

Supporting Information for

Metal-free Aerobic Oxidative Coupling of Amines to Imines

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General Information

D₂O and CDCl₃ were purchased from Cambridge Isotope Laboratory Inc; water was triply distilled and stored under air; other solvents were also distilled before used; all amines purchased from Aldrich or Alfa Aesar were distilled and stored at 4°C; and all other chemicals were purchased from Aldrich or Alfa Aesar unless otherwise noted and used as received. ¹H NMR spectra were recorded on a Bruker AVII⁺-400 spectrometer at ambient temperature. GC-MS results were obtained by the Agilent 7890A/5975C GC/MSD system equipped with the DB-17MS (30m, 0.25mm, 0.25um) column. Mass spectra were taken on a Bruker Apex IV FTMS.

General Procedure for the Oxidative Coupling Reactions

In a typical experiment, one atmosphere dioxygen is pressurized to a 45 ml Schlenk flask containing 4-methylbenzylamine (0.073g, 0.6 mmol) and water. After the reaction mixture is refluxed for 48 hours, the product is simply extracted with diethyl ether and characterized by GC, GC-MS and ¹H NMR.

For the homo-coupling reactions: 4-Methylbenzylamine 0.073 g (0.60 mmol) and water 0.60 ml were added into a Schlenk flask with a high vacuum valve (V = 40 ml) fitting in a Radleys parallel synthesis station. The sample was subjected to three freeze-pump-thaw cycles and then filled with 1 atm O₂. The solution was stirred vigorously and refluxed for 60 hours. After it was cooled down to room temperature, 2 ml of water was added to the solution. The product was extracted for three times with 9 ml of diethyl ether. The organic layers were combined and diluted to 25.00 ml for GC test.

For the cross-coupling reactions: Benzylamine 0.064 g (0.60 mmol), aniline 0.17 g (1.8 mmol) and water 0.60 ml were used instead.

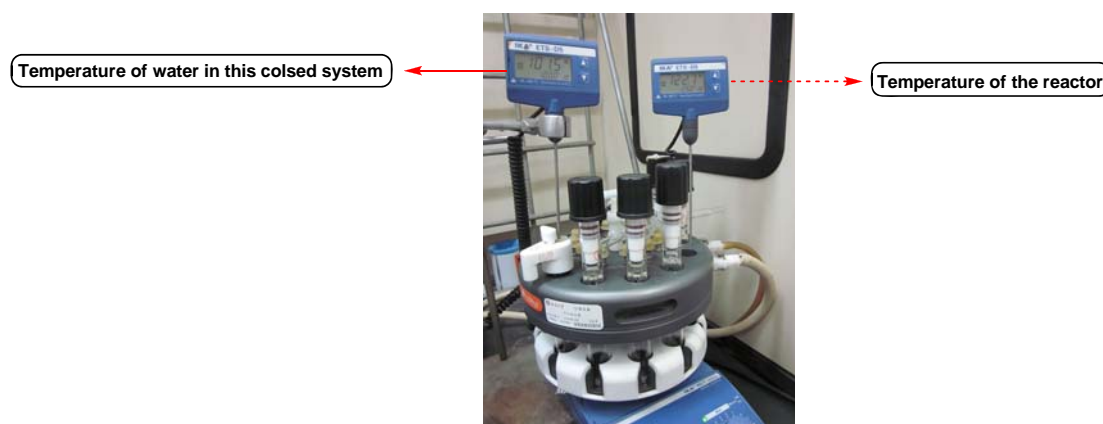


Figure 1S. Radleys parallel synthesis station

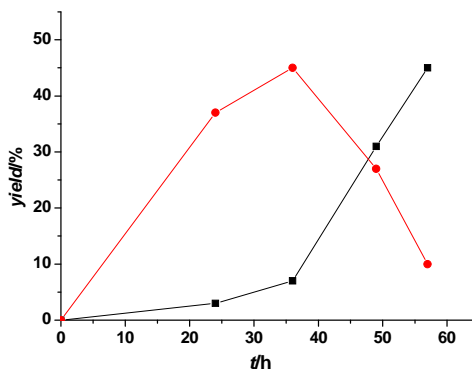
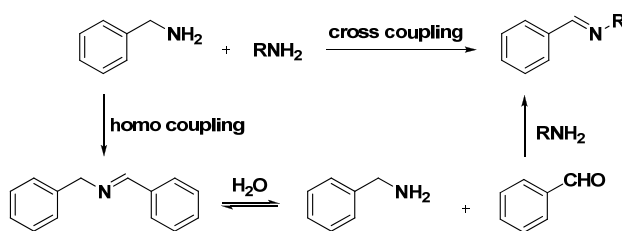


Figure 2S. The kinetics of the formation of N-benzylidene-benzylamine (red) and N-benzylidene-hexamine (black)



General Procedure for the Preparations of Imines

Imines were independently synthesized by condensation of the aldehydes and the amines, and used as standards for GC measurements. The aldehydes and amines were purified by distillation.

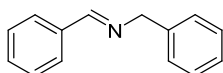
For general imines, the procedure is as follows:¹ To a 25 ml round-bottomed flask was added benzylamine (0.8289 g, 7.74 mmol), 5 ml CH₂Cl₂, and 0.5 g MgSO₄. With stirring, benzaldehyde (0.8201 g, 7.73 mmol) was added. The mixture was stirred at room temperature for 3 hours and then filtered to remove MgSO₄ solid. The filtrated solution was collected and the solvent was removed by rotary evaporation giving a colorless liquid. The excess aldehydes and amines were further removed under high vacuum (< 0.1 Pa) at 60 °C. The yield was 95%.

For the synthesis of N-(diphenylmethylene)-diphenylmethamine, the procedure is as follows:² Benzophenone 2.73 g (15 mmol) and diphenylmethamine 3.02 g (16.5 mmol) were combined and treated with one drop of concentrated H₂SO₄. The Si(OEt)₄ 3.45 g (16.5 mmol) was added and the mixture placed in a flask equipped with a still head. The solution was heated at 160 °C under nitrogen overnight. The distillate (EtOH) was discarded and the residue was dissolved in Et₂O (50 ml) and washed with saturated NaHCO₃ solution and H₂O (25 ml each). The Et₂O solution was dried (MgSO₄) and the solvent was removed under vacuum. Crude products were purified by kugelrohr distillation. For further purification the imine (2 g) was dissolved in 10 ml of 95% EtOH and treated with 2 ml of 1 M KOH in EtOH. The solution was stirred for 15 minutes than filtered and the precipitated washed with Et₂O. The filtrate was washed with H₂O (2 × 20 ml) and dried (MgSO₄). The solvent was removed under vacuum to yield the purified imine.

General Procedure for the Aza-D-A Reactions

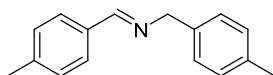
After the oxidative coupling reaction, the product was extracted with diethyl ether. The solvent was removed under vacuum. To the residue was added 2 ml of methanol. Under stirring at room temperature, Danishefsky's diene 58 μL (0.30 mmol) was added dropwise in 10 minutes to the reaction mixture. After stirring for 1 hour at room temperature, another 58 μL of Danishefsky's diene was added dropwise in 10 minutes. The reaction mixture was stirred for another 1 hour at room temperature and quenched with 2 ml of 1.0 M HCl. The product was extracted with diethyl ether and concentrated.³ The crude material was purified by column chromatography with $\text{CH}_2\text{Cl}_2/\text{EA}$ (4:1 V/V) as eluent.

Spectral Data for Products



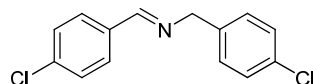
^1H NMR (CDCl_3 , 400MHz): δ 4.80 (s, 2H), 7.19-7.32 (m, 1H), 7.32-7.33 (m, 4H), 7.37-7.41 (m, 3H), 7.76-7.78 (m, 2H), 8.36 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 65.12, 127.06, 128.06, 128.36, 128.57, 128.67, 130.82, 136.30, 139.43, 162.00.



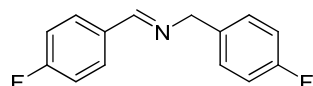
^1H NMR (CDCl_3 , 400MHz): δ 2.32 (s, 3H), 2.36 (s, 3H), 4.75 (s, 2H), 7.13 (d, 2H), 7.20-7.22 (m, 4H), 7.65 (d, 2H), 8.32 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 21.20, 21.59, 64.90, 128.06, 128.35, 129.25, 129.39, 133.80, 136.52, 136.58, 141.03, 161.73.



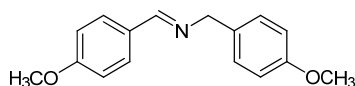
^1H NMR (CDCl_3 , 400MHz): δ 4.74 (s, 2H), 7.24 (d, 2H), 7.28-7.31 (m, 2H), 7.35-7.38 (m, 2H), 7.67-7.70 (m, 2H), 8.30 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 64.23, 128.72, 129.01, 129.35, 129.55, 132.90, 134.58, 136.95, 137.74, 160.88.



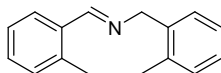
^1H NMR (CDCl_3 , 400MHz): δ 4.75 (s, 2H), 6.99-7.04 (m, 2H), 7.06-7.10 (m, 2H), 7.26-7.30 (m, 2H), 7.74-7.77 (m, 2H), 8.32 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 64.22, 115.30, 115.51, 115.72, 115.93, 129.54, 129.61, 130.23, 130.32, 132.45, 132.48, 135.07, 135.10, 160.62, 160.88, 163.26, 163.31, 165.76.



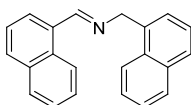
^1H NMR (CDCl_3 , 400MHz): δ 3.77 (s, 3H), 3.81 (s, 3H), 4.71 (s, 2H), 6.86-6.92 (m, 4H), 7.23 (d, 2H), 7.70 (q, 2H), 8.28 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 55.33, 55.41, 64.46, 113.99, 114.06, 129.24, 129.30, 129.89, 131.78, 158.74, 160.99, 161.76.



^1H NMR (CDCl_3 , 400MHz): δ 2.38 (s, 3H), 2.49 (s, 3H), 4.81 (s, 2H), 7.14-7.30 (m, 7H), 7.90-7.92 (m, 1H), 8.65 (s, 1H).

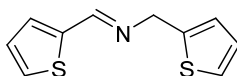
^{13}C NMR (CDCl_3 , 100MHz): δ 19.37, 19.48, 63.38, 126.17, 126.27, 127.15, 127.84, 128.41, 130.21, 130.33, 130.91, 134.35, 136.20, 137.71, 137.82, 160.64.



^1H NMR (CDCl_3 , 400MHz): δ 5.40 (s, 2H), 7.44-7.58 (m, 7H), 7.79-7.93 (m, 5H), 8.24 (d, 1H), 8.93 (d, 1H), 9.07 (s, 1H).

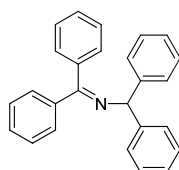
^{13}C NMR (CDCl_3 , 100MHz): δ 63.39, 124.11, 124.61, 125.36, 125.77, 125.84, 126.04, 126.17, 126.27, 127.34, 127.96, 128.75, 128.84, 129.30, 131.27, 131.52, 131.82, 131.86, 133.98, 134.03, 135.67, 162.09.

FTMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{18}\text{N}^+$ ($[\text{M} + \text{H}]^+$): 296.14338; found: 296.14330.



^1H NMR (CDCl_3 , 400MHz): δ 4.92 (s, 2H), 6.95-6.98 (m, 2H), 7.03-7.05 (m, 1H), 7.20-7.22 (m, 1H), 7.29-7.30 (m, 1H), 7.38-7.39 (m, 1H), 8.38 (d, 1H).

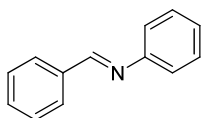
^{13}C NMR (CDCl_3 , 100MHz): δ 58.58, 124.88, 125.34, 126.95, 127.45, 129.39, 131.02, 141.65, 142.23, 155.46.



^1H NMR (CDCl_3 , 400MHz): δ 5.55 (s, 1H), 7.06-7.08 (m, 2H), 7.16-7.20 (m, 2H), 7.24-7.28 (m, 4H), 7.31-7.37 (m, 7H), 7.39-7.43 (m, 3H), 7.74-7.76 (m, 2H).

^{13}C NMR (CDCl_3 , 100MHz): δ 70.02, 126.81, 127.72, 127.90, 128.14, 128.47, 128.54, 128.61, 128.90, 130.19, 136.87, 139.99, 145.03, 167.04.

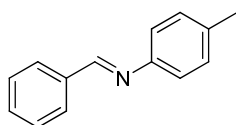
FTMS (ESI): m/z calcd for $\text{C}_{26}\text{H}_{22}\text{N}^+$ ($[\text{M} + \text{H}]^+$): 348.17468; found: 348.17442.



^1H NMR (CDCl_3 , 400MHz): δ 7.20-7.22 (m, 3H), 7.36-7.40 (m, 2H), 7.44-7.47 (m, 3H), 7.88-7.92

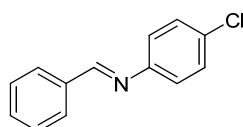
(m, 2H), 8.44 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 120.99, 126.05, 128.89, 128.93, 129.27, 131.48, 136.37, 152.23, 160.49.



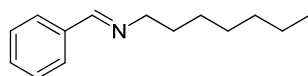
^1H NMR (CDCl_3 , 400MHz): δ 2.36 (s, 3H), 7.13 (d, 2H), 7.18 (d, 2H), 7.44-7.47 (m, 3H), 7.87-7.90 (m, 2H), 8.45 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 21.13, 120.94, 128.83, 128.85, 129.88, 131.31, 135.91, 136.50, 149.60, 159.68.



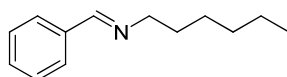
^1H NMR (CDCl_3 , 400MHz): δ 7.12-7.15 (m, 2H), 7.32-7.35 (m, 2H), 7.45-7.49 (m, 3H), 7.87-7.89 (m, 2H), 8.41 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 122.33, 128.94, 129.00, 129.35, 131.58, 131.73, 136.09, 150.64, 160.80.



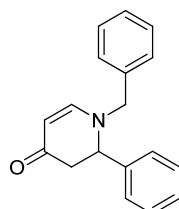
^1H NMR (CDCl_3 , 400MHz): δ 0.88 (t, 3H), 1.28-1.35 (m, 8H), 1.66-1.73 (m, 2H), 3.58-3.62 (m, 2H), 7.36-7.41 (m, 3H), 7.70-7.74 (m, 2H), 8.26 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 14.20, 22.76, 27.46, 29.26, 31.07, 31.95, 61.94, 128.14, 128.68, 130.53, 136.55, 160.79.



^1H NMR (CDCl_3 , 400MHz): δ 0.89 (t, 3H), 1.29-1.38 (m, 6H), 1.66-1.73 (m, 2H), 3.58-3.62 (m, 2H), 7.39-7.40 (m, 3H), 7.70-7.73 (m, 2H), 8.26 (s, 1H).

^{13}C NMR (CDCl_3 , 100MHz): δ 14.19, 22.74, 27.16, 31.02, 31.80, 61.94, 128.13, 128.67, 130.53, 136.52, 160.79.

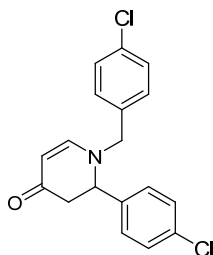


^1H NMR (CDCl_3 , 400MHz): δ 2.68 (dd, 1H), 2.84 (dd, 1H), 4.12 (d, 1H), 4.34 (d, 1H), 4.50 (t, 1H), 5.08 (d, 1H), 7.12 (d, 2H), 7.24-7.25 (m, 2H), 7.28-7.36 (m, 7H).

^{13}C NMR (CDCl_3 , 100MHz): δ 43.80, 57.35, 60.80, 98.84, 127.19, 127.83, 128.31, 128.42, 129.02,

129.13, 136.00, 138.69, 154.26, 190.40.

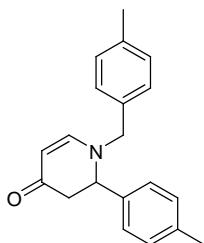
FTMS (ESI): m/z calcd for $C_{18}H_{18}NO^+$ ($[M + H]^+$): 264.13829; found: 264.13800.



1H NMR ($CDCl_3$, 400MHz): δ 2.63 (dd, 1H), 2.80 (dd, 1H), 4.07 (d, 1H), 4.32 (d, 1H), 4.32 (t, 1H), 5.10 (d, 1H), 7.05 (d, 2H), 7.17 (d, 2H), 7.27 (d, 1H), 7.31-7.34 (m, 4H).

^{13}C NMR ($CDCl_3$, 100MHz): δ 43.74, 56.73, 60.22, 99.54, 128.57, 129.15, 129.30, 129.42, 134.25, 134.39, 137.03, 153.95, 190.02.

FTMS (ESI): m/z calcd for $C_{18}H_{16}Cl_2NO^+$ ($[M + H]^+$): 332.06035; found: 332.06008.



1H NMR ($CDCl_3$, 400MHz): δ 2.34 (s, 6H), 2.64 (dd, 1H), 2.77 (dd, 1H), 4.06 (d, 1H), 4.27 (d, 1H), 4.44 (t, 1H), 5.05 (d, 1H), 7.01 (d, 2H), 7.14 (m, 6H), 7.26 (d, 1H).

^{13}C NMR ($CDCl_3$, 100MHz): δ 21.15, 43.81, 56.88, 60.40, 98.48, 127.08, 127.82, 129.59, 129.69, 132.88, 135.72, 137.99, 138.07, 154.17, 190.50.

FTMS (ESI): m/z calcd for $C_{20}H_{22}NO^+$ ($[M + H]^+$): 292.16959; found: 292.16927.

Reference

[1] Incarvito C.; Bosnich B. *Journal of the Chemical Society, Dalton Transactions* **2001**, 23, 3478-3488;

[2] Love B. E. and Ren J., *J. Org. Chem.*, **1993**, 58, 5556-5557.

[3] Y. Yuan, X. Li, K. Ding, *Org. Lett.*, **2002**, 4, 3309-3311;

Spectra of Products

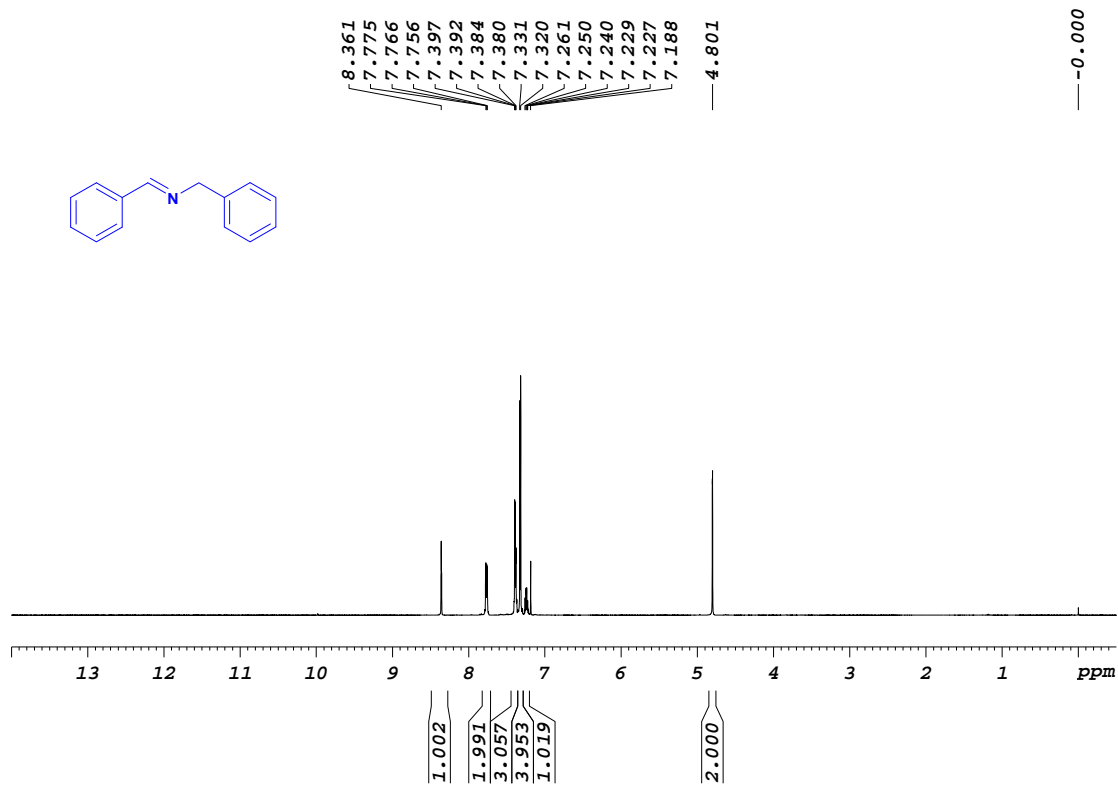


Figure 3S. The ¹H NMR of N-benzylidenebenzylamine

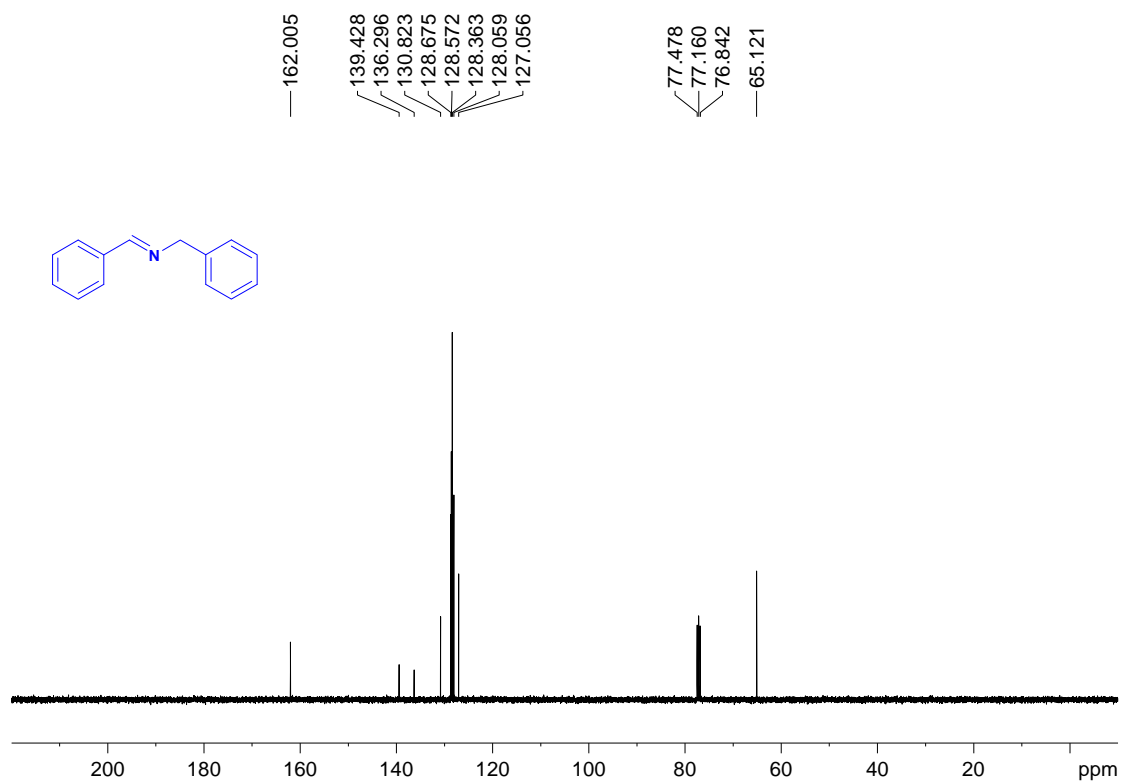


Figure 4S. The ^{13}C NMR of N-benzylidenebenzylamine

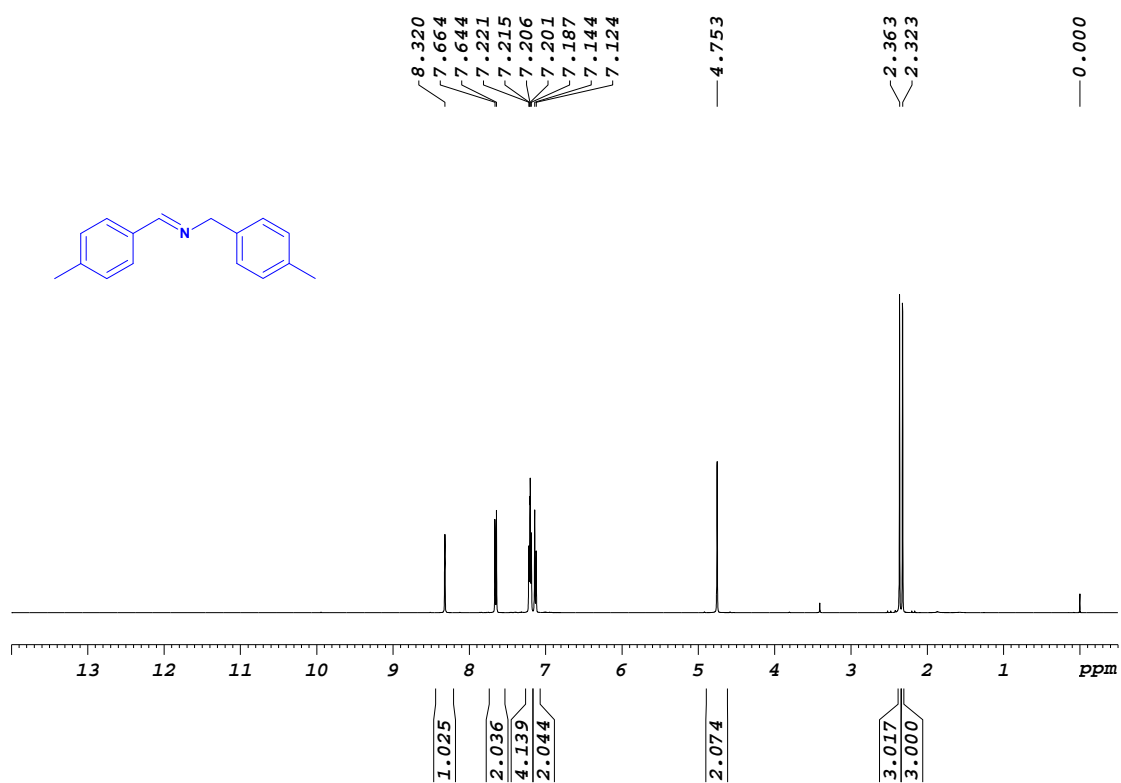


Figure 5S. The ^1H NMR of N-(4-methylbenzylidene)-p-methylbenzylamine

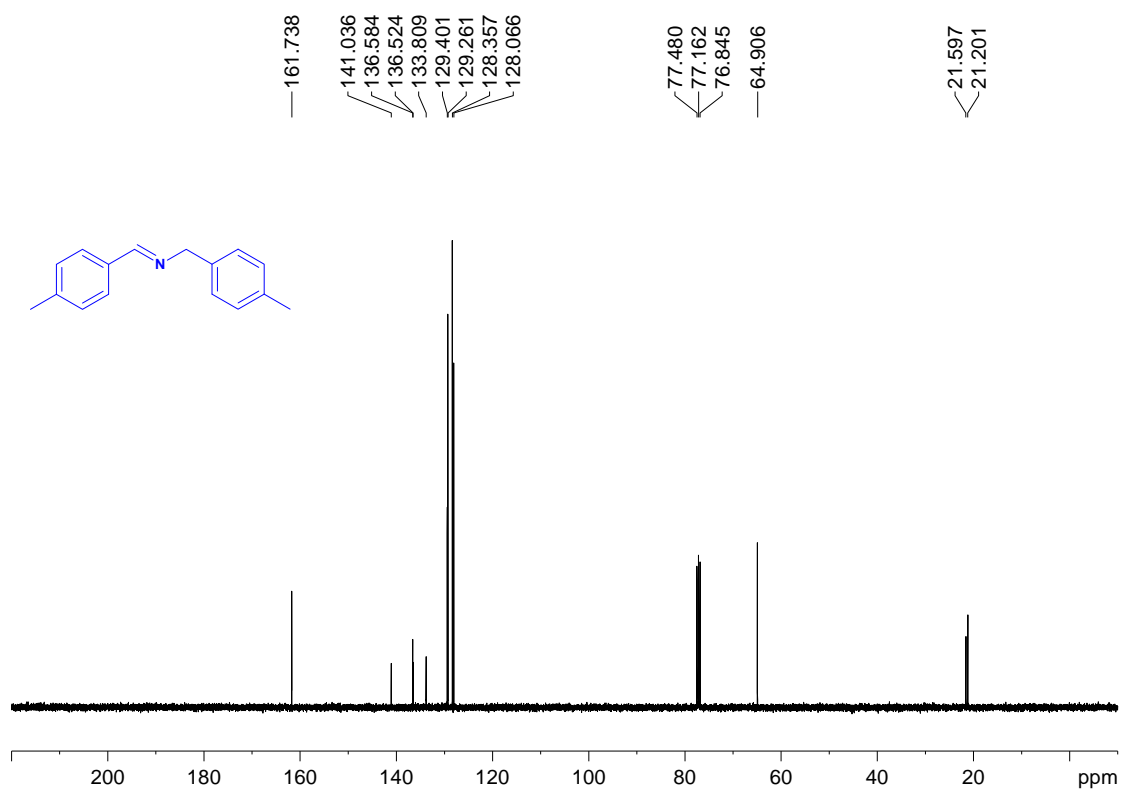


Figure 6S. The ^{13}C NMR of N-(4-methylbenzylidene)-p-methylbenzylamine

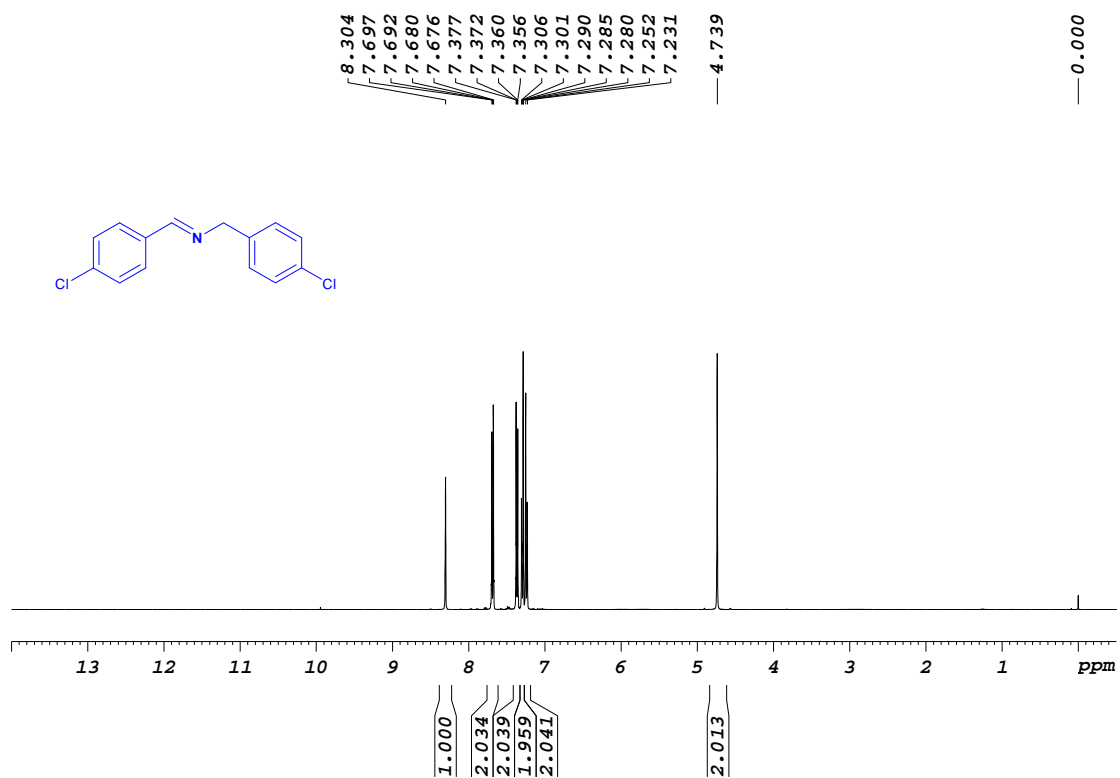


Figure 7S. The ¹H NMR of N-(4-chlorobenzylidene)-p-chlorobenzylamine

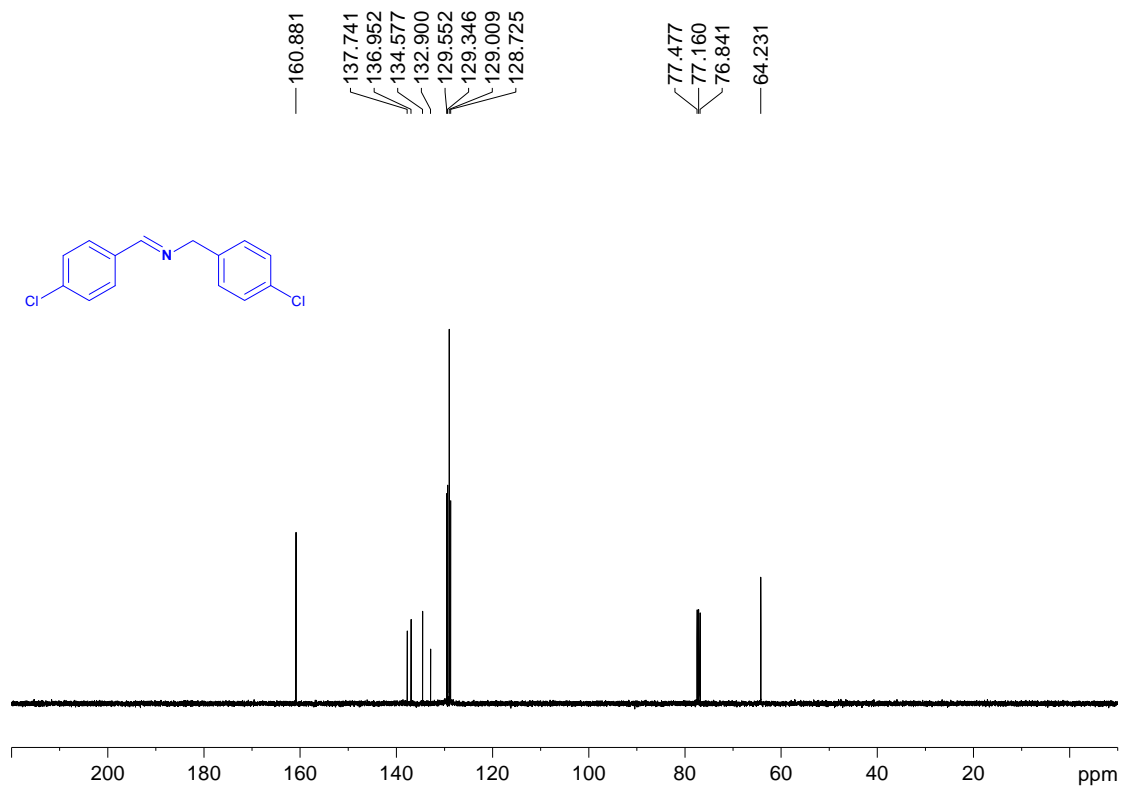


Figure 8S. The ¹³C NMR of N-(4-chlorobenzylidene)-p-chlorobenzylamine

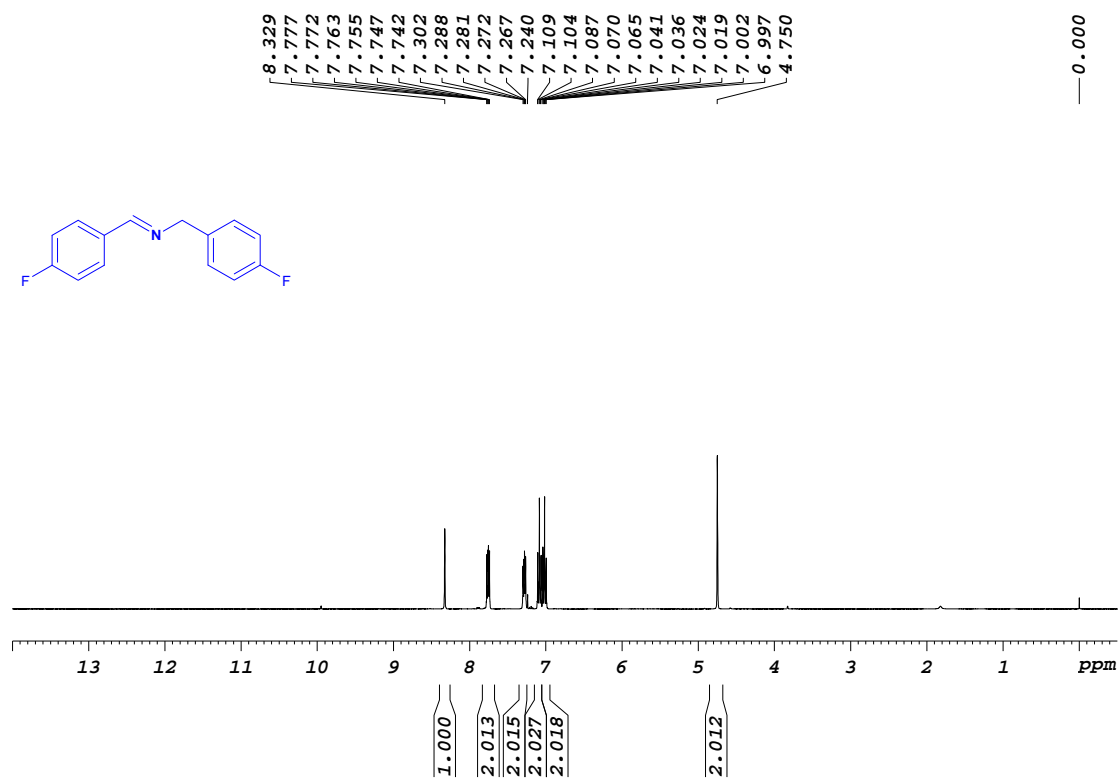


Figure 9S. The ^1H NMR of N-(4-fluorobenzylidene)-p-fluorobenzylamine

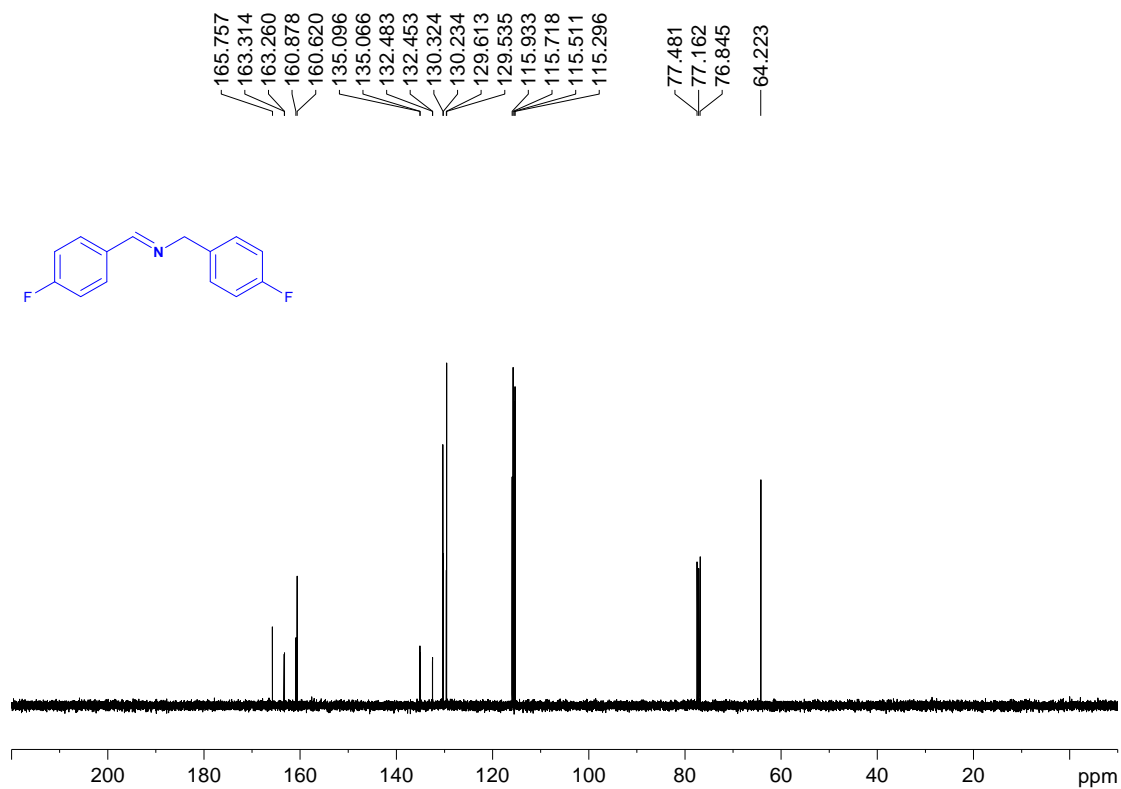


Figure 10S. The ^{13}C NMR of N-(4-fluorobenzylidene)-p-fluorobenzylamine

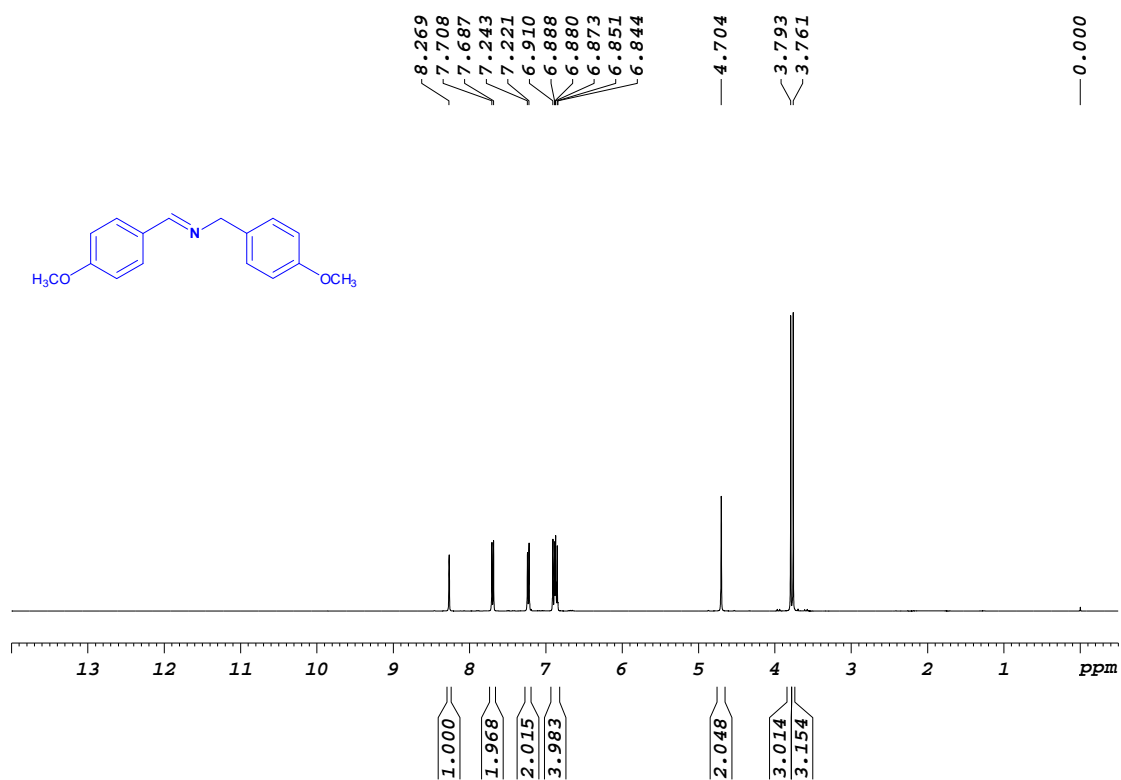


Figure 11S. The ¹H NMR of N-(4-methoxybenzylidene)-p-methoxybenzylamine

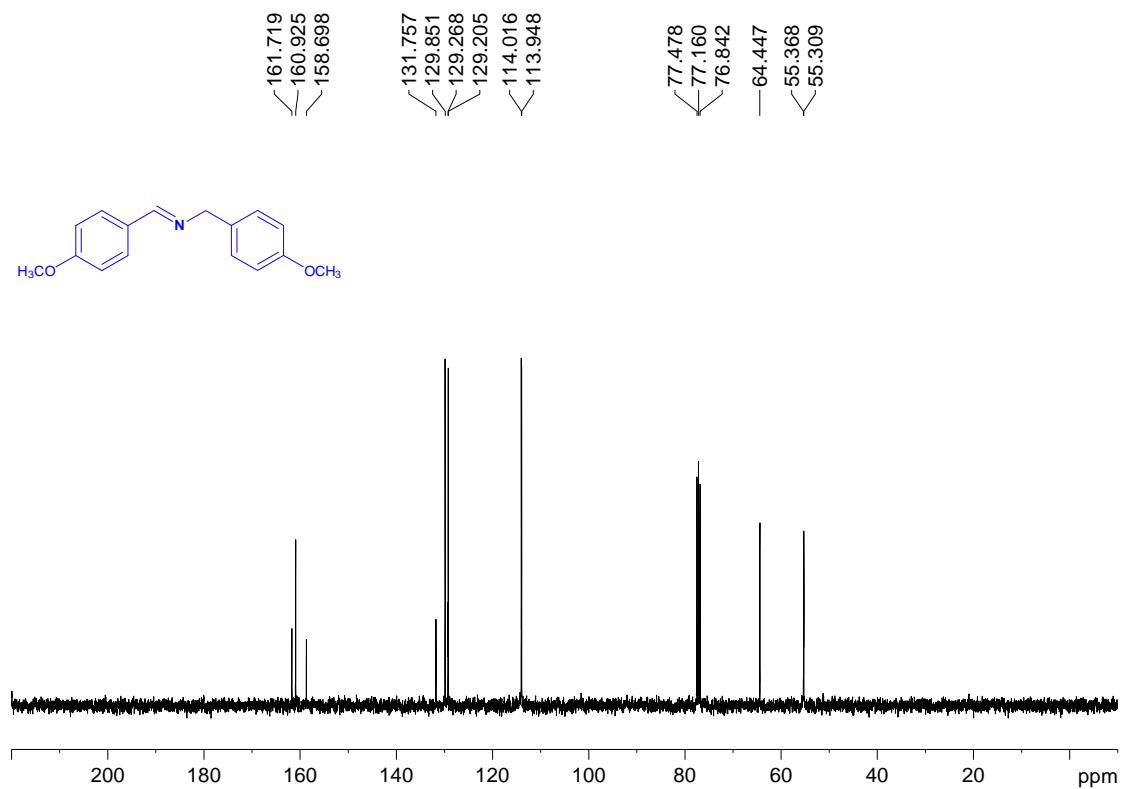


Figure 12S. The ¹³C NMR of N-(4-methoxybenzylidene)-p-methoxybenzylamine

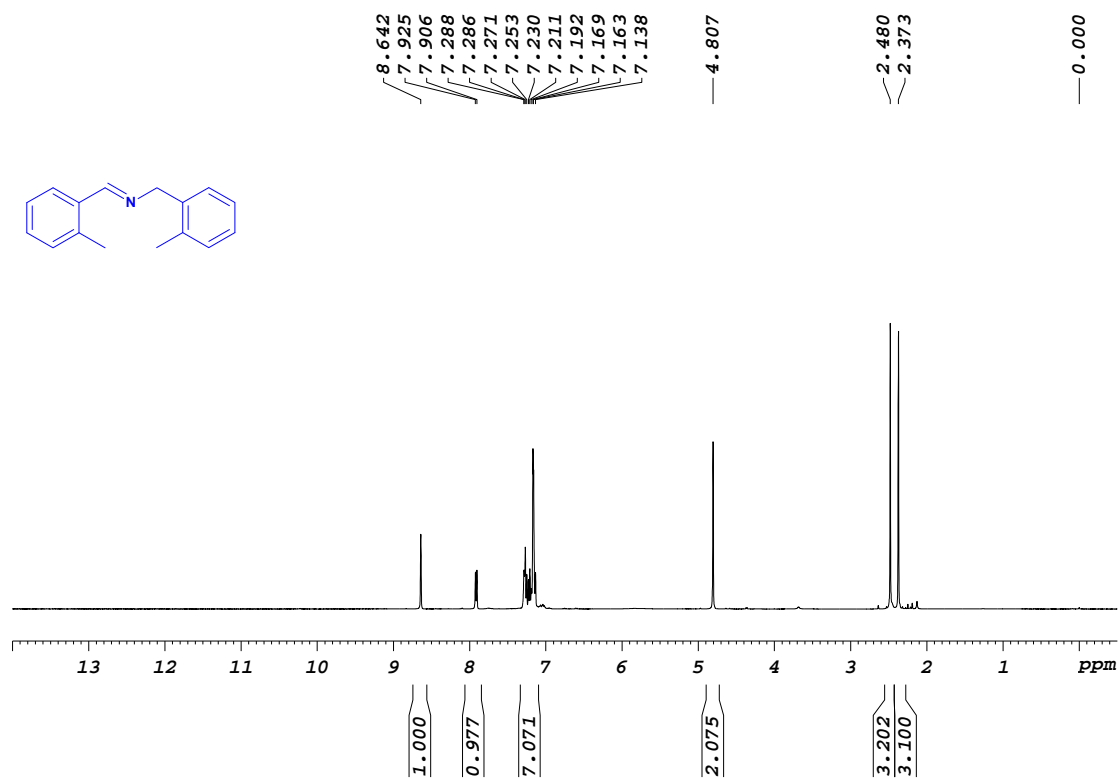


Figure 13S. The ¹H NMR of N-(2-methylbenzylidene)-o-methylbenzylamine

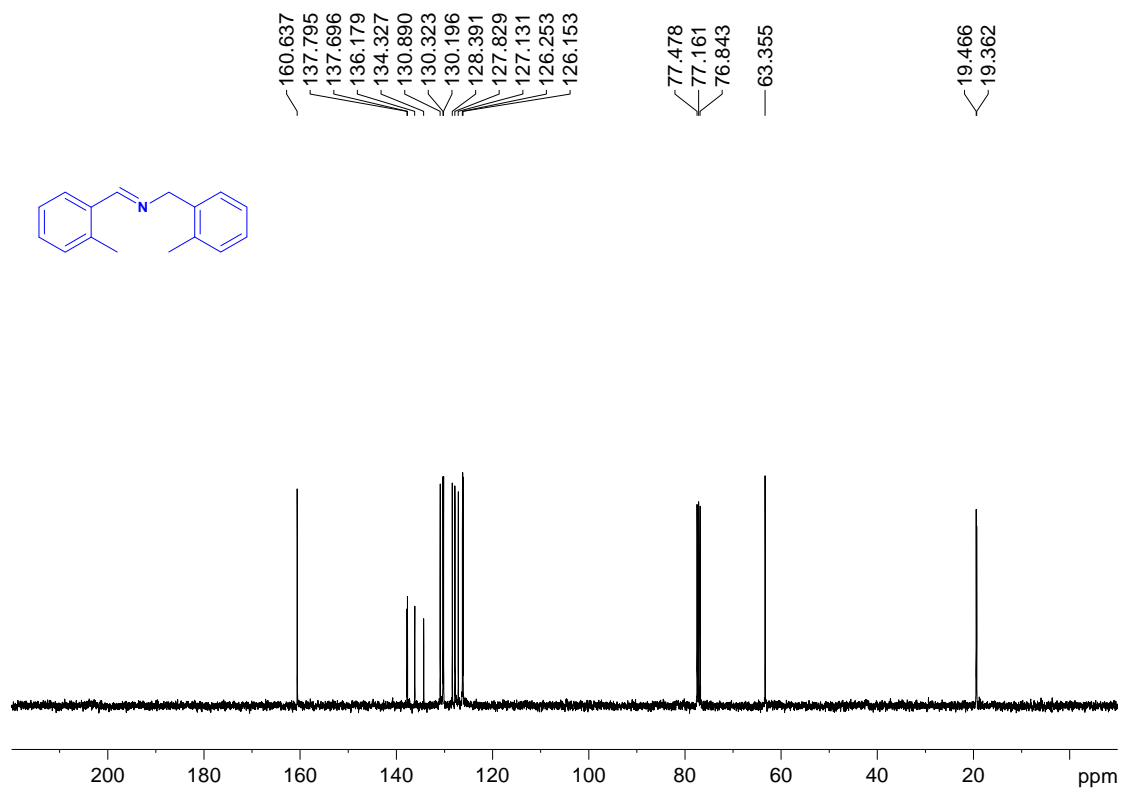


Figure 14S. The ¹³C NMR of N-(2-methylbenzylidene)-o-methylbenzylamine

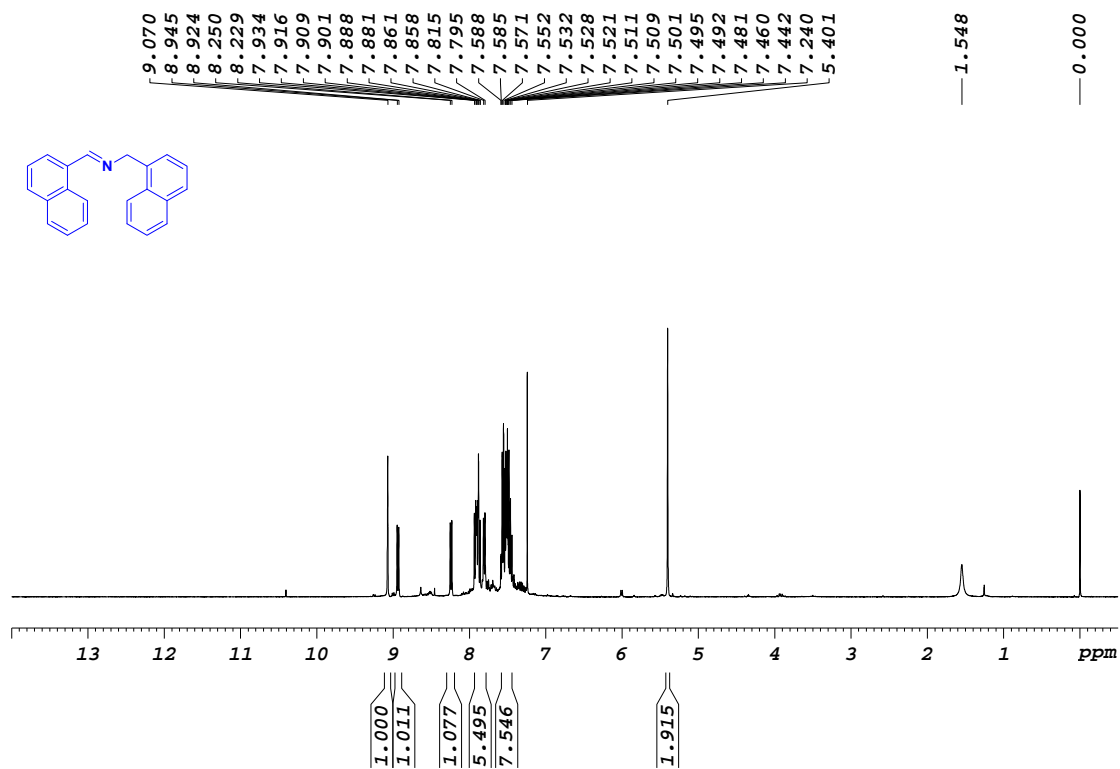


Figure 15S. The ^1H NMR of 1-(naphthalen-1-yl)-N-(naphthalen-1-ylmethylene)methanamine

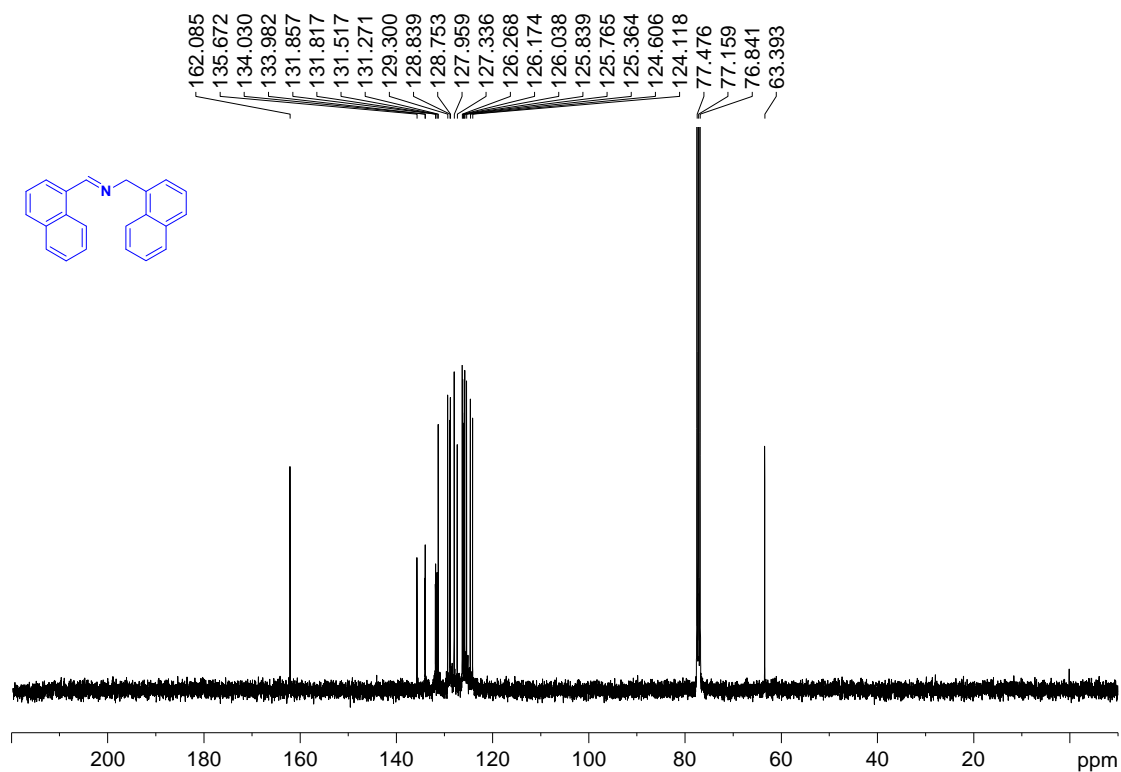


Figure 16S. The ^{13}C NMR of 1-(naphthalen-1-yl)-N-(naphthalen-1-ylmethylene)methanamine

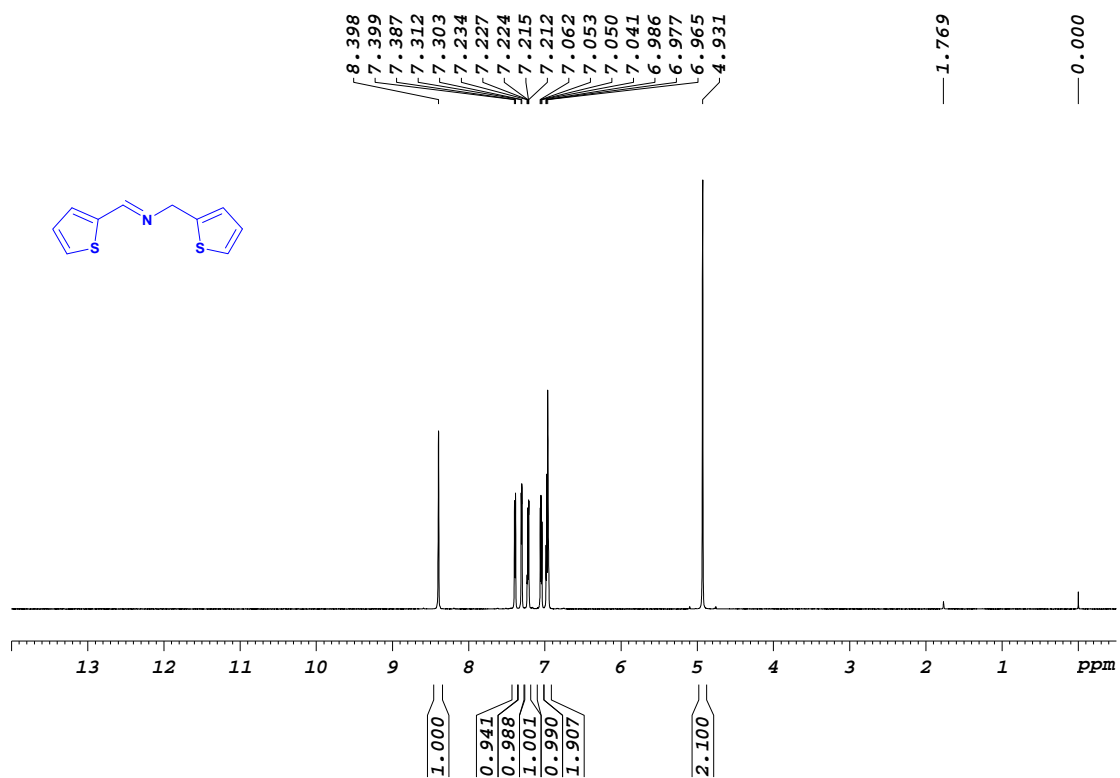


Figure 17S. The ¹H NMR of thiophen-2-yl-N-(thiophen-2-ylmethylene)methanamine

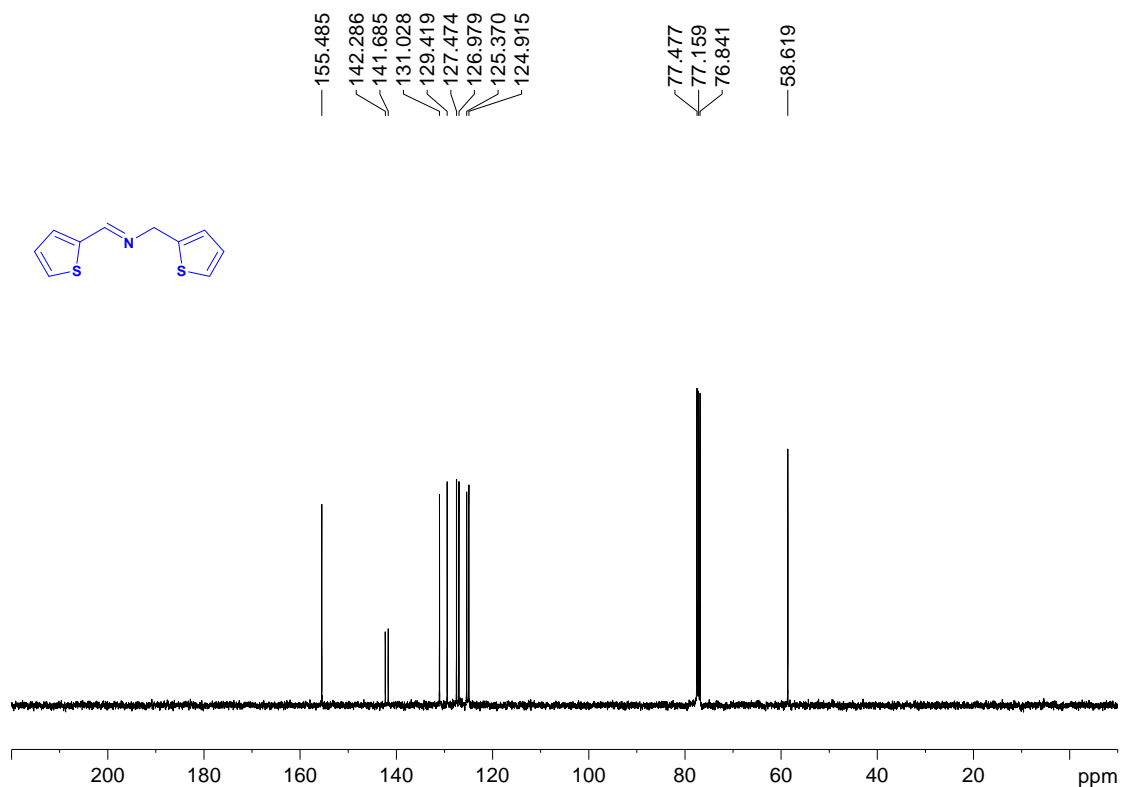


Figure 18S. The ¹³C NMR of thiophen-2-yl-N-(thiophen-2-ylmethylene)methanamine

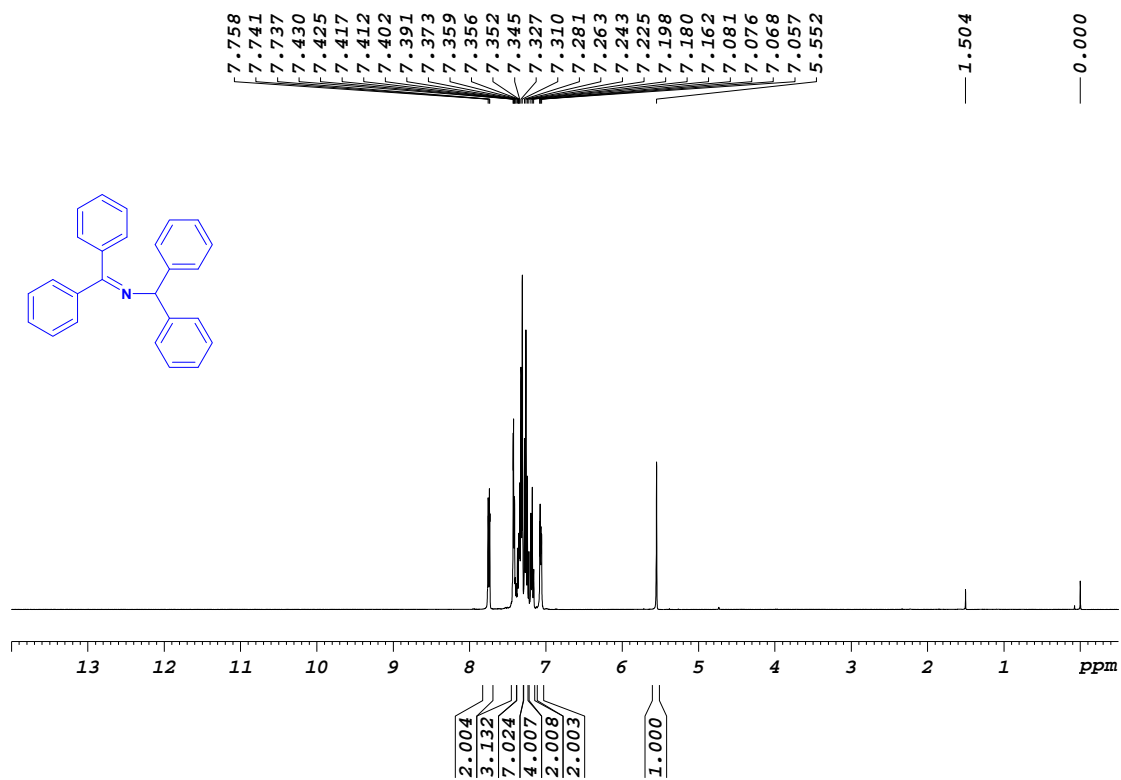


Figure 19S. The ¹H NMR of N-diphenylmethylenediphenylmethanamine

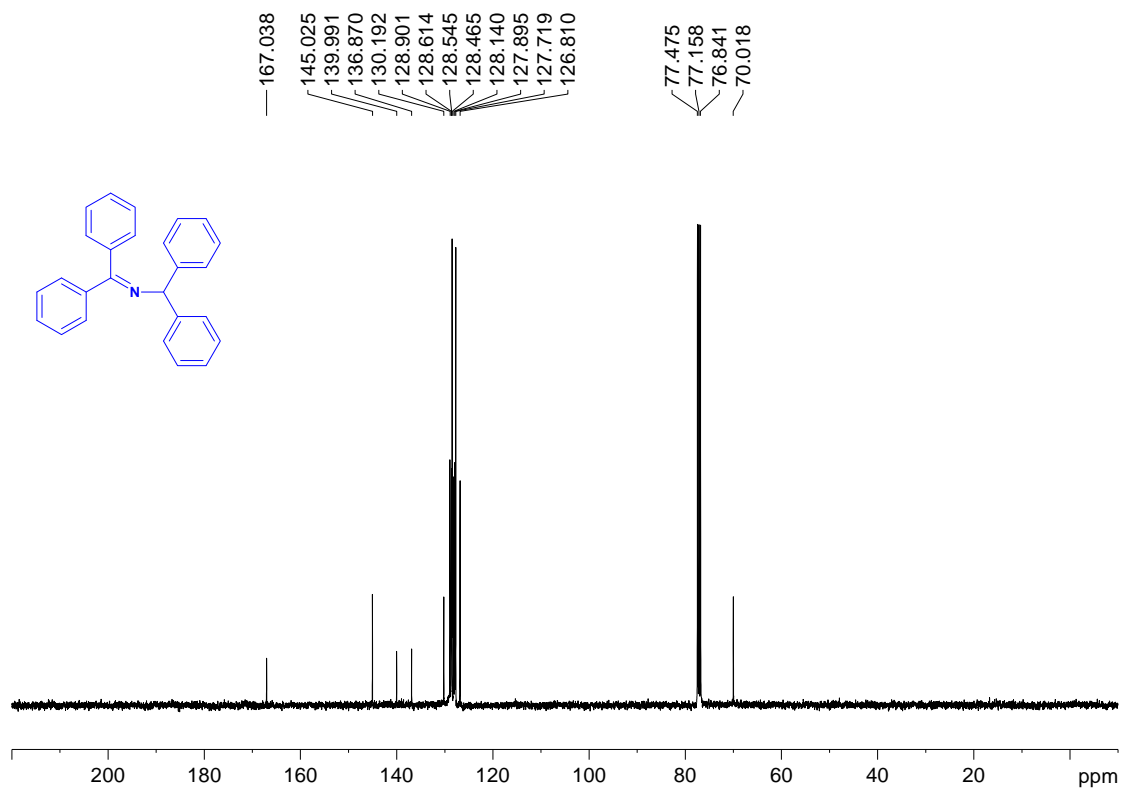


Figure 20S. The ¹³C NMR of N-diphenylmethylenediphenylmethanamine

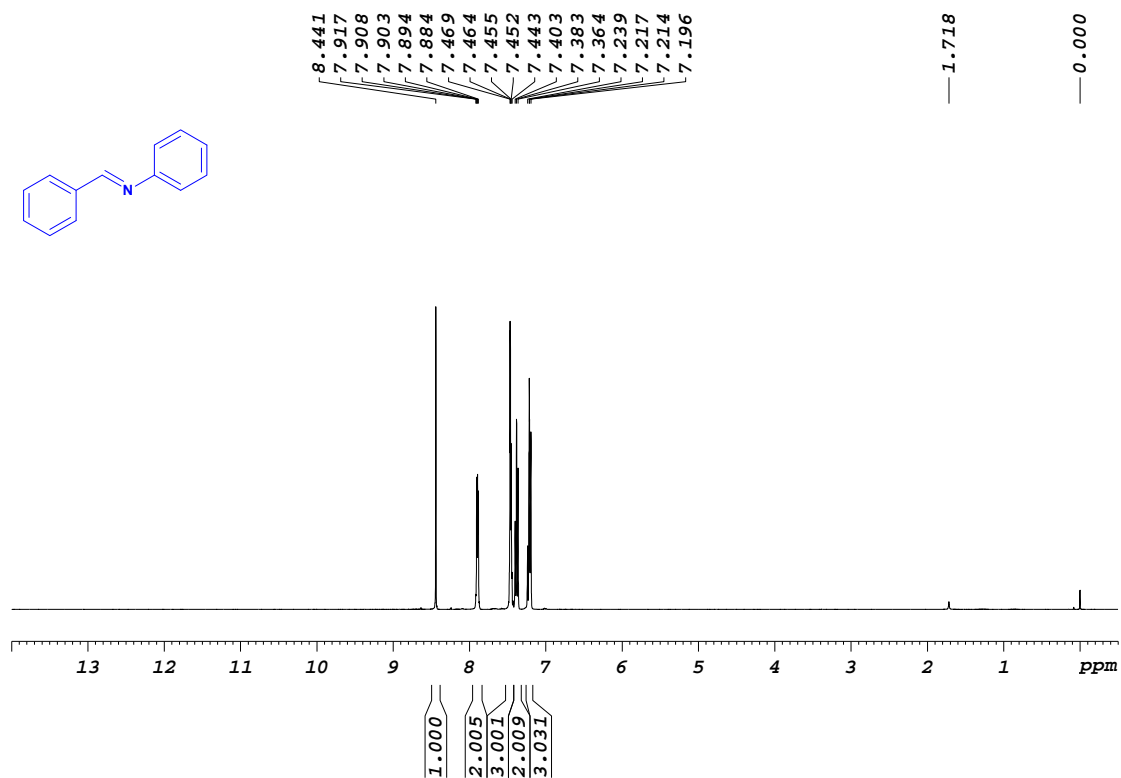


Figure 21S. The ¹H NMR of N-benzylideneaniline

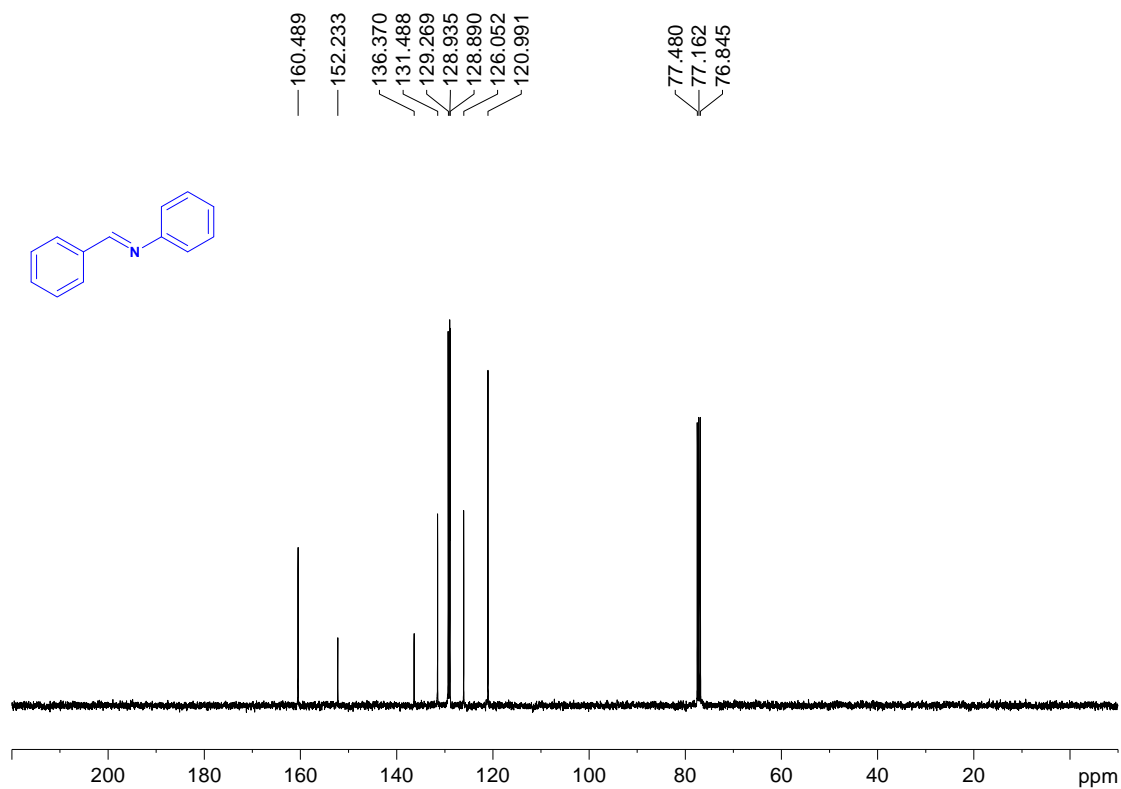


Figure 22S. The ¹³C NMR of N-benzylideneaniline

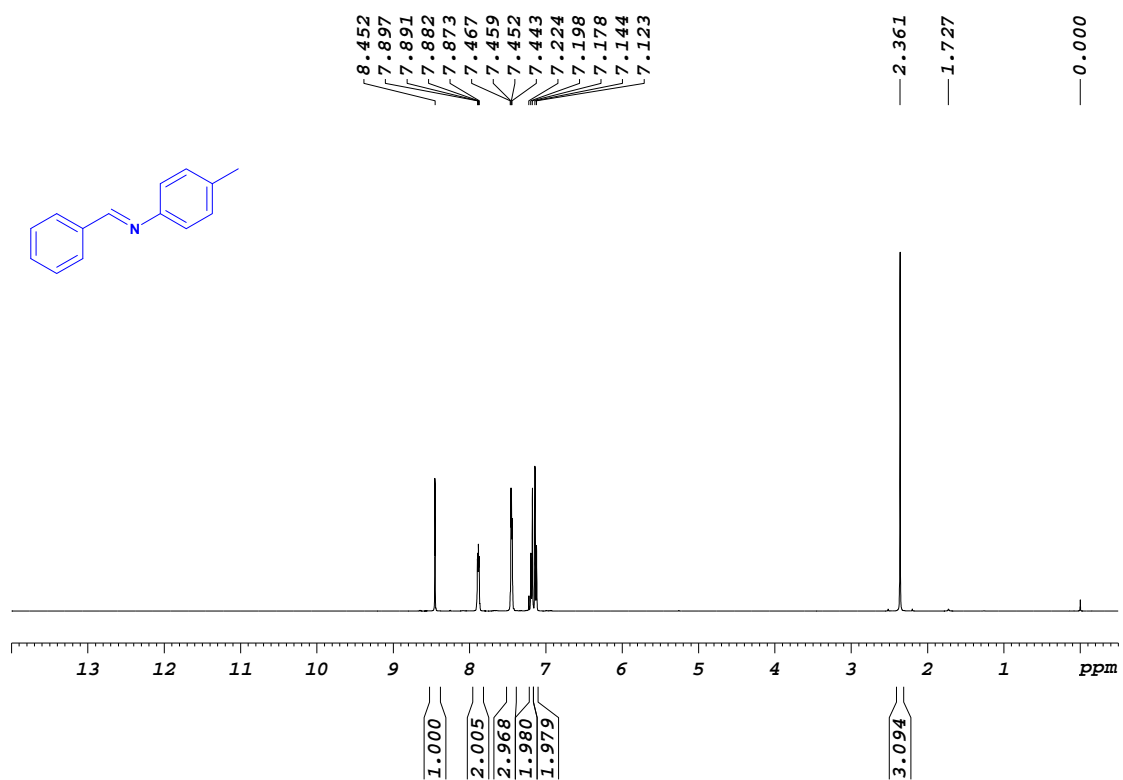


Figure 23S. The ¹H NMR of N-benzylidene-4-methylaniline

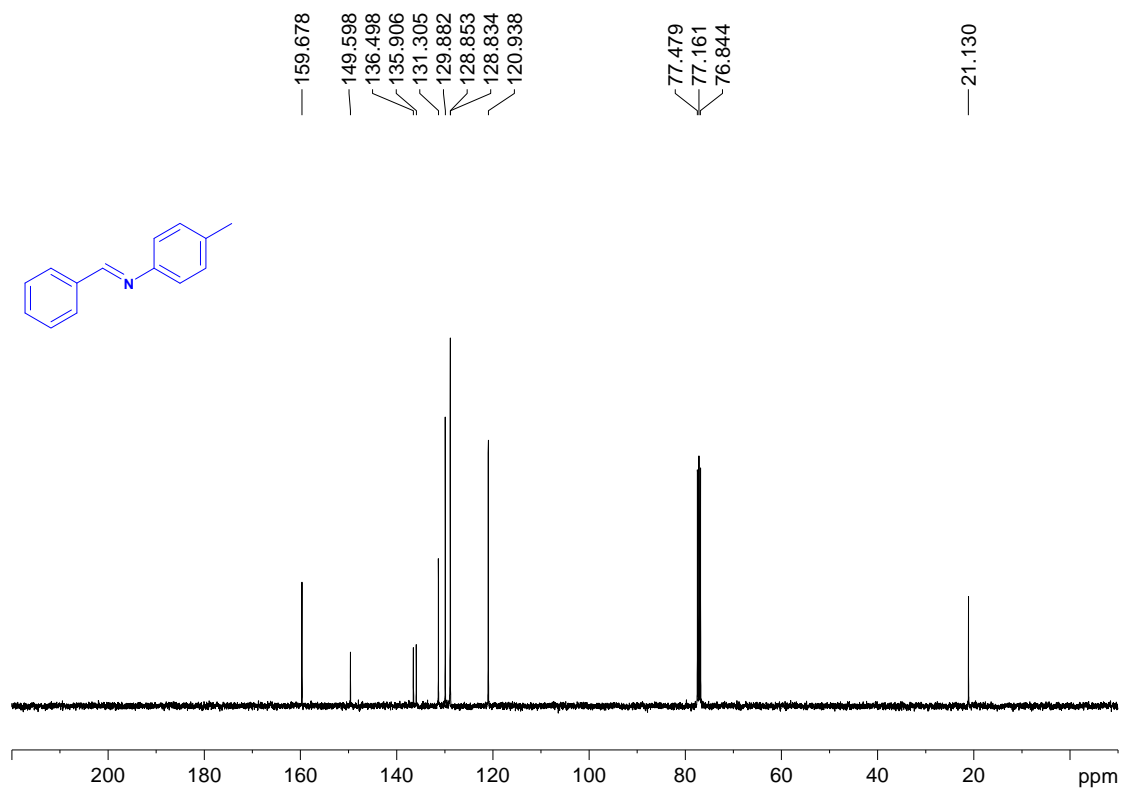


Figure 24S. The ¹³C NMR of N-benzylidene-4-methylaniline

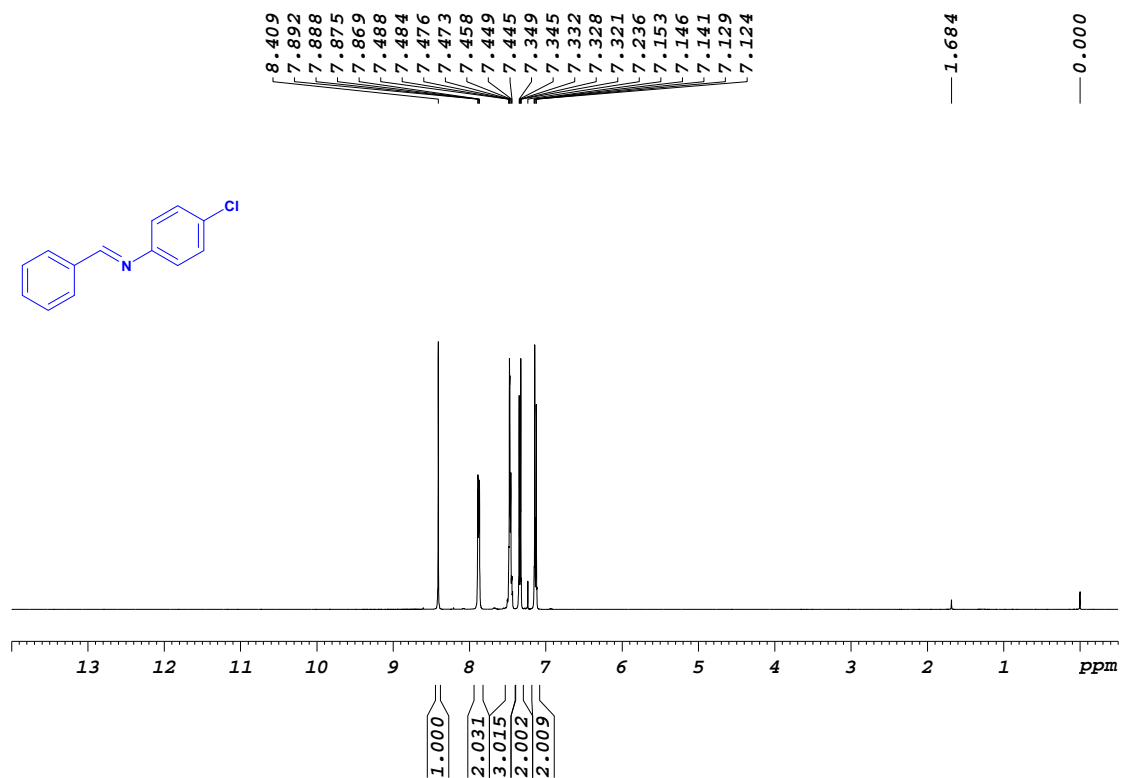


Figure 25S. The ¹H NMR of N-benzylidene-4-chloroaniline

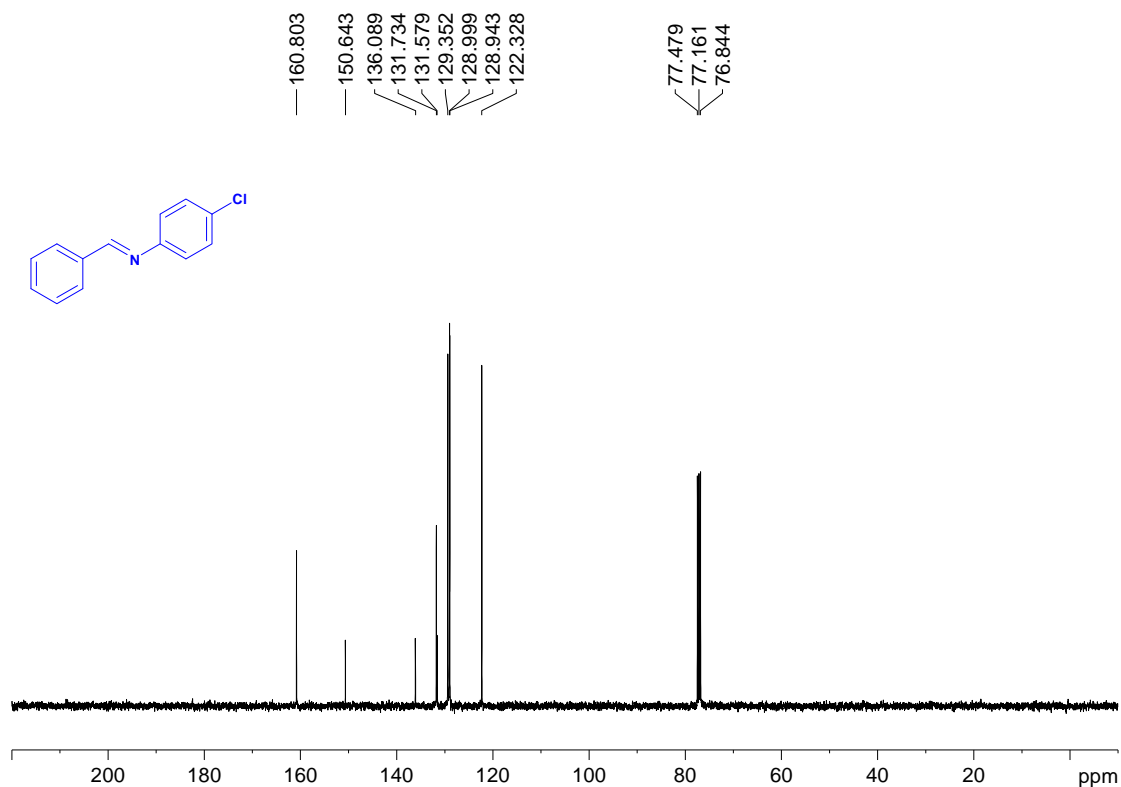


Figure 26S. The ¹³C NMR of N-benzylidene-4-chloroaniline

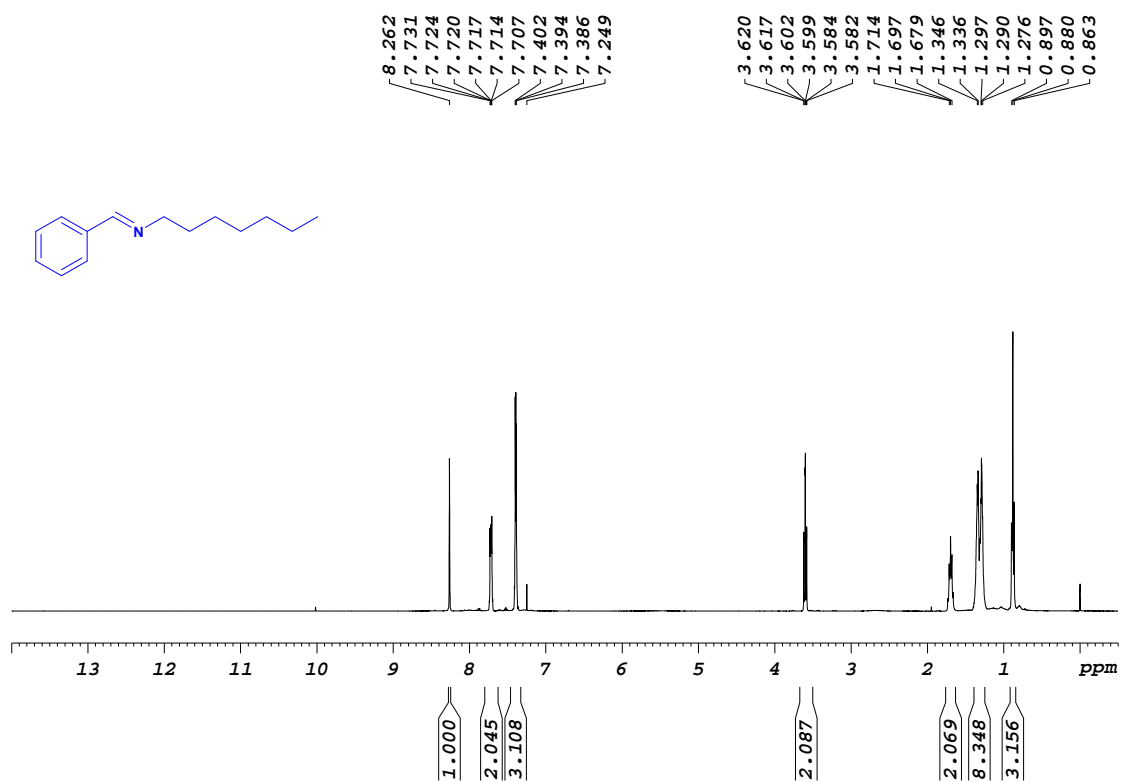


Figure 27S. The ¹H NMR of N-benzylideneheptanamine

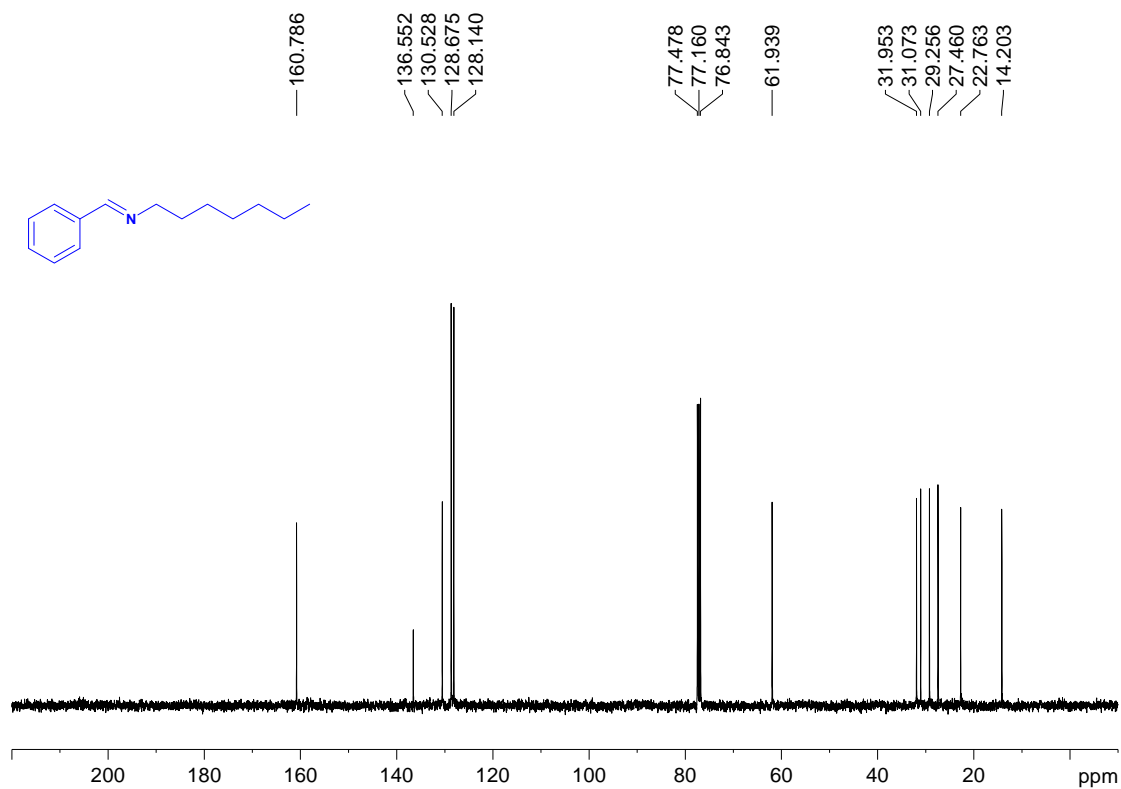


Figure 28S. The ¹³C NMR of N-benzylideneheptanamine

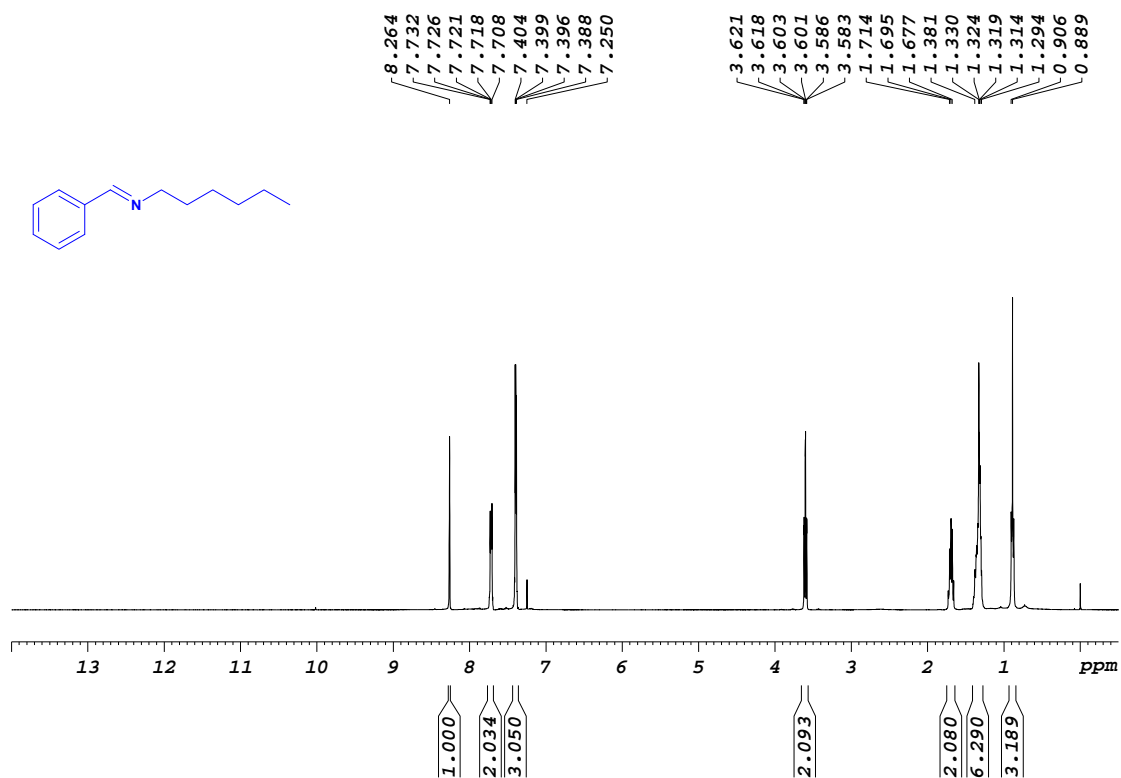


Figure 29S. The ¹H NMR of N-benzylidenehexanamine

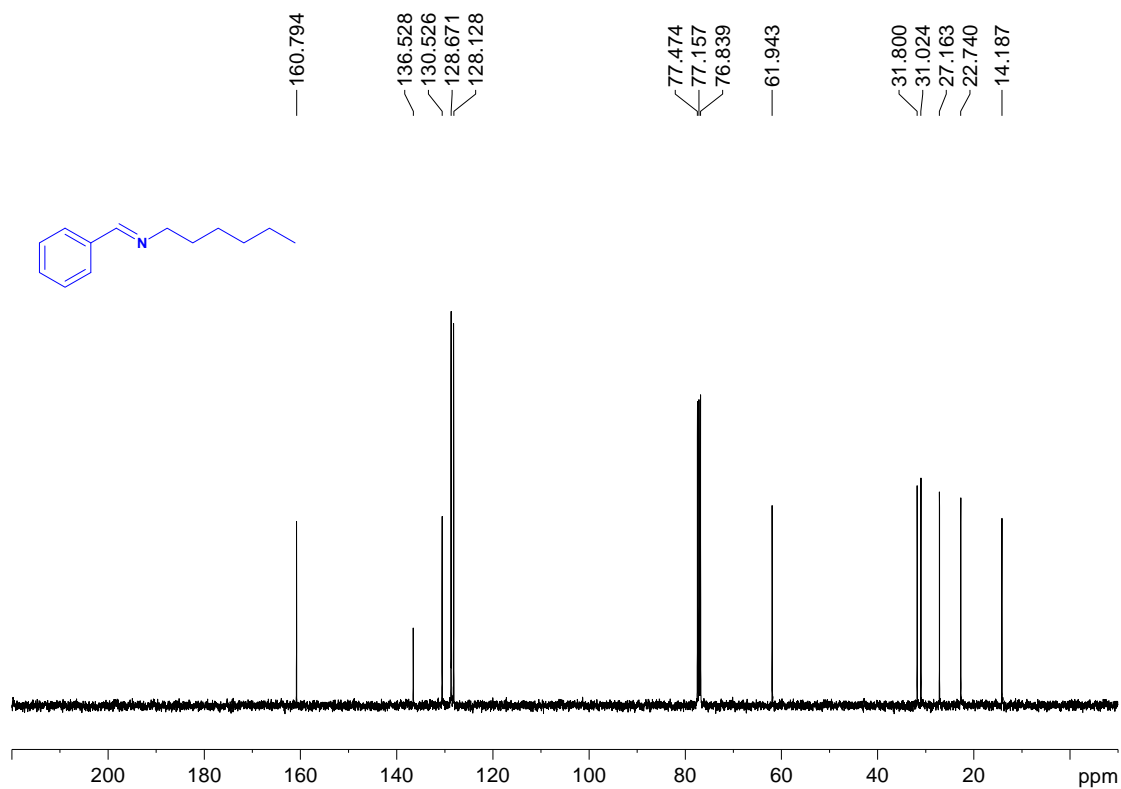


Figure 30S. The ¹³C NMR of N-benzylidenehexanamine

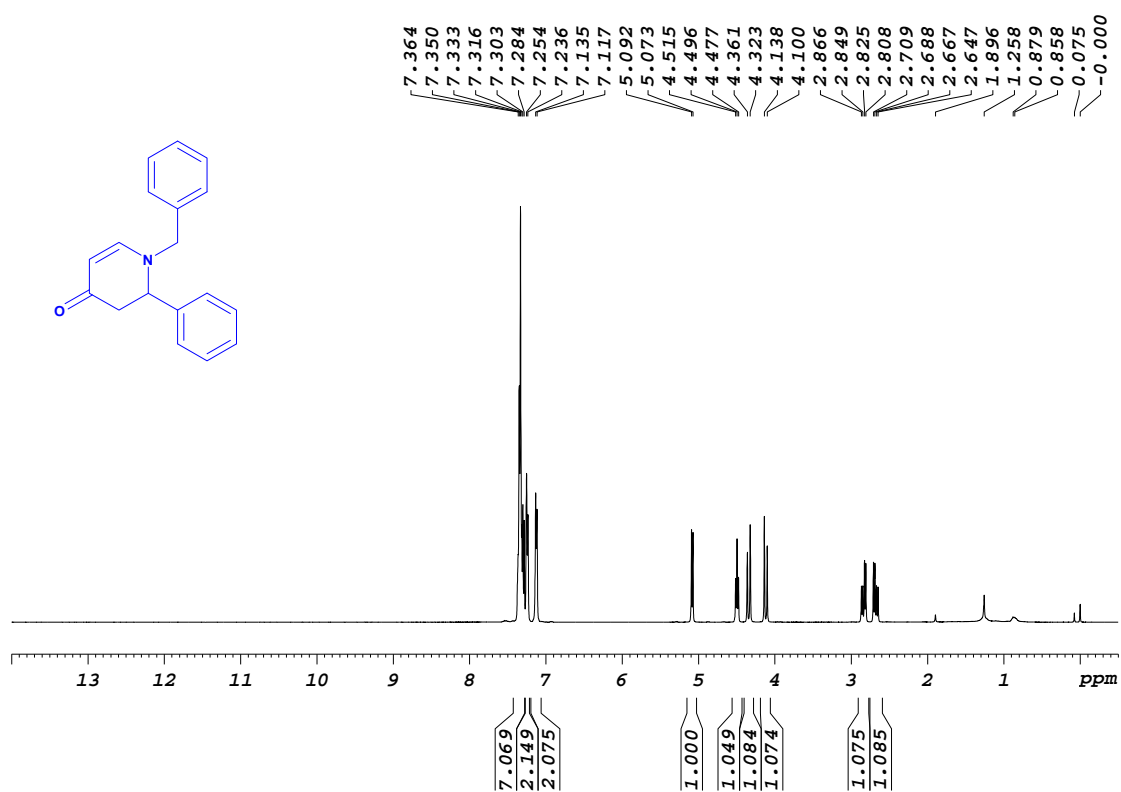


Figure 31S. The ¹H NMR of 1-benzyl-2-phenyl-2,3-dihydropyridin-4(1H)-one

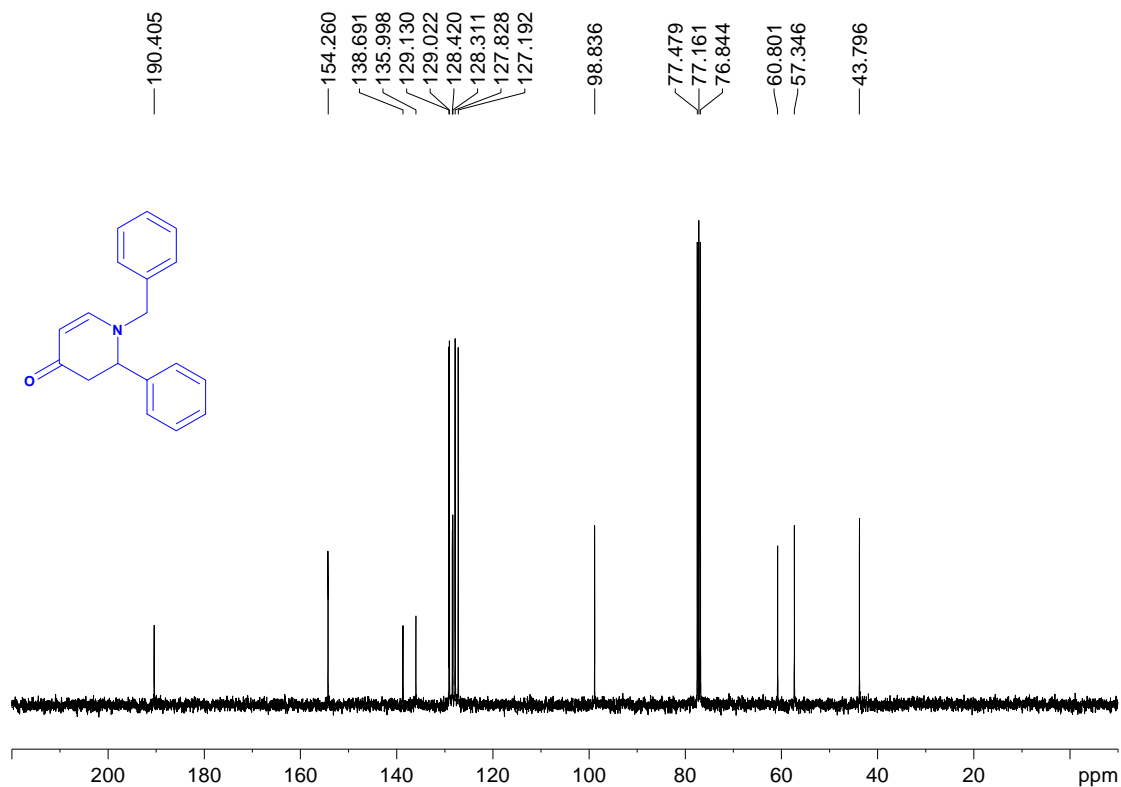


Figure 31S. The ¹³C NMR of 1-benzyl-2-phenyl-2,3-dihydropyridin-4(1H)-one

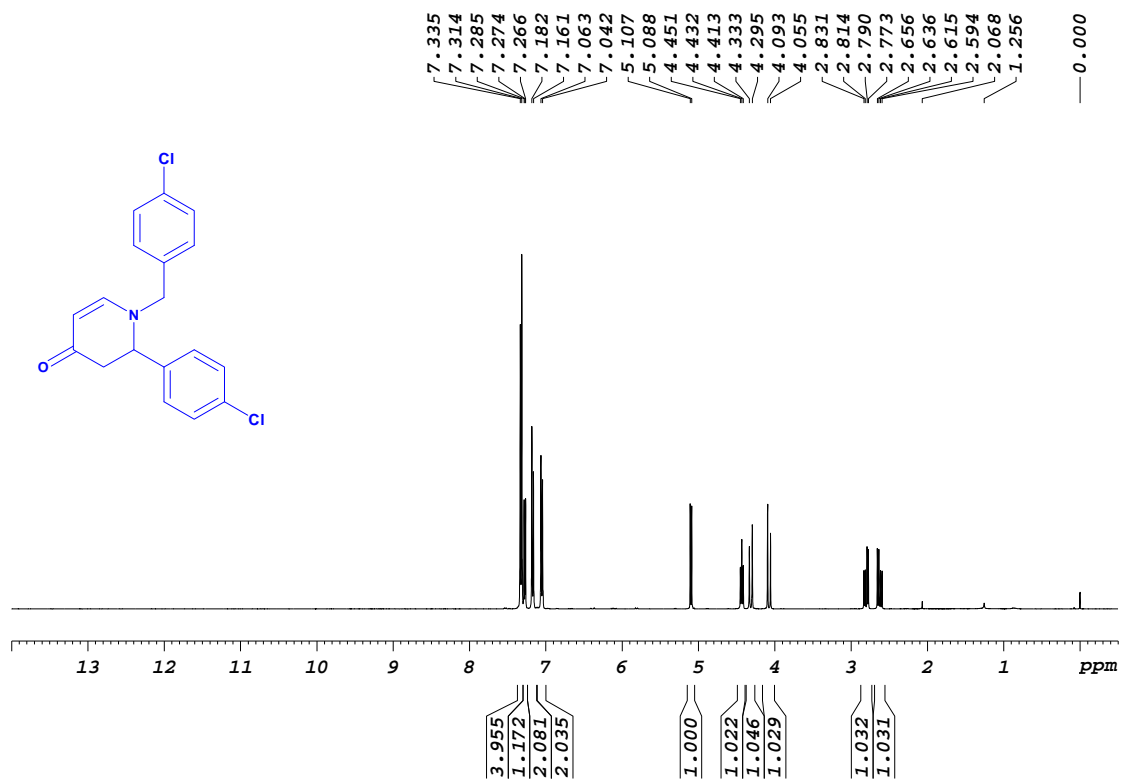


Figure 33S. The ¹H NMR of 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-2,3-dihydropyridin-4(1H)-one

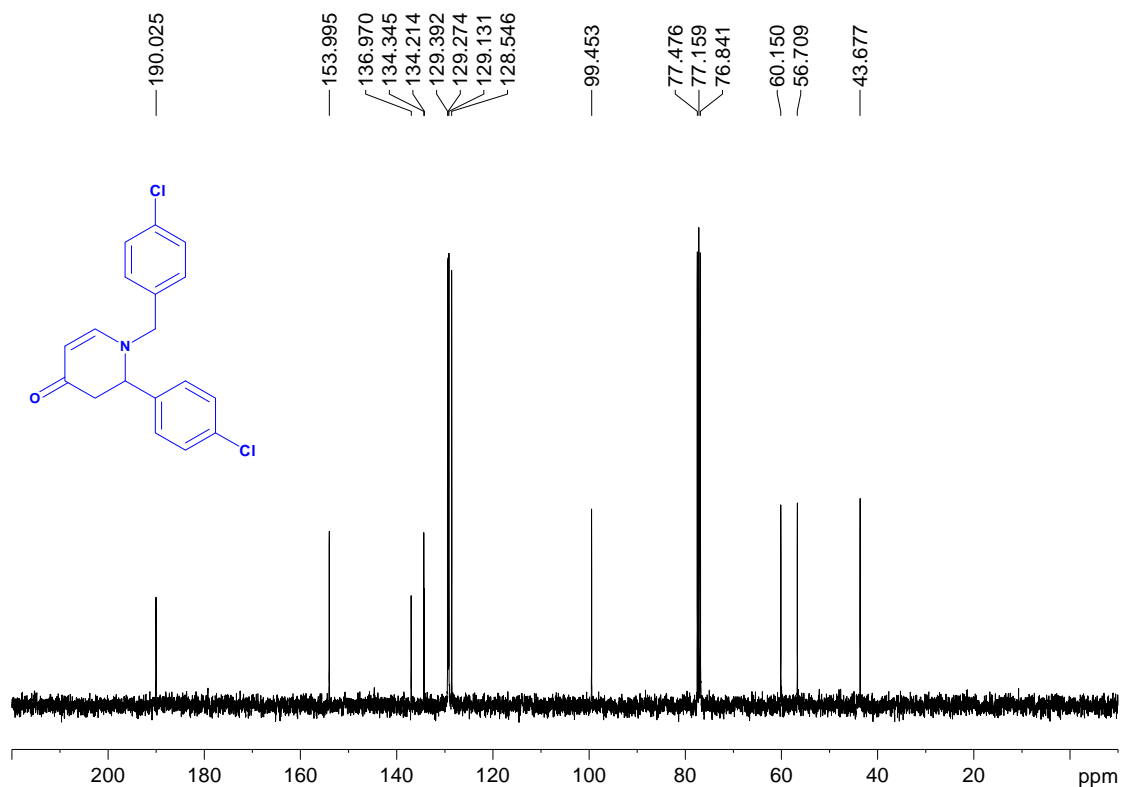


Figure 34S. The ¹³C NMR of 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-2,3-dihydropyridin-4(1H)-one

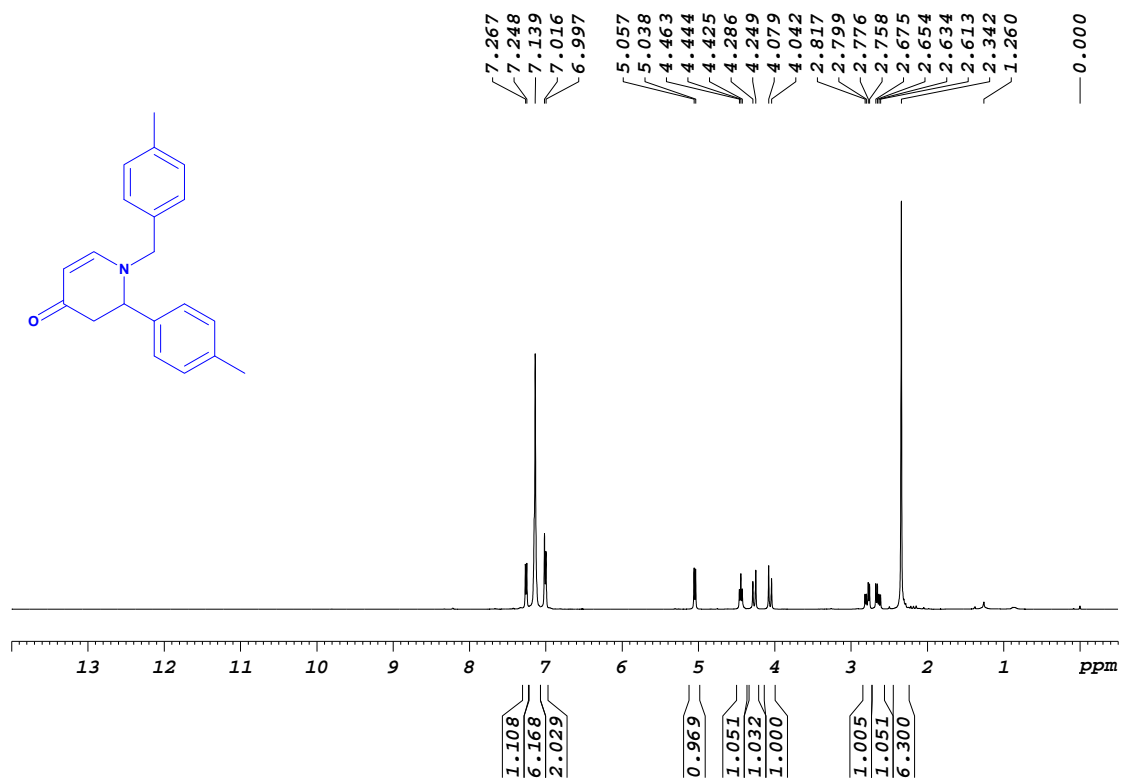


Figure 35S. The ¹H NMR of 1-(4-methylbenzyl)-2-p-tolyl-2,3-dihydropyridin-4(1H)-one

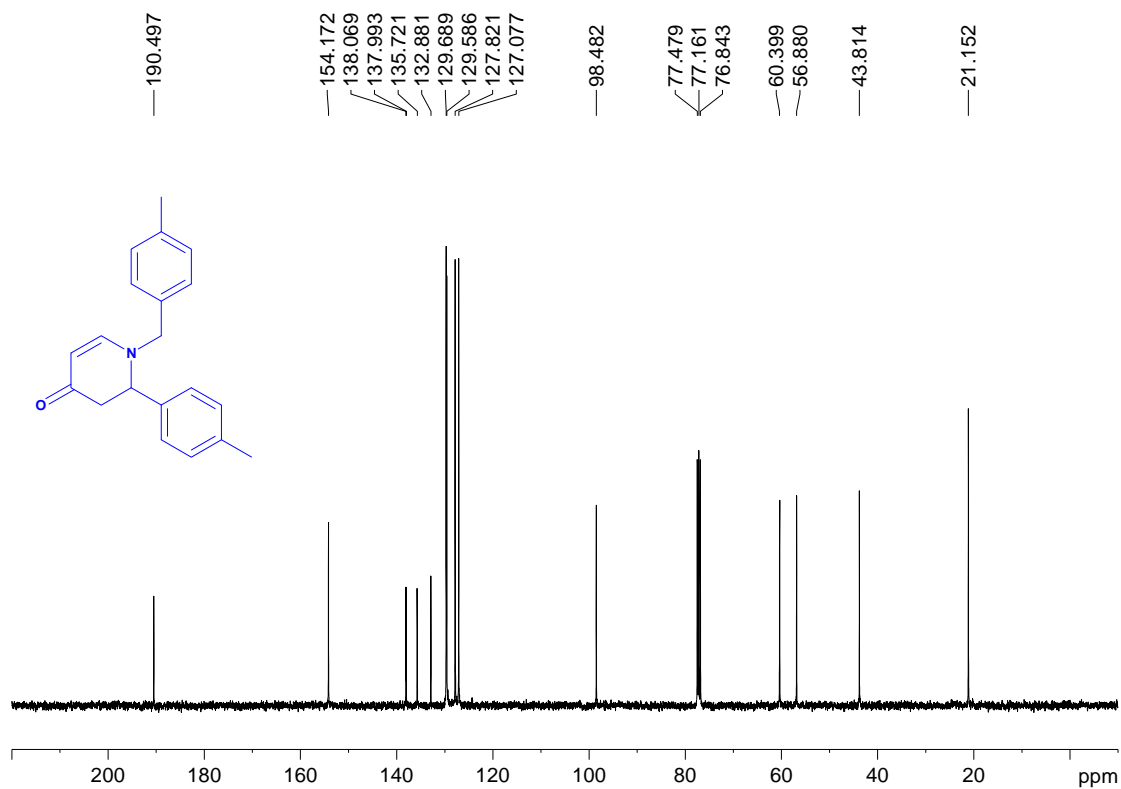


Figure 36S. The ¹³C NMR of 1-(4-methylbenzyl)-2-p-tolyl-2,3-dihydropyridin-4(1H)-one