Supplementary Materials

Synthesis and *in vitro* antitumor activity of novel bivalent β-carboline derivatives with DNA as a potential target

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S.1. General reaction of synthesis of β-carboline monomers (**4A**, **4B**, **4C**, and **4D**)

L-tryptophan (10 g, 49 mmol) was dissolved in ultrapure water (450 mL). And the sulfuric acid (0.1 mol/L) was added dropwise with stirring until the solution became clear. And then 11 mL 37% formaldehyde solution was added and the mixture was reacted at room temperature for about 5 h. Then, the pH of the reaction solution was adjusted to about 6 with the saturated $NaHCO_3$ solution to obtain a white precipitate, and the precipitate was collected by negative-pressure filtration and washed well with water and then dried to obtain the target product **1** (1, 2, 3, 4-tetrahydro-β-carboline-3-carboxylic acid). The yield was about 70% (7.23 g).

The target product **1** (1, 2, 3, 4-tetrahydro-β-carboline-3-carboxylic acid) (500 mg, 2.3 mmol) was dissolved in dried ethanol (20 mL), and thionyl chloride (1 mL) was added under an ice bath. The mixture was refluxed for 15 h and then the pH was adjusted to 8. After extraction with ethyl acetate and purification by column chromatography (PE: EA = 1: 1), the target product **2** (1, 2, 3, 4-tetrahydro-β-carboline-3-carboxylic acid methyl ester) was obtained. The yield was about 63.7% (339 mg).

The target product **2** (1, 2, 3, 4-tetrahydro-β-carboline-3-carboxylic acid methyl ester) (3 g, 13 mmol) was dissolved in xylene with Pd/C (5%) as a catalyst. And the mixture was refluxed for 48 h, then filtered and distilled under negative-pressure. After separation and purification by column chromatography (DCM: EA = 5: 1), the target product **3** (β-carboline-3-carboxylic acid methyl ester) was obtain. The yield was about 81.8% (2.45 g).

The target product **3** (β-carboline-3-carboxylic acid methyl ester) (300 mg, 1.33 mmol) was dissolved in DMF with NaH as reducer. Then, benzyl bromide was added and the mixture was reacted at room temperature for 6 h. After completion of the reaction as indicated by TLC, the reaction was quenched with ice water, and then extracted with ethyl acetate, washed well with saturated NaCl and then dried with anhydrous Na_2SO_4. After separation and purification by column chromatography (DCM: EA = 2: 1), the target product **4A** (9-benzyl-β-carboline-3-carboxylic acid methyl ester) was obtained. The yield was about 80.4% (313.6 mg).

According to the above method, the target product **3** was reacted with *o*-methylbenzyl chloride, *p*-methylbenzyl chloride and *o*-fluorobenzyl chloride, respectively, to obtain monomers 9-*o*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester (**4B**), 9-*p*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester (**4C**), and 9-*o*-fluorobenzyl-β-carboline-3-carboxylic acid methyl ester (**4D**).

S.2. General reaction of synthesis of β-carboline dimers (**6a-6f**, **6g-6l**, **6m-6r**, and **6s-6x**)

Taking the synthesis of the dimer **6a** as an example: **4A** (9-benzyl-β-carboline-3-carboxylic acid methyl ester) (300 mg, 0.95 mmol) was dissolved in THF/CH_3OH. And then the NaOH solution (0.1 mol/L, 38 mL) was added to give a white precipitate. The mixture was reacted at room temperature until the solution became clear (about 24 h). The reaction solution was extracted with ethyl acetate and dichloromethane. The pH of resulting aqueous phase was adjusted to 5 to give the target product **5** (9-benzyl-β-carboline-3-carboxylic acid).

The target product **5** (60 mg, 0.2 mmol) was dissolved in DMF. And K_2CO_3 (41 mg, 0.3 mmol) and 1, 3-dibromopropane (10 μL, 0.1 mmol) were sequentially added, and the mixture was reacted for about 14 h. The miixture was quenched with ice water, and then extracted with dichloromethane, washed with saturated NaCl and dried with anhydrous Na_2SO_4. After separation and purification by column chromatography (DCM: EA = 5: 1), the target product **6a** (propane-1,3-diyl-bis-(9-benzyl-9H-pyrido [3,4-b]indole-3-carboxylate)) was obtained.

Following the same method, 9-benzyl-β-carboline-3-carboxylic acid methyl ester was reacted with dibromobutane, dibromopentane, dibromohexane, dibromooctane, and dibromoxylene, respectively, to give β-carboline-3-carboxylic acid dimers (**6b-6f**).

Following the same method, 9-*o*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester was reacted with dibromopropane, dibromobutane, dibromopentane,

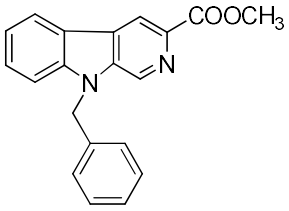
dibromohexane, dibromooctane, and dibromoxylene, respectively, to give different β-carboline-3-carboxylic acid dimers (**6g-6l**).

Following the same method, 9-*p*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester was reacted with dibromopropane, dibromobutane, dibromopentane, dibromohexane, dibromooctane, and dibromoxylene, respectively, to give different β-carboline-3-carboxylic acid dimers (**6m-6r**).

Following the same method, 9-*o*-fluorobenzyl-β-carboline-3-carboxylic acid methyl ester was reacted with dibromopropane, dibromobutane, dibromopentane, dibromohexane, dibromooctane, and dibromoxylene, respectively, to give different β-carboline-3-carboxylic acid dimers (**6s-6x**).

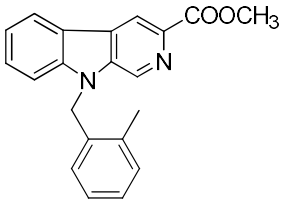
S.3. The data of yield, melting point, nuclear magnetic and mass spectral

4A (9-benzyl-β-carboline-3-carboxylic acid methyl ester):



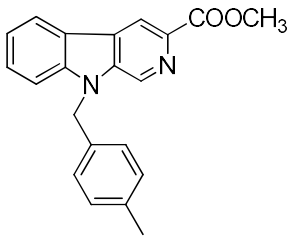
White crystal, yield: 80.4%, m.p.: 186-187 ℃. ESI-MS, m / z: 317.20 $[M+H]^+$. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.95–8.89 (m, 2H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 6.0 Hz, 3H), 7.15 (d, *J* = 7.4 Hz, 2H), 5.62 (s, 2H), 4.06 (s, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 166.47, 141.84, 138.00, 137.55, 135.71, 131.81, 129.22, 129.06, 128.86, 128.12, 126.54, 122.20, 121.51, 121.08, 117.80, 110.25, 52.72, 47.30.

4B (9-*o*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester):



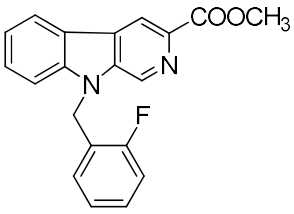
White crystal, yield: 64.7%, m.p.: 147-148 ℃. ESI-MS, m / z: 331.32 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.94 (s, 1H), 8.78 (s, 1H), 8.26 (d, J = 7.8 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.44–7.35 (m, 2H), 7.27–7.22 (m, 1H), 7.19 (t, J = 7.4 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.57 (d, J = 7.7 Hz, 1H), 5.58 (s, 2H), 4.06 (s, 3H), 2.42 (s, 3H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.48, 141.98, 138.16, 137.53, 135.28, 133.32, 131.86, 130.80, 129.23, 128.87, 127.99, 126.59, 125.90, 122.20, 121.48, 121.11, 117.81, 110.32, 52.73, 45.55, 19.37.

4C (9-*p*-methylbenzyl-β-carboline-3-carboxylic acid methyl ester):



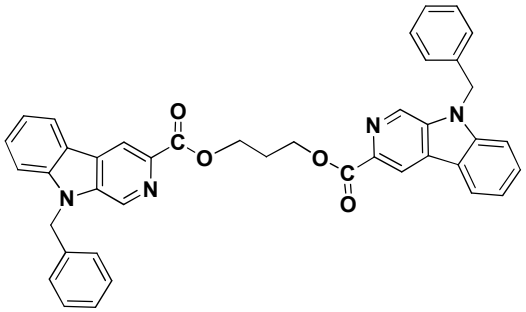
White crystal, yield: 58.9%, m.p.: 157-158 ℃. ESI-MS, m / z: 331.29 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.93 (d, J = 2.2 Hz, 2H), 8.24 (d, J = 7.9 Hz, 1H), 7.66–7.59 (m, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.42–7.35 (m, 1H), 7.26 (s, 1H), 7.07 (q, J = 8.2 Hz, 4H), 5.59 (s, 2H), 4.06 (s, 3H), 2.29 (s, 3H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.35, 141.93, 137.97, 137.23, 132.62, 131.74, 129.72, 129.27, 128.95, 126.57, 122.21, 121.49, 121.08, 117.83, 110.33, 52.75, 47.17, 21.06.

4D (9-*o*-fluorobenzyl-β-carboline-3-carboxylic acid methyl ester):



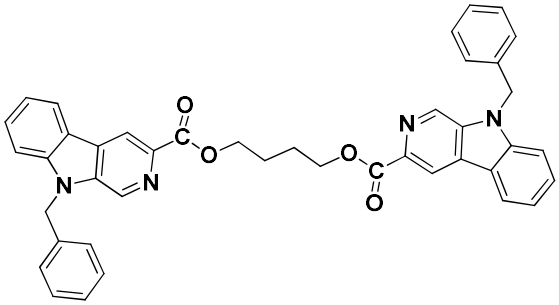
White crystal, yield: 68.3%, m.p.: 175 - 177 ℃. ESI-MS, m / z: 335.30 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 9.00 (s, 1H), 8.93 (s, 1H), 8.24 (d, J = 7.9 Hz, 1H), 7.67 - 7.62 (m, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.15 - 7.08 (m, 1H), 7.00 - 6.94 (m, 1H), 6.91 - 6.85 (m, 1H), 5.68 (s, 2H), 4.07 (s, 3H).

6a propane-1,3-diyl-bis-(9-benzyl-9H-pyrido[3,4-b]indole-3-carboxylate)



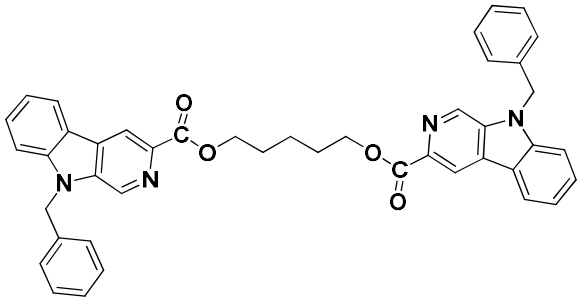
White flake, yield: 57.2%, m.p.: 182-183 ℃. ESI-MS, m / z: 645.38 $[M+H]^{+1}$. H-NMR (500 MHz, CDCl3) δ 8.82 (dd, J = 11.7, 0.7 Hz, 2H), 8.17 (d, J = 7.8 Hz, 1H), 7.61 (ddd, J = 8.2, 7.3, 1.1 Hz, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.26 (d, J = 6.4 Hz, 3H), 7.10 (dd, J = 7.0, 2.4 Hz, 2H), 5.46 (s, 2H), 4.72 (t, J = 6.2 Hz, 2H), 2.50–2.44 (m, 1H). ^{13}C-NMR (126 MHz, CDCl3) δ 165.97, 141.69, 137.87, 137.80, 135.75, 132.04, 129.05, 129.00, 128.52, 128.09, 126.52, 122.22, 121.52, 120.91, 117.76, 110.09, 62.81, 47.11, 28.51.

6b butane-1,4-diyl-bis-(9-benzyl-9H-pyrido[3,4-*b*]indole-3-carboxylate)



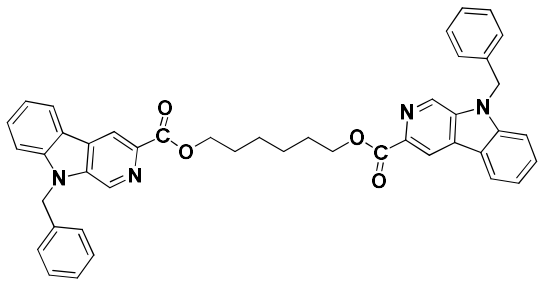
White flake, yield: 56.7%, m.p.: 210-212 ℃. ESI-MS, m / z: 659.40 $[M+H]^{+}$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.89 (d, J = 3.6 Hz, 2H), 8.22 (d, J = 7.8 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.24 (s, 3H), 7.15 – 7.10 (m, 2H), 5.60 (s, 2H), 4.56 (s, 2H), 2.08 (s, 2H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.10, 143.16, 141.86, 138.03, 135.84, 134.33, 132.12, 129.06, 128.74, 128.10, 126.58, 122.23, 121.67, 120.96, 117.71, 110.16, 65.10, 47.32, 25.71.

6c pentane-1,5-diyl-bis-(9-benzyl-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 77.5%, m.p.: 183-184 ℃. ESI-MS, m / z: 673.45 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.92–8.86 (m, 2H), 8.21 (d, J = 7.9 Hz, 1H), 7.63–7.56 (m, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.38–7.32 (m, 1H), 7.26–7.25 (m, 3H), 7.13 (dd, J = 7.2, 2.1 Hz, 2H), 5.58 (s, 2H), 4.51 (t, J = 6.8 Hz, 2H), 2.03–1.95 (m, 2H), 1.70 (dt, J = 15.5, 7.7 Hz, 1H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.15, 141.84, 138.19, 138.01, 135.85, 132.11, 129.08, 129.03, 128.75, 128.12, 126.60, 122.23, 121.66, 120.95, 117.68, 110.15, 65.38, 47.31, 28.65, 22.67.

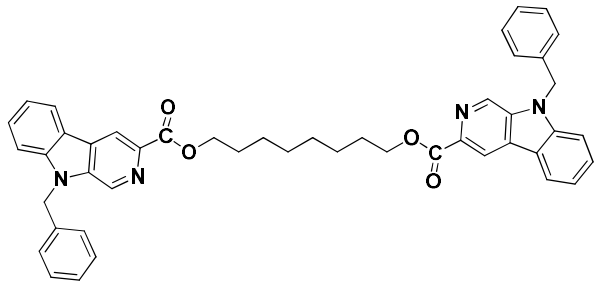
6d hexane-1,6-diyl-bis-(9-benzyl-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White powder, yield: 71%, m.p.: 184-185 ℃. ESI-MS, m / z: 687.41 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.89 (d, J = 10.8 Hz, 2H), 8.23 (d, J = 7.8 Hz, 1H), 7.63–7.58 (m, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.29–7.24 (m, 3H), 7.17–7.11 (m, 2H), 5.60 (s, 2H), 4.48 (t, J = 6.8 Hz, 2H), 1.97–1.87 (m, 2H), 1.60 (dd, J = 8.7, 5.4 Hz, 2H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.20, 141.82, 138.18,

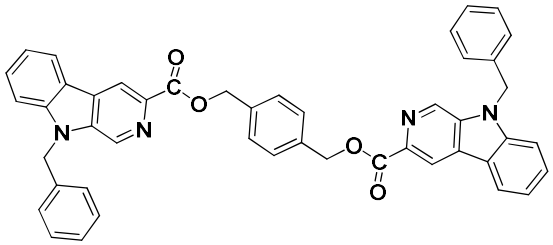
137.99, 135.85, 132.10, 129.07, 129.04, 128.73, 128.11, 126.59, 122.23, 121.63, 120.95, 117.68, 110.16, 65.58, 47.29, 28.85, 25.87.

6e octane-1,8-diyl-bis-(9-benzyl-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White powder, yield: 57.1%, m.p.: 198-199 ℃. ESI-MS, m / z: 715.49 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.90 (d, J = 14.0 Hz, 2H), 8.23 (d, J = 7.8 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.29–7.21 (m, 3H), 7.17–7.11 (m, 2H), 5.61 (s, 2H), 4.46 (t, J = 6.9 Hz, 2H), 1.93 – 1.83 (m, 2H), 1.46 (dd, J = 26.7, 6.3 Hz, 4H). ^{13}C-NMR (126 MHz, CDCl3) δ 166.20, 141.83, 138.21, 137.98, 135.85, 133.96, 132.09, 129.06, 128.73, 128.10, 126.59, 122.19, 121.63, 120.95, 117.66, 110.17, 65.72, 47.29, 29.24, 28.87, 25.96.

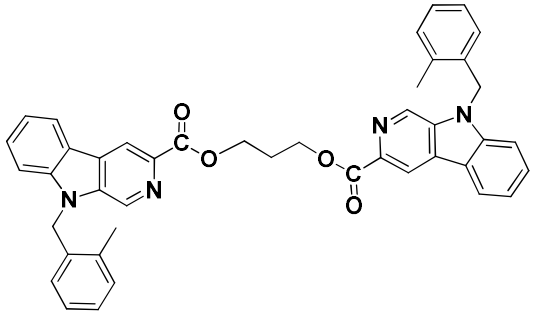
6f 1,4-phenylene-bis-(methylene)-bis-(9-benzyl-9H-pyrido [3,4-*b*]indole-3-carboxylate)



White flake, yield: 53.1%, m.p.: 292-294 ℃. ESI-MS, m / z: 707.22 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.91 (d, J = 8.9 Hz, 2H), 8.23 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.7 Hz, 1H), 7.57 (s, 2H), 7.49 (d, J = 8.3 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.26 (s, 3H), 7.17–7.11 (m, 2H), 5.63 (s, 2H), 5.51 (s, 2H). ^{13}C-NMR (126 MHz, CDCl3) δ

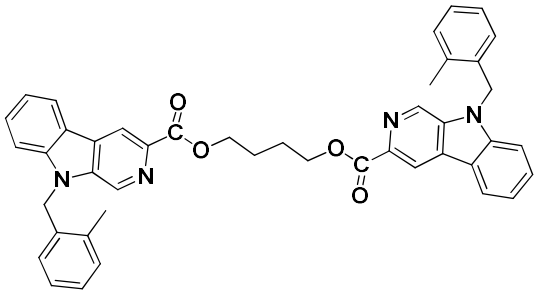
165.90, 141.82, 138.06, 137.78, 136.28, 135.79, 132.18, 129.07, 128.86, 128.71, 128.11, 126.56, 122.24, 121.61, 121.01, 117.96, 110.20, 66.90, 47.31, 29.71.

6g propane-1,3-diyl-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 57.7%, m.p.: 157-158 ℃. ESI-MS, m / z: 673.43 $[M+H]^+$. ^{1}H-NMR (500 MHz, CDCl3) δ 8.77 (s, 1H), 8.65 (s, 1H), 8.18 (d, J = 7.9 Hz, 1H), 7.59 (t, J = 7.7 Hz, 1H), 7.36 (dd, J = 18.8, 8.0 Hz, 2H), 7.26 (s, 1H), 7.21 (d, J = 7.5 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 6.48 (d, J = 7.7 Hz, 1H), 5.32 (s, 2H), 4.72 (t, J = 5.9 Hz, 2H), 2.51–2.42 (m, 1H), 2.37 (s, 3H). ^{13}C-NMR (126 MHz, CDCl3) δ 165.96, 141.77, 137.93, 137.82, 135.18, 133.36, 132.08, 130.75, 128.97, 128.41, 127.93, 126.59, 125.84, 122.26, 121.48, 120.92, 117.71, 110.12, 62.95, 45.22, 28.50, 19.36.

6h butane-1,4-diyl-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 44.2%, m.p.: 211-213 ℃. ESI-MS m / z: 687.40 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (d, *J* = 0.7 Hz, 1H), 8.82 (d, *J* = 0.5 Hz, 1H), 8.30 (d,

190 J = 7.8 Hz, 1H), 7.67–7.60 (m, 1H), 7.46–7.39 (m, 2H), 7.31 (s, 1H), 7.27 (d, J = 7.4

191 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.7 Hz, 1H),

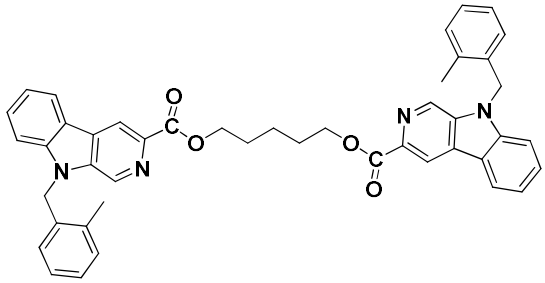
192 5.61 (s, 2H), 4.62 (s, 2H), 2.45 (s, 3H), 2.14 (t, J = 2.7 Hz, 2H). ^{13}C NMR (126 MHz,

193 $CDCl_3$) δ 166.12, 141.94, 138.15, 137.99, 135.28, 133.43, 132.18, 130.78, 129.05,

194 128.70, 127.96, 126.61, 125.99, 122.24, 121.58, 120.99, 117.76, 110.24, 65.12, 45.51,

195 25.69, 19.37.

196 **6i** pentane-1,5-diyl-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



197

198 White flake, yield: 37.9%, m.p.: 145-146 ℃. ESI-MS m / z: 701.57 $[M+H]^+$. ^{1}H

199 NMR (500 MHz, $CDCl_3$) δ 8.93 (d, J = 0.6 Hz, 1H), 8.80 (d, J = 0.4 Hz, 1H), 8.27 (d,

200 J = 7.8 Hz, 1H), 7.66–7.59 (m, 1H), 7.41 (dd, J = 15.6, 7.8 Hz, 2H), 7.31 (s, 1H), 7.27

201 (d, J = 7.4 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H), 6.61 (d, J = 7.7

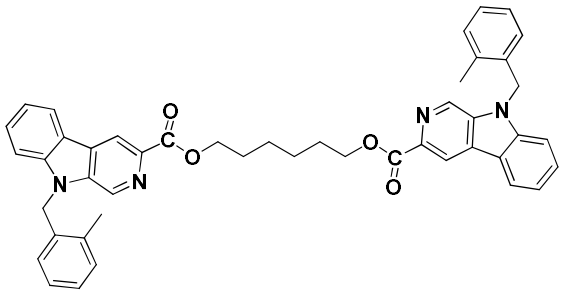
202 Hz, 1H), 5.57 (s, 2H), 4.56 (t, J = 6.8 Hz, 2H), 2.45 (s, 3H), 2.08–1.99 (m, 2H),

203 1.78–1.72 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.15, 141.91, 138.10, 138.07,

204 135.27, 133.43, 132.16, 130.78, 129.01, 128.67, 127.96, 126.60, 125.99, 122.21,

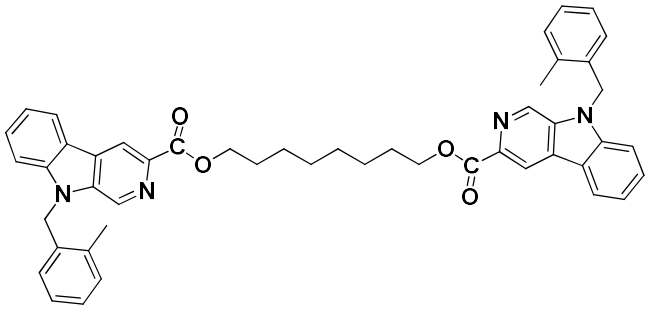
205 121.56, 120.95, 117.68, 110.19, 65.36, 45.47, 28.61, 22.61, 19.36.

206 **6j** hexane-1,6-diyl-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White powder, yield: 32.6%, m.p.: 189-190 ℃. ESI-MS m / z: 715.55 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J* = 0.8 Hz, 1H), 8.77 (d, *J* = 0.7 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.59 (ddd, *J* = 8.2, 7.2, 1.1 Hz, 1H), 7.42–7.34 (m, 2H), 7.26 (s, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 1H), 5.57 (s, 2H), 4.48 (t, *J* = 6.8 Hz, 2H), 2.41 (s, 3H), 1.96–1.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.20, 141.94, 138.13, 135.29, 133.45, 132.16, 130.78, 129.04, 128.71, 127.96, 126.60, 126.00, 122.22, 121.59, 120.97, 117.68, 110.22, 65.58, 45.50, 28.84, 25.86, 19.37.

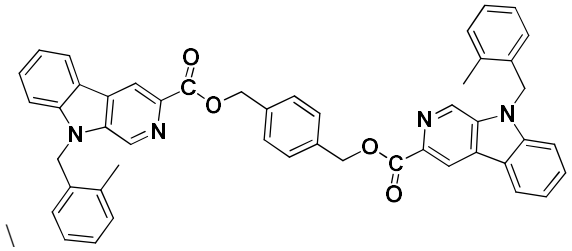
6k octane-1,8-diyl-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White powder, yield: 25.2%, m.p.: 223-225 ℃. ESI-MS m / z: 743.62 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.78 (s, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.42–7.35 (m, 2H), 7.26 (s, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 1H), 5.58 (s, 2H), 4.46 (t, *J* = 6.9 Hz, 2H), 2.41 (s, 3H), 1.92–1.83 (m, 2H), 1.47 (dd, *J* = 32.5, 6.2 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.22, 141.95, 138.18, 138.13, 135.29, 133.46,

132.16, 130.78, 129.04, 128.72, 127.96, 126.60, 126.00, 122.19, 121.58, 120.97, 117.67, 110.23, 65.72, 45.52, 29.24, 28.87, 25.96, 19.37.

6l 1,4-phenylene-bis-(methylene)-bis-(9-(2-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



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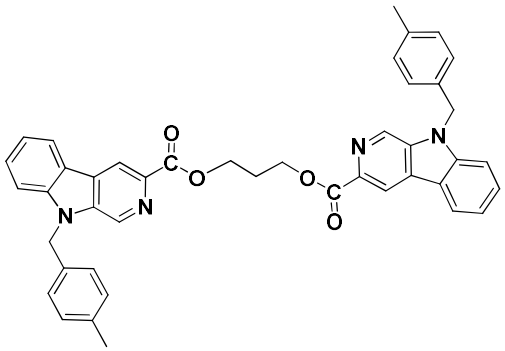
White flake, yield: 59.2%, m.p.: 280-281 ℃. ESI-MS m / z: 735.29 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.84 (s, 1H), 8.29 (d, *J* = 7.9 Hz, 1H), 7.61 (s, 2H), 7.42 (dd, *J* = 16.1, 8.0 Hz, 2H), 7.31 (s, 3H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 5.64 (s, 2H), 5.56 (s, 2H), 2.46 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 165.91, 141.95, 138.21, 137.77, 136.29, 135.29, 133.41, 132.26, 130.79, 129.08, 128.86, 128.70, 127.98, 126.61, 125.98, 122.23, 121.57, 121.02, 117.96, 110.26, 66.89, 45.54, 19.37.

6m propane-1,3-diyl-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 62%, m.p.: 188-189 ℃. ESI-MS m / z: 673.45 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.85 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.66 (t,

240 *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.31 (s, 1H), 7.10

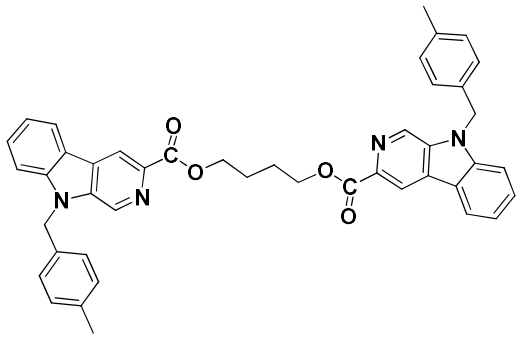
241 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 5.46 (s, 2H), 4.77 (t, *J* = 6.2 Hz, 2H),

242 2.55–2.49 (m, 1H), 2.31 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 165.51, 141.86,

243 137.94, 137.73, 136.95, 132.55, 131.69, 129.69, 129.23, 128.78, 126.54, 122.27,

244 121.38, 121.02, 117.83, 110.23, 62.94, 46.99, 28.42, 21.05.

245 **6n** butane-1,4-diyl-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



246

247 White flake, yield: 47%, m.p.: 223-225 ℃. ESI-MS m / z: 687.46 $[M+H]^+$. ^{1}H

248 NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J* = 8.3 Hz, 2H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.60 (t,

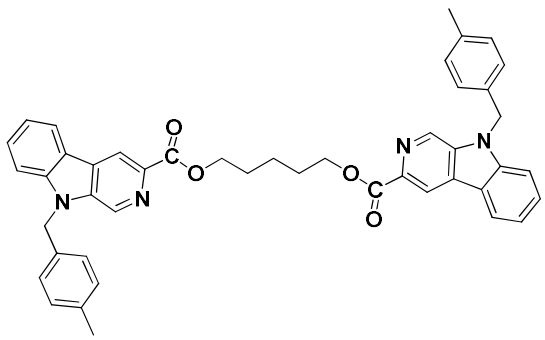
249 *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.37 (s, 1H), 7.26 (s, 1H), 7.06 (q, *J* = 8.2

250 Hz, 4H), 5.57 (s, 2H), 4.57 (s, 2H), 2.28 (s, 3H), 2.10 (s, 2H). ^{13}C NMR (126 MHz,

251 $CDCl_3$) δ 166.14, 141.80, 137.99, 137.89, 137.83, 132.77, 132.15, 129.70, 129.01,

252 128.66, 126.59, 122.21, 121.58, 120.89, 117.77, 110.22, 65.12, 47.10, 25.67, 21.05.

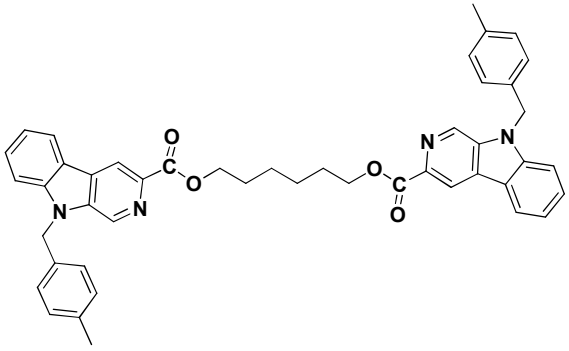
253 **6o** pentane-1,5-diyl-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



254

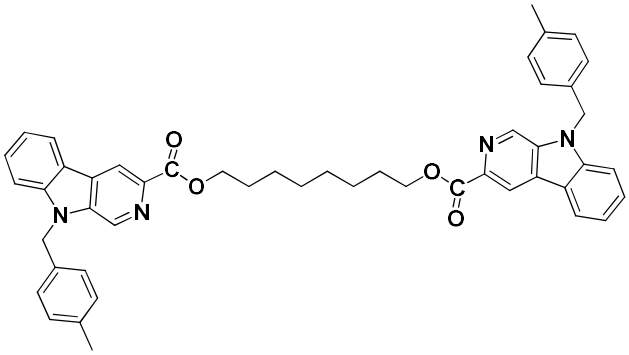
White flake, yield: 50%, m.p.: 109-111 ℃. ESI-MS m / z: 701.67 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, *J* = 10.5 Hz, 2H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.31 (s, 1H), 7.09 (q, *J* = 8.1 Hz, 4H), 5.57 (s, 2H), 4.55 (t, *J* = 6.8 Hz, 2H), 2.32 (s, 3H), 2.18–1.95 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.17, 141.77, 137.95, 137.90, 132.76, 132.13, 129.69, 128.98, 128.65, 126.58, 122.18, 121.55, 120.87, 117.70, 110.18, 109.32, 65.36, 47.07, 28.60, 22.62, 21.05.

6p hexane-1,6-diyl-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



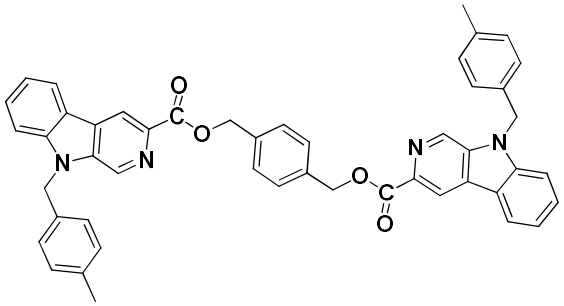
White flake, yield: 69%, m.p.: 115-117 ℃. ESI-MS m / z: 715.59 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J* = 15.9 Hz, 2H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.57 (m, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.38 (s, 1H), 7.26 (s, 1H), 7.06 (q, *J* = 8.3 Hz, 4H), 5.56 (s, 2H), 4.48 (t, *J* = 6.8 Hz, 2H), 2.28 (s, 3H), 1.98–1.88 (m, 2H), 1.62–1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.21, 141.80, 137.97, 137.89, 132.78, 132.13, 129.69, 129.00, 128.67, 126.60, 122.19, 121.59, 120.87, 117.69, 110.20, 65.58, 47.10, 29.71, 28.83, 25.85, 21.05.

6q octane-1,8-diyl-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 47.6%, m.p.: 178-180 ℃. ESI-MS m / z: 743.55 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J* = 17.5 Hz, 2H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.26 (s, 1H), 7.06 (q, *J* = 8.1 Hz, 4H), 5.57 (s, 2H), 4.46 (t, *J* = 6.9 Hz, 2H), 2.28 (s, 3H), 1.93–1.83 (m, 2H), 1.46 (d, *J* = 33.2 Hz, 4H).^{13}C NMR (126 MHz, $CDCl_3$) δ 166.23, 141.81, 138.04, 137.97, 137.90, 132.80, 132.14, 129.69, 129.00, 128.68, 126.60, 122.16, 121.59, 120.87, 117.67, 110.21, 65.72, 47.10, 29.25, 28.86, 25.96, 21.05.

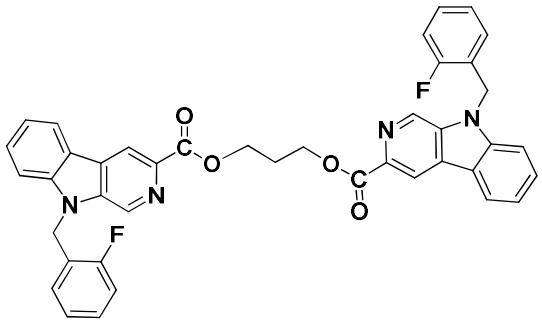
6r 1,4-phenylene-bis-(methylene)-bis-(9-(4-methylbenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 34.4%, m.p.: 266-268 ℃. ESI-MS m / z: 735.32 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.91 (s, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.58 (s, 2H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.26 (s, 2H), 7.06 (dd, *J* = 16.8, 7.8 Hz, 4H), 5.60 (s, 2H), 5.53 (s, 2H), 2.28 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 165.19, 142.11, 138.01, 137.86, 136.61, 136.14, 132.50,

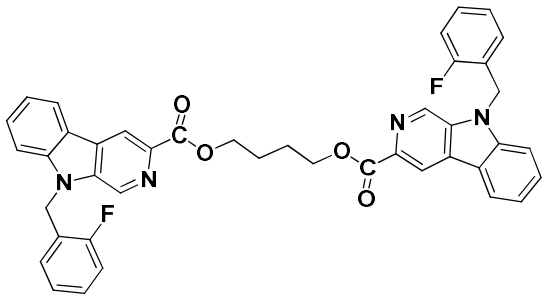
131.64, 129.74, 129.48, 129.15, 128.96, 126.57, 122.35, 121.42, 121.21, 118.05, 110.39, 67.08, 47.26, 21.06.

6s propane-1,3-diyl-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White flake, yield: 65.4%, m.p.: 208-210 ℃. ESI-MS m / z: 681.49 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.77 (s, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.28–7.20 (m, 2H), 7.10 (t, *J* = 9.3 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 5.45 (s, 2H), 4.72 (t, J = 5.8 Hz, 2H), 2.50–2.43 (m, 1H), 1.68 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 165.93, 159.41, 141.50, 137.92, 137.75, 131.94, 129.97, 129.91, 129.09, 128.56, 128.42, 128.39, 124.67, 124.64, 122.86, 122.75, 122.21, 121.49, 121.03, 117.73, 115.87, 115.70, 109.99, 62.95, 40.82, 29.72, 28.51.

6t butane-1,4-diyl-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



Needle crystal, yield: 50%, m.p.: 213-215 ℃. ESI-MS m / z: 695.69 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.90 (s, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.63 (t,

304 J = 7.7 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.29–7.21 (m, 2H),

305 7.15–7.07 (m, 1H), 6.95 (t, J = 7.5 Hz, 1H), 6.86 (t, J = 7.1 Hz, 1H), 5.66 (s, 2H),

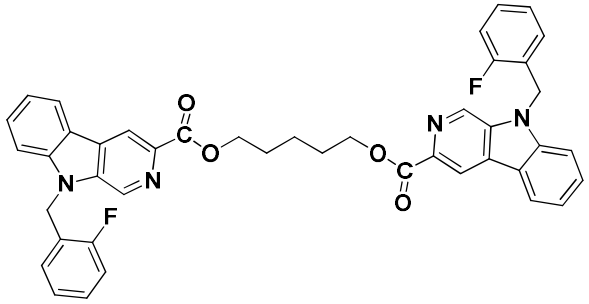
306 4.58 (s, 2H), 2.11 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.08, 161.41, 159.45,

307 141.65, 138.10, 137.91, 132.00, 129.97, 129.91, 129.13, 128.80, 128.47, 128.44,

308 124.67, 124.64, 122.80, 122.24, 121.61, 121.09, 117.75, 115.88, 115.72, 110.09,

309 65.15, 40.99, 29.71, 25.67.

310 **6u** pentane-1,5-diyl-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



311

312 White flake, yield: 67.8%, m.p.: 187-188 ℃. ESI-MS m / z: 709.39 $[M+H]^+$. ^{1}H

313 NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.87 (s, 1H), 8.19 (d, J = 7.8 Hz, 1H), 7.61 (t,

314 J = 7.7 Hz, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.28–7.20 (m, 2H),

315 7.15–7.06 (m, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.84 (t, J = 7.1 Hz, 1H), 5.61 (s, 2H),

316 4.52 (t, J = 6.8 Hz, 2H), 2.07–1.94 (m, 2H), 1.71 (dd, J = 9.3, 6.2 Hz, 1H). ^{13}C NMR

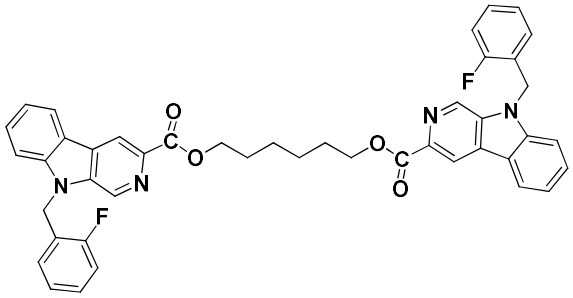
317 (126 MHz, $CDCl_3$) δ 166.11, 161.40, 159.44, 141.61, 138.19, 137.86, 131.99, 129.97,

318 129.91, 129.09, 128.76, 128.47, 128.44, 124.66, 124.63, 122.90, 122.79, 122.19,

319 121.57, 121.05, 117.67, 115.88, 115.71, 110.04, 65.38, 40.98, 40.94, 29.71, 28.59,

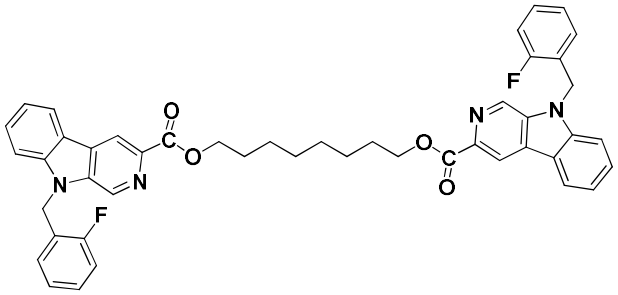
320 22.61.

321 **6v** hexane-1,6-diyl-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White solid, yield: 54.6%, m.p.: 199-201 ℃. ESI-MS m / z: 723.48 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.88 (s, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.29–7.20 (m, 2H), 7.16–7.07 (m, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 5.65 (s, 2H), 4.49 (t, *J* = 6.8 Hz, 2H), 2.05–1.89 (m, 2H), 1.61 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.16, 161.42, 159.45, 141.65, 138.26, 137.88, 131.98, 129.98, 129.91, 129.12, 128.80, 128.49, 128.46, 124.66, 124.64, 122.92, 122.22, 121.61, 121.07, 117.67, 115.88, 115.72, 110.07, 65.61, 41.02, 40.98, 29.71, 28.83, 25.85.

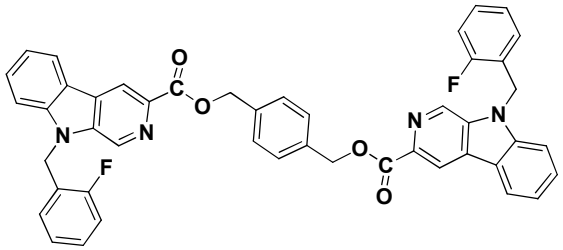
6w octane-1,8-diyl-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)



White solid, yield: 65%, m.p.: 148-150 ℃. ESI-MS m / z: 751.48 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.89 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.25 (dd, *J* = 12.7, 4.3 Hz, 2H), 7.11 (t, *J* = 9.2 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 5.66 (s, 2H), 4.46 (t, *J* = 6.7 Hz, 2H), 1.93–1.83 (m, 2H), 1.50 (s, 2H), 1.43 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.18, 159.46, 141.66, 138.31, 137.89, 131.99, 129.98, 129.92, 129.12, 128.82, 128.47, 124.66, 124.63, 122.93, 122.82, 122.19, 121.62, 121.07, 117.66, 115.89, 115.72, 110.09, 65.75, 41.03, 40.99, 29.71, 29.24, 28.86, 25.95.

6x 1,4-phenylenebis(methylene)-bis-(9-(2-fluorobenzyl)-9H-pyrido[3,4-*b*]indole-3-carboxylate)

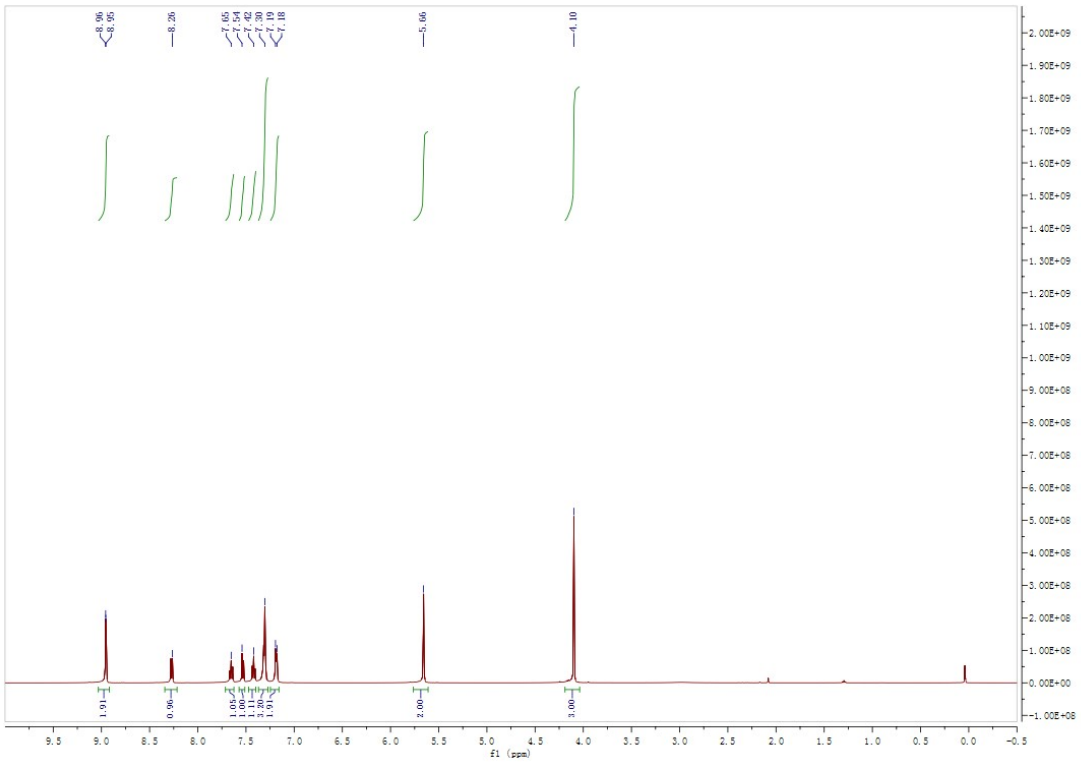


White flake solid, yield: 61.2%, m.p.: 277-279 ℃. ESI-MS m / z: 743.56$[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.91 (s, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.69–7.62 (m, 1H), 7.61–7.54 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.33 (s, 1H), 7.26 (dd, *J* = 13.9, 6.9 Hz, 1H), 7.17–7.09 (m, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.87 (t, *J* = 7.5 Hz, 1H), 5.70 (s, 2H), 5.52 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.71, 141.73, 137.98, 136.13, 131.86, 129.97, 129.91, 129.30, 128.81, 128.38, 124.61, 122.19, 121.42, 121.19, 117.97, 115.83, 115.66, 110.20, 66.91, 49.46, 49.29, 49.12, 48.95, 48.78, 41.08, 29.64.

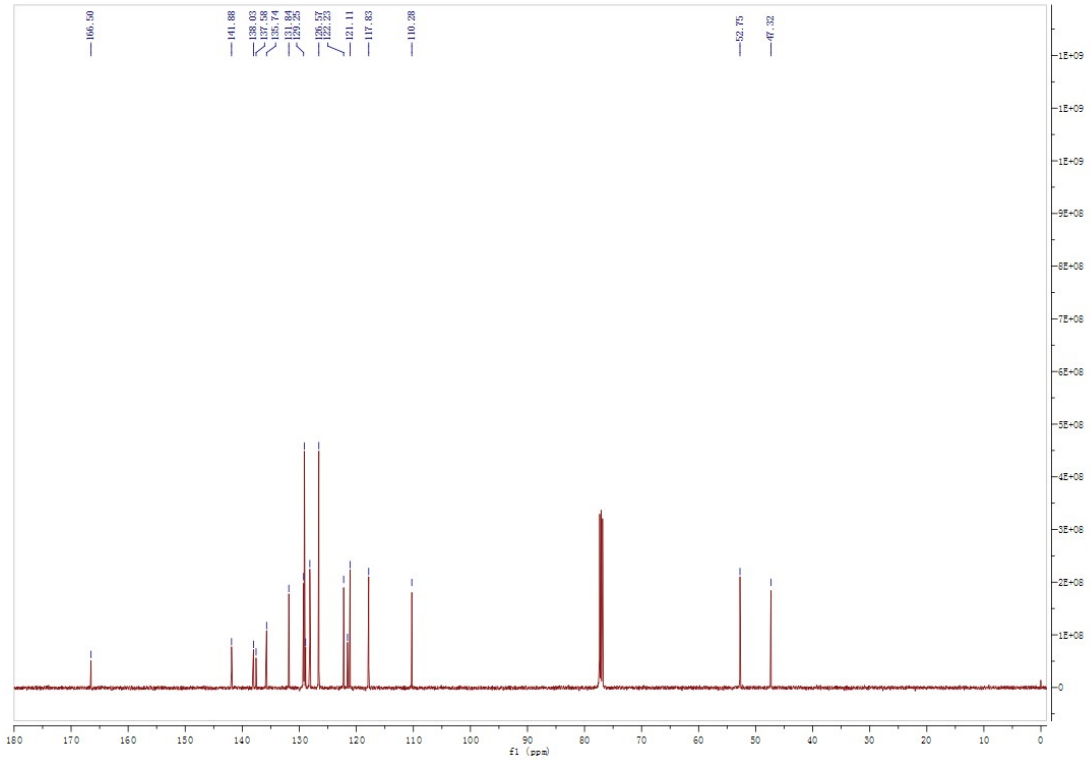
S.4. HNMR and CNMR

4A

H NMR

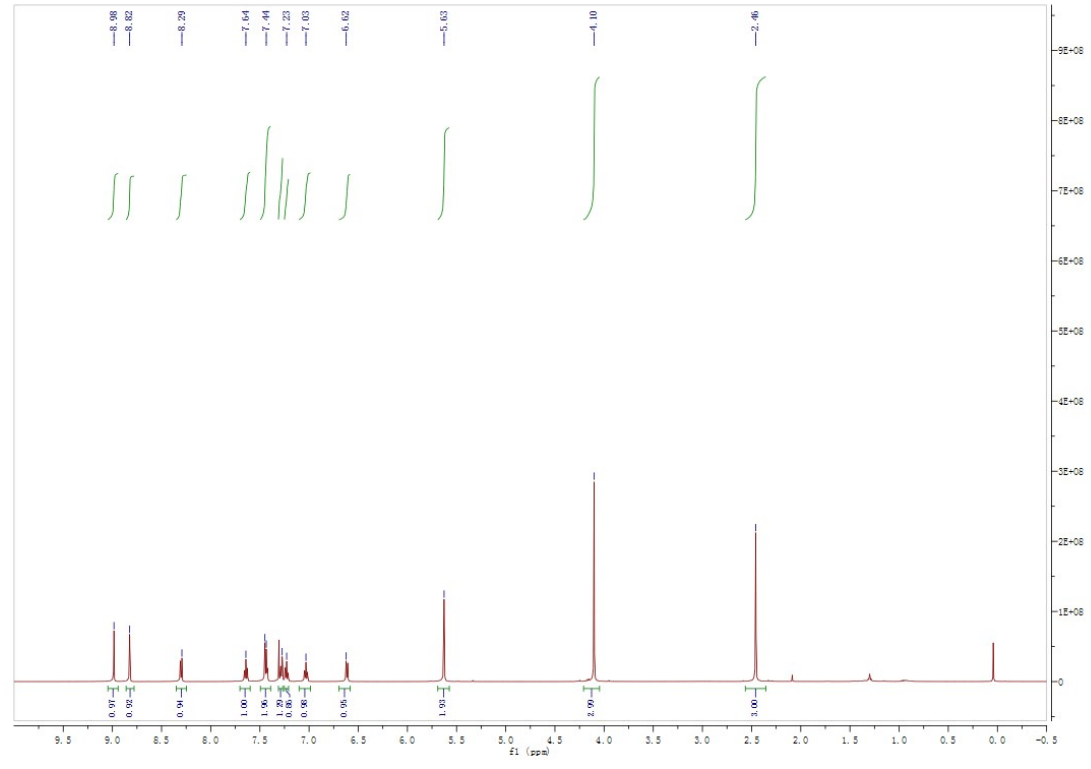


C NMR

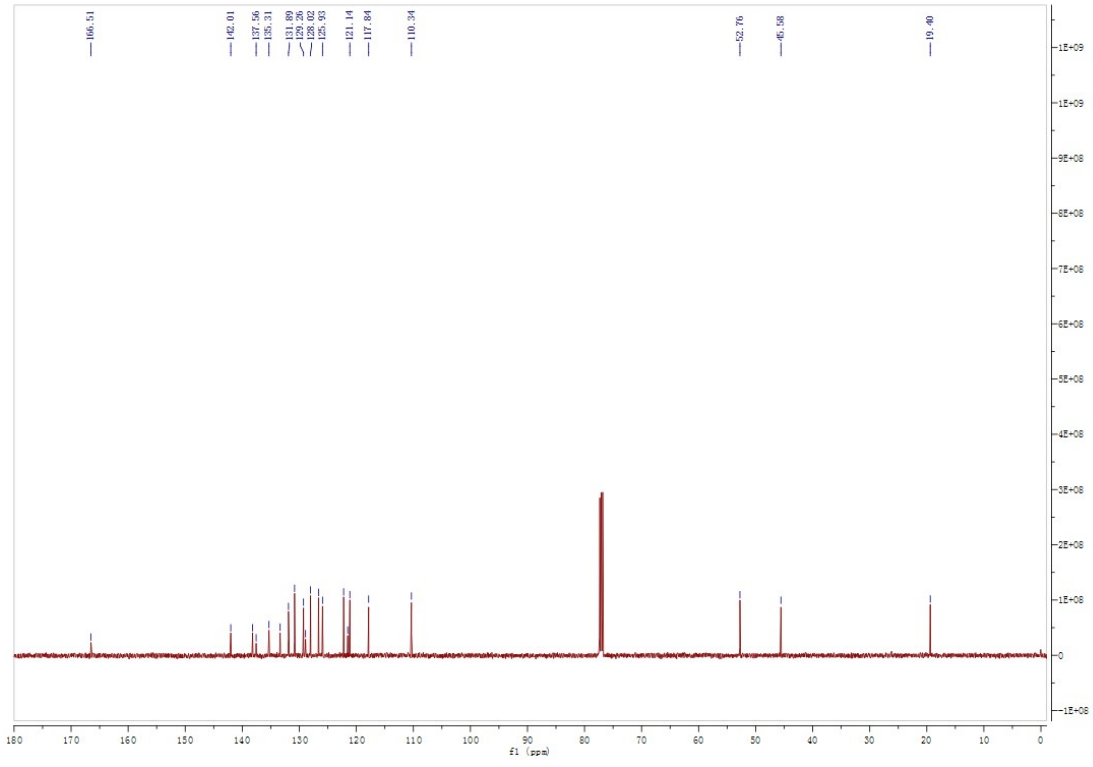

166.50
141.88
138.03
137.98
135.74
131.84
129.36
125.57
122.25
121.11
117.83
110.28
52.75
47.32
f1 (ppm)

4B

H NMR

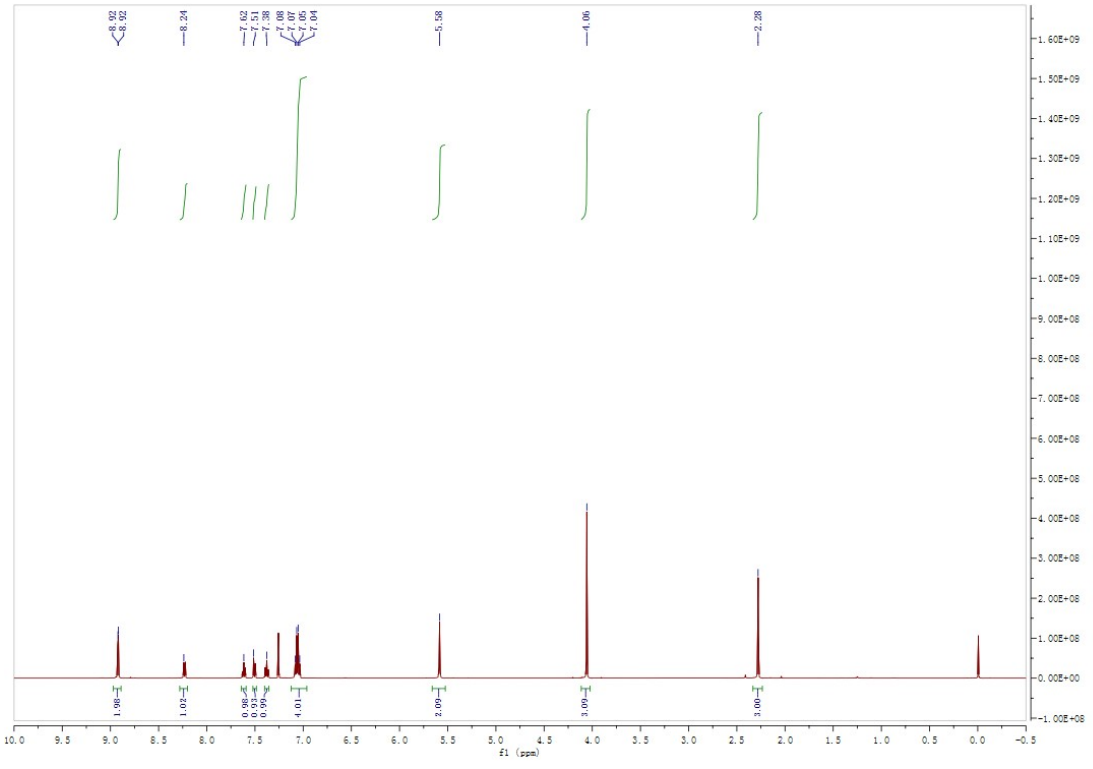

8.98
8.82
8.29
7.64
7.44
7.23
7.03
6.62
5.63
4.10
2.46
f1 (ppm)

C NMR

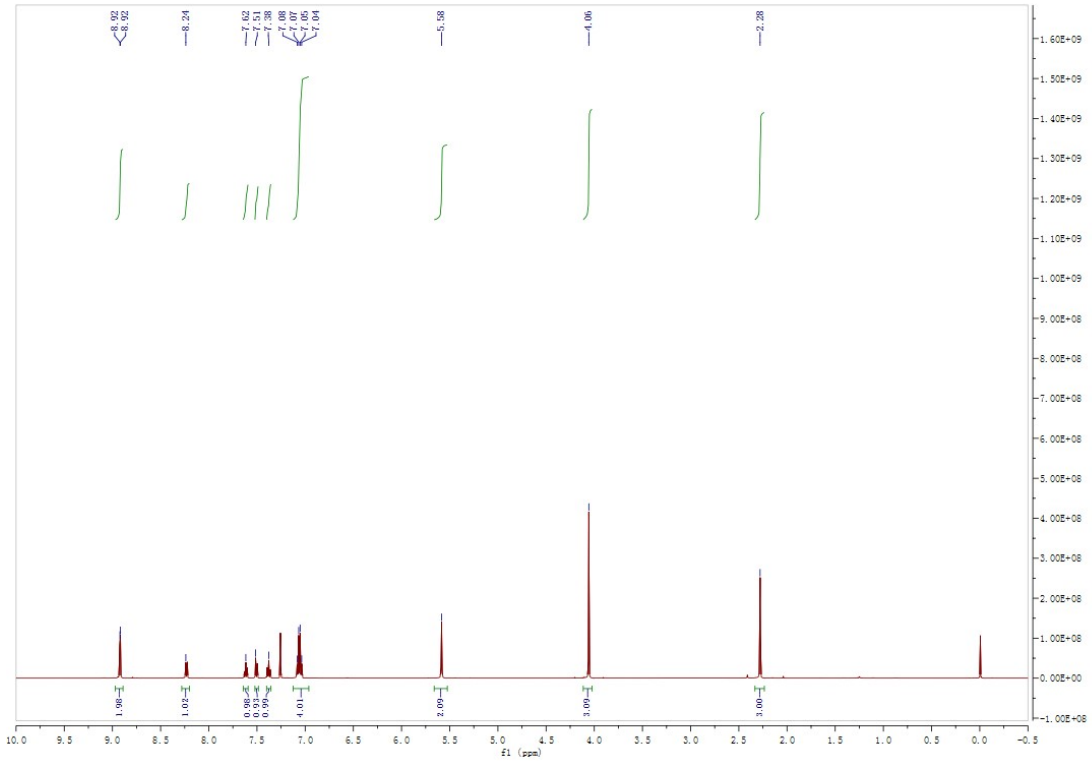

166.51
142.01
137.56
135.31
131.89
129.95
128.02
125.93
121.14
117.84
110.34
52.76
45.58
19.40
f1 (ppm)

4C

H NMR


8.92
8.92
8.24
7.62
7.51
7.38
7.08
7.07
7.05
7.04
5.58
4.06
2.28
1.98
1.03
0.98
0.93
0.99
4.01
2.09
3.09
3.00
f1 (ppm)

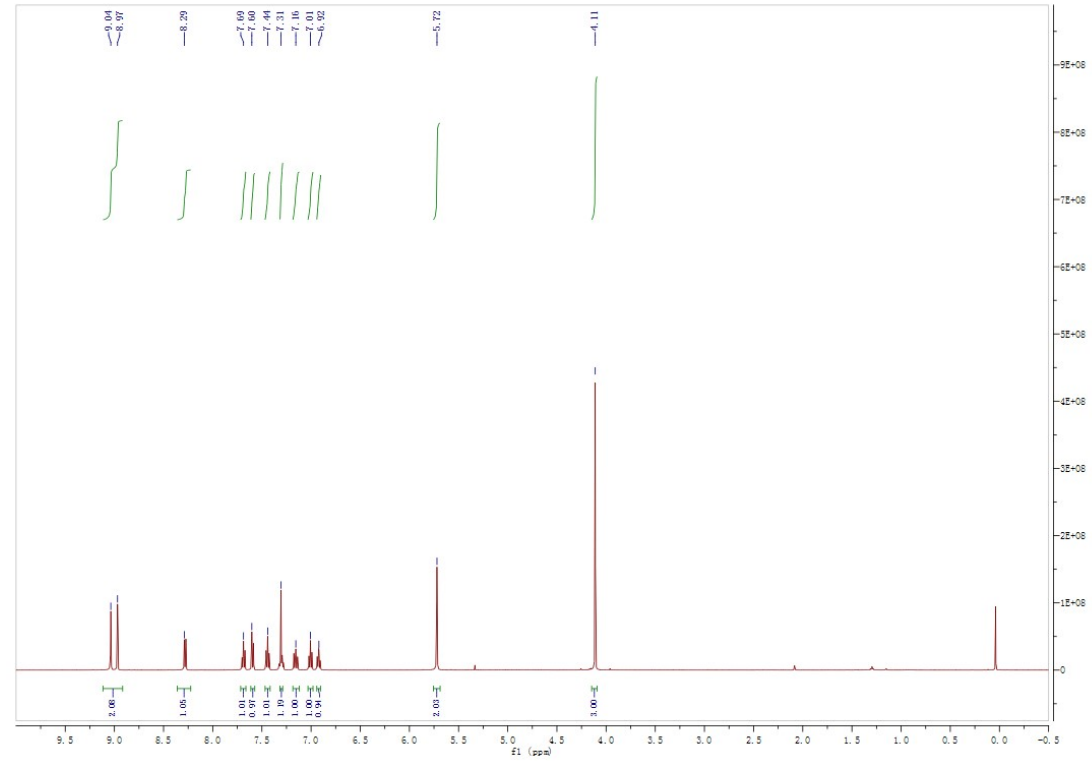
C NMR



369

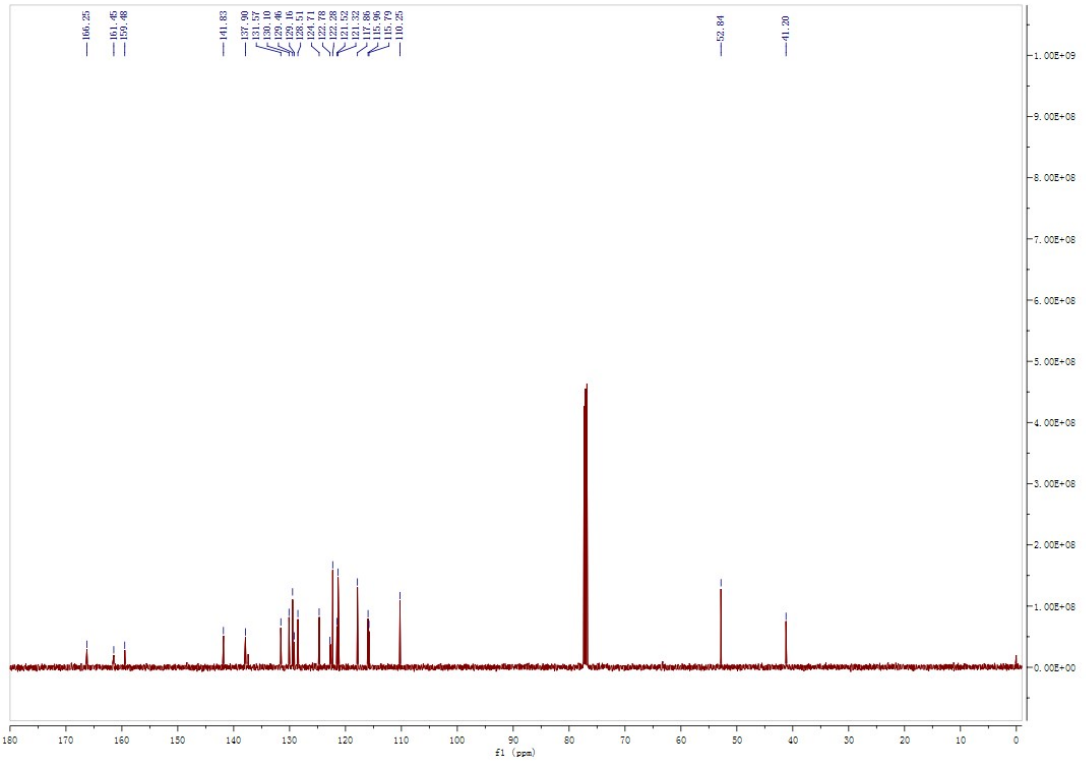
370 **4D**

371 H NMR



372

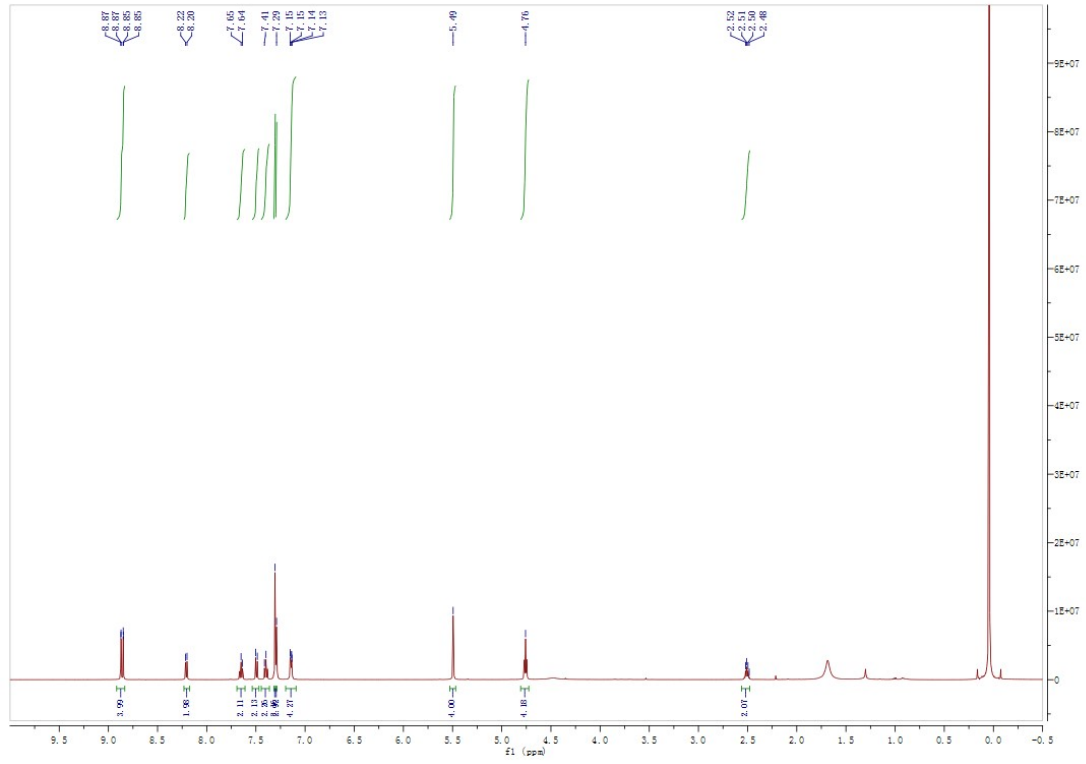
373 C NMR



374

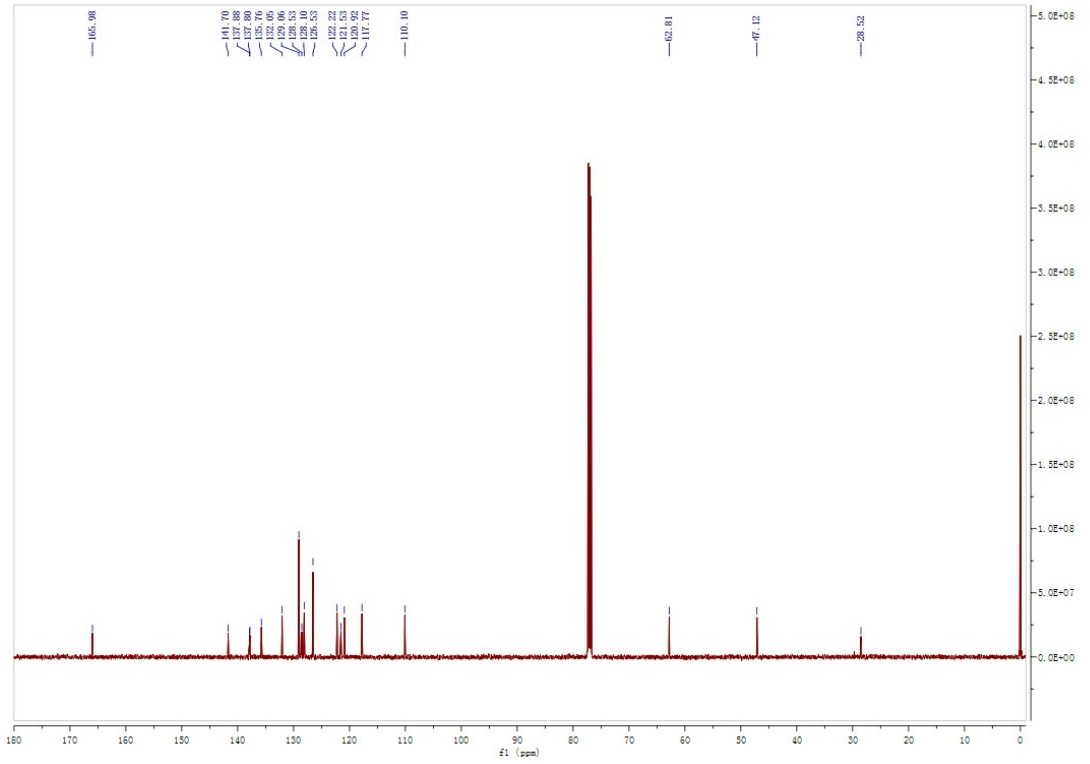
375 **6a**

376 H NMR



377

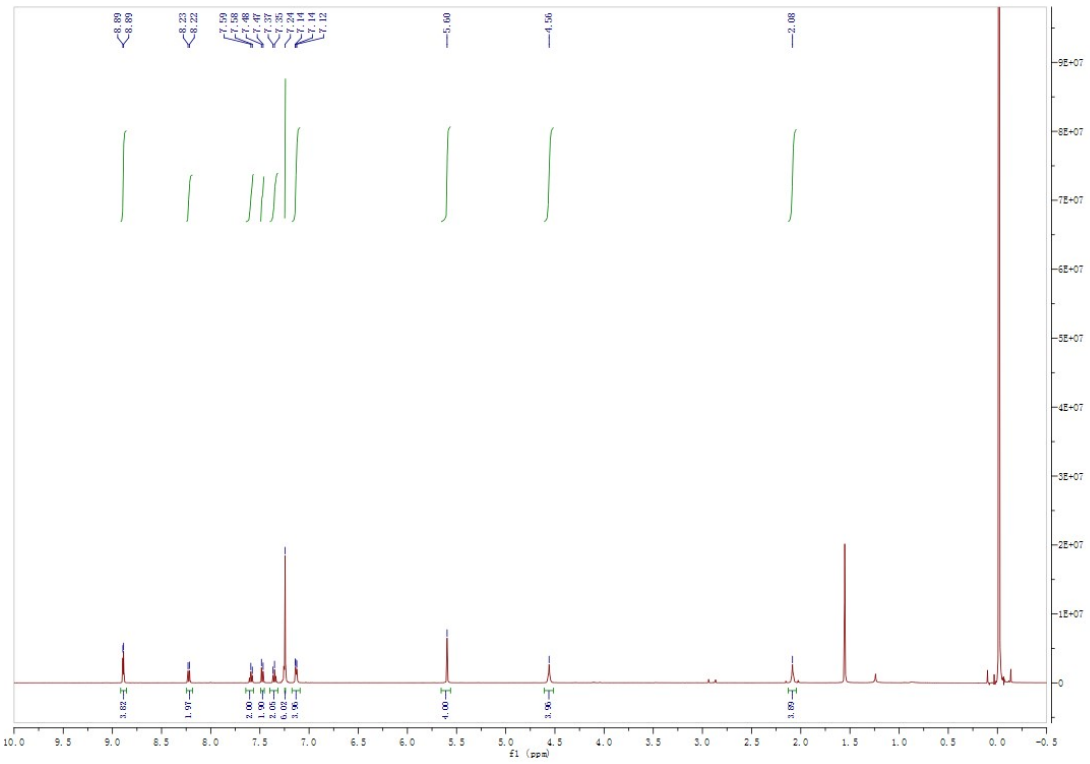
378 C NMR



379

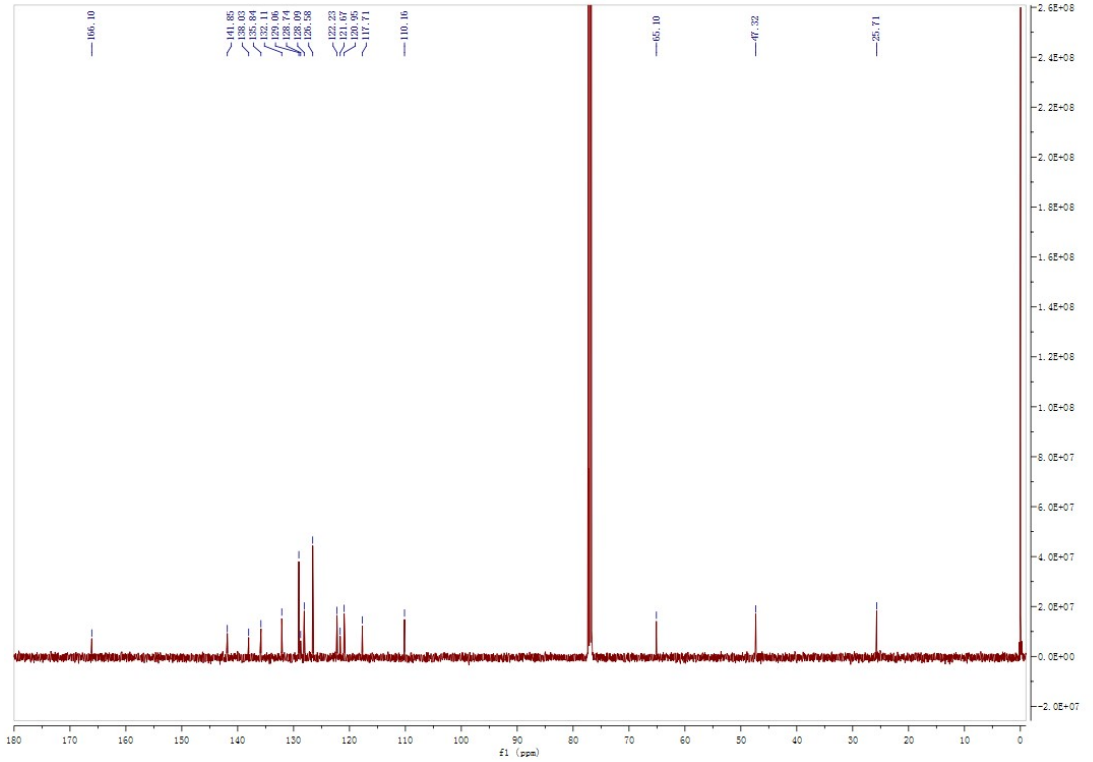
380 **6b**

381 H NMR



382

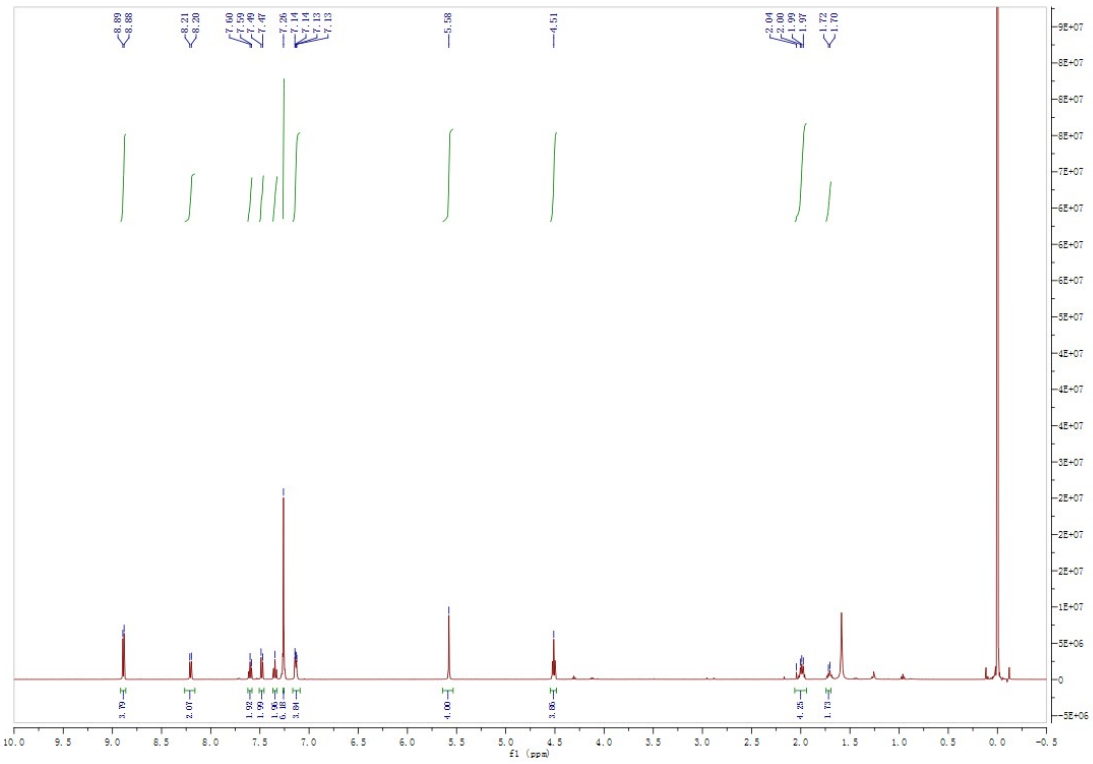
383 C NMR



384

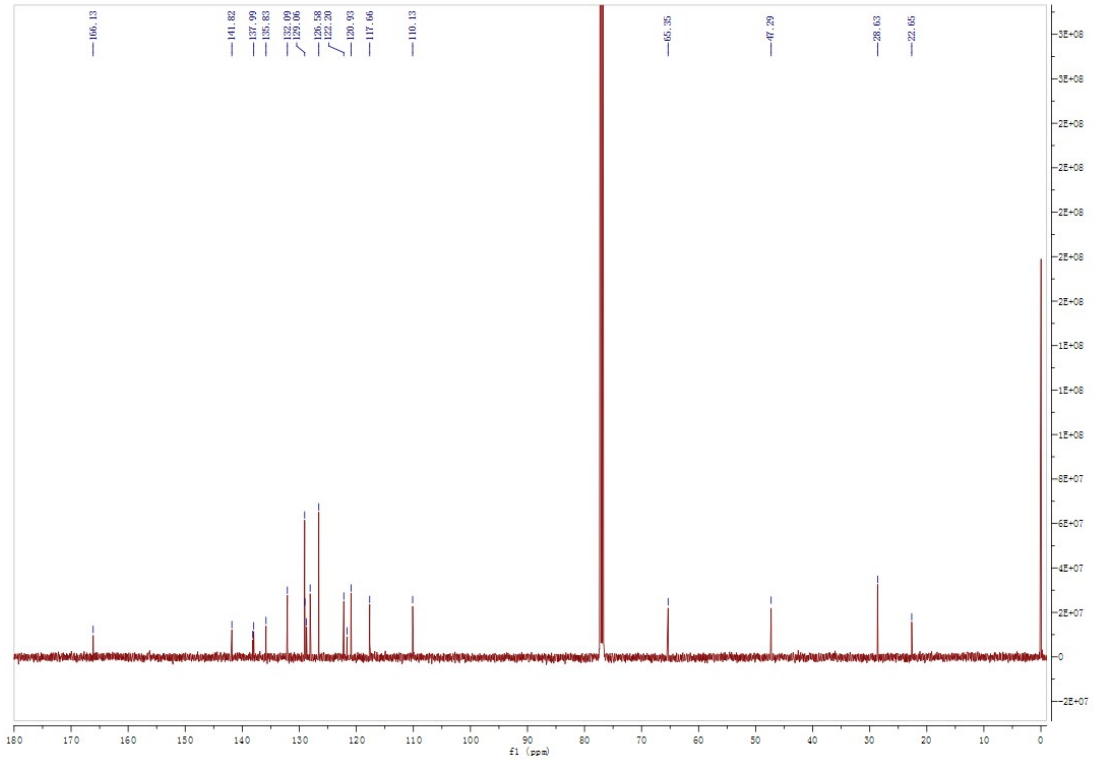
385 **6c**

386 H NMR



387

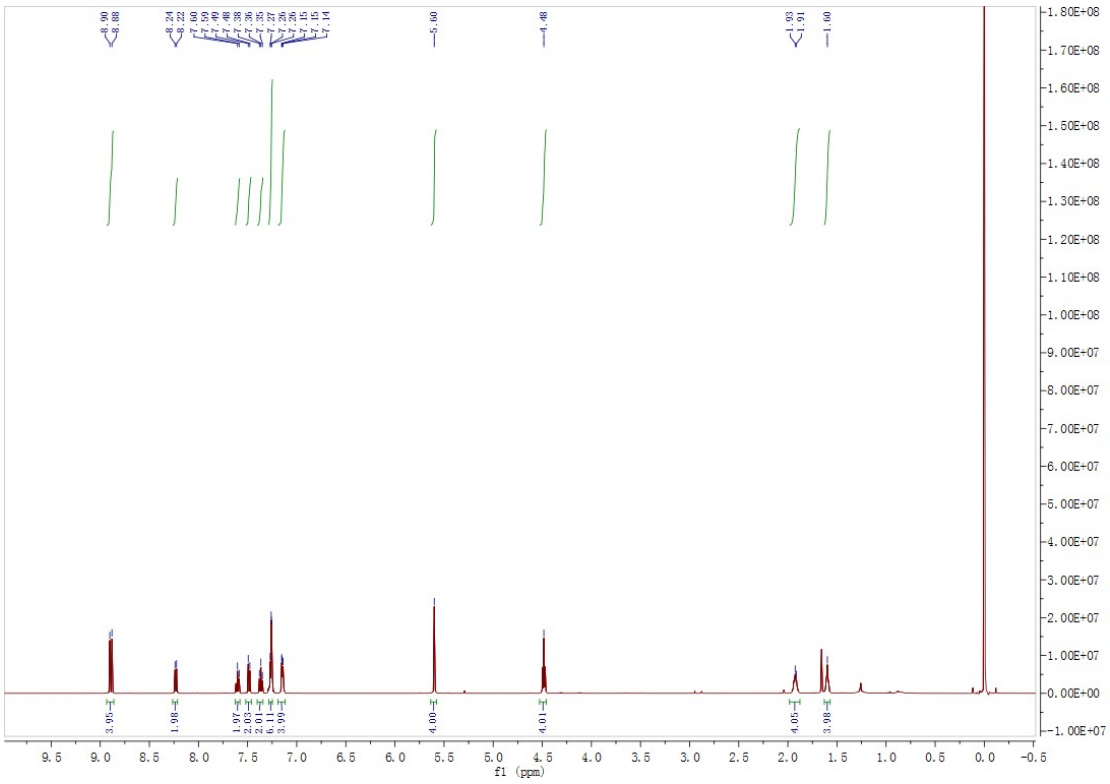
388 C NMR



389

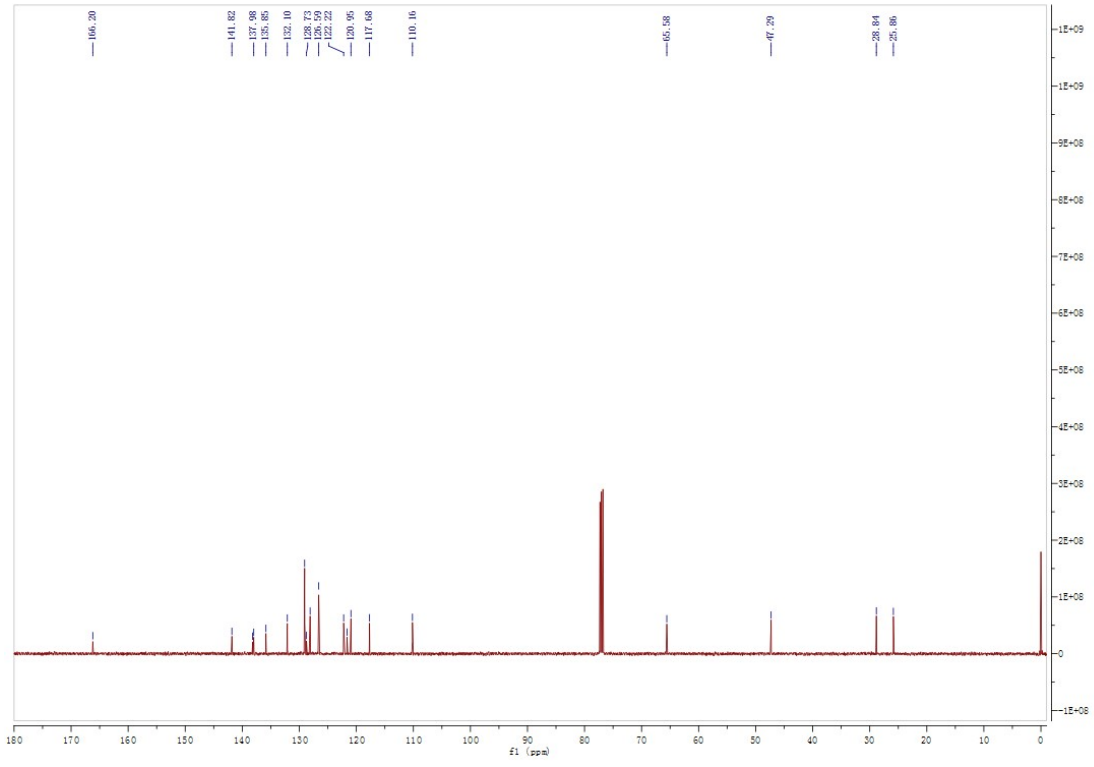
390 **6d**

391 H NMR



392

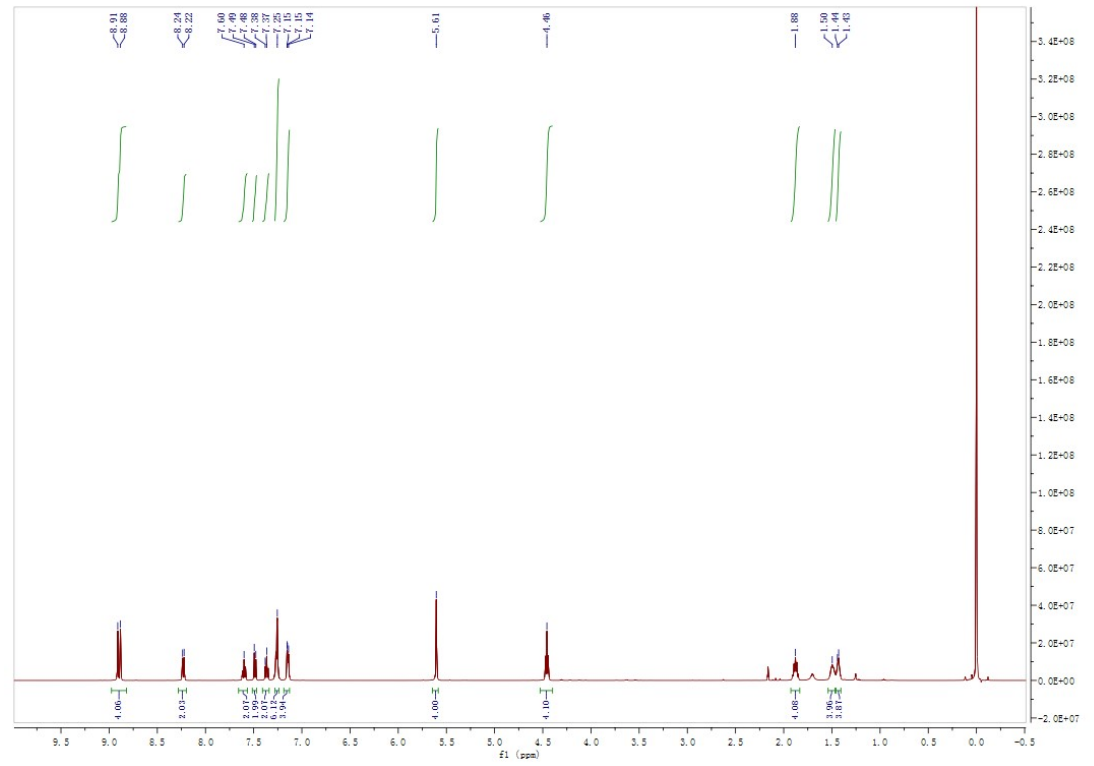
393 C NMR



394

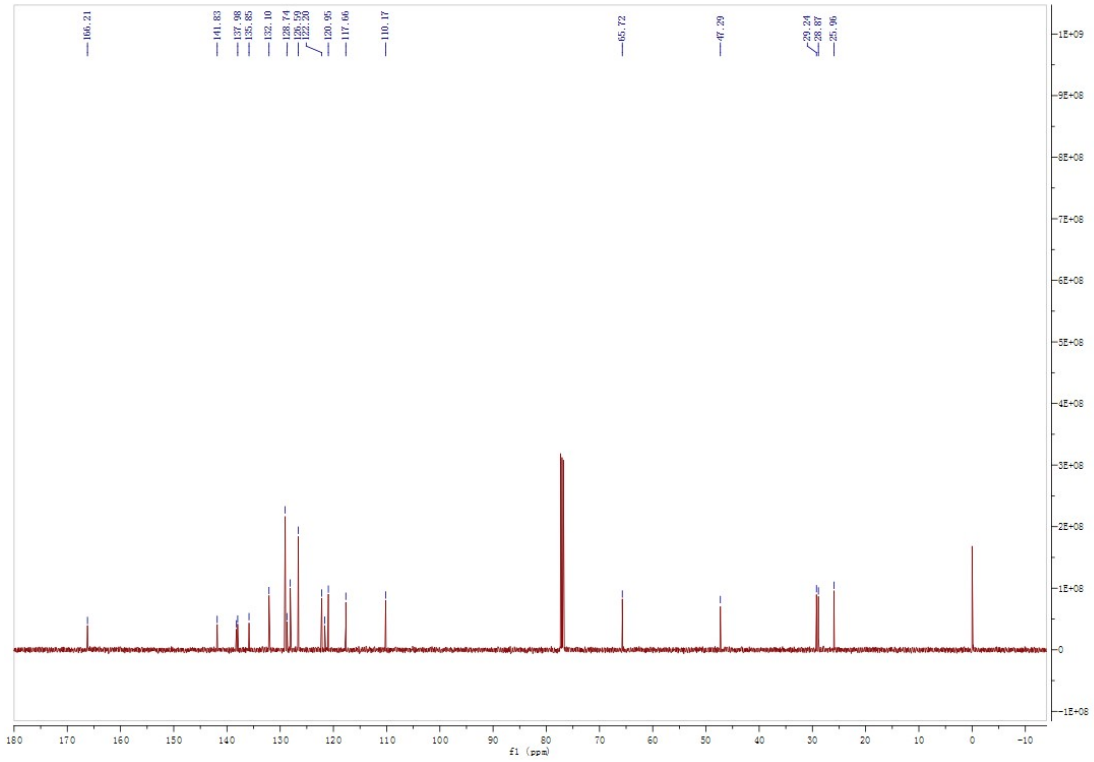
395 **6e**

396 H NMR



397

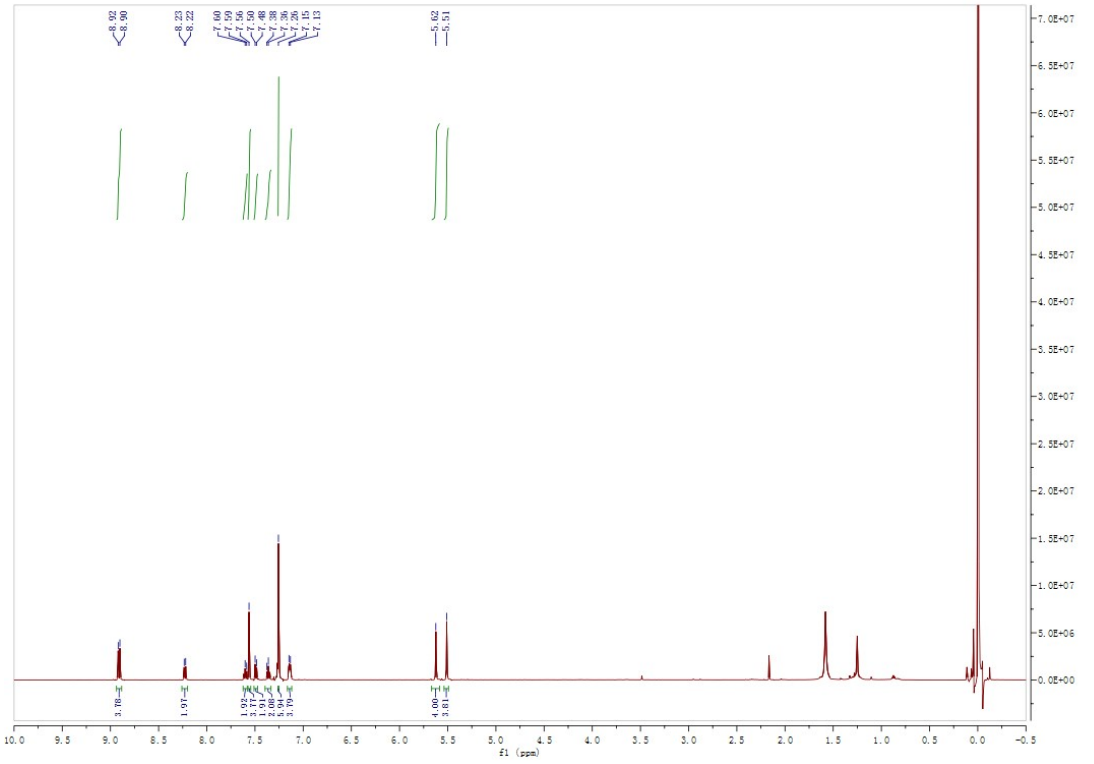
398 C NMR



399

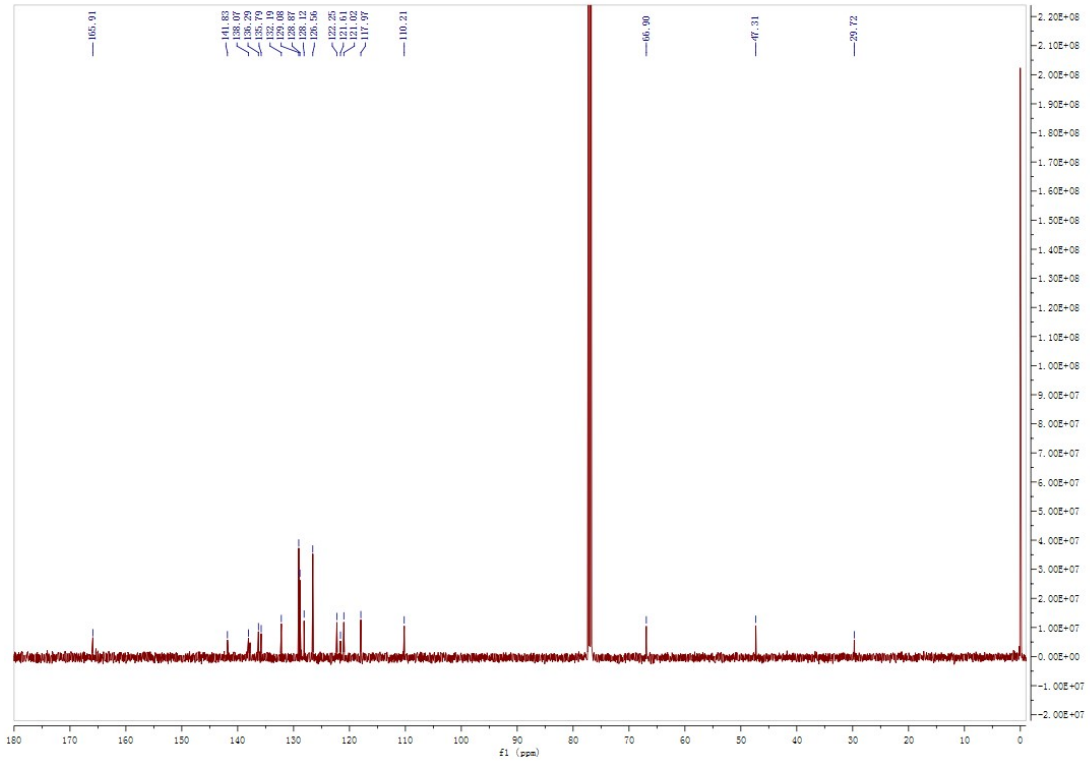
400 **6f**

401 H NMR



402

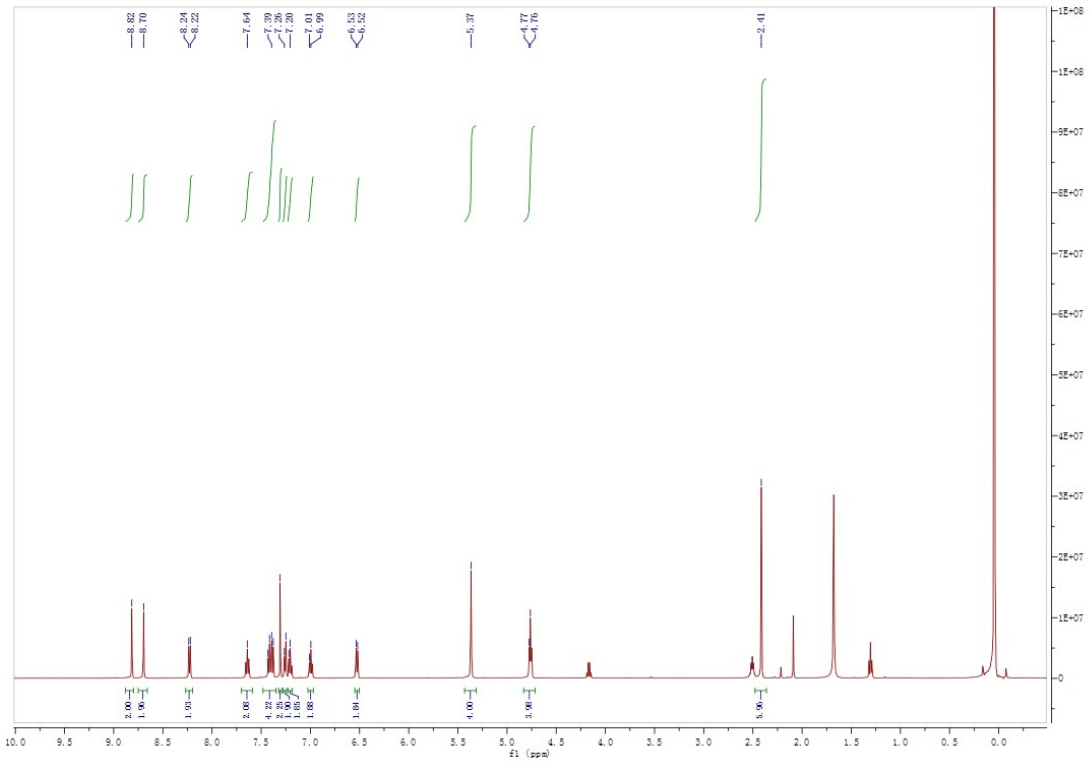
403 C NMR



404

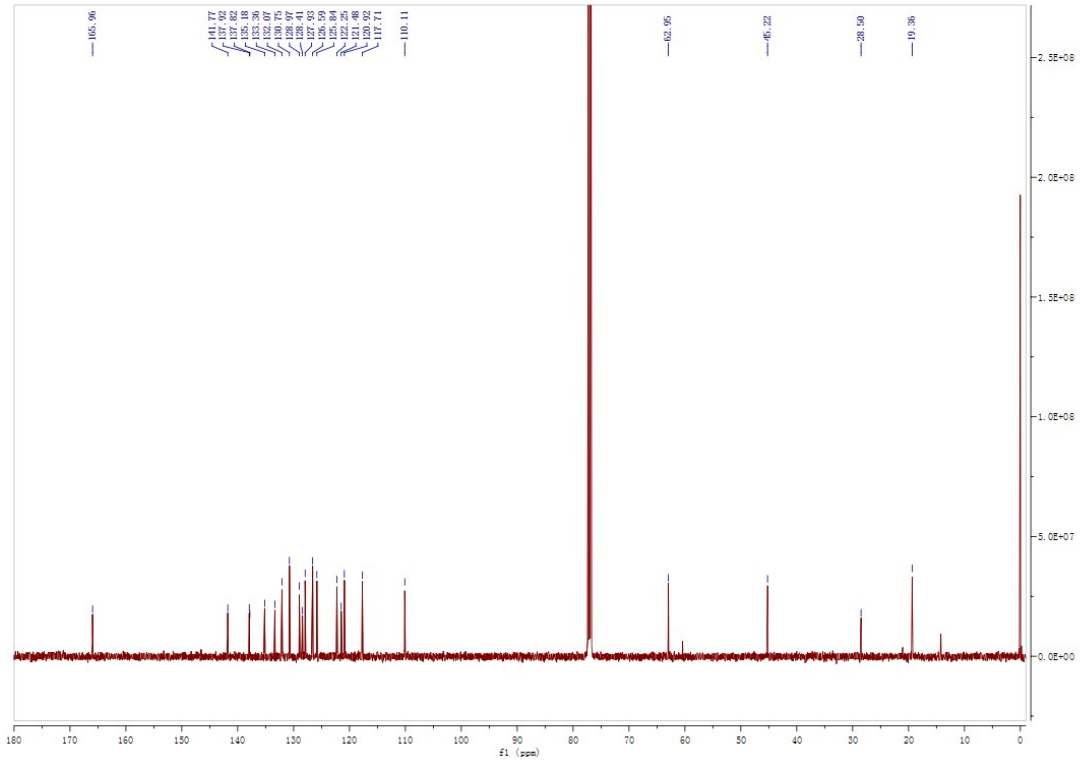
405 **6g**

406 H NMR



407

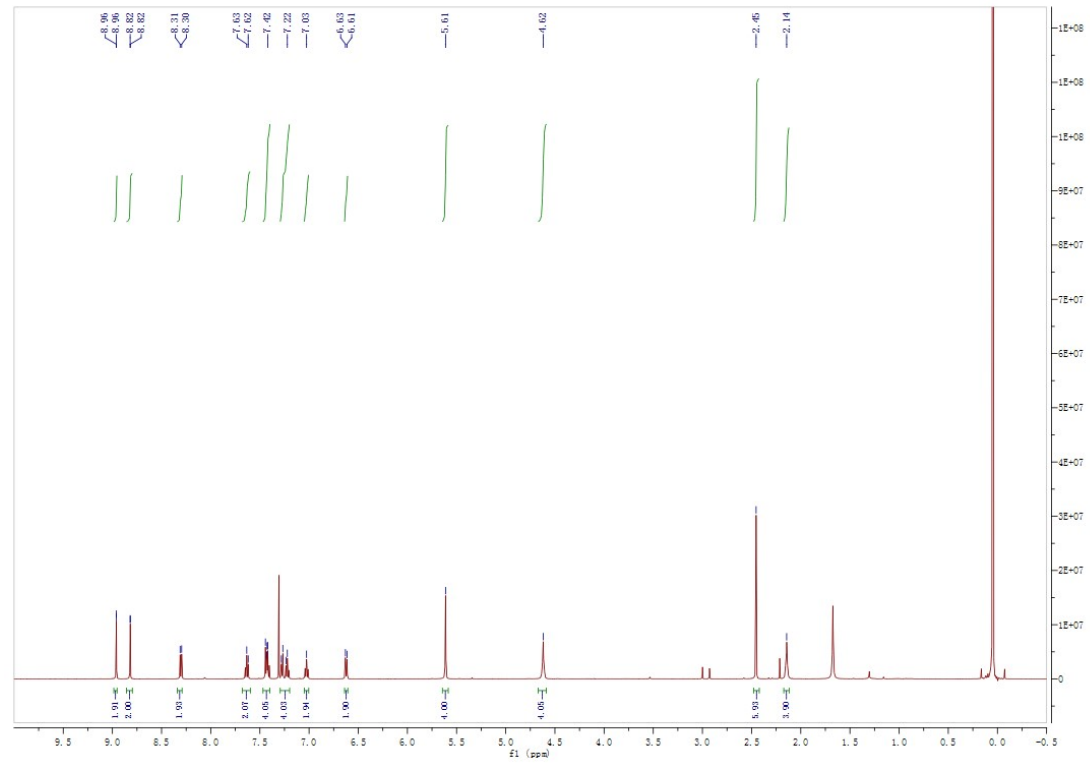
408 C NMR



409

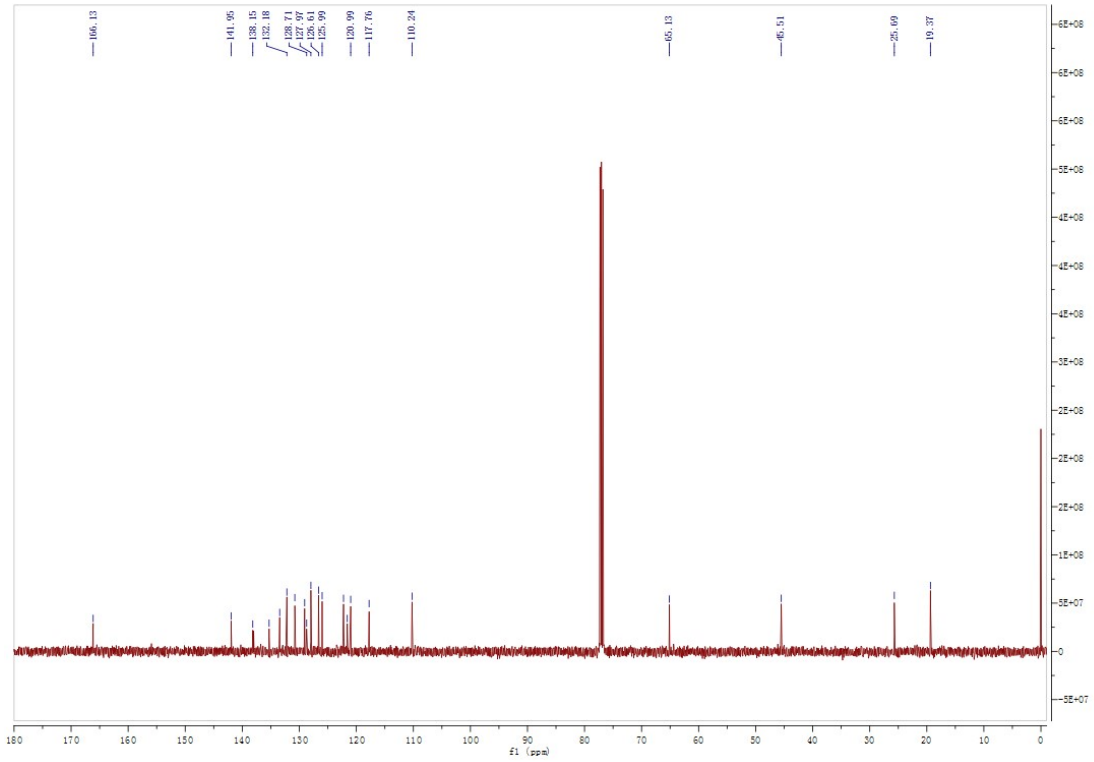
410 **6h**

411 H NMR



412

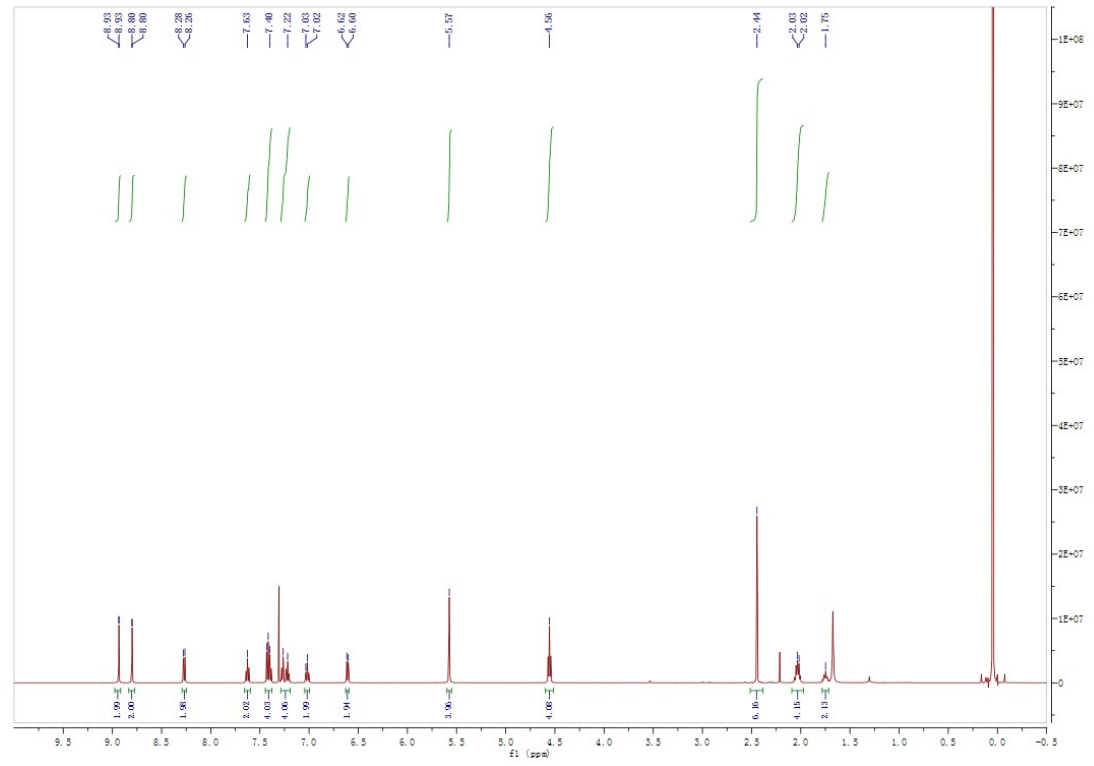
413 C NMR



414

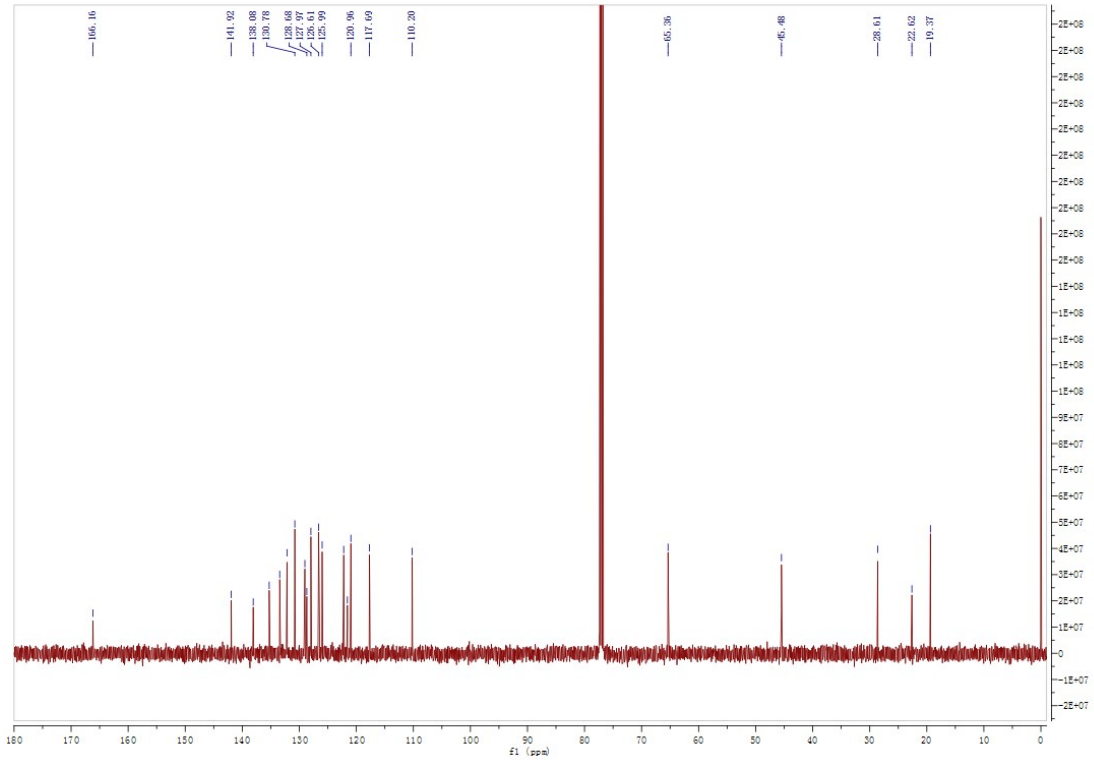
415 **6i**

416 H NMR



417

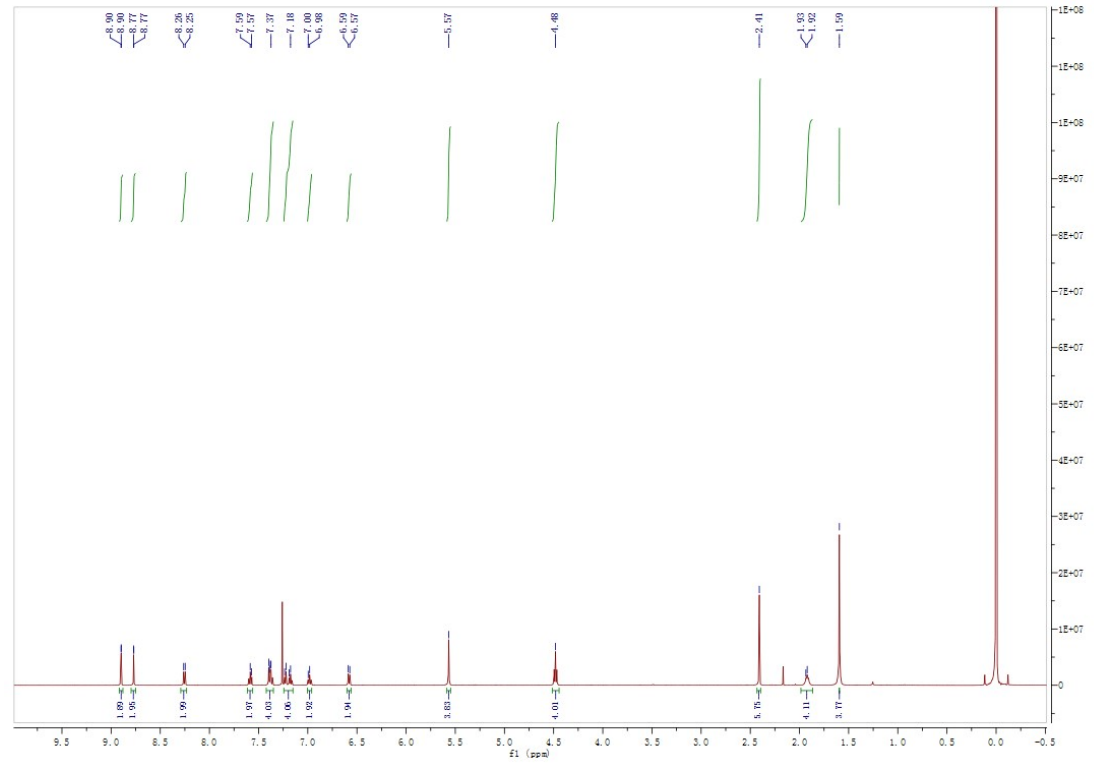
418 C NMR



419

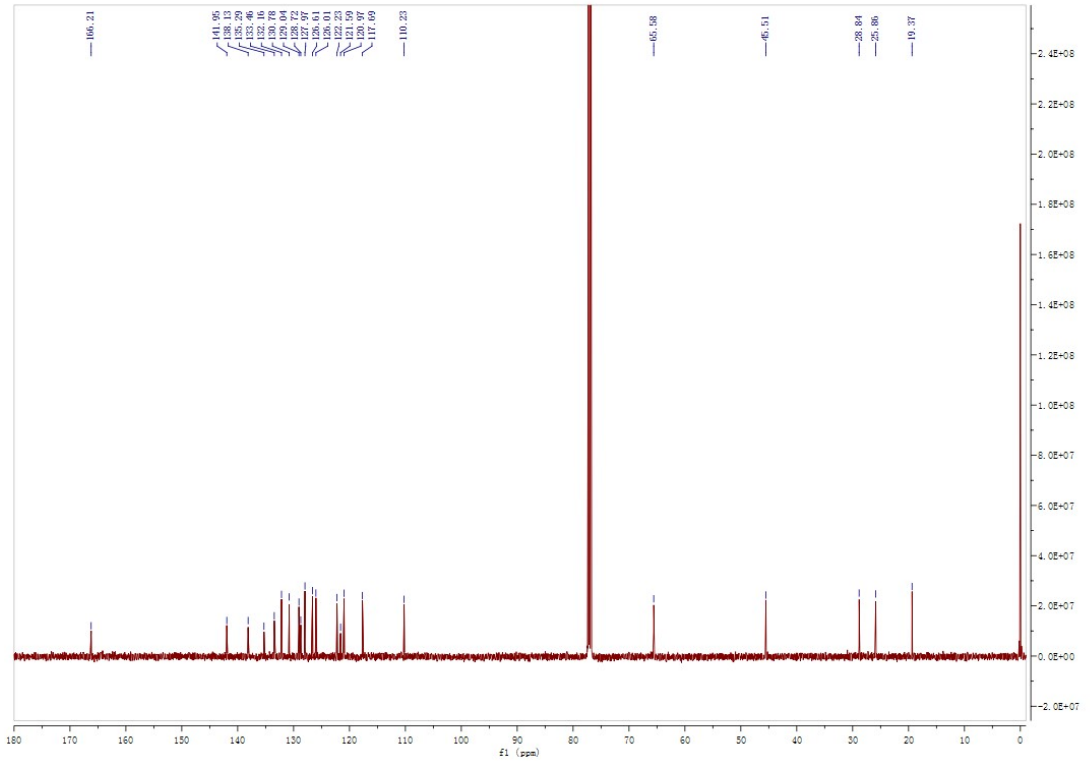
420 **6j**

421 H NMR



422

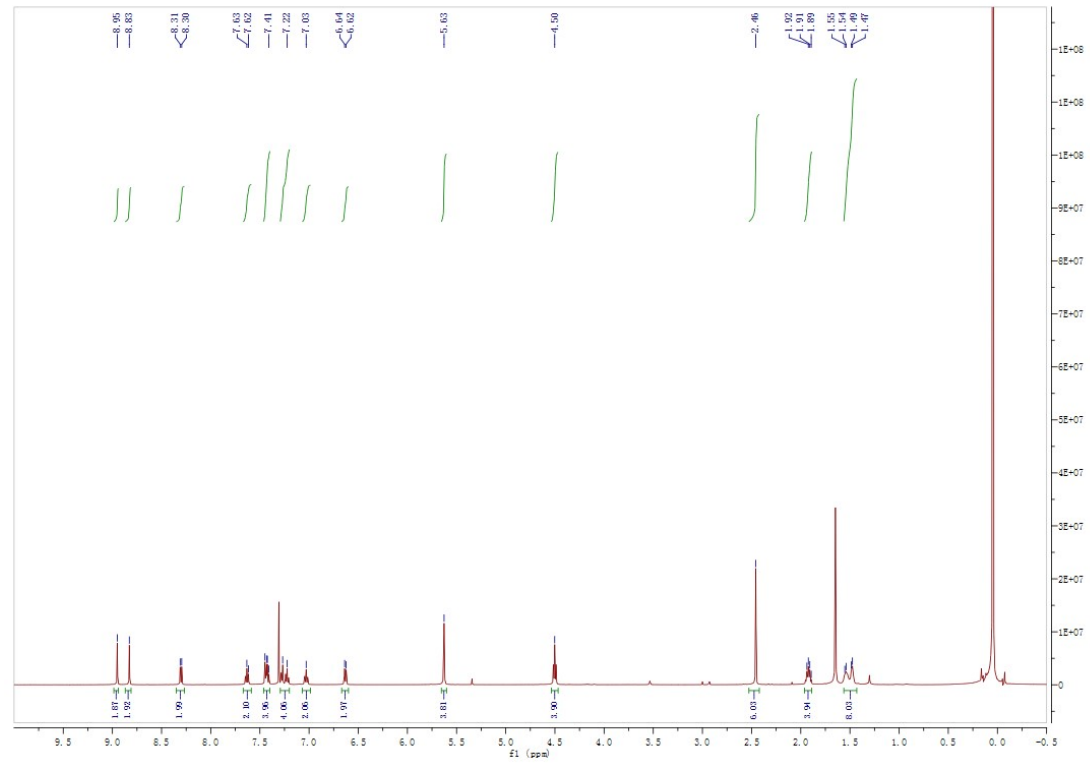
423 C NMR



424

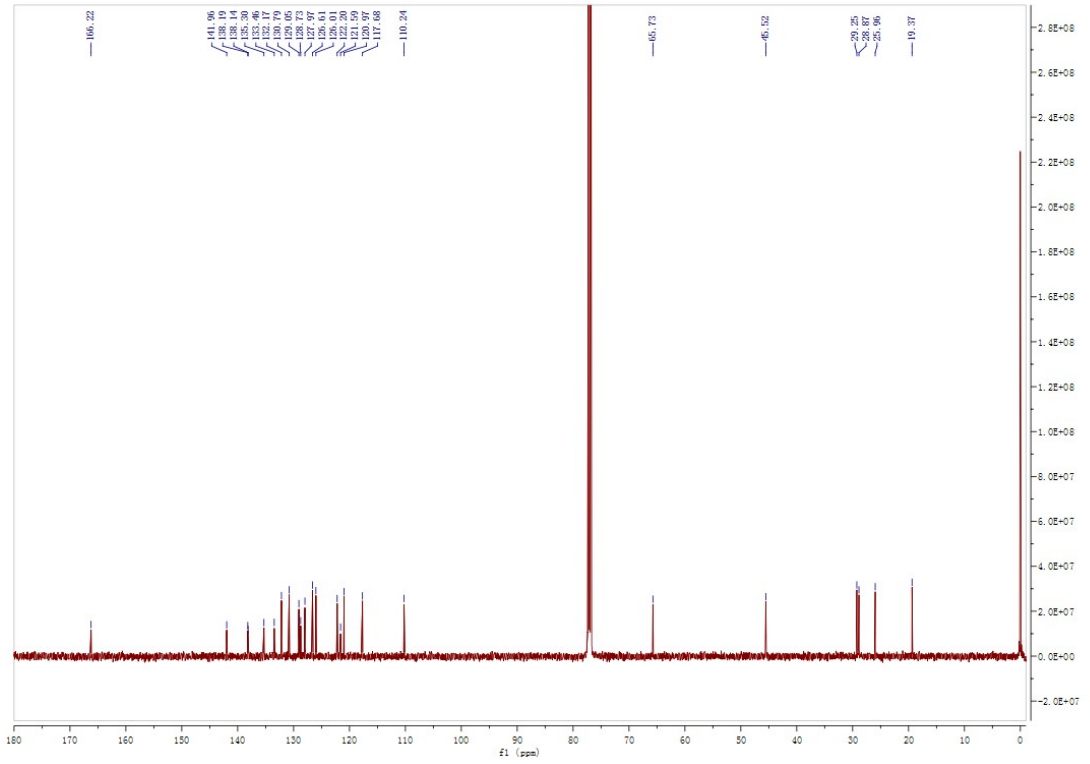
425 **6k**

426 H NMR



427

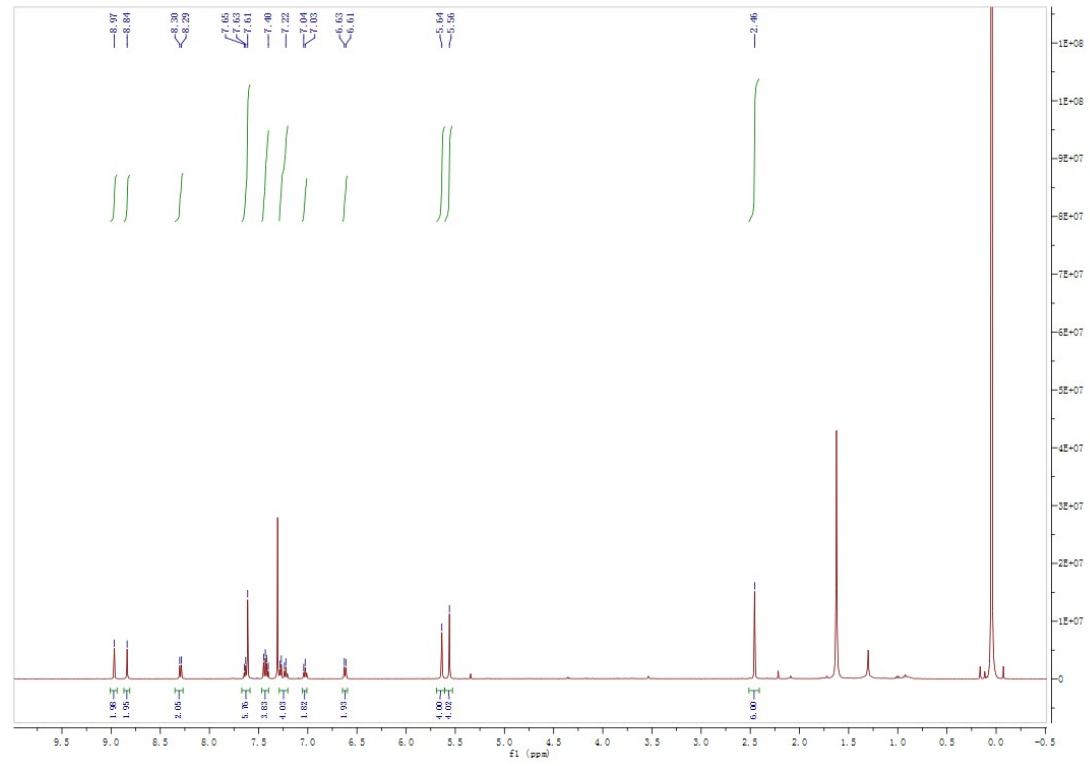
428 C NMR



429

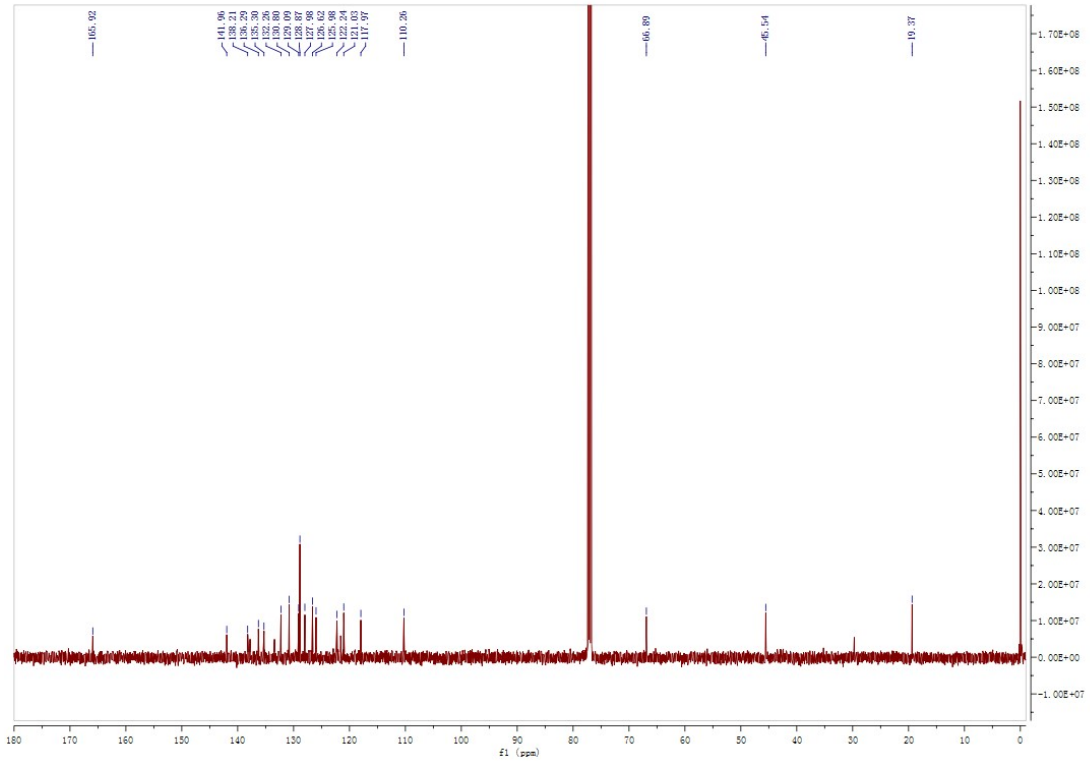
430 **6l**

431 H NMR



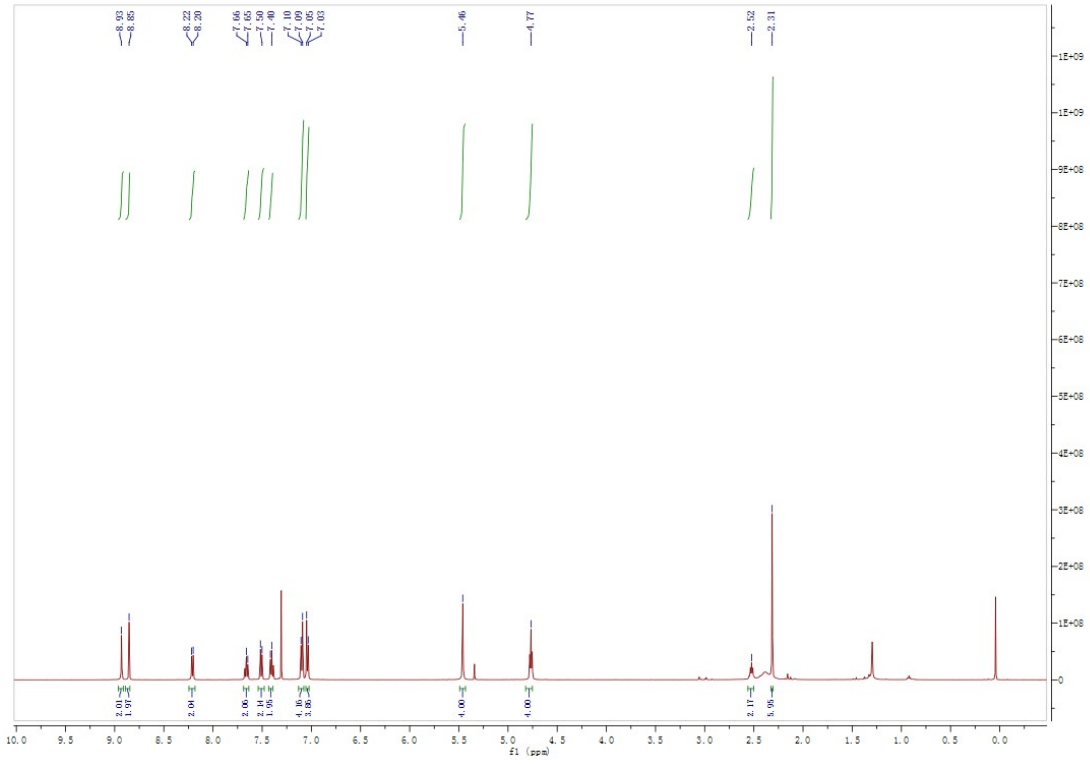
432

433 C NMR

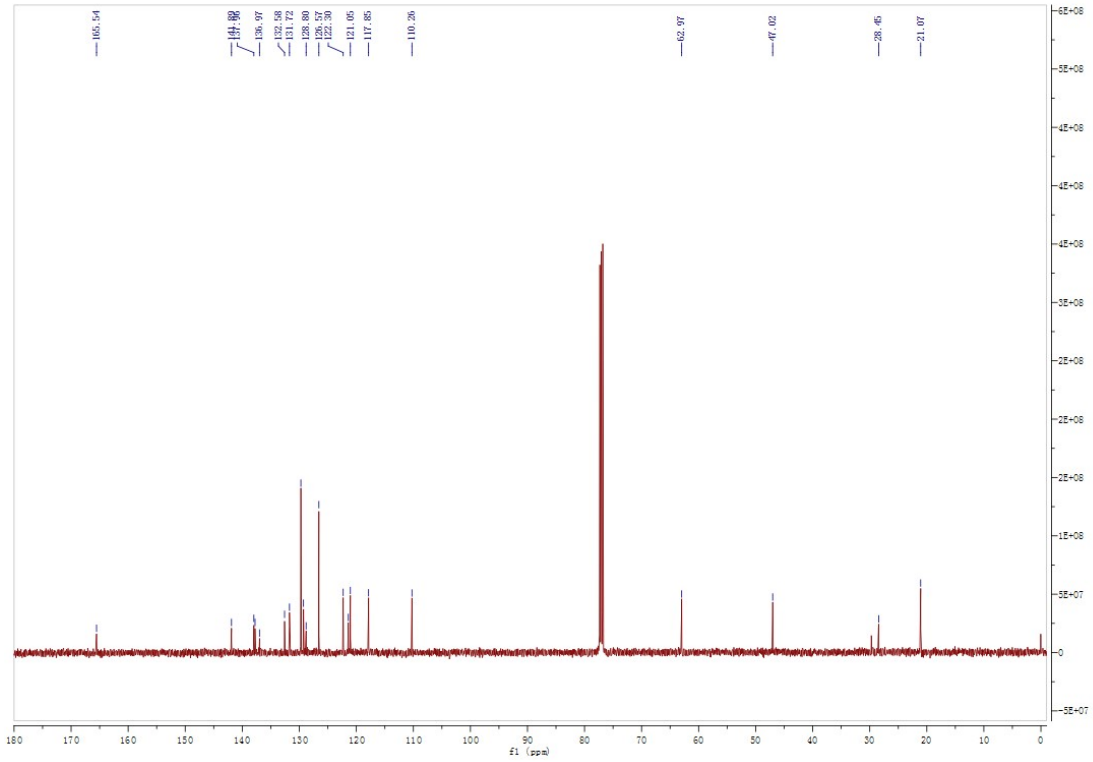

165.92
141.96
138.21
136.20
135.30
132.26
130.60
129.69
128.87
127.88
126.62
125.98
123.34
121.63
117.97
110.26
66.89
45.54
19.37
f1 (ppm)

6m

H NMR


8.93
8.88
8.22
8.20
7.66
7.65
7.50
7.40
7.10
7.09
7.05
7.03
5.46
4.77
2.52
2.31
f1 (ppm)

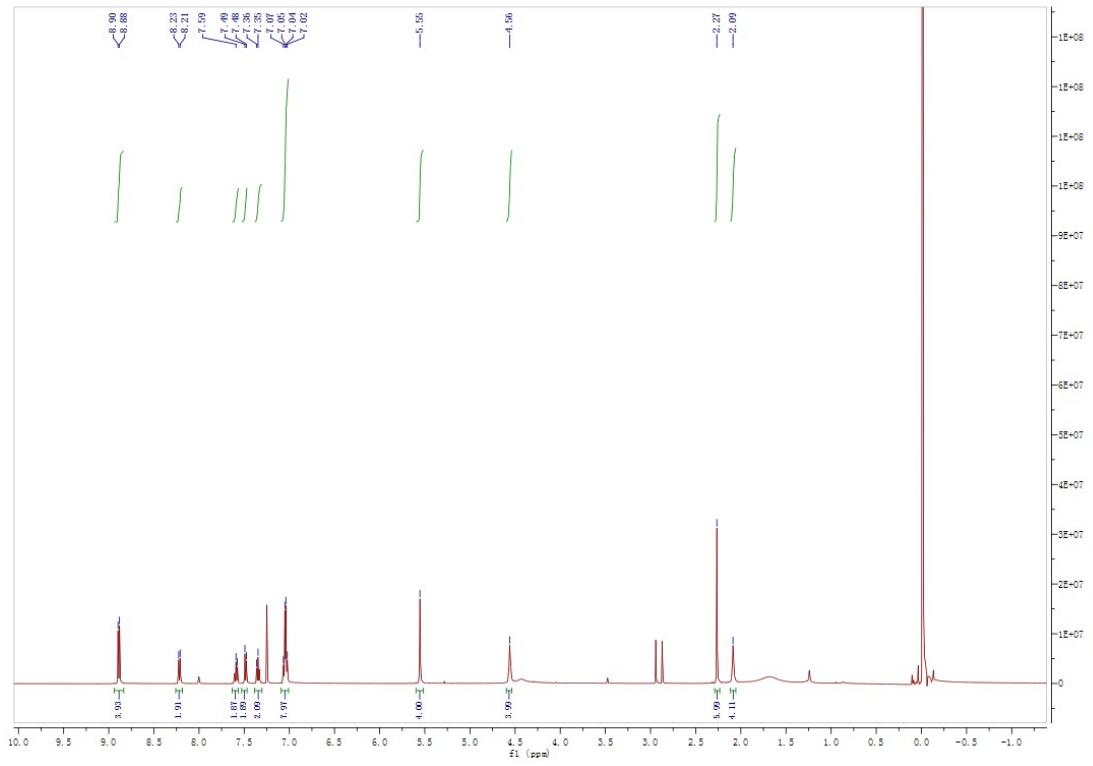
C NMR



439

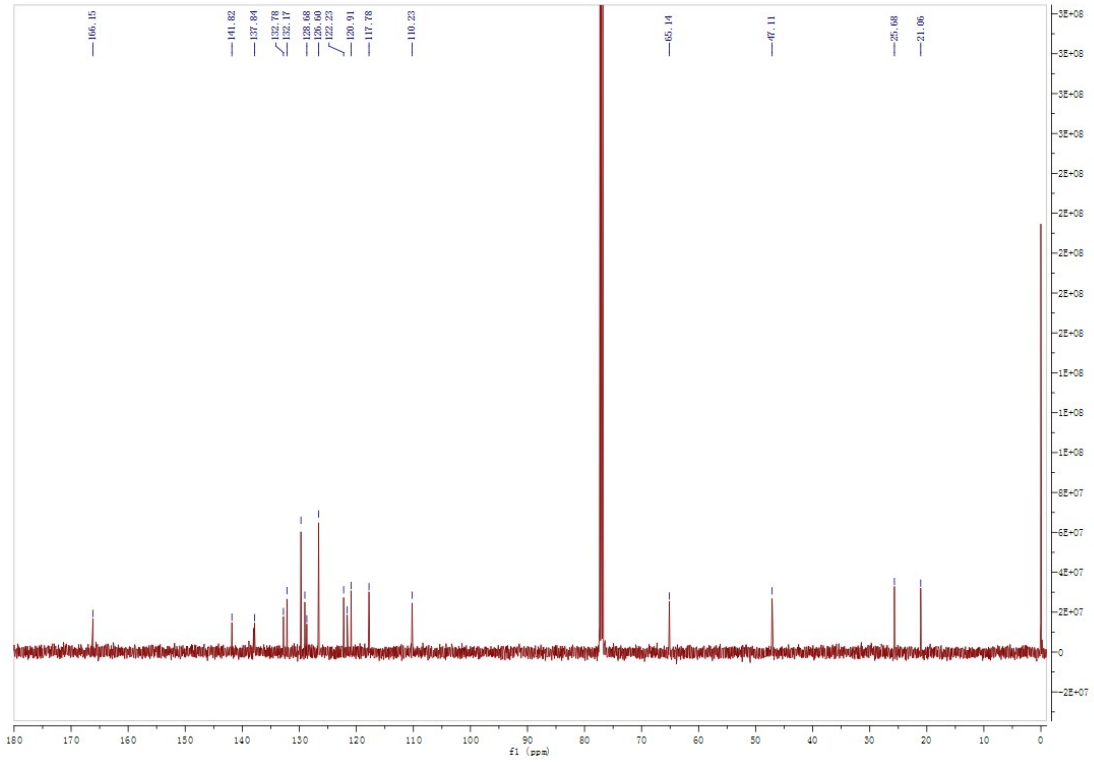
440 **6n**

441 H NMR



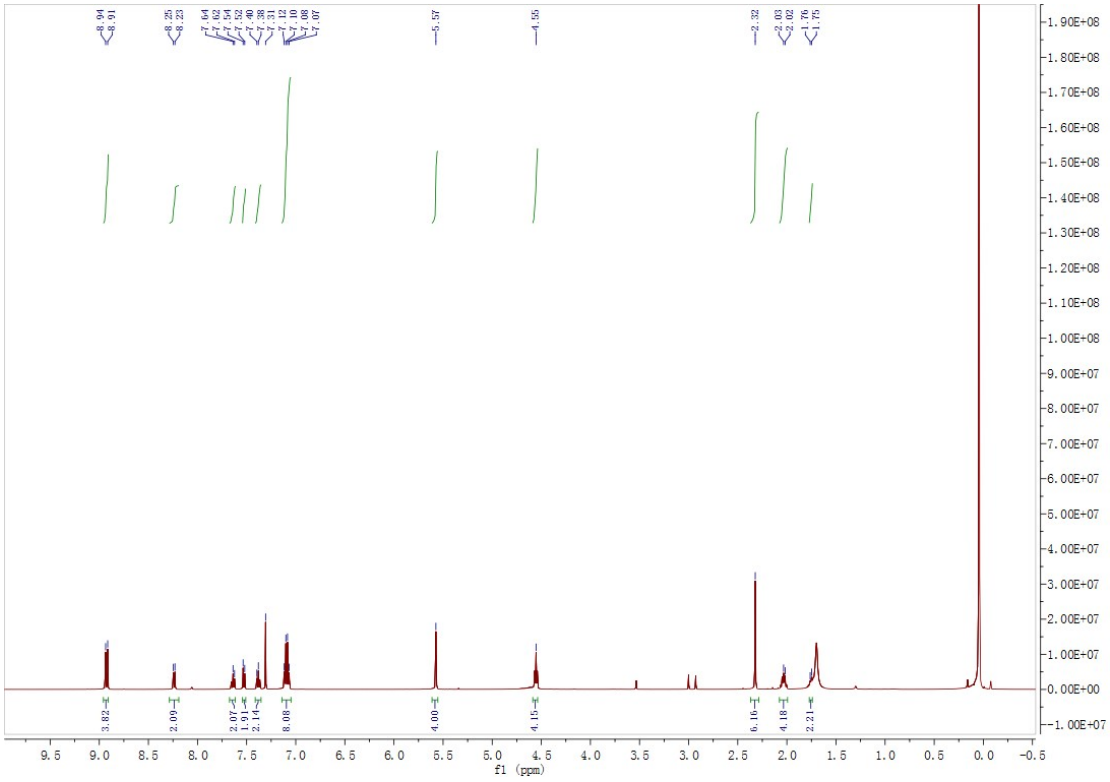
442

443 C NMR


166.15
141.82
137.84
132.78
132.17
128.68
126.60
122.23
120.91
117.78
110.23
65.14
47.11
25.68
21.06
f1 (ppm)

6o

H NMR


8.94
8.91
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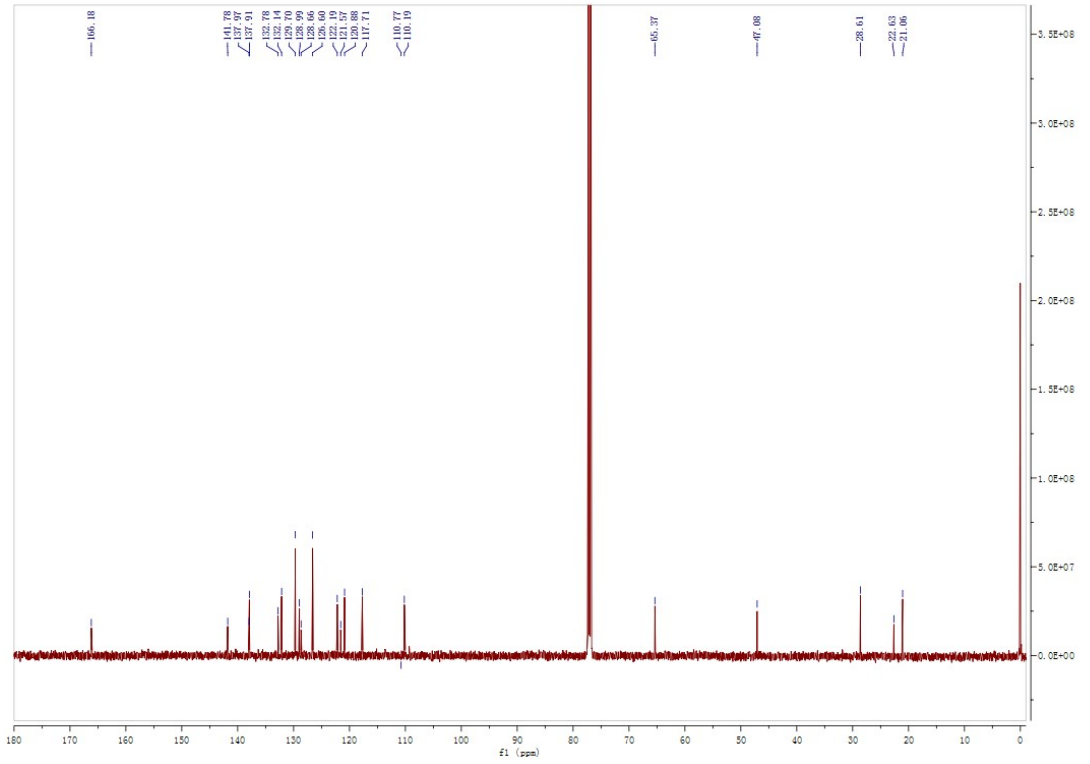
8.23
7.64
7.62
7.54
7.52
7.40
7.38
7.31
7.12
7.10
7.08
7.07
5.57
4.55
2.32
2.03
2.02
1.76
1.75
f1 (ppm)

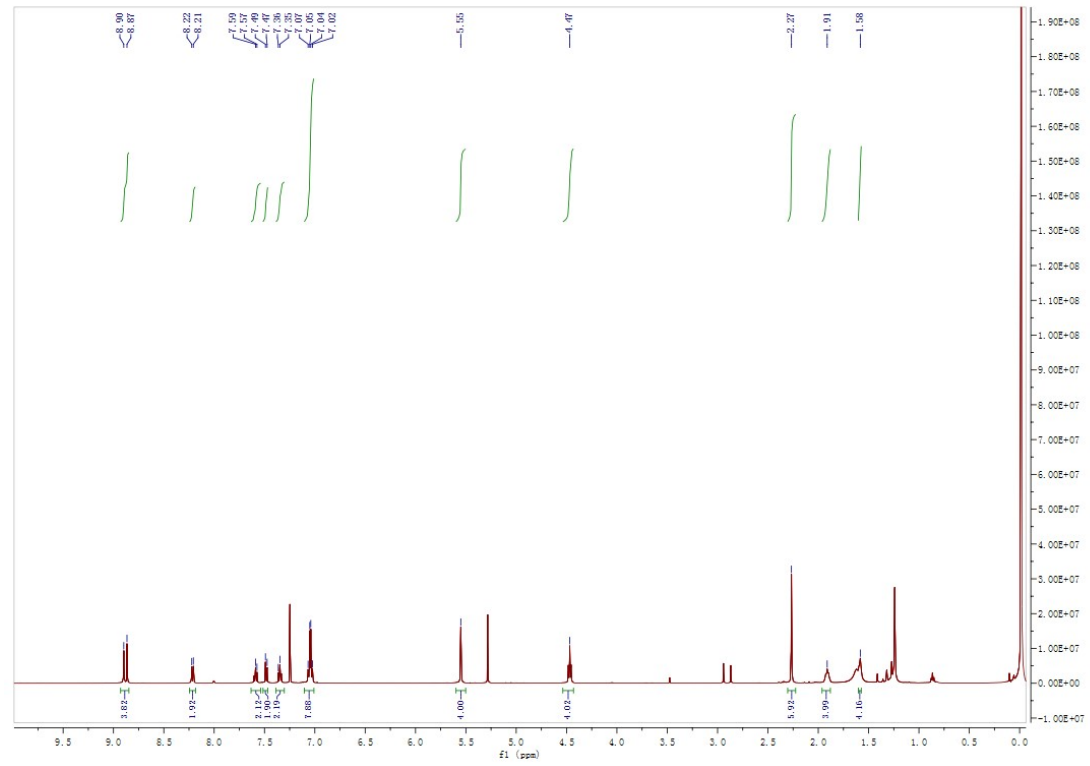
C NMR



449

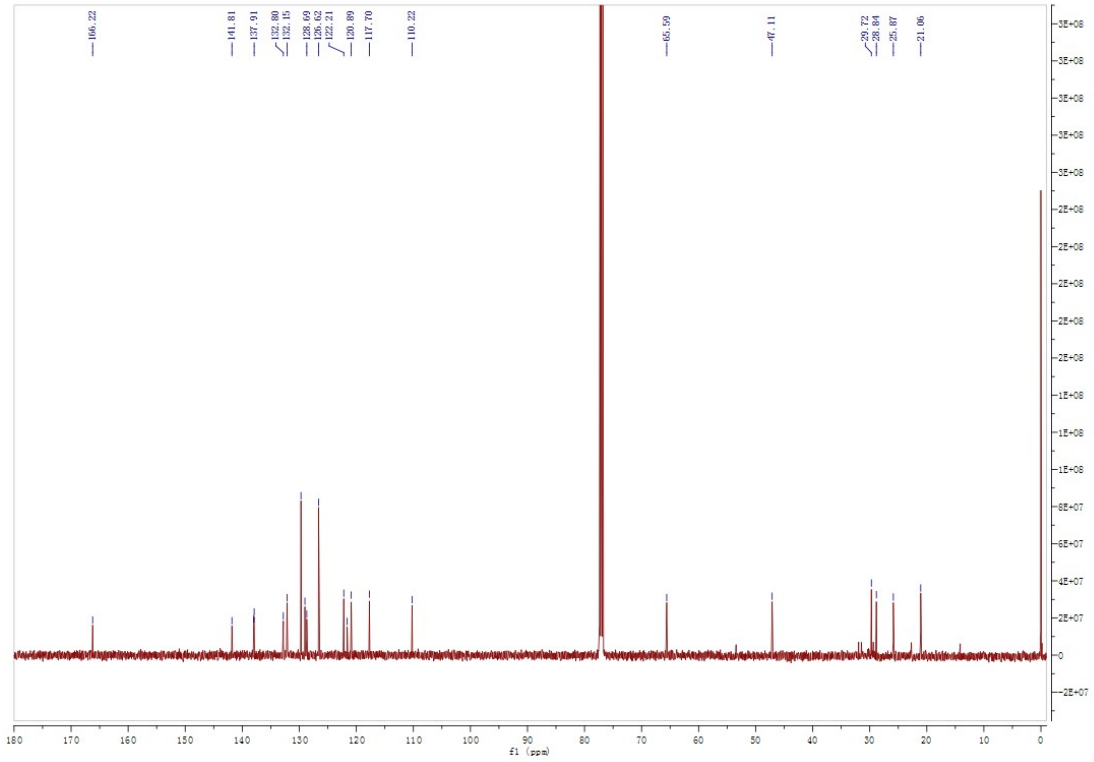
450 **6p**

451 H NMR



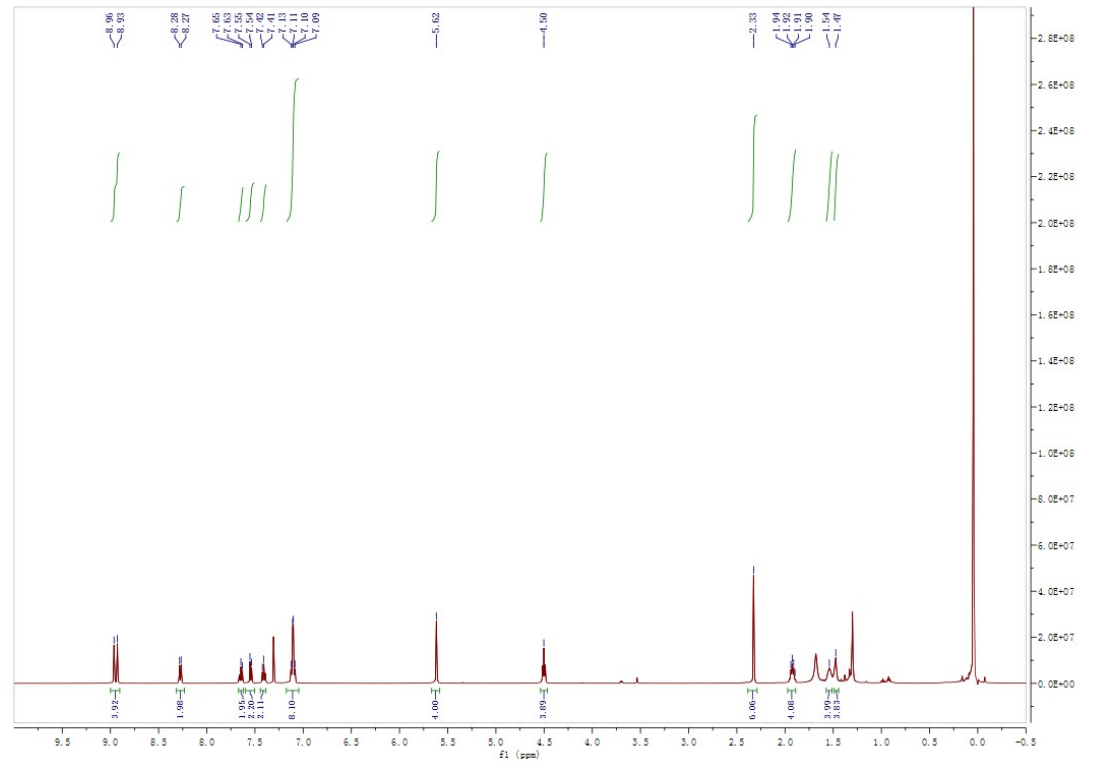
452

453 C NMR

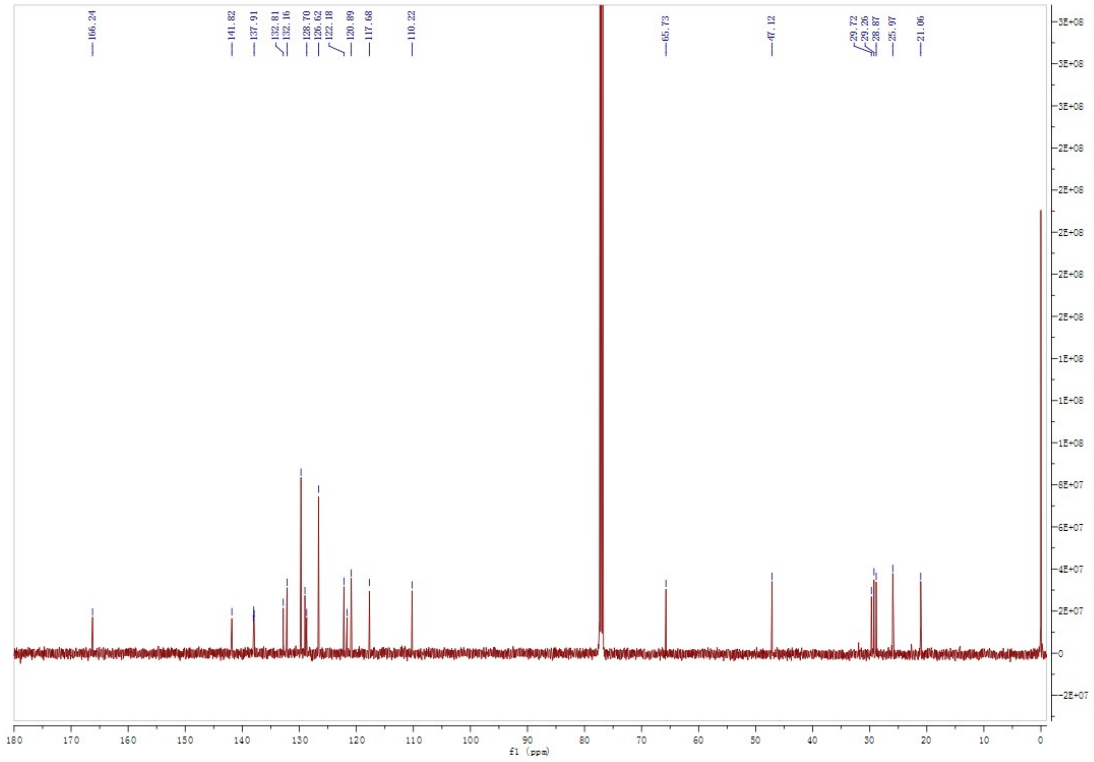

166.22
141.81
137.91
132.80
132.15
128.69
126.62
122.21
120.89
117.70
110.22
65.59
47.11
29.72
28.84
25.87
21.06
f1 (ppm)

6q

H NMR


8.96
8.93
8.28
8.27
7.65
7.63
7.55
7.54
7.42
7.41
7.13
7.10
7.09
5.62
4.50
2.33
1.94
1.92
1.91
1.90
1.54
1.47
3.93
1.98
1.95
2.20
2.11
8.10
4.00
3.89
6.06
4.08
3.99
3.83
f1 (ppm)

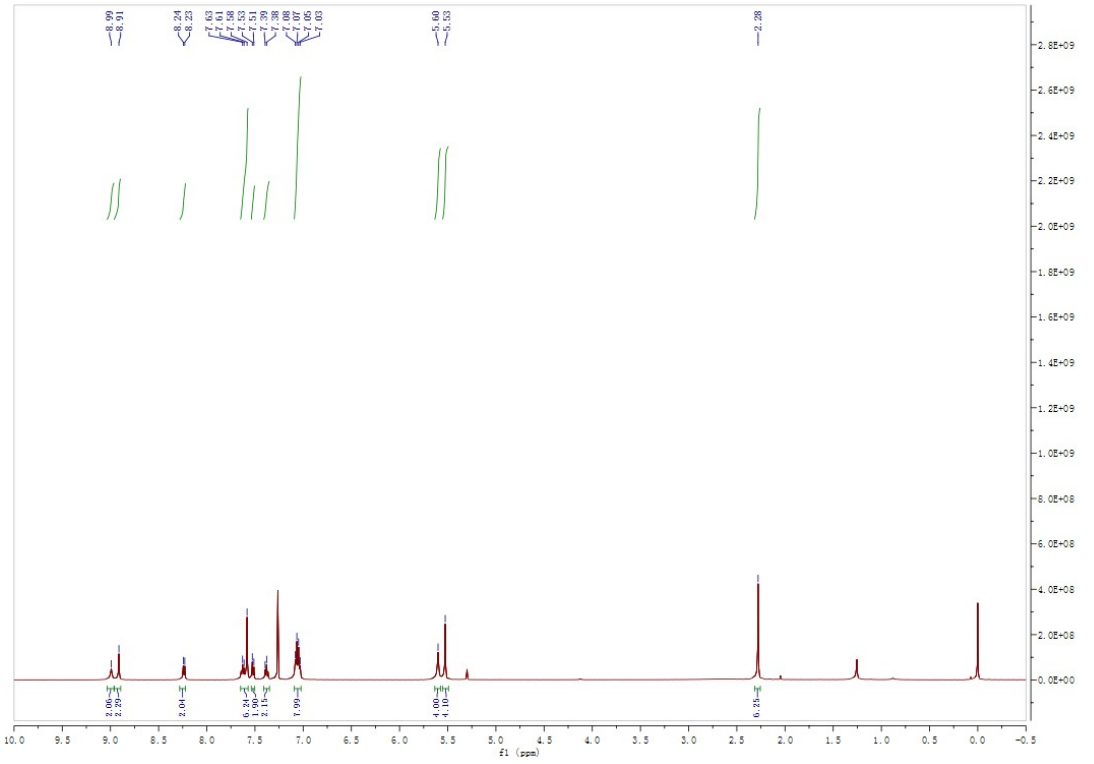
C NMR



459

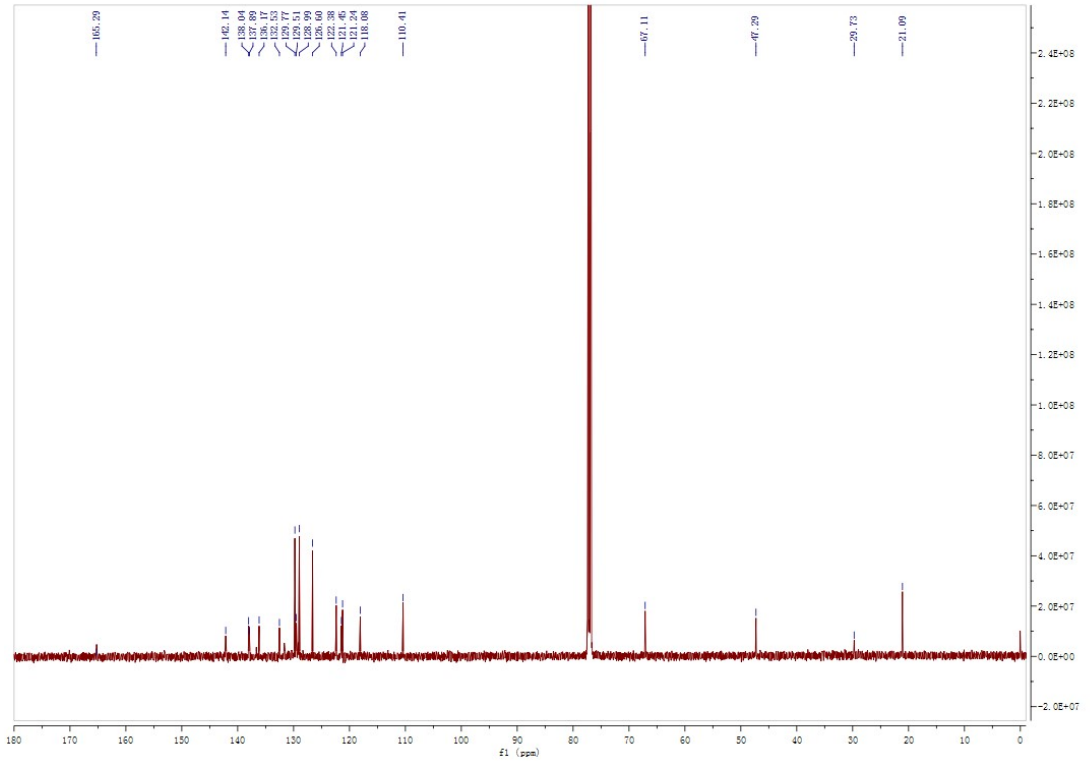
460 **6r**

461 H NMR



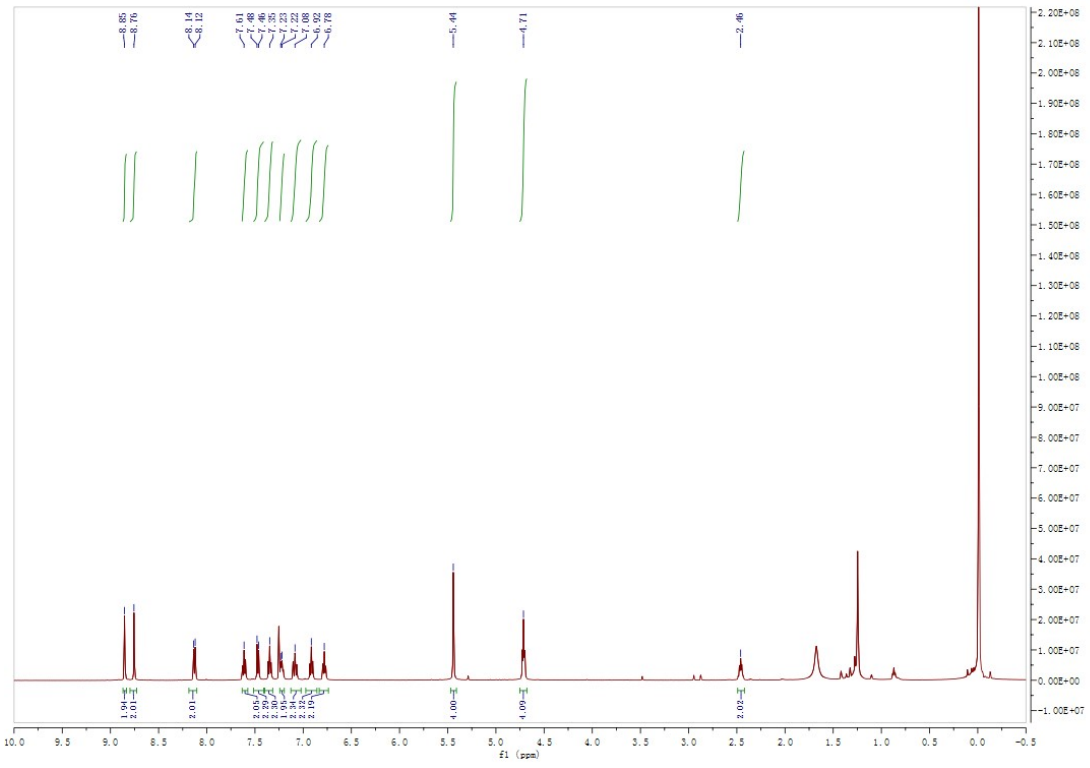
462

463 C NMR

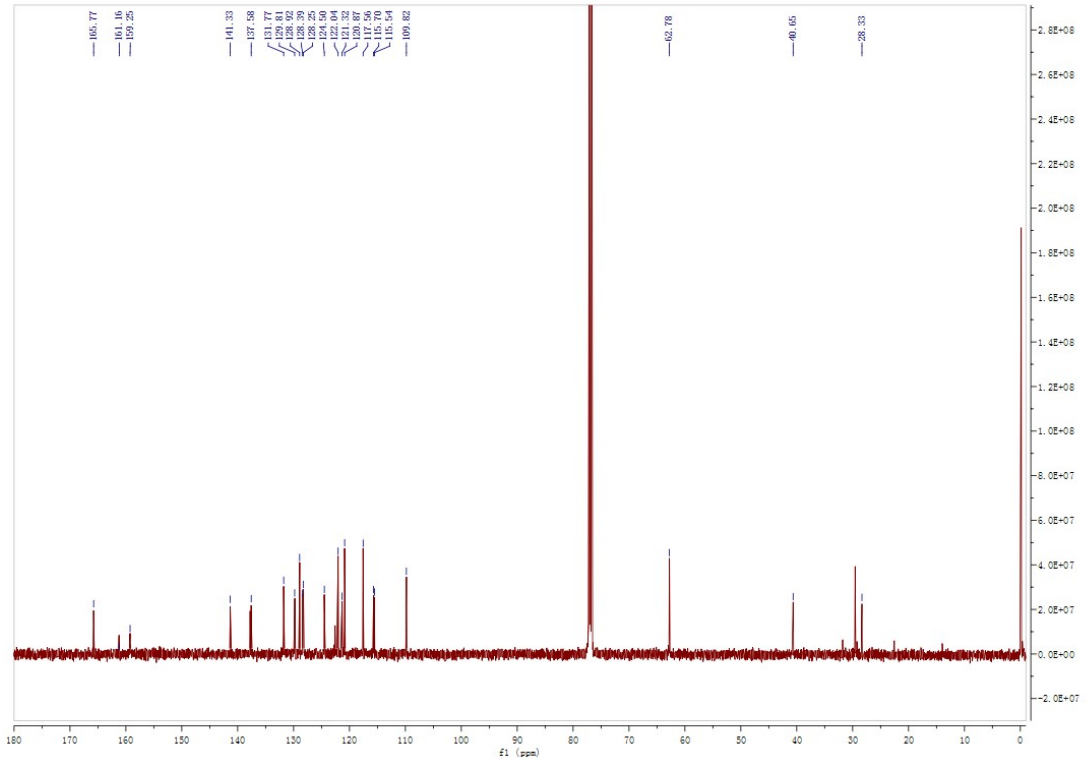

165.29
142.14
138.04
137.89
136.17
133.53
129.77
129.51
128.99
126.60
122.38
121.46
121.24
118.08
110.41
67.11
47.29
29.73
21.09
f1 (ppm)

6s

H NMR


8.85
8.76
8.14
8.12
7.61
7.48
7.46
7.35
7.23
7.22
7.08
6.92
6.78
5.44
4.71
2.46
f1 (ppm)

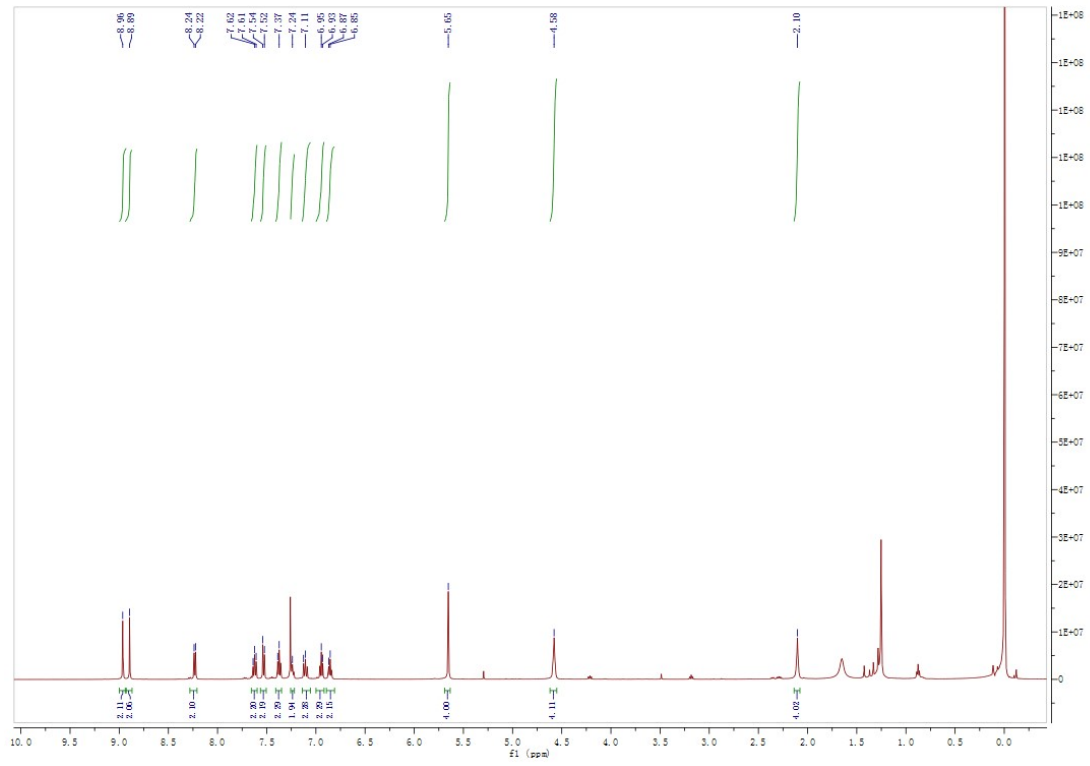
C NMR



469

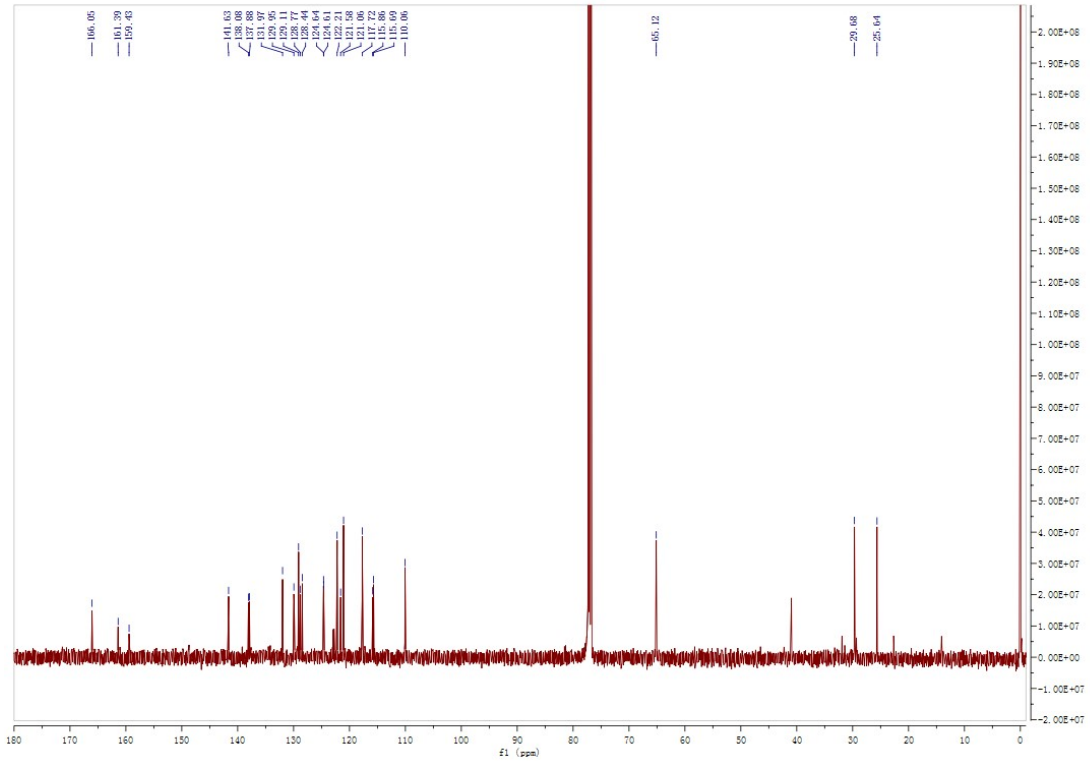
470 **6t**

471 H NMR



472

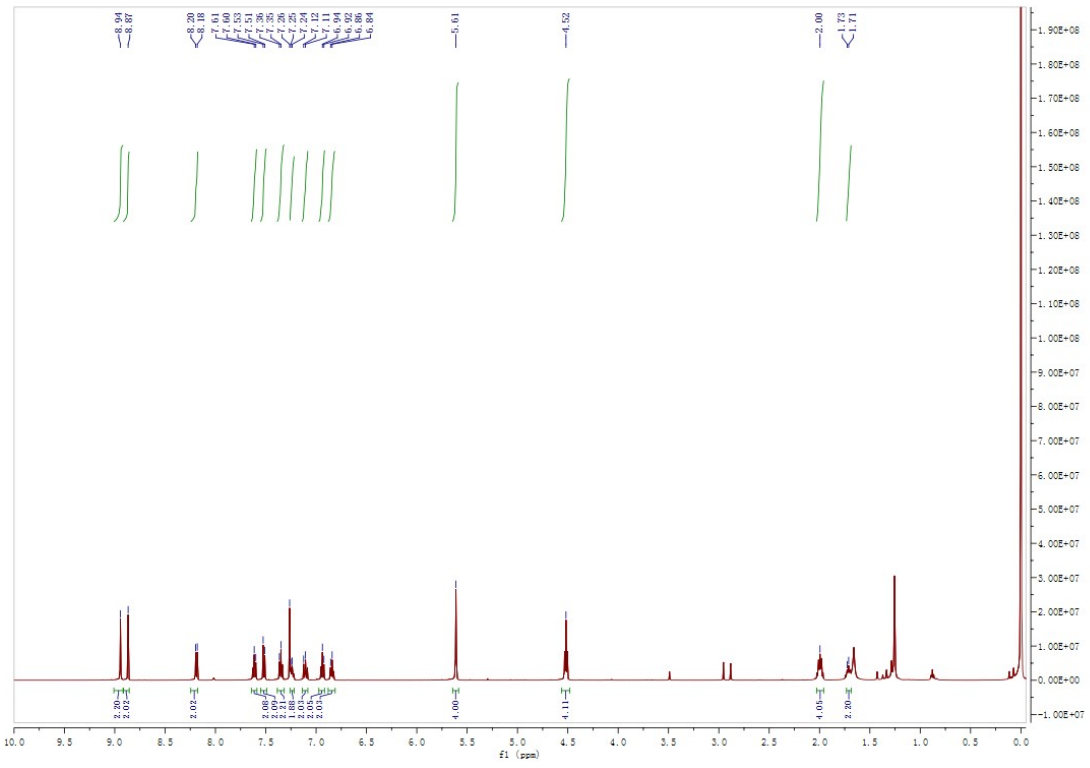
473 C NMR



474

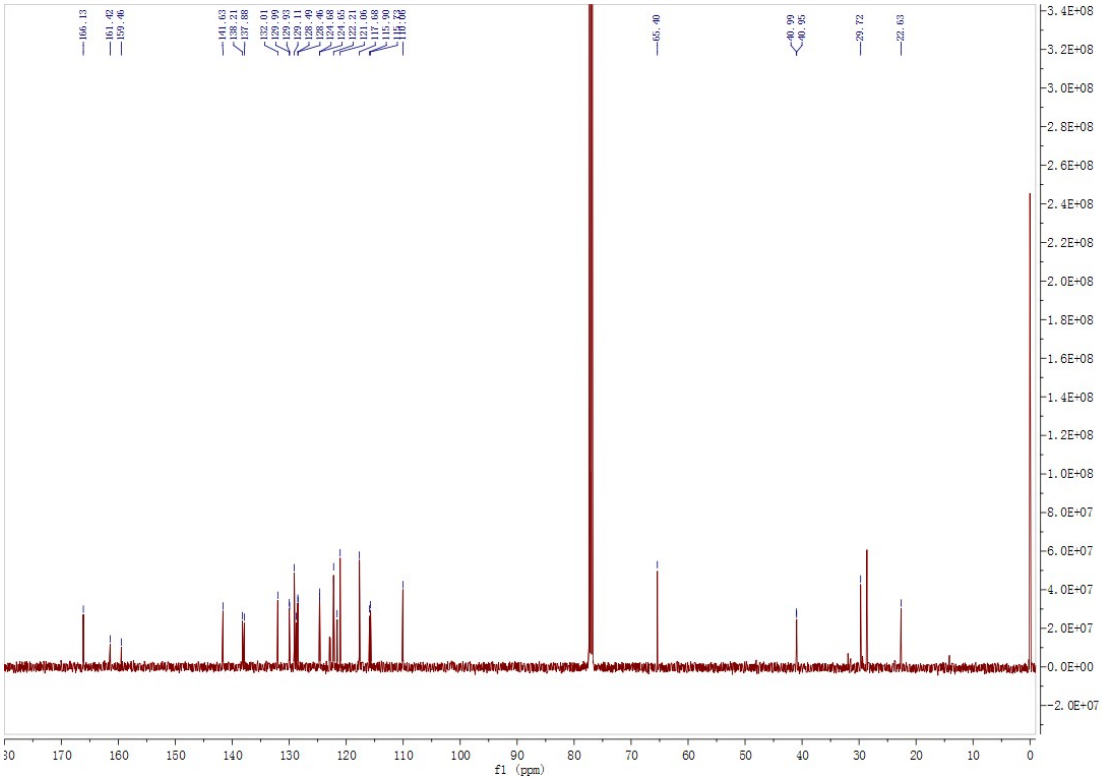
475 **6u**

476 H NMR



477

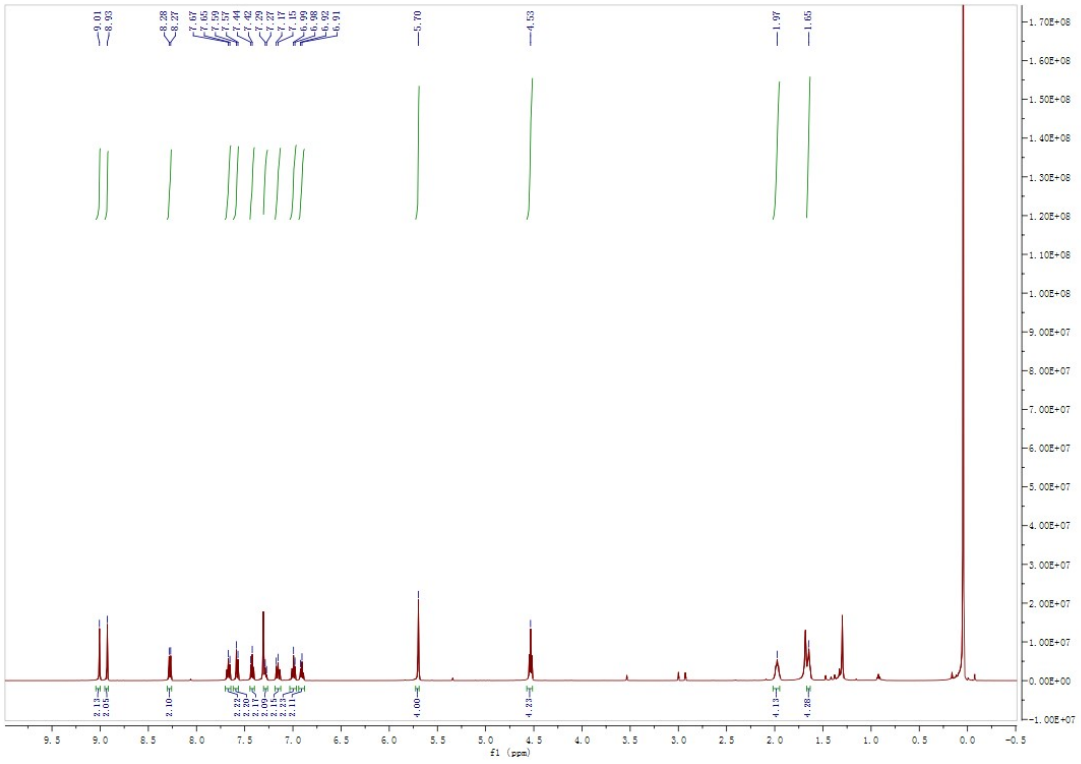
478 C NMR



479

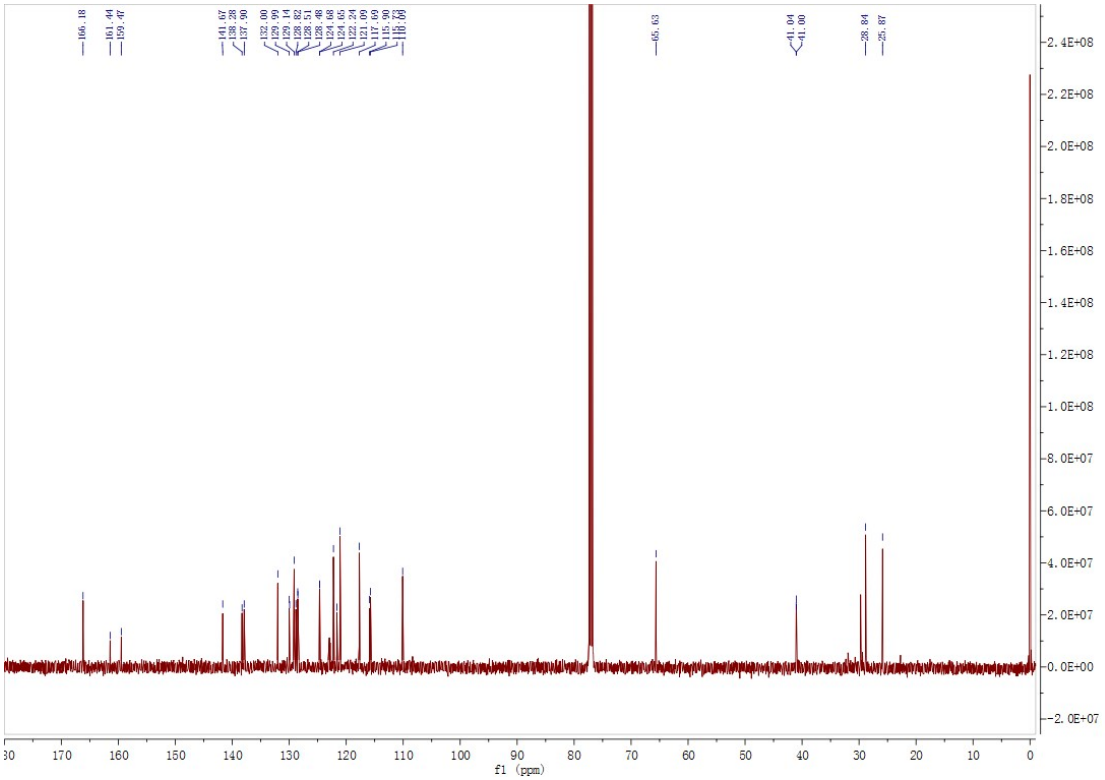
480 **6v**

481 H NMR



482

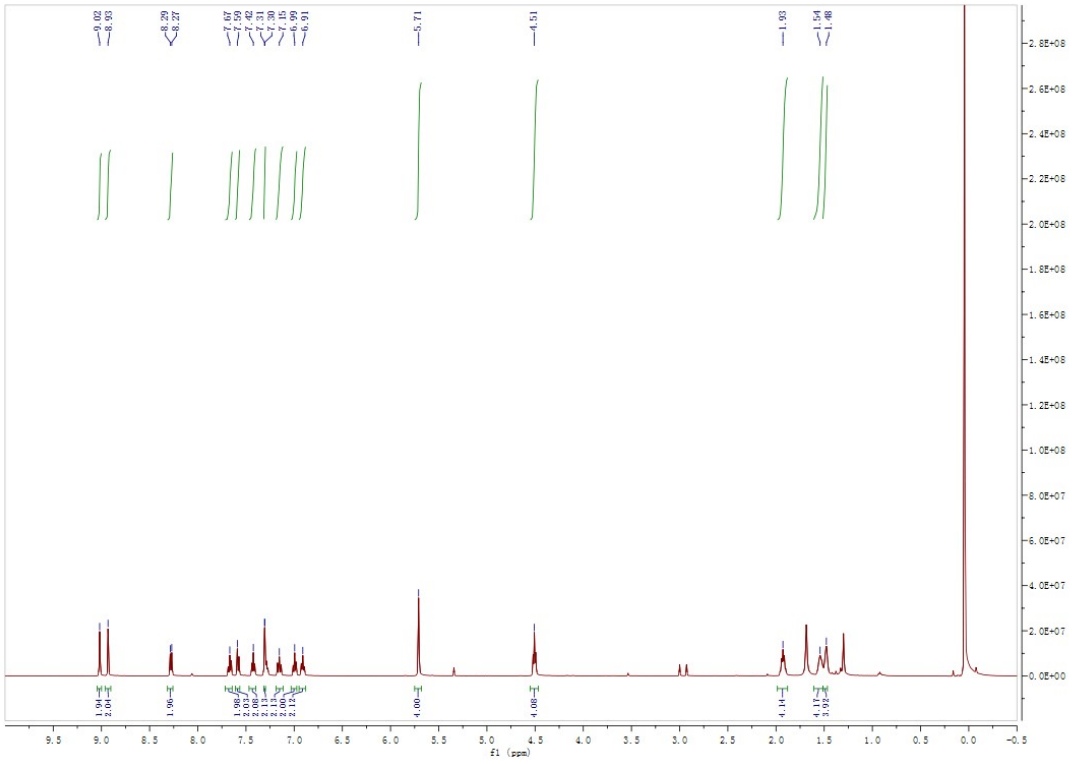
483 C NMR



484

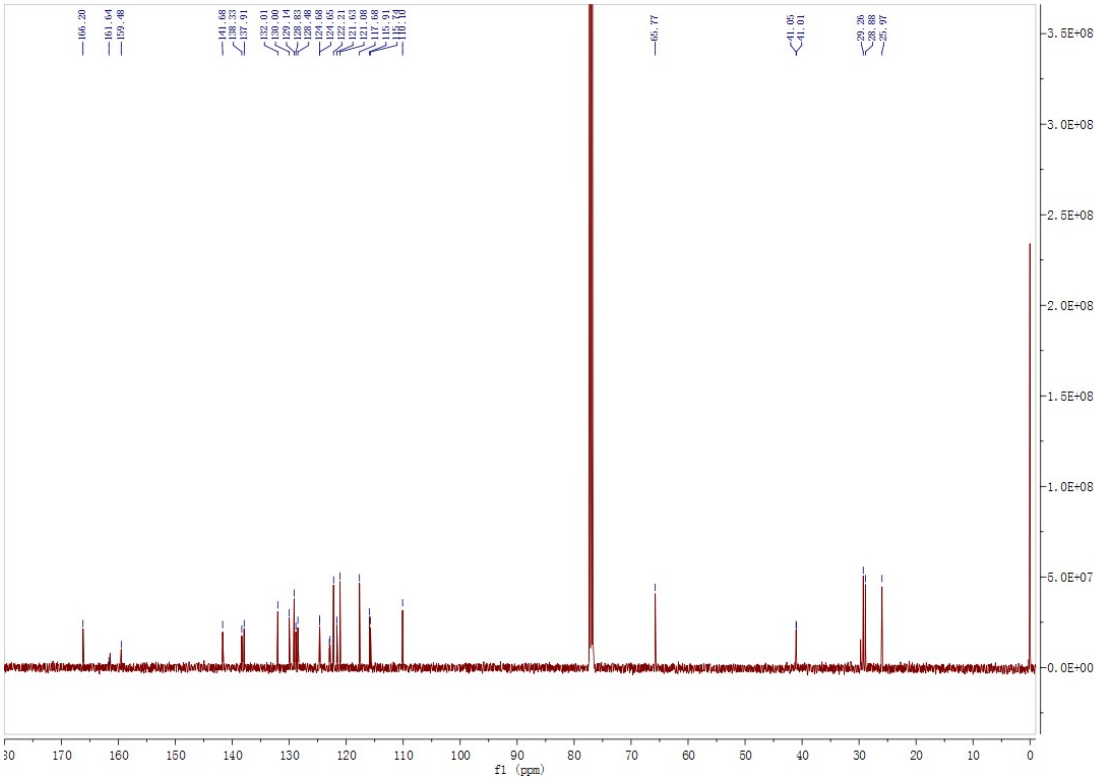
485 **6w**

486 H NMR



487

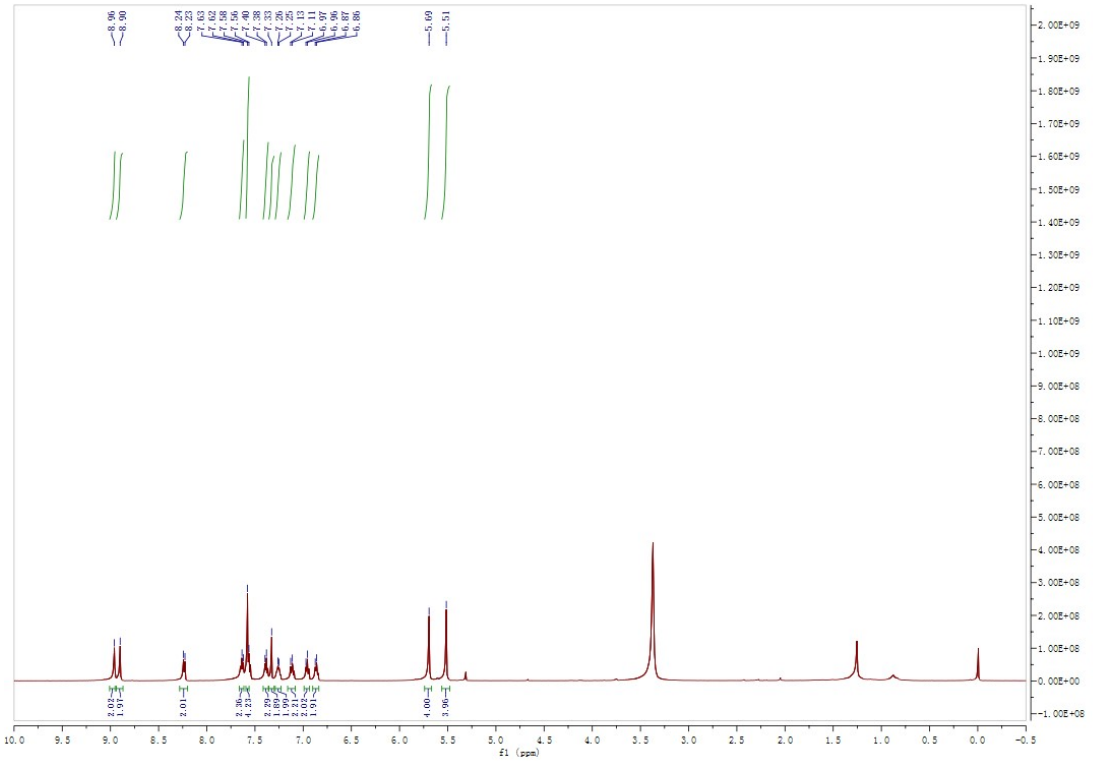
488 C NMR



489

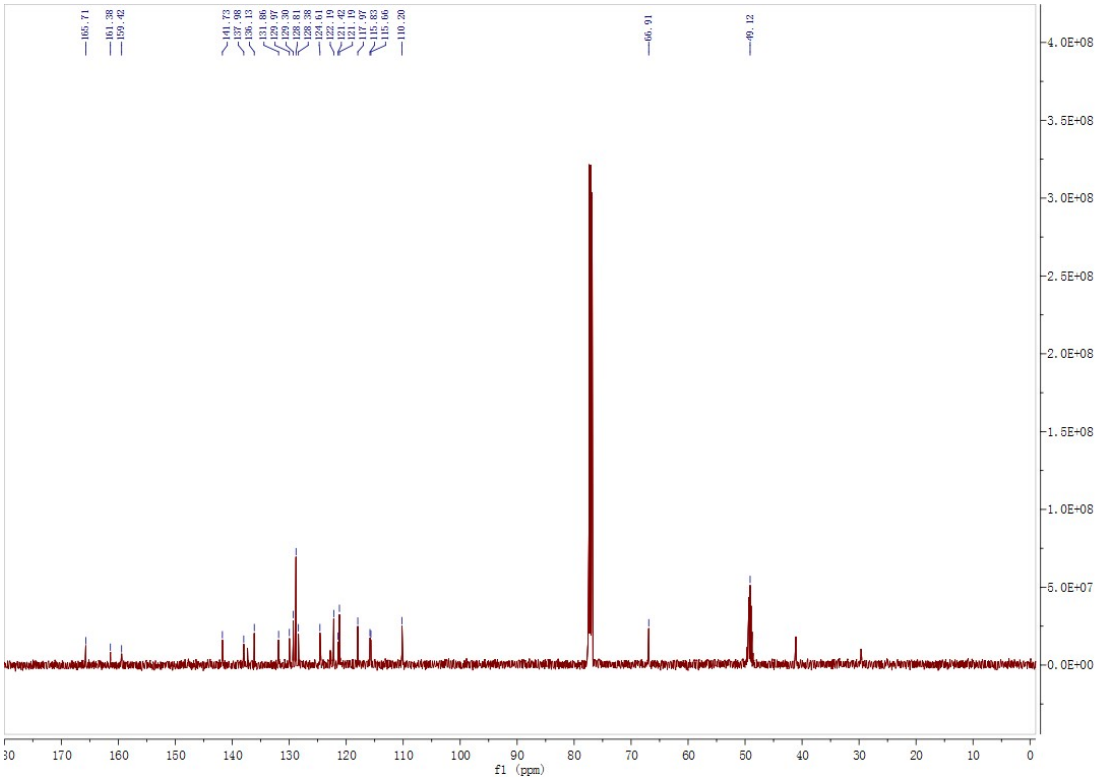
490 **6x**

491 H NMR



492

493 C NMR


165.71
161.38
159.42
141.73
137.98
136.13
131.86
130.07
129.30
128.81
128.38
124.61
122.19
121.42
121.10
117.97
115.83
115.66
110.20
66.91
49.12
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
f1 (ppm)

494