

PVP-Pd nanoparticles as efficient catalyst for nitroarene reduction under mild conditions in aqueous media

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Supplementary Material

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Experimental section

1. General Methods

All materials were commercially available and used as received. PdCl₂, KNO₃, PVP

[poly-(N-vinyl-2-pyrrolidone), $M_w = 10,000$ Da, HCl 35 %, p-chloronitrobenzene, o-chloronitrobenzene, nitrobenzene, p-nitroaniline, p-dinitrobenzene, o-nitrophenol, m-nitrophenol, methyl m-nitrobenzoate, p-nitroacetanilide, 2-chloro-3-nitropyridine, 5-nitroquinoline, styrene, 1,1-diphenylethylene, p-nitroacetophenone, p-chloroaniline, o-chloroaniline, nitrobenzene, p-aminoaniline, o-aminophenol, m-aminophenol, methyl m-aminobenzoate, p-aminoacetanilide, benzophenone, p-iodonitrobenzene, phenylboronic acid, benzaldehyde, di-tert-butyl dicarbonate ((Boc)₂O), ethanol 98 %, methanol HPLC grade, NaBH₄ (AF granules) 98%, Pd(AcO)₂, BINAP, K₃PO₄, K₂CO₃, KI, and Na₂SO₄ were used without purification. Silica gel (0.063-0.200 mm) was used in column chromatography. All solvents were analytical grade and distilled before use.

GC analyses were performed on a gas chromatograph with a flame ionization detector, equipped with VF-5 30 m x 0.25 mm x 0.25 μ m column. GC-MS analyses were performed on a GC/MS QP 5050 spectrometer equipped with a VF-5ms, employing a 30 m x 0.25 mm x 0.33 μ m. Ionization was achieved by electronic impact (70eV) and detection setup positive mode. ¹H and ¹³C NMR spectra were recorded at 400 MHz and 101 MHz respectively on a Brüker Advance II 400 spectrometer in CDCl₃, DMSO-d₆ or acetone-d₆. Coupling constants (*J*) are given in Hz. An Autolab PGSTAT100 (ECO CHEMIE) potentiostat was used for the synthesis of PVP-Pd NPs in the galvanostatic mode. The observation of PVP-Pd NPs by Transmission Electron Microscopy (TEM) was performed with a JEM-Jeol 1120 microscope operating at 80 kV, at the IFFIVE Research Institute, INTA, Córdoba, Argentina. In order to characterize NPs by TEM, samples were prepared depositing a drop of colloidal PVP-Pd NPs dispersion on a formvar-carbon coated copper grid and dried at room temperature. The total content of palladium was determined by Atomic Absorption in a Perkin Elmer Analyst 600, using ET (electro thermal mode with graphite furnace) at the ISIDSA Institute, Universidad Nacional de Córdoba, Córdoba, Argentina. Aqueous solutions were prepared from analytical grade chemicals and Milli-Q-Millipore water.

1.1. Galvanostatic synthesis of PVP-Pd NPs

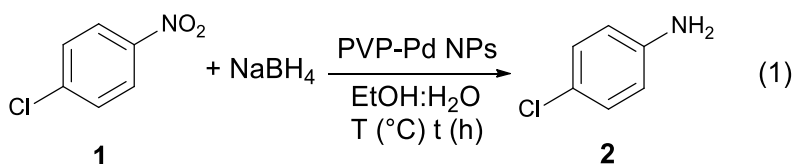
PVP-Pd NPs were electrochemically reduced on polycrystalline Pt disc electrode (geometric area = 0.0746 cm²) employing an aqueous solution of H₂PdCl₄ (0.5 mM) and KNO₃ (0.1 M) containing 16 g/L of poly-(N-vinyl-2-pyrrolidone) polymer (PVP 10 D) as the stabilizing agent by application of a constant current pulse. For that, the electrolyte was prepared by mixing 0.32 g of PVP with 20 mL of an aqueous solution of H₂PdCl₄ and KNO₃.

Complete dissolution of PVP required sonication of the mixture for 10 min. After that, the homogeneous yellow solution obtained was placed in a three electrodes cell and it was deoxygenated by bubbling nitrogen for about 15 min prior to each experiment. The electrochemical experiments were carried out in a glass electrochemical cell provided with a Pt disc working electrode, a very large area sheet of Pt (counter electrode) and a saturated calomel reference electrode. The galvanostatic synthesis of PVP-Pd NPs was performed by applying to the Pt electrode a current density pulse from 0 to a cathodic value of -150 mA cm^{-2} , during 600 seconds. Strong stirring of the solution (1000 rpm) with a magnetic stirrer was kept during the galvanostatic electrolysis. Under these conditions, an abrupt color change from yellow to a dark brown was observed since the first seconds of the galvanostatic pulse, indicating the formation of PVP-Pd NPs. After completion of the reaction the aqueous dispersion of PVP-Pd NPs was placed in a 25 mL volumetric flask to be used as catalyst.

1.2. Representative procedure for the nitroaromatic reduction by PVP-Pd NPs

The following reaction procedure is representative: into a 25 mL bottom round flask equipped with a magnetic stirrer, *p*-chloronitrobenzene **1** (0.25 mmol) was dissolved in EtOH (0.5 mL) and 0.90 mL of colloidal dispersion of PVP-Pd NPs were added. Finally, under vigorous stirring, a solution of 1 mmol of NaBH_4 in H_2O (2 mL) was dropped. At this stage, an intense colour change took place, and effervescence evolution was observed. After 15 minutes under vigorous stirring, a decolouration occurred. The reaction was stirred for 1 hour at room temperature. The mixture was finally diluted with water and then extracted three times with ethyl acetate (5 mL each). The reaction mixture was analysed by GC and GC-MS after being dried with anhydrous Na_2SO_4 . The amine product was compared with authentic samples by GC, GC-MS and ^1H NMR. The product was quantified by CG employing benzophenone as internal standard.

Table S1: Optimization of reaction conditions for Reduction of *p*-chloronitrobenzene (**1**) by PVP-Pd NPs and NaBH₄ in aqueous medium.



Entry	PVP-Pd NPs (mol %)	NaBH ₄ Equiv.	Amine 2 (% Yield) ^b	Conversion (%) ^c
1	0	1.5	0	0
2	0.05	1.5	5	53
3	0.05	3	37	100
4	0.1	1.5	10	74
5	0.1	3	70	93
6	0.1	4	94	98

^a Reaction conditions: 0.25 mmol of **1**, NaBH₄, PVP-Pd NPs, a mixture of EtOH: H₂O 1:6 (final volume 3.5 mL), room temperature, 1 hour. ^b The reaction mixture was extracted with ethyl acetate and quantified by GC analysis with benzophenone as internal standard. ^c Determined based on substrate **1**.

Several reactions were analysed by HPLC. In these cases, once the reaction was completed, MeOH HPLC grade was added until final dilution of 1:100. Then, 1 mL of this solution was filtered and analysed in HPLC equipment, using the external standard method for quantifying the amine products.

For competition reactions: when performing a competition reaction, the same procedure was followed, incorporating alkene 1,1-diphenylethene (**14**) together with *p*-chloronitrobenzene **1**, before adding NaBH₄.

1.3. Representative procedure for one-pot synthesis of *p*-aminebiphenyl (**16**), by consecutive Suzuki- nitro hydrogenation reaction catalyzed by PVP-Pd NPs

For Suzuki cross-coupling reaction: into a 25 mL bottom round flask equipped with a magnetic stirrer, *p*-iodonitrobenzene (0.25 mmol) was dissolved in EtOH (0.5 mL). Then phenylboronic acid (0.375 mmol), K₃PO₄ (1 mmol) and 1 mL of water were added. Finally, 0.90 mL of colloidal dispersion of PVP-Pd NPs were added. The reactions was stirred overnight at 50 °C. After this, the mixture was cooled down before proceeding with the hydrogenation reaction. Hydrogenation of *p*-nitrobiphenyl: to the previous reaction mixture,

EtOH (0.5 mL) and 2 mmol of NaBH₄ in H₂O (4 mL) were dropped. After 45 minutes under vigorous stirring, a decolouration occurred. The reaction was stirred for 2 h at room temperature. Finally, the mixture was diluted with water and then extracted three times with ethyl acetate (5 mL each). The reaction mixture was analysed by GC and GC-MS after being dried with anhydrous Na₂SO₄. The amine product was compared with authentic samples by GC, GC-MS and ¹H NMR. The *p*-aminebiphenyl (**16**) was isolated by column chromatography on silica gel eluting with pentane:ethyl acetate gradient (100:00→70:30), obtained as a yellow solid.

*1.4. Representative procedure for the synthesis of N-protected arylamines with benzaldehyde (**17**) or di-tert-butyl dicarbonate (**18**).*

After the hydrogenation protocol was performed over *p*-chloronitrobenzene **1** (section 1.2), 0.75 mmol of benzaldehyde (**17**) or di-tert-butyl dicarbonate (**18**) were added to the mixture. The reaction was stirred for 3 h at room temperature. The mixture was finally diluted with water and then extracted three times with ethyl acetate (5 mL each). The reaction mixture was analysed by GC and GC-MS after being dried with anhydrous Na₂SO₄. The N-protect amine product was compared with authentic samples by GC, GC-MS and ¹H NMR. Imine product **19** was purified by sublimation in a Buchi microdistillation system at 70 °C, obtained as a white solid. N-Boc protect amine **20** was isolated by column chromatography on silica gel eluting with pentane:ethyl acetate gradient (100:00→70:30), obtained as a pale-yellow solid.

*1.5. Representative procedure for the synthesis of N2-(4-chlorophenyl)pyridine-2,3-diamine (**22**)*

Catalytic amination of 2-chloro-3-nitropyridine: in a Schlenk tube, *p*-chloroaniline **2** (0.25 mmol), 2-chloro-3-nitropyridine **23** (0.25 mmol), K₂CO₃ (1mmol), Pd(AcO)₂ (2 mol%), BINAP (2 mol%), KI (3 mol%), and toluene (1 mL) were placed together with a magnetic stirrer. The reaction was stirred for 24 h at 110 °C in an oil bath. To elaborate the reaction, the mixture was diluted with water, and then extracted three times with ethyl acetate (5 mL each). The reaction mixture was analysed by GC and GC-MS, after being dried with anhydrous Na₂SO₄. Nitro compound **21** was isolated by crystallization from a water:acetone 5:1 mixture as a brown solid compound.

Catalytic hydrogenation of N-(4-chlorophenyl)-3-nitropyridin-2-amine (**21**) by PVP

Pd-NPs: into a 25 mL bottom round flask equipped with a magnetic stirrer, nitro **21** (0.25 mmol) was dissolved in EtOH (0.5 mL) and 0.90 mL of colloidal dispersion of PVP-Pd NPs were added. After that, a solution of 2 mmol of NaBH₄ in H₂O (4 mL) was dropped. After 45 minutes under vigorous stirring, a decolouration occurred. The reaction was stirred for 2.5 h at room temperature. The mixture was finally diluted with water and then extracted three times with ethyl acetate (5 mL each). To isolate amine product **22**, column chromatography on silica gel eluting with pentane:ethyl acetate gradient (100:00→70:30), obtaining amine **22** as an orange solid.

1.6 Catalyst reuse experiment in nitroaromatic hydrogenations by PVP-Pd NPs

In order to perform the reuse test of PVP-Pd nanocatalyst, after carried out the hydrogenation reaction following the procedure previously described in Section 2.1 with 0.2 mol % of Pd, the same reaction mixture was used by addition of fresh amounts of reactants. The experiment was performed five times by consecutive addition of a new batch of *p*-chloronitrobenzene (**1**, 0.25 mmol), NaBH₄ (1 mmol), EtOH (0.5 mL) and water (2 mL). The reaction mixture was stirred at room temperature for 1 h. After this time, the reaction was monitored by CG analyses and no *p*-chloronitrobenzene (**1**) was observed in the reaction mixture after each catalytic.

In order to characterize NPs before and after the catalysis, TEM micrographs analysis was performed. For that, after one reaction cycle the mixture was extracted. Then, aqueous phase was concentrated and centrifuged over 20 minutes in order to obtain a NPs pellet. This pellet was dispersed on milli-Q water, and a drop of colloidal PVP-Pd NPs was deposited on a formvar-carbon coated cooper grid and dried at room temperature. The original colloidal dispersion of PVP-Pd NPs was also centrifuged before deposit a drop of colloidal PVP-Pd NPs dispersion on a formvar-carbon coated cooper grid for TEM measurement.

Figure S1: TEM micrograph of PVP-Pd NPs before their use in nitroaromatic hydrogenation reaction.

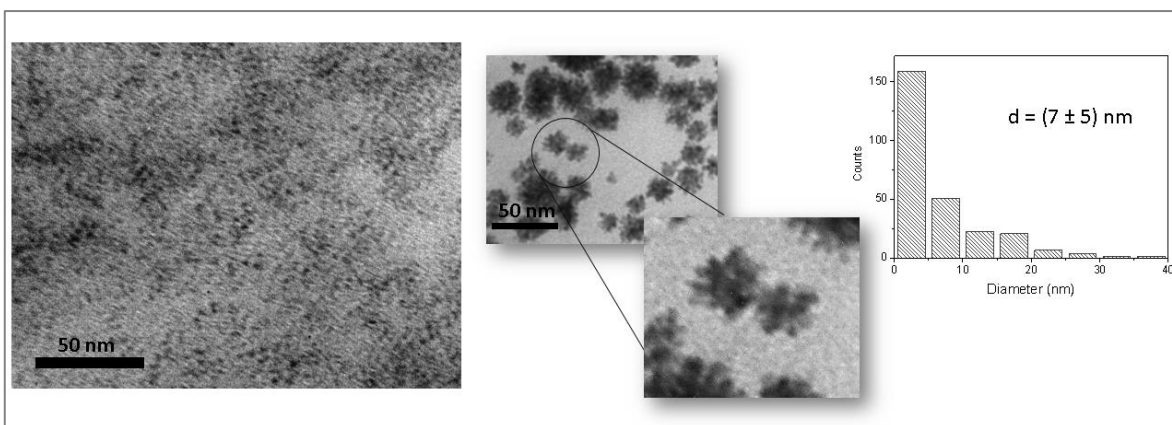
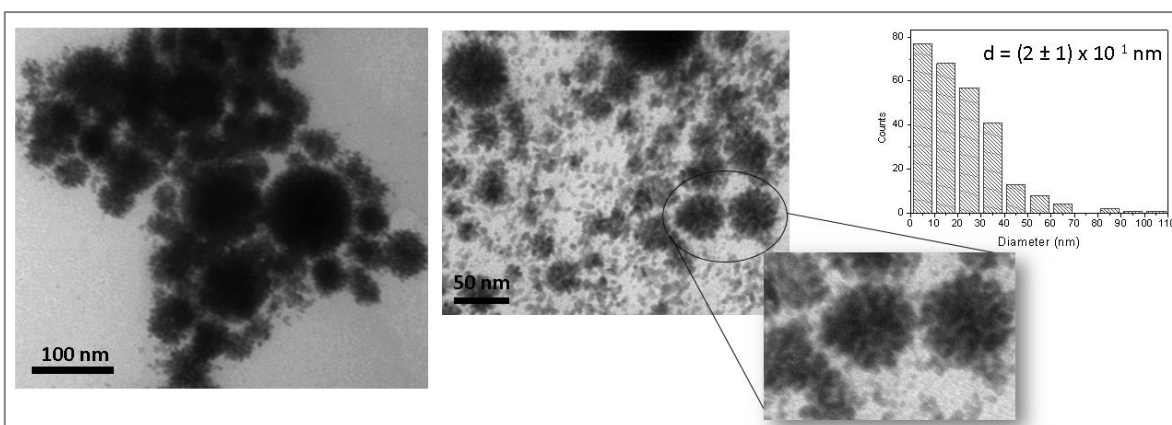
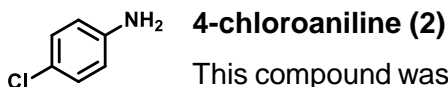


Figure S2: TEM micrograph of PVP-Pd NPs after their use in nitroaromatic hydrogenation reaction.

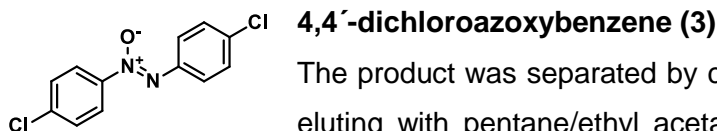


2. Characterization Data

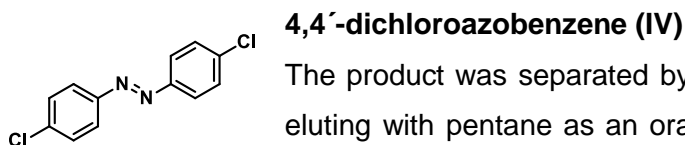
The products were characterized by ^1H NMR, ^{13}C NMR, and GC-MS. All the spectroscopic data were in agreement with those previously reported for the following compounds: 4-chloroaniline (**2**), 4,4'-dichloroazoxybenzene (**3**), 2-chloroaniline (**4**), aniline (**5**), *N*-(4-aminophenyl)acetamide (**6**), methyl 3-aminobenzoate (**7**), 1,4-diaminebenzene (**8**), 4-nitroaniline (**9**), 4-aminophenol (**10**), 3-aminophenol (**11**), 5-chloroquinoline (**12**), 2-chloropyridin-3-amine (**13**), 4-aminobiphenyl (**16**), (*E*)-*N*-benzylidene-4-chloroaniline (**19**), tert-butyl (4-chlorophenyl)carbamate (**20**), *N*-(4-chlorophenyl)-3-nitropyridin-2-amine (**21**), *N*2-(4-chlorophenyl)pyridine-2,3-diamine (**22**), 4,4'-dichloroazobenzene (**IV**), 4-nitrobiphenyl.



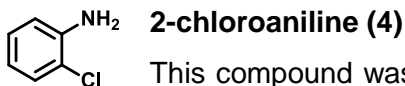
This compound was commercially available and was used as received.¹ CAS: [106-47-8]. ¹H NMR (400 MHz, CDCl₃) δ: 7.09 (dt, *J* = 8.8, 2.6 Hz, 2H), 6.60 (dt, *J* = 8.8, 2.6 Hz, 2H), 3.64 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 145.1 (C), 129.3 (CH), 123.3 (CH), 116.4 (C). GC-MS (70eV) *m/z* (%): 63 (18), 64 (14), 65 (40), 92 (21), 100 (15), [*M*⁺] 127 (100), [*M*⁺+2] 129 (30).



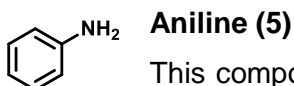
The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→70:30) as an orange solid.² CAS: [614-26-6]. ¹H NMR (400 MHz, CDCl₃) δ: 8.28-8.24 (m, 2H), 8.18-8.14 (m, 2H), 7.50-7.44 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ: 142.3 (C), 138.1 (C), 135.3 (C), 129.4 (C), 129.0 (CH), 128.9 (CH), 127.1 (CH), 123.7 (CH). GC-MS (70eV) *m/z* (%): 50 (19), 63 (20), 75 (54), 90 (21), 111 (100), 113 (35), 125 (23), 139 (28), 266 (9), [*M*⁺] 267 (4).



The product was separated by column chromatography on silica gel eluting with pentane as an orange solid.³ CAS: [1602-00-2]. ¹H NMR (400 MHz, CDCl₃) δ: 7.87 (d, *J* = 8.8 Hz, 4H), 7.49 (d, *J* = 8.8 Hz, 4H). ¹³C NMR (101 MHz, CDCl₃) δ: 150.8 (C), 137.2 (C), 129.4 (CH), 124.2 (CH). GC-MS (70eV) *m/z* (%): 50 (15), 75 (47), 111 (100), 113 (31), 139 (33), 141 (129), [*M*⁺] 250 (13).

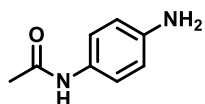


This compound was commercially available and was used as received.¹ CAS: [95-51-2]. ¹H NMR (400 MHz, CDCl₃) δ: 7.23 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.05 (ddd, *J* = 8.0, 7.4, 1.5 Hz, 1H), 6.75 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.68 (ddd, *J* = 7.9, 7.4, 1.5 Hz, 1H), 4.02 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 143.0 (C), 129.5 (CH), 127.8 (CH), 119.4 (C), 119.14 (CH), 116.0 (CH). GC-MS (70eV) *m/z* (%): 45 (33), 52 (13), 64 (63), 65 (53), 91 (16), 92 (41), 100 (20), [*M*⁺] 127 (100), [*M*⁺+2] 129 (75).



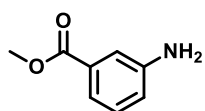
This compound was commercially available and was used as received.¹ CAS: [62-53-3]. ¹H NMR (400 MHz, CDCl₃) δ: 7.15 (q, *J* = 8.4, 1.0 Hz, 2H), 6.75 (t, *J* = 7.4 Hz,

1H), 6.68 (dd, $J = 8.5, 1.0$ Hz, 2H), 3.62 (s, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ : 146.5 (C), 129.4 (CH), 118.7 (CH), 115.2 (CH). GC-MS (70eV) m/z (%): 65 (18), 66 (40), 92 (13), [M^+] 93 (100).



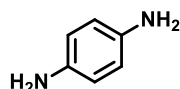
N-(4-aminophenyl)acetamide (6)

The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→50:50) as a yellow solid (i.y.: 61%).¹ CAS: [122-80-5]. ^1H NMR (400 MHz, CDCl_3) δ : 7.25-7.23 (m, 2H), 7.03 (s, 1H), 6.65-6.63 (m, 2H), 3.62 (s, 2H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ : 168.3 (C), 143.5 (C), 129.4 (CH), 122.4 (CH), 115.6 (CH), 24.5 (CH_3). GC-MS (70eV) m/z (%): 43 (11), 53 (13), 80 (31), 81 (14), 107 (42), 108 (100), 109 (11), [M^+] 150 (55).



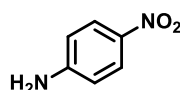
Methyl 3-aminobenzoate (7)

The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→50:50) as a yellow solid (i.y.:44%).⁴ CAS: [4518-10-9]. ^1H NMR (400 MHz, CDCl_3) δ : 7.42 (d, $J = 7.7$ Hz, 1H), 7.35 (t, $J = 1.9$ Hz, 1H), 7.21 (t, $J = 7.8$ Hz, 1H), 6.86 (ddd, $J = 8.0, 2.4, 0.8$ Hz, 1H), 3.89 (s, 4H), 3.77 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ : 167.4 (C), 146.6 (C), 131.3 (C), 129.4 (CH), 119.8 (CH), 119.5 (CH), 115.9 (CH), 52.1 (CH_3). GC-MS (70eV) m/z (%): 63 (11), 64 (12), 65 (44), 92 (100), 93 (24), 120 (95), 121 (11), [M^+] 151 (69).



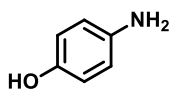
1,4-diaminebenzene (8)

This compound was commercially available and was used as received.¹ CAS: [106-50-3]. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ : 6.34 (s, 4H), 4.15 (s, 4H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ : 138.9 (C), 115.4 (CH). GC-MS (70eV) m/z (%): 52 (12), 53 (18), 54 (17), 80 (43), 81 (22), 107 (31), [M^+] 108 (100).



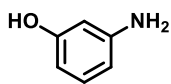
4-nitroaniline (9)

This compound was commercially available and was used as received.⁵ CAS: [100-01-6]. ^1H NMR (400 MHz, acetone- d_6) δ : 8.00 (d, $J = 9.1$ Hz, 2H), 6.76-6.73 (m, 2H), 6.03 (s, 2H). ^{13}C NMR (101 MHz, acetone- d_6) δ : 156.0 (C), 138.3 (C), 127.0 (CH), 113.6 (CH). GC-MS (70eV) m/z (%): 41 (11), 52 (22), 53 (15), 63 (19), 64 (15), 65 (98), 66 (12), 80 (43), 92 (44), 108 (100), 122 (11), [M^+] 138 (99).



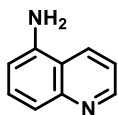
4-aminophenol (10)

This compound was commercially available and was used as received.⁶ CAS: [123-30-8]. ¹H NMR (400 MHz, DMSO-d₆) δ: 8.33 (s, 1H), 6.49-6.46 (m, 2H), 6.43-6.40 (m, 2H), 4.40 (s, 2H). ¹³C NMR (101 MHz, DMSO-d₆) δ: 148.2 (C), 140.6 (C), 115.5 (CH), 115.2 (CH).



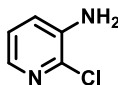
3-aminophenol (11)

This compound was commercially available and was used as received.⁷ CAS: [591-27-5]. ¹H NMR (400 MHz, DMSO-d₆) δ: 8.97 (s, 1H), 6.79-6.75 (m, 1H), 6.02-5.99 (m, 2H), 5.95-5.92 (m, 1H), 4.82 (s, 2H). ¹³C NMR (101 MHz, DMSO-d₆) δ: 158.2 (C), 149.9 (C), 129.8 (CH), 105.9 (CH), 103.8 (CH), 101.4 (CH).



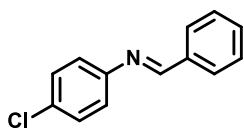
5-aminoquinoline (12)

The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→50:50) as a yellow solid: .⁴ CAS: [611-34-7]. ¹H NMR (400 MHz, CDCl₃) δ: 8.89 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.53-7.49 (m, 1H), 7.35 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.82 (d, *J* = 7.3 Hz, 1H), 4.40 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 150.2 (CH), 149.1 (C), 142.4 (C), 130.2 (CH), 129.8 (CH), 120.1 (CH), 119.7 (CH), 118.9 (C), 110.2 (CH). GC-MS (70eV) *m/z* (%): 89 (16), 90 (15), 116 (18), 117 (32), 143 (13), [*M*⁺] 144 (100), [*M*⁺+1] 145 (12).



2-chloropyridine-3-amine (13)

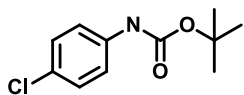
The product was purified by sublimation in a Buchi microdistillation system between 70-75°C as a white solid (i. y.: 63 %).⁸ CAS: [6298-19-7]. ¹H NMR (400 MHz, CDCl₃) δ: 7.80 (dd, *J* = 3.5, 0.72 Hz, 1H), 7.06-7.02 (m, 2H), 4.09 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 139.8 (C), 138.8 (CH), 137.2 (C), 123.5 (CH), 122.5 (CH). GC-MS (70eV) *m/z* (%): 41 (18), 43 (22), 64 (12), 65 (43), 66 (46), 76 (17), 92 (70), 93 (31), 94 (11), 112 (28), [*M*⁺] 128 (100), [*M*⁺+1] 129 (132), [*M*⁺+2] 130 (31).



(*E*)-*N*-benzylidene-4-chloroaniline (18)

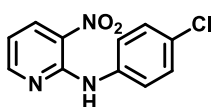
The product was purified by sublimation in a Buchi microdistillation system at 70°C, obtained as a white solid (i.y.: 87 %).⁹ CAS: [780-21-2]. ¹H NMR (400 MHz, CDCl₃) δ: 8.43 (s, 1H), 7.91-7.89 (m, 2H), 7.51-7.48 (m, 3H), 7.36 (d, *J* = 8 Hz, 2 H), 7.14 (d, *J* = 8 Hz, 2 H). ¹³C NMR (101 MHz, CDCl₃) δ: 160.8 (CH), 150.7 (C),

136.1 (C), 131.8 (CH), 131.6 (C), 129.4 (CH), 129.0 (CH), 128.9 (CH), 122.3 (CH). GC-MS (70eV) m/z (%): 50 (9), 51 (13), 63 (6), 75 (30), 76 (19), 77 (22), 89 (32), 111 (36), 113 (12), 138 (15), 151 (6), 152 (5), 180 (6), [M^+] 214 (100), 215 (96), 216 (43), [$M^+ + 3$] 217 (31).



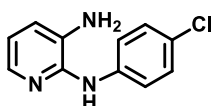
tert-butyl (4-chlorophenyl)carbamate (19)

The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→70:30), obtained as a pale yellow solid (i. y.: 76 %).¹⁰ CAS: [18437-66-6]. ¹H NMR (400 MHz, CDCl₃) δ: 7.32-7.22 (m, 4H), 6.50 (m, 1H), 1.51 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ: 152.7 (C), 137.1 (C), 129.1 (CH), 128.1 (C), 119.9 (CH), 81. (C), 28.5 (CH₃). GC-MS (70eV) m/z: 41 (43), 44 (12), 56 (10), 57 (100), 58 (5), 59 (21), 63 (6), 65 (11), 92 (5), 99 (7), 127 (50), 128 (5), 129 (17), 153 (5), 171 (24), 173 (9), [M^+] 227 (5).



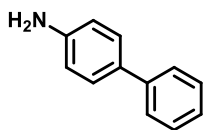
N-(4-chlorophenyl)-3-nitropyridin-2-amine (21)

This compound was recrystallized with a mixture acetone: water 1:5, obtained as a brown solid (i.y.: 75 %).¹¹ CAS: [26820-72-4]. ¹H NMR (400 MHz, CDCl₃) δ: 10.10 (s, 1H), 8.54 (dd, J = 8.3, 1.8 Hz, 1H), 8.49 (dd, J = 4.5, 1.8 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.8 Hz, 2H), 6.87 (dd, J = 8.3, 4.5 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 155.3 (CH), 150.16 (C), 144.52 (C), 136.7 (C), 135.8 (CH), 130.0 (C), 129.2 (CH), 123.8 (CH), 114.4 (CH). GC-MS (70eV) m/z (%): 50 (10), 51 (10), 52 (5), 63 (8), 64 (6), 70 (7), 74 (6), 75 (31), 76 (7), 77 (8), 78 (6), 84 (19), 99 (5), 102 (7), 107 (5), 111 (14), 113 (8), 114 (9), 115 (5), 125 (5), 140 (24), 141 (9), 155 (5), 167 (18), 168 (61), 169 (9), 202 (57), 203 (7), 204 (20), 216 (11), 218 (8), 232 (5), 248 (100), [M^+] 249 (90), 250 (42), [$M^+ + 2$] 251 (26).



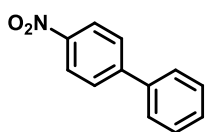
N²-(4-chlorophenyl)pyridine-2,3-diamine (22)

The product was filtrated over celite column washing with ethyl acetate, obtaining an orange solid (i.y.: 83 %).¹¹ CAS: [42048-23-7]. ¹H NMR (400 MHz, CDCl₃) δ: 7.82 (dd, J = 4.7, 1.2 Hz, 1H), 7.29-7.22(m, 4H), 7.02 (dd, J = 7.6, 1 Hz, 1H), 6.77 (dd, J = 7.5, 5 Hz, 1H), 6.44 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 145.4 (C), 140.0 (C), 139.0 (CH), 130.8 (C), 129.0 (CH), 126.0 (C), 123.9 (CH), 119.7 (CH), 117.6 (CH). GC-MS (70eV) m/z (%): 43 (5), 50 (5), 52 (5), 53 (5), 54 (12) 55 (16), 65 (5), 66 (8), 75 (7), 78 (9), 81 (6), 82 (12), 92 (36), 93 (5), 111 (6), 156 (6), 183 (31), 184 (11), 218 (100), [M^+] 219 (71), 220 (41), [$M^+ + 2$] 221 (23).



4-aminebiphenyl (23)

The product was separated by column chromatography on silica gel eluting with pentane/ethyl acetate gradient (100:00→70:30), obtained as a yellow solid (i. y.: 73 %).¹² CAS: [92-67-1]. ¹H NMR (400 MHz, CDCl₃) δ: 7.55 – 7.52 (m, 2H), 7.47 – 7.33 (m, 3H), 7.31 – 7.19 (m, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 3.73 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 145.8 (C), 141.2 (C), 131.6 (C), 128.73 (CH), 128.0 (CH), 126.4 (CH), 126.3 (CH), 115.4 (CH). GC-MS (70eV) *m/z* (%): 70 (5), 84 (9), 85 (9), 115 (8), 141 (8), 167 (13), 168 (22), [*M*⁺] 169 (100), [*M*⁺+1] 170 (13).

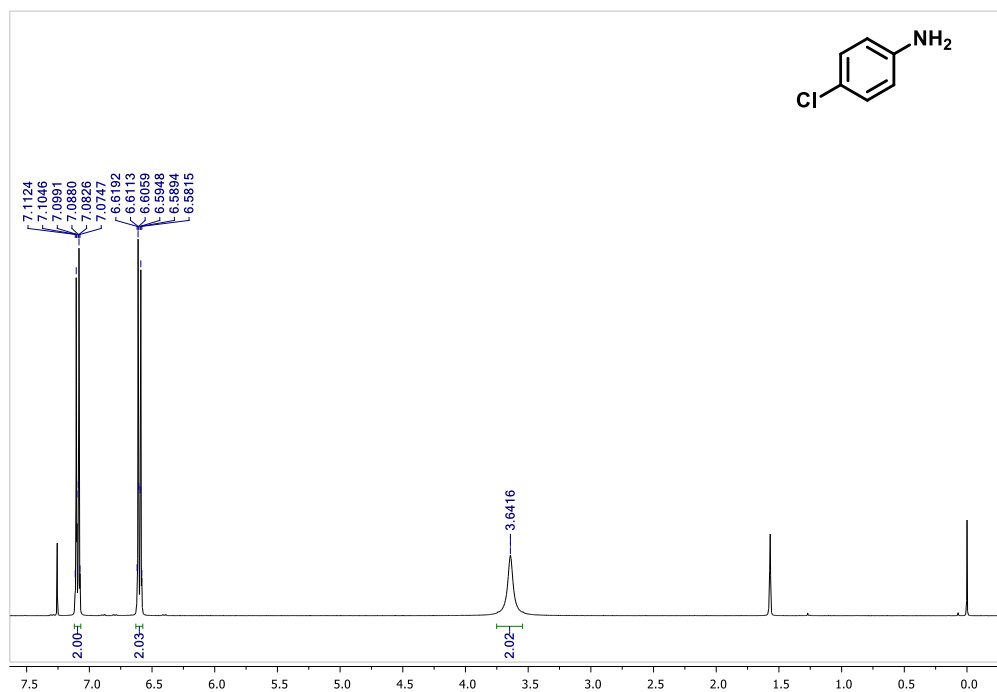


4-nitrobiphenyl

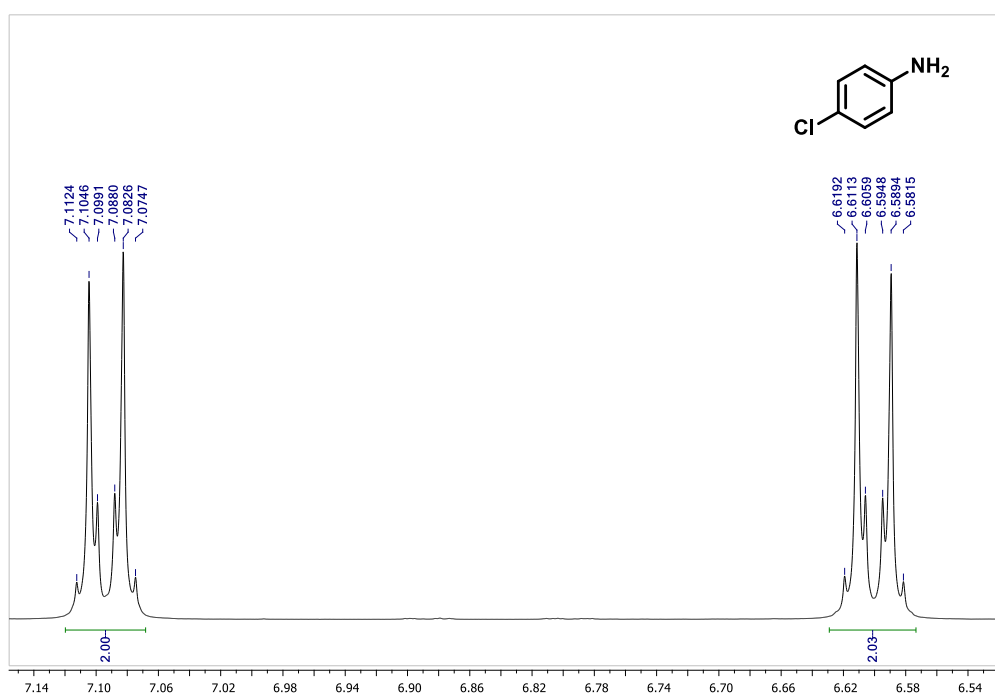
The product was filtrated over a celite column washing with ethyl acetate, obtained as yellow solid.¹² CAS: [92-93-3]. ¹H NMR (400 MHz, CDCl₃) δ: 8.30 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.64-7.62 (m, 2H), 7.52-7.43 (m, 3H). GC-MS (70eV) *m/z* (%): 50 (6), 51 (8), 63 (10), 74 (5), 75 (10), 76 (16), 77 (10), 102 (6), 115 (14), 126 (11), 127 (9), 141 (25), 150 (9), 151 (30), 152 (100), 153 (29), 169 (48), 170 (8), 183 (6), [*M*⁺] 199 (80), [*M*⁺+1] 200 (11).

3. NMR Spectroscopy

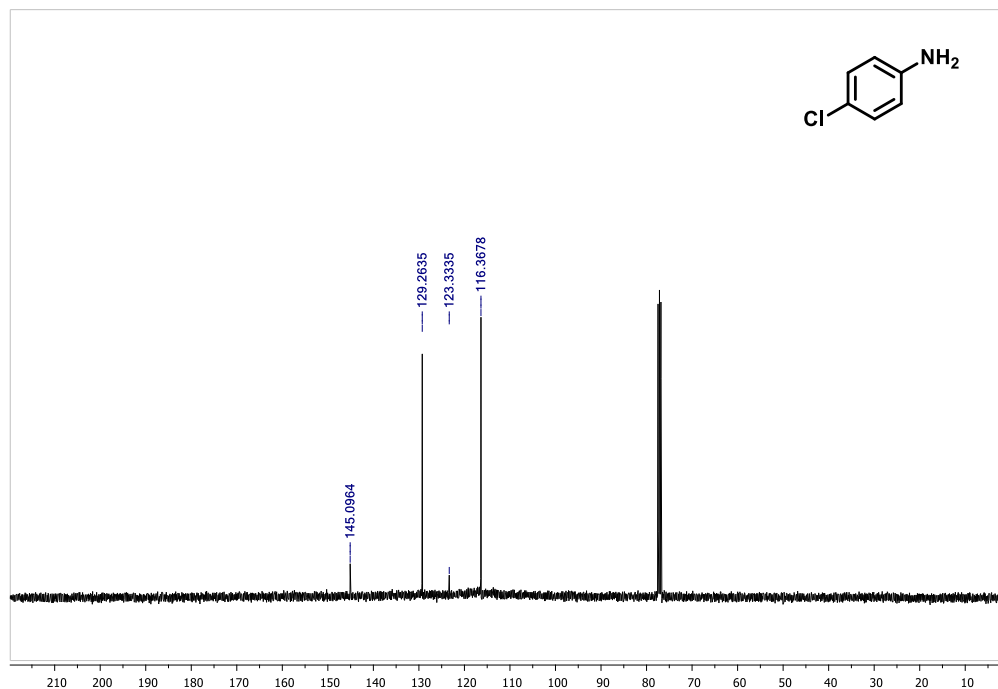
^1H NMR (400 MHz, CDCl_3) **4-chloroaniline (2)**



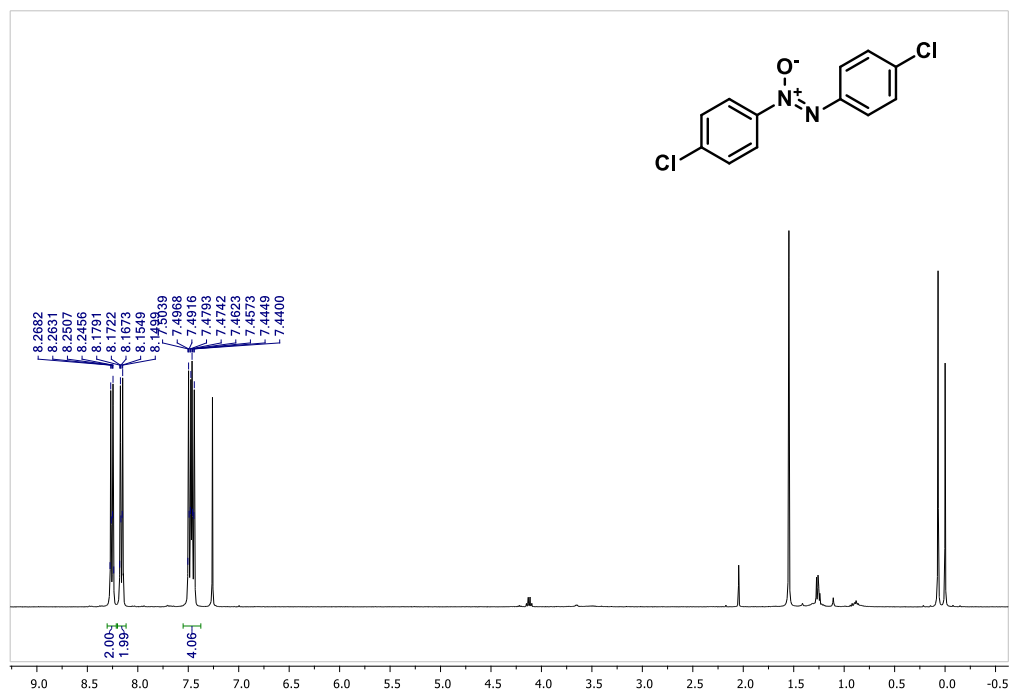
^1H NMR (400 MHz, CDCl_3) **4-chloroaniline (2)**



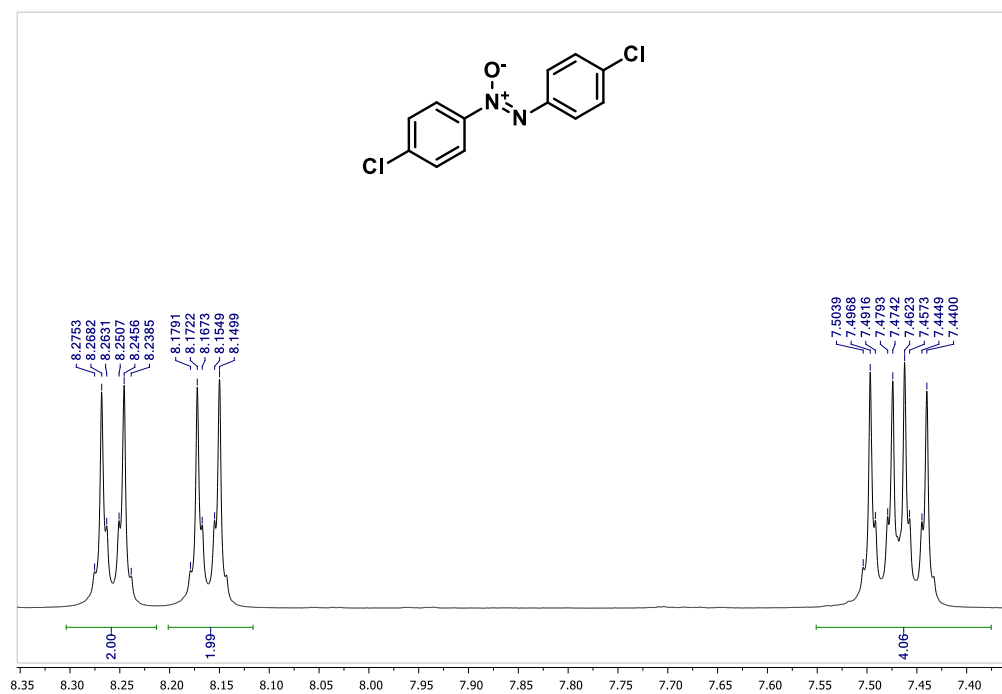
^{13}C NMR (101 MHz, CDCl_3) 4-chloroaniline (2)



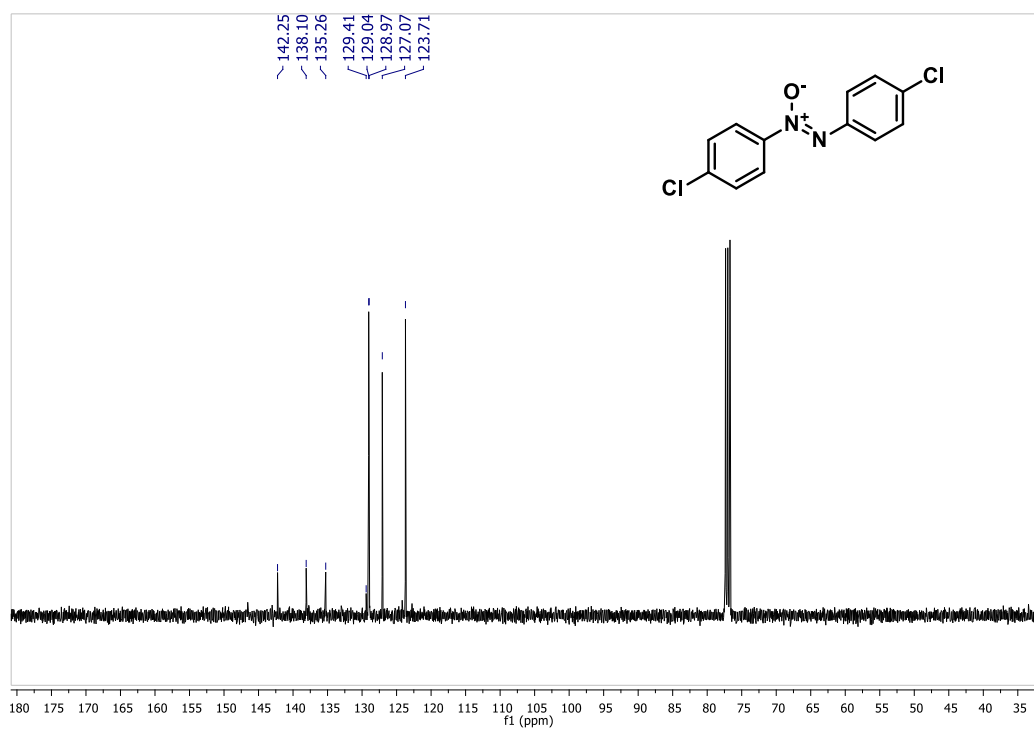
^1H NMR (400 MHz, CDCl_3) 4,4'-dichloroazobenzene (3)



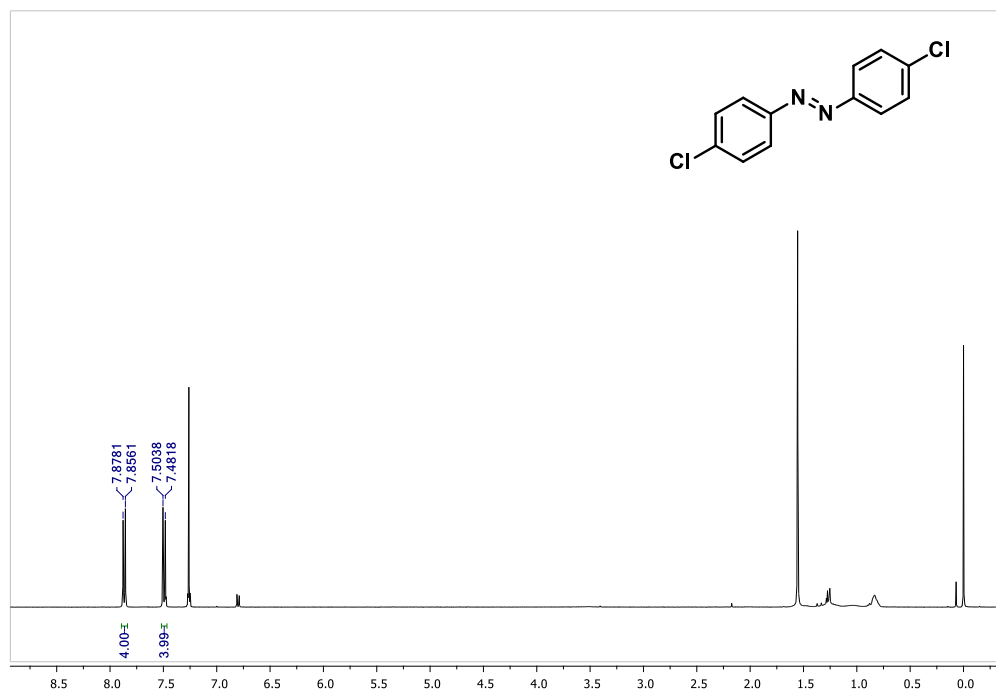
^1H NMR (400 MHz, CDCl_3) 4,4'-dichloroazobenzene (3)



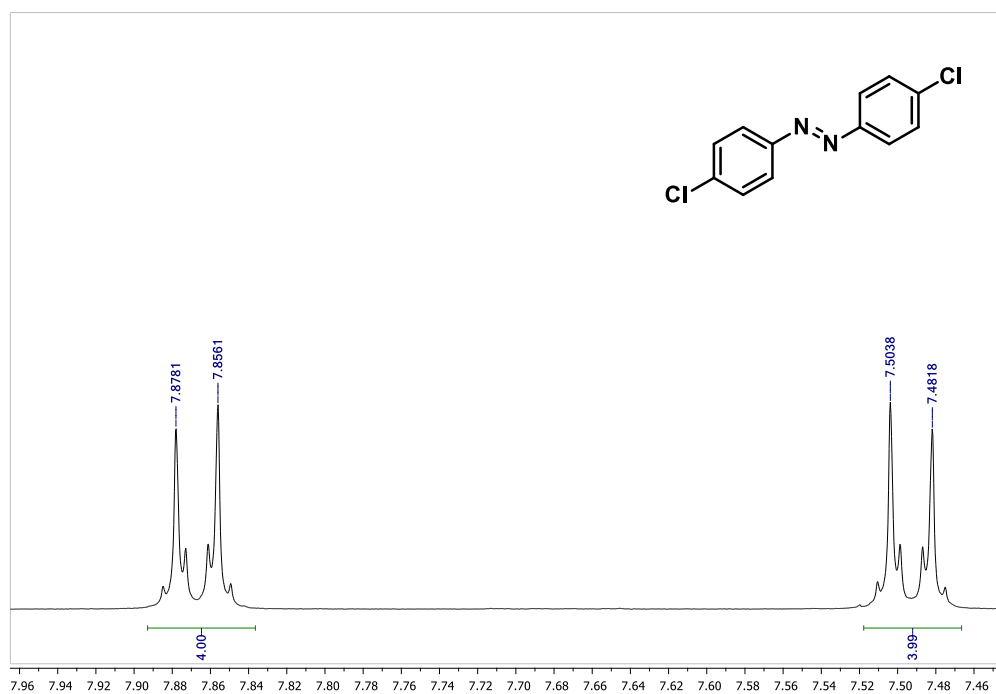
^{13}C NMR (101 MHz, CDCl_3) **4,4'-dichloroazobenzene (3)**



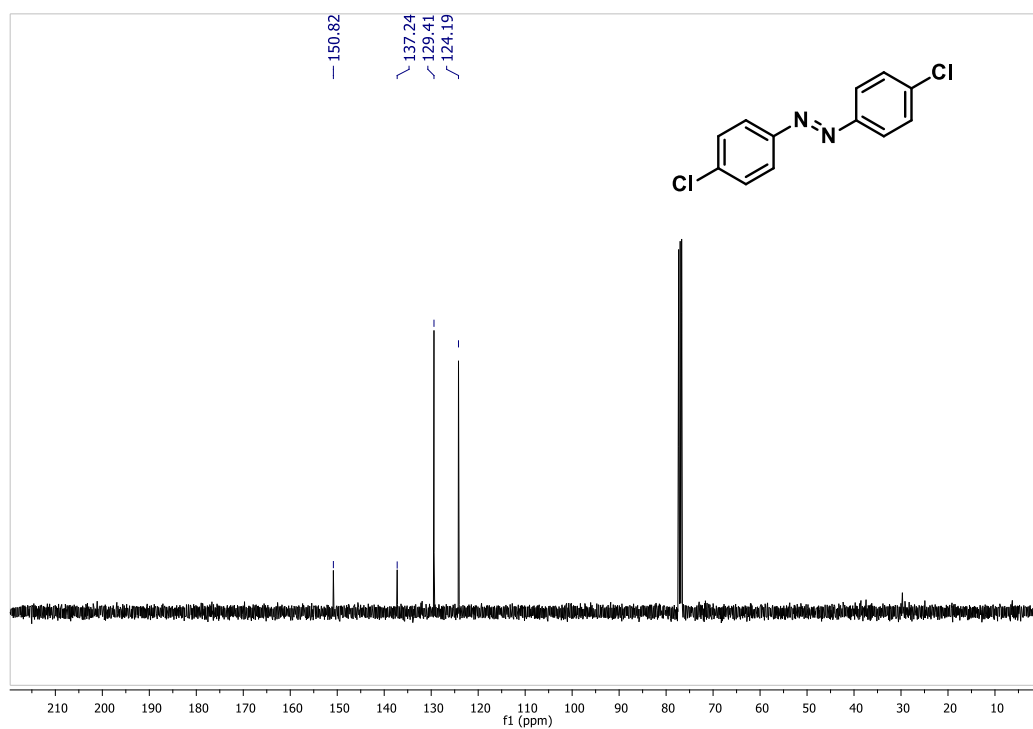
^1H NMR (400 MHz, CDCl_3) **4,4'-dichloroazobenzene (IV)**



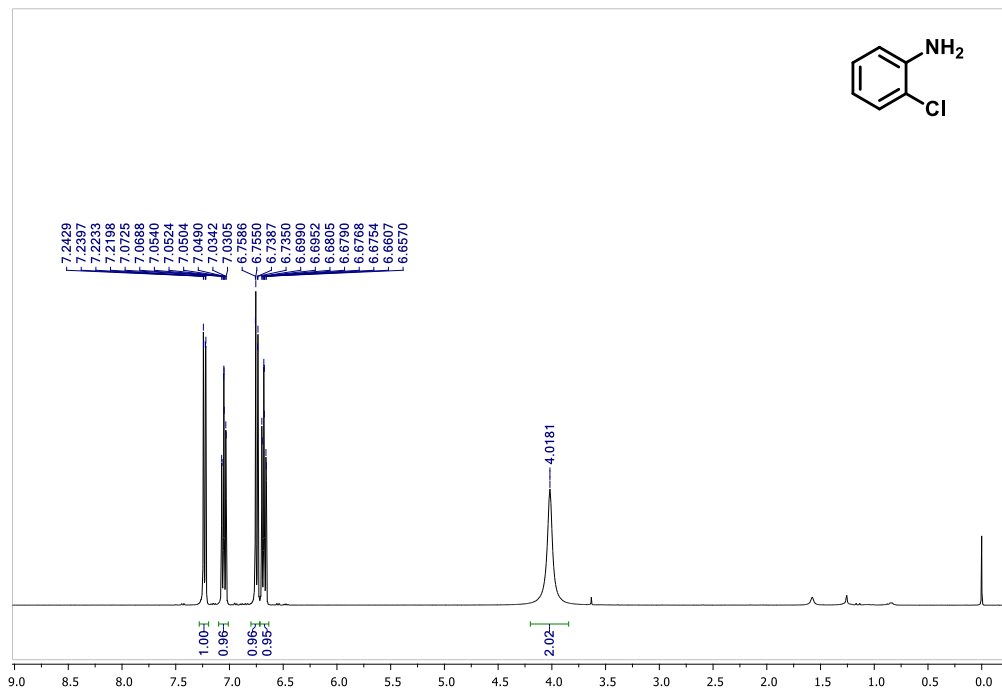
^1H NMR (400 MHz, CDCl_3) **4,4'-dichloroazobenzene (IV)**



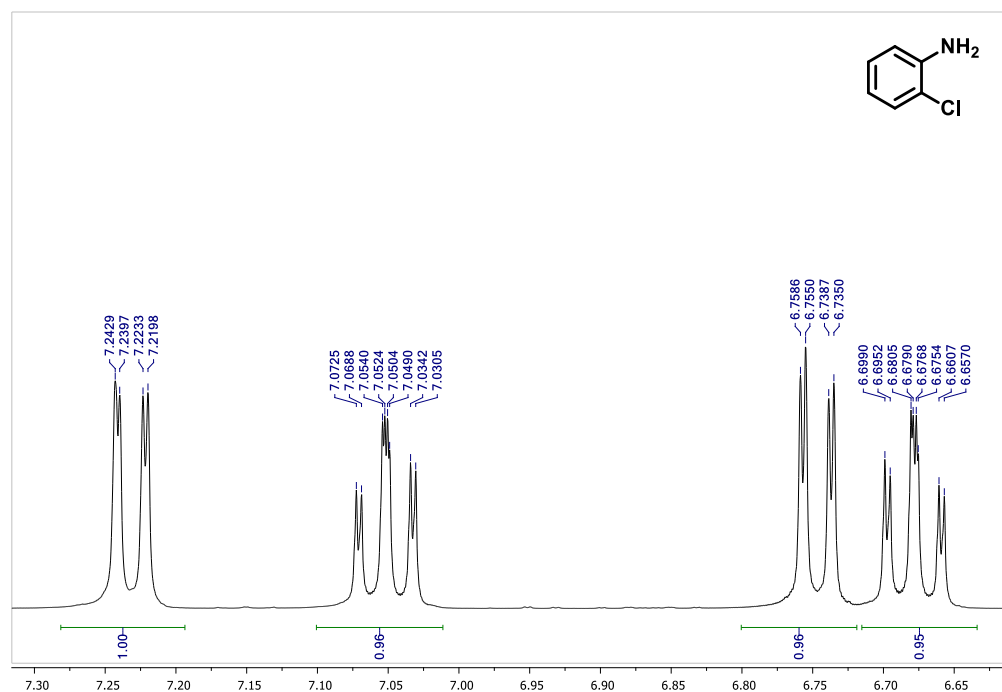
^{13}C NMR (101 MHz, CDCl_3) **4,4'-dichloroazobenzene (IV)**



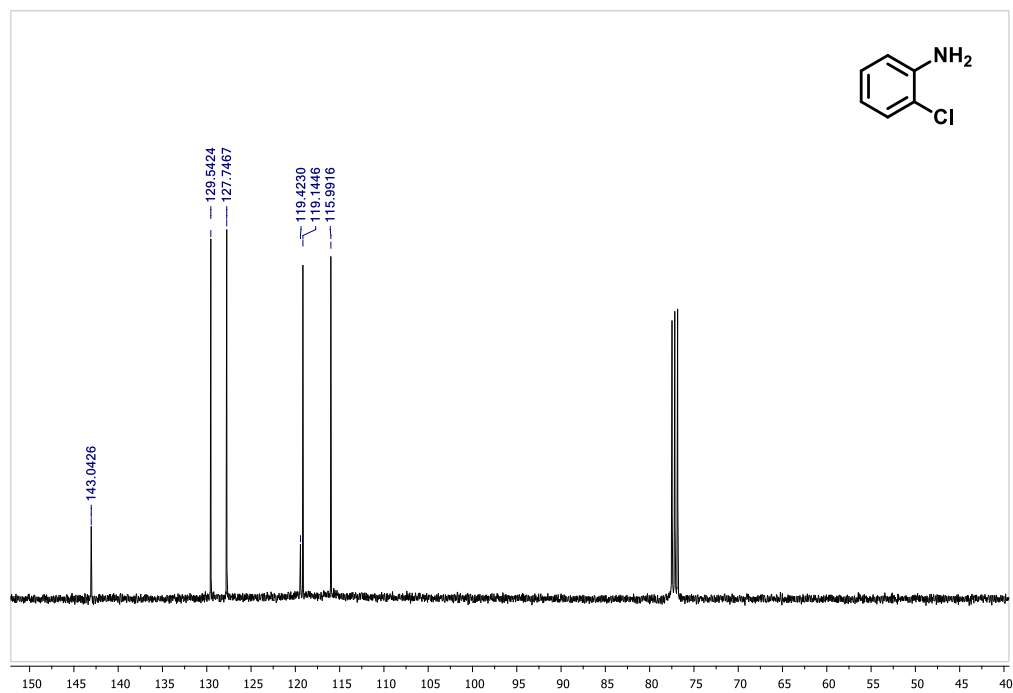
¹H NMR (400 MHz, CDCl₃) **2-chloroaniline (4)**



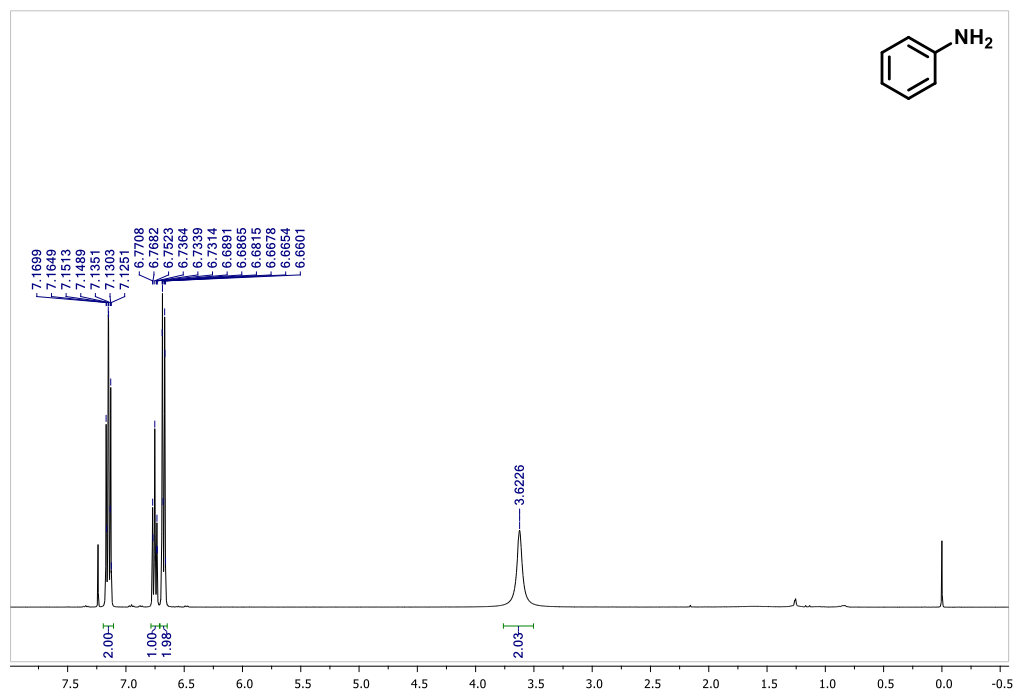
¹H NMR (400 MHz, CDCl₃) **2-chloroanilina (4)**



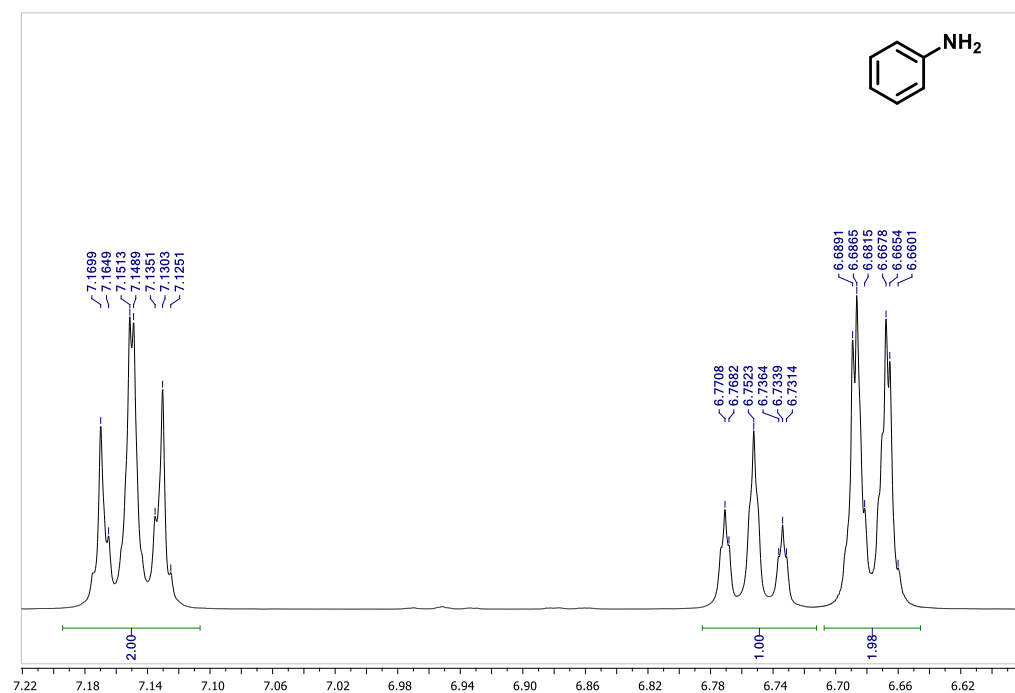
^{13}C NMR (101 MHz, CDCl_3) **2-chloroaniline (4)**



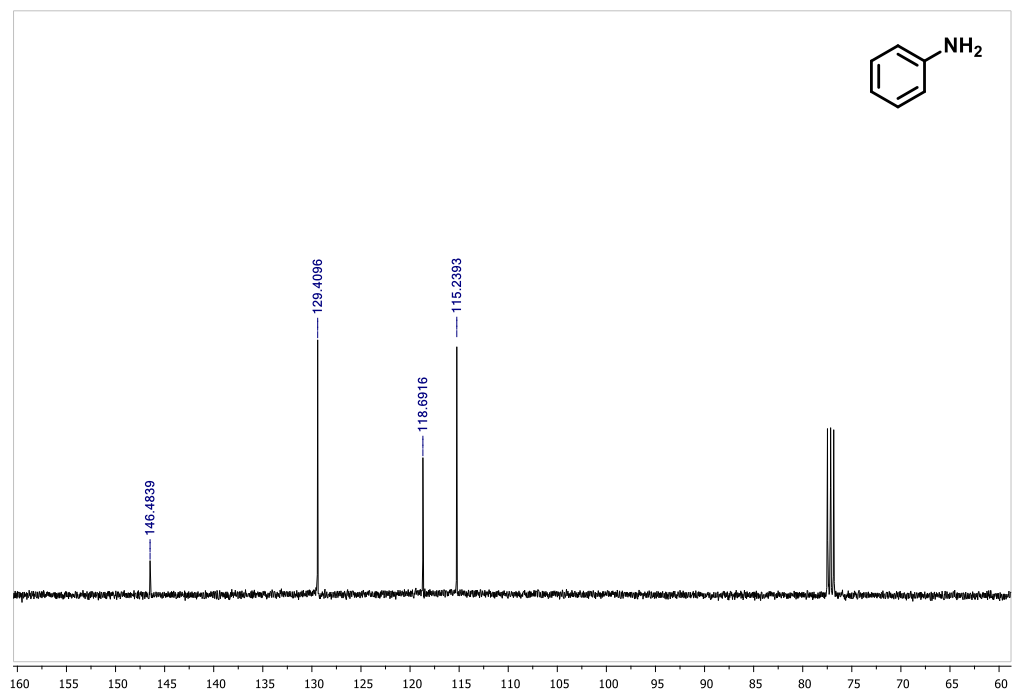
¹H NMR (400 MHz, CDCl₃) **aniline (5)**



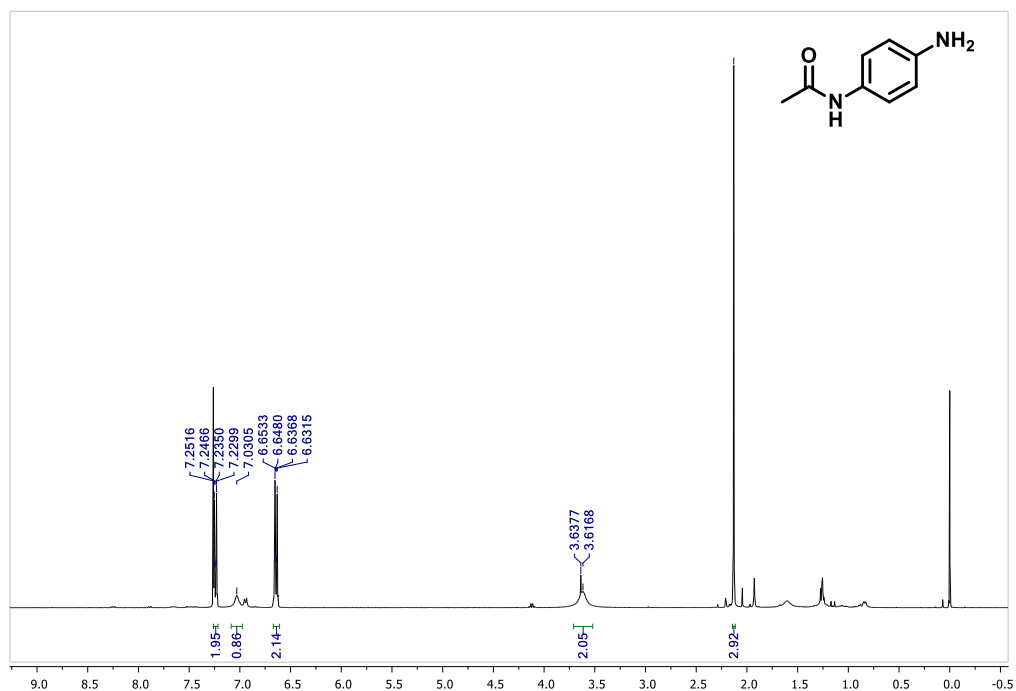
¹H NMR (400 MHz, CDCl₃) **aniline (5)**



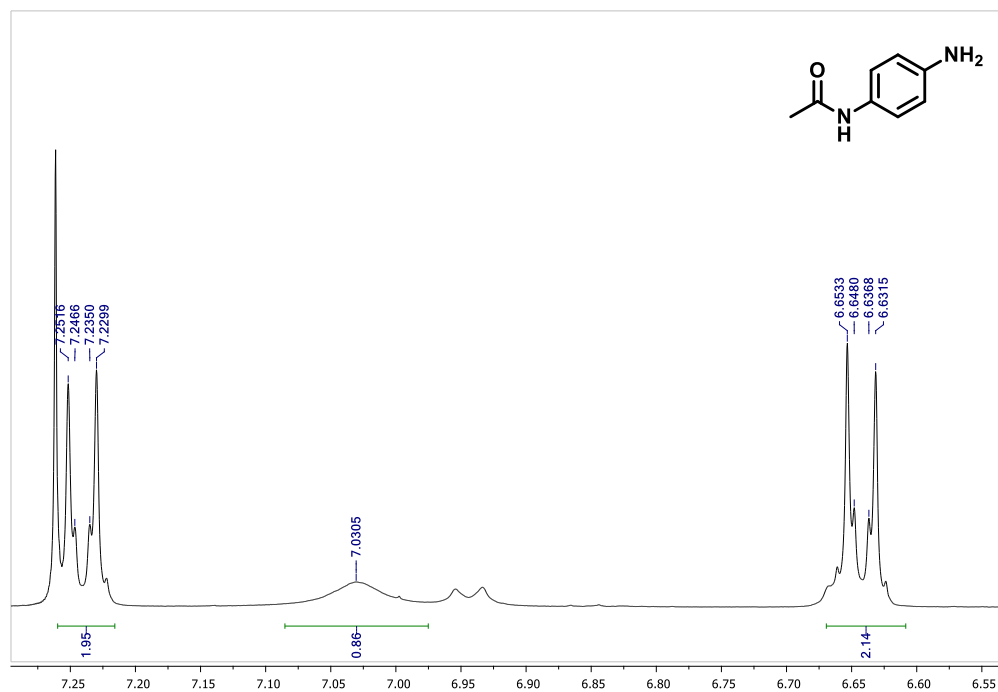
^{13}C NMR (101 MHz, CDCl_3) **aniline (5)**



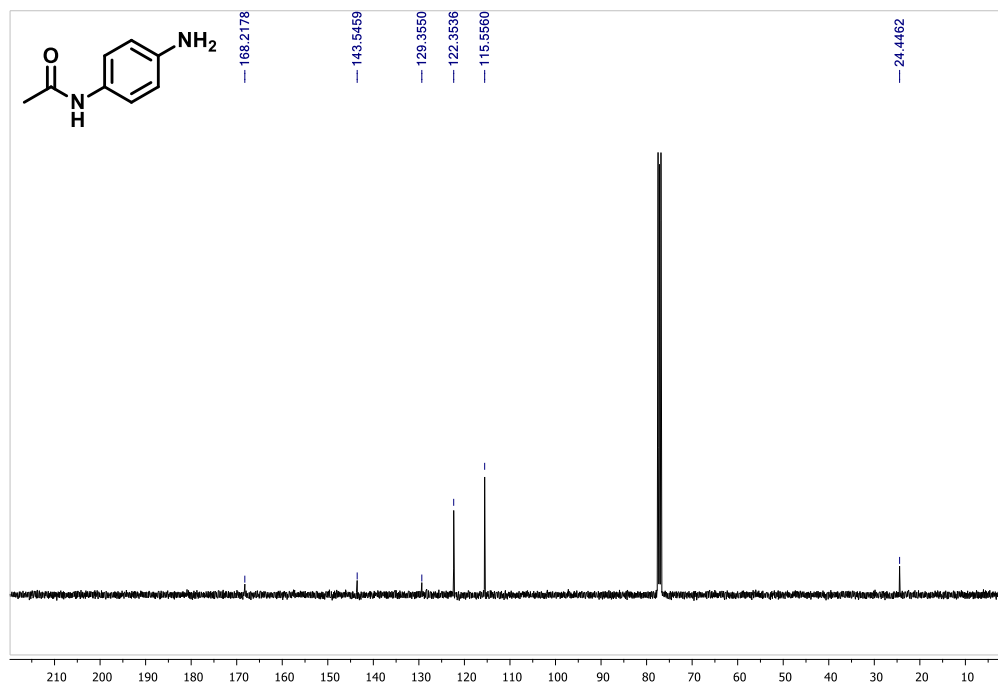
^1H NMR (400 MHz, CDCl_3) ***N*-(4-aminophenyl)acetamide (6)**



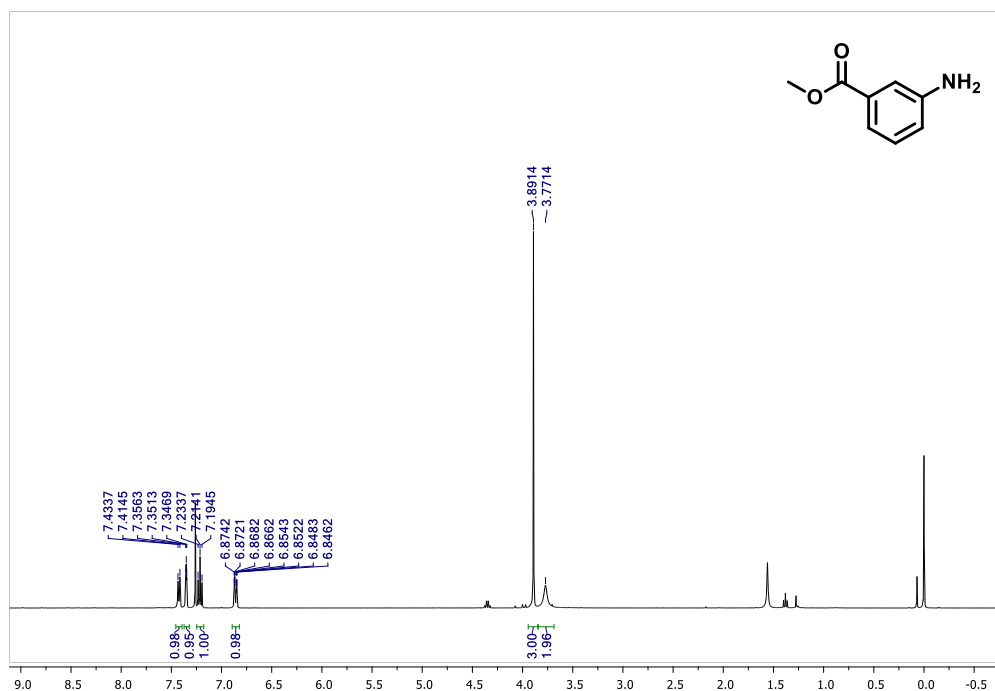
^1H NMR (400 MHz, CDCl_3) ***N*-(4-aminophenyl)acetamide (6)**



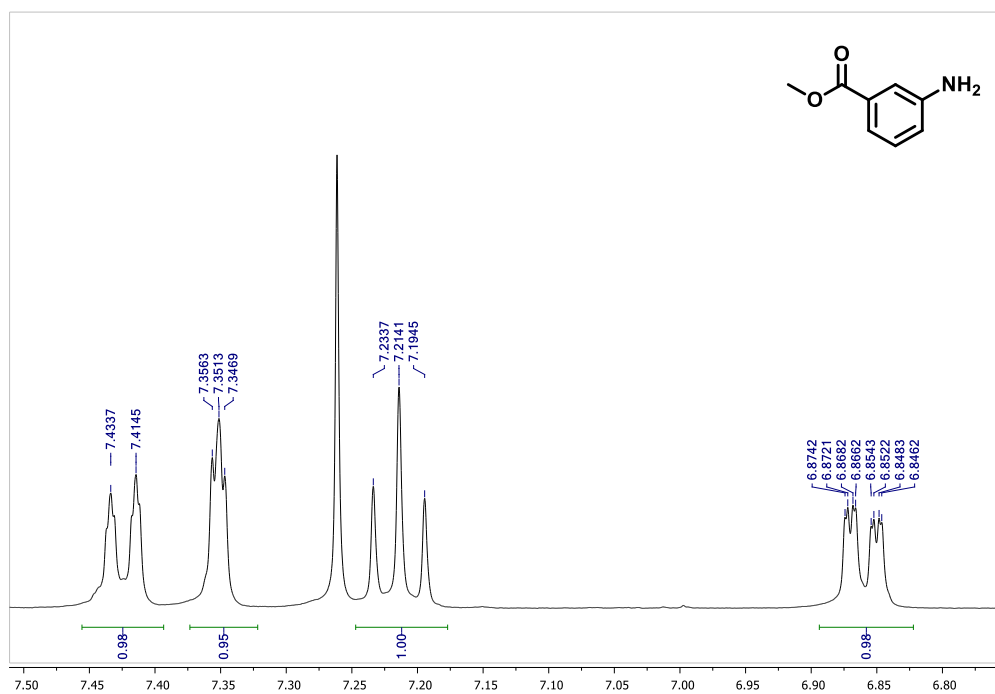
^{13}C NMR (101 MHz, CDCl_3) ***N*-(4-aminophenyl)acetamide (6)**



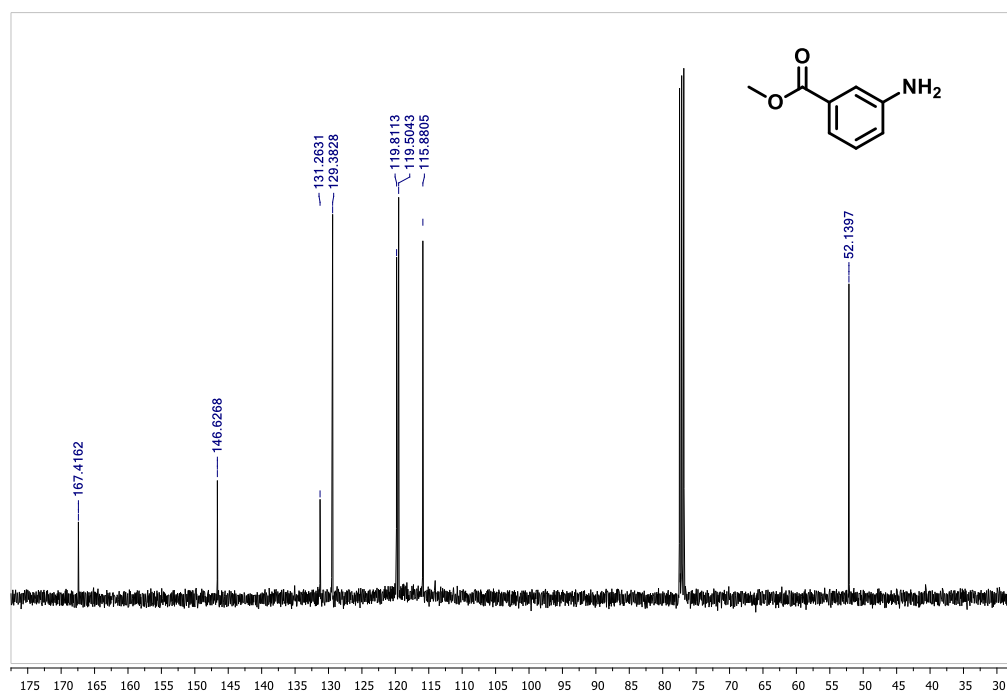
^1H NMR (400 MHz, CDCl_3) methyl 3-aminobenzoato (7)



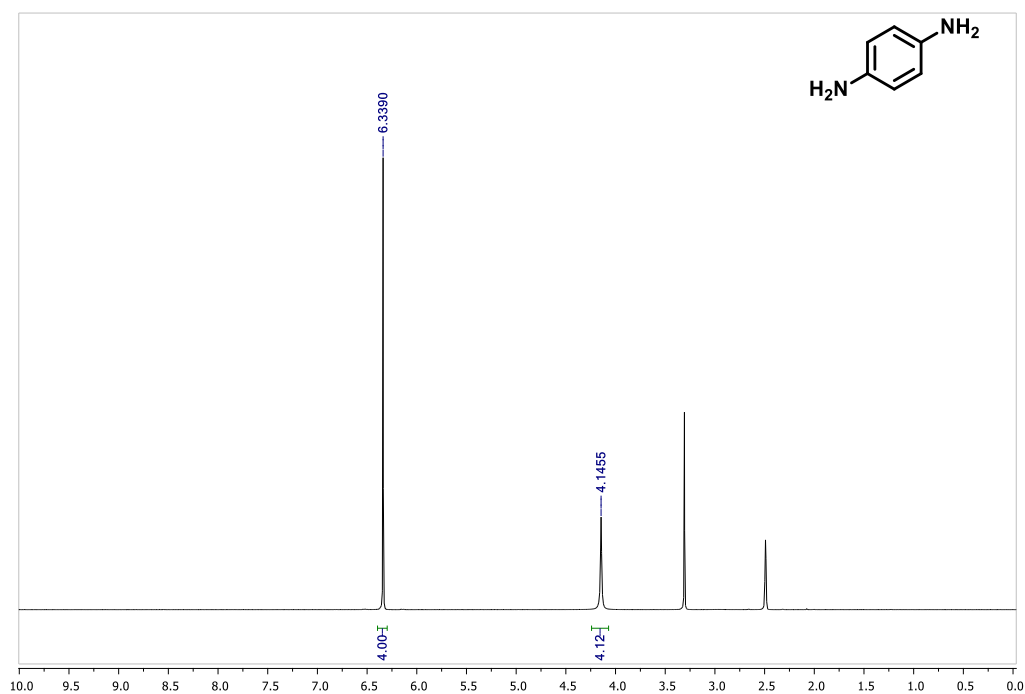
^1H NMR (400 MHz, CDCl_3) methyl 3-aminobenzoato (7)



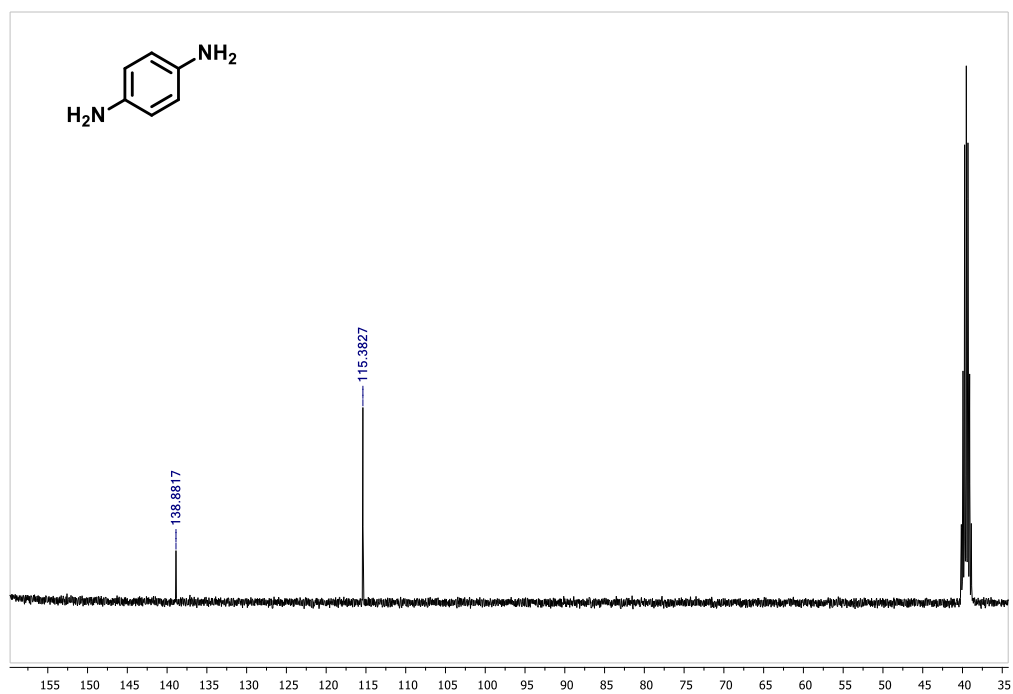
^{13}C NMR (101 MHz, CDCl_3) methyl 3-aminobenzoate (7)



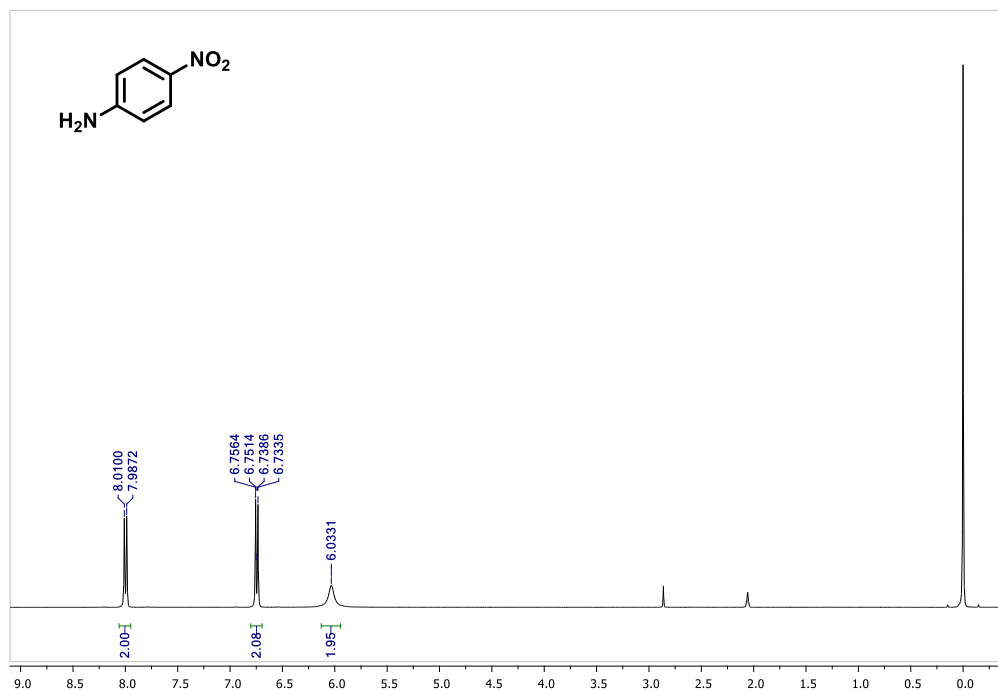
^1H NMR (400 MHz, DMSO- d_6) **1,4-diaminobenzene (8)**



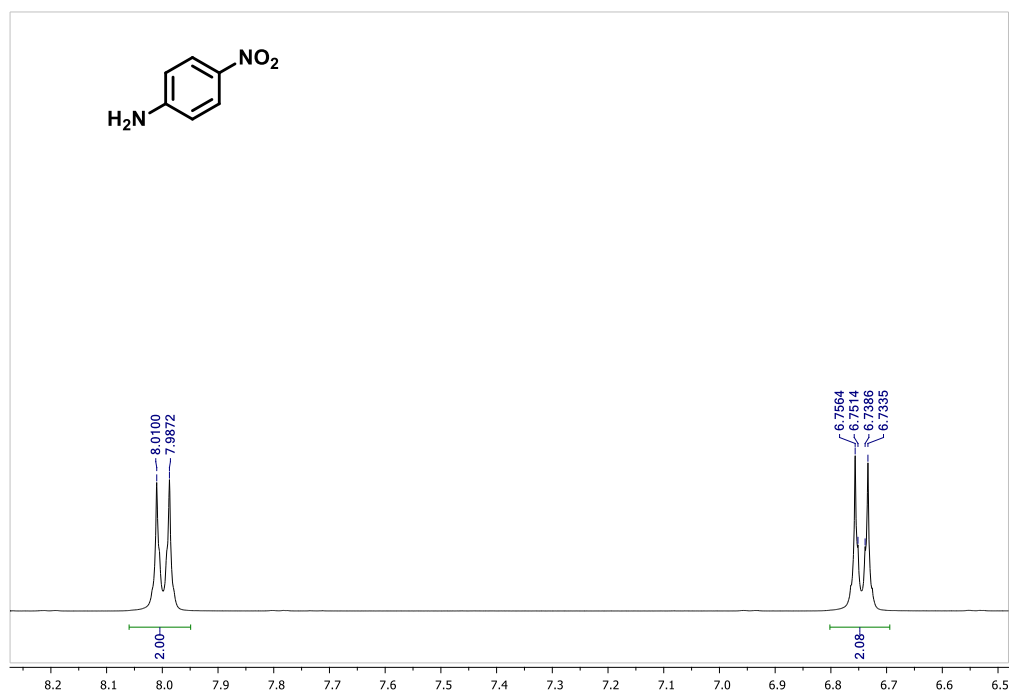
^{13}C NMR (101 MHz, DMSO- d_6) **1,4-diaminobenzene (8)**



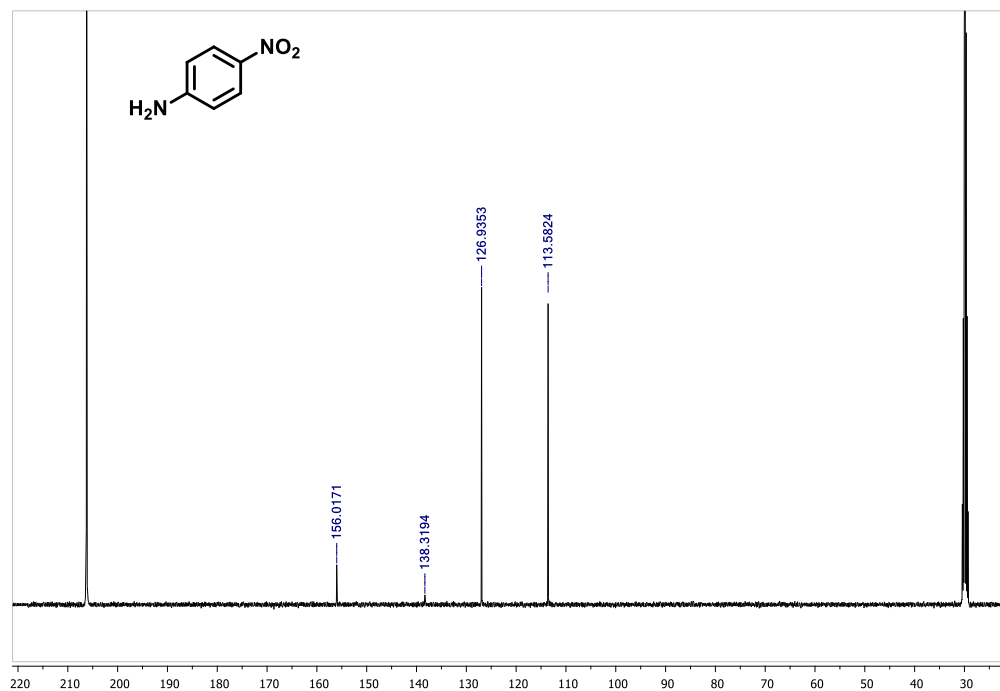
¹H NMR (400 MHz, acetone-d₆) **4-nitroaniline (9)**



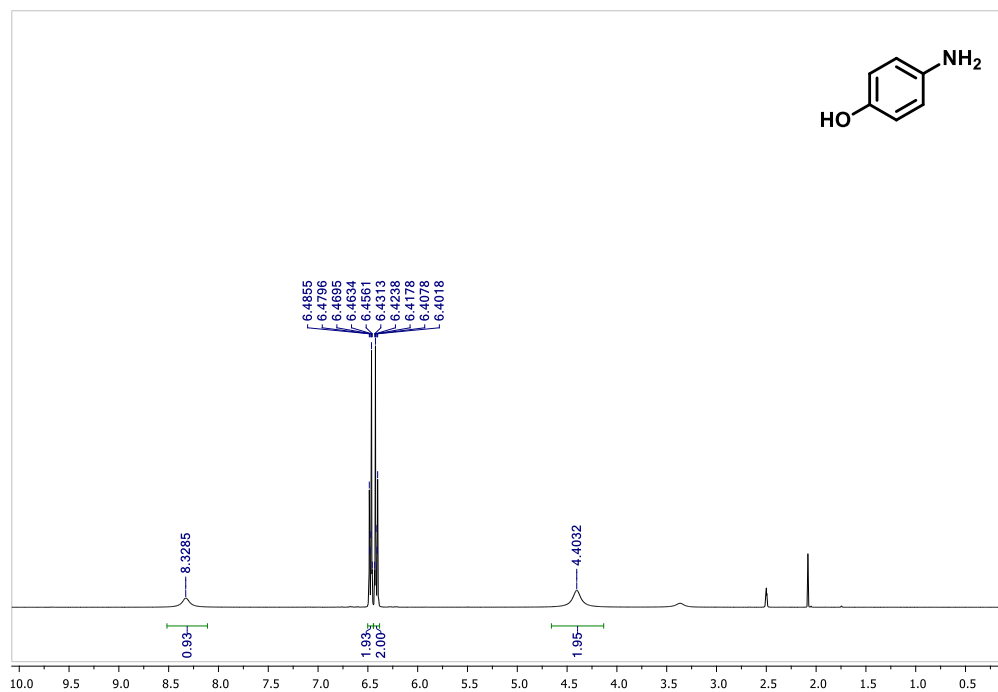
¹H NMR (400 MHz, acetone-d₆) **4-nitroanilina (9)**



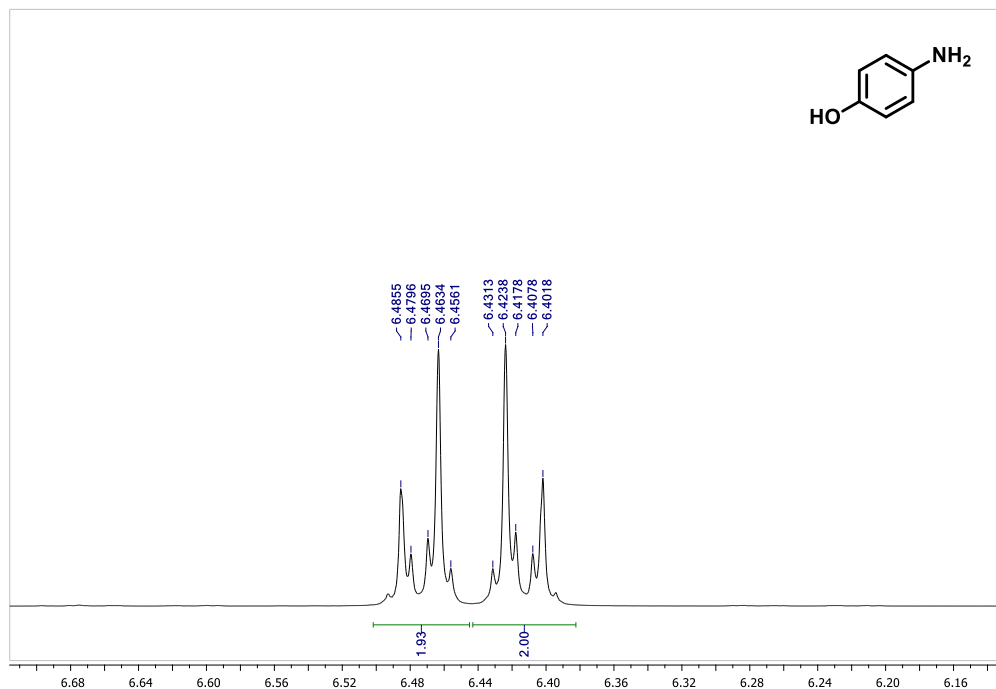
^{13}C NMR (101 MHz, acetone- d_6) **4-nitroaniline (9)**



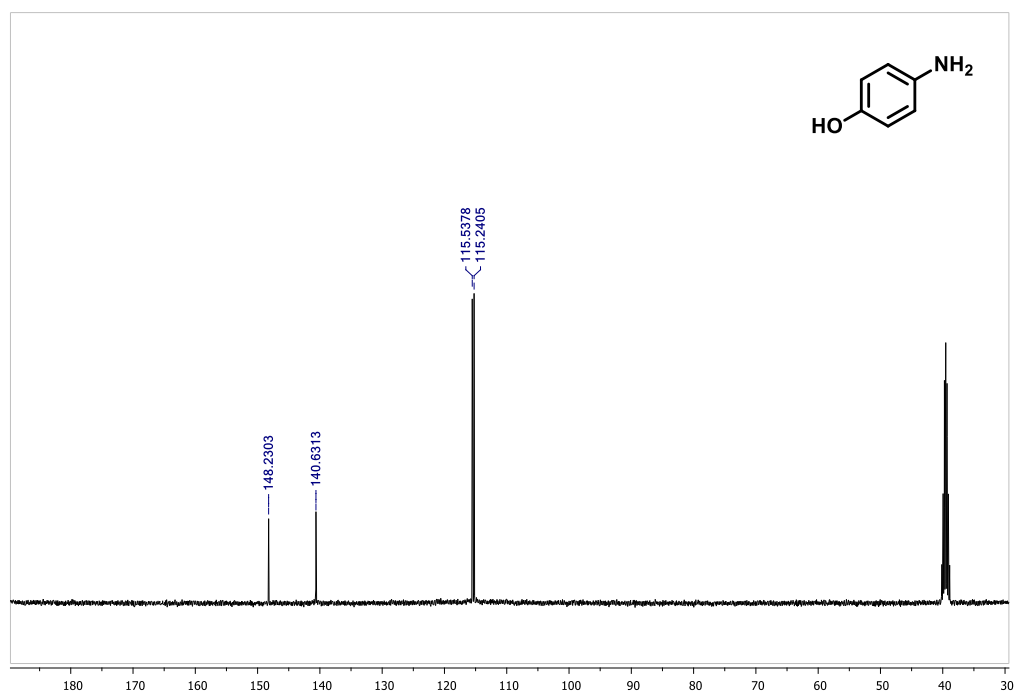
¹H NMR (400 MHz, DMSO-d₆) **4-aminophenol (10)**



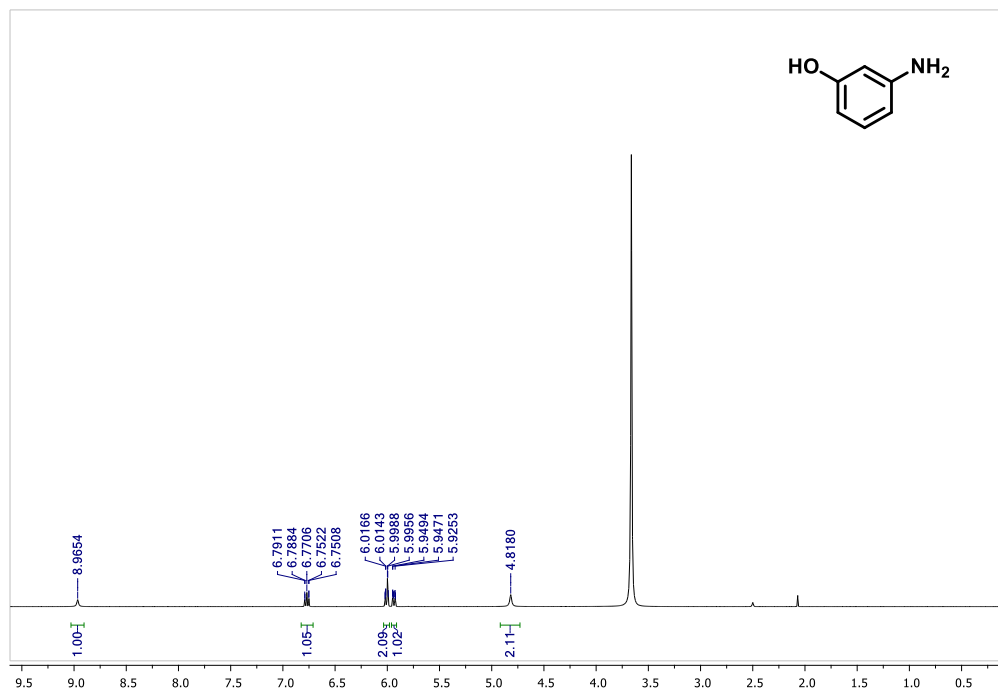
¹H NMR (400 MHz, DMSO-d₆) **4-aminophenol (10)**



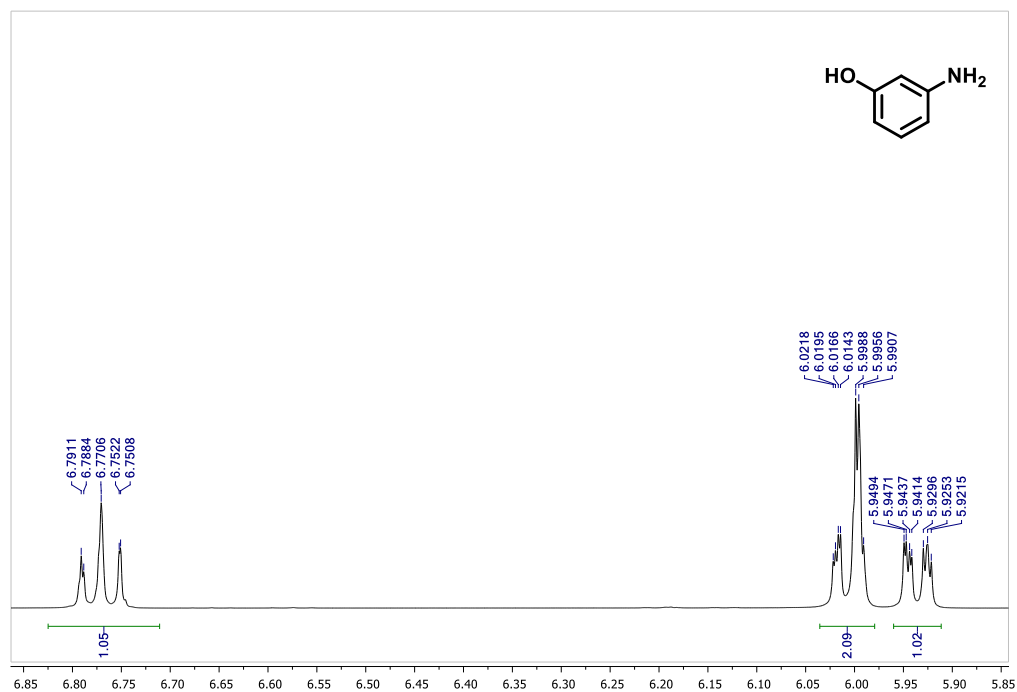
^{13}C NMR (101 MHz, DMSO- d_6) **4-aminophenol (10)**



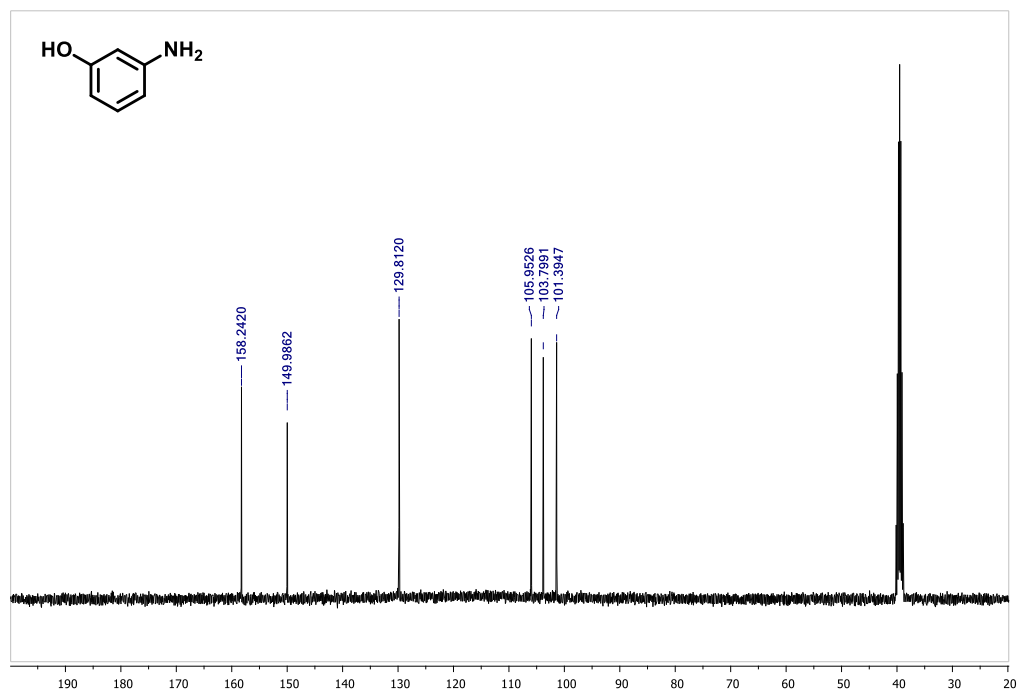
¹H NMR (400 MHz, DMSO-d₆) **3-aminophenol (11)**



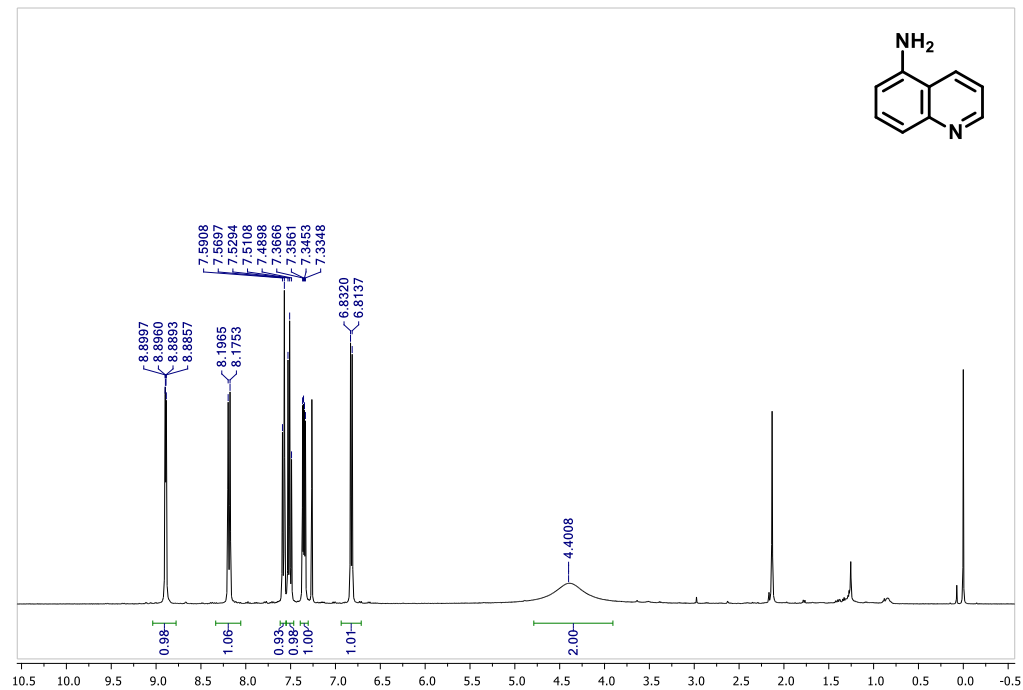
¹H NMR (400 MHz, DMSO-d₆) **3-aminophenol (11)**



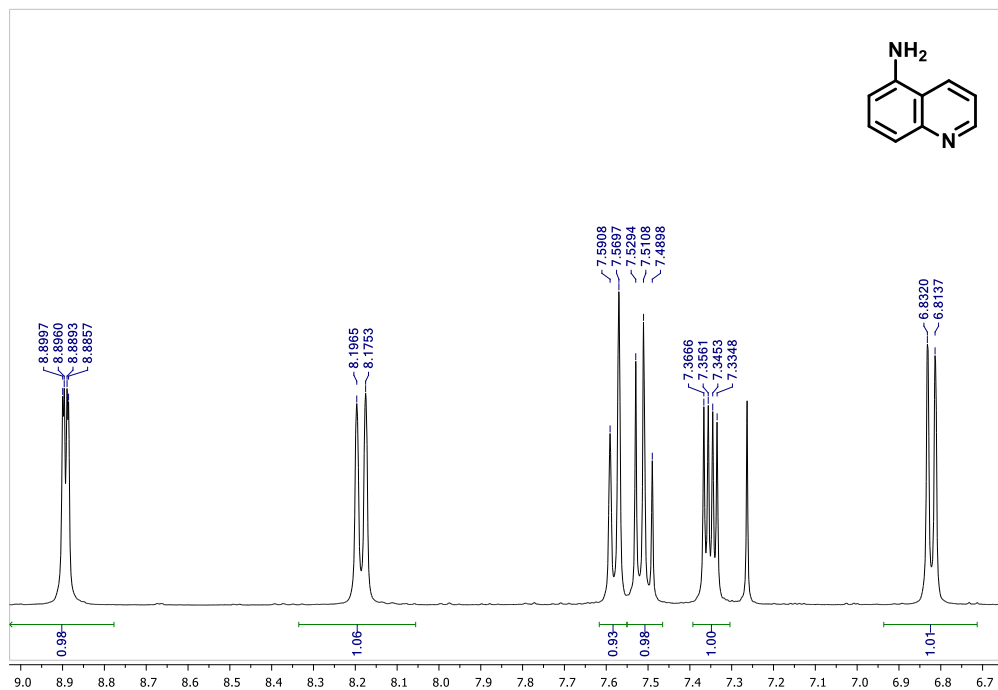
^{13}C NMR (101 MHz, DMSO- d_6) **3-aminophenol (11)**



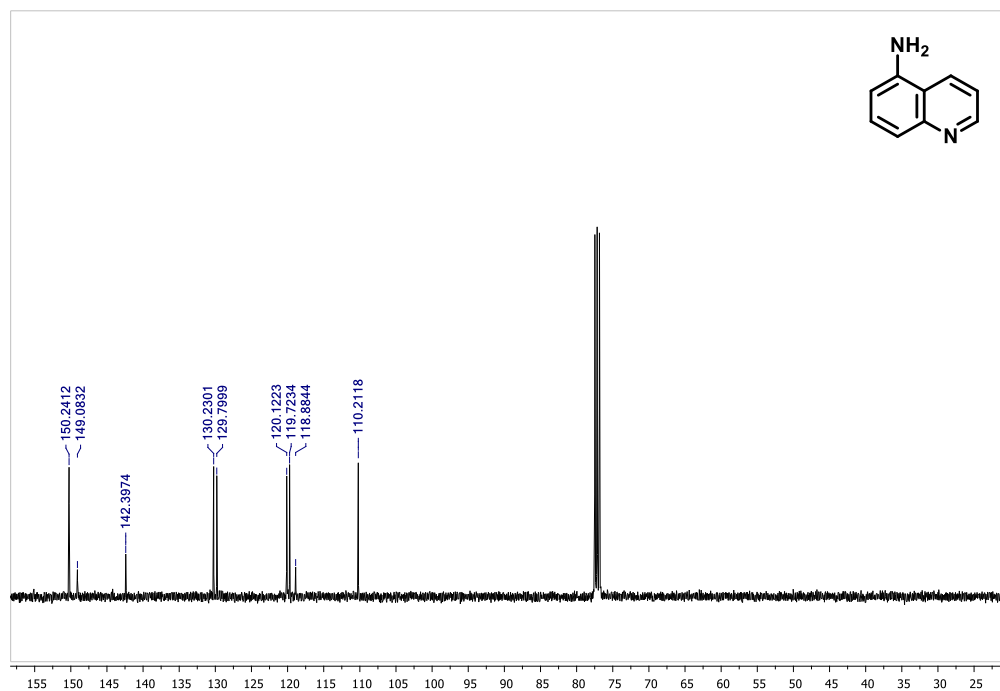
¹H NMR (400 MHz, CDCl₃) **5-aminoquinoline (12)**



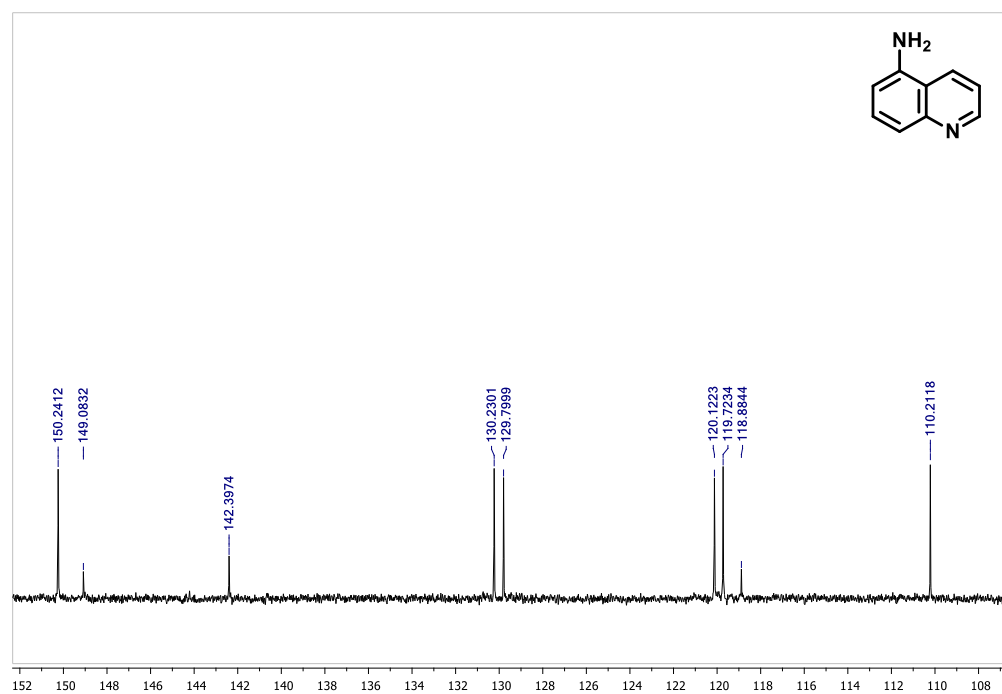
¹H NMR (400 MHz, CDCl₃) **5-aminoquinoline (12)**



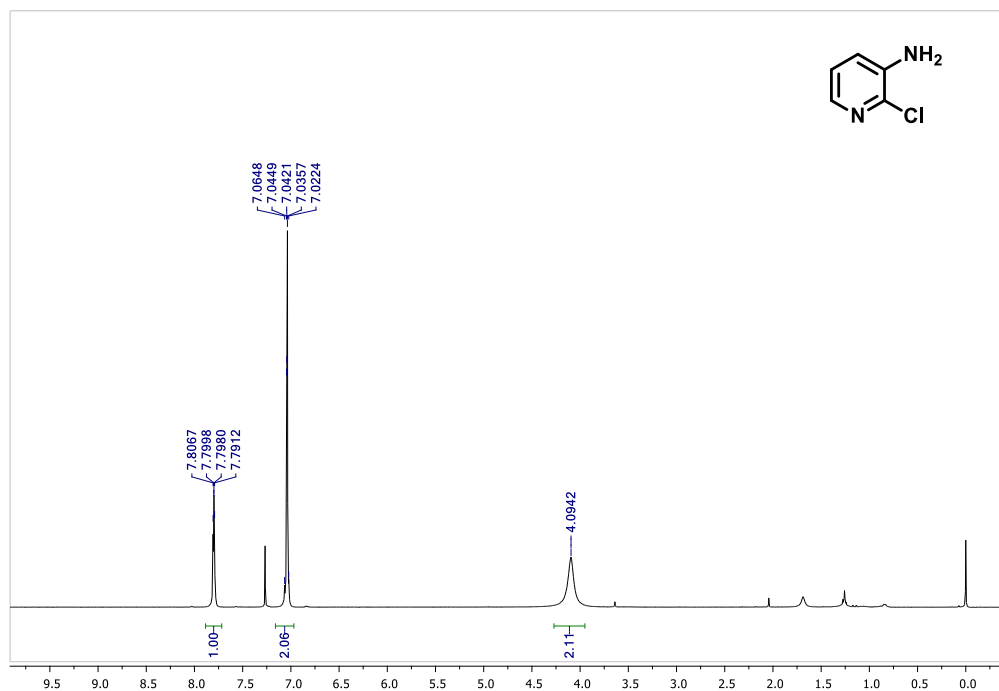
^{13}C NMR (101 MHz, CDCl_3) 5-aminoquinoline (12)



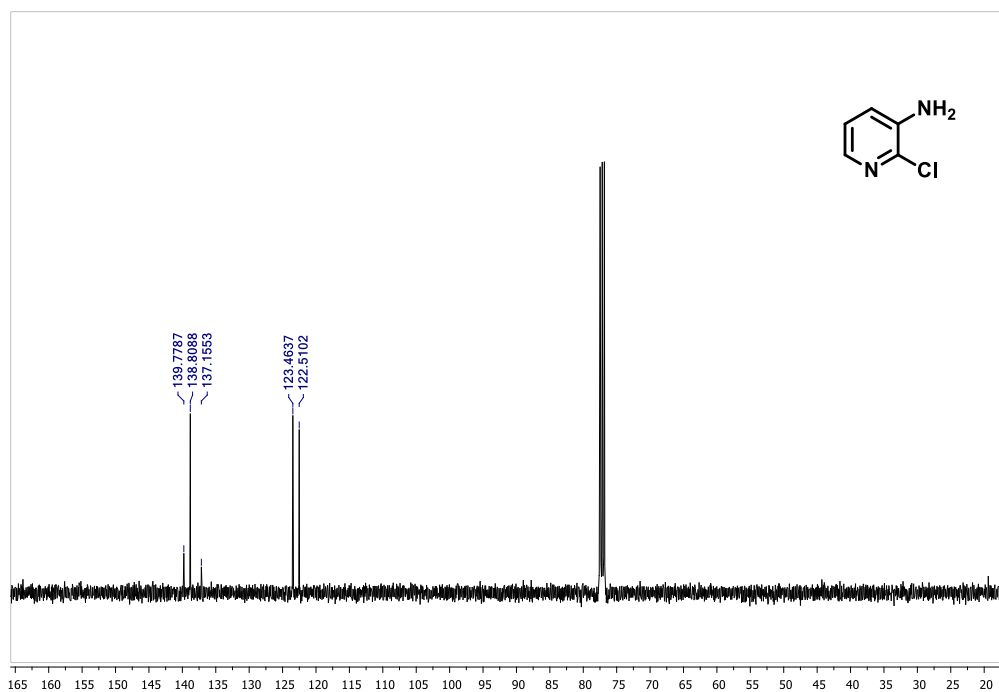
^{13}C NMR (101 MHz, CDCl_3) 5-aminoquinoline (12)



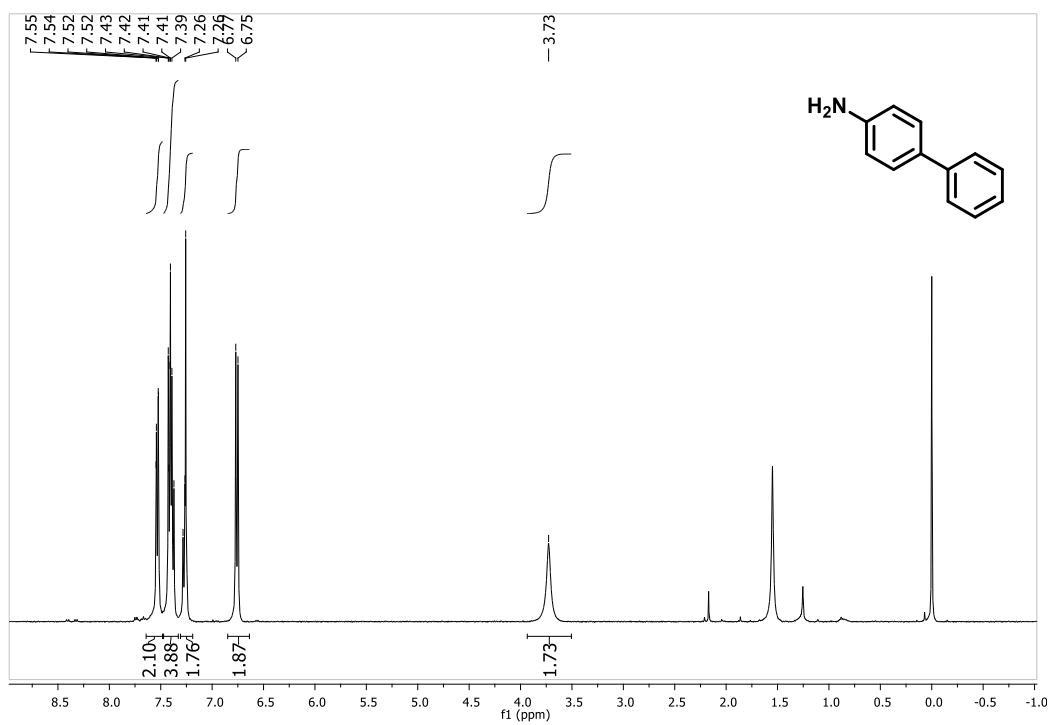
^1H NMR (400 MHz, CDCl_3) **2-chloropyridine-3-amine (13)**



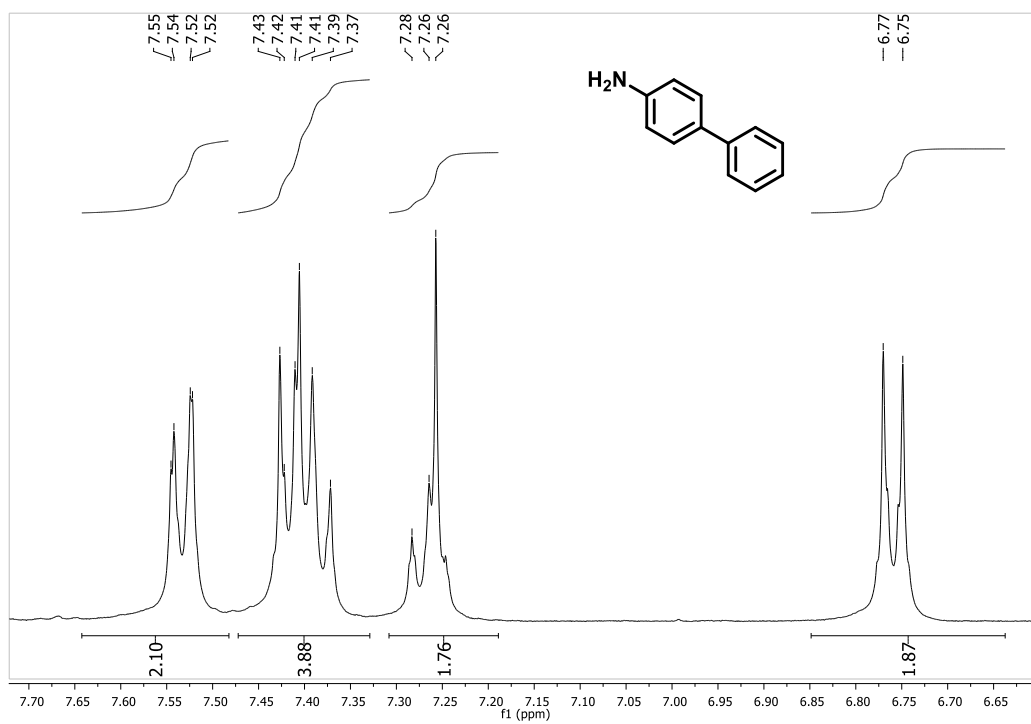
^{13}C NMR (101 MHz, CDCl_3) **2-chloropyridine-3-amine (13)**



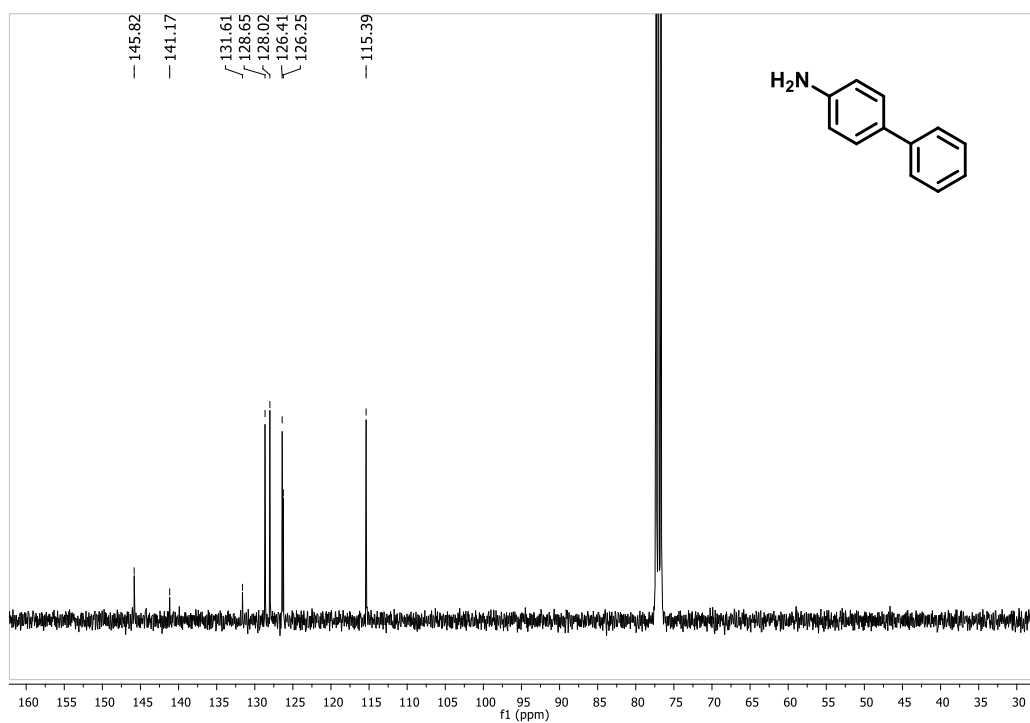
¹H NMR (400 MHz, CDCl₃) 4-aminebiphenyl (16)



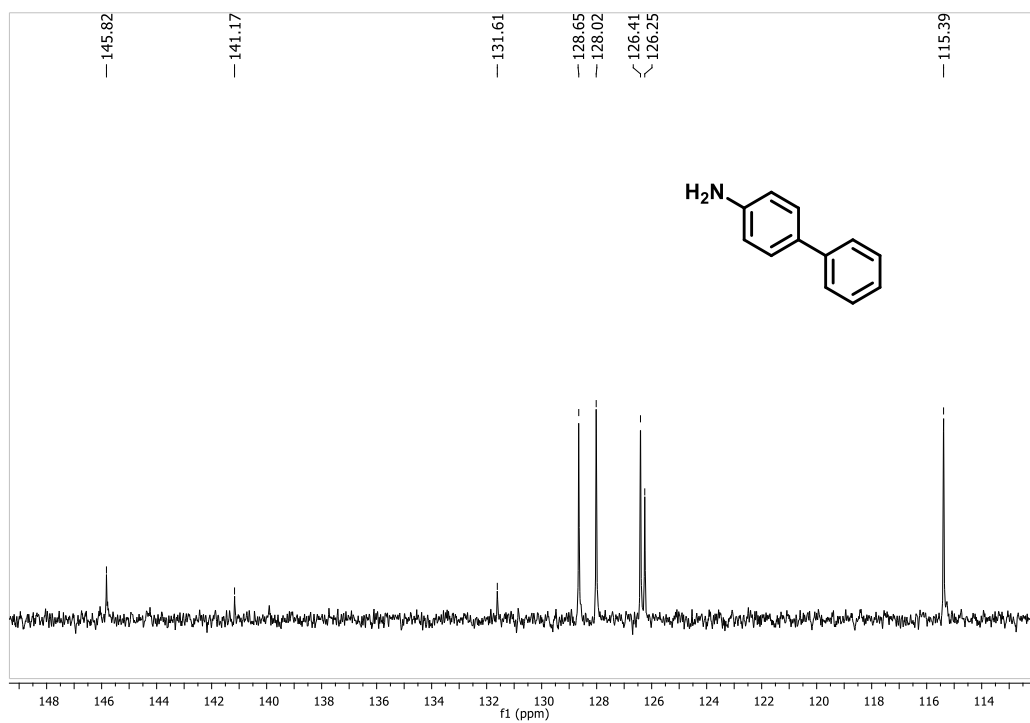
¹H NMR (400 MHz, CDCl₃) 4-aminebiphenyl (16)



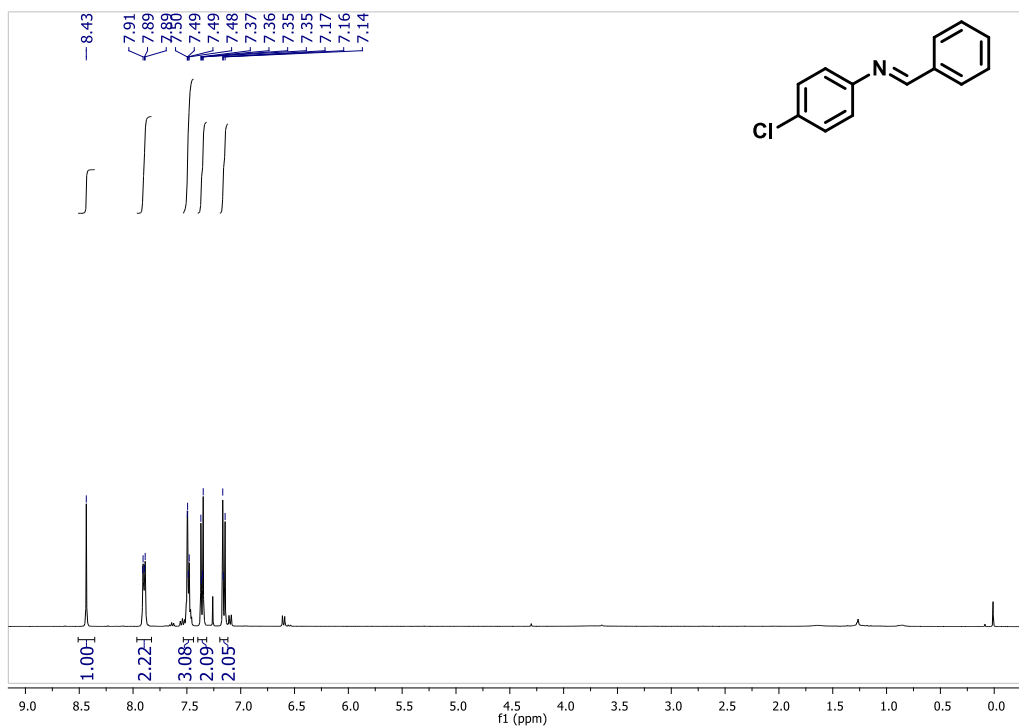
^{13}C NMR (101 MHz, CDCl_3) 4-aminebiphenyl (16)



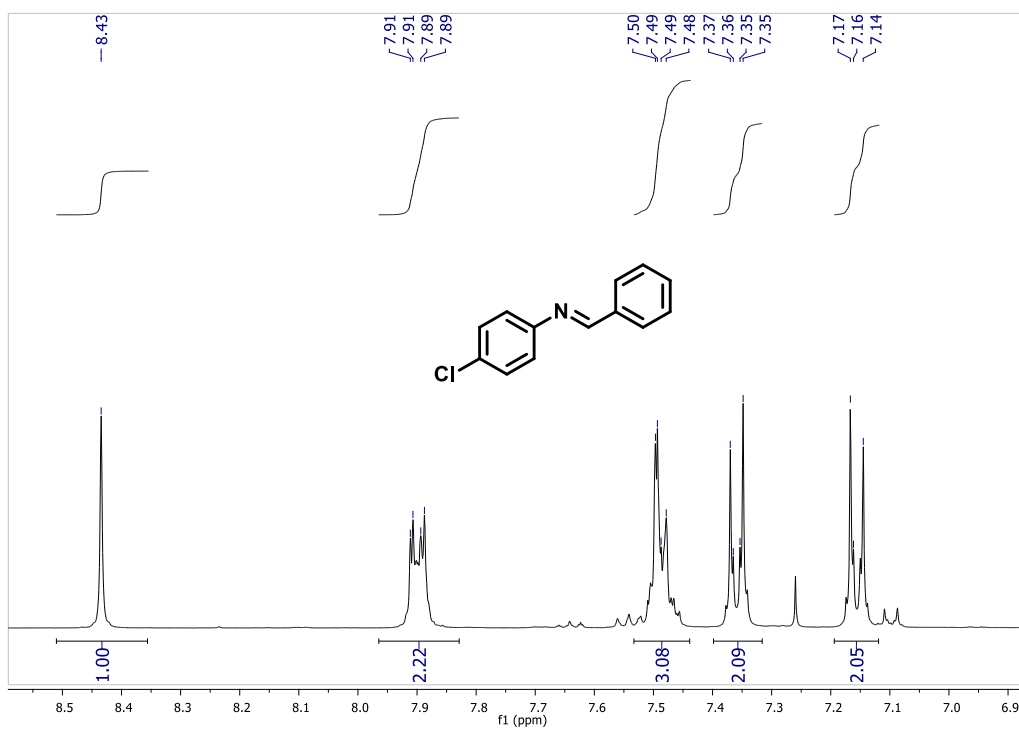
^{13}C NMR (101 MHz, CDCl_3) 4-aminebiphenyl (16)



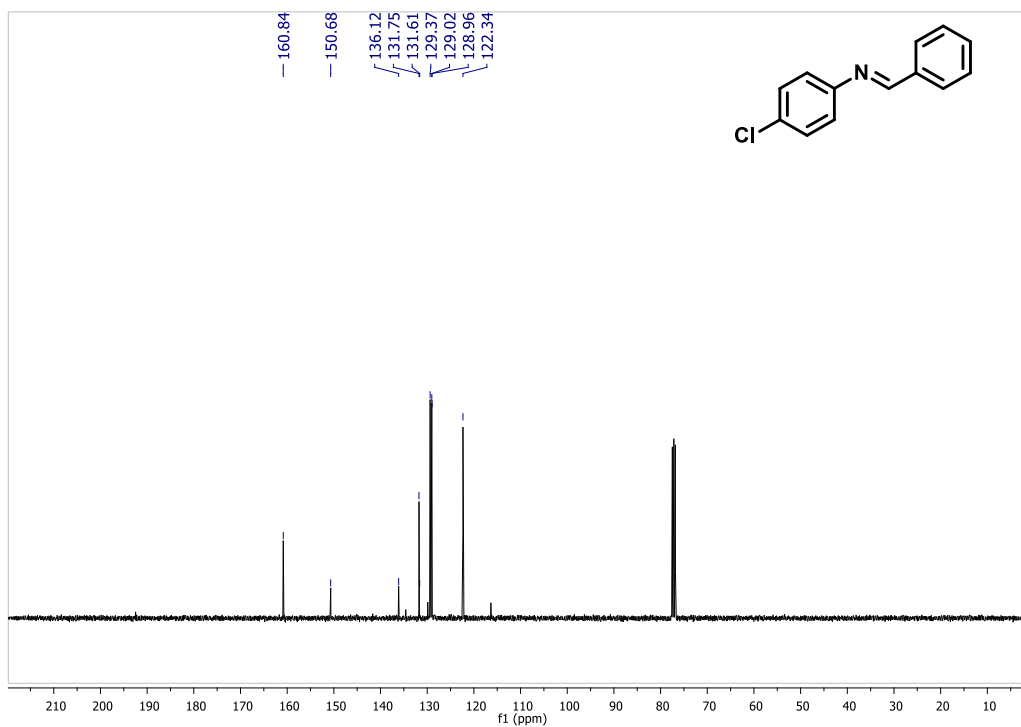
¹H NMR (400 MHz, CDCl₃) (*E*)-*N*-benzylidene-4-chloroaniline (19)



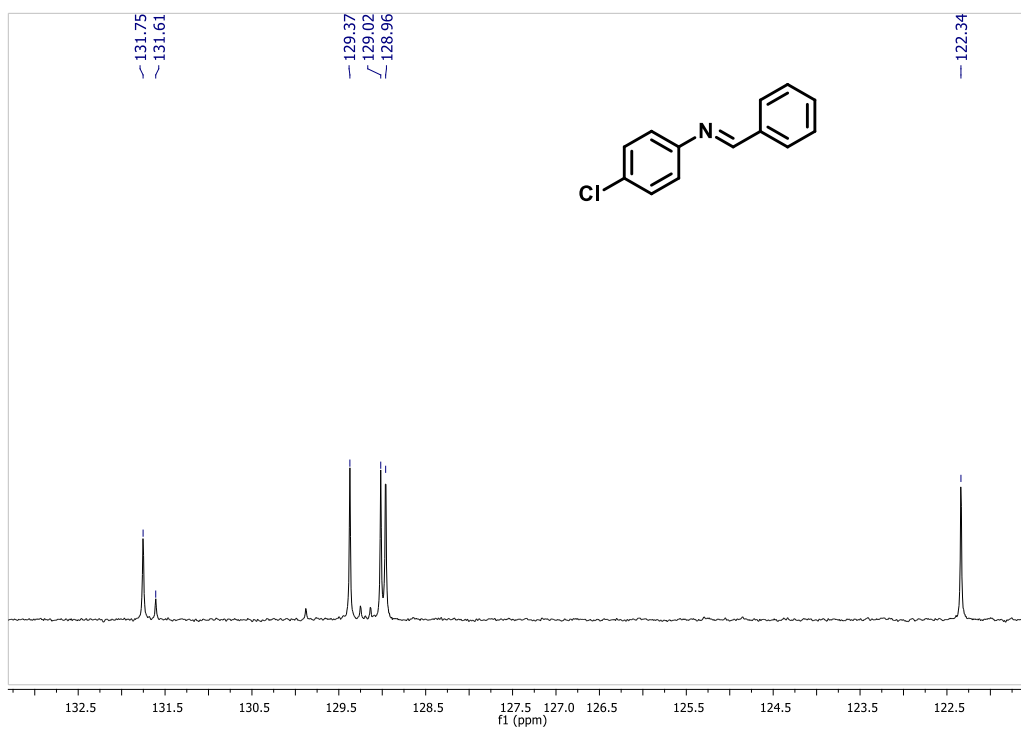
¹H NMR (400 MHz, CDCl₃) (*E*)-*N*-benzylidene-4-chloroaniline (19)



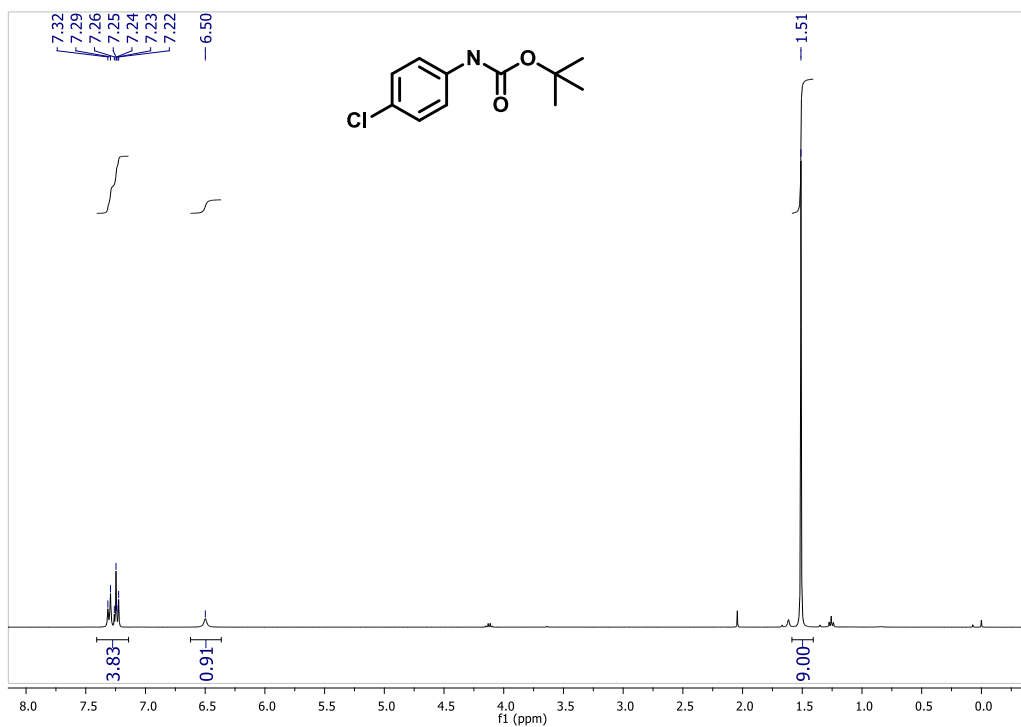
^{13}C NMR (101 MHz, CDCl_3) (*E*)-*N*-benzylidene-4-chloroaniline (19)



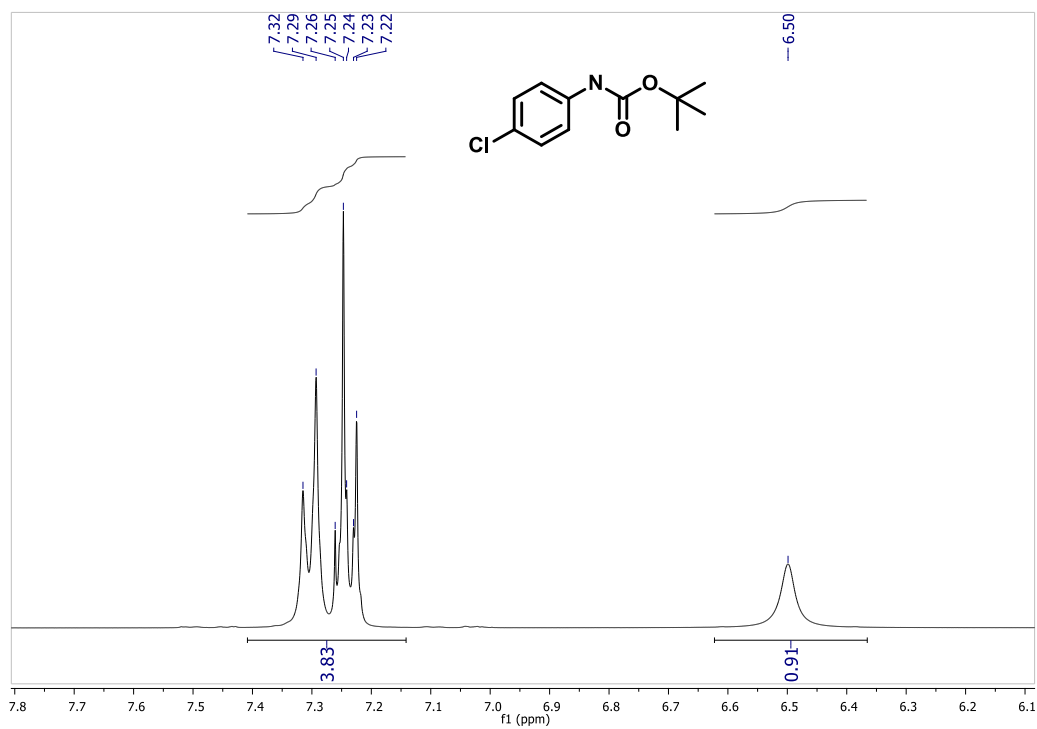
^{13}C NMR (101 MHz, CDCl_3) (*E*)-*N*-benzylidene-4-chloroaniline (19)



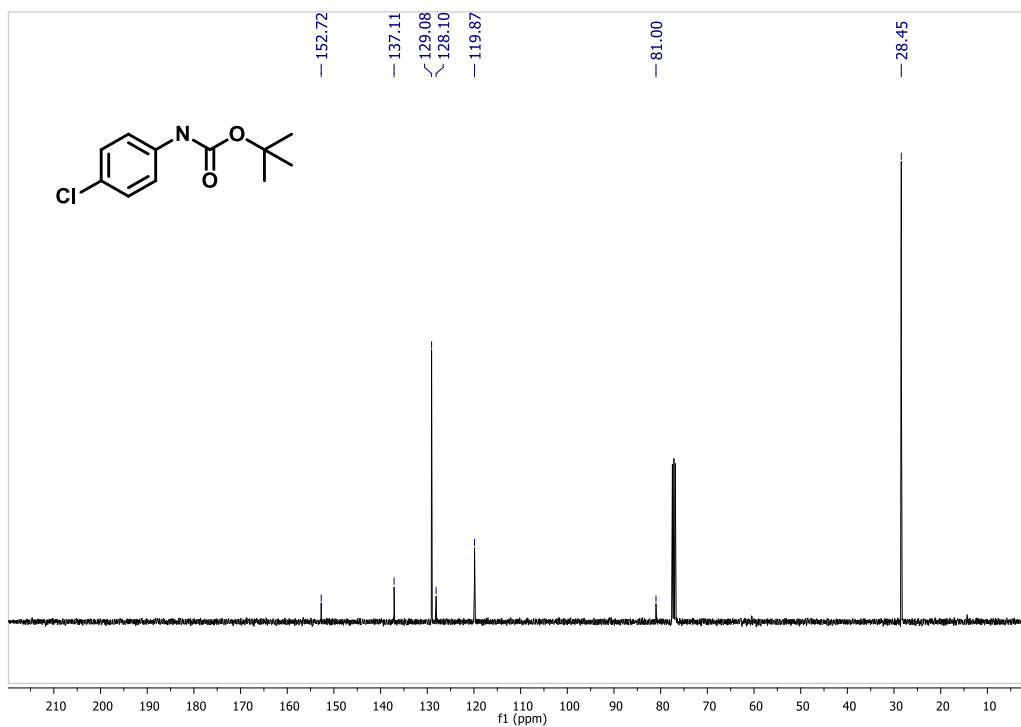
¹H NMR (400 MHz, CDCl₃) tert-butyl (4-chlorophenyl)carbamate (20)



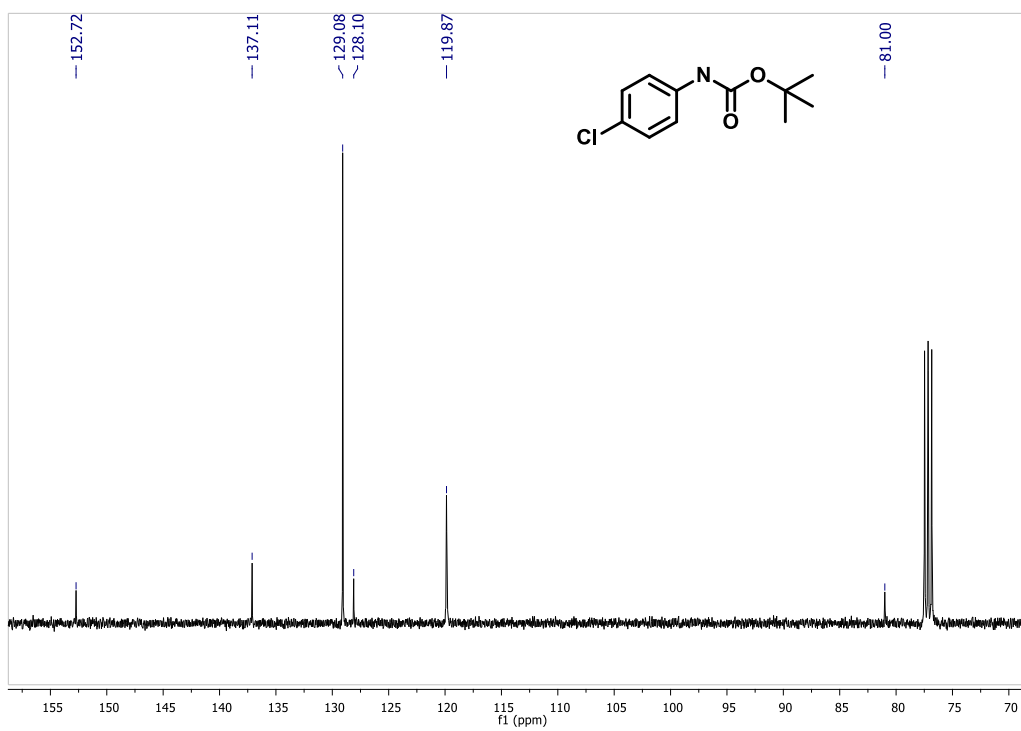
¹H NMR (400 MHz, CDCl₃) tert-butyl (4-chlorophenyl)carbamate (20)



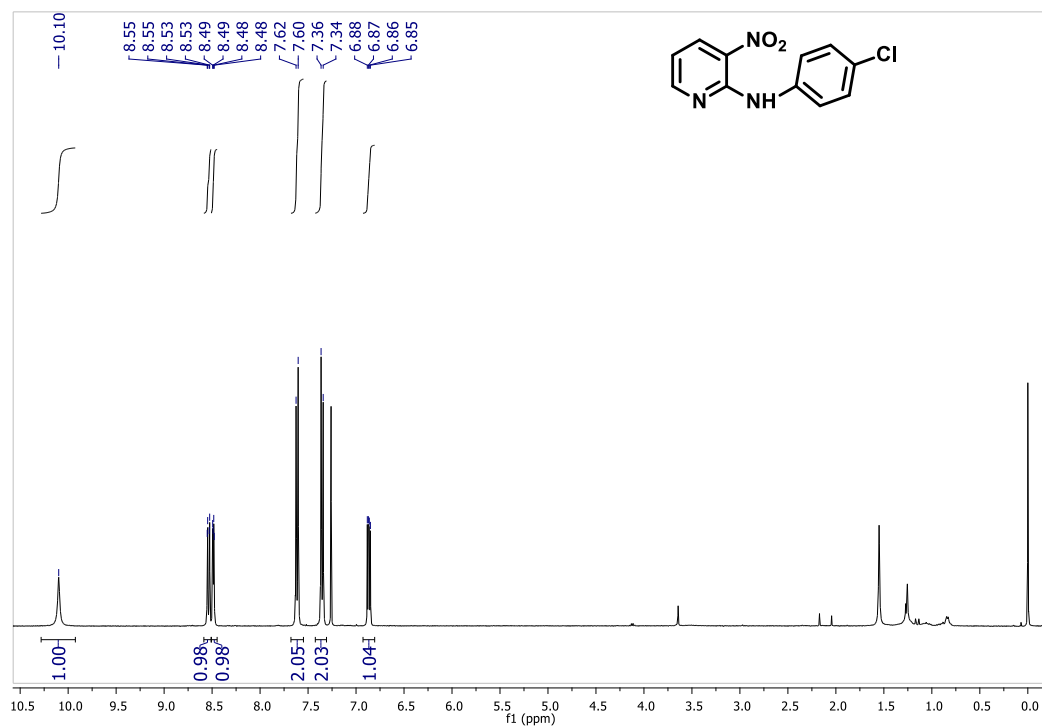
^{13}C NMR (101 MHz, CDCl_3) **tert-butyl (4-chlorophenyl)carbamate (20)**



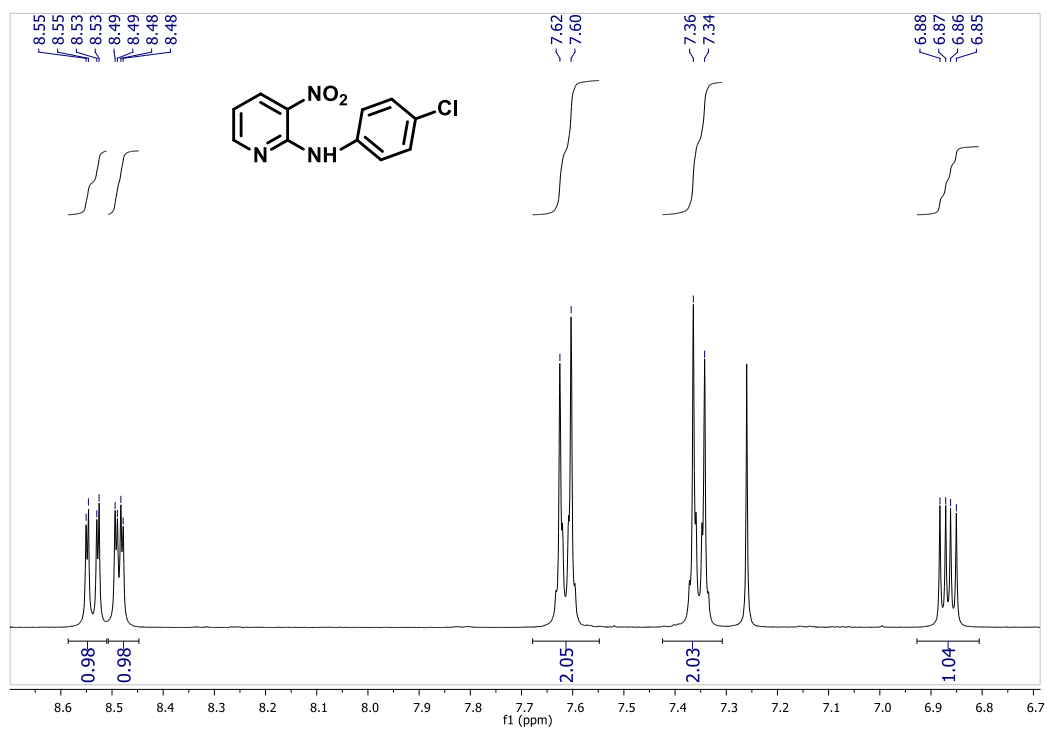
^{13}C NMR (101 MHz, CDCl_3) **tert-butyl (4-chlorophenyl)carbamate (20)**



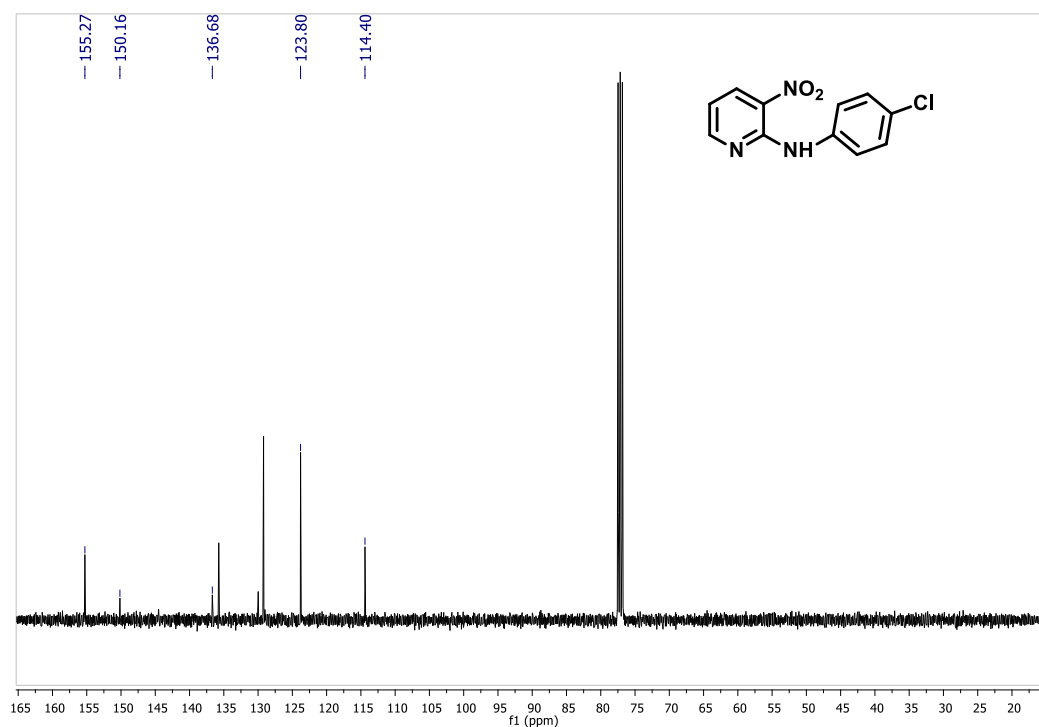
^1H NMR (400 MHz, CDCl_3) ***N*-(4-chlorophenyl)-3-nitropyridin-2-amine (21)**



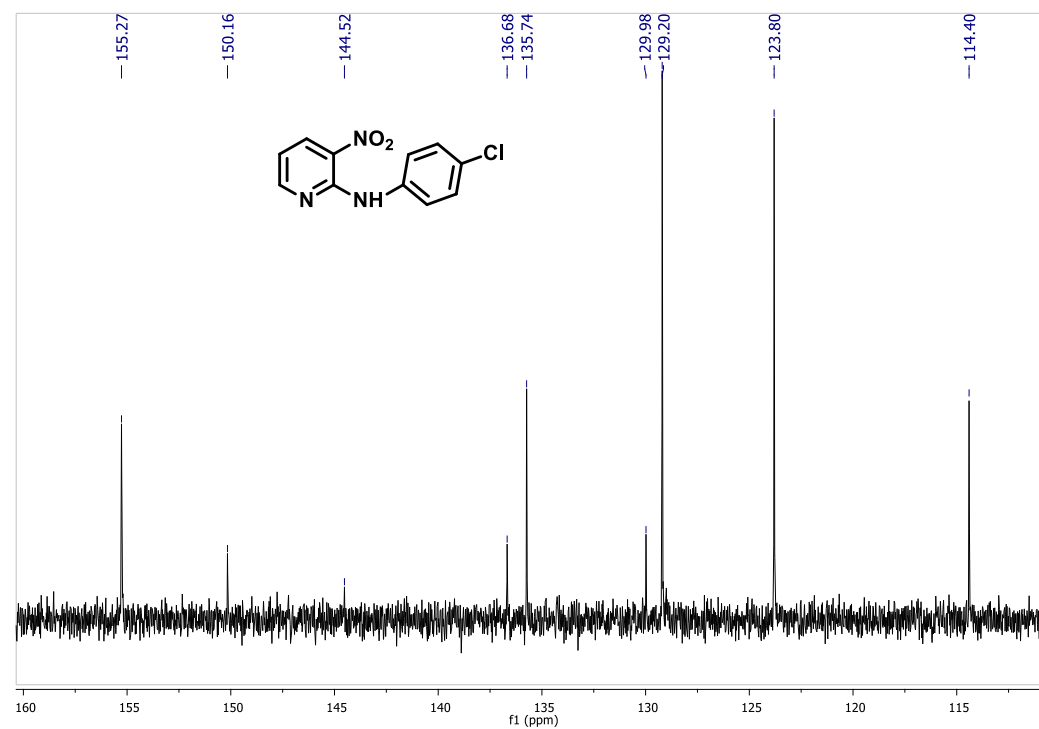
^1H NMR (400 MHz, CDCl_3) ***N*-(4-chlorophenyl)-3-nitropyridin-2-amine (21)**



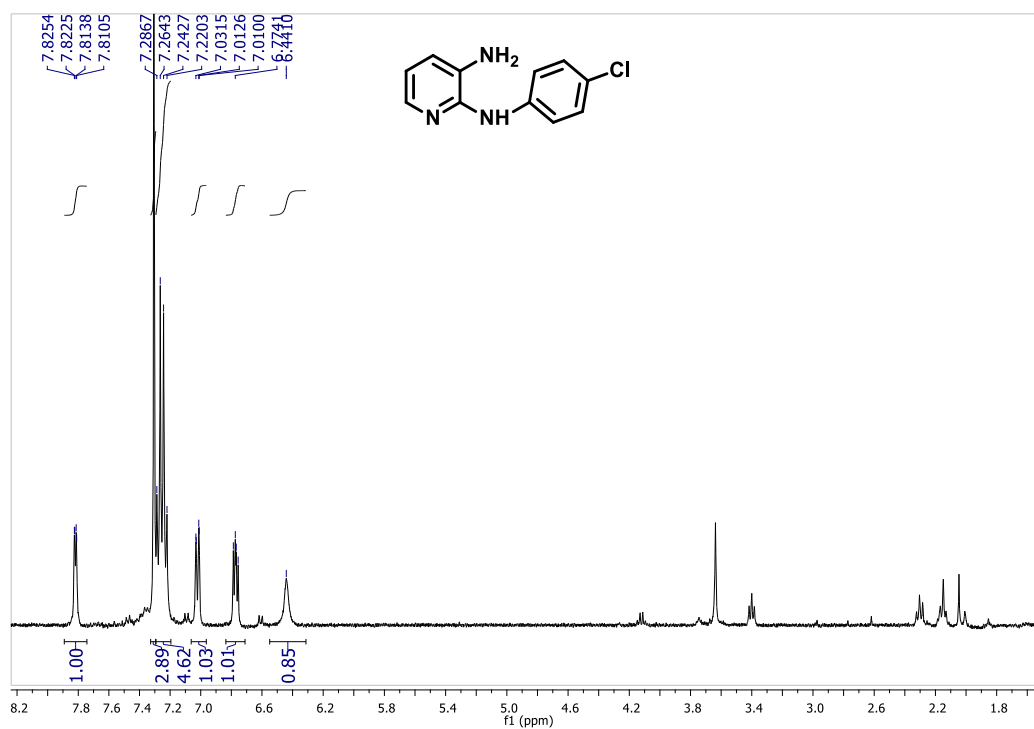
^{13}C NMR (101 MHz, CDCl_3) *N*-(4-chlorophenyl)-3-nitropyridin-2-amine (21)



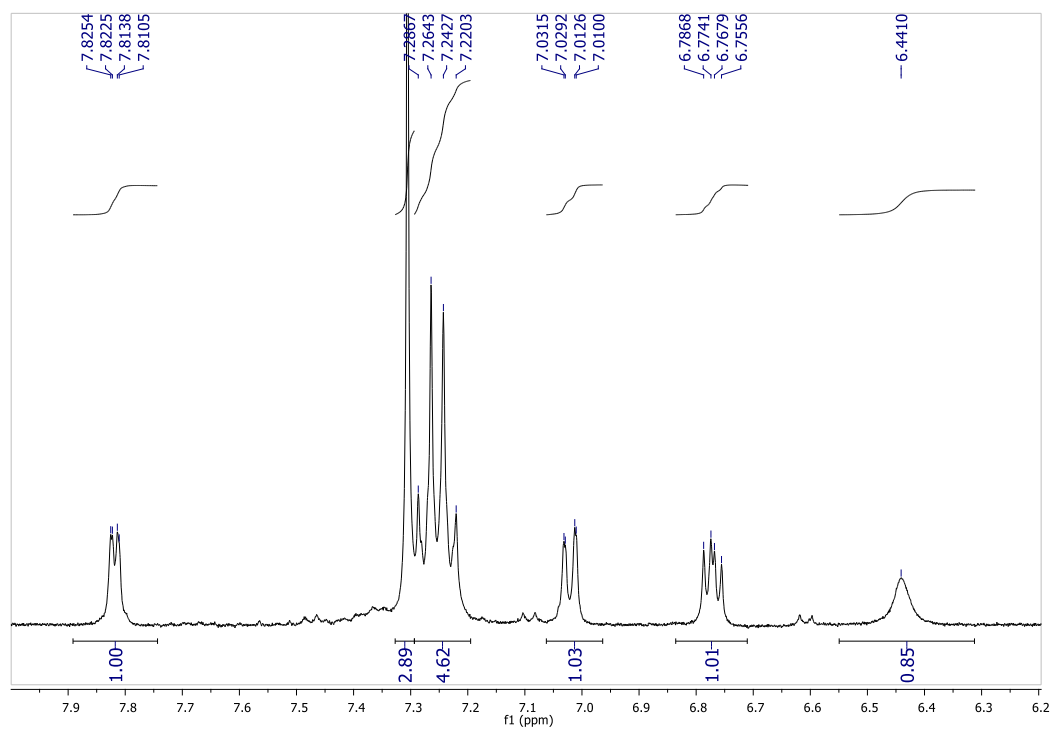
^{13}C NMR (101 MHz, CDCl_3) *N*-(4-chlorophenyl)-3-nitropyridin-2-amine (21)



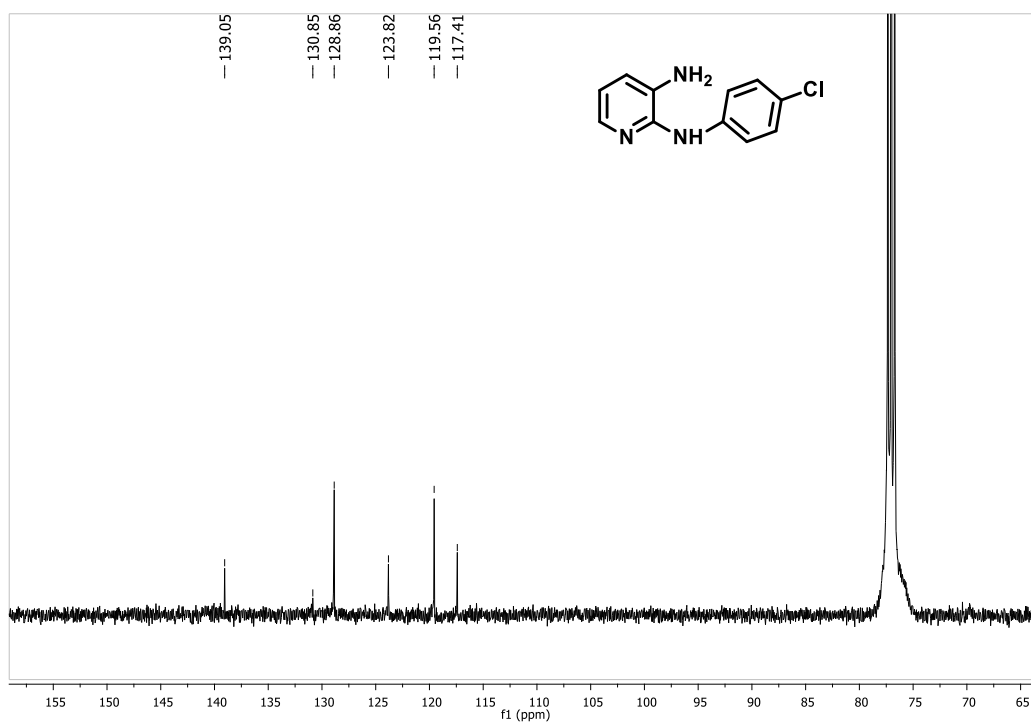
^1H NMR (400 MHz, CDCl_3) **N2-(4-chlorophenyl)pyridine-2,3-diamine (22)**



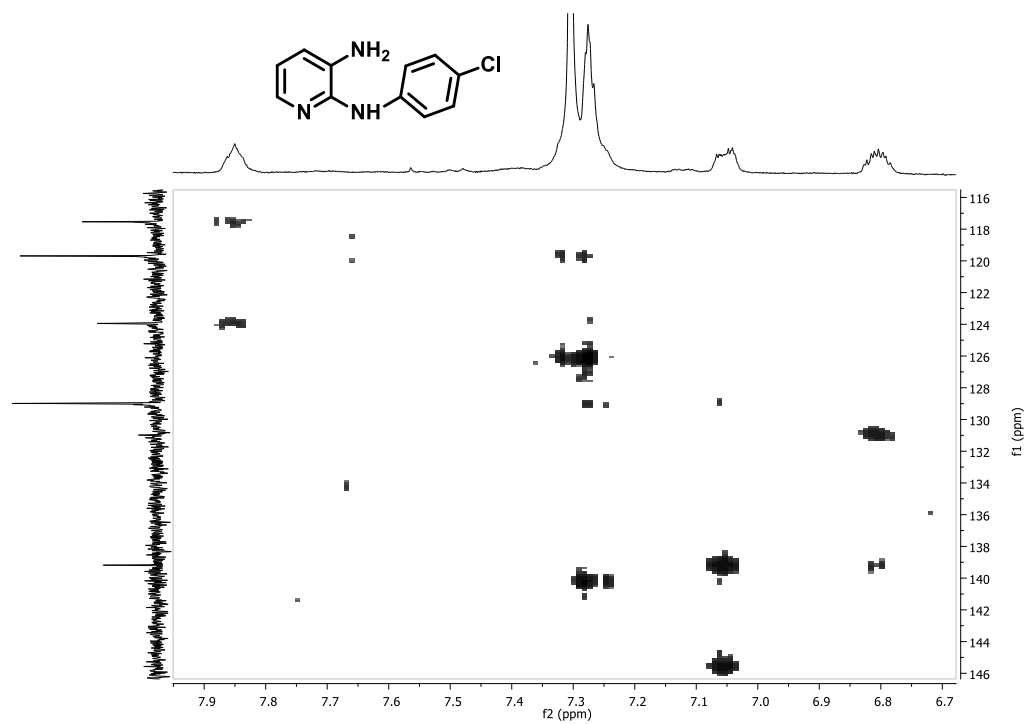
^1H NMR (400 MHz, CDCl_3) **N2-(4-chlorophenyl)pyridine-2,3-diamine (22)**



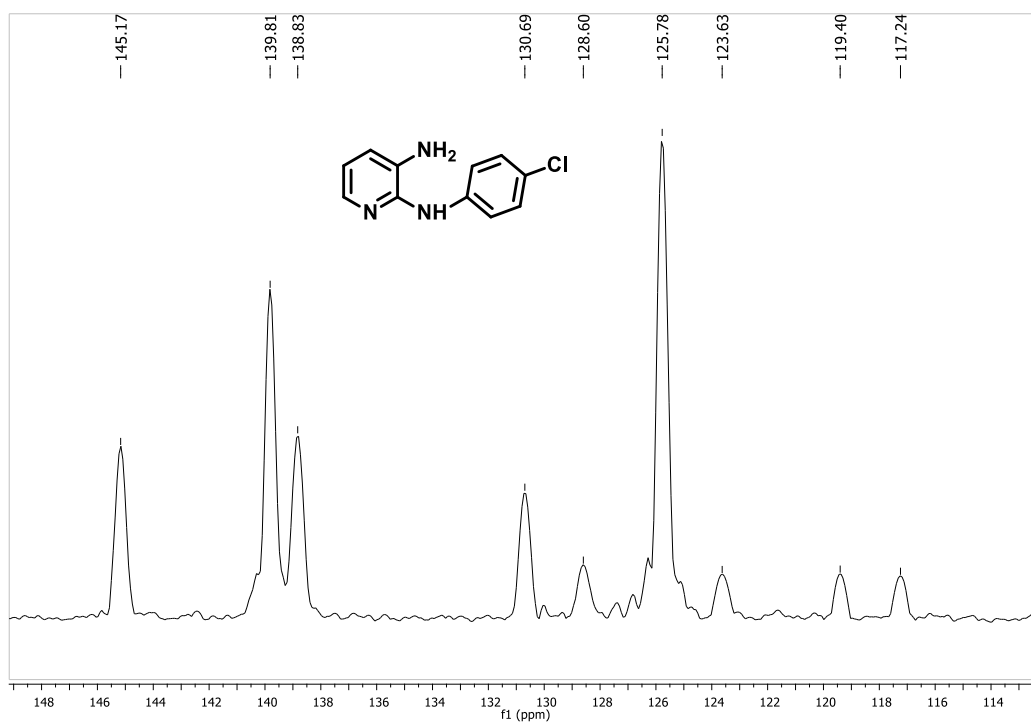
^{13}C NMR (101 MHz, CDCl_3) **N2-(4-chlorophenyl)pyridine-2,3-diamine (22)**



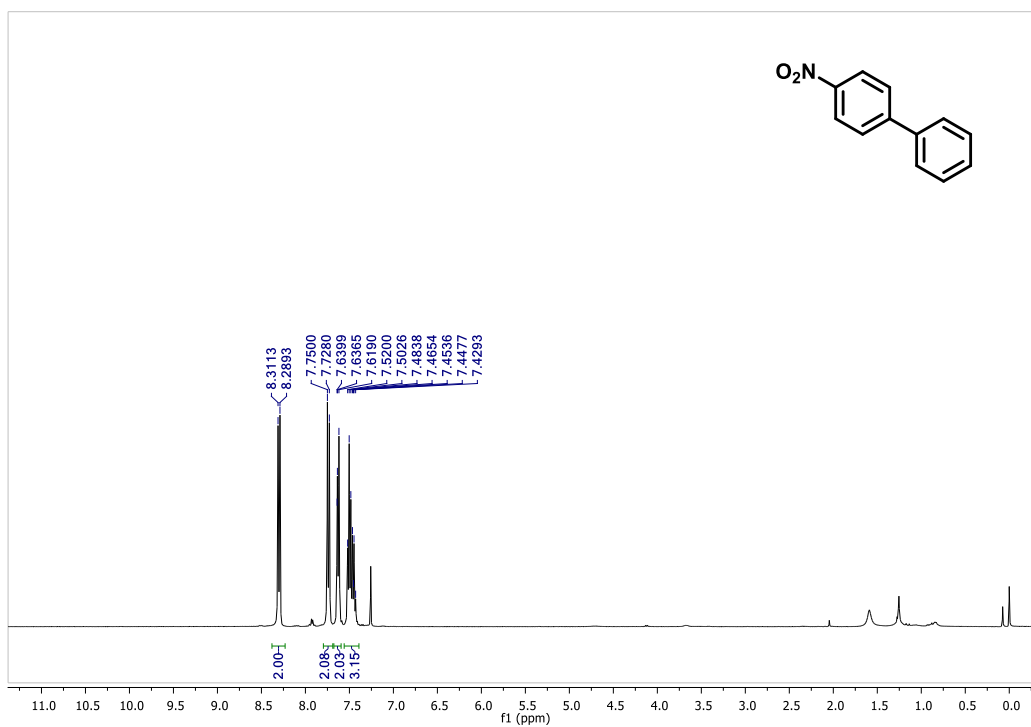
2D HMBC NMR (400 MHz, CDCl_3) **N2-(4-chlorophenyl)pyridine-2,3-diamine (22)**



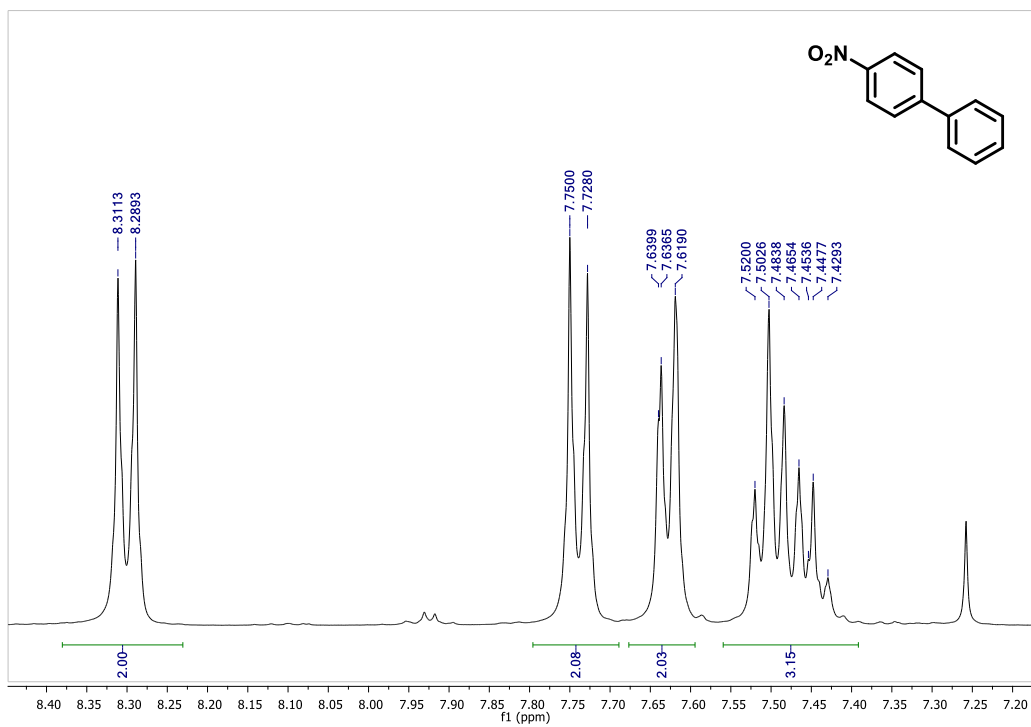
¹³C NMR (101 MHz, CDCl₃) **N2-(4-chlorophenyl)pyridine-2,3-diamine (22)**



¹H NMR (400 MHz, CDCl₃) 4-nitrobiphenyl



¹H NMR (400 MHz, CDCl₃) 4-nitrobiphenyl



4. References

- (1) Cantillo, D.; Moghaddam, M. M.; Kappe, C. O. *J. Org. Chem.* **2013**, *78*, 4530–4542.
- (2) Seth, K.; Nautiyal, M.; Purohit, P.; Parikh, N.; Chakraborti, A. K. *Chem. Commun.* **2015**, *51*, 191–194.
- (3) Thorwirth, R.; Bernhardt, F.; Stolle, A.; Ondruschka, B.; Asghari, J. *Chem. - A Eur. J.* **2010**, *16*, 13236–13242.
- (4) Tundel, R. E.; Anderson, K. W.; Buchwald, S. L. *J. Org. Chem.* **2006**, *71*, 430–433.
- (5) Monguchi, Y.; Maejima, T.; Mori, S.; Maegawa, T.; Sajiki, H. *Chem. - A Eur. J.* **2010**, *16*, 7372–7375.
- (6) Li, L.; Chen, Z.; Zhong, H.; Wang, R. *Chem. - A Eur. J.* **2014**, *20*, 3050–3060.
- (7) Saneyoshi, H.; Ochikubo, T.; Mashimo, T.; Hatano, K.; Ito, Y.; Abe, H. *Org. Lett.* **2014**, *16*, 30–33.
- (8) García, N.; García-García, P.; Fernández-Rodríguez, M. A.; Rubio, R.; Pedrosa, M. R.; Arnáiz, F. J.; Sanz, R. *Adv. Synth. Catal.* **2012**, *354*, 321–327.
- (9) Ulgen, C.-M. L. M.; Gorrod, J. W. *J. Pharm. Pharmacol.* **1994**, *46*, 585–590.
- (10) Sarkar, A.; Roy, S. R.; Parikh, N.; Chakraborti, A. K. *J. Org. Chem.* **2011**, *76*, 7132–7140.
- (11) Kamal, A.; Ali Hussaini, S. M.; Lakshma Nayak, V.; Shaheer Malik, M.; Lakshmi Sucharitha, M.; Shaik, T. B.; Ashraf, M.; Bagul, C. *Bioorg. Med. Chem.* **2014**, *22*, 6755–6767.
- (12) Kumar, A.; Purkait, K.; Dey, S. K.; Sarkar, A.; Mukherjee, A. *RSC Adv.* **2014**, *4*, 35233–35237.