Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Biomimetic Approach to Aerobic Oxidation of Amines in Water *via* a Redox-Active *Cacotheline* Organocatalyst

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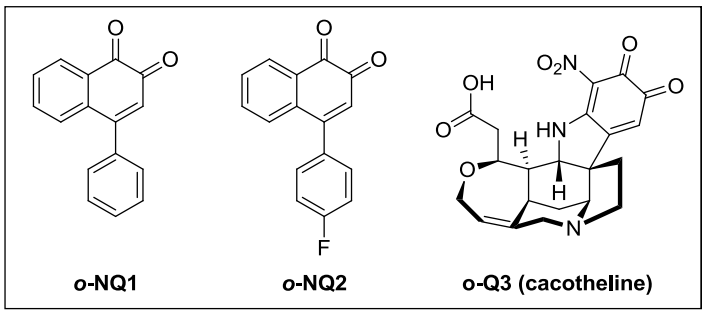
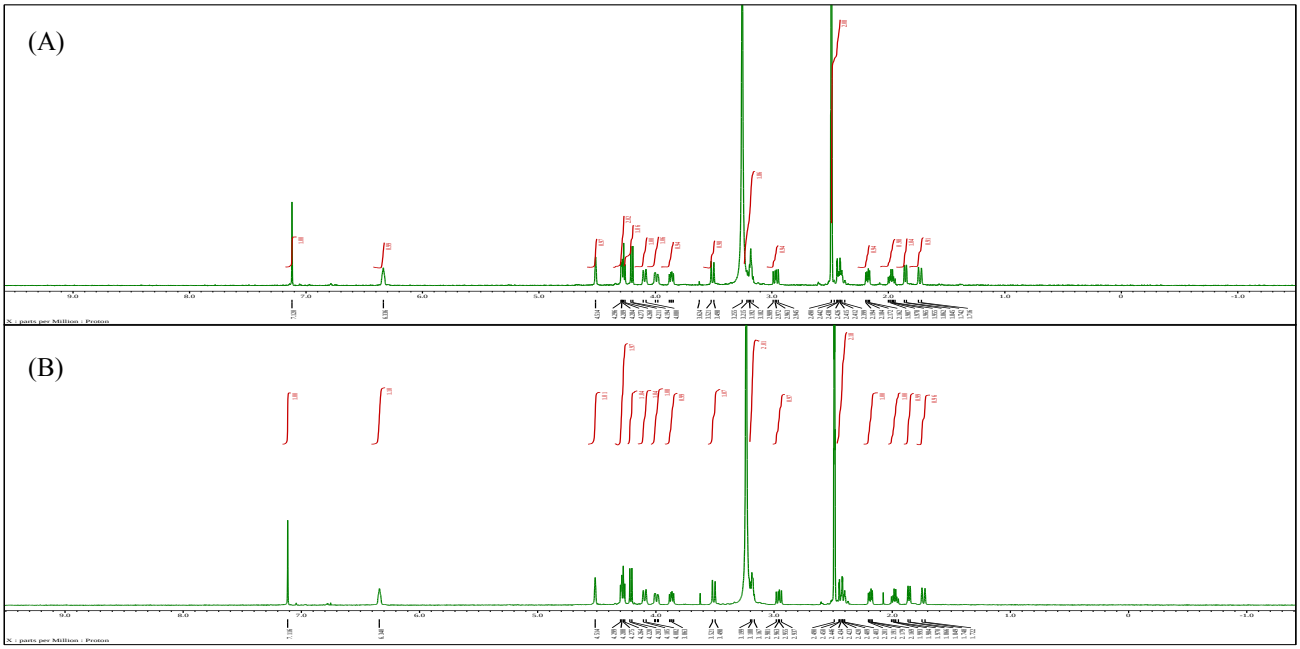
General Methods. All reactions were carried out using oven dried glasswares and monitored by thin layer chromatography (TLC) on 250 μm precoated silica gel plates. TLC spots were visualized by ultraviolet light and *p*-anisaldehyde staining. Column chromatography was performed on silica gel (40-63μm, Merck Silica Gel) column. ^{1}H-, ^{13}C- and ^{19}F-NMR spectra were recorded in $CDCl_3$ on 600 MHz JEOL FT Spectrometer at ambient temperature. The chemical shifts in ^{1}H-NMR spectra were reported in ppm (δ) on a scale downfield from TMS as an internal standard. ^{13}C-NMR spectra were reported in ppm (δ) relative to the central line of triplet for $CDCl_3$ at 77.0 ppm. The signals' multiplicities are indicated as follows: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, and m = multiplet. The coupling constant *J* is given in Hz. The infrared spectra were recorded on Agilent Cary 630 FT-IR. For high resolution mass spectrometry (HRMS), Thermo Fisher Scientific Q Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometer was used and m/z ratios are reported as values in atomic mass units.

Preparation of *ortho*-Quinone Catalysts



Catalysts ***o*-NQ1-2** were synthesized based on the previous work.[1] Commercially available Cacotheline•HNO_3•H_2O (***o*-Q3**) was purchased and used without further purification. For the preparative purpose, the Rao's Cacotheline synthetic precedure was followed,[2] where the commercially available brucine dihydrate (10 g, 25.3 mmol) provided the pure Cacotheline•HNO_3•H_2O (***o*-Q3**) in 91% yield (10.8 g). Briefly, brucine dihydrate (10 g, 25.3 mmol) was dissolved in 3.5 M nitric acid (75 mL) and heated at 60 °C in an oil bath for 2 h with occasional stirring. The reaction mixture was cooled to ambient temperature and kept in an ice bath for 3 h. The precipitates were filtered, washed with water (100 mL), acetone (15 mL) and diethyl ether (30 mL). The cacotheline salt was obtained in 91% yield (10.8 g) after dried in air for 3 h followed by further dry in the oven (set temperature 100 °C) for 6 h. The product was confirmed by comparing ^{1}H NMR spectrum with the authentic sample from commercial source.

^{1}H NMR (DMSO-d_6, 600 MHz): δ 7.11 (s, 1H), 6.36-6.32 (m, 1H), 4.51 (s, 1H), 4.29-4.26 (m, 2H), 4.21 (d, *J* = 10.2 Hz, 1H), 4.09 (d, *J* = 10.2 Hz, 1H), 3.99 (m, 1H), 3.86 (dd, *J* = 12.6, 7.8 Hz, 1H), 3.50 (d, *J* = 13.2 Hz, 1H), 3.19-3.16 (m, 2H), 2.95 (dd, *J* = 15.8, 10.8 Hz, 1H), 2.45-2.40 (m, 2H), 2.18 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.97 (td, 1H, *J* = 13.2, 8.4 Hz), 1.87-1.83 (m, 1H), 1.75-1.72 (m, 1H).

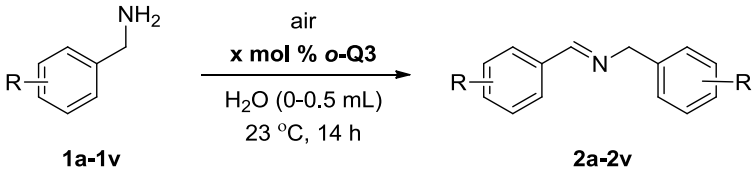


^{1}H-NMR Spectrum of Authentic Cacotheline (A) and Synthetic Cacotheline (B)

Preparation of Starting Materials

All amine starting materials (**1a – 1v**) were commercially available and used without further purification.

General Procedure A: *Cacotheline*-Catalyzed Aerobic Oxidation to Homocoupling

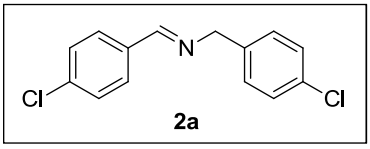


1a-1v **2a-2v**

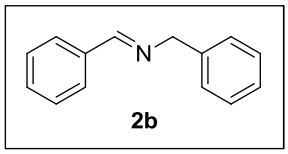
To a 10 mL vial charged with ***o*-Q3** catalyst (1-10 mol %) and amine (**1**, 1.0 equiv, 0.4 mmol) was added water (0-0.5 mL). The reaction was stirred at ambient temperature for 14 h. The reaction mixture was then washed with diethyl ether (2.0 mL x 3). The combined organic layers were dried over Na_2SO_4 and filtered through a short pad of silica gel. After removal of solvent under the reduced pressure, the desired products **2** were obtained without further purification.

[1 g Scale Reaction] An oven dried 25 mL flask was charged with 4-chlorobenzyl amine (**1a**, 1.0 equiv, 7.06 mmol, 1.0 g) and catalyst ***o*-Q3** (1 mol %, 0.0706 mmol, 35.9 mg), and 8.83 mL of water was added to this flask. After stirring at ambient temperature for 24 h, the reaction was extracted with diethyl ether (10 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered through a short pad of silica gel. After concentration *in vacuo*, the product **2a** was obtained without further purification in 97% yield (901.9 mg).

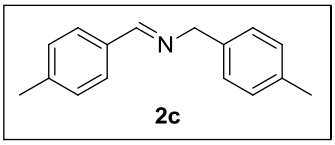
Characterization of the Compounds in Scheme 2



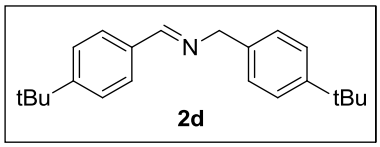
(*E*)-*N*-(4-Chlorobenzylidene)-1-(4-chlorophenyl)methanamine (2a): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) and 0.5 mL of water. 52.6 mg (>99%), off-white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.34 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.32-7.30 (m, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 4.77 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 160.9, 137.7, 137.0, 134.5, 132.9, 129.6, 129.4, 129.0, 128.7, 64.3.



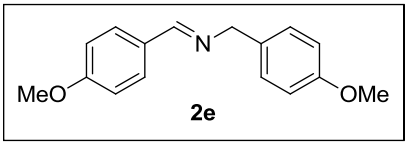
(*E*)-*N*-Benzylidene-1-phenylmethanamine (2b): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) under solvent free condition. 37.4 mg (96%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.41 (s, 1H), 7.80-7.79 (m, 2H), 7.43-7.42 (m, 3H), 7.36-7.34 (m, 4H), 7.29-7.26 (m, 1H), 4.84 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.1, 139.4, 136.3, 130.9, 128.7, 128.6, 128.4, 128.1, 127.1, 65.2.



(*E*)-*N*-(4-Methylbenzylidene)-1-(*p*-tolyl)methanamine (2c): The product was prepared by the General Procedure A with 3 mol % catalyst loading (6 mg) and 0.5 mL of water. 44.1 mg (99%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.34 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.22-7.21 (m, 4H), 7.15 (d, *J* = 8.4 Hz, 2H), 4.77 (s, 2H), 2.38 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.8, 141.1, 136.6, 136.4, 133.7, 129.4, 129.2, 128.3, 128.0, 64.9, 21.6, 21.2.

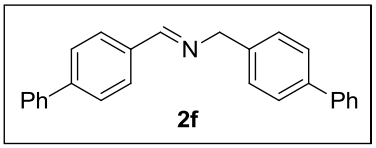


(*E*)-*N*-(4-(*tert*-Butyl)benzylidene)-1-(4-(*tert*-butyl)phenyl)methanamine (2d): The product was prepared by the General Procedure A with 4 mol % catalyst loading (8 mg) under solvent free condition. 61.3 mg (>99 %), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[4] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.36 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 4.78 (s. 2H), 1.33 (s, 9H), 1.31 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.8, 154.2, 149.9, 136.5, 133.7, 128.2, 127.8, 125.6, 125.5, 64.9, 35.0, 34.6, 31.5, 31.3.



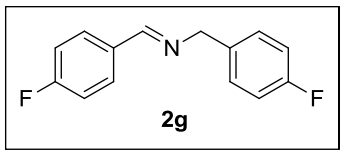
(*E*)-*N*-(4-Methoxybenzylidene)-1-(4-methoxyphenyl)methanamine (2e): The product was prepared by the General Procedure A with 1 mol% catalyst loading (2 mg) under solvent free condition. 50.9 mg (>99 %), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.29 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.25-7.23 (m, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.72 (s, 2H), 3.83 (s, 3H), 3.79

(s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.8, 161.0, 158.7, 131.8, 129.9, 129.3, 128.4, 114.1, 114.0, 64.5, 55.5, 55.4.



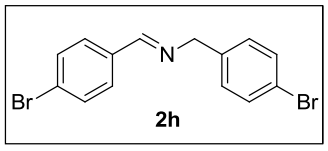
2f

(*E*)-1-([1,1'-Biphenyl]-4-yl)-*N*-([1,1'-biphenyl]-4-ylmethylene)methanamine (2f): The product was prepared by the General Procedure A with 3 mol % catalyst loading (6 mg) and 0.5 mL of water. 67.5 mg (97%), off-white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[5] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.48 (s, 1H), 7.90-7.89 (m, 2H), 7.69-7.60 (m, 8H), 7.48-7.44 (m, 6H), 7.40-7.34 (m, 2H), 4.91 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.8, 143.6, 141.1, 140.5, 140.1, 138.5, 135.2, 129.0, 128.9, 128.8, 128.5, 127.9(1), 127.9(0), 127.4(7), 127.4(3), 127.3, 127.2, 64.9.



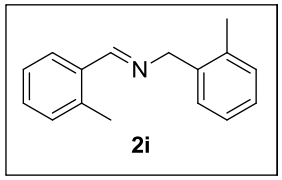
2g

(*E*)-*N*-(4-Fluorobenzylidene)-1-(4-fluorophenyl)methanamine (2g): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) under solvent free condition. 46.1 mg (>99 %), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[4] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.35 (s, 1H), 7.78-7.76 (m, 2H), 7.30-7.28 (m, 2H), 7.10 (t, J = 9.0 Hz, 2H), 7.03 (t, J = 9.0 Hz, 2H), 4.76 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 164.5 (d, J = 248.4 Hz), 162.1 (d, J = 244.0 Hz), 160.6, 135.0 (d, J = 2.8 Hz), 132.4 (d, J = 3.0 Hz), 130.3 (d, J = 8.7 Hz), 129.6 (d, J = 7.2 Hz), 115.8 (d, J = 21.4 Hz), 115.4 (d, J = 21.6 Hz), 64.2; ^{19}F NMR ($CDCl_3$, 564 MHz): δ -109.1, -115.8.



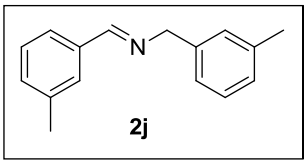
2h

(*E*)-*N*-(4-Bromobenzylidene)-1-(4-bromophenyl)methanamine (2h): The product was prepared by the General Procedure A with 5 mol % catalyst loading (10.2 mg) and 0.5 mL of water. 67.1 mg (95%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[5] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.32 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 4.74 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.1, 138.2, 134.9, 132.0, 131.7, 129.8, 129.7, 125.5, 121.0, 64.3.

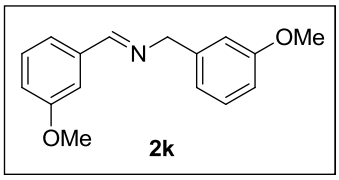


2i

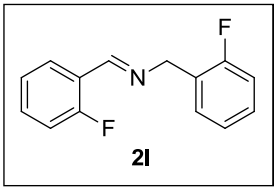
(*E*)-*N*-(2-Methylbenzylidene)-1-(*o*-tolyl)methanamine (2i): The product was prepared by the General Procedure A using 4 mol % catalyst loading (8 mg) under solvent free condition. 44.4 mg (99%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.67 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.31-7.29 (m, 2H), 7.25-7.23 (m, 1H), 7.19-7.17 (m, 4H), 4.83 (s, 2H), 2.51 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 160.6, 137.8, 137.7, 136.2, 134.3, 130.9, 130.3, 130.2, 128.4, 127.8, 127.1, 126.2, 126.1, 63.4, 19.5, 19.4.



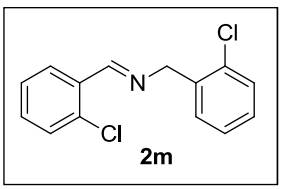
(*E*)-*N*-(3-Methylbenzylidene)-1-(*m*-tolyl)methanamine (2j): The product was prepared by the General Procedure A with 4 mol % catalyst loading (8 mg) under solvent free condition. 44.3 mg (99%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.35 (s, 1H), 7.64 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.23-7.21 (m, 2H), 7.14-7.11 (m, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 4.77 (s, 2H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.2, 139.2, 138.4, 138.2, 136.2, 131.6, 128.8, 128.5(8)(2C), 128.5(1), 127.8, 126.0, 125.1, 65.2, 21.5, 21.3.



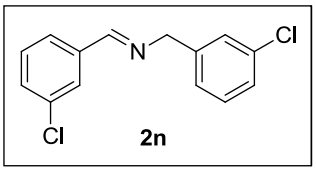
(*E*)-*N*-(3-Methoxybenzylidene)-1-(3-methoxyphenyl)methanamine (2k): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) under solvent free condition. 50.6 mg (99%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[6] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.35 (s, 1H), 7.39 (d, *J* = 1.2 Hz, 1H), 7.33-7.24 (m, 3H), 6.99-6.97 (m, 1H), 6.93-6.90 (m, 2H), 6.81 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.79 (s, 2H), 3.84 (s, 3H), 3.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.1, 160.0, 159.9, 140.9, 137.7, 129.6(9), 129.6(2), 121.7, 120.4, 117.7, 113.7, 112.5, 111.8, 65.0, 55.5, 55.3.



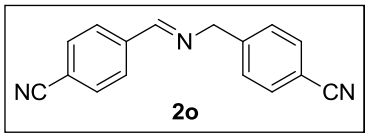
(*E*)-*N*-(2-Fluorobenzylidene)-1-(2-fluorophenyl)methanamine (2l): The product was prepared by the General Procedure A with 5 mol % catalyst loading (10.2 mg) under solvent free condition. 43.0 mg (93%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[6] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.72 (s, 1H), 8.03 (td, *J* = 7.2, 1.2 Hz, 1H), 7.41-7.36 (m, 2H), 7.27-7.23 (m, 1H), 7.17-7.04 (m, 4H), 4.87 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.4 (d, *J* = 251.4 Hz), 160.9 (d, *J* = 245.5 Hz), 156.1 (d, *J* = 4.3 Hz), 132.5 (d, *J* = 8.7 Hz), 130.2 (d, *J* = 4.3 Hz), 128.9 (d, *J* = 7.2 Hz), 127.9 (d, *J* = 2.8 Hz), 126.2 (d, *J* = 15.7 Hz), 124.3(9) (d, *J* = 24.4 Hz), 124.3(7) (d, *J* = 25.8 Hz), 123.8 (d, *J* = 8.7 Hz), 115.8 (d, *J* = 21.6 Hz), 115.4 (d, *J* = 21.4 Hz), 58.6 (d, *J* = 3.0 Hz); ^{19}F NMR ($CDCl_3$, 564 MHz): δ -118.6, -121.6.



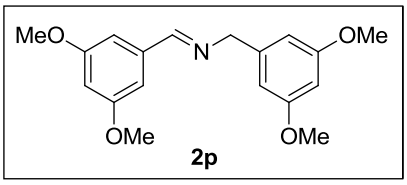
(*E*)-*N*-(2-Chlorobenzylidene)-1-(2-chlorophenyl)methanamine (2m): The product was prepared by the General Procedure A with 3 mol % catalyst loading (6 mg) under solvent free condition. 52.2 mg (99%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.87 (s, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.40-7.34 (m, 3H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.28-7.25 (m, 1H), 7.22 (td, *J* = 7.2, 1.2 Hz, 1H), 4.95 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.8, 136.9, 135.4, 133.5, 133.2, 131.8, 129.9, 129.8, 129.4, 128.6, 128.4, 127.1, 127.0, 62.3.



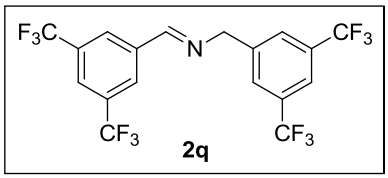
(*E*)-*N*-(3-Chlorobenzylidene)-1-(3-chlorophenyl)methanamine (2n): The product was prepared by the General Procedure A with 3 mol % catalyst loading (6 mg) under solvent free condition. 50.7 mg (96%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.34 (s, 1H), 7.82-7.81 (m, 1H), 7.63 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.42-7.40 (m, 1H), 7.37-7.33 (m, 2H), 7.29-7.21 (m, 3H), 4.79 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.0, 141.1, 137.8, 135.0, 134.5, 131.0, 130.0, 129.9, 128.1(6), 128.1(0), 127.3, 126.7, 126.1, 64.4.



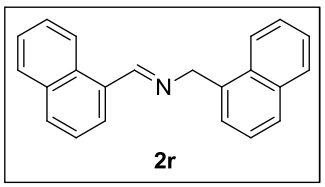
(*E*)-4-(((4-Cyanobenzyl)imino)methyl)benzonitrile (2o): The product was prepared by the General Procedure A using 5 mol % catalyst loading (10.2 mg) in 0.5 mL of water. 46.0 mg (94%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[7] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.45 (s, 1H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 4.90 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.1, 144.3, 139.6, 132.6, 132.5, 128.8, 128.5, 118.9, 118.4, 114.5, 111.1, 64.4.



(*E*)-*N*-(3,5-Dimethoxybenzylidene)-1-(3,5-dimethoxyphenyl)methanamine (2p): The product was prepared by the General Procedure A with 3 mol % catalyst loading (6 mg) under solvent free condition. 59.3 mg (94%), yellow liquid; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.28 (s, 1H), 6.93 (d, *J* = 2.4 Hz, 2H), 6.53 (t, *J* = 2.4 Hz, 1H), 6.50 (d, *J* = 2.4 Hz, 2H), 6.37 (t, *J* = 2.4 Hz, 1H), 4.75 (s, 2H), 3.82 (s, 6H), 3.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.2, 161.0(8), 161.0(6), 141.6, 138.3, 106.1(8), 106.1(3), 103.7, 99.1, 65.0, 55.6, 55.4; IR(neat): 2998, 2937, 2836, 1643, 1589 cm^{-1}; HRMS (ESI): m/z calculated for $C_{18}H_{22}NO_4$ $[M+H]^+$ 316.1543, Found 316.1550.

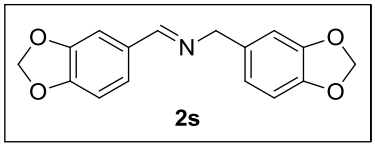


(*E*)-*N*-(3,5-Bis(trifluoromethyl)benzylidene)-1-(3,5-bis(trifluoromethyl)phenyl)methanamine (2q): The product was prepared by the General Procedure A with 10 mol % catalyst loading (20.3 mg) and 0.5 mL of water. 82.1 mg (88%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.55 (s, 1H), 8.25 (s, 2H), 7.97 (s, 1H), 7.83 (s, 3H), 4.97 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 160.2, 141.1, 137.5, 132.5 (q, *J* = 33.0 Hz), 132.0 (q, *J* = 33.0 Hz), 128.3, 128.2, 124.6 (q, *J* = 4.5 Hz), 123.4 (q, *J* = 271.5 Hz), 123.1 (q, *J* = 271.3 Hz), 121.5 (q, *J* = 4.8 Hz), 64.0; ^{19}F NMR ($CDCl_3$, 564 MHz): δ -62.7, -62.9.

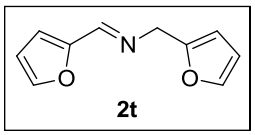


(*E*)-1-(Naphthalen-1-yl)-*N*-(naphthalen-1-ylmethylene)methanamine (2r): The product was prepared by the General Procedure A with 5 mol % catalyst loading (10.2 mg) and 0.5 mL of water. 53.4 mg (90%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[8] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.09 (s, 1H), 8.97 (d, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 9.0 Hz, 1H),

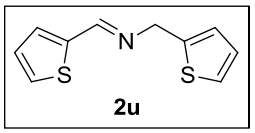
7.96-7.89 (m, 4H), 7.83 (d, J = 7.8 Hz, 1H), 7.61-7.47 (m, 7H), 5.42 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.0, 135.6, 133.9(7), 133.9(2), 131.7(8), 131.7(5), 131.4, 131.2, 129.3, 128.8, 128.7, 127.9, 127.3, 126.2, 126.1, 125.9, 125.8, 125.7, 125.3, 124.5, 124.0, 63.3.



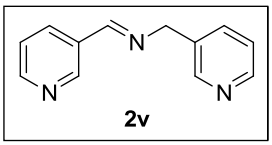
(*E*)-1-(Benzo[d][1,3]dioxol-5-yl)-*N*-(benzo[d][1,3]dioxol-5-ylmethylene) methanamine (2s): The product was prepared by the General Procedure A with 3 mol % of catalyst loading (6 mg) and 0.5 mL of water. 55.2 mg (97%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.23 (s, 1H), 7.39 (d, J = 1.2 Hz, 1H), 7.13 (dd, J = 7.8, 1.2 Hz, 1H), 6.82 (d, J = 7.8 Hz, 2H), 6.77 (s, 2H), 5.99 (s, 2H), 5.93 (s, 2H), 4.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.0, 150.0, 148.4, 147.8, 146.6, 133.4, 131.1, 124.6, 121.1, 108.7, 108.3, 108.1, 106.8, 101.5, 101.0, 64.6.



(*E*)-1-(Furan-2-yl)-*N*-(furan-2-ylmethylene)methanamine (2t): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) and 0.1 mL of water. 26.9 mg (77%), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.11 (s, 1H), 7.51 (s, 1H), 7.37 (s, 1H), 6.78 (d, J = 3.6 Hz, 1H), 6.47 (m, 1H), 6.34-6.33 (m, 1H), 6.27 (d, J = 3.0 Hz, 1H), 4.75 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 151.9, 151.5, 151.4, 145.0, 142.4, 114.6, 111.8, 110.5, 108.0, 56.9.

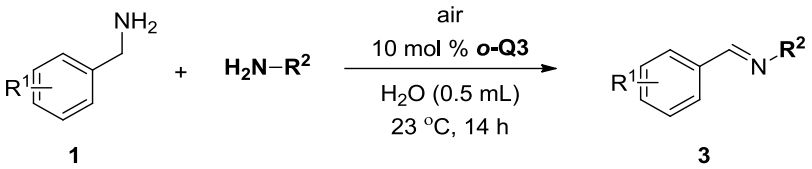


(*E*)-1-(Thiophen-2-yl)-*N*-(thiophen-2-ylmethylene)methanamine (2u): The product was prepared by the General Procedure A with 1 mol % catalyst loading (2 mg) under solvent free condition. 37.4 mg (90%), brown liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.42 (s, 1H), 7.42 (d, J = 4.8 Hz, 1H), 7.33-7.32 (m, 1H), 7.24-7.23 (m, 1H), 7.08-7.07 (m, 1H), 7.00-6.97 (m, 2H), 4.95 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.5, 142.3, 141.7, 131.0, 129.4, 127.5, 127.0, 125.4, 124.9, 58.6.



(*E*)-1-(Pyridin-3-yl)-*N*-(pyridin-3-ylmethylene)methanamine (2v): The product was prepared by the General Procedure A with 5 mol % catalyst loading (10.2 mg) under solvent free condition. 35.6 mg (90%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[9] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.89 (d, J = 1.2 Hz, 1H), 8.66 (dd, J = 4.8, 1.2 Hz, 1H), 8.61 (d, J = 1.2 Hz, 1H), 8.53 (d, J = 5.4 Hz, 1H), 8.47 (s, 1H), 8.16-8.14 (m, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.37-7.35 (m, 1H), 7.29-7.27 (m, 1H), 4.85 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.8, 152.0, 150.5, 149.5, 148.7, 135.7, 134.7, 134.5, 131.5, 123.8, 123.6, 62.6,

General Procedure B: *Cacotheline*-Catalyzed Aerobic Oxidation to Hetero-Coupling of Amines

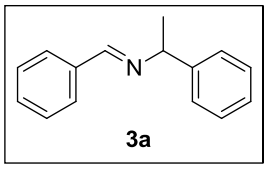


1 3

Benzylamine (**1**, 1.0 equiv, 0.4 mmol), primary amine (R^2NH_2, 1.2 equiv, 0.48 mmol) and catalyst ***o*-Q3** (10 mol %, 20.3 mg) was dissolved in water (0.5 mL) and stirred at ambient temperature for 14 h. After the reaction was complete, the mixture was extracted with diethyl ether (2 mL x 3) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude mixture was purified by column chromatography on deactivated silica gel with 0-20% ethyl acetate in hexanes.

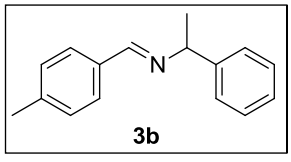
[1 g Scale Reaction] 4-Chlorobenzyl amine (**1a**, 1.0 equiv, 7.06 mmol, 1.0 g), phenylethyl amine (1.2 equiv, 8.47 mmol, 1.03 g) and catalyst ***o*-Q3** (10 mol %, 0.706 mmol, 359 mg) were dissolved in water (8.83 mL) and stirred at 23 °C for 24 h. The reaction mixture was extracted with diethyl ether (10 mL x 3). Combined organic layers were dried with anhydrous Na_2SO_4, and filtered through a short pad of silica gel. After evaporation of organic solvent, the product **3d** was obtained without further purification in 83% yield (1.42 g).

Characterization of the Compounds in Scheme 3



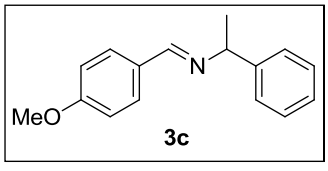
3a

(*E*)-N-Benzylidene-1-phenylethanamine (3a): The product was prepared by the General Procedure B with **1b** and phenylethyl amine, and purified using 100% hexanes. 68.8 mg (82%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.38 (s, 1H), 7.80-7.78 (m, 2H), 7.44-7.40 (m, 5H), 7.36-7.33 (m, 2H), 7.26-7.23 (m, 1H), 4.55 (q, *J* = 6.6 Hz, 1H), 1.60 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.5, 145.3, 136.5, 130.7, 128.6, 128.5, 128.4, 126.9, 126.7, 69.8, 24.9.



3b

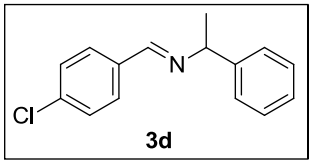
(*E*)-*N*-(4-Methylbenzylidene)-1-phenylethanamine (3b): The product was prepared by the General Procedure B with **1c** and phenylethyl amine, and purified using 100% hexanes. 86.0 mg (96%), off-white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.33 (s, 1H), 7.67 (d, *J* = 7.2 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.34-7.32 (m, 2H), 7.24-7.20 (m, 3H), 4.52 (q, *J* = 6.6 Hz, 1H), 2.37 (s, 3H), 1.59 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.5, 145.4, 140.9, 133.9, 129.3, 128.5, 128.3, 126.9, 126.7, 69.8, 24.9, 21.6.



3c

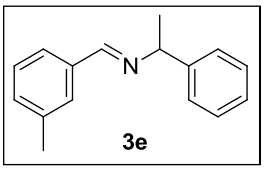
(*E*)-*N*-(4-Methoxybenzylidene)-1-phenylethanamine (3c): The product was prepared by the General Procedure B with **1e** and phenylethyl amine, and purified using 2% ethyl acetate in hexanes. 86.2 mg (90% isolated yield, 98% of ^{1}H NMR yield using dibromomethane internal stanard), yellow solid; ^{1}H NMR and ^{13}C

NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.31 (s, 1H), 7.74-7.72 (m, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 2H), 4.51 (q, *J* = 6.6 Hz, 1H), 3.84 (s, 3H), 1.59 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.6, 158.9, 145.5, 129.9, 129.5, 128.5, 126.8, 126.7, 114.0, 69.7, 55.4, 25.0.



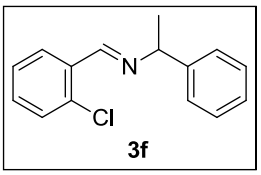
3d

(*E*)-*N*-(4-Chlorobenzylidene)-1-phenylethanamine (3d): The product was prepared by the General Procedure B with **1a** and phenylethyl amine, and purified using 2% ethyl acetate in hexanes. 88.1 mg (90% isolated yield, 97% of ^{1}H NMR yield using dibromomethane internal stanard), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.33 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.37-7.33 (m, 4H), 7.25-7.23 (m, 1H), 4.53 (q, *J* = 6.6 Hz, 1H), 1.58 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 158.1, 145.1, 136.6, 135.0, 129.5, 128.9, 128.6, 127.0, 126.7, 69.8, 24.9.



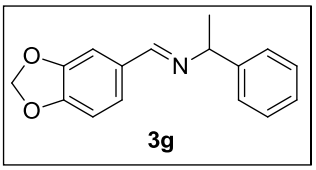
3e

(*E*)-*N*-(3-Methylbenzylidene)-1-phenylethanamine (3e): The product was prepared by the General Procedure B with **1j** and phenylethyl amine, and purified using 100% hexanes. 76.3 mg (85%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.35 (s, 1H), 7.65 (s, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 7.2 Hz, 2H), 7.30 (d, *J* = 7.2 Hz, 1H), 7.26-7.22 (m, 2H), 4.54 (q, *J* = 6.6 Hz, 1H), 2.39 (s, 3H), 1.60 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.8, 145.3, 138.4, 136.4, 131.5(5), 131.5(4), 128.5, 126.9, 126.7(8), 126.7(7), 125.9, 69.8, 24.8, 21.4.



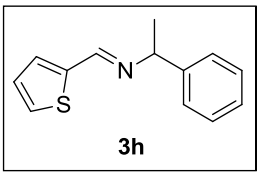
3f

(*E*)-*N*-(2-Chlorobenzylidene)-1-phenylethanamine (3f): The product was prepared by the General Procedure B with **1m** and phenylethyl amine, and purified using 2% ethyl acetate in hexanes. 79.9 mg (82%), colorless liquid; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.82 (s, 1H), 8.13 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.44 (d, *J* = 6.6 Hz, 2H), 7.37-7.24 (m, 6H), 4.62 (q, *J* = 6.6 Hz, 1H), 1.61 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 156.3, 145.1, 135.2, 133.5, 131.5, 129.8, 128.7, 128.6, 127.0(9), 127.0(6), 126.7, 70.1, 25.0; IR(neat): 3015, 2974, 2927, 1634, 1593 cm^{-1}; HRMS (ESI): m/z calculated for $C_{15}H_{15}ClN$ $[M+H]^+$ 244.0887, Found 244.0888.

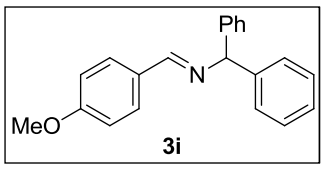


3g

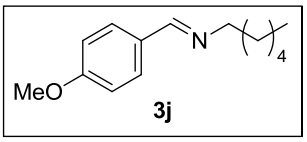
(*E*)-*N*-(Benzo[d][1,3]dioxol-5-ylmethylene)-1-phenylethanamine (3g): The product was prepared by the General Procedure B with **1s** and phenylethyl amine, and purified using 20% ethyl acetate in hexanes. 81.4 mg (80%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.24 (s, 1H), 7.43-7.41 (m, 3H), 7.34-7.32 (m, 2H), 7.24-7.22 (m, 1H), 7.13-7.11 (m, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.98(2) (d, *J* = 2.4 Hz, 1H), 5.98(0) (d, *J* = 2.4 Hz, 1H), 4.50 (q, *J* = 6.6 Hz, 1H), 1.57 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 158.6, 149.9, 148.3, 145.5, 131.4, 128.5, 126.9, 126.7, 124.4, 108.1, 106.9, 101.5, 69.5, 25.0.



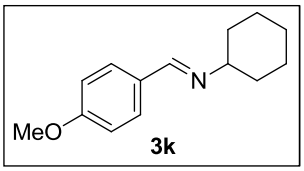
(*E*)-1-Phenyl-*N*-(thiophen-2-ylmethylene)ethanamine (3h): The product was prepared by the General Procedure B with **1u** and phenylethyl amine, and purified using 2% ethyl acetate in hexanes. 76.2 mg (88% isolated yield, 98% of ^{1}H NMR yield using dibromomethane internal stanard), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.44 (s, 1H), 7.42-7.39 (m, 3H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.31 (d, *J* = 3.6 Hz, 1H), 7.27-7.24 (m, 1H), 7.07-7.06 (m, 1H), 4.54 (q, *J* = 6.6 Hz, 1H), 1.61 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.8, 145.0, 142.8, 130.4, 128.9, 128.5, 127.3, 126.9, 126.7, 69.2, 24.8.



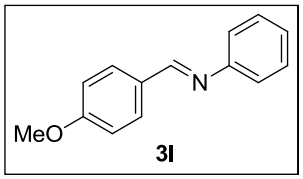
(*E*)-*N*-(4-Methoxybenzylidene)-1,1-diphenylmethanamine (3i): The product was prepared by the General Procedure B with **1e** and benzhydrylamine, and purified using 8% ethyl acetate in hexanes. 119.4 mg (99%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.35 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 4H), 7.31 (t, *J* = 7.8 Hz, 4H), 7.22 (t, *J* = 7.8 Hz, 2H), 6.93-6.92 (m, 2H), 5.57 (s, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.8, 160.2, 144.2, 130.1, 129.5, 128.5, 127.8, 127.0, 114.0, 77.9, 55.5.



(*E*)-*N*-(4-Methoxybenzylidene)hexan-1-amine (3j): The product was prepared by the General Procedure B with **1e** and hexylamine, and purified using 5% ethyl acetate in hexanes. 85.5 mg (97%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.18 (s, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 3.82 (s, 3H), 3.56-3.53 (m, 2H), 1.68-1.64 (m, 2H), 1.35-1.28 (m, 6H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.5, 160.1, 129.6, 129.5, 114.0, 61.8, 55.4, 31.8, 31.1, 27.1, 22.7, 14.2.



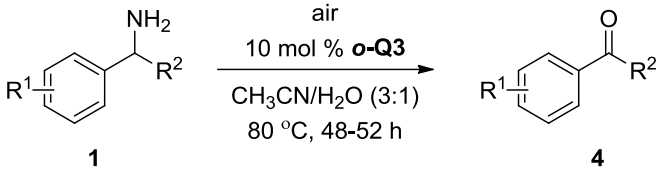
(*E*)-*N*-(4-Methoxybenzylidene)cyclohexanamine (3k): The product was prepared by the General Procedure B with **1e** and cyclohexylamine, and purified using 5% ethyl acetate in hexanes. 81.9 mg (94% isolated yield, 97% of ^{1}H NMR yield using dibromomethane internal stanard), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.24 (s, 1H), 7.66 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.83 (s, 3H), 3.17-3.12 (m, 1H), 1.84-1.80 (m, 2H), 1.74-1.65 (m, 3H), 1.60-1.54 (m, 2H), 1.39-1.32 (m, 2H), 1.28-1.21 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.5, 158.0, 129.7(2C), 114.0, 70.0, 55.4, 34.6, 25.8, 25.0.



(*E*)-*N*-(4-Methoxybenzylidene)aniline (3l): The product was prepared by the General Procedure B with **1e** and phenylamine, and purified using 5% ethyl acetate in hexanes. 82.7 mg (98%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[3] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.39 (s, 1H), 7.86 (d, *J* = 9.0 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.22-7.19 (m, 3H), 6.98

(d, J = 9.0 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.3, 159.8, 152.5, 130.6, 129.4, 129.2, 125.6, 121.0, 114.3, 55.5.

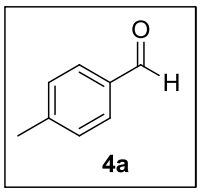
General Procedure C: *Cacotheline*-Catalyzed Aerobic Oxidation of Benzylamines to Carbonyls



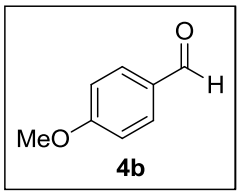
A solution of amine **1** (1.0 equiv, 0.4 mmol) and ***o*-Q3** catalyst (10 mol %, 0.04 mmol, 20.3 mg) dissolved in ACN/H_2O (3:1 (v:v), 3.0 mL) was stirred at 80 °C in an oil bath for 48 h. After cooling down to ambient temperature, the solution was extracted with diethyl ether (2 mL x 3). The organic mixture was dried over Na_2SO_4, filtered through a short pad of silica and concentrated under the reduced pressure. The desired products **4** were obtained without further purification.

[1 g Scale Reaction] To an oven dried 100 mL round bottom flask equipped with a magnetic stir bar were added 4-chlorobenzyl amine (**1a**, 1.0 equiv, 7.06 mmol, 1.0 g), catalyst ***o*-Q3** (10 mol %, 0.706 mmol, 359 mg) and ACN/H_2O (3:1 (v:v), 53 mL) at ambient temperature. The flask was fitted with a condenser and then heated at 80 °C in an oil bath for 96 h. The mixture was cooled to ambient temperature and extracted with diethyl ether (30 mL x 3). The combined organic layers were dried over Na_2SO_4, filtered through a short pad of silica gel and concentrated under reduced pressure. The product **4e** was obtained without further purification in 84% yield (834 mg).

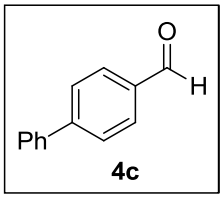
Characterization of the Compounds in Scheme 4



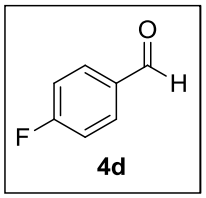
4-Methylbenzaldehyde (4a): The product was prepared by the General Procedure C using **1c**. 45.7 mg (95%), colorless oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.96 (s, 1H), 7.77 (d, J = 7.8 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.1, 145.6, 134.3, 129.9, 129.8, 22.0.



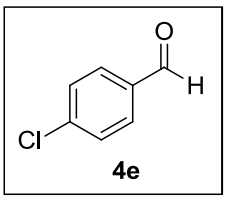
4-Methoxybenzaldehyde (4b): The product was prepared by the General Procedure C using **1e**. 53.7 mg (99%), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.88 (s, 1H), 7.84 (d, J = 9.0 Hz, 2H), 7.00 (d, J = 9.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 190.9, 164.7, 132.0, 130.0, 114.4, 55.6.



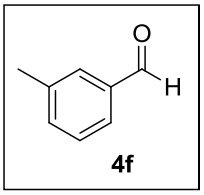
[1,1'-Biphenyl]-4-carbaldehyde (4c): The product was prepared by the General Procedure C using **1f**. 66.9 mg (92%), pale yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 10.06 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.66-7.63 (m, 2H), 7.50-7.47 (m, 2H), 7.43-7.41 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.0, 147.3, 139.8, 135.3, 130.4, 129.1, 128.6, 127.8, 127.5.



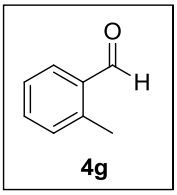
4-Fluorobenzaldehyde (4d): The product was prepared by the General Procedure C using **1g**. 40.1 mg (81% isolated yield, 91% of ^{1}H NMR yield using dibromomethane internal stanard), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.97 (s, 1H), 7.92-7.90 (m, 2H), 7.23-7.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 190.6, 166.6 (d, *J* = 255.6 Hz), 133.1 (d, *J* = 3.0 Hz), 133.1 (d, *J* = 10.0 Hz), 116.5 (d, *J* = 21.6 Hz); ^{19}F NMR ($CDCl_3$, 564 MHz): δ -102.2.



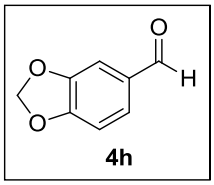
4-Chlorobenzaldehyde (4e): The product was prepared by the General Procedure C using **1a**. 48.9 mg (87%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.98 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 191.0, 141.1, 134.8, 131.0, 129.6.



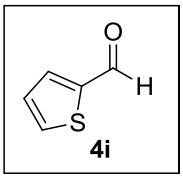
3-Methylbenzaldehyde (4f): The product was prepared by the General Procedure C using **1j**. 45.7 mg (95%), colorless oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[11] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.98 (s, 1H), 7.68-7.67 (m, 2H), 7.45-7.40 (m, 2H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.7, 139.0, 136.6, 135.4, 130.1, 129.0, 127.3, 21.3.



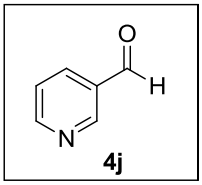
2-Methylbenzaldehyde (4g): The product was prepared by the General Procedure C using **1i**. 43.5 mg (91%), colorless oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[12] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 10.27 (s, 1H), 7.80 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.48 (td, *J* = 7.8, 1.2 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.9, 140.7, 134.3, 133.7, 132.1, 131.9, 126.4, 19.7.



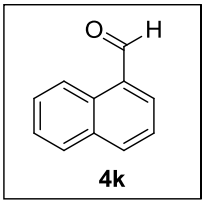
Benzo[*d*][1,3]dioxole-5-carbaldehyde (4h): The product was prepared by the General Procedure C using **1s**. 59.4 mg (99%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.81 (s, 1H), 7.41 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.33 (d, *J* = 1.2 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 190.4, 153.2, 148.8, 132.0, 128.8, 108.5, 107.0, 102.2.



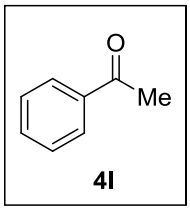
Thiophene-2-carbaldehyde (4i): The product was prepared by the General Procedure C using **1u**. 37.2 mg (83% isolated yield, 92% of ^{1}H NMR yield using dibromomethane internal stanard), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[13] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.95 (s, 1H), 7.79-7.76 (m, 2H), 7.22-7.21 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 183.1, 144.1, 136.4, 135.2, 128.4.



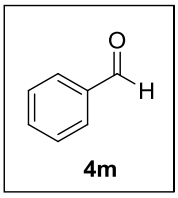
Nicotinaldehyde (4j): The product was prepared by the General Procedure C using **1v** with 52 h reaction time. 32.2 mg (75%), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[13] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 10.11 (s, 1H), 9.07 (s, 1H), 8.84-8.83 (m, 1H), 8.17-8.15 (m, 1H), 7.49-7.47 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 190.8, 154.9, 152.2, 135.9, 131.5, 124.2.



1-Naphthaldehyde (4k): The product was prepared by the General Procedure C using **1r** with 52 h reaction time. 59.1 mg (95%), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[14] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 10.41 (s, 1H), 9.26 (d, J = 9.0 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 6.6 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.71-7.68 (m, 1H), 7.65-7.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 193.6, 136.8, 135.4, 133.8, 131.5, 130.6, 129.2, 128.6, 127.1, 125.0(2), 150.0(1).

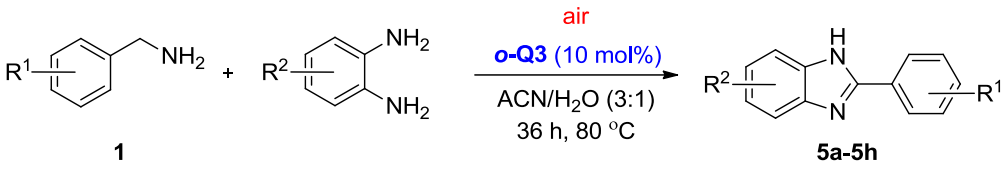


Acetophenone (4l): The product was prepared by the General Procedure C using phenylethyl amine and purified using 3% ethyl acetate in hexanes. 10.8 mg (22% isolated yield, 28% of ^{1}H NMR yield using dibromomethane internal stanard), yellow oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.95 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 2.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 198.2, 137.2, 133.2, 128.6, 128.4, 26.7.



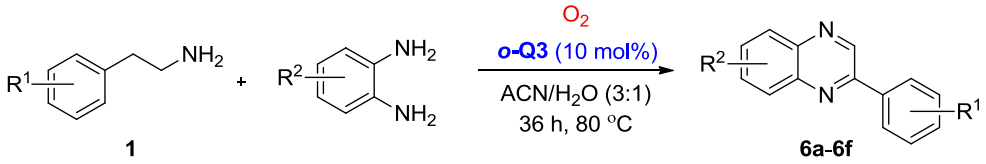
Benzaldehyde (4m): The product was prepared by the General Procedure C using phenylglycine instead of **1b** under concentrated condition (1.0 mL of solvents instead of 3.0 mL) with 5 mol % catalyst loading (10.2 mg) and 60 h reaction time. 17.2 mg (41% isolated yield, 68% of ^{1}H NMR yield using dibromomethane internal stanard), colorless oil; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[10] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 10.02 (s, 1H), 7.89-7.87 (m, 2H), 7.64-7.62 (m, 1H), 7.53 (t, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.5, 136.5, 134.5, 129.8, 129.1.

General Procedure D: *Cacotheline*-Catalyzed Aerobic Oxidation to Benzimidazoles



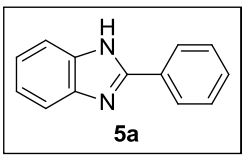
To a 10 mL vial charged with amine (**1**, 1.0 equiv, 0.4 mmol), 2-aminoanilines (1.2 equiv, 0.48 mmol) and ***o*-Q3** catalyst (10 mol %, 0.04 mmol, 20.3 mg) was added ACN/H_2O (3:1 (v:v), 3.0 mL). The reaction was stirred at 80 °C in an oil bath for 36 h. After cooled down to ambient temperature, the reaction mixture was extracted with diethyl ether (2 mL x 3) and combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The reaction mixture was purified by column chromatography on silica gel with 10-30% ethyl acetate in hexanes to provide the compound **5**.

General Procedure E: *Cacotheline*-Catalyzed Aerobic Oxidation to Quinoxalines

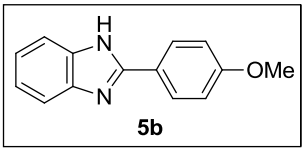


2-Phenylethylamine (3.0 equiv, 1.2 mmol), 2-aminoanilines (1.0 equiv, 0.4 mmol) and ***o*-Q3** Catalyst (10 mol %, 0.04 mmol, 20.3 mg) were dissolved in 3.0 mL of ACN/H_2O (3:1 (v:v)) in a 10 mL vial and then the vial was flushed with O_2. The reaction was heated at 80 °C in an oil bath under O_2 balloon for 36 h. After cooled down to ambient temperature, the reaction mixture was extracted with diethyl ether (2 mL x 3) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The desired product (**6**) was purified by column chromatography on silica gel with 5-10% ethyl acetate in hexanes.

Characterization of the Compounds in Scheme 5

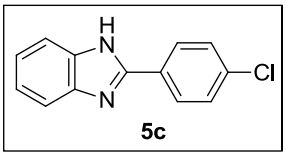


2-Phenyl-1*H*-benzo[*d*]imidazole (5a): The product was prepared by the General Procedure D with **1b** and *o*-phenylenediamine, and purified using 10% ethyl acetate in hexanes. 71.6 mg (92%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 12.91 (brs, 1H), 8.17 (d, J = 7.8 Hz, 2H), 7.59-7.52 (m, 4H), 7.48 (t, J = 7.2 Hz, 1H), 7.20-7.18 (m, 2H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 151.2, 143.8, 135.0, 130.1, 129.8, 128.9, 126.4, 122.5, 121.7, 118.8, 111.3.



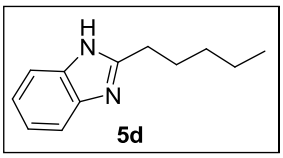
2-(4-Methoxyphenyl)-1*H*-benzo[*d*]imidazole (5b): The product was prepared by the General Procedure D with **1e** and *o*-phenylenediamine, and purified using 30% ethyl acetate in hexanes. 85.8 mg (96%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature

data.[16] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 12.74 (brs, 1H), 8.11 (d, *J* = 9.0 Hz, 2H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.18-7.13 (m, 2H), 7.09 (d, *J* = 9.0 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 160.6, 151.3, 143.9, 135.0, 128.0, 122.7, 122.1, 121.4, 118.5, 114.3, 111.0, 55.3.



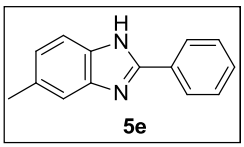
5c

2-(4-Chlorophenyl)-1*H*-benzo[*d*]imidazole (5c): The product was prepared by the General Procedure D with **1a** and *o*-phenylenediamine, and purified using 10% ethyl acetate in hexanes. 78.5 mg (86%), yellow liquid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 12.98 (brs, 1H), 8.17 (d, *J* = 9.0 Hz, 2H), 7.65-7.54 (m, 4H), 7.20 (m, 2H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 150.1, 143.7, 135.0, 134.5, 129.0(9), 129.0(5), 128.1, 122.8, 121.8, 118.9, 111.4.



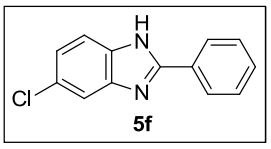
5d

2-Pentyl-1*H*-benzo[*d*]imidazole (5d): The product was prepared by the General Procedure D with 1-hexylamine and *o*-phenylenediamine, and purified using 30% ethyl acetate in hexanes. 44.9 mg (60%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[17] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.54 (m, 2H), 7.22-7.20 (m, 2H), 2.93 (t, *J* = 7.8 Hz, 2H), 1.88-1.83 (m, 2H), 1.36-1.30 (m, 4H), 0.85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.3, 138.6, 122.2, 114.8, 31.6, 29.4, 28.1, 22.4, 14.0.



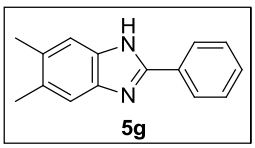
5e

5-Methyl-2-phenyl-1*H*-benzo[*d*]imidazole (5e): The product was prepared by the General Procedure D with **1b** and 3,4-diaminotoluene, and purified using 15% ethyl acetate in hexanes. 69.5 mg (83%), pale yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[18] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 12.75 (brs, 1H), 8.14 (d, *J* = 7.2 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.36 (m, 1H), 2.41 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 150.9, 130.3, 129.6, 128.9, 126.3, 123.5, 21.3.



5f

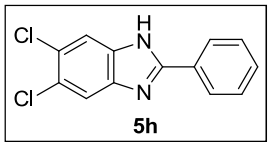
5-Chloro-2-phenyl-1*H*-benzo[*d*]imidazole (5f): The product was prepared by the General Procedure D with **1b** and 4-chloro-*o*-phenylenediamine, and purified using 15% ethyl acetate in hexanes. 80.0 mg (87%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[19] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 13.06 (brs, 1H), 8.15 (d, *J* = 7.2 Hz, 2H), 7.63 (m, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.21 (dd, *J* = 8.4, 1.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 152.6, 130.2, 129.7, 129.0, 126.5, 126.4, 122.3.



5g

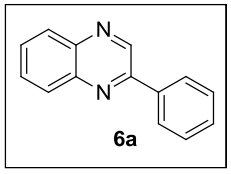
5,6-Dimethyl-2-phenyl-1*H*-benzo[*d*]imidazole (5g): The product was prepared by the General Procedure D with **1b** and 4,5-dimethyl-*o*-phenylenediamine, and purified using 20% ethyl acetate in hexanes. 72.4 mg (81%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[20] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 12.60 (brs, 1H), 8.12 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.45-7.41 (m,

2H), 7.27 (m, 1H), 2.32 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 150.3, 142.5, 133.5, 131.1, 130.4, 129.9, 129.4, 128.8, 126.1, 118.9, 111.3, 20.0(6), 20.0(1).



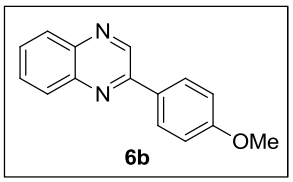
5h

5,6-Dichloro-2-phenyl-1*H*-benzo[*d*]imidazole (5h): The product was prepared by the General Procedure D with **1b** and 4,5-dichloro-*o*-phenylenediamine, and purified using 20% ethyl aceated in hexanes. 83.4 mg (79%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[17] ^{1}H NMR (DMSO-d_6, 600 MHz): δ 13.23 (brs, 1H), 8.15 (dd, *J* = 9.6, 1.2 Hz, 2H), 7.83 (m, 2H), 7.57-7.52 (m, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 153.8, 130.5, 129.3, 129.0, 128.5, 127.7, 126.7, 124.4.



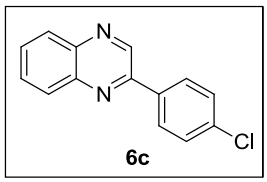
6a

2-Phenylquinoxaline (6a): The product was prepared by the General Procedure E with 2-phenylethylamine and *o*-phenylenediamine, and purified using 5% ethyl acetate in hexanes. 59.5 mg (72%), white solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.33 (s, 1H), 8.21-8.19 (m, 2H), 8.16 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.12 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.80-7.74 (m, 2H), 7.57 (m, 2H), 7.54-7.51 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.0, 143.5, 142.4, 141.7, 136.9, 130.4, 130.3, 129.7(9), 129.7(7), 129.3, 129.2, 127.7.



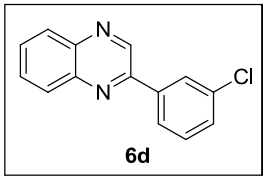
6b

2-(4-Methoxyphenyl)quinoxaline (6b): The product was prepared by the General Procedure E with 2-(4-methoxyphenyl)ethylamine and *o*-phenylenediamine, and purified using 5% ethyl acetate in hexanes. 81.2 mg (86%), pale yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.29 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 8.12 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.76 (t, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.6, 151.5, 143.2, 142.4, 141.3, 130.3, 129.5, 129.4, 129.2, 129.1(9), 129.1(2), 114.7, 55.5.



6c

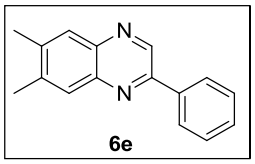
2-(4-Chlorophenyl)quinoxaline (6c): The product was prepared by the General Procedure E with 2-(4-chlorophenyl)ethylamine and *o*-phenylenediamine, and purified using 10% ethyl acetate in hexanes. 68.3 mg (71%), pale yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.26 (s, 1H), 8.13-8.09 (m, 4H), 7.78-7.71 (m, 2H), 7.52-7.49 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.6, 142.9, 142.2, 141.7, 136.6, 135.2, 130.5, 129.8, 129.6, 129.4, 129.2, 128.8.



6d

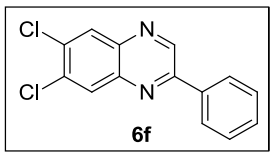
2-(3-Chlorophenyl)quinoxaline (6d): The product was prepared by the General Procedure E with 2-(3-chlorophenyl)ethylamine and *o*-phenylenediamine, and purified using 7% ethyl acetate in hexanes. 61.8 mg (64%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature

data.[15] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.30 (s, 1H), 8.23 (m, 1H), 8.16 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.13 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.07-8.06 (m, 1H), 7.82-7.76 (m, 2H), 7.50-7.49 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.4, 143.1, 142.3, 141.9, 138.6, 135.5, 130.7, 130.5, 130.3, 130.1, 129.8, 129.3, 127.8, 125.6.



6e

6,7-Dimethyl-2-phenylquinoxaline (6e): The product was prepared by the General Procedure E with 2-phenylethylamine and 4,5-dimethyl-*o*-phenylenediamine, and purified using 10% ethyl acetate in hexanes. 78.9 mg (84%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[15] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.21 (s, 1H), 8.16 (d, *J* = 7.2, 1.2 Hz, 2H), 7.90 (s, 1H), 7.84 (s, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 7.51-7.48 (tt, *J* = 7.2, 1.2 Hz,1H), 2.50 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 151.1, 142.5, 141.3, 140.9, 140.6, 140.2, 137.2, 129.9, 129.2, 128.7, 128.2, 127.5, 20.5, 20.4.

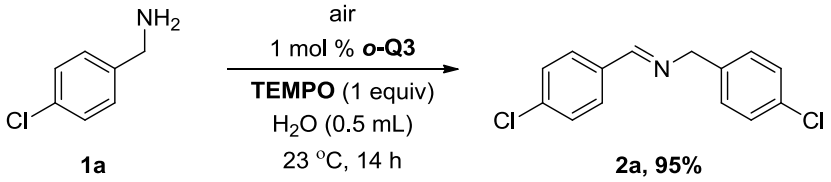


6f

6,7-Dichloro-2-phenylquinoxaline (6f): The product was prepared by the General Procedure E with 2-phenylethylamine and 4,5-dichloro-*o*-phenylenediamine, and purified using 10% ethyl acetate in hexanes. 46.6 mg (42%), yellow solid; ^{1}H NMR and ^{13}C NMR spectra for this compound were consistent with previously reported literature data.[20] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.32 (s, 1H), 8.27 (s, 1H), 8.23 (s, 1H), 8.19-8.18 (m, 2H), 7.59-7.55 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.8, 144.4, 141.2, 140.4, 136.1, 135.0, 134.1, 130.9, 130.3, 129.9, 129.4, 127.7.

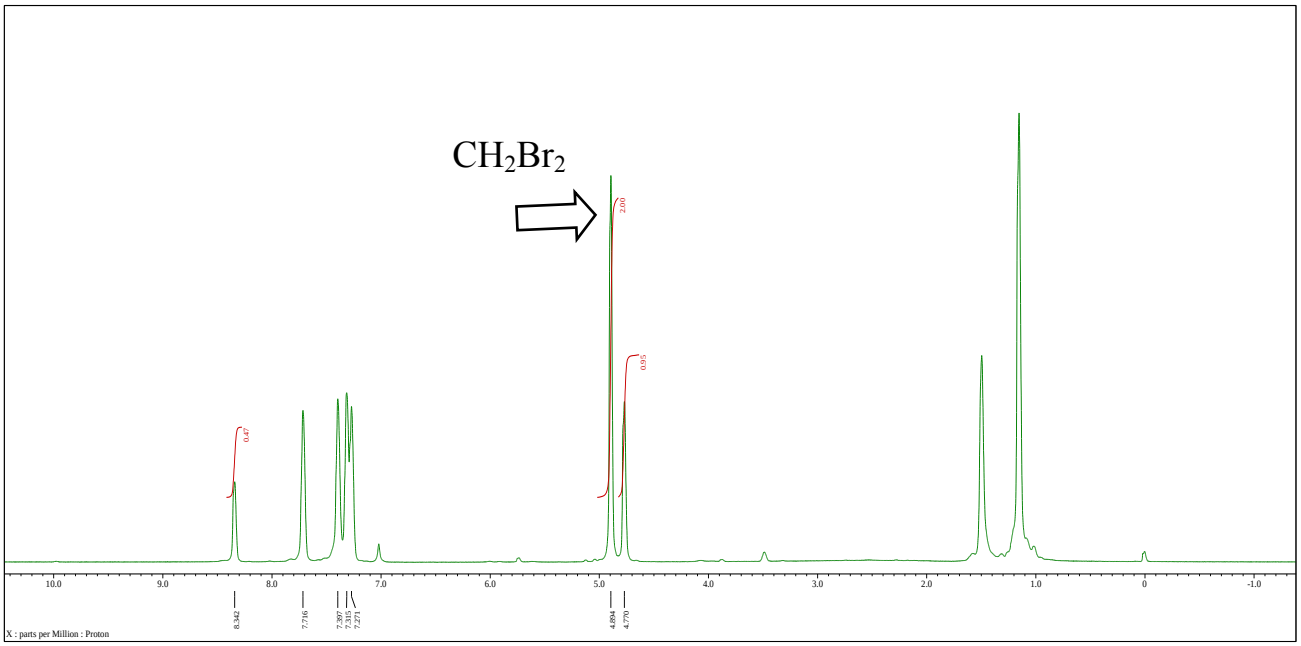
Mechanistic Studies in Scheme 6

(a) Aerobic Oxidation of Amine 1a with TEMPO



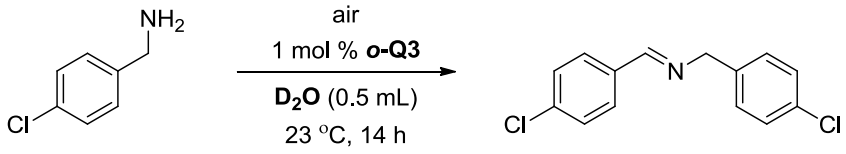
1a **2a, 95%**

The compound **1a** (1 equiv, 0.4 mmol, 56.6 mg), catalyst ***o*-Q3** (1 mol %, 0.004 mmol, 2 mg), TEMPO (1 equiv, 0.4 mmol, 62.5 mg) were dissolved in 0.5 mL of water. The solution was stirred at ambient temperature for 14 h. After the reaction was complete, the reaction mixture was extracted with diethyl ether (2 mL x 3). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. Dibromomethane (1 equiv, 0.4 mmol, 69.5 mg) was then added as an internal standard. Small portions of crude mixture were taken out for ^{1}H NMR analysis.



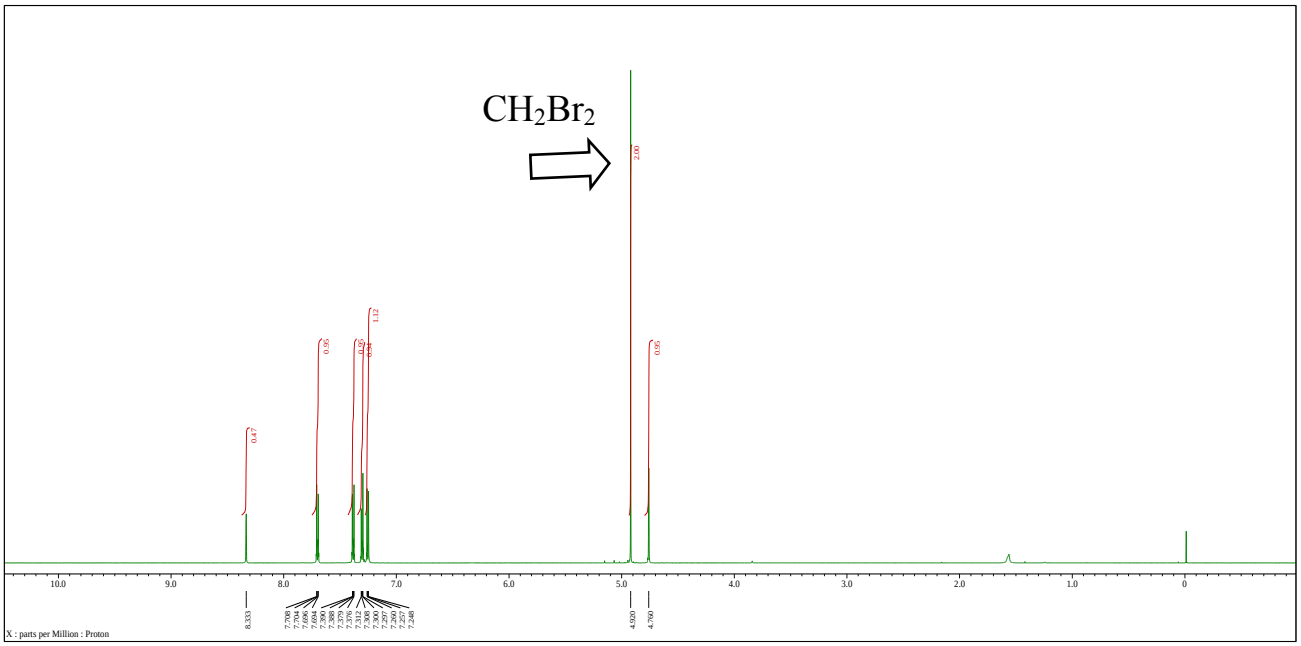
^{1}H-NMR Spectrum of reaction with TEMPO

(b) Mechanistic Studies Using D_2O



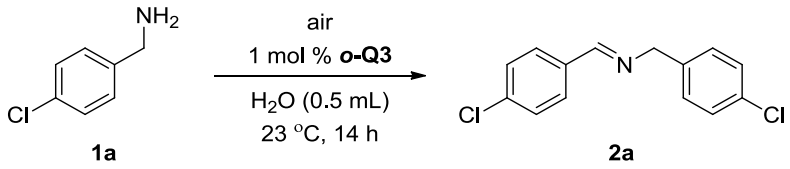
1a **2a, 95%**

Catalyst ***o*-Q3** (1 mol %, 0.004 mmol, 2 mg) was added to a solution of the compound **1a** in 0.5 mL of D_2O and stirred at ambient temperature for 14 h. The solution was extracted with diethyl ether (2 mL x 3). Combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo* after filtration. Dibromomethane (1 equiv, 0.4 mmol, 69.5 mg) was added to this mixture as an internal standard to check the ^{1}H NMR yield.

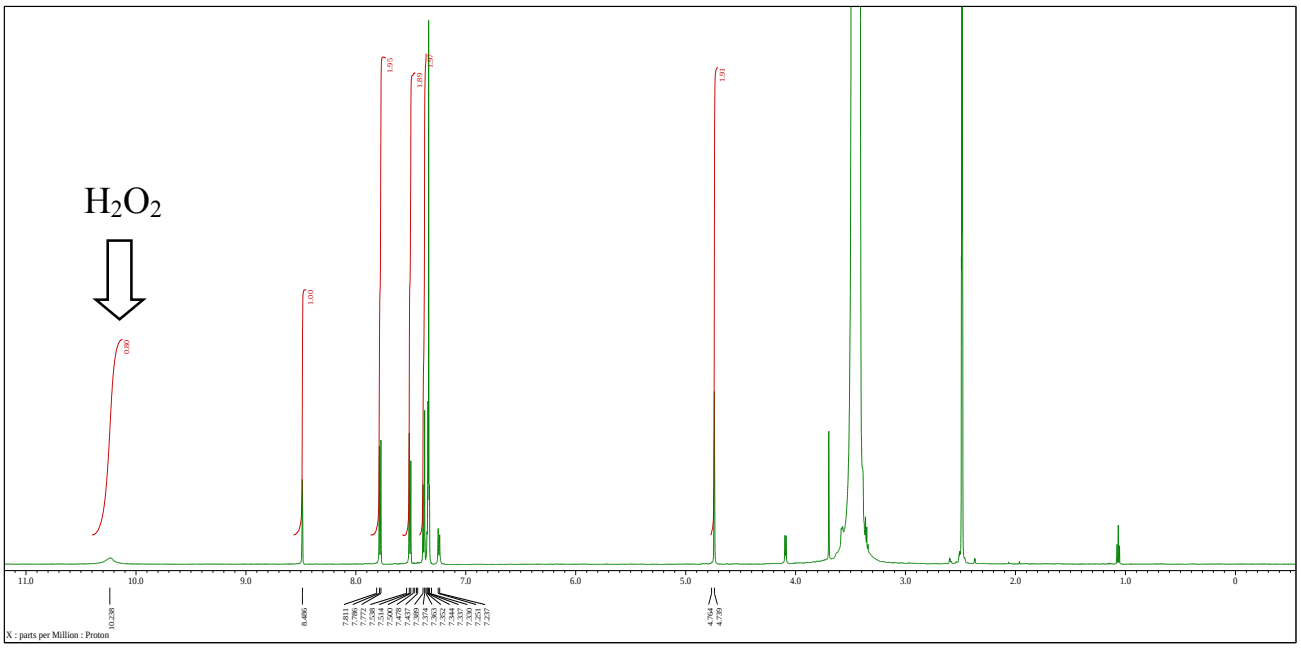


^{1}H-NMR Spectrum of deuterium labeling experiment

(c) Detection of *in-situ* generated H_2O_2 by ^{1}H NMR



A solution of compound **1a** (1.0 equiv, 0.4 mmol, 56.6 mg), catalyst ***o*-Q3** (1 mol %, 0.004 mmol, 2 mg) in water (0.5 mL) was stirred at 23 °C for 14 h. A small portion of crude mixture was taken out for ^{1}H NMR, thereby detecting the in-situ generation of hydrogen peroxide.



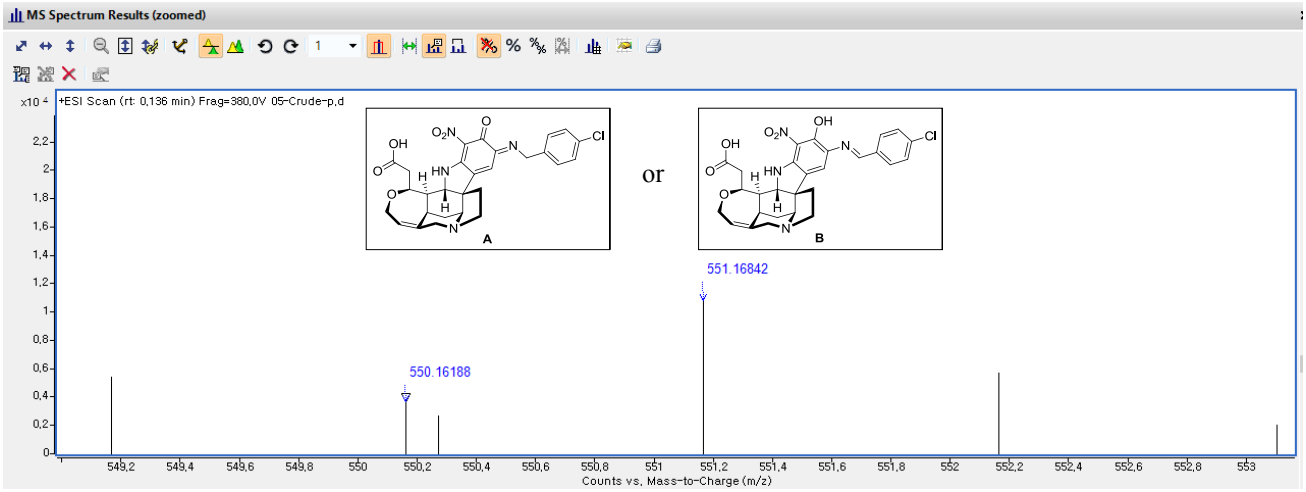
^{1}H-NMR Spectrum of crude mixture

(d) Mechanism Studies by LCMS-ESI Analysis

LCMS-ESI Analysis

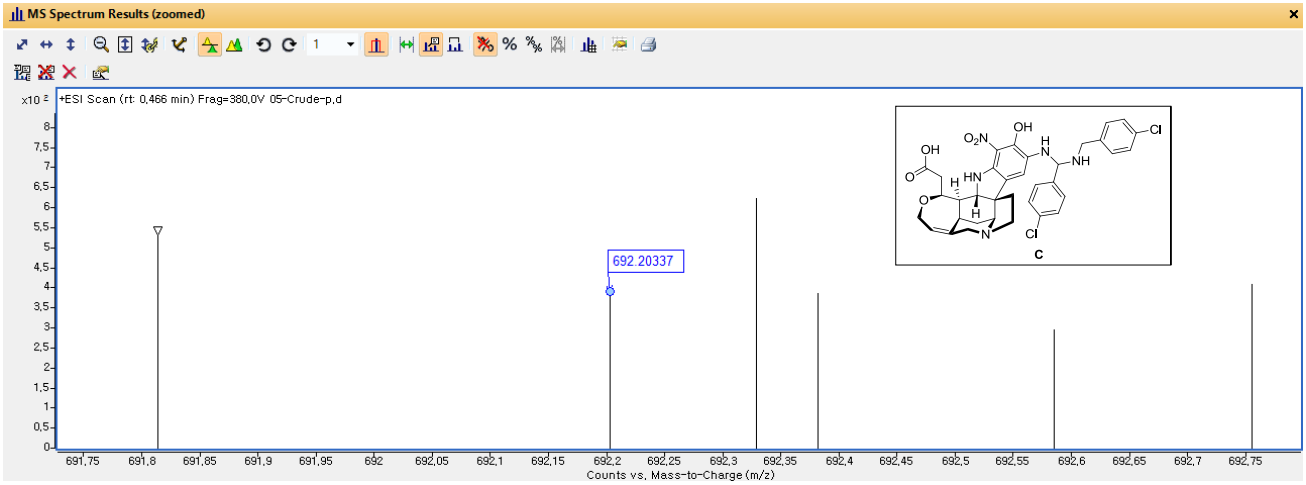
LCMS-ESI analyses were carried out by using Agilent 6550 QTOF mass spectrometer and m/z ratios are reported as values in atomic mass unites. Experiment was carried out in both positive mode and negative mode. ESI-MS condition: flow rate: 0.3 mL/min, solvent: H_2O/CH_3CN (50:50, v/v) in 0.1% formic acid

Positive mode:



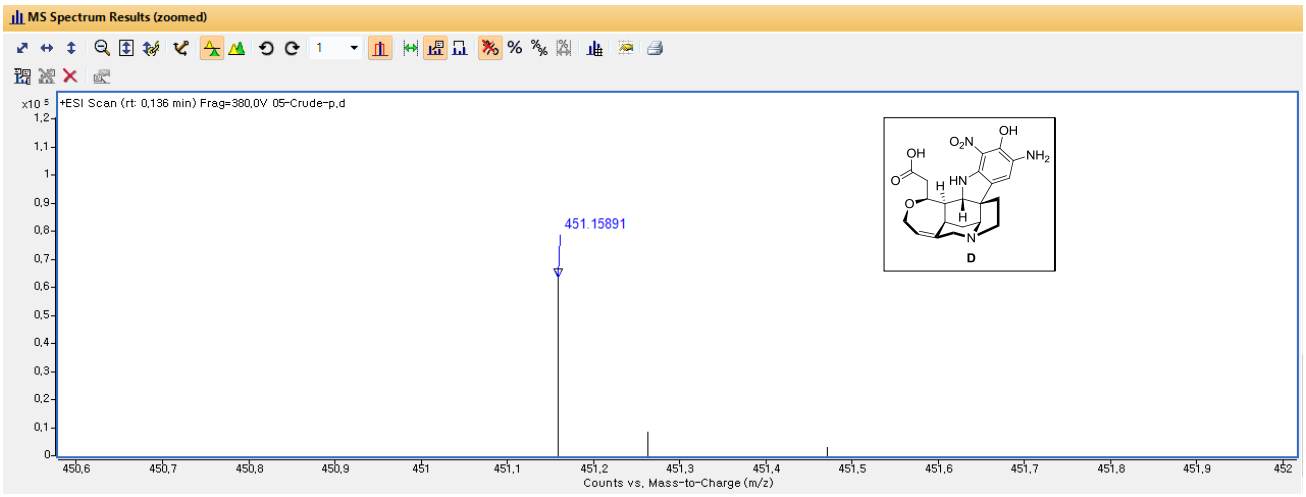
Intermediate	Expected Formula	Theoretical m/z	Observed m/z	Difference (ppm)
A or **B**	$C_{28}H_{27}ClN_4O_6$ $[M]^+$	550.1613	550.1618	0.9451
	$C_{28}H_{28}ClN_4O_6$ $[M+H]^+$	551.1691	551.1684	1.3788

Positive mode:



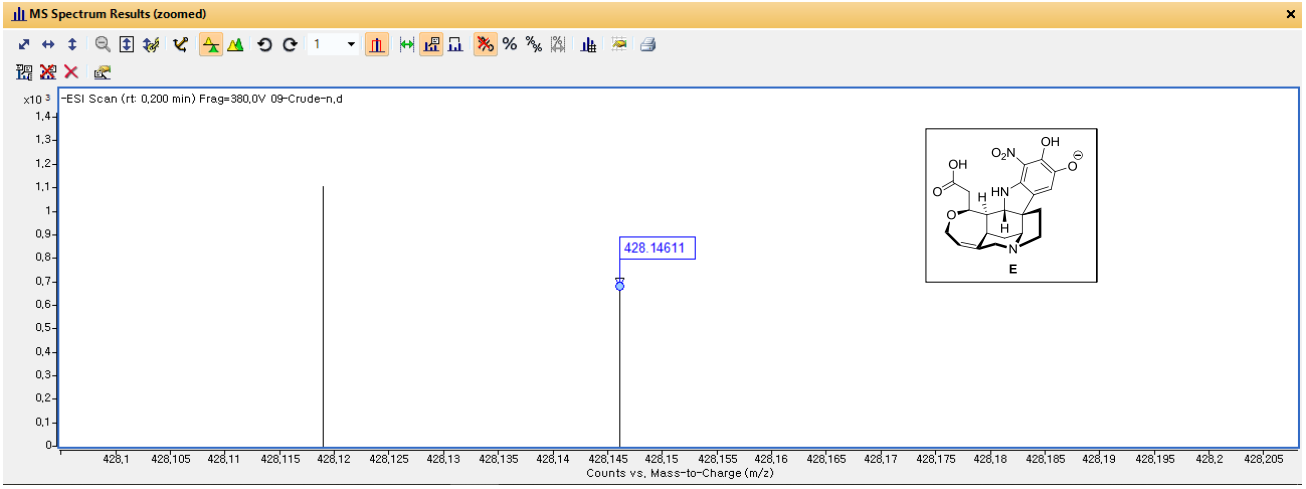
Intermediate	Expected Formula	Theoretical m/z	Observed m/z	Difference (ppm)
C	$C_{35}H_{36}Cl_2N_5O_6$ $[M+H]^+$	692.2037	692.2033	0.4911

Positive mode:



Intermediate	Expected Formula	Theoretical m/z	Observed m/z	Difference (ppm)
D	$C_{21}H_{24}N_4NaO_6$ $[M+Na]^+$	451.1588	451.1589	0.2438

Negative mode:



Intermediate	Expected Formula	Theoretical m/z	Observed m/z	Difference (ppm)
E	$C_{21}H_{22}N_3O_7^-$ $[M]^-$	428.1452	428.1461	2.1021

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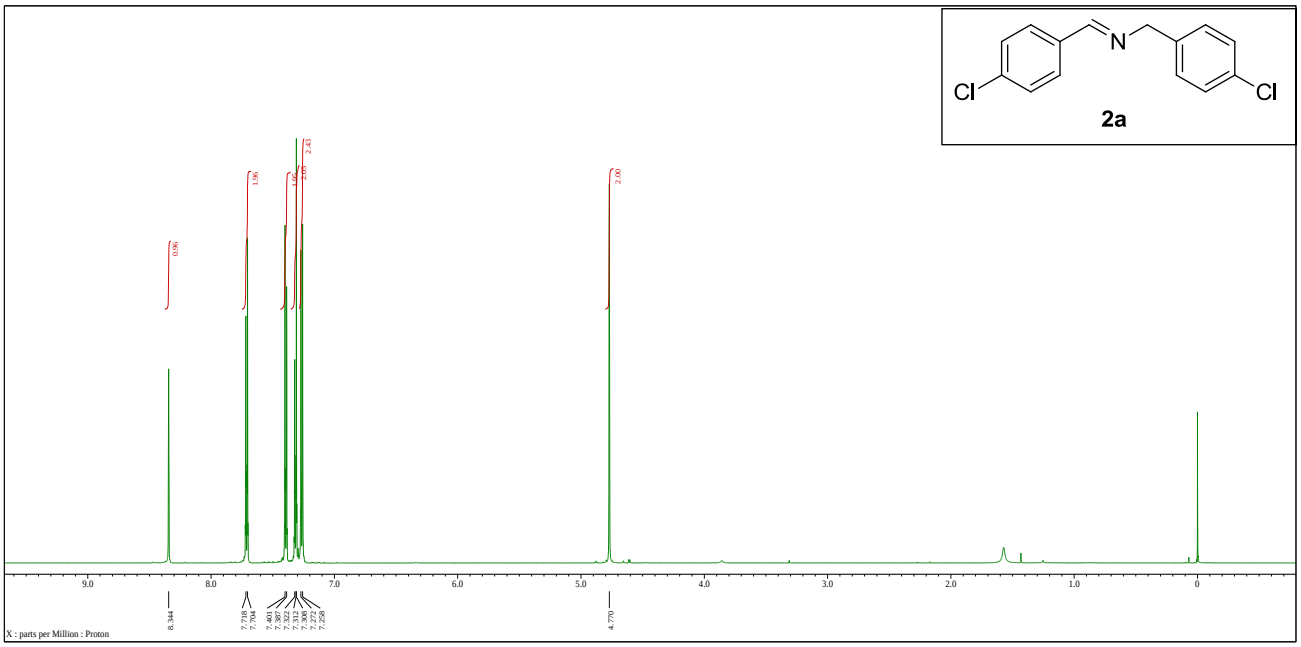
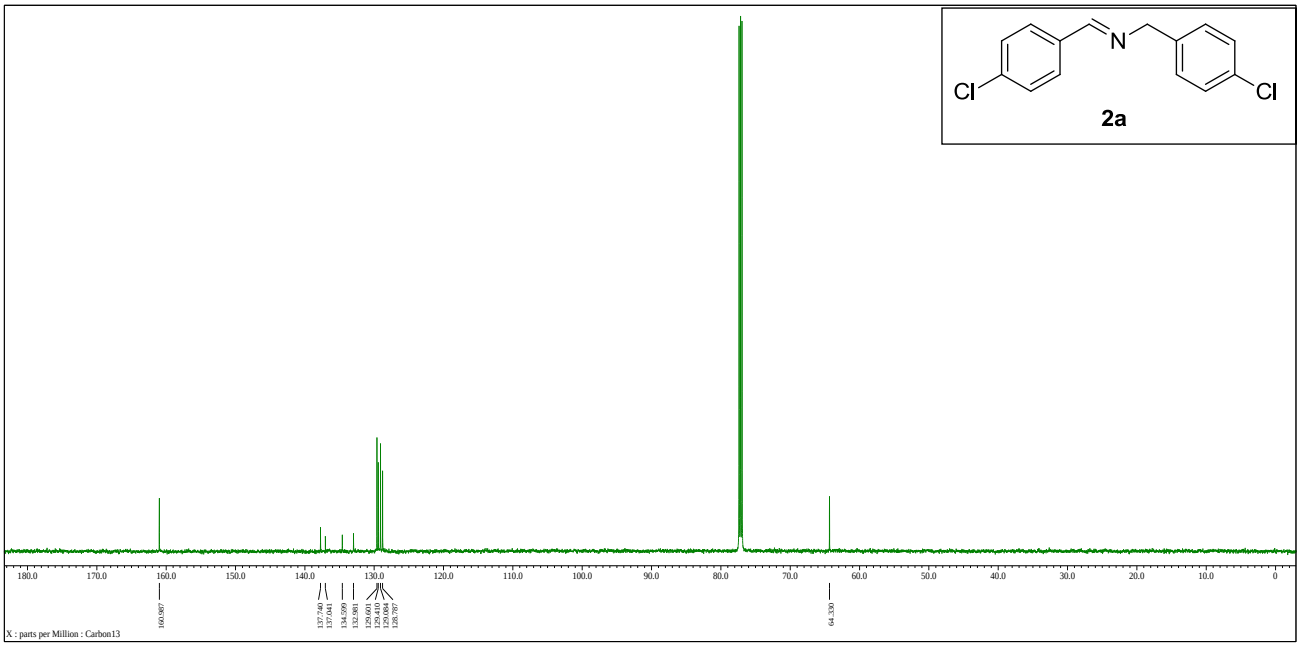
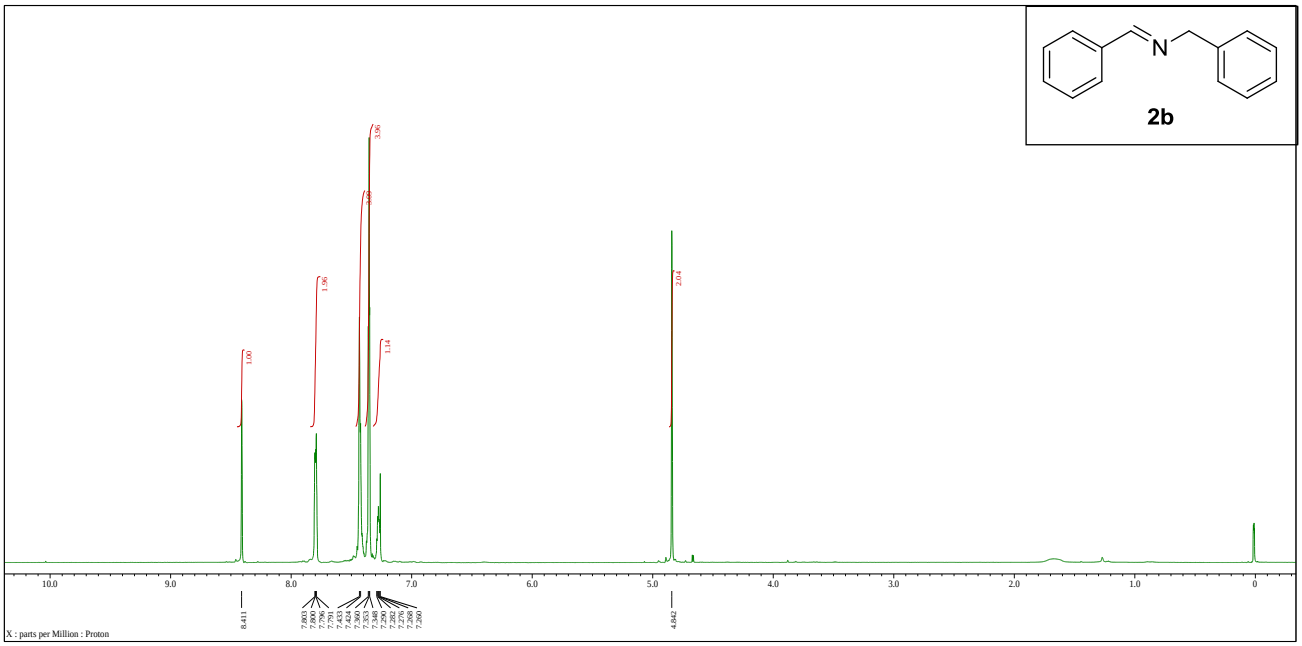
NMR Spectra



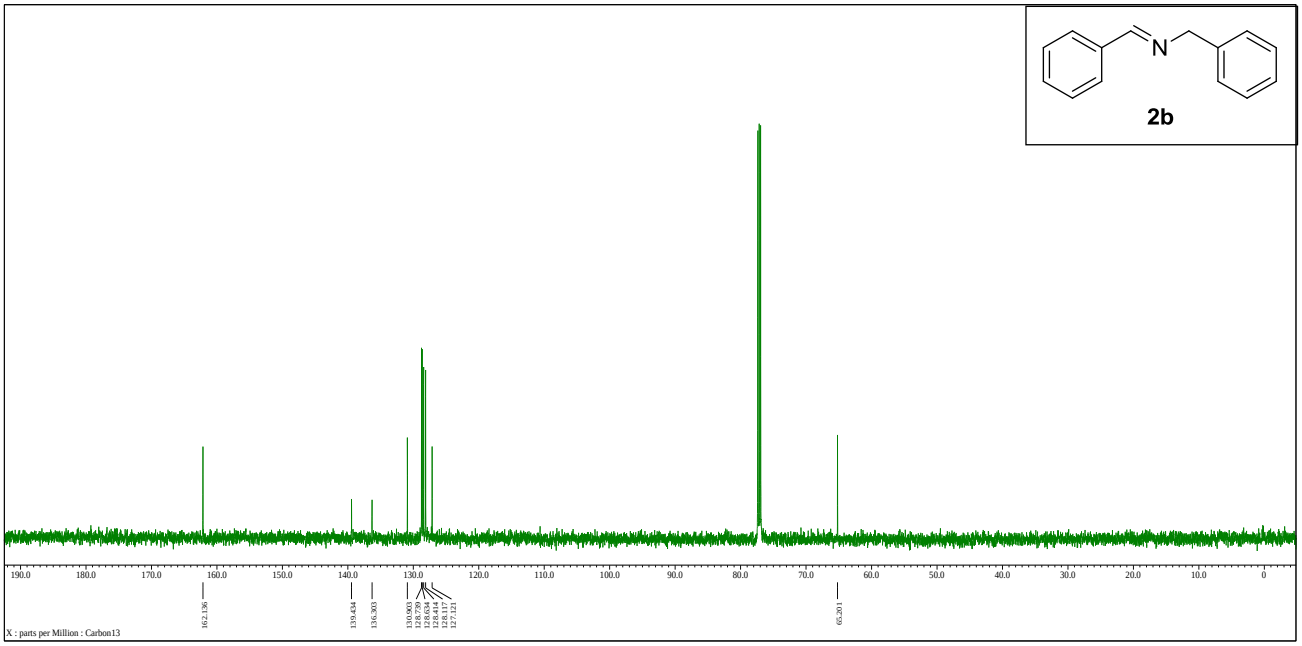
^{1}H-NMR Spectrum of compound **2a** (600 MHz, $CDCl_3$)



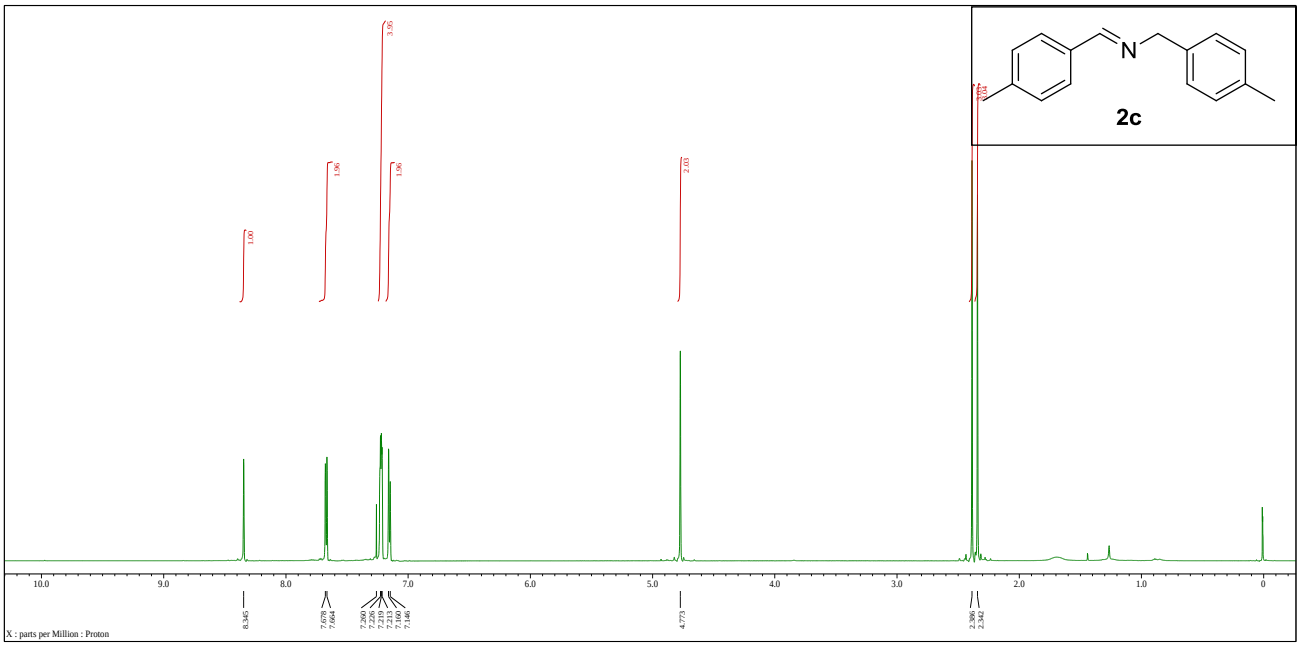
^{13}C-NMR Spectrum of compound **2a** (150 MHz, $CDCl_3$)



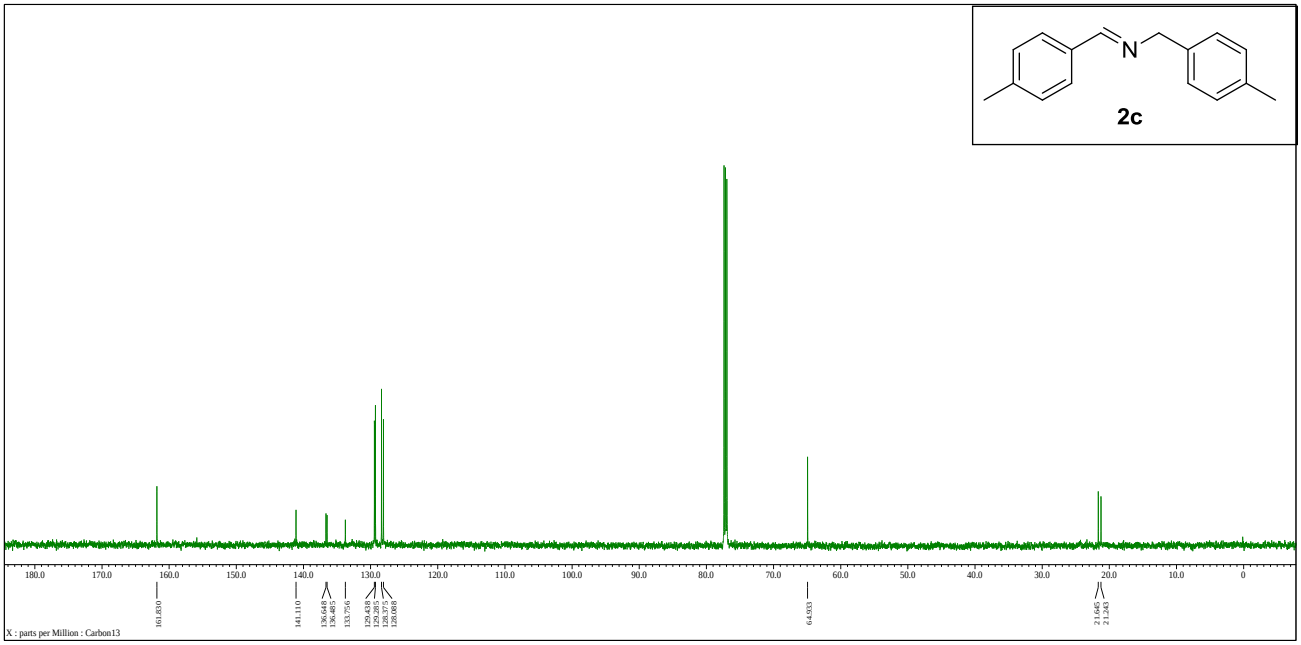
^{1}H-NMR Spectrum of compound **2b** (600 MHz, $CDCl_3$)



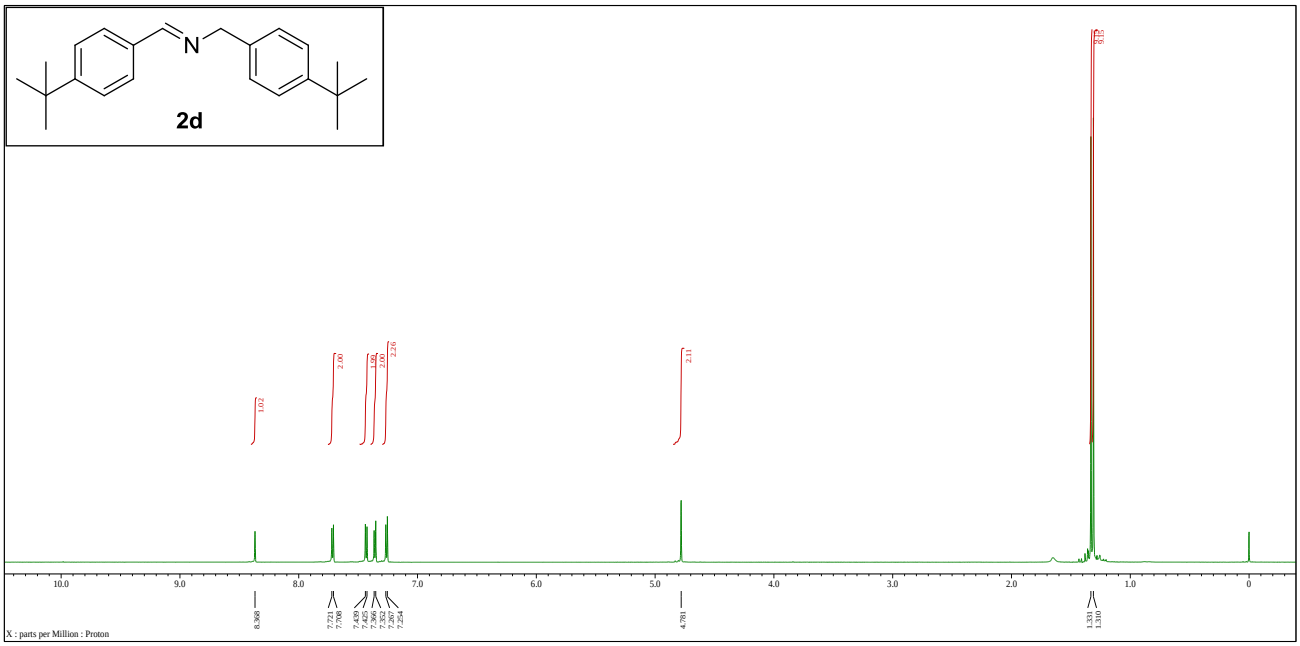
^{13}C-NMR Spectrum of compound **2b** (150 MHz, $CDCl_3$)



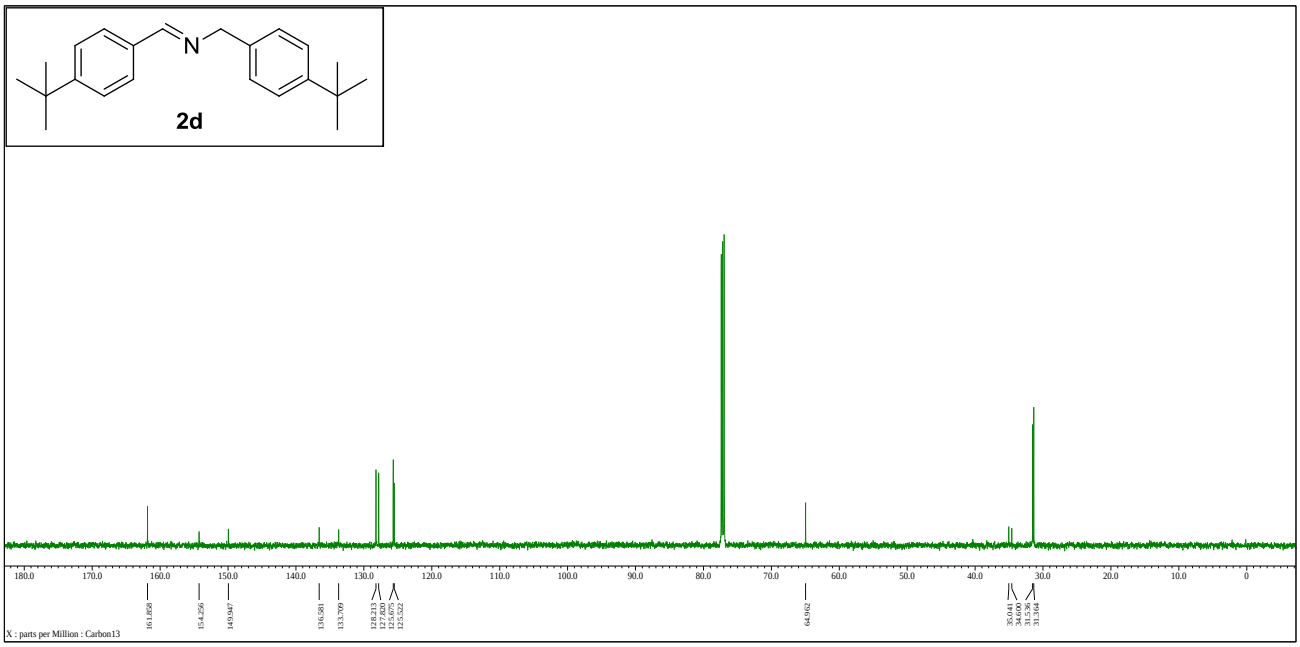
^{1}H-NMR Spectrum of compound **2c** (600 MHz, $CDCl_3$)



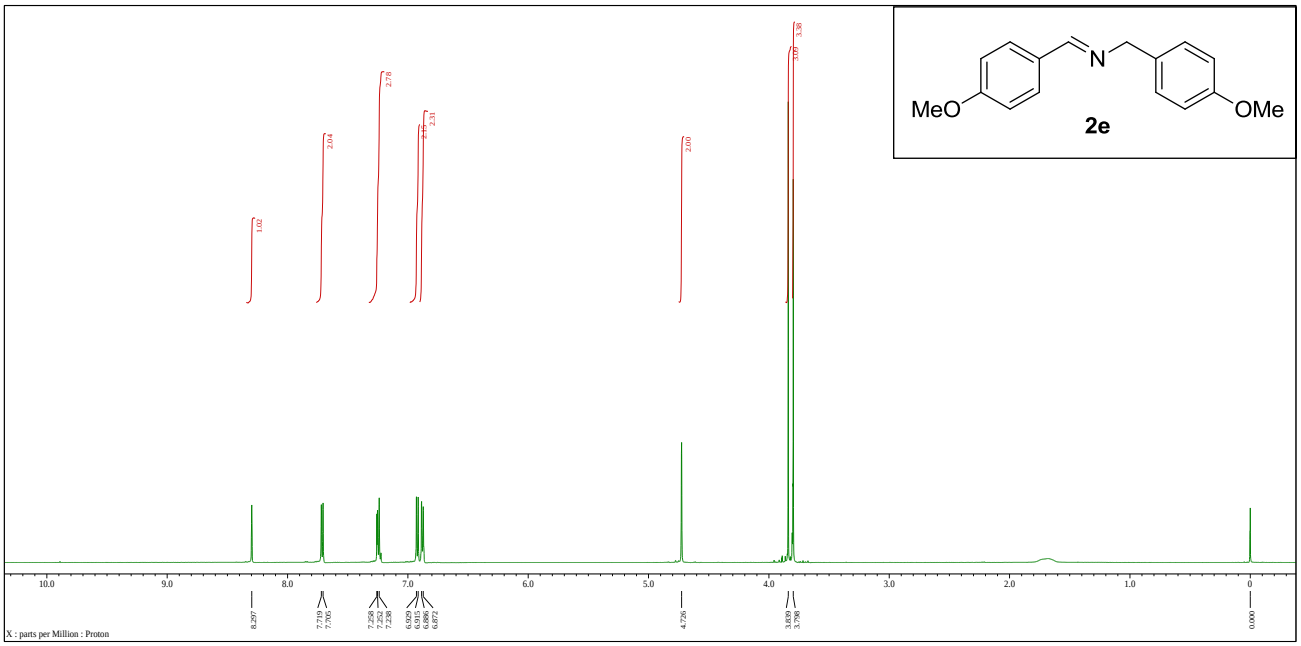
^{13}C-NMR Spectrum of compound **2c** (150 MHz, $CDCl_3$)



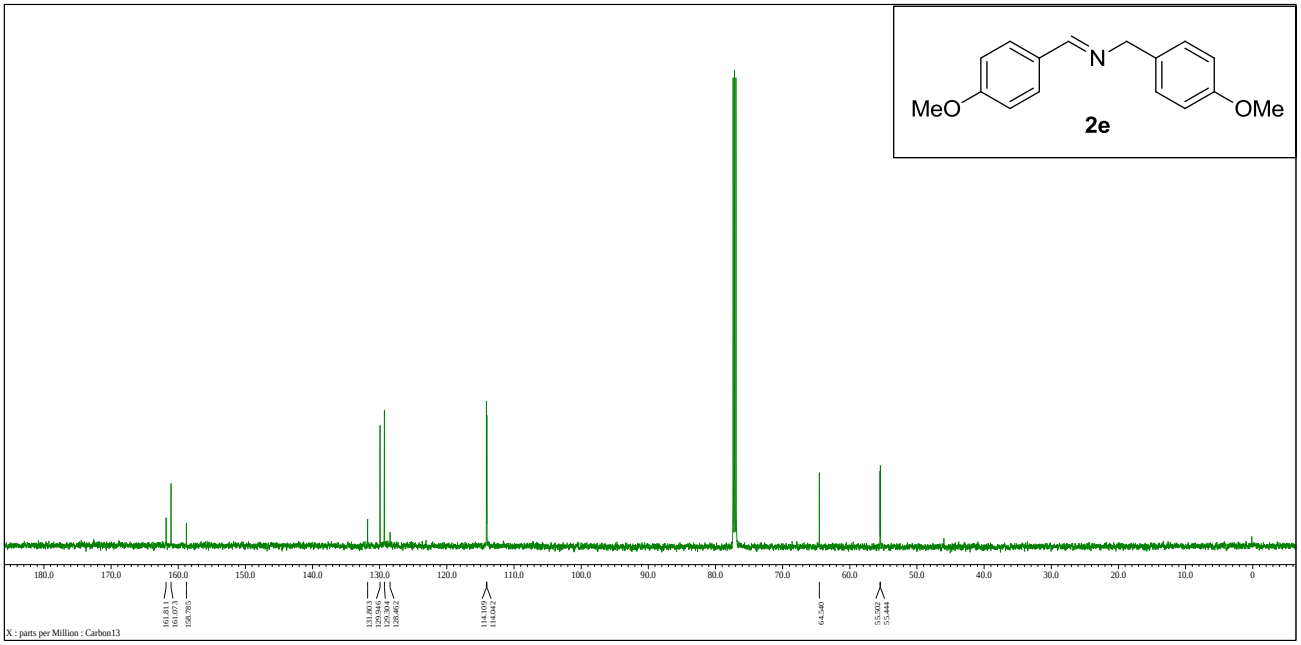
^{1}H-NMR Spectrum of compound **2d** (600 MHz, $CDCl_3$)



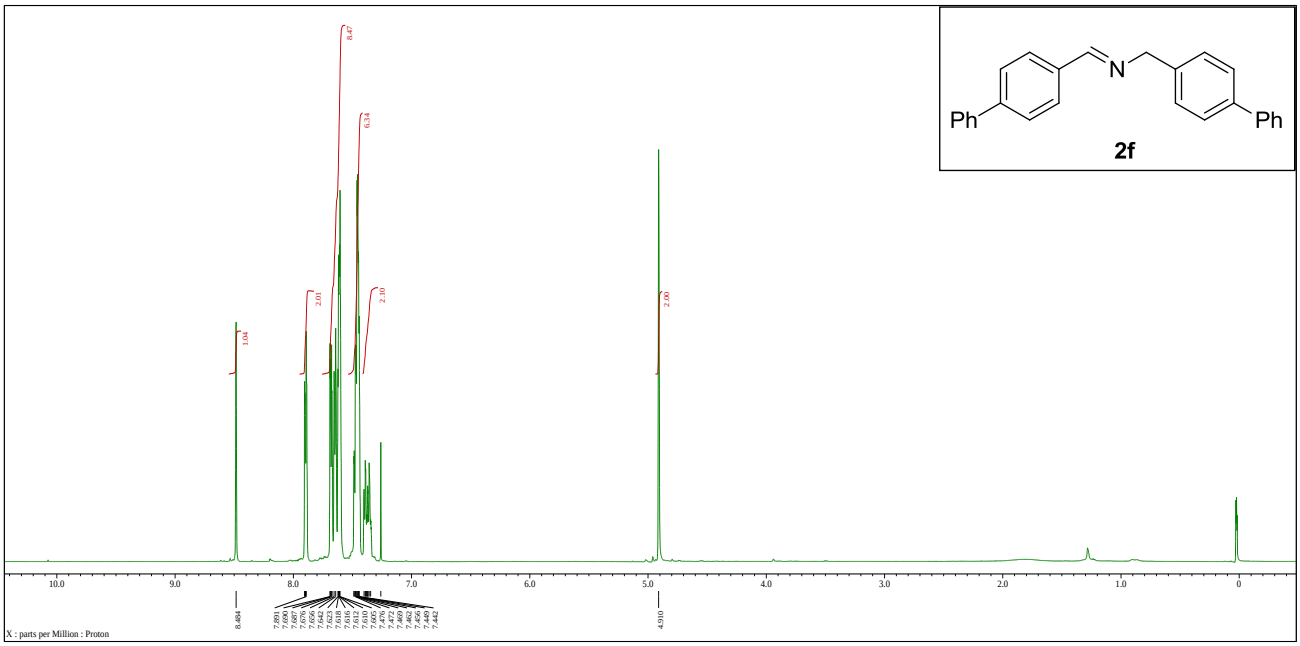
^{13}C-NMR Spectrum of compound **2d** (150 MHz, $CDCl_3$)



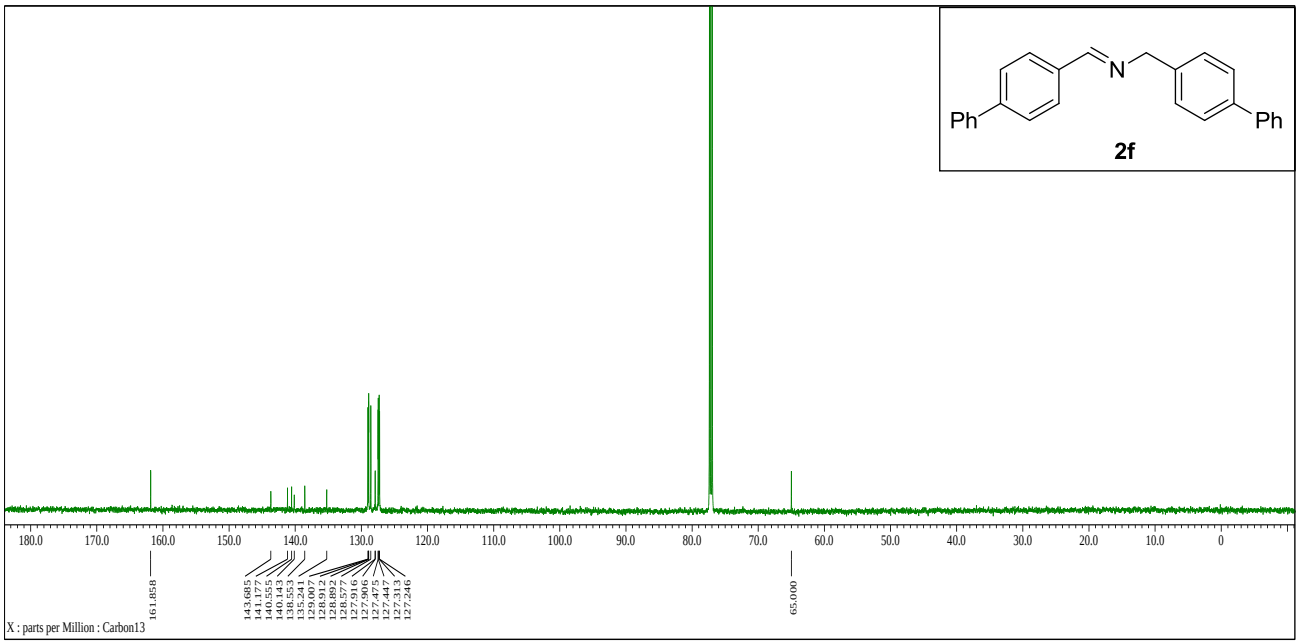
^{1}H-NMR Spectrum of compound **2e** (600 MHz, $CDCl_3$)



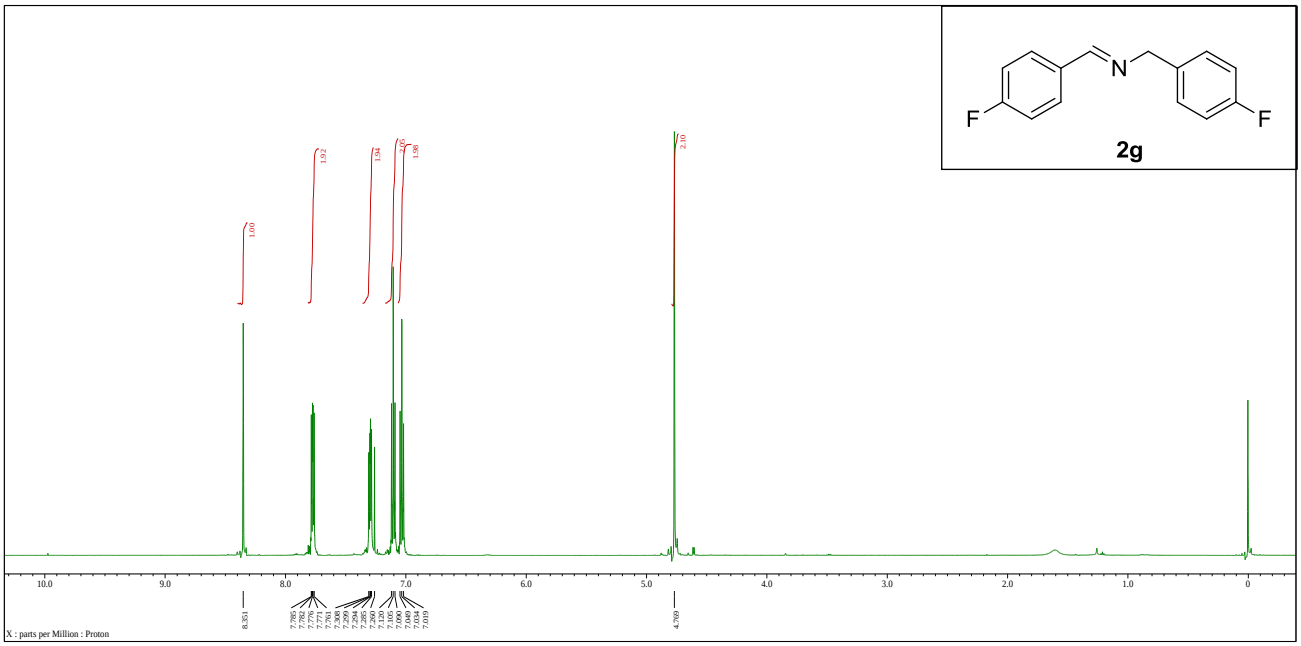
^{13}C-NMR Spectrum of compound **2e** (150 MHz, $CDCl_3$)



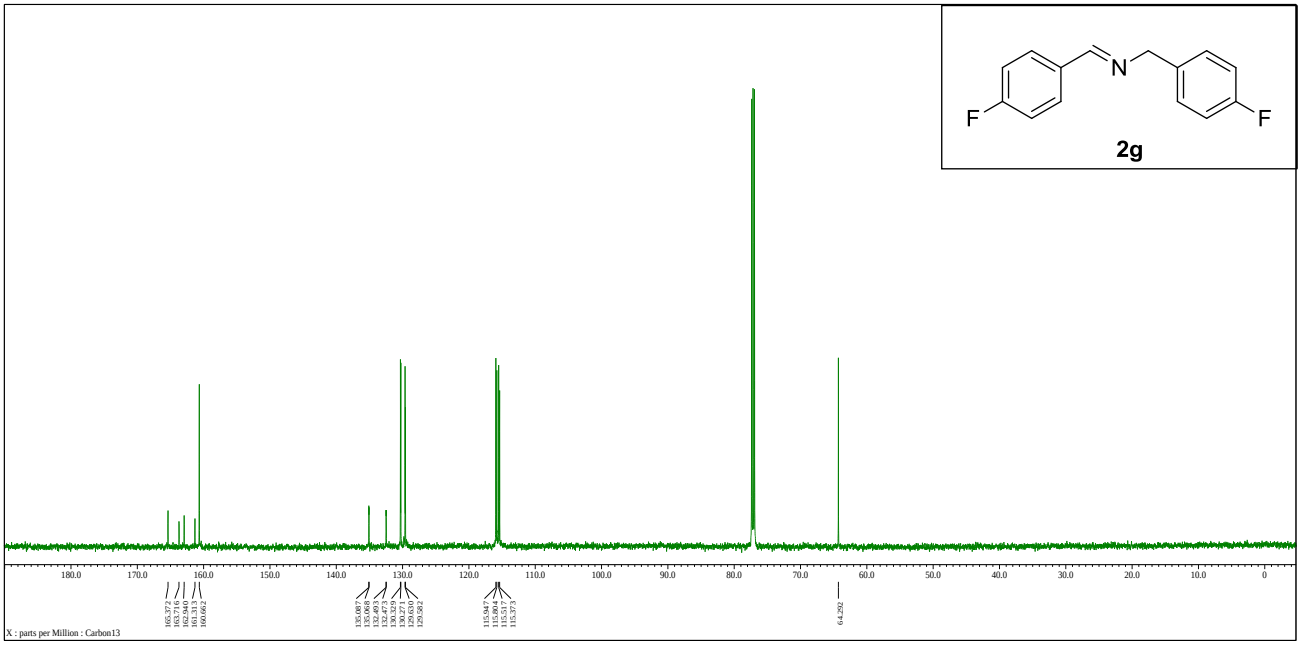
^{1}H-NMR Spectrum of compound **2f** (600 MHz, $CDCl_3$)



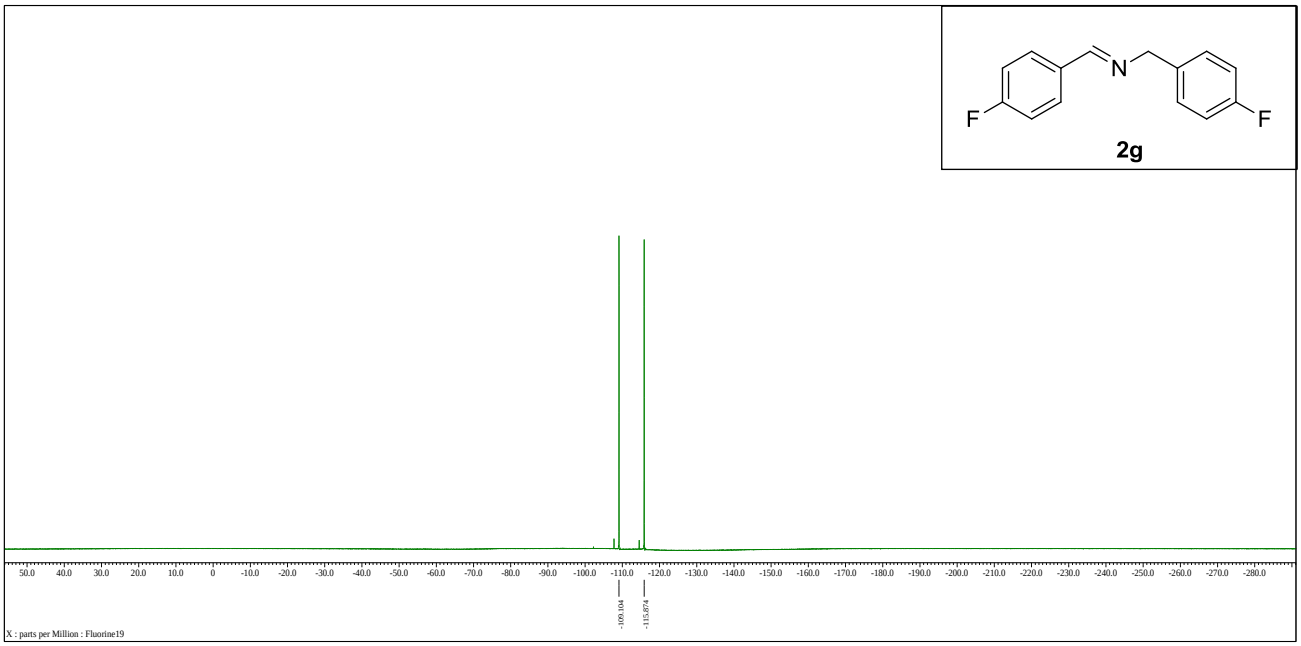
^{13}C-NMR Spectrum of compound **2f** (150 MHz, $CDCl_3$)



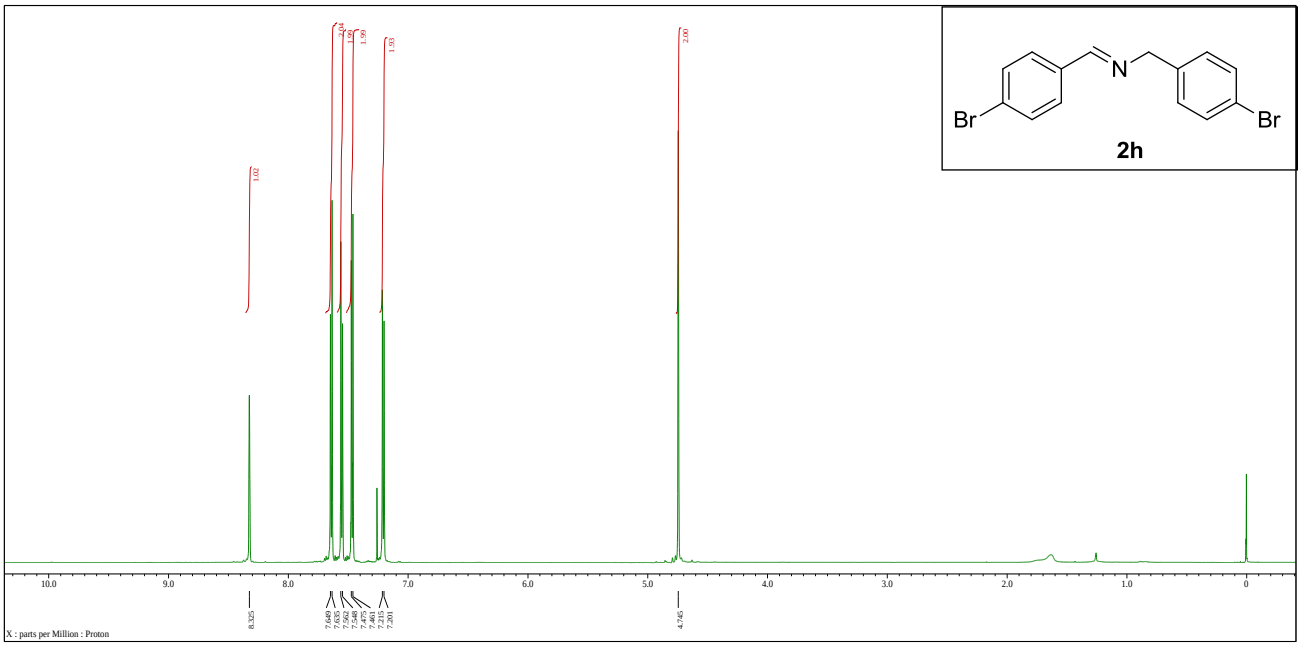
^{1}H-NMR Spectrum of compound **2g** (600 MHz, $CDCl_3$)



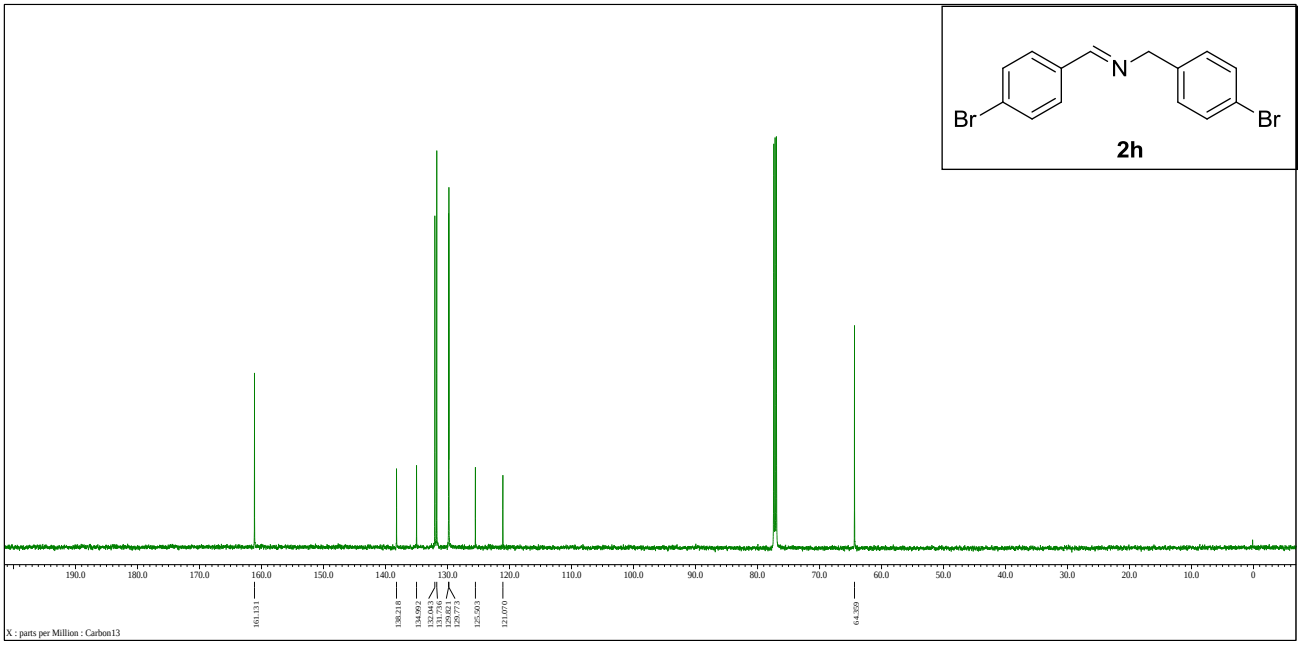
^{13}C-NMR Spectrum of compound **2g** (150 MHz, $CDCl_3$)



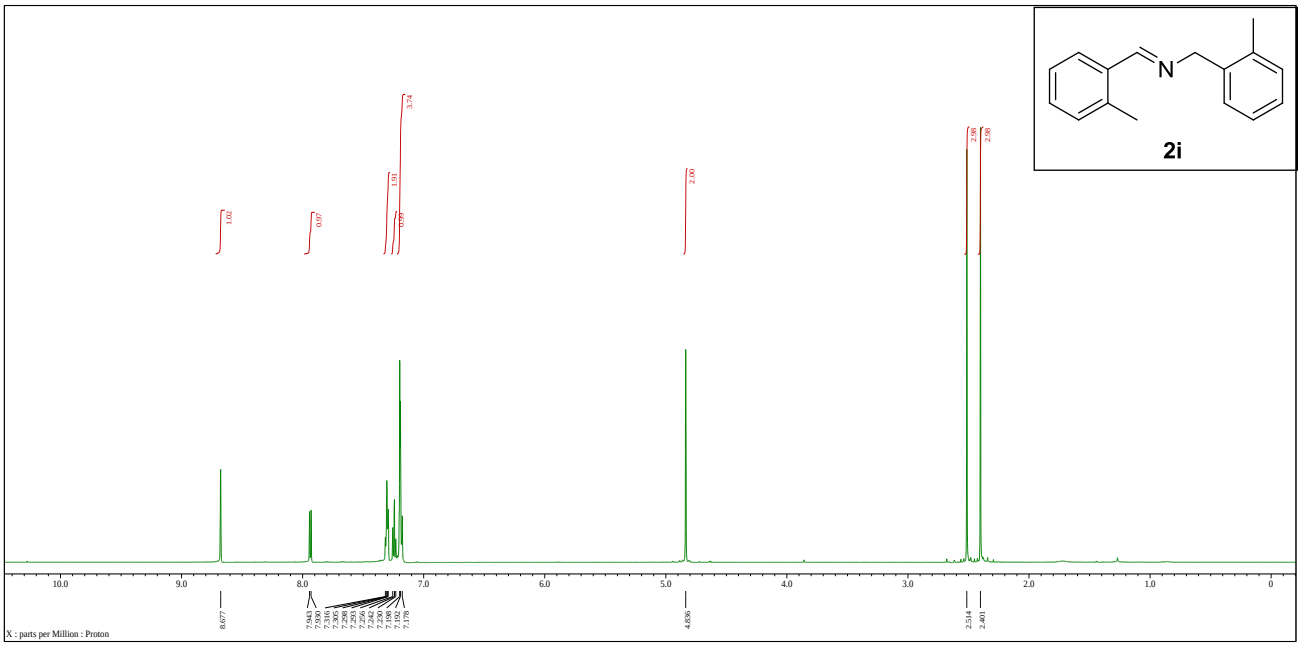
^{19}F-NMR Spectrum of compound **2g** (564 MHz, $CDCl_3$)



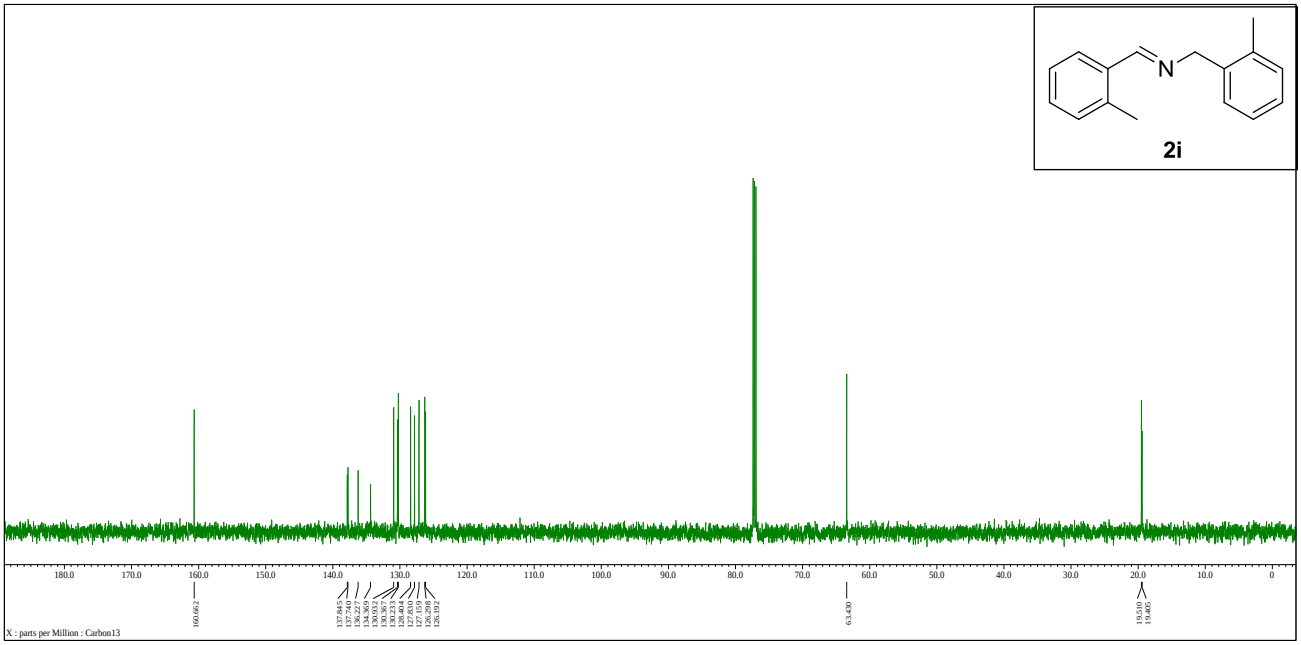
^{1}H-NMR Spectrum of compound **2h** (600 MHz, $CDCl_3$)



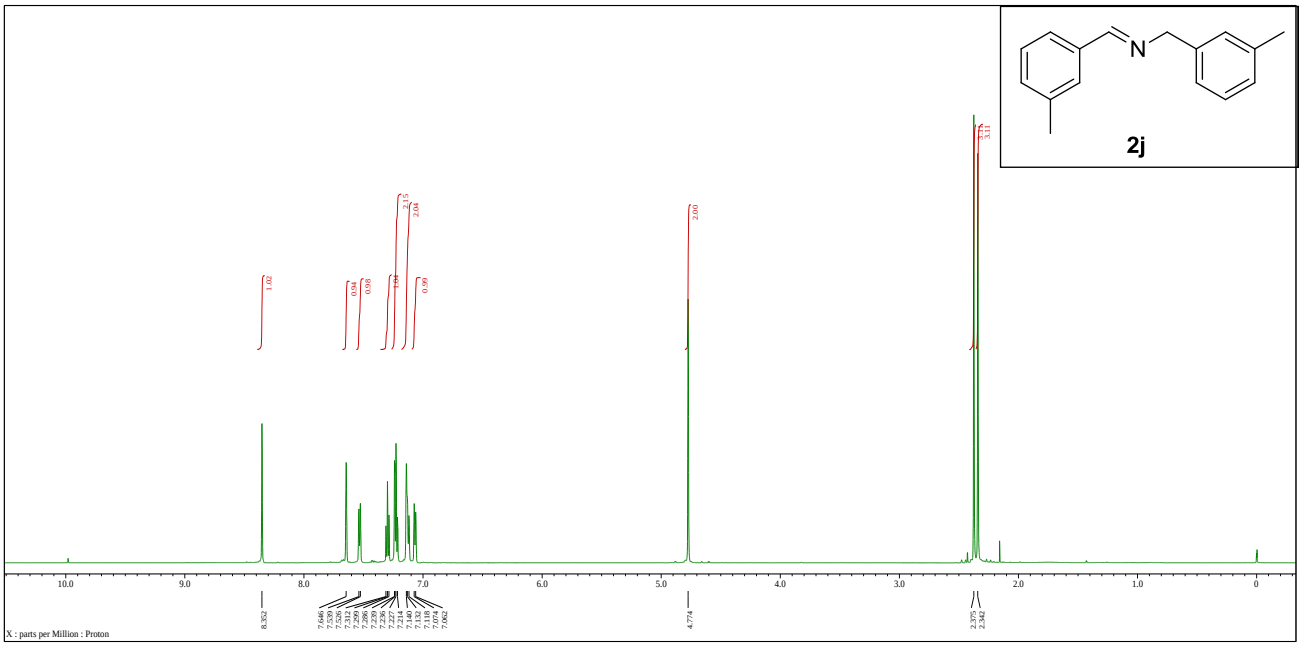
^{13}C-NMR Spectrum of compound **2h** (150 MHz, $CDCl_3$)



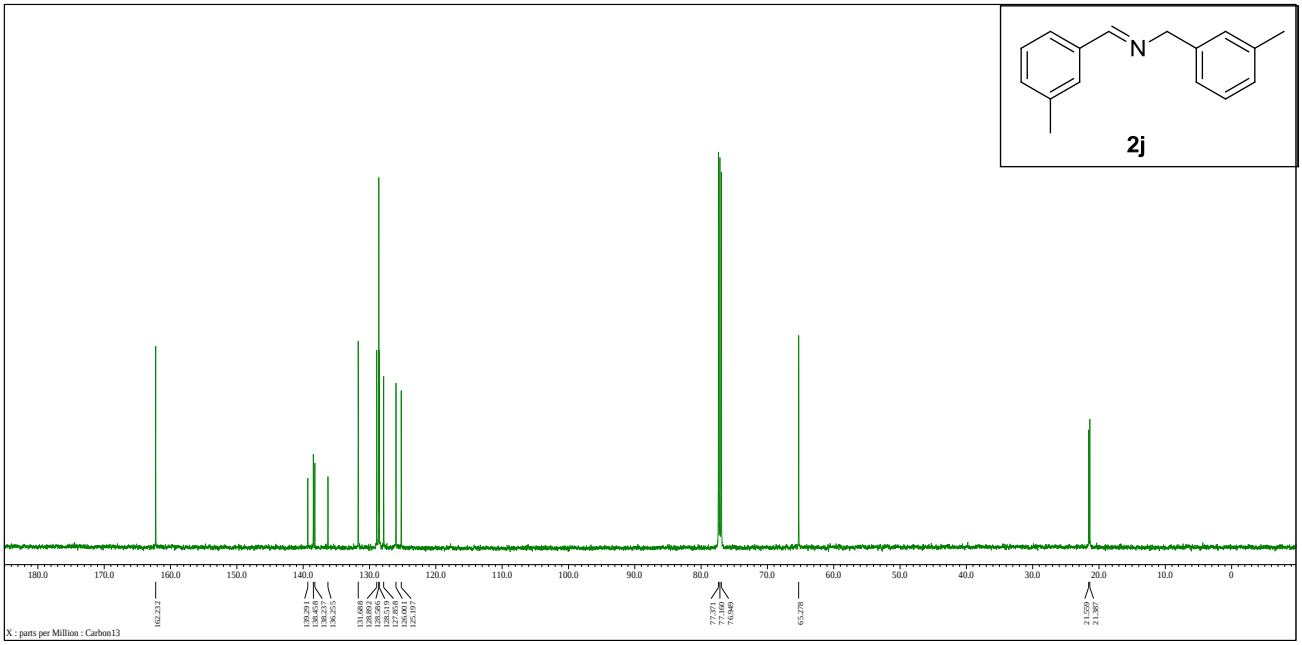
^{1}H-NMR Spectrum of compound **2i** (600 MHz, $CDCl_3$)



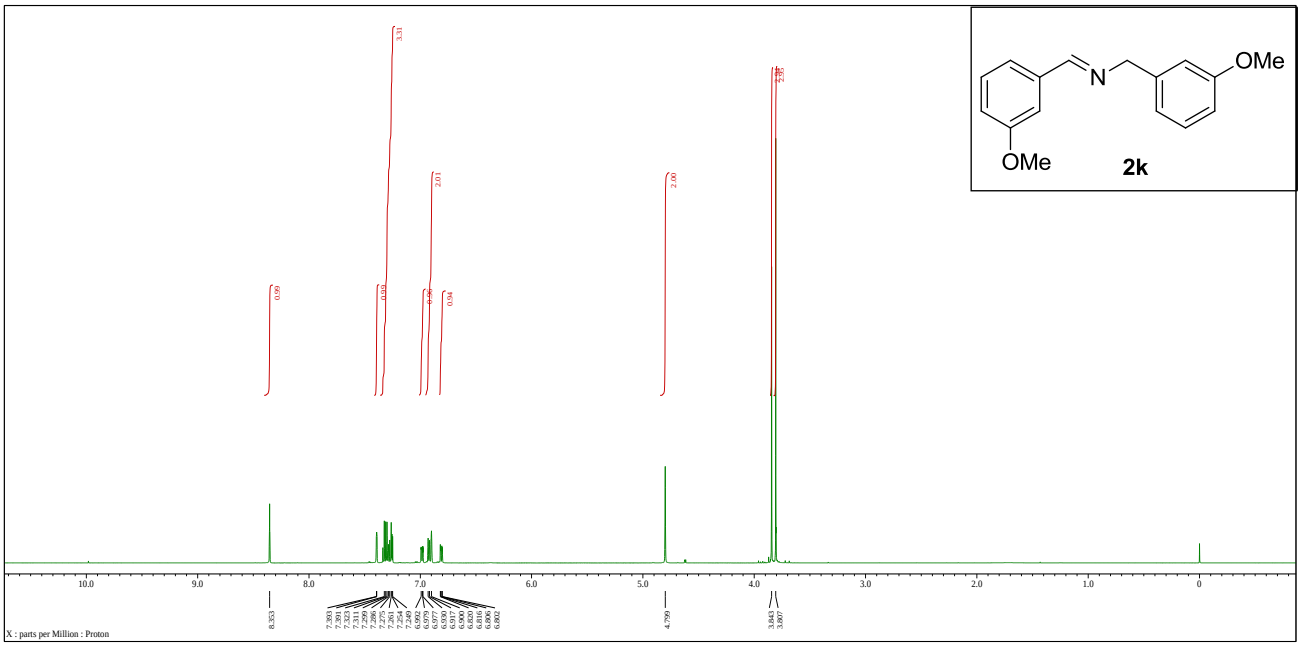
^{13}C-NMR Spectrum of compound **2i** (150 MHz, $CDCl_3$)



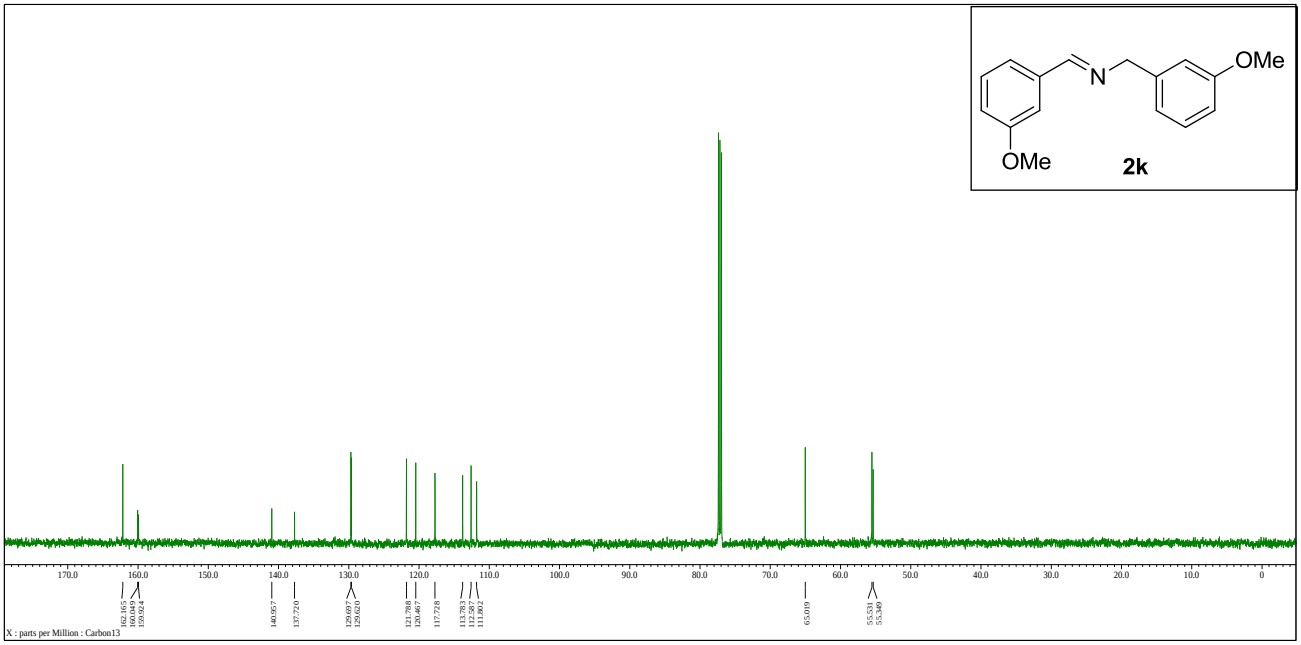
^{1}H-NMR Spectrum of compound **2j** (600 MHz, $CDCl_3$)



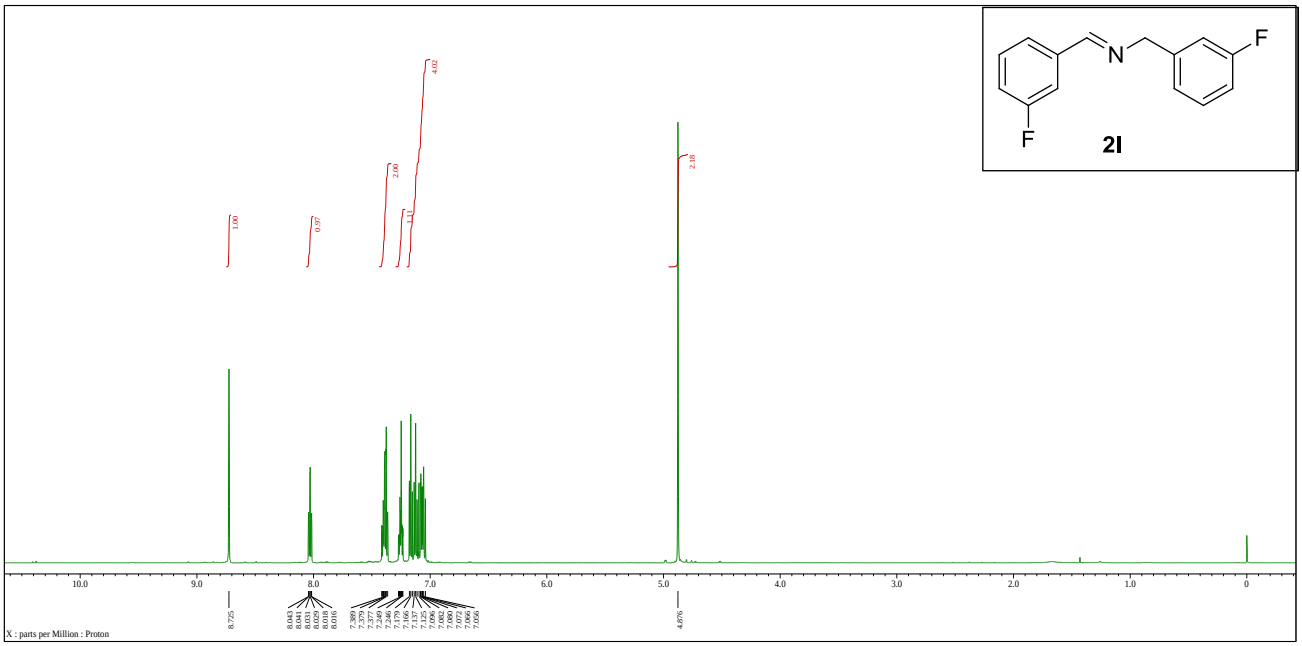
^{13}C-NMR Spectrum of compound **2j** (150 MHz, $CDCl_3$)



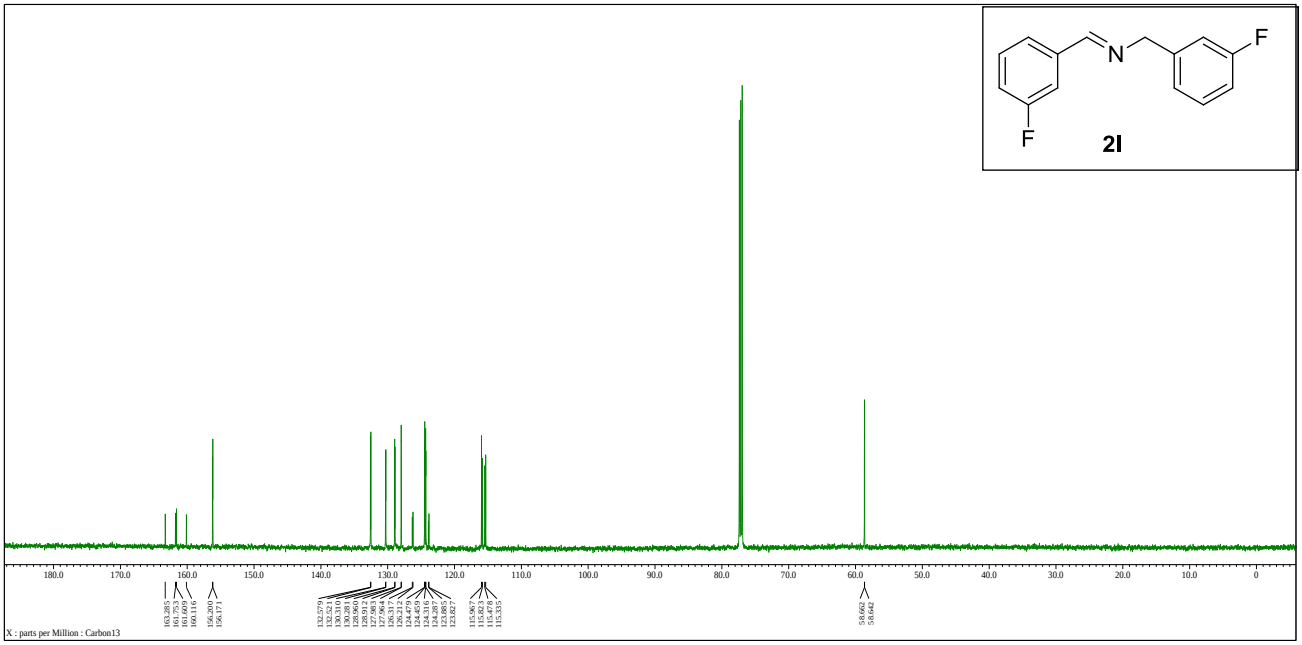
^{1}H-NMR Spectrum of compound **2k** (600 MHz, $CDCl_3$)



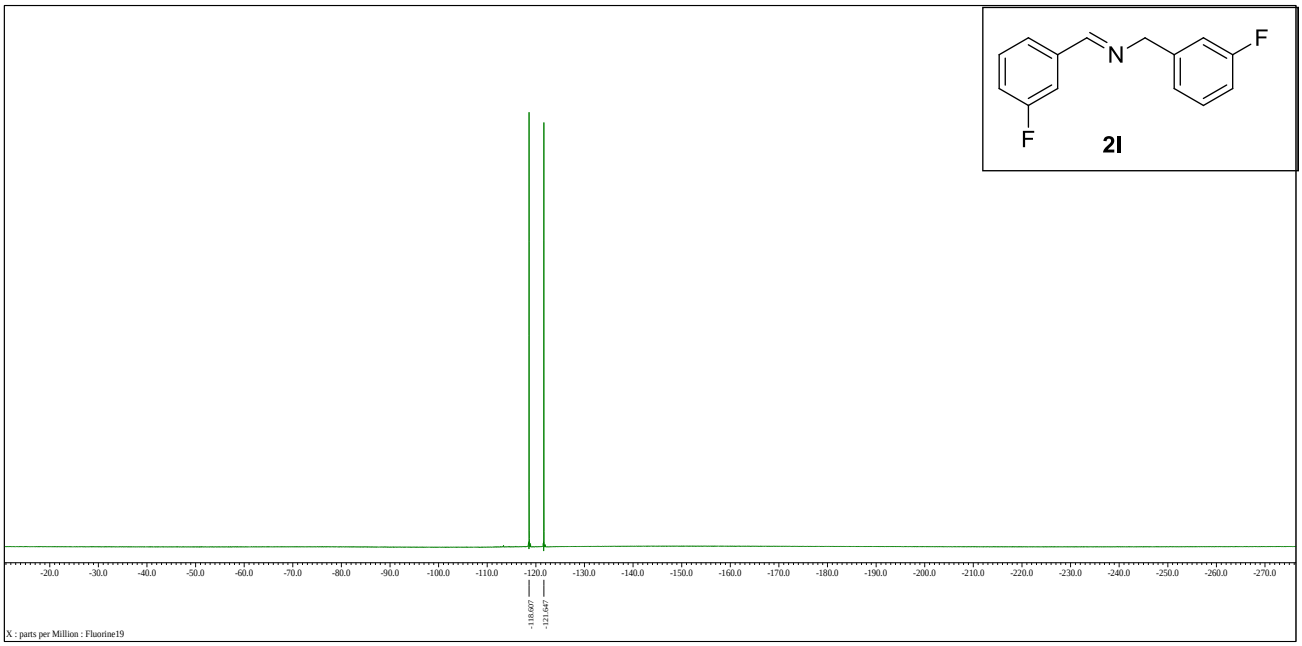
^{13}C-NMR Spectrum of compound **2k** (150 MHz, $CDCl_3$)



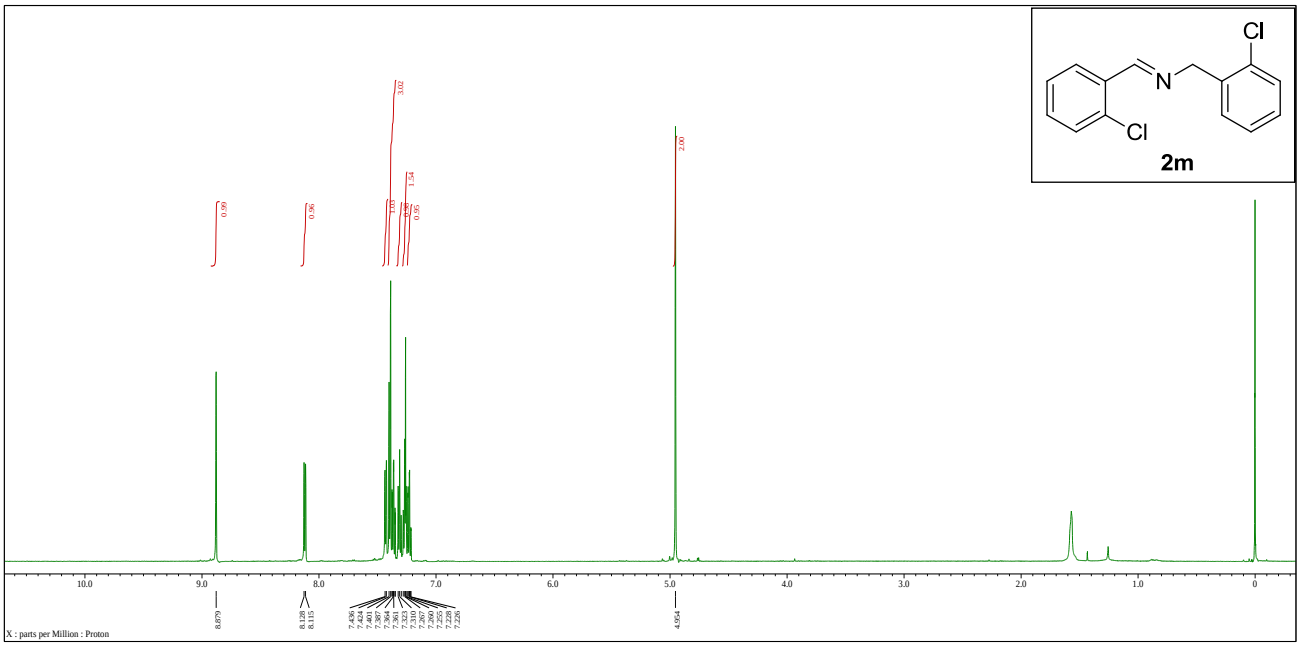
^{1}H-NMR Spectrum of compound **2l** (600 MHz, $CDCl_3$)



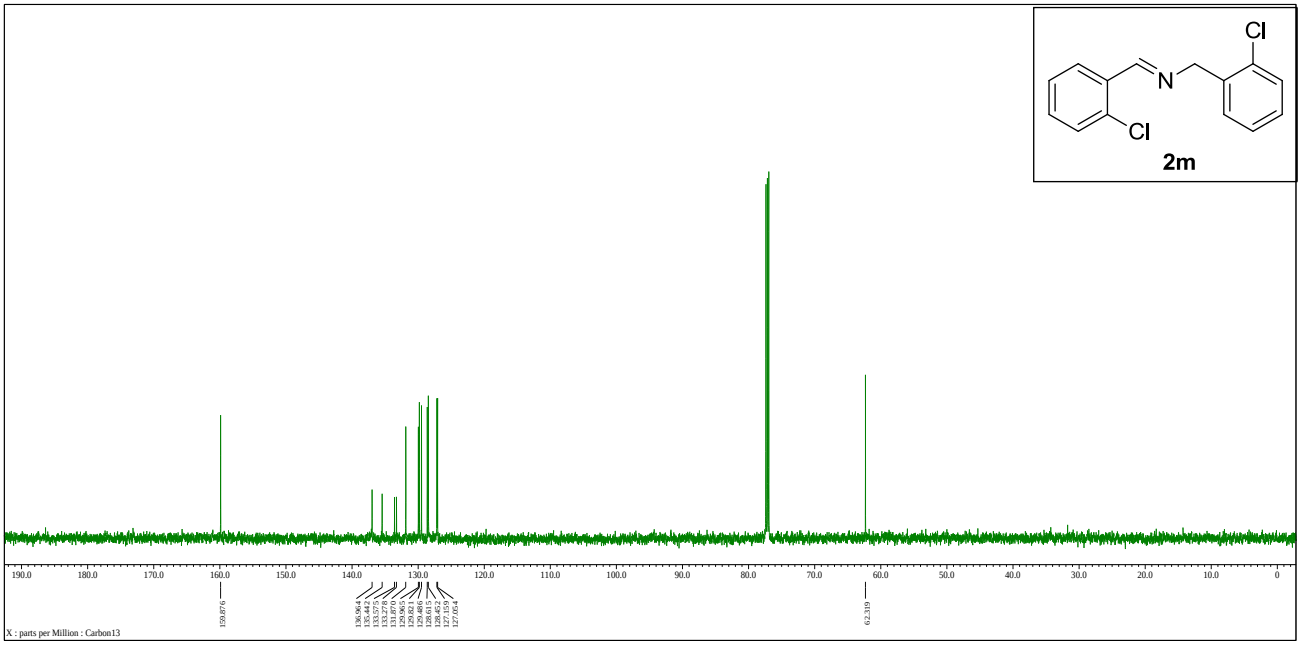
^{13}C-NMR Spectrum of compound **2l** (150 MHz, $CDCl_3$)



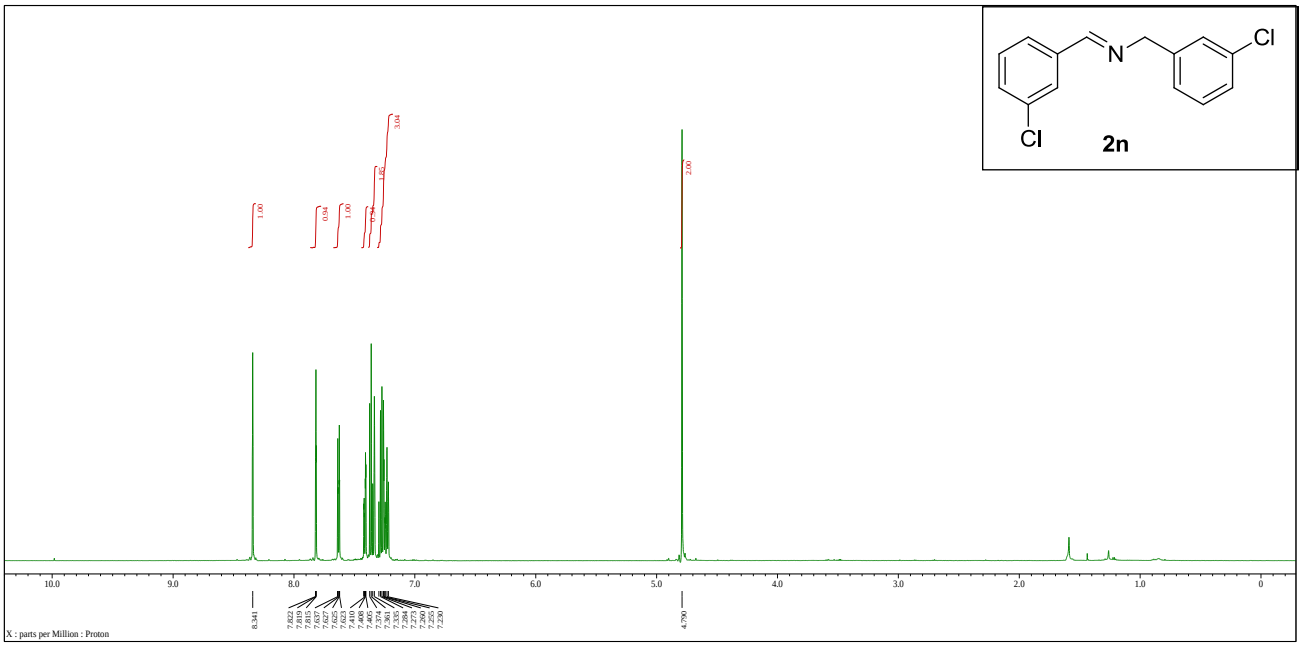
^{19}F-NMR Spectrum of compound **2l** (564 MHz, $CDCl_3$)



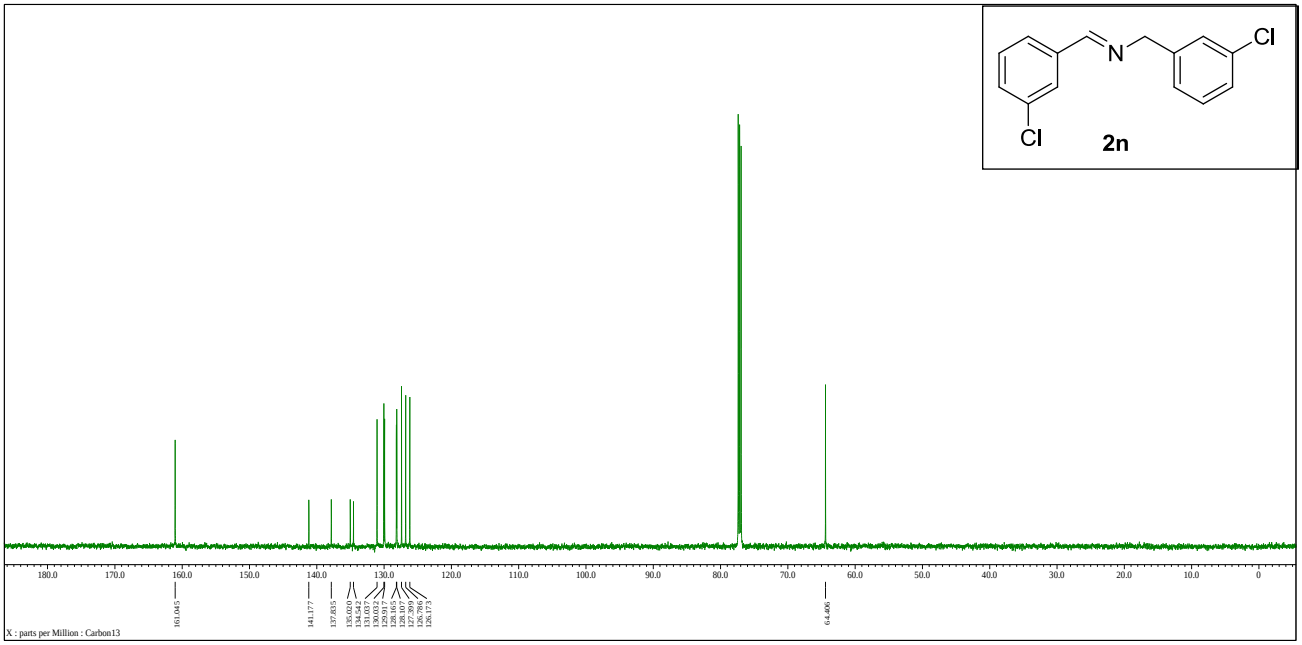
^{1}H-NMR Spectrum of compound **2m** (600 MHz, $CDCl_3$)



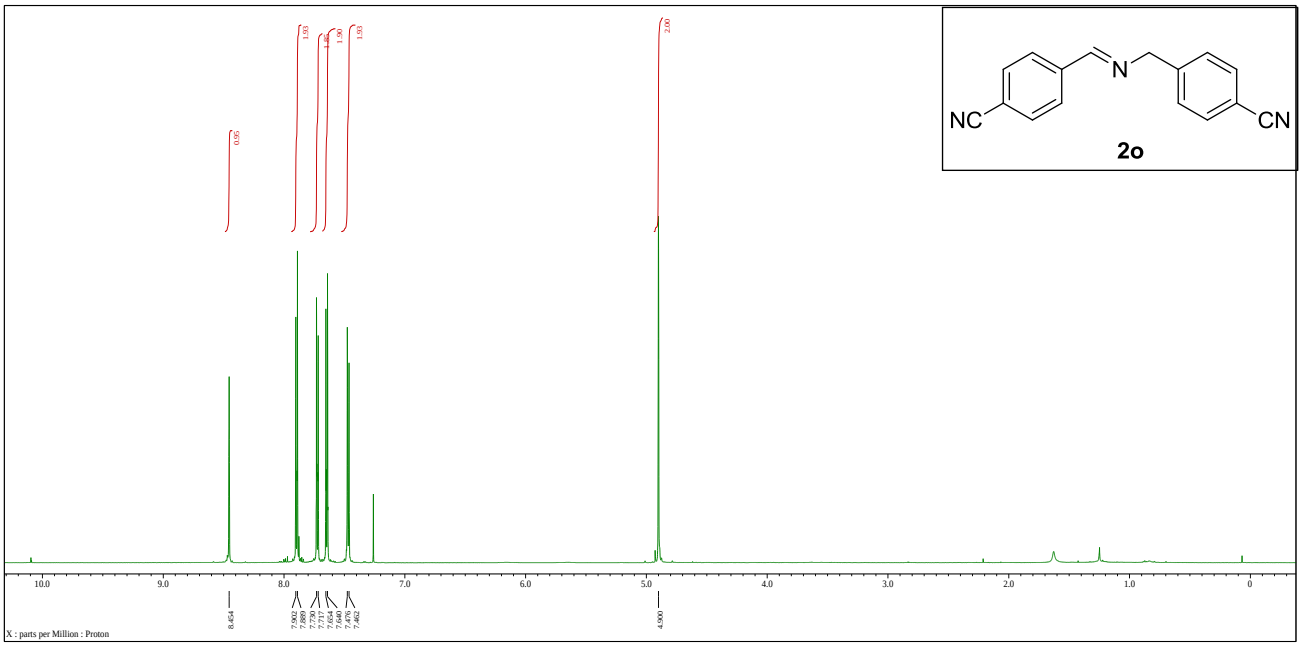
^{13}C-NMR Spectrum of compound **2m** (150 MHz, $CDCl_3$)



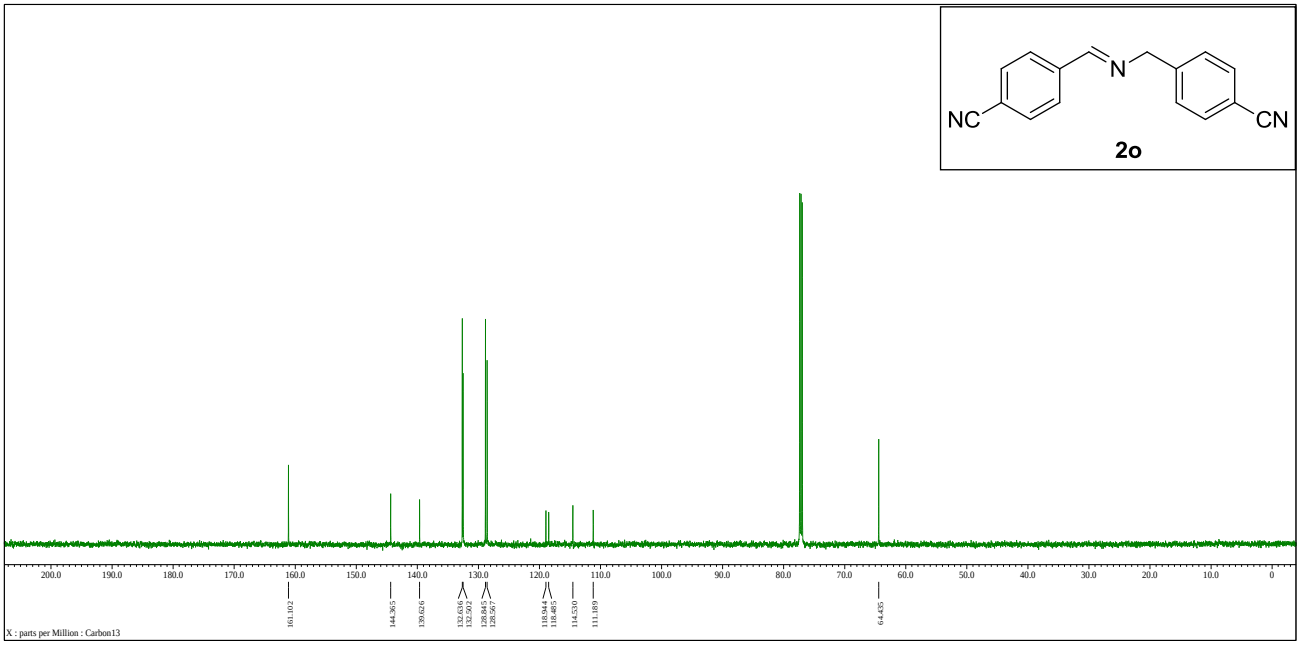
^{1}H-NMR Spectrum of compound **2n** (600 MHz, $CDCl_3$)



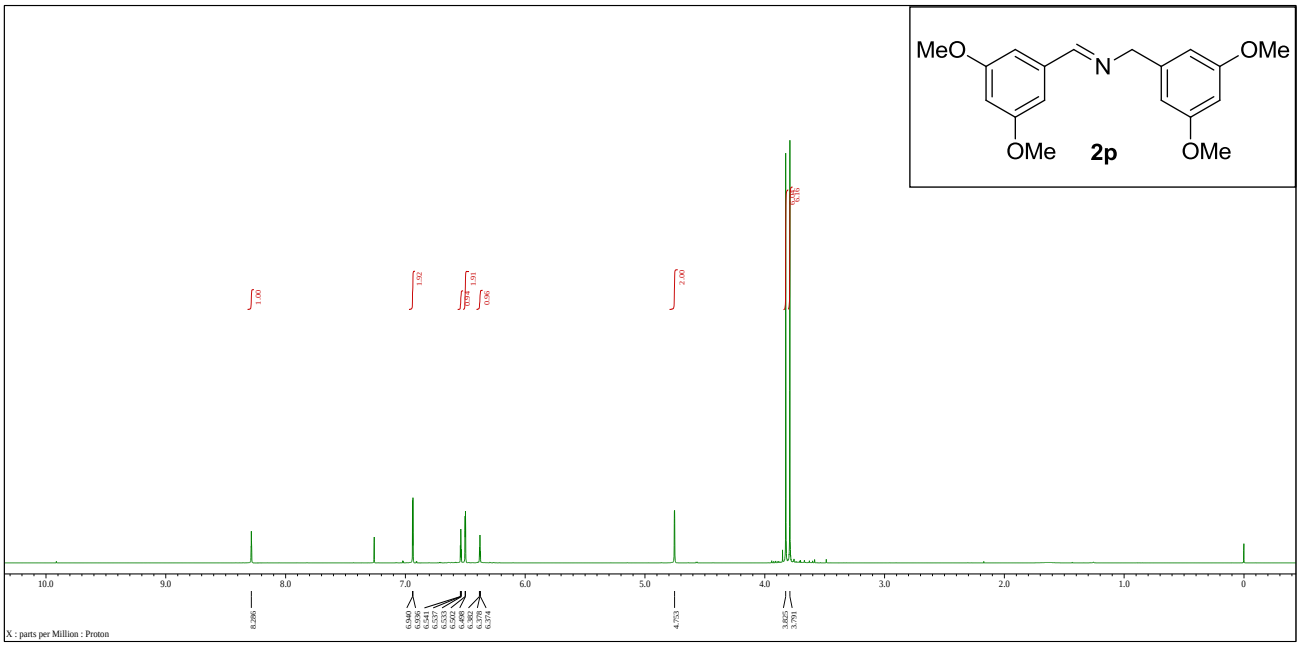
^{13}C-NMR Spectrum of compound **2n** (150 MHz, $CDCl_3$)



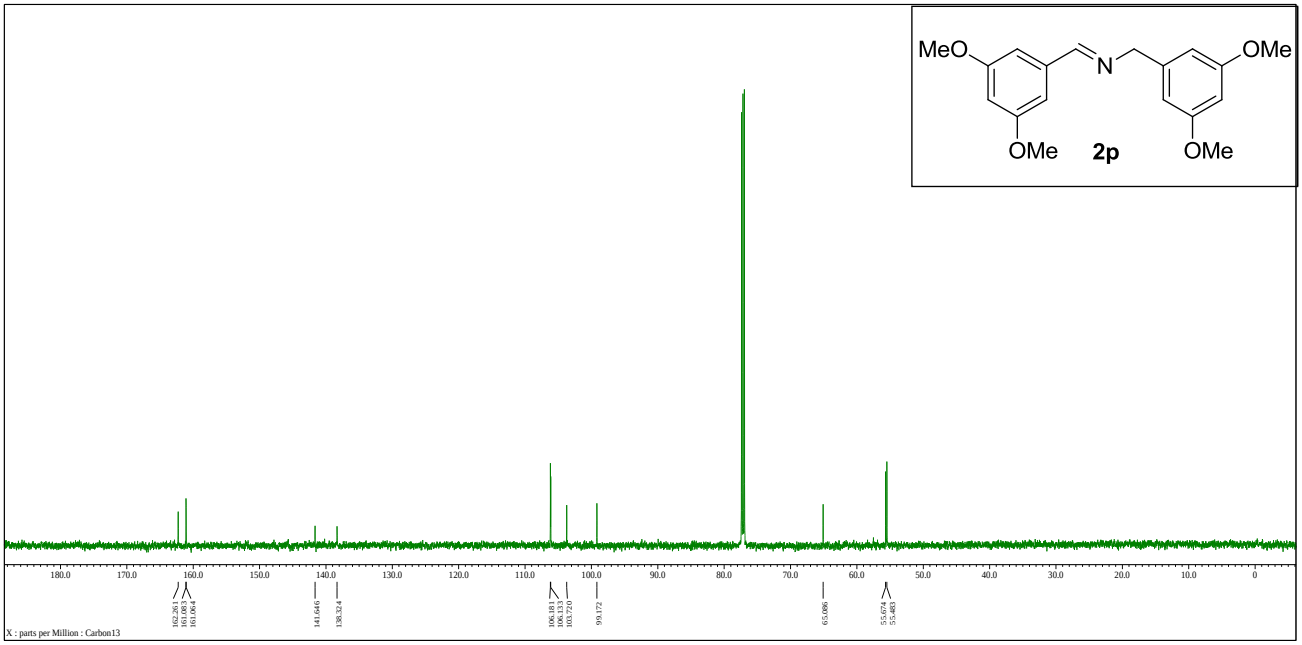
^{1}H-NMR Spectrum of compound **2o** (600 MHz, $CDCl_3$)



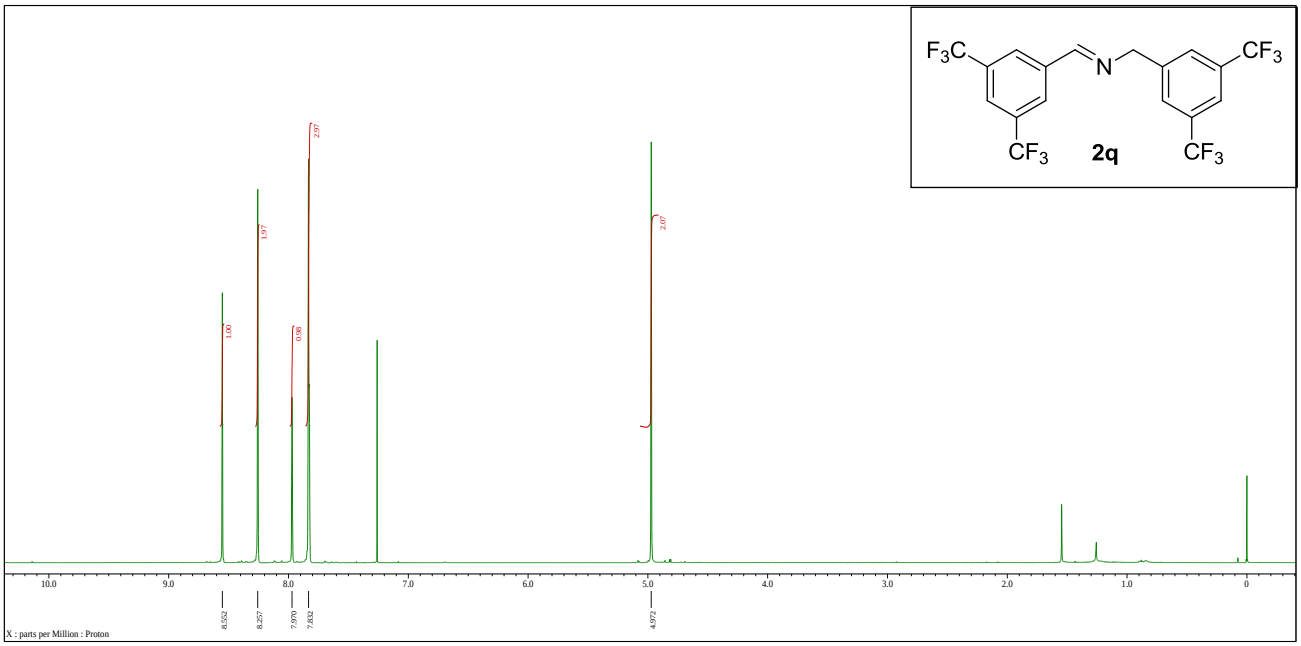
^{13}C-NMR Spectrum of compound **2o** (150 MHz, $CDCl_3$)



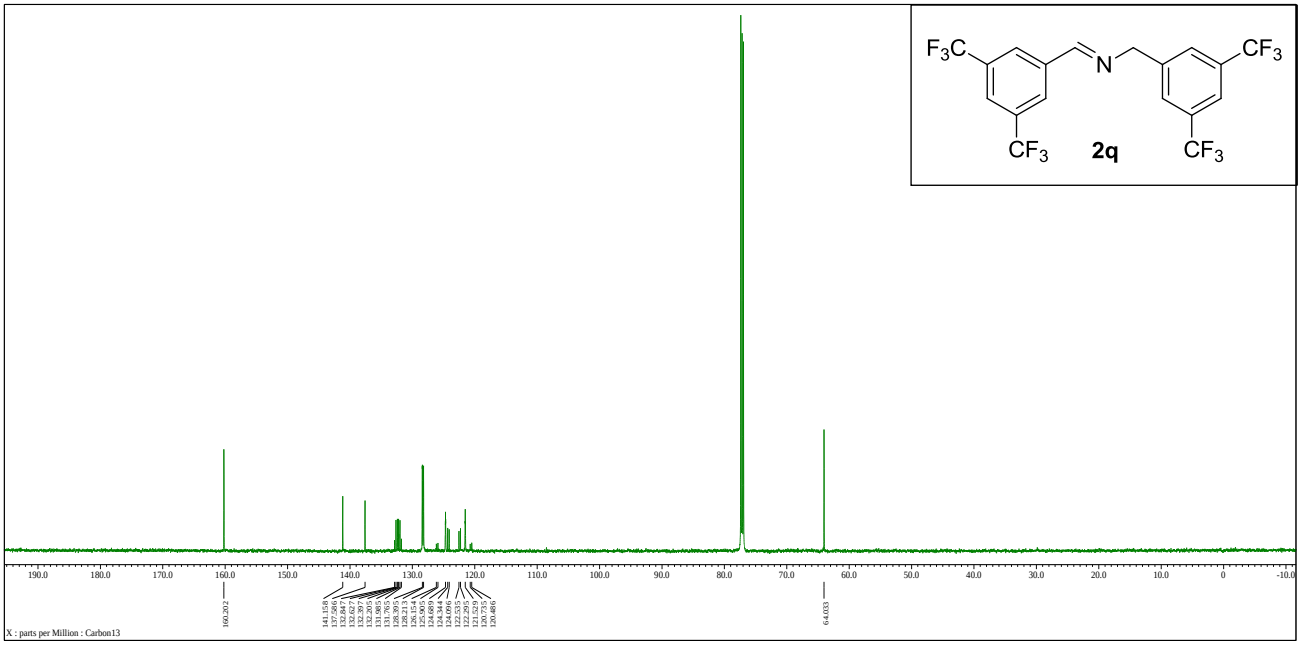
^{1}H-NMR Spectrum of compound **2p** (600 MHz, $CDCl_3$)



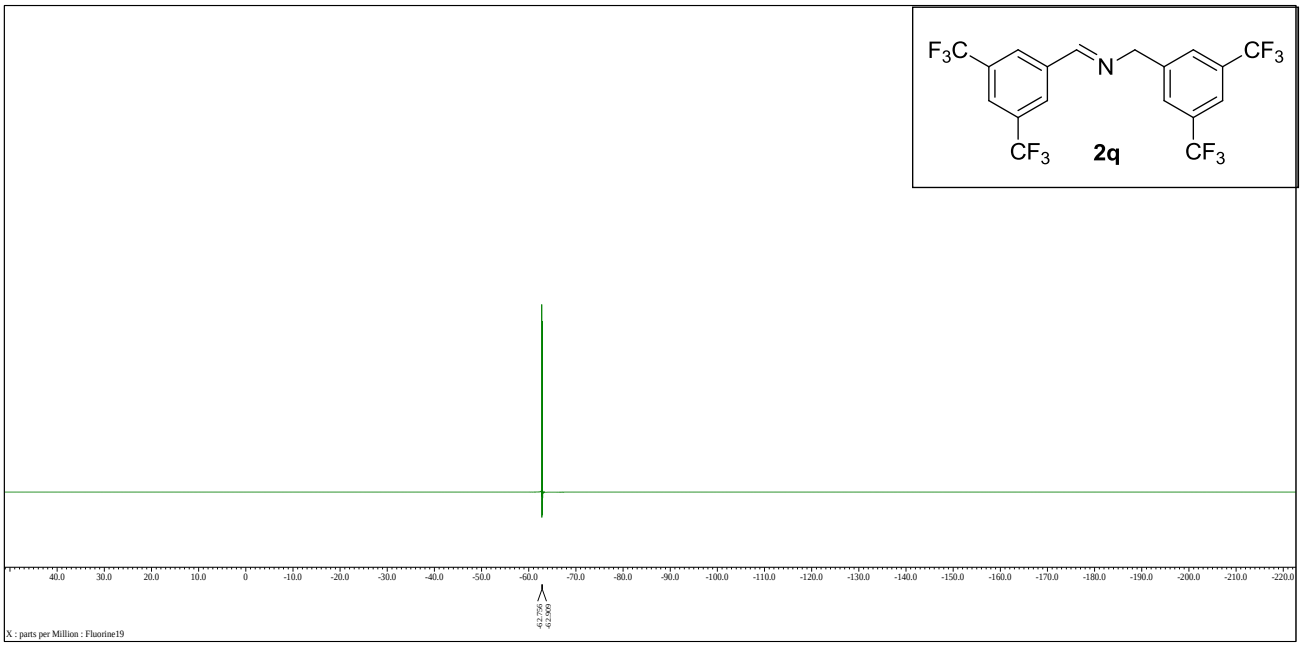
^{13}C-NMR Spectrum of compound **2p** (150 MHz, $CDCl_3$)



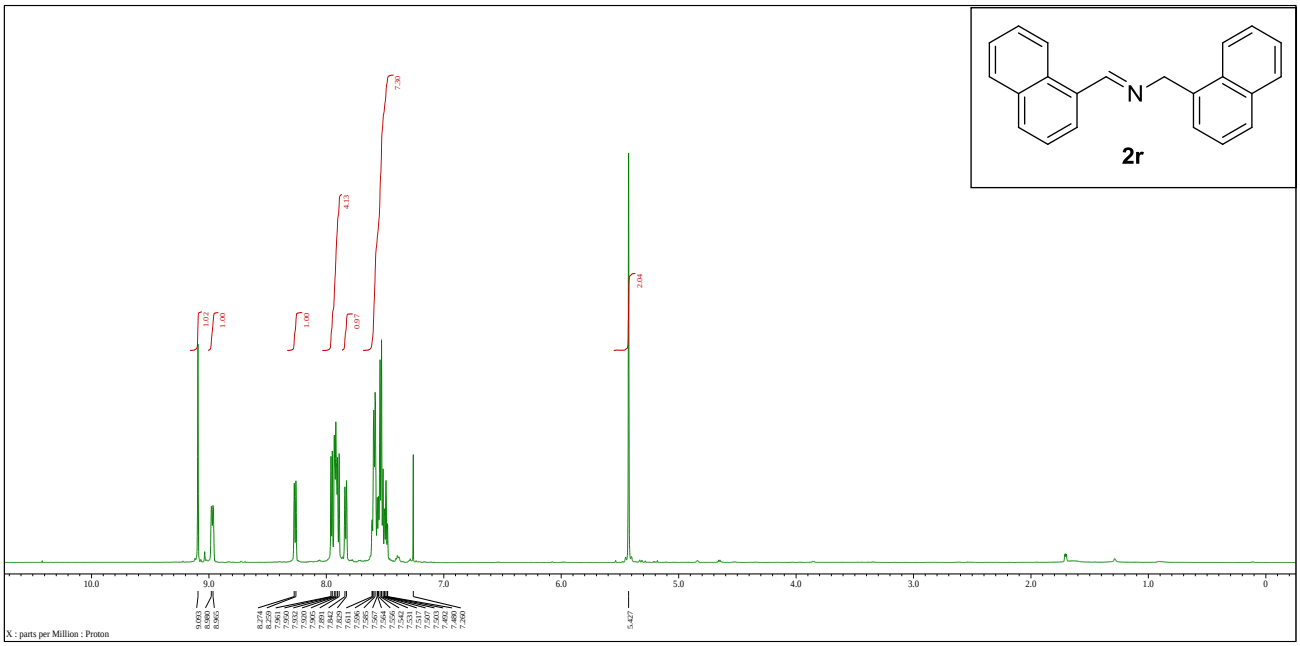
^{1}H-NMR Spectrum of compound **2q** (600 MHz, $CDCl_3$)



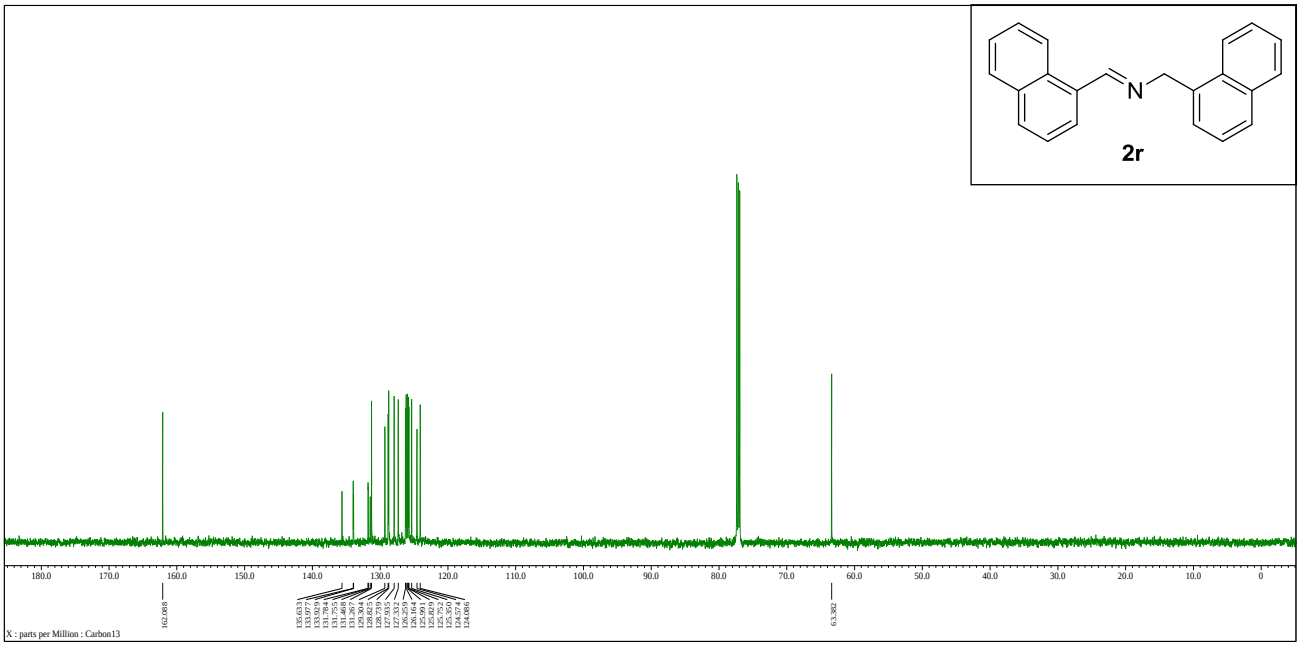
^{13}C-NMR Spectrum of compound **2q** (150 MHz, $CDCl_3$)



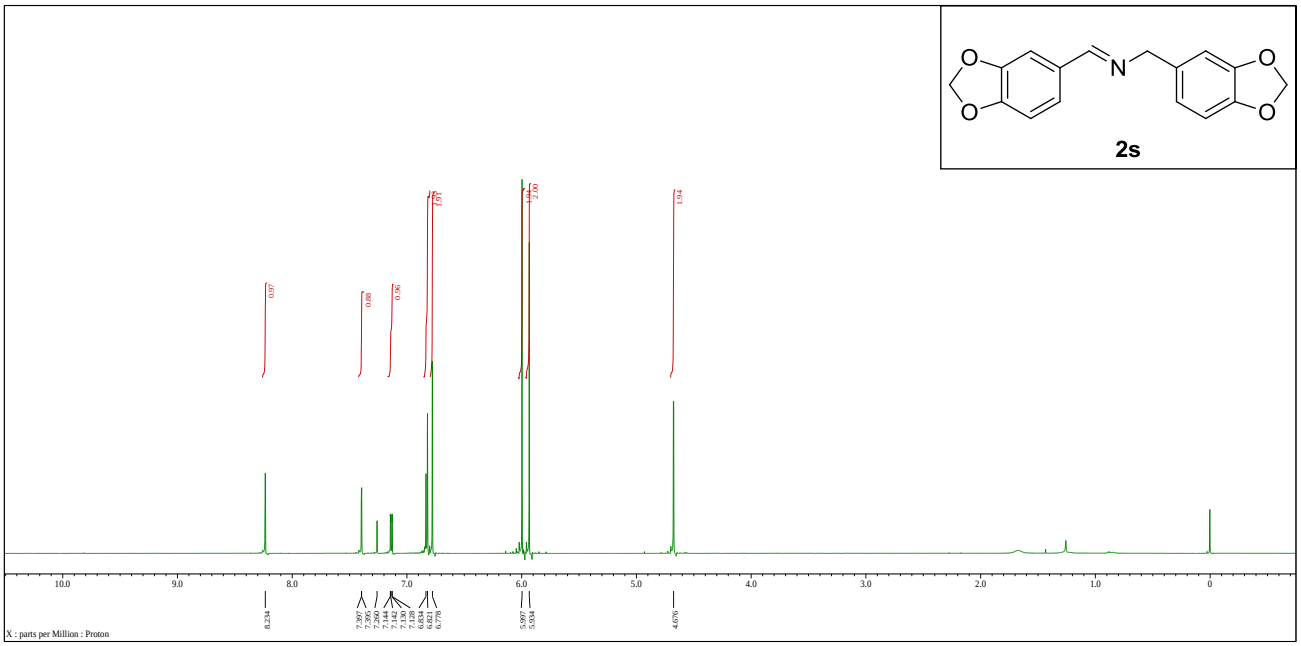
^{19}F-NMR Spectrum of compound **2q** (564 MHz, $CDCl_3$)



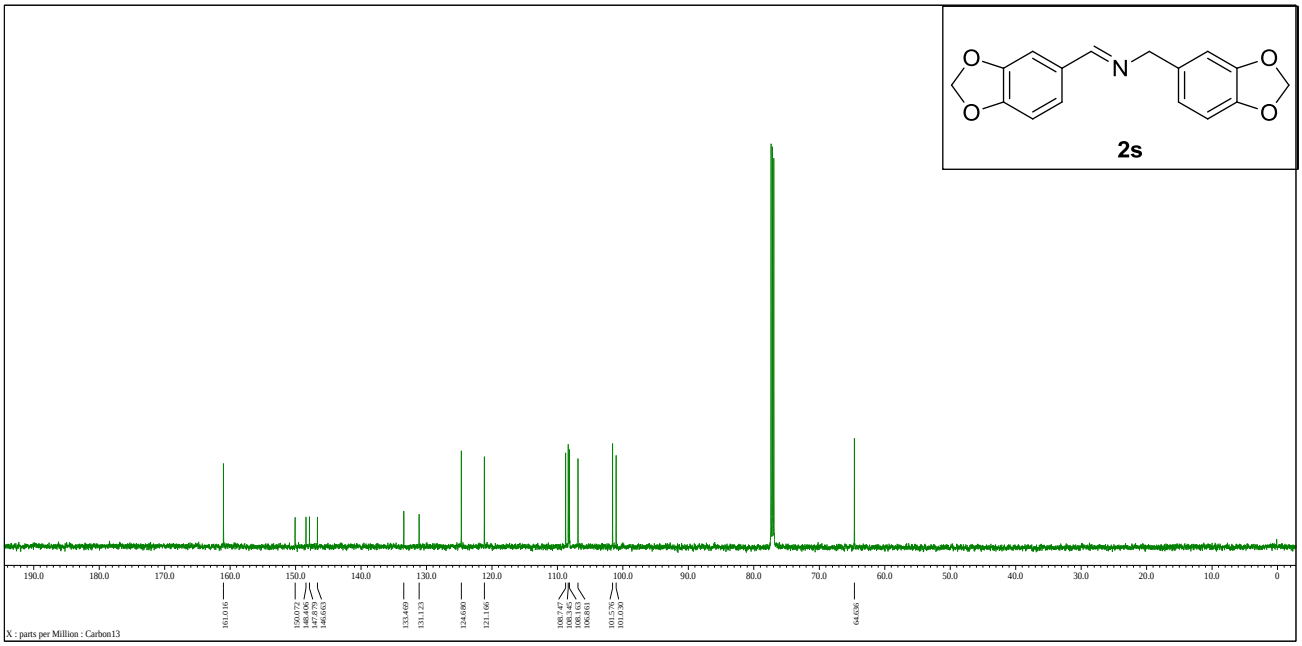
^{1}H-NMR Spectrum of compound **2r** (600 MHz, $CDCl_3$)



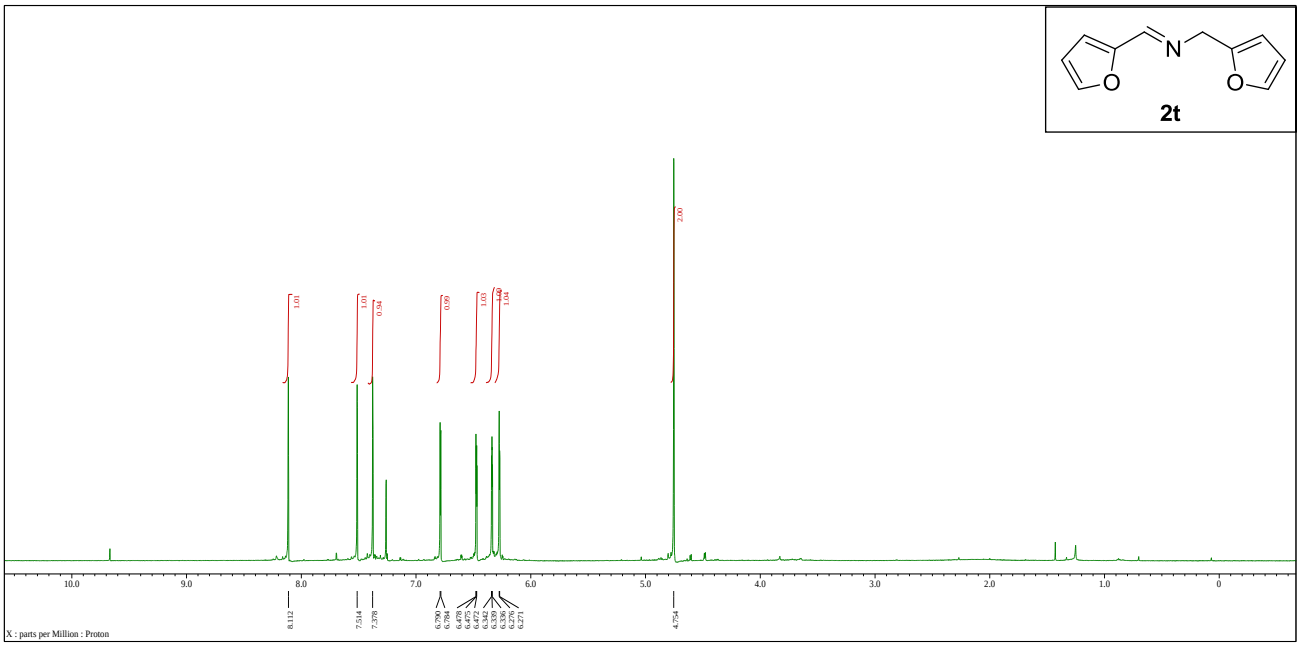
^{13}C-NMR Spectrum of compound **2r** (150 MHz, $CDCl_3$)



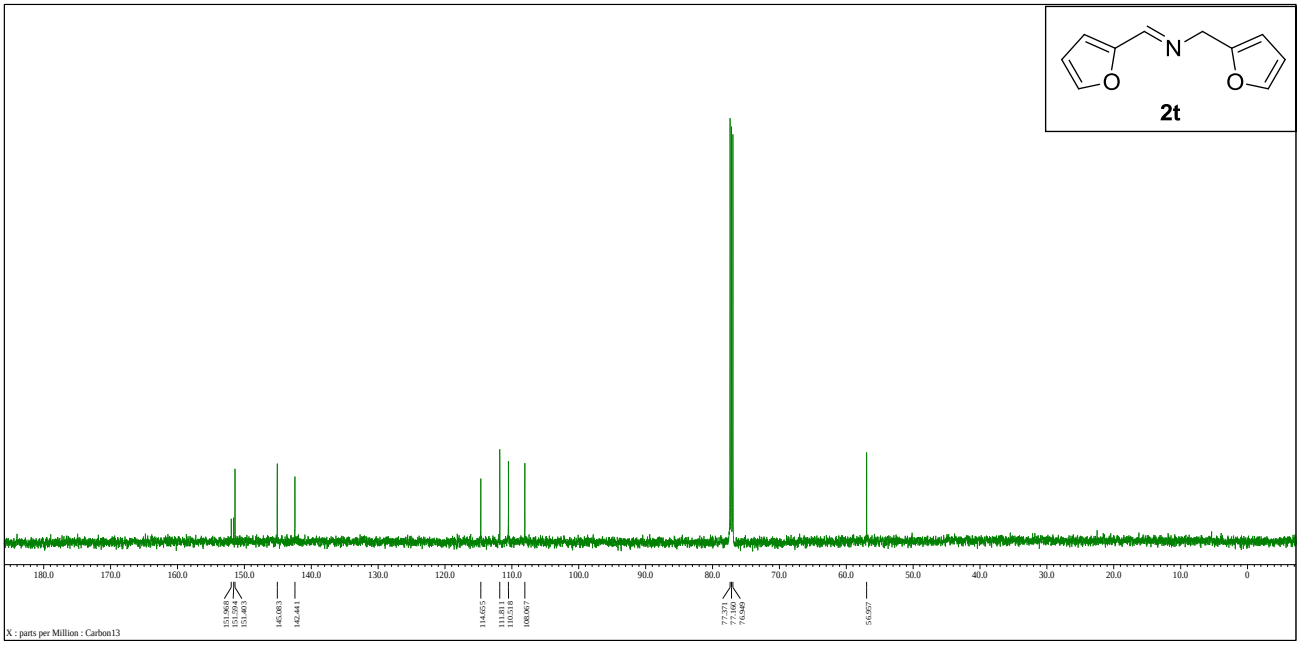
^{1}H-NMR Spectrum of compound **2s** (600 MHz, $CDCl_3$)



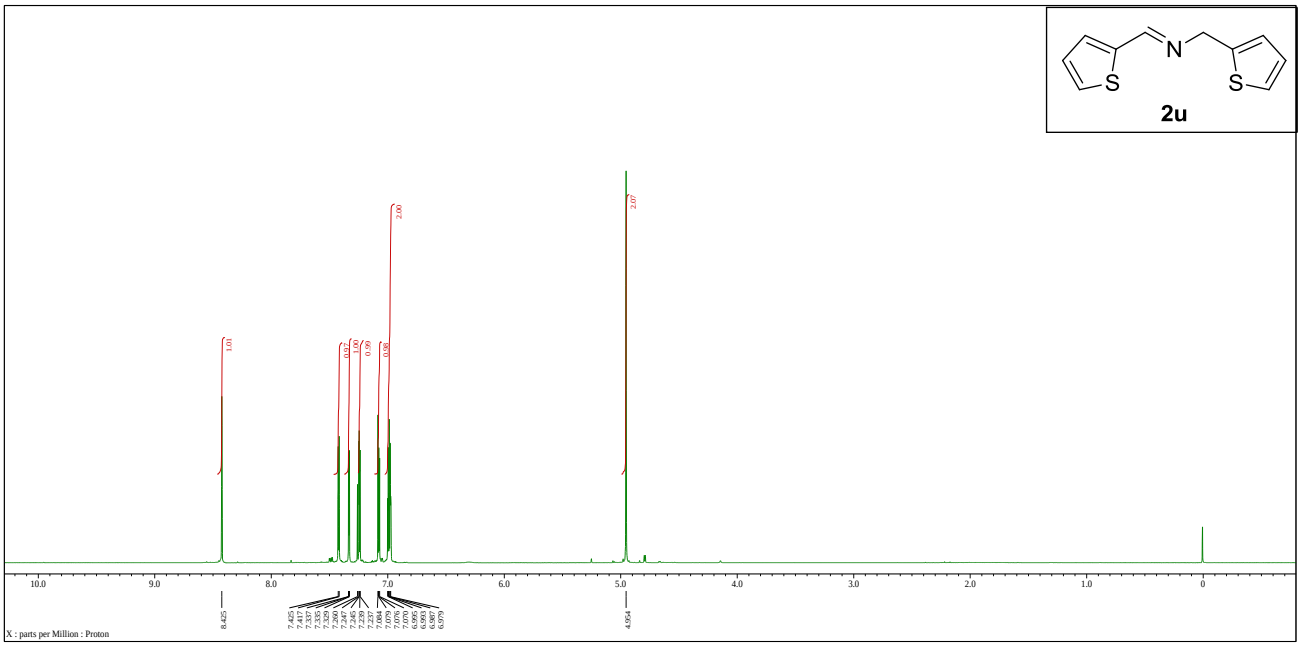
^{13}C-NMR Spectrum of compound **2s** (150 MHz, $CDCl_3$)



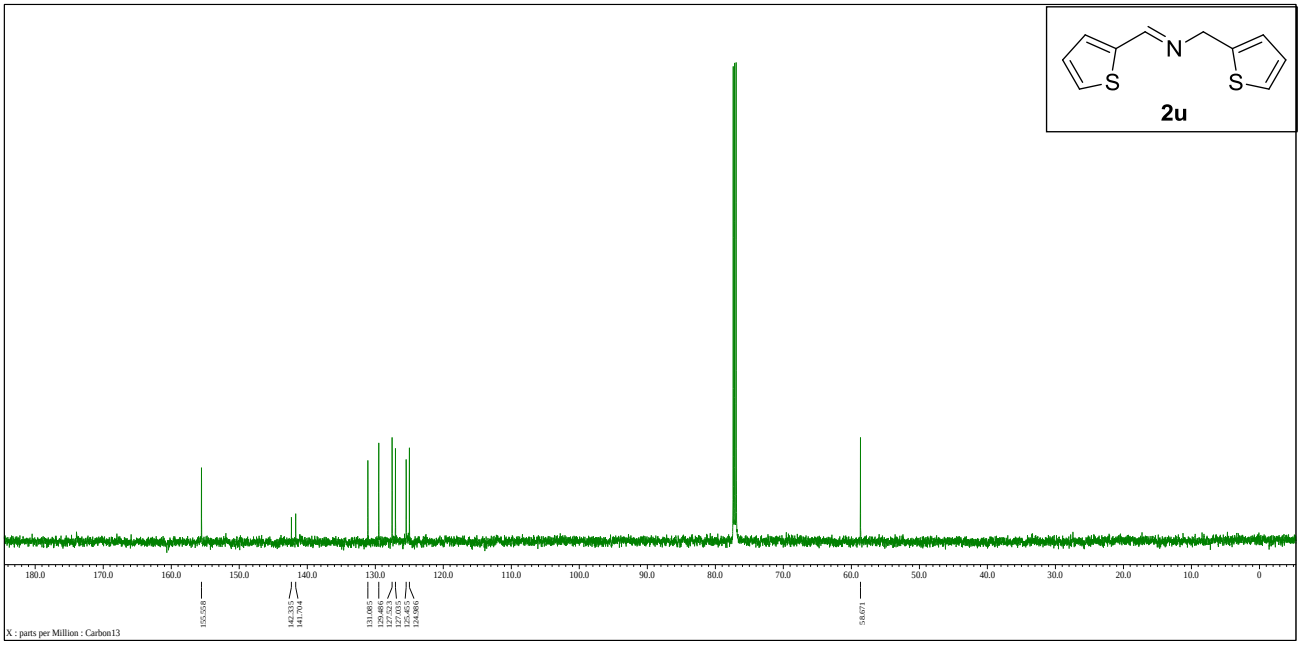
^{1}H-NMR Spectrum of compound **2t** (600 MHz, $CDCl_3$)



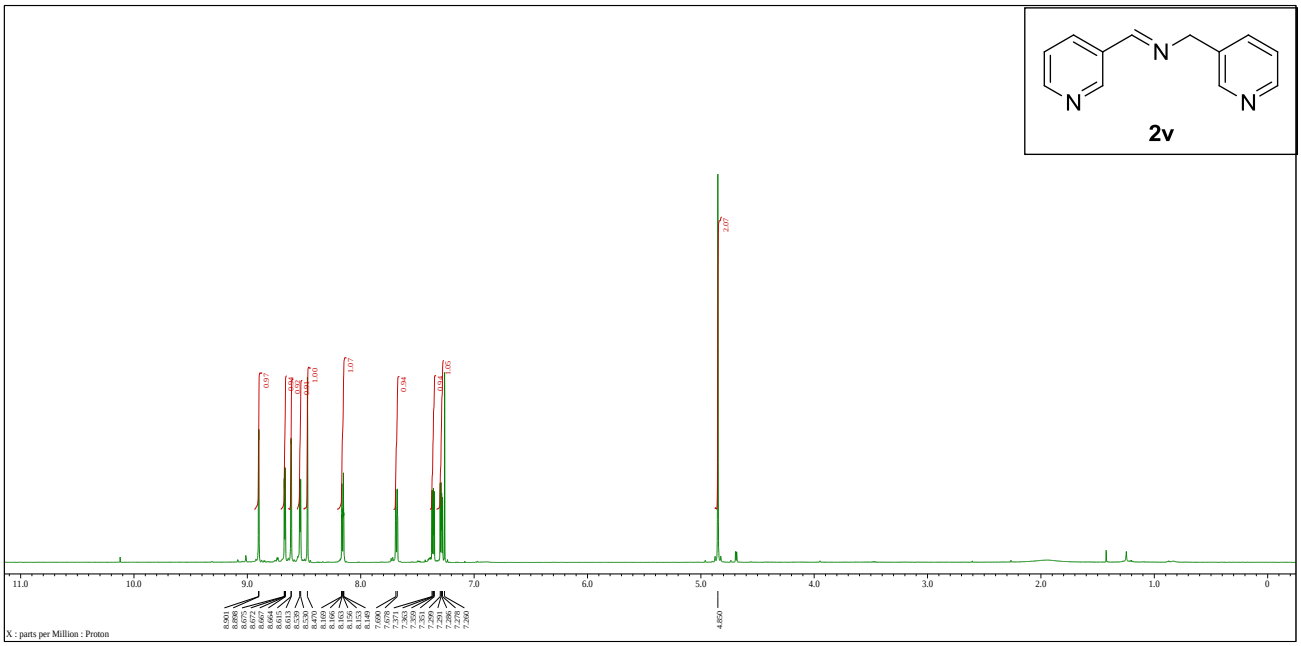
^{13}C-NMR Spectrum of compound **2t** (150 MHz, $CDCl_3$)



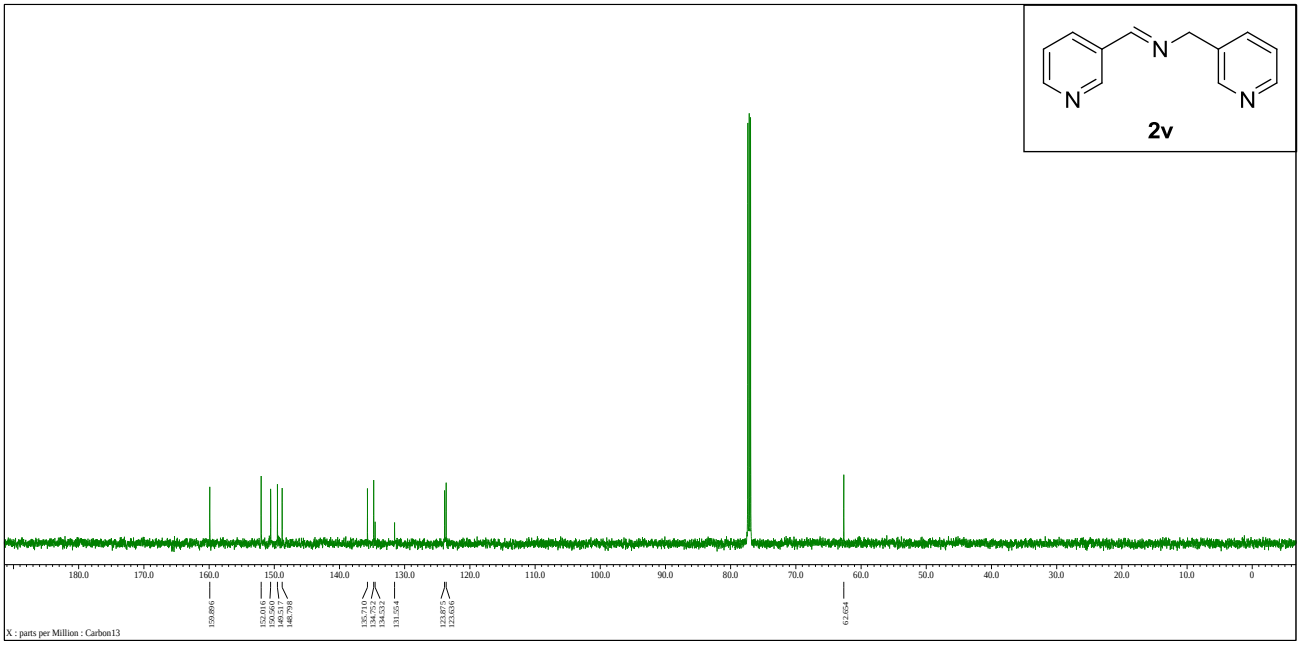
^{1}H-NMR Spectrum of compound **2u** (600 MHz, $CDCl_3$)



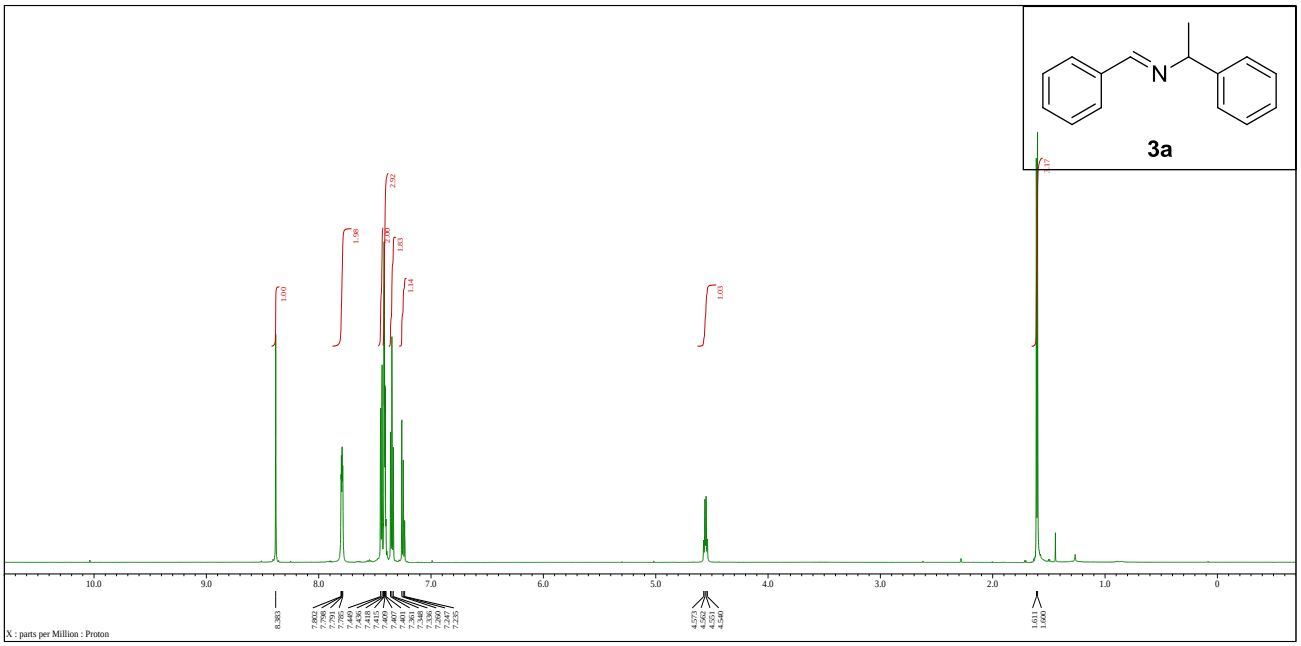
^{13}C-NMR Spectrum of compound **2u** (150 MHz, $CDCl_3$)



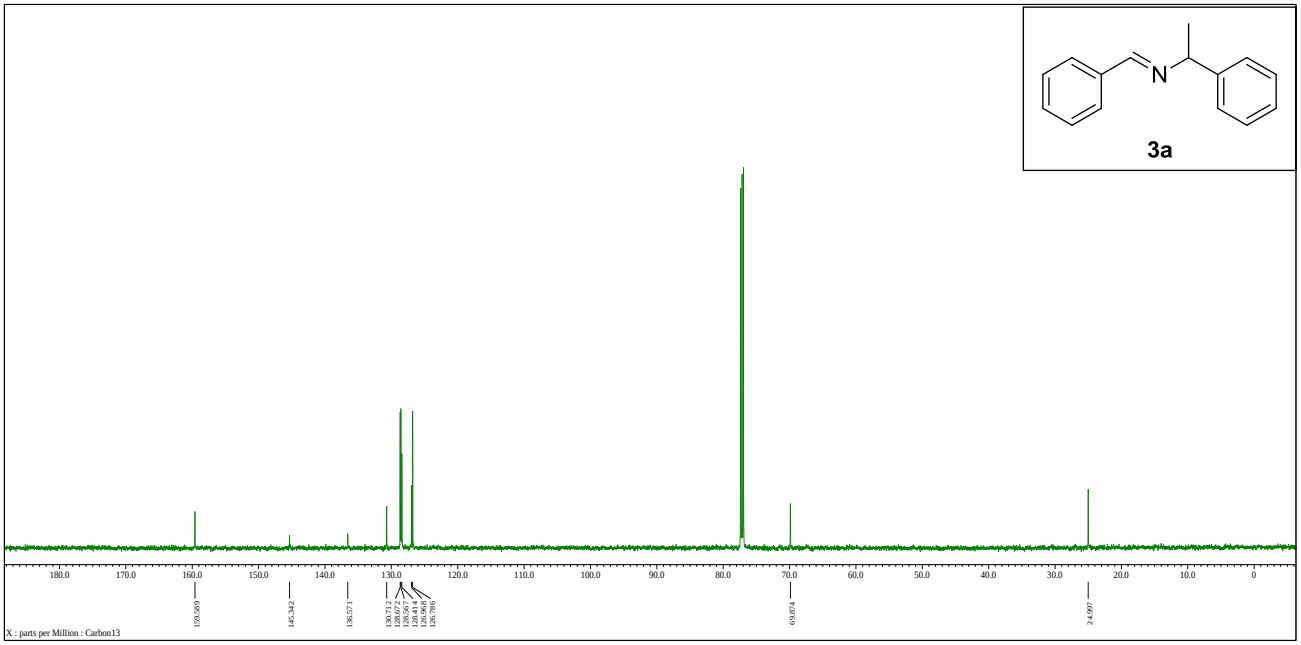
^{1}H-NMR Spectrum of compound **2v** (600 MHz, $CDCl_3$)



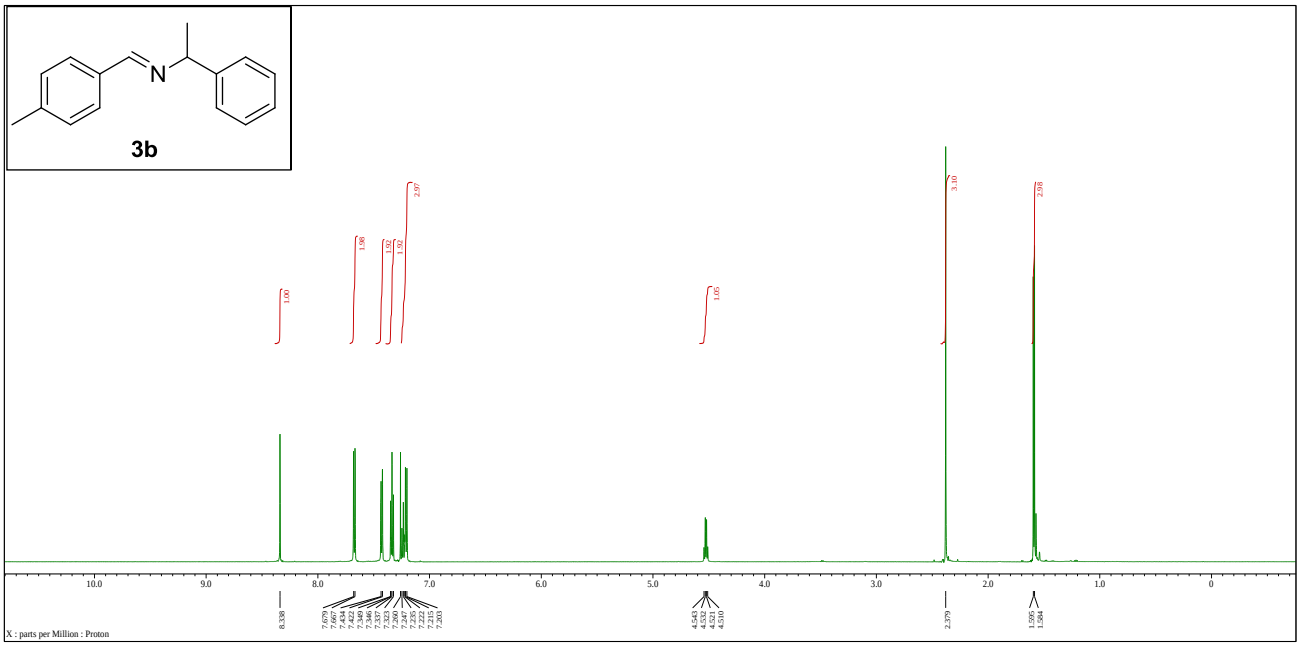
^{13}C-NMR Spectrum of compound **2v** (150 MHz, $CDCl_3$)



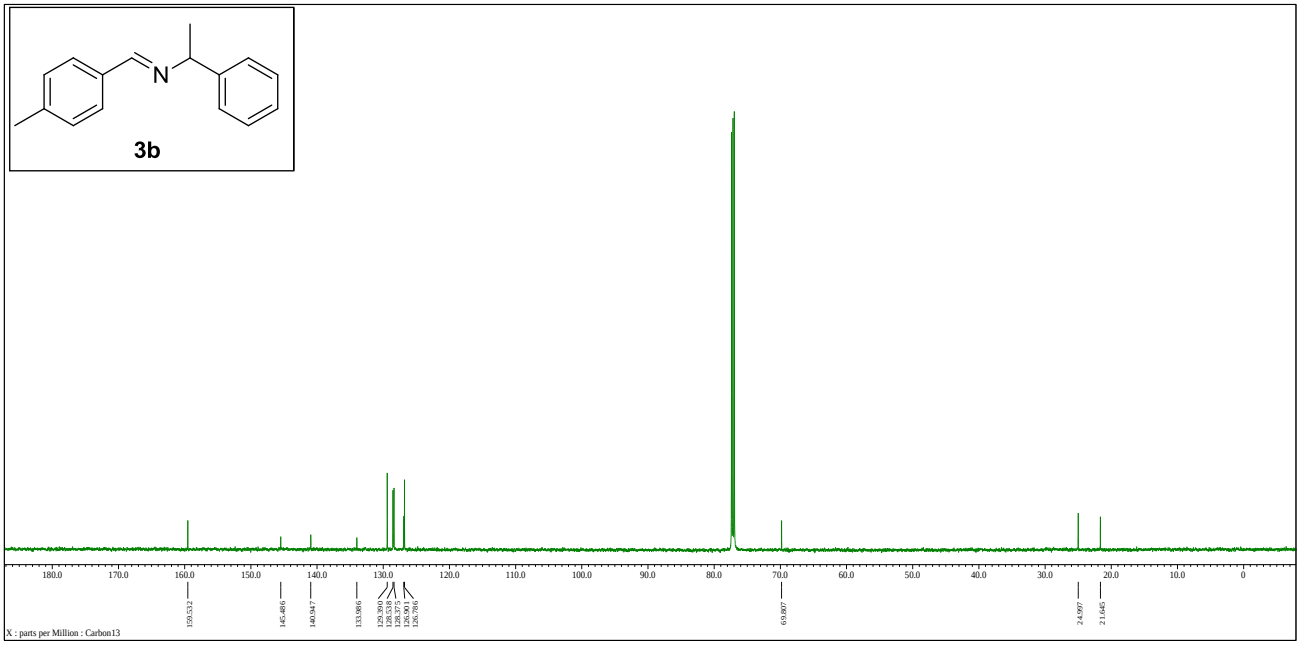
^{1}H-NMR Spectrum of compound **3a** (600 MHz, $CDCl_3$)



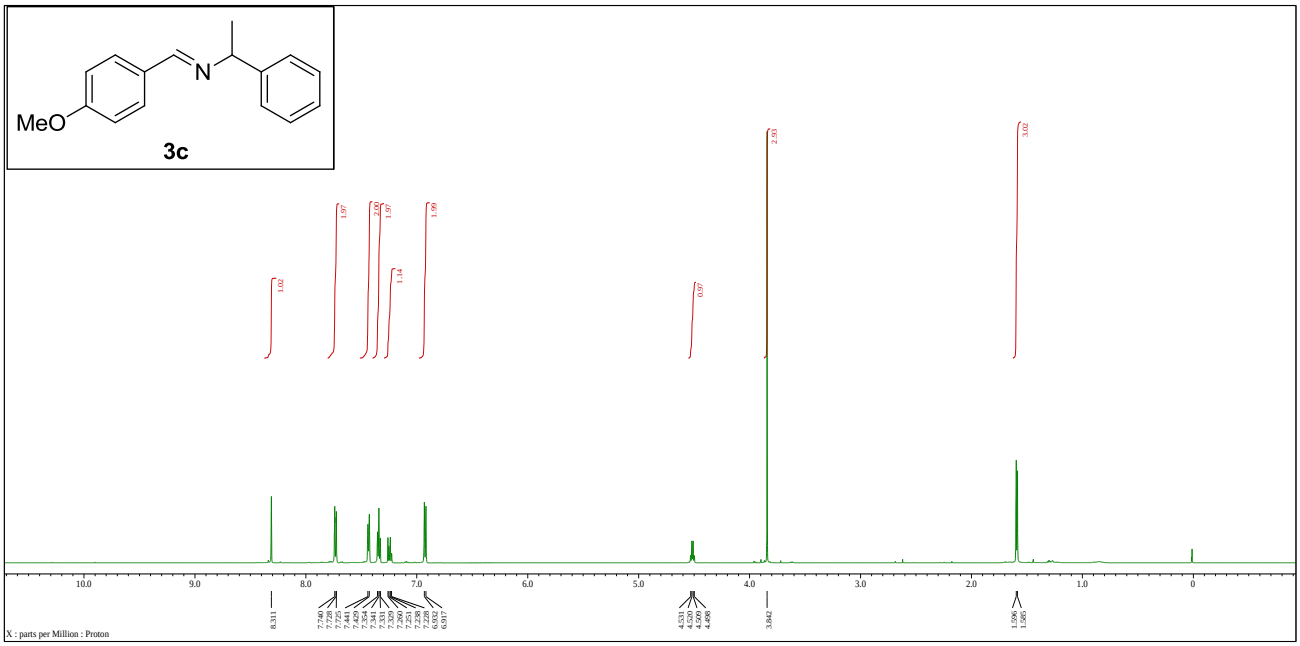
^{13}C-NMR Spectrum of compound **3a** (150 MHz, $CDCl_3$)



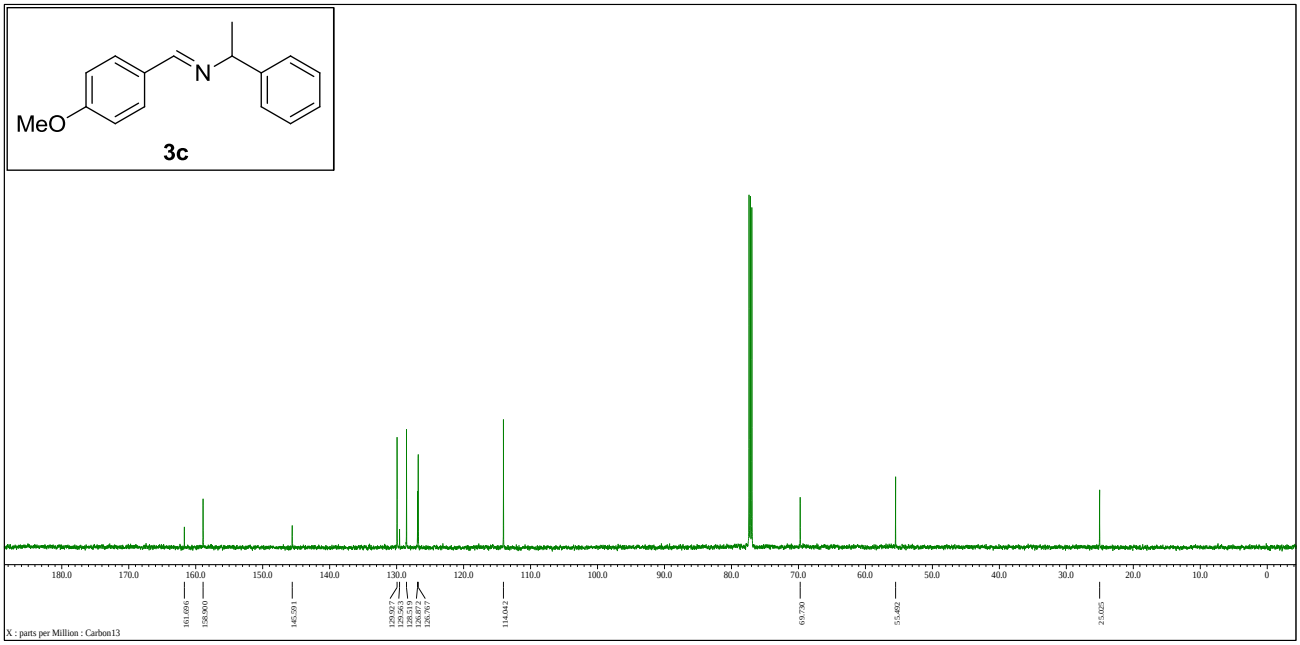
^{1}H-NMR Spectrum of compound **3b** (600 MHz, $CDCl_3$)



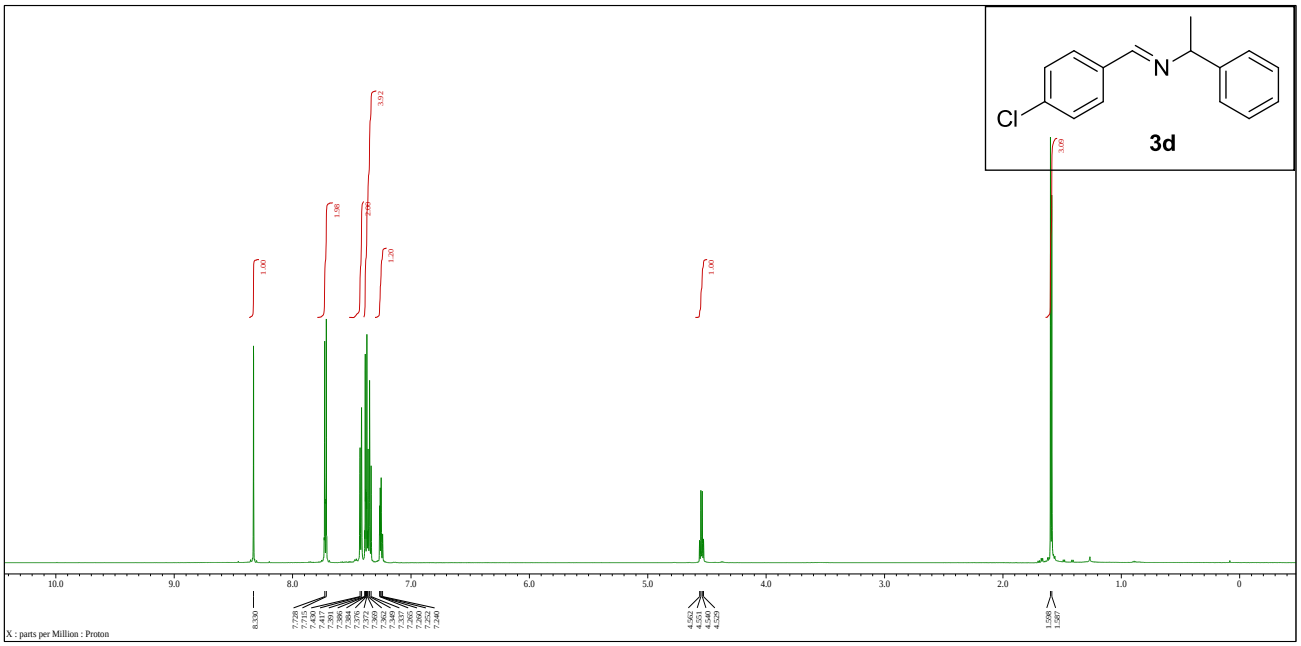
^{13}C-NMR Spectrum of compound **3b** (150 MHz, $CDCl_3$)



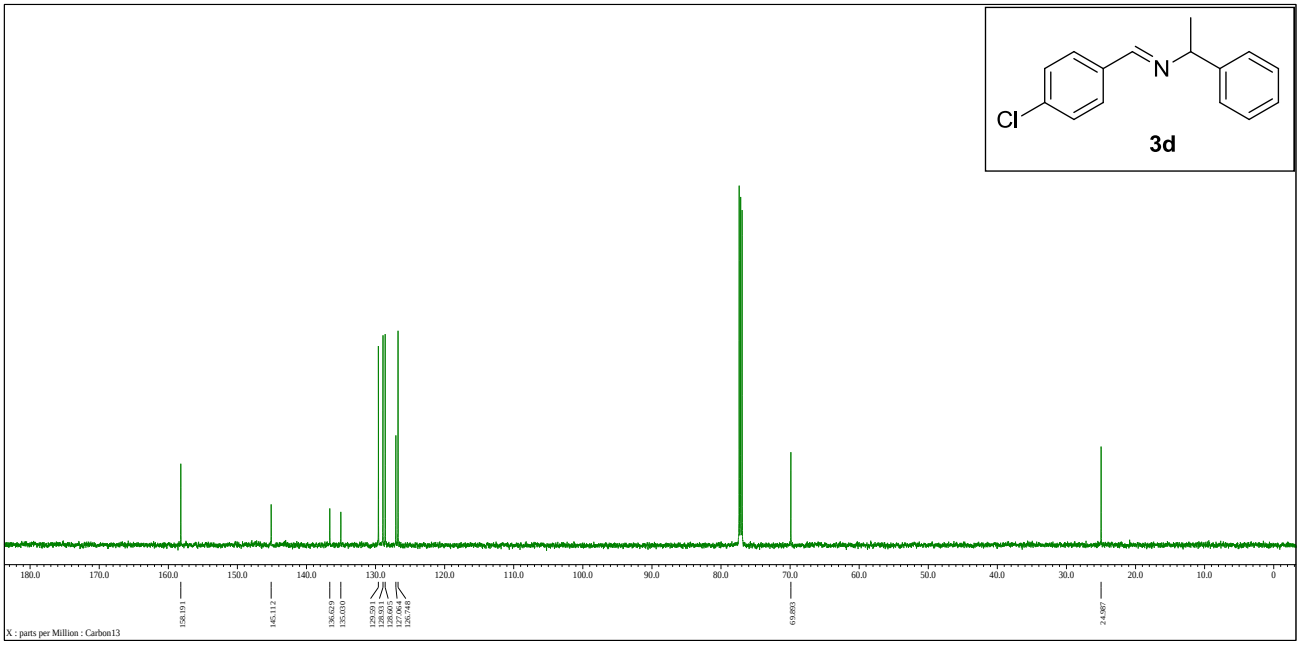
^{1}H-NMR Spectrum of compound **3c** (600 MHz, $CDCl_3$)



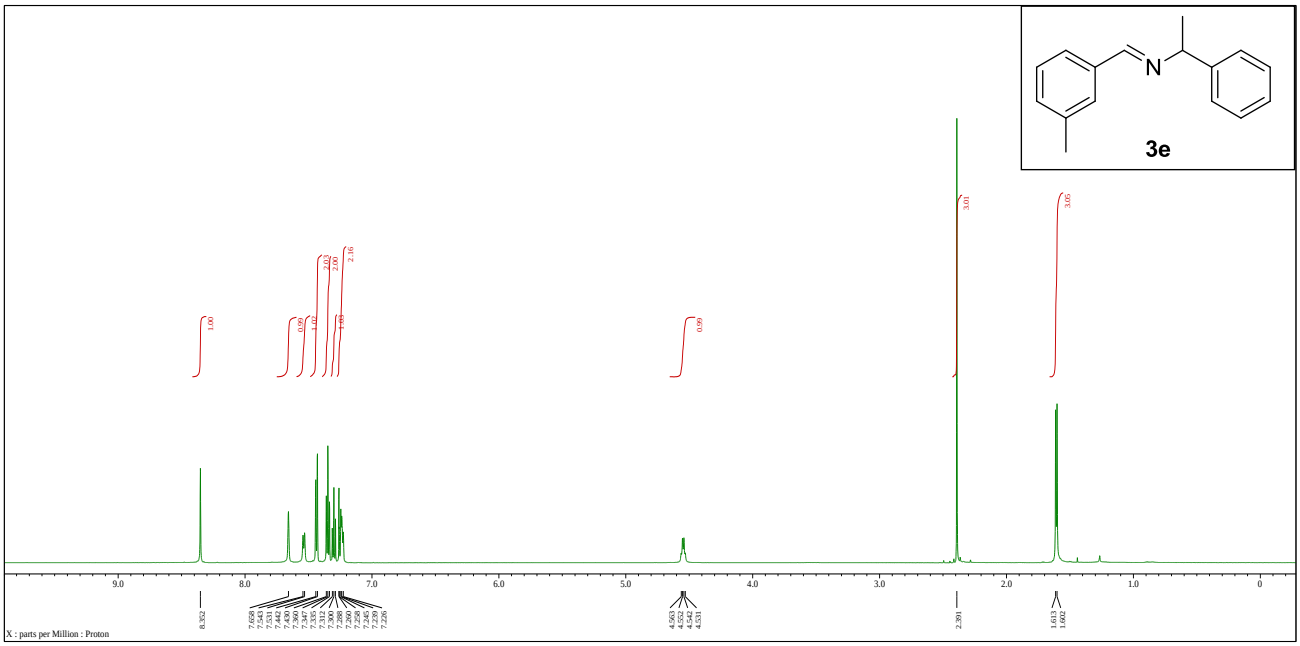
^{13}C-NMR Spectrum of compound **3c** (150 MHz, $CDCl_3$)



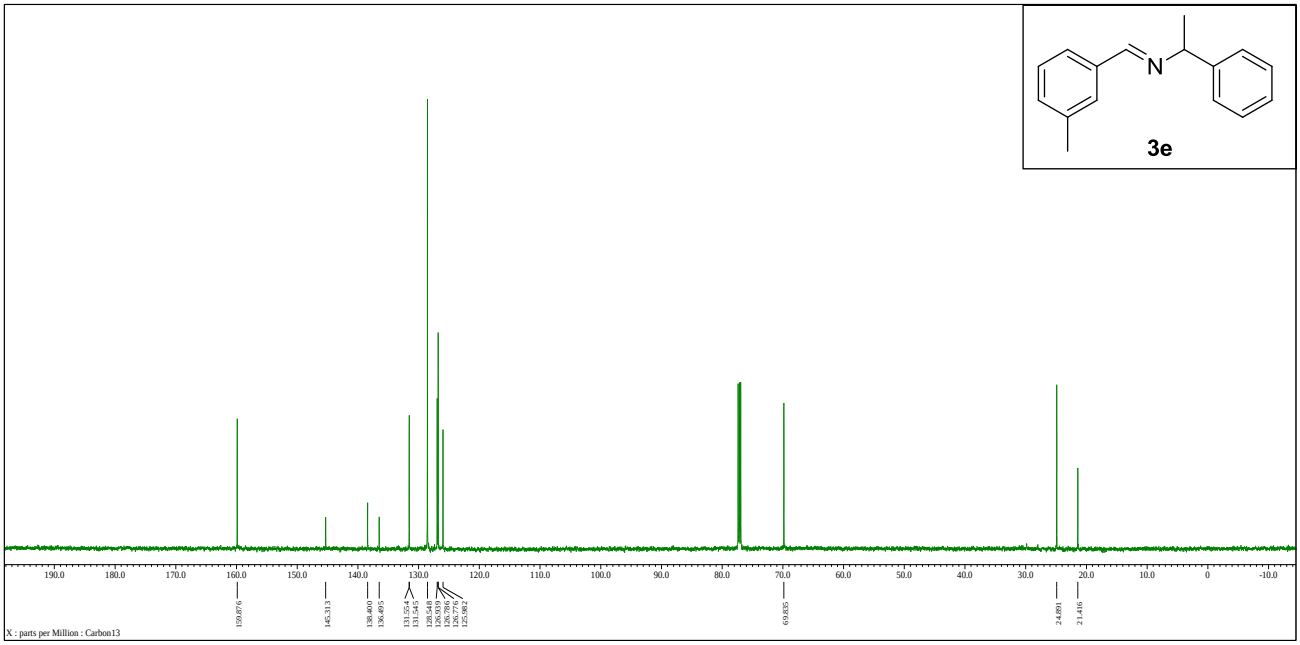
^{1}H-NMR Spectrum of compound **3d** (600 MHz, $CDCl_3$)



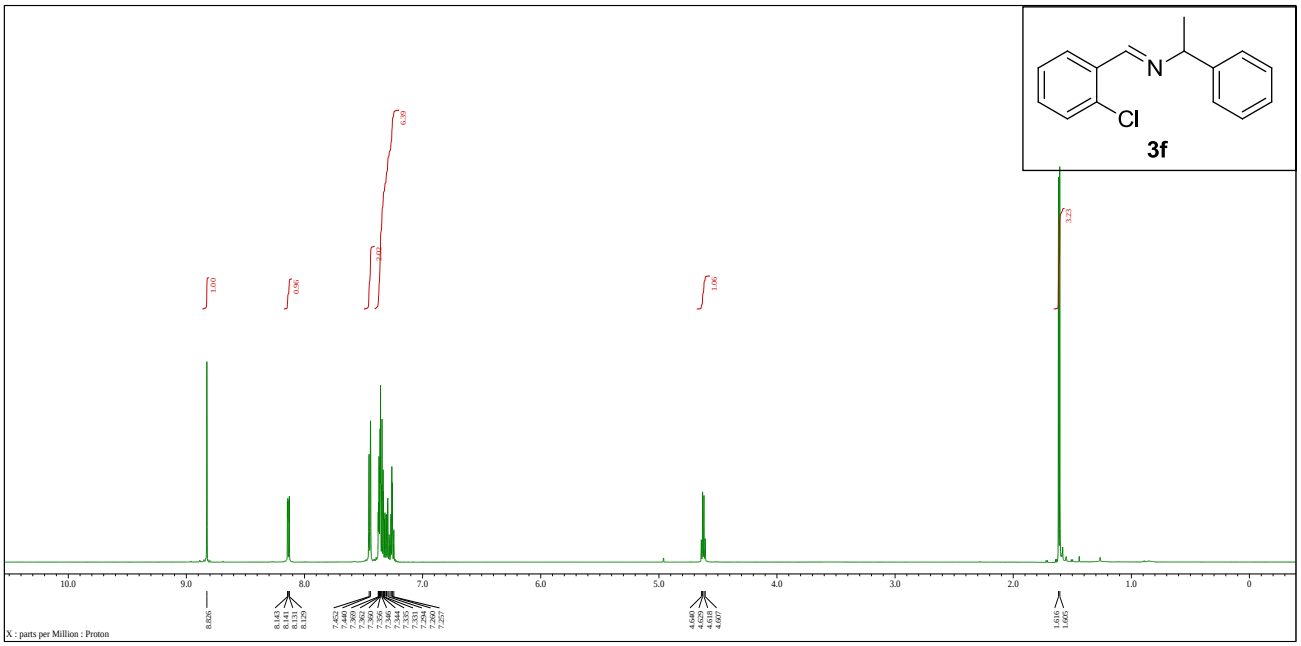
^{13}C-NMR Spectrum of compound **3d** (150 MHz, $CDCl_3$)



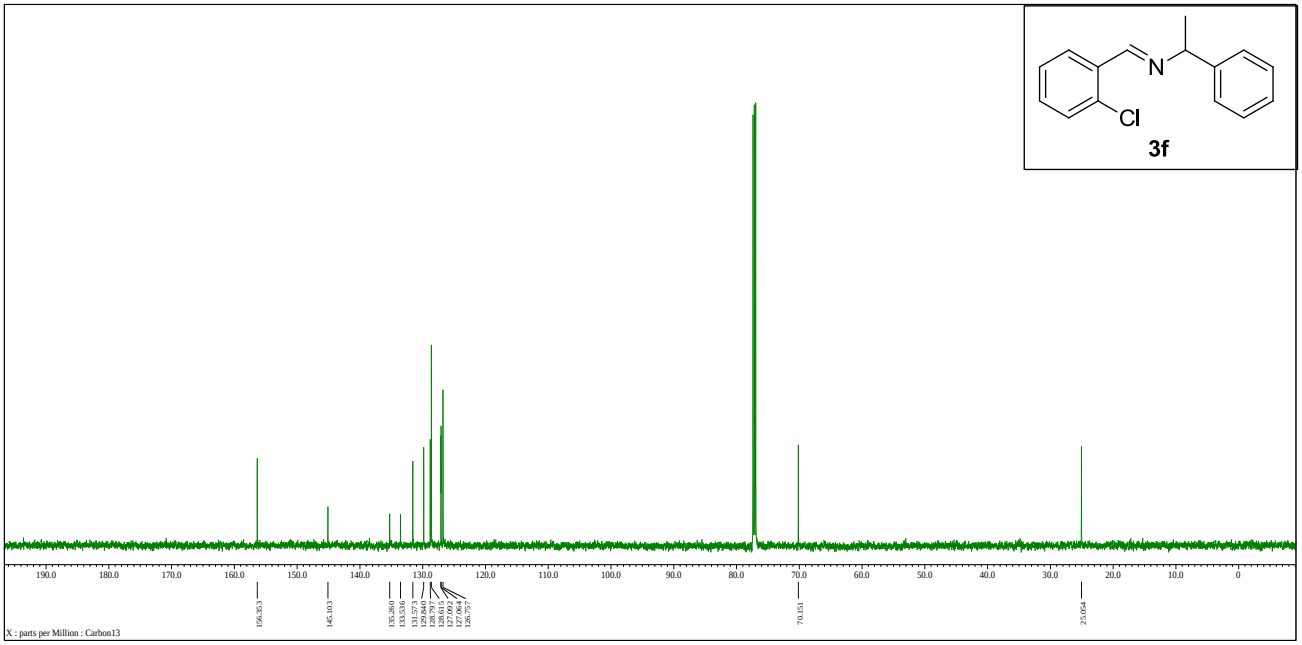
^{1}H-NMR Spectrum of compound **3e** (600 MHz, $CDCl_3$)



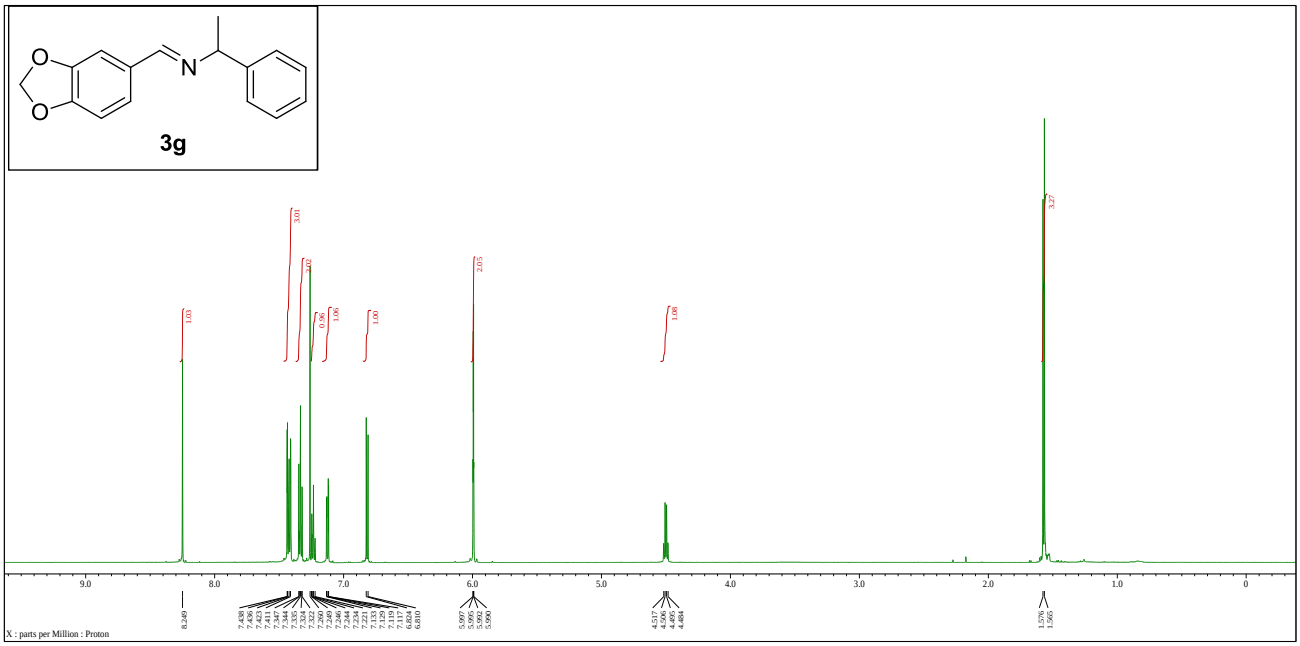
^{13}C-NMR Spectrum of compound **3e** (150 MHz, $CDCl_3$)



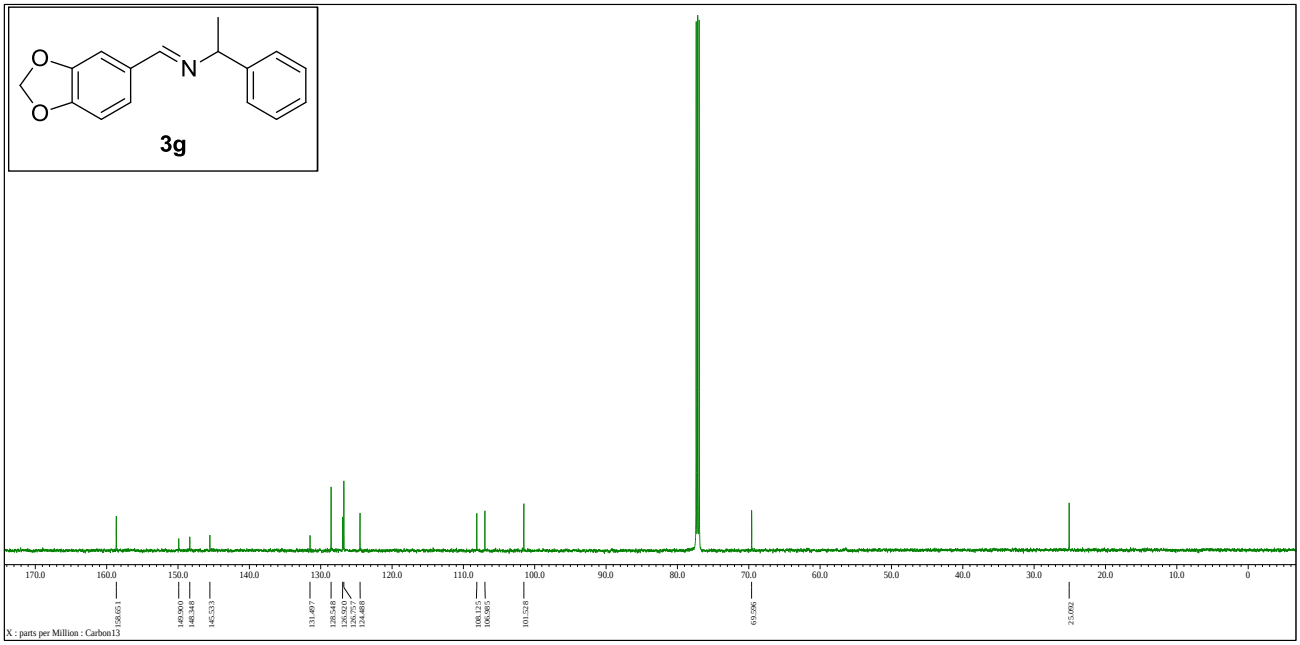
^{1}H-NMR Spectrum of compound **3f** (600 MHz, $CDCl_3$)



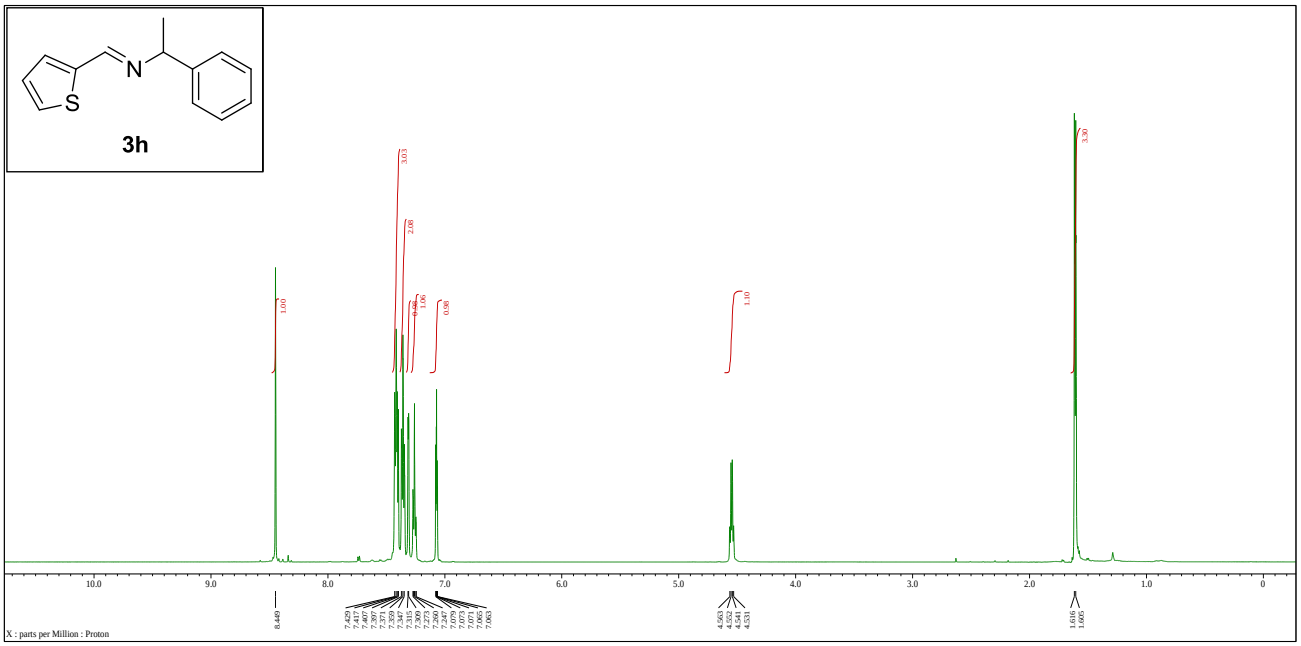
^{13}C-NMR Spectrum of compound **3f** (150 MHz, $CDCl_3$)



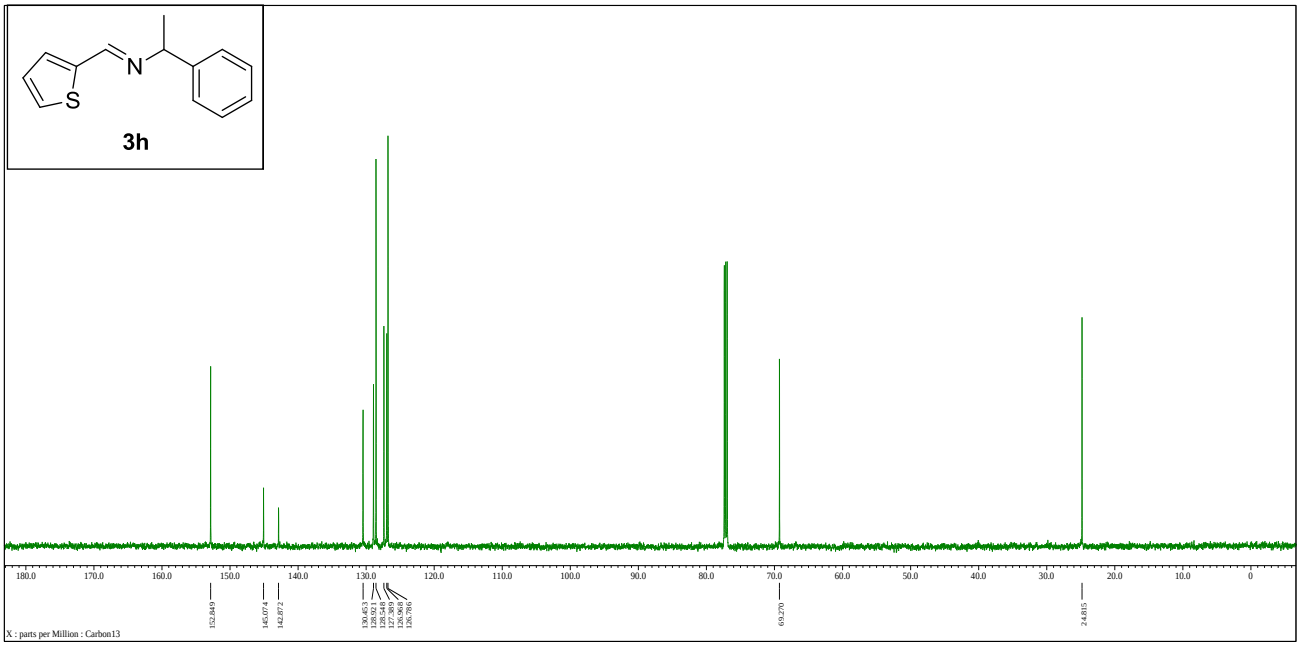
^{1}H-NMR Spectrum of compound **3g** (600 MHz, $CDCl_3$)



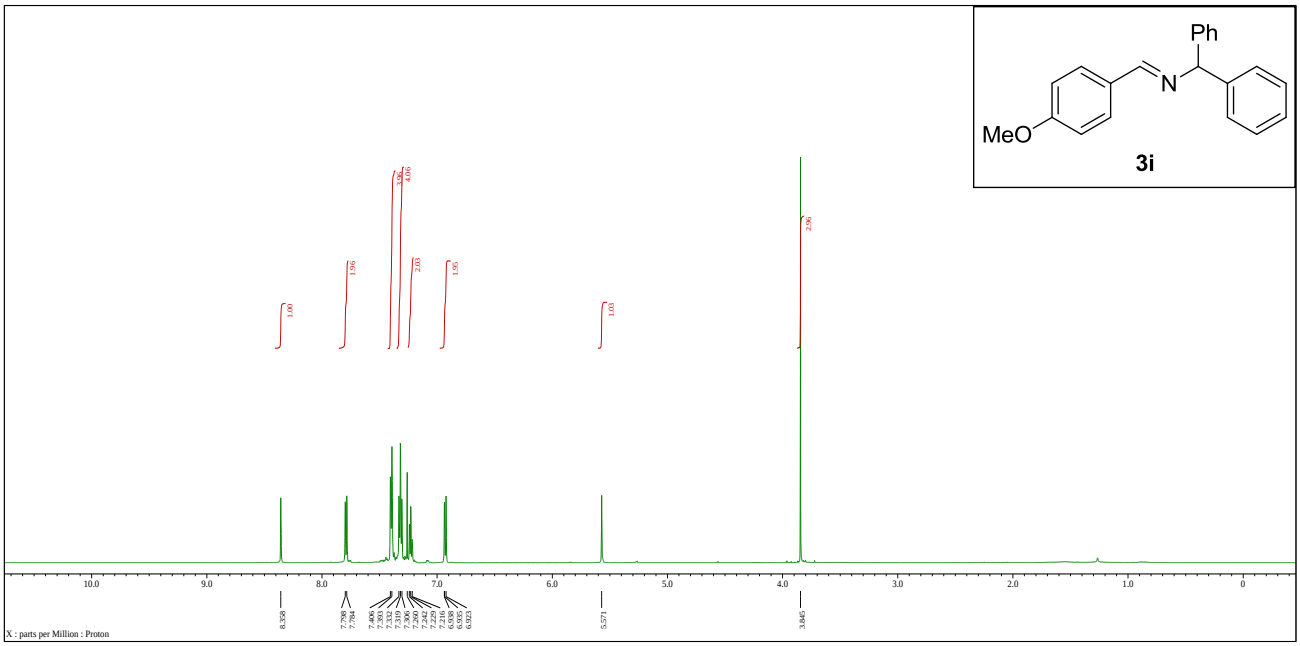
^{13}C-NMR Spectrum of compound **3g** (150 MHz, $CDCl_3$)



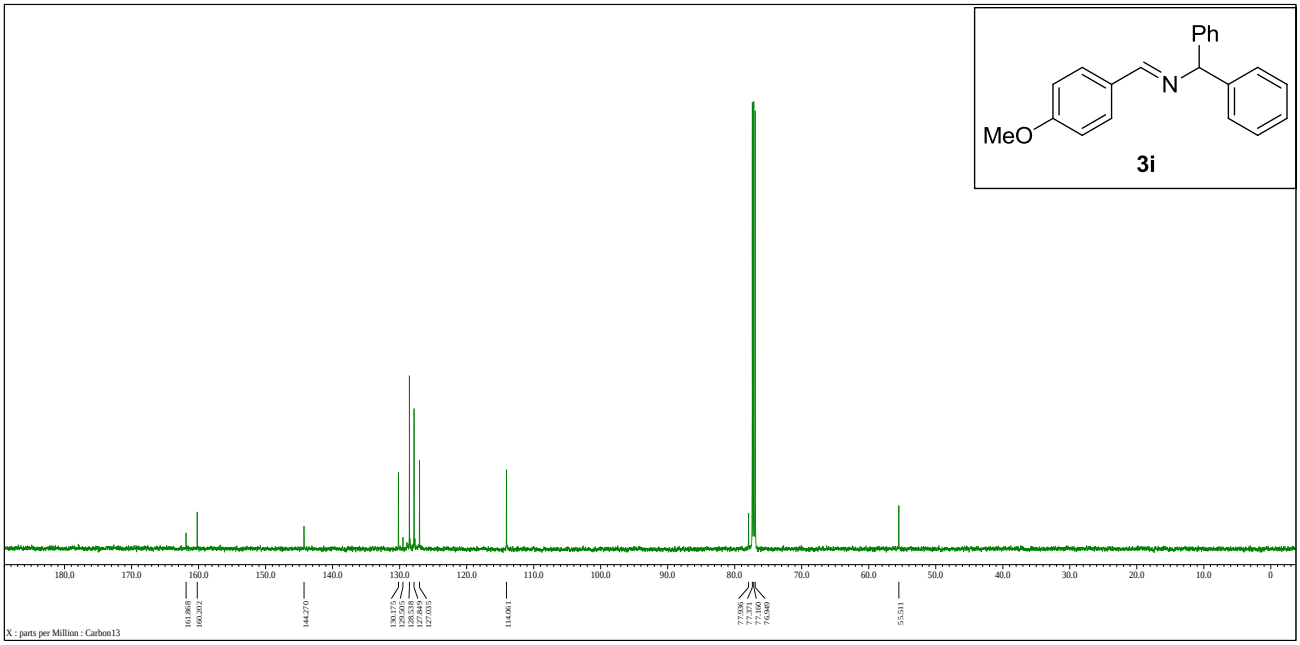
^{1}H-NMR Spectrum of compound **3h** (600 MHz, $CDCl_3$)



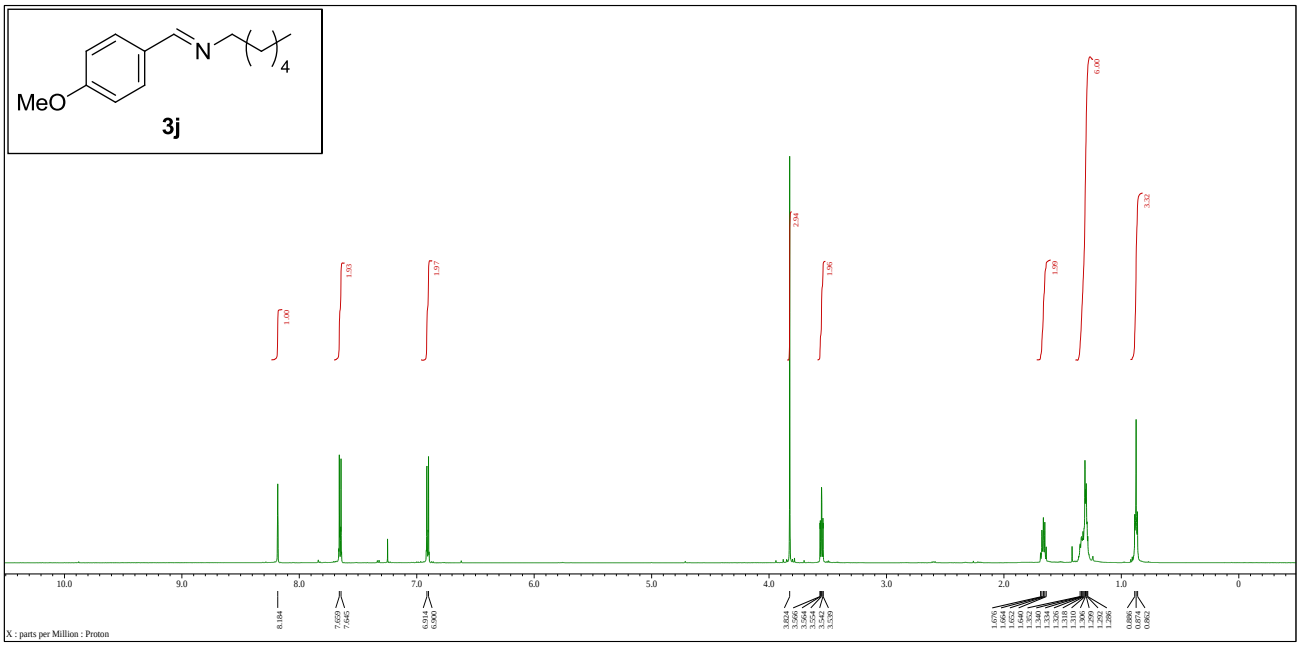
^{13}C-NMR Spectrum of compound **3h** (150 MHz, $CDCl_3$)



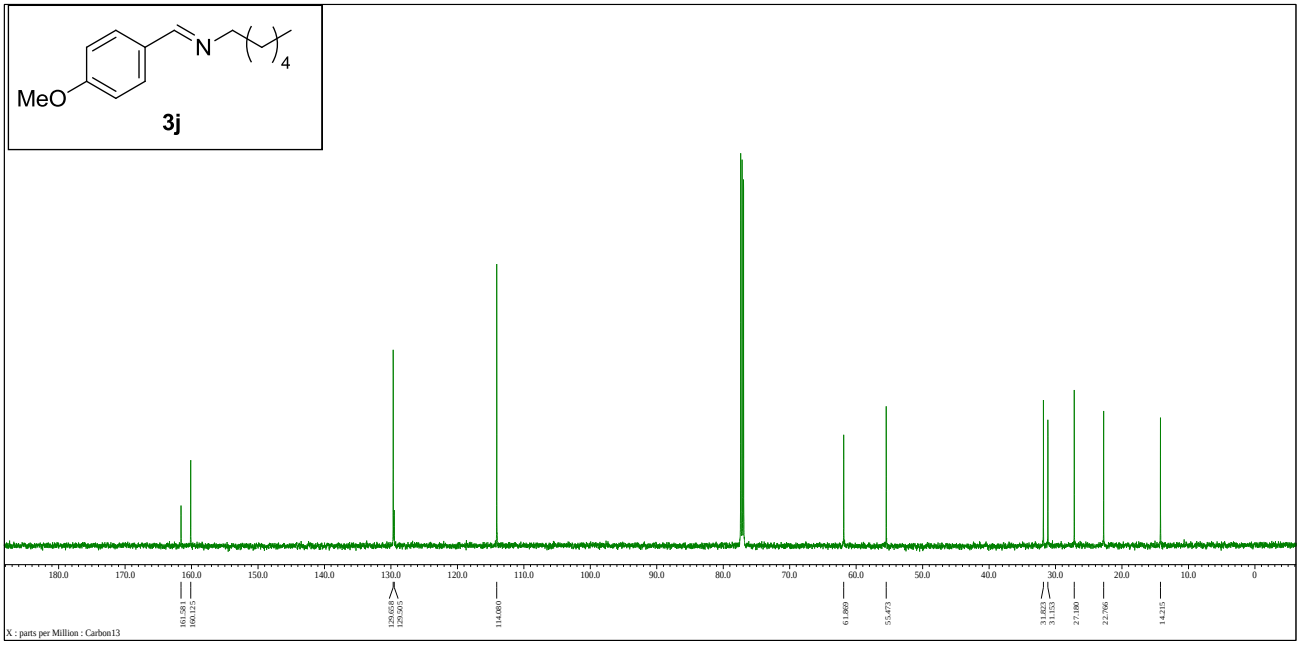
^{1}H-NMR Spectrum of compound **3i** (600 MHz, $CDCl_3$)



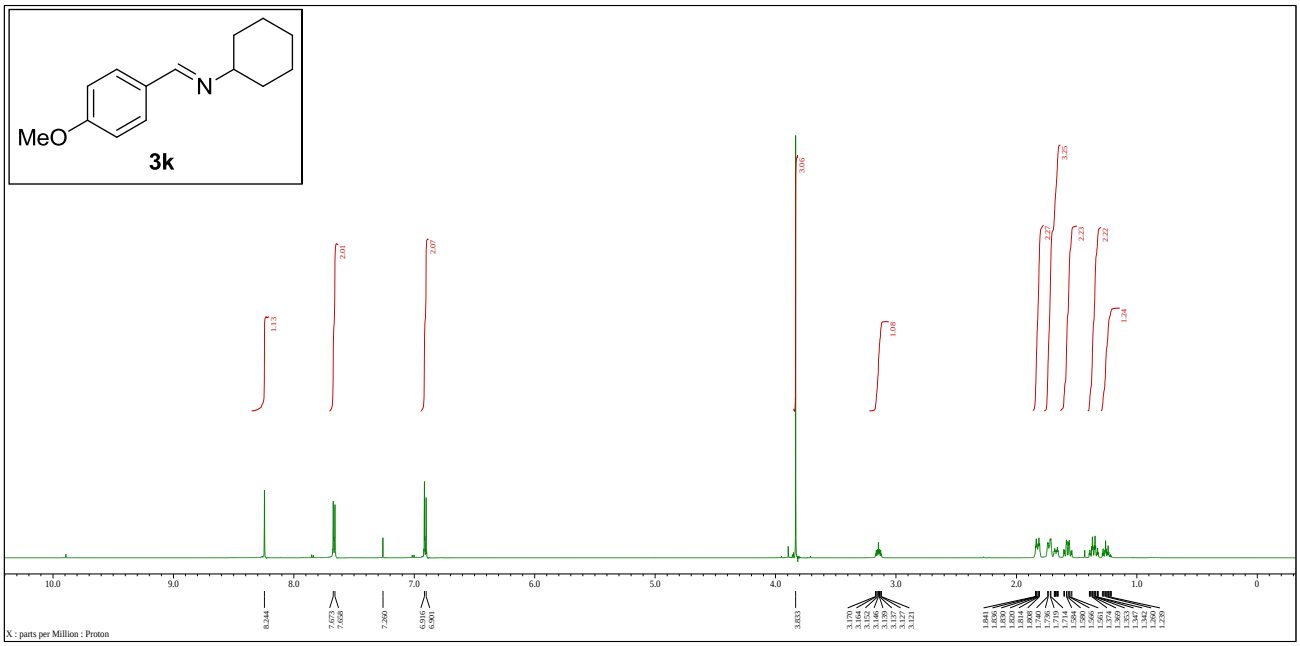
^{13}C-NMR Spectrum of compound **3i** (150 MHz, $CDCl_3$)



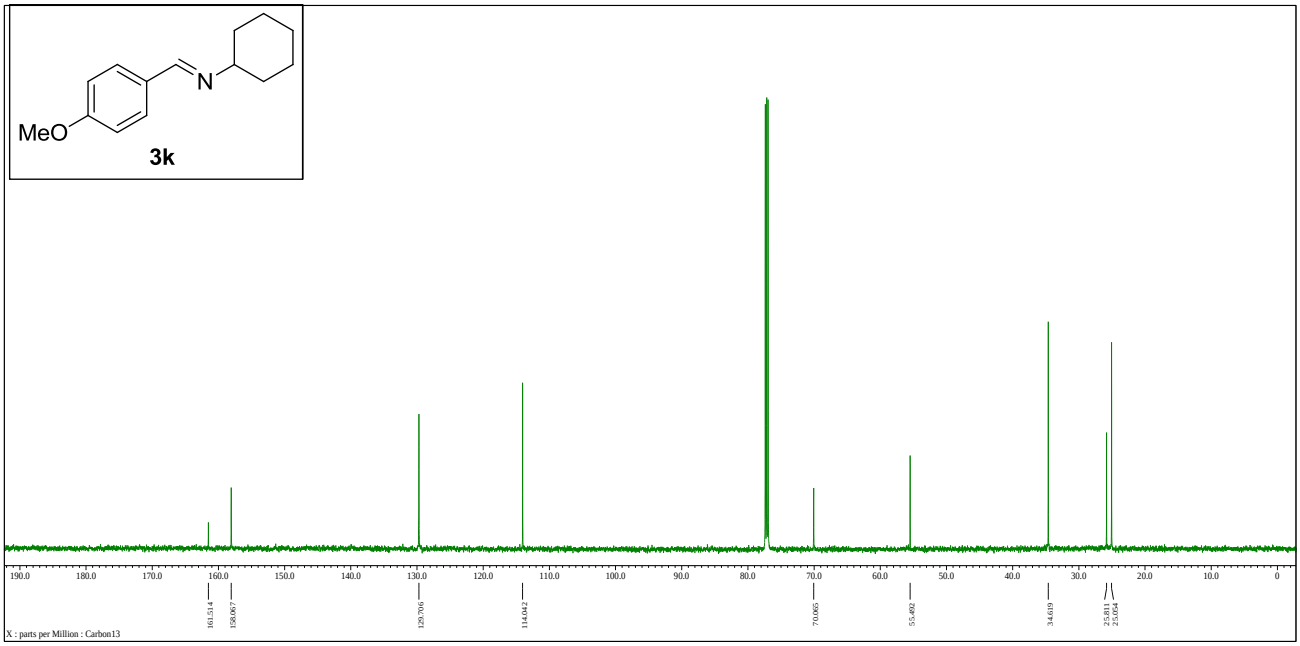
^{1}H-NMR Spectrum of compound **3j** (600 MHz, $CDCl_3$)



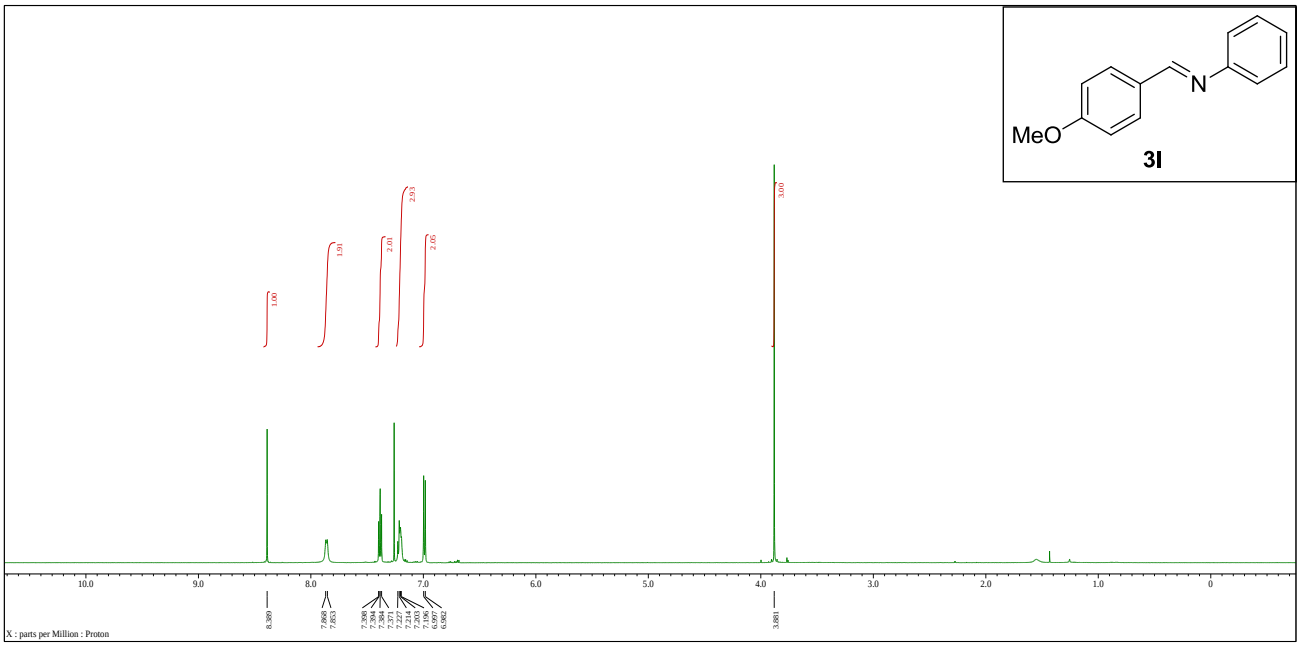
^{13}C-NMR Spectrum of compound **3j** (150 MHz, $CDCl_3$)



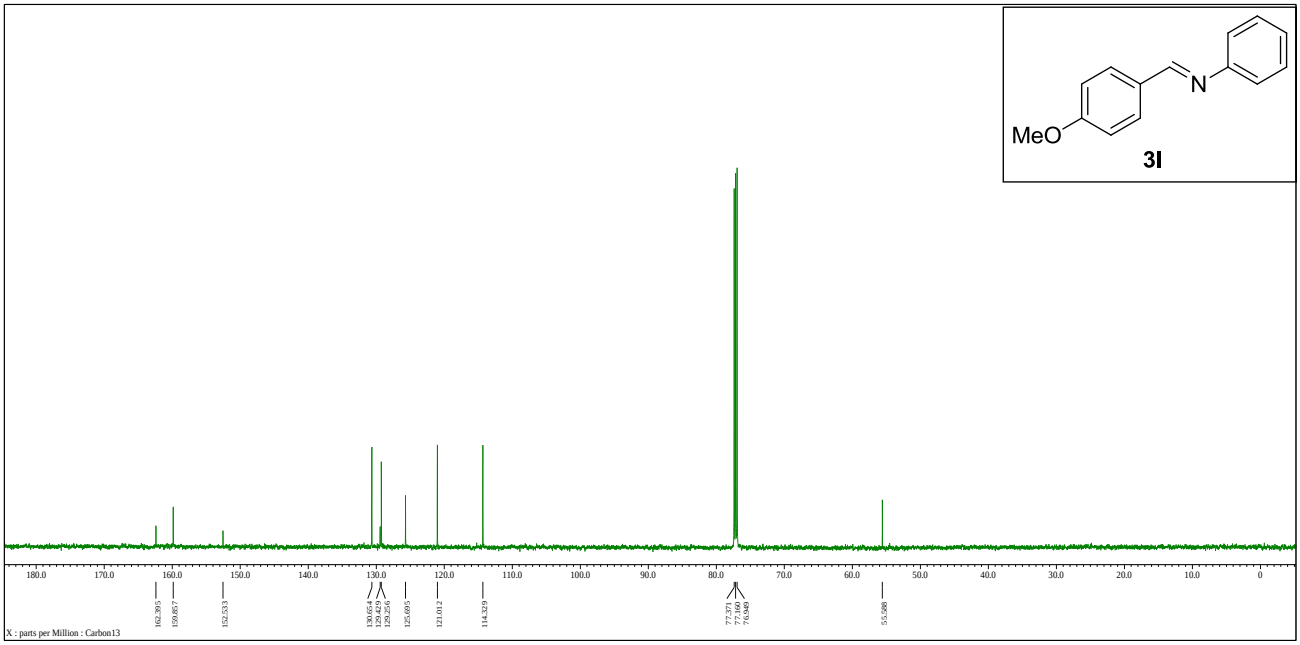
^{1}H-NMR Spectrum of compound **3k** (600 MHz, $CDCl_3$)



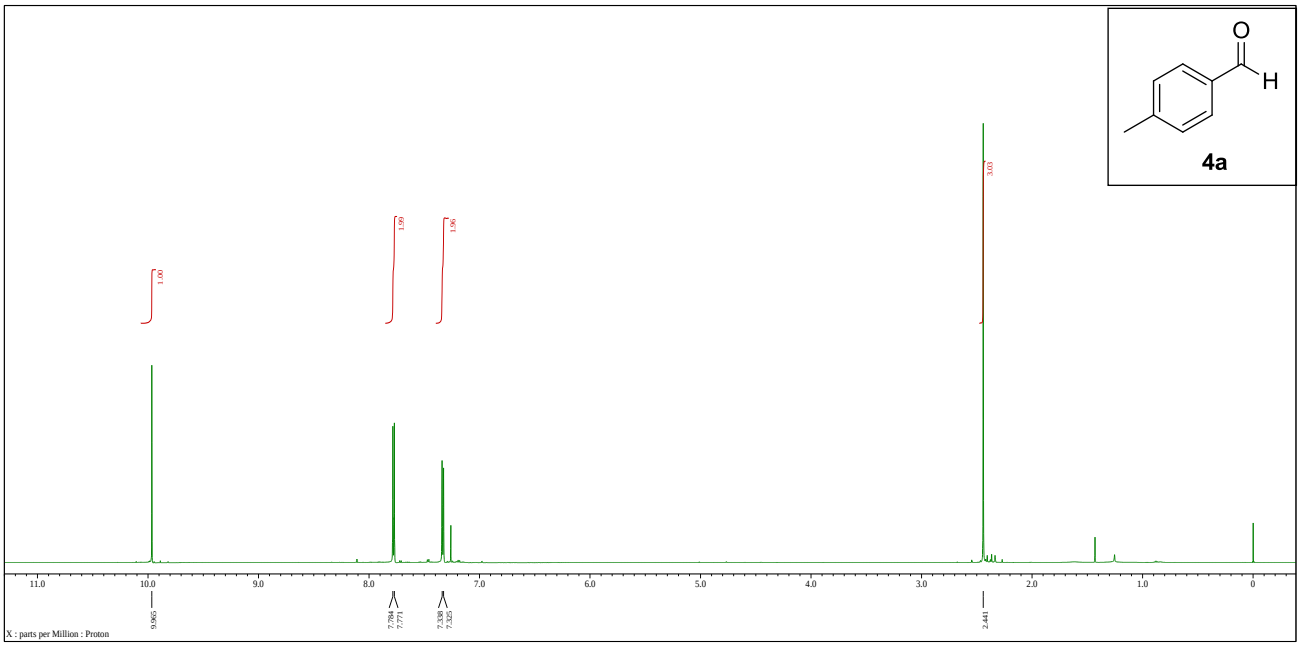
^{13}C-NMR Spectrum of compound **3k** (150 MHz, $CDCl_3$)



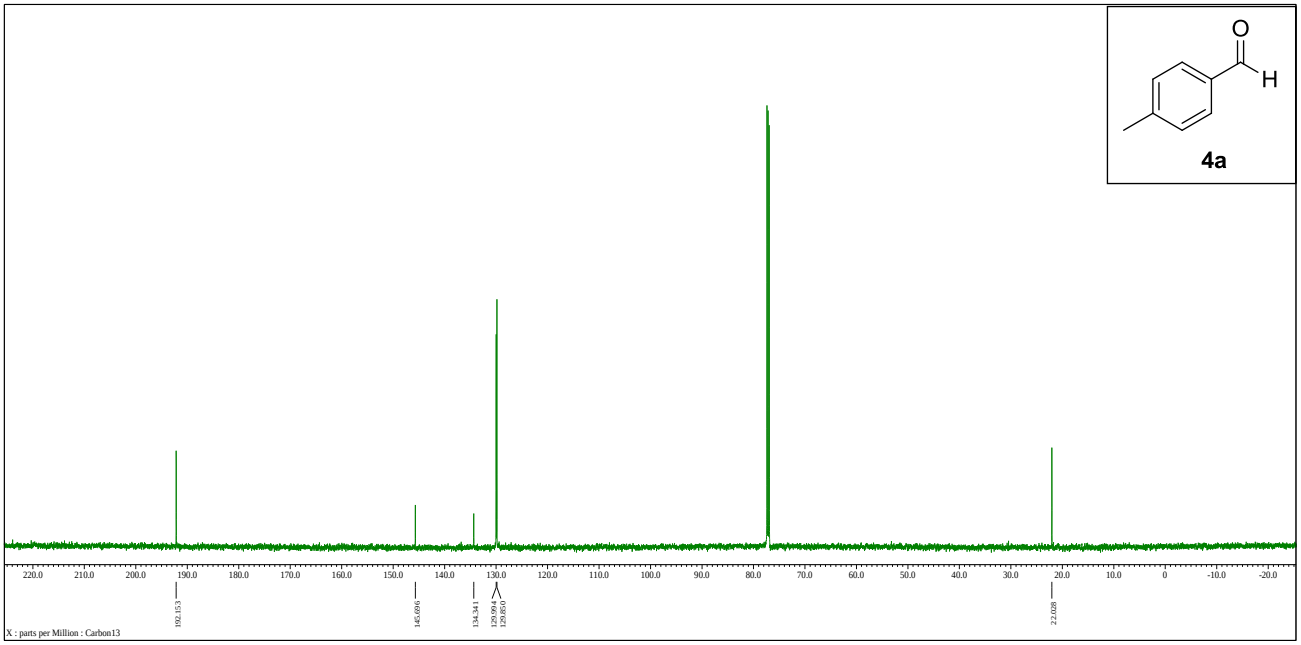
^{1}H-NMR Spectrum of compound **3l** (600 MHz, $CDCl_3$)



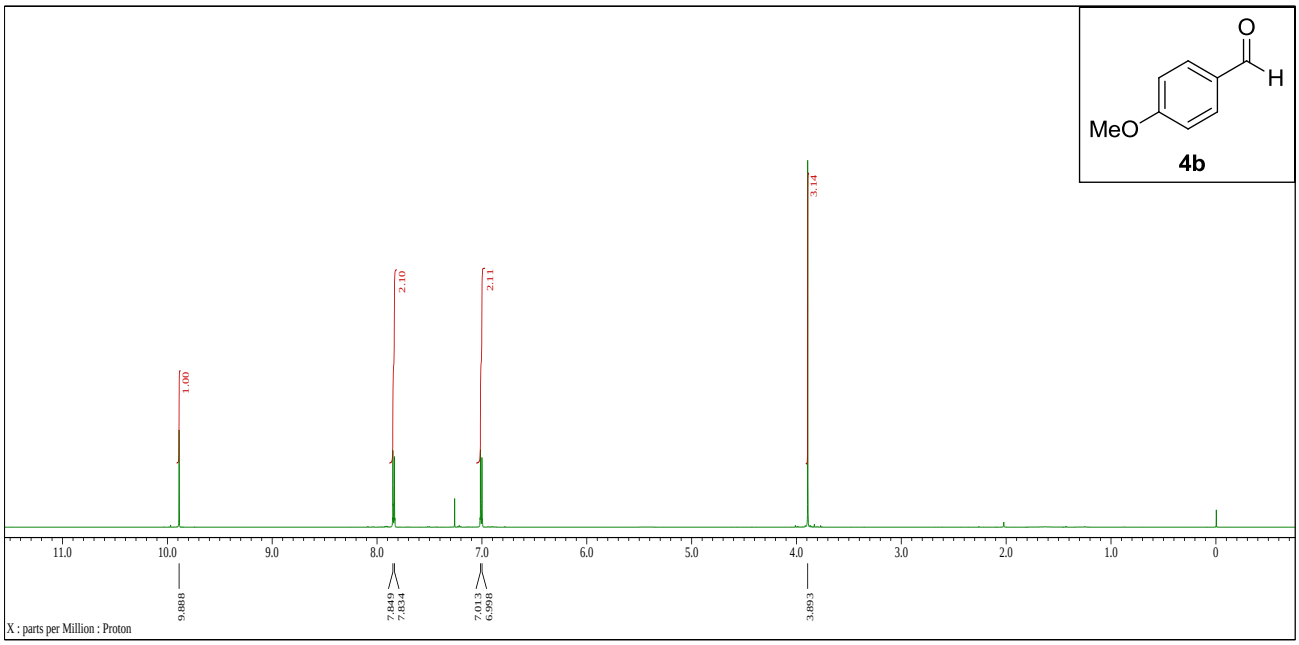
^{13}C-NMR Spectrum of compound **3l** (150 MHz, $CDCl_3$)



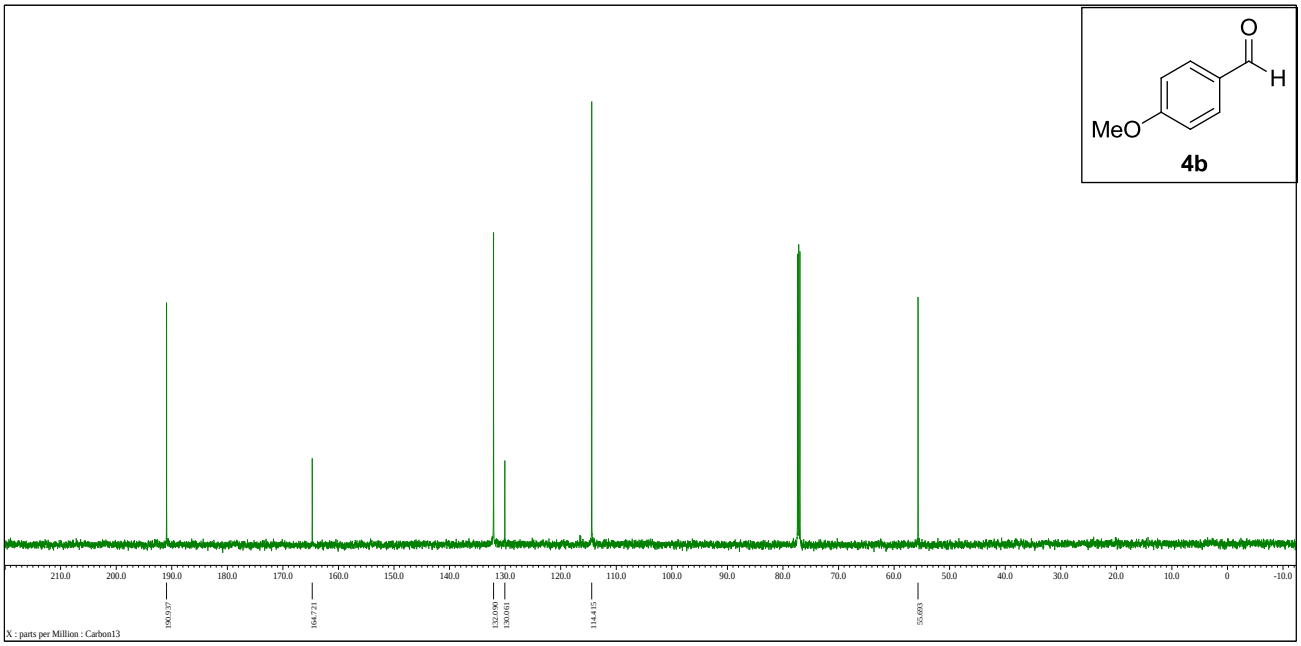
^{1}H-NMR Spectrum of compound **4a** (600 MHz, $CDCl_3$)



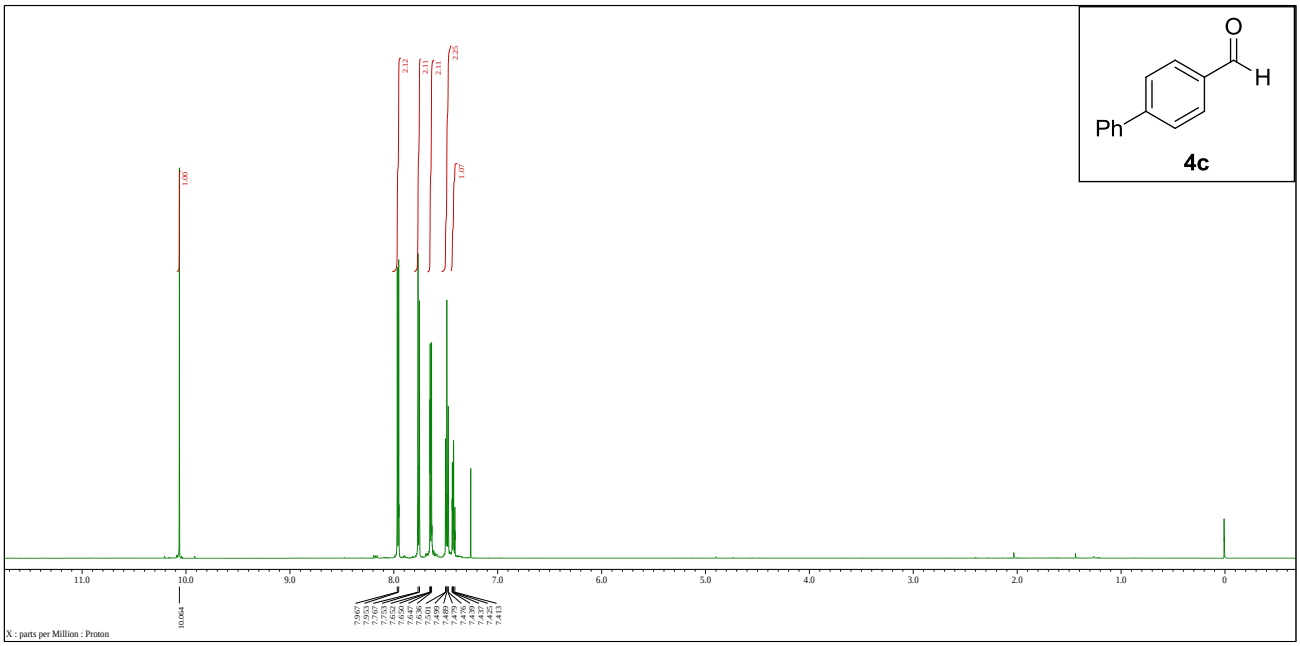
^{13}C-NMR Spectrum of compound **4a** (150 MHz, $CDCl_3$)



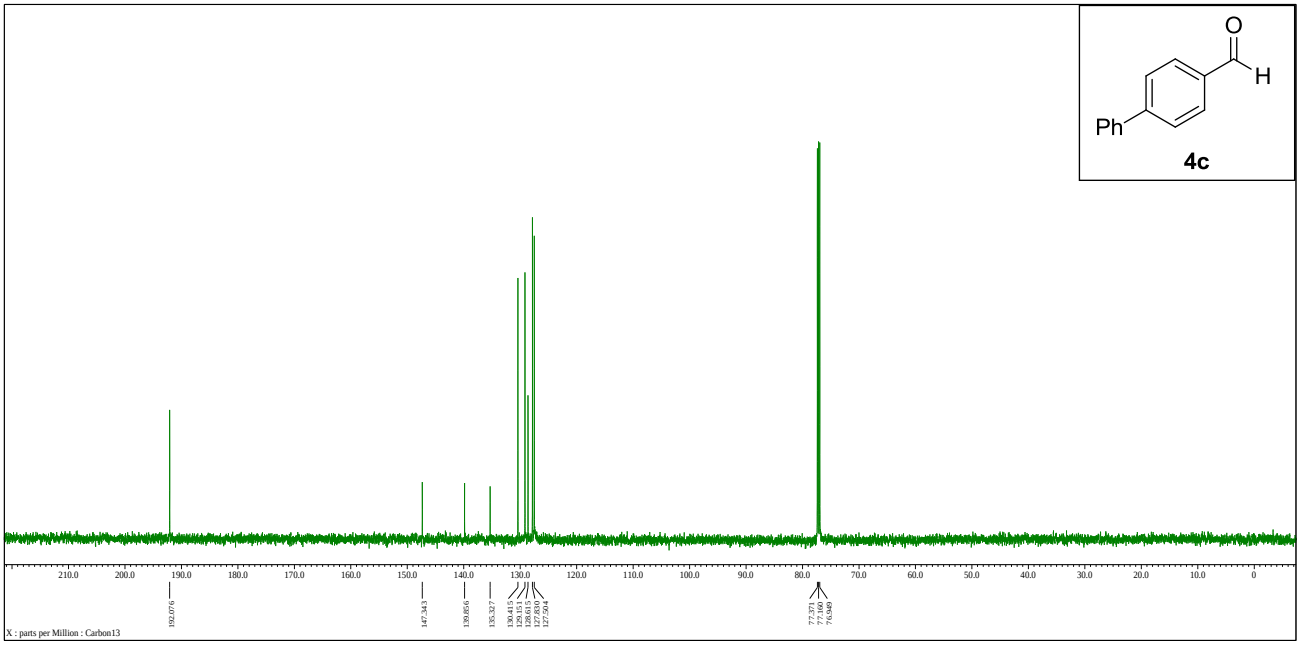
^{1}H-NMR Spectrum of compound **4b** (600 MHz, $CDCl_3$)



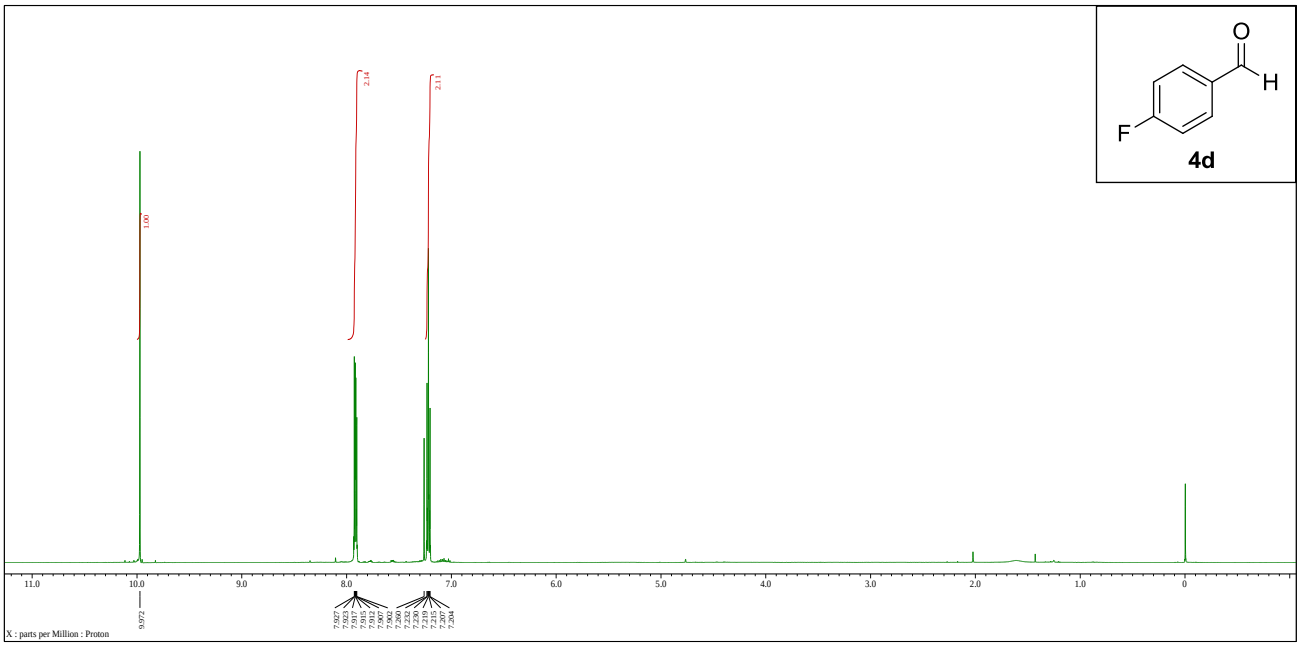
^{13}C-NMR Spectrum of compound **4b** (150 MHz, $CDCl_3$)



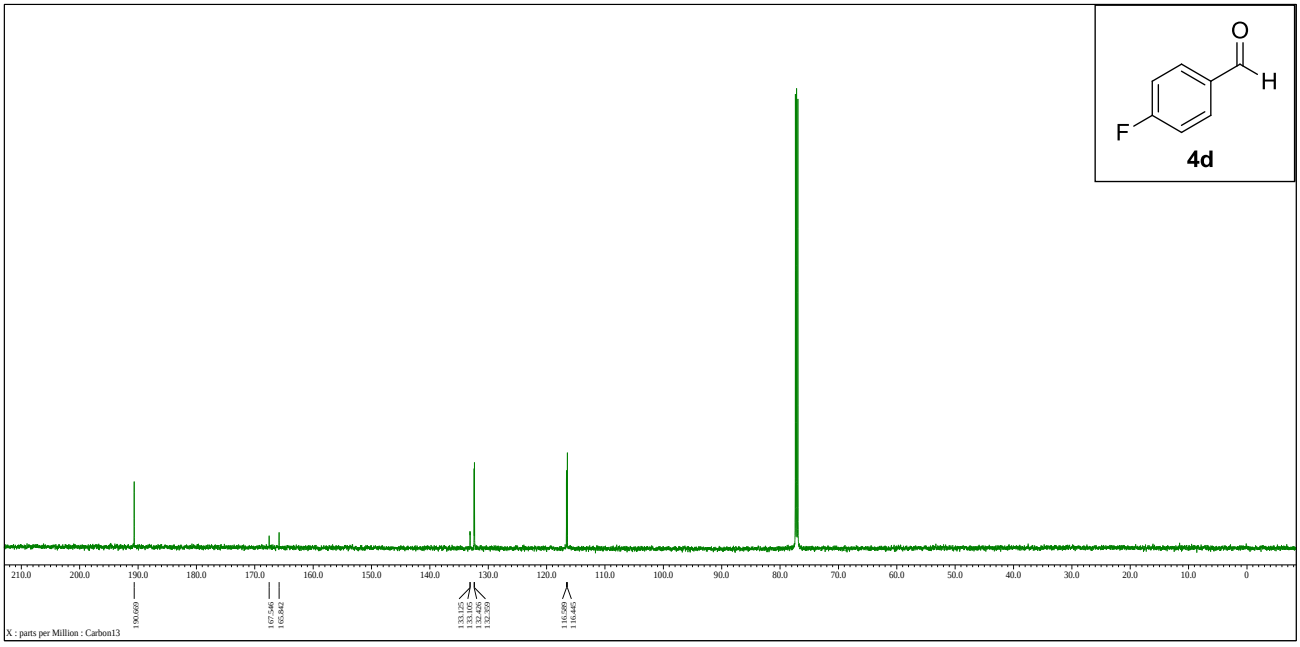
^{1}H-NMR Spectrum of compound **4c** (600 MHz, $CDCl_3$)



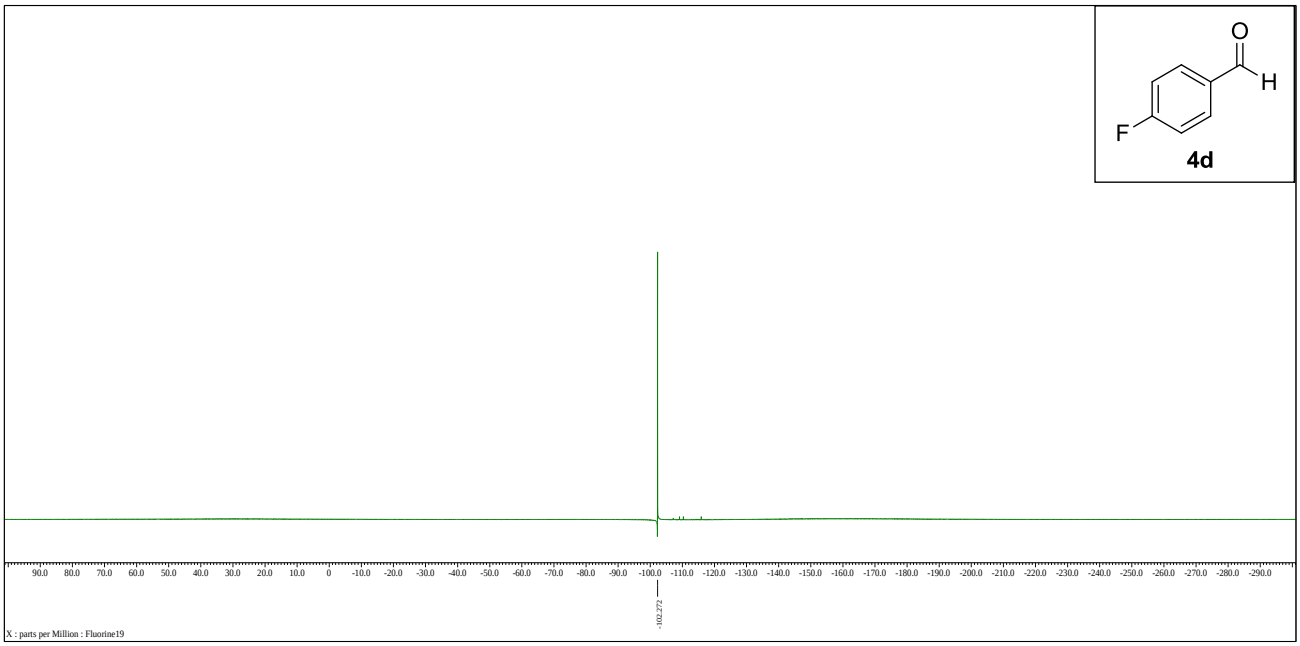
^{13}C-NMR Spectrum of compound **4c** (150 MHz, $CDCl_3$)



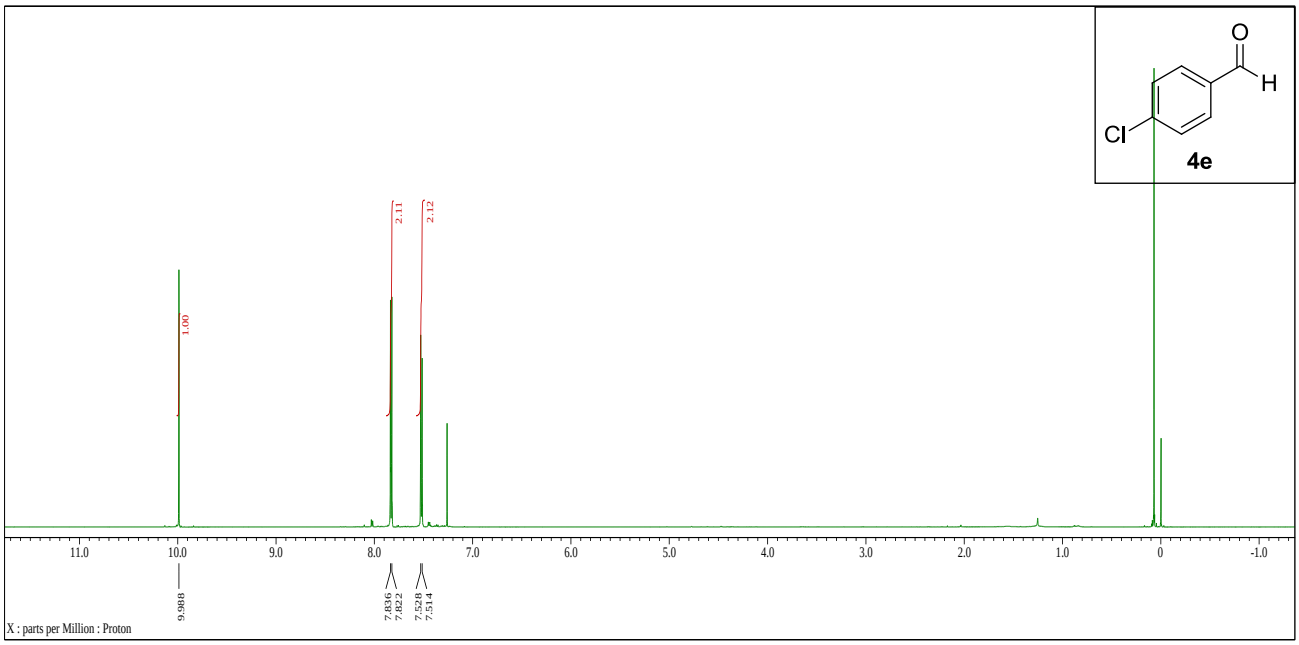
^{1}H-NMR Spectrum of compound **4d** (600 MHz, $CDCl_3$)



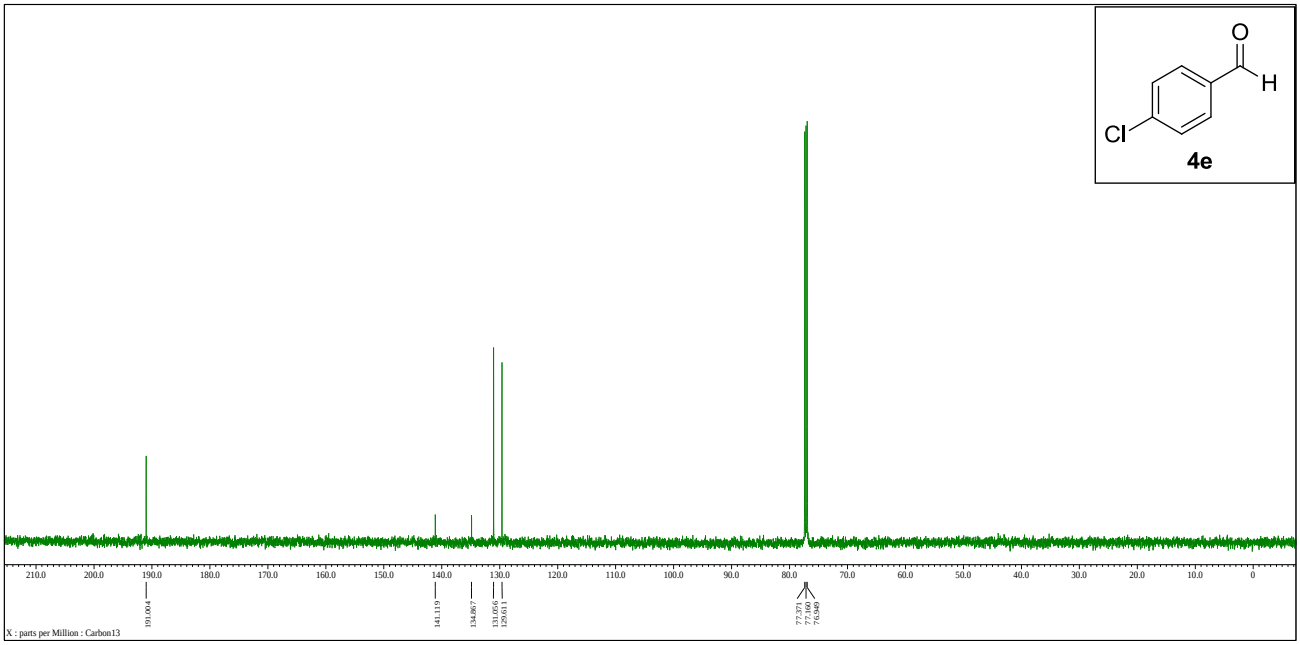
^{13}C-NMR Spectrum of compound **4d** (150 MHz, $CDCl_3$)



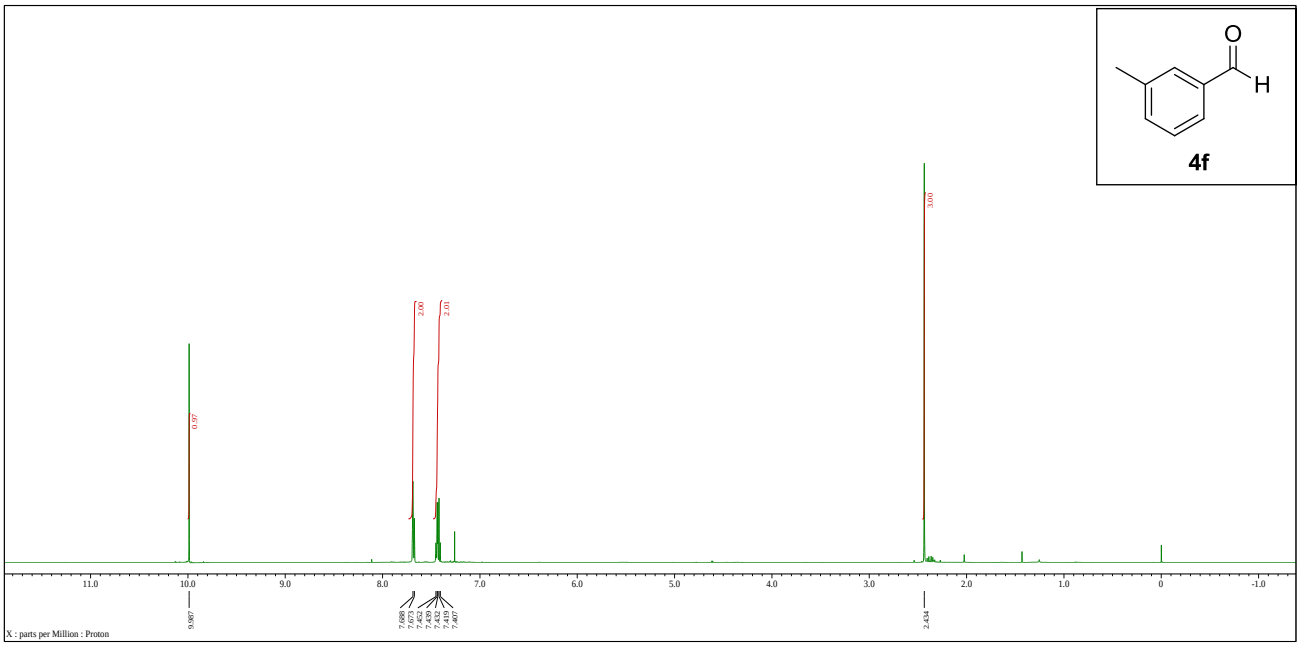
^{19}F-NMR Spectrum of compound **4d** (564 MHz, $CDCl_3$)



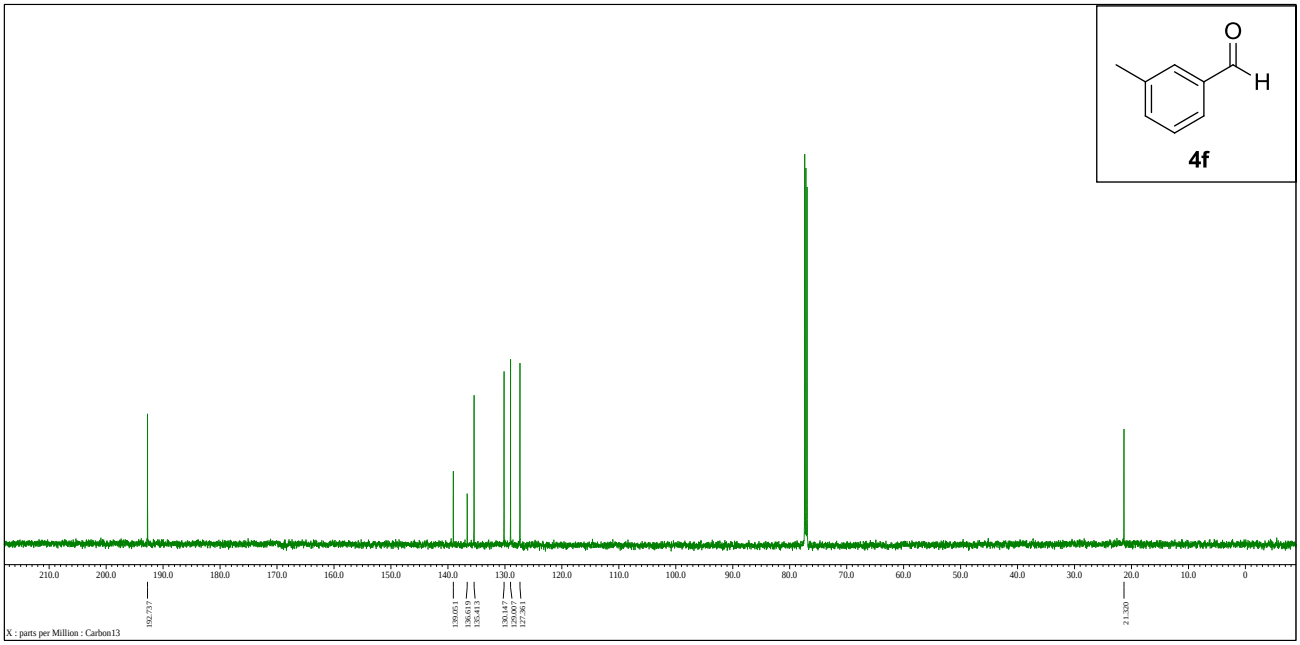
^{1}H-NMR Spectrum of compound **4e** (600 MHz, $CDCl_3$)



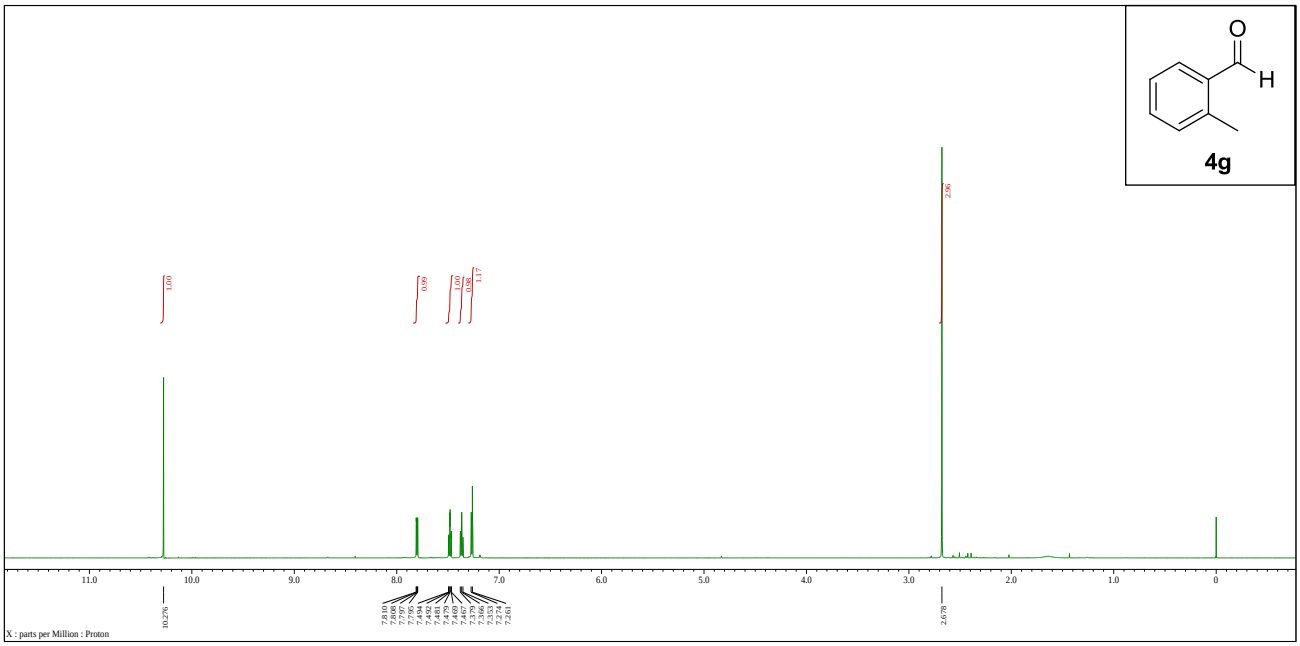
^{13}C-NMR Spectrum of compound **4e** (150 MHz, $CDCl_3$)



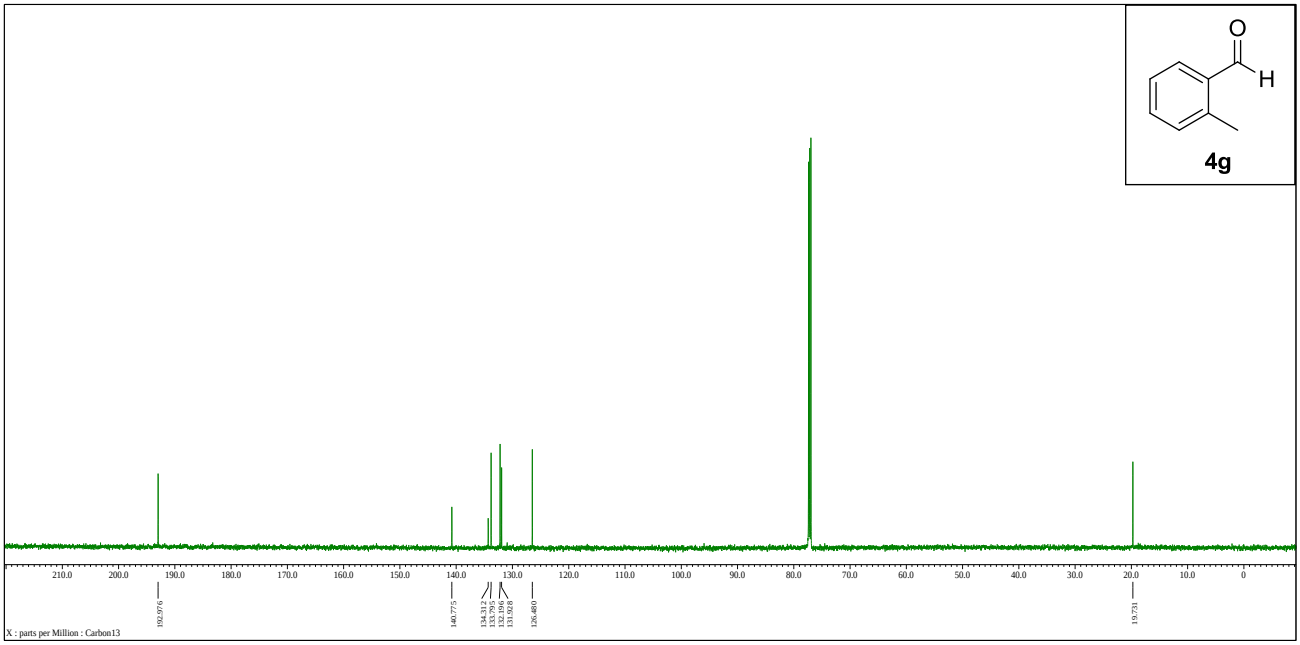
^{1}H-NMR Spectrum of compound **4f** (600 MHz, $CDCl_3$)



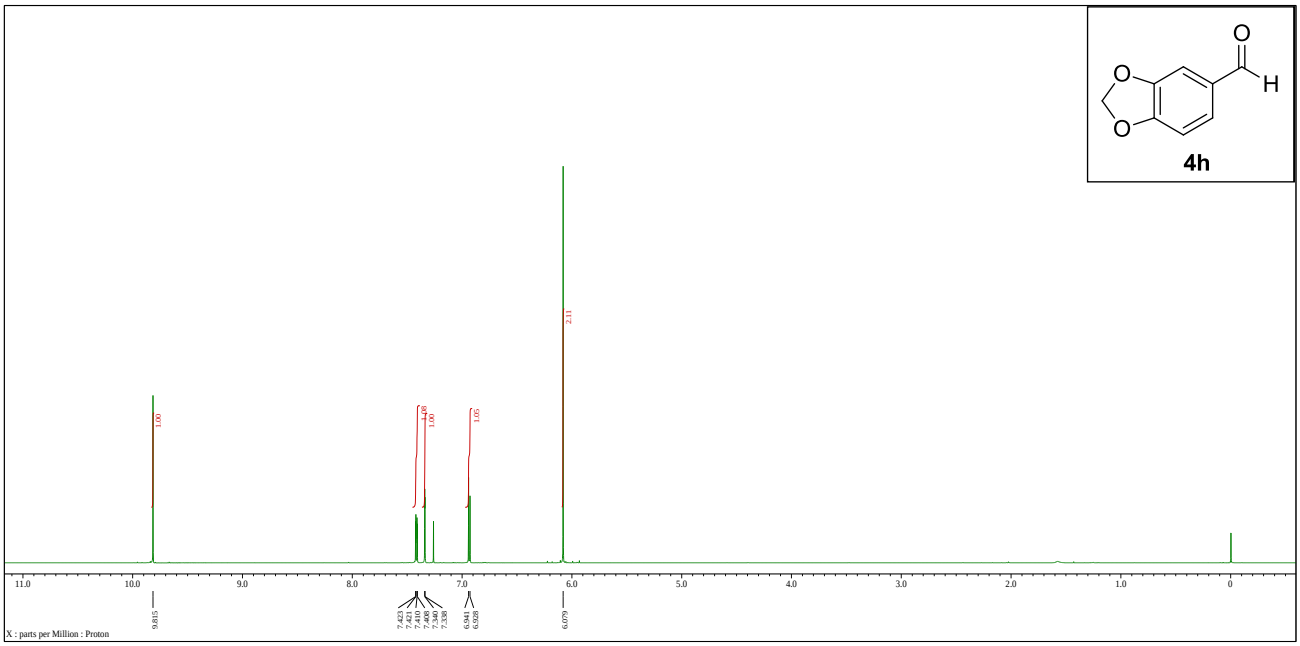
^{13}C-NMR Spectrum of compound **4f** (150 MHz, $CDCl_3$)



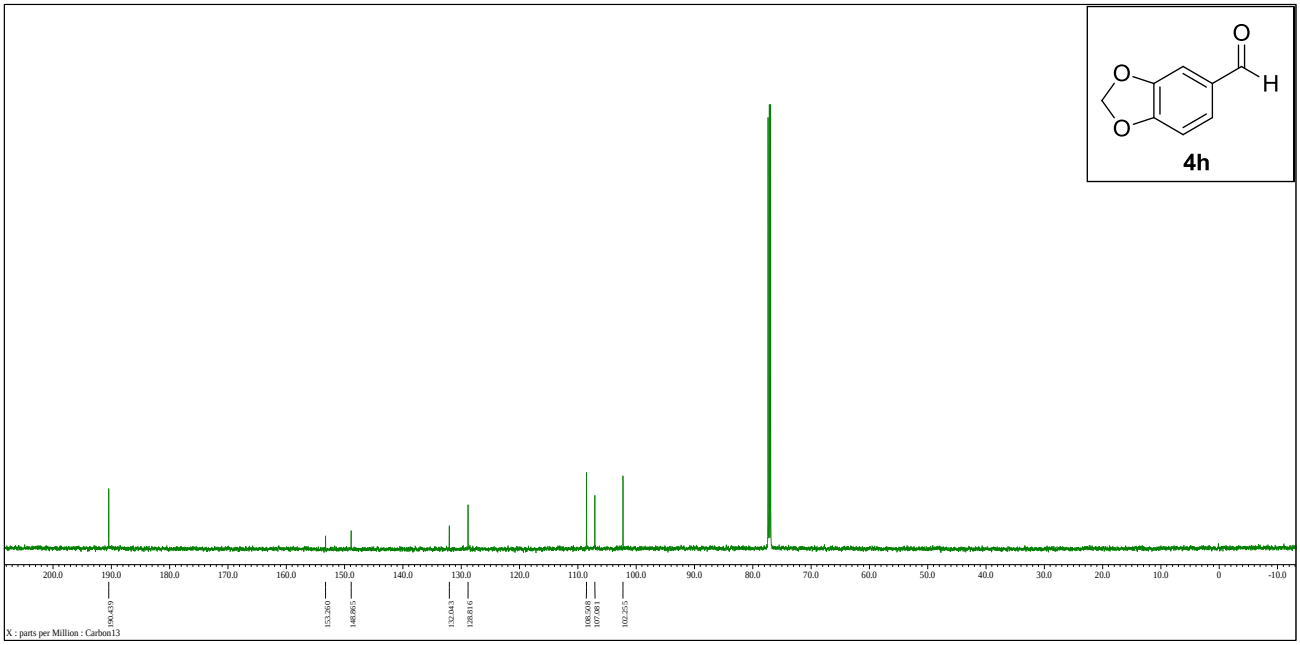
^{1}H-NMR Spectrum of compound **4g** (600 MHz, $CDCl_3$)



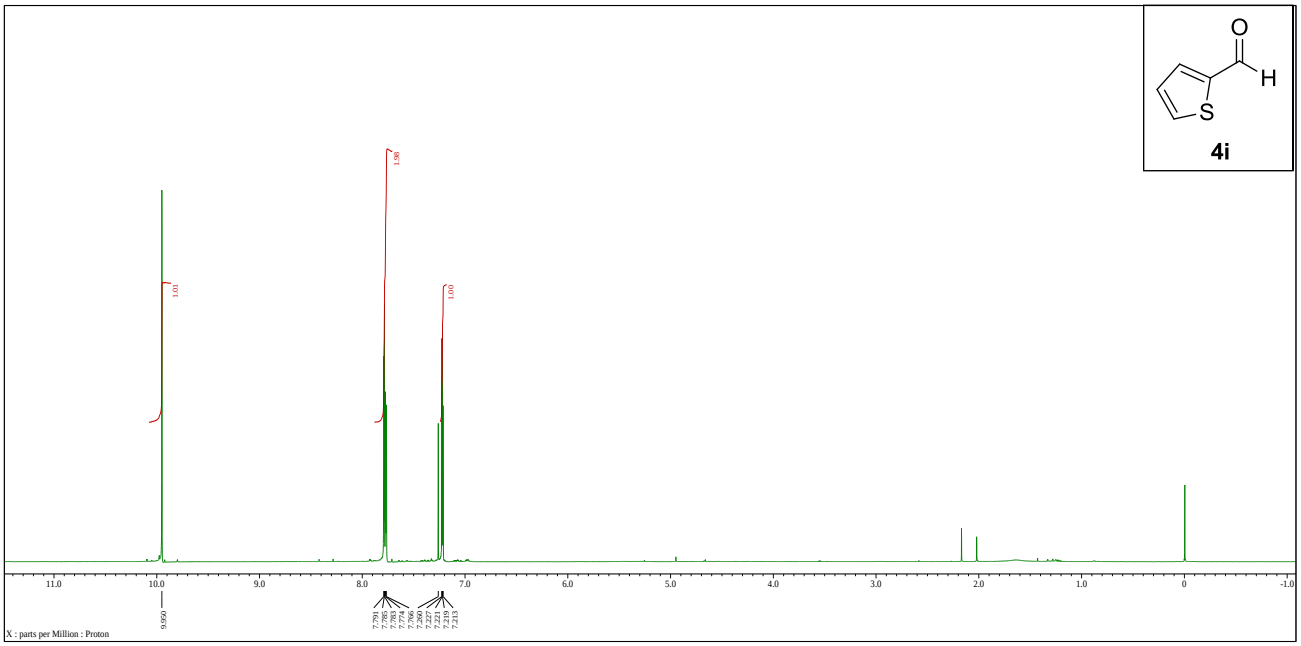
^{13}C-NMR Spectrum of compound **4g** (150 MHz, $CDCl_3$)



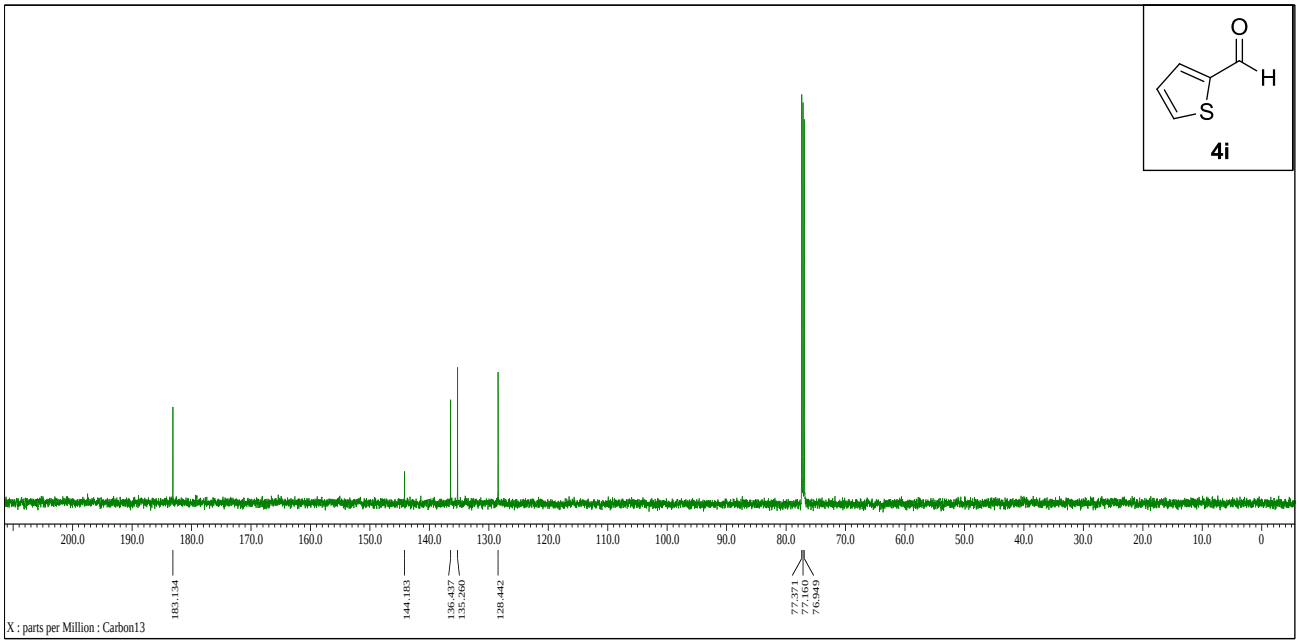
^{1}H-NMR Spectrum of compound **4h** (600 MHz, $CDCl_3$)



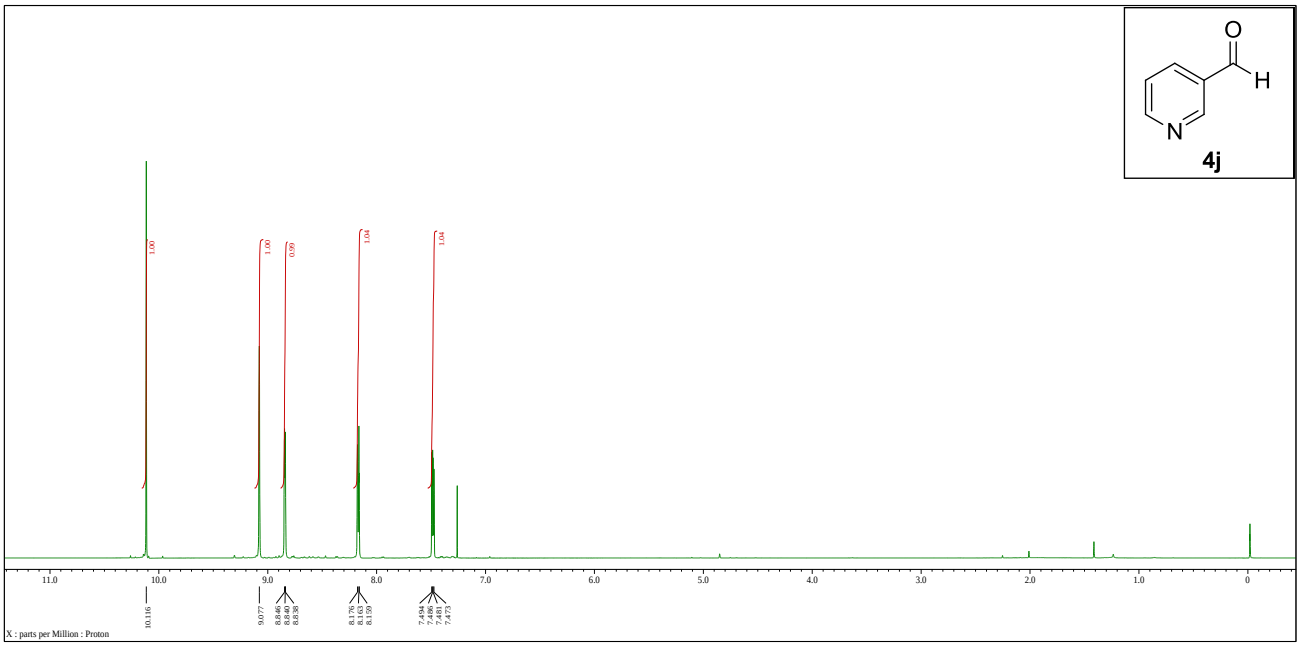
^{13}C-NMR Spectrum of compound **4h** (150 MHz, $CDCl_3$)



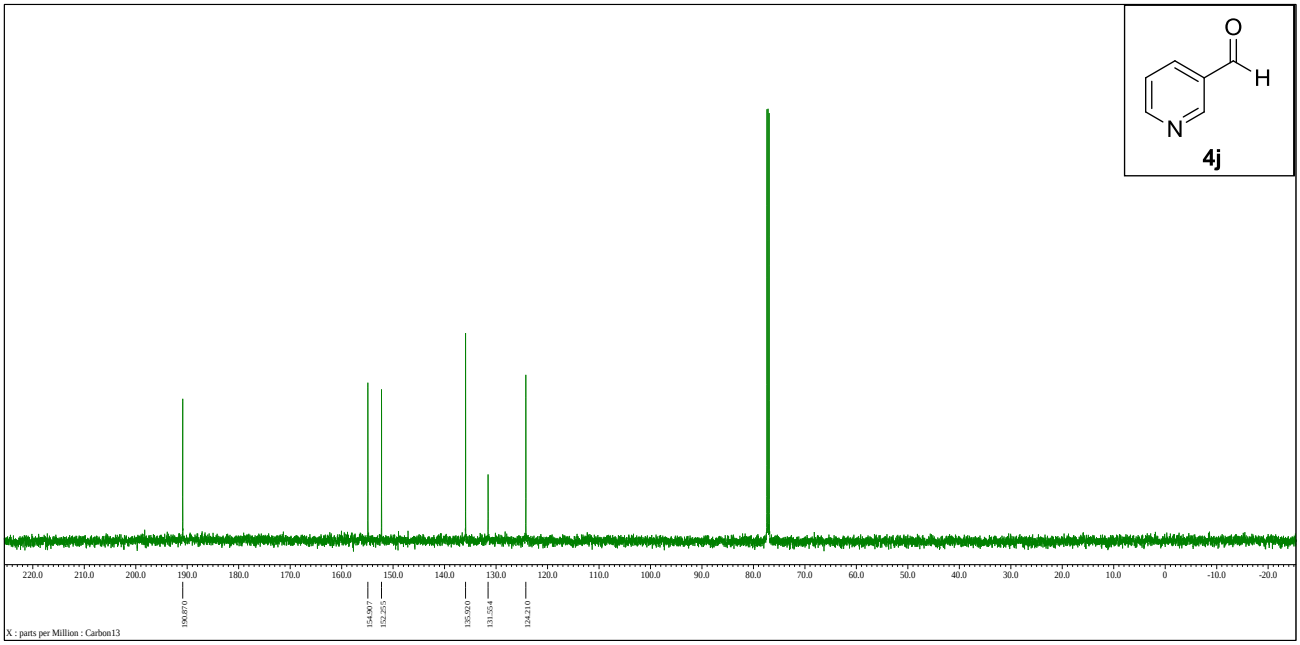
^{1}H-NMR Spectrum of compound **4i** (600 MHz, $CDCl_3$)



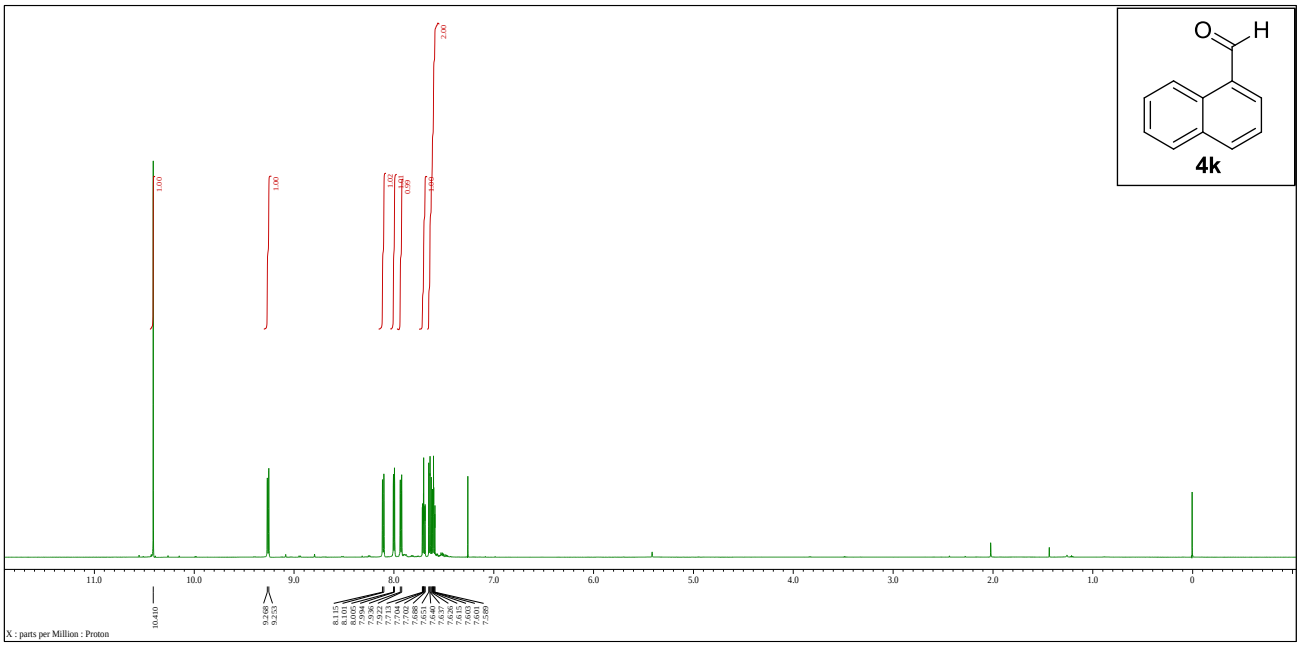
^{13}C-NMR Spectrum of compound **4i** (150 MHz, $CDCl_3$)



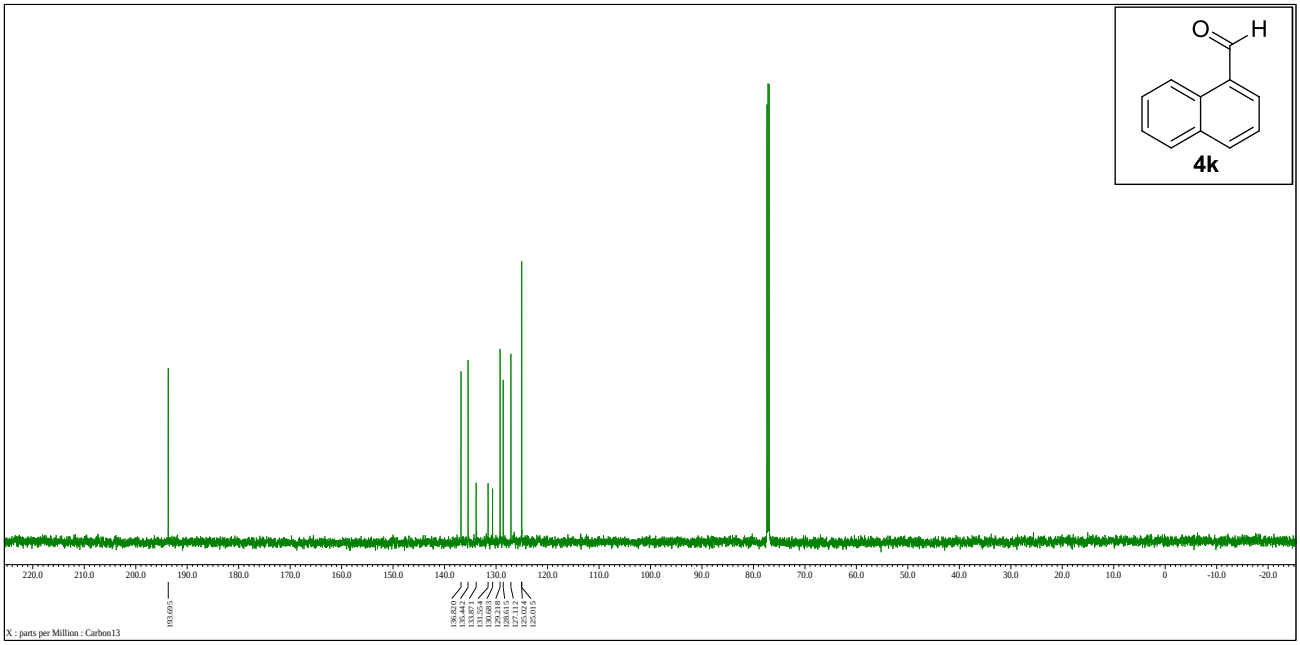
^{1}H-NMR Spectrum of compound **4j** (600 MHz, $CDCl_3$)



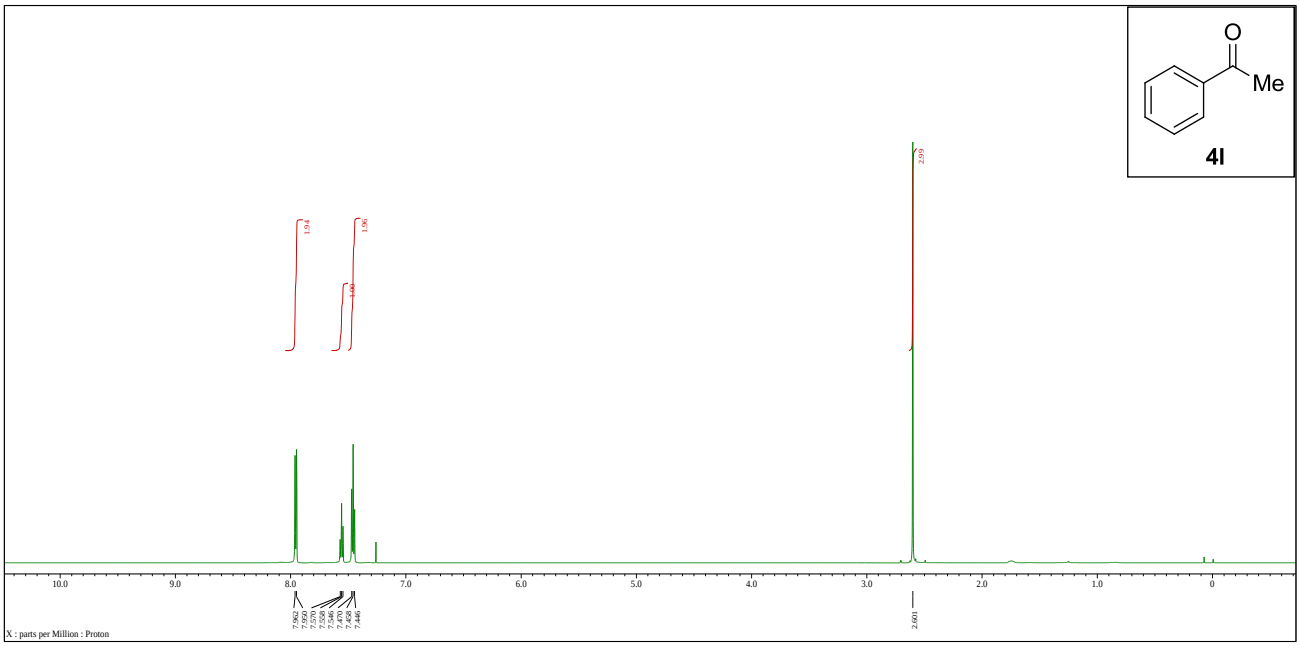
^{13}C-NMR Spectrum of compound **4j** (150 MHz, $CDCl_3$)



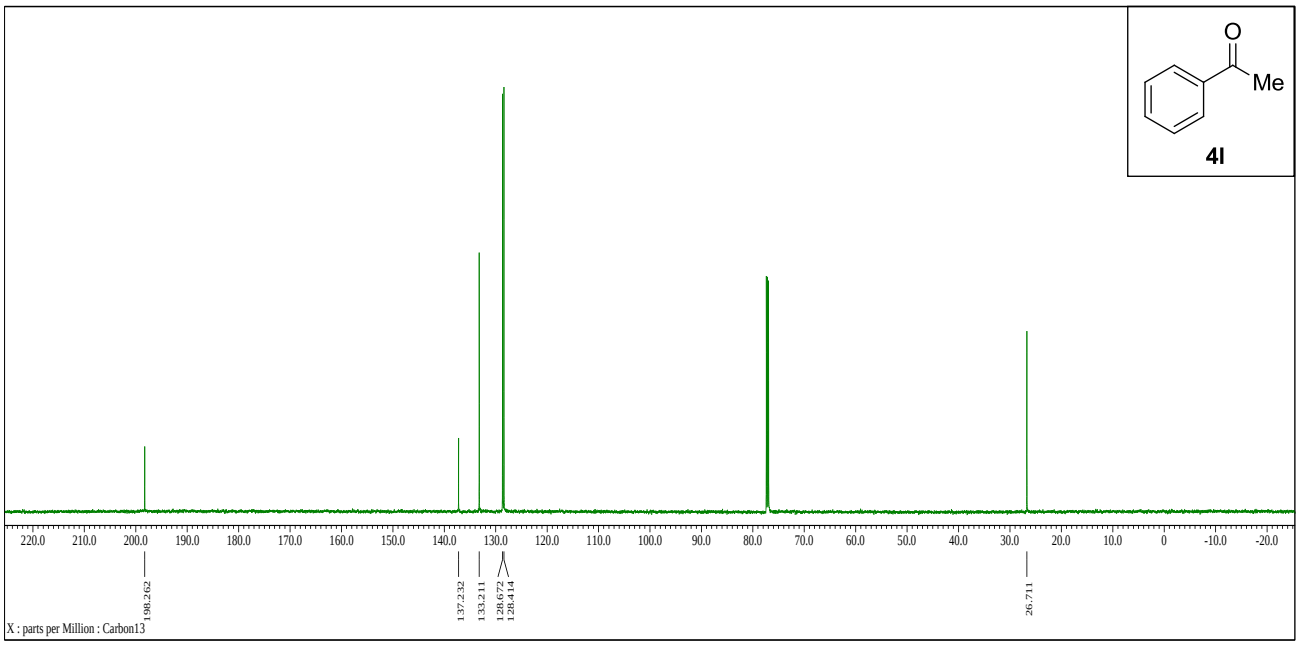
^{1}H-NMR Spectrum of compound **4k** (600 MHz, $CDCl_3$)



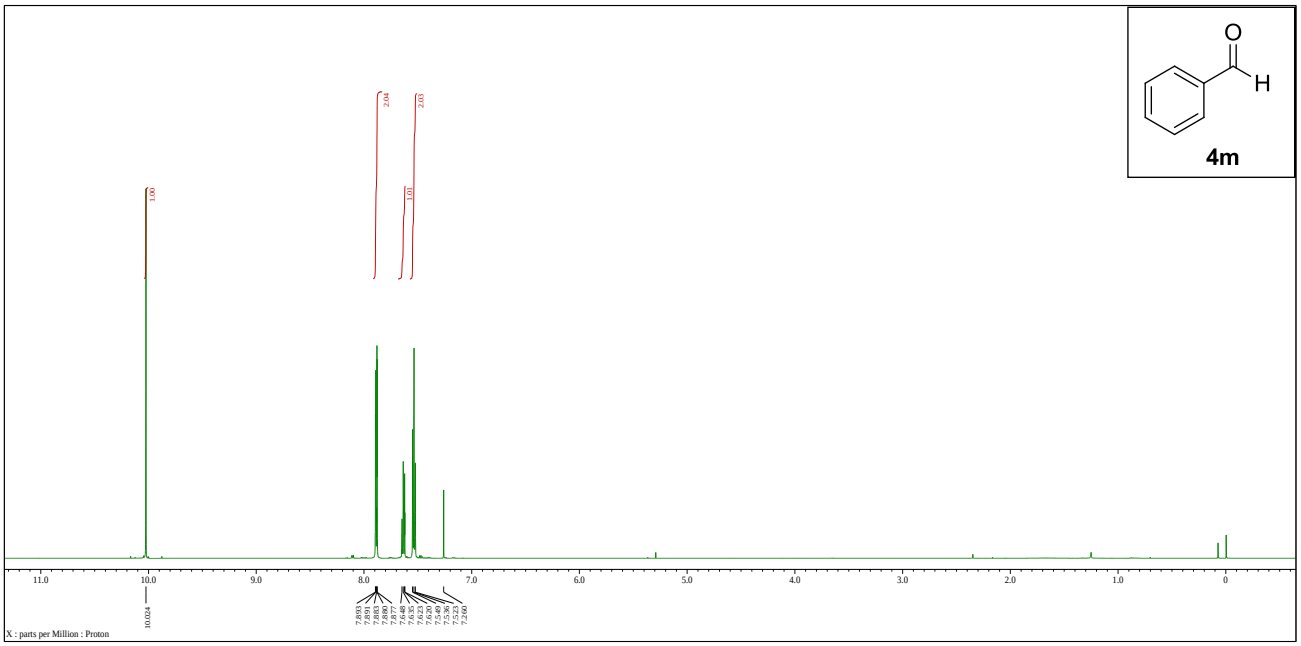
^{13}C-NMR Spectrum of compound **4k** (150 MHz, $CDCl_3$)



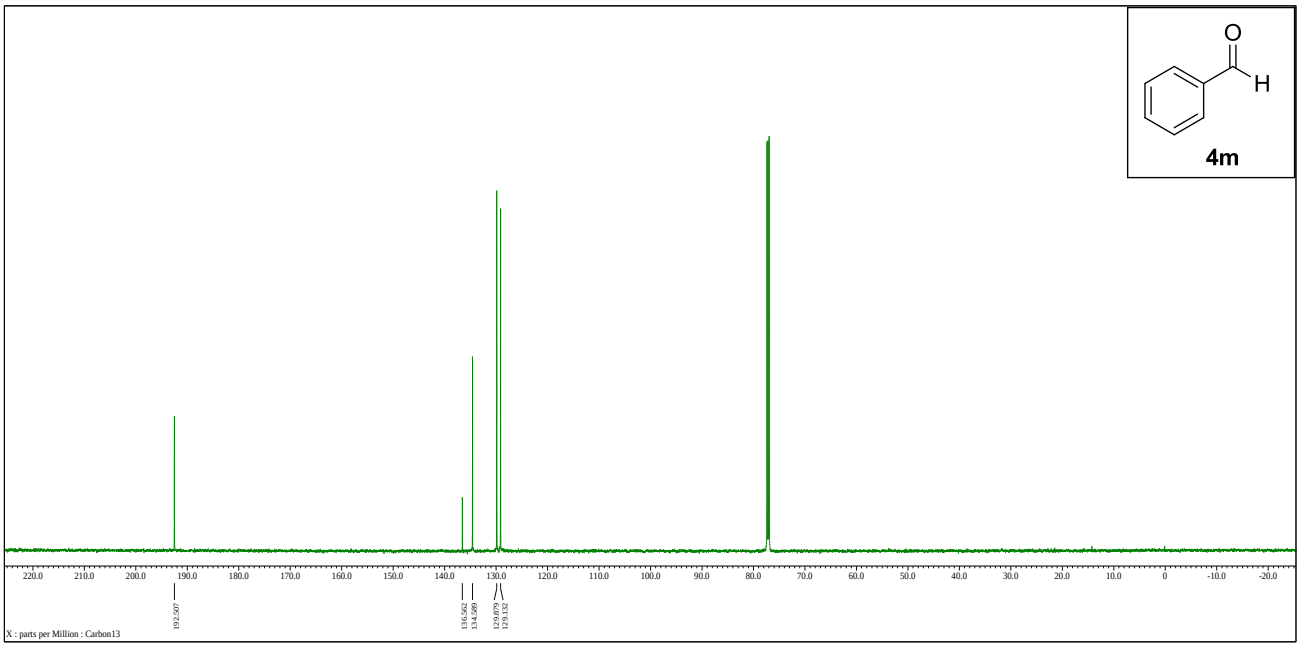
^{1}H-NMR Spectrum of compound **4l** (600 MHz, $CDCl_3$)



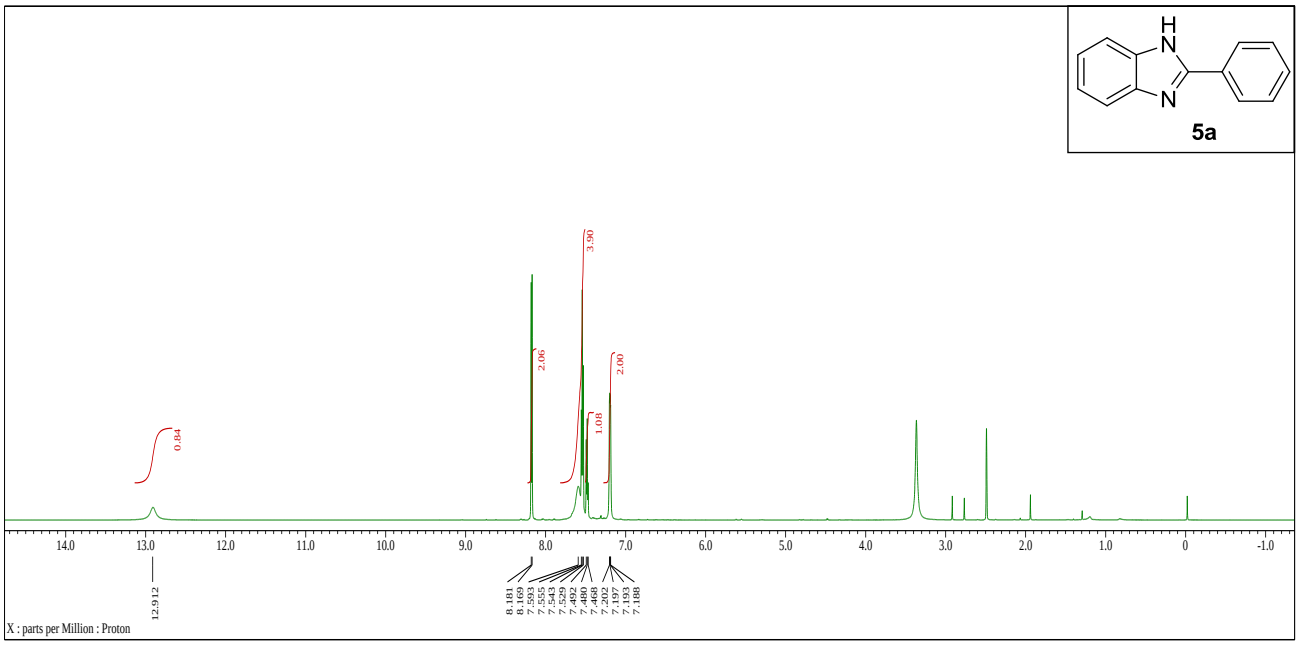
^{13}C-NMR Spectrum of compound **4l** (150 MHz, $CDCl_3$)



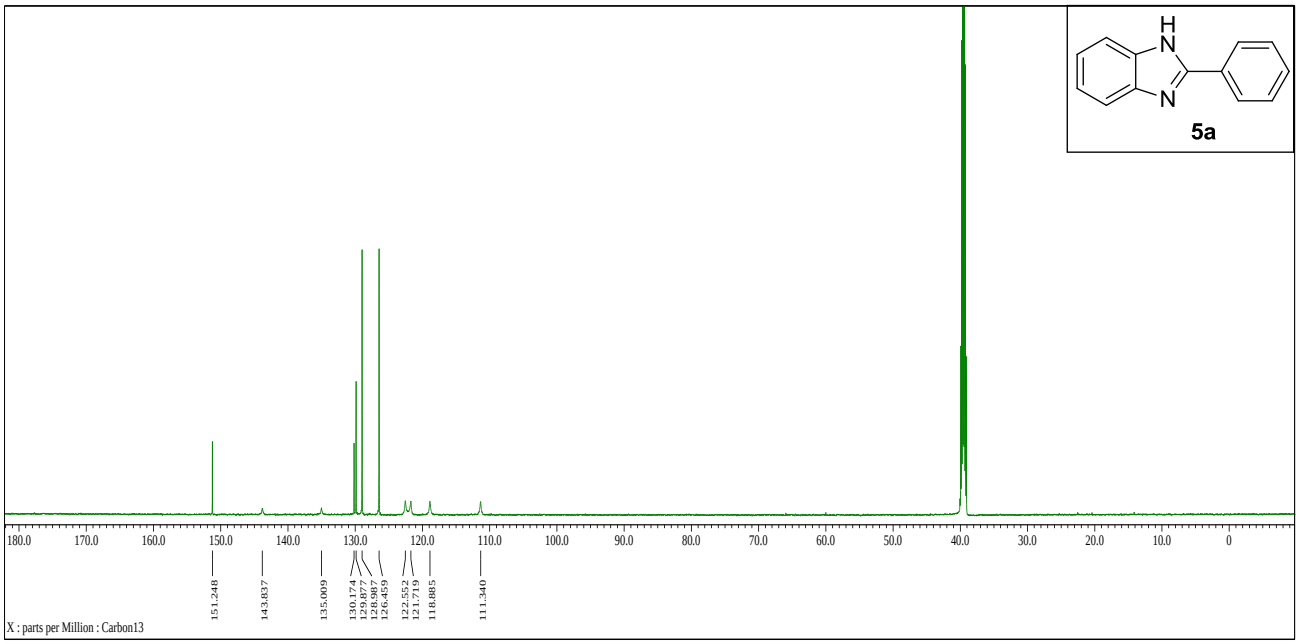
^{1}H-NMR Spectrum of compound **4m** (600 MHz, $CDCl_3$)



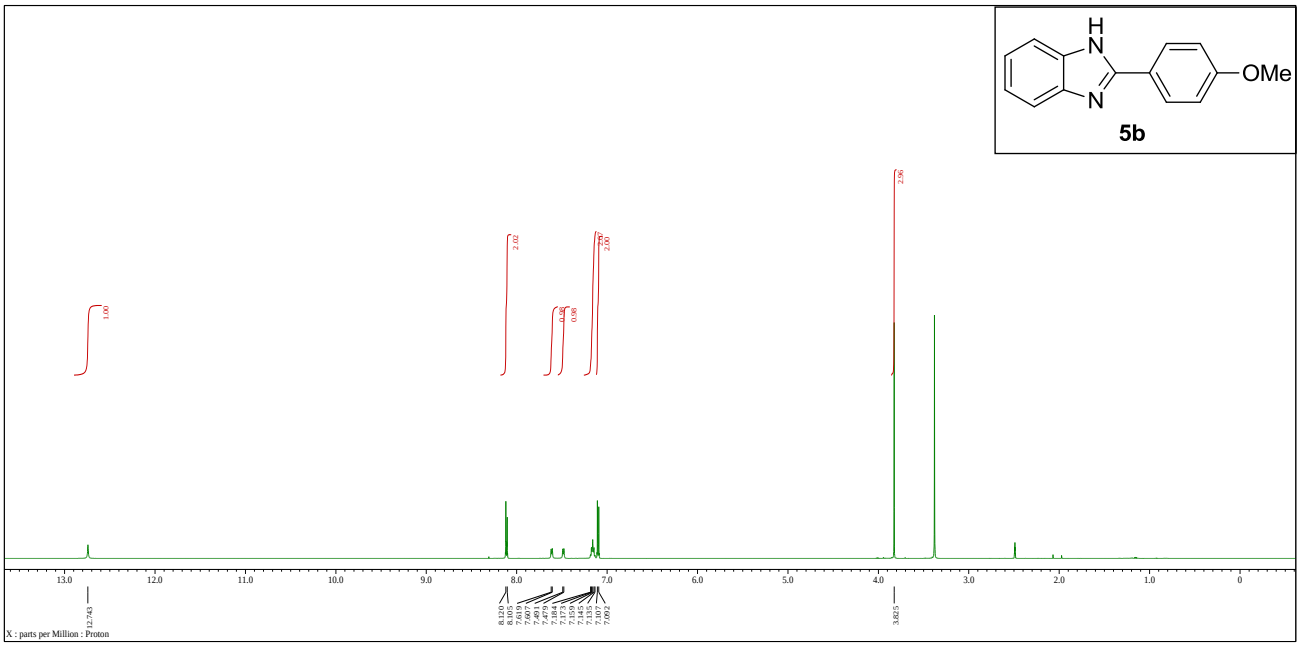
^{13}C-NMR Spectrum of compound **4m** (150 MHz, $CDCl_3$)



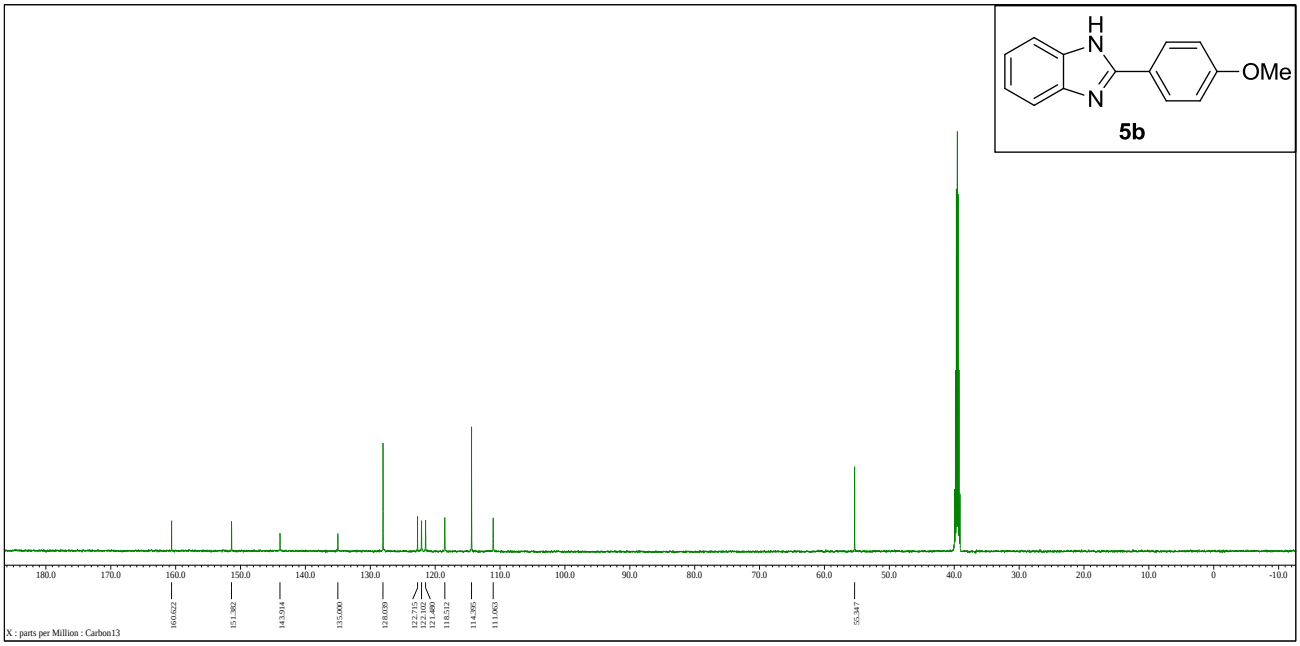
^{1}H-NMR Spectrum of compound **5a** (600 MHz, DMSO-d_6)



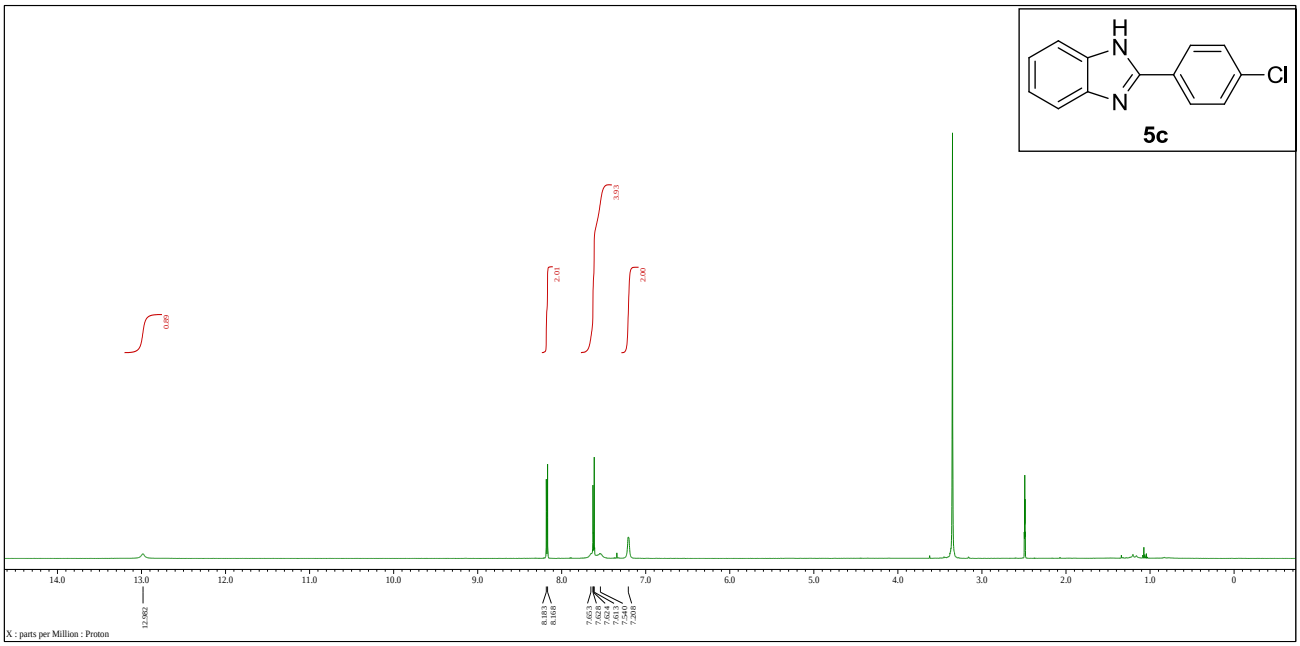
^{13}C-NMR Spectrum of compound **5a** (150 MHz, DMSO-d_6)



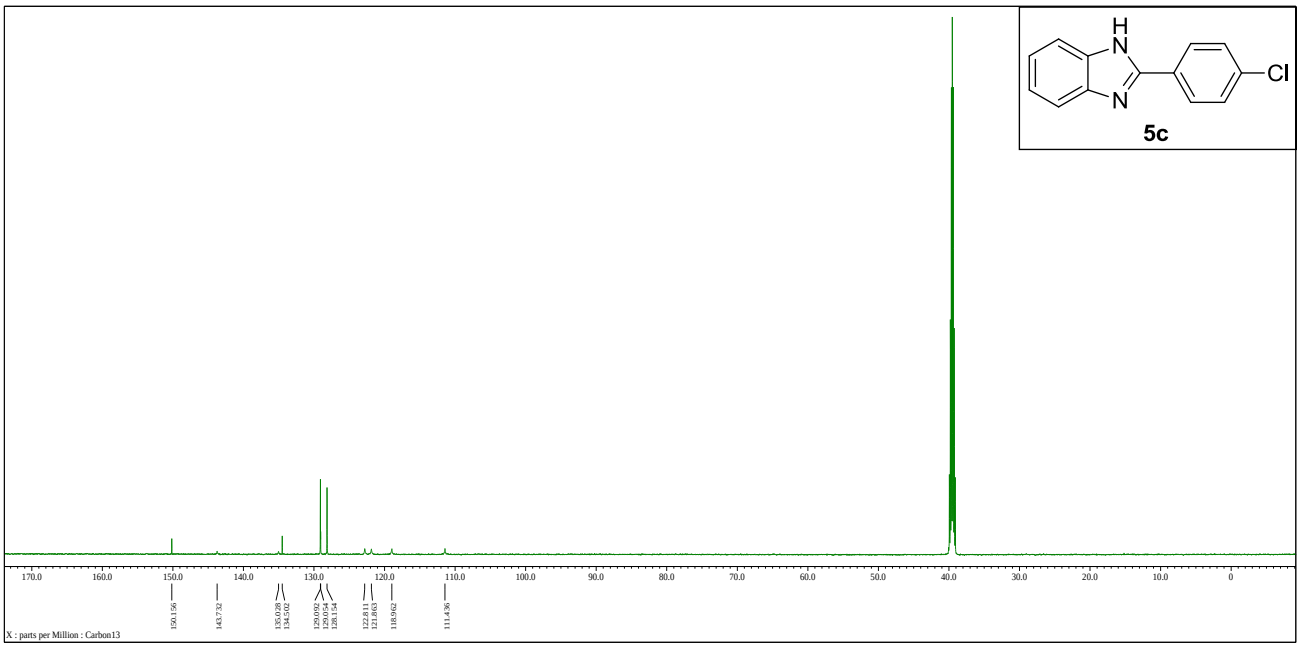
^{1}H-NMR Spectrum of compound **5b** (600 MHz, DMSO-d_6)



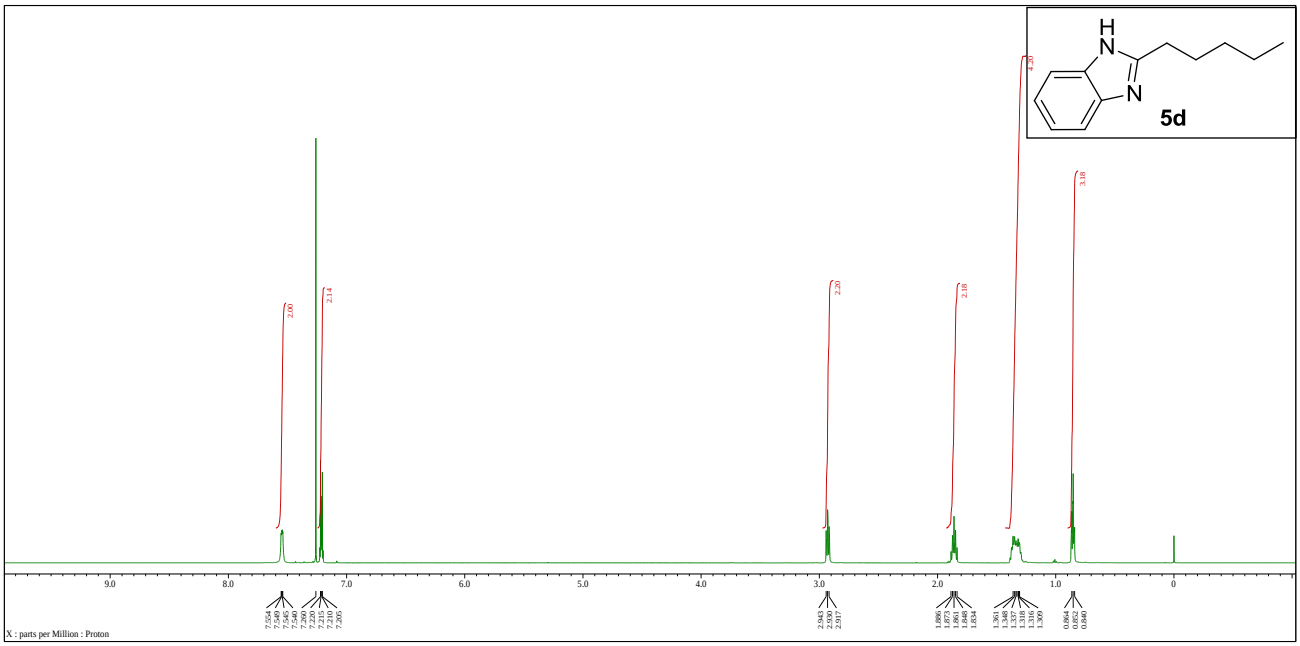
^{13}C-NMR Spectrum of compound **5b** (150 MHz, DMSO-d_6)



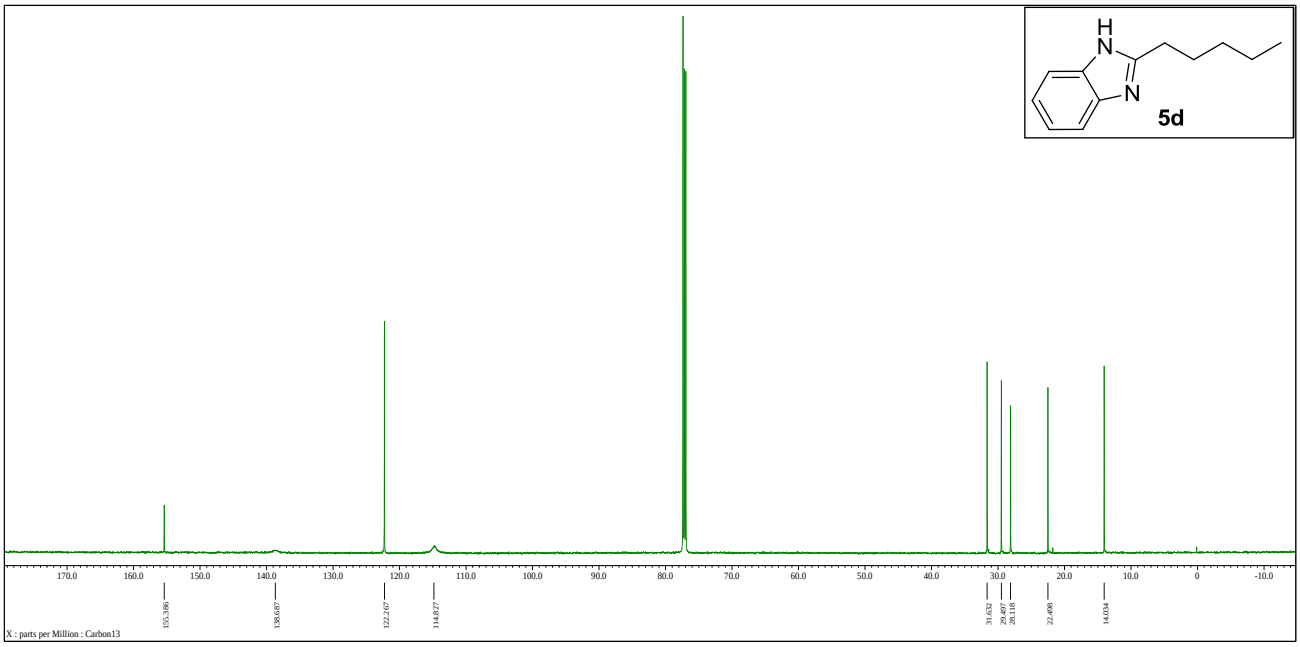
[1]H-NMR Spectrum of compound **5c** (600 MHz, DMSO-d_6)



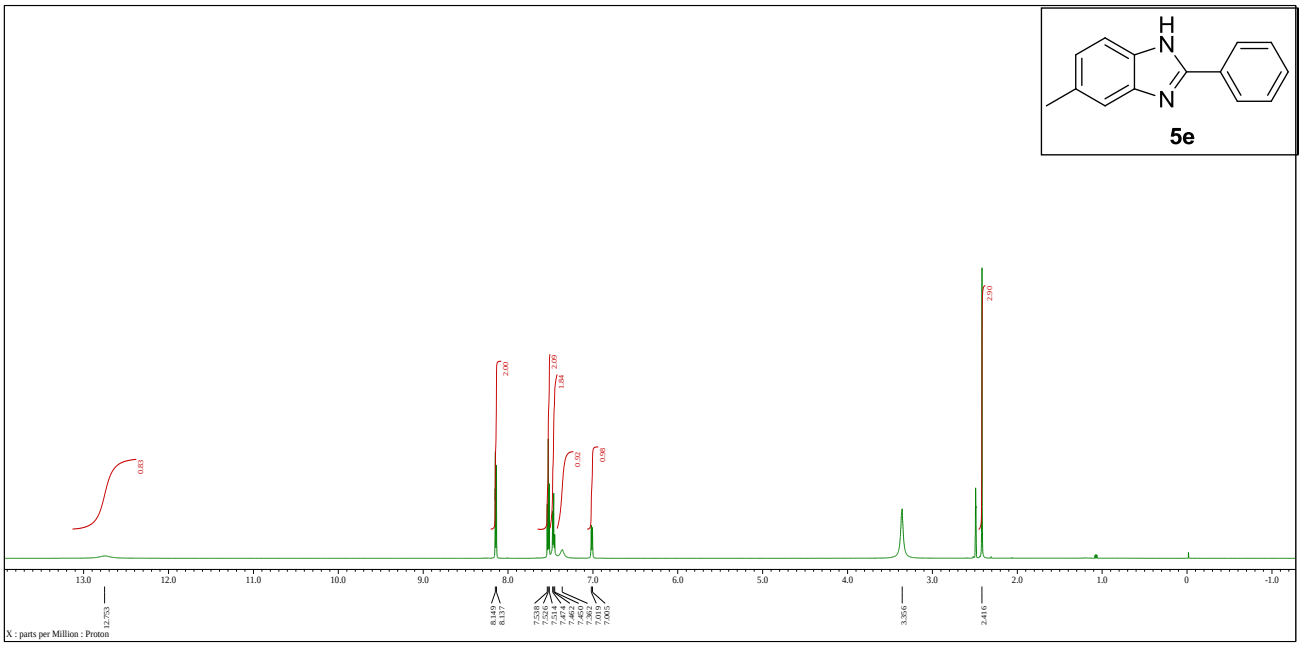
[13]C-NMR Spectrum of compound **5c** (150 MHz, DMSO-d_6)



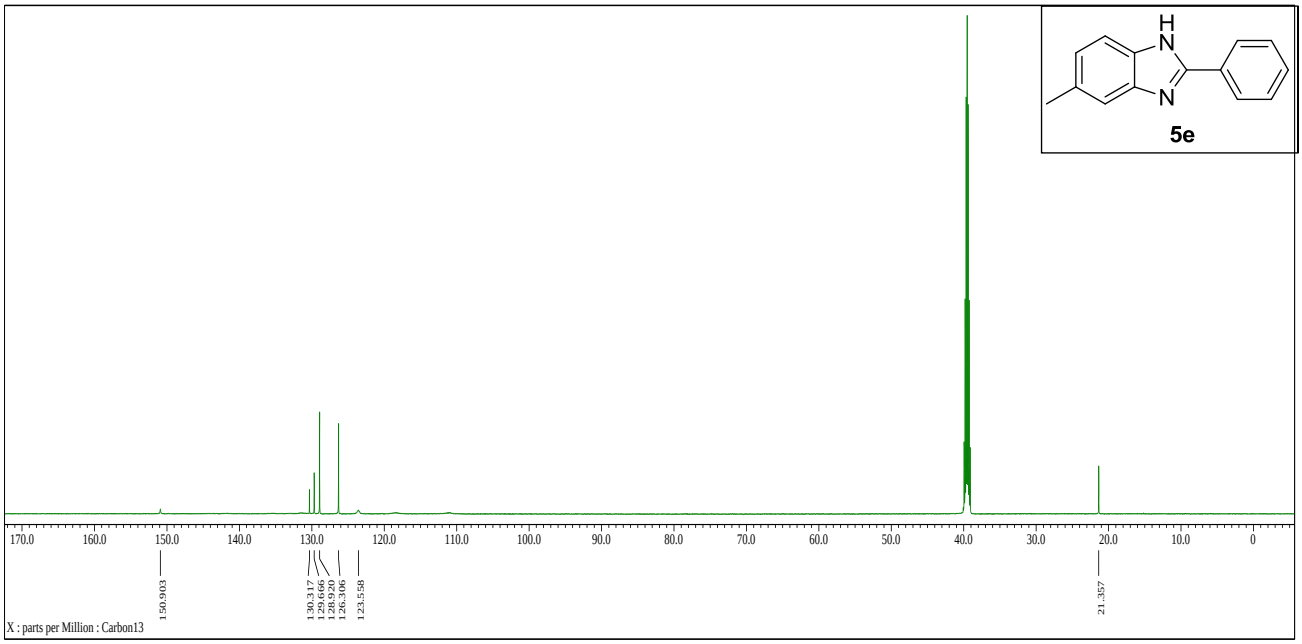
^{1}H-NMR Spectrum of compound **5d** (600 MHz, $CDCl_3$)



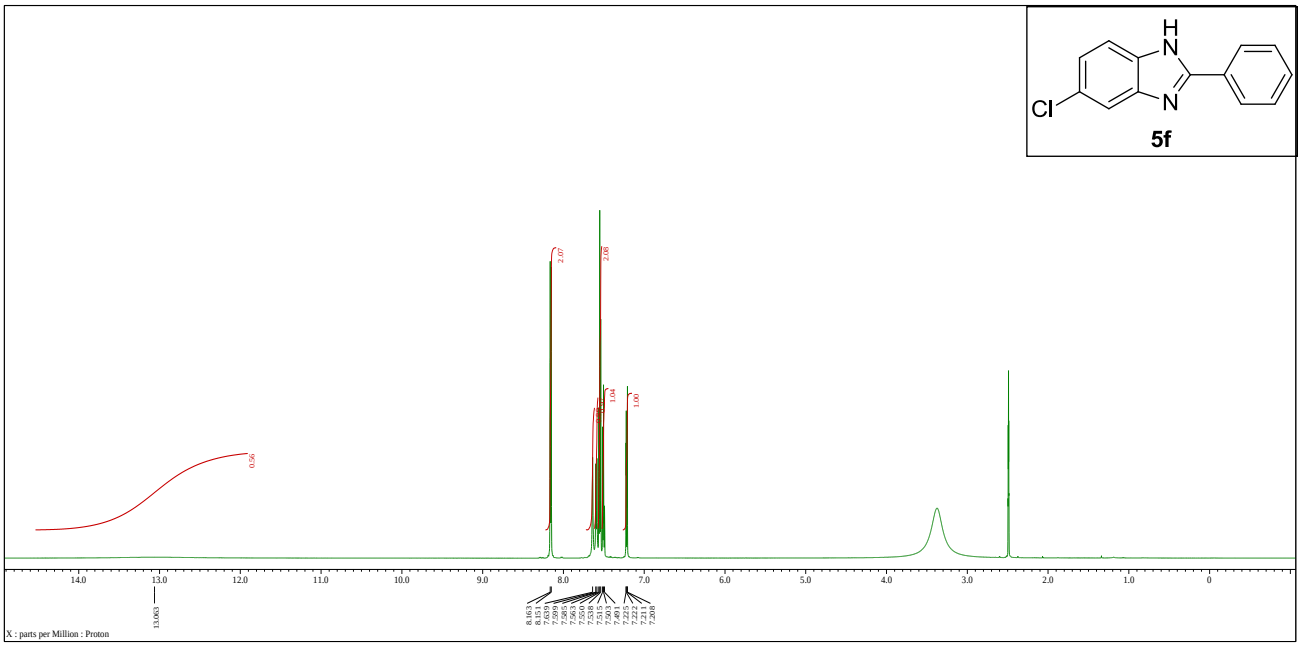
^{13}C-NMR Spectrum of compound **5d** (150 MHz, $CDCl_3$)



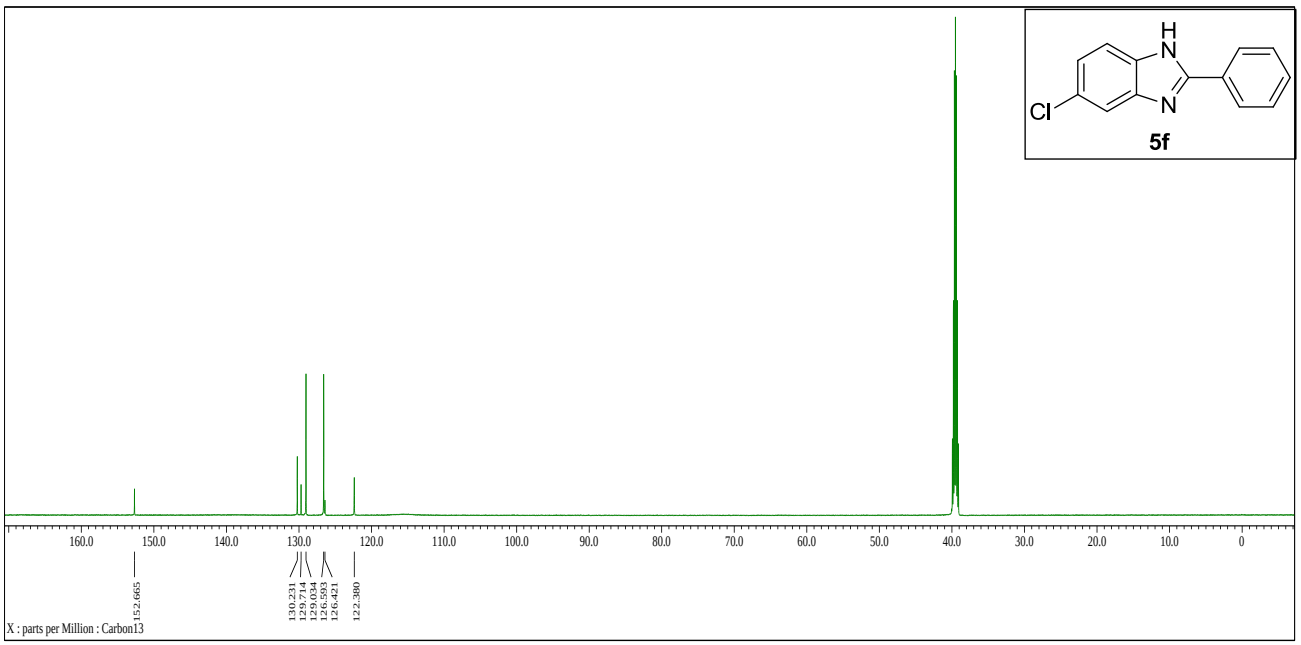
^{1}H-NMR Spectrum of compound **5e** (600 MHz, DMSO-d_6)



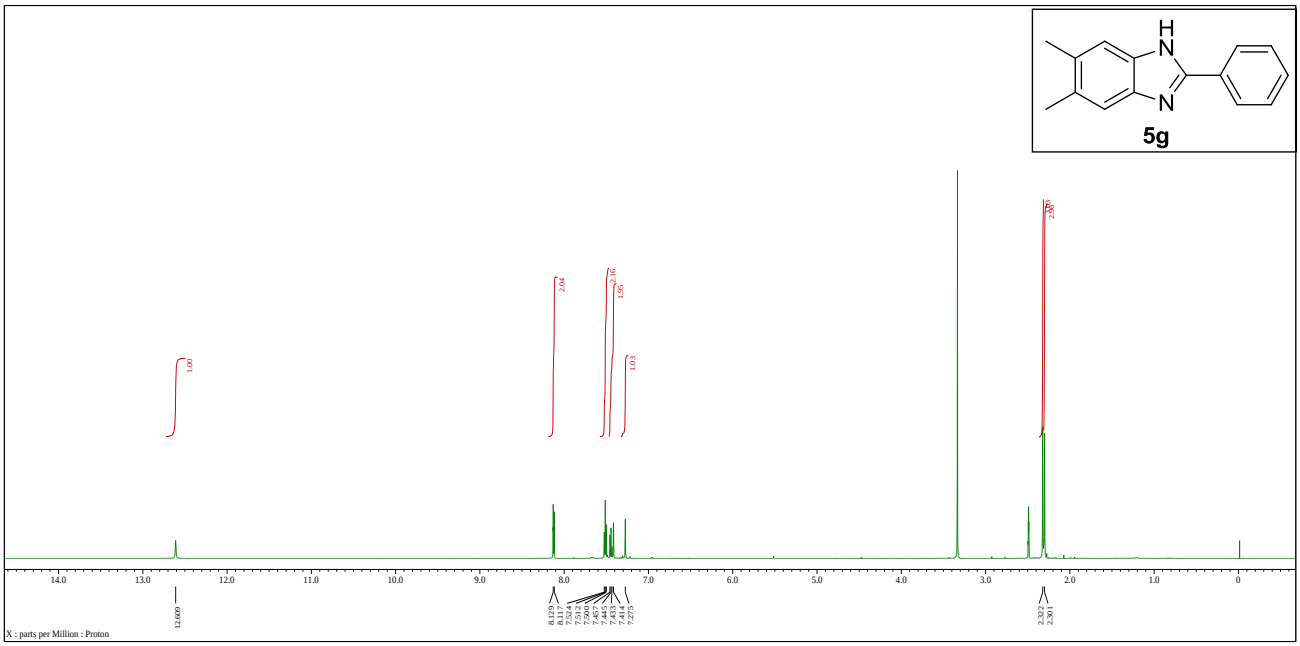
^{13}C-NMR Spectrum of compound **5e** (150 MHz, DMSO-d_6)



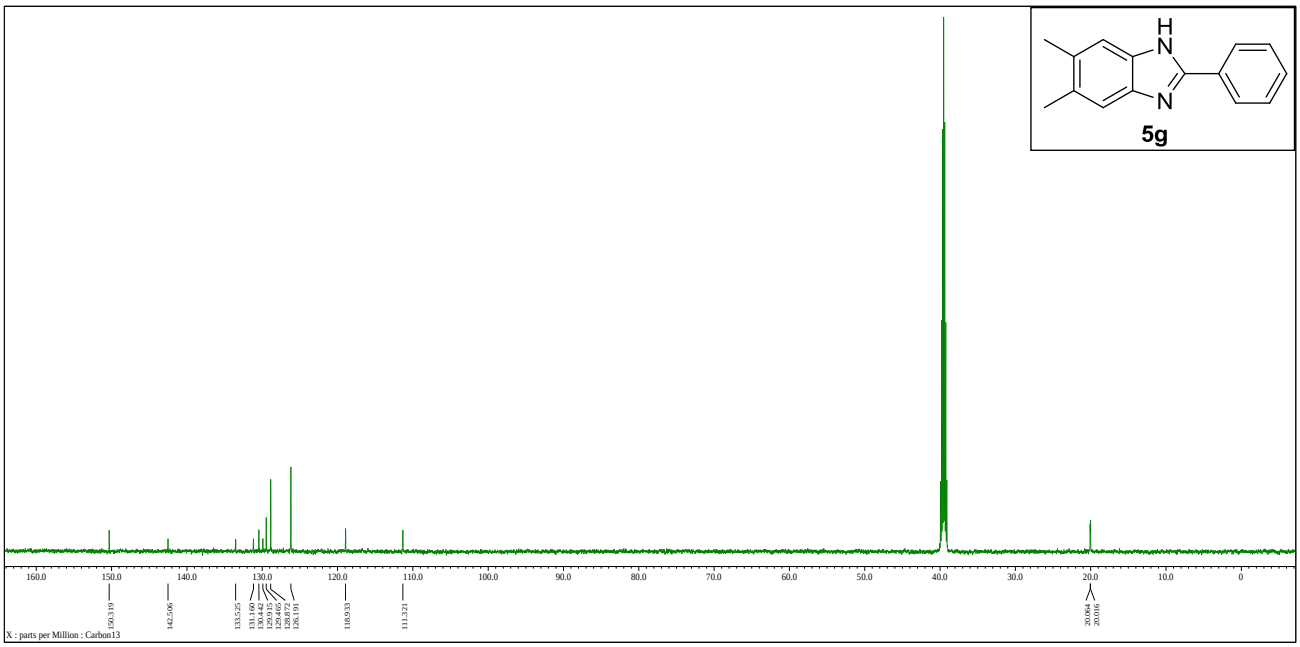
^{1}H-NMR Spectrum of compound **5f** (600 MHz, DMSO-d_6)



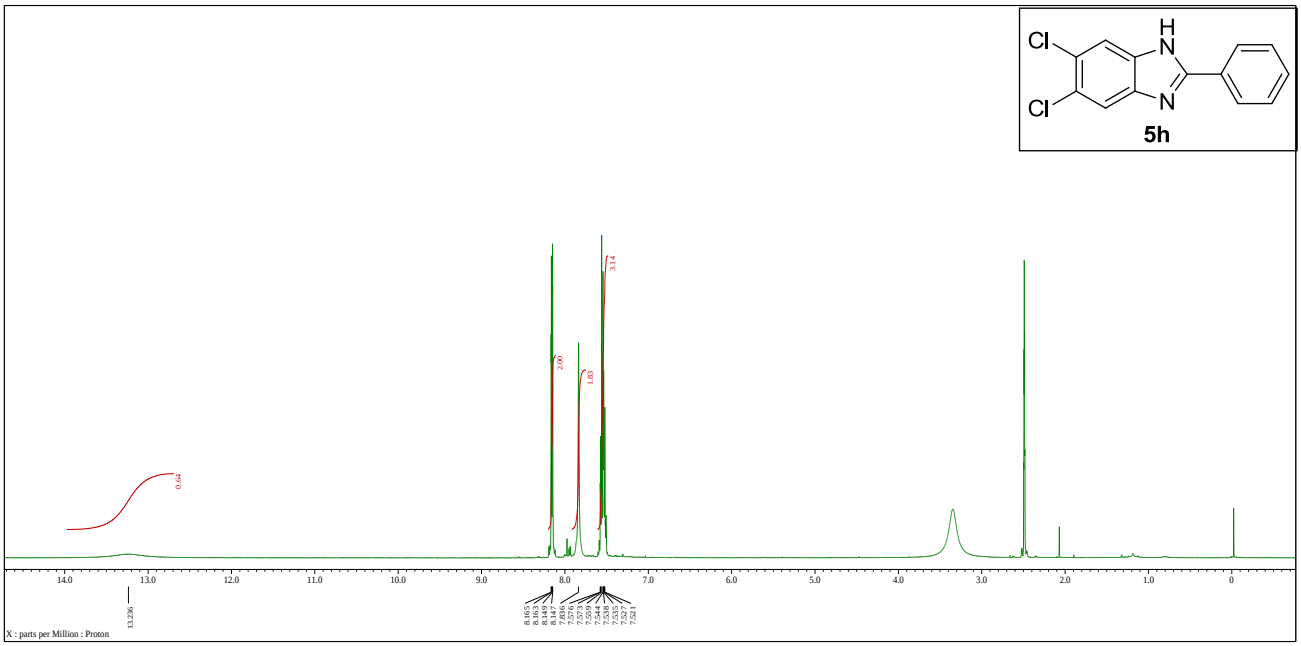
^{13}C-NMR Spectrum of compound **5f** (150 MHz, DMSO-d_6)



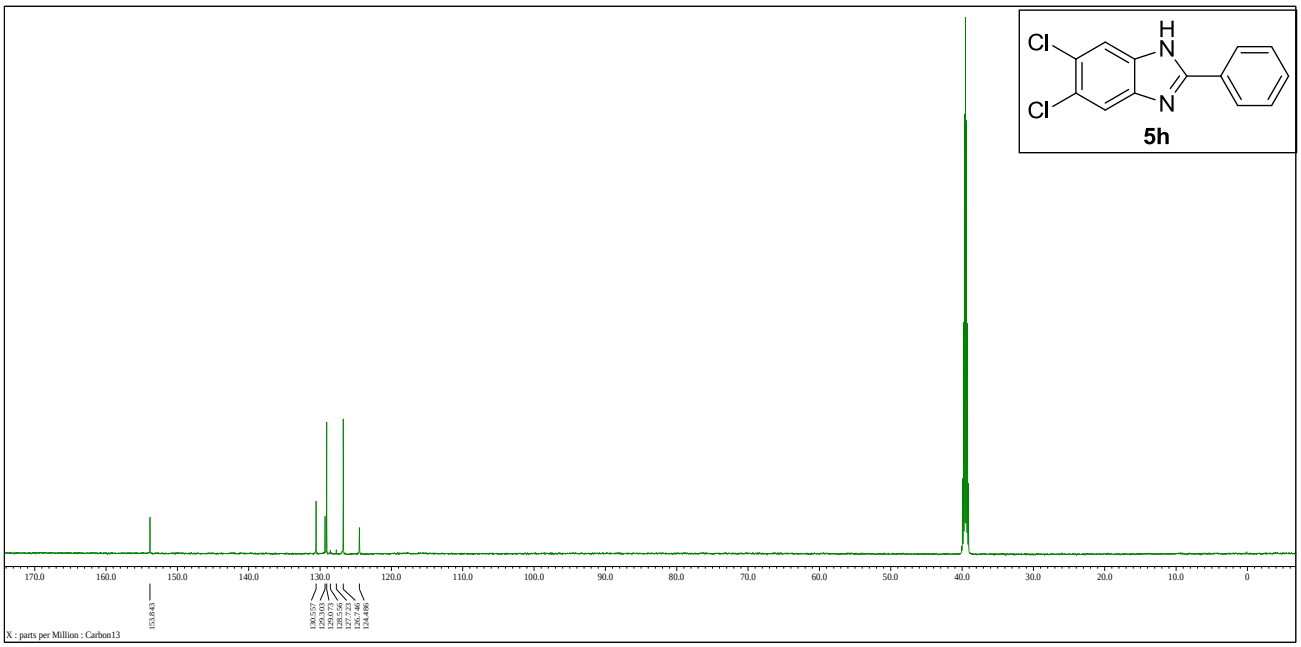
^{1}H-NMR Spectrum of compound **5g** (600 MHz, DMSO-d_6)



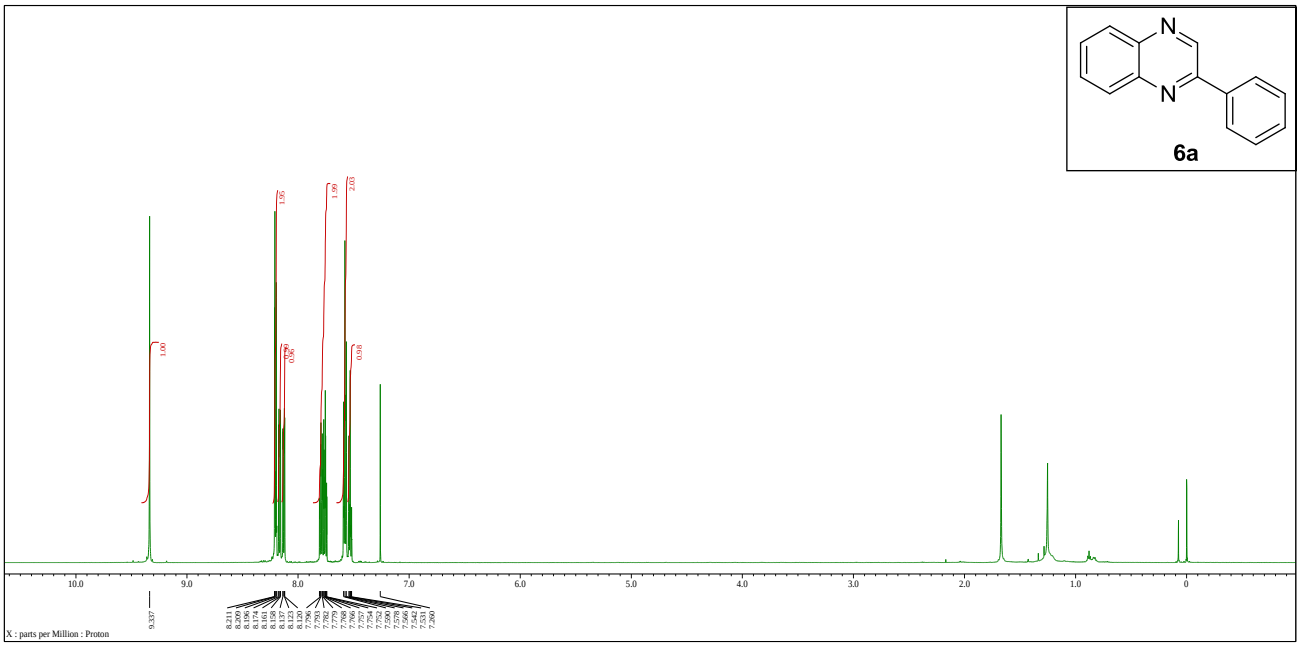
^{13}C-NMR Spectrum of compound **5g** (150 MHz, DMSO-d_6)



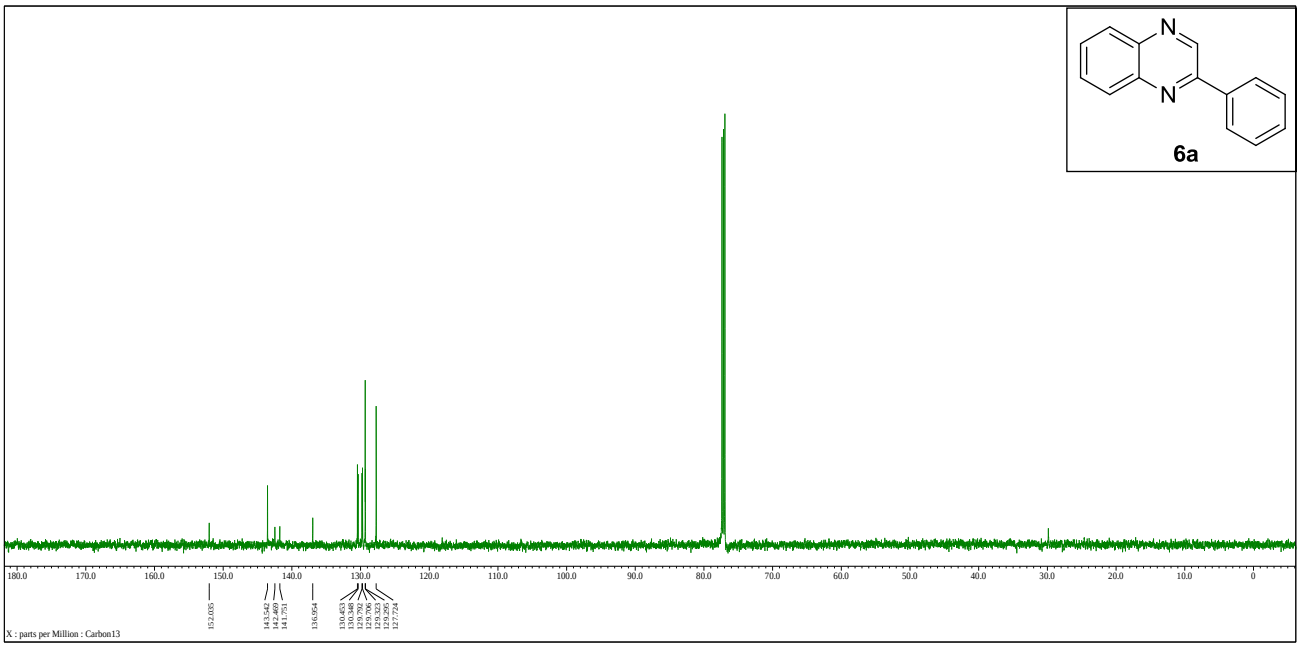
^{1}H-NMR Spectrum of compound **5h** (600 MHz, DMSO-d_6)



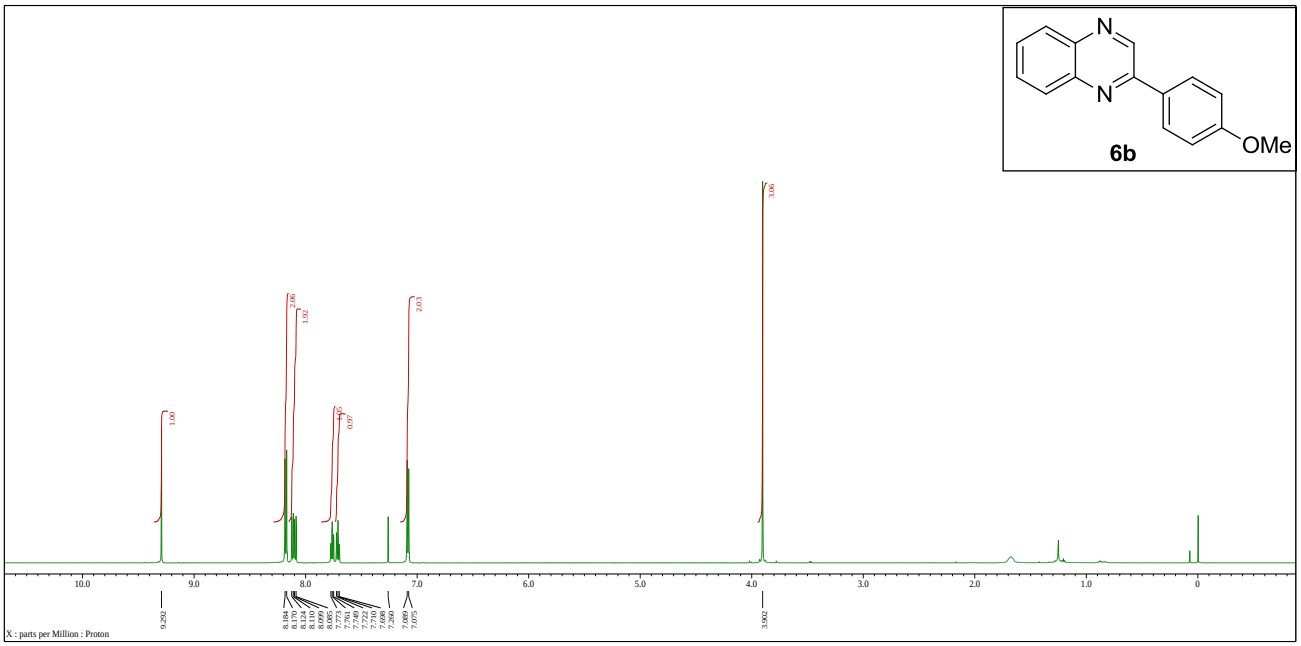
^{13}C-NMR Spectrum of compound **5h** (150 MHz, DMSO-d_6)



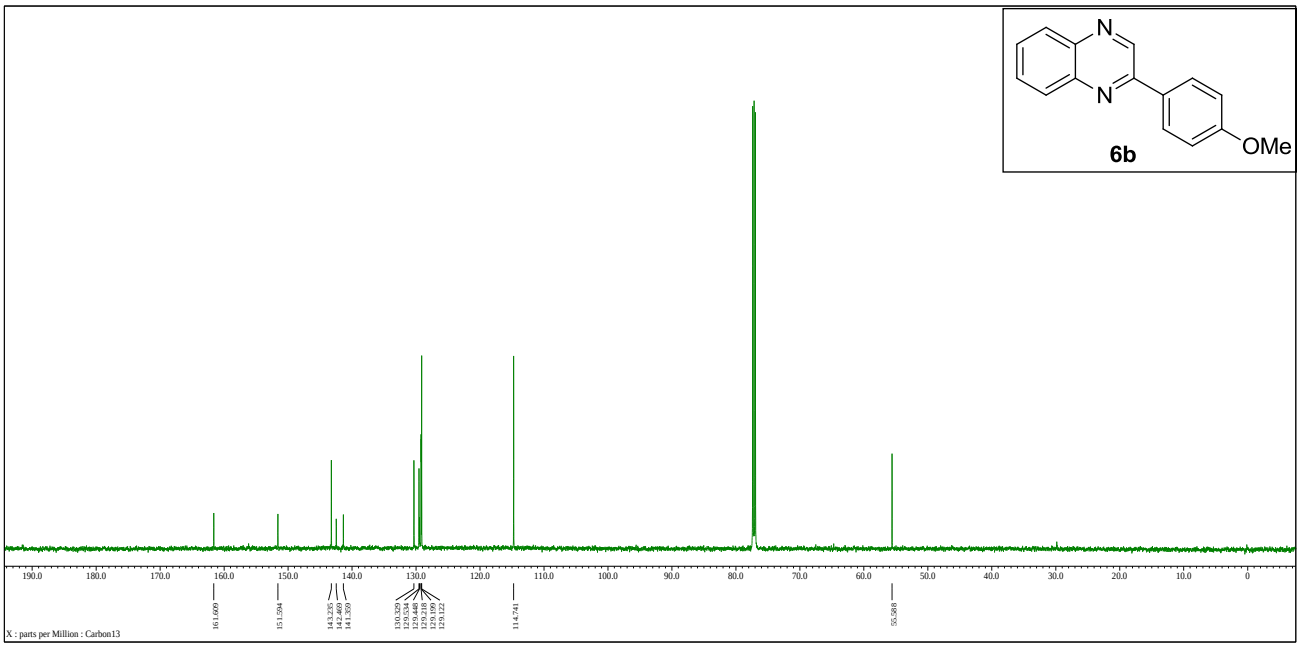
^{1}H-NMR Spectrum of compound **6a** (600 MHz, $CDCl_3$)



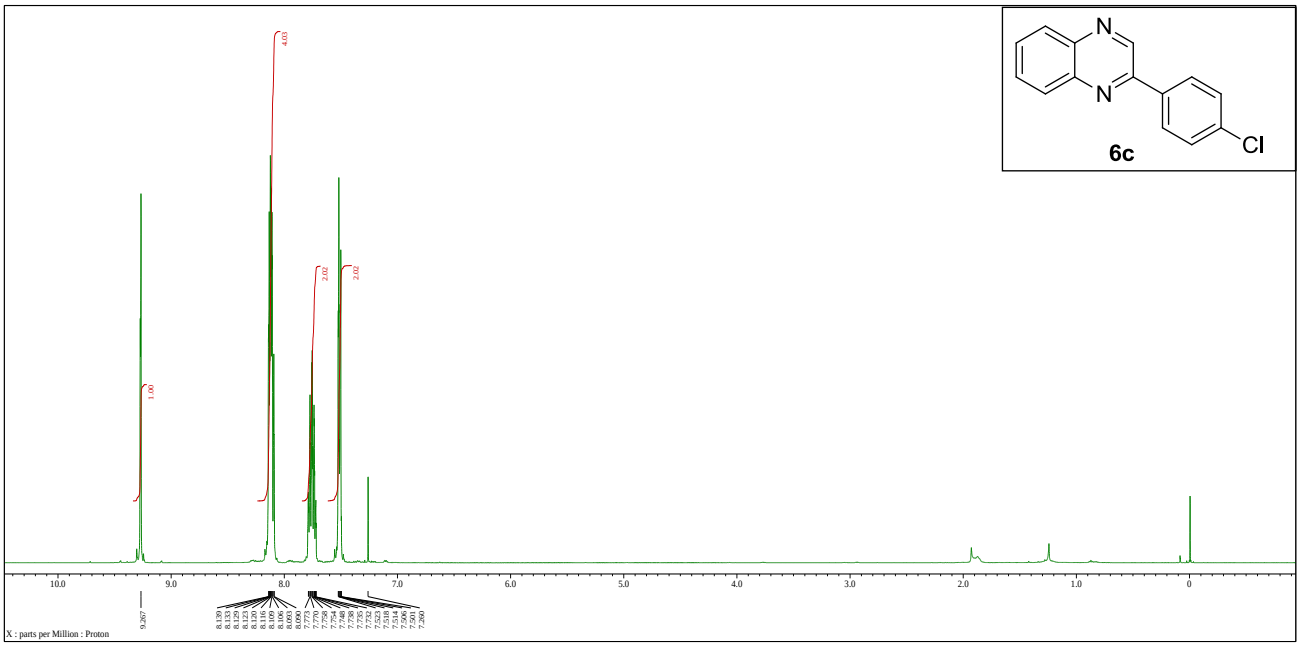
^{13}C-NMR Spectrum of compound **6a** (150 MHz, $CDCl_3$)



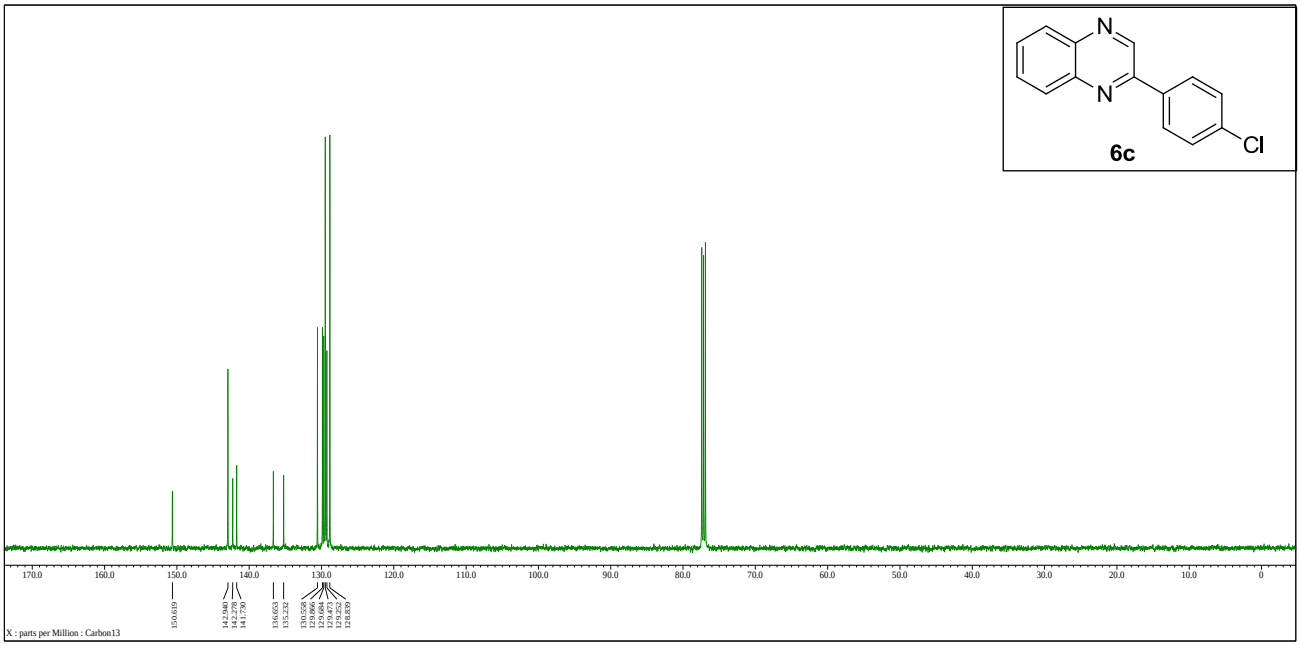
^{1}H-NMR Spectrum of compound **6b** (600 MHz, $CDCl_3$)



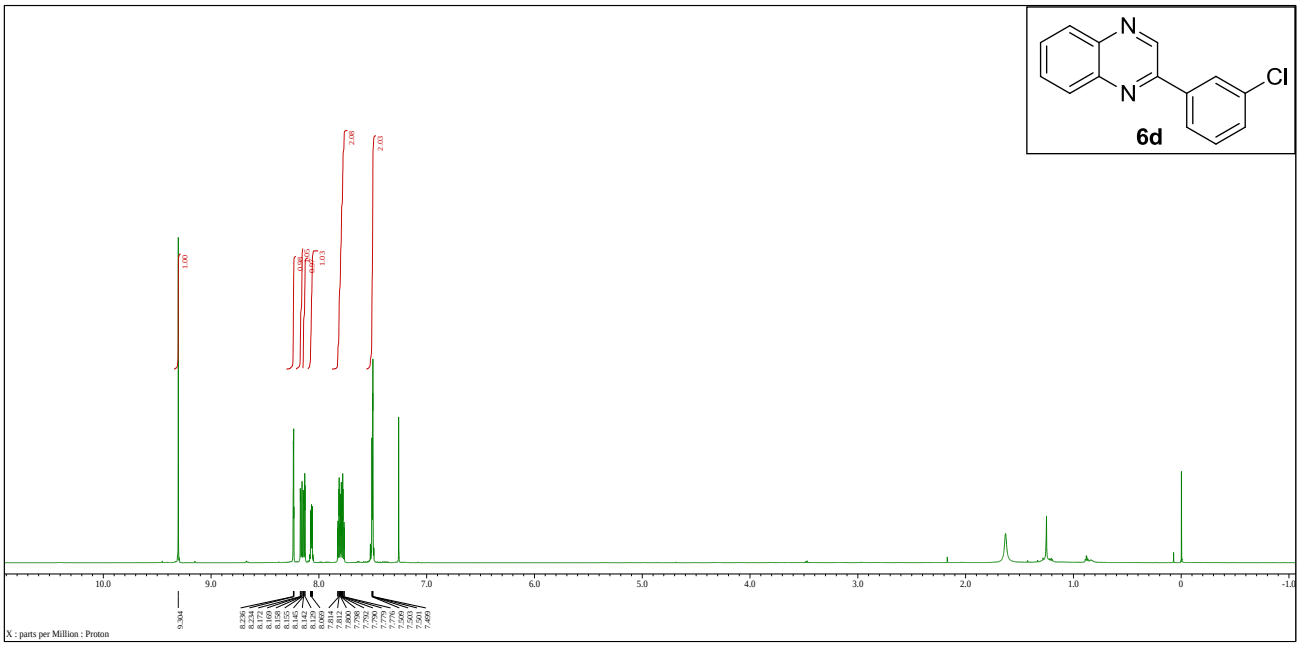
^{13}C-NMR Spectrum of compound **6b** (150 MHz, $CDCl_3$)



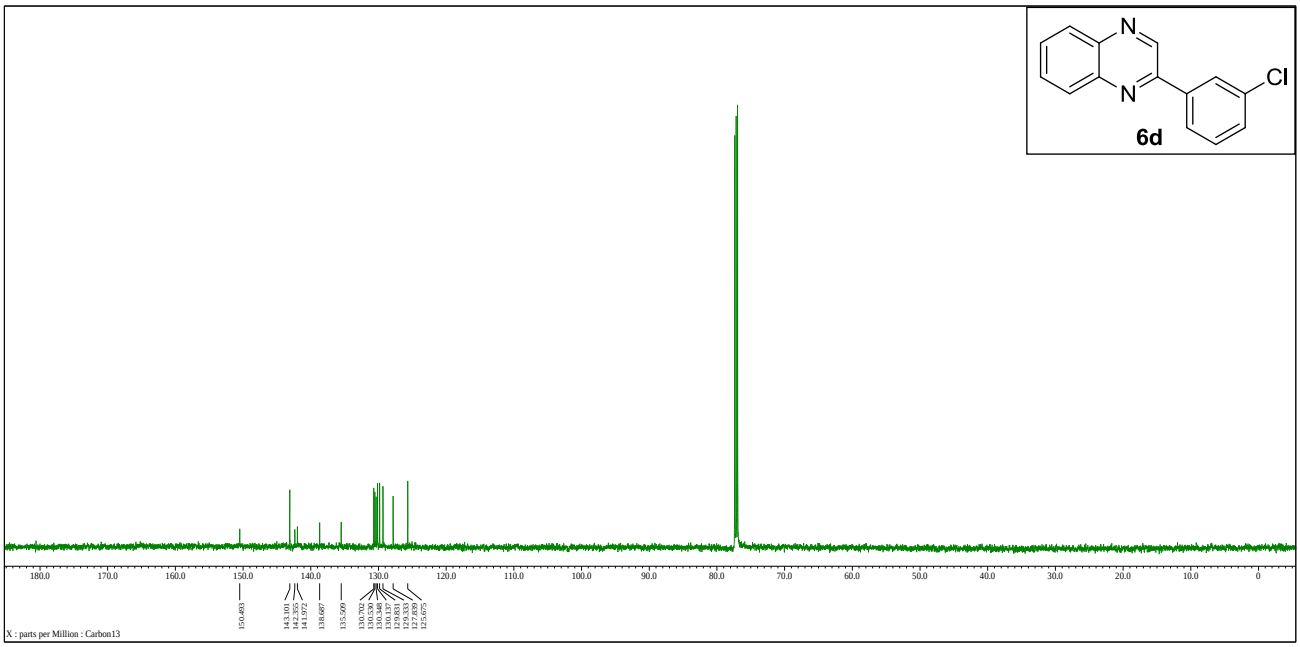
^{1}H-NMR Spectrum of compound **6c** (600 MHz, $CDCl_3$)



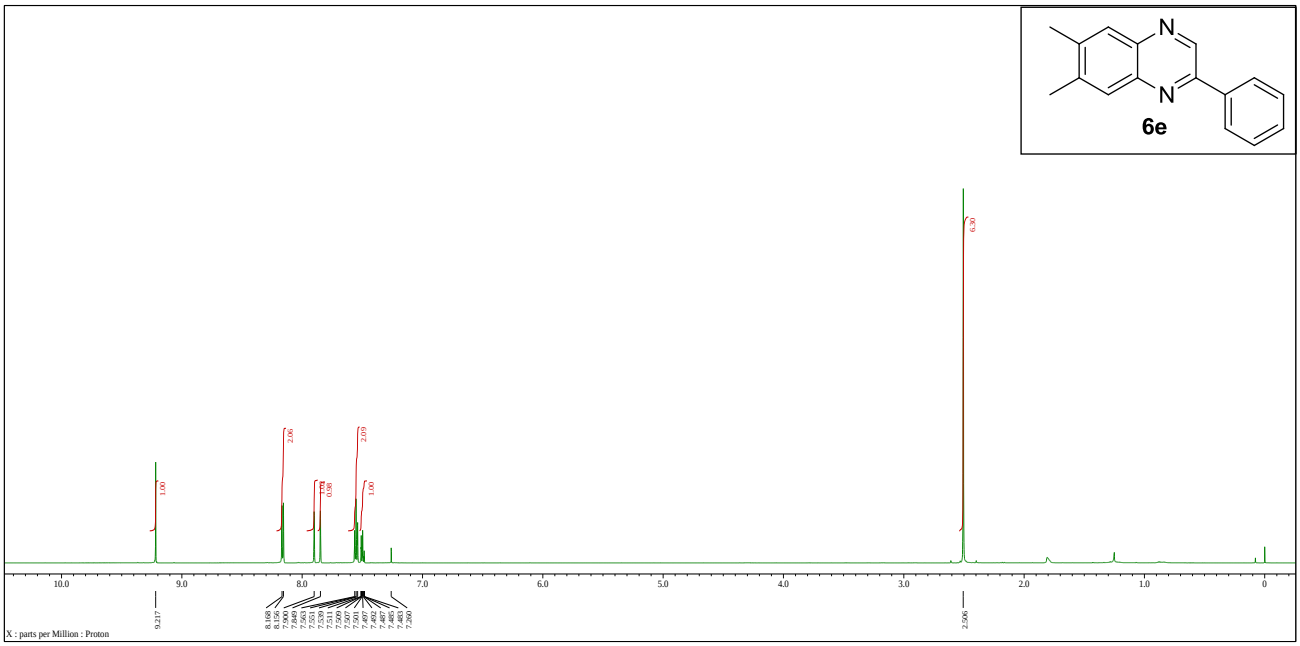
^{13}C-NMR Spectrum of compound **6c** (150 MHz, $CDCl_3$)



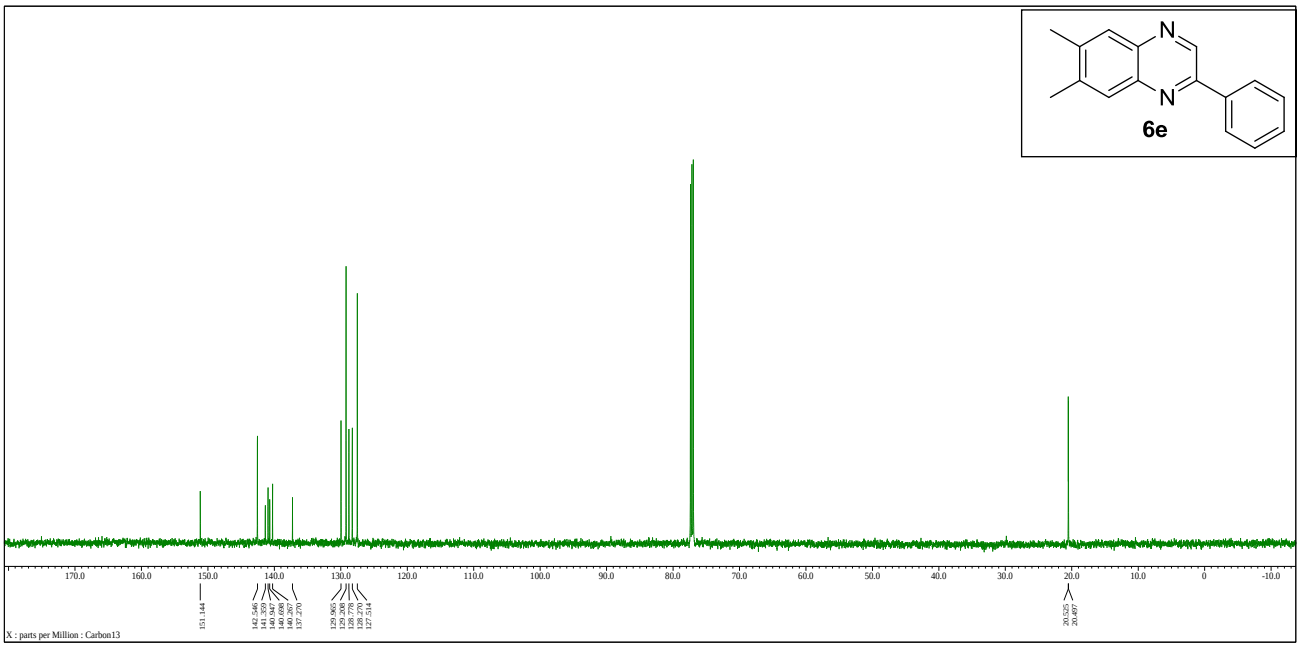
^{1}H-NMR Spectrum of compound **6d** (600 MHz, $CDCl_3$)



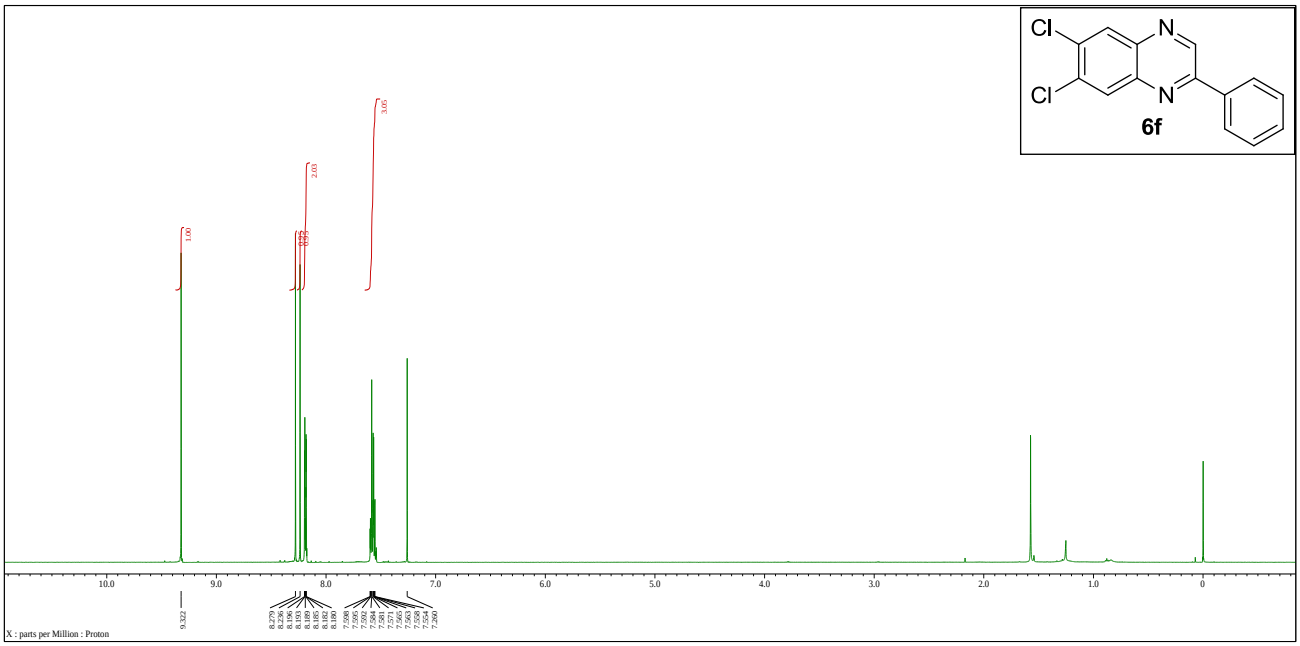
^{13}C-NMR Spectrum of compound **6d** (150 MHz, $CDCl_3$)



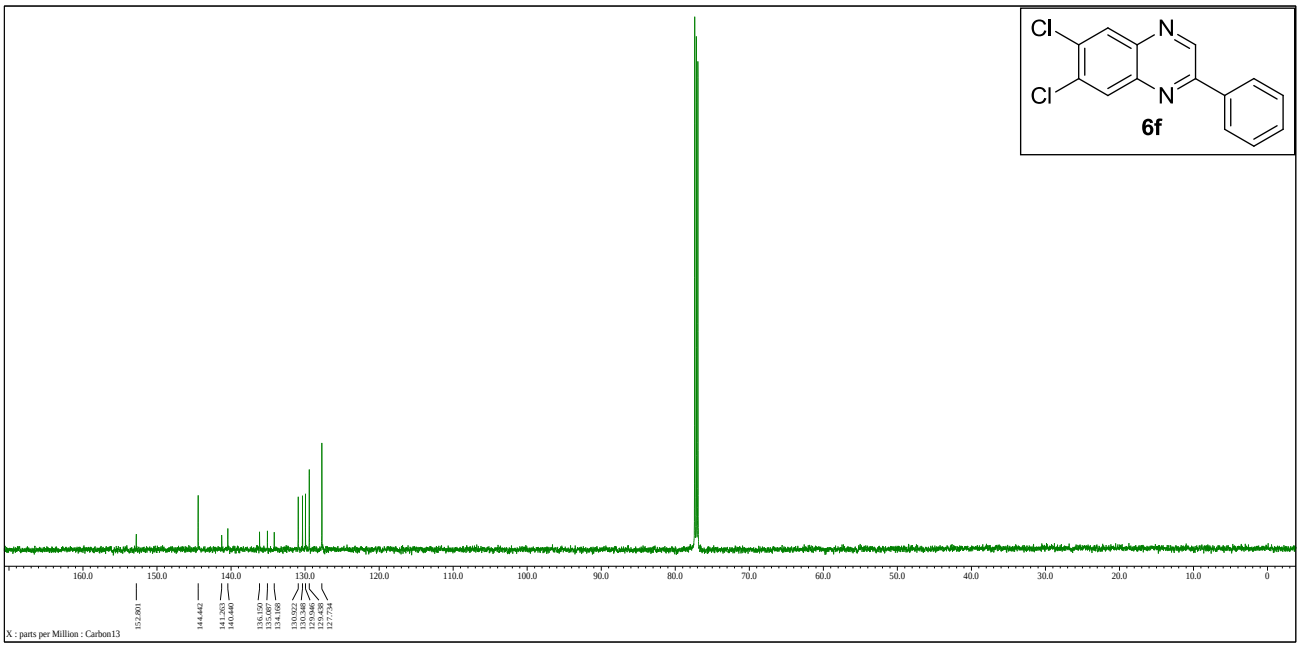
^{1}H-NMR Spectrum of compound **6e** (600 MHz, $CDCl_3$)



^{13}C-NMR Spectrum of compound **6e** (150 MHz, $CDCl_3$)



^{1}H-NMR Spectrum of compound **6f** (600 MHz, $CDCl_3$)



^{13}C-NMR Spectrum of compound **6f** (150 MHz, $CDCl_3$)