Stereocontrolled construction of six vicinal stereogenic centers on hexahydroxanthone framework through a formal [2+1+3] annulation

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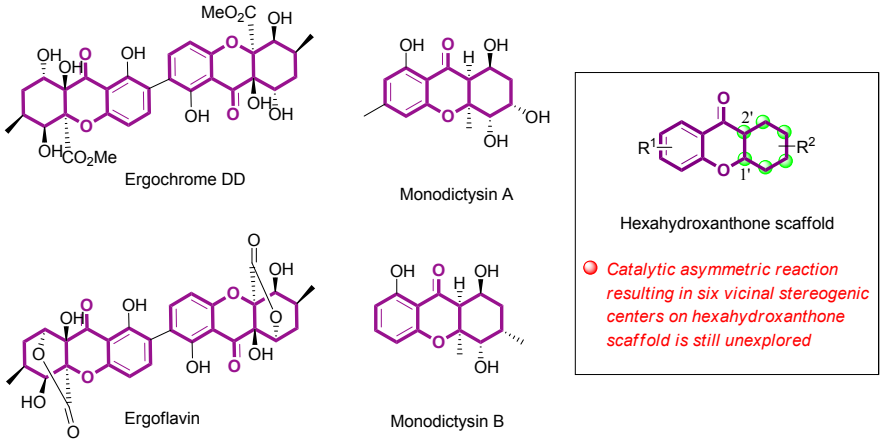
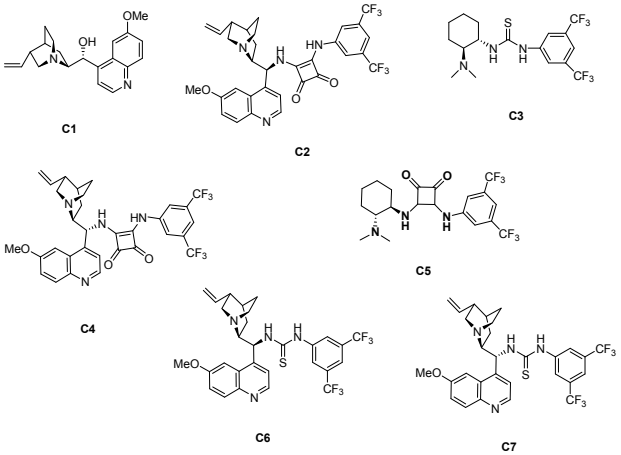
1. General information

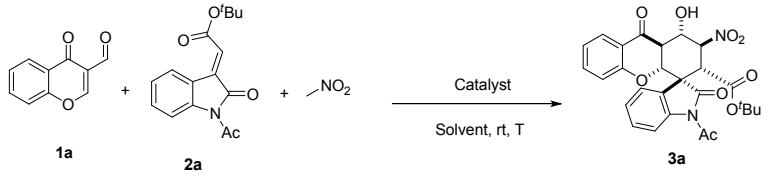
Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refered to pure isolated substances. The ee values were determined by chiral HPLC analysis. The d.r. values were determined by ^{1}H-NMR analysis. ^{1}H and ^{13}CNMR spectra were obtained using a Bruker DPX-400 or DPX-500 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. Optical rotations were measured with a polarimer with the solvent indicated. Melting points were measured on an electrothermal digital melting point apparatus.

2. Fig. S1: representative hexahydroxanthones



3. Table S1: optimization of reaction conditions for synthesis of compound 3a[a]





entry	catalyst	solvent	time[d]	yield [%][b]	d.r.[c]	ee [%][d]
1	**C1**	CH_2Cl_2	3	<10	-	-
2	**C2**	CH_2Cl_2	3	65	5:1	97(-)
3	**C3**	CH_2Cl_2	3	50	3:1	88(-)
4	**C4**	CH_2Cl_2	3	60	5:1	97(+)
5	**C5**	CH_2Cl_2	3	55	5:1	98(+)
6	**C6**	CH_2Cl_2	3	65	3:1	94(-)
7	**C7**	**CH_2Cl_2**	**3**	**76**	**4:1**	**98(+)**
8	**C7**	$CHCl_3$	3	60	4:1	95(+)
9	**C7**	toluene	3	65	4:1	98(+)
10	**C7**	Et_2O	3	<5	-	-
11	**C7**	CH_3CN	3	<5	-	-
12[e]	**C7**	CH_2Cl_2	4	67	4:1	97(+)
13[f]	**C7**	CH_2Cl_2	4	59	3:1	95(+)
14[g]	**C7**	CH_2Cl_2	4	68	4:1	97(+)
15[h]	**C7**	CH_2Cl_2	3	72	4:1	98(+)

[a] Unless otherwise noted, the reactions were carried out with **1a** (0.20 mmol), **2a** (0.30 mmol), nitromethane (0.30 mmol), catalyst (25 mol %) in 1.5 mL solvent at rt for 3 d; [b] Isolated yield; [c] Determined by ^{1}H-NMR analysis; [d] Determined by chiral HPLC analysis; [e] Run with 20 mol % of catalyst **C7**; [f] Run with 10 mol % of catalyst **C7**; [g] Run in 2.0 mL of $CHCl_3$; [h] Run in 1.0 mL of $CHCl_3$.

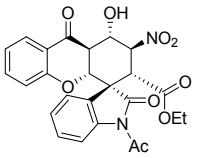
4. Typical experimental procedures for catalytic synthesis of compounds 3

In a sealed tube equipped with a magnetic stirring bar, to the mixture of methyleneindolinone **2** (0.30 mmol) and nitromethane (0.30 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1** (0.2 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired optically active product **3**, using hexane/EtOAc (6/1, v/v) as the eluent.

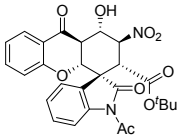
In a sealed tube equipped with a magnetic stirring bar, to the mixture of methyleneindolinone **2** (0.30 mmol) and nitromethane (0.30 mmol) in 1.5 mL of DCM was added racemic Takemoto's catalyst (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1** (0.2 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired racemic product **3**, using

hexane/EtOAc (6/1, v/v) as the eluent.

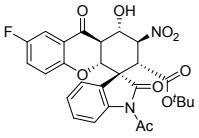
5. Characterization data and HPLC conditions of compounds 3



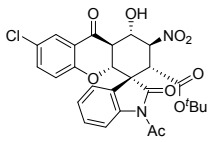
3′a: White solid, m.p. 114.3-115.1 °C; Yield 62%; 85% ee, 3:1 dr; The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 31.97 min; τ_{minor} = 27.08 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 0.82-0.86 (m, 3H), 2.67 (s, 3H), 3.51 (d, *J* = 12.4 Hz, 1H), 3.76-3.84 (m, 2H), 3.90-3.95 (m, 1H), 4.39 (s, 1H), 4.54 (d, *J* = 13.6 Hz, 1H), 4.69-4.74 (m, 1H), 5.54-5.60 (m, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.98-7.01 (m, 1H), 7.19-7.22 (m, 2H), 7.35-7.39 (m, 2H), 7.78-7.80 (m, 1H), 8.23 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.4, 25.7, 45.8, 49.0, 51.4, 61.7, 68.3, 78.7, 85.0, 115.9, 117.0, 118.9, 120.4, 121.8, 124.4, 124.6, 126.1, 129.2, 136.2, 140.3, 159.1, 165.5, 169.7, 174.2, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{25}H_{22}N_2NaO_9$ $[M+Na]^+$: 517.1218; Found: 517.1224.



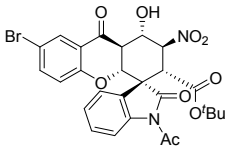
3a: White solid, m.p. 173.5-173.9 °C; Yield 76%; 98% ee, 4:1 dr, $[\alpha]_D^{20}$ = -75.24 (*c* 0.83, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 27.41 min; τ_{minor} = 29.24 min); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.10 (s, 9H), 2.76 (s, 3H), 3.47 (d, *J* = 11.0 Hz, 1H), 4.01-4.05 (m, 1H), 4.43 (s, 1H), 4.63 (d, *J* = 11.0 Hz, 1H), 4.78-4.82 (m, 1H), 5.65-5.69 (m, 1H), 6.72 (d, *J* = 7.0 Hz, 1H), 7.08-7.10 (m, 1H), 7.29-7.30 (m, 2H), 7.45-7.48 (m, 2H), 7.87-7.89 (m, 1H), 8.33 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 26.8, 27.1, 47.0, 51.0, 52.5, 69.3, 79.7, 84.3, 86.0, 116.9, 118.1, 120.0, 121.6, 122.8, 125.5, 127.1, 130.2, 137.2, 141.3, 160.2, 165.3, 170.8, 175.2, 194.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{26}N_2NaO_9$ $[M+Na]^+$: 545.1531; Found: 545.1537.



3b: White solid, m.p. 195.3-195.5 °C; Yield 68%; 96% ee, 13:1 dr, $[\alpha]_D^{20}$ = -39.62 (*c* 0.72, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (70/30 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 25.89 min; τ_{minor} = 11.04 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.01 (s, 9H), 2.67 (s, 3H), 3.35 (d, *J* = 12.4 Hz, 1H), 3.91-3.97 (m, 1H), 4.22-4.25 (m, 1H), 4.52 (d, *J* = 13.2 Hz, 1H), 4.67-4.72 (m, 1H), 5.54-5.59 (m, 1H), 6.61-6.65 (m, 1H), 7.07-7.12 (m, 1H), 7.18-7.23 (m, 2H), 7.35-7.39 (m, 1H), 7.42-7.47 (m, 1H), 8.23 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 25.8, 26.1, 46.0, 50.0, 51.4, 68.1, 79.0, 83.3, 84.8, 111.1 (d, J_{CF} = 23.0 Hz), 115.9, 118.8, 118.9, 119.4, 120.6, 123.7 (d, J_{CF} = 24.3 Hz), 124.3, 124.5, 127.8, 129.2, 129.9, 140.3, 156.7 (d, J_{CF} = 256.5 Hz), 164.2, 169.7, 174.0, 192.2; ^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: -118.86; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}FN_2NaO_9$ $[M+Na]^+$: 563.1436; Found: 563.1441.

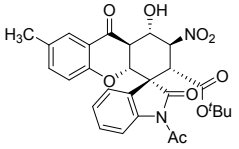


3c: White solid, m.p. 167.5-168.1 °C; Yield 69%; 98% ee, 14:1 dr, $[\alpha]_D^{20}$ = -45.03 (*c* 0.91, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 64.09 min; τ_{minor} = 58.64 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.00 (s, 9H), 2.67 (s, 3H), 3.35 (d, *J* = 12.0 Hz, 1H), 3.91-3.97 (m, 1H), 4.20 (s, 1H), 4.52 (d, *J* = 13.6 Hz, 1H), 4.67-4.72 (m, 1H), 5.53-5.59 (m, 1H), 6.61 (d, *J* = 8.8 Hz, 1H), 7.18-7.24 (m, 2H), 7.29-7.32 (m, 1H), 7.35-7.39 (m, 1H), 7.74 (d, *J* = 2.8 Hz, 1) 8.23 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 25.8, 26.1, 46.0, 50.0, 51.4, 68.0, 78.9, 83.4, 84.8, 115.9, 118.8, 119.7, 120.6, 124.2, 124.6, 125.4, 127.5, 129.2, 135.9, 140.3, 157.6, 164.1, 169.7, 174.0, 191.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}ClN_2NaO_9$ $[M+Na]^+$: 579.1141; Found: 579.1144.

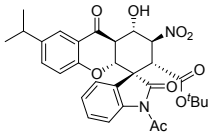


3d: White solid, m.p. 120.5-121.1 °C; Yield 60%; 96% ee, 18:1 dr, $[\alpha]_D^{20}$ = -54.87 (*c* 0.63, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 45.92 min; τ_{minor} = 23.77 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.00 (s, 9H), 2.67 (s, 3H), 3.35 (d, *J* = 12.0 Hz, 1H), 3.91-3.97 (m, 1H), 4.19 (s, 1H),

4.52 (d, J = 13.6 Hz, 1H), 4.67-4.72 (m, 1H), 5.53-5.58 (m, 1H), 6.55 (d, J = 8.8 Hz, 1H), 7.18-7.24 (m, 2H), 7.35-7.39 (m, 1H), 7.43-7.46 (m, 1H), 7.90 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 25.8, 26.1, 45.9, 50.0, 51.4, 68.0, 78.8, 83.4, 84.8, 114.6, 115.9, 119.1, 120.2, 120.6, 124.2, 124.6, 128.5, 129.3, 138.7, 140.3, 158.0, 164.1, 169.7, 174.0, 191.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}BrN_2NaO_9$ $[M+Na]^+$: 623.0636; Found: 623.0637.

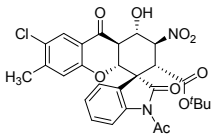


3e: White solid, m.p. 208.9-209.1 ^{o}C; Yield 58%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -39.67 (c 0.75, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 35.03 min; τ_{minor} = 30.00 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10 (s, 9H), 2.30 (s, 3H), 2.75 (s, 3H), 3.46 (d, J = 10.5 Hz, 1H), 3.98-4.02 (m, 1H), 4.47 (s, 1H), 4.58 (d, J = 11.5 Hz, 1H), 4.76-4.80 (m, 1H), 5.64-5.68 (m, 1H), 6.61 (d, J = 7.0 Hz, 1H), 7.26-7.31 (m, 3H), 7.44-7.47 (m, 1H), 7.66 (s, 1H), 8.32 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.4, 26.8, 27.1, 47.0, 51.0, 52.6, 69.3, 79.8, 84.2, 86.0, 116.8, 117.8, 119.6, 121.6, 125.5, 125.6, 126.6, 130.1, 132.5, 138.2, 141.3, 158.4, 165.3, 170.8, 175.2, 194.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_2NaO_9$ $[M+Na]^+$: 559.1687; Found: 559.1684.

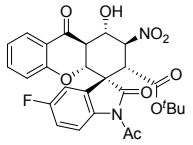


3f: White solid, m.p. 140.1-141.1 ^{o}C; Yield 68%; 95% ee, 6:1 dr, $[\alpha]_D^{20}$ = -166.79 (c 0.76, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 20.92 min; τ_{minor} = 17.38 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.09 (s, 9H), 2.75 (m, 1H), 2.85-2.89 (m, 1H), 3.47 (d, J = 10.0 Hz, 1H), 3.98-4.02 (m, 1H), 4.49 (s, 1H), 4.60 (d, J = 11.0 Hz, 1H), 4.77-4.80 (m, 1H), 5.64-5.68 (m, 1H), 6.65 (d, J = 7.0 Hz, 1H), 7.24-7.27 (m, 1H), 7.28-7.29 (m, 1H), 7.33-7.35 (m, 1H), 7.44-7.47 (m, 1H), 7.71 (d, J = 2.0 Hz, 1H), 8.32 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 23.8, 26.8, 27.1, 33.3, 47.0, 51.0, 52.6, 69.3, 79.7, 84.2, 86.0, 116.8, 118.0, 119.6, 121.6, 124.0, 125.5, 125.6, 130.1, 136.0, 141.3, 143.6, 158.5, 165.3, 170.8, 175.2, 194.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{30}H_{32}N_2NaO_9$

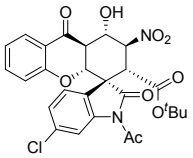
[M+Na]$^+$: 587.2000; Found: 587.2005.



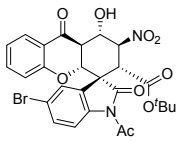
3g: White solid, m.p. 160.1-160.9 ^{o}C; Yield 69%; 97% ee, 10:1 dr, $[\alpha]_D^{20}$ = -91.28 (*c* 0.74, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 33.98 min; τ_{minor} = 29.54 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.10 (s, 9H), 2.31 (s, 3H), 2.76 (s, 3H), 3.45 (d, *J* = 8.4 Hz, 1H), 3.97-4.01 (m, 1H), 4.38 (s, 1H), 4.59 (d, *J* = 9.2 Hz, 1H), 4.76-4.79 (m, 1H), 5.62-5.66 (m, 1H), 6.64 (s, 1H), 7.29-7.32 (m, 2H), 7.45-7.48 (m, 1H), 7.82 (s, 1H), 8.32 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 20.8, 26.8, 27.1, 46.8, 51.0, 52.5, 69.2, 79.9, 84.3, 85.9, 116.9, 118.9, 120.1, 121.6, 125.4, 125.6, 126.7, 129.1, 130.2, 141.3, 146.7, 158.4, 165.2, 170.7, 175.1, 192.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}ClN_2NaO_9$ [M+Na]$^+$: 593.1297; Found: 593.13001.



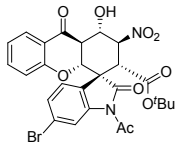
3h: White solid, m.p. 200.1-201.1 ^{o}C; Yield 64%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -96.83 (*c* 0.91, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (70/30 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.68 min; τ_{minor} = 10.60 min); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.14 (s, 9H), 2.74 (s, 3H), 3.44-3.46 (m, 1H), 3.98-4.02 (m, 1H), 4.44 (s, 1H), 4.60-4.62 (m, 1H), 4.76-4.80 (m, 1H), 5.62-5.66 (m, 1H), 6.73 (d, *J* = 7.0 Hz, 1H), 7.04-7.05 (m, 1H), 7.09-7.12 (m, 1H), 7.14-7.18 (m, 1H), 7.47-7.50 (m, 1H), 7.88-7.90 (m, 1H), 8.33-8.35 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 26.7, 27.2, 46.9, 50.7, 52.7, 69.2, 79.6, 84.6, 85.9, 109.4 (d, J_{CF} = 20.1 Hz), 116.7 (d, J_{CF} = 17.5 Hz), 118.0, 119.9, 123.0, 127.2, 137.3, 160.0, 160.3 (d, J_{CF} = 203.8 Hz), 165.1, 170.6, 174.8, 193.7; ^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: -115.05; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}FN_2NaO_9$ [M+Na]$^+$: 563.1436; Found: 563.1439.



3i: White solid, m.p. 203.1-204.1 °C; Yield 70%; 98% ee, 4:1 dr, $[\alpha]_D^{20}$ = -144.07 (*c* 0.80, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 80.15 min; τ_{minor} = 32.75 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.05 (s, 9H), 2.66 (s, 3H), 3.37 (d, *J* = 12.4 Hz, 1H), 3.85-3.91 (m, 1H), 4.35 (s, 1H), 4.51 (d, *J* = 13.6 Hz, 1H), 4.66-4.75 (m, 1H), 5.50-5.56 (m, 1H), 6.64 (d, *J* = 12.4 Hz, 1H), 6.98-7.01 (m, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.20-7.22 (m, 1H), 7.36-7.40 (m, 1H), 7.77-7.79 (m, 1H), 8.31 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 25.7, 26.1, 45.8, 49.7, 51.4, 68.2, 78.5, 83.6, 84.9, 116.4, 117.0, 118.9, 121.5, 121.9, 123.1, 123.7, 124.6, 126.1, 134.9, 136.2, 141.1, 159.0, 164.2, 169.5, 173.8, 192.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}ClN_2NaO_9$ $[M+Na]^+$: 579.1141; Found: 579.1146.

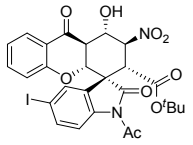


3j: White solid, m.p. 165.1-166.1 °C; Yield 61%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -33.82 (*c* 0.79, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 41.71 min; τ_{minor} = 36.78 min); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.14 (s, 9H), 2.75 (s, 3H), 3.45 (d, *J* = 10.0 Hz, 1H), 3.97-4.01 (m, 1H), 4.44 (s, 1H), 4.61 (d, *J* = 11.0 Hz, 1H), 4.75-4.79 (m, 1H), 5.61-5.65 (m, 1H), 6.75 (d, *J* = 7.0 Hz, 1H), 7.10-7.12 (m, 1H), 7.44 (s, 1H), 7.48-7.51 (m, 1H), 7.58-7.60 (m, 1H), 7.88-7.90 (m, 1H), 8.24 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 26.8, 27.2, 46.9, 50.7, 52.5, 69.2, 79.6, 84.7, 85.8, 118.1, 118.4, 118.5, 119.9, 123.0, 124.9, 127.2, 127.8, 133.1, 137.3, 140.4, 160.0, 165.2, 170.6, 174.4, 193.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}BrN_2NaO_9$ $[M+Na]^+$: 623.0636; Found: 623.0635.

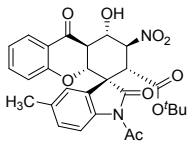


3k: White solid, m.p. 204.1-205.1 °C; Yield 68%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -82.77 (*c* 0.73, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 28.76 min; τ_{minor} = 23.71 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.06 (s, 9H), 3.06 (s, 3H), 3.35 (d, *J* = 12.4 Hz, 1H), 3.86-3.92 (m, 1H), 4.34 (s, 1H),

4.49 (d, J = 13.2 Hz, 1H), 4.65-4.70 (m, 1H), 5.50-5.56 (m, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.99-7.03 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 7.35-7.41 (m, 2H), 7.78-7.80 (m, 1H), 8.47 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 25.7, 26.2, 45.8, 49.6, 51.4, 68.2, 78.5, 83.7, 84.8, 117.0, 118.9, 119.2, 121.7, 121.9, 122.8, 123.6, 126.2, 127.5, 136.2, 141.2, 159.0, 164.2, 169.5, 173.7, 192.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}BrN_2NaO_9$ $[M+Na]^+$: 623.0636; Found: 623.0640.

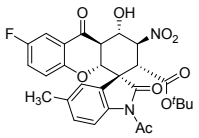


3l: White solid, m.p. 168.5-169.1 ^{o}C; Yield 74%; 97% ee, >20:1 dr, $[\alpha]_D^{20}$ = -120.99 (c 0.50, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 22.57 min; τ_{minor} = 19.57 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.05 (s, 9H), 2.65 (s, 3H), 3.34 (d, J = 12.0 Hz, 1H), 3.87-3.93 (m, 1H), 4.34 (s, 1H), 4.49 (d, J = 13.2 Hz, 1H), 4.65-4.70 (m, 1H), 5.51-5.57 (m, 1H), 6.67 (d, J = 8.8 Hz, 1H), 7.00-7.04 (m, 1H), 7.38-7.42 (m, 1H), 7.50 (s, 1H), 7.67-7.70 (m, 1H), 7.79-7.81 (m, 1H), 8.01 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 25.7, 26.2, 45.9, 49.7, 51.3, 68.2, 78.5, 83.6, 84.7, 117.1, 117.7, 118.9, 121.9, 126.2, 126.9, 129.5, 136.2, 138.0, 140.0, 159.0, 164.2, 169.6, 173.3, 192.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{25}IN_2NaO_9$ $[M+Na]^+$: 671.0497; Found: 671.05001.

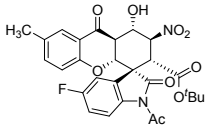


3m: White solid, m.p. 123.2-124.1 ^{o}C; Yield 68%; 96% ee, 11:1 dr, $[\alpha]_D^{20}$ = -127.92 (c 0.77, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (95/5 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 56.92 min; τ_{minor} = 42.03 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.10 (s, 9H), 2.39 (s, 3H), 2.74 (s, 3H), 3.44 (d, J = 10.0 Hz, 1H), 4.01-4.05 (m, 1H), 4.43 (s, 1H), 4.61 (d, J = 9.2 Hz, 1H), 4.76-4.80 (m, 1H), 5.64-5.68 (m, 1H), 6.74 (d, J = 7.0 Hz, 1H), 7.08-7.10 (m, 2H), 7.25 (d, J = 7.0 Hz, 1H), 7.45-7.48 (m, 1H), 7.88-7.89 (m, 1H), 8.19 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.1, 26.8, 27.2, 47.1, 51.0, 52.6, 69.3, 79.8, 84.1, 85.9, 116.7, 118.1, 120.0, 122.2, 122.7, 125.3, 127.1, 130.6, 135.4, 137.1, 139.0, 160.3, 165.2, 170.6, 175.2, 194.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_2NaO_9$ $[M+Na]^+$: 559.1687; Found:

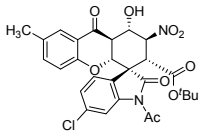
559.1690.



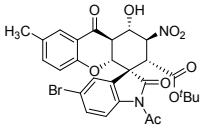
3n: White solid, m.p. 130.1-131.1 °C; Yield 72%; 95% ee, >20:1 dr, $[\alpha]_D^{20}$ = -90.57 (*c* 0.69, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IE column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 84.32 min; τ_{minor} = 18.10 min); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.09 (s, 9H), 2.38 (s, 3H), 2.73 (s, 3H), 3.41 (d, *J* = 12.0 Hz, 1H), 3.99-4.04 (m, 1H), 4.27 (s, 1H), 4.57 (d, *J* = 13.5 Hz, 1H), 4.74-4.78 (m, 1H), 5.62-5.66 (m, 1H), 6.71-6.73 (m, 1H), 7.08 (s, 1H), 7.15-7.19 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.51-7.53 (m, 1H), 8.17 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 21.1, 26.6, 27.2, 47.2, 51.1, 52.6, 69.2, 80.1, 84.2, 86.0, 112.1 (d, J_{CF} = 24.4 Hz), 116.7, 119.9, 122.1, 124.6 (d, J_{CF} = 25.1 Hz), 125.3, 130.6, 135.4, 139.0, 156.5, 157.8 (d, J_{CF} = 243.8 Hz), 165.1, 170.5, 175.1, 193.3; ^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: -118.98; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}FN_2NaO_9$ $[M+Na]^+$: 577.1593; Found: 577.1593.



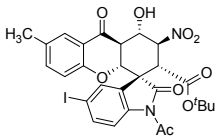
3o: White solid, m.p. 132.1-133.1 °C; Yield 69%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -109.29 (*c* 0.51, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 46.55 min; τ_{minor} = 38.49 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.05 (s, 9H), 2.22 (s, 3H), 2.65 (s, 3H), 3.33 (d, *J* = 12.0 Hz, 1H), 3.85-3.90 (m, 1H), 4.39 (s, 1H), 4.45 (d, *J* = 9.2 Hz, 1H), 4.64-4.69 (m, 1H), 5.52-5.57 (m, 1H), 6.53 (d, *J* = 8.8 Hz, 1H), 6.92-6.95 (m, 1H), 7.04-7.09 (m, 1H), 7.18-7.21 (m, 1H), 7.57 (s, 1H), 8.23-8.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 18.8, 25.1, 25.6, 45.3, 49.1, 51.1, 67.7, 78.0, 83.0, 84.3, 107.7 (d, J_{CF} = 24.2 Hz), 115.0 (d, J_{CF} = 22.5 Hz), 116.2, 116.8, 117.9, 125.1, 126.1, 131.1, 135.8, 136.7, 156.6, 158.7 (d, J_{CF} = 257.0 Hz), 163.5, 169.0, 173.2, 192.3; ^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: -115.14; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}FN_2NaO_9$ $[M+Na]^+$: 577.1593; Found: 577.1597.



3p: White solid, m.p. 167.3-168.1 °C; Yield 73%; 96% ee, 10:1 dr, $[\alpha]_D^{20}$ = -125.98 (*c* 0.76, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 62.49 min; τ_{minor} = 46.11 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.05 (s, 9H), 2.21 (s, 3H), 2.65 (s, 3H), 3.37 (d, *J* = 12.4 Hz, 1H), 3.82-3.88 (m, 1H), 4.39 (s, 1H), 4.46 (d, *J* = 13.2 Hz, 1H), 4.64-4.69 (m, 1H), 5.50-5.55 (m, 1H), 6.54 (d, *J* = 8.8 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.18-7.21 (m, 2H), 4.56 (s, 1H), 8.30 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.4, 25.7, 26.2, 45.8, 49.7, 51.4, 68.3, 78.6, 83.6, 84.9, 116.4, 116.8, 118.5, 121.4, 123.2, 124.5, 125.6, 131.6, 134.9, 137.3, 141.1, 157.2, 164.2, 169.6, 173.8, 193.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}ClN_2NaO_9$ $[M+Na]^+$: 593.1297; Found: 593.1297.

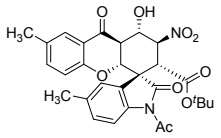


3q: White solid, m.p. 124.1-125.1 °C; Yield 62%; 97% ee, 6:1 dr, $[\alpha]_D^{20}$ = -118.98 (*c* 0.68, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 25.15 min; τ_{minor} = 18.62 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.05 (s, 9H), 2.22 (s, 3H), 2.45 (s, 3H), 3.36 (d, *J* = 12.0 Hz, 1H), 3.83-3.89 (m, 1H), 4.01 (s, 1H), 4.46 (d, *J* = 13.6 Hz, 1H), 4.64-4.69 (m, 1H), 5.51-5.56 (m, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.91 (s, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.47-7.50 (m, 1H), 7.56 (s, 1H), 8.13 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.4, 25.7, 26.2, 45.8, 49.6, 51.5, 68.2, 78.6, 83.6, 84.8, 116.8, 117.3, 117.4, 118.5, 123.7, 123.9, 125.6, 131.6, 132.0, 135.1, 137.3, 157.1, 164.2, 169.6, 173.4, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}BrN_2NaO_9$ $[M+Na]^+$: 637.0792; Found: 637.0795.

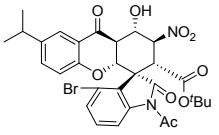


3r: White solid, m.p. 198.1-199.1 °C; Yield 71%; 97% ee, >20:1 dr, $[\alpha]_D^{20}$ = -106.83 (*c* 0.72, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (93/7 hexane/*i*-

PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 36.38 min; τ_{minor} = 27.40 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.05 (s, 9H), 2.22 (s, 3H), 2.64 (s, 3H), 3.35 (d, J = 12.0 Hz, 1H), 3.83-3.89 (m, 1H), 4.38 (s, 1H), 4.47 (d, J = 13.6 Hz, 1H), 4.63-4.68 (m, 1H), 5.50-5.56 (m, 1H), 5.55 (d, J = 8.4 Hz, 1H), 7.19-7.21 (m, 1H), 7.50 (s, 1H), 7.57 (s, 1H), 7.67-7.69 (m, 1H), 8.00 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.4, 25.7, 26.2, 45.8, 49.7, 51.4, 68.2, 78.5, 83.6, 84.8, 116.8, 117.7, 118.5, 125.6, 127.0, 127.8, 129.6, 129.9, 131.6, 137.3, 138.0, 140.0, 157.1, 164.2, 166.7, 169.6, 173.3, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}IN_2NaO_9$ $[M+Na]^+$: 685.0653; Found: 685.0650.

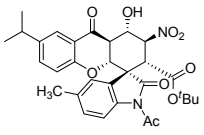


3s: White solid, m.p. 112.4-113.1 °C; Yield 65%; 98% ee, >20:1 dr, $[\alpha]_D^{20}$ = -120.79 (*c* 0.73, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IF column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 37.21 min; τ_{minor} = 24.24 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.10 (s, 9H), 2.31 (s, 3H), 2.39 (s, 3H), 2.73 (s, 3H), 3.43 (d, J = 10.0 Hz, 1H), 3.97-4.01 (m, 1H), 4.57 (d, J = 11.0 Hz, 1H), 4.74-4.78 (m, 1H), 5.64-5.67 (m, 1H), 6.63 (d, J = 7.0 Hz, 1H), 7.09 (s, 1H), 7.23-7.29 (m, 2H), 7.66 (s, 1H), 8.18 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.4, 21.1, 26.8, 27.2, 47.0, 51.0, 52.6, 69.3, 79.8, 84.1, 86.0, 116.6, 117.9, 119.6, 122.2, 125.4, 126.6, 130.5, 132.4, 135.4, 138.2, 139.0, 158.4, 165.2, 170.6, 175.2, 194.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{29}H_{30}N_2NaO_9$ $[M+Na]^+$: 573.1844; Found: 573.1847.

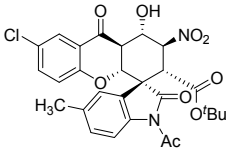


3t: White solid, m.p. 198.7-198.9 °C; Yield 62%; 88% ee, >20:1 dr, $[\alpha]_D^{20}$ = +96.12 (*c* 0.80, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 17.87 min; τ_{minor} = 9.73 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.09 (s, 9H), 1.22 (s, 3H), 1.23 (s, 3H), 2.69 (s, 3H), 2.87-2.92 (m, 1H), 3.03 (d, J = 3.0 Hz, 1H), 4.07-4.09 (m, 1H), 4.85 (d, J = 9.5 Hz, 1H), 5.66 (s, 1H), 5.73-5.76 (m, 1H), 5.85 (d, J = 11.0 Hz, 1H), 6.68 (d, J = 7.0 Hz, 1H), 7.32-7.37 (m, 2H), 7.47-7.49 (m, 1H), 7.76 (d, J = 2.0

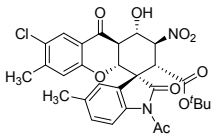
Hz, 1H), 8.35 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 23.9, 26.9, 27.1, 33.3, 42.3, 46.7, 55.7, 66.0, 74.4, 82.5, 82.7, 115.6, 118.0, 118.8, 120.3, 123.7, 124.2, 130.3, 131.2, 135.4, 142.7, 143.1, 158.5, 167.9, 170.5, 174.4, 191.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{30}H_{31}BrN_2NaO_9$ $[M+Na]^+$: 665.1105; Found: 665.1106.



3u: White solid, m.p. 130.1-131.1 °C; Yield 63%; 97% ee, 7:1 dr, $[\alpha]_D^{20}$ = -140.67 (*c* 0.78, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 30.48 min; τ_{minor} = 17.88 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.10 (s, 9H), 1.20 (s, 3H), 1.22 (s, 3H), 2.38 (s, 3H), 2.73 (s, 3H), 3.44 (d, J = 10.5 Hz, 1H), 3.98-4.02 (m, 1H), 4.48 (s, 1H), 4.58 (d, J = 11.0 Hz, 1H), 4.75-4.79 (m, 1H), 5.64-5.68 (m, 1H), 6.67 (d, J = 7.0 Hz, 1H), 7.09 (s, 1H), 7.24 (d, J = 6.5 Hz, 1H), 7.33-7.35 (m, 1H), 7.71 (d, J = 2.0 Hz, 1H), 8.19 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.1, 23.8, 26.8, 27.2, 33.3, 47.0, 51.0, 52.6, 69.3, 79.8, 84.1, 86.0, 116.6, 118.0, 119.6, 122.2, 124.0, 125.4, 130.5, 135.4, 135.9, 138.9, 143.5, 158.6, 165.2, 170.6, 175.2, 194.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{31}H_{34}N_2NaO_9$ $[M+Na]^+$: 601.2157; Found: 601.2153.



3v: White solid, m.p. 125.1-126.1 °C; Yield 67%; 95% ee, 4:1 dr, $[\alpha]_D^{20}$ = -71.57 (*c* 0.52, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (70/30 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 30.11 min; τ_{minor} = 12.68 min); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.01 (s, 9H), 2.30 (s, 3H), 2.65 (s, 3H), 3.33 (d, J = 12.0 Hz, 1H), 3.42 (s, 3H), 3.90-3.96 (m, 1H), 4.51 (d, J = 13.6 Hz, 1H), 4.66-4.71 (m, 1H), 5.53-5.58 (m, 1H), 6.62 (d, J = 8.8 Hz, 1H), 7.00 (s, 1H), 7.15-7.19 (m, 1H), 7.30-7.33 (m, 1H), 7.74 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.7, 25.3, 25.7, 45.6, 49.5, 51.0, 67.6, 78.4, 82.8, 84.4, 115.2, 118.4, 119.3, 120.7, 123.6, 124.9, 127.0, 129.2, 134.0, 135.4, 137.5, 157.2, 163.7, 169.1, 173.6, 191.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{27}ClN_2NaO_9$ $[M+Na]^+$: 593.1297; Found: 593.13002.



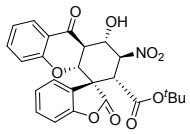
3w: White solid, m.p. 143.1-143.5 °C; Yield 64%; 96% ee, >20:1 dr, $[\alpha]_D^{20}$ = -98.36 (*c* 0.68, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (83/17 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 108.83 min; τ_{minor} = 30.68 min); ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.10 (s, 9H), 2.31 (s, 3H), 2.39 (s, 3H), 2.74 (s, 3H), 3.43 (d, *J* = 10.0 Hz, 1H), 3.97-4.01 (m, 1H), 4.37 (s, 1H), 4.57 (d, *J* = 11.0 Hz, 1H), 4.74-4.78 (m, 1H), 5.62-5.66 (m, 1H), 6.66 (s, 1H), 7.09 (s, 1H), 7.24-7.26 (m, 1H), 7.82 (s, 1H), 8.19 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 20.9, 21.1, 26.8, 27.2, 46.9, 51.0, 52.5, 69.2, 79.9, 84.2, 85.9, 116.7, 118.9, 120.2, 122.1, 125.2, 126.6, 129.1, 130.6, 135.5, 138.9, 146.7, 158.4, 165.2, 170.6, 175.1, 192.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{29}H_{29}ClN_2NaO_9$ $[M+Na]^+$: 607.1454; Found: 607.1457.

6. Typical experimental procedures for catalytic synthesis of compounds 5

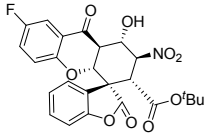
In a sealed tube equipped with a magnetic stirring bar, to the mixture of methylenebenzofuranone **4** (0.30 mmol) and nitromethane (0.30 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1** (0.2 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired optically active product **5**, using hexane/EtOAc (5/1, v/v) as the eluent.

In a sealed tube equipped with a magnetic stirring bar, to the mixture of methylenebenzofuranone **4** (0.30 mmol) and nitromethane (0.30 mmol) in 1.5 mL of DCM was added racemic Takemoto's catalyst (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1** (0.2 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired racemic product **5**, using hexane/EtOAc (5/1, v/v) as the eluent.

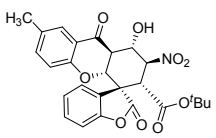
7. Characterization data and HPLC conditions of compounds 5



5a: White solid, m.p. 103.2-103.6 °C; Yield 67%; 94% ee, 5:1 dr, $[\alpha]_D^{20}$ = -58.66 (*c* 0.99, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 27.31 min; τ_{minor} = 24.18 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.09 (s, 9H), 3.39 (d, *J* = 12.0 Hz, 1H), 3.81-3.87 (m, 1H), 4.33 (s, 1H), 4.53 (d, *J* = 13.2 Hz, 1H), 4.68-4.76 (m, 1H), 5.45-5.51 (m, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.98-7.02 (m, 1H), 7.15-7.23 (m, 3H), 7.36-7.39 (m, 1H), 7.77-7.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 26.1, 45.7, 49.2, 51.1, 68.2, 77.9, 83.9, 84.9, 110.2, 117.0, 118.8, 121.3, 121.8, 123.8, 123.9, 126.1, 129.7, 136.2, 153.2, 158.9, 163.8, 172.2, 192.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{25}H_{23}NNaO_9$ $[M+Na]^+$: 504.1265; Found: 504.1268.

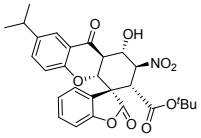


5b: White solid, m.p. 131,2-131.7 °C; Yield 48%; 93% ee, 14:1 dr, $[\alpha]_D^{20}$ = -36.05 (*c* 0.92, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 69.79 min; τ_{minor} = 58.73 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.09 (s, 9H), 3.39 (d, *J* = 12.0 Hz, 1H), 3.81-3.87 (m, 1H), 4.22 (s, 1H), 4.52 (d, *J* = 13.6 Hz, 1H), 4.68-4.73 (m, 1H), 5.44-5.50 (m, 1H), 6.62-6.65 (m, 1H), 7.07-7.72 (m, 1H), 7.15-7.21 (m, 3H), 7.36-7.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 26.1, 45.7, 49.2, 51.0, 68.1, 78.1, 84.0, 84.8, 110.2, 111.0 (d, J_{CF} = 23.2 Hz), 118.8, 118.9, 119.4, 121.3, 123.7 (d, J_{CF} = 20.0 Hz), 123.8, 123.9, 129.8, 153.2, 155.2, 156.8 (d, J_{CF} = 243.3 Hz), 163.7, 172.2, 191.9; ^{19}F NMR ($CDCl_3$, 376 MHz) *δ*: -118.77; HRMS (ESI-TOF) m/z: Calcd. for $C_{25}H_{22}FNNaO_9$ $[M+Na]^+$: 522.1171; Found: 522.1177.

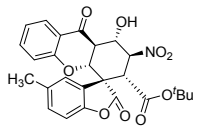


5c: White solid, m.p. 111.4-111.7 °C; Yield 61%; 94% ee, 5:1 dr, $[\alpha]_D^{20}$ = -30.64 (*c* 0.53, CH_2Cl_2);

The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 51.83 min; τ_{minor} = 61.42 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.09 (s, 9H), 2.21 (s, 3H), 3.39 (d, *J* = 12.4 Hz, 1H), 3.77-3.83 (m, 1H), 4.37 (s, 1H), 4.49 (d, *J* = 13.6 Hz, 1H), 4.66-4.72 (m, 1H), 5.44-5.50 (m, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 7.14-7.22 (m, 5H), 7.31-7.41 (m, 1H), 7.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.4, 26.1, 45.7, 49.2, 51.1, 68.3, 77.9, 83.9, 84.9, 110.1, 116.7, 118.4, 121.3, 123.8, 125.5, 129.6, 131.5, 137.3, 153.2, 157.1, 163.8, 172.2, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{26}H_{25}NNaO_9$ $[M+Na]^+$: 518.1422; Found: 518.1426.

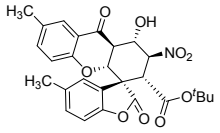


5d: White solid, m.p. 181.2-181.6 °C; Yield 51%; 96% ee, 4:1 dr, $[\alpha]_D^{20}$ = -114.96 (*c* 0.99, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 28.98 min; τ_{minor} = 40.59 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.09 (s, 9H), 1.11 (s, 3H), 1.13 (s, 3H), 2.76-2.82 (m, 1H), 3.39 (d, *J* = 12.4 Hz, 1H), 3.78-3.84 (m, 1H), 4.39 (s, 1H), 4.49 (d, *J* = 13.6 Hz, 1H), 4.67-4.72 (m, 1H), 5.45-5.51 (m, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 7.15-7.19 (m, 3H), 7.22-7.27 (m, 1H), 7.35-7.41 (m, 1H), 7.61 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 22.7, 26.1, 32.3, 45.7, 49.2, 51.1, 68.3, 77.9, 83.9, 84.9, 110.1, 116.9, 118.5, 121.3, 123.0, 123.7, 124.0, 129.6, 135.0, 142.6, 153.2, 157.3, 163.8, 172.2, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{29}NNaO_9$ $[M+Na]^+$: 546.1735; Found: 546.1738.

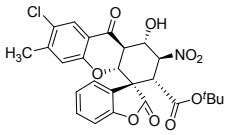


5e: White solid, m.p. 105.5-105.9 °C; Yield 53%; 96% ee, 11:1 dr, $[\alpha]_D^{20}$ = -47.49 (*c* 0.67, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (70/30 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 47.91 min; τ_{minor} = 31.64 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.10 (s, 9H), 2.30 (s, 3H), 3.36 (d, *J* = 12.0 Hz, 1H), 3.81-3.87 (m, 1H), 4.33 (s, 1H), 4.50 (d, *J* = 13.6 Hz, 1H), 4.66-4.71 (m, 1H), 5.45-5.51 (m, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.98-6.99 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.36-7.40 (m, 1H), 7.77-7.80 (m, 1H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.1, 26.1, 45.7, 49.2, 51.1, 68.3, 77.9, 83.8, 84.9, 109.8, 117.0, 118.8, 121.7, 121.8, 123.7, 126.1, 130.0, 133.6, 136.1, 151.1, 159.0, 163.7, 172.5, 192.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{26}H_{25}NNaO_9$ $[M+Na]^+$: 518.1422; Found: 518.1429.

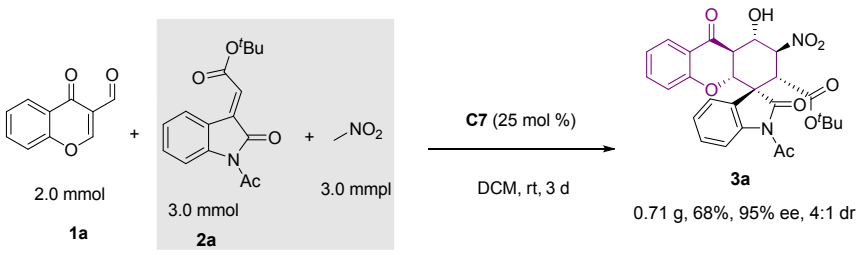


5f: White solid, m.p. 172.0-172.5 °C; Yield 45%; 95% ee, 4:1 dr, $[\alpha]_D^{20}$ = -54.28 (*c* 0.98, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 73.87 min; τ_{minor} = 68.29 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10 (s, 9H), 2.22 (s, 3H), 2.29 (s, 3H), 3.35 (d, *J* = 12.0 Hz, 1H), 3.77-3.83 (m, 1H), 4.37 (s, 1H), 4.46 (d, *J* = 13.2 Hz, 1H), 4.64-4.71 (m, 1H), 5.23 (s, 1H), 5.44-5.50 (m, 1H), 5.54 (d, *J* = 8.8 Hz, 1H), 6.99-7.03 (m, 2H), 7.14-7.19 (m, 2H), 7.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.4, 20.1, 26.1, 45.7, 49.2, 51.2, 68.3, 77.9, 83.8, 84.9, 109.7, 116.8, 118.4, 121.7, 123.7, 125.5, 130.0, 131.4, 133.6, 137.2, 151.1, 157.1, 163.7, 172.5, 192.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}NNaO_9$ $[M+Na]^+$: 532.1578; Found: 532.1573.



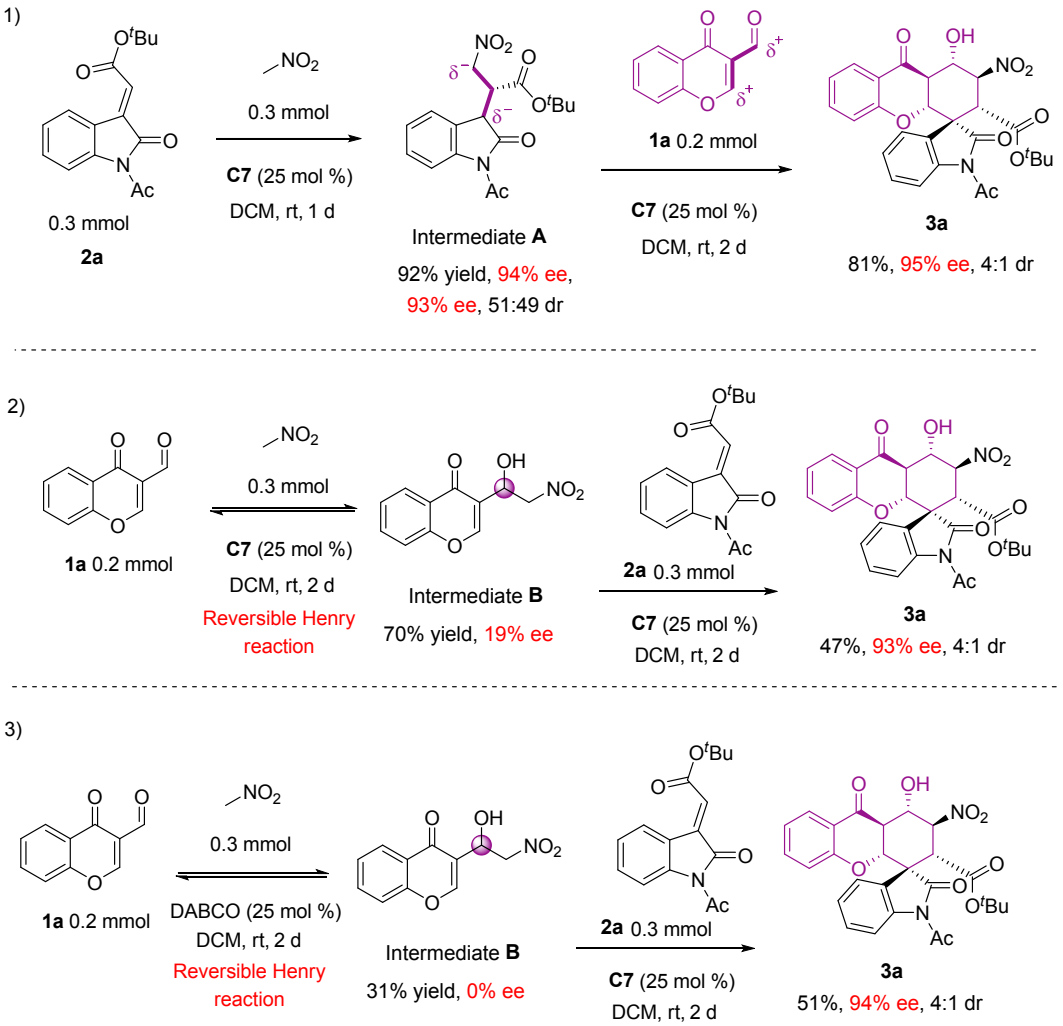
5g: White solid, m.p. 115.8-116.1 °C; Yield 50%; 97% ee, 5:1 dr, $[\alpha]_D^{20}$ = -79.36 (*c* 0.55, CH_2Cl_2); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 71.85 min; τ_{minor} = 58.70 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.09 (s, 9H), 2.22 (s, 3H), 3.37 (d, *J* = 12.4 Hz, 1H), 3.77-3.83 (m, 1H), 4.27 (br s, 1H), 4.49 (d, *J* = 13.6 Hz, 1H), 4.66-4.71 (m, 1H), 5.43-5.49 (m, 1H), 6.54 (s, 1H), 7.15-7.19 (m, 3H), 7.35-7.42 (m, 1H), 7.72 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.8, 26.1, 45.5, 49.2, 51.0, 68.1, 78.0, 84.0, 84.8, 110.2, 117.7, 119.0, 121.3, 123.8, 125.6, 128.2, 129.7, 145.8, 153.2, 157.1, 163.7, 172.1, 191.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{26}H_{24}ClNNaO_9$ $[M+Na]^+$: 552.1032; Found: 552.1034.

8. Scheme S1: gram scale synthesis of the product 3a



In a sealed tube equipped with a magnetic stirring bar, to the mixture of methyleneindolinone **2a** (3.0 mmol) and nitromethane (3.0 mmol) in 15 mL of DCM was added thiourea catalyst **C7** (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1a** (2.0 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3a**, using hexane/EtOAc (6/1, v/v) as the eluent (0.71 g, 68%, 95% ee, 4:1 dr).

9. Scheme S2: control experiments



Control experiment 1).

In a sealed tube equipped with a magnetic stirring bar, to the mixture of methyleneindolinone **2a** (0.3 mmol) and nitromethane (0.3 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %), and was stirred at rt for 1 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired intermediate **A**, using hexane/EtOAc (6/1, v/v) as the eluent (92%, 94% ee, 93% ee, 51:49 dr).

In a sealed tube equipped with a magnetic stirring bar, to the mixture of intermediate **A** and 3-formyl chromone **1a** (2.0 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3a**, using hexane/EtOAc (8/1, v/v) as the eluent (81%, 95% ee, 4:1 dr).

Intermediate **A**: White solid; Yield 92%; 94% ee, 93% ee, 51:49 dr; The ee was determined by

HPLC analysis using a Chiralpak IF column (97/3 hexane/*i*-PrOH; flow rate: 0.8 mL/min; λ = 254 nm; τ_{major1} = 40.56 min; τ_{minor1} = 32.98 min; τ_{major2} = 36.73 min; τ_{minor2} = 44.97 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (major + minor): 1.06 (s, 9H), 1.18 (s, 9H), 2.59 (s, 3H), 2.62 (s, 3H), 3.78 (s, 1H), 3.88-3.93 (m, 2H), 4.07-4.11 (m, 1H), 4.45-4.50 (m, 1H), 4.66-4.71 (m, 1H), 4.83-4.89 (m, 1H), 4.97-5.02 (m, 1H), 7.12-7.21 (m, 4H), 7.28-7.30 (m, 2H), 8.13-8.16 (m, 1H), 8.19-8.21 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (major + minor): 25.6, 25.7, 26.3, 26.5, 43.6, 44.1, 44.2, 44.6, 72.0, 72.3, 82.6, 115.8, 115.9, 122.3, 122.4, 123.0, 123.5, 124.3, 124.4, 128.2, 128.5, 139.7, 140.1, 166.2, 166.8, 169.6, 169.7, 174.5, 174.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{17}H_{20}N_2NaO_6$ $[M+Na]^+$: 371.1214; Found: 371.1217.

Control experiment 2).

In a sealed tube equipped with a magnetic stirring bar, to the mixture of 3-formyl chromone **1a** and nitromethane (0.3 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired intermediate **B**, using hexane/EtOAc (7/1, v/v) as the eluent (70% yield, 19% ee).

In a sealed tube equipped with a magnetic stirring bar, to the mixture of intermediate **B** (19% ee) and methyleneindolinone **2a** (0.3 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3a**, using hexane/EtOAc (8/1, v/v) as the eluent (47%, 93% ee, 4:1 dr).

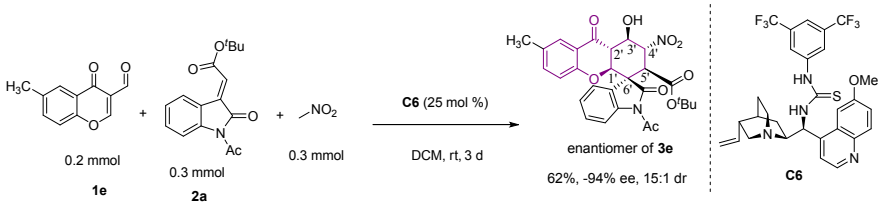
Intermediate **B**: Light yellow solid; Yield 70%; 19% ee; The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 18.87 min; τ_{minor} = 16.05 min); ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 4.49-4.55 (m, 1H), 4.84-4.88 (m, 1H), 5.26 (br s, 1H), 5.42 (d, J = 8.4 Hz, 1H), 7.33-7.37 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.64-7.68 (m, 1H), 7.97-7.99 (m, 1H), 8.16 (s, 1H); ^{13}C NMR (CD_3COCD_3, 100 MHz) δ: 64.8, 79.6, 118.4, 122.6, 123.6, 125.2, 125.5, 134.2, 154.7, 156.4, 175.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{11}H_9NNaO_5$ $[M+Na]^+$: 258.0373; Found: 258.0371.

Control experiment 3).

In a sealed tube equipped with a magnetic stirring bar, to the mixture of 3-formyl chromone **1a** and nitromethane (0.3 mmol) in 1.5 mL of DCM was added catalyst DABCO (25 mol %), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired *rac*-intermediate **B**, using hexane/EtOAc (7/1, v/v) as the eluent (71% yield, 0% ee).

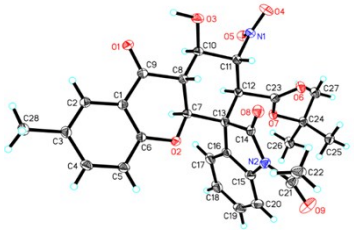
In a sealed tube equipped with a magnetic stirring bar, to the mixture of *rac*-intermediate **B** (0% ee) and methyleneindolinone **2a** (0.3 mmol) in 1.5 mL of DCM was added thiourea catalyst **C7** (25 mol %), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3a**, using hexane/EtOAc (8/1, v/v) as the eluent (51%, 94% ee, 4:1 dr).

10. Scheme S3: catalytic asymmetric synthesis of opposite enantiomer of 3e

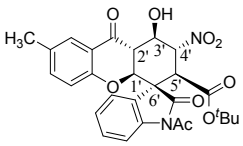


In a sealed tube equipped with a magnetic stirring bar, to the mixture of methyleneindolinone **2a** (0.3 mmol) and nitromethane (0.3 mmol) in 1.5 mL of DCM was added thiourea catalyst **C6** (25 mol %). The reaction mixture was stirred at rt for 1 d, and then was added the 3-formyl chromone **1e** (0.2 mmol), and was stirred at rt for 2 d. The reaction mixture was directly loaded onto a silica gel and purified by flash chromatography to give the enantiomer of **3e**, using hexane/EtOAc (6/1, v/v) as the eluent (62%, -94% ee, 15:1 dr).

11. X-Ray crystal data for opposite enantiomer of 3e



CCDC-1875149



Opposite enantiomer of **3e**

Table S2 Crystal data and structure refinement for opposite enantiomer of 3e

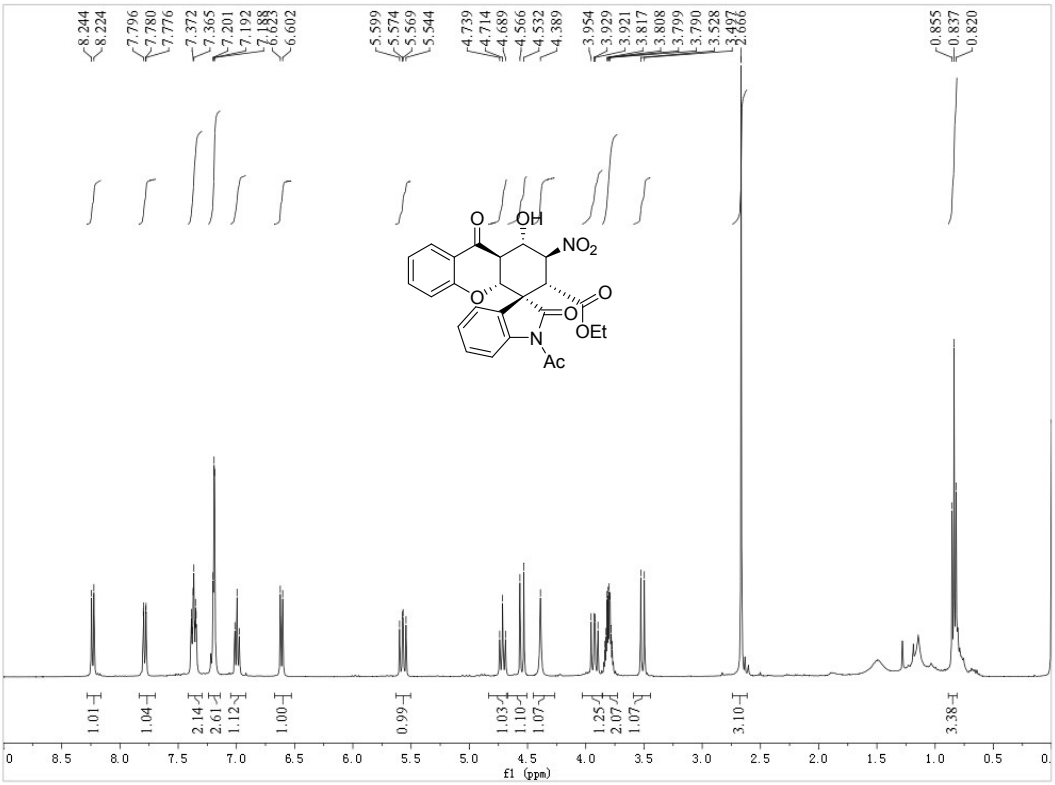
Identification code	opposite enantiomer of **3e**
Empirical formula	$C_{28}H_{28}N_2O_9$
Formula weight	536.52
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	P212121
a/Å, b/Å, c/Å	10.46150(10), 10.51450(10), 23.7246(3)
α/°, β/°, γ/°,	90, 90, 90.
Volume/Å^3	2609.65(5)
Z	4
ρ_{calc}g/cm^3	1.366
μ/mm^{-1}	0.861
F(000)	1128.0
Crystal size/mm^3	0.13 × 0.12 × 0.11
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.452 to 147.158
Index ranges	-13 ≤ h ≤ 9, -13 ≤ k ≤ 12, -29 ≤ l ≤ 29
Reflections collected	15996
Independent reflections	5148 [Rint = 0.0345, Rsigma = 0.0294]
Data/restraints/parameters	5148/0/361
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0460, wR_2 = 0.1226
Final R indexes [all data]	R_1 = 0.0469, wR_2 = 0.1239
Largest diff. peak/hole / e Å^{-3}	0.43/-0.25
Flack/Hooft parameter	0.07(10)/0.08(8)

Crystal structure determination of opposite enantiomer of 3e

Crystal Data for $C_{28}H_{28}N_2O_9$ (M =536.52 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 10.46150(10) Å, b = 10.51450(10) Å, c = 23.7246(3) Å, V = 2609.65(5) Å^3, Z = 4, T = 100.00(10) K, μ(CuKα) = 0.861 mm^{-1}, *Dcalc* = 1.366 g/cm^3, 15996 reflections measured (7.452° ≤ 2Θ ≤ 147.158°), 5148 unique (R_{int} = 0.0345, R_{sigma} = 0.0294) which were used in all calculations. The final R_1 was 0.0460 (I > 2σ(I)) and wR_2 was 0.1239 (all data).

12. The copies of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HPLC spectra for compounds 3 and 5

^{1}H and ^{13}C NMR of 3a'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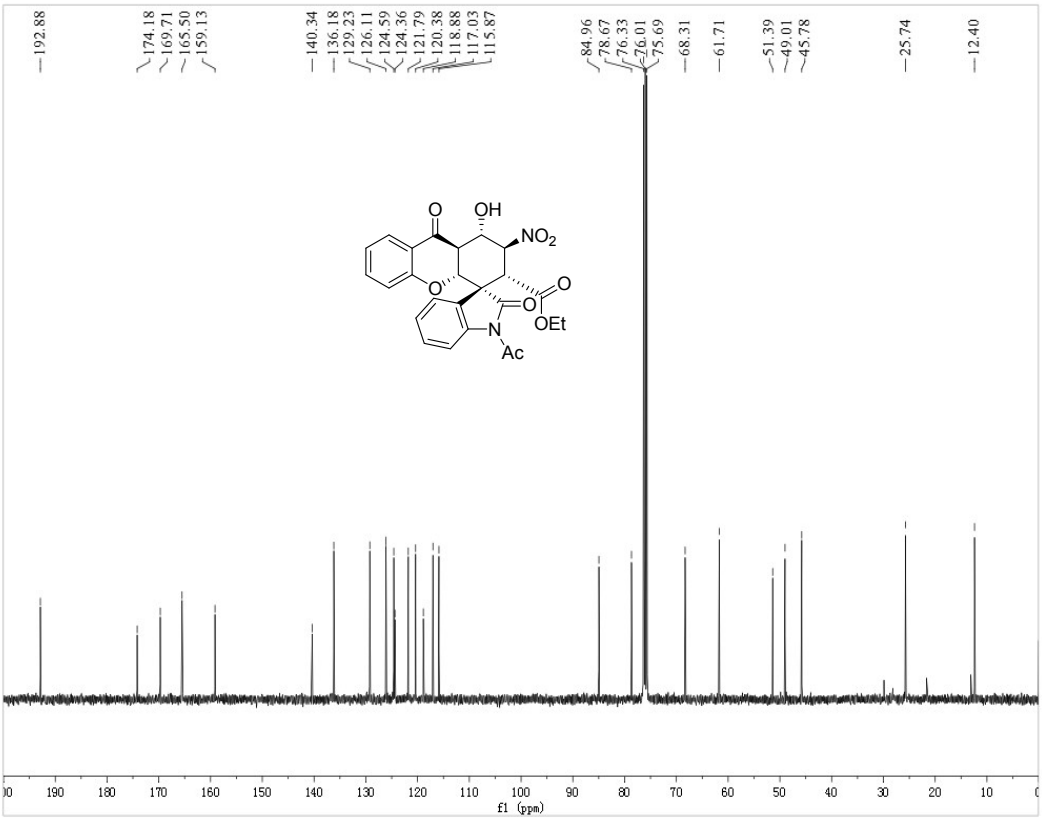
7.372
7.365
7.201
7.192
7.188
6.623
6.602
5.599
5.574
5.569
5.544
4.739
4.714
4.689
4.566
4.532
4.389
3.954
3.929
3.921
3.817
3.808
3.799
3.790
3.528
3.497
2.666
0.855
0.837
0.820
O
OH
NO2
O
O
O
OEt
N
Ac
1.01
1.04
2.14
2.61
1.12
1.00
0.99
1.03
1.10
1.07
1.25
2.07
1.07
3.10
3.38
f1 (ppm)


192.88
174.18
169.71
165.50
159.13
140.34
136.18
129.23
126.11
124.59
124.36
121.79
120.38
118.88
117.03
115.87
84.96
78.67
76.33
76.01
75.69
68.31
61.71
51.39
49.01
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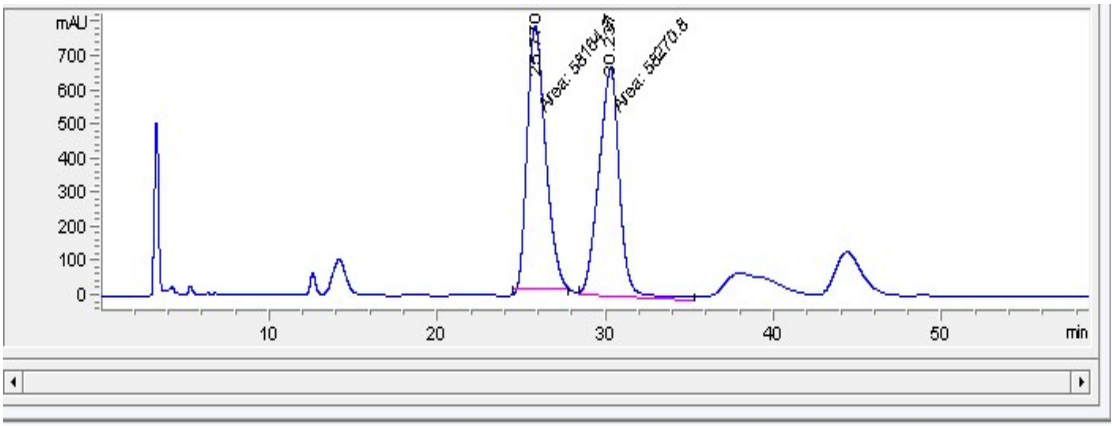
O
OEt
N
Ac
f1 (ppm)

HPLC of 3a'



#	Time	Area	Height	Width	Area%	Symmetry
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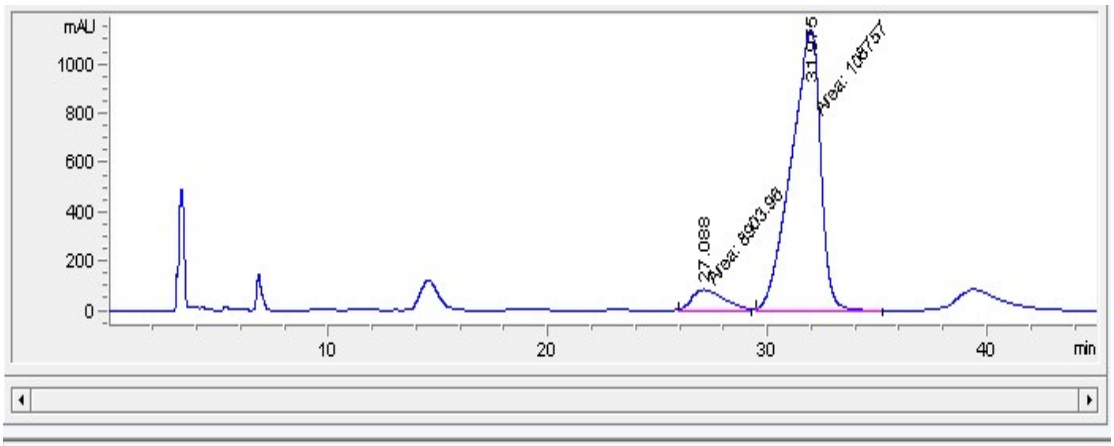
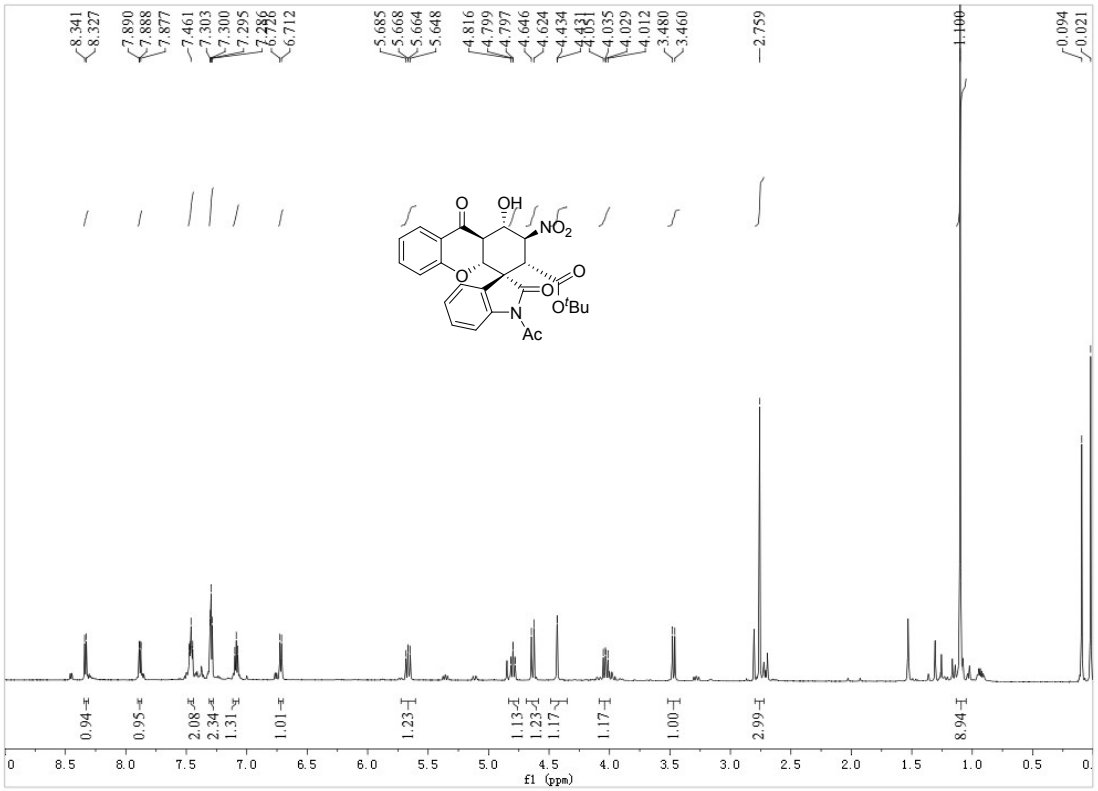


#	Time	Area	Height	Width	Area%	Symmetry
1	27.088	8904	86.3	1.7195	7.567	0.616
2	31.975	108757.1	1144.6	1.5836	92.433	1.984

^{1}H and ^{13}C NMR of 3a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7.877
7.461
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6.712
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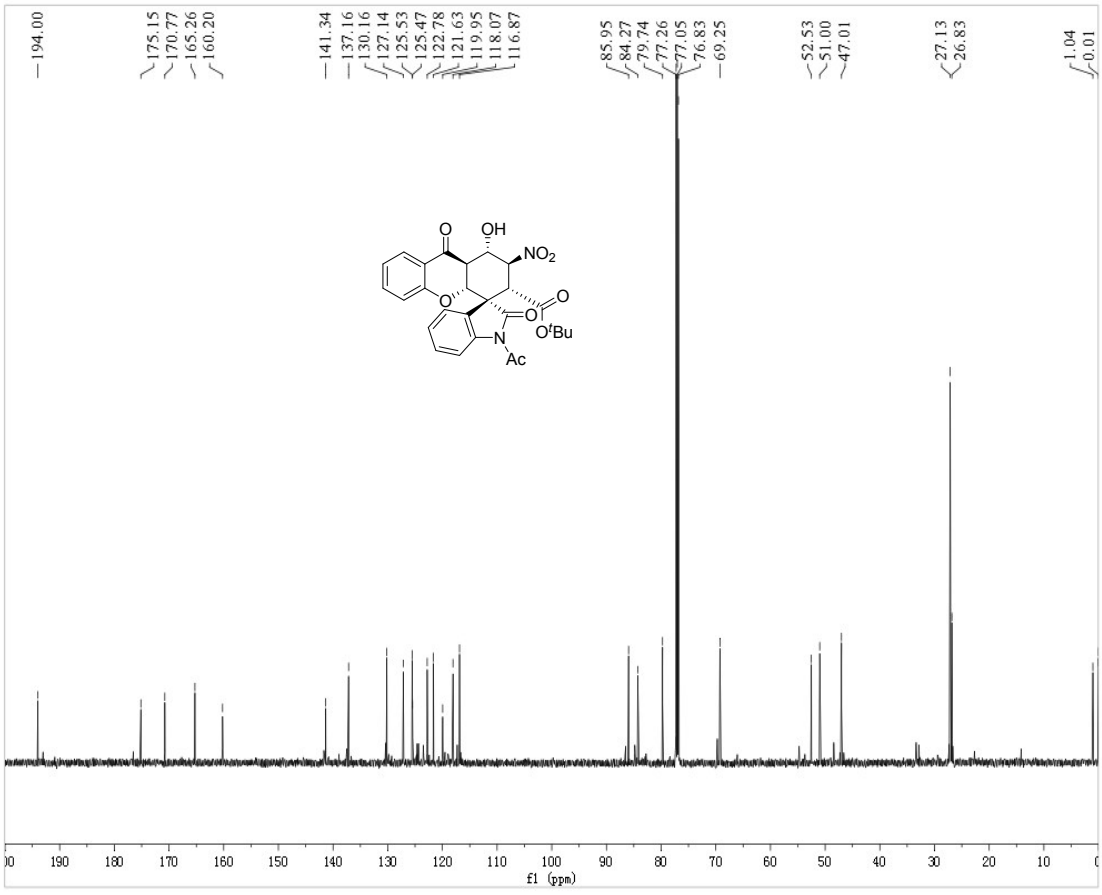
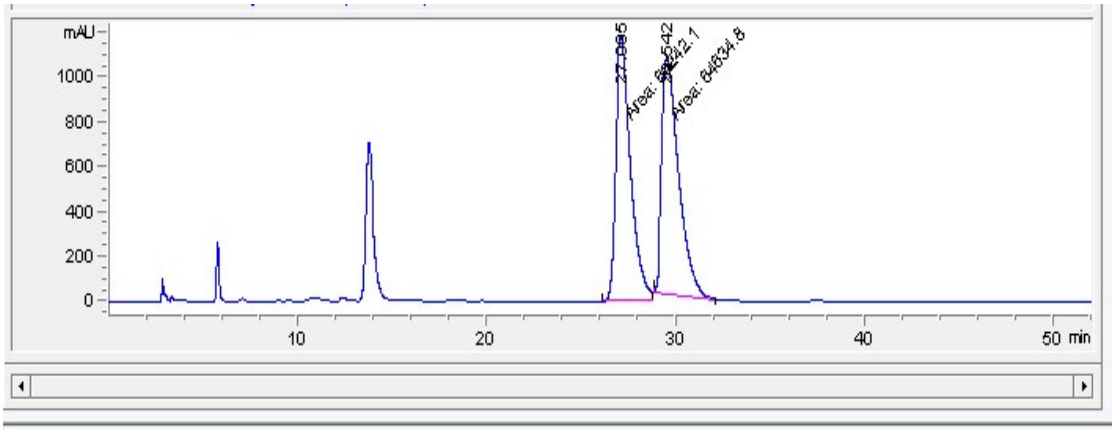
5.668
5.664
5.648
4.816
4.799
4.797
4.646
4.624
4.434
4.431
4.035
4.029
4.012
3.480
3.460
2.759
1.100
0.094
0.021
OH
NO2
O
O
O
O
tBu
N
Ac
0.94
0.95
2.08
2.34
1.31
1.01
1.23
1.13
1.23
1.17
1.17
1.00
2.99
8.94
f1 (ppm)


194.00
175.15
170.77
165.26
160.20
141.34
137.16
130.16
127.14
125.53
125.47
122.78
121.63
119.95
118.07
116.87
85.95
84.27
79.74
77.26
77.05
76.83
69.25
52.53
51.00
47.01
27.13
26.83
1.04
0.01
OH
NO2
O
O
O
O
tBu
N
Ac
f1 (ppm)

HPLC of 3a



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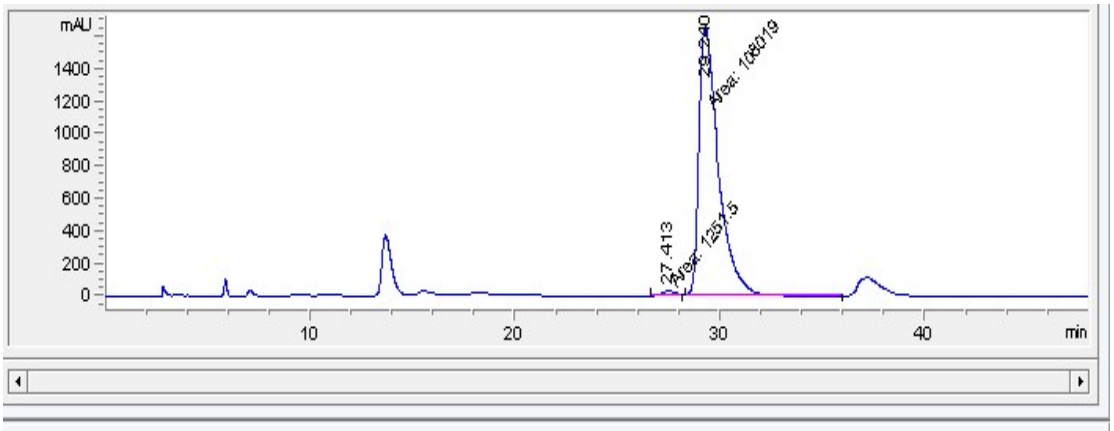
2	29.542	64634.8	1060.4	1.0159	49.766	0.461



#	Time	Area	Height	Width	Area%	Symmetry
1	27.413	1251.5	26.6	0.7836	1.145	0.897
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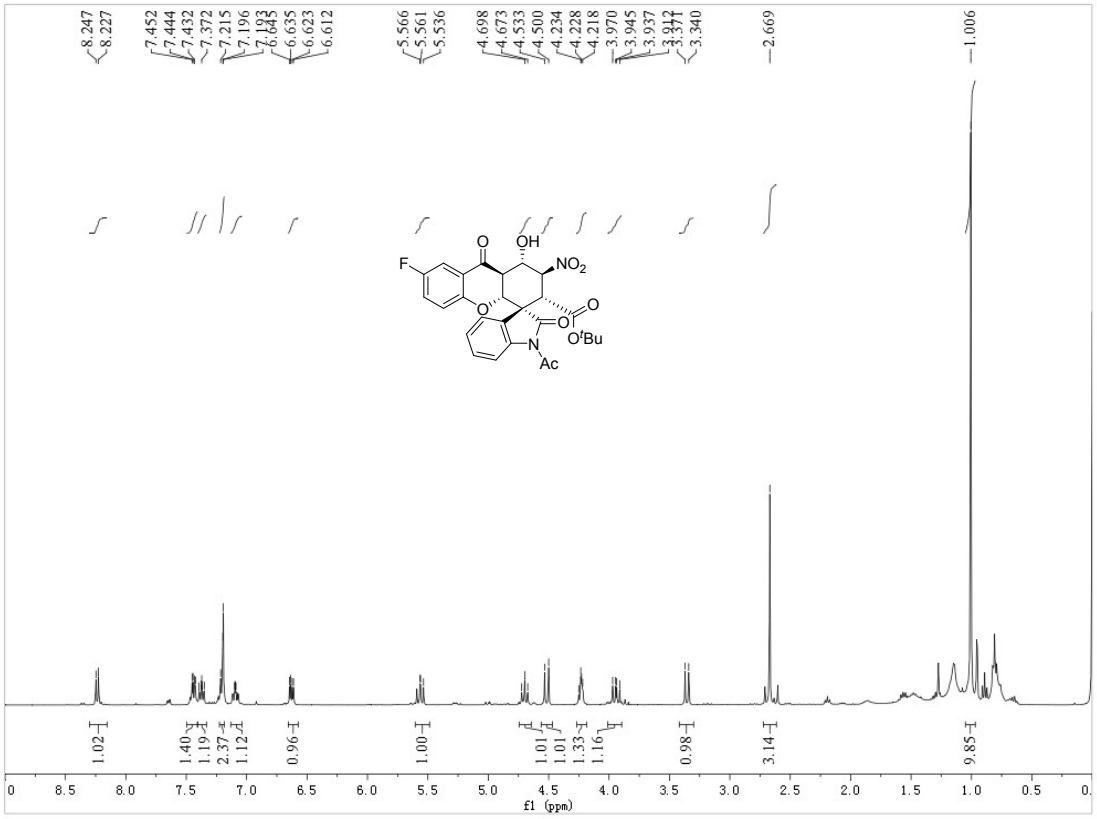
^{1}H and ^{13}C NMR of 3b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5.536
4.698
4.673
4.533
4.500
4.234
4.228
4.218
3.970
3.945
3.937
3.340
2.669
1.006
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F
NO2
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O
O
OtBu
N
Ac
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1.19
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1.01
1.01
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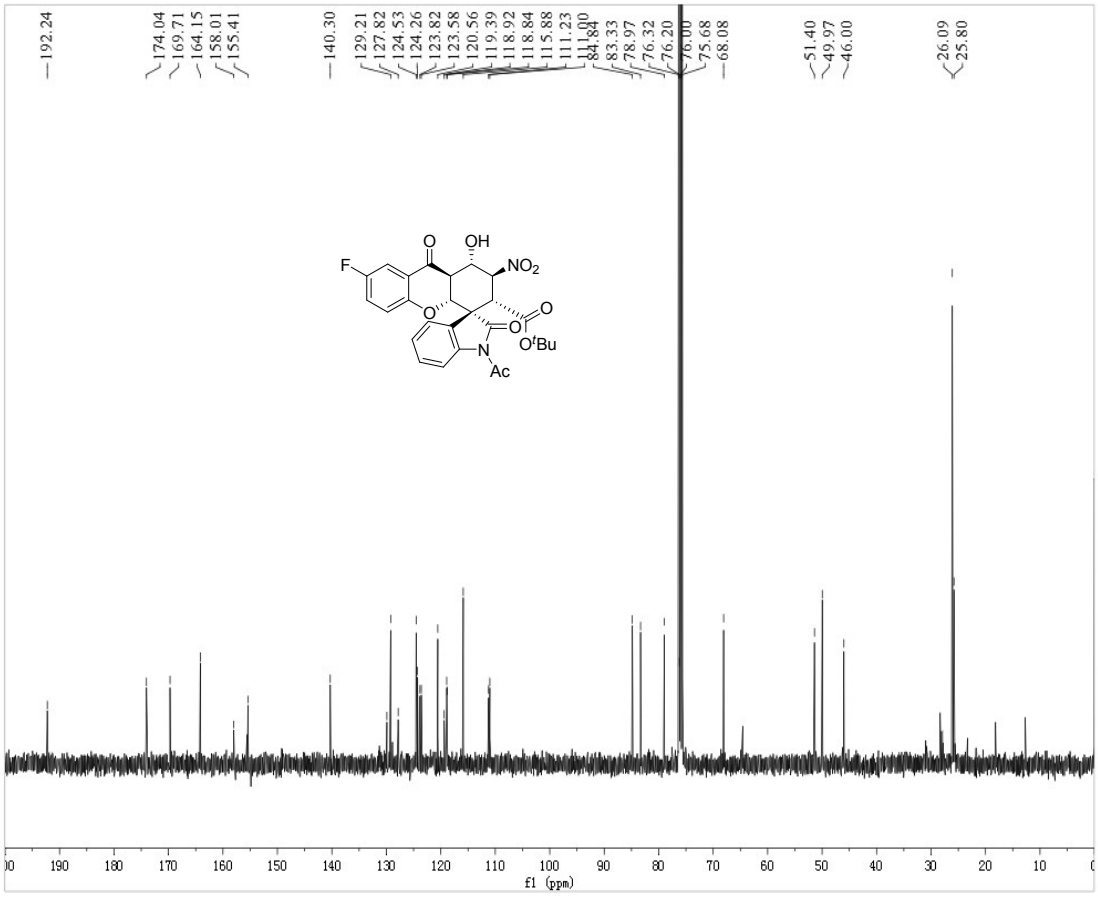
9.85
f1 (ppm)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155.41
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129.21
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124.53
124.26
123.82
123.58
120.56
119.39
118.92
118.84
115.88
111.23
84.84
83.33
78.97
76.32
76.20
76.00
75.68
68.08
51.40
49.97
46.00
26.09
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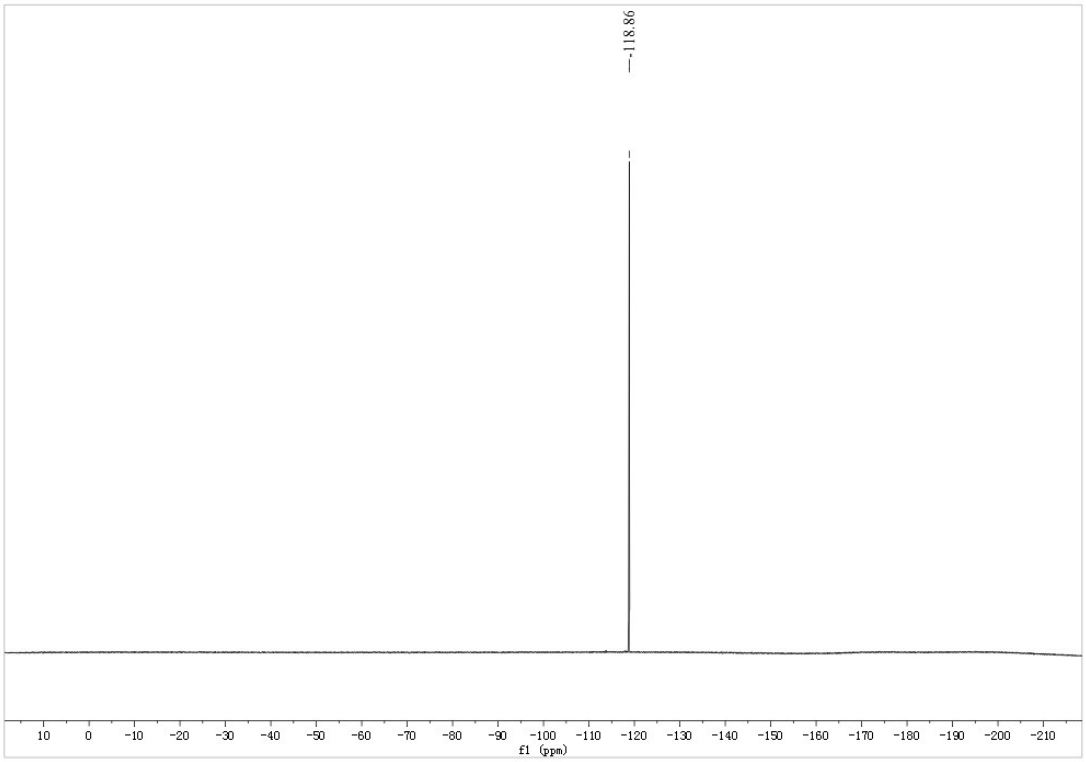
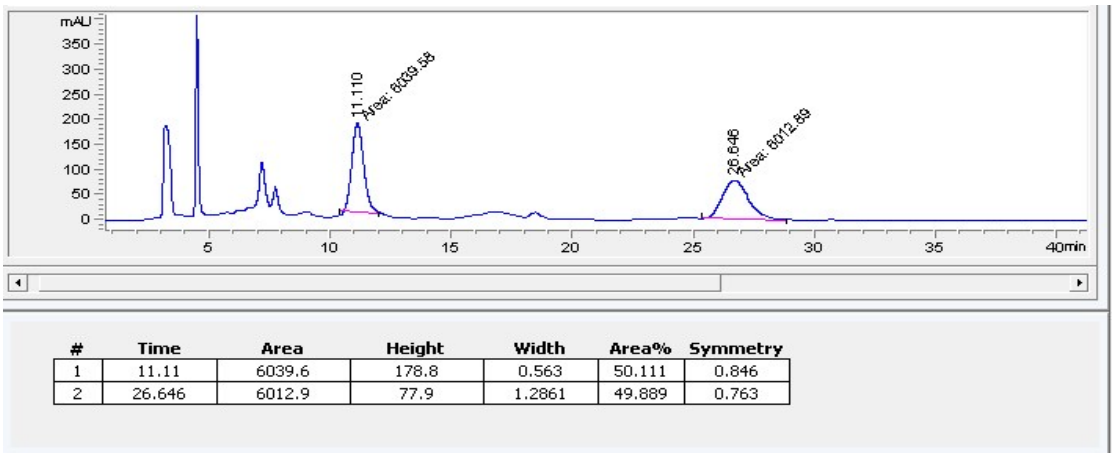
O
OtBu
N
Ac
f1 (ppm)

^{19}F NMR of 3b



HPLC of 3b



#	Time	Area	Height	Width	Area%	Symmetry
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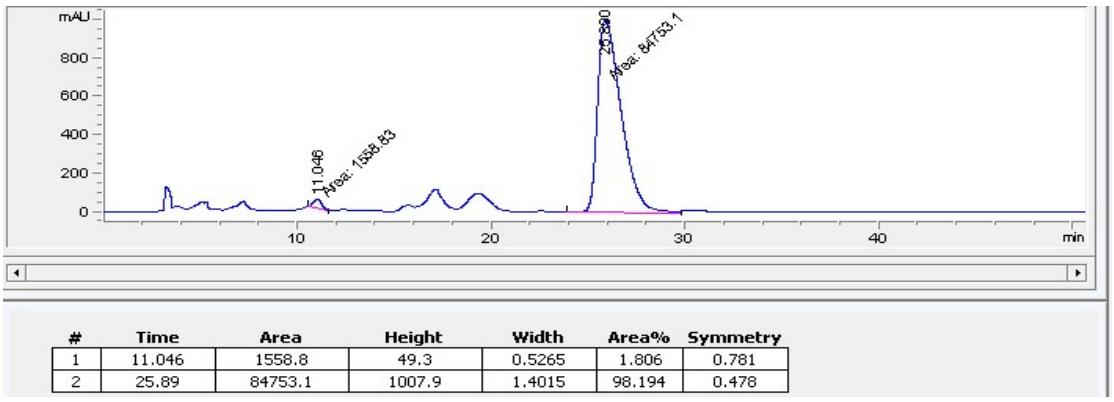

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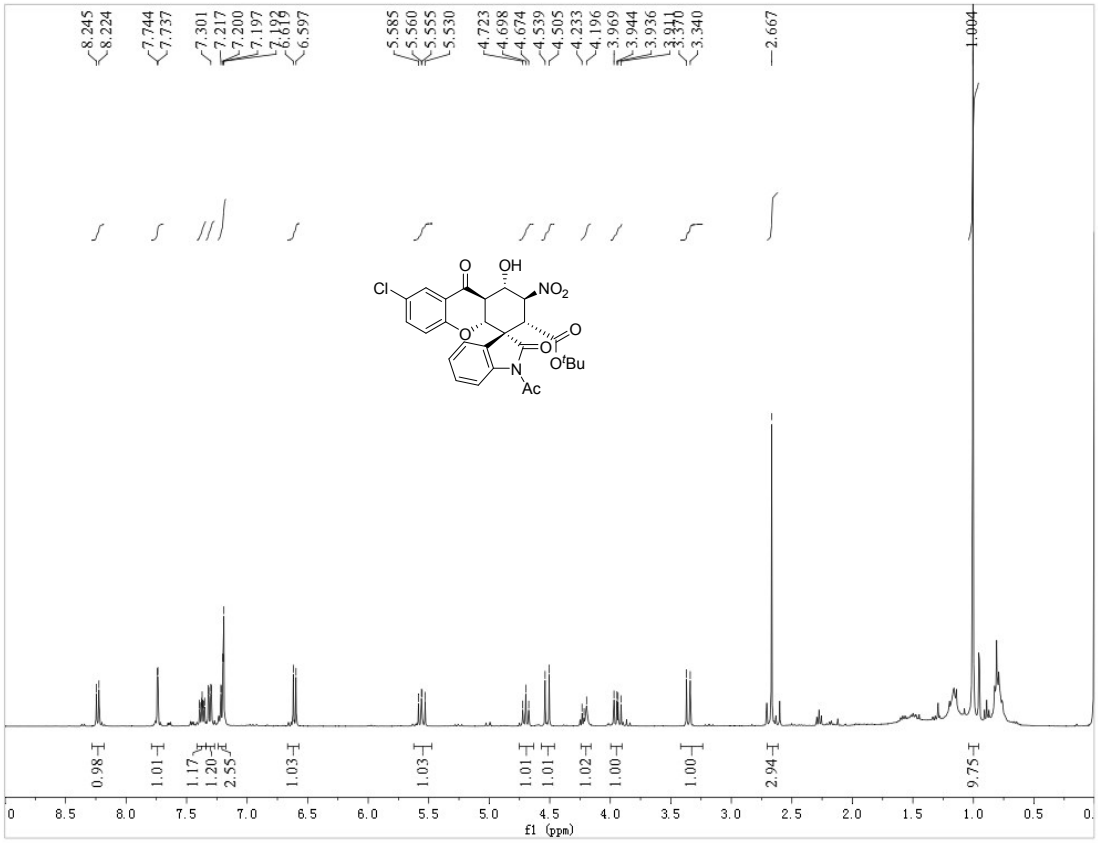
^{1}H and ^{13}C NMR of 3c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5.555
5.530
4.723
4.698
4.674
4.539
4.505
4.233
4.196
3.969
3.944
3.936
3.911
3.370
3.340
2.667
1.004
0.98
1.01
1.17
1.20
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1.03
1.01
1.01
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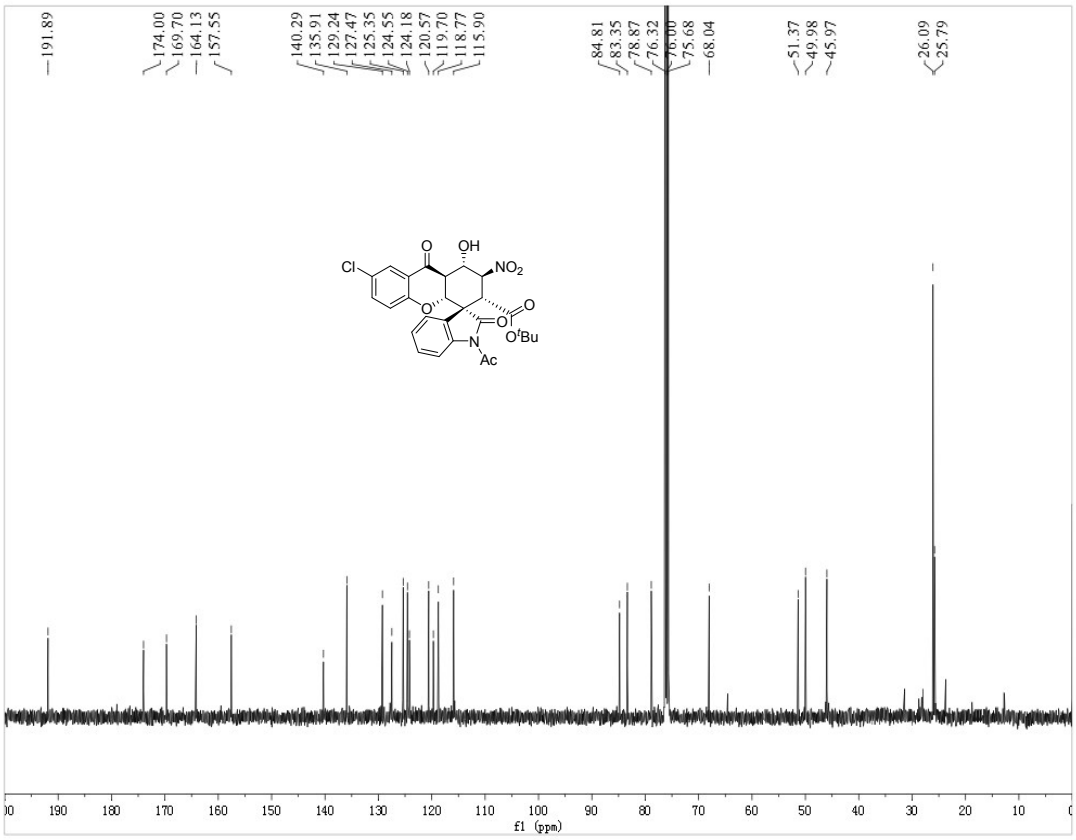
1.00
2.94
9.75
f1 (ppm)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119.70
118.77
115.90
84.81
83.35
78.87
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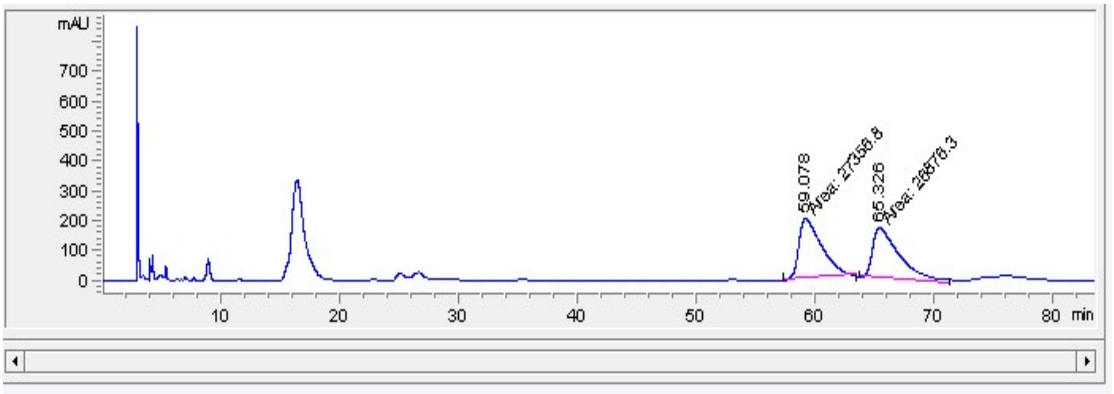
51.37
49.98
45.97
26.09
25.79
f1 (ppm)

HPLC of 3c



#	Time	Area	Height	Width	Area%	Symmetry
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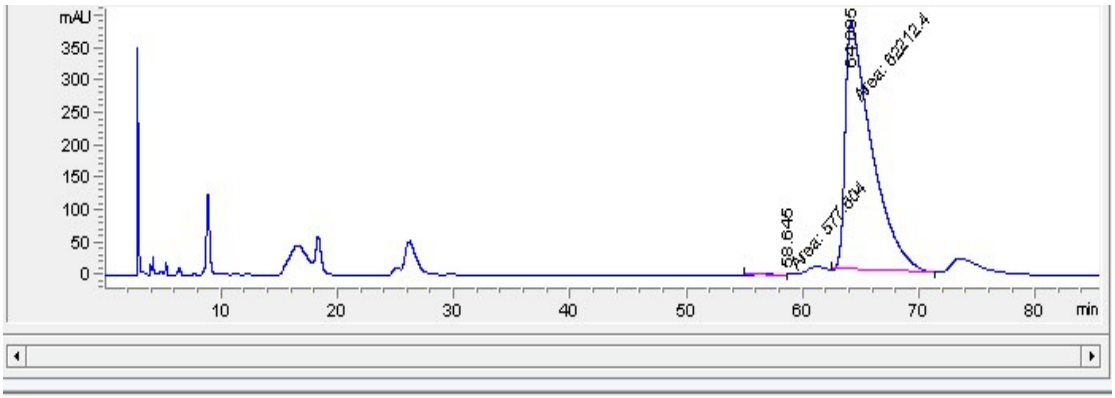
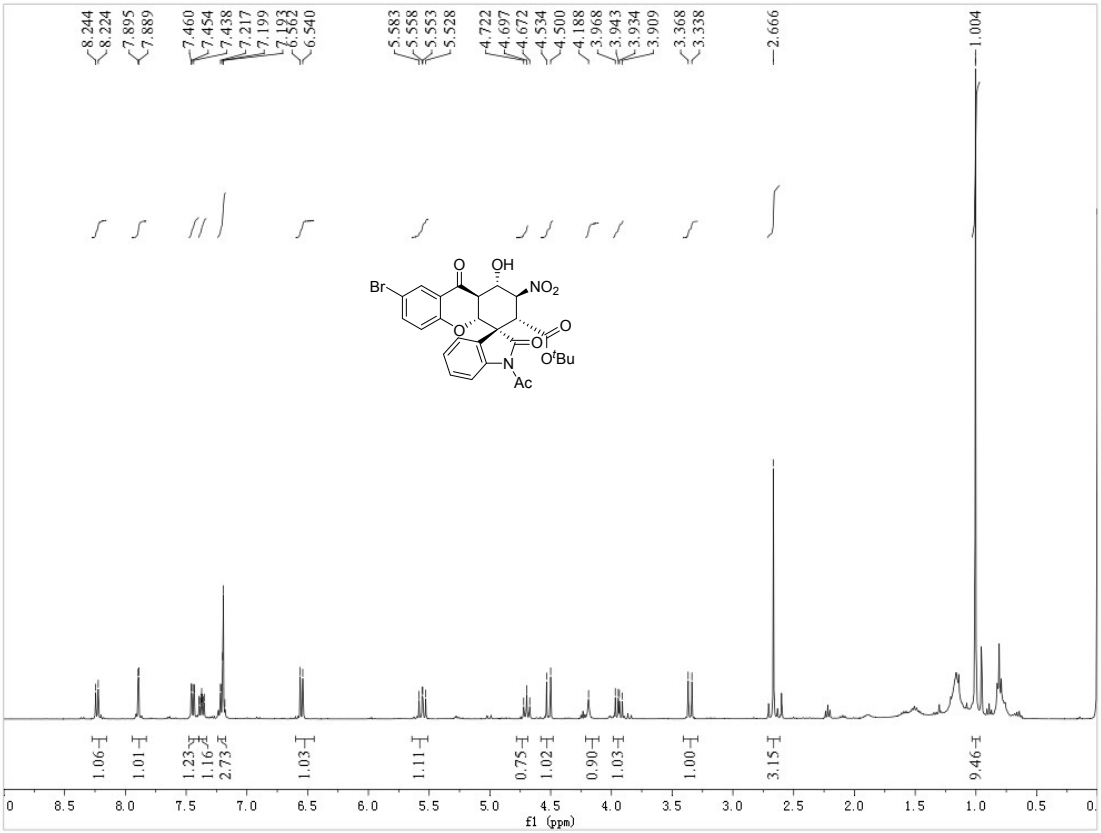


#	Time	Area	Height	Width	Area%	Symmetry
1	58.645	577.6	4.1	2.3253	0.920	0.343
2	64.095	62212.4	383.3	2.7049	99.080	0.288

^{1}H and ^{13}C NMR of 3d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7.460
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7.217
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7.193
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3.909
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3.338
2.666
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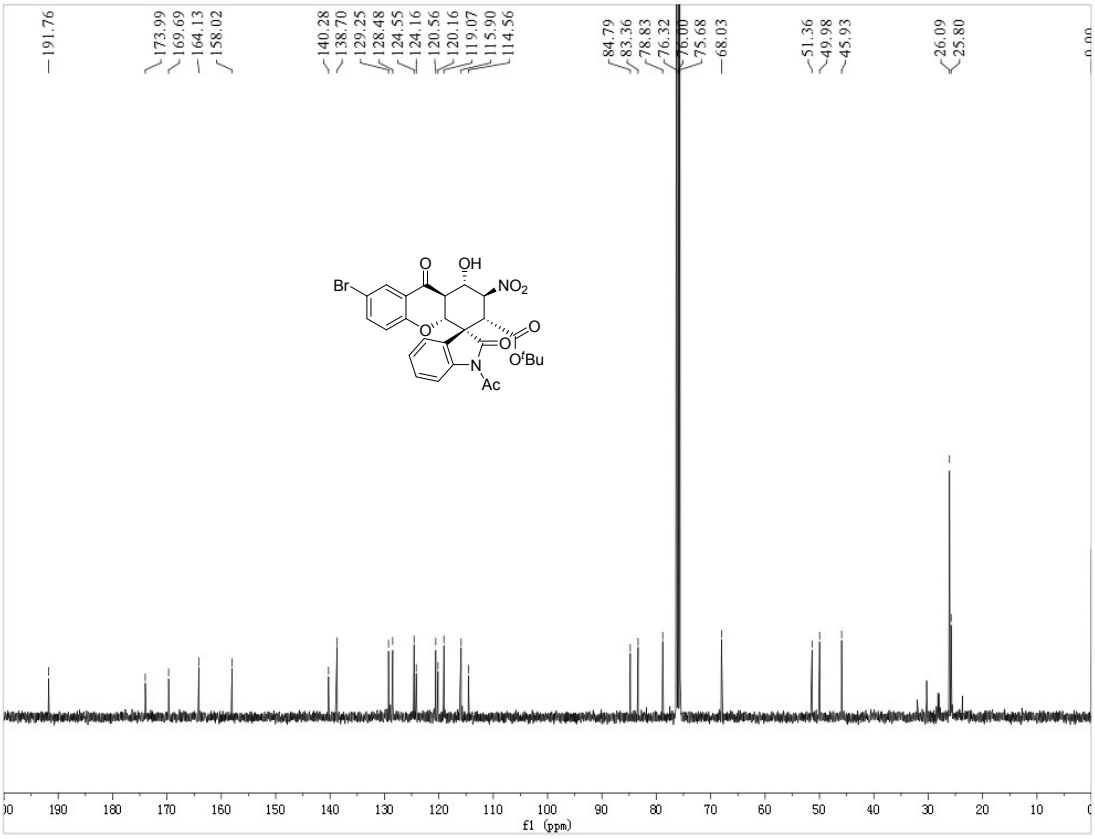
NO2
O
O
O
O
tBu
N
Ac
1.06
1.01
1.23
1.16
2.73
1.03
1.11
0.75
1.02
0.90
1.03
1.00
3.15
9.46
f1 (ppm)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164.13
158.02
140.28
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129.25
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124.55
124.16
120.56
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114.56
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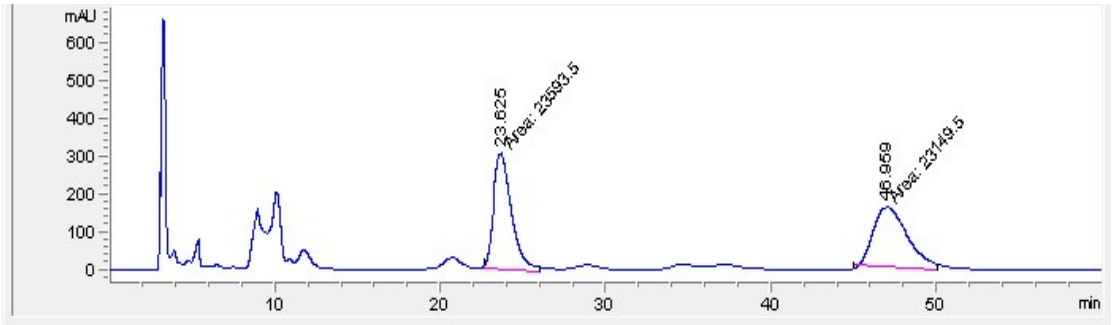
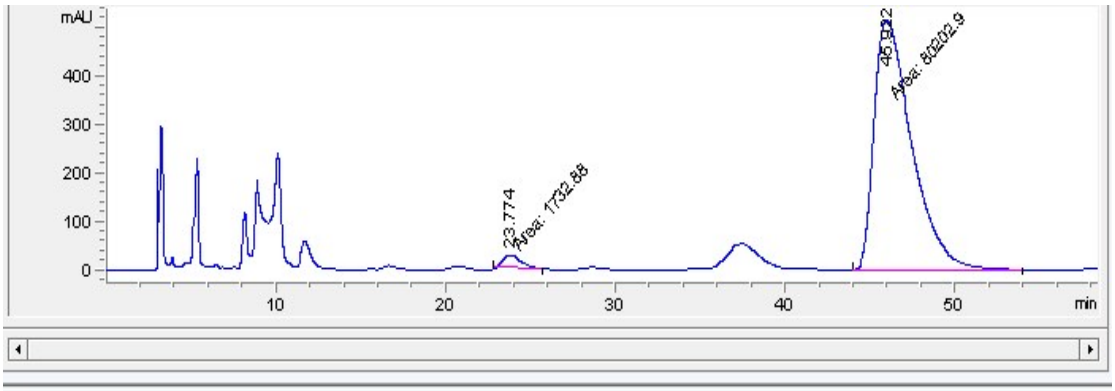
83.36
78.83
76.32
76.00
75.68
68.03
51.36
49.98
45.93
26.09
25.80
Br
O
OH
NO2
O
O
O
O
tBu
N
Ac
f1 (ppm)

HPLC of 3d

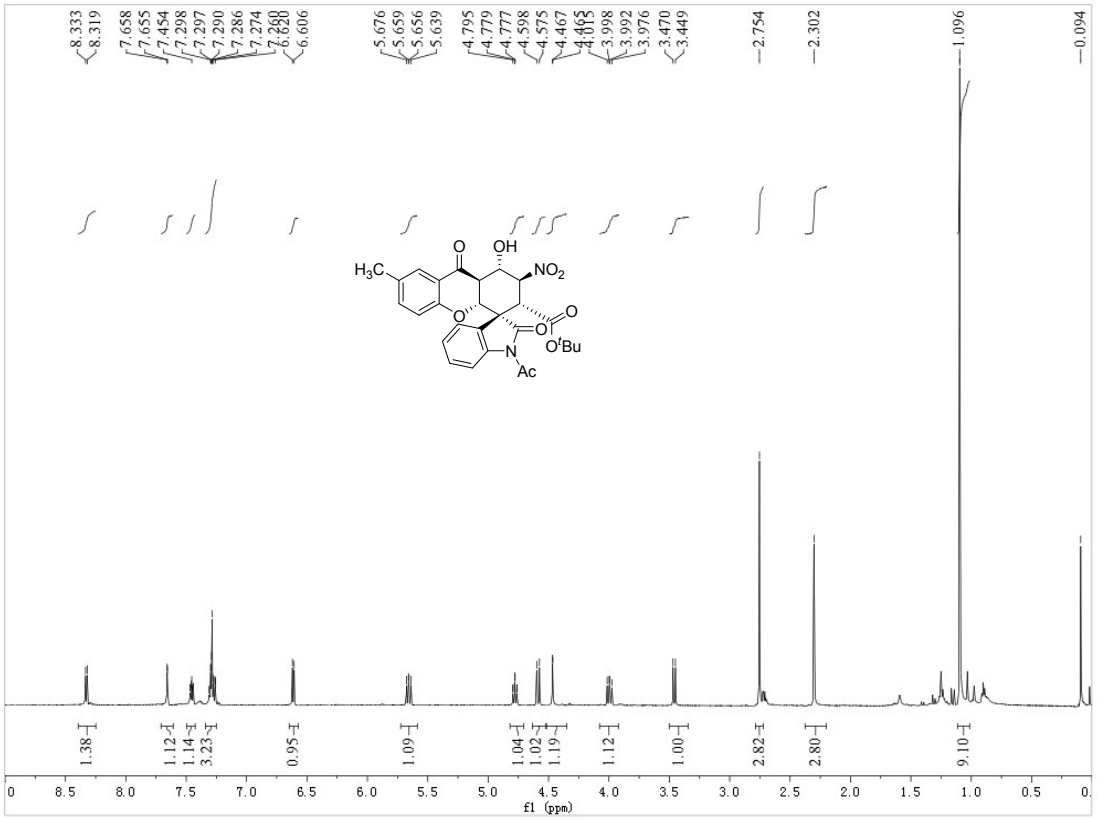


#	Time	Area	Height	Width	Area%	Symmetry
1	23.625	23593.5	306.9	1.2814	50.475	0.664
2	46.959	23149.5	160.1	2.4099	49.525	0.607



#	Time	Area	Height	Width	Area%	Symmetry
1	23.774	1732.9	25	1.154	2.115	0.641
2	45.922	80202.9	518.3	2.5792	97.885	0.466

^{1}H and ^{13}C NMR of 3e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7.655
7.454
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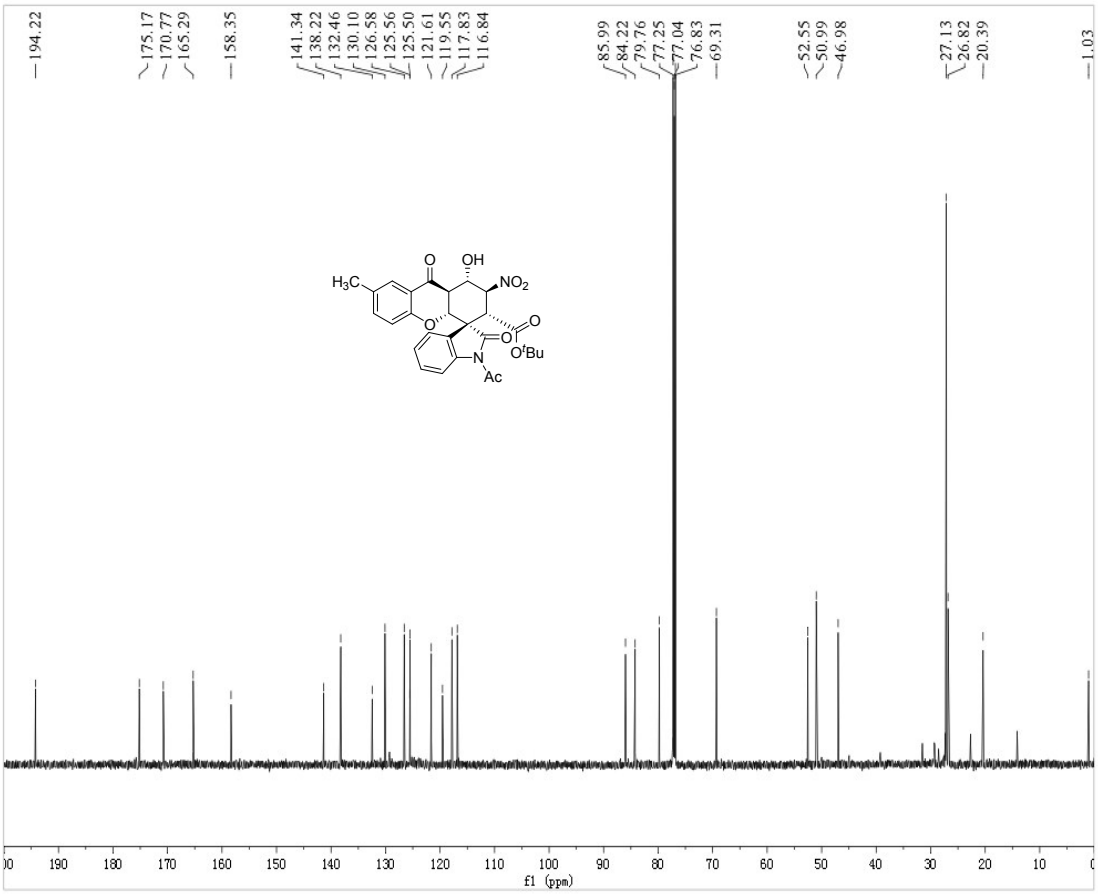
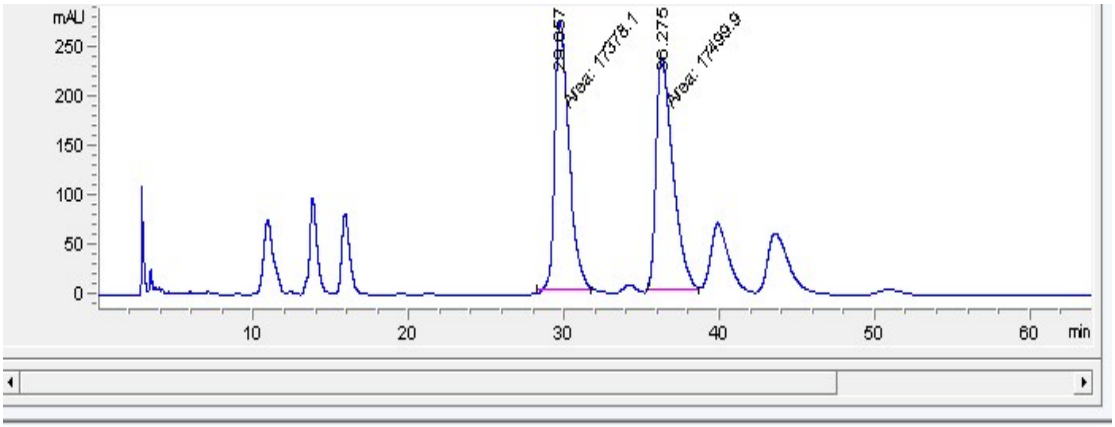
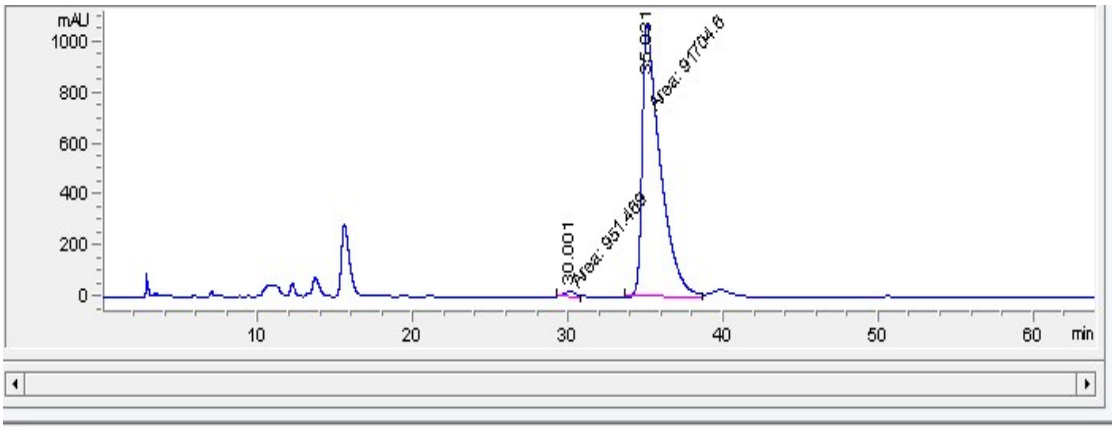
7.297
7.290
7.286
7.274
6.620
6.606
5.676
5.659
5.656
5.639
4.795
4.779
4.777
4.598
4.575
4.467
3.998
3.992
3.976
3.470
3.449
2.754
2.302
1.096
0.094
1.38
1.12
1.14
3.23
0.95
1.09
1.04
1.02
1.19
1.12
1.00
2.82
2.80
9.10
f1 (ppm)


194.22
175.17
170.77
165.29
158.35
141.34
138.22
132.46
130.10
126.58
125.56
125.50
121.61
119.55
117.83
116.84
85.99
84.22
79.76
77.25
77.04
76.83
69.31
52.55
50.99
46.98
27.13
26.82
20.39
1.03
f1 (ppm)

HPLC of 3e

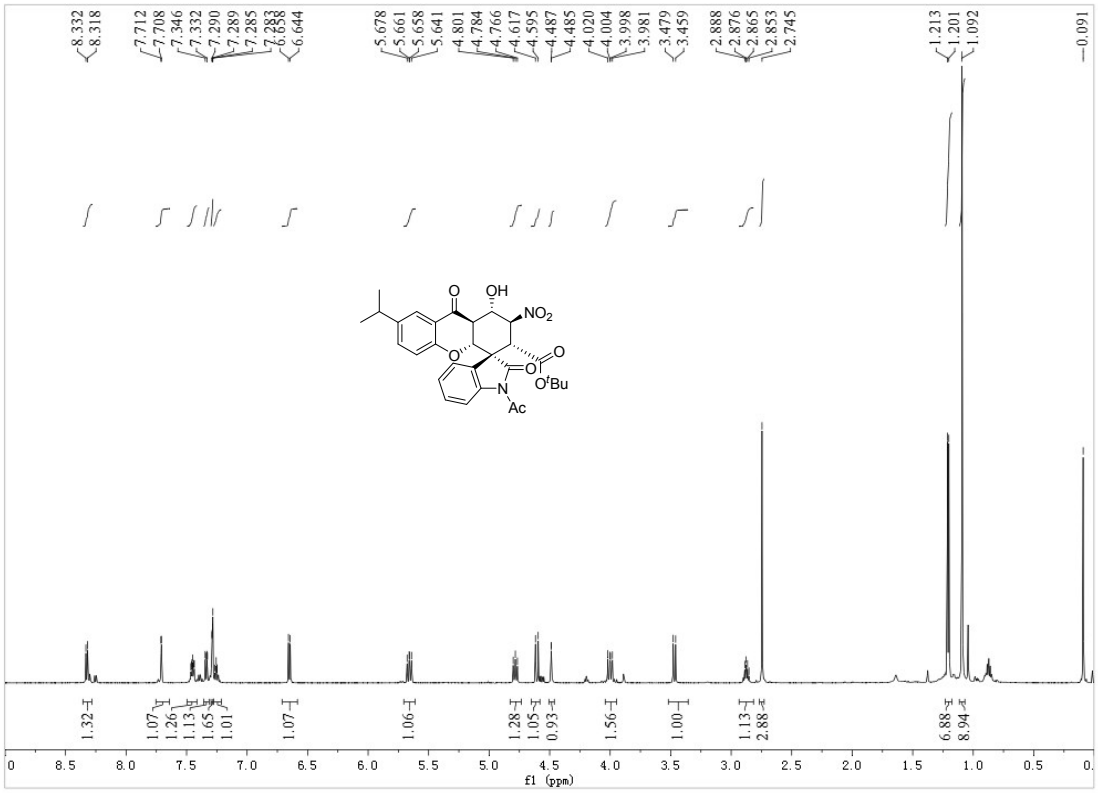


#	Time	Area	Height	Width	Area%	Symmetry
1	29.657	17378.1	271.7	1.0662	49.825	0.52
2	36.275	17499.9	235	1.2409	50.175	0.484



#	Time	Area	Height	Width	Area%	Symmetry
1	30.001	951.5	17.6	0.8998	1.027	0.542
2	35.031	91704.6	1072.7	1.4248	98.973	0.349

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


8.332
8.318
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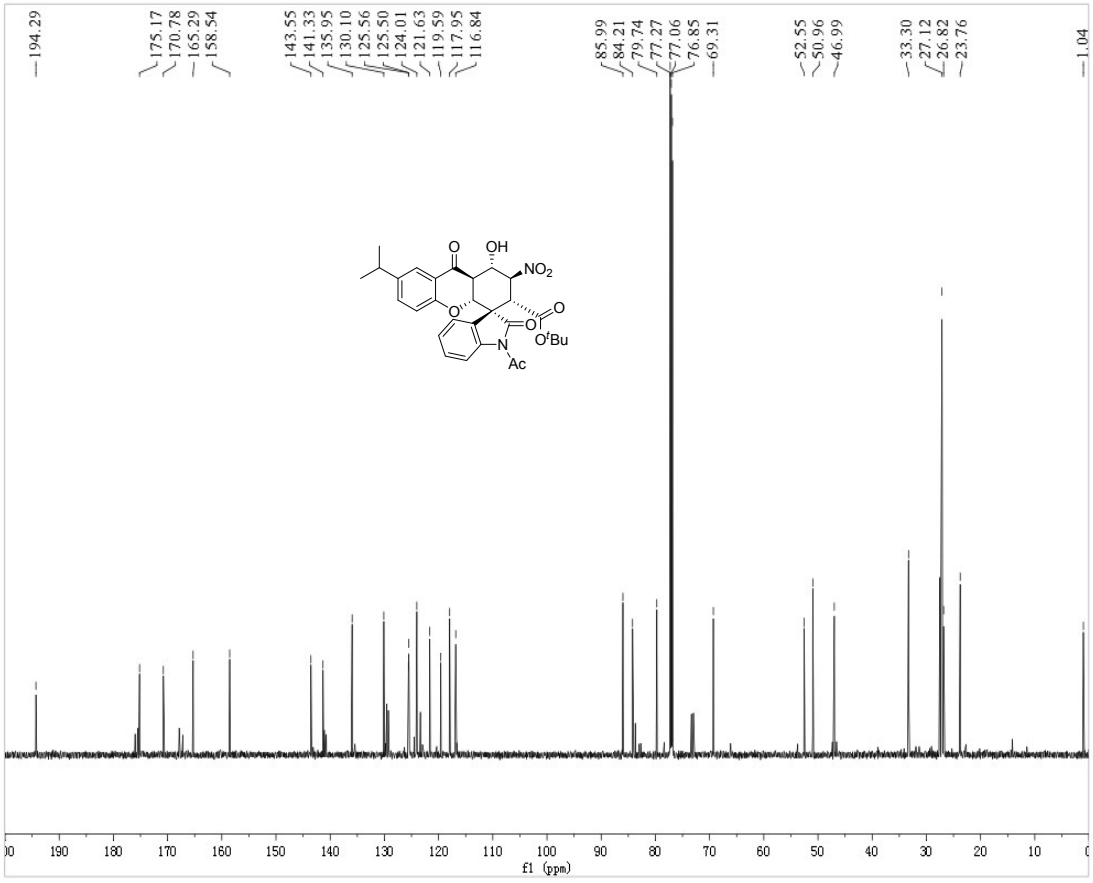
7.708
7.346
7.332
7.290
7.289
7.285
6.644
5.678
5.661
5.658
5.641
4.801
4.784
4.766
4.617
4.595
4.487
4.485
4.020
4.004
3.998
3.981
3.479
3.459
2.888
2.876
2.865
2.853
2.745
1.213
1.201
1.092
0.091
1.32
1.07
1.26
1.13
1.65
1.01
1.07
1.06
1.28
1.05
0.93
1.56
1.00
1.13
2.88
6.88
8.94
f1 (ppm)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158.54
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125.50
124.01
121.63
119.59
117.95
116.84
85.99
84.21
79.74
77.27
77.06
76.85
69.31
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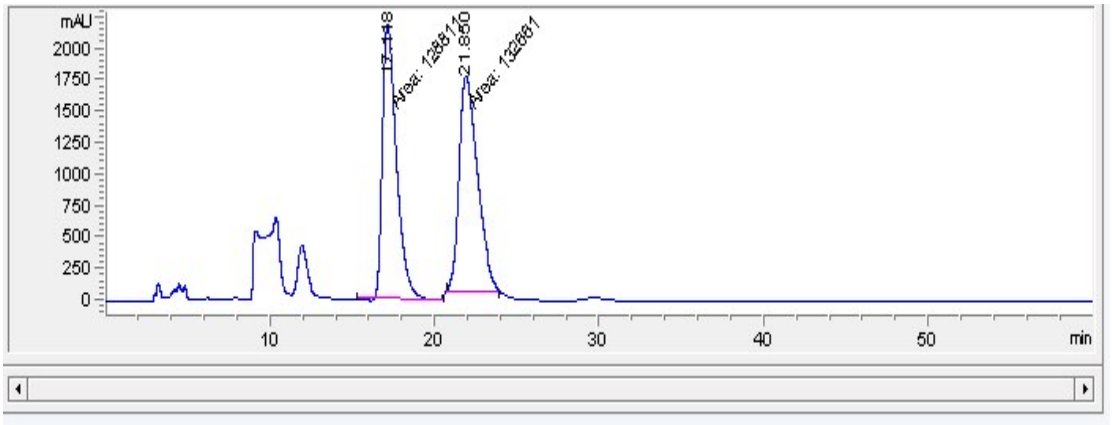
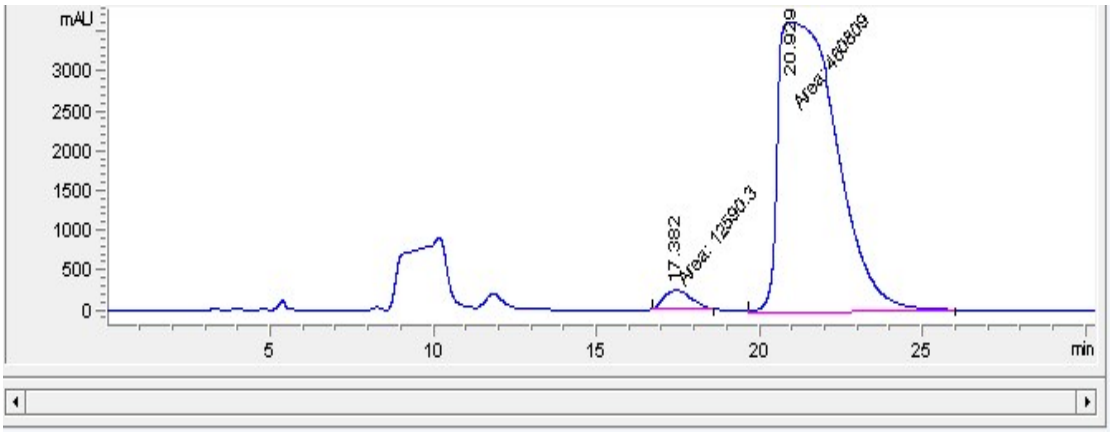
50.96
46.99
33.30
27.12
26.82
23.76
1.04
f1 (ppm)

HPLC of 3f

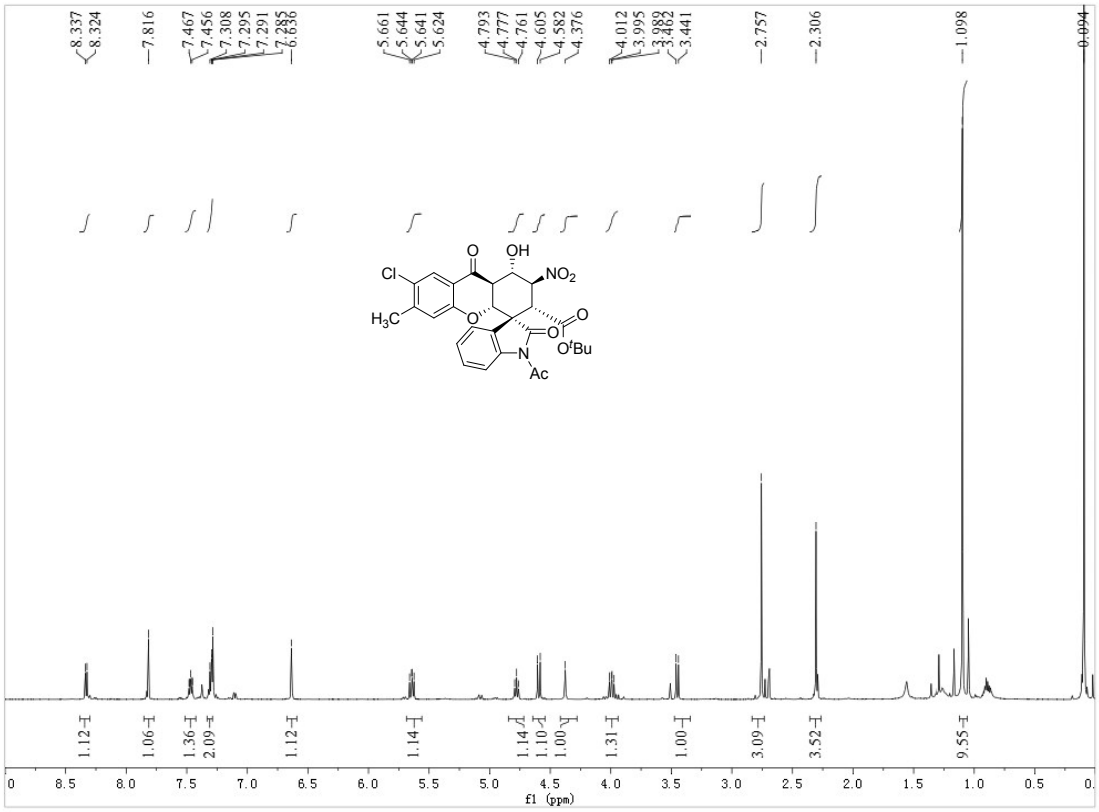


#	Time	Area	Height	Width	Area%	Symmetry
1	17.118	128811.2	2187.6	0.9814	49.264	0.542
2	21.85	132660.9	1722	1.284	50.736	0.577



#	Time	Area	Height	Width	Area%	Symmetry
1	17.382	12590.3	228.8	0.9172	2.660	0.709
2	20.929	460808.9	3641.3	2.1092	97.340	0.27

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


8.337
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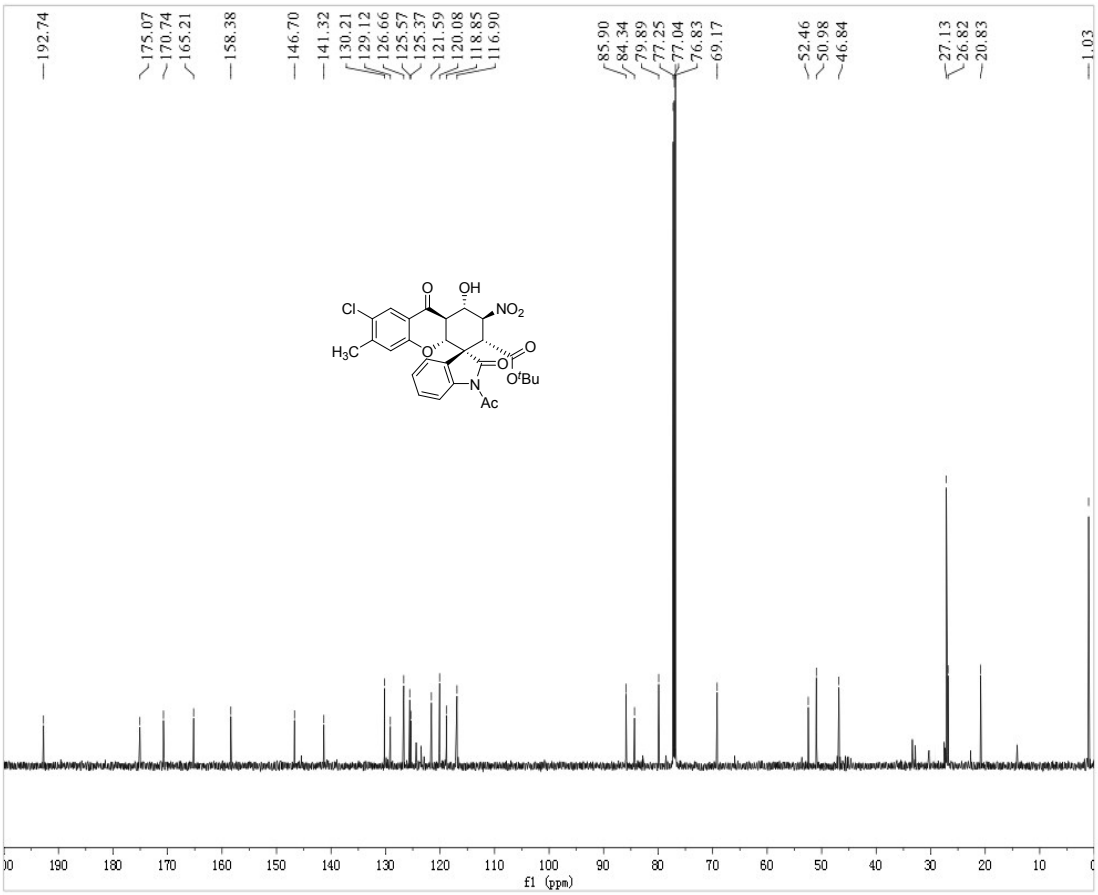
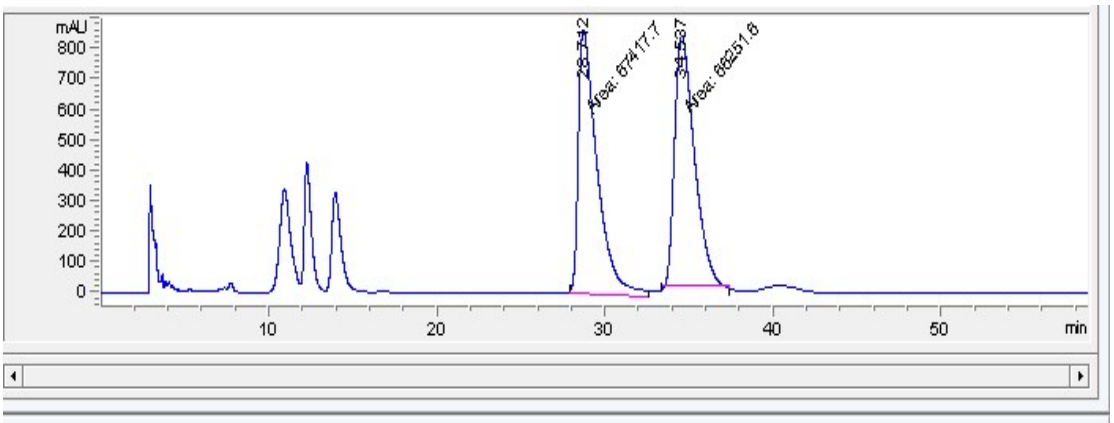
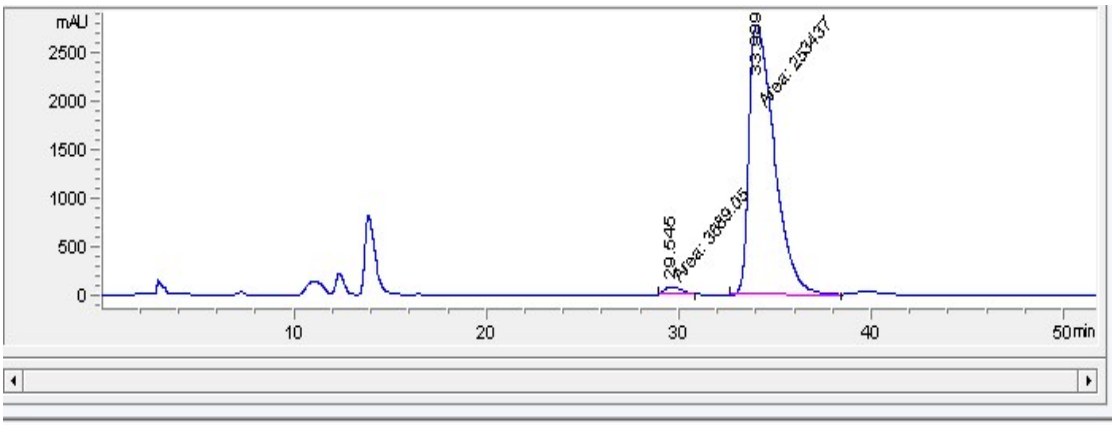
7.308
7.295
7.291
7.285
6.638
5.661
5.644
5.641
5.624
4.793
4.777
4.761
4.605
4.582
4.376
4.012
3.995
3.989
3.482
3.441
2.757
2.306
1.098
0.094
1.12
1.06
1.36
2.09
1.12
1.14
1.14
1.10
1.00
1.31
1.00
3.09
3.52
9.55
f1 (ppm)
Cl
OH
NO2
H3C
O
O
O
OtBu
N
Ac


192.74
175.07
170.74
165.21
158.38
146.70
141.32
130.21
129.12
126.66
125.57
125.37
121.59
120.08
118.85
116.90
85.90
84.34
79.89
77.25
77.04
76.83
69.17
52.46
50.98
46.84
27.13
26.82
20.83
1.03
f1 (ppm)
Cl
OH
NO2
H3C
O
O
O
OtBu
N
Ac

HPLC of 3g

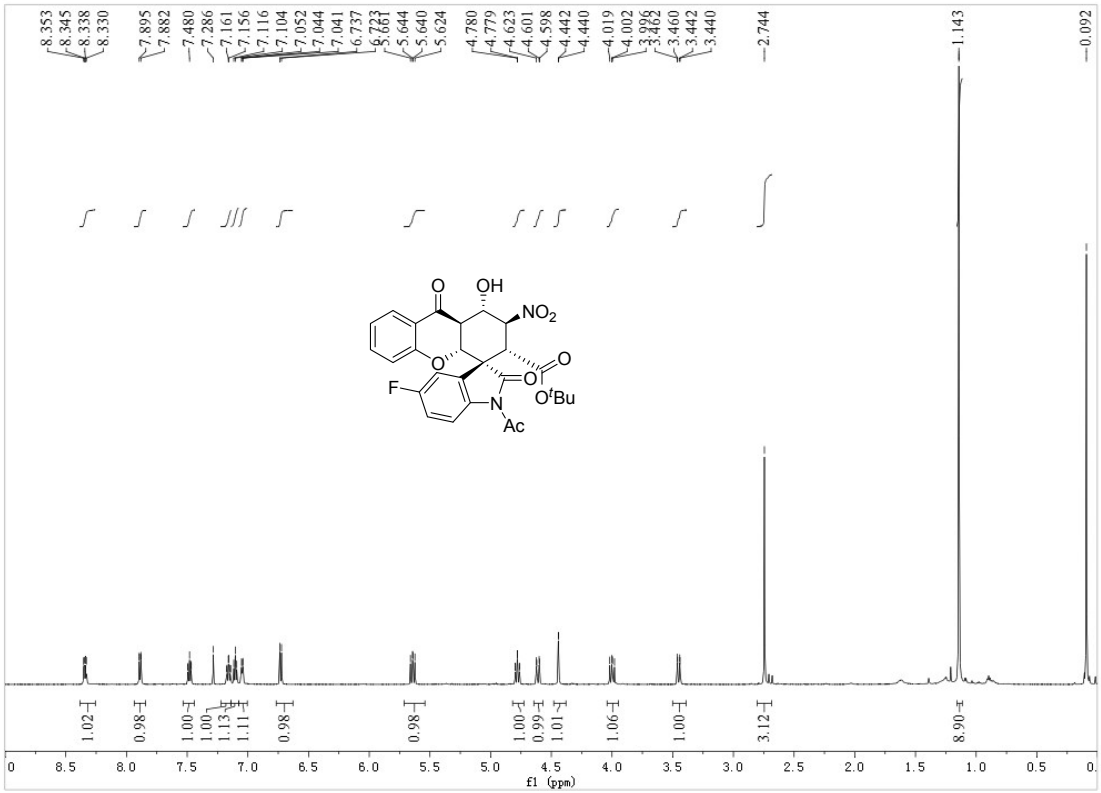


#	Time	Area	Height	Width	Area%	Symmetry
1	28.712	67417.7	864.3	1.3	50.436	0.357
2	34.537	66251.6	819.8	1.347	49.564	0.557



#	Time	Area	Height	Width	Area%	Symmetry
1	29.545	3689.1	68	0.9041	1.435	0.646
2	33.989	253436.8	2782.4	1.5181	98.565	0.401

^{1}H and ^{13}C NMR of 3h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7.286
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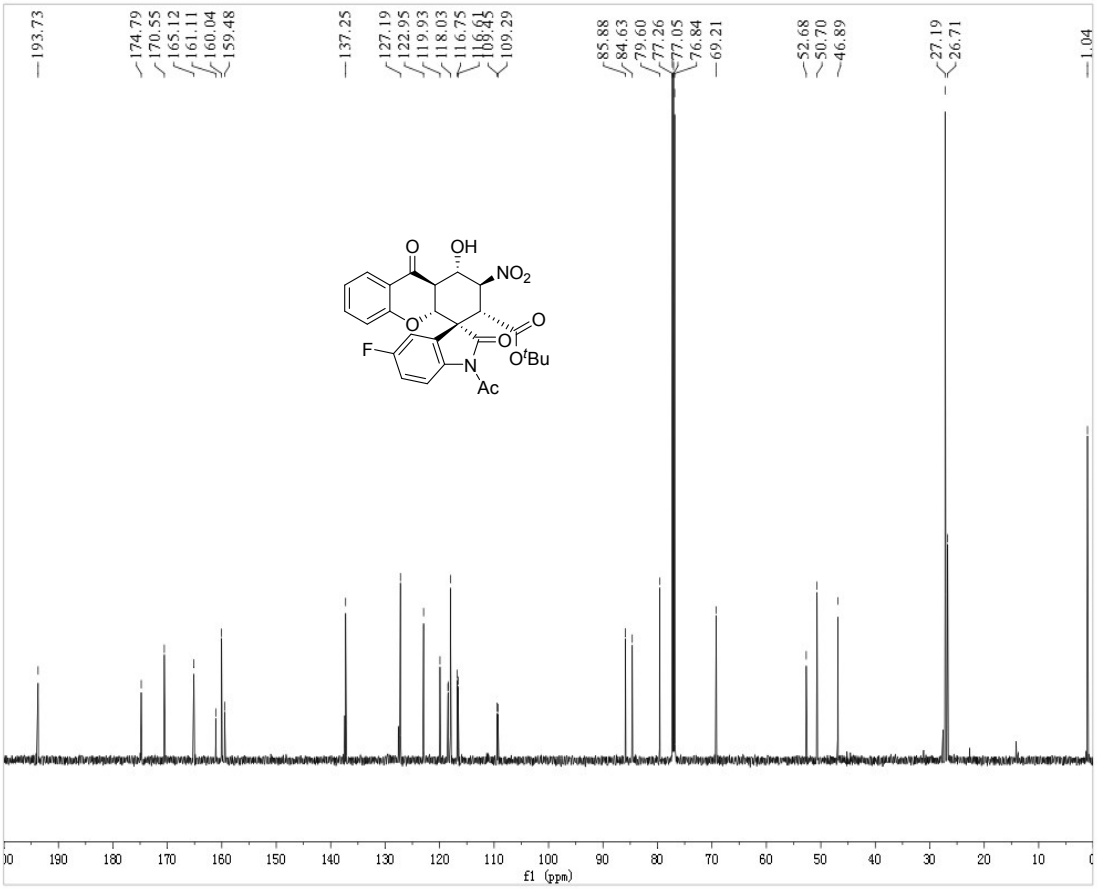
7.156
7.116
7.104
7.052
7.044
7.041
6.737
6.723
5.661
5.644
5.640
5.624
4.780
4.779
4.623
4.601
4.598
4.442
4.440
4.019
4.002
3.996
3.462
3.460
3.442
3.440
2.744
1.143
0.092
1.02
0.98
1.00
1.00
1.13
1.11
0.98
0.98
1.00
0.99
1.01
1.06
1.00
3.12
8.90
f1 (ppm)


193.73
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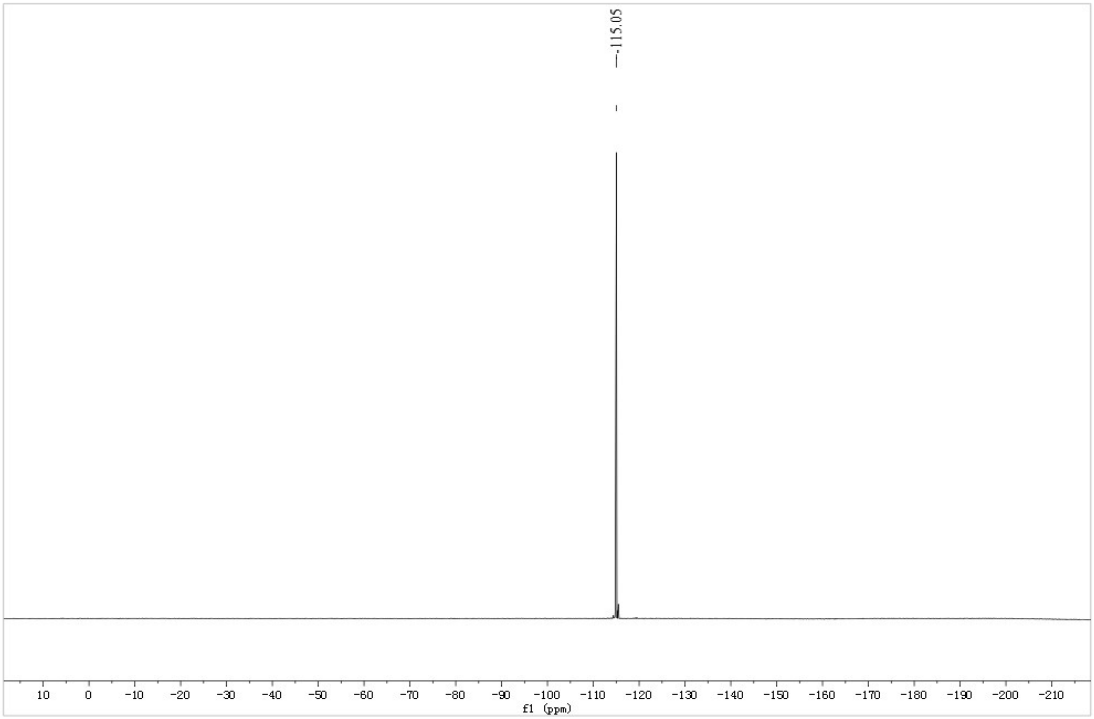
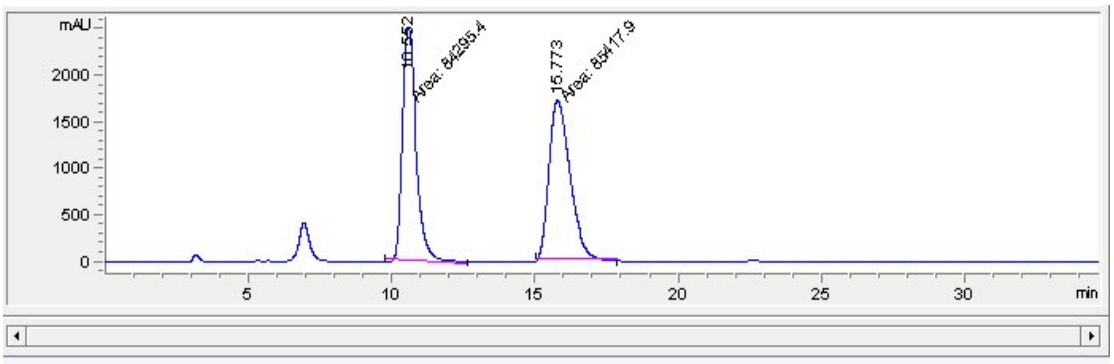
170.55
165.12
161.11
160.04
159.48
137.25
127.19
122.95
119.93
118.03
116.75
109.29
85.88
84.63
79.60
77.26
77.05
76.84
69.21
52.68
50.70
46.89
27.19
26.71
1.04
f1 (ppm)

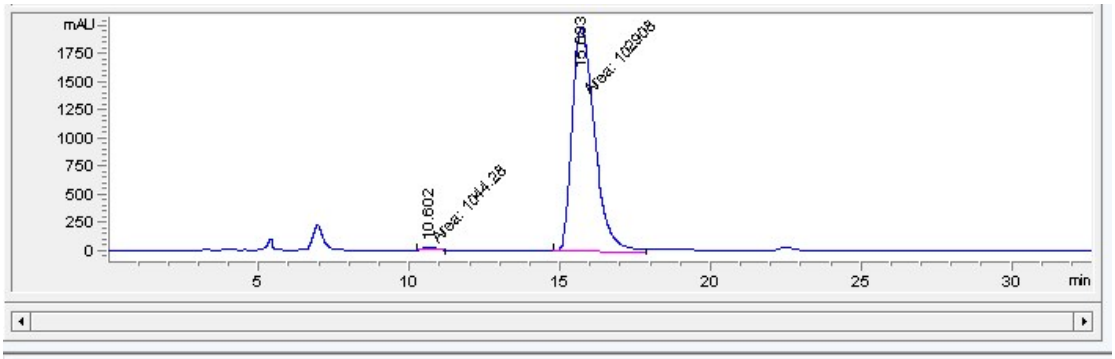
^{19}F NMR of 3h



HPLC of 3h

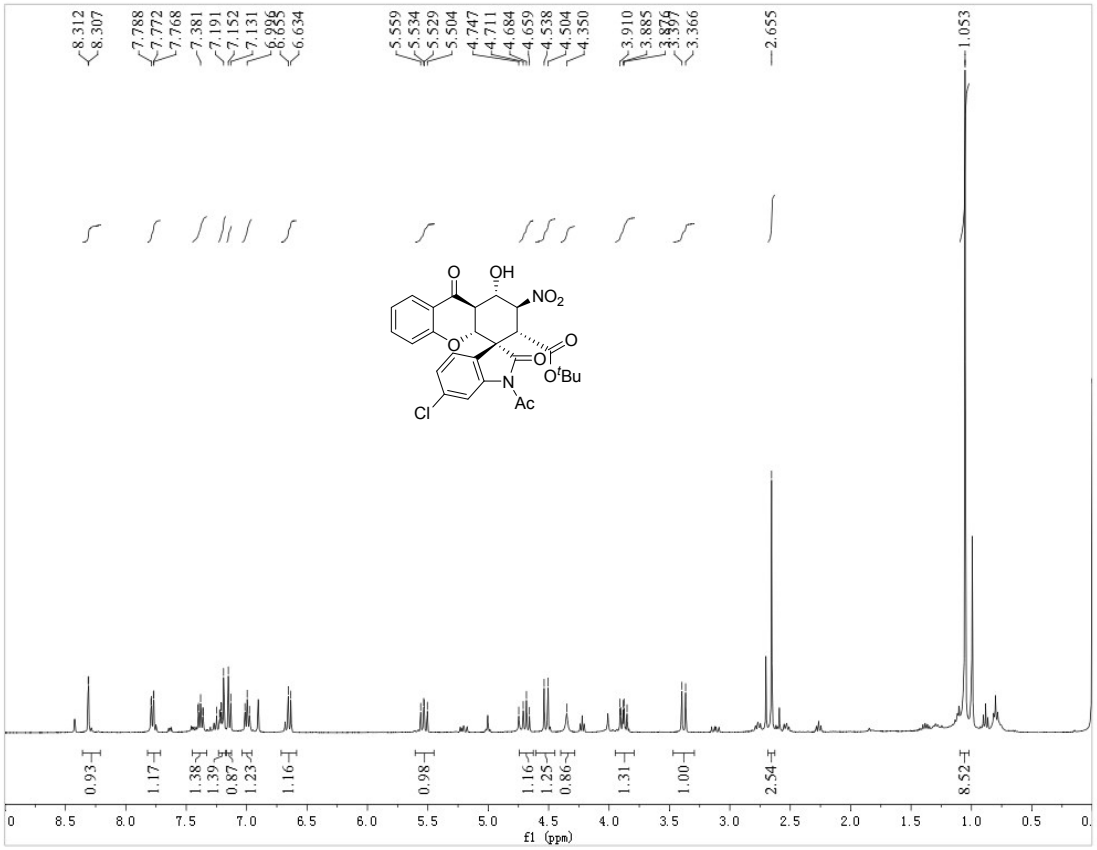


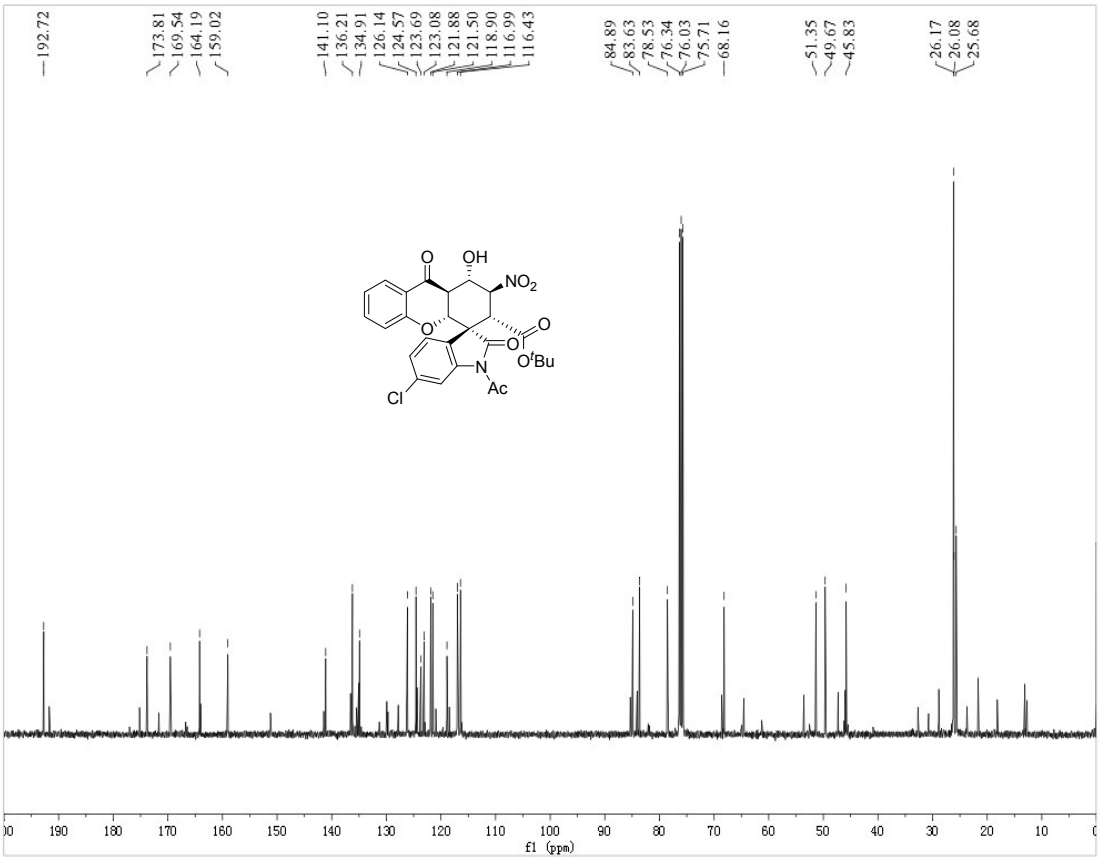
#	Time	Area	Height	Width	Area%	Symmetry
1	10.552	84295.4	2496.8	0.5627	49.669	0.668
2	15.773	85417.9	1720.5	0.8274	50.331	0.661



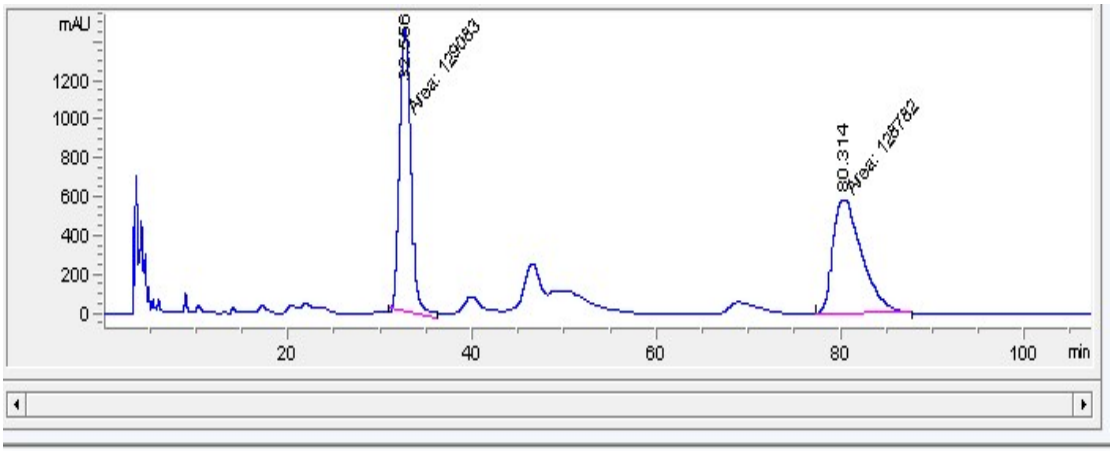
#	Time	Area	Height	Width	Area%	Symmetry
1	10.602	1044.3	32.6	0.5345	1.005	0.723
2	15.683	102907.8	2003	0.8563	98.995	0.633

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

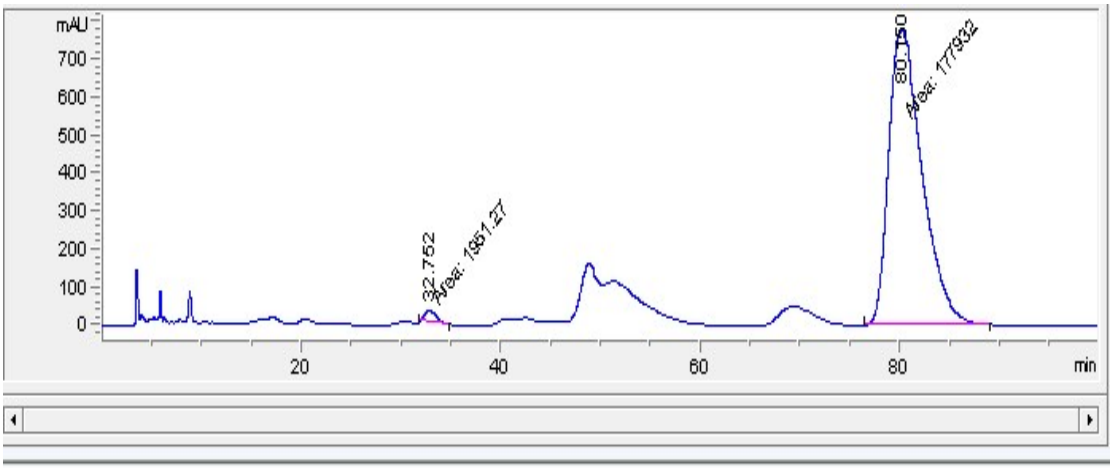




HPLC of 3i

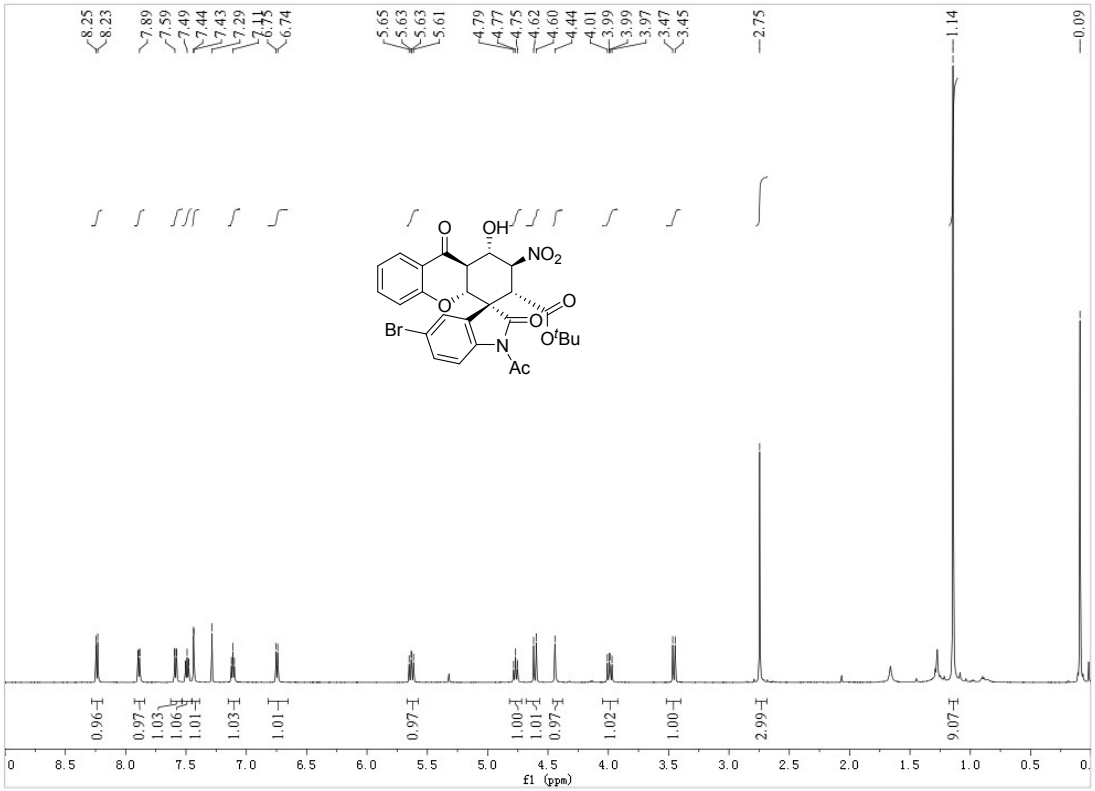


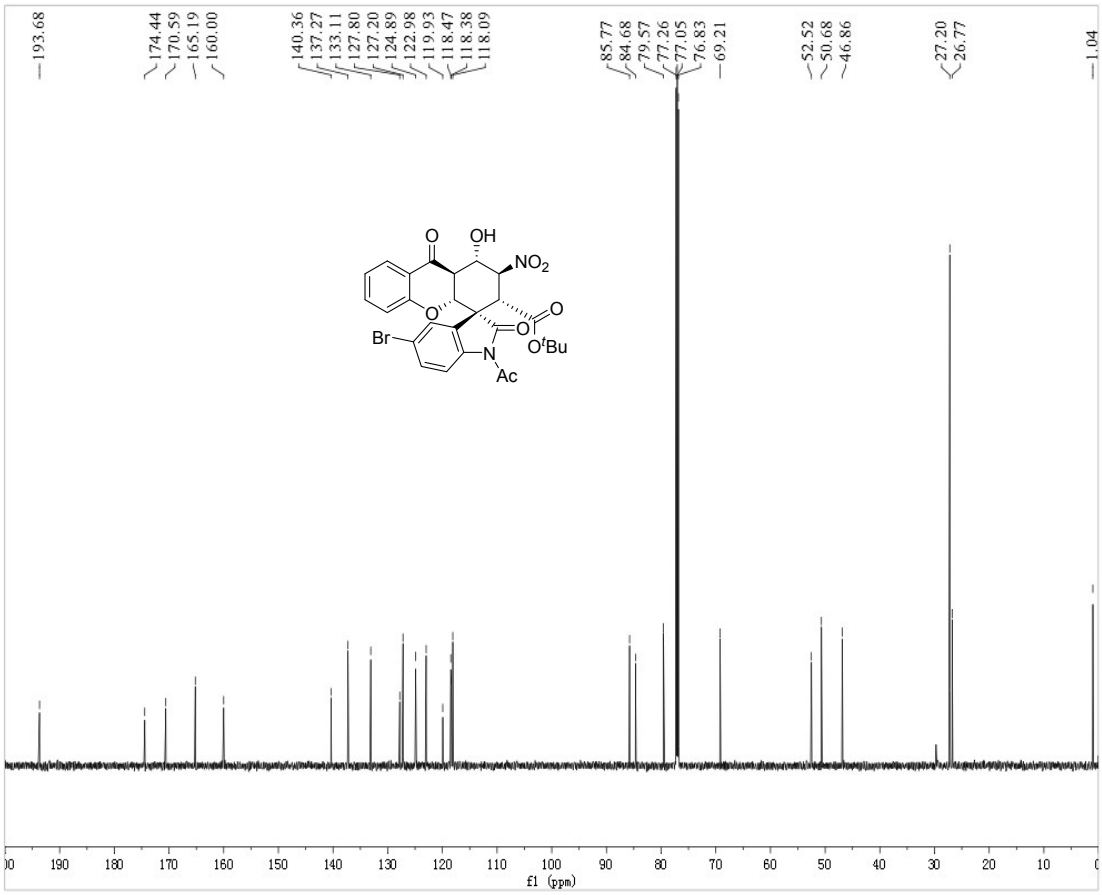
#	Time	Area	Height	Width	Area%	Symmetry
1	32.556	129082.9	1469.2	1.4643	50.058	0.822
2	80.314	128782.2	586	3.6627	49.942	0.58



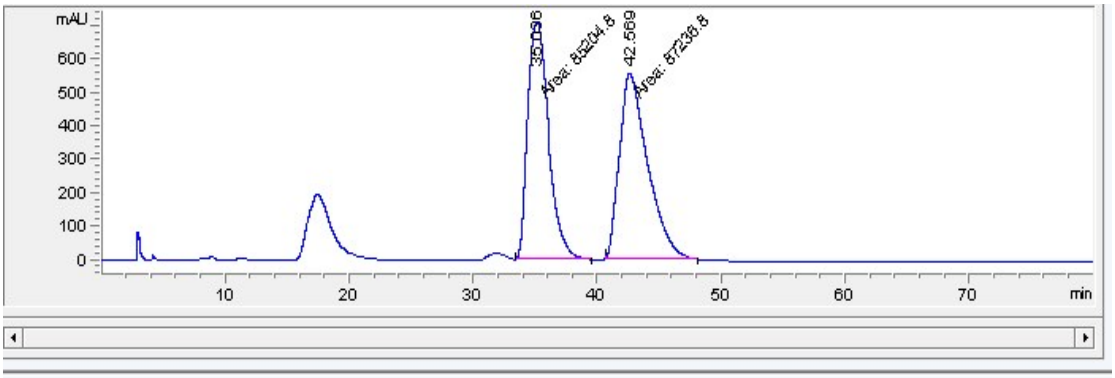
#	Time	Area	Height	Width	Area%	Symmetry
1	32.752	1951.3	28.4	1.1468	1.085	0.484
2	80.15	177931.8	781.7	3.7936	98.915	0.619

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

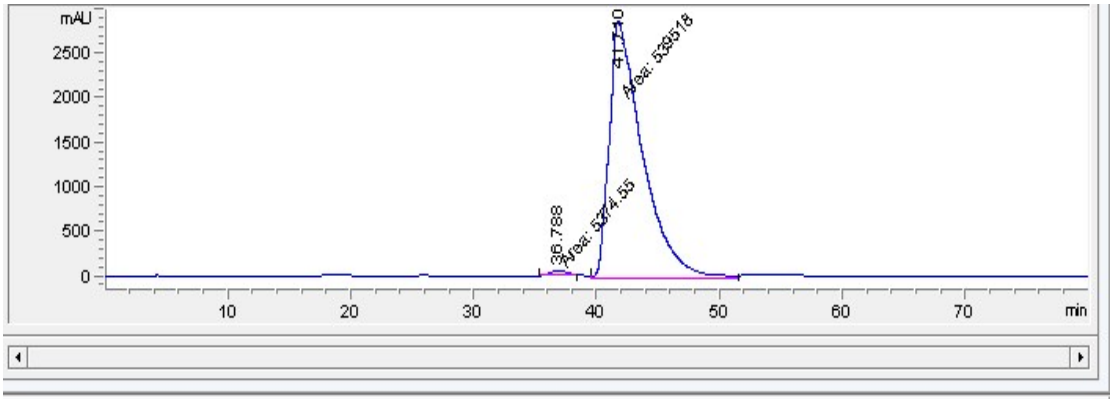




HPLC of 3j

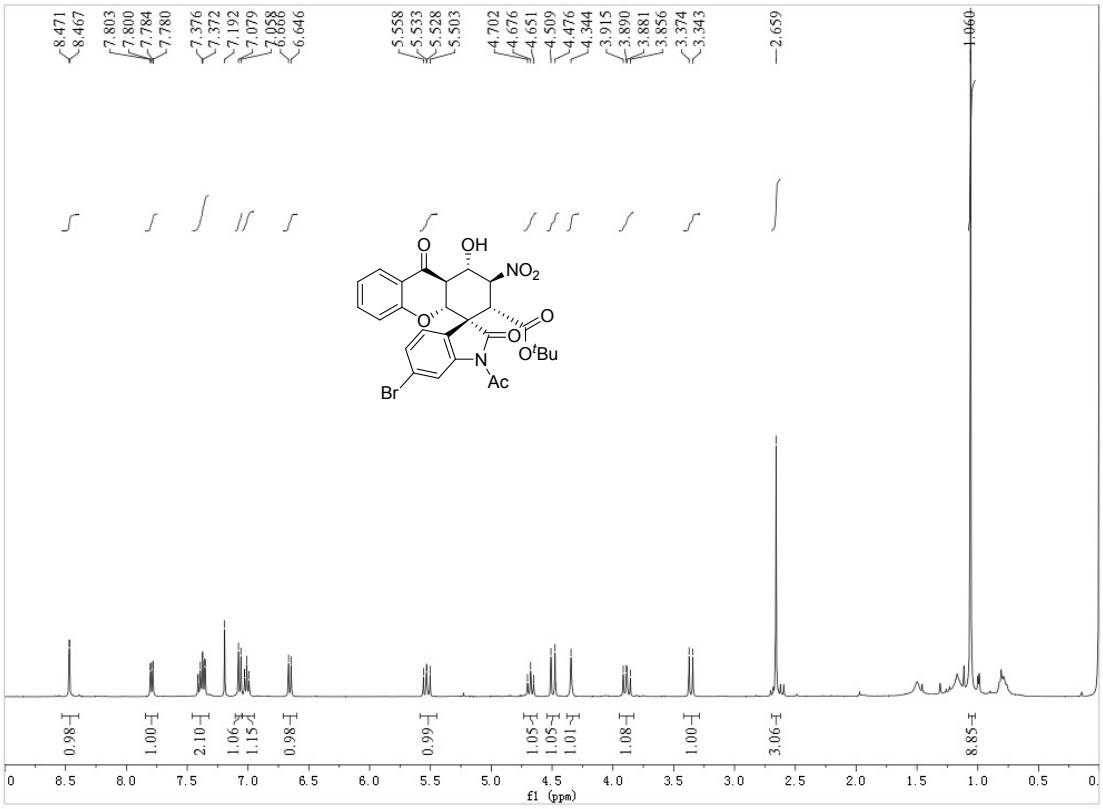


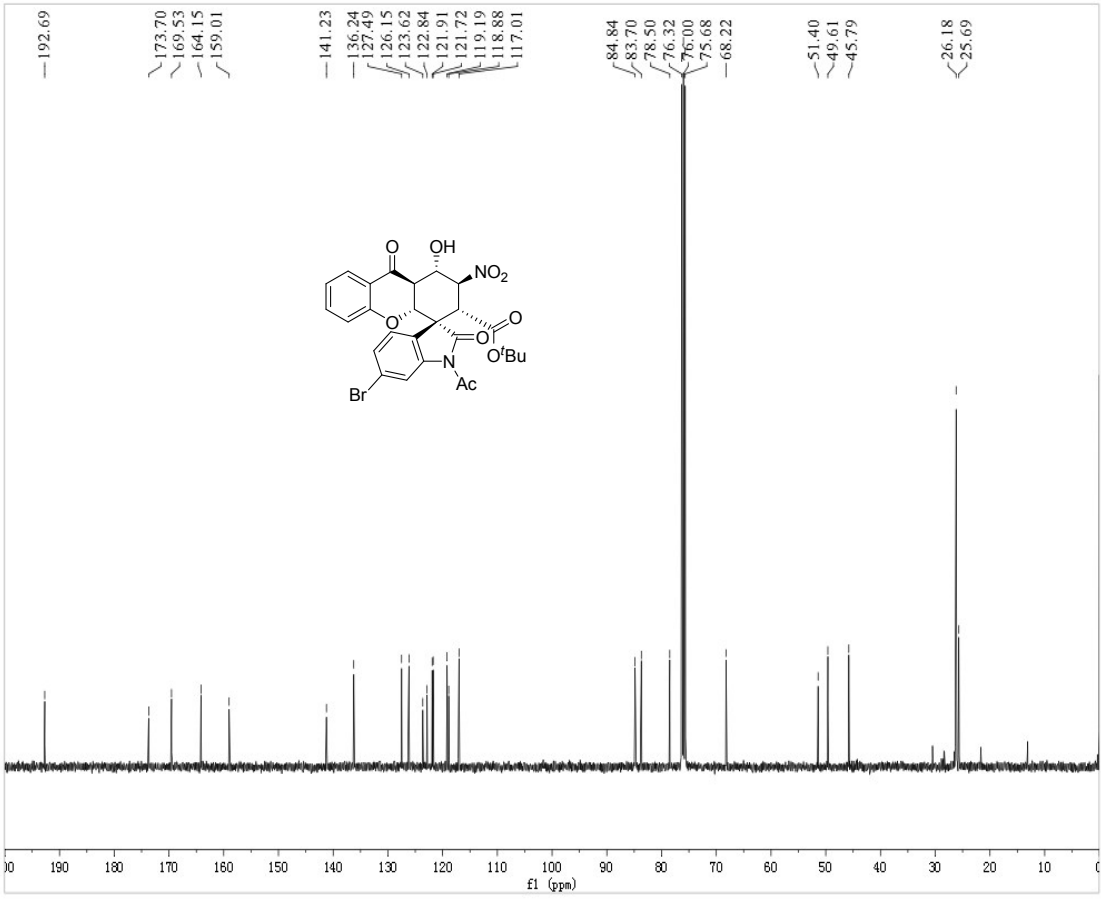
#	Time	Area	Height	Width	Area%	Symmetry
1	35.036	85204.8	708.9	2.0034	49.411	0.715
2	42.569	87236.8	555.9	2.6154	50.589	0.542



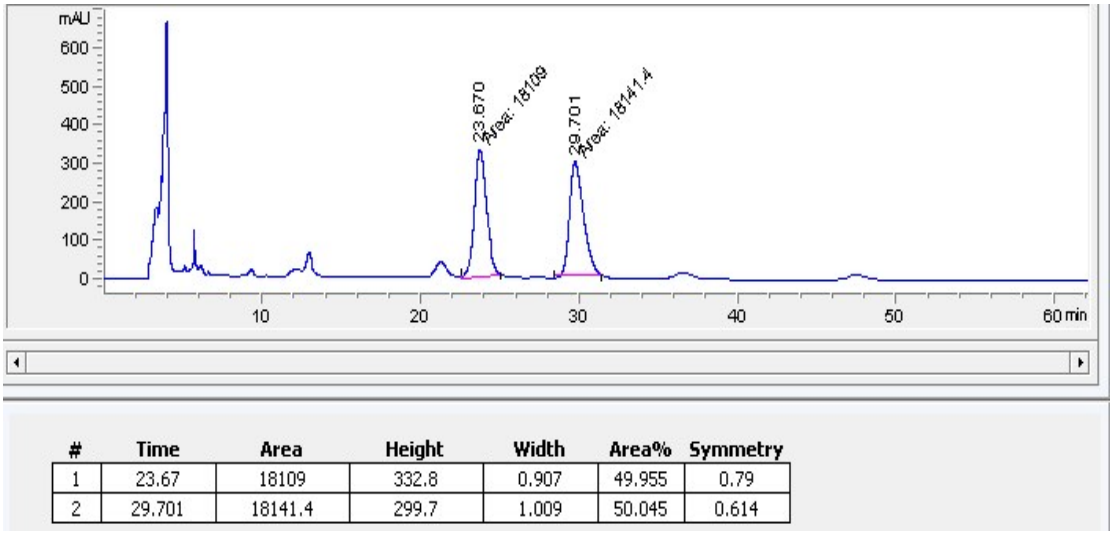
#	Time	Area	Height	Width	Area%	Symmetry
1	36.788	5374.5	49.9	1.7967	0.986	1.075
2	41.71	539518.2	2886.9	3.1147	99.014	0.359

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

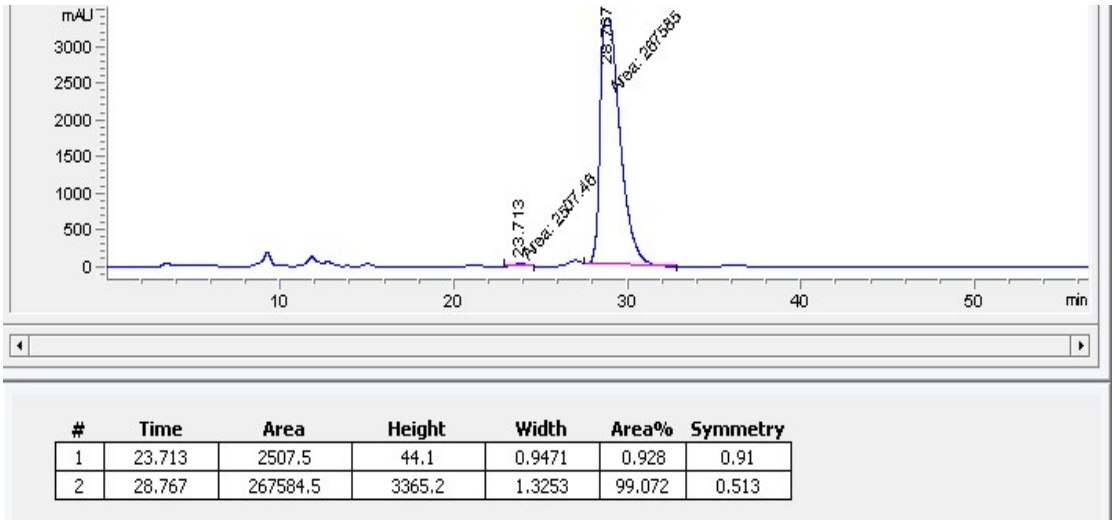




HPLC of 3k

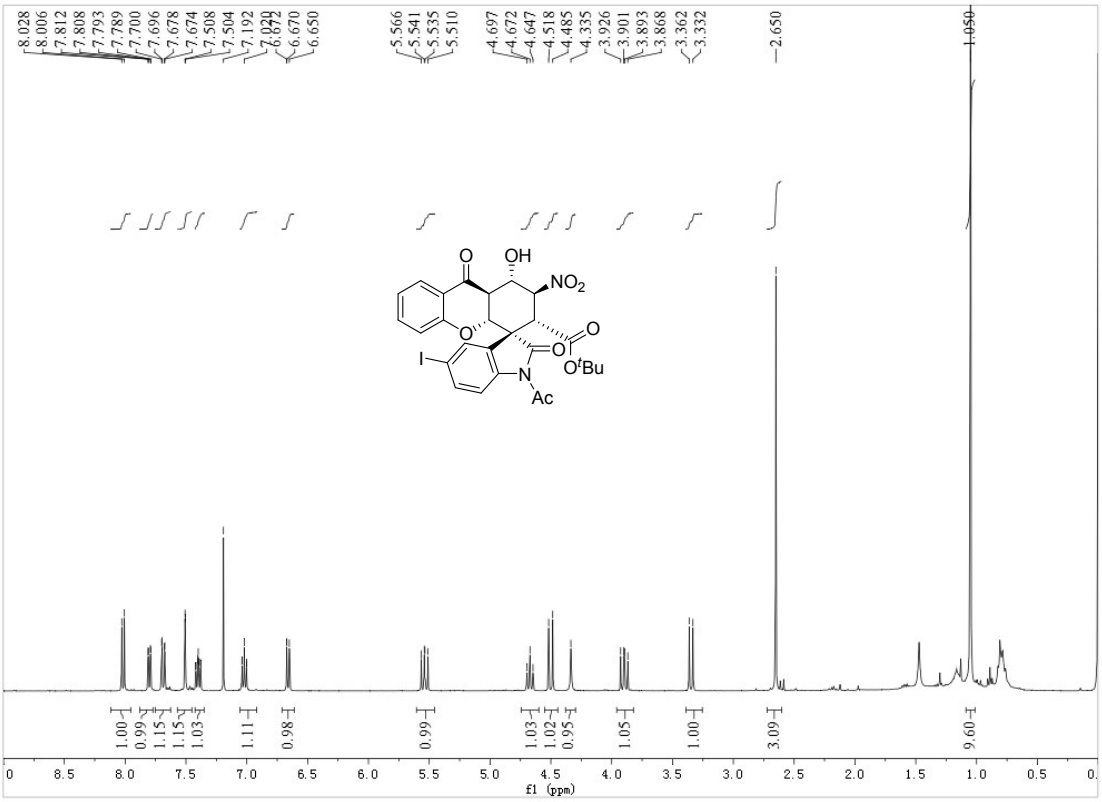


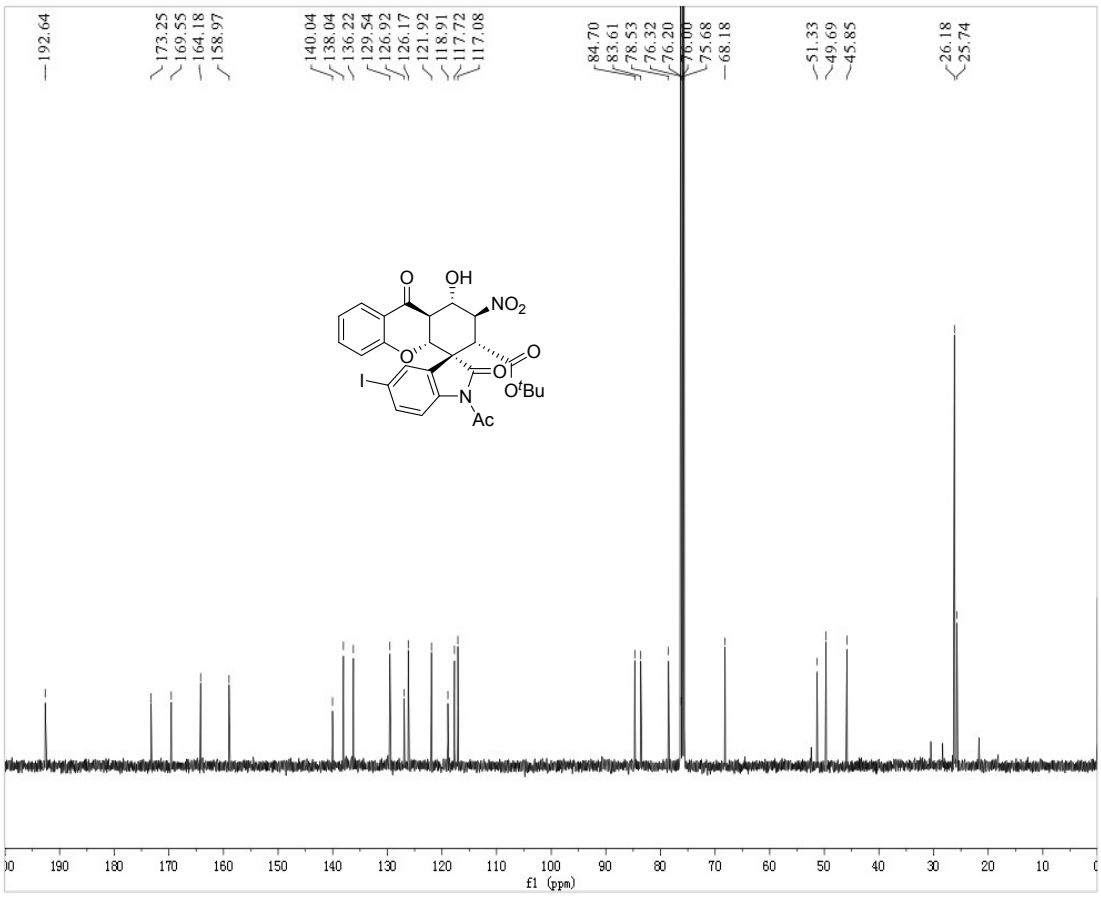
#	Time	Area	Height	Width	Area%	Symmetry
1	23.67	18109	332.8	0.907	49.955	0.79
2	29.701	18141.4	299.7	1.009	50.045	0.614



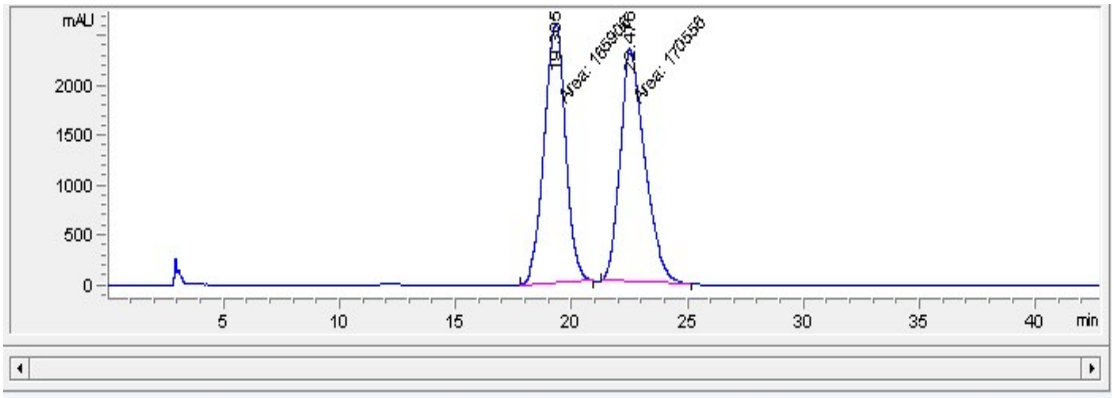
#	Time	Area	Height	Width	Area%	Symmetry
1	23.713	2507.5	44.1	0.9471	0.928	0.91
2	28.767	267584.5	3365.2	1.3253	99.072	0.513

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

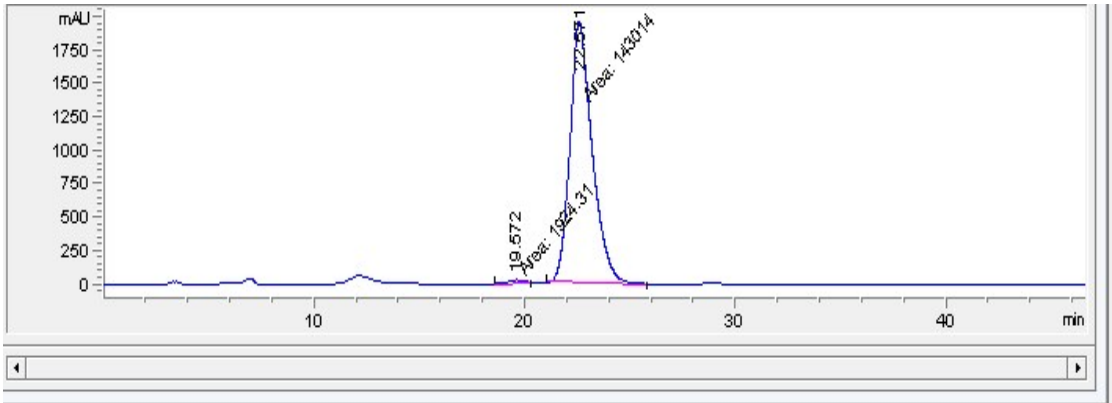




HPLC of 3l

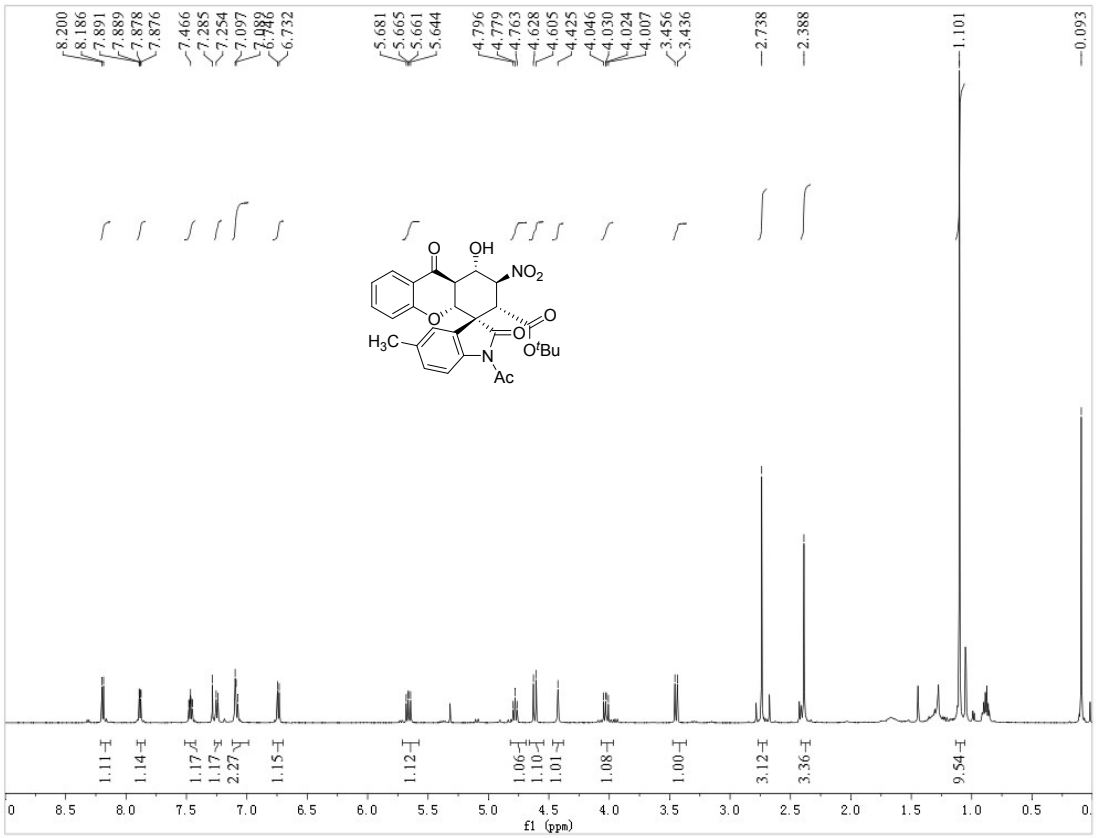


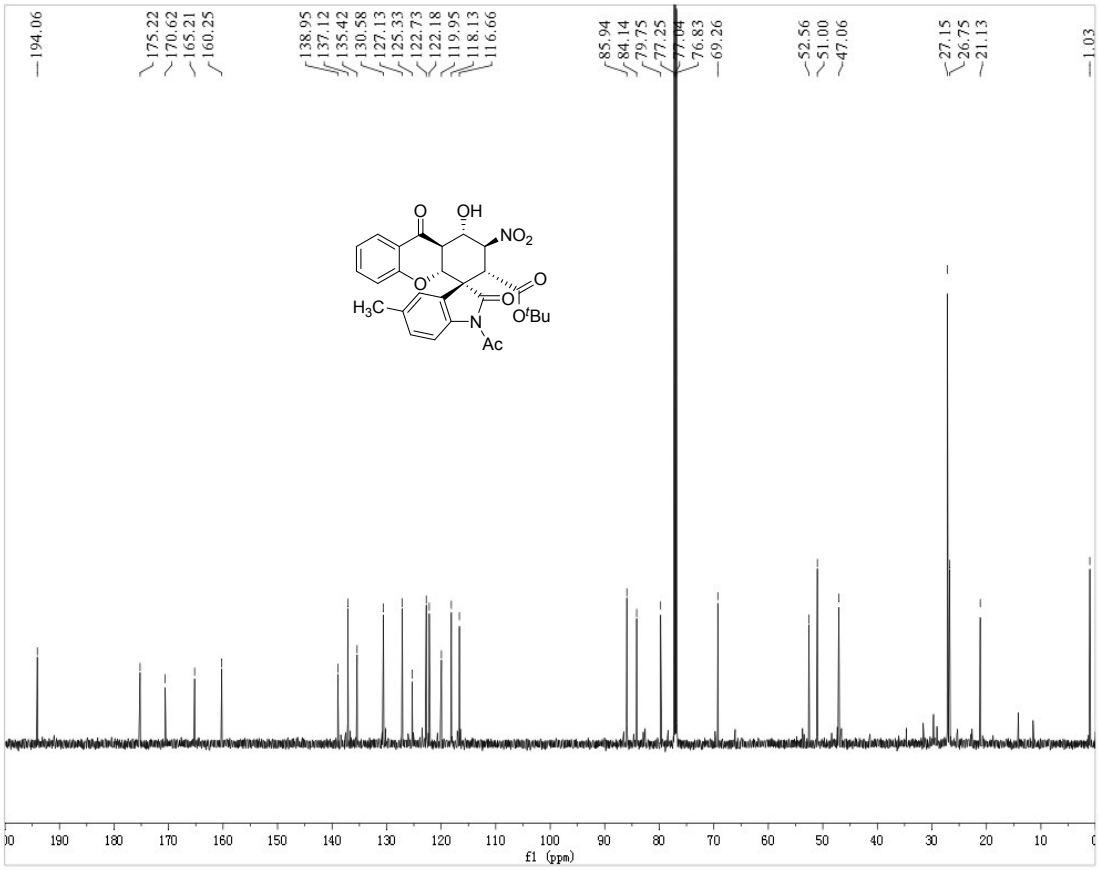
#	Time	Area	Height	Width	Area%	Symmetry
1	19.305	165906	2608.8	1.0599	49.309	1.177
2	22.476	170556.2	2339.1	1.2152	50.691	0.623



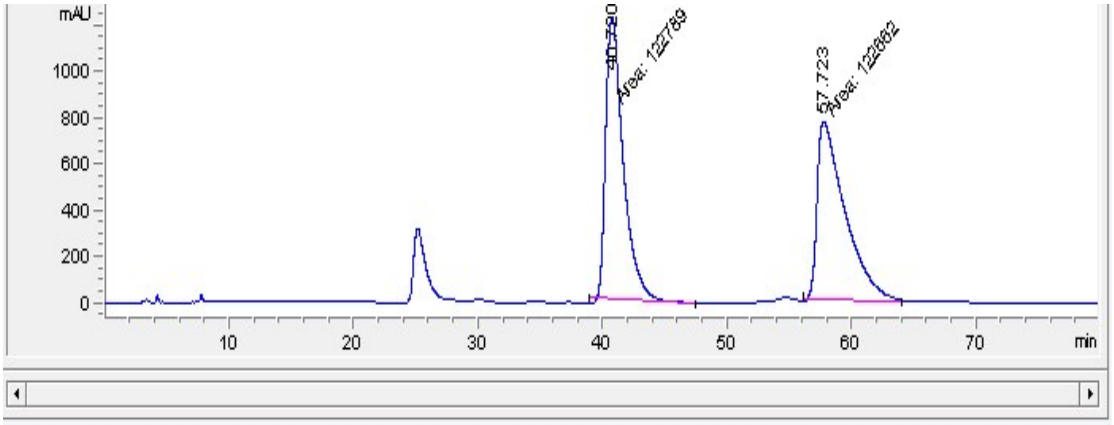
#	Time	Area	Height	Width	Area%	Symmetry
1	19.572	1924.3	29.8	1.0752	1.328	1.41
2	22.571	143013.9	1954.4	1.2196	98.672	0.665

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

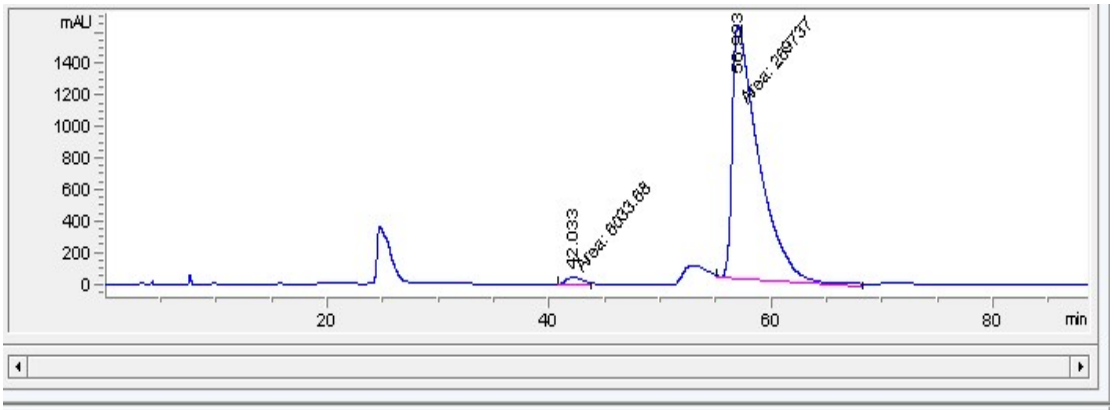




HPLC of 3m

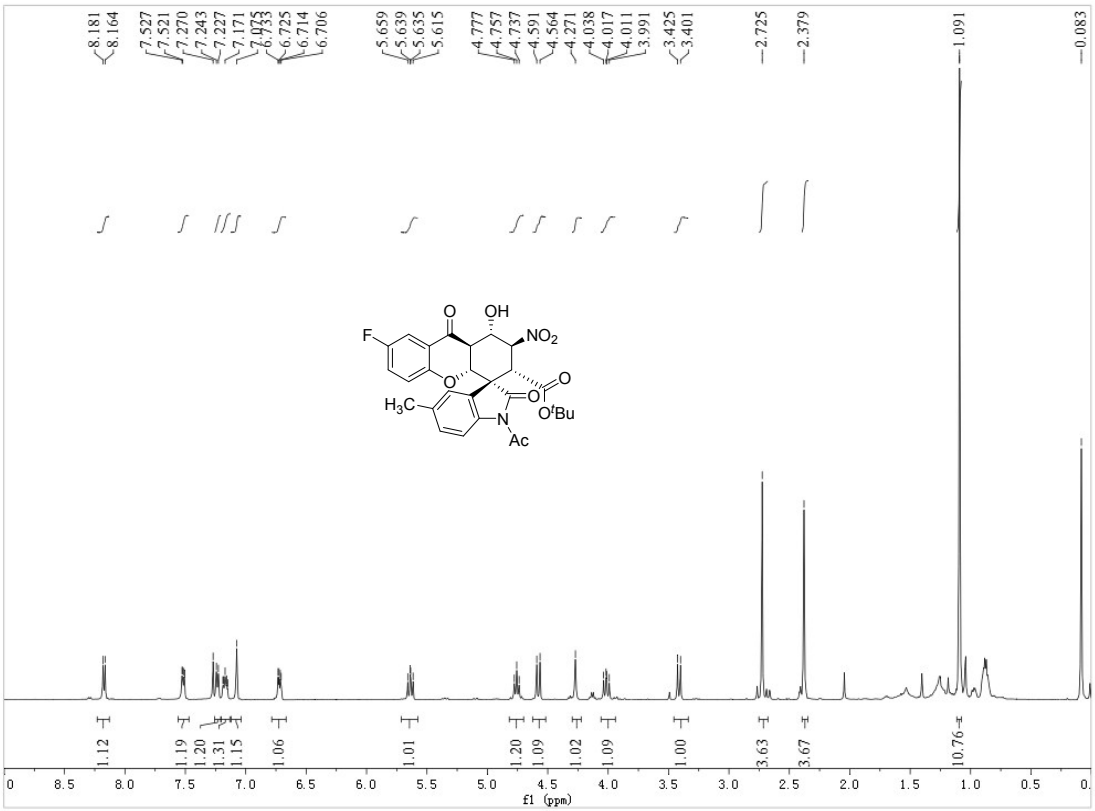


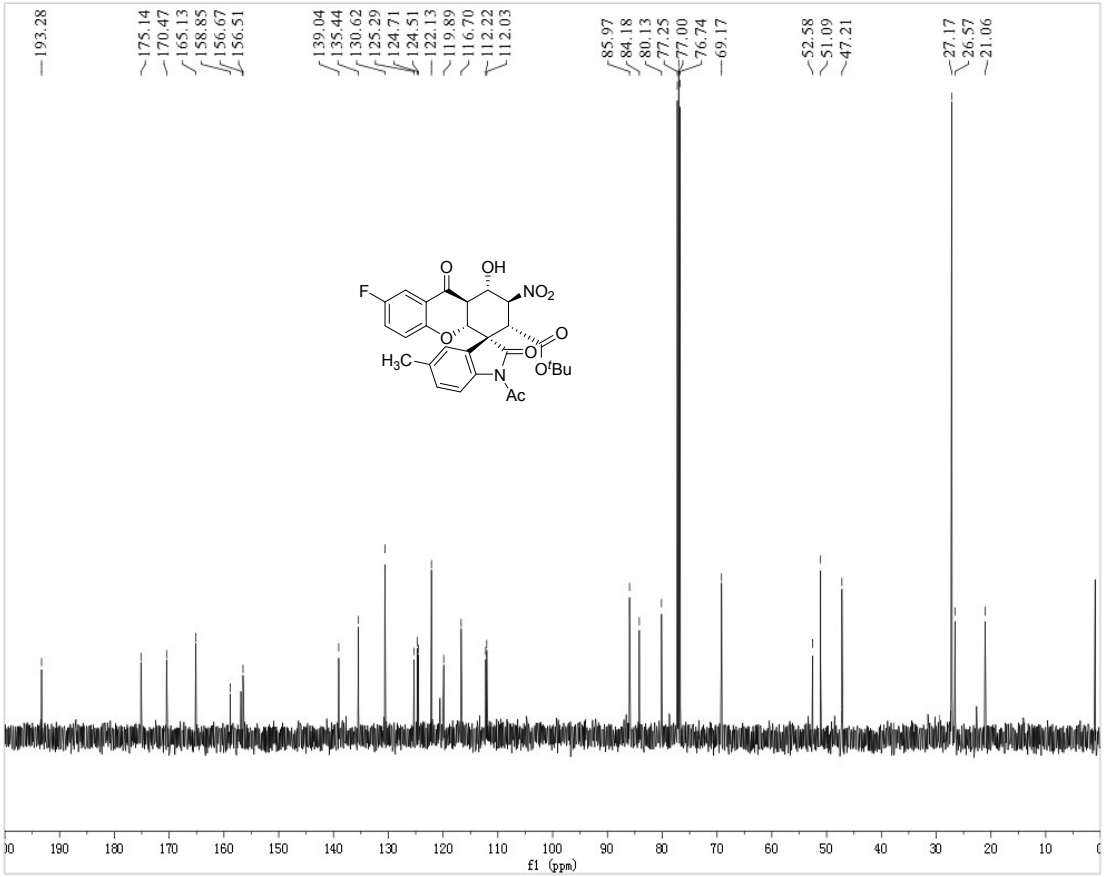
#	Time	Area	Height	Width	Area%	Symmetry
1	40.72	122789.1	1223.8	1.6722	50.026	0.528
2	57.723	122662.3	778.2	2.6271	49.974	0.287



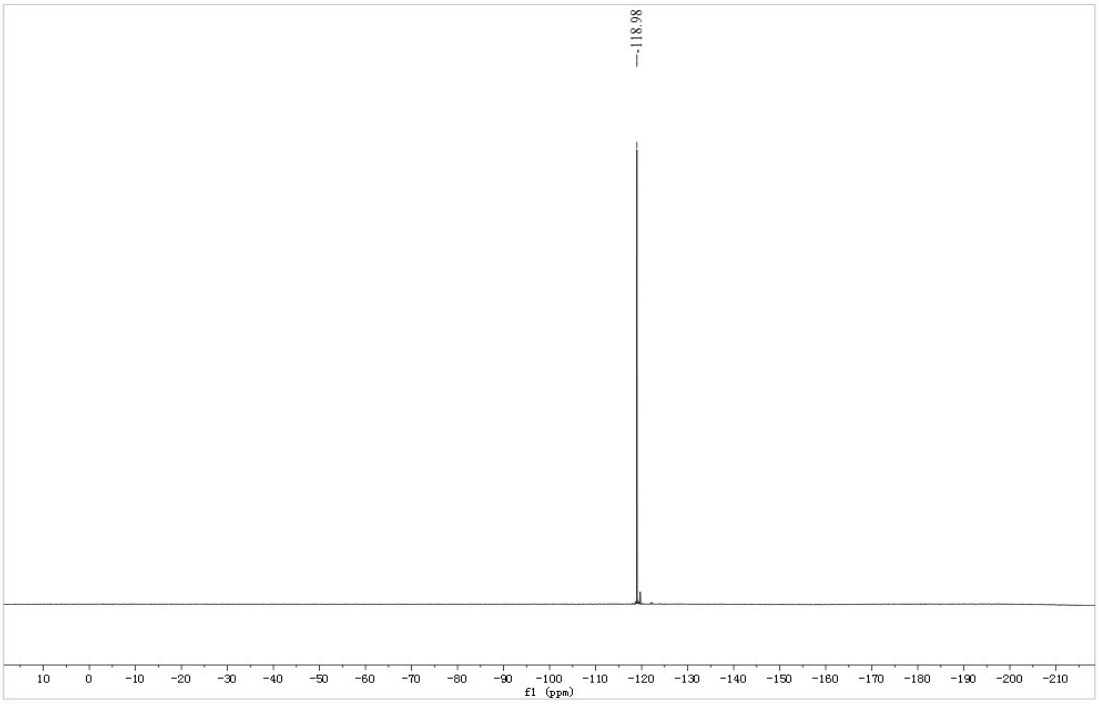
#	Time	Area	Height	Width	Area%	Symmetry
1	42.033	6033.7	52.5	1.9165	2.188	0.514
2	56.923	269736.8	1610.4	2.7916	97.812	0.259

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

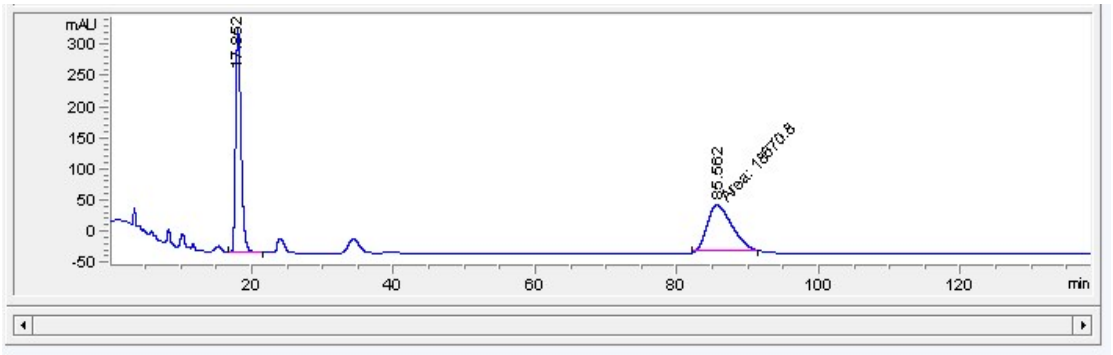




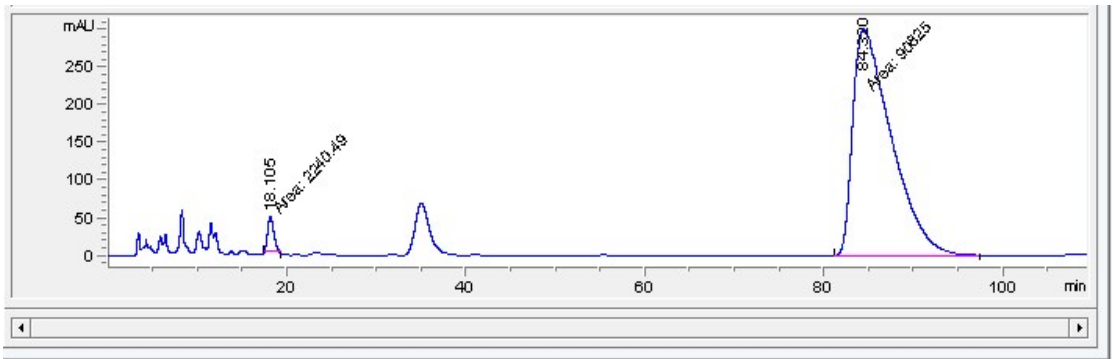
^{19}F NMR of 3n



HPLC of 3n

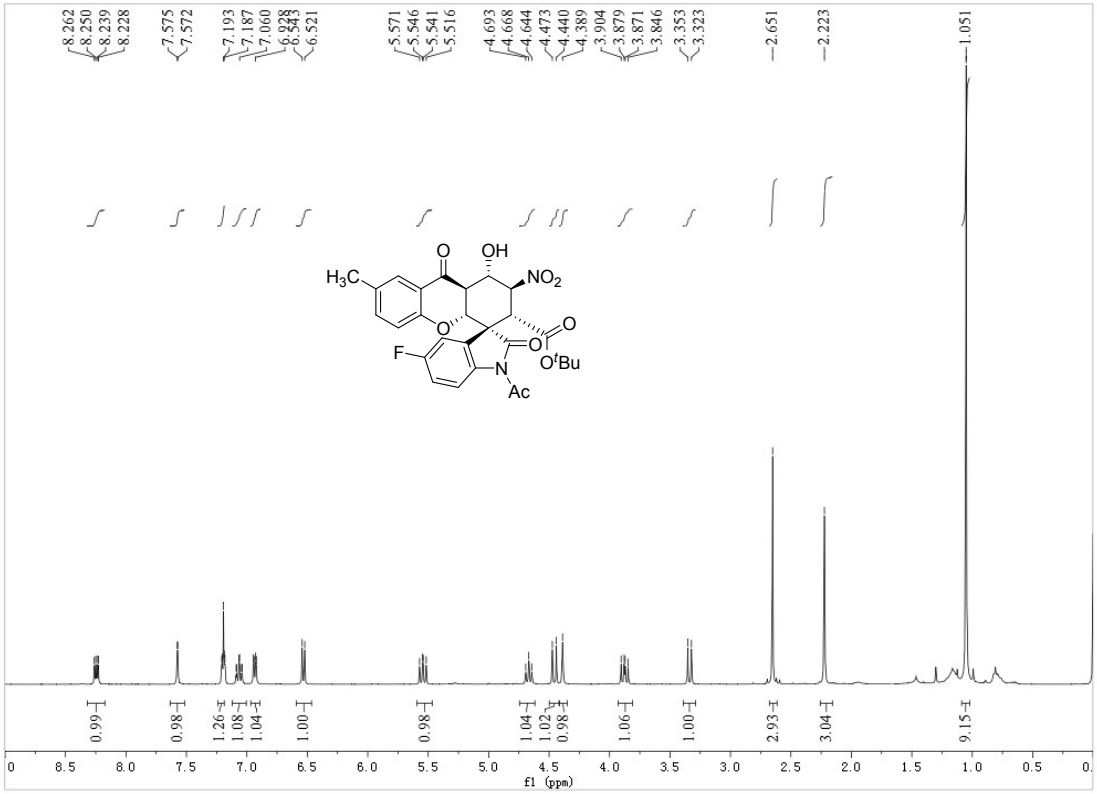


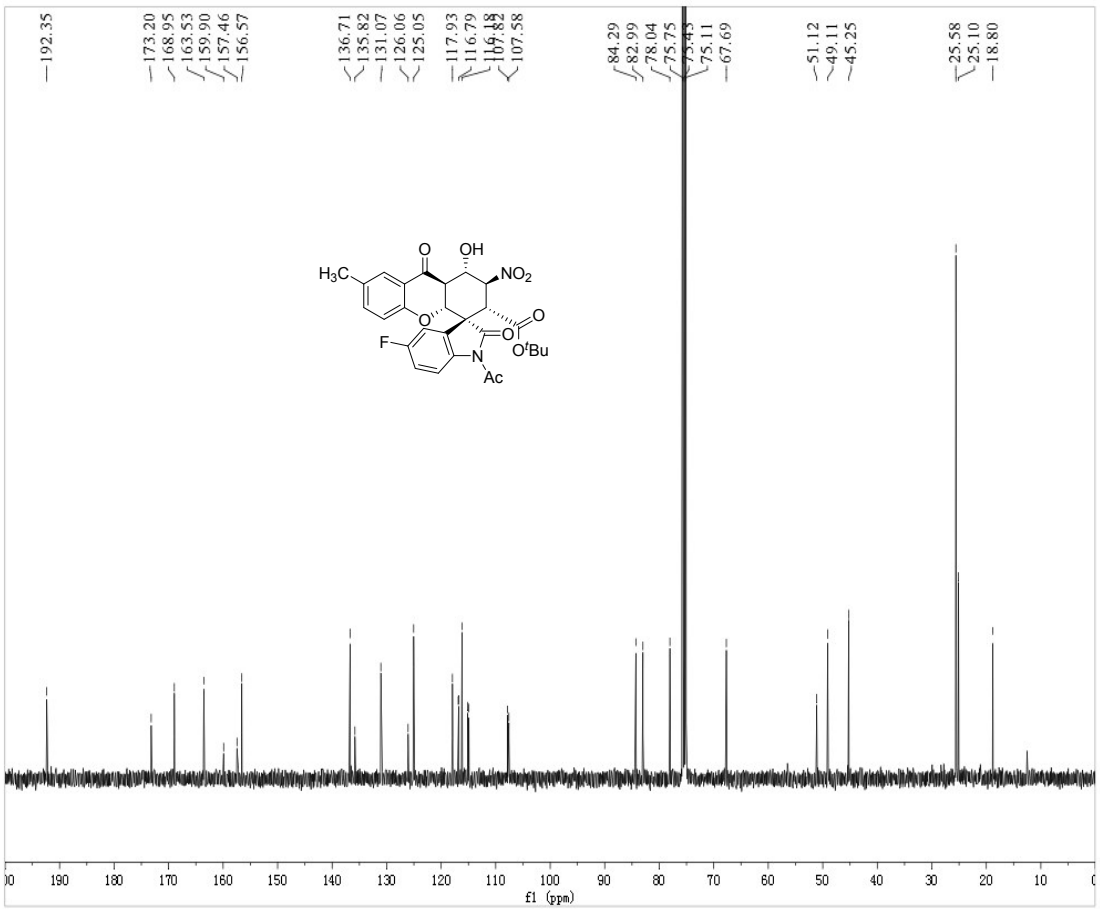
#	Time	Area	Height	Width	Area%	Symmetry
1	17.852	18939.7	361.5	0.8072	50.358	0.676
2	85.562	18670.8	75	4.1473	49.642	0.609



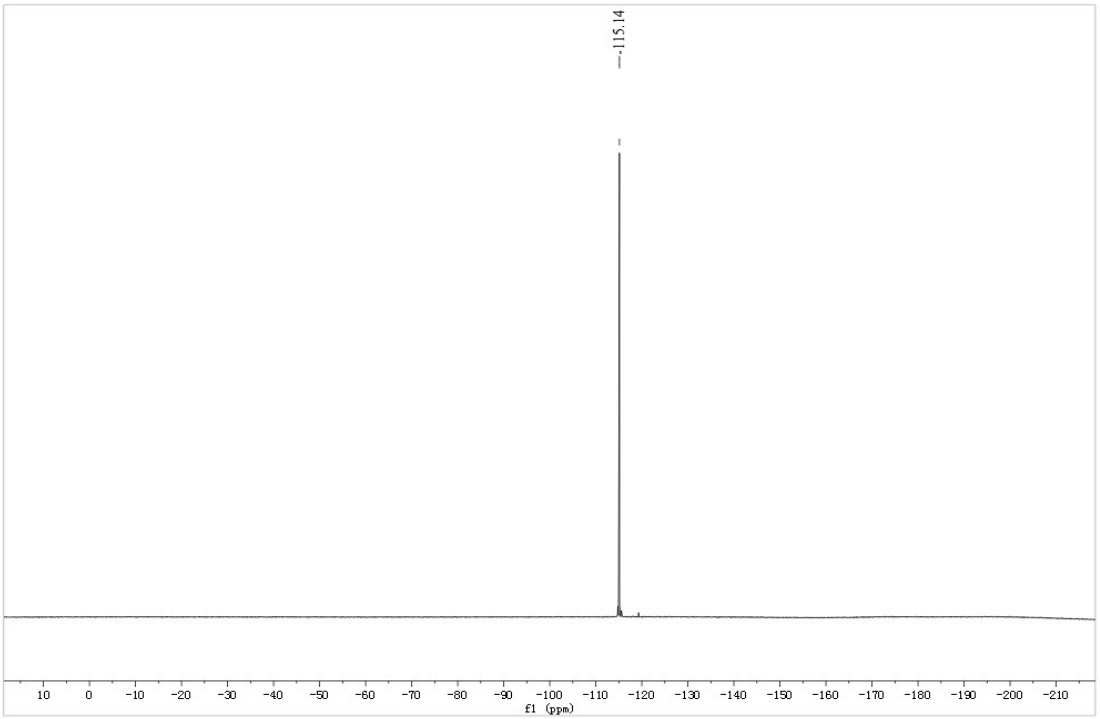
#	Time	Area	Height	Width	Area%	Symmetry
1	18.105	2240.5	46.5	0.8024	2.407	0.743
2	84.32	90825	303	4.9961	97.593	0.36

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

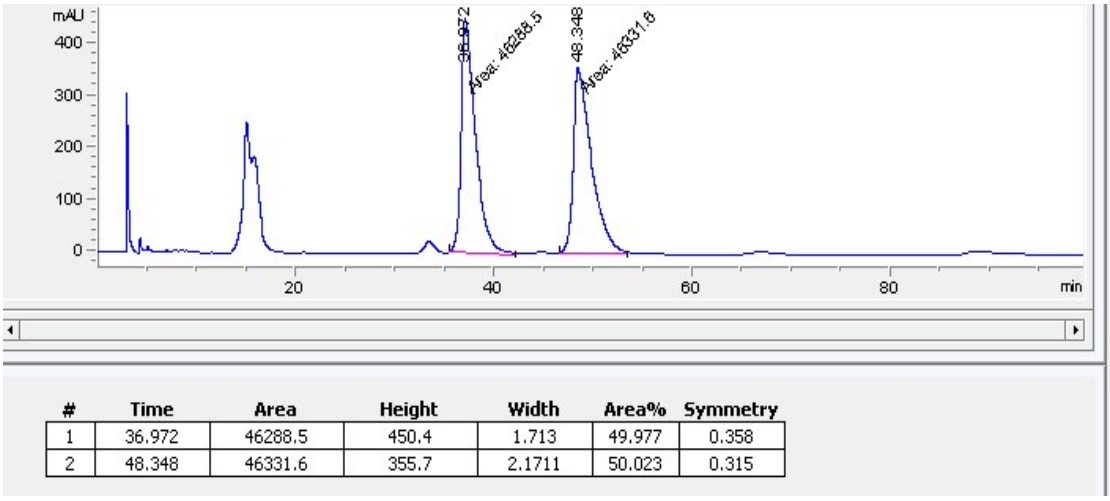




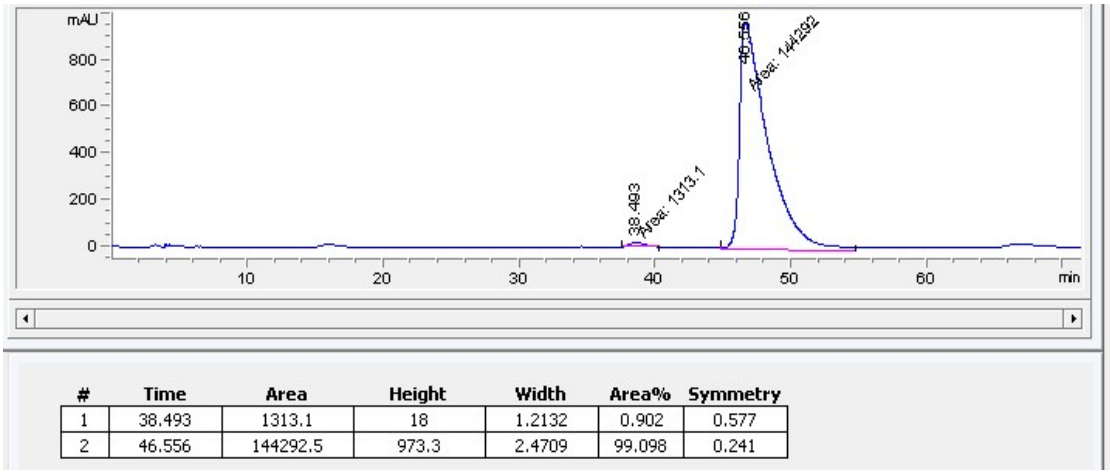
^{19}F NMR of 3o



HPLC of 3o

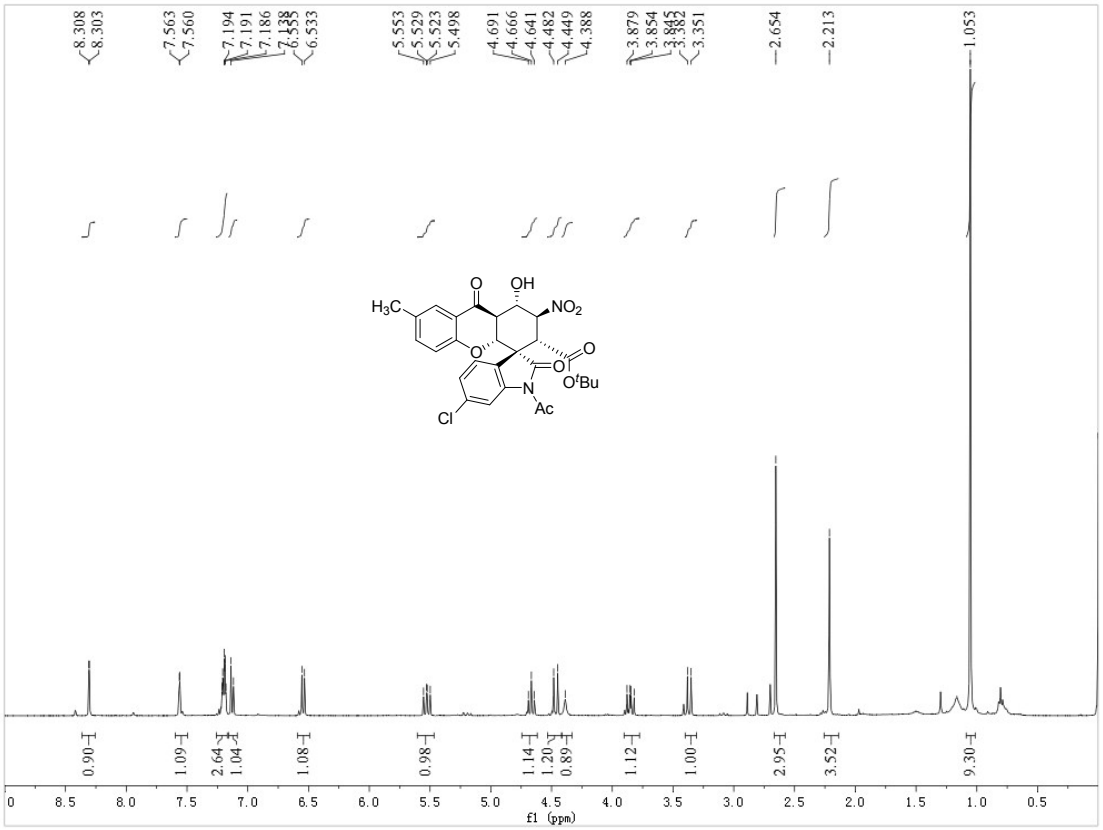


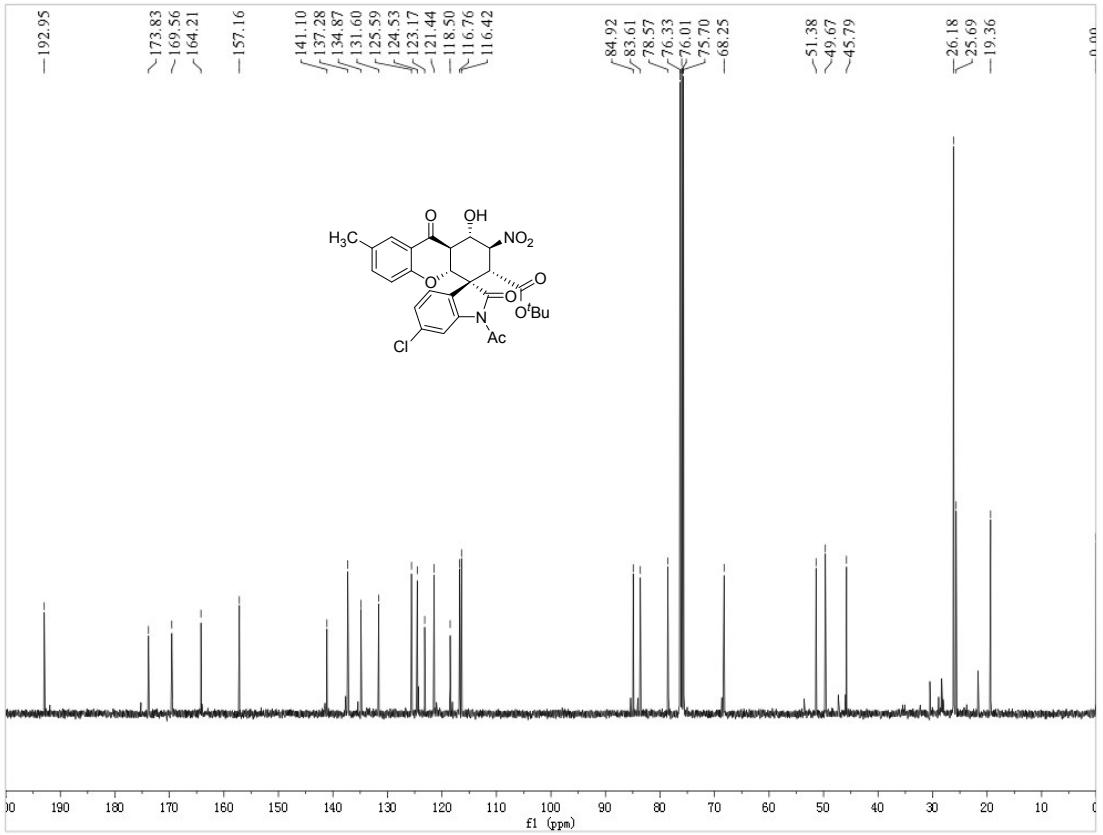
#	Time	Area	Height	Width	Area%	Symmetry
1	36.972	46288.5	450.4	1.713	49.977	0.358
2	48.348	46331.6	355.7	2.1711	50.023	0.315



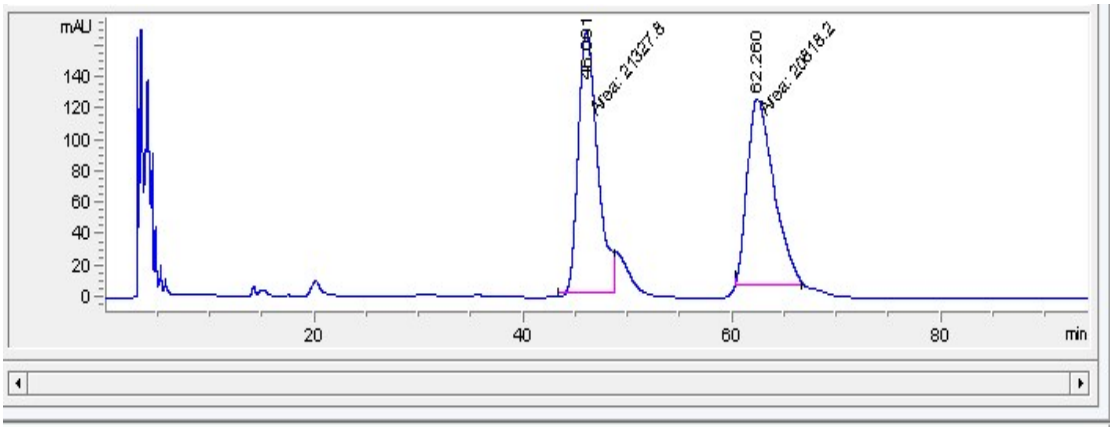
#	Time	Area	Height	Width	Area%	Symmetry
1	38.493	1313.1	18	1.2132	0.902	0.577
2	46.556	144292.5	973.3	2.4709	99.098	0.241

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

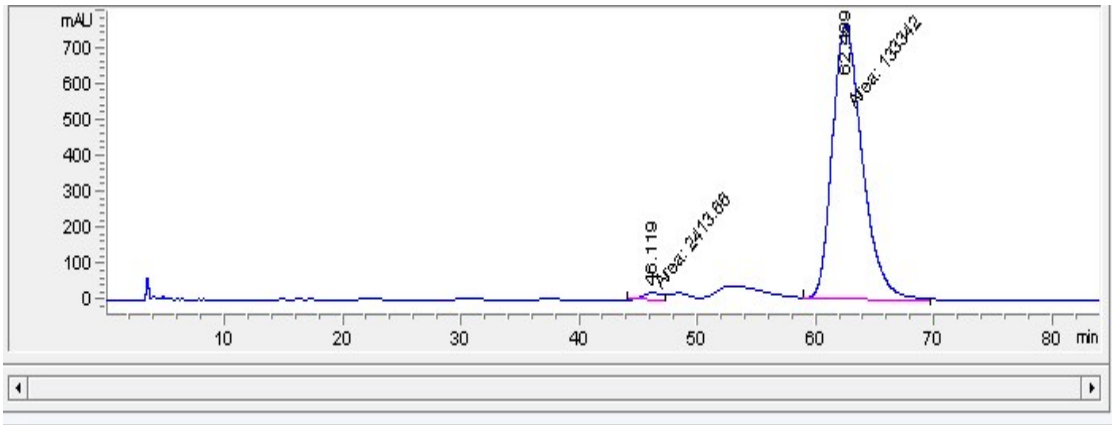




HPLC of 3p

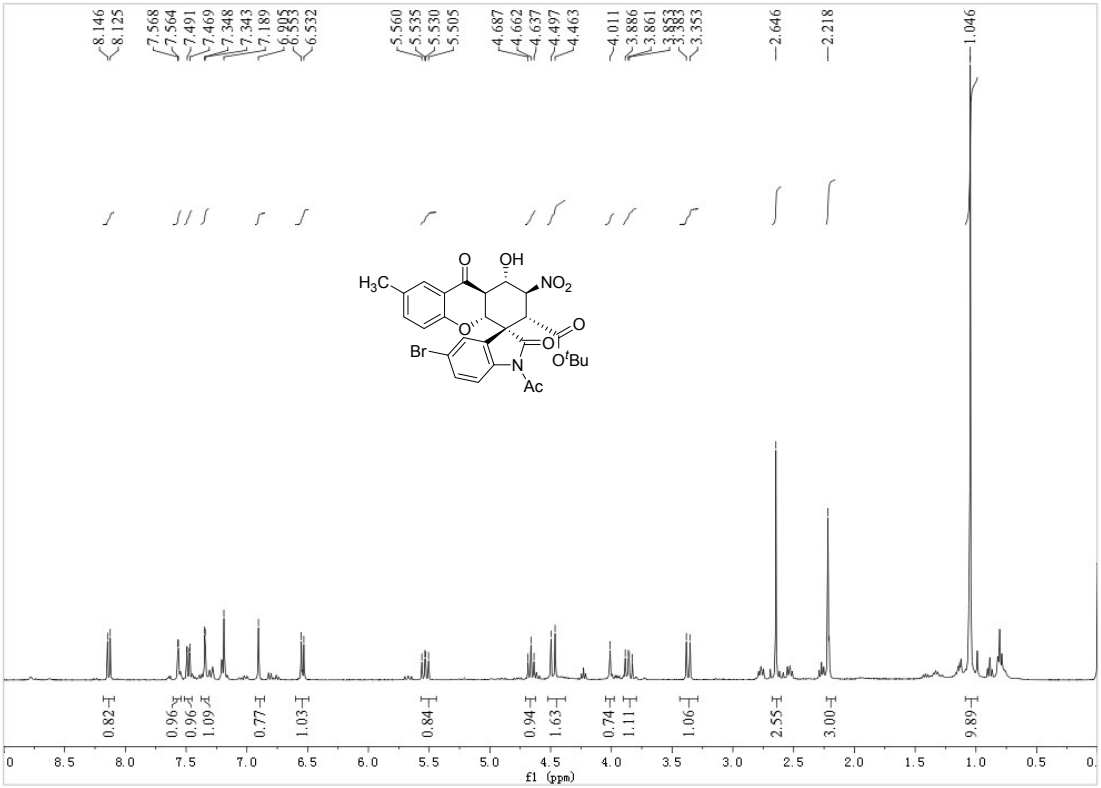


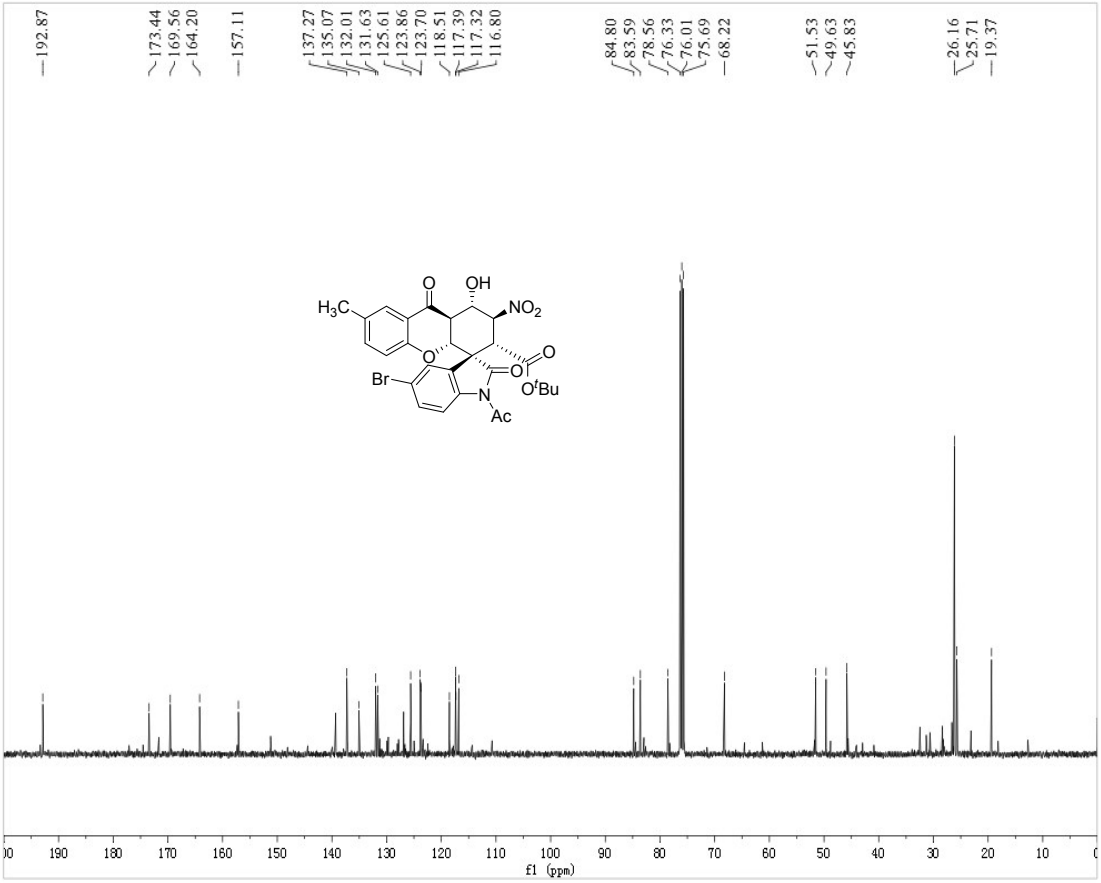
#	Time	Area	Height	Width	Area%	Symmetry
1	46.091	21327.8	166.7	2.1329	50.605	0.752
2	62.26	20818.2	117.6	2.9502	49.395	0.485



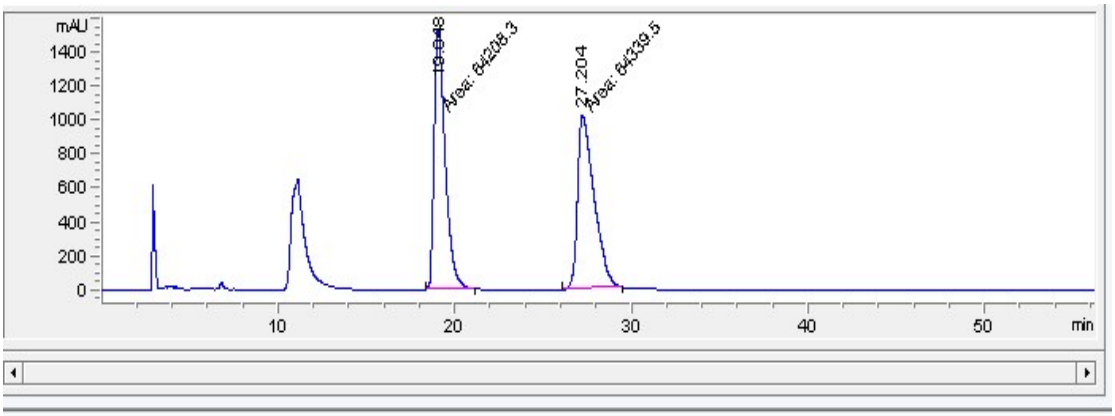
#	Time	Area	Height	Width	Area%	Symmetry
1	46.119	2413.7	20.8	1.9348	1.778	1.073
2	62.499	133342.3	763.3	2.9116	98.222	0.771

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

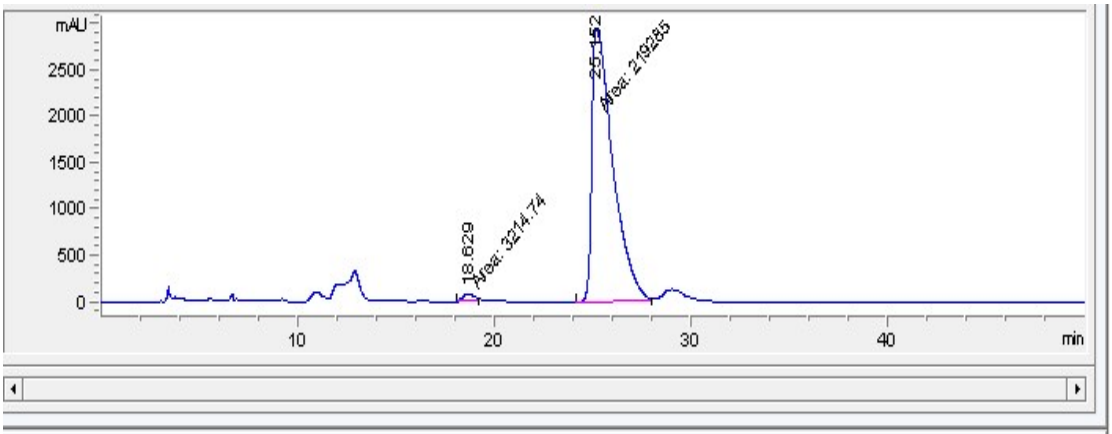




HPLC of 3q

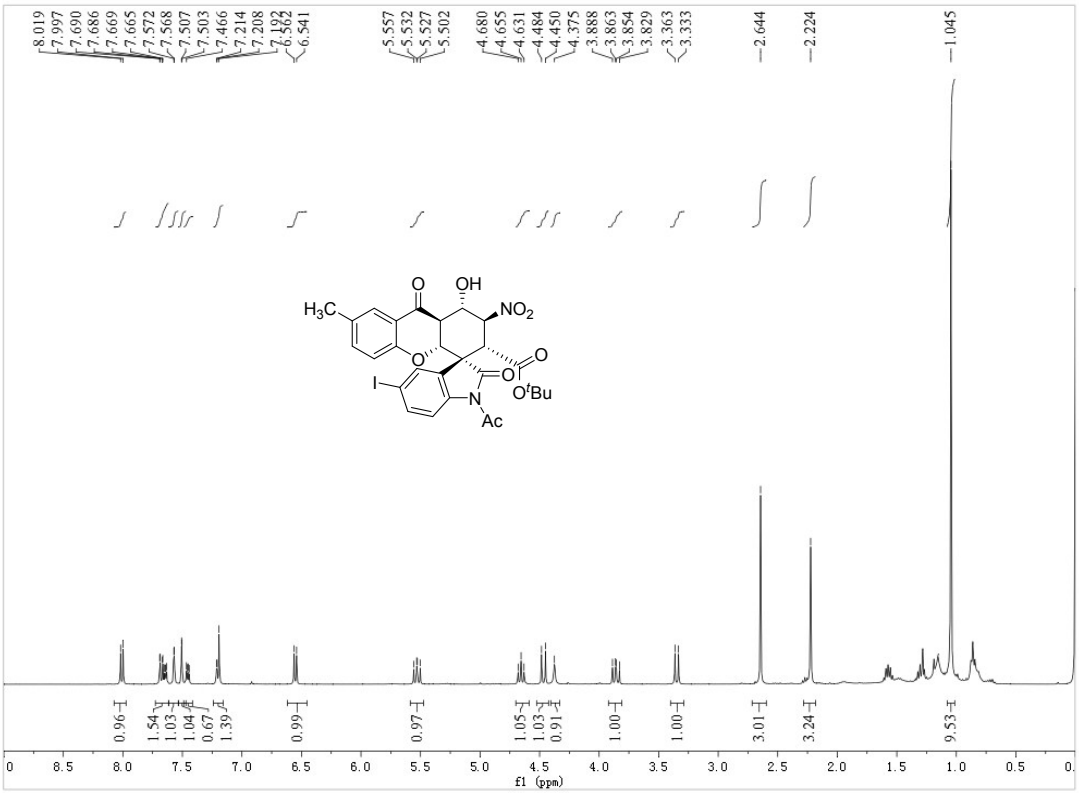


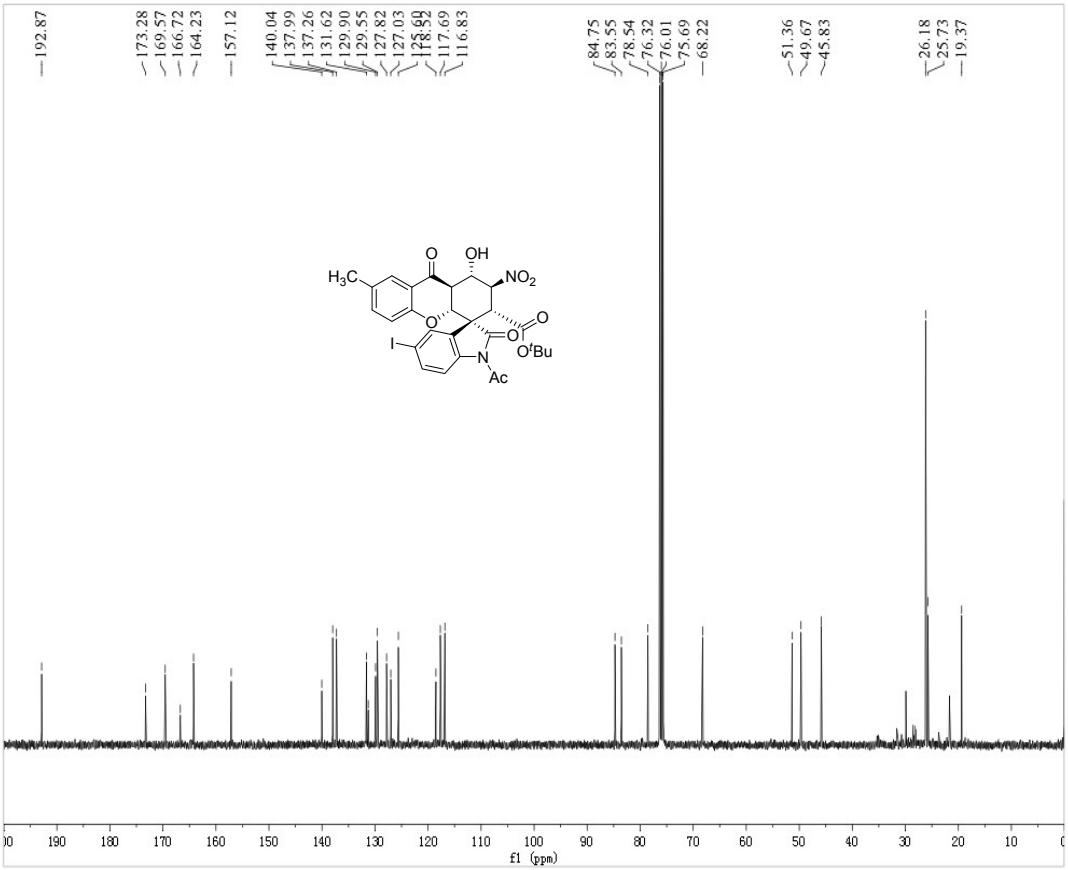
#	Time	Area	Height	Width	Area%	Symmetry
1	19.048	64208.3	1533.2	0.698	49.949	0.546
2	27.204	64339.5	1021.2	1.0501	50.051	0.422



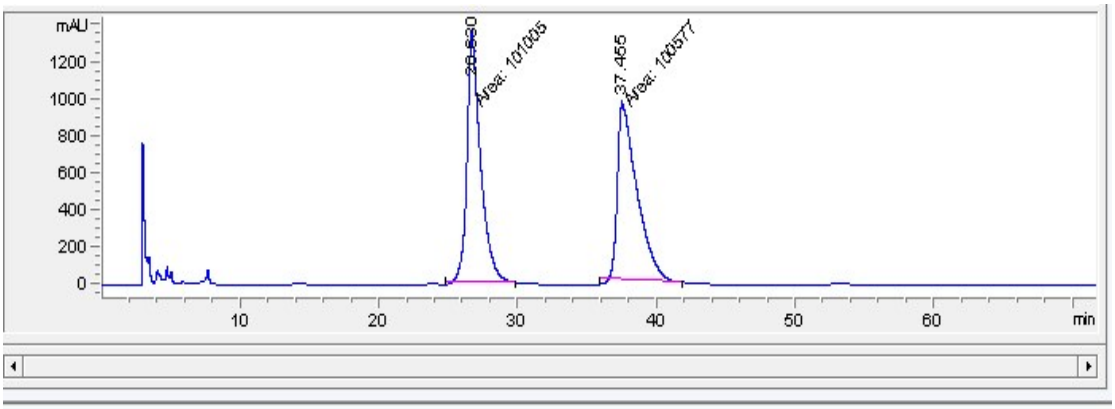
#	Time	Area	Height	Width	Area%	Symmetry
1	18.629	3214.7	83.5	0.6419	1.445	0.784
2	25.152	219285.2	2951.4	1.2383	98.555	0.275

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

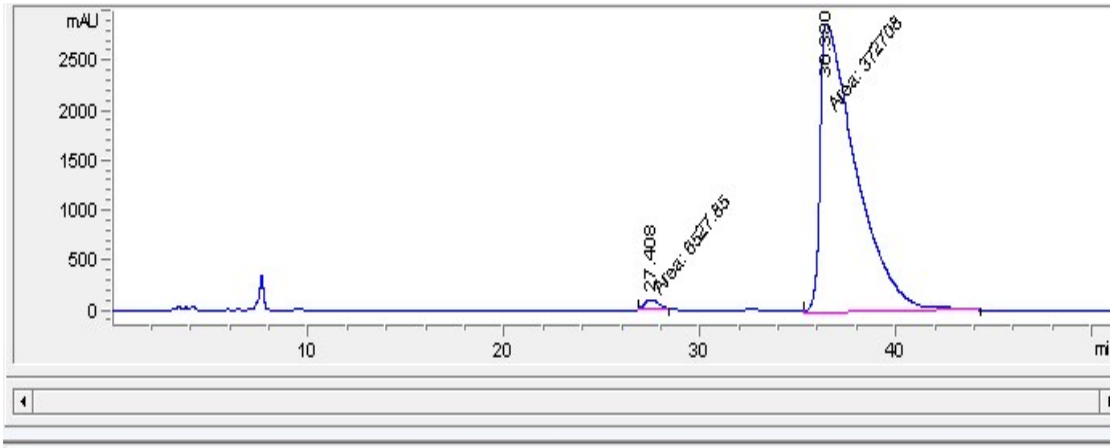




HPLC of 3r

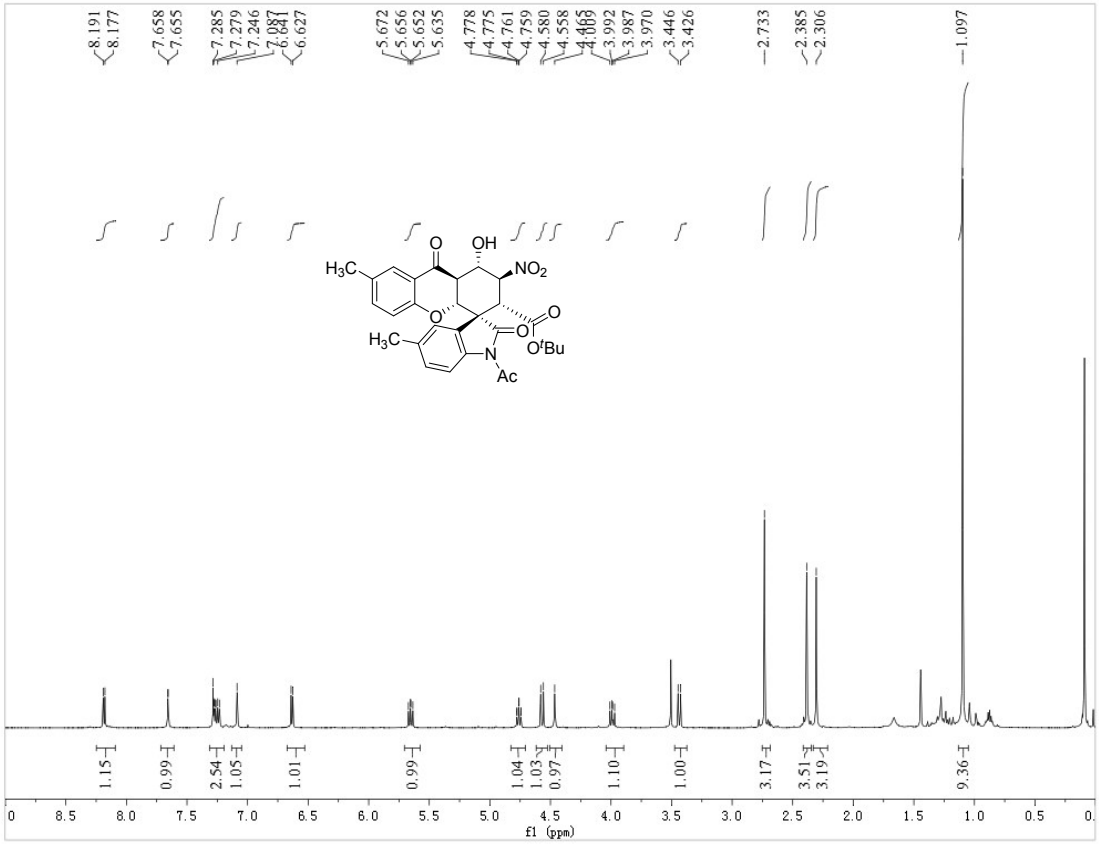


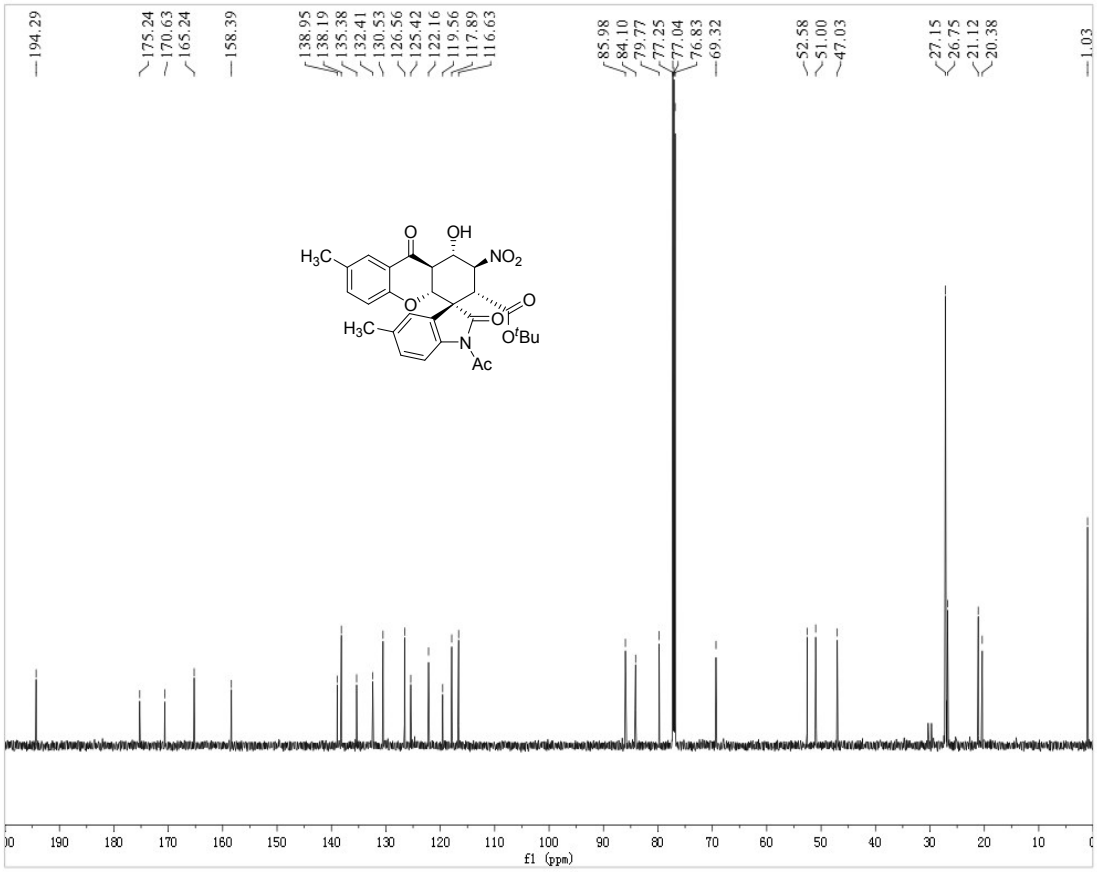
#	Time	Area	Height	Width	Area%	Symmetry
1	26.63	101005.3	1373.5	1.2256	50.106	0.554
2	37.455	100576.5	968.7	1.7304	49.894	0.315



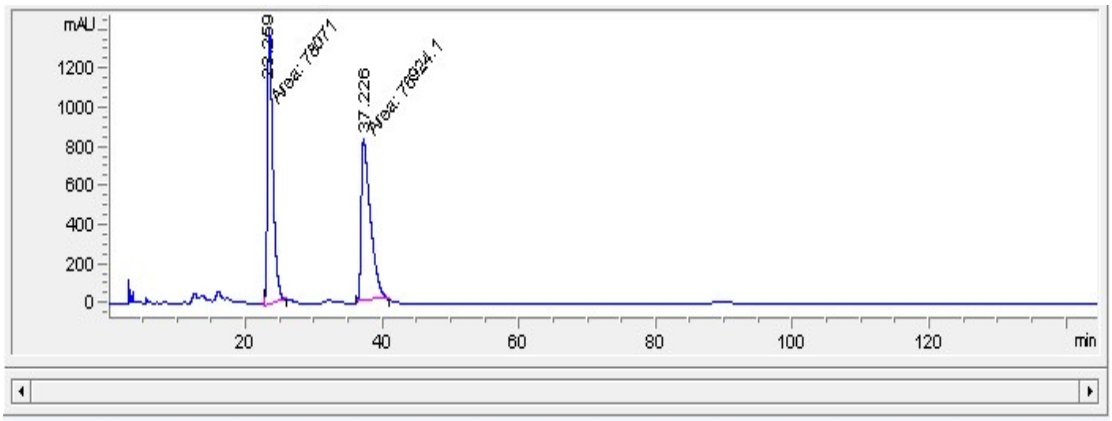
#	Time	Area	Height	Width	Area%	Symmetry
1	27.408	6527.9	112.3	0.9685	1.721	0.595
2	36.38	372707.6	2885.3	2.1529	98.279	0.184

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

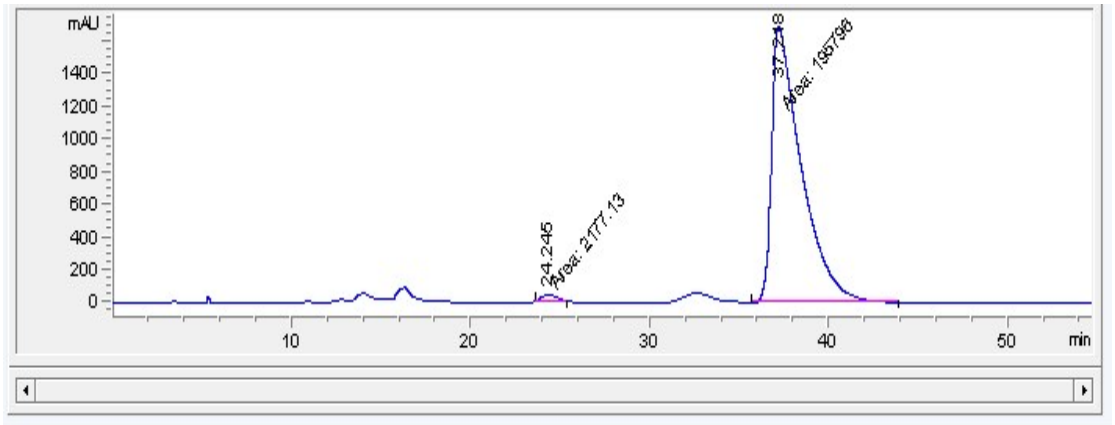




HPLC of 3s

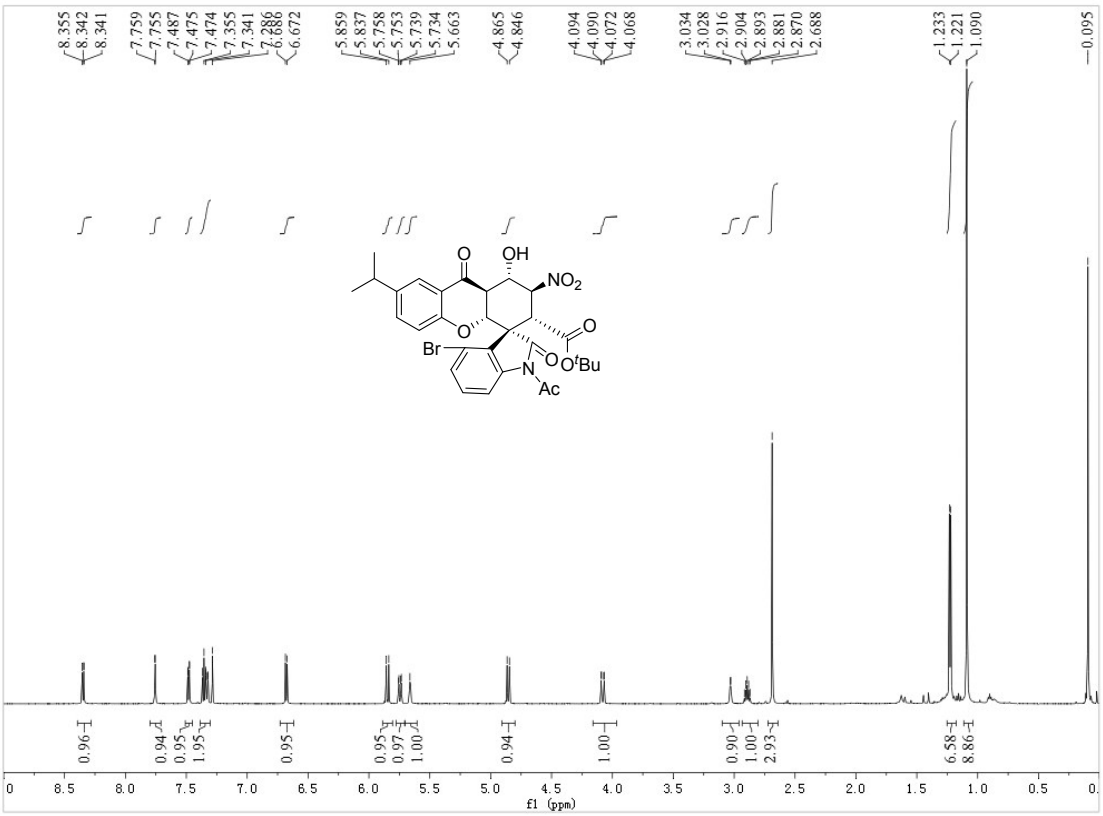


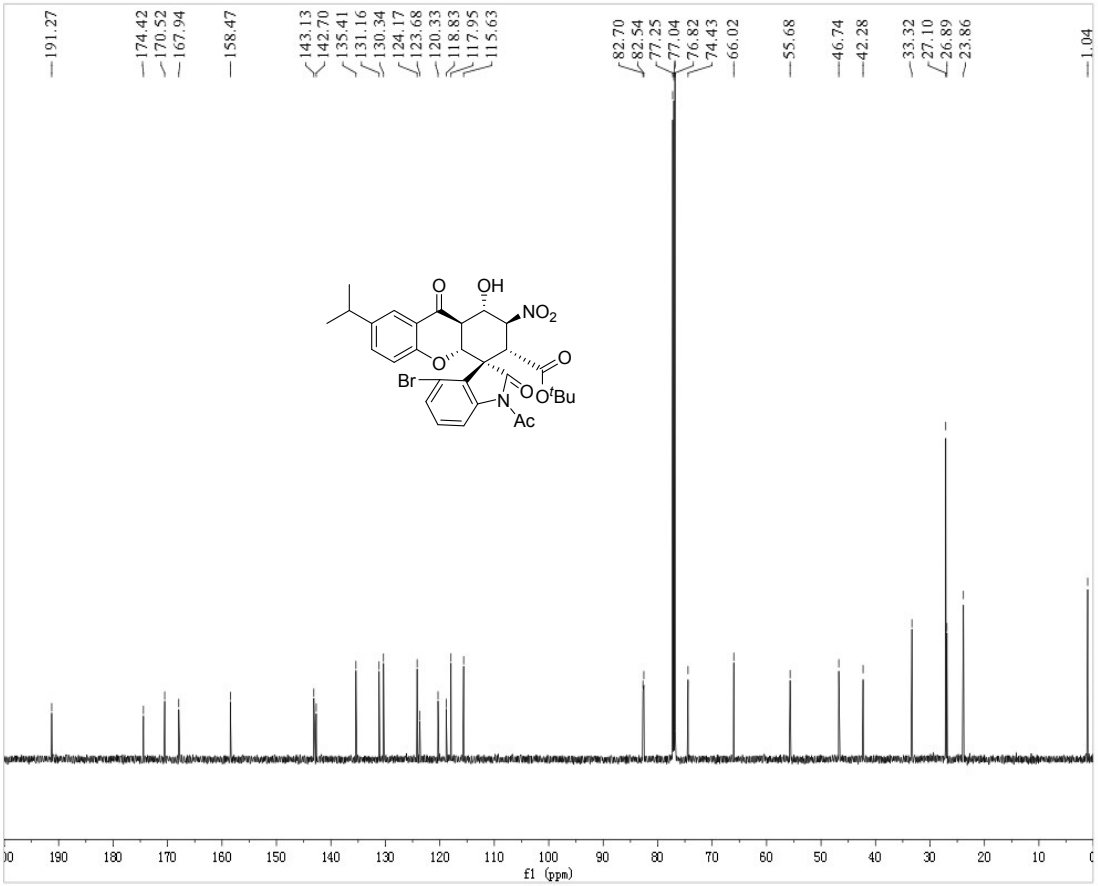
#	Time	Area	Height	Width	Area%	Symmetry
1	23.259	78071	1416.1	0.9188	50.370	0.488
2	37.226	76924.1	824	1.5559	49.630	0.335



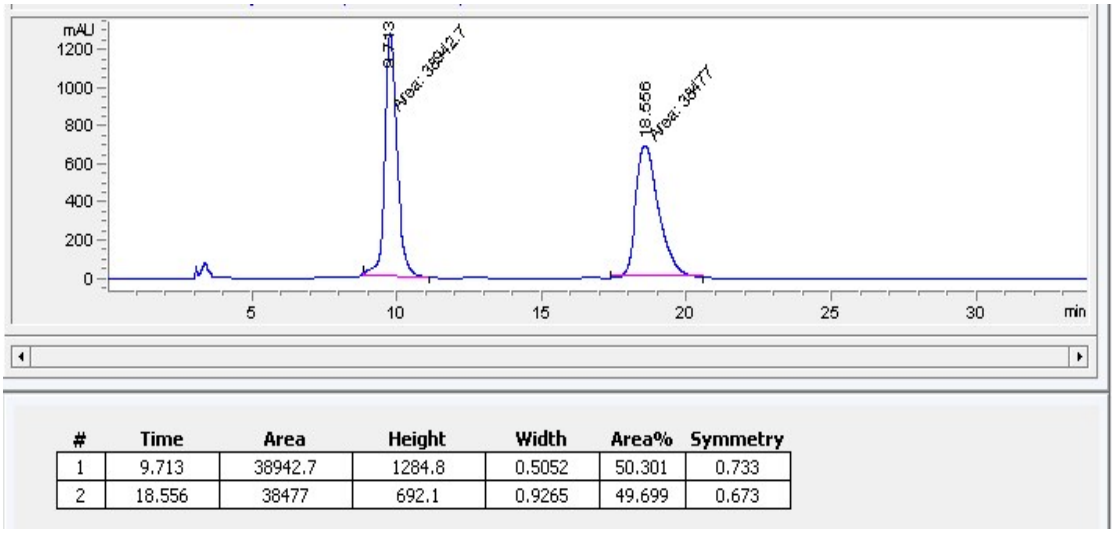
#	Time	Area	Height	Width	Area%	Symmetry
1	24.245	2177.1	42.1	0.8625	1.100	0.784
2	37.218	195795.9	1692	1.9287	98.900	0.315

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

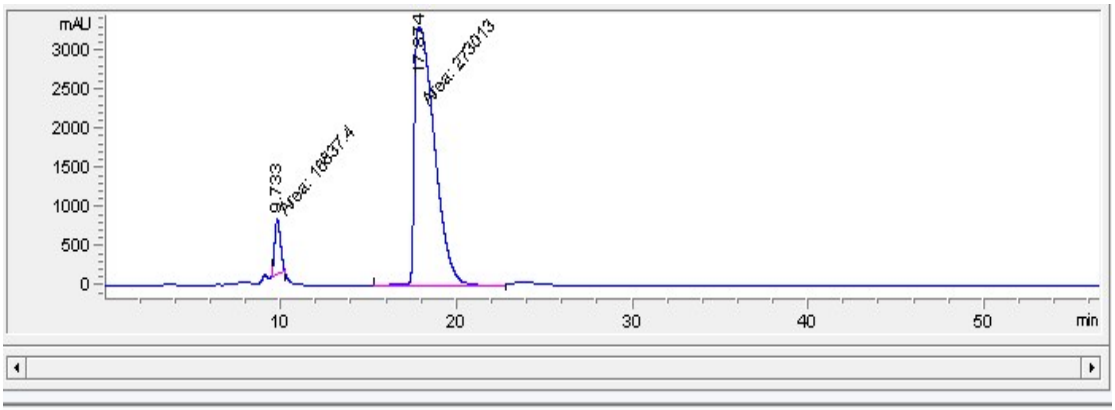




HPLC of 3t

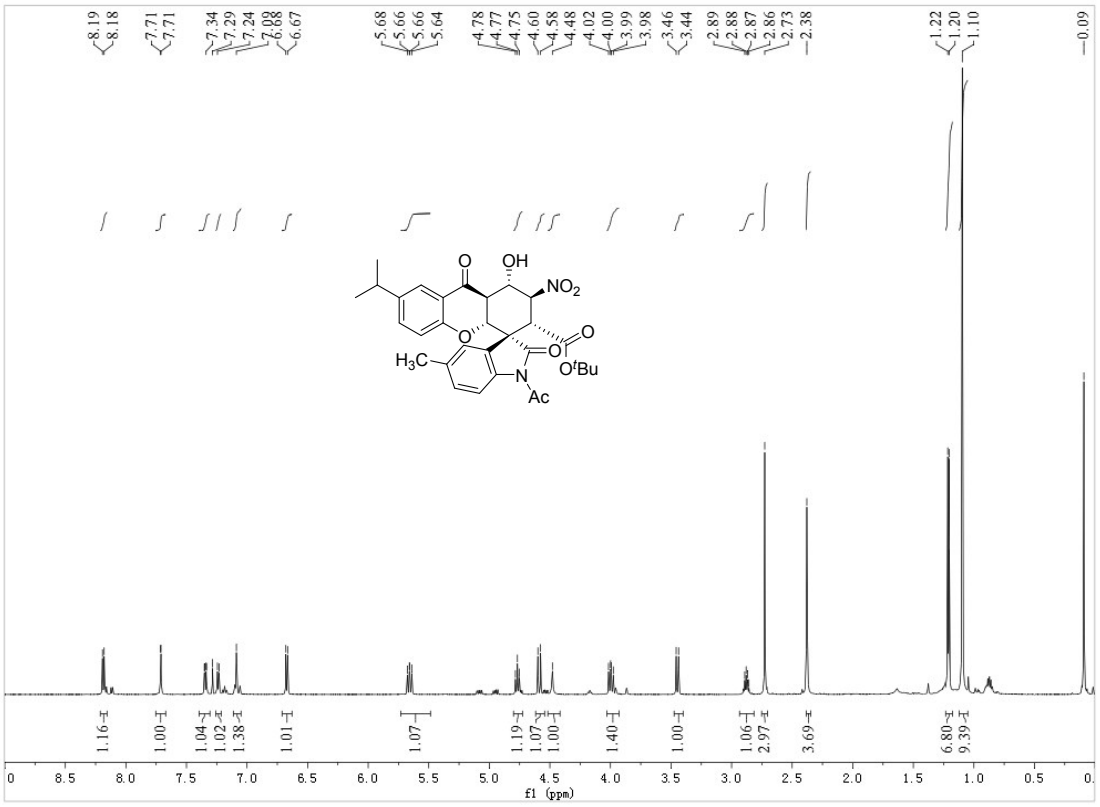


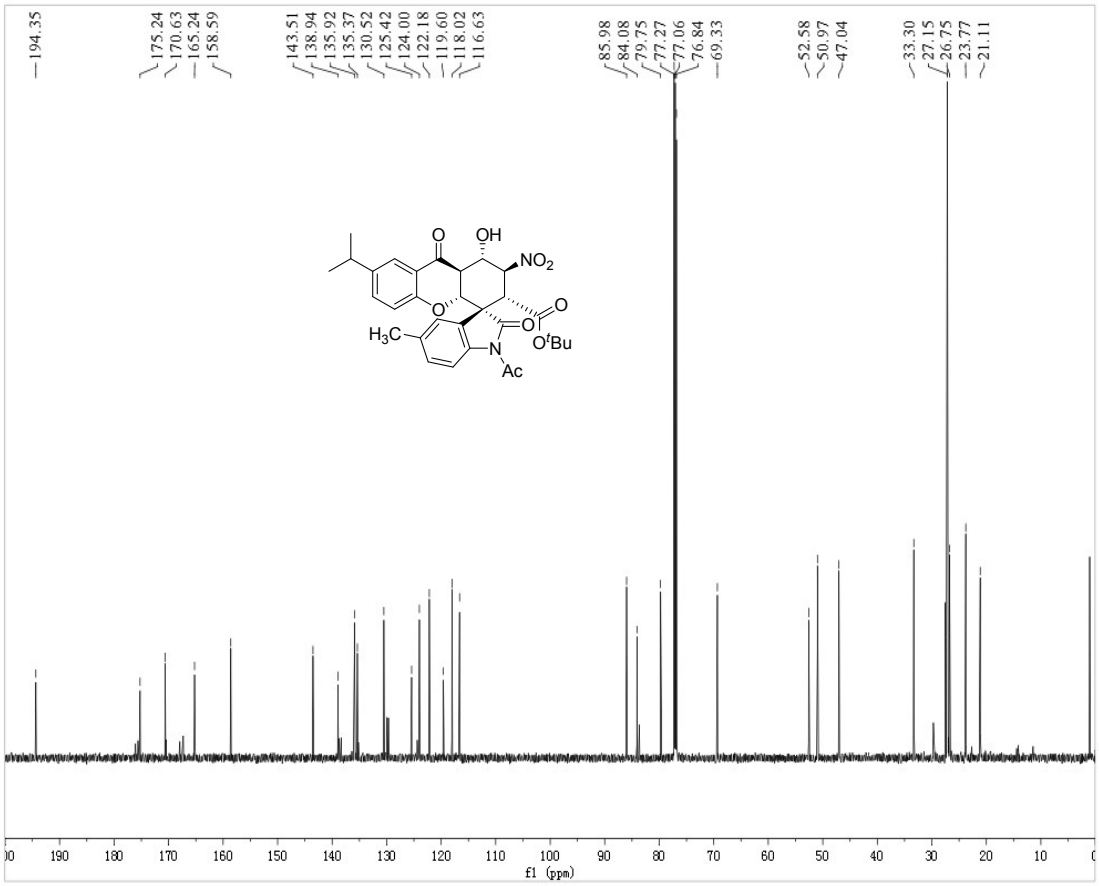
#	Time	Area	Height	Width	Area%	Symmetry
1	9.713	38942.7	1284.8	0.5052	50.301	0.733
2	18.556	38477	692.1	0.9265	49.699	0.673



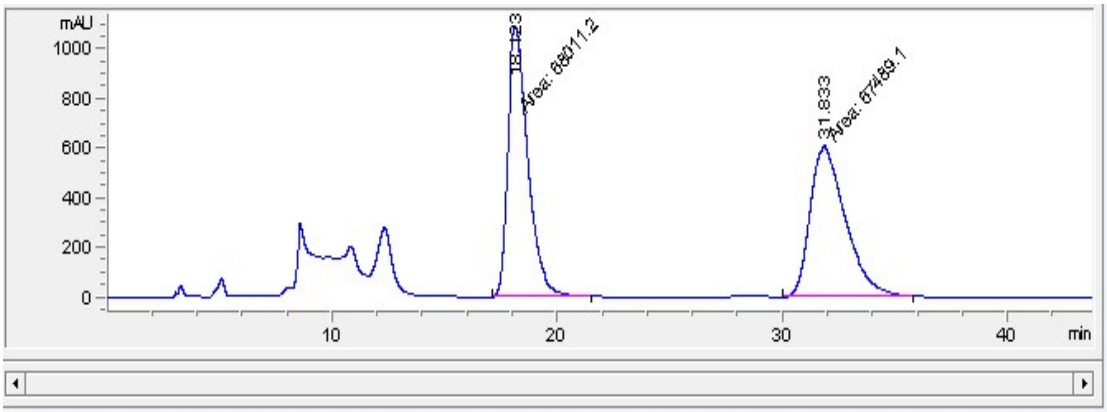
#	Time	Area	Height	Width	Area%	Symmetry
1	9.733	16837.4	730.7	0.3841	5.809	0.757
2	17.874	273013.4	3325.5	1.3683	94.191	0.326

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

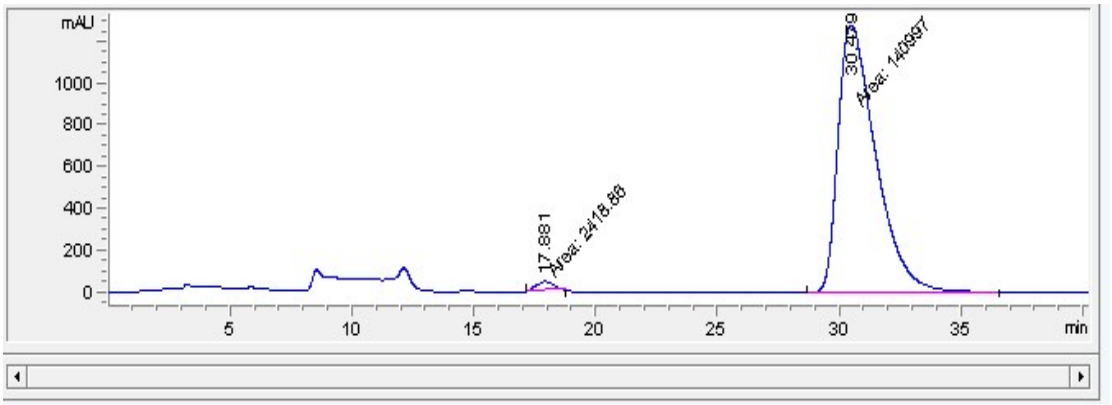




HPLC of 3u

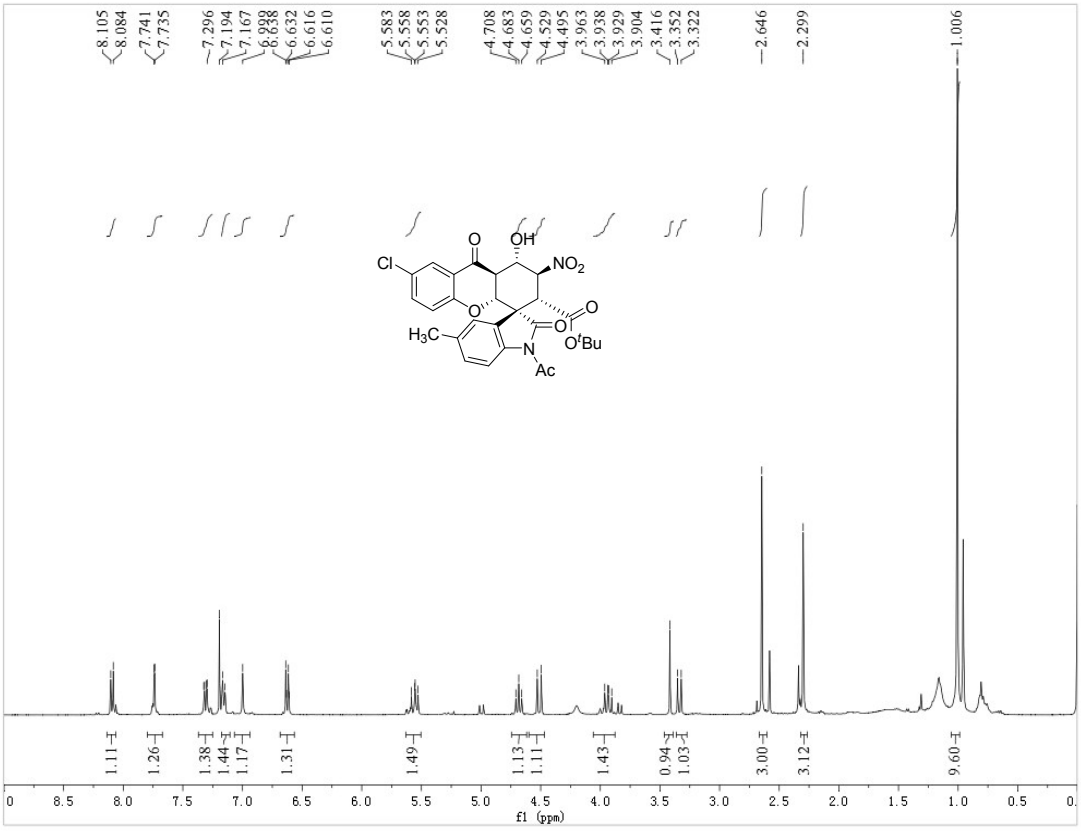


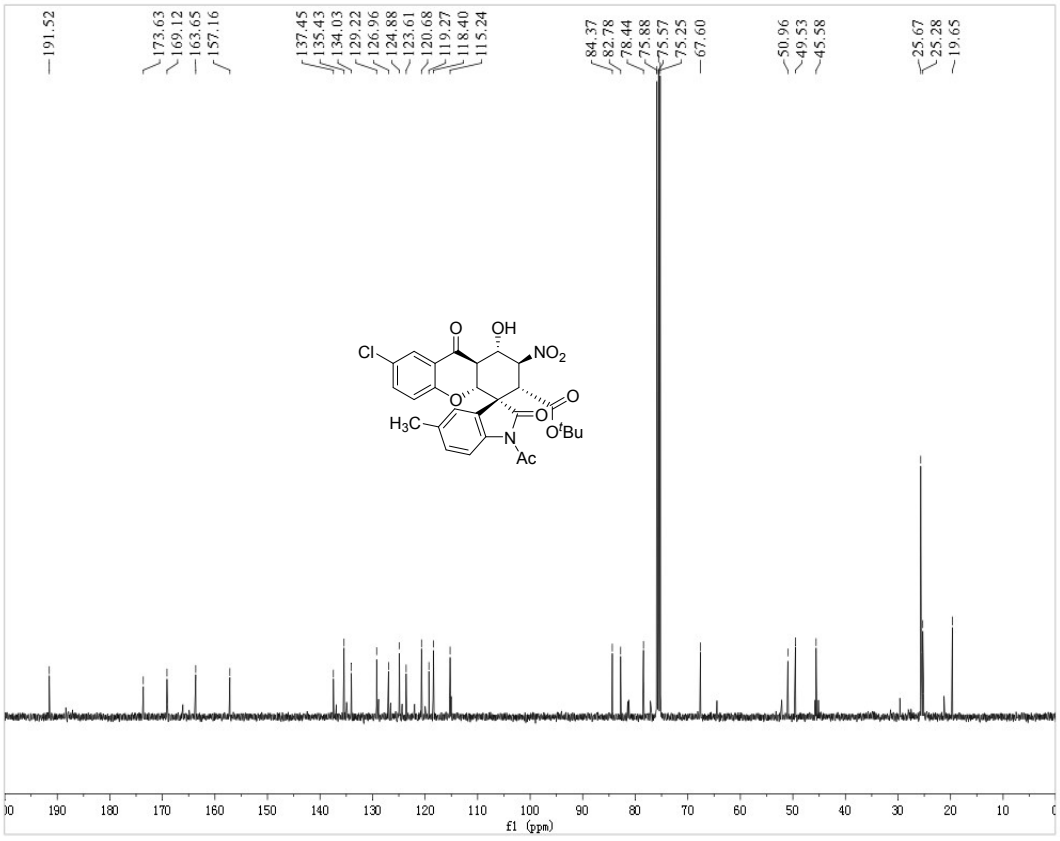
#	Time	Area	Height	Width	Area%	Symmetry
1	18.123	68011.2	1087.2	1.0426	50.193	0.639
2	31.833	67489.1	612.8	1.8356	49.807	0.647



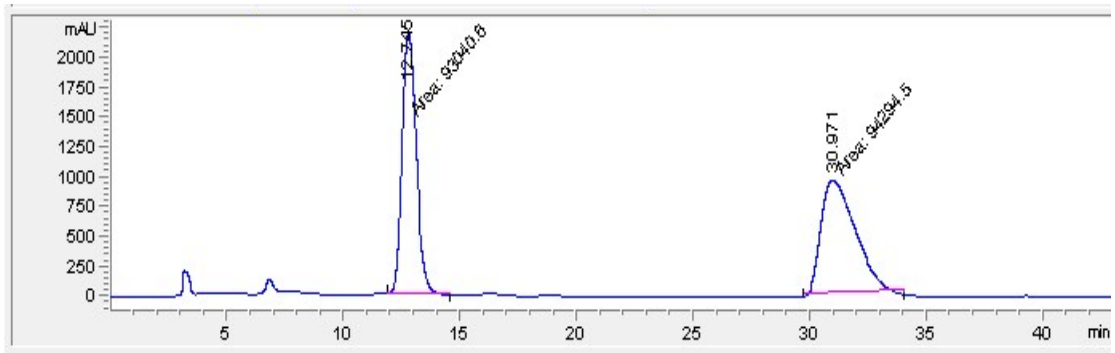
#	Time	Area	Height	Width	Area%	Symmetry
1	17.881	2418.9	47.5	0.8487	1.687	1.02
2	30.479	140996.5	1287.5	1.8252	98.313	0.52

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

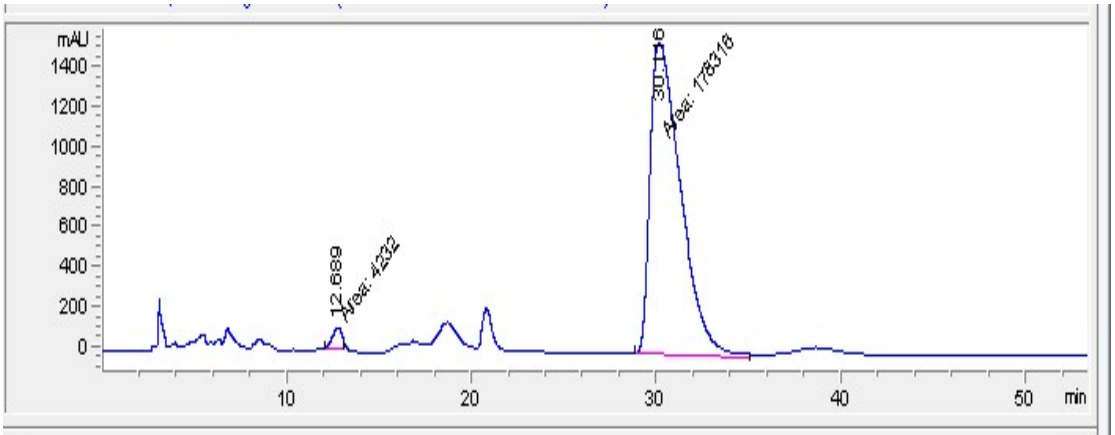




HPLC of 3v

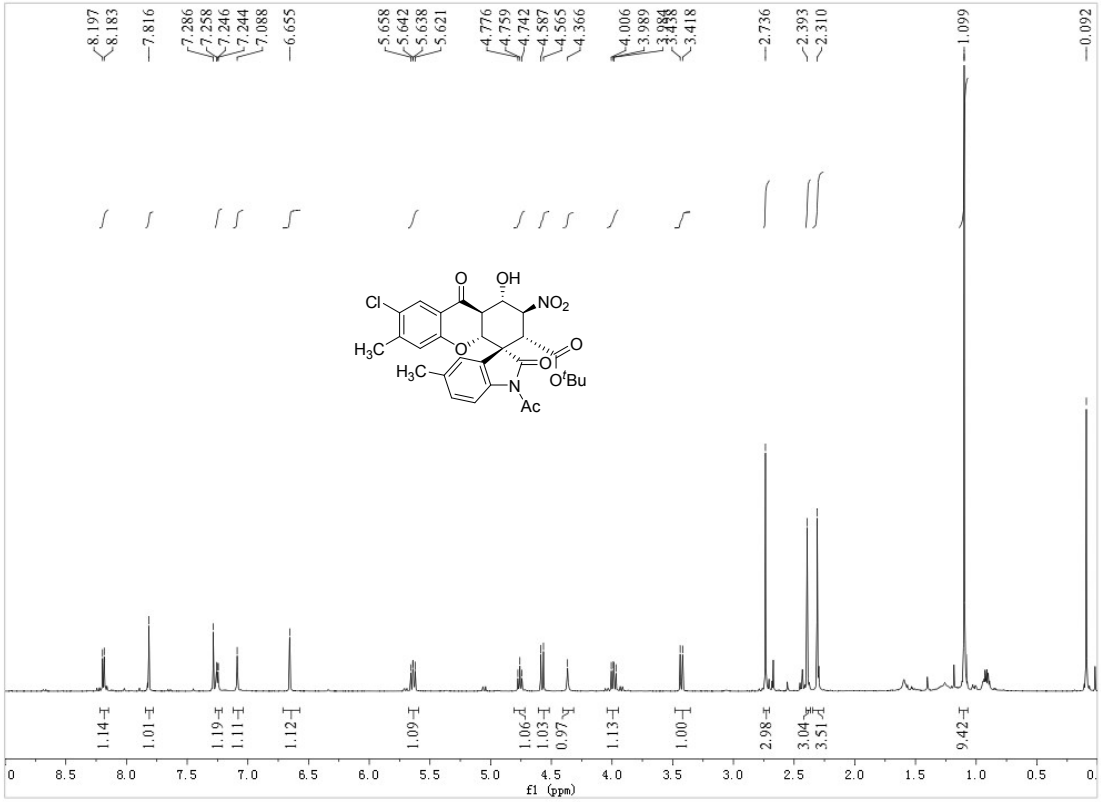


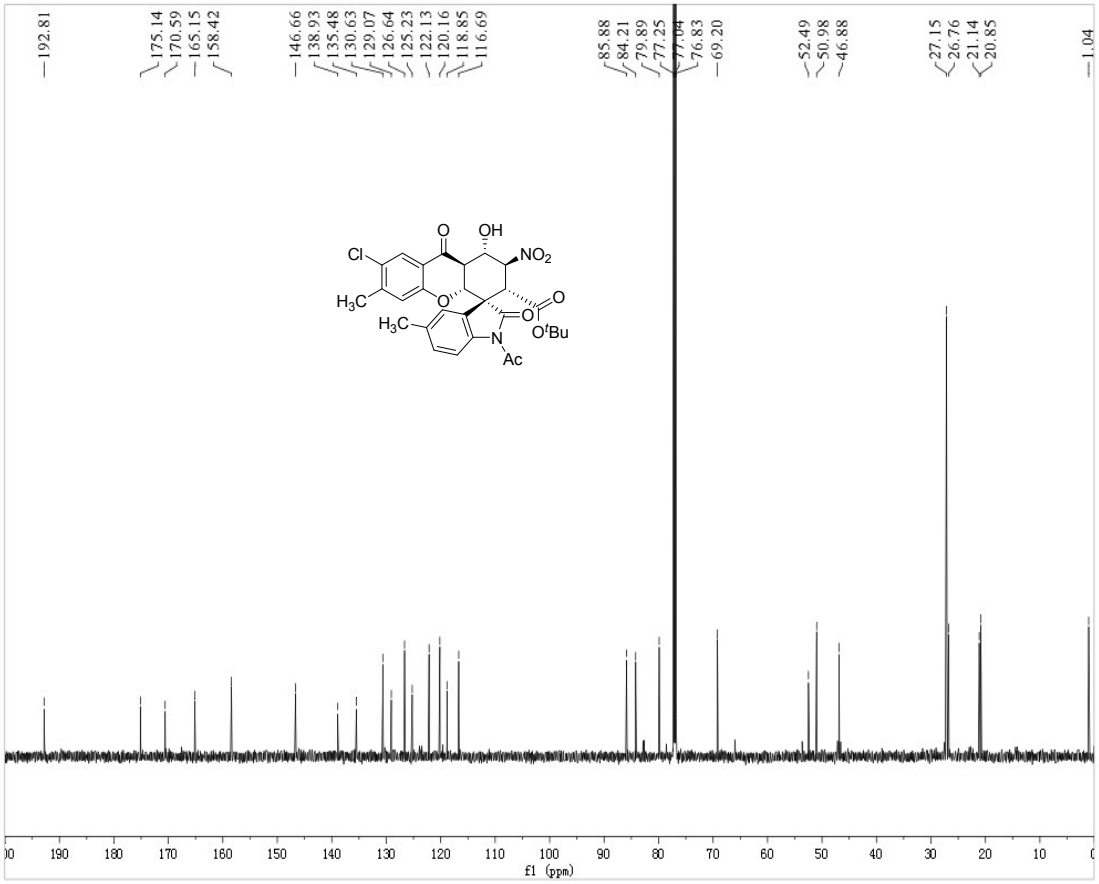
#	Time	Area	Height	Width	Area%	Symmetry
1	12.745	93040.6	2189.9	0.7081	49.665	0.755
2	30.971	94294.5	949.8	1.6546	50.335	0.523



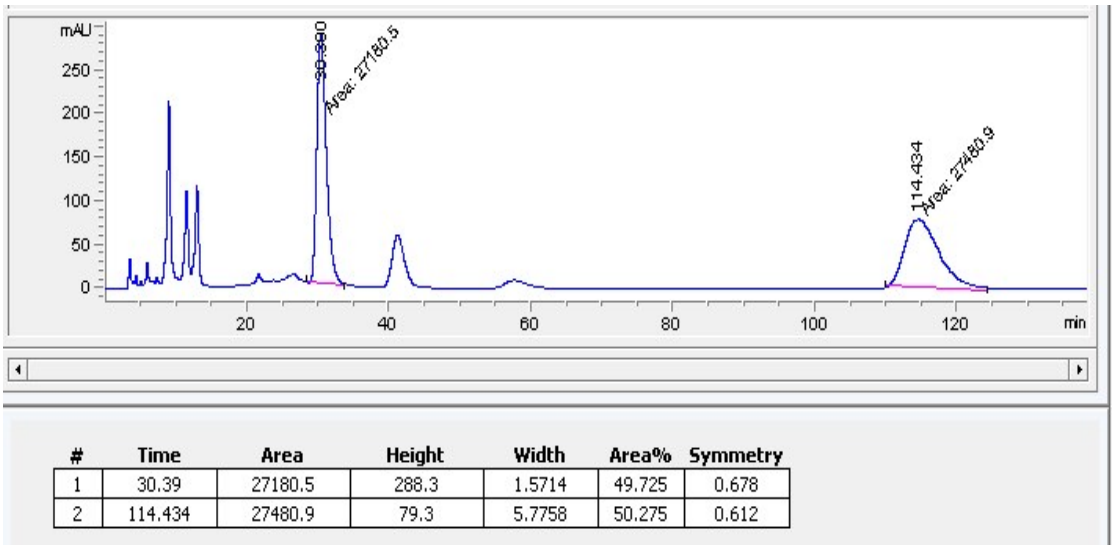
#	Time	Area	Height	Width	Area%	Symmetry
1	12.689	4232	112.4	0.6274	2.318	0.99
2	30.116	178315.9	1554.2	1.9122	97.682	0.395

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

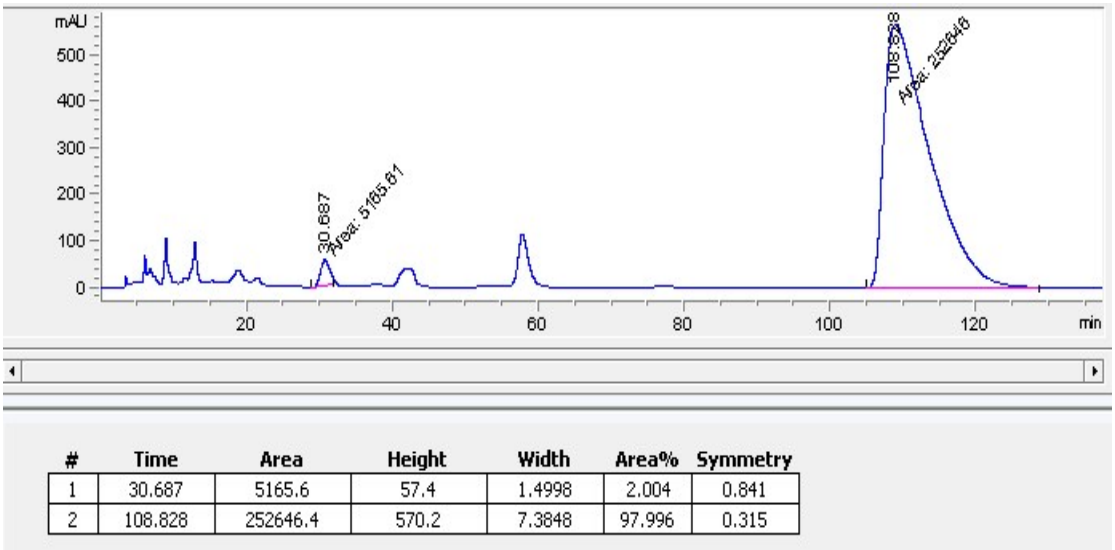




HPLC of 3w

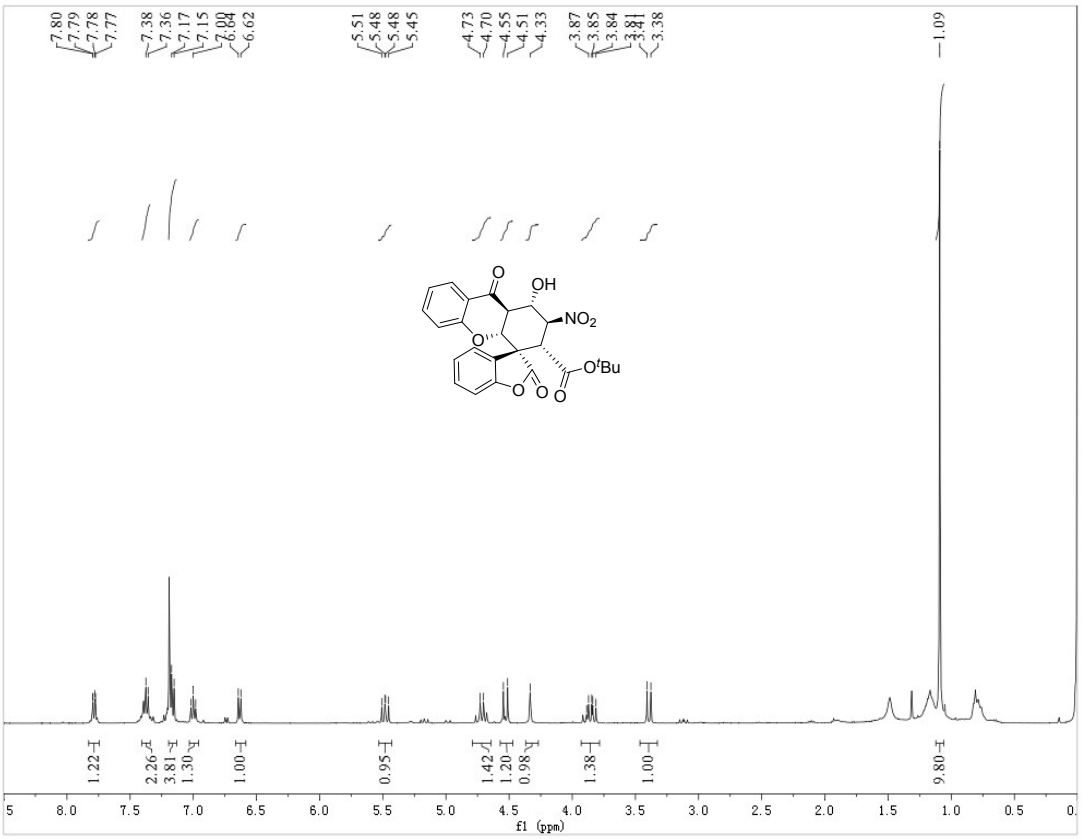


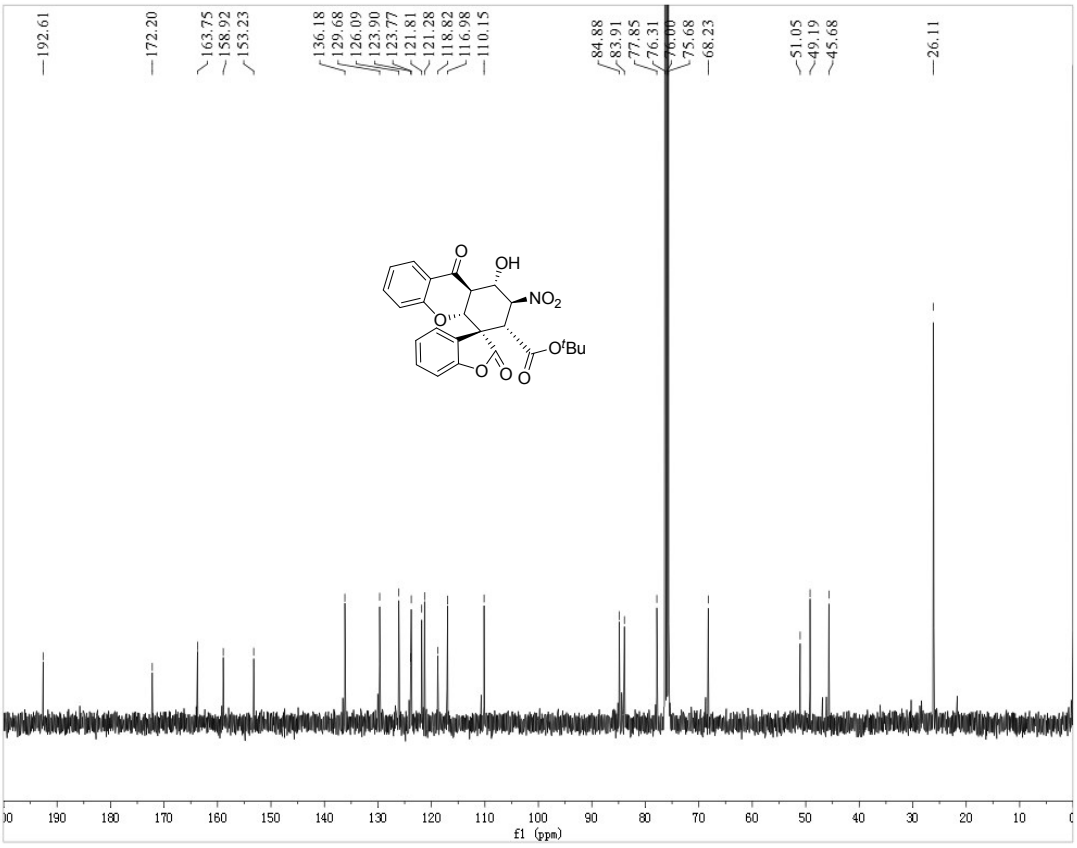
#	Time	Area	Height	Width	Area%	Symmetry
1	30.39	27180.5	288.3	1.5714	49.725	0.678
2	114.434	27480.9	79.3	5.7758	50.275	0.612



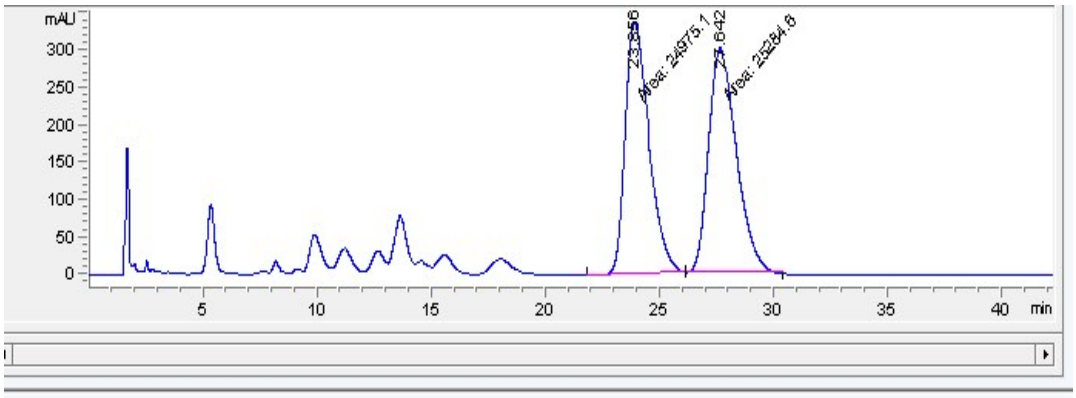
#	Time	Area	Height	Width	Area%	Symmetry
1	30.687	5165.6	57.4	1.4998	2.004	0.841
2	108.828	252646.4	570.2	7.3848	97.996	0.315

^{1}H and ^{13}C NMR of 5a

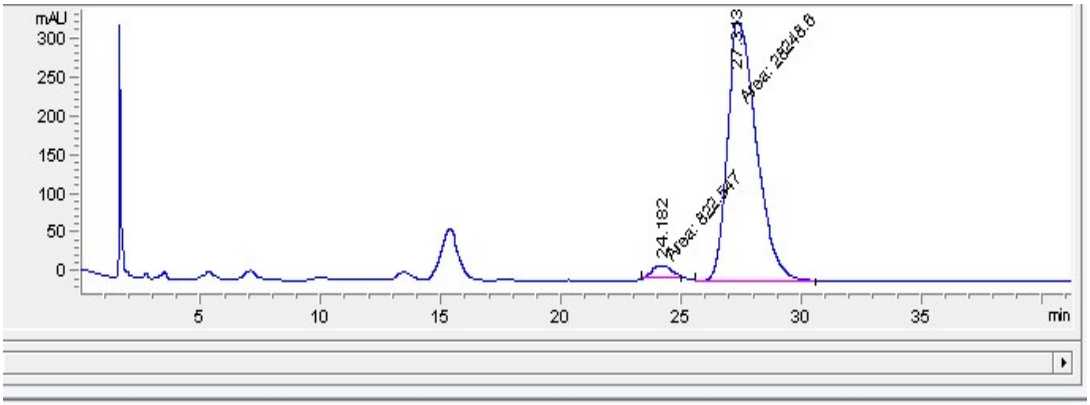




HPLC of 5a

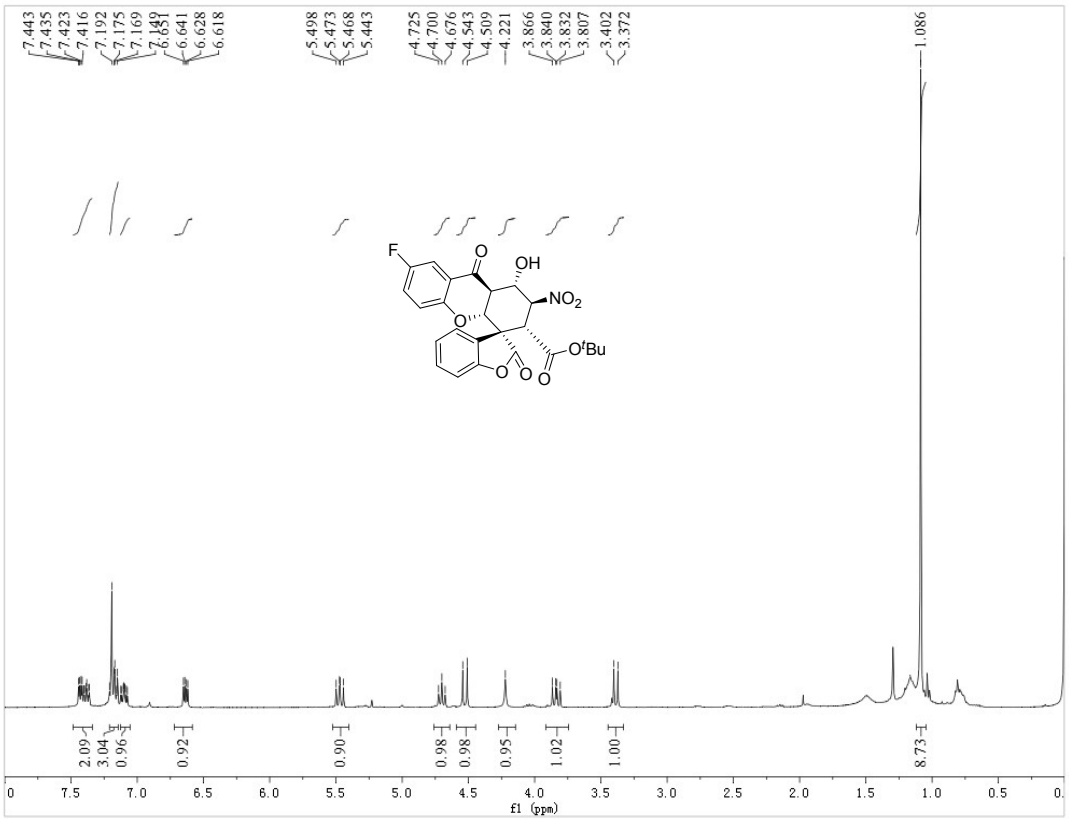


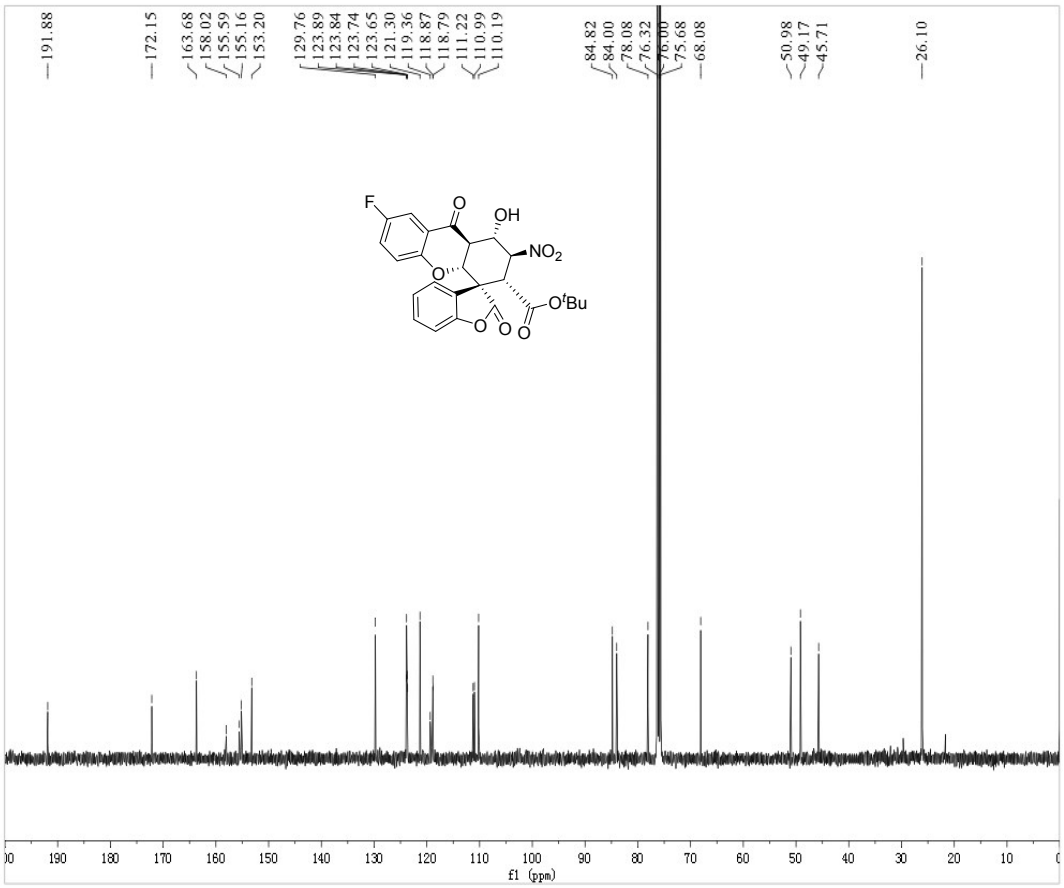
#	Time	Area	Height	Width	Area%	Symmetry
1	23.856	24975.1	337.1	1.2348	49.692	0.588
2	27.642	25284.6	302.7	1.3924	50.308	0.709



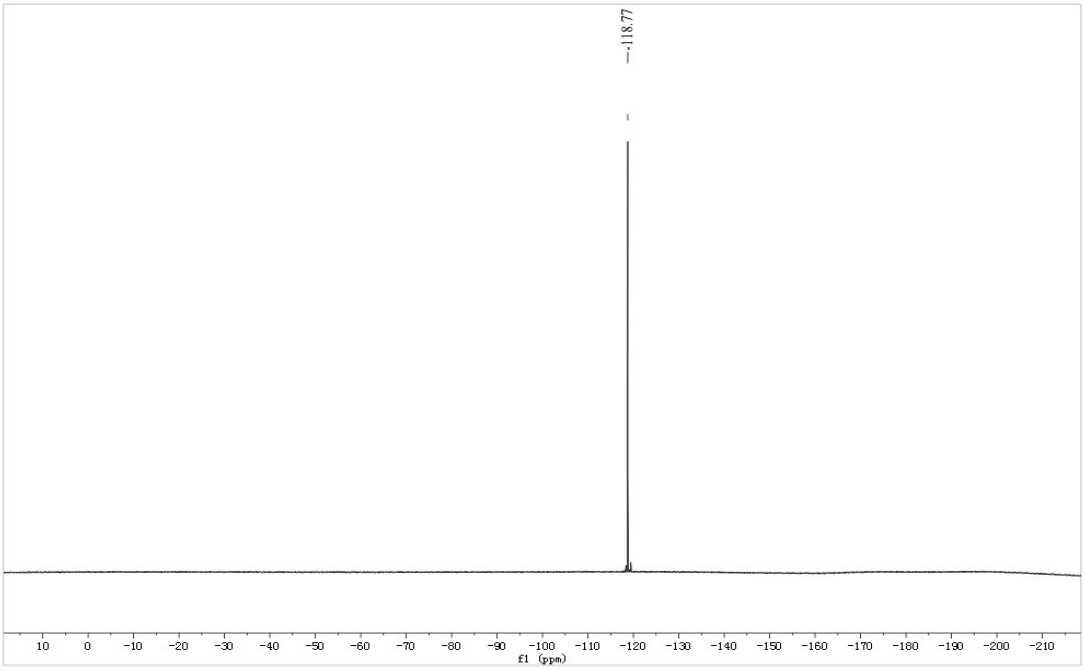
#	Time	Area	Height	Width	Area%	Symmetry
1	24.182	822.5	14.7	0.9299	2.829	0.99
2	27.313	28248.6	333.5	1.4116	97.171	0.532

^{1}H and ^{13}C NMR of 5b

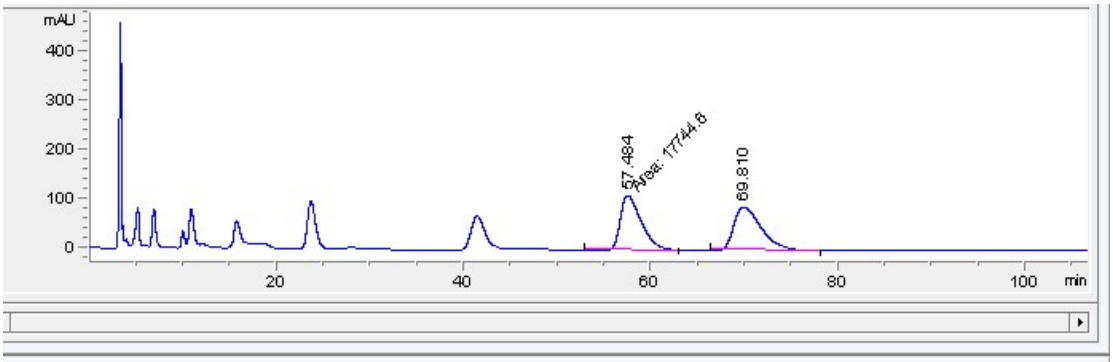




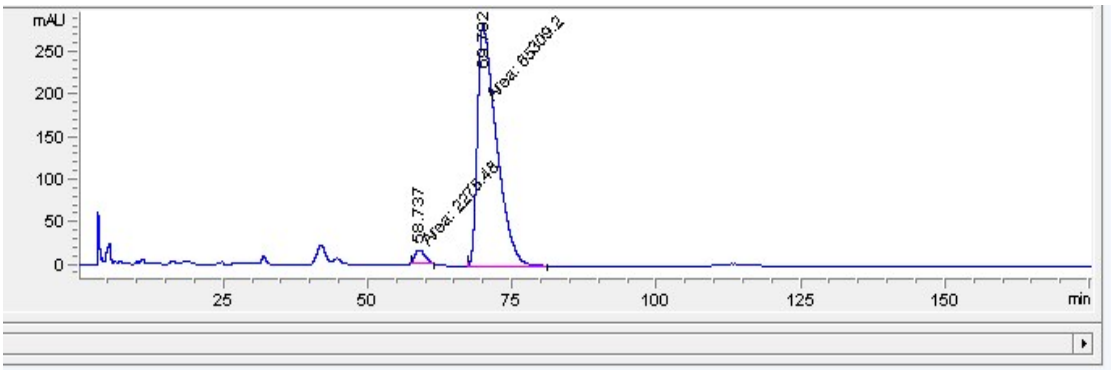
^{19}F NMR of 5b



HPLC of 5b

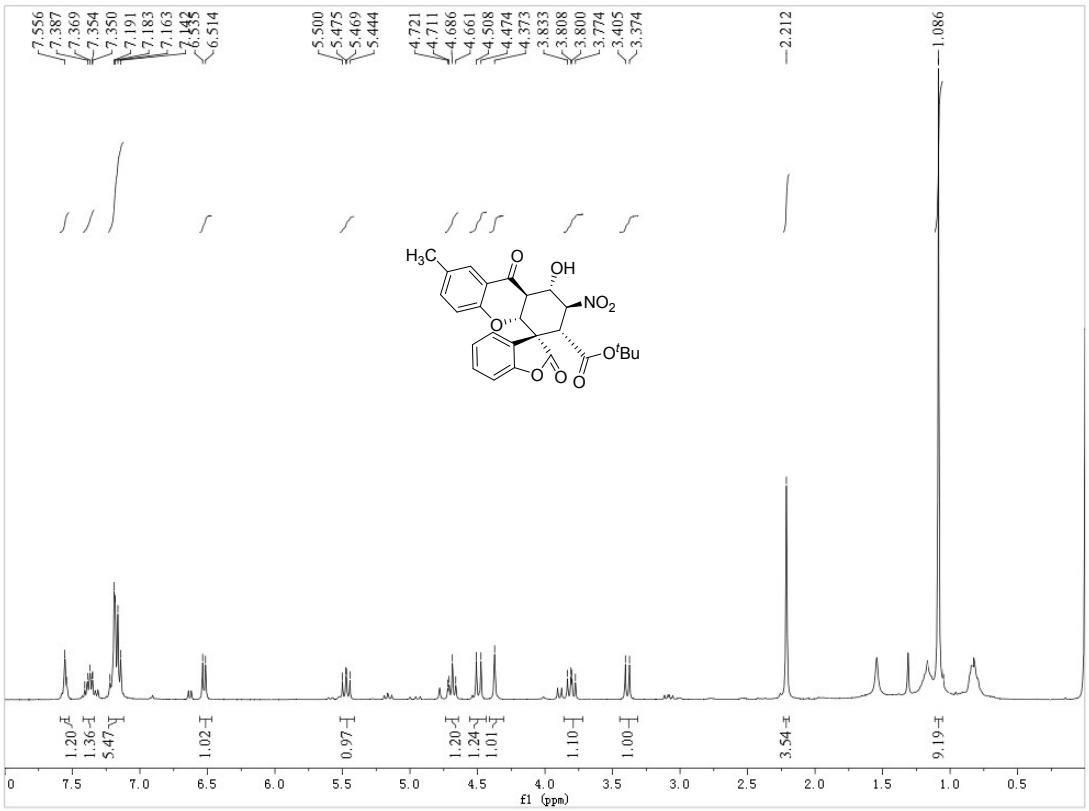


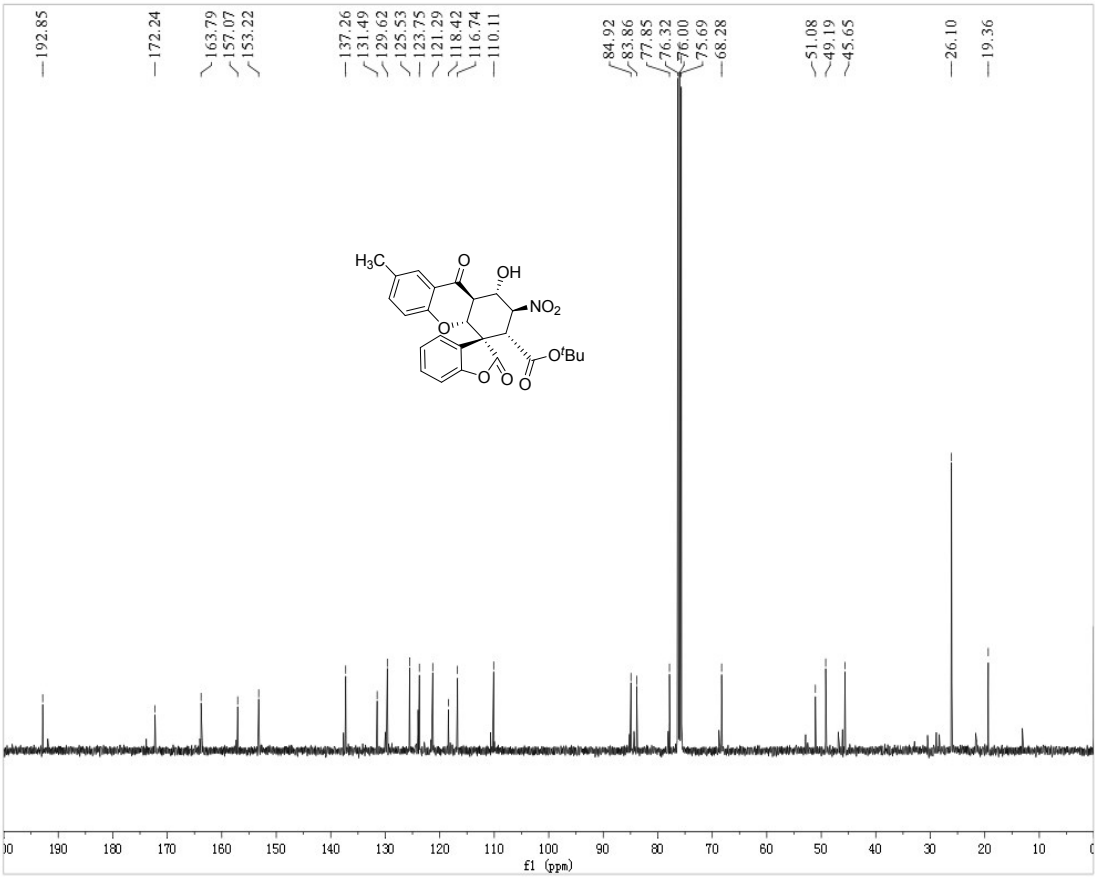
#	Time	Area	Height	Width	Area%	Symmetry
1	57.484	17744.6	111.7	2.647	49.974	0.486
2	69.81	17762.9	88.4	2.6826	50.026	0.503



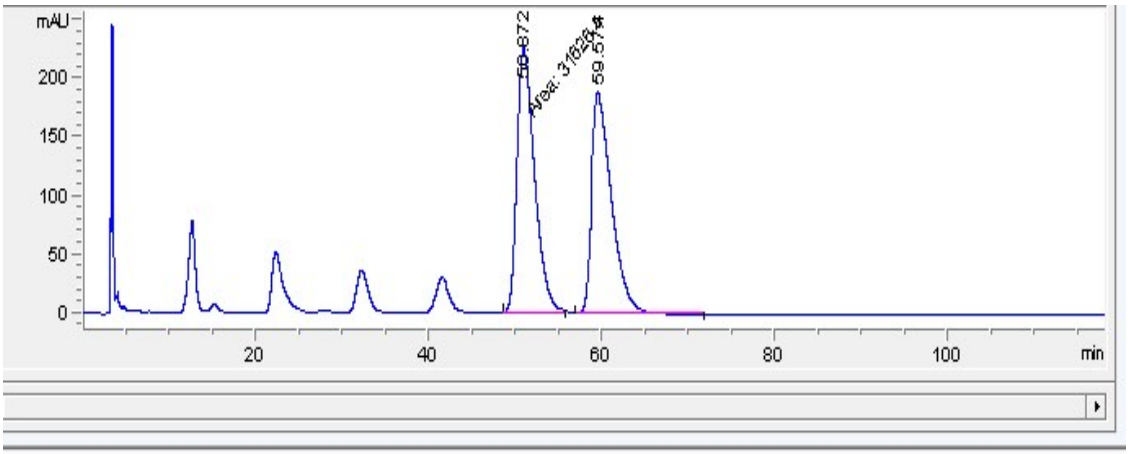
#	Time	Area	Height	Width	Area%	Symmetry
1	58.737	2275.5	17.6	2.1605	3.367	0.665
2	69.792	65309.2	286.3	3.8016	96.633	0.393

^{1}H and ^{13}C NMR of 5c

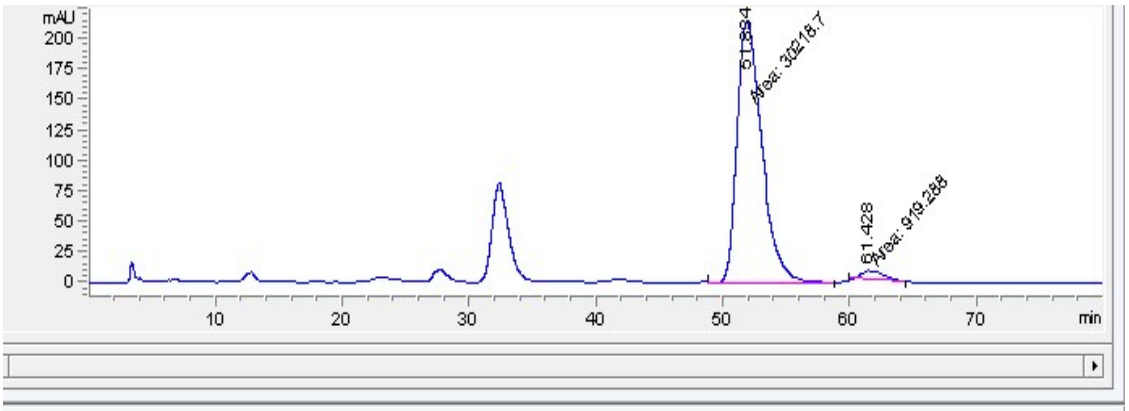




HPLC of 5c

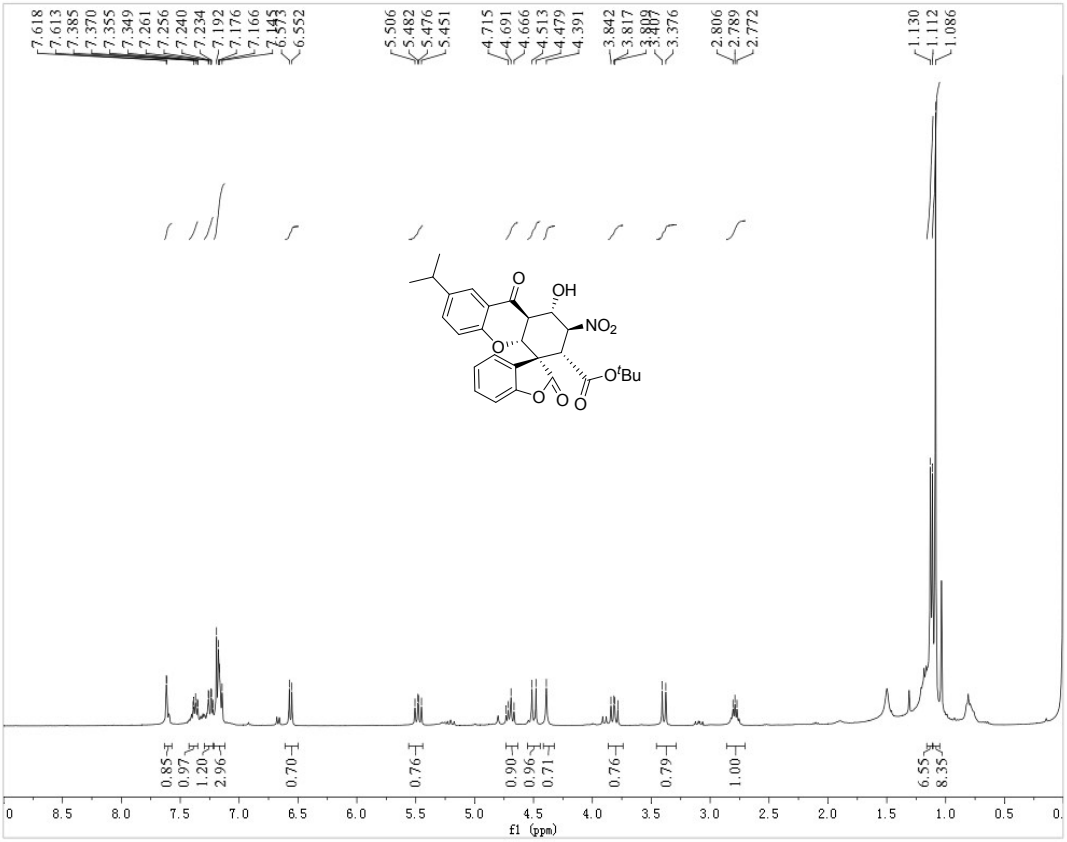


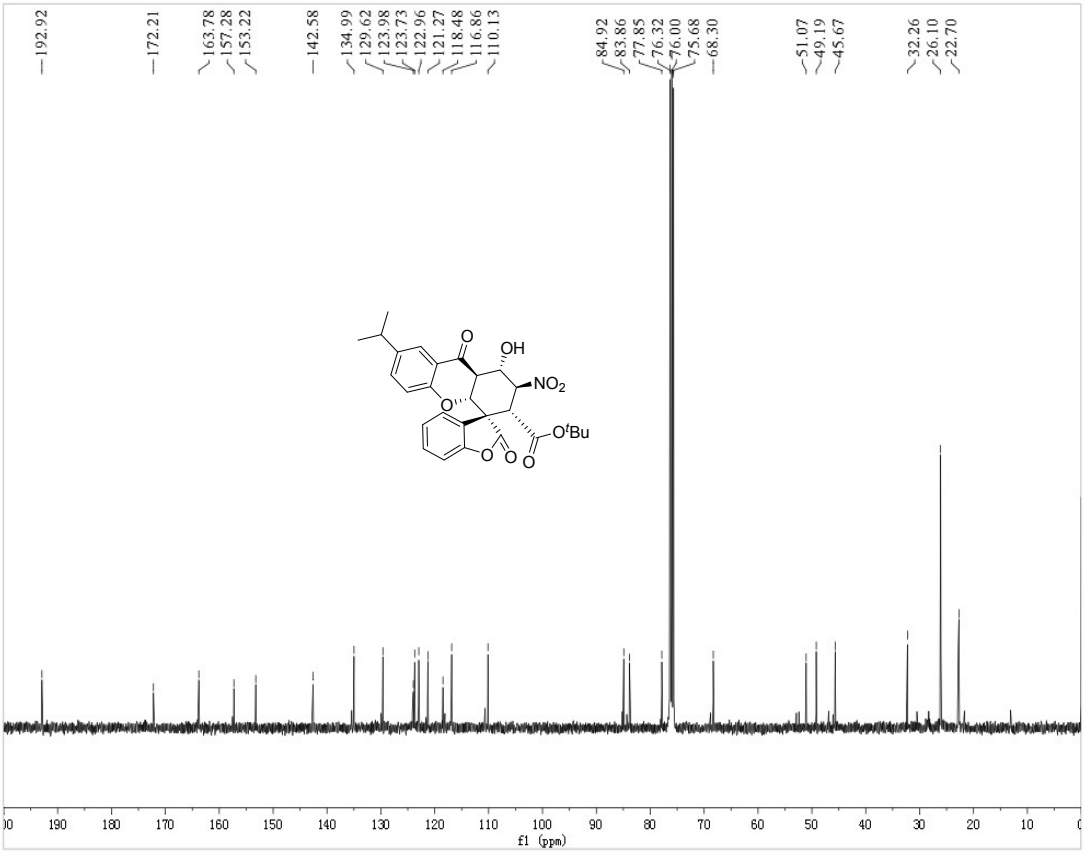
#	Time	Area	Height	Width	Area%	Symmetry
1	50.872	31626.4	227.1	2.3212	50.470	0.588
2	59.574	31037.4	189.5	2.1989	49.530	0.511



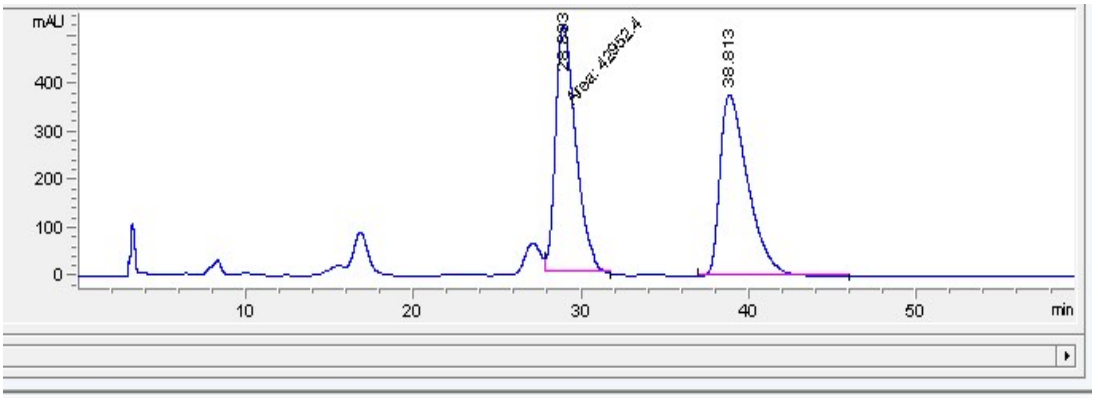
#	Time	Area	Height	Width	Area%	Symmetry
1	51.834	30218.7	215.9	2.3329	97.048	0.626
2	61.428	919.3	7.6	2.0208	2.952	0.521

^{1}H and ^{13}C NMR of 5d

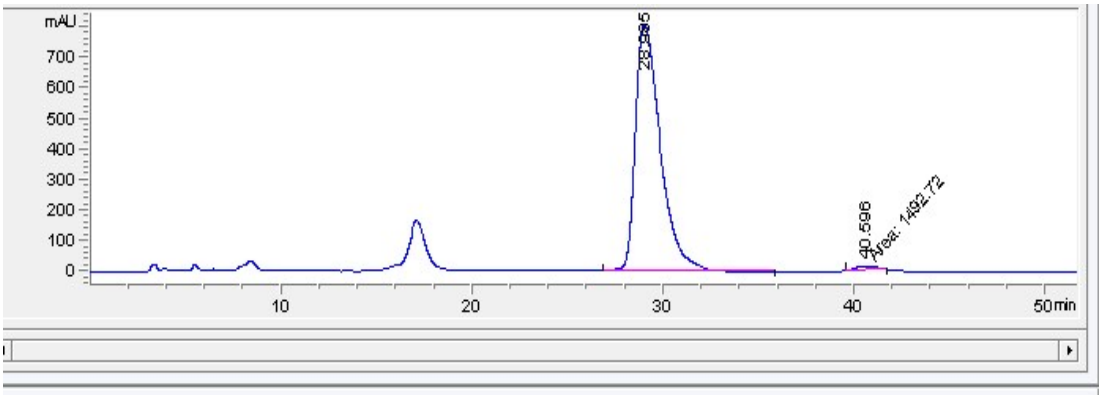




HPLC of 5d

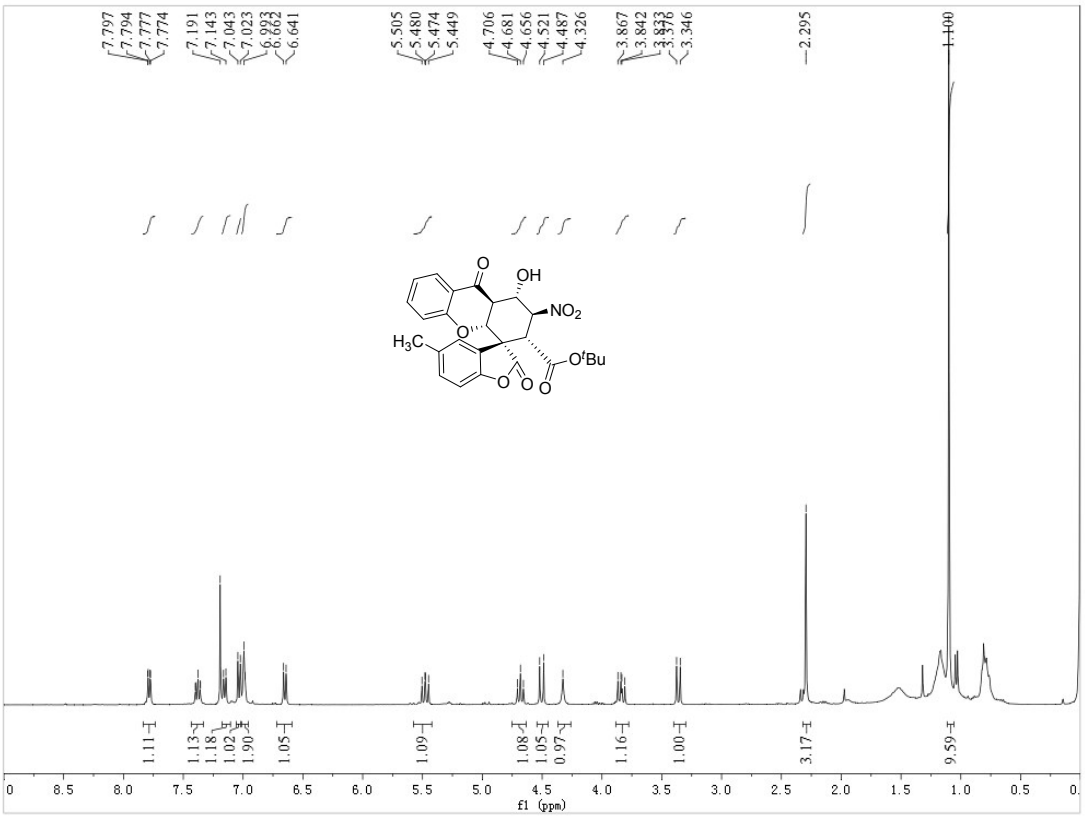


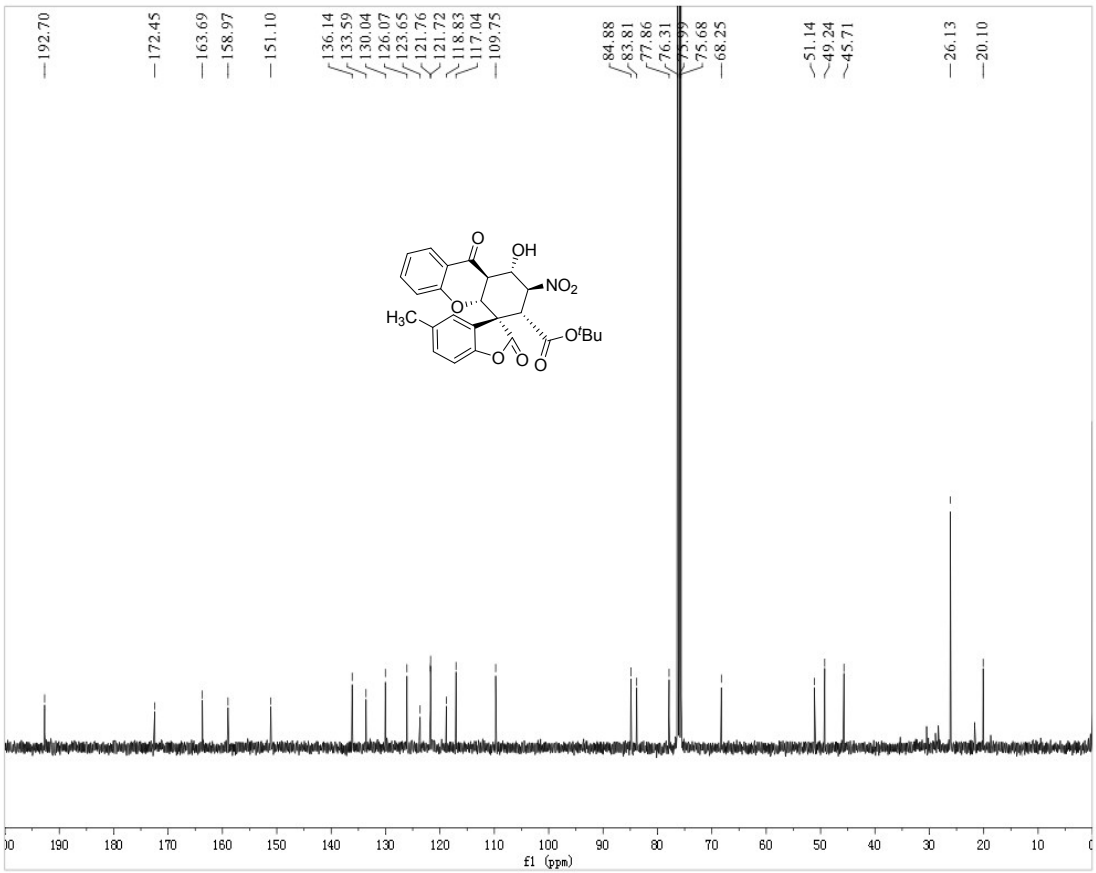
#	Time	Area	Height	Width	Area%	Symmetry
1	28.883	42952.4	516.3	1.3864	49.935	0.595
2	38.813	43063.7	378.4	1.7116	50.065	0.476



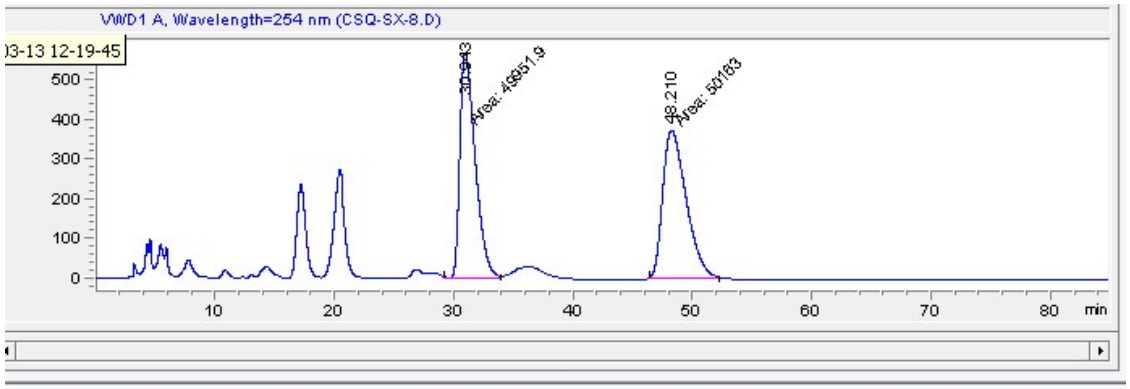
#	Time	Area	Height	Width	Area%	Symmetry
1	28.985	73683.9	808.5	1.3592	98.014	0.508
2	40.596	1492.7	16.9	1.4716	1.986	1.08

^{1}H and ^{13}C NMR of 5e

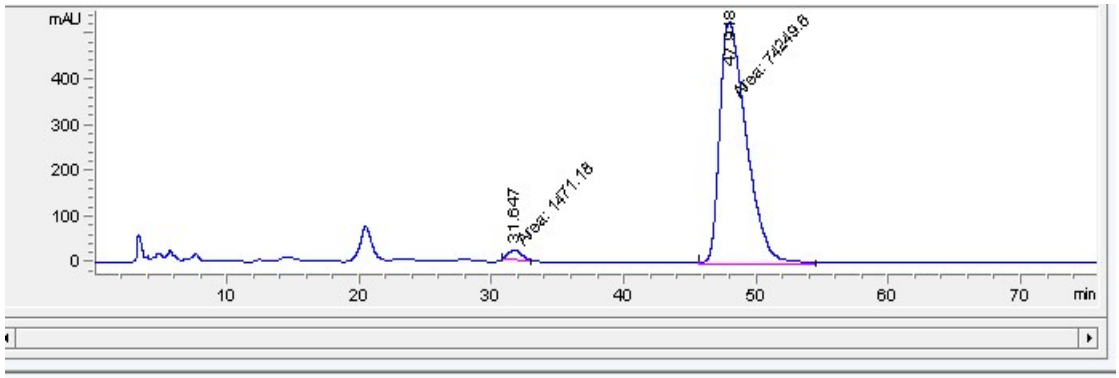




HPLC of 5e

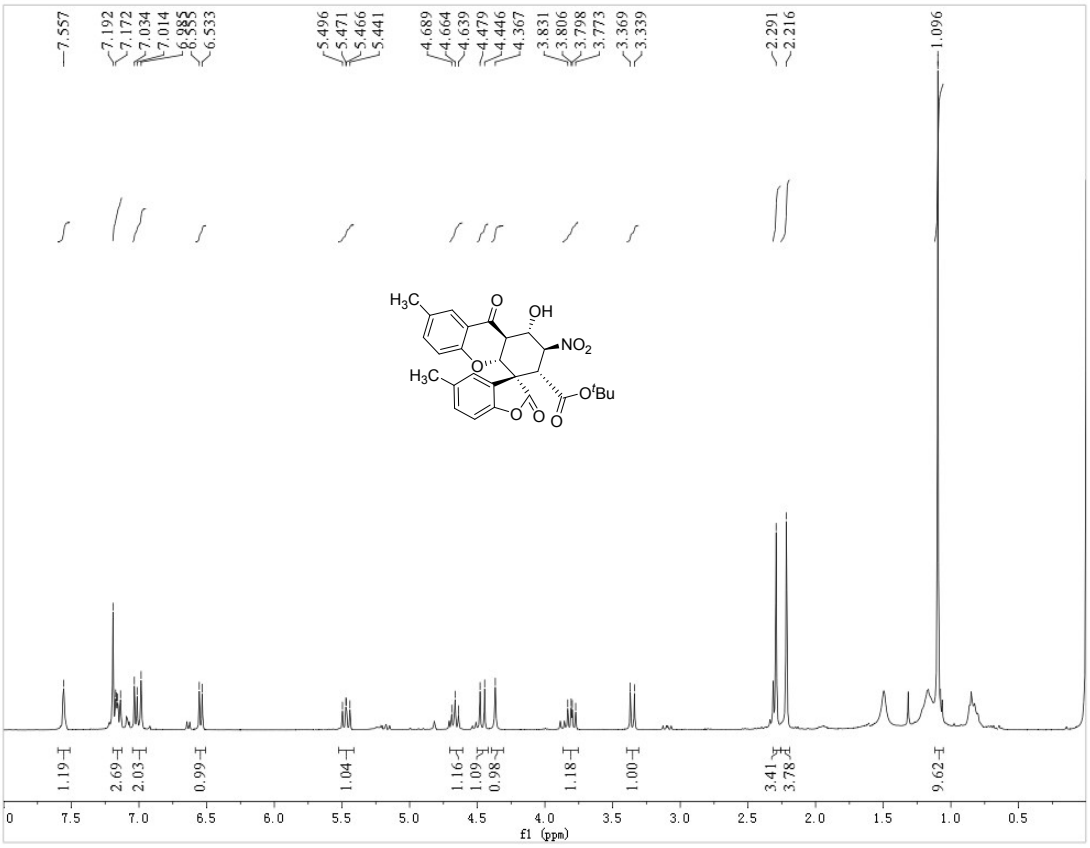


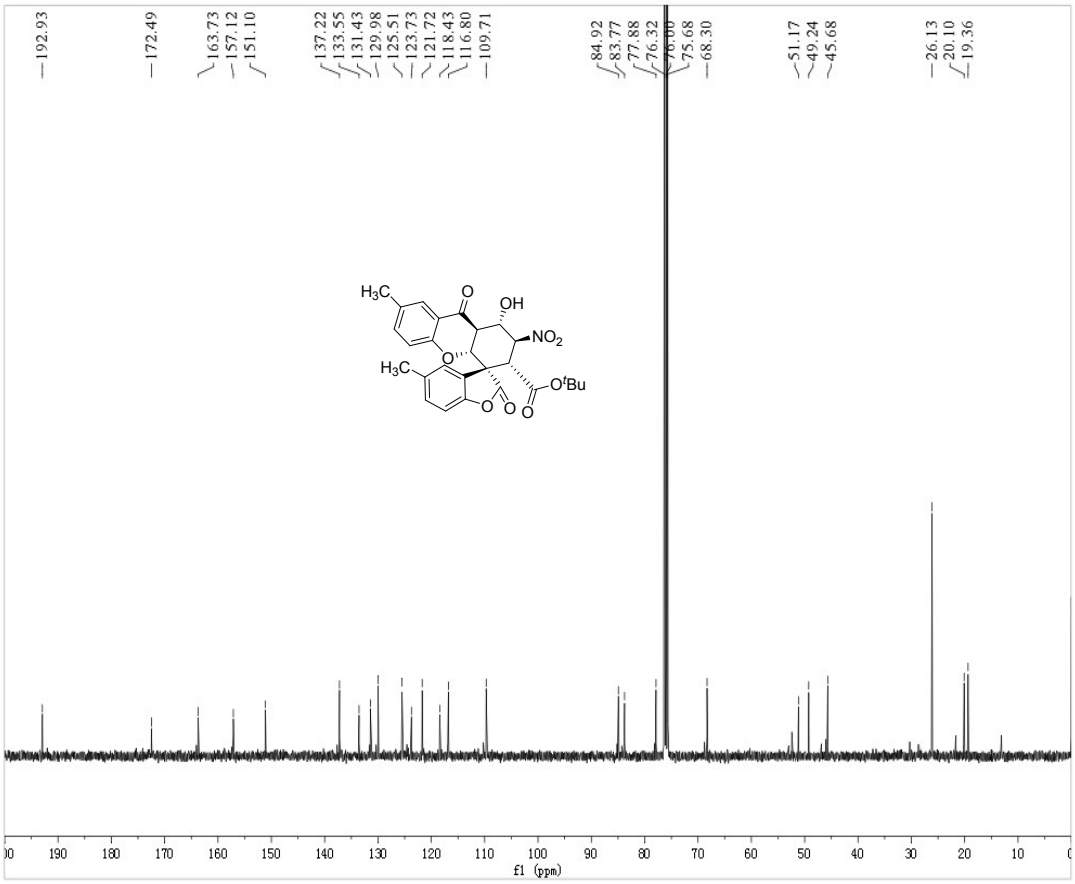
#	Time	Area	Height	Width	Area%	Symmetry
1	30.943	49951.9	568.5	1.4643	49.895	0.52
2	48.21	50163	374	2.2351	50.105	0.582



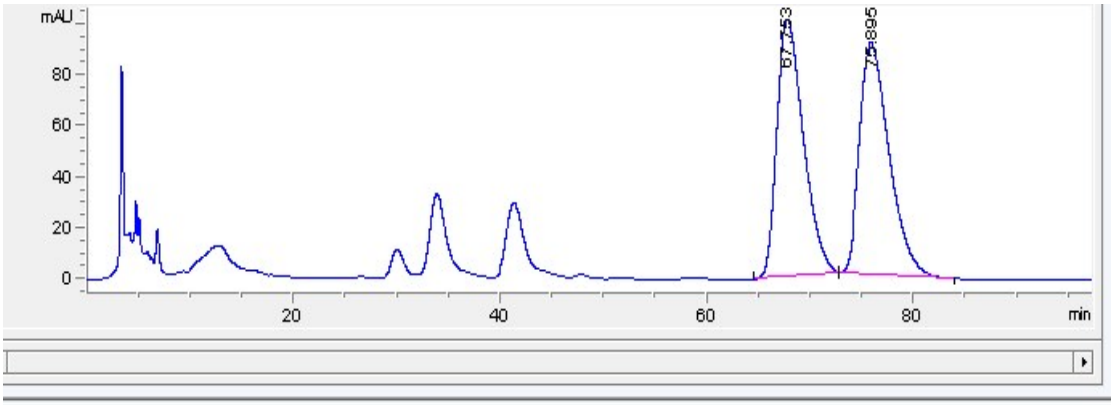
#	Time	Area	Height	Width	Area%	Symmetry
1	31.647	1471.2	21.4	1.1484	1.943	0.711
2	47.918	74249.6	529.6	2.3365	98.057	0.576

^{1}H and ^{13}C NMR of 5f

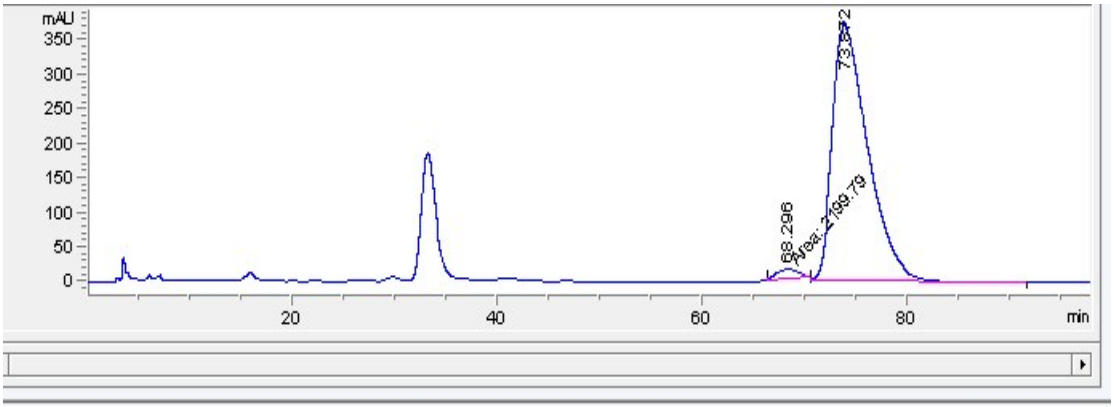




HPLC of 5f

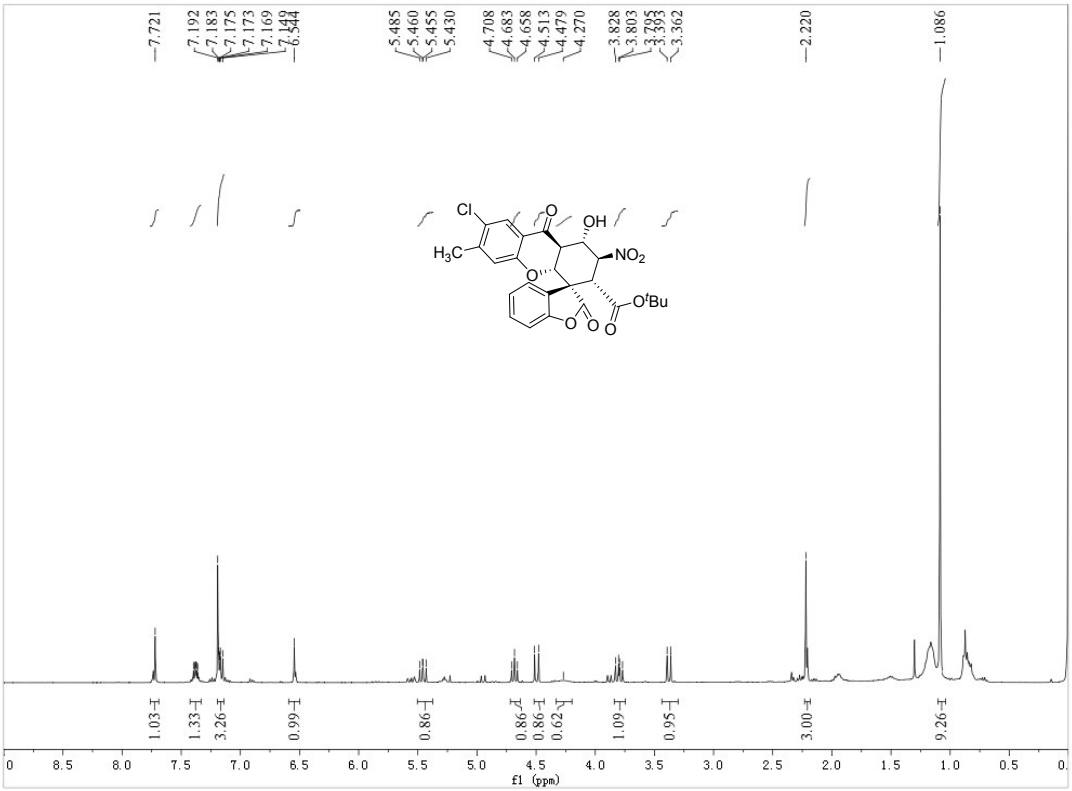


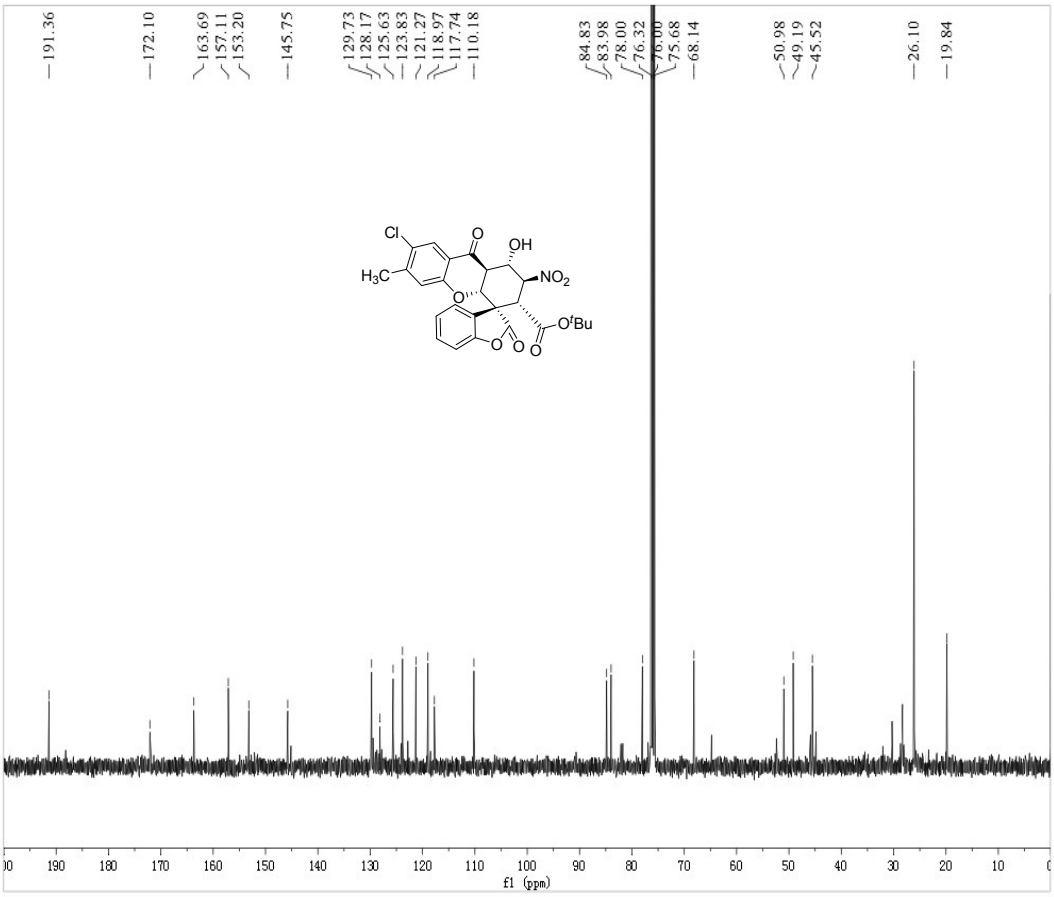
#	Time	Area	Height	Width	Area%	Symmetry
1	67.753	17874.6	101	2.1197	49.612	0.607
2	75.895	18154.5	91.6	2.4117	50.388	0.601



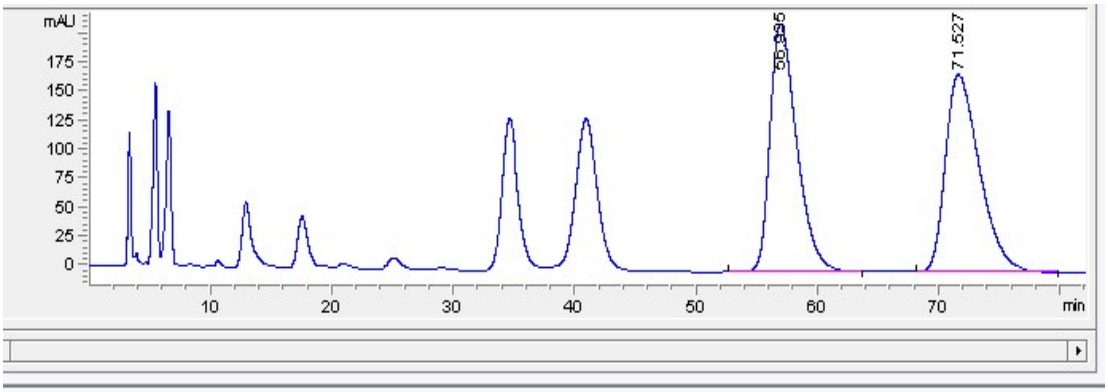
#	Time	Area	Height	Width	Area%	Symmetry
1	68.296	2199.8	14.8	2.4702	2.385	0.939
2	73.872	90044.2	377.3	2.8719	97.615	0.489

^{1}H and ^{13}C NMR of 5g

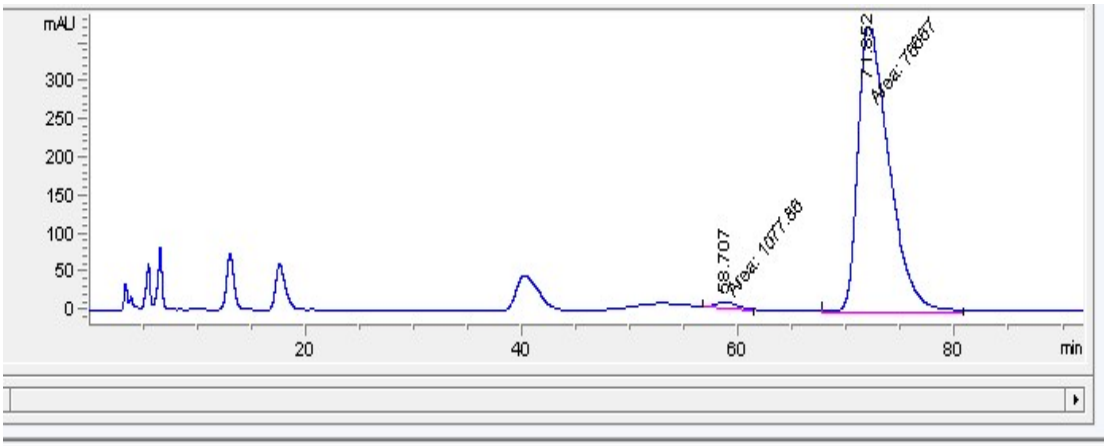




HPLC of 5g

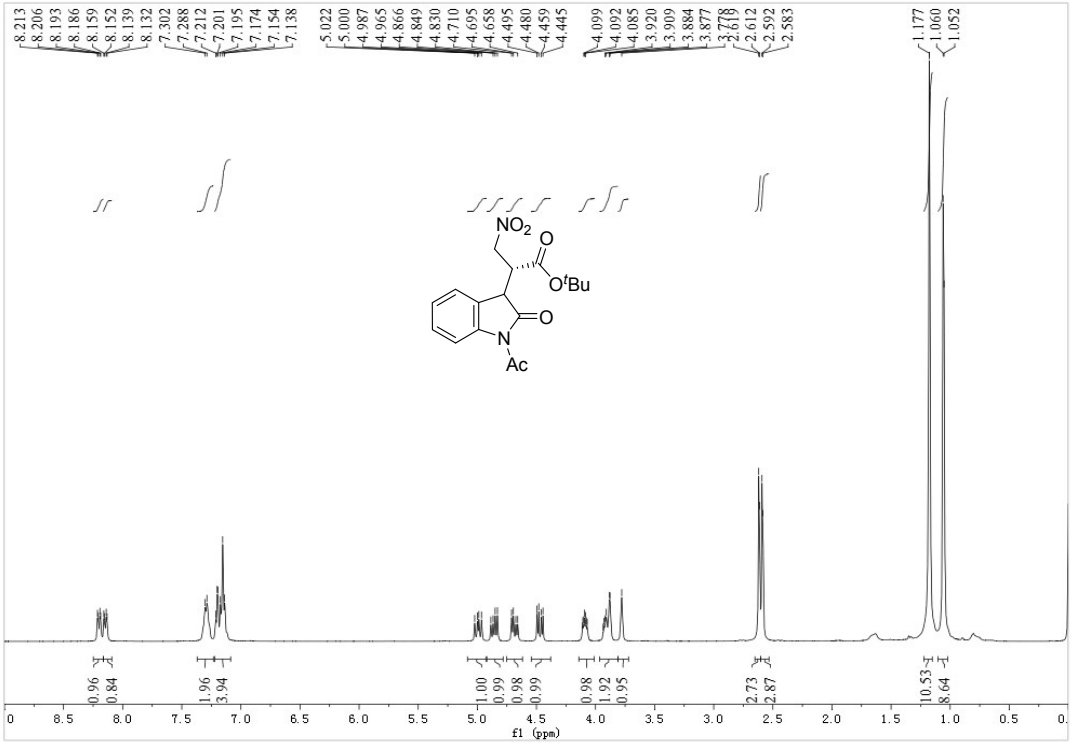


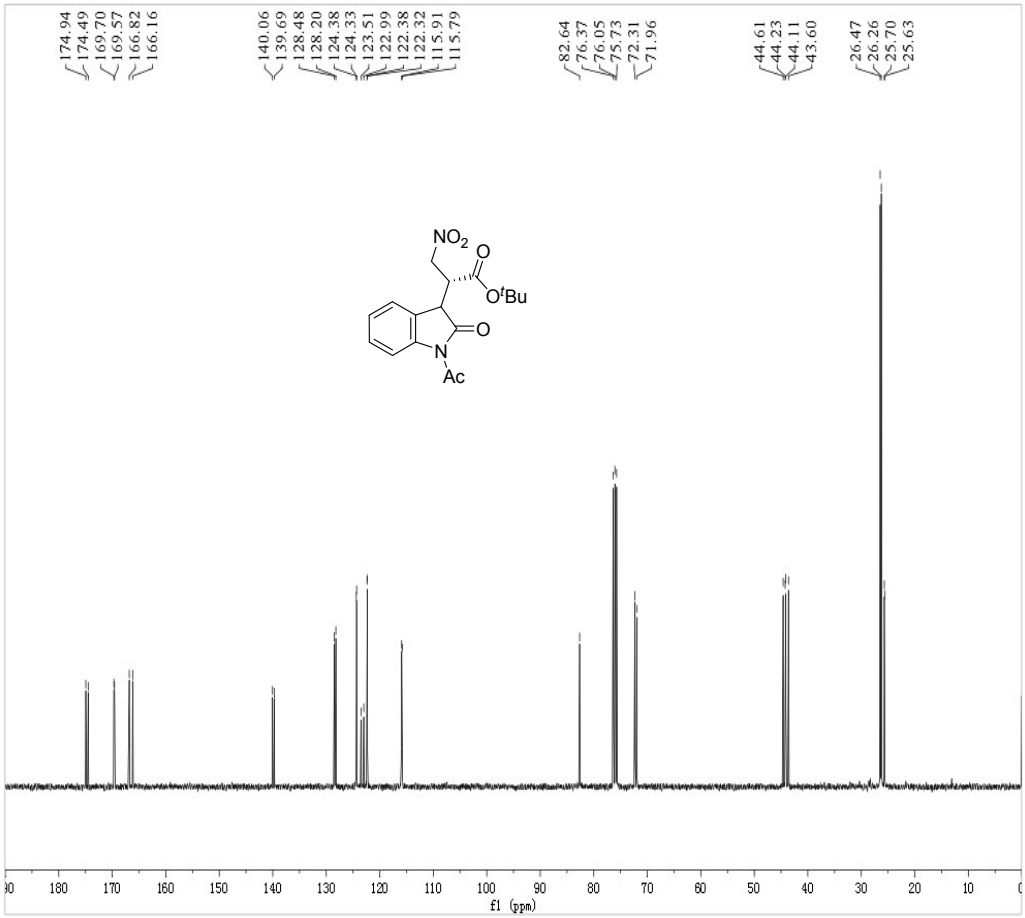
#	Time	Area	Height	Width	Area%	Symmetry
1	56.935	32476.2	213.3	2.1606	49.657	0.629
2	71.527	32924.8	170.1	2.6116	50.343	0.555



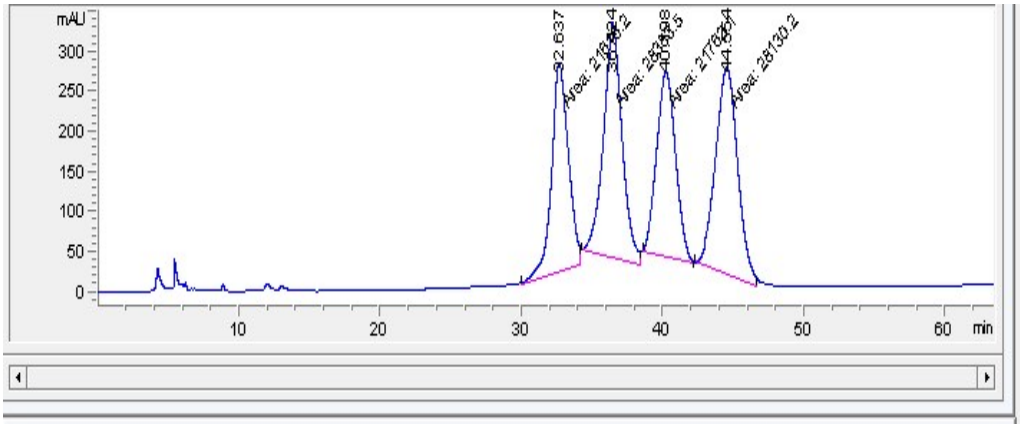
#	Time	Area	Height	Width	Area%	Symmetry
1	58.707	1077.9	7.8	2.2997	1.386	0.666
2	71.852	76667	374.5	3.412	98.614	0.455

^{1}H and ^{13}C NMR of Intermediate A

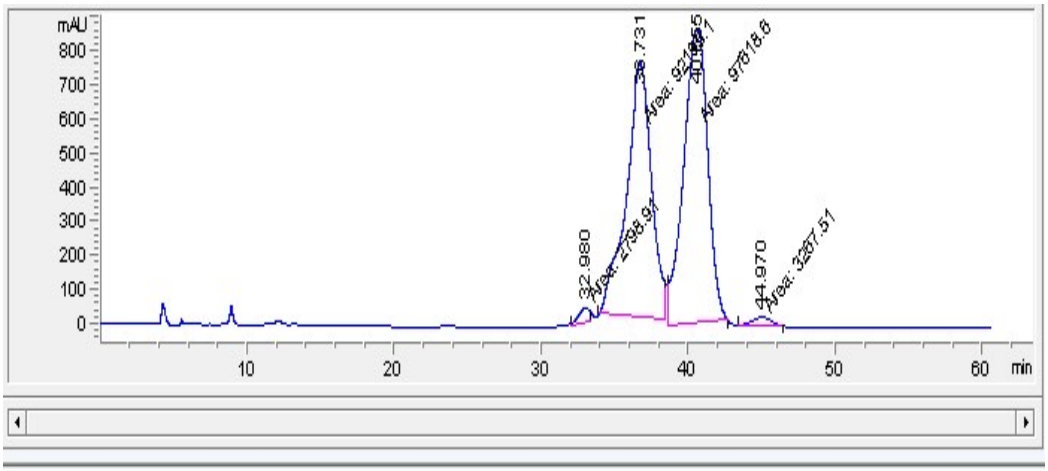




HPLC of Intermediate A

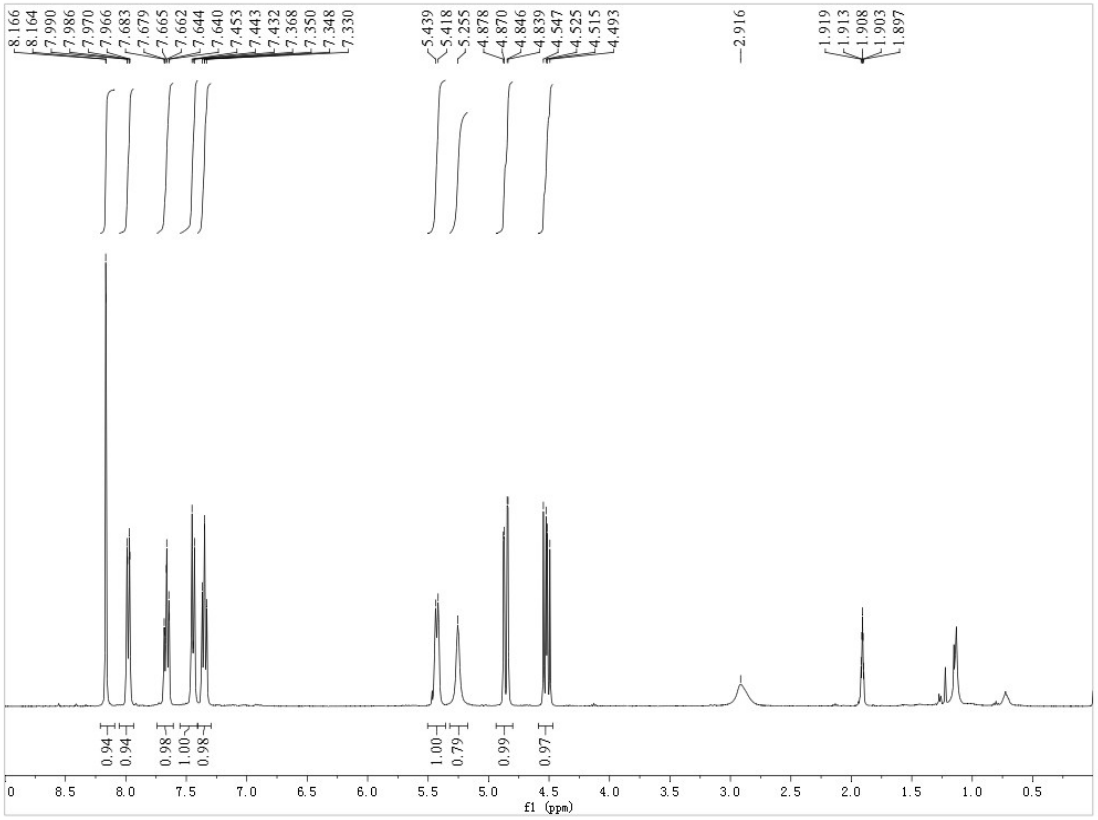


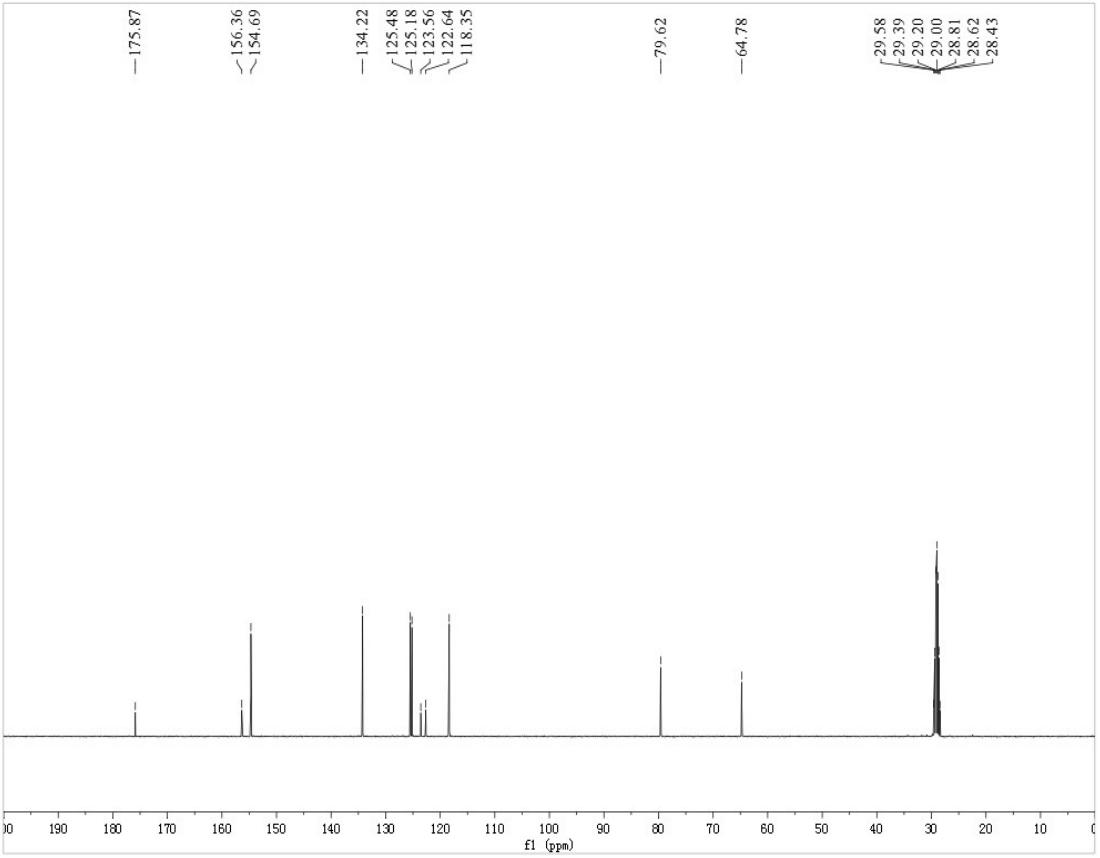
#	Time	Area	Height	Width	Area%	Symmetry
1	32.637	21616.2	263.2	1.3689	21.639	0.823
2	36.424	28383.5	295.3	1.602	28.414	0.925
3	40.198	21763.1	233.5	1.5535	21.786	0.94
4	44.554	28130.2	258.8	1.8118	28.160	1.025



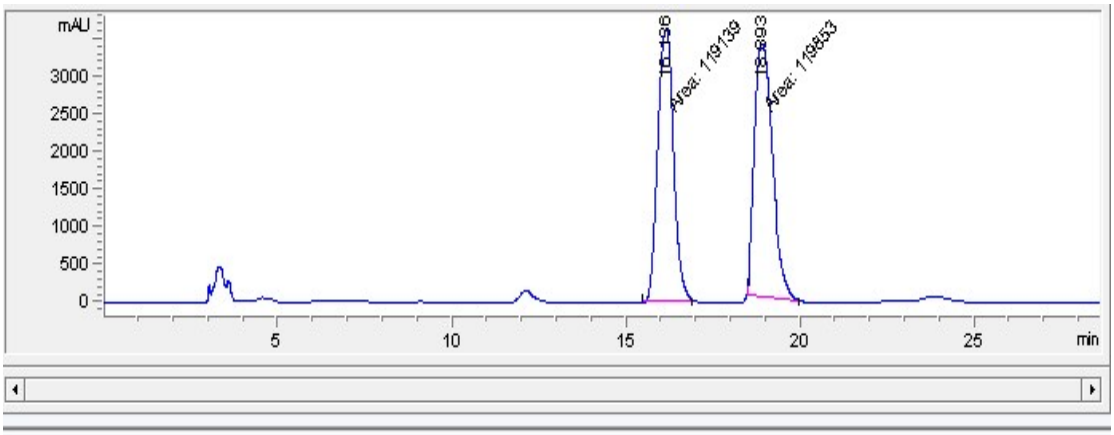
#	Time	Area	Height	Width	Area%	Symmetry
1	32.98	2798.9	49	0.9521	1.429	1.739
2	36.731	92195.1	749.2	2.051	47.067	1.295
3	40.555	97618.6	864.9	1.8811	49.836	1.24
4	44.97	3267.5	31.2	1.7474	1.668	1.11

^{1}H and ^{13}C NMR of Intermediate B

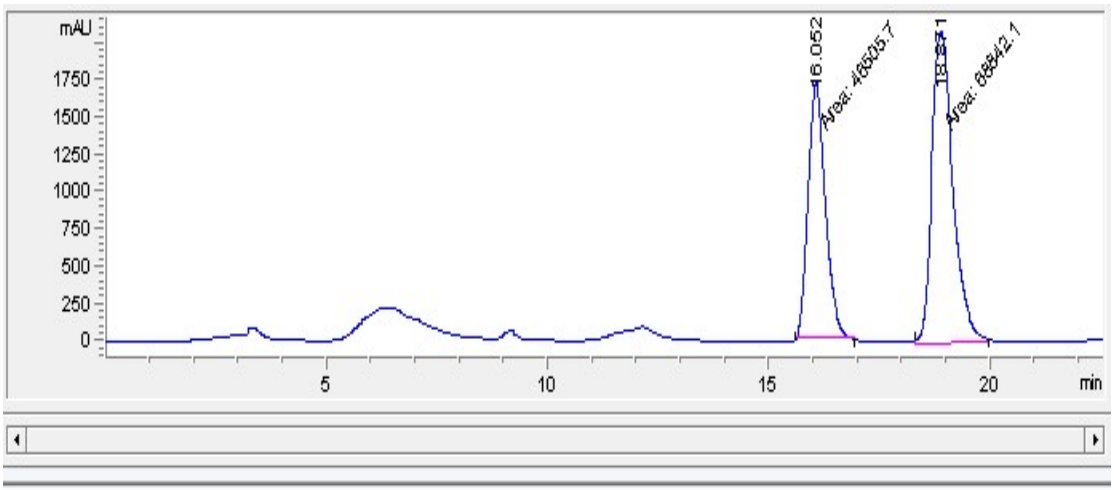




HPLC of Intermediate B



#	Time	Area	Height	Width	Area%	Symmetry
1	16.136	119138.6	3644.6	0.5448	49.851	1.048
2	18.893	119852.9	3379.3	0.5911	50.149	0.684



#	Time	Area	Height	Width	Area%	Symmetry
1	16.052	46505.7	1724.5	0.4495	40.318	0.8
2	18.871	68842.1	2085.7	0.5501	59.682	0.701