Selective Remote Esterification of 8-Aminoquinoline Amides *via* Copper(II)-Catalyzed C(sp^2)-O Cross-Coupling Reactions

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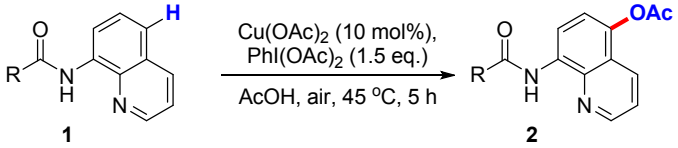
1. General Information

All the chemicals were obtained commercially and used without any prior purification. ^{1}H NMR spectra were recorded on a Bruker AvanceII 500 spectrometer. All products were isolated by short chromatography on a silica gel (200–300 mesh) column using petroleum ether (60-90°C) and ethyl acetate. Unless otherwise noted. All compounds were characterized by ^{1}H NMR, ^{13}C NMR and HRGC- HRMS, which are consistent with those reported in the literature.

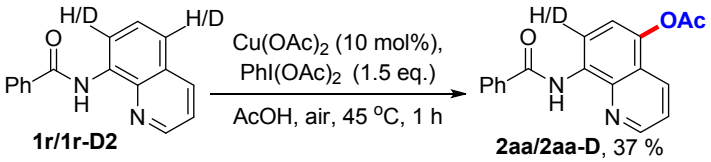
2. Experimental Section

General procedure for preparation acyloxylation of 8-aminoquinoline amides



A mixture of the **1** (0.2 mmol), $PhI(OAc)_2$ (96.6 mg, 1.5 eq), $Cu(OAc)_2$ (3.6 mg, 10 mol %) in AcOH (2.0 mL) was stirred at 45 °C under air atmosphere for 5.0 h. Then the mixture was cooled to room temperature and poured into water (10 mL). The mixture was extracted with EtOAc (6 mL x 3) and the combined organic layer was washed with brine (10 mL), dried with Na_2SO_4, and the solvent was removed under reduced pressure. The product **2** was purified by flash column chromatography using PE/AcOEt as an eluent.

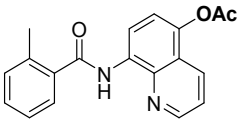
KIE experiment



The reaction of **1r** (62.0 mg, 0.25 mmol), **1r-D2** (62.5 mg, 0.25 mmol), $Cu(OAc)_2$ (9.1 mg, 10 mol %), $PhI(OAc)_2$ (241.5 mg, 1.5 eq) in MeCN (4.0 mL) at 45 °C under air for 1 hour produced **2aa/2aa-D** (37% yield). ^{1}H NMR analysis of the isolated product demonstrated the KIE of 1.0 was resolved for the acyloxylation reaction, this result indicated that the turnover-limiting step does not involve C-H activation.

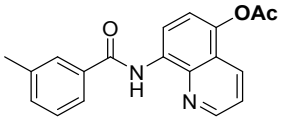
3. Characterization data of the products

8-(2-methylbenzamido)quinolin-5-yl acetate(2a)



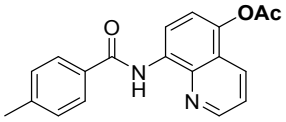
Obtained as a white solid in 80% yield; M.p. 122-123 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.12 (s, 1H), 8.96 (d, *J* = 8.5 Hz, 1H), 8.81 (d, *J* = 2.6 Hz, 1H), 8.20 (d, *J* = 6.9 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.50 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 2.59 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.53, 168.12, 148.65, 140.77, 138.86, 136.72, 136.53, 133.04, 131.40, 130.48, 130.40, 127.25, 126.05, 122.00, 121.89, 119.38, 115.93, 20.92, 20.20. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_3H$, $[M+H]^+$ 321.1234. Found 321.1233.

8-(3-methylbenzamido)quinolin-5-yl acetate(2b)



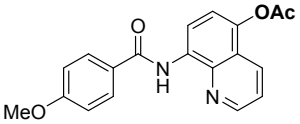
Obtained as a white solid in 78% yield; M.p. 148-149 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.95 (d, *J* = 8.5 Hz, 1H), 8.88 (d, *J* = 2.7 Hz, 1H), 8.21 (d, *J* = 7.0 Hz, 1H), 7.88 (s, 2H), 7.53 (d, *J* = 4.2 Hz, 1H), 7.44 – 7.36 (m, 3H), 2.48 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.50, 165.62, 148.68, 140.67, 139.05, 138.73,135.04, 132.98, 132.68, 130.48, 128.68, 128.07, 124.22, 121.99, 121.89, 119.41, 115.93, 21.50, 20.92. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_3H$, $[M+H]^+$ 321.1234, Found 321.1233.

8-(4-methylbenzamido)quinolin-5-yl acetate(2c)



Obtained as a white solid in 81% yield; M.p. 181-182 °C. ^{1}H NMR (500 MHz, $CDCl_3$)δ 10.60 (s, 1H), 8.89 (dd, *J* = 40.7, 5.6 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 4.2 Hz, 1H), 7.34 (d, *J* = 2.7 Hz, 3H), 2.44 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.51, 165.34, 148.63, 142.44, 140.60, 138.99, 132.99, 132.19, 130.46, 129.49, 127.30, 121.97, 121.88, 119.38, 115.81, 21.56, 20.91. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_3H$, $[M+H]^+$ 321.1234. Found 321.1233.

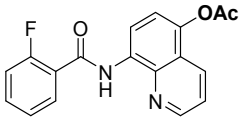
8-(4-methoxylbenzamido)quinolin-5-yl acetate(2d)



Obtained as a white solid in 86% yield; M.p. 159-161 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.58 (s, 1H), 8.90 (dd, *J* = 27.3, 5.5 Hz, 2H), 8.20 (d, *J* = 6.9 Hz, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 4.2 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.05 – 7.02 (m, 2H), 3.89 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.52, 164.93, 162.59, 148.58, 140.50, 138.98,

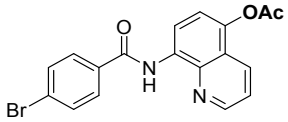
133.08, 130.51, 129.19, 127.32, 121.99, 121.86, 119.43, 115.76, 114.03, 55.50, 20.92. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_4H$, $[M+H]^+$ 337.1183. Found 337.1180.

8-(2-fluorobenzamido)quinolin-5-yl acetate(2e)



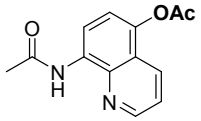
Obtained as a white solid in 75% yield; M.p. 185-186 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.09 (d, *J* = 12.6 Hz, 1H), 8.94 (d, *J* = 39.5 Hz, 2H), 8.22 (d, *J* = 0.9 Hz, 2H), 7.53 (s, 1H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.26 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.47, 161.60, 160.61 (d, *J* = 252.5 Hz), 148.89, 140.99, 139.11, 133.67 (d, *J* = 8.8 Hz), 133.14, 132.09, 132.07, 130.36, 124.91 (d, *J* = 3.8 Hz), 120.00, 121.94 (d, *J* = 12.5 Hz), 119.31, 116.66, 116.37 (d, *J* = 24.0 Hz), 20.93. HRMS(ESI+): Calculated for $C_{18}H_{13}FN_2O_3H$, $[M+H]^+$ 325.0983. Found 325.0985.

8-(4-bromobenzamido)quinolin-5-yl acetate(2f)



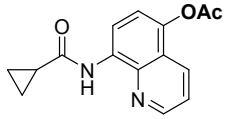
Obtained as a white solid in 81% yield; M.p. 196-197 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.89 (d, *J* = 14.6 Hz, 2H), 8.21 (s, 1H), 7.94 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 169.45, 164.35, 148.73, 140.90, 138.94, 133.84, 132.58, 132.07, 130.59, 128.89, 126.70, 122.01, 121.97, 119.38, 116.05, 20.91. HRMS(ESI+): Calculated for $C_{18}H_{13}BrN_2O_3H$, $[M+H]^+$ 385.0183. Found 385.0187.

8-acetamidoquinolin-5-yl acetate(2g)



Obtained as a white solid in 63% yield; M.p. 124-126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.80 (dd, *J* = 28.9, 6.4 Hz, 2H), 8.18 (d, *J* = 8.5 Hz, 1H), 7.51 (d, *J* = 4.2 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 2.45 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.49, 168.68, 148.46, 140.48, 138.45, 132.81, 130.51, 121.89, 121.80, 119.35, 115.85, 25.10, 20.90. HRMS(ESI+): Calculated for $C_{13}H_{12}N_2O_3H$, $[M+H]^+$ 245.0921, Found 245.0926.

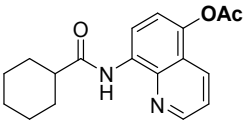
8-(cyclopropanecarboxamido)quinolin-5-yl acetate(2h)



Obtained as a white solid in 69% yield; M.p. 143-145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.74 (d, *J* = 8.5 Hz, 2H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 4.2 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 2.44 (s, 3H), 1.79 (s, 1H), 1.15 (d, *J* = 7.2 Hz, 2H), 0.91 (d, *J* = 4.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.20, 169.50, 148.45, 140.28, 138.45, 133.03, 130.43,

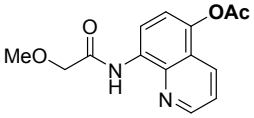
121.89, 121.78, 119.35, 115.74, 20.90, 16.24, 8.20. HRMS(ESI+): Calculated for $C_{15}H_{14}N_2O_3H$, $[M+H]^+$ 271.1077. Found 271.1075.

8-(cyclohexanecarboxamido)quinolin-5-yl acetate(2i)



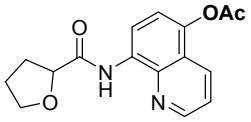
Obtained as a white solid in 75% yield; M.p. 164-165 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.83 (dd, *J* = 16.4, 5.6 Hz, 2H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 4.3 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 2.50 (s, 1H), 2.44 (s, 3H), 2.08 (d, *J* = 10.9 Hz, 2H), 1.88 (d, *J* = 13.2 Hz, 2H), 1.64 (d, *J* = 3.2 Hz, 5H), 0.88 (s, 1H). ^{13}C NMR (126 MHz, CDCl3) δ 174.89, 169.48, 148.23, 140.36, 138.35, 132.82, 130.87, 121.97, 121.71, 119.52, 116.21, 46.81, 29.74, 25.78, 25.74, 20.89. HRMS(ESI+): Calculated for $C_{18}H_{20}N_2O_3H$,$[M+H]^+$ 313.1547, Found 313.1540.

8-(2-methoxyacetamido)quinolin-5-yl acetate(2j)



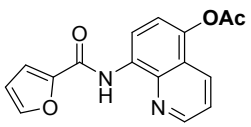
Obtained as a white solid in 58% yield; M.p. 116-117 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.85 (dd, *J* = 38.2, 5.5 Hz, 2H), 8.18 (d, *J* = 6.8 Hz, 1H), 7.50 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 4.15 (s, 2H), 3.60 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.46, 168.19, 148.97, 140.92, 139.10, 132.15, 130.26, 121.95, 121.83, 119.16, 116.11, 72.72, 59.56, 20.91. HRMS(ESI+): Calculated for $C_{14}H_{14}N_2O_4H$, $[M+H]^+$ 275.1027, Found 275.1022.

8-(tetrahydrofuran-2-carboxamido)quinolin-5-yl acetate(2k)



Obtained as a white solid in 71% yield; M.p. 166-168 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.83 (s, 1H), 8.85 (dd, *J* = 43.4, 5.6 Hz, 2H), 8.18 (d, *J* = 6.9 Hz, 1H), 7.50 (d, *J* = 4.2 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 4.62 (d, *J* = 2.8 Hz, 1H), 4.22 (d, *J* = 7.5 Hz, 1H), 4.07 (d, *J* = 7.5 Hz, 1H), 2.45 (s, 3H), 2.39 (d, *J* = 8.1 Hz, 1H), 2.26 (d, *J* = 5.9 Hz, 1H), 2.01 – 1.96 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.07, 169.47, 148.96, 140.88, 139.12, 132.23, 130.31, 121.98, 121.81, 119.19, 115.99, 79.13, 69.80, 30.47, 25.56, 20.91. HRMS(ESI+): Calculated for $C_{16}H_{16}N_2O_4H$, $[M+H]^+$ 301.1183, Found 301.1186.

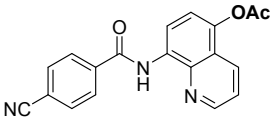
8-(furan-2-carboxamido)quinolin-5-yl acetate(2l)



Obtained as a white solid in 61% yield; M.p. 163-166 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.68 (s, 1H), 8.90 (dd, *J* = 14.3, 5.6 Hz, 2H), 8.20 (d, *J* = 7.0 Hz, 1H), 7.62 (d, *J* = 0.8 Hz,

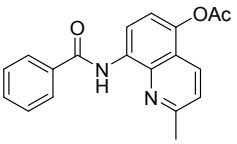
1H), 7.53 (d, *J* = 4.2 Hz, 1H), 7.33 (d, *J* = 30.5 Hz, 2H), 6.59 (d, *J* = 1.7 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.48, 156.31, 148.80, 148.25, 144.58, 140.82, 138.90, 132.49, 130.43, 122.00, 121.93, 119.33, 116.05, 115.25, 112.49, 20.92. HRMS(ESI+): Calculated for $C_{16}H_{12}N_2O_4H$, $[M+H]^+$ 297.0870, Found 297.0875.

8-(4-cyanobenzamido)quinolin-5-yl acetate(2n)



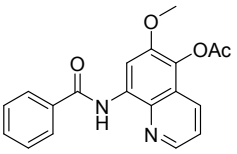
Obtained as a white solid in 30% yield; M.p. 190-192 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.69 (s, 1H), 8.92 (d, *J* = 8.5 Hz, 2H), 8.26 – 8.23 (m, 1H), 8.17 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 12.7 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.42, 163.40, 148.87, 141.30, 138.84, 132.71, 132.32, 132.18, 130.77, 130.61, 127.99, 122.11, 119.40, 118.05, 116.39, 115.46, 20.92. HRMS(ESI+): Calculated for $C_{19}H_{13}N_3O_3H$, $[M+H]^+$ 332.1030, Found 332.1039.

8-benzamido-2methylquinolin-5-yl acetate(2p)



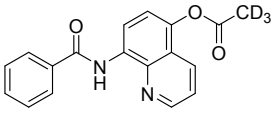
Obtained as a white solid in 73% yield; M.p. 154-156 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 10.64 (s, 1H), 8.83 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 3H), 7.49 (d, *J* = 7.4 Hz, 3H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 1H), 2.71 (s, 3H), 2.37 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 168.49, 164.23, 156.79, 139.86, 137.44, 134.17, 131.19, 130.80, 129.61, 127.80, 126.24, 121.70, 119.06, 117.32, 115.01, 24.34, 19.89. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_3H$, $[M+H]^+$321.1234, Found 321.1237.

8-benzamido-6-methoxyquinolin-5-yl acetate(2q)



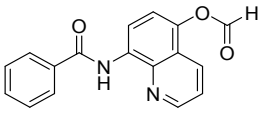
Obtained as a white solid in 75% yield; M.p. 159-161 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 10.65 (s, 1H), 8.95 (s, 1H), 8.64 (d, *J* = 2.6 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 6.8 Hz, 2H), 7.49 (d, *J* = 7.4 Hz, 3H), 7.38 (d, *J* = 4.3 Hz, 1H), 3.98 (s, 3H), 2.38 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 168.00, 164.47, 147.47, 145.25, 133.77, 132.86, 132.78, 131.03, 128.18, 127.86, 126.23, 125.94, 121.96, 121.38, 103.93, 55.75, 19.48. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_4H$, $[M+H]^+$337.1183, Found 337.1189.

4-benzamidonaphthalen-1-yl aetate-*d*$_3$(2r)



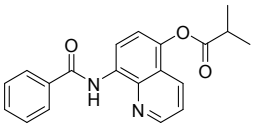
Obtained as a white solid in 82% yield; M.p. 177-178 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.96 (d, *J* = 8.5 Hz, 1H), 8.89 (d, *J* = 2.6 Hz, 1H), 8.21 (s, 1H), 8.08 (d, *J* = 6.7 Hz, 2H), 7.56 (d, *J* = 7.3 Hz, 4H), 7.38 (d, *J* = 8.5 Hz, 1H). HRMS(ESI+): Calculated for $C_{18}H_{11}D_3N_2O_3H$, $[M+H]^+$ 310.1266, Found 310.1269.

8-benzamidoquinolin-5-yl formate(2s)



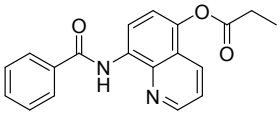
Obtained as a white solid in 58% yield; M.p. 230-231 °C. ^{1}H NMR (400 MHz, DMSO) δ 10.34 (s, 1H), 9.94 (s, 1H), 8.78 (d, *J* = 2.7 Hz, 1H), 8.53 (d, *J* = 8.5 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 7.5 Hz, 3H),7.42 (d, *J* = 4.2 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 164.31, 161.43, 149.03, 148.85, 139.38, 135.24, 131.87, 131.74, 128.91, 127.03, 126.44, 120.59, 120.02, 117.63, 108.34. HRMS(ESI+): Calculated for $C_{17}H_{12}N_2O_3H$, $[M+H]^+$ 293.0921, Found 293.0923.

8-benzamidoquinolin-5-yl isobutyrate(2t)



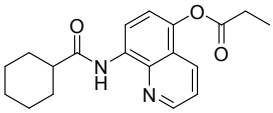
Obtained as a white solid in 47% yield; M.p. 115-116 °C. ^{1}H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 8.99 (d, *J* = 2.8 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H), 8.30 – 8.26 (m, 1H), 8.01 (d, *J* = 6.9 Hz, 2H), 7.69 (s, 1H), 7.58 (s, 3H), 7.42 (d, *J* = 8.4 Hz, 1H), 3.02 (s, 1H), 1.32 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 175.75, 164.95, 150.13, 141.34, 139.07, 134.76, 132.62, 132.60, 131.08, 129.44, 127.50, 123.22, 122.27, 119.62, 116.73, 33.81, 19.21. HRMS(ESI+): Calculated for $C_{20}H_{18}N_2O_3H$, $[M+H]^+$ 335.1390, Found 335.1398.

8-benzamidoquinolin-5-yl propionate(2u)



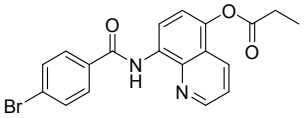
Obtained as a white solid in 62% yield; M.p. 108-109 °C. ^{1}H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 8.99 (d, *J* = 4.0 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 2H), 7.69 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.67 – 7.49 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 1H), 2.80 (q, *J* = 7.4 Hz, 2H), 1.18 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.43, 164.97, 150.13, 141.43, 139.10, 134.77, 132.73, 132.60, 131.43, 129.45, 127.51, 123.12, 122.34, 119.68, 116.78, 27.15, 9.31. HRMS(ESI+): Calculated for $C_{19}H_{16}N_2O_3H$, $[M+H]^+$ 321.1234, Found 321.1230.

8-(cyclohexanecarboxamido)quinolin-5-yl propionate(2v)



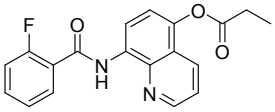
Obtained as a white solid in 42% yield; M.p. 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.77 (d, *J* = 8.3 Hz, 2H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.44 (d, *J* = 3.1 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 2.70 (d, *J* = 7.6 Hz, 2H), 2.41 (d, *J* = 15.1 Hz, 1H), 2.02 (s, 2H), 1.82 (s, 2H), 1.59 (d, *J* = 12.2 Hz, 3H), 1.40 – 1.24 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.71, 172.96, 148.40, 140.34,138.63, 132.78, 130.34, 121.88, 121.68, 119.22, 115.69, 46.78, 29.70, 27.58, 25.73, 25.70, 9.21. HRMS(ESI+): Calculated for $C_{19}H_{22}N_2O_3H$, $[M+H]^+$ 327.1703, Found 327.1700.

8-(4-bromobenzamido)quinolin-5-yl propionate(2w)



Obtained as a white solid in 48% yield; M.p. 126-127 °C. ^{1}H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 8.96 (s, 1H), 8.61 (s, 1H), 8.35 (s, 1H), 7.91 (s, 2H), 7.77 (s, 2H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 2.79 (d, *J* = 7.5 Hz, 2H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.37, 164.09, 150.10, 141.60, 139.20, 133.83, 132.44, 132.36, 131.36, 129.65, 126.34, 123.06, 122.32, 119.61, 117.17, 27.16, 9.30. HRMS(ESI+): Calculated for $C_{19}H_{15}BrN_2O_3H$, $[M+H]^+$ 399.0339, Found 399.0332.

8-(2-fluorobenzamido)quinolin-5-yl propionate(2x)



Obtained as a white solid in 51% yield; M.p. 117-118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (d, *J* = 12.7 Hz, 1H), 8.92 (d, *J* = 31.2 Hz, 2H), 8.18 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 5.0 Hz, 2H), 7.29 (d, *J* = 41.3 Hz, 3H), 2.75 (d, *J* = 7.6 Hz, 2H), 1.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.93, 161.78, 160.41 (d, *J* = 278.5 Hz), 148.77, 141.00, 139.00, 133.61 (d, *J* = 8.8 Hz), 132.93, 132.03, 132.01, 130.39, 124.86 (d, *J* = 3.8 Hz), 121.97 (d, *J* = 12.5 Hz), 121.83, 119.25, 116.73, 116.32 (d, *J* = 24.0 Hz), 27.65, 9.23. HRMS(ESI+): Calculated for $C_{19}H_{15}FN_2O_3H$, $[M+H]^+$ 339.1140, Found 339.1148.

4. X-ray Crystal Data for 2c

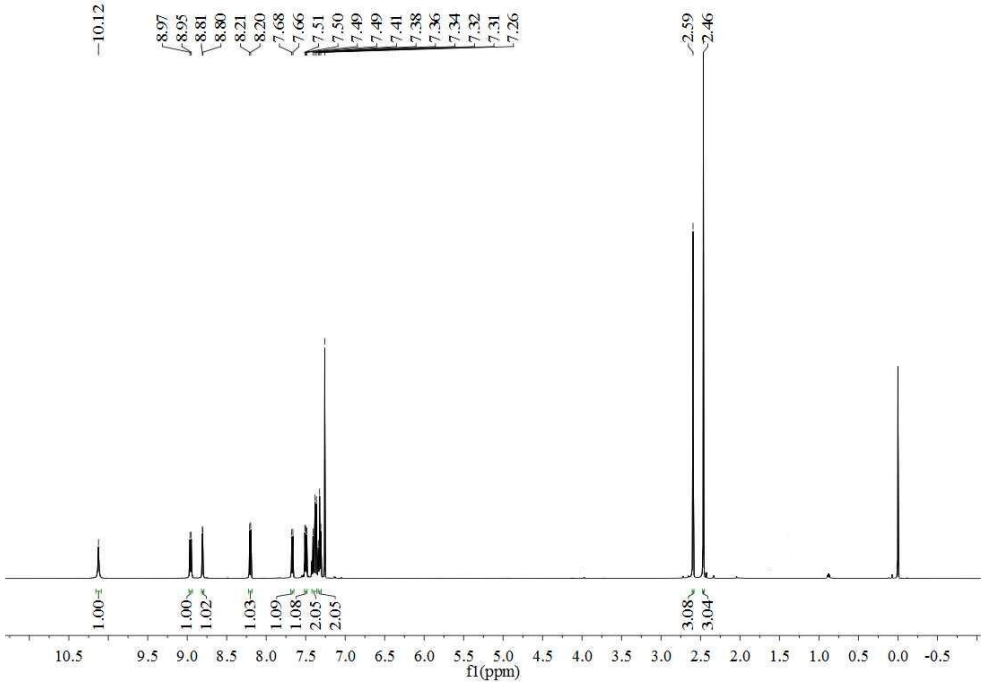
Crystals of **2c** ($C_{19}H_{16}N_2O_3$) was recrystallized from $CDCl_3$. The single colourless transparent granular crystal which was suitable for X-ray diffraction measurements was mounted on a glass fiber. Unit cell measurements and intensity data collections were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo Ka. The data reduction included a correction for Lorentz and polarization effects, with an applied multi-scan absorption correction (SADABS). The crystal structure was solved and refined using the SHELXTL-97 program suite. Direct methods yielded all non-hydrogen atoms which were refined with anisotropic thermal parameters. The obtained crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1508095 (**2c**, CCDC NO.). The crystallographic data and refinement parameters of them are listed in **Table S1**.

Table S1 Crystallographic data and structure refinement for **2c.**

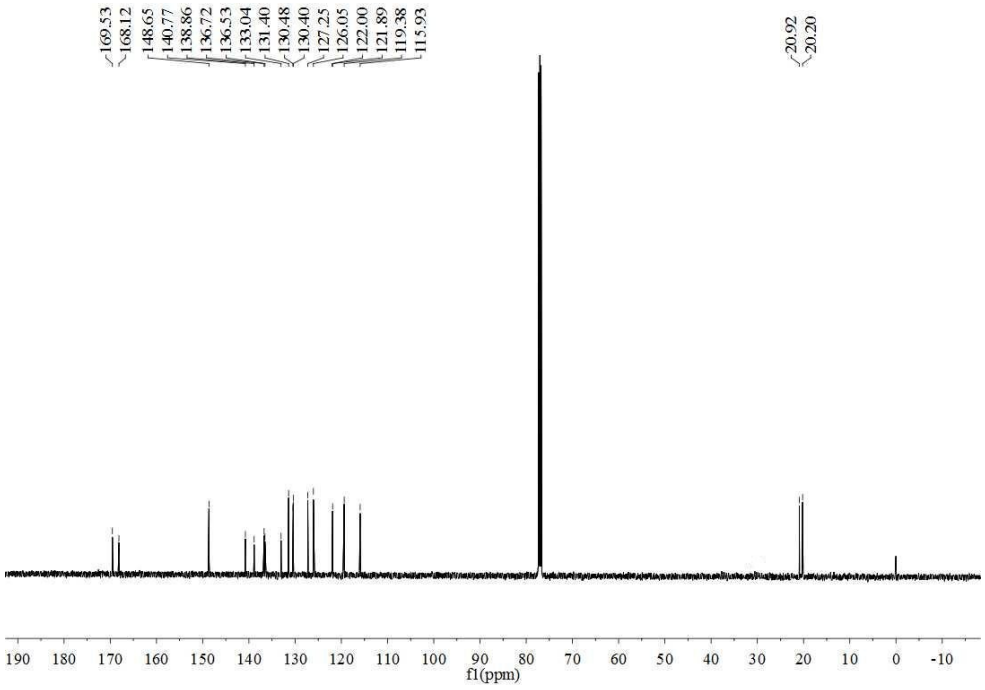
Empirical formula	$C_{19}H_{16}N_2O_3$
Formula weight	320.34
Temperature, K	100(2)
Wavelength, Å	0.71073
Crystal system	Monoclinic
Space group	P1 21/c 1
Unit cell dimensions	
a, *b*, *c*, Å	6.1225(6), 16.4269(15), 15.5669(14)
α, β, γ, °	90.00, 93.055(3), 90.00
Volume, $Å^3$	1563.4(3)
Z	4
Calculated density, Mg/m^3	1.361
Absorption coefficient, mm^{-1}	0.093
F (000)	672
Crystal size, mm	0.317 x 0.309 x 0.112
Theta range for data collection, °	3.333 to 25.137
Limiting indices	-7<=h<=7, -19<=k<=19, -18<=l<=18
Absorption correction	multi-scan
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2751 / 0 / 218
Goodness of fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0455, wR2 = 1.248
R indices (all data)	R1 = 0.0636, wR2 = 1.390

5. ^{1}H and ^{13}C NMR spectra of the products

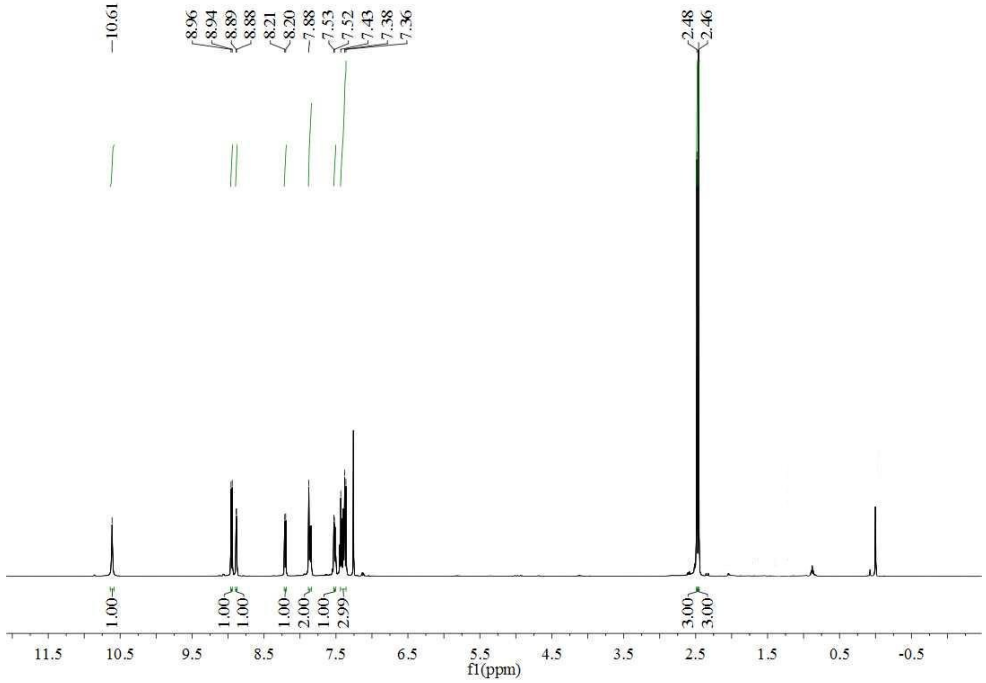
2a ^{1}H NMR



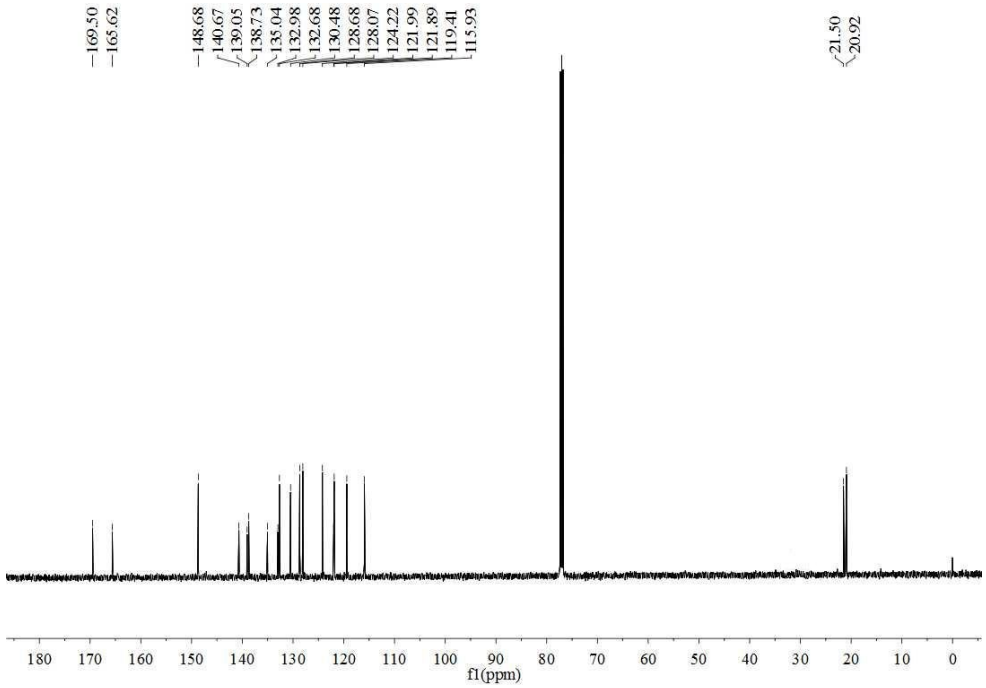
2a ^{13}C NMR



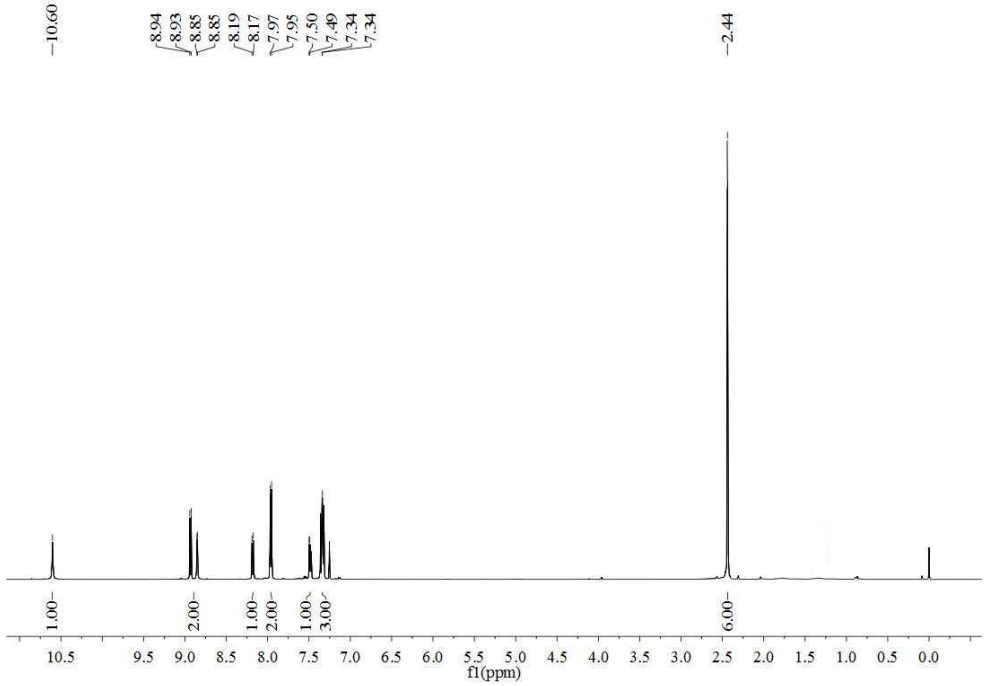
2b ^{1}H NMR



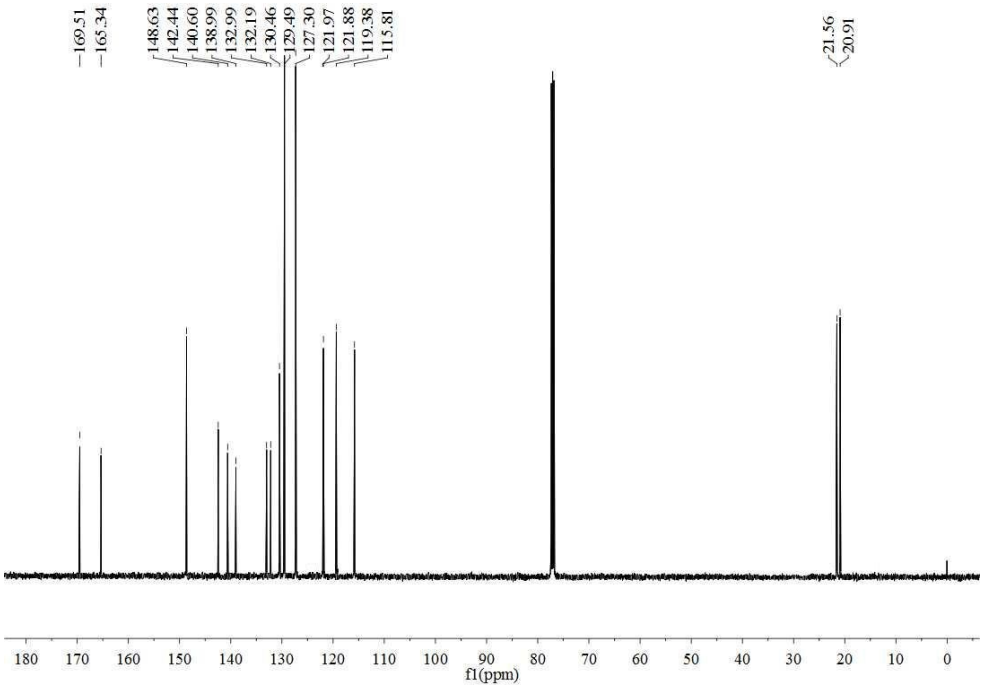
2b ^{13}C NMR



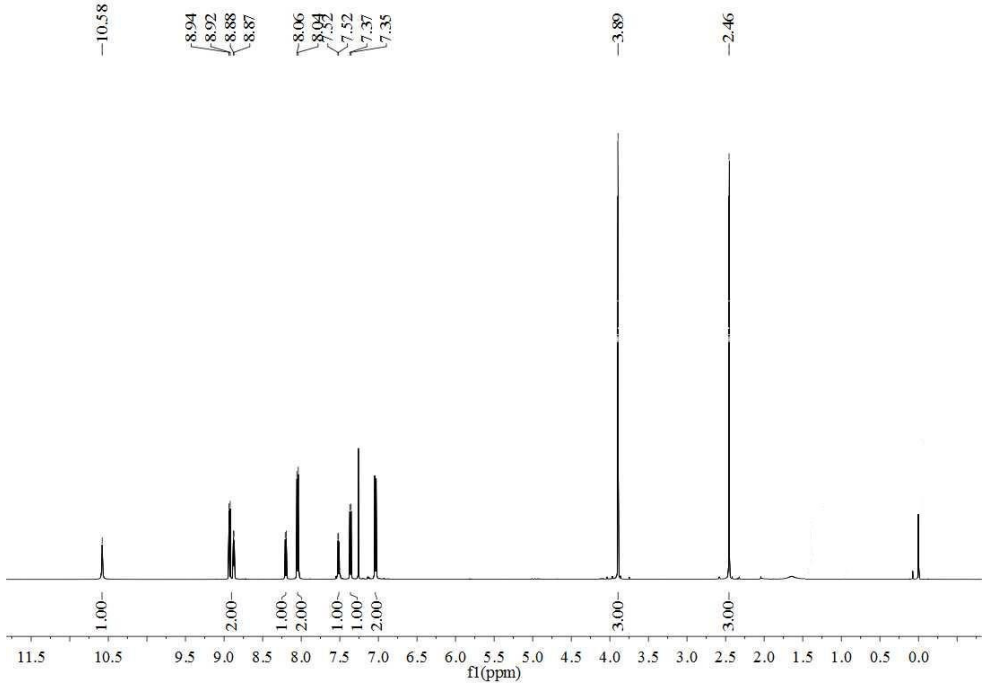
2c ^{1}H NMR



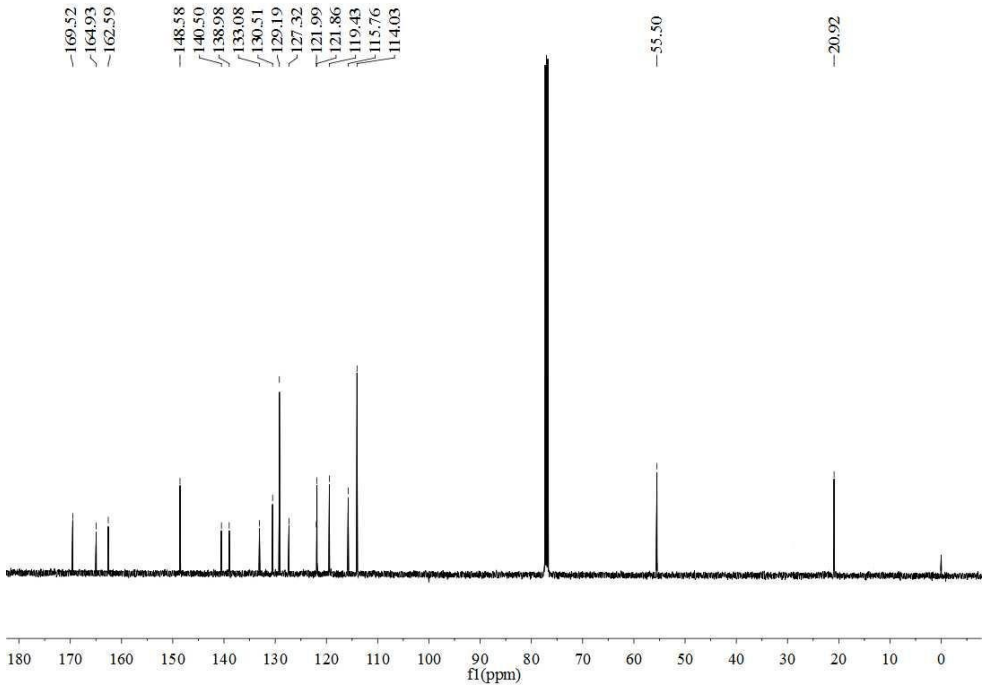
2c ^{13}C NMR



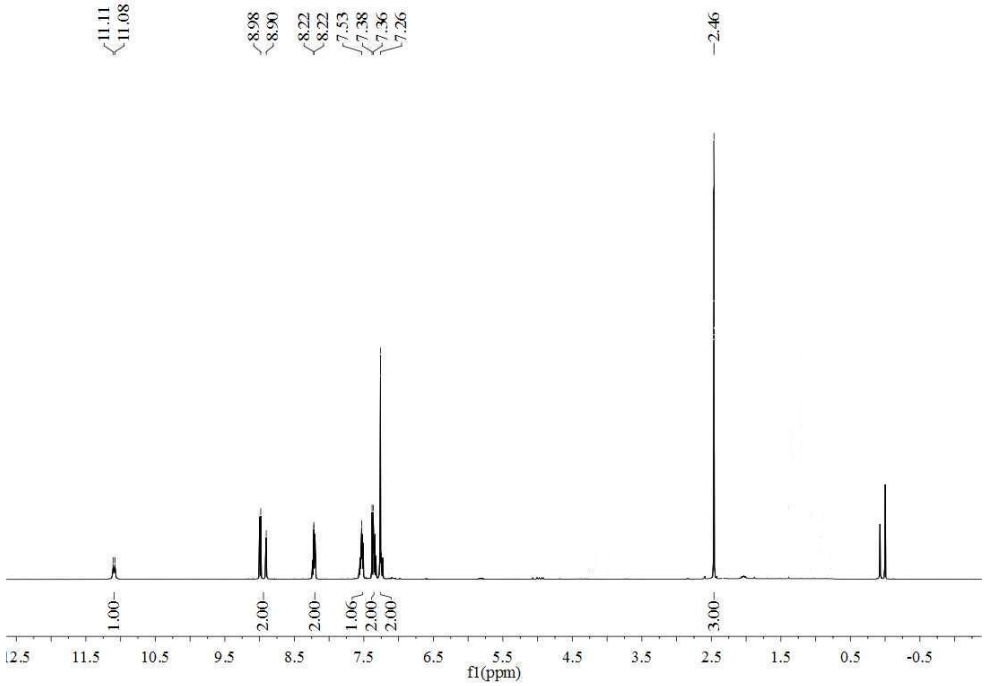
2d ^{1}H NMR



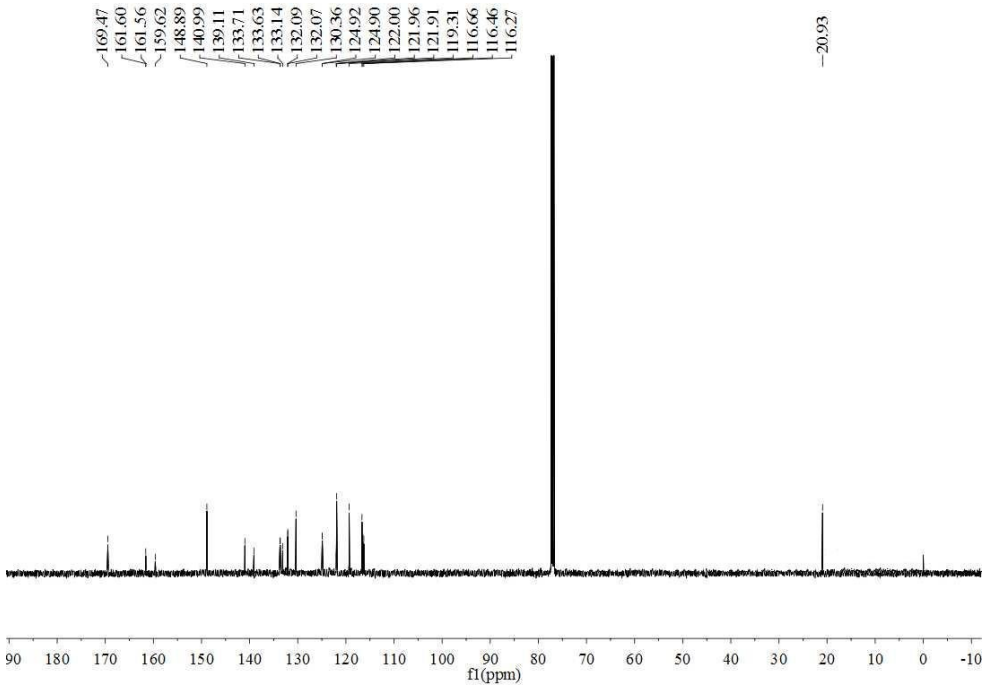
2d ^{13}C NMR



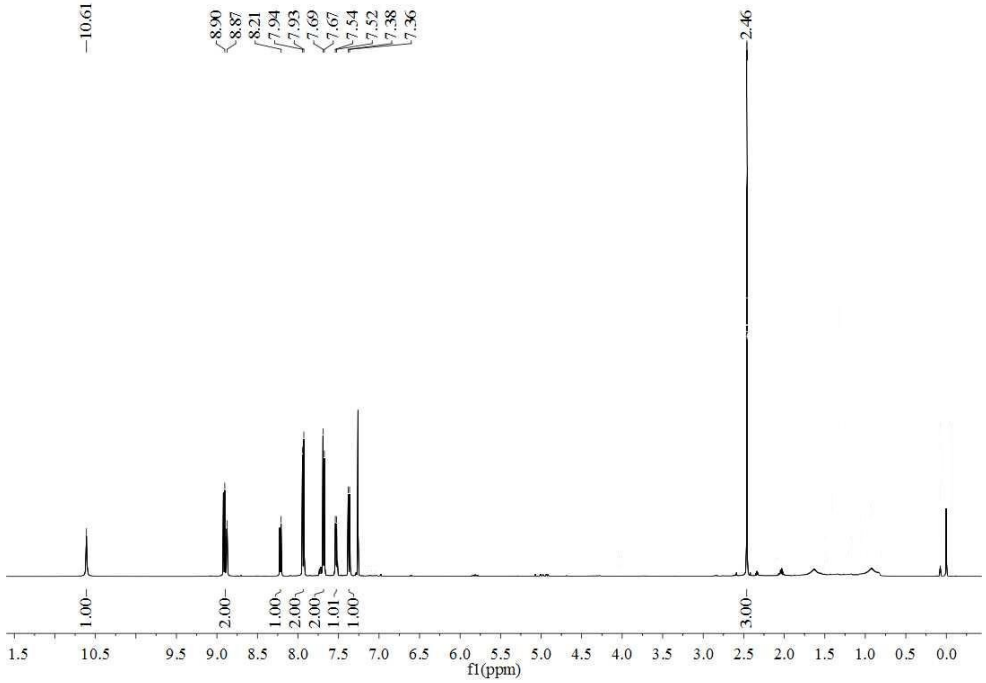
2e ^{1}H NMR



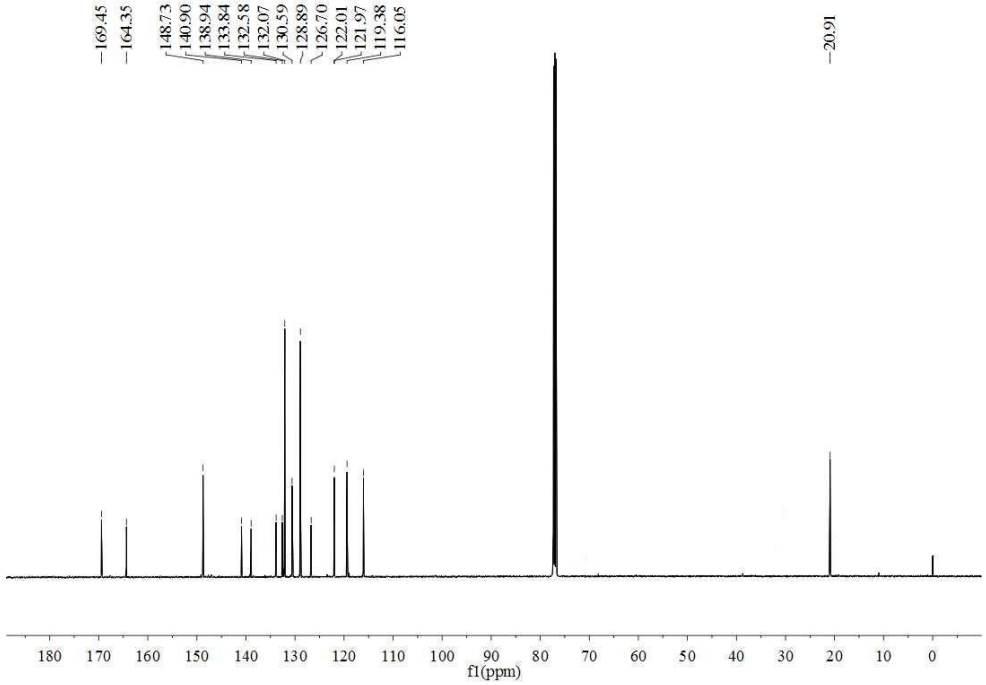
2e ^{13}C NMR



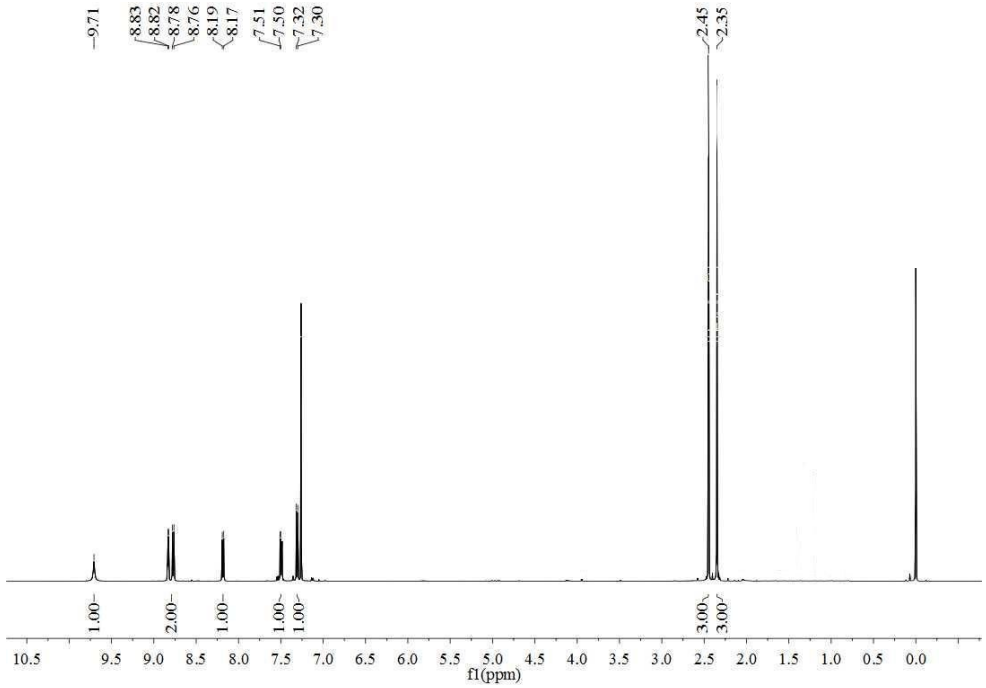
2f ^{1}H NMR



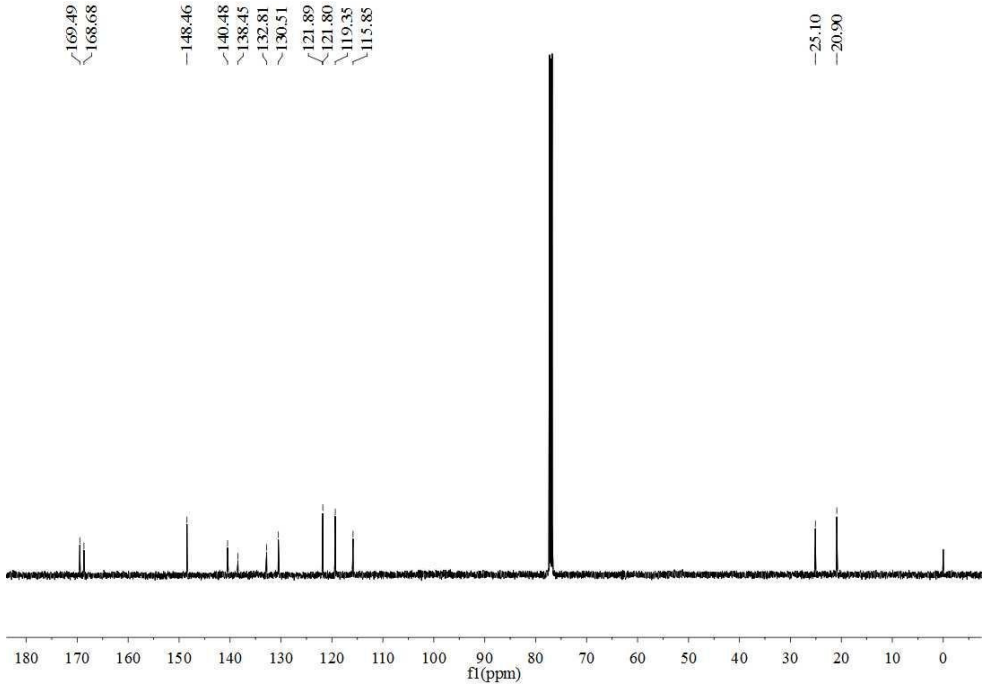
2f ^{13}C NMR



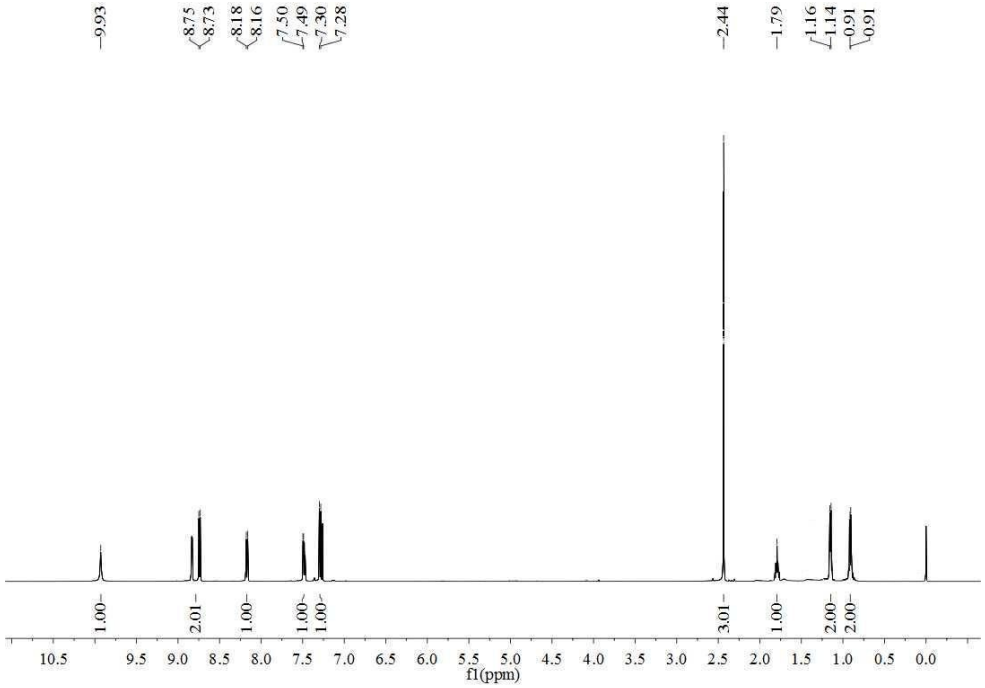
2g ^{1}H NMR



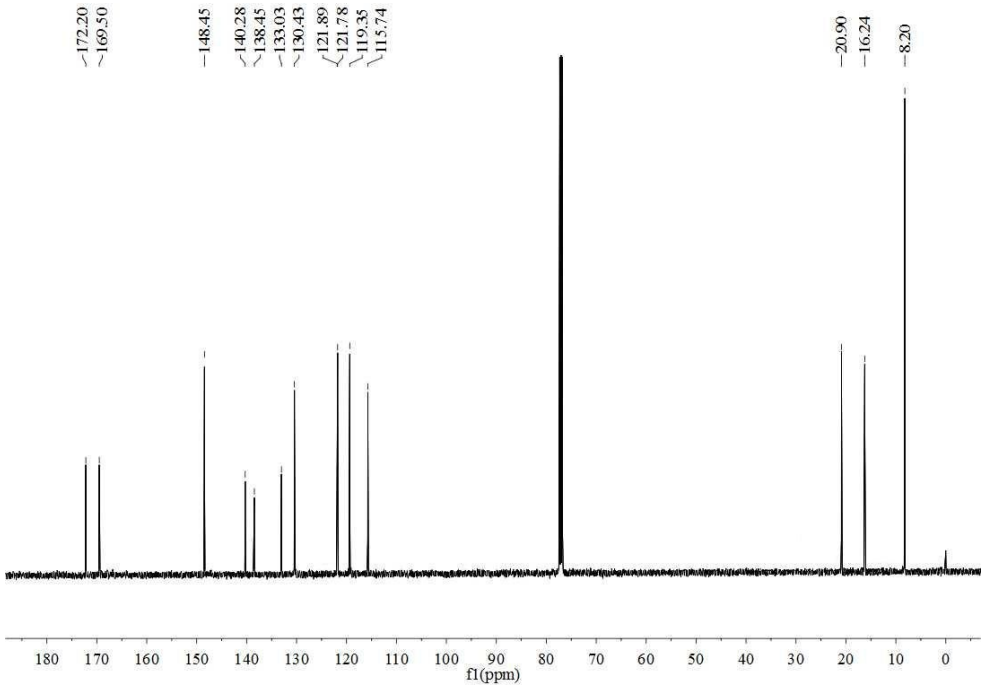
2g ^{13}C NMR



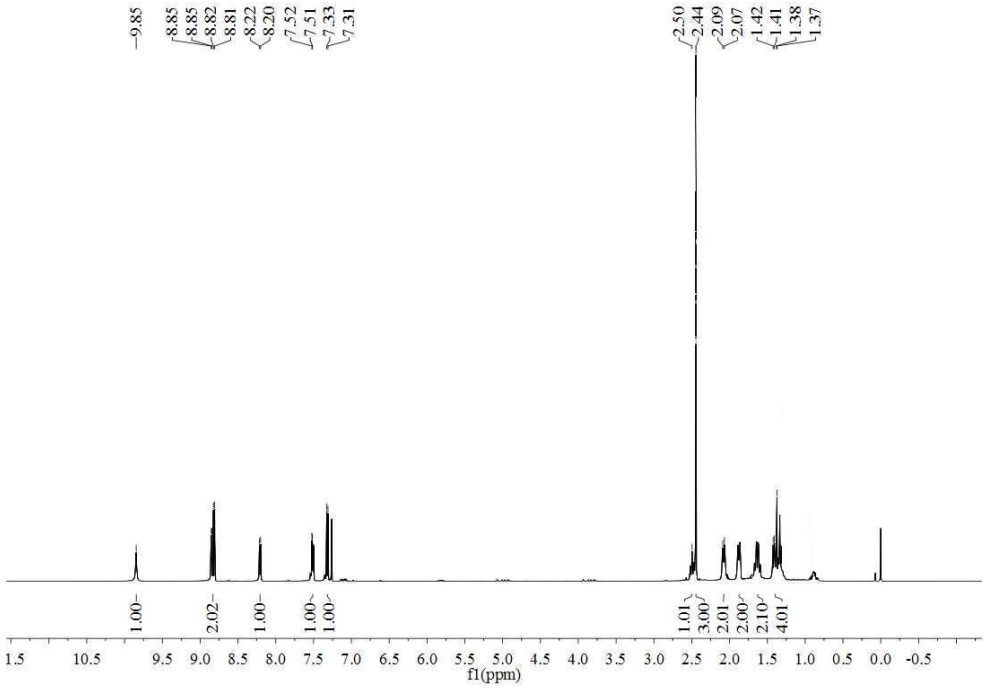
2h ^{1}H NMR



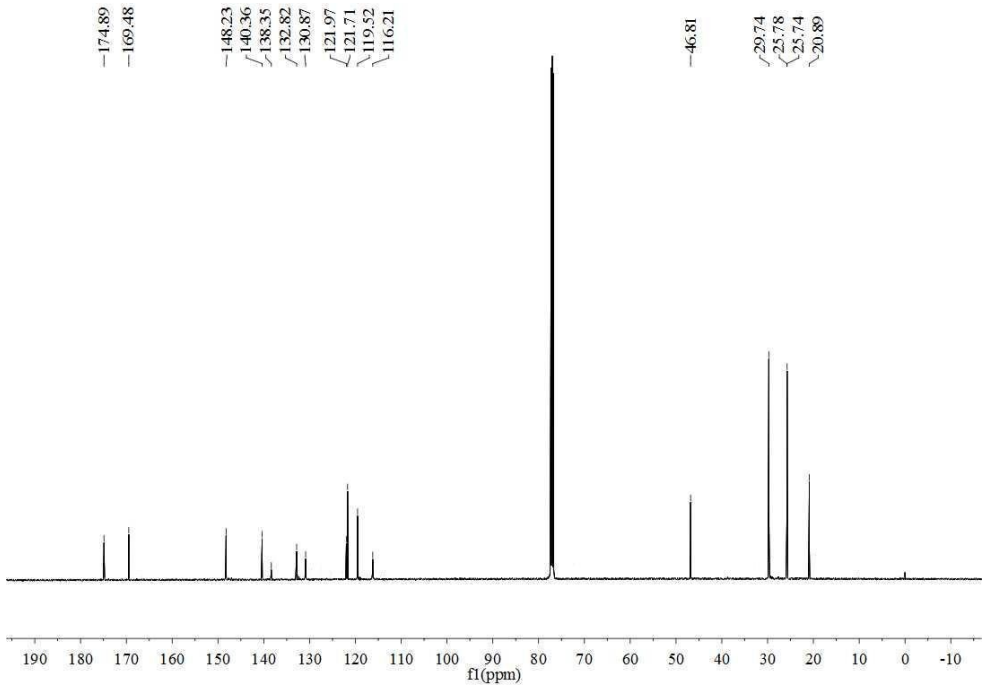
2h ^{13}C NMR



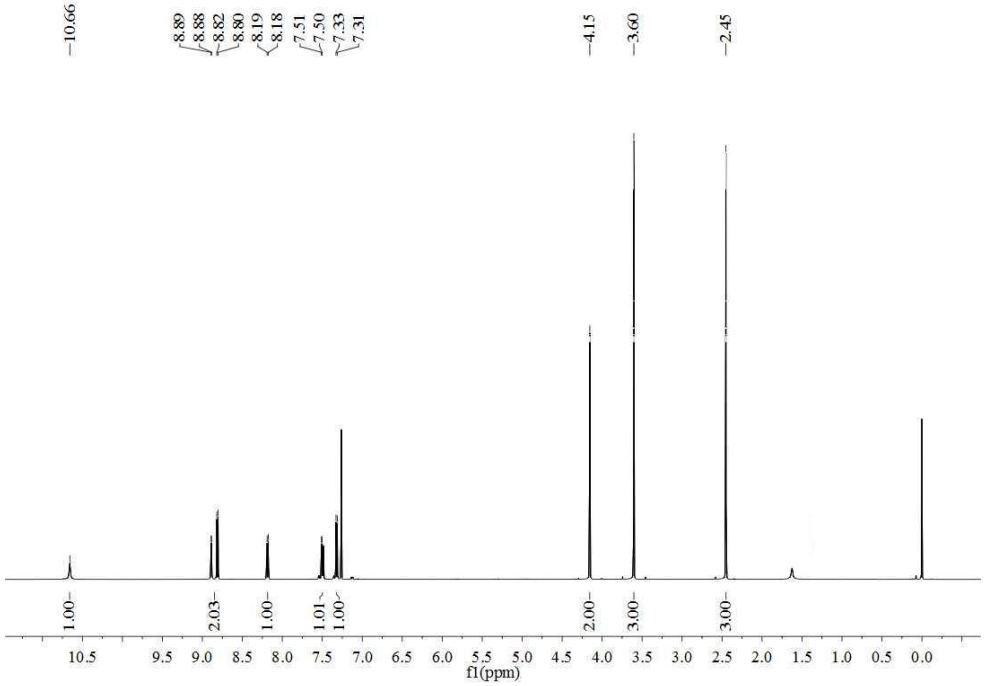
2i ^{1}H NMR



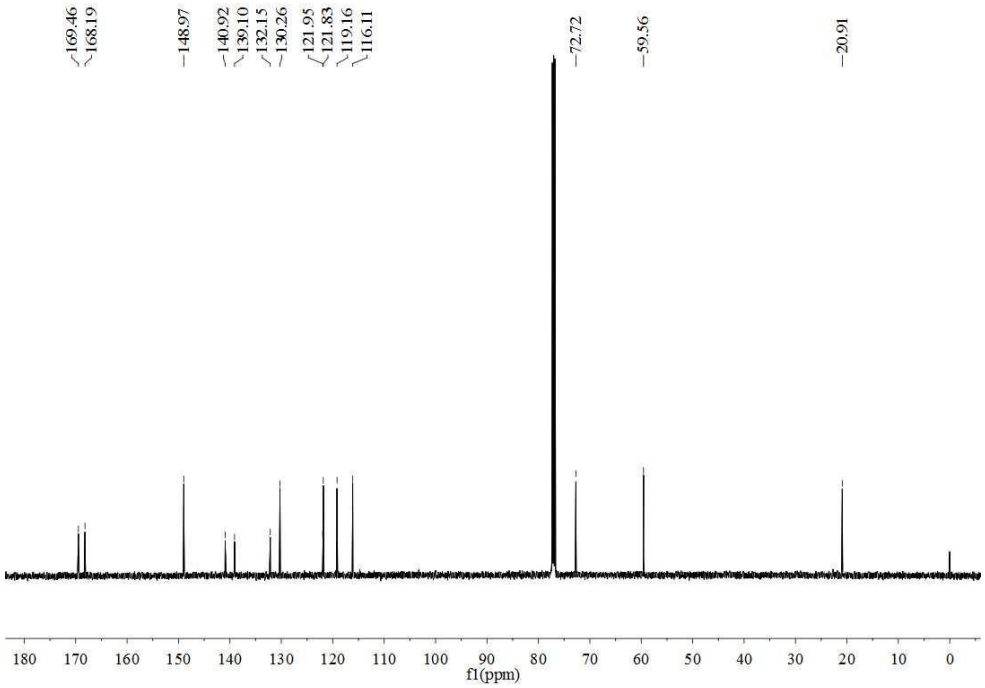
2i ^{13}C NMR



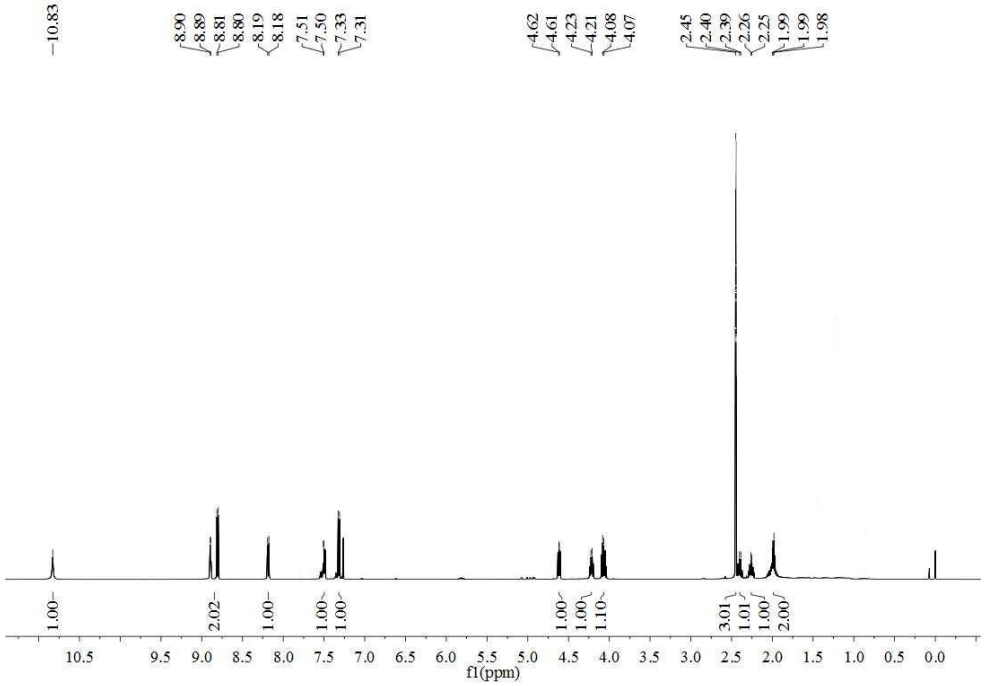
2j ^{1}H NMR



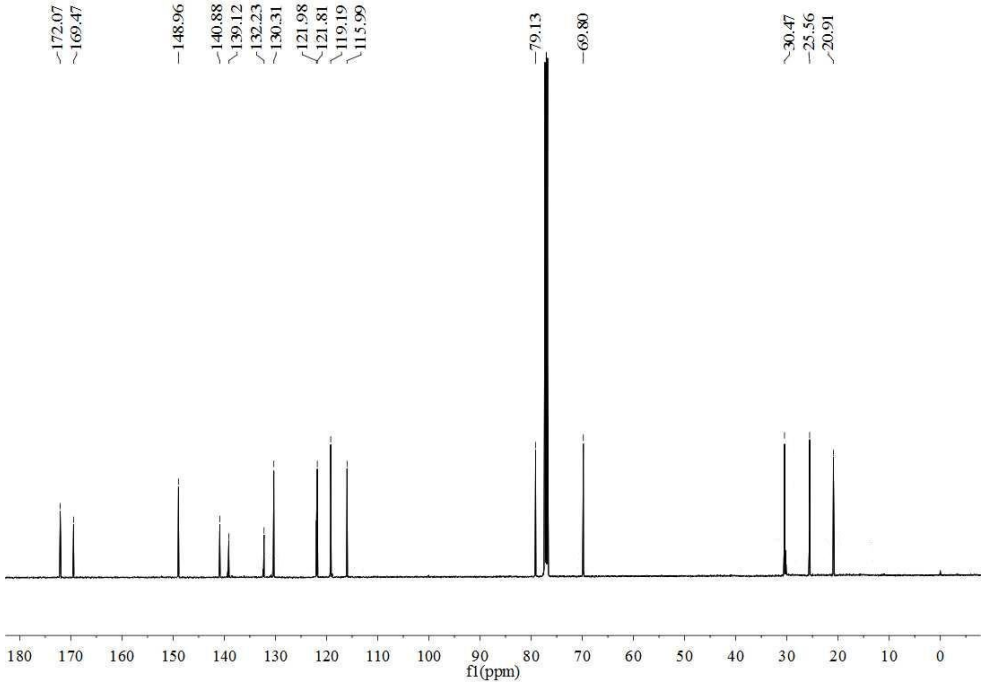
2j ^{13}C NMR



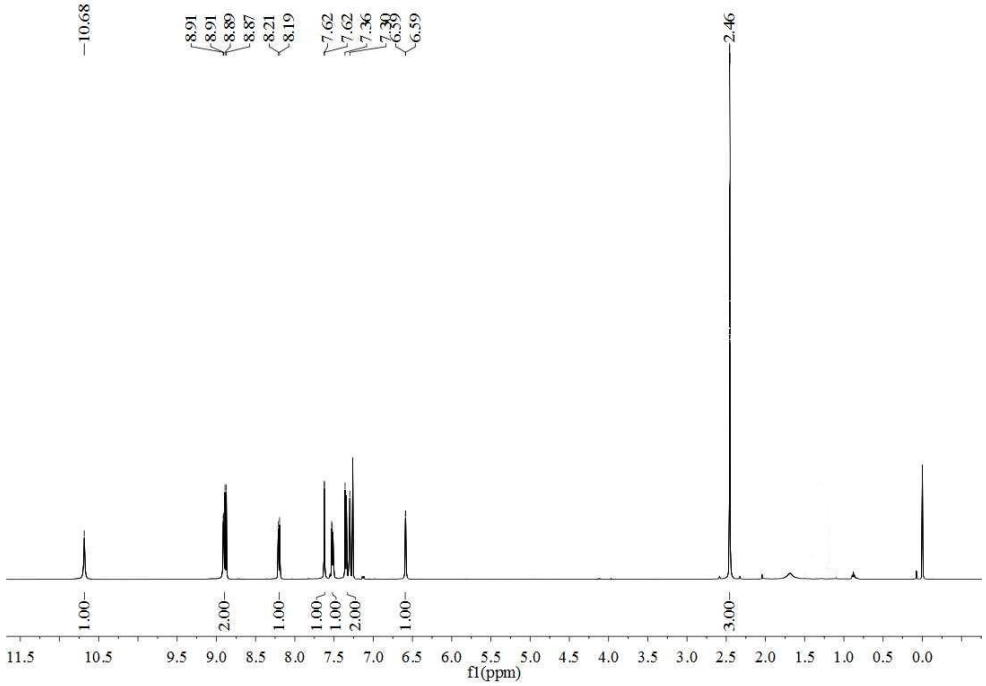
2k ^{1}H NMR



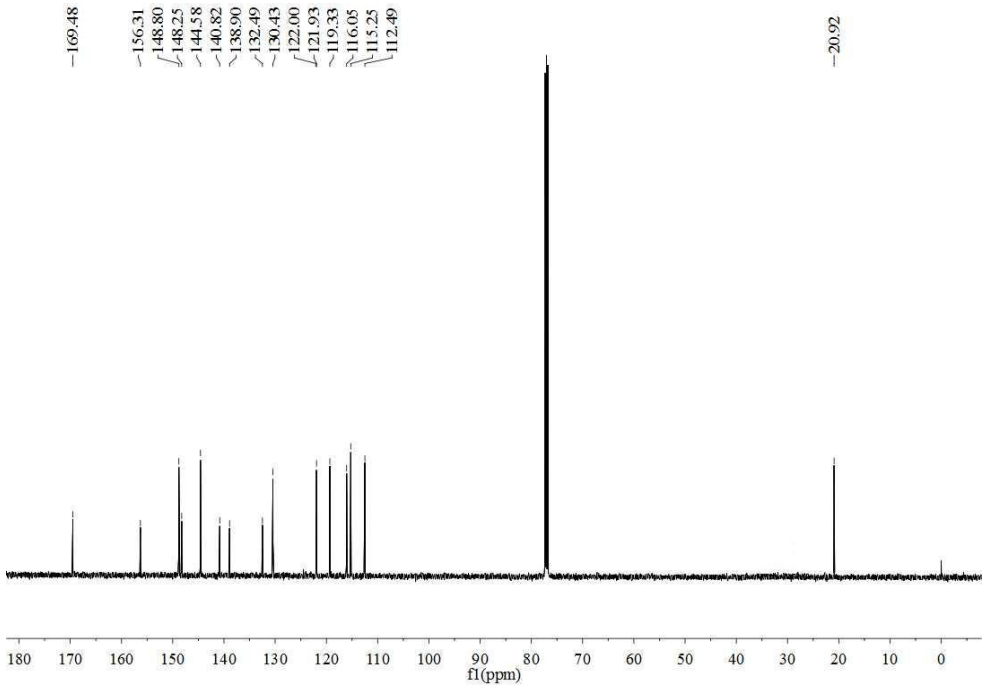
2k ^{13}C NMR



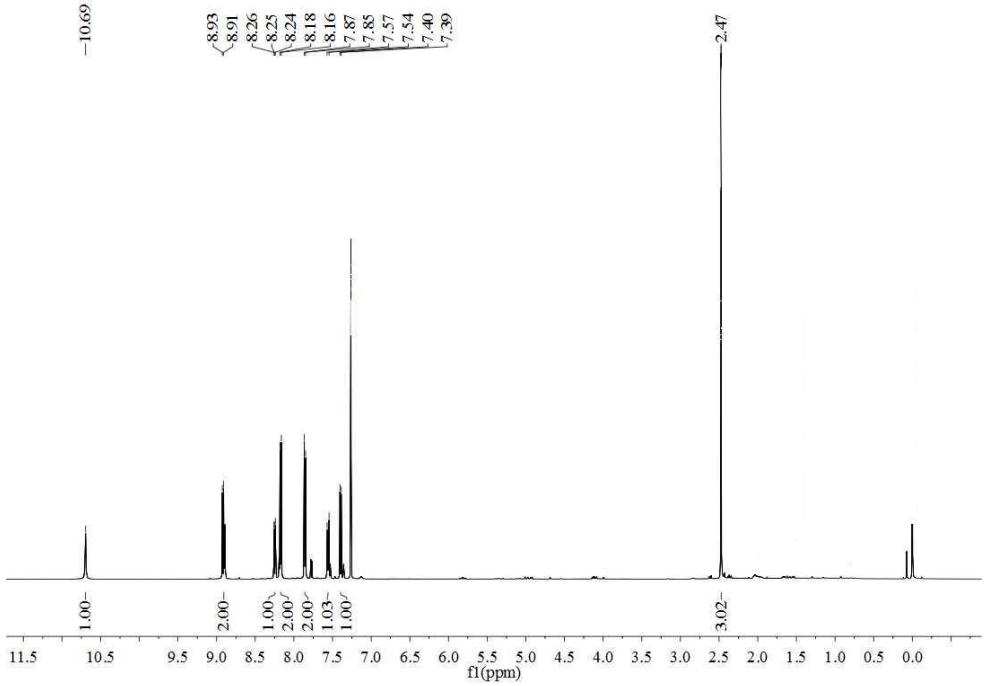
2l ^{1}H NMR



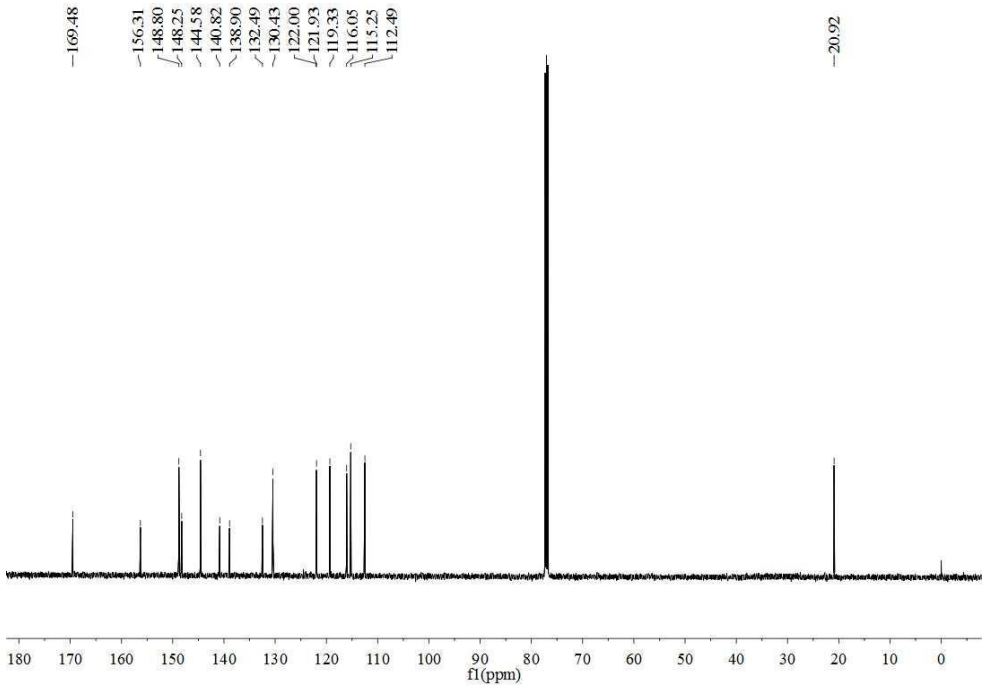
2l ^{13}C NMR



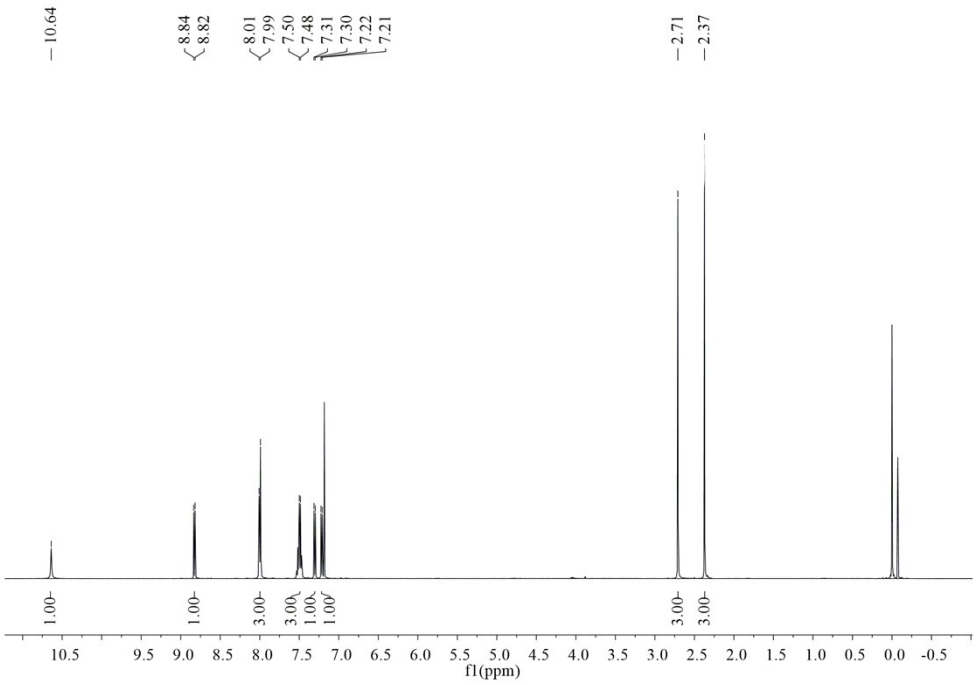
2n ^{1}H NMR



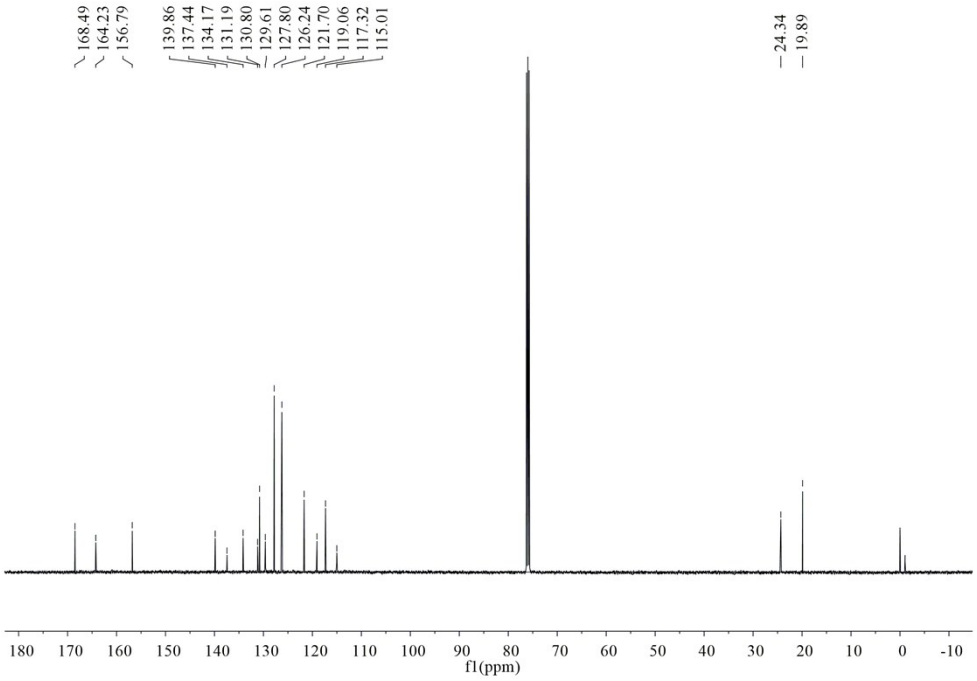
2n ^{13}C NMR



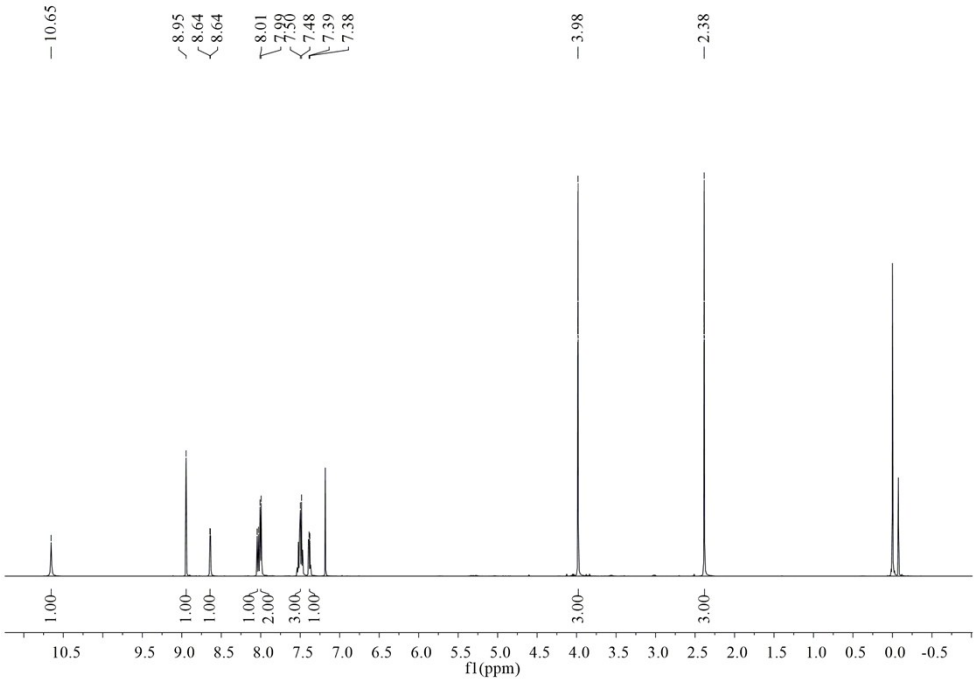
2p ^{1}H NMR



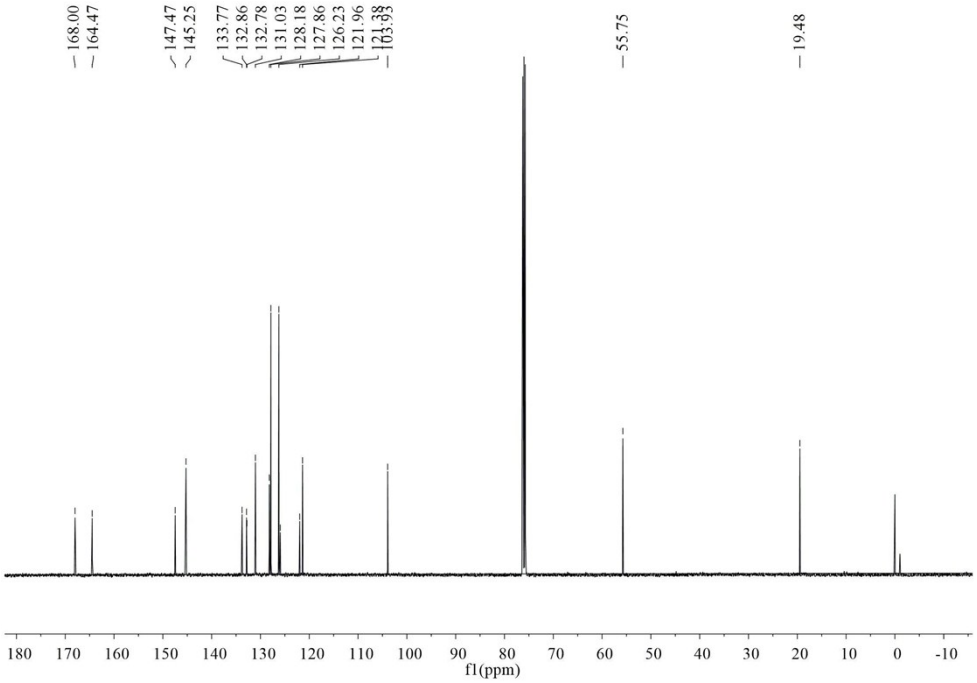
2p ^{13}C NMR



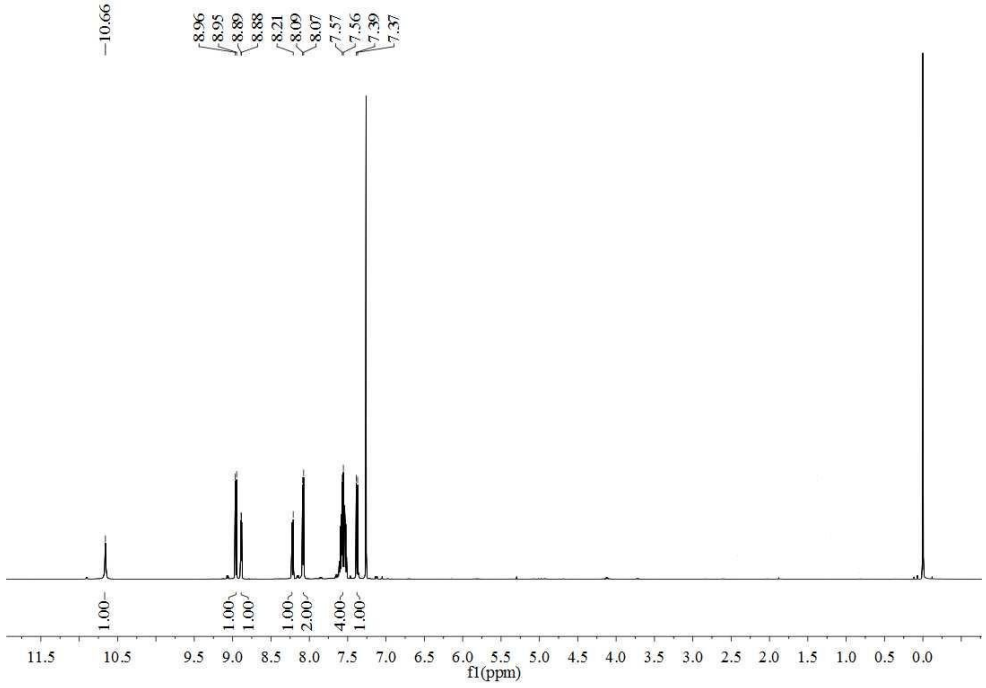
2q ^{1}H NMR



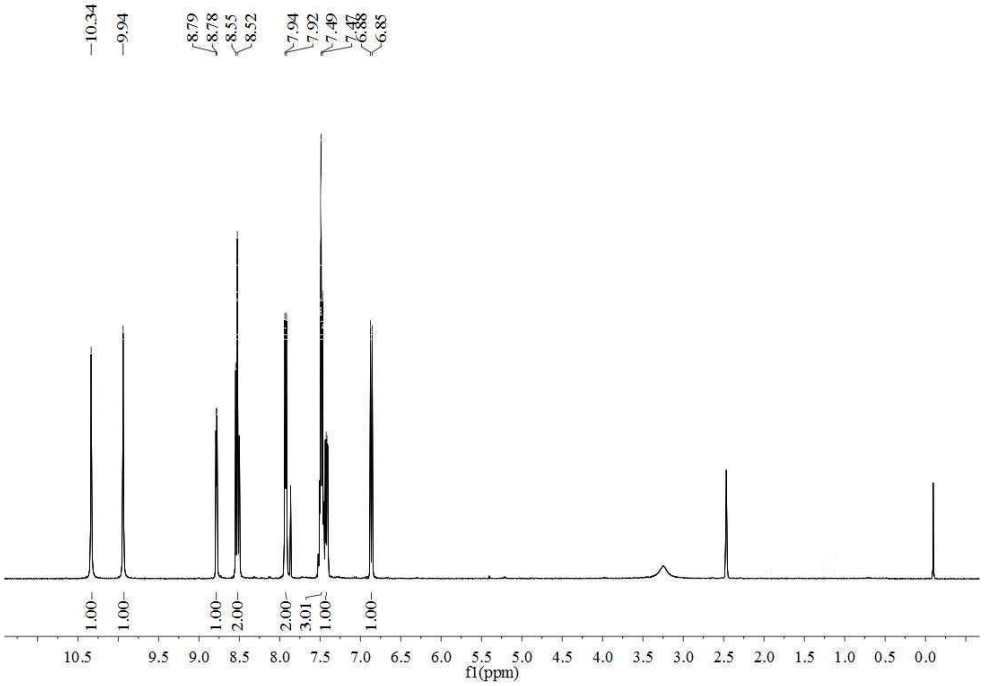
2q ^{13}C NMR



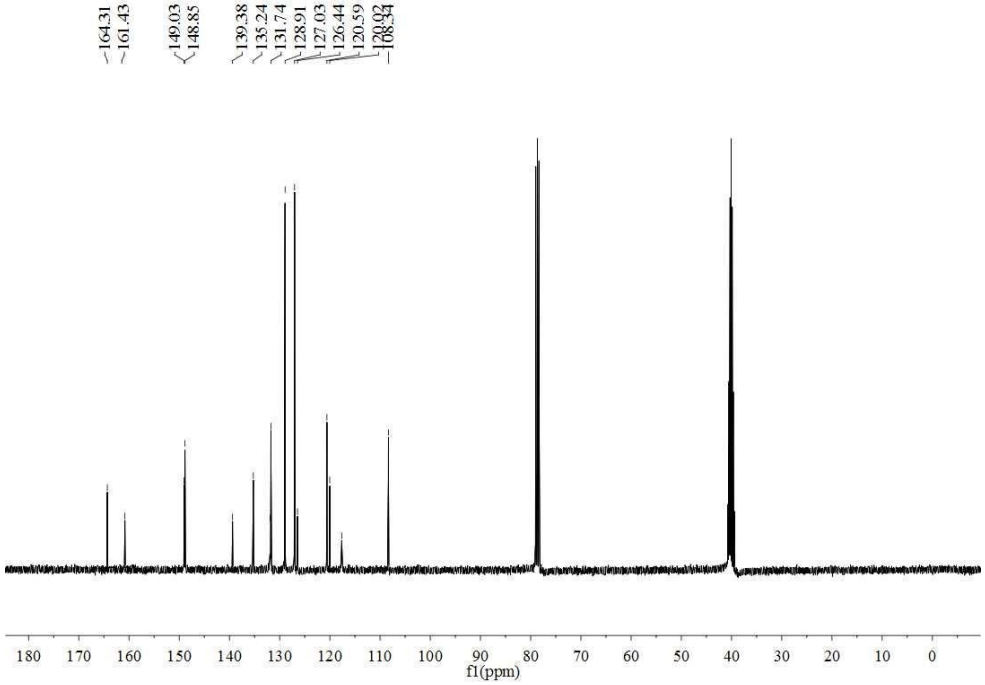
2r ^{1}H NMR


10.66
8.96
8.95
8.89
8.88
8.21
8.09
8.07
7.57
7.56
7.39
7.37
1.00
1.00
1.00
1.00
2.00
4.00
1.00
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1(ppm)

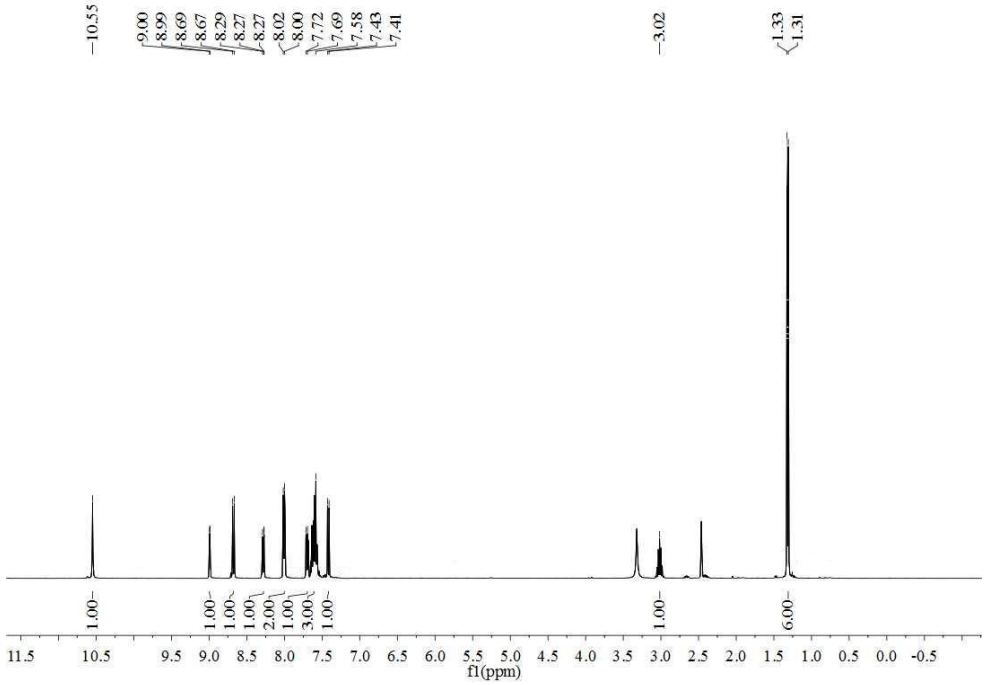
2s ^{1}H NMR



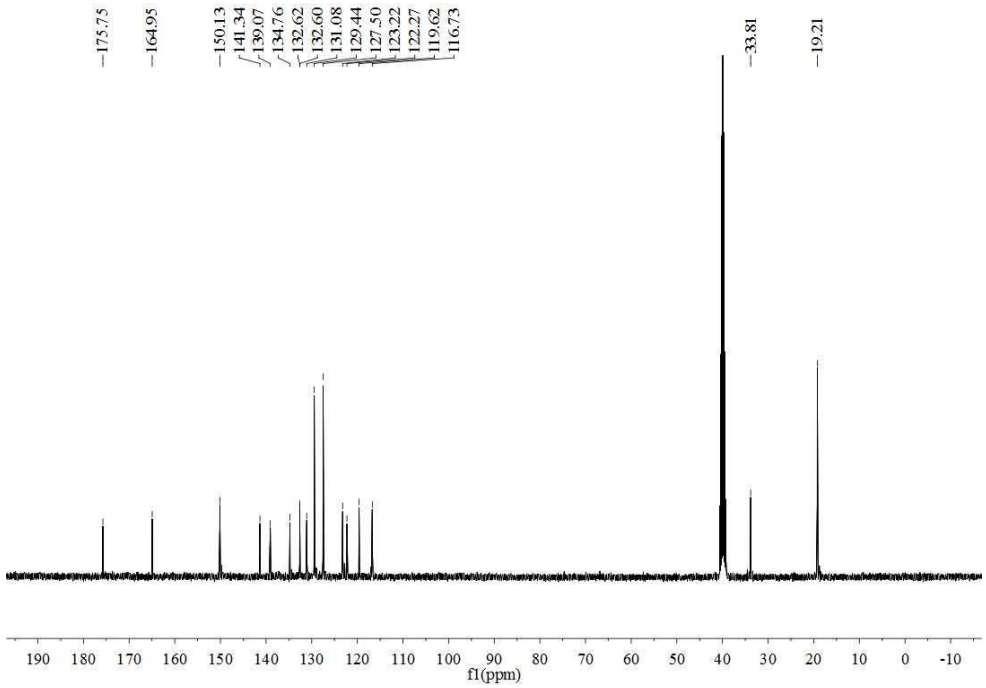
2s ^{13}C NMR



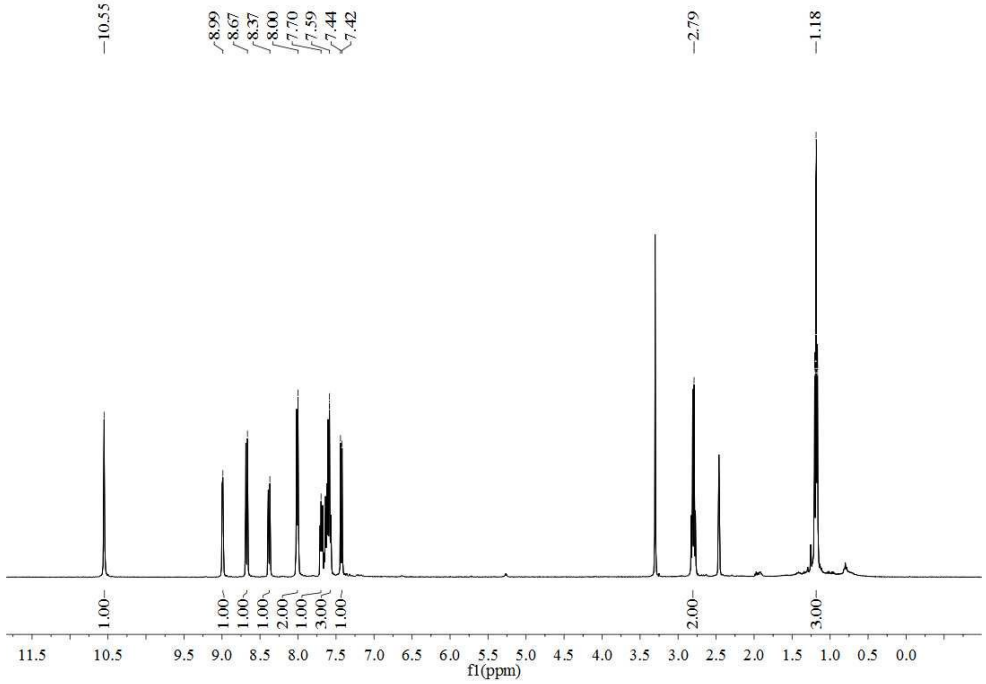
2t ^{1}H NMR



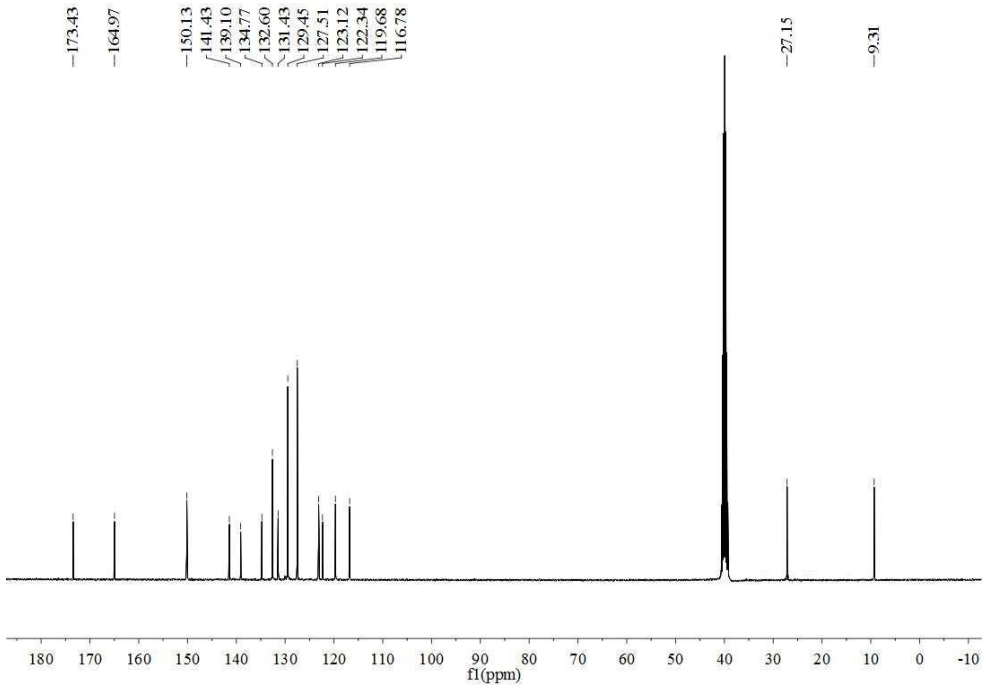
2t ^{13}C NMR



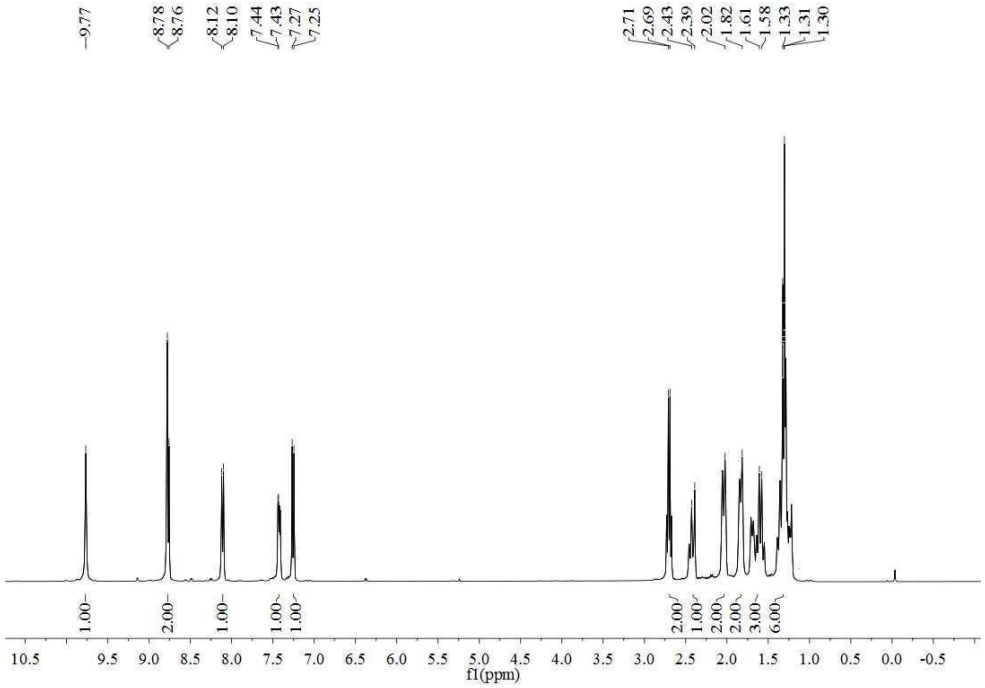
2u ^{1}H NMR



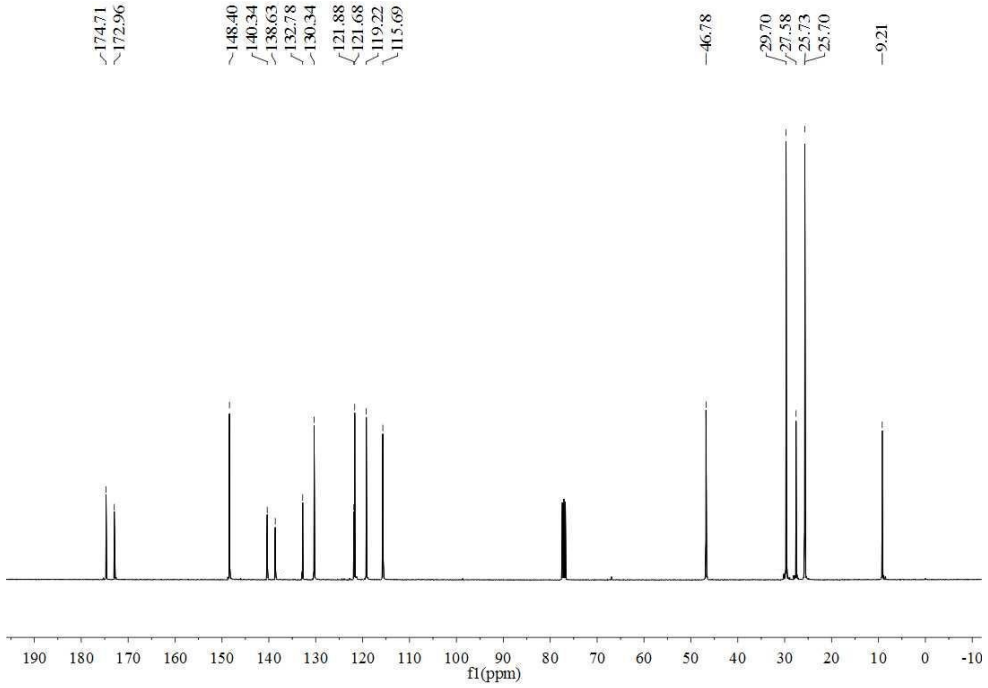
2u ^{13}C NMR



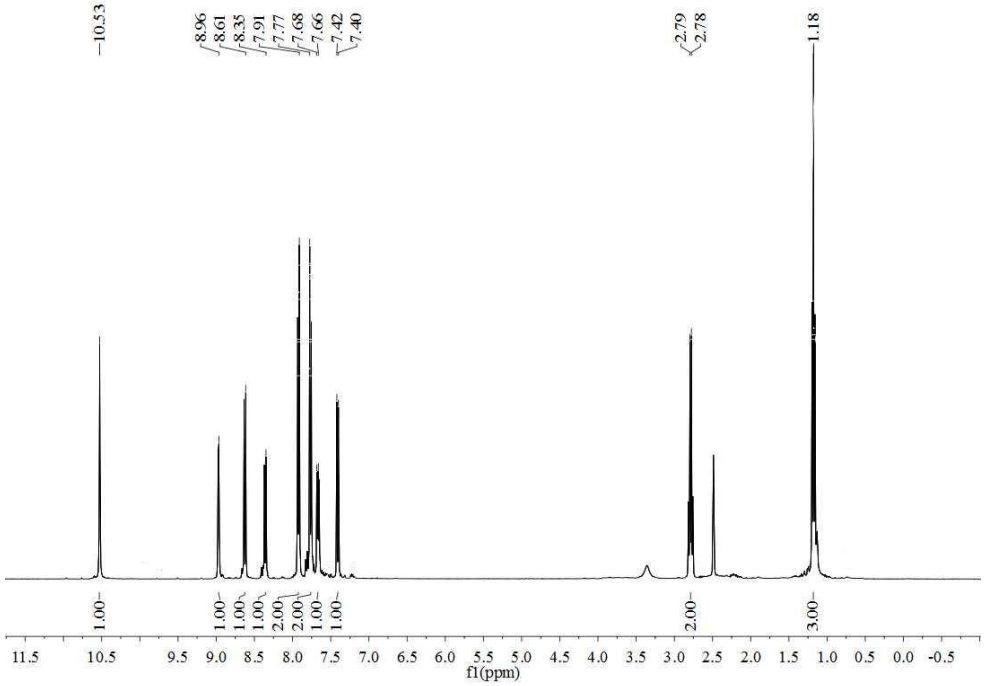
2v ^{1}H NMR



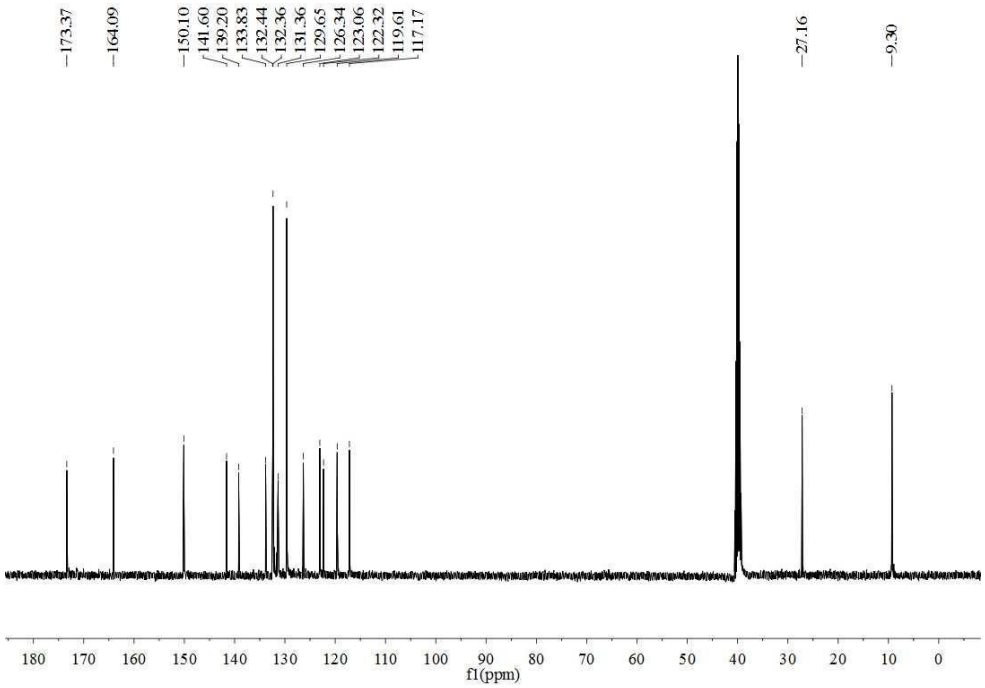
2v ^{13}C NMR



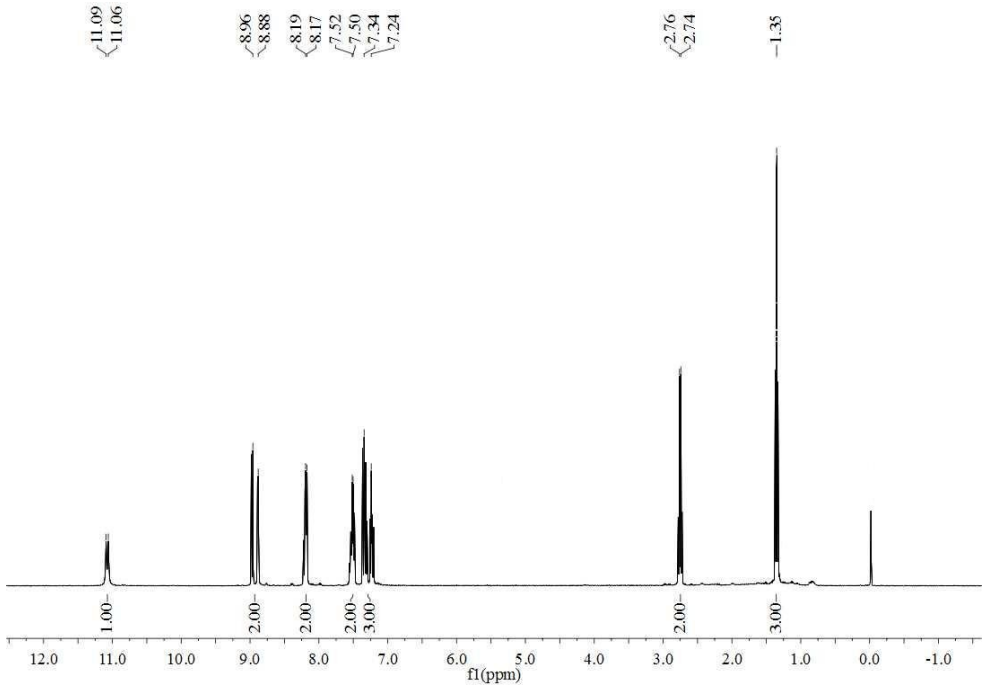
2w ^{1}H NMR



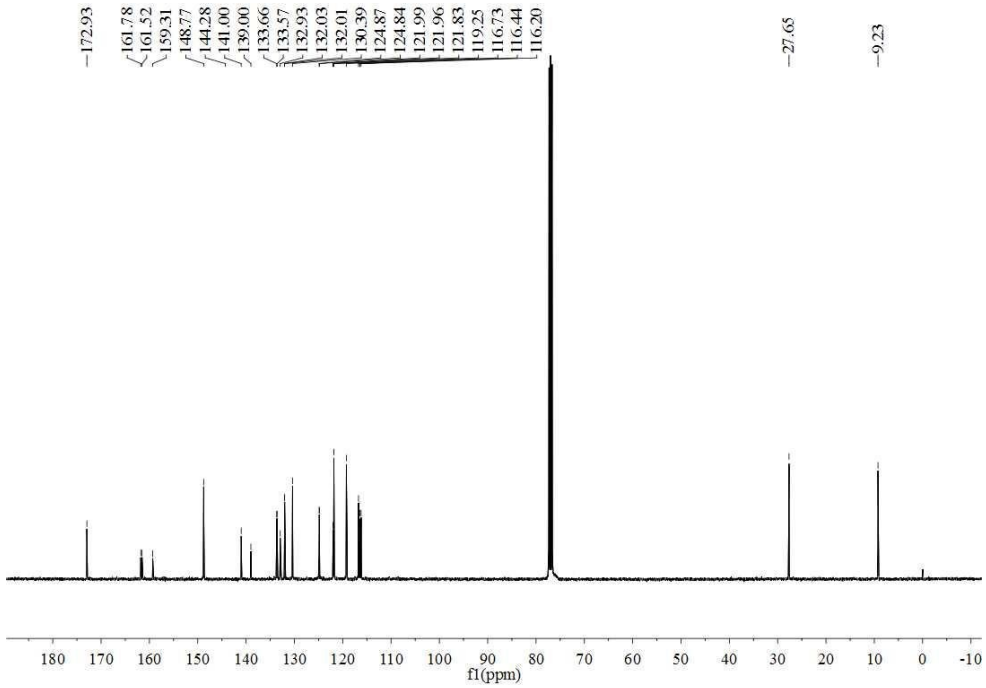
2w ^{13}C NMR



2x ^{1}H NMR



2x ^{13}C NMR



2aa/2aa-D ^{1}H NMR