SUPPORTING INFORMATION

Radical C-H arylations of (hetero)arenes catalysed by gallic acid

Marcelle D. Perretti, Diego M. Monzón, Fernando P. Crisóstomo, Víctor S. Martín and Romen Carrillo*

Departamento de Química Orgánica, Instituto Universitario de Bio-Orgánica "Antonio González" (IUBO), Centro de Investigaciones Biomédicas de Canarias (CIBICAN), Universidad de La Laguna. Avda. Astrofísico Fco. Sánchez 2, Apdo. Correos 456, 38200 – La Laguna, S/C. de Tenerife (Spain).

rocarril@ull.es

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Materials and methods.

^{1}H NMR spectra were recorded at 600 MHz and 500MHz, ^{13}C NMR spectra were recorded at 150 MHz. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^{1}H NMR spectrum as 0.00 ppm (chloroform, 7.26 ppm; acetone-d_6 2.05 ppm). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, ddd = double double doublet, m =multiplet and br = broad), coupling constant (*J* values) in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in ppm from tetramethylsilane using the central peak of $CDCl_3$ (77.16 ppm), acetone (209.68 ppm) as the internal standard. Accurate mass (HRMS) were determined by electrospray ionization (ESI-TOF) and electronic impact (EI-TOF). Flash column chromatography was performed using silica gel, 60 Å and 0.2-0.5 mm with the indicated solvent system according to standard techniques. Compounds were visualized on TLC plates by use of UV light, or vanillin with acetic and sulfuric acid in ethanol with heating. Anilines were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Gallic acid and tannic acid from ALDRICH were employed. Anhydrous magnesium sulfate was used for drying solutions.

General Procedures

Synthesis of diazonium tetrafluoroborate salts.

Aniline (10 mmol) was dissolved in a mixture of 4 mL of distilled water and 3.4 mL of 50% hydrofluoroboric acid. After cooling the reaction mixture to 0°C, sodium nitrite (0.69 g) dissolved in 1.5 mL of water, was added dropwise. The resulting mixture was stirred for 1h and the precipitate was collected by filtration, washed with water and re-dissolved in minimum amount of acetone. Diethyl ether was added until precipitation of the corresponding diazonium tetrafluoroborate, which is filtered, washed several times with diethyl ether and dried under vacuum.

Synthesis of N-(tert-butoxycarbonyl)-pyrrole.

Based on a literature procedure,[1,2] DMAP (0.12 g, 1 mmol) and di-t-butyl dicarbonate (2.62 g, 12 mmol) were added to a solution of pyrrole (0.69 mL, 10 mmol) in acetonitrile (10 mL) and the solution was stirred at room temperature for 24 hours. The reaction

mixture was diluted with Et_2O and washed with $NaHCO_3$ and then brine. The organic layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography Hex/AcOEt (99:1), yielding the title compound (1.44 g, 86%) as a colourless oil.

General procedure for coupling.

A 10 mL round bottom flask with a Teflon-coated stirrer bar was charged with gallic acid (0.05 mmol, 8.5 mg). Then, 2ml of acetone and 1ml of water were added by syringe, followed by the addition of the corresponding arene (5 mmol when furan or thiophene, 1 mmol when pyrrole or quinones, and 1ml when benzene) under an atmosphere of dry argon. The resulting solution was stirred at room temperature while a solution of the arenediazonium tetrafluoroborate (0.5 mmol) in 1 ml of acetone was added dropwise. The reaction mixture turns light orange and a fine bubbling starts thereafter. The reaction mixture was stirred at ambient temperature for 12 h. The crude was adsorbed in silica gel, and purified by flash chromatography (SiO_2, hexane/ethyl acetate), yielding the corresponding (hetero)biaryl.

Reaction of arylation with other polyphenolic compounds.

Other polyphenolic compounds, different from gallic acid, were explored as promoters of this reaction. The main aim of these experiments is to understand which parts of the polyphenolic reducing agent are important for an optimal activity. As it can be seen in table S1, in all cases the yields were lower than that obtained with gallic acid. As expected, 3,4,5-trimethoxybenzoic acid gave traces of final compound, proving that free OH groups are essential for a good reactivity. Syringic acid, also led to traces, which could be rationalized by the lack of two stabilizing H-bond interactions in the syringoyl radical. On the other hand, resorcinol and propyl gallate led to moderate yields, slightly worse than gallic acid. It is obvious then, that the trihydroxy system is the most relevant part of the promoter. Regarding propyl gallate and its yield, lower than one could expect, we hypothesized that solubility of the gallic acid in water plays a role in reactivity. Indeed, very recently it has been pointed out how biphasic radical arylations, where radical is generated in the aqueous phase, could improve the reaction yield by inhibiting unproductive pathways that are accessed when free radical concentration in the vicinity of reactants is too high.[3] In our case, although acetone and water are miscible, a biphasic system is clearly appreciable in the reaction.

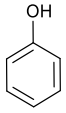
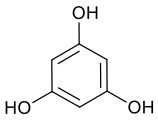
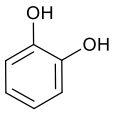
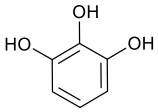
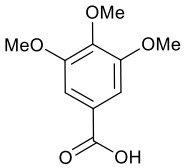
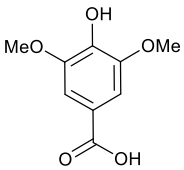
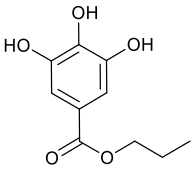
Entry	Phenolic Compound	Yield
1	 phenol	2
2	 phloroglucinol	4
3	 catechol	17
4	 resorcinol	49
5	 3,4,5-trimethoxybenzoic acid	Traces
6	 Syringic acid	2
7	 Propyl gallate	22

Table S1. *Arylation of furan with p-chlorobenzenediazonium tetrafluoroborate in the optimized conditions, but substituting gallic acid by the corresponding 10mol% of phenolic compound.*

Additionally, the rest of polyphenolic compounds assayed were worse promoters, confirming the importance of a proper stabilization of the corresponding phenoxyl radical generated in the reaction, either by captodative effect or by H-bond.

Finally, tannic acid was also evaluated. In this case, considering its structure (Fig. S1) where 10 gallates are pending on a glucose, only 1 mol% of tannic acid was added to the reaction. The yield of this non-optimized reaction was 54%. In fact, considering the lower yields obtained with syringic acid and with catechol, it would be probably more sensible to employ 2 mol%. In any case, the actual aim of this last experiment was to explore the possibilities of using bio-waste rich in tannins such as grape pomace to promote this reaction. In the next section, preliminary results are presented on such issue.

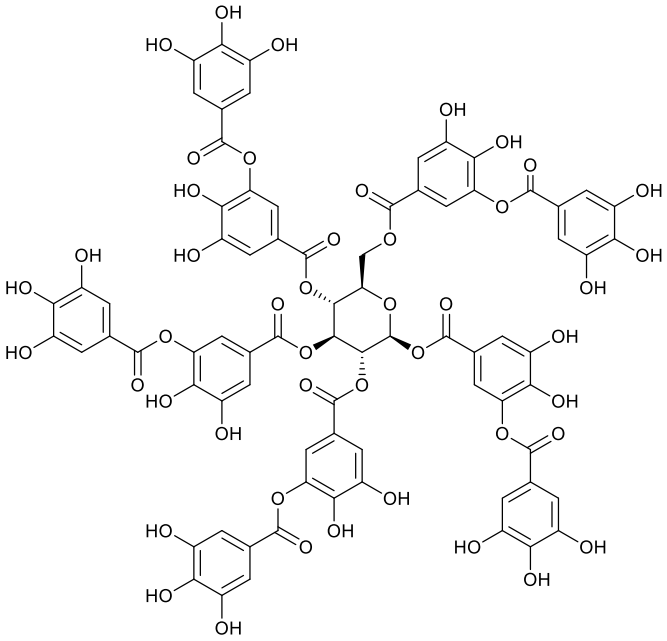


Fig S1. *Tannic acid*

Reaction of arylation with Grape Pomace Extract: Preliminary results.

In order to test the robustness of this arylation reaction and, at the same time, to highlight its greater sustainability compared to many other analogous reported methodologies, grape pomace extract was used as promoter instead of pure gallic acid. Indeed, grape pomace is an abundant agricultural residue: The wine industry produces millions of tons of grape by-products called pomaces, which account for about 20% of the weight of the grapes used to make wine. Considering that grape is the world's largest fruit crop, such grape pomace represents a waste management issue both ecologically and economically. Additionally, it is well known that grape pomace is very rich in polyphenols, such as tannins and anthocyanins. Particularly abundant is gallic acid and its derivatives (although

most of the polyphenols could probably act as radical promoters). Thus, we decided to explore a grape pomace extract as promoter of this arylation reaction.

For this experiment, grape pomace from a local winery was employed (E. Páez winery). The red grapes *Vitis vinifera L*. (*Listan Negro*, a local cultivar) were cultivated in the Canary Islands, specifically in the north of Tenerife (Finca Los Angostos, La Cruz Santa, Los Realejos) and harvested at the beginning of October 2015. The grapes were pressed right after the harvest and left in contact with the grape juice for one week, while fermentation was going on. Grape seeds and skins were pressed and dried at air for two days. The extraction method was analogous to other previously reported.[4] Fortunately, many extraction methods employ acetone/water, which is the solvent used for our methodology. Thus, the grape pomace was left with acetone/water/HCl (37%) (7:2.9:0.1) (3ml per g of pomace), for 3 days, and then filtered. The grape pomace extract was kept at 5ºC.

The reaction was set up by adding 0.5 mmol of p-cyanobenzenediazonium tetrafluoroborate solved in 1ml of acetone, to a mixture of 2 ml of grape pomace extract and furan (5 mmol) under argon. The reaction mixture was stirred at ambient temperature for 12 h. The crude was adsorbed in silica gel, and purified by flash chromatography (SiO_2, hexane/ethyl acetate). The yield of compound **3c** for this un-optimized reaction was 71%. Obviously, some parameters like pH, grape varieties or extraction method should be tuned. Further experiments on this issue are being carried out in our lab and the results will be published elsewhere in due time.

Radical Capturing Experiments.

An oven-dried 10 mL round bottom flask with a Teflon-coated stirrer bar was charged with gallic acid (0.05 mmol) and 2,2,6,6-tetramethylpiperidine-1-oxy radical (TEMPO) (1 mmol) under an atmosphere of dry argon. Acetone (2 mL) was added by syringe. The resulting solution was stirred at room temperature until the reagents were dissolved and a solution of 4-nitrobenzenediazonium tetrafluoroborate (0.5 mmol) in acetone (1 ml) was added by syringe. The reaction mixture was stirred at ambient temperature for 12 h. The crude was adsorbed in silica gel, and purified by flash chromatography (SiO2, hexane/ethyl acetate 95:5), yielding the trapped compound **10** (112 mg, 81%) as a white-yellowish solid.

Catalytic behavior of gallic acid.

In order to check if gallic acid was present in the reaction mixture once full conversion was reached, the optimized reaction with p-chlorobenzenediazonium tetrafluoroborate and furan was set up in deuterated solvents, and NMR analysis of the mixture was performed before diazonium salt was added and after 12h of the addition. The optimized conditions of the reaction were applied, although 25 mol% of gallic acid was employed for visualization ease. As it is shown in Fig. S2, the aromatic singlet of gallic acid is clearly seen before and after the reaction is complete. Analogously, gallic acid is detected by C^{13}NMR. Worth to mention, addition of more gallic acid to the reaction mixture, made the mentioned peaks increase, confirming thus that those peaks correspond to gallic acid.

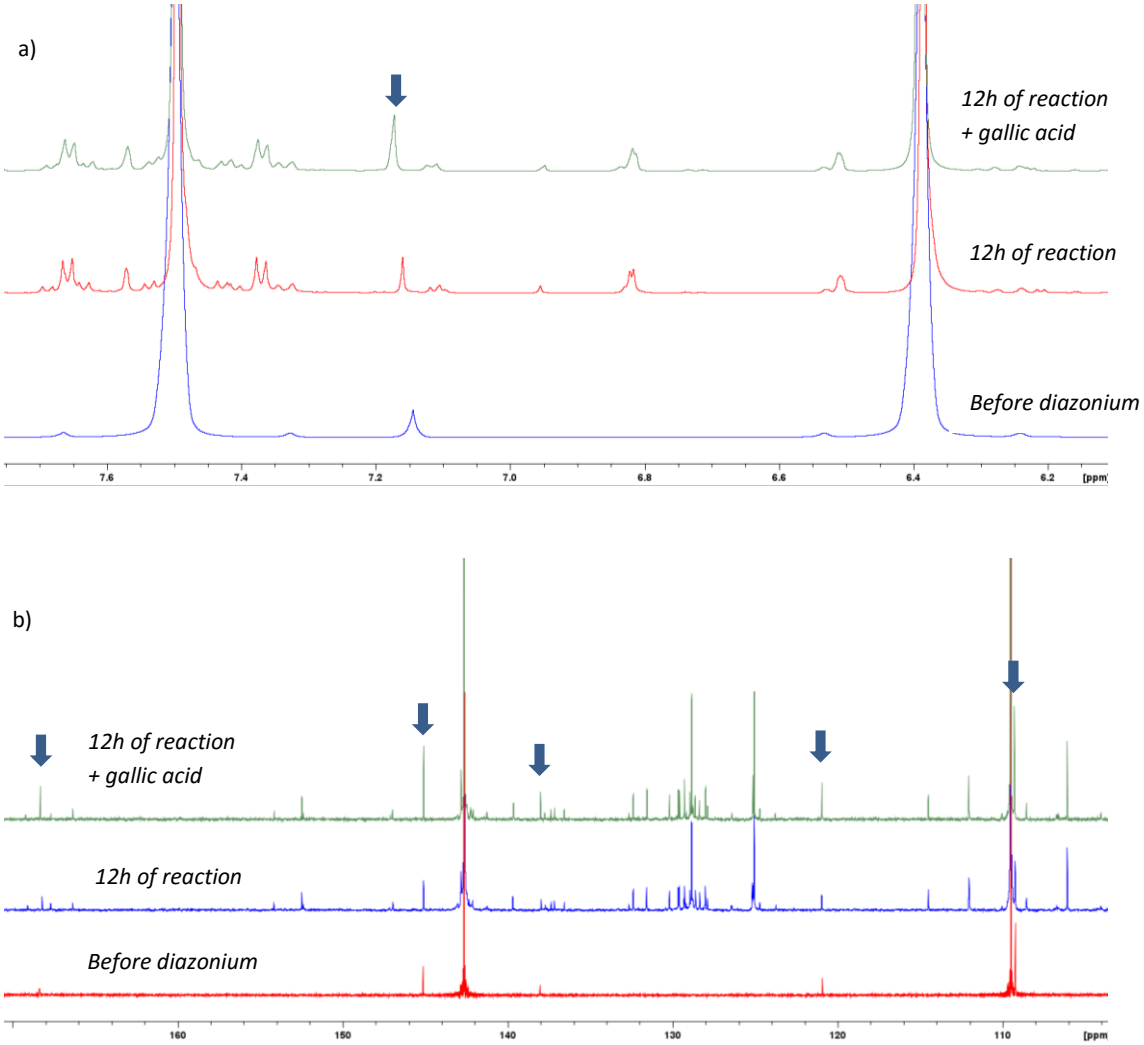
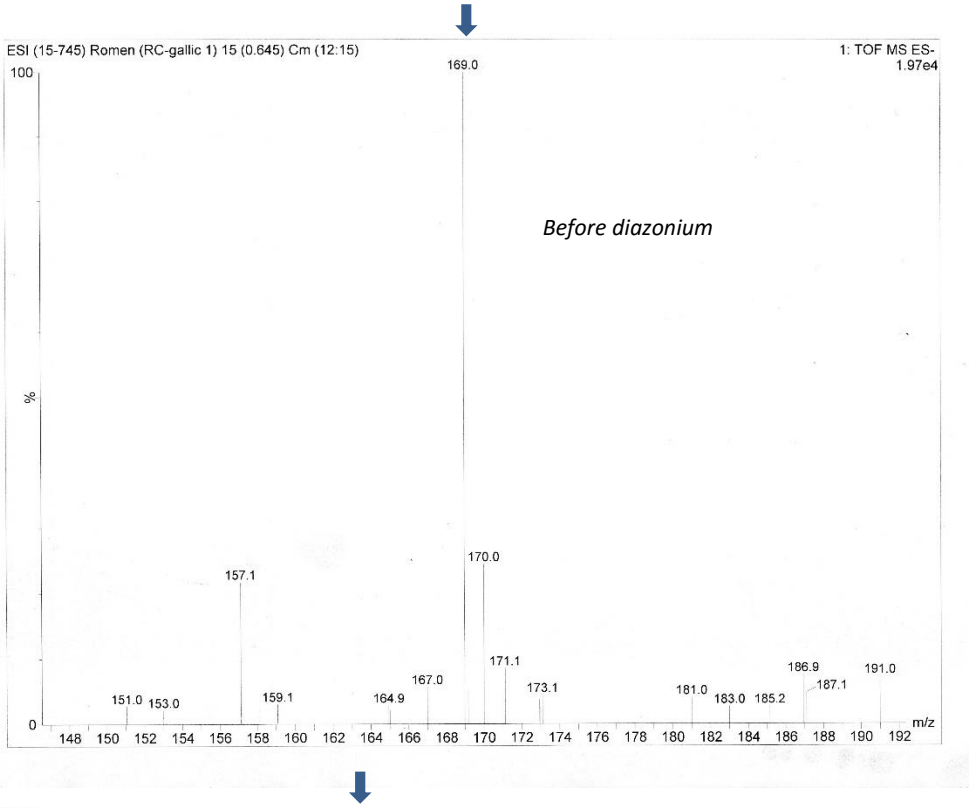
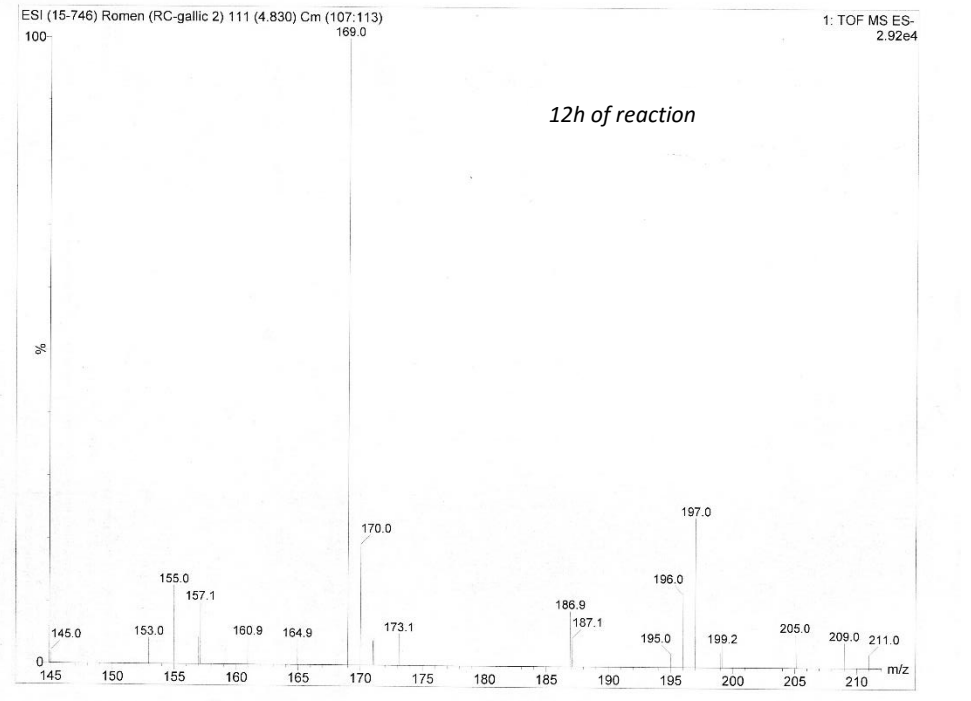
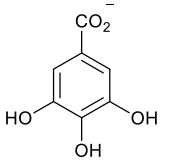


Fig. S2. *(a) Stacked plot of the ^{1}HNMR of the reaction before the addition of diazonium salt, after 12 h of reaction, and 12h of reaction + addition of more gallic acid (b) Stacked plot of the ^{13}CNMR of the reaction before the addition of diazonium salt, after 12 h of reaction, and 12h of reaction + addition of more gallic acid.*

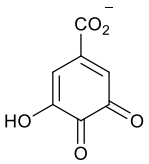






Chemical Formula: $C_7H_5O_5^-$
Exact Mass: 169,0142

Gallate



Chemical Formula: $C_7H_3O_5^-$
Exact Mass: 166,9986

Hydroxy-o-quinone

Fig S3*. ESI of the crude reaction before addition of diazonium salt and after 12h of reaction.*

Additionally ESI mass spectra (negative ion mode) of the above samples were also recorded, and the peak of gallic acid was detected (M^- =169.013), while no peak was detected for the hydroxy-o-quinone (M^- =166.998) in the reaction sample, which is the main decomposition product of galloyl radical (Fig S3). The small peak 167.0 observed in the control sample, before the addition of diazonium salt, might be due to an unappropriate manipulation of the sample which was left under air for 48h before the MS was performed.

Additional comments on the scope

Several heterocycle diazonium salts were tested. However, as expected, they were much more reactive than arenediazonium salts, which resulted in traces of final products due to the presence of water in this methodology. Indeed, the outcome of the reaction is probably the addition of water to form an alcohol, which has been reported before.[5] It might be possible that in some specific examples the reaction works well, however we have to conclude that this methodology is not an optimal choice for the coupling of two heterocycles.

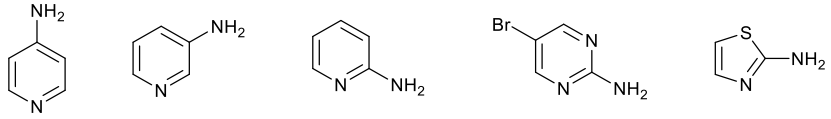
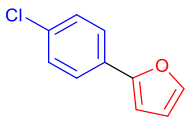


***Fig S4**. Heterocyclic amines tested. In all cases traces of final product was obtained.*

Characterization of products



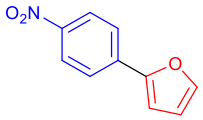
3a,74%

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.59 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 1.3 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 3.4 Hz, 1H), 6.47 (dd, *J* = 1.7, 3.4 Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 153.1, 142.5, 133.1, 129.5, 129.1, 129.0, 125.1, 111.9, 105.6

HRMS (EI): m/z: calcd for $C_{10}H_7O^{35}Cl$ [M^+]: 178.0185, found: 178.0189/ calcd for $C_{10}H_7O^{37}Cl$ [M^+]: 180.0156, found: 180.0147

Column Chromatography: 98:2 (Hex-AcOEt)

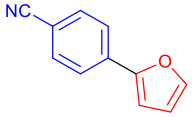


3b, 92% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.22 (d, *J* = 8.9 Hz, 2H), 7.76 (d, *J* = 8.9 Hz, 2H), 7.56 (d, *J* = 1.0 Hz, 1H), 6.87 (d, *J* = 2.9 Hz, 1H), 6.54 (dd, *J* = 1.8, 3.4 Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 151.6, 146.3, 144.1, 136.4, 124.2, 123.8, 112.4, 108.9

HRMS (ESI): m/z: calcd for $C_{10}H_7NO_3Na$ [M + Na^+]: 212.0324, found: 212.0329.

Column Chromatography: 95:5 (Hex-AcOEt)

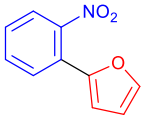


3c,96% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.74 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 1.3 Hz, 1H), 6.81 (d, *J* = 3.4 Hz, 1H), 6.53 (dd, *J* = 1.8, 3.4 Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 152.0, 143.8, 134.7, 132.7, 124.0, 119.1, 112.3, 110.3, 108.3

HRMS (ESI): m/z: calcd for $C_{11}H_7NONa$ [M^+] : 192.0425; found: 192.0421.

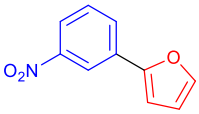
Column Chromatography: 95:5 (Hex:AcOEt)



3d,85% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.72 (dd, *J* = 1.1, 7.8 Hz, 1H), 7.68 (dd, *J* = 1.0, 8.0 Hz, 1H), 7.58 (ddd, *J* = 1.1, 7.6, 7.6 Hz, 1H), 7.52(d, *J* = 1.7 Hz, 1H), 7.41 (ddd, *J* = 1.3, 7.9, 7.9 Hz, 1H), 6.67 (d, *J* = 3.5 Hz, 1H), 6.50 (dd, *J* = 1.8, 3.4 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 148.5, 147.6, 143.9, 132.0, 129.0, 128.4, 124.2, 124.0, 112.0, 109.8.

HRMS (ESI): m/z: calcd for $C_{10}H_7NO_3$ [M^+]: 212.0324, found: 212.0319.



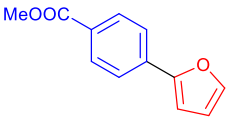
3e, 76%

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 8.52-8.49 (m, 1H), 8.09 (ddd, *J* = 8.2, 2.1, 0.8 Hz, 1H), 7.98-7.95 (m, 1H), 7.57-7.53 (m, 2H), 6.82 (d, *J* = 3.4 Hz, 1H), 6.53 (dd, J_1 = 1.8, 3.4, Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 151.5, 148.7, 143.3, 132.4, 129.7, 129.2, 121.7, 118.5, 112.1, 107.3

HRMS (EI): m/z: calcd for $C_{10}H_7NO_3$ [M^+]: 189.0426, found: 189.0422

Column Chromatography: Gradient (98:2) (Hex-AcOEt)



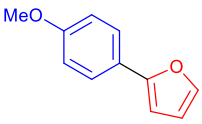
3f, 64%

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 8.05 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 1.2 Hz, 1H), 6.79 (d, *J* = 3.4 Hz, 1H), 6.51 (dd, *J* = 1.8, 3.4 Hz, 1H), 3.92 (s, 3H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 166.8, 152.9, 143.1, 134.7, 130.1, 128.5, 123.4, 112.0, 107.2, 52.1

HRMS (ESI): m/z: calcd for $C_{12}H_{10}O_3Na$ [M + Na^+]: 225.0528; found: 225.0527.

Column Chromatography: 95:5 (Hex-AcOEt)



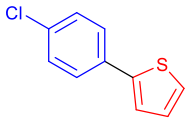
3g, 2%

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.60 (d, *J* = 8.9 Hz, 2H), 7.42 (d, *J* = 1.2 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 6.51 (d, *J* = 3.3 Hz, 1H), 6.44 (dd, *J* = 1.8, 3.3 Hz, 1H), 3.84 (s, 3H)

^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 159.1, 154.1, 141.3, 125.2, 124.1, 114.1, 111.5, 103.3, 55.3

HRMS (EI): m/z: calcd for $C_{11}H_{10}O_2$ [M^+]: 174.0681, found: 174.0684

Column Chromatography: (98:2) (Hex:AcOEt)

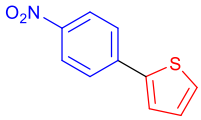


5a, 56% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.53 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.30-7.29 (m, 2H), 7.08 (dd, *J* = 3.8, 4.9 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 143.2, 133.3, 133.0, 129.1, 128.3, 127.2, 125.3, 123.6

HRMS (EI): m/z: calcd for $C_{10}H_7SCl$ [M^+]: 193.9957; found: 193.9966.

Column Chromatography: 95:5 (Hex:AcOEt)

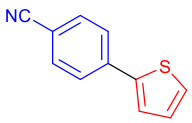


5b, 67% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 8.22 (d, *J* = 8.9 Hz, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 7.47 (dd, *J* = 1.1, 3.6 Hz, 1H), 7.44 (dd, *J* = 1.1, 5.0 Hz, 1H), 7.15 (dd, *J* = 3.6, 5.0 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 146.5, 141.5, 140.5, 128.6, 127.6, 126.0, 125.7, 124.4.

HRMS (ESI): m/z: calcd for $C_{10}H_7NO_2SNa$ [M + Na^+]: 228.0095; found: 228.0098.

Column Chromatography: 95:5 (Hex:AcOEt)

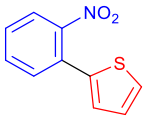


5c, 72% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.70 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.43 (dd, *J* = 0.8, 3.6 Hz, 1H), 7.40 (dd, *J* = 0.8, 5.1 Hz, 1H), 7.13 (dd, *J* = 3.8, 5.1 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 142.1, 138.7, 132.8, 128.6, 127.2, 126.9, 126.1, 125.2, 118.9, 110.6.

HRMS (ESI): m/z: calcd for $C_{11}H_7NSNa$ [M + Na^+]: 208.0197; found: 208.0204.

Column Chromatography: 95:5 (Hex:AcOEt)

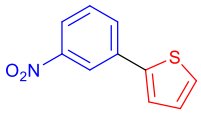


5d, 70% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.75 (d, *J* = 1.9 Hz, 1H), 7.60-7.54 (m, 2H), 7.47 (ddd, *J* = 2.2, 6.7, 8.9 Hz, 1H), 7.42 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.10-7.07 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.6, 137.2, 132.4, 132.0, 128.7, 128.5, 127.9, 127.3 (x2), 124.0.

HRMS (ESI): m/z: calcd for $C_{10}H_7NO_2S$ [M^+]: 228.0095, found: 228.0092.

Column Chromatography: (Hex-AcOEt) (95:5)

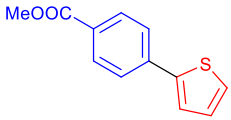


5e, 50% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.46-8.44 (m, 1H), 8.14-8.02 (m, 1H), 7.93-7.89 (m, 1H), 7.57-7.53 (m, 1H), 7.44 (dd, *J* = 0.9, 3.6 Hz, 1H), 7.37 (dd, *J* = 0.9, 5.1 Hz, 1H), 7.14 (dd, *J* = 3.6, 5.1 Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 148.75, 141.53, 136.11, 131.57, 129.89, 128.48, 126.55, 124.82, 121.92, 120.47

HRMS (EI): m/z: calcd for $C_{10}H_7NO_2S$ [M^+]: 205.0198, found: 205.0202

Column Chromatography: Gradient (98:2) (Hex-AcOEt)

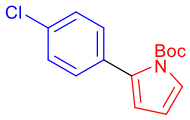


5f, 48% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): *δ* ppm** 8.04 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 3.6 Hz, 1H), 7.36 (d, *J* = 5.0 Hz, 1H), 7.11 (dd, *J* = 3.6, 5.0 Hz, 1H), 3.93 (s, 3H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): *δ* ppm 166.7, 143.0, 138.6, 130.2, 128.7, 128.3, 126.3, 125.5, 124.4, 52.1.

HRMS (ESI): *m/z:* calcd for: $C_{12}H_{10}O_2SNa$ [M + Na^+]: 241.0299; found: 241.0297.

Column Chromatography: 95:5 (Hex-AcOEt)

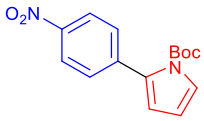


7a,37% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.34 (dd, J_1 = 1.8 Hz; J_2 = 3.3 Hz, 1H), 7.32 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 8.6 Hz, 2H), 6.22 (t, J = 3.3 Hz, 1H), 6.18 (dd, J_1 = 1.8 Hz; J_2 = 3.2 Hz, 1H), 1.39 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.3, 133.9, 133.3, 132.9, 130.6 (x2), 127.9 (x2), 123.0, 114.9, 110.8, 84.0, 27.8

HRMS (ESI): m/z: calcd for $C_{15}H_{16}NO_2{}^{35}ClNa$ [M + Na^+]: 300.0767, found: 300.0774/ calcd for $C_{15}H_{16}NO_2{}^{37}ClNa$ [M^+]: 302.0738, found: 302.0739

Column Chromatography: n-Hexane

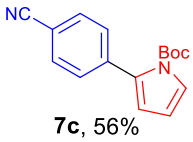


7b, 55% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.22 (d, J = 8.9 Hz, 2H), 7.51 (d, J = 8.9 Hz, 2H), 7.40 (dd, J = 1.7, 3.2 Hz, 1H), 6.32 (dd, J = 1.7, 3.2 Hz, 1H), 6.27 (t, J = 3.3 Hz, 1H), 1.43 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.0, 146.7, 140.8, 132.9, 129.6 (x2), 124.4, 123.0, 116.6, 111.3, 84.6, 27.8

HRMS (ESI): m/z: calcd for $C_{15}H_{16}N_2O_4$ [M^+]: 311.1008, found: 311.1009.

Column Chromatography: (Hex-AcOEt) (95:5)

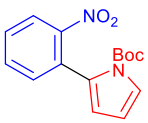


7c, 56% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.63 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.3 Hz, 2H), 7.38 (dd, J = 1.8, 3.2 Hz, 1H), 6.27 (dd, J = 1.8, 3.3 Hz, 1H), 6.27 (t, J = 3.3 Hz, 1H), 1.41 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.1, 138.9, 133.2, 131.5, 129.7, 124.1, 119.2, 116.2, 111.2, 110.7, 84.5, 27.8.

HRMS (ESI): m/z: calcd for $C_{16}H_{16}N_2O_2$ [M^+]: 291.1109, found: 291.1109.

Column Chromatography: (Hex-AcOEt) (95:5)



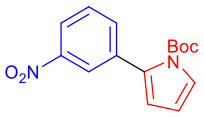
7d, 71% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.11 (dd, J = 0.8, 8.2 Hz, 1H), 7.62 (ddd, J = 1.0, 7.5, 7.5 Hz, 1H), 7.51 (ddd, J = 1.3, 8.0, 8.0 Hz, 1H), 7.46 (dd, J = 1.1,

7.6 Hz, 1H), 7.41 (dd, *J* = 1.8, 3.1 Hz, 1H), 6.27 (t, *J* = 1.7 Hz, 1H), 6.20 (dd, *J* = 1.8, 3.1 Hz, 1H), 1.33 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.0, 148.6, 133.0, 132.8, 130.2, 129.6, 128.7, 124.5, 122.7, 114.9, 111.0, 84.2, 27.6 (¿x3?).

HRMS (ESI): m/z: calcd for $C_{15}H_{16}N_2O_4$ [M^+]: 311.1008, found: 311.1009.

Column Chromatography: (Hex-AcOEt) (95:5)

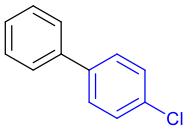


7e, 55% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.25-8.22 (m, 1H), 8.15 (ddd, *J* = 0.9, 2.2, 8.2Hz, 1H), 7.71-7.67 (m, 1H), 7.54-7.49 (m, 1H), 7.40 (dd, *J* = 1.8, 3.2 Hz, 1H), 6.31-6.28 (m, 1H), 6.28-6.25 (m, 1H)

^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 148.98, 147.67, 135.84, 135.05, 132.33, 128.46, 124.17, 123.69, 121.92, 115.96, 110.97, 84.42, 27.71

HRMS (EI): m/z: calcd for $C_{15}H_{16}N_2O_4$ [M^+]: 288.1110, found: 288.1109

Column Chromatography: Gradient (98:2) (Hex-AcOEt)

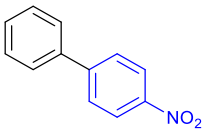


9a, 28% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 7.57-7.52 (m, 4H), 7.46-7.37 (m, 5H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 140.1, 139.8, 133.5, 129.0, 129.0, 128.5, 127.7, 127.1.

HRMS (EI): m/z: calcd for: $C_{12}H_9Cl$ [M^+]: 188.0393; found: 188.0330.

Column Chromatography: 98:2 (Hex-AcOEt)

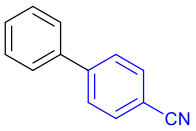


9b, 50% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 8.29 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 2H), 7.63 (m, 2H), 7.50 (m, 2H), 7.45 (m, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 147.7, 147.1, 138.8, 129.3, 129.0, 127.9, 127.5, 124.2.

HRMS (EI): m/z: calcd for: $C_{12}H_9NO_2$ [M^+]: 199.0633; found: 199.0634.

Column Chromatography: 98:2 (Hex-AcOEt)

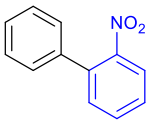


9c, 55% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.73 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.59 (m, 2H), 7.48 (m, 2H), 7.42 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 145.8, 139.3, 132.7, 129.2, 128.8, 127.8, 127.3, 119.1, 111.0.

HRMS (EI): m/z: calcd for: $C_{13}H_9N$ [M^+]: 179.0735; found: 179.0731.

Column Chromatography: 98:2 (Hex-AcOEt)



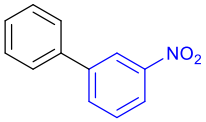
9d, 24% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.86 (dd, *J* = 0.9, 8.1 Hz, 1H), 7.62 (ddd, *J* = 1.1, 7.6, 7.6 Hz, 1H), 7.49 (ddd, *J* = 1.2, 7.9, 7.9 Hz, 1H), 7.47-7.40 (m, 4H), 7.33 (d, *J* = 1.7 Hz, 1H), 7.32 (d, *J* = 1.2 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 149.3, 137.4, 136.4, 132.3, 132.0, 128.7, 128.3, 128.2, 127.9, 124.1.

HRMS (ESI): m/z: calcd for $C_{12}H_9NO_2$ [M^+]: 222.0531, found: 228.0527.

Column Chromatography: (Hex-AcOEt) (95:5)

Column Chromatography: 98:2 (Hex-AcOEt)

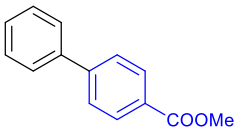


9e, 37% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 8.47-8.45 (m, 1H), 8.22-8.19 (m, 1H), 7.94-7.90 (m, 1H), 7.65-7.59 (m, 3H), 7.53-7.41 (m, 3H)

^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 148.74, 142.90, 138.69, 133.08, 129.74, 129.19, 128.57, 127.19, 122.07, 121.99

HRMS (EI): m/z: calcd for $C_{12}H_9NO_2$ [M^+]: 199.0633, found: 199.0640

Column Chromatography: Gradient (95:5) (Hex-AcOEt)

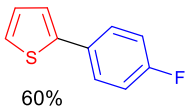


9f, 41% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 8.11 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.63 (m, 2H), 7.47 (m, 2H), 7.40 (m, 1H), 3.95 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 167.2, 145.8, 140.1, 130.2, 129.1, 129.0, 128.3, 127.4, 127.2, 52.3.

HRMS (ESI): m/z: calcd for: $C_{14}H_{12}O_2Na$ [M + Na^+]: 235.0735; found: 235.0741.

Column Chromatography: 98:2 (Hex-AcOEt)

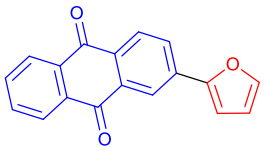


60% **^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm** 7.64-7.61 (m, 2H), 7.33-7.29 (m, 2H), 7.14-7.12 (m, 3H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 162.4 (d, *J* = 246.3 Hz), 143.4, 130.8 (d, J = 2.9 Hz), 128.2, 127.7 (d, J = 8.0 Hz), 124.9, 123.2, 115.9 (d, J = 21.8 Hz).

HRMS (EI): m/z: calcd for: $C_{10}H_7FS$ [M^+]: 178.0252; found: 177.9959.

Column Chromatography: 98:2 (Hex-AcOEt)

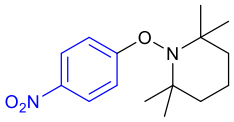


3h, 41% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 8.56 (d, *J* = 1.6 Hz, 1H), 8.34-8.32 (m, 3H), 8.07 (dd, *J* = 1.7, 8.2 Hz, 1H), 7.82-7.80 (m, 2H), 7.60 (d, *J* = 1.2 Hz, 1H), 6.98 (d, *J* = 3.4 Hz, 1H), 6.58 (dd, *J* = 1.7, 3.4 Hz, 1H)

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 183.3, 182.7, 152.3, 144.1, 136.1, 134.4, 134.2, 134.1, 133.8, 133.7, 131.8, 128.5, 128.3, 127.4, 127.4, 122.1, 112.6, 109.1.

HRMS (EI): m/z: calcd for: $C_{18}H_{10}O_3$ [M^+]: 274.0630; found: 274.0629.

Column Chromatography: 95:5 (Hex-AcOEt)



10, 81% **^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ ppm** 8.14 (d, *J* = 8.4 Hz, 2H), 7.29 (br, 2H), 1.65-1.60 (m, 5H), 1.45-1.43 (m, 1H), 1.24 (s, 6H), 0.98 (s, 6H).

^{13}C NMR (150 MHz, $CDCl_3$, 298 K): δ ppm 168.8, 141.2, 125.7, 114.3, 61.0, 39.8, 32.4, 20.6, 17.0.

HRMS (ESI): m/z: calcd for: $C_{15}H_{22}N_2O_3Na$ [M + Na^+]: 301.1528; found: 301.1524.

Column Chromatography: 95:5 (Hex-AcOEt)

References

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4. M. R. González-Centeno, M. Jourdes, A. Femenia, S. Simal, C. Rosselló and P.-L. Teissedre, *J. Agric. Food Chem.*, 2012, **60**, 11850-11858.

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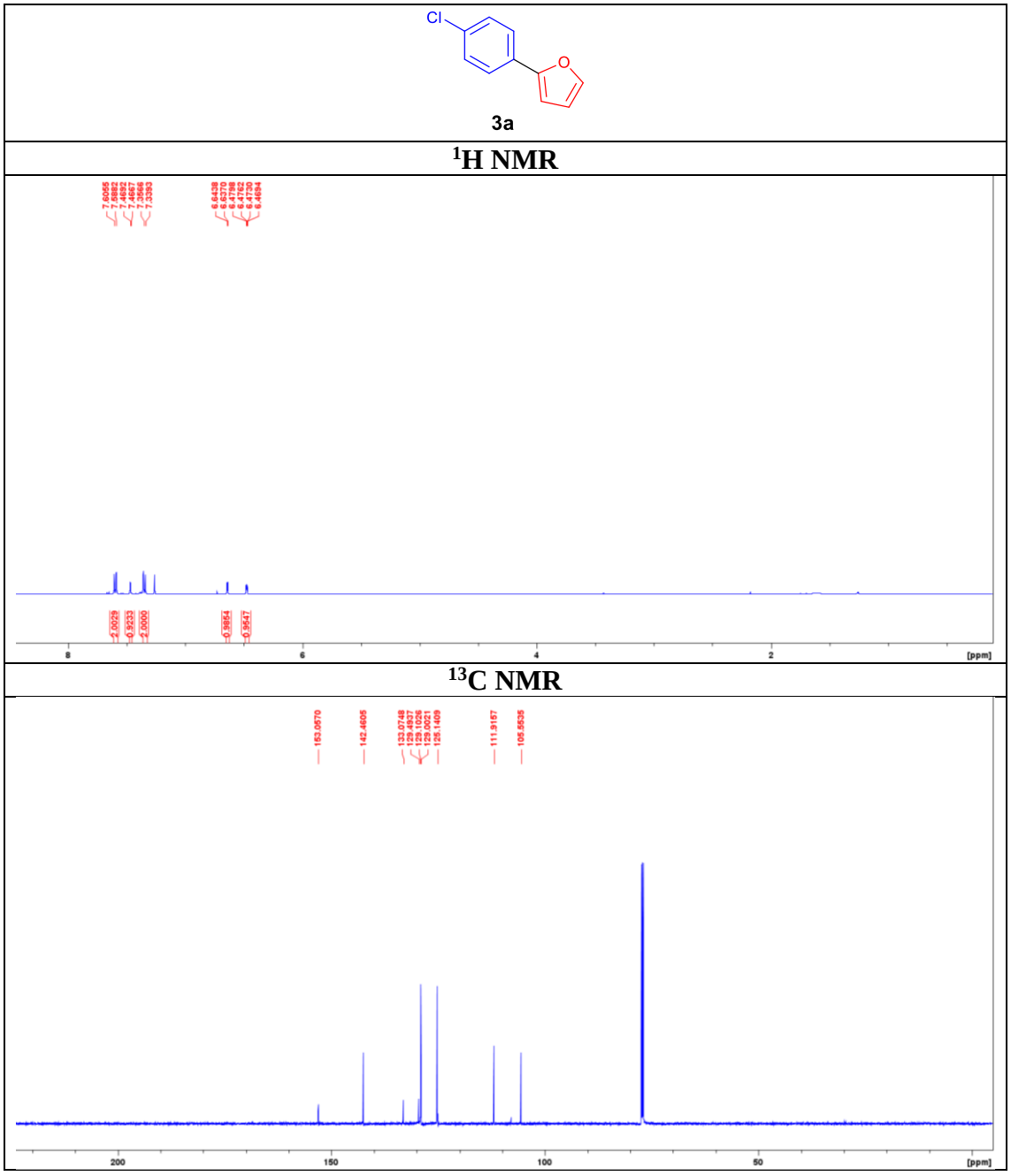
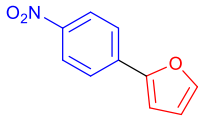
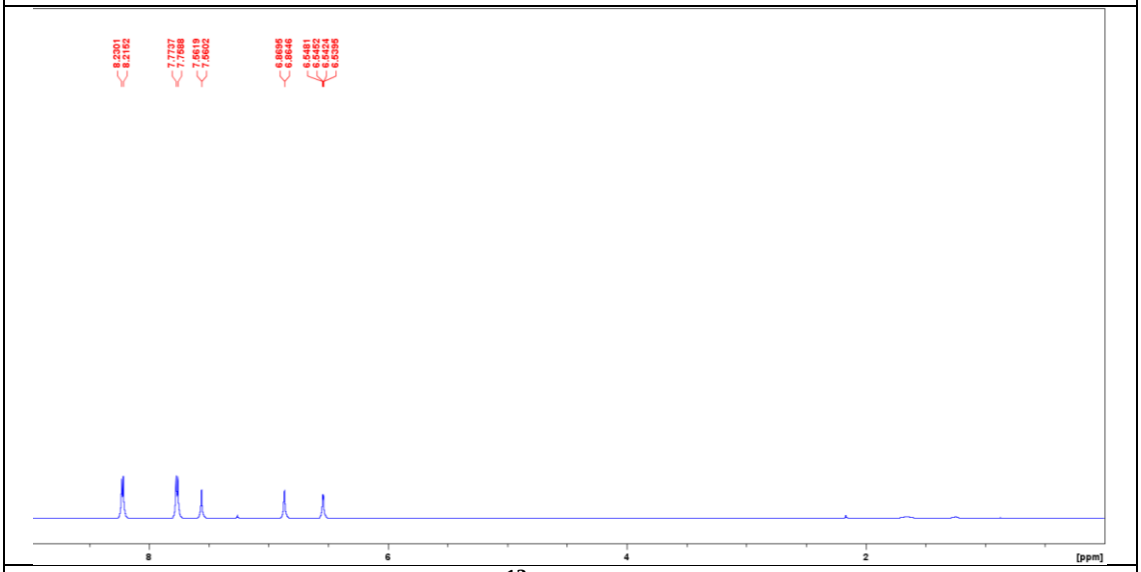
NMR spectra



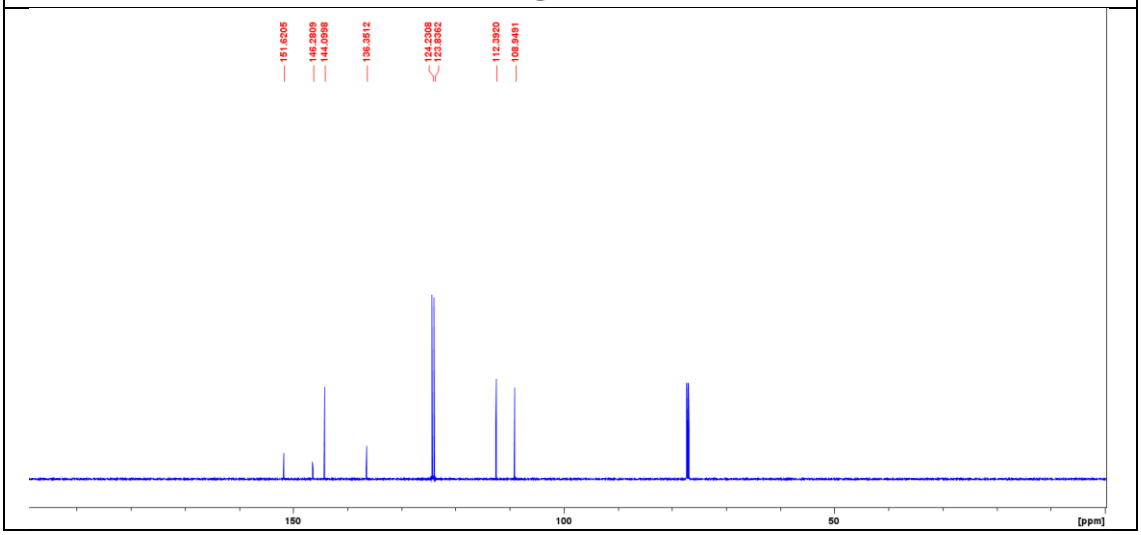


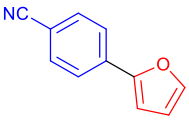
3b

^{1}H NMR



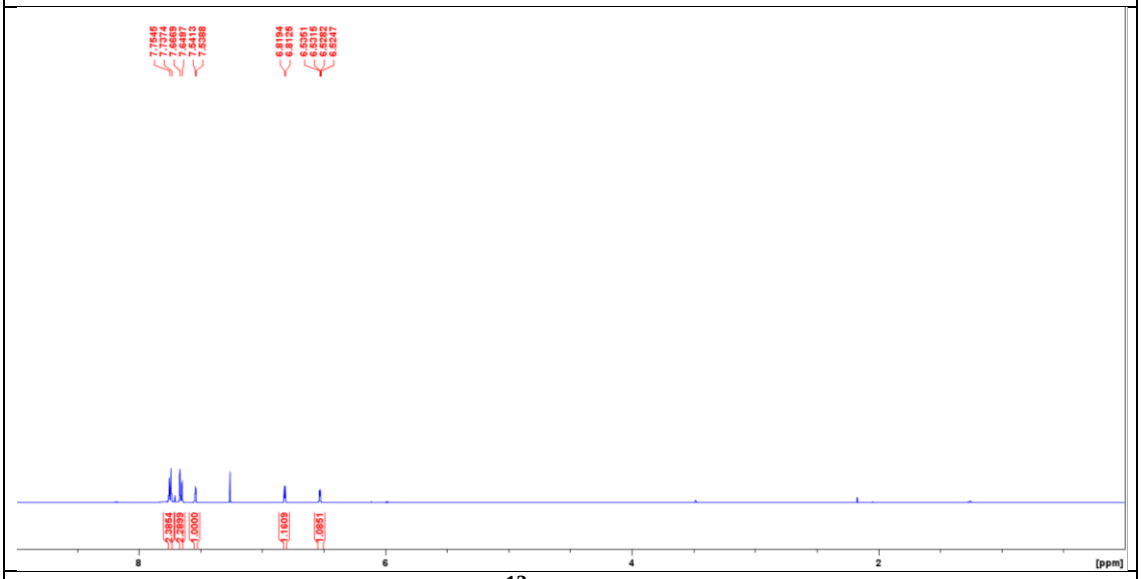
^{13}C NMR



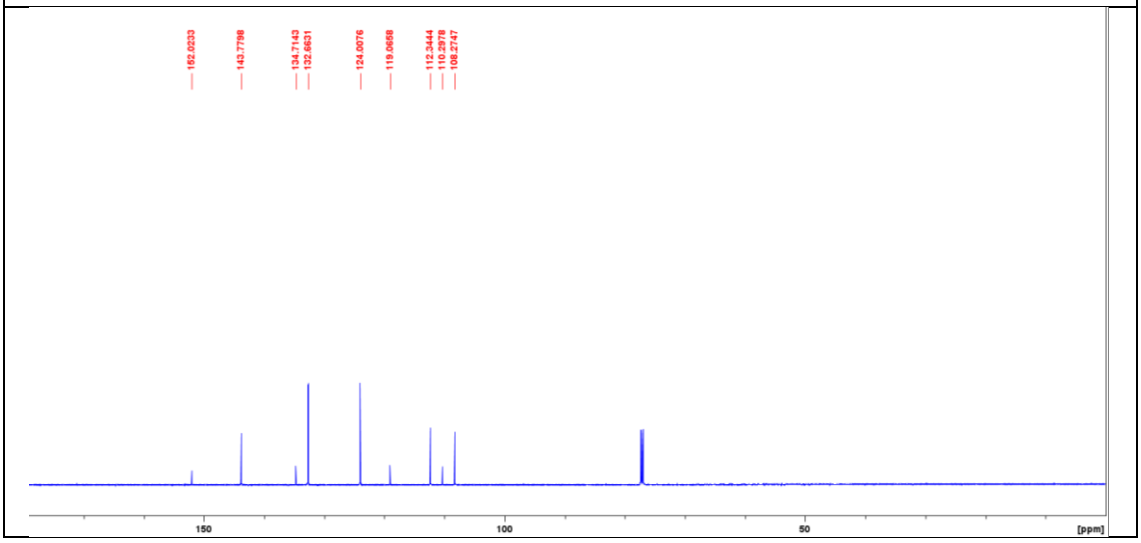


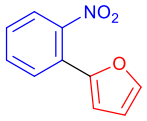
3c

^{1}H NMR



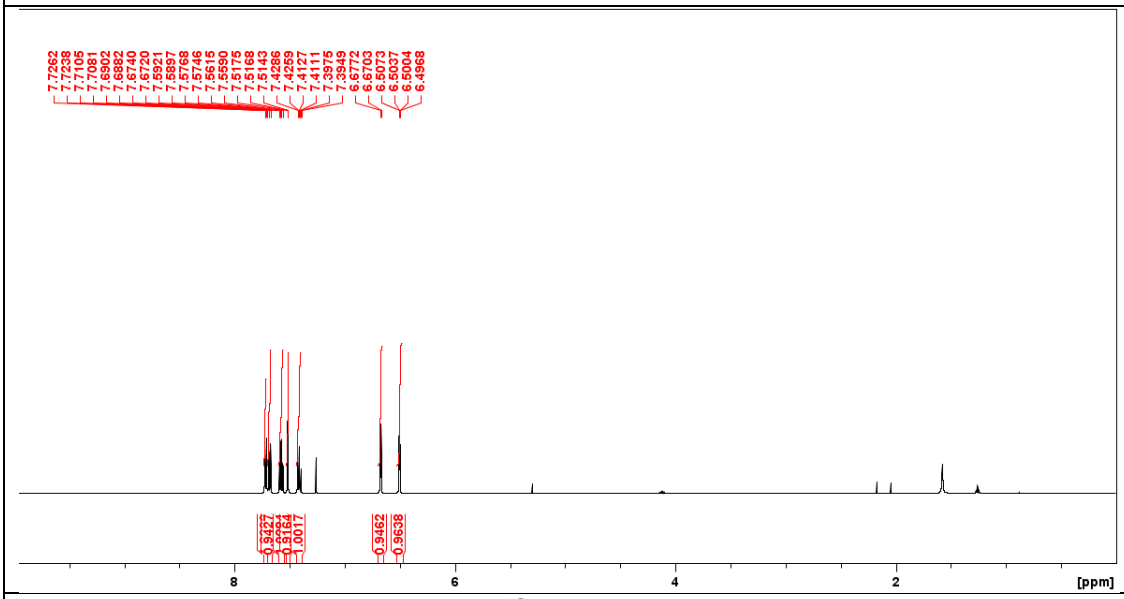
^{13}C NMR



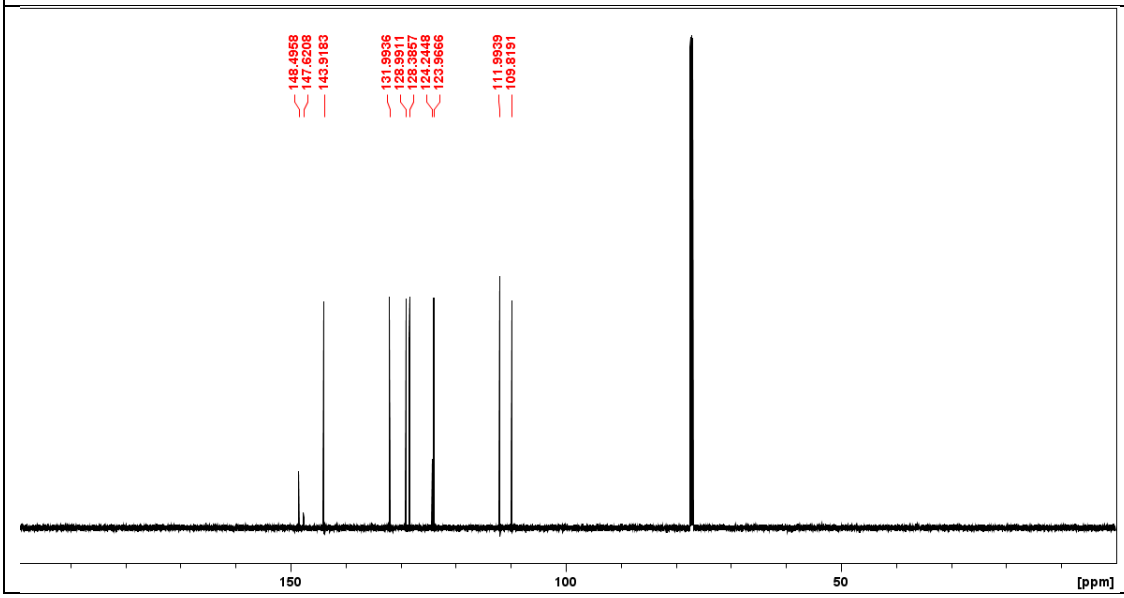


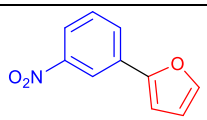
3d

^{1}H NMR



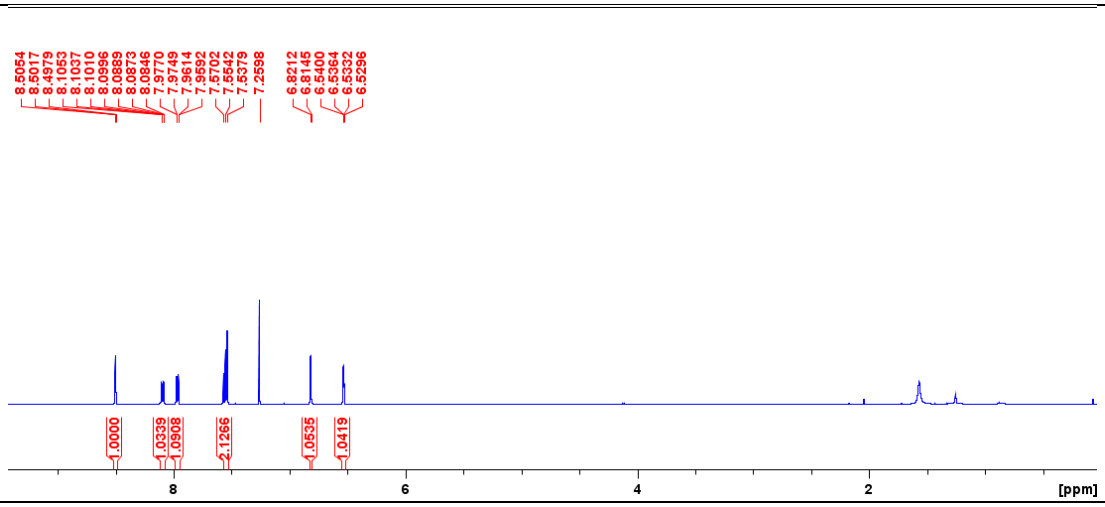
^{13}C NMR





3e

^{1}H NMR



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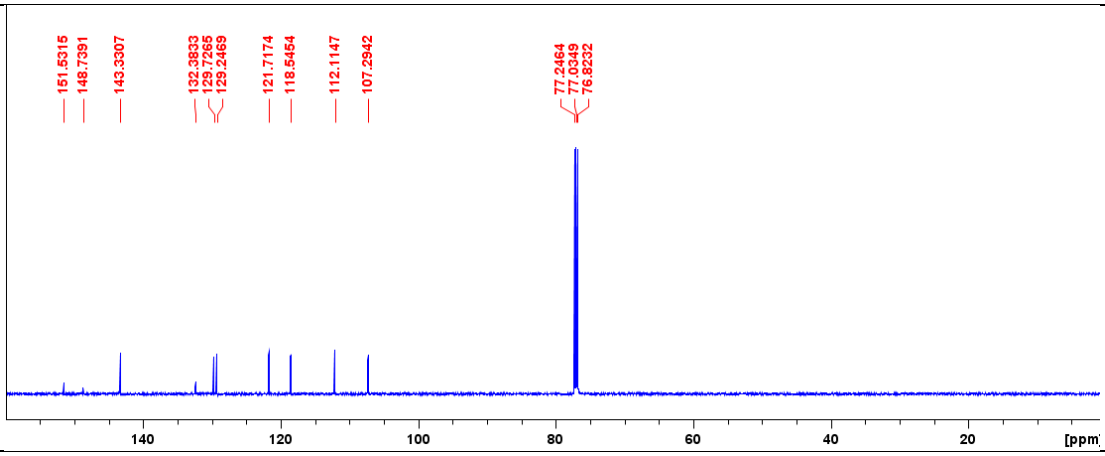

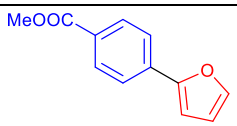

3f

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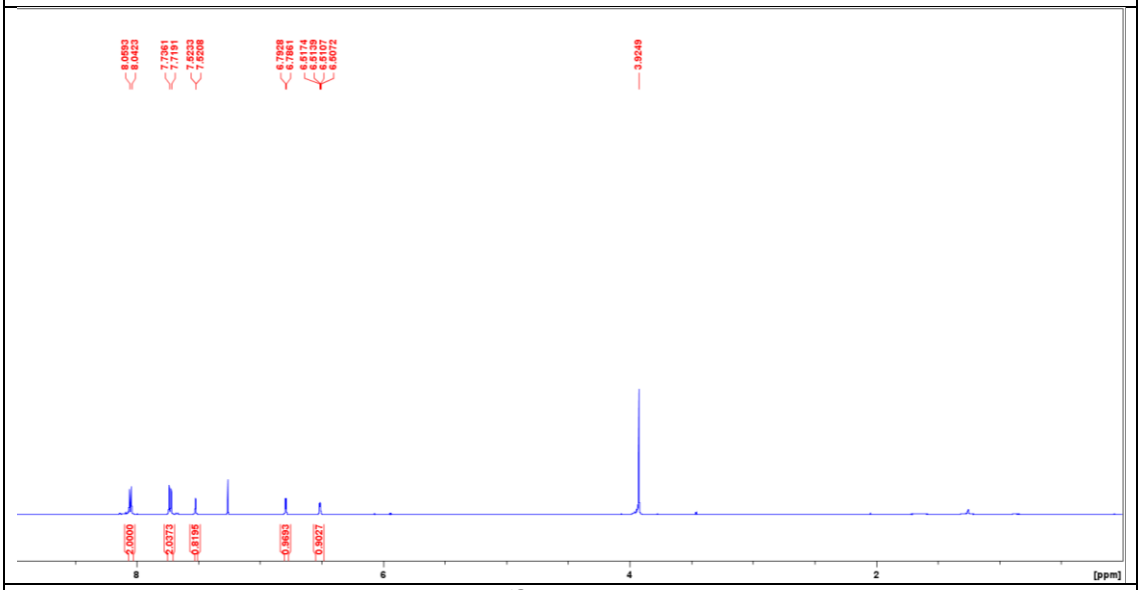
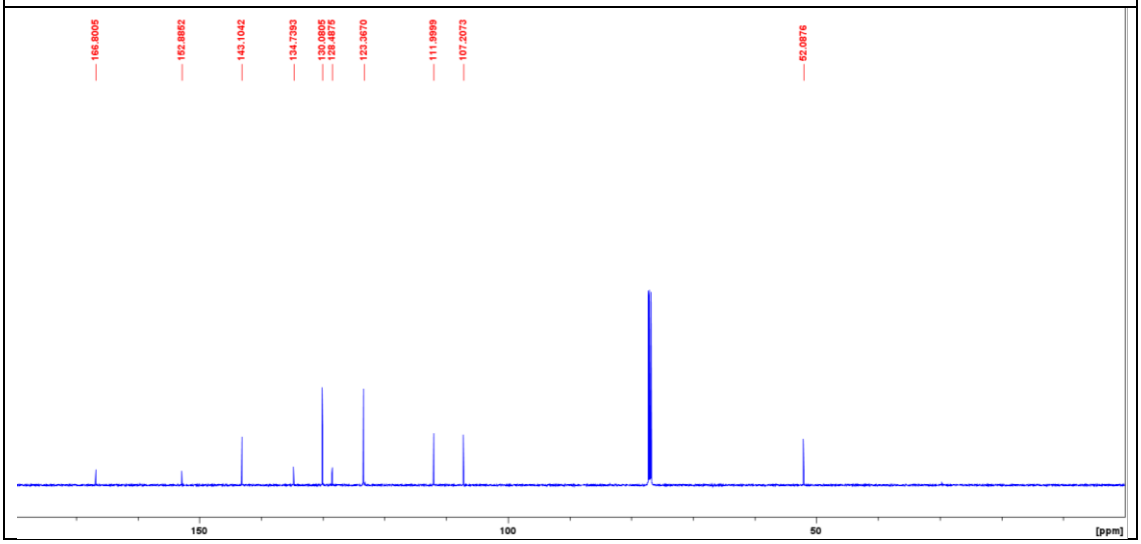
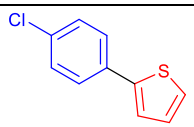


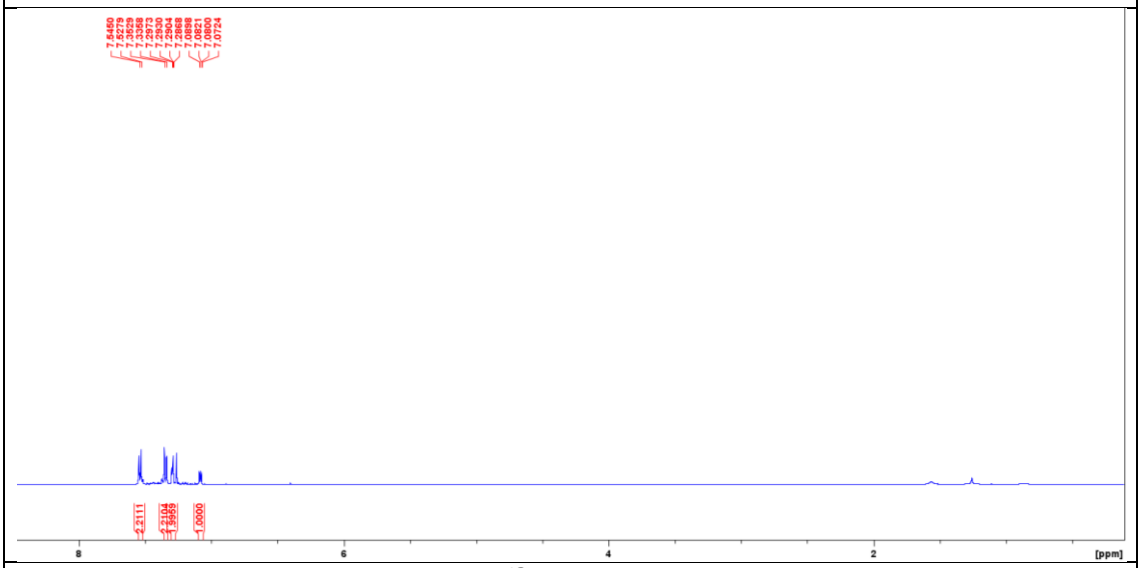
^{13}C NMR



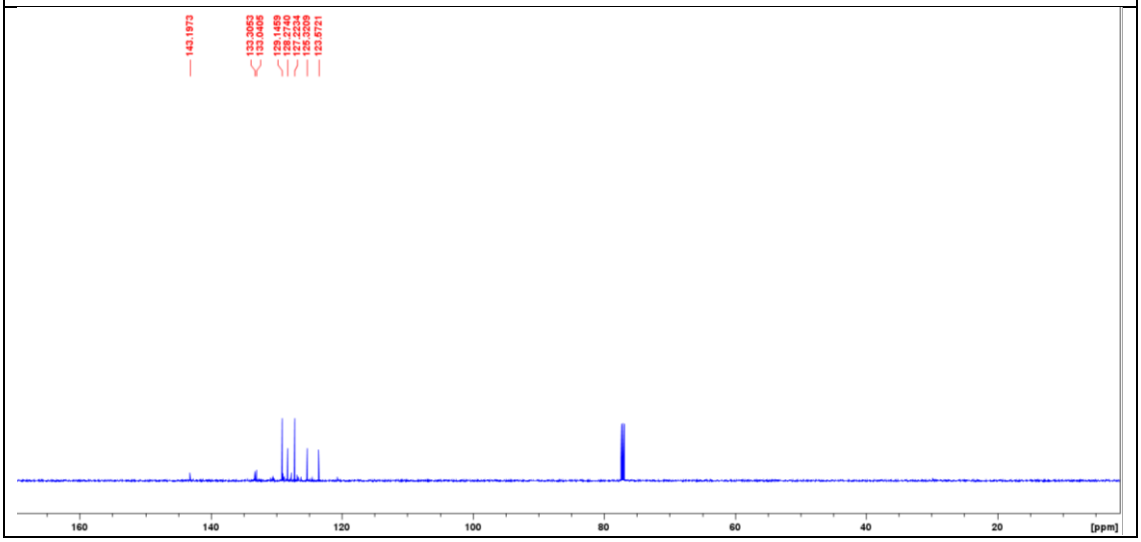


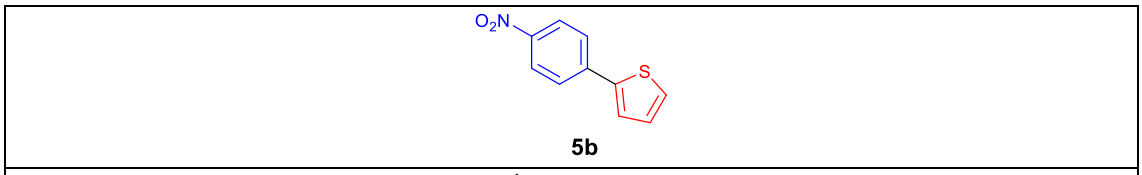
5a

^{1}H NMR



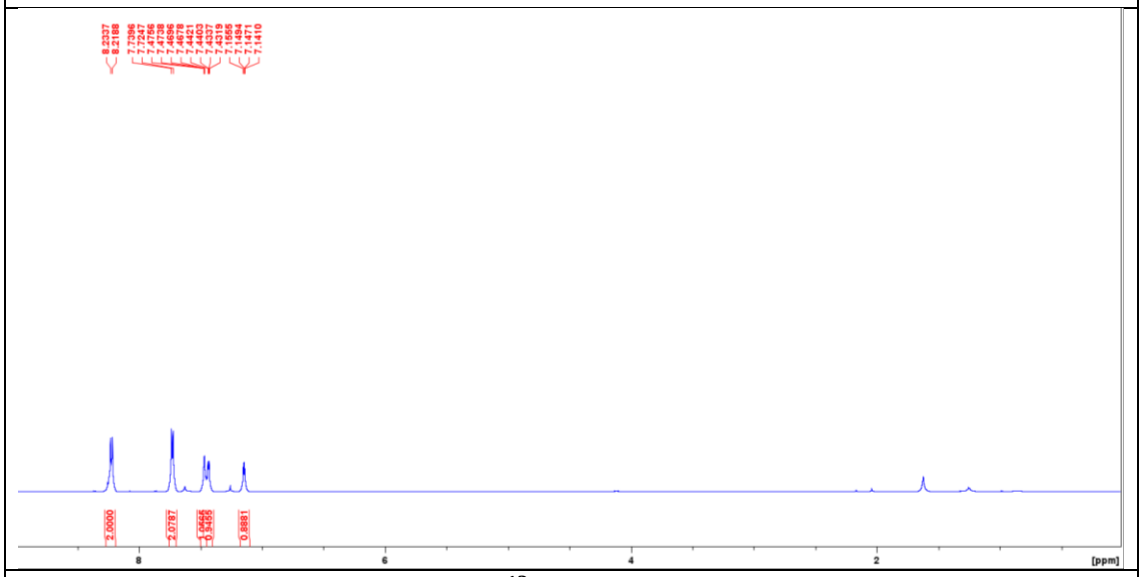
^{13}C NMR





5b

^{1}H NMR



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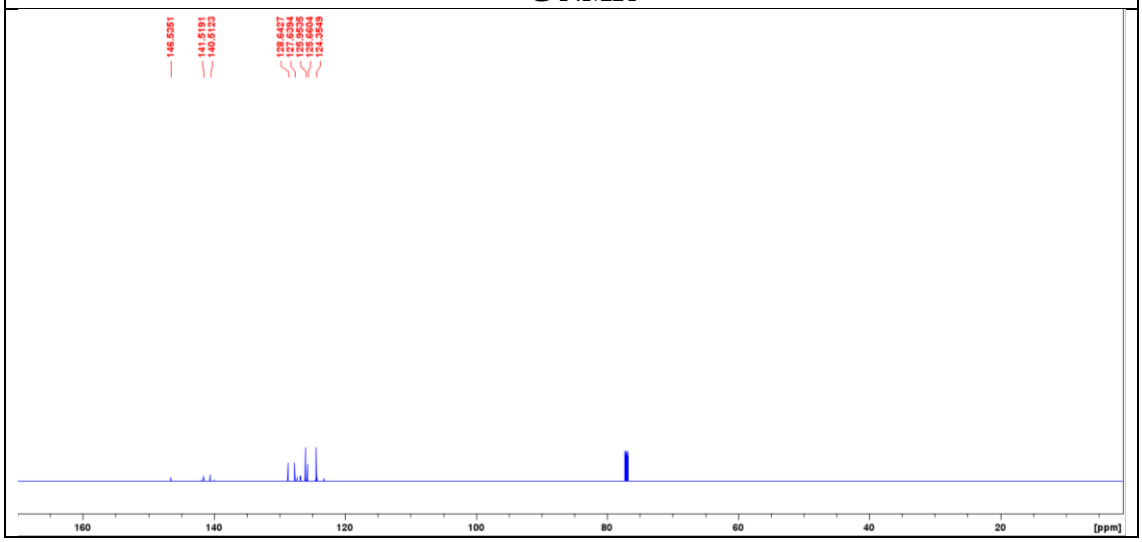

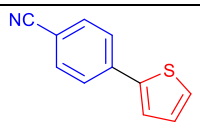

5c

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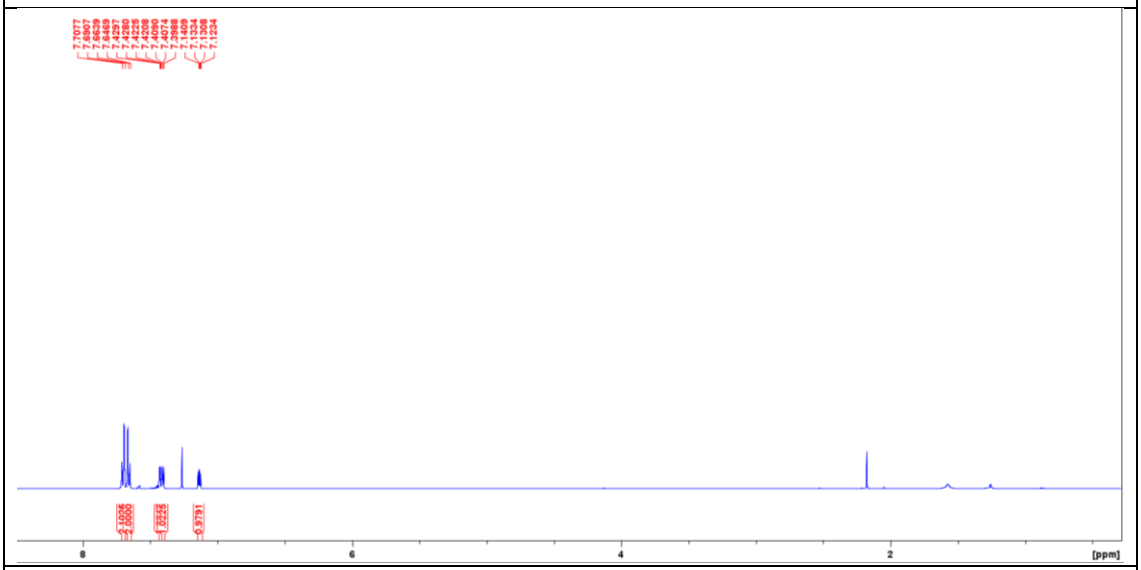
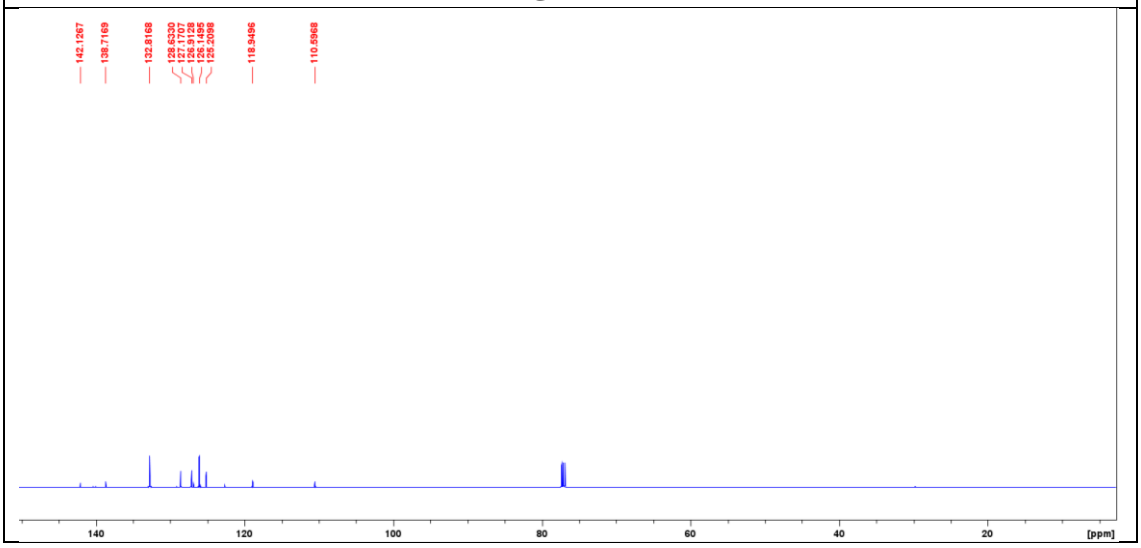
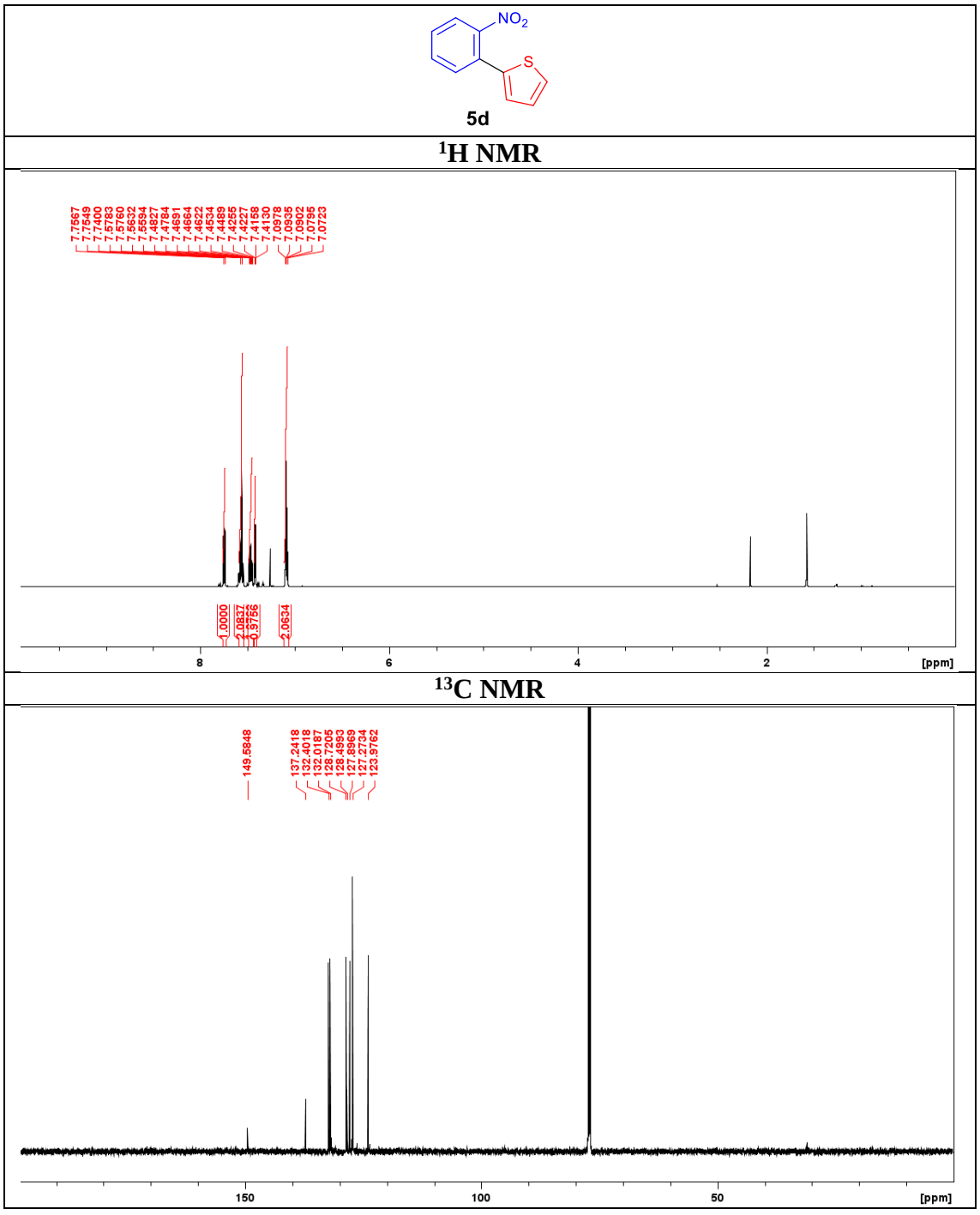


^{13}C NMR




NO2
S
5d
1H NMR
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7.7400
7.5783
7.5769
7.5632
7.5594
7.4827
7.4784
7.4691
7.4664
7.4622
7.4534
7.4489
7.4255
7.4227
7.4158
7.4130
7.0978
7.0935
7.0902
7.0795
7.0723
1.0000
2.0837
0.9756
2.0634
8
6
4
2
[ppm]
13C NMR
149.5848
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128.4993
127.8969
127.2734
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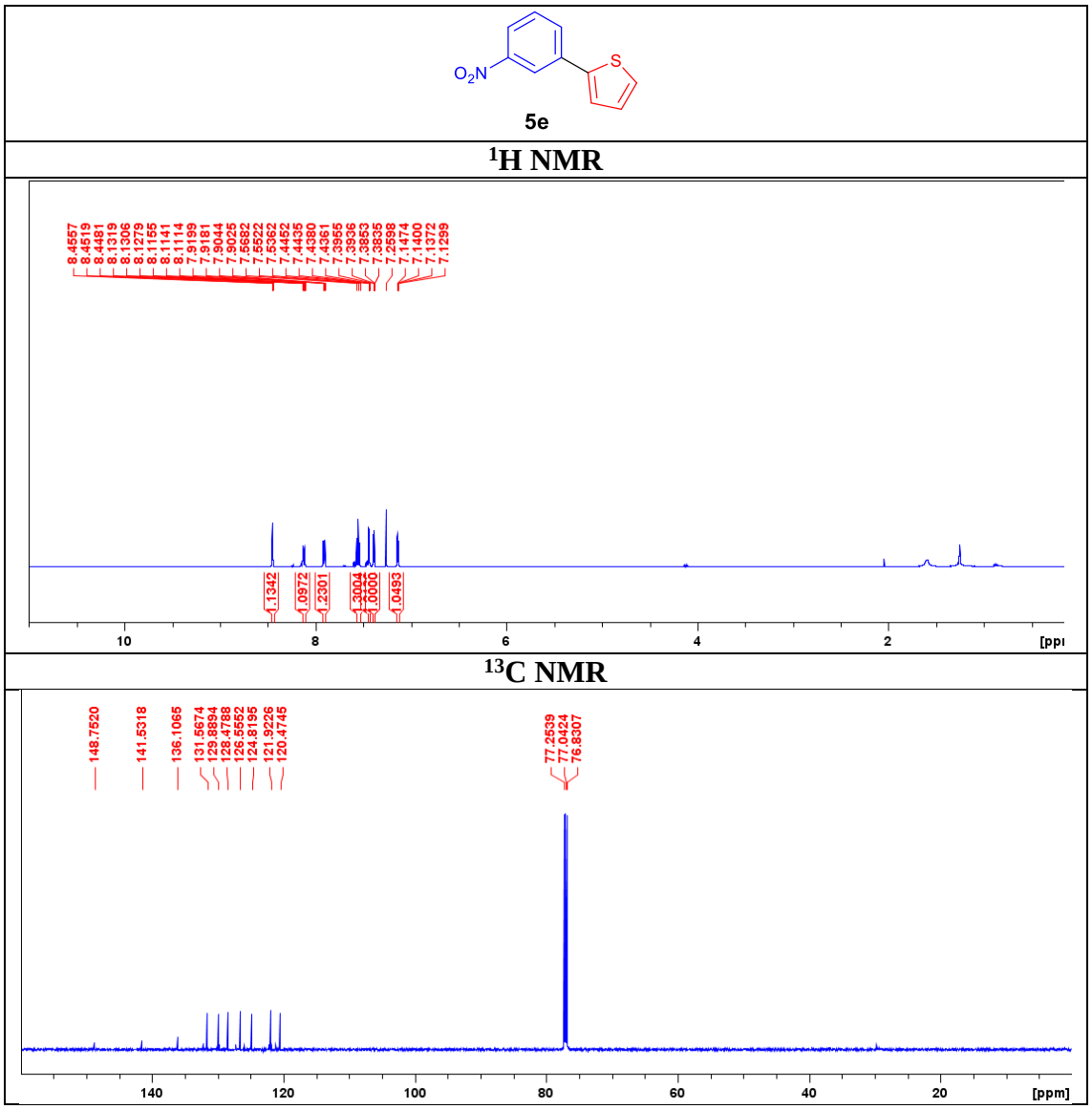
50
[ppm]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S
5e
1H NMR
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8.1319
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8.1279
8.1155
8.1141
8.1114
7.9199
7.9181
7.9044
7.9025
7.5682
7.5522
7.5362
7.4452
7.4435
7.4380
7.4361
7.3955
7.3936
7.3853
7.3835
7.2598
7.1474
7.1400
7.1372
7.1299
1.1342
1.0972
1.2301
1.3004
1.0000
1.0493
10
8
6
4
2
[ppı
13C NMR
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131.5674
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128.4788
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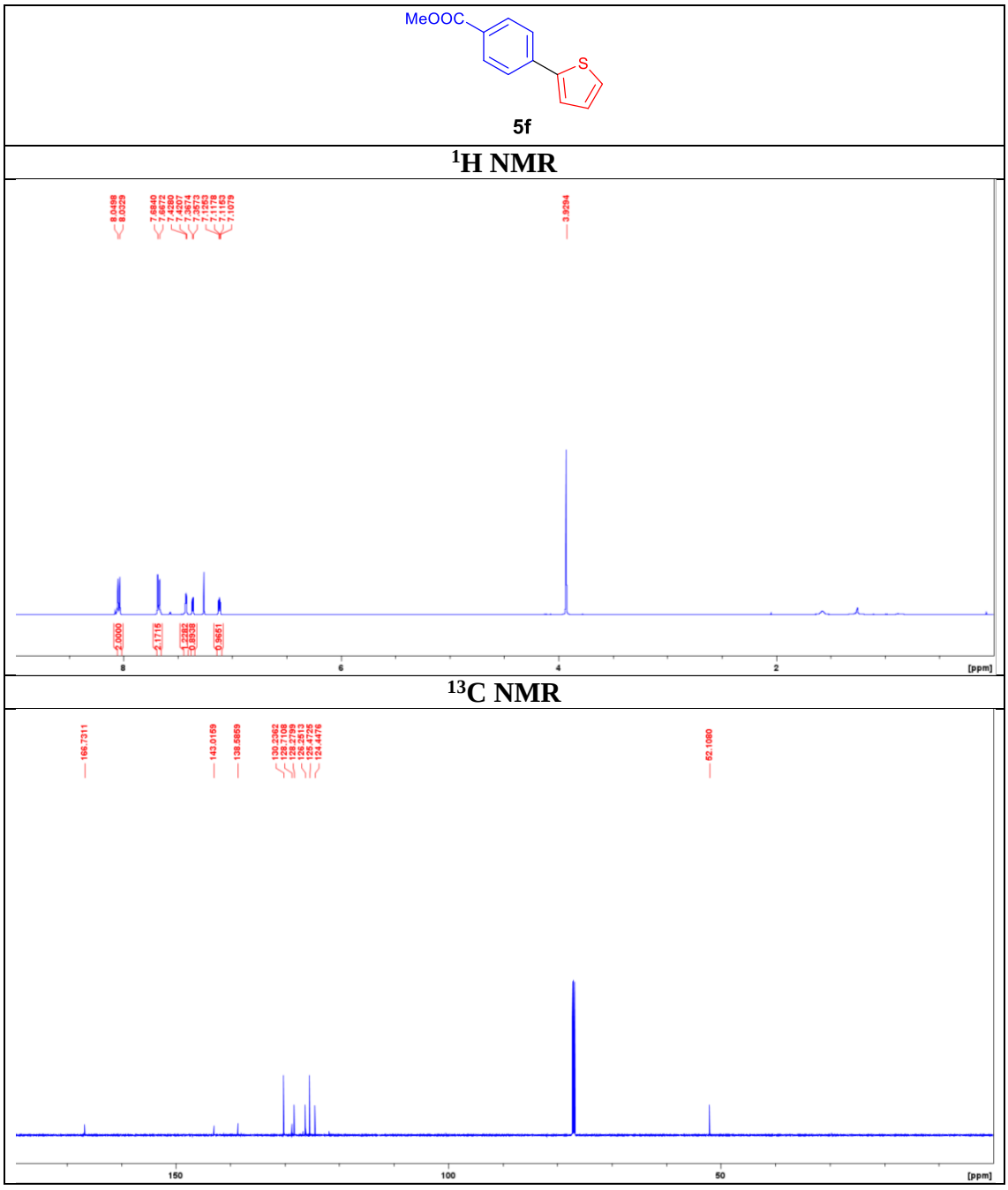
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5f
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7.3807
7.1253
7.1178
7.1165
7.1079
3.9294
2.0000
2.1715
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0.8938
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6
4
2
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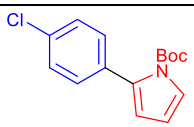
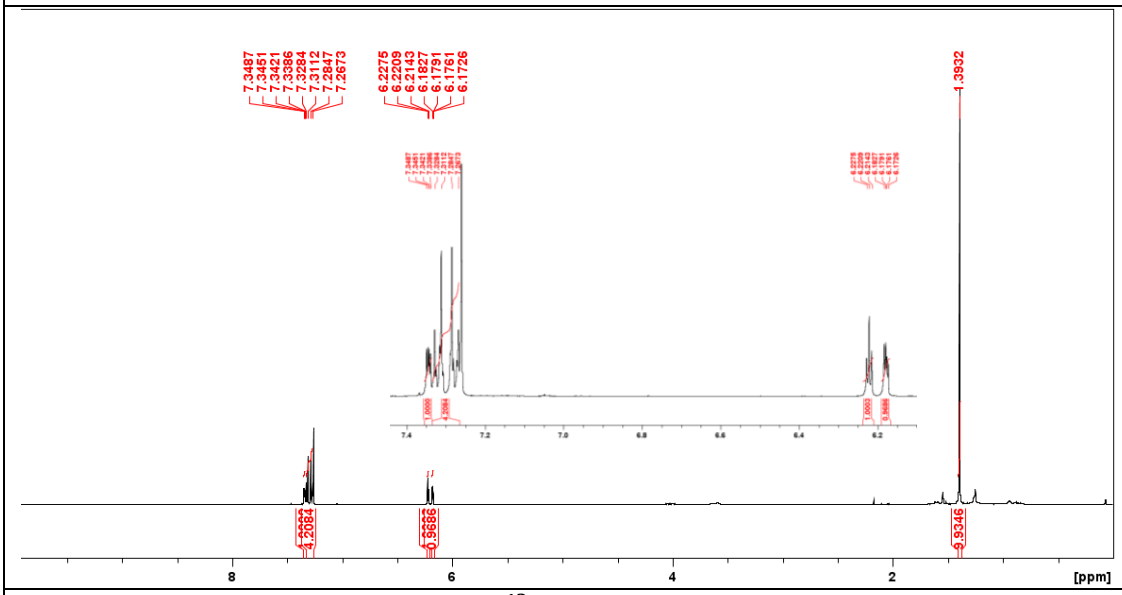
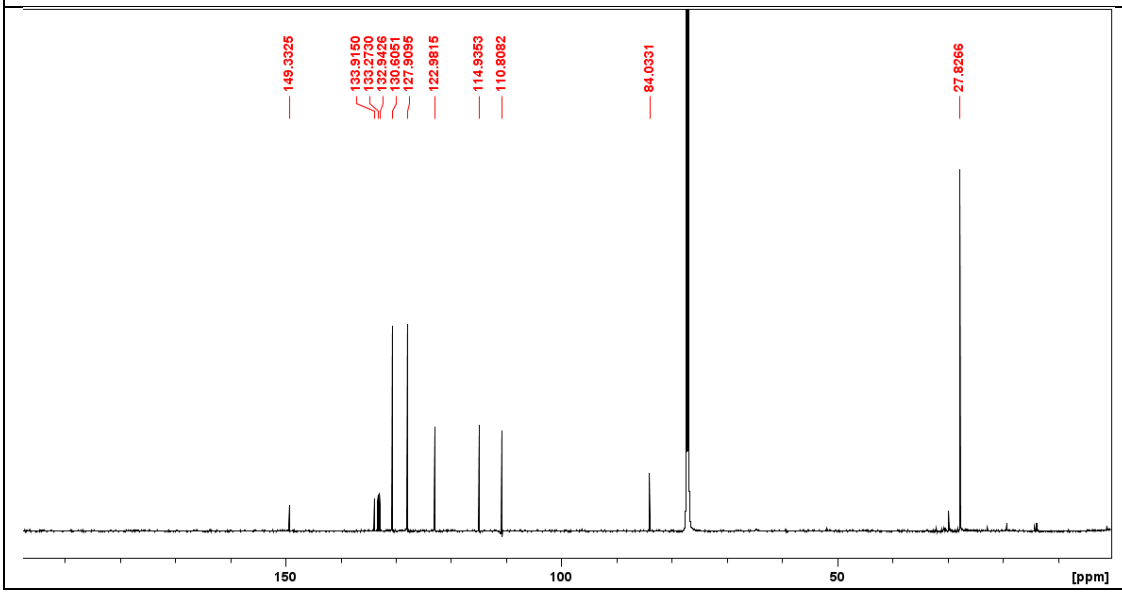


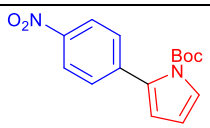
7a

^{1}H NMR



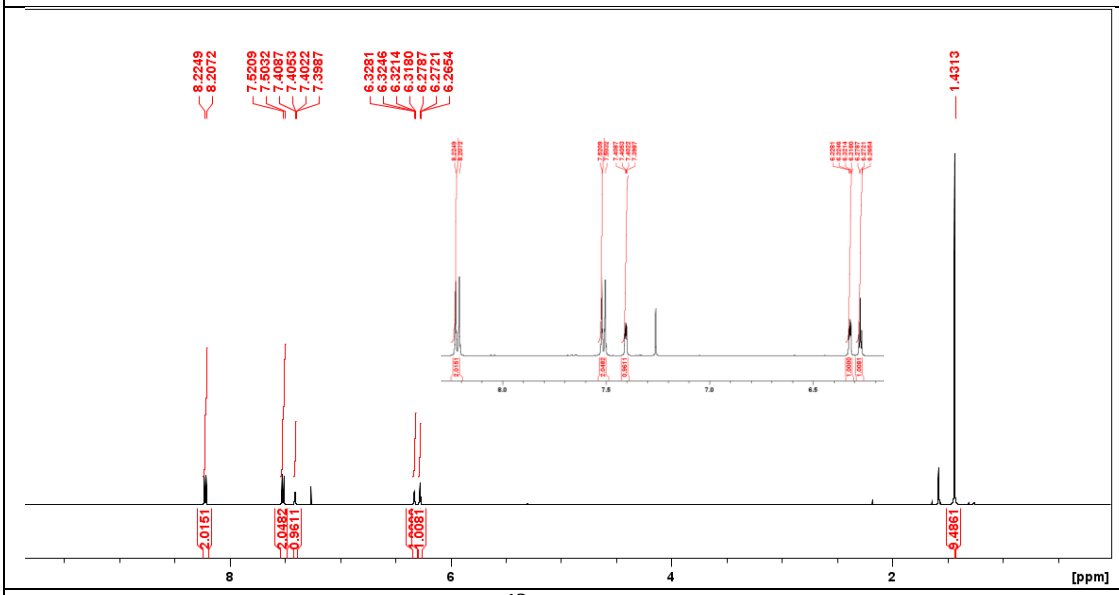
^{13}C NMR



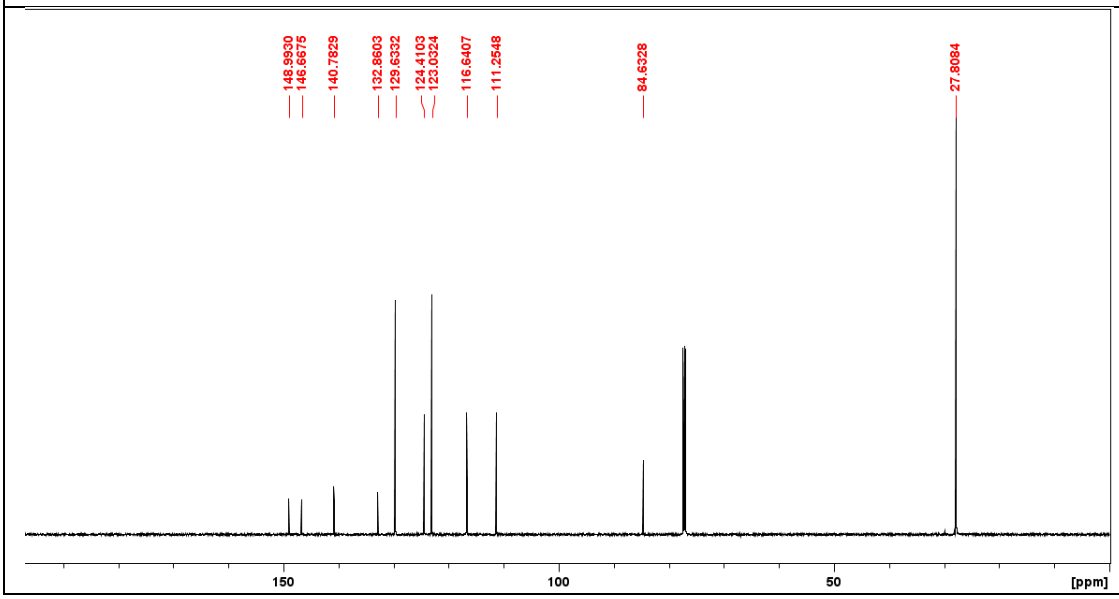


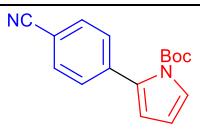
7b

^{1}H NMR



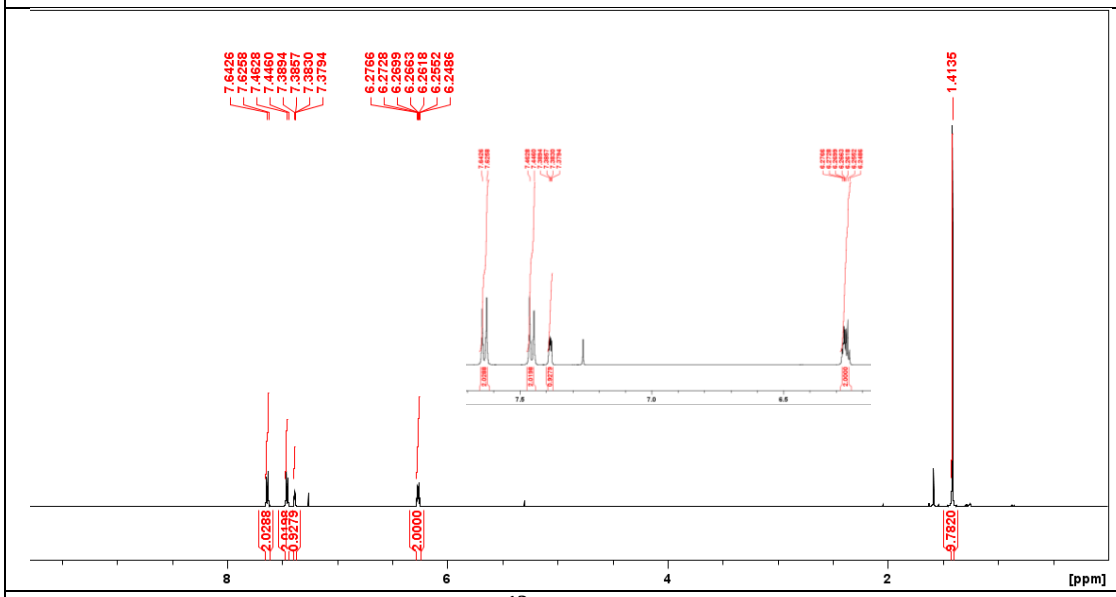
^{13}C NMR



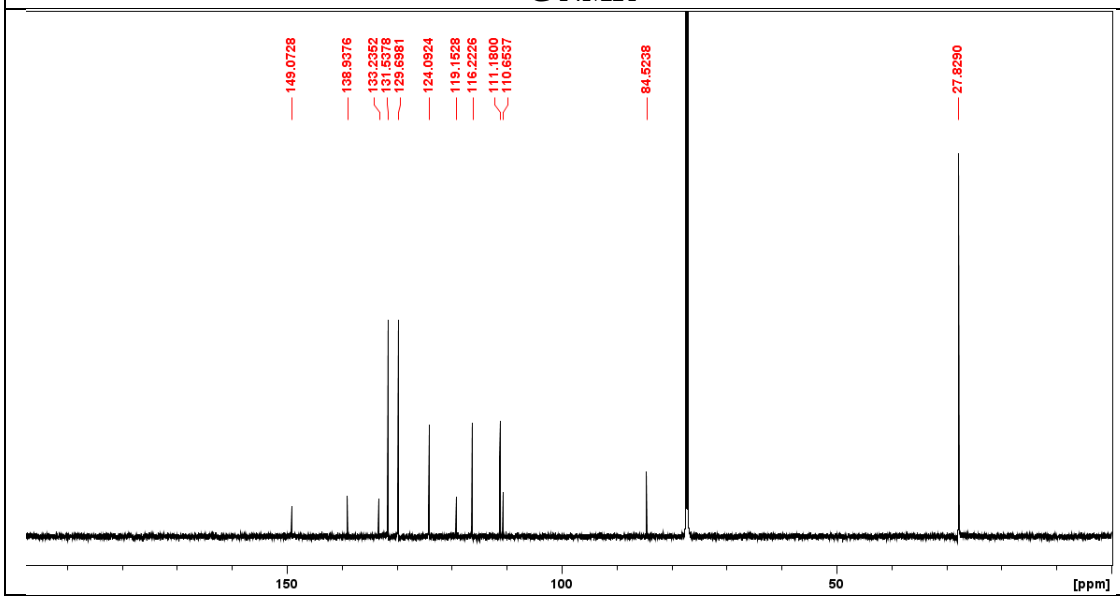


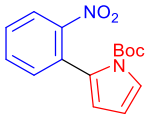
7c

^{1}H NMR



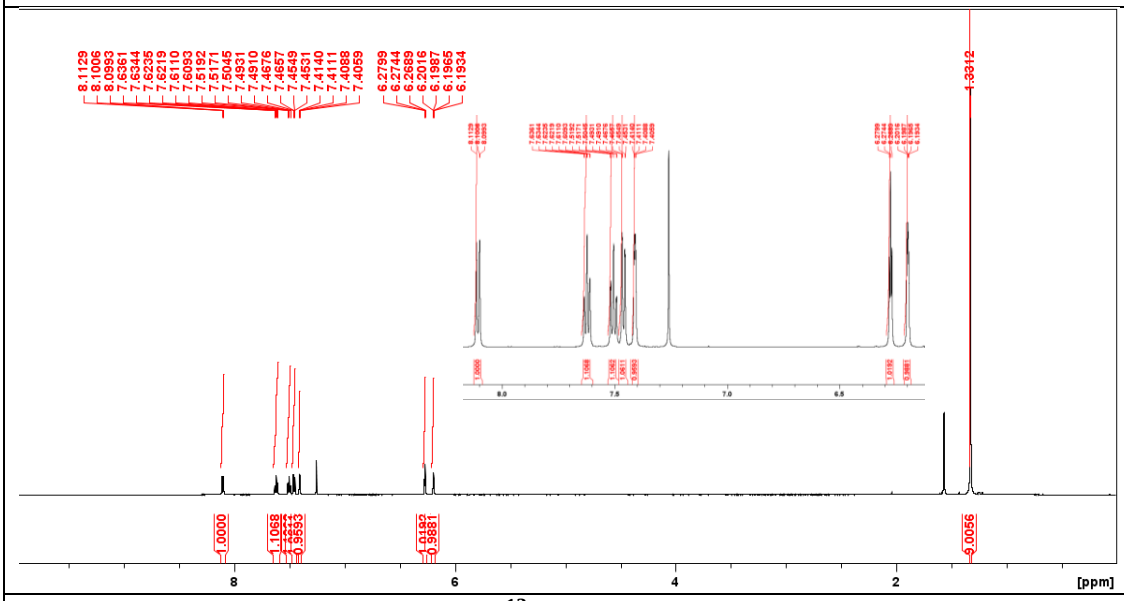
^{13}C NMR



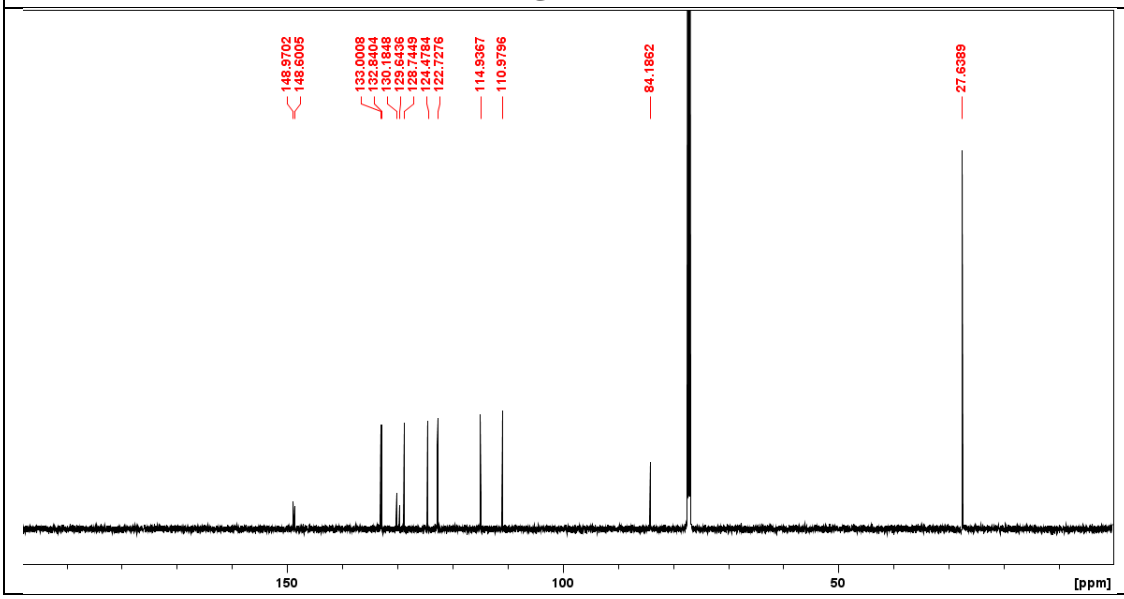


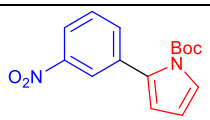
7d

^{1}H NMR



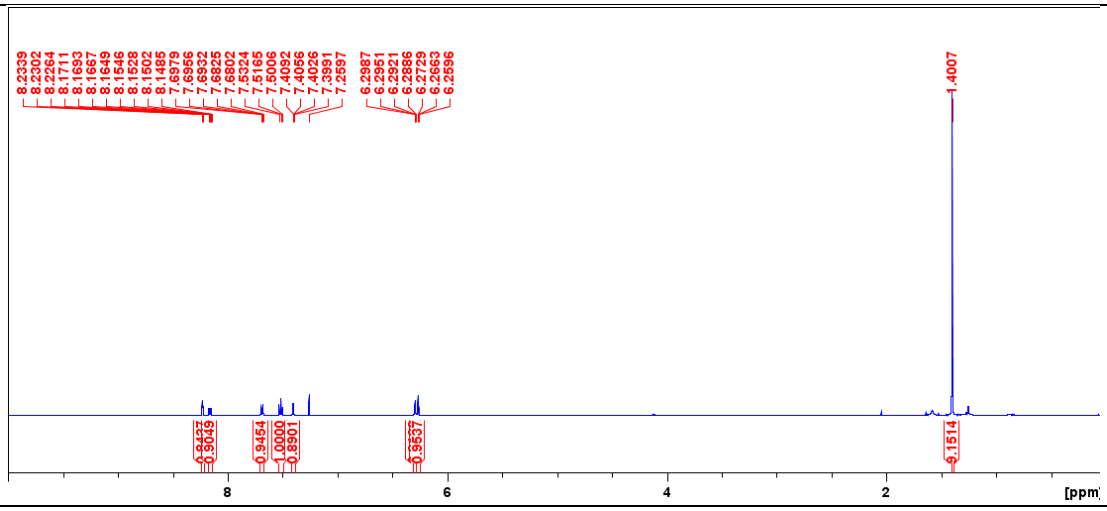
^{13}C NMR



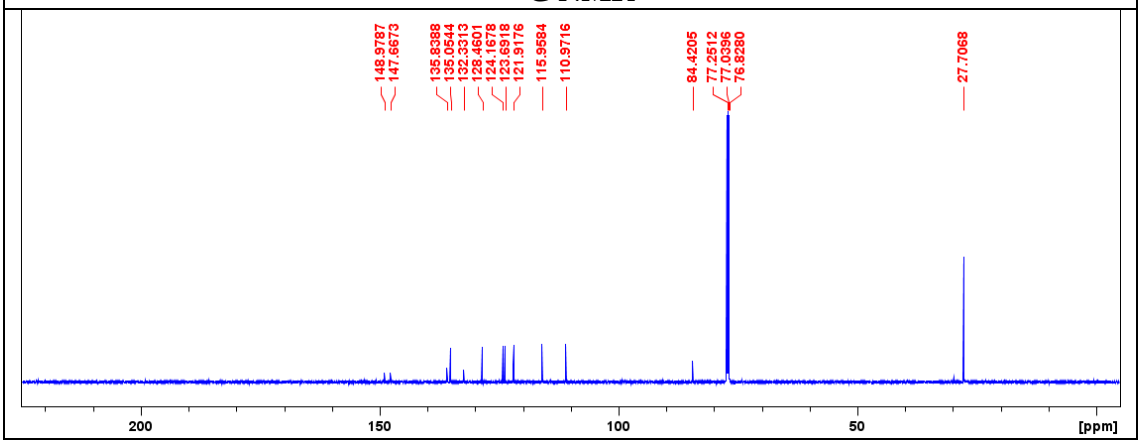


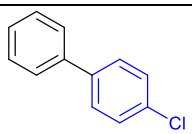
7e

^{1}H NMR



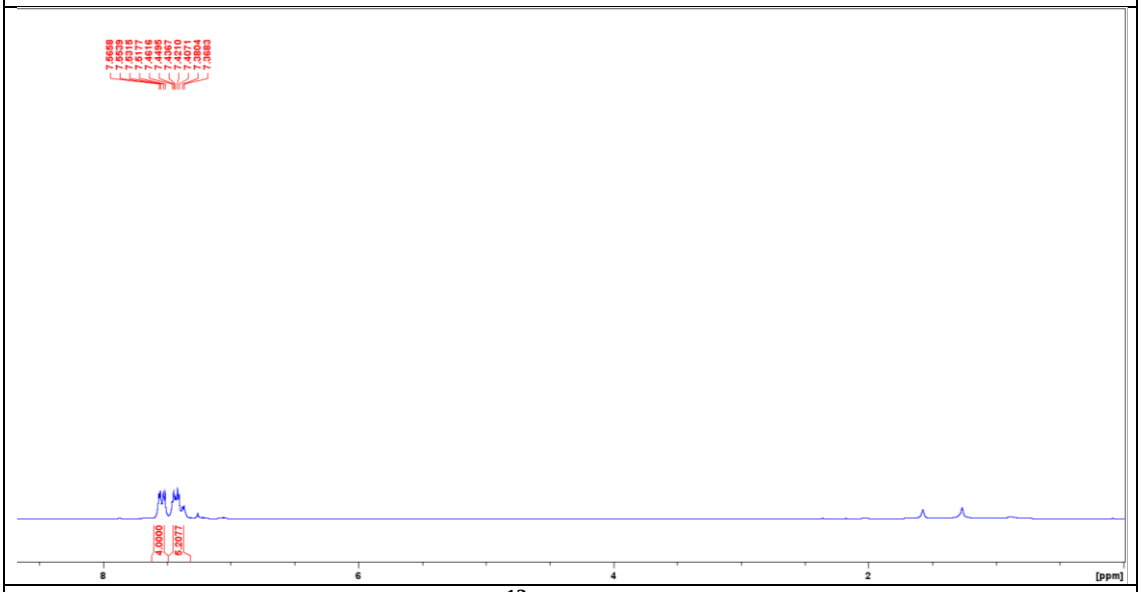
^{13}C NMR



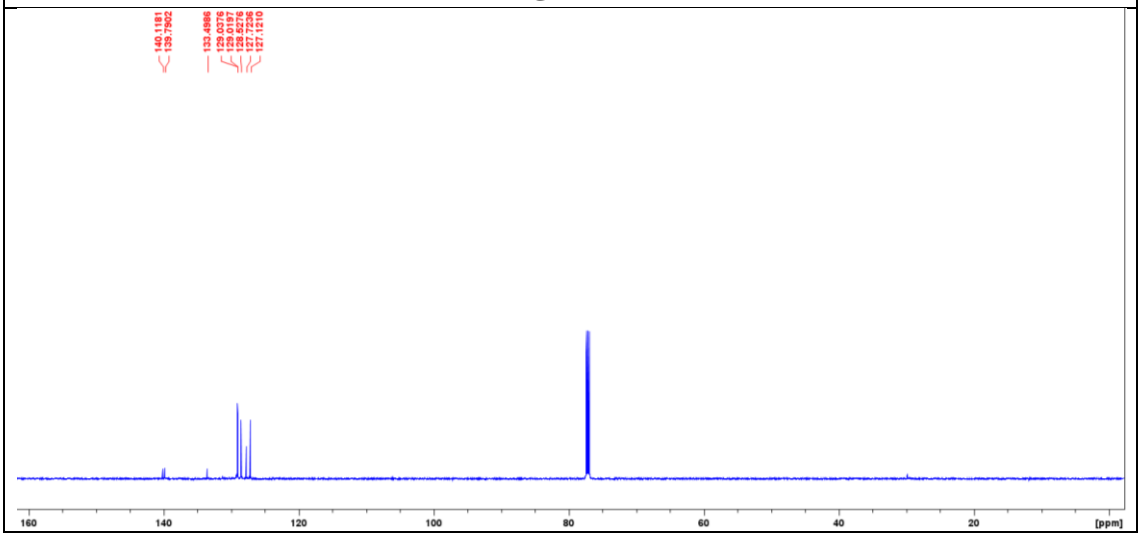


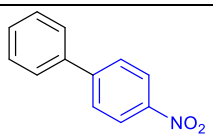
9a

^{1}H NMR



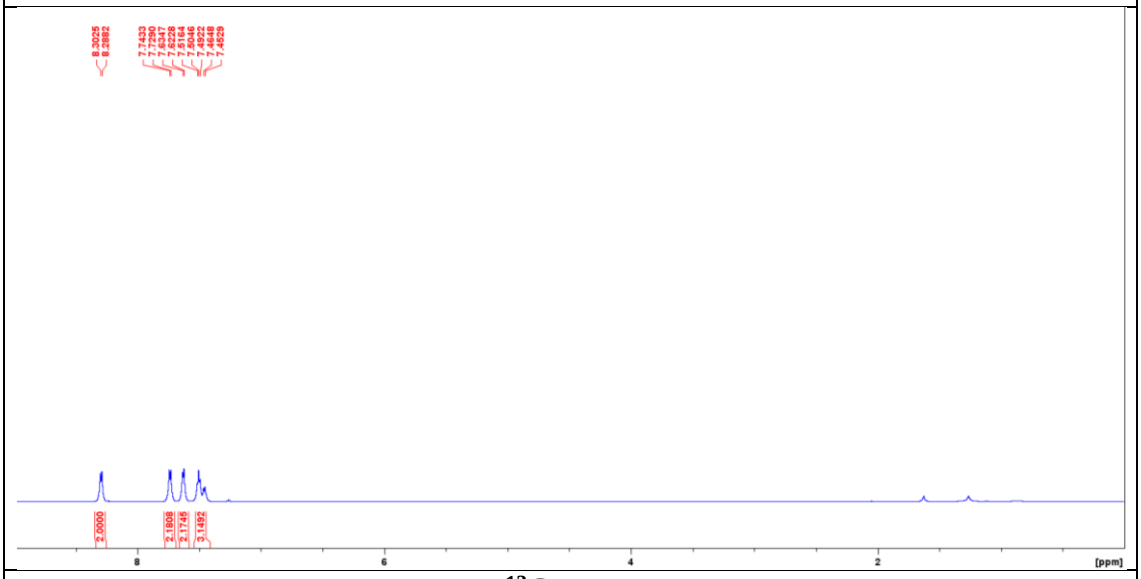
^{13}C NMR



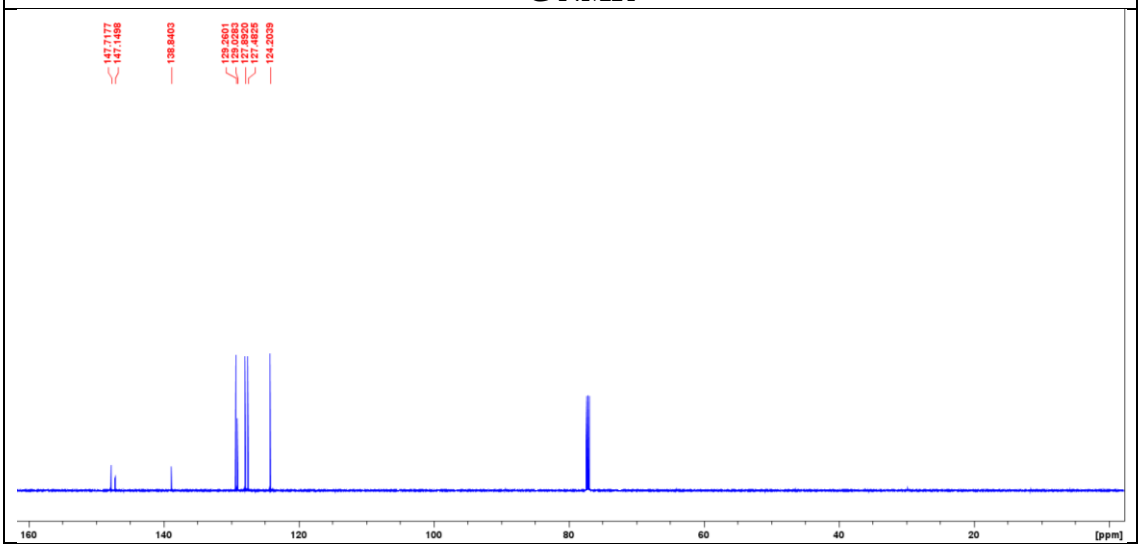


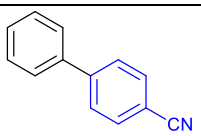
9b

^{1}H NMR



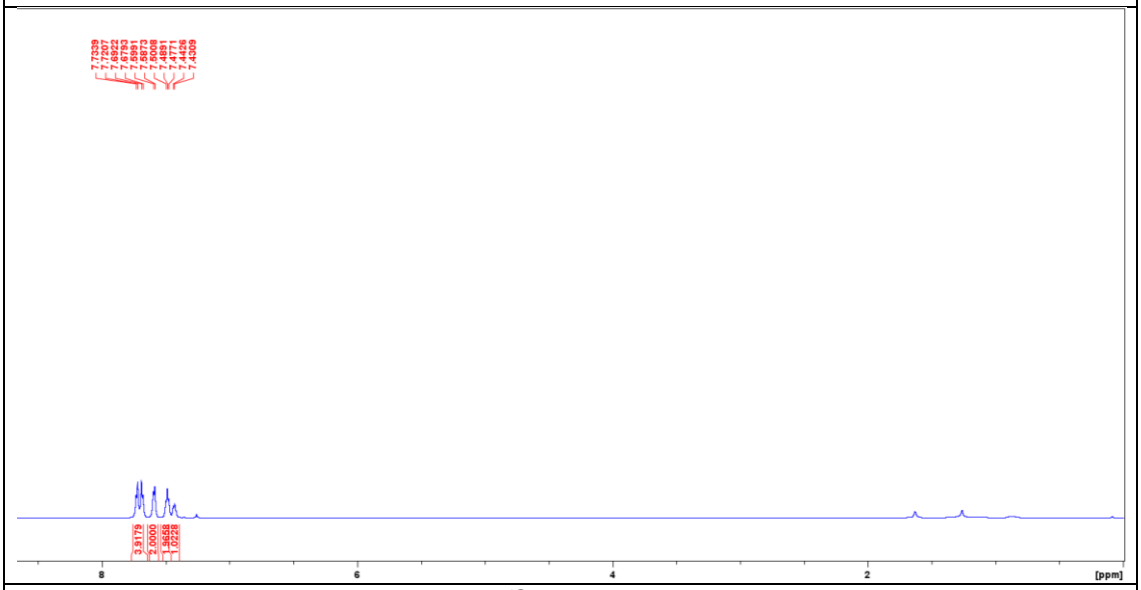
^{13}C NMR



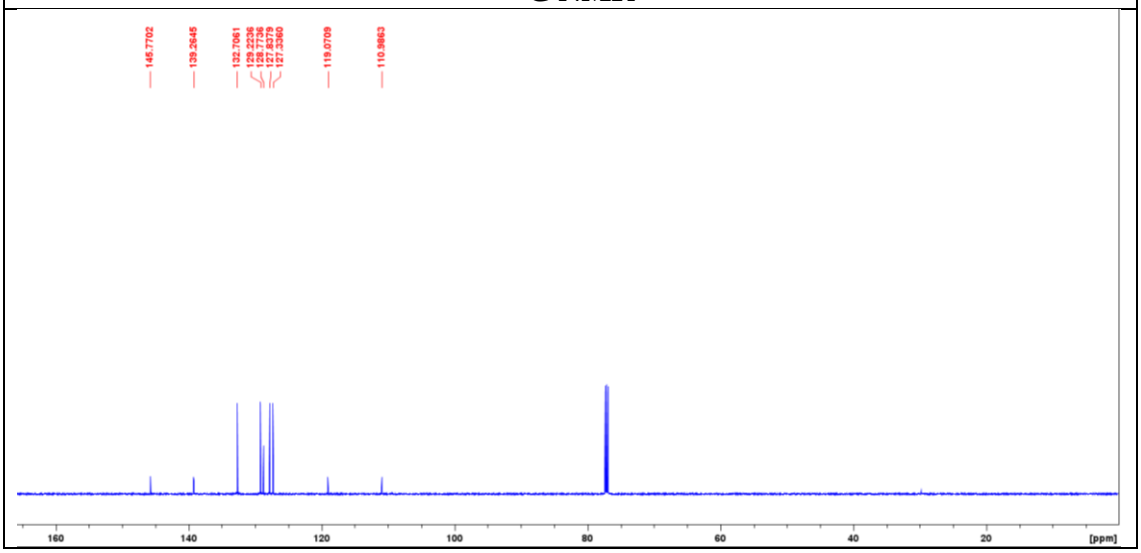


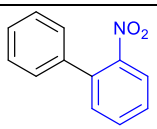
9c

^{1}H NMR



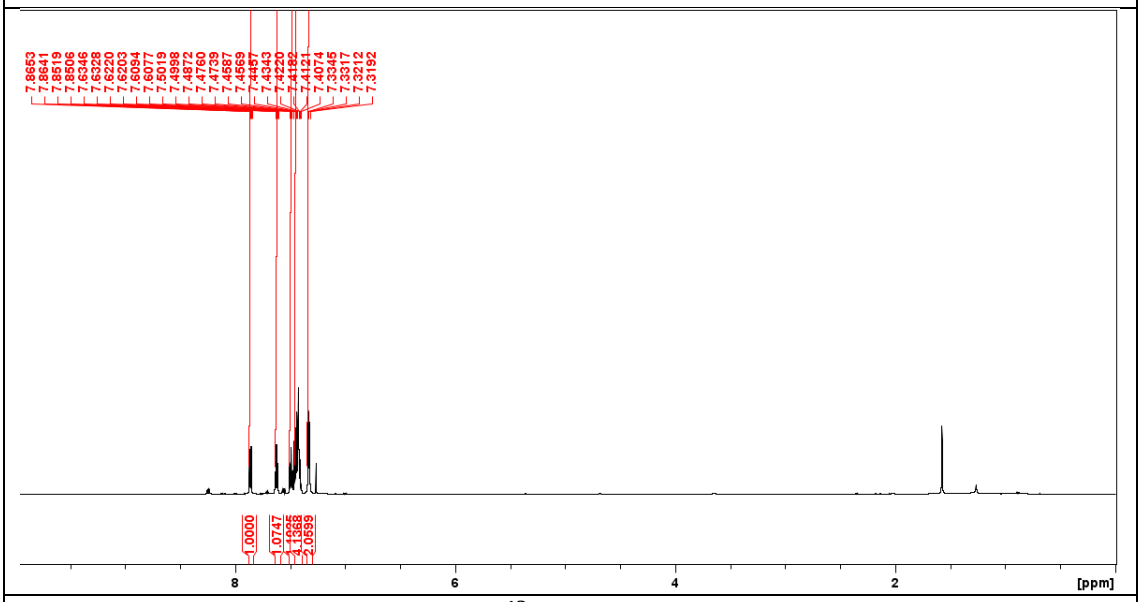
^{13}C NMR



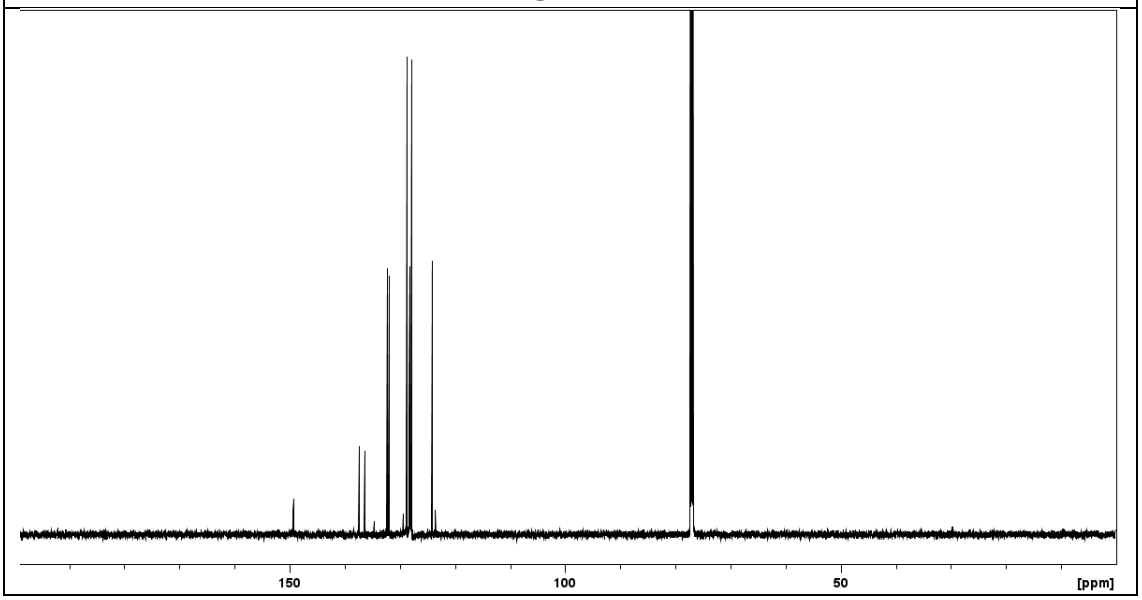


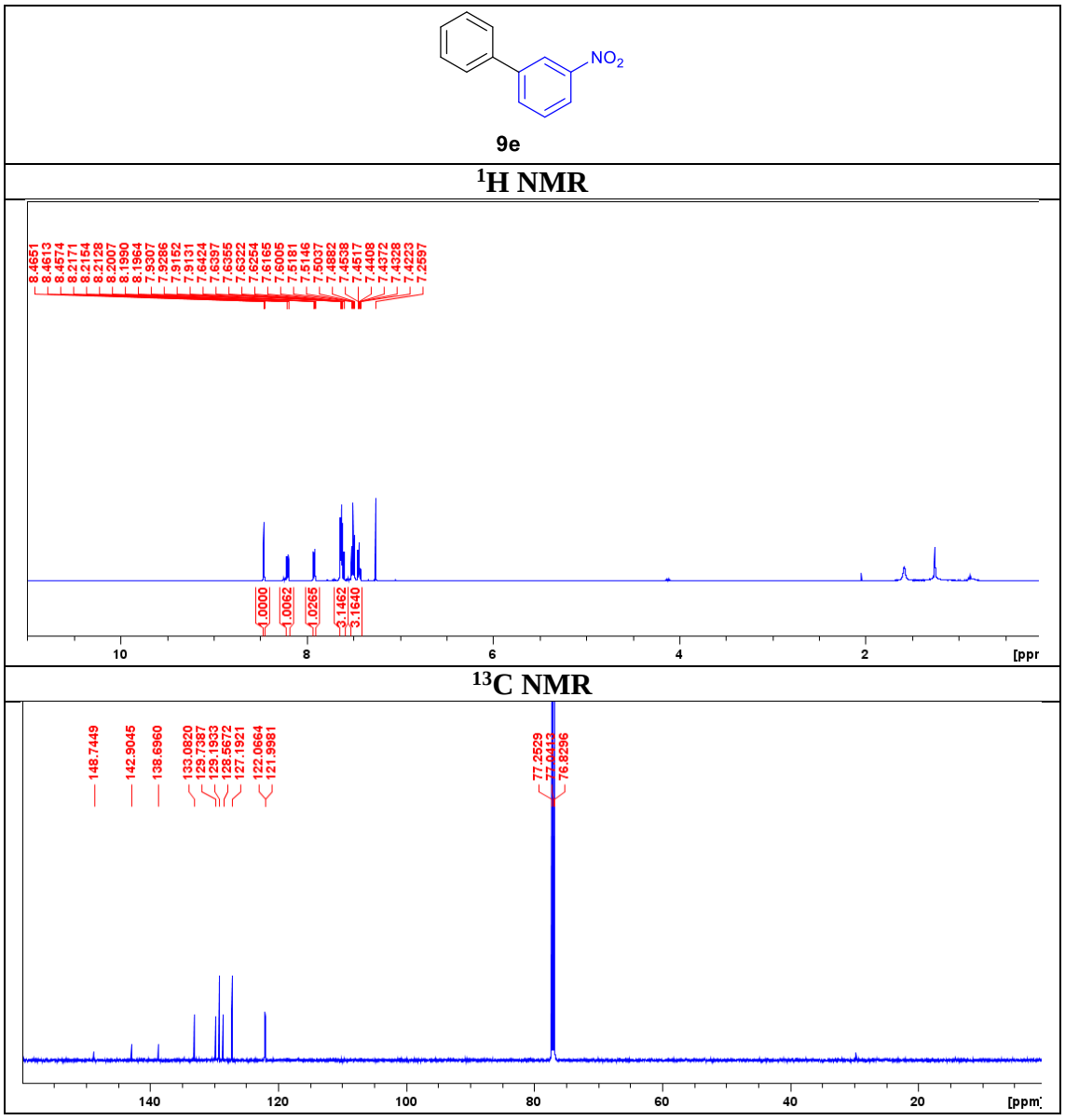
9d

^{1}H NMR



^{13}C NMR

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8.2128
8.2007
8.1990
8.1964
7.9307
7.9286
7.9152
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10
8
6
4
2
[ppr
13C NMR
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138.6960
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20
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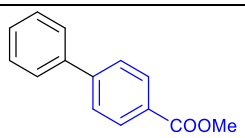
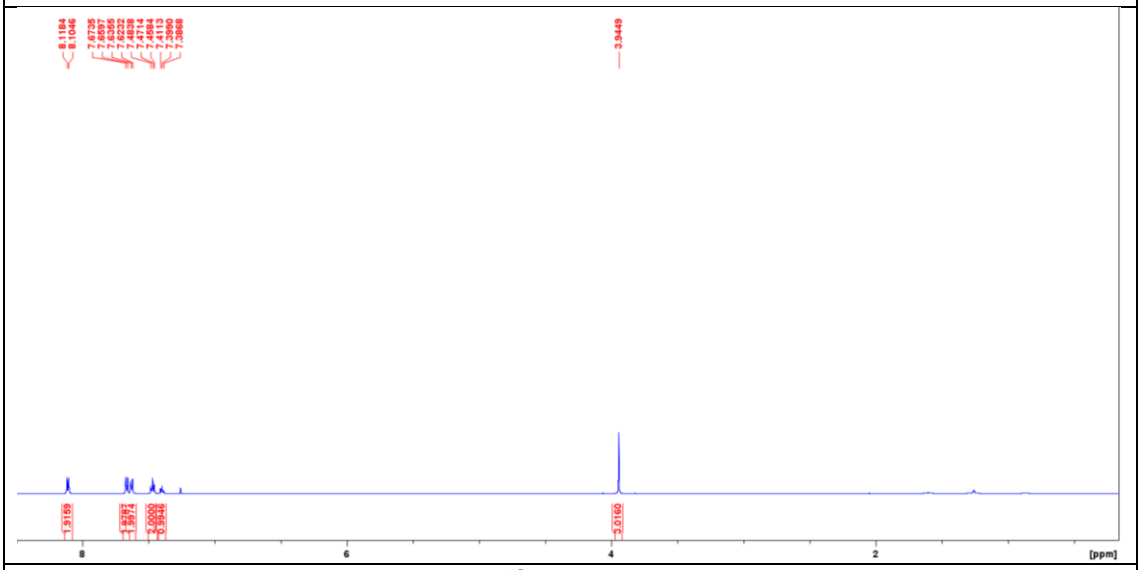


9f

^{1}H NMR



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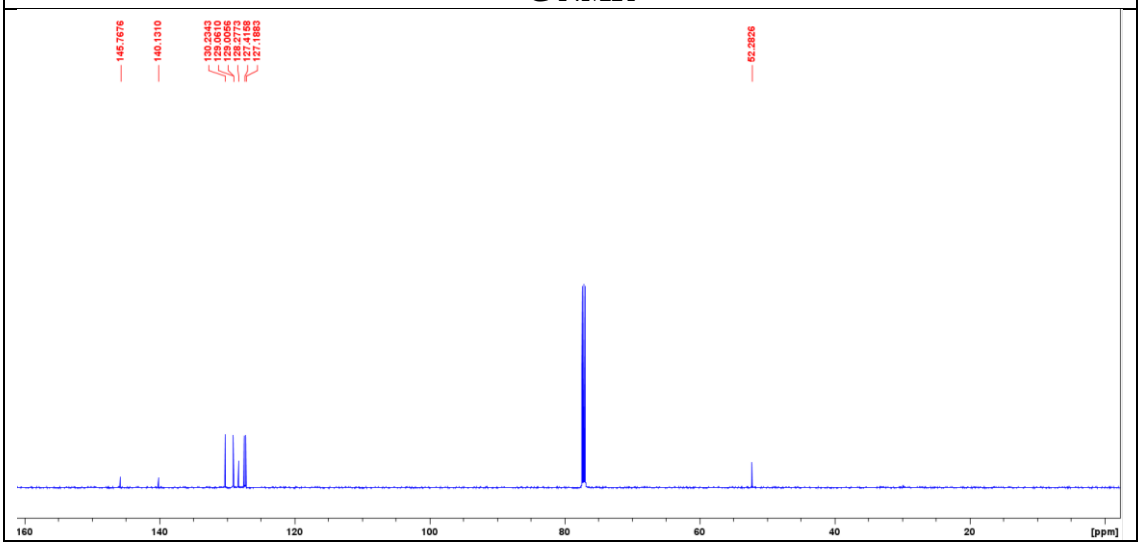

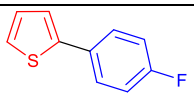

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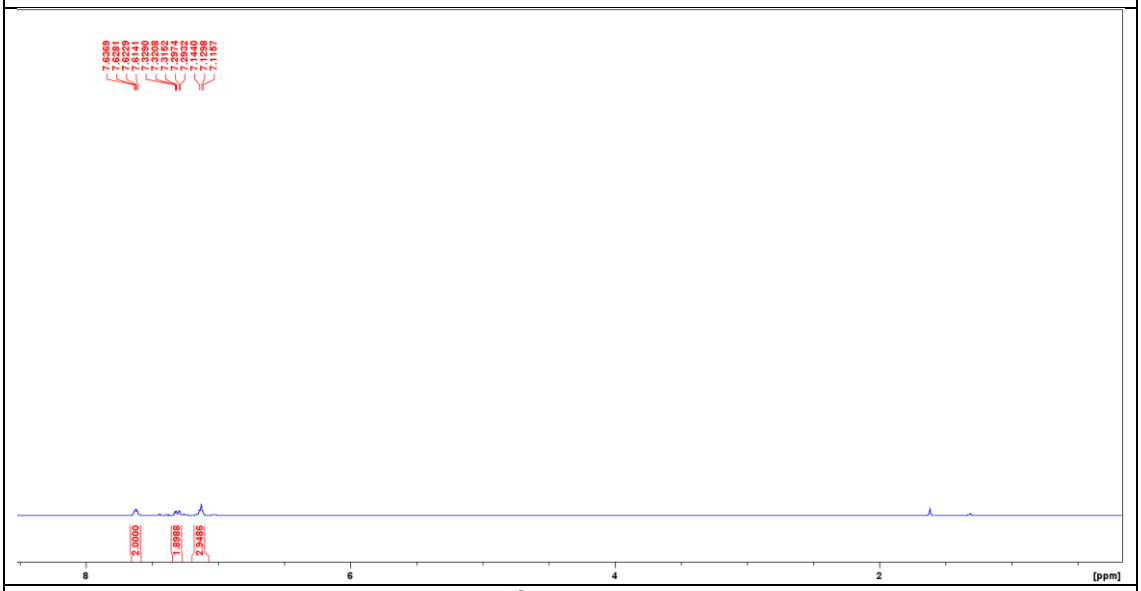

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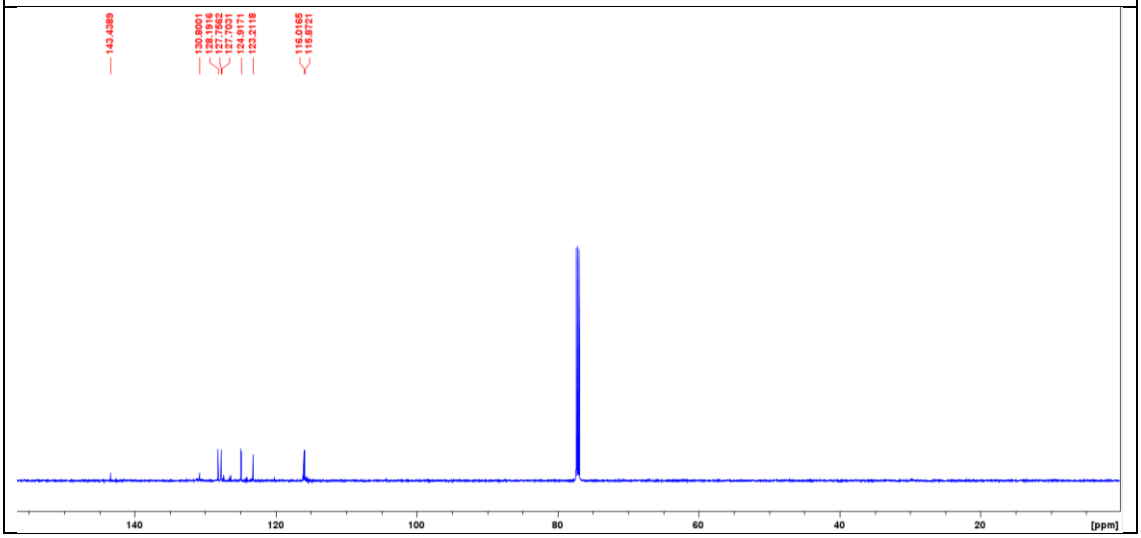
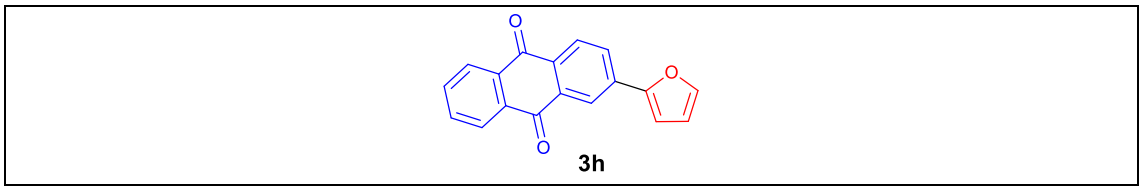
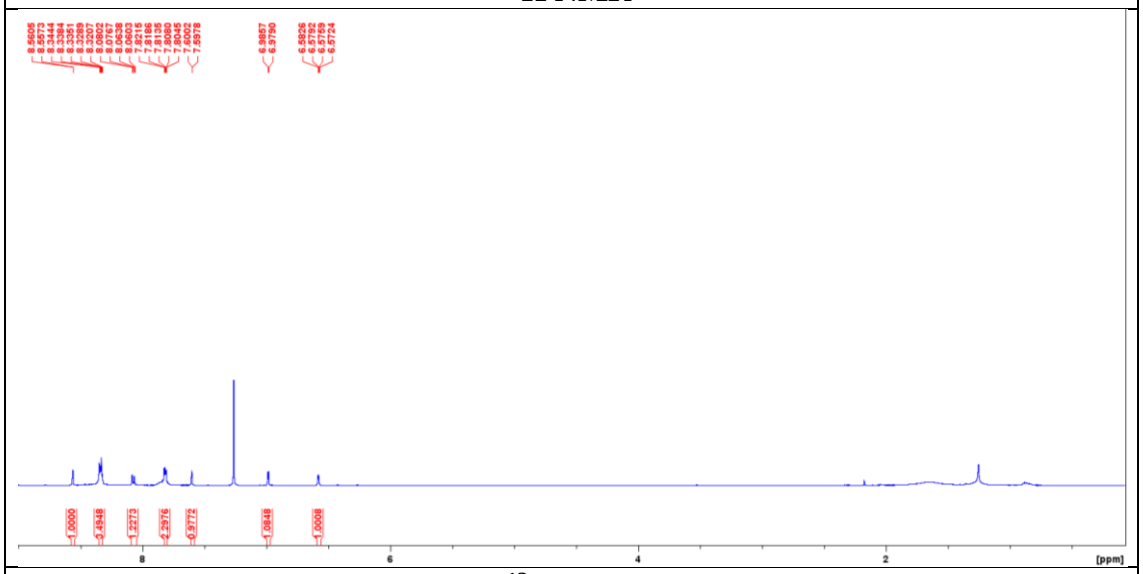




3h

^{1}H NMR



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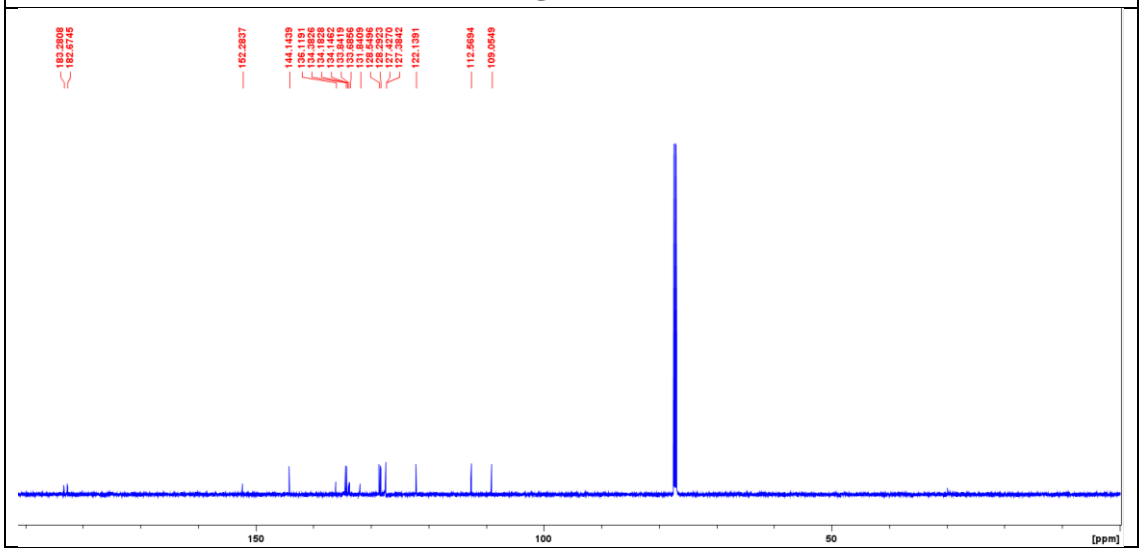
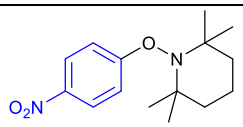
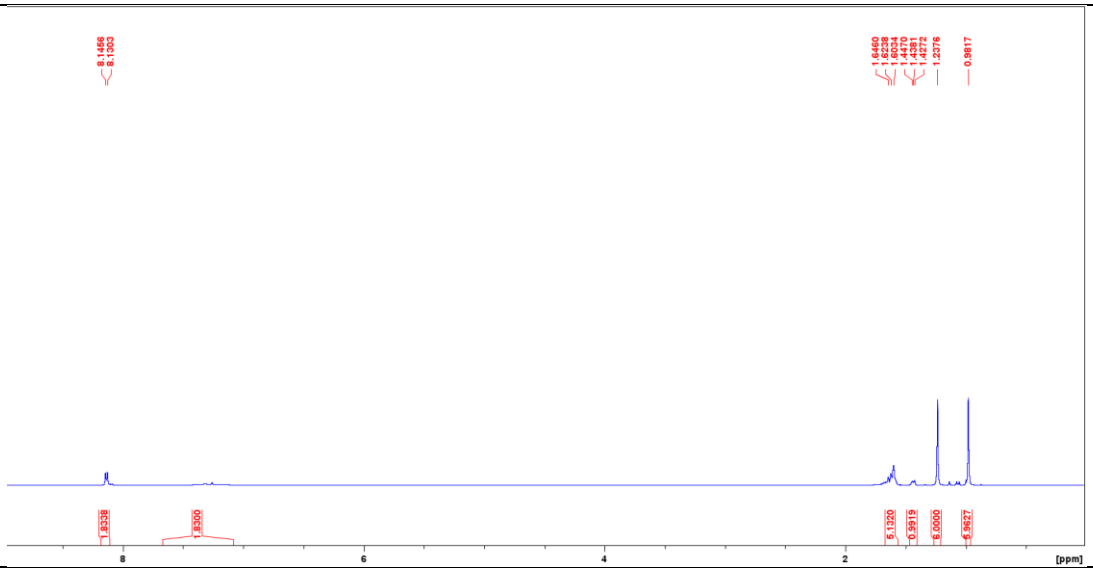




10

^{1}H NMR



^{13}C NMR