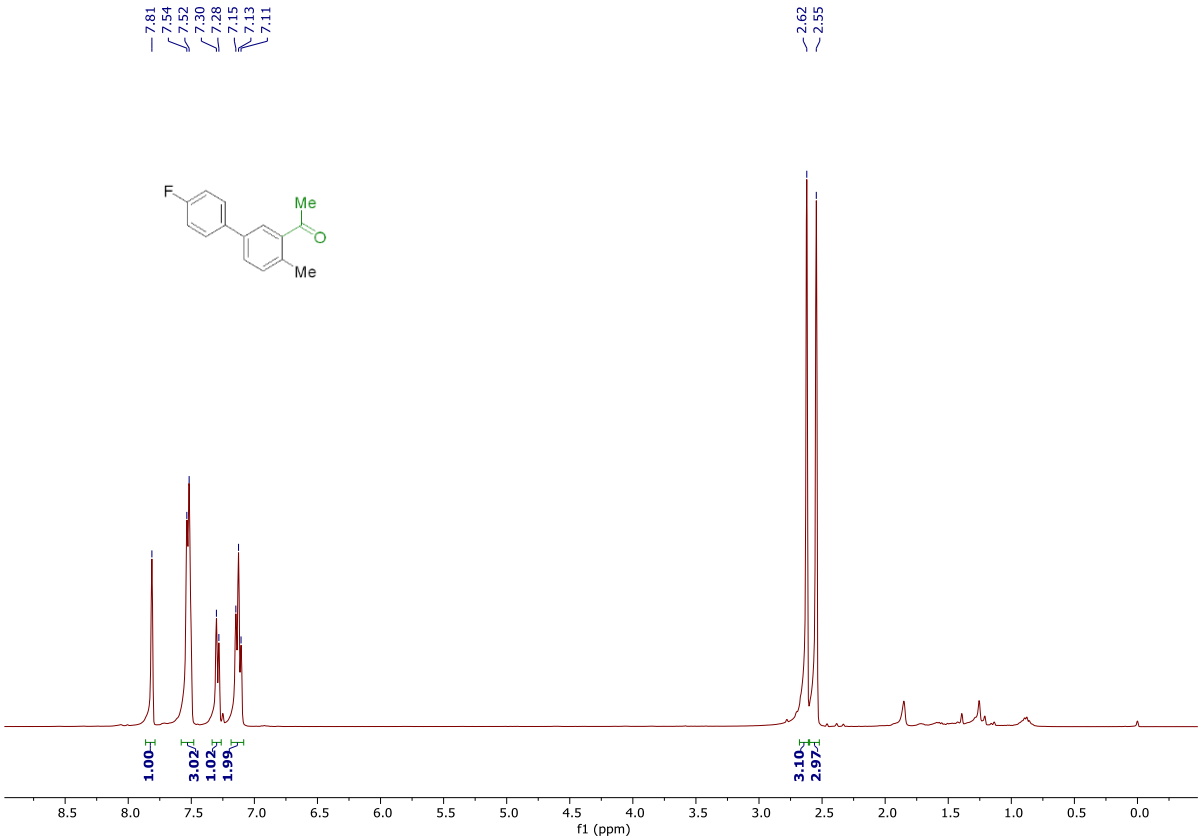


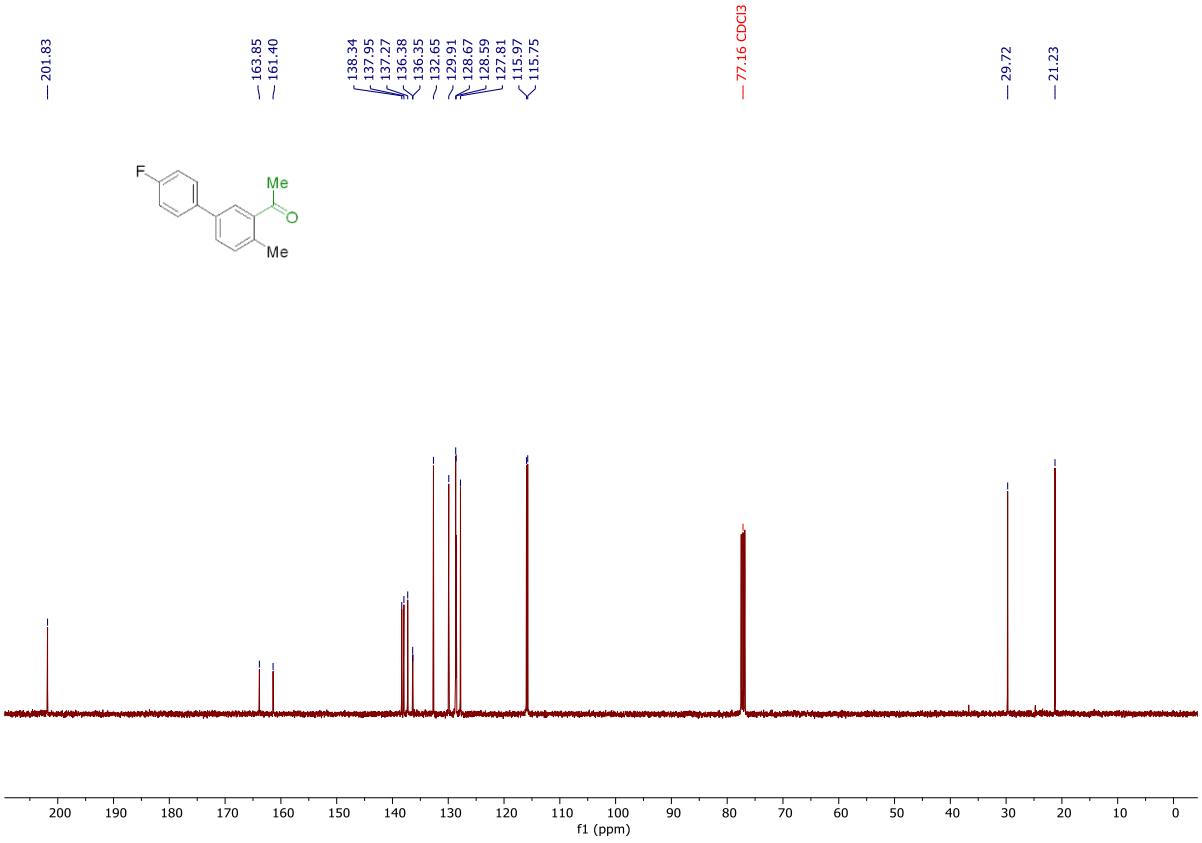
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1e



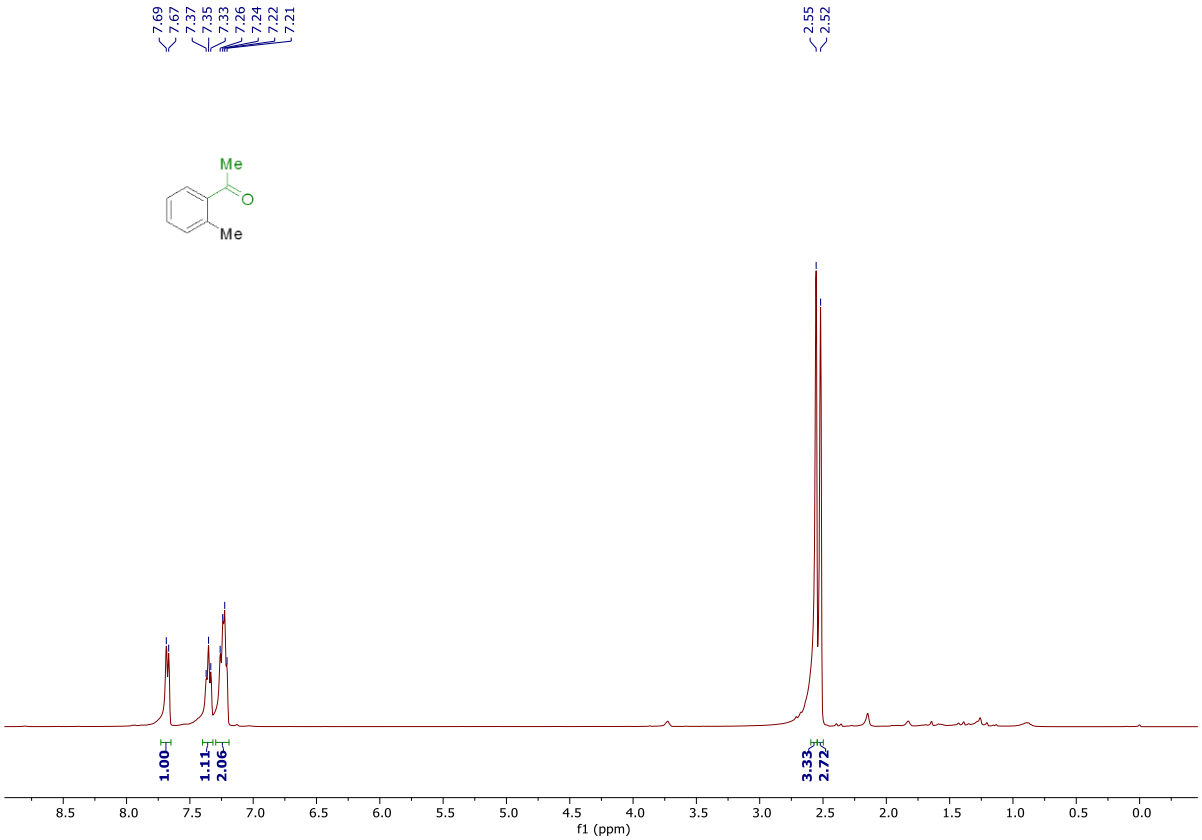


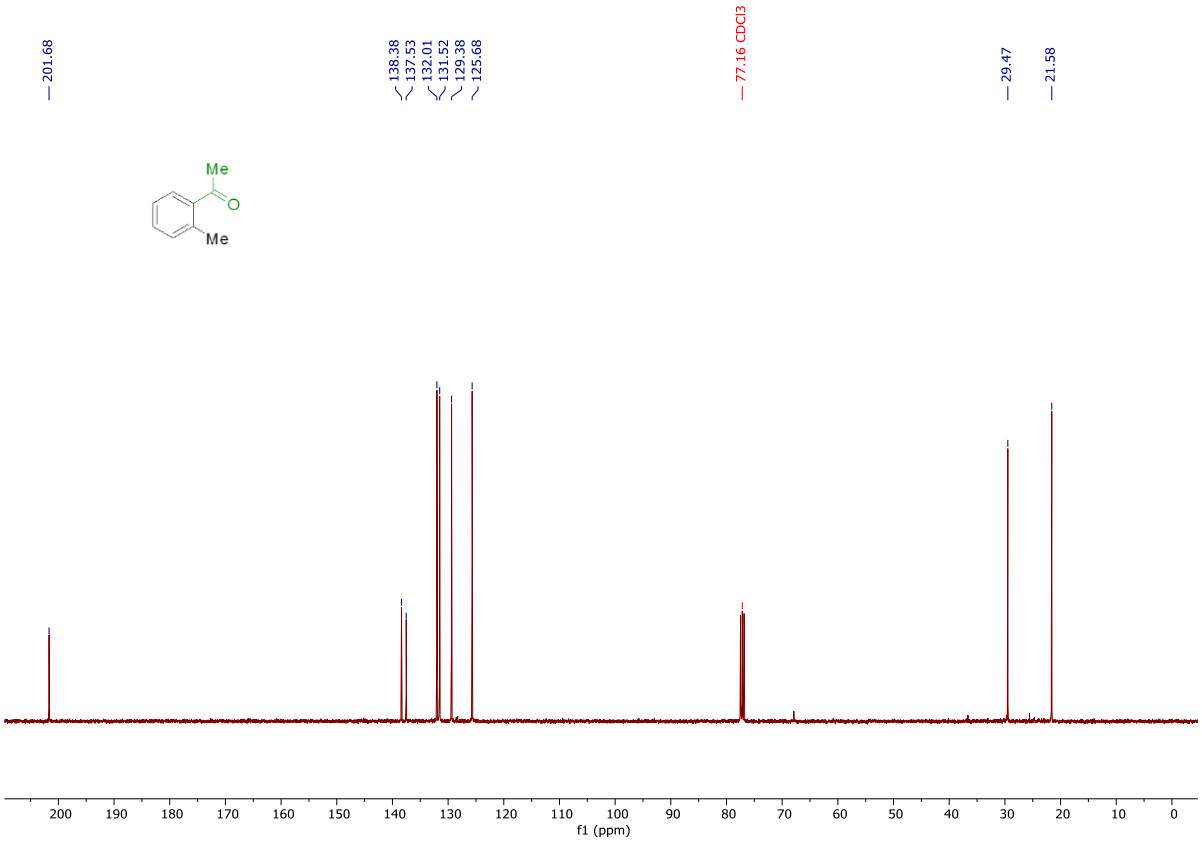
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1g



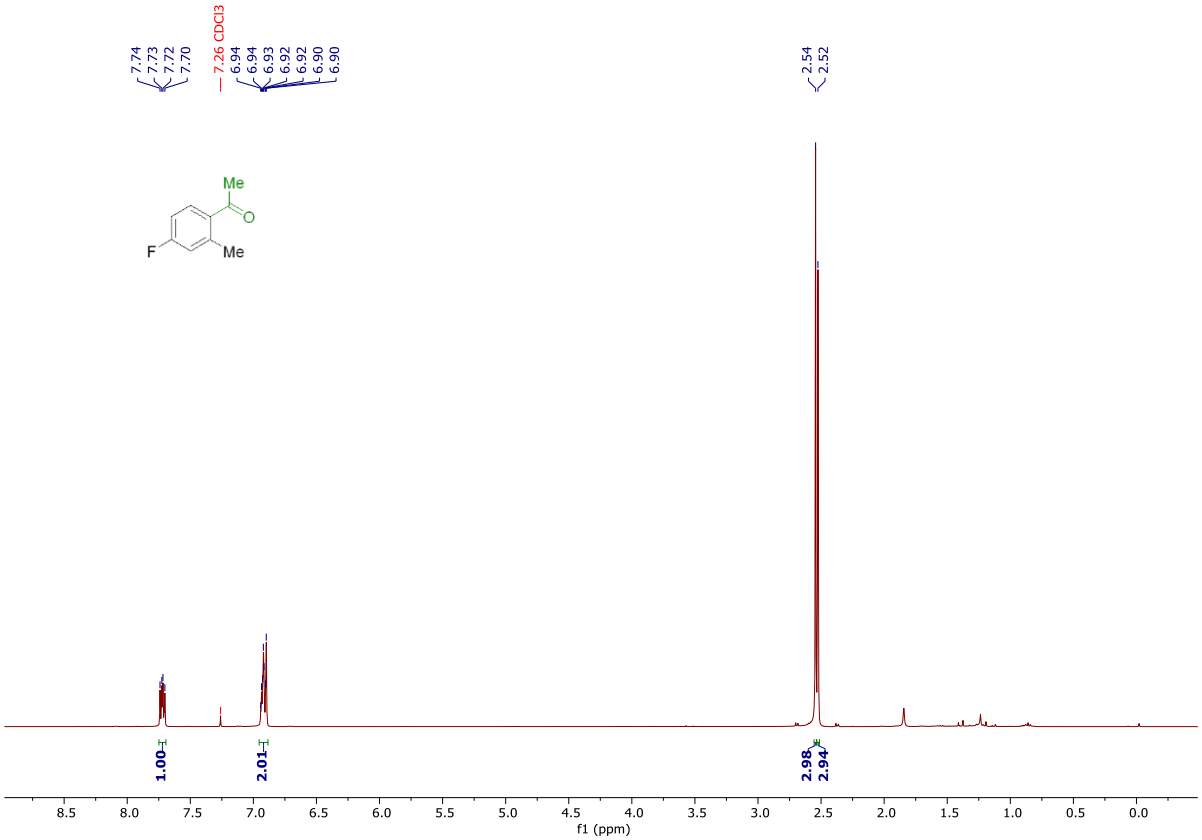


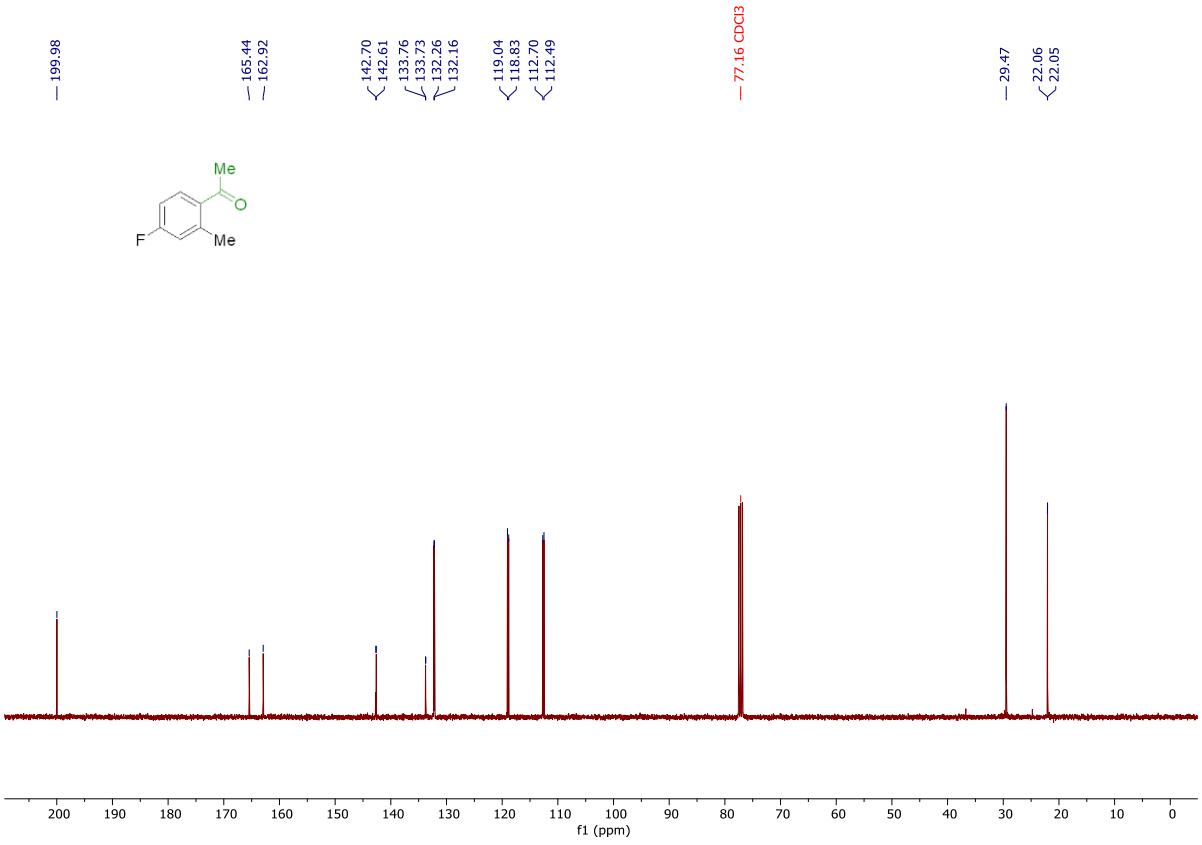
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1h



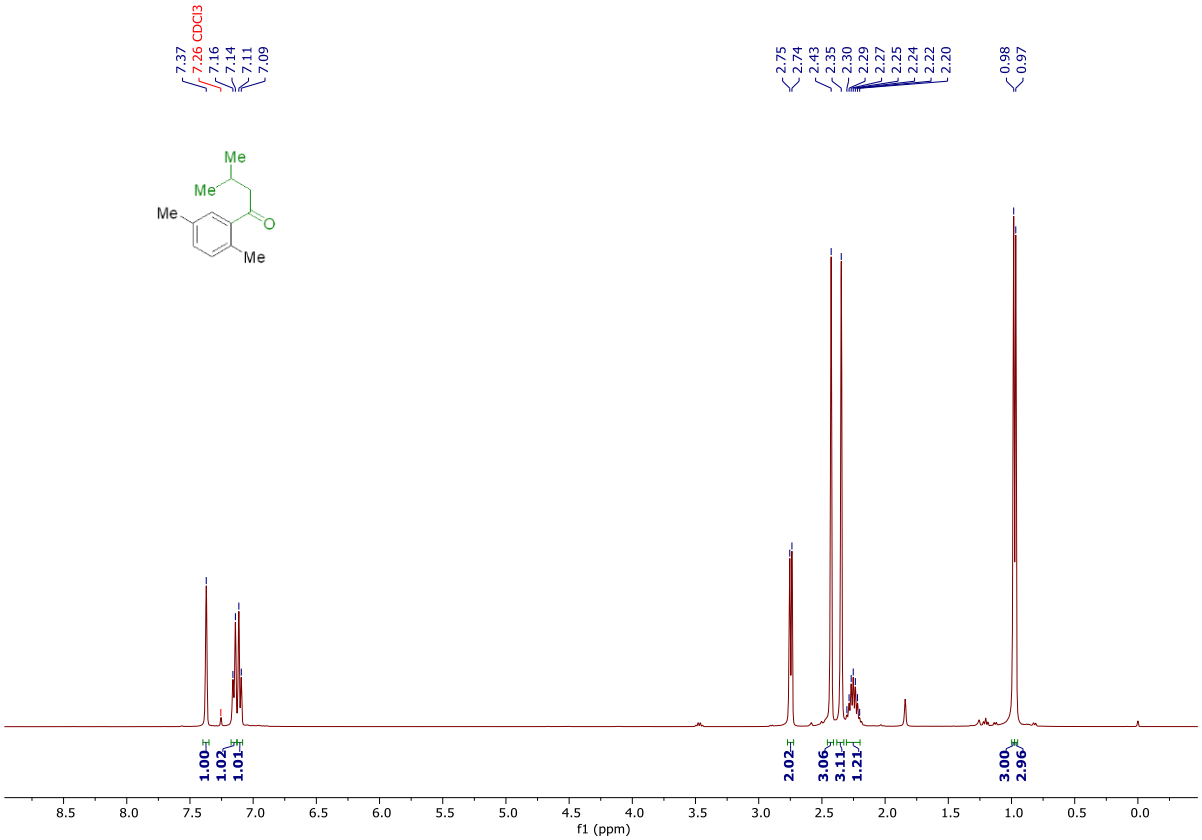


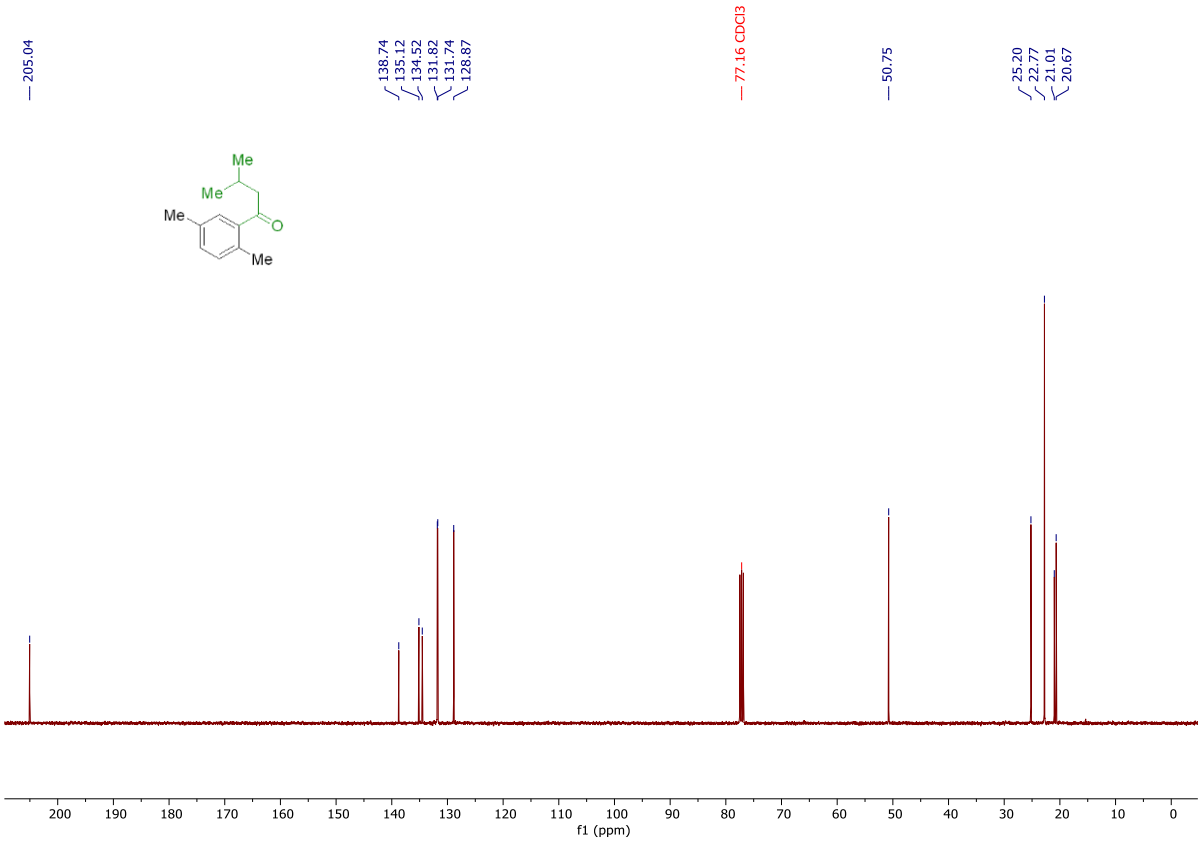
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 1i



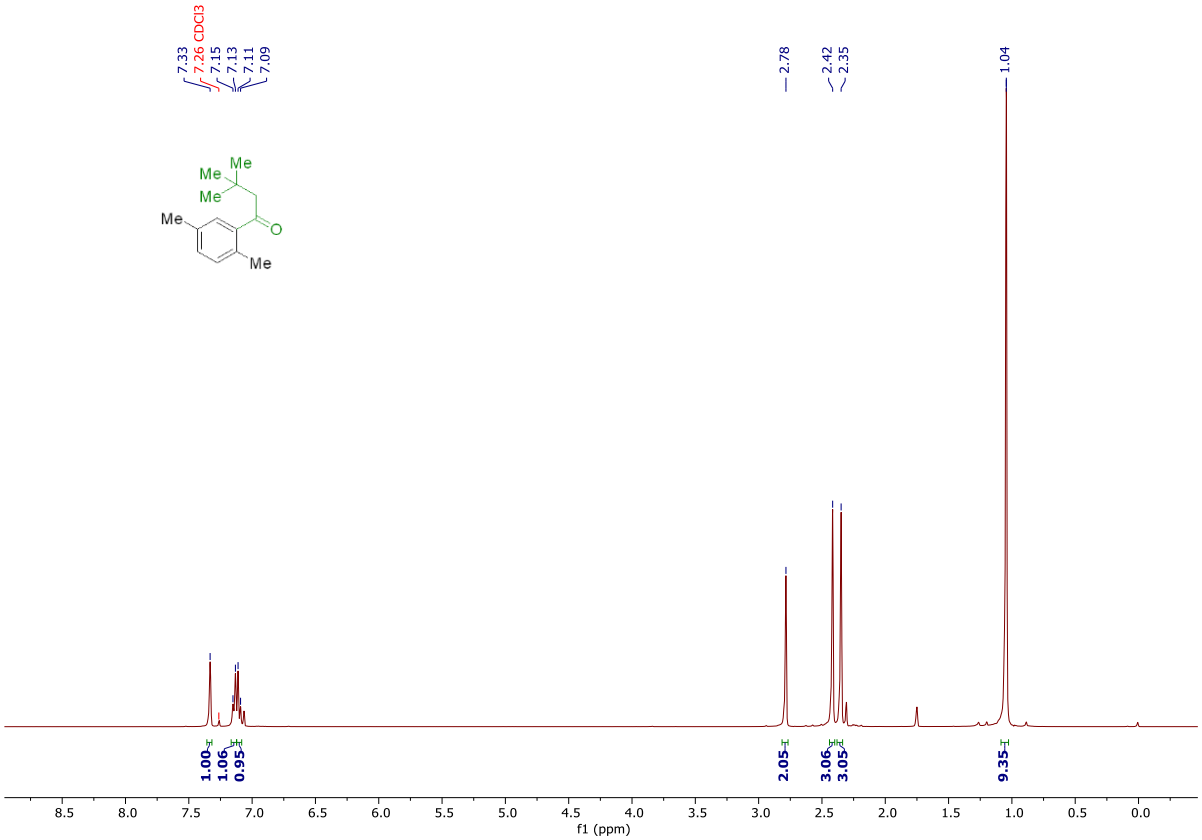


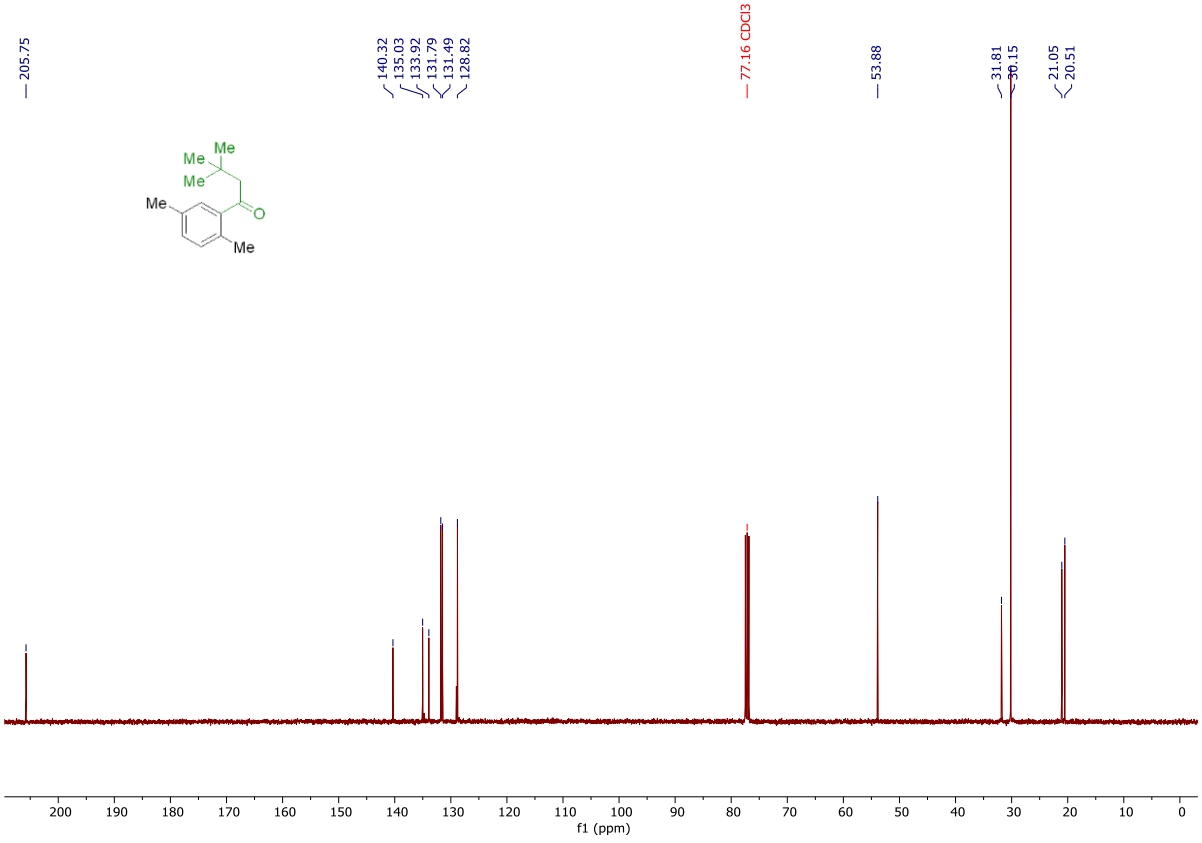
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4b



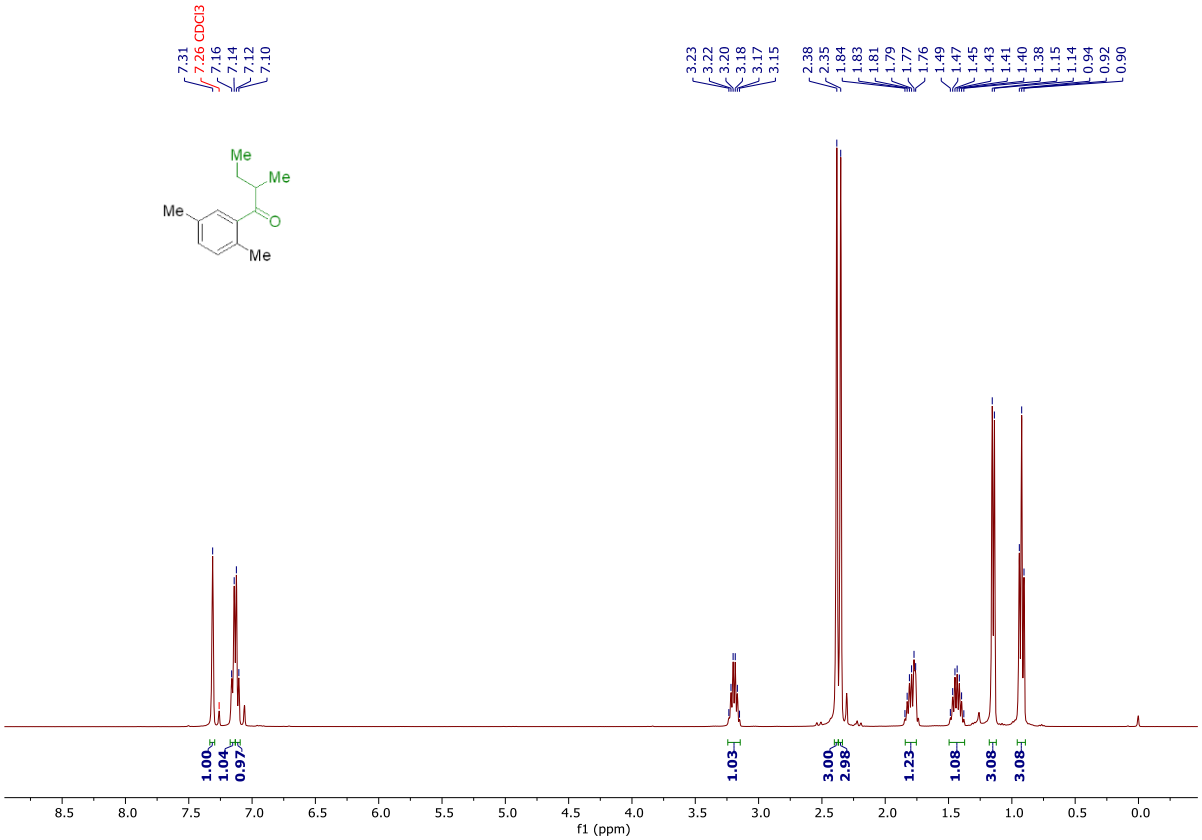


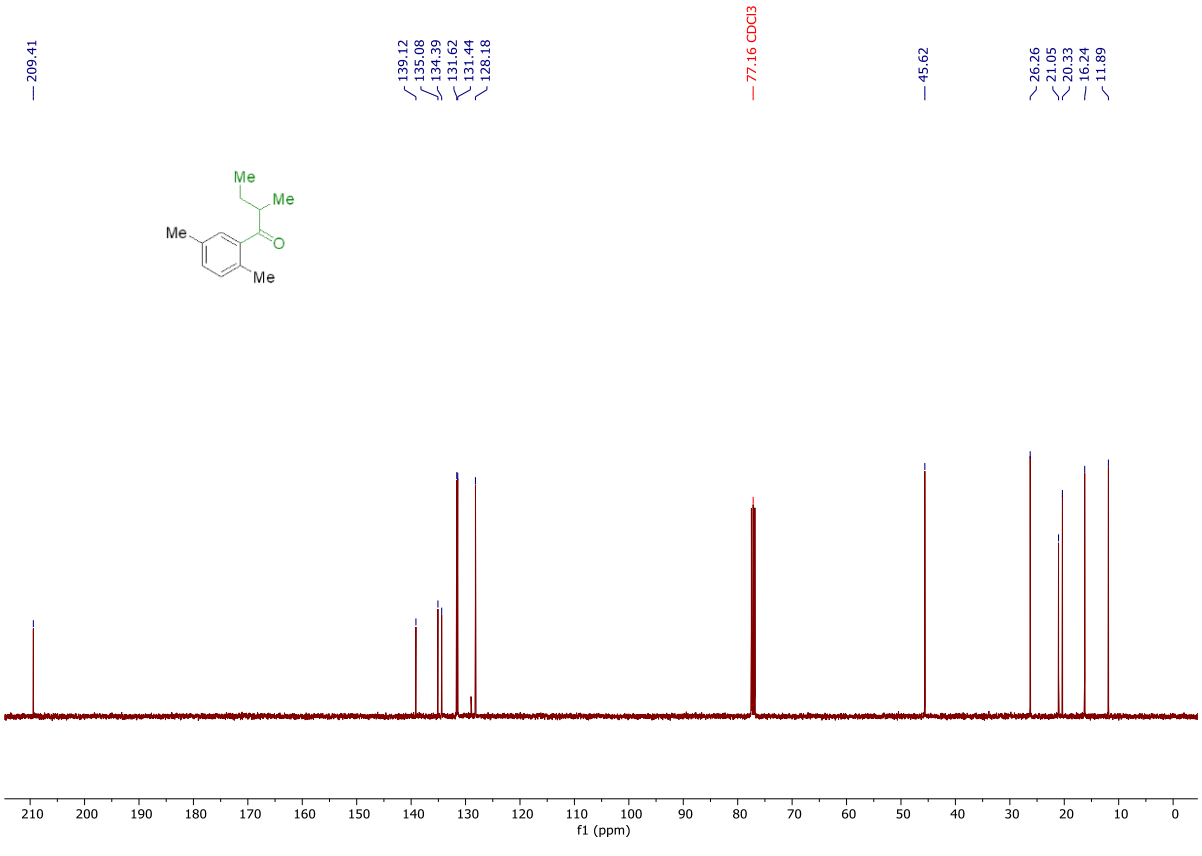
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4c



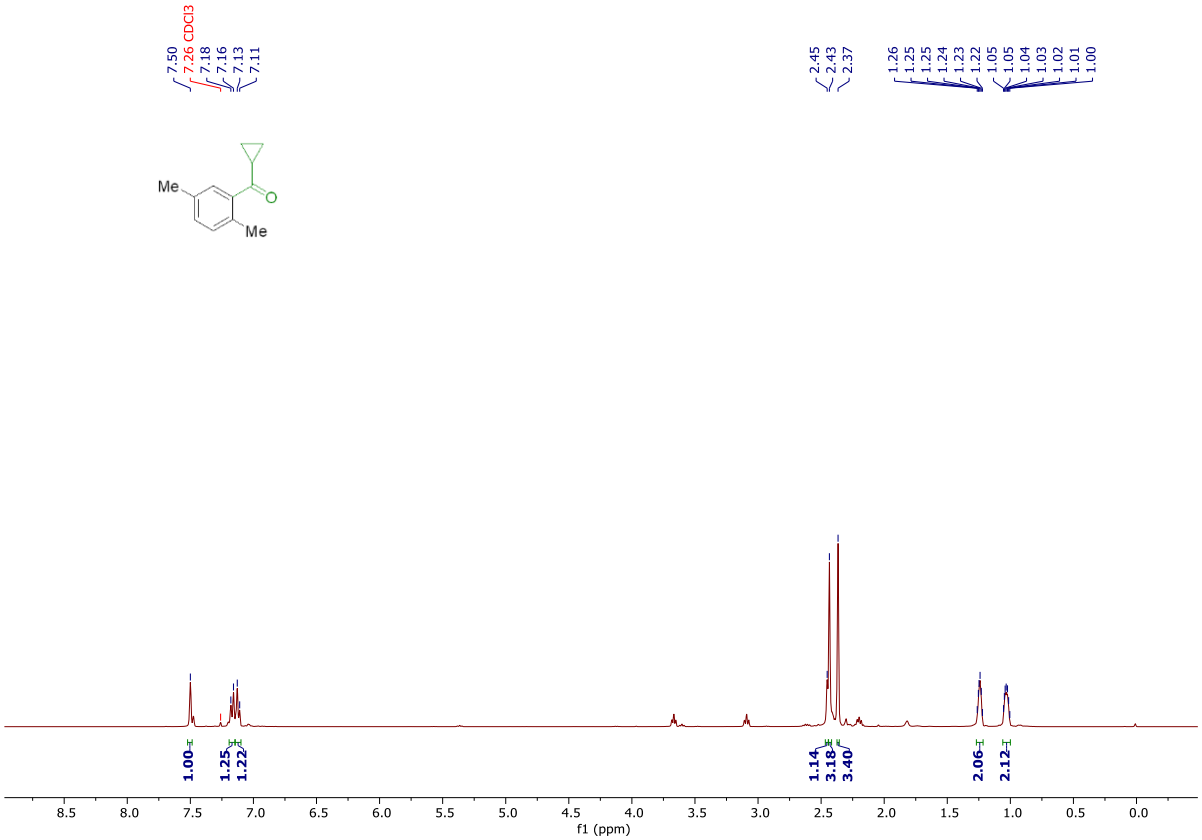


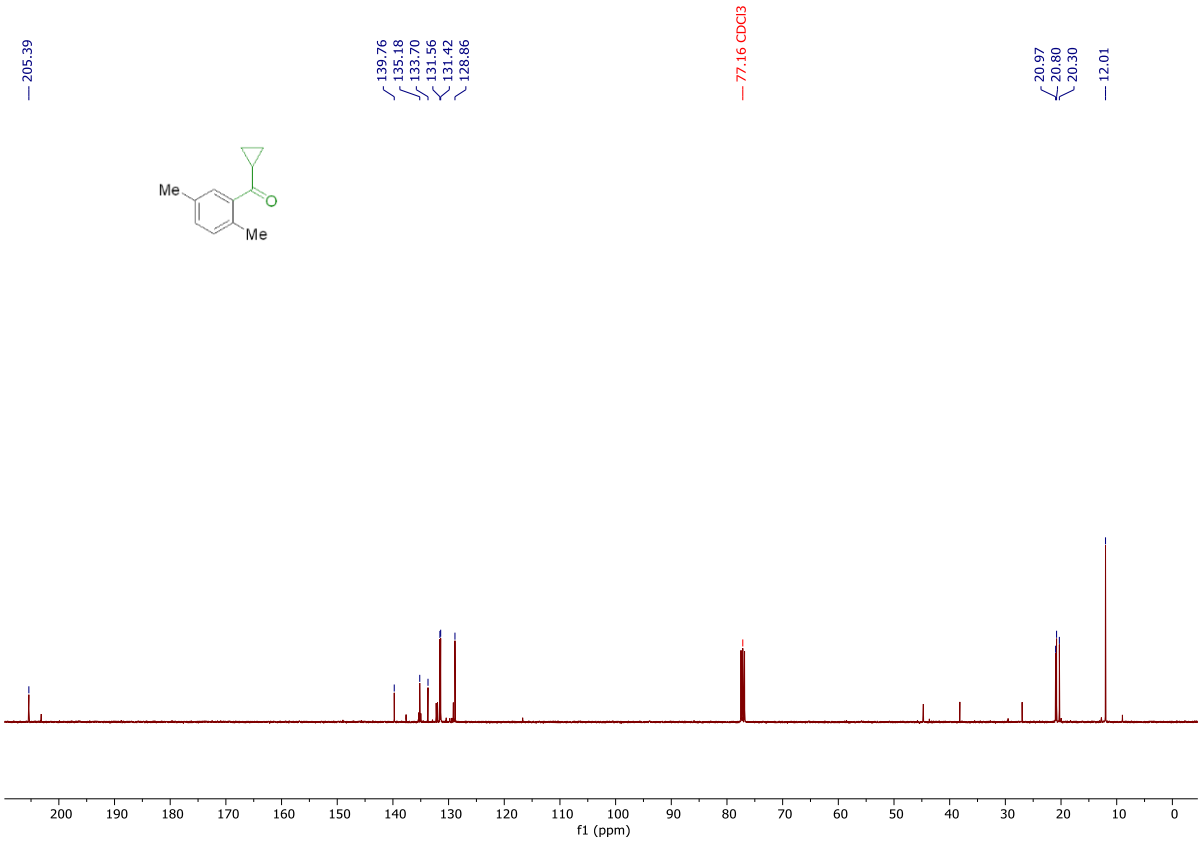
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4d



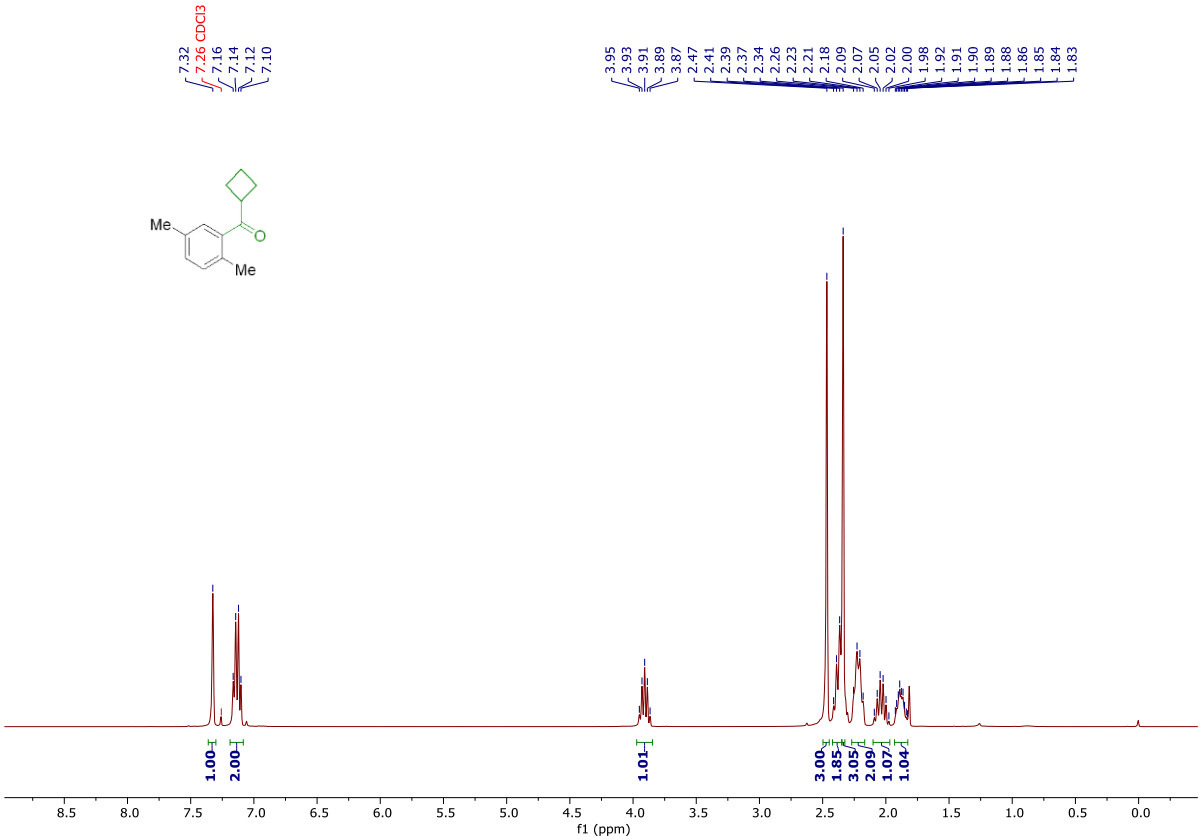


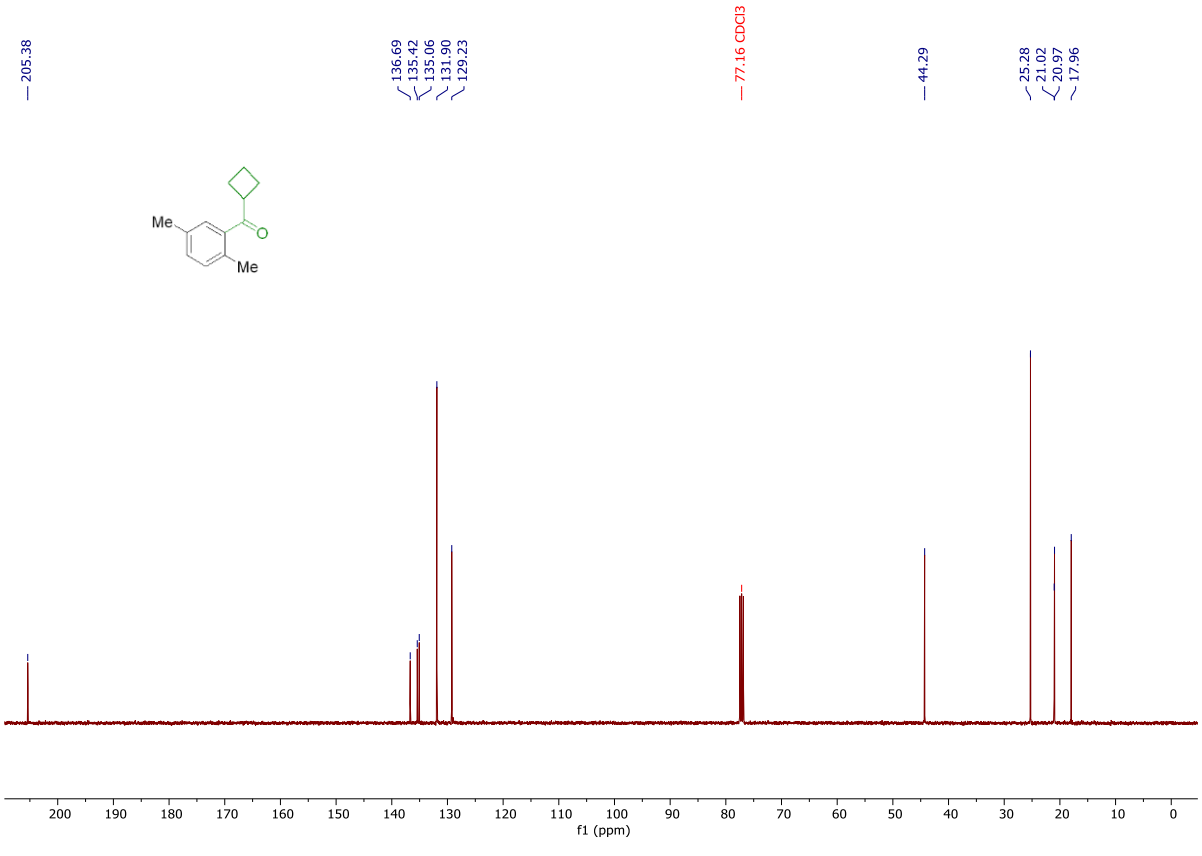
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4e



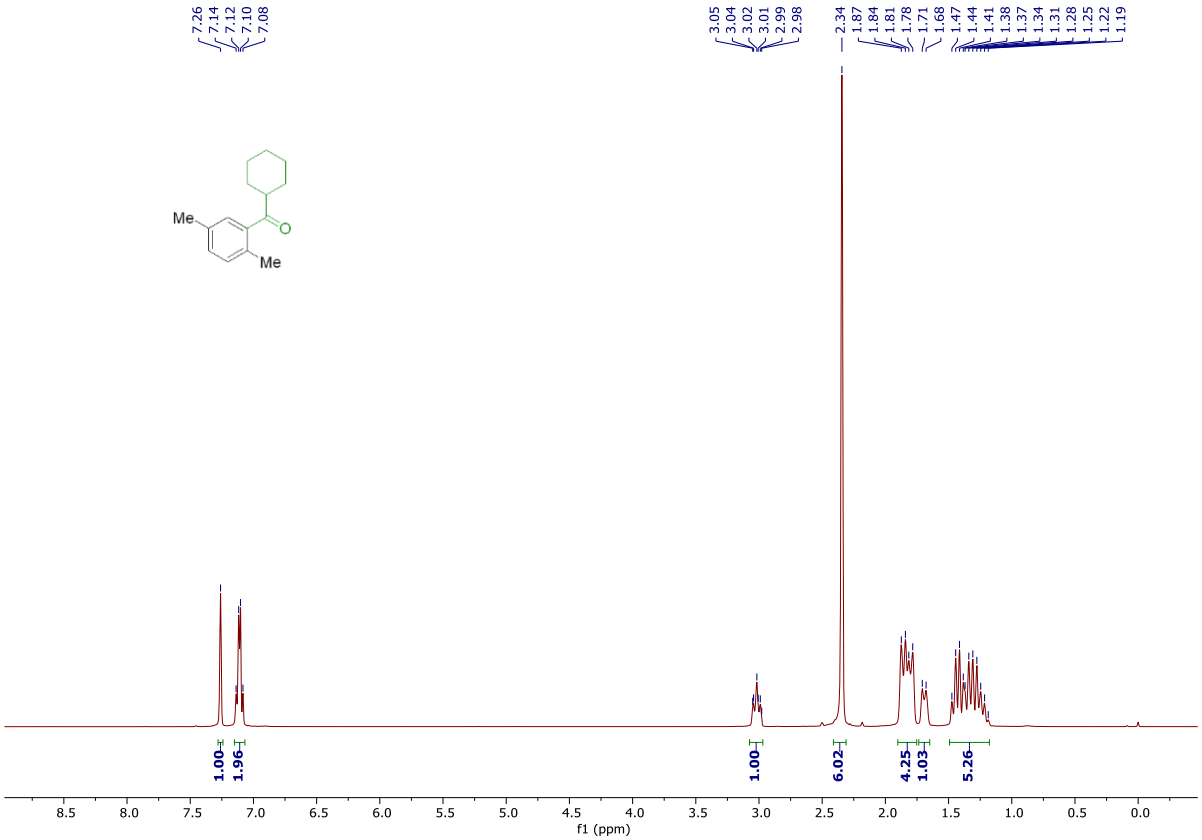


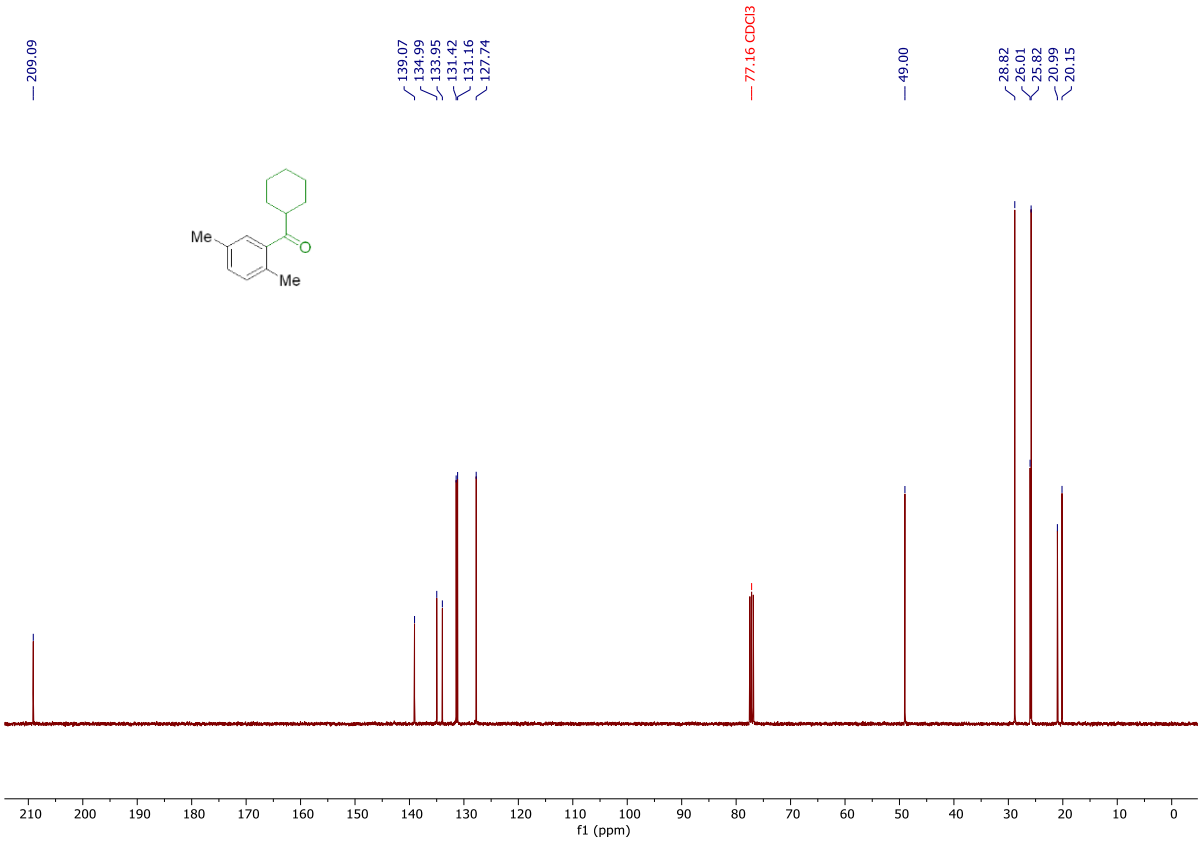
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4f



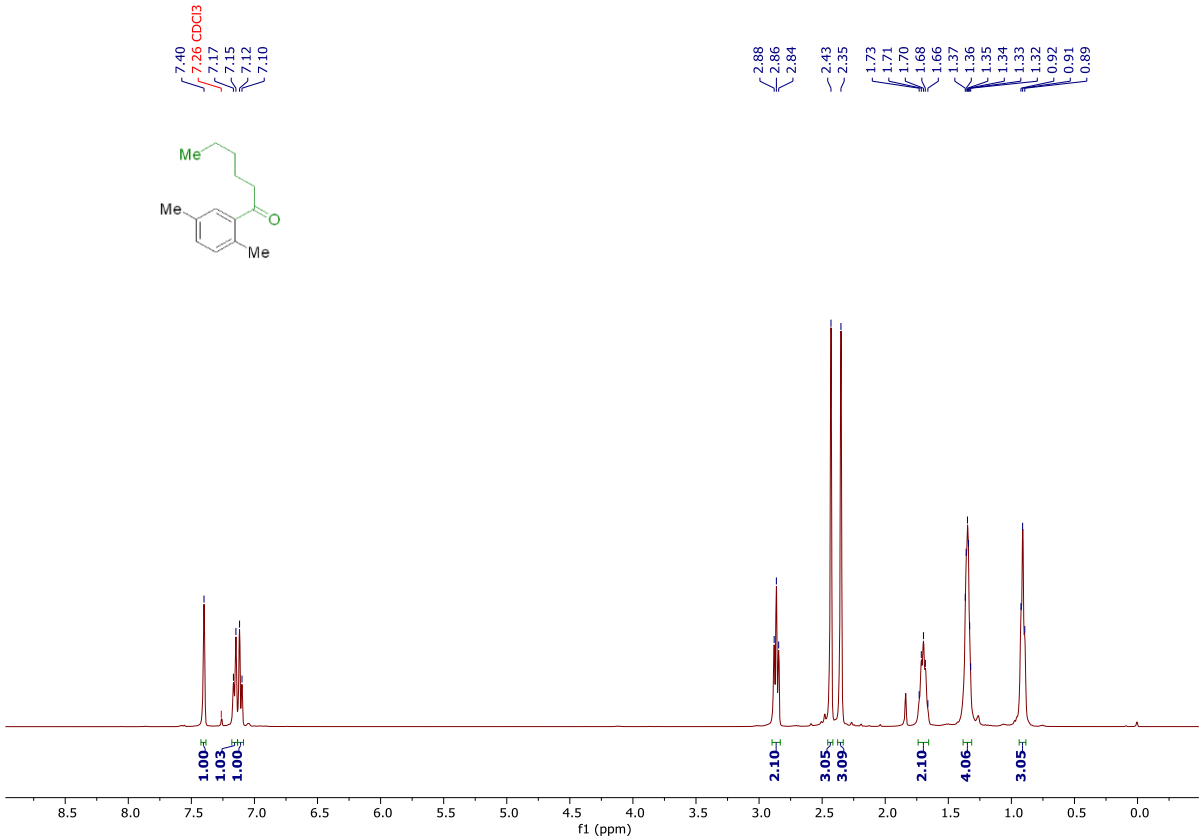


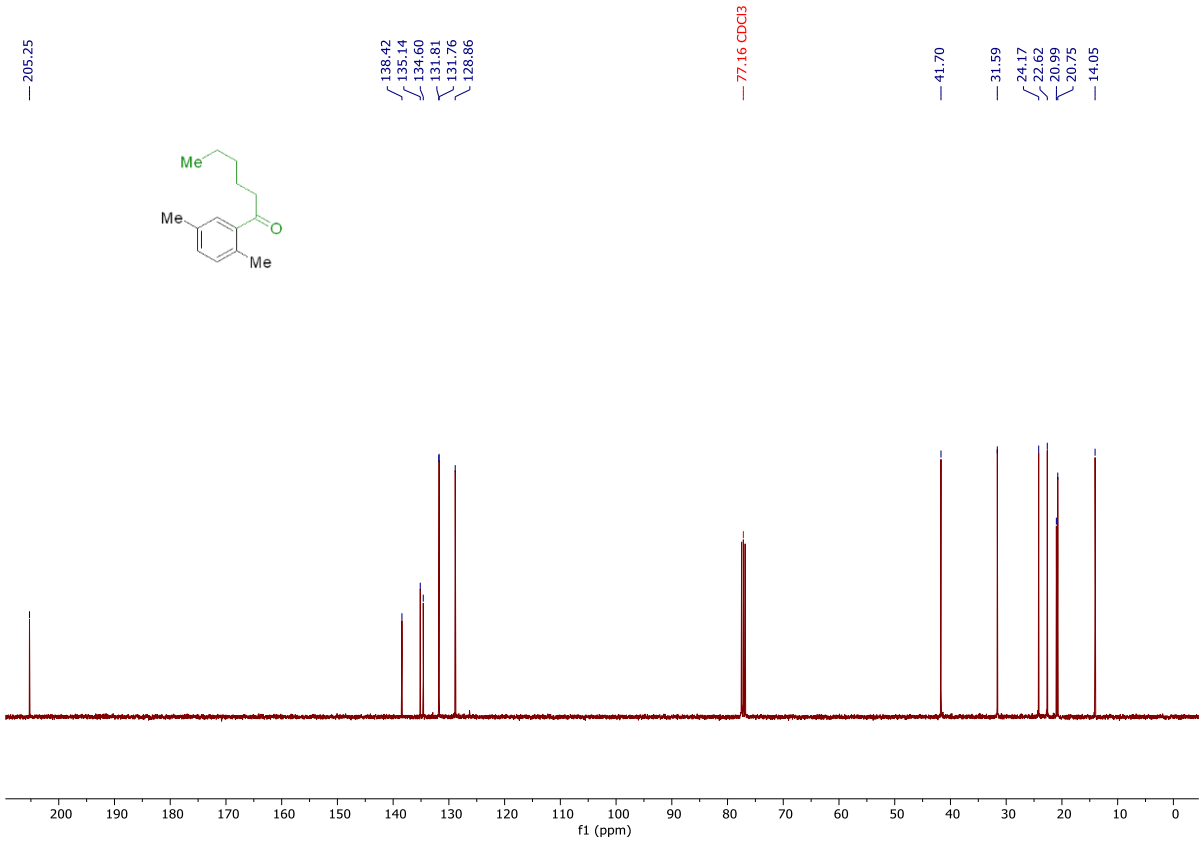
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4g



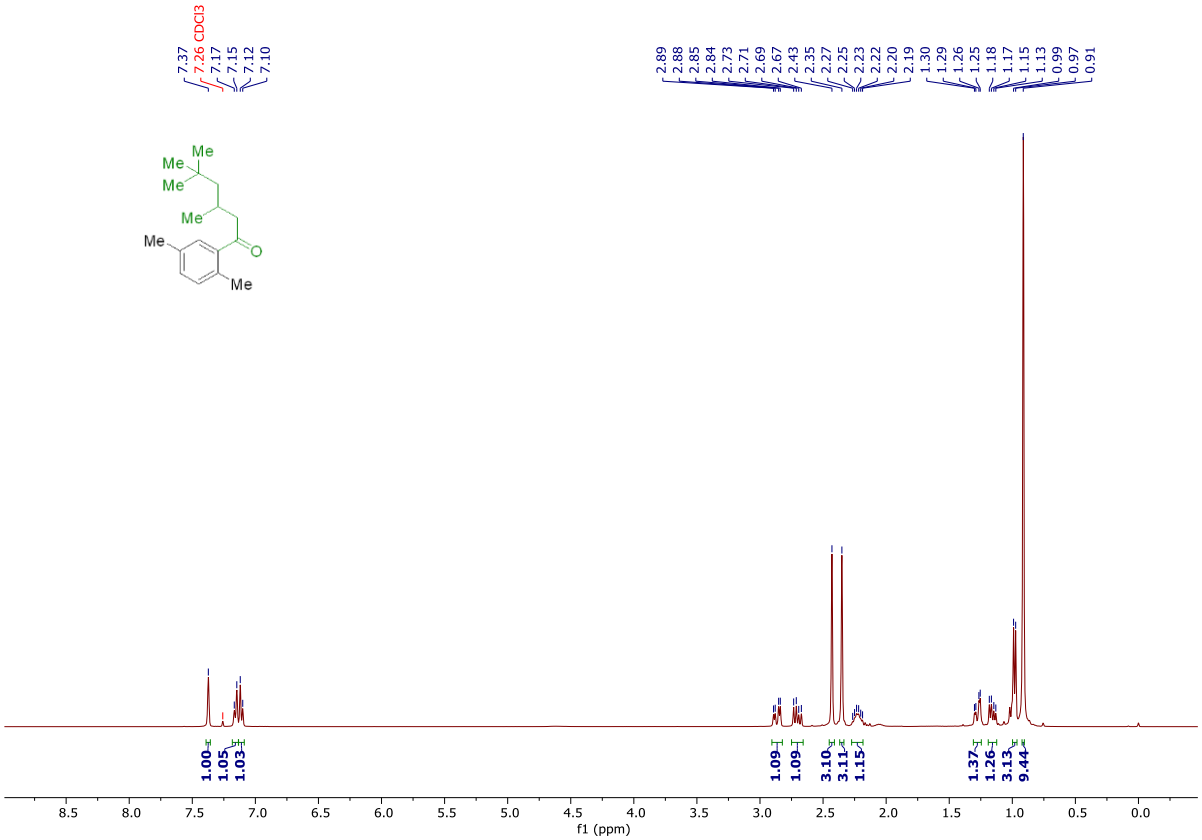


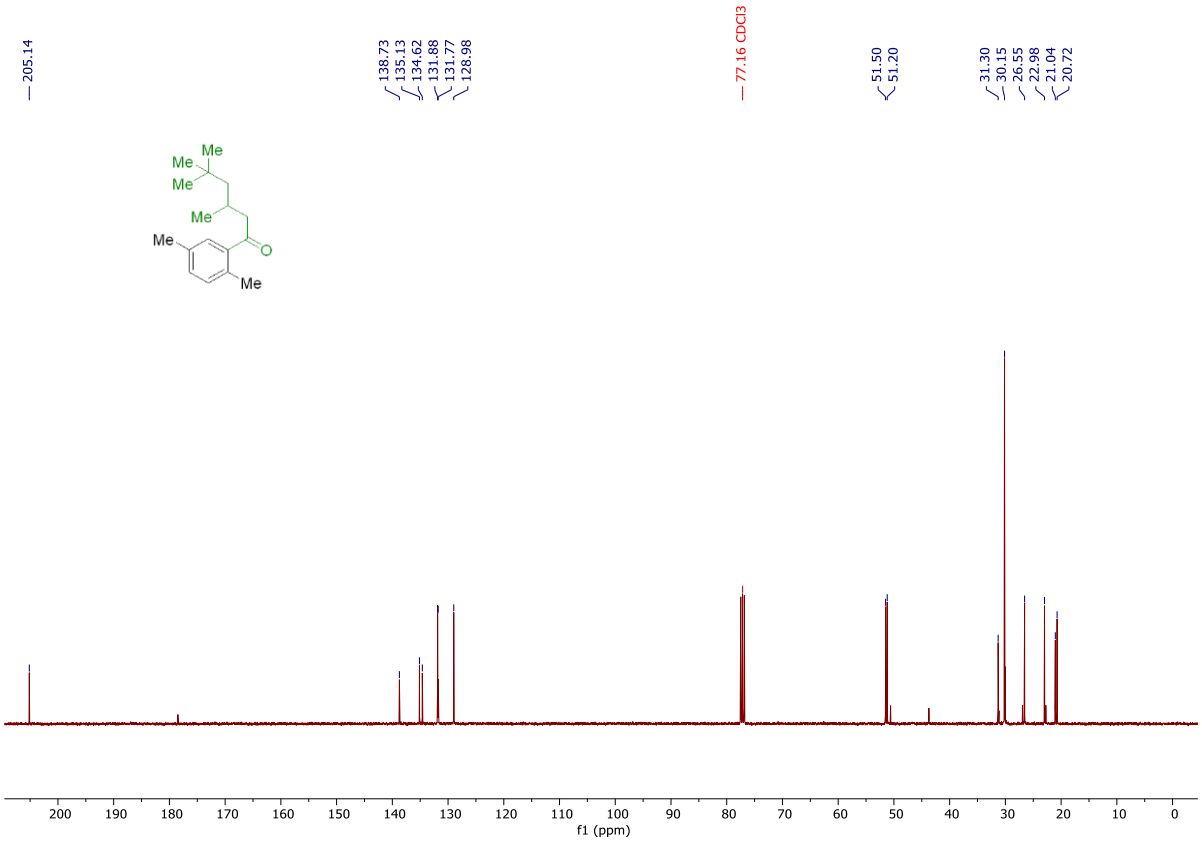
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4h



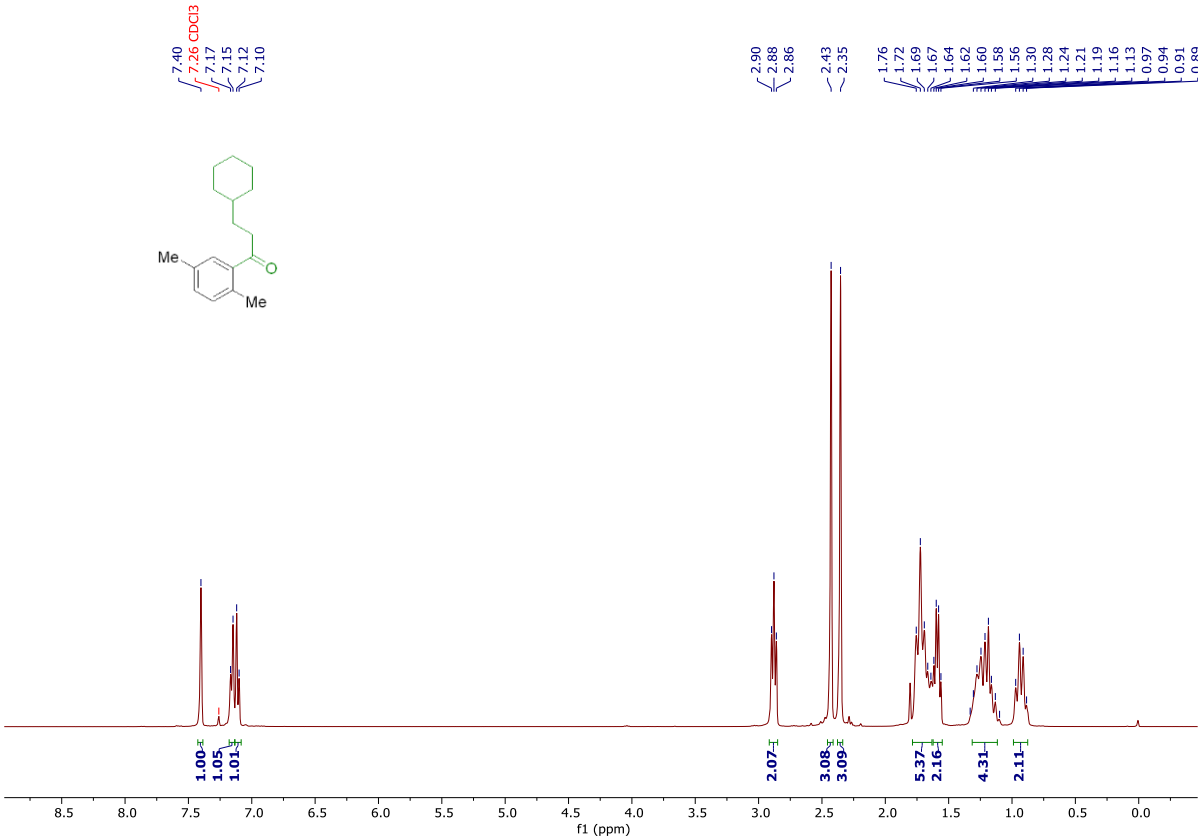


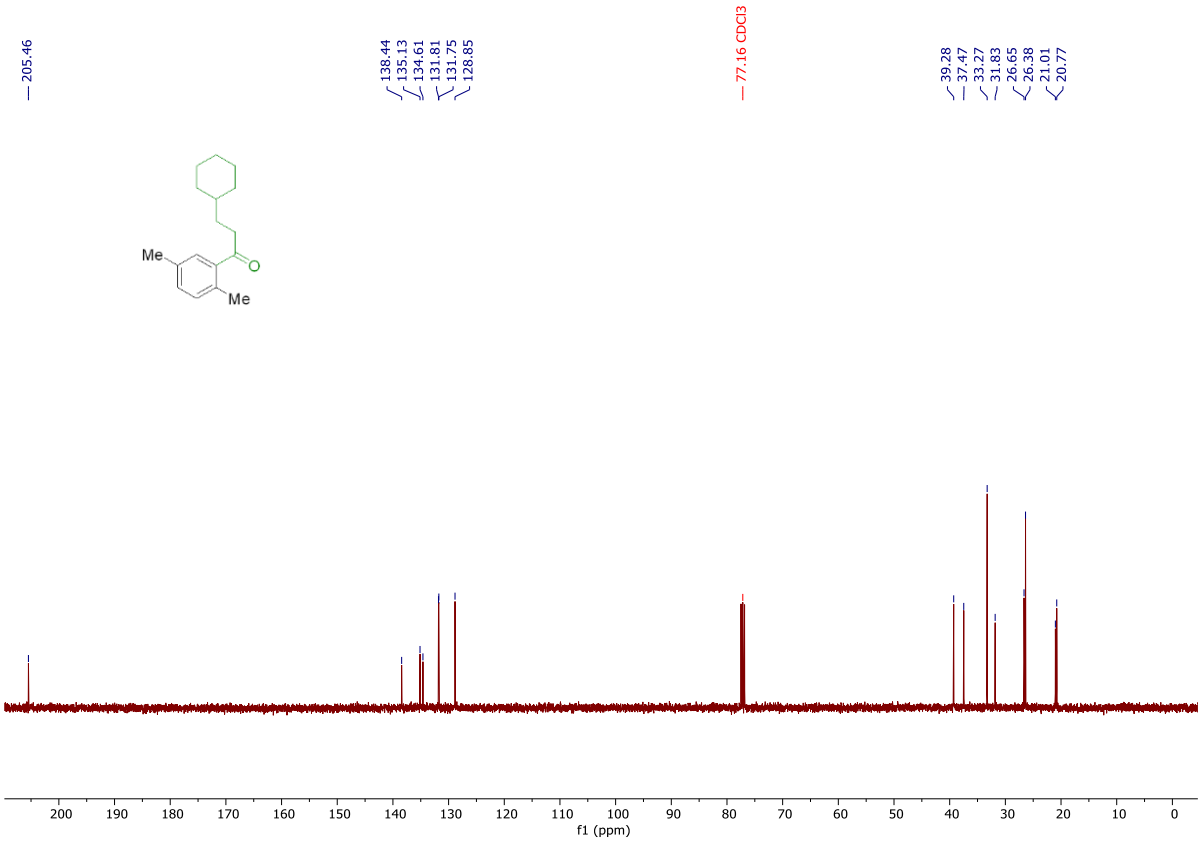
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4j



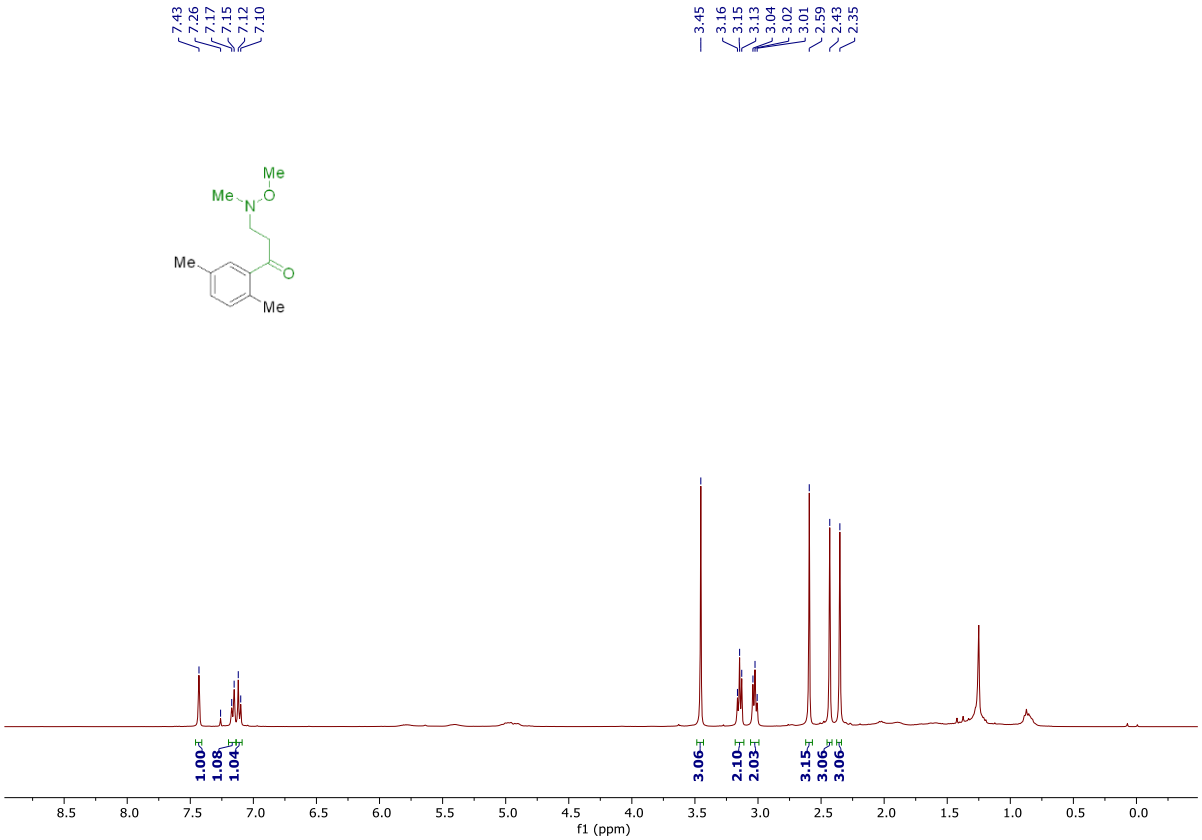


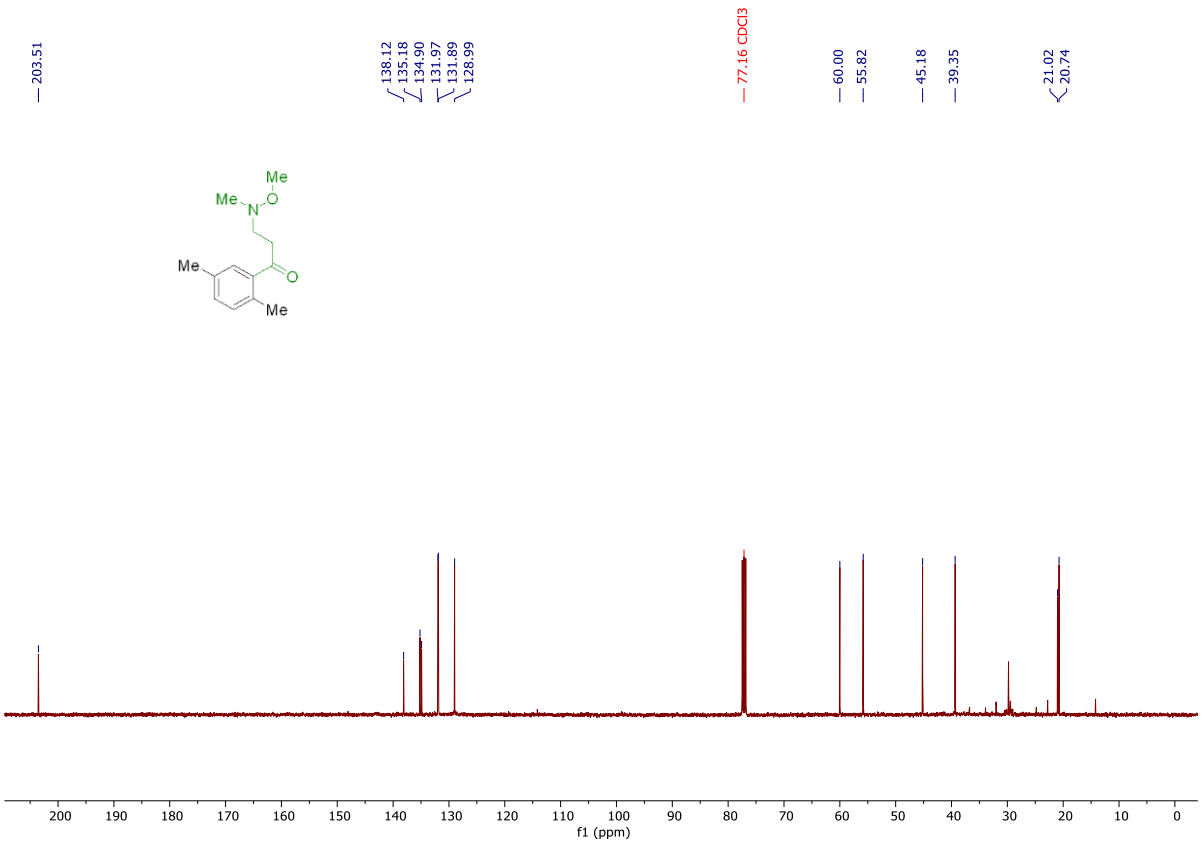
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4k



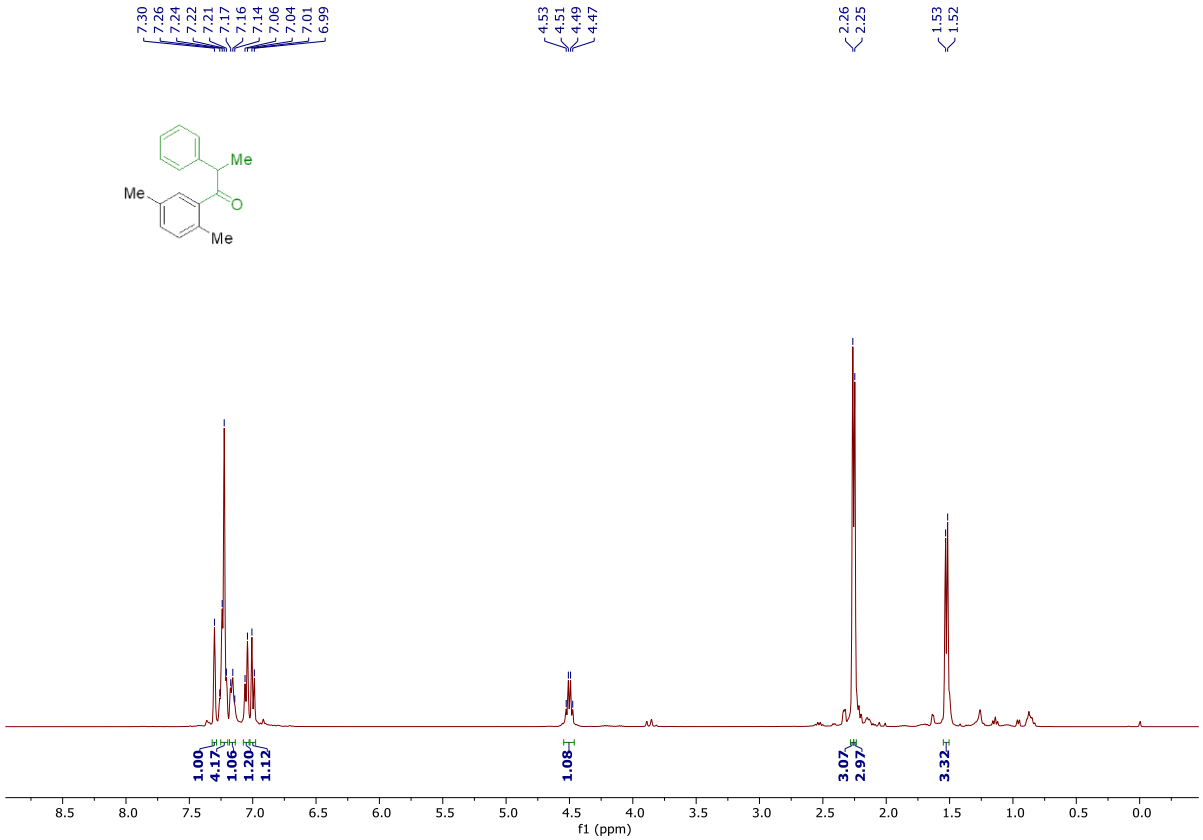


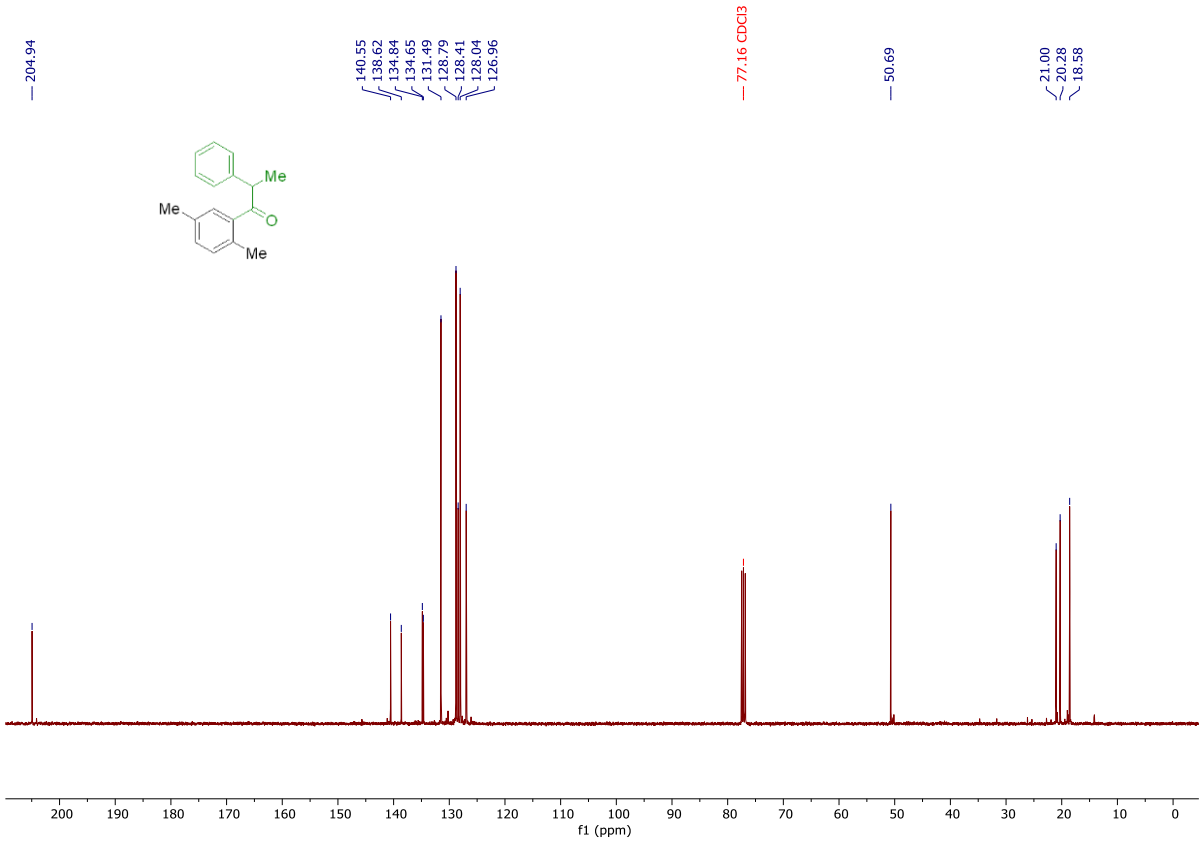
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4l



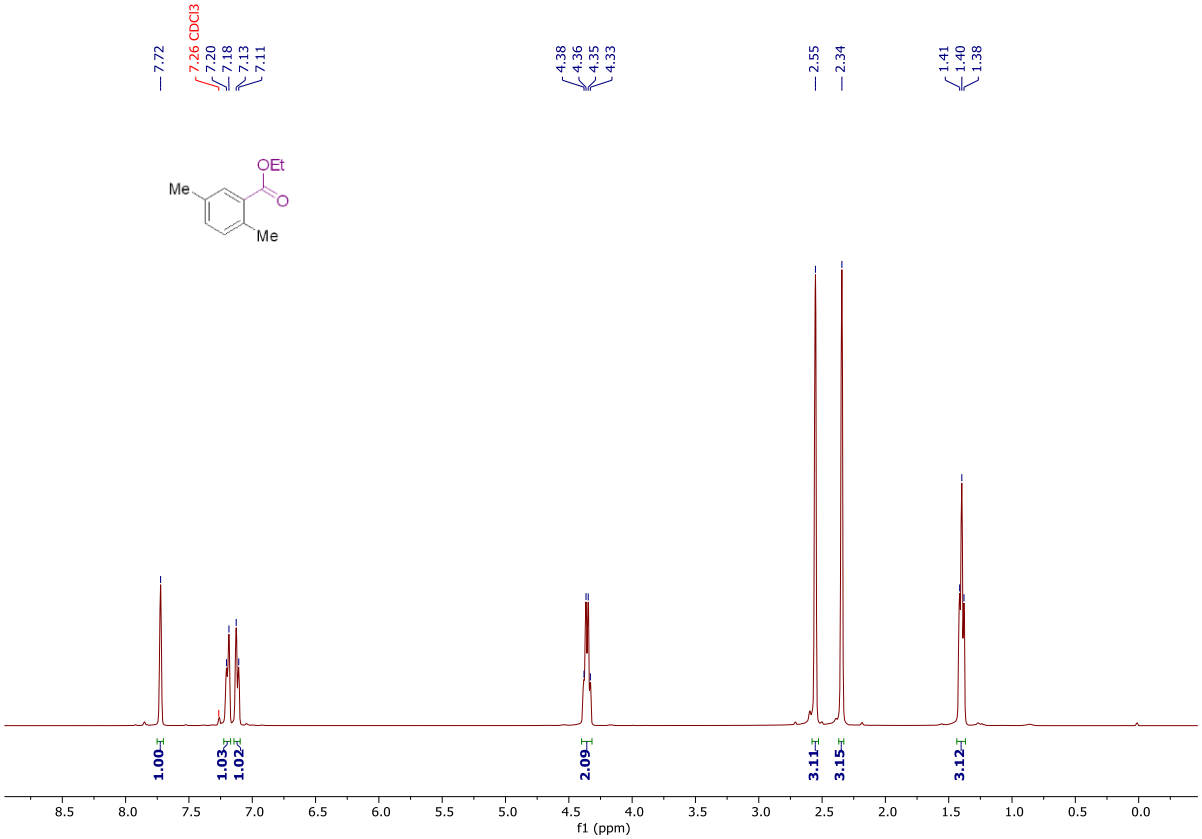


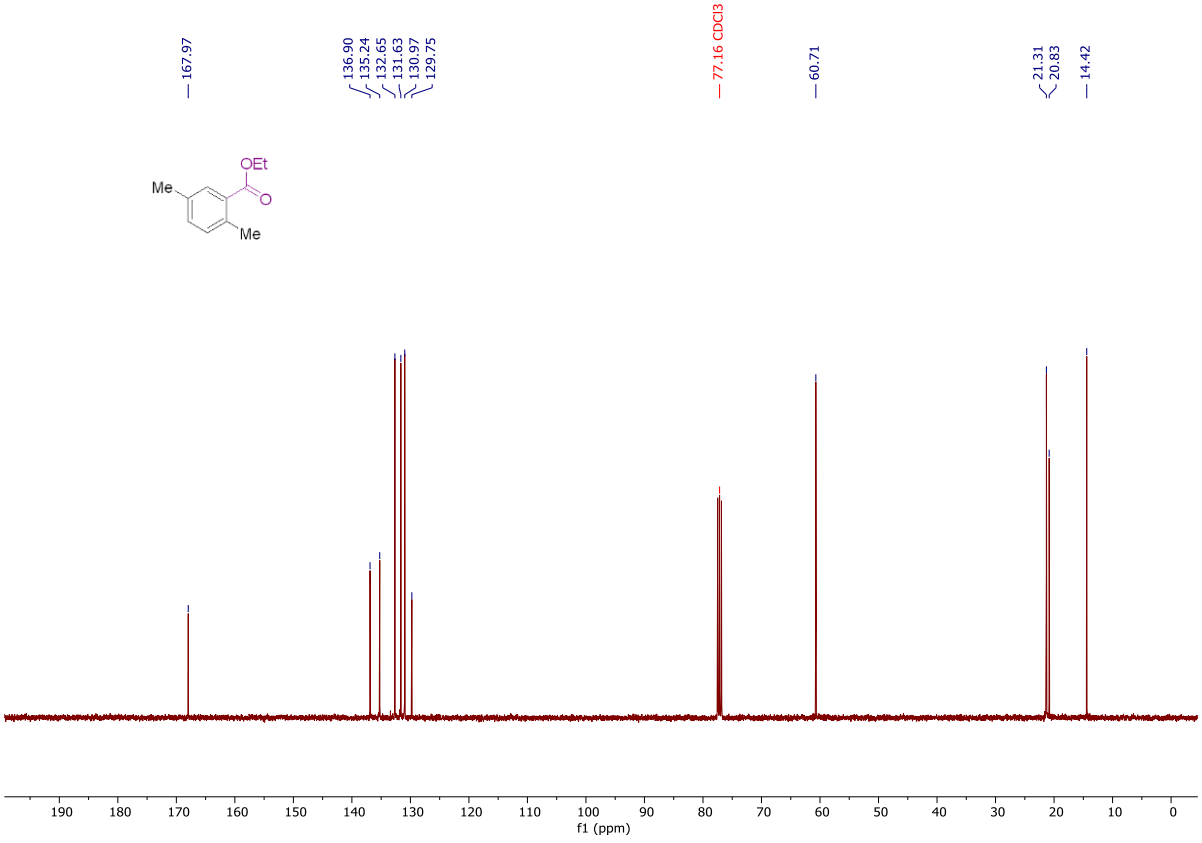
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4m



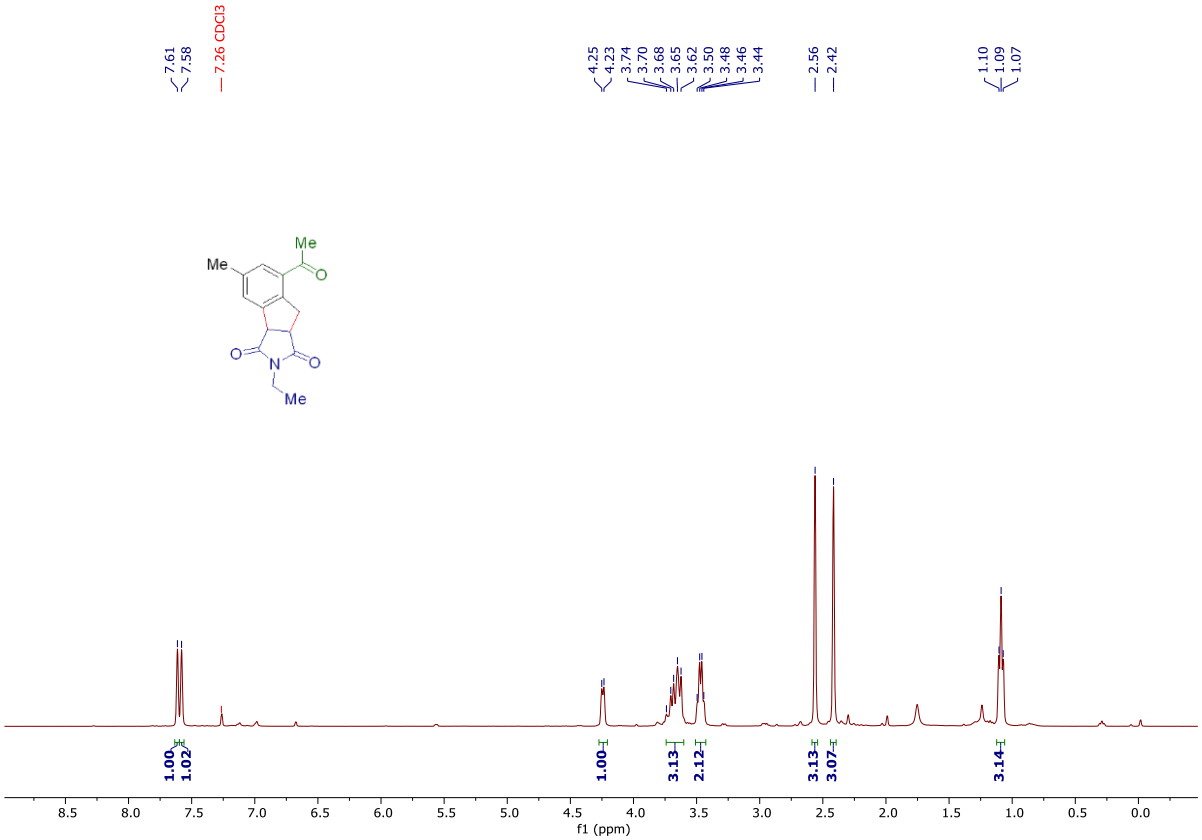


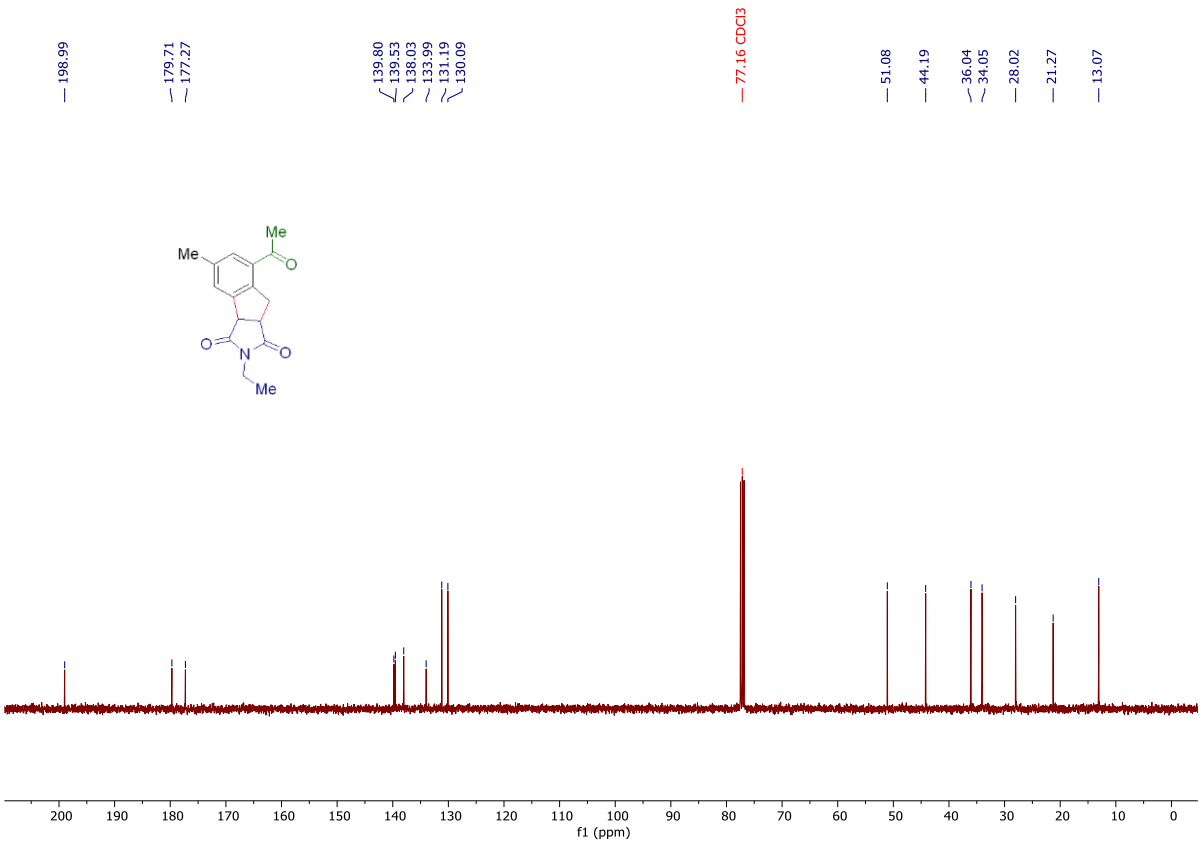
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 4o



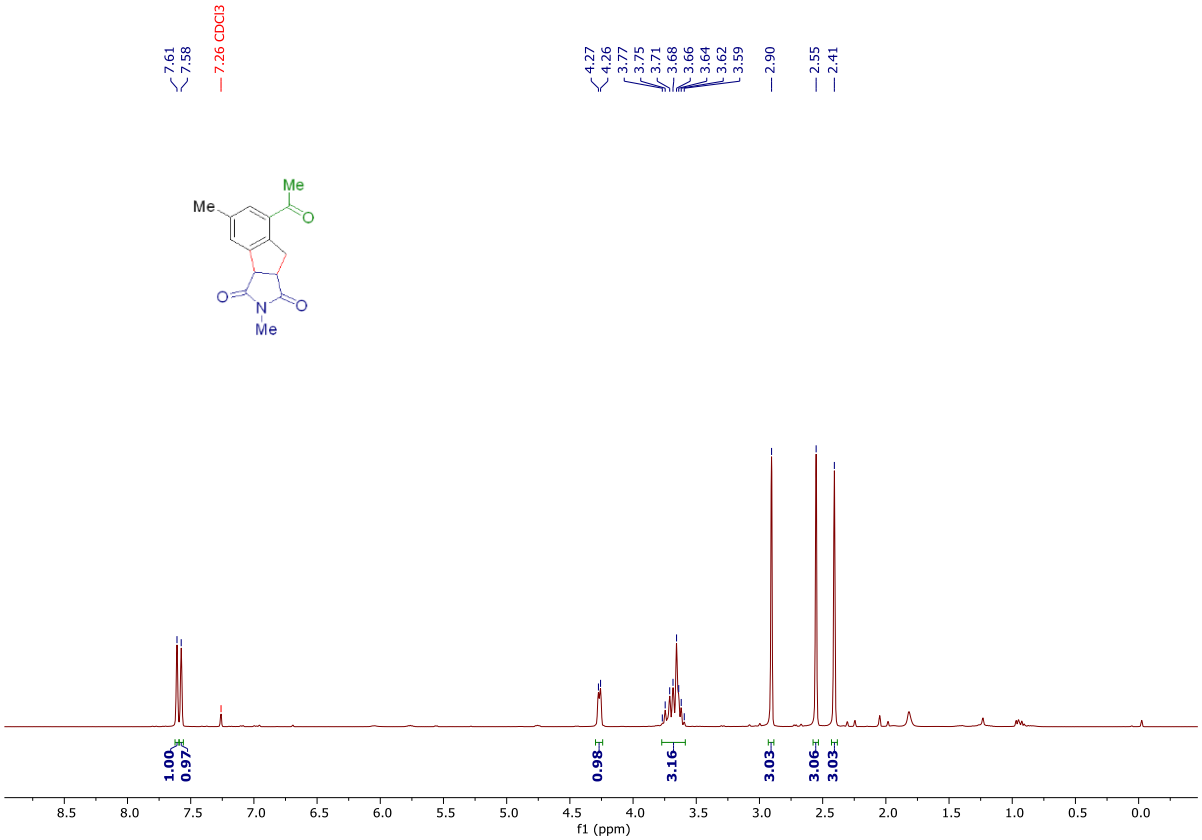


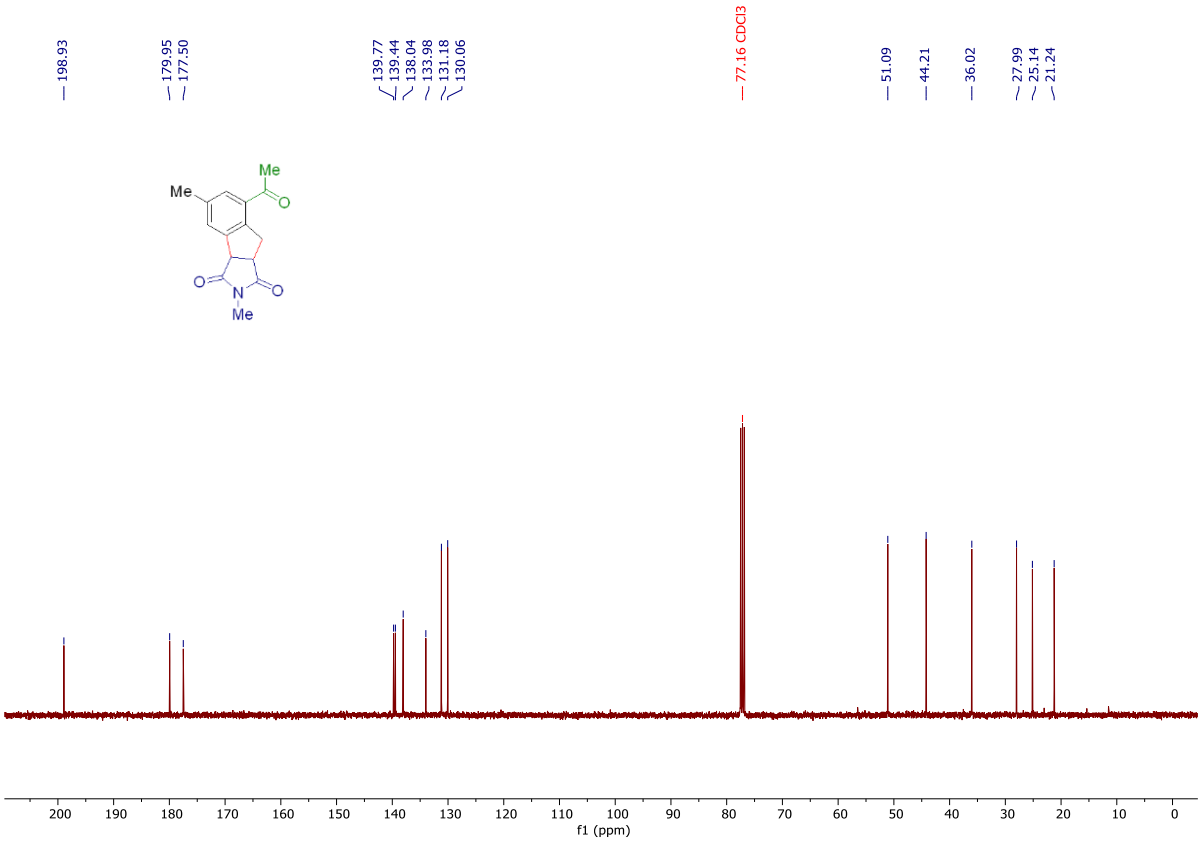
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3aa



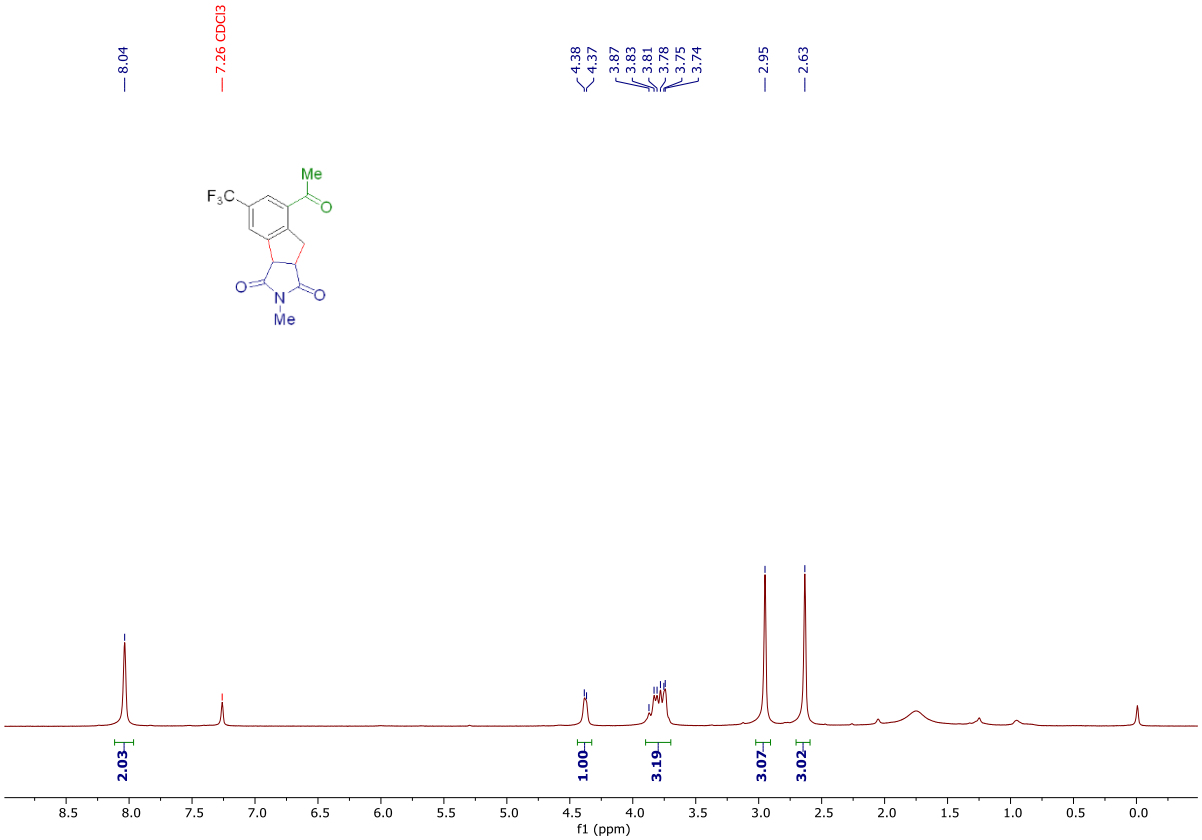


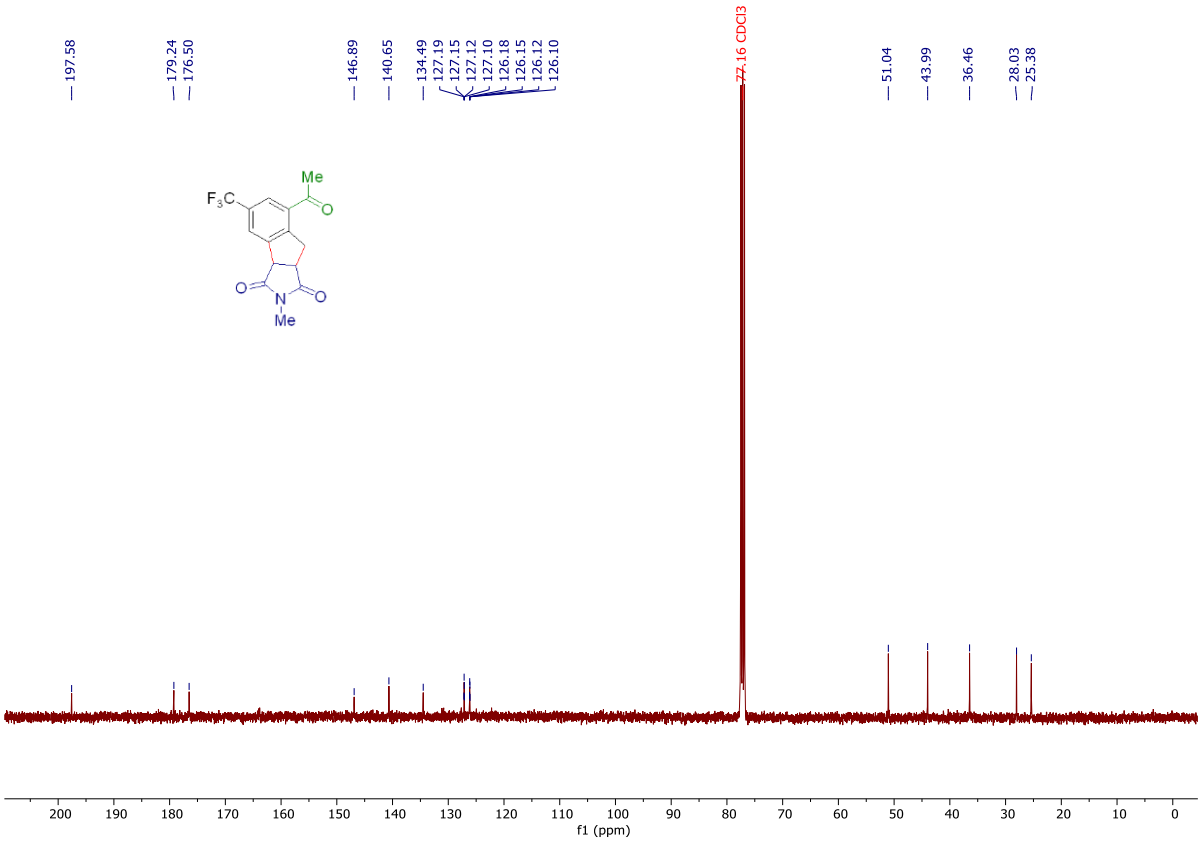
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ab



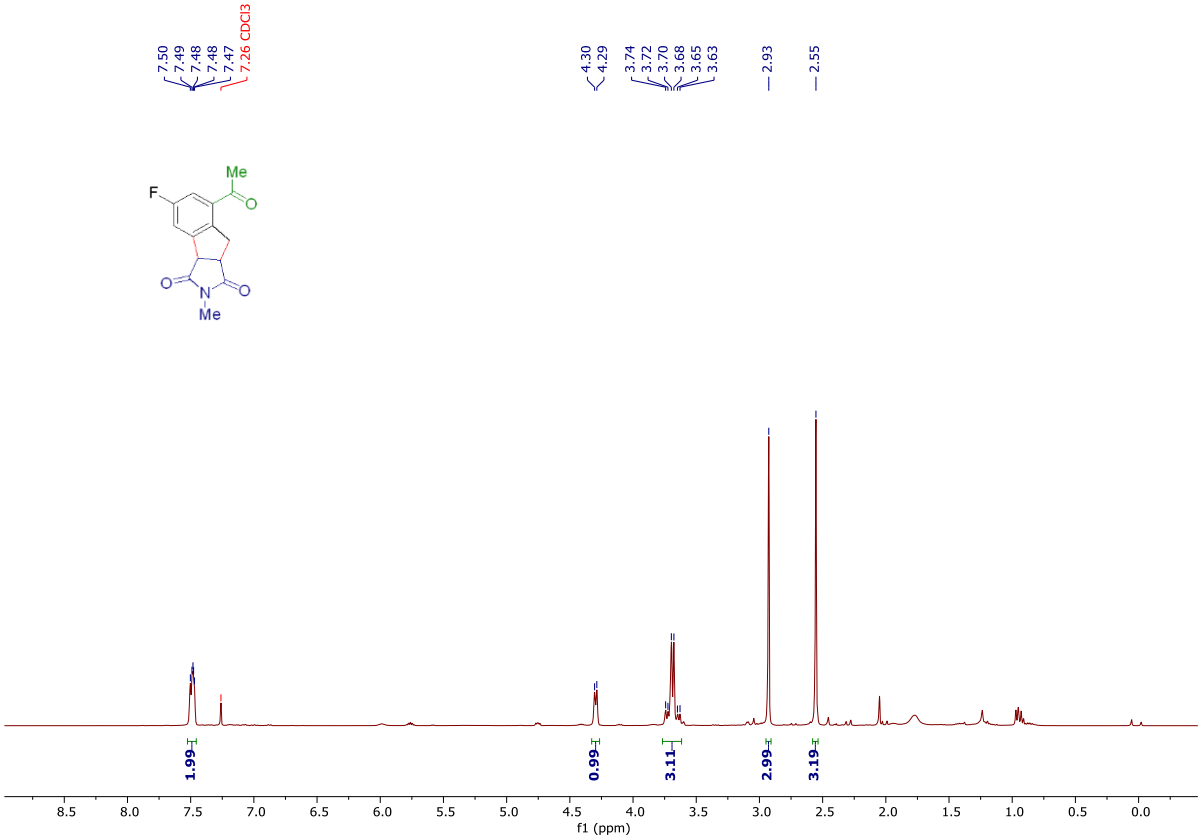


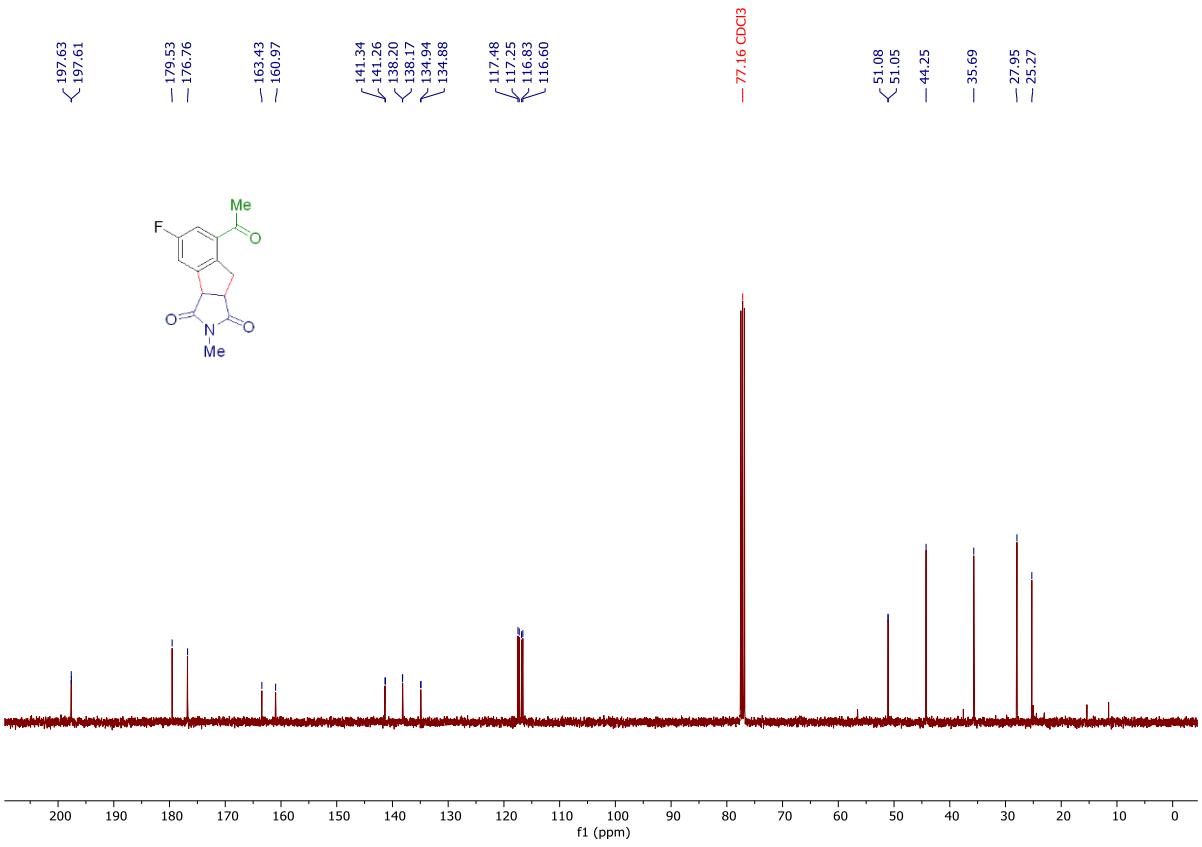
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3bb



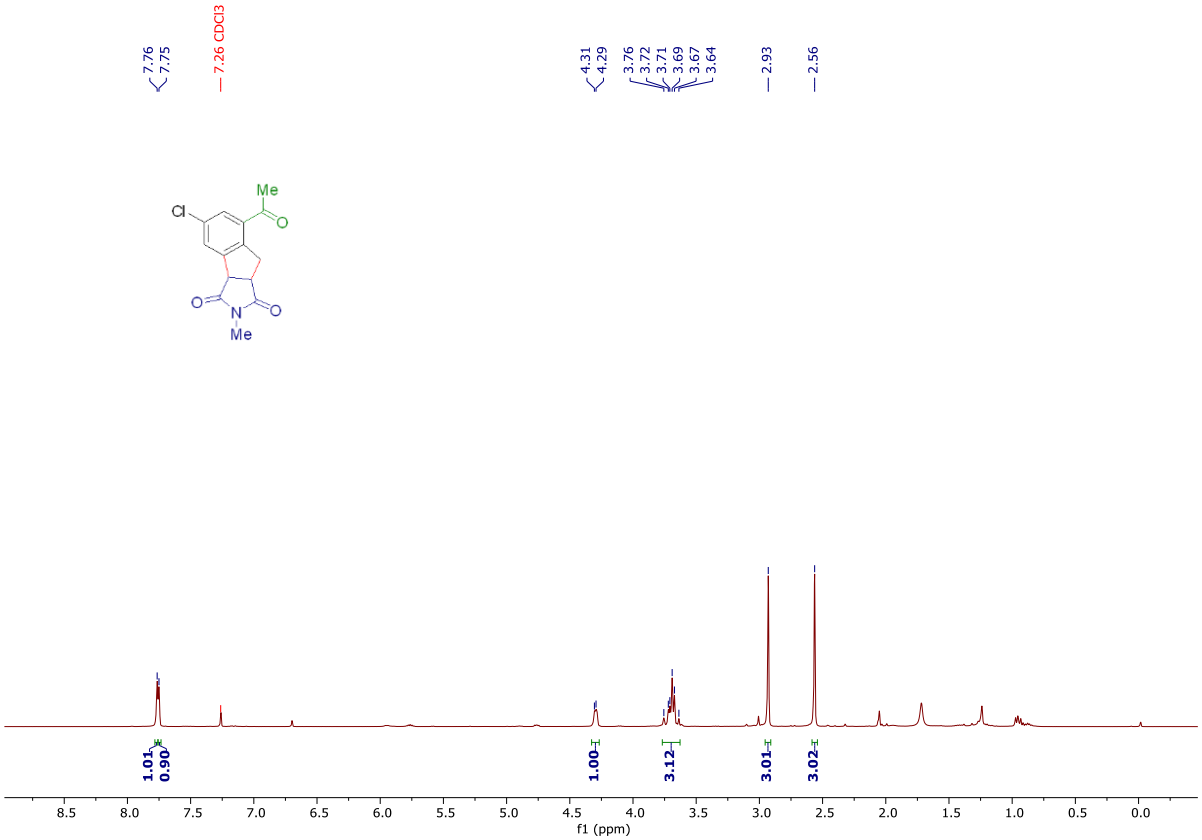


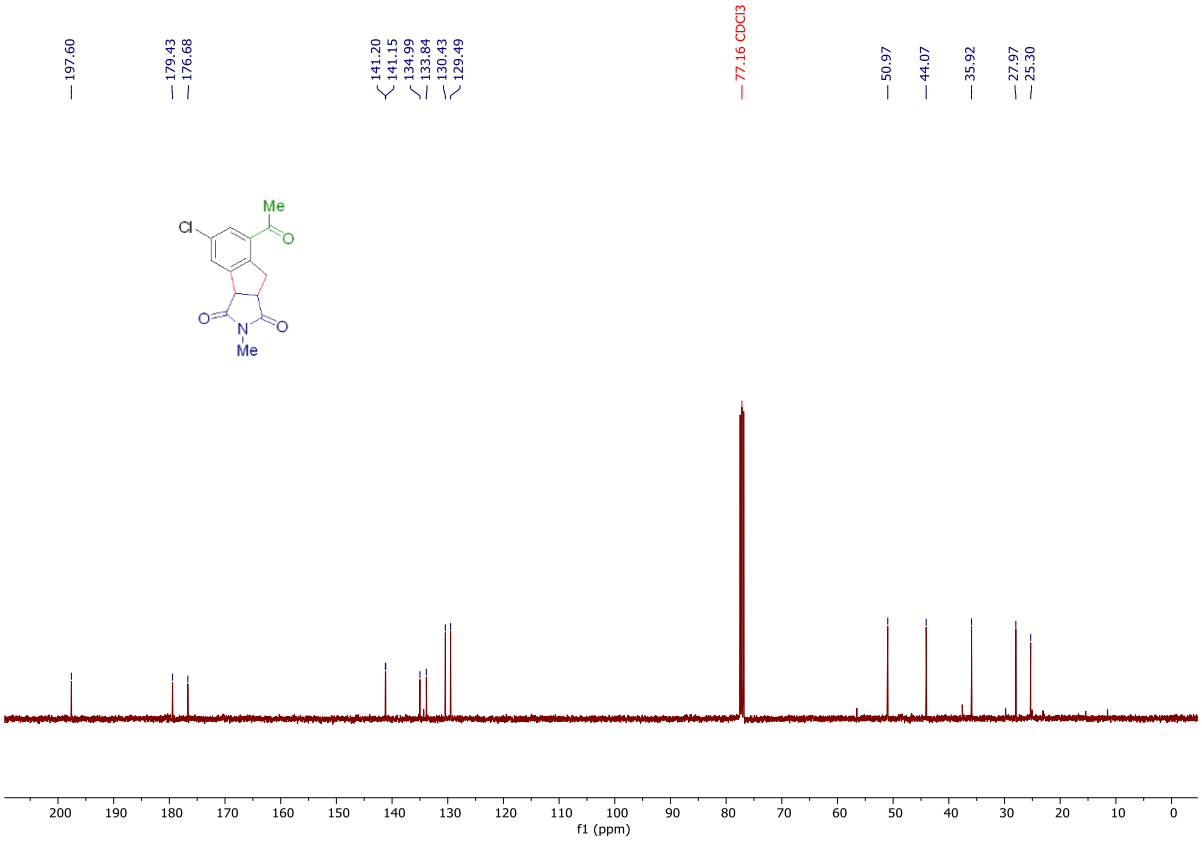
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3cb



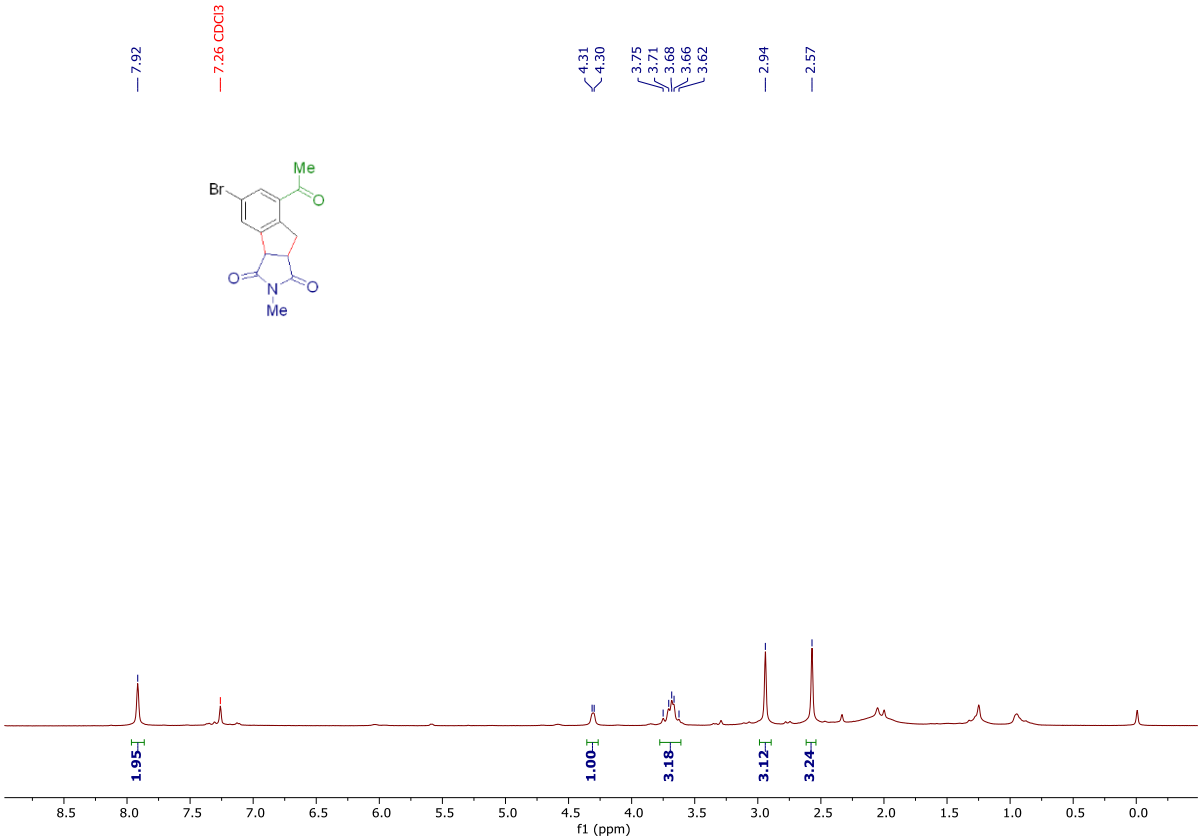


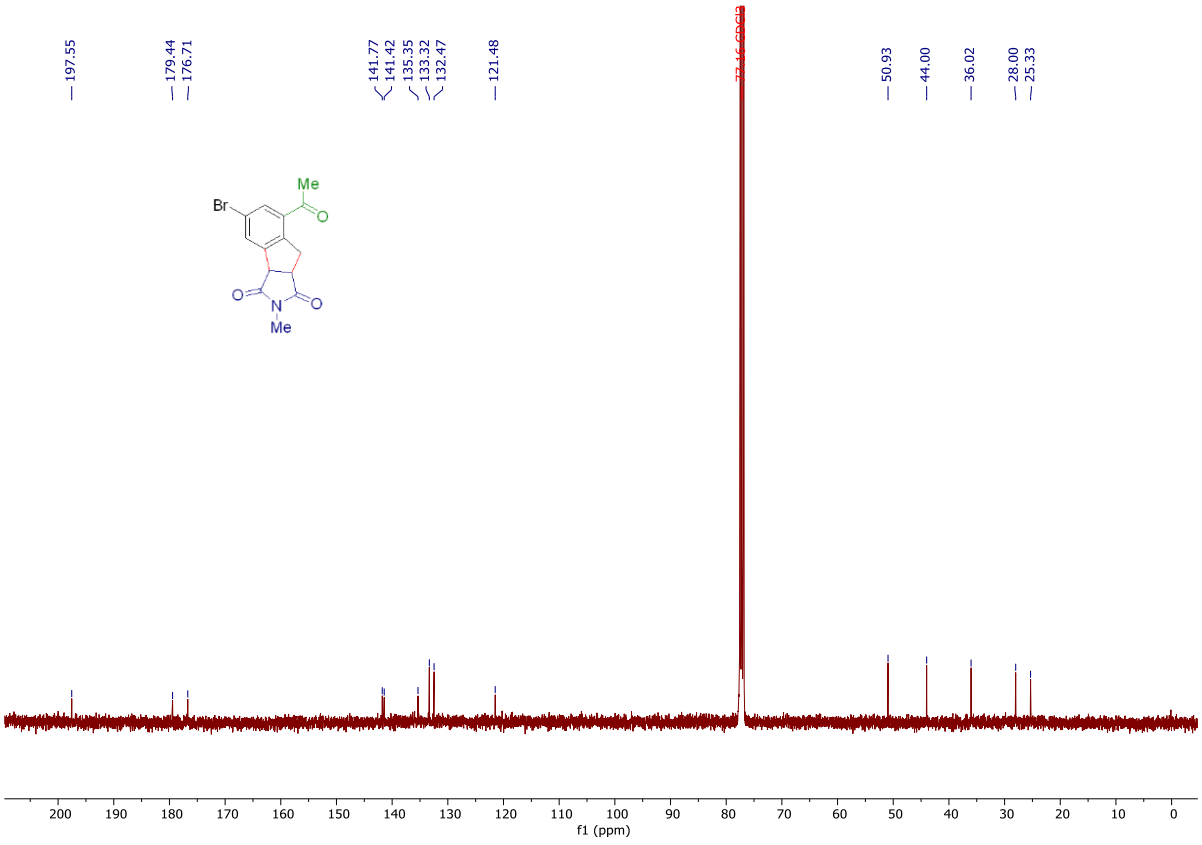
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3db



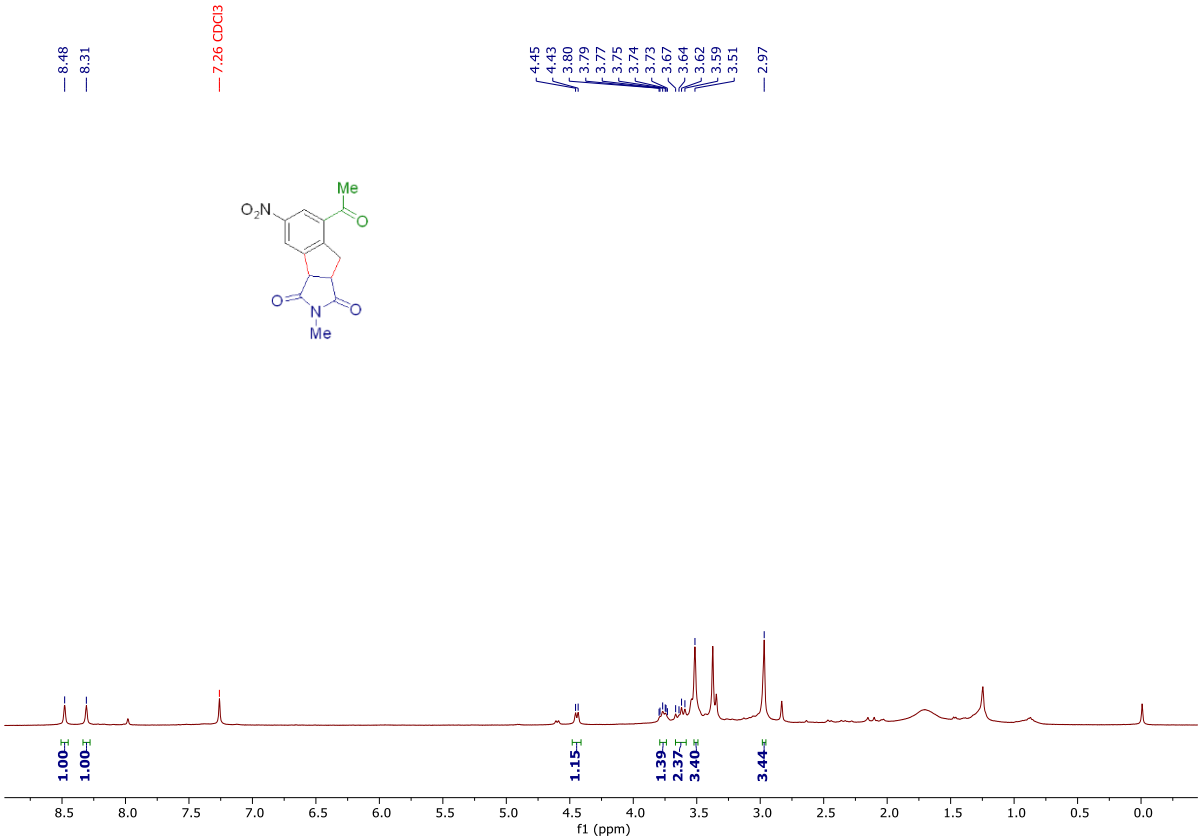


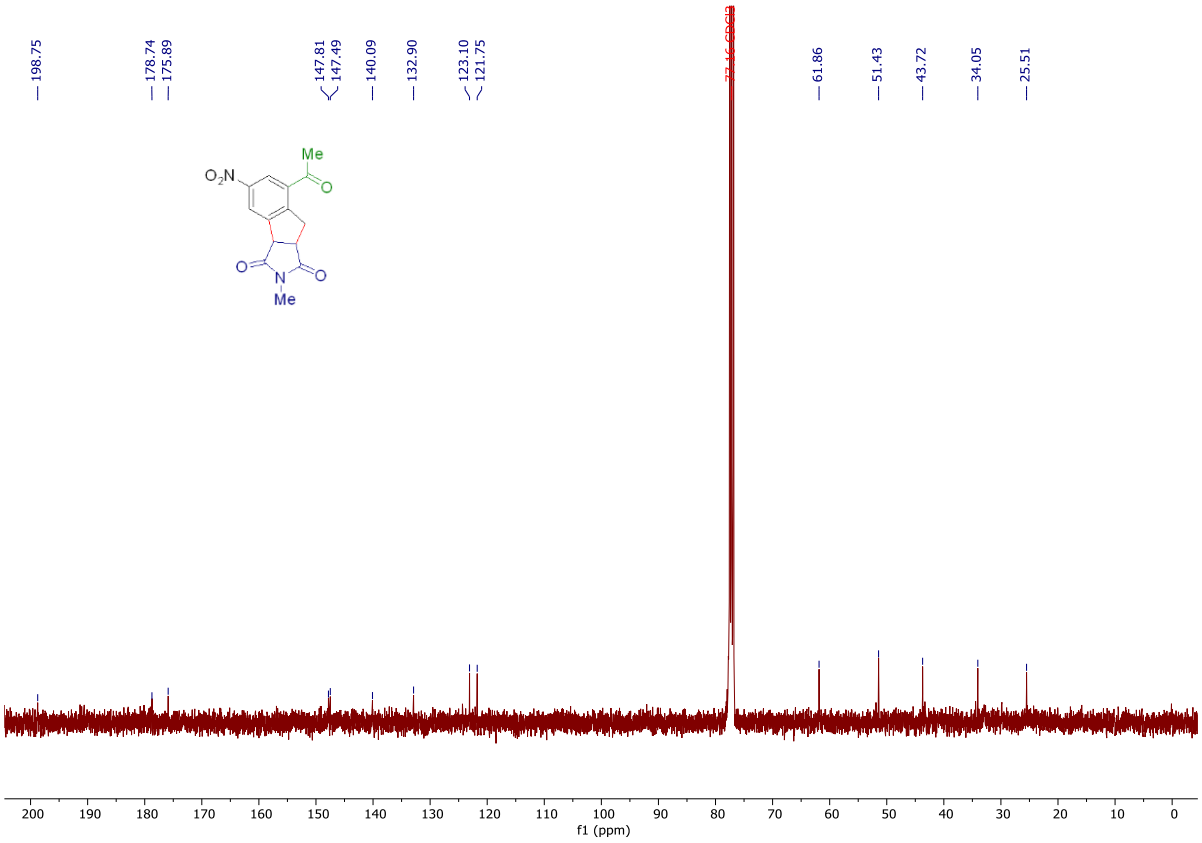
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3eb



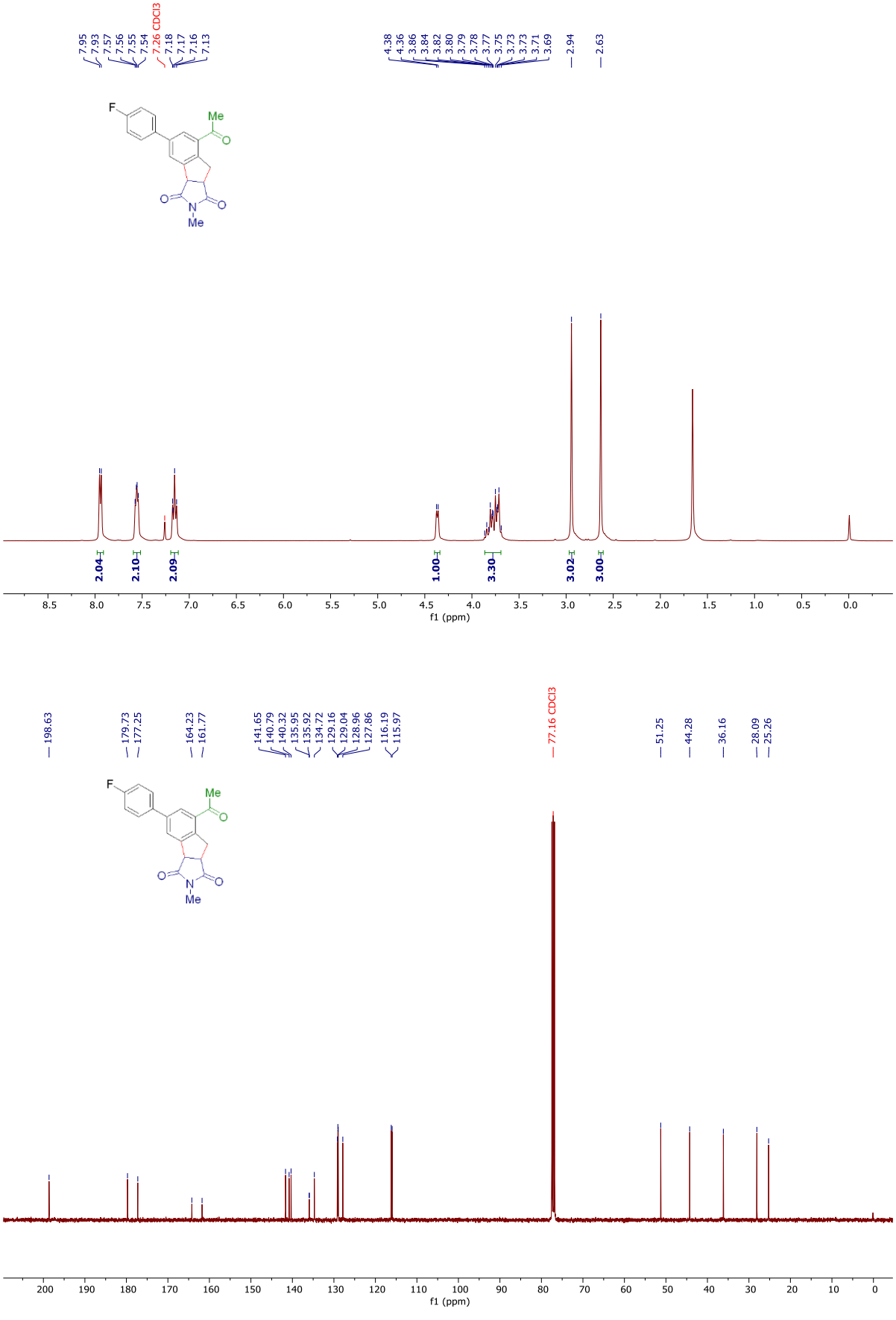


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3fb

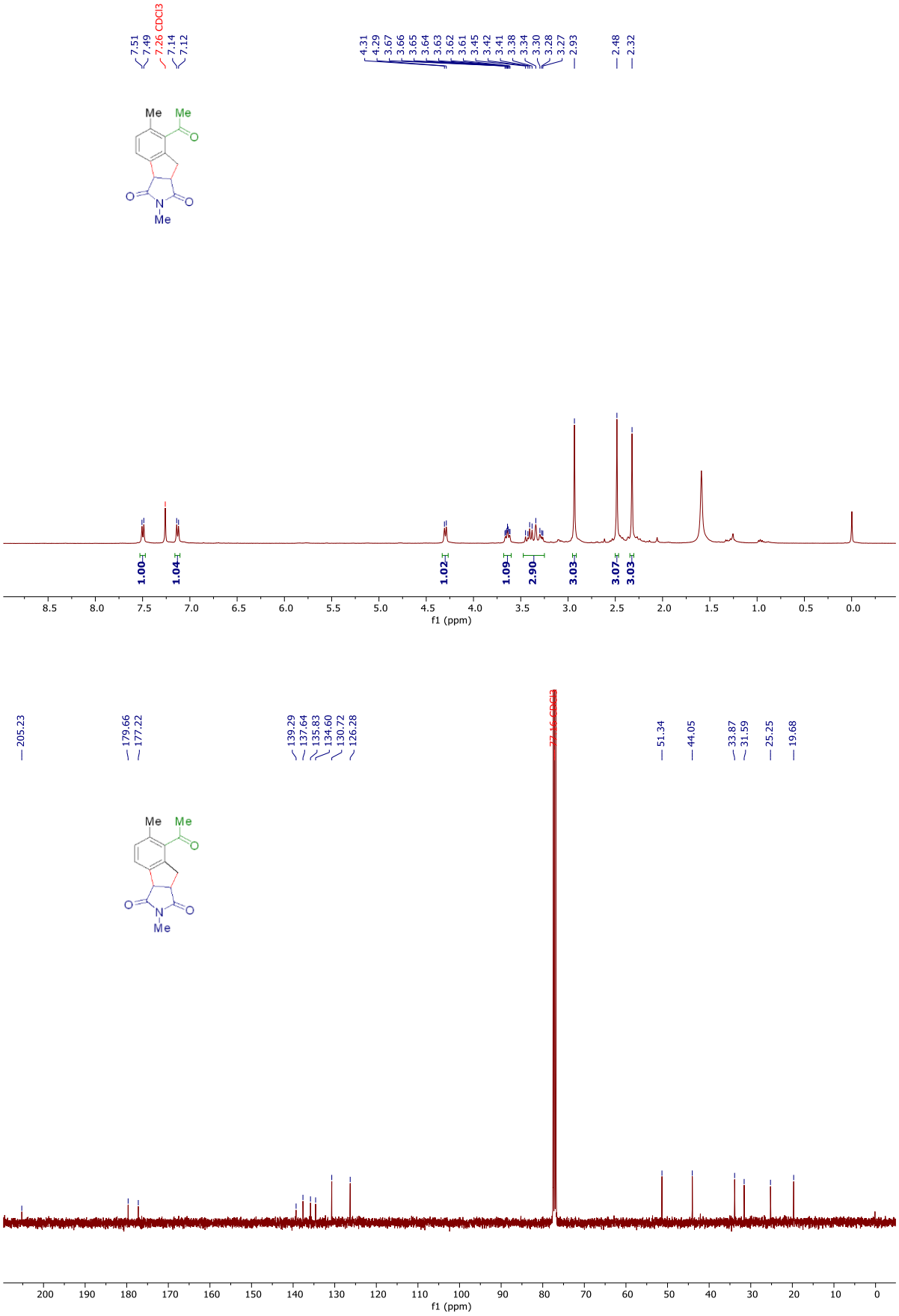




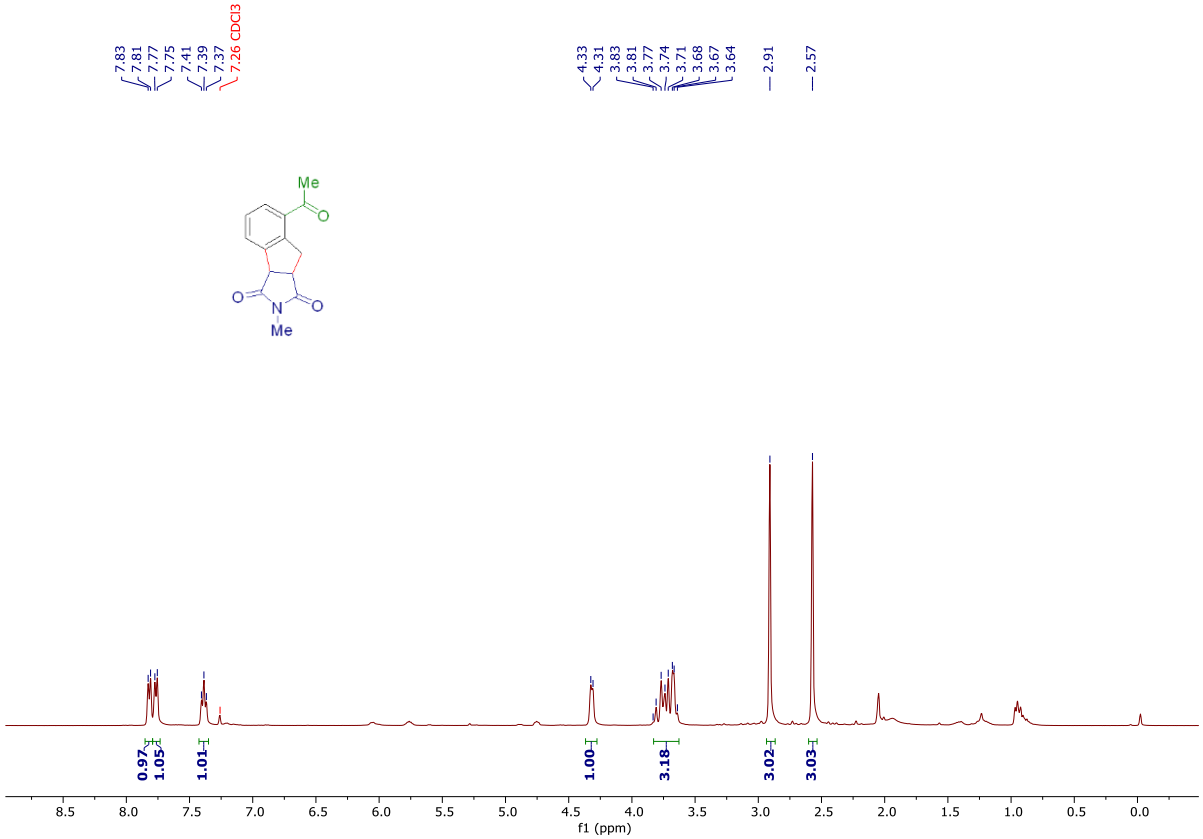
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3gb

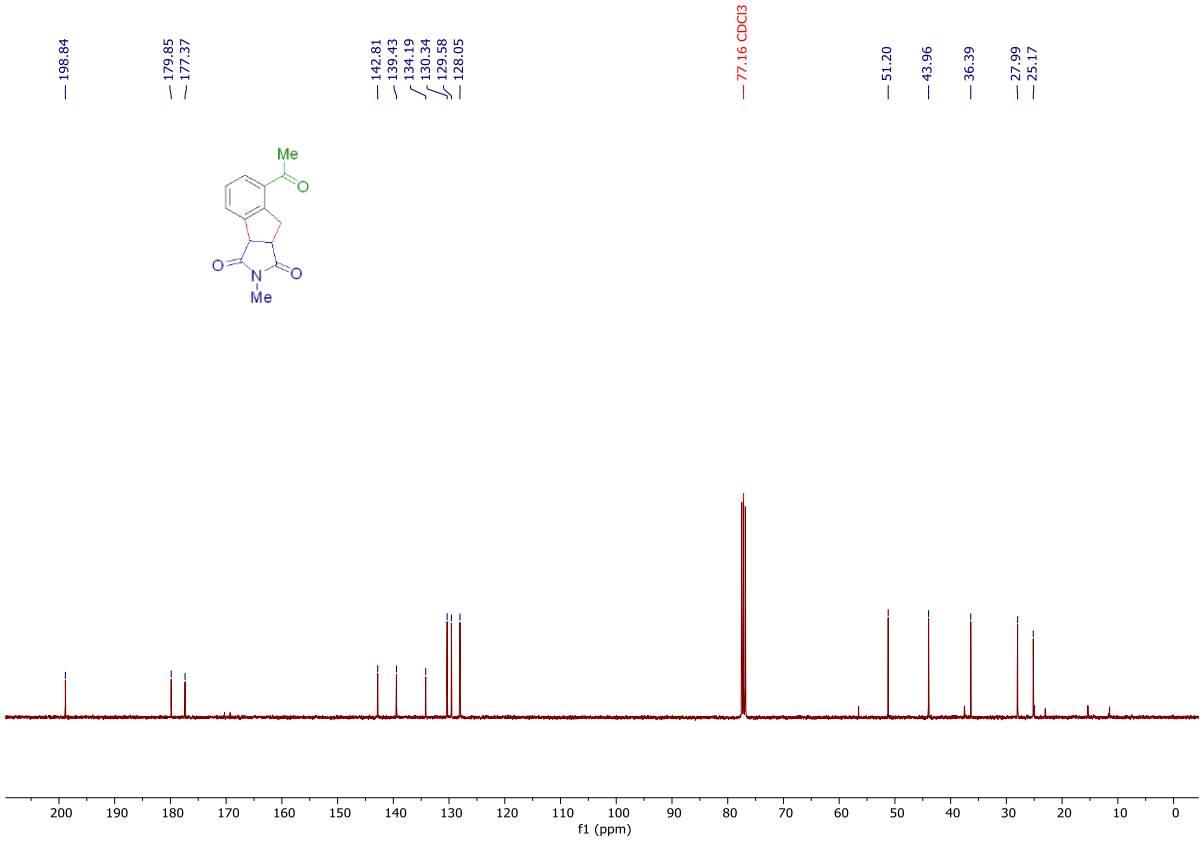


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3hb

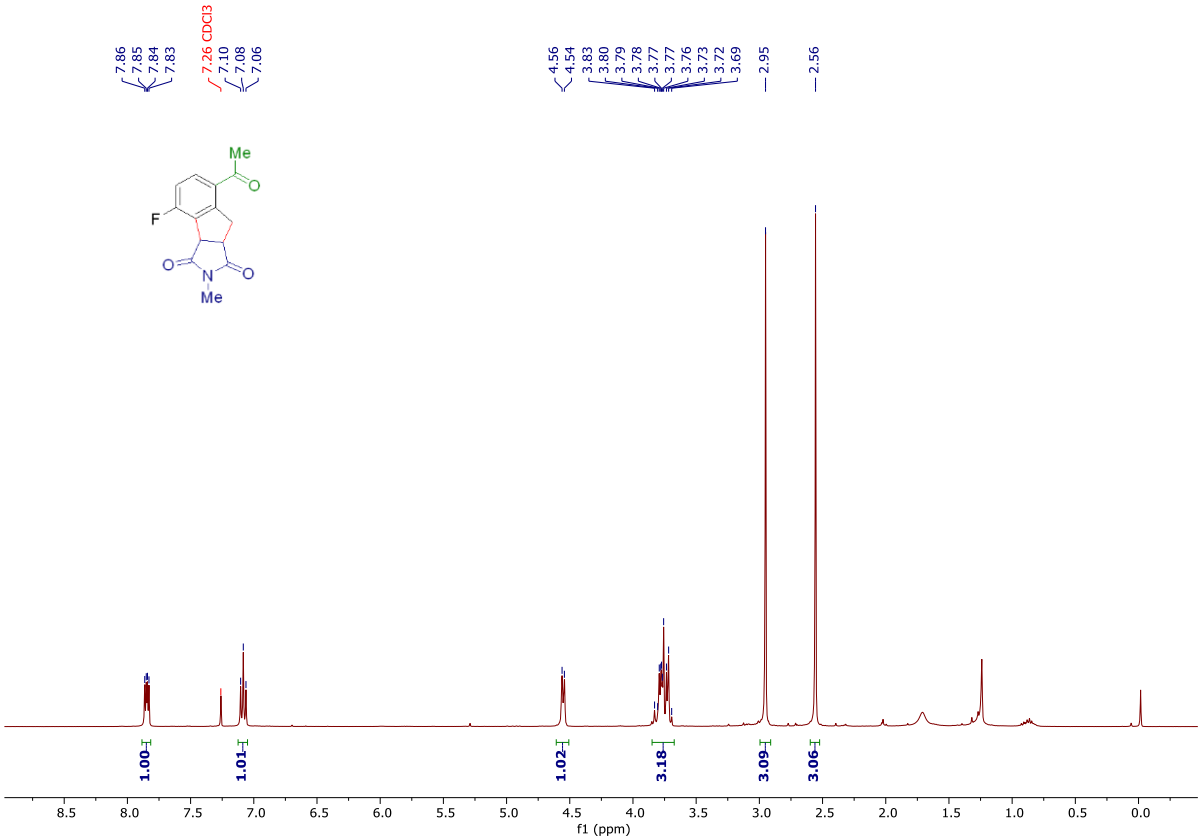


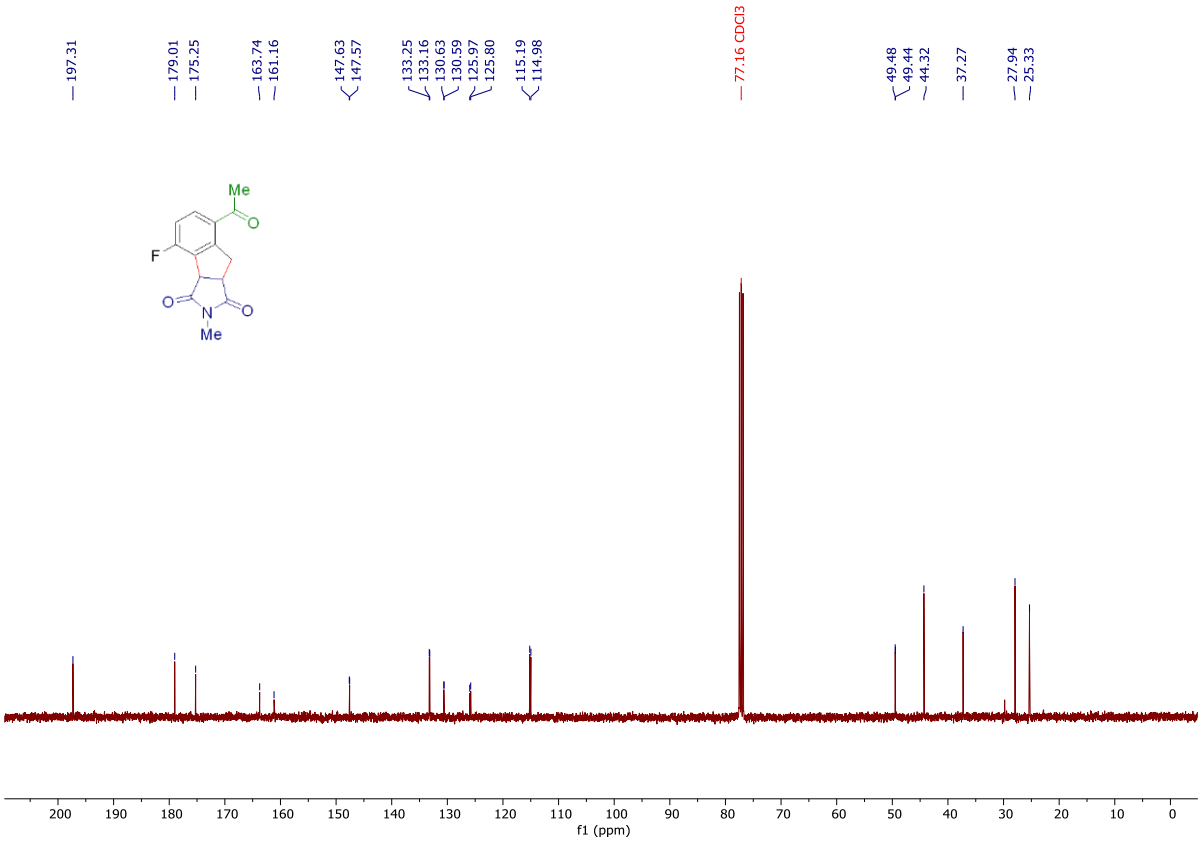
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ib



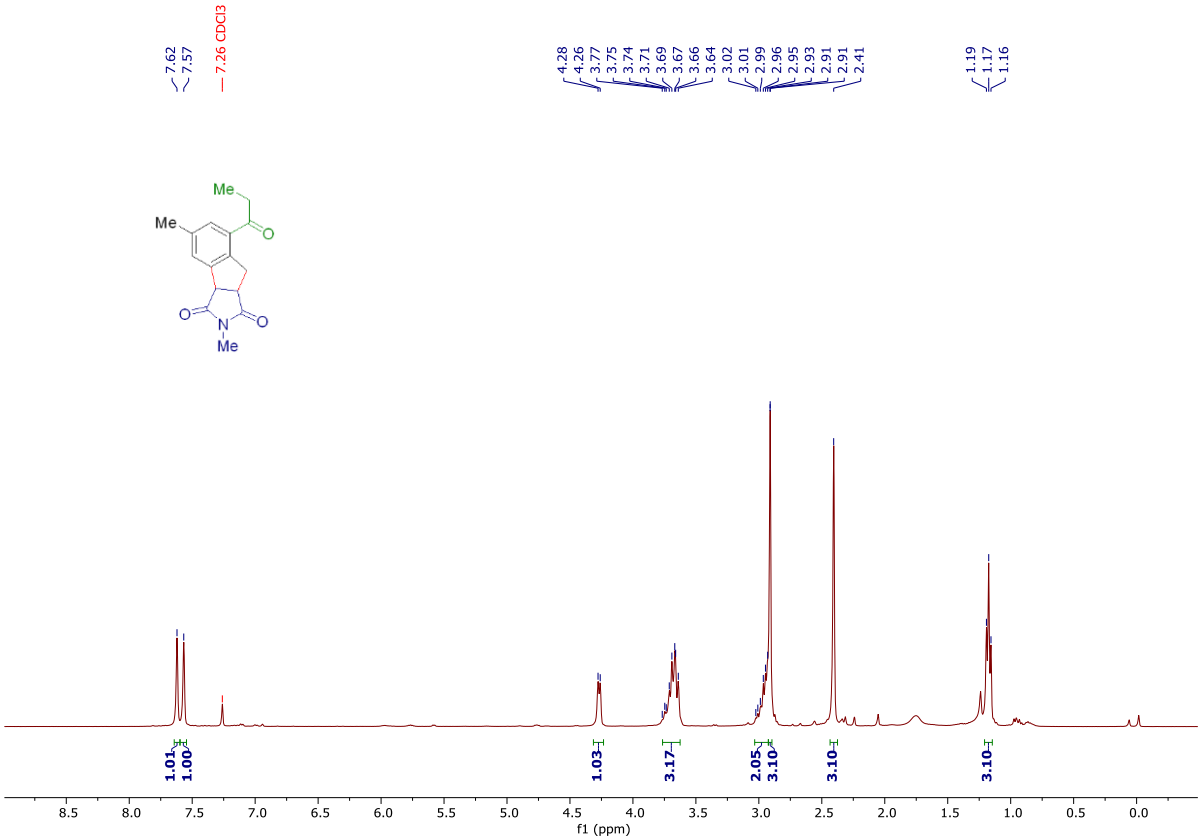


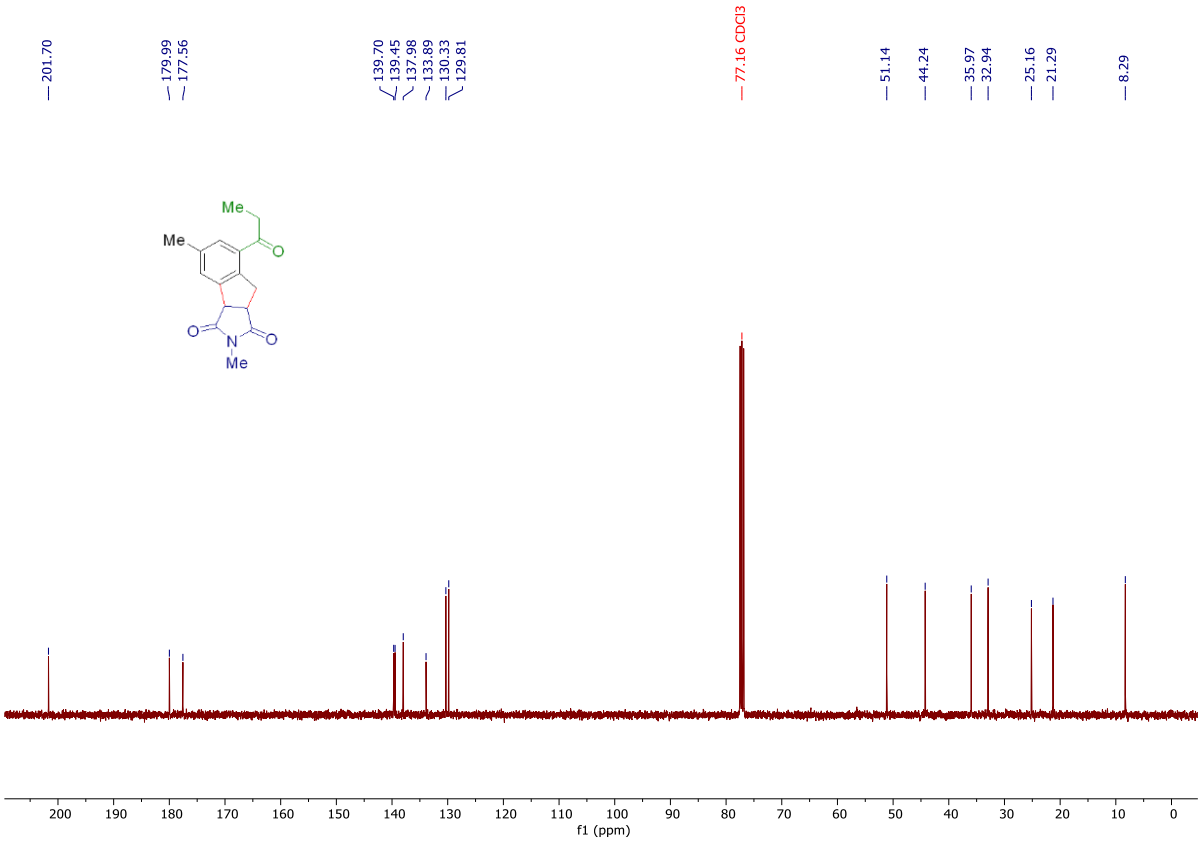
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3jb



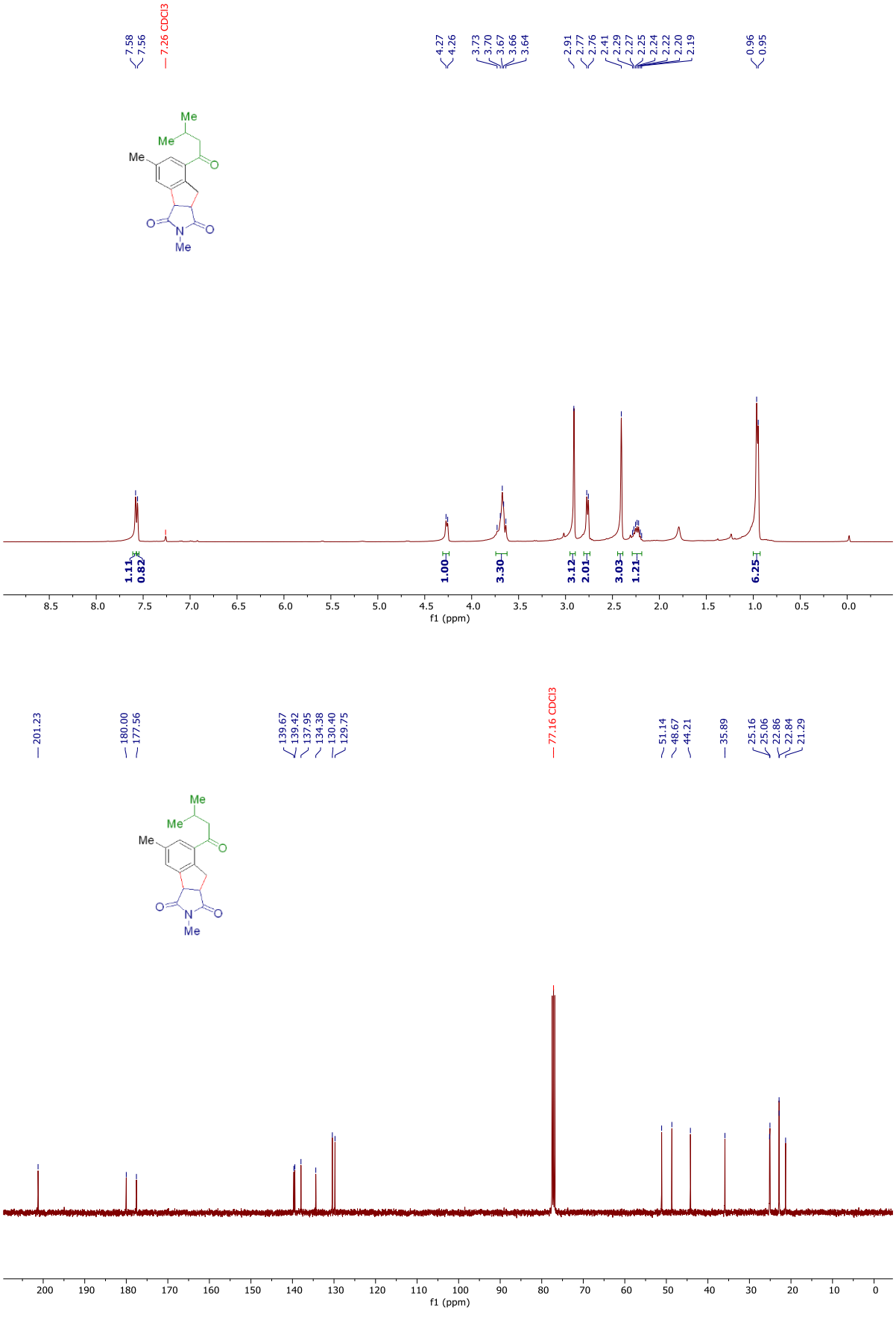


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5ab

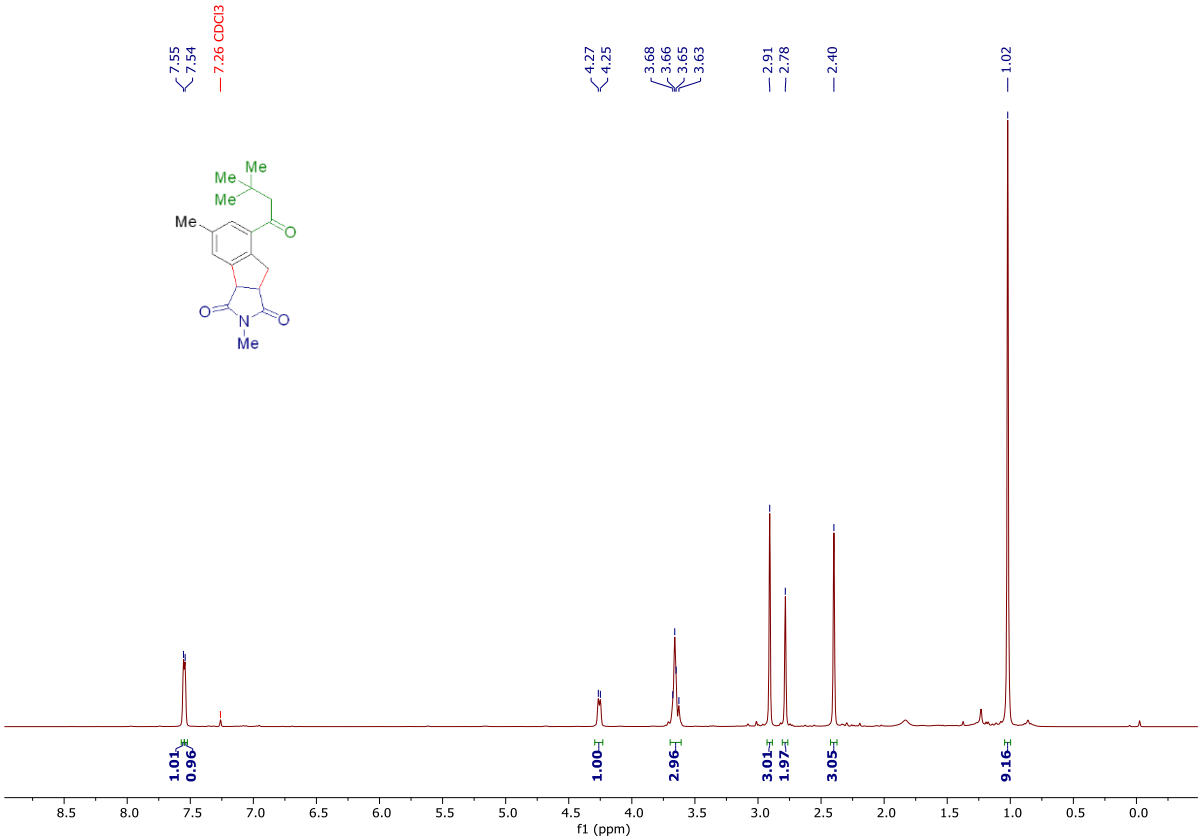


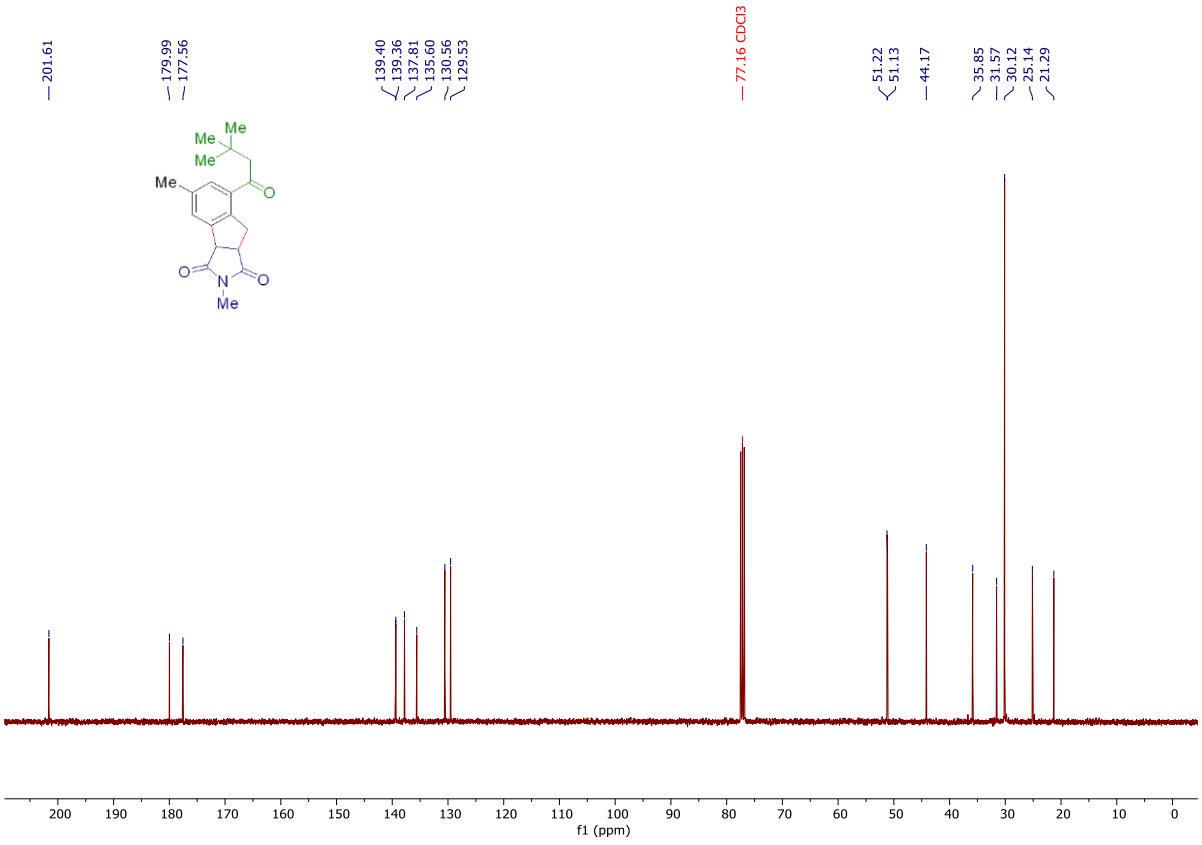


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5bb

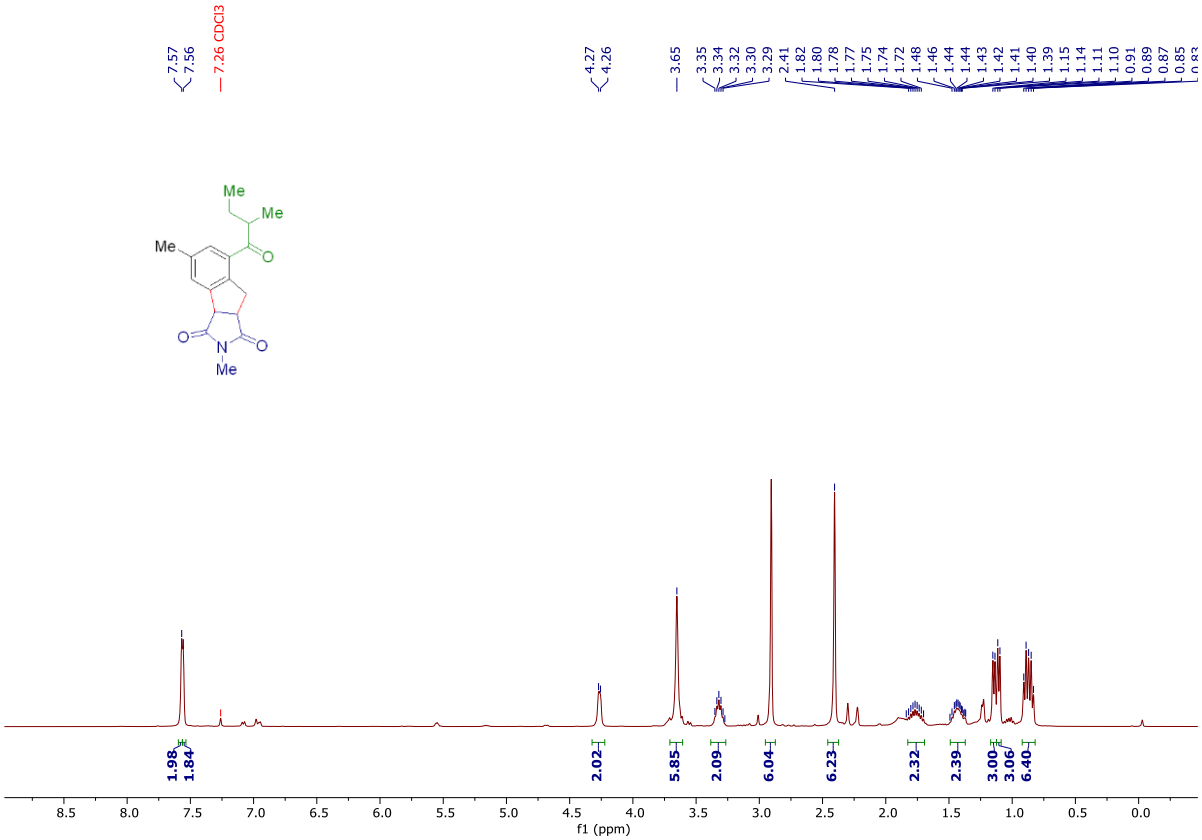


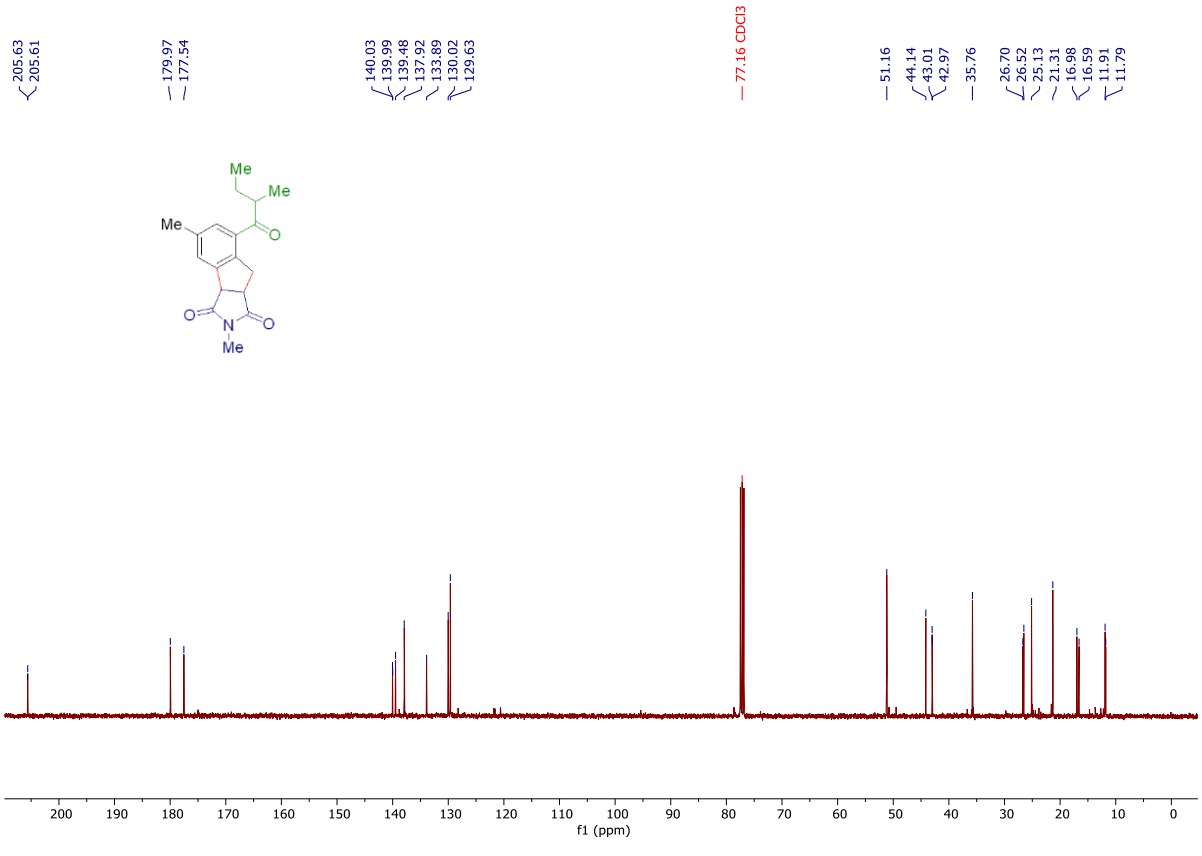
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5cb



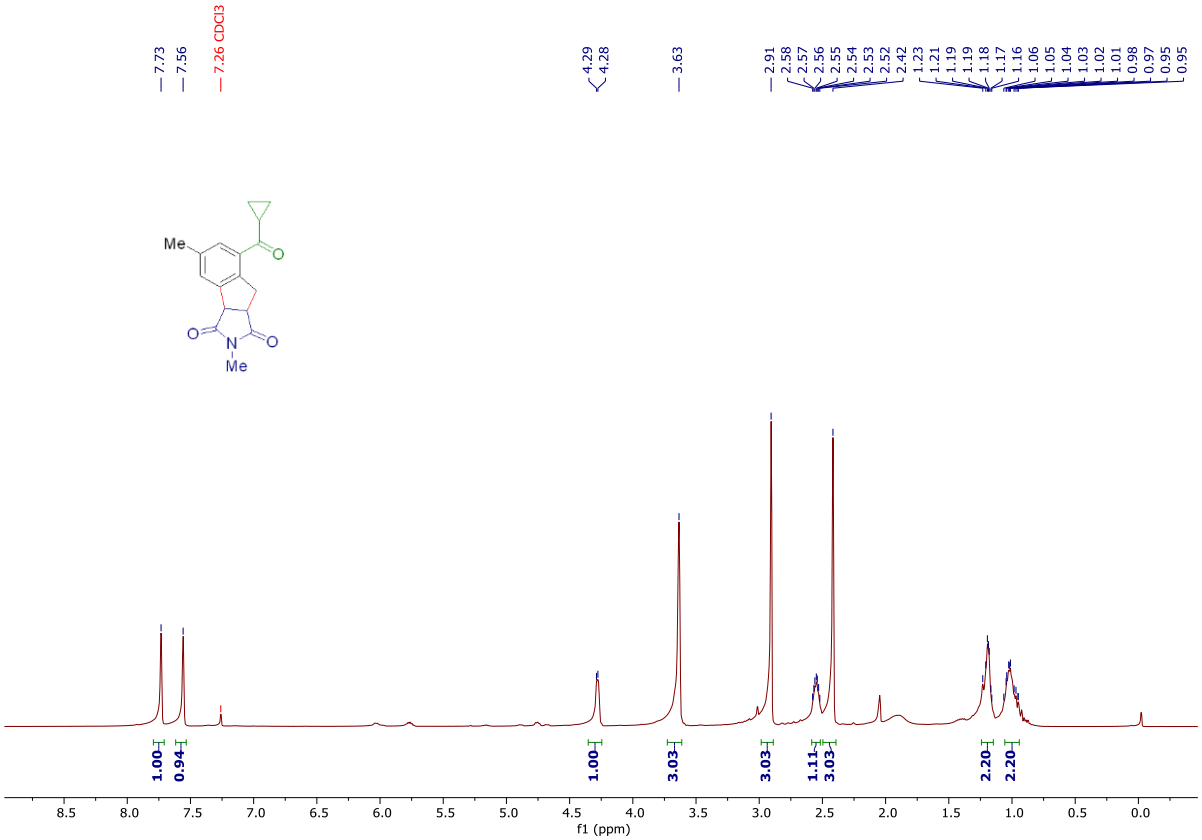


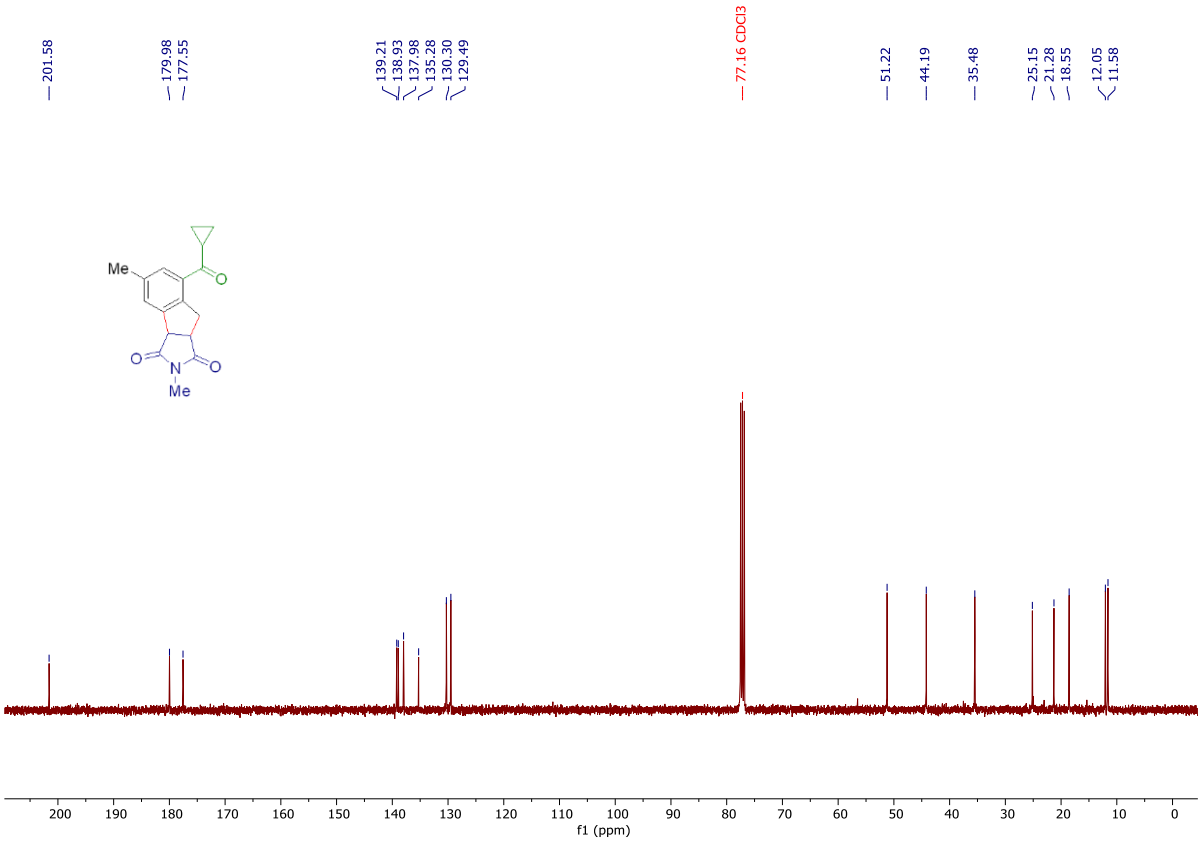
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5db



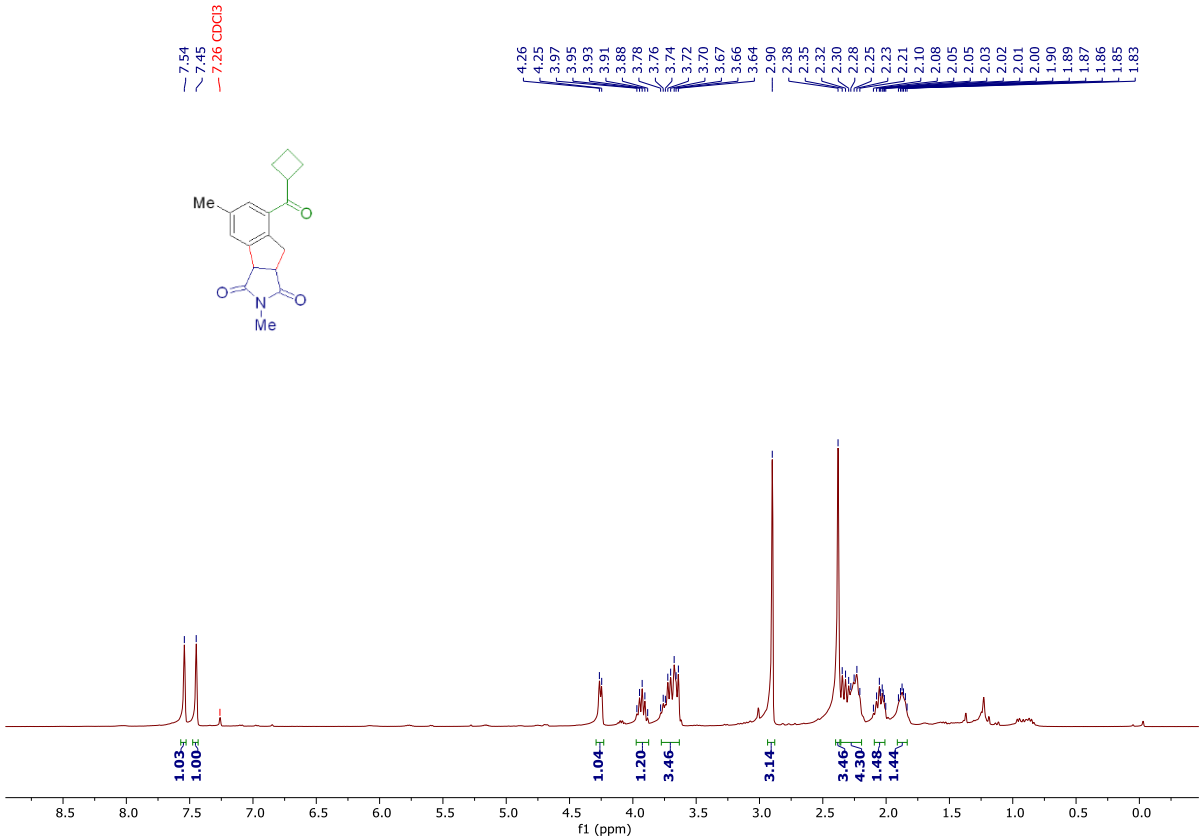


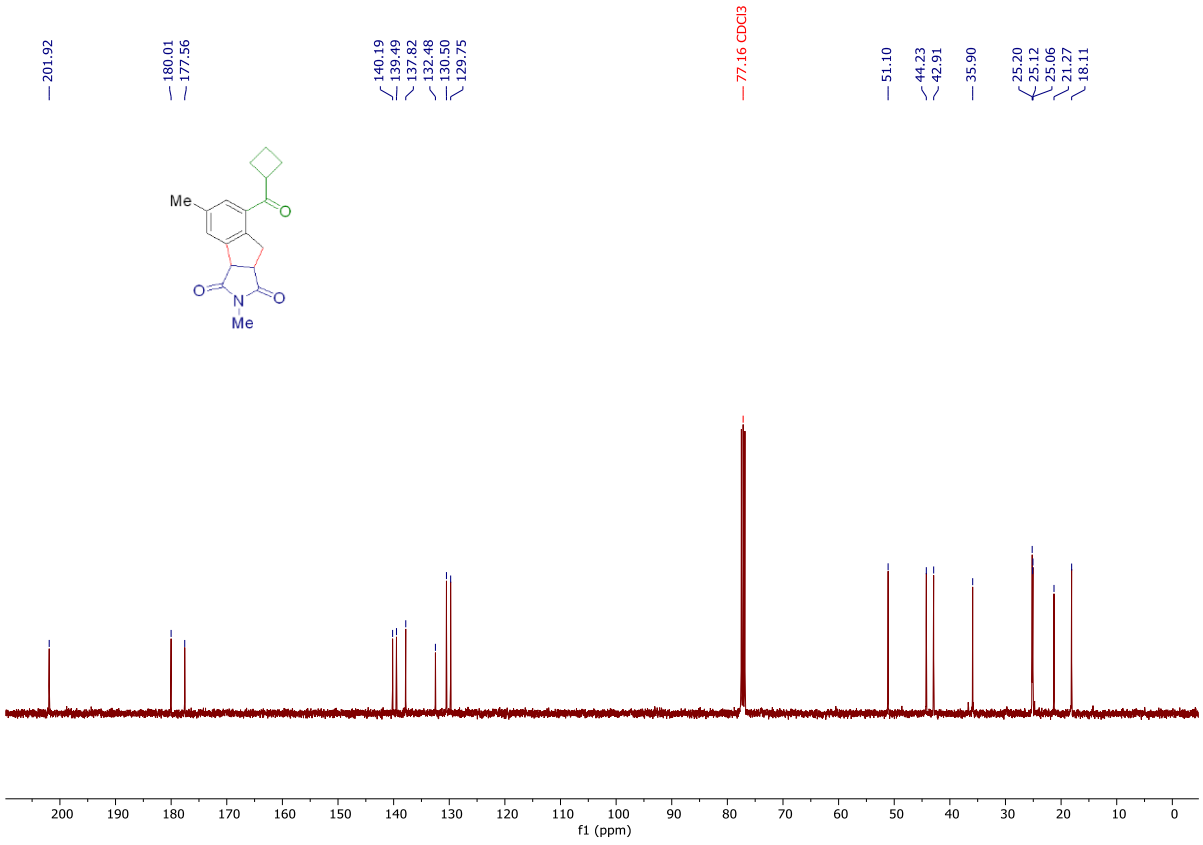
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5eb



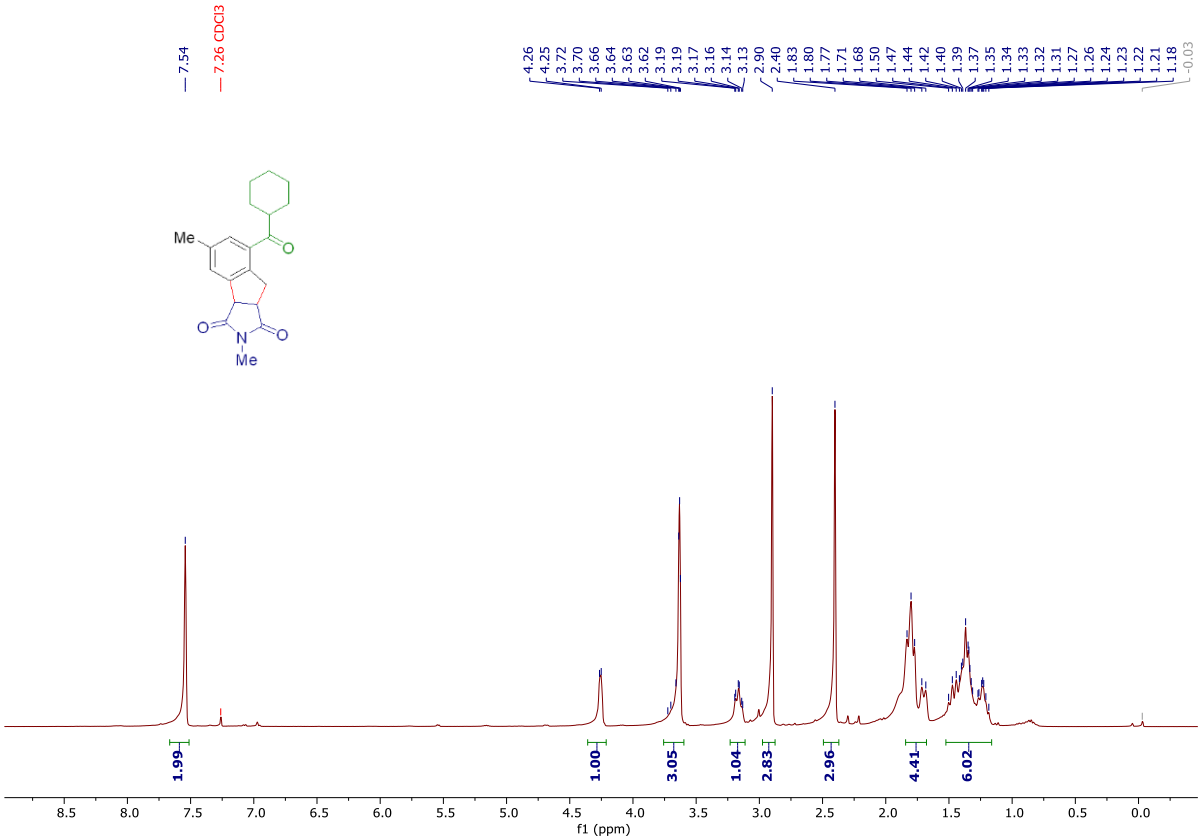


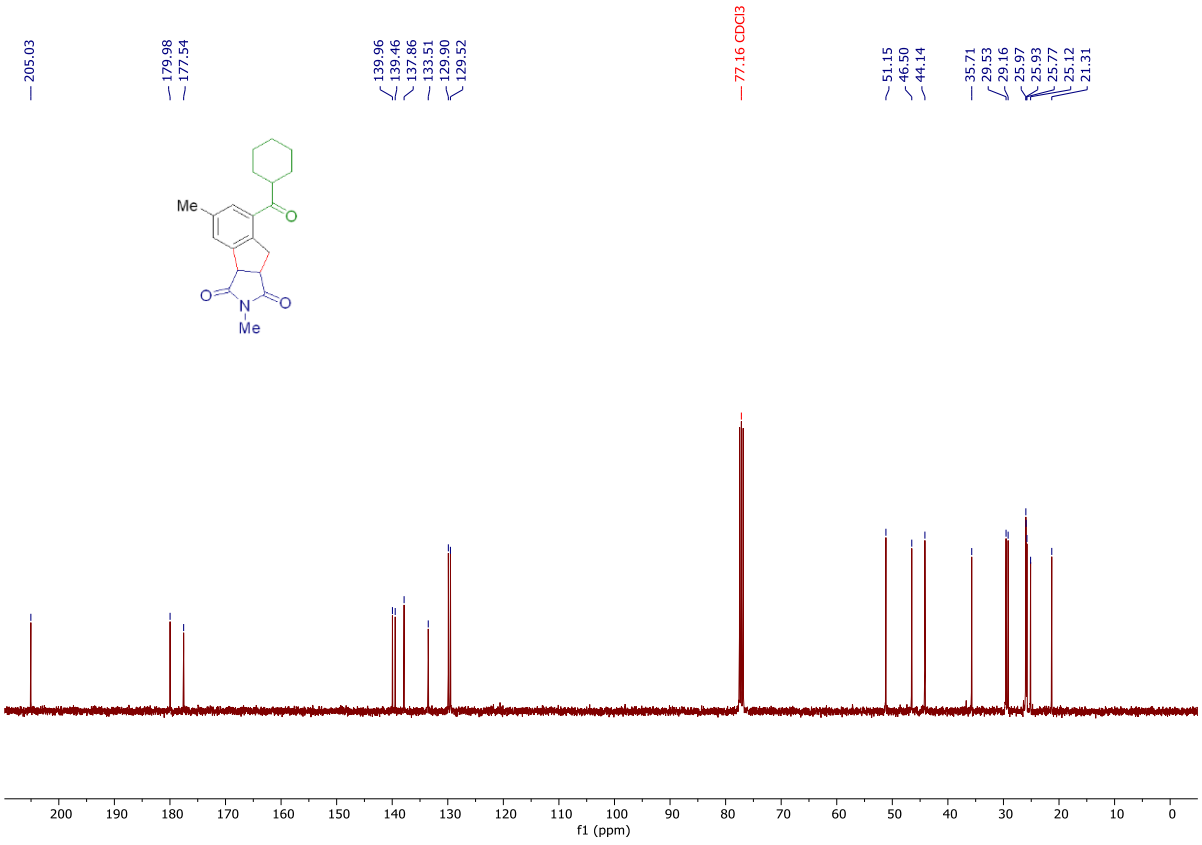
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5fb



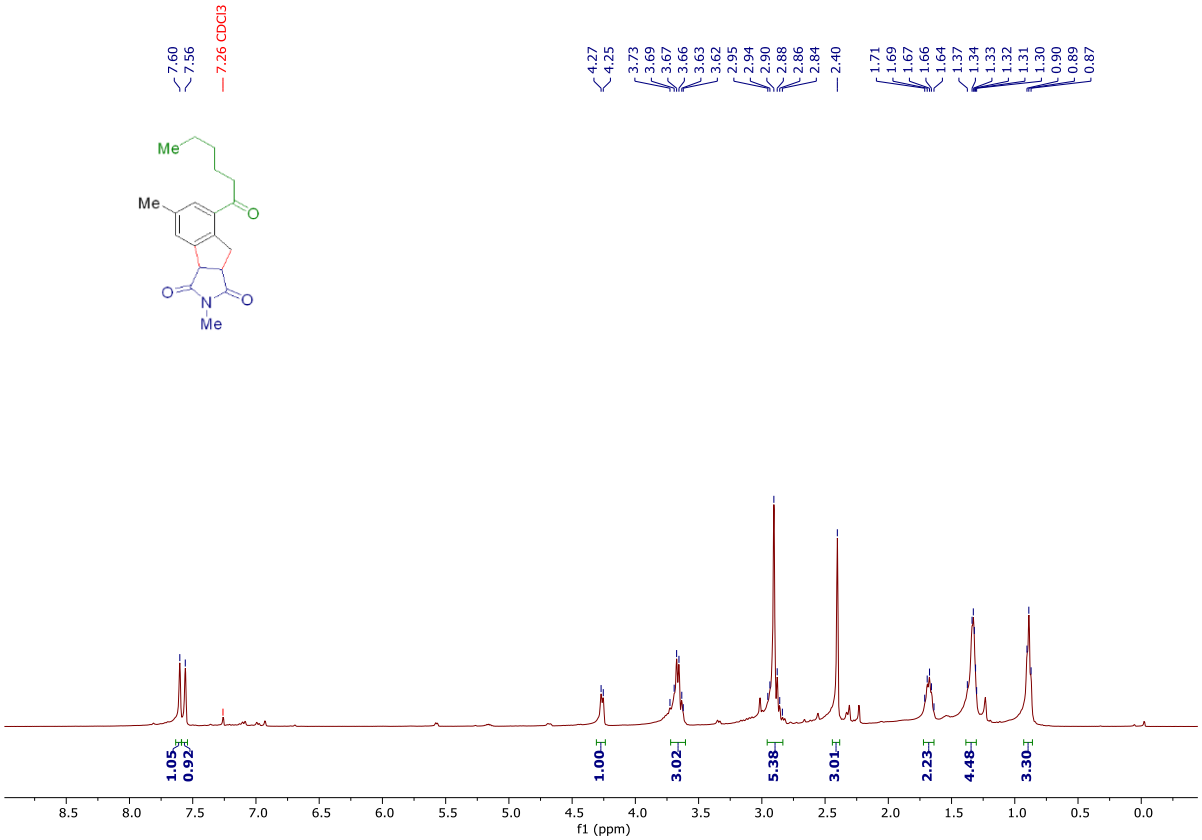


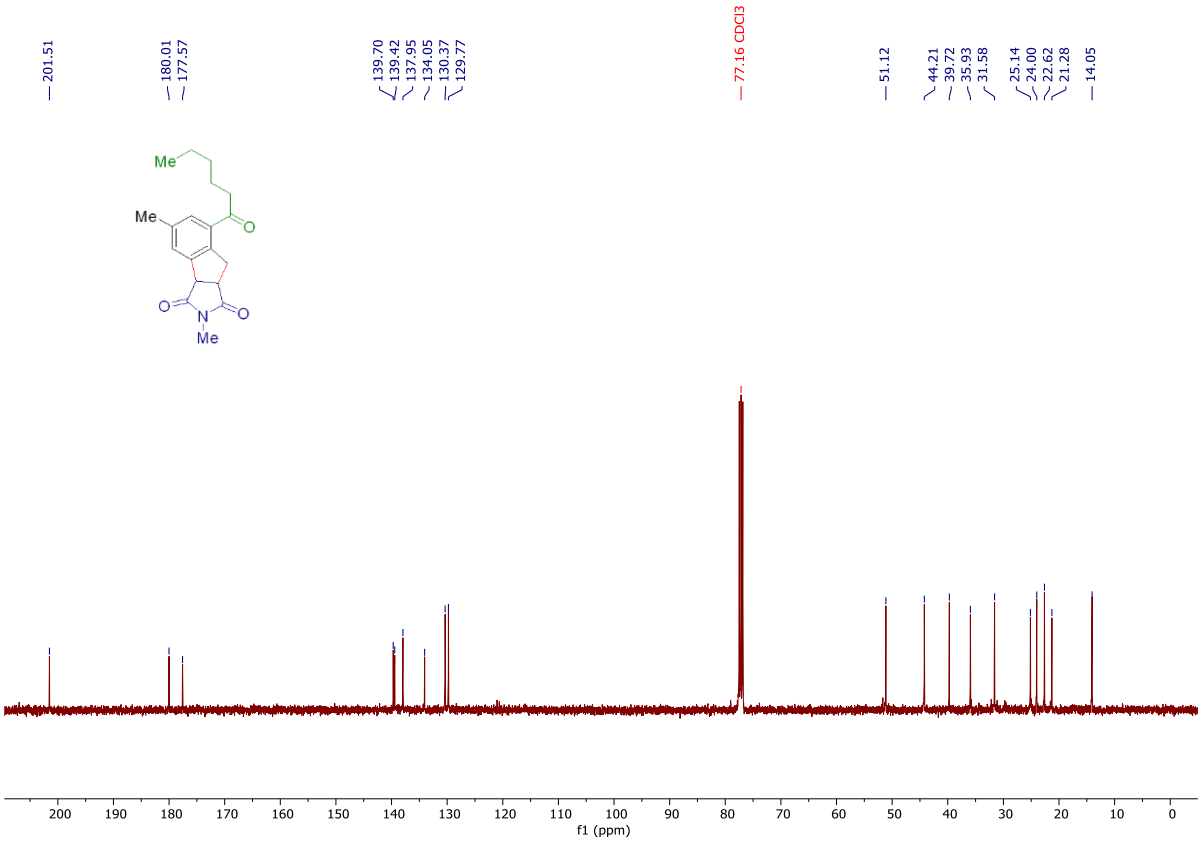
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5gb



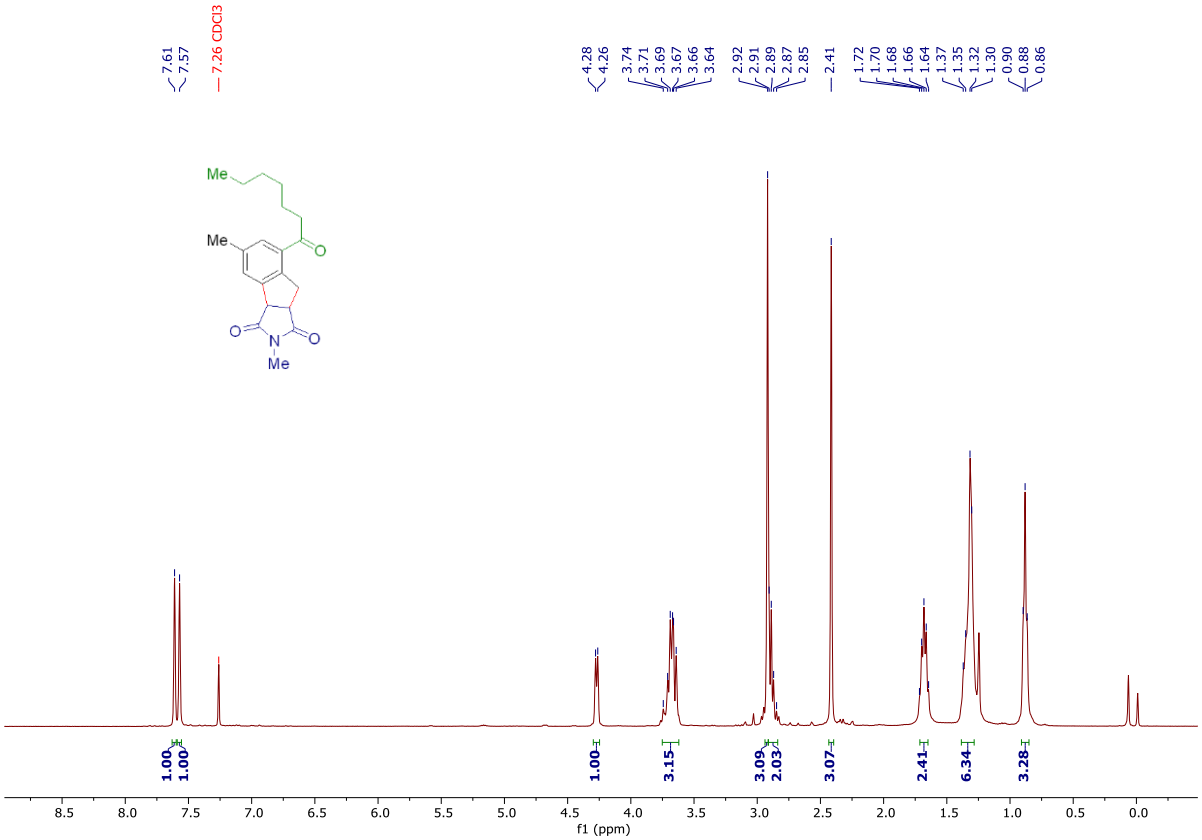


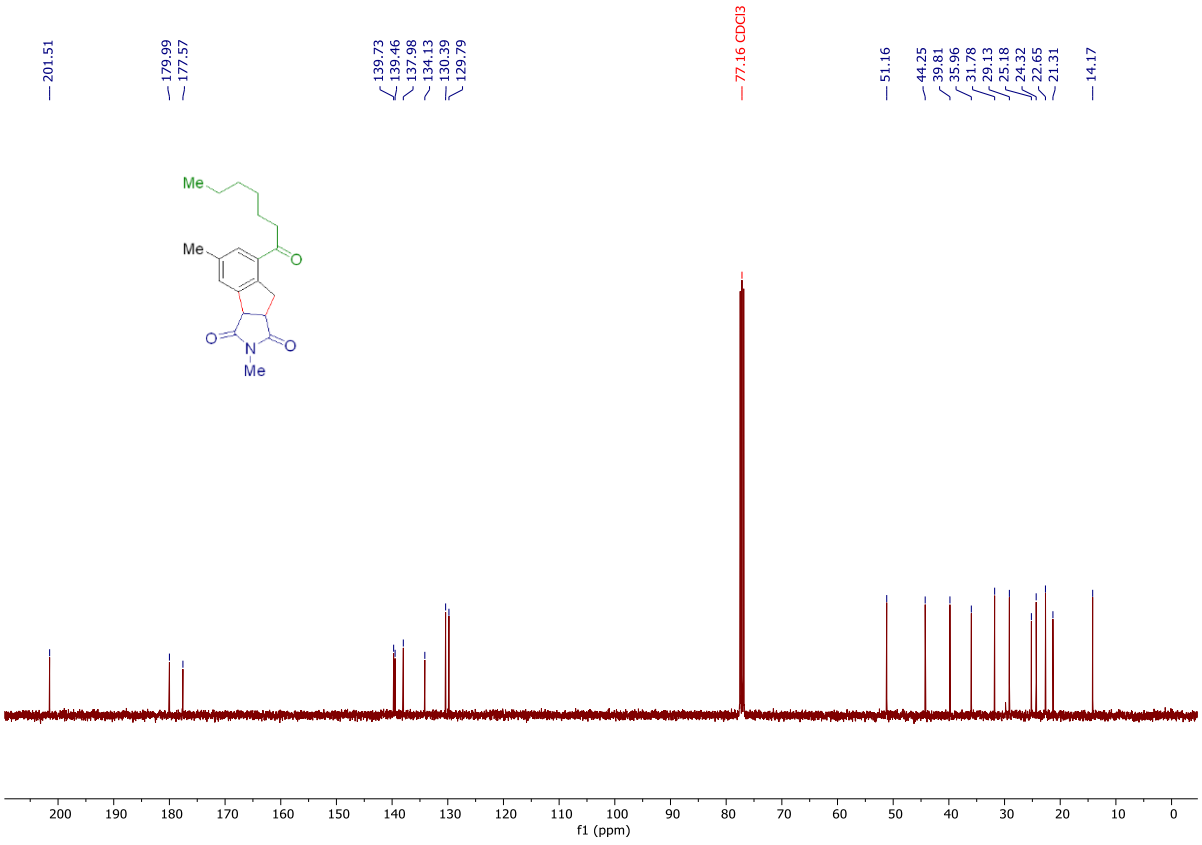
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5hb



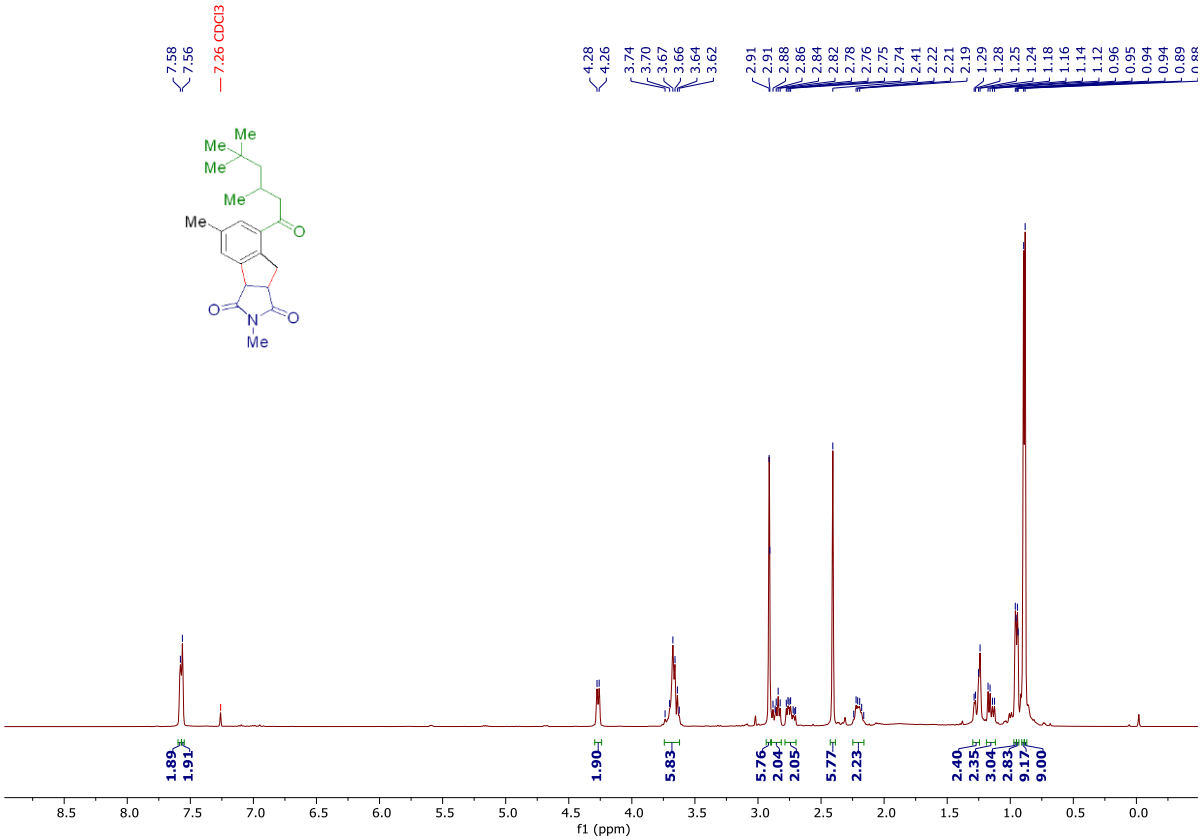


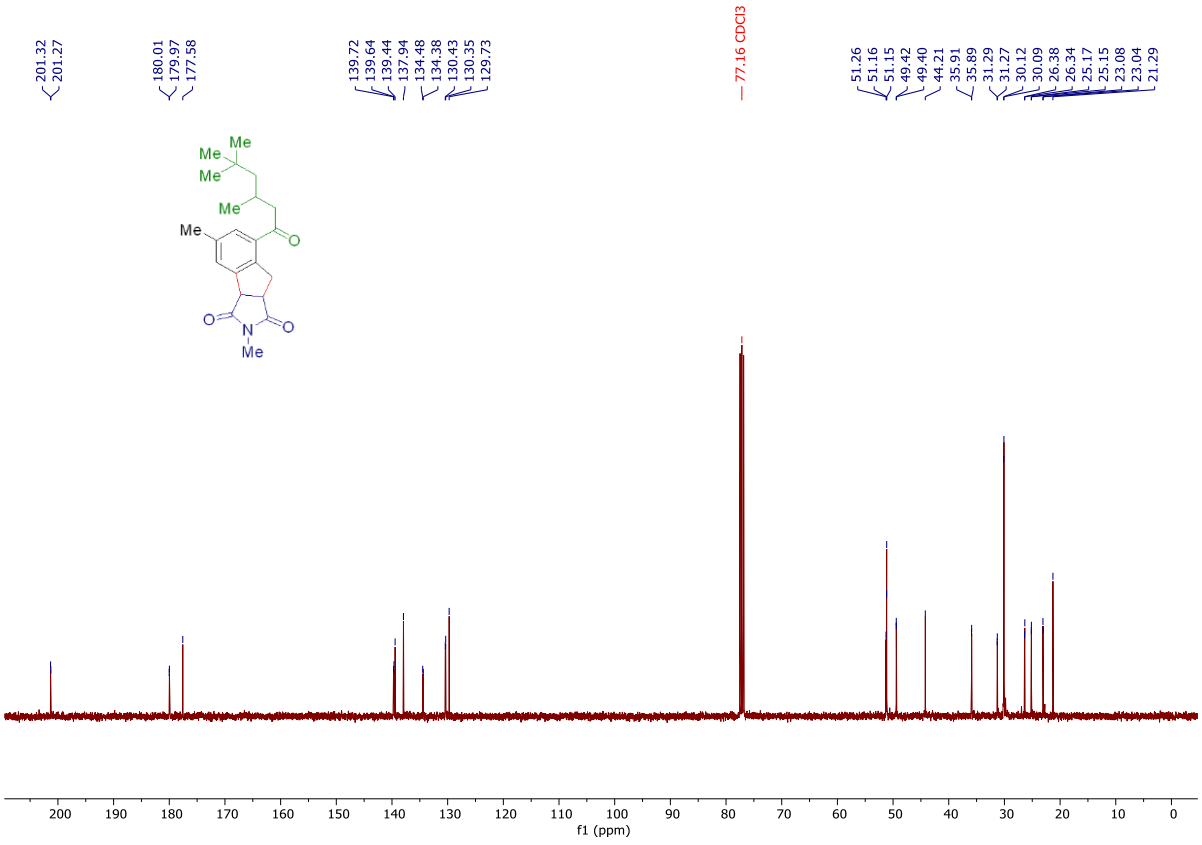
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5ib



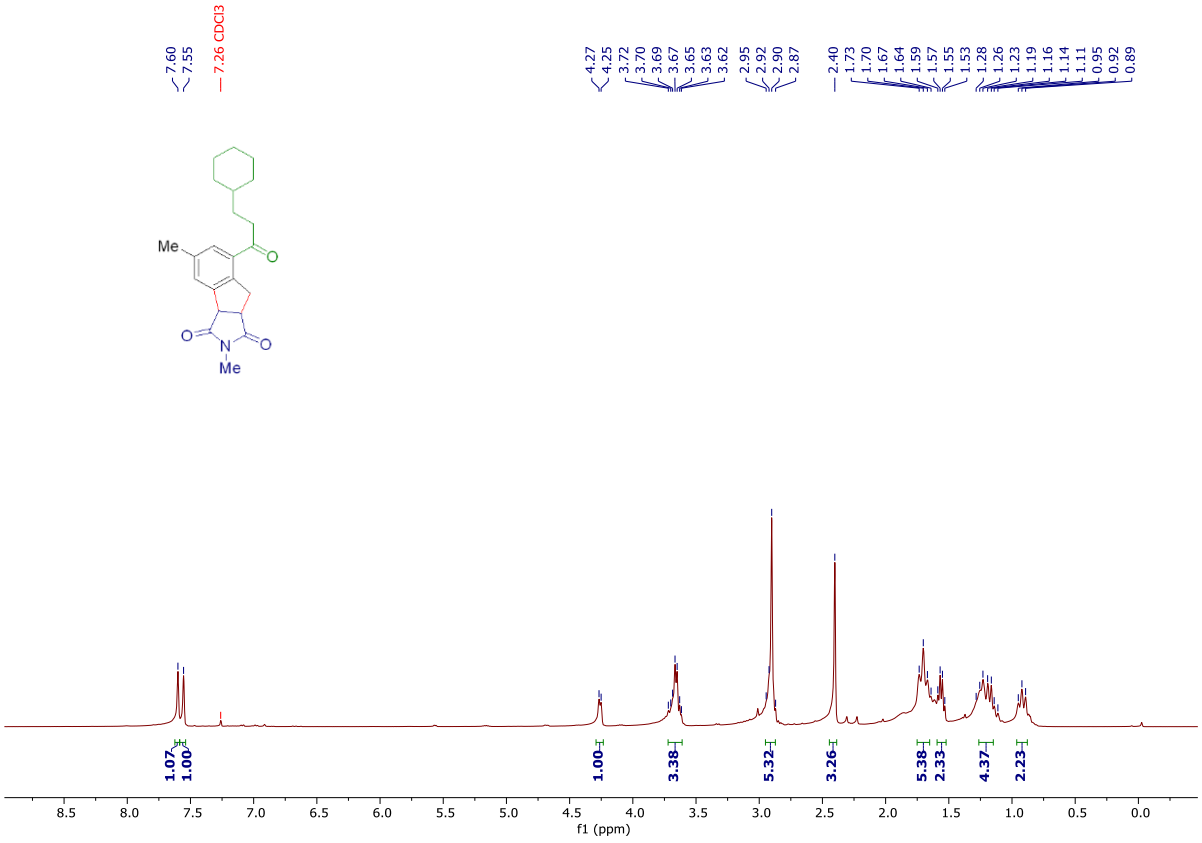


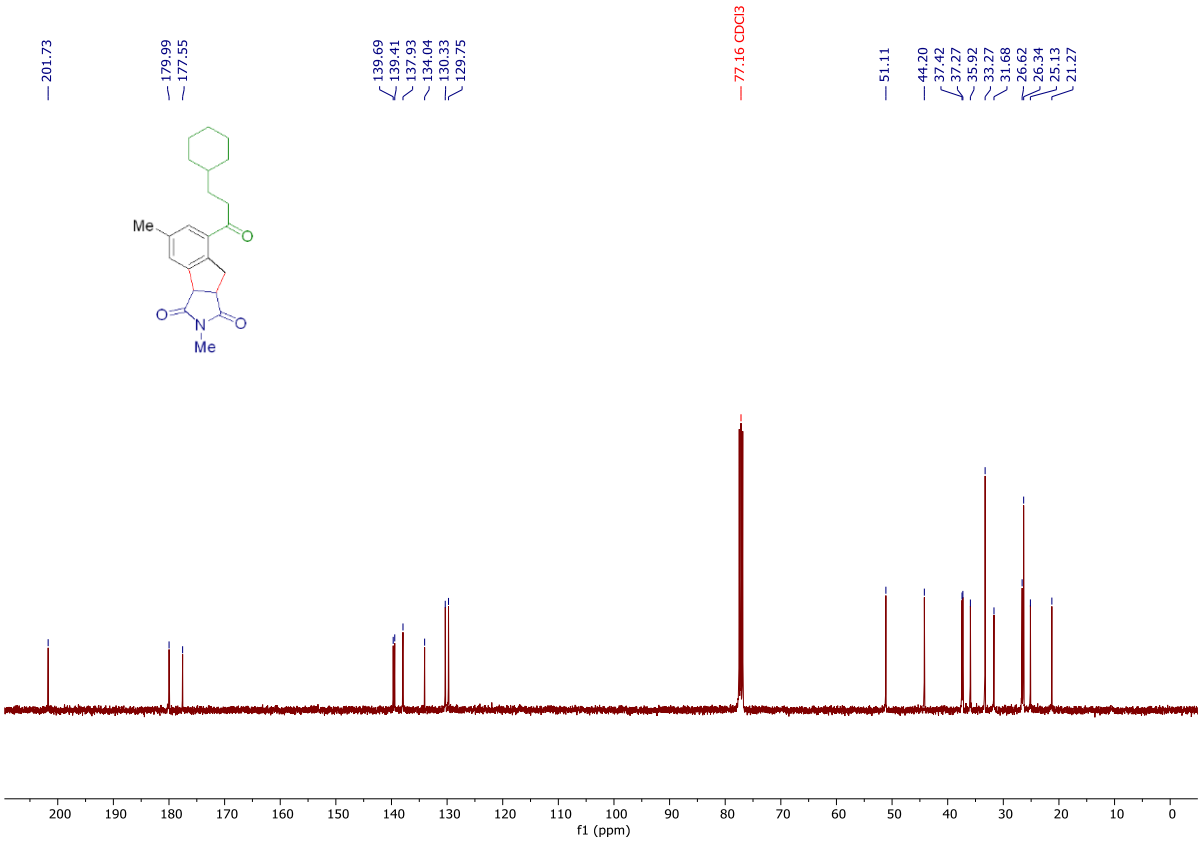
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5jb



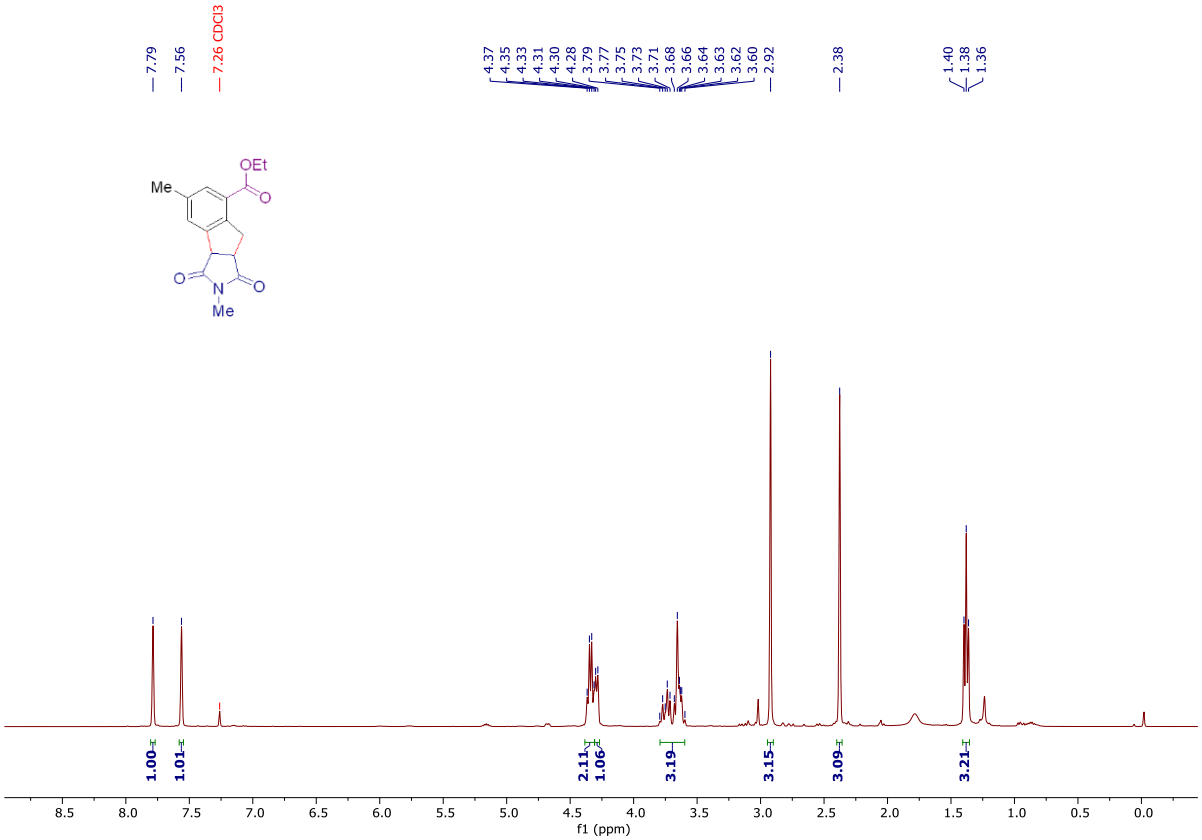


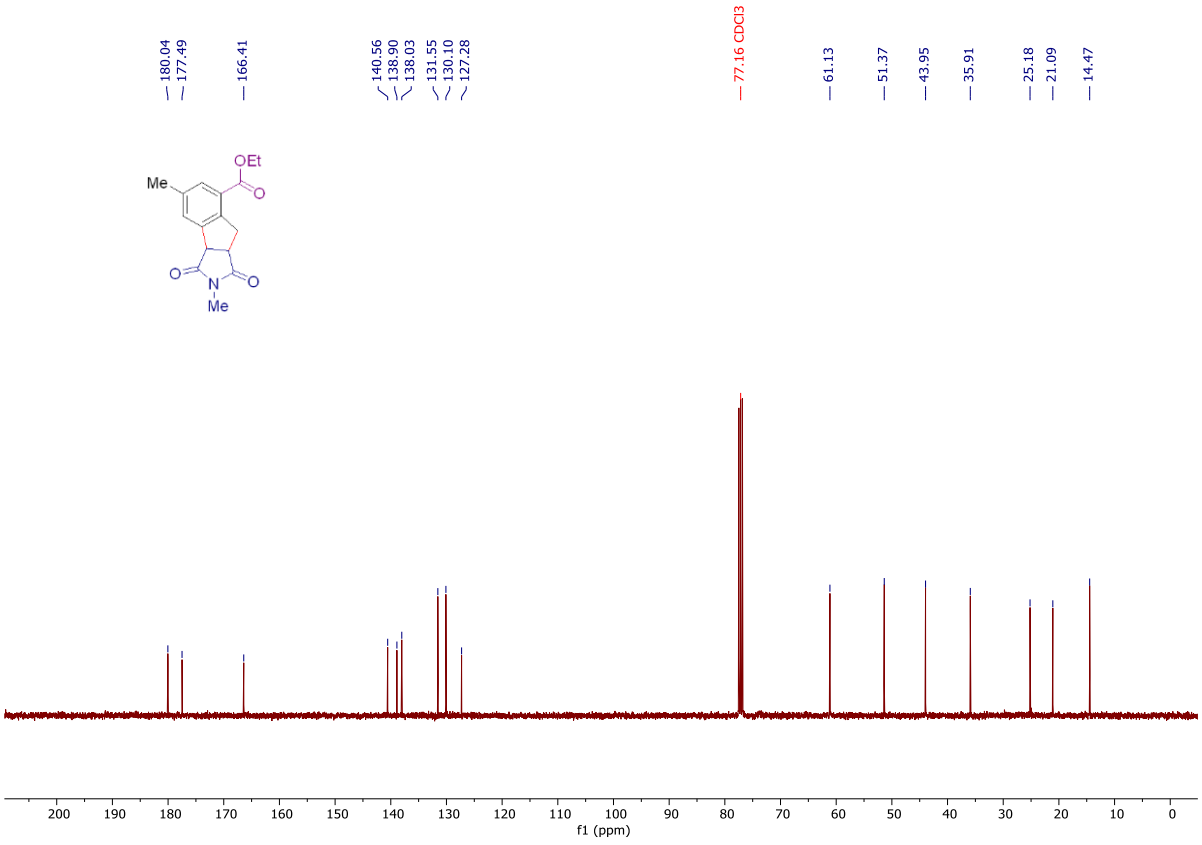
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5kb



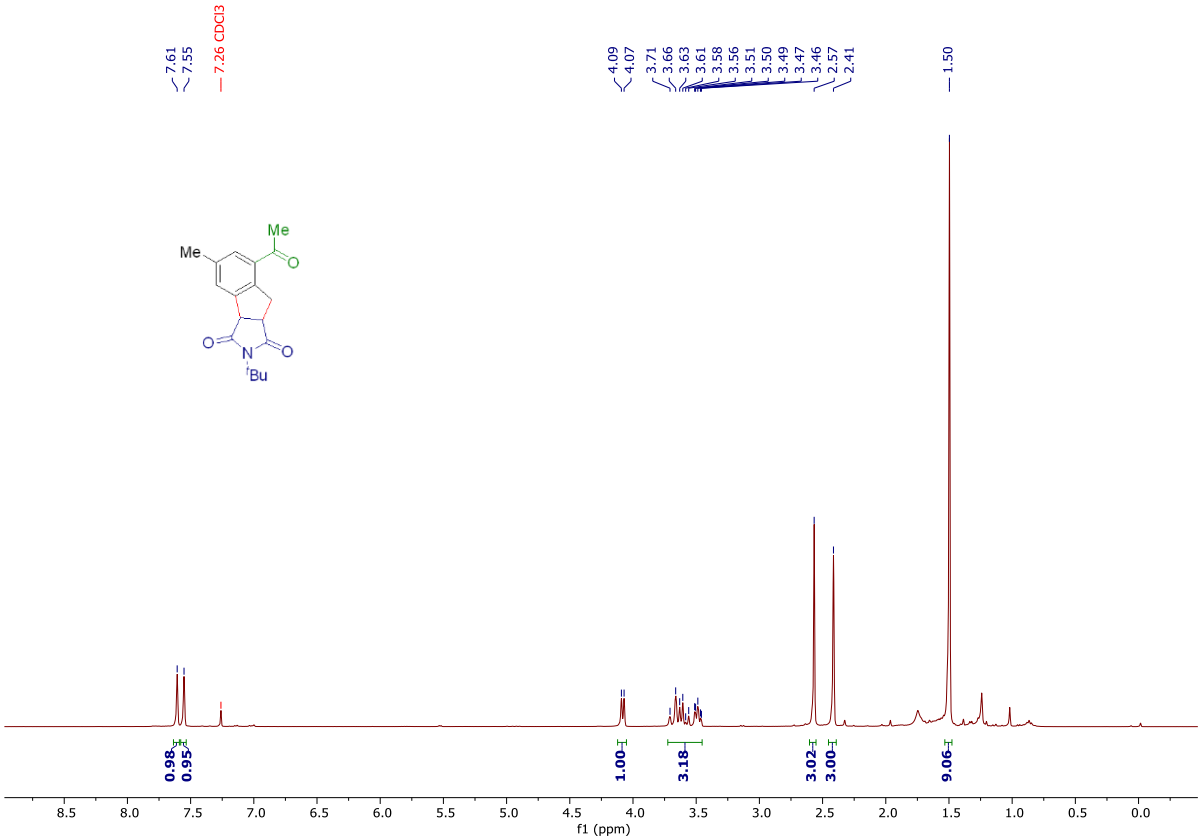


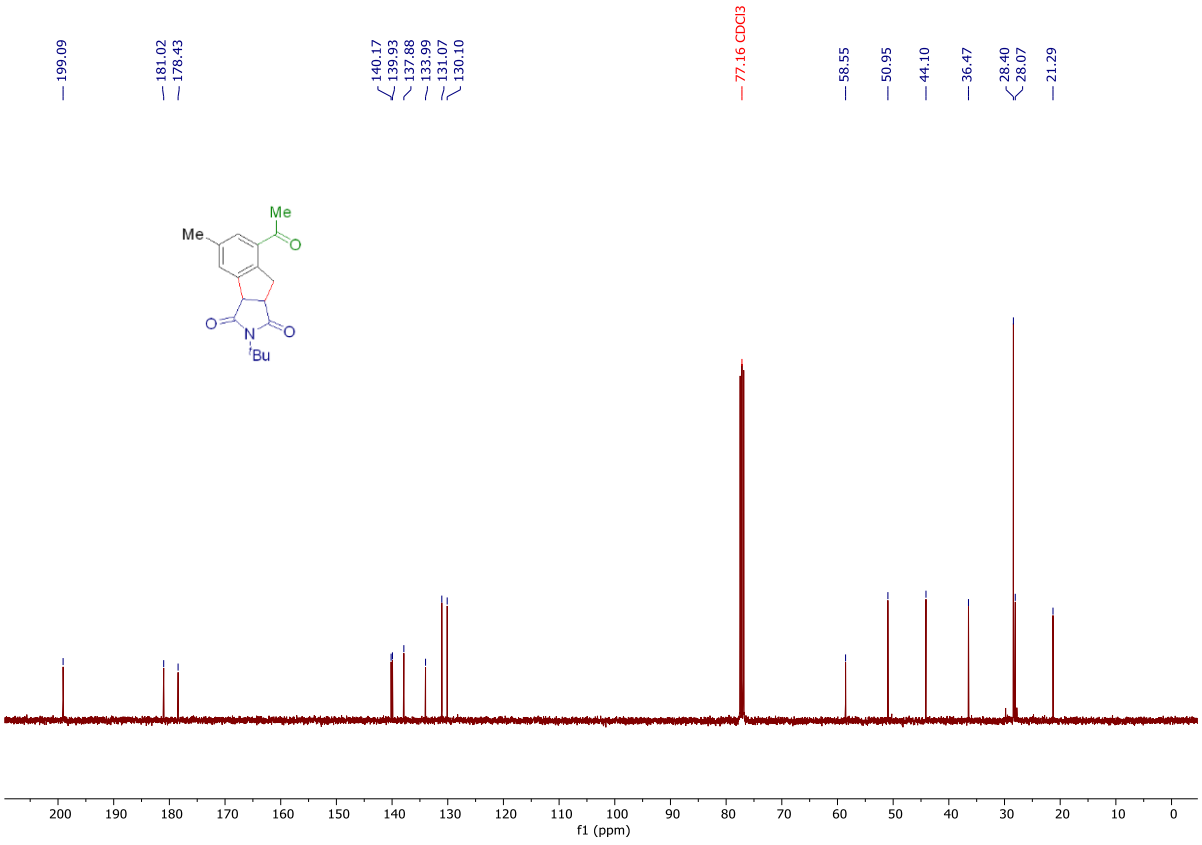
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 5ob



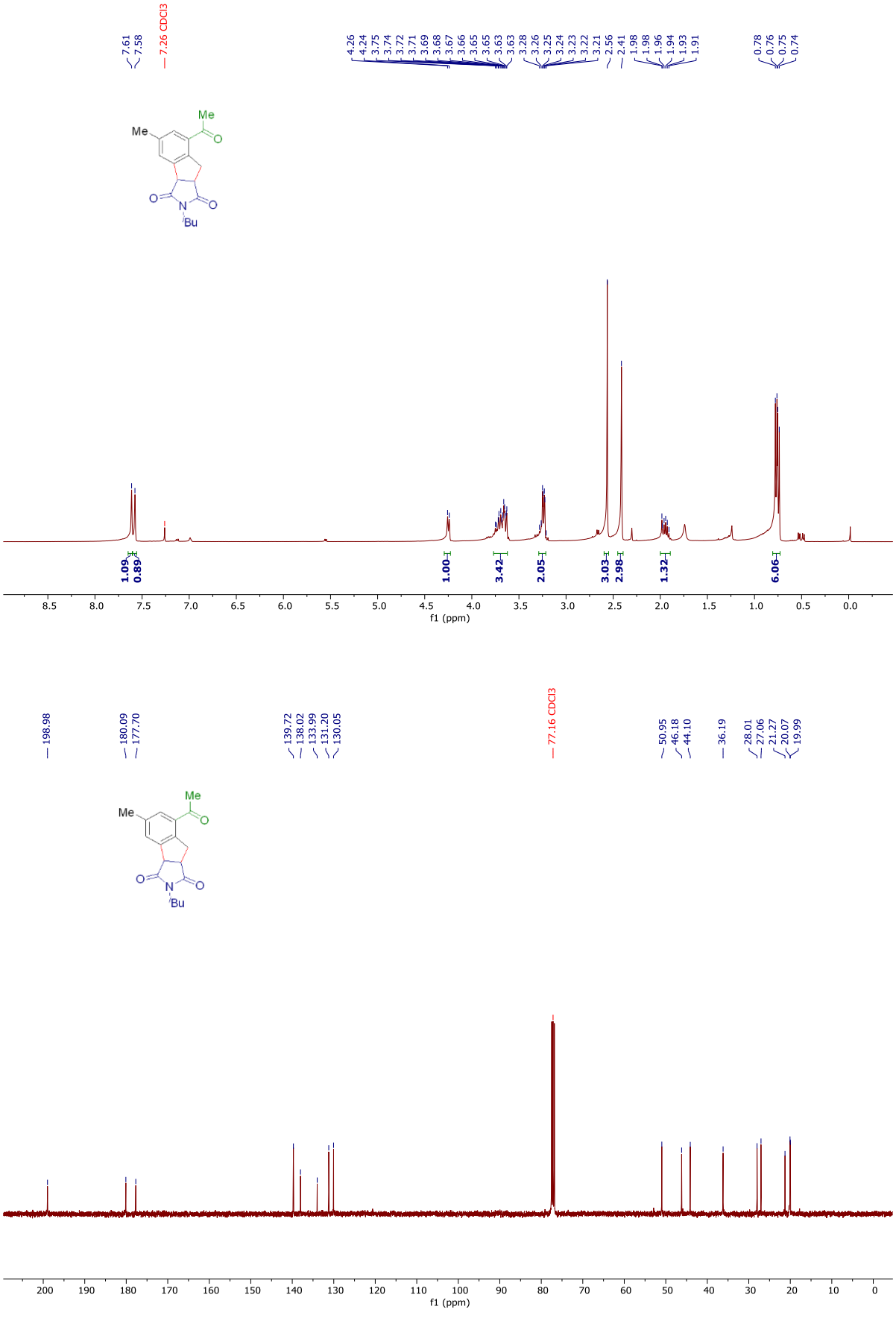


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ac

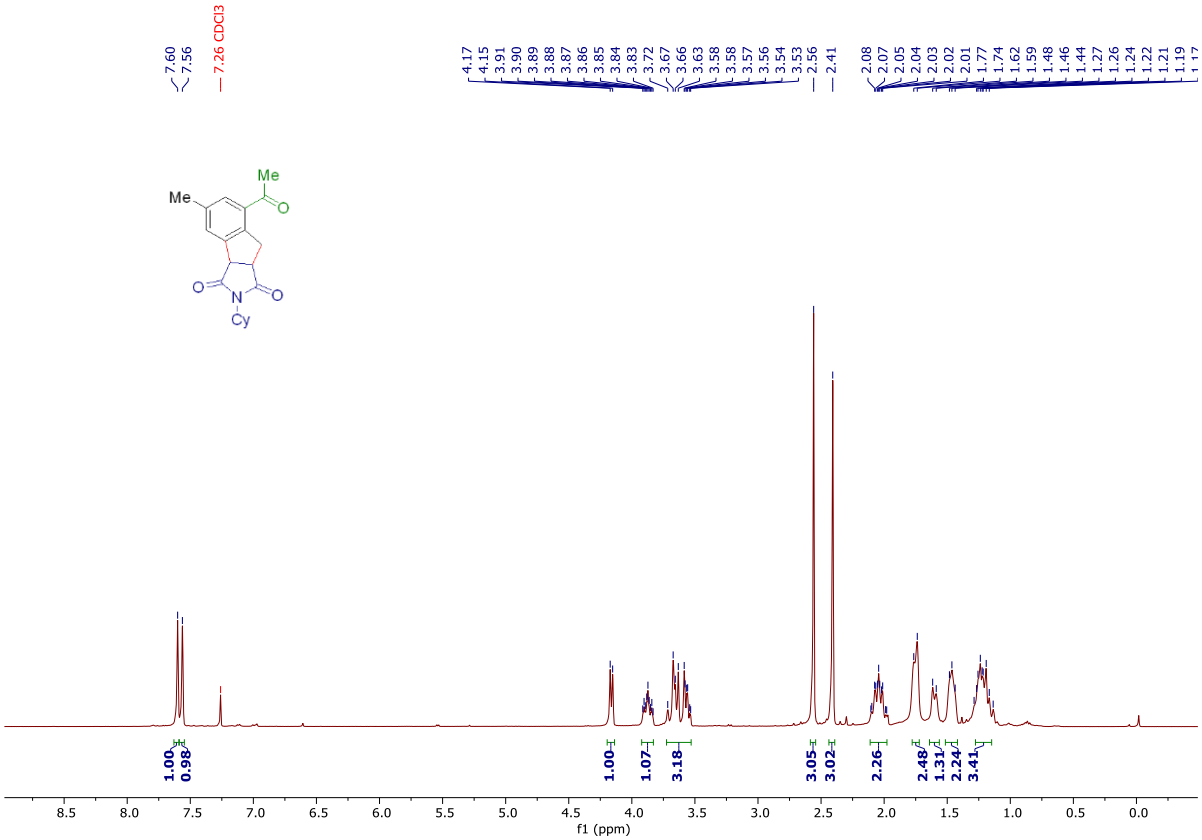


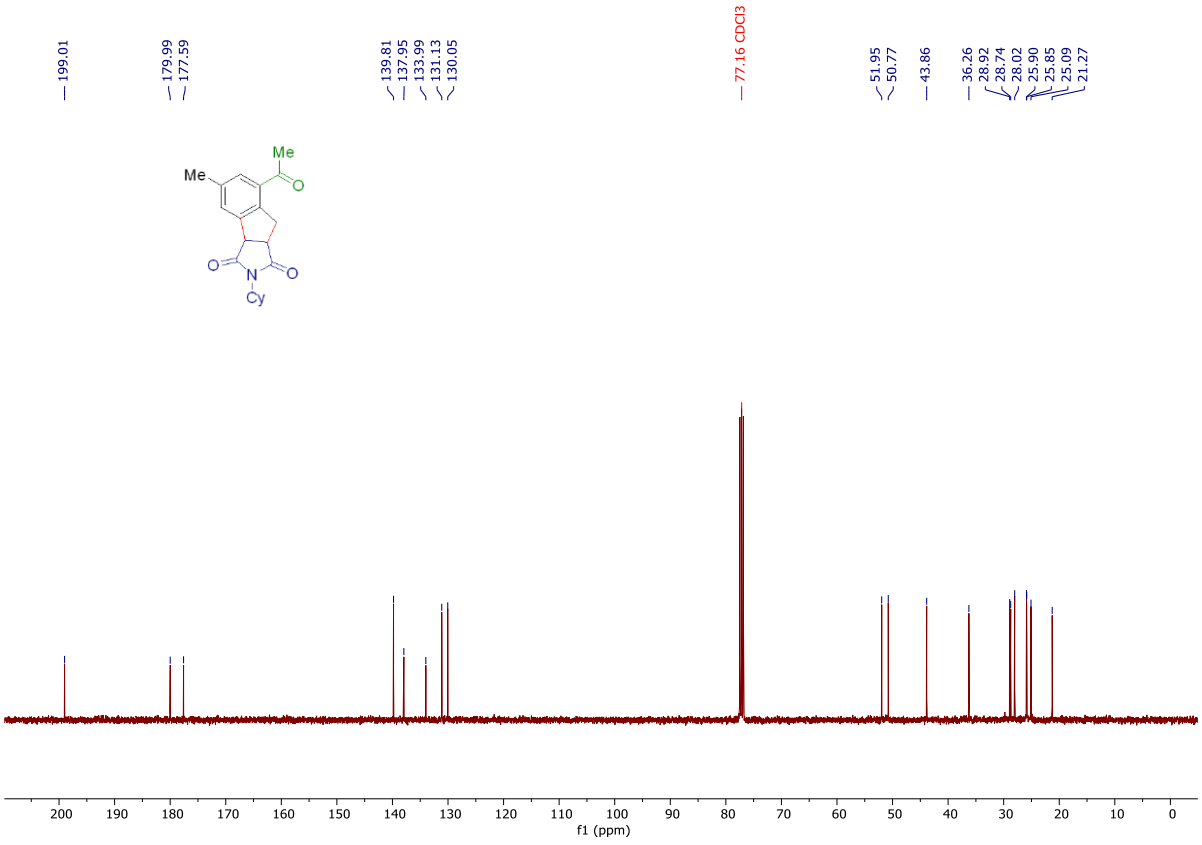


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ad

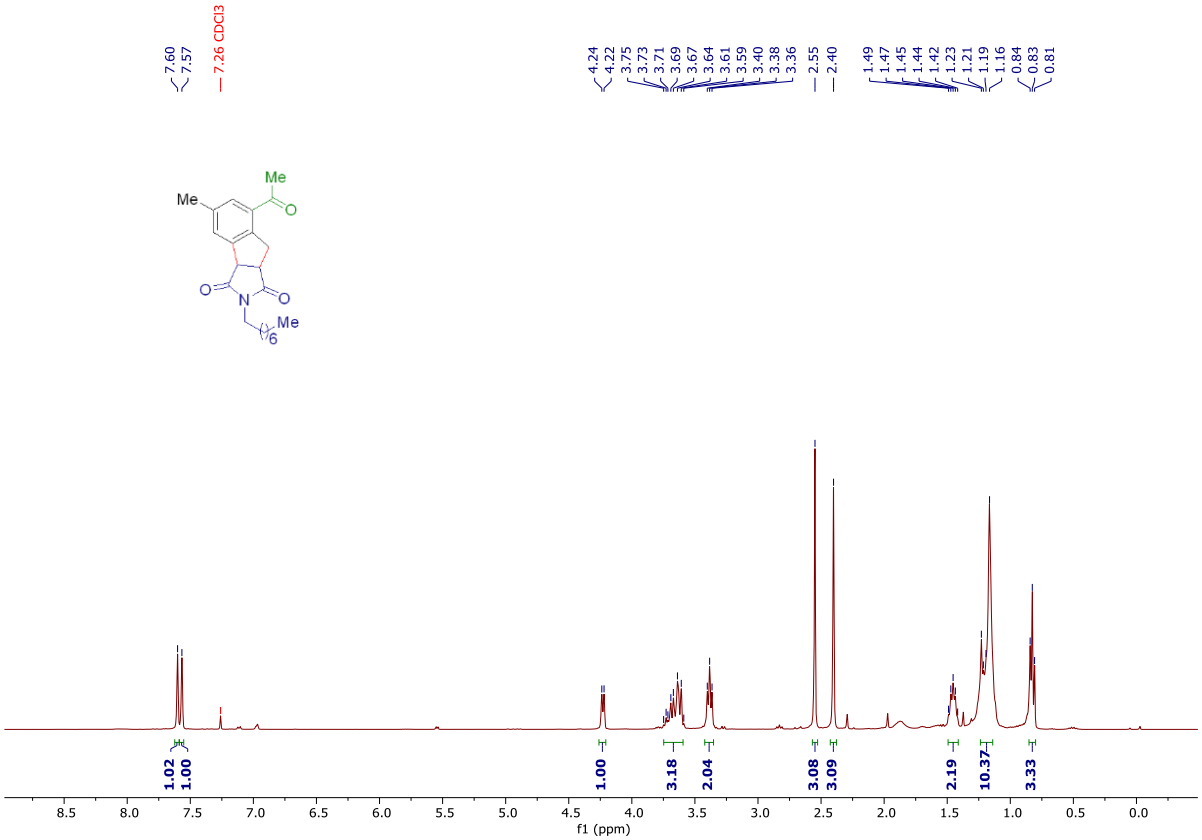


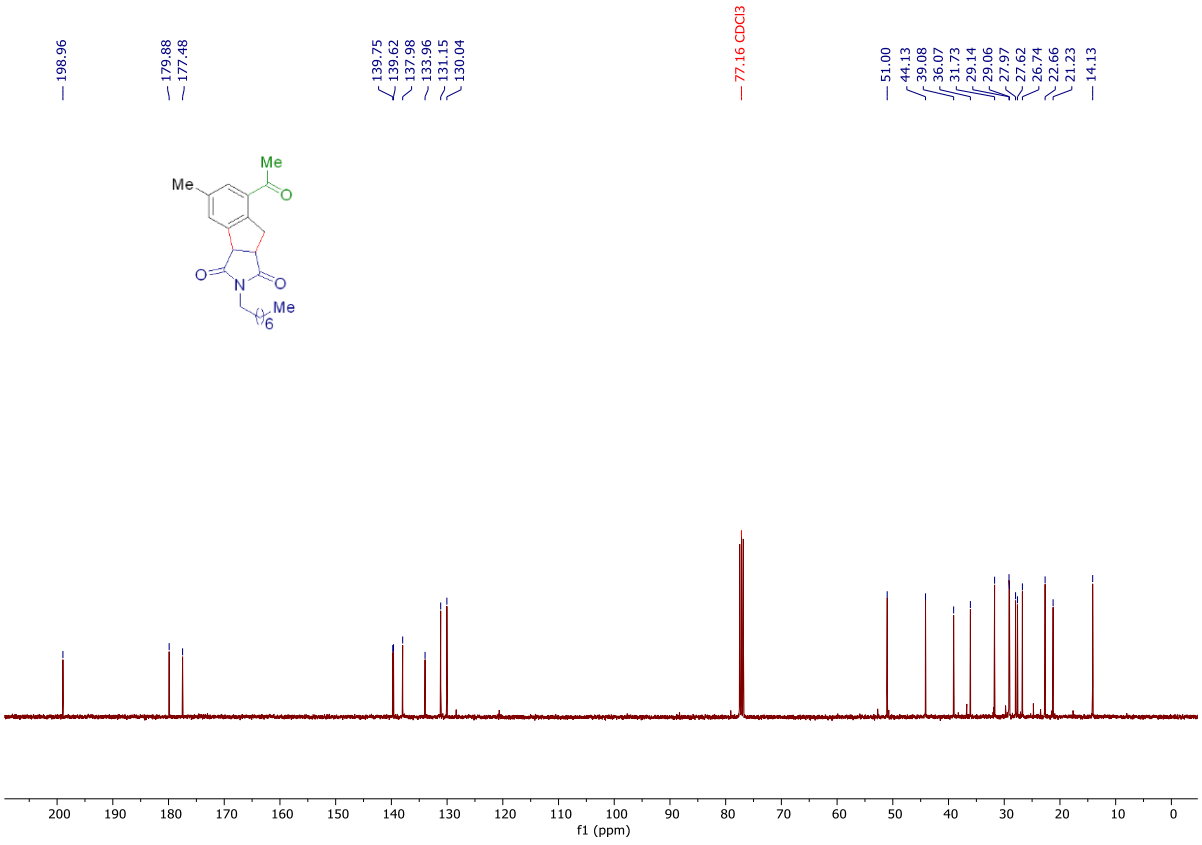
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ae



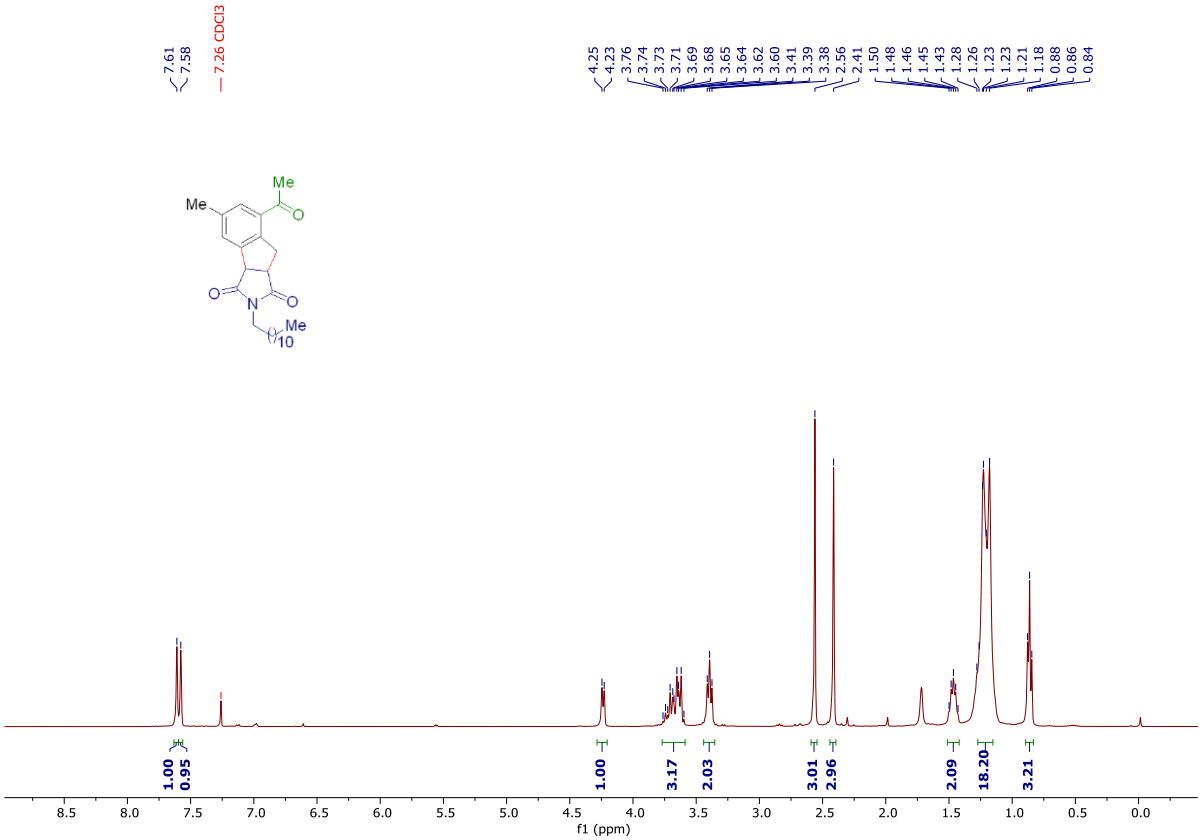


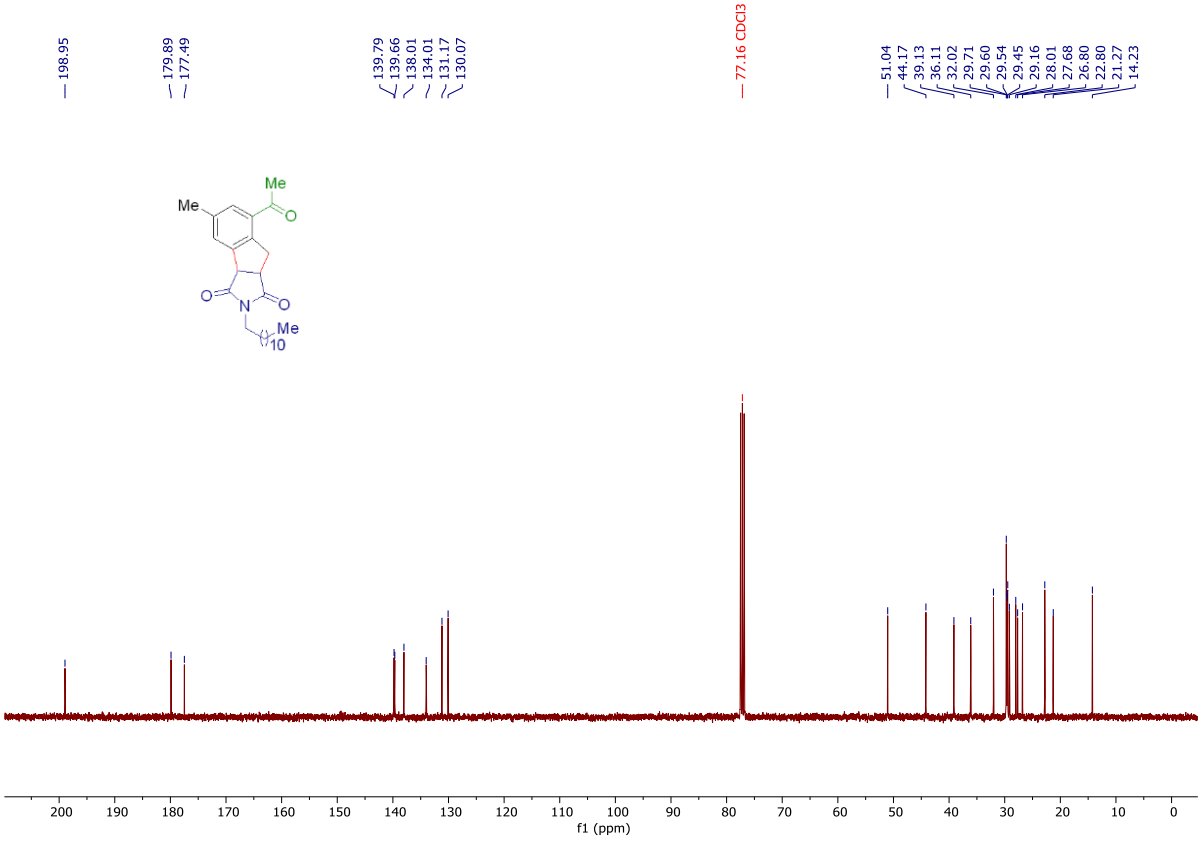
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3af



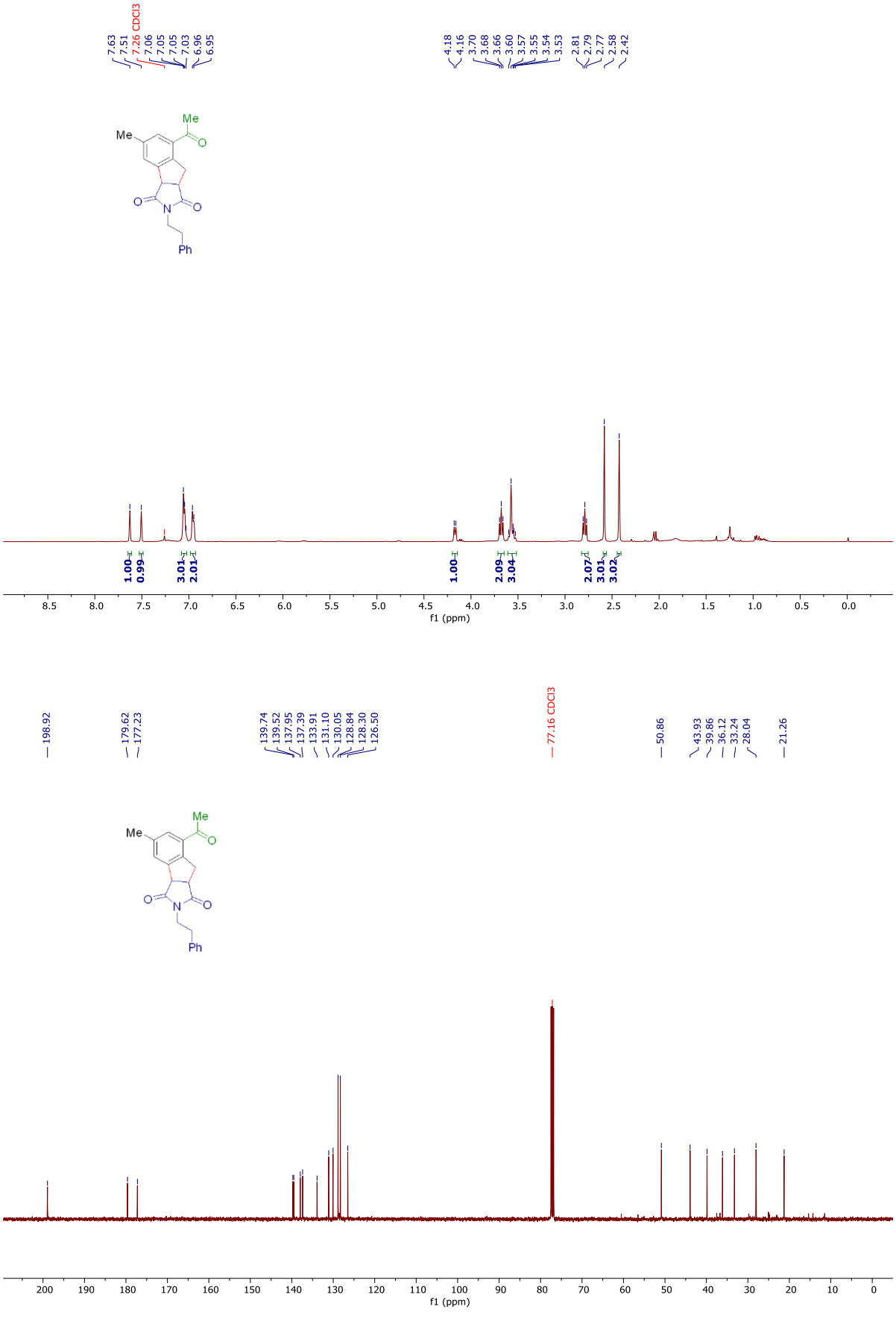


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ag

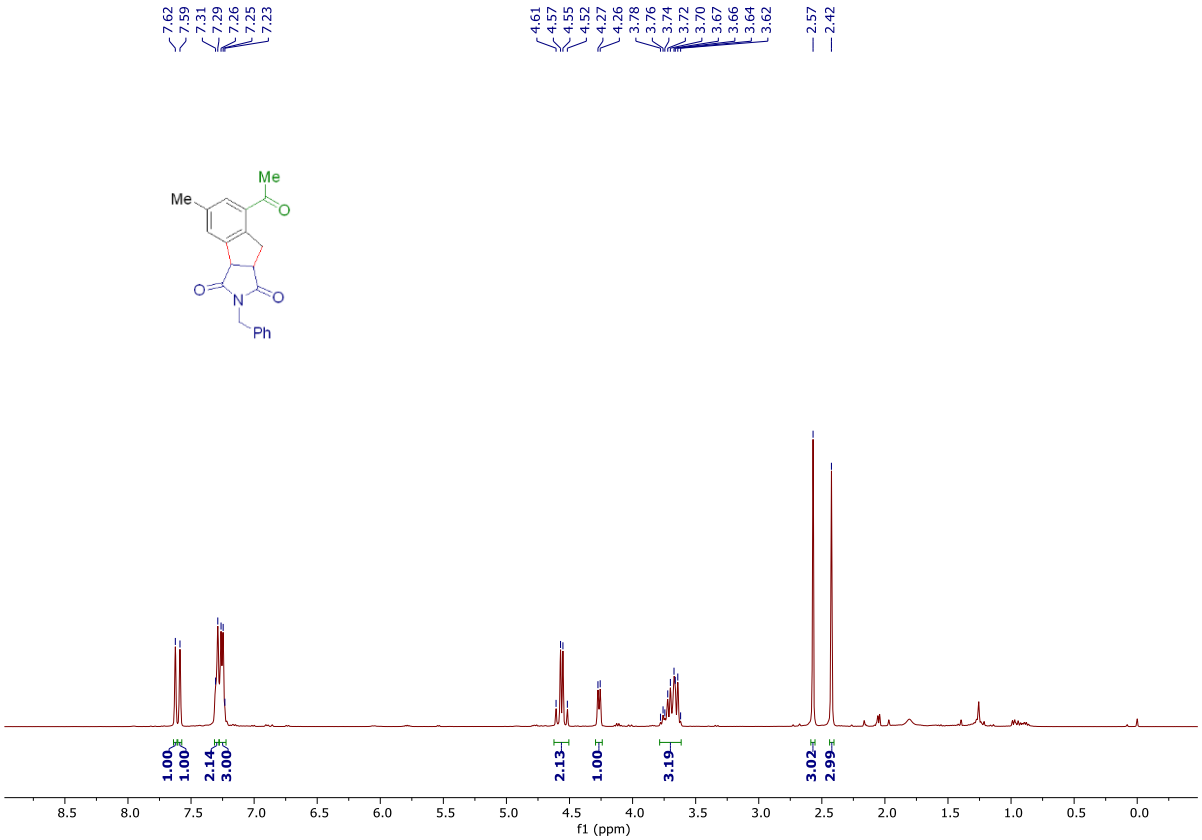


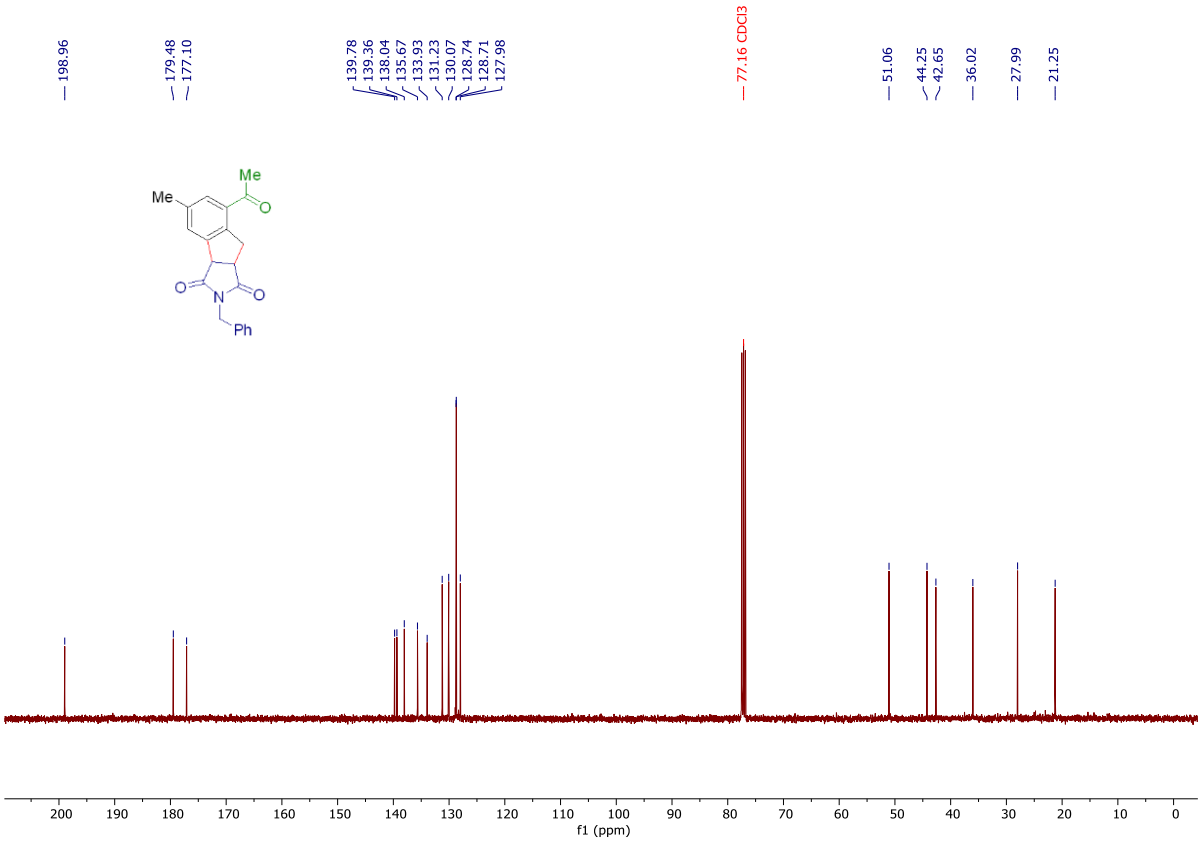


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ah

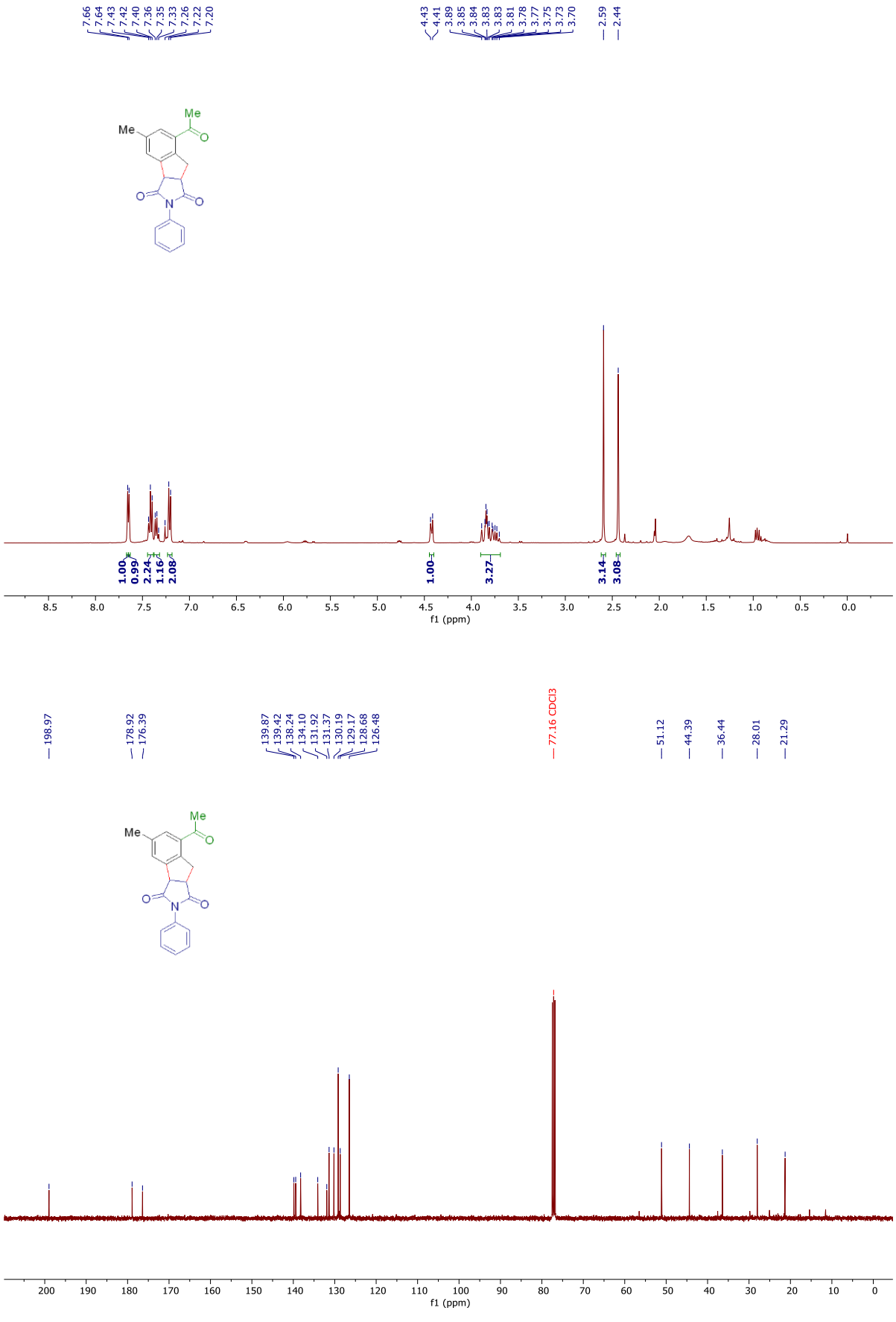


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ai

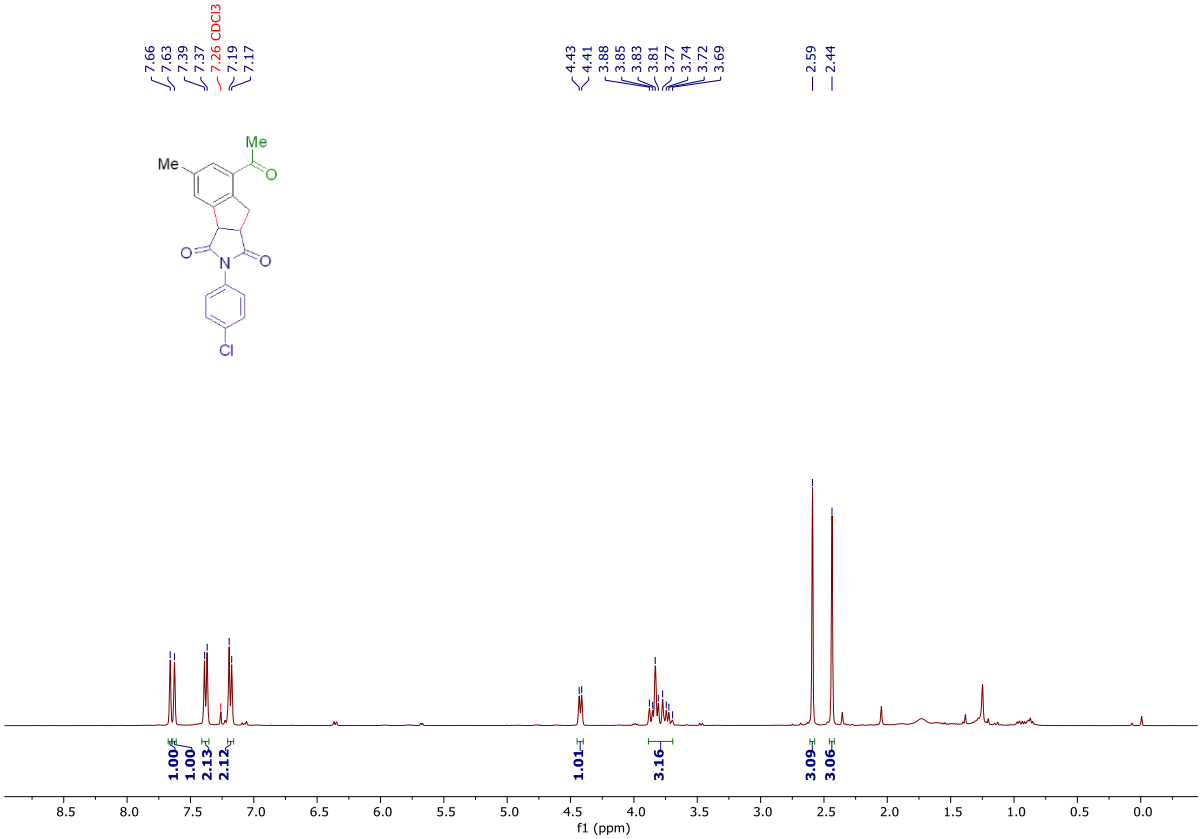


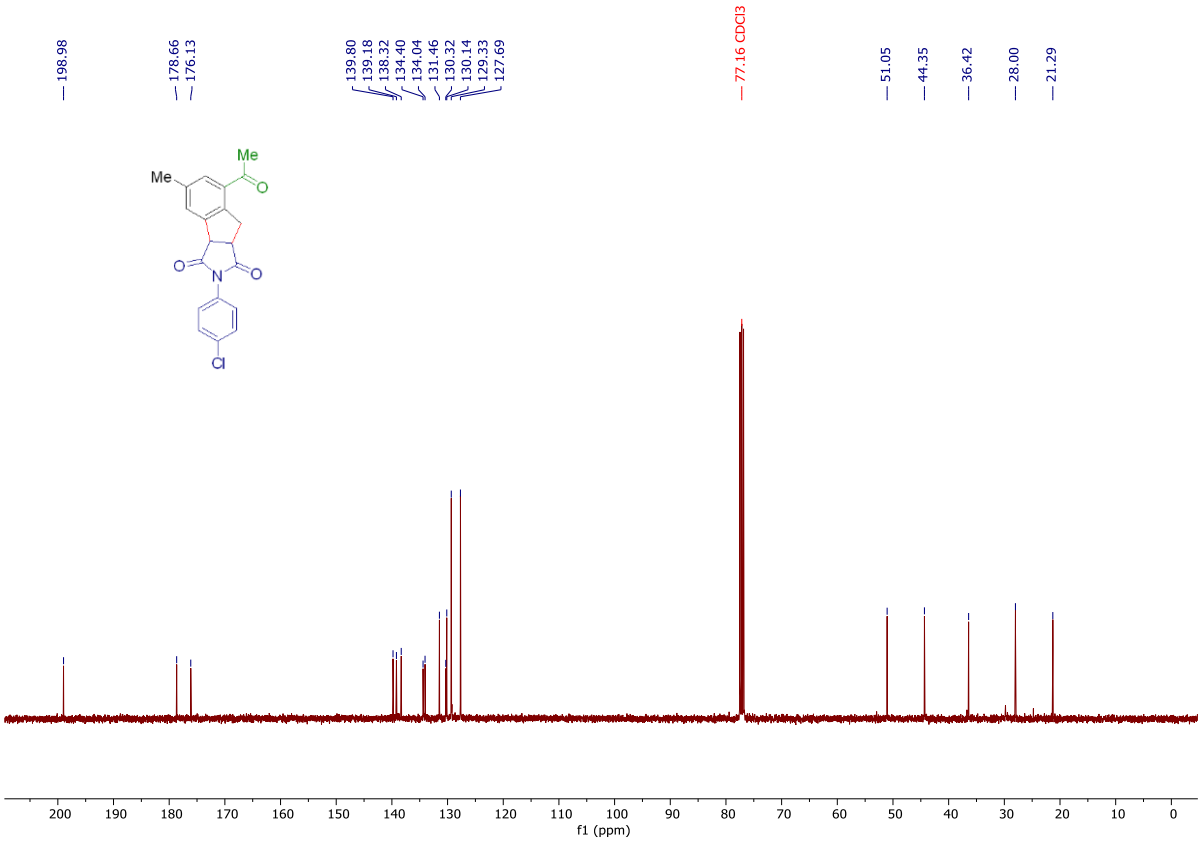


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3aj

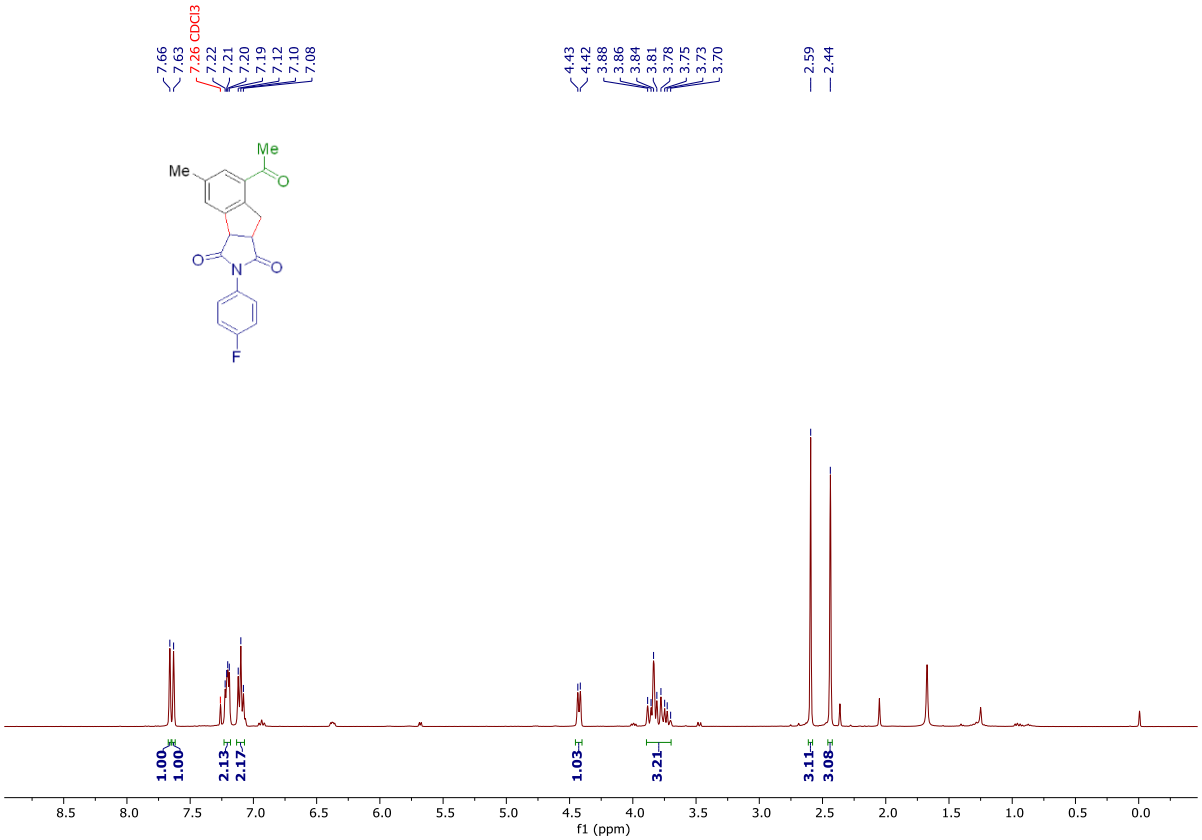


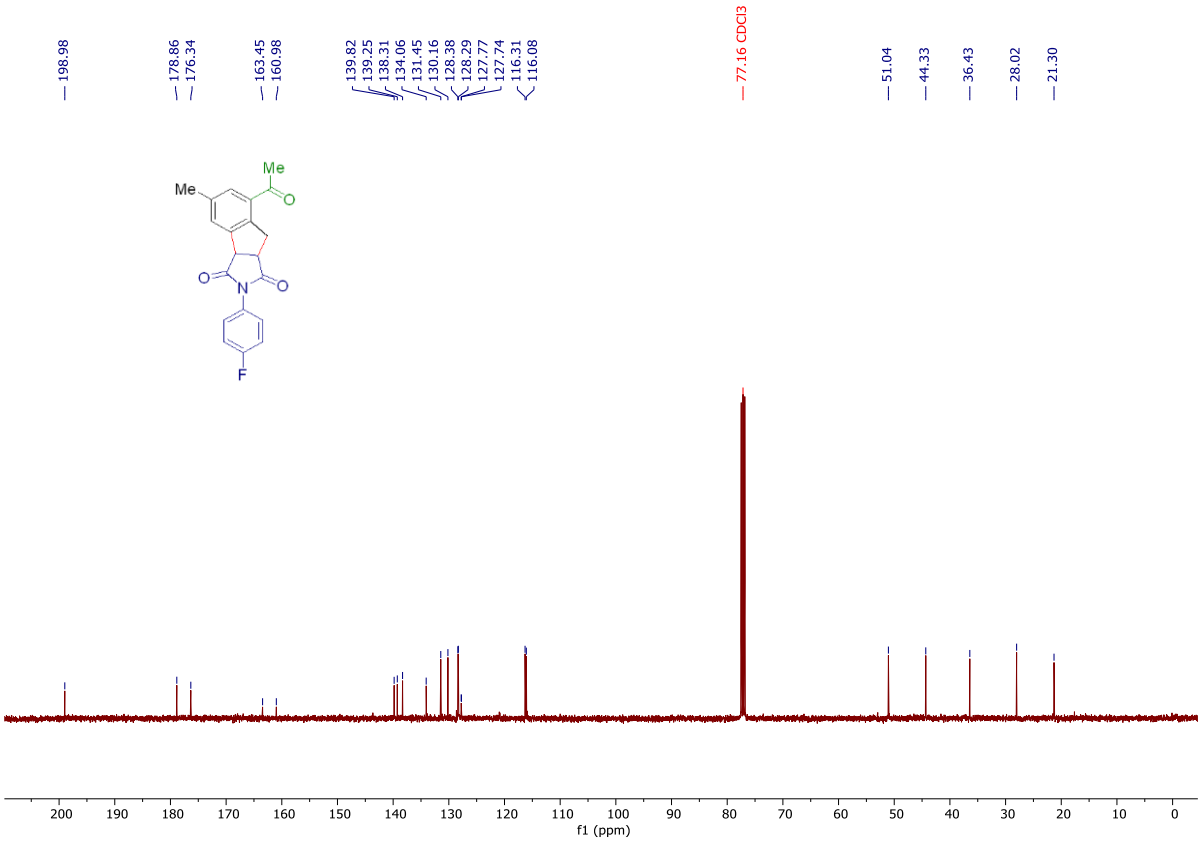
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3ak



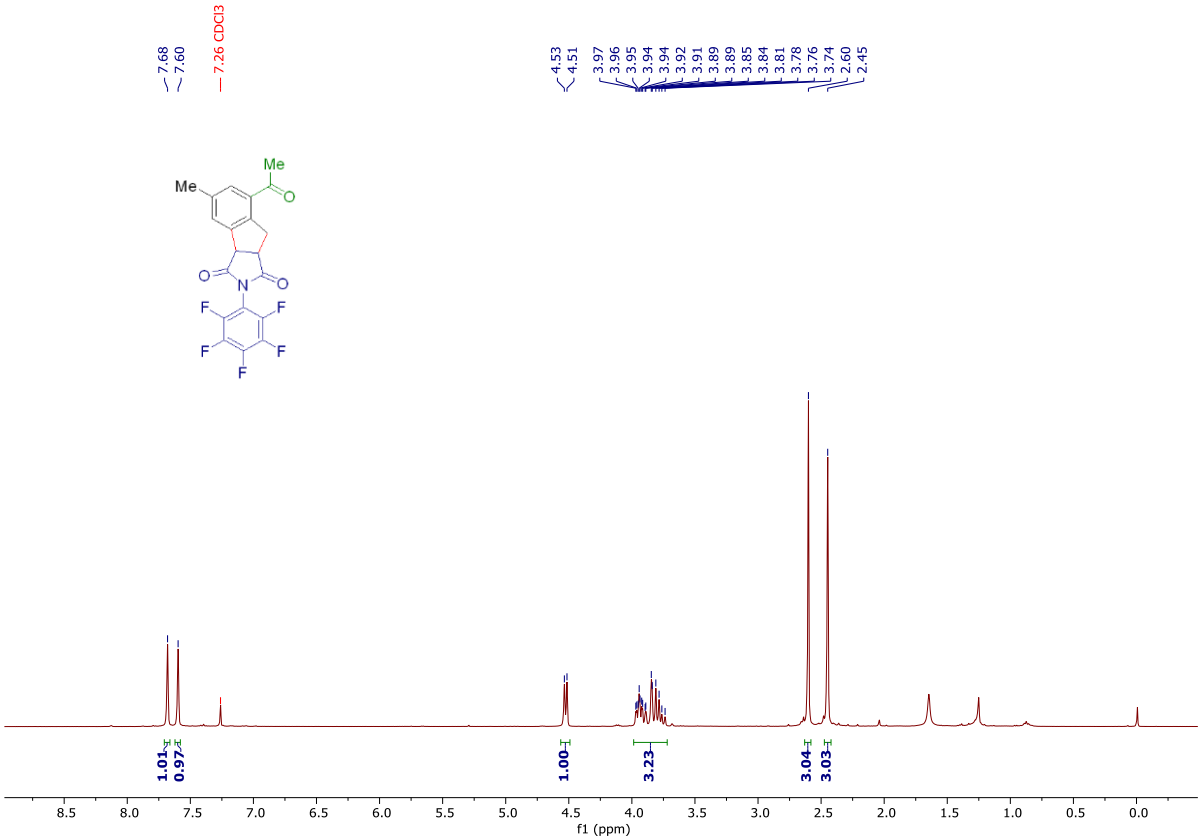


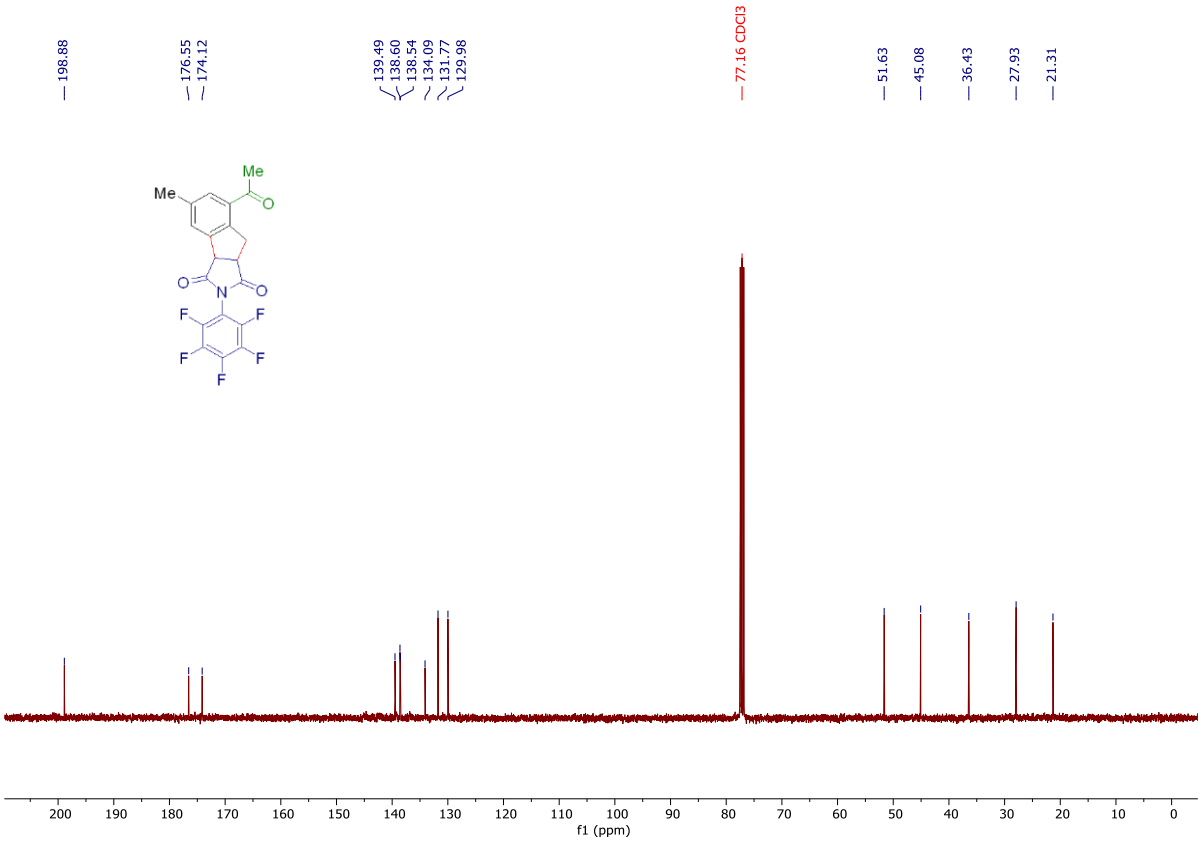
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3al



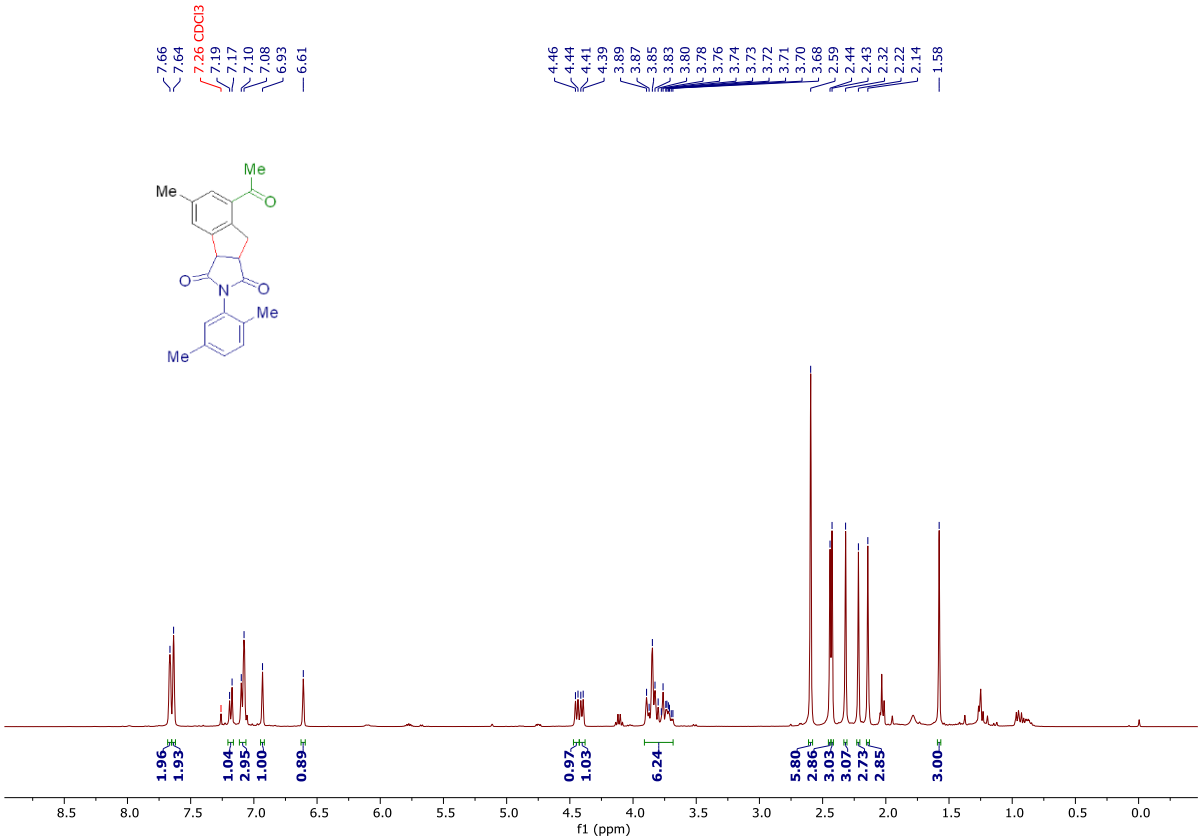


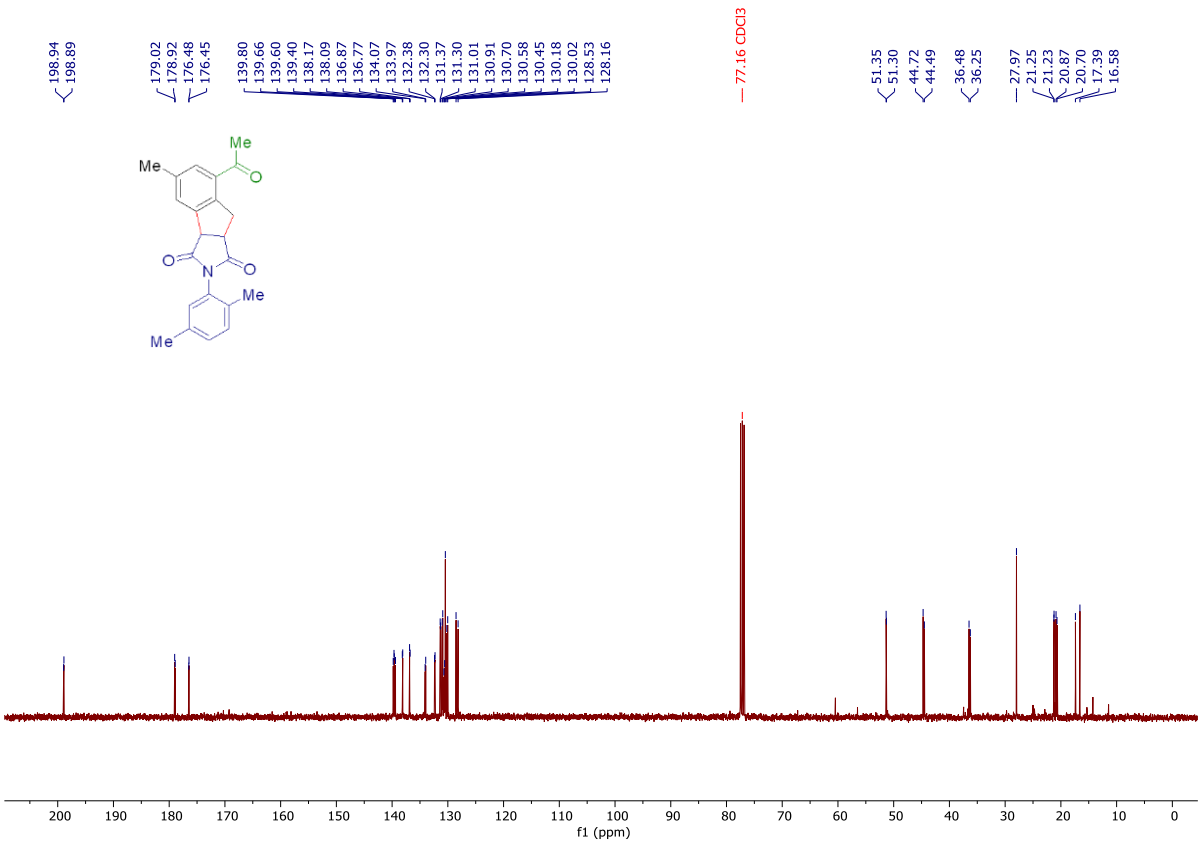
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3am



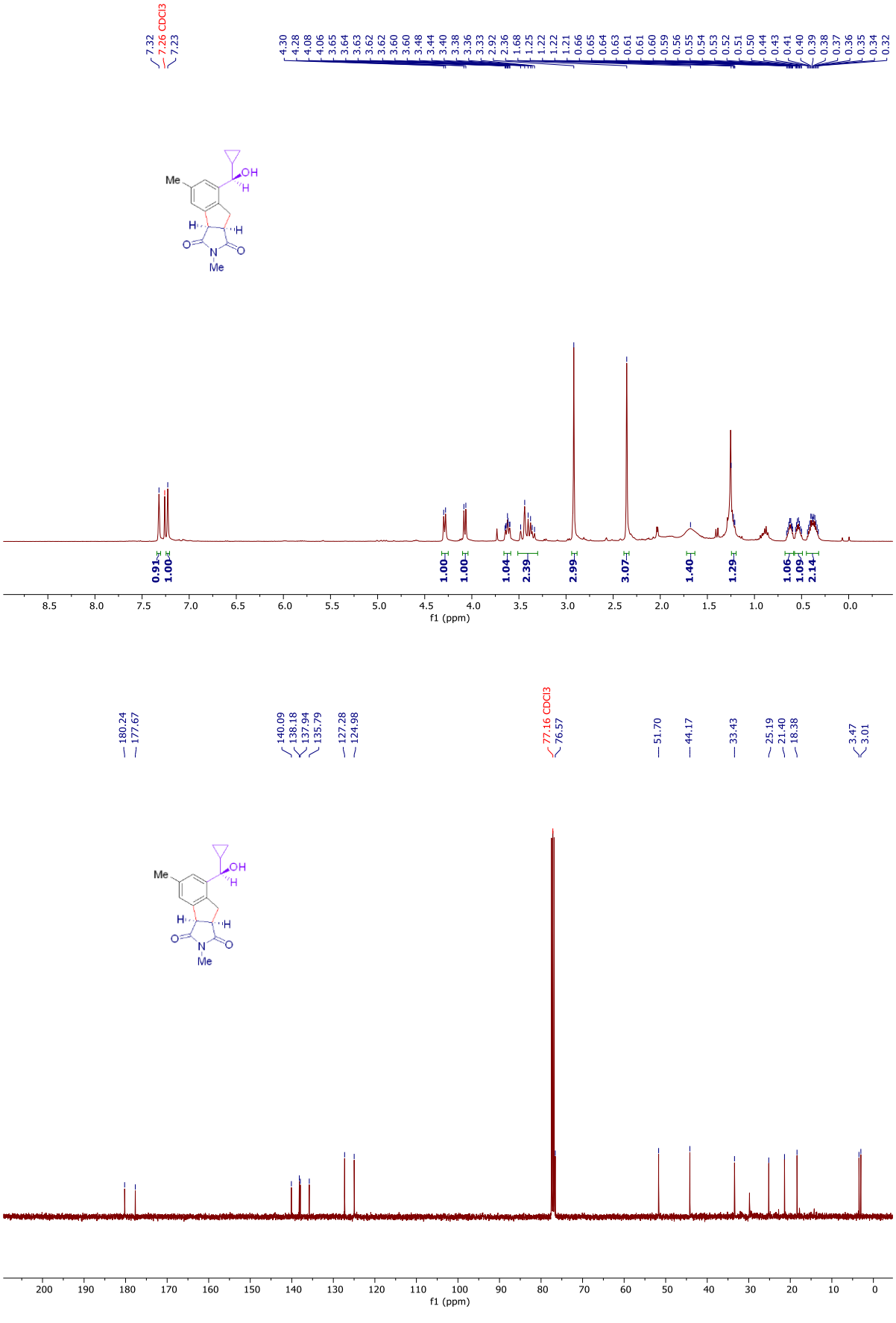


^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 3an

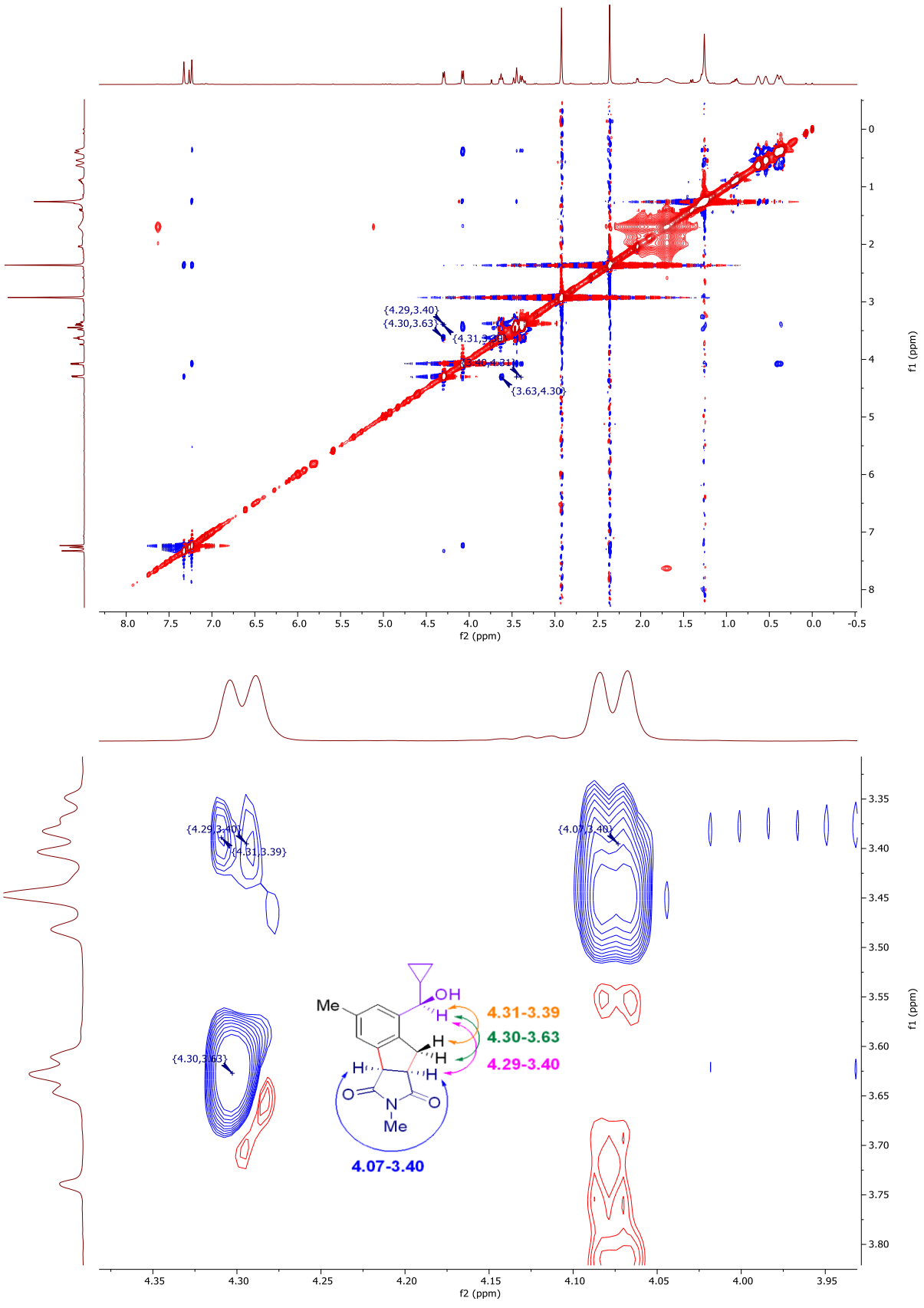




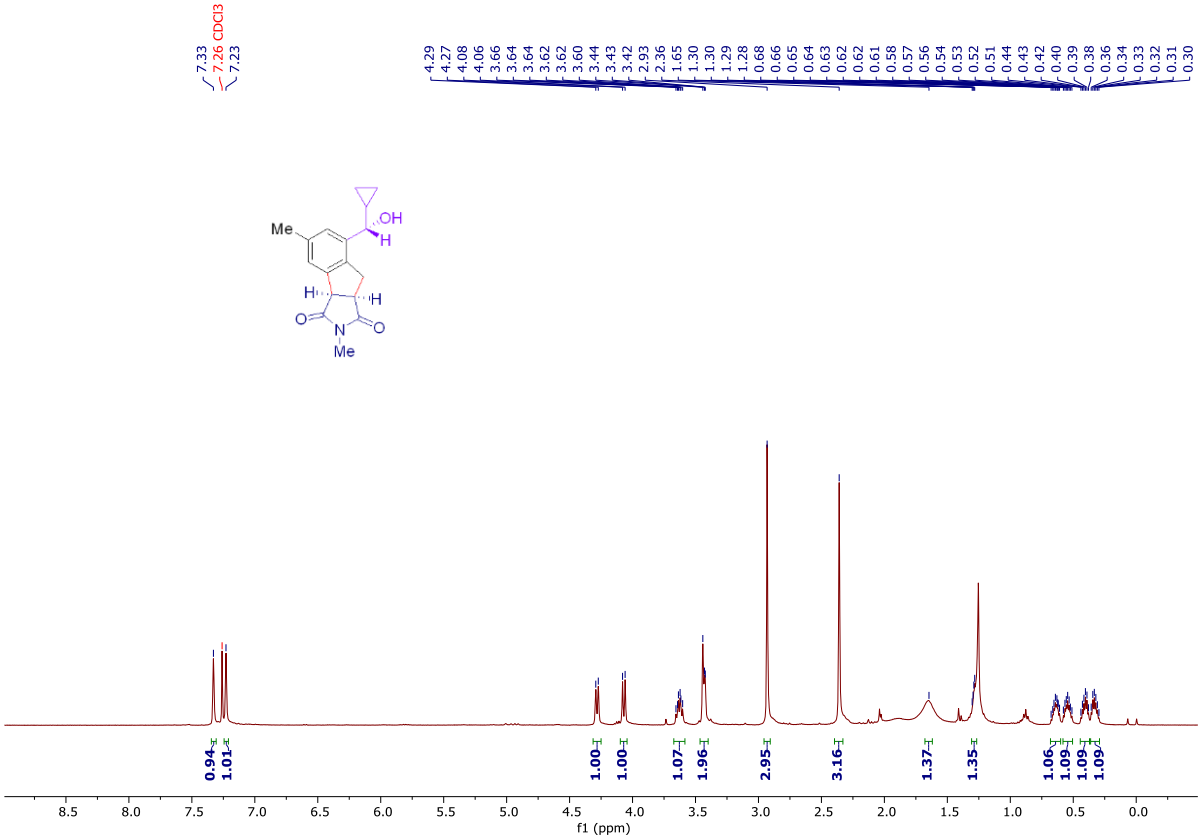
^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 6R

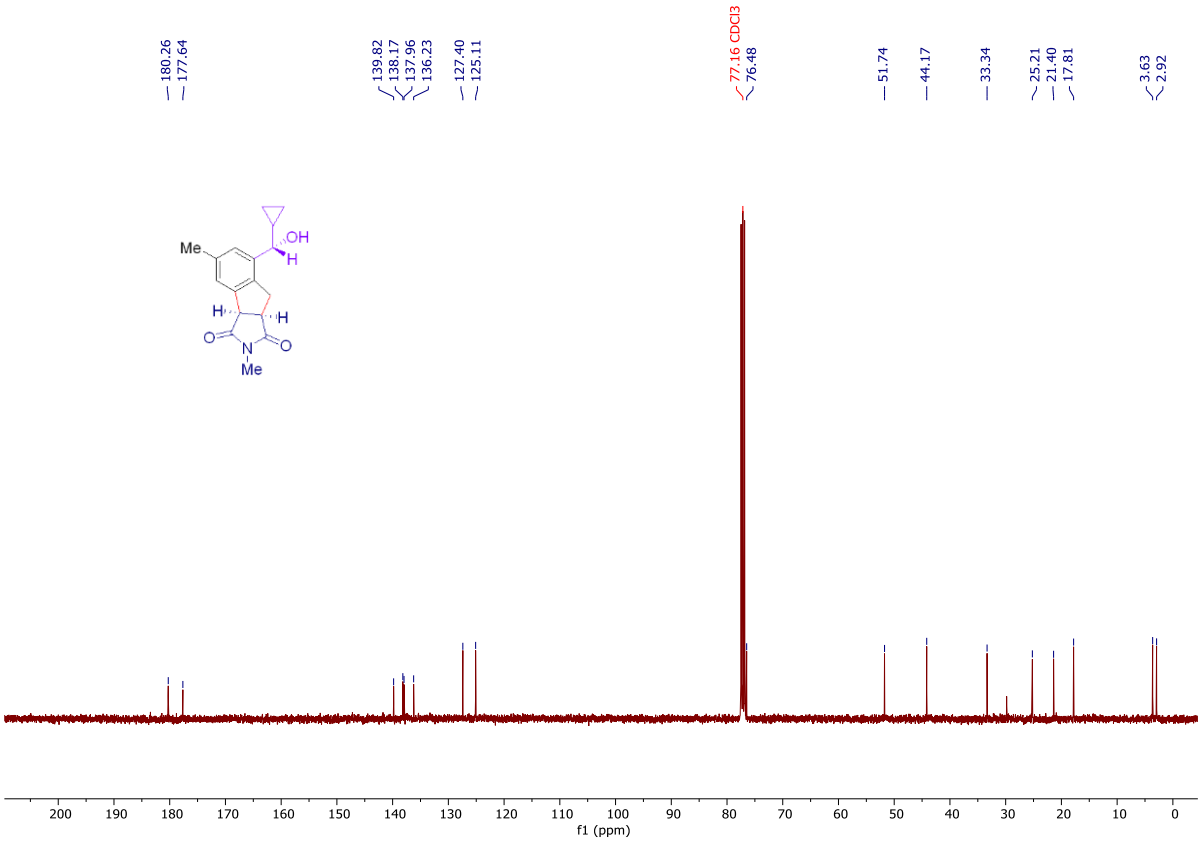


NOESY (500 Hz) NMR Spectra of 6R



^{1}H (400 Hz) and ^{13}C (101 Hz) NMR Spectra of 6S





NOESY (500 Hz) NMR Spectra of 6S