Selectfluor-induced C(sp^2)-O Coupling Reaction of *N*-substituted Anilines with Hydroxylamine Derivatives

Bin Sun,[a] Shi Yin,[b] Xiaohui Zhuang,[b] Can Jin,*[b] and Weike Su*[a,b]

[a] Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology, Hangzhou, P. R. China.

[b] College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou, P. R. China.

Supporting Information

Contents

1、General and Experimental Information

Melting points were determined using a digital melting point apparatus and uncorrected. ^{1}H NMR spectra were recorded at 400, 500 and 600MHz using TMS as internal standard, ^{13}C NMR spectra were recorded at 100, 125 and 150 MHz using TMS as internal standard. All chemical shifts were reported as δ values (ppm) relative to TMS and observed coupling constants (*J*) are given in Hertz (Hz). Mass spectra were measured with a HRMS-ESI instrument. All chemical reagents were purchased from commercial source and without prior purification. Column Chromatography was performed on silica gel (200-300 mesh) and the elution was performed with *n*-hexane/ethyl acetate.

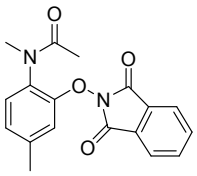
(i) General Procedure for the synthesis of 2a-2s2, 6ab-6gb (2a as example):

A suspension of *N*-substituted anilines **1a** (0.5 mmol), NHPI (0.6 mmol) and Selectfluor (1.0 mmol) in CH_3CN was stirred at 40 ^{o}C for 2 h. After cooling, water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and then concentrated under reduced pressure. The residues were purified by flash column chromatography (*n*-hexane-EtOAc) to afford the desired product **2a**.

(ii) General Procedure for the Synthesis of 2t'-2z3' (2t' as example)

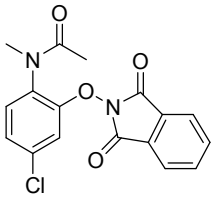
A suspension of **2t** (Prepared according to **(i)**), $NH_2OH{\cdot}HCl$ (1.5 mmol) and K_2CO_3 (1.5 mmol) in MeOH:$CHCl_3$(1:2)(6 mL) was stirred at 25 ^{o}C for 16 h. When the reaction was finished, water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and then Ac_2O (3.0 mmol), DMAP (0.05 mmol) was added. After being stirred for 2 h at 25 ^{o}C, the organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane-EtOAc) to afford the desired product **2t'**.

2、Characterization Data for the products



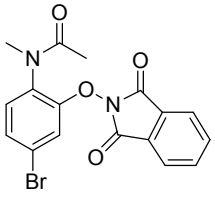
(2a)

2a: white solid; yield 85% (138 mg); m.p. 152.8-153.6 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96-7.93 (m, 2H), 7.88-7.85 (m, 2H), 7.16 (d, J = 7.8 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.84 (s, 1H), 3.33 (s, 3H), 2.33 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 162.6, 153.7, 140.2, 135.1, 129.3, 128.9, 128.8, 125.7, 124.1, 113.7, 36.2, 22.0, 21.5. HRMS: $C_{18}H_{17}N_2O_4$ $[M+H]^+$; calculated: 325.1183, found: 325.1183.



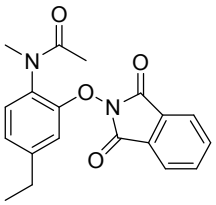
(2b)

2b: white solid; yield 65% (112 mg); m.p. 176.2-176.6 °C; ^{1}H NMR (600 MHz, DMSO-d^6): δ 7.98-7.90 (m, 4H), 7.85 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 3.16 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 163.3, 154.9, 135.4, 134.5, 131.8, 129.9, 129.7, 125.4, 124.1, 114.6, 35.9, 22.2. HRMS: $C_{17}H_{13}N_2O_4ClNa$ $[M+Na]^+$; calculated: 367.0456, found: 367.0453.



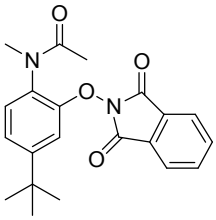
(2c)

2c: white solid; yield 60% (116 mg); m.p. 174.0-174.5 °C; ^{1}H NMR (500 MHz, DMSO-d^6): δ 8.16-7.73 (m, 5H), 7.46 (s, 2H), 3.15 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.9, 163.4, 154.9, 135.4, 132.1, 130.3, 129.8, 128.4, 124.1, 122.6, 117.2, 35.8, 22.2. HRMS: $C_{17}H_{13}N_2O_4BrNa$ $[M+Na]^+$; calculated: 410.9951, found: 410.9938.



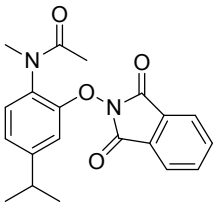
(2d)

2d: white solid; yield 77% (130 mg); m.p. 160.4-160.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97-7.94 (m, 2H), 7.88-7.86 (m, 2H), 7.19 (d, J = 7.8 Hz, 1H), 7.02 (d, J = 7.8, 1H), 6.86 (s, 1H), 3.34 (s, 3H), 2.62 (q, J = 7.8 Hz, 2H), 2.03 (s, 3H), 1.21 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 162.7, 153.9, 146.5, 135.1, 129.4, 129.1, 128.8, 124.3, 124.1, 112.7, 36.2, 28.7, 22.0, 15.2. HRMS: $C_{19}H_{18}N_2NaO_4[M+Na]^+$; calculated: 361.1159, found: 361.1156.



(2e)

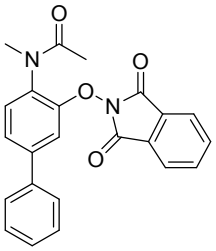
2e: white solid; yield 72% (132 mg); m.p. 166.3-167.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98-7.95 (m, 2H), 7.89-7.86 (m, 2H), 7.22-7.19 (m, 2H), 7.05 (s, 1H), 3.35 (s, 3H), 2.03 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 162.9, 153.6, 153.5, 135.1, 129.0, 128.8, 124.1, 122.2, 110.6, 36.2, 35.0, 31.2, 22.1. HRMS: $C_{21}H_{22}N_2NaO_4[M+Na]^+$; calculated: 389.1472, found: 389.1469.



(2f)

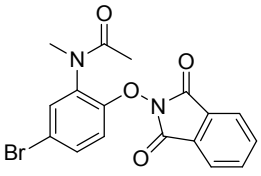
2f: white solid; yield 75% (132 mg); m.p. 145.8-146.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96-7.94 (m, 2H), 7.88-7.86 (m, 2H), 7.20 (d, J = 7.8 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 6.87 (s, 1H), 3.34 (s, 3H), 2.90-2.83 (m, 1H),

2.03 (s, 3H), 1.21 (d, J = 7.2 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.6, 162.8, 153.8, 151.1, 135.1, 129.4, 129.1, 128.8, 124.1, 122.7, 111.6, 36.2, 34.1, 23.8, 22.1. HRMS: $C_{20}H_{20}N_2NaO_4[M+Na]^+$; calculated: 375.1315, found: 375.1305.



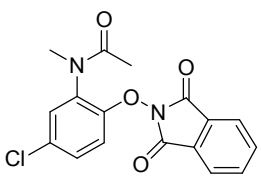
(2g)

2g: white solid; yield 80% (154 mg); m.p. 174.5-175.6 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97-7.94 (m, 2H), 7.88-7.85 (m, 2H), 7.51-7.49 (m, 2H), 7.43-7.35 (m, 5H), 7.22 (s, 1H), 3.40 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.4, 162.7, 154.3, 143.2, 139.4, 135.2, 130.6, 130.0, 128.9, 128.8, 128.2, 127.2, 124.2, 123.8, 112.1, 36.2, 22.2. HRMS: $C_{23}H_{18}N_2NaO_4[M+Na]^+$; calculated: 409.1159, found: 409.1140.



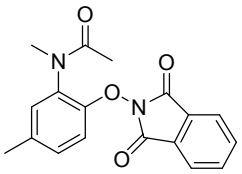
(2h)

2h: white solid; yield 35% (68 mg); m.p. 171.2-172.0 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.93 (m, 4H), 7.82 (s, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 3.20 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.8, 163.1, 153.8, 135.6, 133.0, 132.9, 132.4, 129.3, 124.2, 116.2, 35.9, 22.2. HRMS: $C_{17}H_{13}BrN_2NaO_4[M+Na]^+$; calculated: 410.9951, found: 410.9951.



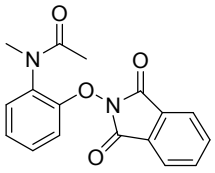
(2i)

2i: white solid; yield 31% (53 mg); m.p. 174.0-175.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.94 (m, 4H), 7.71 (s, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 3.20 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.8, 163.1, 153.4, 135.6, 132.2, 130.3, 130.0, 129.3, 128.6, 124.2, 115.9, 35.9, 22.2. HRMS: $C_{17}H_{13}ClN_2NaO_4[M+Na]^+$; calculated: 367.0456, found: 367.0441.



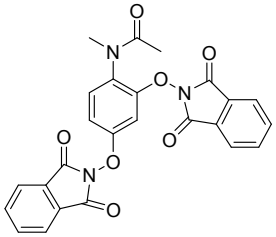
(2j)

2j: white solid; yield 39% (63 mg); m.p. 153.0-154.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93-7.90 (m, 2H), 7.86-7.82 (s, 2H), 7.09-7.08 (m, 2H), 6.94 (d, J = 9.0 Hz, 1H), 3.33 (s, 3H), 2.34 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.3, 162.6, 152.0, 135.1, 135.0, 131.3, 130.0, 129.9, 128.8, 124.0, 113.4, 36.2, 22.0, 20.5. HRMS: $C_{18}H_{17}N_2O_4[M+H]^+$; calculated: 325.1183, found: 325.1181.



(2k)

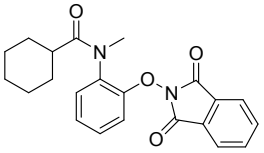
2k: white solid; yield 43% (67 mg); m.p. 153.7-154.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95-7.93 (m, 2H), 7.87-7.85 (m, 2H), 7.33-7.28 (m, 2H), 7.20 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 3.36 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.3, 162.6, 154.2, 135.1, 131.6, 129.8, 129.6, 128.7, 125.1, 124.1, 113.3, 36.1, 22.0. HRMS: $C_{17}H_{15}N_2O_4[M+H]^+$; calculated: 311.1026, found: 311.1030.



(2k')

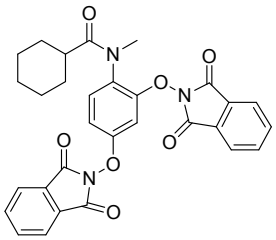
2k': white solid; yield 23% (54 mg); m.p. 186.7-187.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98-7.93 (m, 4H), 7.89-7.84 (m, 4H), 7.25 (d, J = 6.0 Hz,

1H), 7.04 (d, J = 2.4 Hz, 1H), 6.90 (d, J = 4.8 Hz, 1H), 3.33 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 162.7, 162.4, 159.1, 155.2, 135.3, 135.2, 130.7, 128.8, 128.7, 128.1, 124.3, 124.2, 109.3, 101.6, 36.2, 22.1. HRMS: $C_{25}H_{18}N_3O_7$ $[M+H]^+$; calculated: 472.1139, found: 472.1130.



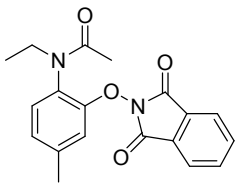
(2l)

2l: white solid; yield 41% (77 mg); m.p. 178.5-179.2 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95-7.92 (m, 2H), 7.88-7.84 (m, 2H), 7.34-7.27 (m, 2H), 7.18 (t, J = 11.4 Hz, 1H), 7.03 (d, J = 12.6 Hz, 1H), 3.34 (s, 3H), 2.33-2.26 (m, 1H), 1.92-1.89 (m, 1H), 1.76-1.48 (m, 6H), 1.24-1.19 (m, 2H), 1.07-0.98 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 162.5, 154.1, 135.1, 130.9, 129.9, 129.4, 128.8, 124.7, 124.1, 112.5, 41.6, 36.2, 29.9, 29.0, 25.7, 25.4. HRMS: $C_{22}H_{22}N_2NaO_4$ $[M+Na]^+$; calculated: 401.1472, found: 401.1491.



(2l')

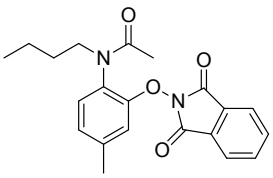
2l': white solid; yield 24% (65 mg); m.p. 142.0-143.1 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97-7.92 (m, 4H), 7.89-7.84 (m, 4H), 7.22 (d, J = 13.2 Hz, 1H), 7.01 (d, J = 6.3 Hz, 1H), 6.88 (dd, J_1 = 13.2 Hz, J_2 = 6.3 Hz, 1H), 3.30 (s, 3H), 2.31-2.27 (m, 1H), 1.78-1.76 (m, 1H), 1.59-1.47 (m, 5H), 1.24-1.08 (m, 2H), 0.92-0.89 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 162.7, 162.3, 159.0, 155.1, 135.3, 135.2, 130.7, 128.8, 128.6, 127.4, 124.3, 124.2, 108.8, 101.0, 41.4, 36.4, 29.9, 29.0, 25.7, 25.6, 25.3. HRMS: $C_{30}H_{25}N_3NaO_7$ $[M+Na]^+$; calculated: 562.1585, found: 562.1577.



(2m)

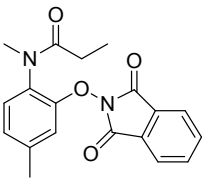
2m: white solid; yield 71% (120 mg); m.p. 151.4-151.7 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97-7.94 (m, 2H), 7.89-7.86 (m, 2H), 7.12 (d, J = 8.4 Hz,

1H), 6.98 (d, J = 7.8 Hz, 1H), 6.82 (s, 1H), 3.97-3.92 (m, 1H), 3.76-3.70 (m, 1H), 2.34 (s, 3H), 2.02 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 162.6, 153.9, 140.2, 135.1, 130.4, 128.8, 127.0, 125.3, 124.1, 113.0, 43.2, 22.4, 21.4, 13.1. HRMS: $C_{19}H_{19}N_2O_4$ $[M+H]^+$; calculated: 339.1339, found: 339.1348.



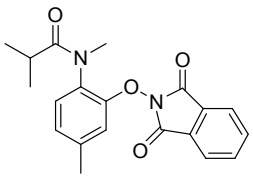
(2n)

2n: white solid; yield 81% (148 mg); m.p. 144.5-145.0 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94-7.93 (m, 2H), 7.87-7.85 (m, 2H), 7.11 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 6.80 (s, 1H), 3.94-3.89 (m, 1H), 3.64-3.59 (m, 1H), 2.32 (s, 3H), 2.01 (s, 3H), 1.62-1.54 (m, 2H), 1.40-1.33 (m, 2H), 0.93 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2, 162.6, 153.9, 140.1, 135.1, 130.4, 128.8, 127.4, 125.3, 124.1, 113.0, 48.1, 30.0, 22.4, 21.5, 20.2, 13.9. HRMS: $C_{21}H_{23}N_2O_4$ $[M+H]^+$; calculated: 367.1652, found: 367.1660.



(2o)

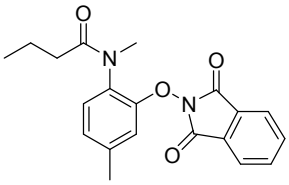
2o: white solid; yield 74% (125 mg); m.p. 164.3-165.0 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97-7.94 (m, 2H), 7.88-7.85 (m, 2H), 7.14 (d, J = 7.8 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 6.84 (s, 1H), 3.34 (s, 3H), 2.37-2.31 (m, 4H), 2.20-2.14 (m, 1H), 1.13 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.7, 162.6, 153.8, 140.1, 135.1, 129.6, 128.8, 128.5, 125.6, 124.1, 113.6, 36.2, 27.1, 21.5, 9.5. HRMS: $C_{19}H_{18}N_2O_4Na$ $[M+Na]^+$; calculated: 361.1159, found: 361.1153.



(2p)

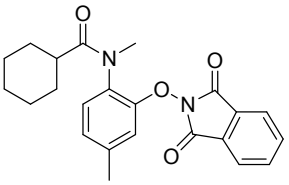
2p: white solid; yield 84% (148 mg); m.p. 180.5-181.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93-7.91 (m, 2H), 7.85-7.83 (m, 2H), 7.13 (d, J = 8.0 Hz,

1H), 6.98 (d, J = 7.5 Hz, 1H), 6.80 (s, 1H), 3.31 (s, 3H), 2.63-2.58 (m, 1H), 2.31 (s, 3H), 1.14 (d, J = 6.5 Hz, 3H), 1.05 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 162.5, 153.7, 140.0, 135.1, 129.5, 128.7, 128.2, 125.4, 124.0, 113.1, 36.2, 31.2, 21.4, 20.0, 19.4. HRMS: $C_{20}H_{21}N_2O_4$ $[M+H]^+$; calculated: 353.1496, found: 353.1497.



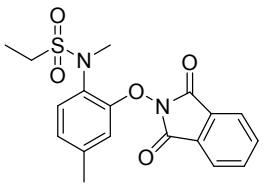
(2q)

2q: white solid; yield 88% (155 mg); m.p. 169.0-169.5 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95-7.92 (m, 2H), 7.87-7.83 (m, 2H), 7.12 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.82 (s, 1H), 3.32 (s, 3H), 2.32-2.25 (m, 4H), 2.15-2.09 (m, 1H), 1.72-1.61 (m, 2H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 162.6, 153.7, 140.1, 135.1, 129.6, 128.8, 128.5, 125.5, 124.1, 113.5, 36.1, 35.6, 21.5, 18.6, 13.9. HRMS: $C_{20}H_{21}N_2O_4$ $[M+H]^+$; calculated: 353.1496, found: 353.1497.



(2r)

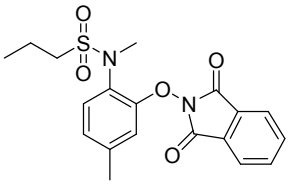
2r: white solid; yield 76% (149 mg); m.p. 170.0-170.5 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95-7.93 (m, 2H), 7.86-7.85 (m, 2H), 7.13 (d, J = 7.8 Hz, 1H), 6.96 (d, J = 7.8 Hz, 1H), 6.80 (s, 1H), 3.31 (s, 3H), 2.34-2.29 (m, 4H), 1.90-1.88 (m, 1H), 1.76-1.46 (m, 6H), 1.23-1.20 (m, 2H), 1.06-1.00 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 162.6, 153.7, 140.0, 135.1, 129.5, 128.8, 128.3, 125.4, 124.1, 113.0, 41.5, 36.3, 29.9, 29.0, 25.8, 25.7, 25.4, 21.5. HRMS: $C_{20}H_{25}N_2O_4$ $[M+H]^+$; calculated: 393.1809, found: 393.1823.



(2s1)

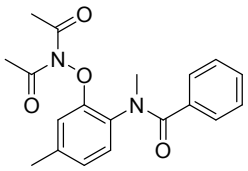
2s1: white solid; yield 65% (121 mg); m.p. 129.1-129.9 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98-7.94 (m, 2H), 7.90-7.86 (m, 2H), 7.42 (d, J = 8.0 Hz,

1H), 6.95 (d, J = 8.0 Hz, 1H), 6.75 (s, 1H), 3.44 (s, 3H), 3.27 (q, J = 7.5 Hz, 2H), 2.29 (s, 3H), 1.43 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 154.5, 140.4, 135.2, 132.9, 128.7, 125.4, 124.5, 124.2, 112.6, 46.2, 38.5, 21.4, 8.1. HRMS: $C_{18}H_{19}N_2O_5S$ $[M+H]^+$; calculated: 375.1009, found: 375.1007.



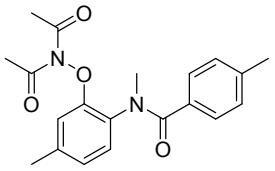
(2s2)

2s2: white solid; yield 70% (136 mg); m.p. 136.3-137.0 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00-7.97 (m, 2H), 7.91-7.88 (m, 2H), 7.43 (d, J = 7.8 Hz, 1H), 6.96 (d, J = 7.8 Hz, 1H), 6.76 (s, 1H), 3.45 (s, 3H), 3.25-3.22 (m, 2H), 2.31 (s, 3H), 1.98-1.91 (m, 2H), 1.07 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.6, 154.6, 140.5, 135.2, 133.0, 128.8, 125.4, 124.6, 124.2, 112.5, 53.4, 38.3, 21.5, 17.1, 13.1. HRMS: $C_{19}H_{21}N_2O_5S$ $[M+H]^+$; calculated: 389.1166, found: 389.1180.



(2t')

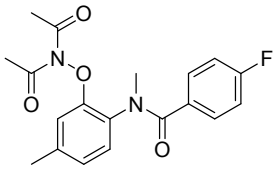
2t': white solid; yield 85% (145 mg); m.p. 134.2-134.8 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49 (d, J = 7.2 Hz, 2H), 7.27-7.20 (m, 3H), 6.95 (d, J = 7.8 Hz, 1H), 6.76 (d, J = 7.2 Hz, 1H), 6.51 (s, 1H), 3.48 (s, 3H), 2.38 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 168.9, 152.2, 139.4, 135.7, 130.3, 129.8, 129.1, 128.5, 127.7, 124.8, 111.4, 37.4, 24.6, 21.5. HRMS: $C_{19}H_{21}N_2O_4$ $[M+H]^+$; calculated: 341.1496, found: 341.1498.



(2u')

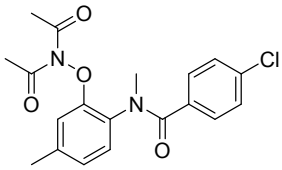
2u': white solid; yield 76% (135 mg); m.p. 155.5-156.1 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 (d, J = 7.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 7.2 Hz, 1H), 6.76 (d, J = 7.2 Hz, 1H), 6.54 (s, 1H), 3.44 (s, 3H), 2.41 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 169.0, 152.2,

140.0, 139.3, 132.7, 130.3, 129.4, 128.6, 128.3, 124.8, 111.3, 37.5, 24.6, 21.5, 21.3. HRMS: $C_{20}H_{23}N_2O_4$ $[M+H]^+$; calculated: 355.1652, found: 355.1654.



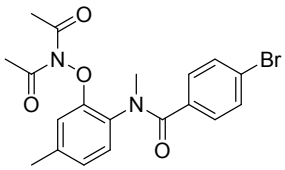
(2v')

2v': white solid; yield 60% (107 mg); m.p. 134.3-134.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54-7.52 (m, 2H), 6.91-6.88 (m, 3H), 6.77 (d, J = 7.8 Hz, 1H), 6.54 (s, 1H), 3.45 (s, 3H), 2.41 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 168.8, 163.4 (d, $J_{C\text{-}F}$ = 248.7 Hz), 152.2, 139.7, 131.7, 130.9 (d, $J_{C\text{-}F}$ = 8.4 Hz), 130.2, 129.0, 124.9, 114.8 (d, $J_{C\text{-}F}$ = 21.6 Hz), 111.5, 37.6, 24.7, 21.5. HRMS: $C_{19}H_{20}FN_2O_4$ $[M+H]^+$; calculated: 359.1402, found: 359.1397.



(2w')

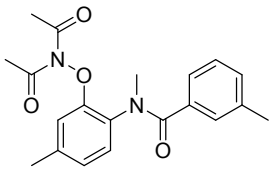
2w': white solid; yield 74% (138 mg); m.p. 152.8-153.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 (d, J = 7.2 Hz, 2H), 7.18 (d, J = 6.6 Hz, 2H), 6.89 (d, J = 6.6 Hz, 1H), 6.76 (d, J = 6.6 Hz, 1H), 6.54 (s, 1H), 3.44 (s, 3H), 2.40 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 168.8, 152.2, 139.8, 135.9, 134.0, 130.2, 130.0, 128.8, 128.0, 125.0, 111.5, 37.5, 24.7, 21.5. HRMS: $C_{19}H_{20}N_2O_4Cl$ $[M+H]^+$; calculated: 375.1106, found: 375.1102.



(2x')

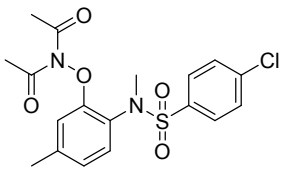
2x': white solid; yield 69% (144 mg); m.p. 159.8-160.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 (d, J = 7.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 7.8 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 6.54 (s, 1H), 3.45 (s, 3H), 2.42 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 168.8, 152.2, 139.8, 134.5, 131.0, 130.2, 128.8, 125.0, 124.3, 111.5, 37.5, 24.7, 21.6.

HRMS: $C_{19}H_{20}N_2O_4Br$ $[M+H]^+$; calculated: 419.0601, found: 419.0611.



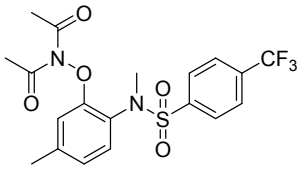
(2y')

2y': white solid; yield 85% (150 mg); m.p. 124.4-124.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 (s, 1H), 7.19 (s, 1H), 7.03 (s, 2H), 6.92 (d, J = 6.0 Hz, 1H), 6.73 (d, J = 6.0 Hz, 1H), 6.50 (s, 1H), 3.45 (s, 3H), 2.36 (s, 6H), 2.25 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.3, 168.9, 152.2, 139.3, 137.4, 135.6, 130.5, 130.3, 129.2, 127.4, 125.5, 124.8, 111.3, 37.3, 24.6, 21.5, 21.1. HRMS: $C_{20}H_{23}N_2O_4$ $[M+H]^+$; calculated: 355.1652, found: 355.1657.



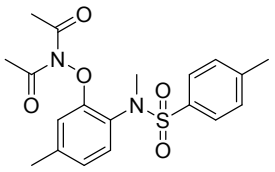
(2z1')

2z1': white solid; yield 67% (137 mg); m.p. 150.8-151.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.59 (s, 1H), 3.29 (s, 3H), 2.41 (s, 6H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 140.7, 139.1, 138.2, 130.1, 129.3, 129.0, 124.7, 124.5, 111.6, 38.3, 24.7, 21.6. HRMS: $C_{18}H_{19}N_2O_5ClSNa$ $[M+Na]^+$; calculated: 433.0595, found: 433.0588.



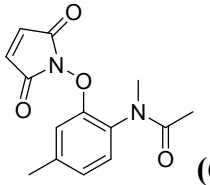
(2z2')

2z2': white solid; yield 65% (144 mg); m.p. 143.0-144.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 7.8 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.61 (s, 1H), 3.34 (s, 3H), 2.40 (s, 6H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 143.3, 140.8, 134.3 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.3, 128.0, 126.2 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.6, 124.4, 123.3 (d, $J_{C\text{-}F}$ = 271.4 Hz), 111.7, 38.4, 24.6, 21.6. HRMS: $C_{19}H_{19}F_3N_2O_5SNa$ $[M+Na]^+$; calculated: 467.0859, found: 467.0874.



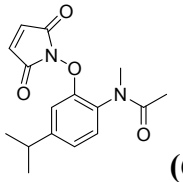
(2z3')

2z3': white solid; yield 76% (148 mg); m.p. 148.4-149.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 6.93 (d, J = 7.8 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 6.59 (s, 1H), 3.28 (s, 3H), 2.46 (s, 3H), 2.42 (s, 6H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 154.7, 143.4, 140.3, 136.7, 130.1, 129.6, 127.7, 125.2, 124.4, 111.5, 38.3, 24.7, 21.6, 21.5. HRMS: $C_{19}H_{22}N_2O_5SNa$ $[M+Na]^+$; calculated: 413.1142, found: 413.1129.



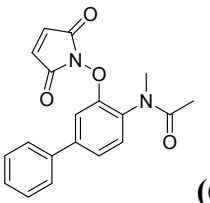
(6ab)

6ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.85 (s, 2H), 6.82 (s, 1H), 3.27 (s, 3H), 2.36 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 164.9, 153.7, 140.2, 132.8, 129.3, 128.8, 125.7, 113.7, 36.2, 22.0, 21.5. HRMS: $C_{14}H_{14}N_2NaO_4$ $[M+Na]^+$; calculated: 297.0850, found: 297.0850.



(6fb)

6fb: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.92-6.77 (m, 3H), 3.28 (s, 3H), 2.93-2.84 (m, 1H), 1.96 (s, 3H), 1.24 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 165.0, 153.8, 151.1, 132.8, 129.4, 129.0, 122.8, 111.5, 36.2, 34.1, 23.8, 23.7, 22.0. HRMS: $C_{16}H_{18}N_2NaO_4$ $[M+Na]^+$; calculated: 325.1148, found: 325.1159.

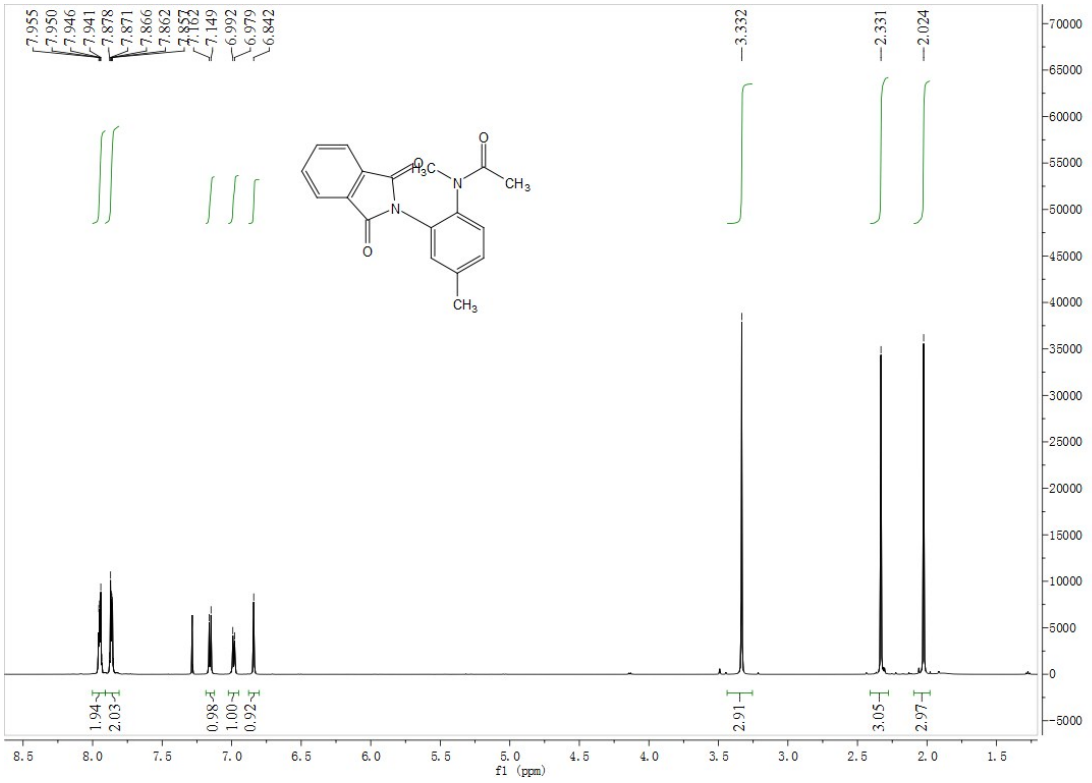


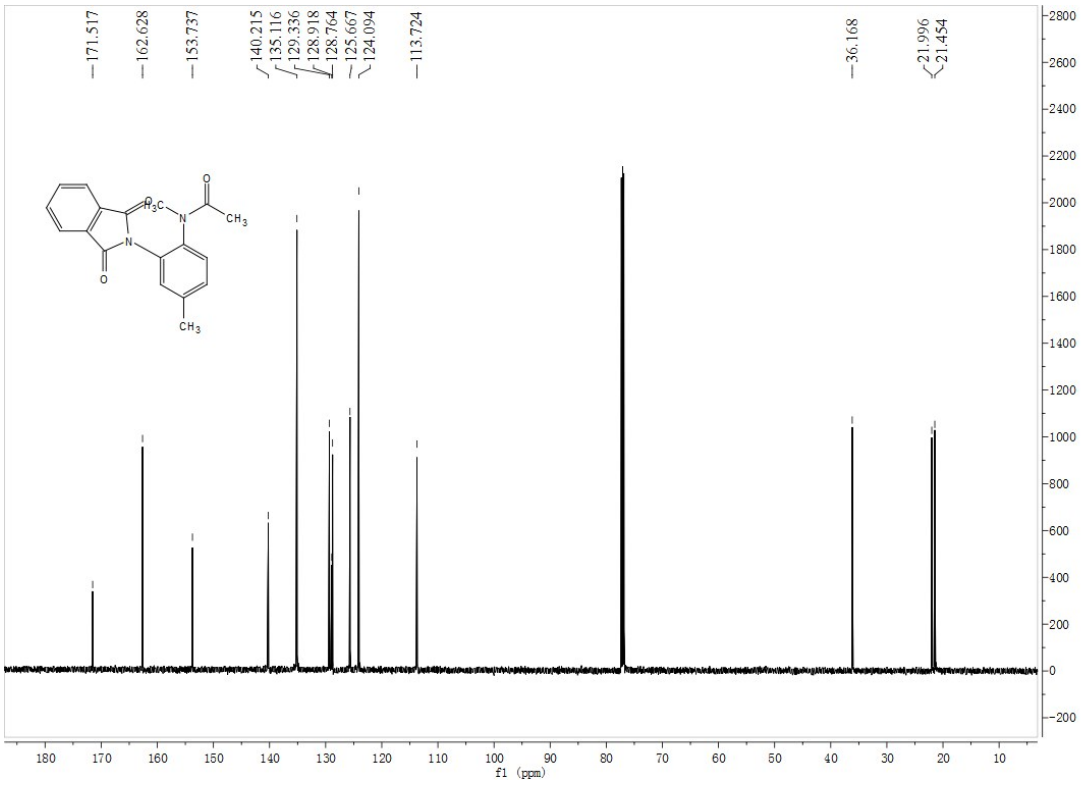
(6gb)

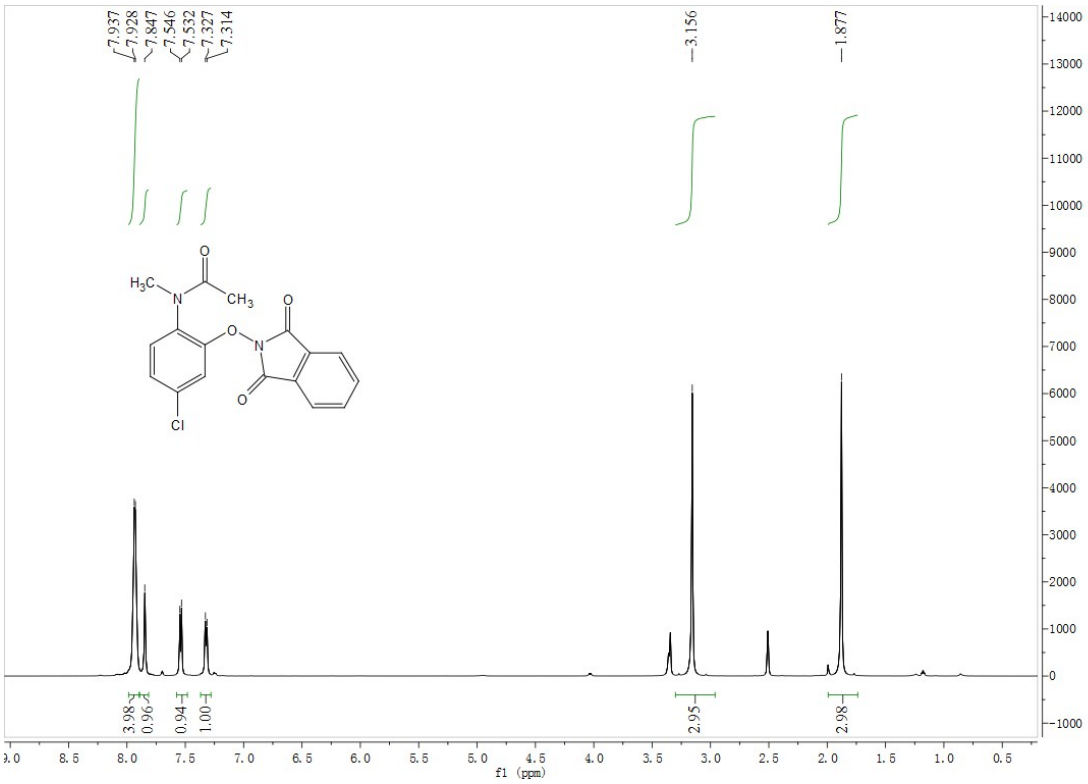
6gb: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.50 (m, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.43–7.37 (m, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 1.6 Hz, 1H),

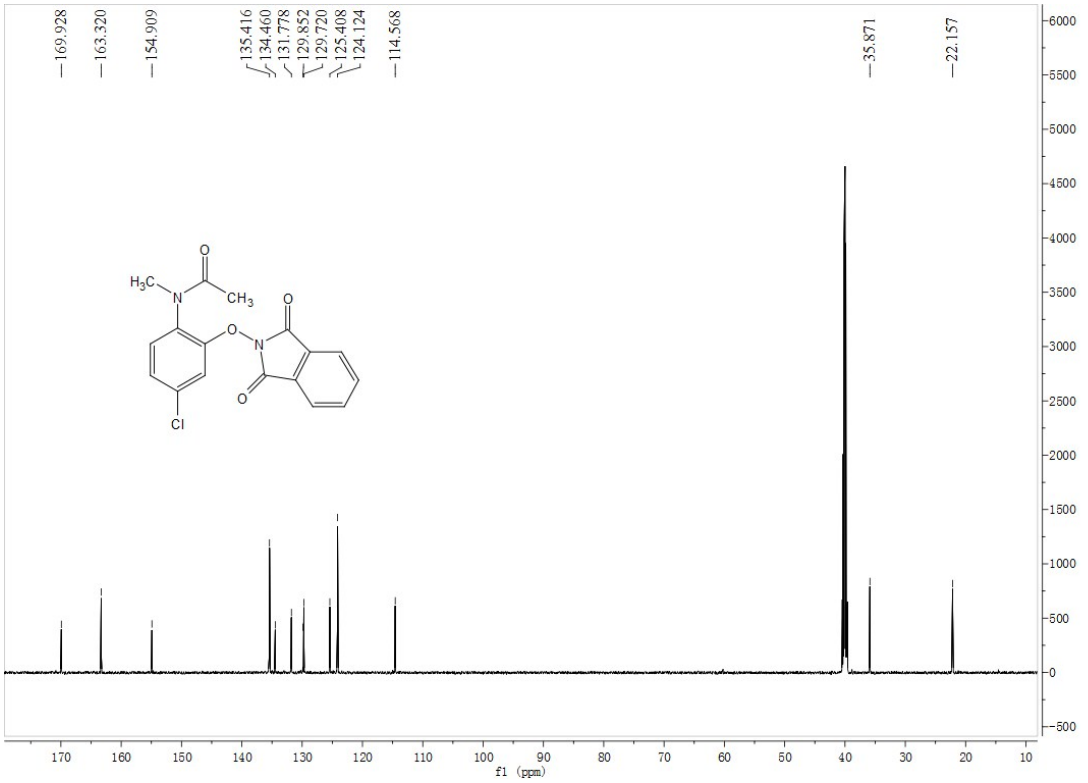
6.86 (s, 2H), 3.34 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 164.9, 154.3, 143.2, 139.5, 132.9, 130.5, 129.9, 129.0, 128.2, 127.2, 123.8, 112.1, 36.2, 22.1. HRMS: $C_{19}H_{16}N_2NaO_4$ $[M+Na]^+$; calculated: 359.1002, found: 359.0990.

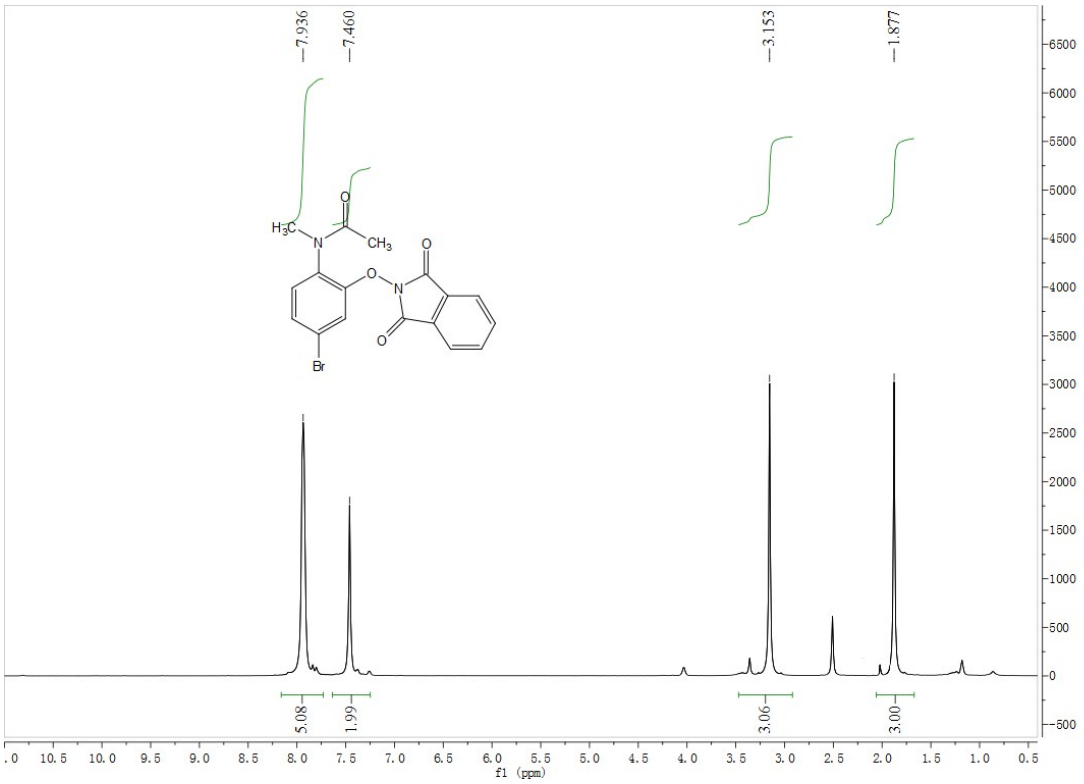
Copies of NMR Spectra

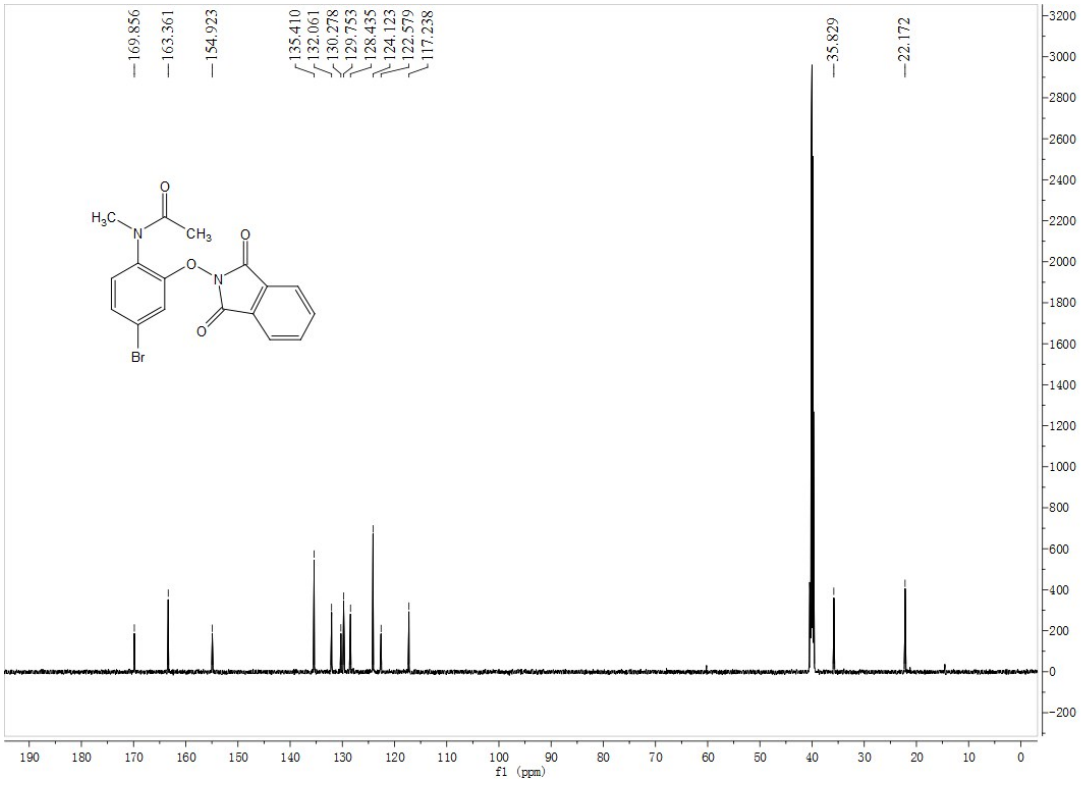


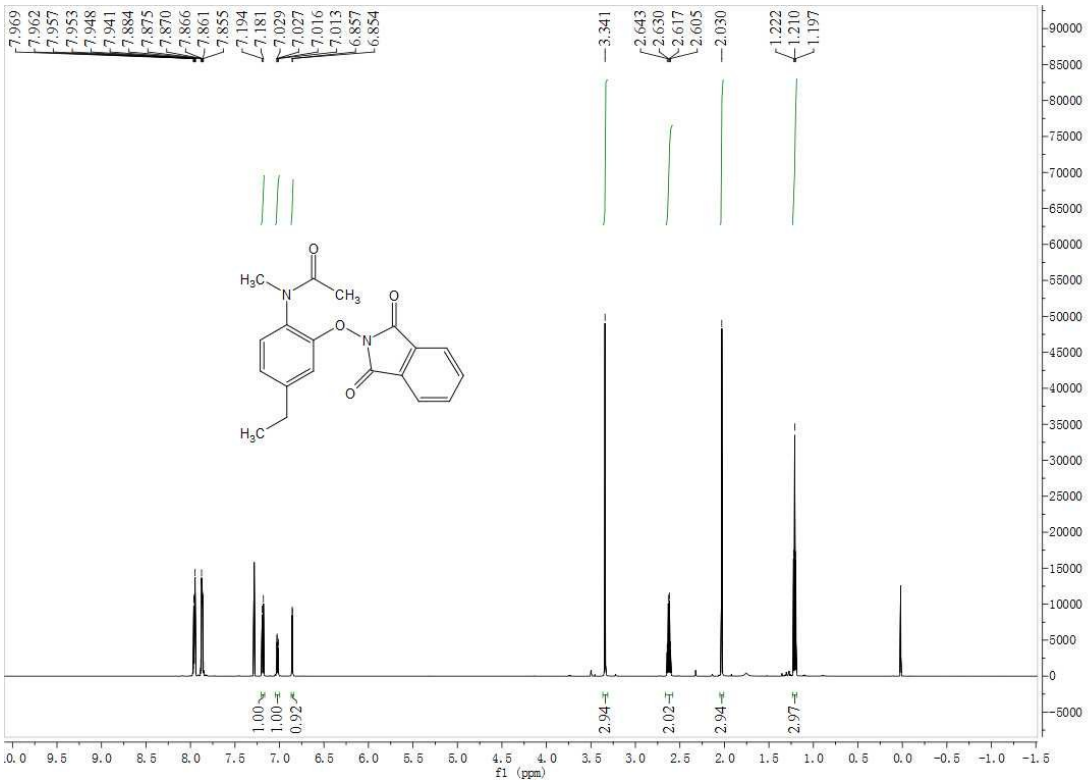


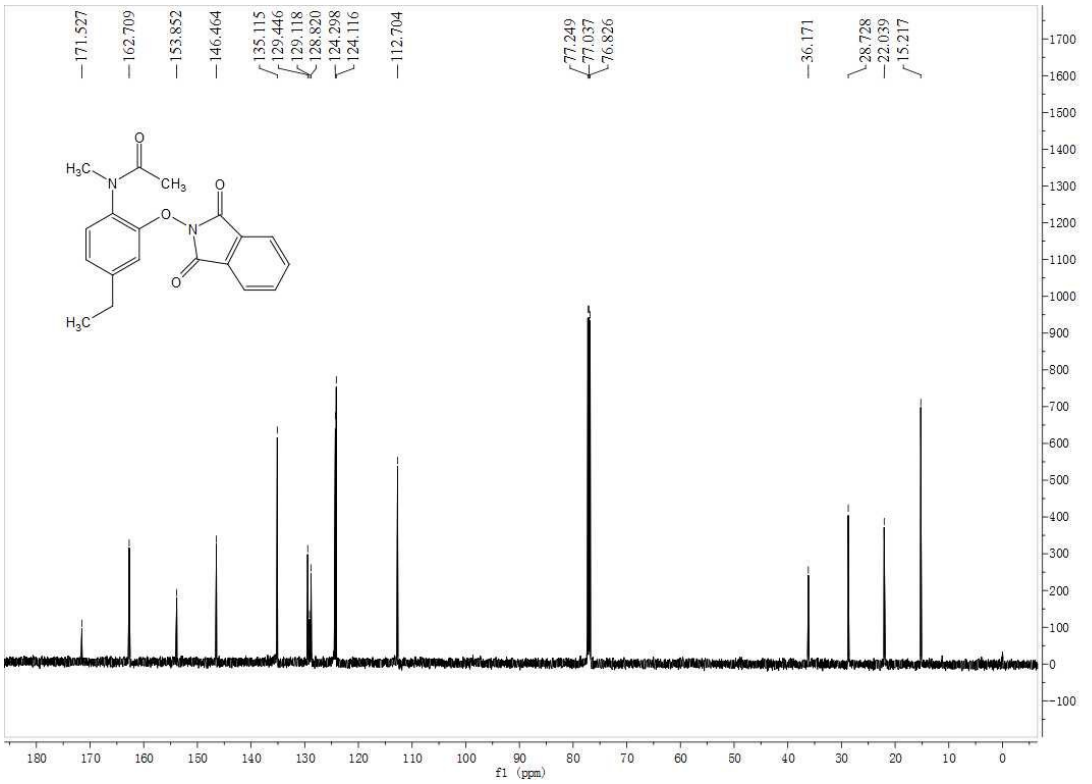

7.937
7.928
7.847
7.546
7.532
7.327
7.314
3.156
1.877
3.98
0.96
0.94
1.00
2.95
2.98
f1 (ppm)

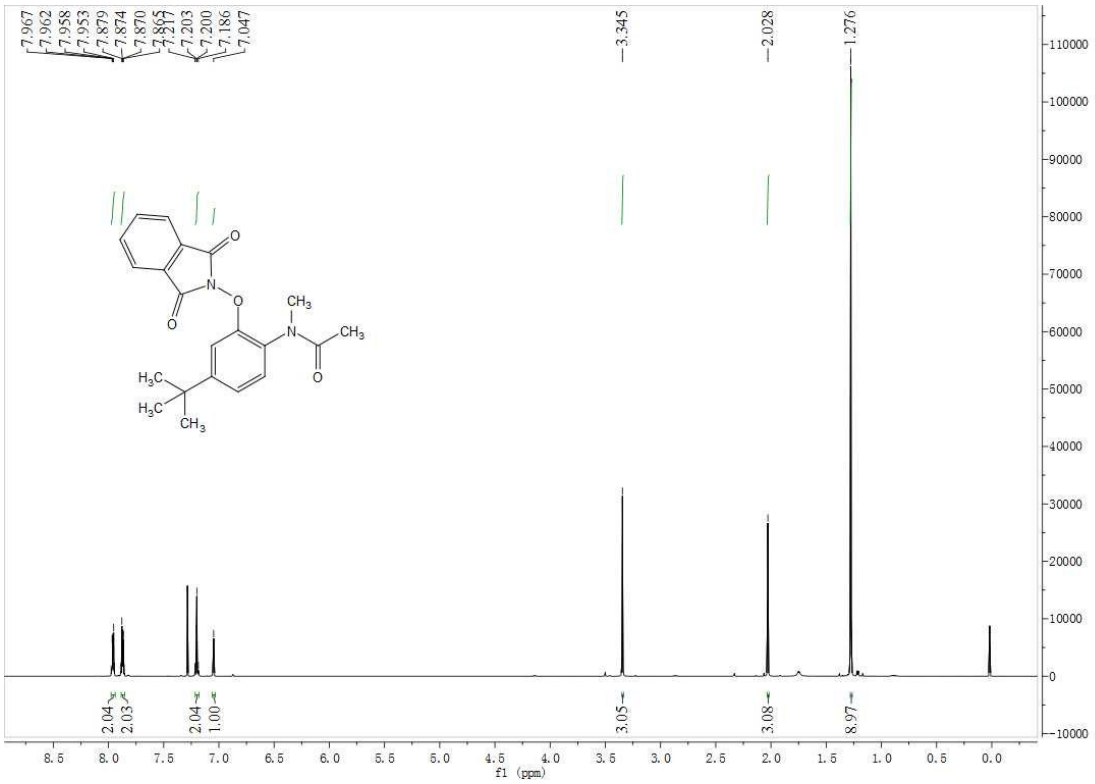

169.928
163.320
154.909
135.416
134.460
131.778
129.852
129.720
125.408
124.124
114.568
35.871
22.157
f1 (ppm)

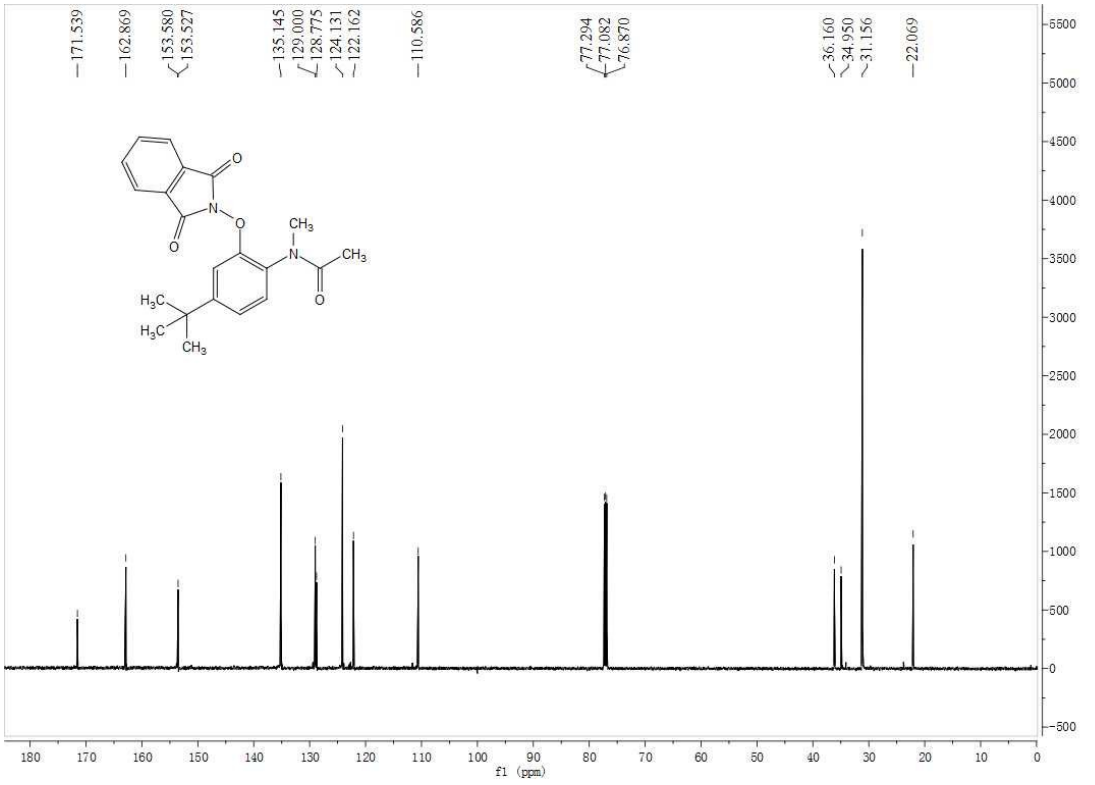

7.936
7.460
3.153
1.877
5.08
1.99
3.06
3.00
f1 (ppm)

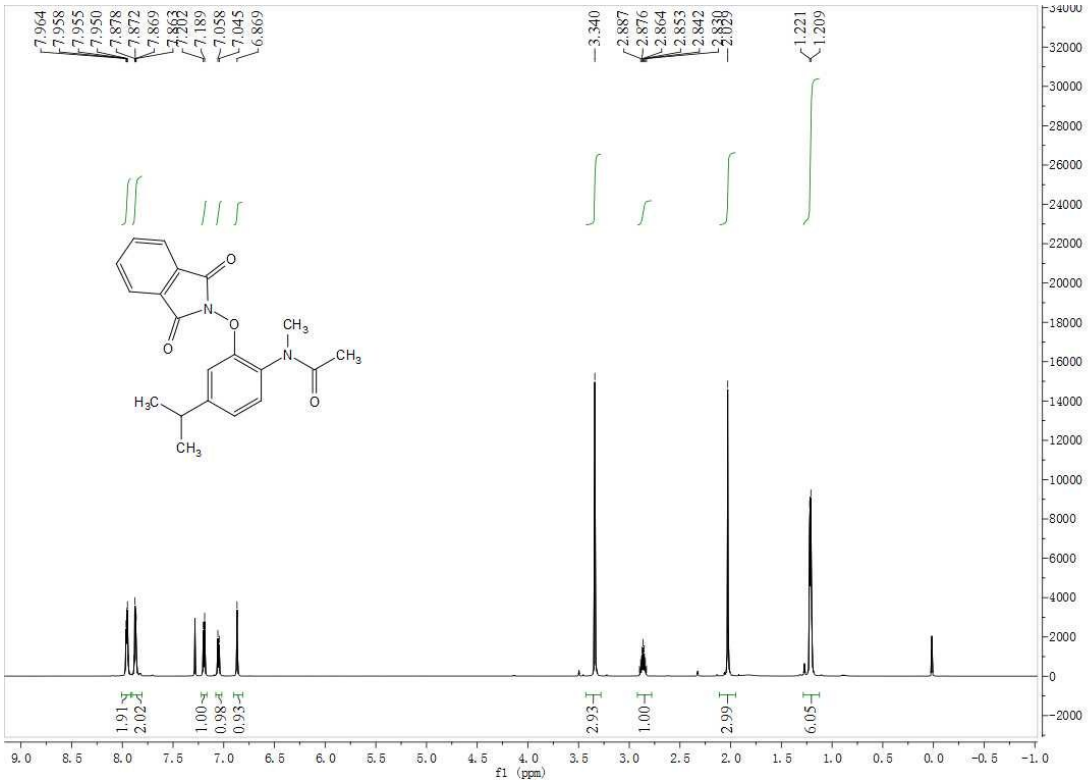

169.856
163.361
154.923
135.410
132.061
130.278
129.753
128.435
124.123
122.579
117.238
35.829
22.172
f1 (ppm)

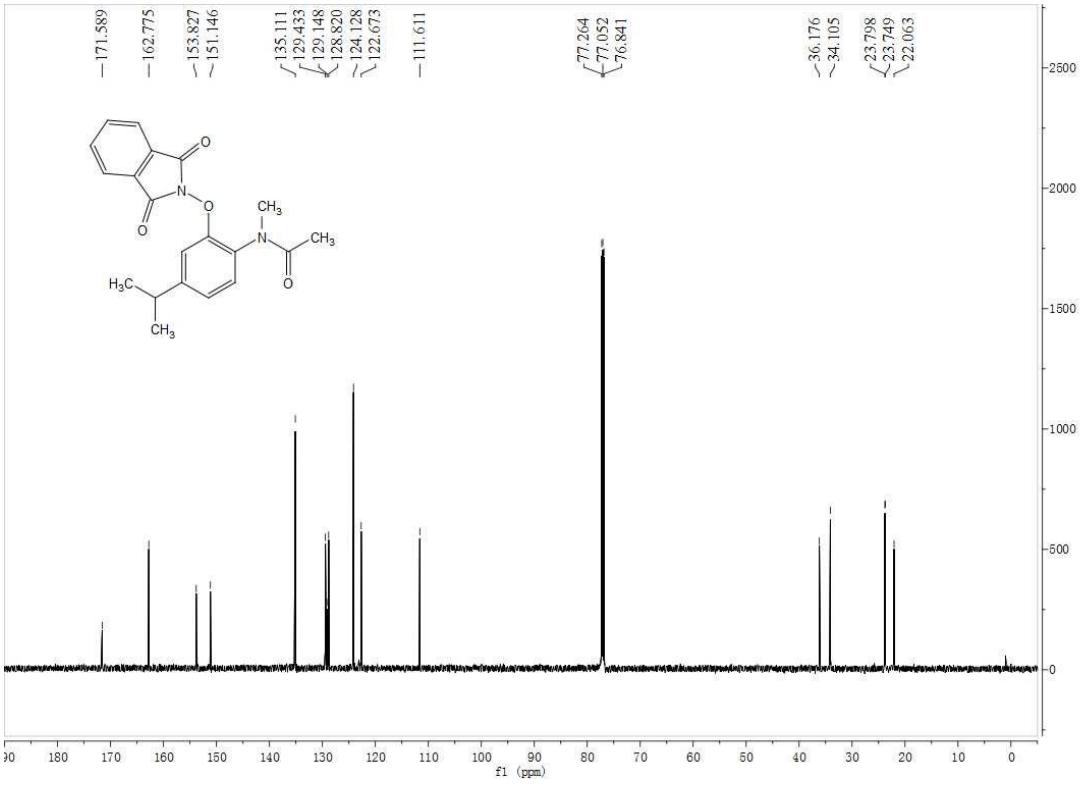

7.969
7.962
7.957
7.953
7.948
7.941
7.884
7.875
7.870
7.866
7.861
7.855
7.194
7.181
7.029
7.027
7.016
7.013
6.857
6.854
3.341
2.643
2.630
2.617
2.605
2.030
1.222
1.210
1.197
1.00
1.00
0.92
2.94
2.02
2.94
2.97
f1 (ppm)

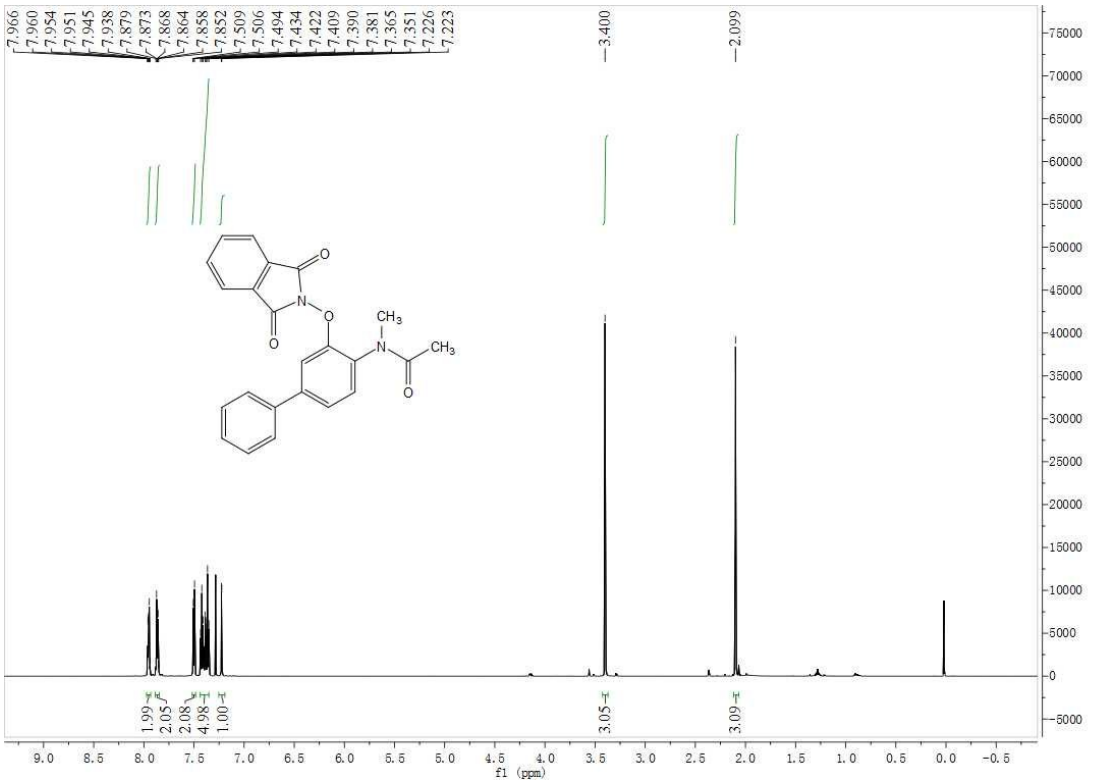

171.527
162.709
153.852
146.464
135.115
129.446
129.118
128.820
124.298
124.116
112.704
77.249
77.037
76.826
36.171
28.728
22.039
15.217
f1 (ppm)

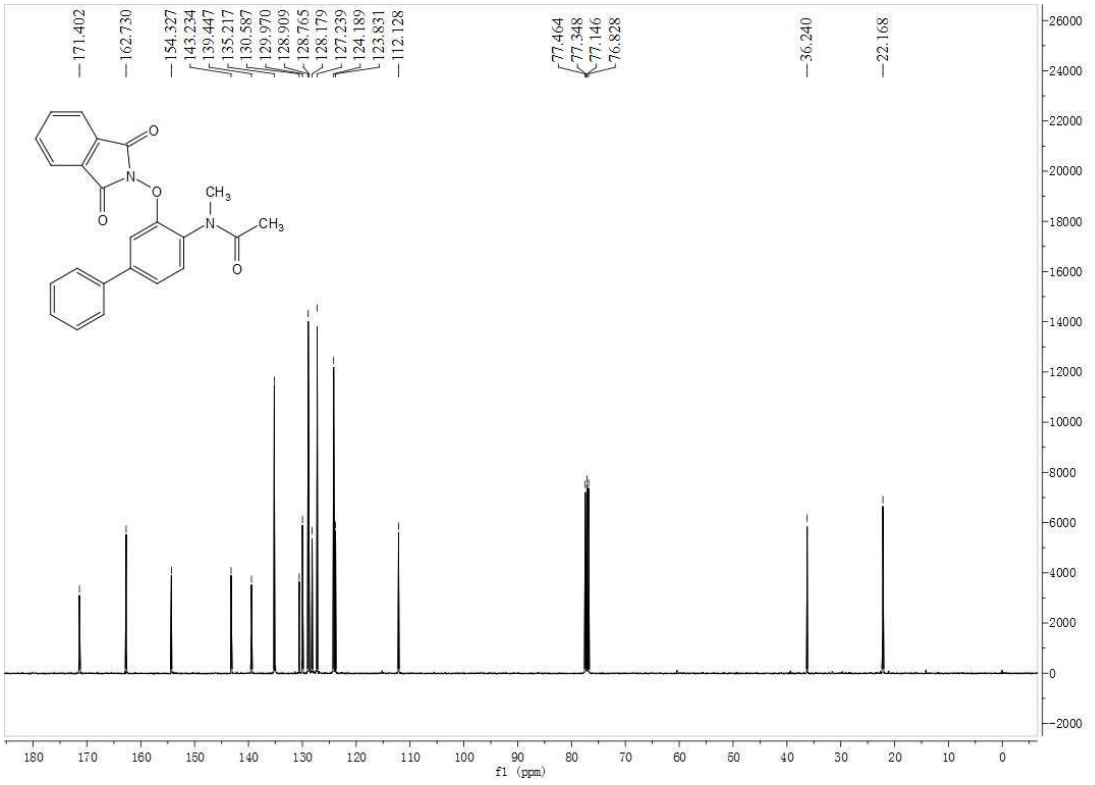

7.967
7.962
7.958
7.953
7.879
7.874
7.870
7.865
7.217
7.203
7.200
7.186
7.047
3.345
2.028
1.276
2.04
2.03
2.04
1.00
3.05
3.08
8.97
f1 (ppm)

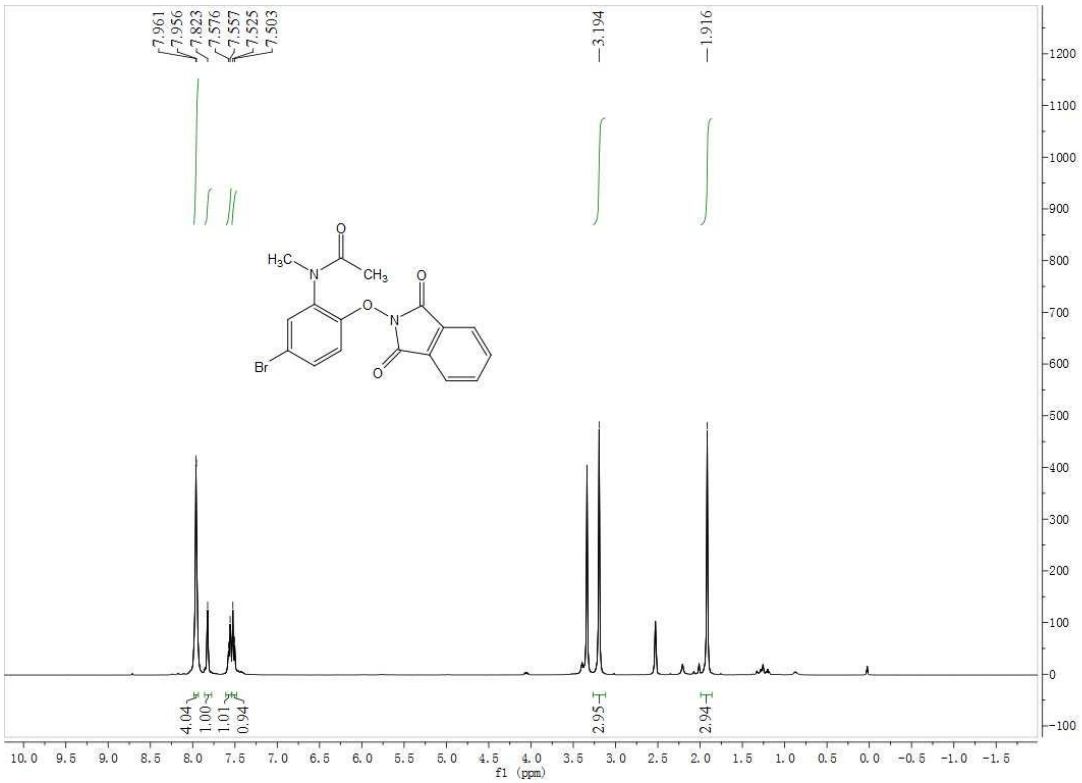

171.539
162.869
153.580
153.527
135.145
129.000
128.775
124.131
122.162
110.586
77.294
77.082
76.870
36.160
34.950
31.156
22.069
f1 (ppm)

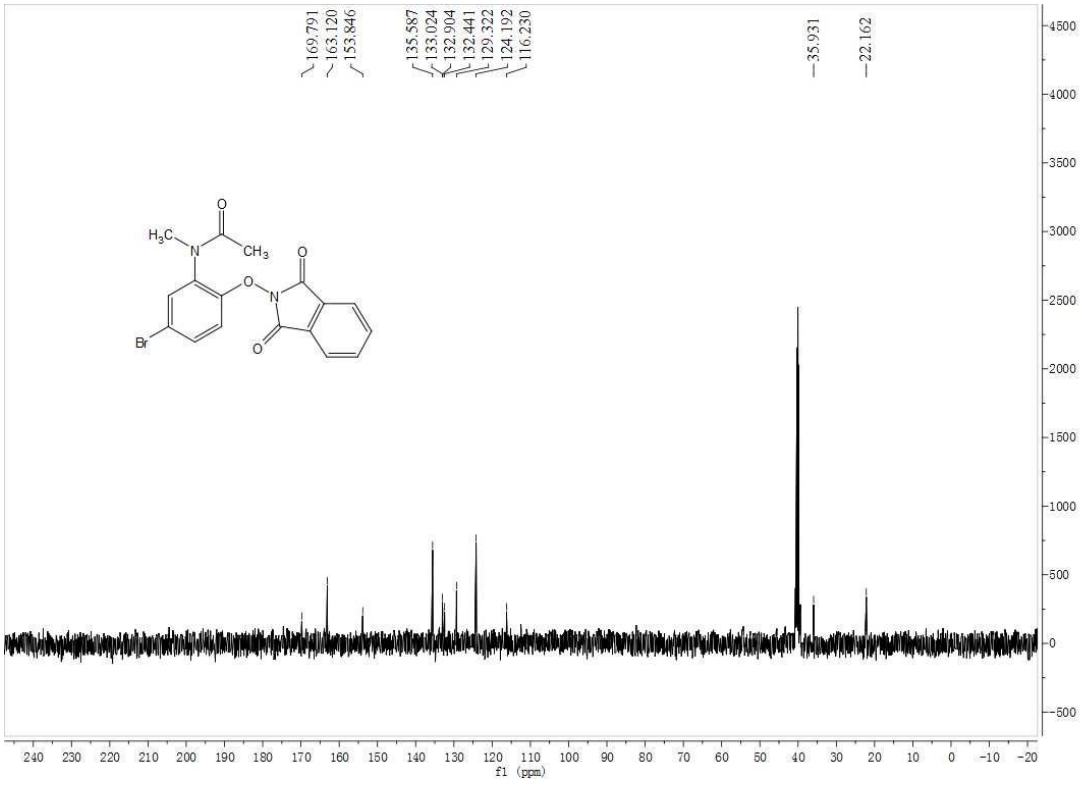

7.964
7.958
7.955
7.950
7.878
7.872
7.869
7.189
7.058
7.045
6.869
3.340
2.887
2.876
2.864
2.853
2.842
1.221
1.209
1.91
2.02
1.00
0.98
0.93
2.93
1.00
2.99
6.05
f1 (ppm)

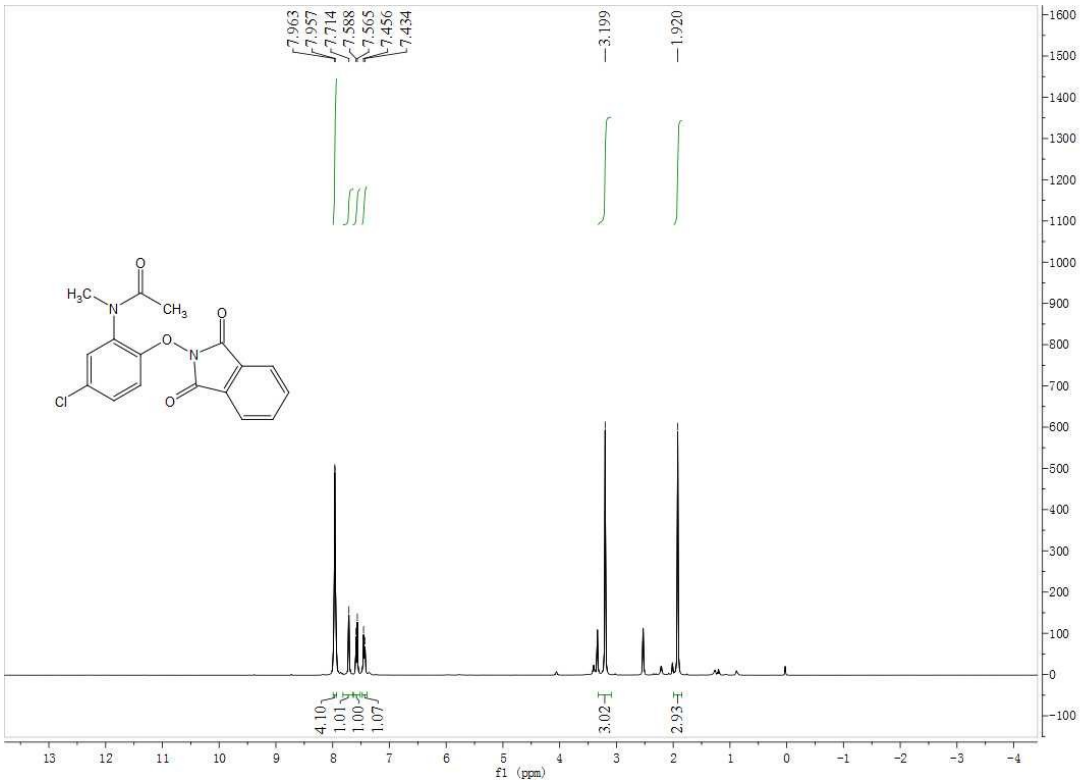

171.589
162.775
153.827
151.146
135.111
129.433
129.148
128.820
124.128
122.673
111.611
77.264
77.052
76.841
36.176
34.105
23.798
23.749
22.063
f1 (ppm)

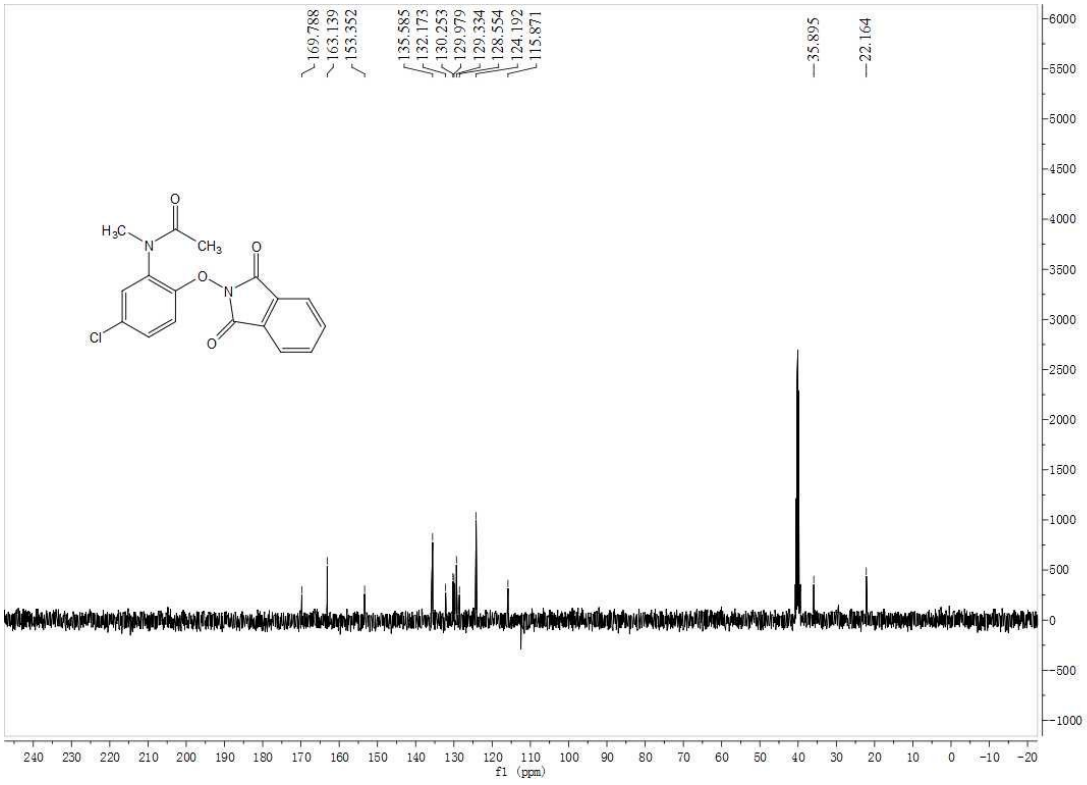

7.966
7.960
7.954
7.951
7.945
7.938
7.879
7.873
7.868
7.864
7.858
7.852
7.509
7.506
7.494
7.434
7.422
7.409
7.390
7.381
7.365
7.351
7.226
7.223
3.400
2.099
1.99
2.05
2.08
4.98
1.00
3.05
3.09
f1 (ppm)

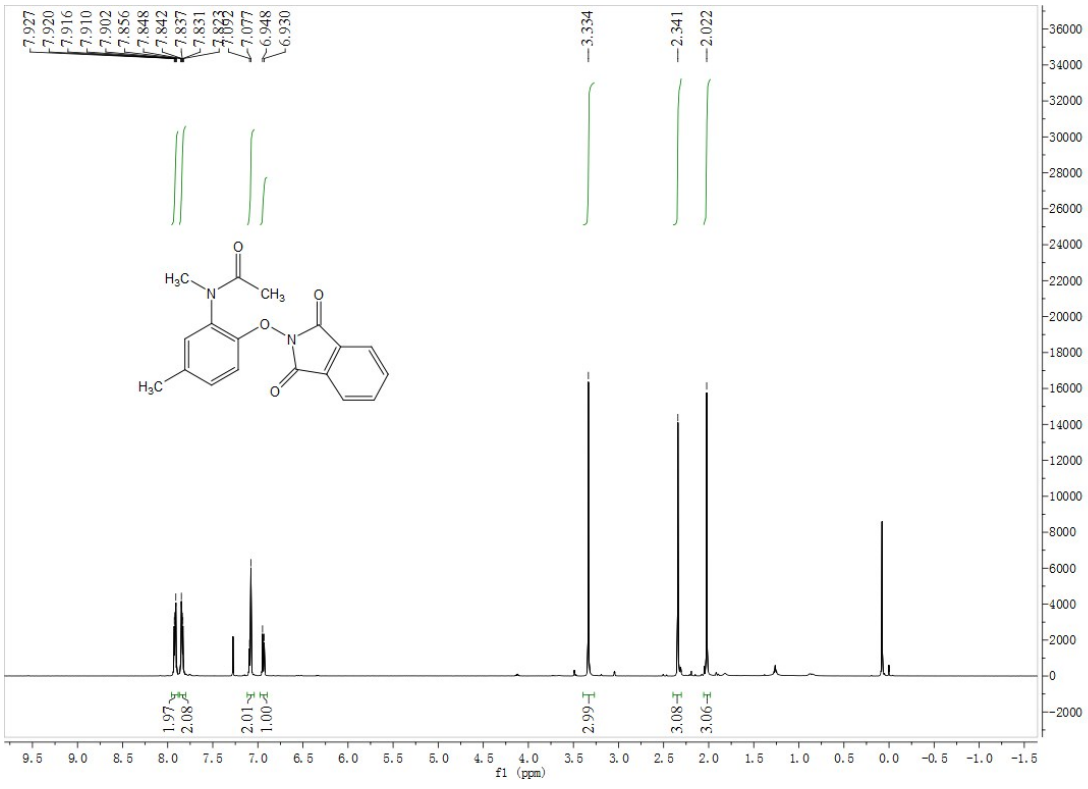

171.402
162.730
154.327
143.234
139.447
135.217
130.587
129.970
128.909
128.765
128.179
127.239
124.189
123.831
112.128
77.464
77.348
77.146
76.828
36.240
22.168
f1 (ppm)

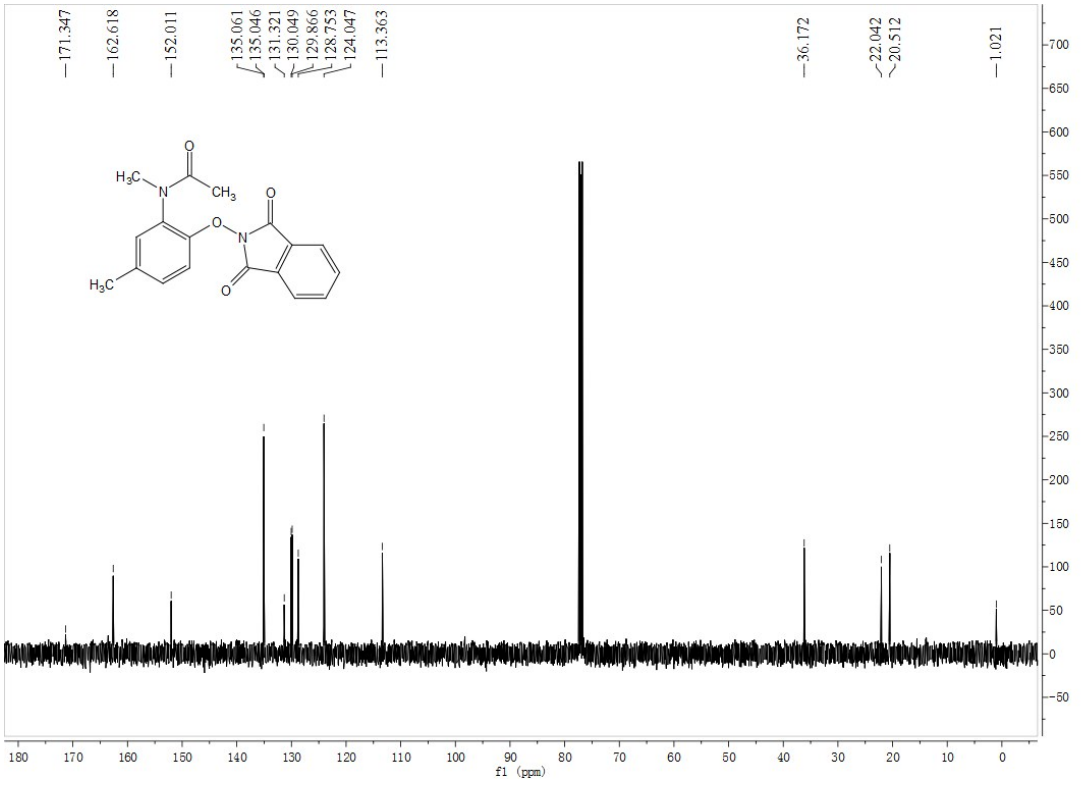

7.961
7.956
7.823
7.576
7.557
7.525
7.503
3.194
1.916
4.04
1.00
1.01
0.94
2.95
2.94
f1 (ppm)

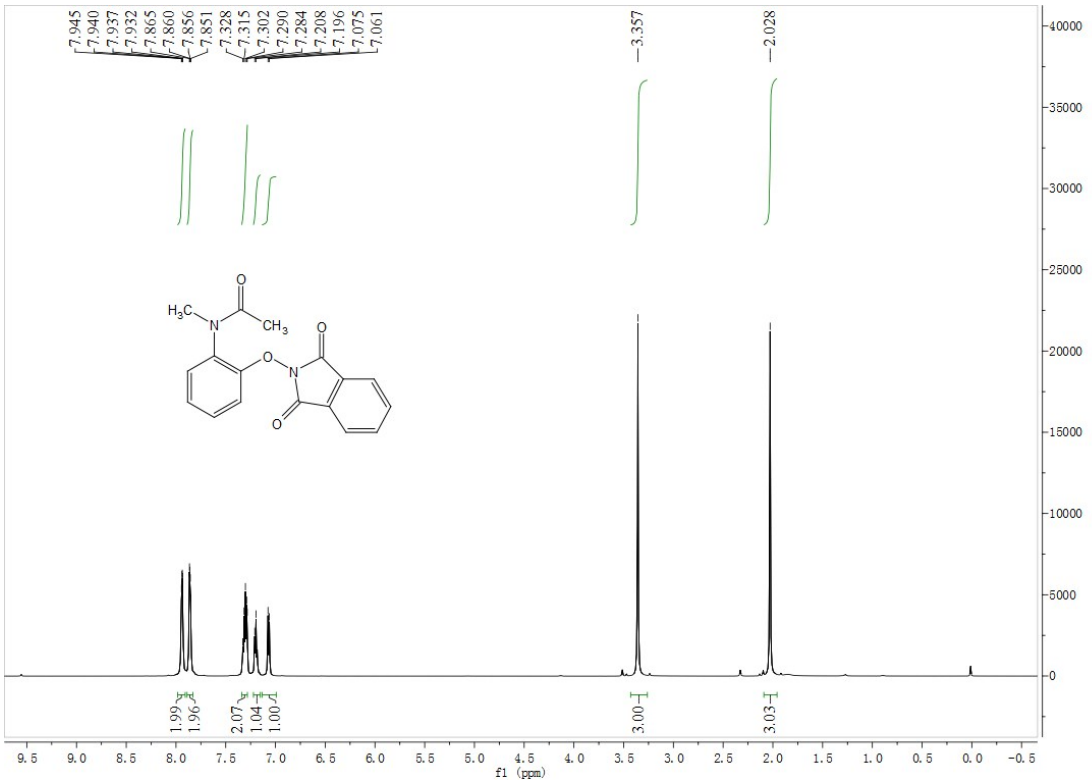

169.791
163.120
153.846
135.587
133.024
132.904
132.441
129.322
124.192
116.230
35.931
22.162
f1 (ppm)

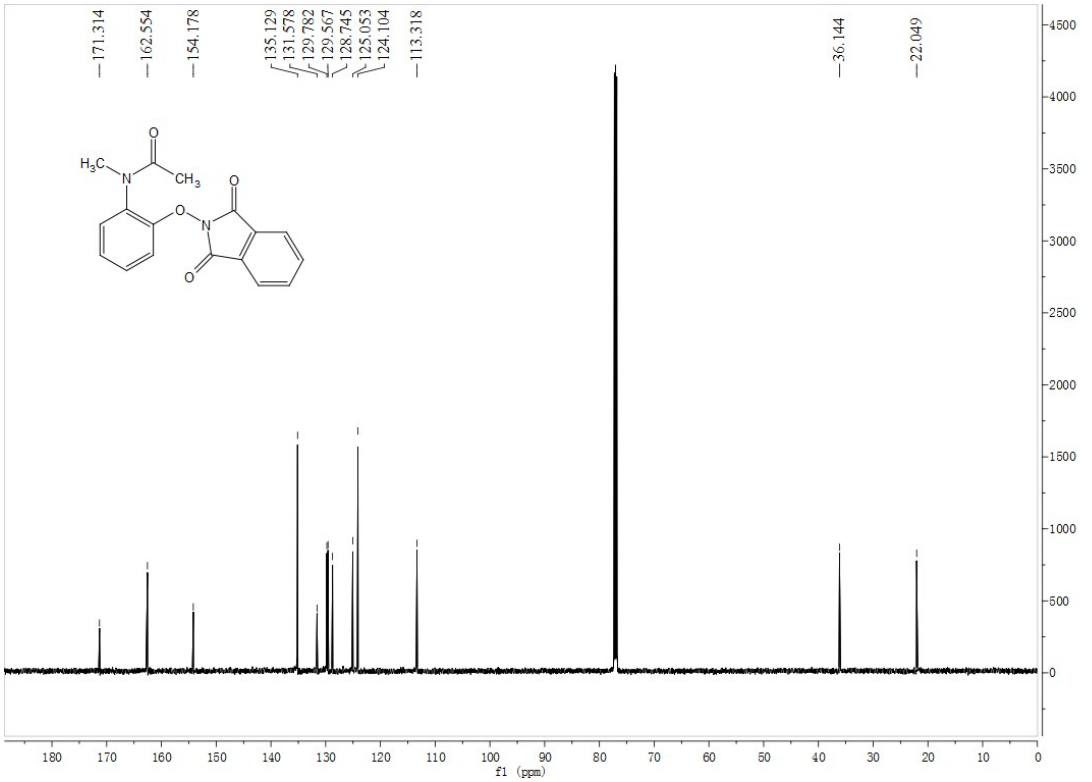

7.963
7.957
7.714
7.588
7.565
7.456
7.434
3.199
1.920
4.10
1.01
1.00
1.07
3.02
2.93
f1 (ppm)

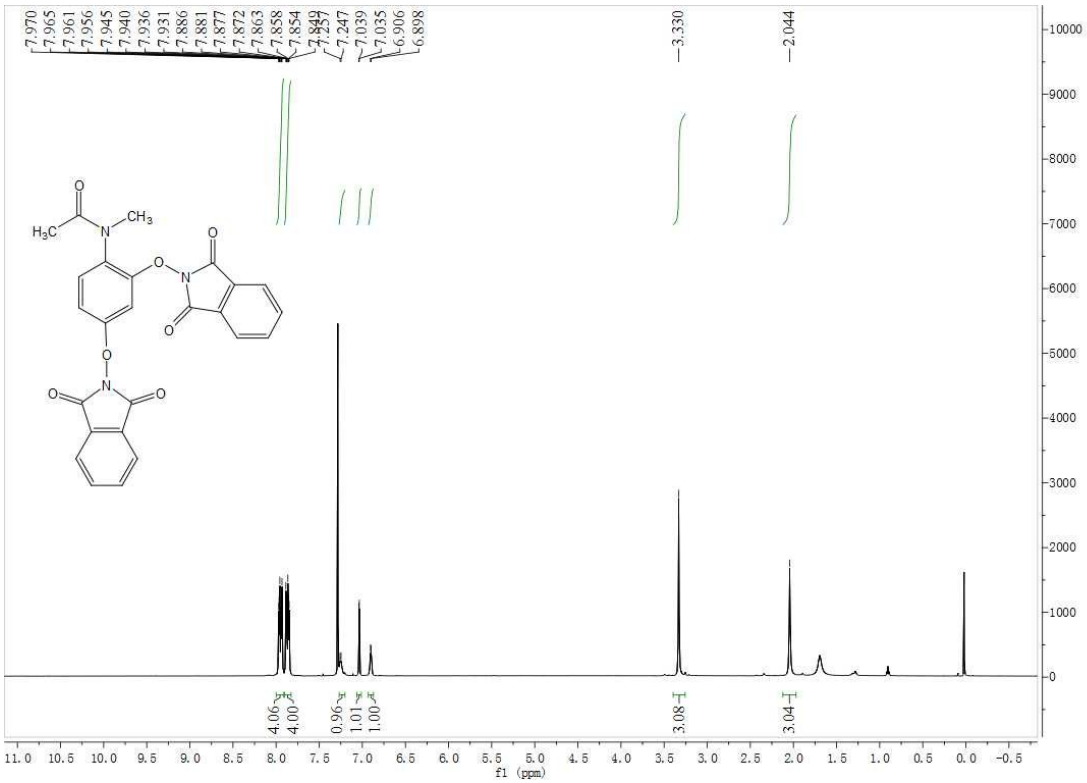

169.788
163.139
153.352
135.585
132.173
130.253
129.979
129.334
128.554
124.192
115.871
35.895
22.164
f1 (ppm)

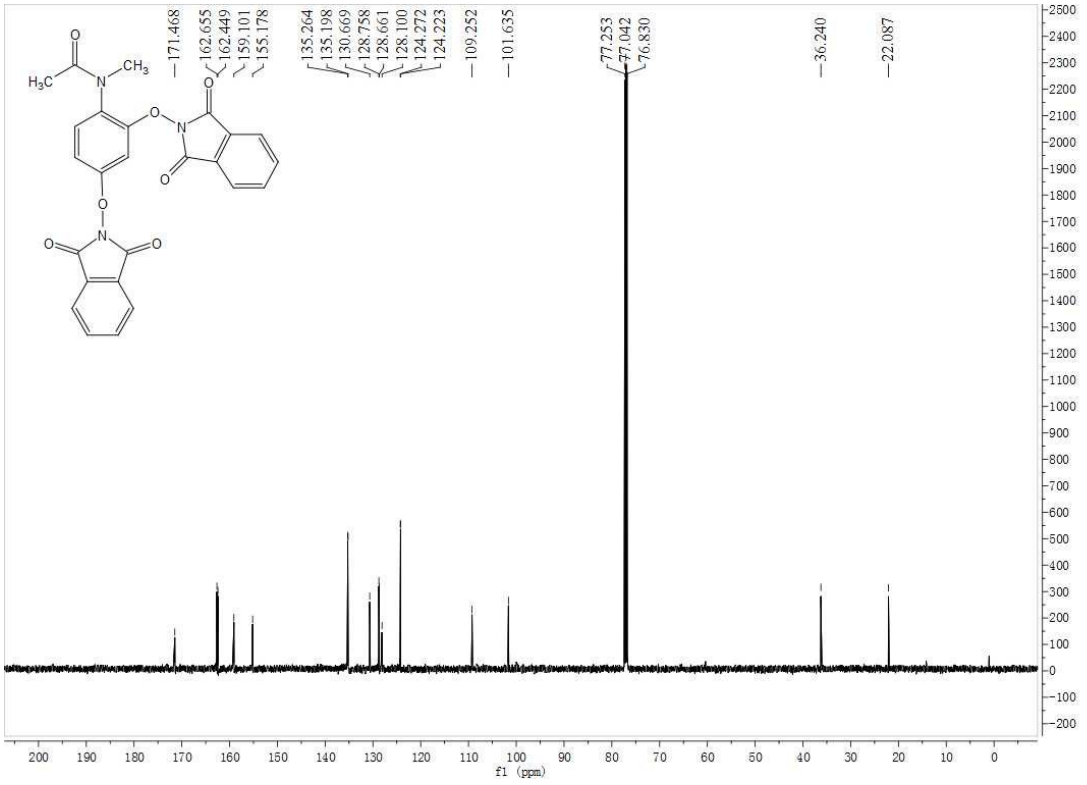

7.927
7.920
7.916
7.910
7.902
7.856
7.848
7.842
7.837
7.831
7.823
7.092
7.077
6.948
6.930
3.334
2.341
2.022
1.97
2.08
2.01
1.00
2.99
3.08
3.06
f1 (ppm)

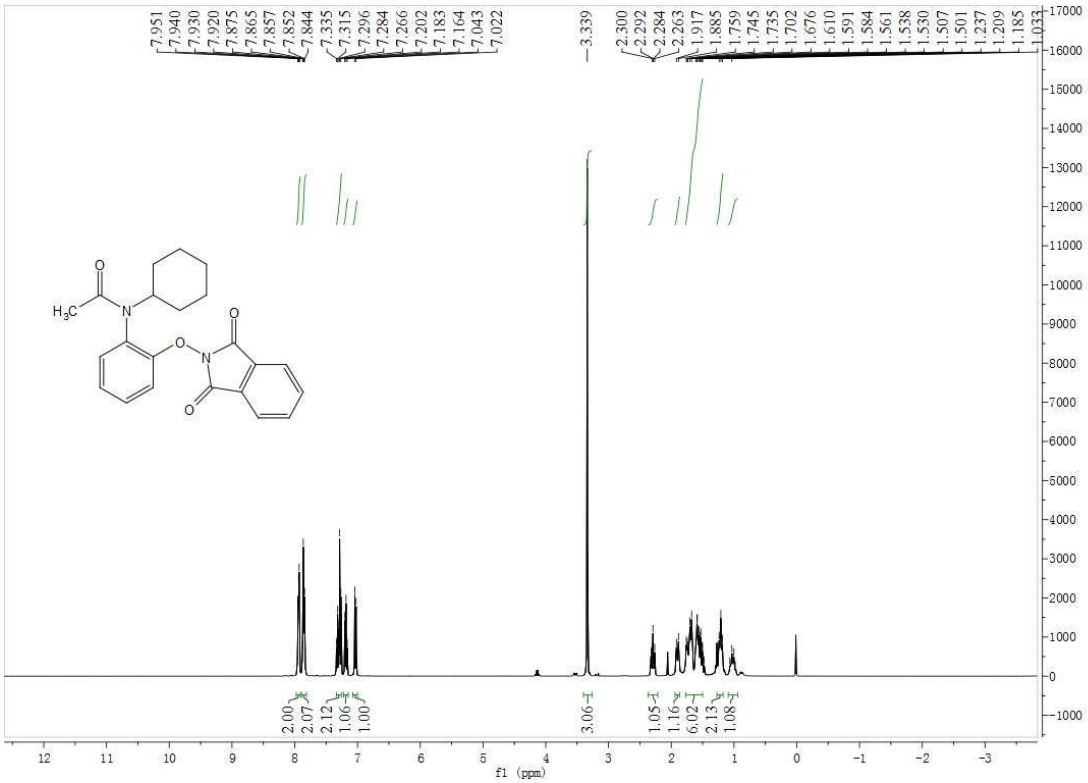

171.347
162.618
152.011
135.061
135.046
131.321
130.049
129.866
128.753
124.047
113.363
36.172
22.042
20.512
1.021
f1 (ppm)

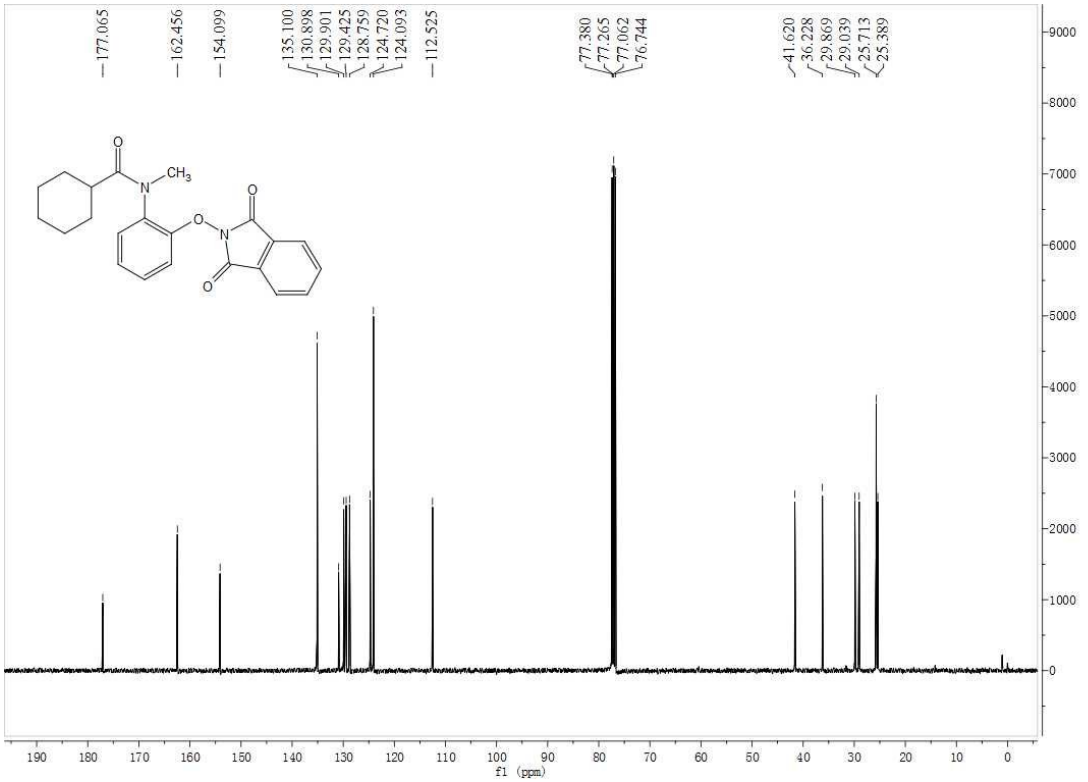

7.945
7.940
7.937
7.932
7.865
7.860
7.856
7.851
7.328
7.315
7.302
7.290
7.284
7.208
7.196
7.075
7.061
3.357
2.028
1.99
1.96
2.07
1.04
1.00
3.00
3.03
f1 (ppm)

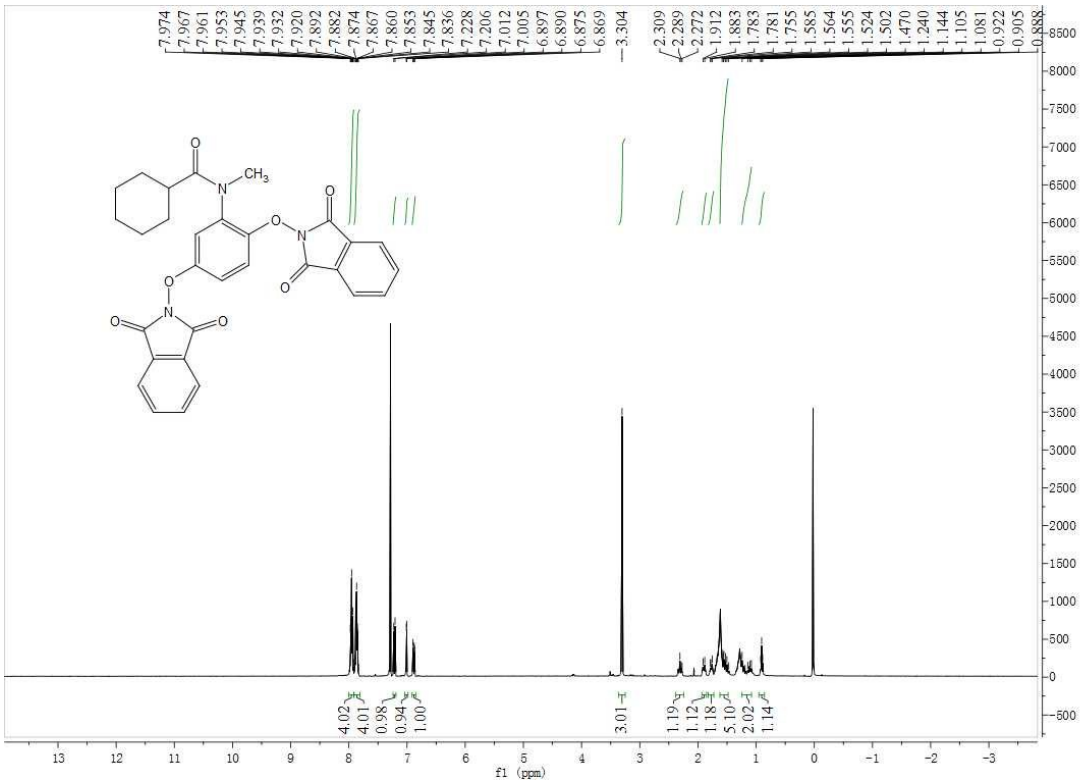

171.314
162.554
154.178
135.129
131.578
129.782
129.567
128.745
125.053
124.104
113.318
36.144
22.049
f1 (ppm)

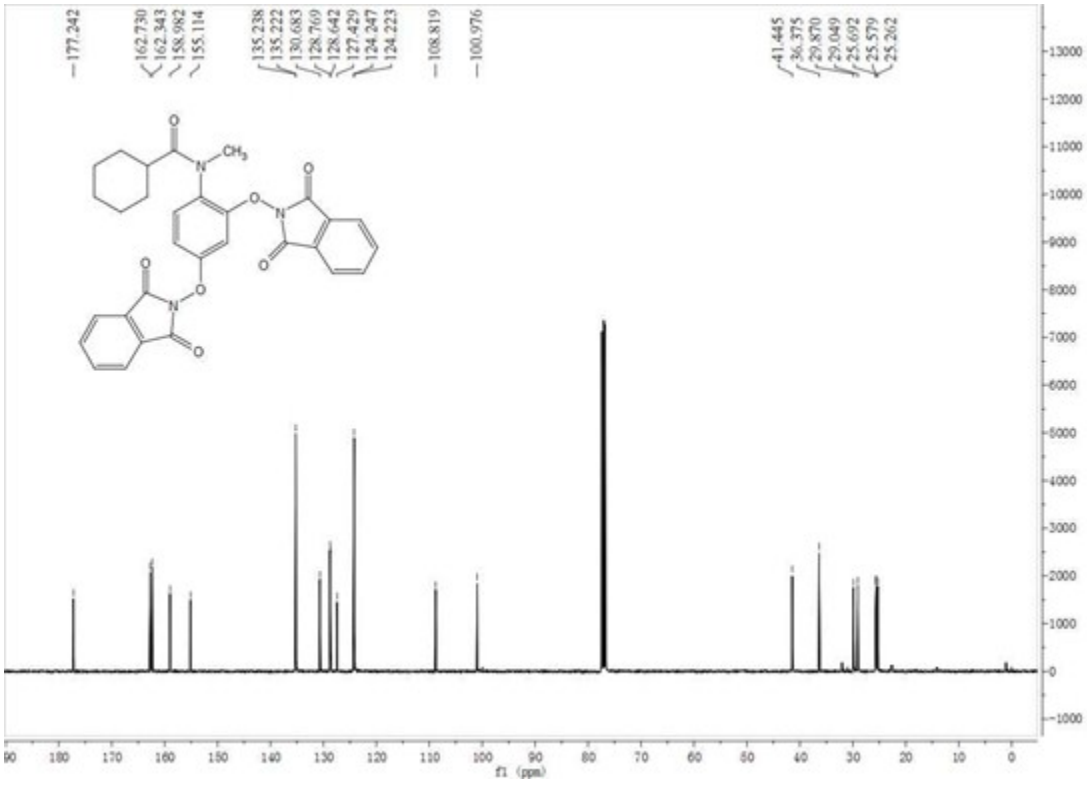

7.970
7.965
7.961
7.956
7.945
7.940
7.936
7.931
7.886
7.881
7.877
7.872
7.863
7.858
7.854
7.849
7.247
7.039
7.035
6.906
6.898
3.330
2.044
4.06
4.00
0.96
1.01
1.00
3.08
3.04
f1 (ppm)

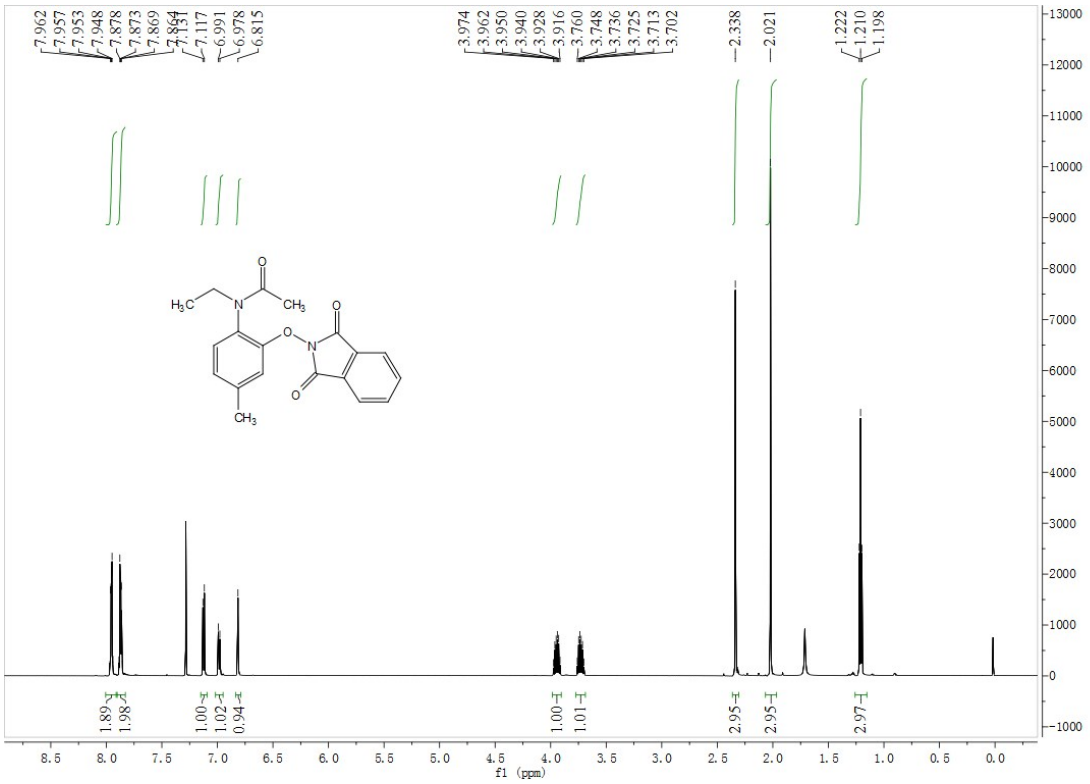

171.468
162.655
162.449
159.101
155.178
135.264
135.198
130.669
128.758
128.661
128.100
124.272
124.223
109.252
101.635
77.253
77.042
76.830
36.240
22.087
f1 (ppm)

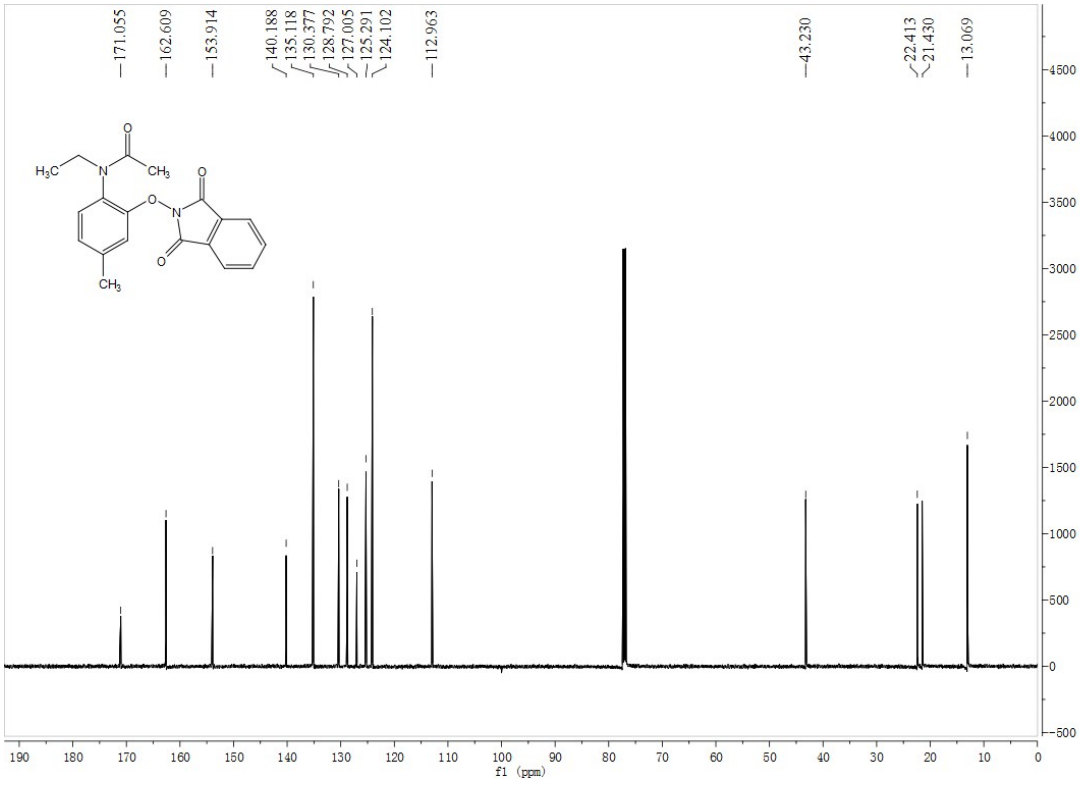

7.951
7.940
7.930
7.920
7.875
7.865
7.857
7.852
7.844
7.335
7.315
7.296
7.284
7.266
7.202
7.183
7.164
7.043
7.022
3.339
2.300
2.292
2.284
2.263
1.917
1.885
1.759
1.745
1.735
1.702
1.676
1.610
1.591
1.584
1.561
1.538
1.530
1.507
1.501
1.237
1.209
1.185
1.033
2.00
2.07
2.12
1.06
1.00
3.06
1.05
1.16
6.02
2.13
1.08
f1 (ppm)

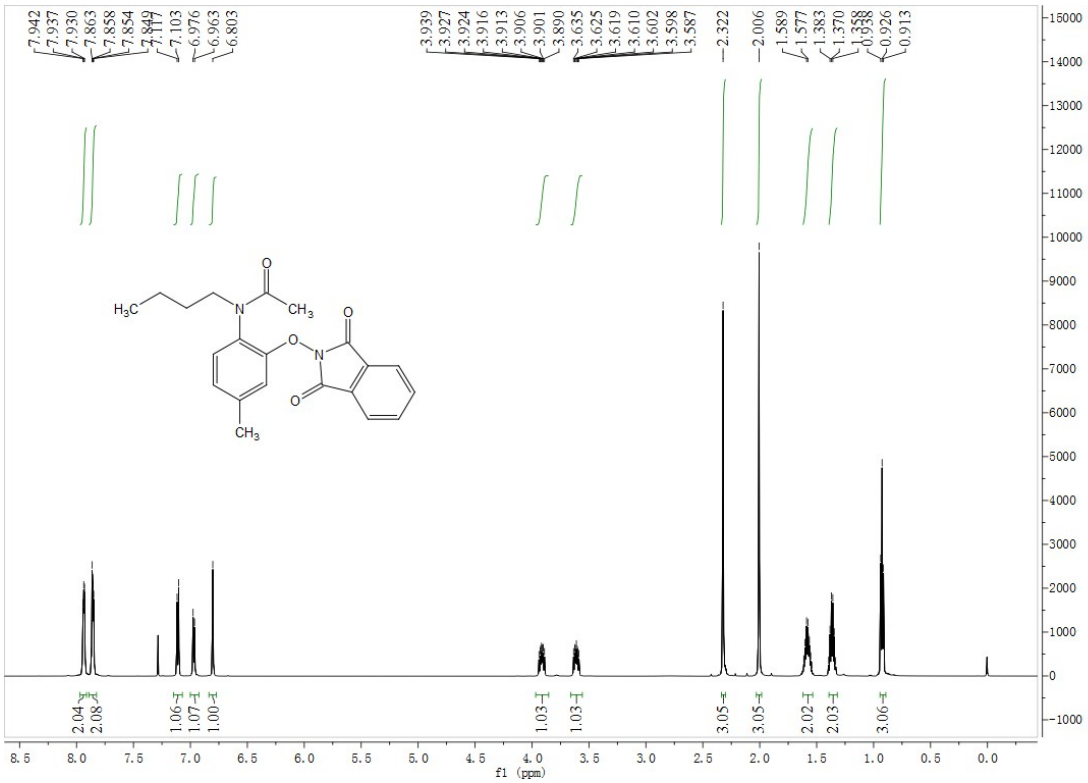

177.065
162.456
154.099
135.100
130.898
129.901
129.425
128.759
124.720
124.093
112.525
77.380
77.265
77.062
76.744
41.620
36.228
29.869
29.039
25.713
25.389
f1 (ppm)

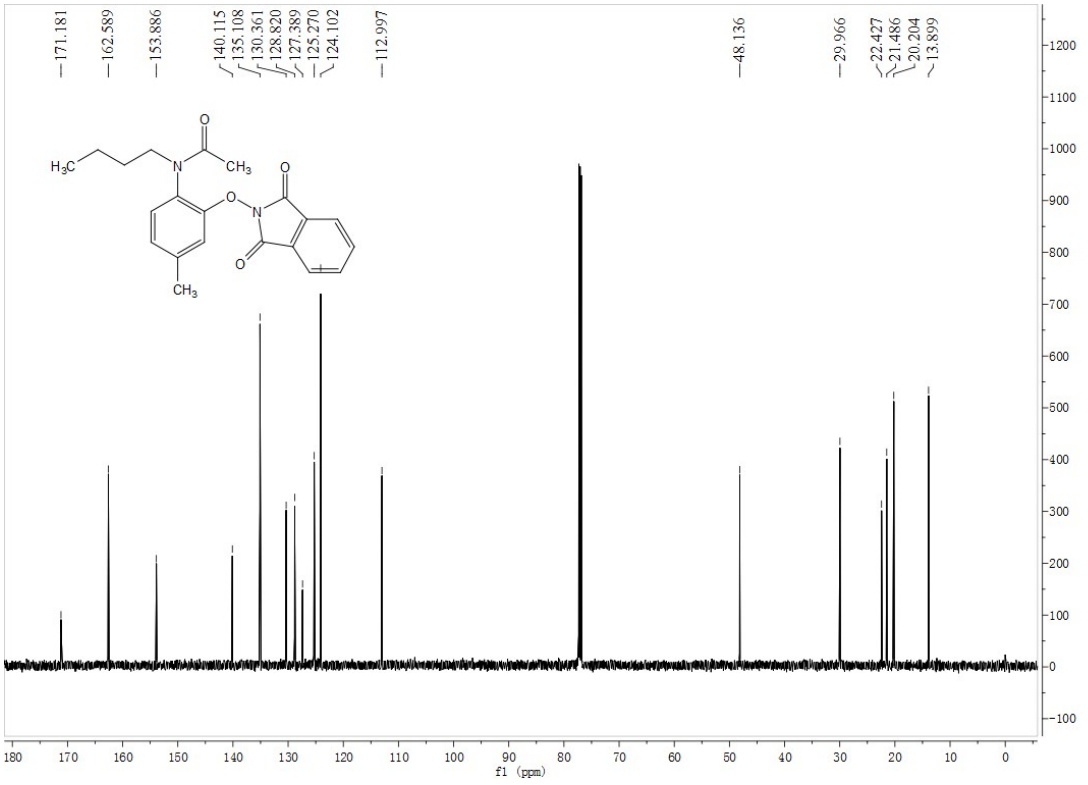

7.974
7.967
7.961
7.953
7.945
7.939
7.932
7.920
7.892
7.882
7.874
7.867
7.860
7.853
7.845
7.836
7.228
7.206
7.012
7.005
6.897
6.890
6.875
6.869
3.304
2.309
2.289
2.272
1.912
1.883
1.783
1.781
1.755
1.585
1.564
1.555
1.524
1.502
1.470
1.240
1.144
1.105
1.081
0.922
0.905
0.888
4.02
4.01
0.98
0.94
1.00
3.01
1.19
1.12
1.18
5.10
2.02
1.14
f1 (ppm)

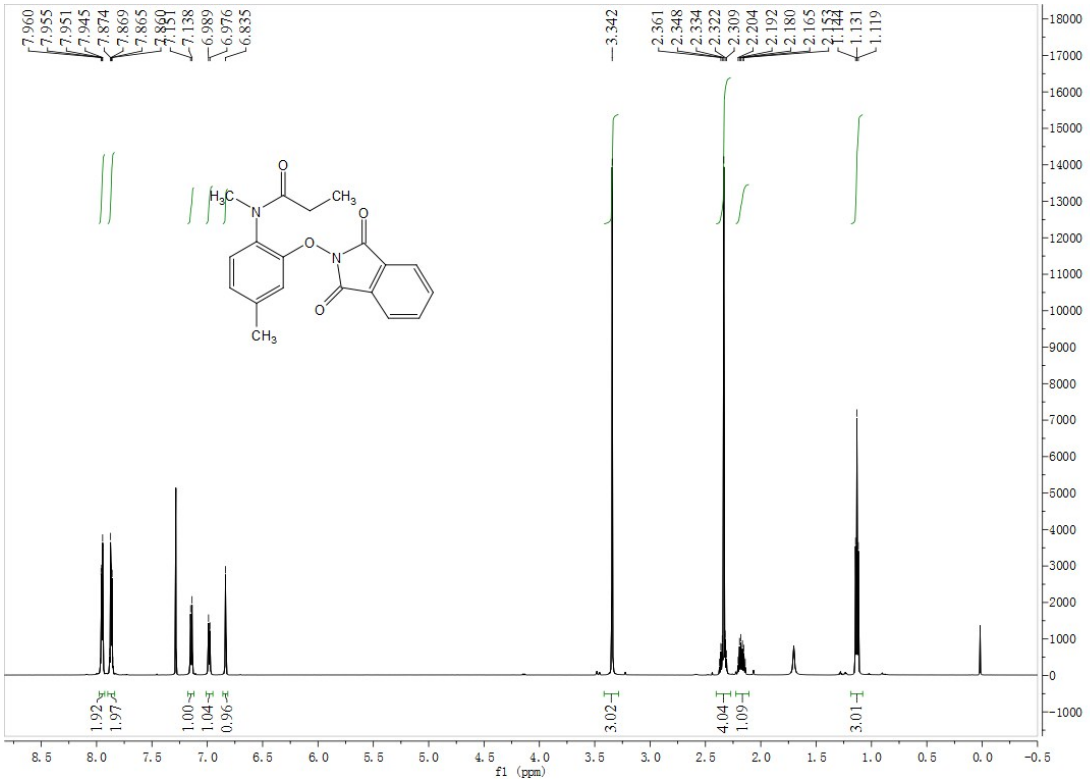

177.242
162.730
162.343
158.982
155.114
135.238
135.222
130.683
128.769
128.642
127.429
124.247
124.223
108.819
100.976
41.445
36.375
29.870
29.049
25.692
25.579
25.262
f1 (ppm)

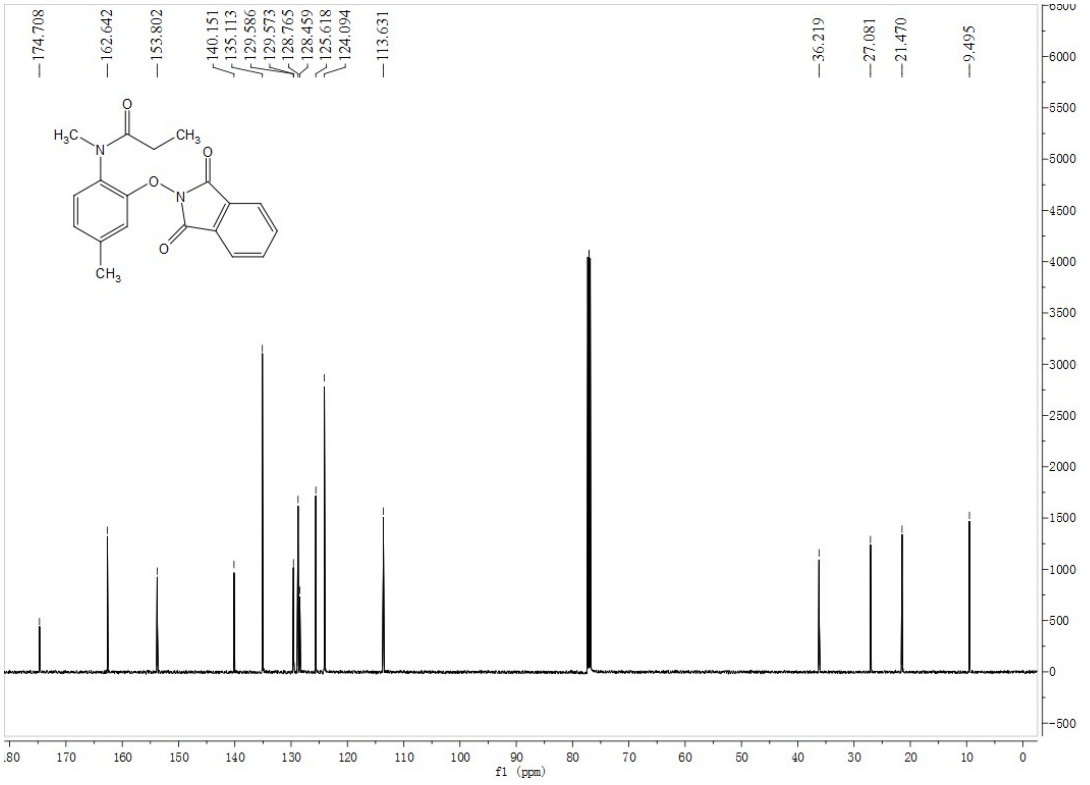

7.962
7.957
7.953
7.948
7.878
7.873
7.869
7.864
7.131
7.117
6.991
6.978
6.815
3.974
3.962
3.950
3.940
3.928
3.916
3.760
3.748
3.736
3.725
3.713
3.702
2.338
2.021
1.222
1.210
1.198
1.89
1.98
1.00
1.02
0.94
1.00
1.01
2.95
2.95
2.97
f1 (ppm)

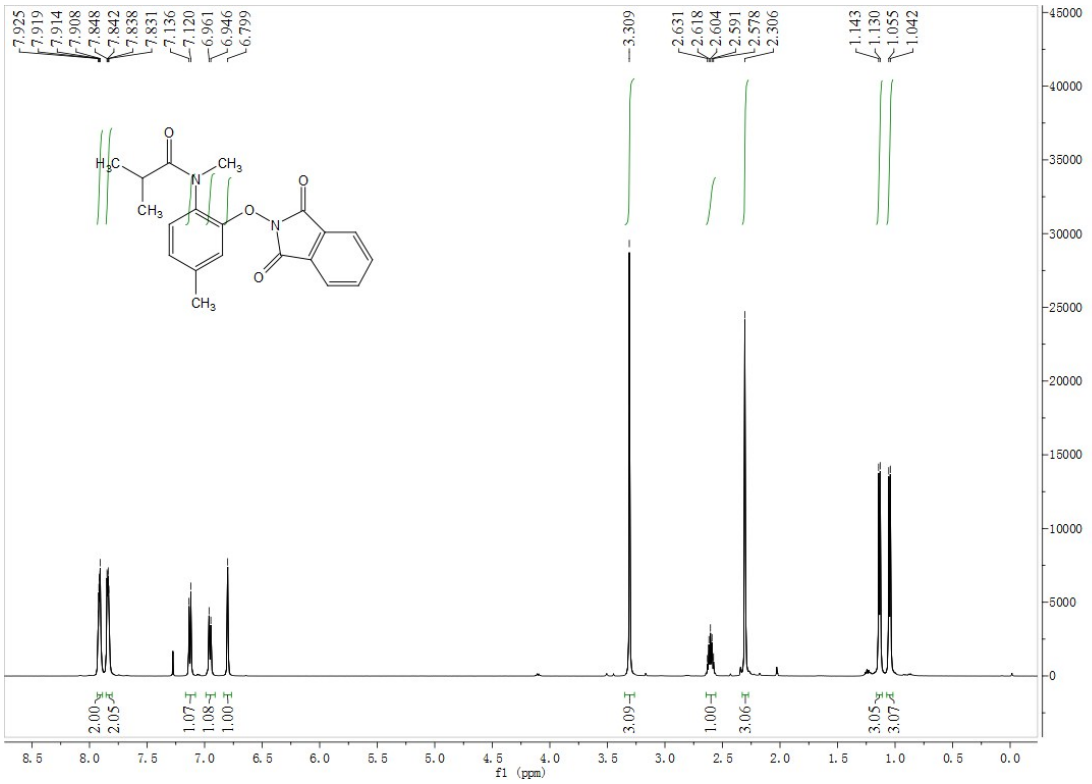

171.055
162.609
153.914
140.188
135.118
130.377
128.792
127.005
125.291
124.102
112.963
43.230
22.413
21.430
13.069
f1 (ppm)

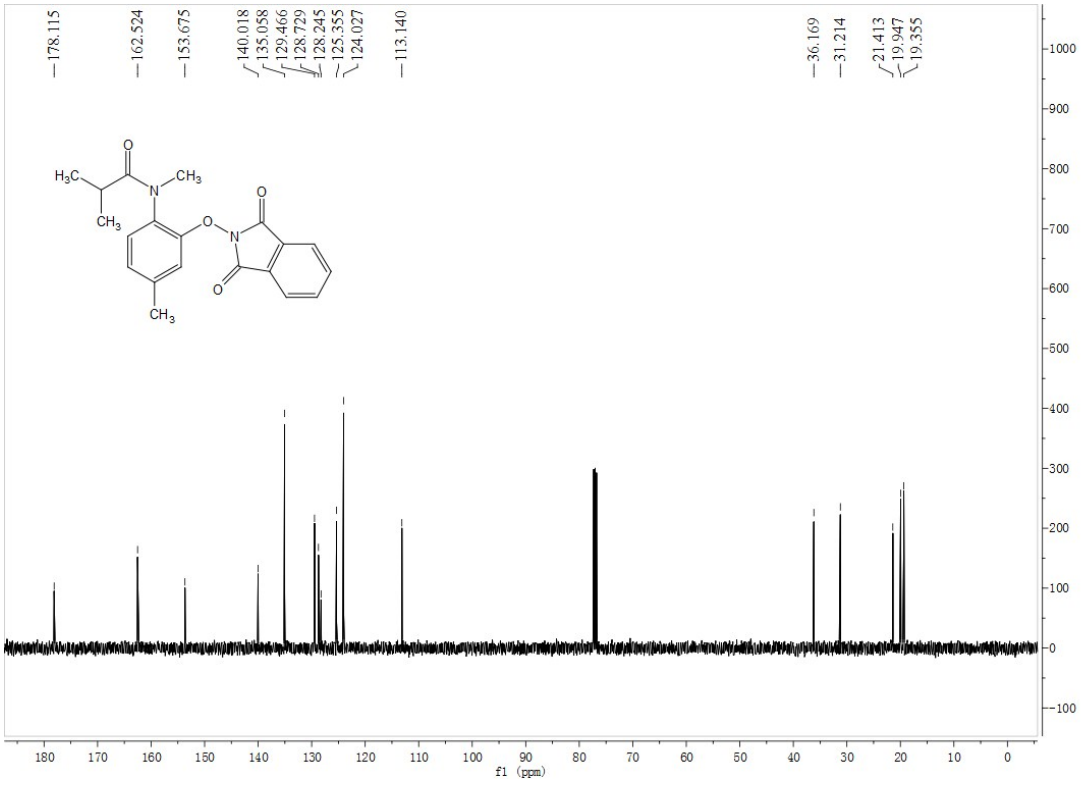

7.942
7.937
7.930
7.863
7.858
7.854
7.849
7.117
7.103
6.976
6.963
6.803
3.939
3.927
3.924
3.916
3.913
3.906
3.901
3.890
3.635
3.625
3.619
3.610
3.602
3.598
3.587
2.322
2.006
1.589
1.577
1.383
1.370
1.358
0.938
0.926
0.913
2.04
2.08
1.06
1.07
1.00
1.03
1.03
3.05
3.05
2.02
2.03
3.06
f1 (ppm)

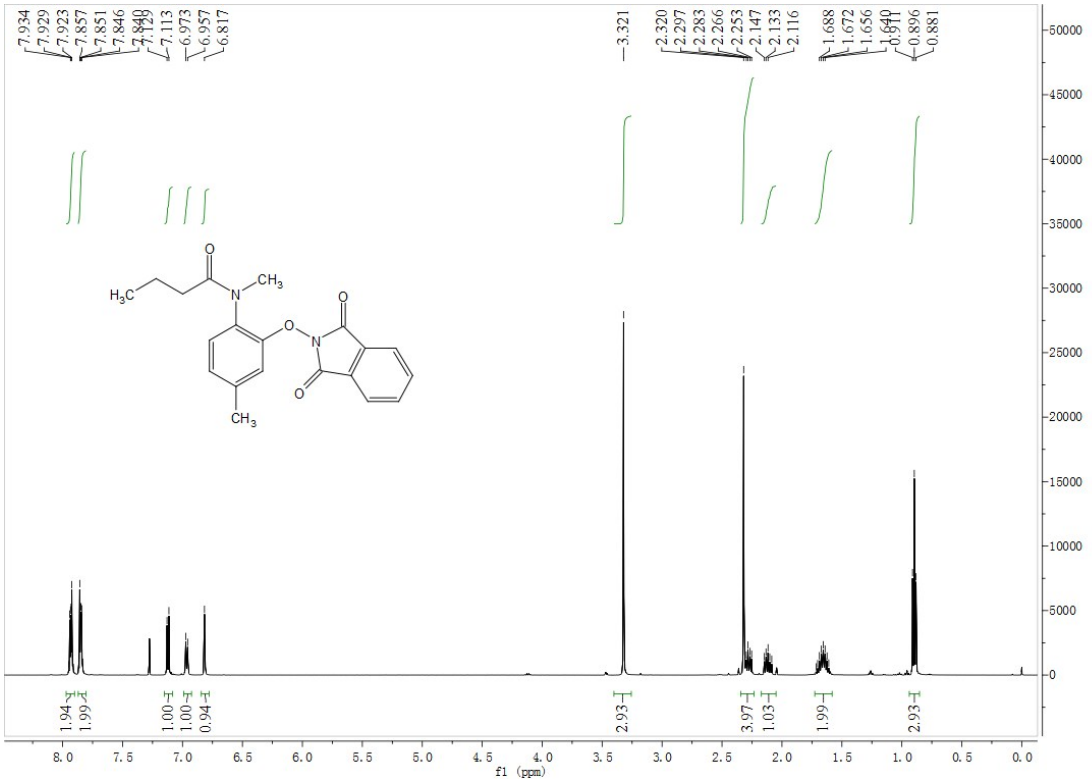

171.181
162.589
153.886
140.115
135.108
130.361
128.820
127.389
125.270
124.102
112.997
48.136
29.966
22.427
21.486
20.204
13.899
f1 (ppm)

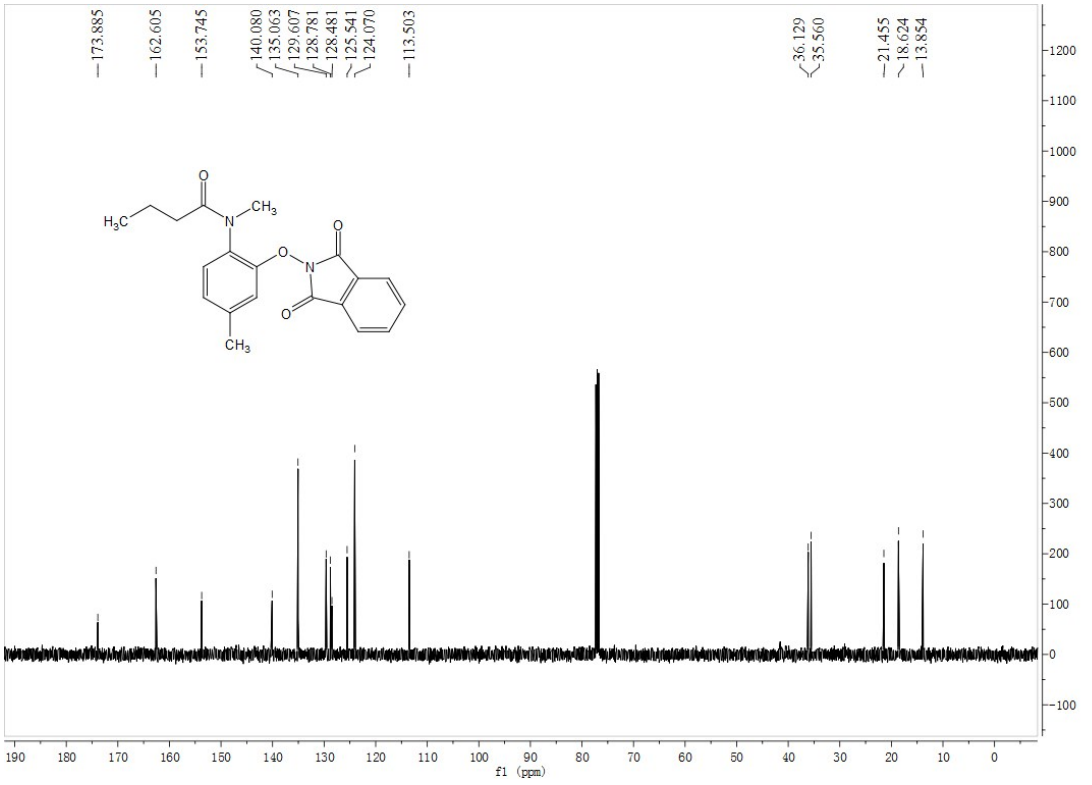

7.960
7.955
7.951
7.945
7.874
7.869
7.865
7.860
7.151
7.138
6.989
6.976
6.835
3.342
2.361
2.348
2.334
2.322
2.309
2.204
2.192
2.180
2.165
2.153
1.144
1.131
1.119
1.92
1.97
1.00
1.04
0.96
3.02
4.04
1.09
3.01
f1 (ppm)

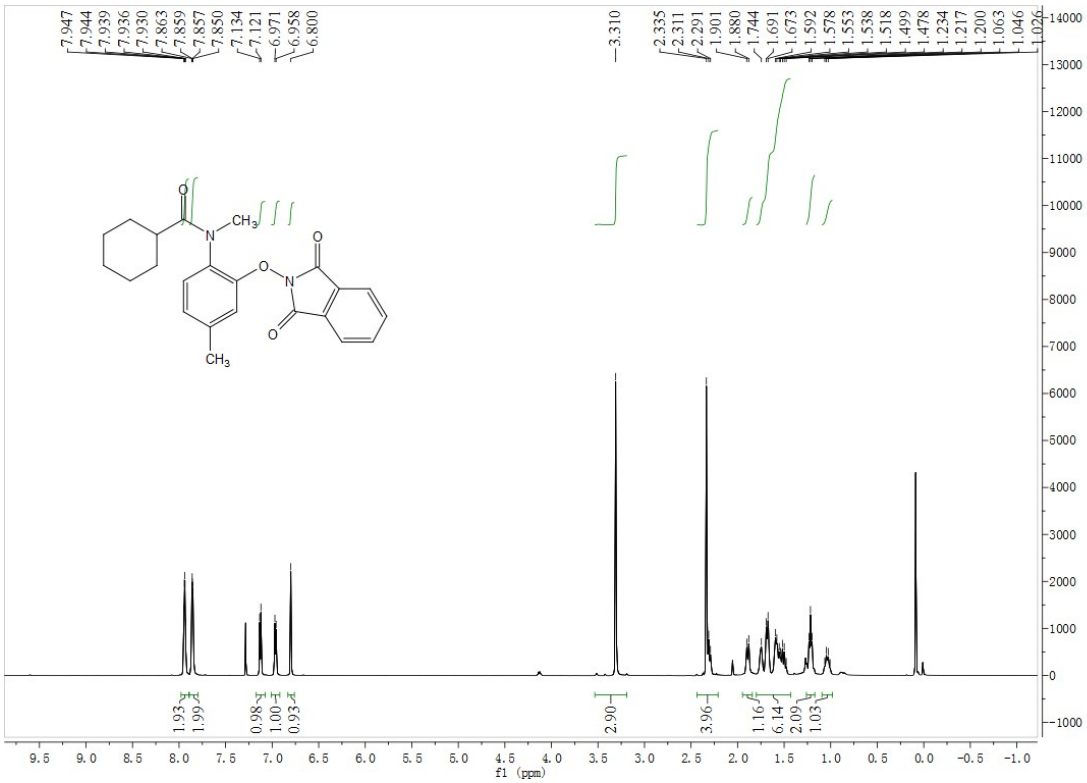

174.708
162.642
153.802
140.151
135.113
129.586
129.573
128.765
128.459
125.618
124.094
113.631
36.219
27.081
21.470
9.495
f1 (ppm)

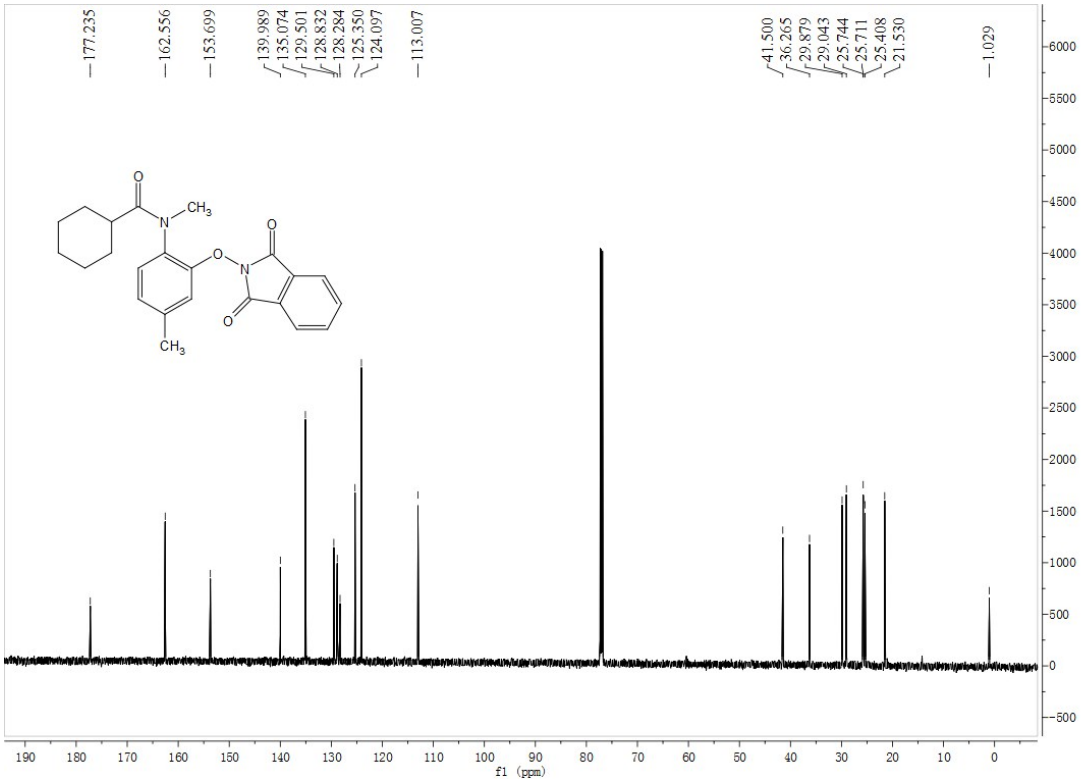

7.925
7.919
7.914
7.908
7.848
7.842
7.838
7.831
7.136
7.120
6.961
6.946
6.799
3.309
2.631
2.618
2.604
2.591
2.578
2.306
1.143
1.130
1.055
1.042
2.00
2.05
1.07
1.08
1.00
3.09
1.00
3.06
3.05
3.07
f1 (ppm)

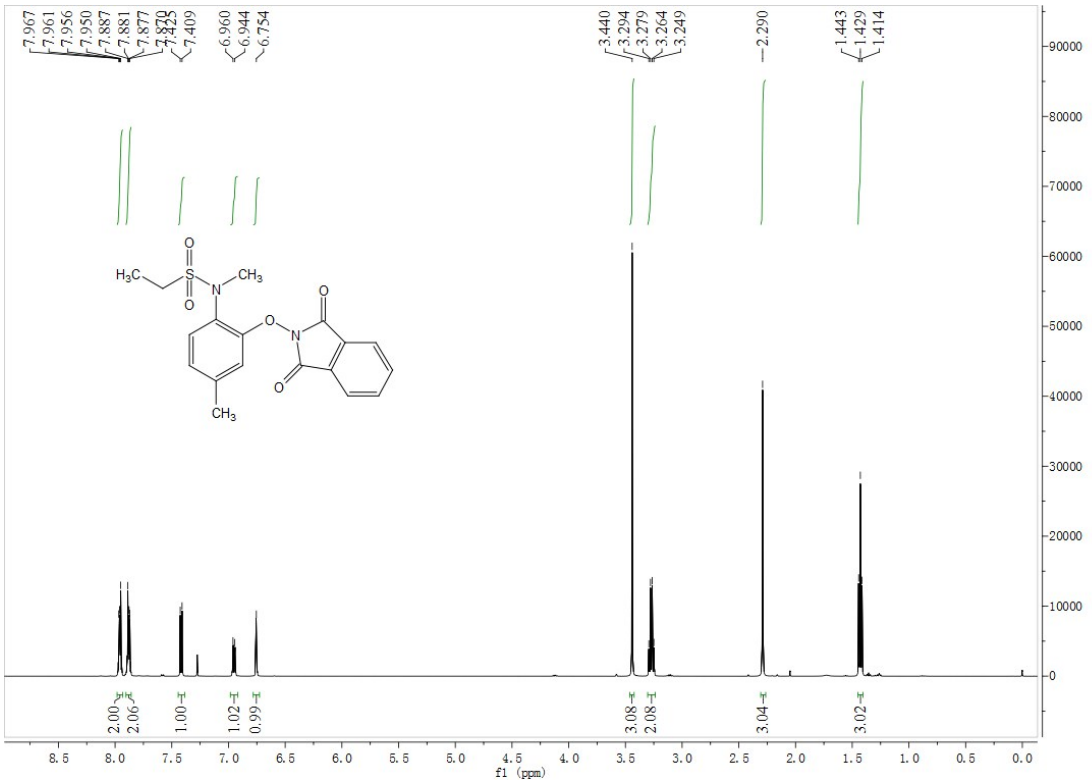

178.115
162.524
153.675
140.018
135.058
129.466
128.729
128.245
125.355
124.027
113.140
36.169
31.214
21.413
19.947
19.355
f1 (ppm)

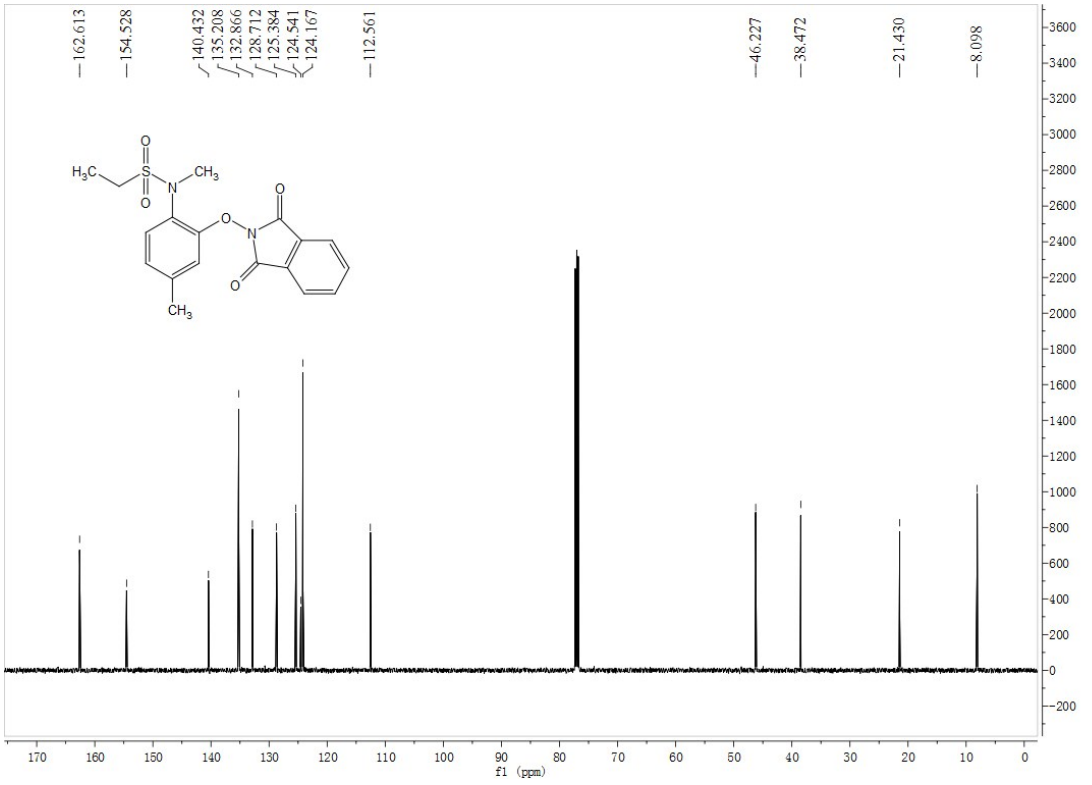

7.934
7.929
7.923
7.857
7.851
7.846
7.840
7.129
7.113
6.973
6.957
6.817
3.321
2.320
2.297
2.283
2.266
2.253
2.147
2.133
2.116
1.688
1.672
1.656
1.640
0.941
0.896
0.881
1.94
1.99
1.00
1.00
0.94
2.93
3.97
1.03
1.99
2.93
f1 (ppm)

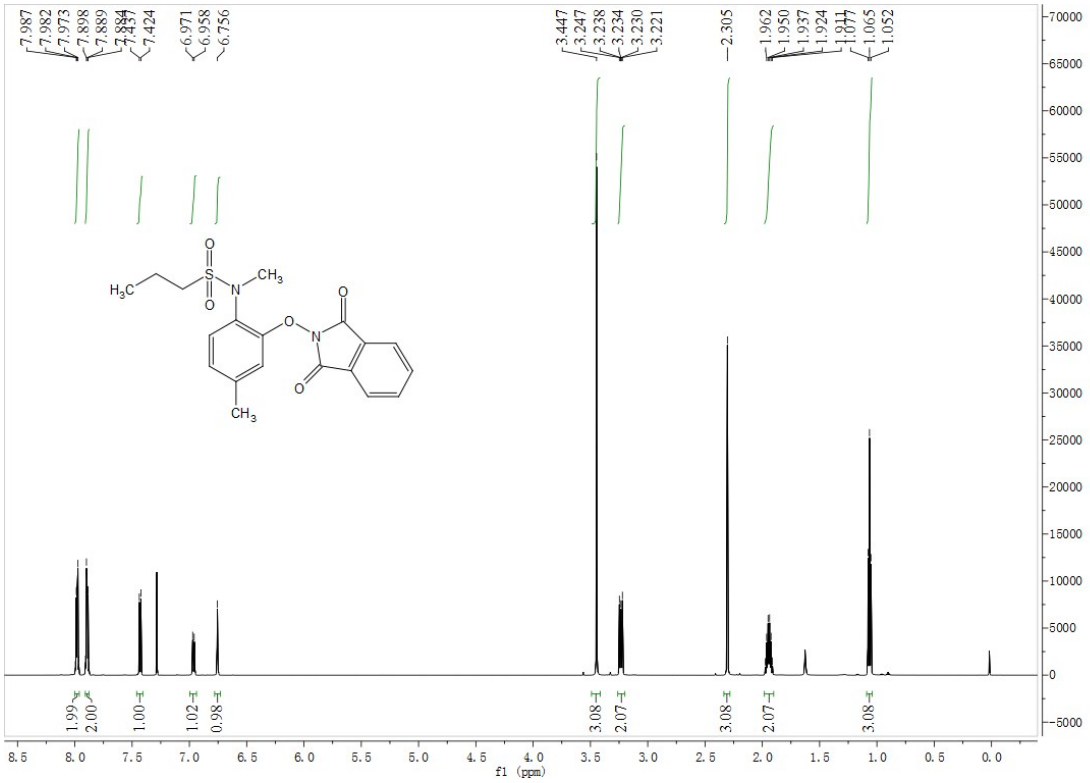

173.885
162.605
153.745
140.080
135.063
129.607
128.781
128.481
125.541
124.070
113.503
36.129
35.560
21.455
18.624
13.854
f1 (ppm)

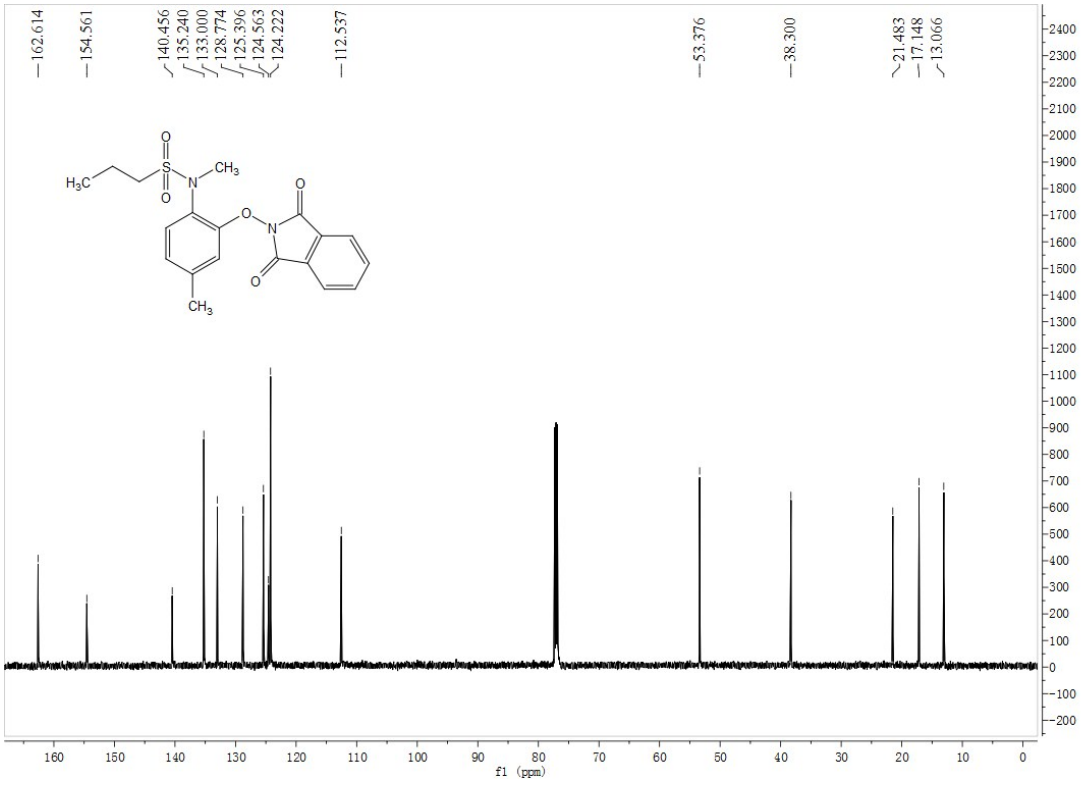

7.947
7.944
7.939
7.936
7.930
7.863
7.859
7.857
7.850
7.134
7.121
6.971
6.958
6.800
3.310
2.335
2.311
2.291
1.901
1.880
1.744
1.691
1.673
1.592
1.578
1.553
1.538
1.518
1.499
1.478
1.234
1.217
1.200
1.063
1.046
1.026
1.93
1.99
0.98
1.00
0.93
2.90
3.96
1.16
6.14
2.09
1.03
f1 (ppm)

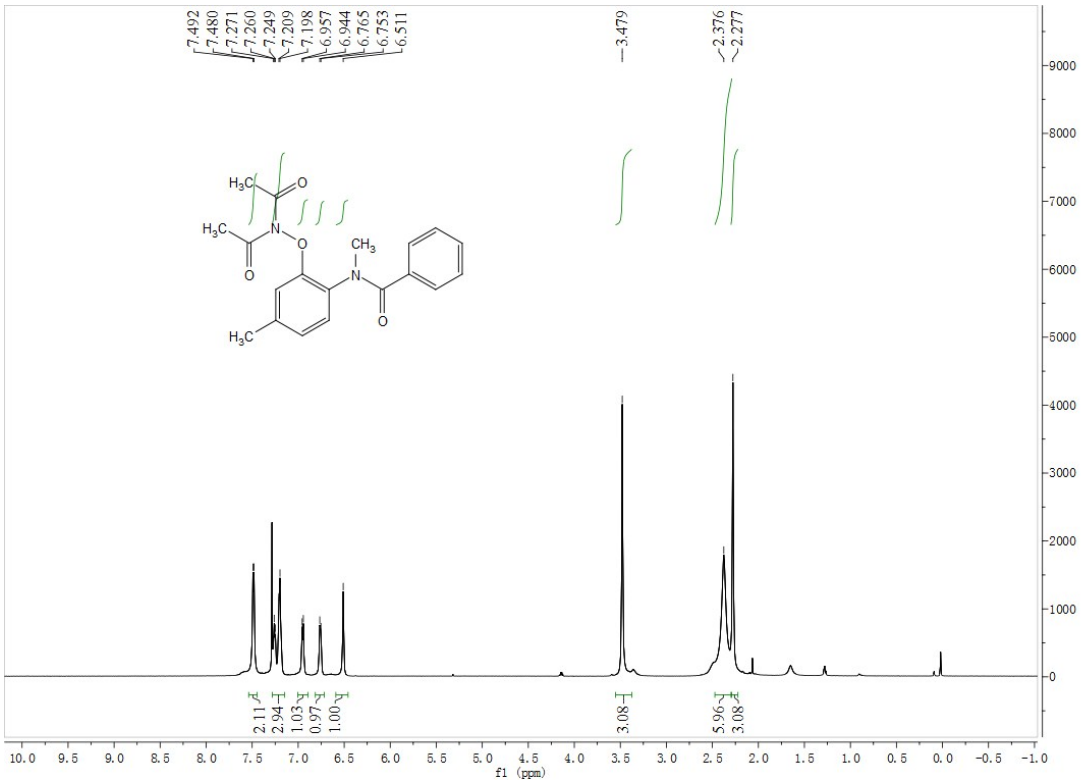

177.235
162.556
153.699
139.989
135.074
129.501
128.832
128.284
125.350
124.097
113.007
41.500
36.265
29.879
29.043
25.744
25.711
25.408
21.530
1.029
f1 (ppm)

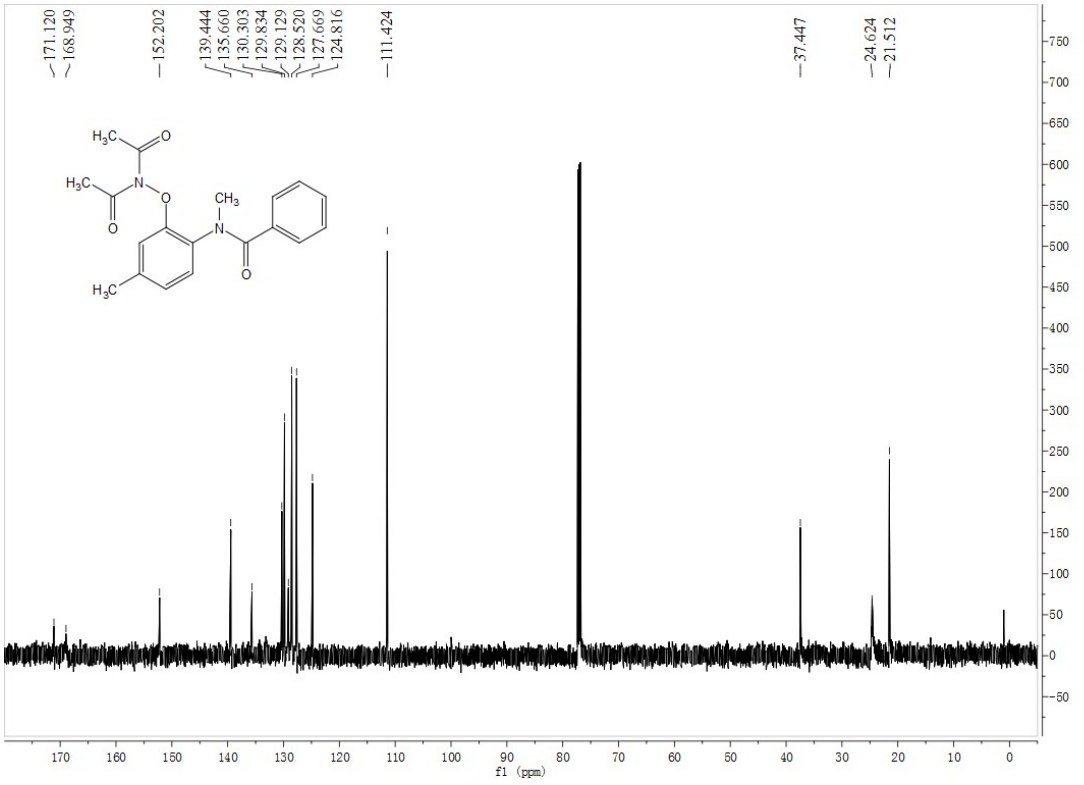

7.967
7.961
7.956
7.950
7.887
7.881
7.877
7.870
7.425
7.409
6.960
6.944
6.754
3.440
3.294
3.279
3.264
3.249
2.290
1.443
1.429
1.414
2.00
2.06
1.00
1.02
0.99
3.08
2.08
3.04
3.02
f1 (ppm)

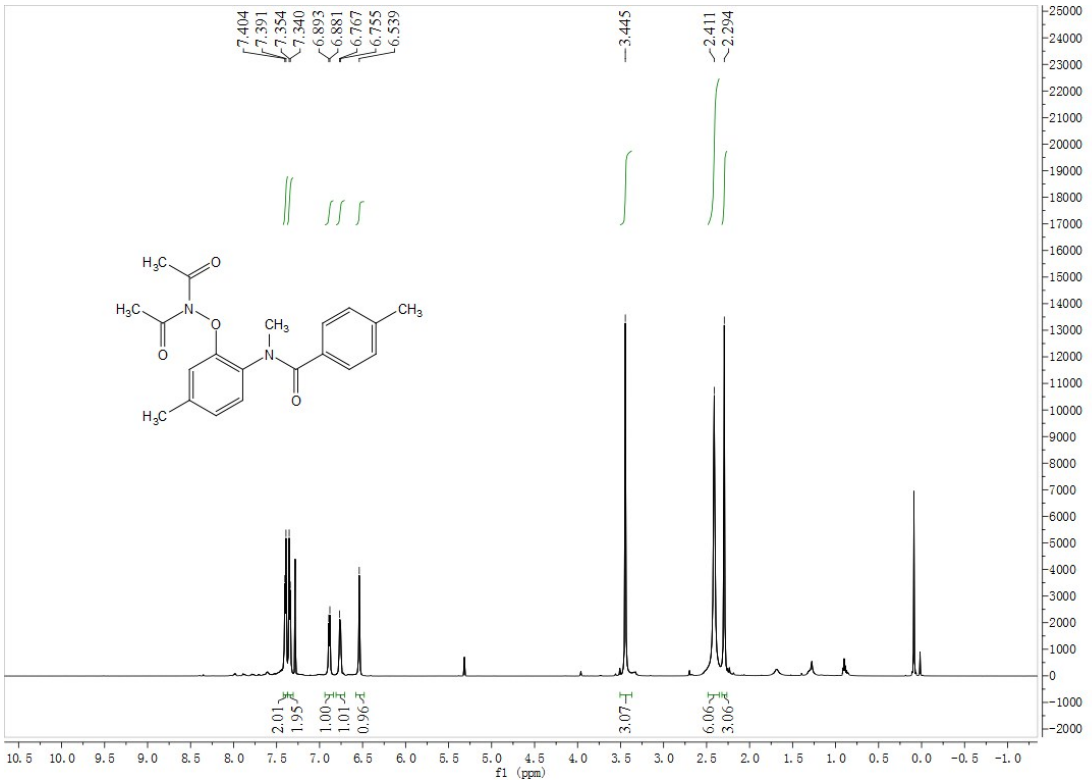

162.613
154.528
140.432
135.208
132.866
128.712
125.384
124.541
124.167
112.561
46.227
38.472
21.430
8.098
f1 (ppm)

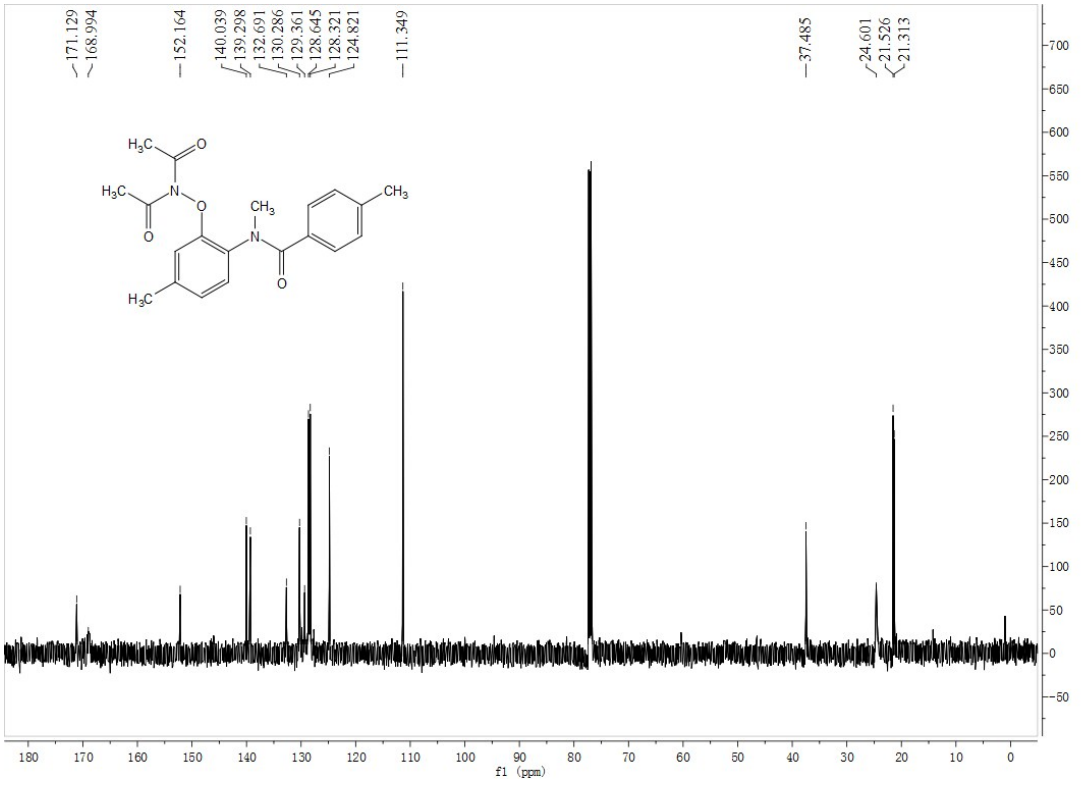

7.987
7.982
7.973
7.898
7.889
7.884
7.437
7.424
6.971
6.958
6.756
3.447
3.247
3.238
3.234
3.230
3.221
2.305
1.962
1.950
1.937
1.924
1.911
1.077
1.065
1.052
1.99
2.00
1.00
1.02
0.98
3.08
2.07
3.08
2.07
3.08
f1 (ppm)

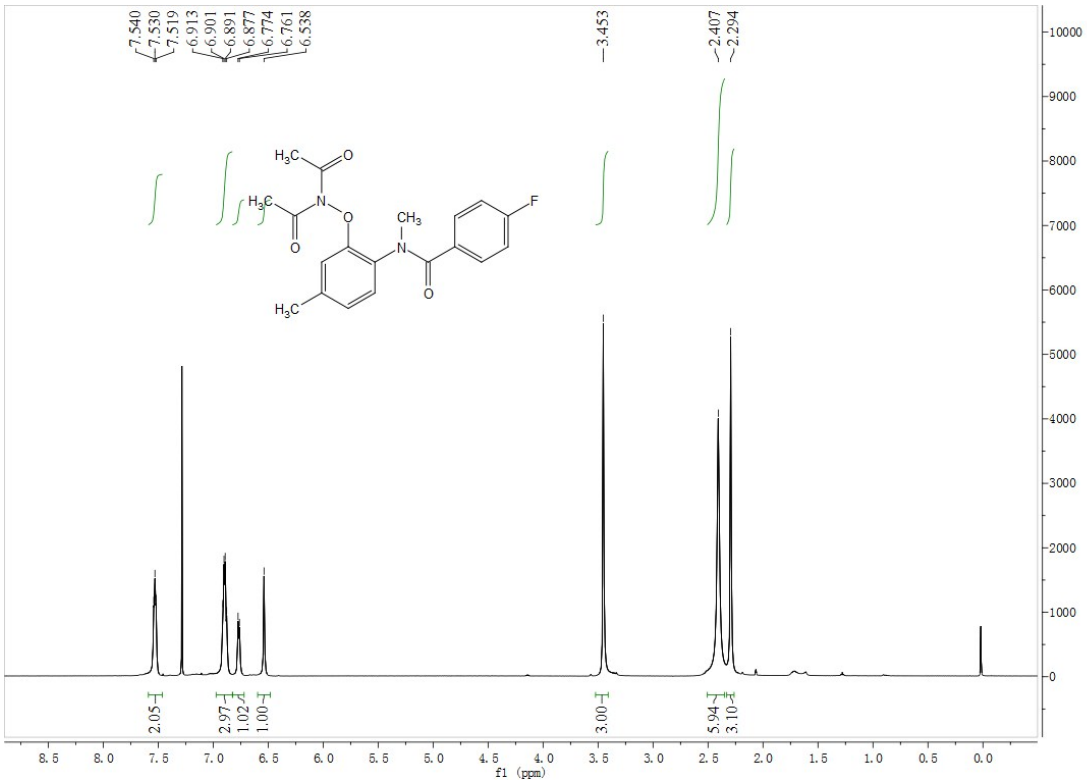

162.614
154.561
140.456
135.240
133.000
128.774
125.396
124.563
124.222
112.537
53.376
38.300
21.483
17.148
13.066
f1 (ppm)

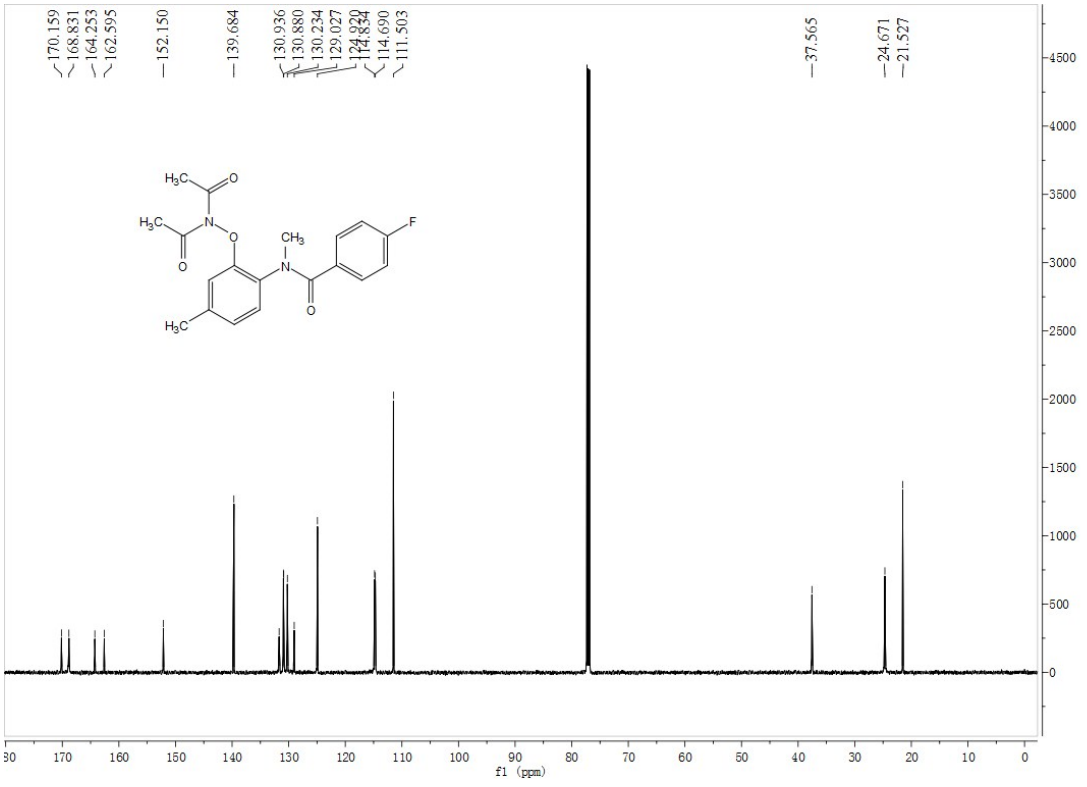

7.492
7.480
7.271
7.260
7.249
7.209
7.198
6.957
6.944
6.765
6.753
6.511
3.479
2.376
2.277
2.11
2.94
1.03
0.97
1.00
3.08
5.96
3.08
f1 (ppm)

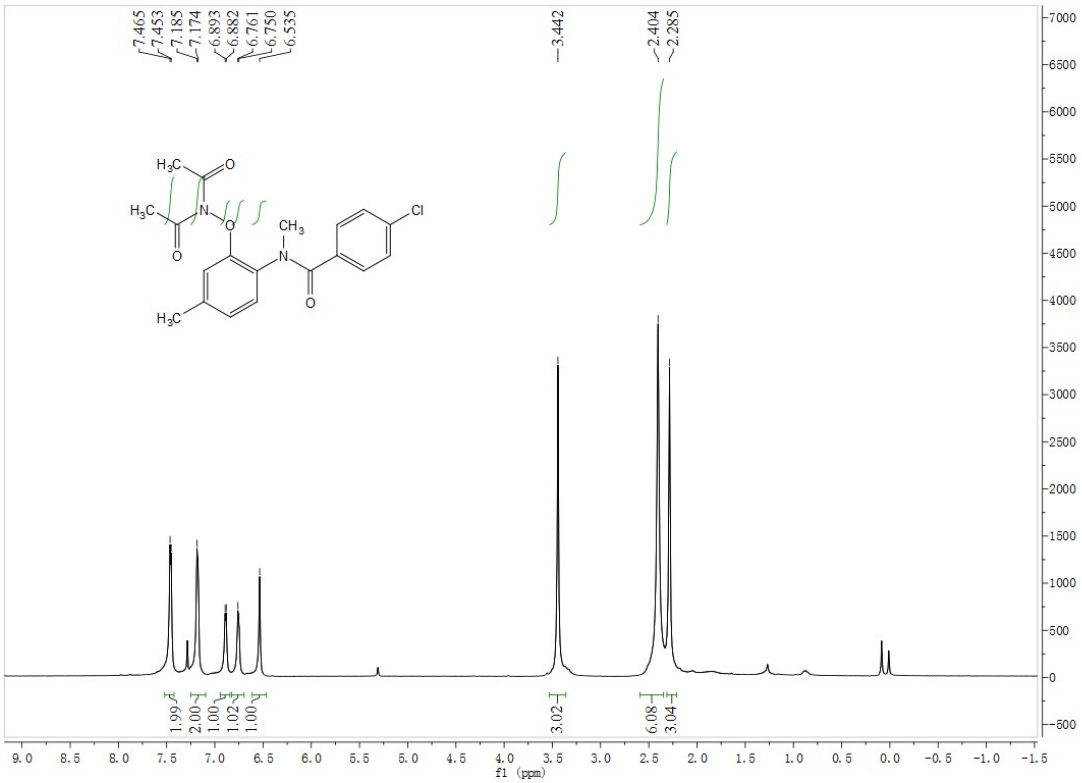

171.120
168.949
152.202
139.444
135.660
130.303
129.834
129.129
128.520
127.669
124.816
111.424
37.447
24.624
21.512
f1 (ppm)

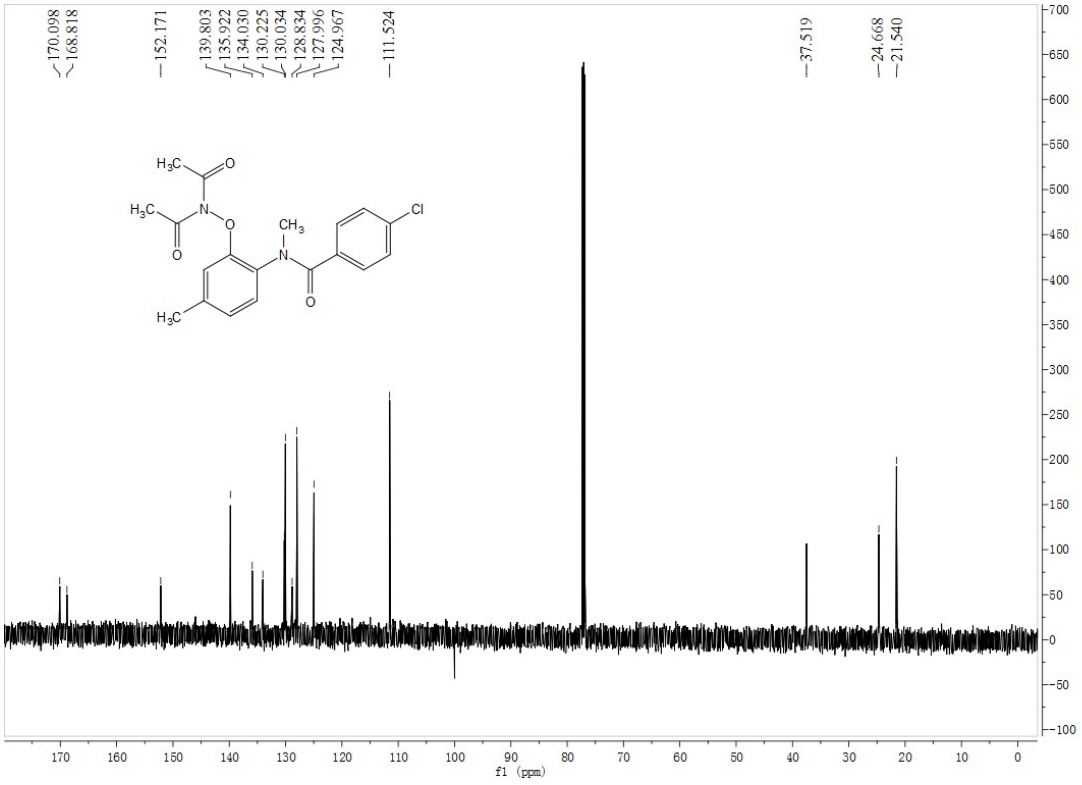

7.404
7.391
7.354
7.340
6.893
6.881
6.767
6.755
6.539
3.445
2.411
2.294
2.01
1.95
1.00
1.01
0.96
3.07
6.06
3.06
f1 (ppm)

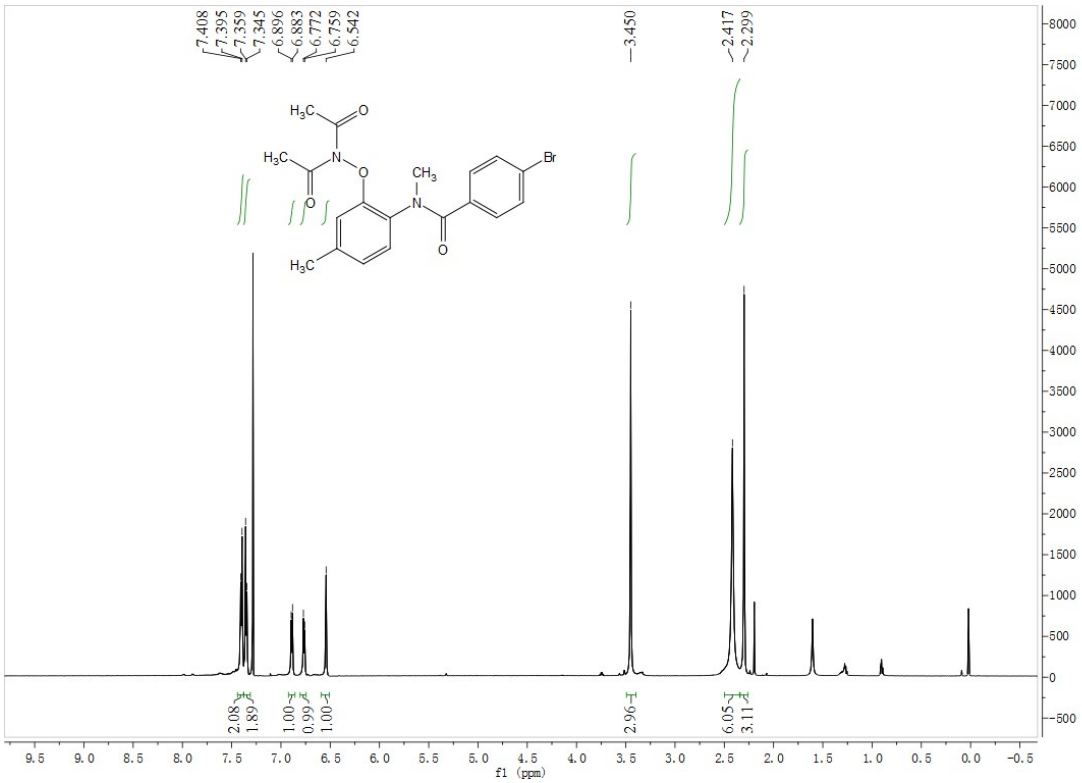

171.129
168.994
152.164
140.039
139.298
132.691
130.286
129.361
128.645
128.321
124.821
111.349
37.485
24.601
21.526
21.313
f1 (ppm)

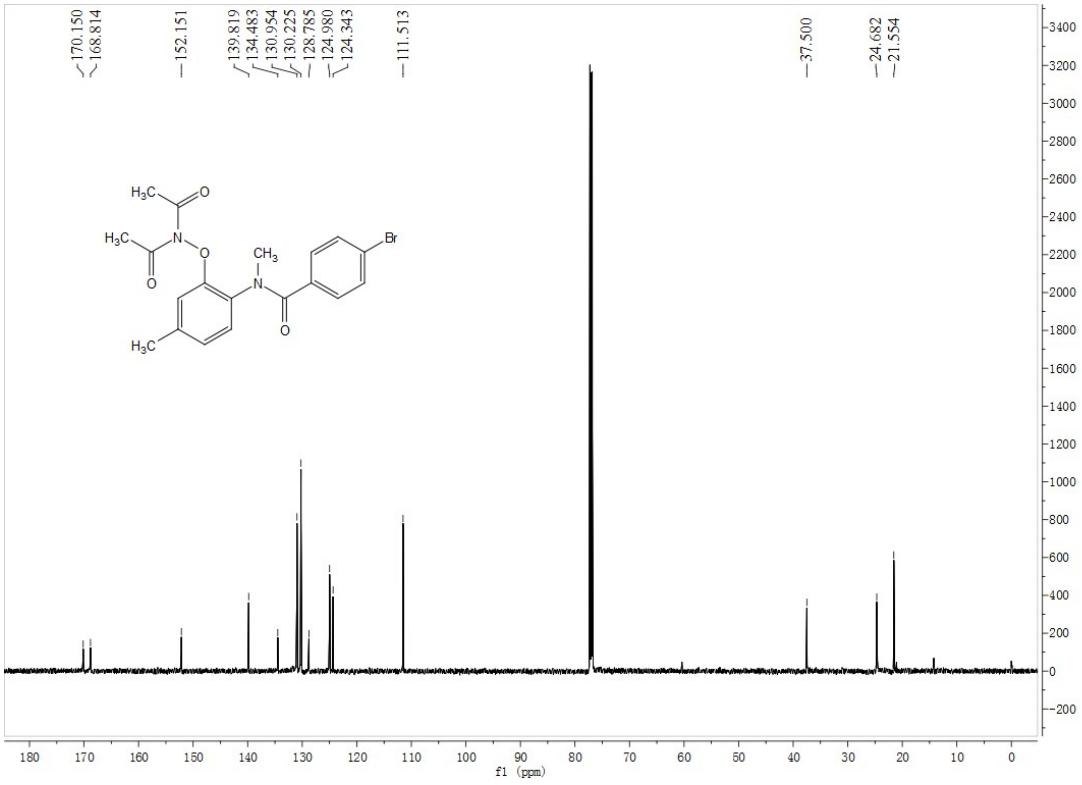

7.540
7.530
7.519
6.913
6.901
6.891
6.877
6.774
6.761
6.538
3.453
2.407
2.294
2.05
2.97
1.02
1.00
3.00
5.94
3.10
f1 (ppm)

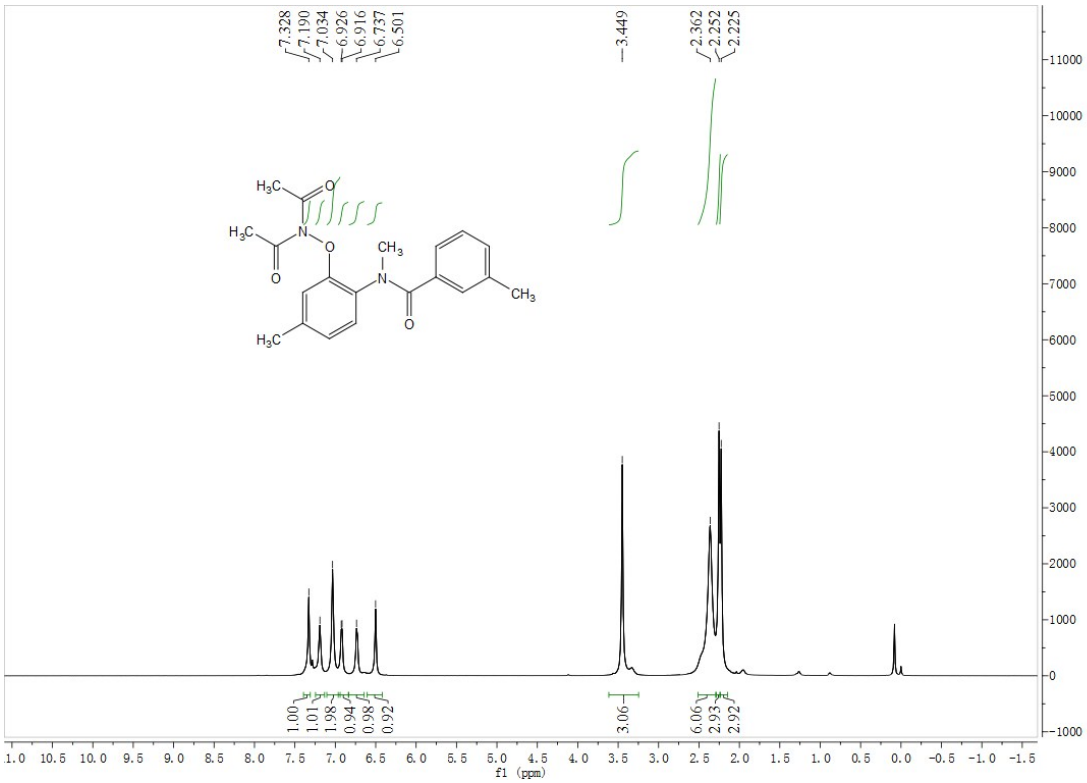

170.159
168.831
164.253
162.595
152.150
139.684
130.936
130.880
130.234
129.027
114.690
111.503
37.565
24.671
21.527
f1 (ppm)

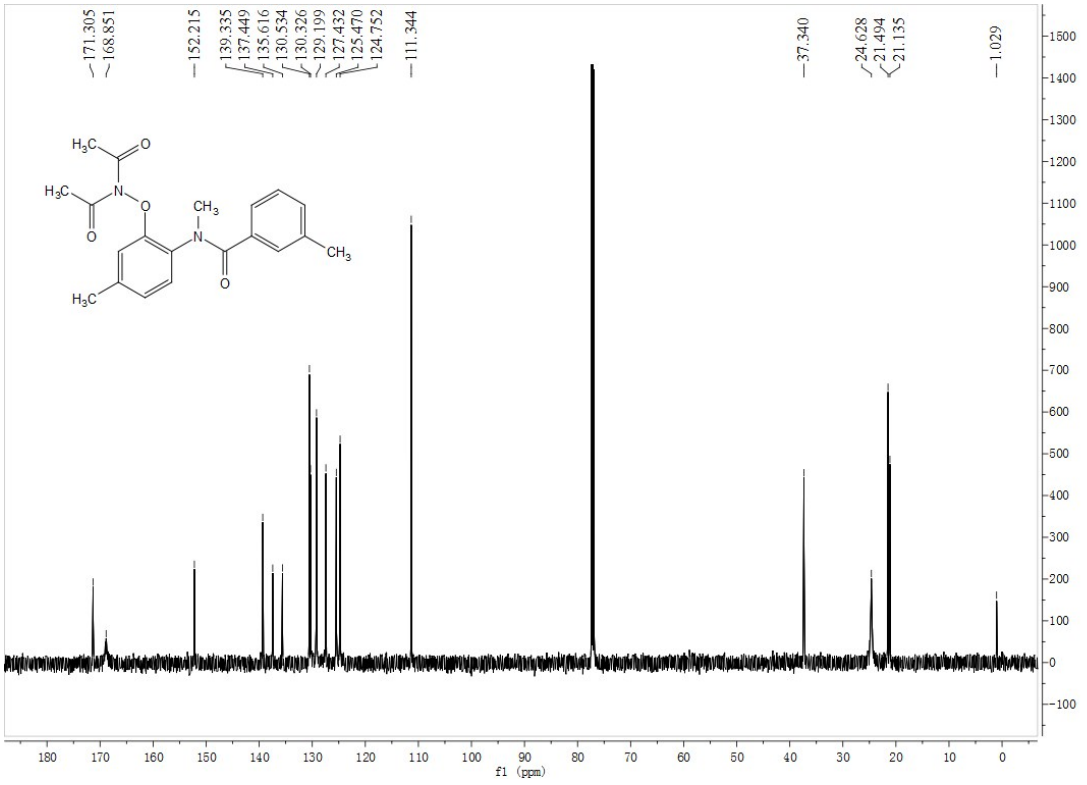

7.465
7.453
7.185
7.174
6.893
6.882
6.761
6.750
6.535
3.442
2.404
2.285
1.99
2.00
1.00
1.02
1.00
3.02
6.08
3.04
f1 (ppm)

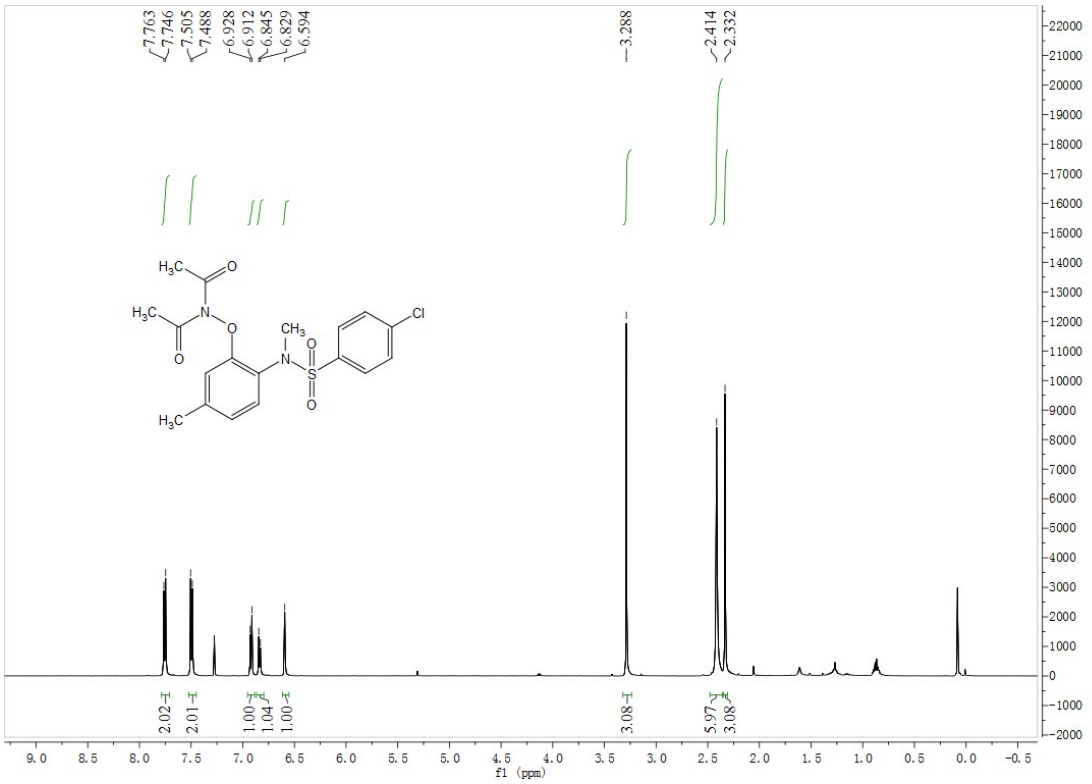

170.098
168.818
152.171
139.803
135.922
134.030
130.225
130.034
128.834
127.996
124.967
111.524
37.519
24.668
21.540
f1 (ppm)

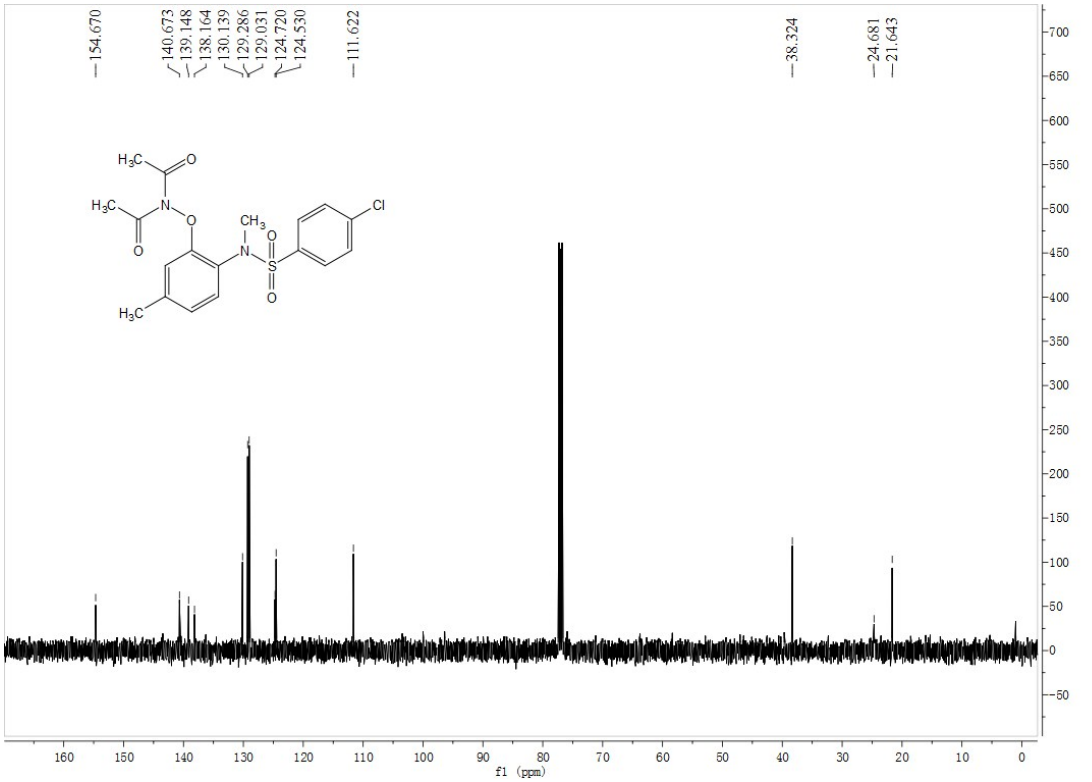

7.408
7.395
7.359
7.345
6.896
6.883
6.772
6.759
6.542
3.450
2.417
2.299
2.08
1.89
1.00
0.99
1.00
2.96
6.05
3.11
f1 (ppm)

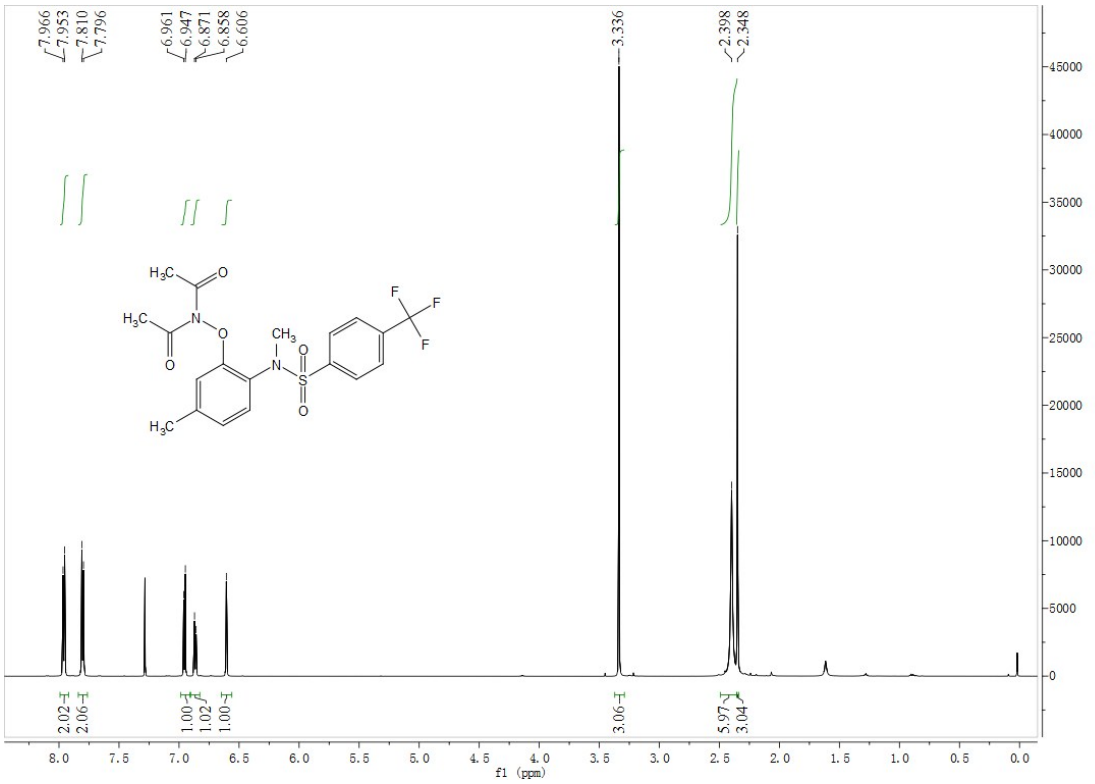

170.150
168.814
152.151
139.819
134.483
130.954
130.225
128.785
124.980
124.343
111.513
37.500
24.682
21.554
f1 (ppm)

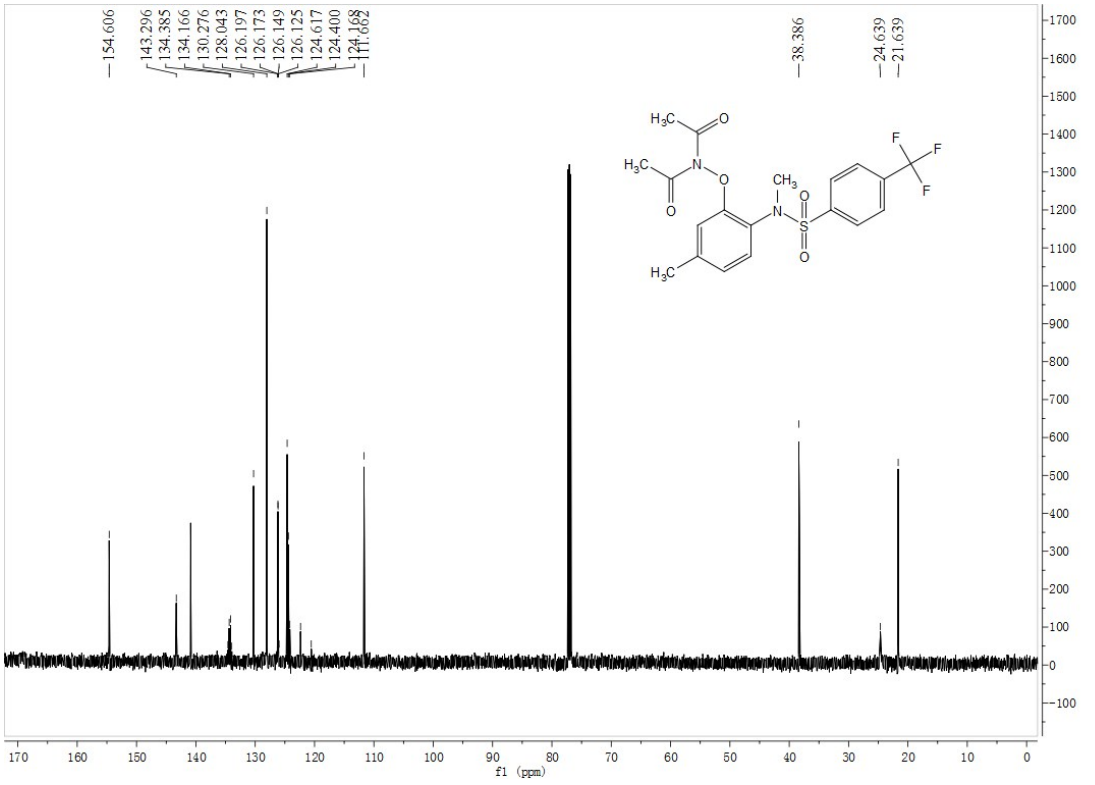

7.328
7.190
7.034
6.926
6.916
6.737
6.501
3.449
2.362
2.252
2.225
1.00
1.01
1.98
0.94
0.98
0.92
3.06
6.06
2.93
2.92
f1 (ppm)

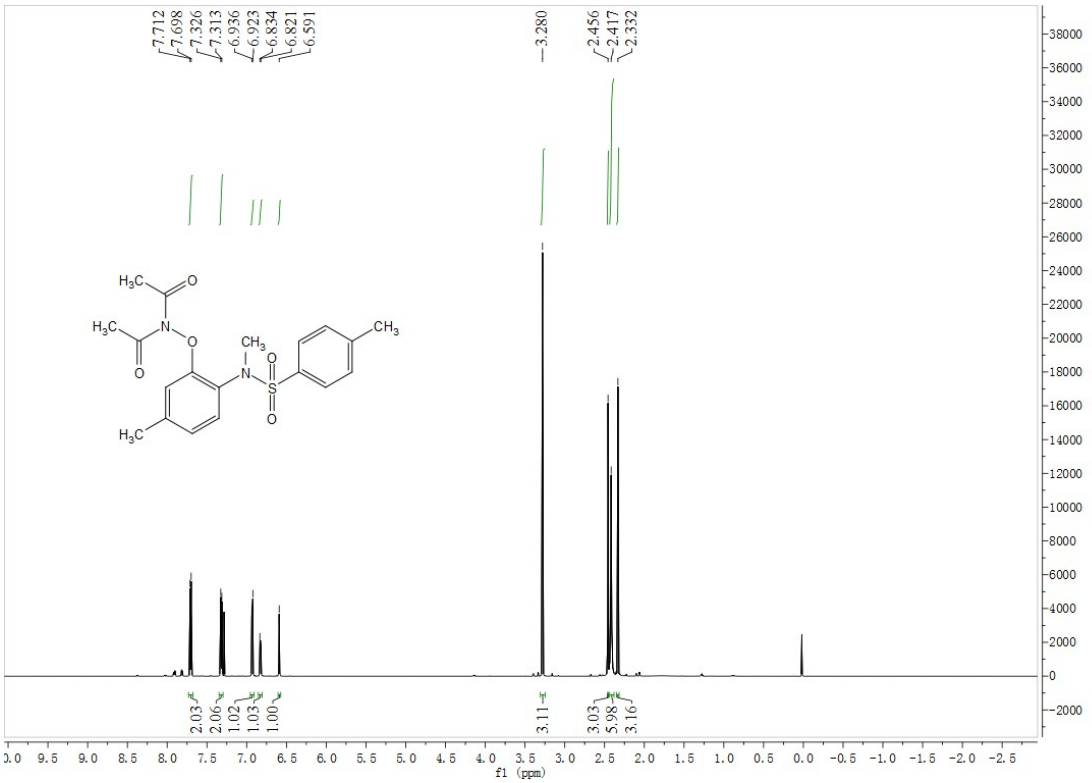

171.305
168.851
152.215
139.335
137.449
135.616
130.534
130.326
129.199
127.432
125.470
124.752
111.344
37.340
24.628
21.494
21.135
1.029
f1 (ppm)

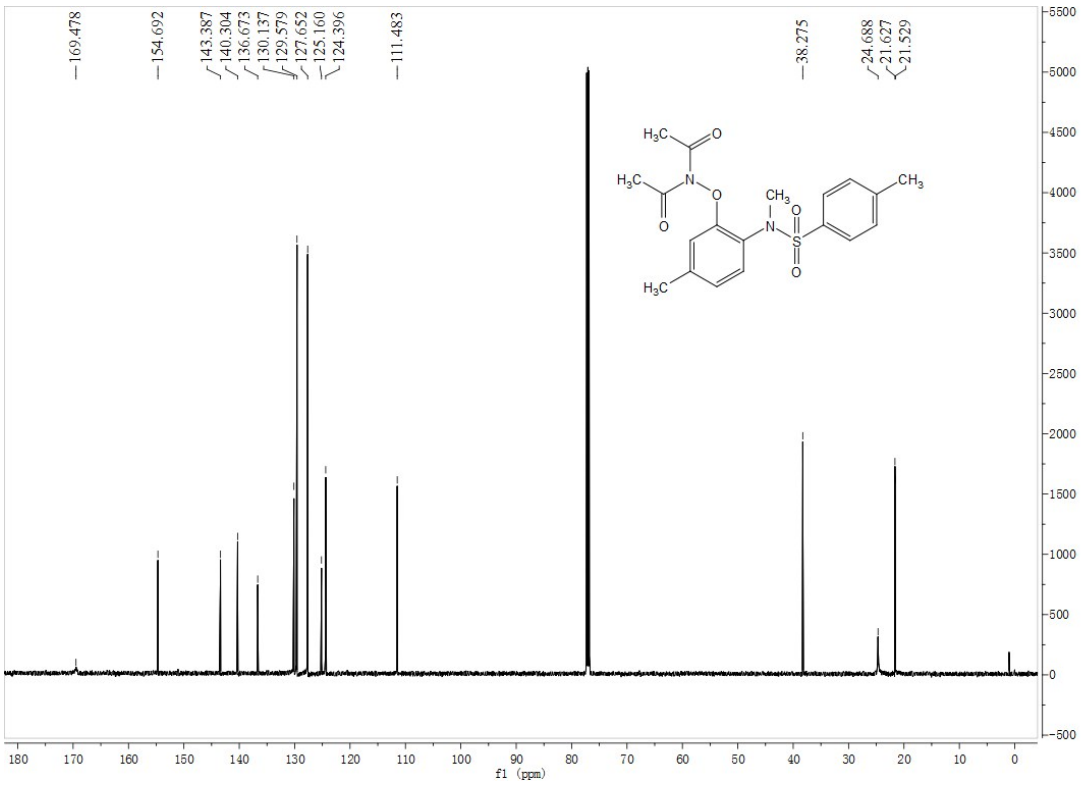

7.763
7.746
7.505
7.488
6.928
6.912
6.845
6.829
6.594
3.288
2.414
2.332
2.02
2.01
1.00
1.04
1.00
3.08
5.97
3.08
f1 (ppm)

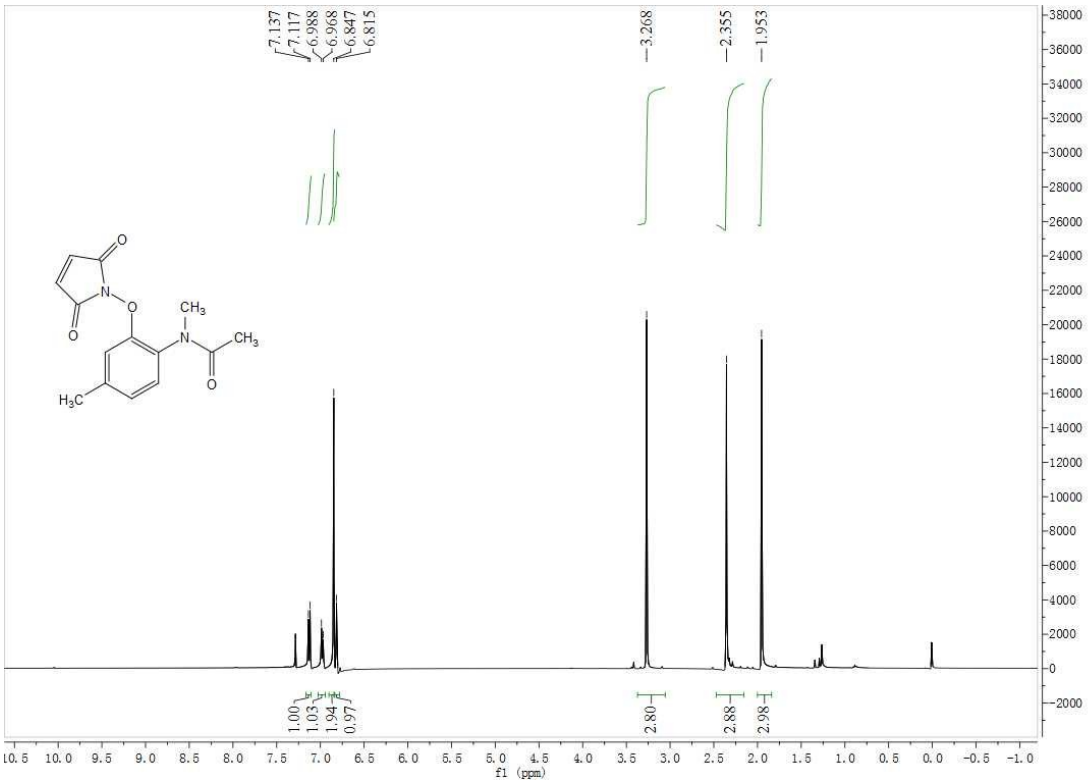

154.670
140.673
139.148
138.164
130.139
129.286
129.031
124.720
124.530
111.622
38.324
24.681
21.643
f1 (ppm)

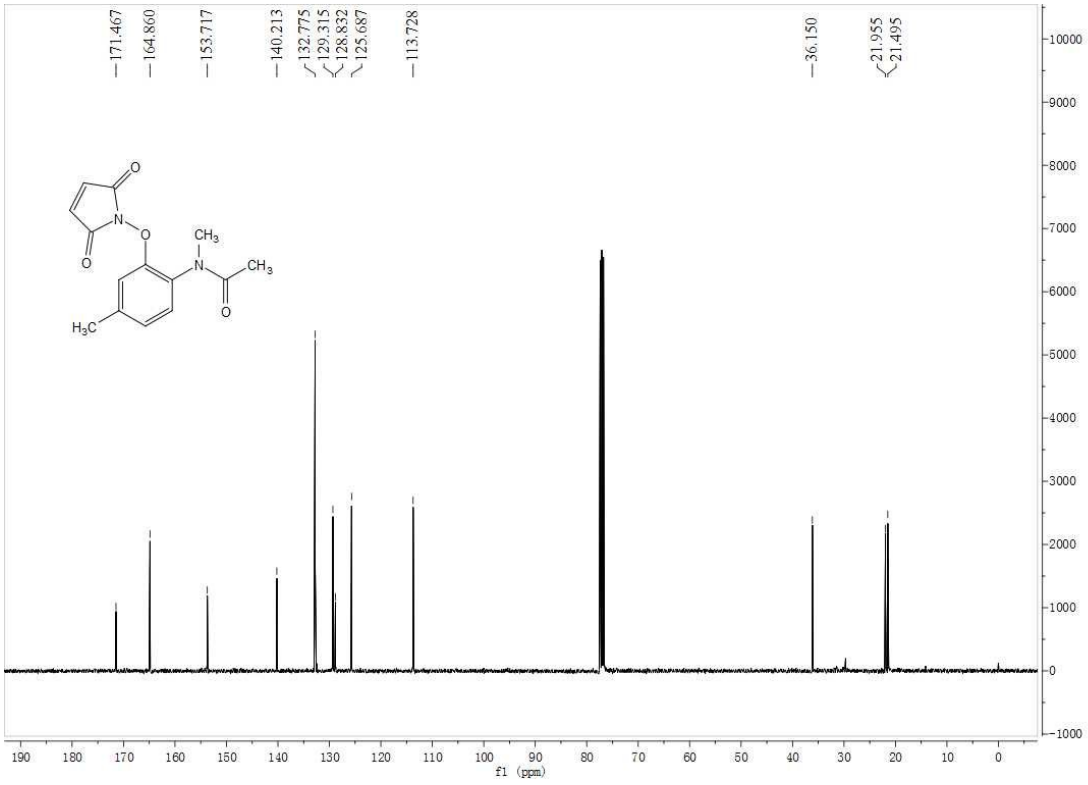

7.966
7.953
7.810
7.796
6.961
6.947
6.871
6.858
6.606
3.336
2.398
2.348
2.02
2.06
1.00
1.02
1.00
3.06
5.97
3.04
f1 (ppm)

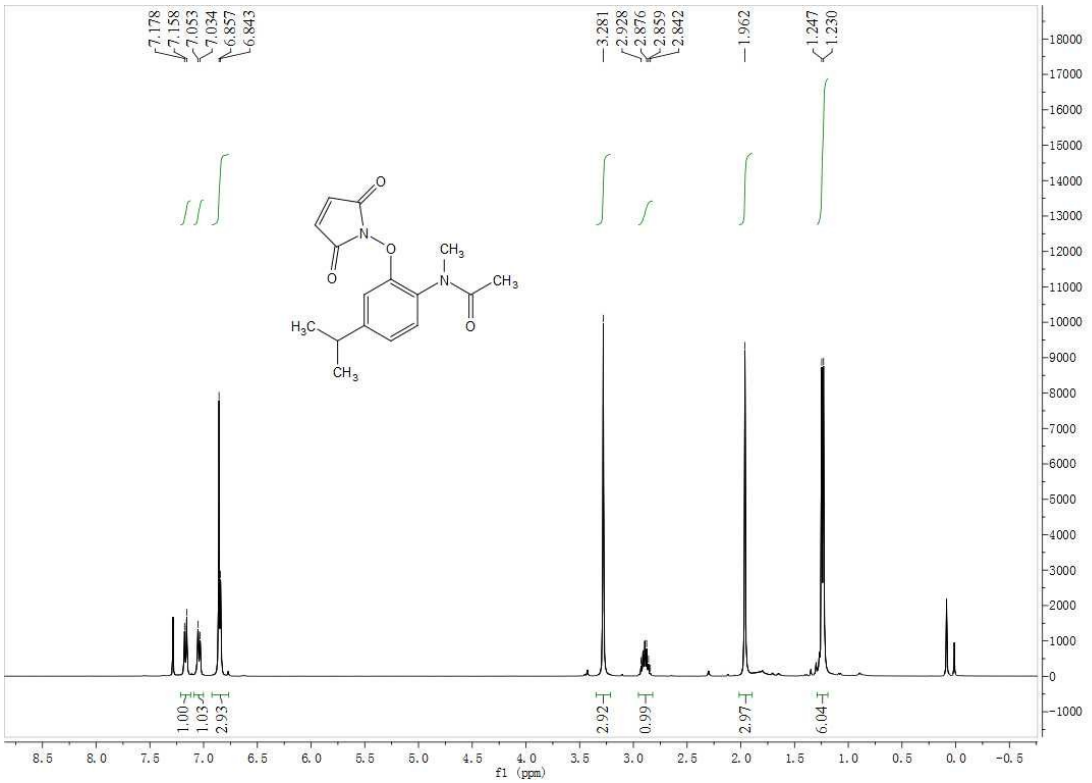

154.606
143.296
134.385
134.166
130.276
128.043
126.197
126.173
126.149
126.125
124.617
124.400
124.168
111.062
38.386
24.639
21.639
f1 (ppm)

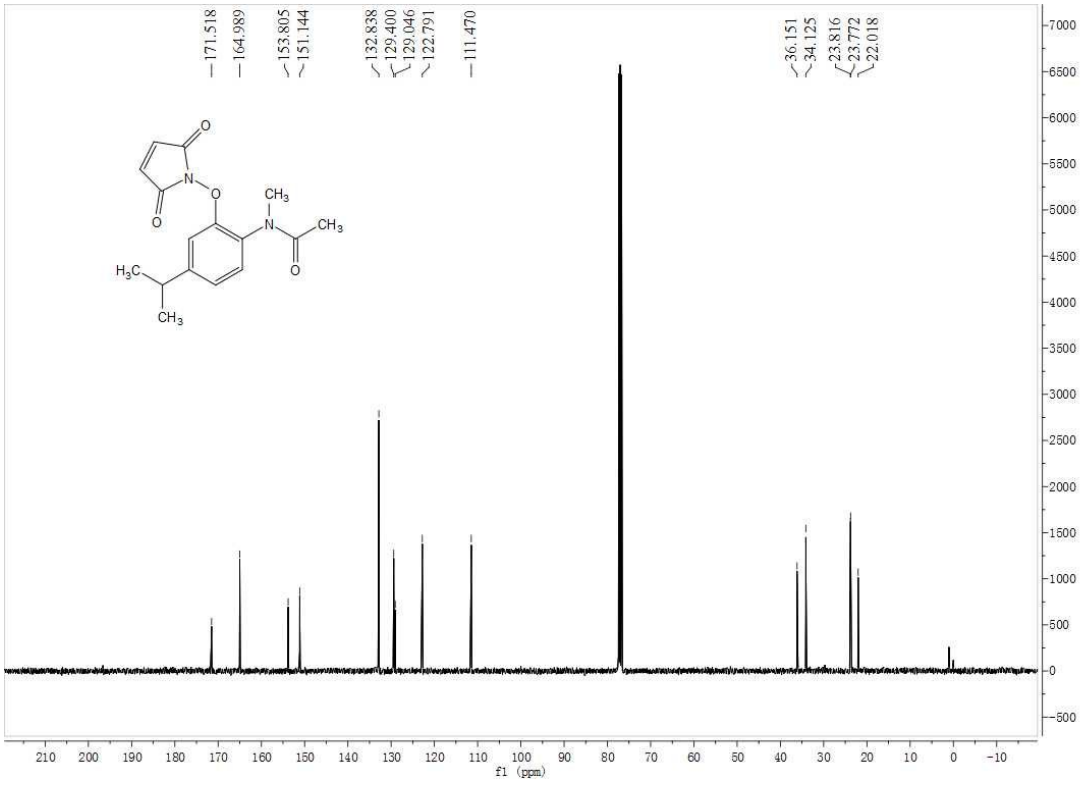

7.712
7.698
7.326
7.313
6.936
6.923
6.834
6.821
6.591
3.280
2.456
2.417
2.332
2.03
2.06
1.02
1.03
1.00
3.11
3.03
5.98
3.16
f1 (ppm)

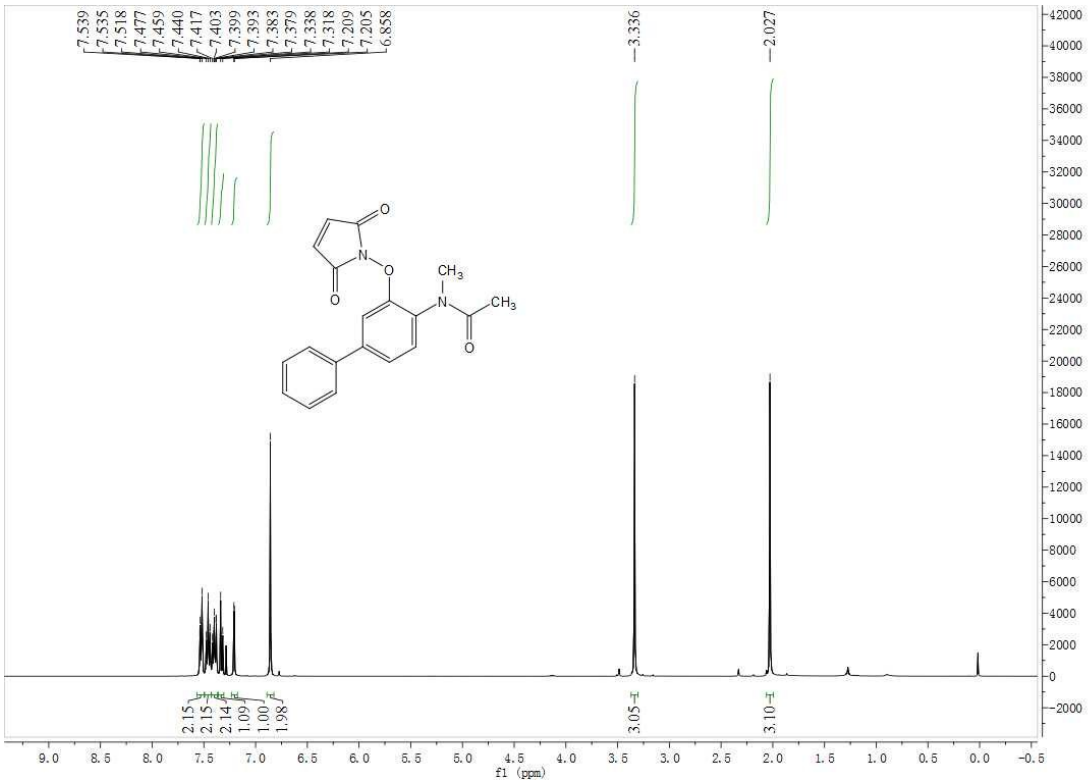

169.478
154.692
143.387
140.304
136.673
130.137
129.579
127.652
125.160
124.396
111.483
38.275
24.688
21.627
21.529
f1 (ppm)

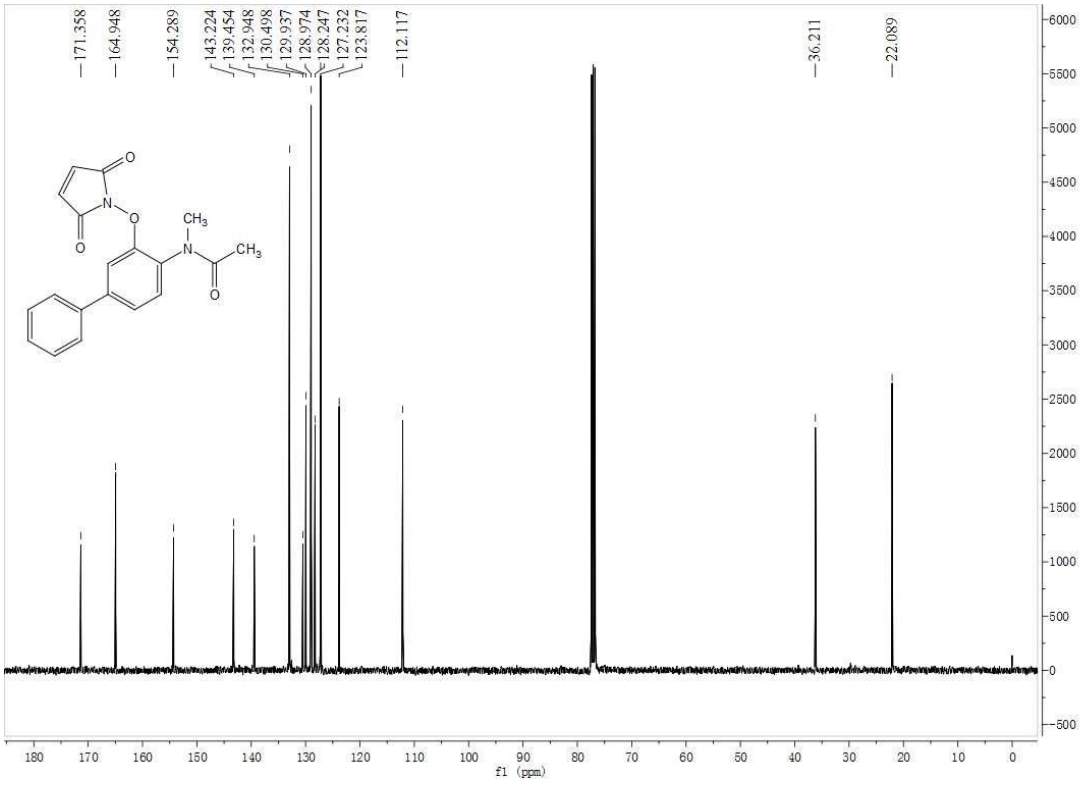

7.137
7.117
6.988
6.968
6.847
6.815
3.268
2.355
1.953
1.00
1.03
1.94
0.97
2.80
2.88
2.98
f1 (ppm)


171.467
164.860
153.717
140.213
132.775
129.315
128.832
125.687
113.728
36.150
21.955
21.495
f1 (ppm)


7.178
7.158
7.053
7.034
6.857
6.843
3.281
2.928
2.876
2.859
2.842
1.962
1.247
1.230
1.00
1.03
2.93
2.92
0.99
2.97
6.04
f1 (ppm)


171.518
164.989
153.805
151.144
132.838
129.400
129.046
122.791
111.470
36.151
34.125
23.816
23.772
22.018
f1 (ppm)


7.539
7.535
7.518
7.477
7.459
7.440
7.417
7.403
7.399
7.393
7.383
7.379
7.338
7.318
7.209
7.205
6.858
3.336
2.027
2.15
2.15
2.14
1.09
1.00
1.98
3.05
3.10
f1 (ppm)


171.358
164.948
154.289
143.224
139.454
132.948
130.498
129.937
128.974
128.247
127.232
123.817
112.117
36.211
22.089
f1 (ppm)