Highly chemo- and diastereo-selective synthesis of 2,6-diazabicyclo[3.2.0]heptan-7-ones, pyrrolidines and perhydroazirino[2,3-*c*]pyrroles

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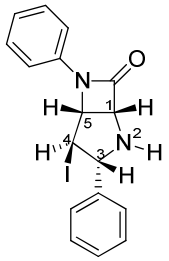
1. General Information

Materials and methods

Oxygen- and moisture-sensitive reactions were carried out under nitrogen atmosphere. Solvents were purified and dried by standard methods prior to use. All commercially available reagents and solvents (purchased from Aldrich, Merck, Spectrochem, Acros) were used without further purification unless otherwise noted. Analytical thin layer chromatography (TLC) was conducted on Merck Kieselgel 60 F254. Compounds were visualized with both short- and long-wavelength UV light. Column chromatography was performed on silica gel (100-200 mesh). Melting points were determined in capillary tubes using a Mel-Temp apparatus and are not corrected. Infrared spectra were obtained as films on KBr salt plates except where otherwise specified, using a Perkin Elmer FT-IR spectrometer. ^{1}H NMR spectra were obtained with $CDCl_3$ at 300 & 500 MHz, using Bruker spectrometers (residual chloroform referenced to 7.26 ppm) or DMSO-*d*6 (residual DMSO referenced to 2.50 ppm and residual water in DMSO-*d*6 appearing at 3.33 ppm). Chemical shift values are expressed as parts per million downfield from TMS and *J* values are in hertz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet, dd: double doublet, ddd: doublet of a doublet of a doublet, and br: broad peak. ^{13}C NMR spectra were recorded with $CDCl_3$ at 75 MHz, using Bruker spectrometers (residual chloroform referenced to 77.0 ppm) or DMSO-*d*6 (residual DMSO referenced to 39.5 ppm). Infrared spectra were recorded on a Perkin Elmer FT-IR spectrometer. HRMS were recorded on Bruker high resolution spectrometer (BrukermicrOTOF QII).

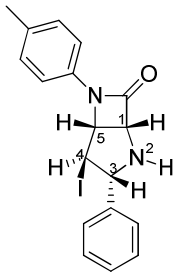
2. General procedure for synthesis of compound 4-halo-3,6-diaryl-2,6-diaza-bicyclo[3.2.0]heptan-7-one 2. To a solution of compounds 1 (0.1 g, 1 equiv) in DCM (10 ml) was added bromine/iodine (1.2 equiv). The reaction was stirred for 10 minutes. This was followed by addition of K_2CO_3 at 0 ^{o}C. The solution was stirred at 0 ^{o}C for 1–2 h. The progress of the reaction was monitored with the help of tlc. After completion of the reaction, reaction mixture was diluted with DCM and washed with $Na_2S_2O_3$/water solution followed by brine solution. The dichloromethane solution was dried over anhydrous Na_2SO_4 and solvent was evaporated. Crude residue was purified by flash column chromatography using silica gel (100:200 mesh) in EtOAc/cyclohexane (2:8) as an elutent system to get compounds 2.



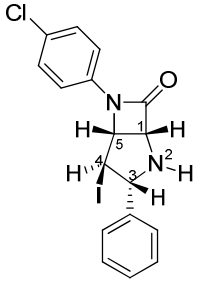
4-Iodo-3,6-diphenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2a). Yield: 90%; White solid, Mp: 118–119 ºC; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.36 (d, *J* = 7.2 Hz, 2H), 7.10-7.19 (m 5H), 6.97-7.04 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 2H), 5.02 (d, *J* = 3.9 Hz, 2H), 4.94 (bs, 1H), 4.91 (d,

J = 3.6 Hz, 1H). δ_C NMR (75 MHz, $CDCl_3$) δ 164.2, 139.6, 136.1, 129.0, 128.2, 127.2, 125.3, 124.4, 116.8, 74.7, 71.8, 67.8, 30.7. MS (EI) *m/z* 391 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1755, HRMS calculated for $C_{17}H_{15}IN_2O$ $(M+H)^+$ 391.0307, found 391.0314.

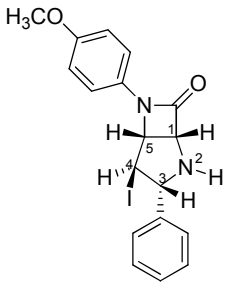
X-Ray crystal data and structure refinement. CCDC 972460 contains the supplementary crystallographic data. $C_{17}H_{15}I_1N_2O_1$, V = 2958.9(2) $Å^3$ Mr = 390.21, Z = 8 , orthorhombic, a = 9.8710(5) Å, *m* = 2.165 mm^{-1}, b = 16.0822(8) Å, T = 100(2) K, c = 18.6387(8) Å, *a* = 90, *b* = 90 *g* = 90; b = 104.719(2), T_{min} = 0.655, T_{max} = 0.677, R_{int} = 0.0252, 3047 measured reflections, wR(F2) = 0.0759, S = 1.155



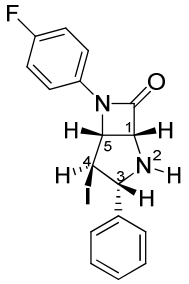
4-Iodo-3-phenyl-6-(p-tolyl)-2,6-diazabicyclo[3.2.0]heptan-7-one (2b). Yield: 82%; White solid, Mp: 129–131 ºC; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.37 (dd, *J* = 6.9 , 0.9 Hz, 2H), 7.11-7.21 (m, 3H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.78 (dd, *J* = 6.6, 1.8 Hz, 2H), 5.01 (d, *J* = 3.6 Hz, 2H), 4.91 (bs, 2H), 2.24 (s, 3H). δ_C NMR (75 MHz, $CDCl_3$) δ 163.9, 139.7, 134.2, 133.6, 129.5, 128.2, 127.1, 125.4, 116.8, 74.8, 71.8, 67.8, 30.8, 20.9. MS (EI) *m/z* 405 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1755, HRMS calculated for $C_{18}H_{17}IN_2O$ $(M+H)^+$ 405.0464, found 405.0488..



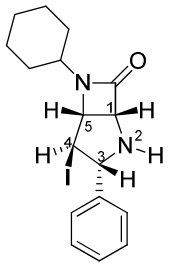
6-(4-Chlorophenyl)-4-iodo-3-phenyl-2,6-diazabicycle[3.2.0]heptan-7-one (2c). Yield: 65%; Pale yellow solid, Mp: 143–144; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.35 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.10-7.20 (m, 5H), 6.83 (d, *J* = 6.6 Hz, 2H), 5.01 (d, *J* = 3.6 Hz, 2H), 4.92 (bs, 2H). δ_C NMR (75 MHz, $CDCl_3$) δ 164.1, 139.5, 134.6, 129.1, 128.9, 128.3, 127.2, 125.3, 118.0, 74.5, 72.2, 67.9, 30.3. MS (EI) *m/z* 425 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1755, HRMS calculated for $C_{17}H_{14}ClIN_2O$ $(M+H)^+$ 424.9918, found 424.9915.



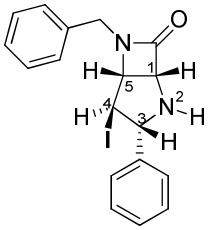
4-Iodo-6-(4-methoxyphenyl)-3-phenyl-2,6-diazabicyclo[3. 2.0]heptan-7-one (2d). Yield: 66%; White solid, Mp: 137-139; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.37 (d, *J* = 7.2 Hz, 2H), 7.10-7.19 (m, 5H), 6.80 (dd, *J* = 6.6, 1.8 Hz, 2H), 5.01 (d, *J* = 3.6 Hz, 2H), 4.91 (bs, 2H), 3.21 (s, 3H). δ_C NMR (75 MHz, $CDCl_3$) *δ* 164.0, 139.7, 134.2, 133.7, 129.5, 128.2, 127.1, 125.3, 116.8, 74.8, 71.7, 67.8, 55.9, 30.8. MS (EI) *m/z* 421 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1755, HRMS calculated for $C_{18}H_{17}IN_2O_2$ $(M+H)^+$ 421.0413, found 421.0411.



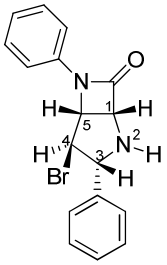
6-(4-fluorophenyl)-4-iodo-3-phenyl-2,6-diazabicycle[3.2.0]heptan-7-one (2e). Yield: 62%; Pale yellow solid, Mp: 124–127; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.34-7.37 (m, 2H, ArH), 7.10-7.26 (m, 5H, ArH), 6.82-6.85 (m, 2H, ArH), 5.00 (d, *J* = 3.6 Hz, 2H, H_3 & H_4), 4.92 (m, 2H, H_1 & H_5). δ_C NMR (75 MHz, $CDCl_3$) *δ* 163.9, 139.7, 134.2, 133.7, 129.6, 128.3, 128.0, 127.2, 125.4, 116.9, 74.8, 71.8, 67.9, 30.8. MS (EI) *m/z* 409 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1750, HRMS calculated $(M+H)^+$ 409.0213, found 409.0207, Anal. Calc. for $C_{17}H_{14}FIN_2O$: C, 50.02; H, 3.46; N, 6.86; found: C, 50.06; H, 3.51; N, 6.81.



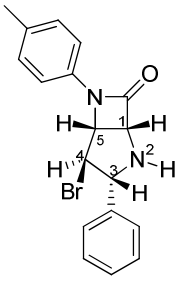
6-cyclohexyl-4-iodo-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2f). Yield: 75%; Pale yellow solid, Mp: 110–111; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.18-7.39 (m, 5H, ArH), 5.07 (d, *J* = 4.0 Hz, 2H, H_3 & H_4), 5.02 (s, 1H, H_1) 5.00 (d, *J* = 3.5 Hz, 1H, H_5), 3.57-3.62 (m, 1H, cyclohexyl-H), 0.85-1.95(m, 10H, cyclohexyl-H), δ_C NMR (75 MHz, $CDCl_3$) *δ* 164.5, 128.8, 128.7, 126.7 123.6, 74.7, 71.8, 67.9, 52.7, 31.8, 30.6, 29.7, 25.0. MS (EI) *m/z* 397 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1755, HRMS calculated $(M+H)^+$ 397.0777, found 397.0773, Anal. Calc. for $C_{17}H_{21}IN_2O$: C, 51.53; H, 5.34; N, 7.07; found: C, 51.60; H, 5.39; N, 7.04.



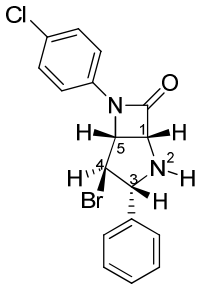
6-benzyl-4-iodo-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2g). Yield: 60%; Yellow solid, Mp: 125–126; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.21-7.36 (m, 10H, ArH), 5.04 (d, *J* = 3.5 Hz, 2H, H_3 & H_4), 4.94 (s, 1H, H_1) 4.92 (d, *J* = 3.5 Hz, 1H, H_5), 4.09-4.14 (m, 2H, CH_2). δ_C NMR (75 MHz, $CDCl_3$) δ 170.1, 143.4, 128.8, 128.7, 128.5, 127.9, 127.2, 126.6, 123.5, 74.4, 70.3, 65.8, 47.26, 29.7. MS (EI) *m/z* 405 $(M+1)^+$, ν_{max} (KBr)/cm^{-1} 1752, HRMS calculated $(M+H)^+$ 405.0464, found 405.0462, Anal. Calc. for $C_{18}H_{17}IN_2O$: C, 53.48; H, 4.24; N, 6.93; found: C, 53.52; H, 4.29; N, 6.89.



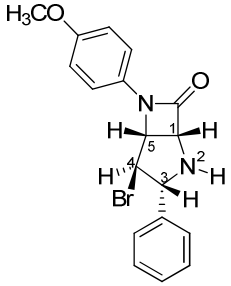
***4-bromo-3,6-diphenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2h)*.** Yield: 61%; Brown solid, Mp: 131–132; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.38 (m, 2H, ArH), 7.10-7.22 (m, 5H, ArH), 6.97-7.04 (m, 1H, ArH), 6.93 (m, 2H, ArH), 5.02 (bs, 1H, H_3), 4.92 (d, *J* = 3.6 Hz, 1H, H_4), 4.91 (bs, 1H, H_1), 4.83 (d, *J* = 3.6 Hz, 1H, H_5). δ_C NMR 75 MHz, $CDCl_3$) δ 164.1, 139.0, 136.1, 129, 128.2, 127.2, 125.4, 124.5, 116.7, 73.1, 71.7, 66.1, 52.7. MS (EI) *m/z* 343 $(M+1)^+$, Anal. Calc. for $C_{17}H_{15}BrN_2O$: C, 59.49; H, 4.41; N, 8.16; found: C, 59.41; H, 4.38; N, 8.20.



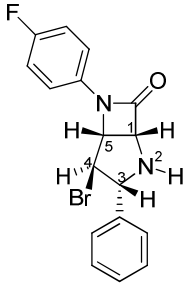
***4-bromo-3-phenyl-6-(p-tolyl)-2,6-diazabicyclo[3.2.0]heptan-7-one (2i)*.** Yield: 55%; Brown solid; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.39(m, 2H, ArH), 7.10-7.23 (m, 3H, ArH), 6.97 (m, 2H, ArH), 6.80 (m, 2H, ArH), 5.02 (s, 1H, H_3), 4.91 (d, *J* = 3.6 Hz, 1H, H_4), 4.90 (bs, 1H, H_1), 4.81 (d, *J* = 3.6 Hz, 1H, H_5), 2.24 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 163.8, 139.0, 134.2, 133.6, 129.5, 128.2, 127.2, 125.4, 116.8, 73.1, 71.6, 66.2, 52.7, 20.9. MS (EI) *m/z* 357 $(M+1)^+$, Anal. Calc. for $C_{18}H_{17}BrN_2O$: C, 60.52; H, 4.80; N, 7.84; found: C, 60.49; H, 4.75; N, 7.87.



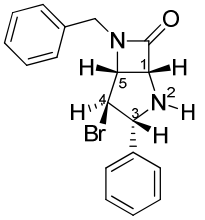
***4-bromo-6-(4-chlorophenyl)-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2j)*.** Yield: 50%; Light brown solid, δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.30-7.40 (m, 3H, ArH), 7.16-7.22 (m, 2H), 7.13 (m, 2H, ArH), 6.86 (m, 2H, ArH), 5.02 (s, 1H, H_3), 4.93 (d, *J* = 3.6 Hz, 1H, H_4), 4.89 (s, 1H, H_1), 4.81 (d, *J* = 3.6 Hz, 1H, H_5). δ_C NMR (75 MHz, $CDCl_3$) δ 163.5, 134.5, 129.6, 129.1, 128.8, 128.3, 127.5, 125.5, 117.9, 73.0, 71.5, 66.0, 51.6. MS (EI) *m/z* 377 $(M+1)^+$, Anal. Calc. for $C_{17}H_{14}BrClN_2O$: C, 54.06; H, 3.74; N, 7.42; found: C, 54.03; H, 3.68; N, 7.45.



***4-bromo-6-(4-methoxyphenyl)-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2k)*.** Yield: 55%; Brown solid, δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.37-7.51 (m, 4H, ArH), 7.10-7.18 (m, 2H, ArH), 7.06 (m, 2H, ArH), 6.86 (m, 2H, ArH), 5.01 (s, 1H, H_3), 4.92 (d, *J* = 3.6 Hz, 1H, H_4), 4.91 (s, 1H, H_1), 4.83 (d, *J* = 3.6 Hz, 1H, H_5), 3.18 (s, 3H, OCH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 164.0, 134.3, 129.7, 129.2, 128.8, 128.3, 127.5, 125.4, 116.8, 73.1, 71.6, 66.2, 57.8, 52.7. MS (EI) *m/z* 373 $(M+1)^+$, Anal. Calc. for $C_{18}H_{17}BrN_2O_2$: C, 57.92; H, 4.59; N, 7.51; found: C, 57.91; H, 4.55; N, 7.57.

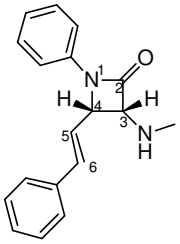


4-bromo-6-(4-fluorophenyl)-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2l). Yield: 60%; Brown solid, δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.02-7.29 (m, 7H, ArH), 6.78-6.81 (m, 2H, ArH), 4.76-4.96 (m, 2H, H_3 & H_4), 4.66 (t, *J* = 3.3 Hz, 1H, H_5), 4.66 (s, 1H, H_1). δ_C NMR (75 MHz, $CDCl_3$) δ 163.5, 134.5, 129.6, 129.1, 128.8, 128.3, 127.5, 125.5, 117.9, 73.0, 71.5, 66.0, 51.6. MS (EI) *m/z* 361 $(M+1)^+$, Anal. Calc. for $C_{17}H_{14}FBrN_2O$: C, 56.53; H, 3.91; N, 7.76; found: C, 56.55; H, 3.96; N, 7.73.

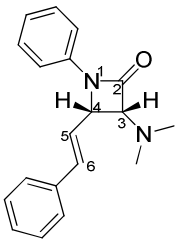


6-benzyl-4-bromo-3-phenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (2m). Yield: 45%; Yellow solid, δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.23-7.37 (m, 10H, ArH), 5.01 (s, 1H, H_3), 4.93 (d, *J* = 3.5 Hz, 1H, H_4), 4.81 (s, 1H, H_1), 4.68 (d, *J* = 3.5 Hz, 1H, H_5), 4.10-4.15 (m, 2H, CH_2). δ_C NMR (75 MHz, $CDCl_3$) δ 169.1, 143.4, 128.8, 128.7, 128.6, 127.8, 127.2, 126.7, 123.5, 73.0, 69.9, 65.8, 50.6, 47.2. MS (EI) *m/z* 357 $(M+1)^+$, Anal. Calc. for $C_{18}H_{17}IN_2O$: C, 60.52; H, 4.80; N, 7.84; found: C, 60.54; H, 4.85; N, 7.80.

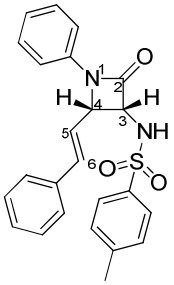
3. General procedure for synthesis of compound 4-halo-2-alkyl-3,6-diaryl-2,6-diazabicyclo[3.2.0]heptan-7-one 6. To a solution of compounds **5** (0.1 g, 1 equiv) in DCM (10 ml) was added bromine/iodine (1.2 equiv). The reaction was stirred for 10 minutes. This was followed by addition of K_2CO_3 at 0 ^oC. The solution was stirred at 0 ^oC. The progress of the reaction was monitored with the help of tlc. After completion of the reaction, reaction mixture was diluted with DCM and washed with $Na_2S_2O_3$/water solution followed by brine solution. The dichloromethane solution was dried over anhydrous Na_2SO_4 and solvent was evaporated. Crude residue was purified by flash column chromatography using silica gel (100:200 mesh) in EtOAc/cyclohexane (2:8) as an elutent system to get compounds 6.



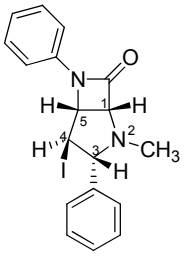
3-(methylamino)-1-phenyl-4-((E)-styryl)azetidin-2-one (5a). White solid, δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.48 (m, 2H, ArH), 7.43-7.45 (m, 2H, ArH), 7.28-7.38 (m, 5H, ArH), 7.10 (m, 1H, ArH), 6.85 (d, *J* = 16.5 Hz, 1H, H_6), 6.53 (dd, *J* = 16.0, 8.0 Hz, 1H, H_5), 4.86 (t, *J* = 6.5 Hz, 1H, H_3), 4.46 (d, *J* = 5.5 Hz, 1H, H_3), 2.90 (s, 3H, NCH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 165.9, 138.3, 136.0, 135.3, 129.1, 128.3, 128.1, 126.6, 124.3, 116.7, 57.5, 56.1, 32.4. MS (EI) *m/z* 279 $(M+1)^+$, Anal. Calc. for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06; found: C, 77.71; H, 6.54; N, 10.02.



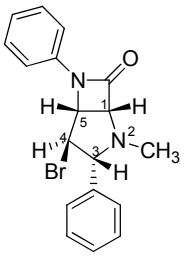
3-(dimethylamino)-1-phenyl-4-((E)-styryl)azetidin-2-one (5b). White solid, δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.46-7.51 (m, 4H, ArH), 7.28-7.40 (m, 5H, ArH), 7.07 (m, 1H, ArH), 6.75 (d, *J* = 16.0 Hz, 1H, H_6), 6.30 (dd, *J* = 15.5, 9.0 Hz, 1H, H_5), 4.88 (t, *J* = 6.5 Hz, 1H, H_3), 4.45 (d, *J* = 6.0 Hz, 1H, H_3), 2.92 (s, 6H, $N(CH_3)_2$). δ_C NMR (75 MHz, $CDCl_3$) δ 165.9, 138.7, 136.6, 135.6, 130.1, 128.7, 128.1, 126.6, 124.6, 124.3, 116.3, 57.5, 56.8, 38.3. MS (EI) *m/z* 293 $(M+1)^+$, Anal. Calc. for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89; N, 9.58; found: C, 78.11; H, 6.93; N, 9.54.



4-methyl-N-(2-oxo-1-phenyl-4-((E)-styryl)azetidin-3-yl)benzenesulfonamide (5c). White solid, δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.74-7.77 (m, 2H, ArH), 7.06-7.31 (m, 12H, ArH), 6.45 (d, *J* = 15.5 Hz, 1H, H_6), 5.93 (dd, *J* = 16.0, 9.0 Hz, 1H, H_5), 5.06 (t, *J* = 6.5 Hz, 1H, H_3), 4.78 (d, *J* = 6.5 Hz, 1H, H_3), 2.71 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 166.2, 139.4, 137.0, 136.3, 136.0, 135.3, 131.5, 130.1, 129.4, 128.7, 128.1, 126.6, 124.6, 124.3, 117.1, 57.5, 56.1, 16.2. MS (EI) *m/z* 419 $(M+1)^+$, Anal. Calc. for $C_{24}H_{22}N_2O_3S$: C, 68.88; H, 5.30; N, 6.69; found: C, 68.95; H, 5.33; N, 6.65.

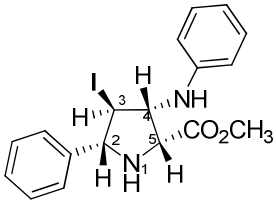


4-iodo-2-methyl-3,6-diphenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (6a). Yield: 75%; White solid, δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.43-7.45 (m, 2H, ArH), 7.28-7.38 (m, 5H, ArH), 7.10 (m, 1H, ArH), 6.92 (m, 1H, ArH), 5.03 (d, *J* = 4.0 Hz, 2H, H_3 & H_4), 4.95 (s, 1H, H_1), 4.92 (d, *J* = 3.0 Hz, 1H, H_5), 2.40 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 163.9, 139.4, 136.3, 129.4, 128.3, 127.4, 125.3, 124.6, 116.3, 74.7, 71.6, 67.5, 43.7, 30.7. MS (EI) *m/z* 405 $(M+1)^+$, HRMS calculated $(M+H)^+$ 405.0464, found 405.0655, Anal. Calc. for $C_{18}H_{17}IN_2O$: C, 53.48; H, 4.24; N, 6.93; found: C, 53.54; H, 4.30; N, 6.89.

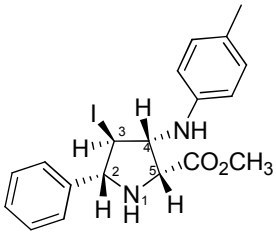


4-bromo-2-methyl-3,6-diphenyl-2,6-diazabicyclo[3.2.0]heptan-7-one (6b). Yield: 40%; Brown solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.43-7.49 (m, 4H, ArH), 7.28-7.37 (m, 5H, ArH), 7.10 (m, 1H, ArH), 5.00 (s, *1*H, H_3), 4.81-4.89 (m, 2H, H_1 & H_4), 4.82 (d, *J* = 3.5 Hz, 1H, H_5), 2.44 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 165.3, 138.0, 135.6, 129.1, 128.7, 128.4, 126.7, 124.3, 117.0, 73.8, 71.9, 66.2, 52.7, 45.8. (EI) *m/z* 357 $(M+1)^+$, Anal. Calc. for $C_{18}H_{17}BrN_2O$: C, 60.52; H, 4.80; N, 7.84; found: C, 60.50; H, 4.71; N, 7.78.

4. Typical procedure for the preparation of Alkyl 4-iodo-5-aryl-3-(arylamino)pyrrolidine-2-carboxylate 7. To a solution of compounds **2** (30mg, 1 eq) in methanol/ethanol (5 ml), NaOMe/NaOEt (3 eq) was added and the reaction mixture was stirred at 0 ^oC for 1.5 h. The progress of the reaction was monitored with the help of TLC. After completion of the reaction, the mixture was quenched with ice and pH adjust to 6-7 extracted with ethyl acetate (3 times). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated to get compound (**7**) as a pure product as solid.

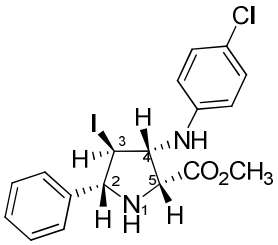


Methyl 4-iodo-5-phenyl-3-(phenylamino)pyrrolidine-2-carboxylate (7a). Yield: 85%; White solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.52 (m, 2H, ArH), 7.31-7.39 (m, 3H, ArH), 7.19 (t, *J* = 7.5 Hz, 2H, ArH), 6.76 (t, *J* = 7.5 Hz, 1H, ArH), 6.63 (d, *J* = 7.8 Hz, 2H, ArH), 4.70 (d, *J* = 7.5 Hz, 1H, H_2), 4.46 (bs, 2H, H_3 & H_4), 4.11 (d, *J* = 7.2 Hz, 1H, H_5), 3.64 (s, 3H, $COOCH_3$). δ_C NMR (75 MHz, $CDCl_3$) δ 172.1, 145.8, 139.3, 129.3, 128.9, 128.4, 127, 118.7, 113.9, 71.0, 66.0, 61.7, 52.3, 29.3. MS (EI) *m/z* 423 $(M+1)^+$, HRMS calculated $(M+H)^+$ 423.0569, found 423.0561, Anal. Calc. for $C_{18}H_{19}IN_2O_2$: C, 51.20; H, 4.54; N, 6.63; found: C, 51.12; H, 4.49; N, 6.69.

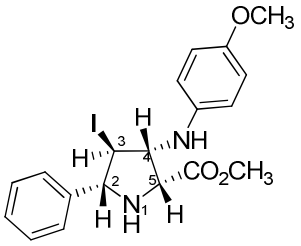


***Methyl 4-iodo-5-phenyl-3-(p-tolylamino)pyrrolidine-2-carboxylate (7b)*.** Yield: 88%; White solid; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.51 (m, 2H, ArH), 7.31-7.38 (m, 3H, ArH), 6.99 (m, 2H, ArH), 6.53 (d, *J* = 8.4 Hz, 2H, ArH), 4.69 (d, *J* = 7.2 Hz, 1H, H_2), 4.43 (bs, 2H, H_3 & H_4), 4.06-4.10 (m, 1H, H_5), 3.66

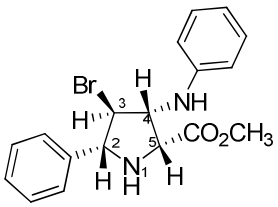
(s, 3H, $COOCH_3$), 2.23 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 172.3, 143.5, 140.1, 129.6, 128.7, 128.2, 126.9, 120.3, 114.1, 71.3, 66.5, 61.8, 52.2, 33.9, 20.4. MS (EI) *m/z* 437 $(M+1)^+$, HRMS calculated $(M+H)^+$ 437.0726, found 437.0726, Anal. Calc. for $C_{19}H_{21}IN_2O_2$: C, 52.31; H, 4.85; N, 6.42; found: C, 52.29; H, 4.80; N, 6.44.



Methyl 3-((4-chlorophenyl)amino)-4-iodo-5-phenylpyrrolidine-2-carboxylate (7c). Yield: 75%; White solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.43-7.45 (m, 2H, ArH), 7.28-7.39 (m, 3H, ArH), 7.12 (d, *J* = 8.0 Hz, 2H, ArH), 6.81-6.89 (m, 2H, ArH), 4.69 (d, *J* = 6.0 Hz, 1H, H_2), 4.48 (bs, 2H, H_3 & H_4), 4.12 (d, *J* = 7.0 Hz, 1H, H_5), 3.63 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 171.4, 146.6, 139.4, 129.1, 128.5, 128.4, 127.1, 117.3, 114.2, 71.2, 65.8, 61.8, 52.6, 29.7. MS (EI) *m/z* 457 $(M+1)^+$, HRMS calculated $(M+H)^+$ 457.0180, found 457.0177, Anal. Calc. for $C_{18}H_{18}ClIN_2O_2$: C, 47.34; H, 3.97; N, 6.13; found: C, 47.31; H, 3.92; N, 6.17.

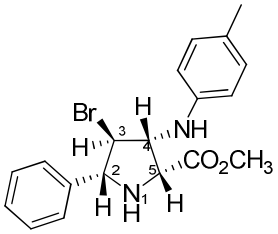


Methyl 4-iodo-3-((4-methoxyphenyl)amino)-5-phenylpyrrolidine-2-carboxylate (7d). Yield: 79%; White solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.32-7.38 (m, 4H, ArH), 7.10-7.25 (m, 3H, ArH), 6.83-6.87 (m, 2H, ArH), 4.69 (d, *J* = 6.5 Hz, 1H, H_2), 4.49 (bs, 2H, H_3 & H_4), 4.15 (d, *J* = 7.5 Hz, 1H, H_5), 3.77 (s, 3H, OCH_3), 3.60 (s, 3H, $COOCH_3$). δ_C NMR (75 MHz, $CDCl_3$) δ 169.0, 145.6, 137.7, 129.1, 128.7, 128.3, 127.0, 117.0, 113.6, 71.2, 66.5, 61.3, 55.8, 52.0, 29.6. MS (EI) *m/z* 453 $(M+1)^+$, HRMS calculated (M+H) 453.0675, found 453.0669, Anal. Calc. for $C_{19}H_{21}IN_2O_3$: C, 50.46; H, 4.68; N, 6.19; found: C, 50.39; H, 4.63; N, 6.21.

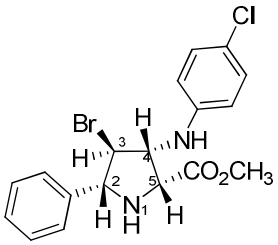


Methyl 4-bromo-5-phenyl-3-(phenylamino)pyrrolidine-2-carboxylate (7e). Yield: 87%; White solid; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.50 (m, 2H, ArH), 7.29-7.38 (m, 3H, ArH), 7.17 (t, *J* = 6.6 Hz, 2H, ArH), 6.75 (t, *J* = 7.5 Hz, 1H, ArH), 6.61 (d, *J* = 7.8 Hz, 2H, ArH), 4.60 (d, *J* = 6.0 Hz, 1H, H_2), 4.48

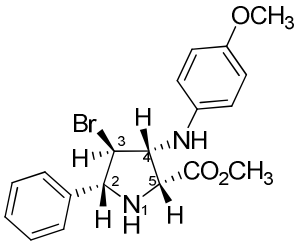
(d, *J* = 6 Hz, 1H, H_5), 4.40 (bs, 1H, H_3), 4.07 (dd, *J* = 3.9, 2.1 Hz, 1H, H_4), 3.68 (s, 3H, $COOCH_3$). δ_C NMR (75 MHz, $CDCl_3$) δ 171.6, 145.6, 139.4, 129.4, 128.8, 126.9, 118.7, 113.9, 69.8, 64.5, 61.8, 56.3, 52.3, 33.8. MS (EI) *m/z* 375 $(M+1)^+$, HRMS calculated $(M+H)^+$ 375.0708, found 375.0704, Anal. Calc. for $C_{18}H_{19}BrN_2O_2$: C, 57.61; H, 5.10; N, 7.47; found: C, 57.59; H, 5.04; N, 7.50.



Methyl 4-bromo-5-phenyl-3-(p-tolylamino)pyrrolidine-2-carboxylate (7f). Yield: 90%; White solid; δ_H ^{1}H NMR (300 MHz, $CDCl_3$) 7.5 (m, 2H, ArH), 7.28-7.38 (m, 3H, ArH), 6.98 (d, *J* = 7.8 Hz, 2H, ArH), 6.51 (d, *J* = 7.8 Hz, 2H, ArH), 4.60 (d, *J* = 5.7 Hz, 1H, H_2), 4.47 (d, *J* = 5.7 Hz, 1H, H_5), 4.36 (bs, 1H, H_3), 4.06 (dd, *J* = 6, 3.6 Hz, 1H, H_4), 3.68 (s, 3H, $COOCH_3$), 2.22 (s, 3H, CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 171.8, 143.3, 139.9, 129.8, 128.8, 128.2, 128.0, 126.8, 114.1, 70.0, 64.9, 61.9,56, 52.2, 29.7, 20.4. MS (EI) *m/z* 389 $(M+1)^+$, HRMS calculated $(M+H)^+$ 389.0865, found 389.0852, Anal. Calc. for $C_{19}H_{21}BrN_2O_2$: C, 58.62; H, 5.44; N, 7.20; found: C, 58.60; H, 5.41; N, 7.28.

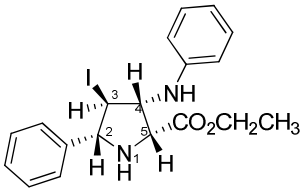


Methyl 4-bromo-3-((4-chlorophenyl)amino)-5-phenylpyrrolidine-2-carboxylate (7g). Yield: 80%; Brown solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.42-7.45 (m, 2H, ArH), 7.28-7.38 (m, 3H, ArH), 7.11 (t, *J* = 6.5 Hz, 2H, ArH), 6.81-6.87 (m, 2H, ArH), 4.62 (d, *J* = 5.5 Hz, 1H, H_2), 4.46 (d, *J* = 5.5 Hz, 1H, H_5), 4.37 (bs, 1H, H_3), 4.08 (dd, *J* = 6.0 & 3.0 Hz, 1H, H_4), 3.65 (s, 3H, $COOCH_3$). δ_C NMR (75 MHz, $CDCl_3$) δ 169.7, 145.2, 139.0, 129.6, 129.1, 128.7, 125.1, 116.7, 114.3, 70.9, 64.7, 60.9, 56.1, 53.0. MS (EI) *m/z* 409$(M+1)^+$, HRMS calculated $(M+H)^+$ 409.0318, found 409.0313, Anal. Calc. for $C_{18}H_{18}BrClN_2O_2$: C, 52.77; H, 4.43; N, 6.84; found: C, 52.73; H, 4.39; N, 6.87.

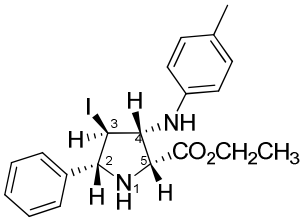


Methyl 4-bromo-3-((4-methoxyphenyl)amino)-5-phenylpyrrolidine-2-carboxylate (7h). Yield: 82%; Brown solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.47-7.49 (m, 2H, ArH), 7.28-7.42 (m, 3H, ArH), 7.22-7.23 (m, 2H, ArH), 7.04-7.06 (m, 2H, ArH), 4.61 (d, *J* = 6.0 Hz, 1H, H_2), 4.46 (d, *J* = 5.5 Hz, 1H,

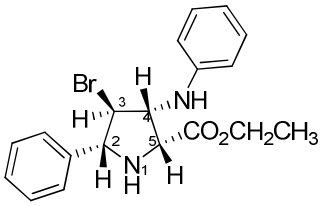
H_5), 4.34 (bs, 1H, H_3), 4.09 (dd, *J* = 6.5 & 3.5 Hz, 1H, H_4), 3.69 (s, 3H, OCH_3), 3.52 (s, 3H, $COOCH_3$). δ_C NMR (75 MHz, $CDCl_3$) δ 171.8, 146.0, 139.0, 129.1, 128.7, 128.1, 126.6, 118.4, 114.3, 70.9, 64.7, 61.3, 57.5, 56.1, 52.7. MS (EI) *m/z* 405 $(M+1)^+$, HRMS calculated $(M+H)^+$ 405.0814, found 405.0806, Anal. Calc. for $C_{19}H_{21}BrN_2O_3$: C, 56.31; H, 5.22; N, 6.91; found: C, 56.29; H, 5.17; N, 6.96.



Ethyl 4-iodo-5-phenyl-3-(phenylamino)pyrrolidine-2-carboxylate (7i). Yield: 86%; White solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.28-40 (m, 5H, ArH), 7.06-7.12 (m, 2H, ArH), 6.76 (t, *J* = 7.5 Hz, 1H, ArH), 6.62 (d, *J* = 7.5 Hz, 2H, ArH), 4.70 (d, *J* = 6.0 Hz, 1H, H_2), 4.46 (m, 2H, H_3 & H_4), 4.17 (m, 2H, CH_2), 4.08 (d, *J* = 7.0 Hz, 1H, H_5), 1.27 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 170.7, 145.6, 139.4, 129.4, 128.7, 128.3, 127.0, 118.7, 113.6, 71.2, 66.1, 61.3, 60.3, 29.3, 14.5. MS (EI) *m/z* 437 $(M+1)^+$, HRMS calculated (M+H) 437.0726, found 437.0720, Anal. Calc. for $C_{19}H_{21}IN_2O_2$: C, 52.31; H, 4.85; N, 6.42; found: C, 52.27; H, 4.79; N, 6.47.

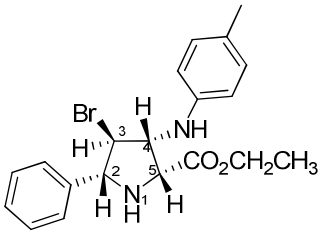


Ethyl 4-iodo-5-phenyl-3-(p-tolylamino)pyrrolidine-2-carboxylate (7j). Yield: 82%; White solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.35-7.49 (m, 4H, ArH), 7.22-7.28 (m, 3H, ArH), 7.05 (d, *J* = 8.5 Hz, 2H, ArH), 4.68 (d, *J* = 7.0 Hz, 1H, H_2), 4.39-4.50 (m, 2H, H_3 & H_4), 4.10-4.18 (m, 3H, CH_2 & H_5), 2.27 (s, 3H, CH_3), 1.28 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 171.4, 143.5, 139.4, 129.4, 128.7, 128.1, 126.3, 120.8, 114.3, 71.2, 66.5, 62.0, 60.3, 33.8, 20.7, 13.8. MS (EI) *m/z* 451 $(M+1)^+$, HRMS calculated $(M+H)^+$ 451.0882, found 451.0879, Anal. Calc. for $C_{20}H_{23}IN_2O_2$: C, 53.34; H, 5.15; N, 6.22; found: C, 53.31; H, 5.10; N, 6.27.



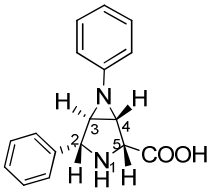
Ethyl 4-bromo-5-phenyl-3-(phenylamino)pyrrolidine-2-carboxylate (7k). Yield: 73%; Brown solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.50 (m, 2H, ArH), 7.32-7.48 (m, 5H, ArH), 7.23-7.28 (m, 2H, ArH), 7.02 (t, *J* = 7.5 Hz, 1H, ArH), 4.61 (d, *J* = 5.5 Hz, 1H, H_2), 4.46 (d, *J* = 5.5 Hz, 1H, H_5), 4.39 (bs,

1H, H_3), 4.06-4.13 (m, 3H, CH_2 & H_4), 1.19 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 171.1, 145.2, 139.4, 129.4, 129.1, 127.8, 126.3, 118.7, 114.0, 69.9, 64.4, 61.6, 60.6, 56.9, 14.5. MS (EI) *m/z* 390 $(M+1)^+$, HRMS calculated $(M+H)^+$ 389.0865, found 389.0855, Anal. Calc. for $C_{19}H_{21}BrN_2O_2$: C, 58.62; H, 5.44; N, 7.20; found: C, 58.59; H, 5.36; N, 7.24.

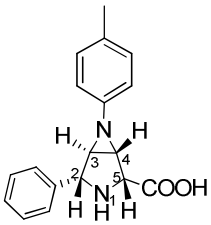


Ethyl 4-bromo-5-phenyl-3-(p-tolylamino)pyrrolidine-2-carboxylate (7l). Yield: 81%; Brown solid; δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 7.28-7.49 (m, 5H, ArH), 7.22 (m, 2H, ArH), 7.05 (m, 2H, ArH), 4.59 (d, *J* = 6.0 Hz, 1H, H_2), 4.47 (d, *J* = 6.0 Hz, 1H, H_5), 4.36 (bs, 1H, H_3), 4.08-4.17 (m, 3H, CH_2 & H_4), 2.21 (s, 3H, CH_3), 1.28 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). δ_C NMR (75 MHz, $CDCl_3$) δ 170.1, 143.4, 139.8, 129.7, 129.4, 128.7, 128.1, 126.6, 114.3, 70.3, 64.7, 62.0, 60.6, 56.1, 29.7, 21.5, 13.7. MS (EI) *m/z* 404 $(M+1)^+$, HRMS calculated $(M+H)^+$ 403.1021, found 403.1014, Anal. Calc. for $C_{20}H_{23}BrN_2O_2$: C, 59.56; H, 5.75; N, 6.95; found: C, 59.51; H, 5.73; N, 6.98.

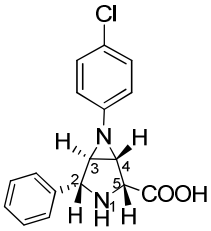
5. Typical procedure for the preparation of 4,6-diaryl-3,6-diazabicyclo[3.1.0] hexane-2-carboxylic acid 8. To a solution of compound 2 (30mg, 1 eq) in methanol/ethanol (5 ml), NaOMe/NaOEt (6.5 eq) was added and the reaction mixture was stirred at room temperature for 1 hr. Then the reaction mixture was heated upto 50°C for 30 minutes. The progress of the reaction was monitored with the help of TLC. After completion of the reaction, the mixture was quenched with ice and pH adjust to 6-7. Now, the reaction mixture was concentrated under reduced pressure and purified *via* flash column chromatography using silica gel (100:200 mesh) in MeOH/DCM (1:9) as an elutent system to get compound 6 as a pure product.



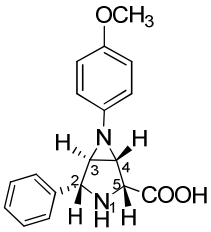
4,6-diphenyl-3,6-diazabicyclo[3.1.0]hexane-2-carboxylic acid (8a). Yield: 90%; Brown solid; δ_H ^{1}H NMR (300 MHz, MeOD) 7.68 (dd, *J* = 8.4 & 1.5 Hz, 2H, ArH), 7.31-7.42 (m, 3H, ArH), 7.12 (t, *J* = 7.8 Hz, 2H, ArH), 6.58 (d, *J* = 7.8 Hz, 3H, ArH), 4.10 (d, *J* = 1.8 Hz, 1H, H_2), 3.68 (d, *J* = 1.8 Hz, 1H, H_5), 3.23 (dd, *J* = 4.5, 2.1 Hz, 1H, H_3), 3.08 (dd, *J* = 4.5, 2.1 Hz, 1H, H_4). δ_C NMR (75 MHz, $DMSOD_6$) δ 173.8, 154.1, 141.8, 129.07, 128.6, 127.8, 127.5, 121.7, 120.9, 64.3, 63.6, 49.7, 49.0. MS (EI) *m/z* 281 $(M+1)^+$, HRMS calculated $(M+H)^+$ 281.1290, found 281.1289, Anal. Calc. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99; found: C, 72.78; H, 5.71; N, 10.02.



4-phenyl-6-(p-tolyl)-3,6-diazabicyclo[3.1.0]hexane-2-carboxylic acid (8b). Yield: 88%; Brown solid; δ_H ^{1}H NMR (500 MHz, MeOD) 7.51 (m, 2H, ArH), 7.25-7.48 (m, 3H, ArH), 7.03 (m, 2H, ArH), 6.70 (d, *J* = 7.5 Hz, 2H, ArH), 4.09 (d, *J* = 2.0 Hz, 1H, H_2), 3.65 (d, *J* = 2.0 Hz, 1H, H_5), 3.19 (dd, *J* = 4.0, 2.0 Hz, 1H, H_3), 3.08 (dd, *J* = 4.5, 2.0 Hz, 1H, H_4), 2.27 (s, 3H, CH_3). δ_C NMR (75 MHz, $DMSOD_6$) δ 172.8, 154.5, 141.7, 129.1, 128.5, 127.5, 127.4, 121.8, 121.3, 64.3, 63.9, 49.8, 49.2, 21.4. MS (EI) *m/z* 295 $(M+1)^+$, HRMS calculated $(M+H)^+$ 295.1447, found 295.1440, Anal. Calc. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52; found: C, 73.38; H, 6.10; N, 9.54.



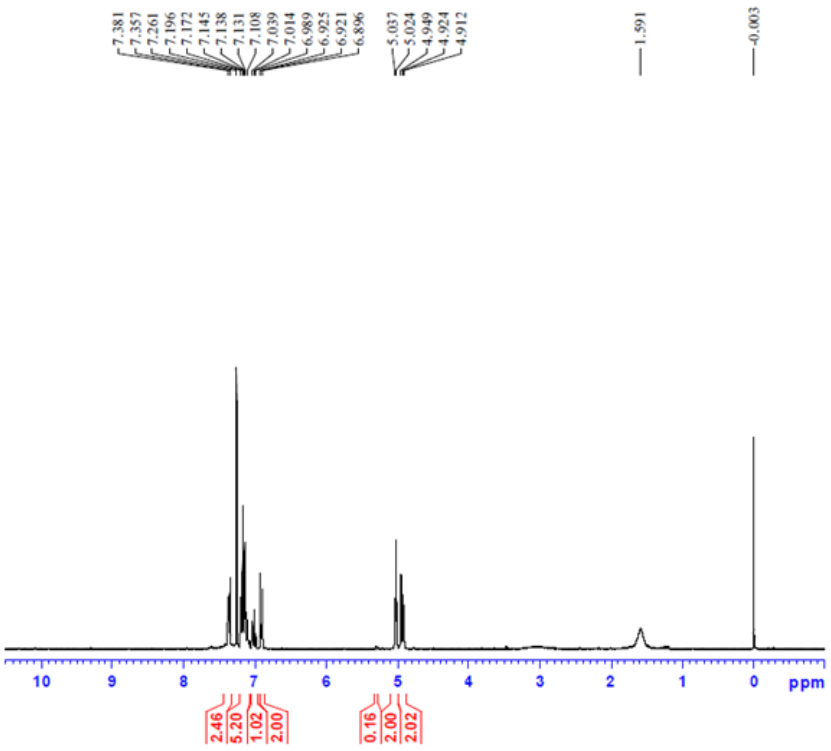
6-(4-chlorophenyl)-4-phenyl-3,6-diazabicyclo[3.1.0]hexane-2-carboxylic acid (8c). Yield: 82%; Brown solid; δ_H ^{1}H NMR (500 MHz, MeOD) 7.25-7.51 (m, 5H, ArH), 6.99-7.02 (m, 2H, ArH), 6.71-6.76 (m, 2H, ArH), 4.10 (d, *J* = 2.0 Hz, 1H, H_2), 3.64 (d, *J* = 2.0 Hz, 1H, H_5), 3.20 (dd, *J* = 4.5, 2.0 Hz, 1H, H_3), 3.08 (m, 1H, H_4). δ_C NMR (75 MHz, $DMSOD_6$) δ 172.1, 154.5, 141.8, 129.4, 128.3, 127.4, 127.0, 121.5, 120.8, 64.4, 63.3, 48.9, 47.9. MS (EI) *m/z* 315 $(M+1)^+$, HRMS calculated $(M+H)^+$ 315.0900, found 315.0891, Anal. Calc. for $C_{17}H_{15}ClN_2O_2$: C, 64.87; H, 4.80; N, 8.90; found: C, 64.85; H, 4.85; N, 8.96.



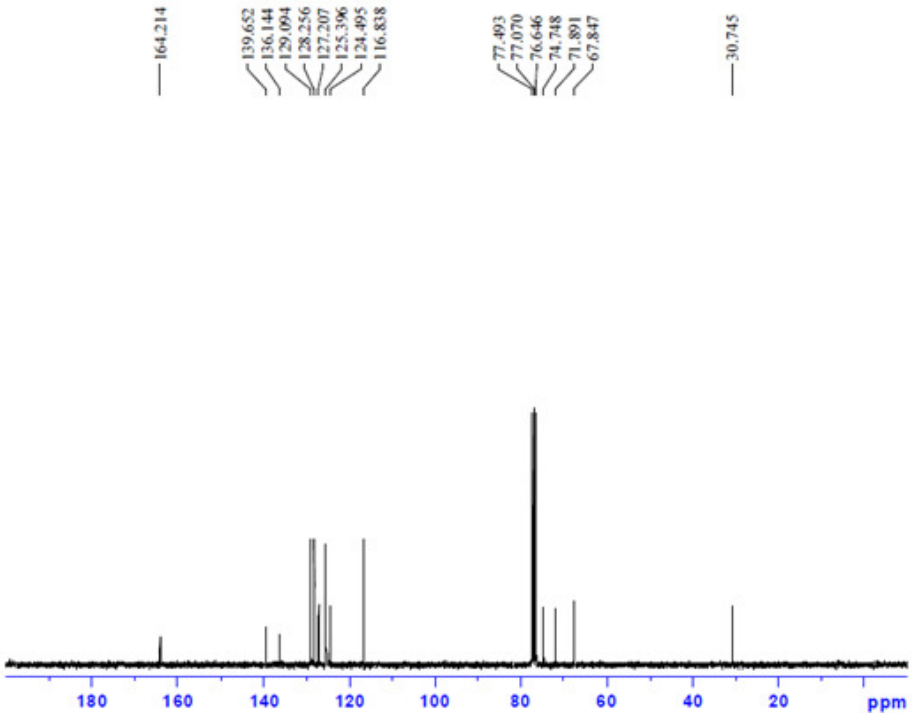
6-(4-methoxyphenyl)-4-phenyl-3,6-diazabicyclo[3.1.0]hexane-2-carboxylic acid (8d). Yield: 85%; Brown solid; δ_H ^{1}H NMR (500 MHz, MeOD) 7.23-7.53 (m, 5H, ArH), 6.74-7.02 (m, 4H, ArH), 4.10 (d, *J* = 1.5 Hz, 1H, H_2), 3.66 (d, *J* = 1.5 Hz, 1H, H_5), 3.23 (dd, *J* = 4.5, 2.0 Hz, 1H, H_3), 3.19 (s, 3H, OCH_3) 3.07 (dd, *J* = 4.5 & 2.0 Hz, 1H, H_4). δ_C NMR (75 MHz, $DMSOD_6$) δ 173.8, 154.2, 141.5, 129.8, 128.7, 127.7, 127.4, 121.9, 120.4, 64.4, 63.0, 55.8, 49.9, 48.9. MS (EI) *m/z* 311 $(M+1)^+$, HRMS calculated $(M+H)^+$ 311.1396, found 310.1388, Anal. Calc. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03; found: C, 69.63; H, 5.78; N, 9.08.

6. Copies of ^{1}H, ^{13}C NMR spectra

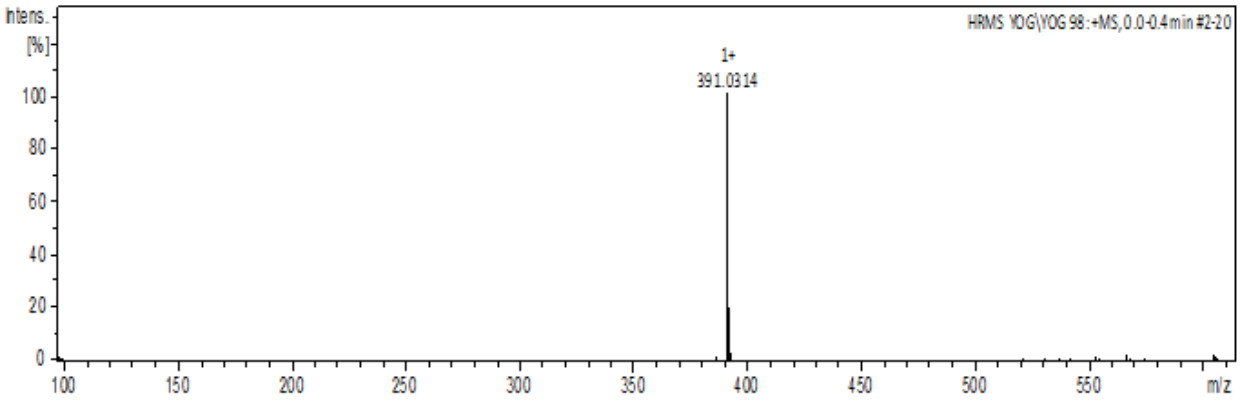
^{1}H NMR spectrum of **2a:**



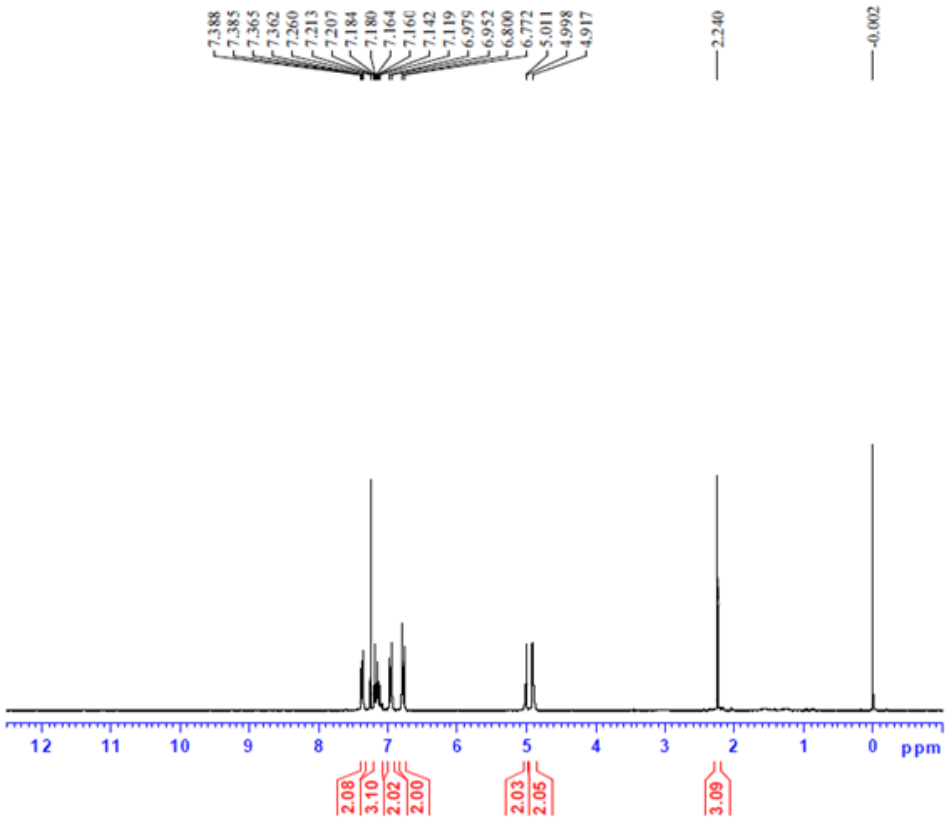
^{13}C NMR spectrum of **2a**:



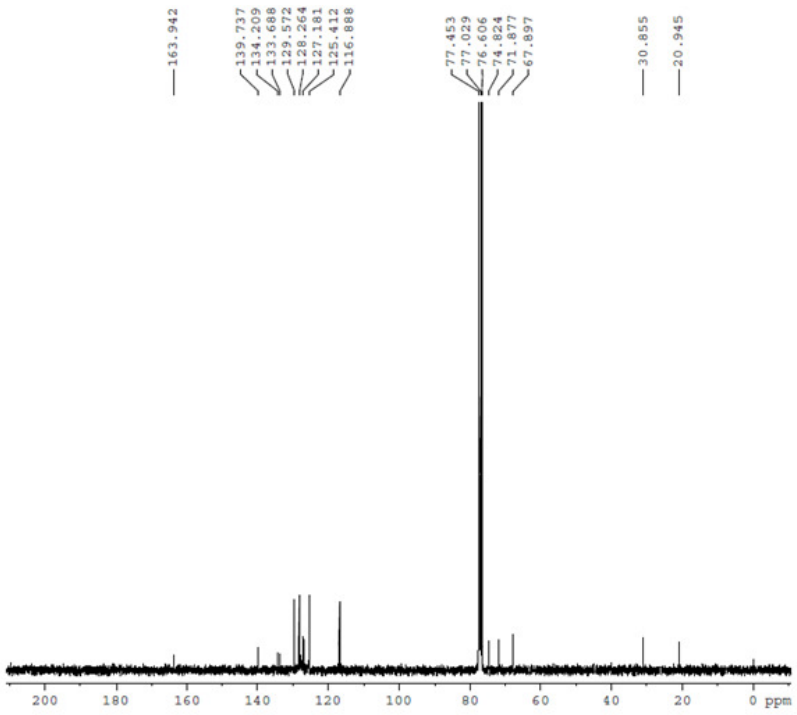
Mass spectrum of **2a**:



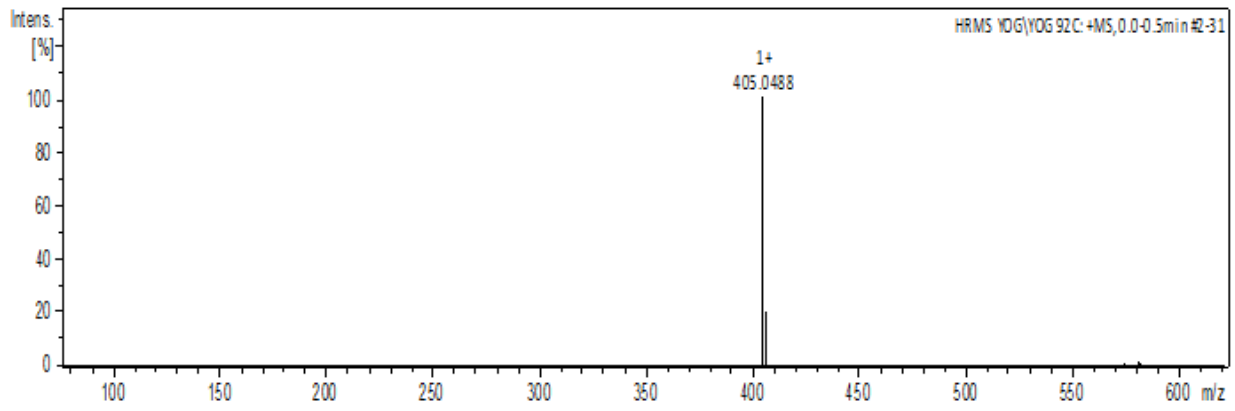
^{1}H NMR spectrum of **2b:**



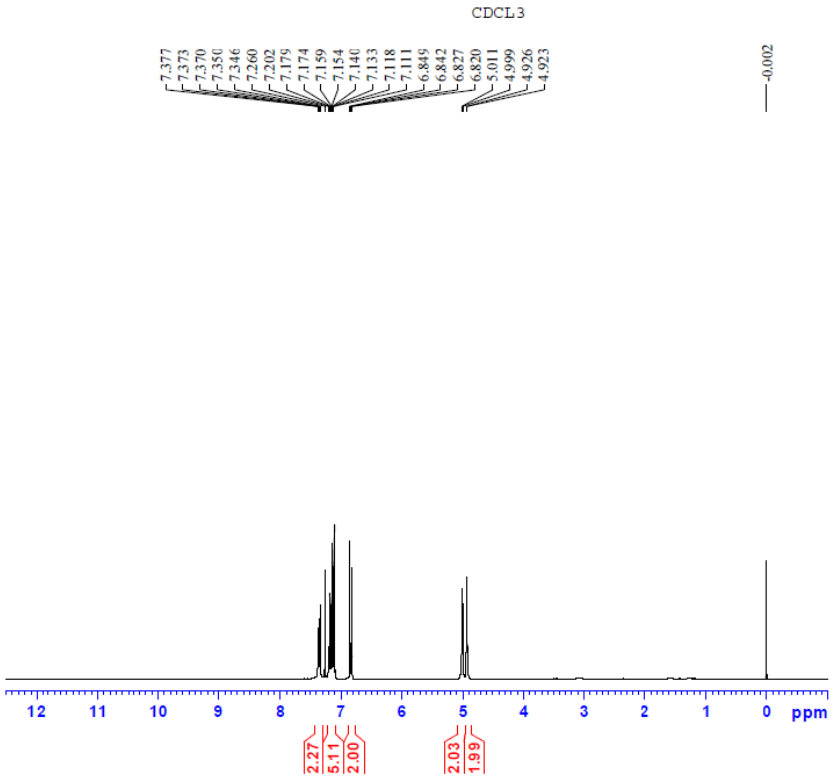
^{13}C NMR spectrum of **2b**:



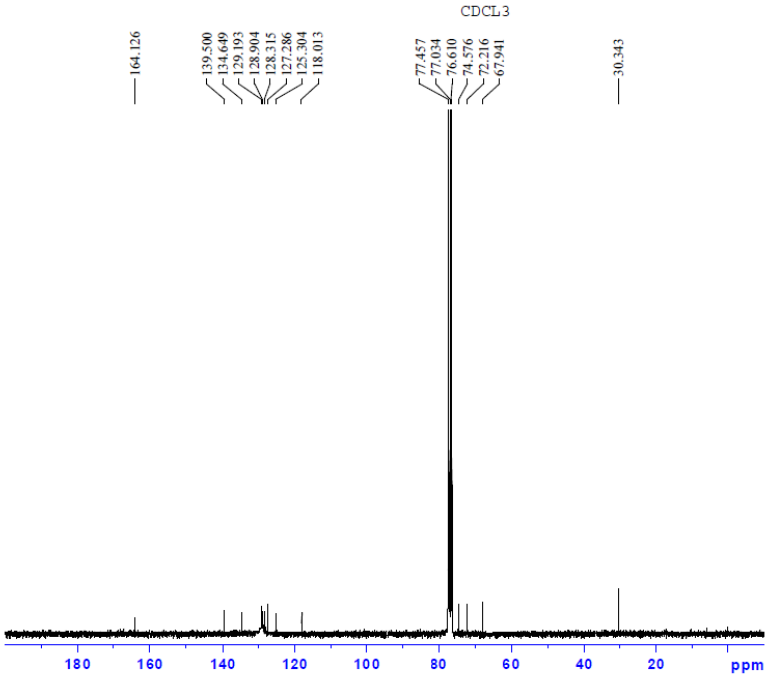
HRMS spectrum of **2b**:



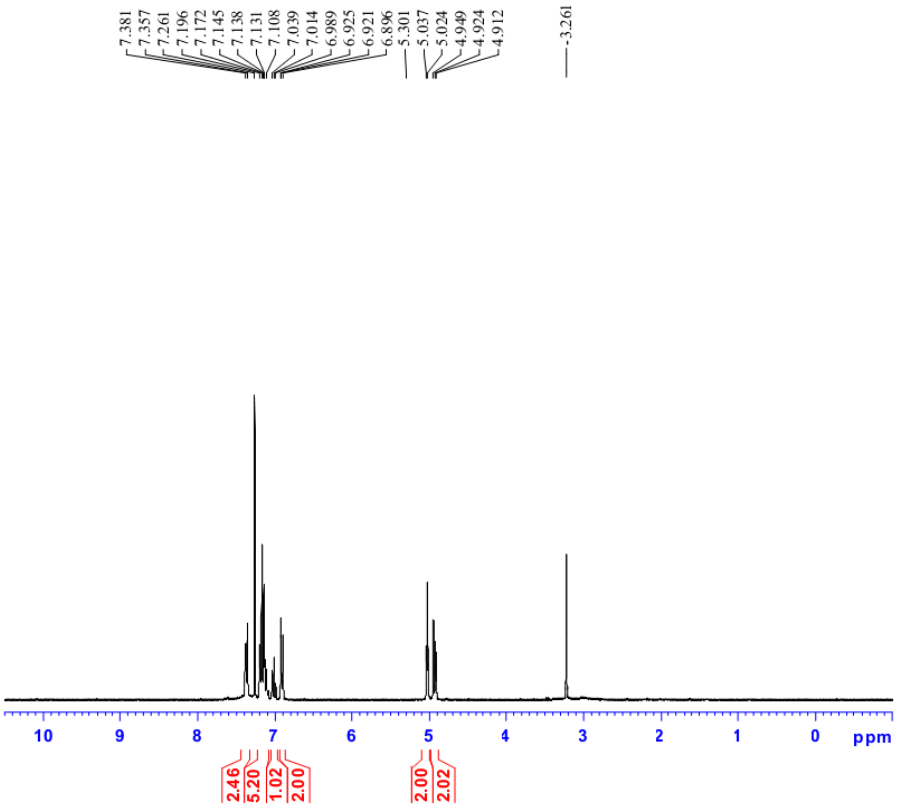
^{1}H NMR spectrum of **2c:**



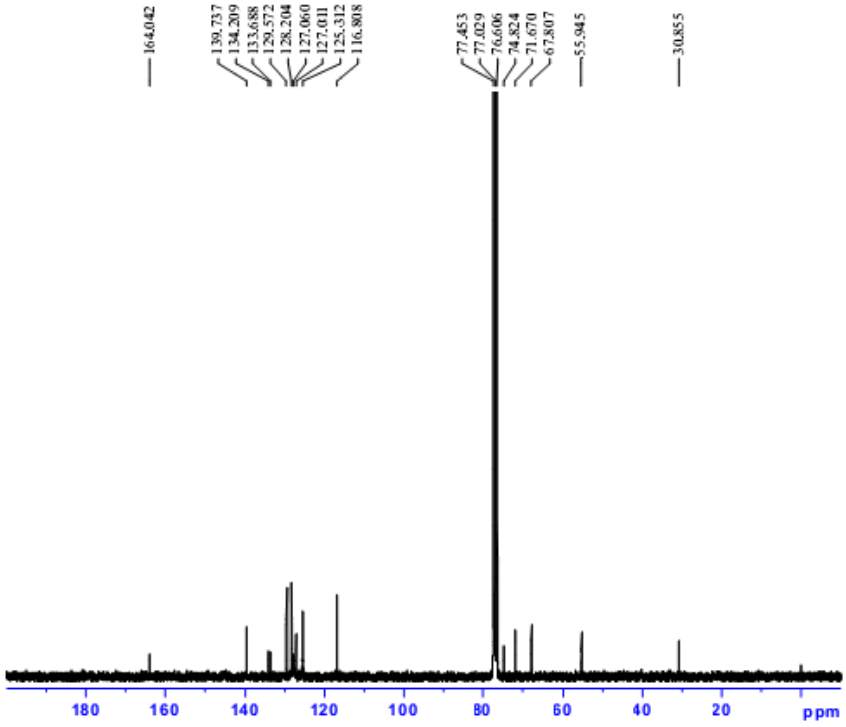
^{13}C NMR spectrum of **2c**:



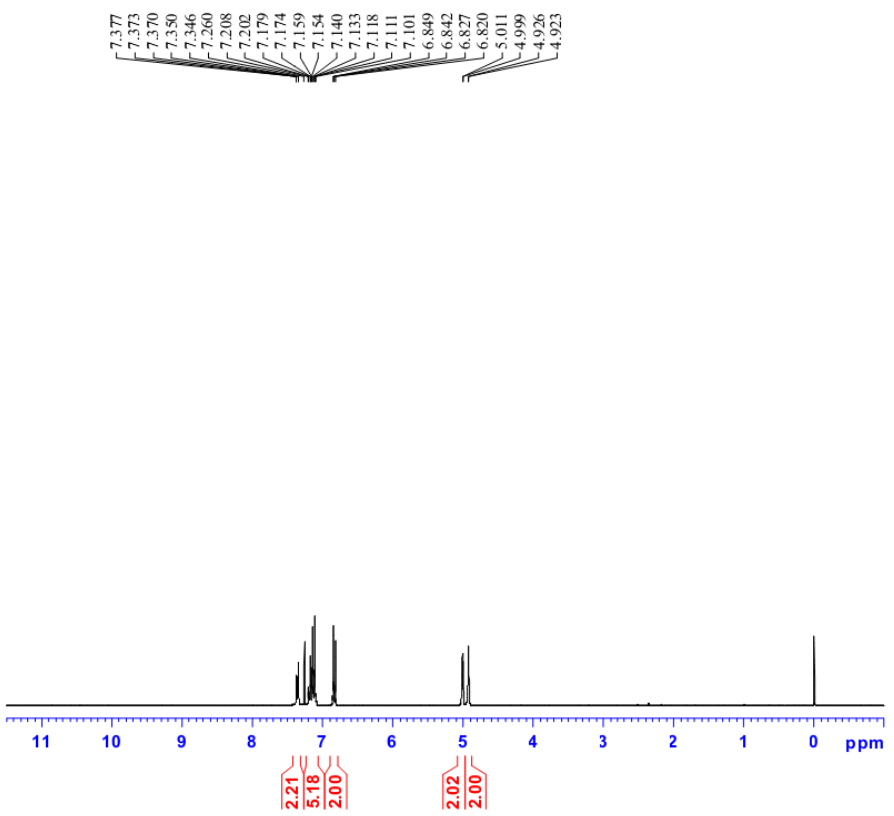
^{1}H NMR spectrum of **2d:**



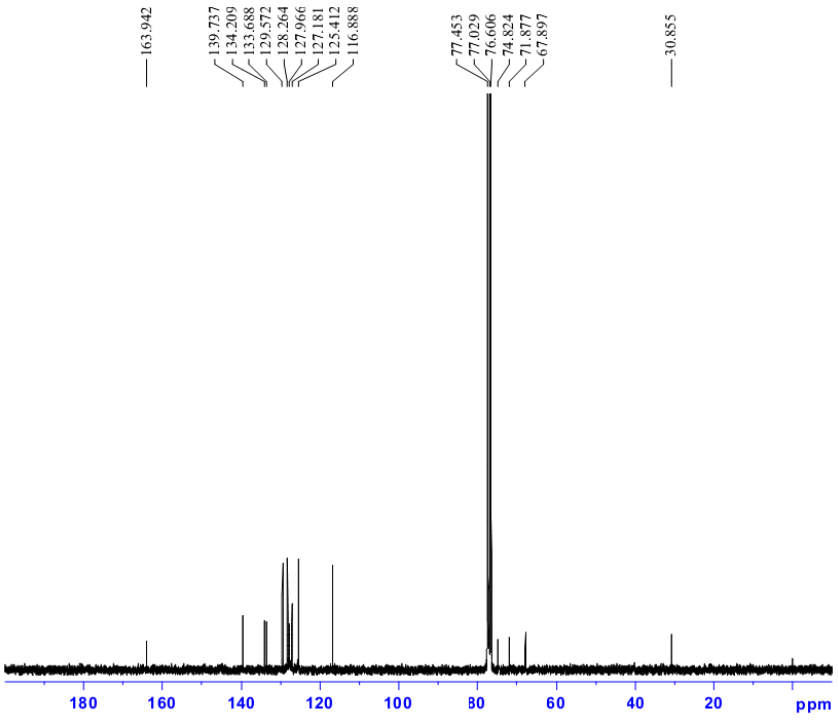
^{13}C NMR spectrum of **2d**:



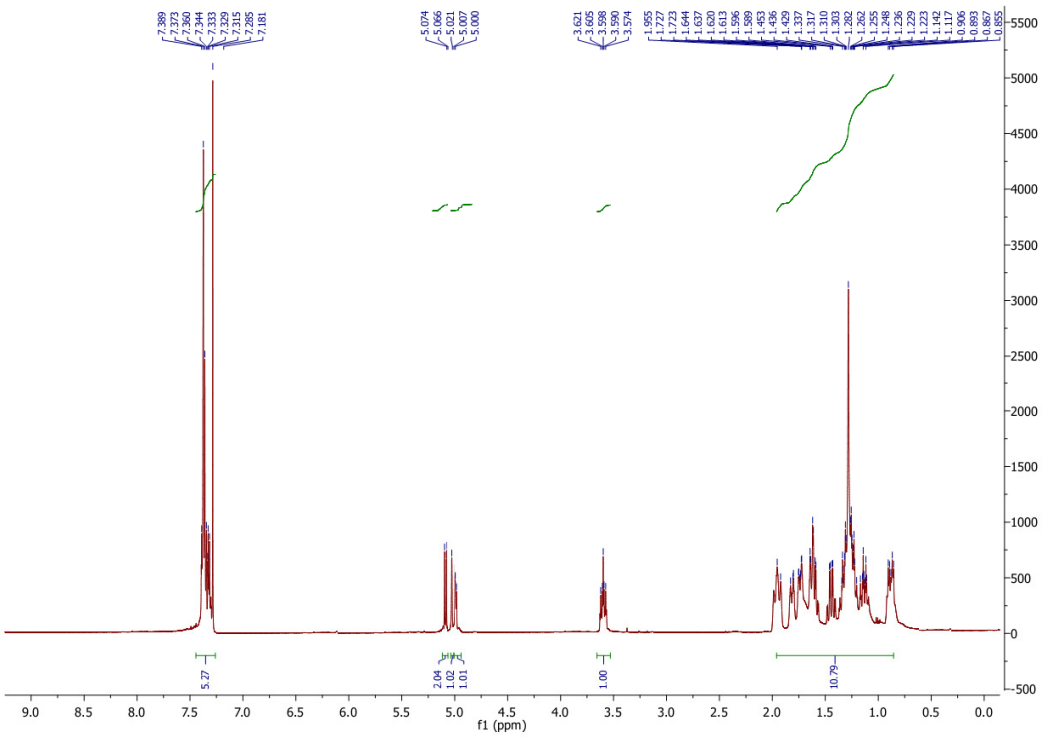
^{1}H NMR spectrum of **2e:**



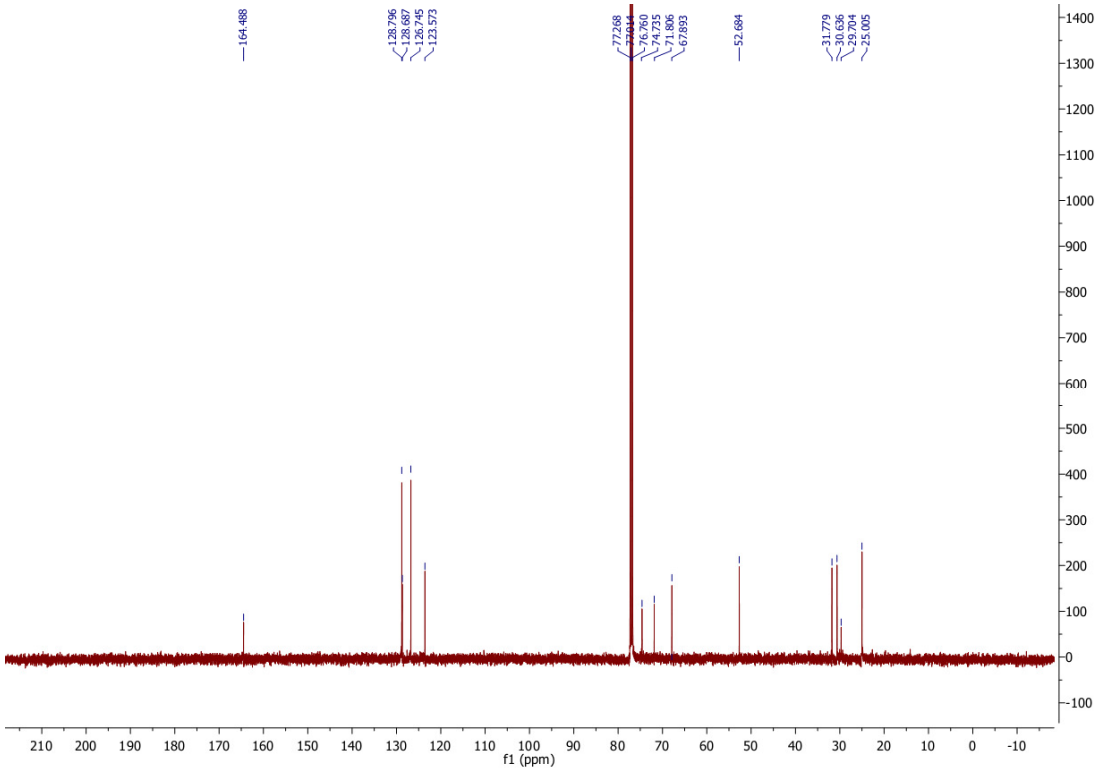
^{13}C NMR spectrum of **2e**:



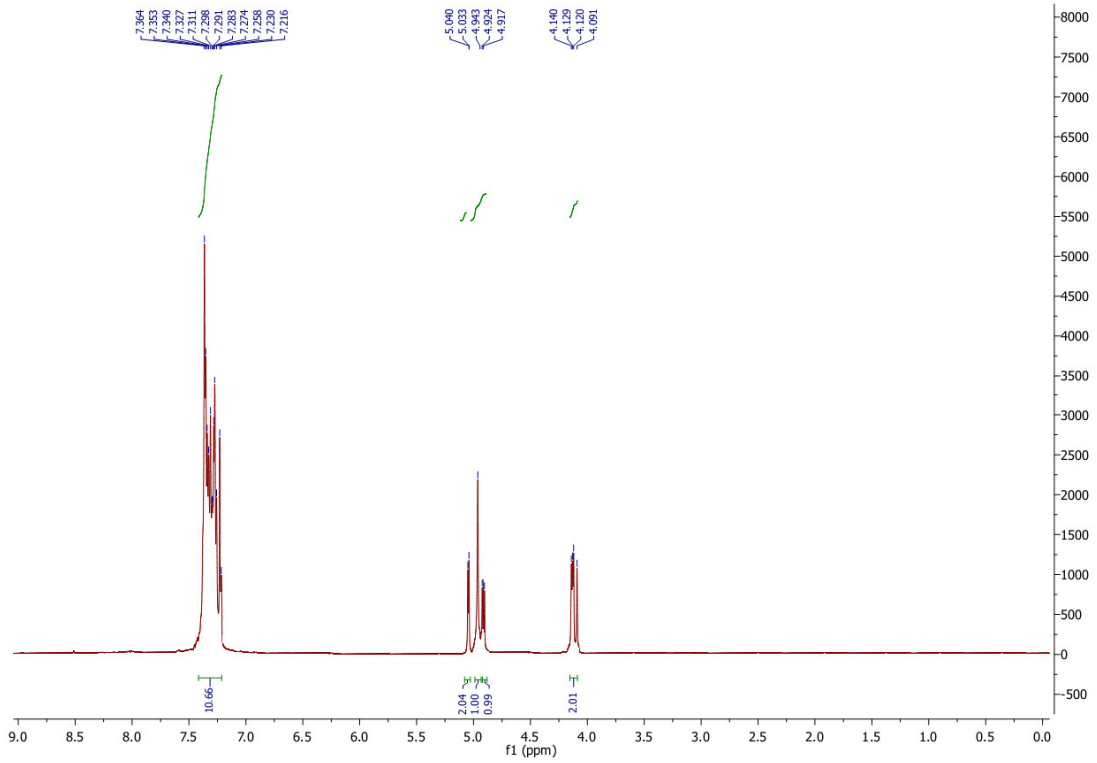
^{1}H NMR spectrum of **2f:**



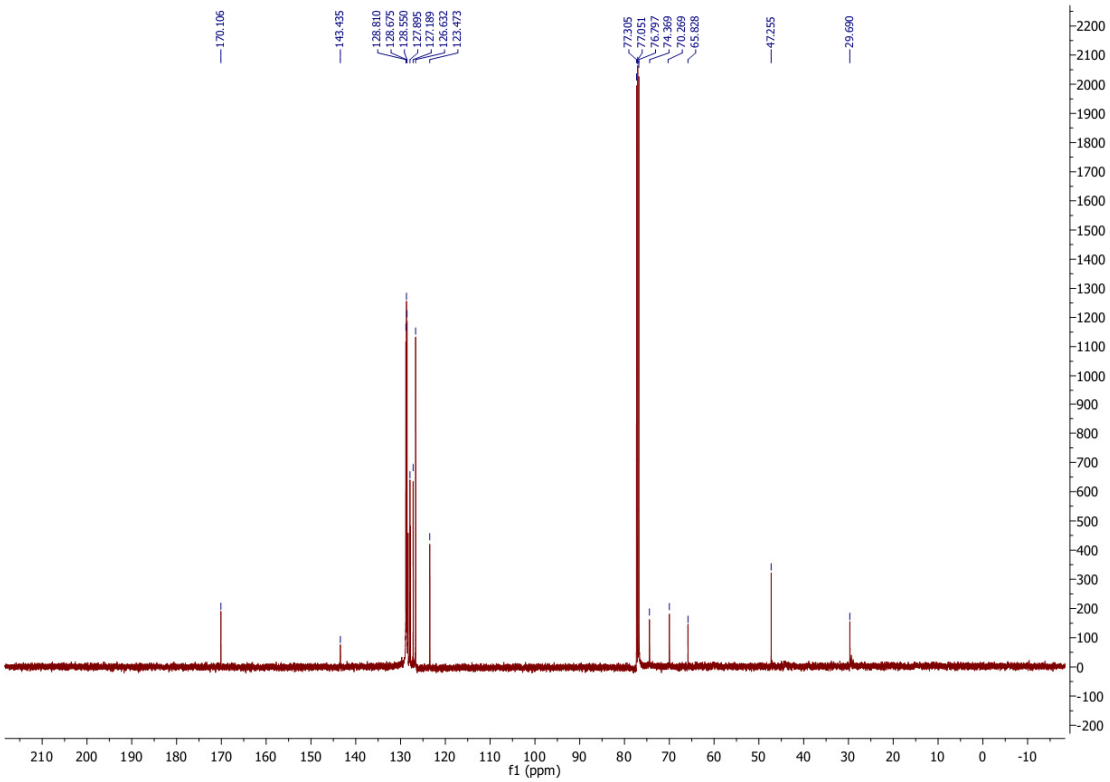
^{13}C NMR spectrum of **2f**:



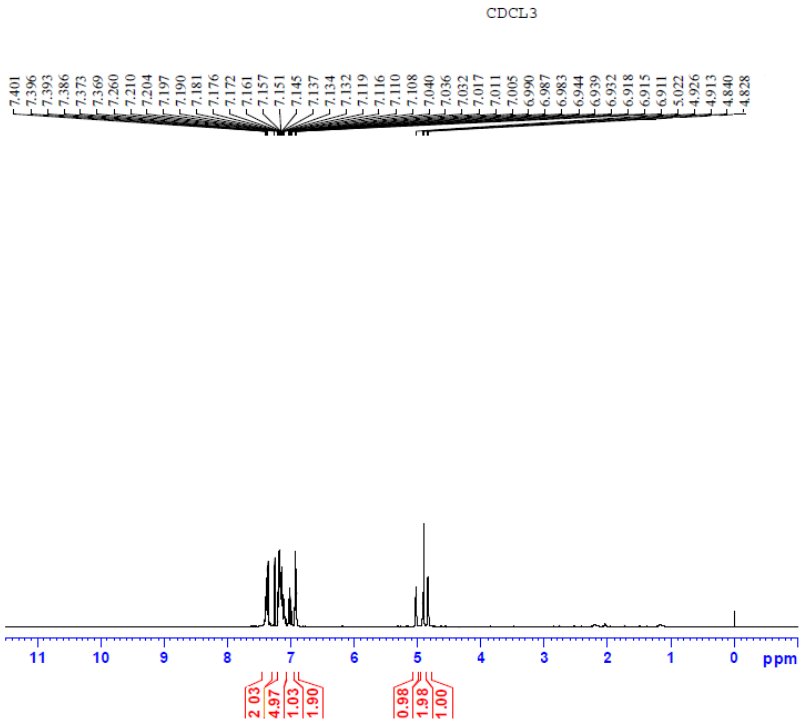
^{1}H NMR spectrum of **2g:**



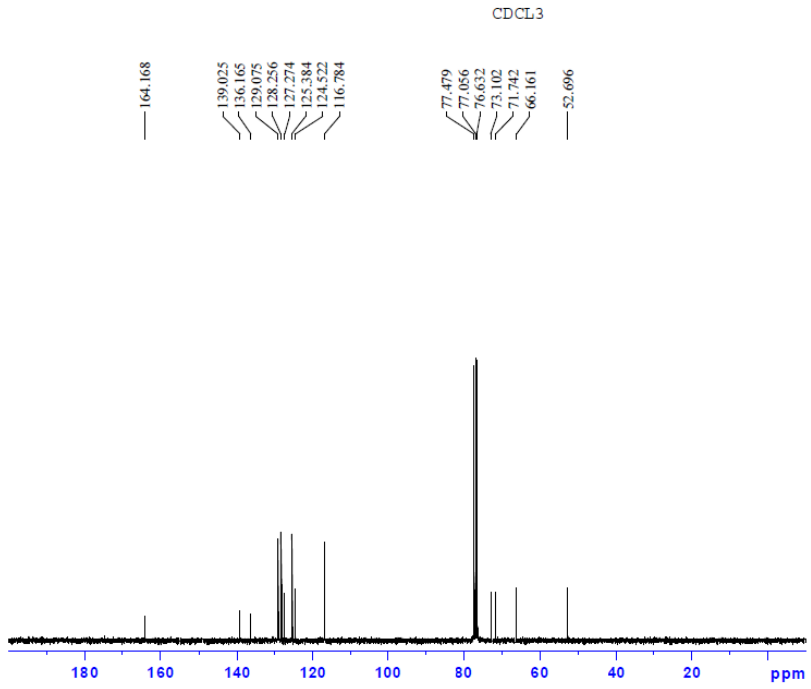
^{13}C NMR spectrum of **2g**:



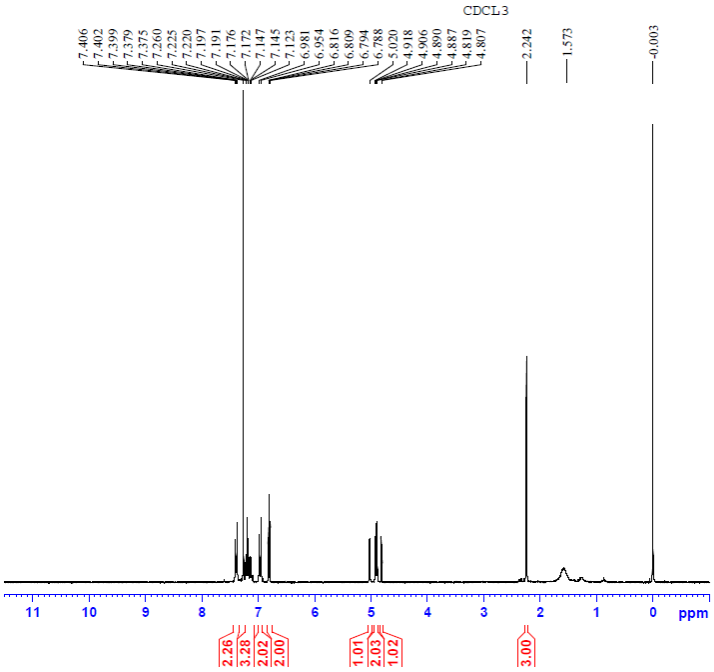
^{1}H NMR spectrum of **2h:**



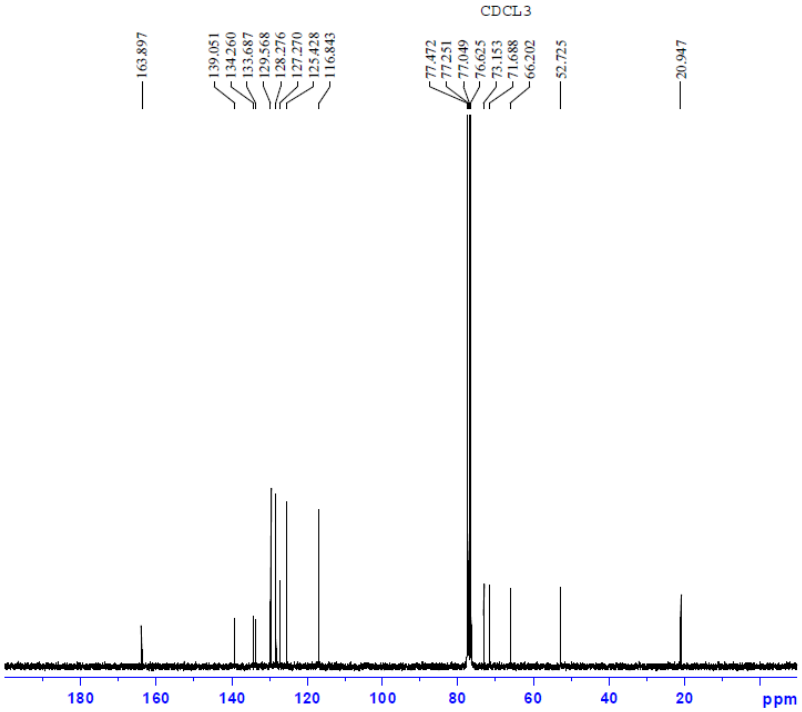
^{13}C NMR spectrum of **2h**:



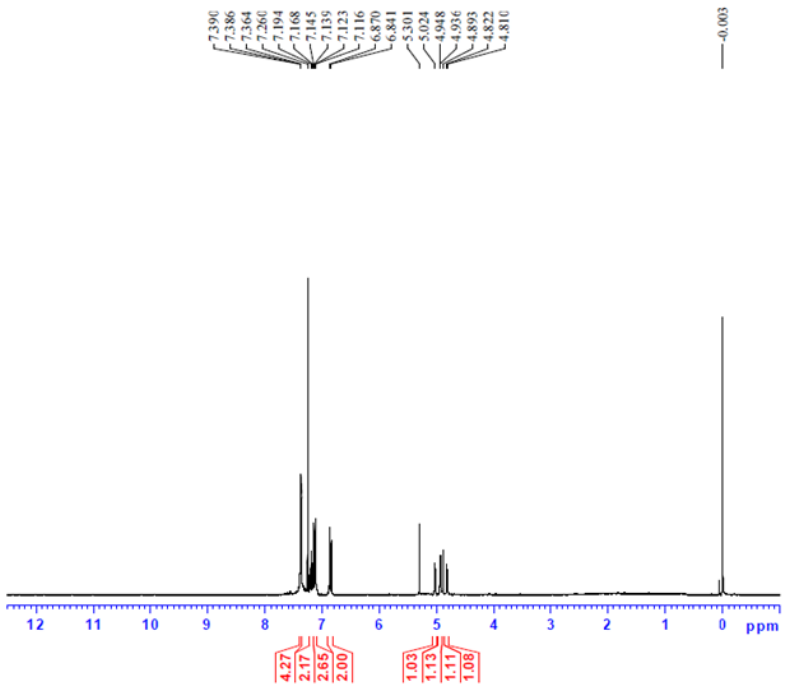
^{1}H NMR spectrum of **2i:**



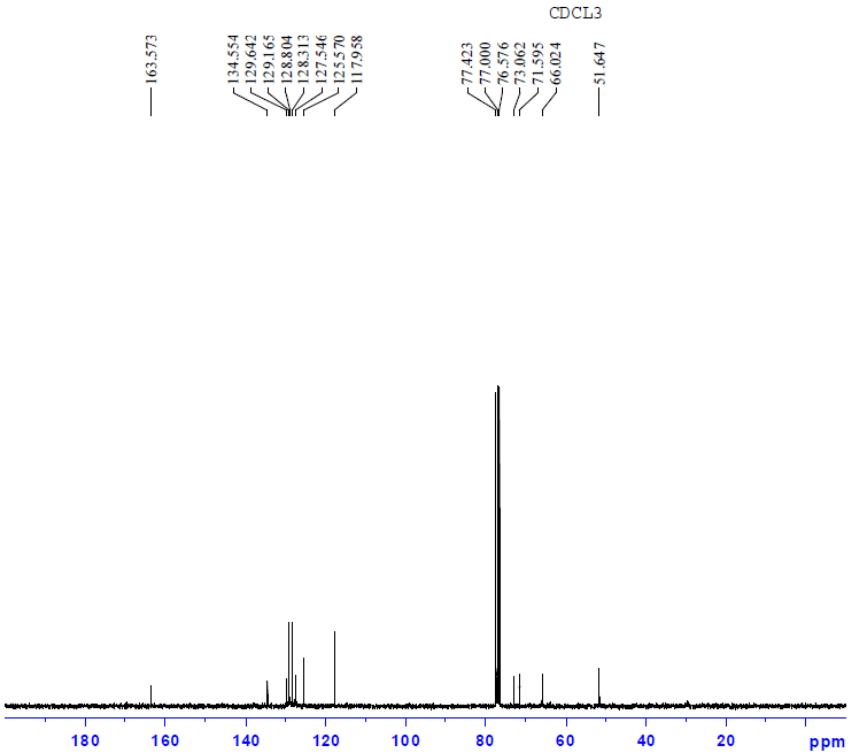
^{13}C NMR spectrum of **2i**:



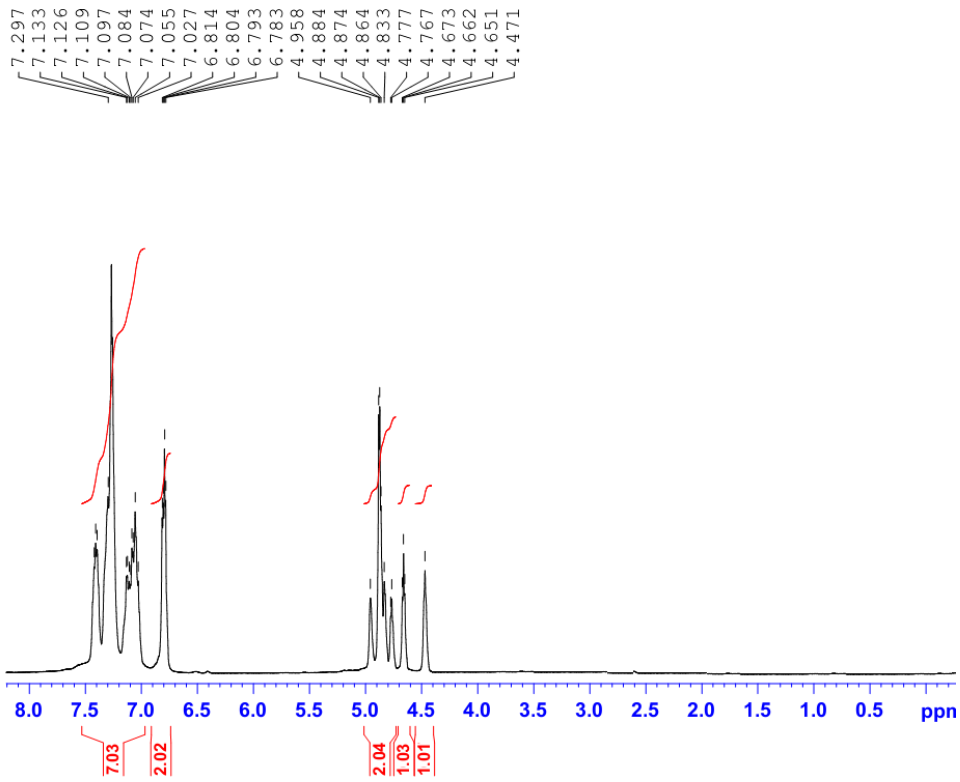
^{1}H NMR spectrum of **2j:**



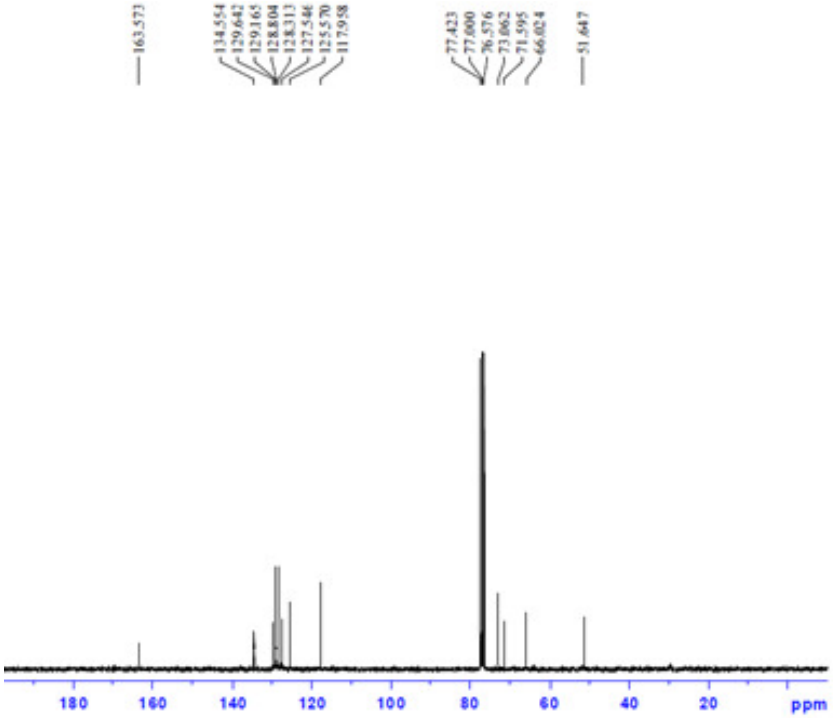
^{13}C NMR spectrum of **2j**:



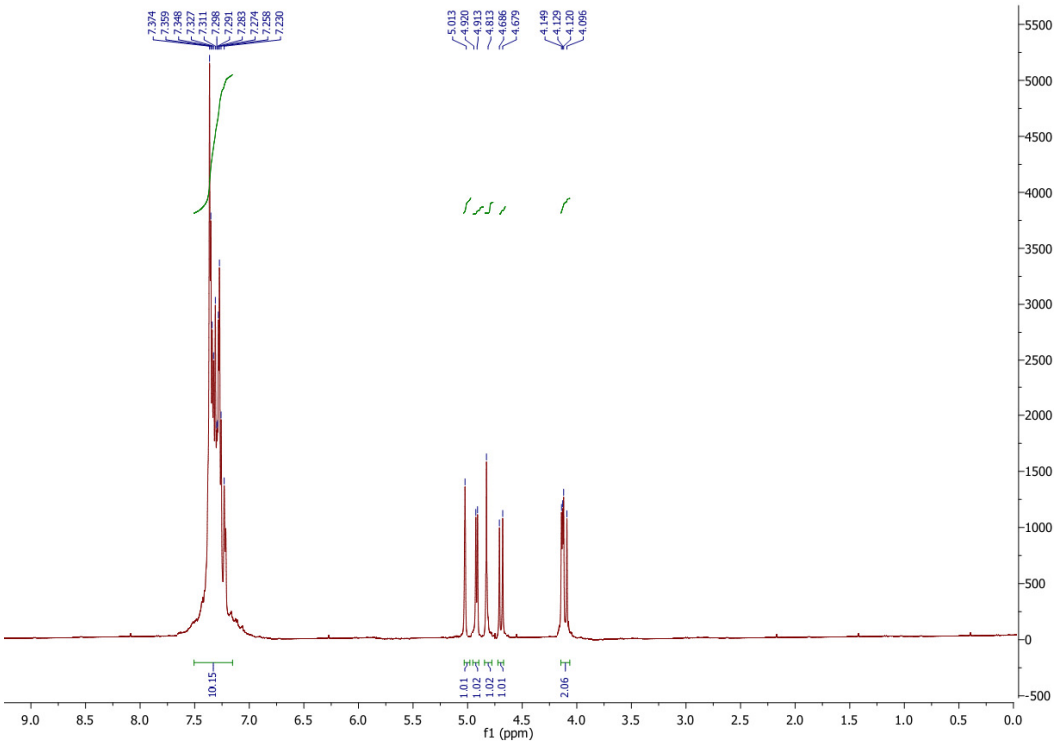
^{1}H NMR spectrum of **2l:**



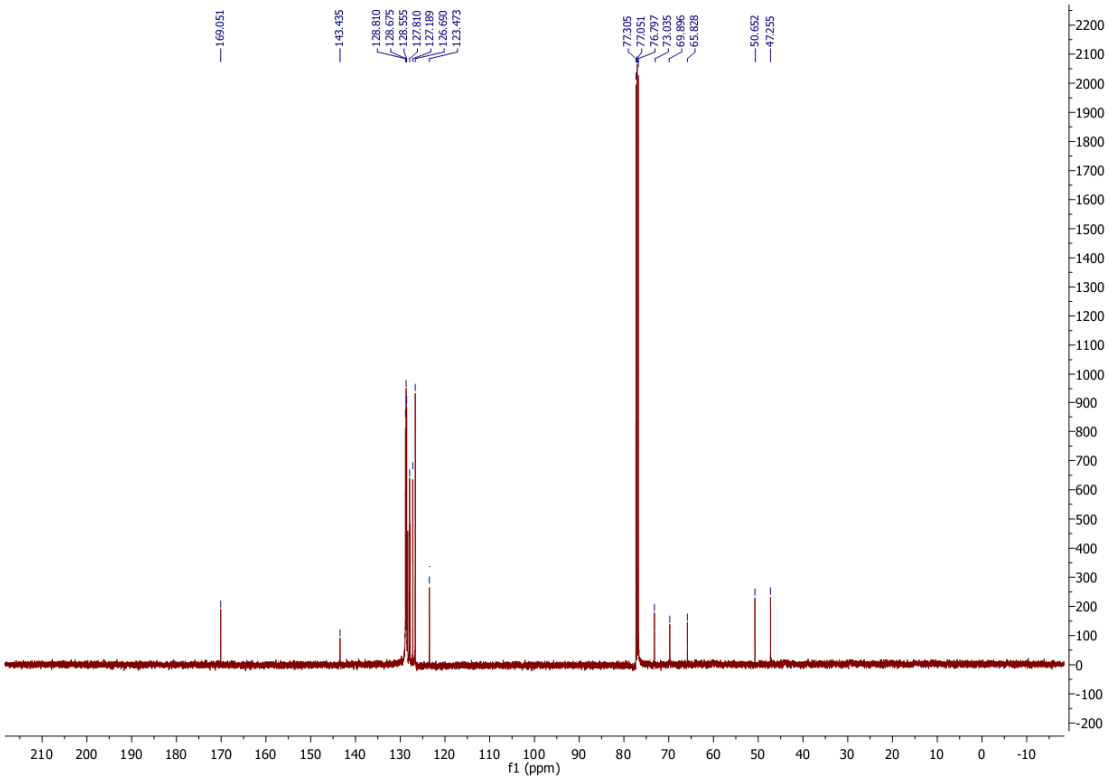
^{13}C NMR spectrum of **2l**:



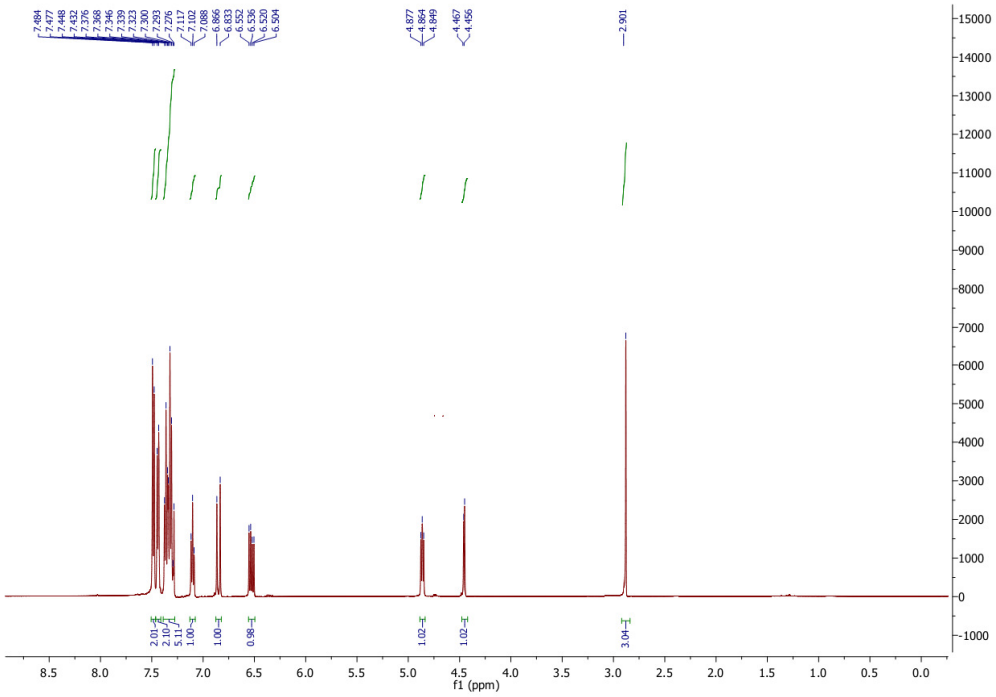
^{1}H NMR spectrum of **2m:**



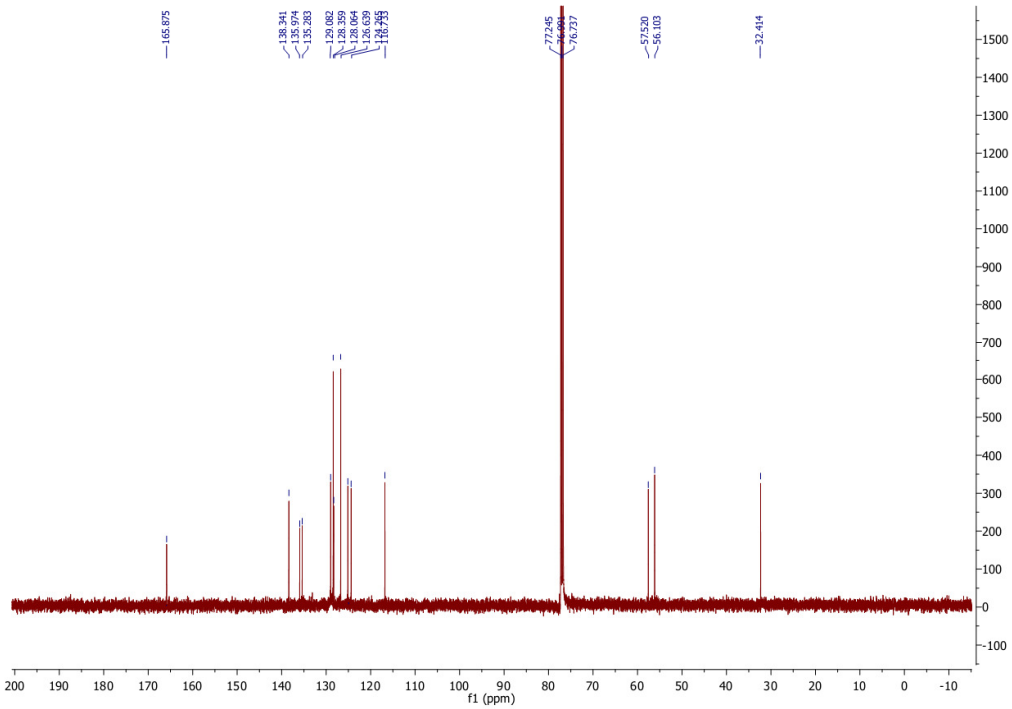
^{13}C NMR spectrum of **2m**:



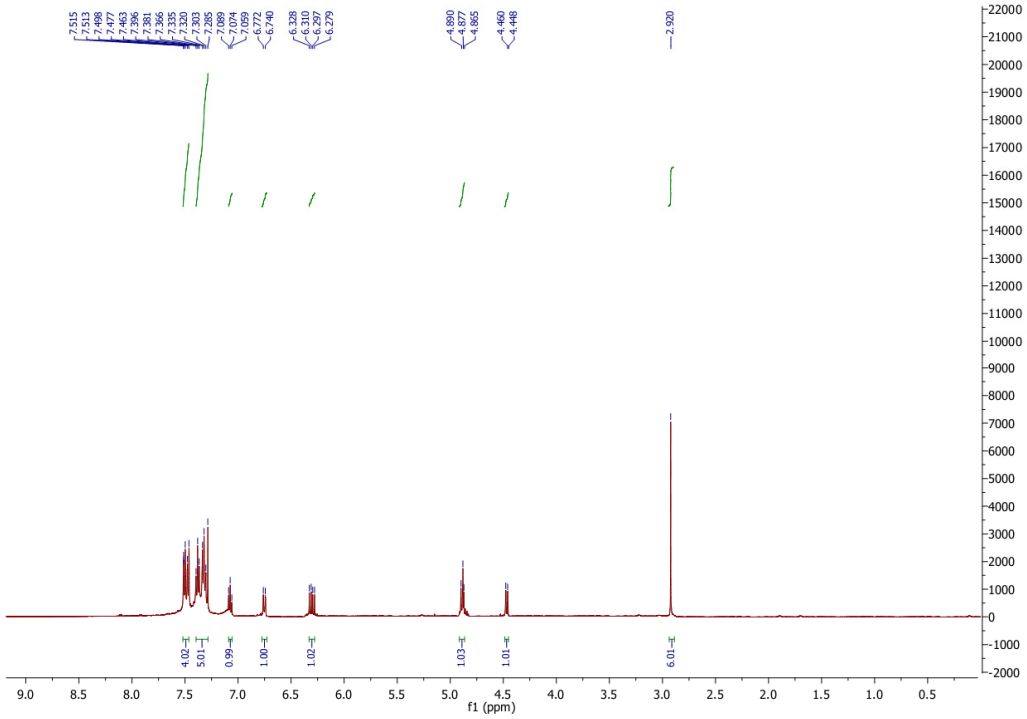
^{1}H NMR spectrum of **5a:**



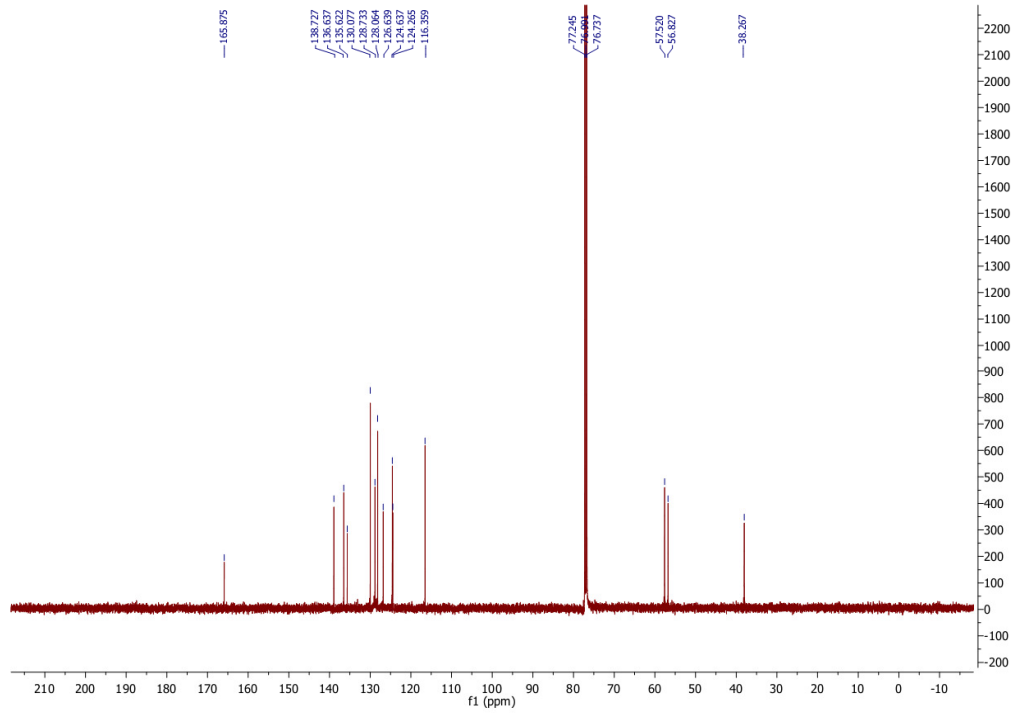
^{13}C NMR spectrum of **5a**:



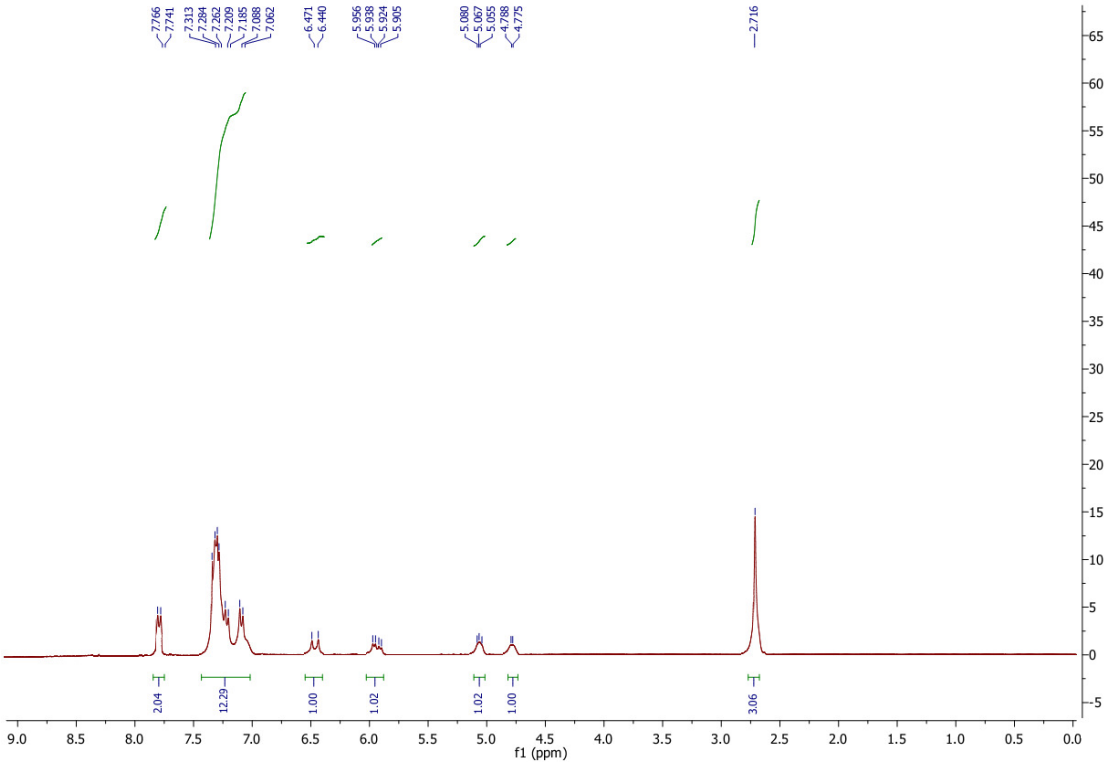
^{1}H NMR spectrum of **5b:**



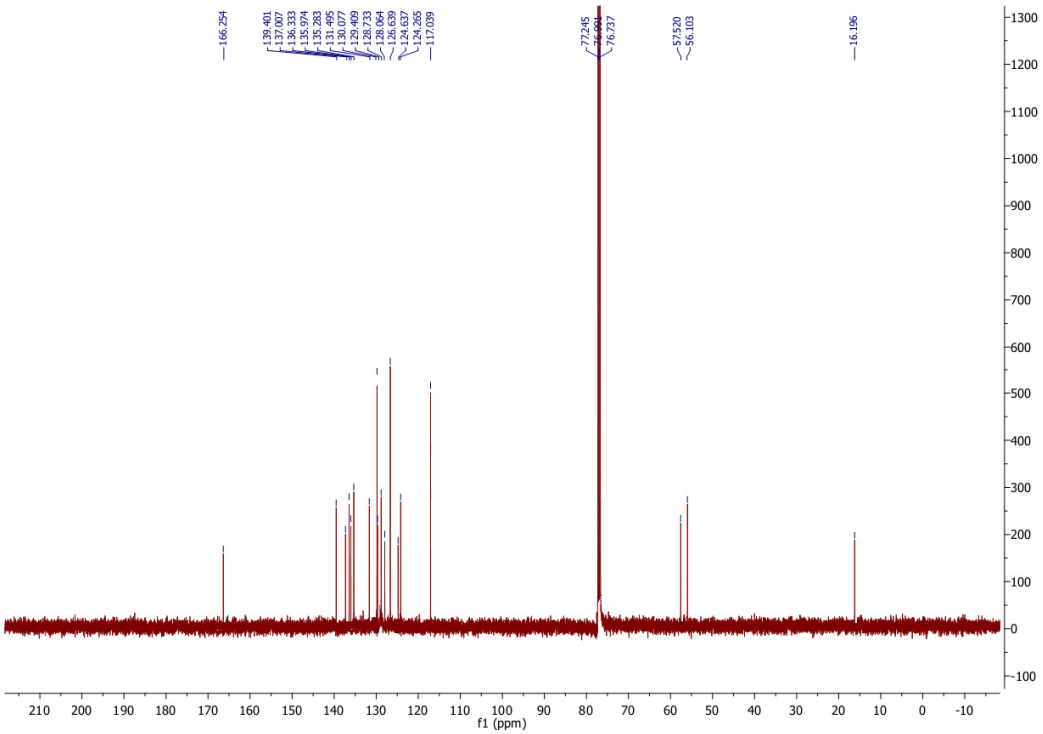
^{13}C NMR spectrum of **5b**:



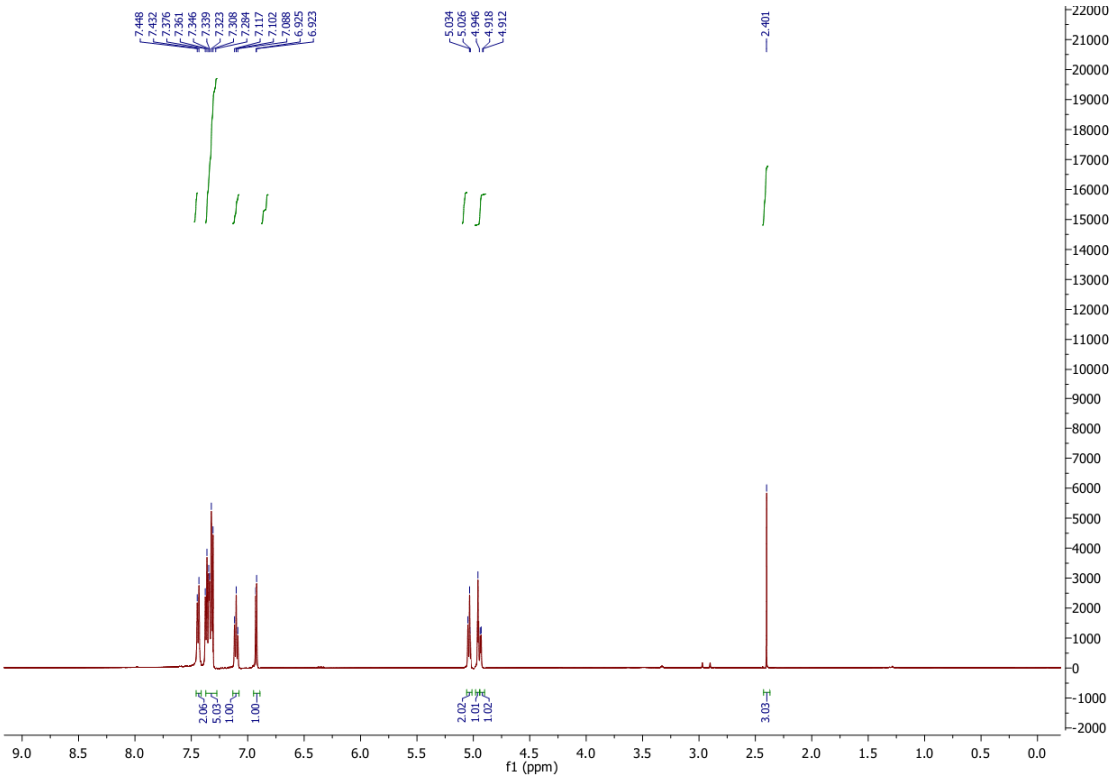
^{1}H NMR spectrum of **5c:**



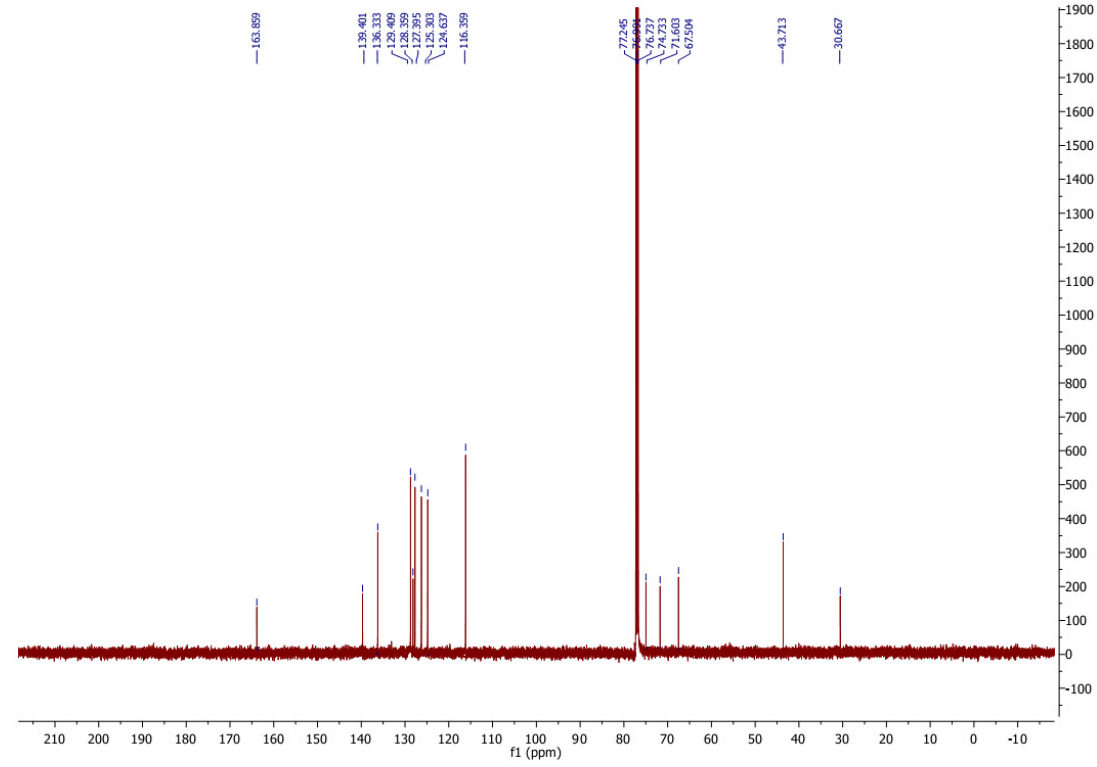
^{13}C NMR spectrum of **5c**:



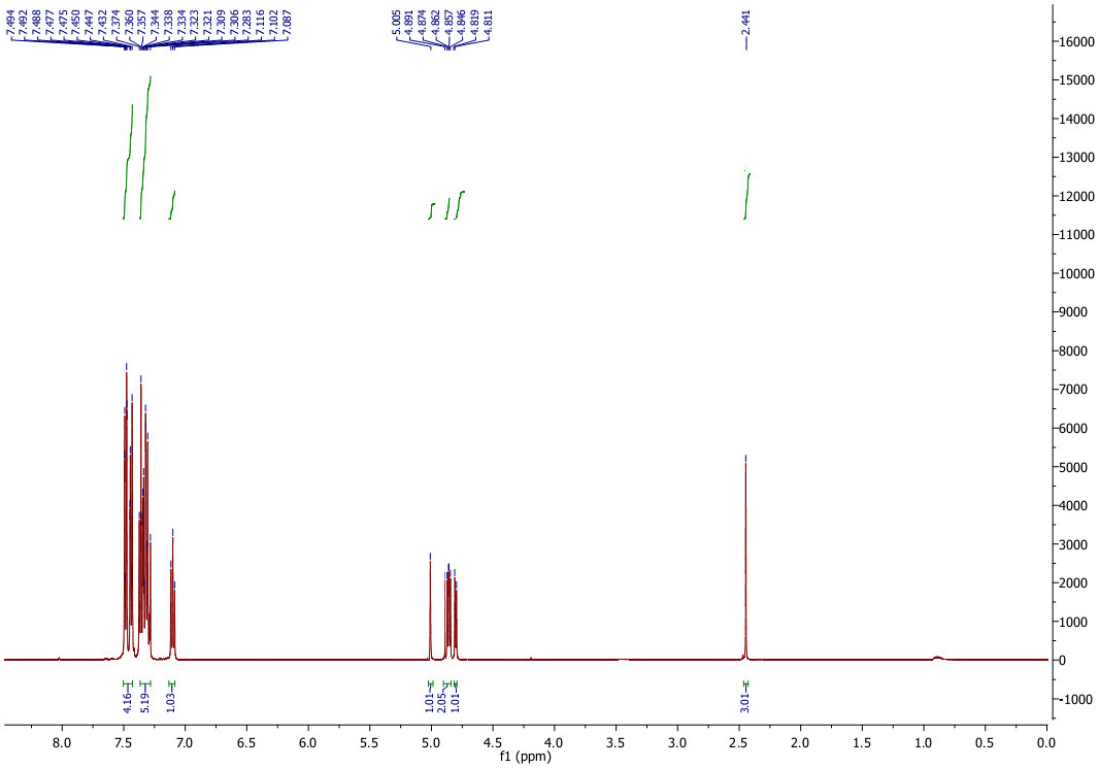
^{1}H NMR spectrum of **6a:**



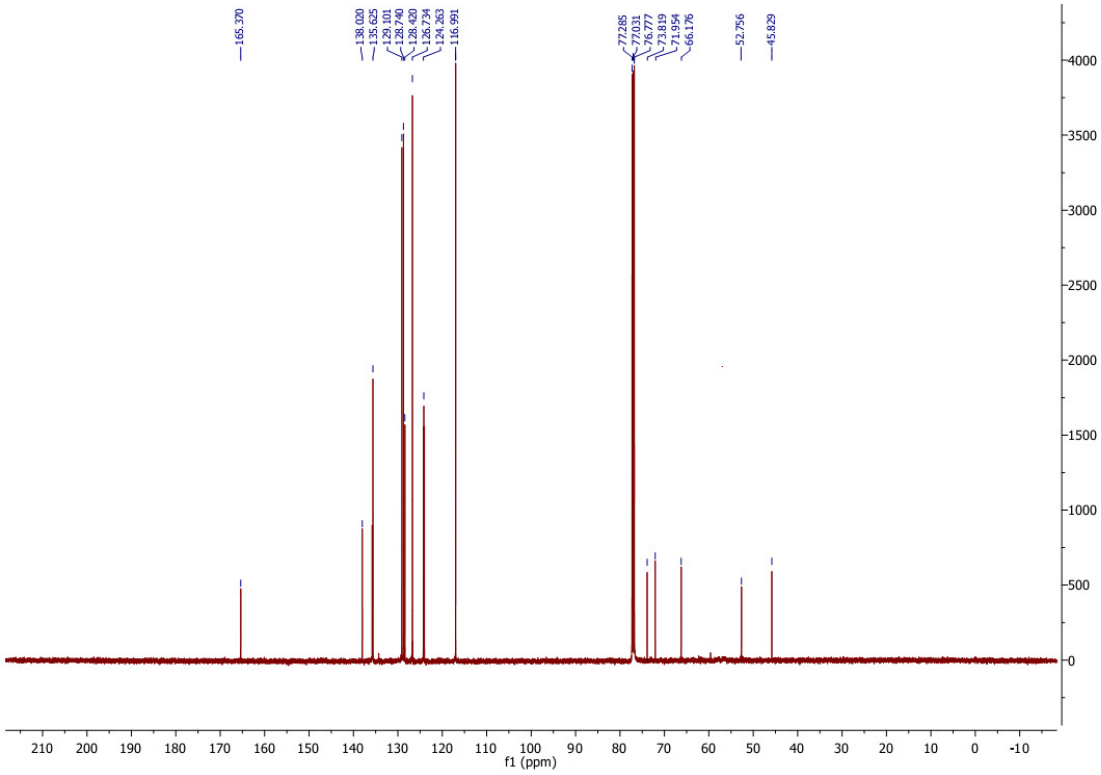
^{13}C NMR spectrum of **6a**:



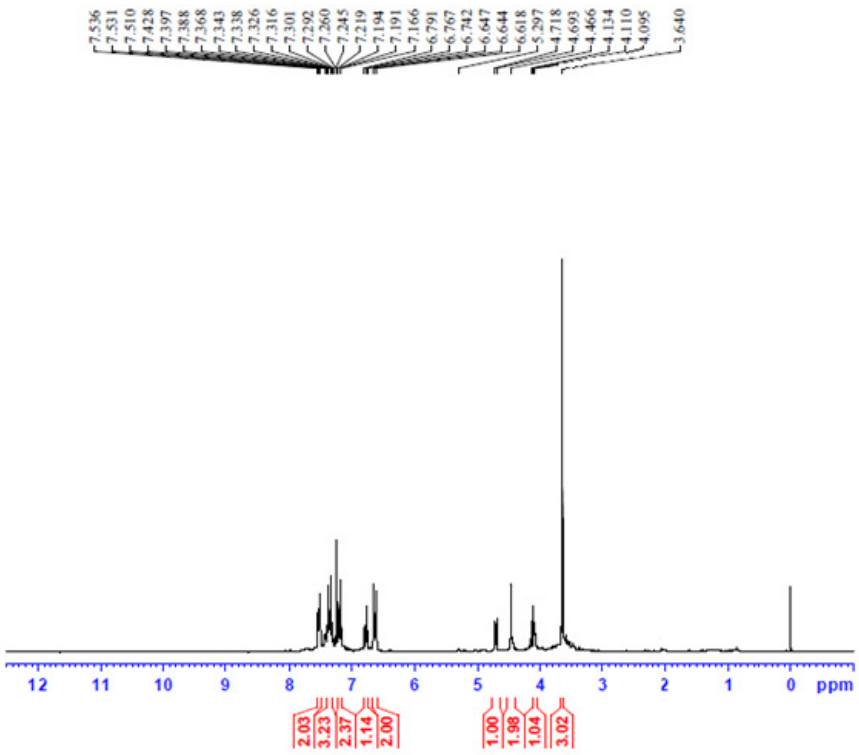
^{1}H NMR spectrum of **6b:**



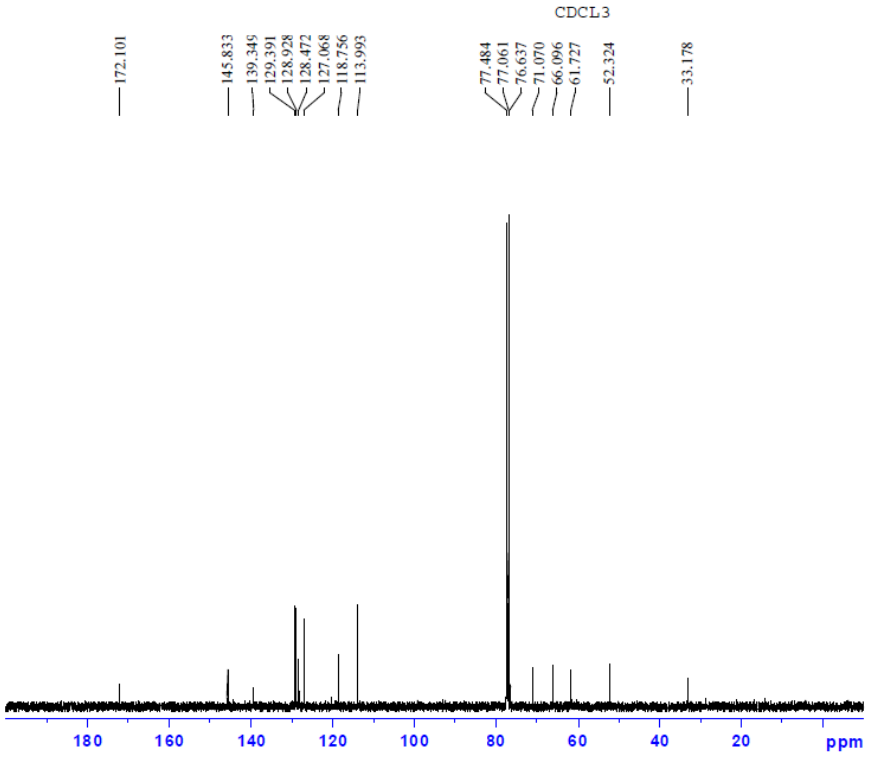
^{13}C NMR spectrum of **6b**:



^{1}H NMR spectrum of **7a:**

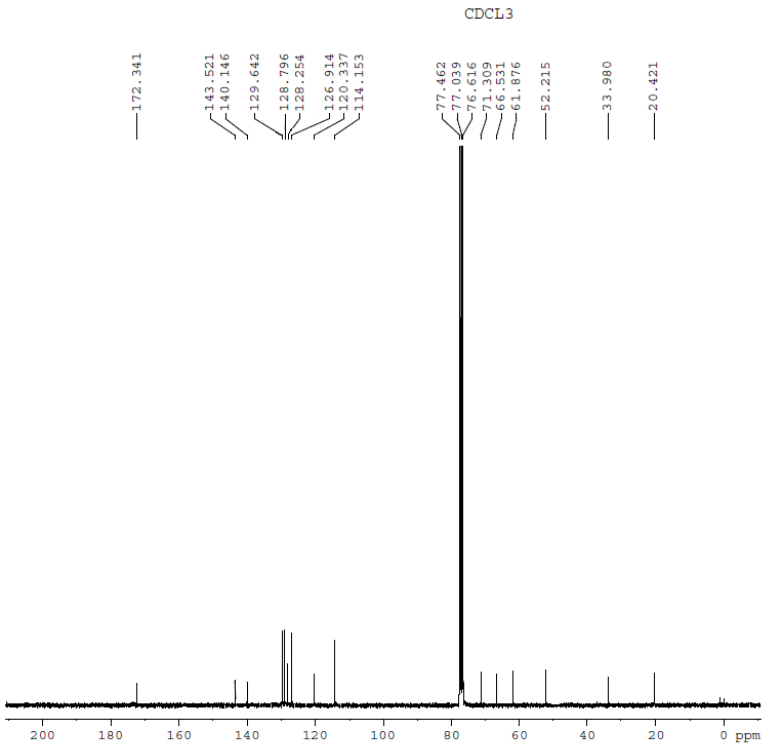


^{13}C NMR spectrum of **7a**:

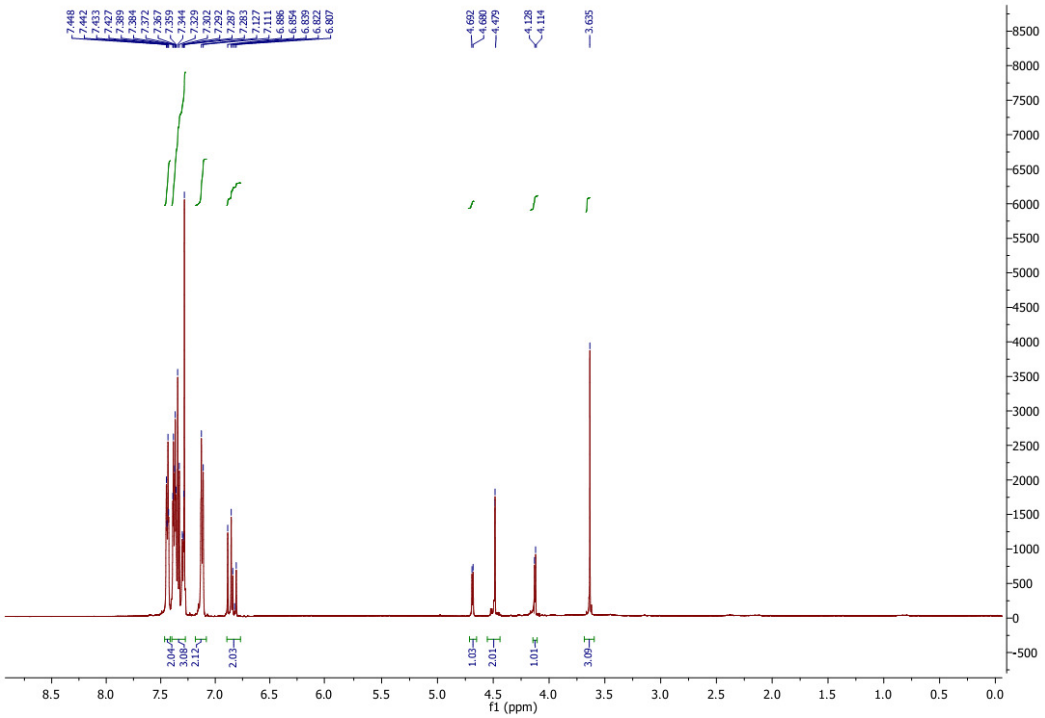


^{1}H NMR spectrum of **7b:**

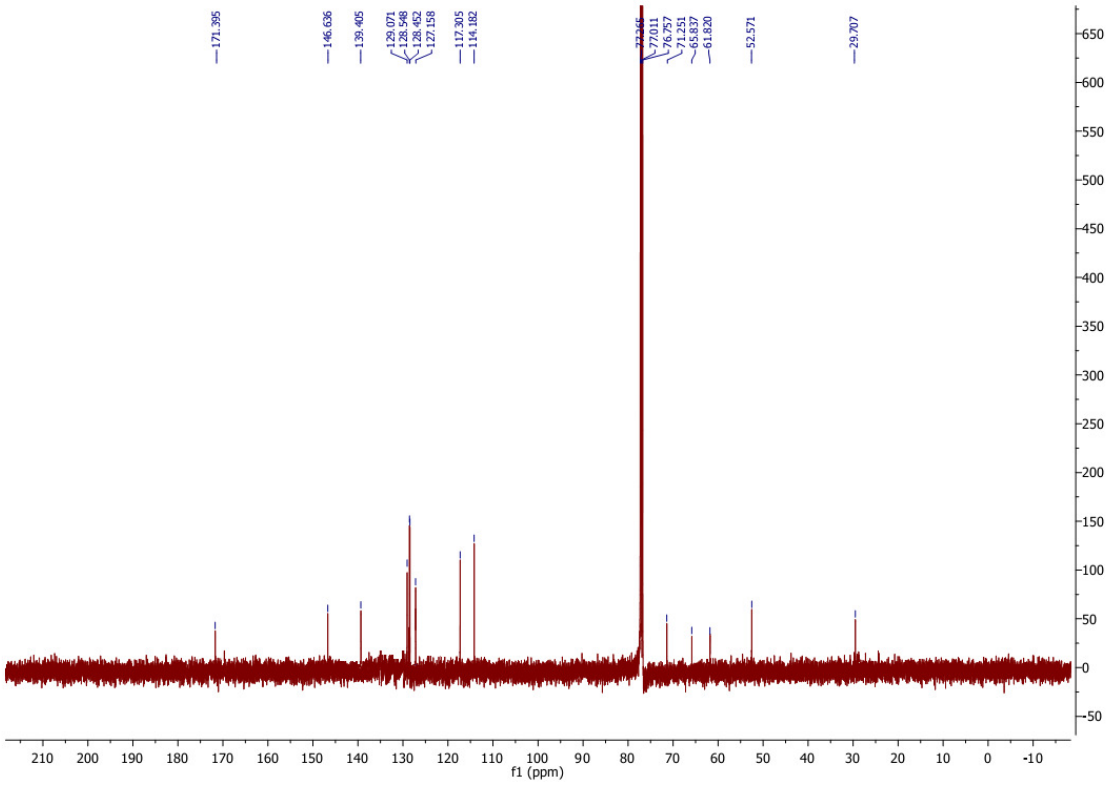
^{13}C NMR spectrum of **7b**:



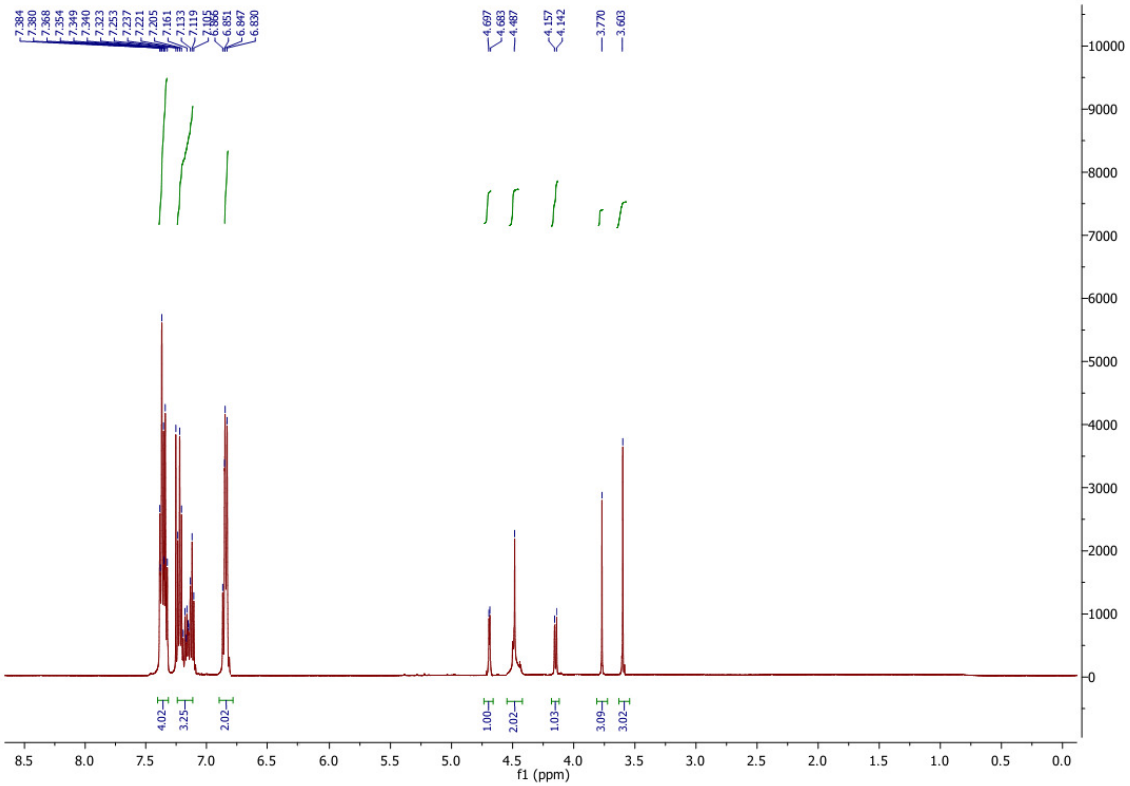
^{1}H NMR spectrum of **7c:**



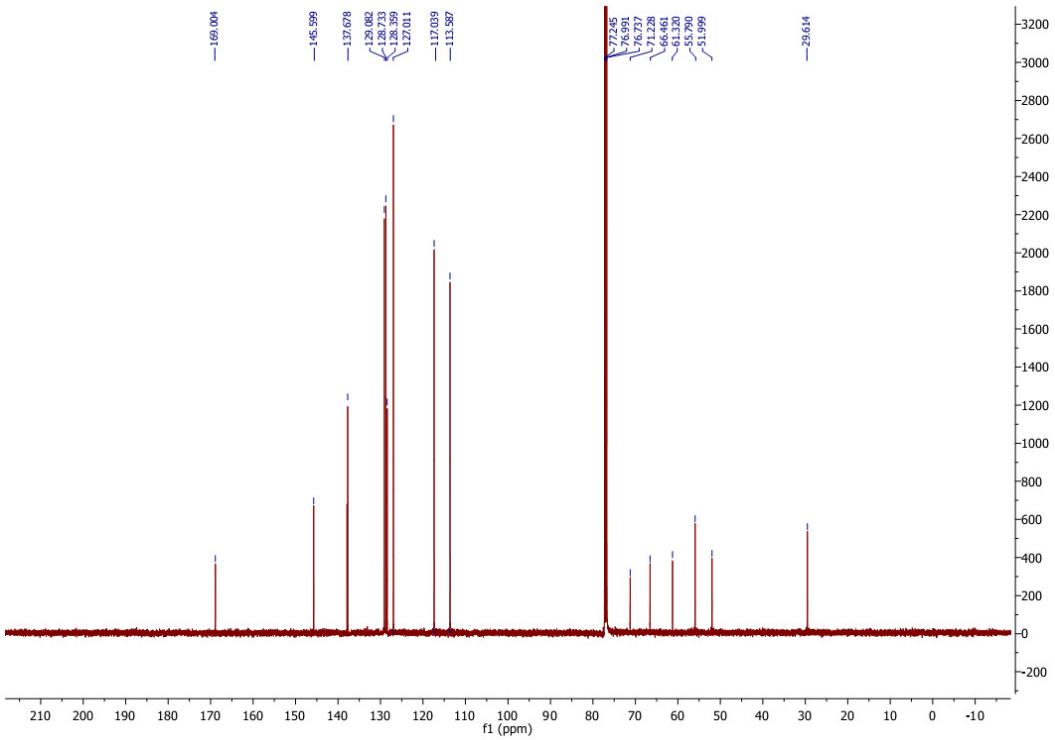
^{13}C NMR spectrum of **7c**:



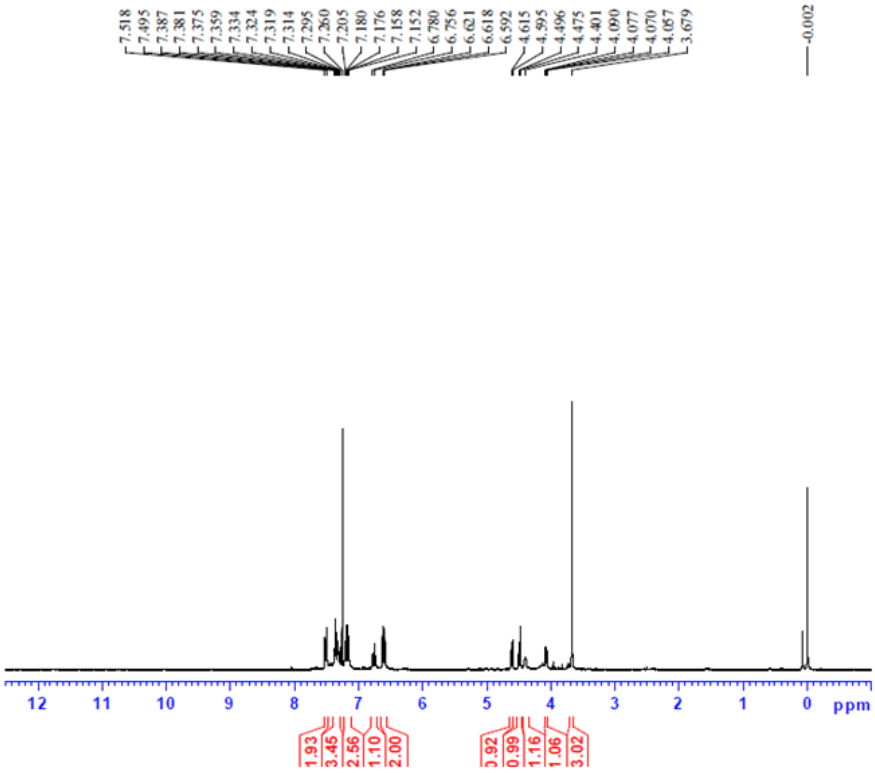
^{1}H NMR spectrum of **7d:**



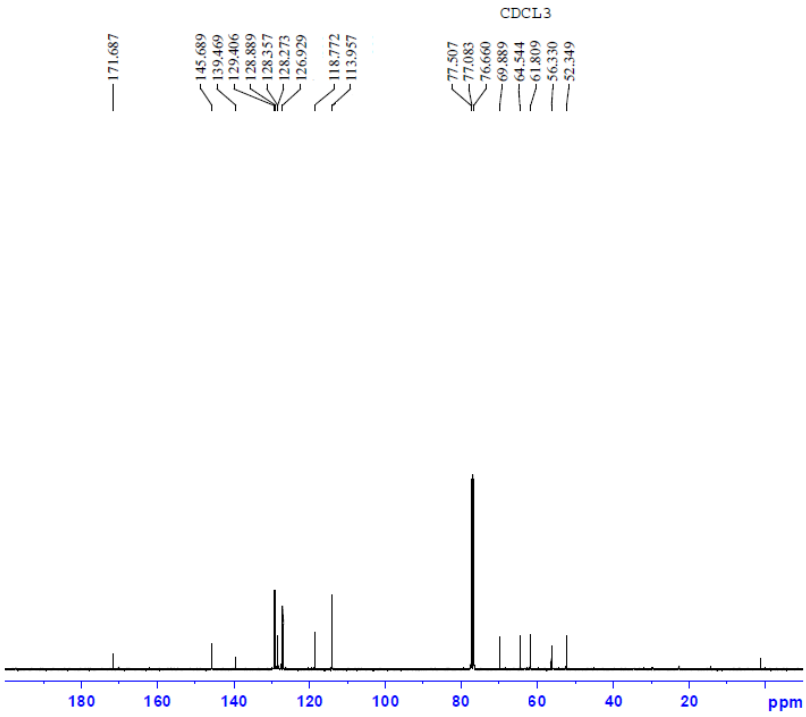
^{13}C NMR spectrum of **7d**:



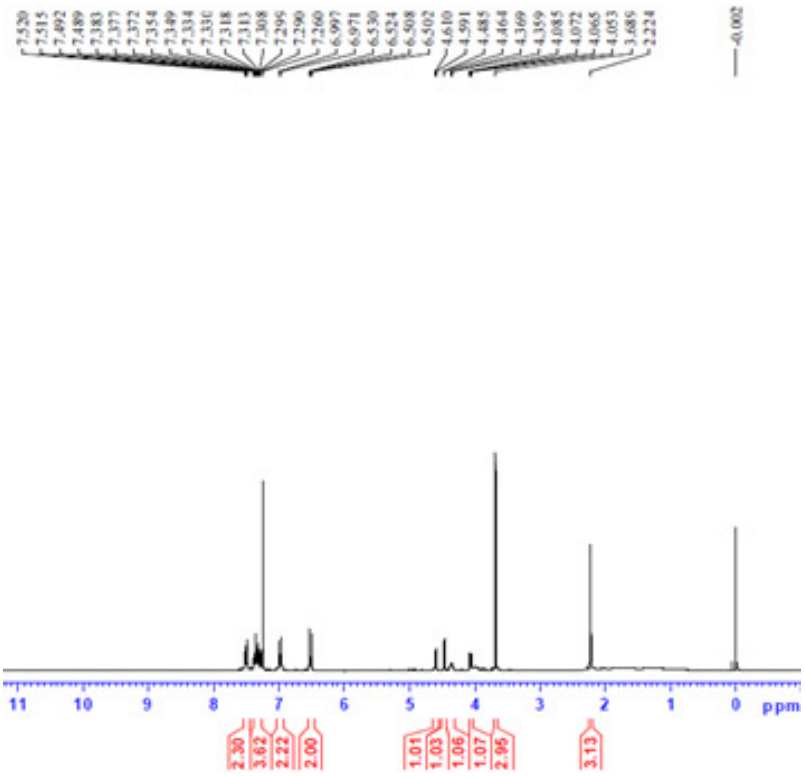
^{1}H NMR spectrum of **7e:**



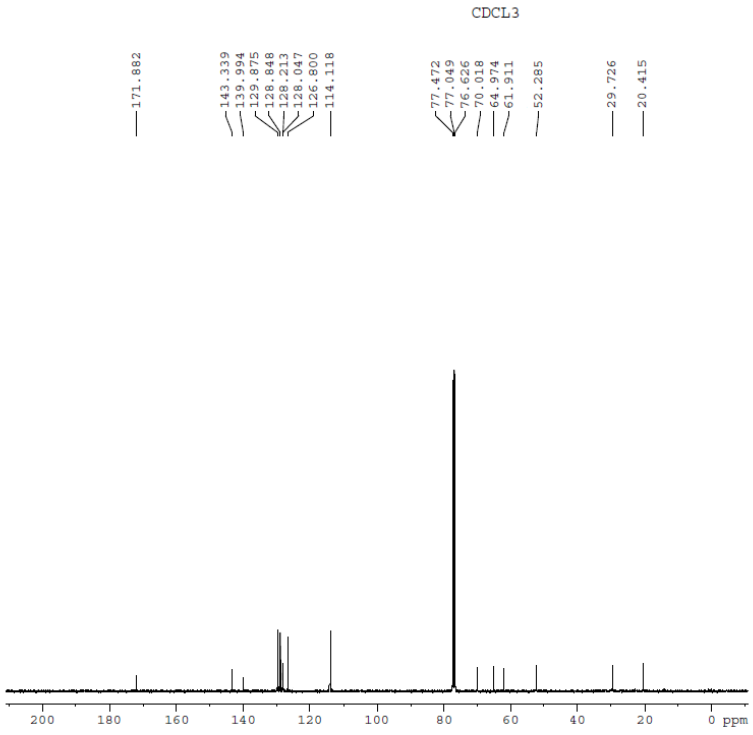
^{13}C NMR spectrum of **7e**:



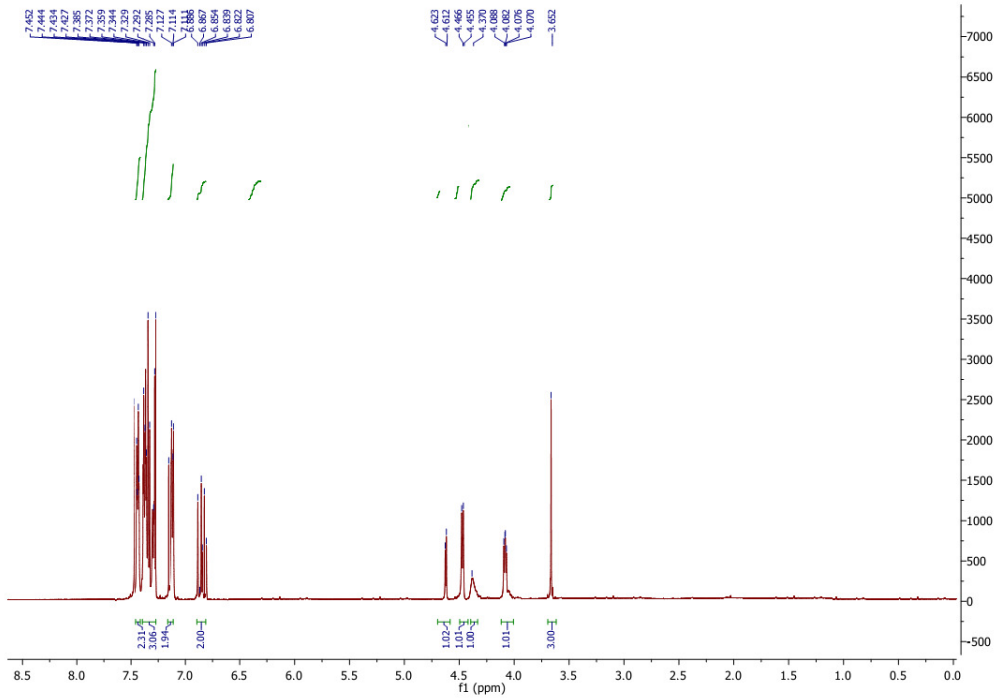
^{1}H NMR spectrum of **7f:**



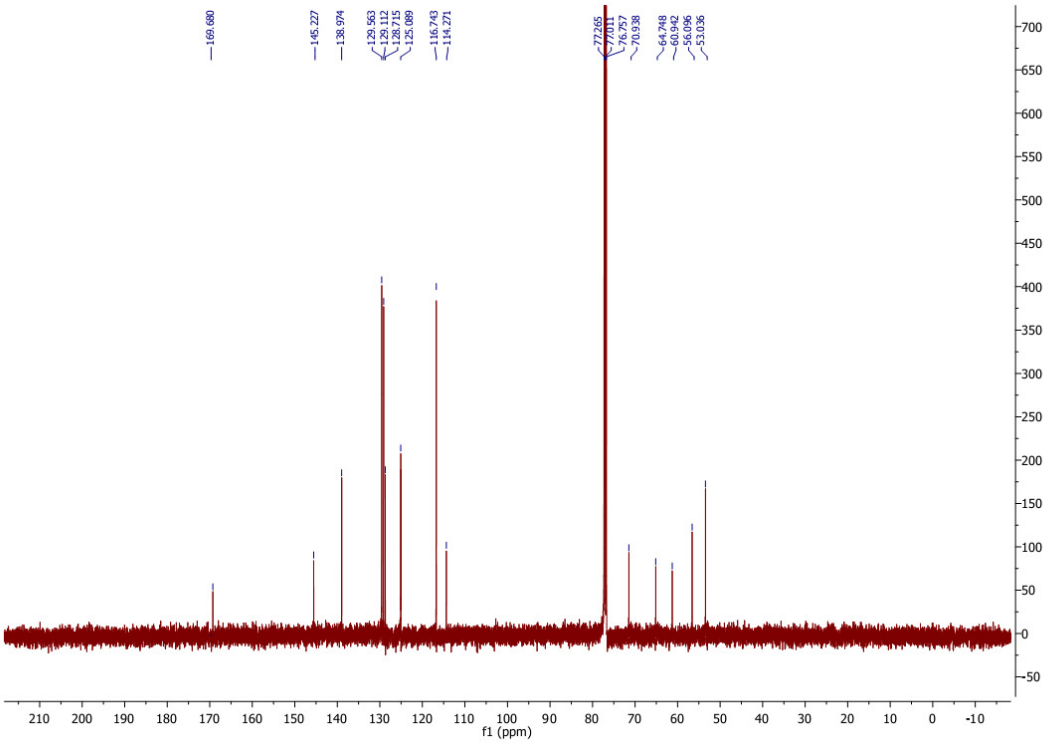
^{13}C NMR spectrum of **7f**:



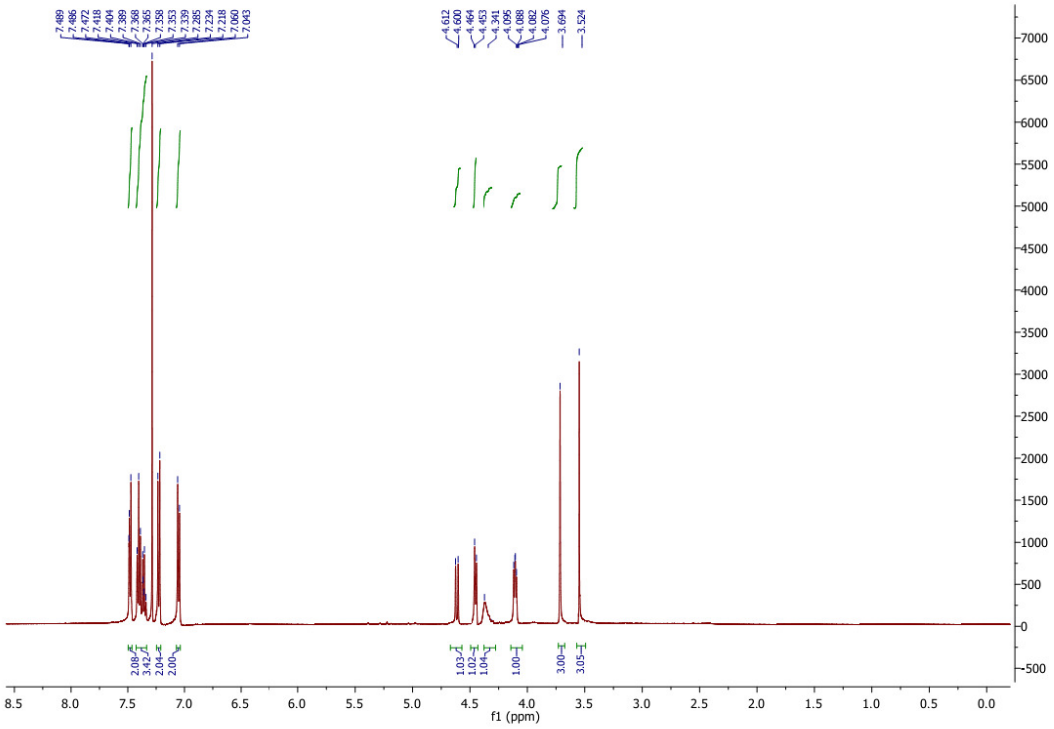
^{1}H NMR spectrum of **7g:**



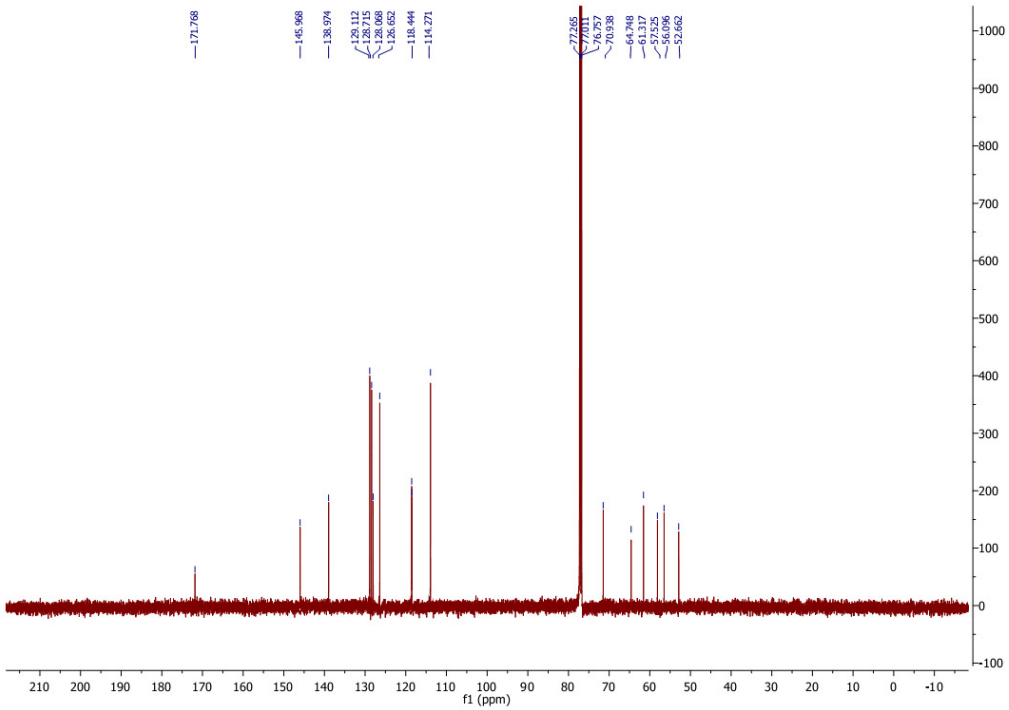
^{13}C NMR spectrum of **7g**:



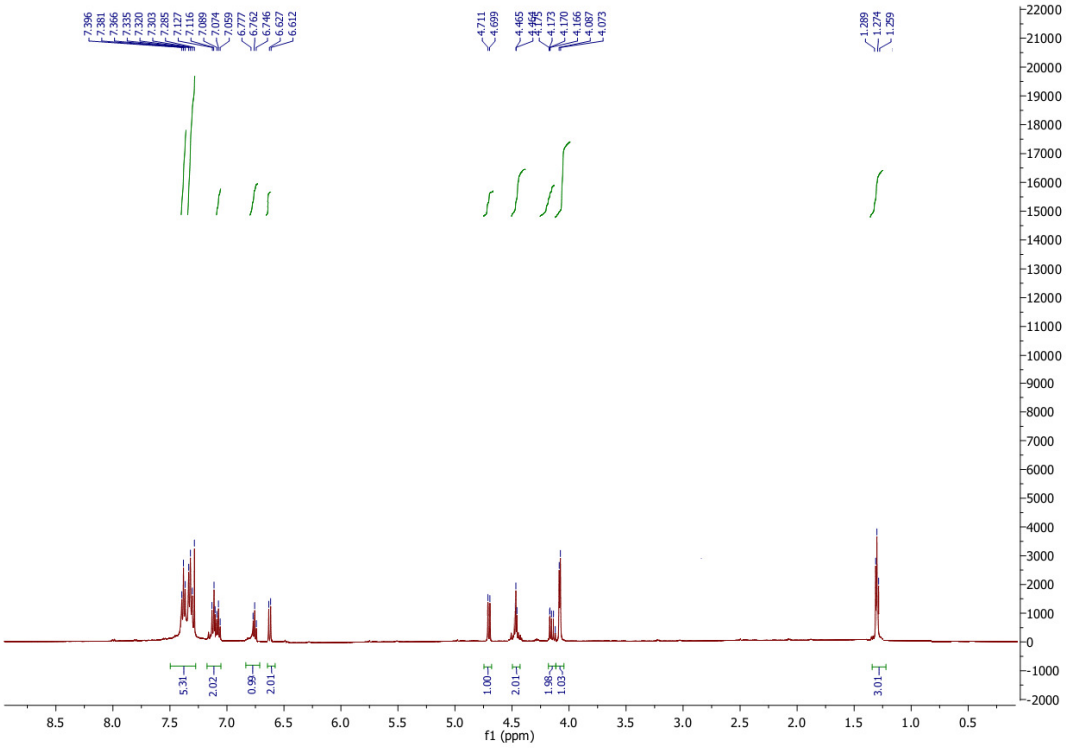
^{1}H NMR spectrum of **7h:**



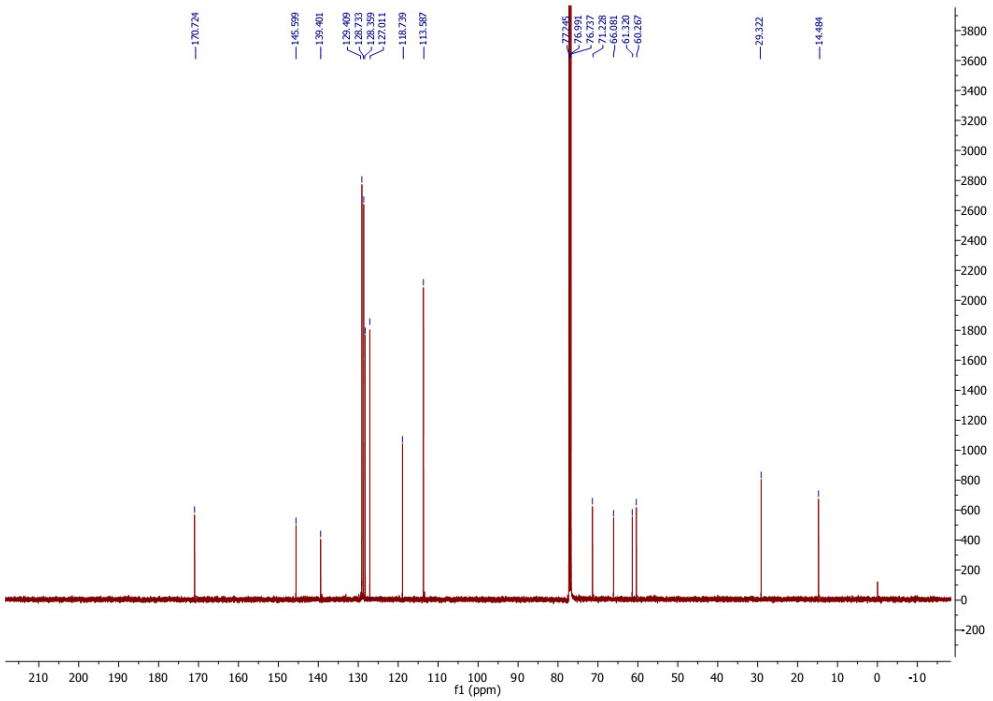
^{13}C NMR spectrum of **7h**:



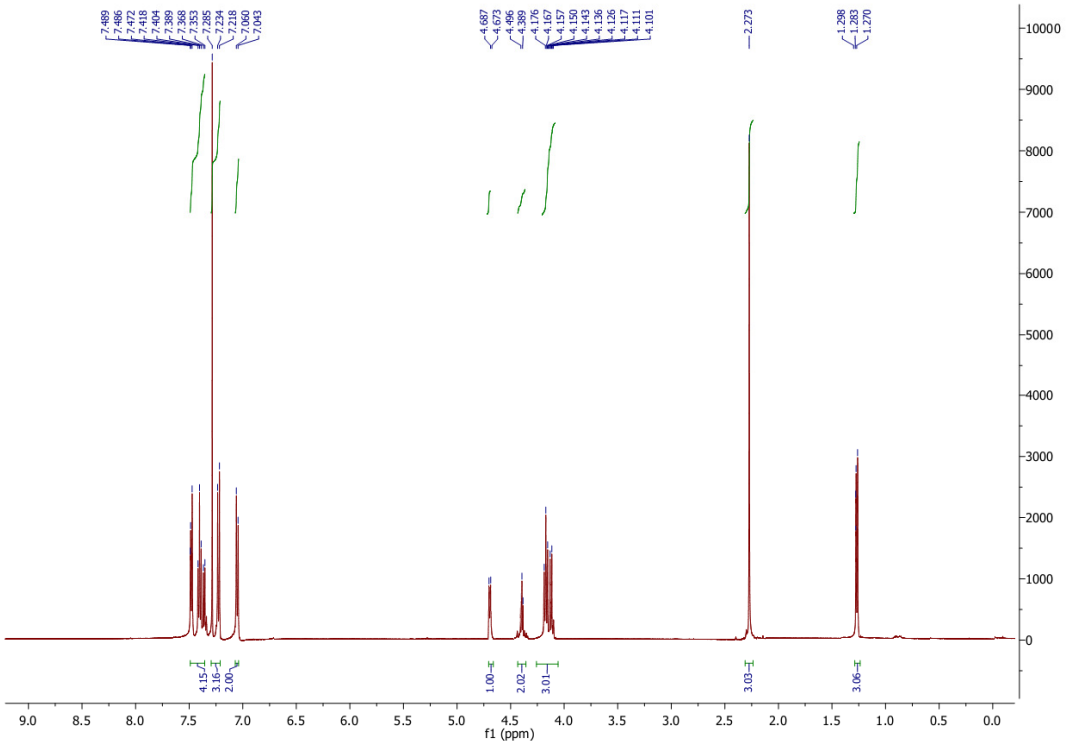
^{1}H NMR spectrum of **7i:**



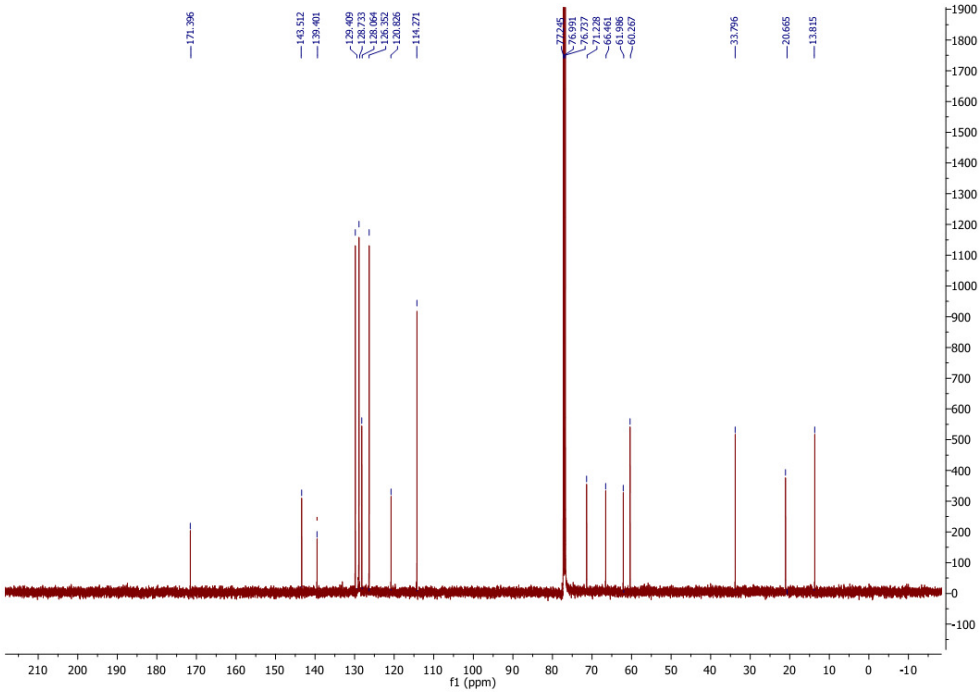
^{13}C NMR spectrum of **7i**:



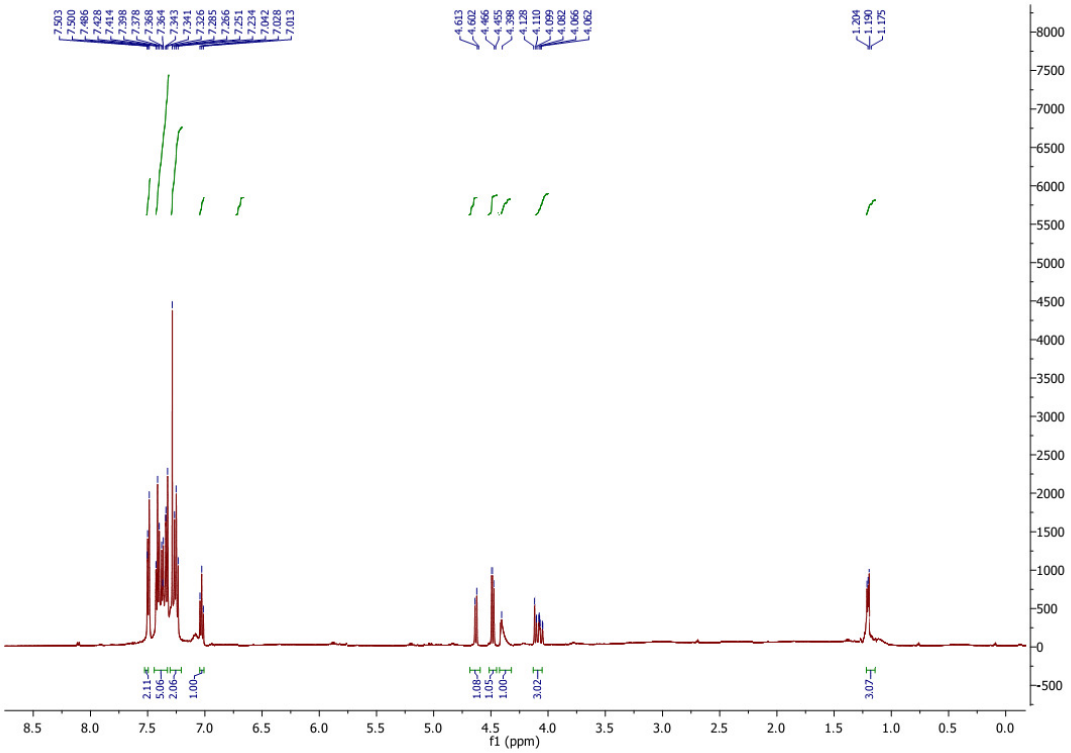
^{1}H NMR spectrum of **7j:**



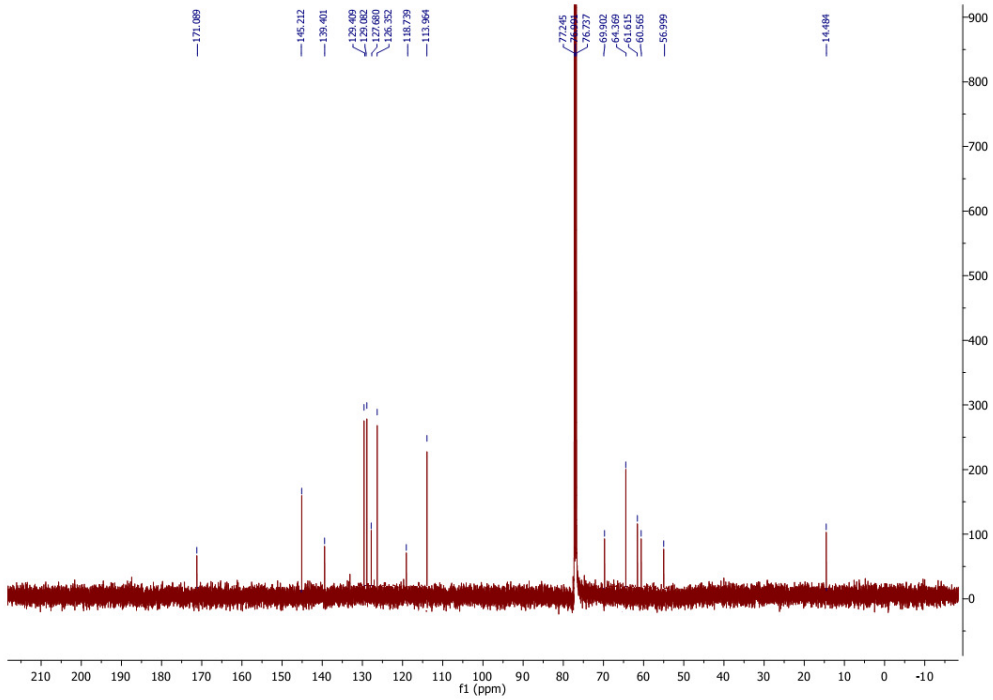
^{13}C NMR spectrum of **7j**:



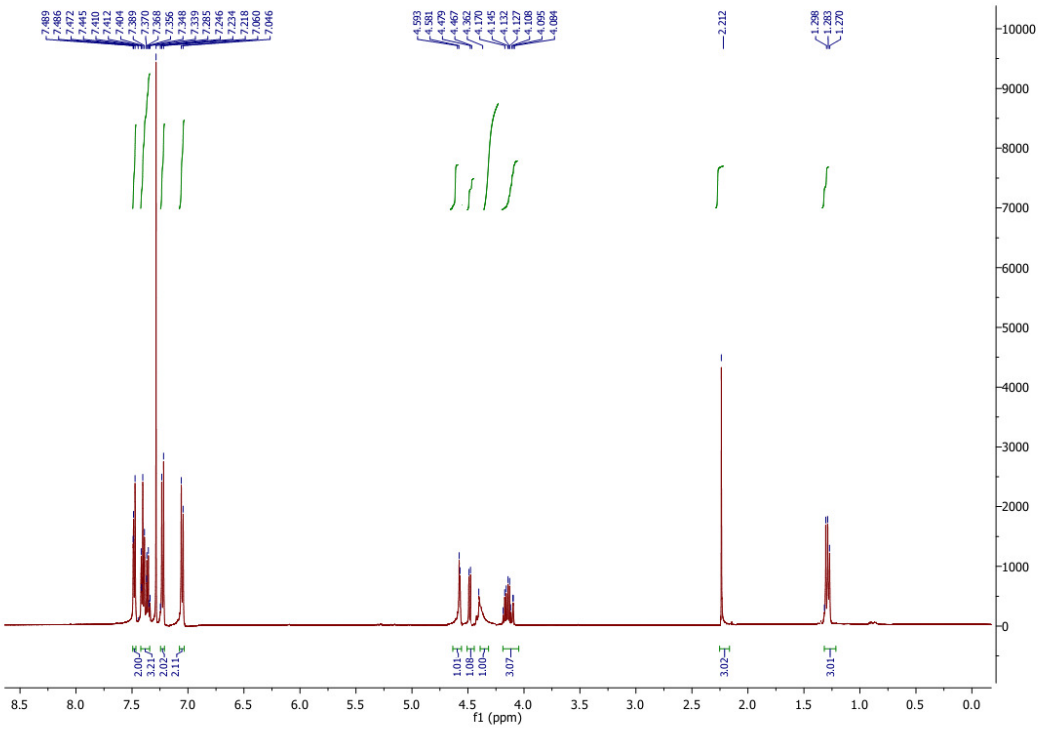
^{1}H NMR spectrum of **7k:**



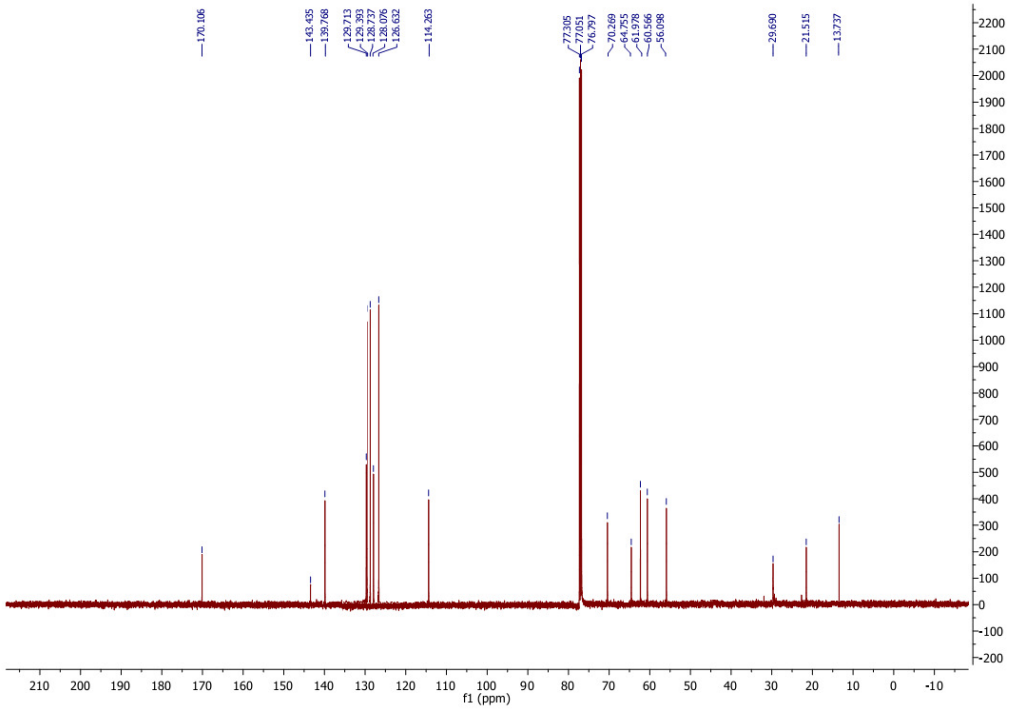
^{13}C NMR spectrum of **7k**:



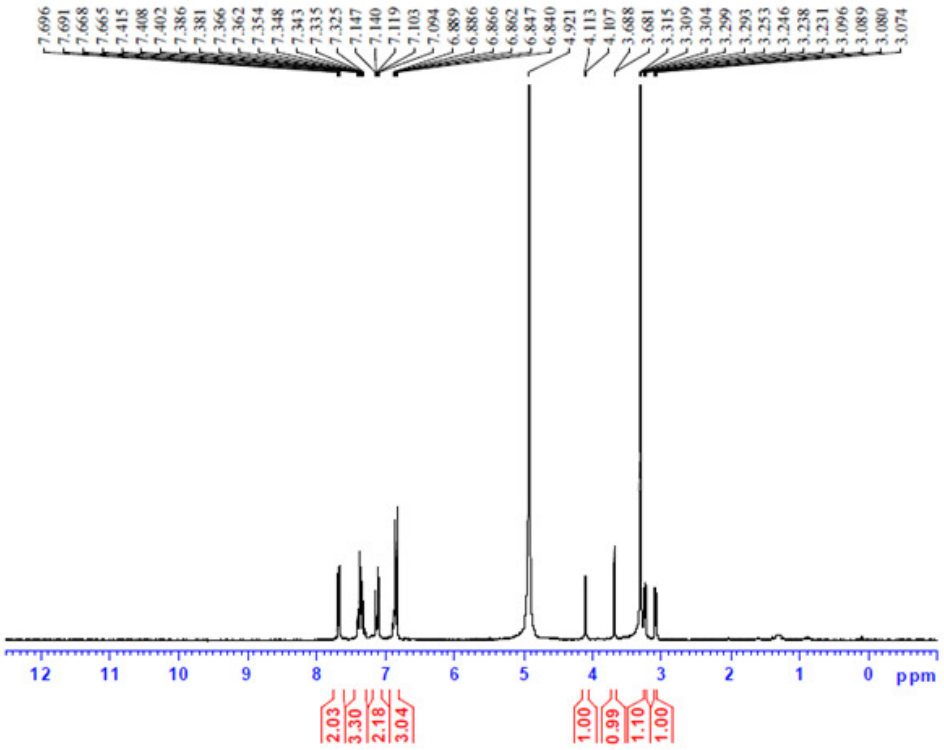
^{1}H NMR spectrum of **7l:**



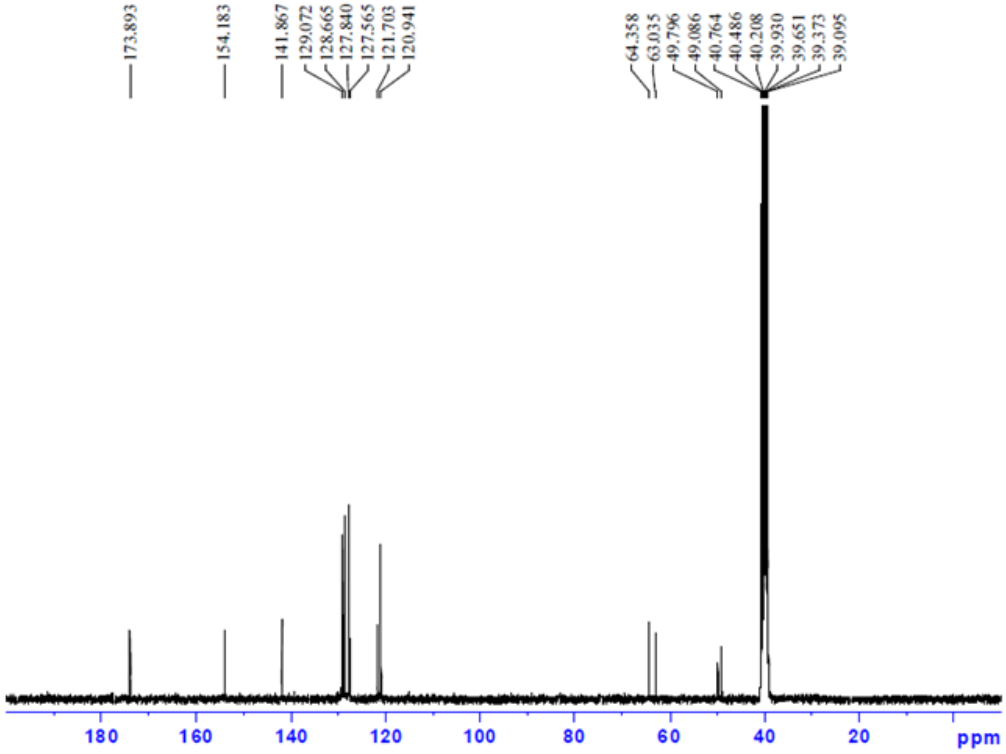
^{13}C NMR spectrum of **7l**:



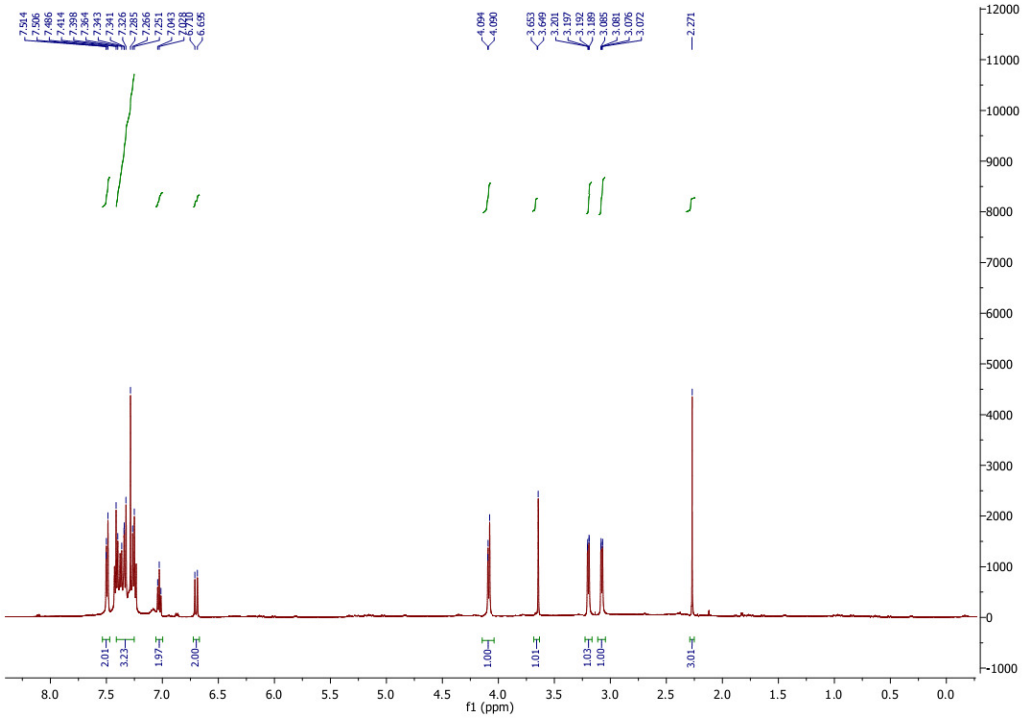
^{1}H NMR spectrum of **8a:**



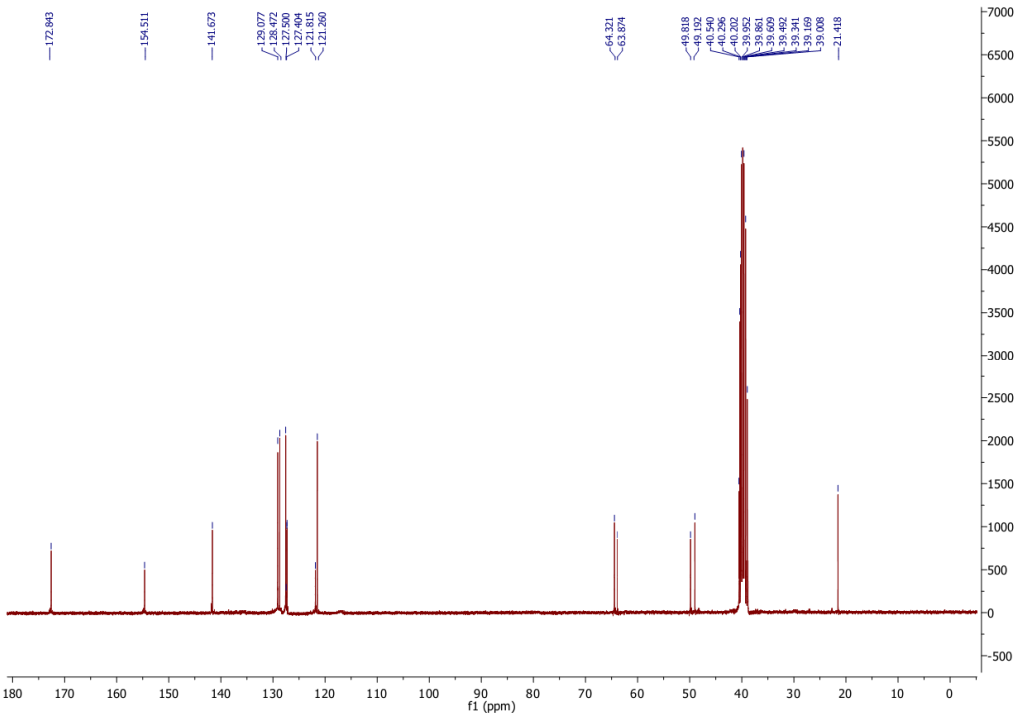
^{13}C NMR spectrum of **8a**:



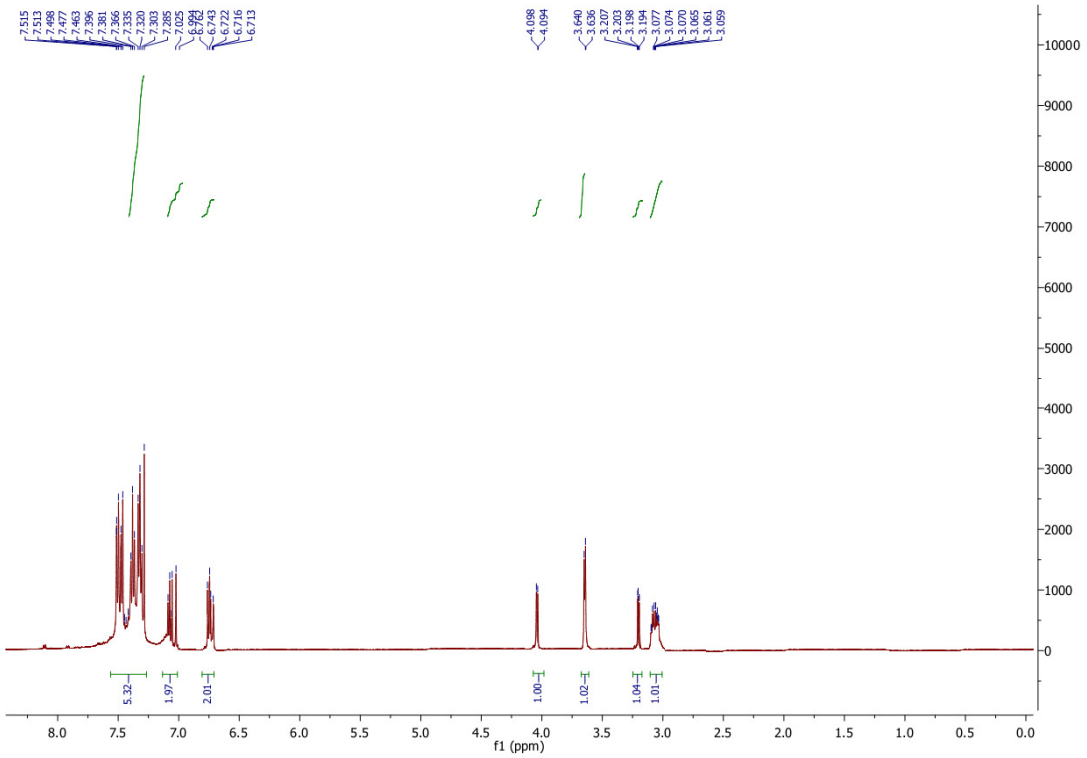
^{1}H NMR spectrum of **8b:**



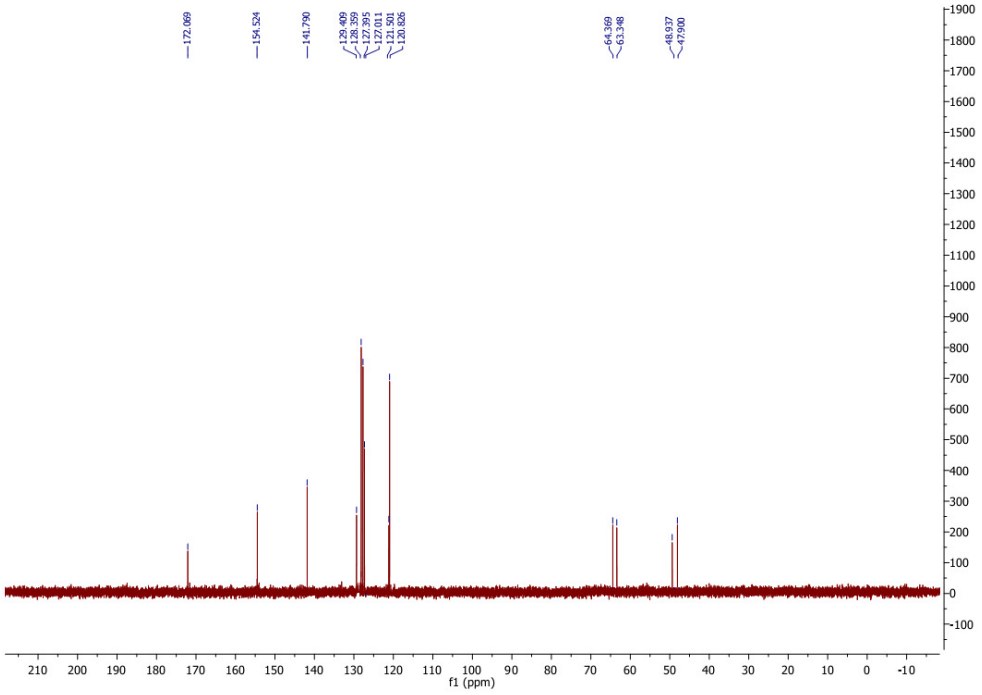
^{13}C NMR spectrum of **8b**:



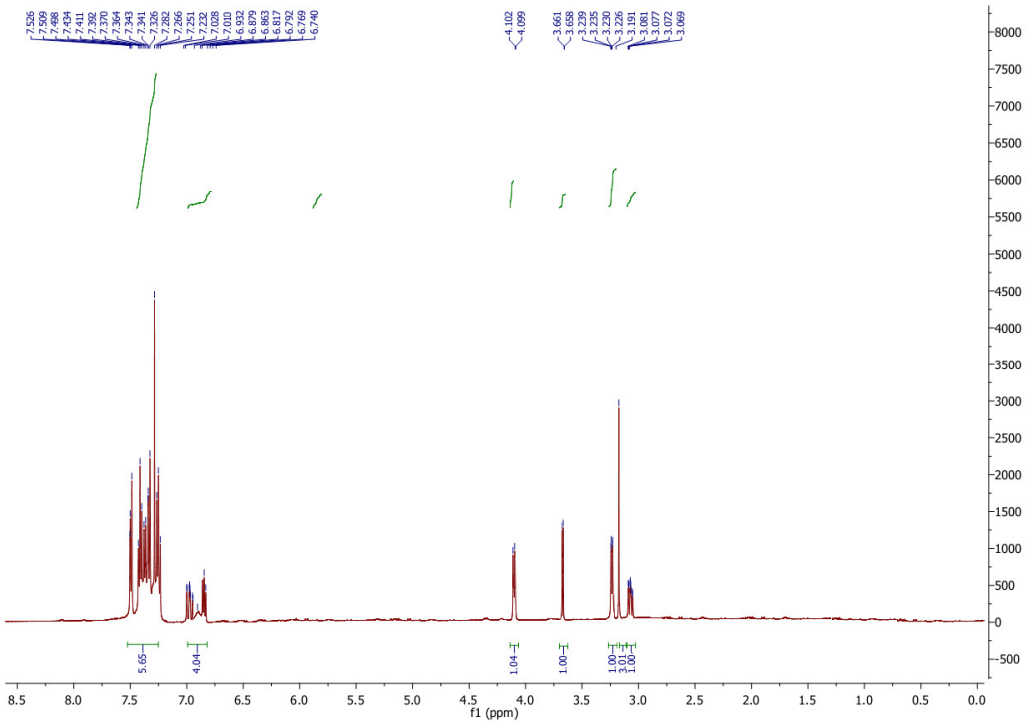
^{1}H NMR spectrum of **8c:**



^{13}C NMR spectrum of **8c**:



^{1}H NMR spectrum of **8d:**



^{13}C NMR spectrum of **8d**: