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Supporting Information

Direct amidation of acids in a screw reactor for the continuous flow synthesis of amides

Ranjit S. Atapalkar[a, b] and Amol A. Kulkarni[a, b]*

[a]Chem. Eng. & Proc. Dev. Div., CSIR-National Chemical Laboratory, Pune 411008, India.

E-mail: aa.kulkarni@ncl.res.in

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, 201002, India.

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General Methods

All the reagents and solvents (commercial grade) were used as received. All the reactions were carried out in a single screw reactor (Teflon reactor) at room temperature. All the reactions were monitored by thin layer chromatography (TLC) on Merck silica gel 60-F254 coated 0.25 mm plates, detected by UV. Flash chromatography was performed with the indicated solvents on silica gel (particle size 0.064−0.210 mm). Yields reported are for isolated, spectroscopically pure compounds. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 200 MHz instrument with TMS as the internal standard. Chemical shifts are given in ppm (δ), referenced to tetramethylsilane (TMS) for ^{1}H NMR and the ^{13}C resonances of $CDCl_3$ (= 77.0 ppm) for ^{13}C NMR as internal standards and DMSO-d6 (= 40.0 ppm) for ^{13}C NMR. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiples, b=broad, respectively) coupling constant (J, Hz), and integration.

General experimental procedure

Note: After the reaction was over as monitored by TLC, the remained product in the groves of screw was removed by using respective solvents used for the particular reaction followed by vacuum evaporation so as to avoid the loss in product yields.

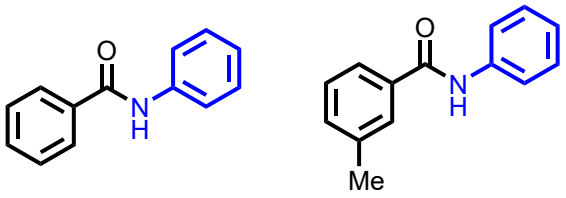
1. **General procedure for continuous flow synthesis of amide by mechanochemical approach**

Acid (1 mmol, 2 g) was fed from solid dosing 1 and the mixture of aniline (1 mmol) and EDC.HCl (1.1 mmol) fed from solid dosing 2 in a screw reactor rotating 20-300 rpm and temperature was maintained at ~27 °C. The total residence time for amide and its derivative formation was only 30 – 300 sec. A colourless solid/ powder slurry was collected and monitored on TLC complete starting material consumed with the formation of desired amide products. The collected sample was washed by water (20 X 3) to remove the EDAC urea formed in stoichiometric amounts and filtered the product on whatmann-41 filter paper, precipitated product was collected and then final sample was dried at room temperature at overnight. We have achieved the final products yield is 65-95% with high purity. The final amide products were analysed by using ^{1}H NMR and ^{13}C NMR spectroscopy. By using this procedure, we have performed 36 examples with 2 APIs with good to excellent yield. We would like to mention that 1 gram of EDC.HCl required for the amide bond formation, we got the 0.91 gram of urea as a by-product, which is recovered after workup.

2. **General procedure for scale up for continuous flow synthesis of amides by mechanochemical approach**

Acid (1 mmol, 50 g) was fed from solid dosing 1 and the mixture of aniline (1 mmol) and EDC.HCl (1.1 mmol) fed from solid dosing 2 in a screw reactor rotating 20-300 rpm and temperature was maintained at ~27 °C. The total residence time for amide and its derivative formation was only 30 – 300 sec. A colourless solid/ powder slurry was collected

and monitored on TLC complete starting material consumed with the formation of desired amide products. The collected sample was washed by water (20 X 3) to remove the EDAC urea formed in stoichiometric amounts and filtered the product on whatmann-41 filter paper, precipitated product was collected and then final sample was dried at room temperature at overnight. We have achieved final amide products yield is 46-88% with high purity. The final amide products (**7a** and **7b)** were analysed by using ^{1}H NMR and ^{13}C NMR spectroscopy.

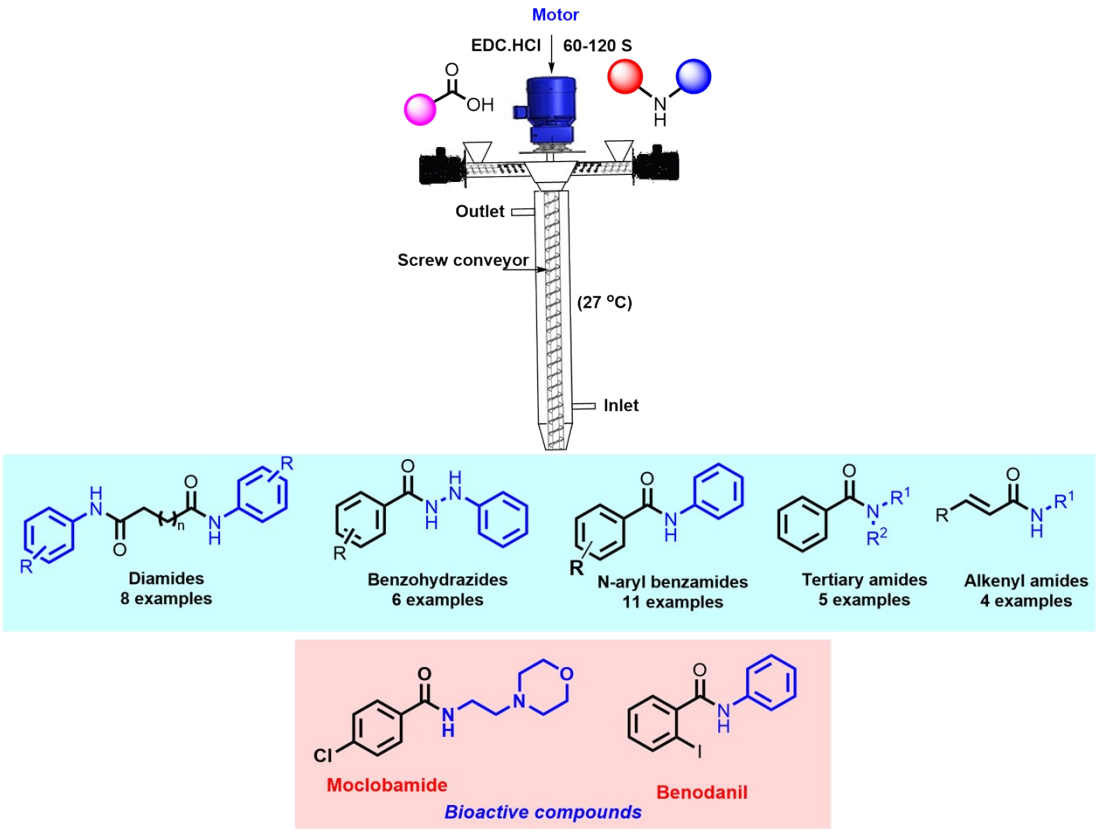


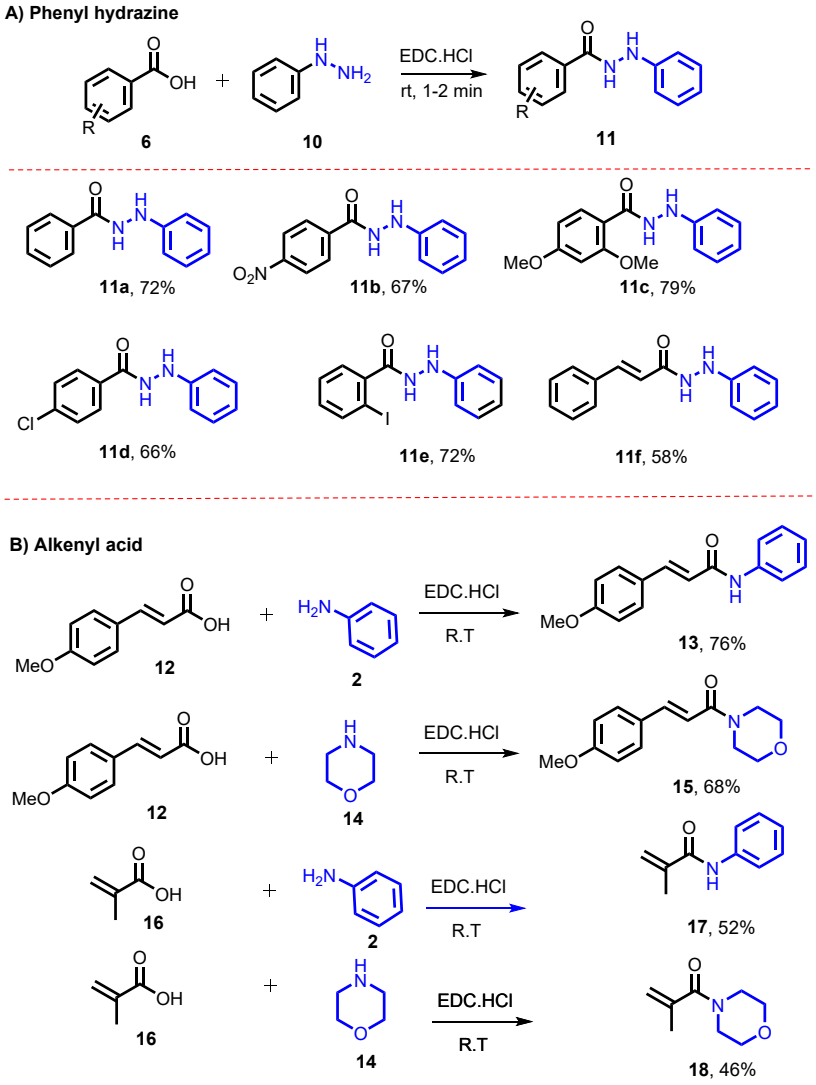
7a, 95%
50 g/hr

7b, 93%
50 g/hr

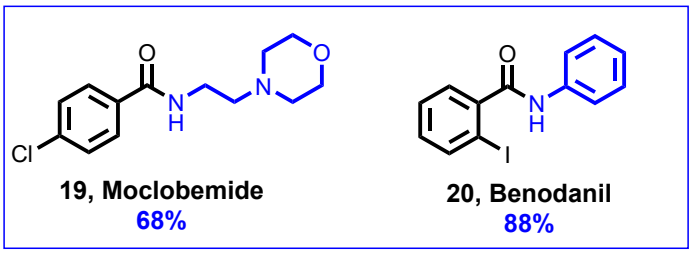
Scale up for continuous flow synthesis of amides (*7a and 7b*).

3. **General experimental setup for amide and its derivatives by using screw reactor[1, 2]**





Scheme S1: EDC.HCl promoted direct amidation of acids with amines: (A) Scope of aromatic acids with phenyl hydrazine (B) Scope of alkenyl acid with primary and secondary amine



Scheme S2: Active pharmaceutical ingredients (APIs) and agrochemicals (fungicide)

4. Details of the screw reactor

A jacketed single-screw reactor (glass-Teflon) have used for continuous flow mechanochemical synthesis of amides. We have purchased a glass-Teflon reactor from (D. M. Solutions Pvt. Ltd, India.) which allows us to monitor the changes occurring visibly during the course of the reaction. We used the vertical alignment for the screw reactor (having a glass jacket with 42 mm outer diameter and 18 mm inner diameter and a 340 mm long PTFE screw with 17.5 mm diameter). This leaves a gap of only 0.25 mm between the jacket wall and the screw threads, the screw reactor as shown in figure 1. The inlet and outlet ports of the jacket are connected to a constant temperature circulation bath (Julabo GmBH, Germany). The residence time was controlled using the rotation speed of the screw, controlled using a precision motor (Remi, India). The screw reactor parameters can be tuned to optimize the process for the amide synthesis with good to excellent yield with short residence time including the screw profile, feed rate, screw speed, and temperature. Furthermore, various output parameters can be monitored both during and after the reactive extrusion, and these parameters includes throughput rate, which is the amount product (g) produced (per hour or per day) and residence time, which is the time required for the solid material to pass through the using screw extruder (from a few second to few minutes) depending on screw speed. For a few experiments to check the reproducibility, experiments were carried out using tiny screw reactors (diameter 10 mm, screw pitch 2 mm, screw depth 2 mm and screw height 200 mm). For scale-up experiments a 20 ml volume screw reactor (diameter 25.4 mm, screw pitch 10 mm, screw depth 2 mm and screw height 400 mm) was used having

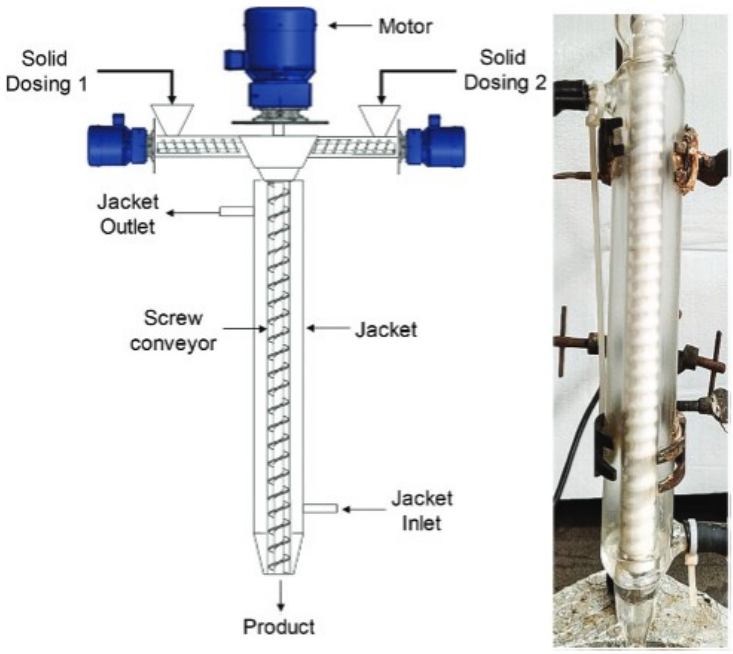
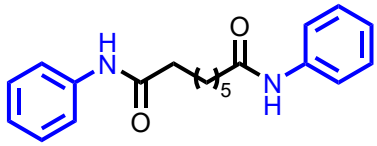


Figure 1: General setup for the continuous flow mechanochemical synthesis of amides using a screw reactor

Spectral data of the synthesized compounds (without any purification)

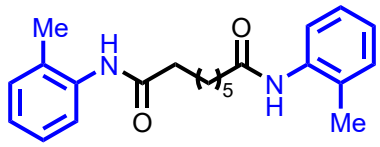
Characterization Data:

N1, N8-diphenyloctanediamide (3a)



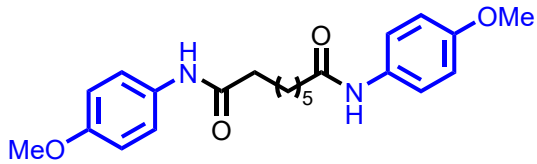
(White solid, 87%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 9.85 (br. s., 2H), 7.59 (d, *J* = 7.6 Hz, 4H), 7.27 (t, *J* = 7.6 Hz, 4H), 7.13 - 6.85 (m, 2H), 2.30 (t, *J* = 7.1 Hz, 4H), 1.60 (br. s., 4H), 1.33 (br. s., 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 171.6, 139.8, 129.0, 123.3, 119.4, 36.8, 28.9, 25.4.

N1, N8-di-o-tolyloctanediamide (3b)



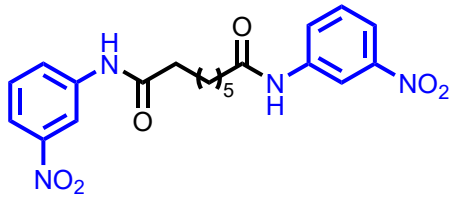
(White solid, 82%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 9.23 (br. s., 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.14 (t, *J* = 7.3 Hz, 2H), 7.10 - 7.00 (m, 2H), 2.33 (t, *J* = 7.3 Hz, 4H), 2.18 (s, 6H), 1.62 (br. s., 4H), 1.37 (br. s., 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 171.5, 136.9, 132.2, 130.6, 126.2, 125.6, 125.4, 36.2, 28.9, 25.7, 18.3.

N1, N8-bis (4-methoxyphenyl)octanediamide (3c)



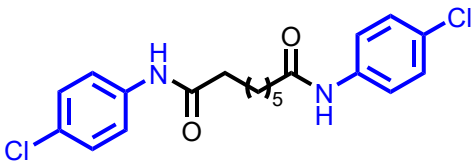
(White solid, 85%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 9.70 (s, 2H), 7.48 (d, *J* = 9.0 Hz, 4H), 6.85 (d, *J* = 9.0 Hz, 4H), 3.70 (s, 6H), 2.25 (t, *J* = 7.4 Hz, 4H), 1.70 - 1.47 (m, 4H), 1.32 (br. s., 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 170.9, 155.2, 132.7, 120.8, 113.9, 55.3, 36.4, 28.7, 25.3.

N1, N8-bis (3-nitrophenyl)octanediamide (3d)



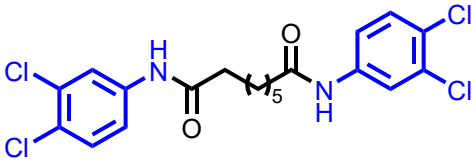
(Yellow solid, 65%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 10.34 (s, 2H), 8.63 (br. s., 2H), 7.87 (t, *J* = 7.5 Hz, 4H), 7.56 (t, *J* = 8.1 Hz, 2H), 2.43 - 2.29 (m, 4H), 1.62 (br. s., 4H), 1.43 - 1.27 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 172.0, 147.9, 140.4, 130.0, 124.9, 117.4, 113.0, 36.3, 28.4, 24.8.

N1, N8-bis (4-chlorophenyl)octanediamide (3e)



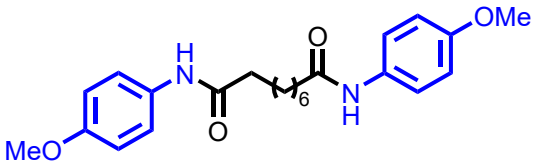
(White solid, 78%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 9.98 (s, 2H), 7.61 (d, *J* = 8.6 Hz, 4H), 7.32 (d, *J* = 8.5 Hz, 4H), 2.29 (t, *J* = 7.3 Hz, 4H), 1.59 (br. s., 4H), 1.44 - 1.14 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 171.6, 138.5, 128.7, 126.6, 120.7, 36.5, 28.7, 25.1.

N1, N8-bis (3, 4-dichlorophenyl)octanediamide (3f)



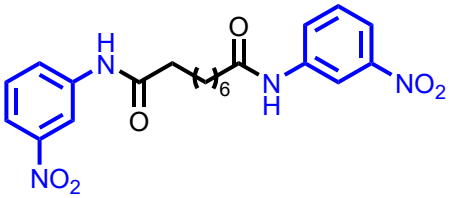
(White solid, 75%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 10.18 (s, 2H), 8.01 (d, *J* = 1.9 Hz, 2H), 7.63 - 7.34 (m, 4H), 2.33 (t, *J* = 7.3 Hz, 4H), 1.60 (br. s., 4H), 1.33 (br. s., 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 171.9, 139.6, 131.1, 130.7, 124.5, 120.3, 119.2, 36.5, 28.6, 25.0.

N1, N9-bis (4-methoxyphenyl)nonanediamide (3g)



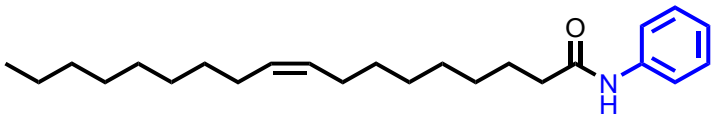
(White solid, 90%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 9.70 (s, 2H), 7.49 (d, *J* = 8.9 Hz, 4H), 6.85 (d, *J* = 8.9 Hz, 4H), 3.70 (s, 6H), 2.25 (t, *J* = 7.3 Hz, 4H), 1.57 (br. s., 4H), 1.30 (br. s., 7H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 170.7, 155.0, 132.5, 120.5, 113.7, 55.1, 36.3, 28.7, 28.6, 25.2.

N1, N9-bis (3-nitrophenyl)nonanediamide (3h)



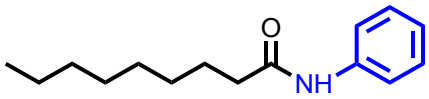
(Yellow solid, 68%), ^{1}H NMR (400 MHz, DMSO-d_6) δ= 10.43 (br. s., 2H), 8.66 (br. s., 2H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.58 (t, *J* = 8.1 Hz, 2H), 2.37 (t, *J* = 7.3 Hz, 4H), 1.62 (br. s., 4H), 1.33 (br. s., 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ= 172.0, 147.9, 140.4, 130.1, 124.9, 117.4, 113.0, 28.5, 28.5, 24.9.

N-phenyloleamide (5a)



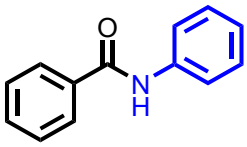
(White solid, 85%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.76 (br. s., 1H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.21 - 7.03 (m, 1H), 5.36 (d, *J* = 2.3 Hz, 2H), 2.69 (s, 1H), 2.37 (t, *J* = 7.4 Hz, 2H), 2.03 (d, *J* = 5.7 Hz, 4H), 1.80 - 1.59 (m, 2H), 1.29 (s, 11H), 1.32 (s, 8H), 0.90 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 172.0, 138.3, 130.2, 129.9, 129.1, 124.3, 120.1, 43.2, 37.9, 32.1, 30.0, 29.9, 29.7, 29.5, 29.3, 27.4, 25.9, 22.9, 14.3.

N-phenylnonanamide (5b)



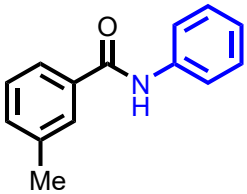
(White solid, 91%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.65 - 7.42 (m, 3H), 7.41 - 7.26 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 2.37 (t, *J* = 7.6 Hz, 2H), 1.74 (quin, *J* = 7.3 Hz, 2H), 1.47 - 1.34 (m, 2H), 1.30 (dd, *J* = 5.1, 10.5 Hz, 8H), 0.90 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 171.9, 138.2, 129.2, 124.3, 120.1, 38.0, 32.0, 29.6, 29.5, 29.4, 25.9, 22.9, 14.3.

N-phenylbenzamide (7a)



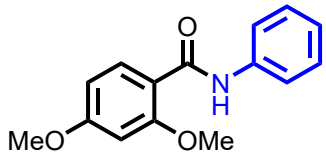
(White solid, 95%), ^{1}H NMR (500 MHz ,$CDCl_3$) δ= 7.99 (br. s., 1H), 7.89 (d, *J* = 7.2 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.1 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 165.9, 138.0, 135.0, 131.8, 129.1, 128.8, 127.1, 124.6, 120.3, 77.3, 77.1, 76.8.

3-methyl-N-phenylbenzamide (7b)



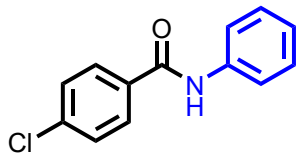
(White solid, 86%), ^{1}H NMR (400MHz, $CDCl_3$) δ= 7.62 (d, *J* = 7.6 Hz, 2H), 7.55 - 7.43 (m, 2H), 7.41 - 7.31 (m, 3H), 7.30 - 7.24 (m, 2H), 7.18 - 7.12 (m, 1H), 2.50 (s, 3H). ^{13}C NMR (101MHz, $CDCl_3$) δ= 168.1, 138.0, 136.5, 131.3, 130.3, 129.1, 126.6, 125.9, 124.6, 119.9, 19.8.

2, 4-dimethoxy-N-phenylbenzamide (7c)



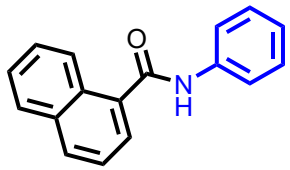
(White solid, 89%), ^{1}H NMR (500 MHz ,$CDCl_3$) δ= 9.72 (br. s., 1H), 8.28 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.67 (dd, *J* = 1.9, 8.8 Hz, 1H), 6.60 - 6.46 (m, 1H), 4.04 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 163.8, 163.1, 158.6, 138.6, 134.2, 128.9, 123.9, 120.4, 114.7, 105.7, 98.8, 56.2, 55.6.

4-chloro-N-phenylbenzamide (7d)



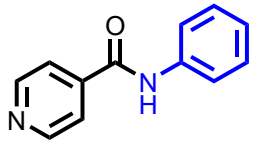
(White solid, 69%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 10.32 (s, 1H), 7.99 (d, *J* = 8.5 Hz, 2H), 7.86 - 7.71 (m, *J* = 7.9 Hz, 2H), 7.67 - 7.54 (m, *J* = 8.5 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 164.3, 138.8, 136.2, 133.5, 129.5, 128.5, 128.3, 123.6, 120.3.

N-phenyl-1-naphthamide (7e)



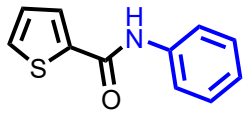
(White solid, 78%), ^{1}H NMR (500 MHz ,$CDCl_3$) δ= 8.38 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.95 - 7.87 (m, 2H), 7.81 (br. s., 1H), 7.78 - 7.66 (m, 3H), 7.66 - 7.55 (m, 2H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 167.6, 138.1, 134.5, 133.8, 131.1, 130.1, 129.2, 128.4, 127.4, 126.6, 125.3, 125.1, 124.8, 124.7, 120.0.

N-phenylisonicotinamide (7f)



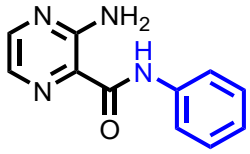
(White solid, 79%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 8.77 (d, *J* = 4.6 Hz, 2H), 8.10 (br. s., 1H), 7.71 (d, *J* = 5.3 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.25 - 7.10 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 163.8, 150.7, 142.1, 137.2, 129.2, 125.3, 120.9, 120.4.

N-phenylthiophene-2-carboxamide (7g)



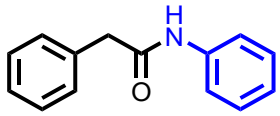
(White solid, 92%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.93 (br. s., 1H), 7.79 - 7.60 (m, 3H), 7.56 (d, *J* = 4.2 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.24 - 7.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 160.1, 139.3, 137.6, 130.8, 129.1, 128.5, 127.8, 124.6, 120.3.

3-amino-N-phenylpyrazine-2-carboxamide (7h)



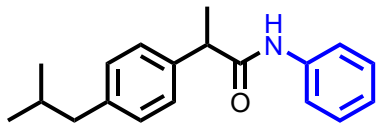
(White solid, 76%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.81 (br. s., 1H), 8.19 (br. s., 1H), 7.85 (br. s., 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 163.6, 155.1, 146.7, 137.1, 131.2, 128.8, 125.9, 124.1, 119.5

N, 2-diphenylacetamide (7i)



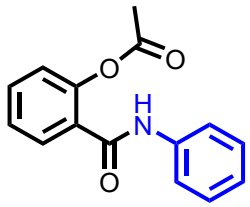
(White solid, 89%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.46 (d, *J* = 8.0 Hz, 3H), 7.43 - 7.39 (m, 2H), 7.36 (d, *J* = 6.1 Hz, 3H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.20 - 7.03 (m, 1H), 3.74 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 169.3, 137.7, 134.5, 129.5, 129.2, 128.9, 127.6, 124.5, 119.9, 44.8.

2-(4-isobutylphenyl)-N-phenylpropanamide (7j)



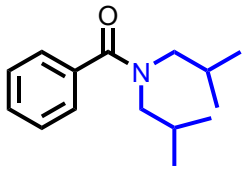
(White solid, 82%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.44 (d, *J* = 7.6 Hz, 2H), 7.29 (br. s., 4H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.14 - 6.92 (m, 2H), 3.72 (d, *J* = 6.9 Hz, 1H), 2.50 (d, *J* = 6.9 Hz, 2H), 2.00 - 1.79 (m, 1H), 1.62 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 172.6, 141.1, 138.0, 137.9, 129.9, 128.9, 127.5, 124.2, 119.6, 47.8, 45.0, 30.2, 22.4, 18.5.

2-(phenylcarbamoyl) phenyl acetate (7l)



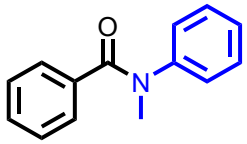
(White solid, 89%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 8.06 (br. s., 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 6.9 Hz, 3H), 7.23 - 7.12 (m, 2H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 169.3, 163.6, 147.7, 137.8, 132.2, 130.0, 129.2, 126.6, 124.7, 123.4, 121.2, 119.9, 21.1.

N, N-diisobutylbenzamide (9a)



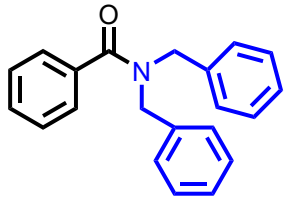
(Clear liquid, 79%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 - 7.29 (m, 5H), 3.34 (d, *J* = 6.9 Hz, 2H), 3.08 (d, *J* = 6.1 Hz, 2H), 2.16 - 2.04 (m, 1H), 1.82 (br. s., 1H), 0.97 (d, *J* = 5.3 Hz, 6H), 0.81 - 0.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 172.5, 137.5, 129.0, 128.4, 128.3, 127.0, 126.4, 56.6, 51.2, 44.6, 26.8, 26.2, 20.2, 19.8.

N-methyl-N-phenylbenzamide (9b)



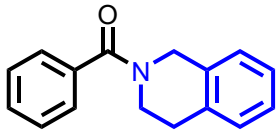
(Clear liquid, 72%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 - 7.26 (m, 2H), 7.23 - 7.17 (m, 3H), 7.16 - 7.09 (m, 3H), 7.03 (d, *J* = 7.6 Hz, 2H), 3.49 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 170.1, 144.3, 135.4, 129.1, 128.6, 128.2, 127.2, 126.4, 126.0, 111.8, 37.9.

N, N-dibenzylbenzamide (9c)



(Clear liquid, 86%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.52 (br. s., 2H), 7.47 - 7.30 (m, 11H), 7.17 (br. s., 2H), 4.73 (br. s., 2H), 4.42 (br. s., 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 172.2, 136.9, 136.4, 136.1, 129.6, 128.8, 128.7, 128.5, 128.4, 127.6, 127.0, 126.7, 51.5, 46.8.

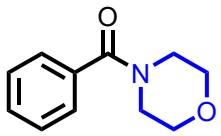
(3, 4-dihydroisoquinolin-2(1H)-yl)(Phenyl)methanone (9d)



(Clear liquid, 76%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 (br. s., 5H), 7.17 (br. s., 3H), 4.91 (br. s., 1H), 4.59 (br. s., 1H), 4.00 (br. s., 1H), 3.64 (br. s., 1H), 2.99 (br. s., 1H), 2.88 (br. s., 1H). ^{13}C NMR (126

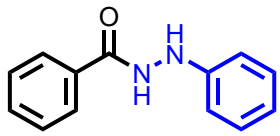
MHz, $CDCl_3$) δ= 170.6, 135.7, 132.5, 129.4, 128.1, 126.5, 126.2, 125.5, 49.4, 44.9, 44.5, 40.2, 29.2, 27.9.

morpholino(phenyl)methanone (9e)



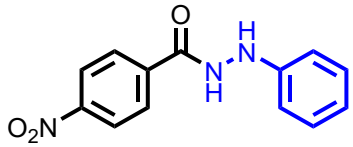
(Clear liquid, 82%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 (br. s., 5H), 3.75 - 3.52 (m, 6H), 3.38 (br. s., 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 170.2, 135.0, 129.6, 128.3, 126.8, 66.6.

N'-phenylbenzohydrazide (11a)



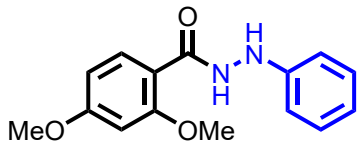
(Red solid, 72%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 10.47 - 10.27 (m, 1H), 8.04 - 7.85 (m, 3H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 7.9 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 166.5, 149.7, 133.2, 131.8, 128.9, 128.7, 127.5, 118.8, 112.5.

4-nitro-N'-phenylbenzohydrazide (11b)



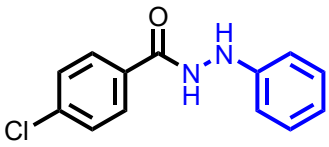
(Red solid, 67%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 10.71 (br. s., 1H), 8.43 - 8.32 (m, *J* = 8.5 Hz, 2H), 8.20 - 8.13 (m, *J* = 8.2 Hz, 2H), 8.06 (br. s., 1H), 7.18 (t, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.75 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 164.6, 149.1, 148.9, 138.5, 128.7, 128.7, 123.5, 118.7, 112.2.

2, 4-dimethoxy-N'-phenylbenzohydrazide (11c)



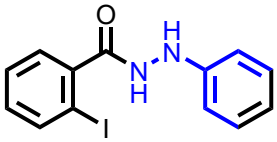
(Red solid, 79%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 9.65 (d, *J* = 3.1 Hz, 1H), 7.90 (d, *J* = 3.1 Hz, 1H), 7.71 (d, *J* = 8.9 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 6.75 - 6.68 (m, 2H), 6.65 (dd, *J* = 2.1, 8.5 Hz, 1H), 3.94 (s, 3 H), 3.85 - 3.82 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 165.1, 162.7, 158.5, 149.4, 131.8, 128.5, 118.3, 114.4, 112.2, 105.4, 98.3, 55.8, 55.4.

4-chloro-N'-phenylbenzohydrazide (11d)



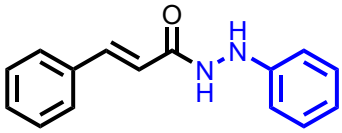
(Red solid, 66%),[1]H NMR (500 MHz ,DMSO-d_6) δ= 10.47 (br. s., 1H), 7.96 (d, *J* = 7.3 Hz, 3H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 2H), 6.80 (d, *J* = 7.9 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 165.5, 149.5, 136.7, 131.9, 129.4, 128.9, 128.8, 118.9, 112.5.

2-iodo-N'-phenylbenzohydrazide (11e)



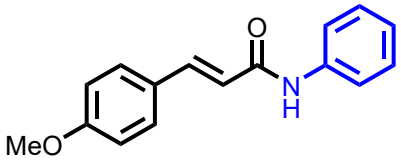
(Red solid, 72%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 10.17 (br. s., 1H), 8.00 (br. s., 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.59 - 7.40 (m, 2H), 7.29 - 7.13 (m, 3H), 6.91 (d, *J* = 7.6 Hz, 2H), 6.84 - 6.62 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 168.7, 149.1, 141.2, 139.4, 131.3, 128.7, 128.5, 128.1, 118.6, 112.4, 93.7.

N'-phenylcinnamohydrazide (11f)



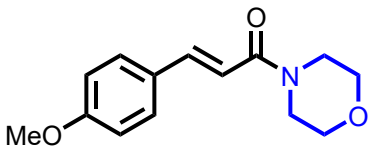
(Red solid, 58%), ^{1}H NMR (500 MHz, DMSO-d_6) δ= 10.06 - 9.82 (m, 1H), 7.97 - 7.79 (m, 1H), 7.61 (d, *J* = 7.3 Hz, 2H), 7.57 - 7.51 (m, 1H), 7.47 - 7.34 (m, 4H), 7.15 (t, *J* = 7.8 Hz, 2H), 6.79 - 6.74 (m, 2H), 6.73 - 6.68 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ= 164.7, 148.9, 139.3, 134.4, 129.4, 128.6, 128.4, 127.5, 127.4, 127.3, 119.5, 118.2, 111.9.

(E)-3-(4-methoxyphenyl)-N-phenylacrylamide (13)



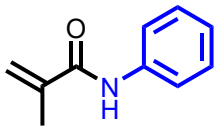
(White solid, 76%), ^{1}H NMR (400 MHz, $CDCl_3$) δ= 8.13 - 7.84 (m, 1H), 7.84 - 7.60 (m, 3H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.41 (d, *J* = 7.1 Hz, 2H), 7.37 - 7.29 (m, 2H), 7.12 (br. s., 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 7.1 Hz, 2H), 6.49 (d, *J* = 15.4 Hz, 1H), 3.90 - 3.76 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 161.0, 141.9, 138.2, 130.0, 129.5, 129.0, 127.3, 124.2, 120.0, 118.4, 114.3, 114.2, 55.3.

(E)-3-(4-methoxyphenyl)-1-morpholinoprop-2-en-1-one (15)



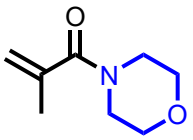
(White solid, 68%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.66 (d, *J* = 15.3 Hz, 1H), 7.55 - 7.37 (m, *J* = 8.0 Hz, 2H), 7.00 - 6.81 (m, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 15.3 Hz, 1H), 3.83 (s, 3H), 3.78 (br. s., 1H), 3.71 (br. s., 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 165.9, 161.0, 142.9, 129.4, 127.9, 114.2, 114.0, 66.9, 55.4.

N-phenylmethacrylamide (17)



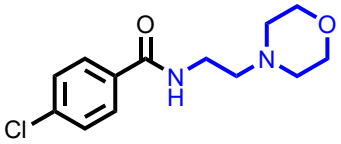
(White solid, 52%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.65 (br. s., 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 5.79 (s, 1H), 5.46 (s, 1H), 2.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 166.4, 140.6, 137.5, 128.7, 124.1, 119.8, 119.5, 18.5.

2-methyl-1-morpholinoprop-2-en-1-one (18)



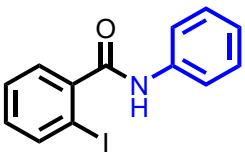
(White solid, 46%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 5.00 (br. s., 1H), 4.81 (s, 1H), 3.44 (br. s., 4H), 3.38 (br. s., 4H), 1.73 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 170.8, 139.6, 115.4, 66.5, 20.1.

4-chloro-N-(2-morpholinoethyl)benzamide (Moclobemide) (19)



(Yellow solid, 68%), ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.72 (d, *J* = 7.4 Hz, 2H), 7.40 (dd, *J* = 2.5, 8.5 Hz, 2H), 6.88 (br. s., 1H), 3.73 (br. s., 4H), 3.61 - 3.47 (m, 2H), 2.69 - 2.56 (m, 2H), 2.51 (br. s., 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ= 166.7, 137.9, 133.1, 129.1, 128.6, 67.2, 57.1, 53.5, 36.3.

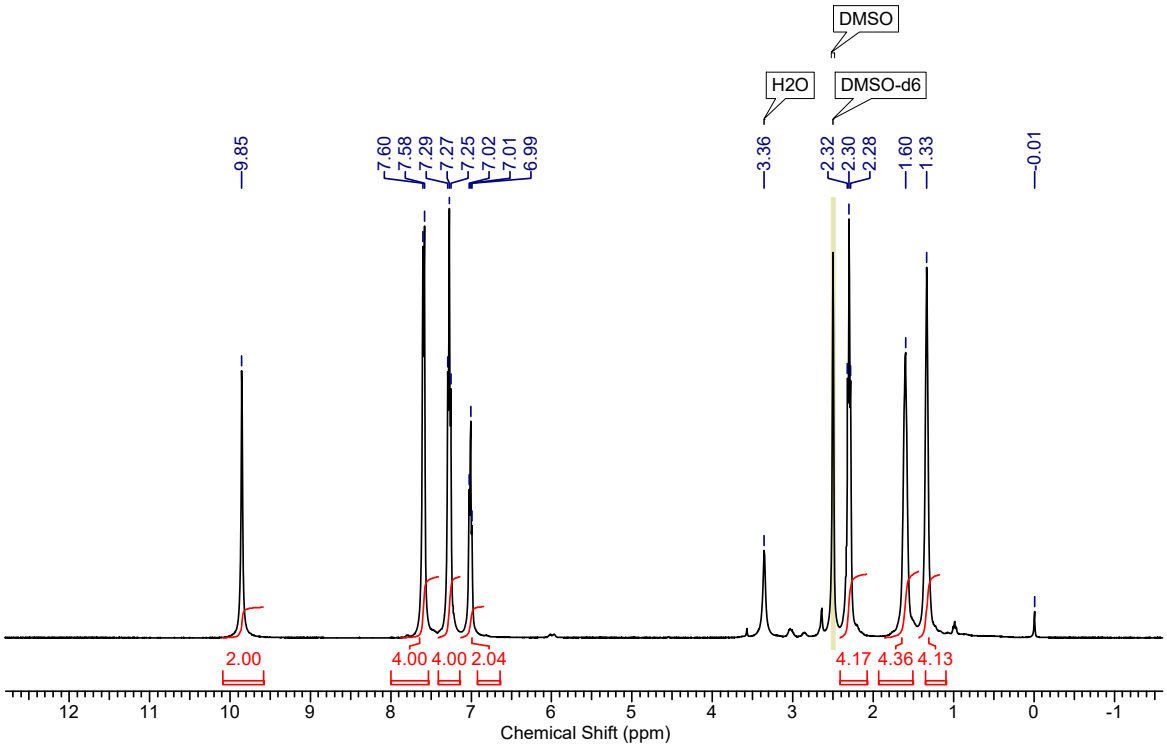
2-iodo-N-phenylbenzamide (Benodanil) (20)



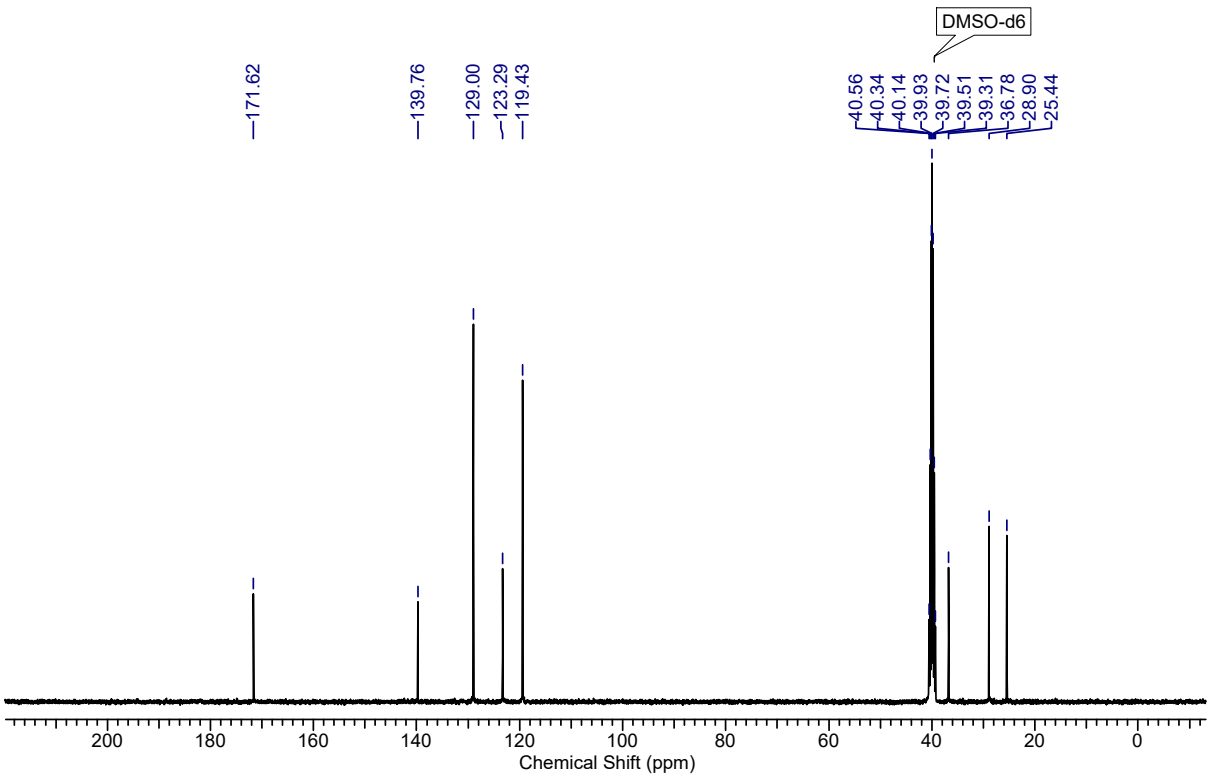
(White solid, 88%), ^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.88 (d, *J* = 6.9 Hz, 1H), 7.75 (br. s., 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.47 (br. s., 1H), 7.43 - 7.29 (m, 3H), 7.18 (t, *J* = 7.1 Hz, 1H), 7.12 (br. s., 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ= 167.5, 142.2, 140.2, 137.8, 131.6, 129.3, 128.7, 128.5, 125.1, 120.4, 92.6.

Spectroscopic Data:

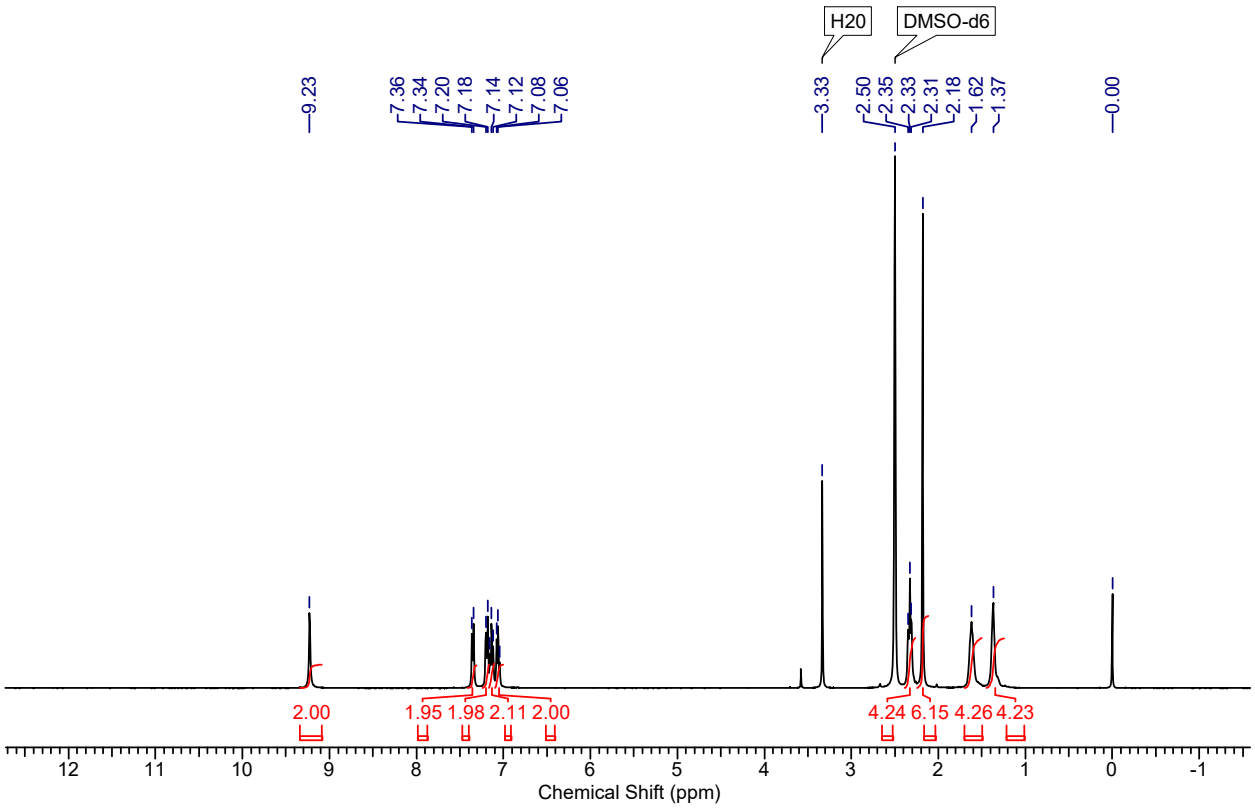
^{1}H NMR- of N1, N8-diphenyloctanediamide (3a)



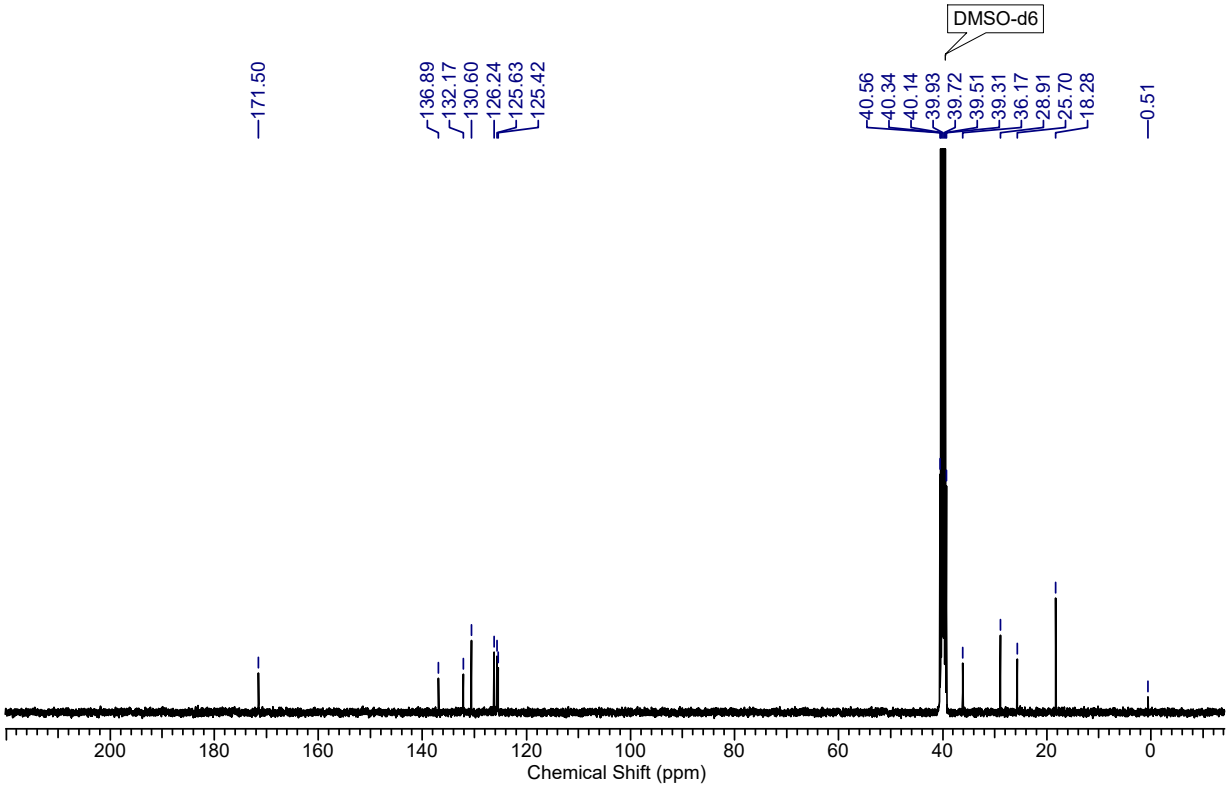
^{13}C NMR of N1, N8-diphenyloctanediamide (3a)



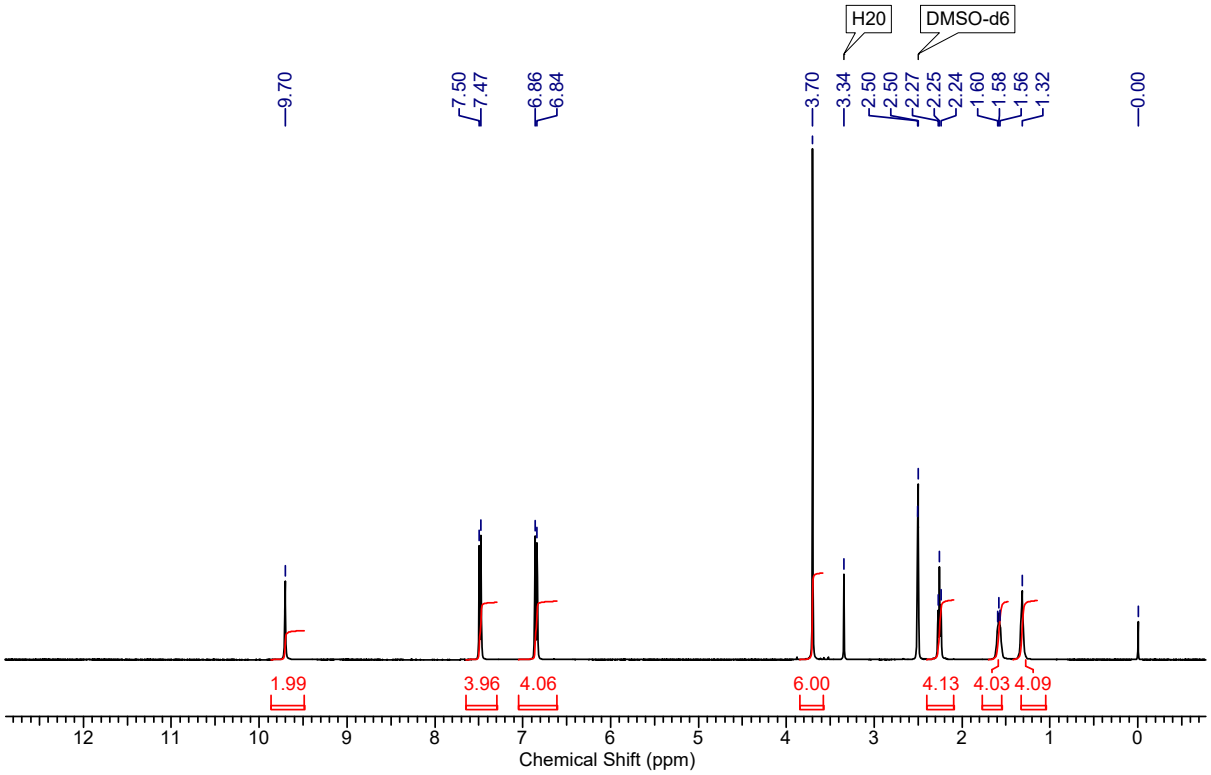
^{1}H NMR of N1, N8-di-o-tolyloctanediamide (3b)



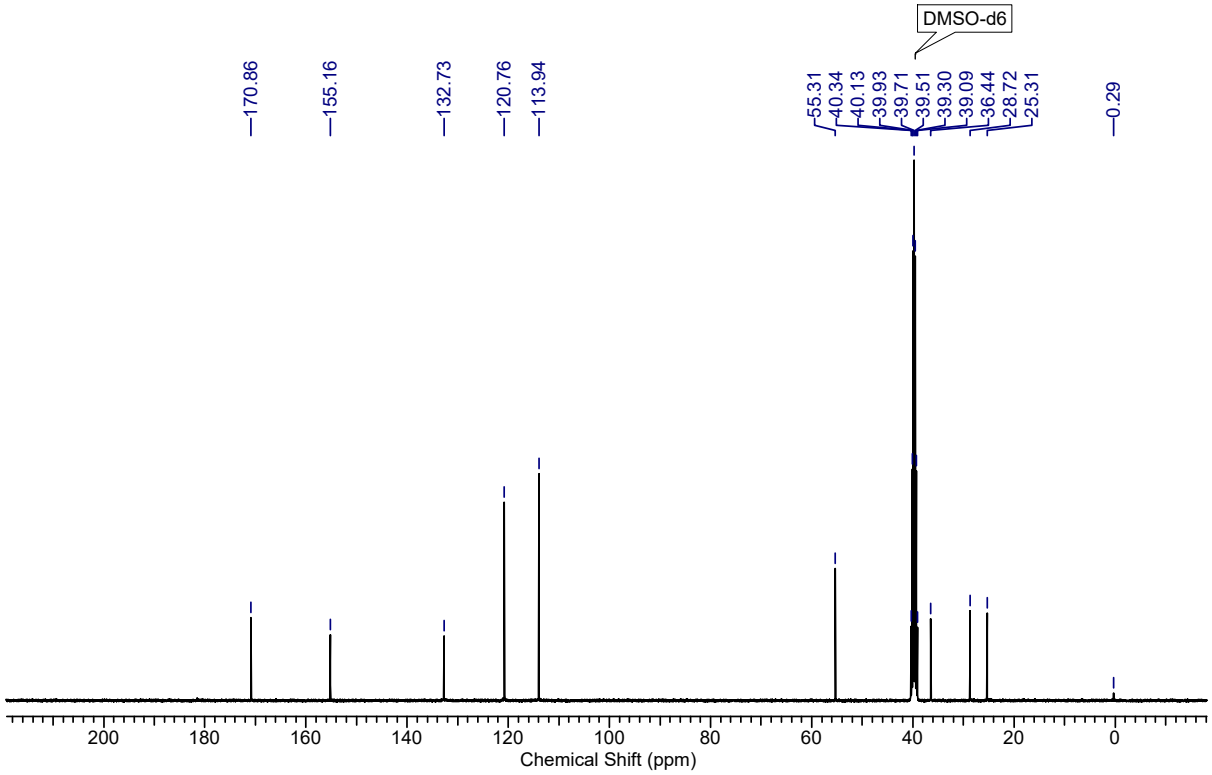
^{13}C NMR of N1, N8-di-o-tolyloctanediamide (3b)



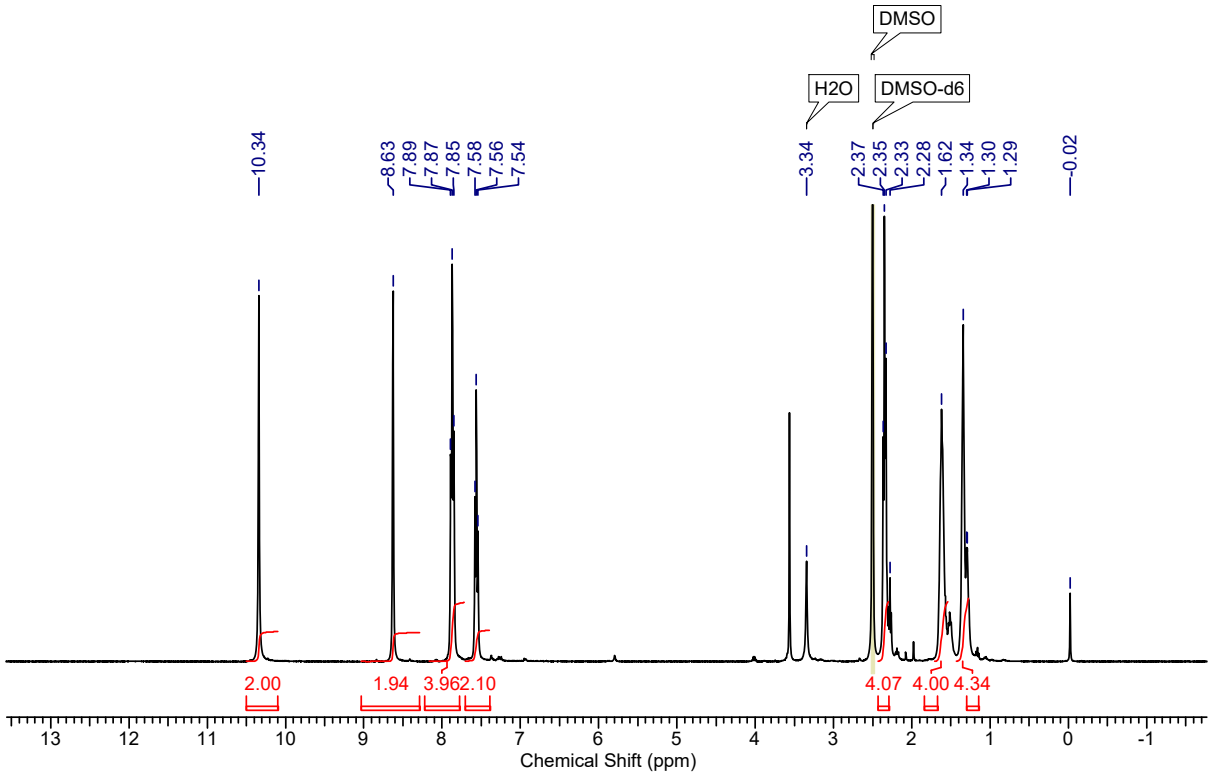
[1]H NMR of N1, N8-bis (4-methoxyphenyl)octanediamide (3c)



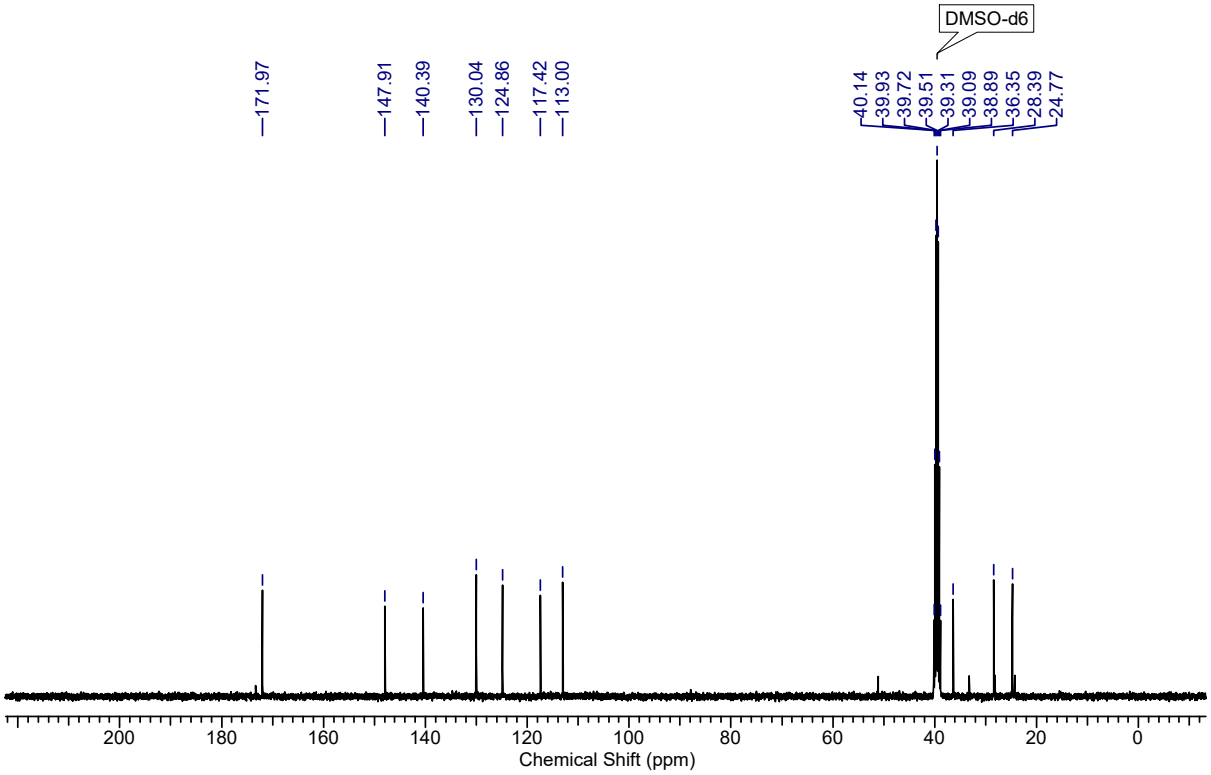
[13]C NMR of N1, N8-bis (4-methoxyphenyl)octanediamide (3c)



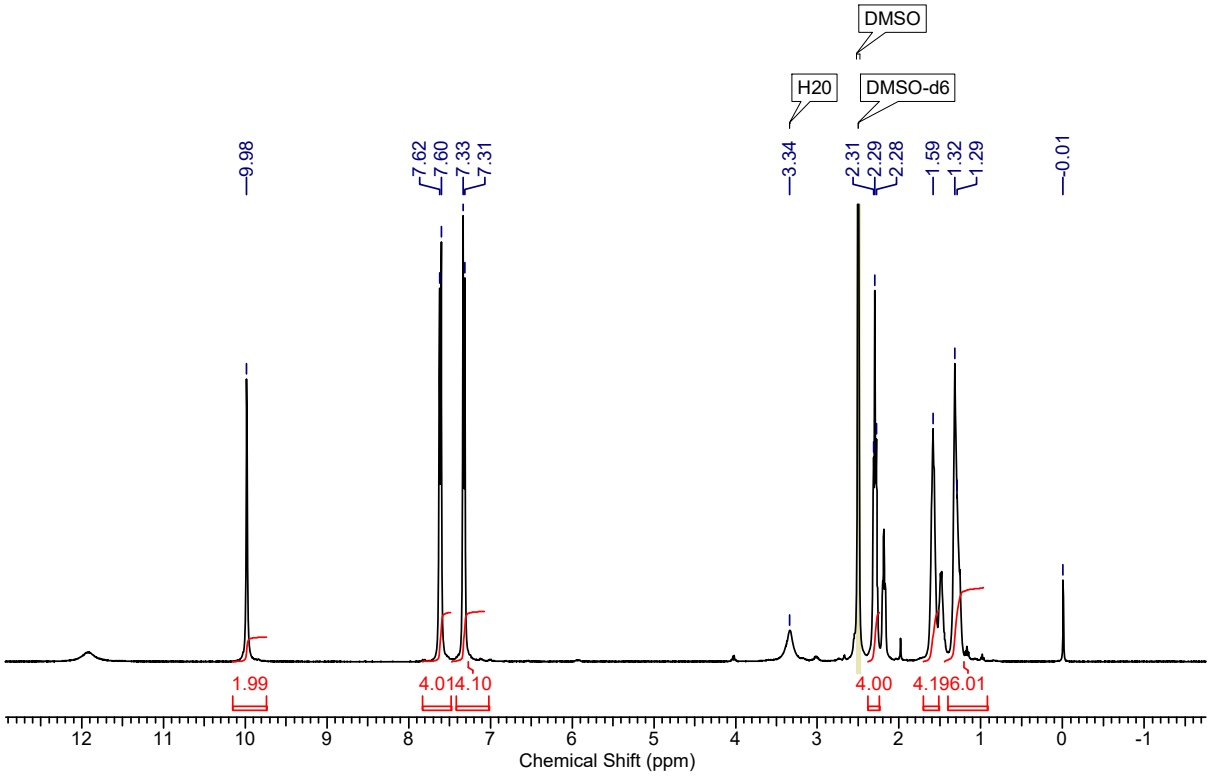
[1]H NMR of N1, N8-bis (3-nitrophenyl)octanediamide (3d)



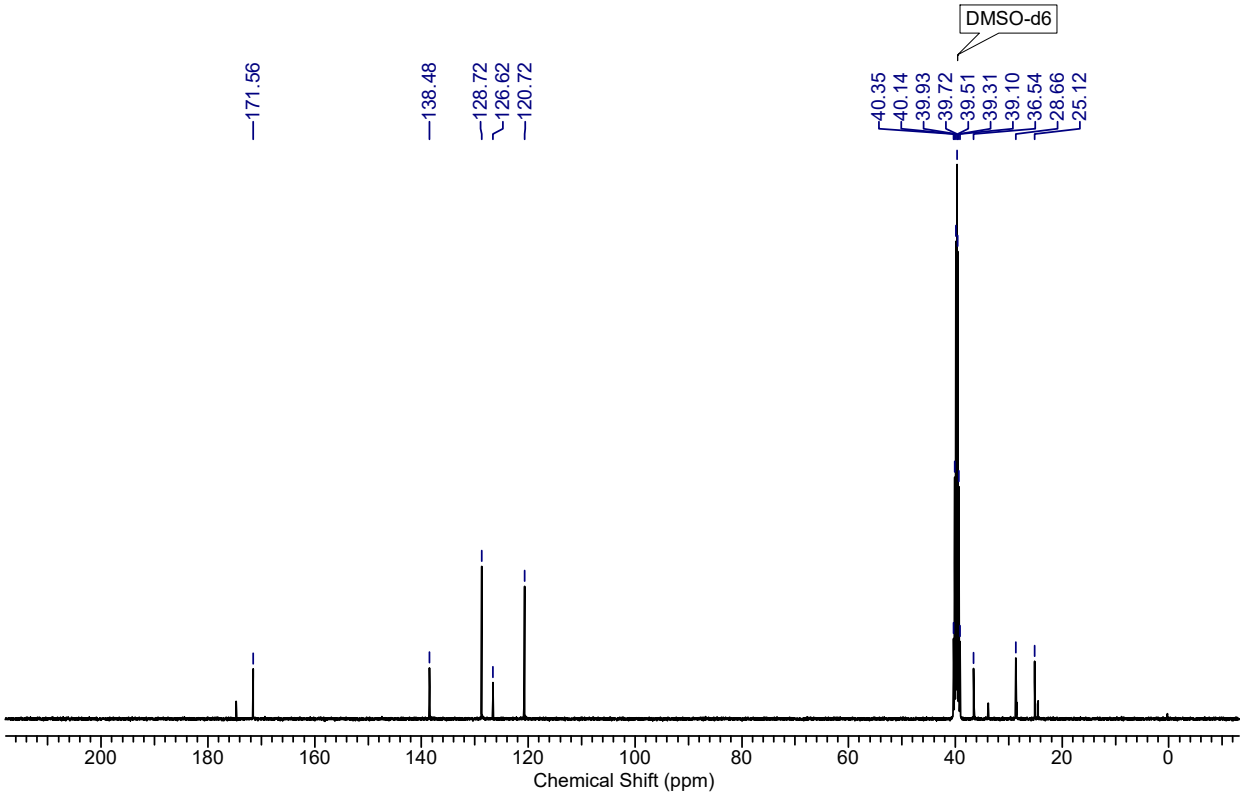
[13]C NMR of N1, N8-bis (3-nitrophenyl)octanediamide (3d)



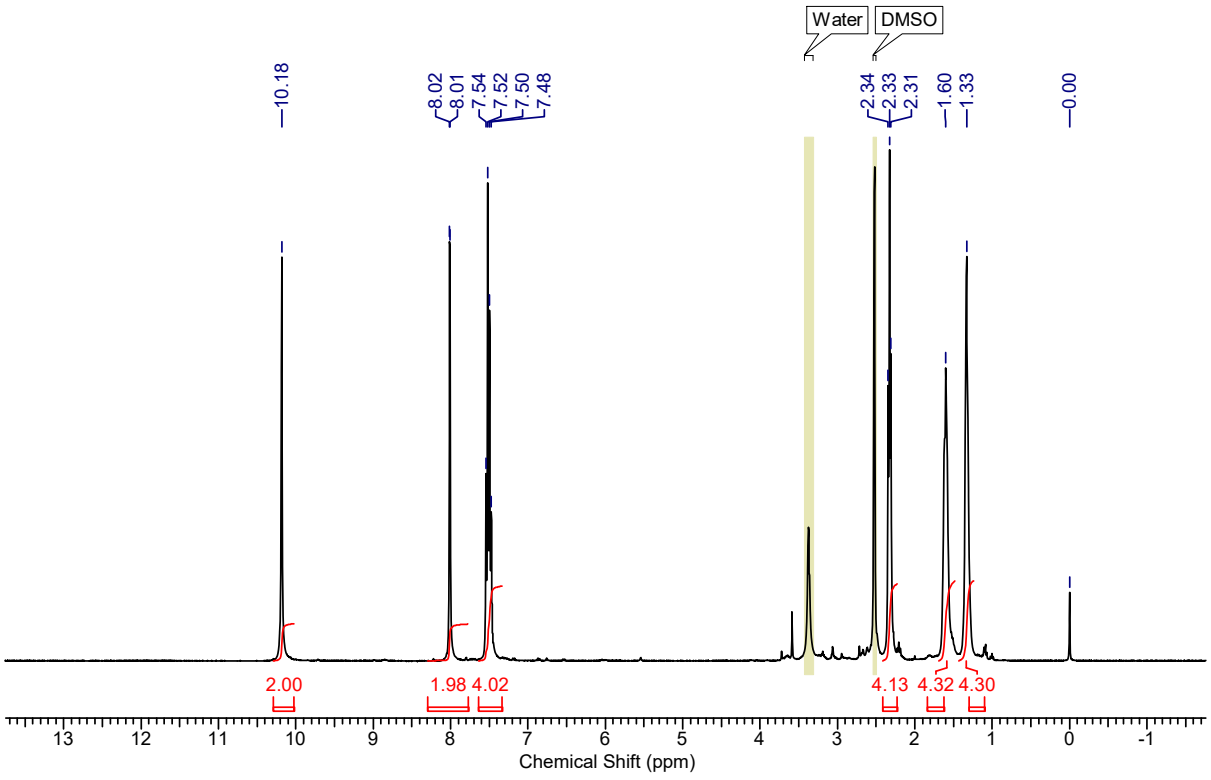
^{1}H NMR of N1, N8-bis (4-chlorophenyl)octanediamide (3e)



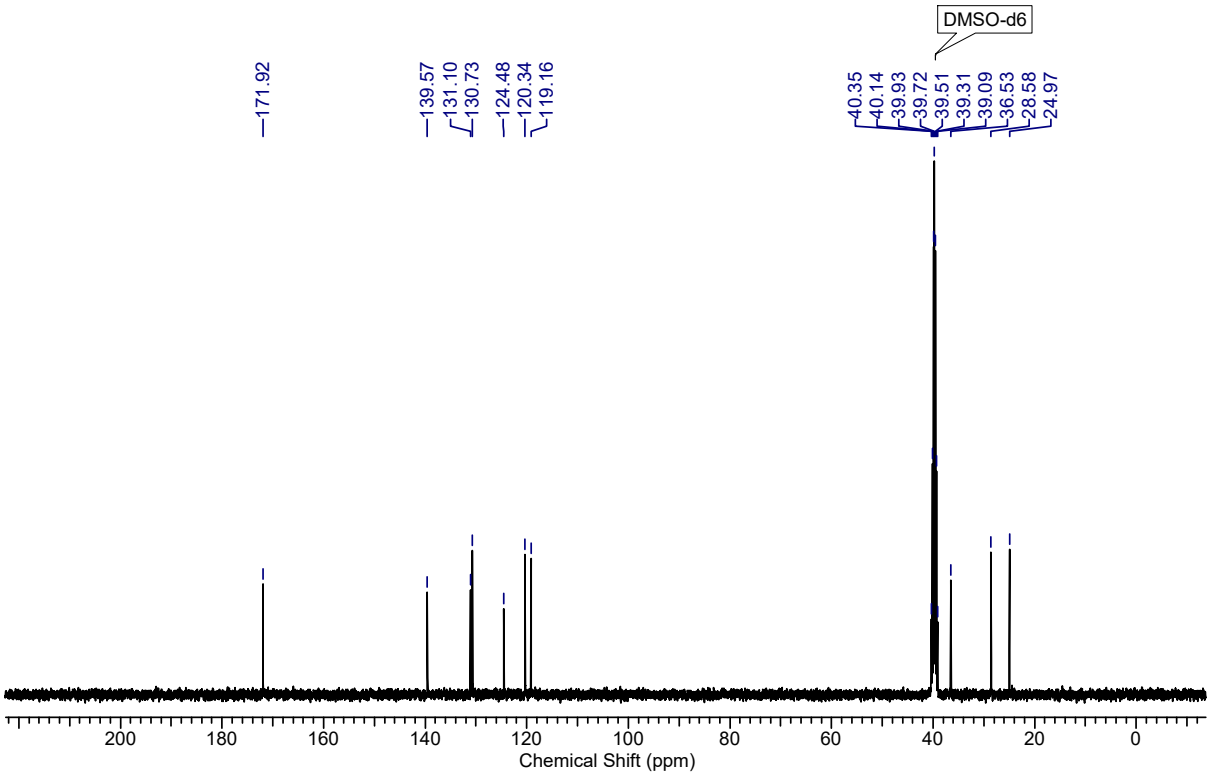
^{13}C NMR of N1, N8-bis (4-chlorophenyl)octanediamide (3e)



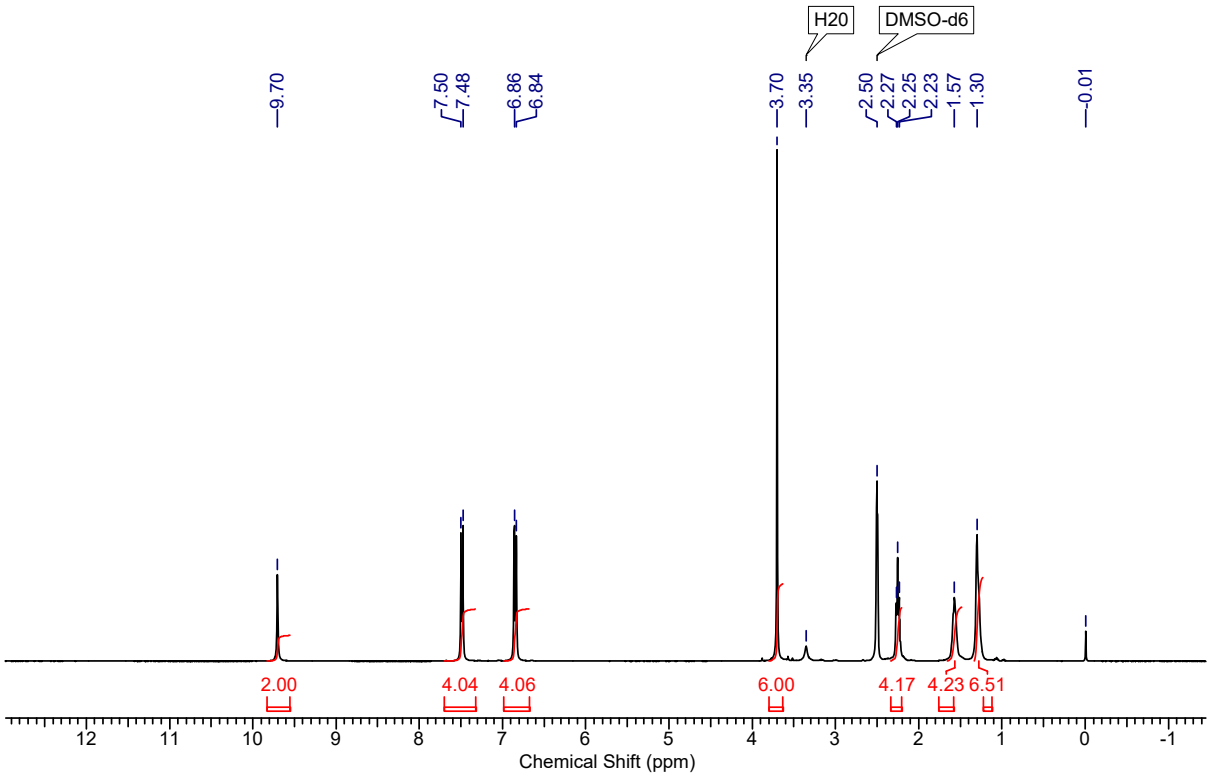
^{1}H NMR of N1, N8-bis (3, 4-dichlorophenyl)octanediamide (3f)



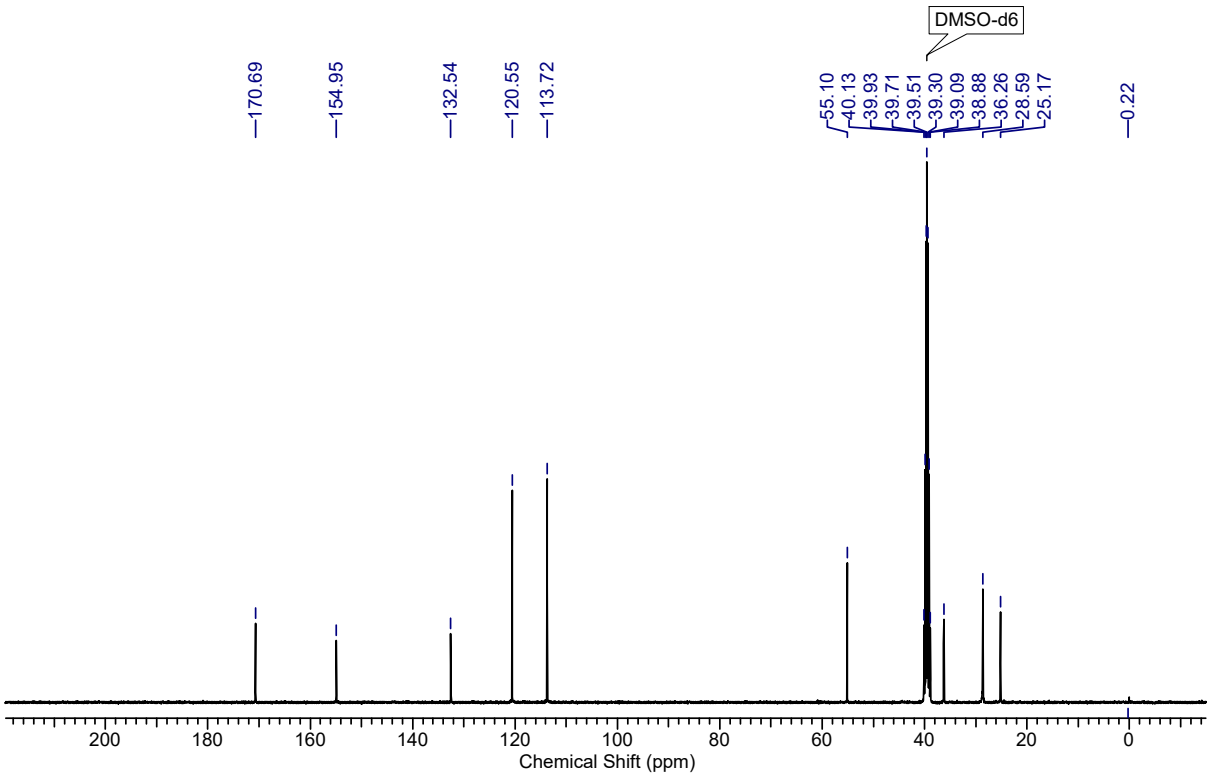
^{13}C NMR of N1, N8-bis (3, 4-dichlorophenyl)octanediamide (3f)



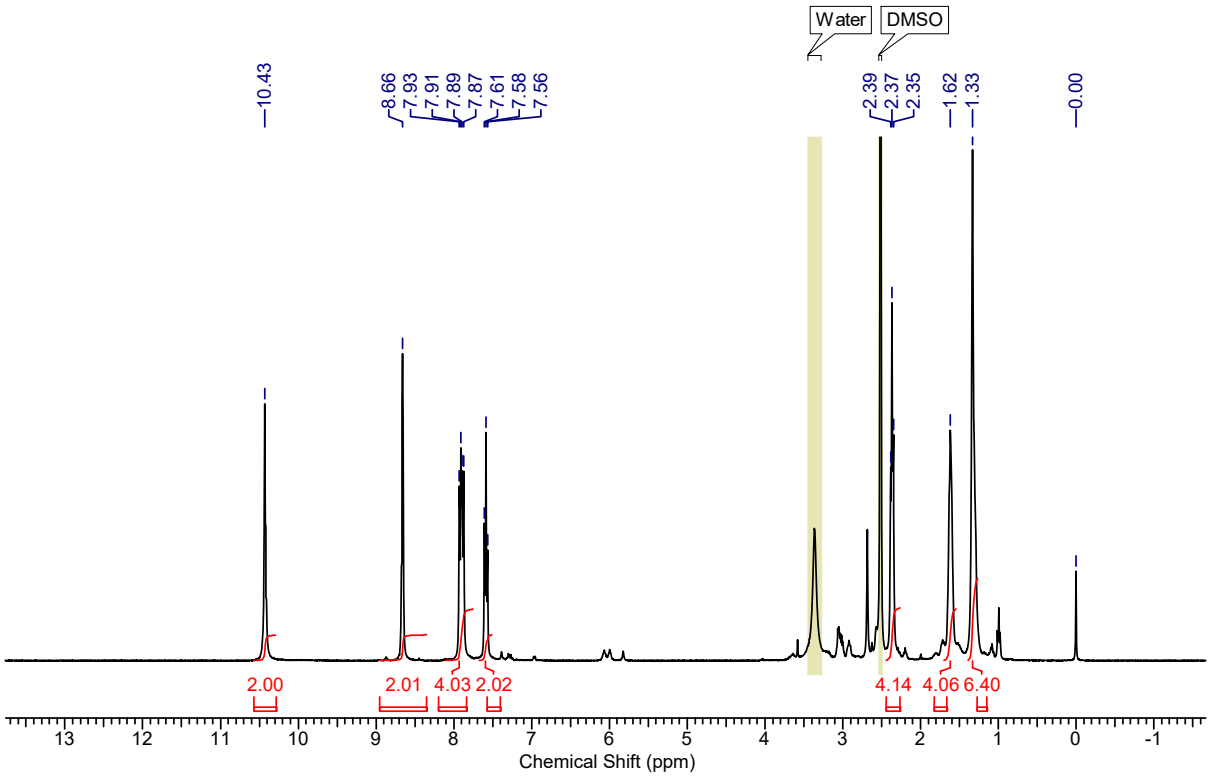
^{1}H NMR of N1, N9-bis (4-methoxyphenyl)nonanediamide (3g)



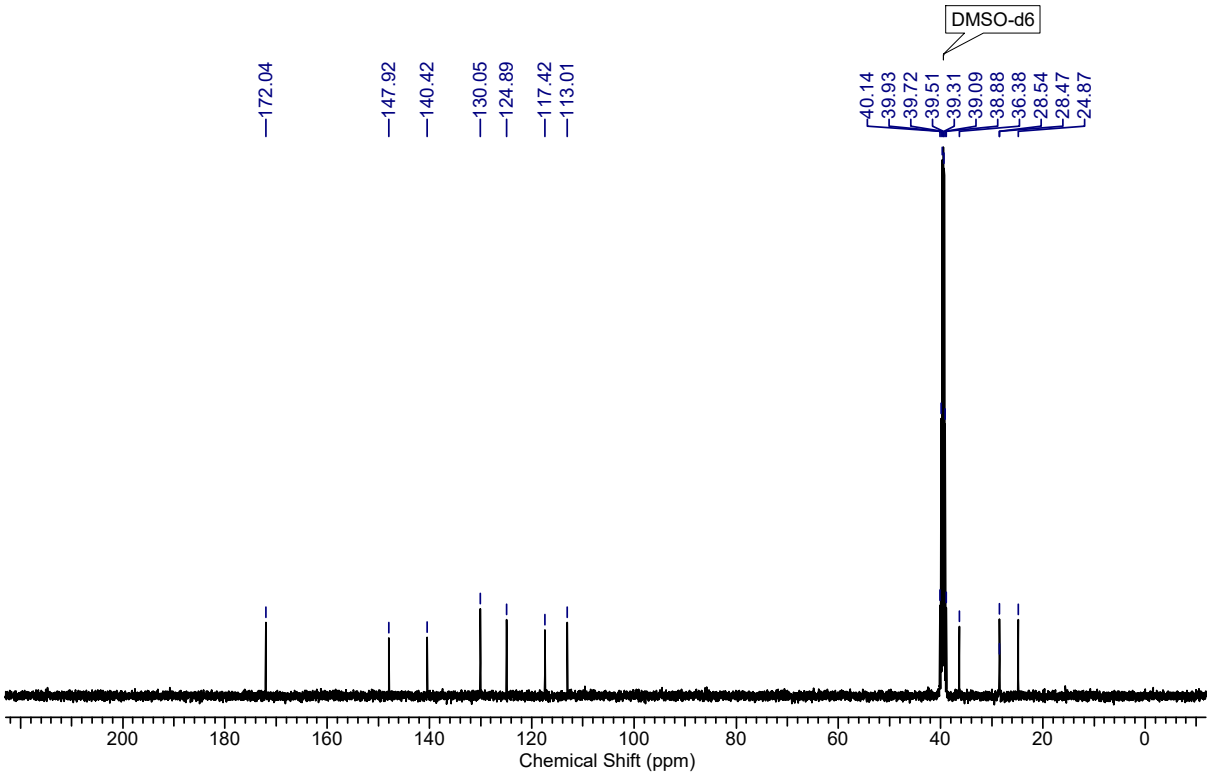
^{13}C NMR of N1, N9-bis (4-methoxyphenyl)nonanediamide (3g)



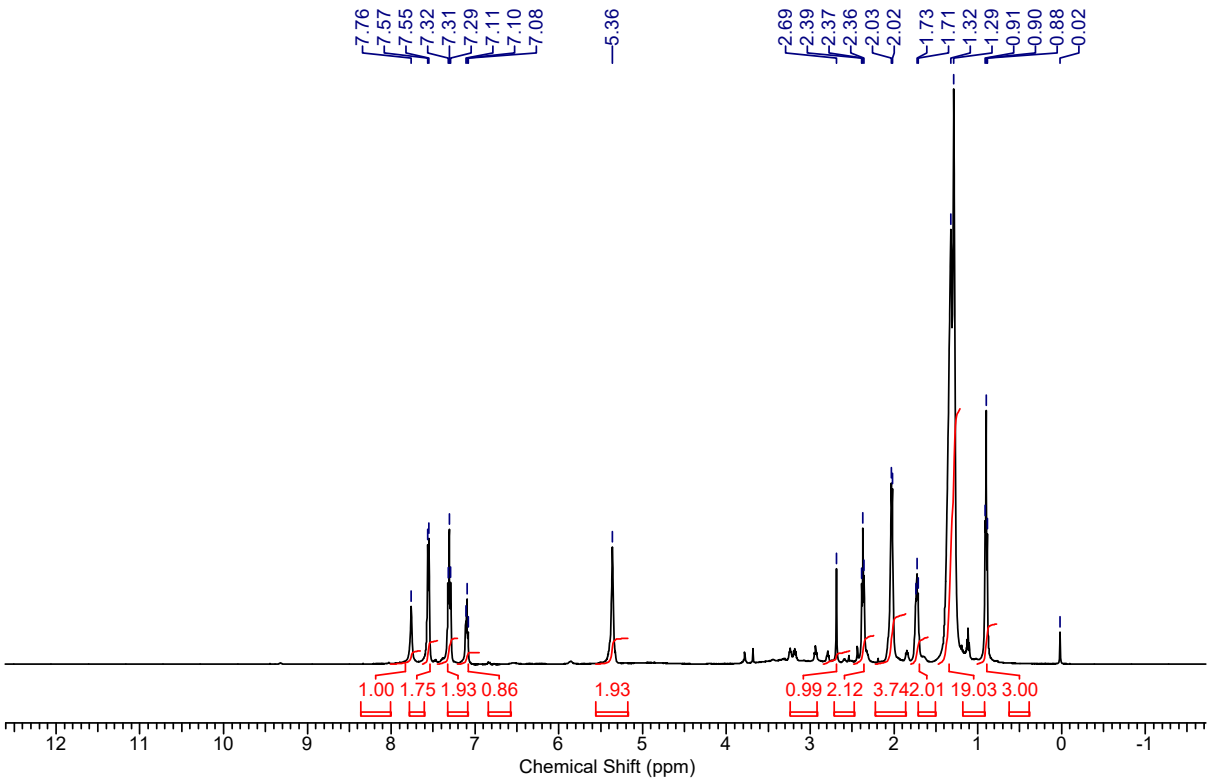
^{1}H NMR of N1, N9-bis (3-nitrophenyl)nonanediamide (3h)



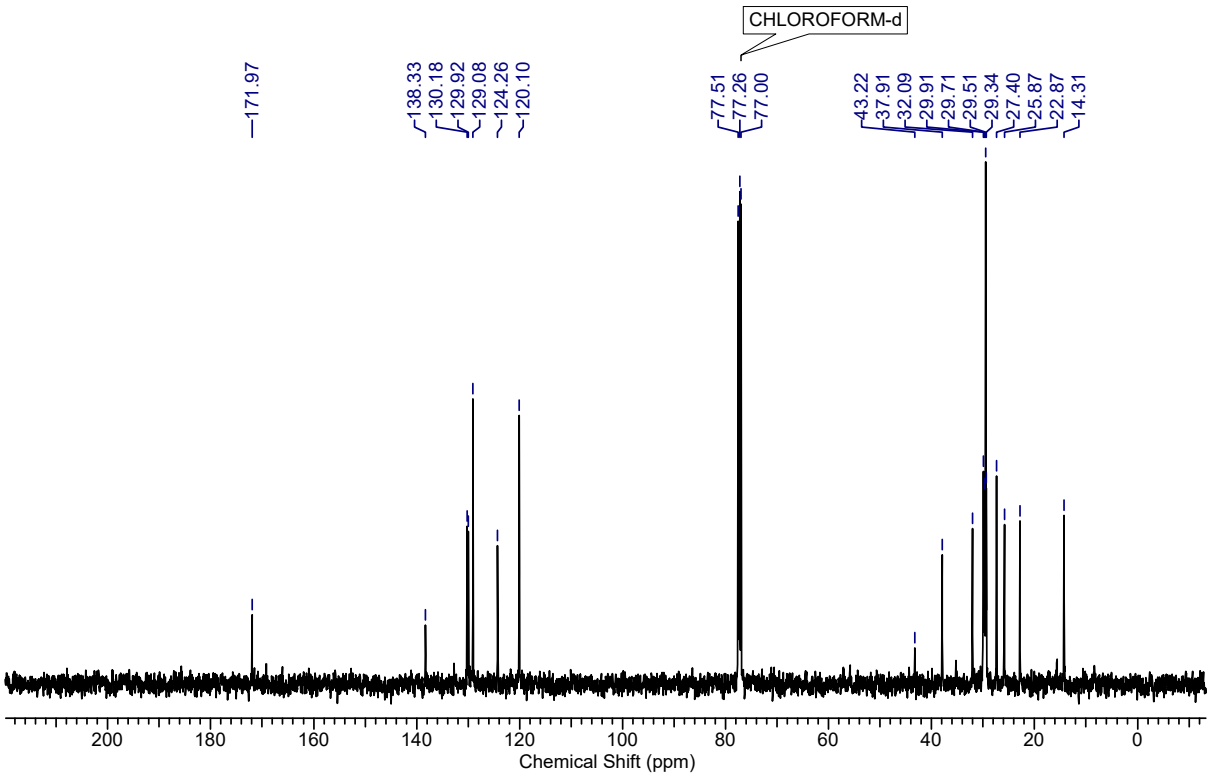
^{13}C NMR of N1, N9-bis (3-nitrophenyl)nonanediamide (3h)



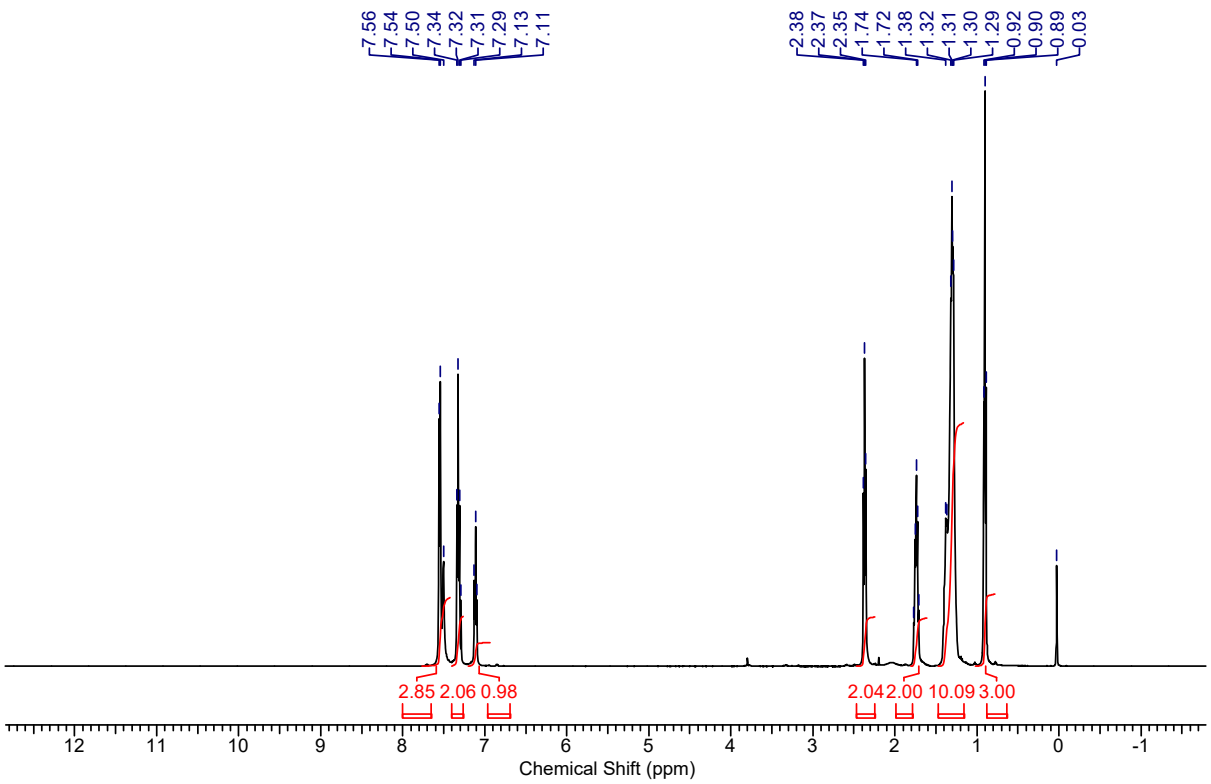
^{1}H NMR of N-phenyloleamide (5a)



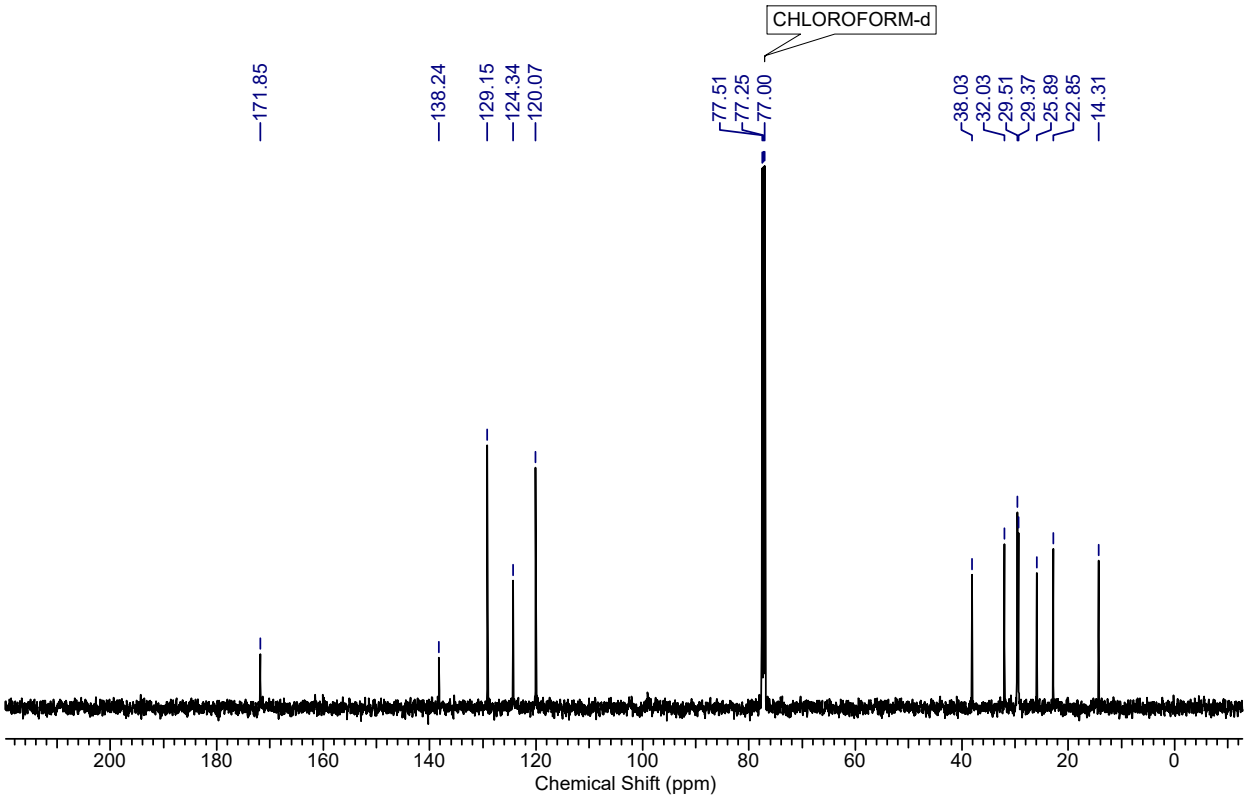
^{13}C NMR of N-phenyloleamide (5a)



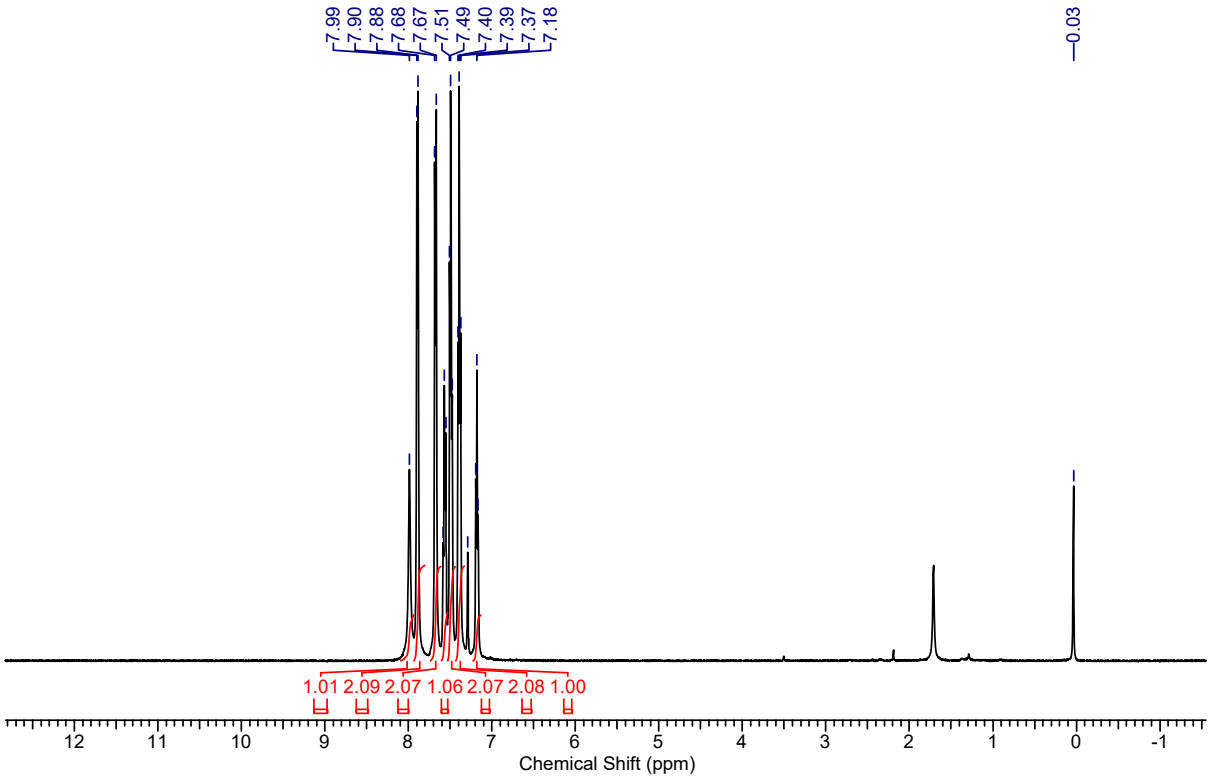
^{1}H NMR of N-phenylnonanamide (5b)



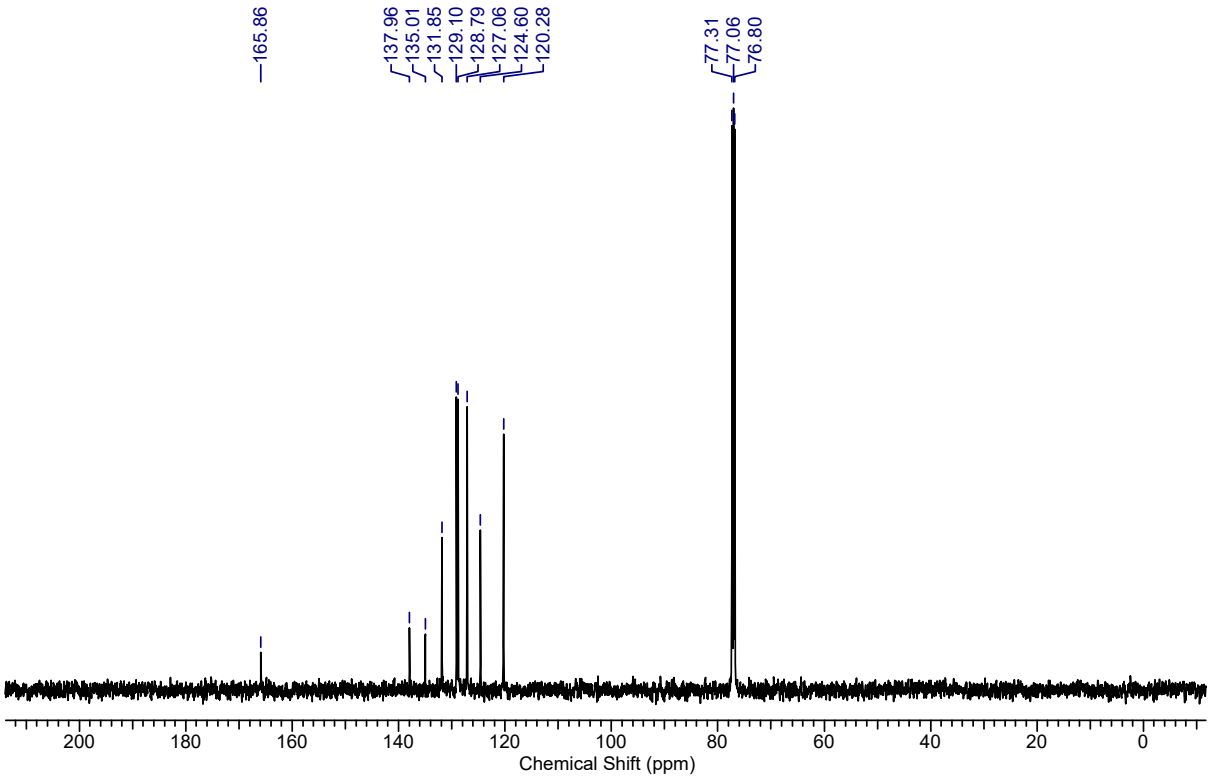
^{13}C NMR of N-phenylnonanamide (5b)



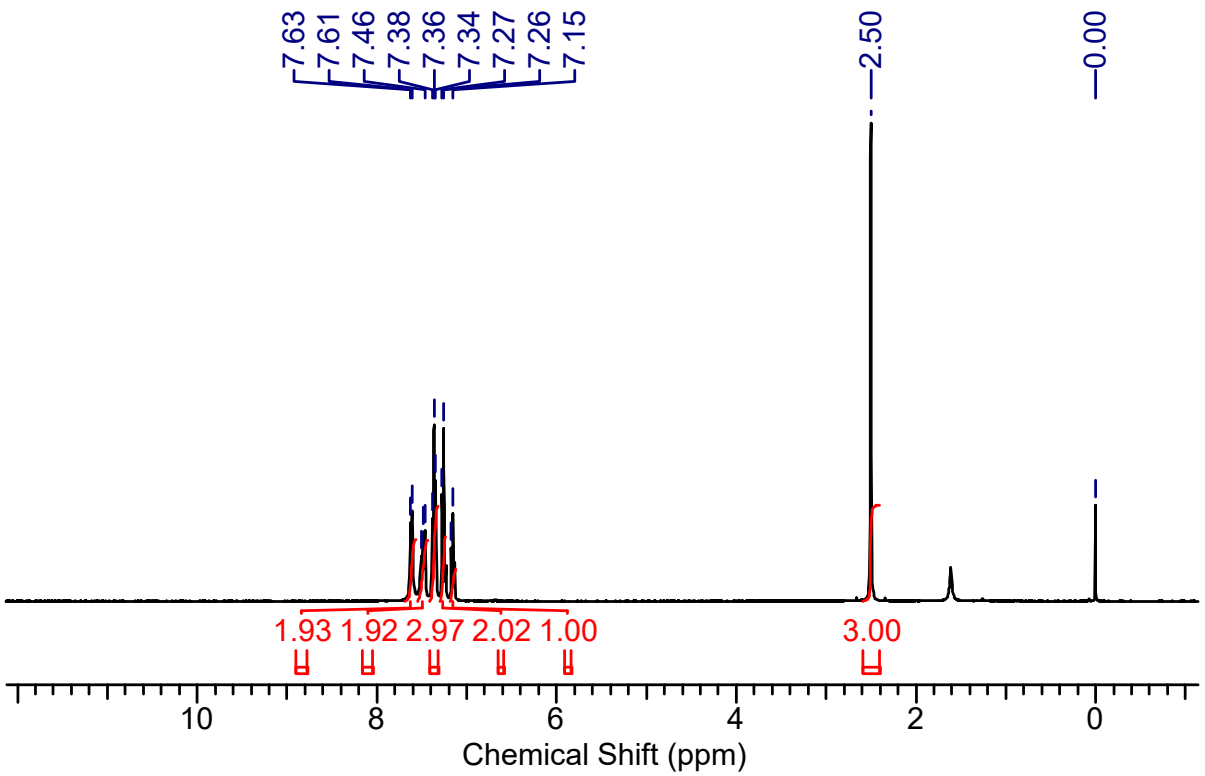
^{1}H NMR of N-phenylbenzamide (7a)



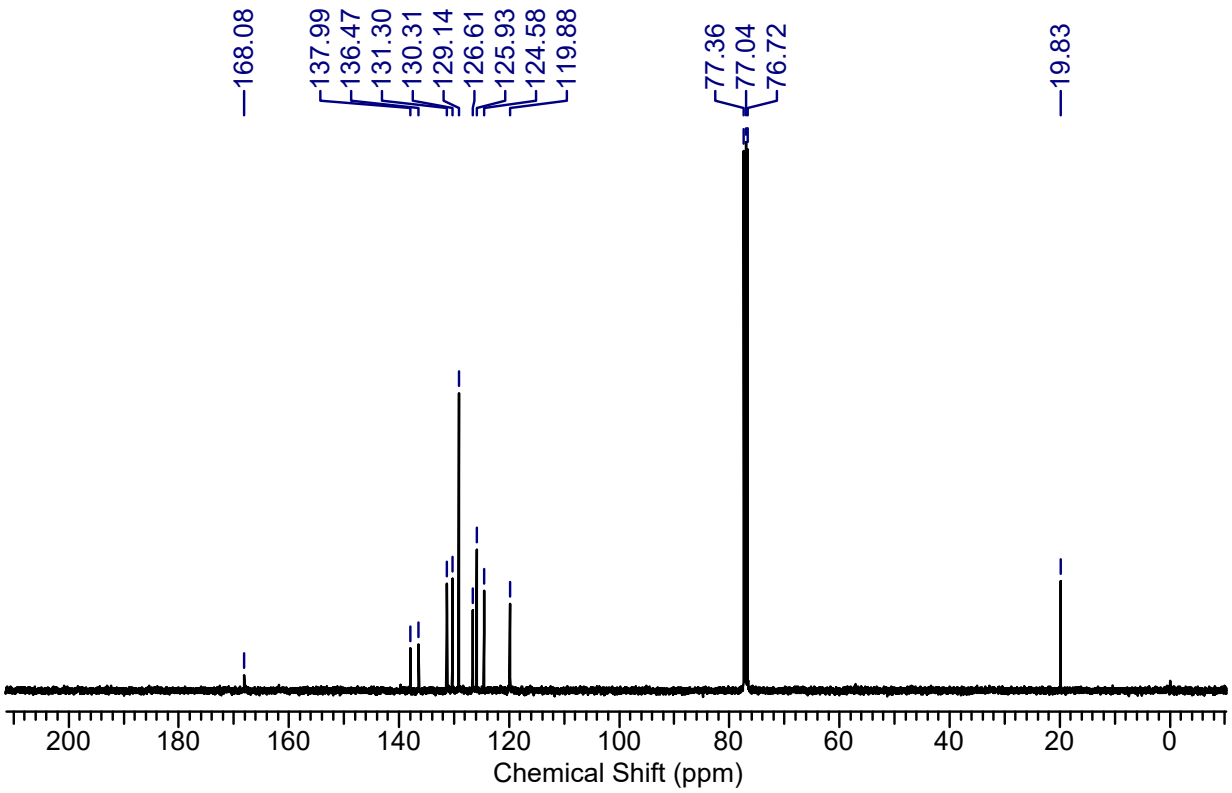
^{13}C NMR of N-phenylbenzamide (7a)



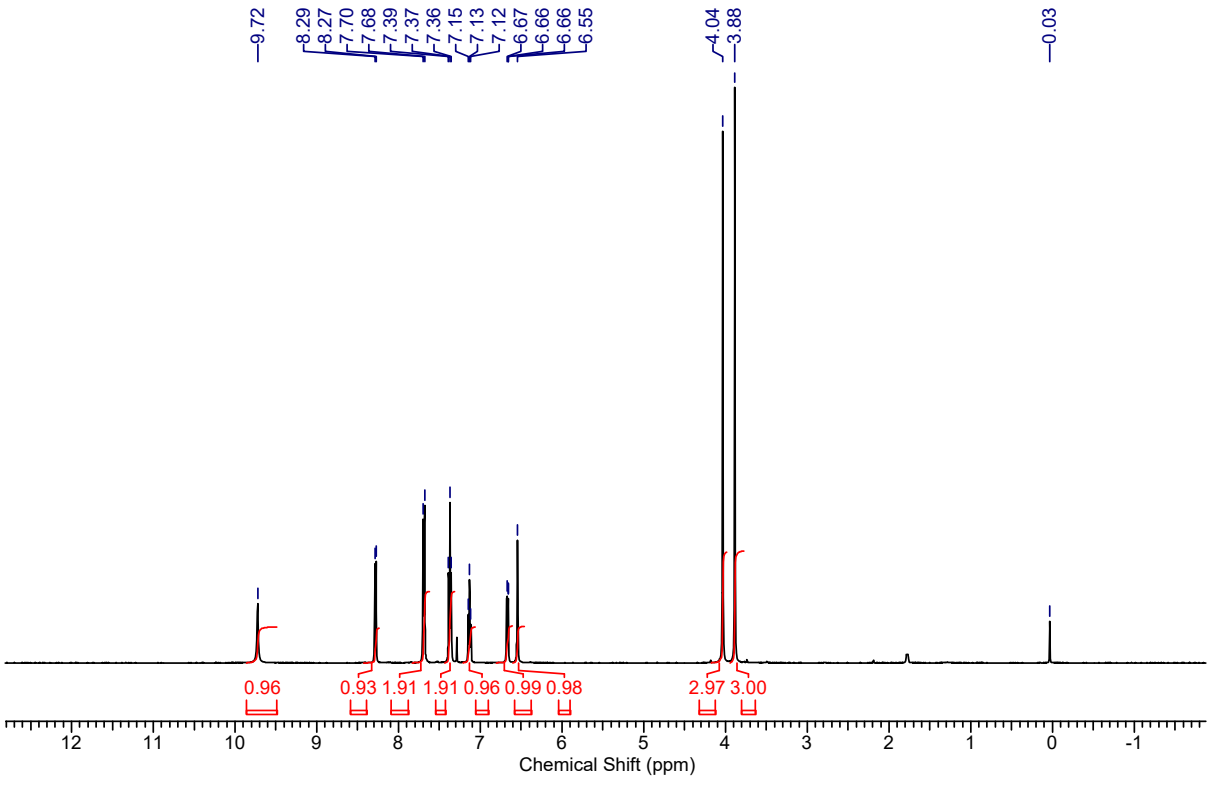
^{1}H NMR of 3-methyl-N-phenylbenzamide (7b)



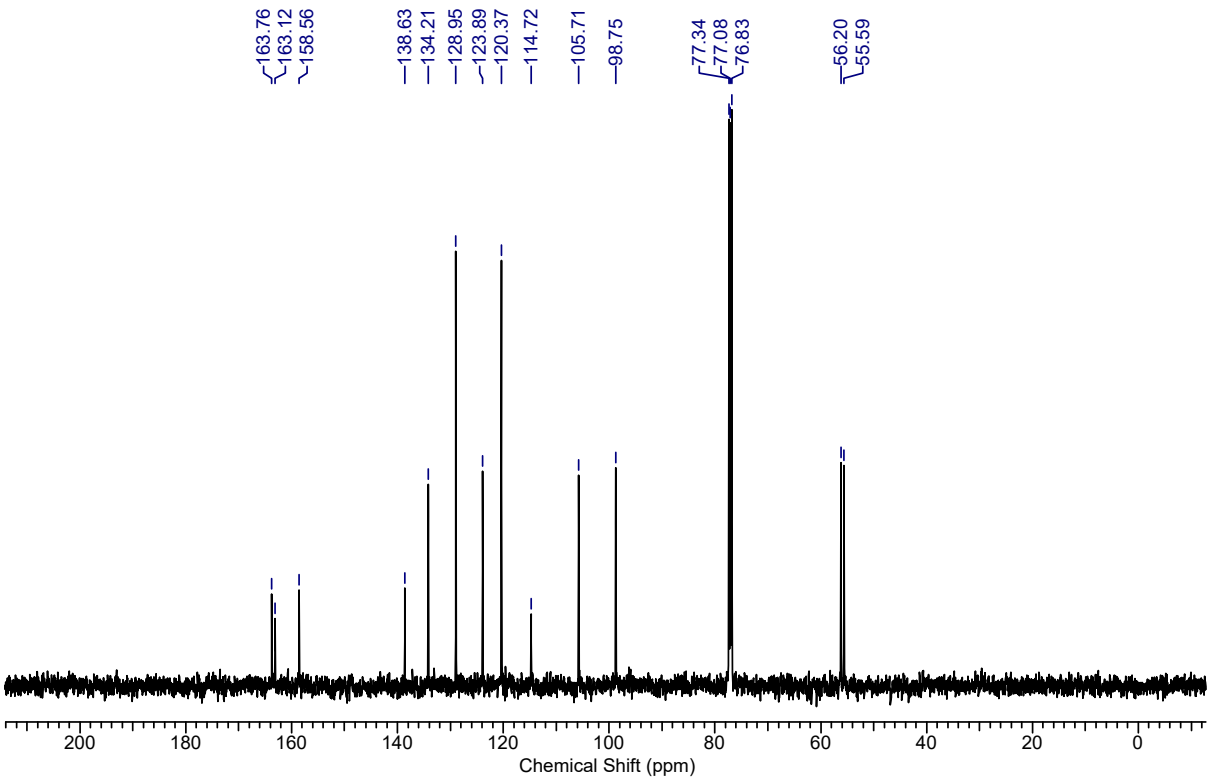
^{13}C NMR of 3-methyl-N-phenylbenzamide (7b)



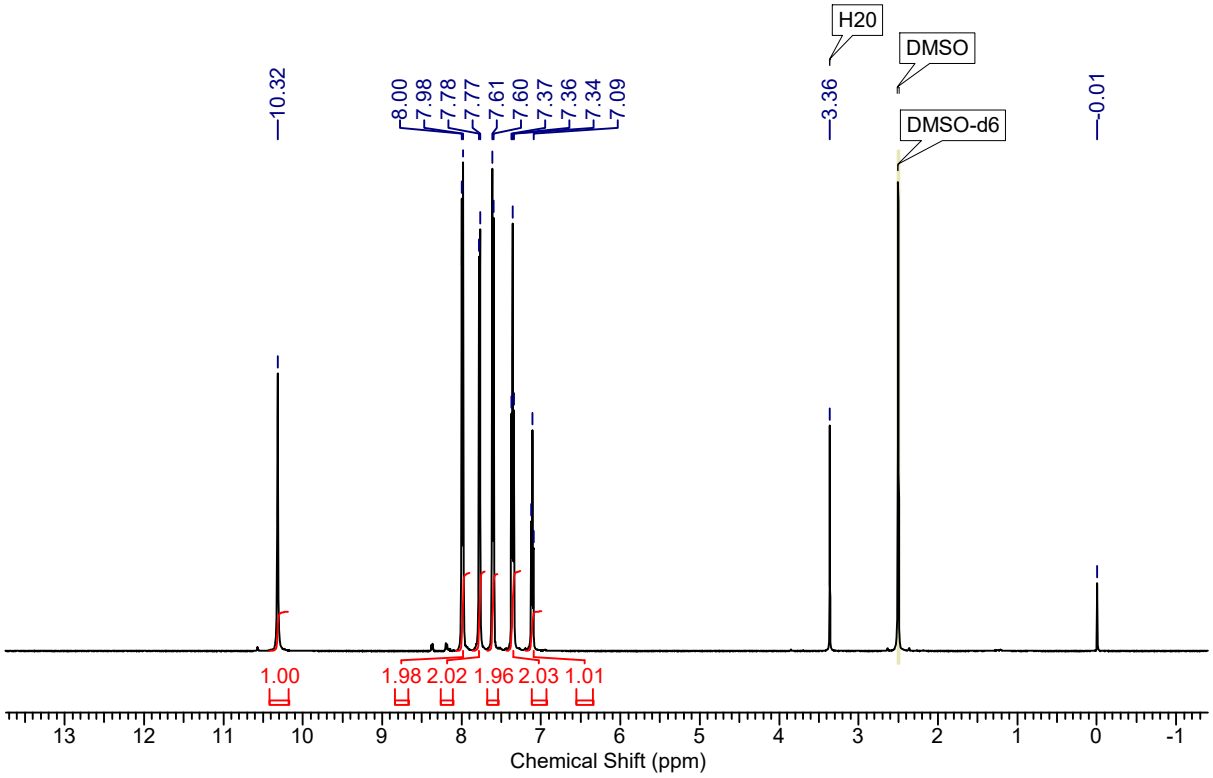
^{1}H NMR of 2, 4-dimethoxy-N-phenylbenzamide (7c)



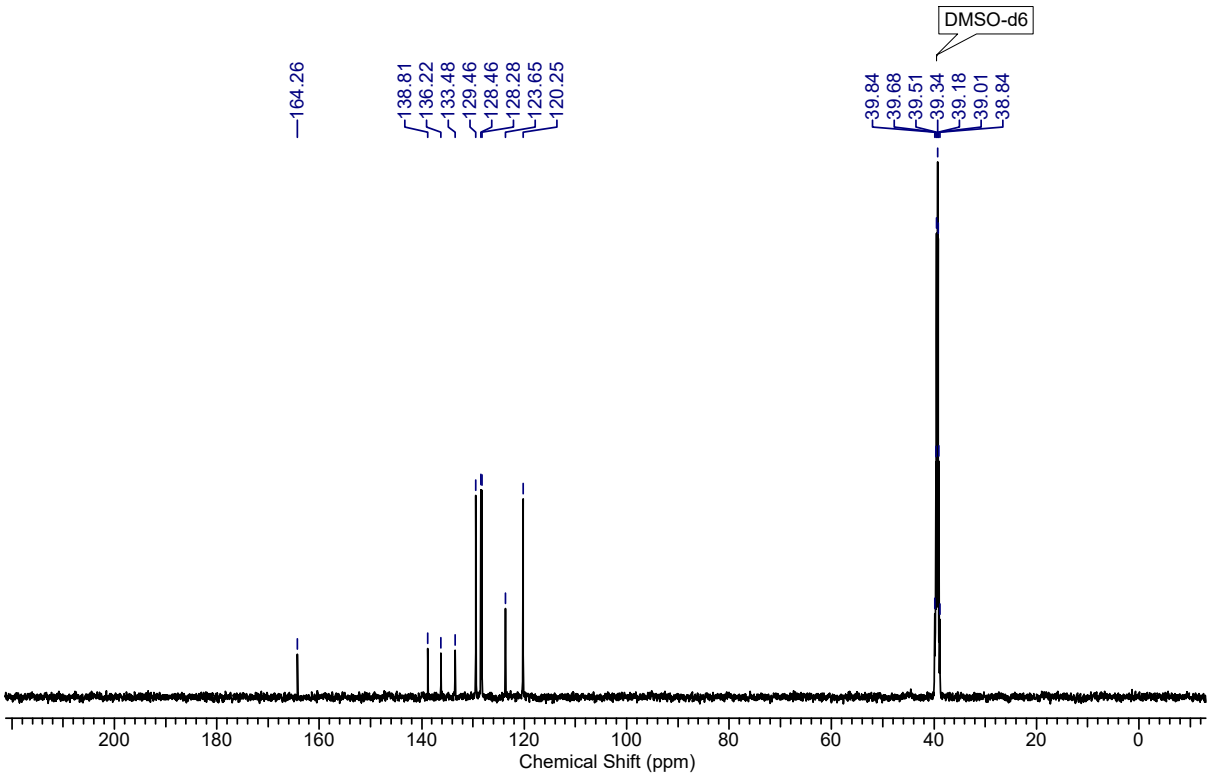
^{13}C NMR of 2, 4-dimethoxy-N-phenylbenzamide (7c)



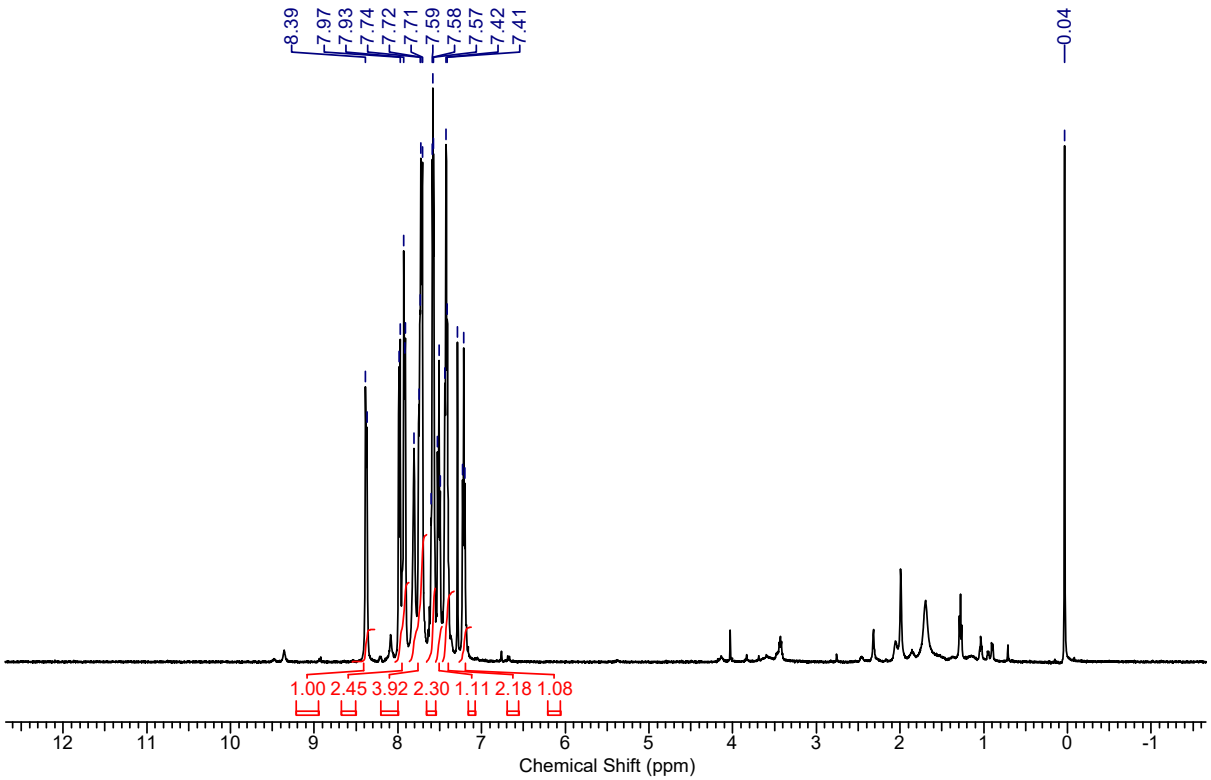
^{1}H NMR of 4-chloro-N-phenylbenzamide (7d)



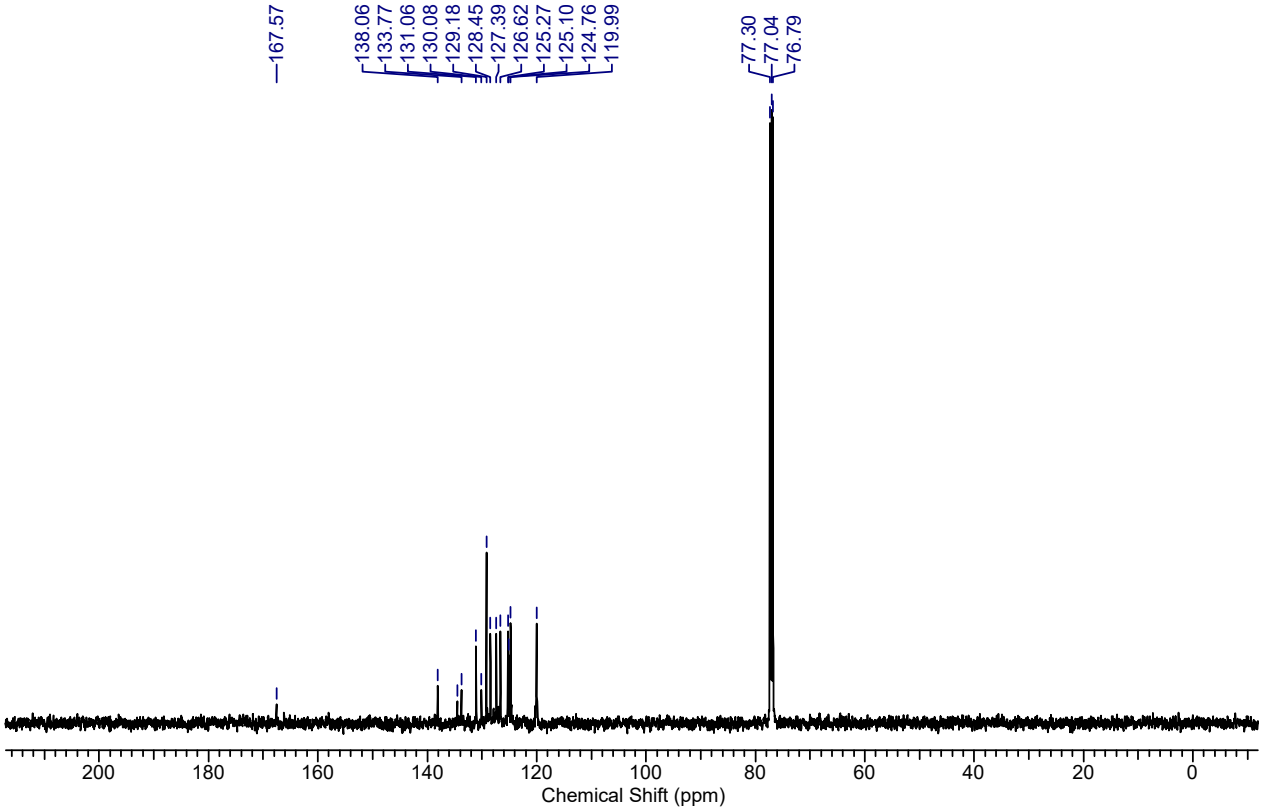
^{13}C NMR of 4-chloro-N-phenylbenzamide (7d)



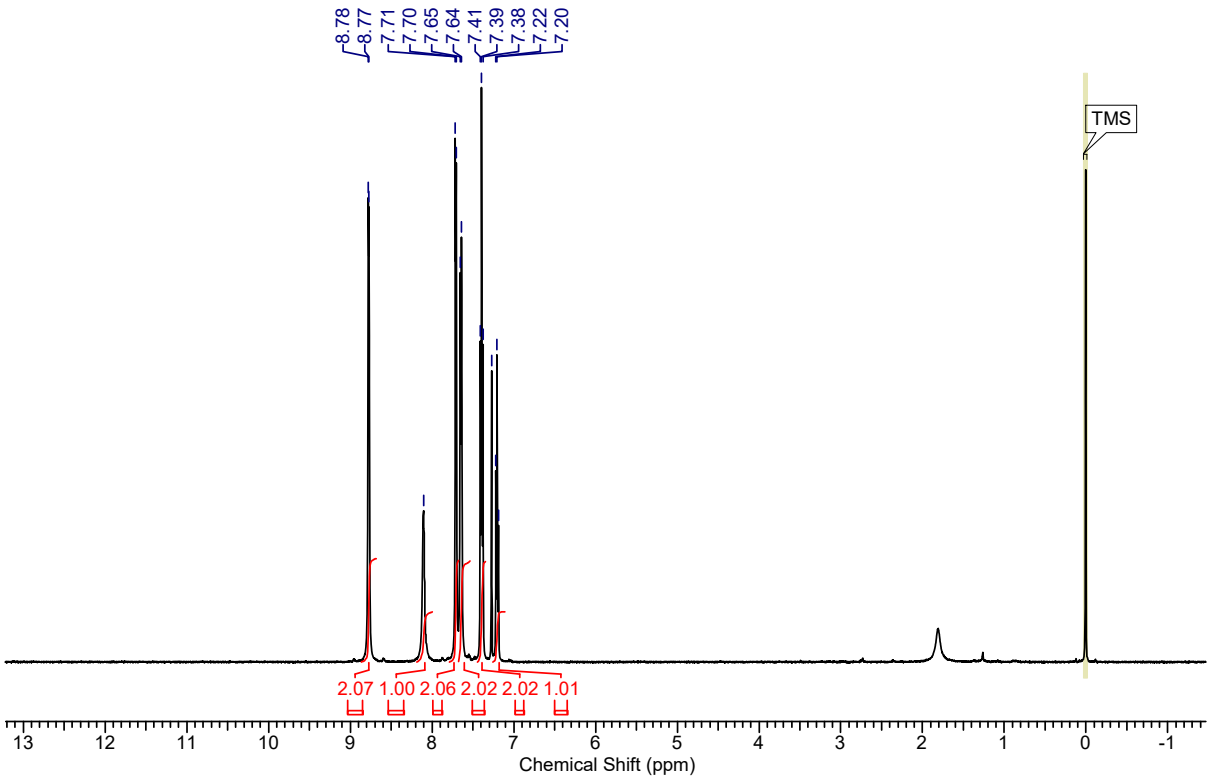
^{1}H NMR of N-phenyl-1-naphthamide (7e)



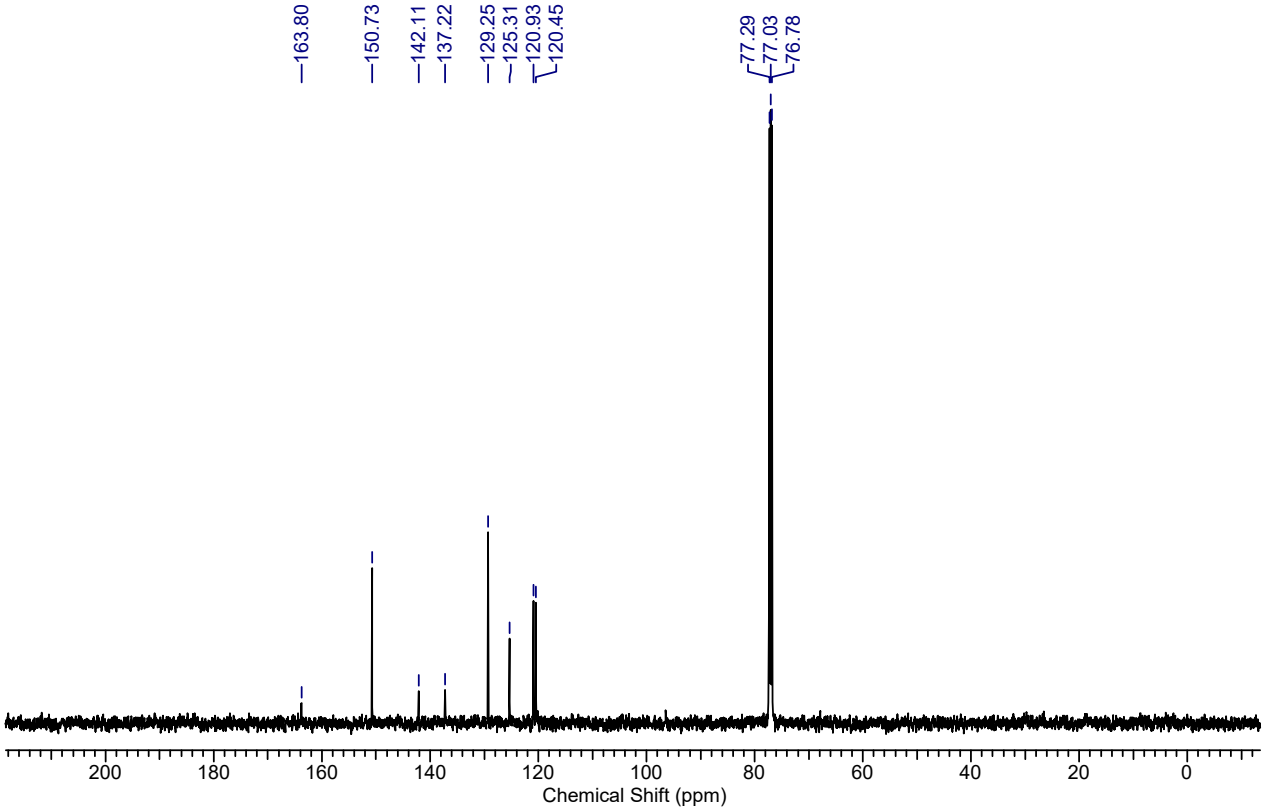
^{13}C NMR of N-phenyl-1-naphthamide (7e)



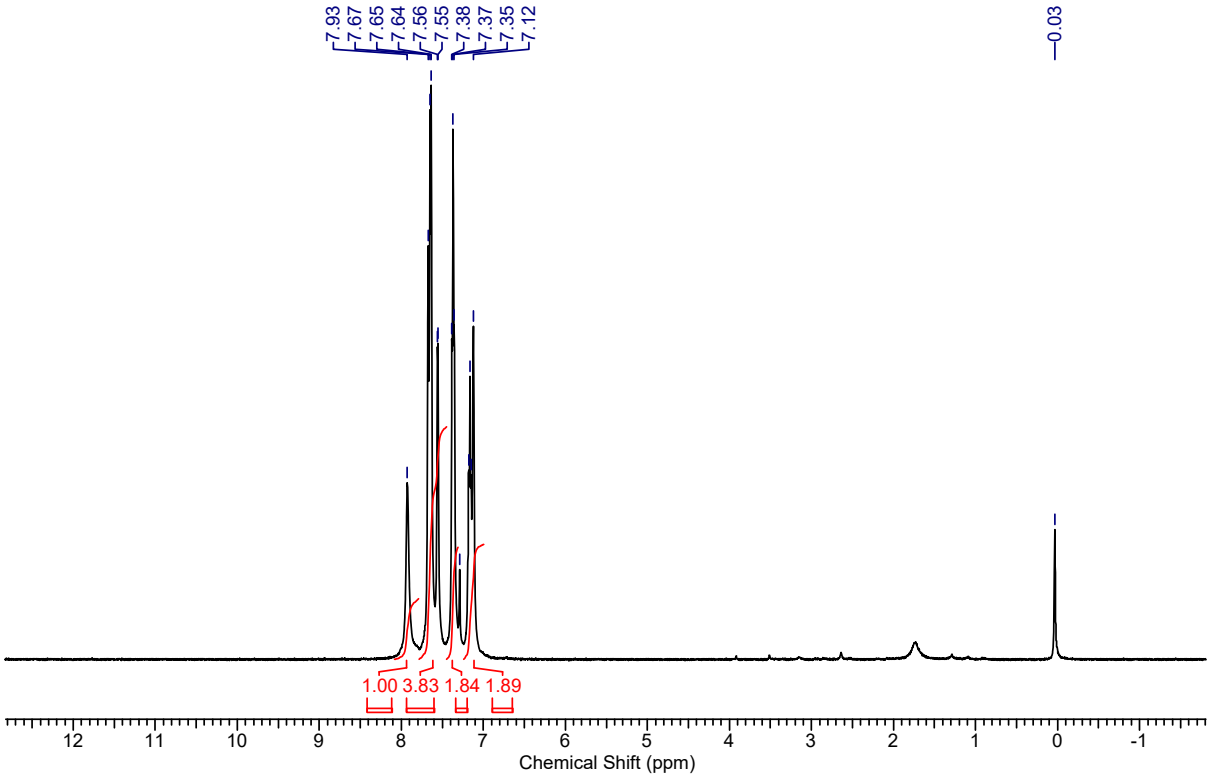
^{1}H NMR of N-phenylisonicotinamide (7f)



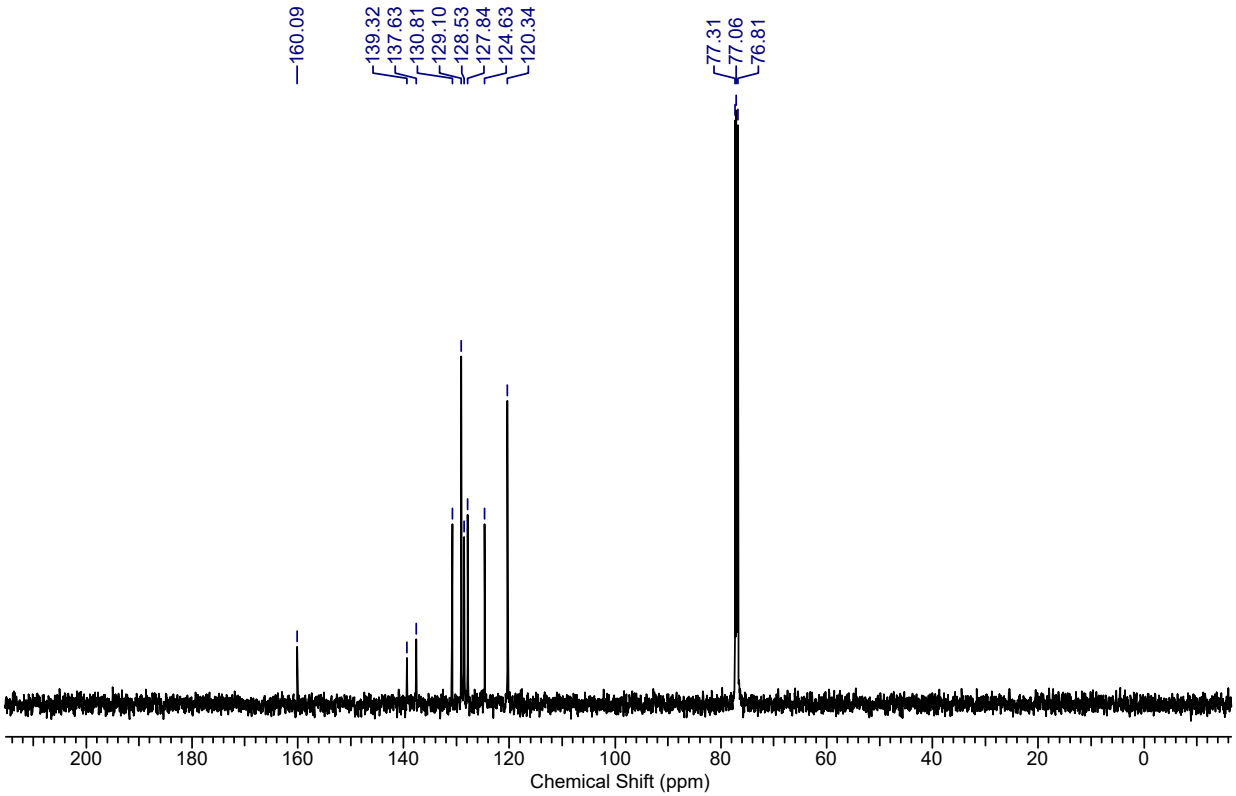
^{13}C NMR of N-phenylisonicotinamide (7f)



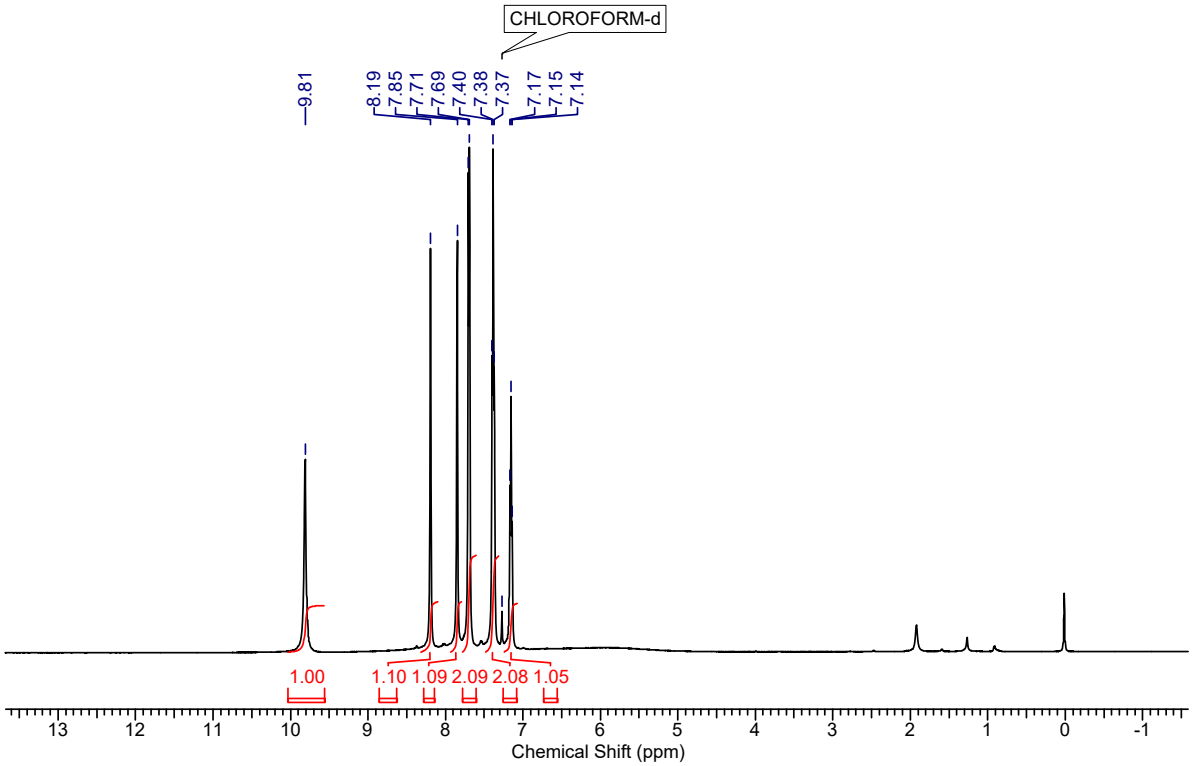
1H NMR of N-phenylthiophene-2-carboxamide (7g)



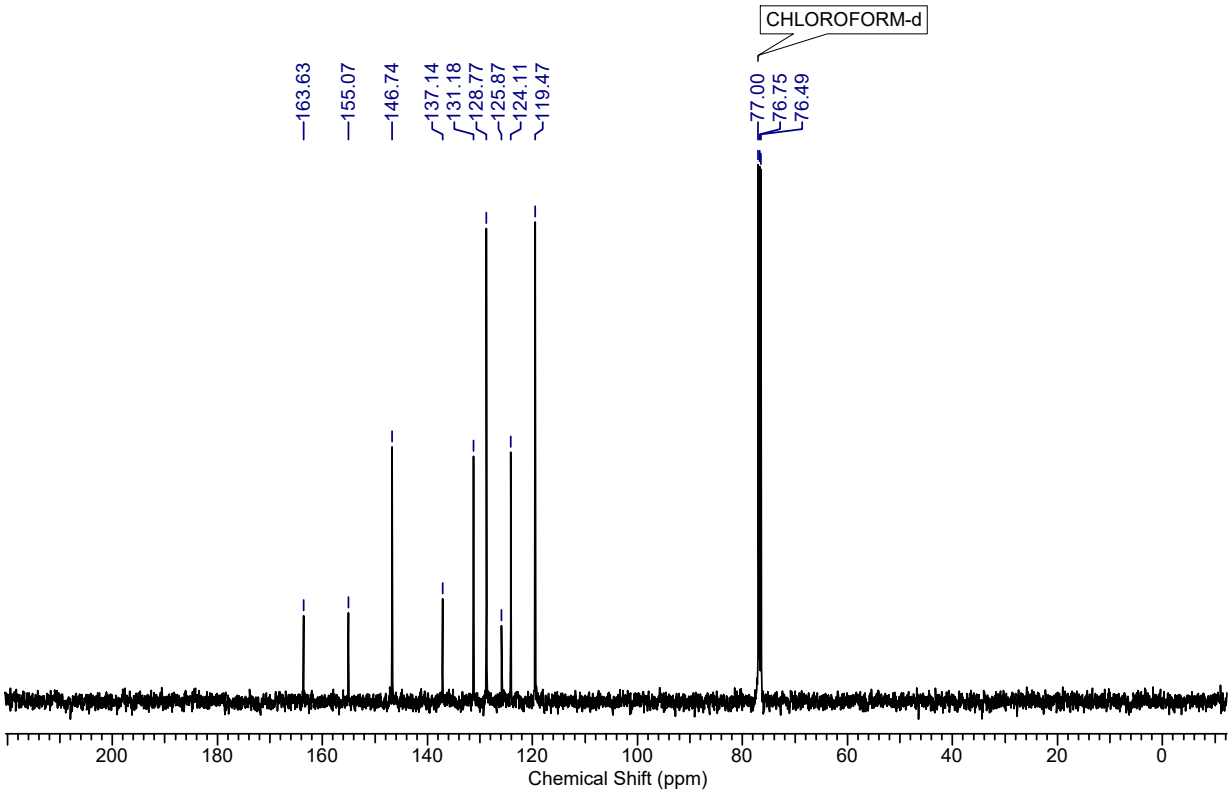
1H NMR of N-phenylthiophene-2-carboxamide (7g)



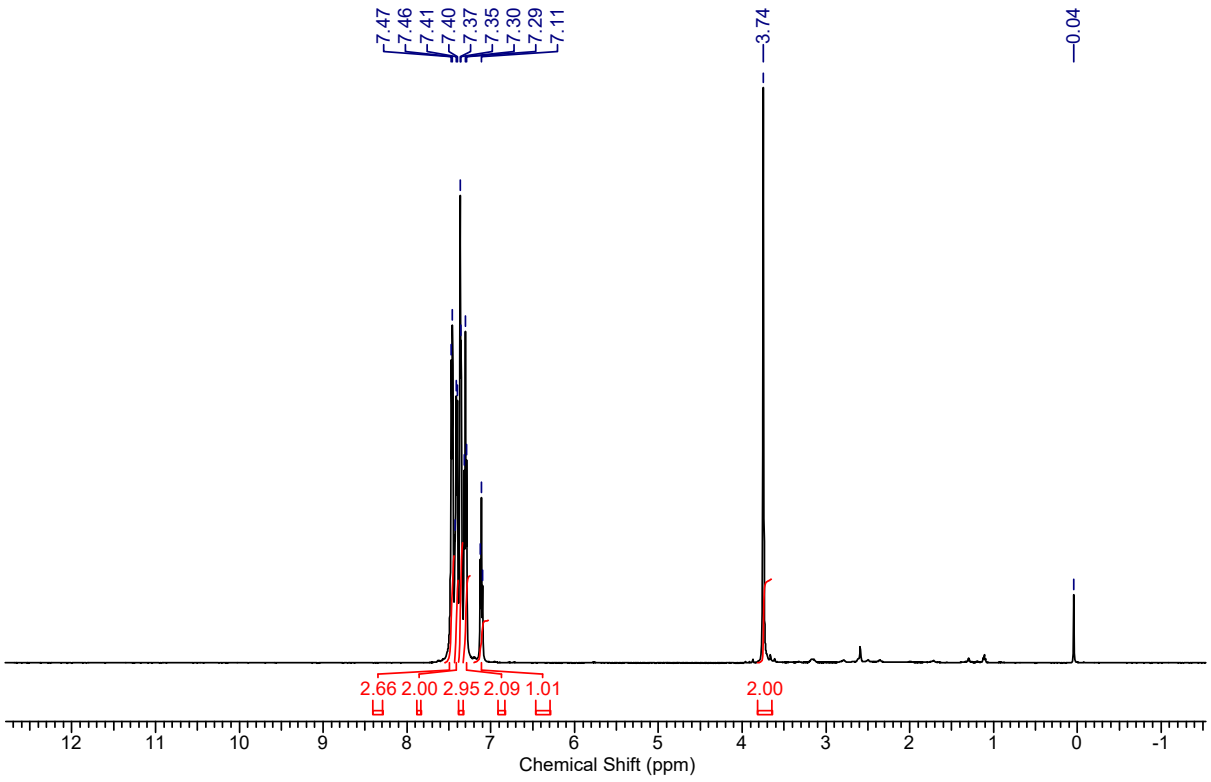
^{1}H NMR of 3-amino-N-phenylpyrazine-2-carboxamide (7h)



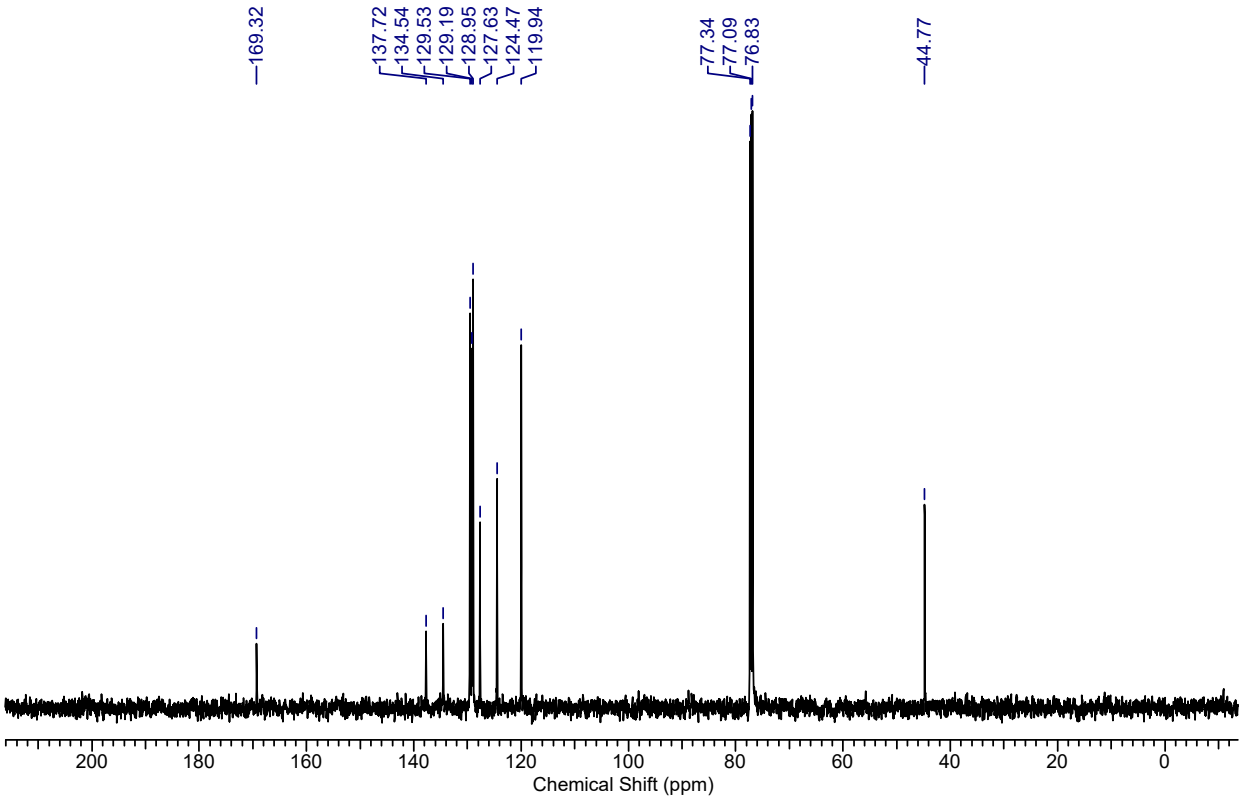
^{13}C NMR of 3-amino-N-phenylpyrazine-2-carboxamide (7h)



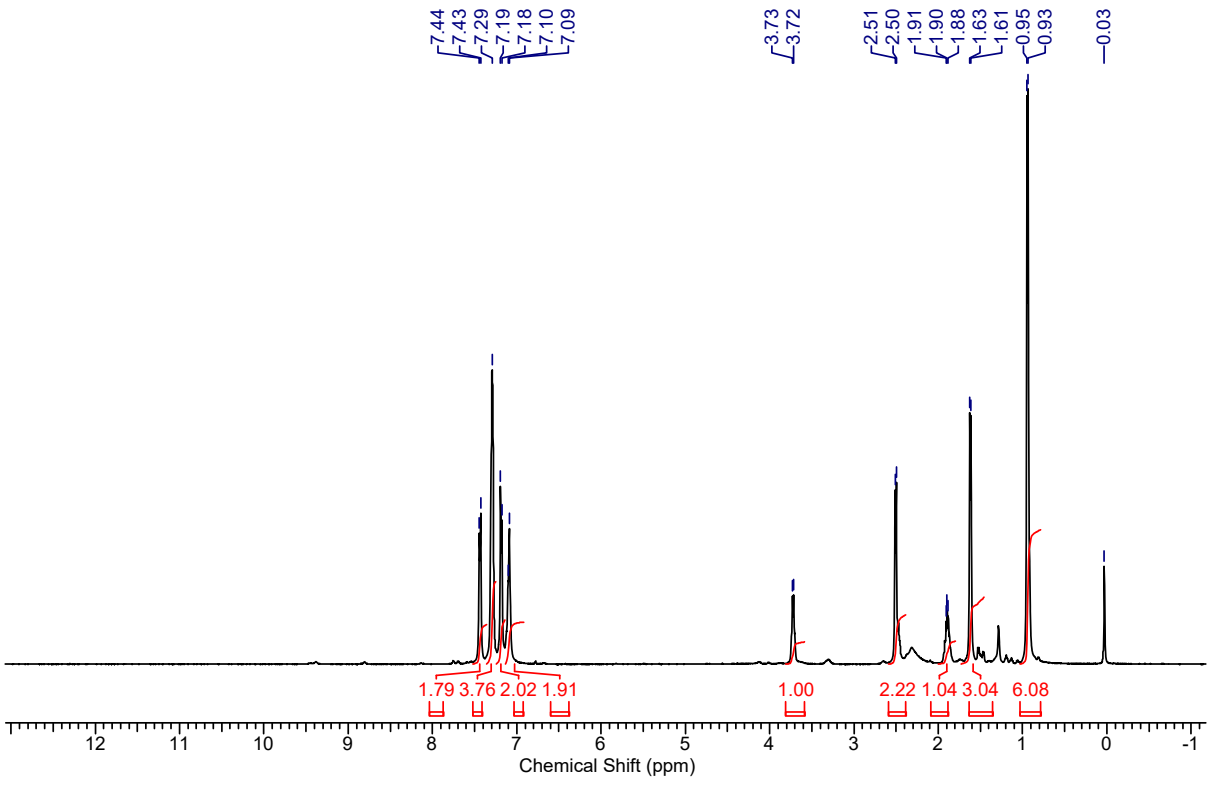
^{1}H NMR of N, 2-diphenylacetamide (7i)



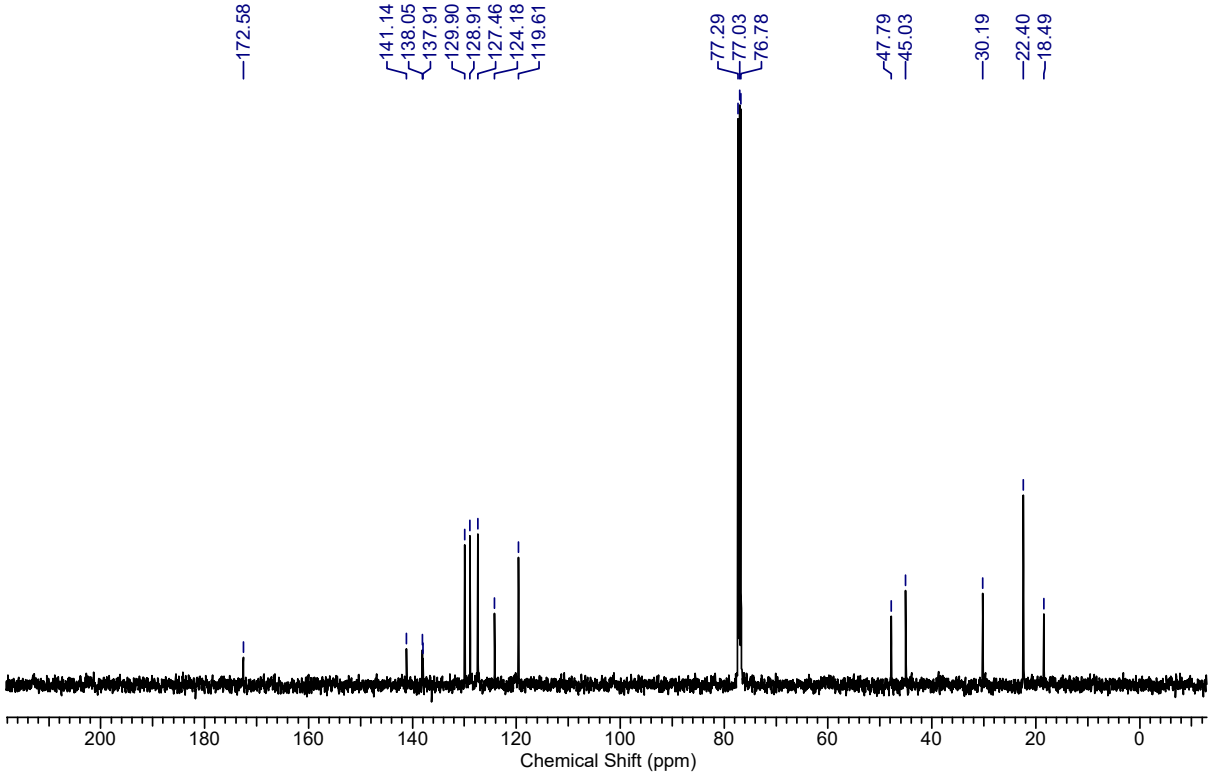
^{13}C NMR of N, 2-diphenylacetamide (7i)



^{1}H NMR of 2-(4-isobutylphenyl)-N-phenylpropanamide (7j)

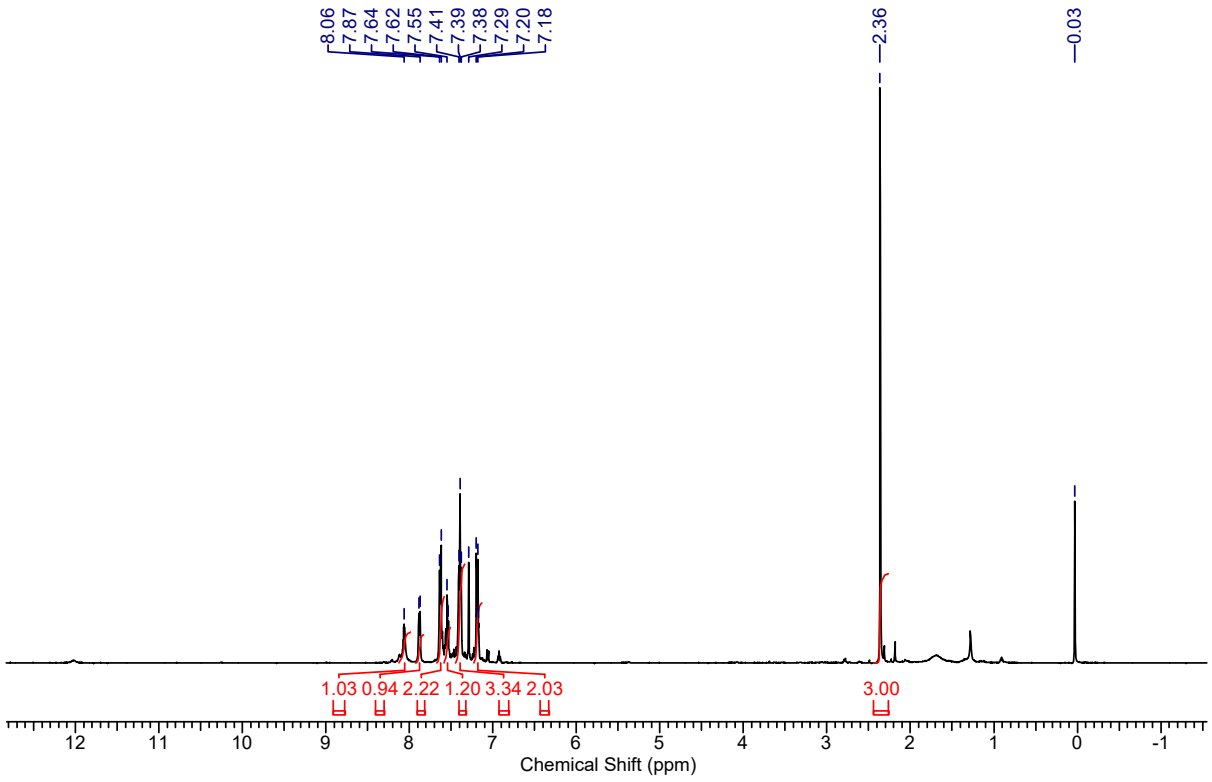


^{13}C NMR of 2-(4-isobutylphenyl)-N-phenylpropanamide (7j)

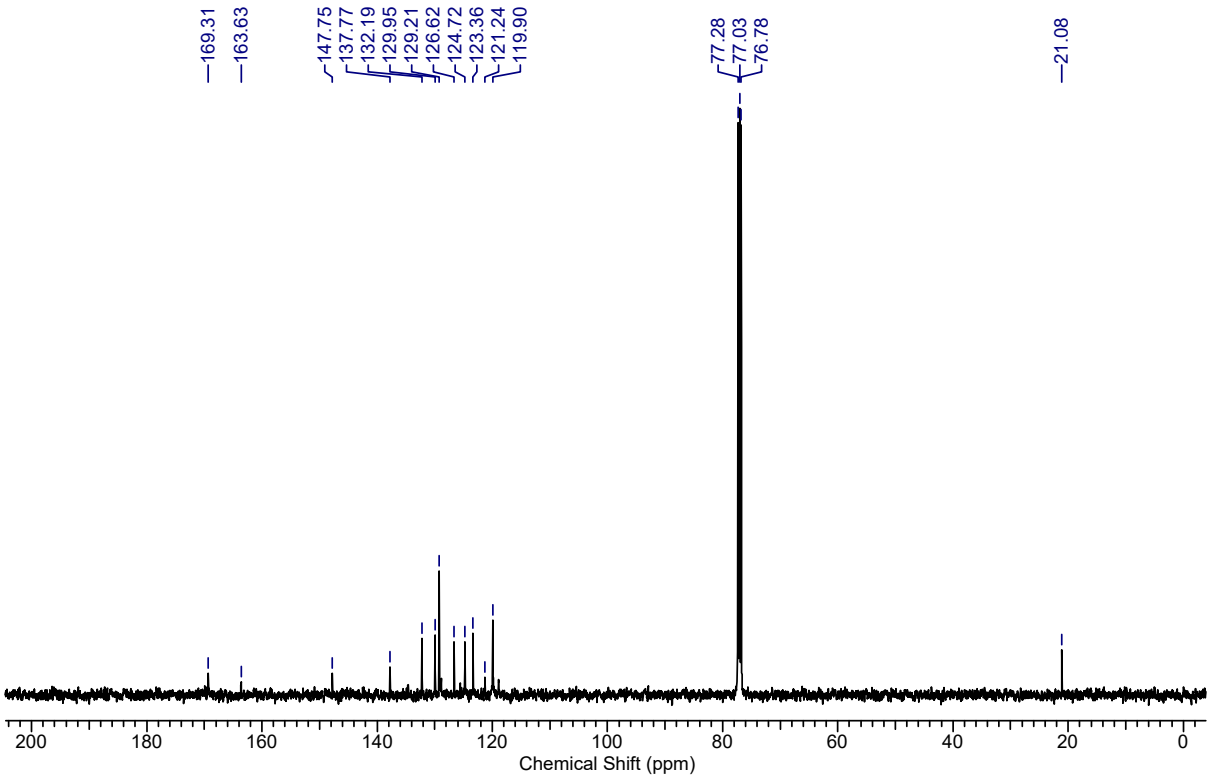


^{1}H NMR of 2-(phenylcarbamoyl) phenyl acetate (7l)

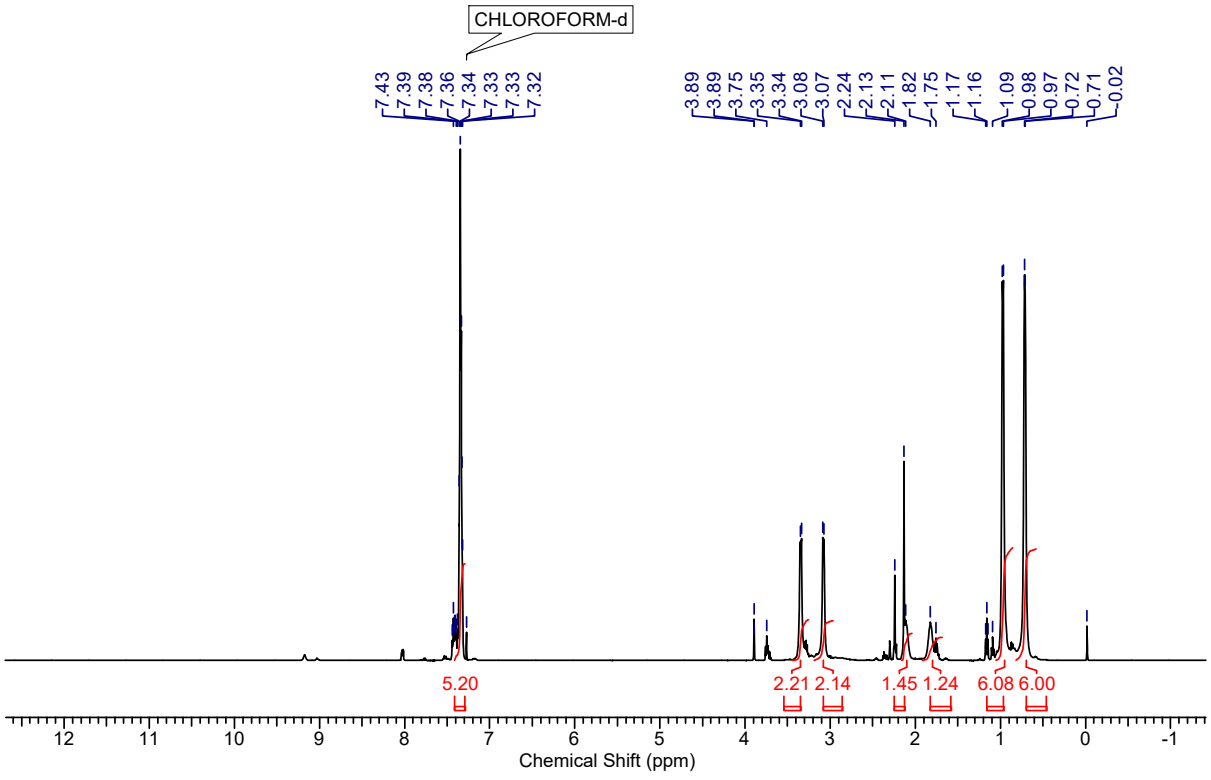
a



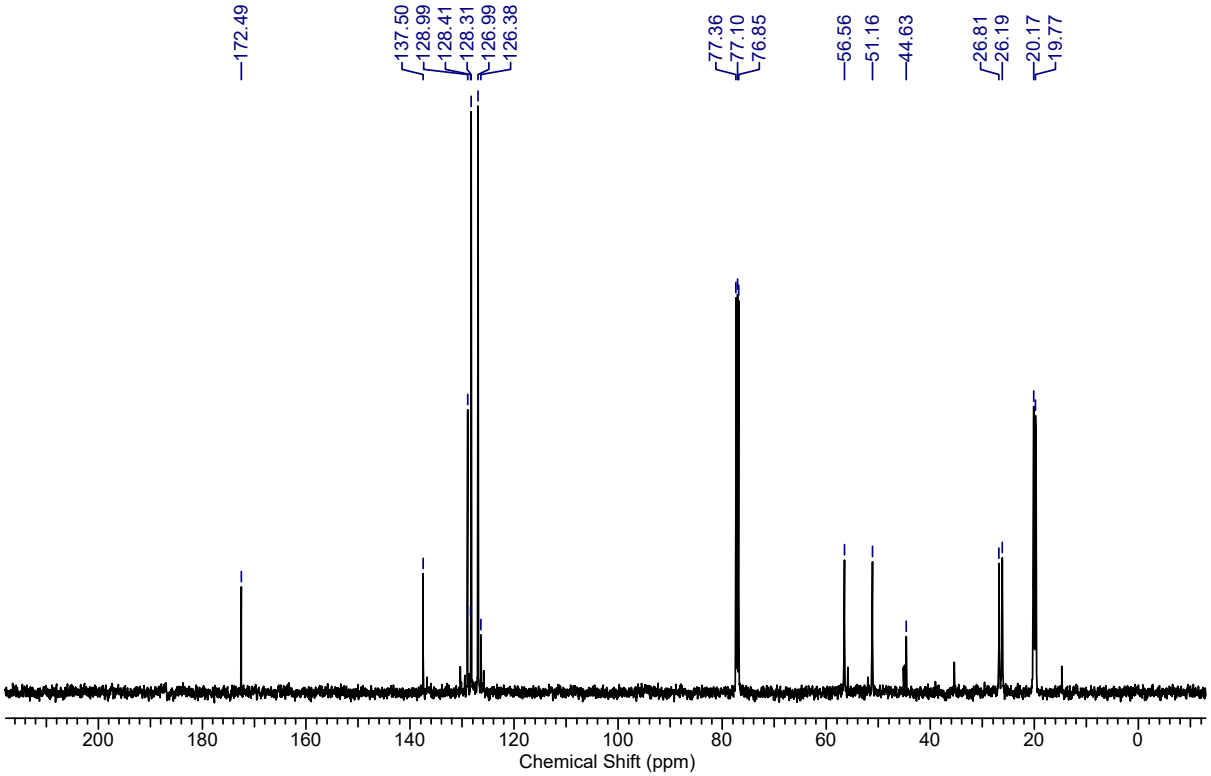
^{13}C NMR of 2-(phenylcarbamoyl) phenyl acetate (7l)



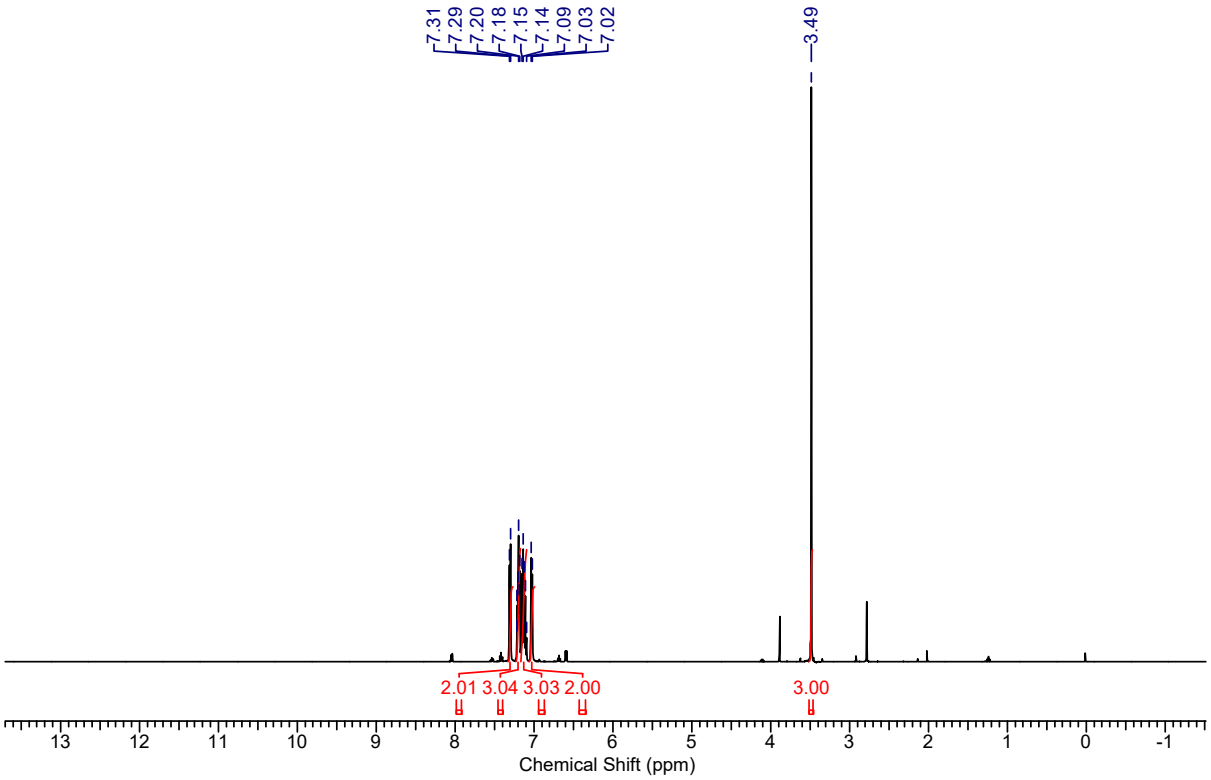
^{1}H NMR of N, N-diisobutylbenzamide (9a)



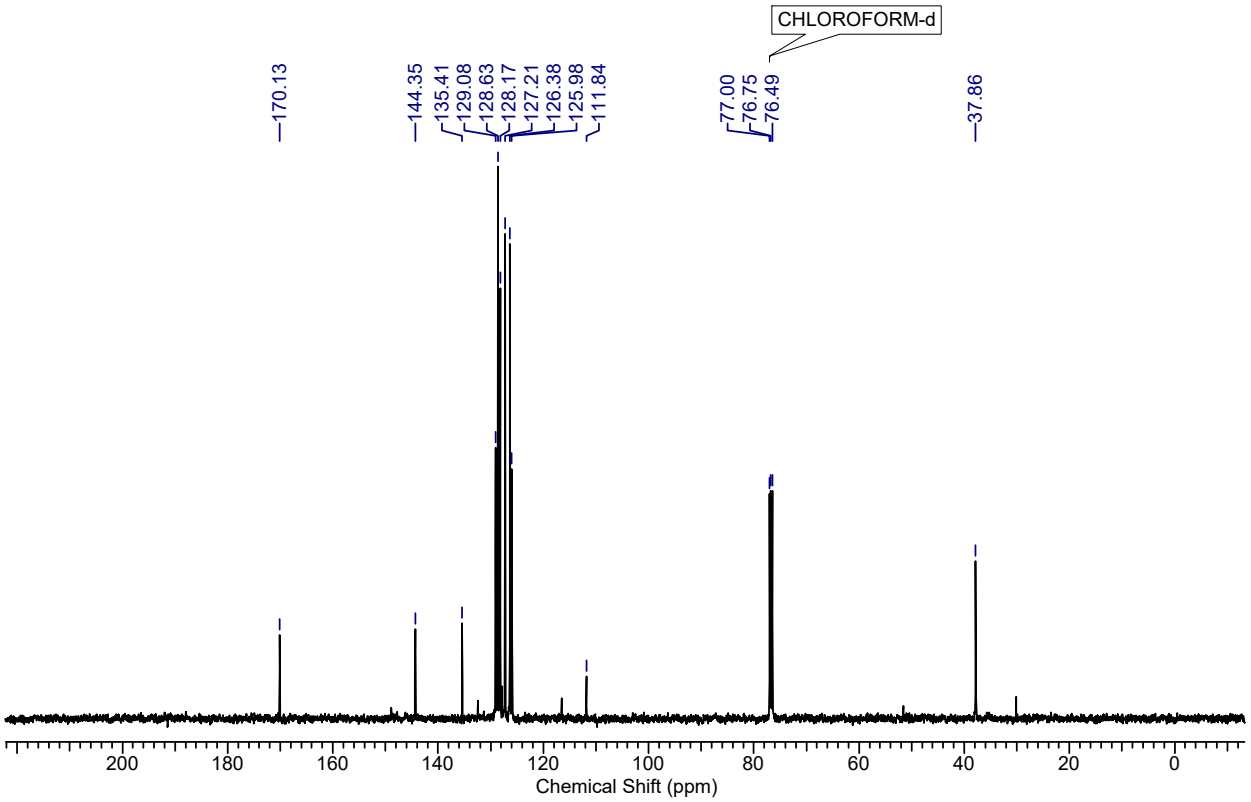
^{13}C NMR of N, N-diisobutylbenzamide (9a)



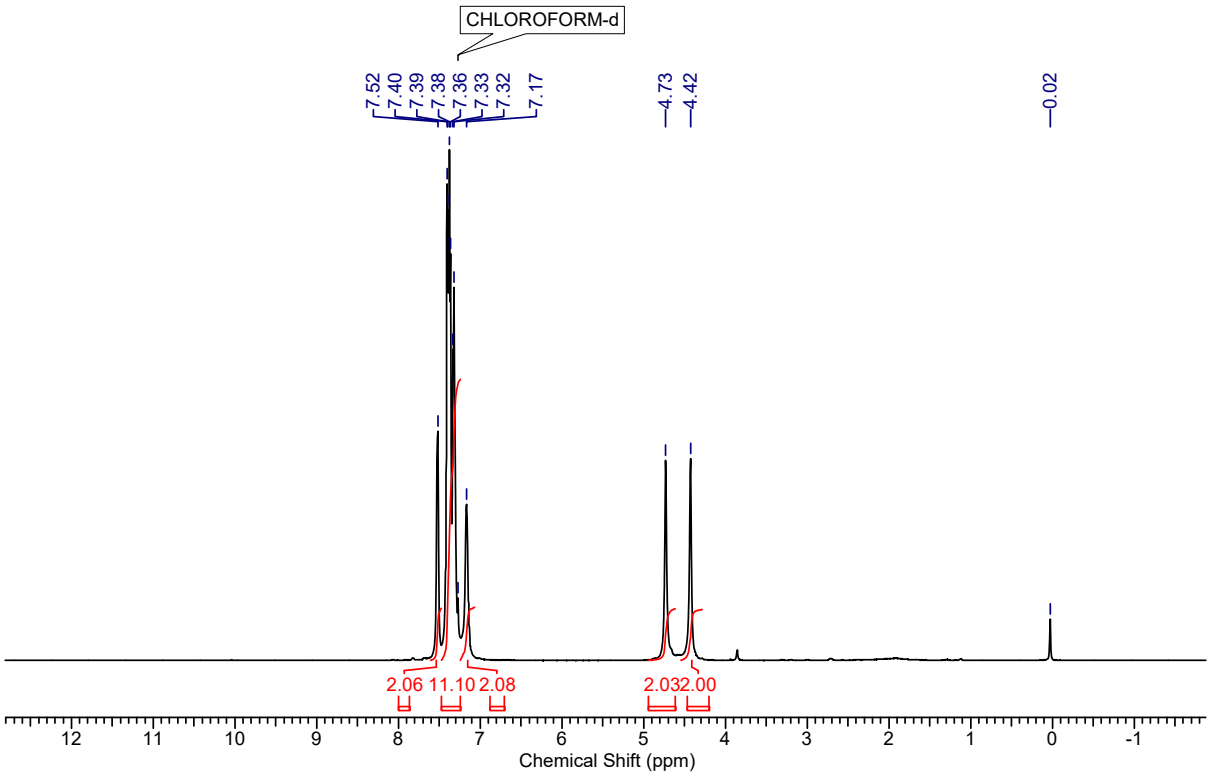
^{1}H NMR of N-methyl-N-phenylbenzamide (9b)



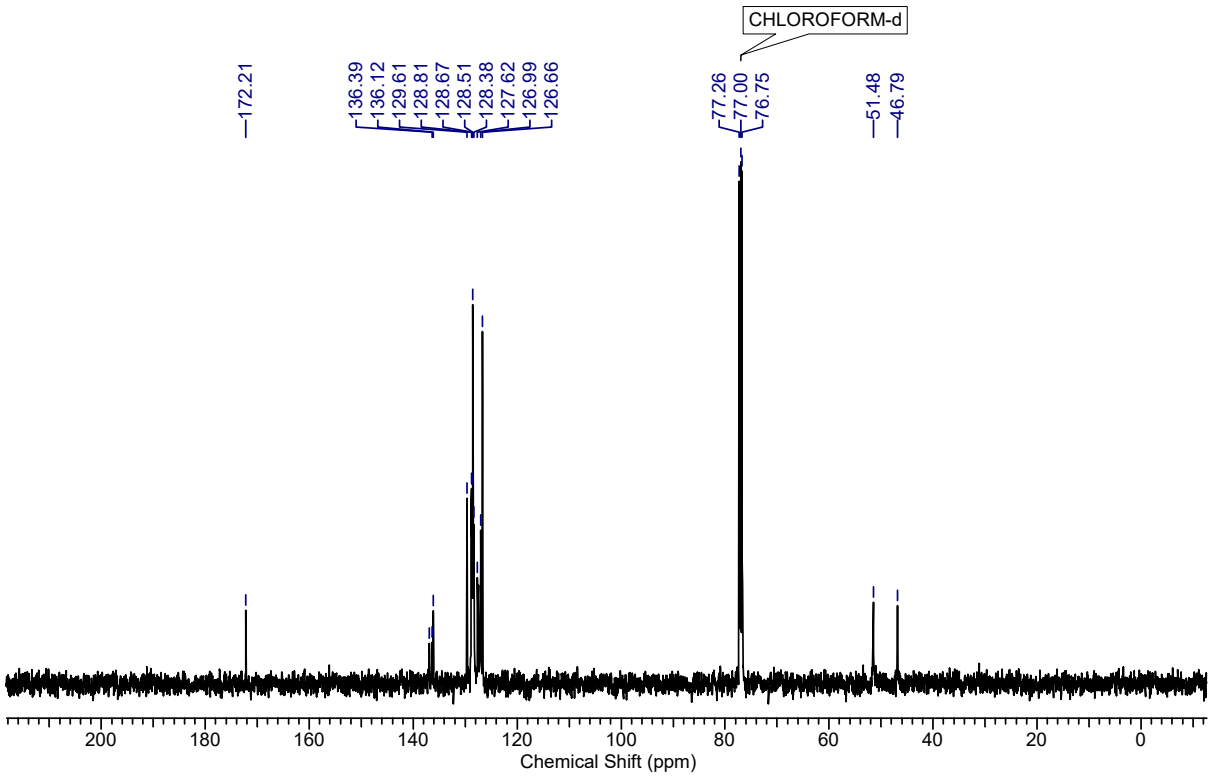
^{13}C NMR of N-methyl-N-phenylbenzamide (9b)



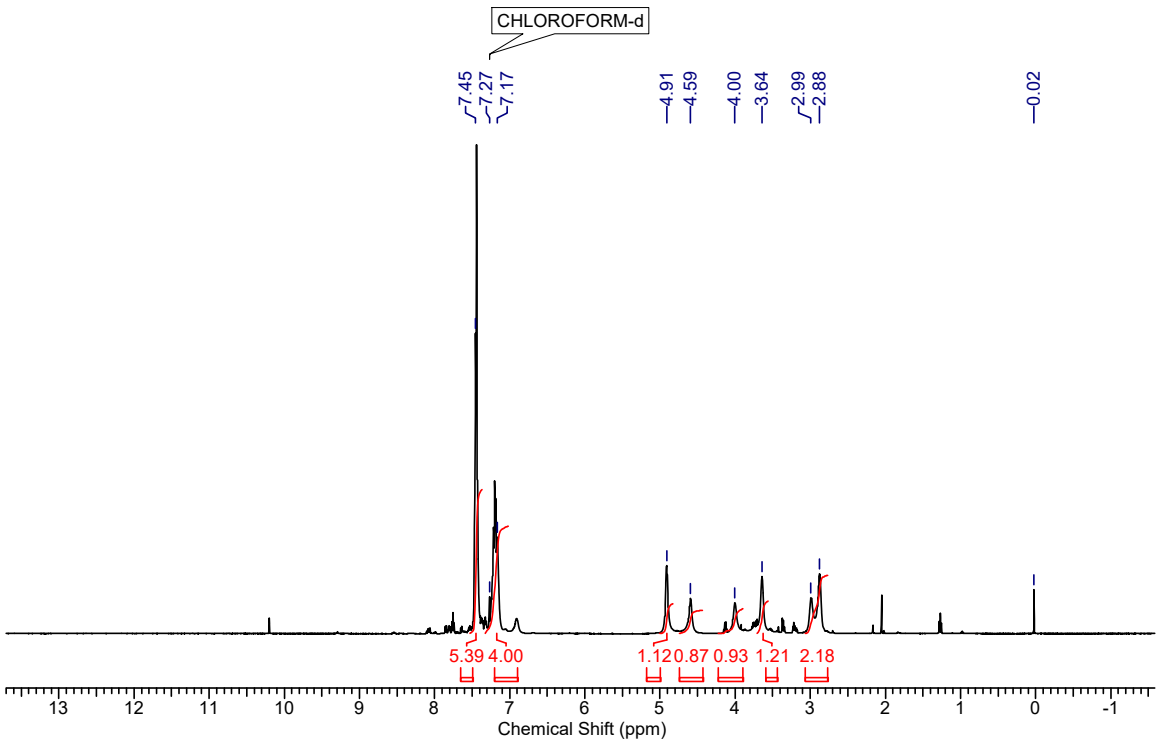
^{1}H NMR of N, N-dibenzylbenzamide (9c)



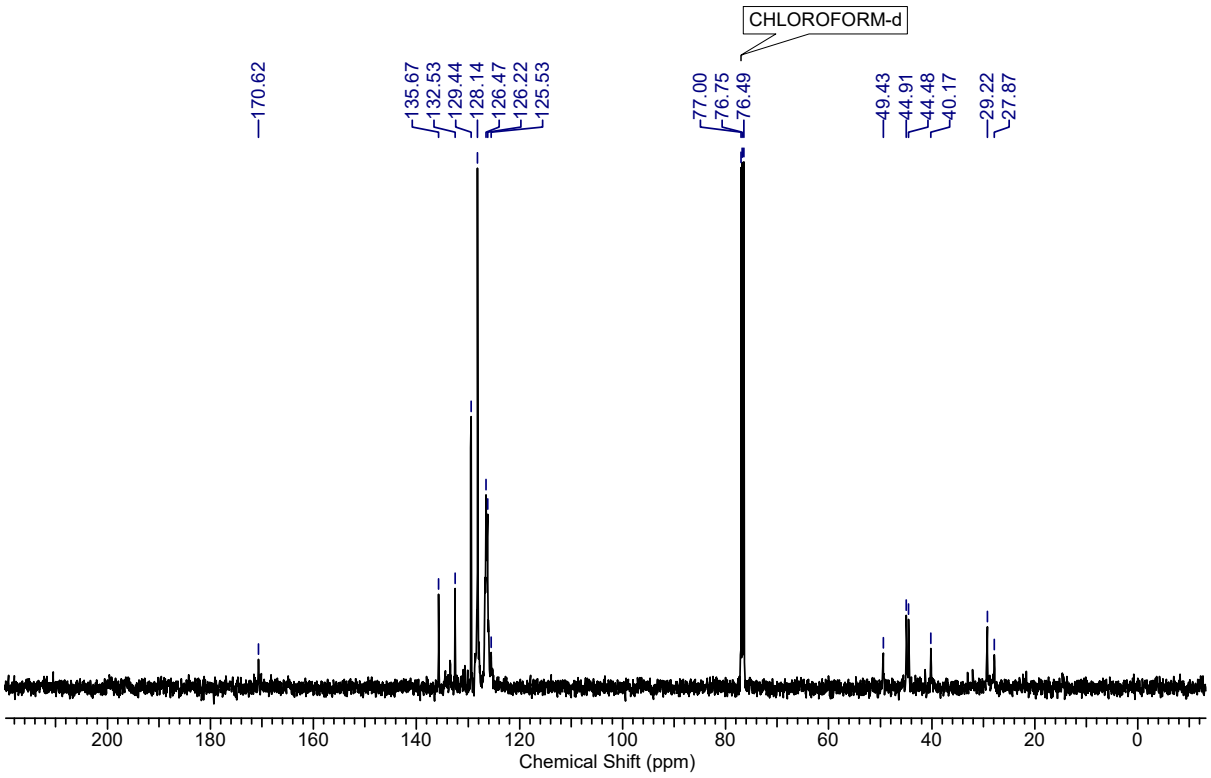
^{13}C NMR of N, N-dibenzylbenzamide (9c)



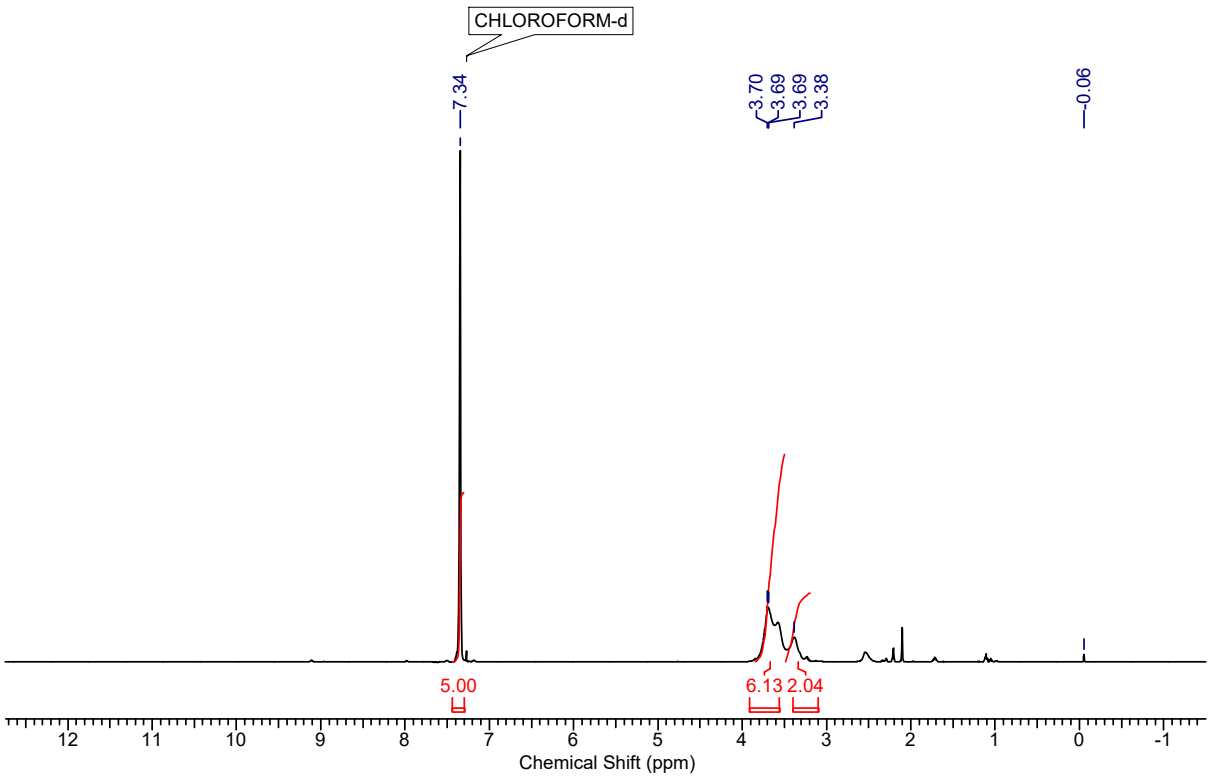
^{1}H NMR of (3, 4-dihydroisoquinolin-2(1H)-yl)(Phenyl)methanone (9d)



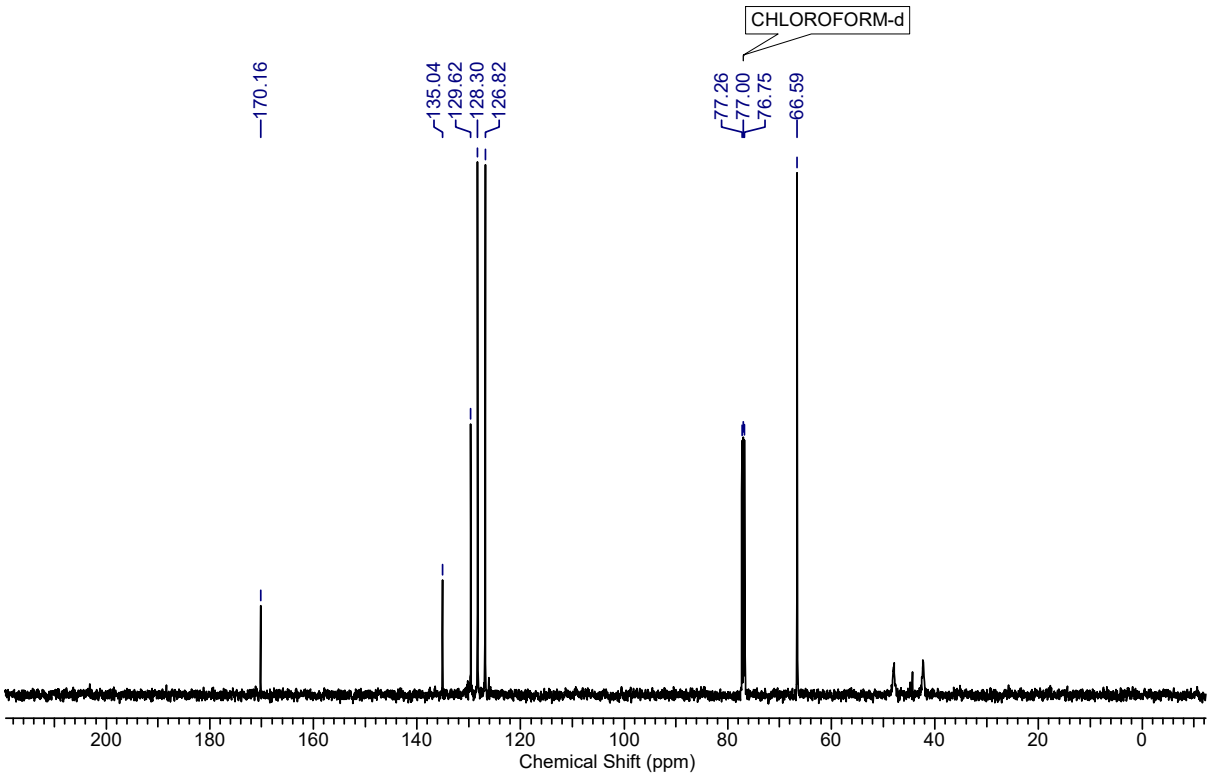
^{13}C NMR of (3, 4-dihydroisoquinolin-2(1H)-yl)(Phenyl)methanone (9d)



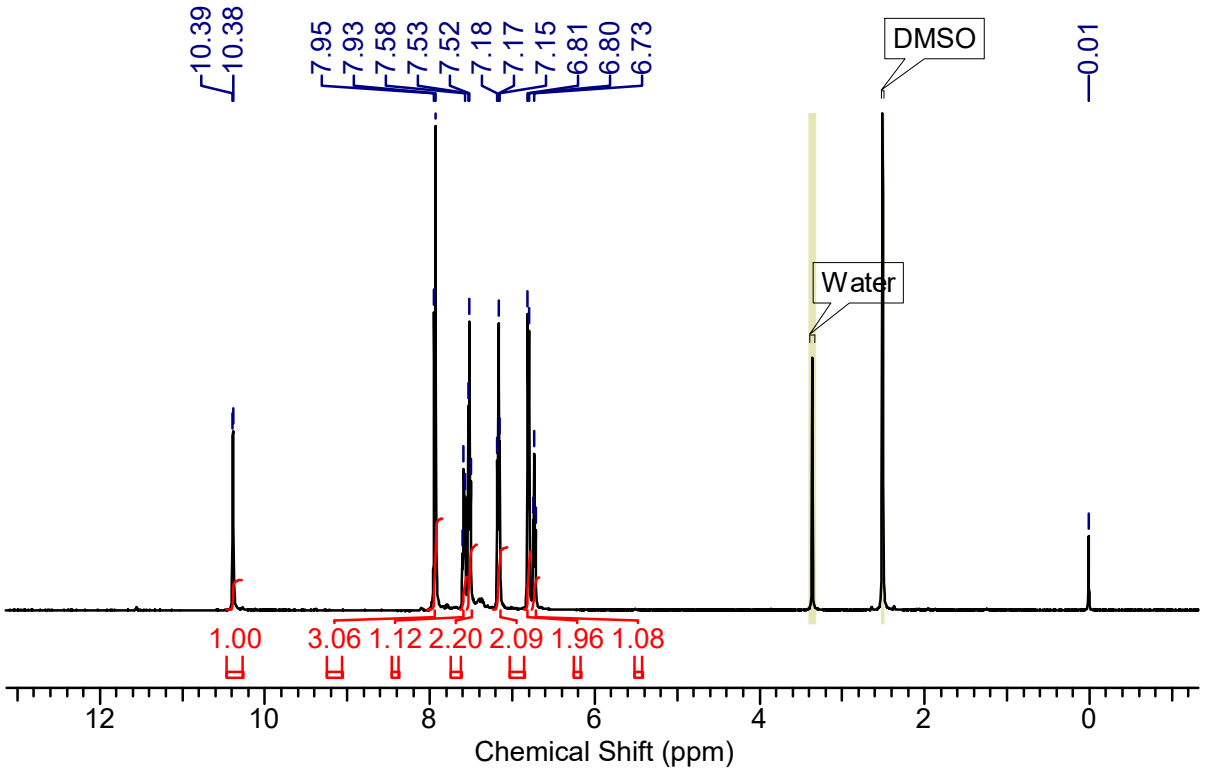
^{1}H NMR of morpholino(phenyl)methanone (9e)



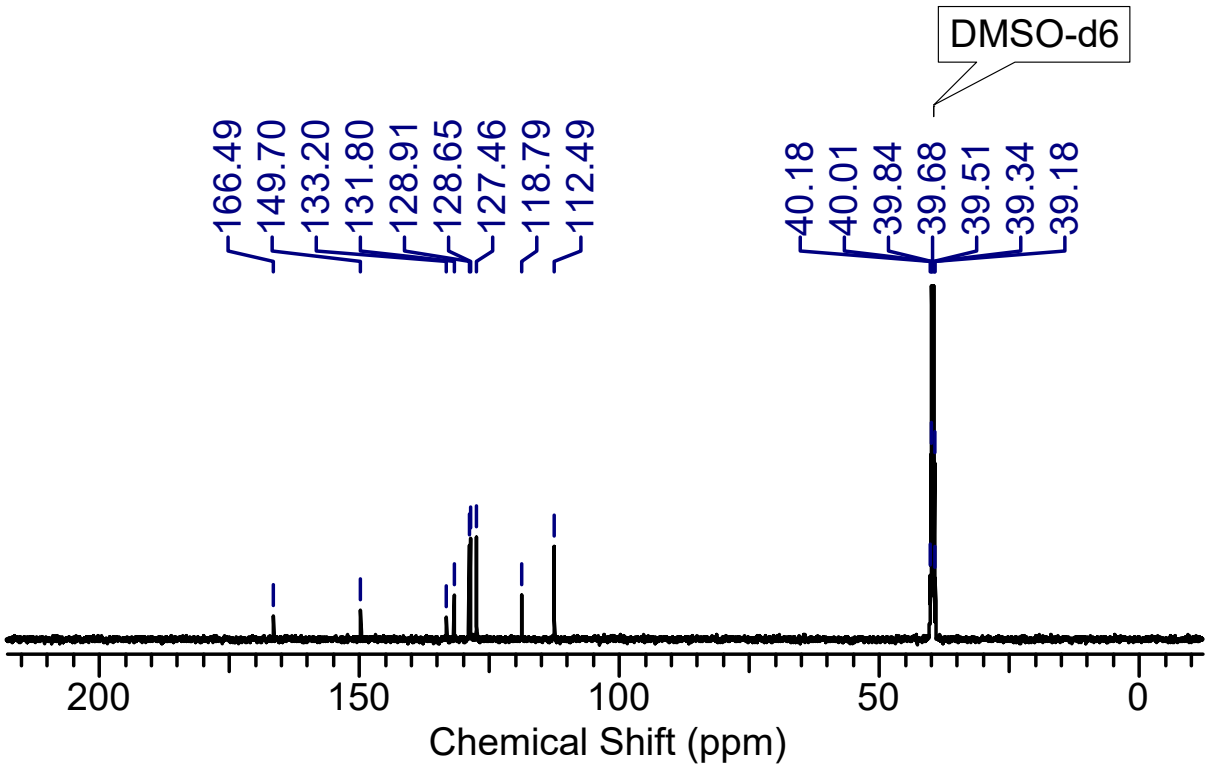
^{13}C NMR of morpholino(phenyl)methanone (9e)



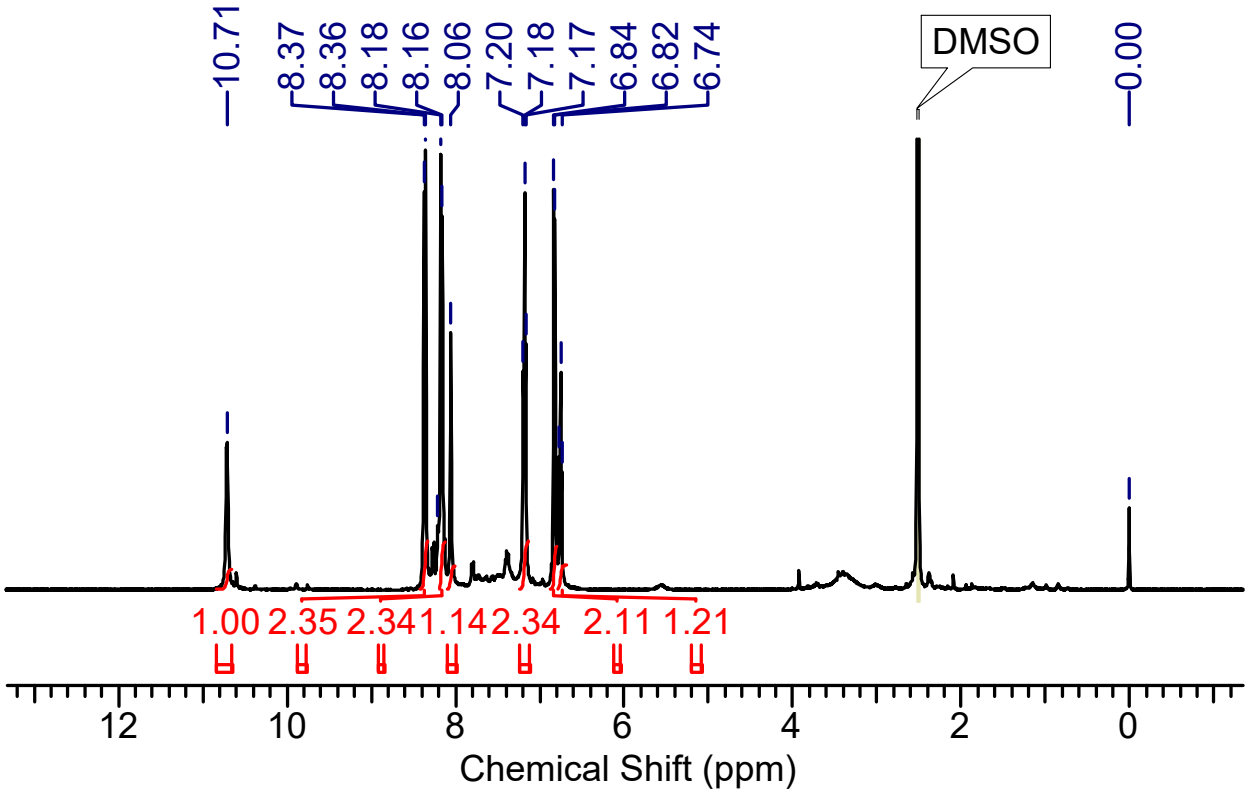
^{1}H NMR of N'-phenylbenzohydrazide (11a)



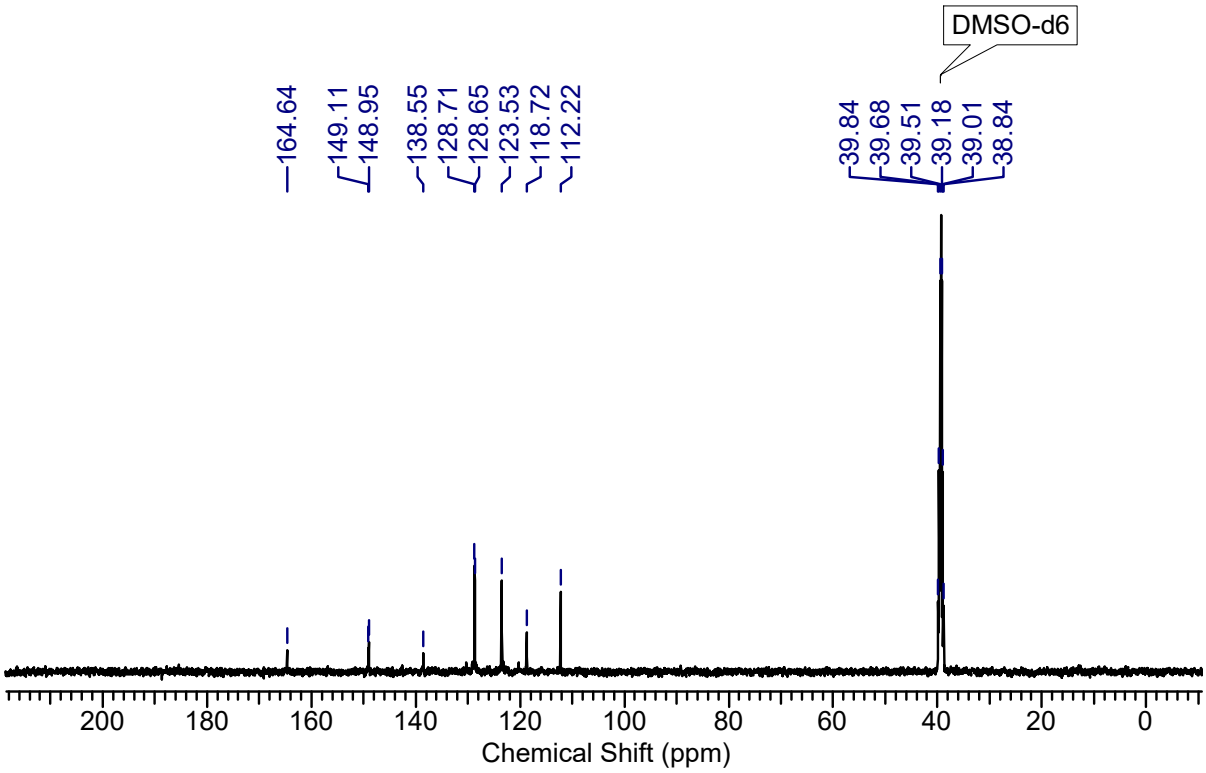
^{13}C NMR of N'-phenylbenzohydrazide (11a)



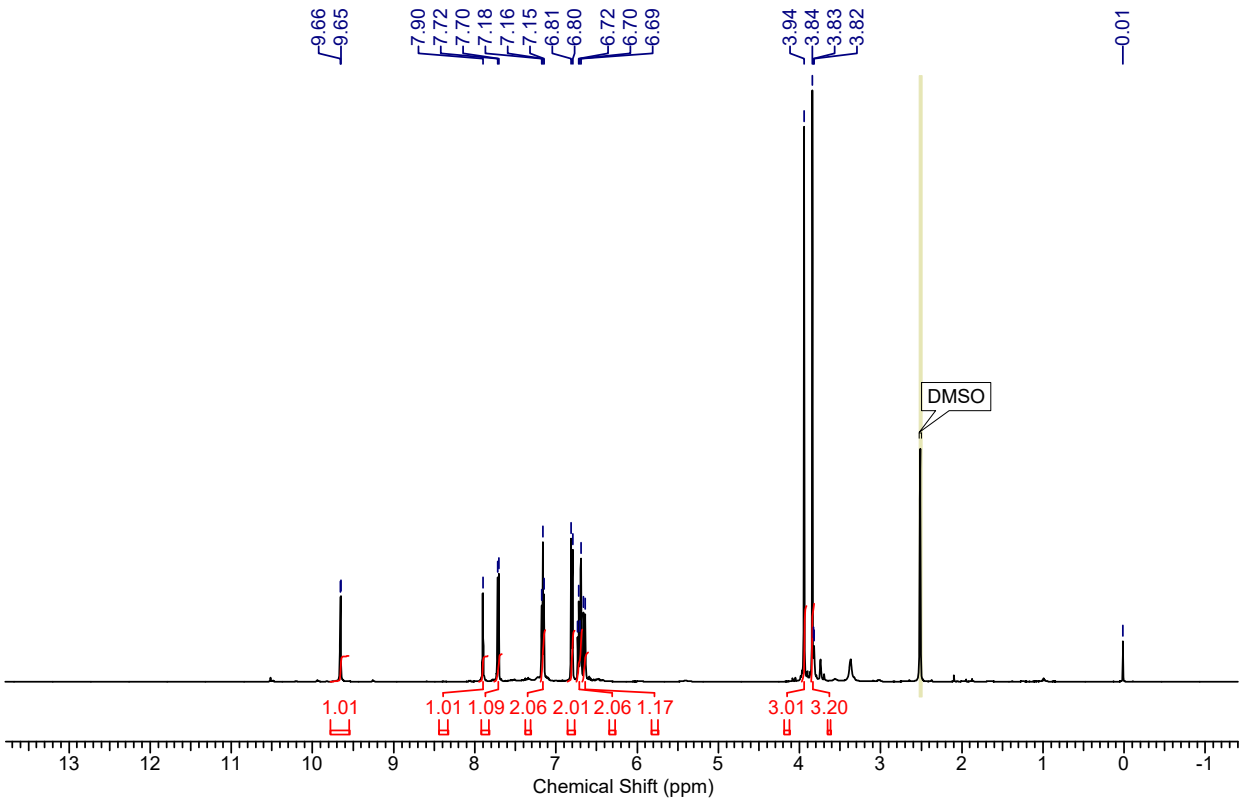
^{1}H NMR of 4-nitro-N'-phenylbenzohydrazide (11b)



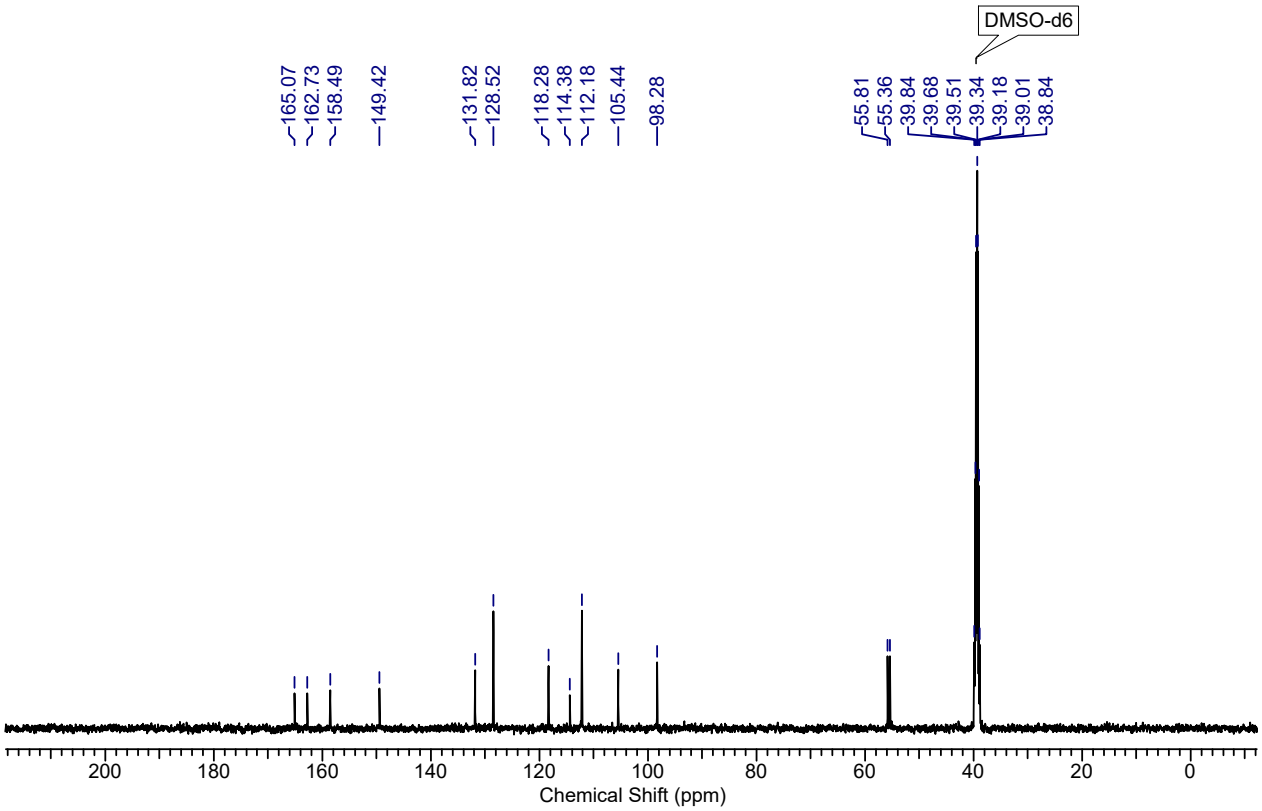
^{13}C NMR of 4-nitro-N'-phenylbenzohydrazide (11b)



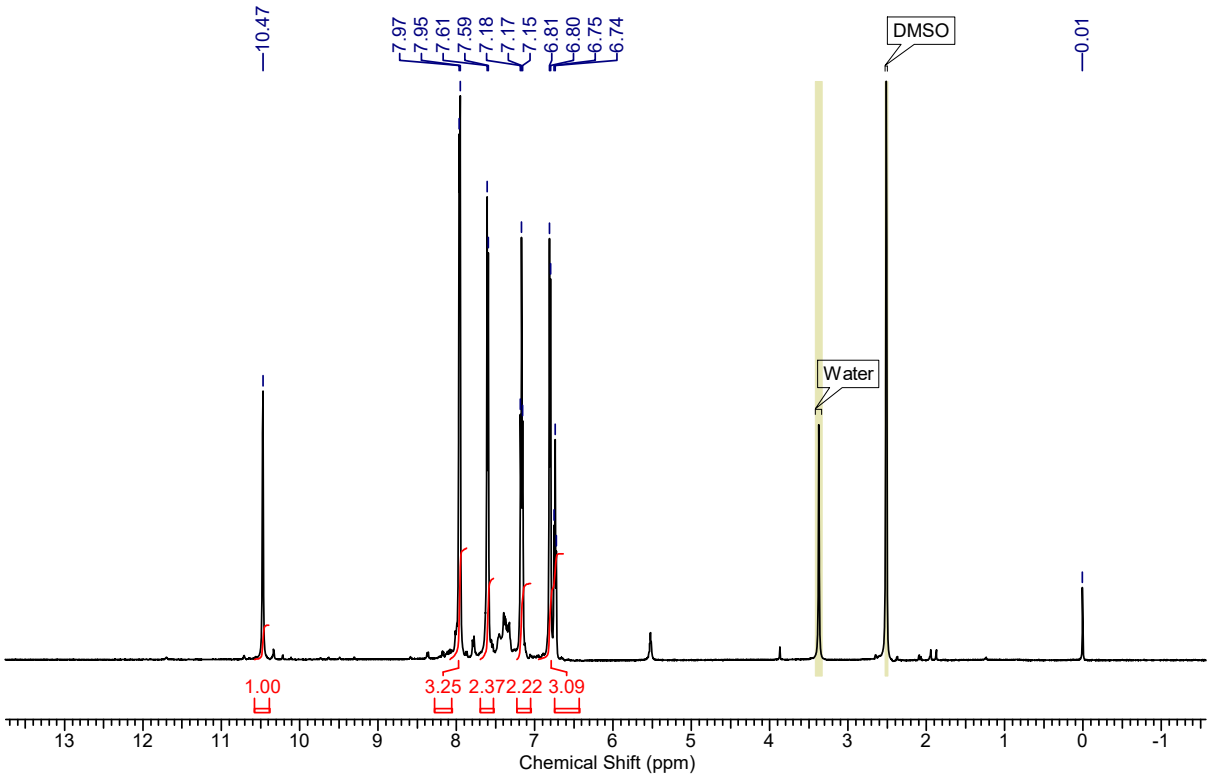
^{1}H NMR of 2, 4-dimethoxy-N'-phenylbenzohydrazide (11c)



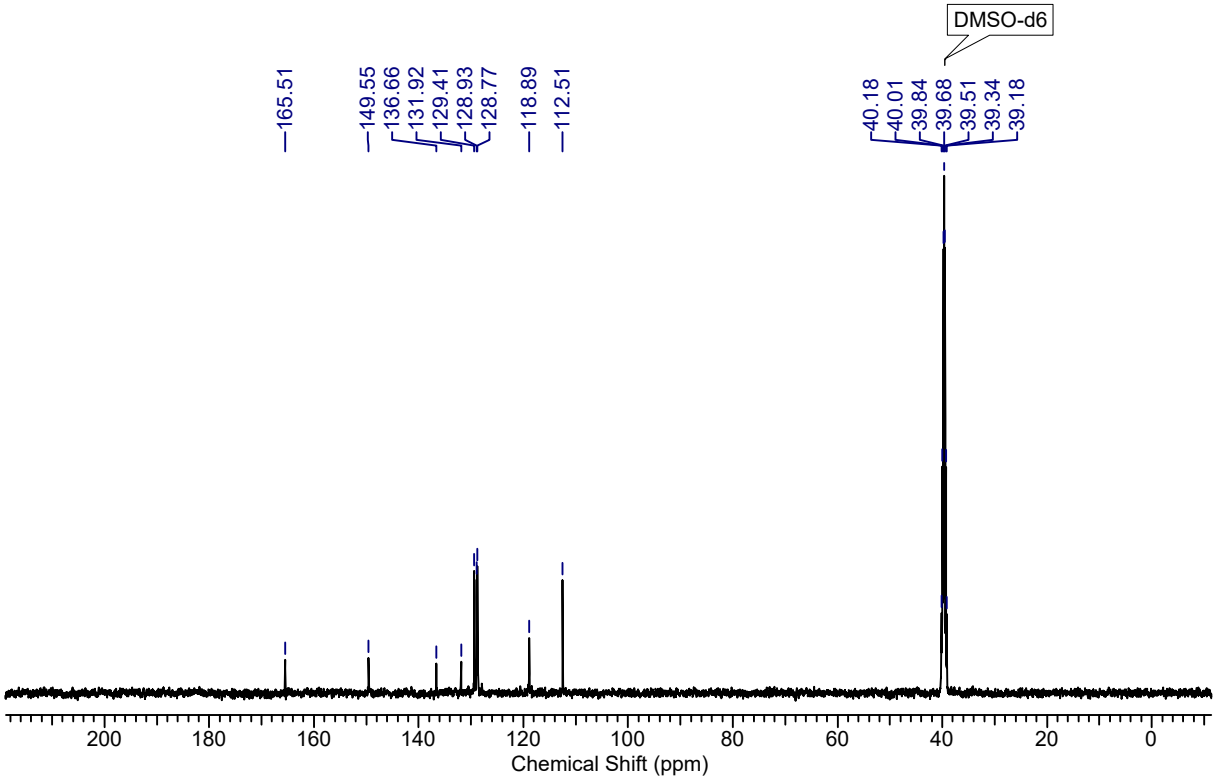
^{13}C NMR of 2, 4-dimethoxy-N'-phenylbenzohydrazide (11c)



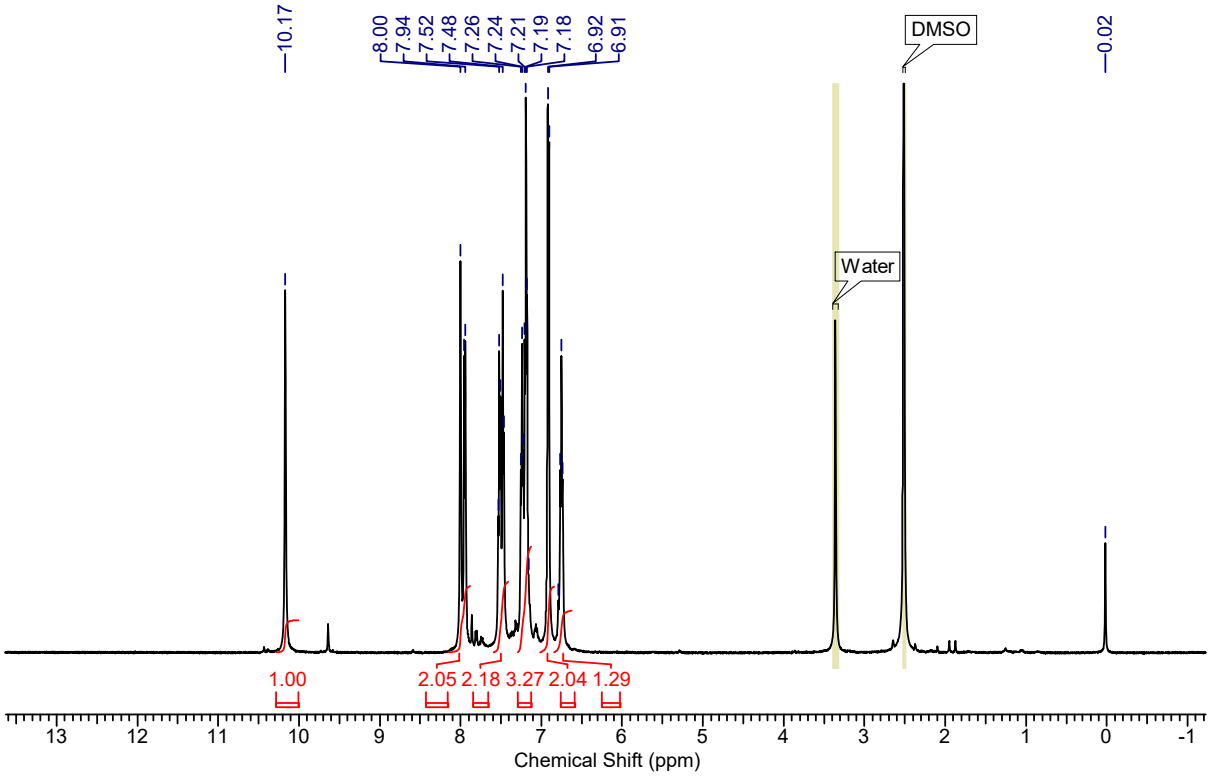
^{1}H NMR of 4-chloro-N'-phenylbenzohydrazide (11d)



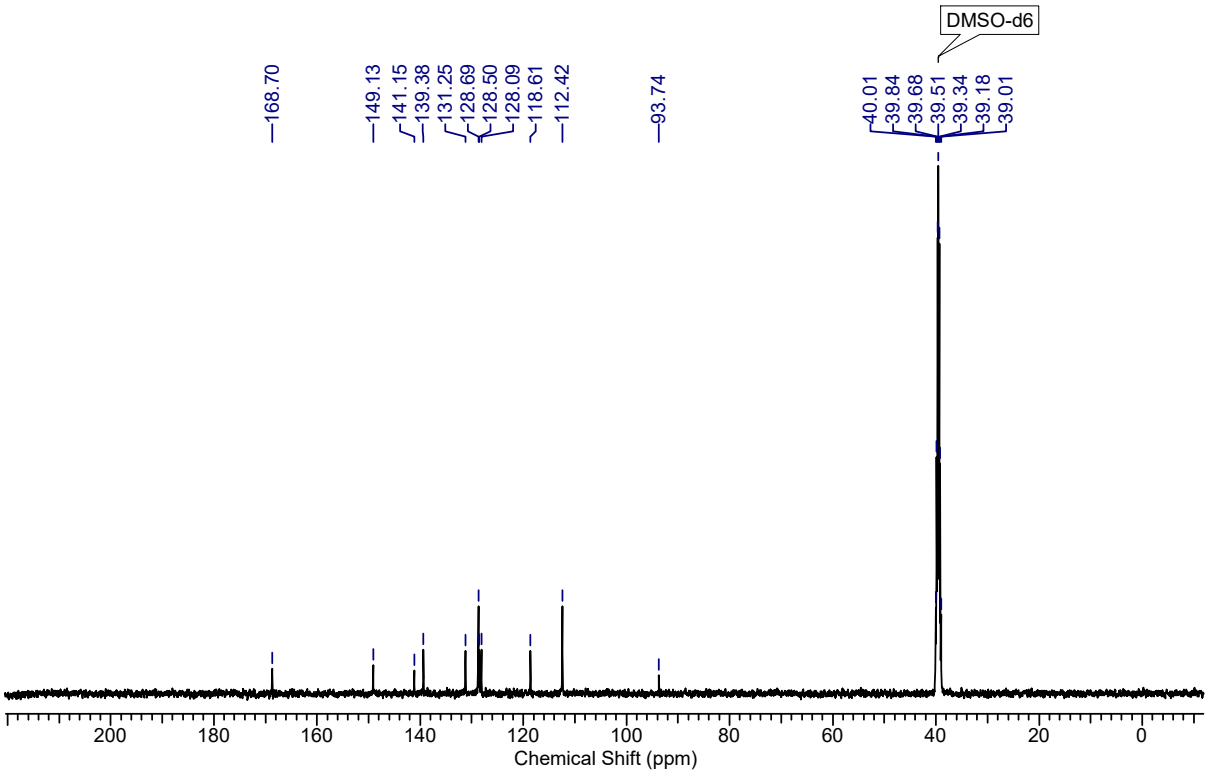
^{13}C NMR of 4-chloro-N'-phenylbenzohydrazide (11d)



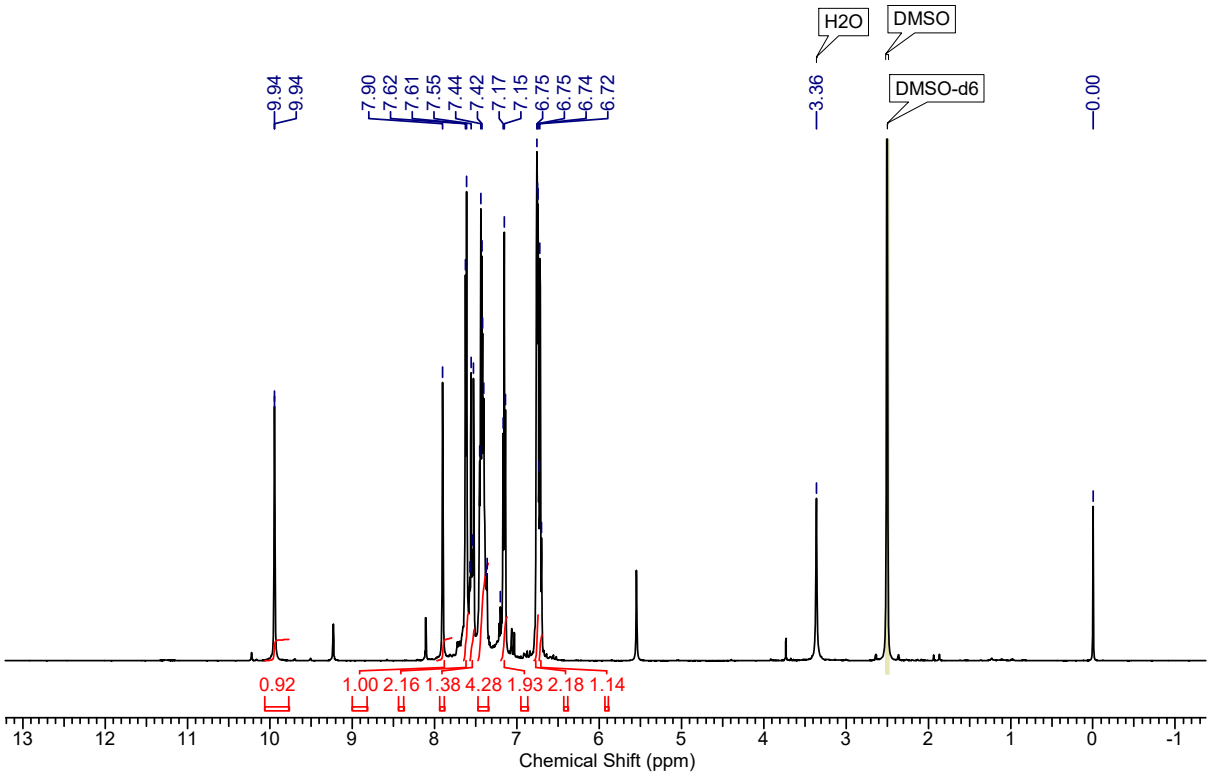
^{1}H NMR of 2-iodo-N'-phenylbenzohydrazide (11e)



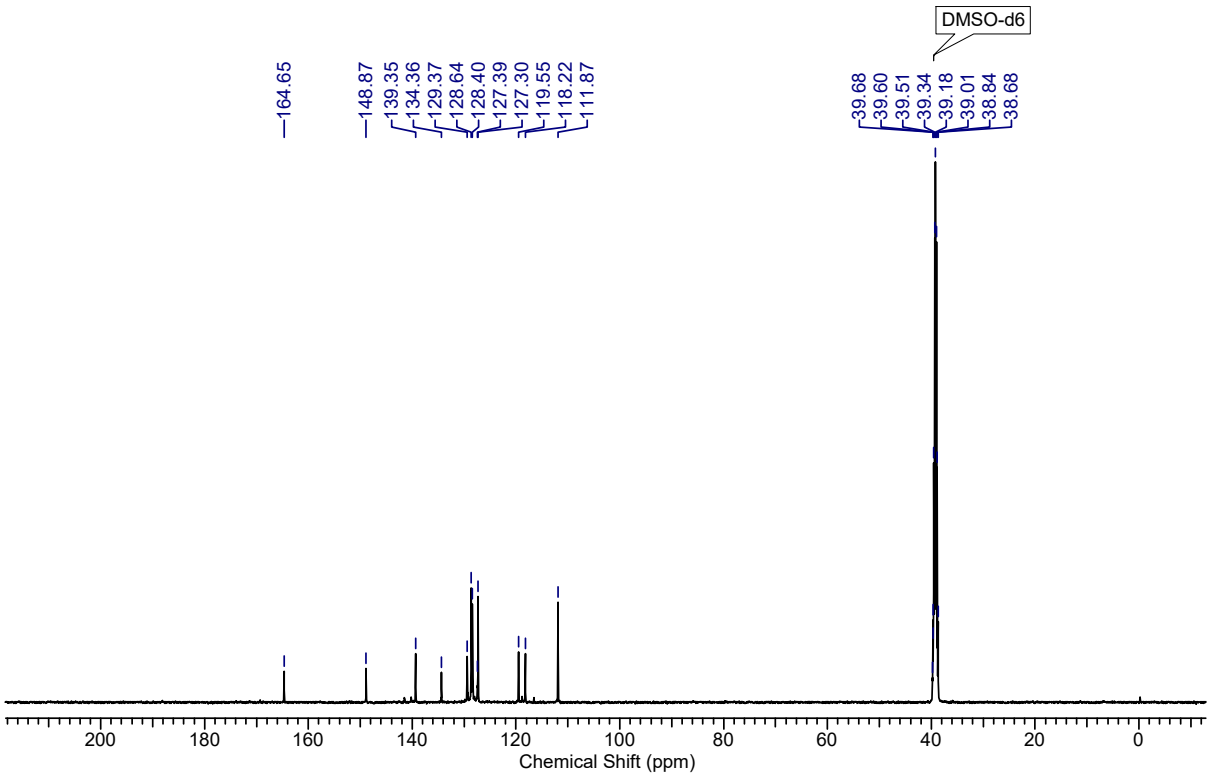
^{13}C NMR of 2-iodo-N'-phenylbenzohydrazide (11e)



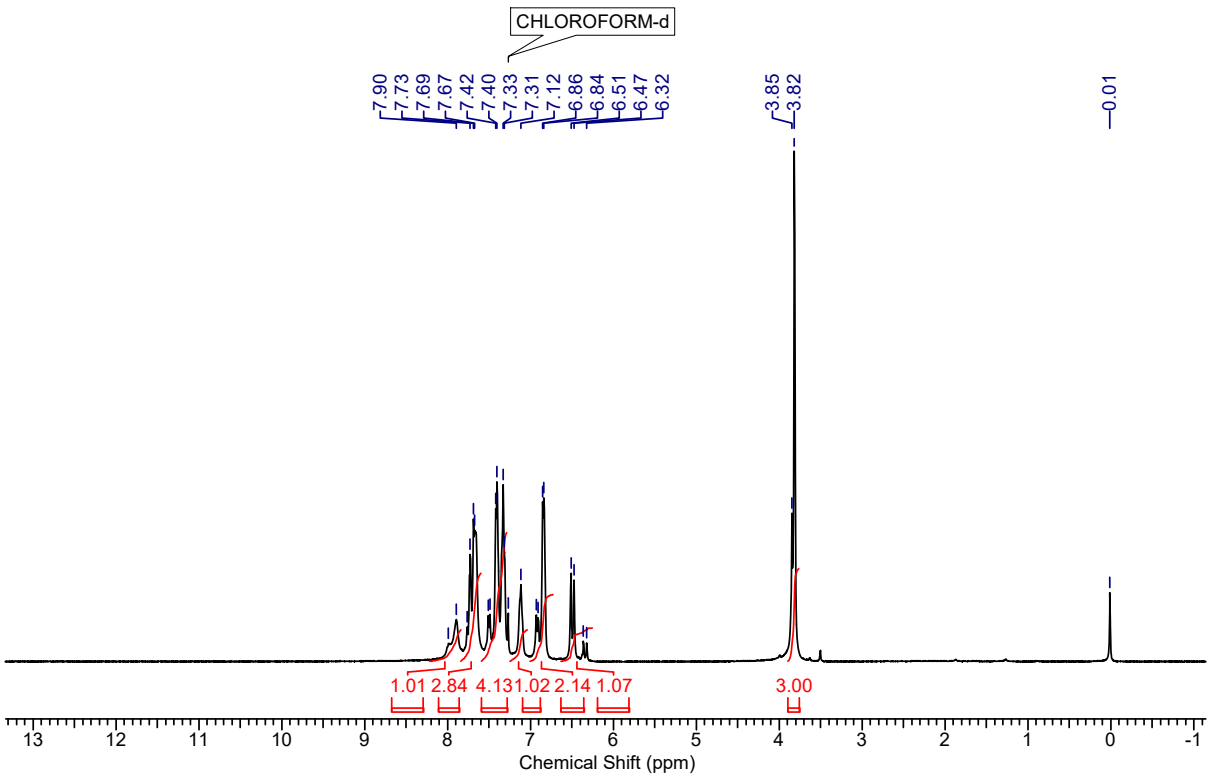
^{1}H NMR of N'-phenylcinnamohydrazide (11f)



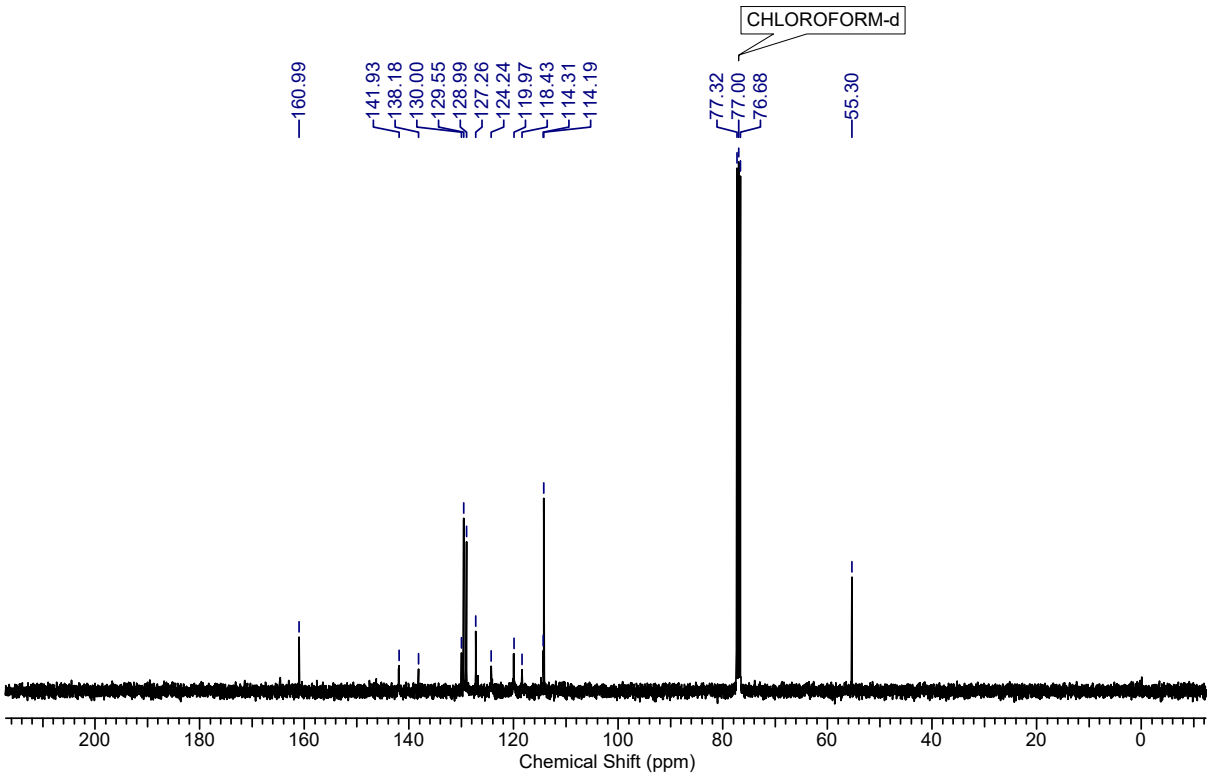
^{13}C NMR of N'-phenylcinnamohydrazide (11f)



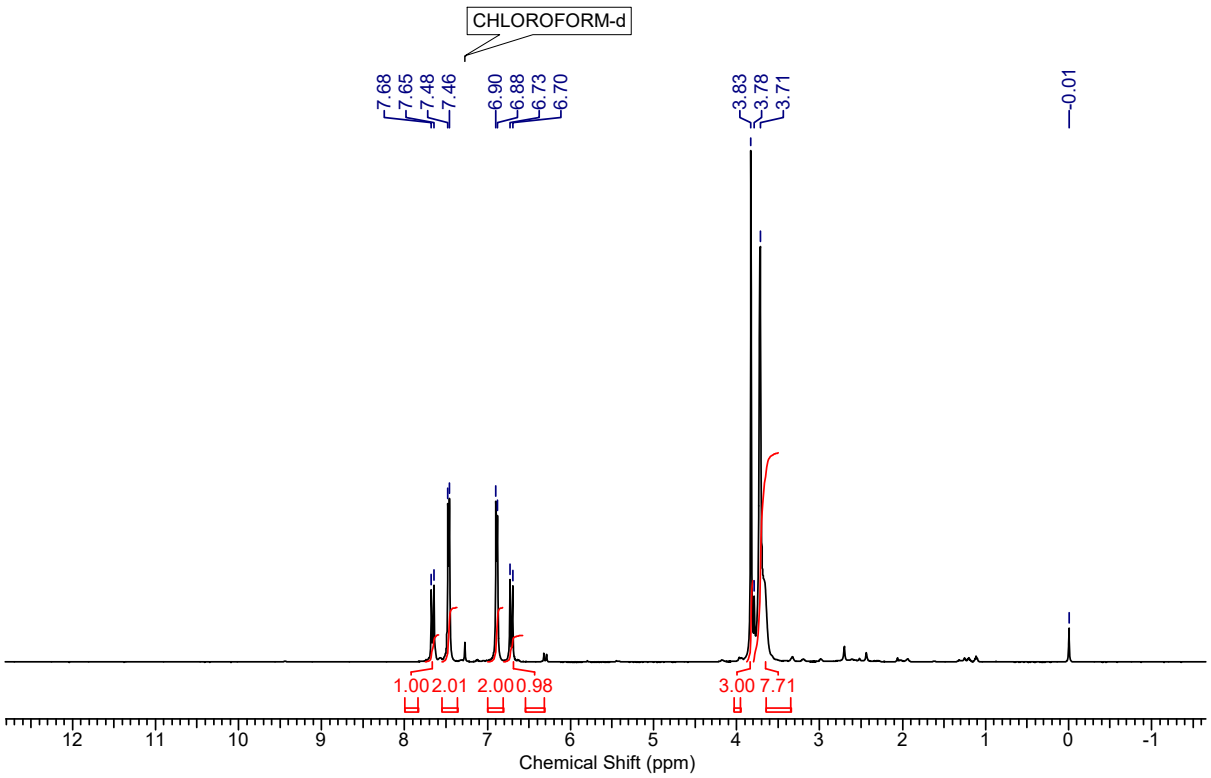
^{1}H NMR of (E)-3-(4-methoxyphenyl)-N-phenylacrylamide (13)



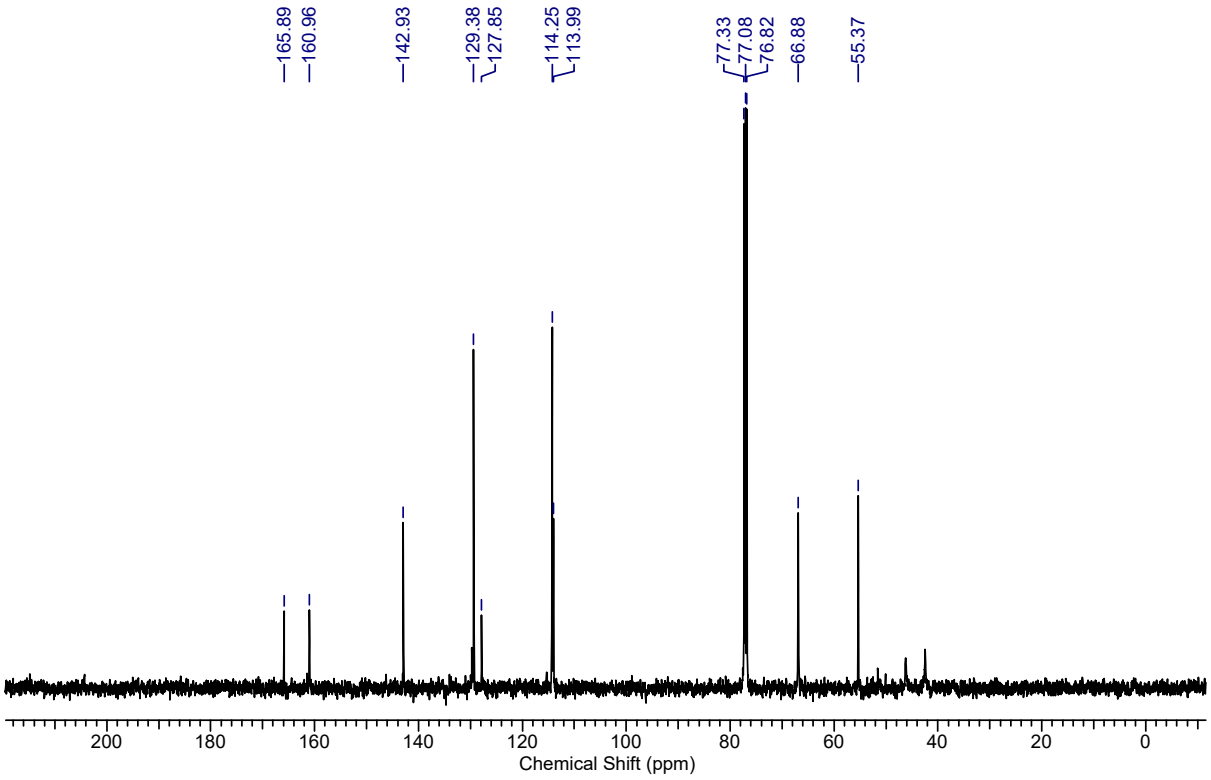
^{13}C NMR of (E)-3-(4-methoxyphenyl)-N-phenylacrylamide (13)



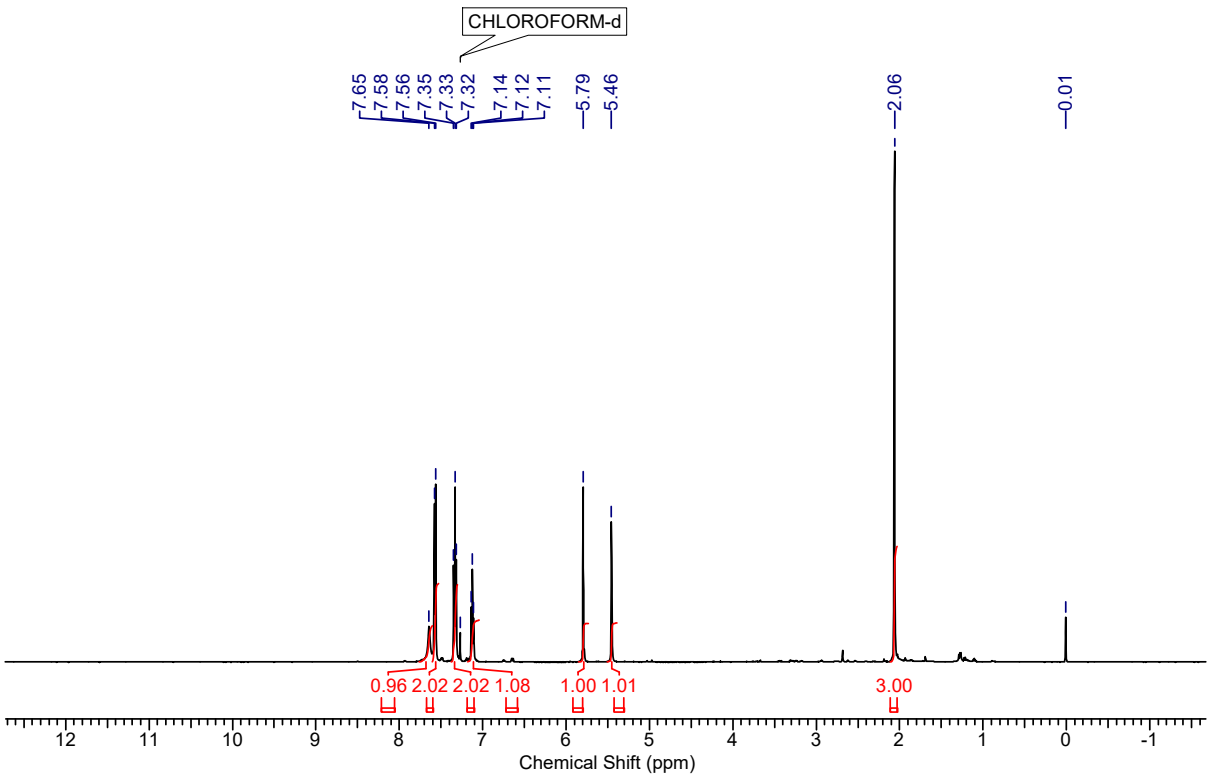
^{1}H NMR of (E)-3-(4-methoxyphenyl)-1-morpholinoprop-2-en-1-one (15)



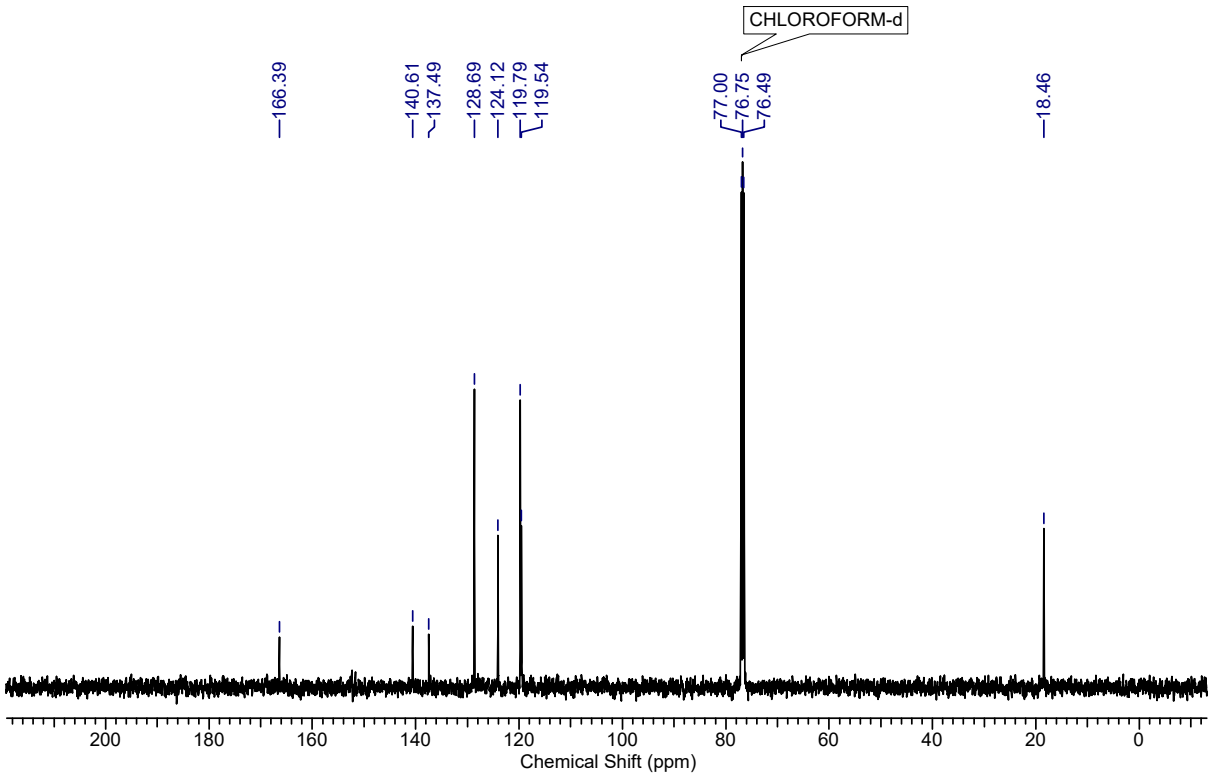
^{13}C NMR of (E)-3-(4-methoxyphenyl)-1-morpholinoprop-2-en-1-one (15)



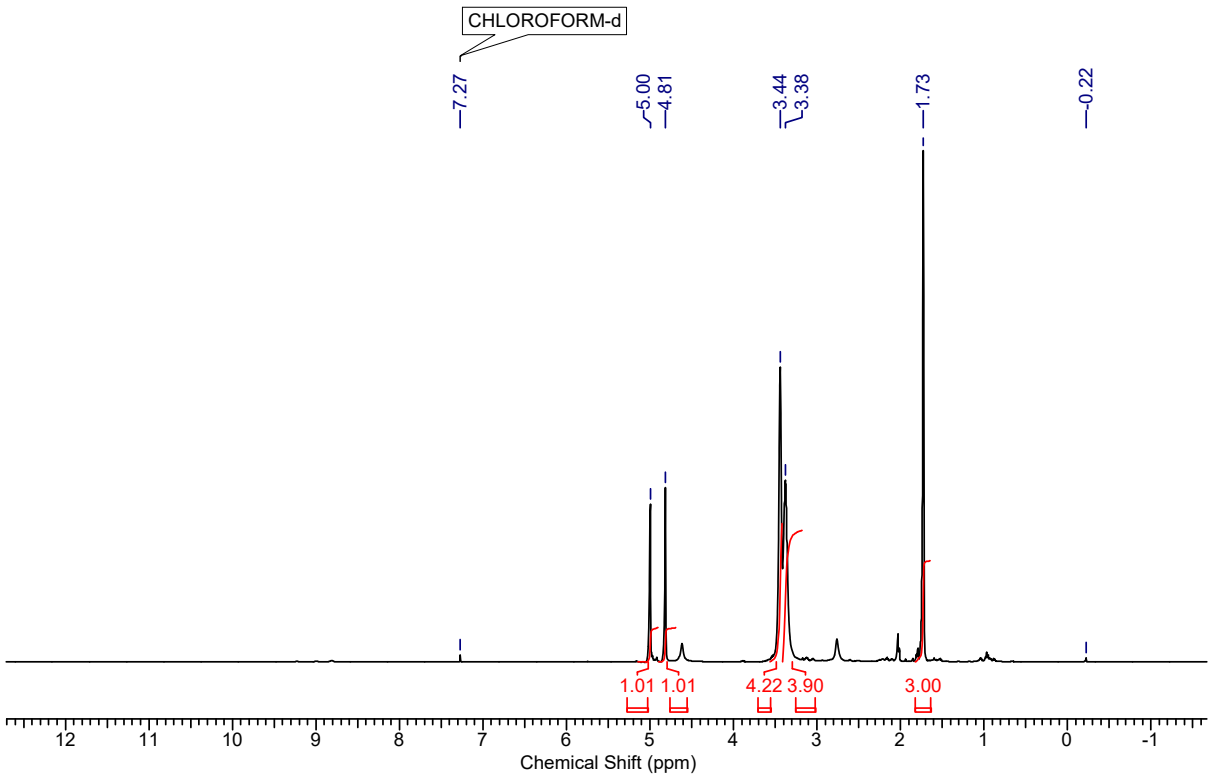
^{1}H NMR of N-phenylmethacrylamide (17)



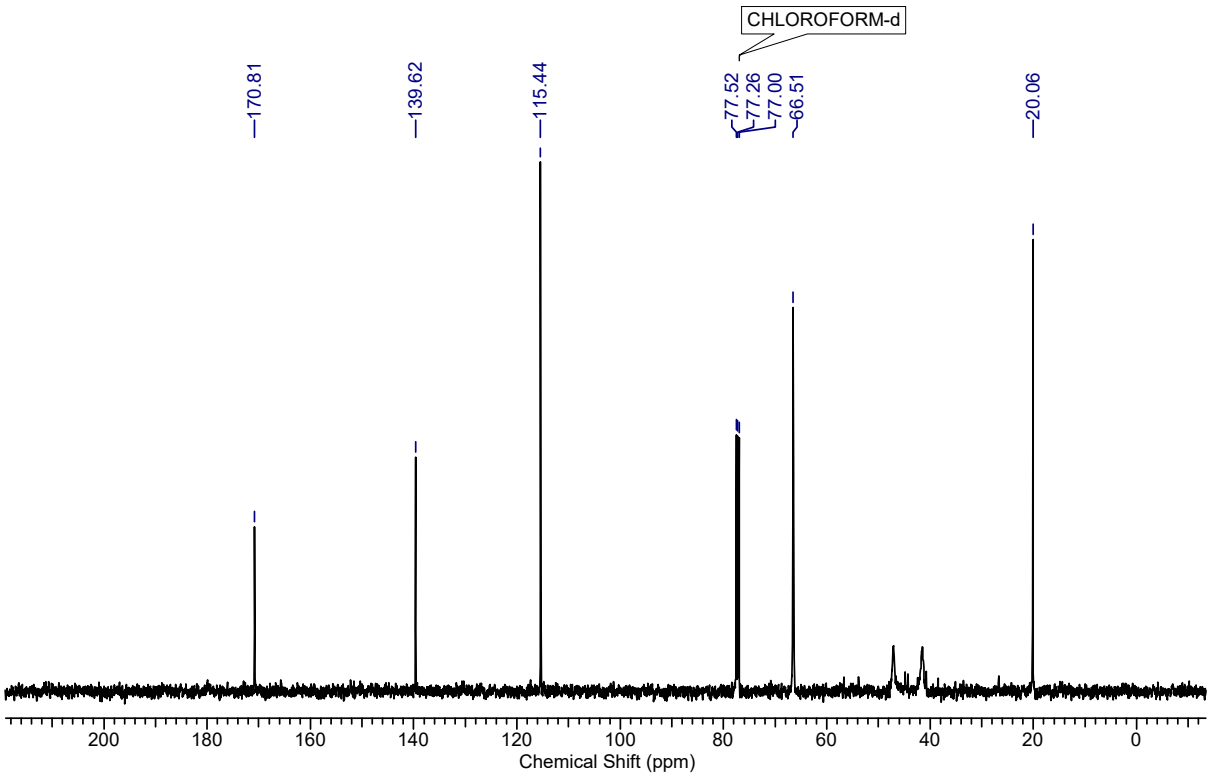
^{1}H NMR of N-phenylmethacrylamide (17)



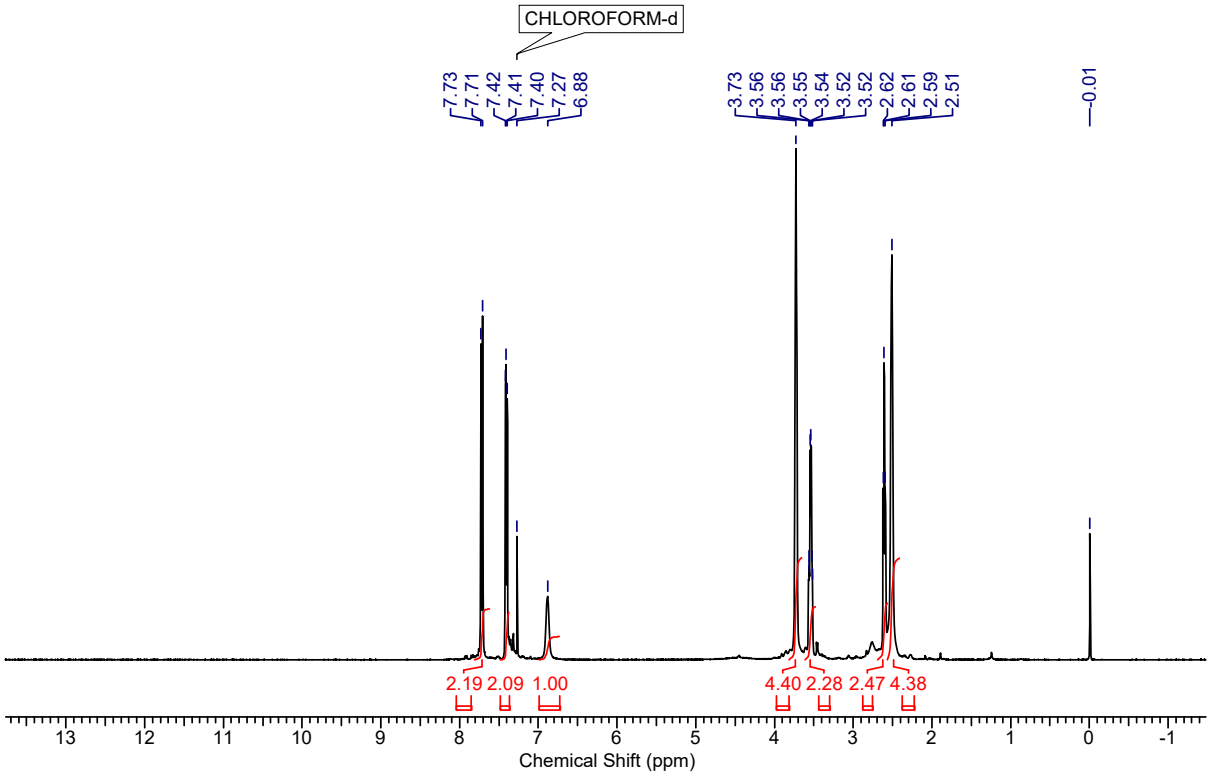
^{1}H NMR of 2-methyl-1-morpholinoprop-2-en-1-one (18)



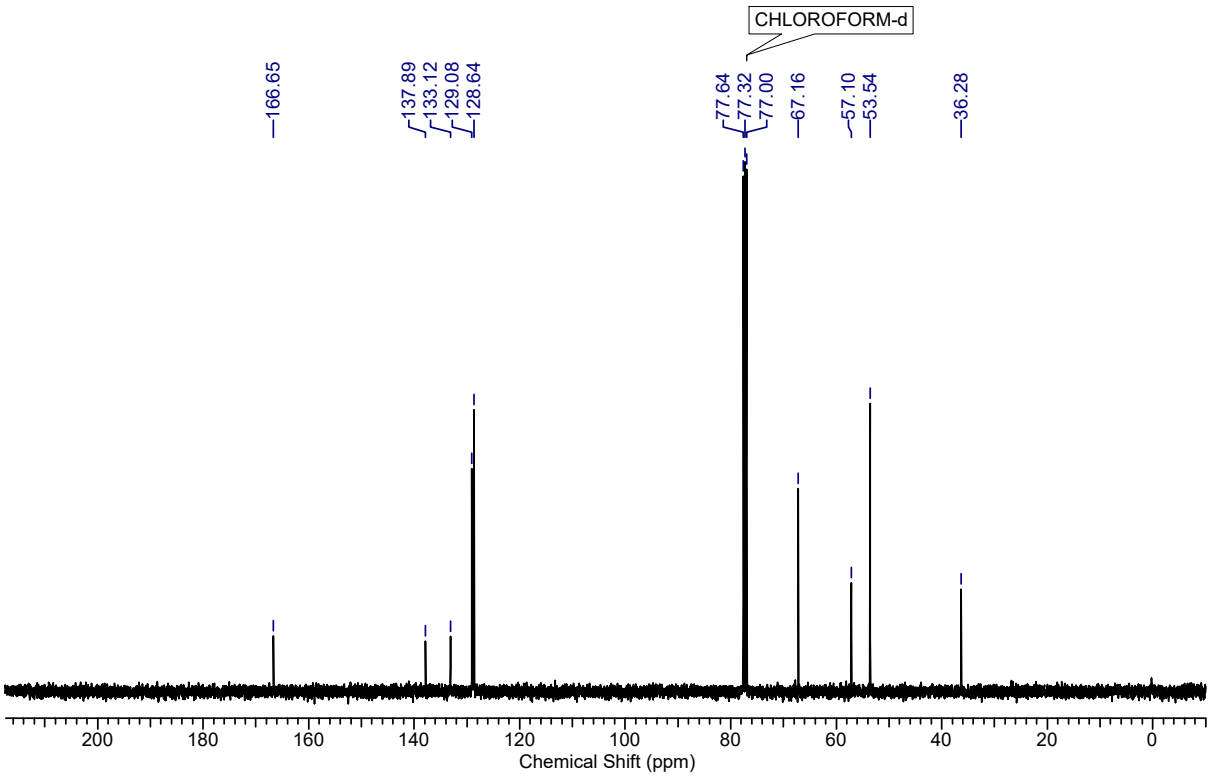
^{13}C NMR of 2-methyl-1-morpholinoprop-2-en-1-one (18)



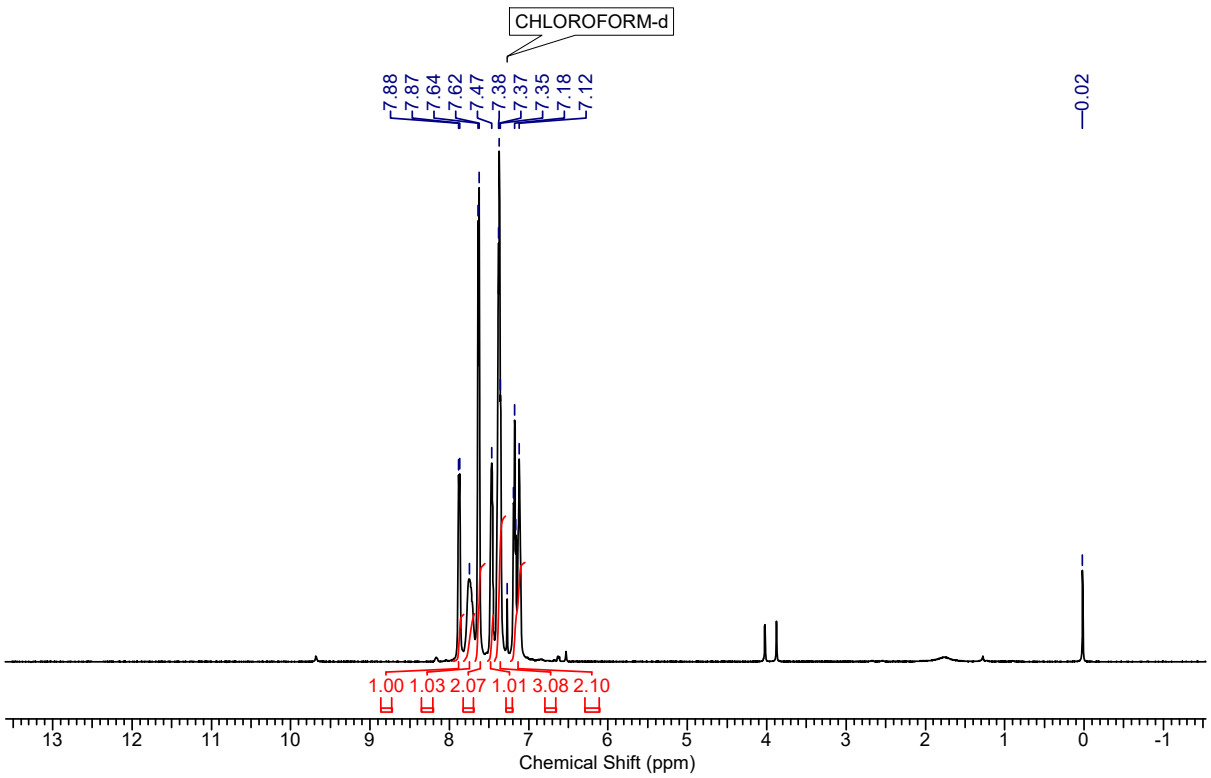
^{1}H NMR of 4-chloro-N-(2-morpholinoethyl)benzamide (moclobemide) (19)



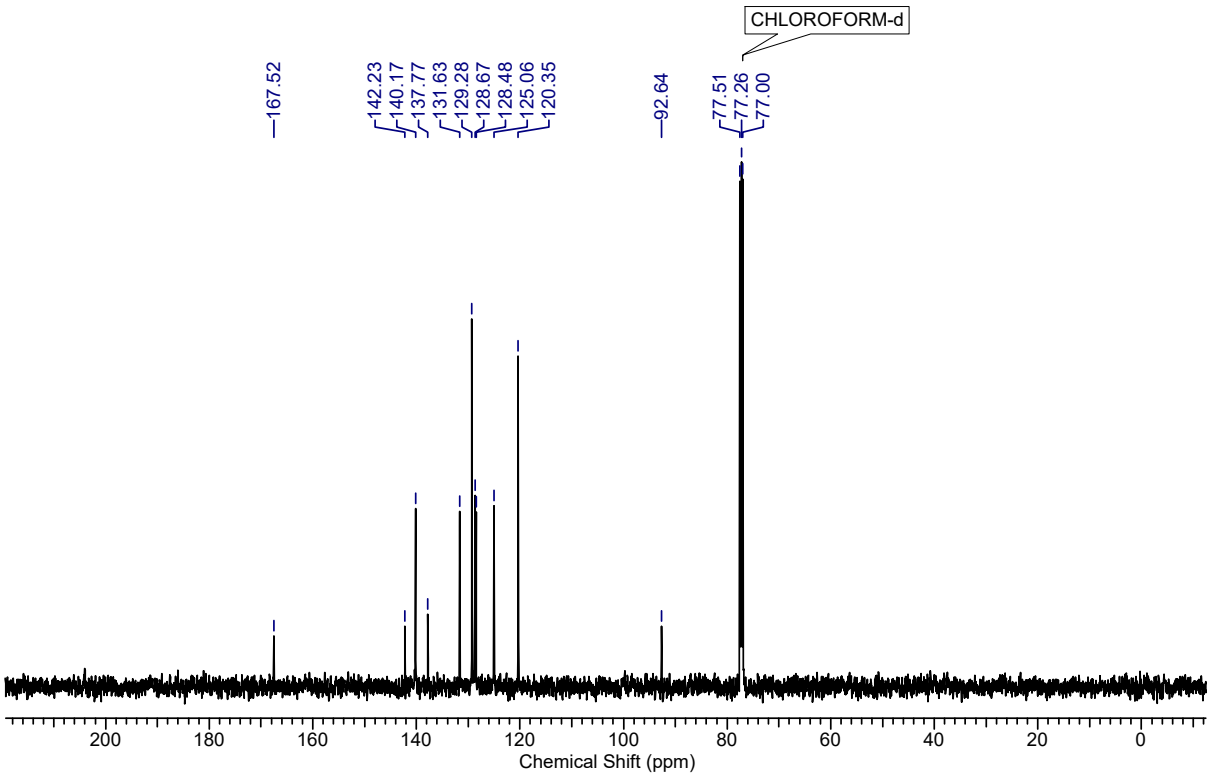
^{13}C NMR of 4-chloro-N-(2-morpholinoethyl) benzamide (moclobemide) (19)



^{1}H NMR of 2-iodo-N-phenylbenzamide (Benodanil) (20)



^{13}C NMR of 2-iodo-N-phenylbenzamide (Benodanil) (20)



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1. B. M. Sharma, R. S. Atapalkar and A. A. Kulkarni, *Green Chem* **2019,** *21*, 5639-5646.
2. M. S. Said, N. S. Khonde, M. N. Thorat, R. S. Atapalkar, A. A. Kulkarni, J. Gajbhiye, S. G. Dastager, *Asian J Org Chem* **2020**, *9*, 1022-1026