Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Informations

Visible/Solar-Light-Driven Thiyl-Radical-Triggered Synthesis of Multi-Substituted Pyridines

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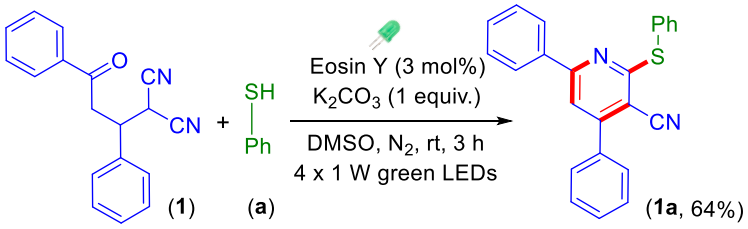
Contents:

1. General Procedures

(A) General Procedure for 5 mmol Scale Reaction for the Synthesis of 4,6-Diphenyl-2-(phenylthio)nicotinonitrile (1a):

To an oven-dried 50 mL borosilicate round bottom flask, 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (5 mmol, 1.37 g), eosin Y (3 mol%, 0.135 g), and K_2CO_3 (1 equiv, 0.966 g). Then to the reaction mixture benzene thiol (**a**) (10.0 mmol, 1.10 g) in 2 mL of DMSO was added and stirred at room temperature under N_2 atmosphere for 3 h, tentatively at a distance of ~1–2 cm from four 1 W green LEDs. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (50 mL) and the organic layer was washed with ice-cooled water (20 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60–120 mesh) using hexane and ethyl acetate (98:2) as eluent to afford the 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) in 64% yield (Scheme S3). The identity and purity of the product was confirmed by spectroscopic analysis.

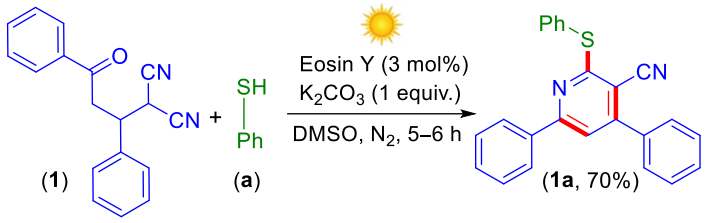


Scheme S1. Large-scale synthesis.

(B) General Procedure for the Synthesis of 4,6-Diphenyl-2-(phenylthio)nicotinonitrile (1a) in the Presence of Sunlight:

To an oven-dried 25 mL borosilicate round bottom flask, was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), eosin Y (3 mol%, 5 mg), and K_2CO_3 (1 equiv., 34 mg). Then to the reaction mixture benzene thiol (**a**) (0.5 mmol, 55 mg), in 1 mL DMSO was added and stirred at room temperature under N_2 atmosphere for 5–6 h, with the surrounding temperature 30–35 ^oC. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethylacetate (20 mL) and the organic layer was washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the

solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60-120 mesh) using hexane and ethyl acetate (98:2) as eluent to afford the 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) in 70% yield (Scheme S4). The identity and purity of the product was confirmed by spectroscopic analysis.



Scheme S2. Reaction performed in sunlight.

2. Light Information and Reaction Set-up:

Luxeon star 4 x 1 W green LEDs were used as a light source for this light promoted reaction without using any filter. The measured wavelength is 523 nm with measured flux of 39 mW/cm^2, and borosilicate glass vial was used as a reaction vessel. Distance from the light source to the irradiation vessel ~1–2 cm. Regular fan was used for proper aeration to maintain the temperature 28–30 ^{o}C (Fig. S1).

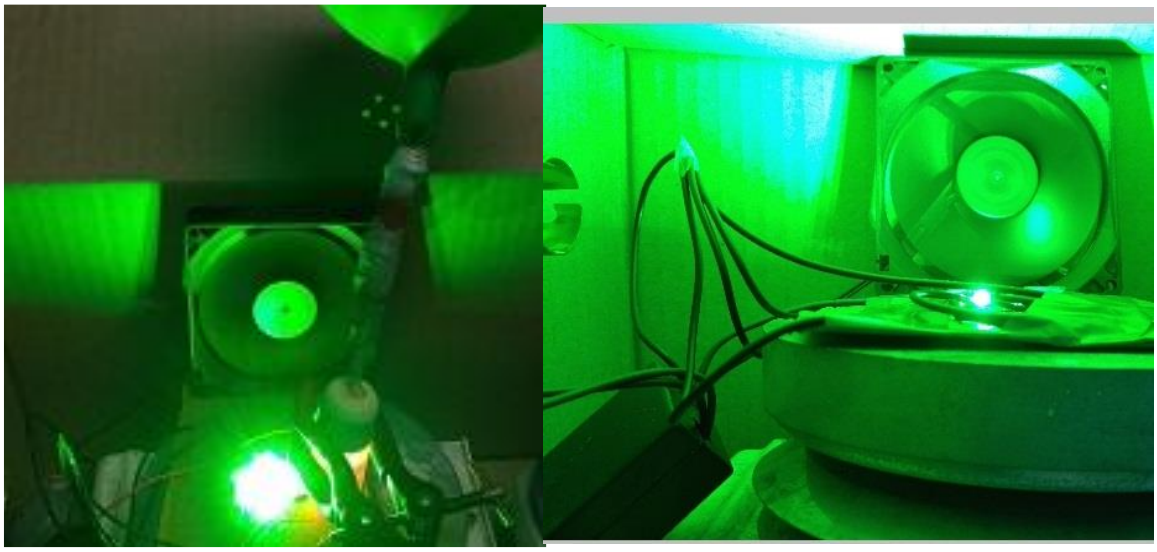


Fig. S1. Photochemical reaction set-up (outside & inside view).

3. Crystallographic Information:

(A) Sample Preparation:

The single crystal of compound **1f** was prepared by the slow evaporation method for which 10 mg of the compound (**1f**) was dissolved in 1 mL of DCM in a clean and dry 10 mL glass vial. MeOH (0.5 mL) was added to this solution slowly with a dropper. The mouth of the glass vial was covered with a cap having a small hole and kept it for slow evaporation at room temperature. Transparent white needle-like single crystals of **1f** was obtained after 2–3 days.

(B) Crystallographic Description of 2-(4-Fluorophenyl)thio)-4,6-diphenylnicotinonitrile (1f):

Diffraction data were collected at 292 K with MoKα radiation (λ = 0.71073 Å) using a Bruker Nonius SMART APEX CCD diffractometer equipped with graphite monochromator and Apex CD camera. The SMART software was used for data collection and for indexing the reflections and determining the unit cell parameters. Data reduction and cell refinement were performed using SAINT[1,2] software and the space groups of these crystals were determined from systematic absences by XPREP and further justified by the refinement results. The structures were solved by direct methods and refined by full-matrix least-squares calculations using SHELXTL-97[3] software. All the non-H atoms were refined in the anisotropic approximation against F^2 of all reflections.

1. G. M. Sheldrick, SADABS, 1996, based on the method described in: R. H. Blessing, *Acta Crystallogr.* 1995, **A51**, 33–38.
2. SMART and SAINT, Siemens Analytical X-ray Instruments Inc., Madison, WI, 1996.
3. G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112–122.

$C_{24}H_{15}FN_2S$, crystal dimensions 0.35 x 0.31 x 0.29 mm, M_r = 382.44, monoclinic, space group P 21/c, a = 13.2258 (5), b = 8.0745 (3), c = 19.2139 (8) Å, α = 90°, β = 109.317 (1)°, γ = 90°, V = 1936.37 (13) Å^3, Z = 4, ρ_{calcd} = 1.312 g/cm^3, μ = 0.188 mm^{-1}, F(000)= 792.0, reflection collected / unique = 32809 / 3414, refinement method = full-matrix least-squares on F^2, final R indices [I> 2\s(I)]:R_1 = 0.0407, wR_2 = 0.0973, R indices (all data): R_1 = 0.0601, wR_2 = 0.1182, goodness of fit = 1.037. CCDC-2201897 for 2-((4-fluorophenyl)thio)-4,6-diphenylnicotinonitrile **(1f)** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

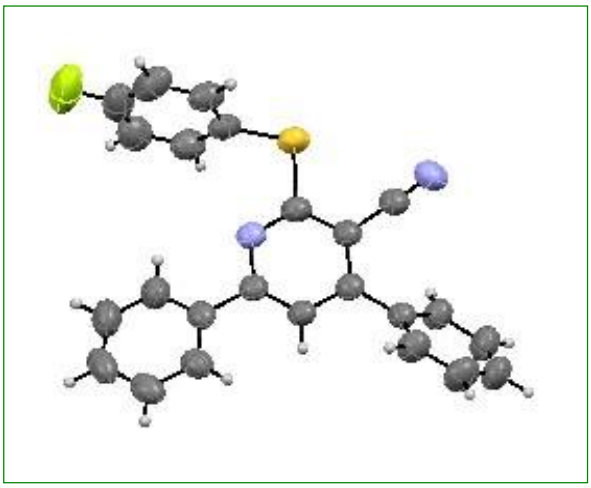
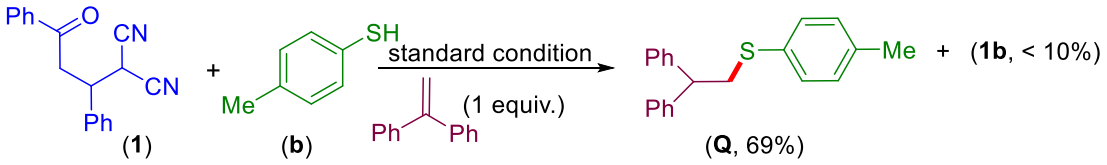


Fig. S2. ORTEP diagram of 2-((4-fluorophenyl)thio)-4,6-diphenylnicotinonitrile (**1f**) with 40% ellipsoid probability (CCDC 2201897).

4. Mechanistic Investigation:

(A) Radical-trapping Experiments:

(i) To an oven-dried 10 mL borosilicate vial was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), *p*-methyl benzene thiol (**b**) (0.5 mmol, 62 mg), eosin Y (3 mol%, 5 mg), and K_2CO_3 (1 equiv., 34 mg). Then 1,1-diphenyl ethylene (1 equiv, 45 mg) in 1 mL of DMSO was added and stirred at room temperature under N_2 atmosphere for 3 h tentatively at a distance of ~1–2 cm from four 1 W green LEDs. It was found that in the presence of diphenyl ethylene <10% of the product (**1b**) and exclusive thiyl radical trapped adduct (**Q**, 69%) was observed (Scheme S5). The structure of the adduct (**Q**) was confirmed by HRMS (Fig. S3) and ^{1}HNMR analysis (Fig. S4).



Scheme S3. Radical-trapping experiment.

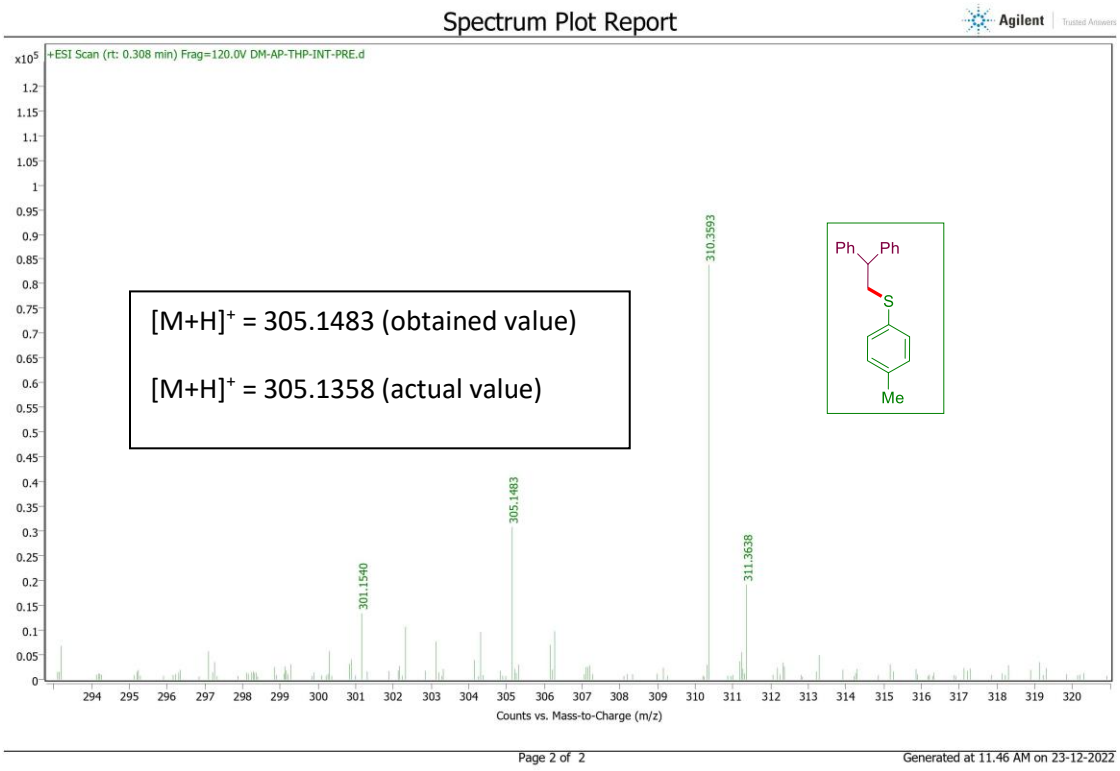


Fig. S3. HRMS spectra of thiyl-radical trapped adduct (**Q**).

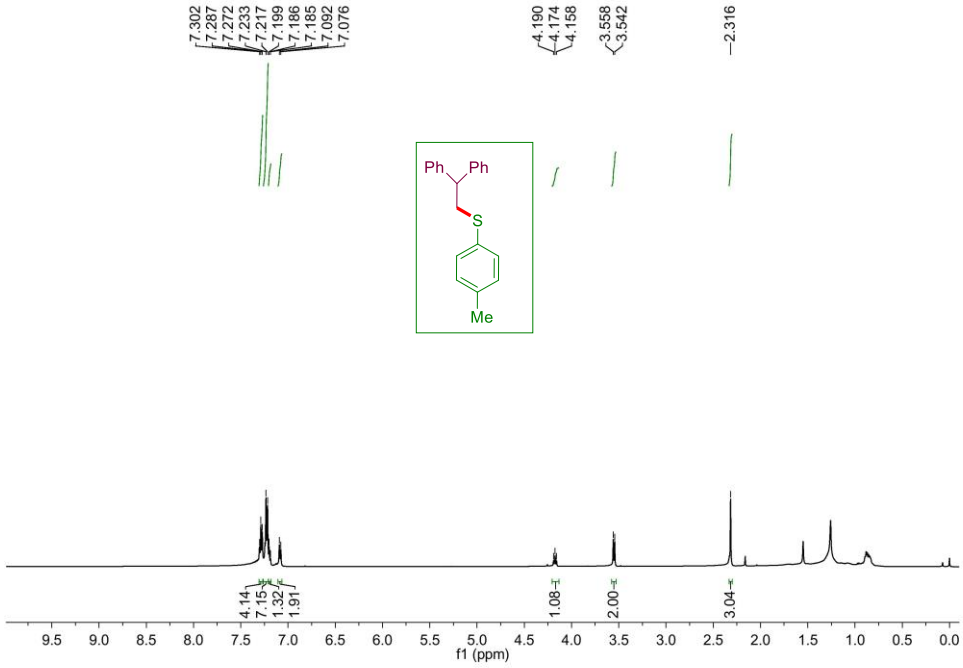


Fig. S4. ^{1}HNMR spectra of thiyl-radical trapped adduct (**Q**).

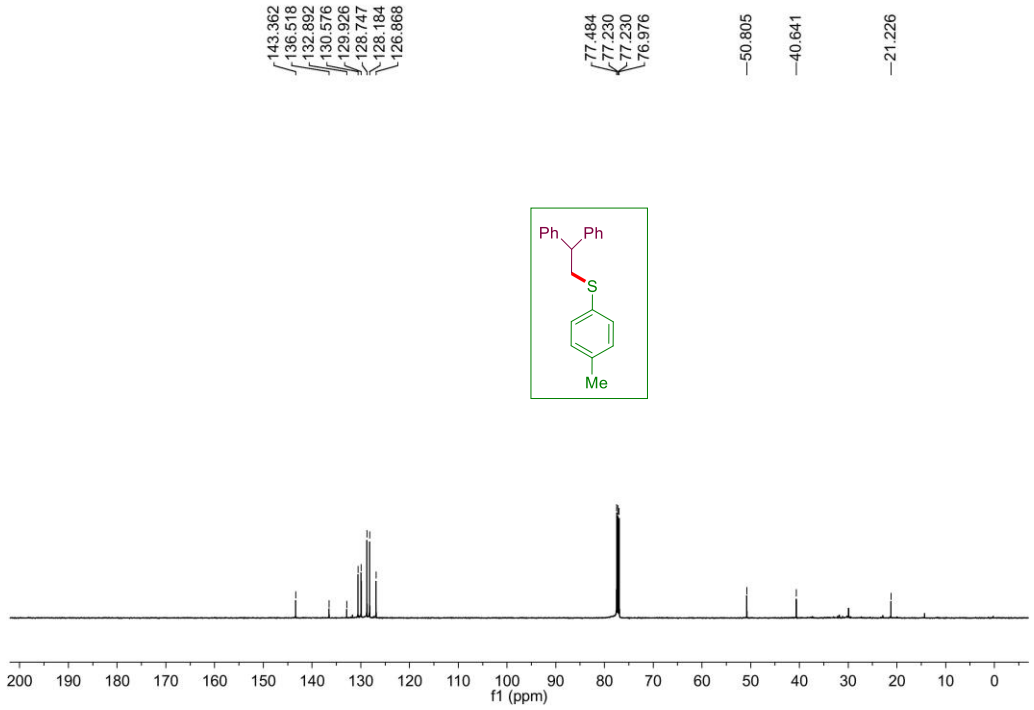


Fig. S5. $^{13}C\{1H\}$ NMR spectra of thiyl-radical trapped adduct (**Q**).

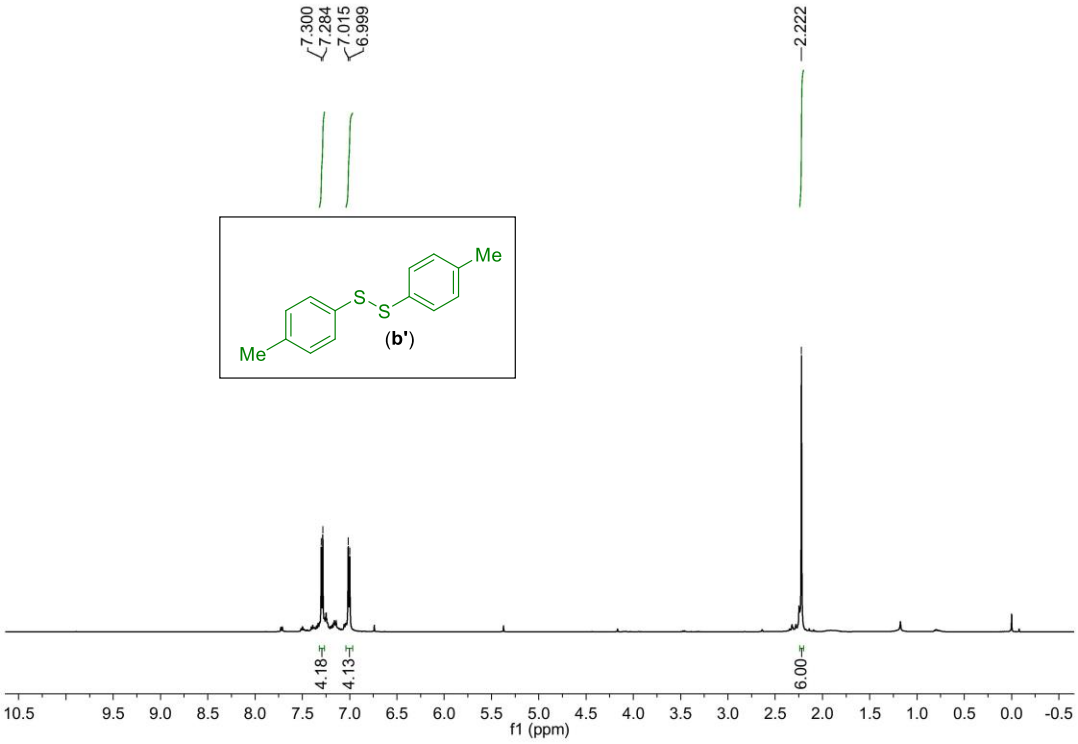


Fig. S6. ^{1}H NMR spectra of (**b′**).

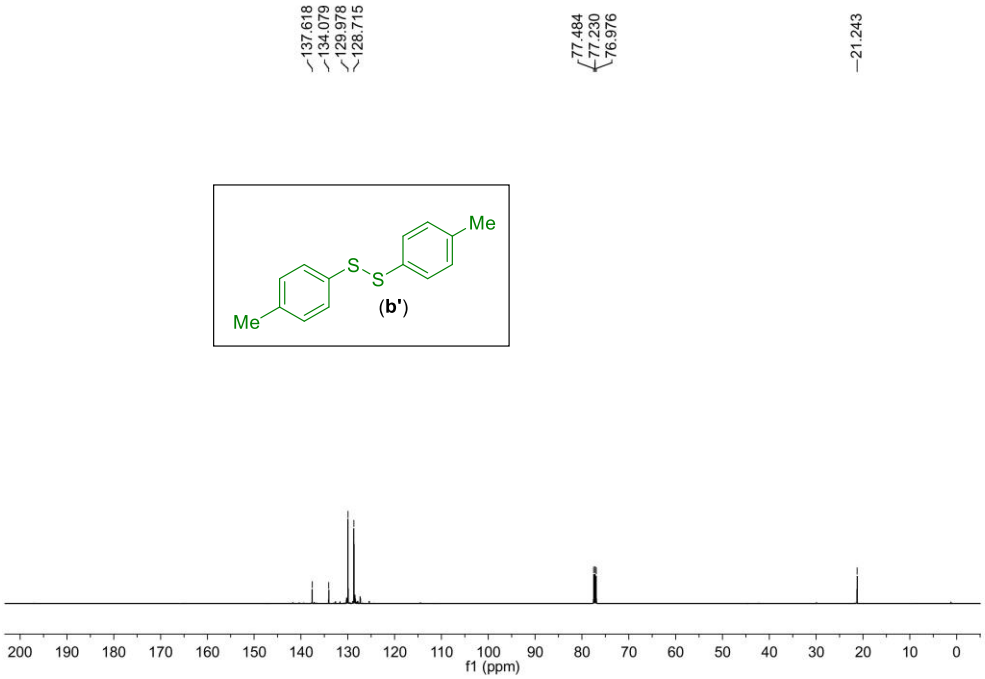
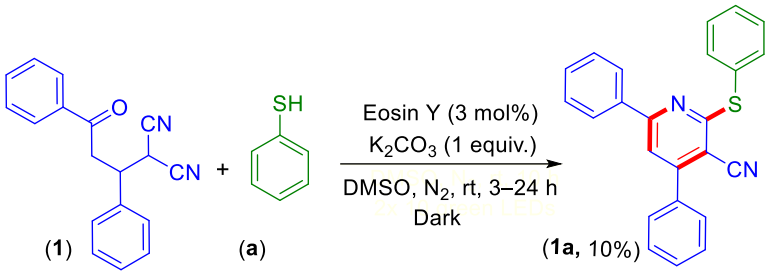


Fig. S7. $^{13}C\{^{1}H\}$ NMR spectra of (**b′**).

(B) Control experiments

(I) In the Absence of Light:

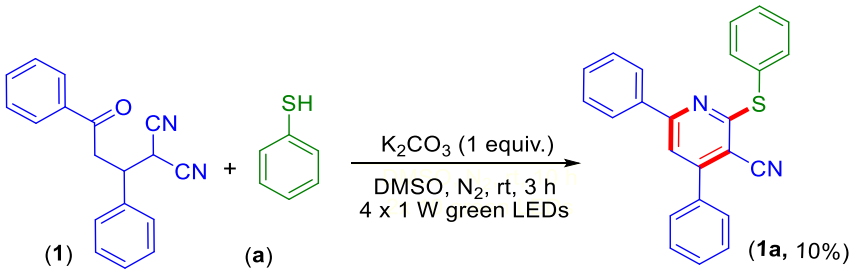
To an oven-dried 10 mL borosilicate vial was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), eosin Y (3 mol%, 5 mg), and K_2CO_3 (1 equiv., 34 mg). Then benzene thiol (**a**) (0.5 mmol, 55 mg), in 1 mL of DMSO was added and then covered with an aluminium foil so that light cannot interact with the reaction mixture. Then the reaction mixture stirred at room temperature under N_2 atmosphere for 3 h. It was observed that around 10% of **1a** was formed (monitored by TLC analysis). Then the reaction was continued for 24 h to check the further progress. After completion of the reaction, the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer was washed with ice-cooled water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60−120 mesh) using hexane and ethyl acetate (98:2) as an eluent to afford the 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) in 10% yield. The identity and purity of the product were confirmed by spectroscopic analysis (Scheme S6).



Scheme S4. Reaction performed in the dark.

(II) In the Absence of Catalyst:

To an oven-dried 10 mL borosilicate vial were added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), and K_2CO_3 (1 equiv, 34 mg). Then benzene thiol (**a**) (0.5 mmol, 55 mg) in 1 mL of DMSO was added and stirred at room temperature under N_2 atmosphere for 3 h, tentatively at a distance of ~1−2 cm from four 1 W green LEDs. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer is washed with ice-cooled water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60−120 mesh) using hexane and ethyl acetate (98:2) as an eluent to afford the 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) in 10% yield suggesting the crucial role of catalyst in the generation of thiyl radical. The identity and purity of the product were confirmed by spectroscopic analysis (Scheme S7).

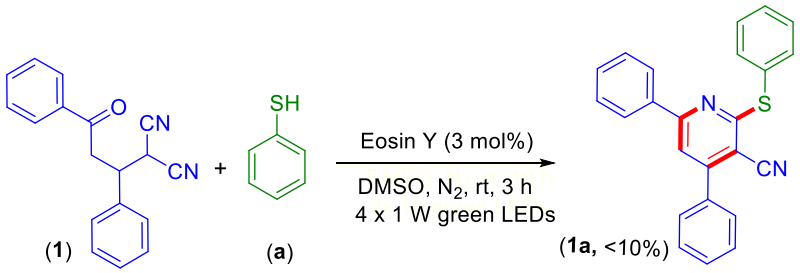


Scheme S5. Reaction in the absence of catalyst

(III) Reaction in the Absence of Base

To an oven-dried 10 mL borosilicate vial was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), and eosin Y (3 mol%, 5 mg). Then

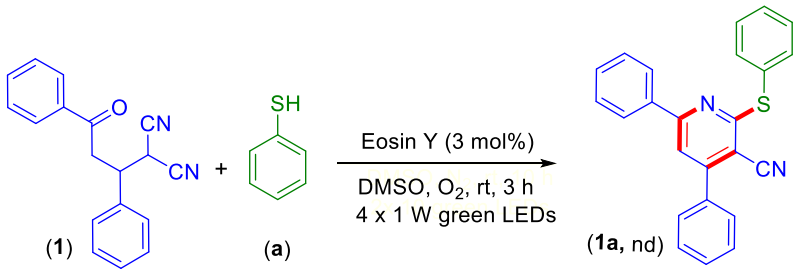
benzene thiol (**a**) (0.5 mmol, 55 mg) in 1 mL of DMSO was added and stirred at room temperature under N_2 atmosphere for 10 h, tentatively at a distance of ~1−2 cm from four 1 W green LEDs. It was found that a trace amount (<10%) of the product (**1a**) was obtained (as monitored by TLC) suggesting the necessity of the base in the present protocol (Scheme S8).



Scheme S6. Reaction in absence of base

(IV) Reaction in the Absence of Base and in the Presence of Oxygen

To an oven-dried 10 mL borosilicate vial was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), and eosin Y (3 mol%, 5 mg). Then benzene thiol (**a**) (0.5 mmol, 55 mg), in 1 mL of DMSO was added and stirred at room temperature under O_2 atmosphere for 3 h, tentatively at a distance of ~1−2 cm from four 1 W green LEDs. It was found that no desired product (**1a**) was obtained (as monitored by TLC) suggesting the silence of oxygen in the present protocol (Scheme S9).

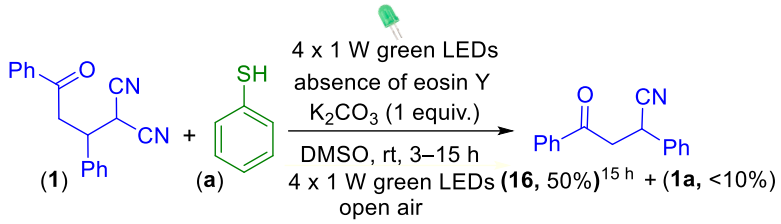


Scheme S7. Reaction in absence of base and presence of oxygen.

(V) Reaction in the Absence of Photosensitizer in Open Air

To an oven-dried 10 mL borosilicate vial were added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), and K_2CO_3 (1 equiv., 34 mg). Then benzene thiol (**a**) (0.5 mmol, 55 mg) in 1 mL of DMSO was added and stirred at room temperature under open air for 3 h, tentatively at a distance of ~1−2 cm from four 1 W green LEDs. It was observed that the desired product **1a** was obtained in <10% yield, while to see the

further conversion the reaction was continued for 15 h and it was observed that (**1**) consumed completely and a new spot was formed. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer is washed with ice-cooled water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60−120 mesh) using hexane and ethyl acetate (98:2) as an eluent to afford the 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) in <10% yield and 4-oxo-2,4-diphenylbutanenitrile (16), in 50% yield (Scheme S10). The identity of the product was confirmed by ^{1}HNMR analysis (Fig. S5).



Scheme S8. Reaction in the absence of Eosin Y in open air

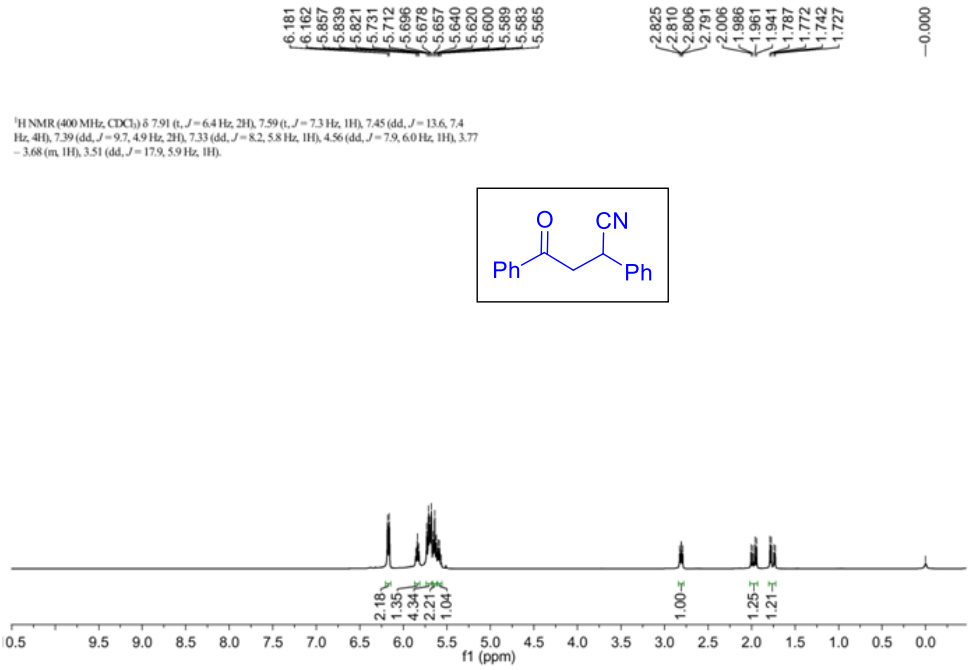
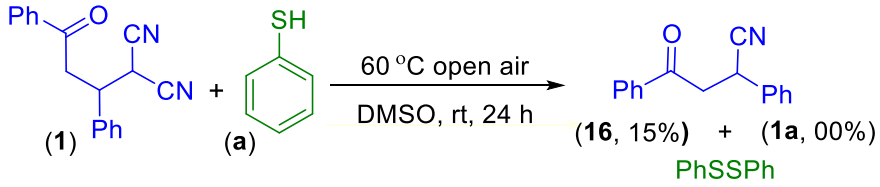


Fig. S8. ^{1}H NMR spectra of (**16**).

(VI) Reaction under Thermal Condition in the Absence of Base and Eosin Y in Open Air

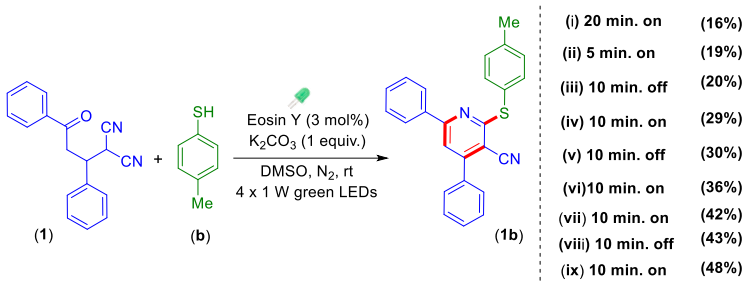
To an oven-dried 10 mL round bottom flask were added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol, 68 mg), benzene thiol (**a**) (0.5 mmol, 55 mg) in 1 mL of DMSO was added and stirred at 60 °C under open air for 24 h. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer is washed with ice-cooled water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (60−120 mesh) using hexane and ethyl acetate (98:2) as an eluent to afford the 4-oxo-2,4-diphenylbutanenitrile (**16**), in 15% yield (Scheme S11). The identity of the product was confirmed by ^{1}HNMR analysis. No trace of the desired product 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) was obtained.



Scheme S9. Reaction under thermal condition in the absence of Eosin Y and base in open air.

(C) On-off Experiments

The reaction mixture was stirred and irradiated by 4 x 1 W green LEDs at room temperature under a nitrogen atmosphere for 20 minutes, and the corresponding product (**1b**) was isolated in 16% yield. Then the reaction mixture was continuously stirred for further 5 minutes and the desired product (**1b**) was obtained in 19% yield. When the reaction mixture was continued under dark for another 10 min the desired product (**1b**) was obtained in 20% yield. Furthermore, when the reaction mixture was stirred and irradiated by 4 x 1 W green LEDs at room temperature under a nitrogen atmosphere for 10 minutes, the desired product (**1b**) was isolated in 29% yield. This procedure was repeated at regular time intervals and the above results indicated that continuous visible light irradiation is essential for promoting this transformation (Figure S7). The NMR spectra were recorded taking nitromethane as the internal standard $CDCl_3$ as the solvent.



Scheme S10. On-off experiments

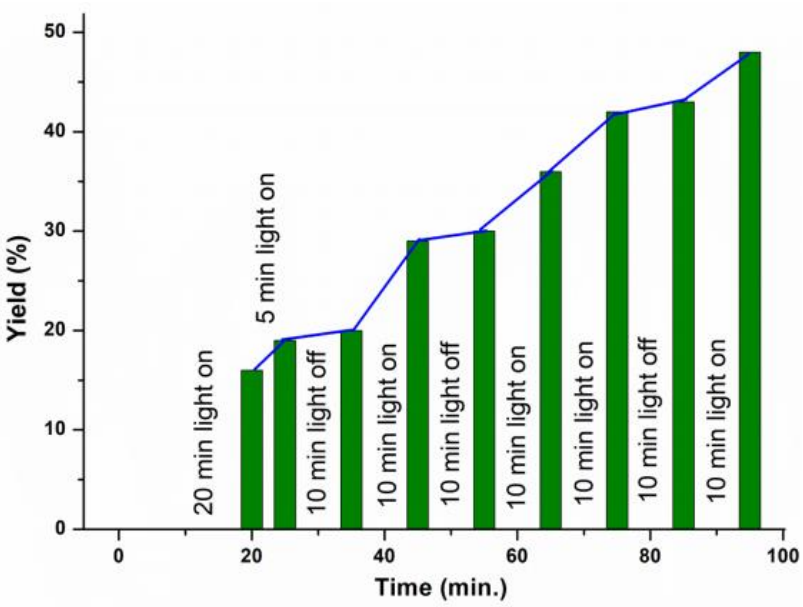


Fig. S9 Stair type graph for on-off experiments.

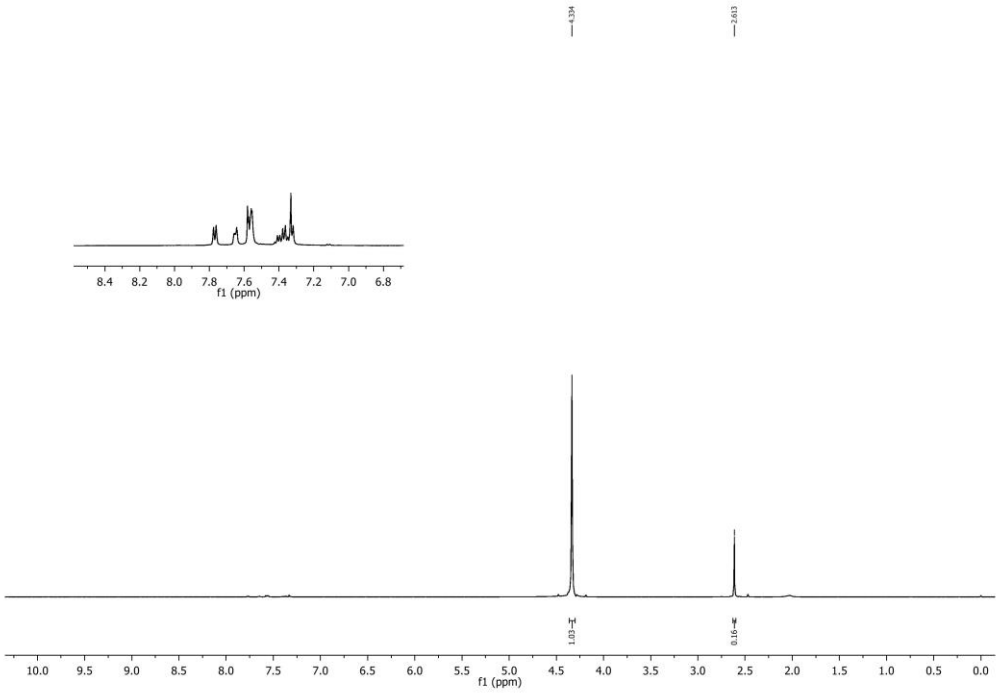


Fig. S10. ^{1}H NMR spectra of the on-off experiment (20 min. light on).

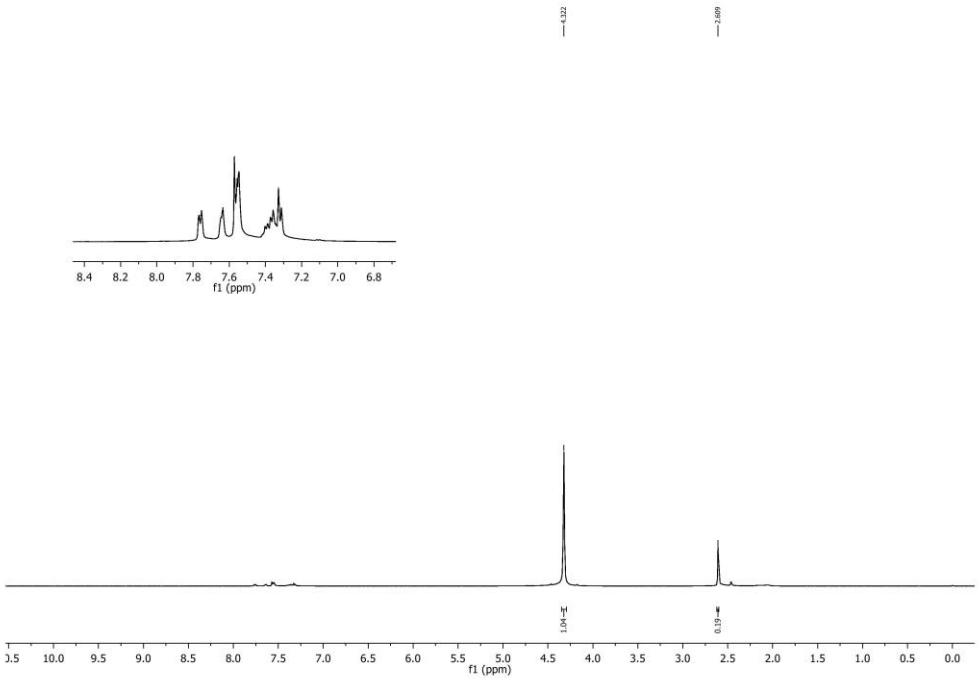


Fig. S11. ^{1}H NMR spectra of the on-off experiment (further 5 min. light on).

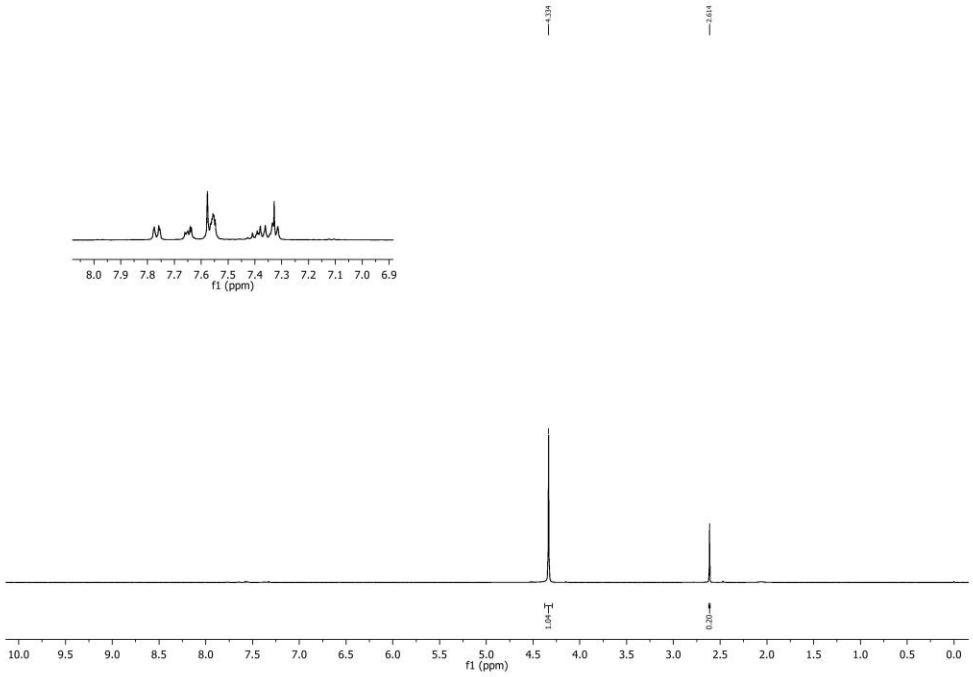


Fig. S12. ^{1}H NMR spectra of the on-off experiment (further 10 min. light off).

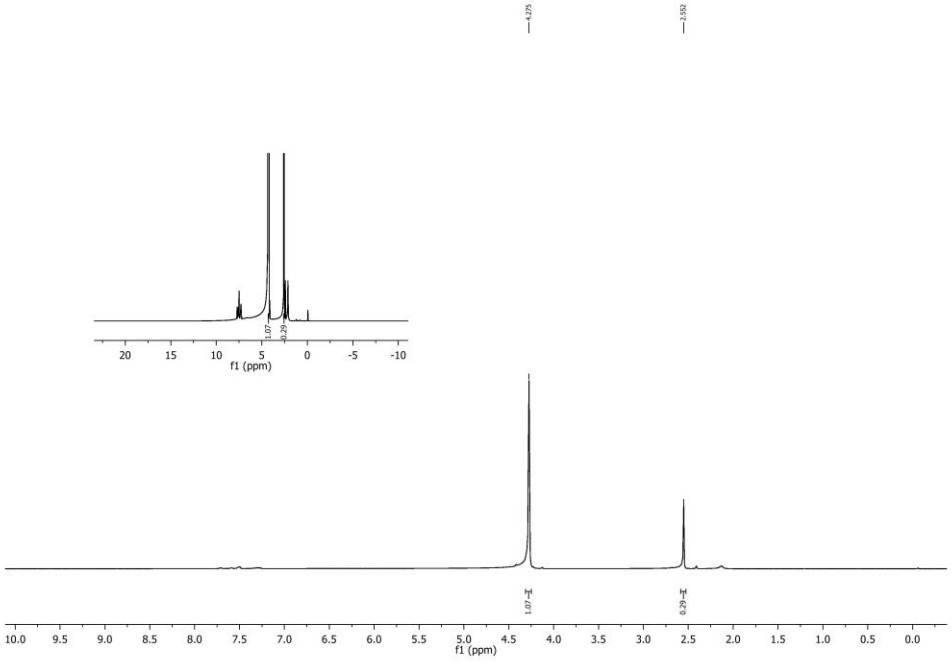


Fig. S13. ^{1}H NMR spectra of the on-off experiment (further 10 min. light on).

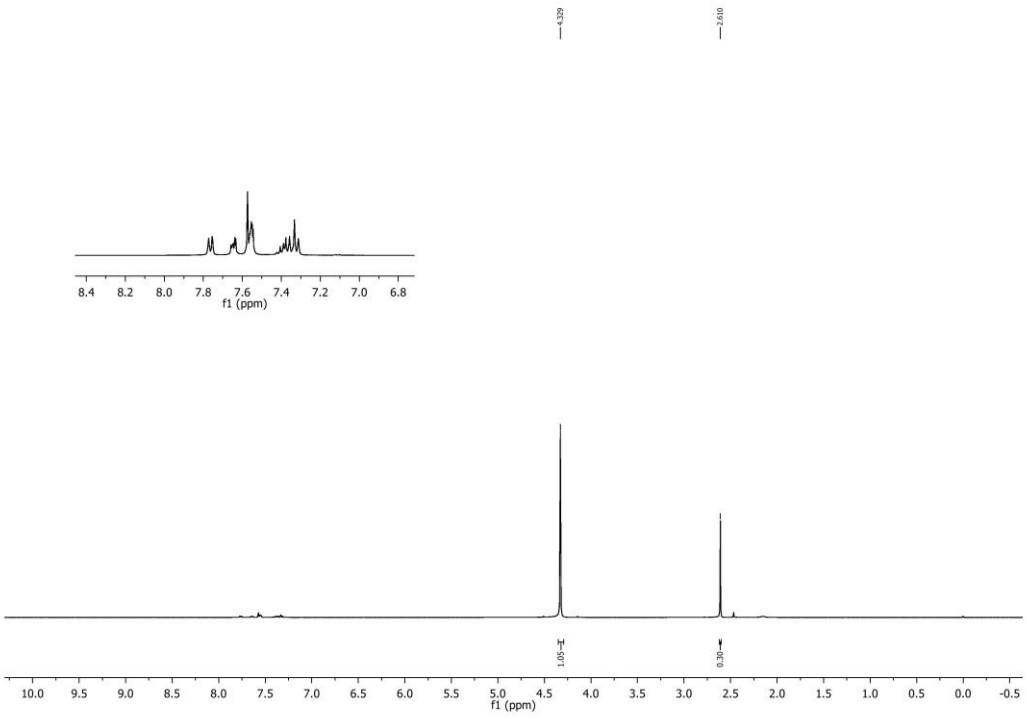


Fig. S14. ^{1}H NMR spectra of the on-off experiment (further 10 min. light off).

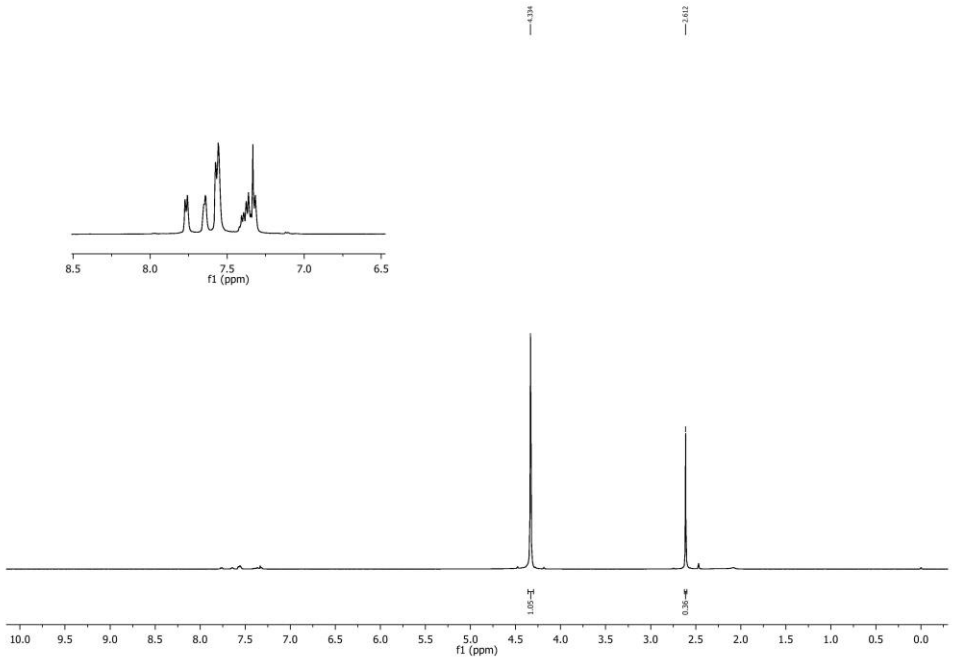


Fig. S15. ^{1}H NMR spectra of the on-off experiment (further 10 min. light on).

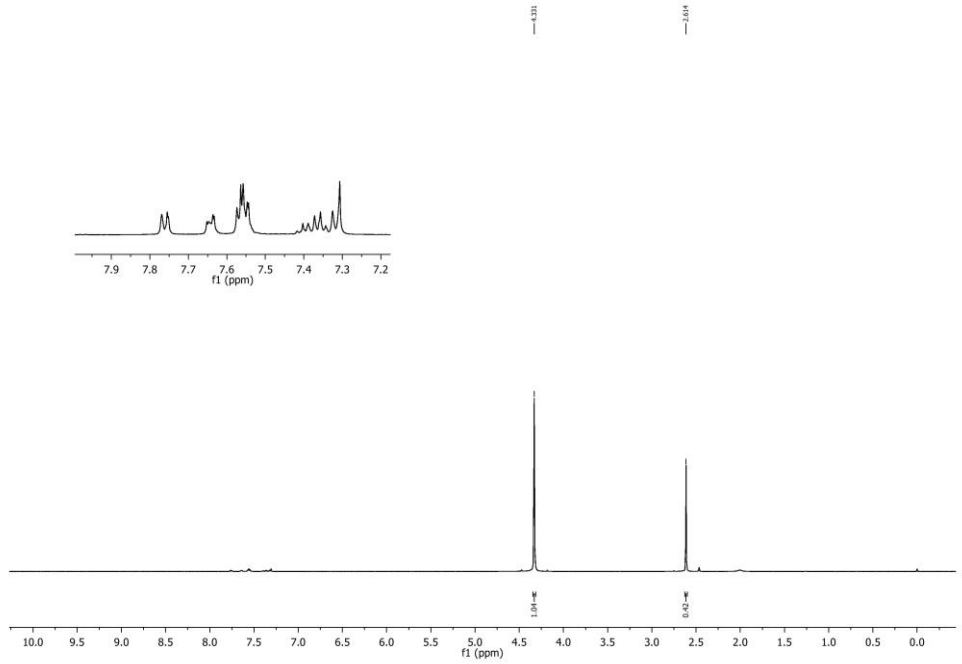


Fig. S16. ^{1}H NMR spectra of the on-off experiment (further 10 min. light on).

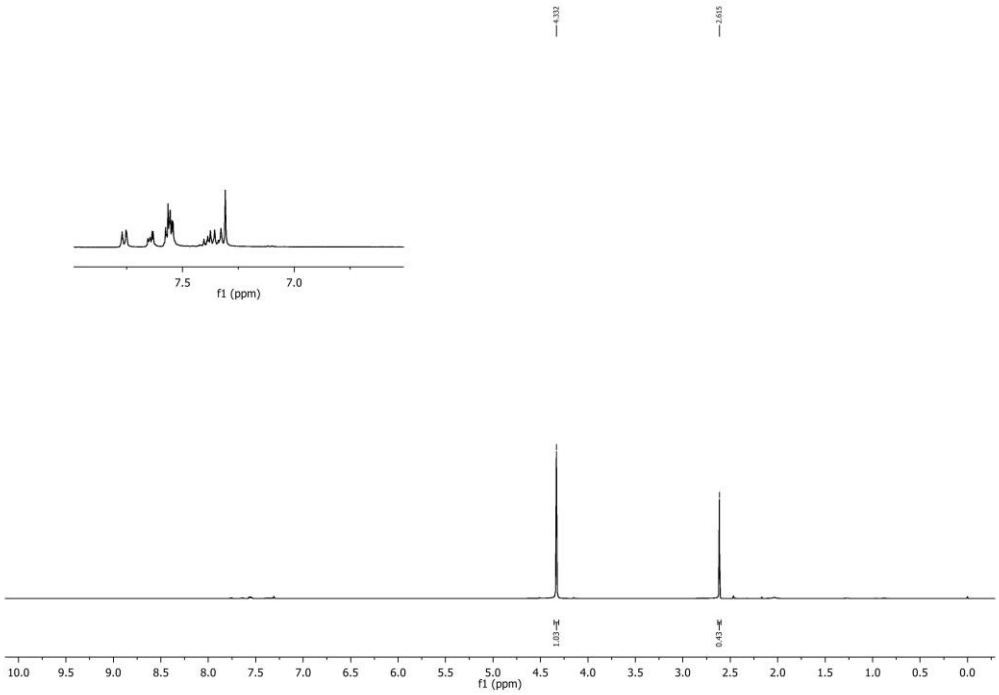


Fig. S17. ^{1}H NMR spectra of the on-off experiment (further 10 min. light off).

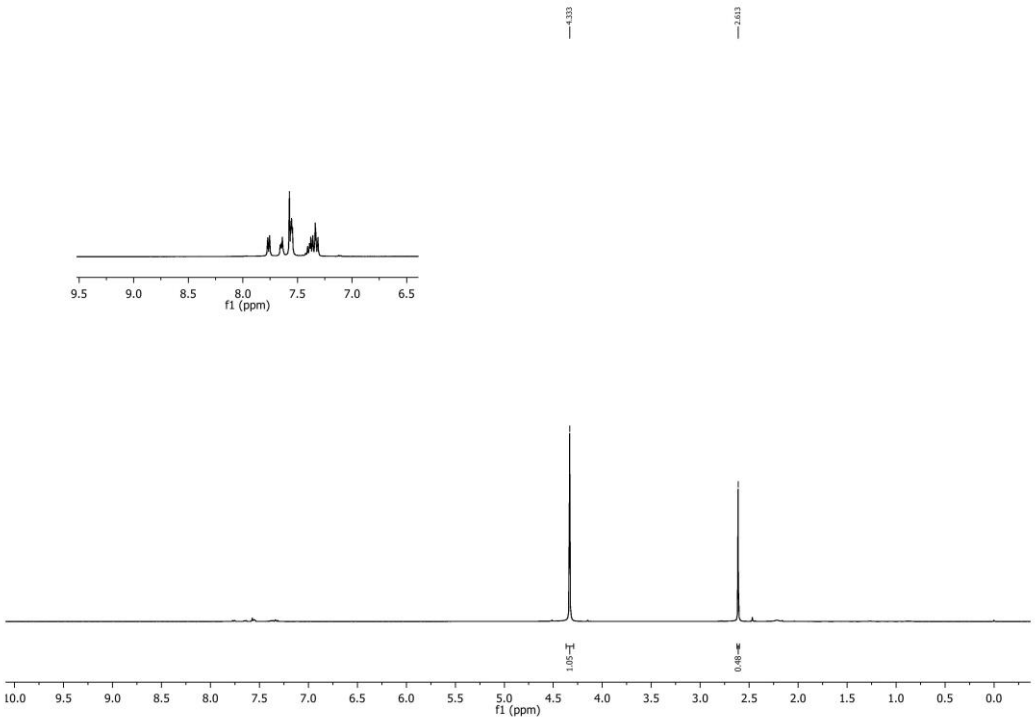


Fig. S18. ^{1}H NMR spectra of the on-off experiment (further 10 min. light on).

ESI-MS studies of the reaction mixtures:

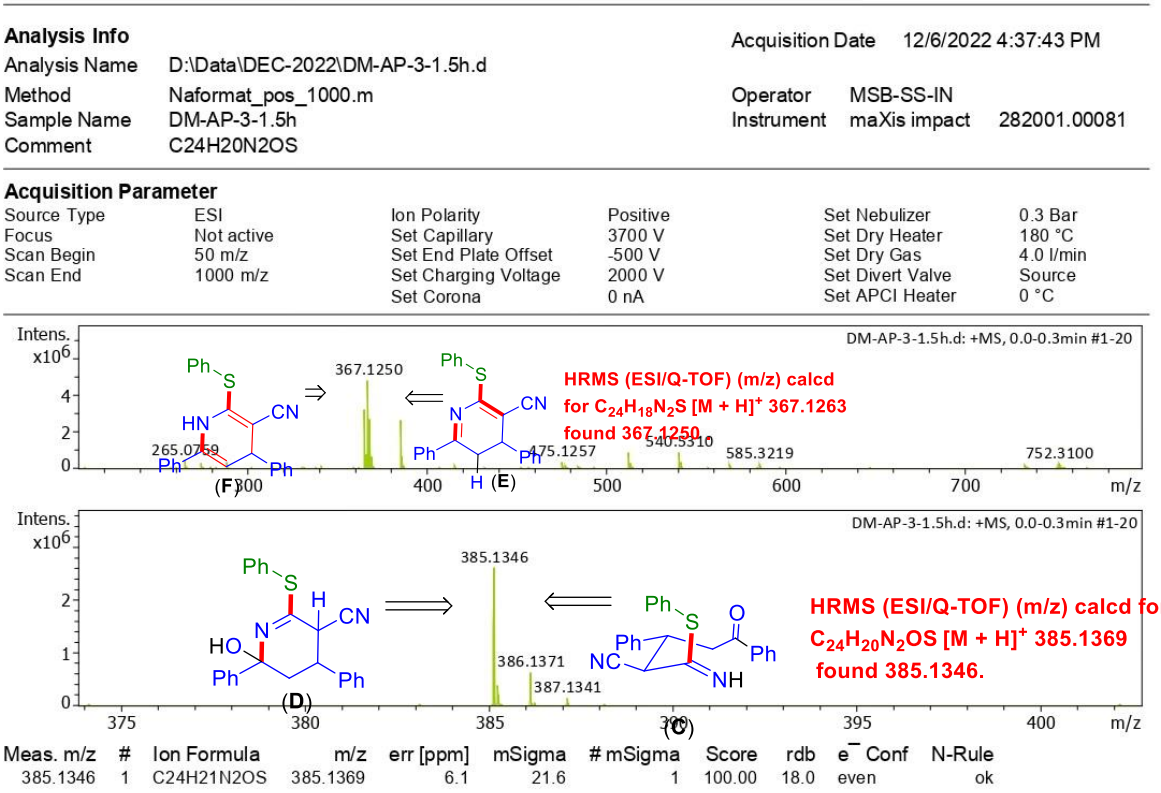


Fig. S19. HRMS spectrum after 1.5 h

5. SV Experiments:

A 1 mM solution was prepared by mixing eosin Y in water by an appropriate dilution of 0.01 M stock solution and taken in a quartz UV cuvette of a 1 cm path length. The UV−visible spectroscopy showed λmax of 515 nm. For the fluorescence measurement, the sample was excited at 515 nm, and the emission was observed at 560 nm. For each fluorescence quenching experiment, a 5 μL (1 M) solution of benzene thiol (a) was added to eosin Y solution (1 mM) taken in a fluorescence cuvette, and fluorescence emission spectra were recorded after each addition (Figure S6). As evident from Figure S6, a decrease in emission intensity was observed after each addition of thiophenol (a) concentration (5−75 mM). This suggests that a facile electron transfer is possible between the catalyst and the quencher PhSH. This indicates that eosin Y might be helping in the generation of thiyl radical from the PhSH. With these data, the Stern−Volmer graph was plotted using the equation I0/It =1+ KSV [Q], where I0 and It are the integrated emission intensity in the absence and presence of quencher and Ksv is the quenching constant. A linear quenching was observed (Figure S6).

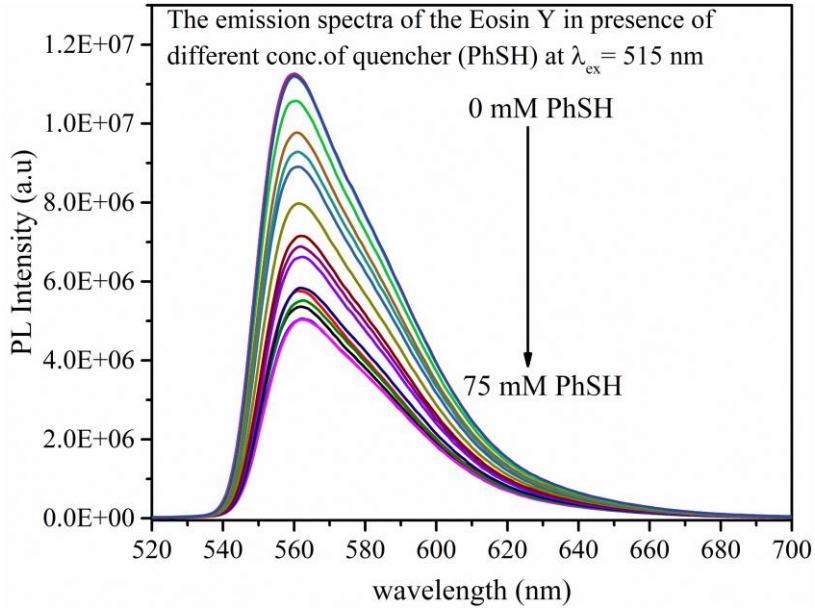


Fig. S20. Fluorescence emission spectra of eosin Y at varied conc. Of quencher thiophenol (**a**) when excited at 515 nm

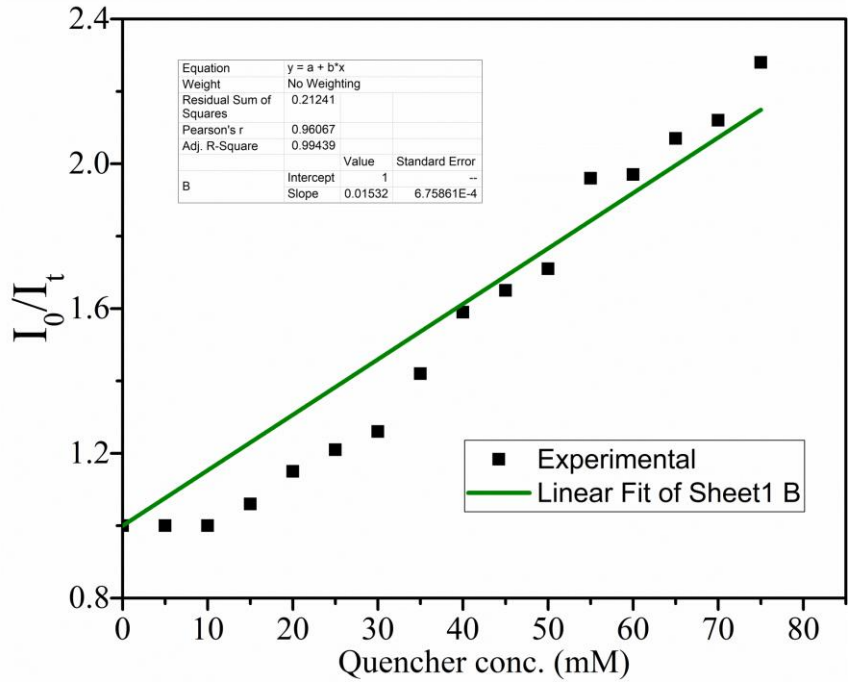


Fig. S21 Eosin Y emission quenching by quencher thiophenol (**a**)
(Linear quenching is observed)

A 1 mM solution was prepared by mixing eosin Y in water by an appropriate dilution of 0.01 M stock solution and taken in a quartz UV cuvette of a 1 cm path length. The UV−visible spectroscopy showed λmax of 515 nm. For the fluorescence measurement, the sample was excited at 515 nm, and the emission was observed at 560 nm. For each fluorescence quenching experiment, a 5 μL (1 M) solution of benzene thiol (a) was added to eosin Y solution (1 mM) taken in a fluorescence cuvette, and fluorescence emission spectra were recorded after each addition (Figure S6). As evident from Figure S6, a decrease in emission intensity was not uniform upon addition of thiolate anion (thiophenol + base) concentration (5−110 mM). This suggests that the electron transfer between the eosin Y and thiophenols is more facile as compared to that between eosin Y and thiolate anion. With these data, the Stern−Volmer graph was plotted using the equation I0/It =1+ KSV [Q], where I0 and It are the integrated emission intensity in the absence and presence of quencher and Ksv is the quenching constant. No linear quenching was observed (Figure S6).

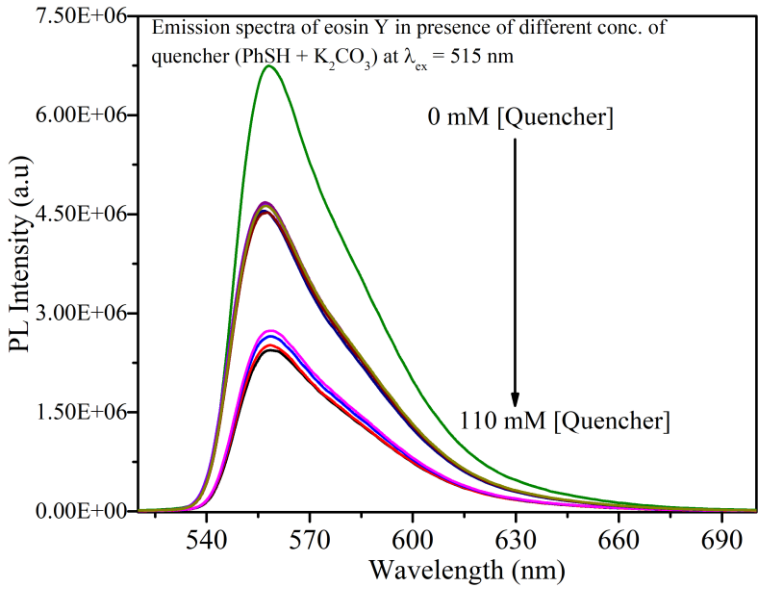


Fig. S22. Fluorescence emission spectra of eosin Y at varied conc. of quencher thiolate anion (thiol **(a)** + base) when excited at 515 nm.

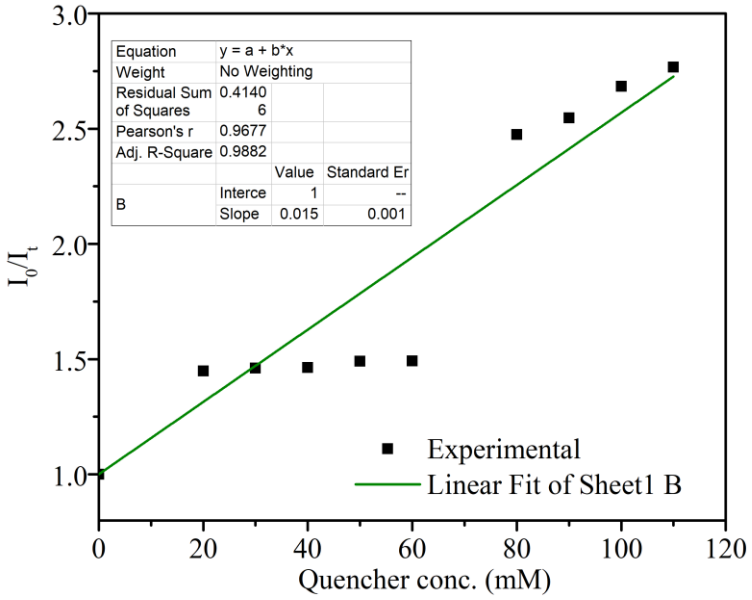


Fig. S23 Eosin Y emission quenching by quencher thiolate anion (thiol **(a)** + base)

6. CV Experiments:

(A) CV Experiments Performed to Determine the Redox Potentials.

Cyclic voltammetry (CV) was performed using a three-electrode cell configuration comprising a glassy carbon, a platinum wire, and Ag(s)/AgCl (0.01 M) as the working, auxiliary, and reference electrodes, respectively. Cyclic voltammetry experiment of PhSH and *β*-ketodinitrile (**1**) taken at a scan rate 100 mv/s. Experiment conditions: init E = 2.0 V, high E = 2.0 V, low E = −2.0 V, init P/N = N, scan rate = 0.1 V/s, sample interval = 0.001 V, quiet time = 2s, sensitivity = 2e−4 A/ V]. The supporting electrolyte used was tetraethylammonium hexafluorophosphate (TEAHFP) $(C_2H_5)_4N(PF_6)$. Samples were prepared with a substrate concentration of 0.01 M in a 0.1 M TEAHFP in an acetonitrile electrolyte solution. From the result, it was found that the oxidation potential of thiophenol ($E_{1/2\ ox}$ = +0.25 V vs SCE) is lower than the oxidation potential of Eosin Y ($E_{1/2\ ox}$ = +0.83 V vs SCE for excited state of eosin Y). Similarly, the reduction potential of thiophenol (**a**) ($E_{1/2\ red}$ = -1.35 V vs SCE) is lower than the reduction potential value of Eosin Y ($E_{1/2\ red}$ = -1.06 V vs SCE for excited state of eosin Y This indicates that thiophenols can be easily oxidized by the eosin Y which also confirms the role of eosin Y as an oxidizing agent and helps in the facile generation of the thiyl radical. Further, the CV value of thiolate anion ($E_{1/2\ ox}$ = +0.35 V *vs*. SCE) shows that it has a stronger tendency to gain electron than PhSH ($E_{1/2\ ox}$ = +0.25 V *vs*. SCE) or PhSH has a better tendency to lose

electron than thiolate anion (Fig. S6). While comparing these values with the oxidation potential of eosin Y ($E_{1/2\ ox}$ = +0.83 V *vs*. SCE for excited state of eosin Y) it is clear that EY* will preferably accept an electron from PhSH rather than from the thiyl anion.[1] The $E_{1/2\ Oxd}$ of γ-ketodinitriles (**1**) is found to be 0.38 V + 2.13 V & vs SCE (Fig. S7).

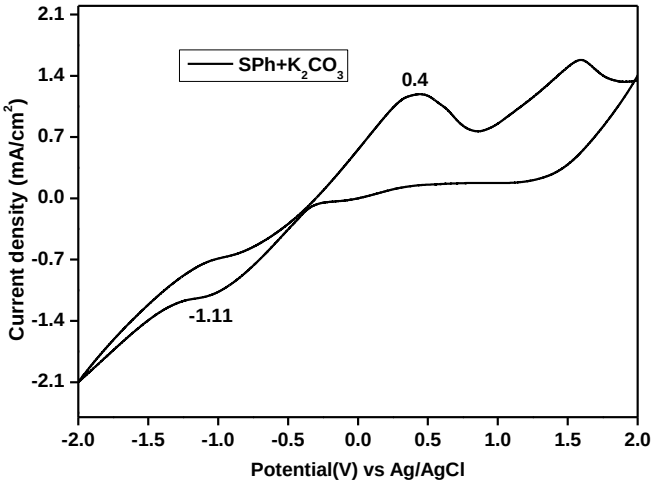


Fig. S24A. CV Graph of thiophenol (**a**) + K_2CO_3 recorded in a 0.1 M TEAHFP as supporting electrolyte at 100 mV scan rate. working electrode: glassy carbon electrode; counter electrode: plantinum wire; reference electrode: Ag/AgCl.

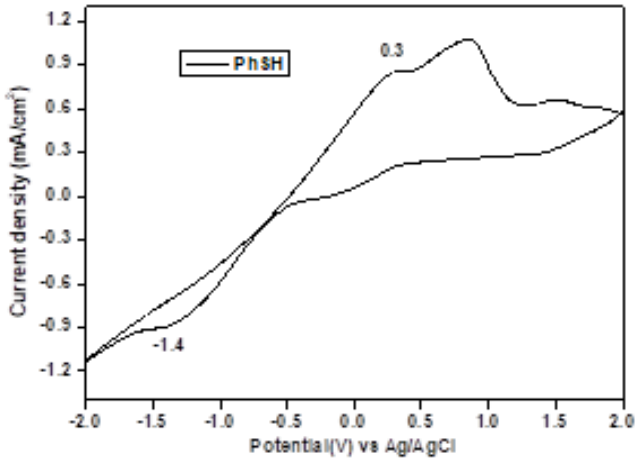


Fig. S24B. CV Graph of thiophenol (**a**) recorded in a 0.1 M TEAHFP as supporting electrolyte at 100 mV scan rate. working electrode: glassy carbon electrode; counter electrode: plantinum wire; reference electrode: Ag/AgCl.

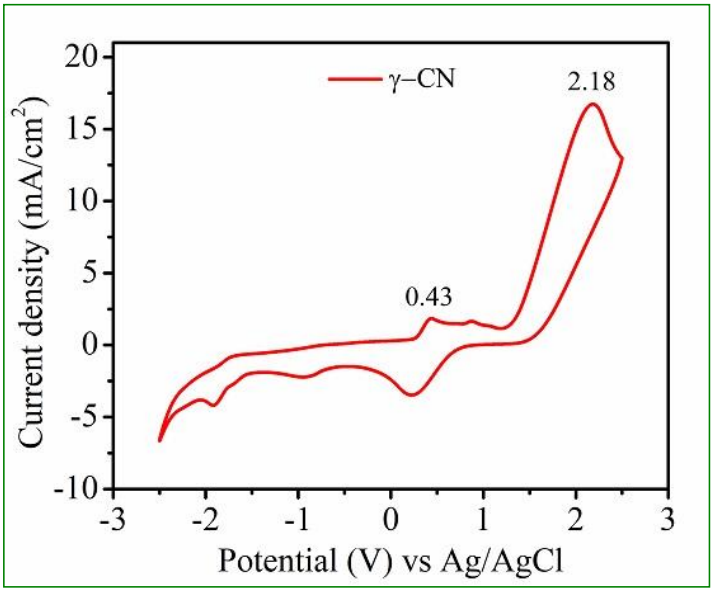


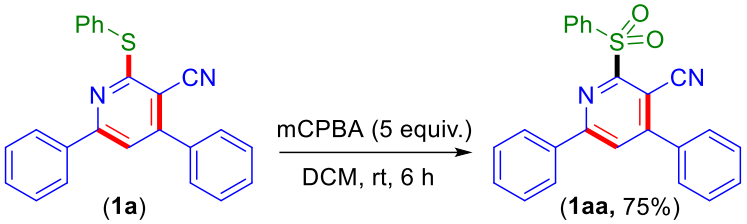
Fig. S25. CV Graph of *γ*-ketodinitriles (**1**) recorded in a 0.1 M TEAHFP as Supporting Electrolyte at 100 mV Scan rate. Working electrode: glassy carbon electrode; Counter electrode: platinum wire; Reference electrode: Ag/AgCl.

7. Post Synthetic Applications:

(A) General Procedure for the Synthesis of 4,6-diphenyl-2-(phenylsulfonyl)nicotinonitrile (1aa) from 4,6-diphenyl-2-(phenylthio)nicotinonitrile (1a):

The synthesis was carried out following the modified literature procedure.[1]

To a 10 mL round bottom flask was added 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) (91 mg, 0.25 mmol) and DCM. Then the reaction mixture was stirred under ice-cooled condition. Then to the reaction mixture mCPBA (215 mg, 1.25 mmol) was added pinch wise over a period of 5 minute. Then the reactions mixture was stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC analysis), the solvent was evaporated and the reaction mixture was admixed with ethyl acetate (15 mL) and the organic layer was washed with saturated bicarbonate solution (5 mL). The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel using 8% ethyl acetate in hexane to give pure 4,6-diphenyl-2-(phenylsulfonyl)nicotinonitrile (**1aa**) in 75% yield (Scheme S13). The identity and purity of the product was confirmed by spectroscopic analysis.

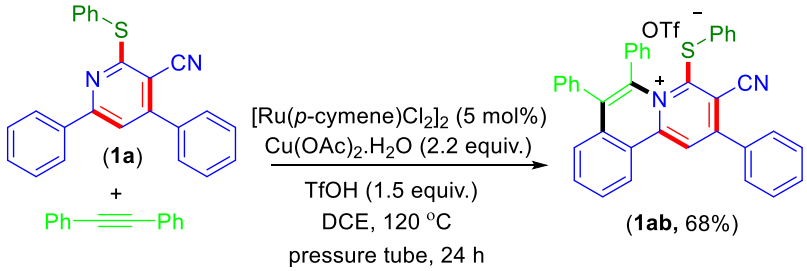


Scheme S11. Oxidation of 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) with mCPBA.

(B) General Procedure for the Synthesis of 3-cyano-2,6,7-triphenyl-4-(phenylthio)pyrido[2,1-*a*]isoquinolin-5-ium (1ab) from 4,6-diphenyl-2-(phenylthio)nicotinonitrile (1a) and Diphenyl Acetylene.

The synthesis was carried out following the modified literature procedure.[2]

To an oven-dried pressure tube containing a magnetic bar was added 4,6-diphenyl-2-(phenylthio)nicotinonitrile (1a) (0.20 mmol, 72 mg), diphenylacetylene (0.024 mmol, 43 mg), [Ru(*p*-cymene)Cl_2]$_2$ (0.01 mmol, 6 mg), Cu(OAc)$_2$.H_2O (0.44 mmol, 84 mg), TfOH (0.30 mmol, 45mg) and DCE (2 mL). The reactions mixture was stirred in an oil bath preheated at 120 ^oC for 24 h. After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer was washed with saturated sodium bicarbonate solution (10 mL). The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), and solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel using 2% methanol in DCM to give pure 3-cyano-2,6,7-triphenyl-4-(phenylthio)pyrido[2,1-*a*]isoquinolin-5-ium (**1ab**) in 68% yield. The identity and purity of the product was confirmed by spectroscopic analysis (Scheme S14).

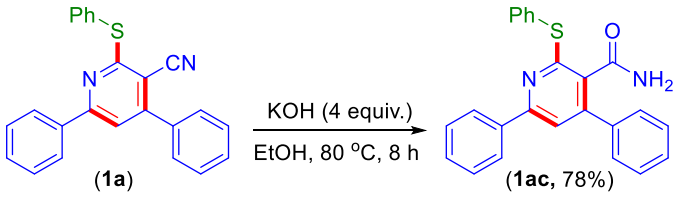


Scheme S12. Ru(II)-catalyzed annulation with diphenyl acetylene.

(C) General Procedure for the Synthesis Of 4,6-diphenyl-2-(phenylthio)nicotinamide (1ac) from 4,6-diphenyl-2-(phenylthio)nicotinonitrile (1a):

The synthesis was carried out following the modified literature procedure.[3]

To a oven-dried round bottom flask was added 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**) (0.20 mmol, 72 mg), KOH (0.8 mmol, 44 mg), and ethanol (2 mL). Then the reaction mixture was stirred under ice-cooled condition for 8 h. After completion of the reaction (monitored by TLC analysis), the solvent was evaporated and the reaction mixture was admixed with ethyl acetate (20 mL) and the organic layer was washed with water (10 mL). The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel using 20% ethyl acetate in hexane to give pure 4,6-diphenyl-2-(phenylthio)nicotinamide (**1ac**) in 78% yield (Scheme S15). The identity and purity of the product was confirmed by spectroscopic analysis



Scheme S13. Synthesis of nicotinamide from 4,6-diphenyl-2-(phenylthio)nicotinonitrile (**1a**).

8. References

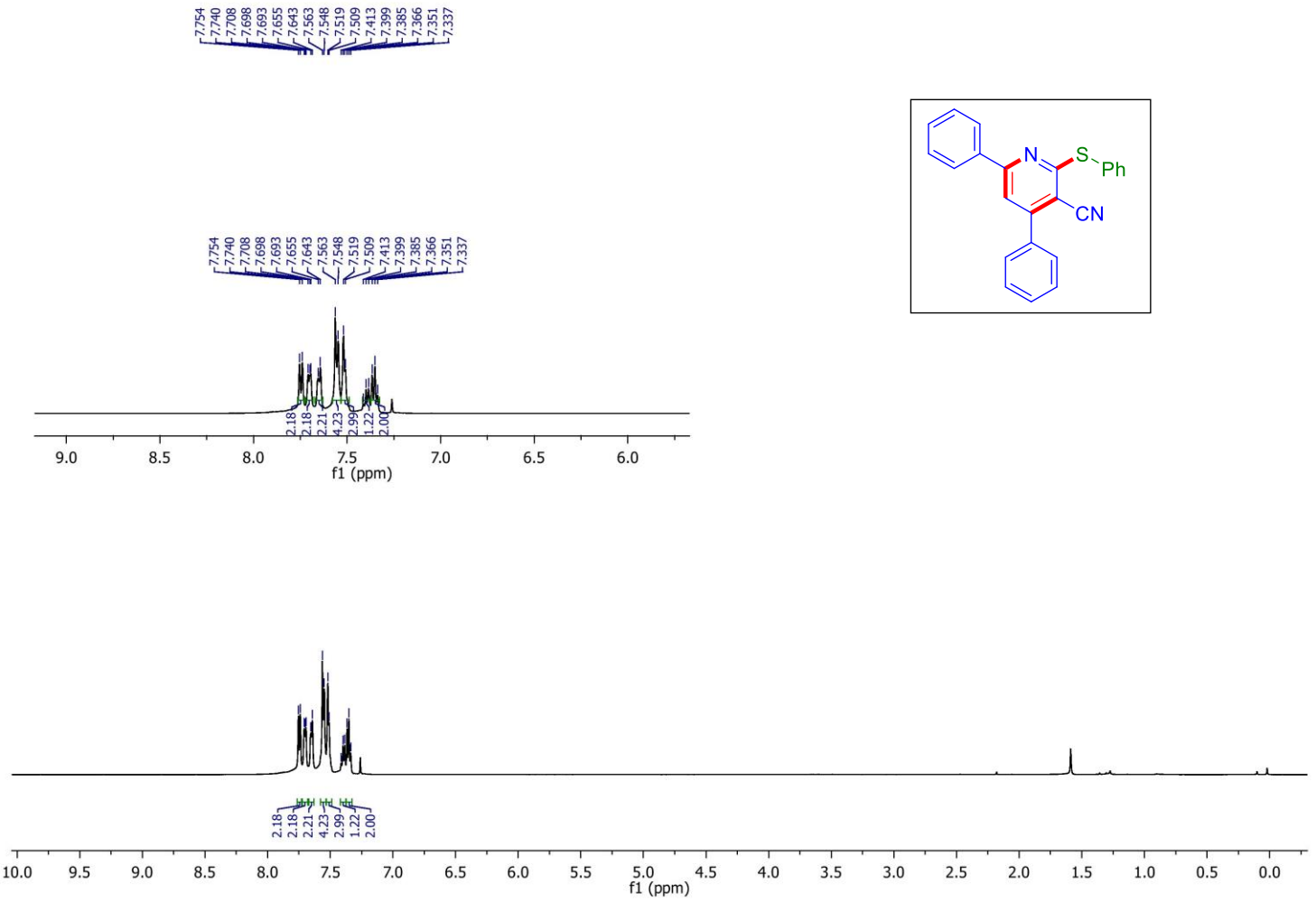
1. A. A. Dar, N. Enjamuri, Md. Shadab, N. Ali and A. T. Khan, *ACS Comb. Sci.*, 2015, **17**, 671−681.

2. S. Ghosh, S. Pal, S. Rajamanickam, R. Shome, P. R. Mohanta, S. S. Ghosh and B. K. Patel, *ACS Omega*, 2019, **4**, 5565−5577.

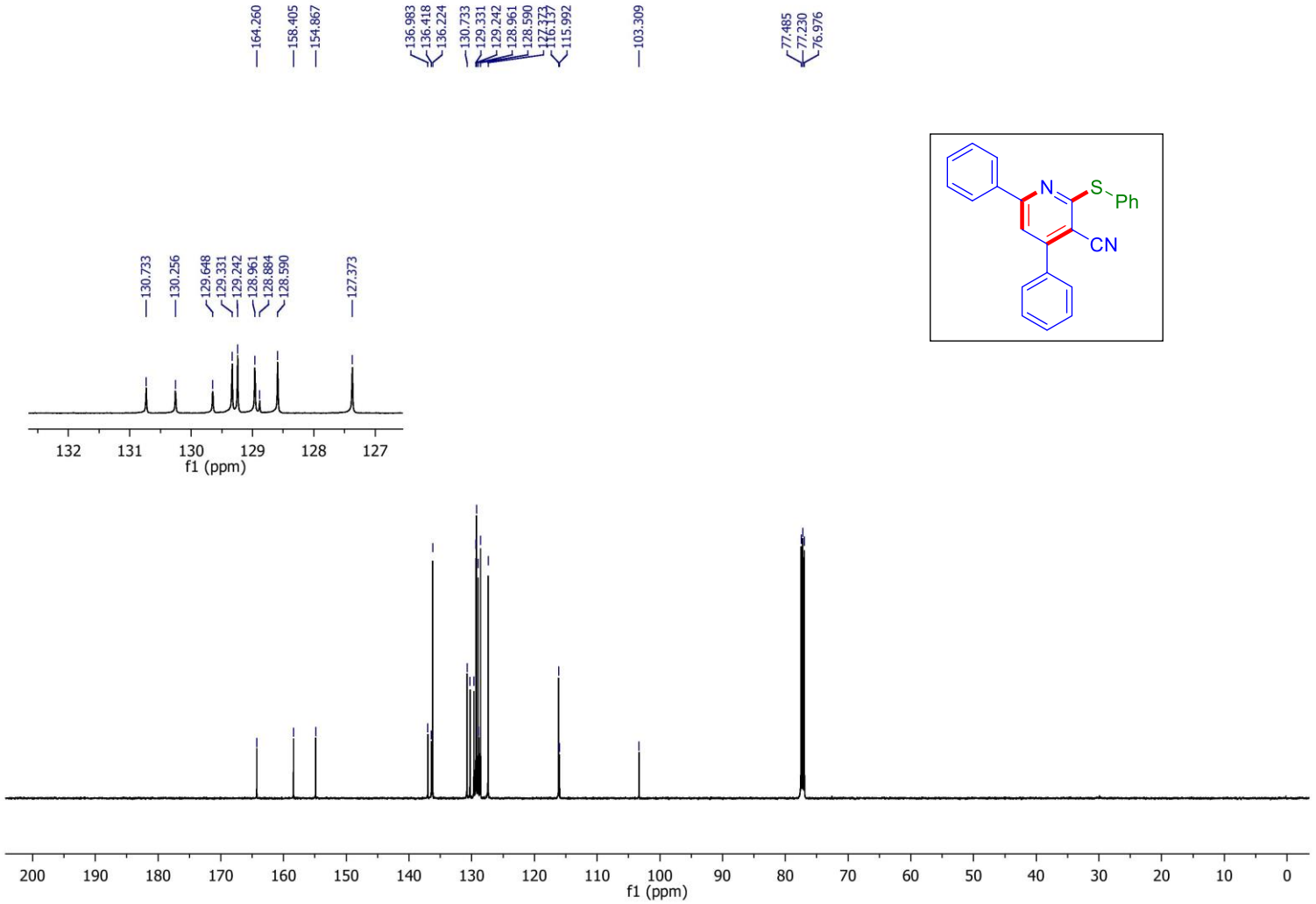
3. J. H. Hall and M. A. Gisler, *J. Org. Chem.*, 1976, **41**, 3769–3770.

9. Spectra :

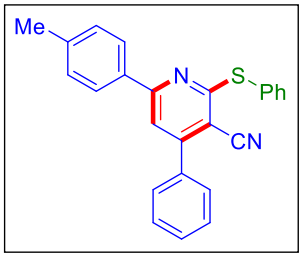
4,6-Diphenyl-2-(phenylthio)nicotinonitrile (1a) : ^{1}H NMR ($CDCl_3$, 500 MHz)

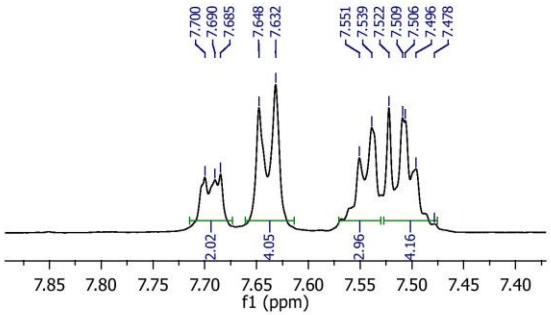


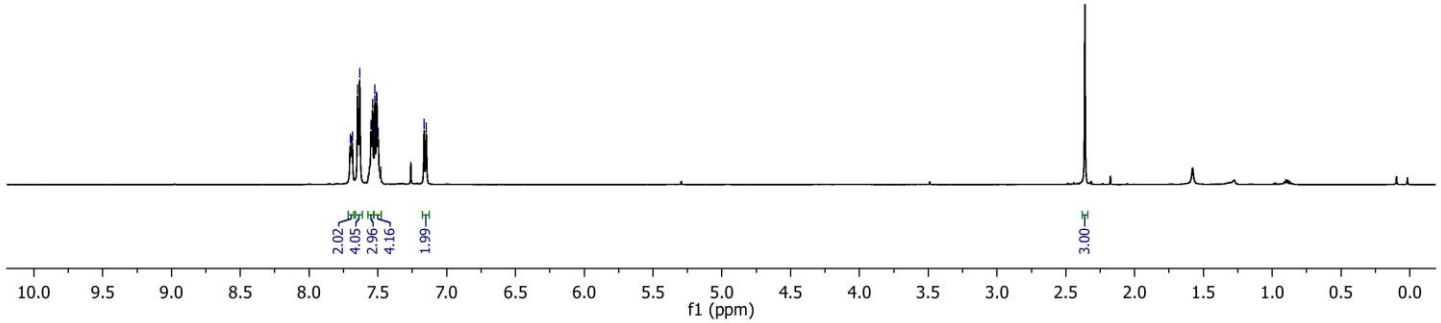
4,6-Diphenyl-2-(phenylthio)nicotinonitrile (1a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



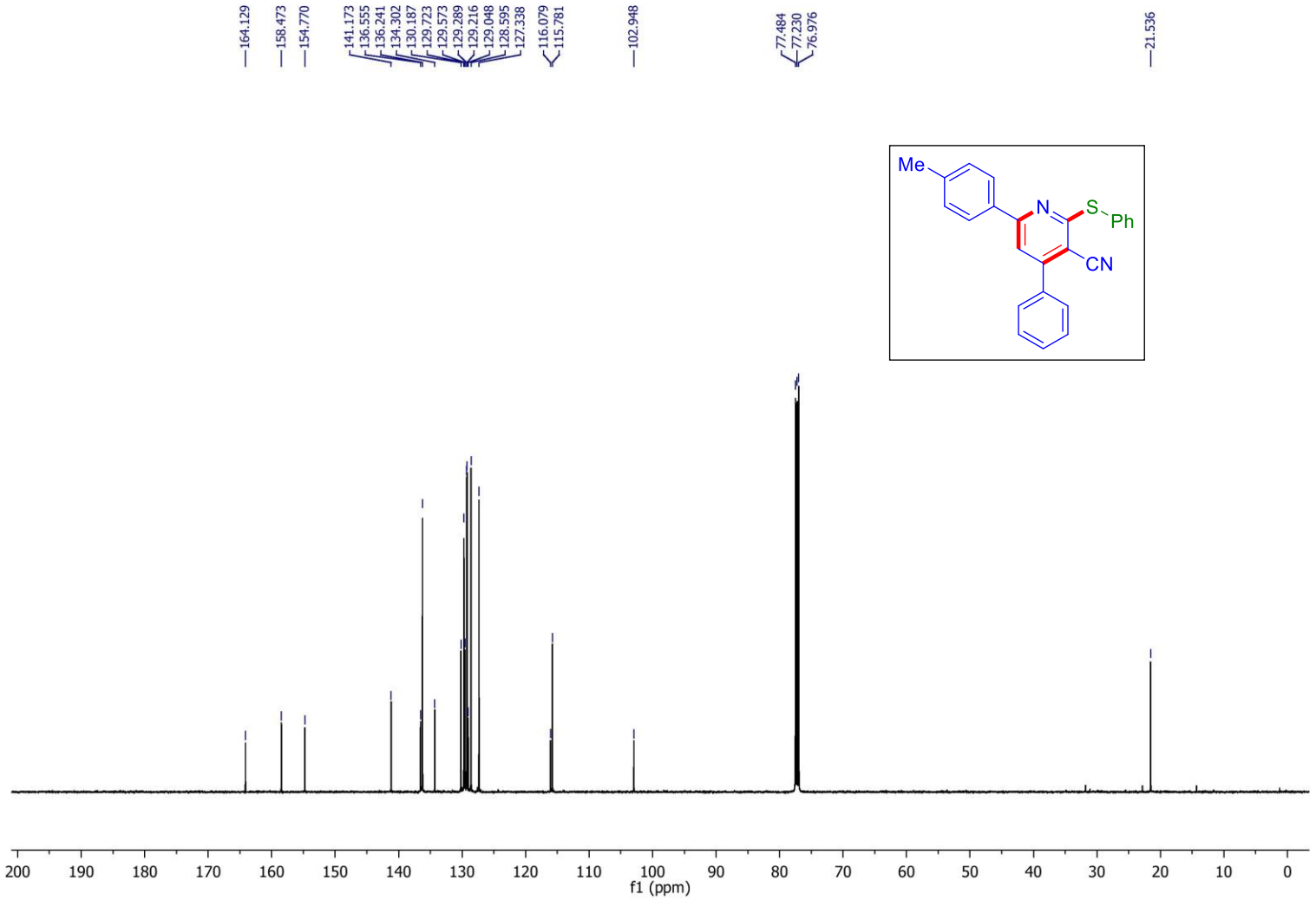
4-Phenyl-2-(phenylthio)-6-(p-tolyl)nicotinonitrile (2a): ^{1}H NMR ($CDCl_3$, 500 MHz)



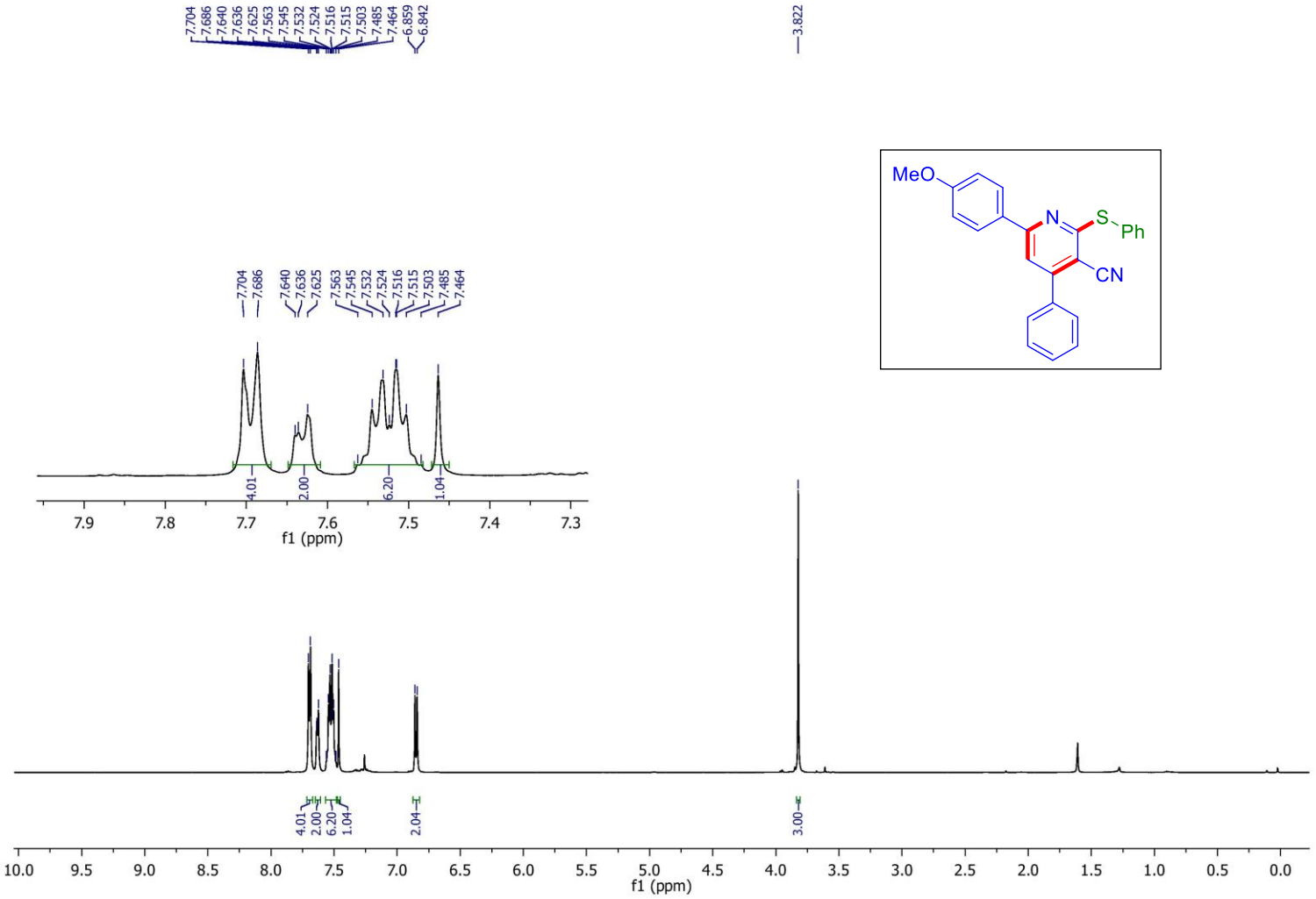




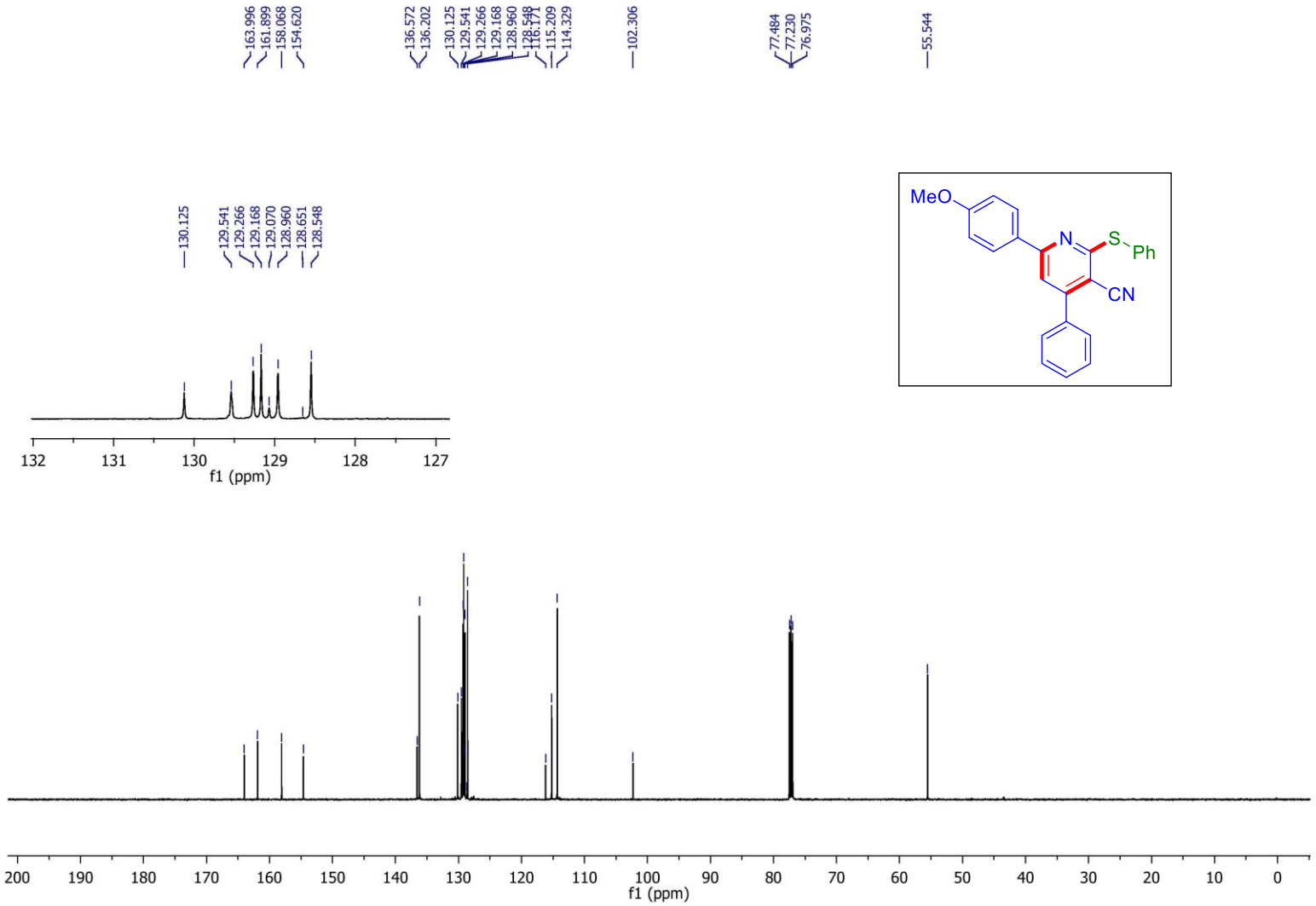
4-Phenyl-2-(phenylthio)-6-(p-tolyl)nicotinonitrile (2a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



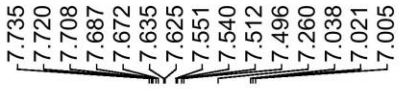
6-(4-Methoxyphenyl)-4-phenyl-2-(phenylthio)nicotinonitrile (3a): ^{1}H NMR (CDCl$_3$, 500 MHz)

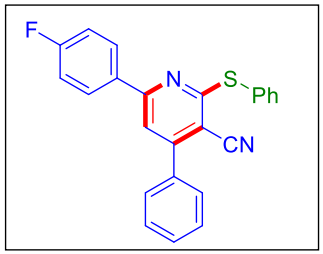


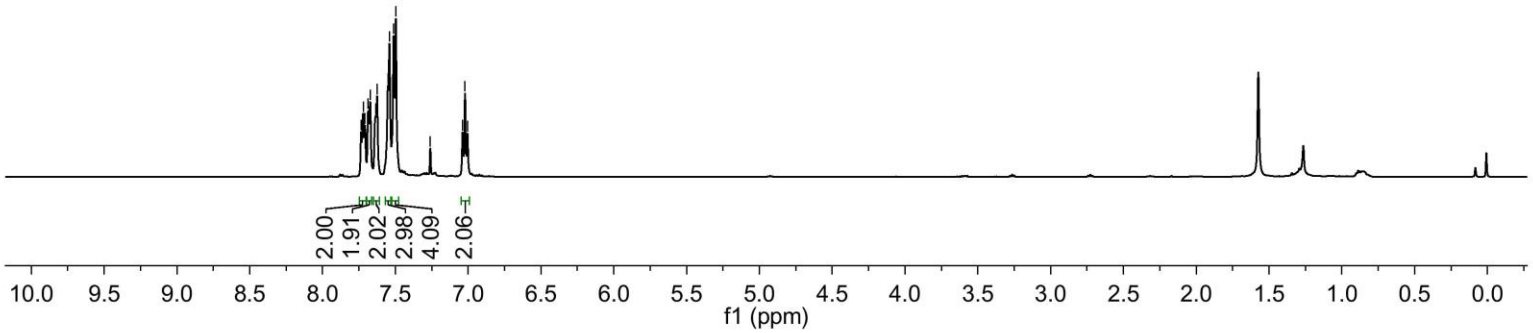
6-(4-Methoxyphenyl)-4-phenyl-2-(phenylthio)nicotinonitrile (3a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



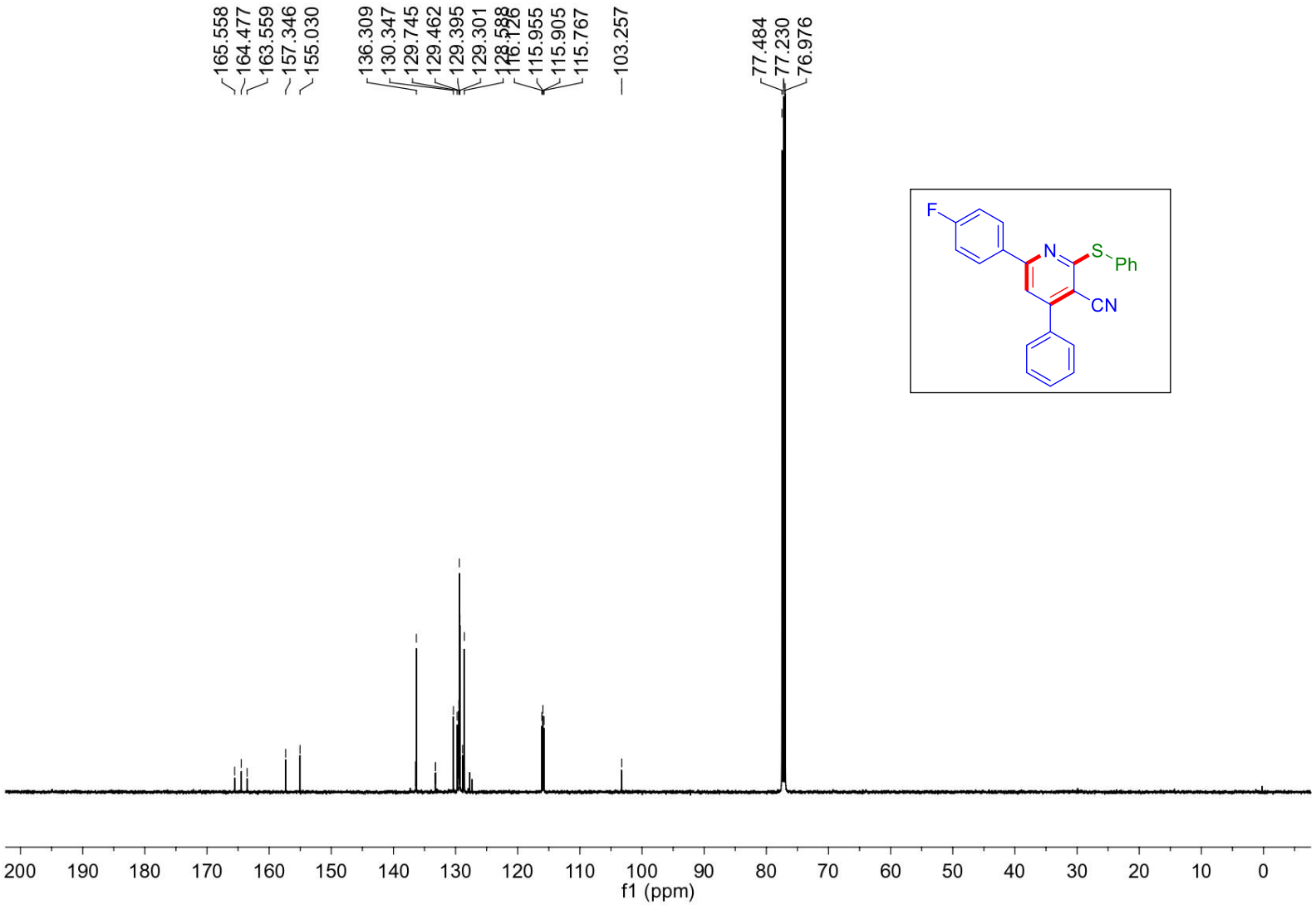
6-(4-Fluorophenyl)-4-phenyl-2-(phenylthio)nicotinonitrile* (*4a*):^{1}*H NMR (CDCl$_3$, 500 MHz)



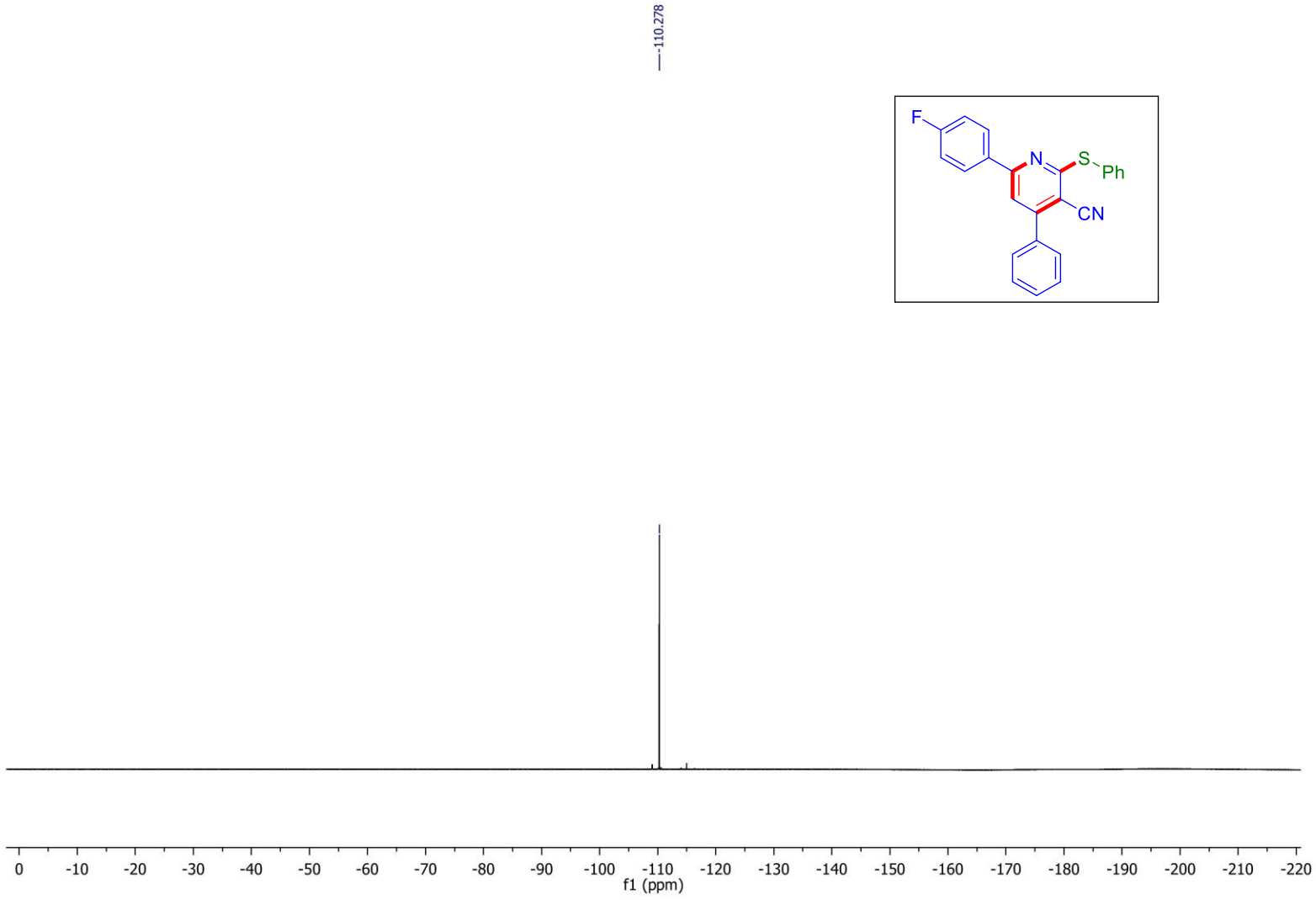




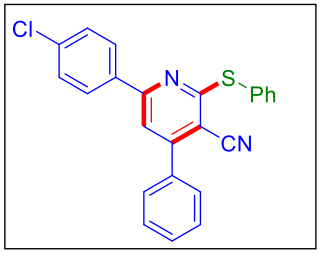
***6-(4-Fluorophenyl)-4-phenyl-2-(phenylthio)nicotinonitrile* (*4a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz)**

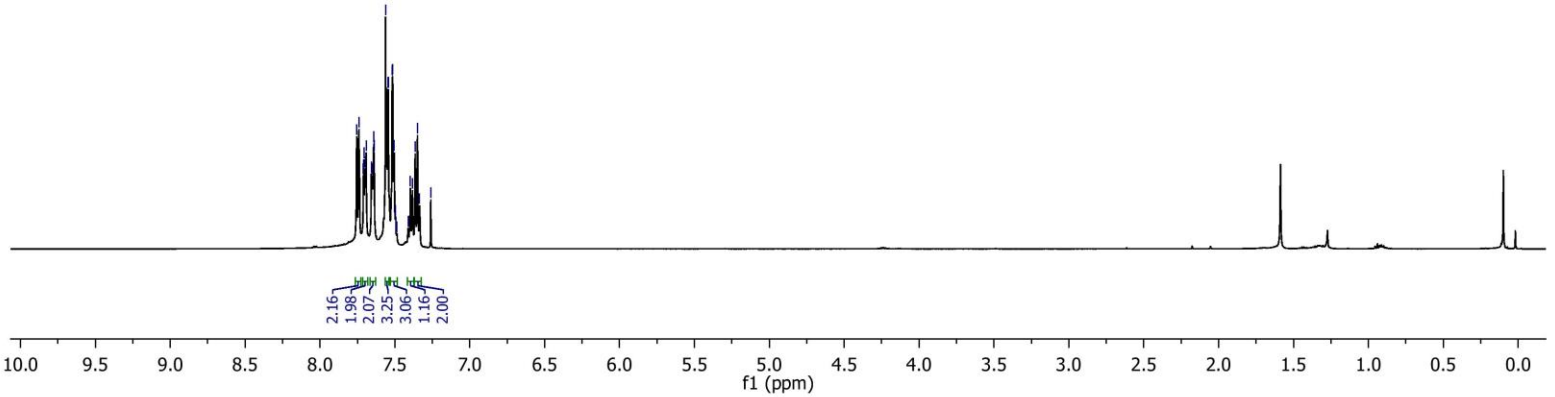


***6-(4-Fluorophenyl)-4-phenyl-2-(phenylthio)nicotinonitrile* (*4a*): ^{19}F NMR ($CDCl_3$, 471 MHz)**

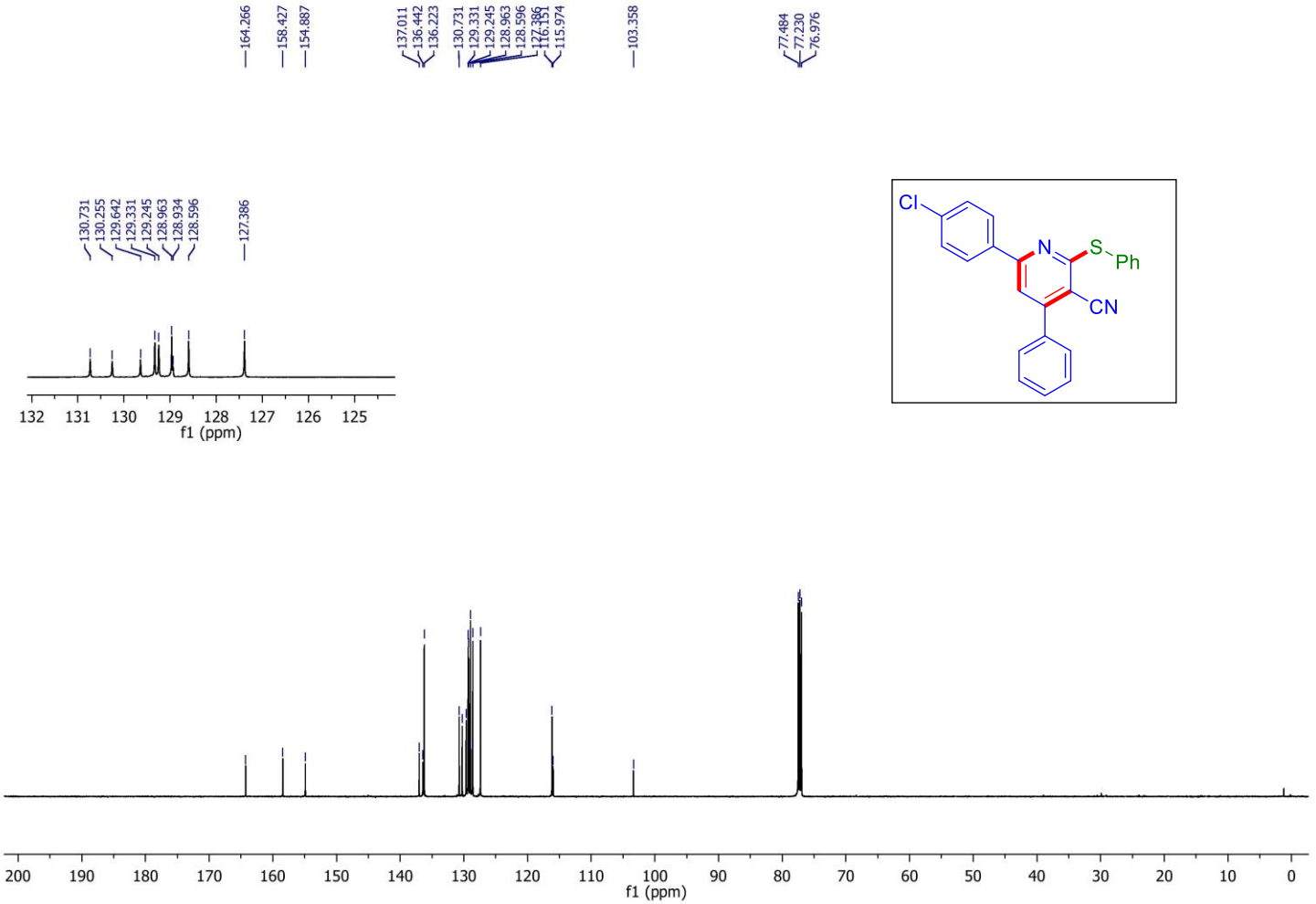


6-(4-Chlorophenyl)-4-phenyl-2-(phenylthio)nicotinonitrile (5a): ^{1}H NMR ($CDCl_3$, 500 MHz)

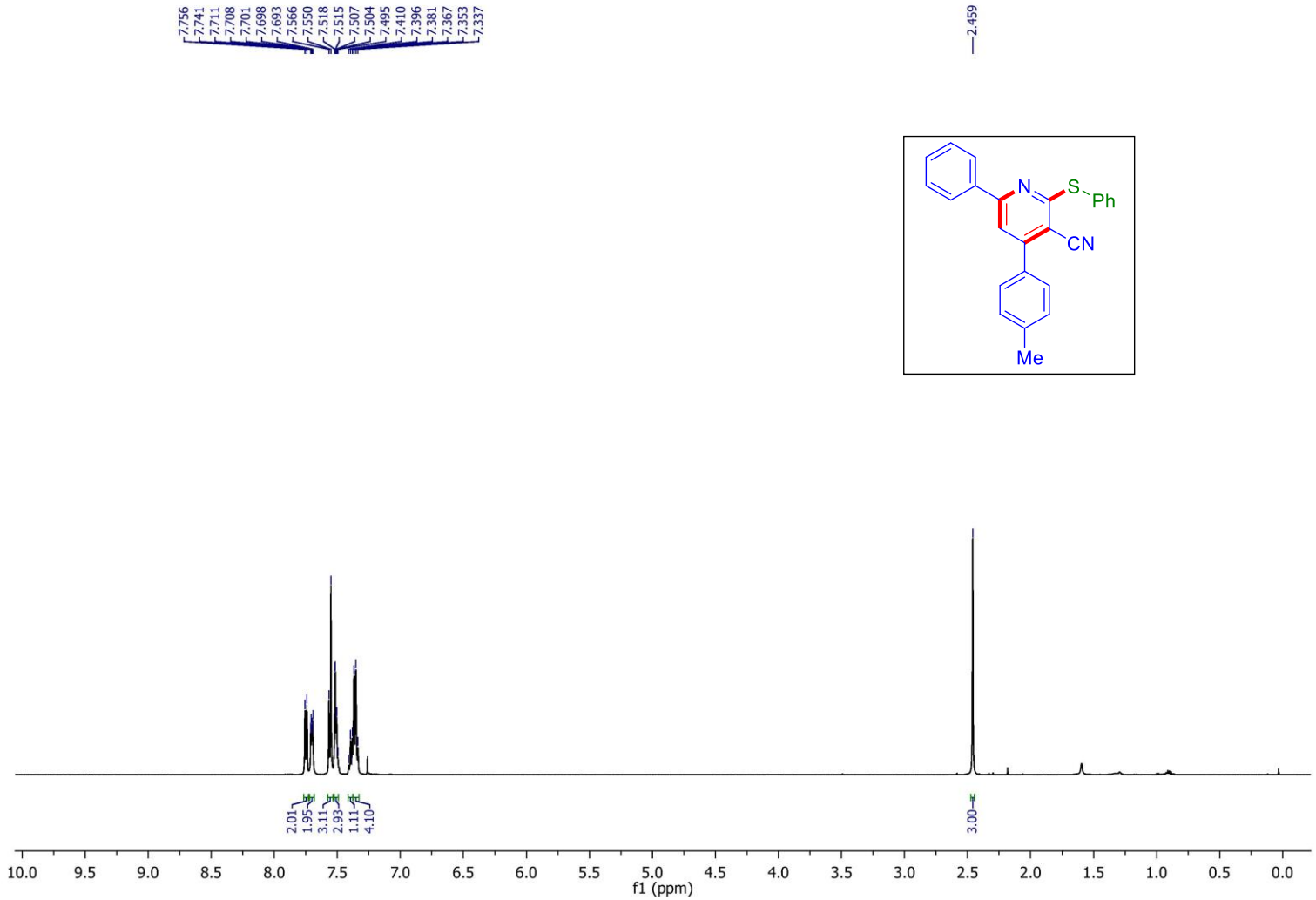




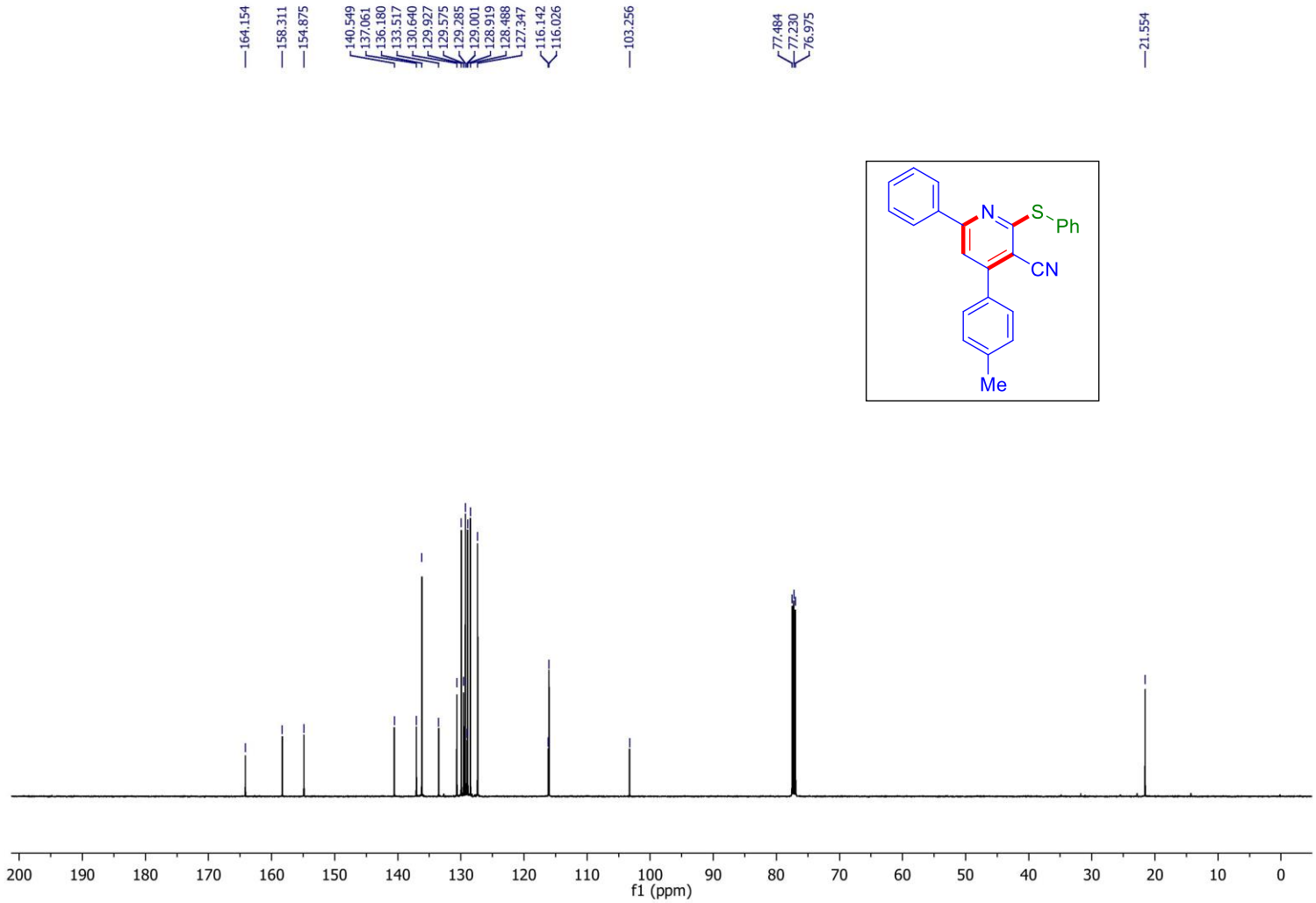
6-(4-Chlorophenyl)-4-phenyl-2-(phenylthio)nicotinonitrile (5a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



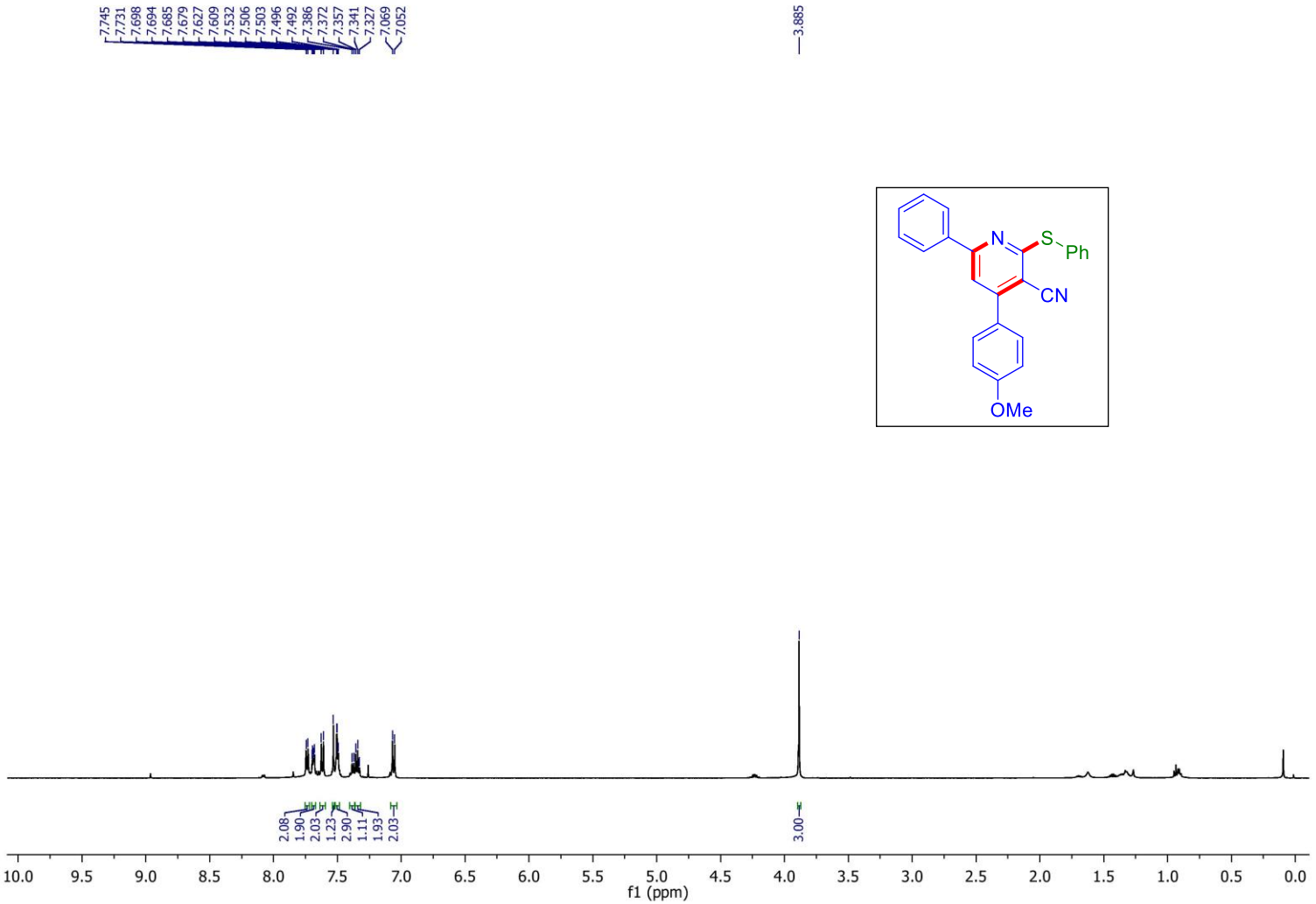
6-Phenyl-2-(phenylthio)-4-(p-tolyl)nicotinonitrile* (*6a*): ^{1}*H NMR (CDCl$_3$, 500 MHz)



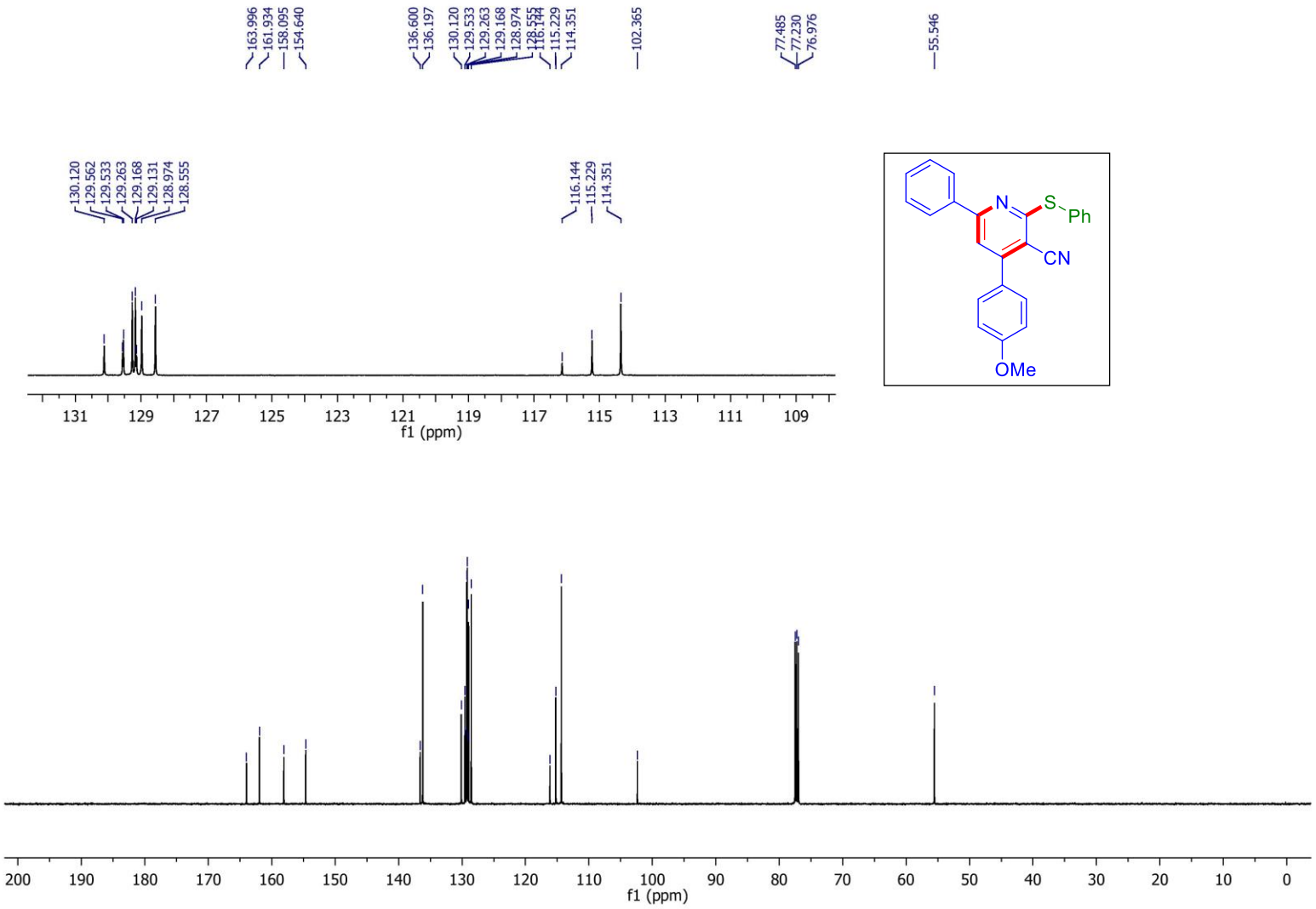
6-Phenyl-2-(phenylthio)-4-(p-tolyl)nicotinonitrile (6a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



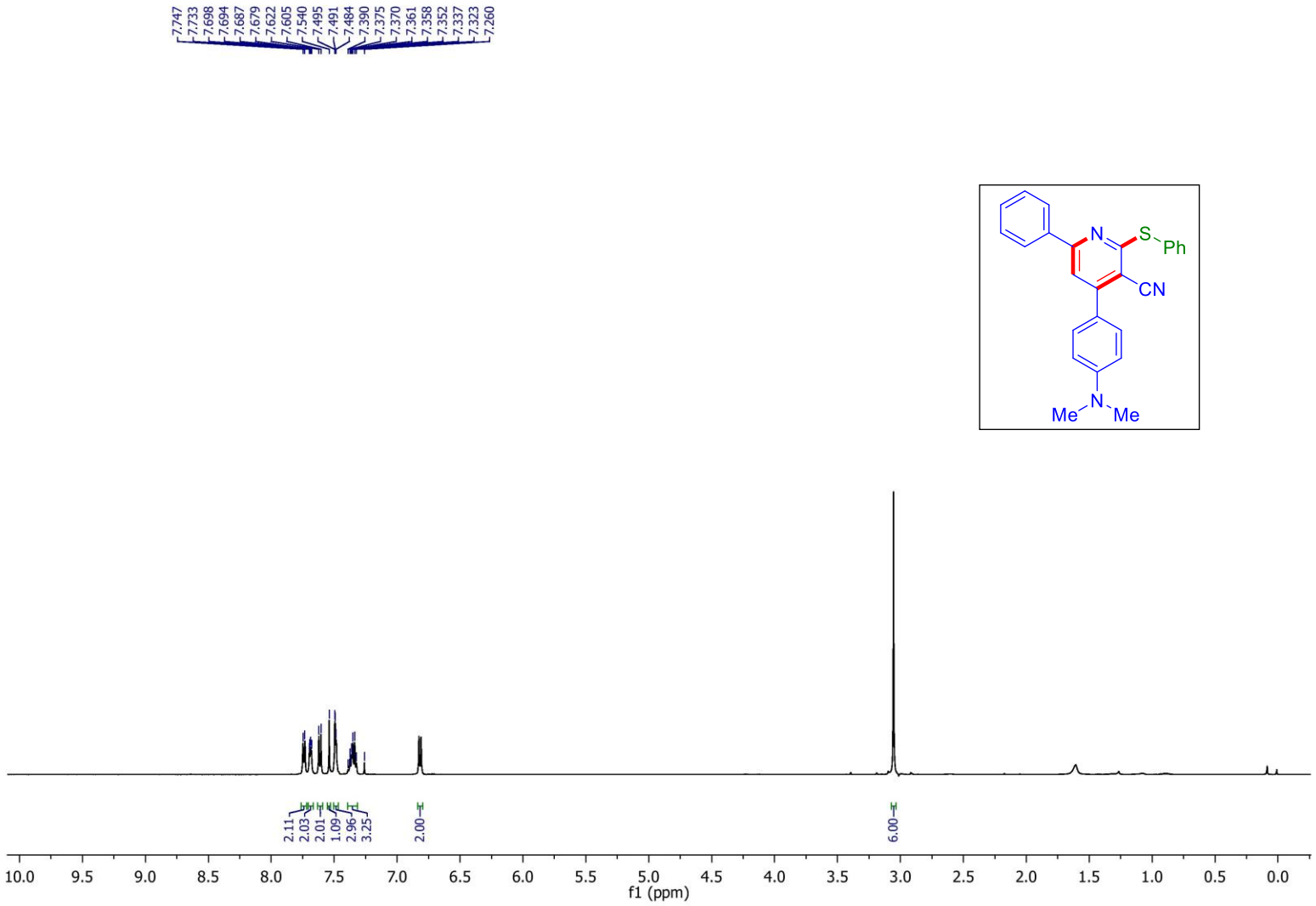
4-(4-Methoxyphenyl)-6-phenyl-2-(phenylthio)nicotinonitrile (7a): ^{1}H NMR (CDCl$_3$, 500 MHz)



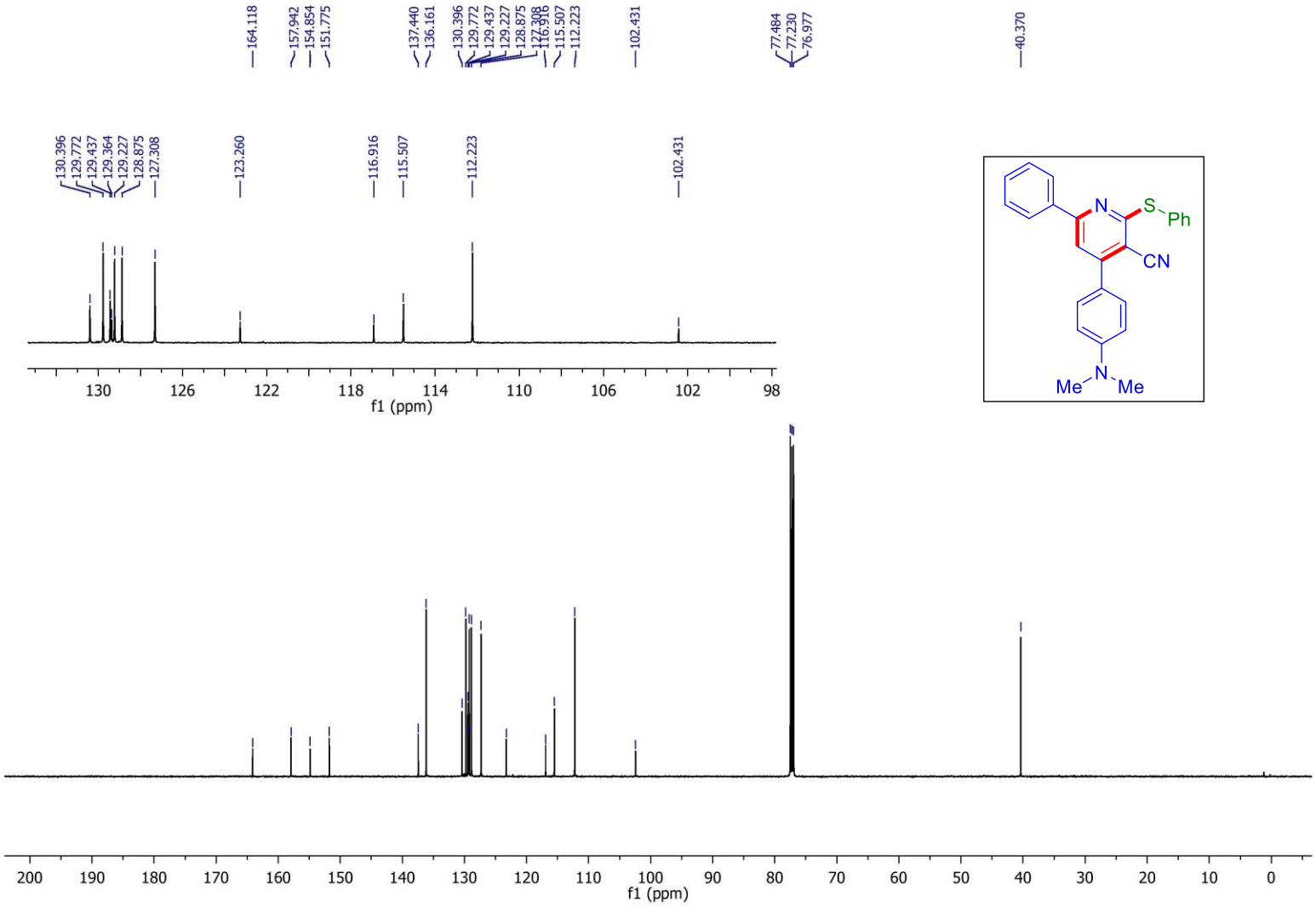
***4-(4-Methoxyphenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*7a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



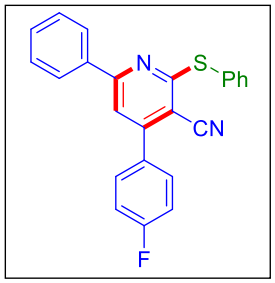
4-(4-(Dimethylamino)phenyl)-6-phenyl-2-(phenylthio)nicotinonitrile (8a): ^{1}H NMR ($CDCl_3$, 500 MHz)

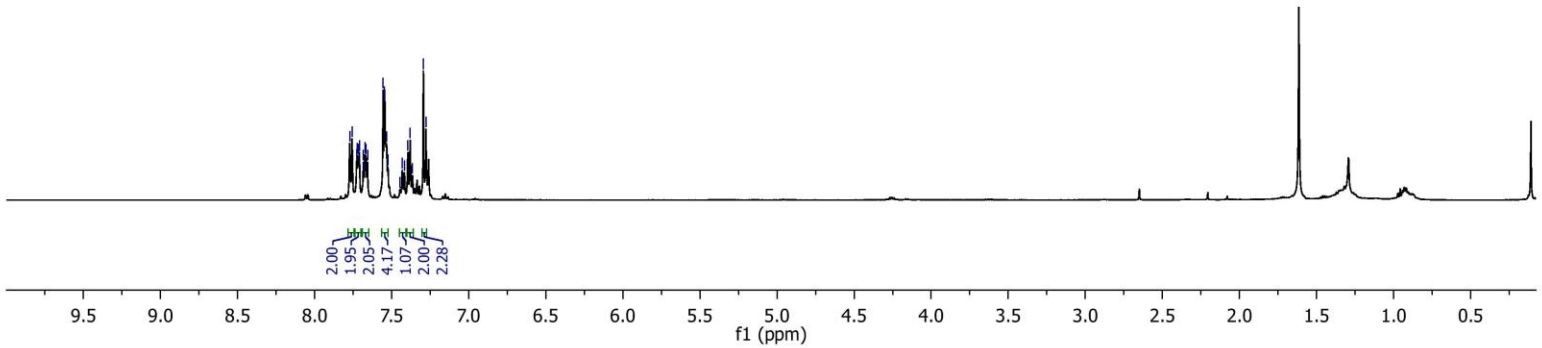


4-(4-(Dimethylamino)phenyl)-6-phenyl-2-(phenylthio)nicotinonitrile (8a): $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz)

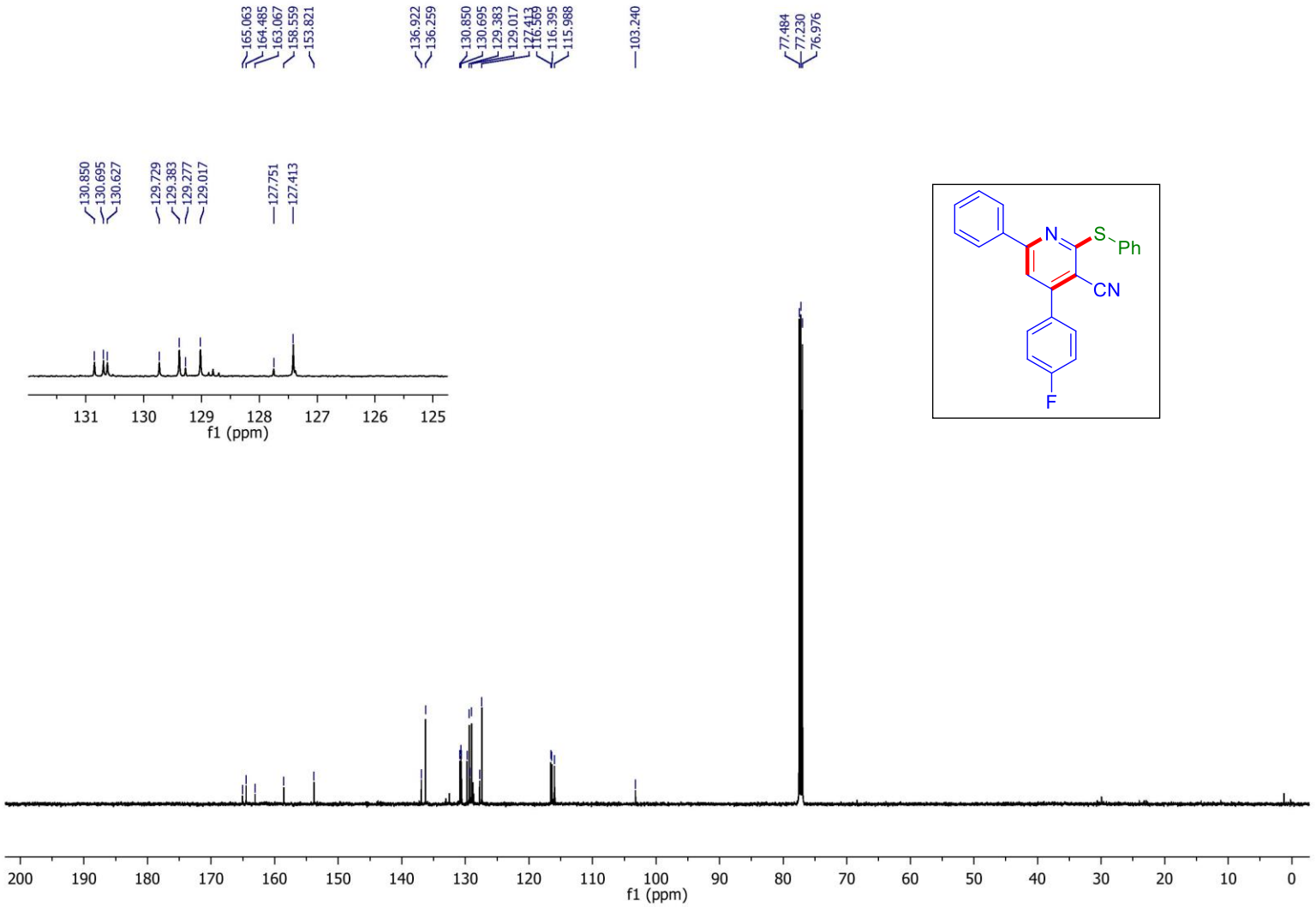


4-(4-Fluorophenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*9a*): *^{1}H NMR ($CDCl_3$, 500 MHz)

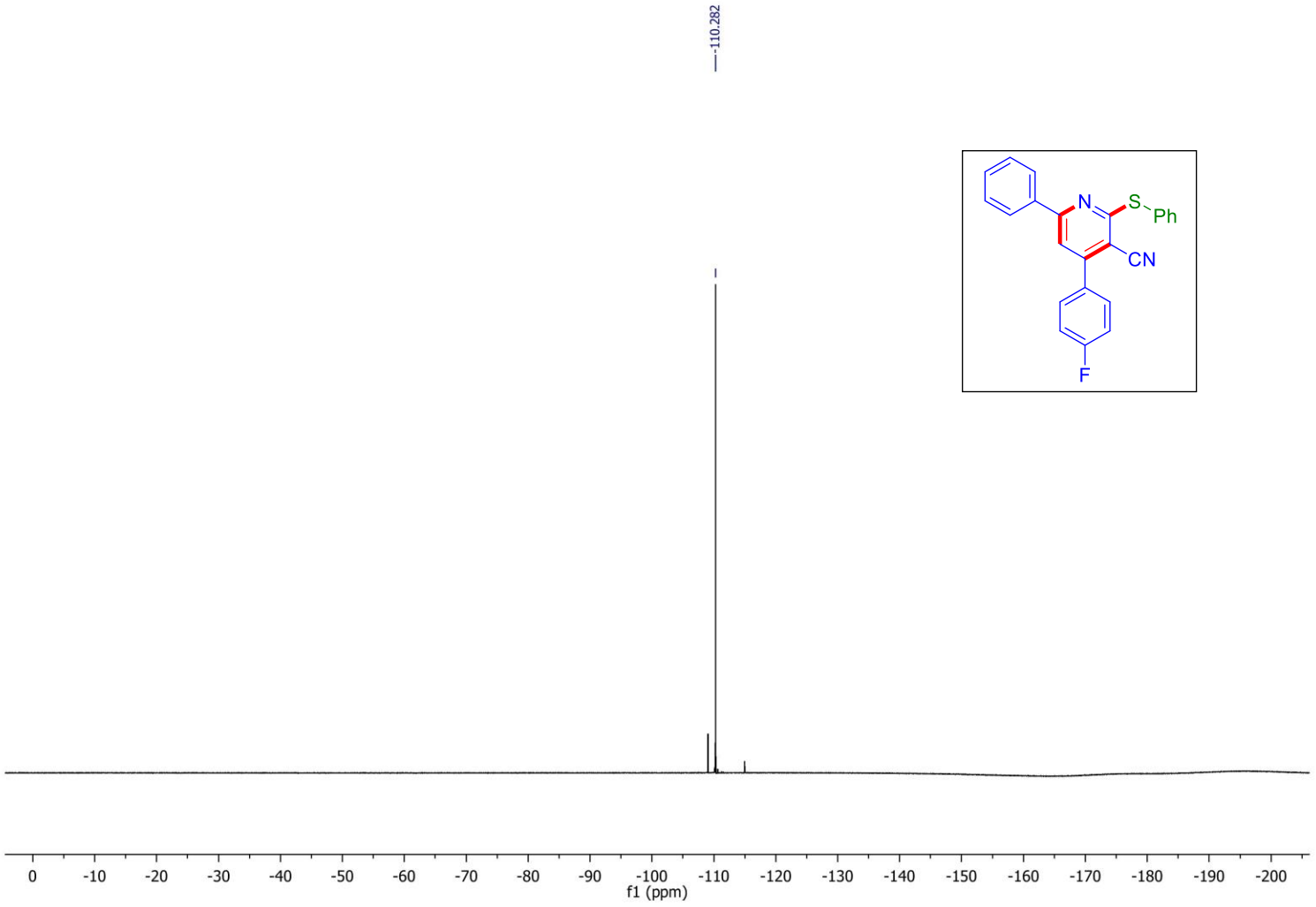




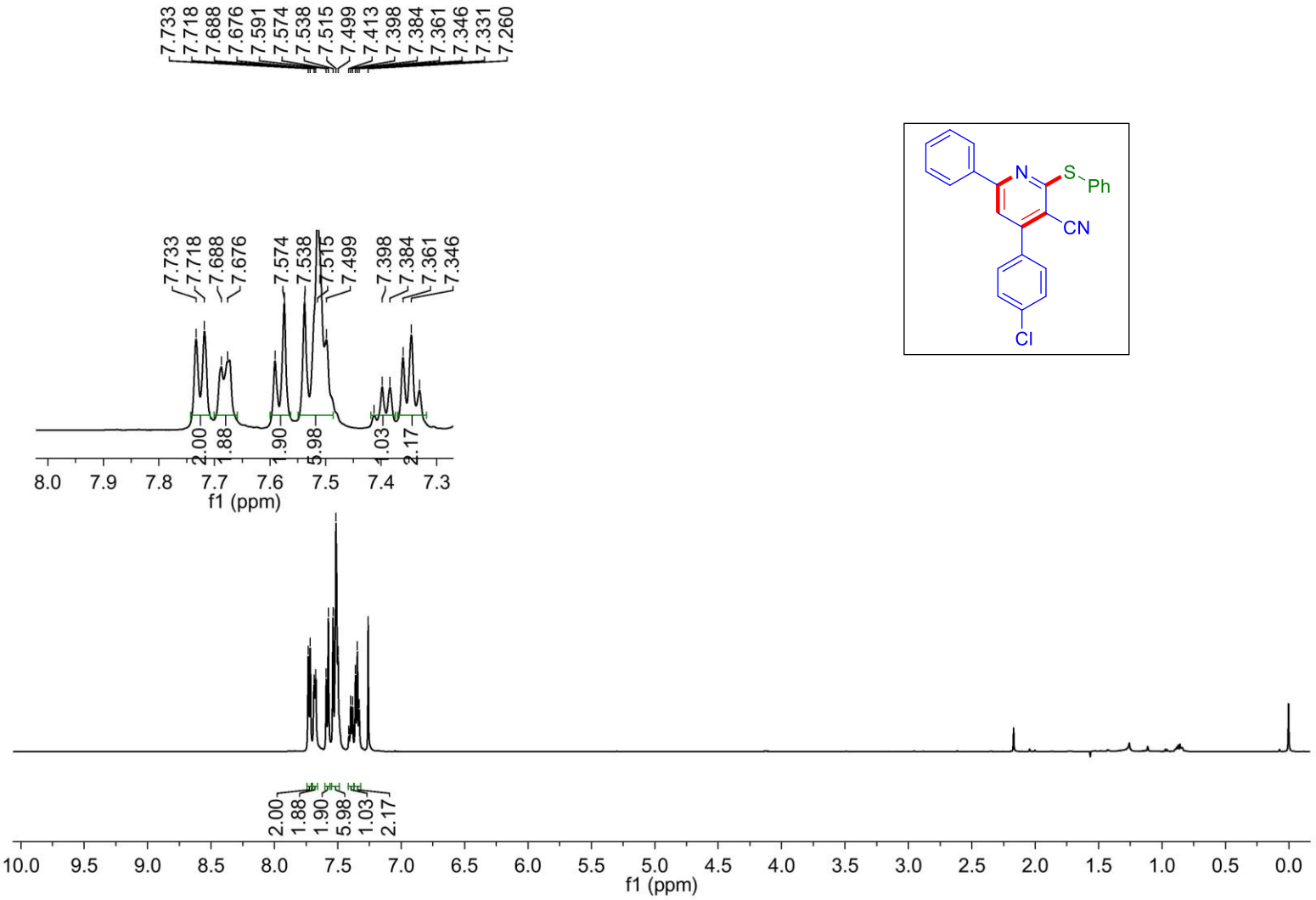
***4-(4-Fluorophenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*9a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



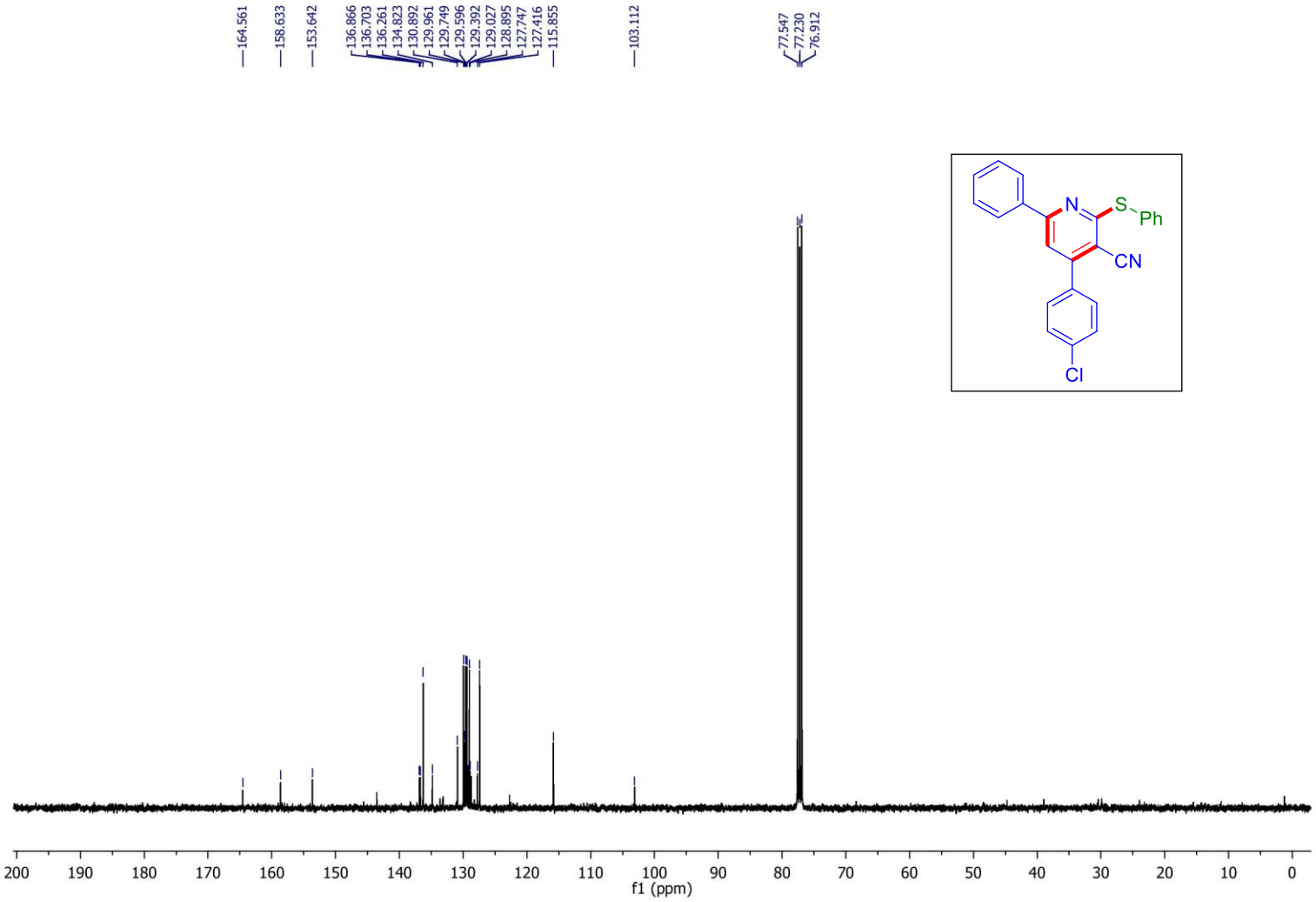
***4-(4-Fluorophenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*9a*): ^{19}F NMR ($CDCl_3$, 471 MHz)**



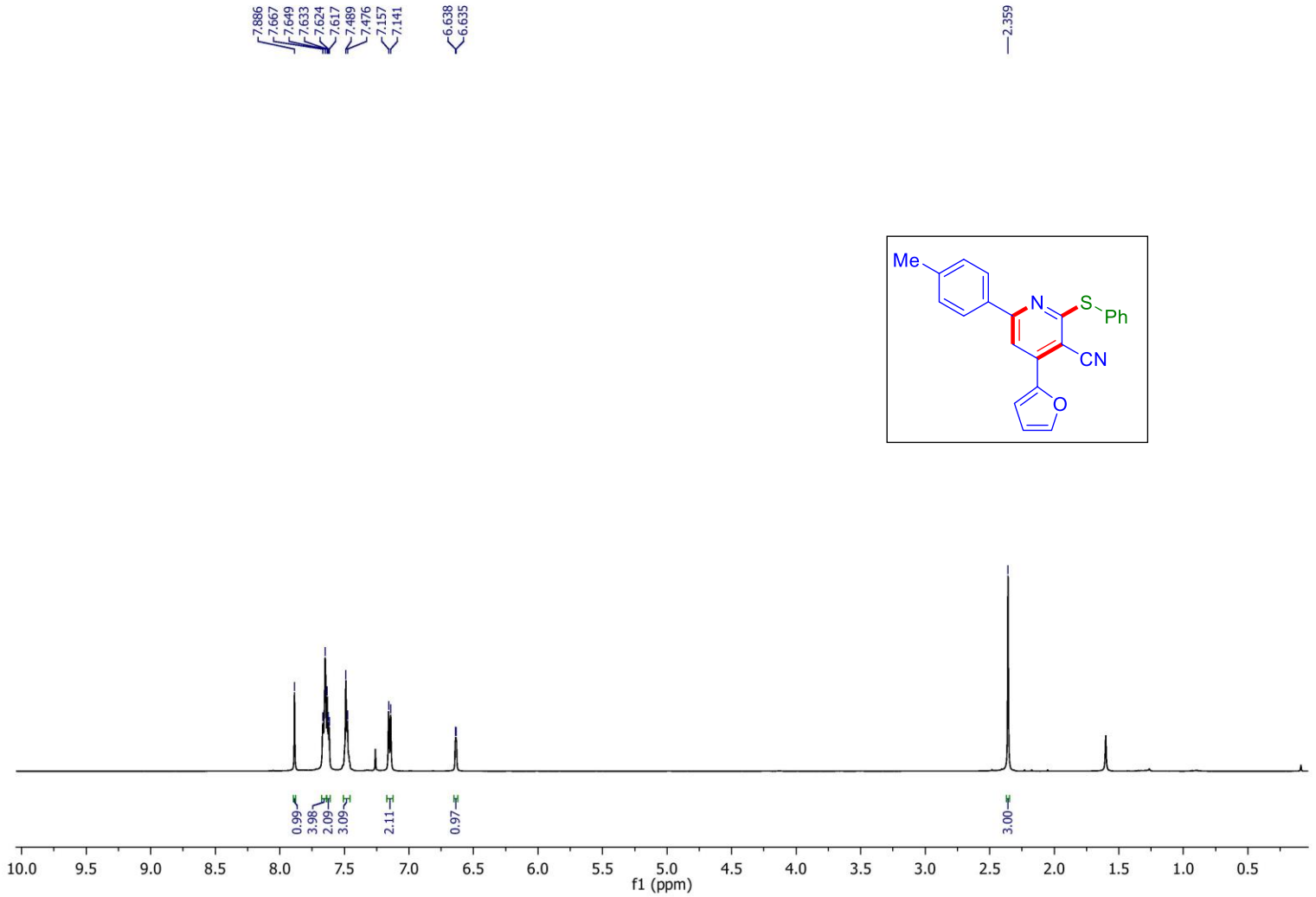
***4-(4-Chlorophenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*10a*): ^{1}H NMR ($CDCl_3$, 125 MHz)**



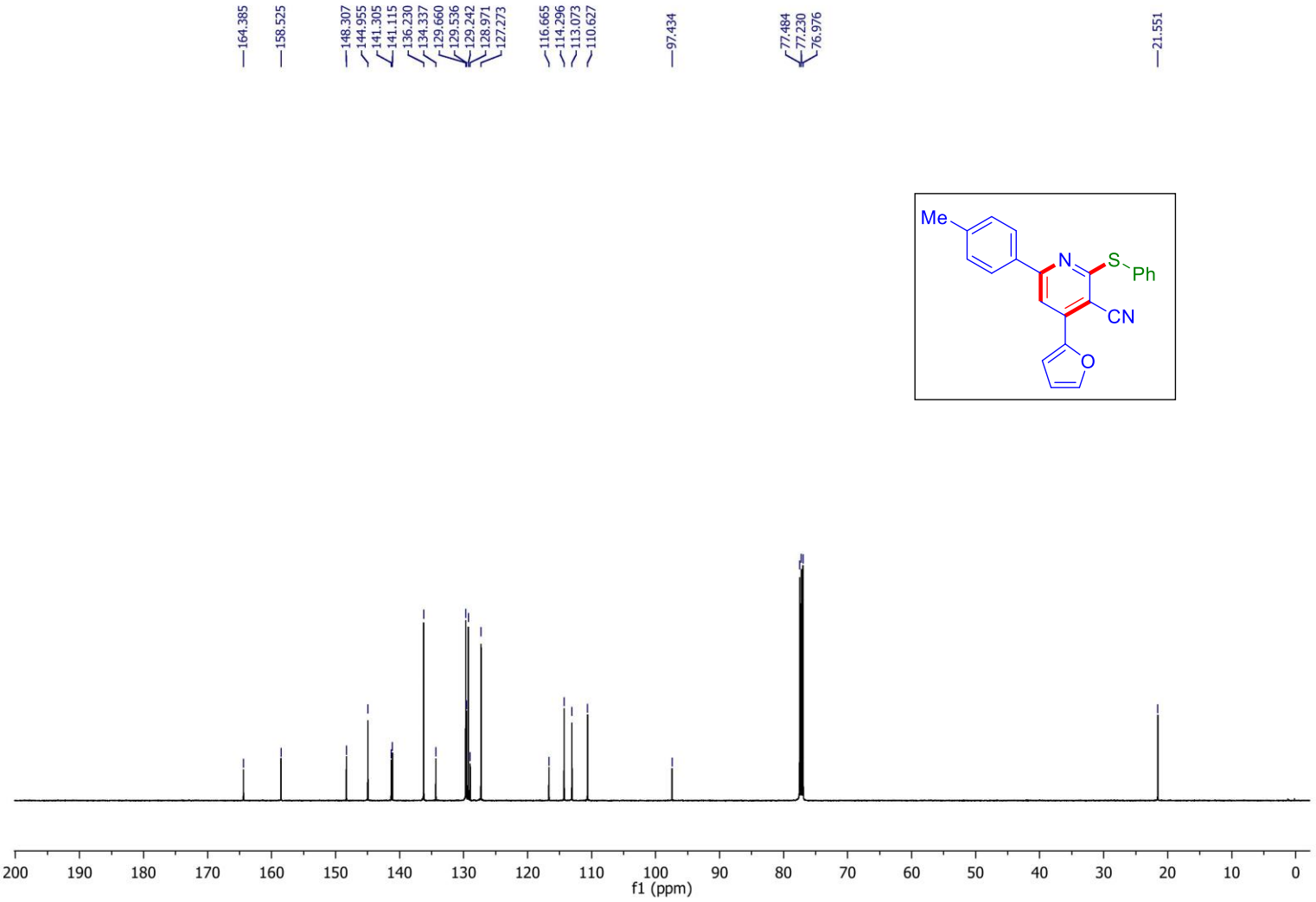
***4-(4-Chlorophenyl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*10a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



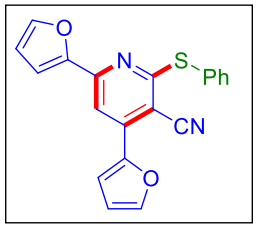
4-(Furan-2-yl)-2-(phenylthio)-6-(p-tolyl)nicotinonitrile* (*11a*): ^{1}H *NMR (*$CDCl_3$*, 500 MHz)

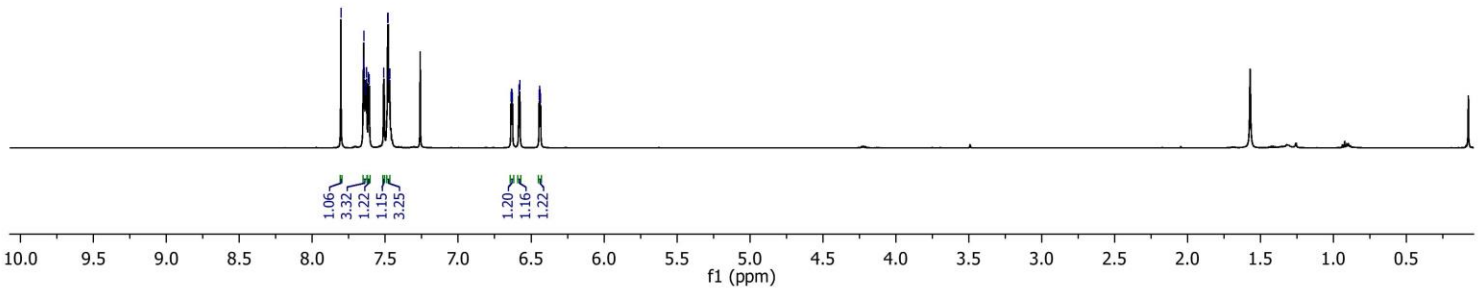


***4-(Furan-2-yl)-2-(phenylthio)-6-(p-tolyl)nicotinonitrile* (*11a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**

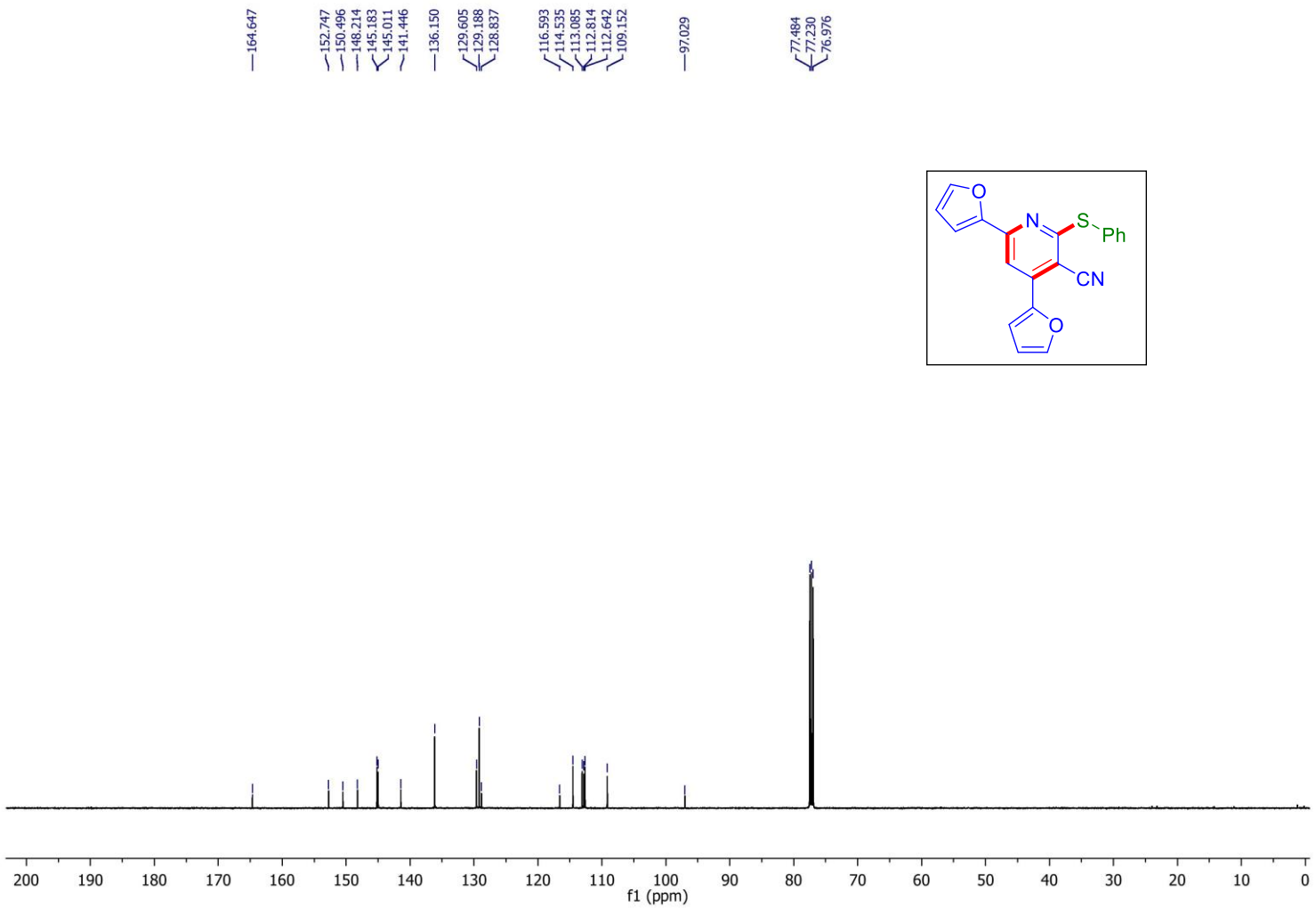


***4,6-Di(furan-2-yl)-2-(phenylthio)nicotinonitrile* (*12a*): ^{1}H NMR ($CDCl_3$, 500 MHz)**

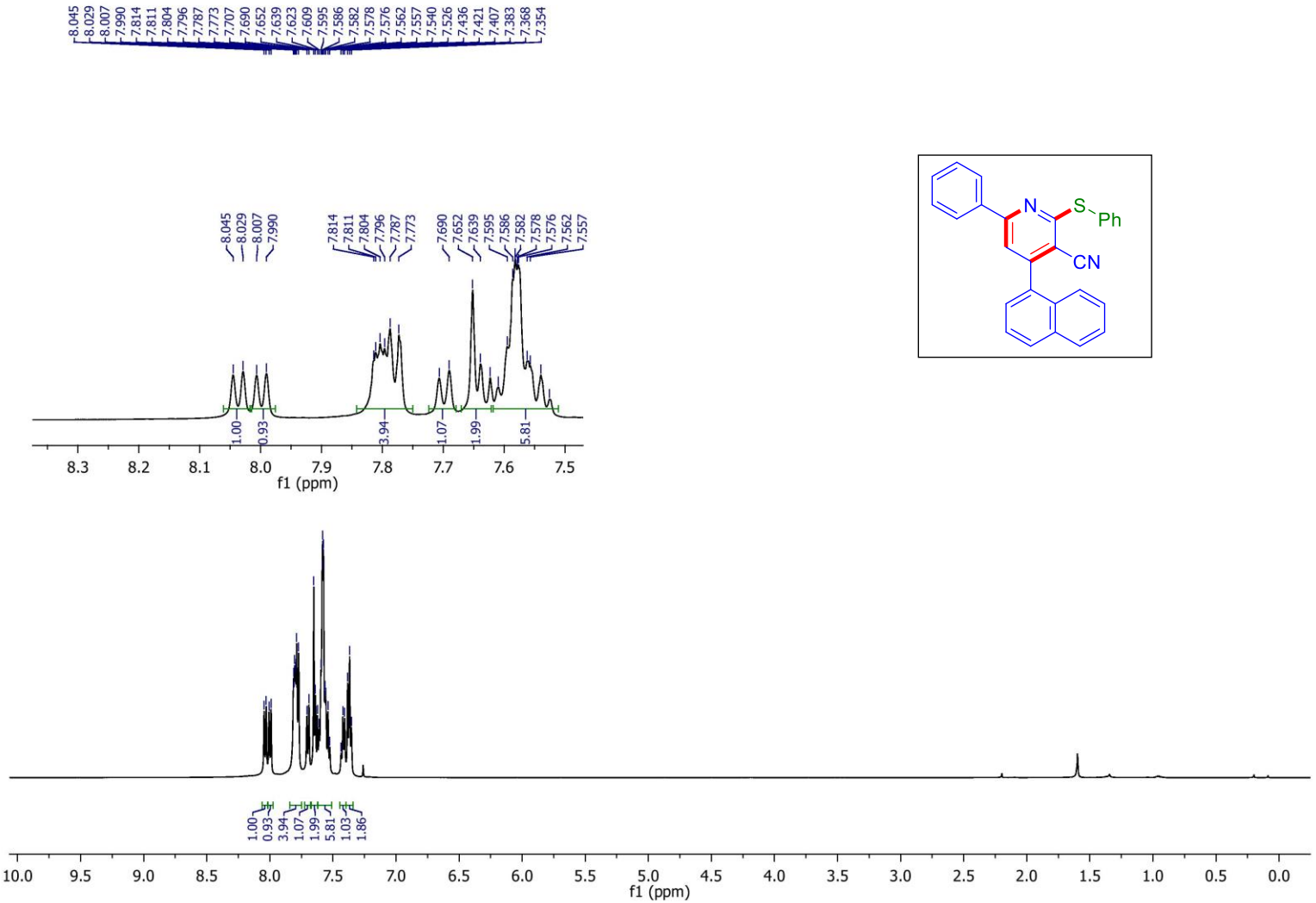




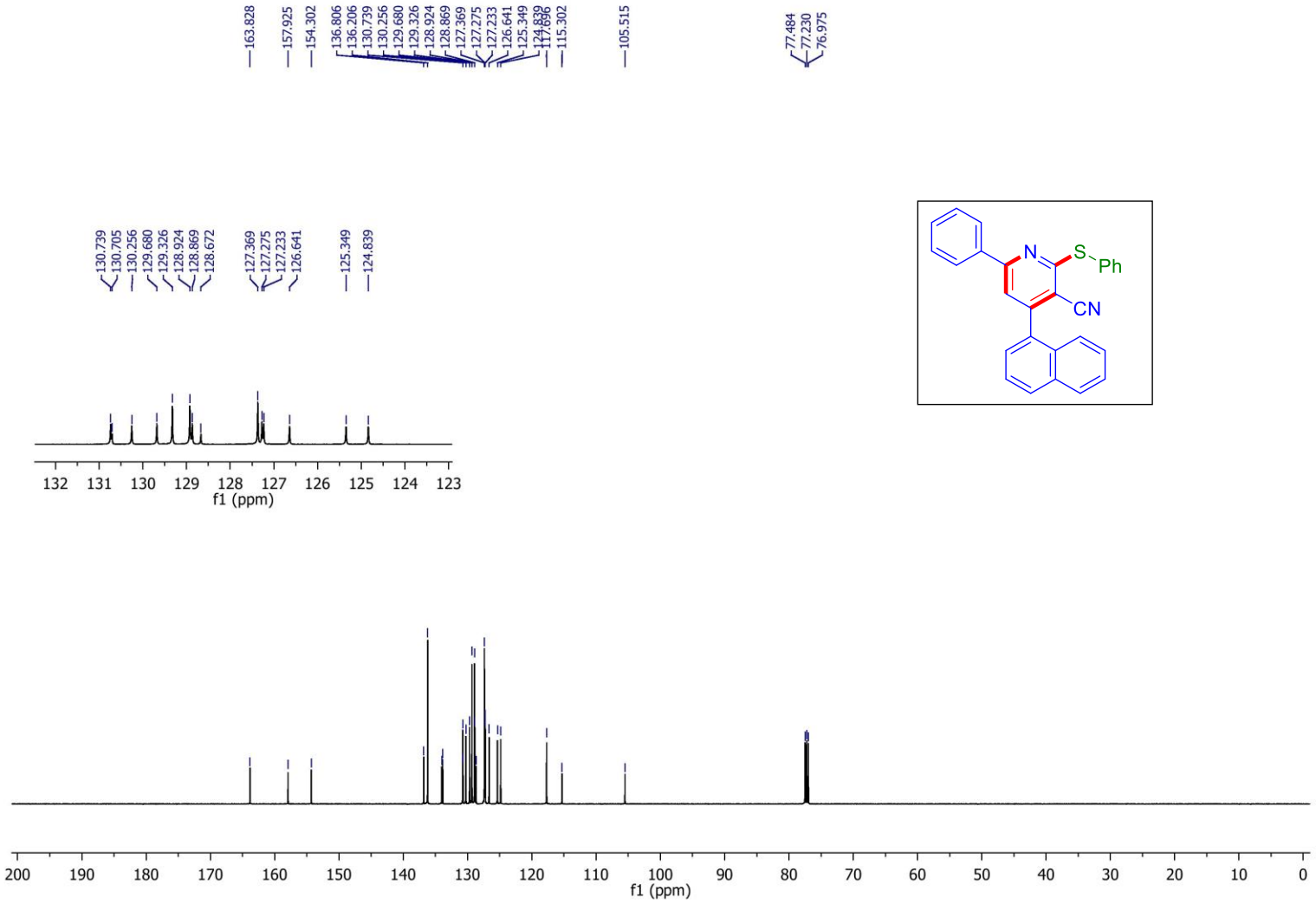
***4,6-Di(furan-2-yl)-2-(phenylthio)nicotinonitrile* (*12a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



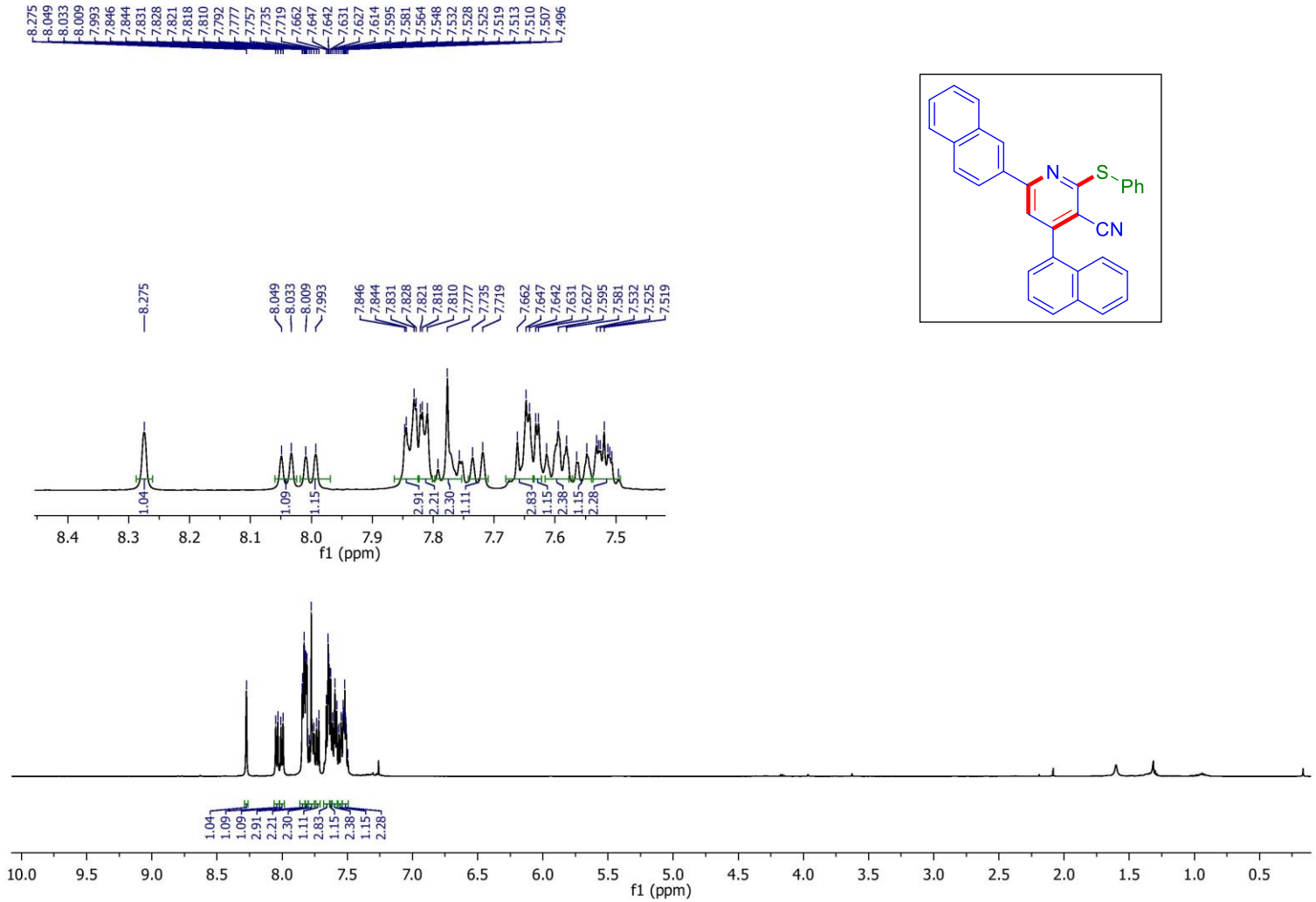
4-(Naphthalen-1-yl)-6-phenyl-2-(phenylthio)nicotinonitrile (13a): ^{1}H NMR (CDCl$_3$, 500 MHz)



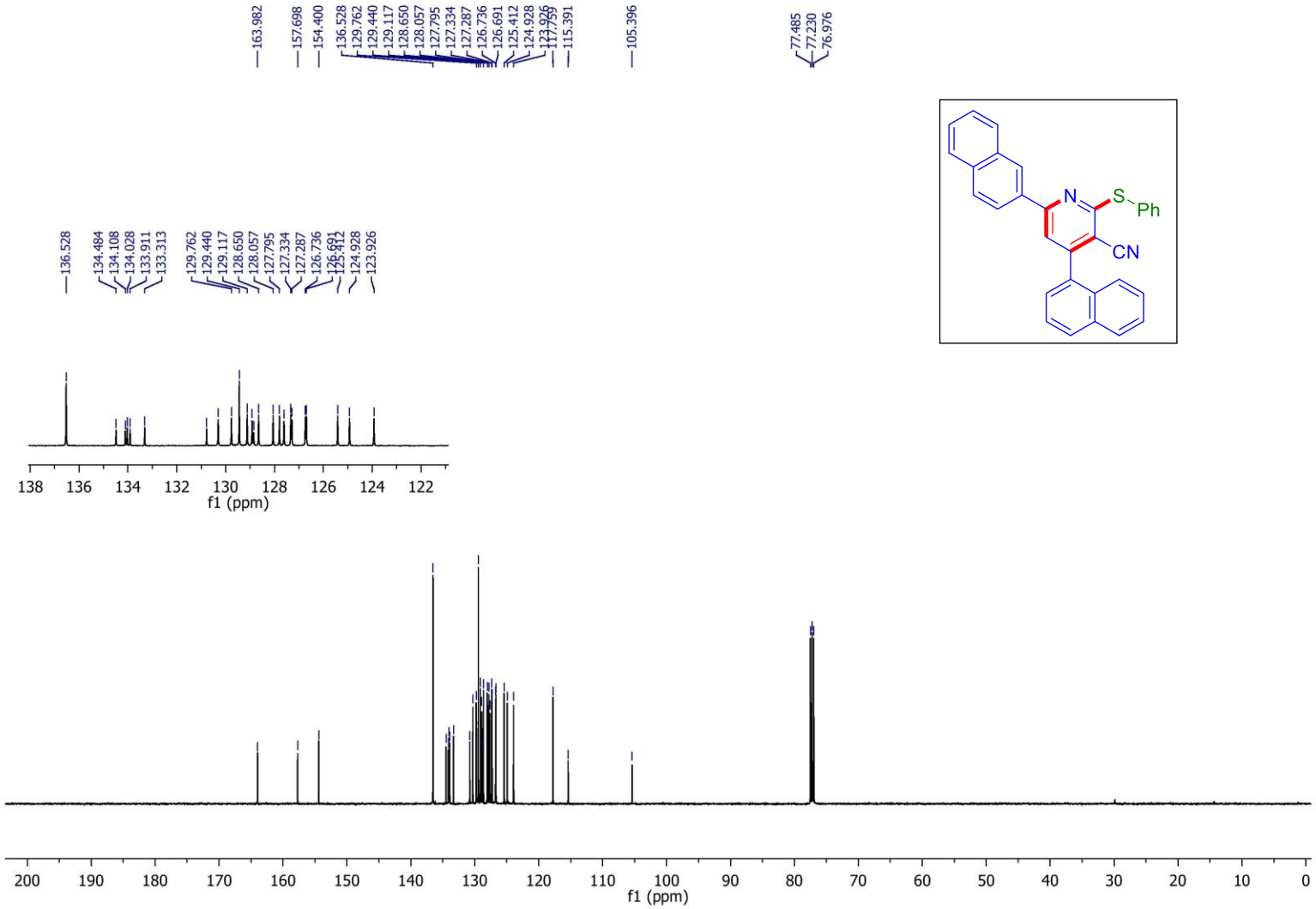
***4-(Naphthalen-1-yl)-6-phenyl-2-(phenylthio)nicotinonitrile* (*13a*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



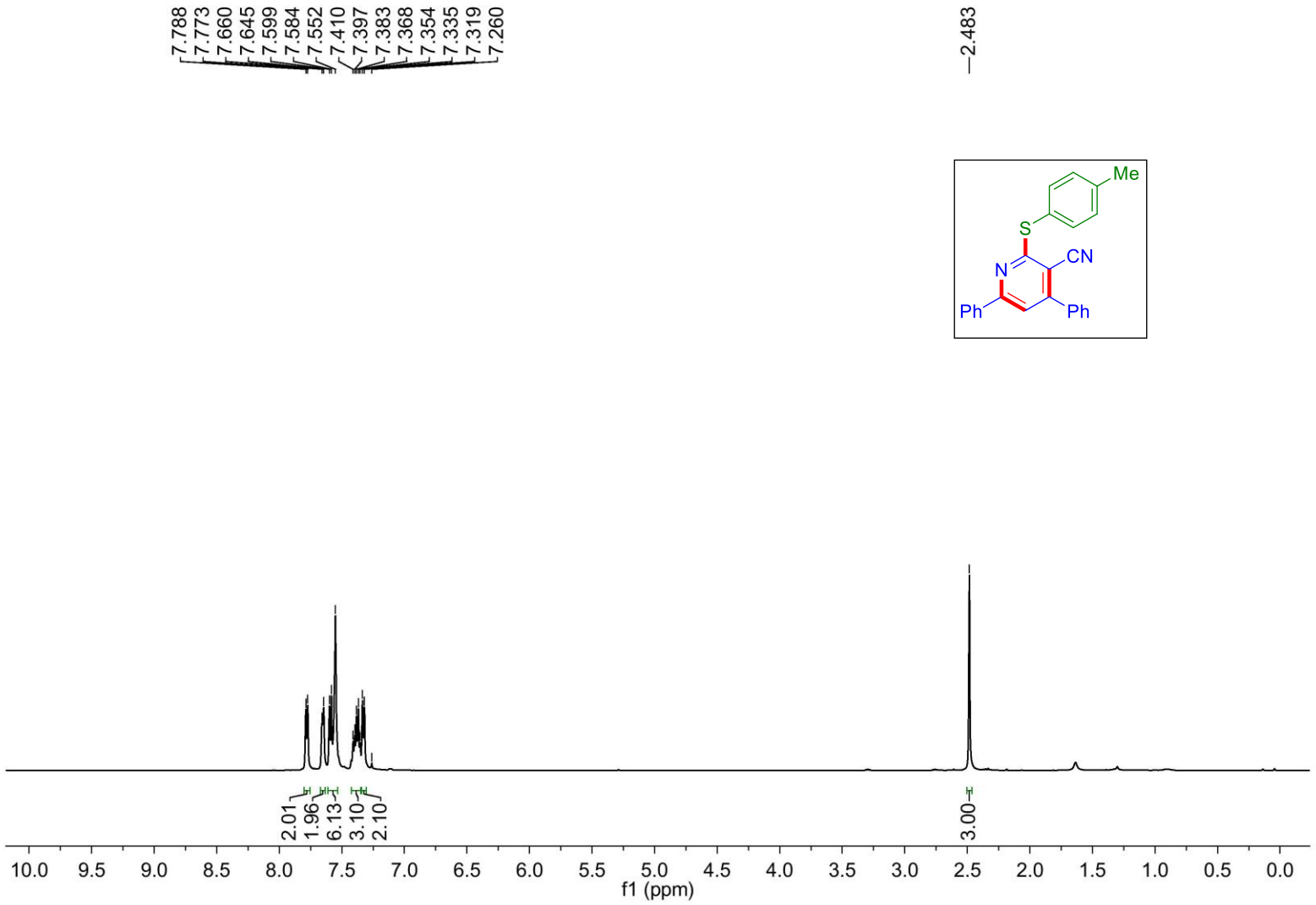
***4-(Naphthalen-1-yl)-6-(naphthalen-2-yl)-2-(phenylthio)nicotinonitrile* (*14a*): ^{1}H NMR ($CDCl_3$, 500 MHz)**



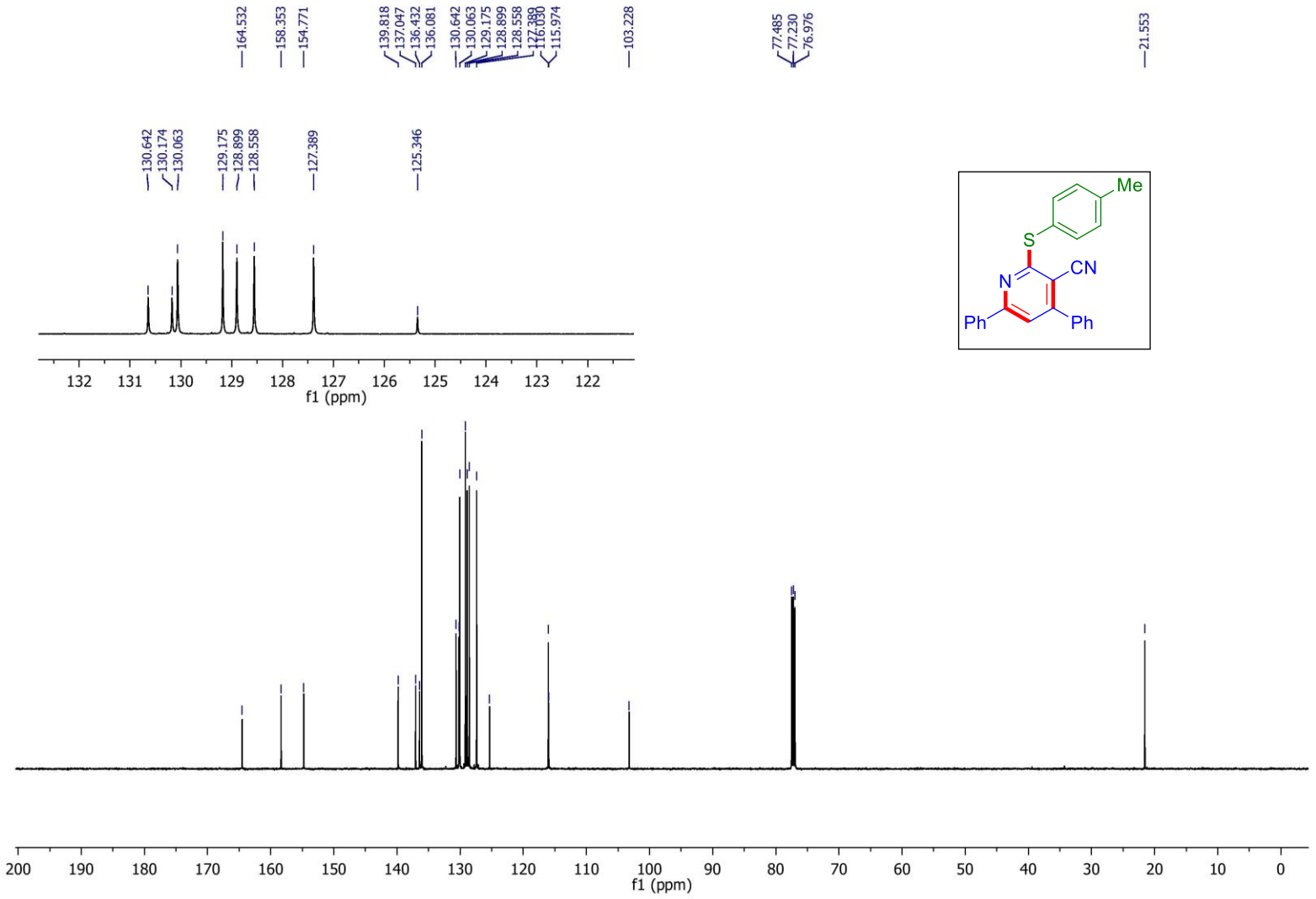
4-(Naphthalen-1-yl)-6-(naphthalen-2-yl)-2-(phenylthio)nicotinonitrile (14a): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



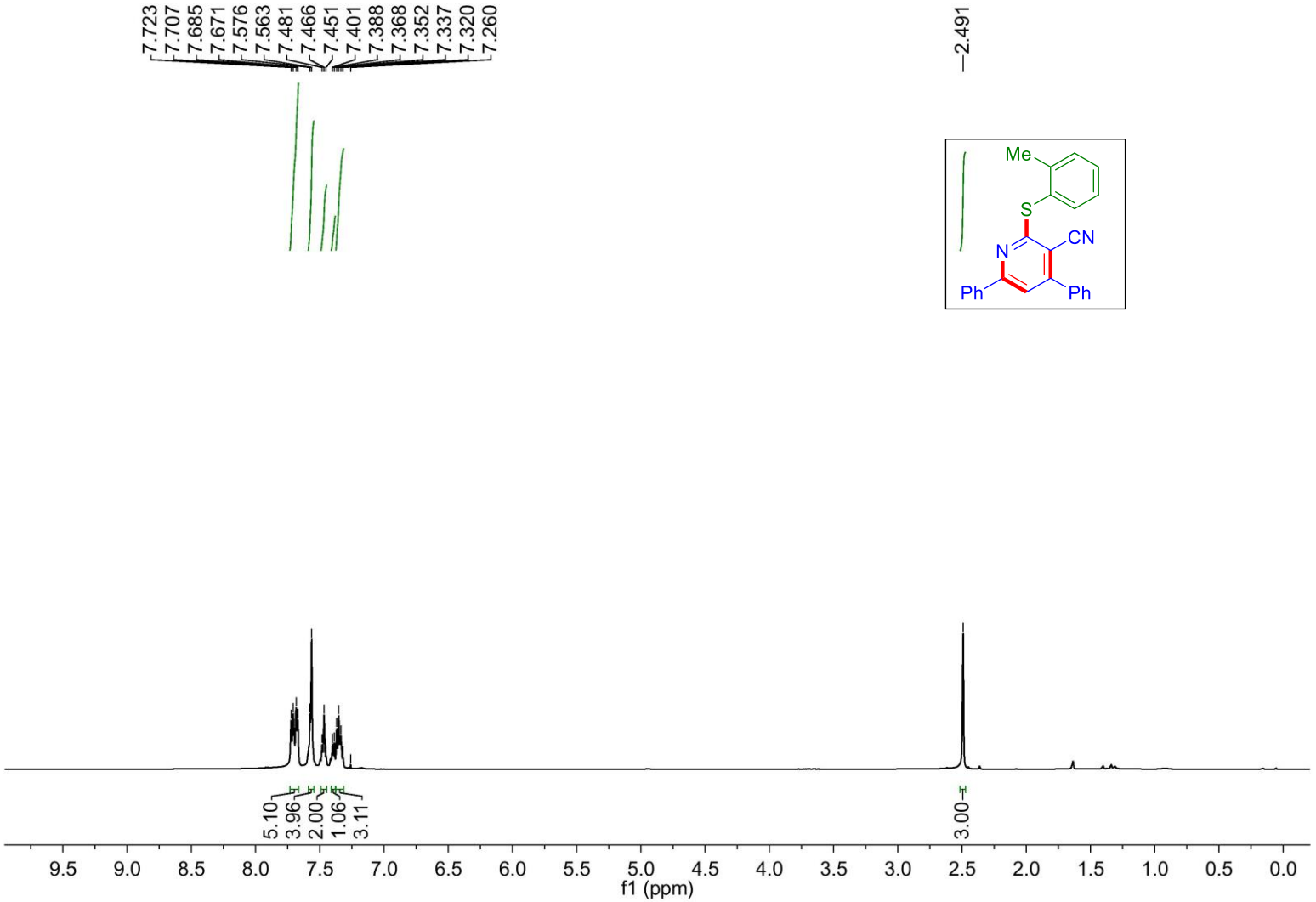
4,6-Diphenyl-2-(p-tolylthio)nicotinonitrile (1b): ^{1}H NMR ($CDCl_3$, 500 MHz)



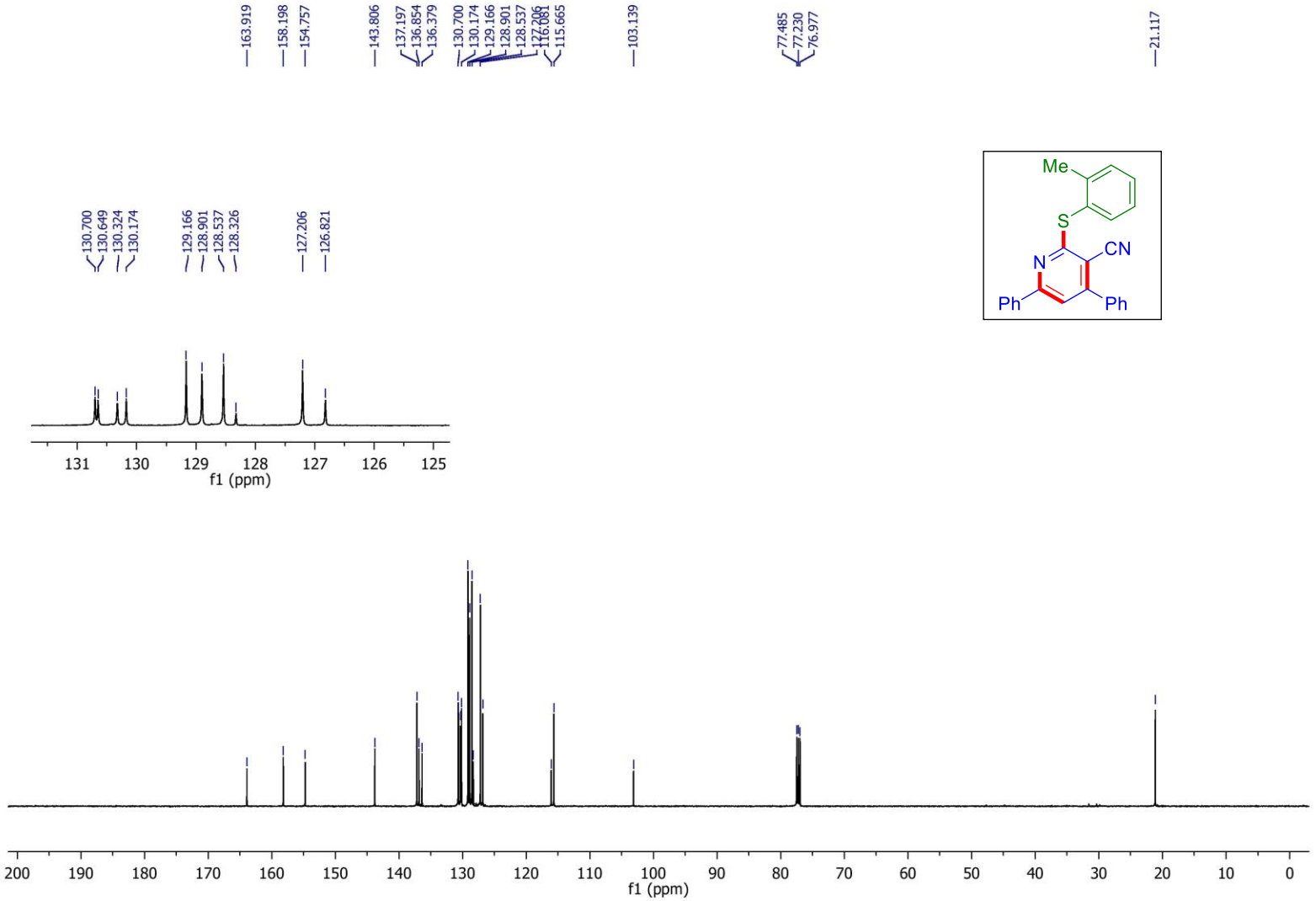
4,6-Diphenyl-2-(p-tolylthio)nicotinonitrile (1b): $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz)



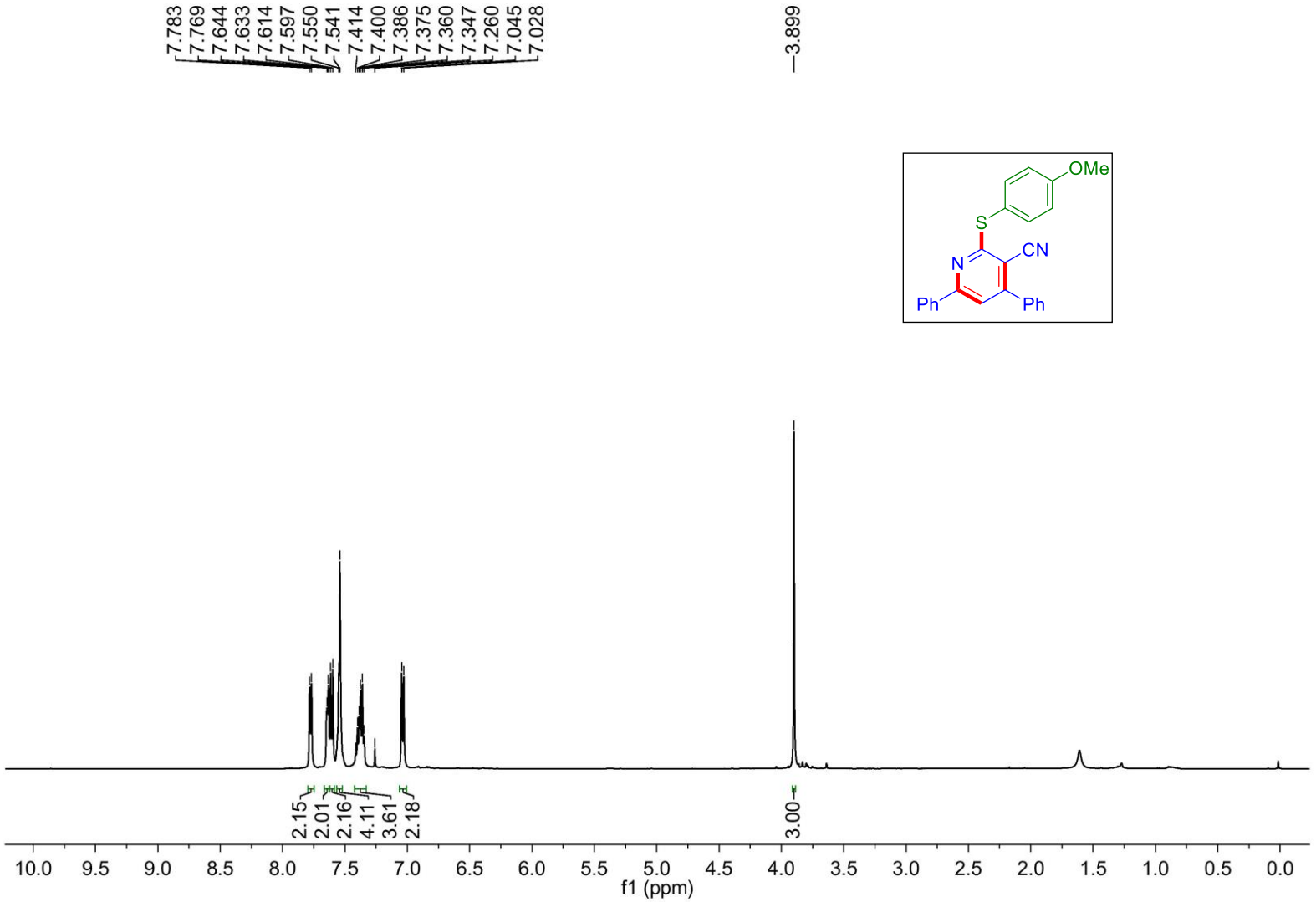
4,6-Diphenyl-2-(o-tolylthio)nicotinonitrile (1c): ^{1}H NMR ($CDCl_3$, 500 MHz)



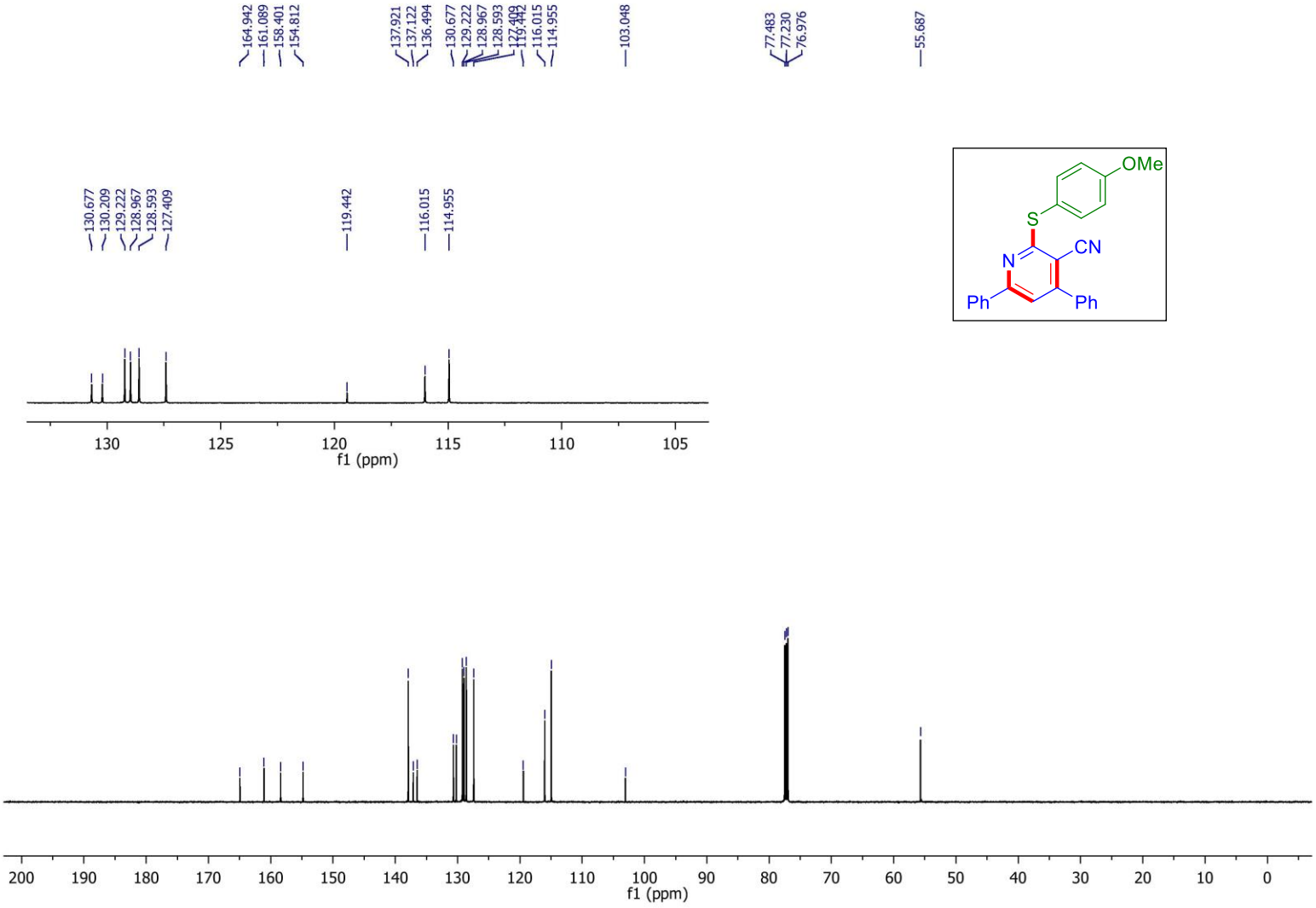
4,6-Diphenyl-2-(o-tolylthio)nicotinonitrile (1c): $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz)



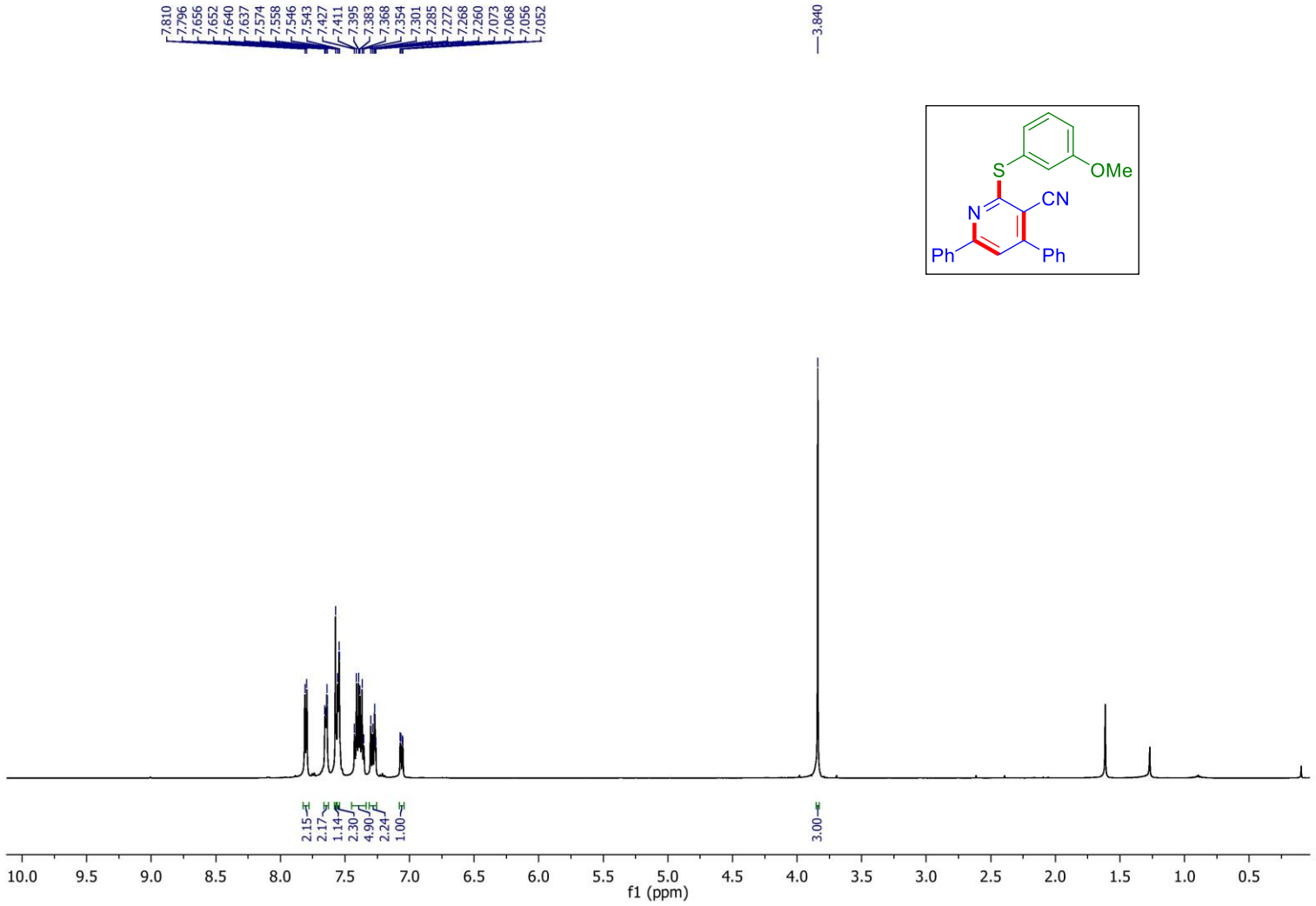
***2-((4-Methoxyphenyl)thio)-4,6-diphenylnicotinonitrile* (*1d*): ^{1}H NMR ($CDCl_3$, 500 MHz)**



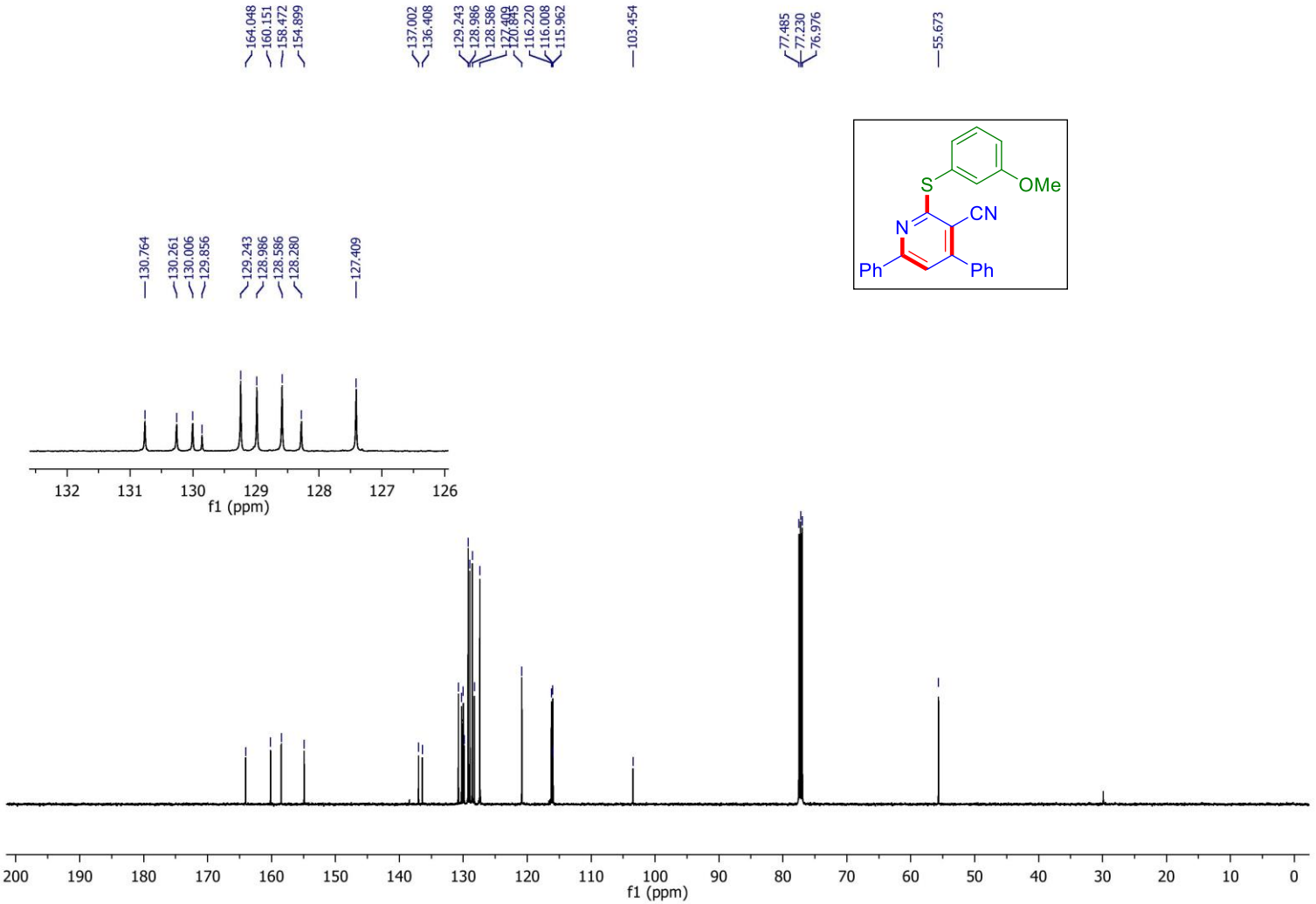
***2-((4-Methoxyphenyl)thio)-4,6-diphenylnicotinonitrile* (*1d*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



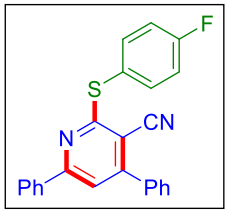
***2-((3-Methoxyphenyl)thio)-4,6-diphenylnicotinonitrile* (*1e*): ^{1}H NMR ($CDCl_3$, 500 MHz)**

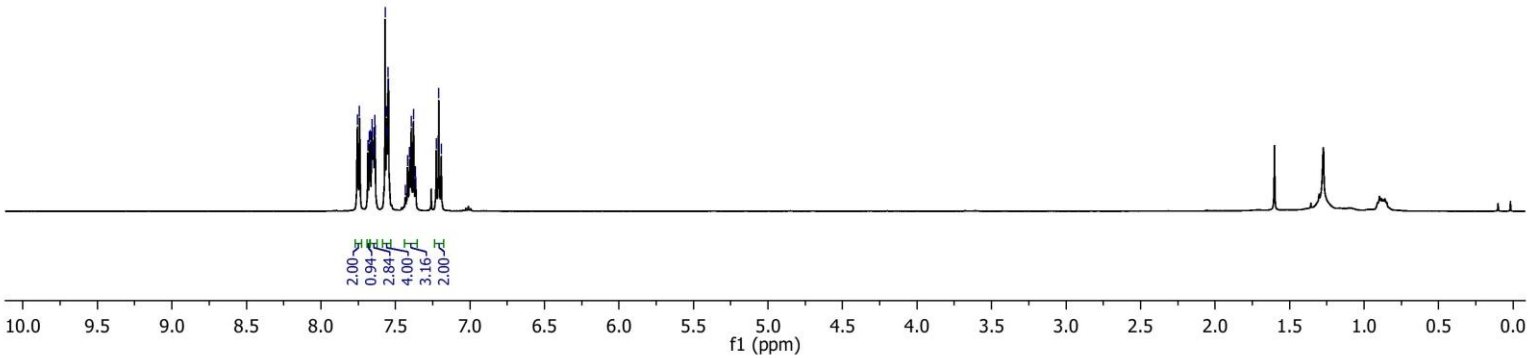


***2-((3-Methoxyphenyl)thio)-4,6-diphenylnicotinonitrile* (*1e*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**

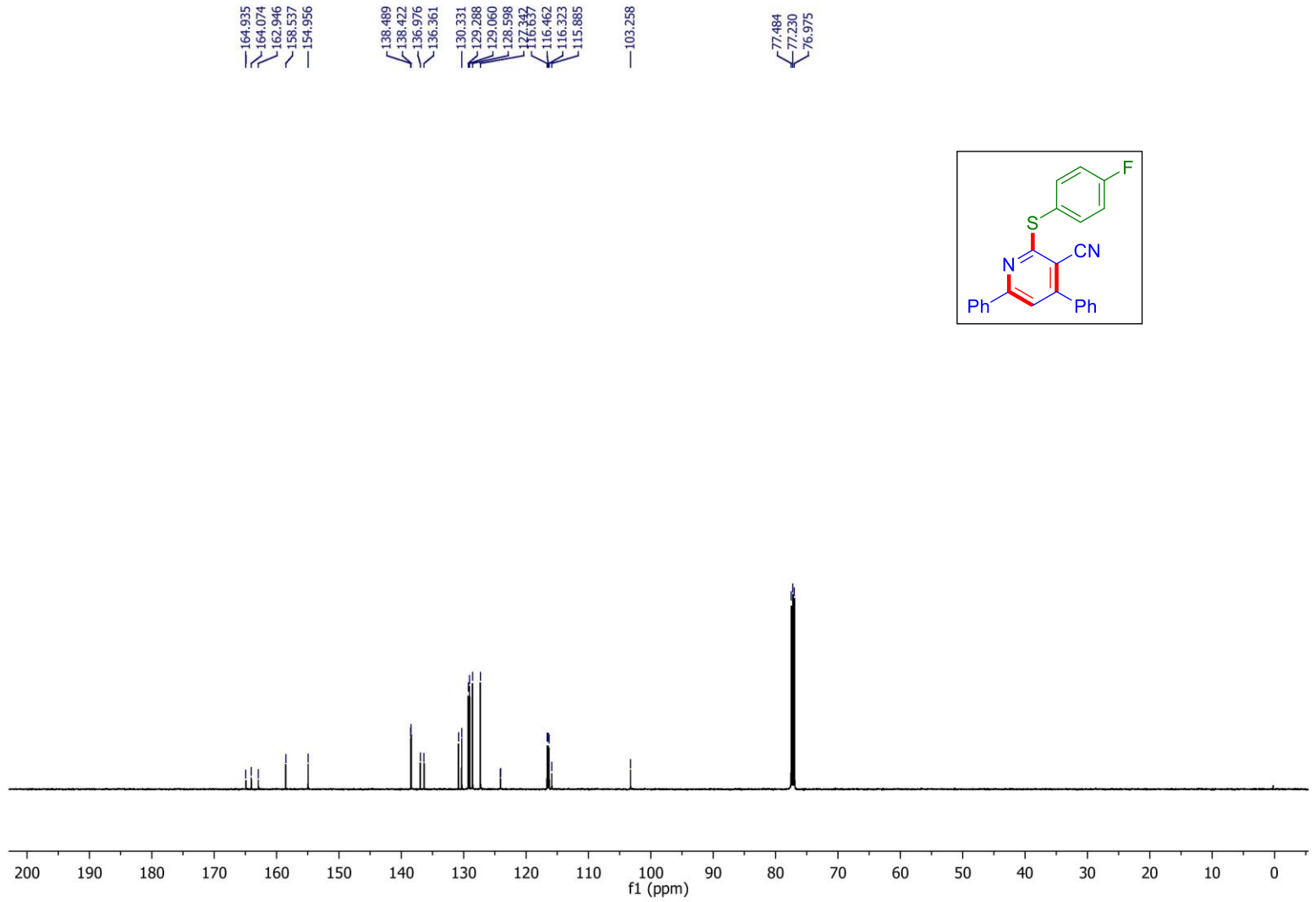


2-((4-Fluorophenyl)thio)-4,6-diphenylnicotinonitrile (1f): ^{1}H NMR ($CDCl_3$, 500 MHz)

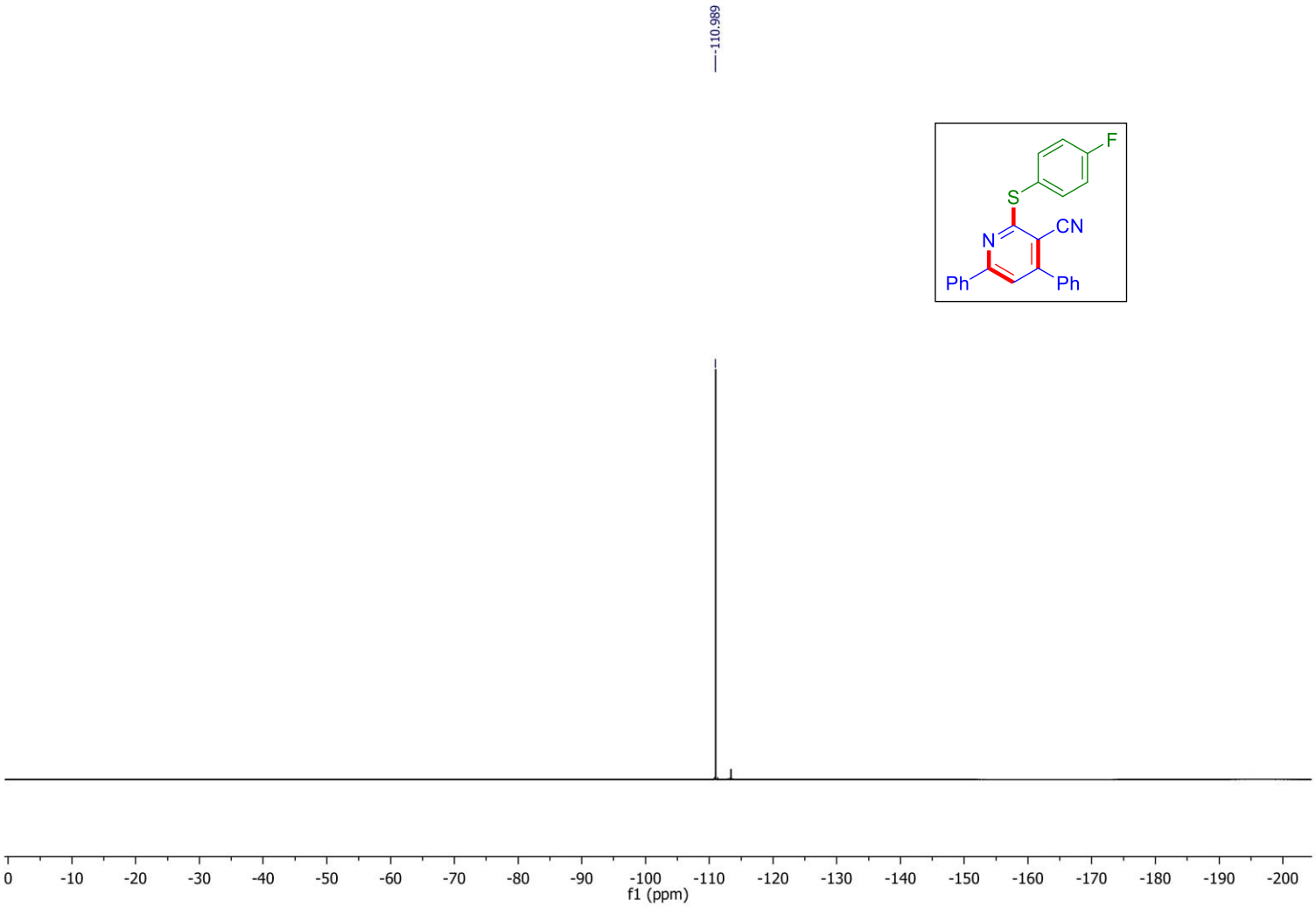




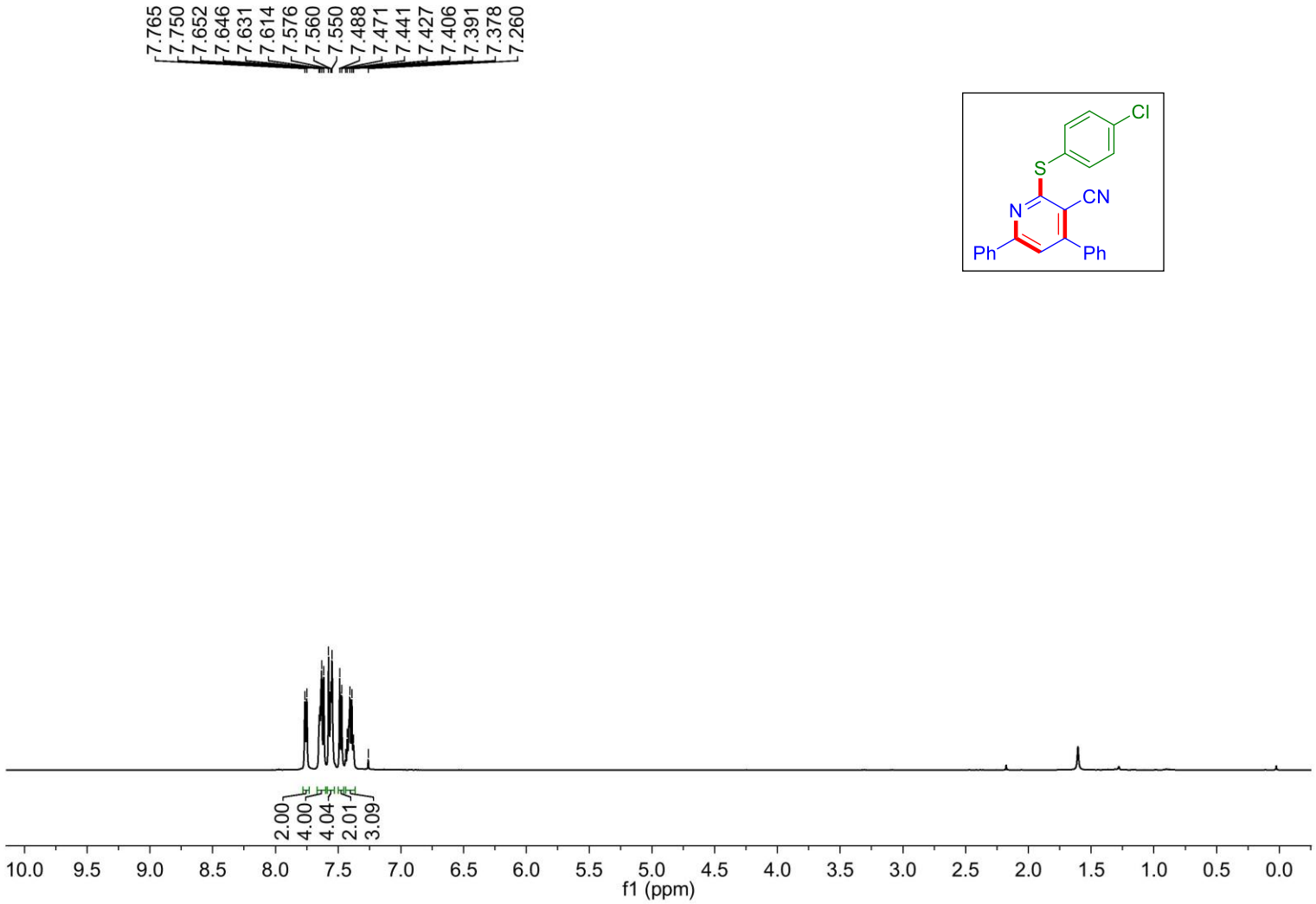
2-((4-Fluorophenyl)thio)-4,6-diphenylnicotinonitrile (1f): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



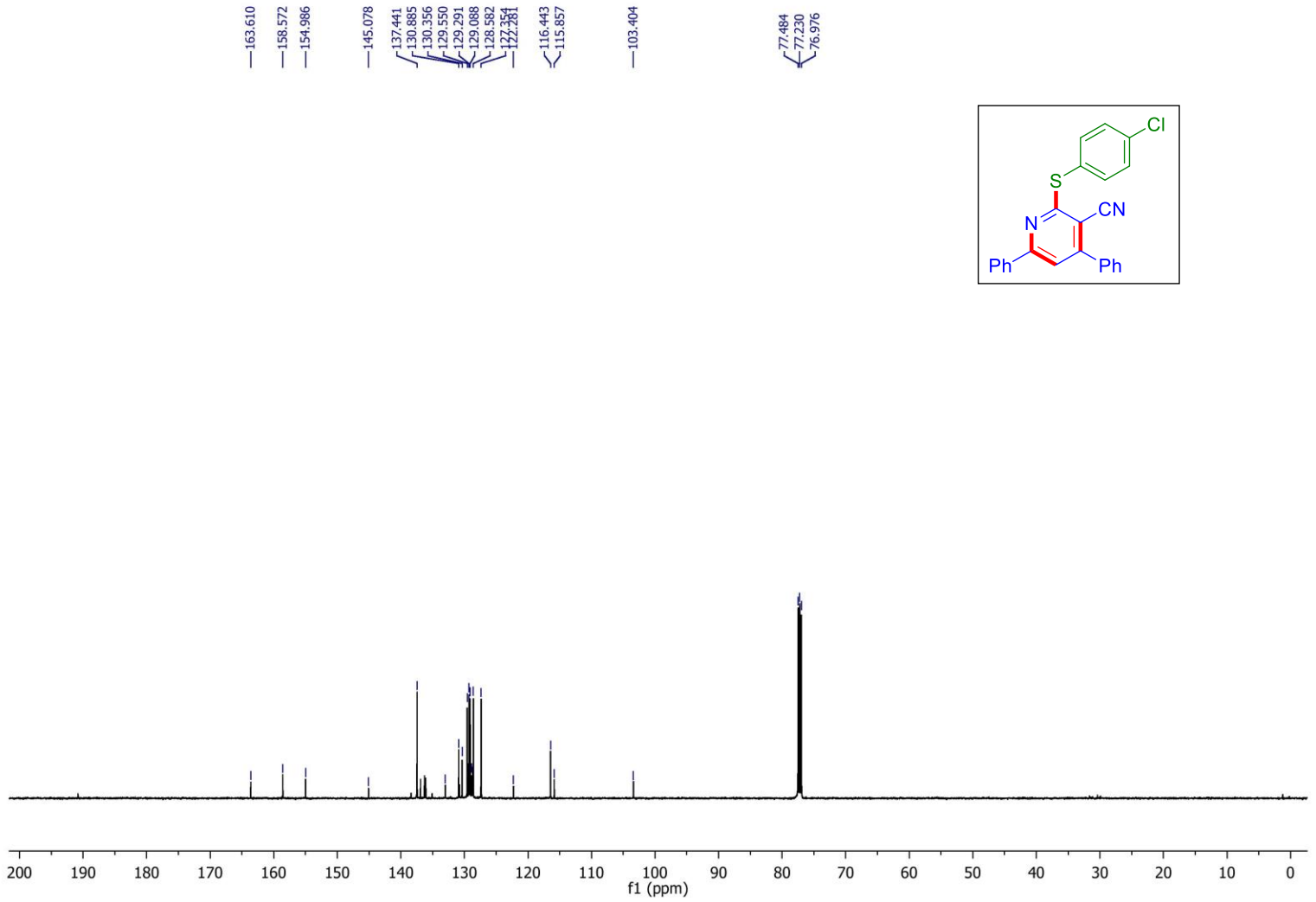
2-((4-Fluorophenyl)thio)-4,6-diphenylnicotinonitrile (1f): ^{19}F NMR ($CDCl_3$, 471 MHz)



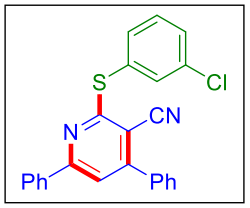
2-((4-Chlorophenyl)thio)-4,6-diphenylnicotinonitrile (1g): ^{1}H NMR ($CDCl_3$, 500 MHz)

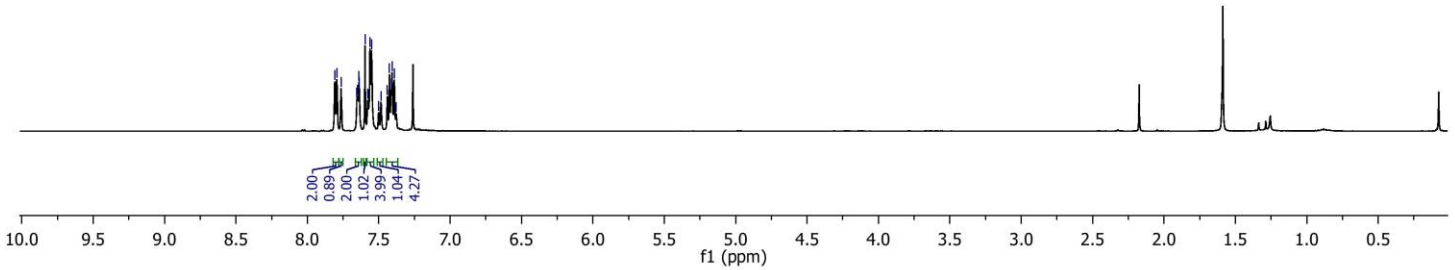


2-((4-Chlorophenyl)thio)-4,6-diphenylnicotinonitrile (1g): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)

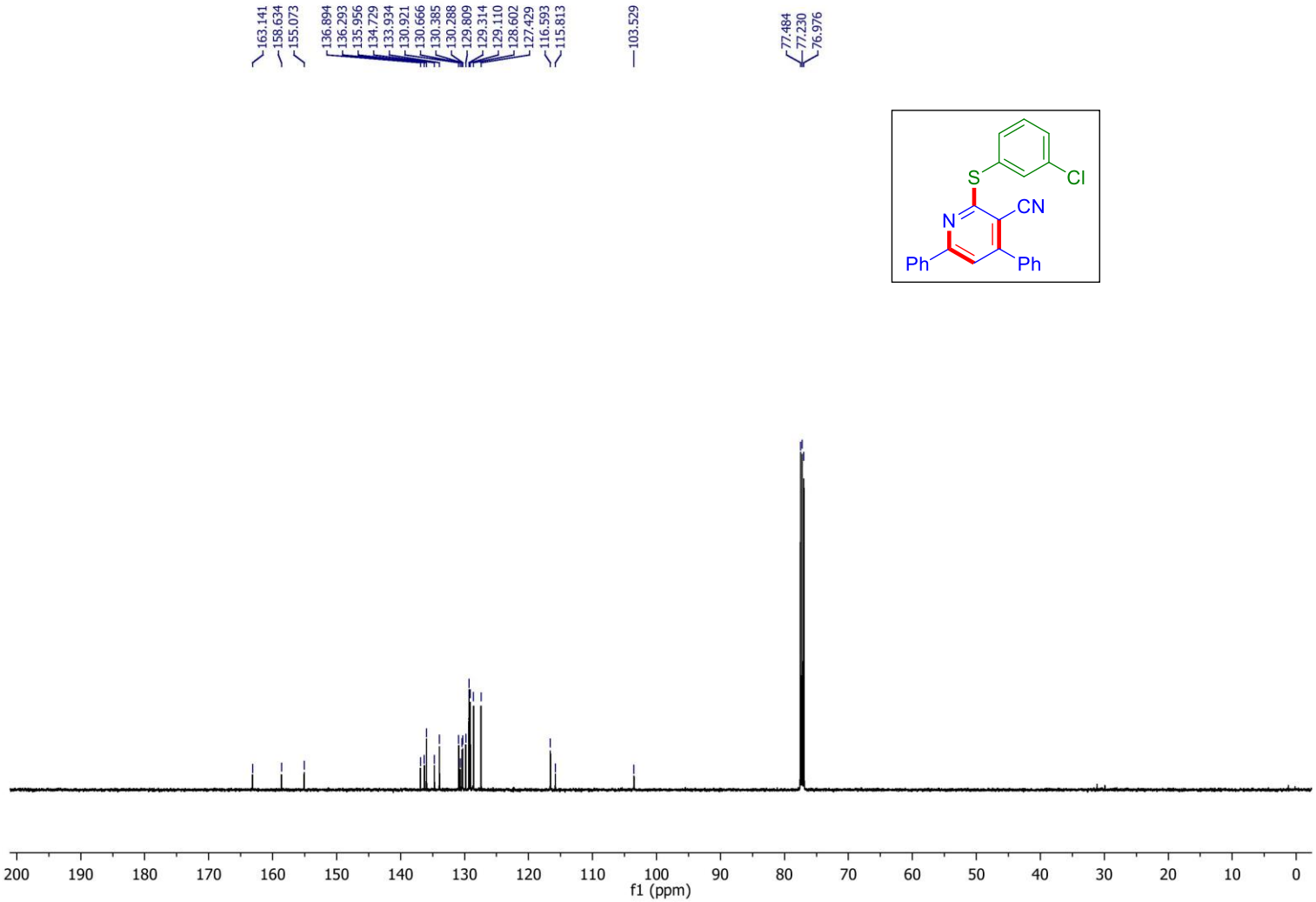


***2-((3-Chlorophenyl)thio)-5-phenyl-1H-pyrrole-3-carbonitrile* (*1h*): ^{1}H NMR ($CDCl_3$, 500 MHz)**

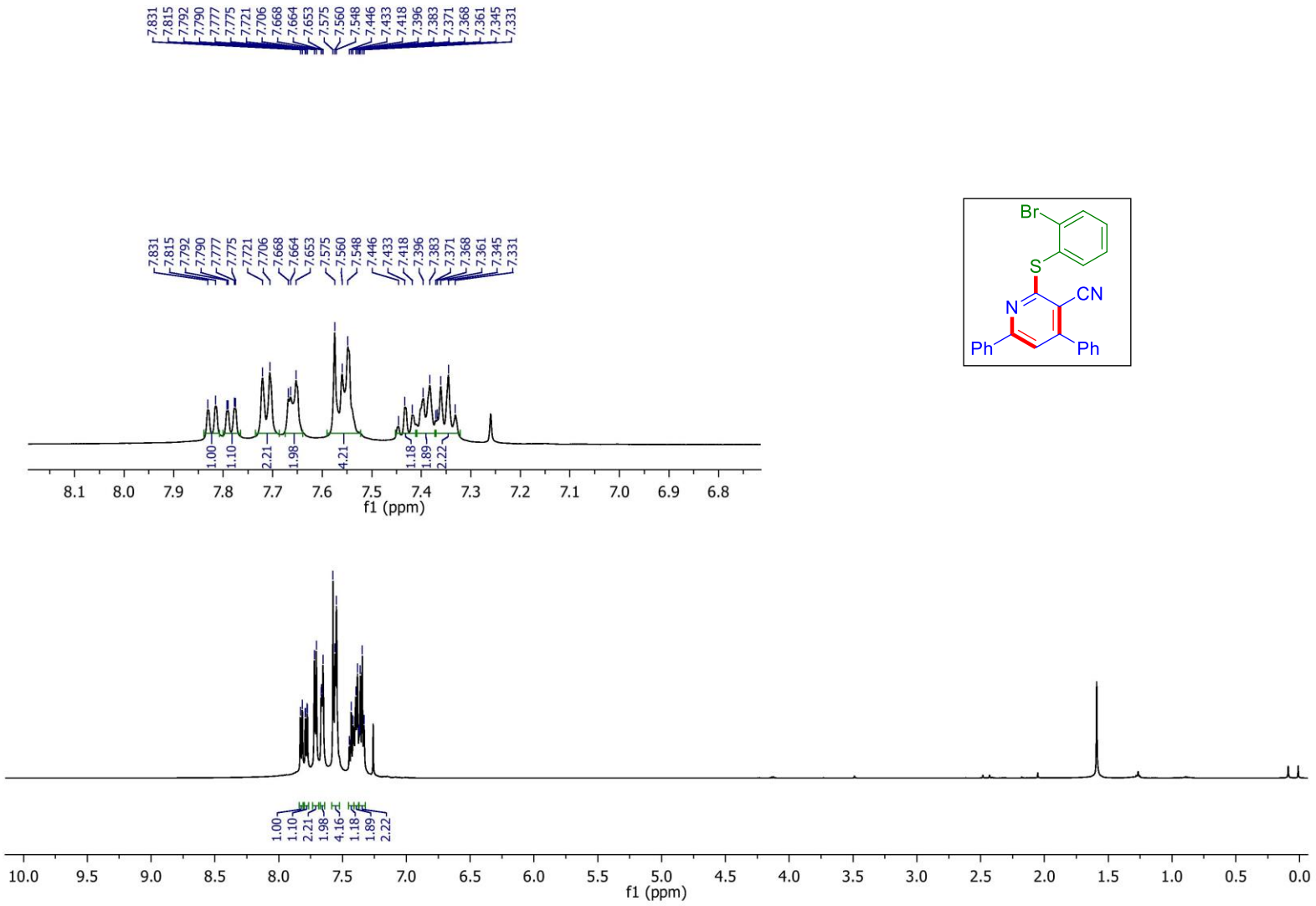




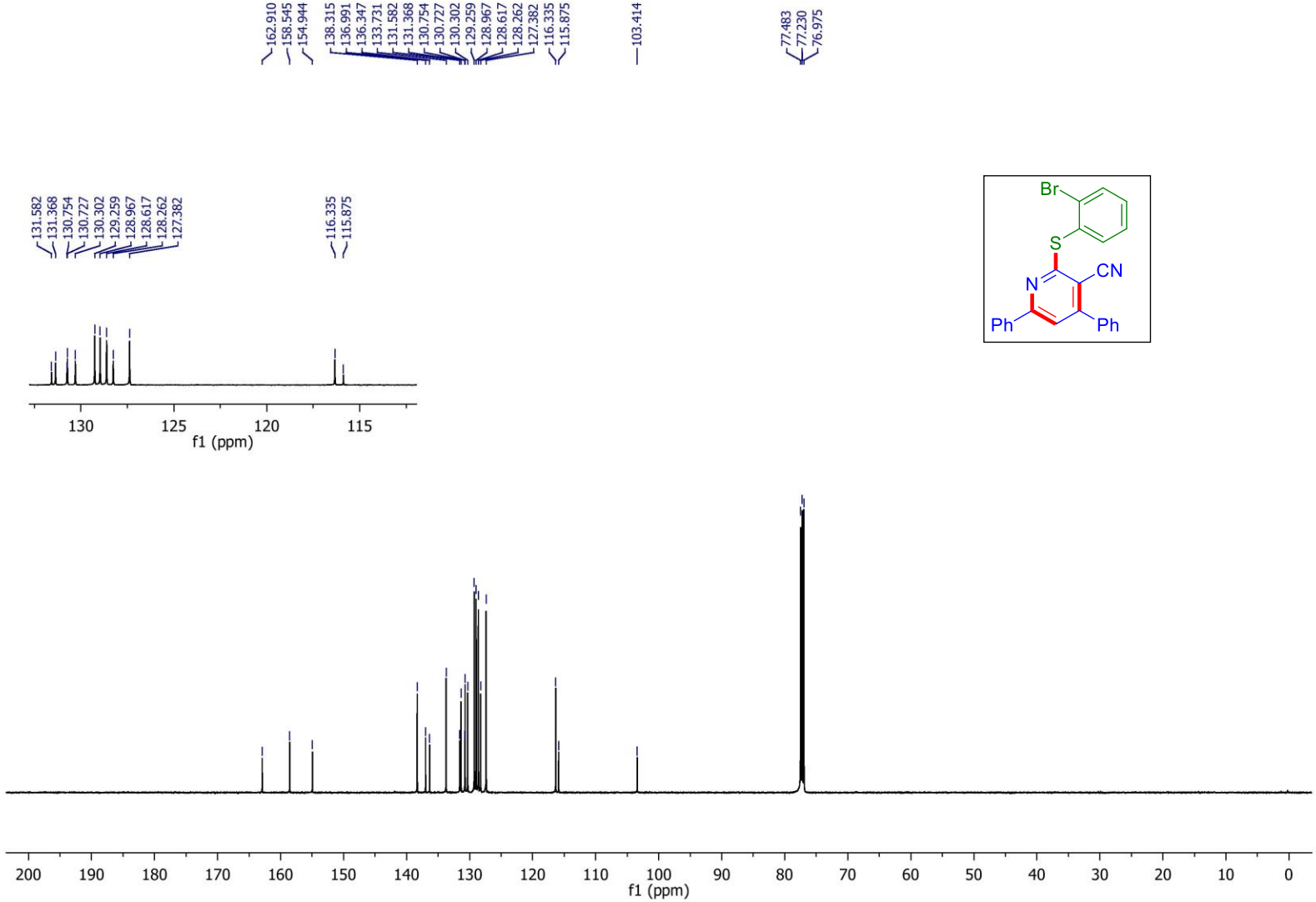
***2-((3-Chlorophenyl)thio)-5-phenyl-1H-pyrrole-3-carbonitrile* (1h): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



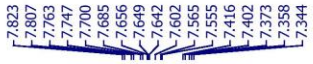
***2-((2-Bromophenyl)thio)-4,6-diphenylnicotinonitrile* (*1i*): ^{1}H NMR ($CDCl_3$, 500 MHz)**

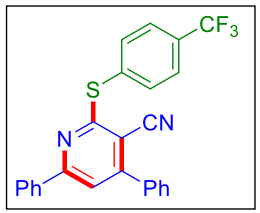


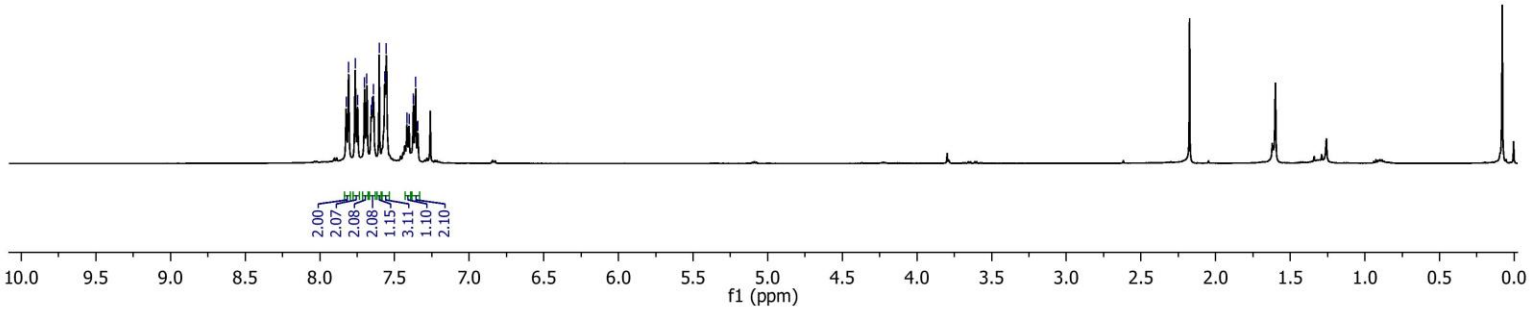
***2-((2-Bromophenyl)thio)-4,6-diphenylnicotinonitrile* (*1i*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



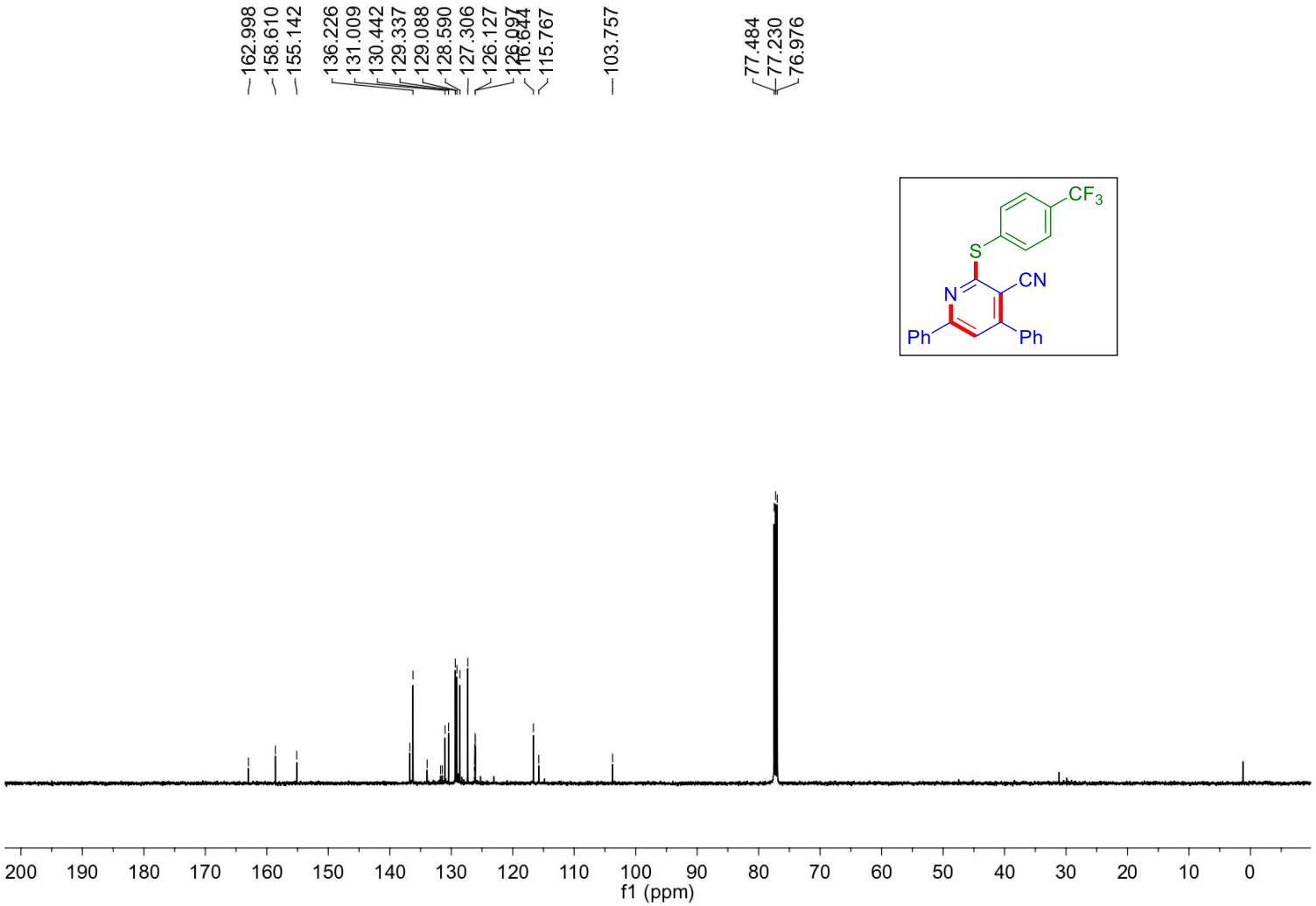
***4,6-Diphenyl-2-((4-(trifluoromethyl)phenyl)thio)nicotinonitrile* (*1j*): ^{1}H NMR ($CDCl_3$, 500 MHz)**



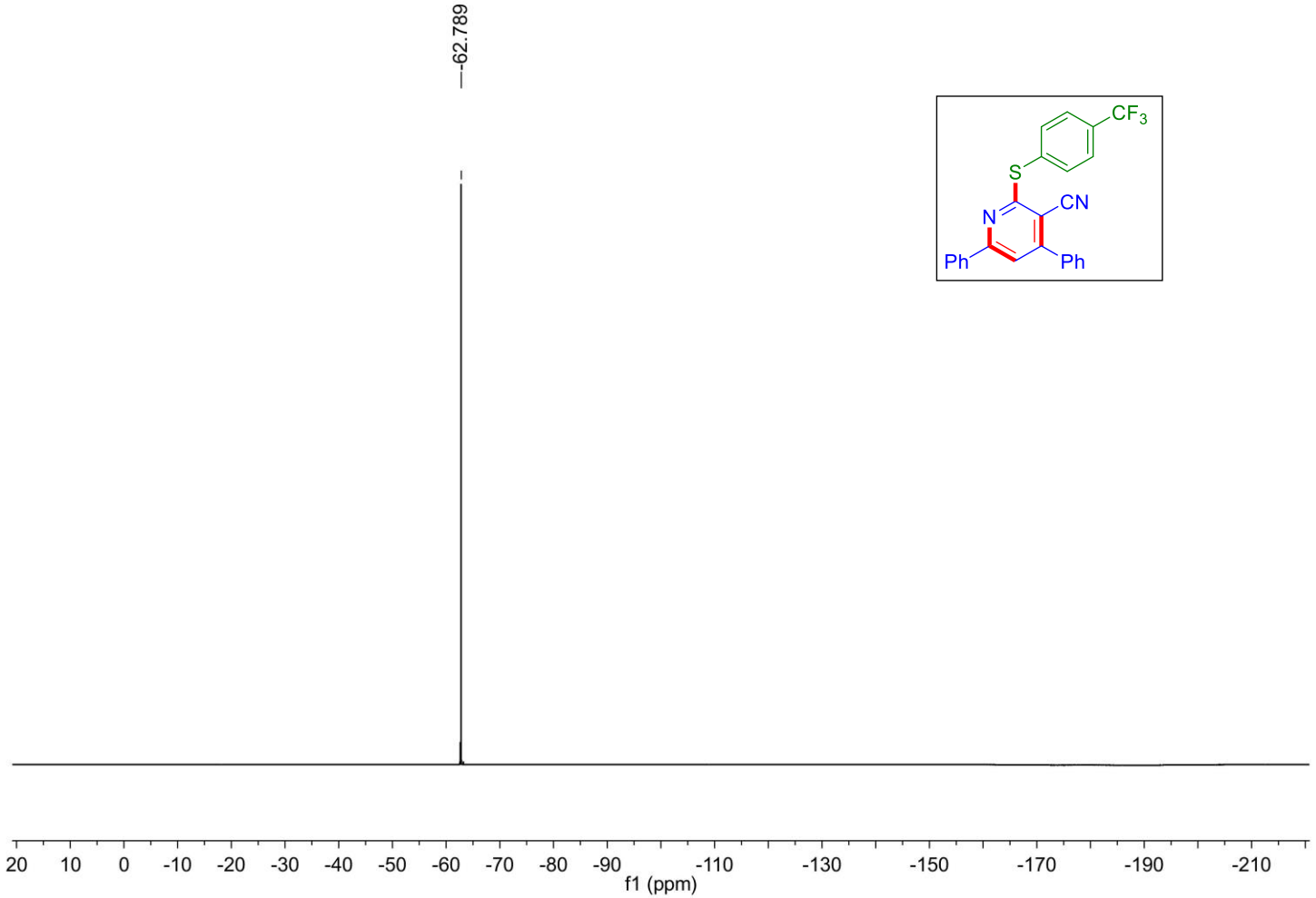




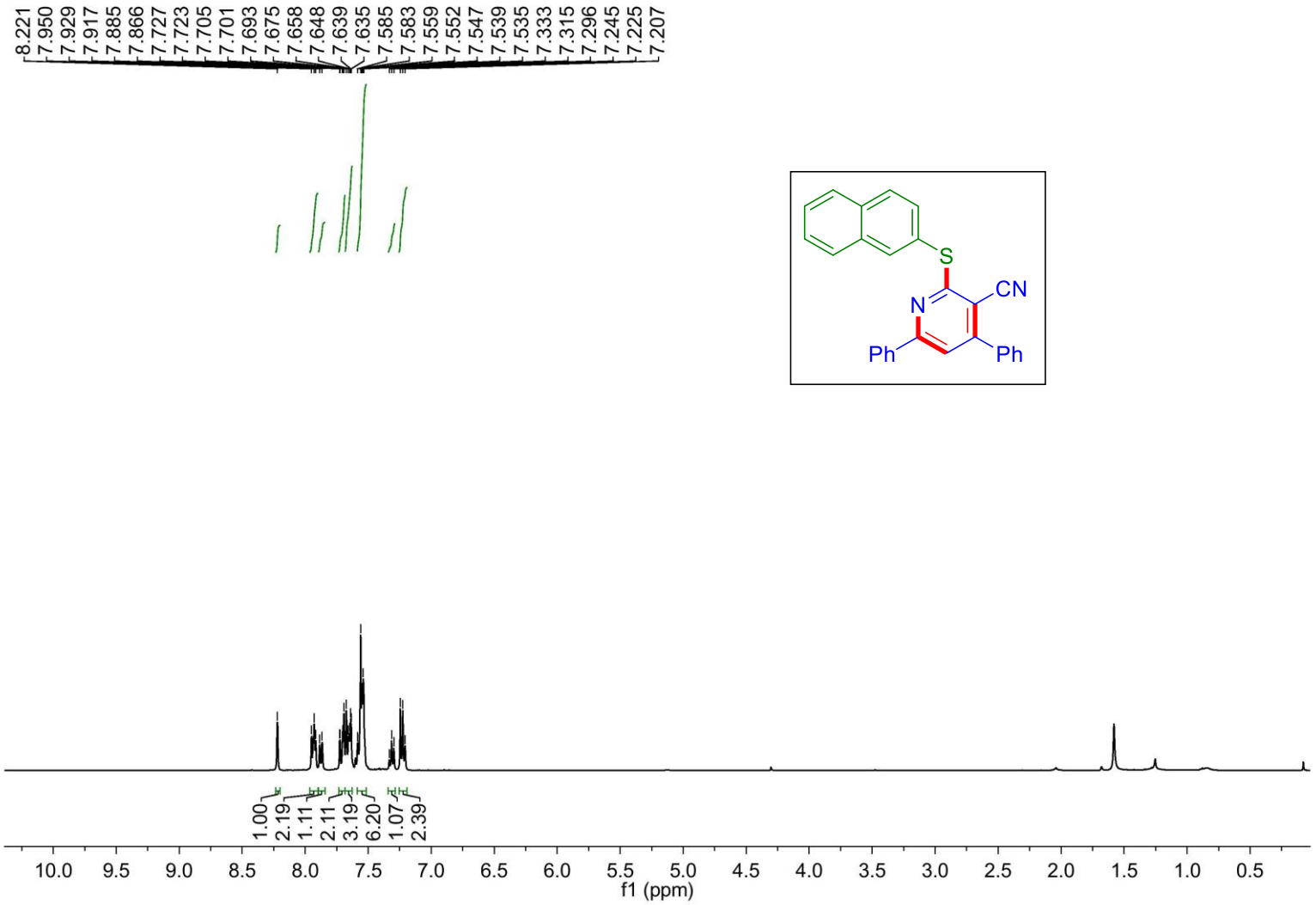
***4,6-Diphenyl-2-((4-(trifluoromethyl)phenyl)thio)nicotinonitrile* (*1j*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



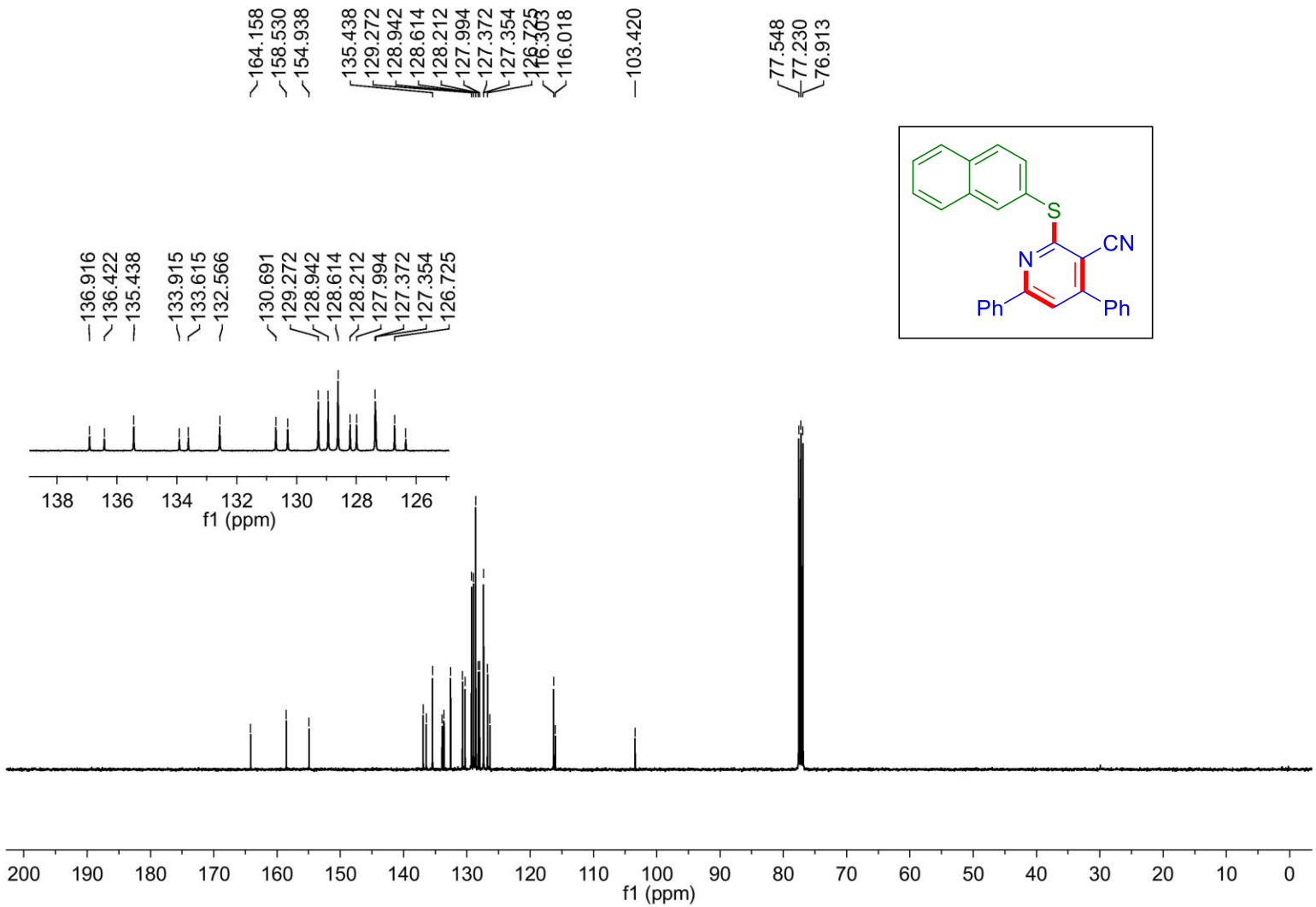
***4,6-Diphenyl-2-((4-(trifluoromethyl)phenyl)thio)nicotinonitrile* (*1j*): ^{19}F NMR ($CDCl_3$, 471 MHz)**



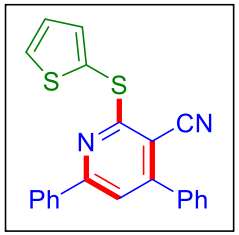
2-(naphthalen-2-ylthio)-4,6-diphenylnicotinonitrile* (1k)*: ^{1}H NMR ($CDCl_3$, 400 MHz)

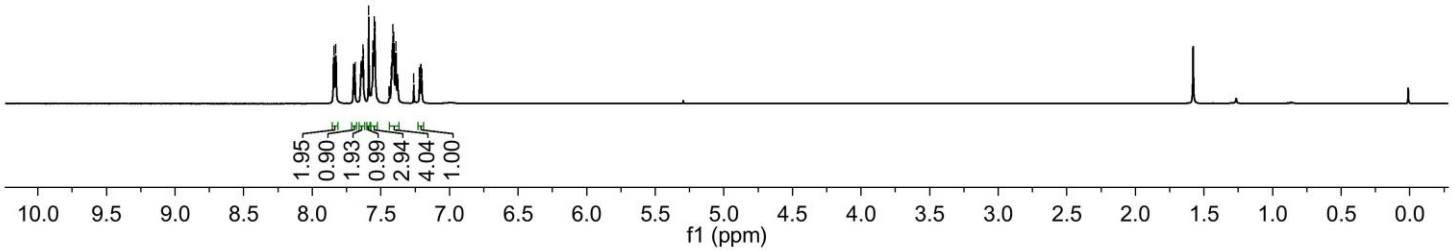


***2-(naphthalen-2-ylthio)-4,6-diphenylnicotinonitrile* (1k): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz)**

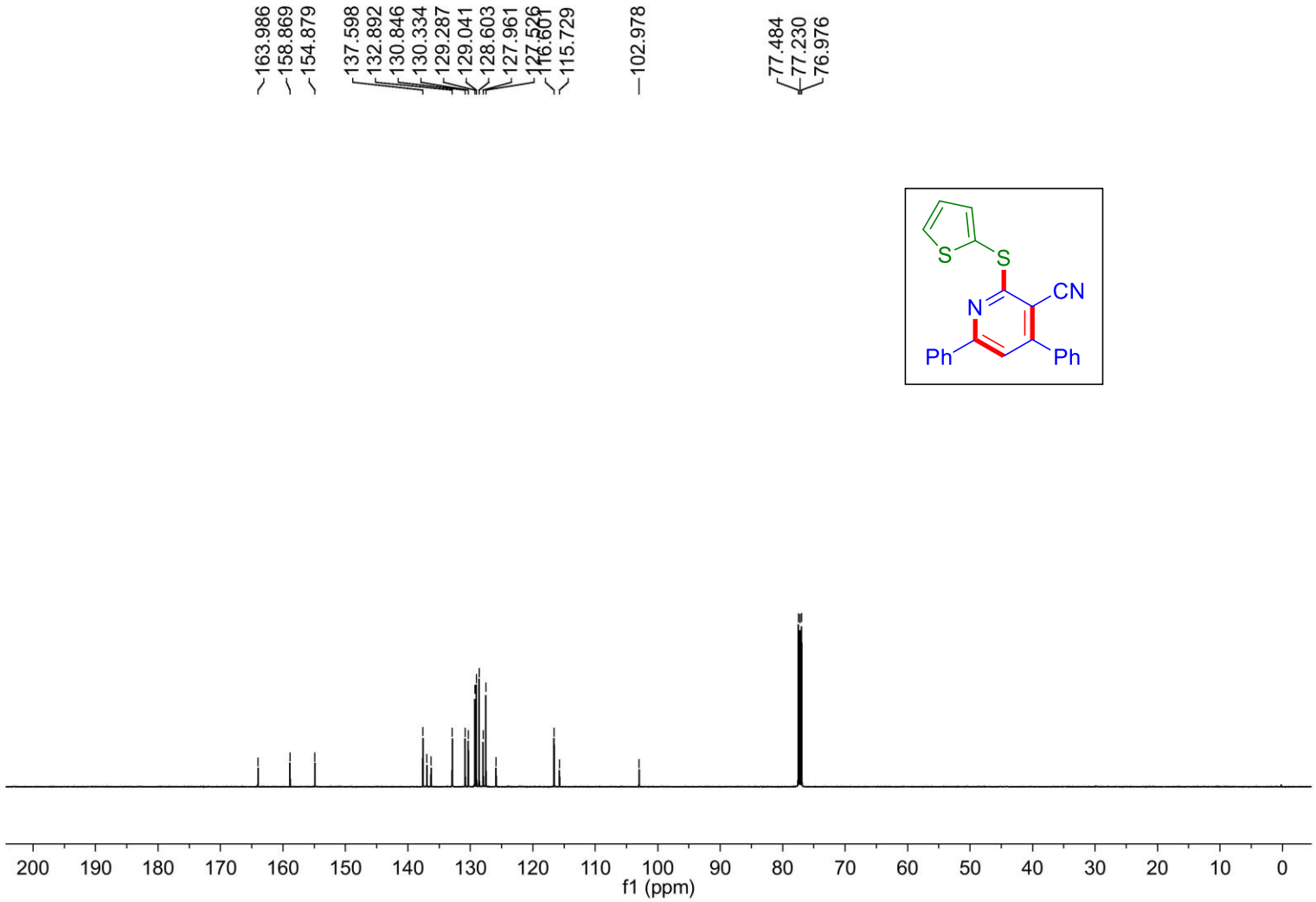


***4,6-Diphenyl-2-(thiophen-2-ylthio)nicotinonitrile* (*1l*): ^{1}H NMR ($CDCl_3$, 500 MHz)**

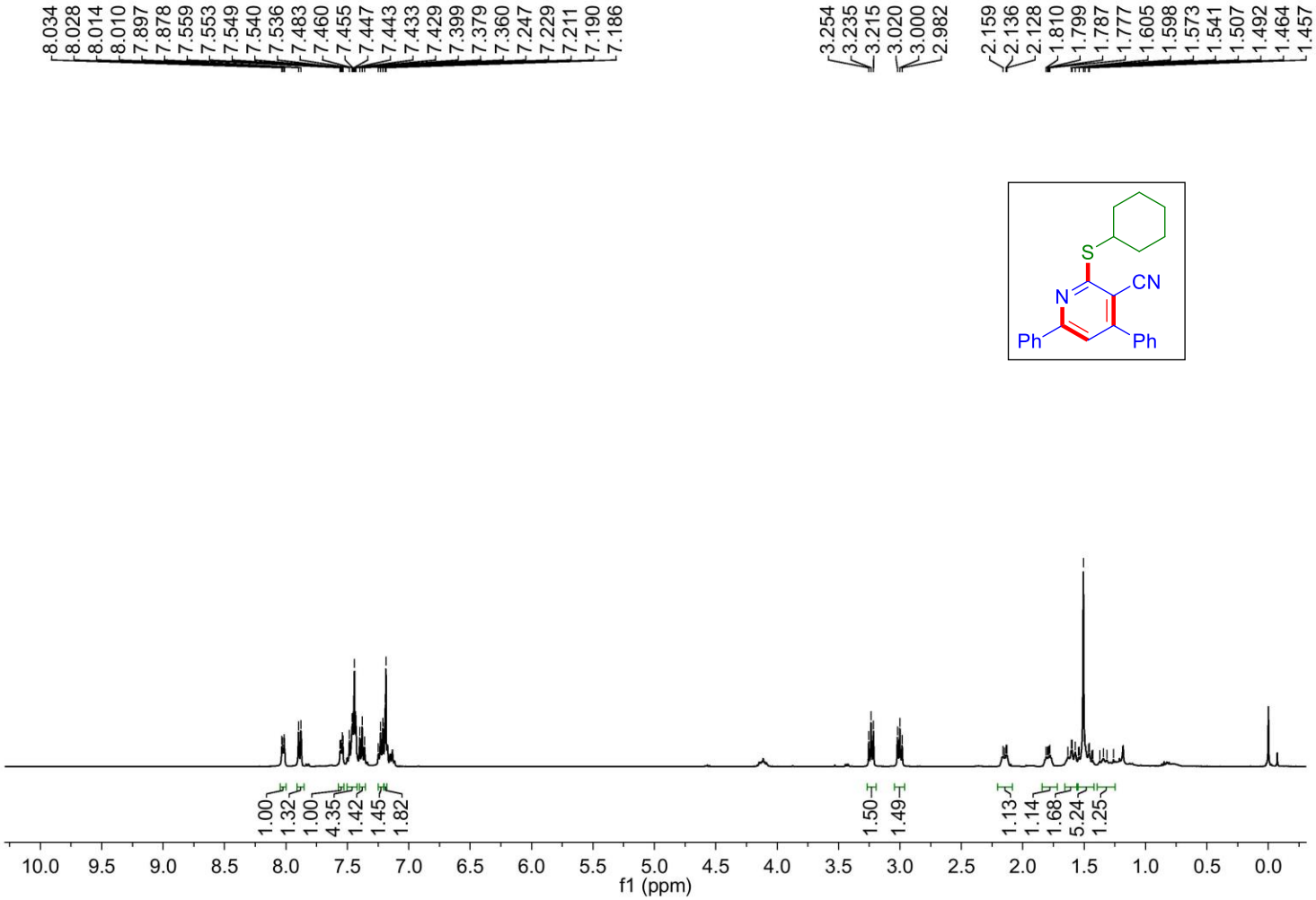




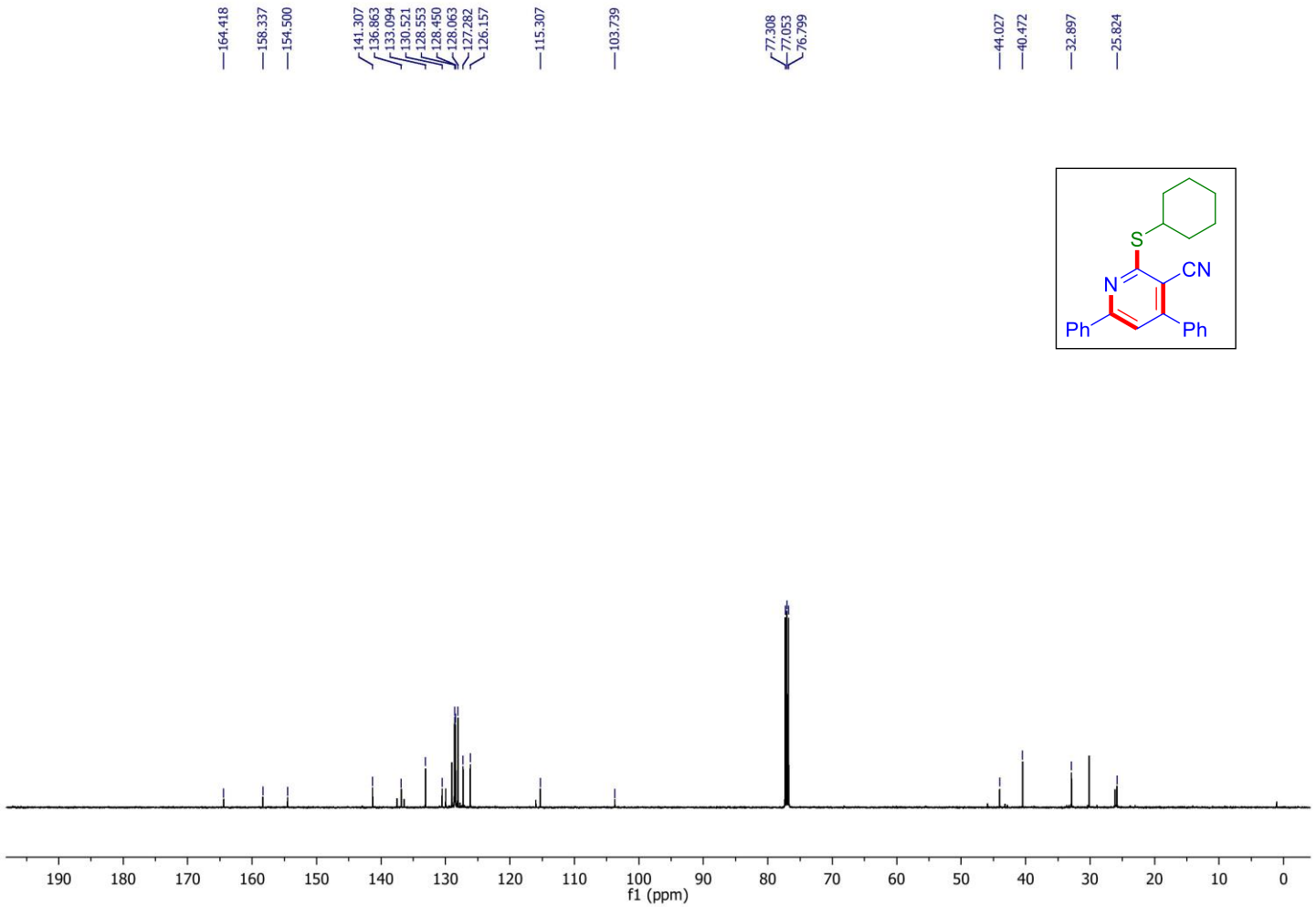
***4,6-Diphenyl-2-(thiophen-2-ylthio)nicotinonitrile* (*1l*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



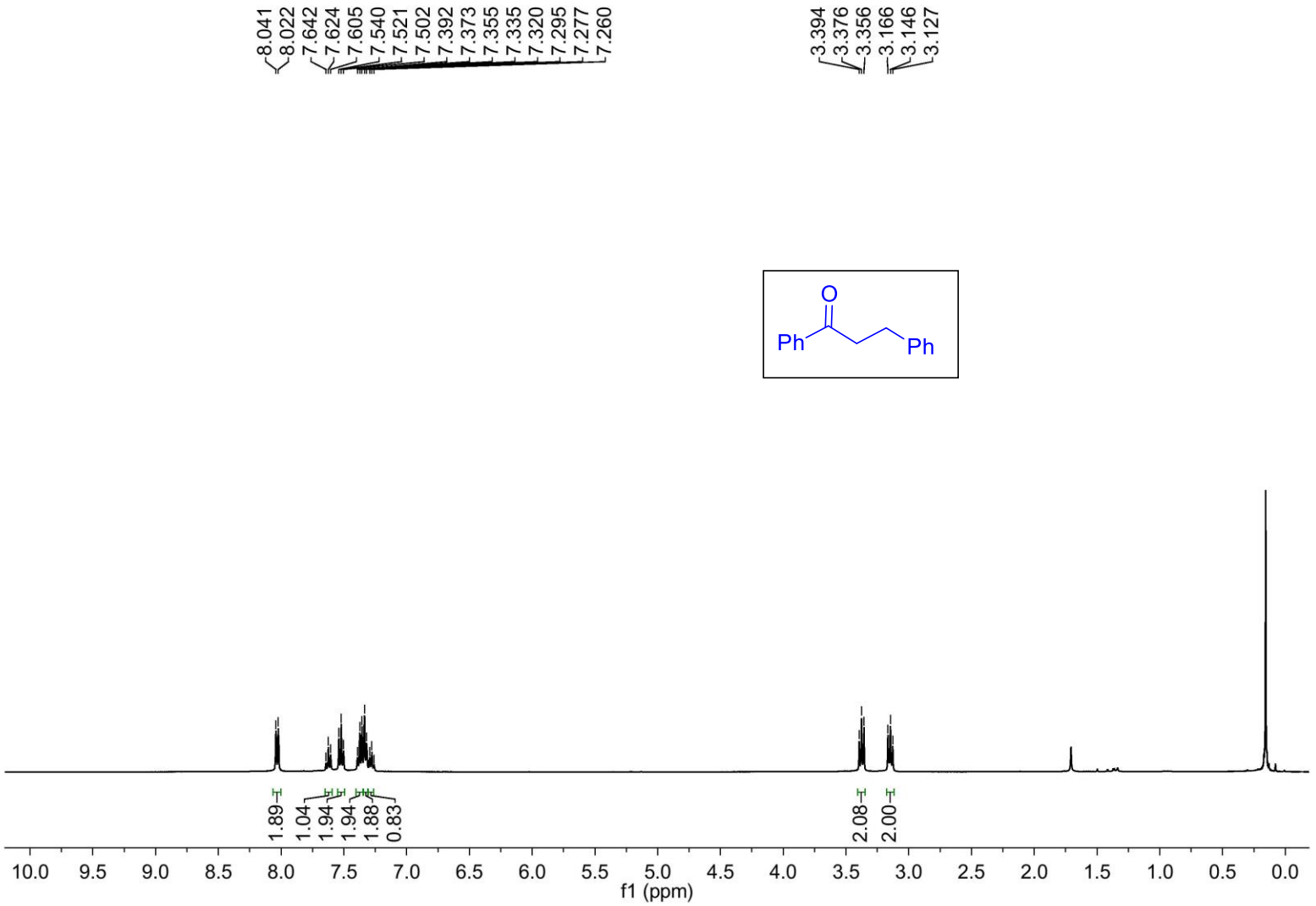
2-(Cyclohexylthio)-4,6-diphenylnicotinonitrile* (1m)*: ^{1}H NMR ($CDCl_3$, 400 MHz)



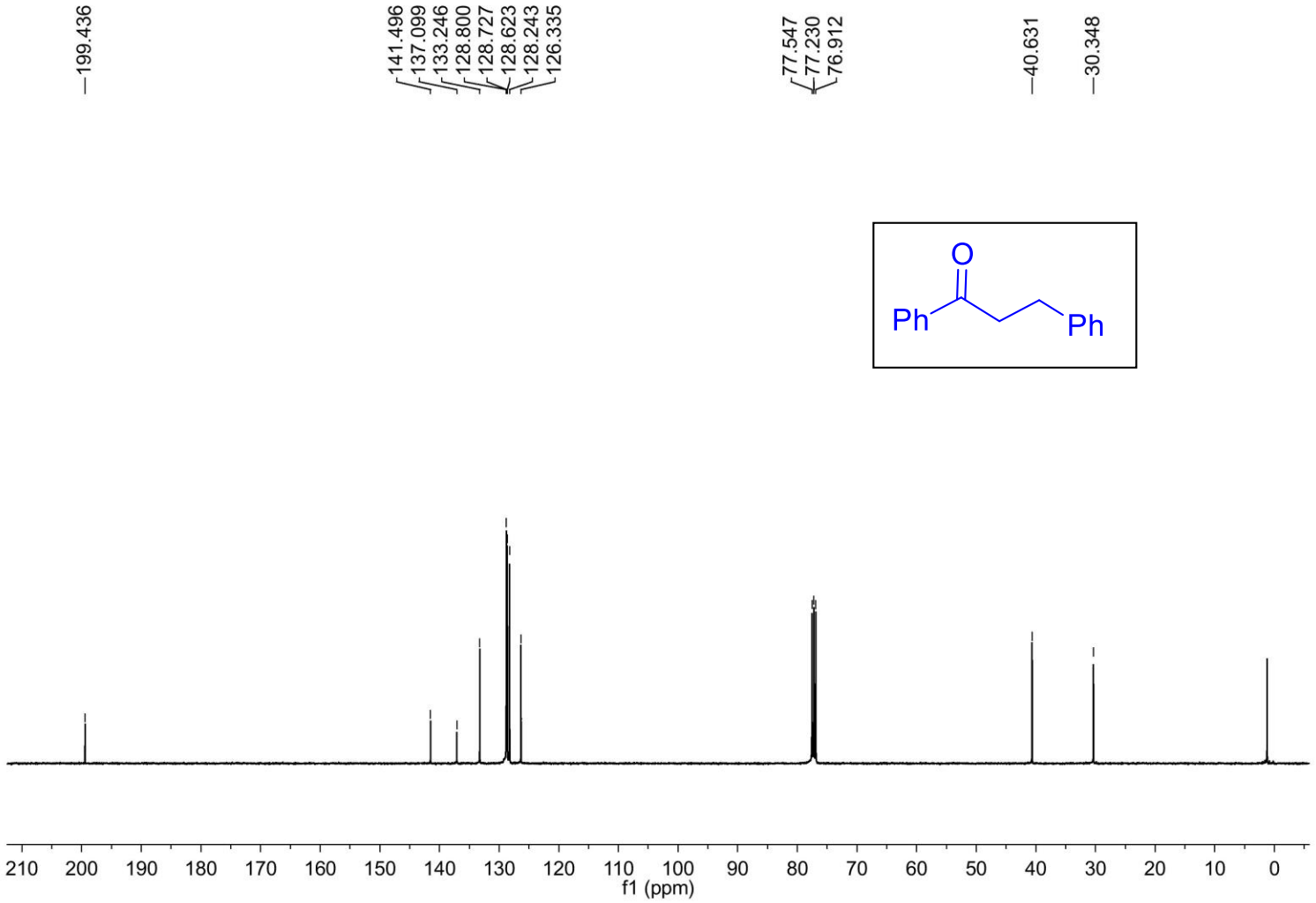
***2-(Cyclohexylthio)-4,6-diphenylnicotinonitrile* (1m): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



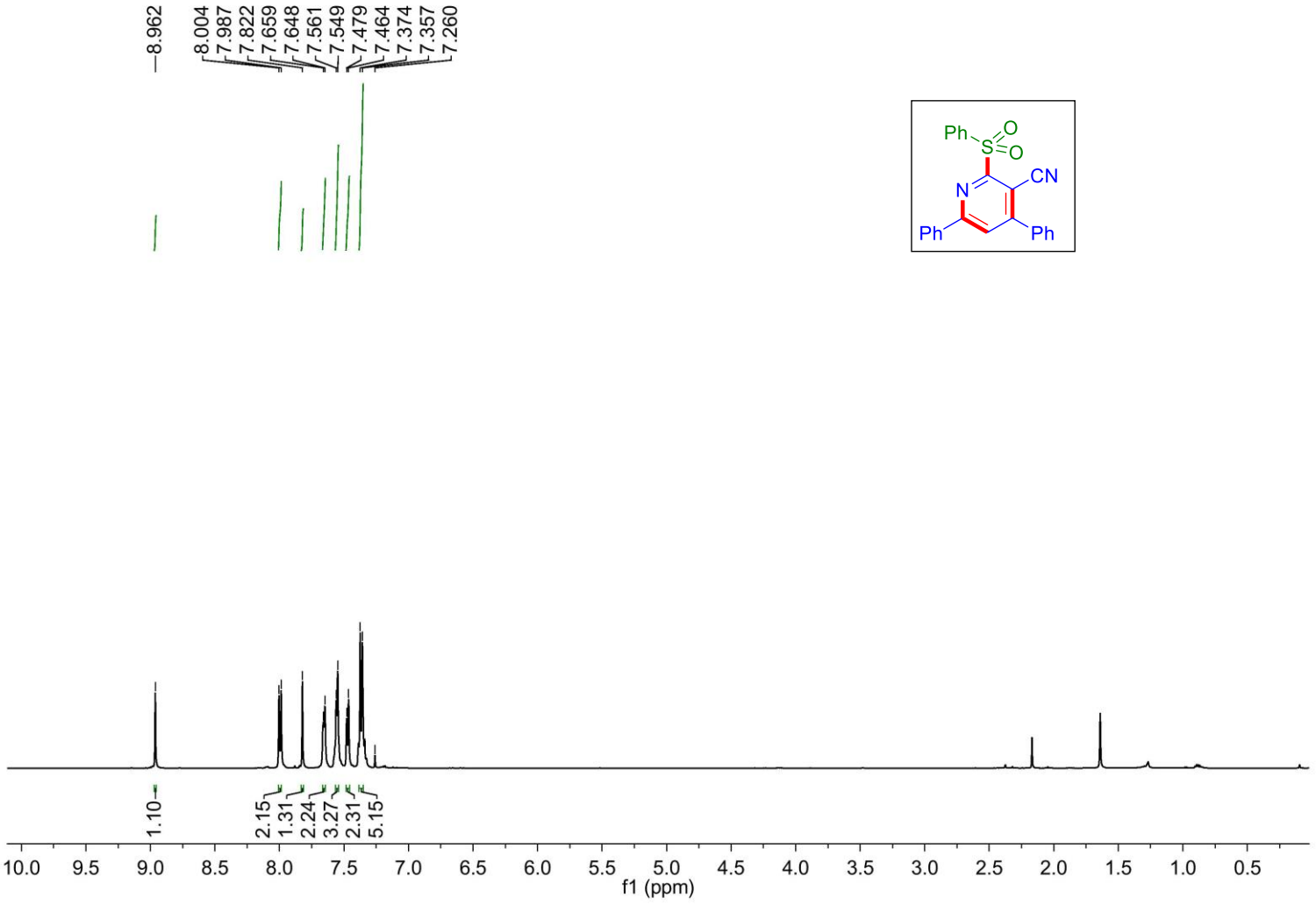
***1,3-Diphenylpropan-1-one* (*1'*): ^{1}H NMR ($CDCl_3$, 400 MHz)**



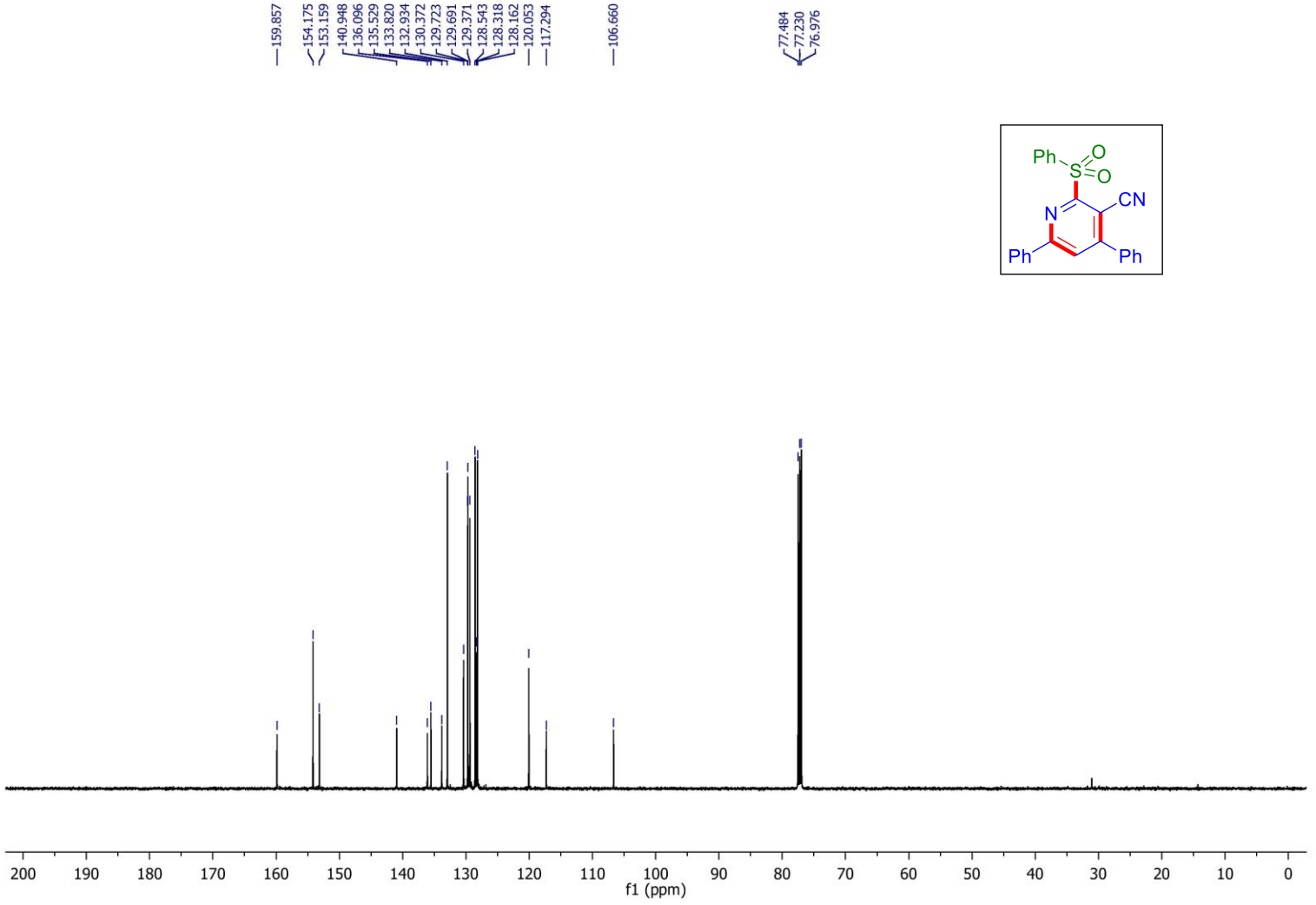
***1,3-Diphenylpropan-1-one* (*1'*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz)**



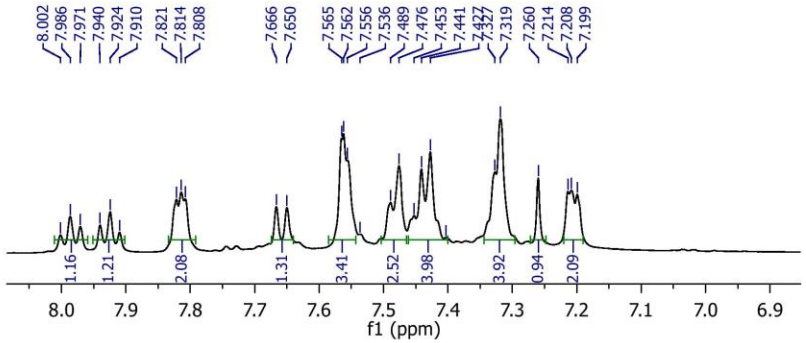
4,6-Diphenyl-2-(phenylsulfonyl)nicotinonitrile (1aa): ^{1}H NMR ($CDCl_3$, 500 MHz)

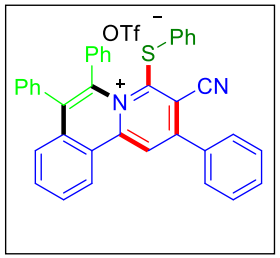


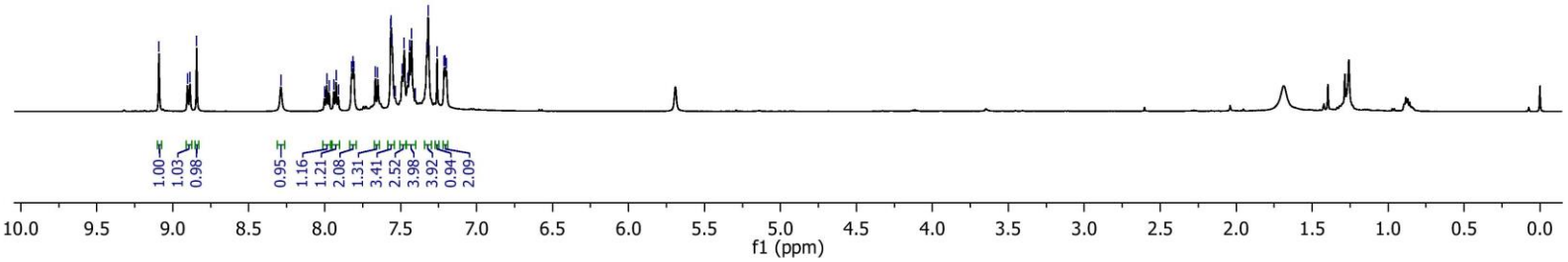
4,6-Diphenyl-2-(phenylsulfonyl)nicotinonitrile (1aa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)



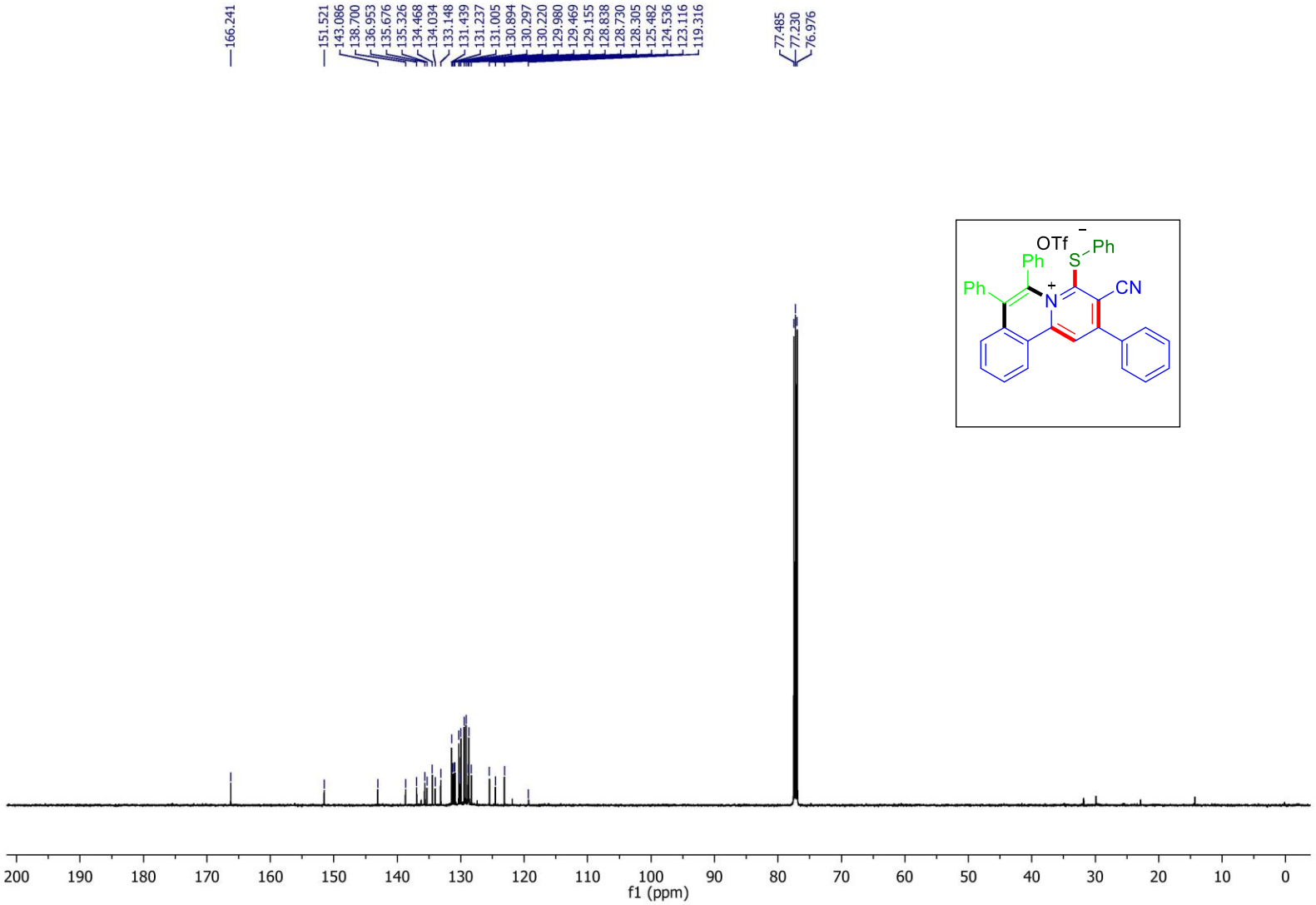
***3-Cyano-2,6,7-triphenyl-4-(phenylthio)pyrido[2,1-a]isoquinolin-5-ium* (*1ab*): ^{1}H NMR ($CDCl_3$, 500 MHz)**



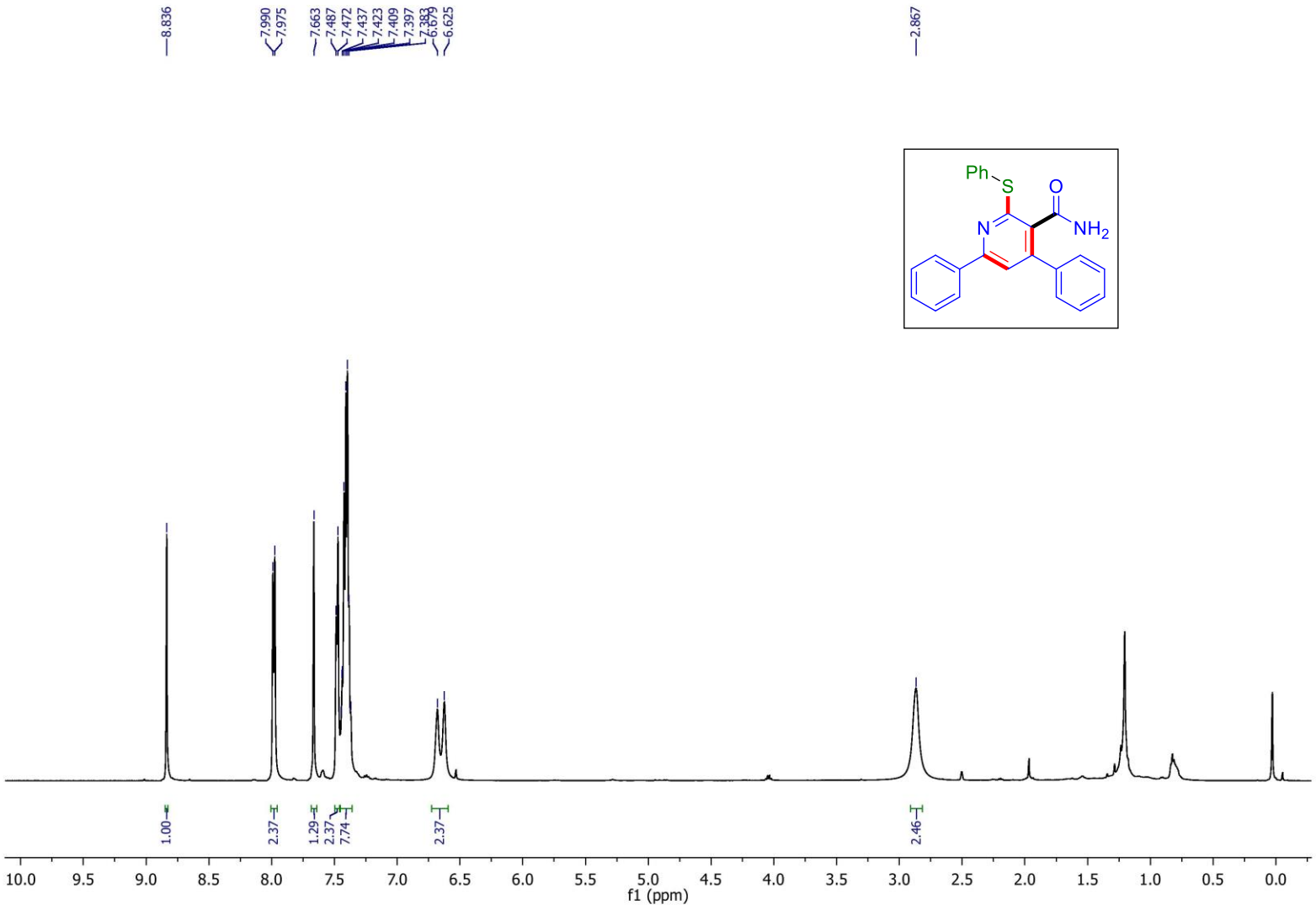




***3-Cyano-2,6,7-triphenyl-4-(phenylthio)pyrido[2,1-a]isoquinolin-5-ium* (*1ab*): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz)**



4,6-Diphenyl-2-(phenylthio)nicotinamide(1ac): ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 500 MHz)



4,6-Diphenyl-2-(phenylthio)nicotinamide(1ac): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$ + DMSO-d_6, 150 MHz)