Supplementary Information (SI) for Chemical Science.
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Supporting information

Non-Innocent Behaviour of Aromatic Isocyanides under Visible Light: A Pathway to Thioformimidates and Dehydroalanine

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Contents

1. General information

Commercially available reagents were purchased from Sigma-Aldrich, Fischer Scientific, TCI Chemicals, or Fluorochem and were used as purchased unless mentioned otherwise. Solvents were purchased from VWR Chemicals or Sigma-Aldrich and used without purification unless stated otherwise, and deuterated solvents were used as purchased (Chloroform-d, D_2O, acetone-D_6, CD_3CN). Thin layer chromatography (TLC) was performed using plates from Merck (SiO_2, Kieselgel 60 F254 neutral, on aluminium with

fluorescence indicator) and compounds were visualized by UV detection (254 nm), $KMnO_4$, and/or *p*-anisaldehyde stain. Flash column chromatography was performed by employing silica (200-300 mesh) as support and *n*-heptane/ethyl acetate. NMR spectra were recorded on a Brüker Avance 300 using the residual $CDCl_3$ as internal reference (^1H: δ 7.26 ppm, ^{13}C: δ 77.16 ppm). Chemical shifts (δ) are given in ppm and coupling constants (*J*) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), br (broad singlet), and m (multiplet) or combinations thereof. Ultra-high-resolution mass-spectrometer Bruker solariX XR FT-ICR-MS was used for accurate mass measurements. Samples were ionized by electrospray ionization (ESI) in positive ion mode. NMR Data were processed with Mestre nova version 14. UV−vis absorption spectra were recorded on an Agilent Cary 60 spectrophotometer in a quartz cuvette with a 1 cm path length.

Photochemical experiments were performed in a 10 mL microwave (MW) vial equipped with teflon septa. The tubes were irradiated with blue light (456 nm) using a Kessil LED light of power 40W. To maintain a constant reaction temperature of 30°C, the setup was cooled by a constant airflow (Figure S1).

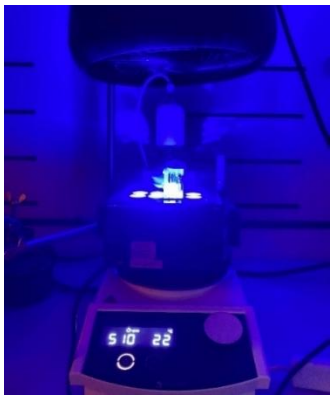
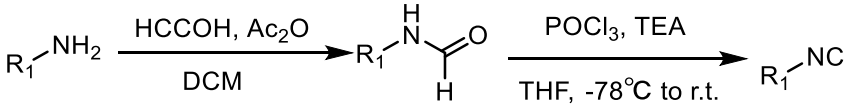
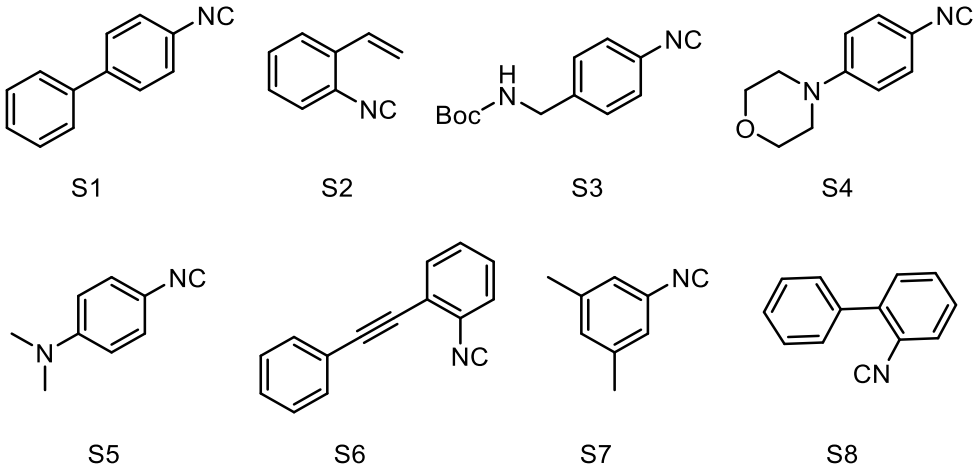


Figure S1: Batch reaction setup.

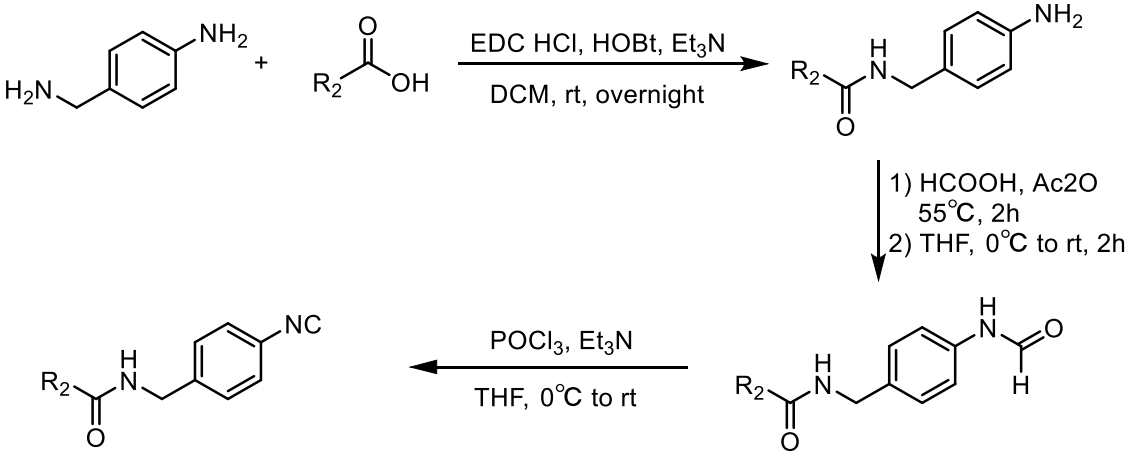
2. Synthesis and characterization of starting materials

2.1 **Isocyanide Synthesis: Isocyanides were synthesized according to previous literature.**[1–3]





2.2 Functionalized isocyanides



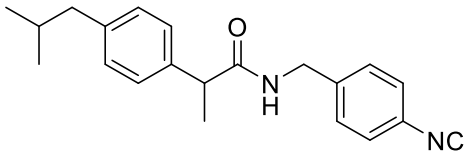
Step 1: In a 100 mL round bottom flask equipped with a magnetic stir bar, the desired carboxylic acid (1 equiv.) was dissolved in DCM (0.08 M), followed by the addition of EDC.HCl (1.5 equiv.), HOBt (1.5 equiv.), Et_3N (1.2 equiv.), and 4-aminobenzylamine (1.2 equiv.). The resulting mixture

was stirred overnight at room temperature and then washed with water (x 3). The organic phase was dried over sodium sulfate, filtered, and concentrated under vacuum to give a crude mixture which was purified via column chromatography (*n*-hexane/EtOAc) to afford the functionalized aniline derivative to be used in the following step (79-94% yields).

Step 2: In a 50 mL two-necked round bottom flask, a mixture of formic acid (2.7 equiv.) and acetic anhydride (2.3 equiv.) was stirred at 55° C for 2 h. After the reaction was cooled at room temperature, the crude mixture was added dropwise to a solution of the desired aniline (1 equiv.) in THF (0.6 M), at 0° C. The resulting mixture was stirred at room temperature for 2 h, until completion of the reaction, as monitored by TLC. Then the mixture was cooled to 0° C and a saturated aqueous solution of $NaHCO_3$ was added slowly under vigorous stirring until neutral pH was reached. EtOAc was added, and the two phases were separated; the aqueous layer was further extracted with EtOAc (x 2), then the combined organic extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated under vacuum to give the resulting formamide in quantitative yield. The crude material was used in the next step without further purification.

Step 3: In a 100 ml round bottom flask equipped whit a magnetic stir bar, the desired formamide was dissolved in THF (0.6 M), and Et_3N (6.7 equiv.) was added to the solution. After cooling to 0°C, $POCl_3$ (1.7 equiv.) was added dropwise under argon atmosphere to the reaction mixture, which was stirred at room temperature for 1 h. After completion of the reaction, as monitored by TLC, the mixture was cooled to 0° C and a saturated aqueous solution of Na_2CO_3 was added slowly under vigorous stirring, until pH ~ 9. Then DCM was added, and the two phases were separated; the aqueous layer was further extracted with DCM (x 2), then the combined organic extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated under vacuum to give a crude mixture which was purified via column chromatography (*n*-hexane/EtOAc) to afford the desired functionalized isocyanides (53-83% yields).

2-(4-Isobutylphenyl)-*N*-(4-isocyanobenzyl)propenamide S9

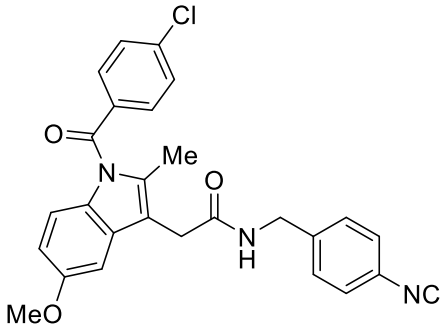


The title compound was synthesized according to the reported general procedure starting from ibuprofen (2.4 mmol) and isolated as a brownish solid (528.1 mg, 69% yield over 3 steps).

Column Chromatography: Silica, gradient 20-30% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.21 – 7.16 (m, 2H), 7.14 – 7.10 (m, 2H), 7.08 – 7.03 (m, 4H), 5.65 (brt, -*N*H), 4.38 – 4.25 (m, 2H), 3.52 (q, *J* = 7.1 Hz, 1H), 2.39 (d, *J* = 7.2 Hz, 2H), 1.83 – 1.73 (m, 1H), 1.47 (d, *J* = 7.2 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR**: (101 MHz, $CDCl_3$) δ 174.6, 164.1, 141.1, 140.3, 138.3, 129.8, 128.2, 127.3, 126.6, 125.6 (t, *J* = 11.6 Hz), 46.8, 45.0, 42.8, 30.2, 22.4, 18.3; **HRMS (ESI$^+$)**: $[M + H]^+$calcd for: 321.1961, found: 321.1951

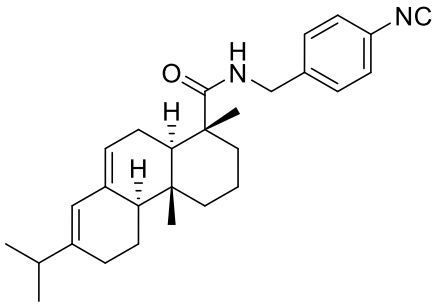
2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-*N*-(4-isocyanobenzyl)acetamide S10



The title compound was synthesized according to the reported general procedure starting from indomethacin (1.4 mmol) and isolated as a light-yellow solid (310.1 mg, 47% yield over 3 steps). **Column Chromatography**: Silica, gradient 30-40% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, DMSO-d_6) δ 8.57 (brt, -N*H*), 7.74 – 7.60 (m, 4H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 2.6 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.72 (dd, J_a = 9.0, J_b = 2.5 Hz, 1H), 4.31 (d, *J* = 5.9 Hz, 2H), 3.74 (s, 3H), 3.60 (s, 2H), 2.22 (s, 3H); **^{13}C NMR**: (101 MHz, DMSO-d_6) δ 170.2, 168.4, 164.2, 156.1, 142.2, 138.1, 135.7, 134.7, 131.6, 131.3, 130.8, 129.5, 128.9, 126.7, 124.7 (t, *J* = 10.5 Hz), 115.1, 114.6, 111.8, 102.3, 55.9, 42.3, 31.6, 13.9; **HRMS (ESI$^+$)**: $[M + H]^+$calcd for: 472.1422, found: 472.1411

(1*R*,4a*R*,4b*R*,10a*R*)-*N*-(4-isocyanobenzyl)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,4b,5,6,10,10a-decahydrophenanthrene-1-carboxamide S11



The title compound was synthesized according to the reported general procedure starting from abietic acid (1.6 mmol) and isolated as off-white crystals (440.9 mg, 66% yield over 3 steps).

Column Chromatography: Silica, gradient 10-15% EtOAc/*n*-hexane.

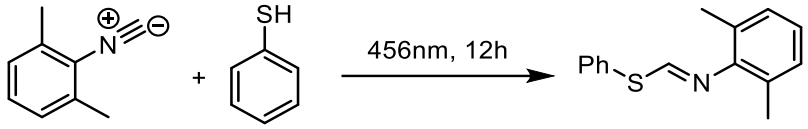
^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.28 – 7.26 (m, 2H), 6.10 (brt, -N*H*), 5.75 (s, 1H), 5.33 – 5.30 (m, 1H), 4.49 – 4.36 (m, 2H), 2.25 – 2.18 (m, 1H), 2.10 – 2.03 (m, 2H), 2.03 – 1.86 (m, 4H), 1.84 – 1.75 (m, 3H), 1.59 – 1.53 (m, 2H), 1.28 (s, 3H), 1.22 (s, 1H), 1.22 – 1.14 (m, 2H), 1.02 – 0.99 (m, 6H), 0.83 (s, 3H); **^{13}C NMR**: (101 MHz, $CDCl_3$) δ 178.5, 164.1, 145.5, 140.6, 135.7, 128.6, 126.7, 122.3, 120.2, 51.0, 46.5, 45.8, 43.2, 38.3, 37.8, 34.9, 34.7, 27.4, 25.4, 22.5, 21.4, 20.9, 18.3, 17.1, 14.2; **HRMS (ESI$^+$)**: $[M + H]^+$calcd for: 417.2900, found: 417.2891

3. Optimization studies

General procedure for optimization

An oven-dried 10 mL MW vial equipped with a magnetic stirring bar was charged with 2-isocyano-1,3-dimethylbenzene (**1a**) and benzenethiol (**1b**). Afterwards, solvent was added followed by additives. The MW vial was then closed with a cap containing a teflon septum and degassed with nitrogen for 5-10 min. The vial was then placed for irradiation with a Kessil blue LEDs as shown in figure S1 (40W, 456 nm). The progress of the reaction was monitored through TLC and LC/MS. After completion, the solvent was removed in vacuum and the reaction yield was calculated through the ^{1}H-NMR integration method using CH_2Br_2 as an internal standard.

Table S1. Optimization results of solvents, ratio and concentration.[a]



1a **1b** **2**

Entry	Ratio (1a:1b)	Base	Light (456nm)	Solvent (0.1M)	Yield (isolated%)
Solvents Screening					
1	1.2:1	no	Yes	MeCN	81
2	1.2:1	no	Yes	DMSO	46
3	1.2:1	no	Yes	acetone	7
4	1.2:1	no	Yes	Chlorobenzene	2
5	1.2:1	no	Yes	2Me-THF	60
6	1.2:1	no	Yes	H_2O	87 (75)
7[b]	1.2:1	no	Yes	H_2O	11
8	1.2:1	no	Yes	cyclohexane	31
9	**1.2:1**	**no**	**Yes**	**DCE**	**91**

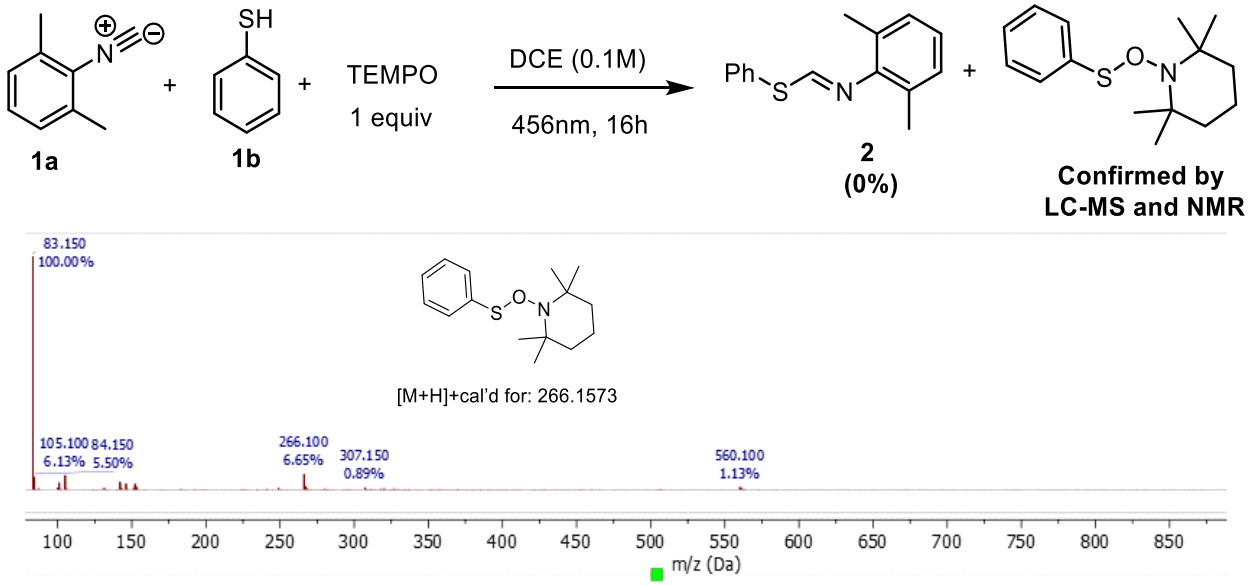
Base Screening[c]					
10	1.2:1	Cs_2CO_3	Yes	DCE	8
11	1.2:1	Cs_2CO_3 + $NaHCO_2$	Yes	DCE	80
13	1.2:1	DIPEA	Yes	DCE	10
14	1.2:1	2,6-lutidine	Yes	DCE	10
15	1.2:1	Na_2CO_3	Yes	DCE	56
Ratio & Concentration Screening					
16	1:1	no	Yes	DCE	80
17	1.5:1	no	Yes	DCE	82
18	1:1.5	no	yes	DCE	30
19	1.2:1	no	Yes	DCE (0.5M)	83
20	1.2:1	no	Yes	DCE (0.2M)	84
21	1.2:1	no	Yes	DCE (0.05M)	67
Effect of Light					
22	1.2:1	no	no	DCE	0%
23	1.2:1	no	No (80°C)	DCE	0%

[a]Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard. [b]Meglumine (2 equiv). [c]1 equiv. of base.

4. Mechanistic investigations

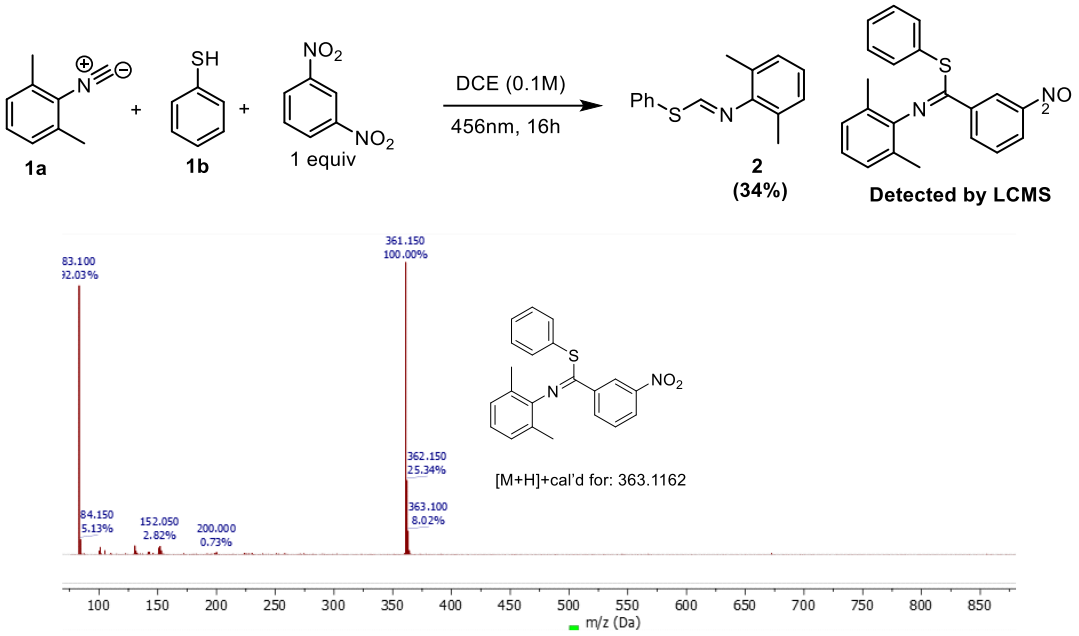
4.1 Radical Quenching Experiments

A) Under our optimized reaction conditions, we added 1 equiv of TEMPO. The reaction mixture was analyzed by NMR and LC-MS. We observed the thiyl radical adduct with TEMPO suggesting the formation of thiyl radical under our optimized conditions.



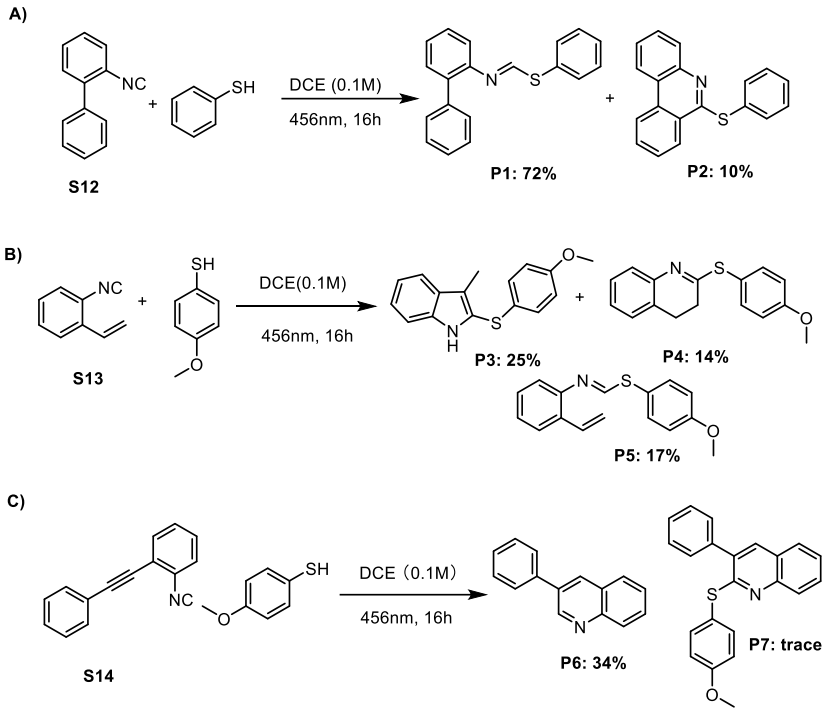
Scheme S1: Radical inhibition experiment with TEMPO and analysis of the adduct by LC-MS.

B) Under our optimized reaction conditions, we added 1 equiv of 1,3-dinitrobenzene. The reaction mixture was analyzed by NMR and LC-MS. We observed lower product formation with a trace amount of substitution products. Since the ionic reaction between isocyanide and 1,3-nitrobenzene is difficult, the substitution product can be derived from the attack of the imidoyl radical intermediate on the 1,3-dinitrobenzene followed by re-aromatization. The lower yield of our desired product could be due to the fact that dinitrobenzene absorbs strongly in the visible region, and therefore the number of photons available for isocyanide or diphenyl sulfide will be lower.



Scheme S2: Radical inhibition experiment with 1,3-dinitrobenzene and analysis of side products by LC-MS.

4.2 **Imidoyl radical trapping experiments**



Scheme S3: Intramolecular imidoyl radical trapping experiments.

Implication: To analyze the possibility of a radical initiation step, we employed S12. We observed P1 as the major product and P2 as the minor product. The formation of P2 indicates that the thiyl radical attacks the free isocyanide, continuing the chain propagation step as explained in the main paper.

When we employed the isocyanide S13, we obtained three major products in different ratios. Since 5-exo cyclization is favored over 6-endo cyclization, P3 was the major product. The formation of P5 supports the radical termination step in our mechanism, where the first step is protonation followed by radical-radical combination.

Knowing that arylthiols under our optimized conditions generate a small amount of disulfide, which undergoes homolytic cleavage to produce thiyl radicals, we then employed isocyanide S14. In this case, we only observed the aza-Bergman cyclization product, as reported by Ogawa and co-workers[4] without any 5-exo cyclization product[5]. This suggests that thiyl radical generation from the homolytic cleavage of disulfide contributes only minimally under our reaction conditions.

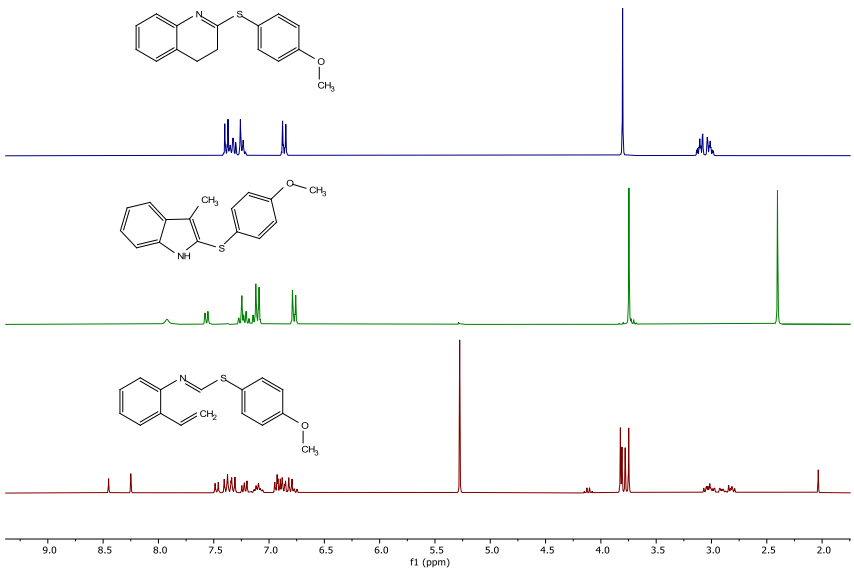


Figure S2: 1-isocyano-2-vinylbenzene reaction analysis through ^{1}H NMR.

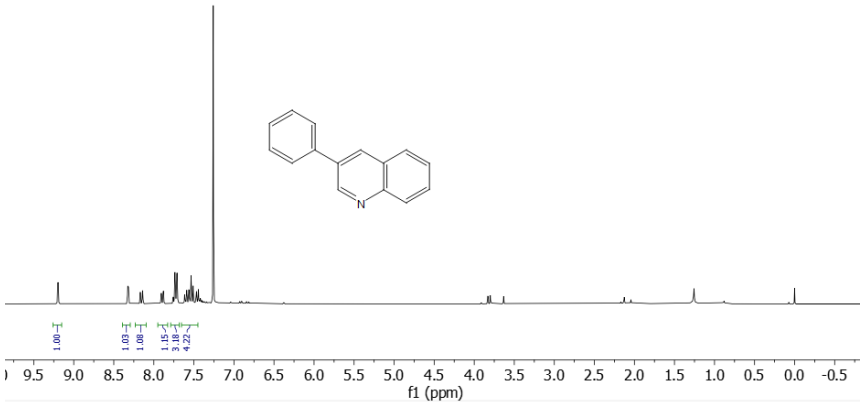


Figure S3: 1-isocyano-2-(phenylethynyl)benzene reaction analysis through ^{1}H NMR.

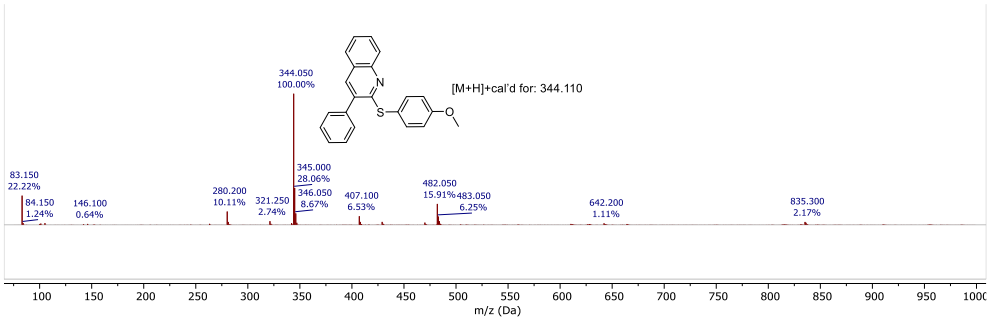
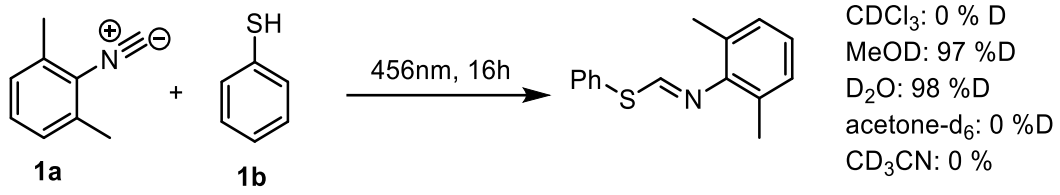


Figure S4: 1-isocyano-2-(phenylethynyl)benzene reaction analysis through LC-MS.

4.3 Deuteration experiment



Scheme S4: Deuterium labelling experiments.

Implication:

We observed no deuteriation in aprotic solvents but a high percentage of deuteriation with protic solvents. These results indicate that HAT from the solvent is unlikely, and that the hydrogen comes from the thiol.

4.4 UV-Vis Spectrum

UV−vis absorption spectra were recorded on an Agilent Cary 60 spectrophotometer and Shimadzu UV-Vis Spectrophotometer UV-3600 in a quartz cuvette with a 10 mm path length.

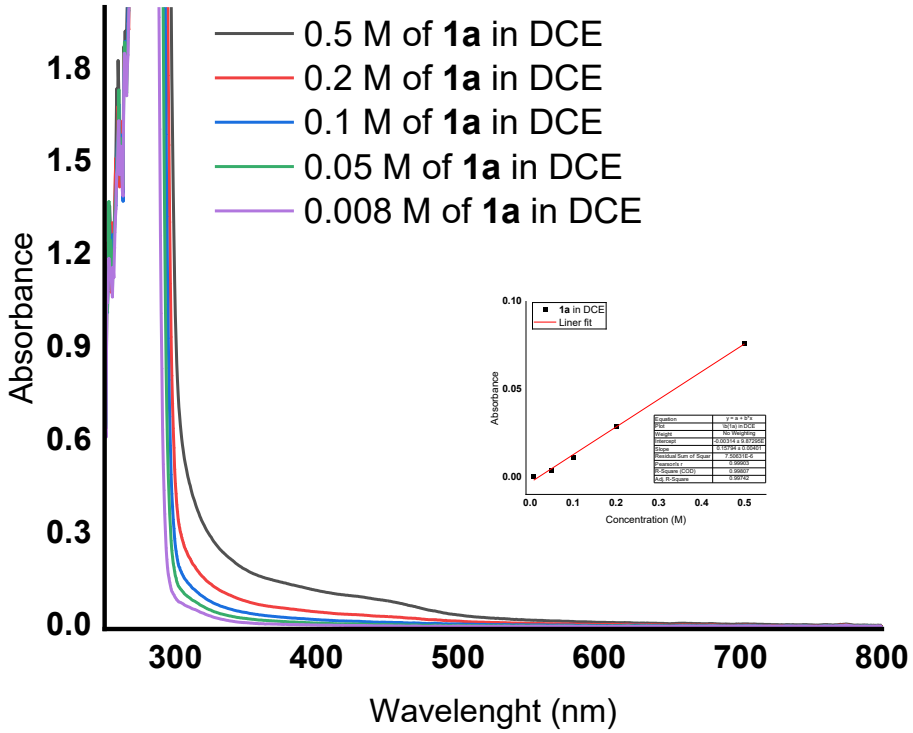


Figure S5: Absorption spectra of **1a** at different concentrations in DCE using Cary60 spectrophotometer.

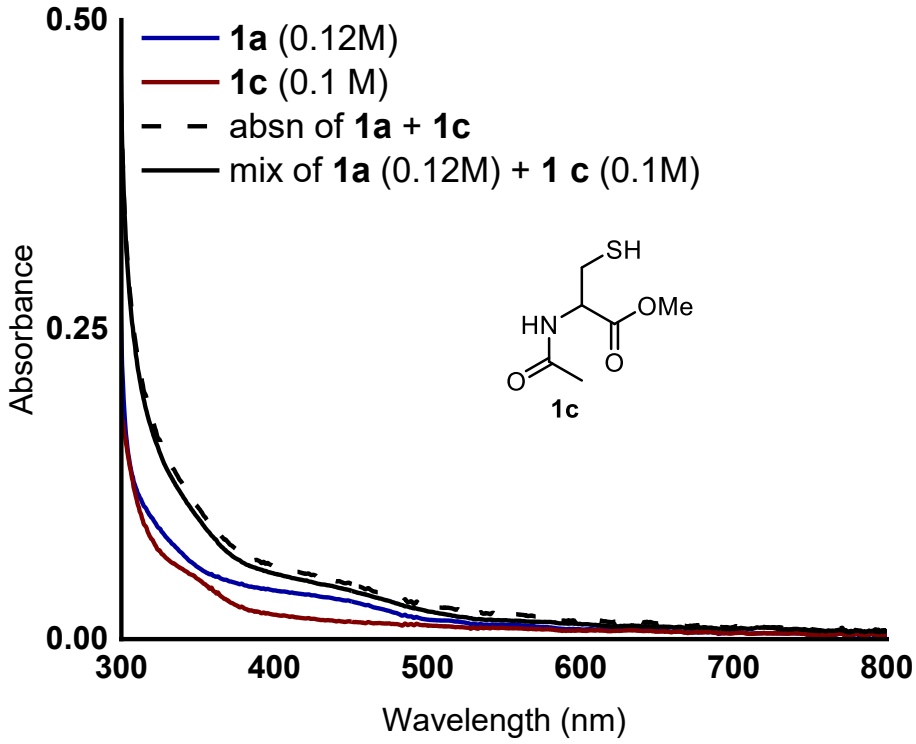


Figure S6: Absorption spectra of **1a**, **1c** and mixture of **1a** and **1c** in DMF using Cary60 spectrophotometer.

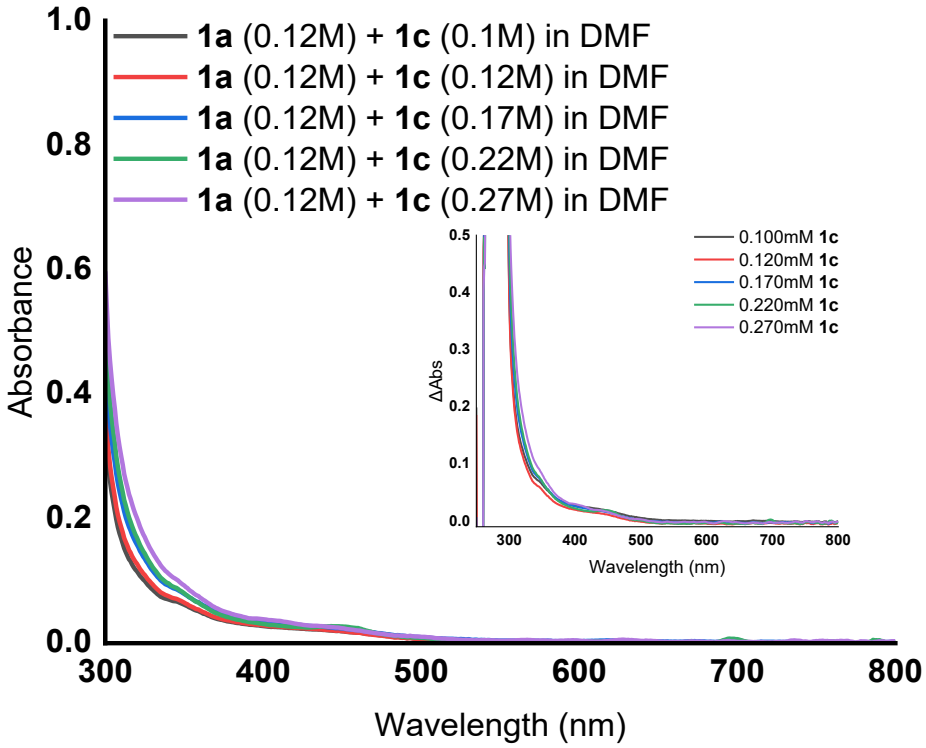


Figure S7: Absorption spectra of mixture of **1a** and **1c** with varying concentration of **1c** in DMF using Cary60 spectrophotometer.

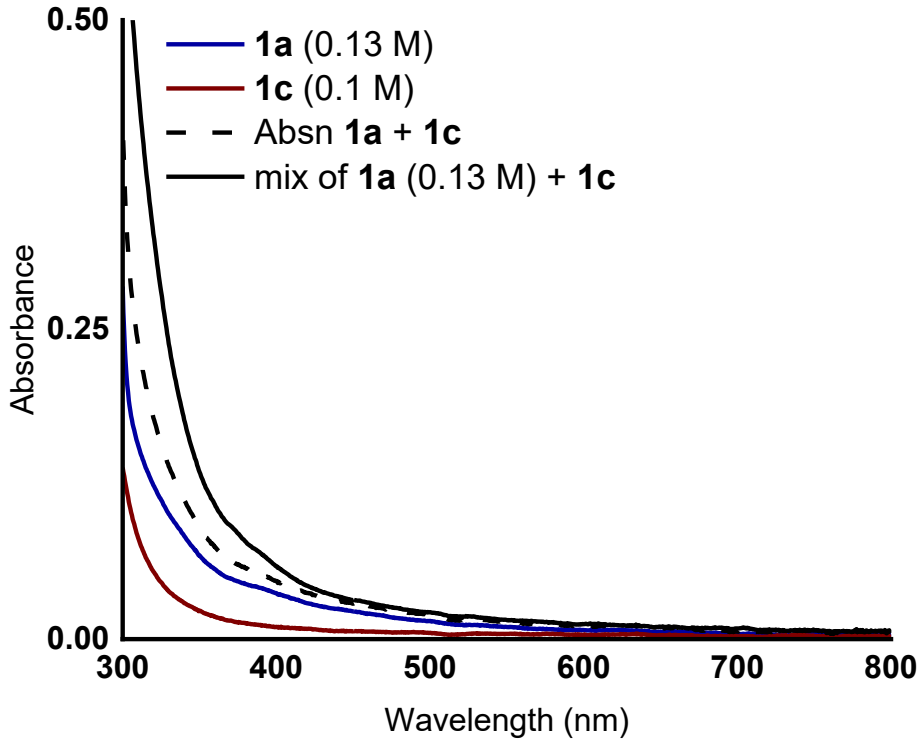


Figure S8: Absorption spectra of **1a**, **1c** and mixture of **1a** and **1c** in 40% MeCN in DCE using Cary60 spectrophotometer.

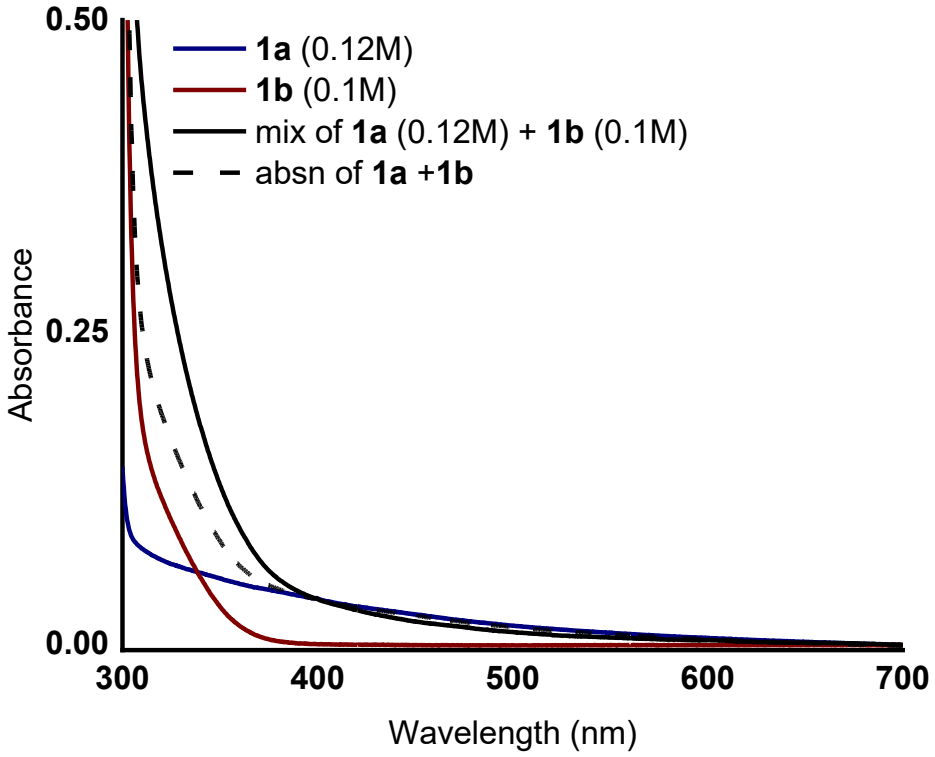


Figure S9: Absorption spectra of **1a**, **1b** and mixture of **1a** and **1b** in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

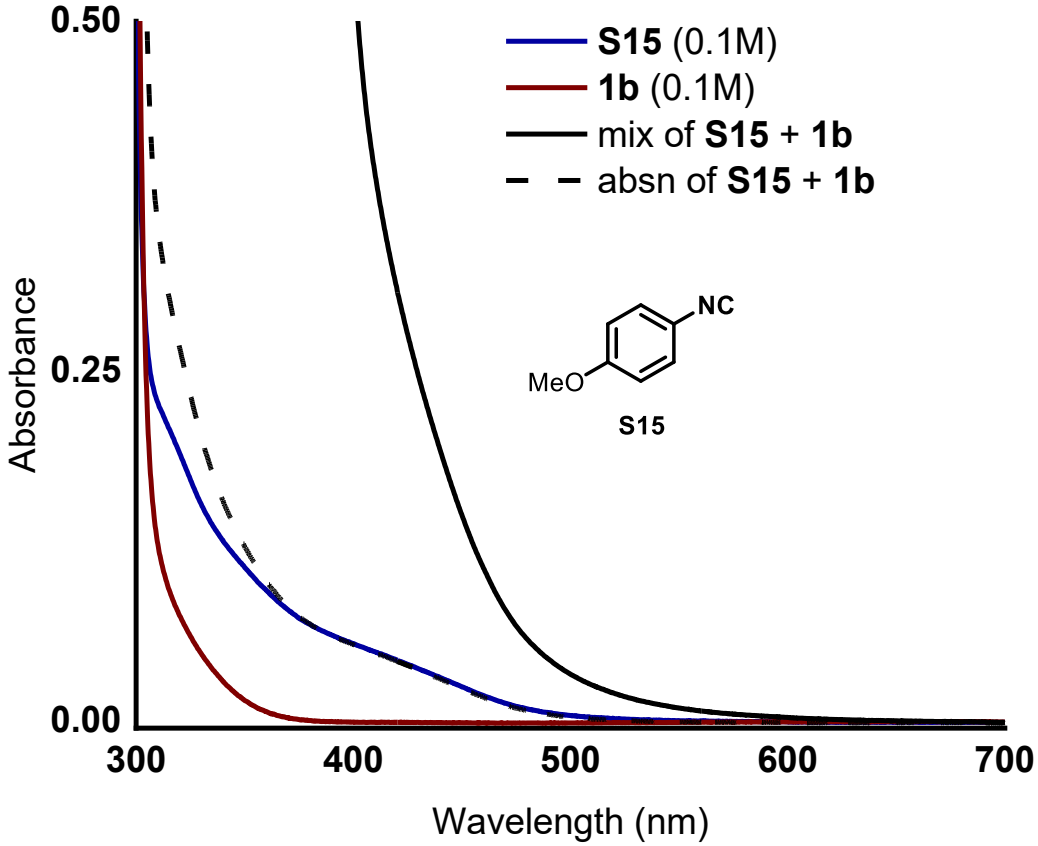


Figure S10: Absorption spectra of **S15**, **1b** and mixture of **S15** and **1b** in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

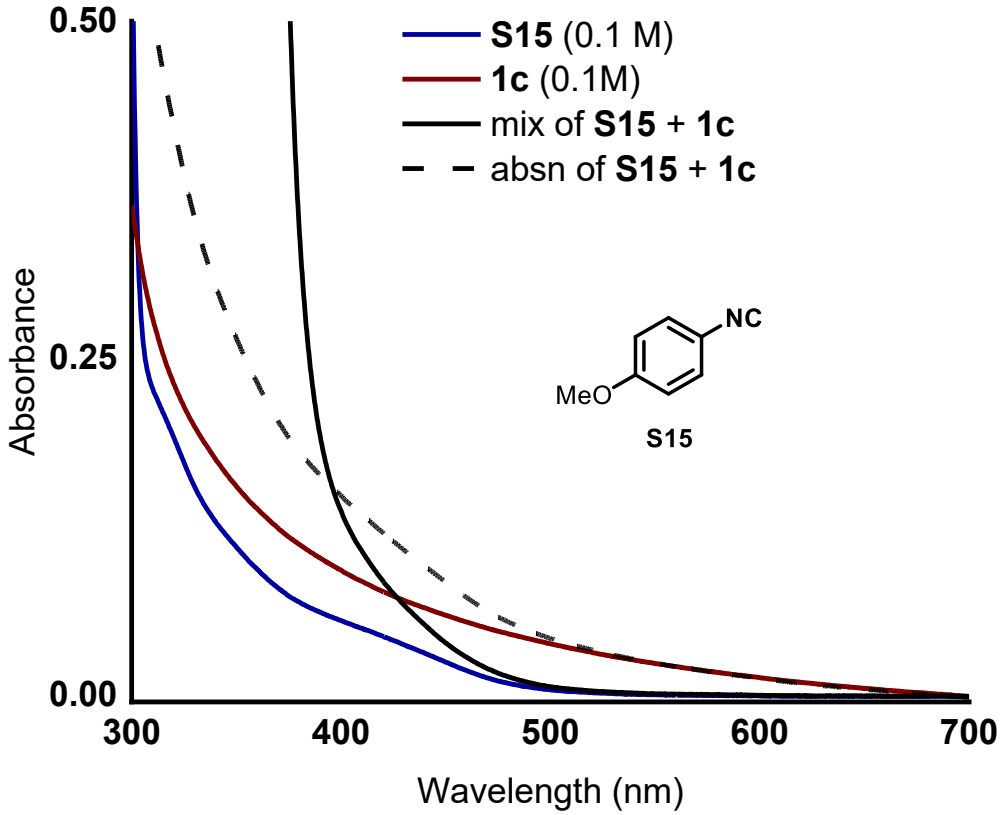


Figure S11: Absorption spectra of **S15**, **1c** and mixture of **S15** and **1c** in 40% MeCN in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

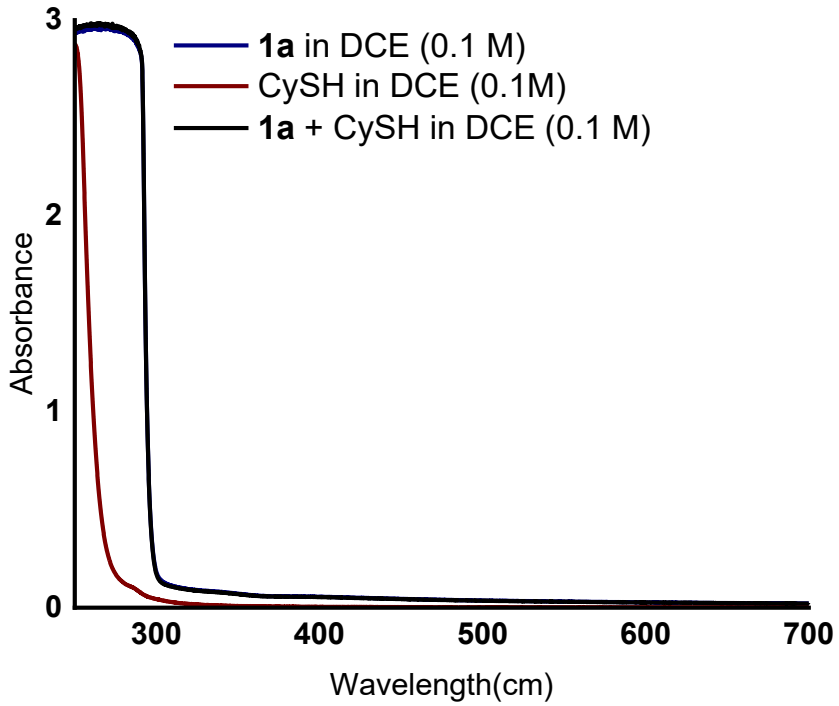


Figure S12: Absorption spectra of **1a,** cychexyl thiol(**CySH)** and mixture of **1a** and **CySH** in in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

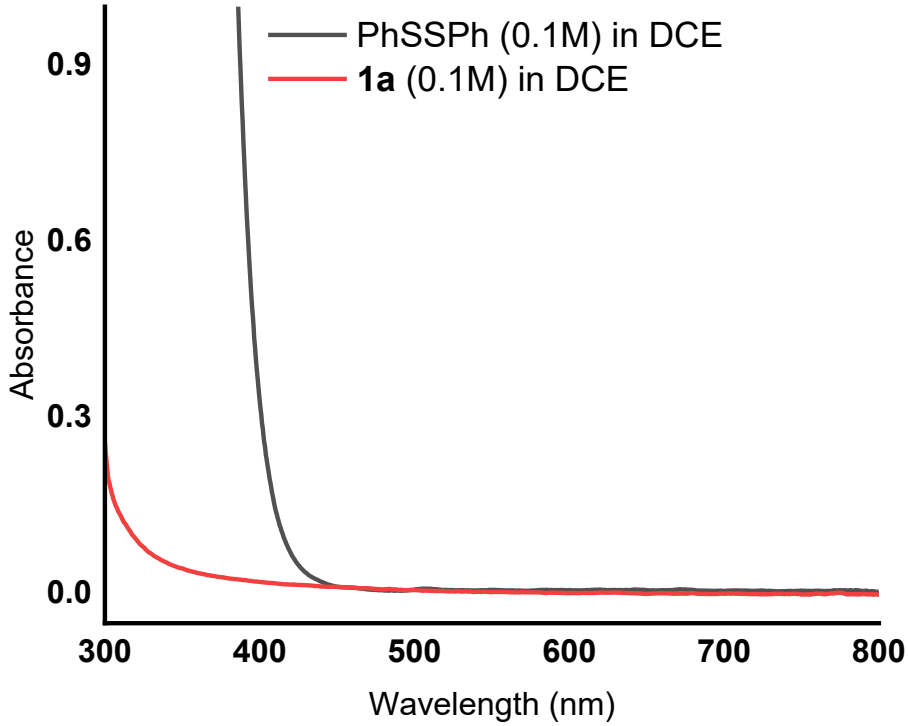


Figure S13: Absorption spectra of **PhSSPh** and **1a** at 0.1M concentration in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

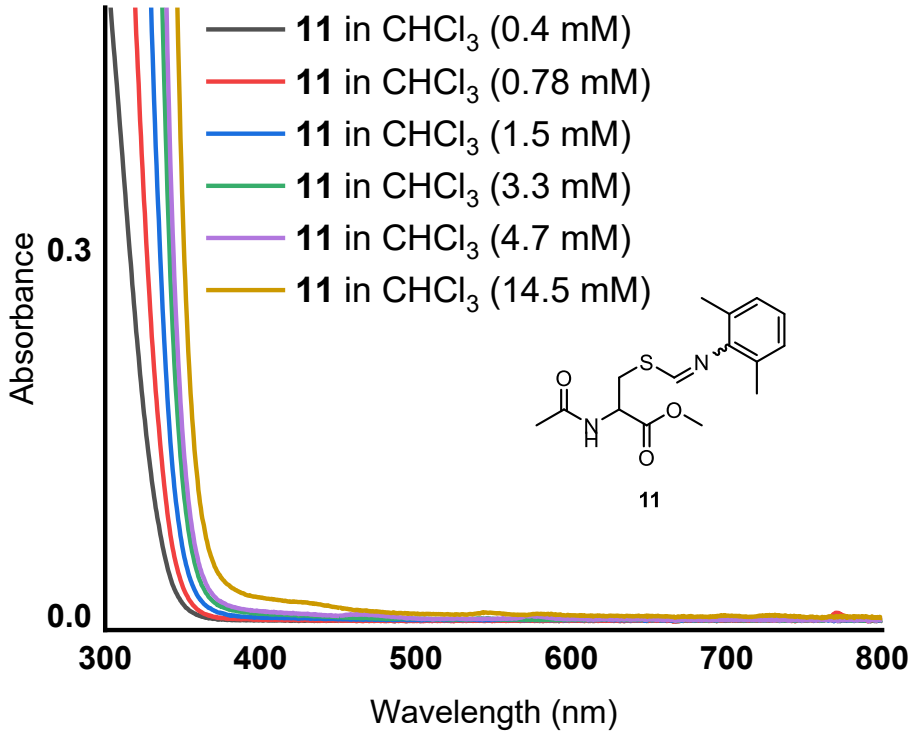


Figure S14: Absorption spectrum of **11** at different concentrations in $CHCl_3$ using Cary60 spectrophotometer.

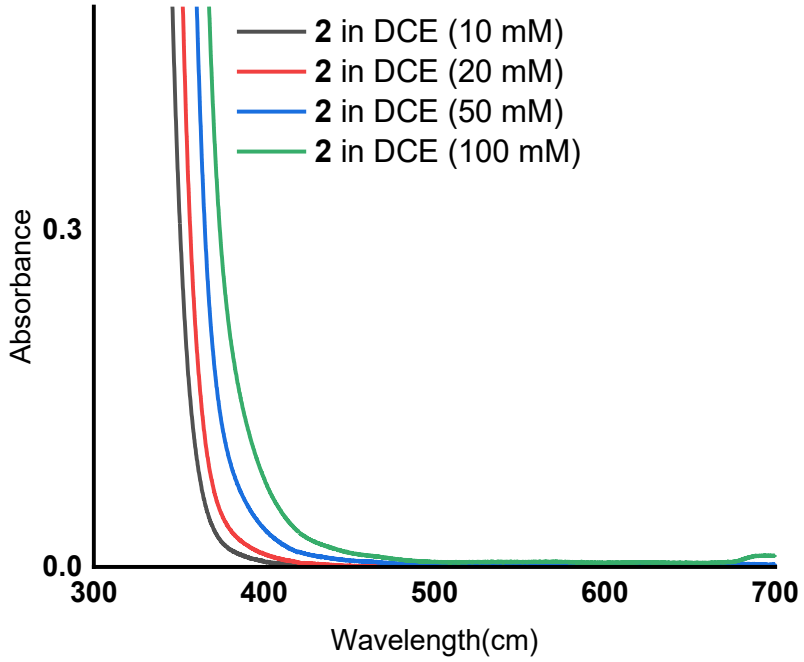


Figure S15: Absorption spectra of **2** at different concentrations in DCE using Shimadzu UV-Vis Spectrophotometer UV-3600.

Implication:

From the UV-Vis experiments, we can rule out the formation of a ground-state electron donor-acceptor complex between compound **1a** and aliphatic and aromatic thiols or disulfides in DCE, DMF, or their mixtures. Furthermore, the thioformimidates derived from both aliphatic and aromatic thiols exhibit absorption in the visible region, depending on their concentration. Notably, the observed UV-Vis absorption peak of the thioformimidate product suggests its potential applicability as a photocatalyst in future studies. Detailed photophysical characterization is presented in the following section.

4.5 Steady state photoluminescence

Steady-state photoluminescence spectra were recorded on an Edinburgh Instruments FS5 Spectrofluorometer. The steady-state photoluminescence spectra were recorded using a 150 W Xenon arc lamp as the excitation source. The photoluminescence was detected at a right angle to the excitation beam using a single photon counting PMT-900 in a temperature stabilized housing. The spectra were integrated at 0.1 s. Steady-state photoluminescence spectra were corrected for

the instrument's spectral response. All room-temperature spectra were obtained from Argon-sparged solutions unless otherwise mentioned.

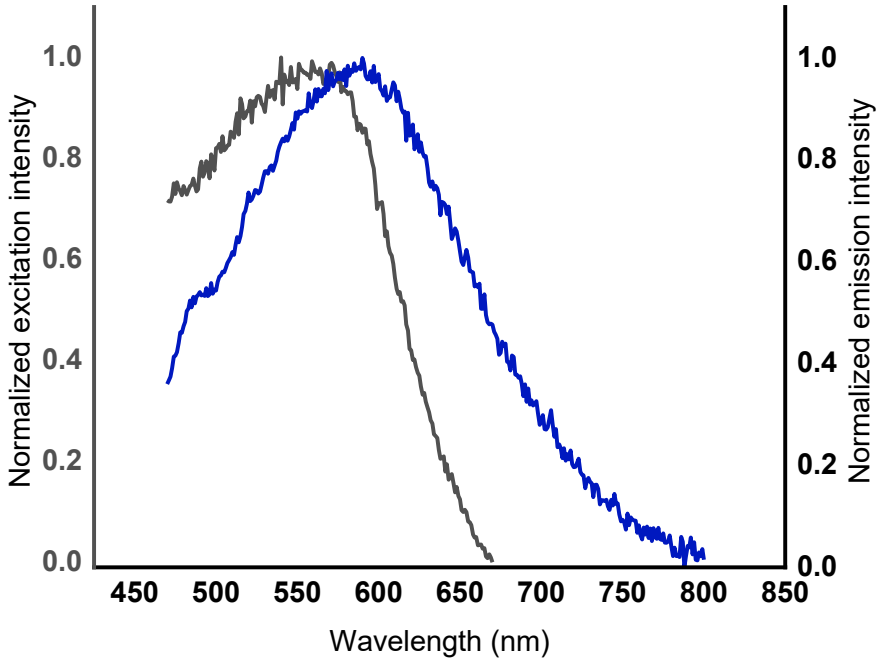


Figure S16: Excitation and emission spectra of **1a** (0.1M) in $CHCl_3$.

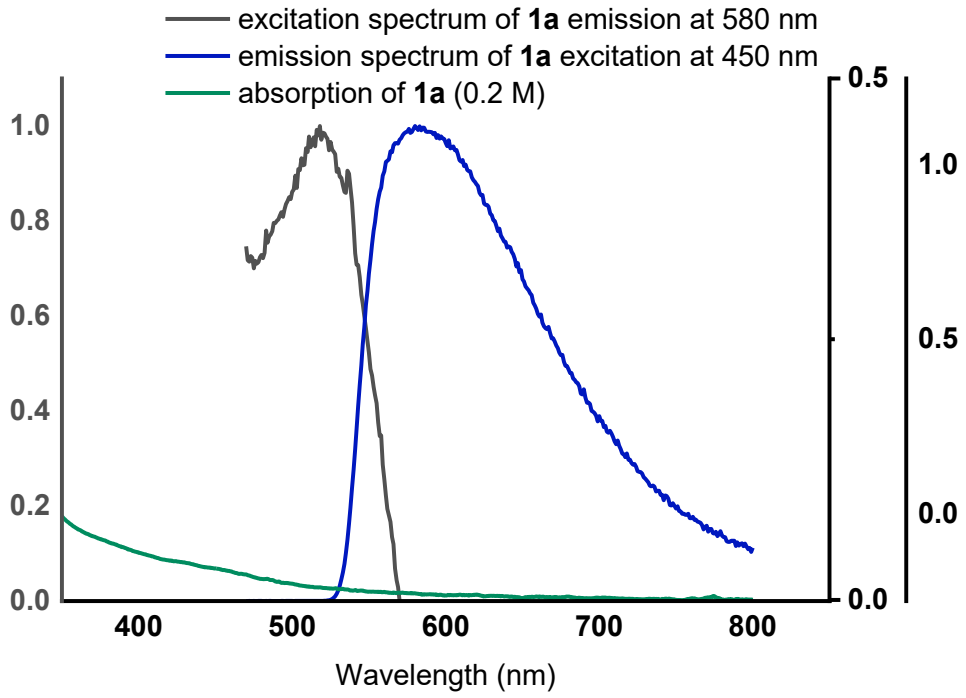


Figure S17: Absorption, excitation and emission spectra of **1a** in DCE; to avoid scattered light from solvent in emission spectra, 550 nm band pass filter was used.

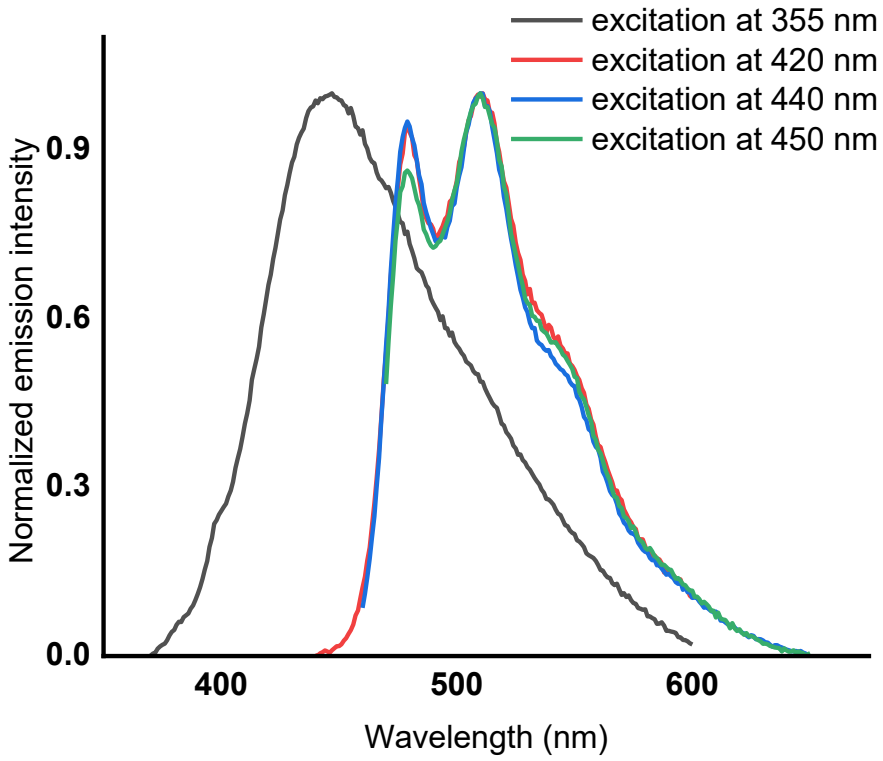


Figure S18: Emission spectra of **11** (14mM) in $CHCl_3$ at different excitation wavelengths.

4.6 Fluorescence lifetime measurement (TCSPC) and quenching experiments

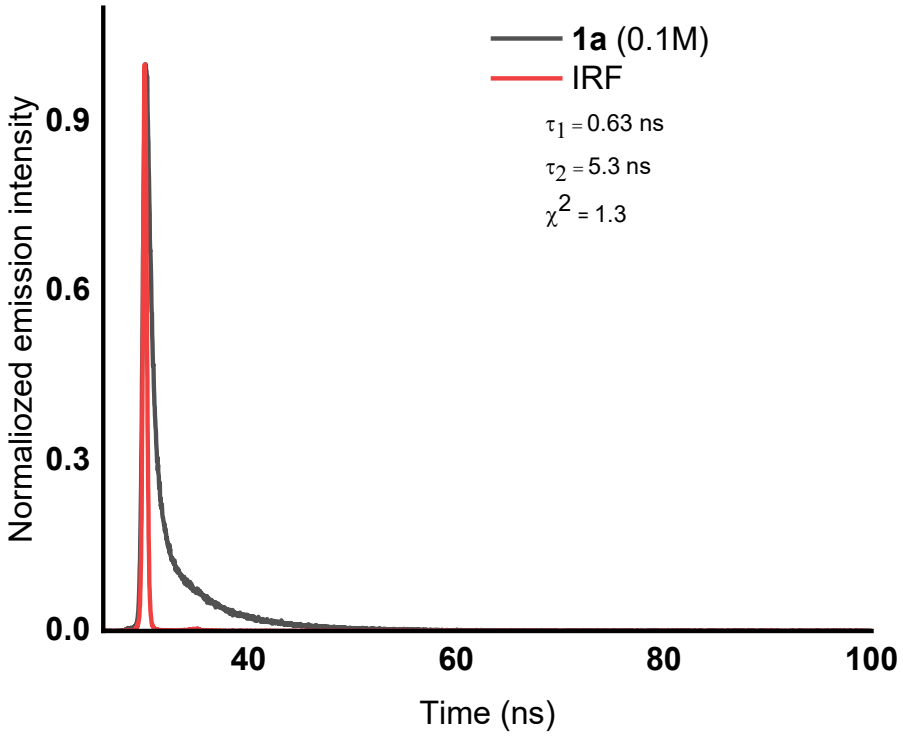


Figure S19: Fluorescence emission lifetime of **1a** (100 mM) in deaerated $CHCl_3$ was measured using the TCSPC technique, with excitation at 450 nm and emission decay monitored at 600 nm.

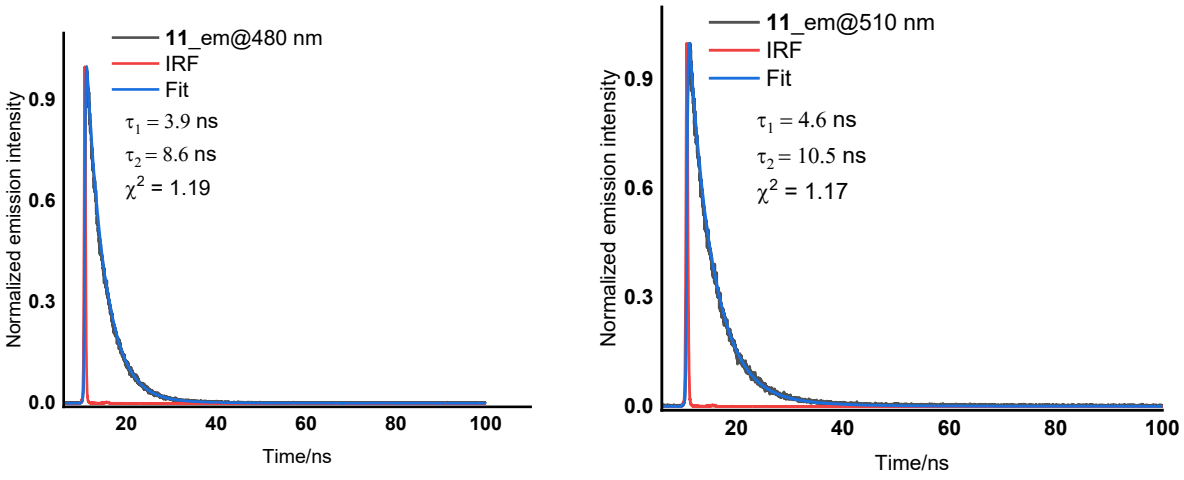


Figure S20: Fluorescence emission lifetime of **11** (15 mM) in deaerated $CHCl_3$ was measured using the TCSPC technique, with excitation at 450 nm and emission decay monitored at 480 and 510 nm.

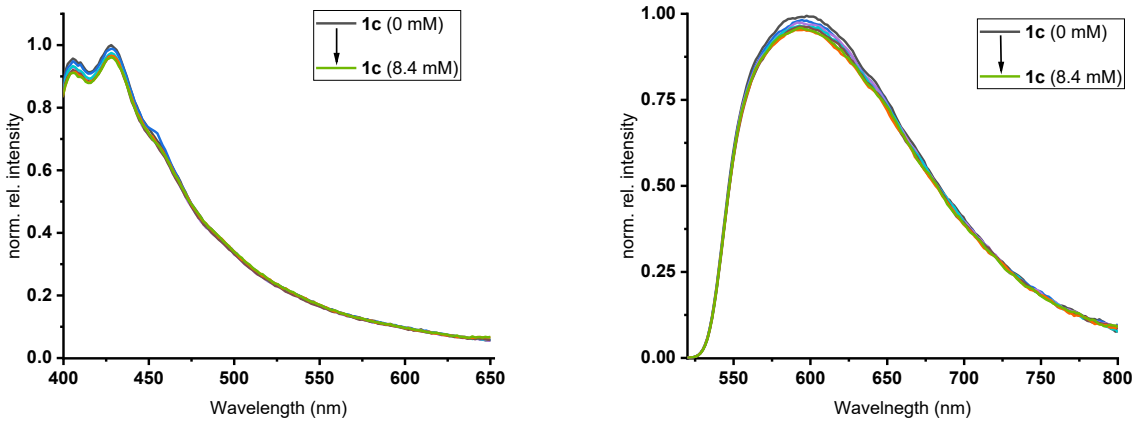


Figure S21: Fluorescence quenching of **1a** with **1c** were recorded with excitation at 355 nm in a mixture of $CHCl_3$ and MeCN (left); fluorescence quenching of **1a** with **1c** were recorded with excitation at 450 nm in a mixture of $CHCl_3$ and MeCN (550 nm band-pass filter was used to avoid scattered light from the solvent in the emission spectra) (right).

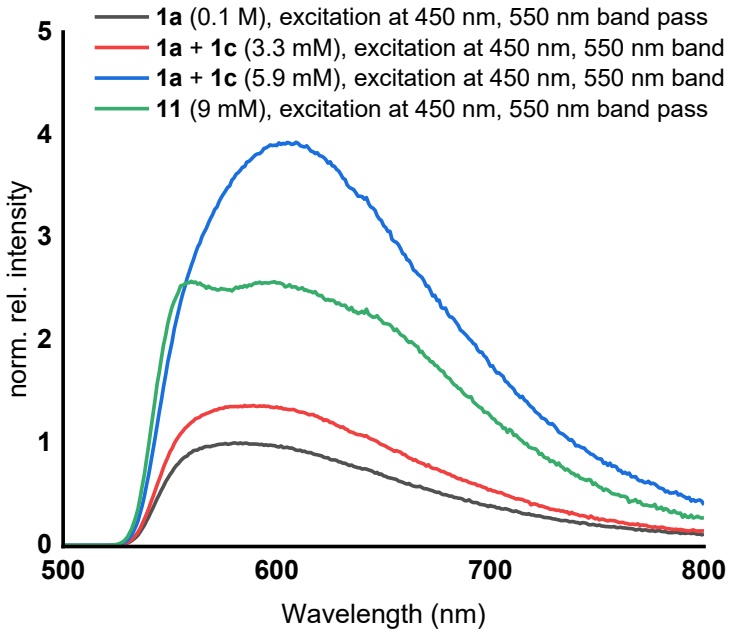


Figure S22: Fluorescence quenching of **1a** with **1c** and the emission spectrum of **11** were recorded with excitation at 450 nm. To avoid scattered light from the solvent in the emission spectra, a 550 nm band-pass filter was used. For these quenching studies, **1c** was dissolved in a 0.1 M solution of **1a**.

Implications:

We observed photoluminescence quenching of **1a** with **1c** as a quencher, as shown in Figure S21. However, Stern-Volmer constant was very low (3 M^{-1} excitation at 355 nm and 8 M^{-1} excitations at 450 nm)). The observed low quenching efficiency can be attributed to the short excited state lifetime of **1a** (Figure S19). To observe an appreciable quenching, higher quencher concentration would be required, but the solubility of **1c** and **1a** was the limiting factor in these experiments. In addition, when the emission spectrum of product **11**, derived from **1a** and **1c**, was recorded, significant spectral overlap was observed (Figure S18 and S22). Considering these results, it is apparent that the excited state of **1a** is involved in the radical initiation step. However, we cannot overrule the other mechanistic pathway at this stage.

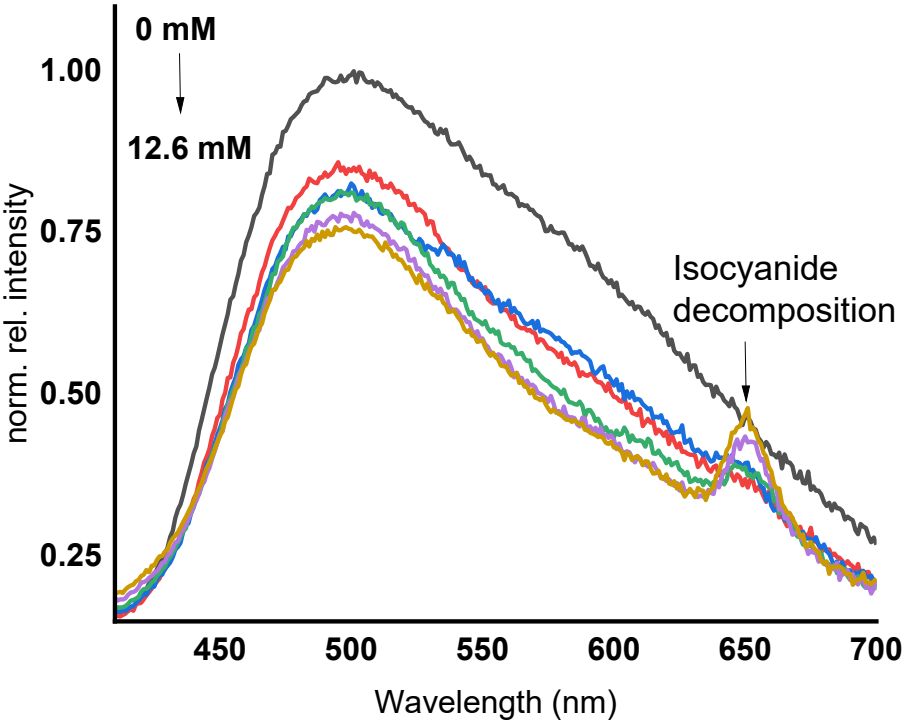


Figure S23: Fluorescence quenching of **4-Isocyanoanisole** with **1c** were recorded with excitation at 360 nm. For these quenching studies, **1c** was dissolved in a solution of **4-Isocyanoanisole** (40% MeCN in $CHCl_3$).

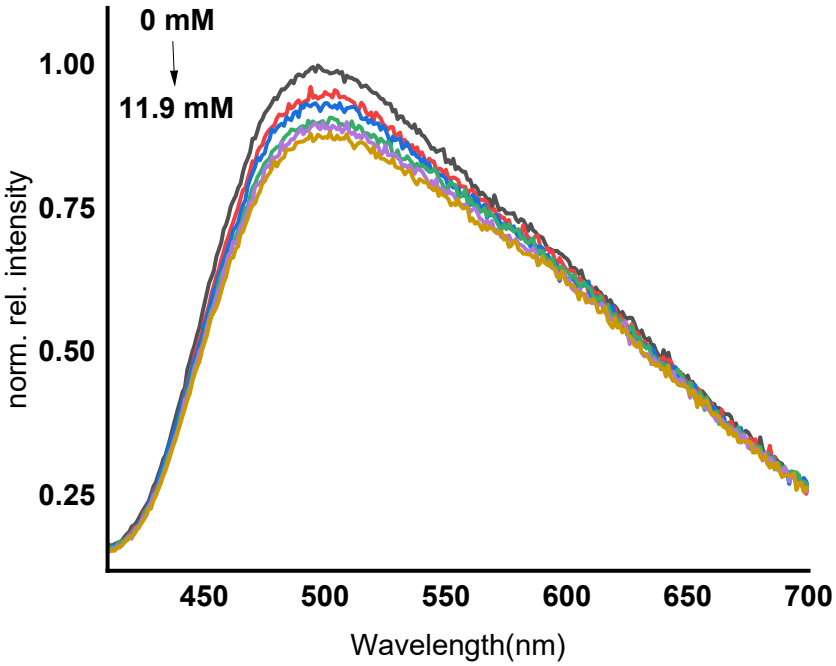


Figure S24: Fluorescence quenching of **4-Isocyanoanisole** with **phenol** were recorded with excitation at 360 nm. For these quenching studies, **phenol** was dissolved in a solution of **4-Isocyanoanisole** (40% MeCN in $CHCl_3$).

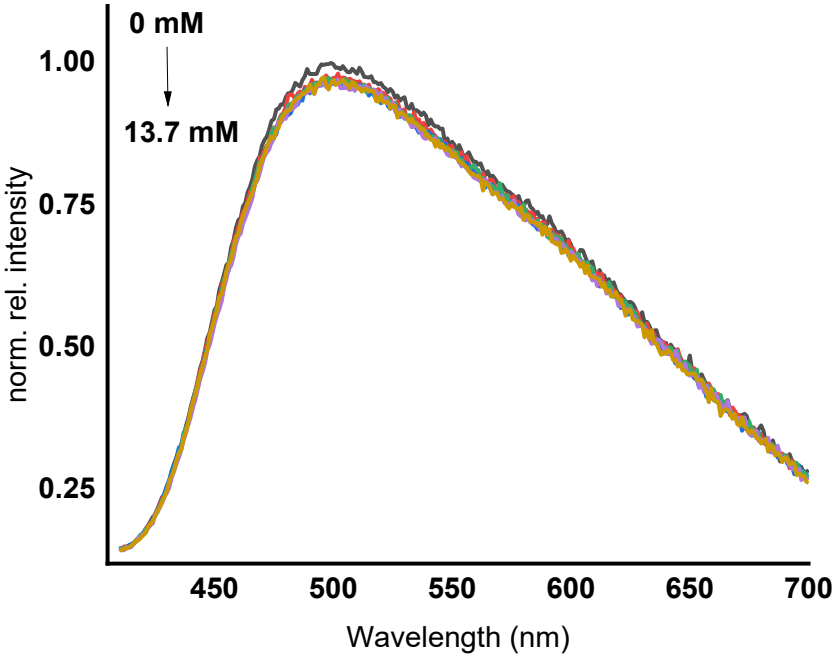


Figure S25: Fluorescence quenching of **4-Isocyanoanisole** with **1,3,5-trimethoxybenzene** were recorded with excitation at 360 nm. For these quenching studies, **1,3,5-trimethoxybenzene** was dissolved in a solution of **4-Isocyanoanisole** (40% MeCN in $CHCl_3$).

Implications:

We selected another isocyanide, 4-isocyanoanisole, which was expected to exhibit better charge-transfer characteristics due to the presence of an electron-donating methoxy group. In this case, excitation at 360 nm was chosen to minimize scattering and obtain cleaner emission spectra. Under these conditions, distinct quenching was observed with both thiol and phenol. However, due to the unavailability of a TCSPC laser module source below 410 nm in our laboratory, fluorescence lifetime quenching experiments could not be performed.

4.7 Time resolved fluorescence

Time resolved fluorescence measurements were recorded on a LP980-K spectrometer from Edinburgh Instruments equipped with an iCCD detector from Andor (DH320T). The excitation source was a tunable Nd:YAG Laser NT342 Series from EKSPLA. The third harmonic (355 nm) at 150 mJ was directed into an optical parametric oscillator (OPO) to enable wavelength tuning starting from 410 nm. The laser power was then attenuated to reach appreciable signal/noise and the integrity of the samples was verified by UV-vis measurements. measurements were performed in argon-purged acetonitrile at room temperature. An average of 10 scans per measurement was used.

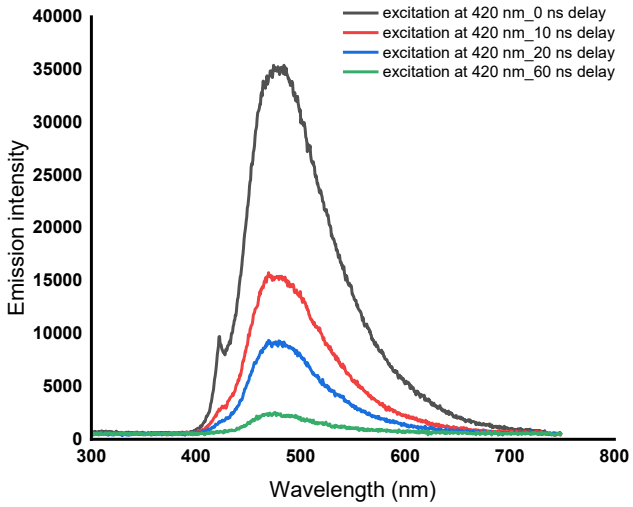


Figure S26: Time resolved fluorescence spectra of **1a** (0.1M) in DCE acquired in an LP980 with an ICCD detector at different times after the pump pulse (indicated in the graph); gate width = 200 ns, BW = 2 nm.

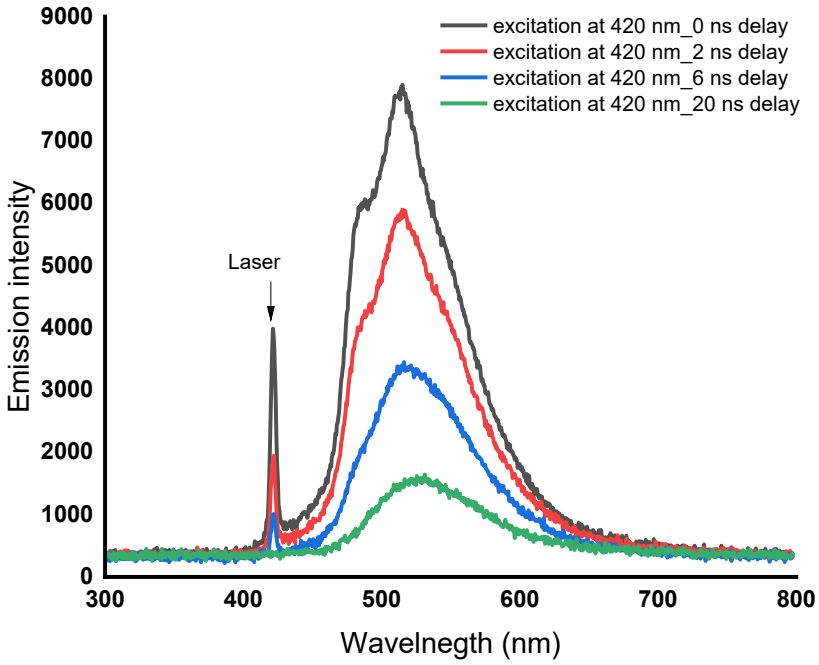
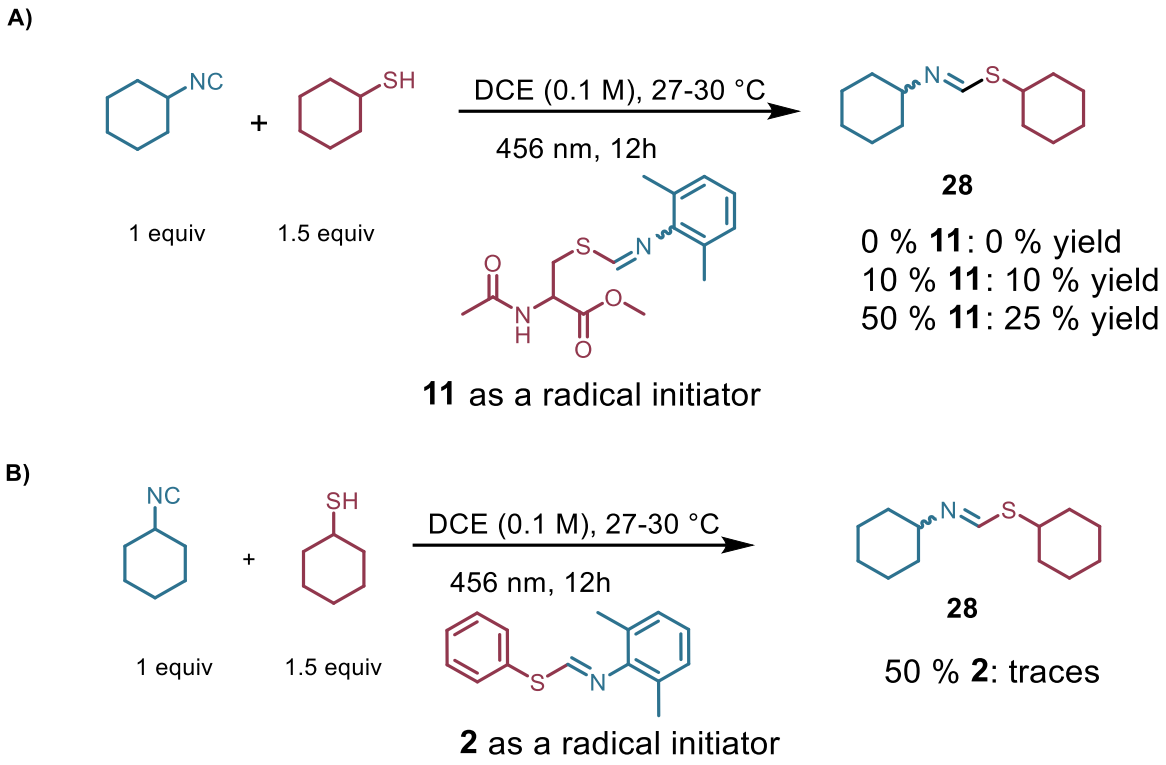


Figure S27: Time resolved fluorescence spectra of **11** (14 mM) in $CHCl_3$ acquired in an LP980 with an ICCD detector at different times after the pump pulse (indicated in the graph); gate width = 200 ns, BW = 2 nm.

4.8 Product as a radical initiator



Scheme S5: Investigation of the use of thioformimidate as a radical initiator.

We performed the reaction of aliphatic thiol and aliphatic isocyanide in the presence of product **11** and product **2** as radical initiators. In the case of product **11,** we can see the formation of the desired product. However, no product formation was detected in the presence of product **2** as a radical initiator. At this stage, we do not have a clear mechanistic rationale for this behaviour, but, we can say that, in some cases, the reaction product can act as a radical initiator or sustain the radical chain mechanism.

4.9 Thiol-disulfide exchange

To understand the mechanism of product formation involving an aliphatic isocyanide and an aromatic thiol, we investigated the possibility of disulfide formation under our reaction conditions. UV-Vis spectroscopy revealed the absorption of visible light in the case of diphenyl disulfide, which can homolytically (S—S BDE 43 kcal/mol) cleave under visible light (456 nm).[6] We conducted a thiol-disulfide exchange experiment in DMSO. Using thiophenol as a model compound, we observed that over time, thiophenol was converted to diphenyl disulfide upon exposure to light. We hypothesized that this conversion was facilitated by residual oxygen

dissolved in the solvent.[7] To confirm this, we performed a freeze-pump-thaw process to completely remove dissolved oxygen. Interestingly, even under these oxygen-depleted conditions, diphenyl disulfide formation persisted, albeit at a significantly reduced rate. When we conducted a similar experiment with cyclohexyl thiol we did not see any formation of disulfide bond.

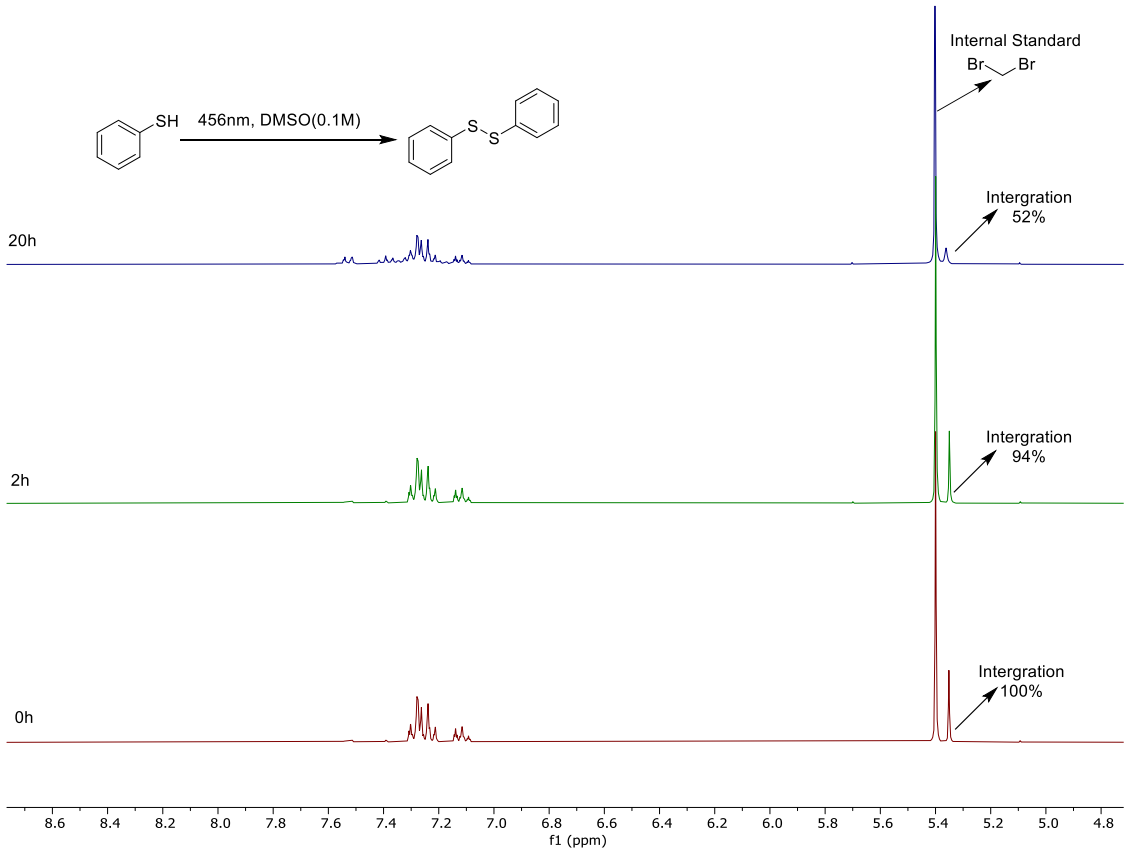


Figure S28: Thiophenol to diphenyl disulfide formation under our reaction conditions.

5. Quantum yield

The quantum yield of the reaction was determined according to a reported procedure.[8] The photon flux of the blue LED system was determined through standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (736 mg) in 10.0 mL of 0.05 M aqueous sulfuric acid. A buffered solution of 1,10- phenanthroline was prepared by dissolving 1,10-phenanthroline (50 mg) and sodium acetate (11.25 g) in 50 mL of 0.5 M aqueous sulfuric acid. To a 10 mL MW vial equipped with a stirring bar, 1 mL of the ferrioxalate

solution was added. The vial was sealed and placed 4 cm away from the walls of the irradiation system as shown in figure S1 and irradiated for the indicated time (see Table S2). After irradiation for the indicated time, 20 µL of the irradiated solutions were added to 2 mL of the phenanthroline solution. The resulting reaction mixture was left equilibrating in the dark for 1 h. Next, the resultant reaction solutions were further diluted by taking 50 µL and adding 3 mL of distilled water. The final solution was analyzed via UV-Vis spectroscopy. The absorbance of the resulting solution in a cuvette (l = 10 mm) at 510 nm was measured by a UV-Vis spectrometer. The procedure was repeated at different reaction times and the absorbance of a non-irradiated sample was measured as well.

To calculate the amount of Fe^{2+}, the following equation was used:

$$mol\ Fe^{2+} = \frac{V \times \Delta A}{l \times \varepsilon}$$

Where V is the total volume (0.00305 L), ΔA is the difference in the absorbance at 510 nm between the irradiated and non-irradiated sample, l is the path length (1.00 cm), and ε is the molar absorptivity at 510 nm (11, 100 L/mol x cm).

Table S2: ferrioxalate actinometry obtained from UV-Vis spectrometry

Time (s)	ΔA510nm	mol Fe^{2+}
0	0	0
5	0.00661607	1.81793E-06
10	0.0124289	3.41515E-06
15	0.0199769	5.48915E-06
20	0.0280143	7.69762E-06
25	0.0330874	9.09158E-06

According to the ferrioxalate actinometry, the correlation of mol Fe^{2+} and time can be plotted as follows.

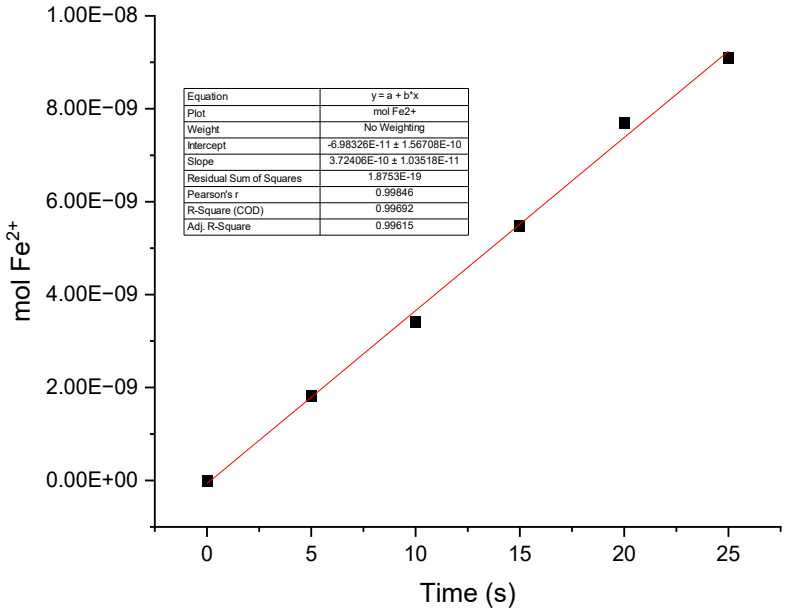


Figure S29: Plot of the moles of Fe^{2+} vs time to calculate the photon flux.

From the graph,

Slope = $((F \times \Phi \times f) = 3.72406 \times 10^{-10}$

The photon flux (F) was calculated as follows:

$$F = \frac{mol\ Fe^{2+}}{\phi \times t \times f}$$

Then

$$Slope = F \times \phi \times f = 3.72406\text{E} - 10$$

So

$$F = \frac{3.72406\text{E} - 10}{\phi \times f} = 4.40717\text{E} - 10$$

Where Φ is the quantum yield for the ferrioxalate actinometer (approximated as 0.845, which was reported for a 0.15 M solution at λ = 457.9 nm) and *f* is the fraction of light absorbed (close to 1).

Quantum yield determination: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, **1a** (1.2 equiv. 0.24 mmol) and **1c** (1.0 equiv. 0.2 mmol) were added, followed by the addition of 40% MeCN in DCE (0.1M). The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with one

Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 2 h. The yield was calculated as 12% through the ^{1}H-NMR integration method using CH_2Br_2 as an internal standard.

The quantum yield was calculated through the formula:

$$\phi = \frac{mol\ product}{F \times t \times f}$$

Where flux is the photon flux determined by ferrioxalate actinometry (4.40717E^{-10} Einstein/s), t is the time (3600 s), and *f* is the fraction of light absorbed by reaction mixture in 40% MeCN in DCE at 456 nm (0.069, average of three measurements). The fraction of light absorbed at 456 nm was calculated: $f = 1.0000 - 10^{-0.069}$

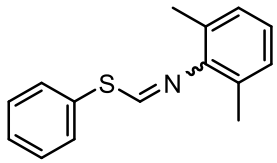
So, the calculated quantum yield is 104. This is in line with the chain propagation mechanism.

6. General procedure for the synthesis of thioformimidates

GP1: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, isocyanide (1.2 equiv. 0.24 mmol) and thiol (1 equiv. 0.2 mmol) were added, followed by the addition of dry DCE (2mL). The MW vial was then closed with a teflon septum cap and degassed with nitrogen for 5 min. (in the case of volatile thiols, freeze-thaw process was used) The vial was then placed for irradiation with one Kessil blue LEDs as shown in Figure S1 (40W, 456 nm) for 16 h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was concentrated under reduced pressure. The product was isolated through an auto column using an Eco flex silica column (0-30 % EtOAc/heptane).

7. Product Characterization

phenyl *N*-(2,6-dimethylphenyl)-methanimidothioate

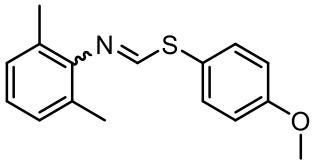


Compound **2** was prepared according to the general procedure (GP1) and isolated as colorless oil. Spectroscopic data were consistent with literature values.[9]

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.51 – 7.46 (m, 2H), 7.42-7.37 (m, 3H), 7.08 (d, *J* = 7.4 Hz, 2H), 7.02 – 6.95 (m, 1H), 2.19 (s, 6H).

4-methoxyphenyl *N*-(2,6-dimethylphenyl)methanimidothioate

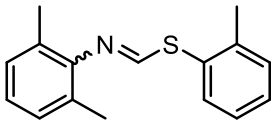


Compound **3** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.44 – 7.38 (m, 2H), 7.08 (m, 2H), 7.02 – 6.97 (m, 1H), 6.96 – 6.90 (m, 2H), 3.83 (s, 3H), 2.20 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.05, 160.57, 147.90, 135.05, 128.16, 126.12, 124.16, 121.52, 115.16, 55.45, 17.71; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 272.1105, found: 272.1093

o-tolyl *N*-(2,6-dimethylphenyl)methanimidothioate

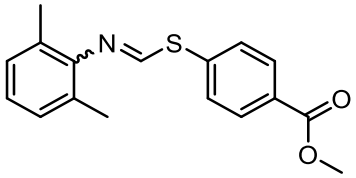


Compound **4** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.53 – 7.47 (m, 1H), 7.34 – 7.29 (m, 2H), 7.28 – 7.22 (m, 1H), 7.10 (d, *J* = 7.4 Hz, 2H), 7.00 (dd, *J* = 8.4, 6.5 Hz, 1H), 2.42 (s, 3H), 2.22 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.12, 147.97, 141.24, 134.69, 131.07, 130.48, 129.72, 128.31, 127.23, 126.32, 124.29, 21.37, 17.79; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 256.11544, found: 256.11518

methyl 4-((((2,6-dimethylphenyl)imino)methyl)thio)benzoate

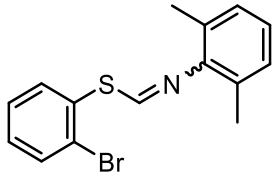


Compound **5** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 30 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 – 8.02 (m, 2H), 7.57 – 7.50 (m, 2H), 7.09 (d, *J* = 7.3 Hz, 2H), 7.04 – 6.97 (m, 1H), 3.94 (s, 3H), 2.19 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.23, 157.77, 147.79, 137.23, 131.90, 130.58, 130.37, 128.27, 126.02, 124.47, 52.39, 17.69; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 300.10526, found: 300.10456

2-bromophenyl N-(2,6-dimethylphenyl)methanimidothioate

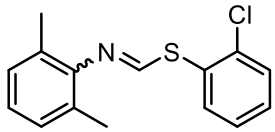


Compound **6** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.37 (s, 1H), 7.70 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.60 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.35 (td, *J* = 7.6, 1.5 Hz, 1H), 7.25 (td, *J* = 7.6, 1.7 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 2H), 7.02-6.99 (m, 1H), 2.22 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 158.17, 147.20, 135.13, 133.62, 132.01, 130.46, 128.51, 128.05, 127.92, 126.03, 124.06, 17.42; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 320.01035, found: 320.00932

2-chlorophenyl *N*-(2,6-dimethylphenyl)methanimidothioate

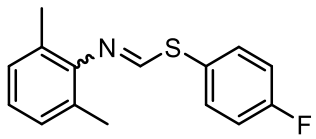


Compound **7** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.59 (dd, *J* = 7.3, 2.1 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.39-7.28 (m, 2H), 7.10 (d, *J* = 7.3 Hz, 2H), 7.03-6.98 (m, 1H), 2.23 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 158.36, 147.64, 138.06, 135.58, 130.80, 130.71, 130.27, 128.34, 127.79, 126.40, 124.48, 17.77; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 276.06082, found: 276.05985

4-fluorophenyl *N*-(2,6-dimethylphenyl)methanimidothioate



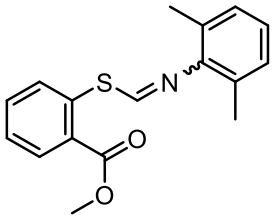
Compound **8** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.50 – 7.44 (m, 2H), 7.16 – 7.06 (m, 4H), 7.03-6.98 (m, 1H), 2.20 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.14, 161.83, 159.73, 147.87, 135.36 (d, *J* = 8.4 Hz), 128.33, 126.14, 124.44, 116.94 (d, *J* = 22.1 Hz) 17.79; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.38.

HRMS (ESI^+): $[M+H]^+$ cal'd for: 260.09036, found: 260.08969

methyl 2-((((2,6-dimethylphenyl)imino)methyl)thio)benzoate

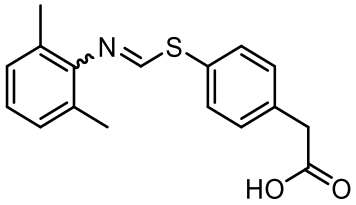


Compound **9** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.52 (s, 0.9H), 8.38 (s, 0.10H), 7.89 (dd, *J* = 7.6, 1.5 Hz, 0.9H), 7.62 – 7.50 (m, 2H), 7.47 – 7.36 (m, 1H), 7.09 – 7.04 (m, 2H), 7.02 – 6.94 (m, 1H), 3.89 (s, 3H), 2.19 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.75, 158.88, 147.59, 133.96, 133.63, 133.10, 132.59, 132.35, 131.48, 130.92, 128.56, 128.20, 126.15, 125.86, 125.50, 124.25, 52.50, 52.41, 17.70; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 300.1053, found: 300.1042

2-(4-((((2,6-dimethylphenyl)imino)methyl)thio)phenyl)acetic acid



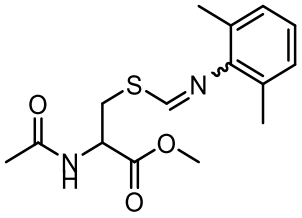
Compound **10** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 50 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.61 (s, 1H), 7.48 – 7.41 (m, 2H), 7.36 – 7.29 (m, 2H), 7.11-7.08 (m, 2H), 7.05 – 6.98 (m, 1H), 3.66 (s, 2H), 2.19 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$)

δ 175.91, 161.99, 147.18, 135.09, 133.22, 130.83, 129.78, 128.39, 126.65, 124.79, 40.77, 17.77; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 300.1053, found: 300.1046

methyl *N*-acetyl-S-(((2,6-dimethylphenyl)imino)methyl)cysteinate

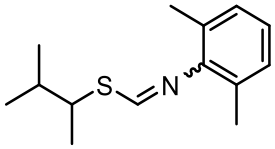


Compound **11** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.36 (s, 0.6H), 8.20 (s, 0.4H), 7.02 (d, *J* = 6.6 Hz, 2H), 7.00 – 6.87 (m, 1H), 6.41 (s, 0.4H), 6.32 (s, 0.6H), 4.94-4.86 (m, 1H), 3.79 (s, 2H), 3.75 (s, 1H), 3.64 – 3.33 (m, 1H), 3.04 – 2.97 (m, 1H), 2.12 (s, 2H), 2.07 (s, 4H), 2.03 (s, 2H), 1.98 (s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 170.94, 170.76, 170.19, 170.04, 159.45, 159.36, 128.35, 128.27, 127.73, 126.03, 124.32, 124.22, 53.67, 53.15, 53.02, 52.95, 52.82, 52.80, 34.12, 30.50, 27.00, 23.28, 23.20, 18.41, 17.61; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 309.12673, found: 309.12789

3-methylbutan-2-yl N-(2,6-dimethylphenyl)methanimidothioate

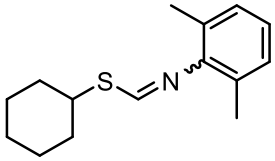


Compound **12** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers**)** δ 8.54 (s, 0.72H), δ 8.21 (s, 0.28H), 7.07 – 6.99 (m, 2H), 6.98 – 6.86 (m, 1H), 3.95 (qd, *J* = 7.1, 4.6 Hz, 0.29H), 3.16 (qd, *J* = 7.1, 4.6 Hz, 0.76H), 2.11 (s, 6H), 2.05 – 1.97 (m, 0.20H), 1.95 – 1.84 (m, 0.80H), 1.41 (d, *J* = 7.2 Hz, 1H), 1.34 (d, *J* = 7.0 Hz, 2H), 1.04 (dd, *J* = 6.8, 4.0 Hz, 1.5H), 0.95 (t, *J* = 6.3 Hz, 4.5H); **^{13}C NMR (**75 MHz, $CDCl_3$**)** δ 160.71, 159.89, 148.53, 128.13, 127.82, 123.94, 123.53, 49.66, 44.75, 34.10, 33.11, 19.63, 19.54, 19.43, 19.40, 18.45, 18.41, 17.72; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 236.14673, found: 236.14708

cyclohexyl *N*-(2,6-dimethylphenyl)methanimidothioate

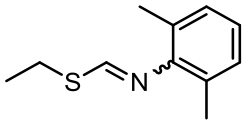


Compound **13** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 30 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.59 (s, 0.75H), 8.19 (s, 0.25H), 7.04 – 7.04 (m, 2H), 6.97 – 6.86 (m, 1H), 3.83 (td, *J* = 10.1, 5.1 Hz, 0.26H), 3.15 (td, *J* = 10.3, 4.2 Hz, 0.74H), 2.12 (s, 1.45H), 2.10 (s, 4.55H), 2.06 – 1.97 (m, 2H), 1.82 – 1.71 (m, 2H), 1.68 – 1.19 (m, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 160.00, 159.65, 148.60, 128.12, 126.12, 123.97, 123.54, 45.25, 41.78, 34.48, 33.36, 26.04, 25.92, 25.81, 25.38, 18.47, 17.70; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 248.14673, found: 248.14656

ethyl (E)-N-(2,6-dimethylphenyl)methanimidothioate

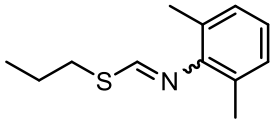


Compound **14** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.52 (s, 0.6H), 8.21 (s, 0.4H), 7.04 – 7.01 (m, 2H), 6.97 – 6.87 (m, 1H), 3.16 (q, *J* = 7.4 Hz, 0.8H), 2.91 (q, *J* = 7.5 Hz, 1.2H), 2.11 (s, 6H), 1.43 (t, *J* = 7.4 Hz, 1.2H), 1.36 (t, *J* = 7.5 Hz, 1.8H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 160.94, 159.30, 148.52, 128.17, 128.14, 127.81, 126.13, 124.07, 123.62, 26.29, 23.07, 18.43, 17.71, 16.57, 14.92; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 194.09979, found: 194.09954

propyl (E)-*N*-(2,6-dimethylphenyl)methanimidothioate

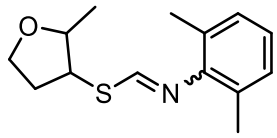


Compound **15** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 0- 40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.50 (s, 0.6H), 8.21 (s, 0.4H), 7.03 (t, *J* = 6.4 Hz, 2H), 6.97 – 6.88 (m, 1H), 3.13 (t, *J* = 7.2 Hz, 0.7H), 2.87 (t, *J* = 7.2 Hz, 1.7H), 2.11 (s, 6H), 1.84 – 1.61 (m, 3H), 1.09 – 0.99 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 161.31, 159.57, 148.49, 128.17, 128.13, 127.79, 126.15, 124.03, 123.59, 34.25, 30.52, 24.65, 23.07, 18.43, 17.70, 13.61, 13.07; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 208.1154, found: 208.1148

2-methyltetrahydrofuran-3-yl (E)-*N*-(2,6-dimethylphenyl)methanimidothioate

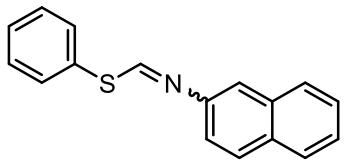


Compound **16** was prepared according to the general procedure (GP) and isolated as yellow oil.

Column Chromatography: Silica, gradient 0- 40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.55 (s, 0.55H), 8.20 (s, 0.45H), 7.06 – 6.99 (m, 2H), 6.98 – 6.87 (m, 1H), 4.50 – 4.43 (m, 0.5H), 4.31 (p, *J* = 6.1 Hz, 0.5H), 4.22 – 4.12 (m, 0.5H), 4.08 – 3.89 (m, 1H), 3.85 – 3.70 (m, 1.5H), 2.64 – 2.47 (m, 1H), 2.11 (s, 6H), 1.36 (d, *J* = 6.3 Hz, 1.2H), 1.25 (d, *J* = 6.3 Hz, 1.8H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 159.43, 158.76, 128.23, 127.72, 124.22, 123.77, 77.33, 66.16, 65.93, 48.83, 45.13, 34.64, 33.85, 18.54, 17.72, 17.39, 17.29; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 250.1260, found: 250.1249

phenyl *N*-(naphthalen-2-yl)methanimidothioate

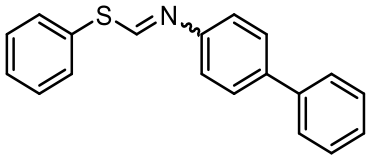


Compound **17** was prepared according to the general procedure (GP1) and isolated as brown oil.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.76 (s, 0.5H), 8.49 (s, 0.5H), 7.91 – 7.74 (m, 4H), 7.64 – 7.60 (m, 1H), 7.59 – 7.53 (m, 1H), 7.50 – 7.48 (m, 1H), 7.47 – 7.40 (m, 4H), 7.32 – 7.28 (m, 0.6H), 7.25 – 7.20 (m, 0.4H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 163.56, 160.09, 148.51, 147.50, 134.10, 134.02, 133.41, 133.15, 131.88, 131.74, 131.42, 130.17, 129.75, 129.67, 129.37, 129.25, 129.15, 129.10, 128.04, 128.02, 127.95, 127.91, 127.85, 127.81, 127.65, 126.57, 126.55, 125.46, 125.34, 121.02, 120.61, 117.52, 116.41; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 264.0841, found: 264.0833

phenyl *N*-([1,1'-biphenyl]-4-yl)methanimidothioate

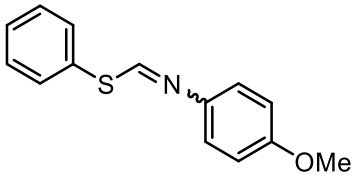


Compound **18** was prepared according to the general procedure (GP1) and isolated as an orange solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.70 (s, 0.5H), 8.46 (s, 0.5H), δ 7.68 – 7.57 (m, 3H), 7.55 – 7.51 (m, 1H), 7.49 – 7.34 (m, 8H), 7.10-7.00 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 163.58, 159.92, 151.32, 150.20, 142.38, 142.34, 140.83, 140.73, 133.32, 133.07, 131.65, 130.02, 129.65, 129.63, 129.55, 129.14, 129.05, 128.80, 127.52, 127.49, 127.23, 127.17, 124.59, 123.91, 119.54, 119.46, 118.83, 118.66; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 290.0998, found: 290.0974

phenyl *N*-(4-methoxyphenyl)methanimidothioate

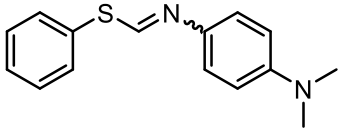


Compound **19** was prepared according to the general procedure (GP1) and isolated as brown oil.

Column Chromatography: Silica, gradient 40- 50 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.60 (s, 0.55H), 8.35 (s, 0.45H), 7.59 – 7.56 (m, 1H), 7.53 – 7.49 (m, 1H), 7.44 – 7.39 (m, 3H), 7.08 – 7.01 (m, 2H), 6.97 – 6.92 (m, 1H), 6.88 – 6.82 (m, 1H), 3.83 (s, 1.4H), 3.79 (s, 1.6H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 161.29, 158.64, 144.00, 133.30, 133.17, 129.73, 129.62, 129.08, 121.91, 121.73, 114.49, 114.46, 55.62, 55.59; **HRMS** (ESI^+): $[M+H]^+$ cal'd for: 244.0791, found: 244.0787

Phenyl *N*-(4-(dimethylamino)phenyl)methanimidothioate

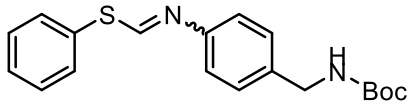


Compound **20** was prepared according to the general procedure (GP1) and isolated as yellowish oil.

Column Chromatography: Silica, gradient 0-5% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, $CDCl_3$, mixture of E/Z isomers) 8.59 (s, 0.6H), 8.26 (s, 0.4H), 7.58 – 7.54 (m, 1.2H), 7.54 – 7.50 (m, 0.8H), 7.44 – 7.37 (m, 3H), 7.10 – 7.04 (m, 2H), 6.80 – 6.75 (m, 0.8H), 6.71 – 6.66 (m, 1.2H), 2.98 (s, 2.6H), 2.94 (s, 3.6H); **^{13}C NMR**: (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 158.71, 156.22, 149.43, 148.75, 140.23, 138.99, 133.13, 133.09, 132.67, 131.09, 129.65, 129.56, 128.90, 128.84, 122.20, 121.85, 113.03, 112.85, 40.89; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 257.1107, found: 257.1100

Phenyl N-(4-(((tert-butoxycarbonyl)amino)methyl)phenyl)methanimidothioate

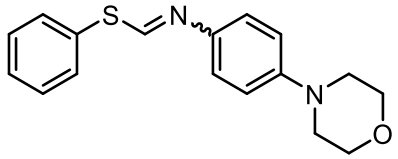


Compound **21** was prepared according to the general procedure (GP) and isolated as yellowish oil.

Column Chromatography: Silica, gradient 5-15% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.61 (s, 0.4H), 8.39 (s, 0.4H), 7.60 – 7.53 (m, 0.9H), 7.53 – 7.46 (m, 0.9H), 7.45 – 7.37 (m, 2.7H), 7.33 – 7.30 (m, 1.6H), 7.25 – 7.22 (m, 0.9H), 7.06 – 6.96 (m, 1.9H), 4.91 (brs, -N*H*), 4.30 (m, 2H), 1.47 (m, 4H), 1.45 (m, 5H); **^{13}C NMR**: (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 163.42, 159.86, 156.01, 155.99, 150.08, 149.01, 136.65, 135.80, 133.37, 133.18, 131.67, 130.17, 129.76, 129.66, 129.23, 129.18, 128.59, 128.47, 128.33, 126.70, 120.98, 120.27, 79.65, 44.49, 44.38, 28.55, 28.52; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for $C_{19}H_{23}N_2O_2S^+$: 343.14746, found: 343.14658

Phenyl *N*-(4-morpholinophenyl)methanimidothioate

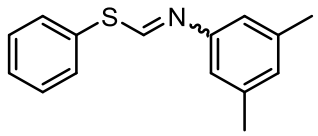


Compound **22** was prepared according to the general procedure (GP) and isolated as yellowish oil.

Column Chromatography: Silica, gradient 10-15% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.60 (s, 0.5H), 8.33 (s, 0.4H), 7.59 – 7.53 (m, 1H), 7.53 – 7.49 (m, 1H), 7.43 – 7.40 (m, 3H), 7.07 – 7.04 (m, 2H), 6.98 – 6.92 (m, 1H), 6.90 – 6.84 (m, 1H), 3.89 – 3.83 (m, 4H), 3.19 – 3.16 (m, 1.8H), 3.14 – 3.12 (m, 2.2H); **^{13}C NMR:** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 160.78, 158.05, 149.83, 149.09, 143.28, 142.16, 133.26, 133.17, 132.24, 130.69, 129.73, 129.62, 129.05, 121.77, 121.71, 116.33, 116.27, 67.09, 67.01, 49.66, 49.63; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 299.12125, found: 299.11968

Phenyl *N*-(4-(dimethylamino)phenyl)methanimidothioate

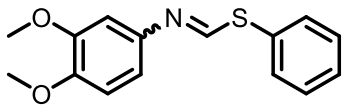


Compound **23** was prepared according to the general procedure (GP) and isolated as yellowish oil.

Column Chromatography: Silica, gradient 0-5% EtOAc/*n*-hexane.

^{1}H NMR: (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.60 (s, 0.5H), 8.37 (s, 0.4H), 7.60 – 7.55 (m, 1H), 7.54 – 7.48 (m, 1H), 7.43 – 7.40 (m, 3H), 6.83 (s, 1H), 6.69 (s, 1H), 6.65 (s, 1H), 2.35 (s, 3H), 2.29 (s, 3H); **^{13}C NMR:** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 162.82, 159.08, 150.98, 149.88, 139.05, 138.96, 133.36, 133.14, 132.06, 130.43, 129.72, 129.62, 129.13, 129.04, 127.60, 126.91, 118.54, 117.56, 21.54, 21.37; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for :242.09979, found: 242.09984

phenyl *N*-(3,4-dimethoxyphenyl)methanimidothioate

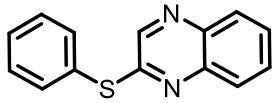


Compound **24** was prepared according to the general procedure (GP1) and isolated as a colorless solid.

Column Chromatography: Silica, gradient 10-30% EtOAc/*n*-heptane.

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.61 (s, 0.6H), 8.35 (s, 0.4H), 7.60 – 7.56 (m, 1H), 7.54 – 7.50 (m, 1H), 7.44 – 7.40 (m, 3H), 6.91 – 6.88 (m, 0.5H), 6.81 (d, J = 8.5 Hz, 0.6H), 6.71 (d, J = 2.4 Hz, 0.5H), 6.68 – 6.67 (m, 0.7H), 6.65 (t, J = 2.2 Hz, 0.5H), 6.63 (d, J = 2.4 Hz, 0.2H), 3.91 (d, J = 2.7 Hz, 3H), 3.87 (d, J = 1.9 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 160.52, 147.90, 142.93, 129.76, 129.62, 128.77, 128.32, 128.05, 126.46, 124.21, 22.55, 17.74; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 274.0896, found: 274.0888

2-(phenylthio)quinoxaline

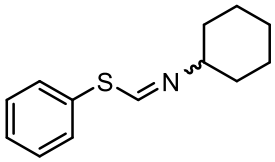


Compound **25** was prepared according to the general procedure (GP1) and isolated as a white solid. Spectroscopic data were consistent with literature values.[10]

Column Chromatography: Silica, gradient 10-30% EtOAc/*n*-heptane.

^{1}H NMR (400 MHz, $CDCl_3$,) δ 8.42 (s, 1H), 7.99 – 7.95 (m, 1H), 7.89 – 7.87 (m, 1H), 7.71 – 7.60 (m, 4H), 7.48 – 7.44 (m, 3H).

phenyl *N*-cyclohexylmethanimidothioate

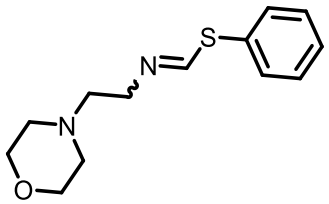


Compound **26** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 20-50% EtOAc/*n*-heptane.

^{1}H NMR (300 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.38 (s, 0.3H), 8.04 (d, J = 1.7 Hz, 0.7H), 7.52 – 7.46 (m, 2H), 7.42 – 7.34 (m, 3H), 3.43 – 3.32 (m, 0.8H), 3.14 – 3.00 (m, 0.2H), 1.90 – 1.61 (m, 5H), 1.57 – 1.14 (m, 5H); **^{13}C NMR** (75 MHz, $CDCl_3$, mixture of E/Z isomers) δ 160.03, 154.34, 133.15, 133.05, 132.22, 129.64, 129.46, 128.75, 128.62, 69.89, 63.46, 34.41, 32.83, 25.78, 25.62, 24.86, 24.72; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for : 220.11544, found: 220.11553

phenyl N-(2-morpholinoethyl)methanimidothioate

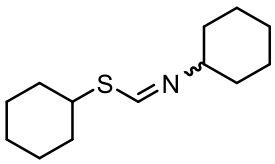


Compound **27** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 60%-80% (1%TEA and EtOAc/n-hexane). Some unknown impurities were still along with the desired product.

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.35-8.43 (m, 0.2H), 8.15 (t, J = 2.4 Hz, 0.8H), 7.50 – 7.44 (m, 2H), 7.41 – 7.32 (m, 3H), 3.75-3.72 (m, 3.5H), 3.56 (t, 0.5H), 3.50 (td, J = 6.6, 2.5 Hz, 2H), 2.75 (t, J = 6.6 Hz, 1.5H), 2.69 – 2.62 (m, 0.5H), 2.59 (t, J = 6.7 Hz, 0.5H)., 2.56 – 2.51 (m, 3.5H); **^{13}C NMR** (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 157.99, 133.12, 131.53, 129.67, 128.93, 66.98, 58.90, 53.98, 51.45; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 251.12125, found: 251.12090

cyclohexyl N-cyclohexylmethanimidothioate

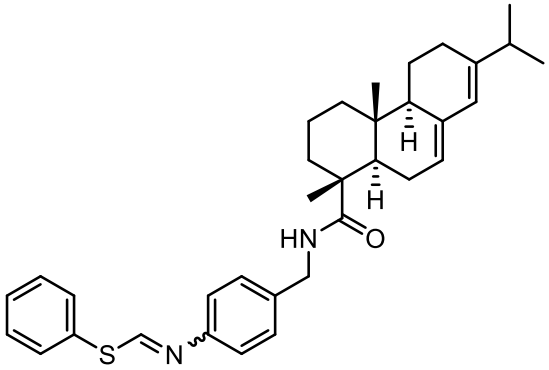


Compound **28** was prepared according to the general procedure (GP1) and isolated as a colorless oil.

Column Chromatography: Silica, gradient 10-20% EtOAc/*n*-heptane.

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.24 (s, 0.4H), 8.07 (s, 0.6H), 3.43 – 3.36 (m, 0.3H), 3.24 – 3.18 (m, 0.7H), 3.06– 32.98 (m, 1H), 2.06 – 1.91 (m, 2H), 1.82 – 1.67 (m, 6H), 1.66 – 1.53 (m, 3H), 1.47 – 1.18 (m, 10H); **^{13}C NMR** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 155.46, 154.43, 69.77, 63.08, 45.60, 42.29, 34.47, 34.45, 33.53, 32.65, 25.94, 25.77, 25.74, 25.69, 25.44, 24.77, 24.72; **HRMS (ESI$^+$)**: $[2M + H]^+$calcd for: 451.3175, found: 451.3188

phenyl *N*-(4-(((1R,4aR,4bR,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,4b,5,6,10,10a-decahydrophenanthrene-1-carboxamido)methyl)phenyl)methanimidothioate

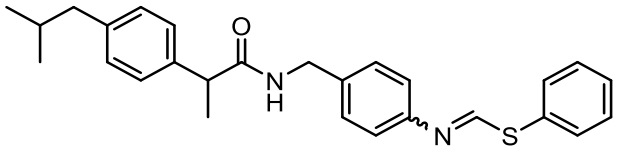


Compound **29** was prepared according to the general procedure (GP1) and isolated as a white solid.

Column Chromatography: Silica, gradient 0- 20 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.61 – 8.60 (m, 0.5H), 8.39 (s, 0.5H), 7.58 – 7.55 (m, 1H), 7.52 – 7.47 (m, 1H), 7.43 – 7.38 (m, 2H), 7.32 – 7.25 (m, 2H), 7.22 – 7.17 (m, 1H), 7.05 – 6.97 (m, 2H), 6.12-6.05 (m, 1H), 5.74 (s, 1H), 5.35-5.30 (m, 1H), 4.54 – 4.30 (m, 2H), 2.85 – 2.75 (m, 0.3H), 2.24-2.21 (m, 1H), 2.08-2.02 (m, 2.7H), 1.90 – 1.73 (m, 4H), 1.63 – 1.52 (m, 3H), 1.42 (s, 1H), 1.30 – 1.15 (m, 7H), 1.02 – 0.97 (m, 4H), 0.82 (d, J = 4.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 178.35, 178.32, 163.55, 159.92, 150.04, 148.99, 145.31, 145.25, 136.42, 135.63, 135.61, 135.55, 133.32, 133.13, 131.56, 130.09, 129.74, 129.63, 129.22, 129.16, 128.80, 128.71, 122.49, 122.46, 121.01, 120.58, 120.51, 120.32, 51.00, 46.46, 46.43, 45.79, 45.76, 43.60, 43.49, 38.34, 37.76, 34.95, 34.72, 27.48, 26.99, 25.45, 22.54, 21.50, 20.94, 18.37, 17.16, 17.13, 14.24; **HRMS (ESI$^+$)**: $[M + H]^+$calcd for :527.30904, found: we could not see the right mass in HRMS or LC-MS using ESI mode.

phenyl *N*-(4-((2-(4-isobutylphenyl)propanamido)methyl)phenyl)methanimidothioate

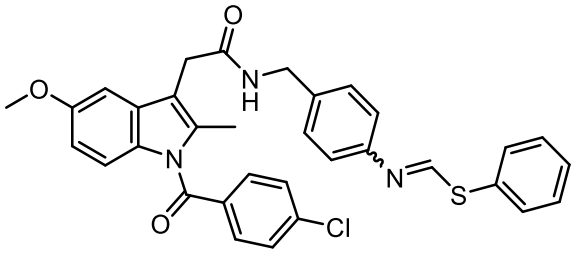


Compound **30** was prepared according to the general procedure (GP1) and isolated as yellow oil.

Column Chromatography: Silica, gradient 20- 30 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.57 (s, 0.4H), 8.37 (s, 0.4H), 7.57 – 7.54 (m, 1H), 7.50 – 7.47 (m, 1H), 7.43 – 7.40 (m, 3H), 7.25 – 7.16 (m, 2H), 7.15 – 7.05 (m, 4H), 6.96 – 6.90 (m, 2H), 5.83 (brs, 1H), 4.39 (dd, *J* = 5.8, 2.7 Hz, 1H), 4.34 (d, *J* = 5.8 Hz, 1H), 3.58 (dq, *J* = 10.0, 7.2 Hz, 1H), 2.45 (dd, *J* = 7.2, 3.5 Hz, 2H), 1.84 (td, *J* = 6.8, 4.8 Hz, 1H), 1.54 (dd, *J* = 9.3, 7.2 Hz, 3H), 0.89 (dd, *J* = 6.6, 4.6 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 174.47, 174.45, 163.43, 159.83, 149.90, 148.85, 140.81, 138.59, 138.55, 136.09, 135.24, 133.29, 133.09, 131.53, 130.05, 129.72, 129.70, 129.61, 129.20, 129.14, 128.40, 128.31, 127.42, 127.40, 120.87, 120.18, 46.81, 46.77, 45.06, 45.04, 43.18, 43.07, 30.24, 30.23, 22.46, 22.44, 18.57, 18.51; **HRMS (ESI$^+$)**: $[M + H]^+$calcd for: 431.21515, found: 432.21370

phenyl *N*-(4-((2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)methyl)phenyl)methanimidothioate



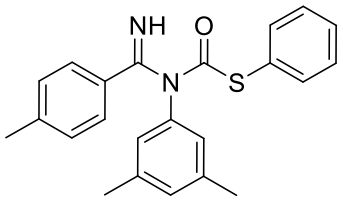
Compound **31** was prepared according to the general procedure (GP1) and isolated as a yellow solid.

Column Chromatography: Silica, gradient 20- 30 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$, mixture of E/Z isomers) δ 8.55 (s, 0.4H), 8.34 (s, 0.4H), 7.57 – 7.49 (m, 3H), 7.48 – 7.37 (m, 6H), 7.15 (d, *J* = 8.3 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 6.94 – 6.85 (m, 3H), 6.84 – 6.79 (m, 1H), 6.68 – 6.62 (m, 1H), 6.18 – 6.03 (m, 0.8H), 6.01 – 5.95 (m, 0.1H), 4.64 (d, *J* = 7.4 Hz, 0.2H), 4.39 (d, *J* = 5.9 Hz, 0.8H), 4.34 (d, *J* = 6.0 Hz, 0.8H), 4.29 (d, *J* = 5.7 Hz, 0.2H), 3.79 – 3.74 (m, 3H), 3.70 – 3.64 (m, 2H), 2.34 (s, 1.3H), 2.3 2(s, 1.7H); **^{13}C NMR** (101 MHz, $CDCl_3$, mixture of E/Z isomers) δ 170.01, 169.97, 168.35, 163.56, 159.94, 156.39, 156.36,

150.02, 148.98, 139.60, 139.55, 136.44, 136.41, 135.77, 134.96, 133.63, 133.58, 133.33, 133.10, 131.47, 131.20, 130.95, 130.94, 130.38, 130.35, 129.74, 129.62, 128.85, 128.42, 128.39, 55.83, 55.78, 43.19, 43.10, 32.34, 32.29, 13.45, 13.41; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 582.16125, found: 582.16084

***S*-phenyl (3,5-dimethylphenyl)(imino(*p*-tolyl)methyl)carbamothioate**



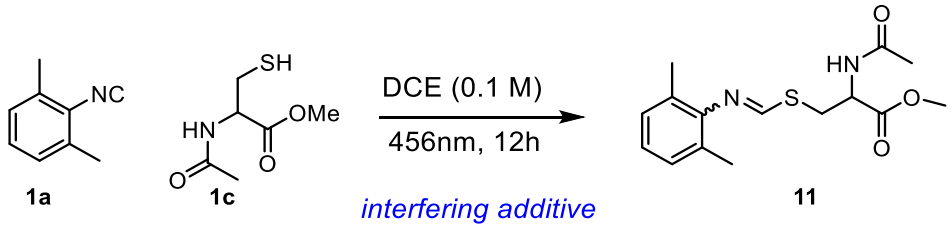
Compound **43** was prepared according to the procedure described below.

To a 4 mL colourless screw-cap glass vial equipped with a magnetic stir bar, 2,6-dimethylphenyl isocyanide (0.24 mmol, 1.2 equiv.) and thiophenol (0.2 mmol, 1 equiv.) were added, followed by anhydrous DCE (2 mL, 0.1 M). The reaction mixture was purged with N_2 gas for ~ 5 minutes, then the vial was sealed and the mixture stirred in a PhotoRedOx Box (EvoluChem™), under 30 W blue LEDs irradiation, at room temperature, for 20 hours. Upon completion of the reaction, as monitored by TLC, (*Z*)-*N*-hydroxy-4-methylbenzimidoyl chloride (0.2 mmol, 1 equiv.) and Et_3N (0.22 mmol, 1.1 equiv.) were added *in situ*, and the resulting mixture was stirred at room temperature for additional 24 hours. Then the solvent was removed under vacuum and the crude material was purified by silica gel chromatography (97:3 hex/EtOAc) to afford the product as an off-white solid (24.8 mg, 33% yield over 2 steps).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.00 (brs, -N*H*), 7.27 – 7.24 (m, 2H), 7.23 – 7.10 (m, 7H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.76 (s, 1H), 2.30 (s, 6H), 2.27 (s, 3H); **^{13}C NMR**: (101 MHz, $CDCl_3$) δ 162.4, 151.4, 140.3, 138.8, 136.8, 134.9, 129.3, 129.1, 129.0, 128.8, 128.7, 126.0, 117.4, 21.4, 21.4; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 375.15255, found: we could not see the right mass in HRMS or LC-MS using ESI mode.

8. Dehydroalanine Synthesis

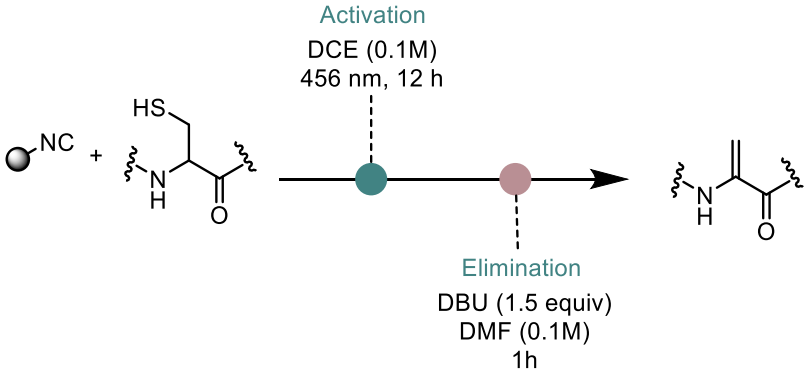
Table S3: Effect of additives and concentration on thioformimidate formation with methyl acetylcysteinate



Entry	Additive	Concentration	Yield (%)[a]
Concentration effect			
1	no	0.1M	68
2	no	0.02M	58
3	no	0.01M	26
4	no	0.005M	8
Additive effect			
5	imidazole	0.1M	83
6	Ethanol	0.1M	58
7	Ethanamine	0.1M	20
8	Guanidine	0.1M	33
9	Acetic acid	0.1M	68
10	iso-Butyramide	0.1M	65
11	Phosphate buffer (pH: 6, 2M)	0.1 M	55

[a]Yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard.

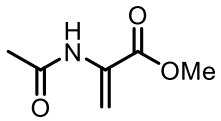
8.1 General procedure for the dehydroalanine synthesis from thioforimidate



GP2: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, isocyanide (1 to 10 equiv) and amino acid (1 equiv 0.2 mmol) were added, followed by the addition of dry DCE (2mL).

The MW vial was then closed with a teflon septum cap and degassed with nitrogen for 5 min..The vial was then placed for irradiation with one Kessil blue LEDs as shown in Figure S1 (40W, 456 nm) for 12-20 h. The progress of the reaction was monitored through LC/MS. After completion, the solvent was removed. The crude reaction mixture was then dissolved in DMF (0.1M) followed by DBU (1.5 equiv). This mixture was then stirred for 1h. After completion, the solution was diluted with EtOAc and transferred in a separatory funnel containing deionized water. The organic layer was separated and washed with water followed by brine. Organic layer was then dried over Na_2SO_4. Purification was performed by SiO_2 column chromatography or prep HPLC.

methyl 2-acetamidoacrylate

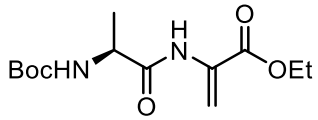


Compound **32** was prepared according to the general procedure (GP2) and isolated as colorless oil. Spectroscopic data were consistent with literature values.[11]

Column Chromatography: Silica, gradient 60- 80 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 6.59 (s, 1H), 5.88 (d, *J* = 1.5 Hz, 1H), 3.84 (s, 3H), 2.13 (s, 3H).

ethyl (S)-2-(2-((tert-butoxycarbonyl)amino)propanamido)acrylate

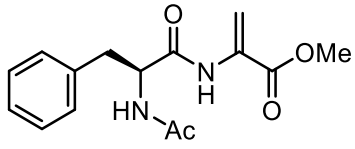


Compound **33** was prepared according to the general procedure (GP2) and isolated as colorless oil. Spectroscopic data were consistent with literature values.[12]

Column Chromatography: Silica, gradient 20- 30 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 6.58 (s, 1H), 5.91 (d, *J* = 1.5 Hz, 1H), 4.96 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.63 (s, 2H), 1.45 (s, 9H), 1.40 (d, *J* = 7.1, 0.7 Hz, 3H), 1.34 (t, *J* = 7.2, 0.7 Hz, 3H).

methyl (S)-2-(2-acetamido-3-phenylpropanamido)acrylate

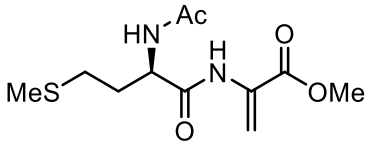


Compound **34** was prepared according to the general procedure (GP2) and isolated as colorless oil. Spectroscopic data were consistent with literature values.[11]

Column Chromatography: Silica, gradient 60- 80 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.33 – 7.21 (m, 3H), 7.21 – 7.15 (m, 2H), 6.55 (s, 1H), 6.14 (s, 1H), 5.89 (d, *J* = 1.5 Hz, 1H), 4.75 (q, *J* = 7.2 Hz, 1H), 3.78 (s, 3H), 3.10 (d, *J* = 7.0 Hz, 2H), 1.99 (s, 3H).

methyl (R)-2-(2-acetamido-4-(methylthio)butanamido)acrylate

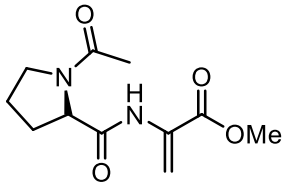


Compound **35** was prepared according to the general procedure (GP2) and isolated as colorless oil.

Column Chromatography: Silica, gradient 60- 80 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.53 (s, 1H), 5.91 (d, *J* = 1.4 Hz, 1H), 4.70 (td, *J* = 7.6, 6.2 Hz, 1H), 3.83 (s, 3H), 2.63 – 2.46 (m, 2H), 2.19 – 2.11 (m, 1H), 2.10 – 2.08 (m, 3H), 2.03 (d, *J* = 0.9 Hz, 3H), 2.00 – 1.92 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.54, 170.25, 164.15, 130.95, 109.94, 53.12, 53.10, 31.24, 30.25, 23.16, 15.34; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 275.1060, found: 275.1054

methyl (S)-2-(1-acetylpyrrolidine-2-carboxamido)acrylate

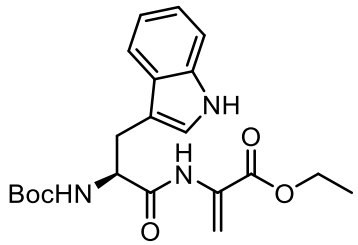


Compound **36** was prepared according to the general procedure (GP2) and isolated as white solid.

Column Chromatography: Silica, gradient 80- 100 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 6.52 (s, 1H), 5.86 (d, *J* = 1.4 Hz, 1H), 4.66 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.82 (s, 3H), 3.58 (ddd, *J* = 9.8, 8.1, 2.9 Hz, 1H), 3.44 (td, *J* = 9.7, 7.0 Hz, 1H), 2.43 (ddt, *J* = 12.3, 6.4, 2.4 Hz, 1H), 2.13 (s, 3H), 2.12 – 1.81 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.27, 170.02, 164.31, 131.60, 109.11, 60.47, 52.96, 48.34, 27.39, 25.09, 22.44; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 241.1183, found: 241.1175

ethyl (S)-2-(2-((tert-butoxycarbonyl)amino)-3-(1H-indol-3-yl)propanamido)acrylate

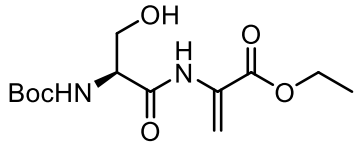


Compound **37** was prepared according to the general procedure (GP2) and isolated as colorless oil.

Column Chromatography: Silica, gradient 40- 60 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.19 (s, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.18 (td, *J* = 6.9, 1.2 Hz, 1H), 7.11 (td, *J* = 7.0, 1.1 Hz, 1H), 7.03 (s, 1H), 6.60 (s, 1H), 5.87 (s, 1H), 5.16 (s, 1H), 4.54 (s, 1H), 4.18 (q, *J* = 7.2 2H), 3.40 – 3.19 (m, 2H), 1.42 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.90, 163.57, 155.66, 136.37, 130.98, 127.51, 123.27, 122.37, 119.85, 118.84, 111.34, 110.22, 109.01, 80.52, 62.17, 56.08, 28.33, 28.11, 14.11; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for : 402.2023, found: 402.2011

ethyl (S)-2-(2-((tert-butoxycarbonyl)amino)-3-hydroxypropanamido)acrylate

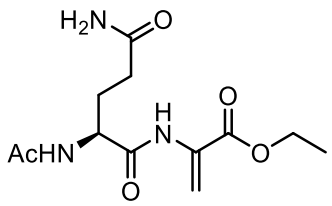


Compound **38** was prepared according to the general procedure (GP2) and isolated as colorless oil.

Column Chromatography: Silica, gradient 20- 30 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 6.56 (s, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 5.61 (s, 1H), 4.29 (q, *J* = 7.1, 0.8 Hz, 3H), 4.20 – 4.11 (m, 1H), 3.72 (t, *J* = 6.7 Hz, 1H), 1.46 (m, 9H), 1.33 (t, *J* = 7.2, 0.8 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.21, 163.68, 156.18, 131.20, 109.52, 80.84, 62.56, 62.29, 56.03, 28.33, 14.15; **HRMS (ESI$^+$)**: $[M + Na]^+$ calcd for : 325.1370, found: 325.1358

ethyl (S)-2-(2-acetamido-5-amino-5-oxopentanamido)acrylate

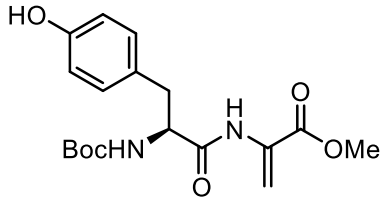


Compound **39** was prepared according to the general procedure (GP2) and isolated as yellow oil.

Column Chromatography: Silica, gradient 80- 100 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.22 (d, *J* = 7.0 Hz, 1H), 6.51 (s, 1H), 6.21 (s, 1H), 5.91 (d, *J* = 1.3 Hz, 2H), 4.55 (td, *J* = 7.7, 4.7 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.55 – 2.46 (m, 1H), 2.40 – 2.31 (m, 1H), 2.21 – 2.12 (m, 1H), 2.04 (s, 3H), 2.03 – 1.98 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.63, 171.21, 170.61, 163.78, 131.37, 109.74, 62.32, 53.80, 32.04, 28.04, 23.15, 14.18; **HRMS (ESI$^+$)**: $[M + H]^+$ calcd for: 286.1397, found: 286.1392

methyl (S)-2-(2-((tert-butoxycarbonyl)amino)-3-(4-hydroxyphenyl)propanamido)acrylate

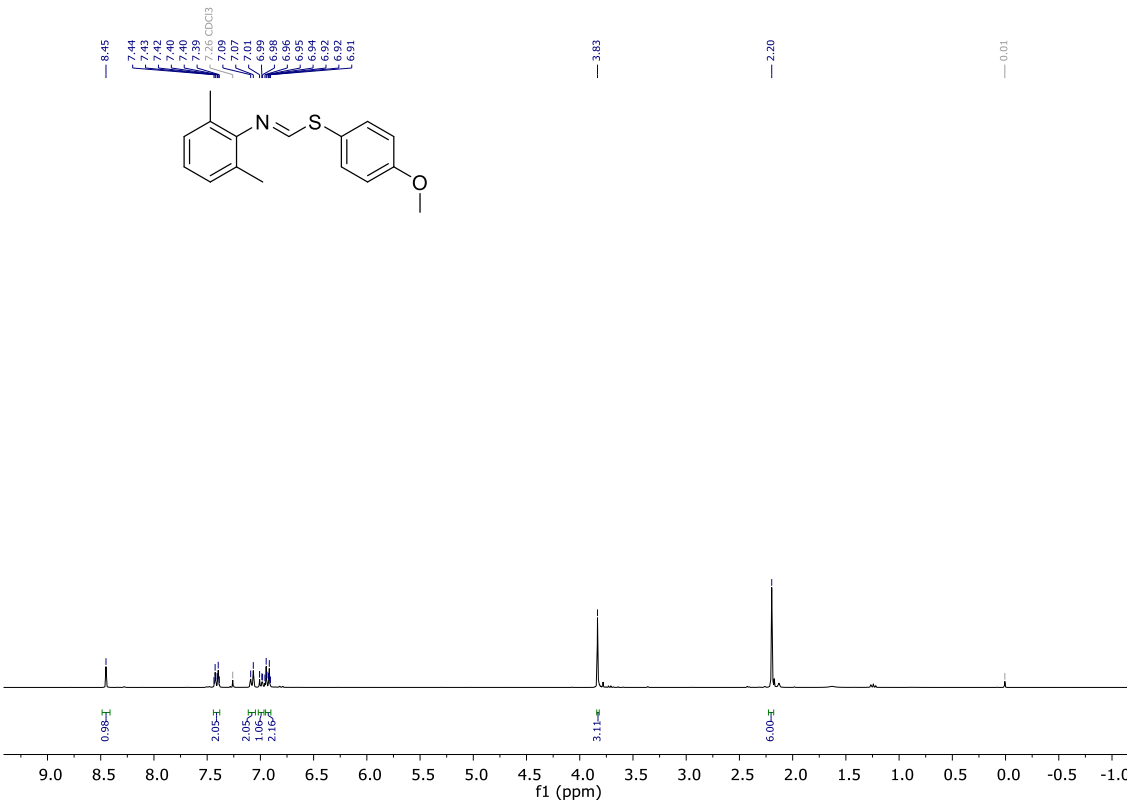


Compound **40** was prepared according to the general procedure (GP2) and isolated as colorless oil. Spectroscopic data were consistent with literature values.[13]

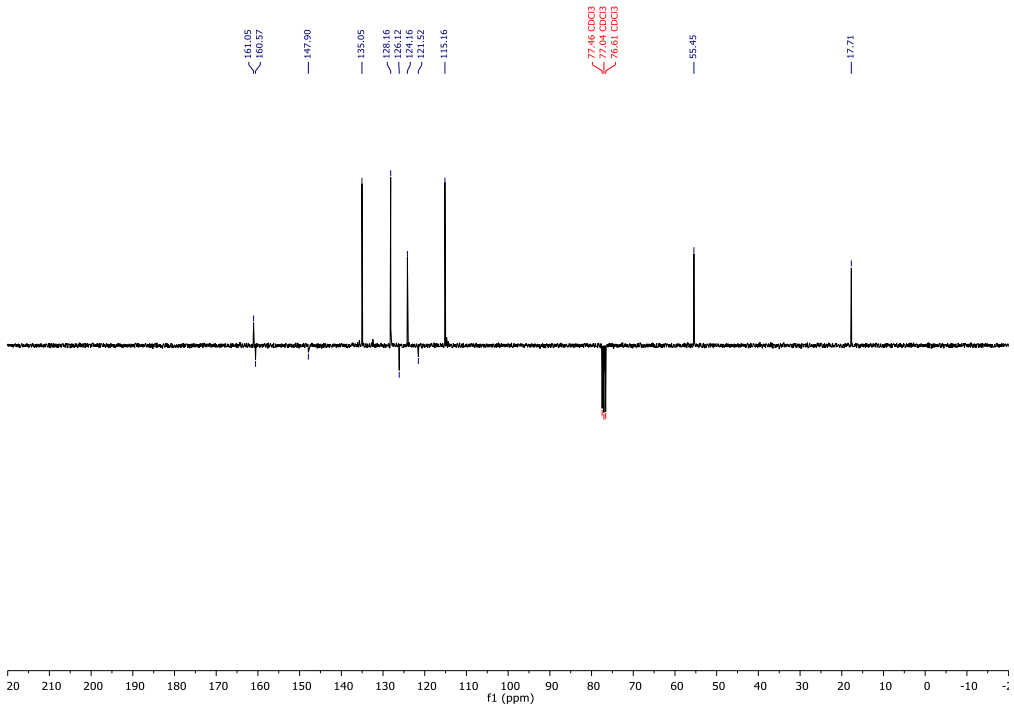
Column Chromatography: Silica, gradient 30- 40 % EtOAc/Heptane

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.60 (s, 1H), 5.89 (s, 1H), 4.98 (s, 1H), 4.37 (s, 1H), 3.80 (s, 3H), 3.03 (d, *J* = 6.7 Hz, 2H), 1.42 (s, 9H).

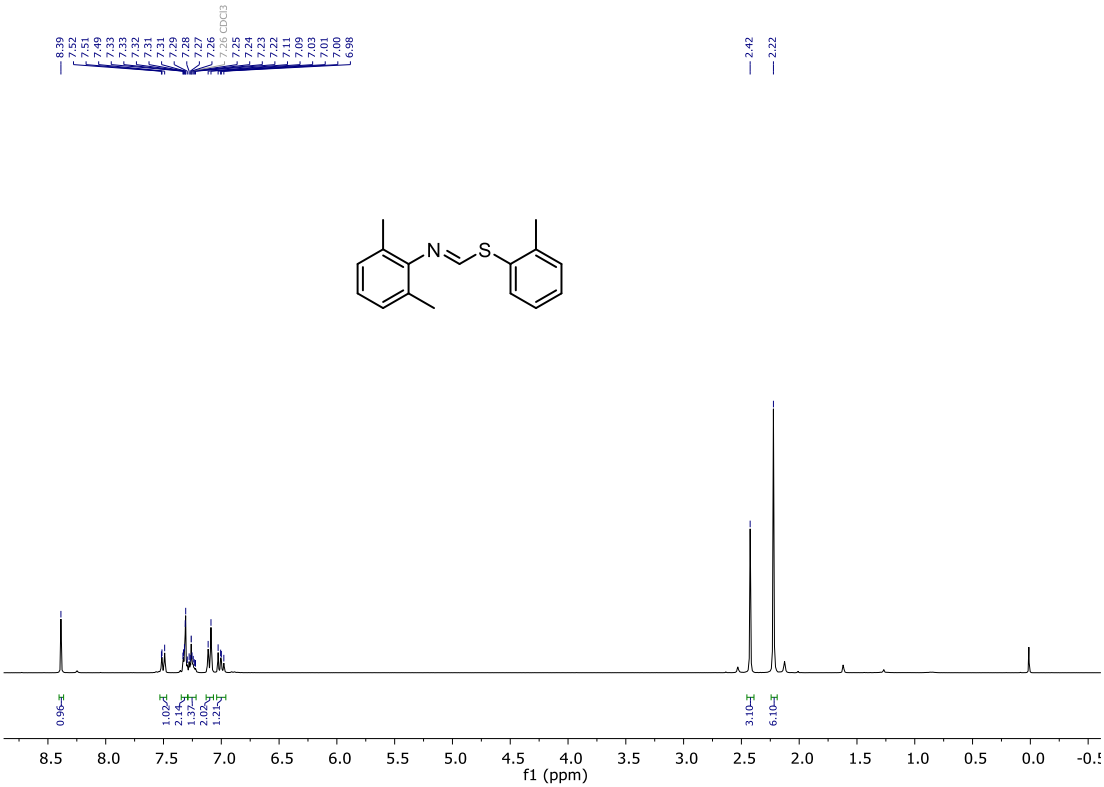
9. NMR Spectra



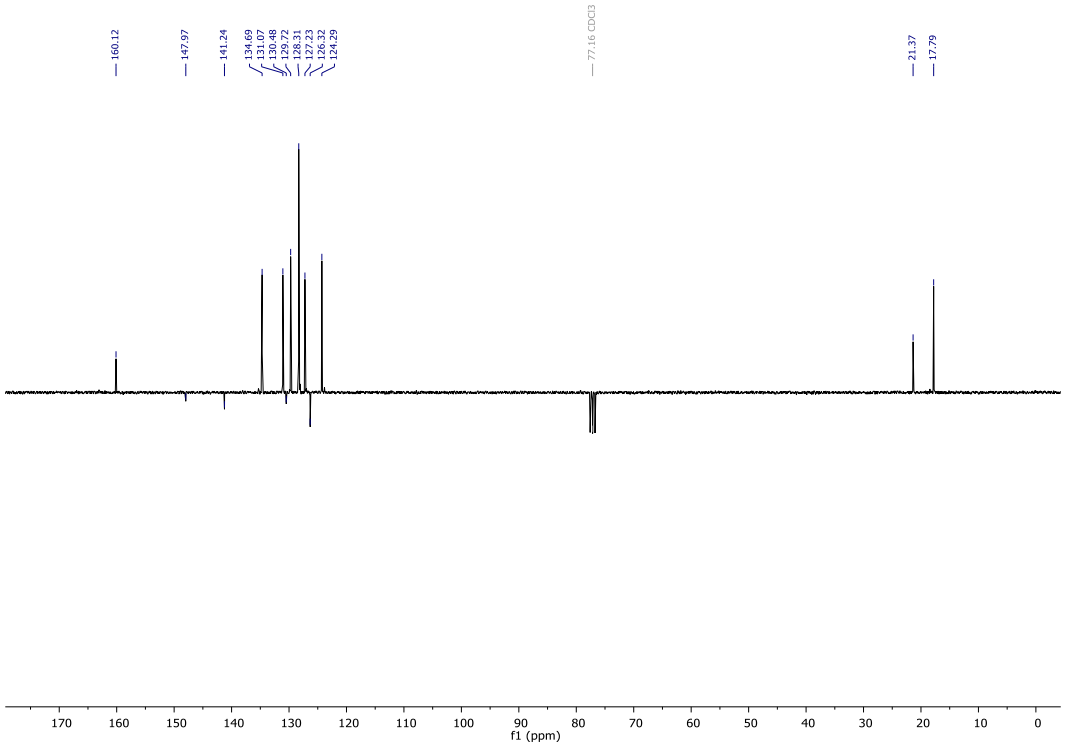
^{1}H NMR spectra of **3**



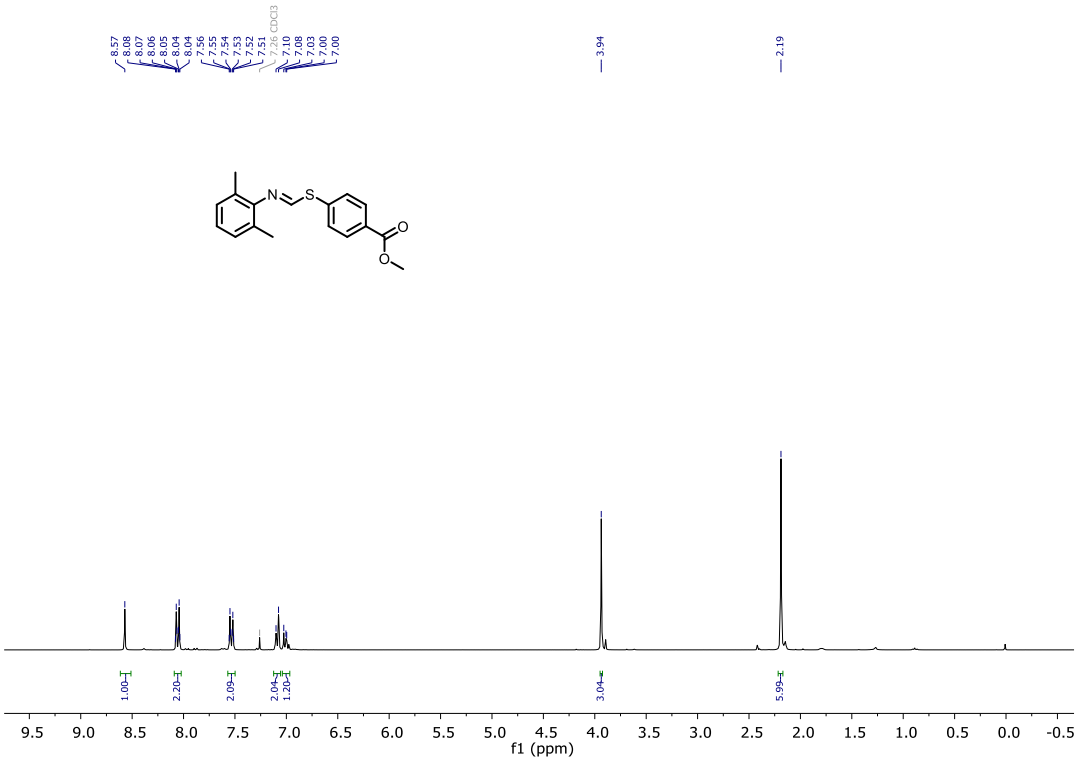
^{13}C NMR spectra of **3**



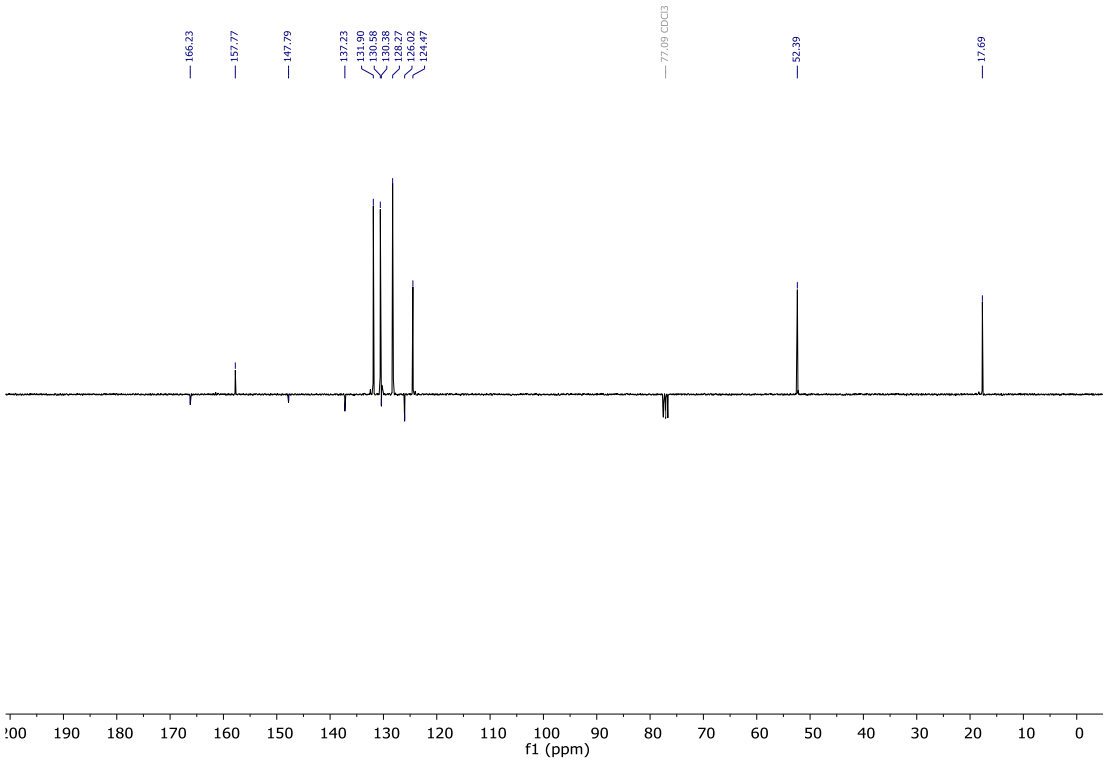
^{1}H NMR spectra of **4**



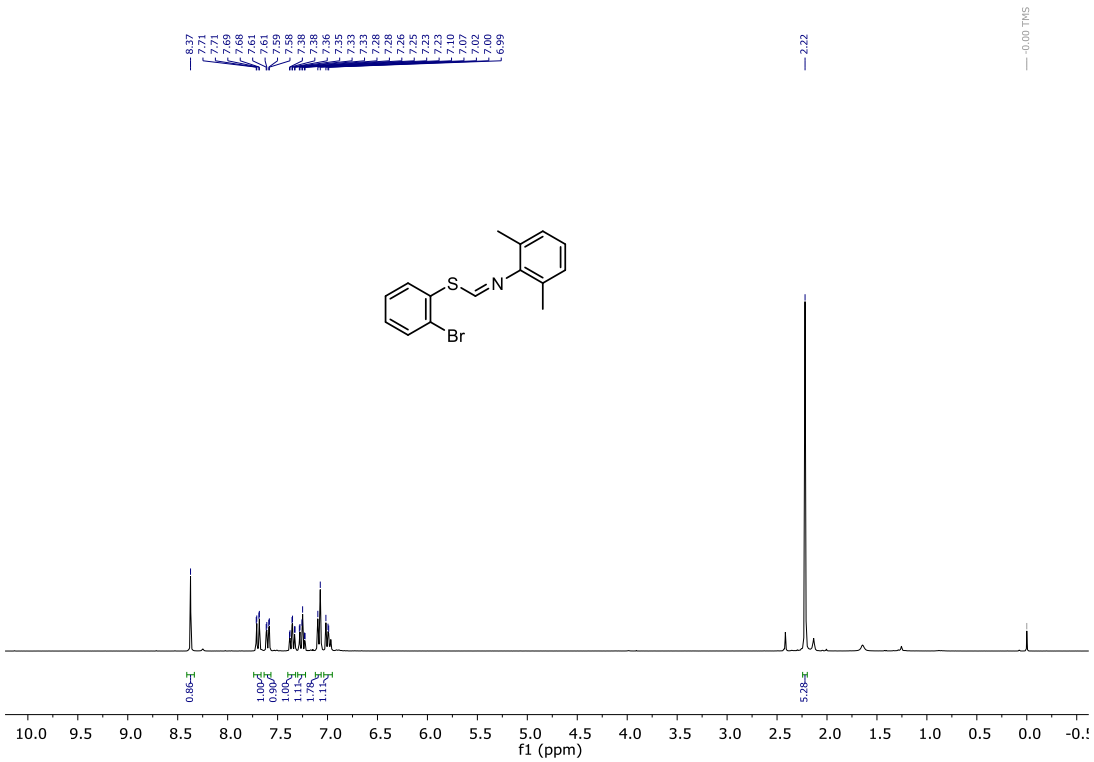
^{13}C NMR spectra of **4**



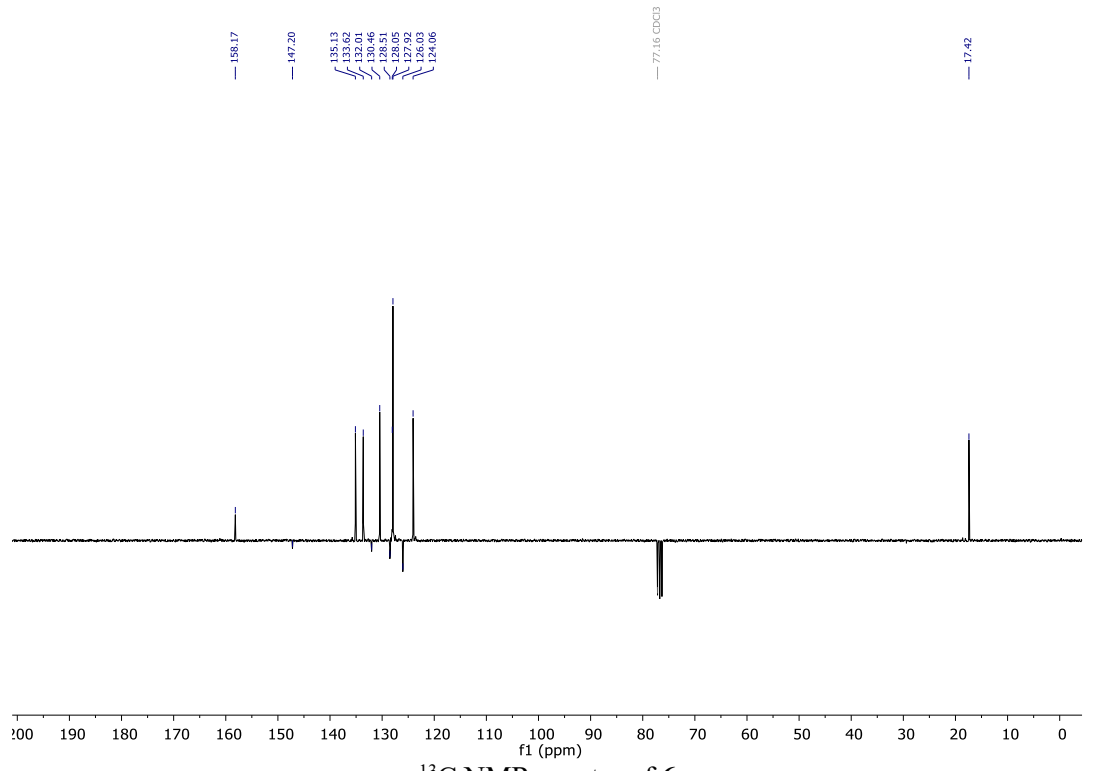
^{1}H NMR spectra of **5**



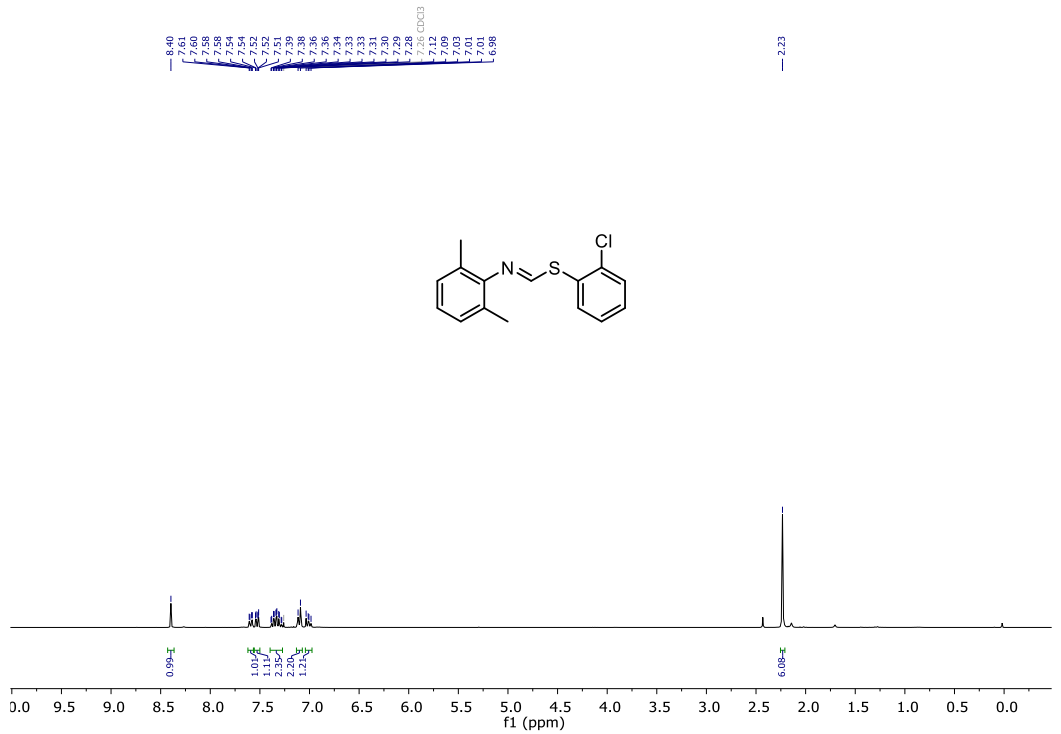
^{13}C NMR spectra of **5**



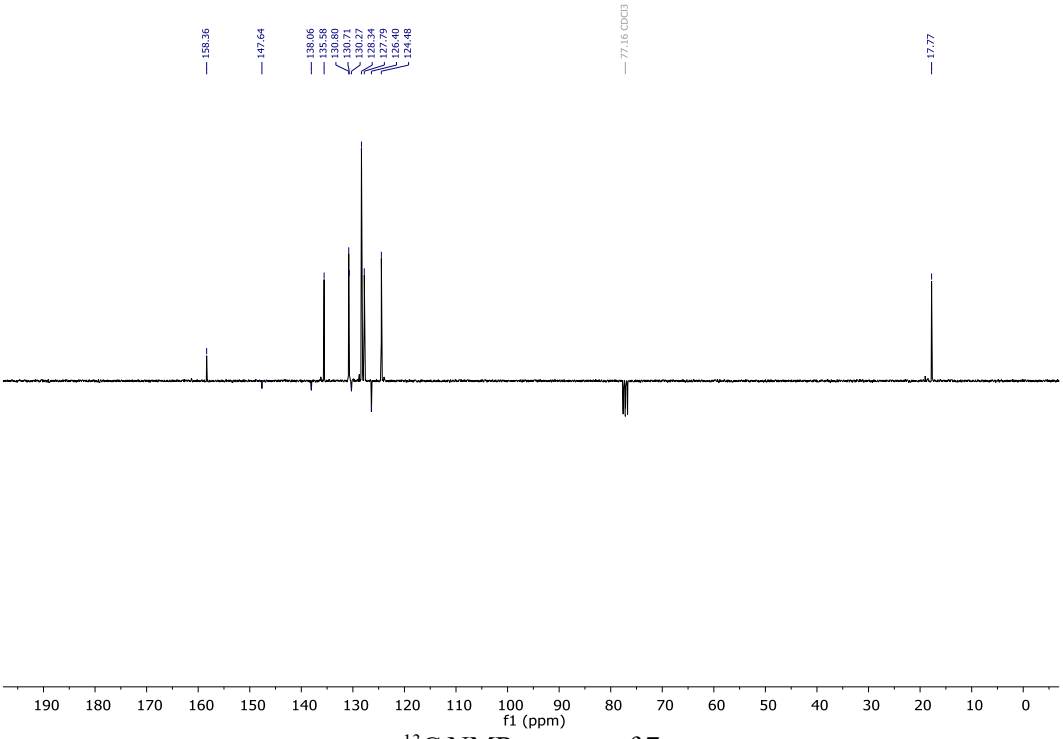
^{1}H NMR spectra of **6**



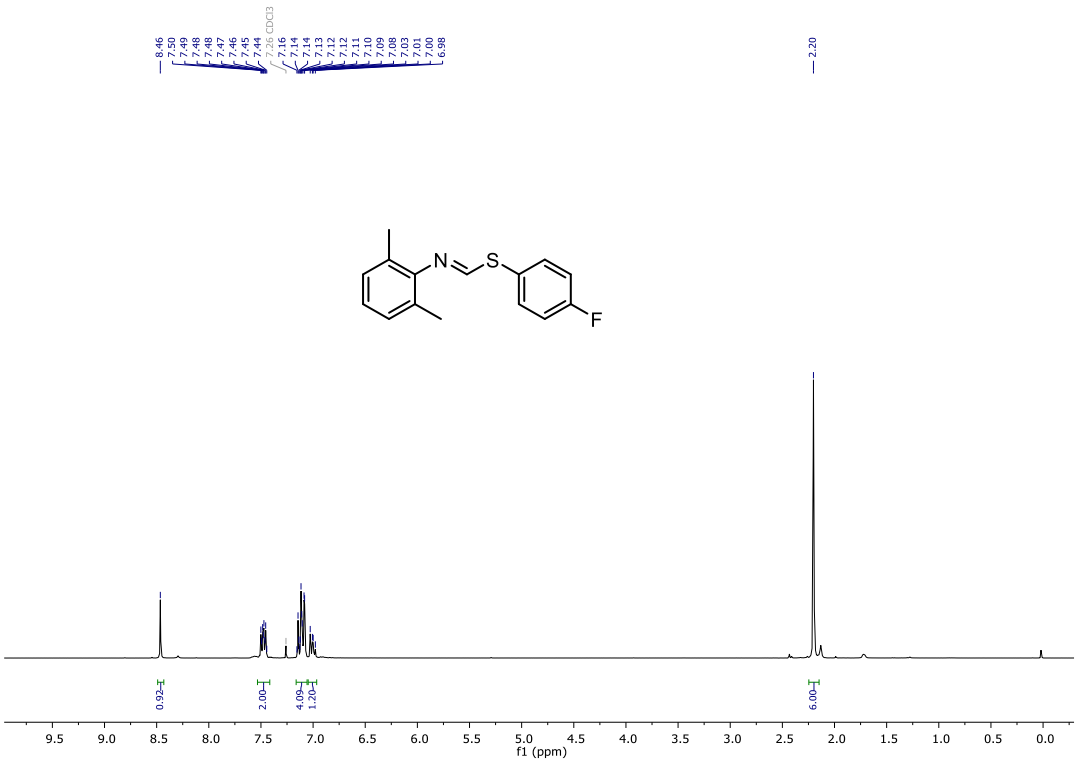
^{13}C NMR spectra of **6**



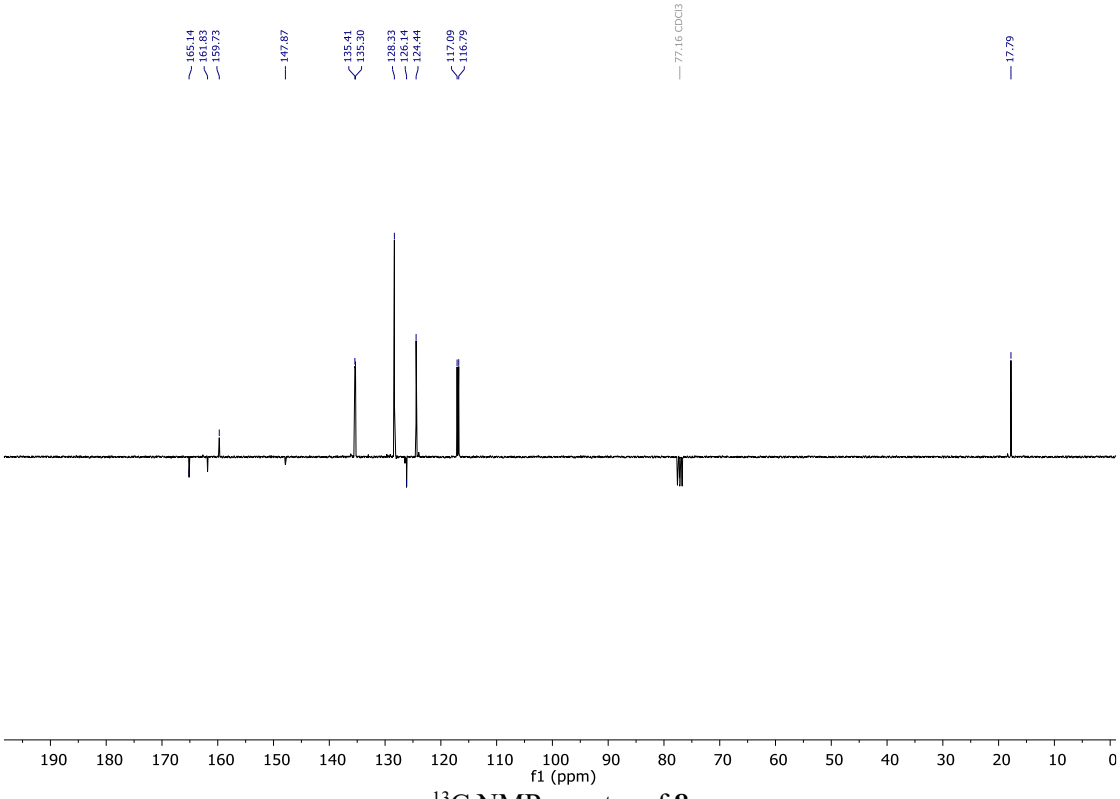
^{1}H NMR spectra of **7**



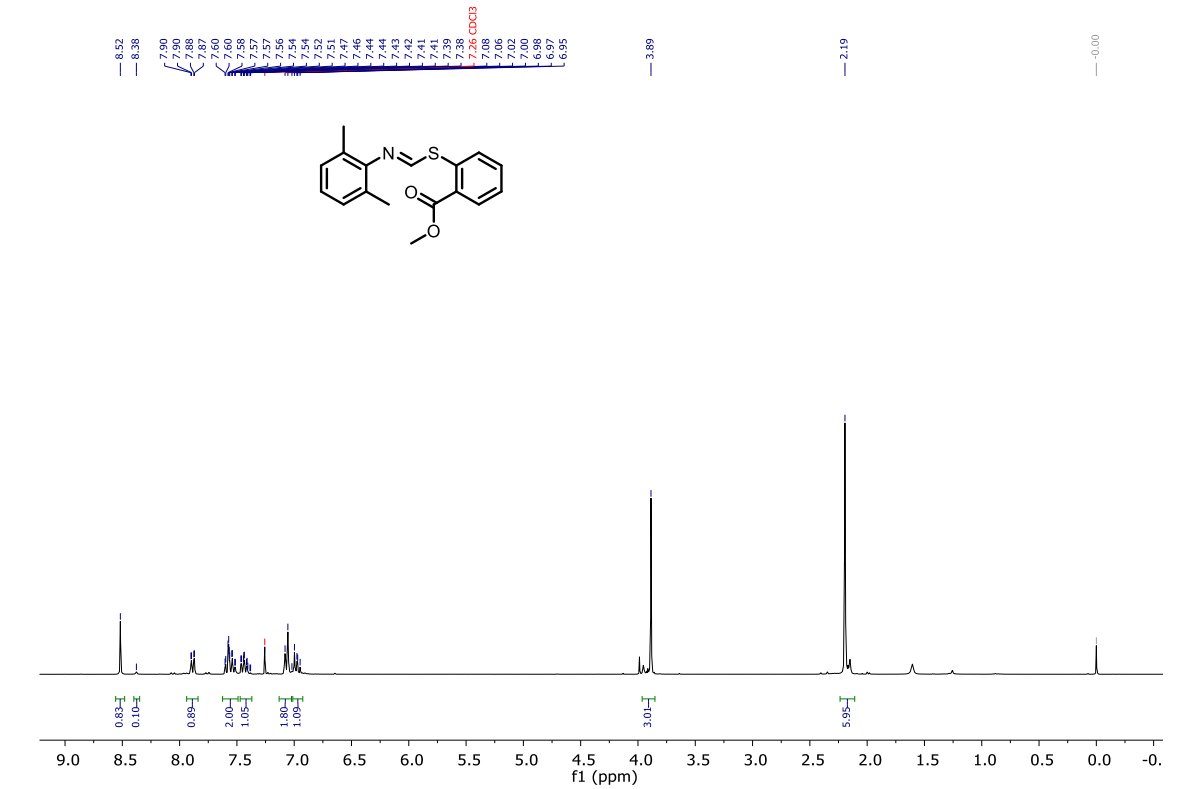
^{13}C NMR spectra of **7**



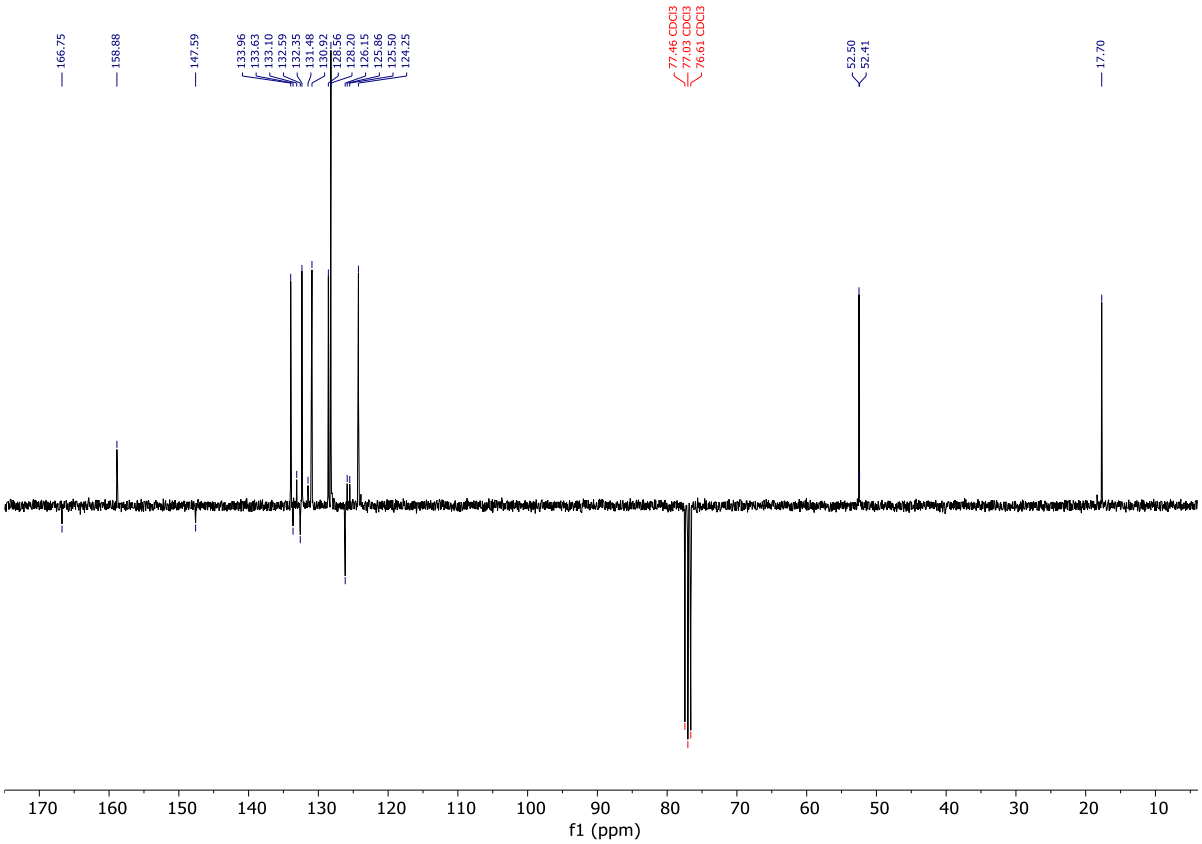
^{1}H NMR spectra of **8**



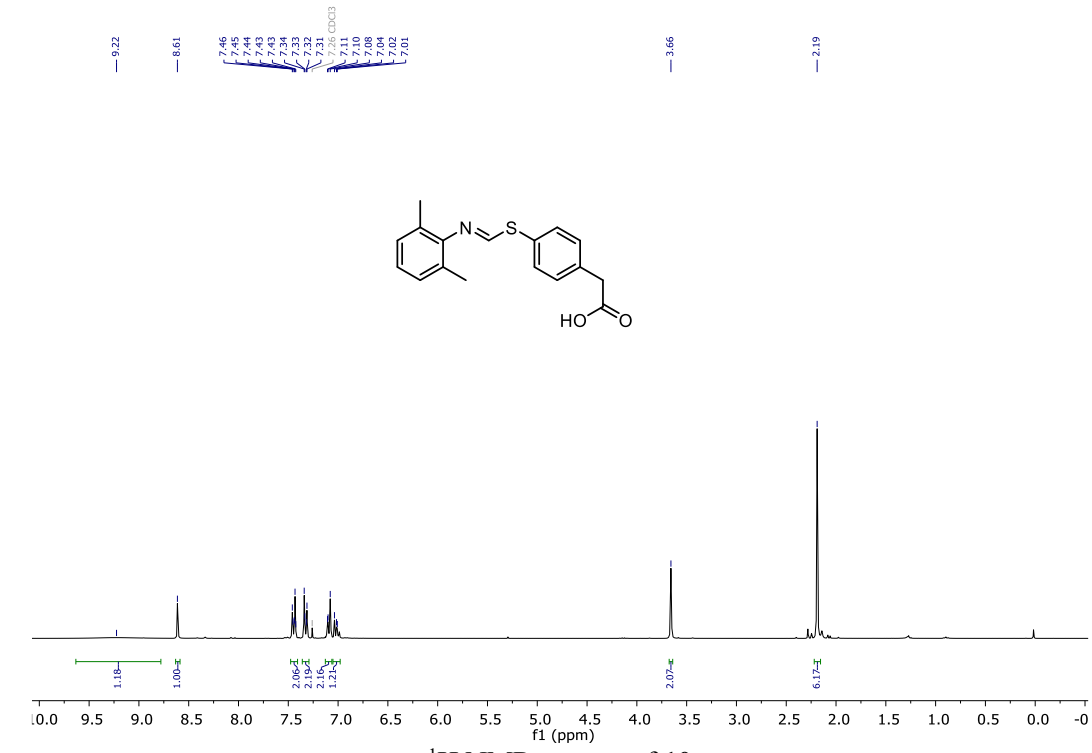
^{13}C NMR spectra of **8**



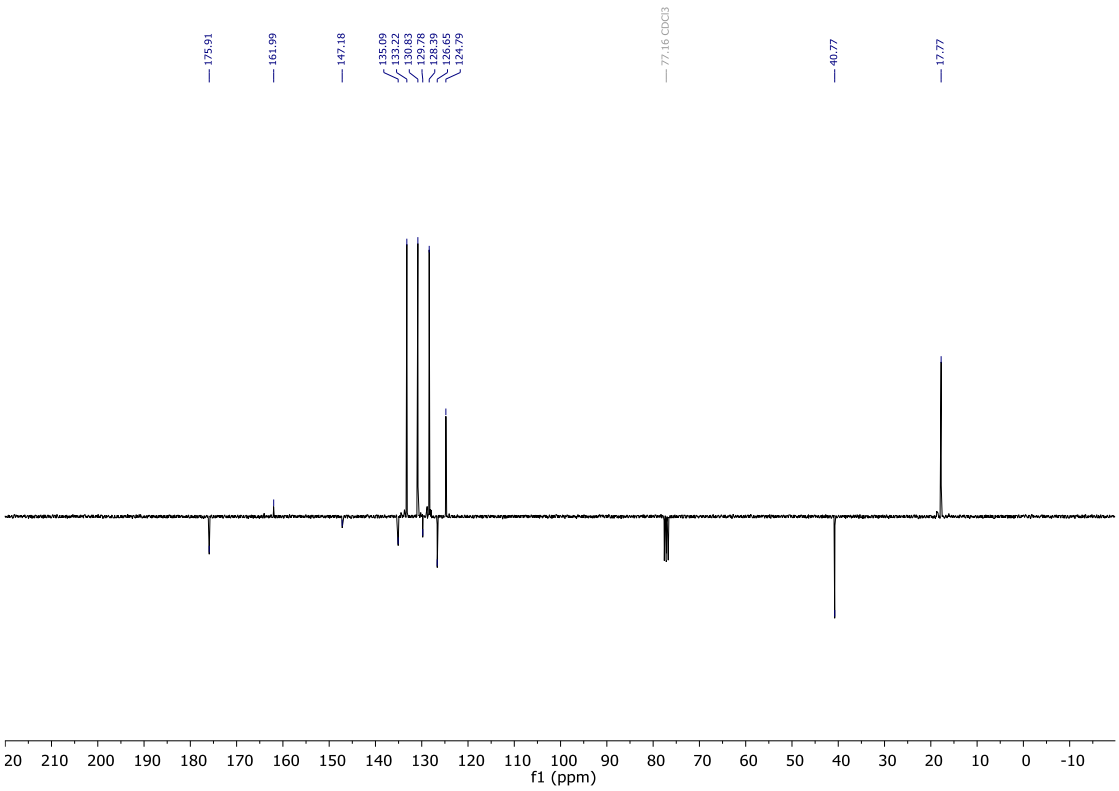
^{1}H NMR spectra of **9**



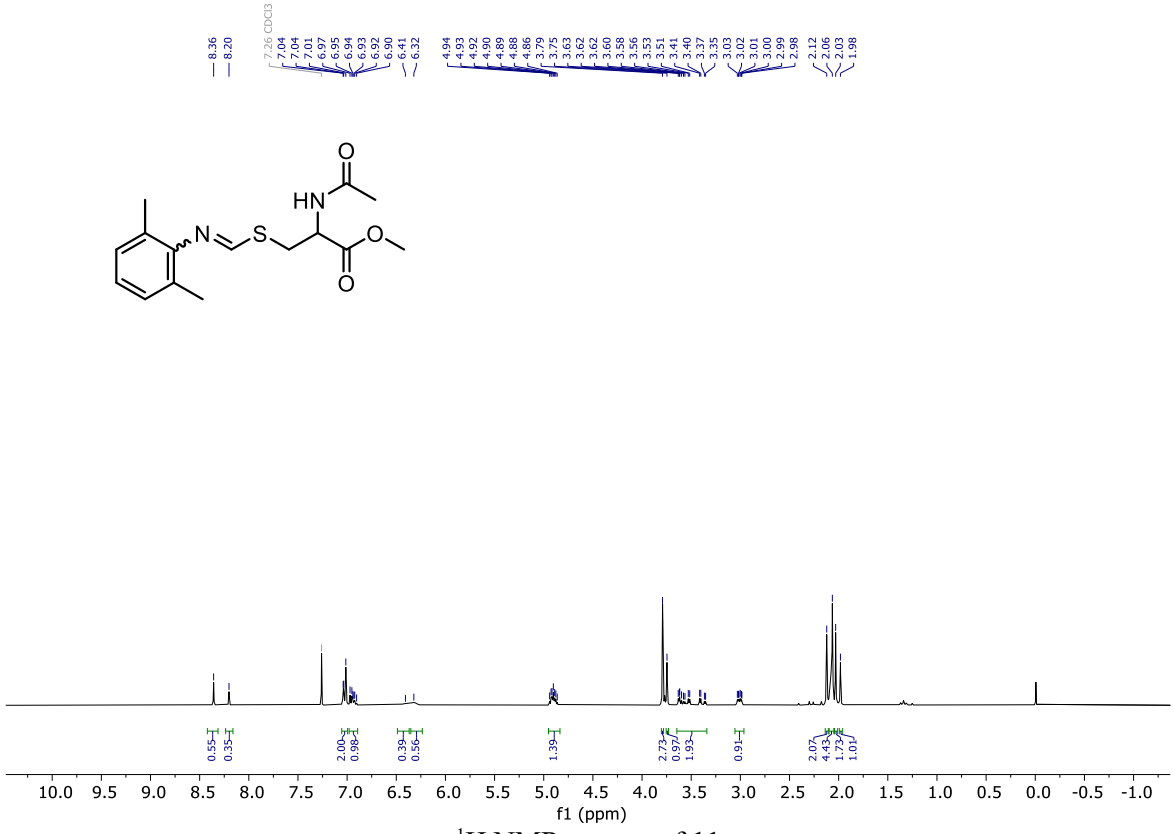
^{13}C NMR spectra of **9**



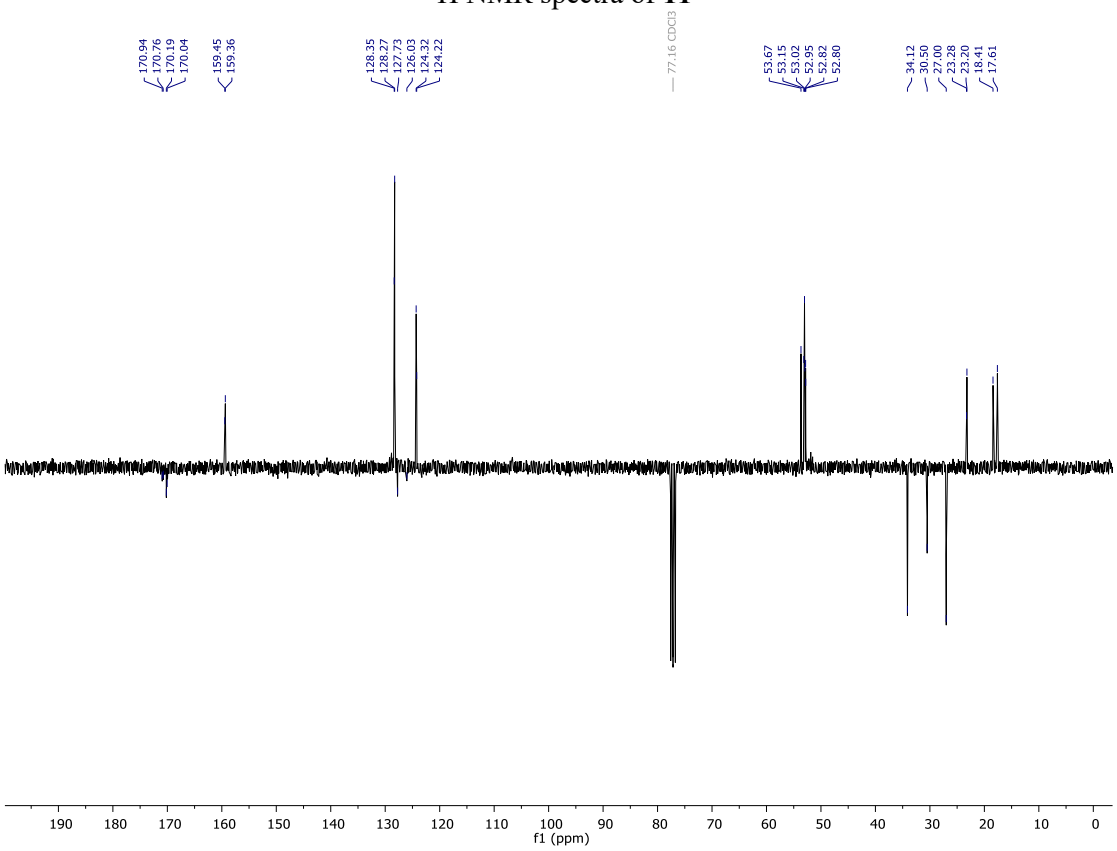
^{1}H NMR spectra of **10**



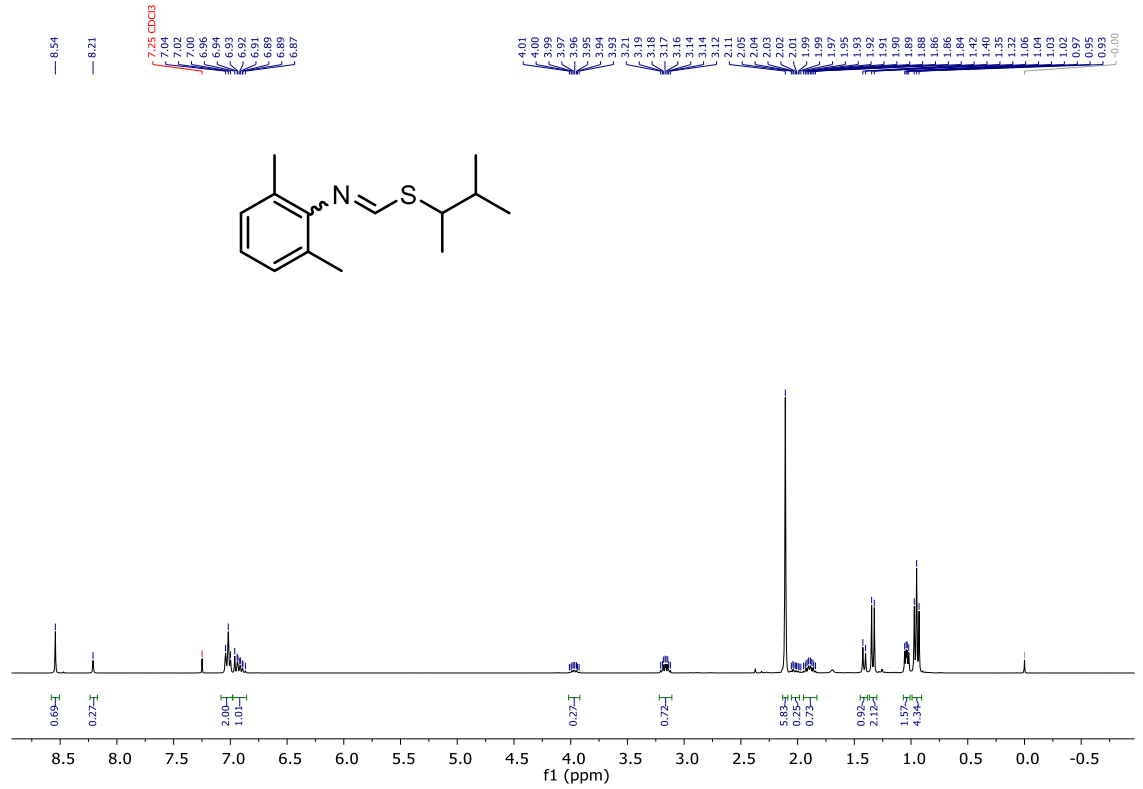
^{13}C NMR spectra of **10**



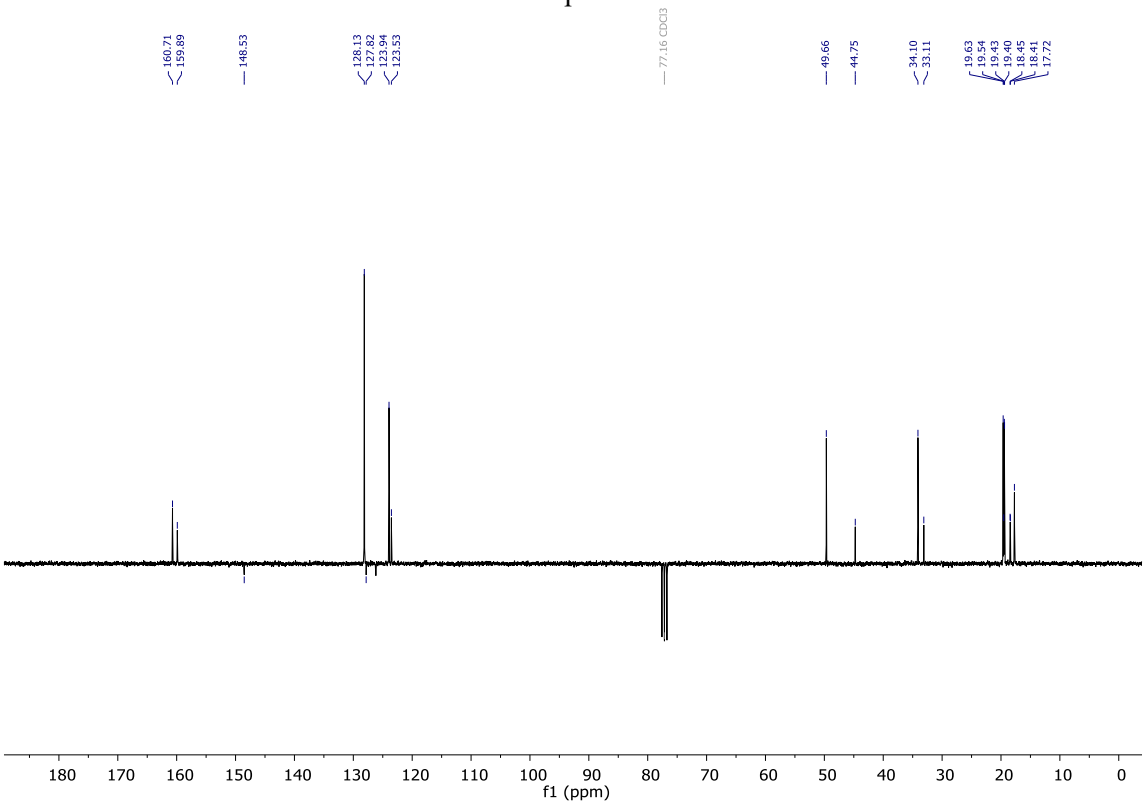
^{1}H NMR spectra of **11**



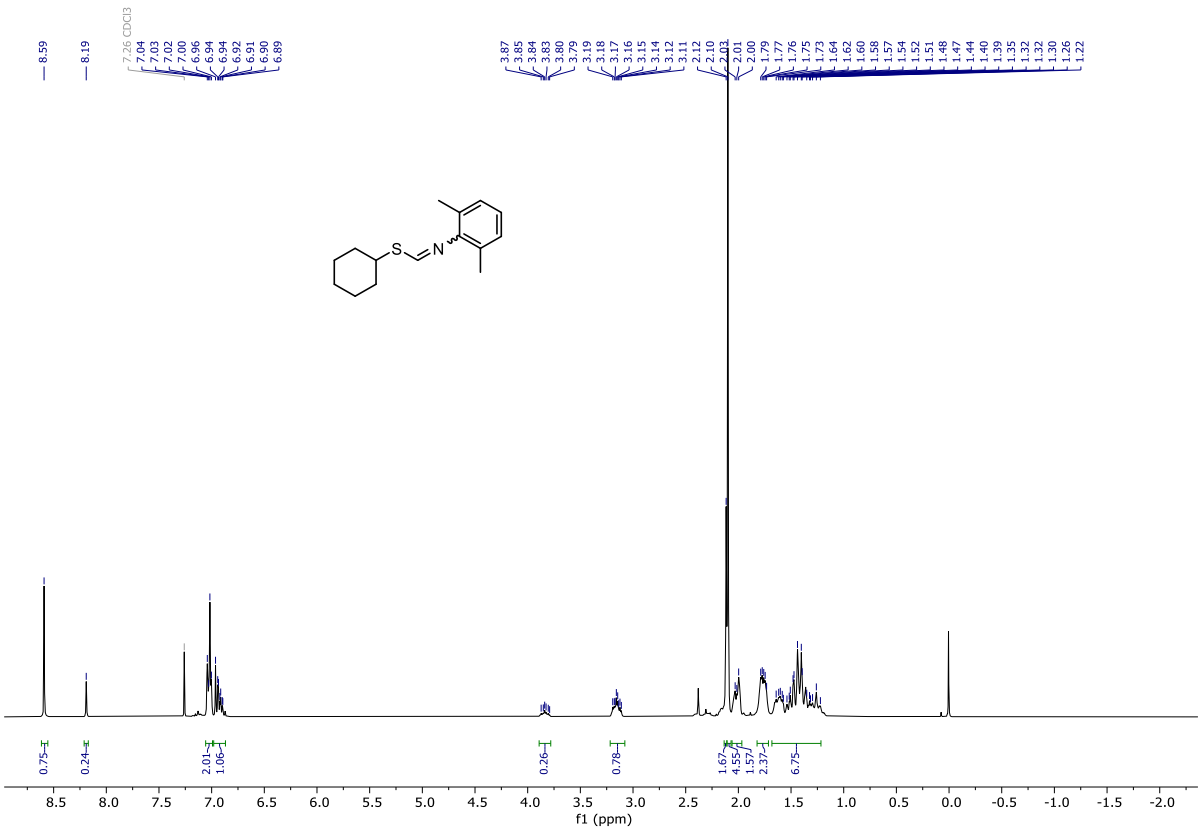
^{13}C NMR spectra of **11**



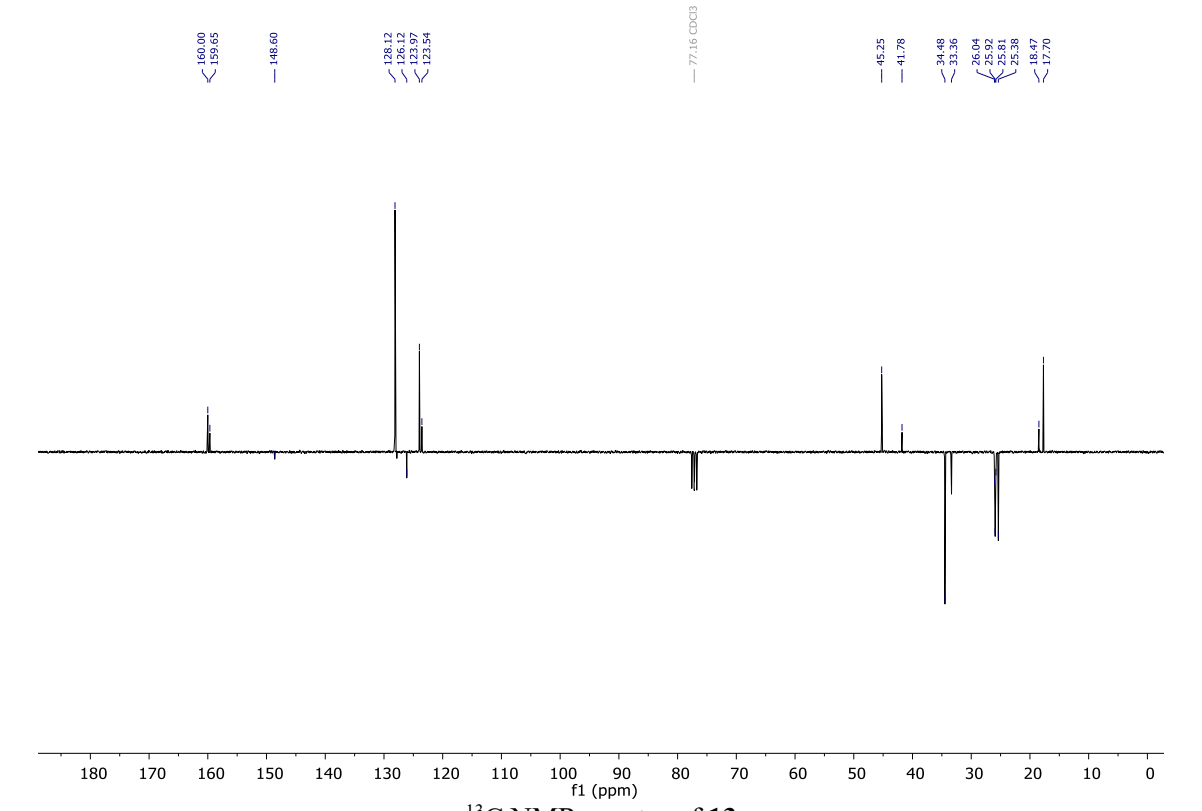
^{1}H NMR spectra of **12**



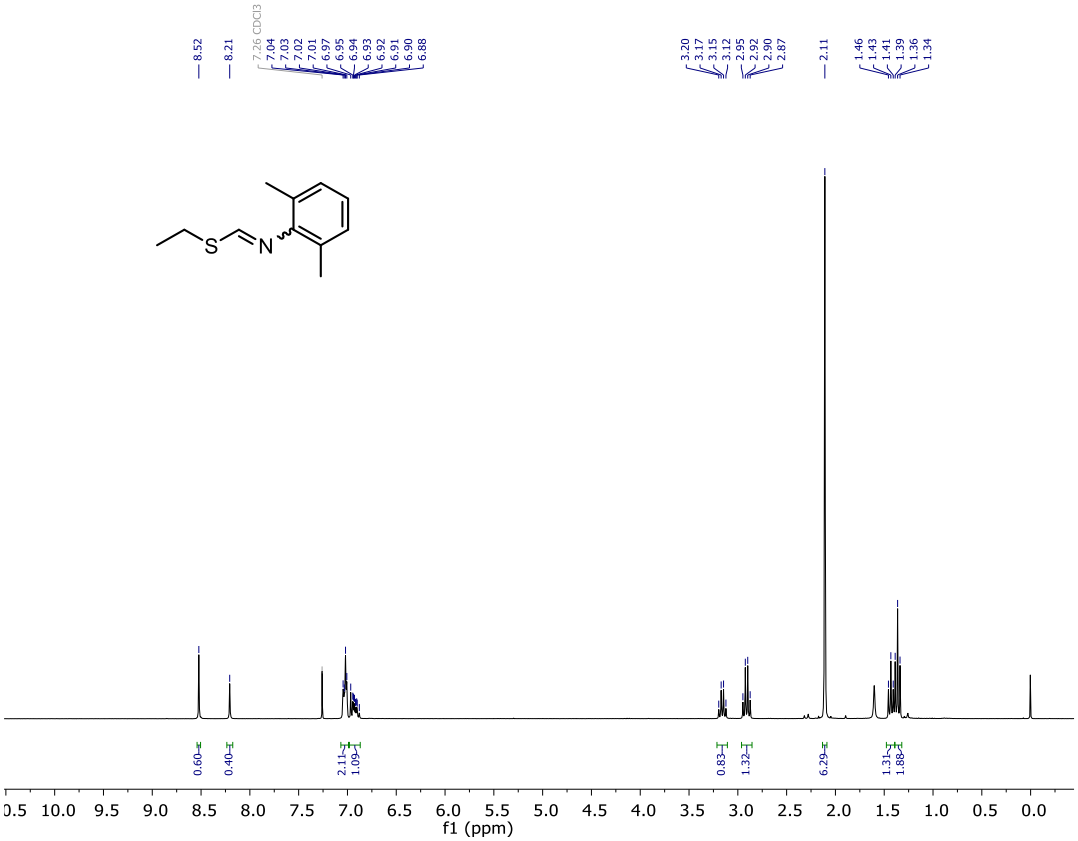
^{13}C NMR spectra of **12**



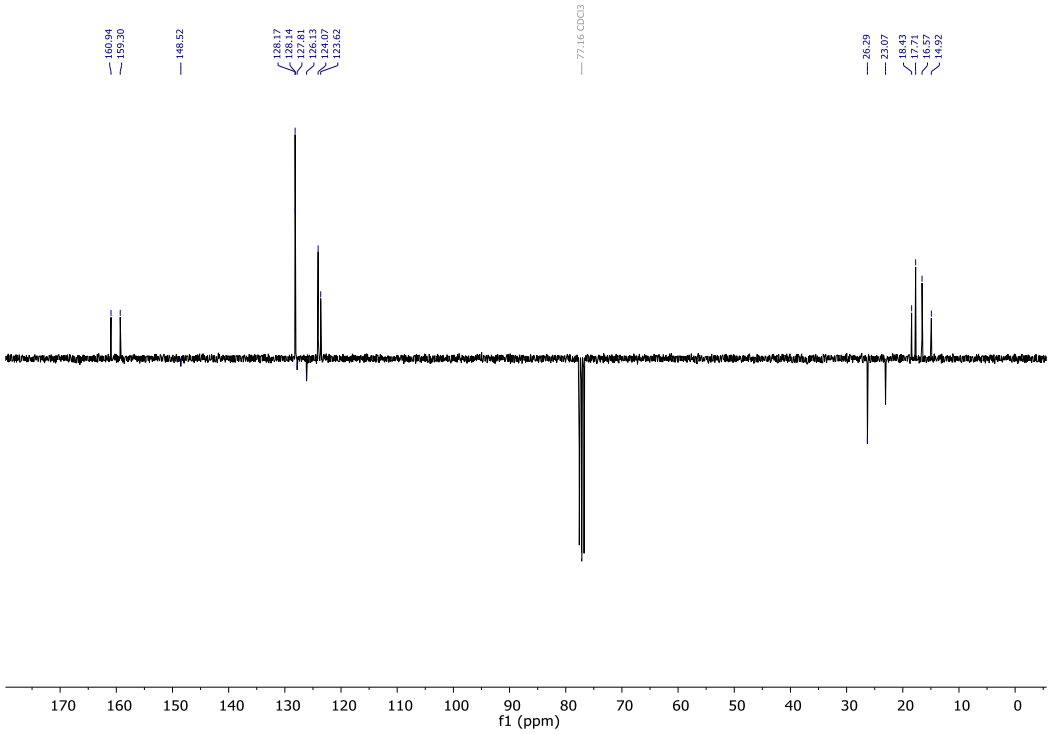
^{1}H NMR spectra of **13**



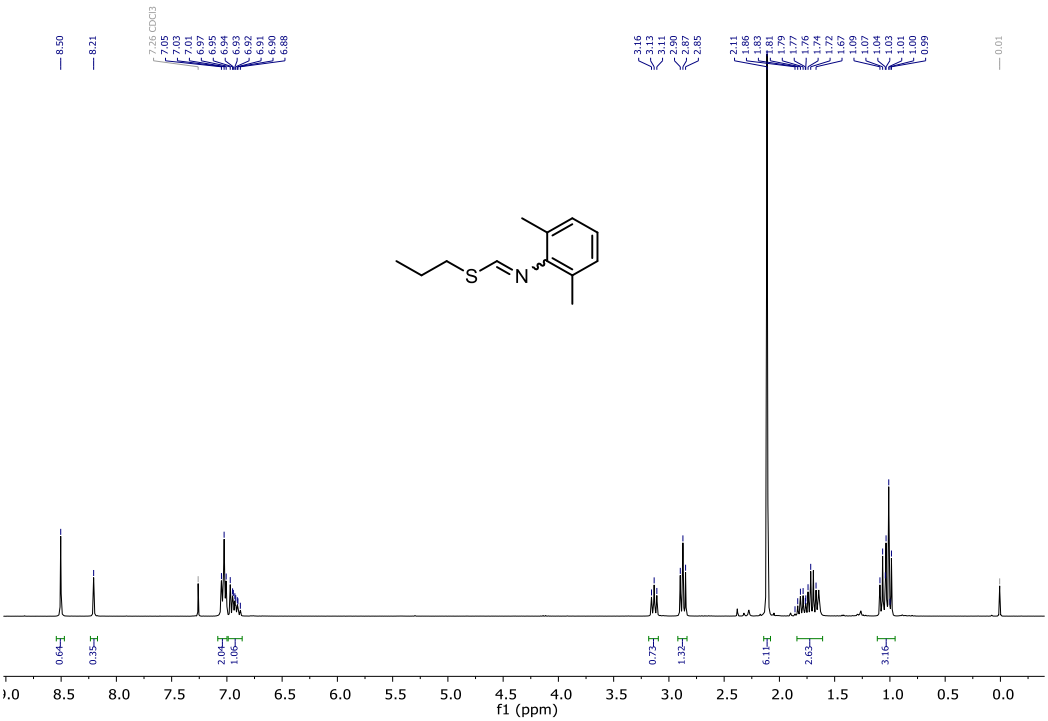
^{13}C NMR spectra of **13**



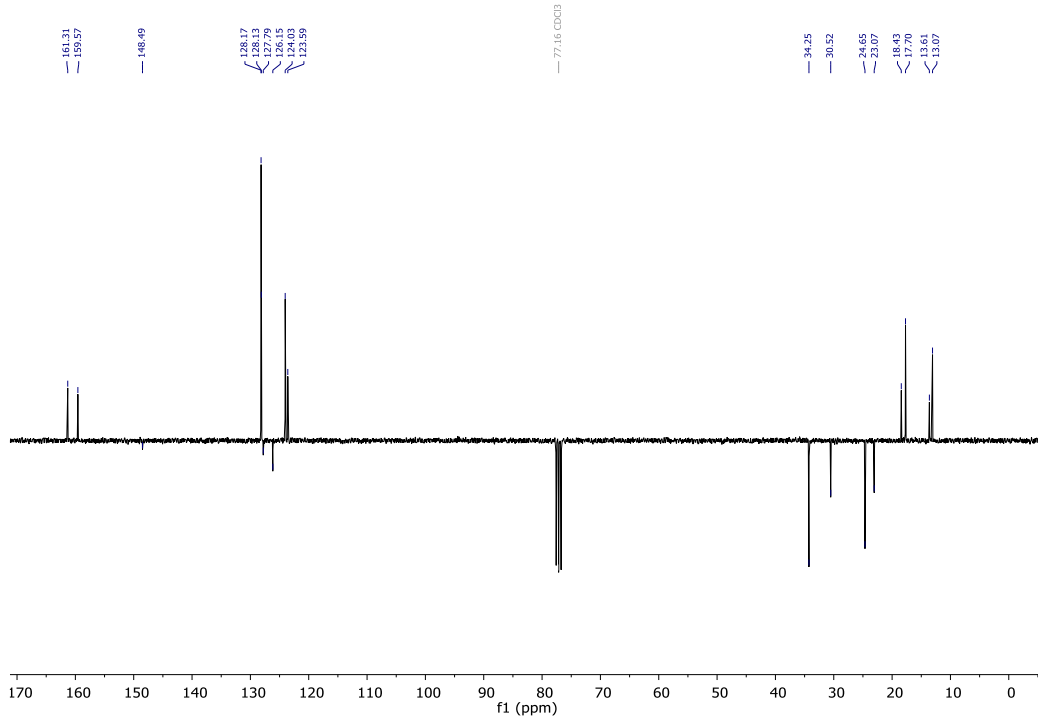
^{1}H NMR spectra of **14**



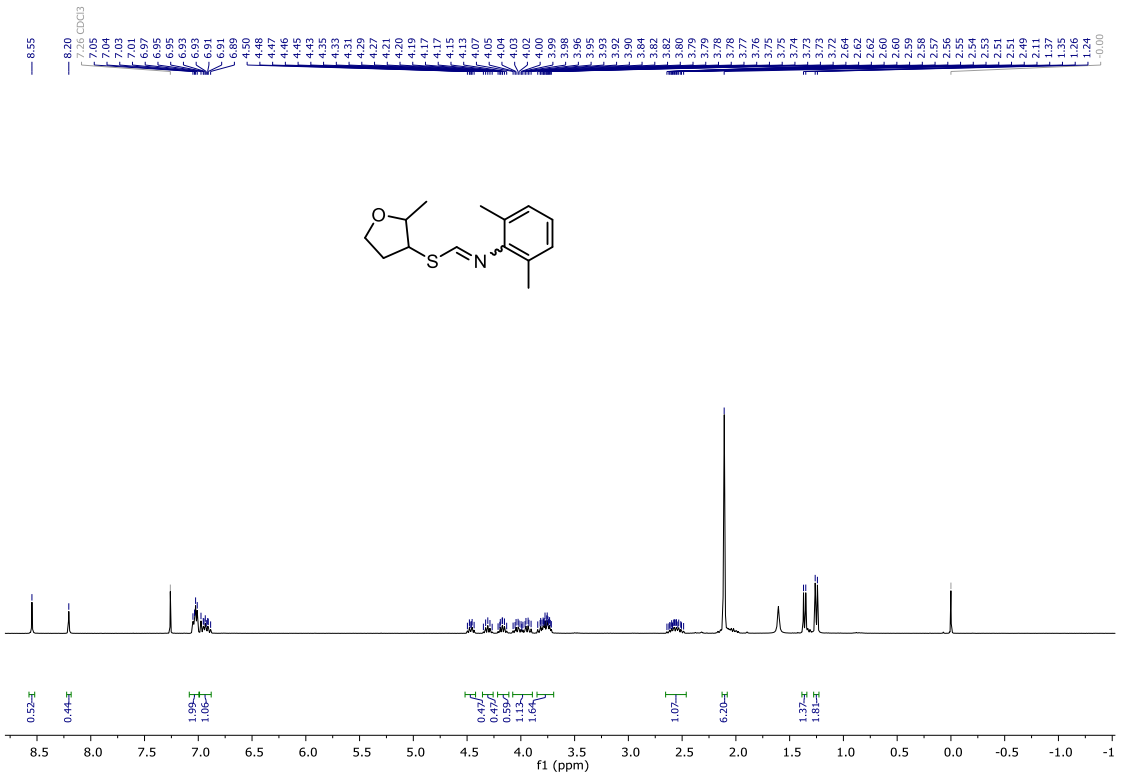
^{13}C NMR spectra of **14**



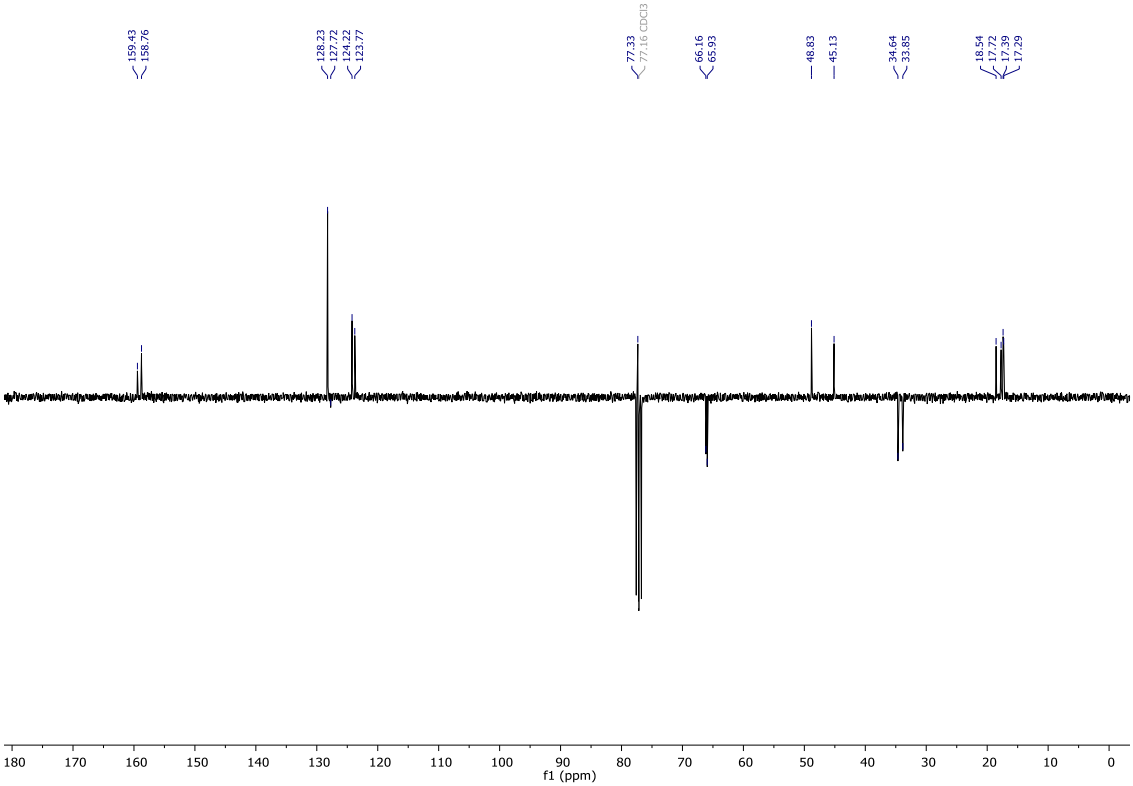
^{1}H NMR spectra of **15**



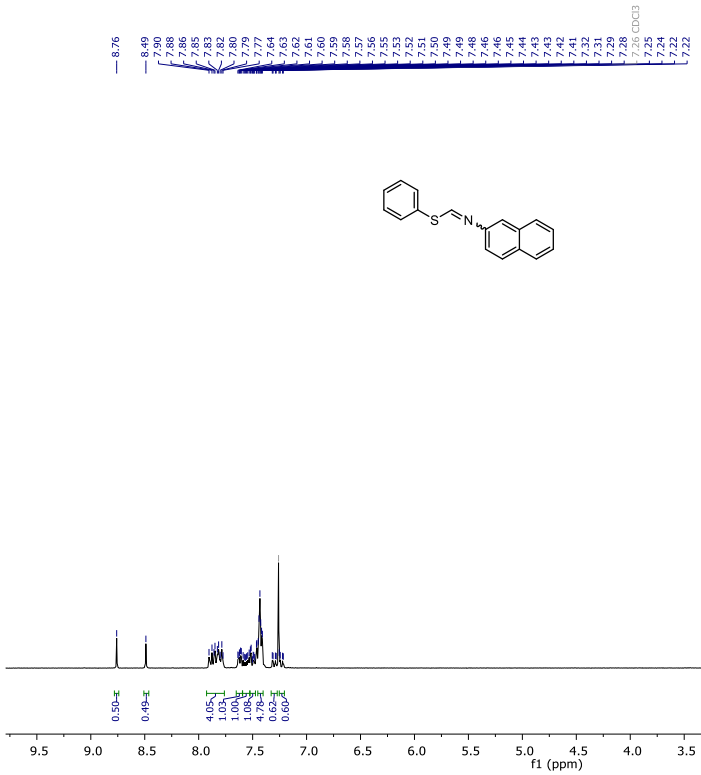
^{13}C NMR spectra of **15**



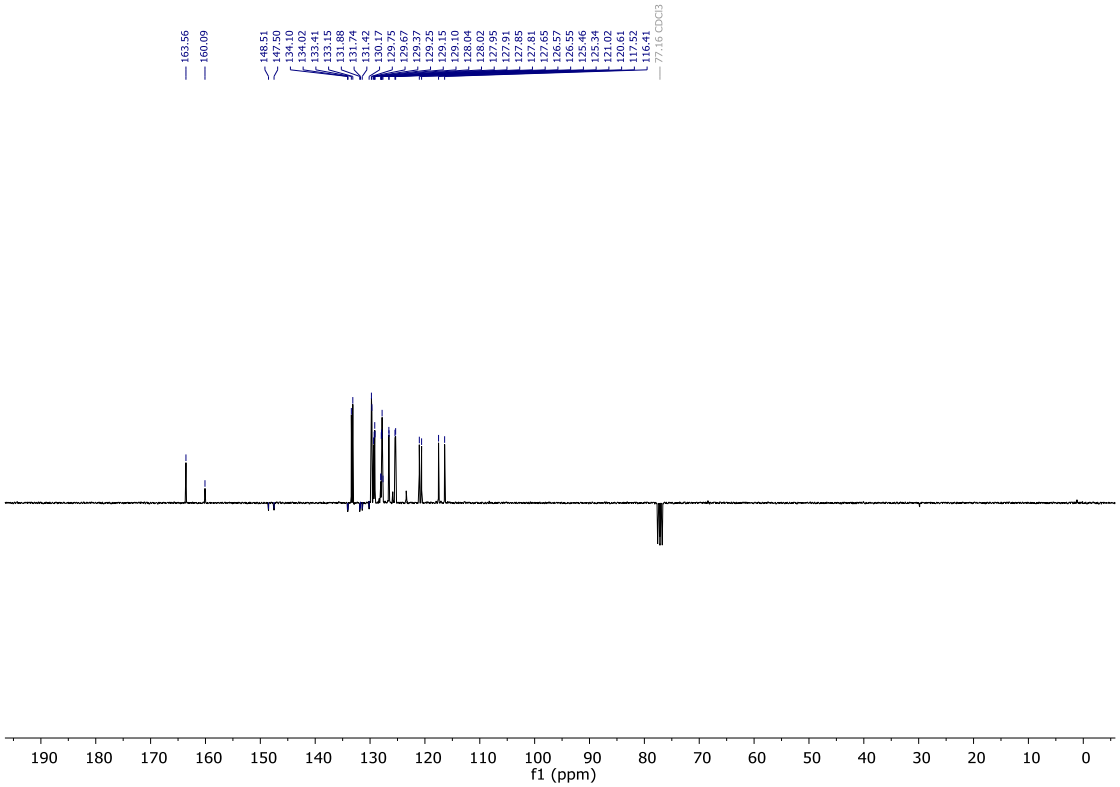
^{1}H NMR spectra of **16**



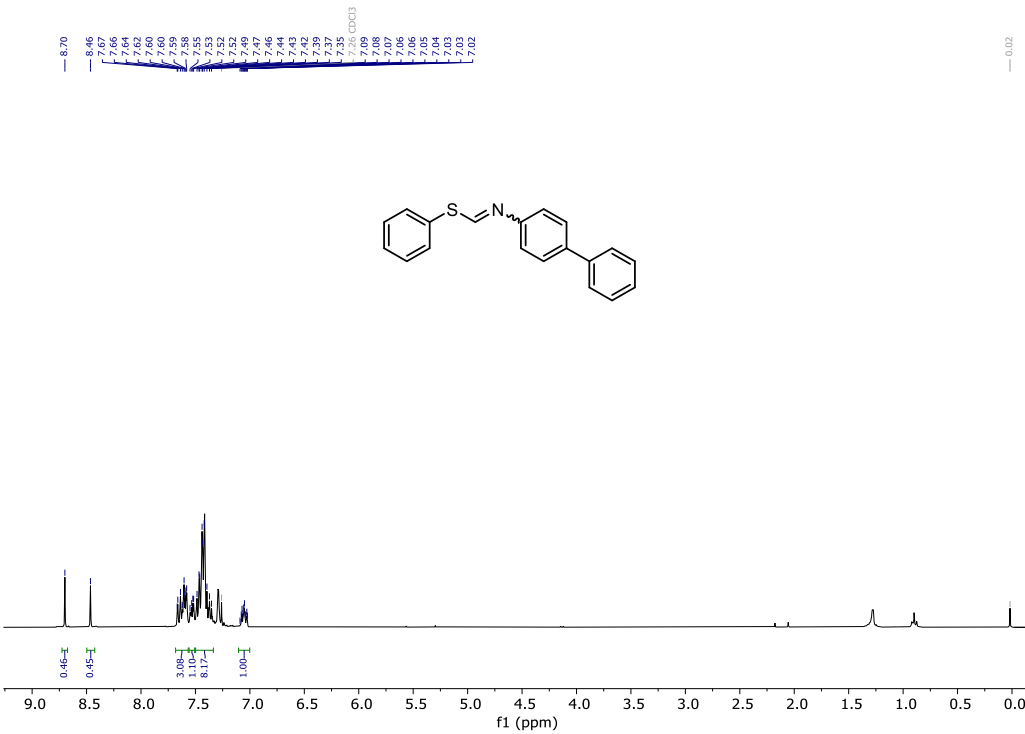
^{13}C NMR spectra of **16**



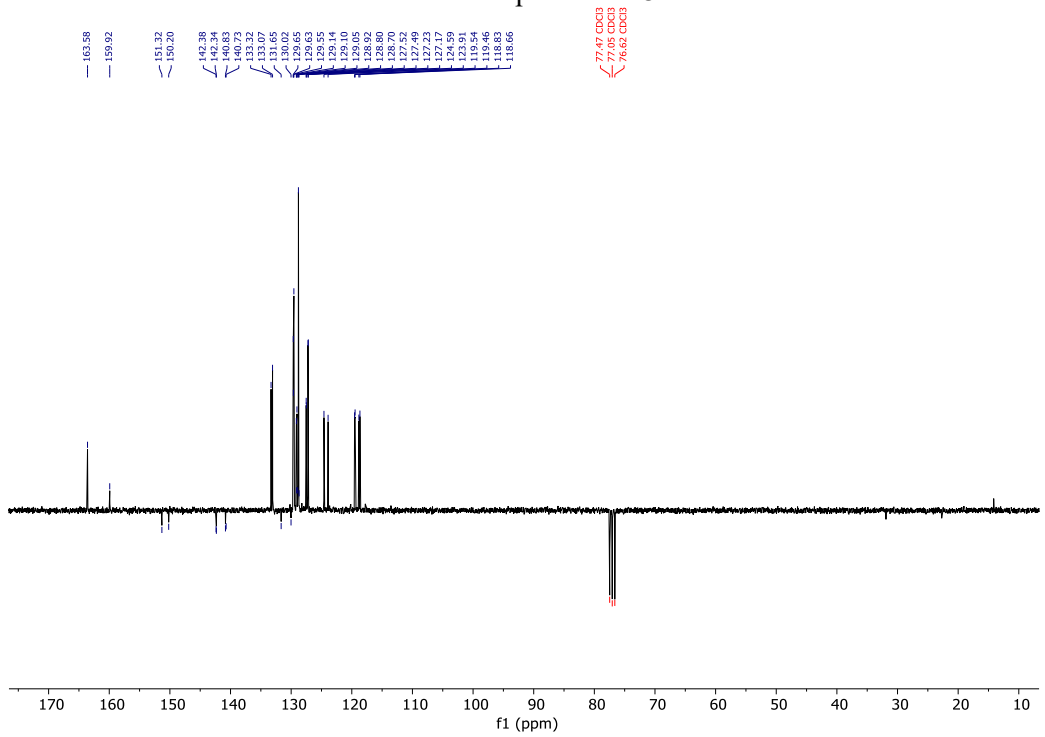
^{1}H NMR spectra of **17**



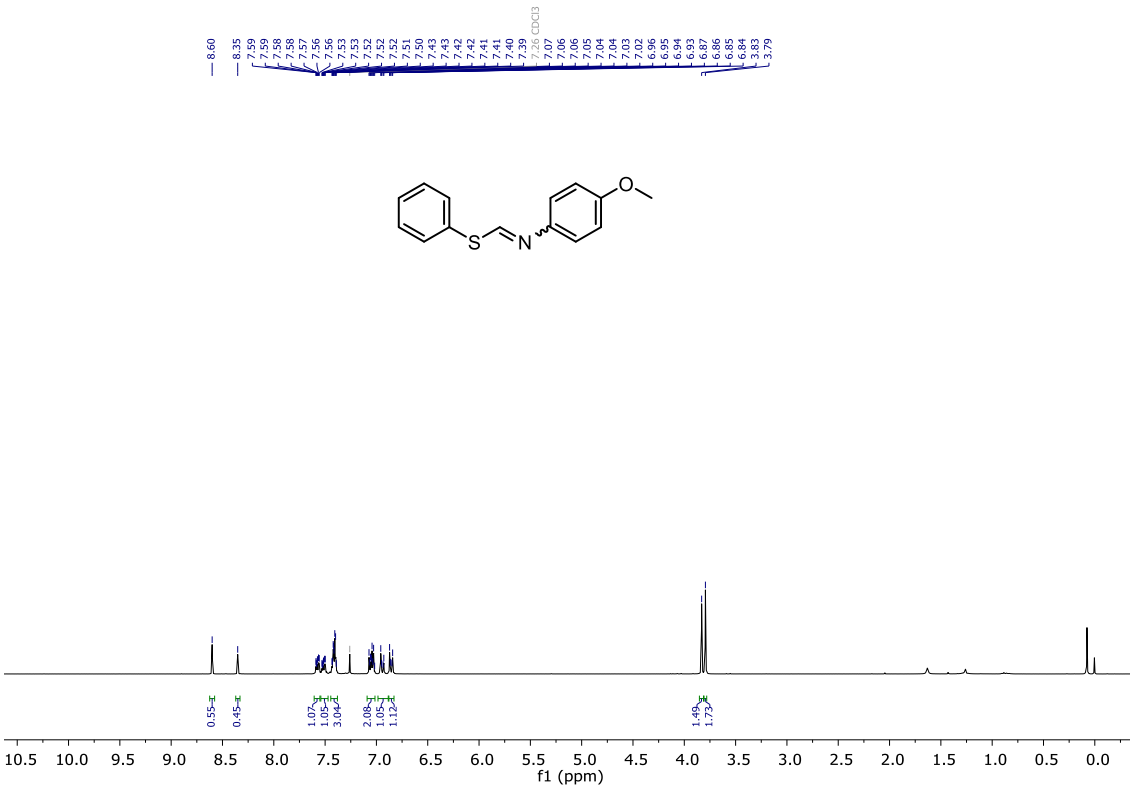
^{13}C NMR spectra of **17**



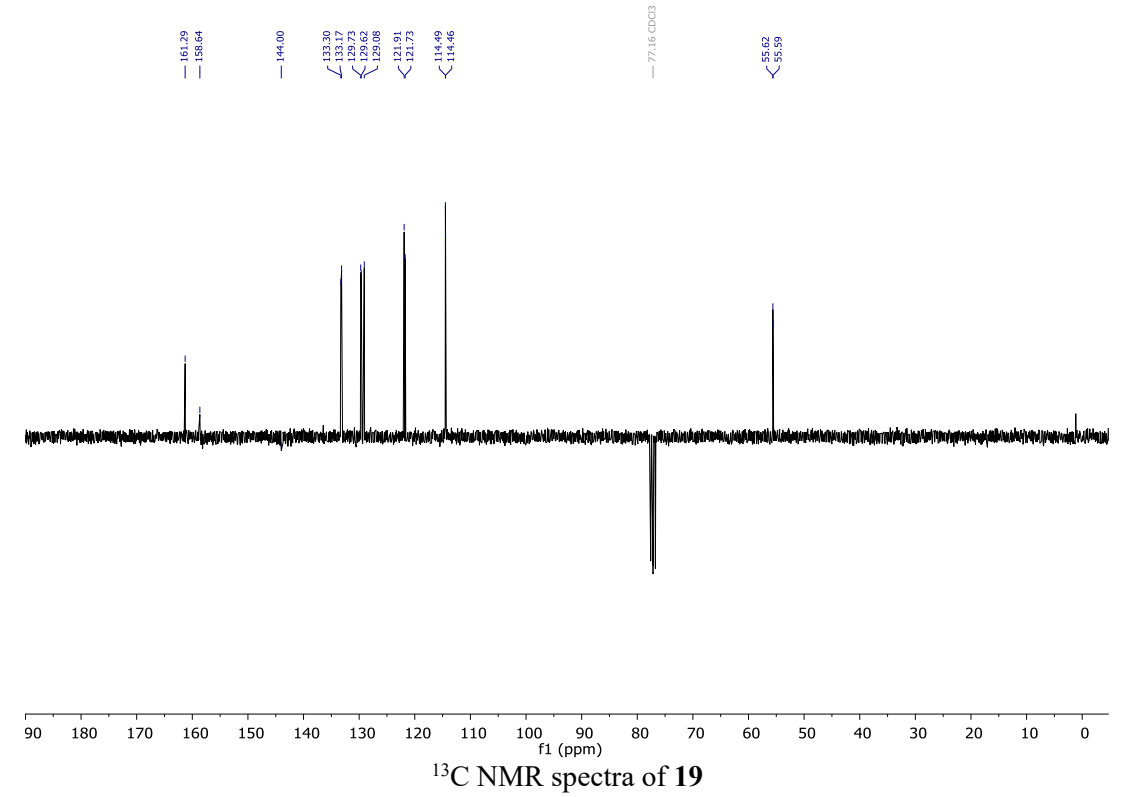
^{1}H NMR spectra of **18**



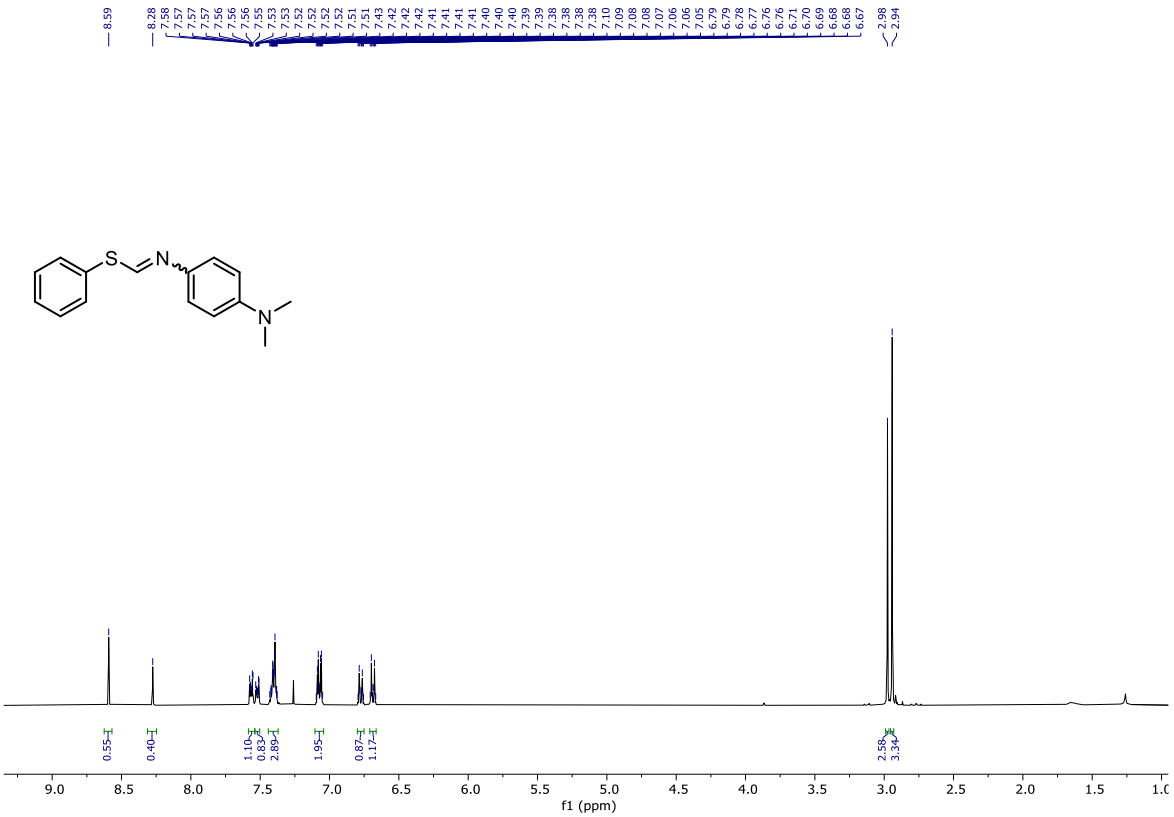
^{13}C NMR spectra of **18**



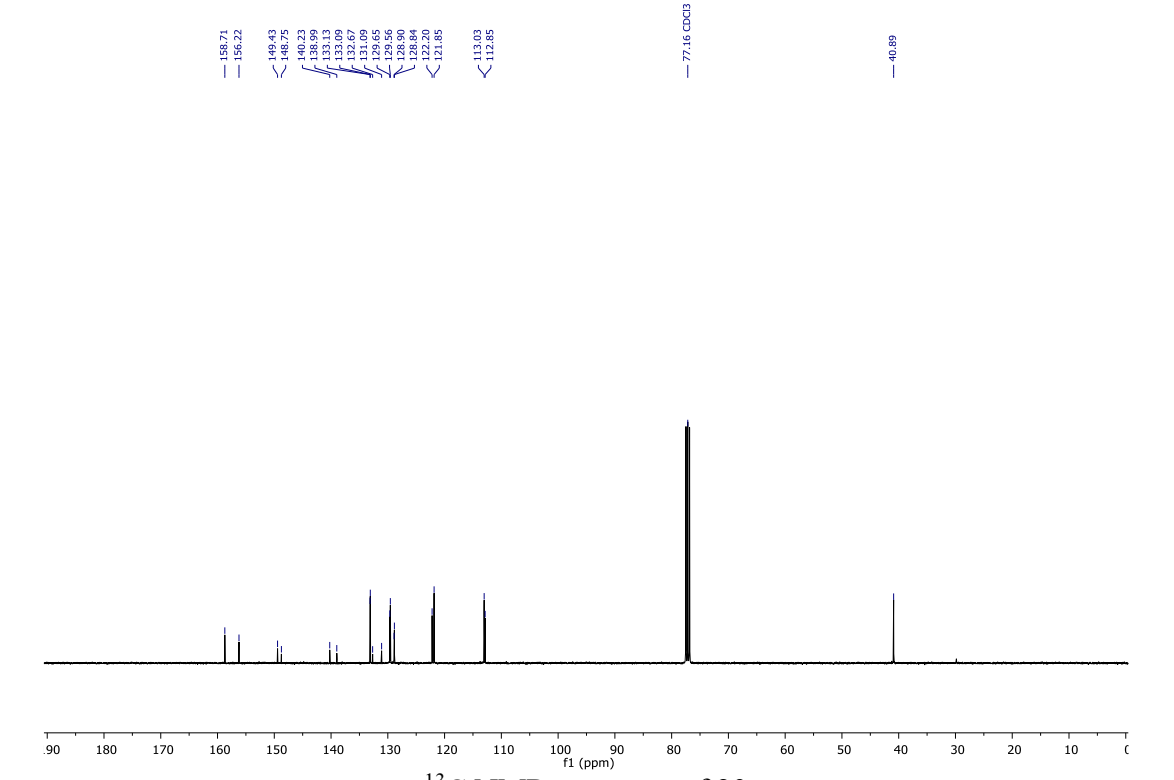
^{1}H NMR spectra of **19**



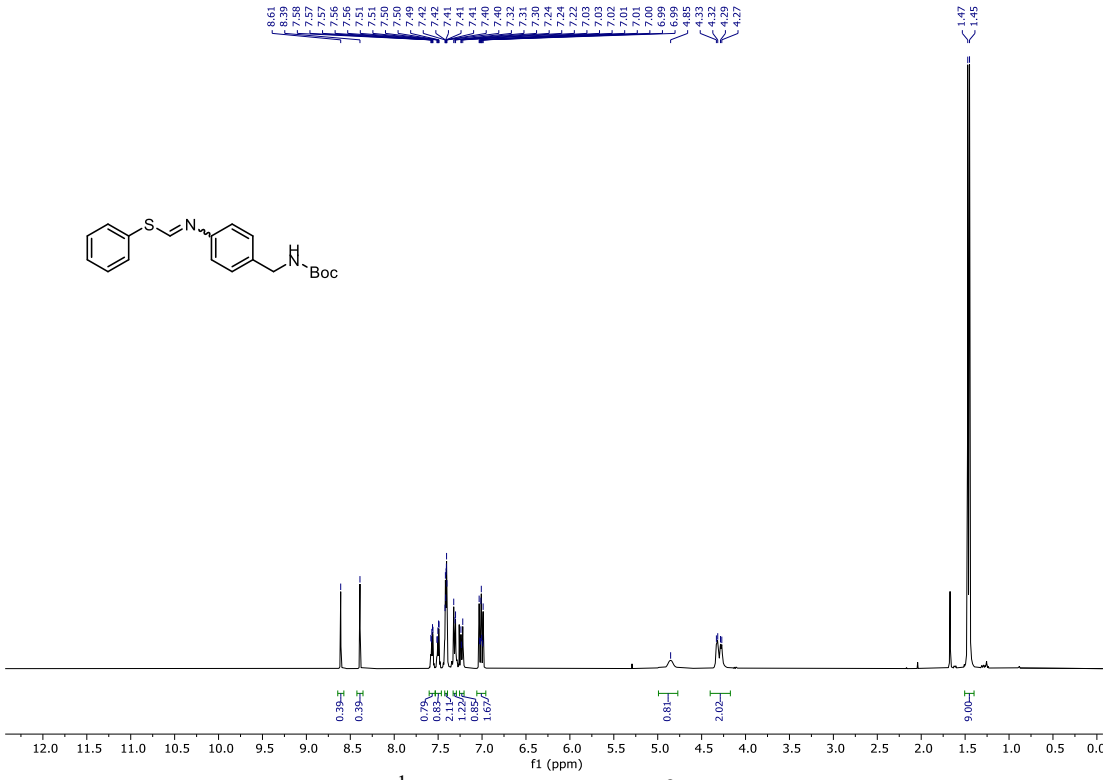
^{13}C NMR spectra of **19**



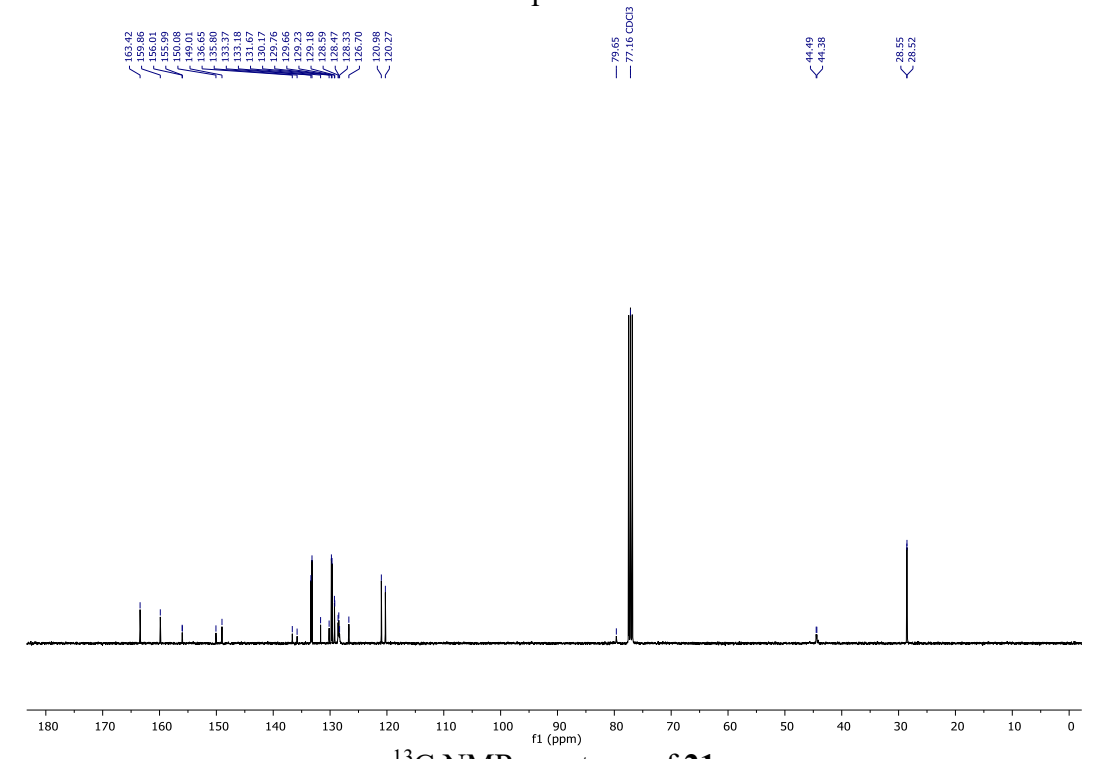
^{1}H NMR spectrum of **20**



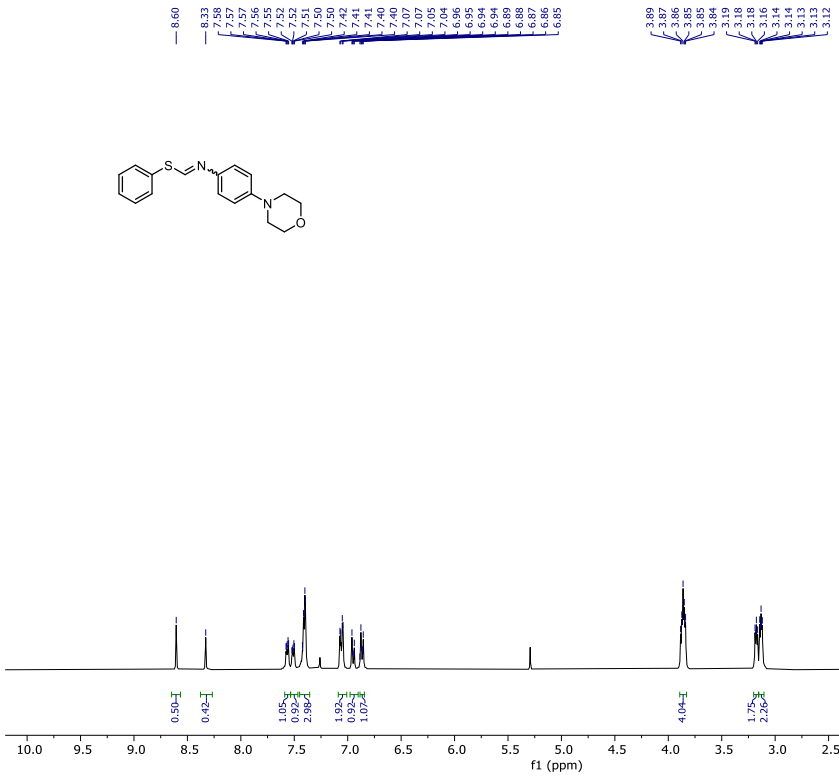
^{13}C NMR spectrum of **20**



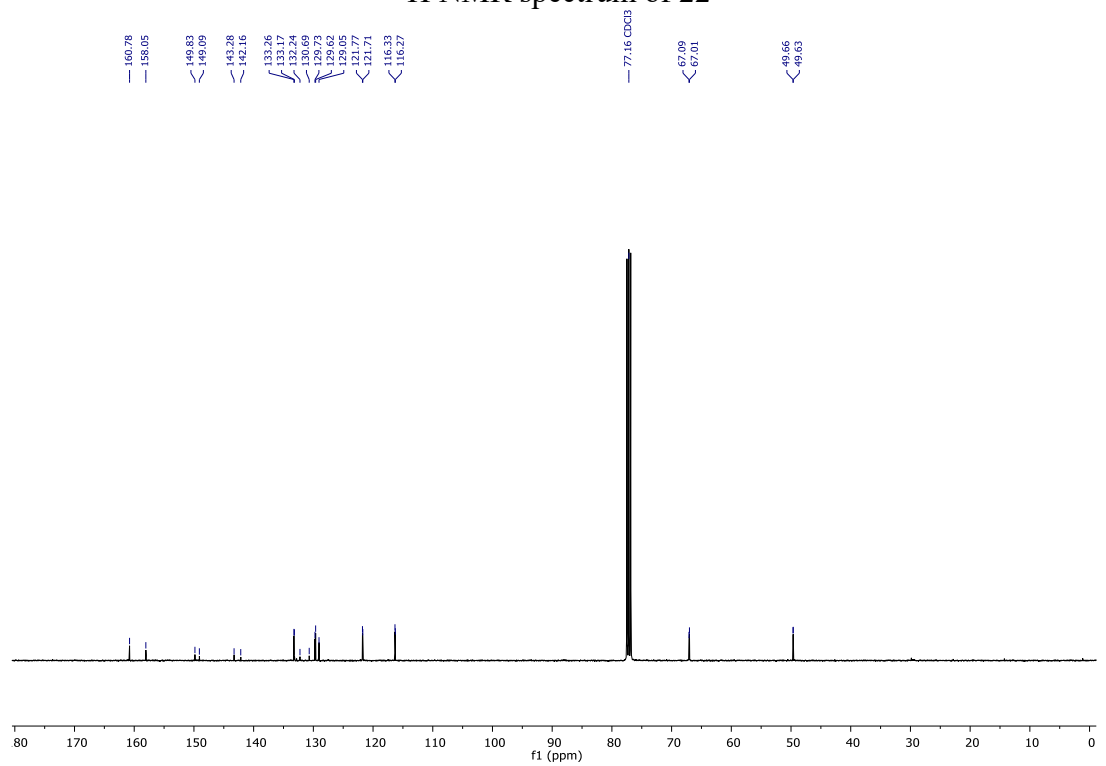
^{1}H NMR spectrum of **21**



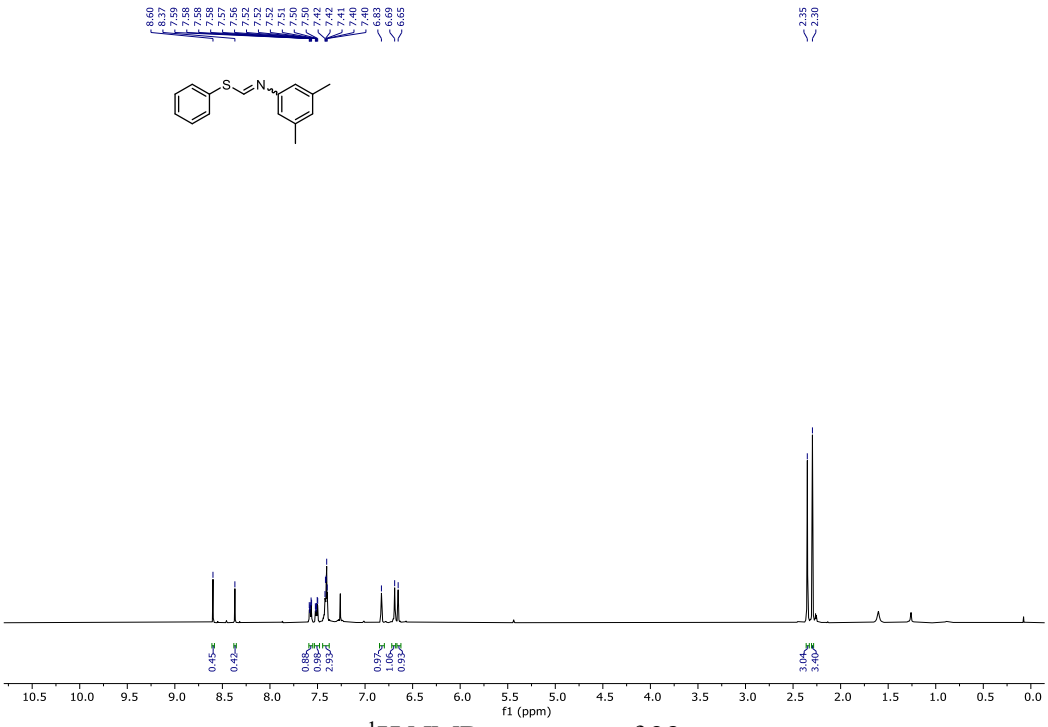
^{13}C NMR spectrum of **21**



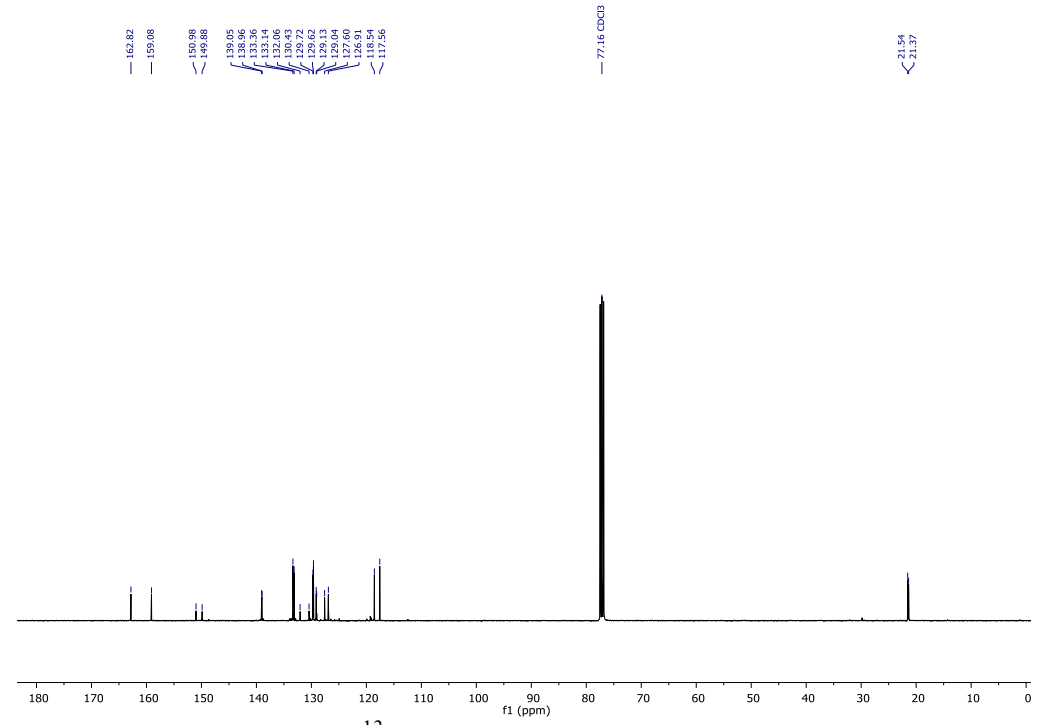
^{1}H NMR spectrum of **22**



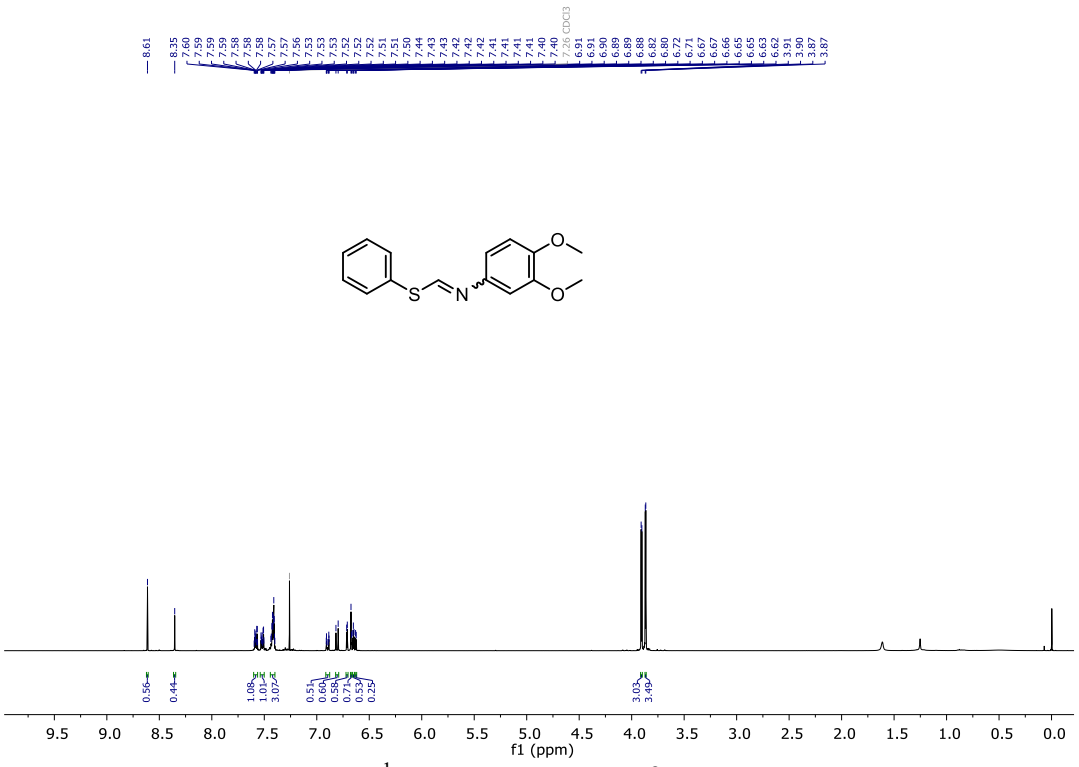
^{13}C NMR spectrum of **22**



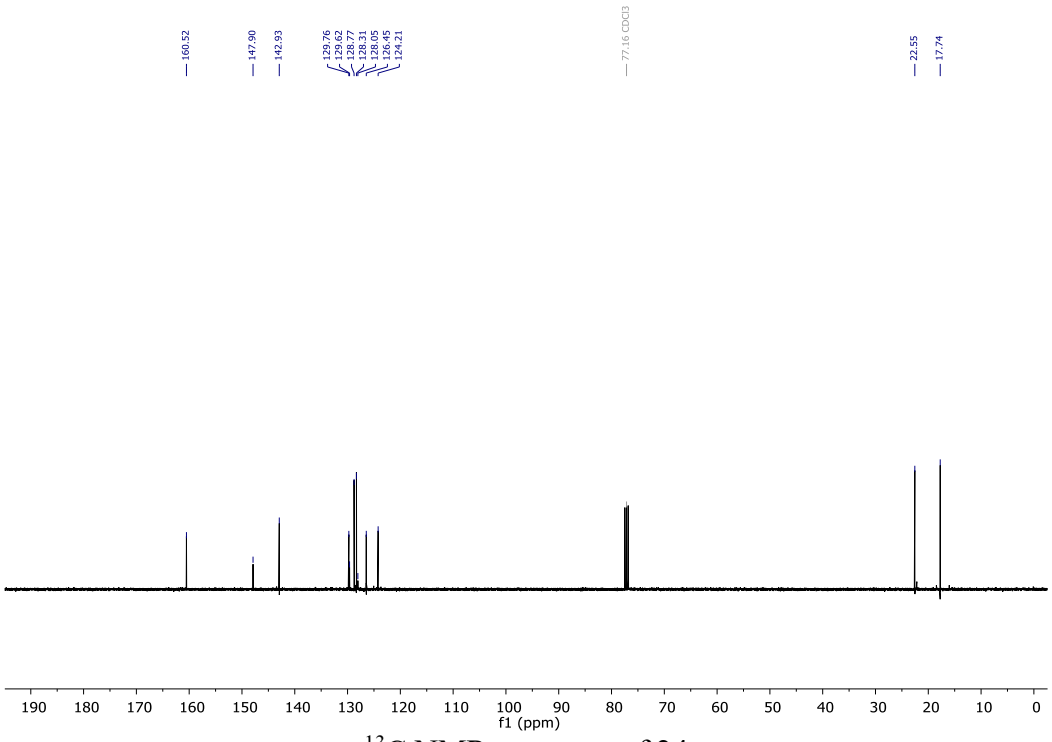
^{1}H NMR spectrum of **23**



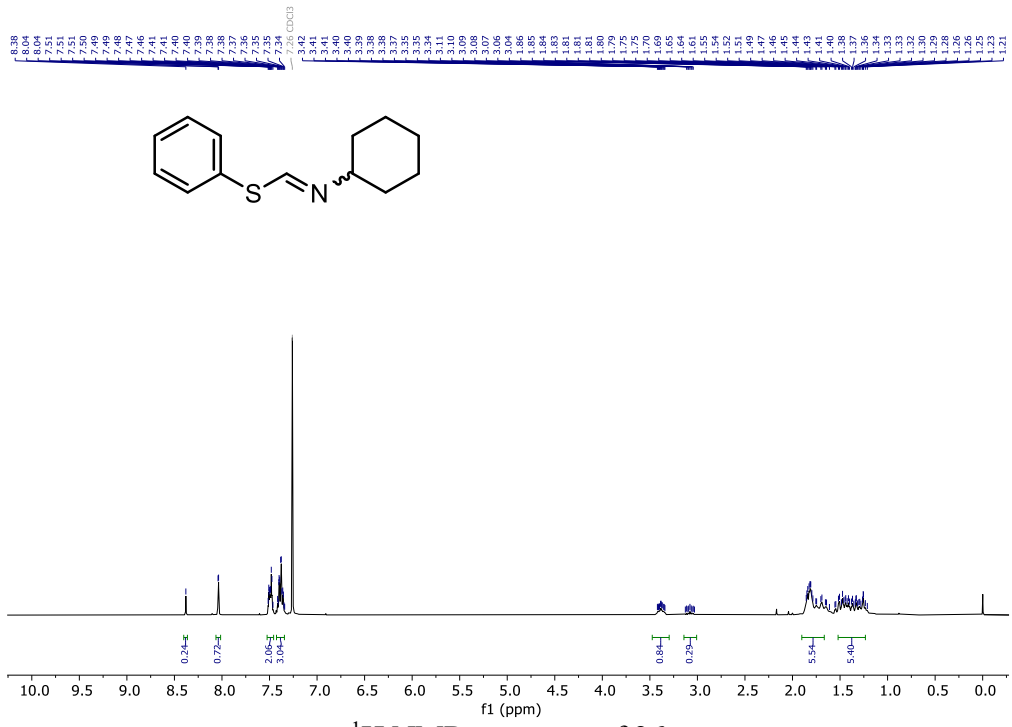
^{13}C NMR spectrum of **23**



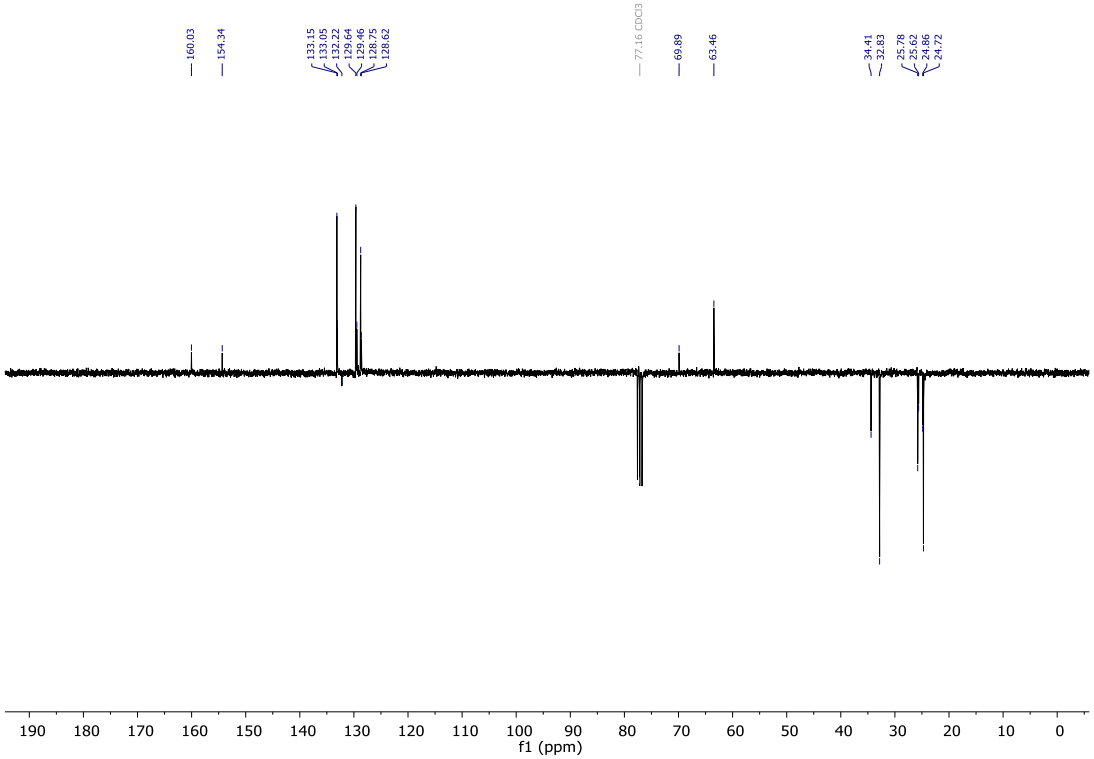
^{1}H NMR spectrum of **24**



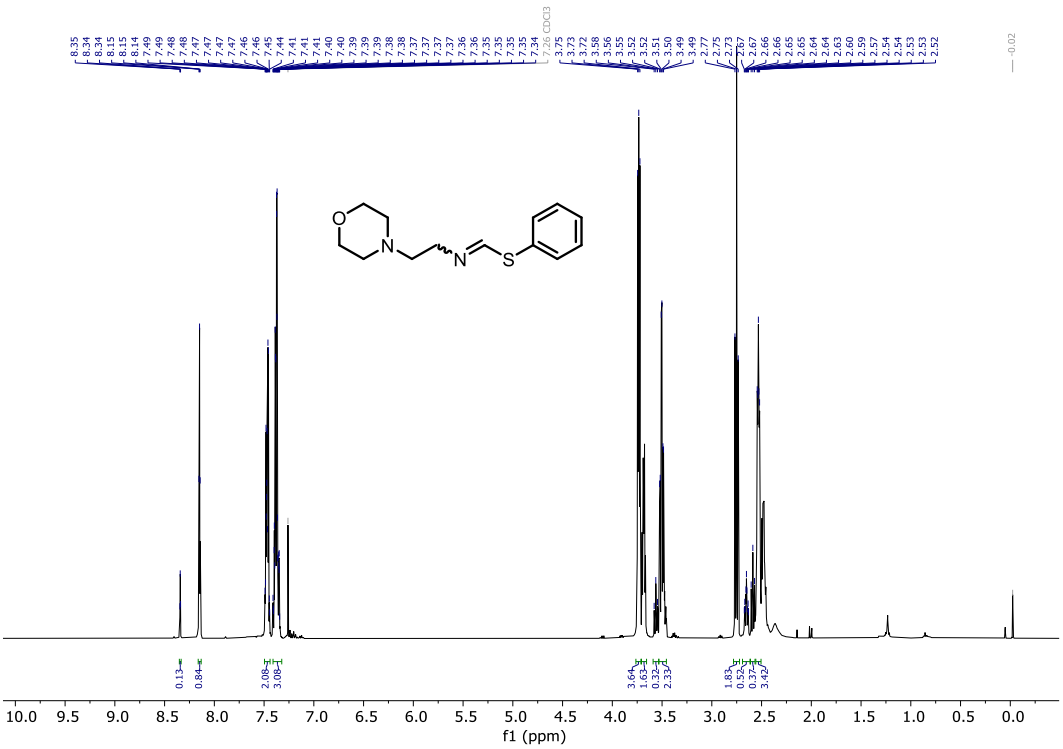
^{13}C NMR spectrum of **24**



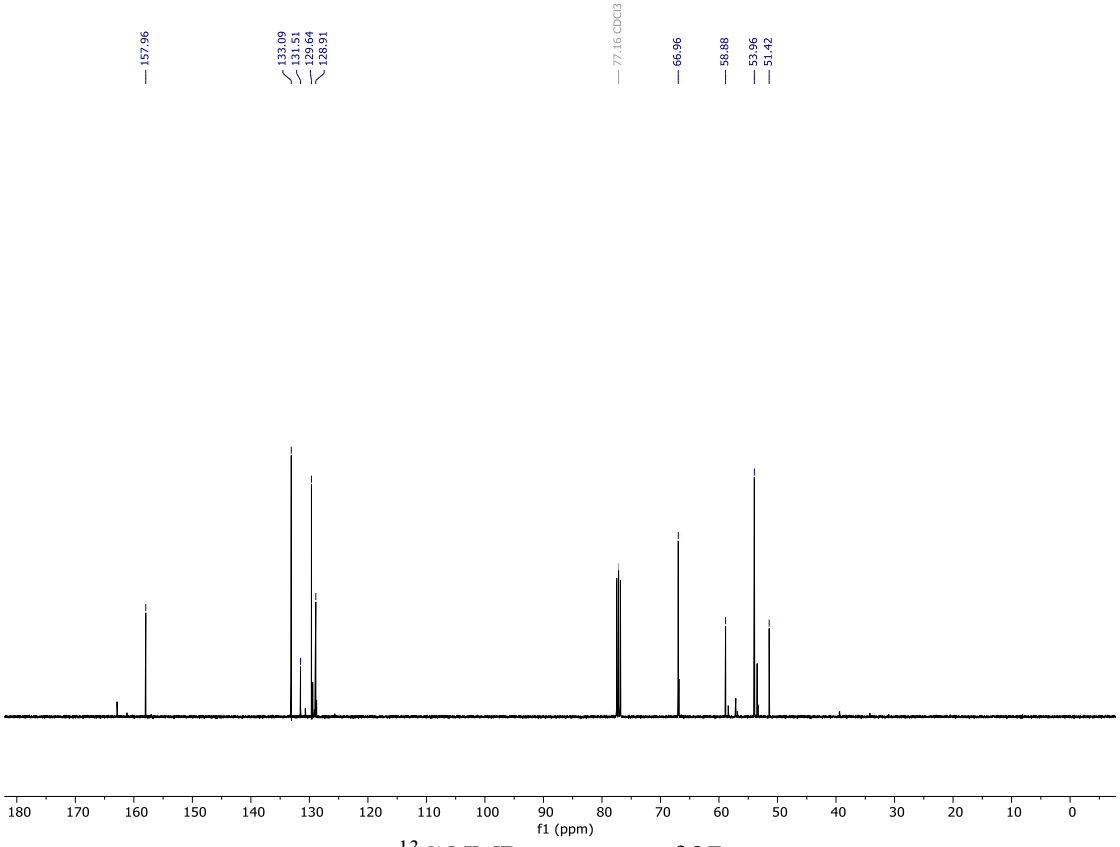
^{1}H NMR spectrum of **26**



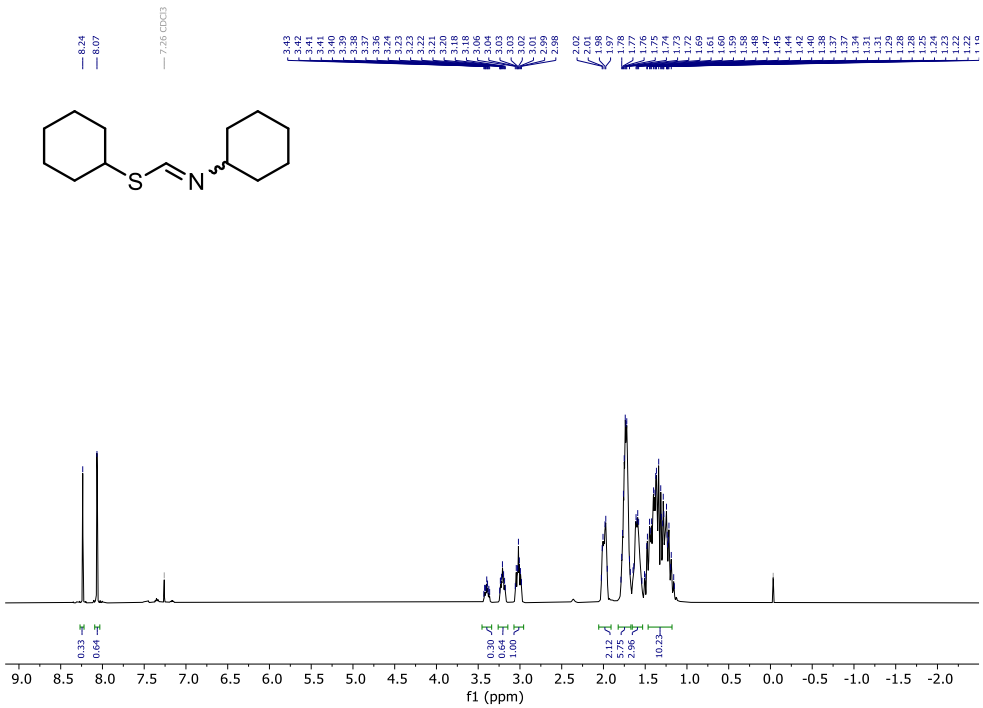
^{13}C NMR spectrum of **26**



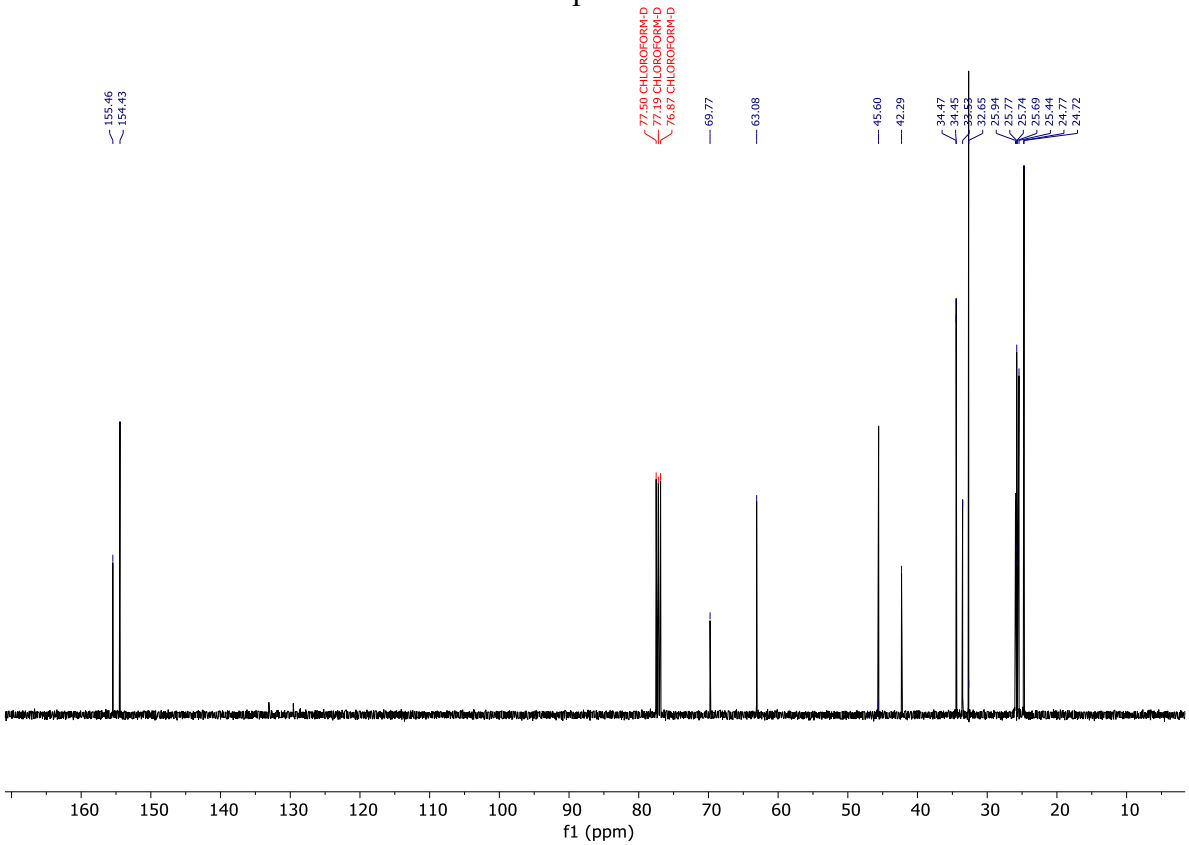
^{1}H NMR spectrum of **27**



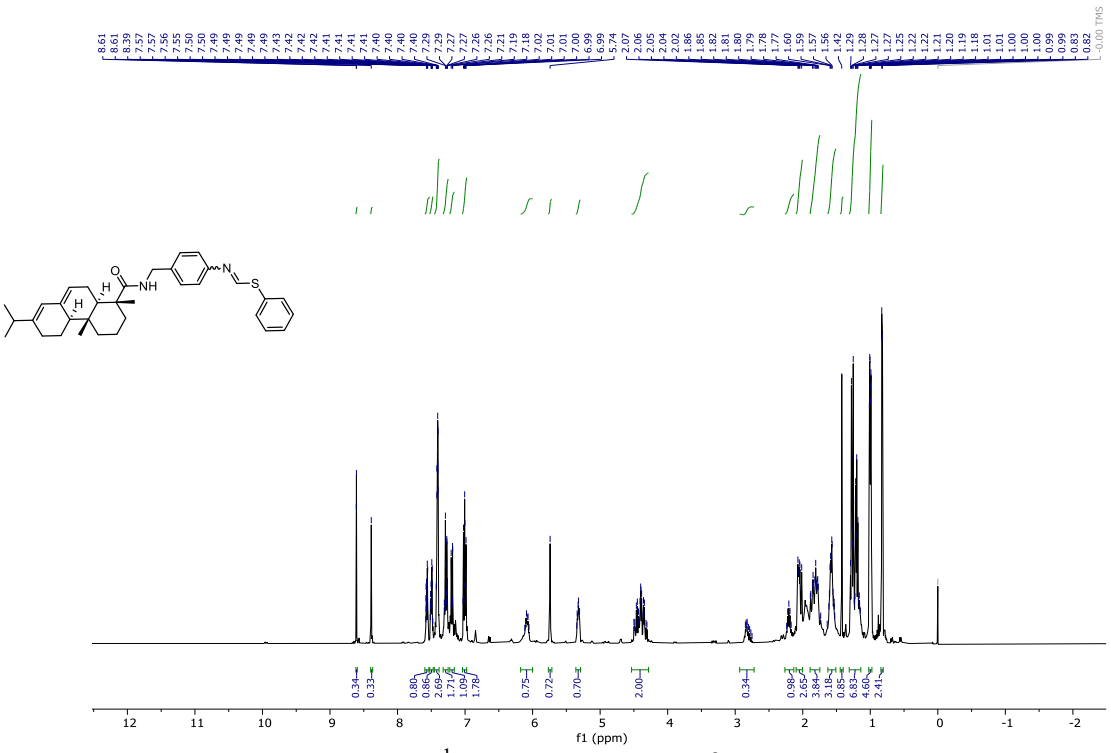
^{13}C NMR spectrum of **27**



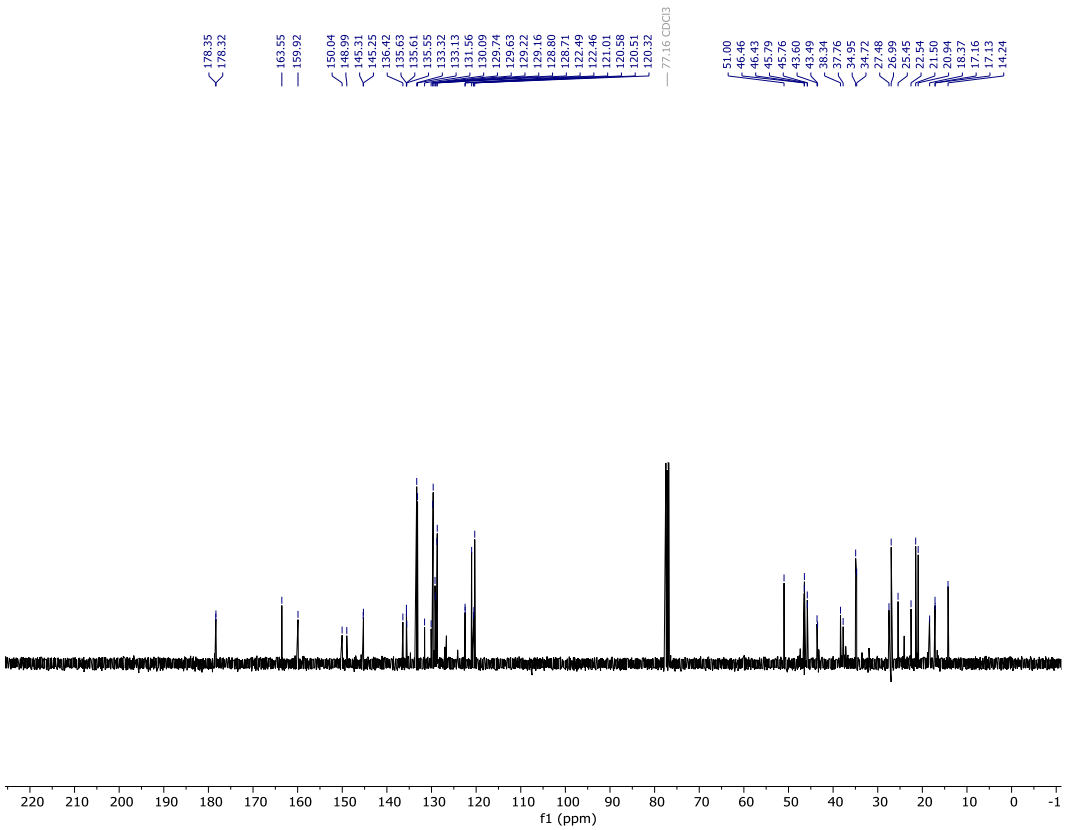
^{1}H NMR spectrum of **28**



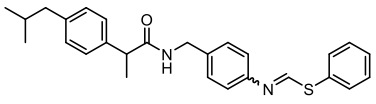
^{13}C NMR spectrum of **28**

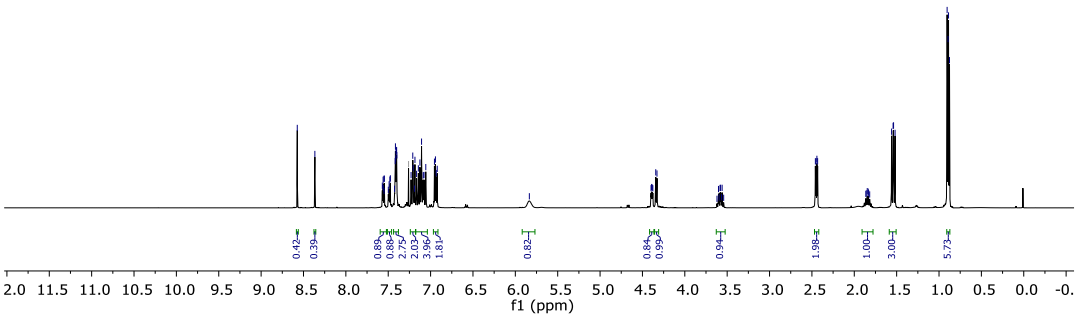


^{1}H NMR spectrum of **29**

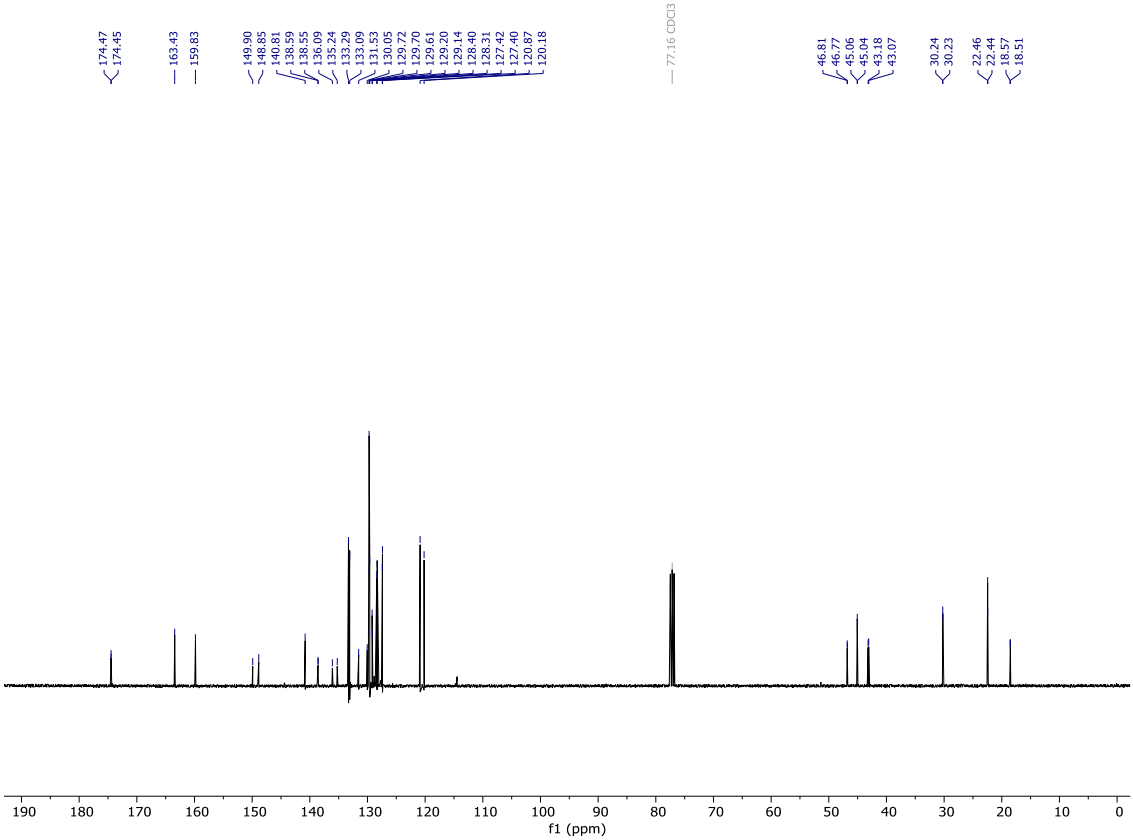


^{13}C NMR spectrum of **29**

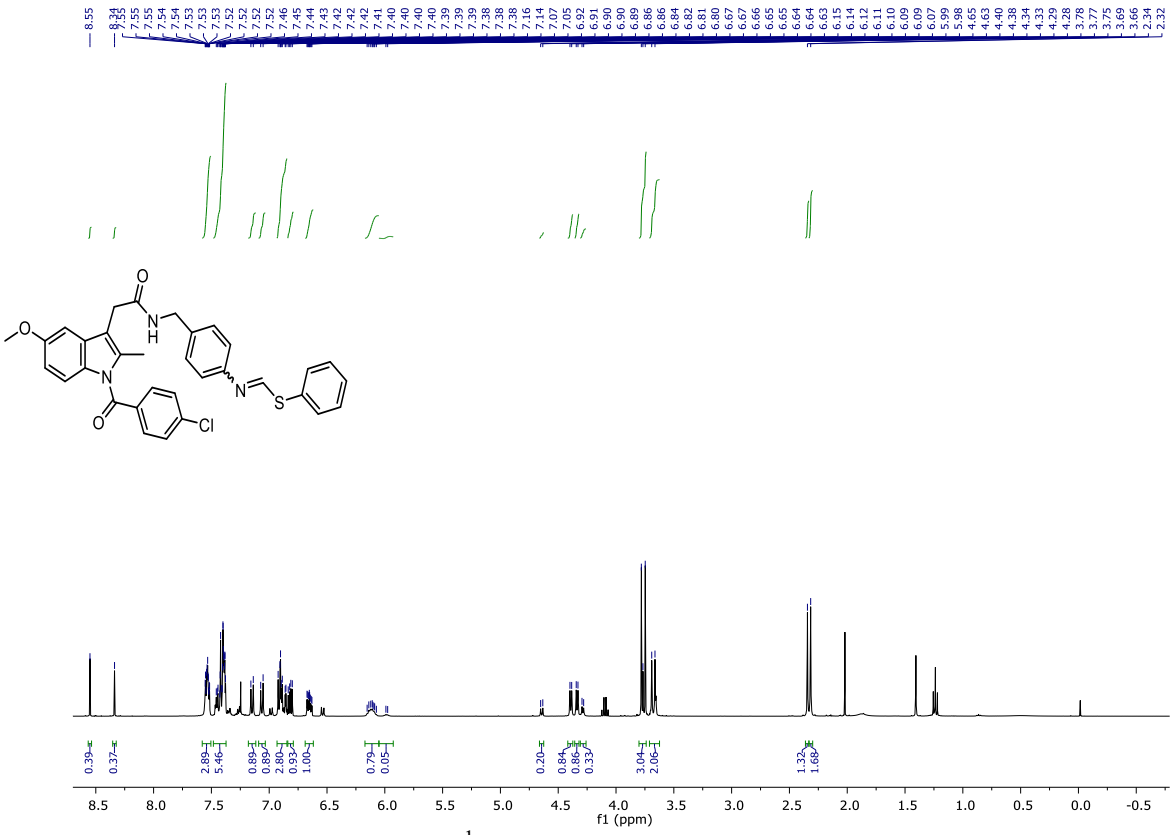




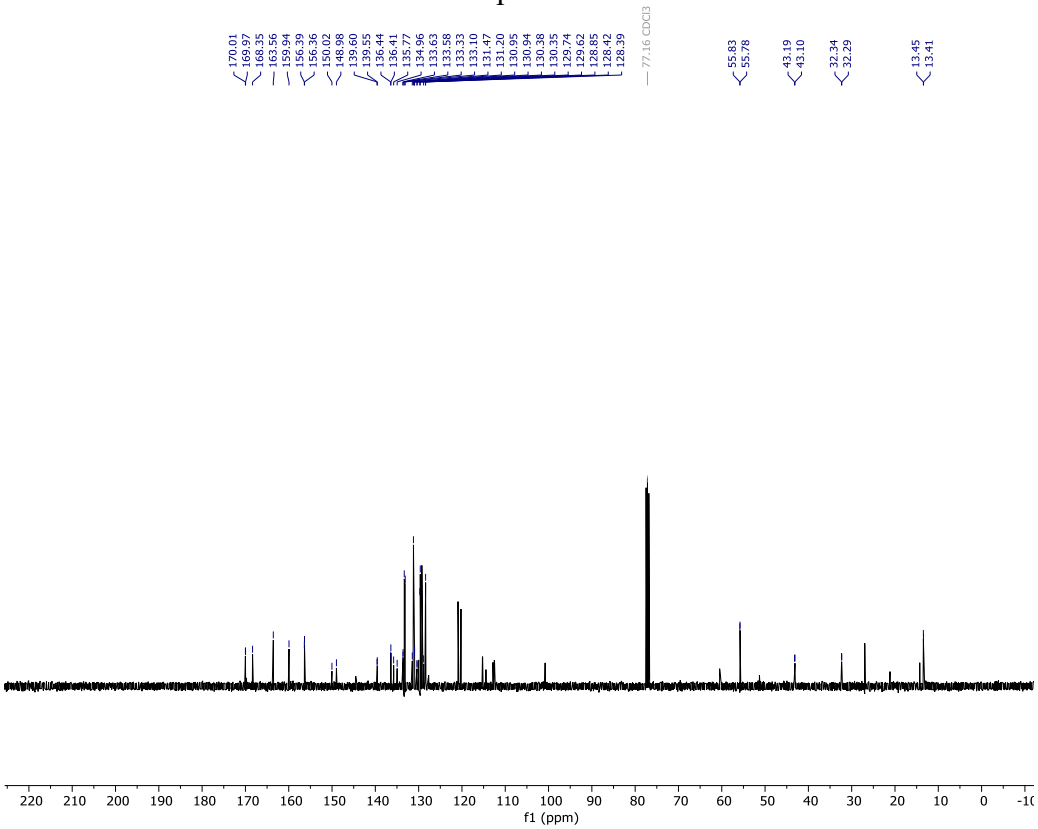
^{1}H NMR spectrum of **30**



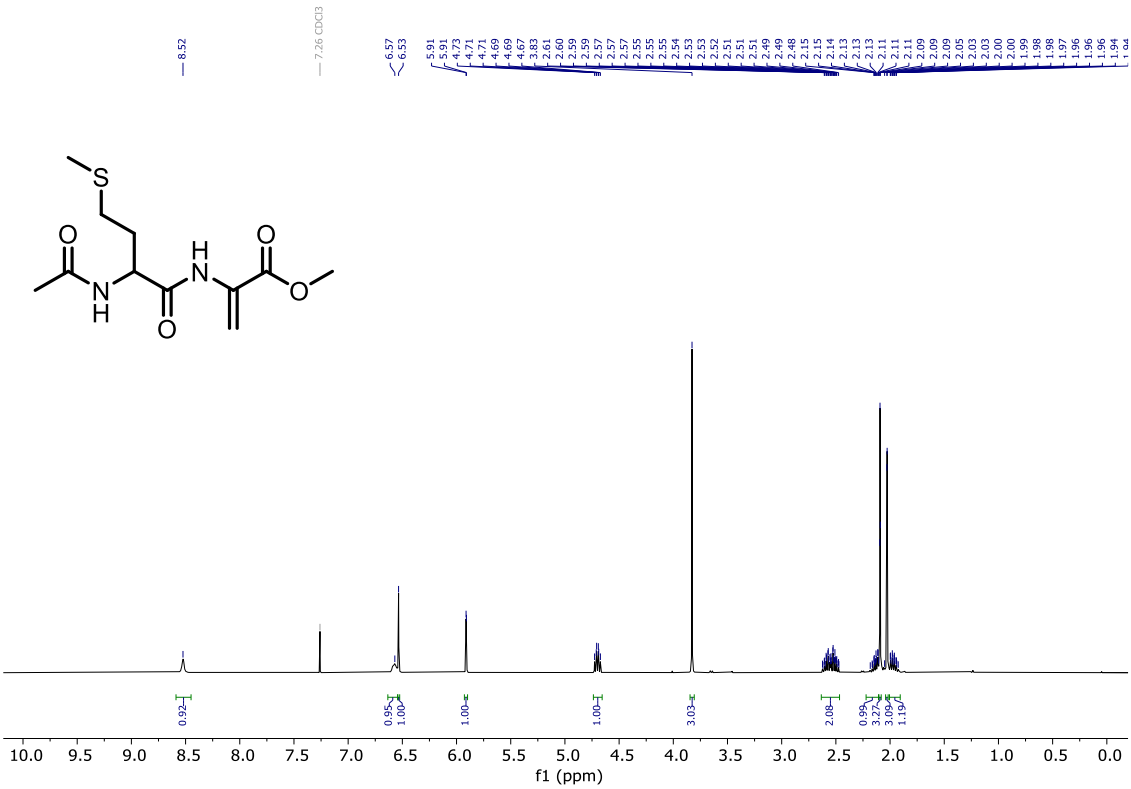
^{13}C NMR spectrum of **30**



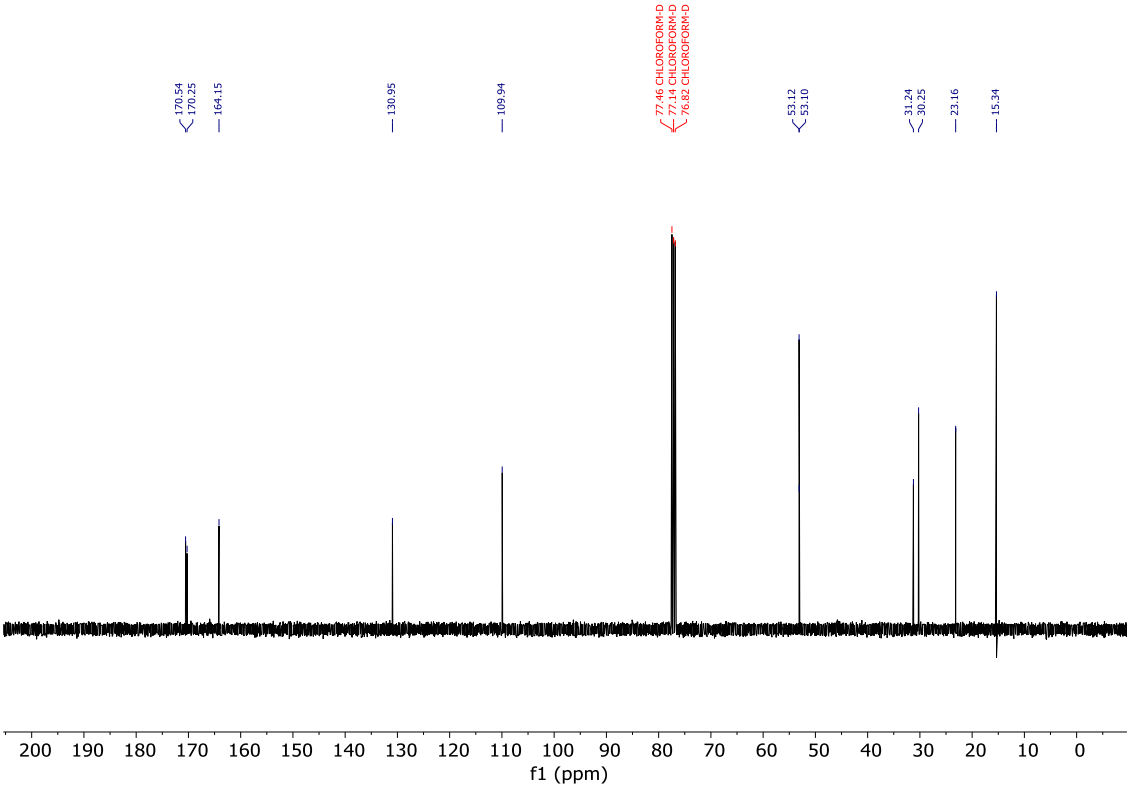
^{1}H NMR spectrum of **31**



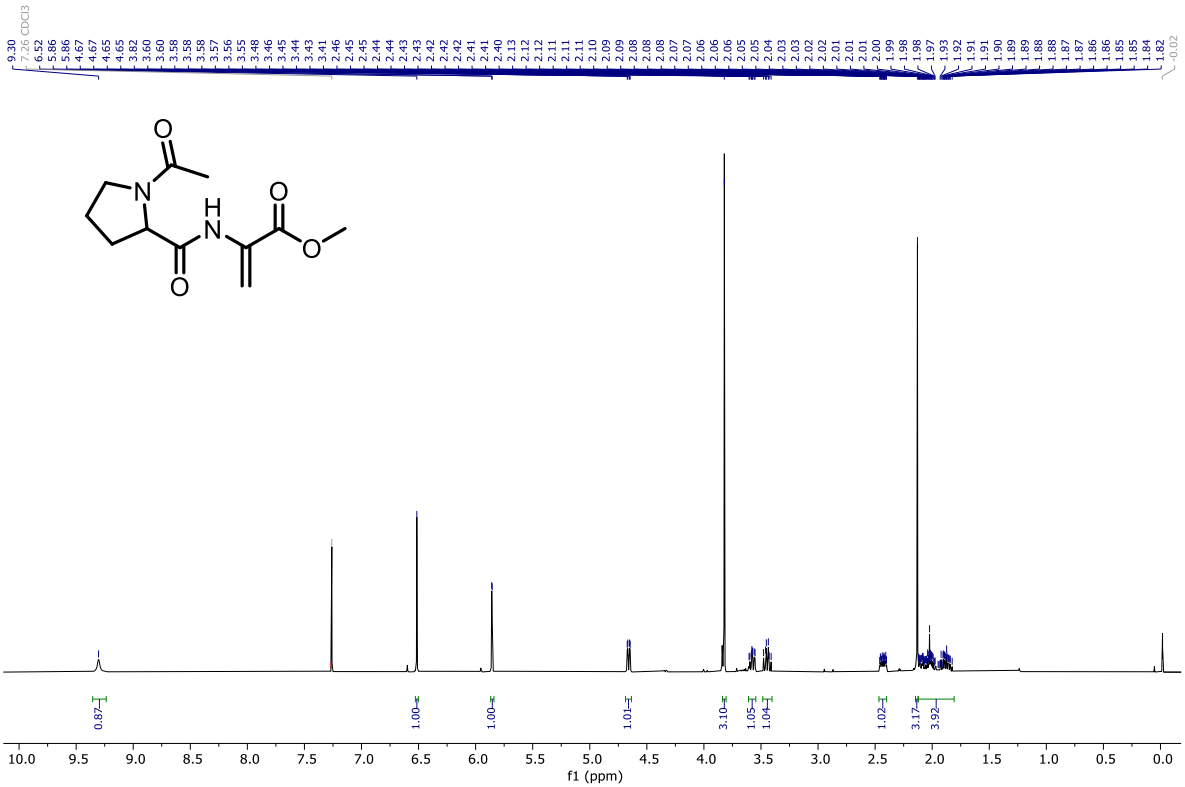
^{13}C NMR spectrum of **31**



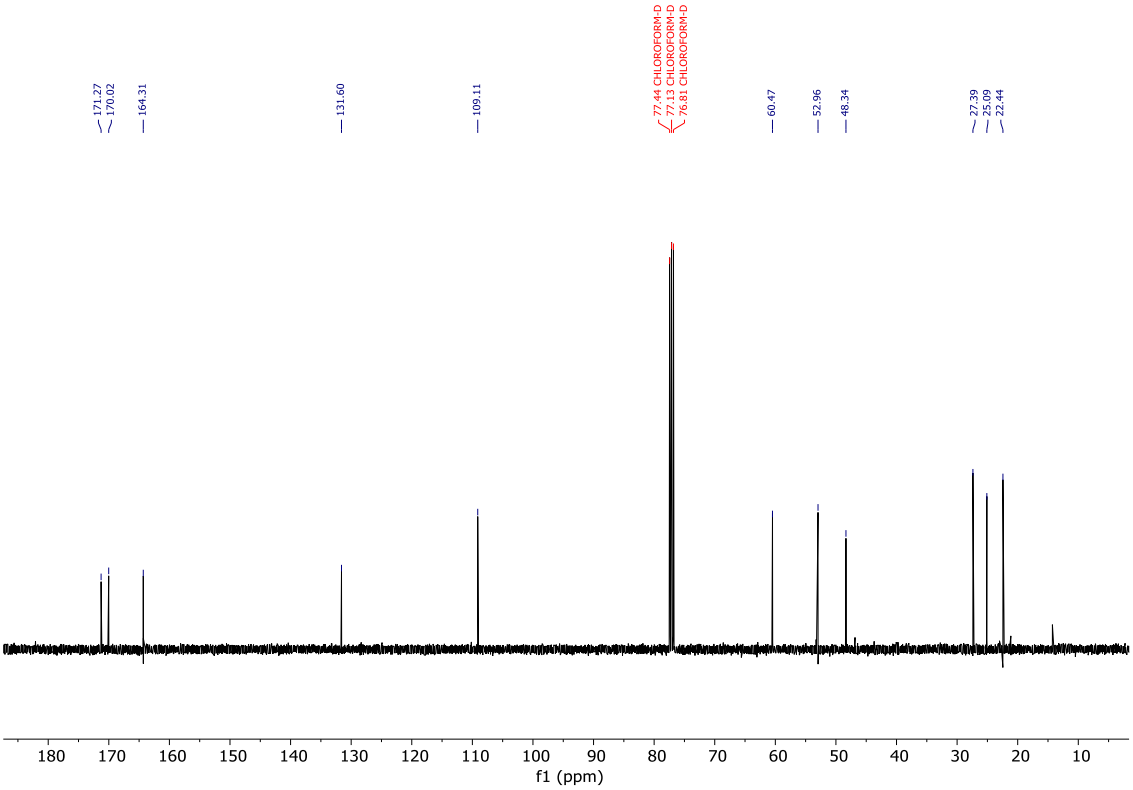
^{1}H NMR spectrum of **35**



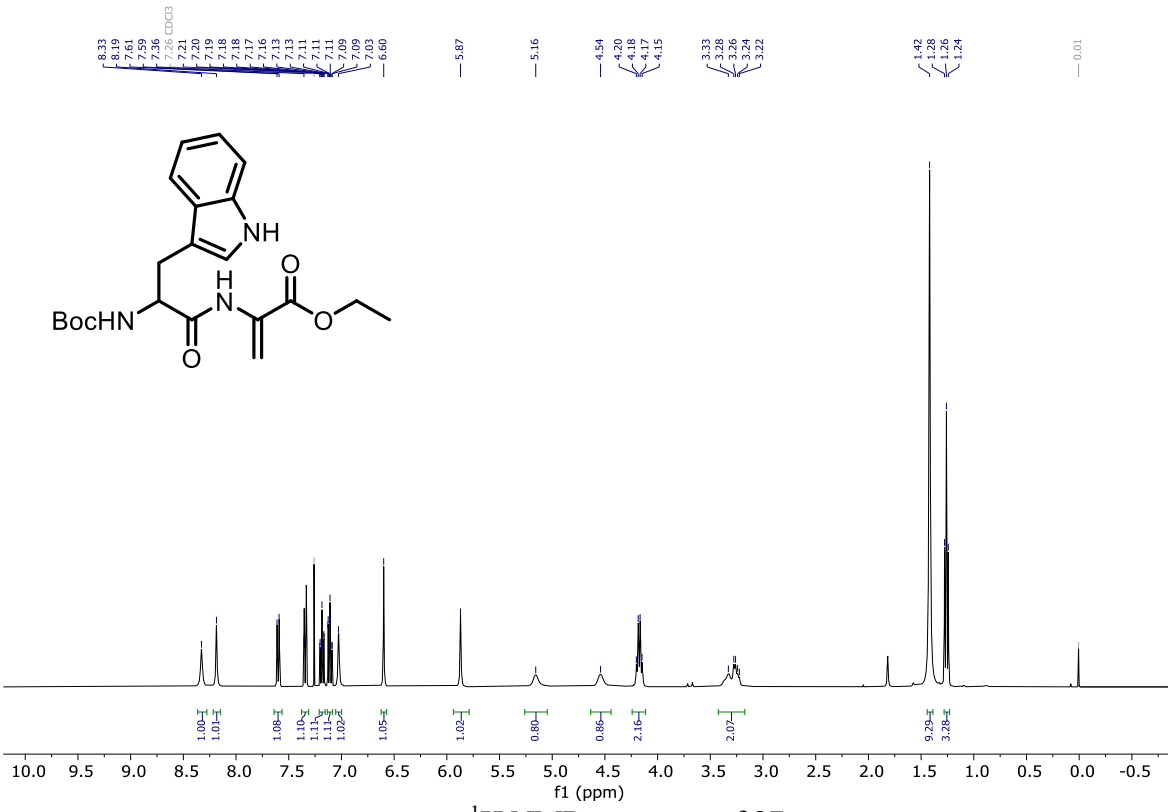
^{13}C NMR spectrum of **35**



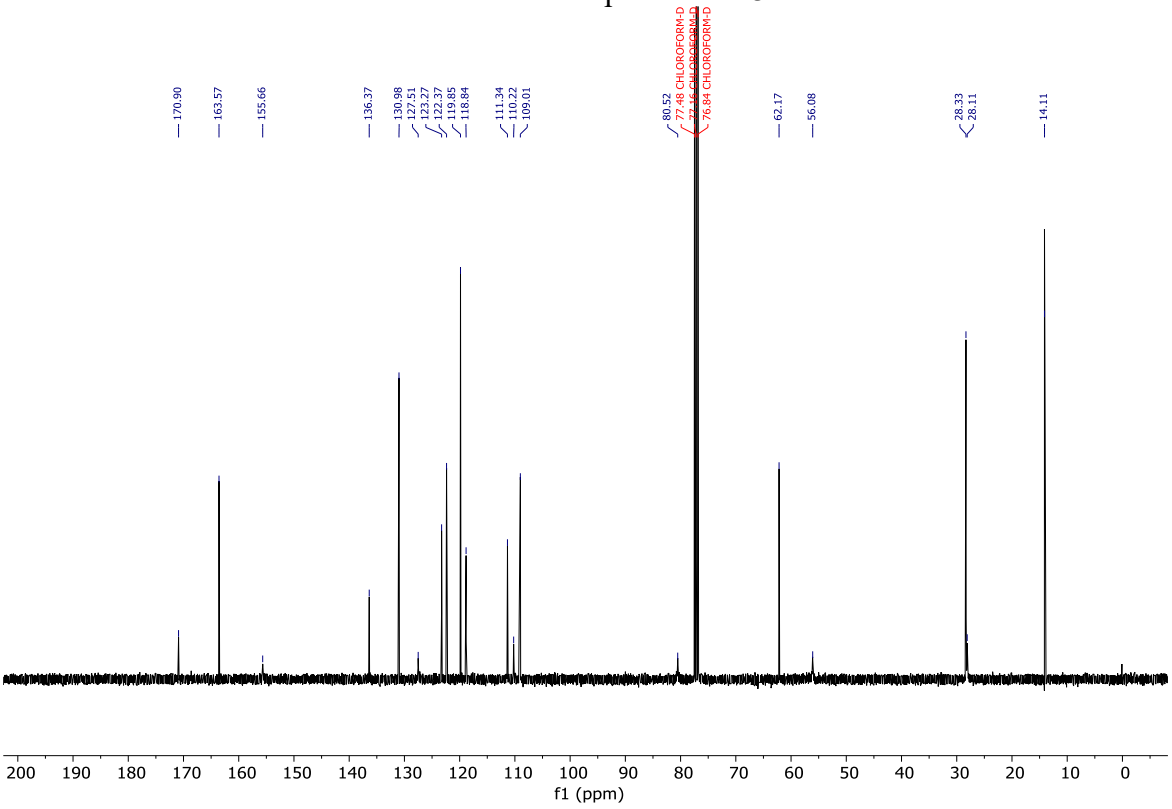
^{1}H NMR spectrum of **36**



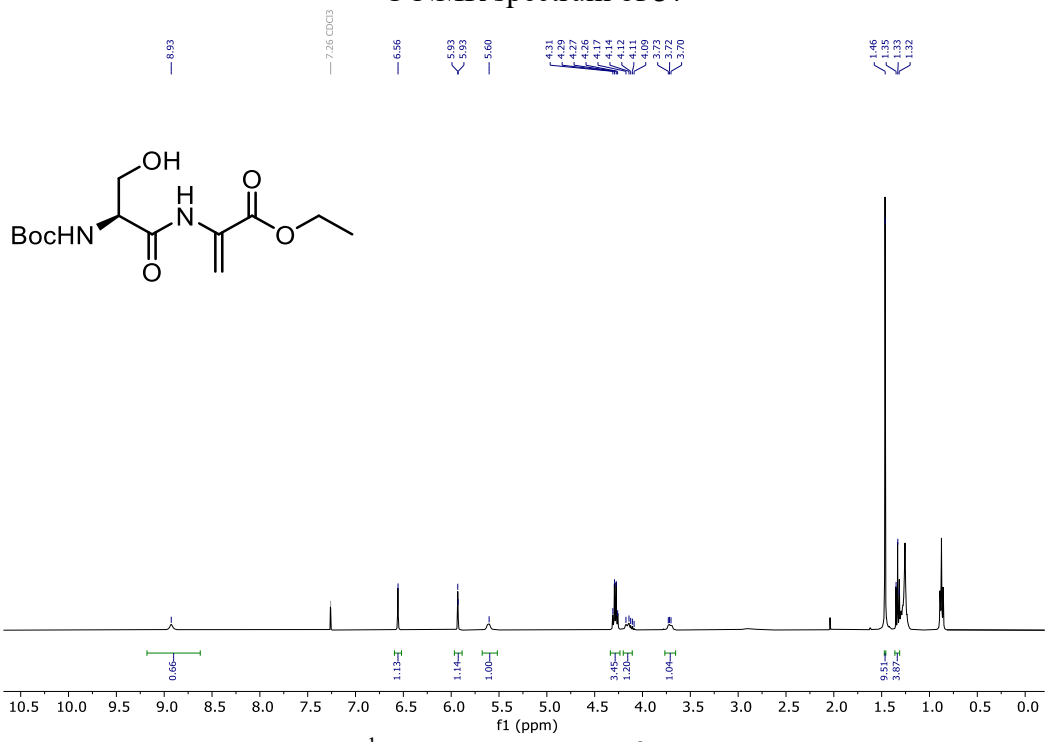
^{13}C NMR spectrum of **36**



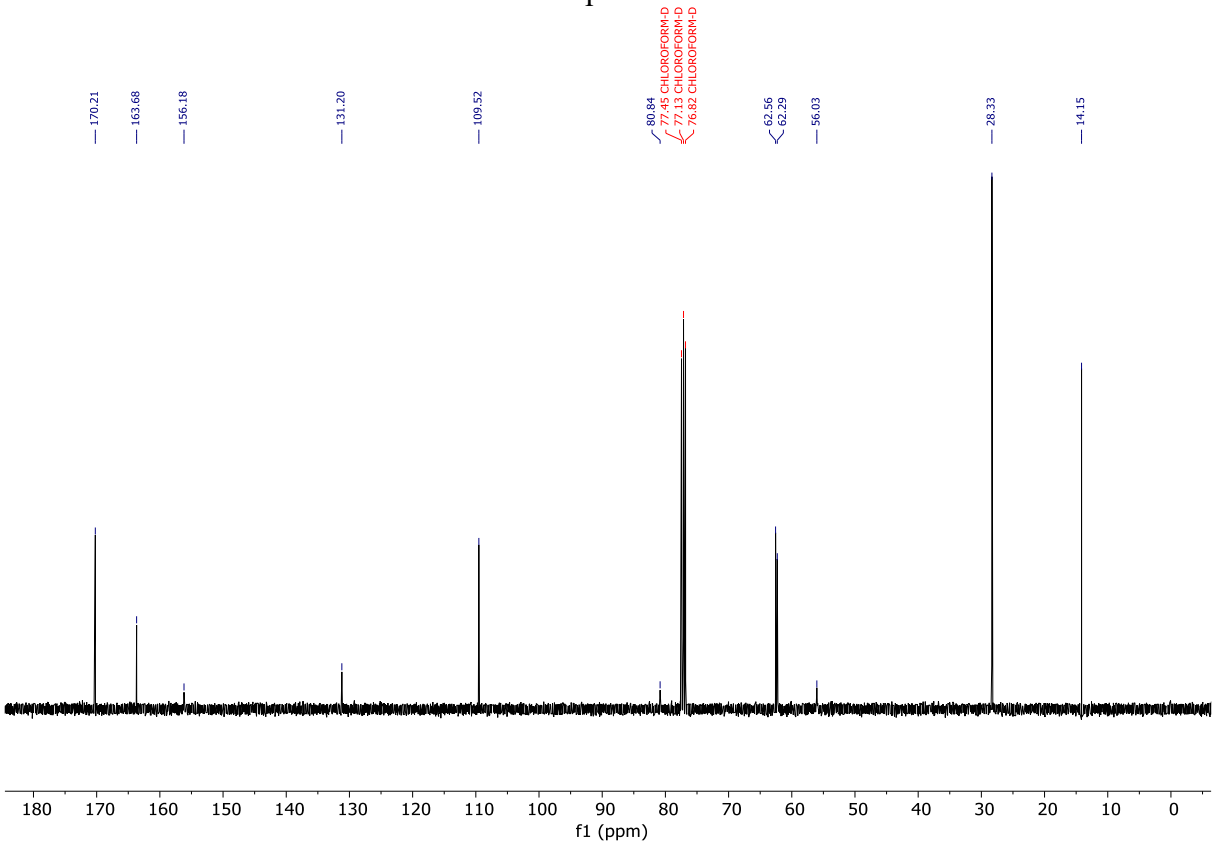
^{1}H NMR spectrum of **37**



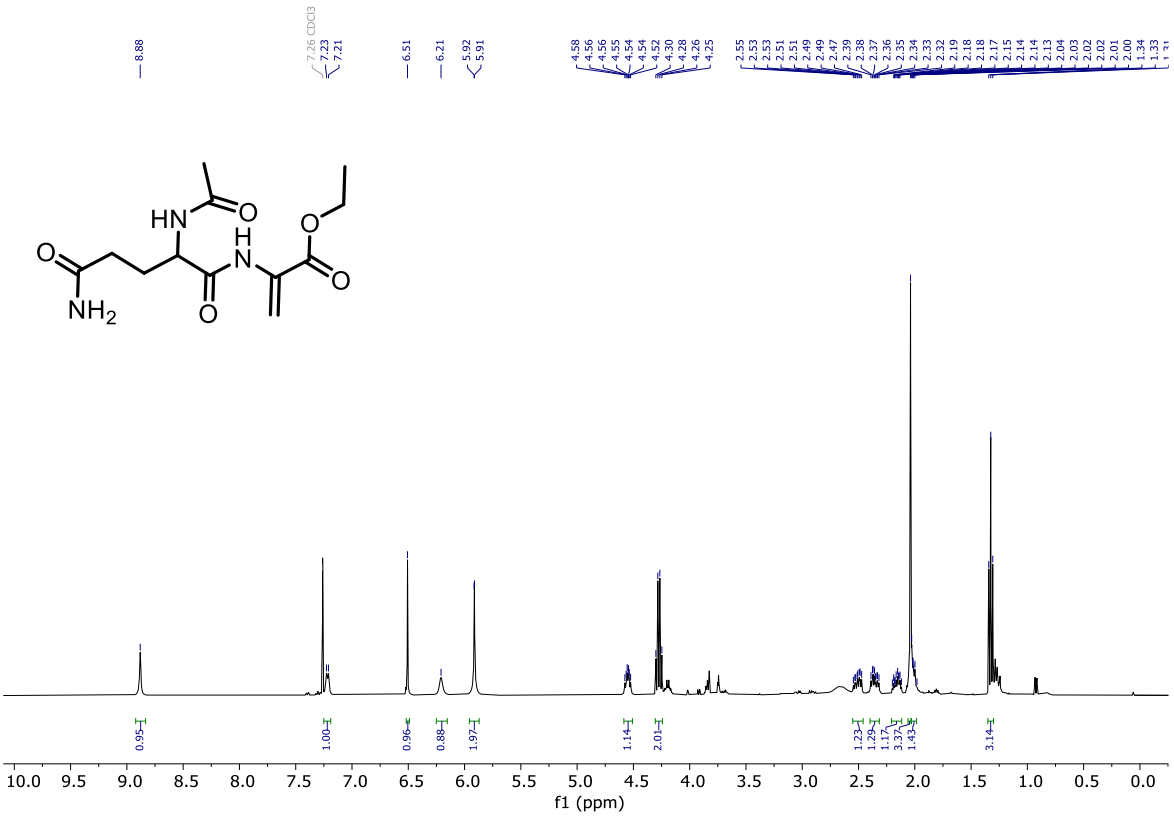
^{13}C NMR spectrum of **37**



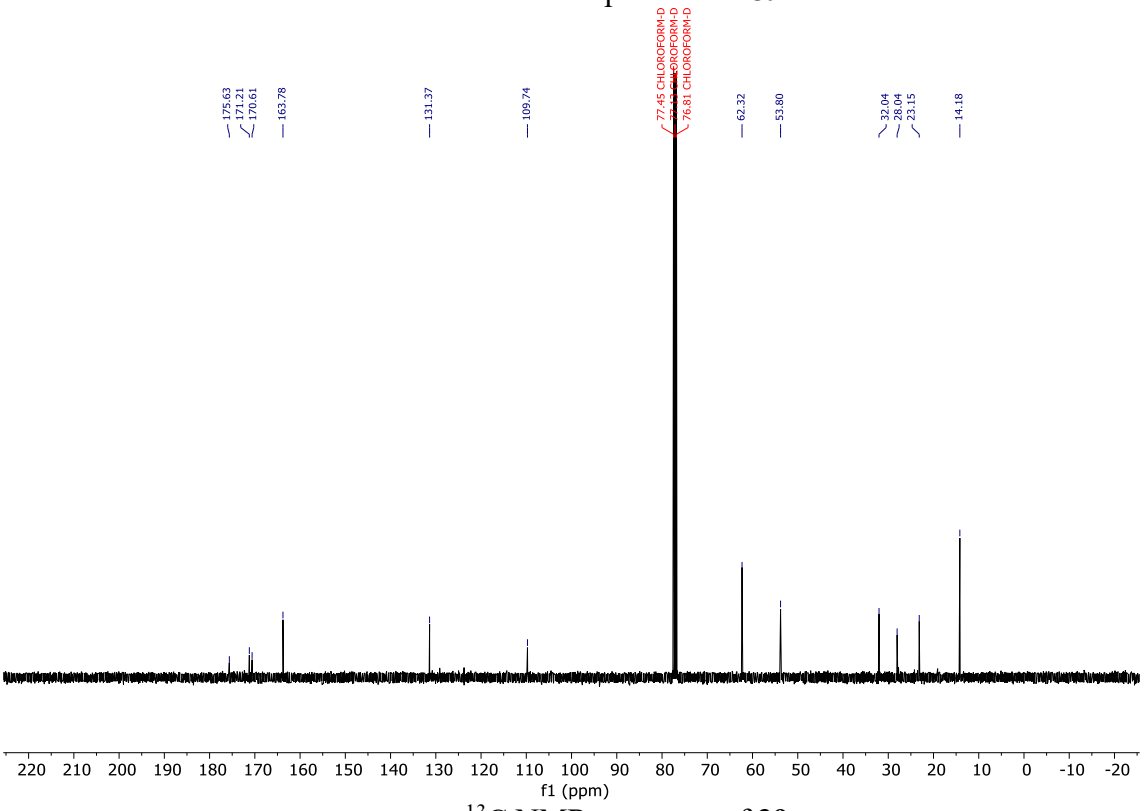
^{1}H NMR spectrum of **38**



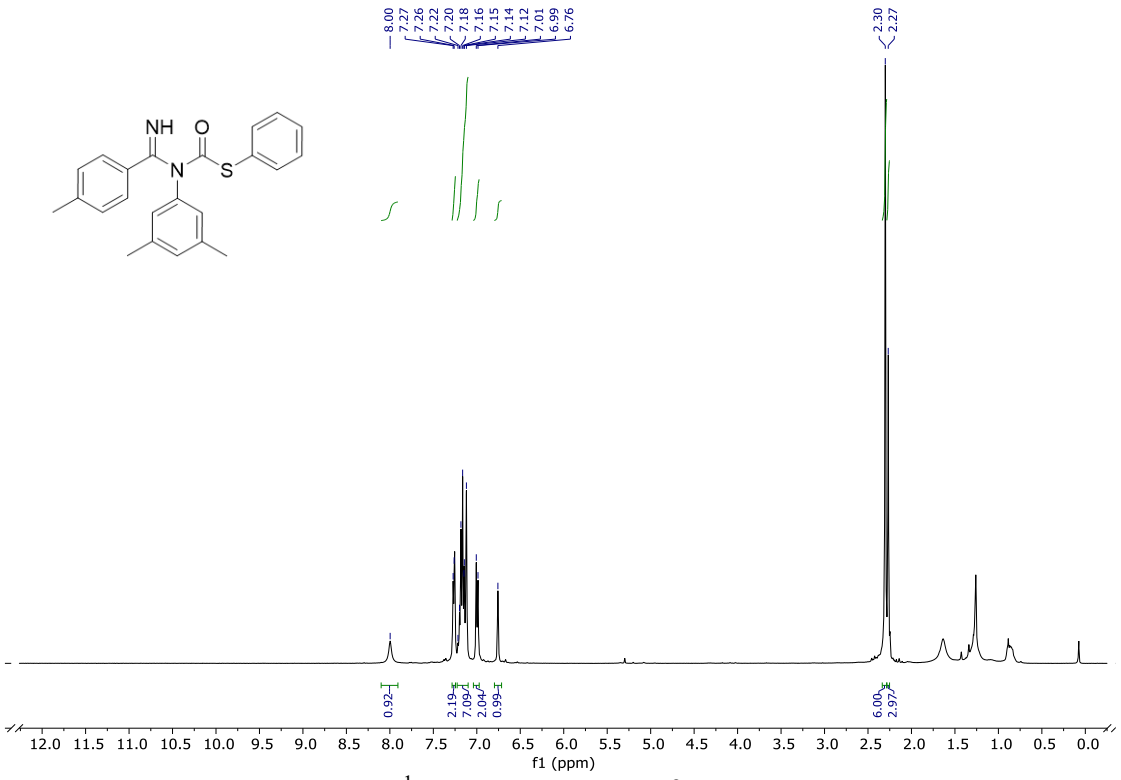
^{13}C NMR spectrum of **38**



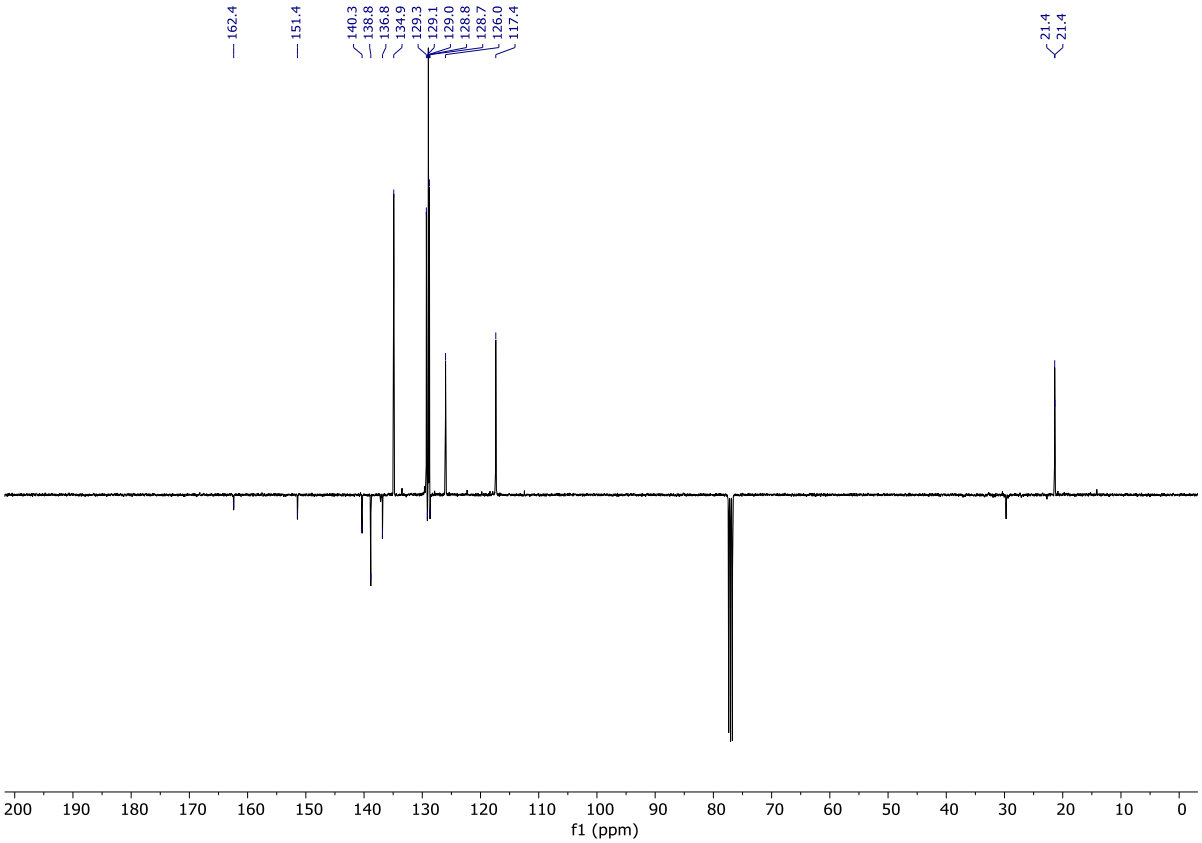
^{1}H NMR spectrum of **39**



^{13}C NMR spectrum of **39**



^{1}H NMR spectrum of **43**



^{13}C NMR spectrum of **43**

10. TD-DFT

Computational methodology: Geometry optimizations were carried out at the WB97XD/cc-pVTZ level with CPCM (dichloroethane) solvation using Gaussian 16 package.[14] Excited-state calculations were performed using time-dependent density functional theory (TD-DFT) at the same level of theory. Interfragment charge transfer in the S1 state was quantified using the IFCT method implemented in Multiwfn,[14] based on Hirshfeld partitioning.

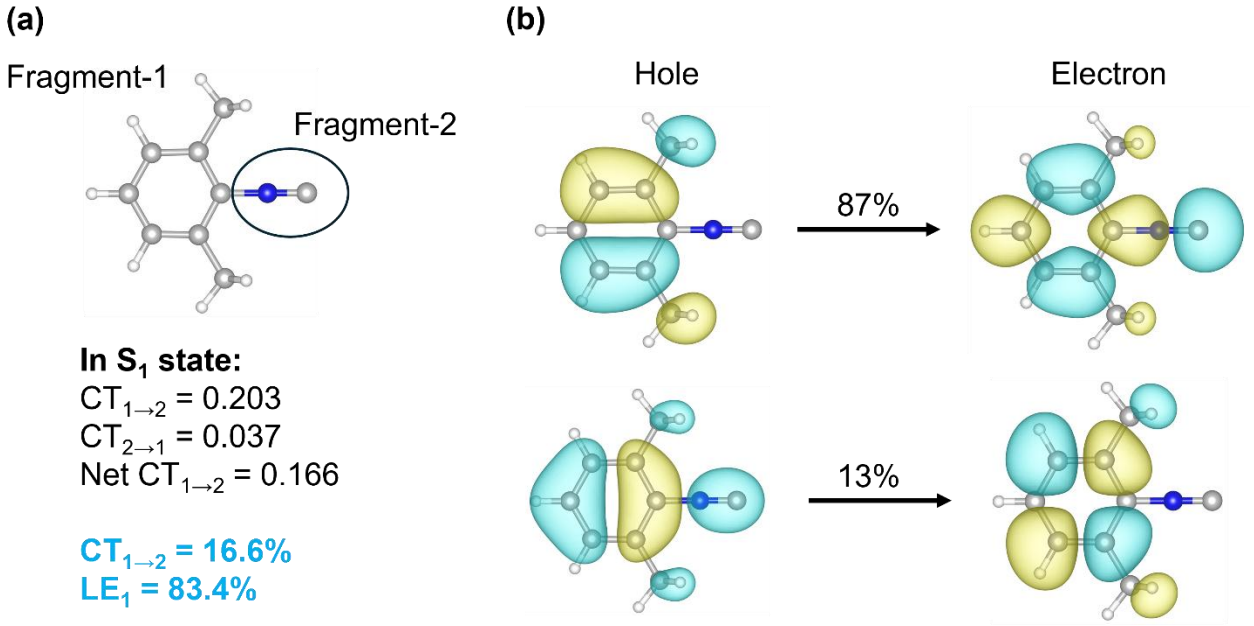


Figure S30. (a) Fragmentation scheme used to partition the isocyanide molecule into two fragments, where fragment-1 corresponds to the main molecular framework and fragment-2 represents the isocyanide (–NC) unit. The parameter Net $CT_{1\rightarrow2}$ denotes the net charge transfer from fragment-1 to fragment-2, while LE_1 refers to the locally excited character confined to fragment 1 in S_1 excited state. (b) Natural transition orbitals (NTOs) associated with the $S_0\rightarrow S_1$ excitation of the isocyanide molecule. The percentages indicated above the arrows represent the relative weight of each NTO pair.

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