A transition-metal-free cascade benzannulation for the synthesis of 2-hydroxybenzophenones

Xue-Wen He,[a] Wei Zhou,[a] Min Zhang,[a] Min-Yi Tian,[a] Hui-Juan Wang,*[a] You-Ping Tian[b] and Xiong-Li Liu*[a]

[a] National & Local Joint Engineering Research Center for the Exploition of Homology Resources of Medicine and Food, Guizhou University, Guiyang, 550025, China.

[b] College of Pharmaceutical Sciences, Guizhou University of Traditional Chinese Medicine, Guiyang, Guizhou 550025, P. R. China.

E-mail: xlliu1@gzu.edu.cn and xuchwhj@163.com

Table of Contents

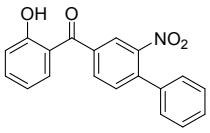
1. General experimental information

Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refered to pure isolated substances. ^{1}H and ^{13}CNMR spectra were obtained using a Bruker DPX-400 spectrometer. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Melting points were measured on an electrothermal digital melting point apparatus. Reagents were purchased from commercial sources and were used as received unless mentioned otherwise.

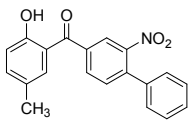
2. Typical experimental procedures for synthesis of compounds 3

In a sealed tube containing air with a magnetic stirring bar, to the mixture of γ-nitroaldehyde **1** (0.20 mmol) and chromone-3-carboxaldehyde **2** (0.30 mmol) in 1.0 mL of DCM was added DBU (1.2 eq). The reaction mixture was stirred at rt for 2 d in the air. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3**, using hexane/EtOAc (8/1, v/v) as the eluent.

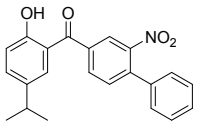
3. Characterization data of compounds 3



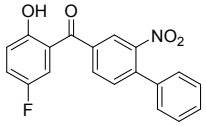
3a: Light yellow solid, m.p. 99.2-100.7 ^{o}C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.86-6.90 (m, 1H), 7.04-7.06 (m, 1H), 7.29-7.31 (m, 2H), 7.36-7.43 (m, 3H), 7.48-7.55 (m, 3H), 7.84-7.87 (m, 1H), 8.09 (s, 1H), 11.67 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 117.5, 117.9, 118.2, 123.8, 126.8, 127.9, 128.0, 131.2, 131.4, 131.9, 135.2, 136.2, 136.7, 138.4, 148.0, 162.4, 197.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{12}NO_4$ $[M-H]^{-}$: 318.0766; Found: 318.0763.



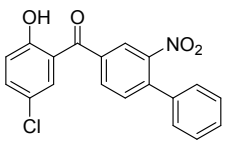
3b: Light yellow solid, m.p. 181.6-183.2 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.22 (s, 3H), 6.95 (d, J = 8.4 Hz, 1H), 7.28-7.32 (m, 4H), 7.39-7.42 (m, 3H), 7.54 (d, J = 8.0 Hz, 1H), 7.83-7.85 (m, 1H), 8.08 (s, 1H), 11.45 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 117.2, 117.6, 123.7, 126.8, 127.4, 127.9, 131.2, 131.3, 131.4, 135.3, 136.9, 137.3, 138.3, 148.0, 160.3, 197.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{14}NO_4$ [M-H]$^-$: 332.0923; Found: 332.0927.



3c: Light yellow solid, m.p. 118.7-119.2 °C; yield 53%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.14 (s, 3H), 1.15 (s, 3H), 2.76-2.83 (m, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.31-7.34 (m, 3H), 7.38-7.42 (m, 4H), 7.55 (d, J = 8.0 Hz, 1H), 8.11 (s, 1H), 11.49 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.9, 32.2, 117.1, 117.7, 124.0, 126.8, 127.9, 128.0, 129.0, 131.2, 131.4, 134.7, 135.3, 136.8, 138.4, 138.6, 148.0, 160.5, 197.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{18}NO_4$ [M-H]$^-$: 360.1230; Found: 360.1235.

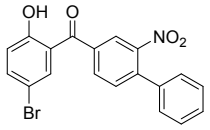


3d: Light yellow solid, m.p. 124.9-126.3 °C; yield 52%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.01-7.04 (m, 1H), 7.18-7.31 (m, 4H), 7.39-7.42 (m, 3H), 7.55 (d, J = 7.6 Hz, 1H), 7.83-7.86 (m, 1H), 8.09 (s, 1H), 11.39 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 116.5 (d, J_{CF} = 24.1 Hz), 116.9 (d, J_{CF} = 7.2 Hz), 119.3, 119.4, 123.7, 123.8 (d, J_{CF} = 23.4 Hz), 126.8, 127.9, 131.2, 131.3, 135.1, 136.1, 138.8, 148.2, 153.4, 153.7 (d, J_{CF} = 239.3 Hz), 158.6, 196.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{11}FNO_4$ [M-H]$^-$: 336.0674; Found: 336.0675.

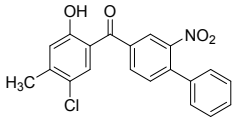


3e: Light yellow solid, m.p. 210.0-211.5 °C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.01 (d, J = 8.8 Hz, 1H), 7.30-7.32 (m, 2H), 7.40-7.48 (m, 5H), 7.56 (d, J = 8.0 Hz, 1H), 7.82-7.85 (m, 1H), 8.09 (s, 1H), 11.55 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 118.1, 119.6, 123.0, 123.7, 126.8,

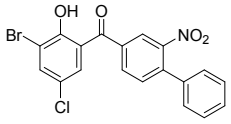
128.0, 128.1, 130.6, 131.2, 131.4, 135.1, 136.0, 136.1, 138.8, 148.3, 160.8, 196.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{11}ClNO_4$ [M-H]$^-$: 352.0378; Found: 352.0382.



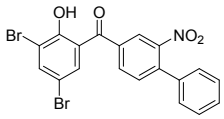
3f: Light yellow solid, m.p. 163.6-165.1 ^{o}C; yield 50%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.97 (d, J = 8.8 Hz, 1H), 7.30-7.33 (m, 2H), 7.40-7.43 (m, 3H), 7.56-7.59 (m, 2H), 7.62 (d, J = 2.4 Hz, 1H), 7.82-7.85 (m, 1H), 8.09 (s, 1H), 11.56 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 109.8, 118.8, 119.9, 123.7, 126.8, 128.0, 128.1, 131.2, 131.4, 133.6, 135.1, 136.0, 138.8, 148.3, 161.3, 196.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{11}BrNO_4$ [M-H]$^-$: 395.9874; Found: 395.9878.



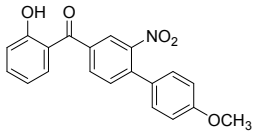
3g: Light yellow solid, m.p. 173.6-175.1 ^{o}C; yield 50%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.35 (s, 3H), 6.94 (s, 1H), 7.29-7.32 (m, 2H), 7.38-7.42 (m, 3H), 7.46 (s, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.81-7.83 (m, 1H), 8.07 (s, 1H), 11.55 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.0, 116.4, 119.9, 123.6, 123.7, 126.8, 127.9, 128.0, 131.0, 131.2, 131.3, 135.2, 136.3, 138.6, 145.8, 148.2, 160.8, 196.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{13}ClNO_4$ [M-H]$^-$: 366.0534; Found: 366.0530.



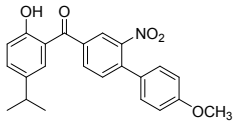
3h: Light yellow solid, m.p. 167.8-169.3 ^{o}C; yield 49%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.29-7.32 (m, 2H), 7.40-7.42 (m, 3H), 7.48 (d, J = 2.4 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 2.4 Hz, 1H), 7.82-7.85 (m, 1H), 8.09 (s, 1H), 12.09 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 112.4, 118.5, 123.3, 123.8, 126.7, 128.0, 128.1, 130.0, 131.3, 131.5, 134.9, 135.4, 138.6, 139.2, 148.3, 157.4, 196.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}BrClNO_4$ [M-H]$^-$: 429.9484; Found: 429.9486.



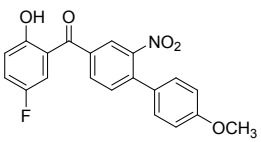
3i: Light yellow solid, m.p. 201.2-202.7 °C; yield 47%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.30-7.32 (m, 2H), 7.40-7.42 (m, 3H), 7.57-7.61 (m, 2H), 7.82-7.85 (m, 1H), 7.89 (d, J = 2.4 Hz, 1H), 8.09 (s, 1H), 12.11 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 109.8, 112.8, 119.2, 123.9, 126.8, 128.0, 128.2, 131.3, 131.5, 132.9, 134.9, 135.4, 139.3, 141.1, 148.3, 157.8, 196.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}Br_2NO_4$ $[M-H]^-$: 473.8977; Found: 473.8981.



3j: Light yellow solid, m.p. 116.6-118.1 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.80 (s, 3H), 6.86-6.90 (m, 1H), 6.91-6.95 (m, 1H), 7.04-7.06 (m, 1H), 7.23-7.26 (m, 2H), 7.48-7.54 (m, 3H), 7.82-7.85 (m, 1H), 8.04 (s, 1H), 11.67 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 54.4, 113.5, 117.6, 117.8, 118.2, 123.8, 127.2, 128.1, 131.1, 131.3, 131.9, 136.1, 136.2, 138.0, 148.1, 159.3, 162.3, 197.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{14}NO_5$ $[M-H]^-$: 348.0874; Found: 348.0871.

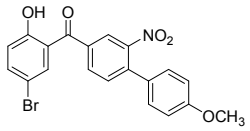


3k: Light yellow solid, m.p. 131.3-132.6 °C; yield 51%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.13 (s, 3H), 1.15 (s, 3H), 2.75-2.82 (m, 1H), 3.79 (s, 3H), 6.92 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 1H), 7.24-7.27 (m, 2H), 7.33 (d, J = 2.4 Hz, 1H), 7.37-7.40 (m, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.82-7.85 (m, 1H), 8.06 (d, J = 1.6 Hz, 1H), 11.49 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.9, 32.2, 54.4, 113.5, 117.2, 117.6, 124.1, 127.3, 128.2, 129.0, 131.0, 131.3, 134.7, 136.3, 137.9, 138.5, 148.0, 159.3, 160.5, 197.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{23}H_{20}NO_5$ $[M-H]^-$: 390.1343; Found: 390.1346.

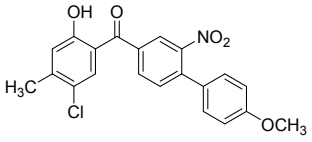


3l: Light yellow solid, m.p. 153.3-154.8 °C; yield 50%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.80 (s,

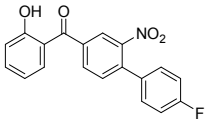
3H), 6.93 (d, J = 8.8 Hz, 2H), 7.01-7.05 (m, 1H), 7.20-7.28 (m, 4H), 7.54 (d, J = 8.0 Hz, 1H), 7.81-7.84 (m, 1H), 8.05 (s, 1H), 11.40 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 54.4, 113.5, 116.5 (d, J_{CF} = 24.1 Hz), 117.0 (d, J_{CF} = 6.4 Hz), 119.2 (d, J_{CF} = 8.1 Hz), 123.8 (d, J_{CF} = 24.2 Hz), 127.1, 128.2, 131.1, 131.2, 135.6, 138.4, 148.2, 153.7 (d, J_{CF} = 238.3 Hz), 158.5, 159.4, 196.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{13}FNO_5$ [M-H]$^-$: 366.0780; Found: 366.0784.



3m: Light yellow solid, m.p. 177.5-179.2 ^{o}C; yield 49%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.80 (s, 3H), 6.92-6.97 (m, 3H), 7.25 (d, J = 8.8 Hz, 2H), 7.54-7.62 (m, 3H), 7.79-7.82 (m, 1H), 8.04 (s, 1H), 11.56 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 54.4, 109.7, 113.5, 118.8, 119.9, 123.8, 127.1, 128.2, 131.2, 133.6, 135.4, 138.4, 138.7, 159.4, 161.2, 196.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{13}BrNO_5$ [M-H]$^-$: 425.9981; Found: 425.9977.

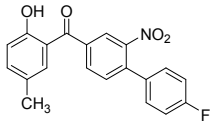


3n: Light yellow solid, m.p. 173.6-175.1 ^{o}C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.35 (s, 3H), 3.79 (s, 3H), 6.91-6.94 (m, 3H), 7.24 (d, J = 8.4 Hz, 2H), 7.46 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.78-7.81 (m, 1H), 8.03 (s, 1H), 11.56 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.9, 54.4, 113.5, 116.5, 119.8, 123.6, 123.7, 127.2, 128.2, 131.0, 131.1, 131.2, 135.7, 138.2, 145.7, 148.2, 159.3, 160.7, 196.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{15}ClNO_5$ [M-H]$^-$: 396.0640; Found: 396.0644.

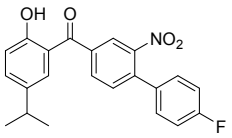


3o: Light yellow solid, m.p. 123.1-124.6 ^{o}C; yield 47%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.86-6.90 (m, 1H), 7.04-7.12 (m, 3H), 7.26-7.30 (m, 2H), 7.49-7.53 (m, 3H), 7.85-7.87 (m, 1H), 8.09 (s, 1H), 11.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 115.1 (d, J_{CF} = 22.3 Hz), 117.5, 117.9, 118.2, 123.9, 128.7 (d, J_{CF} = 8.1 Hz), 131.3 (d, J_{CF} = 26.0 Hz), 136.2, 136.9, 137.3, 148.0, 162.4,

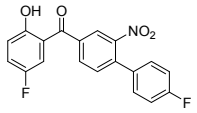
162.6 (d, J_{CF} = 248.3 Hz), 197.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{11}FNO_4$ $[M-H]^-$: 336.0675; Found: 336.0673.



3p: Light yellow solid, m.p. 203.4-204.9 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.22 (s, 3H), 6.95 (d, J = 8.4 Hz, 1H), 7.07-7.12 (m, 2H), 7.26-7.33 (m, 4H), 7.51 (d, J = 7.6 Hz, 1H), 7.83-7.85 (m, 1H), 8.08 (s, 1H), 11.47 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 115.1 (d, J_{CF} = 21.1 Hz), 117.2, 117.7, 123.8, 128.7 (d, J_{CF} = 8.3 Hz), 131.1, 131.4, 137.1, 137.2, 137.4, 148.0, 160.4, 161.6 (d, J_{CF} = 248.1 Hz), 197.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{13}FNO_4$ $[M-H]^-$: 350.0832; Found: 350.0827.

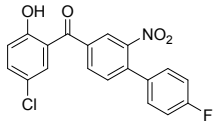


3q: Light yellow solid, m.p. 166.4-167.9 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.13 (s, 3H), 1.15 (s, 3H), 2.75-2.82 (m, 1H), 6.98 (d, J = 21.0 Hz, 1H), 7.07-7.11 (m, 2H), 7.28-7.32 (m, 3H), 7.38-7.41 (m, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.85-7.87 (m, 1H), 8.11 (s, 1H), 11.46 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.9, 32.2, 115.0 (d, J_{CF} = 22.1 Hz), 117.1, 117.7, 124.1, 128.7, 128.9 (d, J_{CF} = 21.2 Hz), 131.1, 131.2, 131.3, 131.5, 134.8, 137.0, 137.3, 138.6, 148.0, 160.5, 161.7 (d, J_{CF} = 248.3 Hz), 197.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{17}FNO_4$ $[M-H]^-$: 378.1144; Found: 378.1142.

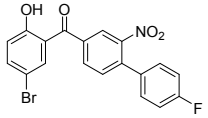


3r: Light yellow solid, m.p. 152.2-153.7 °C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.02-7.05 (m, 1H), 7.08-7.13 (m, 2H), 7.17-7.20 (m, 1H), 7.23-7.30 (m, 3H), 7.53 (d, J = 7.6 Hz, 1H), 7.84-7.86 (m, 1H), 8.10 (s, 1H), 11.38 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 115.1 (d, J_{CF} = 21.2 Hz), 116.4 (d, J_{CF} = 23.3 Hz), 116.9 (d, J_{CF} = 7.2 Hz), 119.4 (d, J_{CF} = 7.0 Hz), 124.0 (d, J_{CF} = 23.3 Hz), 128.7, 131.3, 136.3, 137.7, 148.2, 153.7 (d, J_{CF} = 249.4 Hz), 158.6, 162.2 (d, J_{CF} = 238.4 Hz), 196.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}F_2NO_4$ $[M-H]^-$: 354.0579; Found:

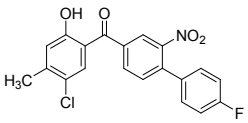
354.0582.



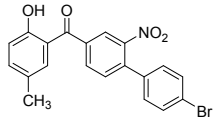
3s: Light yellow solid, m.p. 223.5-225.2 °C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.01-7.03 (m, 1H), 7.08-7.13 (m, 2H), 7.27-7.31 (m, 2H), 7.44-7.46 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.82-7.85 (m, 1H), 8.10 (s, 1H), 11.53 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 115.1 (d, J_{CF} = 21.3 Hz), 118.1, 119.6, 123.0, 123.8, 128.7 (d, J_{CF} = 9.1 Hz), 130.6, 131.3 (d, J_{CF} = 6.2 Hz), 136.1, 136.2, 137.8, 148.2, 160.8, 162.2 (d, J_{CF} = 249.3 Hz), 196.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}ClFNO_4$ $[M-H]^-$: 370.0285; Found: 370.0283.



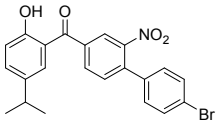
3t: Light yellow solid, m.p. 245.3-246.8 °C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.97 (d, J = 8.4 Hz, 1H), 7.09-7.13 (m, 2H), 7.28-7.32 (m, 2H), 7.54-7.61 (m, 3H), 7.82-7.85 (m, 1H), 8.10 (s, 1H), 11.55 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 109.8, 115.1 (d, J_{CF} = 22.3 Hz), 118.7, 120.0, 123.8, 128.7 (d, J_{CF} = 8.3 Hz), 131.0, 131.1, 131.3 (d, J_{CF} = 6.3 Hz), 133.6, 136.2, 137.8, 138.9, 148.2, 4161.3, 162.2 (d, J_{CF} = 249.3 Hz), 196.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}BrFNO_4$ $[M-H]^-$: 413.9780; Found: 413.9779.



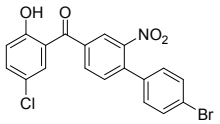
3u: Light yellow solid, m.p. 145.1-146.7 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.35 (s, 3H), 6.94 (s, 1H), 7.07-7.12 (m, 2H), 7.27-7.30 (m, 2H), 7.44 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.81-7.83 (m, 1H), 8.08 (s, 1H), 11.53 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.0, 115.1 (d, J_{CF} = 22.3 Hz), 116.4, 119.9, 123.6, 123.7, 128.7 (d, J_{CF} = 9.1 Hz), 131.0, 131.2, 131.3, 136.5, 137.5, 145.9, 148.2, 161.8 (d, J_{CF} = 248.1 Hz), 195.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{12}ClFNO_4$ $[M-H]^-$: 384.0441; Found: 384.0442.



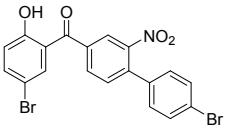
3v: Light yellow solid, m.p. 215.4-216.9 °C; yield 51%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.22 (s, 3H), 6.95 (d, J = 8.4 Hz, 1H), 7.17-7.19 (m, 2H), 7.25 (s, 1H), 7.31-7.33 (m, 1H), 7.49-7.55 (m, 3H), 7.83-7.86 (m, 1H), 8.10 (s, 1H), 11.46 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 117.1, 117.7, 122.5, 123.9, 127.5, 128.4, 131.0, 131.1, 131.3, 131.5, 134.3, 137.1, 137.3, 137.4, 147.8, 160.4, 197.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{13}BrNO_4$ [M-H]$^-$: 410.0030; Found: 410.0034.



3w: Light yellow solid, m.p. 149.2-150.7 °C; yield 56%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.13 (s, 3H), 1.15 (s, 3H), 2.75-2.82 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.18-7.20 (m, 2H), 7.31 (d, J = 2.4 Hz, 1H), 7.38-7.41 (m, 1H), 7.50-7.55 (m, 3H), 7.86-7.88 (m, 1H), 8.13 (s, 1H), 11.46 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.9, 32.2, 117.1, 117.7, 122.5, 124.2, 128.4, 128.9, 131.0, 131.1, 131.6, 134.3, 134.8, 137.2, 138.6, 147.7, 160.6, 197.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{17}BrNO_4$ [M-H]$^-$: 438.0342; Found: 438.0339.

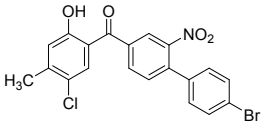


3x: Light yellow solid, m.p. 213.7-215.2 °C; yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.01 (d, J = 9.6 Hz, 1H), 7.17-7.19 (m, 2H), 7.44-7.47 (m, 2H), 7.52-7.55 (m, 3H), 7.83-7.85 (m, 1H), 8.11 (s, 1H), 11.52 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 118.0, 119.6, 122.6, 123.0, 123.9, 128.4, 130.6, 131.2, 131.4, 134.1, 136.2, 136.4, 137.7, 148.0, 160.9, 196.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}BrClNO_4$ [M-H]$^-$: 429.9484; Found: 429.9489.



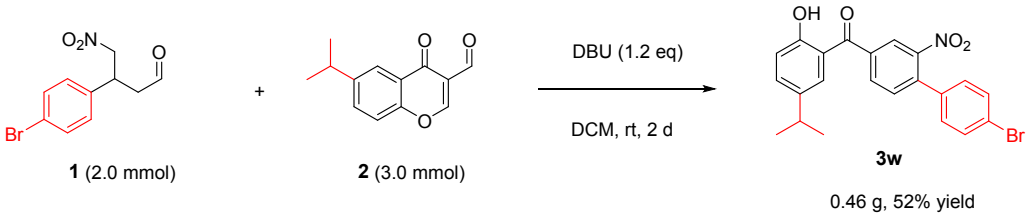
3y: Light yellow solid, m.p. 224.9-226.4 °C; yield 50%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.96-6.98 (m, 1H), 7.17-7.19 (m, 2H), 7.52-7.60 (m, 5H), 7.83-7.85 (m, 1H), 8.11 (s, 1H), 11.54 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 109.8, 118.7, 120.0, 122.6, 123.9, 128.4, 131.2, 131.4, 133.6, 134.1, 136.4, 137.7, 138.9, 148.0, 161.3, 196.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{19}H_{10}Br_2NO_4$

[M-H]$^-$: 473.8977; Found: 473.8982.



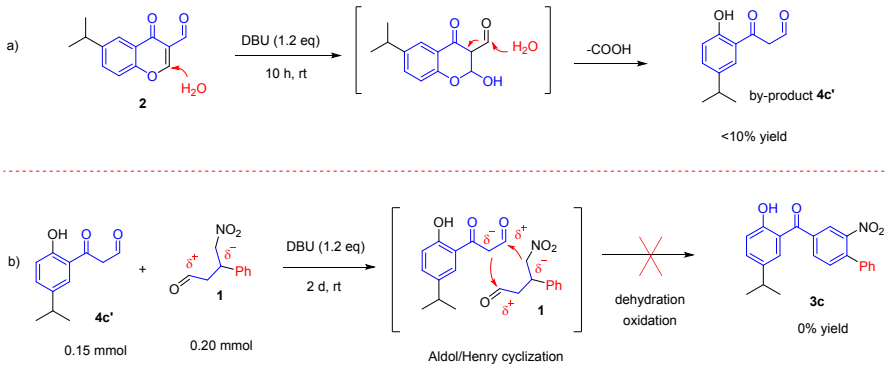
3z: Light yellow solid, m.p. 149.6-151.1 ^{o}C; yield 52%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.36 (s, 3H), 6.95 (s, 1H), 7.17-7.19 (m, 2H), 7.44 (s, 1H), 7.51-7.56 (m, 3H), 7.82-7.84 (m, 1H), 8.10 (s, 1H), 11.53 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.0, 116.4, 119.9, 122.5, 123.7, 123.8, 128.4, 131.0, 131.2, 131.3, 134.1, 136.7, 137.5, 145.9, 147.9, 160.8, 195.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{12}BrClNO_4$ [M-H]$^-$: 443.9641; Found: 443.9637.

4. Scheme S1: large-scale synthesis of product 3w



In a sealed tube containing air with a magnetic stirring bar, to the mixture of γ-nitroaldehyde **1** (2.0 mmol) and chromone-3-carboxaldehyde **2** (3.0 mmol) in 10.0 mL of DCM was added DBU (1.2 eq). The reaction mixture was stirred at rt for 2 d in the air. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3w**, using hexane/EtOAc (8/1, v/v) as the eluent (0.46 g, 52% yield).

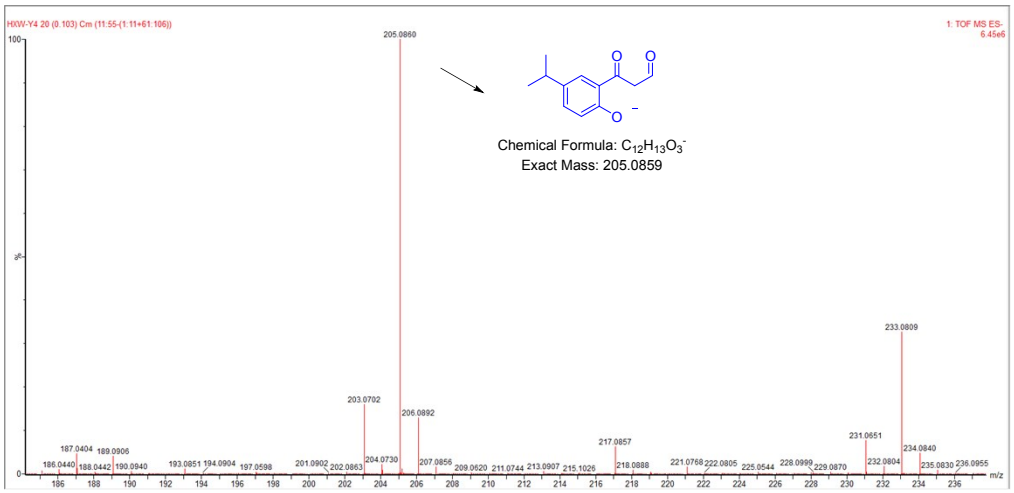
5. Scheme S2: control experiments



In a sealed tube containing air with a magnetic stirring bar, to the mixture of chromone-3-carboxaldehyde **2** (0.2 mmol) in 1.0 mL of DCM was added DBU (1.2 eq). The reaction mixture was stirred at rt for 10 h in the air. The mixture was directly detected by HRMS analysis (HRMS

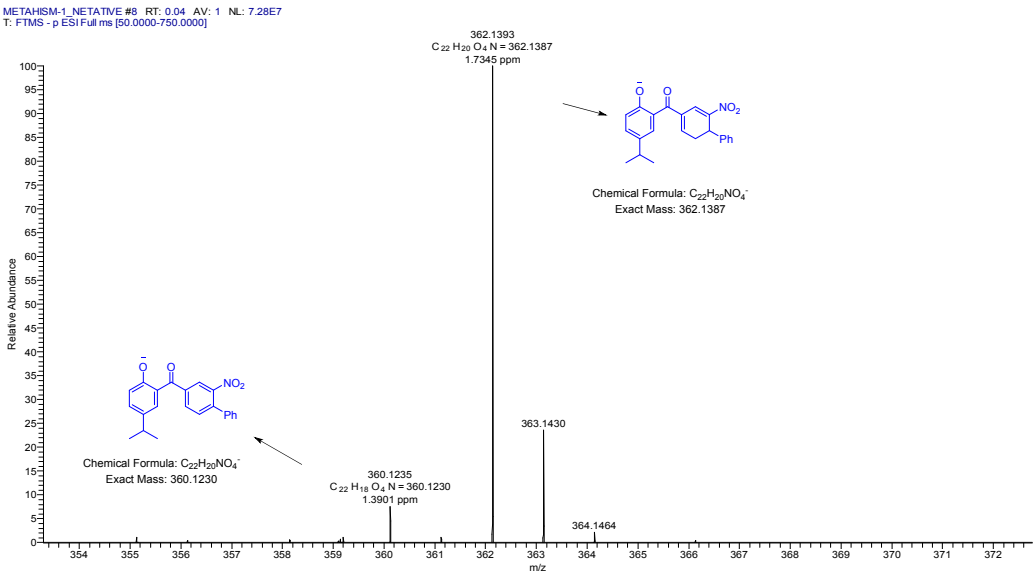
(ESI) exact mass calcd for $C_{12}H_{13}O_3^-$ requires m/z 205.0859, found m/z 205.0860).

In a sealed tube containing air with a magnetic stirring bar, to the mixture of chromone-3-carboxaldehyde **2** (0.20 mmol) and the *β*-keto aldehyde **4c′** (0.15 mmol) in 1.0 mL of DCM was added DBU (1.2 eq). The reaction mixture was stirred at rt for 2 d in the air. However, the reaction did not provide the desired product **3c**.



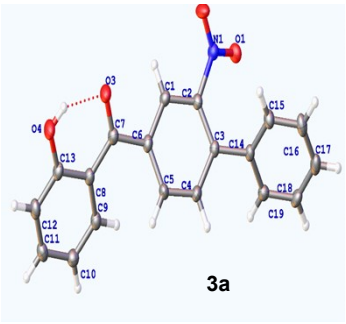
program: a solution of substrate **2** and DBU was stirred at rt for 4 h

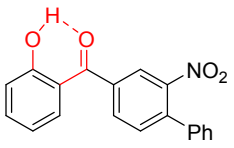
6. Figure S1: intermediate III detected by ESI-MS analysis in reaction solution.



program: a solution of substrate **2**, DBU and γ-nitroaldehyde **1** was stirred at rt for 4 h

7. X-Ray crystal data for compounds 3a and 3f



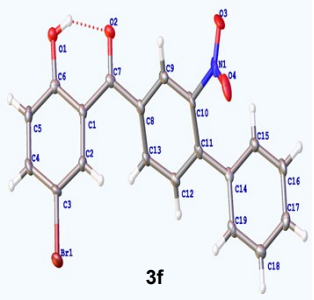


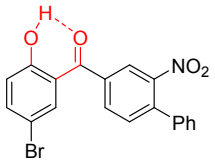
3a

Table S1 Crystal data and structure refinement for 3a

Identification code	**3a**
Empirical formula	$C_{19}H_{13}NO_4$
Formula weight	319.30
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å, b/Å, c/Å	4.2074(4), 12.9179(9), 27.180(2)
α/°, β/°, γ/°,	90, 94.001(7), 90.
Volume/Å^3	1473.7(2)
Z	4
ρ_{calc}g/cm^3	1.439
μ/mm^{-1}	0.843
F(000)	664.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.52 to 146.668
Index ranges	-2 ≤ h ≤ 5, -15 ≤ k ≤ 14, -33 ≤ l ≤ 33
Reflections collected	6110
Independent reflections	2894 [R_{int} = 0.0505, R_{sigma} = 0.0559]
Data/restraints/parameters	2894/0/218
Goodness-of-fit on F^2	1.133
Final R indexes [I>=2σ (I)]	R_1 = 0.0771, wR_2 = 0.2231
Final R indexes [all data]	R_1 = 0.0845, wR_2 = 0.2291
Largest diff. peak/hole / e Å^{-3}	0.35/-0.44

Crystal data for **3a**: **Crystal Data** for $C_{19}H_{13}NO_4$ (*M* =319.30 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 4.2074(4) Å, *b* = 12.9179(9) Å, *c* = 27.180(2) Å, *β* = 94.001(7)°, *V* = 1473.7(2) Å^3, *Z* = 4, *T* = 100.01(10) K, μ(Cu Kα) = 0.843 mm^{-1}, *Dcalc* = 1.439 g/cm^3, 6110 reflections measured (6.52° ≤ 2Θ ≤ 146.668°), 2894 unique (R_{int} = 0.0505, R_{sigma} = 0.0559) which were used in all calculations. The final R_1 was 0.0771 (I > 2σ(I)) and wR_2 was 0.2291 (all data).





3f

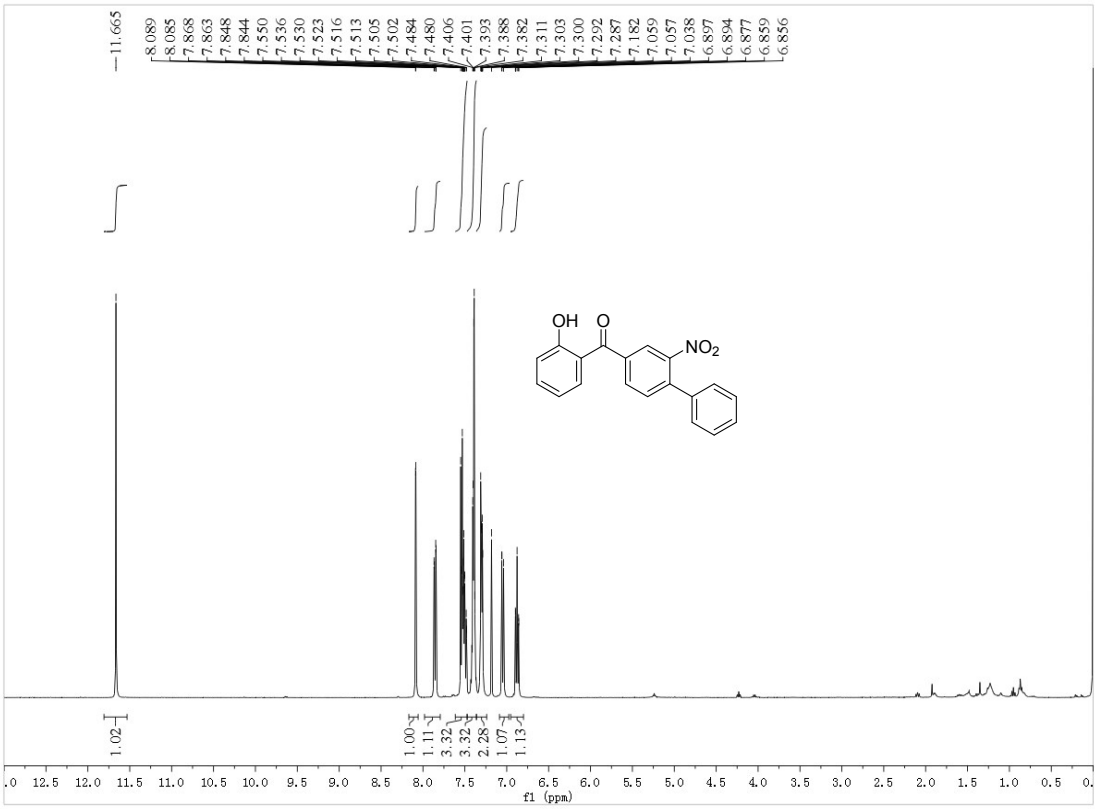
Table S2 Crystal data and structure refinement for 3f

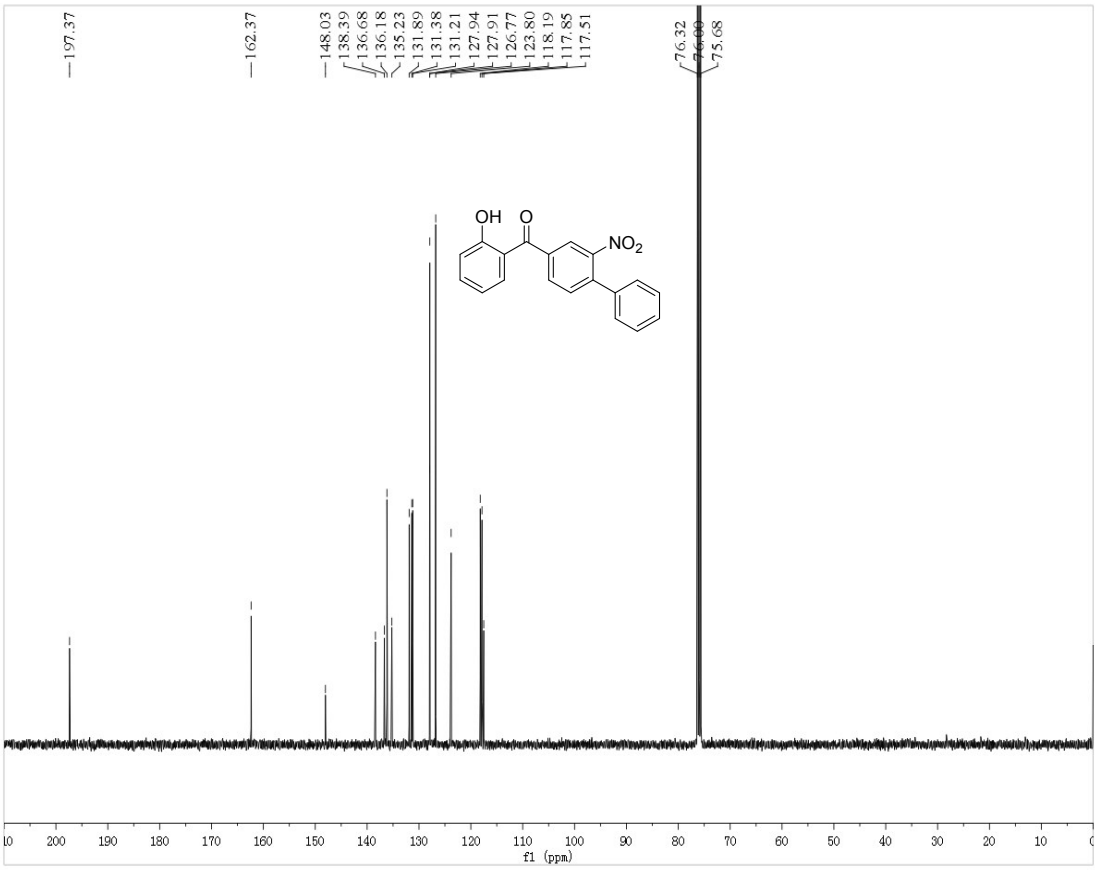
Identification code	**3f**
Empirical formula	$C_{19}H_{12}BrNO_4$
Formula weight	398.21
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å, b/Å, c/Å	12.5309(7), 7.1686(4), 17.8685(10)
α/°, β/°, γ/°,	90, 94.845(5), 90.
Volume/Å^3	1599.37(16)
Z	4
ρ_{calc}g/cm^3	1.654
μ/mm^{-1}	2.595
F(000)	800.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.576 to 50
Index ranges	-14 ≤ h ≤ 12, -7 ≤ k ≤ 8, -21 ≤ l ≤ 18
Reflections collected	6396
Independent reflections	2818 [R_{int} = 0.0314, R_{sigma} = 0.0469]
Data/restraints/parameters	2818/0/227
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0328, wR_2 = 0.0683
Final R indexes [all data]	R_1 = 0.0439, wR_2 = 0.0725
Largest diff. peak/hole / e Å^{-3}	0.36/-0.40

Crystal data for **3f**: **Crystal Data** for $C_{19}H_{12}BrNO_4$ (M =398.21 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 12.5309(7) Å, b = 7.1686(4) Å, c = 17.8685(10) Å, β = 94.845(5)°, V = 1599.37(16) Å^3, Z = 4, T = 100.00(10) K, μ(Mo Kα) = 2.595 mm^{-1}, $Dcalc$ = 1.654 g/cm^3, 6396 reflections measured (4.576° ≤ 2Θ ≤ 50°), 2818 unique (R_{int} = 0.0314, R_{sigma} = 0.0469) which were used in all calculations. The final R_1 was 0.0328 (I > 2σ(I)) and wR_2 was 0.0725 (all data)..

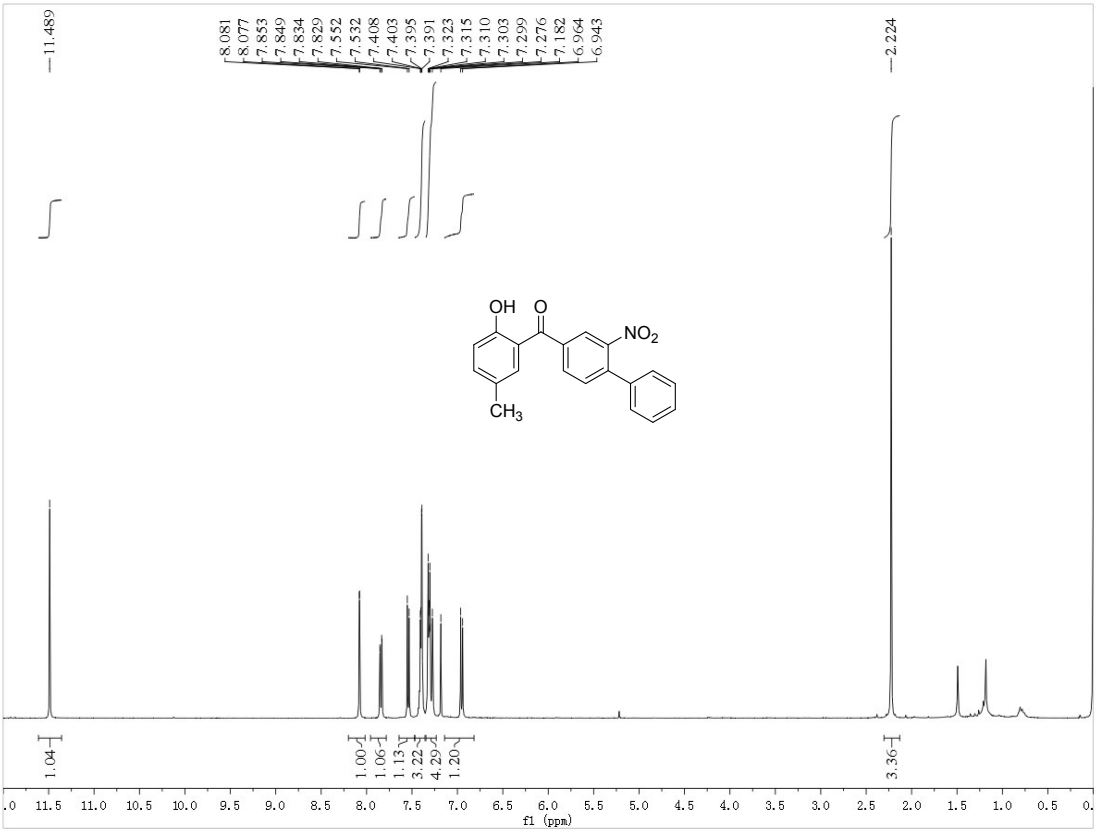
8. The copies of ^{1}H NMR and ^{13}C NMR spectra for compounds 3

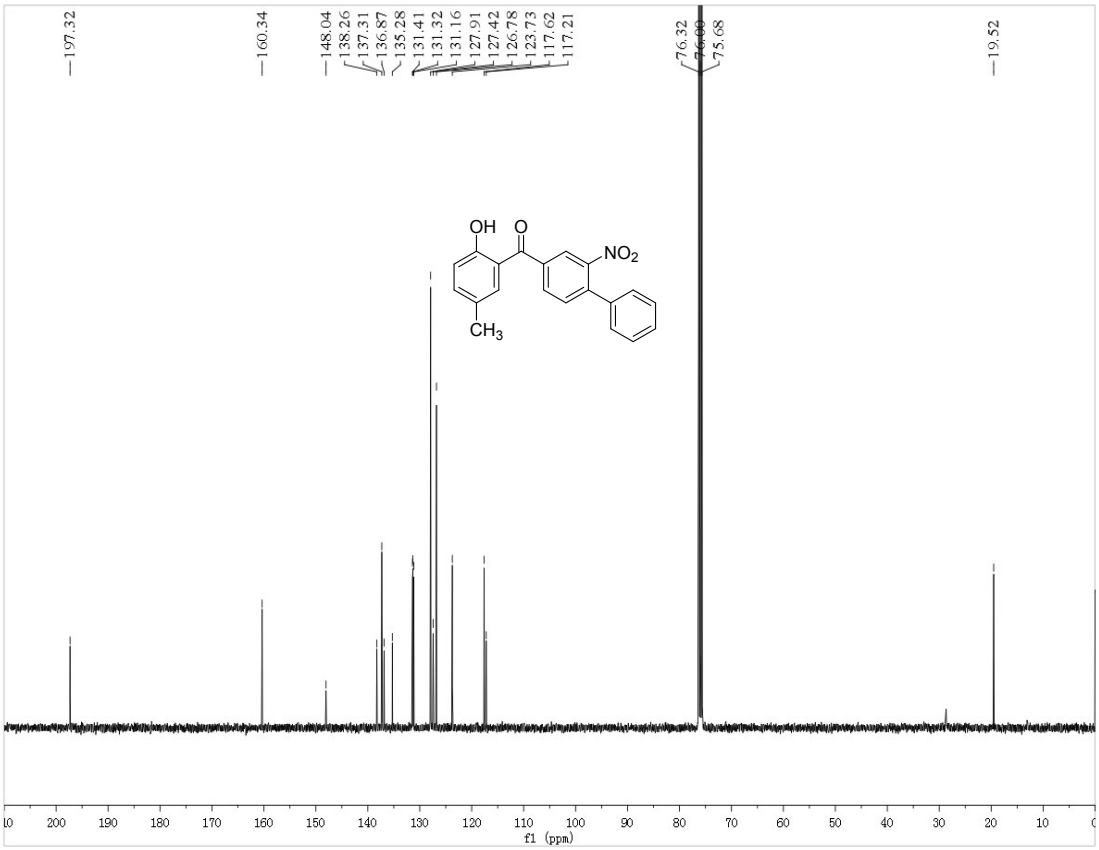
^{1}H and ^{13}C NMR of 3a



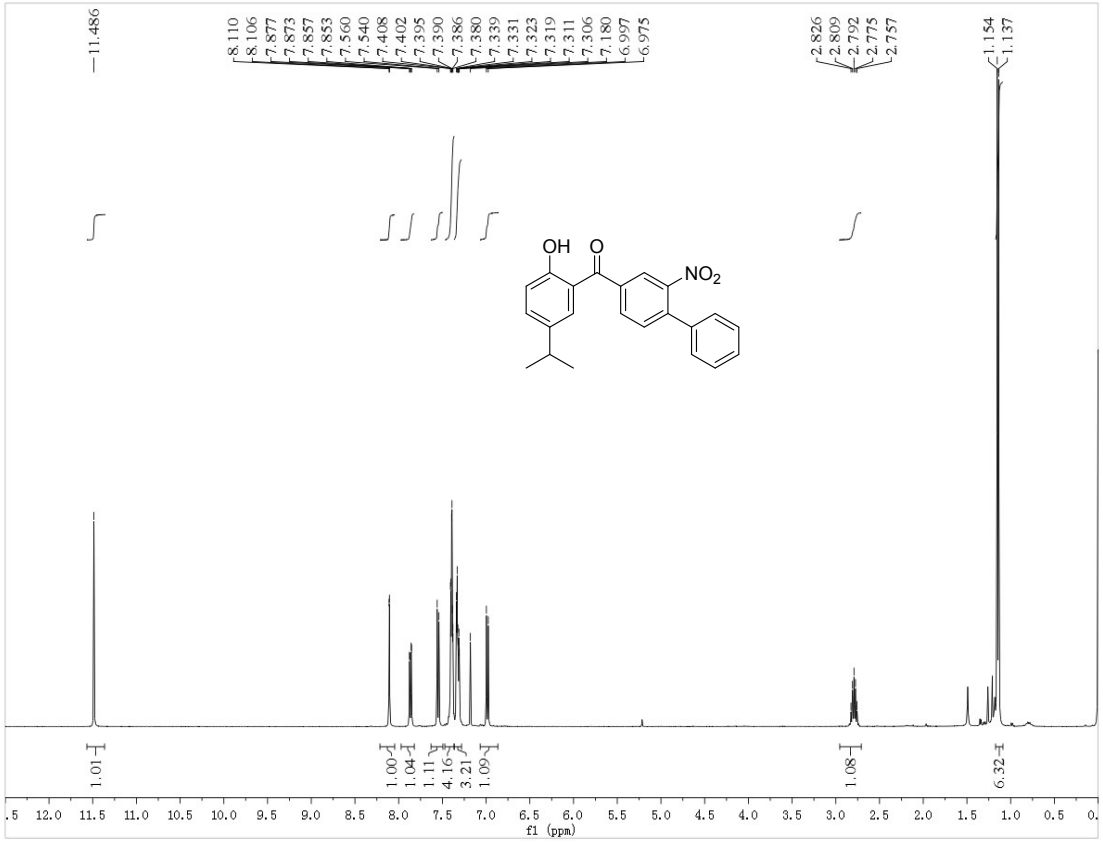


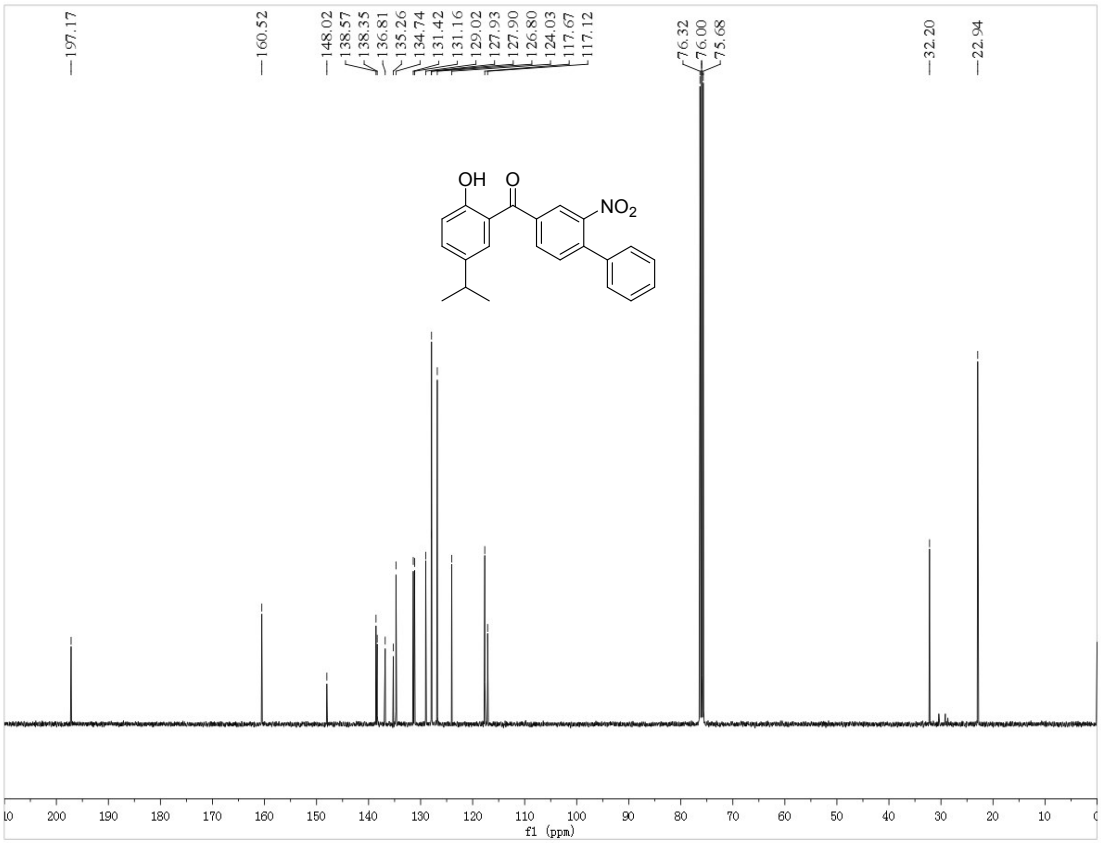
^{1}H and ^{13}C NMR of 3b



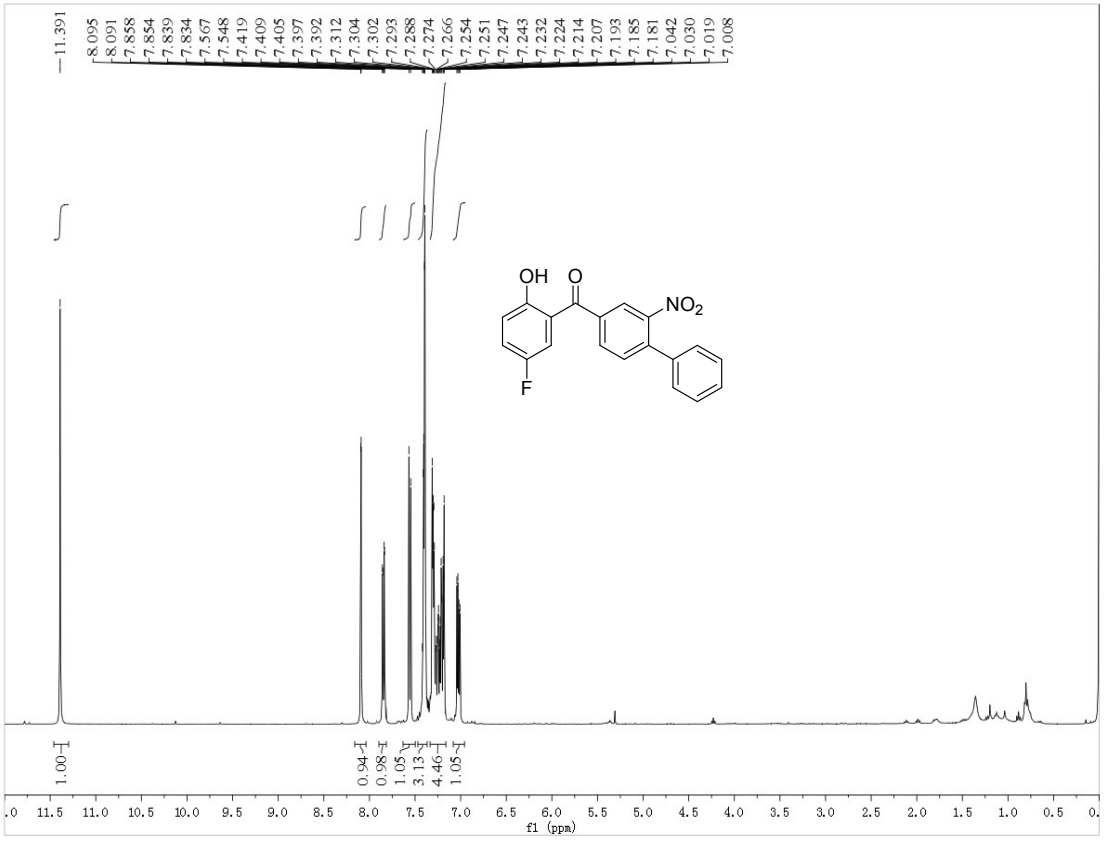


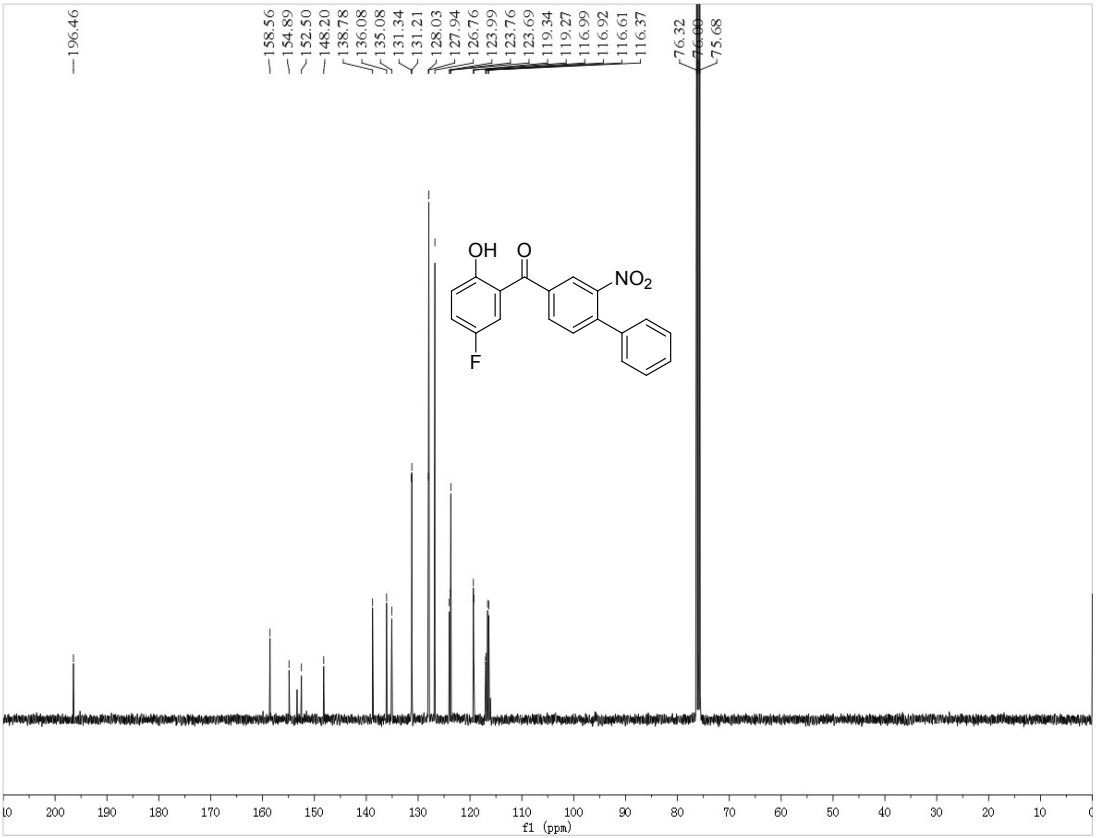
^{1}H and ^{13}C NMR of 3c



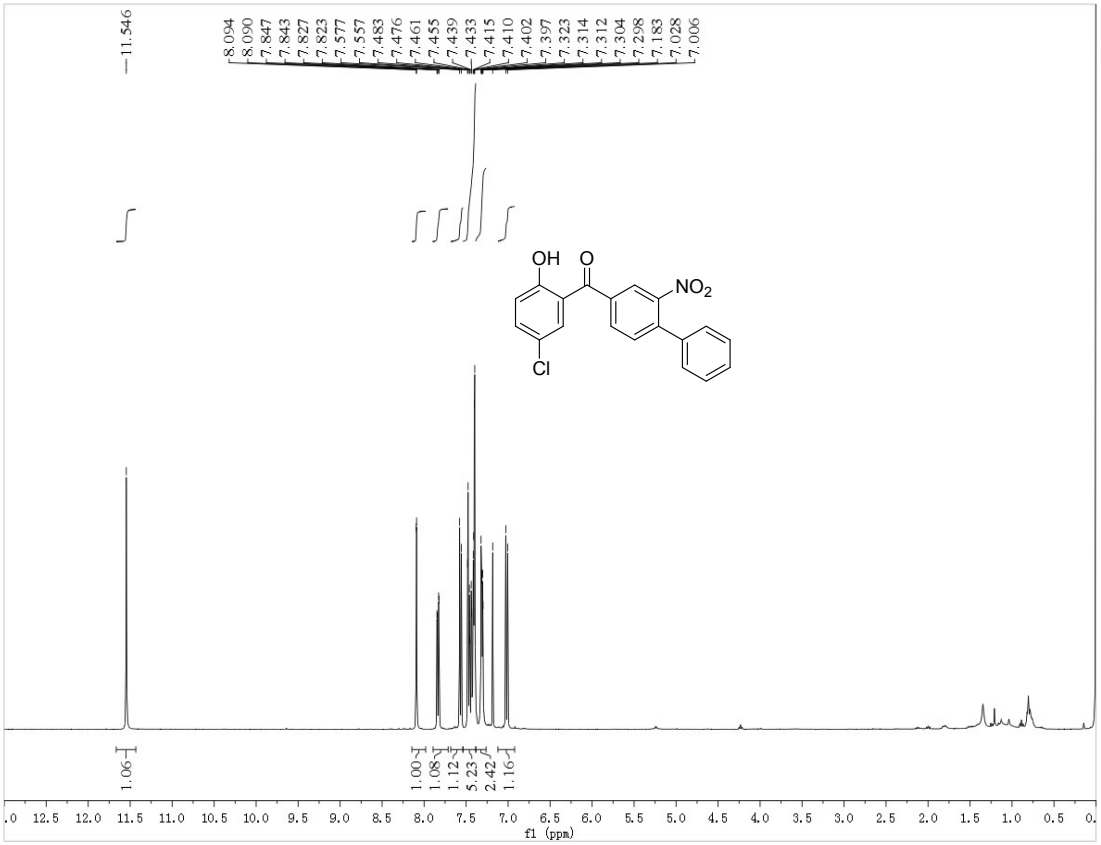


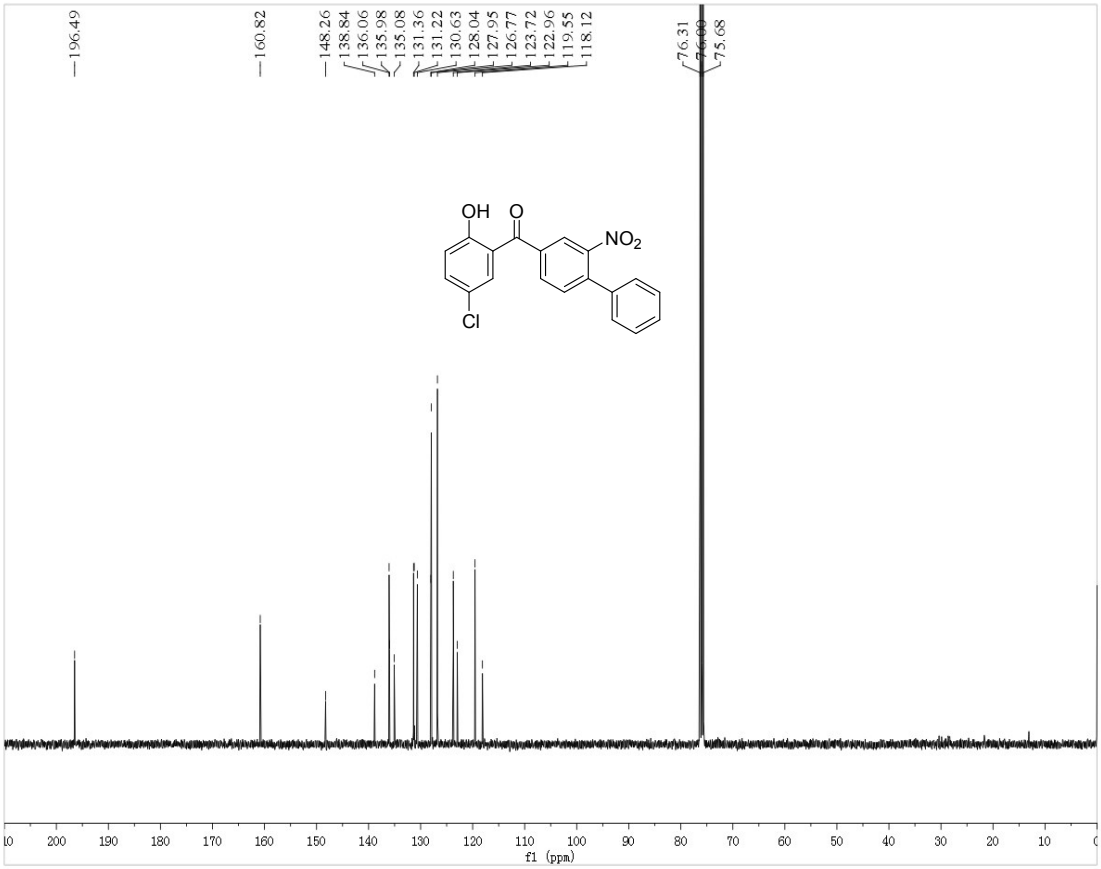
^{1}H and ^{13}C NMR of 3d



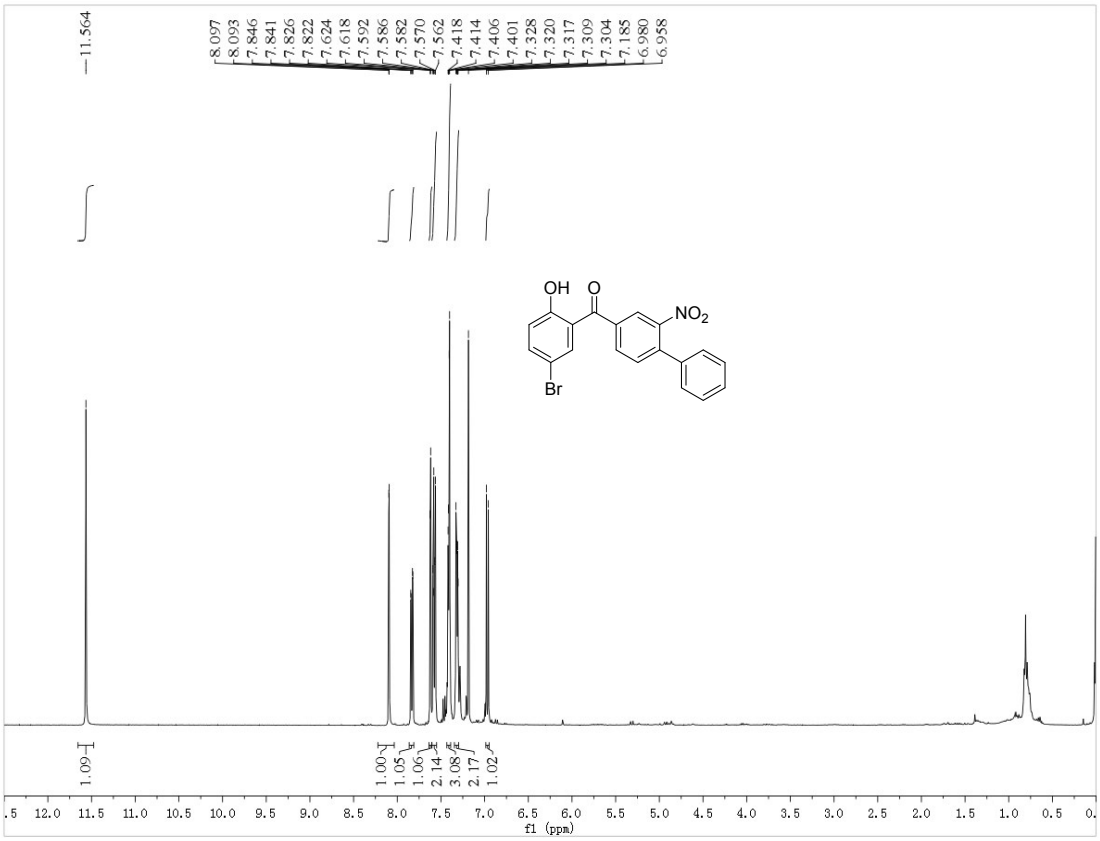


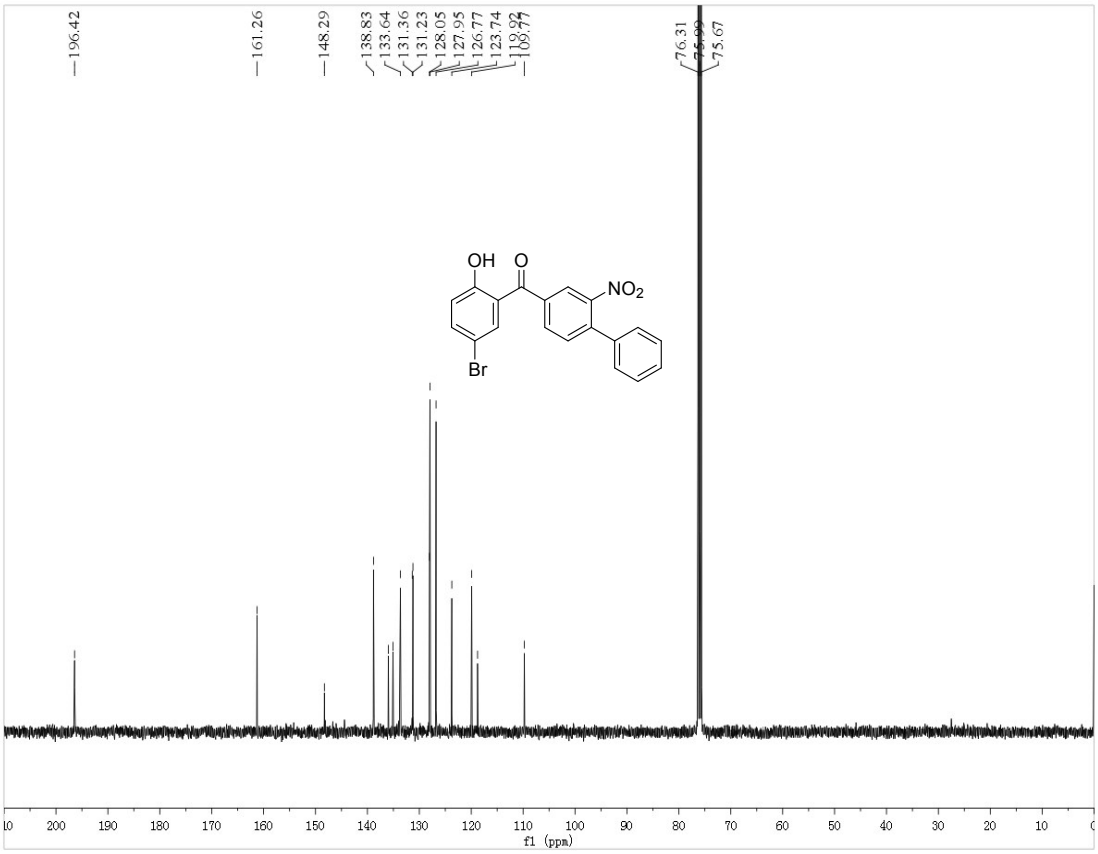
^{1}H and ^{13}C NMR of 3e



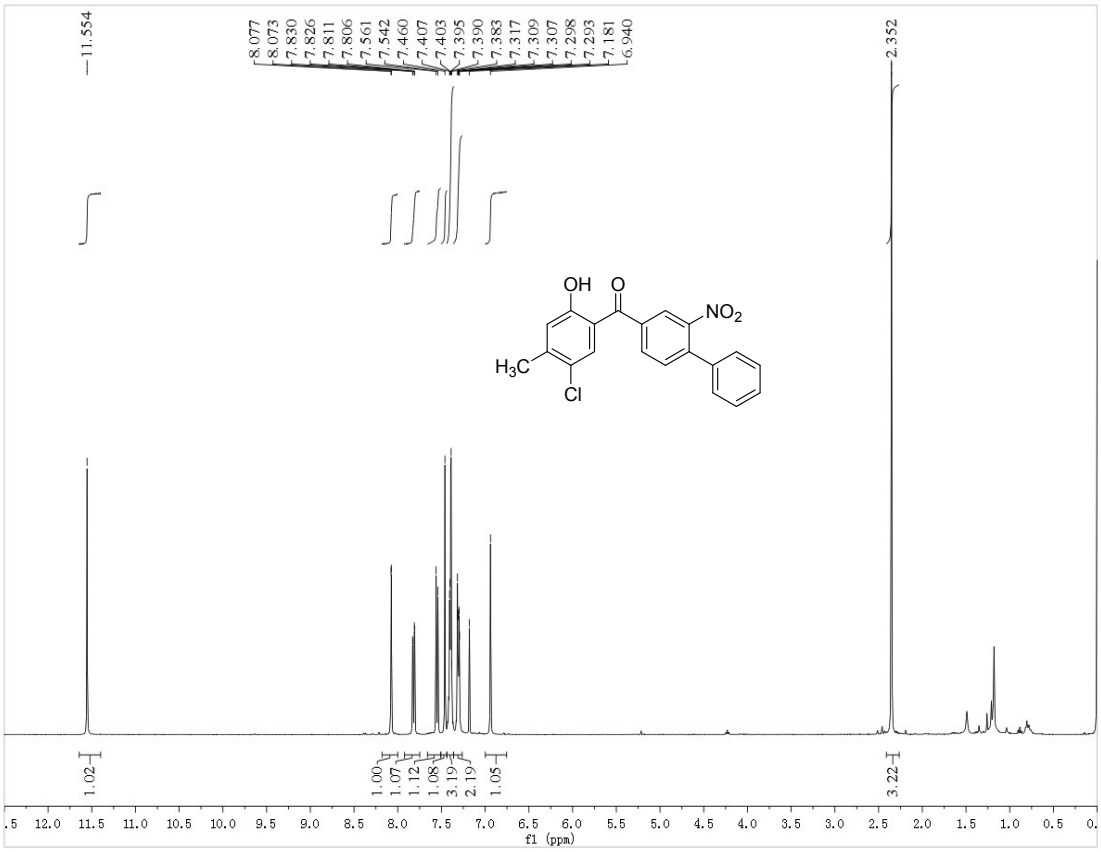


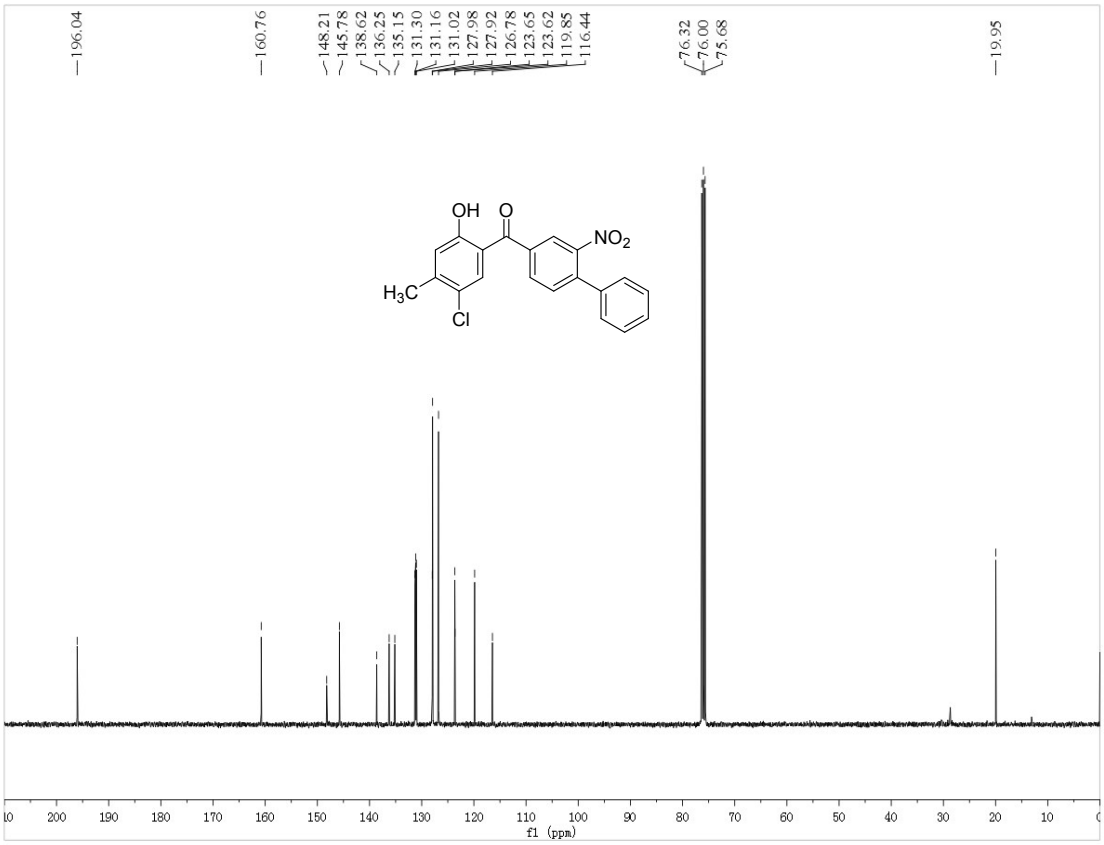
^{1}H and ^{13}C NMR of 3f



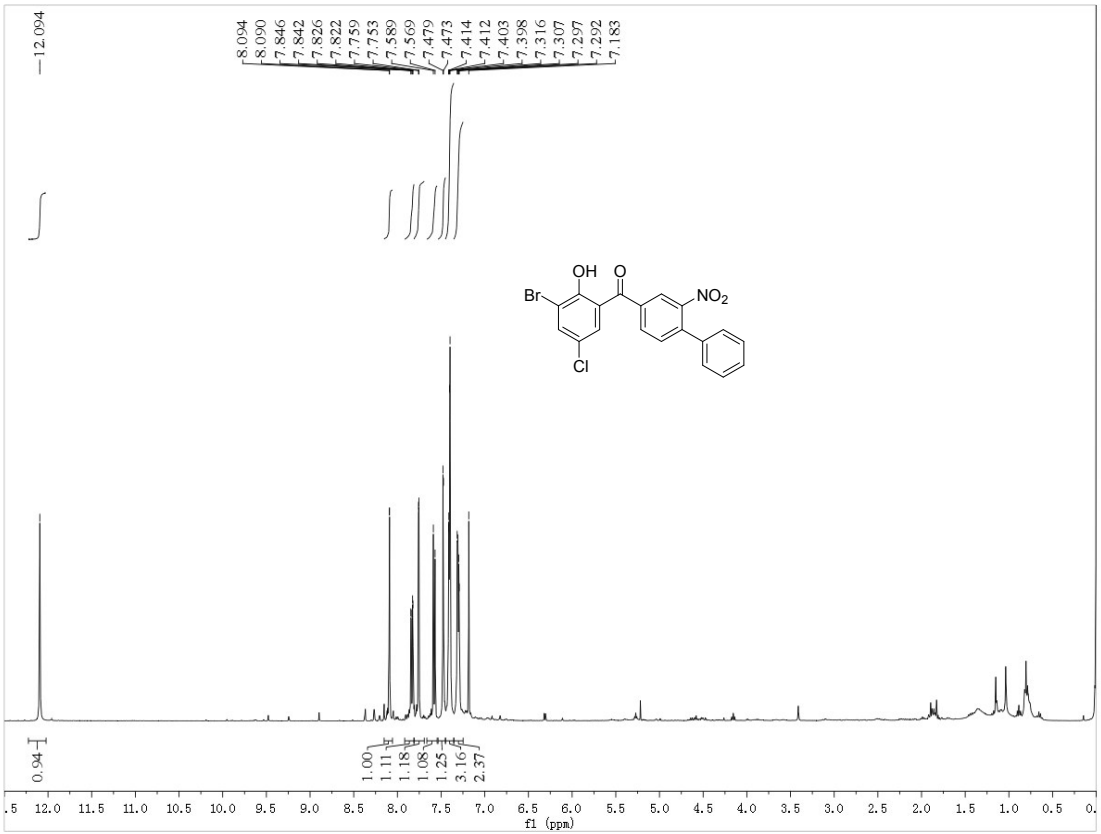


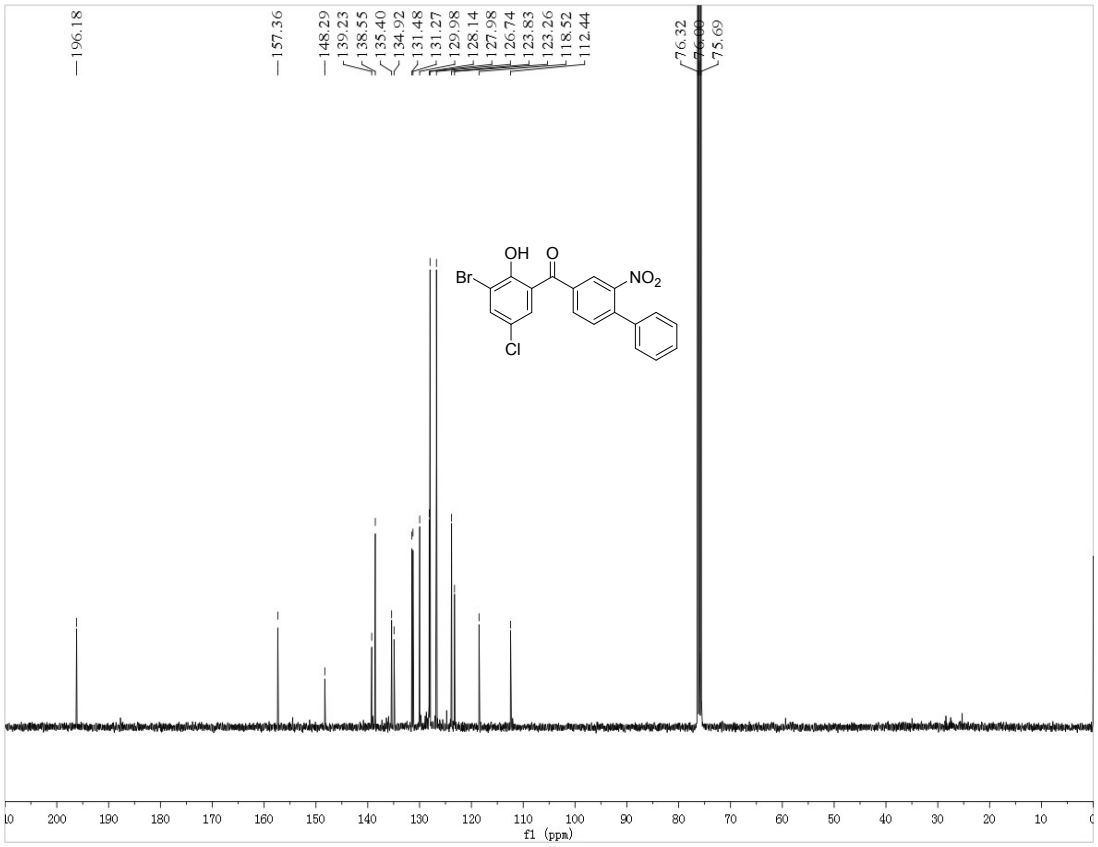
^{1}H and ^{13}C NMR of 3g



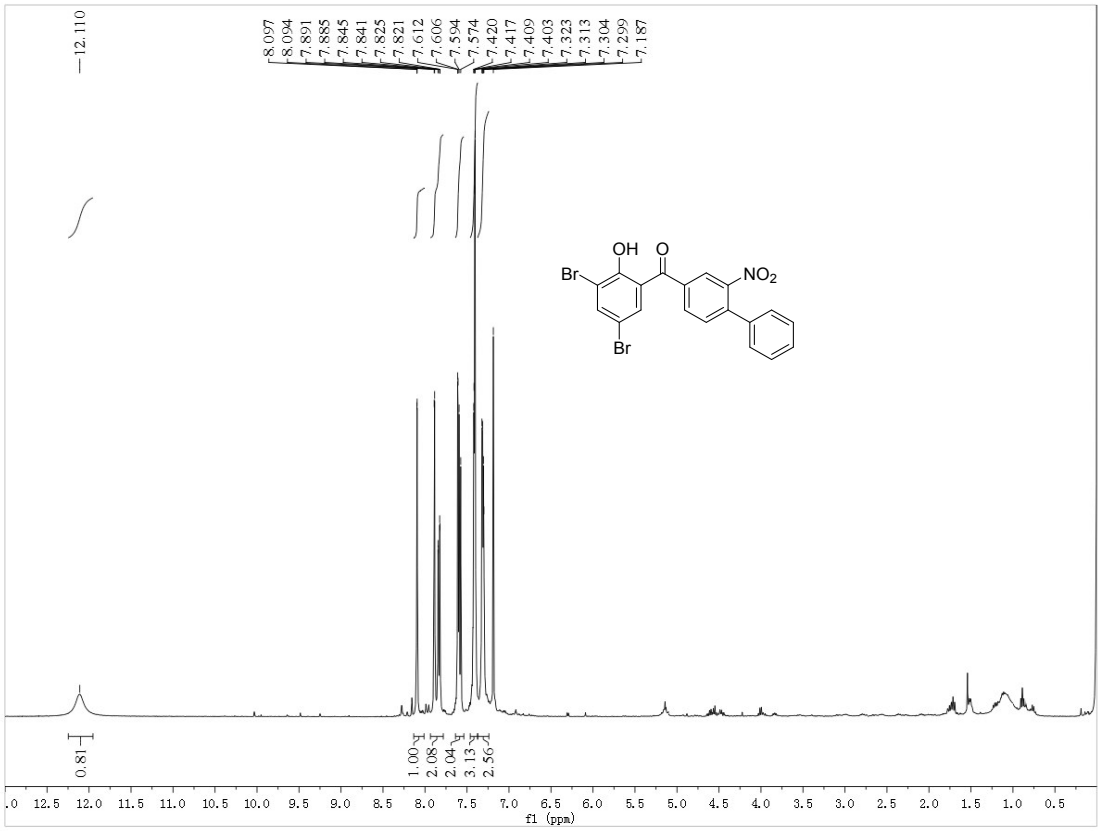


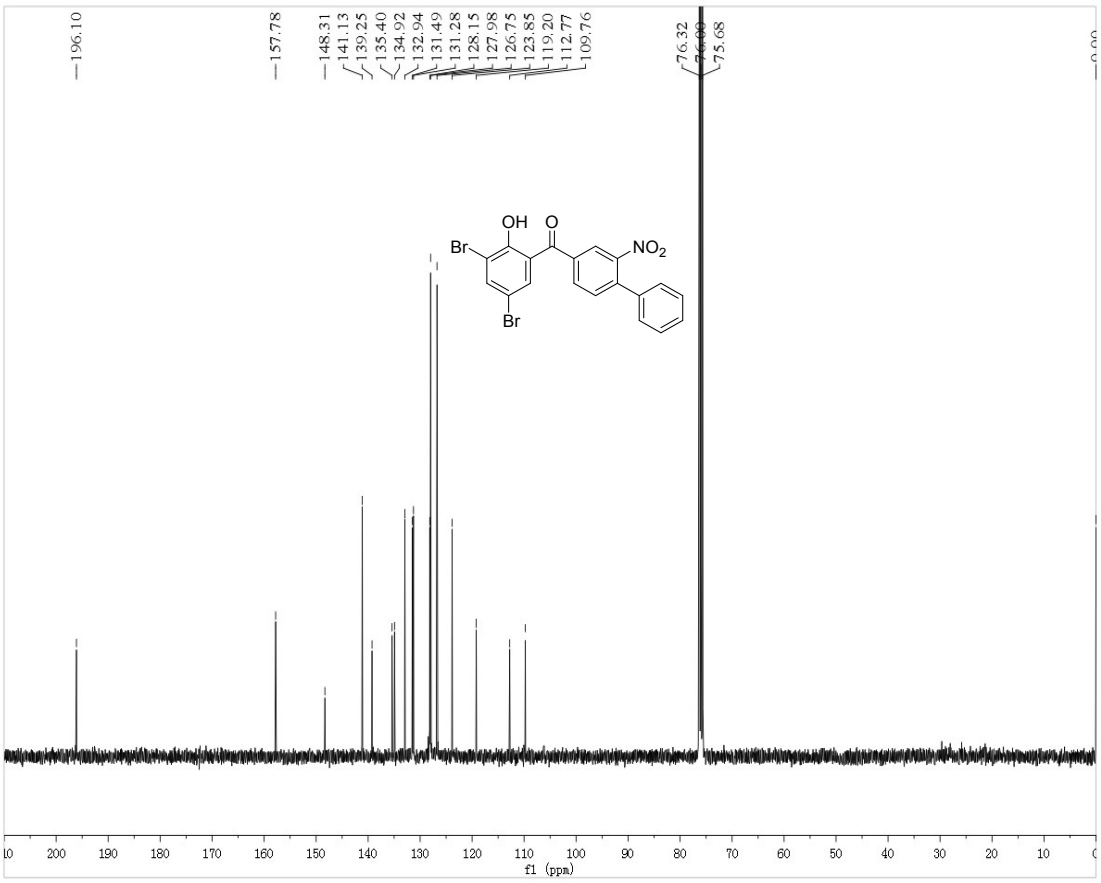
^{1}H and ^{13}C NMR of 3h



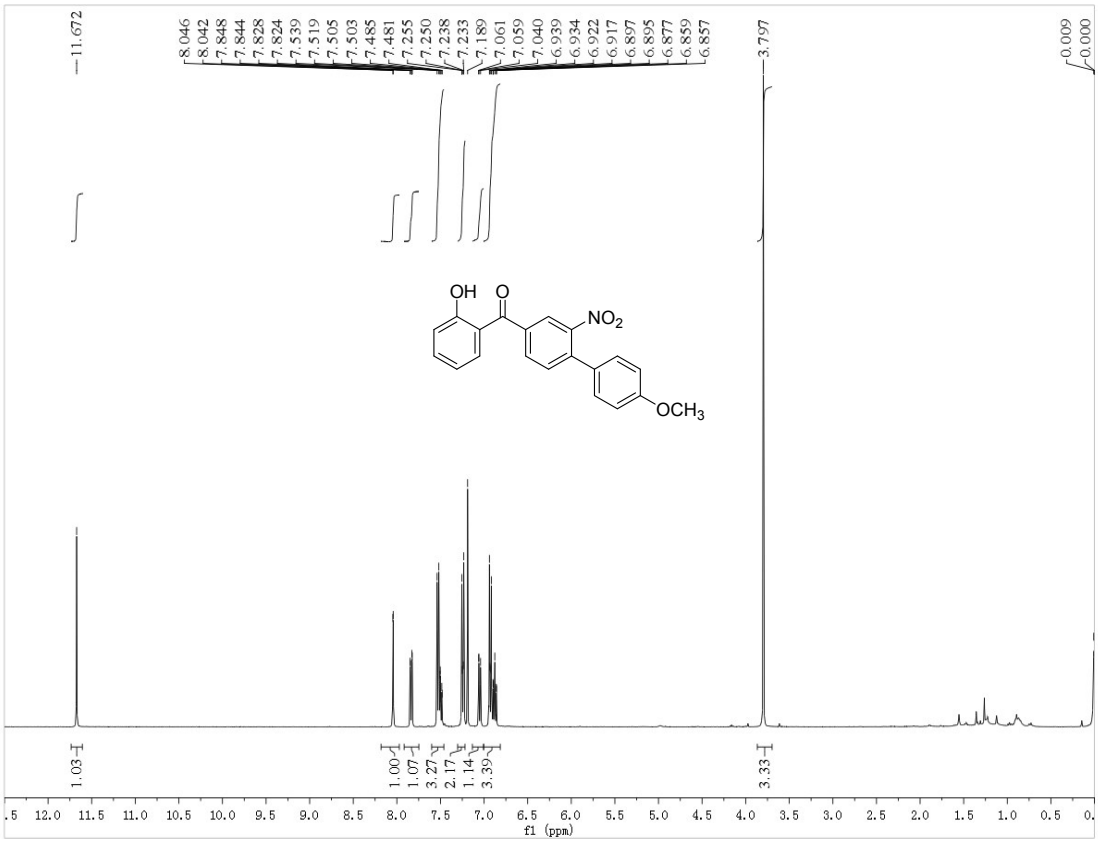


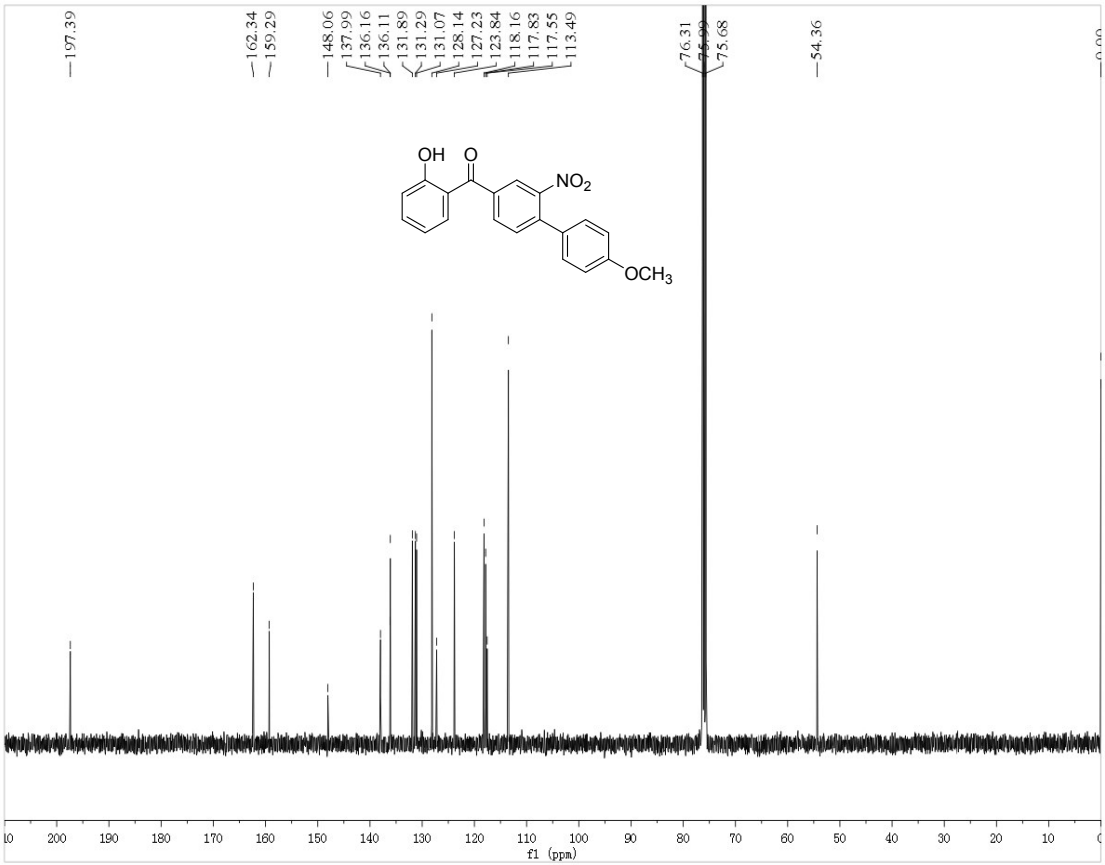
^{1}H and ^{13}C NMR of 3i



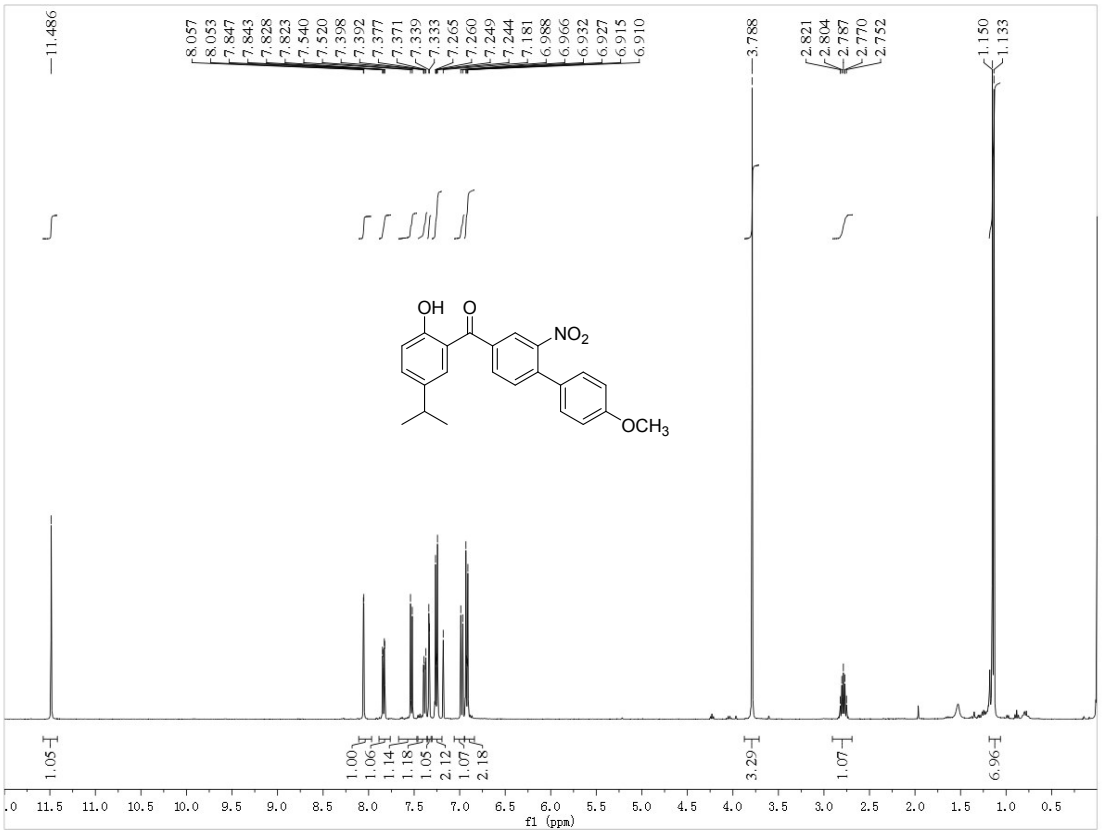


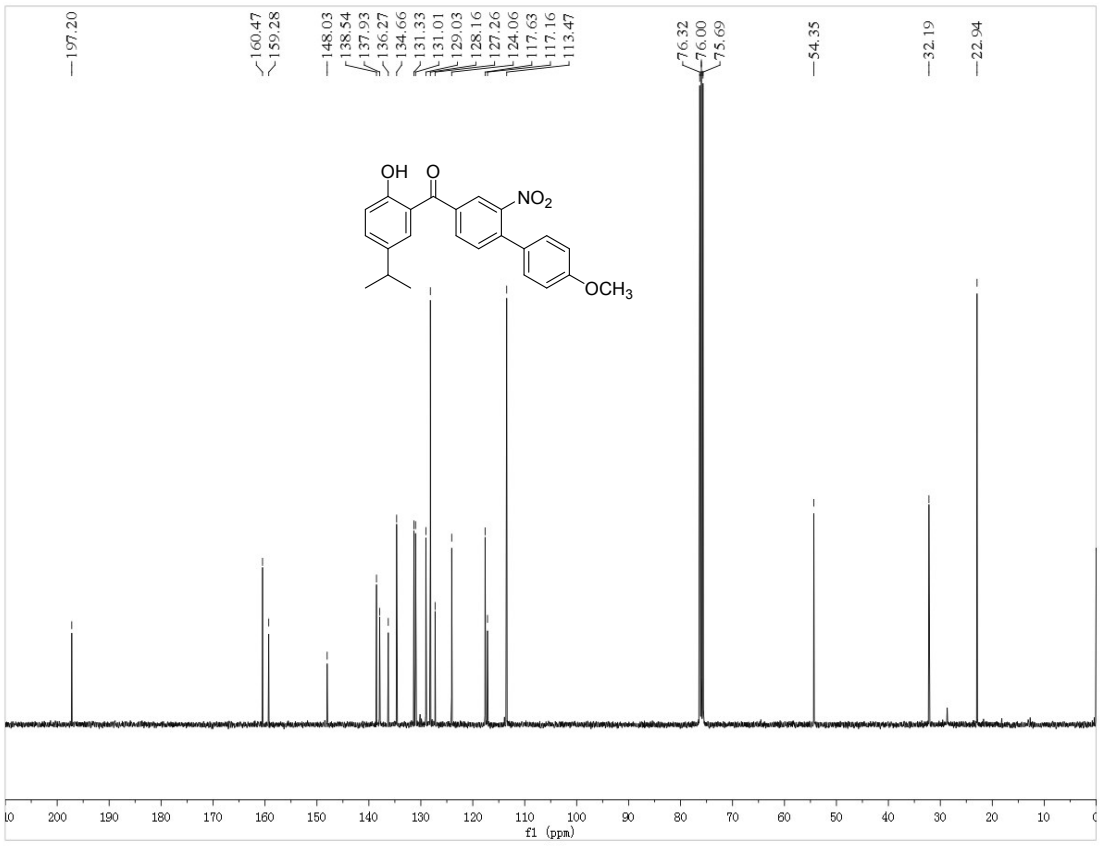
^{1}H and ^{13}C NMR of 3j



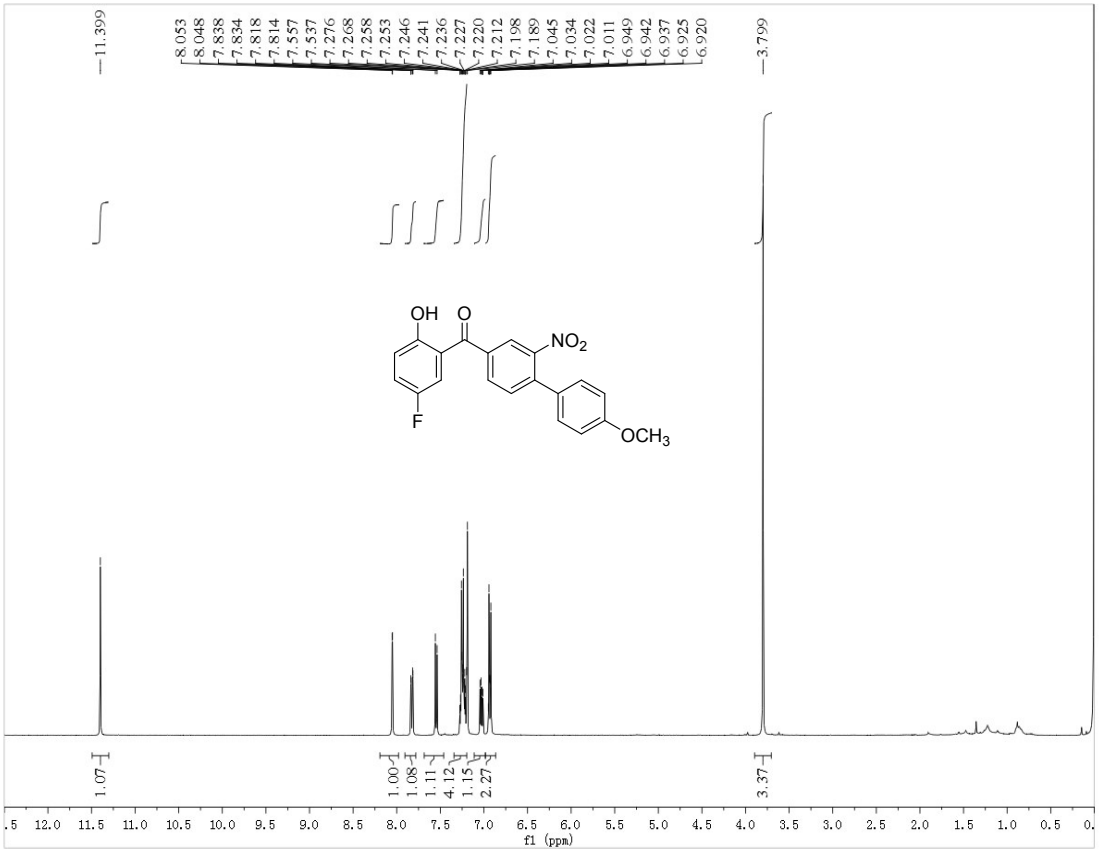


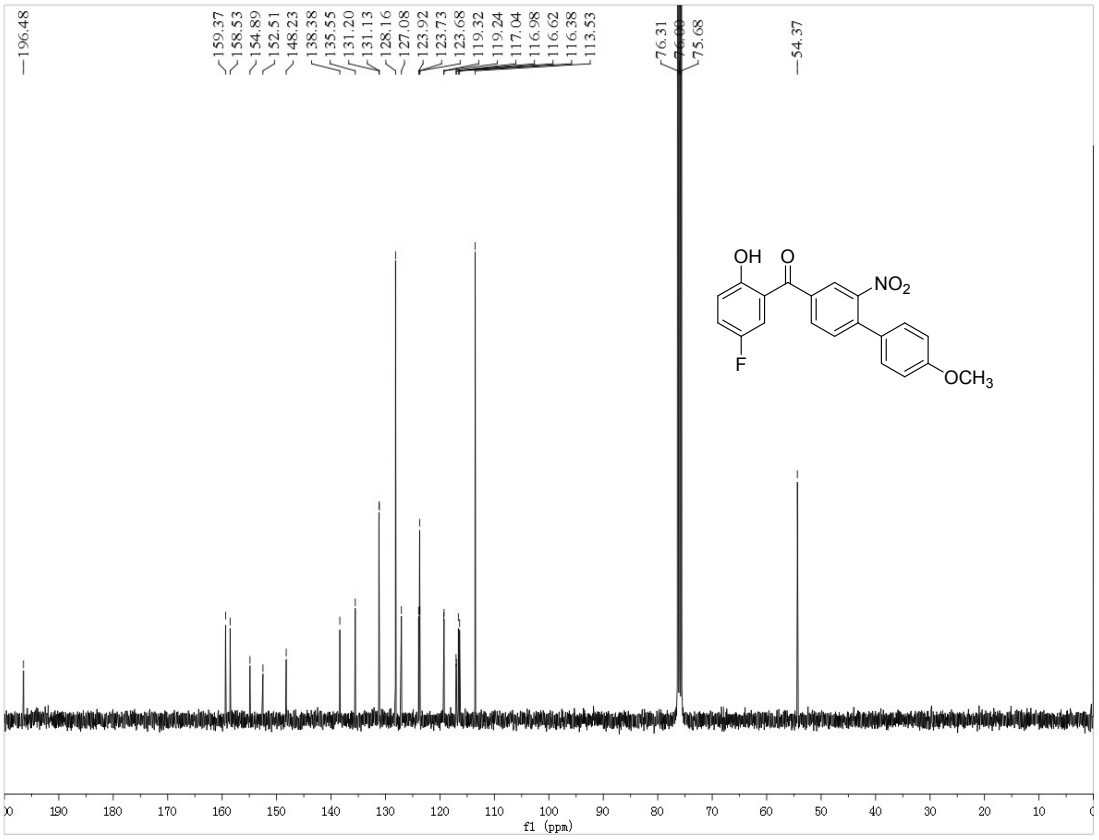
^{1}H and ^{13}C NMR of 3k



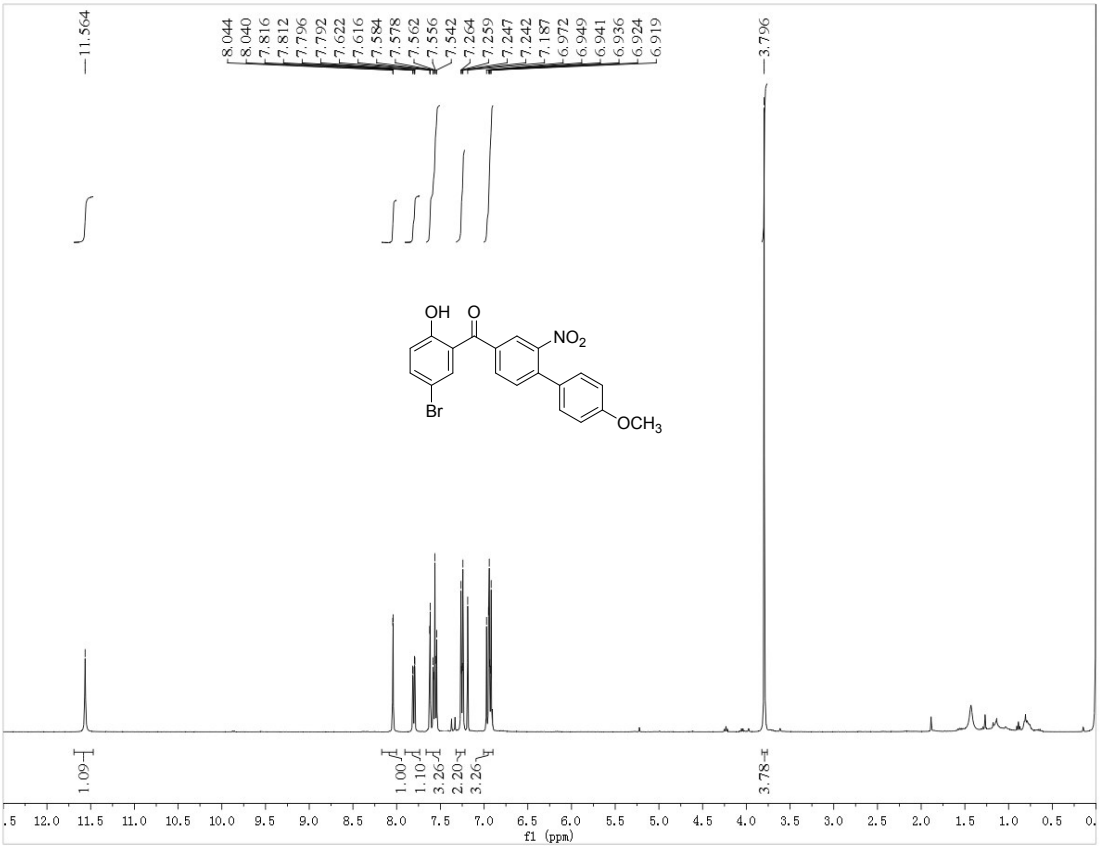


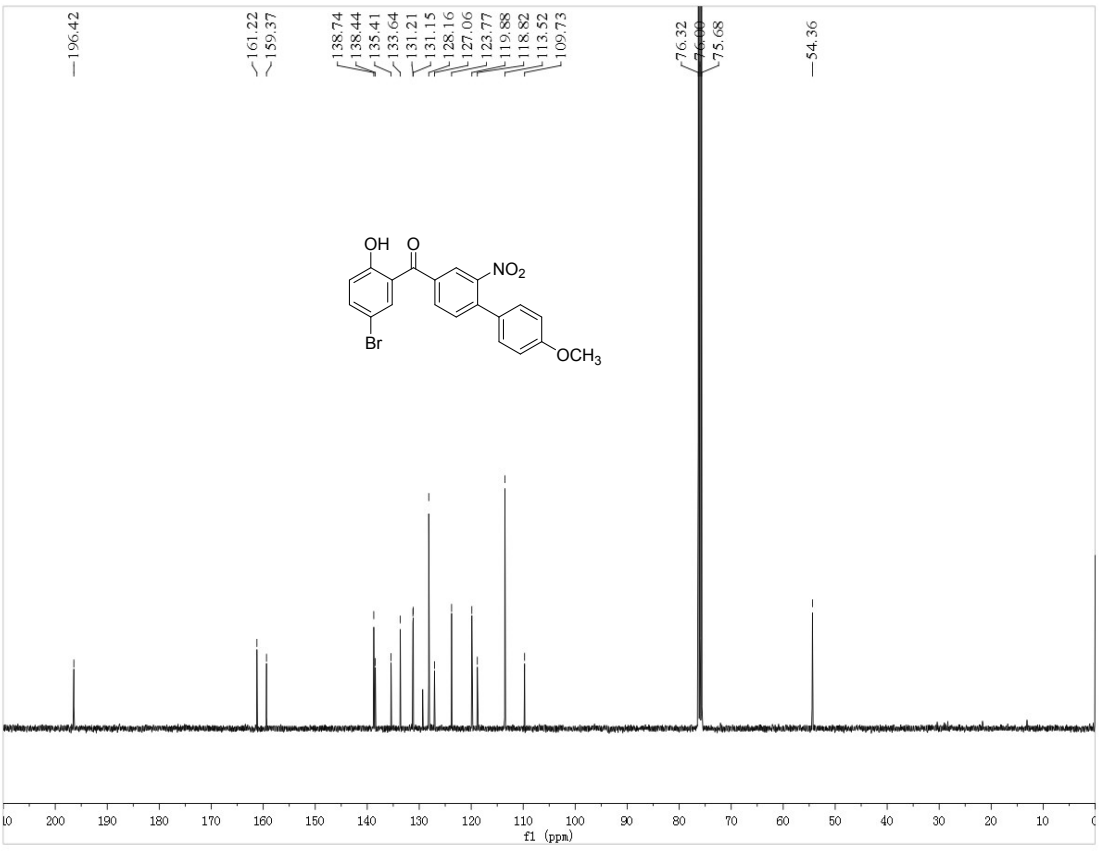
^{1}H and ^{13}C NMR of 3l



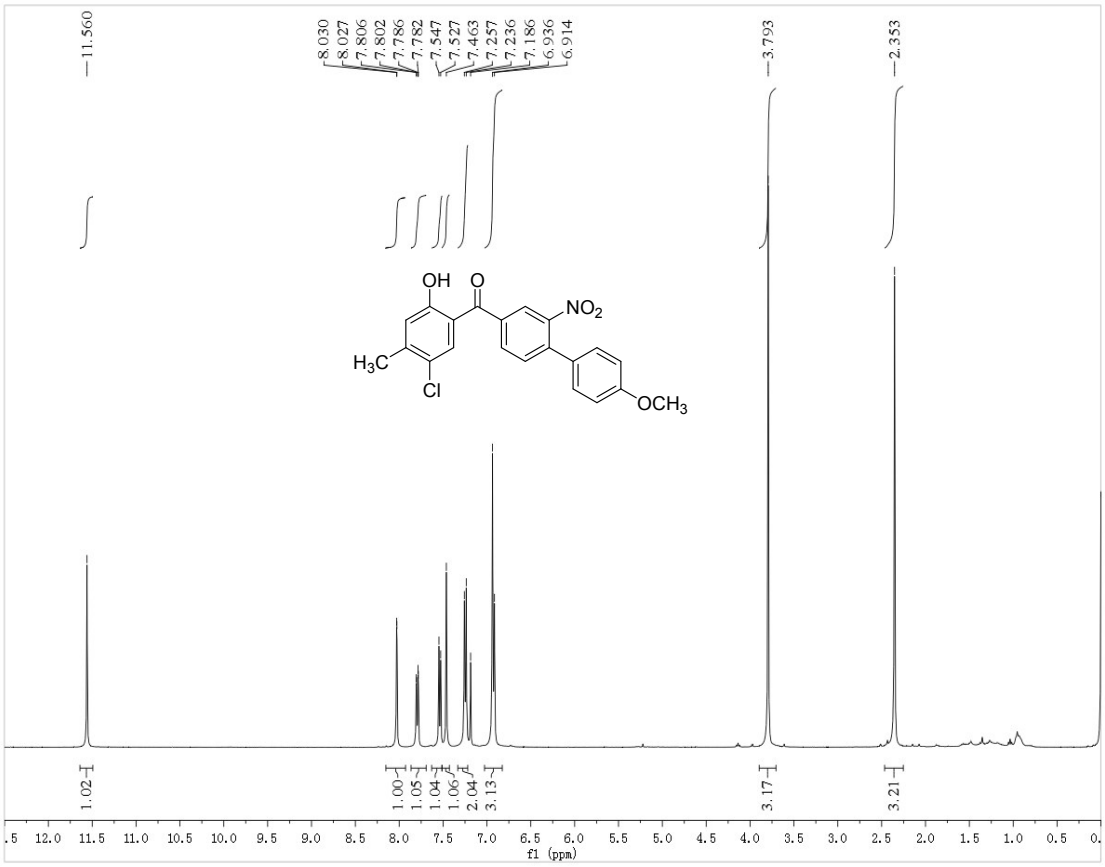


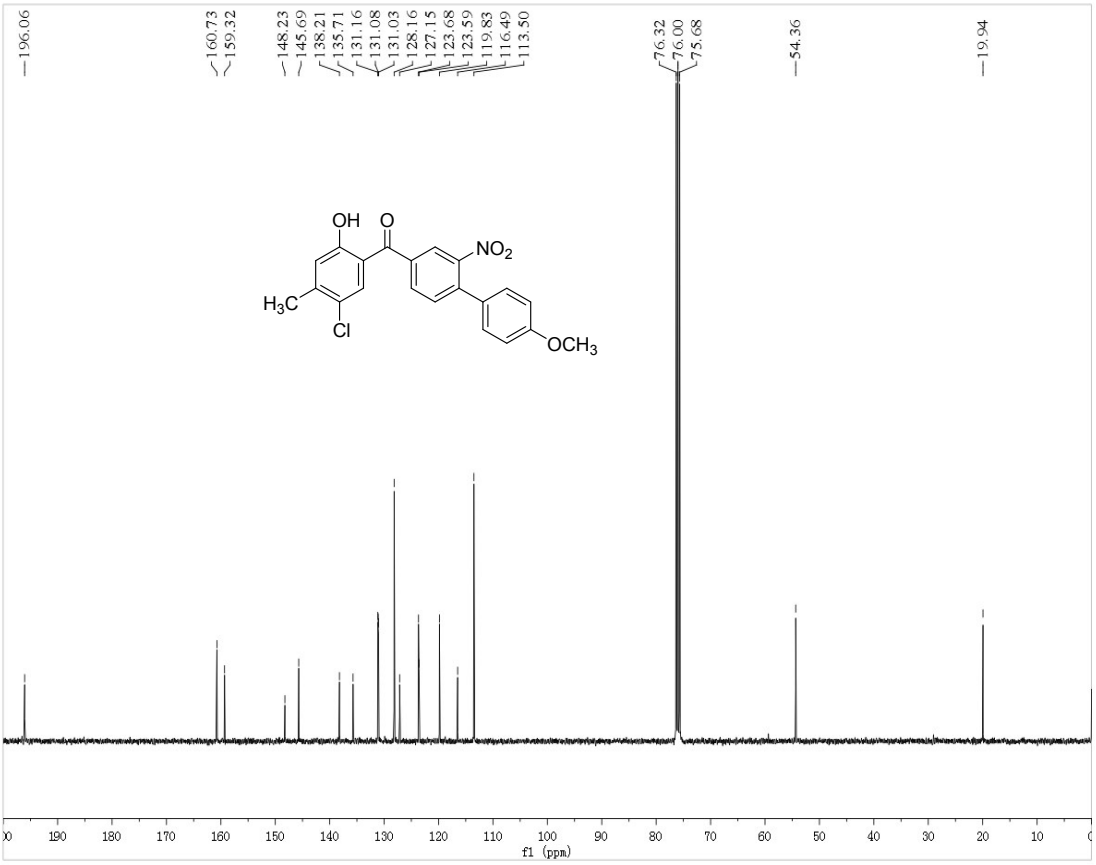
^{1}H and ^{13}C NMR of 3m



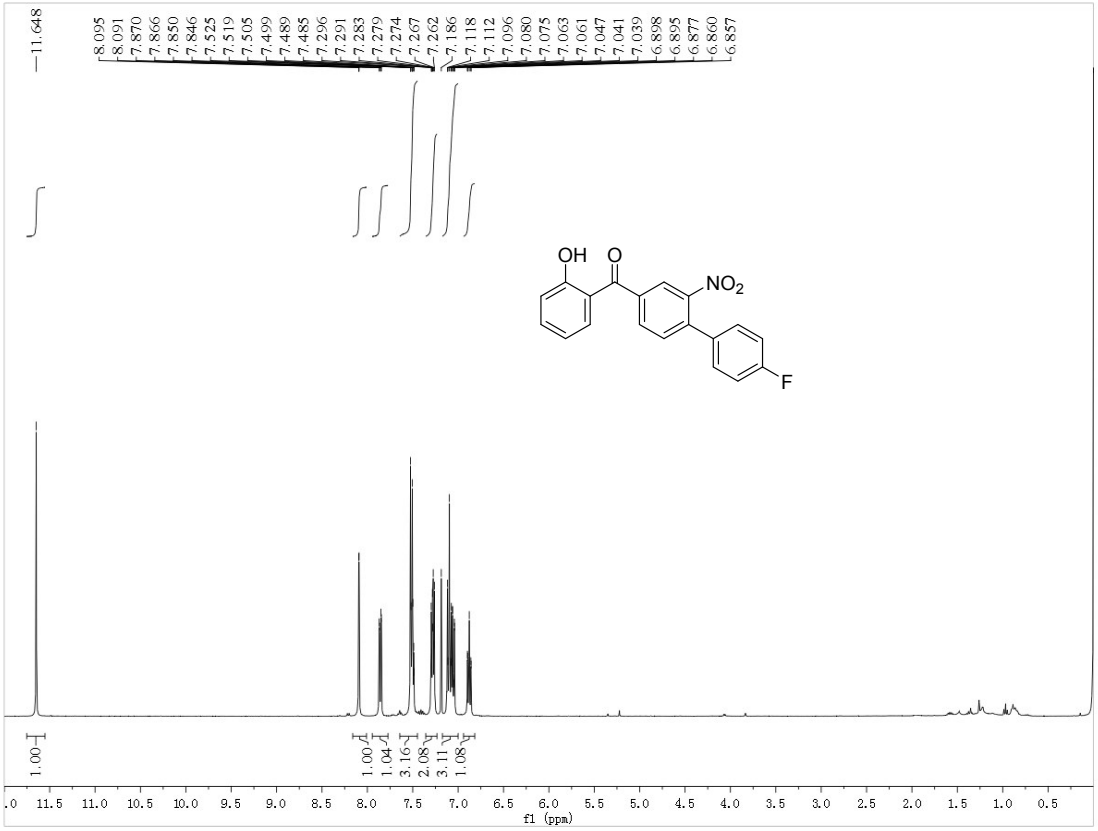


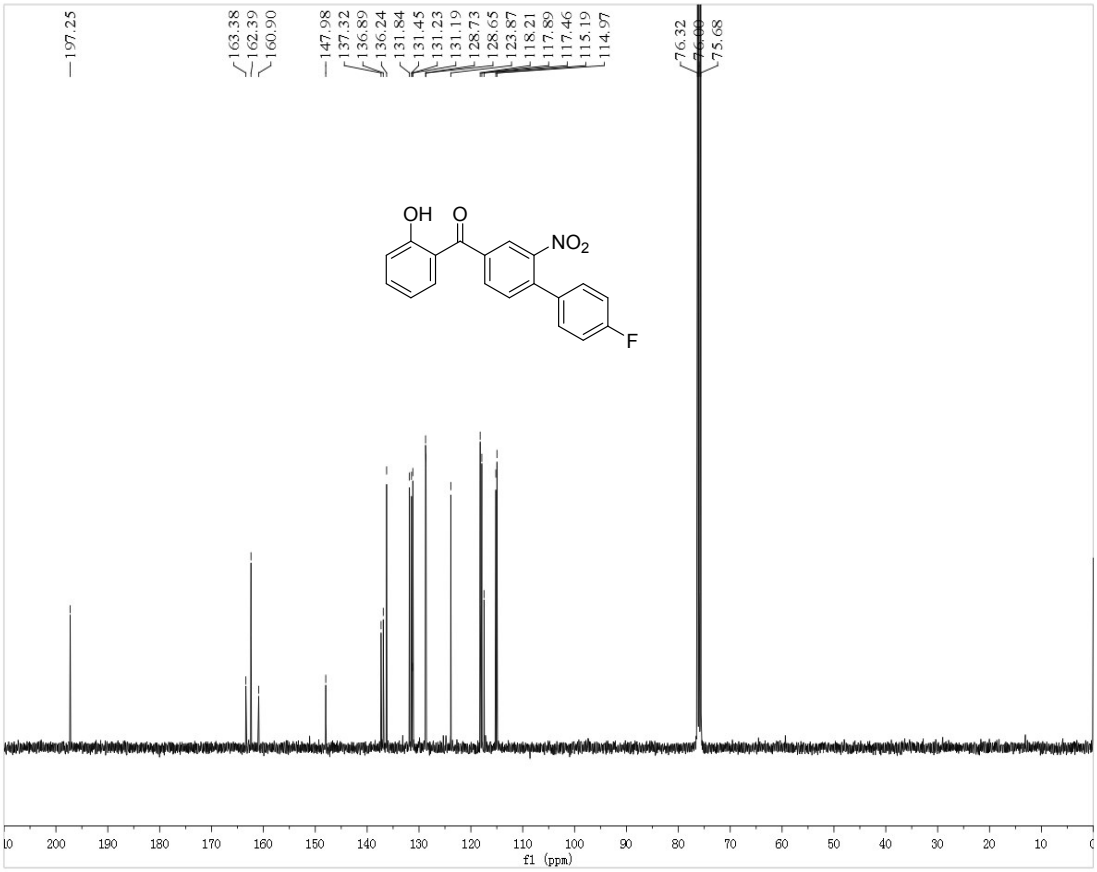
^{1}H and ^{13}C NMR of 3n


11.560
8.030
8.027
7.806
7.802
7.786
7.782
7.547
7.527
7.463
7.257
7.236
7.186
6.936
6.914
3.793
2.353
OH
O
NO2
H3C
Cl
OCH3
1.02
1.00
1.05
1.04
1.06
2.04
3.13
3.17
3.21
f1 (ppm)

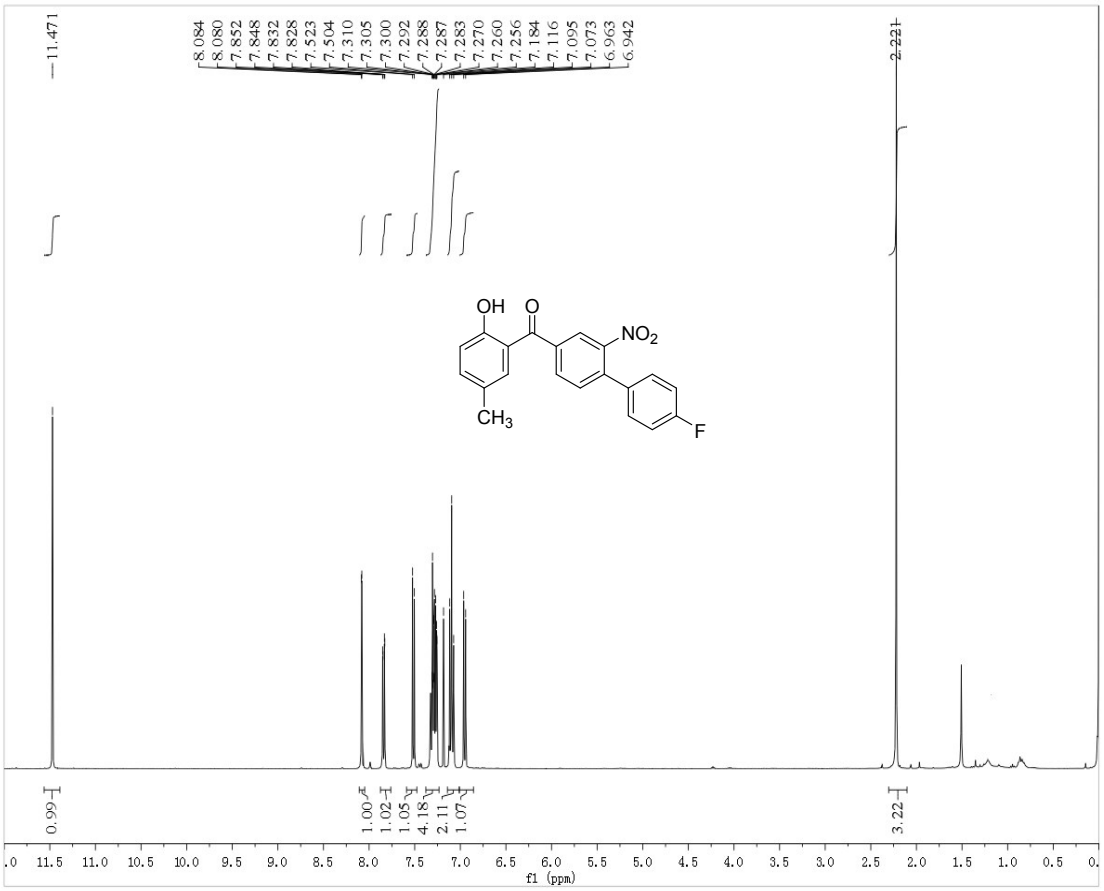

196.06
160.73
159.32
148.23
145.69
138.21
135.71
131.16
131.08
131.03
128.16
127.15
123.68
123.59
119.83
116.49
113.50
76.32
76.00
75.68
54.36
19.94
OH
O
NO2
H3C
Cl
OCH3
f1 (ppm)

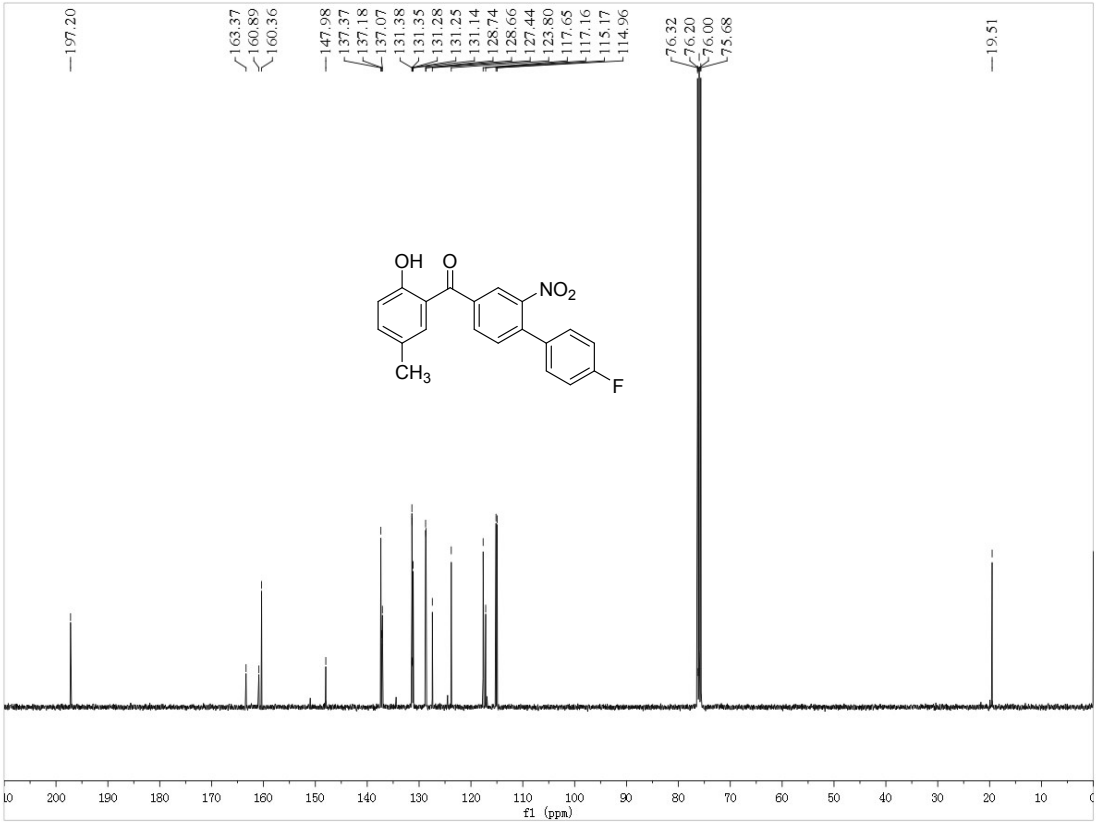
^{1}H and ^{13}C NMR of 3o



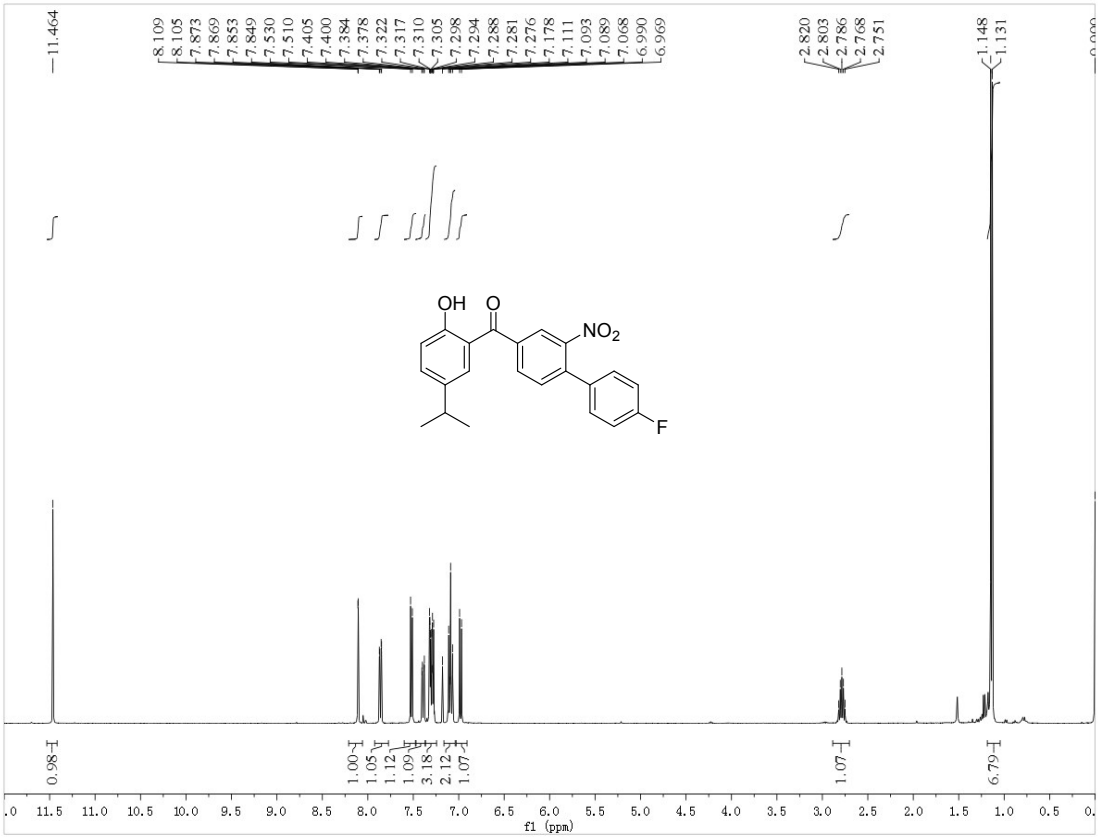


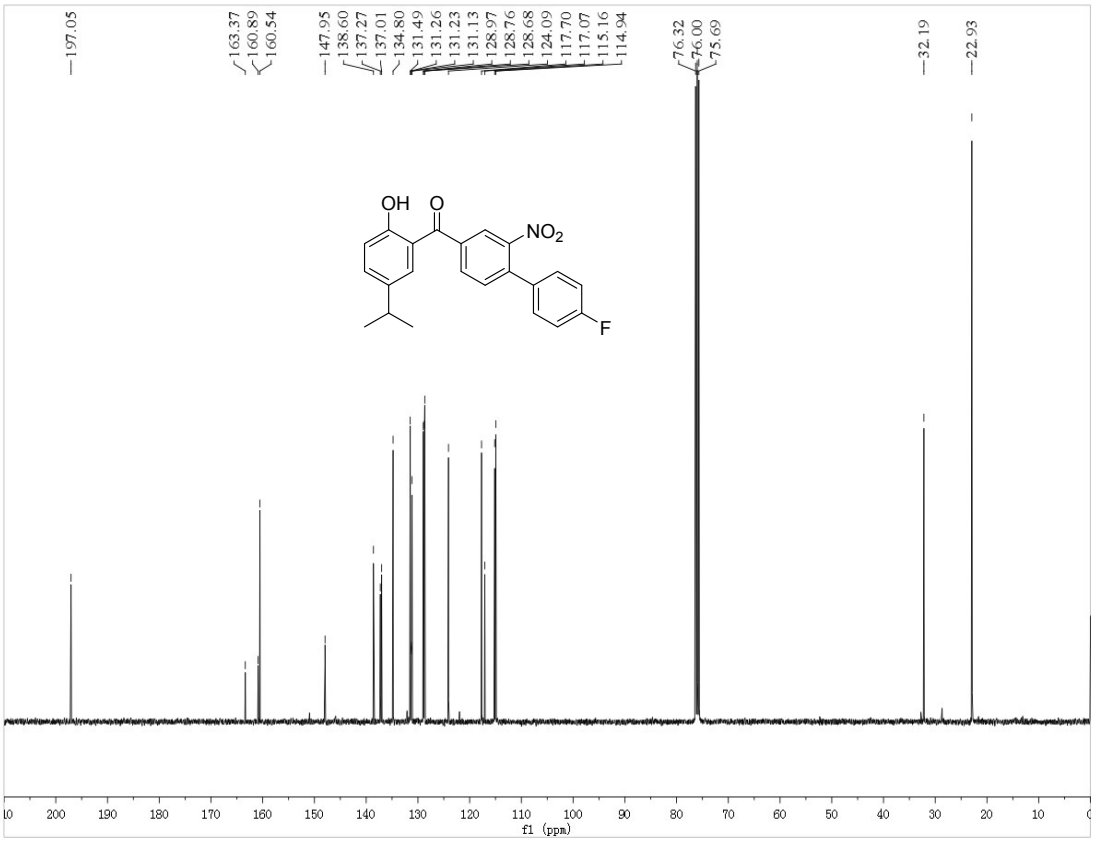
^{1}H and ^{13}C NMR of 3p



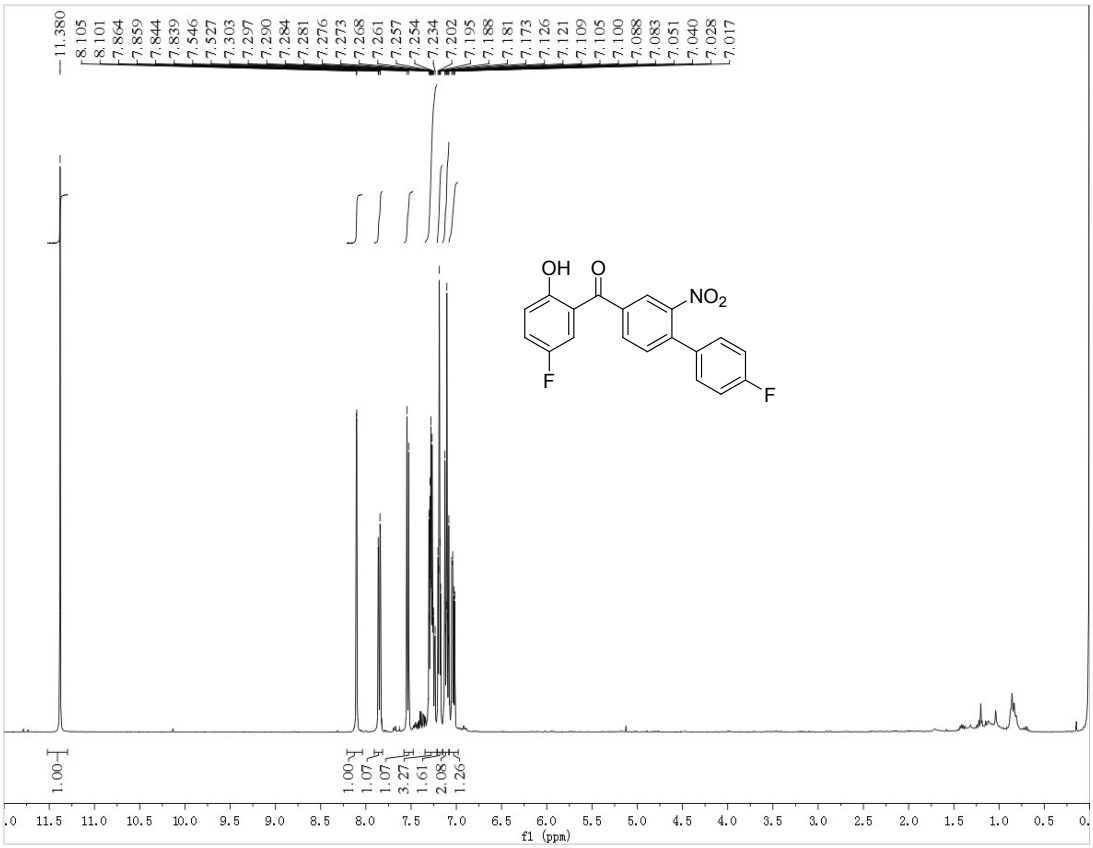


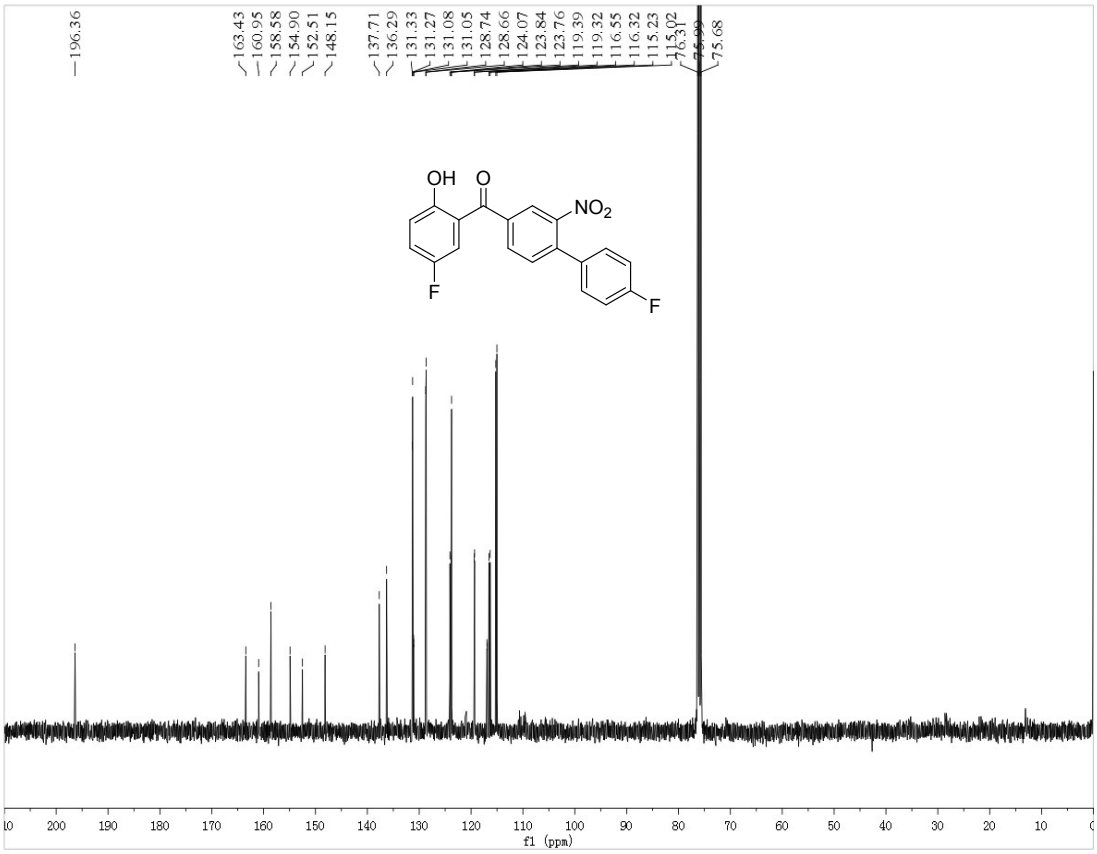
^{1}H and ^{13}C NMR of 3q



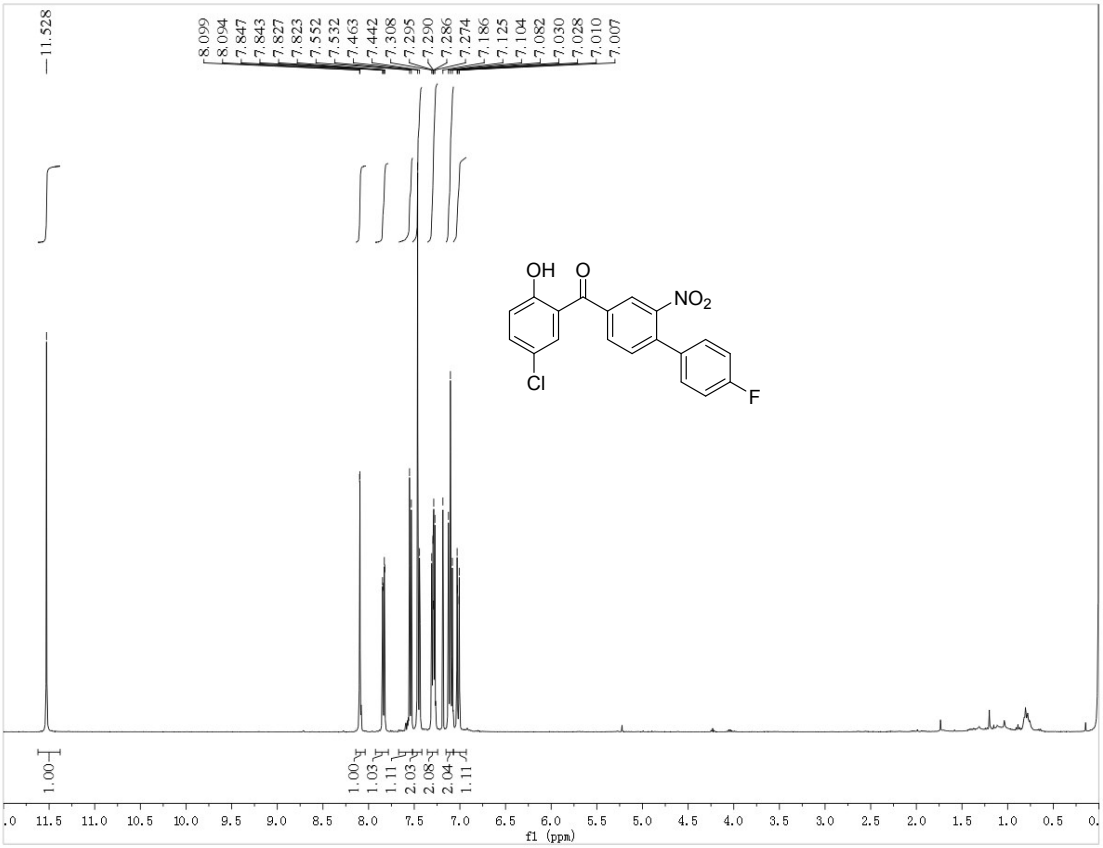


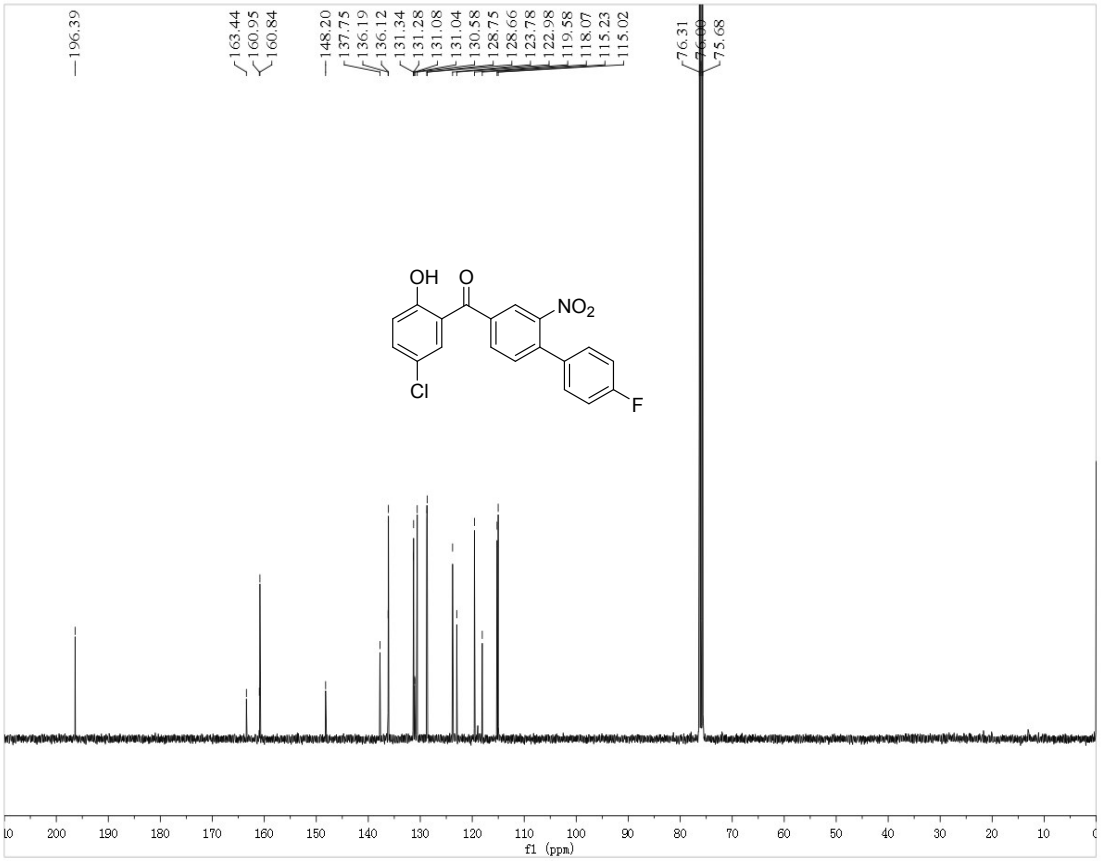
^{1}H and ^{13}C NMR of 3r



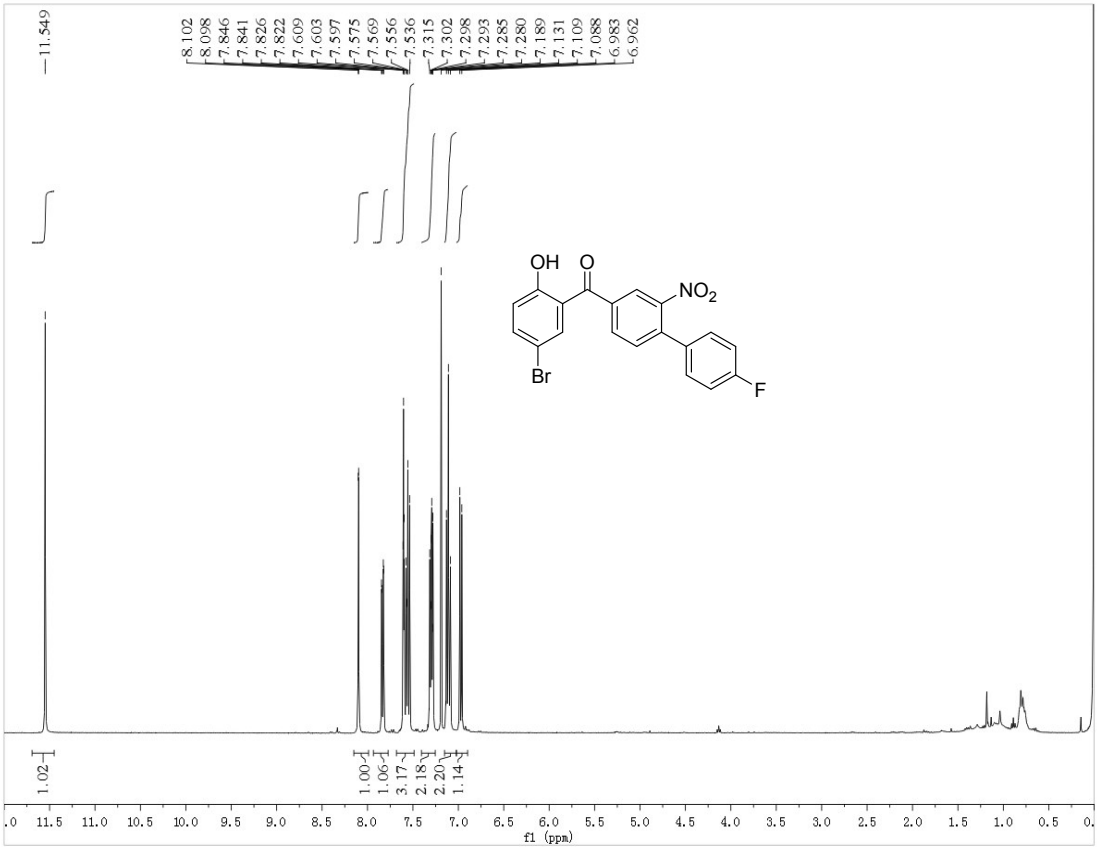


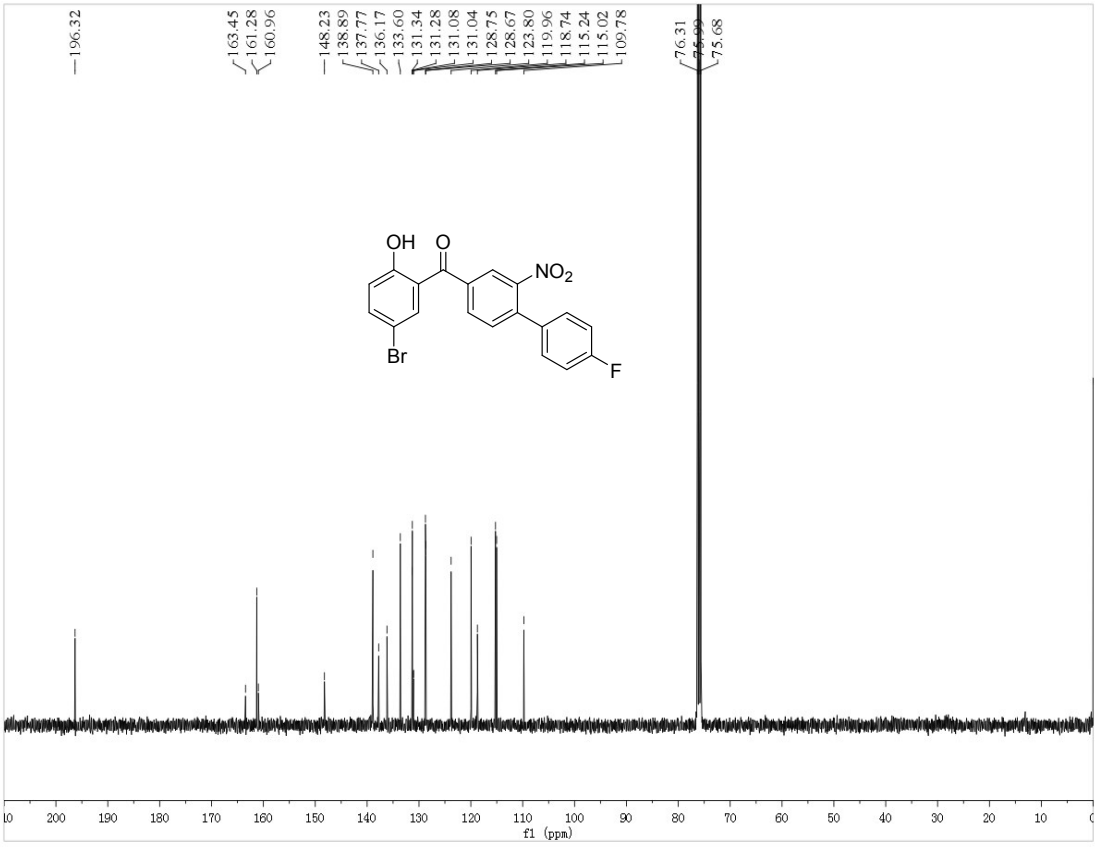
^{1}H and ^{13}C NMR of 3s



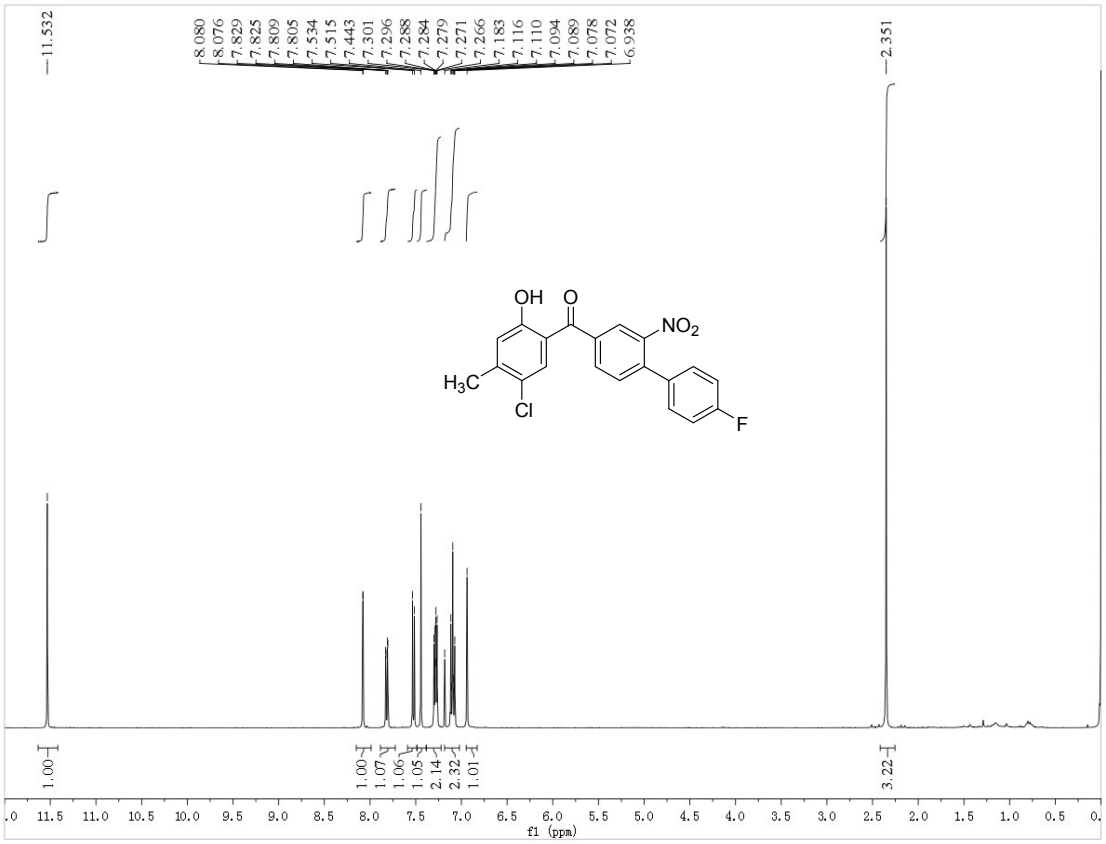


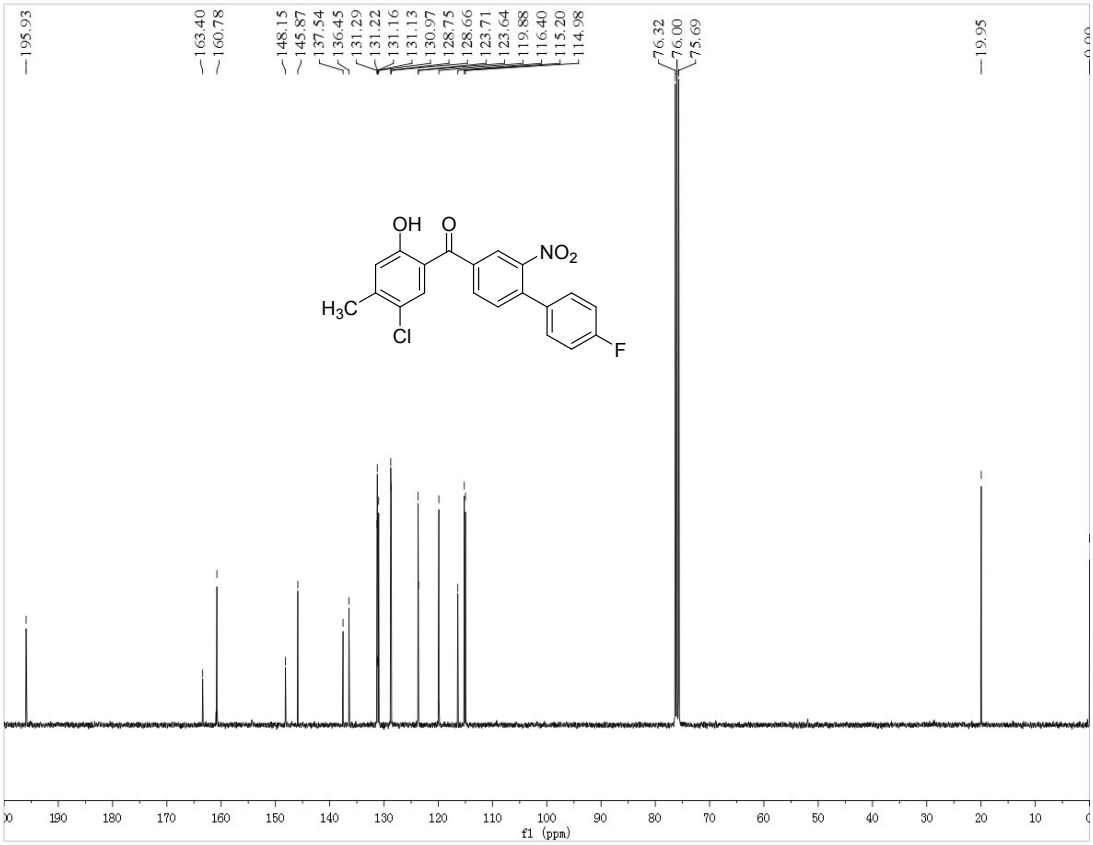
^{1}H and ^{13}C NMR of 3t



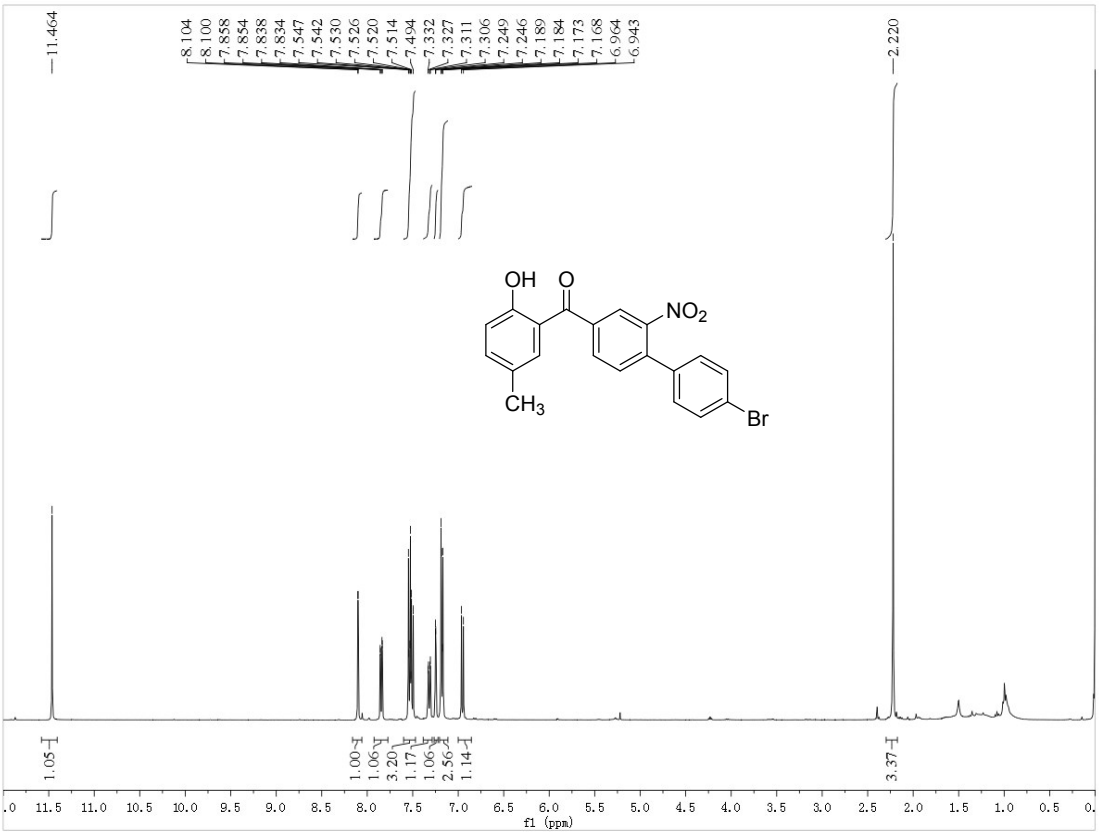


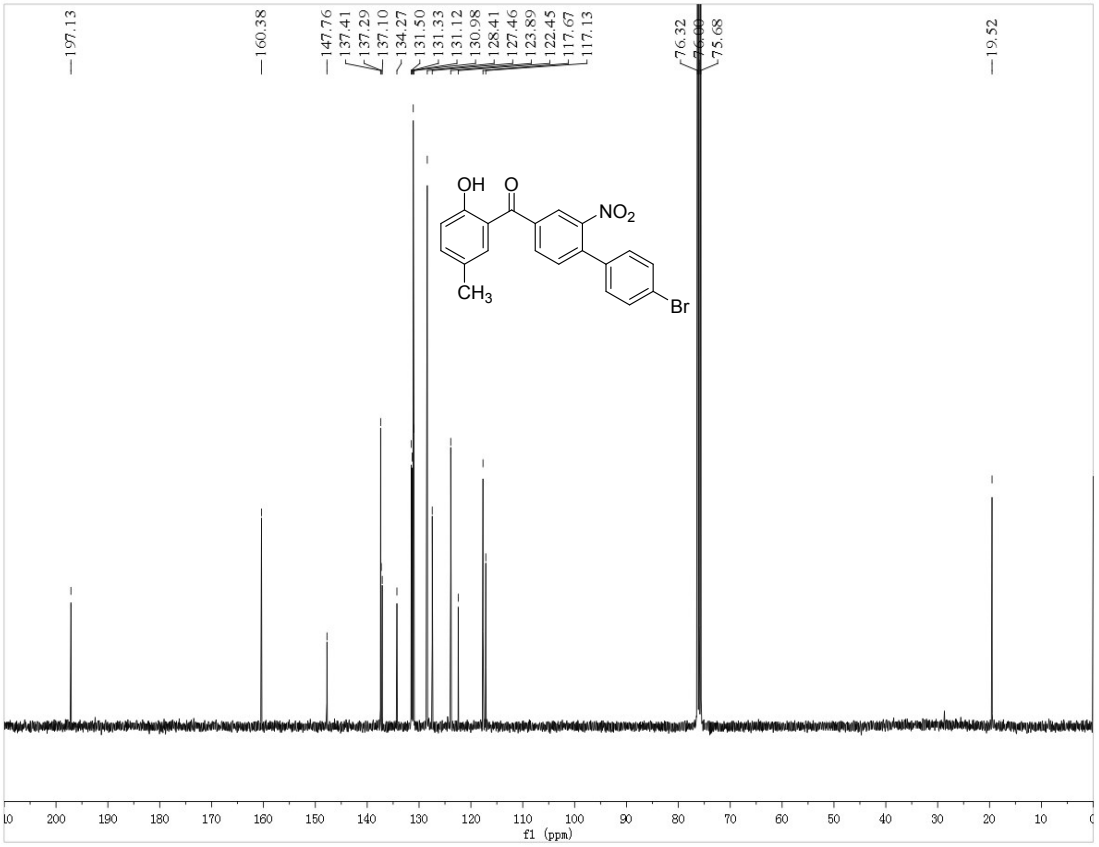
^{1}H and ^{13}C NMR of 3u



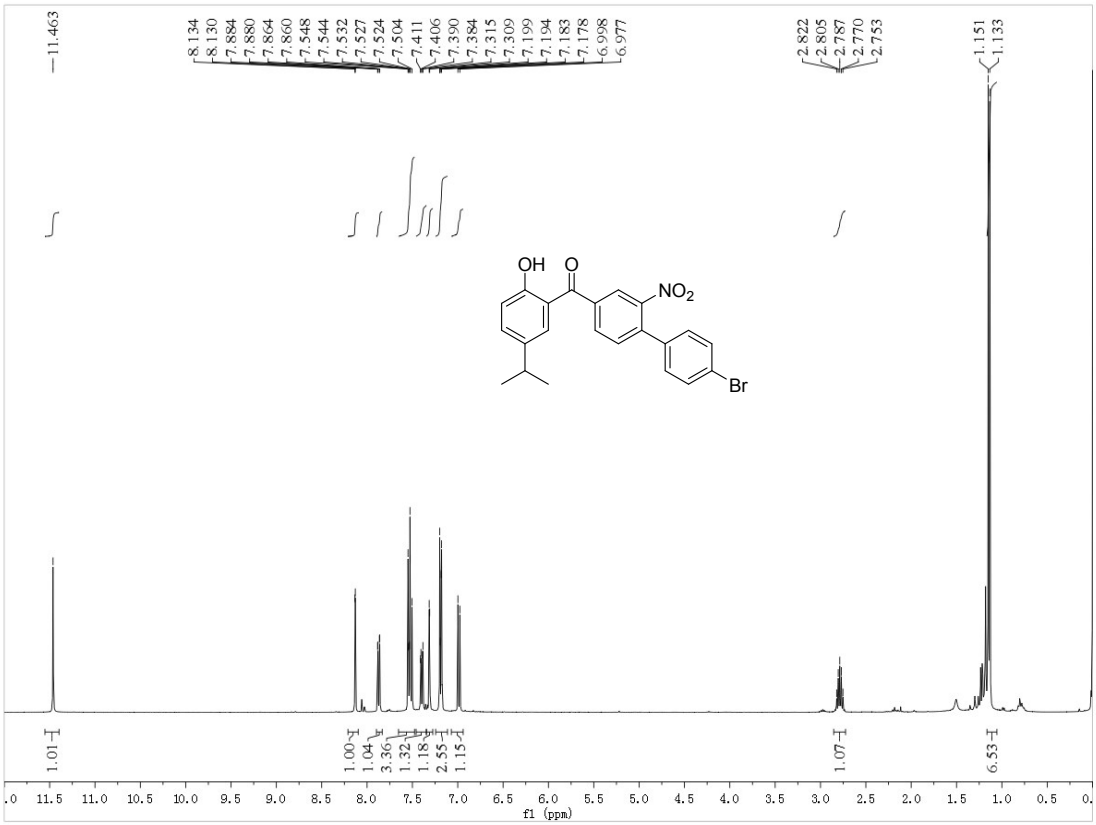


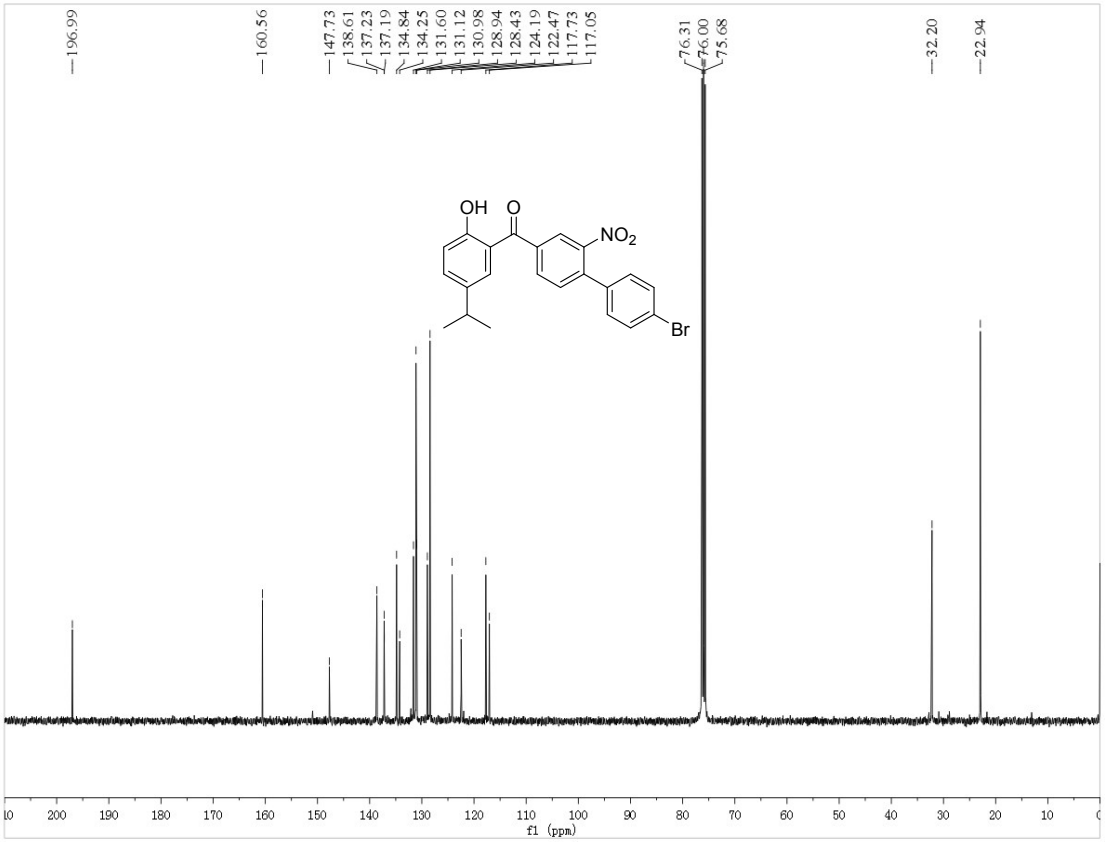
^{1}H and ^{13}C NMR of 3v



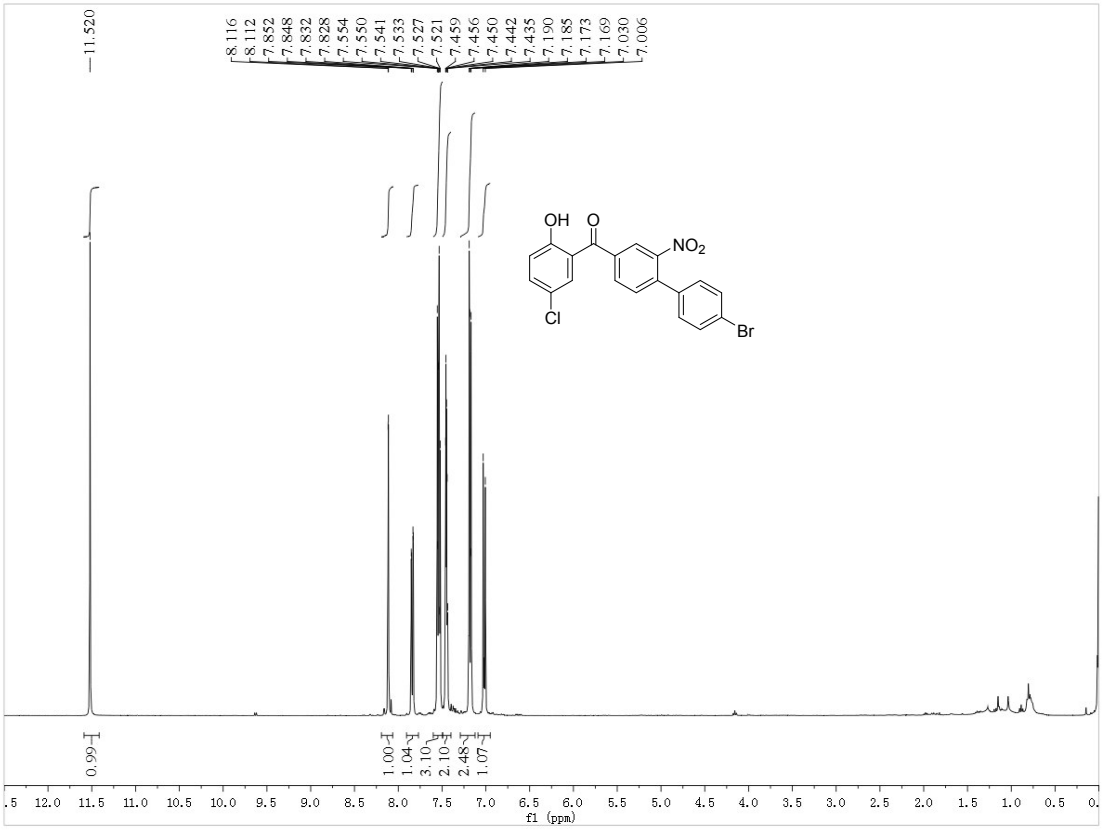


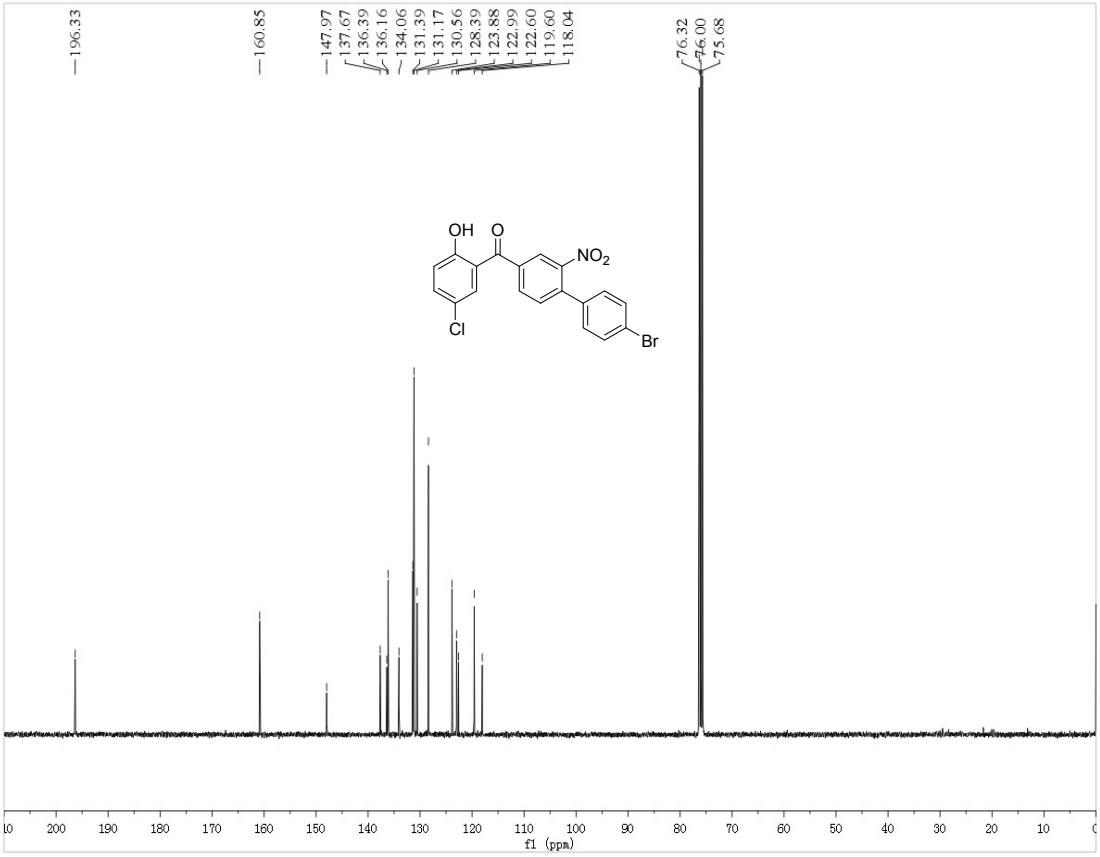
^{1}H and ^{13}C NMR of 3w



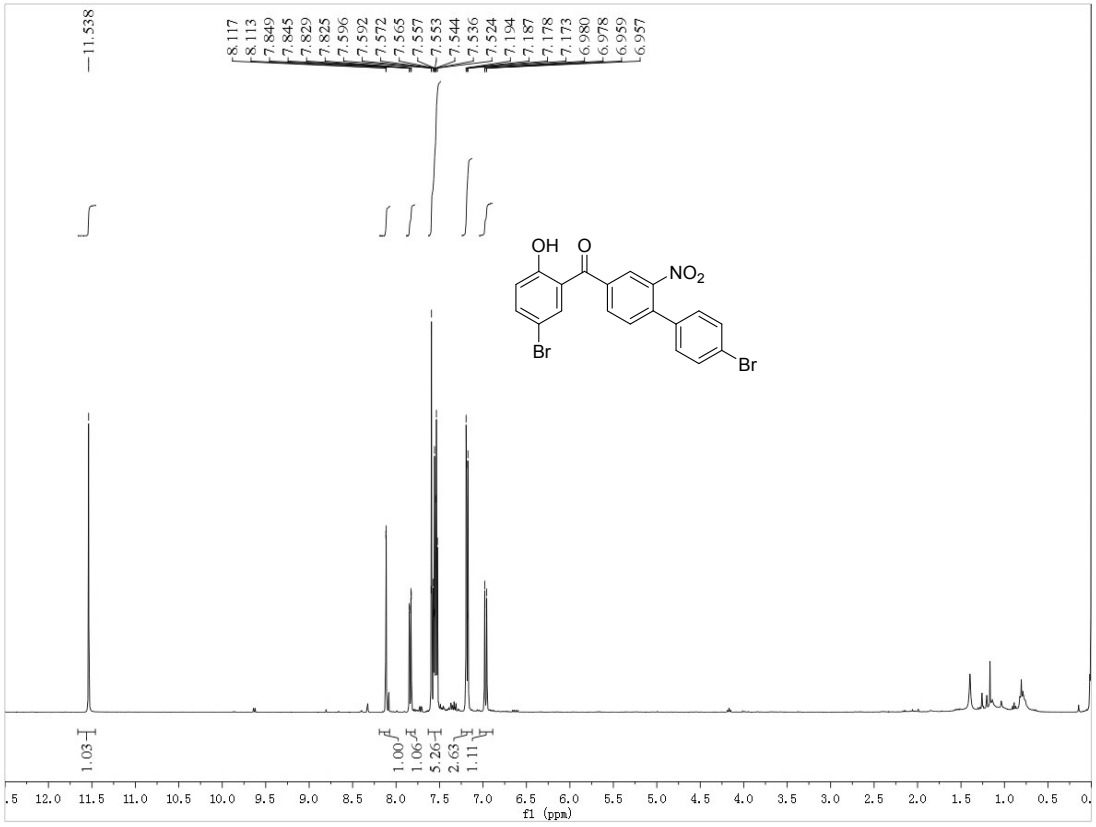


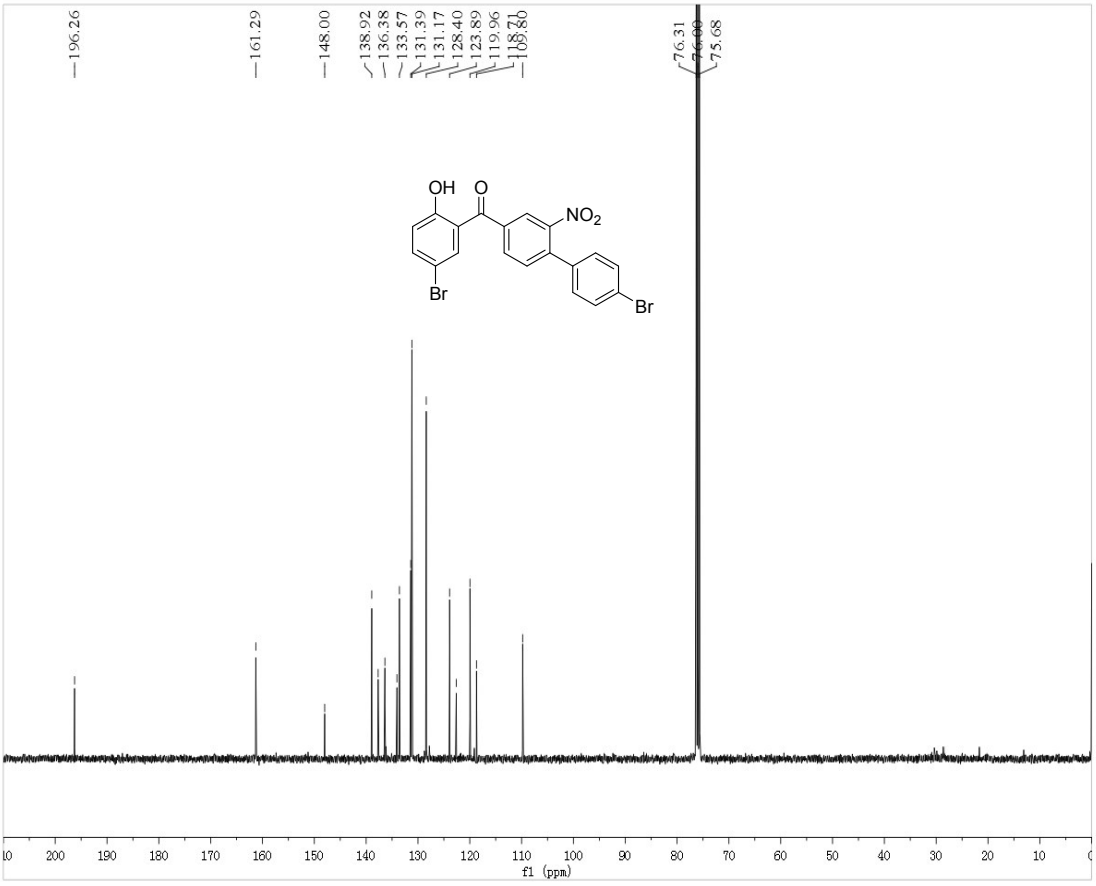
^{1}H and ^{13}C NMR of 3x





^{1}H and ^{13}C NMR of 3y





^{1}H and ^{13}C NMR of 3z