A $B_2(OH)_4$-Mediated Synthesis of 2-Substitued Indazolone and Its Application in DNA-Encoded Library

Yapeng Bao,† Zongfa Deng,† Jing Feng,* Weiwei Zhu, Jin Li, Jinqiao Wan,* Guansai Liu*

†Discovery Chemistry Unit, HitGen Inc., Building 6, No. 8 Huigu 1st East Road, Tianfu International Bio-Town, Shuangliu District, Chengdu 610200, Sichuan, P. R. China.

*E-mail: gs.liu@hitgen.com
*E-mail: jing.feng@hitgen.com
*E-mail: jq.wan@hitgen.com

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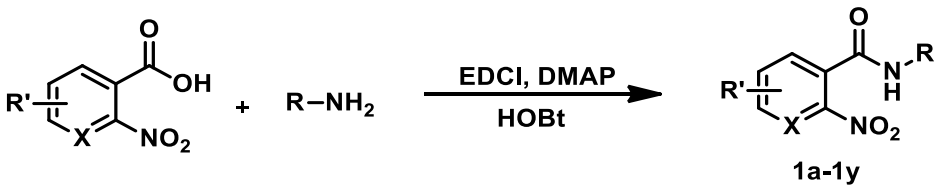
1. General Information and Experimental Procedures of Small Molecule Synthesis

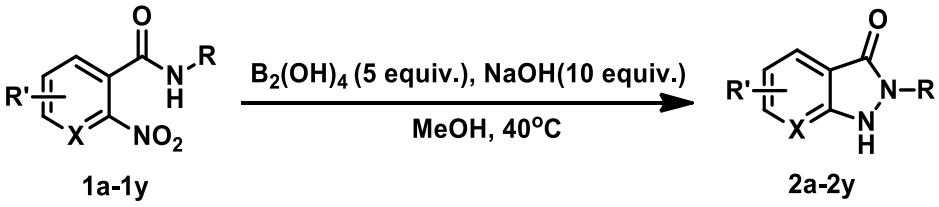
All the reagents were used as received, unless otherwise indicated. TLC analysis was performed using pre-coated glass plates. Analytical TLC was performed using pre-coated plates (silica gel 60 F254) and visualized with UV light or an I_2 chamber. Heating was performed by using oil bath. NMR spectra were recorded with a 400 MHz Bruker spectrometer for ^{1}H NMR and 100 MHz for ^{13}C NMR, respectively, and TMS was used as an internal standard. The following abbreviations (or combinations thereof) were used to explain multiplicities: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet, *br* = broad. Coupling constants, *J* were reported in Hertz unit (Hz). Mass spectra were measured LC-2030C with liquid chromatograph. Samples were injected into a mixture of 0.05%TFA Water and 0.05%TFA CAN Gradient: B from 5% to 95% for 4.0 min and hold 95% at for 1.0 min; Flow Rate: 2.5 mL/min; Column Temperature: 40^{0}C. High resolution mass spectral (HRMS) analyze were measured using ESI techniques with quadrupole time of flight mass spectrometer.

General procedures of synthesis of amide derivatives (1a-1y)[1]:



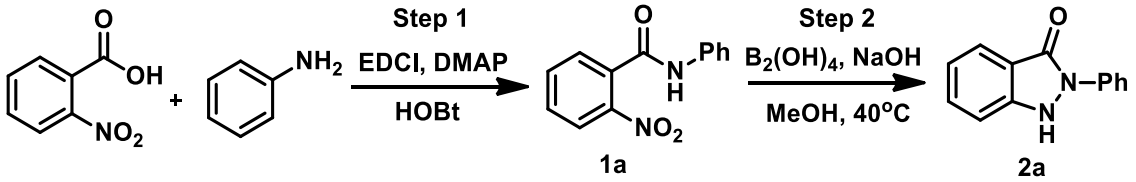
To the solution of 2-nitrobenzoic acid derivatives (2.99 mmol, 1.0 equiv.) in 12.5 mL DCM and 0.5 mL DMF was added EDCI (3.29 mmol, 1.1 equiv.), HOBt (3.29 mmol, 1.1 equiv.) and DMAP (0.15 mmol, 0.05 equiv.) at r.t.. Then amine (5.98 mmol, 2.0 equiv.) was added dropwise. The mixture was heat to reflux with 60°C oil bath and stirred for 4 hours. The reaction mixture was poured into water (40 mL) and extracted with dichloromethane (30 mL x 3). The combined organic layers were washed with saturated NaCl solution (30 mL x 2), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (PE/EtOAc 3:1 to 1:1 v/v) to obtain the desired product **1a**-**1y**.

General procedure of indazolone formation on small molecules (2a-2y)



To the solution of compound **1a-1y** (1.0 equiv., dissolved in MeOH, 0.08 M) was added $B_2(OH)_4$ (5.0 equiv.). The mixture was then cooled down to 0°C and NaOH (0.80 M in MeOH, 10 equiv.) was added dropwise. After stirring at 0°C for another 10 min, the mixture was warmed up to 40°C (oil bath) and react at 40°C overnight. The reaction mixture was mixed with silica gel and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (PE/EtOAc 3:1 to 1:1) to obtain the desired product **2a-2y**.

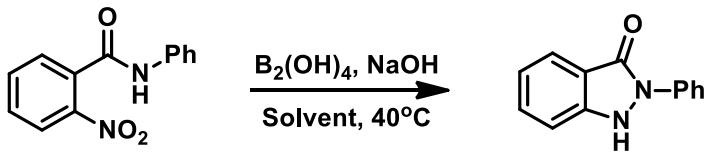
Case representation for large scale synthesis of compound 2a:



Step 1: To the solution of 2-nitrobenzoic acid (500.0 mg, 2.99 mmol, 1.0 equiv.) in 12.5 mL DCM and 0.5 mL DMF was added EDCI (631.0 mg, 3.29 mmol, 1.1 equiv.), HOBt (445.0 mg, 3.29 mmol, 1.1 equiv.) and DMAP (18.3 mg, 0.15 mmol, 0.05 equiv.) at r.t.. Then aniline (556.0 mg, 5.98 mmol, 2.0 equiv.) was added dropwise. The mixture was heat to reflux with 60 °C oil bath and stirred for 4 hours. The reaction mixture was poured into water (40 mL) and extracted with dichloromethane (30 mL x 3). The combined organic layers were washed with saturated NaCl solution (30 mL x 2), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (PE/EtOAc=3:1) to obtain the desired product **1a** (593.0 mg, 82%) as a white solid.

Step 2: to the solution of compound **1a** (242.0 mg, 1.0 mmol, 1.0 equiv.) in MeOH (12.5 mL) was added $B_2(OH)_4$ (448.8 mg, 5.0 mmol, 5.0 equiv.). The mixture was then cooled down to 0°C and NaOH solution (0. 80 M in MeOH, 12.5 mL, 10 equiv.) was added dropwise. After stirring at 0°C for another 10 min, the mixture was warmed up to 40°C (oil bath) and react at 40°C overnight. The reaction mixture was mixed with silica gel (3.0 g) and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (PE/EtOAc=2:1) to obtain the desired product **2a** (188.1 mg, 89%) as a light red solid.

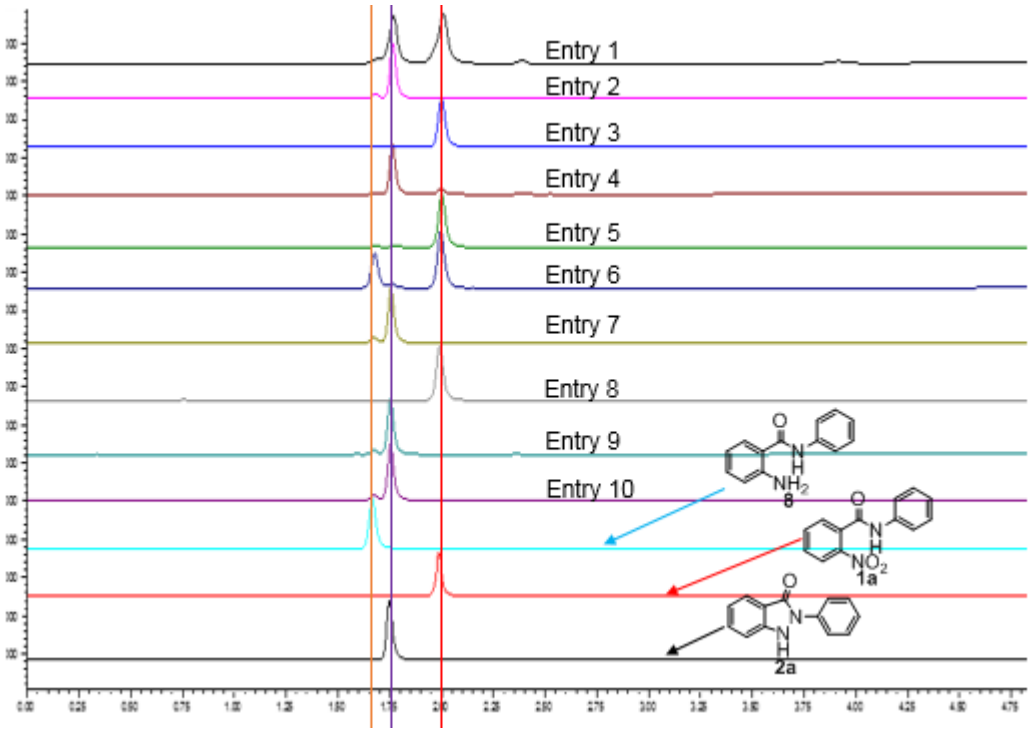
2. Condition optimization for $B_2(OH)_4$-mediated cyclization.



1a 2a

entry[a]	solvent	$B_2(OH)_4$ (equiv.)	NaOH (equiv.)	yield (%[b])
1	MeOH	5	10	49%[c]
2	MeOH	5	10	90 (89[d])
3	MeOH	5	0	0
4	EtOH	5	10	85
5	DMA	5	10	trace
6	DMSO	5	10	trace
7	MeOH/H_2O=9:1	5	10	89
8[e]	MeOH	5	10	0
9[e]	MeOH	100	200	91
10[e]	MeOH/H_2O=9:1	100	200	90

To the solution of compound **1a** (0.040 mmol in 0.5 mL solvent, 1.0 equiv.) was added $B_2(OH)_4$. The mixture was then cooled down to 0°C and NaOH (0.80 M in solvent) was added dropwise. After stirring at 0°C for 10 min, the mixture was warmed up to 40 °C and react at 40 °C overnight; [b]Conversion was determined by LC-MS; [c]react at 40°c for 2h; [d]Isolated yield (1.0 mmol); [e]the final concentration of compound **1a** was 0.002 M.



*HPLC condition: Column: Waters Xbridge-Shield-RP-C18 50 mm*4.6 mm 3.5 um Mobile Phase: A: 0.05%TFA Water B: 0.05%TFA CAN. Gradient : B from 5% to 95% for 4.0 min and hold 95% for 1.0 min; Flow Rate: 2.5 mL/min; Column Temperature:40 ℃.

HPLC Comparison of starting material (1a), non-cyclization product (8) and desired product (2a)

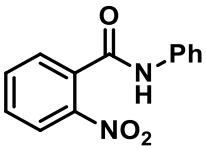
3. Structure confirmation of 2a.

^{1}H NMR reported in literature[2] (A_{ppm}) (400 MHz, DMSO-d_6)	Observed ^{1}H NMR (B_{ppm}) (400 MHz, DMSO-d_6)	δ_Δ (A_{ppm}-B_{ppm})
10.67	10.64	0.03
7.95-7.91	7.93-7.92	0.02-(-0.01)
7.76	7.75	0.01
7.65-7.59	7.62-7.60	0.03-(-0.01)
7.54-7.48	7.52-7.48	0.02-0
7.37	7.36	0.01
7.26-7.18	7.25-7.19	0.01-(-0.01)

^{13}C NMR reported in literature[2] (A_{ppm}) (100 MHz, DMSO-d_6)	Observed ^{13}C NMR (B_{ppm}) (100 MHz, DMSO-d_6)	δ_Δ (A_{ppm}-B_{ppm})
160.7	160.1	0.6
147.1	146.5	0.6
138.1	137.5	0.6
133.0	132.5	0.5
129.5	129.0	0.5
125.4	124.8	0.6
123.9	123.3	0.6
122.3	121.8	0.5
119.4	118.8	0.6
118.6	118.0	0.6
113.1	112.6	0.5

4. Starting materials for indazolone cyclization

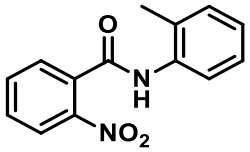
2-nitro-N-phenylbenzamide (1a)



The product was obtained as a white solid (purified by PE:EA=3:1), 593 mg, 82% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 7.5 Hz,

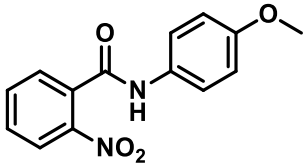
1H), 7.81 – 7.77 (m, 1H), 7.76 (dd, *J* = 10.8, 4.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.14 (td, *J* = 7.5, 3.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 147.0, 139.3, 134.6, 133.2, 131.4, 129.8, 129.3, 124.7, 124.4, 120. 1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{13}H_{11}N_2O_3]^+$ 243.0764; found: 243.0767.

2-nitro-N-(o-tolyl)benzamide (1b)



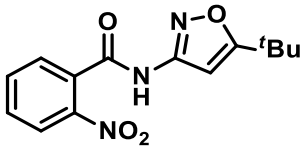
The product was obtained as a white solid (purified by PE:EA=3:1), 560 mg, 73% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 7.4 Hz, 1H), 7.80 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.25 (dd, *J* = 13.7, 7.5 Hz, 2H), 7.16 (t, *J* = 6.9 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 147.1, 136.1, 134.5, 133.3, 131.3, 130.9, 129.8, 126.5, 126.2, 124.7, 18.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_3]^+$ 257.0921; found: 257.0918.

N-(4-methoxyphenyl)-2-nitrobenzamide (1c)



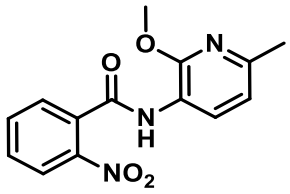
The product was obtained as a white solid (purified by PE:EA=3:1), 520 mg, 74% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.51 (s, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.85 (dd, *J* = 10.7, 4.2 Hz, 1H), 7.74 (dd, *J* = 12.4, 4.4 Hz, 2H), 7.58 (d, *J* = 9.0 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 2H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 156.2, 147.1, 134.5, 133.2, 132.4, 131.3, 129.7, 124.7, 121.67, 114.4, 55.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_4]^+$ 273.0870; found: 273.0866.

N-(5-(tert-butyl)isoxazol-3-yl)-2-nitrobenzamide (1d)



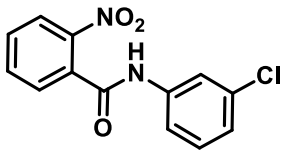
The product was obtained as a white solid (purified by PE:EA=3:1), 553 mg, 64% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.71 (s, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.86 (t, *J* = 7.3 Hz, 1H), 7.76 (t, *J* = 8.6 Hz, 2H), 6.69 (s, 1H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.3, 164.9, 158.1, 146.8, 134.7, 132.0, 131.9, 129.8, 124.8, 93.8, 33.1, 28.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{16}N_3O_4]^+$ 290.1136; found: 290.1139.

N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1e)



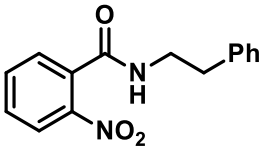
The product was obtained as a white solid (purified by PE:EA=2:1), 218 mg, 64% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 8.21 – 8.07 (m, 2H), 7.84 (t, J = 7.1 Hz, 1H), 7.72 (dd, J = 16.7, 8.4 Hz, 2H), 6.88 (d, J = 7.8 Hz, 1H), 3.88 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 154.8, 151.1, 146.8, 134.5, 133.1, 131.5, 131.2, 129.8, 124.5, 119.5, 116.1, 53.7, 23.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{14}N_3O_4]^+$ 288.0979; found: 288.0987.

N-(3-chlorophenyl)-2-nitrobenzamide (1f)[2]



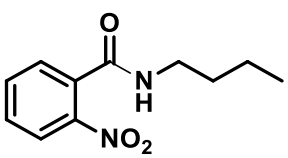
The product was obtained as a white solid (purified by PE:EA=3:1), 545 mg, 66% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.83 (s, 1H), 8.17 – 8.11 (m, 1H), 7.86 (dt, J = 3.7, 1.6 Hz, 2H), 7.76 (ddd, J = 9.6, 7.7, 4.6 Hz, 2H), 7.50 (ddd, J = 8.2, 1.9, 0.9 Hz, 1H), 7.37 (t, J = 8.1 Hz, 1H), 7.17 (ddd, J = 8.0, 2.1, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 146.8, 140.8, 134.7, 133.6, 132.7, 131.7, 131.1, 129.8, 124.9, 124.2, 119.5, 118.5.

2-nitro-N-phenethylbenzamide (1g)



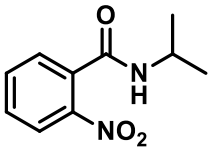
The product was obtained as a white solid (purified by PE:EA=2:1), 654 mg, 81% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.78 (t, J = 5.5 Hz, 1H), 8.02 (dd, J = 8.1, 1.1 Hz, 1H), 7.77 (td, J = 7.5, 1.2 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.52 (dd, J = 7.5, 1.4 Hz, 1H), 7.35 – 7.25 (m, 4H), 7.25 – 7.19 (m, 1H), 3.46 (dd, J = 13.9, 6.5 Hz, 2H), 2.84 (t, J = 7.4 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.8, 147.6, 139.8, 134.0, 133.1, 131.1, 129.4, 129.2, 128.8, 126.6, 124.5, 41.2, 35.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{15}H_{15}N_2O_3]^+$ 271.1077; found: 271.1077.

N-butyl-2-nitrobenzamide (1h)



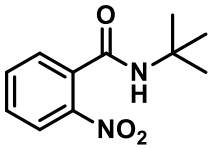
The product was obtained as a white solid (purified by PE:EA=2:1), 416 mg, 63% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.62 (s, 1H), 8.02 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.77 (td, *J* = 7.5, 1.2 Hz, 1H), 7.67 (td, *J* = 7.9, 1.4 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.3 Hz, 1H), 3.21 (d, *J* = 6.1 Hz, 2H), 1.57 – 1.42 (m, 2H), 1.42 – 1.28 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 147.5, 134.0, 133.3, 131.0, 129.5, 124.5, 39.2, 31.3, 20.0, 14.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{11}H_{15}N_2O_3]^+$ 223.1077; found: 223.1078.

N-isopropyl-2-nitrobenzamide (1i)



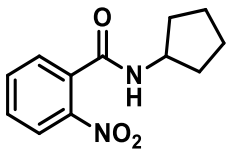
The product was obtained as a white solid (purified by PE:EA=2:1), 414 mg, 66% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (d, *J* = 7.4 Hz, 1H), 8.03 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.77 (td, *J* = 7.5, 1.1 Hz, 1H), 7.67 (td, *J* = 7.9, 1.4 Hz, 1H), 7.56 (dd, *J* = 7.5, 1.3 Hz, 1H), 4.07 – 3.92 (m, 1H), 1.14 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 147.3, 134.1, 133.5, 130.9, 129.6, 124.4, 41.5, 22.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{10}H_{13}N_2O_3]^+$ 209.0921; found: 209.0926.

N-(tert-butyl)-2-nitrobenzamide (1j)



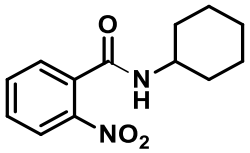
The product was obtained as a white solid (purified by PE:EA=2:1), 445 mg, 67% (3.00 mmol starting material).^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (s, 1H), 8.03 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.75 (td, *J* = 7.5, 1.2 Hz, 1H), 7.68 – 7.60 (m, 1H), 7.53 (dd, *J* = 7.5, 1.4 Hz, 1H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 146.9, 134.3, 134.1, 130.5, 129.7, 124.3, 51.4, 28.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{11}H_{15}N_2O_3]^+$ 223.1077; found: 223.1077.

N-cyclopentyl-2-nitrobenzamide (1k)



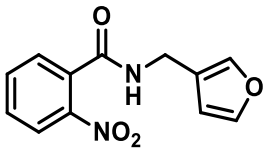
The product was obtained as a white solid (purified by PE:EA=2:1), 437 mg, 63% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (d, *J* = 6.9 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.80 – 7.73 (m, 1H), 7.71 – 7.62 (m, 1H), 7.56 (dd, *J* = 7.5, 1.0 Hz, 1H), 4.15 (dd, *J* = 12.0, 6.3 Hz, 1H), 1.85 (dd, *J* = 11.9, 5.7 Hz, 2H), 1.75 – 1.58 (m, 2H), 1.54 (d, *J* = 8.3 Hz, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 147.3, 134.1, 133.5, 130.8, 129.6, 124.4, 51.4, 32.3, 24.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{15}N_2O_3]^+$ 235.1077; found: 235.1077.

N-cyclohexyl-2-nitrobenzamide (1l)



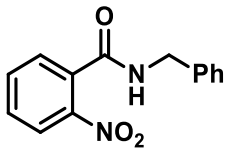
The product was obtained as a white solid (purified by PE:EA=2:1), 537 mg, 73% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (d, J = 7.8 Hz, 1H), 8.03 (dd, J = 8.1, 1.1 Hz, 1H), 7.77 (td, J = 7.5, 1.2 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.55 (dd, J = 7.5, 1.4 Hz, 1H), 3.68 (tdt, J = 11.4, 7.4, 3.7 Hz, 1H), 1.90 – 1.52 (m, 5H), 1.37 – 1.06 (m, 5H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 147.3, 134.1, 133.6, 130.8, 129.6, 124.4, 48.6, 32.4, 25.7, 25.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{13}H_{17}N_2O_3]^+$ 249.1234; found: 249.1240.

N-(furan-3-ylmethyl)-2-nitrobenzamide (1m)



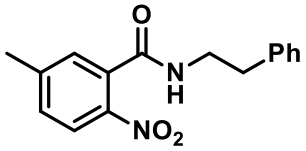
The product was obtained as a white solid (purified by PE:EA=2:1), 254 mg, 75% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (t, J = 5.5 Hz, 1H), 8.03 (dd, J = 8.1, 0.9 Hz, 1H), 7.78 (td, J = 7.5, 1.1 Hz, 1H), 7.69 (td, J = 7.8, 1.4 Hz, 1H), 7.66 – 7.58 (m, 3H), 6.49 (d, J = 0.7 Hz, 1H), 4.29 (d, J = 5.7 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 147.6, 143.9, 140.3, 134.1, 132.9, 131.2, 129.6, 124.5, 123.2, 111.0, 34.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{11}N_2O_4]^+$ 247.0714; found: 247.0710.

N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1n)[3]



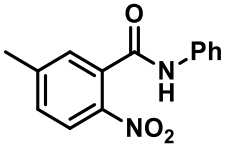
The product was obtained as a white solid (purified by PE:EA=2:1), 601 mg, 78% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.21 (t, J = 5.6 Hz, 1H), 8.08 – 8.00 (m, 1H), 7.79 (td, J = 7.5, 1.0 Hz, 1H), 7.69 (td, J = 7.9, 1.4 Hz, 1H), 7.67 (s, 1H), 7.35 (dd, J = 8.5, 5.5 Hz, 4H), 7.31 – 7.23 (m, 1H), 4.46 (d, J = 6.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 147.6, 139.4, 134.1, 132.9, 131.3, 129.6, 128.8, 127.8, 127.4, 124.6, 43.1.

5-methyl-2-nitro-N-phenethylbenzamide (1o)



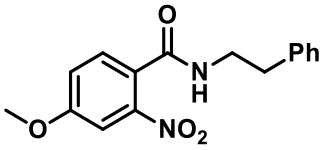
The product was obtained as a white solid (purified by PE:EA=2:1), 550 mg, 65% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (t, J = 5.5 Hz, 1H), 7.94 (d, J = 8.3 Hz, 1H), 7.46 (dd, J = 8.3, 1.2 Hz, 1H), 7.35 – 7.25 (m, 5H), 7.22 (t, J = 7.0 Hz, 1H), 3.44 (dd, J = 13.4, 7.2 Hz, 2H), 2.83 (t, J = 7.4 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.1, 145.0, 139.8, 133.4, 131.1, 129.8, 129.2, 128.8, 126.6, 124.6, 41.2, 35.2, 21.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{16}H_{17}N_2O_3]^+$ 285.1234; found: 285.1238.

5-methyl-2-nitro-N-phenylbenzamide (1p)



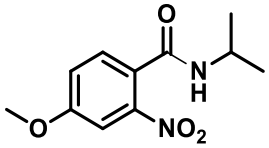
The product was obtained as a white solid (purified by PE:EA=2:1), 537 mg, 70% (2.99 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 8.07 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.61 – 7.51 (m, 2H), 7.36 (t, J = 7.8 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 145.8, 144.5, 139.4, 133.4, 131.5, 130.0, 129.3, 124.8, 124.3, 120.1, 21.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_3]^+$ 257.0921; found: 257.0927.

4-methoxy-2-nitro-N-phenethylbenzamide (1q)



The product was obtained as a white solid (purified by PE:EA=1:1), 592 mg, 66% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.68 (s, 1H), 7.49 (dd, J = 11.0, 5.4 Hz, 2H), 7.34 – 7.18 (m, 6H), 3.87 (s, 3H), 3.42 (dd, J = 13.5, 6.7 Hz, 2H), 2.82 (t, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 160.8, 149.5, 139.8, 130.6, 129.2, 128.8, 126.6, 124.6, 118.7, 109.8, 56.7, 41.2, 35.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{16}H_{17}N_2O_4]^+$ 301.1183; found: 301.1185.

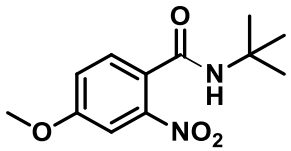
N-isopropyl-4-methoxy-2-nitrobenzamide (1r)



The product was obtained as a white solid (purified by PE:EA=1:1), 508 mg, 71% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (d, J = 7.6 Hz, 1H), 7.61 – 7.48 (m, 2H), 7.29 (dd, J =

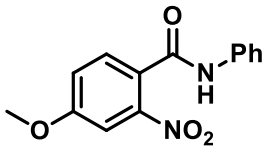
8.5, 2.6 Hz, 1H), 3.97 (td, *J* = 13.3, 6.6 Hz, 1H), 3.87 (s, 3H), 1.14 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 160.5, 149.2, 130.7, 125.2, 118.9, 109.6, 56.8, 41.5, 22.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{11}H_{15}N_2O_4]^+$ 239.1027; found: 239.1024.

N-(tert-butyl)-4-methoxy-2-nitrobenzamide (1s)



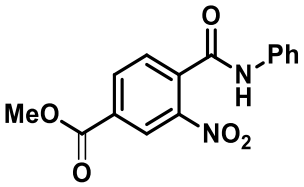
The product was obtained as a white solid (purified by PE:EA=2:1), 607 mg, 80% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (s, 1H), 7.51 (d, *J* = 2.5 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.28 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.87 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 160.2, 148.7, 130.9, 126.5, 119.1, 109.4, 56.6, 51.3, 28.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{17}N_2O_4]^+$ 253.1183; found: 253.1181.

4-methoxy-2-nitro-N-phenylbenzamide (1t)



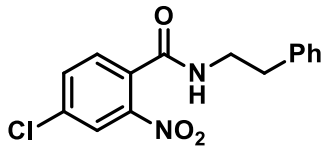
The product was obtained as a white solid (purified by PE:EA=2:1), 704 mg, 86% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.62 (d, *J* = 2.5 Hz, 1H), 7.39 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 161.0, 148.9, 139.4, 131.1, 129.3, 125.0, 124.3, 120.1, 119.3, 109.9, 56.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_4]^+$ 273.0870; found: 273.0877.

Methyl 3-nitro-4-(phenylcarbamoyl) benzoate (1u)



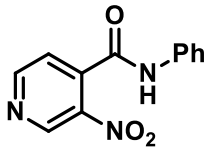
The product was obtained as a white solid (purified by PE:EA=2:1), 477 mg, 53% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.56 (d, *J* = 1.5 Hz, 1H), 8.38 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.9 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 163.7, 146.9, 139.0, 136.7, 134.7, 132.2, 130.7, 129.4, 125.2, 124.7, 120.2, 53.5. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{15}H_{13}N_2O_5]^+$ 301.0819; found: 301.0828.

4-chloro-2-nitro-N-phenethylbenzamide (1v)



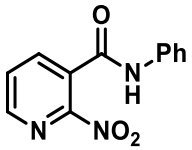
The product was obtained as a white solid (purified by PE:EA=2:1), 608 mg, 94% (2.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.84 (t, J = 5.5 Hz, 1H), 8.16 (d, J = 2.1 Hz, 1H), 7.87 (dd, J = 8.2, 2.1 Hz, 1H), 7.55 (d, J = 8.2 Hz, 1H), 7.38 – 7.17 (m, 5H), 3.45 (dd, J = 13.8, 6.5 Hz, 2H), 2.83 (t, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 148.5, 139.7, 135.2, 133.6, 131.4, 131.0, 129.2, 128.8, 126.7, 124.5, 41.2, 35.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{15}H_{14}ClN_2O_3]^+$ 305.0688; found: 305.0685.

3-nitro-N-phenylisonicotinamide (1w)



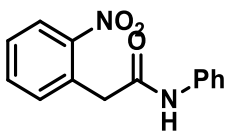
The product was obtained as a white solid (purified by DCM:MeOH=10:1), 277 mg, 57% (2.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.81 (s, 1H), 9.37 (s, 1H), 9.06 (d, J = 4.9 Hz, 1H), 7.87 (d, J = 4.9 Hz, 1H), 7.65 (d, J = 7.6 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 155.5, 145.9, 142.4, 139.8, 138.8, 129.5, 124.9, 123.6, 120.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{10}N_3O_3]^+$ 244.0717; found: 244.0714.

2-nitro-N-phenylnicotinamide (1x)



The product was obtained as a white solid (purified by PE:EA=3:1), 417 mg, 62% (2.79 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 8.74 (dd, J = 4.7, 1.5 Hz, 1H), 8.44 (dd, J = 7.7, 1.5 Hz, 1H), 7.99 (dd, J = 7.7, 4.7 Hz, 1H), 7.65 (d, J = 7.9 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.15 (t, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 155.4, 150.3, 140.6, 138.9, 129.4, 129.4, 127.2, 124.8, 120.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{10}N_3O_3]^+$ 244.0717; found: 244.0715.

N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1y)

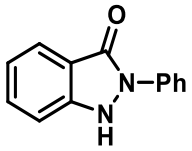


The product was obtained as a yellow solid (purified by PE:EA=2:1), 511 mg, 67% (3.00 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.71 (t, J = 7.5 Hz,

1H), 7.56 (t, *J* = 8.1 Hz, 4H), 7.29 (t, *J* = 7.9 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 4.13 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.0, 149.5, 139.6, 134.1, 131.1, 129.2, 128.9, 125.0, 123.6, 119.5, 41.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_3]^+$ 257.0921; found: 257.0924.

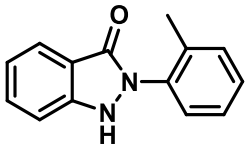
5. Analytical data for the indazolone products

2-phenyl-1,2-dihydro-3H-indazol-3-one (2a)[4,5]



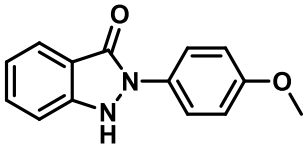
The product was obtained as a light red solid (purified by PE:EA=2:1), 188.1 mg, 89% yield (1.0 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.65 (s, 1H), 7.93 (dd, *J* = 8.7, 1.1 Hz, 2H), 7.79 – 7.72 (m, 1H), 7.62 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.24 – 7.17 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 147.1, 138.1, 133.0, 129.6, 125.4, 123.9, 122.4, 119.4, 118.6, 113.1.

6-methoxy-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2b)



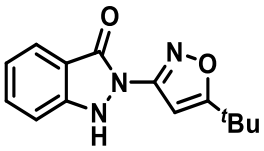
The product was obtained as a red oil (purified by PE:EA=2:1 to 1:1), 19.8 mg, 91% yield (0.0967 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.35 (tdd, *J* = 12.8, 7.3, 2.5 Hz, 4H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 147.6, 136.3, 136.0, 132.3, 131.2, 128.9, 127.9, 127.0, 123.9, 121.8, 117.3, 112.8, 18.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O]^+$ 225.1023; found: 225.1026.

2-(4-methoxyphenyl)-1,2-dihydro-3H-indazol-3-one (2c)[4,6]



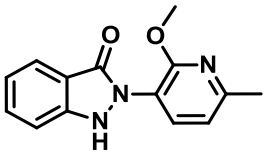
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 29.6 mg, 67% yield (0.183 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 7.80 (d, *J* = 9.1 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.54 (m, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.11 – 7.00 (m, 2H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.2, 157.1, 146.8, 132.6, 131.3, 123.8, 122.2, 121.5, 118.6, 114.7, 113.0, 55.8.

2-(5-(tert-butyl)isoxazol-3-yl)-1,2-dihydro-3H-indazol-3-one (2d)



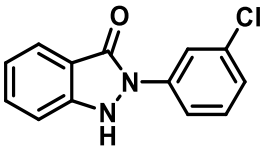
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 25 mg, 80% yield (0.121 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.70 – 7.55 (m, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 6.91 (s, 1H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.4, 160.62, 155.7, 148.2, 134.3, 124.2, 122.5, 116.5, 113.4, 91.6, 33.3, 28.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{16}N_3O_2]^+$ 258.1237; found: 258.1243.

2-(2-methoxy-6-methylpyridin-3-yl)-1, 2-dihydro-3H-indazol-3-one (2e)



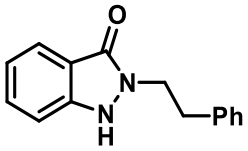
The product was obtained as a red solid (purified by PE:EA=2:1 to 1:1), 35 mg, 68% yield (0.200 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 7.7 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 8.3 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 7.7 Hz, 1H), 3.85 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 158.4, 156.5, 147.7, 138.4, 132.2, 123.7, 121.1, 118.2, 116.9, 116.5, 113.0, 53.9, 24.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{14}N_3O_2]^+$ 256.1081; found: 256.1077.

2-(3-chlorophenyl)-1,2-dihydro-3H-indazol-3-one 2f)[7]



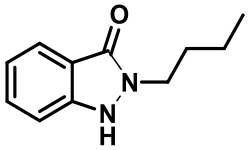
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 19.8 mg, 45% yield (0.179 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 8.02 (t, J = 2.0 Hz, 1H), 7.87 (ddd, J = 8.3, 2.1, 0.8 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.61 (ddd, J = 8.3, 7.2, 1.1 Hz, 1H), 7.51 (t, J = 8.2 Hz, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.28 (ddd, J = 8.0, 2.0, 0.7 Hz, 1H), 7.22 – 7.15 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 147.4, 139.2, 134.0, 133.5, 131.3, 125.0, 124.1, 122.6, 118.5, 118.3, 117.3, 113.2.

2-phenethyl-1,2-dihydro-3H-indazol-3-one (2g)[4]



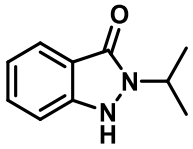
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 42.3 mg, 84% yield (0.210 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.51 (ddd, J = 8.3, 7.1, 1.2 Hz, 1H), 7.31 – 7.17 (m, 6H), 7.13 – 7.07 (m, 1H), 4.02 (dd, J = 8.1, 6.9 Hz, 2H), 3.06 – 2.97 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 146.5, 138.9, 131.8, 129.1, 128.9, 126.8, 123.4, 121.3, 117.9, 112.6, 44.9, 34.1.

2-butyl-1,2-dihydro-3H-indazol-3-one (2h)[4,8]



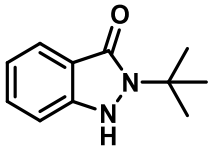
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 35.9 mg, 84% yield (0.224 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.25 (d, J = 8.2 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 3.79 (t, J = 7.0 Hz, 2H), 1.72 – 1.62 (m, 2H), 1.32 – 1.21 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 146.4, 131.6, 123.4, 121.5, 117.9, 112.5, 43.1, 30.3, 19.7, 13.9.

2-isopropyl-1,2-dihydro-3H-indazol-3-one (2i)[4,8]



The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 27.4 mg, 81% yield (0.191 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (d, J = 7.4 Hz, 1H), 8.03 (dd, J = 8.1, 1.1 Hz, 1H), 7.77 (td, J = 7.5, 1.2 Hz, 1H), 7.74 – 7.60 (m, 1H), 7.56 (dd, J = 7.5, 1.4 Hz, 1H), 4.00 (dq, J = 13.2, 6.6 Hz, 1H), 1.15 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 147.3, 134.1, 133.5, 130.9, 129.6, 124.4, 41.5, 22.4.

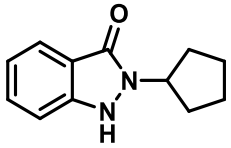
2-(tert-butyl)-1,2-dihydro-3H-indazol-3-one (2j)[4]



The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 33.8 mg, 79% yield (0.224 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.63 (s, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz,

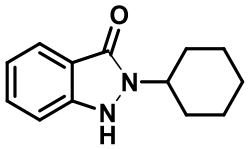
DMSO-d_6) δ 162.9, 146.9, 131.7, 123.1, 121.3, 119.8, 112.9, 57.8, 27.7.

2-cyclohexyl-1,2-dihydro-3H-indazol-3-one (2k)[4]



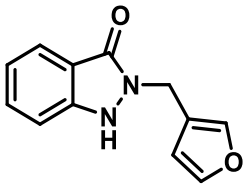
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 32.4 mg, 75% yield (0.213 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 8.2 Hz, 1H), 7.10 (t, J = 7.2 Hz, 1H), 4.88 – 4.73 (m, 1H), 1.99 – 1.86 (m, 2H), 1.79 (s, 4H), 1.61 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d6) δ 161.5, 147.0, 131.7, 123.3, 121.4, 118.3, 112.9, 54.5, 30.2, 24.7.

2-cyclohexyl-1,2-dihydro-3H-indazol-3-one (2l)[4]



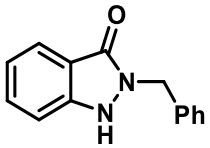
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 41.5 mg, 95% yield (0.201 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.98 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.49 (ddd, J = 8.3, 7.1, 1.2 Hz, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.12 – 7.05 (m, 1H), 4.21 (s, 1H), 1.88 – 1.59 (m, 7H), 1.47 – 1.30 (m, 2H), 1.24 – 1.06 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 146.8, 131.6, 123.3, 121.2, 118.2, 112.7, 53.1, 31.1, 25.6, 25.5.

2-(furan-3-ylmethyl)-1,2-dihydro-3H-indazol-3-one (2m)



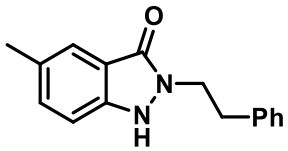
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 21.7 mg, 50% yield (0.202 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (s, 1H), 7.68 – 7.63 (m, 2H), 7.61 (t, J = 1.6 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.42 (d, J = 1.0 Hz, 1H), 4.81 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 146.8, 144.2, 141.4, 131.9, 123.5, 121.4, 121.1, 117.7, 112.7, 111.1, 38.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{11}N_2O_2]^+$ 215.0815; found: 215.0824.

2-benzyl-1,2-dihydro-3H-indazol-3-one (2n)[4]



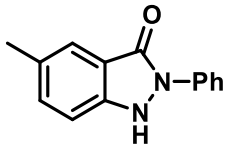
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 35.3 mg, 81% yield (0.194 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H), 7.34 (t, J = 7.1 Hz, 2H), 7.25 (td, J = 12.8, 7.6 Hz, 4H), 7.11 (t, J = 7.5 Hz, 1H), 4.99 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 146.6, 137.4, 132.0, 129.0, 128.1, 128.0, 123.5, 121.4, 117.6, 112.7, 47.2.

5-methyl-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2o)[4]



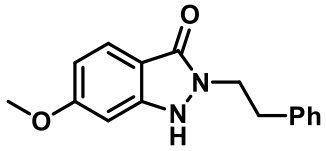
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 33.7 mg, 79% yield (0.168 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 7.40 (s, 1H), 7.36 – 7.15 (m, 7H), 3.99 (t, J = 7.5 Hz, 2H), 2.99 (t, J = 7.4 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 145.1, 138.9, 133.2, 130.5, 129.1, 128.9, 126.8, 122.7, 118.4, 112.5, 44.9, 34.2, 21.0.

5-methyl-2-phenyl-1,2-dihydro-3H-indazol-3-one (2p)



The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 30.1 mg, 69% yield (0.194 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 7.92 (d, J = 8.8 Hz, 2H), 7.47 (ddd, J = 13.2, 9.9, 6.1 Hz, 4H), 7.38 – 7.14 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 145.5, 138.2, 134.5, 131.6, 129.5, 125.2, 123.2, 119.2, 118.9, 113.1, 21.0. HRMS (ESI) m/z: [M + H]$^+$ calcd for $[C_{14}H_{13}N_2O]^+$ 225.1023; found: 225.1029.

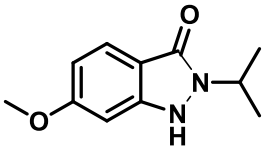
6-methoxy-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2q)



The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 32.4 mg, 91% yield (0.132 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.15 (s, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.33 – 7.17 (m, 5H), 6.72 (d, J = 2.0 Hz, 1H), 6.67 (dd, J = 8.6, 2.1 Hz, 1H), 3.98 – 3.92 (m, 2H), 3.82 (s, 3H), 3.03 – 2.92 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 161.3, 148.4, 139.0, 129.1, 128.9,

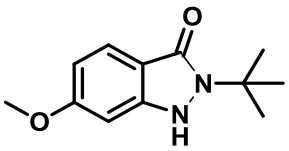
126.8, 124.5, 94.9, 56.0, 45.0, 34.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{16}H_{17}N_2O_2]^+$ 269.1285; found: 269.1288.

2-isopropyl-6-methoxy-1,2-dihydro-3H-indazol-3-one (2r)[4]



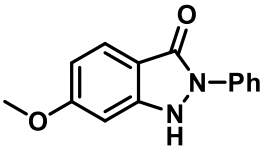
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 40.1 mg, 93% yield (0.208 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.49 (d, J = 8.8 Hz, 1H), 6.81 – 6.36 (m, 2H), 4.52 (m, J = 6.7 Hz, 1H), 3.81 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 161.5, 149.0, 124.4, 111.6, 111.3, 95.1, 55.9, 45.7, 20.7.

2-(tert-butyl)-6-methoxy-1,2-dihydro-3H-indazol-3-one (2s)



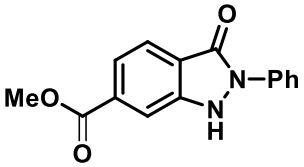
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 37.6 mg, 86% yield (0.198 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 7.44 (d, J = 9.2 Hz, 1H), 6.68 – 6.63 (m, 2H), 3.80 (s, 3H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.5, 163.0, 149.0, 124.3, 113.0, 111.3, 95.2, 57.7, 55.9, 27.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{17}N_2O_2]^+$ 221.1285; found: 221.1286.

6-methoxy-2-phenyl-1,2-dihydro-3H-indazol-3-one (2t)



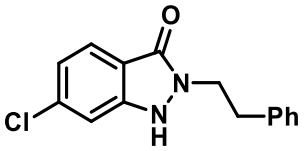
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 18.7 mg, 71% yield (0.109 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.87 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 8.6 Hz, 1H), 7.48 (t, J = 8.0 Hz, 2H), 7.21 (t, J = 7.4 Hz, 1H), 6.83 – 6.73 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.9, 160.7, 149.2, 138.4, 129.5, 125.1, 124.9, 95.4, 56.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{13}N_2O_2]^+$ 241.0972; found: 241.0970.

Methyl 3-oxo-2-phenyl-2,3-dihydro-1H-indazole-6-carboxylate (2u)



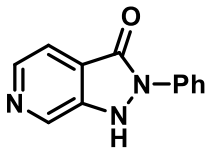
The product was obtained as a pale yellow amorphous solid (purified by PE:EA=2:1 to 1:1), 53.6 mg, 60% yield (0.332 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 7.93 (d, J = 7.7 Hz, 2H), 7.89 (d, J = 7.6 Hz, 2H), 7.73 (d, J = 9.2 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.30 (t, J = 7.4 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 159.6, 146.3, 137.6, 133.6, 129.7, 125.9, 124.5, 122.3, 121.7, 119.7, 114.2, 53.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{15}H_{13}N_2O_3]^+$ 269.0921; found: 269.0923.

6-chloro-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2v)



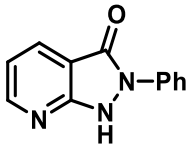
The product was obtained as a white solid (purified by PE:EA=2:1 to 1:1), 19.8 mg, 35% yield (0.207 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 7.58 (d, J = 8.3 Hz, 1H), 7.36 (d, J = 1.5 Hz, 1H), 7.31 – 7.13 (m, 6H), 7.06 (dd, J = 8.3, 1.7 Hz, 1H), 4.33 – 3.71 (m, 2H), 2.96 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.0, 146.5, 138.7, 136.6, 129.1, 128.9, 126.8, 125.2, 121.6, 116.4, 112.1, 44.9, 34.1. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $[C_{15}H_{13}ClN_2NaO]^+$ 295.0614; found: 295.0612.

2-phenyl-1,2-dihydro-3H-pyrazolo[3,4-c]pyridin-3-one (2w)



The product was obtained as a pale yellow amorphous solid (purified by PE:EA=1:1 to pure EA), 32.6 mg, 75% yield (0.205 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d6) δ 11.31 (s, 1H), 8.87 (s, 1H), 8.19 (s, 1H), 8.03 (d, J = 7.4 Hz, 2H), 7.76 (dd, J = 5.3, 0.8 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.1, 140.1, 134.5, 127.6, 124.2, 118.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{10}N_3O]^+$ 212.0819; found: 212.0820.

2-phenyl-1,2-dihydro-3H-pyrazolo[3,4-b]pyridin-3-one (2x)

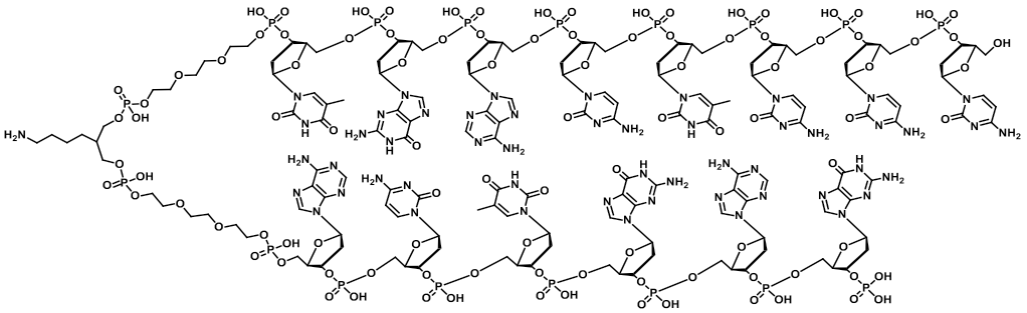


The product was obtained as a white solid (purified by PE:EA=1:1 to pure EA), 11.8 mg, 21% yield (0.265 mmol starting material). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.44 (d, J = 4.6 Hz, 1H), 8.22 (dd, J = 7.5, 1.6 Hz, 1H), 8.00 (d, J = 7.8 Hz, 2H), 7.66 – 7.38 (m, 2H), 7.22 (t, J = 7.4 Hz, 1H), 7.07 – 6.88 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.0, 138.6, 136.1, 129.4, 125.3, 119.7, 112.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{12}H_{10}N_3O]^+$ 212.0819; found: 212.0822.

6. General information for on-DNA chemistry

6-1). Materials and equipment. The chemically modified DNA oligonucleotide headpiece (HP, 5'-/5Phos/GAGTCA/iSp9/iUniAmM/iSp9/TGACTCCC-3', Figure S1) was synthesized at HitGen Inc.. T4 ligase was expressed at HitGen Inc. and its activity was determined through testing DNA oligomer ligations on HP. All buffer and ionic solutions, including ligation buffer, aq. NaOH (1 M), aq. NaOH (200 mM), aq. NaCl (5 M), aq. HCl (1 M), basic borate buffer (250 mM sodium borate/boric acid, pH=9.4), phosphate buffer (250 mM sodium dihydrogen phosphate/disodium hydrogen phosphate, pH=5.5), acetate buffer (3 M sodium acetate/acetic acid, pH=4.8) were prepared in-house. Heating was performed by using PCR inhibitor.

Chemical building block and reagents were sourced from a variety of vendors, and were generally used from aliquots dissolved in DMSO, DMA, MeCN or THF depending on solubility and optimized reaction conditions.



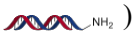
(abbreviated as: )

Figure S1 Headpiece (5'-/5Phos/GAGTCA/iSp9/iUniAmM/iSp9/TGACTCCC-3'), MW = 4937

6-2). General procedure for the analysis of oligonucleotide compositions. DNA was characterized on UPLC-MS system equipped with PDA and QDa mass detector (Waters, MA, USA). The UPLC system was set as following. Column: Acquity UPLC Oligonucleotide BEH C18 Column, 130A, 1.7 μm, 2.1 mm × 50 mm, and maintained at 40 °C. Mobile phases: 0.75% HFIP/0.0375% DIPEA/10 μM EDTA in HPLC grade water (A) and 0.75% HFIP/0.0375% DIPEA/10 μM EDTA in 80/20 HPLC grade methanol/water (B). Eluting gradient: from 26% to 46% of B in 1.2 minutes, flow rate 0.3 mL/min. Absorption was detected at 260 nm. Electrospray ionization (ESI) probe temperature was 600 °C, source temperature was 120 °C and ESI capillary was 0.8 kV. Mass detector (QDa) was operated at negative full scan mode in the range of 500-1200 (m/z). Data was analyzed by ProMass HR 2.0 (Novatia, Pennsylvania, USA) and MassLynx4.1 (Waters, MA, USA).

6-3). General procedure for ethanol precipitation. To a DNA reaction mixture was added 10% (V/V)

5 M NaCl solution and 3 times the volume of absolute ethanol. The solution was then incubated in dry ice for 2 h. The precipitated material was then isolated as a pellet by centrifugation and subsequent removal of the supernatant. 75% aq. ethanol was then added to the pellet and the mixture was centrifuged again. The supernatant again was discarded and the DNA pellet was dried in air or under gentle vacuum.

6-4). General procedures for HP-AOP-NH_2 synthesis.

Elaboration of HP to HP-AOP-NH_2 for substrate preparation. All substrates were prepared on HP that had been further elaborated by a long amino-terminating linker. This elaborated HP, HP-AOP-NH_2, was prepared through amidation of 1-(9H-fluoren-9-yl)-3-oxo-2,7,10,13,16-pentaoxa-4-azanonadecan-19-oic acid through the general acylation procedure and Fmoc deprotection.

The preparation of Fmoc protected HP (Figure S2). In a 15 mL Falcon tube, HP (2 μmol) was dissolved in sodium borate buffer (250 mM, pH=9.4, 2 mL). The stock solutions of 1-(9H-fluoren-9-yl)-3-oxo-2,7,10,13,16- pentaoxa-4-azanonadecan-19-oic acid (10 equiv., 100 μL, 200 mM in DMA), HATU (10 equiv., 50 μL, 400 mM in DMA), and DIPEA (10 equiv., 50 μL, 400 mM in DMA) were first chilled at 0 °C for 5 minutes and then mixed. The mixed reagents were further chilled at 4 °C for 5 minutes and finally added to HP solution in sodium borate buffer. The reaction was proceeded at room temperature for 30 minutes. The product was obtained by ethanol precipitation as described above. The DNA pellet was re-dissolved in 2 mL dd-H_2O and used directly without further purification (98% yield). Calculated MS=5406.7, found MS=5407.2, observed m/z (product) =900.2 $[M-6H]^{6-}$

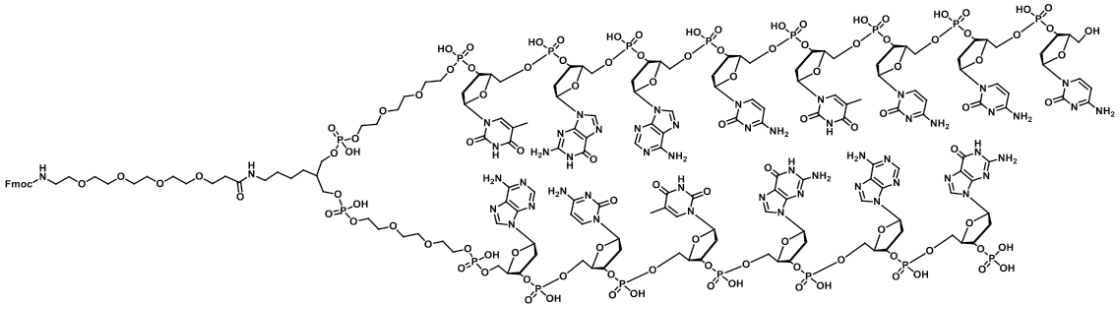


Figure S2 Fmoc protected HP-AOP (MW=5406.72)

The preparation of HP-AOP-NH_2 (Figure S3). In a 15 mL Falcon tube (Corning), 200 μL piperidine was added to a solution of Fmoc protected HP (2 μmoL in 2 mL dd-H_2O, Figure S2). The reaction was proceeded at room temperature for 30 minutes. The product was obtained by ethanol precipitation as described above (95% yield). Calculated MS=5184.4, found MS=5184.8, observed m/z (product) = 647.1 $[M-8H]^{8-}$

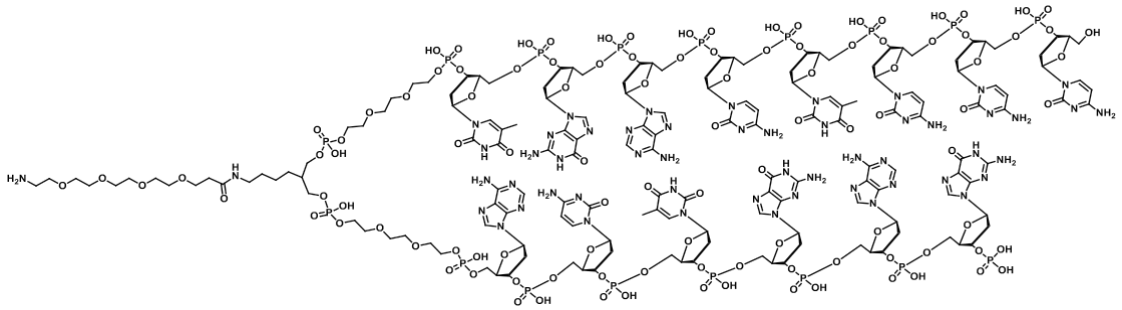
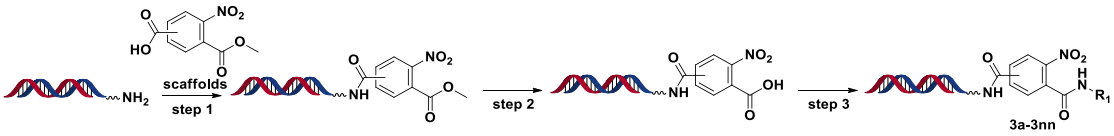


Figure S3 HP-AOP-NH_2 (MW=5184.4)

7. Procedures of on-DNA material synthesis

Synthesis of substrates 3a-3nn.

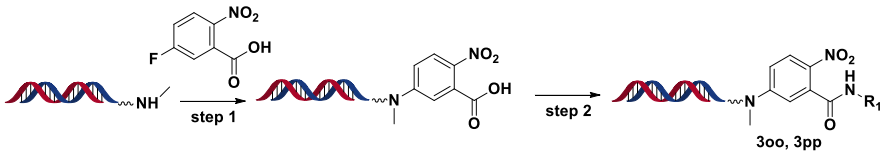


Step 1-amide formation. HP-AOP-NH_2 was dissolved in sodium borate buffer (250 mM, pH=9.4) to make 1 mM solution. Acid (200 mM in DMA, 50 equiv.), HATU (200 mM in DMA, 50 equiv.), and DIPEA (200 mM in DMA, 50 equiv.) were firstly chilled at 4 °C for 5 minutes, and then mixed together. The mixture was chilled at 4 °C for 5 minutes, then transferred to HP-AOP-NH_2 solution. The reaction was allowed to proceed at room temperature overnight prior to ethanol precipitation.

Step 2-ester hydrolysis formation. Product of Step 1 was dissolved in H_2O to make 0.5 mM solution. and NaOH (1000 mM in H_2O, 300 equiv.) were mixed together. The reaction was allowed to proceed at 60 °C for 1 h prior to ethanol precipitation.

Step 3-amide formation (synthesis of substrate 3a-3nn). Product of Step 2 was dissolved in sodium borate buffer (500 mM, pH=9.4) to make 1 mM solution. Amine (300 mM in V_{MeCN}:V_{H2O}=1:1, 300 equiv.), HOAt (600 mM in DMSO, 600 equiv.), and DIC (600 mM in DMSO, 600 equiv.) was added into the DNA solution and vortexed. The reaction mixture was allowed to proceed at room temperature for 1 h prior to ethanol precipitation.

Synthesis of substrate 3oo-3pp.

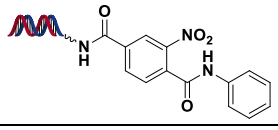
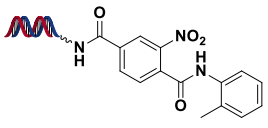
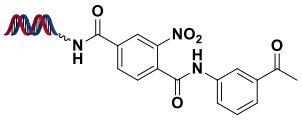
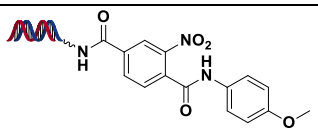
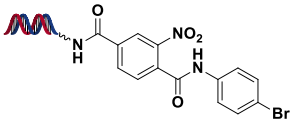


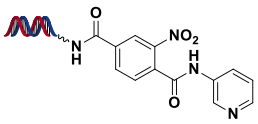
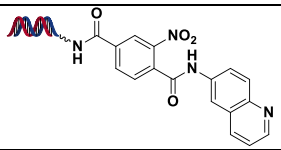
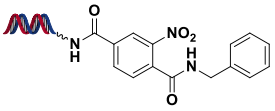
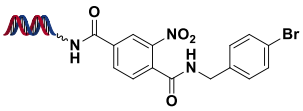
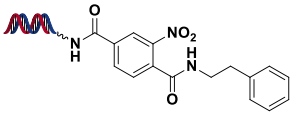
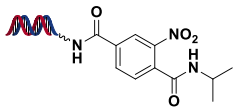
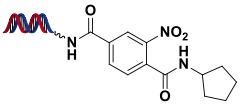
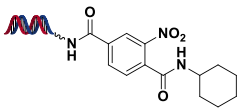
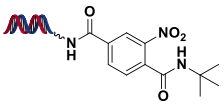
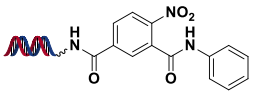
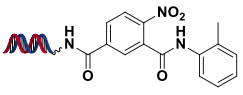
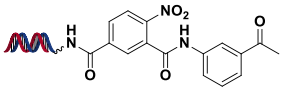
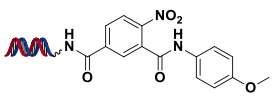
Step 1 C-N bond formation. HP-AOP-$NHCH_3$ was dissolved in sodium borate buffer (250 mM, pH=9.4) to make 1 mM solution. 5-fluoro-2-nitrobenzoic acid (200 mM in DMSO, 100 equiv.), and DIPEA (400 mM in DMSO, 100 equiv.) was added. The reaction was allowed to proceed at 60 ºC overnight prior to ethanol precipitation.

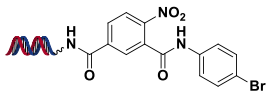
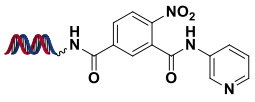
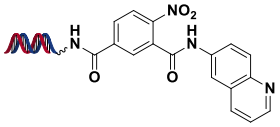
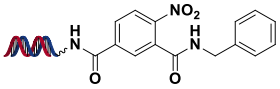
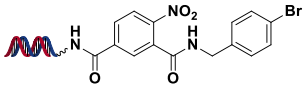
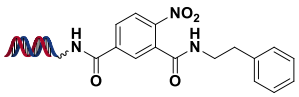
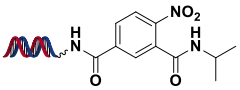
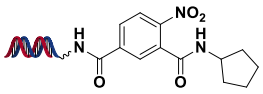
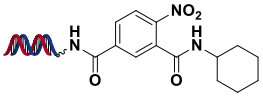
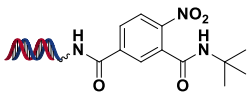
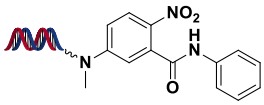
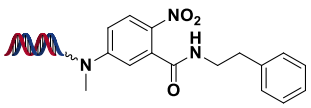
The product was re-dissolved in sodium borate buffer (250 mM, pH=9.4) to make 1 mM solution. 5-fluoro-2-nitrobenzoic acid (200 mM in DMSO, 100 equiv.), and DIPEA (400 mM in DMSO, 100 equiv.) was added into the DNA solution and vortexed. The reaction was allowed to proceed at 60 ºC overnight prior to ethanol precipitation.

Step 2 amide formation (synthesis of substrate 3oo-3pp). Product of Step 1 was dissolved in sodium borate buffer (500 mM, pH=9.4) to make 1 mM solution. Amine (300 mM in V_{MeCN}:V_{H2O}=1:1, 300 equiv.), HOAt (600 mM in DMSO, 600 equiv.), and DIC (600 mM in DMSO, 600 equiv.) was added into the DNA solution and vortexed. The reaction mixture was allowed to proceed at room temperature for 1 h prior to ethanol precipitation.

The on-DNA substrates were listed as below:

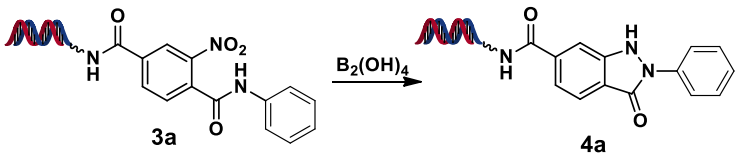
Substrate	Structure	Expected MW	Observed MW	Conversions of amide formation step
3a		5452	5452.4	98%
3b		5466	5466.0	97%
3c		5494	5494.7	96%
3d		5482	5482.7	99%
3e		5531	5530.9	97%

3f		5453	5454.1	96%
3g		5503	5503.6	97%
3h		5466	5465.8	97%
3i		5545	5545.1	95%
3j		5480	5481.4	99%
3k		5418	5418.3	89%
3l		5444	5444.7	97%
3m		5458	5458.1	86%
3n		5432	5432.5	37%
3aa		5452	5452.9	98%
3bb		5466	5466.8	91%
3cc		5494	5494.9	88%
3dd		5482	5482.2	93%

3ee		5531	5531.3	90%
3ff		5453	5453.3	96%
3gg		5503	5503.2	91%
3hh		5466	5466.7	93%
3ii		5545	5545.7	95%
3jj		5480	5480.7	99%
3kk		5418	5418.3	91%
3ll		5444	5444.6	92%
3mm		5458	5458.6	93%
3nn		5432	5432.5	43%
3oo		5438	5438.3	96%
3pp		5466	5466.1	99%

8. Procedures for on-DNA indazolone formation

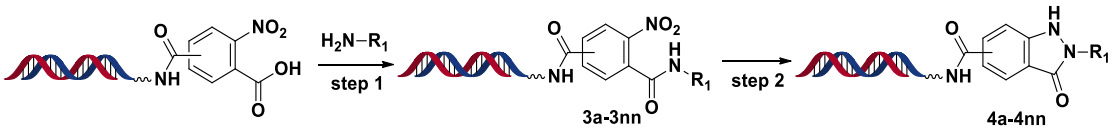
Condition optimization for on-DNA indazolone formation.



entry[a]	$B_2(OH)_4$ (X equiv.)	NaOH (Y equiv.)	EtOH (Z v/v)	4a (%)[b]
1	80	300	0	87%
2	80	300	6%	95%
3[c]	150	500	30%	95%
4[c]	150	500	6%	93%
5[c]	80	500	6%	94%

[a]NaOH (1.0 M in H_2O, Y equiv.) and conjugate **3a** (20 nmol in 20 μ L H_2O, 1.0 equiv.) were pre-mixed together, then EtOH (Z v/v) was added, which was followed by adding $B_2(OH)_4$ (100 mM in H_2O, X equiv.). The mixture was vortexed and reacted at room temperature for 2 hours; [b]Conversion was determined by LC-MS; [c]NaOH (500 mM in H_2O) was used.

Syntheses of substrate 4a-4nn.

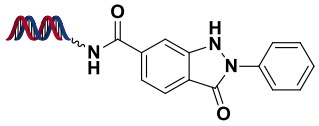
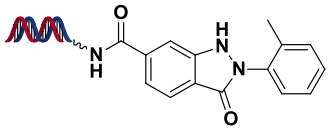
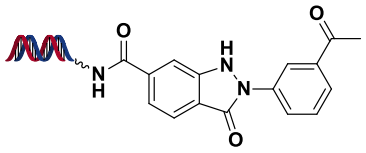
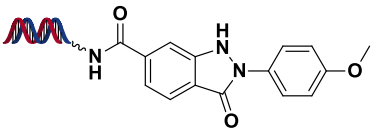
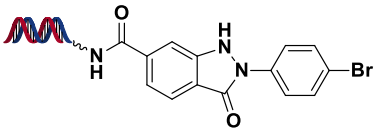
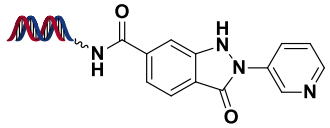
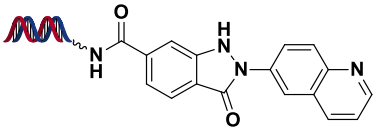
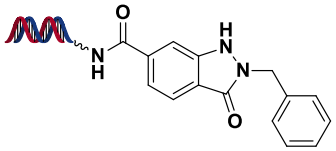


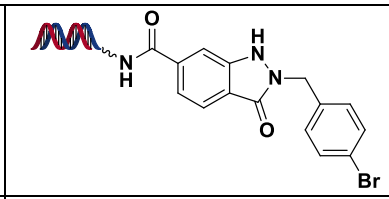
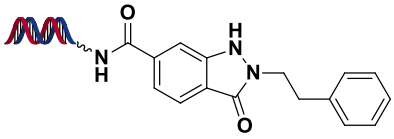
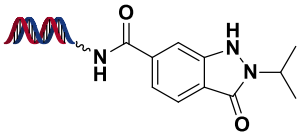
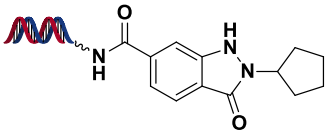
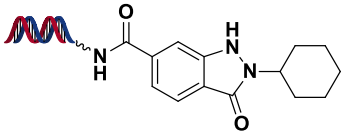
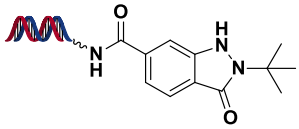
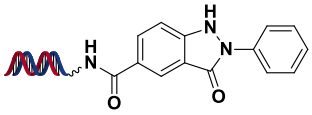
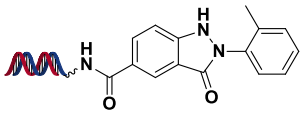
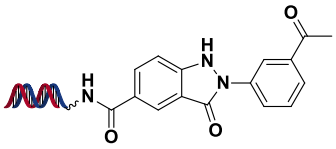
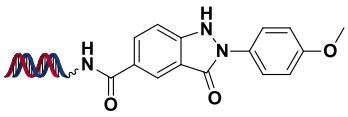
Step 1-amide formation (synthesis of substrate 3a-3nn). on-DNA acid was dissolved in sodium borate buffer (500 mM, pH=9.4) to make 1 mM solution. Amine (300 mM in V_{MeCN}:V_{H2O}=1:1, 300 equiv.), HOAt (600 mM in DMSO, 600 equiv.), and DIC (600 mM in DMSO, 600 equiv.) was added into the DNA solution and vortexed. The reaction mixture was allowed to proceed at room temperature for 1 h prior to ethanol precipitation.

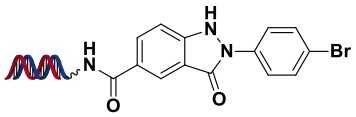
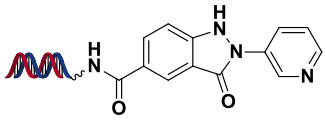
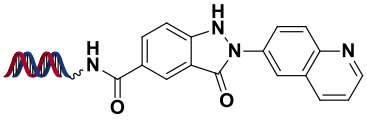
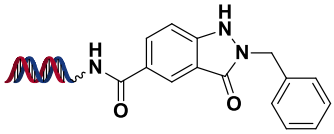
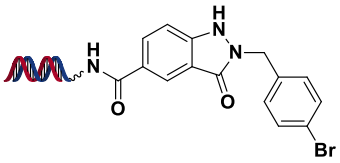
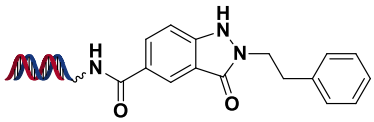
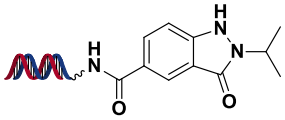
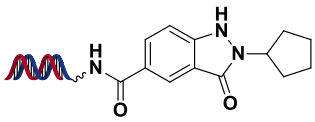
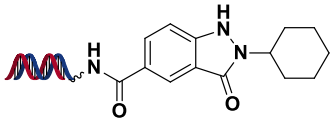
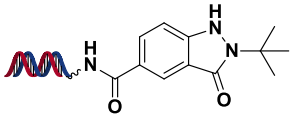
Step 2-indazolone formation (synthesis of conjugate 4a-4nn). Conjugate **3a-3nn** (20 nmol, 1.0 equiv.) was dissolved in H_2O to make 1 mM solution, which was premixed with NaOH (6 μmol in 6 μL H_2O, 300 equiv.) and vortexed. Then EtOH (2.6 μL, 6% v/v) was added, which was followed

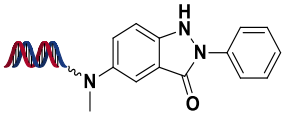
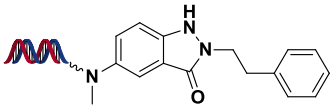
by adding $B_2(OH)_4$ (1.6 μmol in 16 μL H_2O, 80 equiv.). The mixture was vortexed and reacted at room temperature for 2h;

The on-DNA substrates were listed as below:

Entry	structure	Conversion of step 1	Conversion of step 2	2-step Conversion
4a		98%	95%	93%
4b		97%	81%	79%
4c		96%	91%	87%
4d		99%	92%	91%
4e		97%	68%	66%
4f		96%	57%	55%
4g		97%	93%	90%
4h		97%	47%	46%

4i		95%	52%	49%
4j		99%	63%	62%
4k		89%	42%	37%
4l		97%	42%	41%
4m		86%	40%	34%
4n		37%	25%	9%
4aa		98%	95%	93%
4bb		91%	95%	87%
4cc		88%	92%	81%
4dd		93%	95%	88%

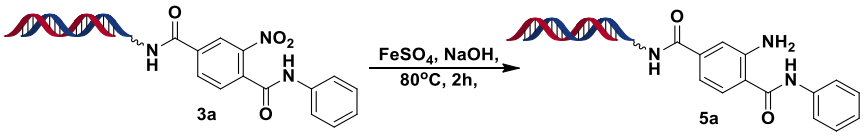
4ee		90%	74%	67%
4ff		96%	95%	91%
4gg		91%	94%	86%
4hh		93%	79%	74%
4ii		95%	79%	75%
4jj		99%	73%	72%
4kk		91%	75%	68%
4ll		92%	74%	68%
4mm		93%	64%	60%
4nn		43%	47%	20%

4oo		96%	/	/
4pp		99%	/	/

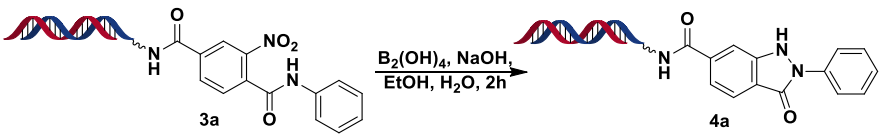
9. On-DNA structure confirmation

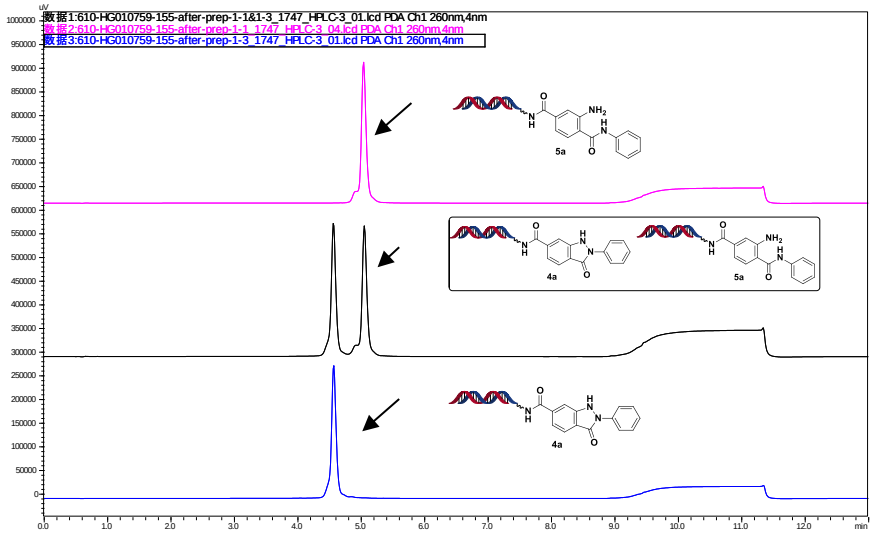
9-1) Co-injection of conjugate 5a and 4a

DNA-conjugated substrate **3a** was dissolved in sodium borate buffer (250 mM, pH=9.4) to make 1 mM solution. $FeSO_4$ (200 mM in dd-H_2O, 100 equiv.) and NaOH (1 M in dd-H_2O, 300 equiv.) were added into the DNA solution, then vortex, the reaction was allowed to proceed at 80 °C for 2 hours.



To a solution of DNA-conjugated substrate **3a** was dissolved in H_2O to make 1 mM solution, and NaOH (300 equiv., 1000 mM in H_2O) were mixed together. And then EtOH (10% equiv v/v of total volume of NaOH and DNA) was added, which is followed by adding $B_2(OH)_4$ (80 equiv., 100 mM in H_2O). The mixture was vortexed and reacted at room temperature for 2 h.

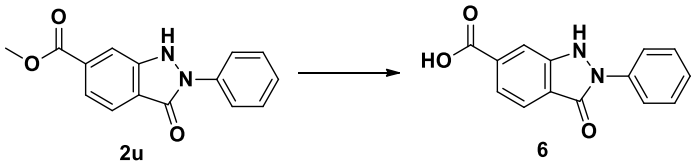




*HPLC condition: Method : Column: XBridge Shield RP 18 3.5um 4.6*50mm; Mobile Phase: A:100mM TEAA Water B:CAN;Gradient : B from 5% to 34% in 7 min and hold 95% for 2.0 min;

Figure S4. HPLC analysis between **5a** and **4a**

9-2) Co-injection of conjugate 4a and 7



To a stirred solution of Compound **2u** (70 mg, 0.26 mmol) in a mixture of THF/H_2O (6:1, 1.6 mL) was added aq 4 M LiOH (1.3 mL, 5.2 mmol). The mixture was stirred at r.t. for 16 h, then diluted with water (10 mL) and acidified to pH=3-4 using aq. saturated citric acid. Collecting the precipitate gave Compound **6** (64 mg, 97%) as a pale yellow amorphous solid, HRMS (ESI) m/z: $[M + H]^+$ calcd for $[C_{14}H_{11}N_2O_3]^+$ 255.0764; found: 255.0769.

Synthesis of DNA conjugate **7**. The synthesis protocol was the same as acylation as above.

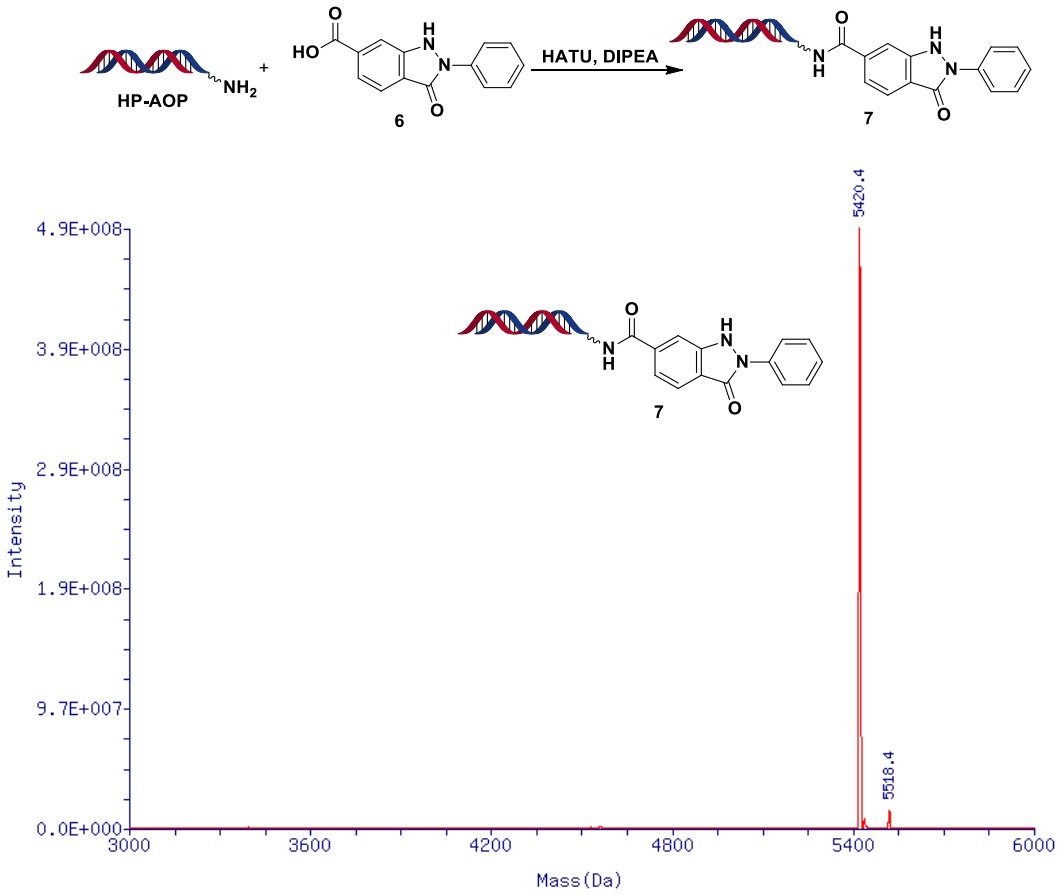
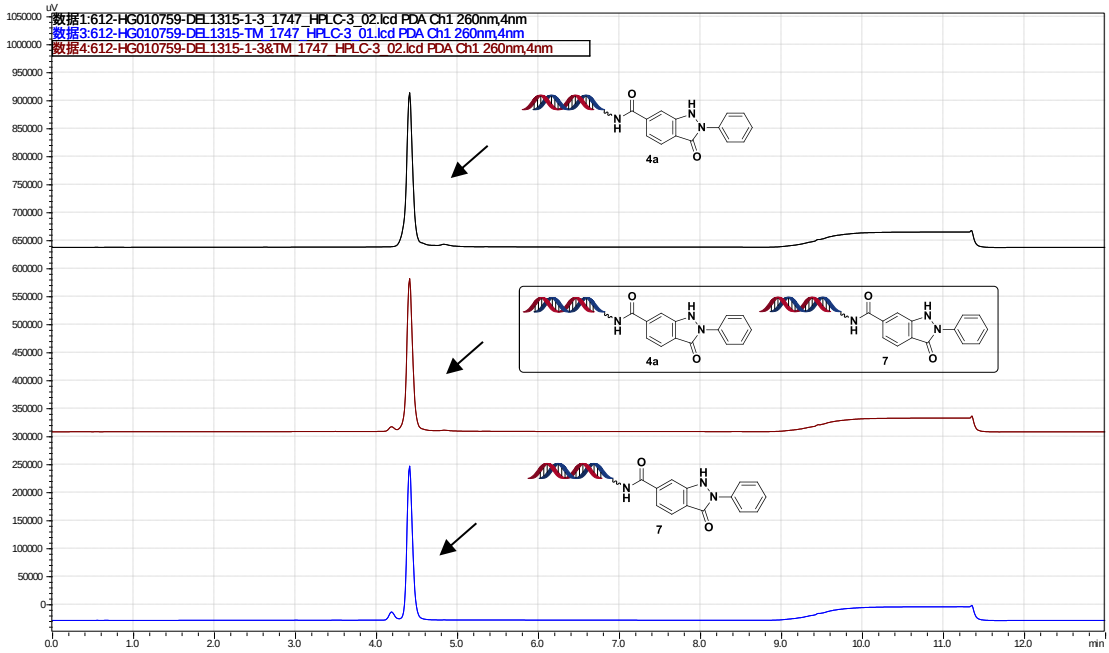


Figure S5. Deconvoluted mass spectrum of DNA conjugate 7, expected: 5420.5; observed 5420.4

Co-injection experiment by HPLC.

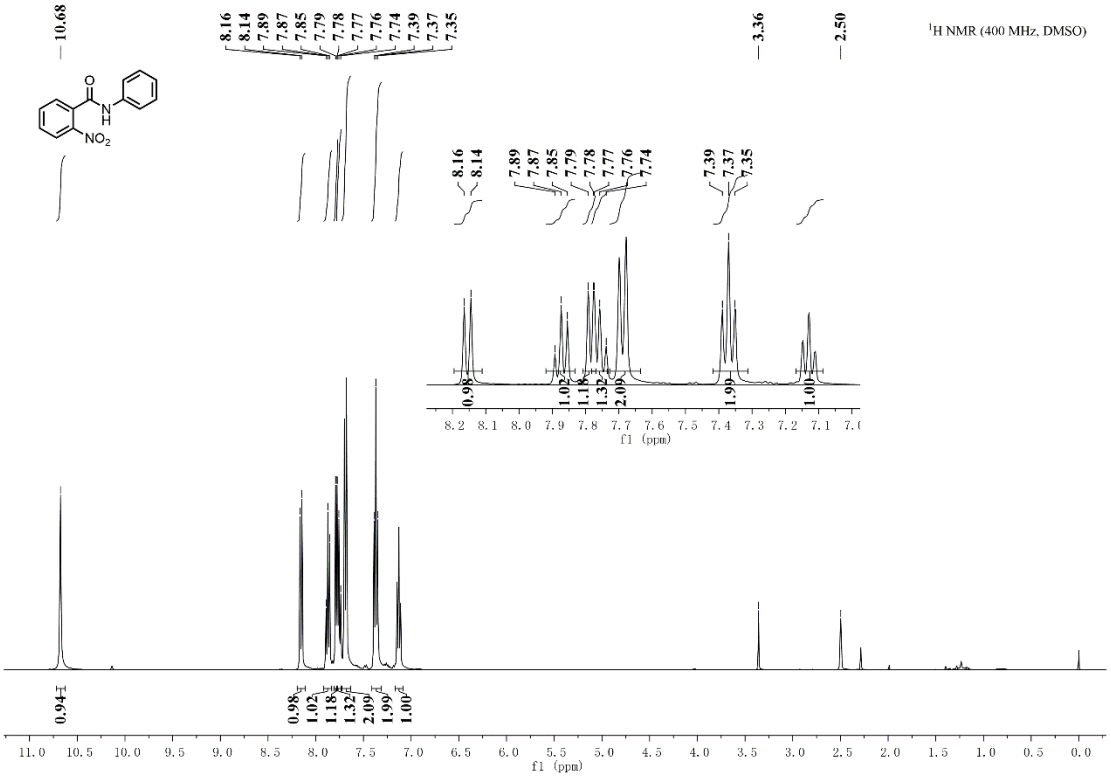


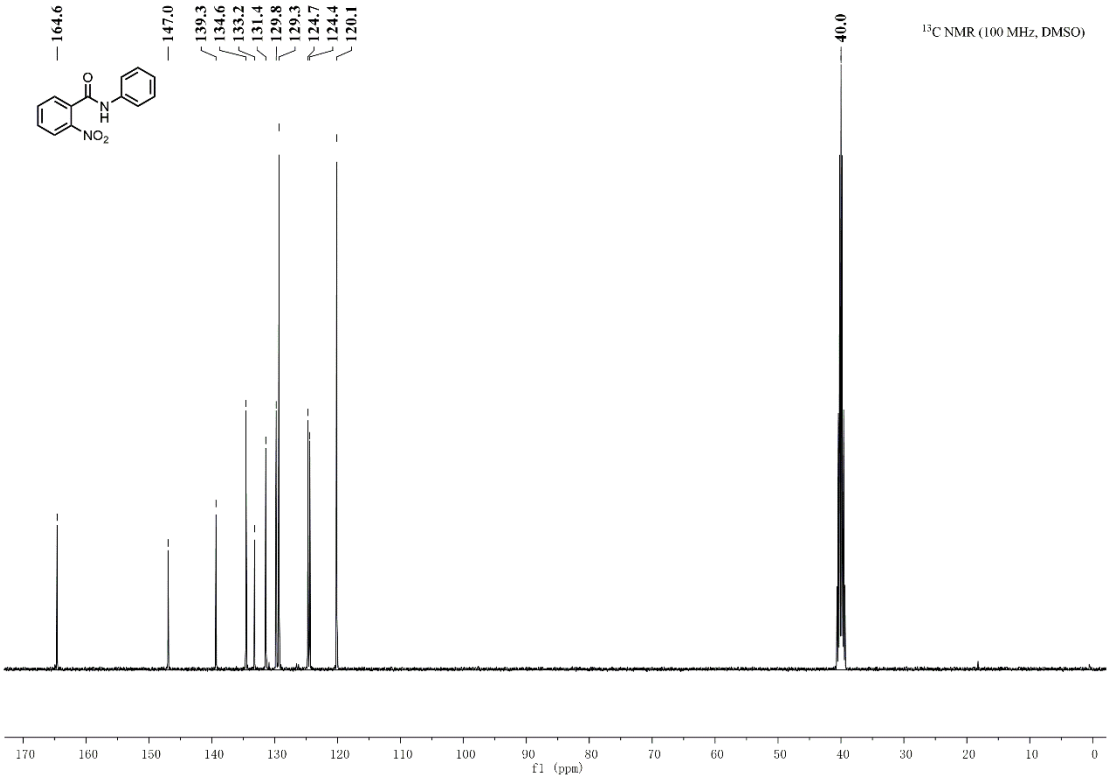
*HPLC condition: Method : Column: XBridge Shield RP 18 3.5um 4.6*50mm; Mobile Phase: A:100mM TEAA Water B:CAN;Gradient : B from 5% to 34% in 7 min and hold 95% for 2.0 min;

Figure S6. HPLC analysis between 7 and 4a.

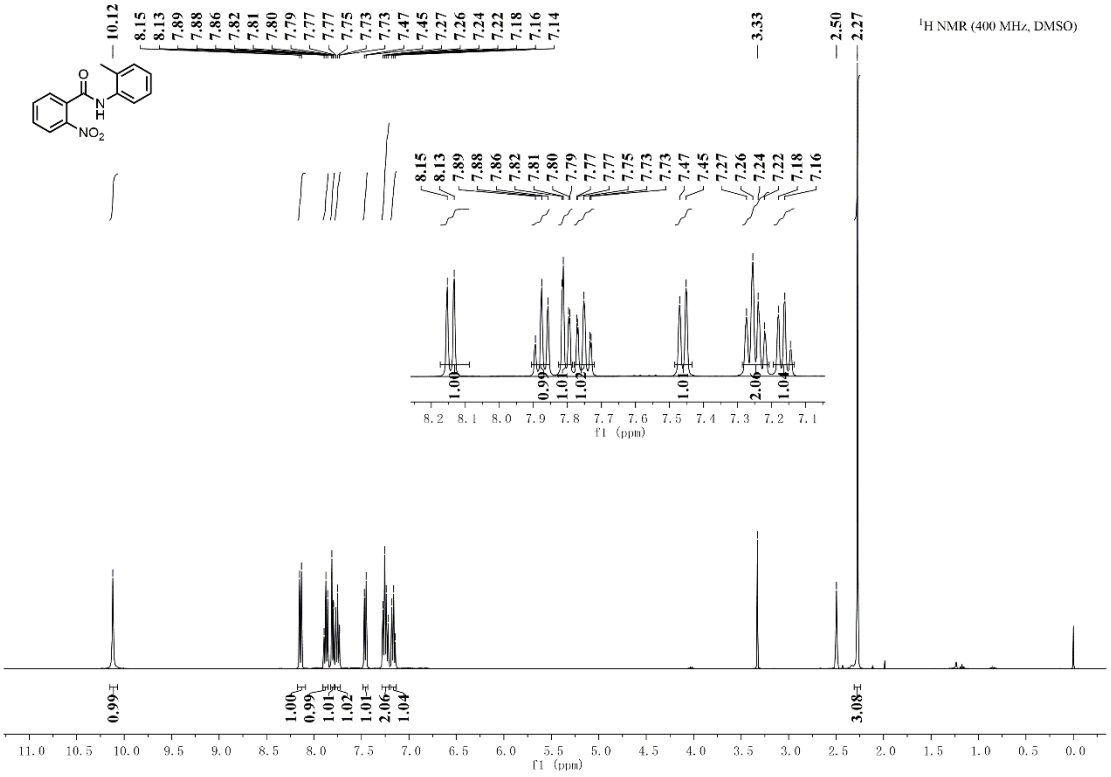
10. ^{1}H and ^{13}C NMR spectra of small molecules

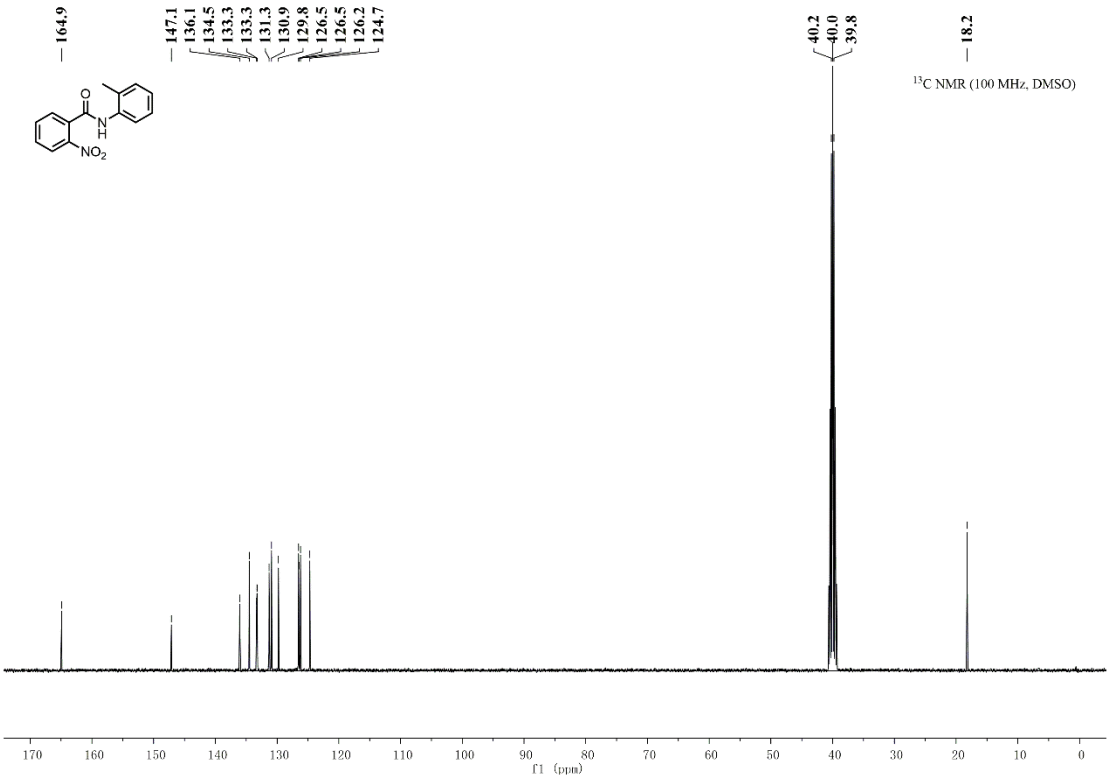
2-nitro-N-phenylbenzamide (1a)



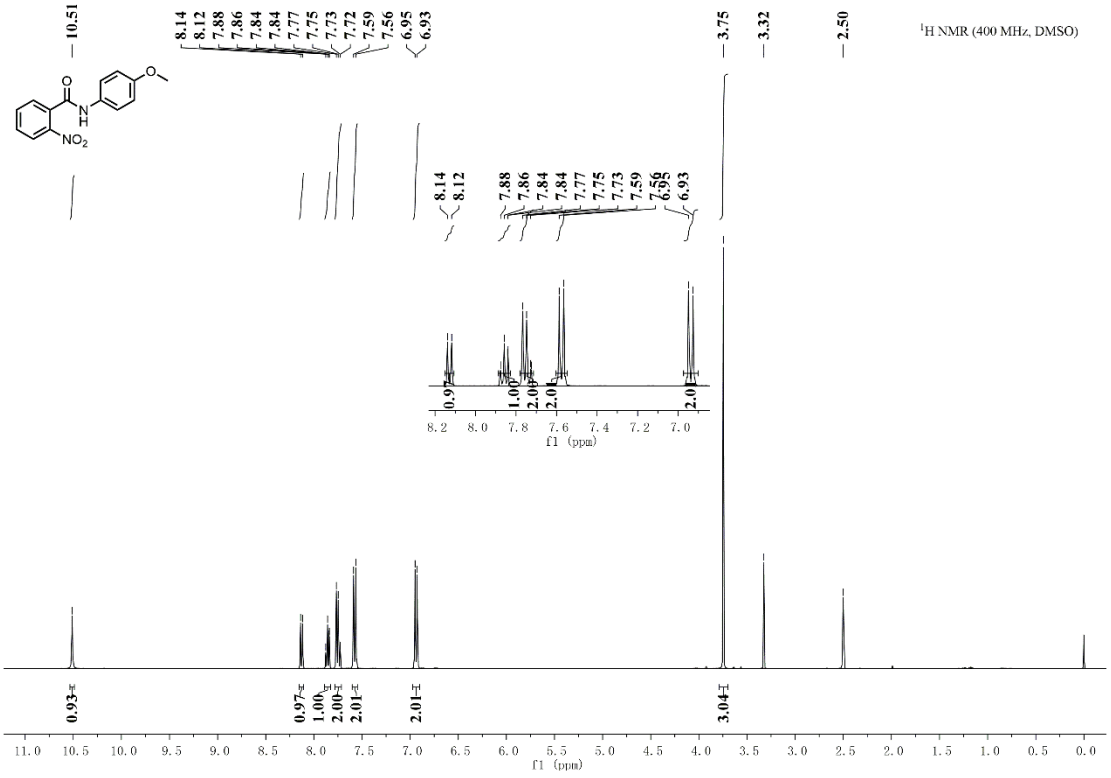


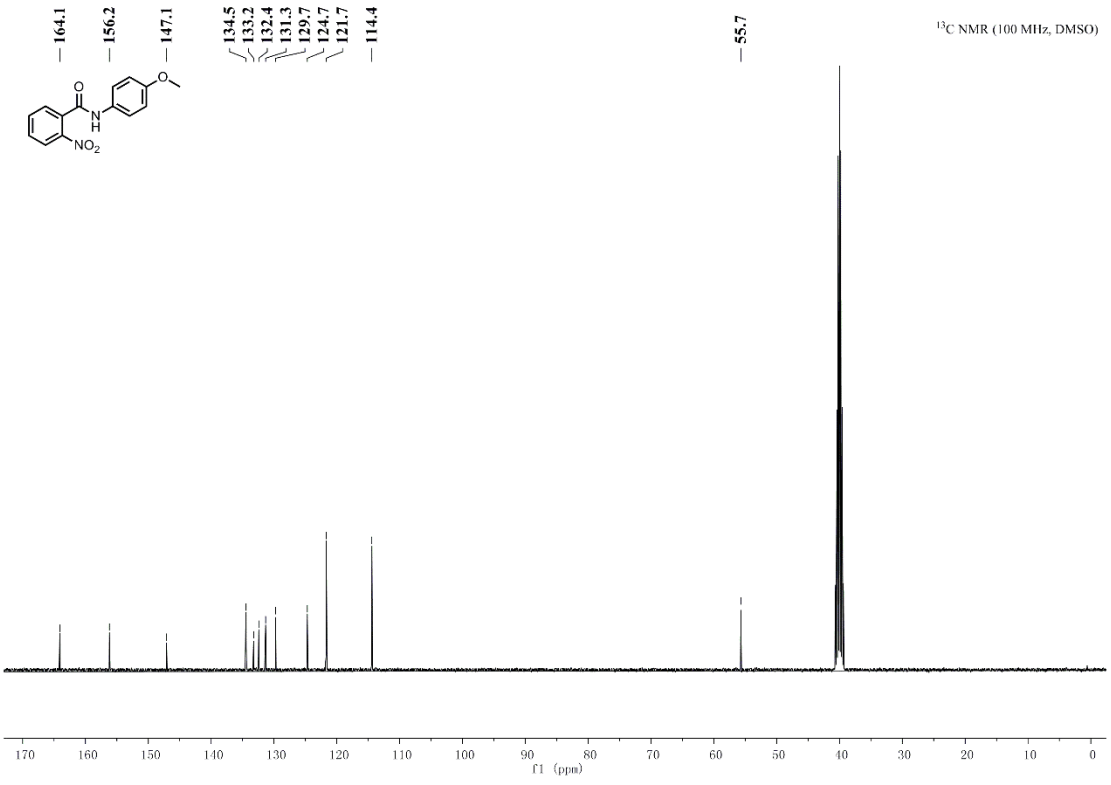
2-nitro-N-(o-tolyl)benzamide (1b)





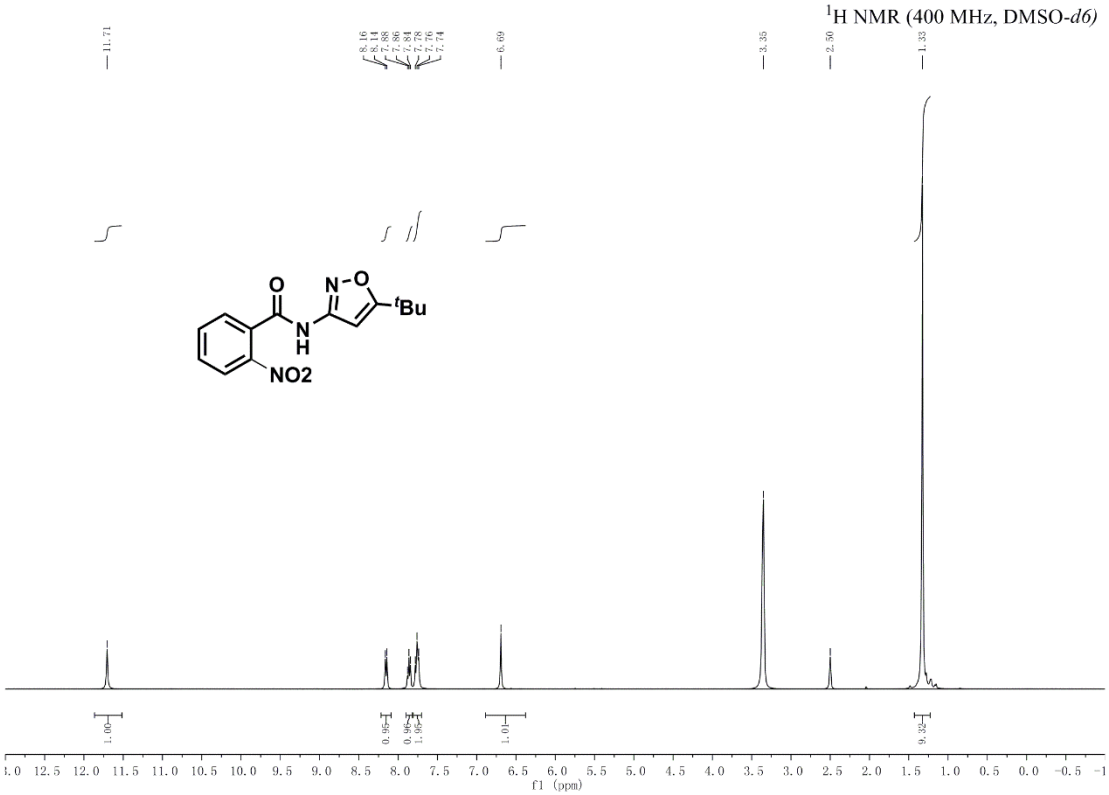
N-(4-methoxyphenyl)-2-nitrobenzamide (1c)



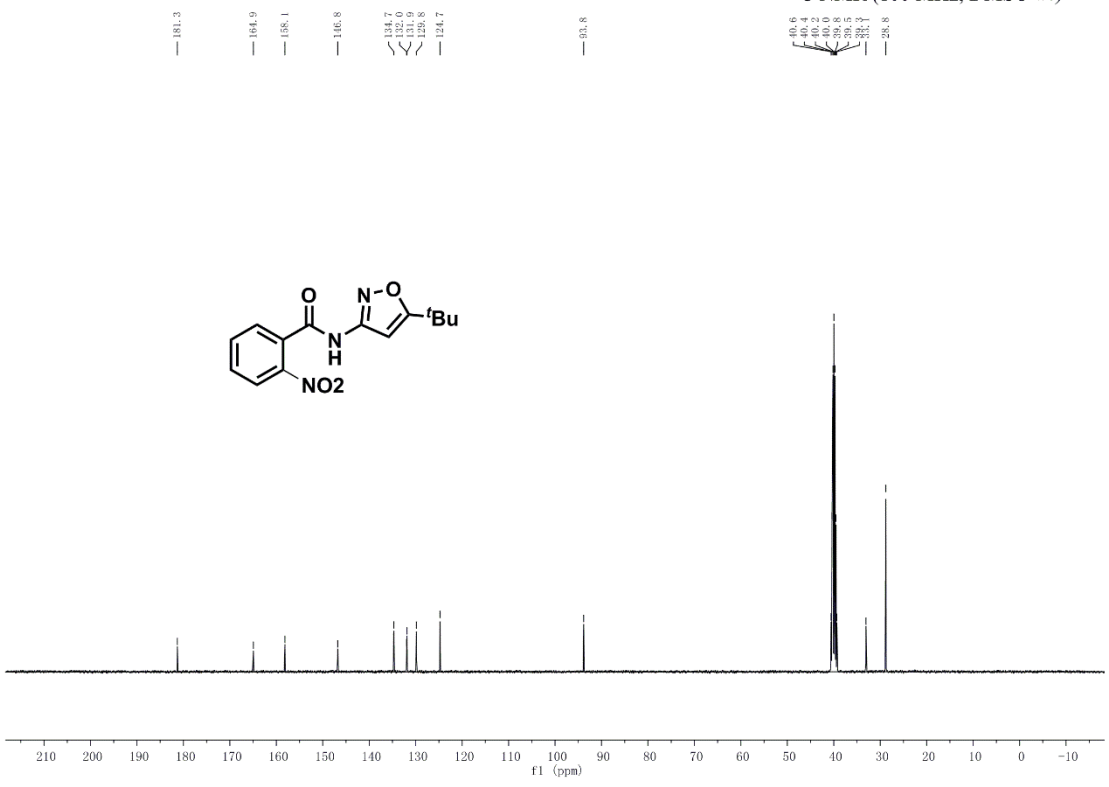


N-(5-(tert-butyl)isoxazol-3-yl)-2-nitrobenzamide (1d)

^{1}H NMR (400 MHz, DMSO-*d6)*

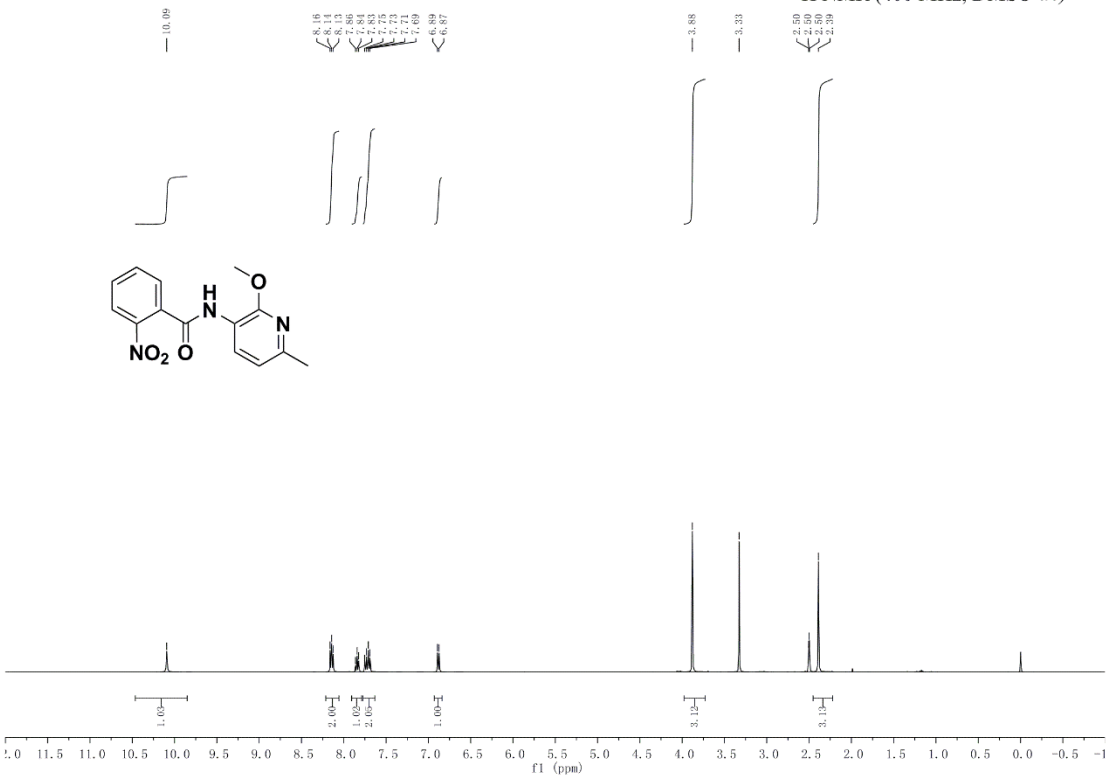


^{13}C NMR (100 MHz, DMSO-*d6)*

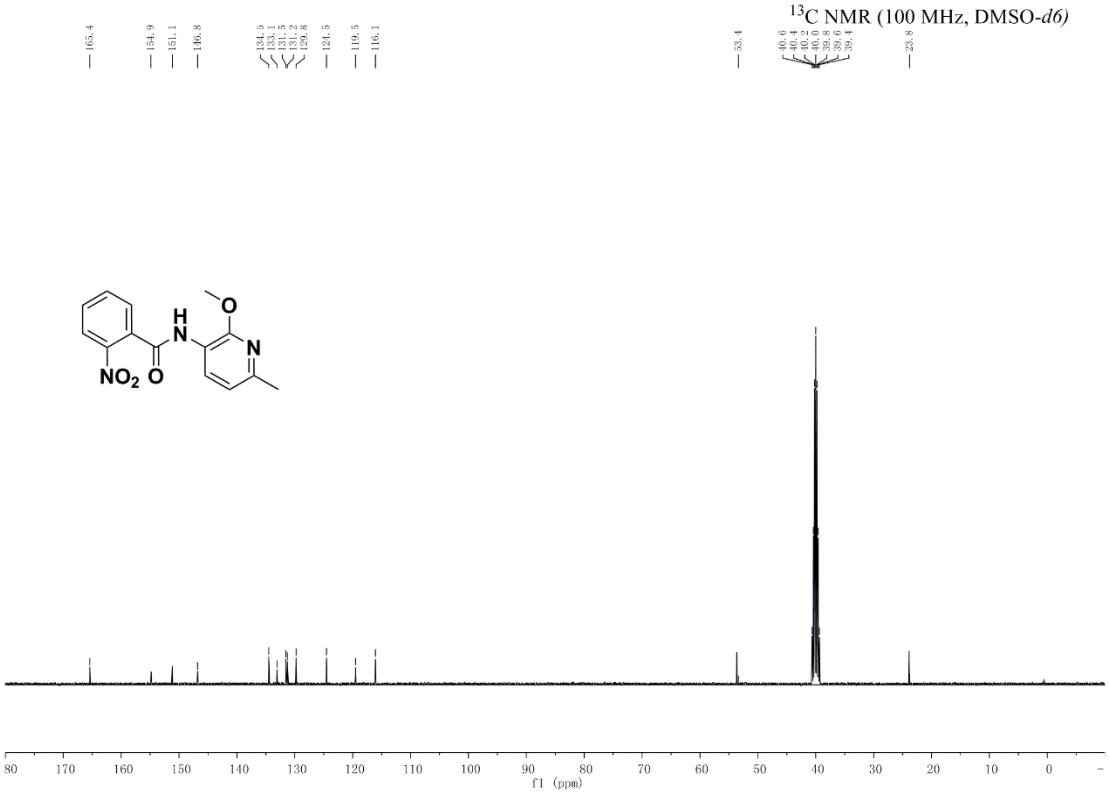


N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1e)

^{1}H NMR (400 MHz, DMSO-*d6*)

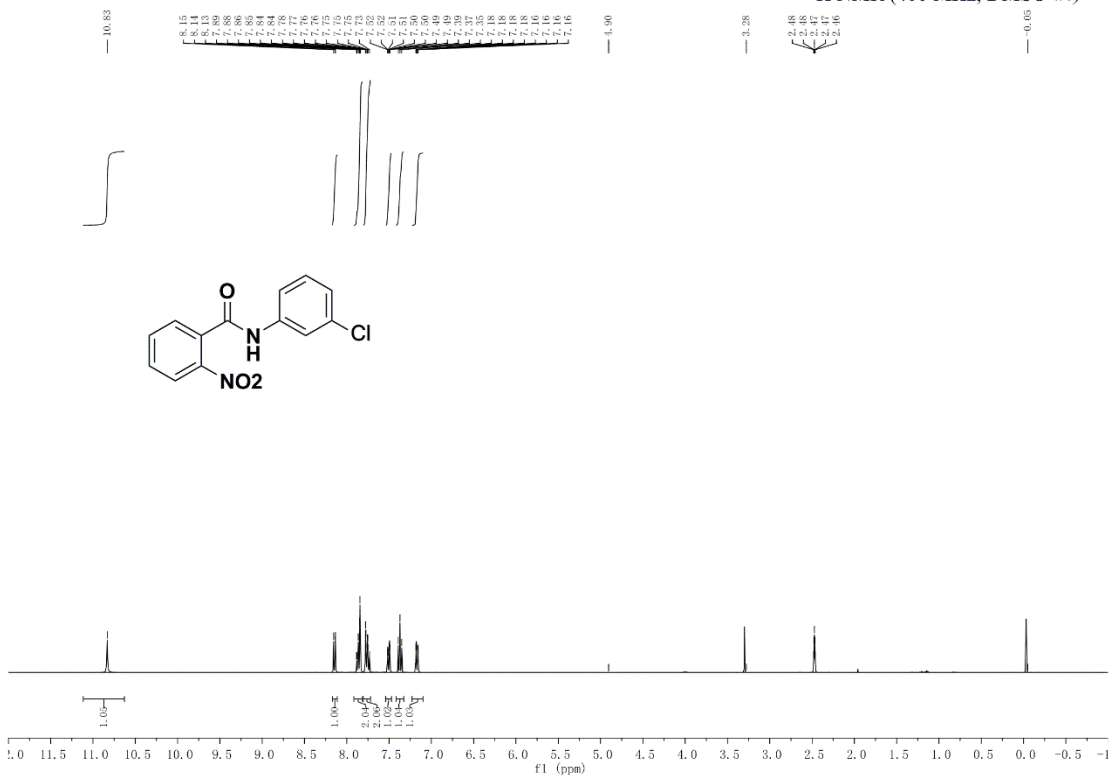


^{13}C NMR (100 MHz, DMSO-*d6*)

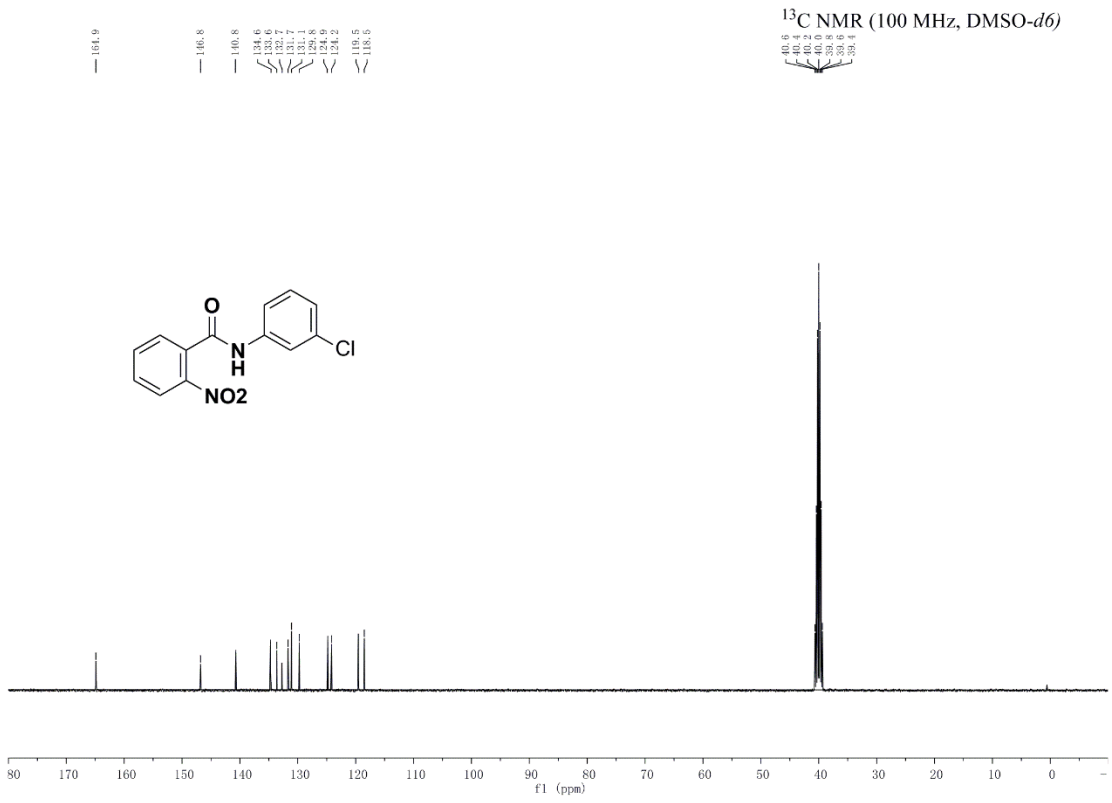


N-(3-chlorophenyl)-2-nitrobenzamide (1f)

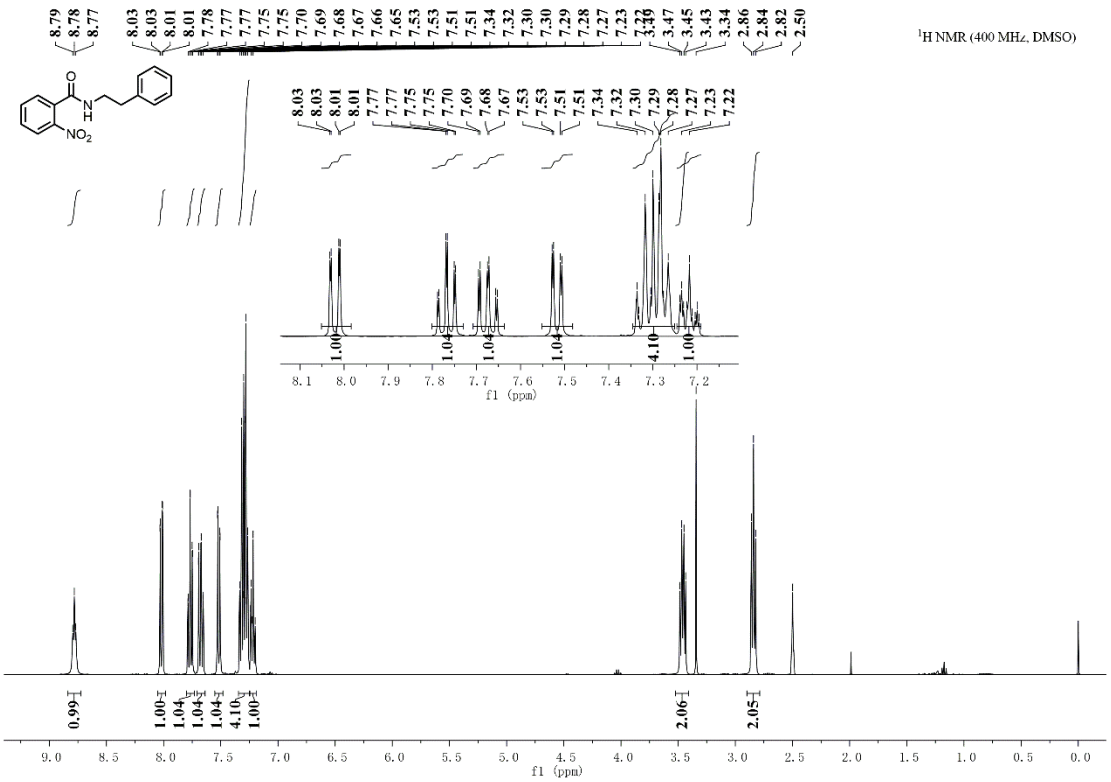
^{1}H NMR (400 MHz, DMSO-*d6*)

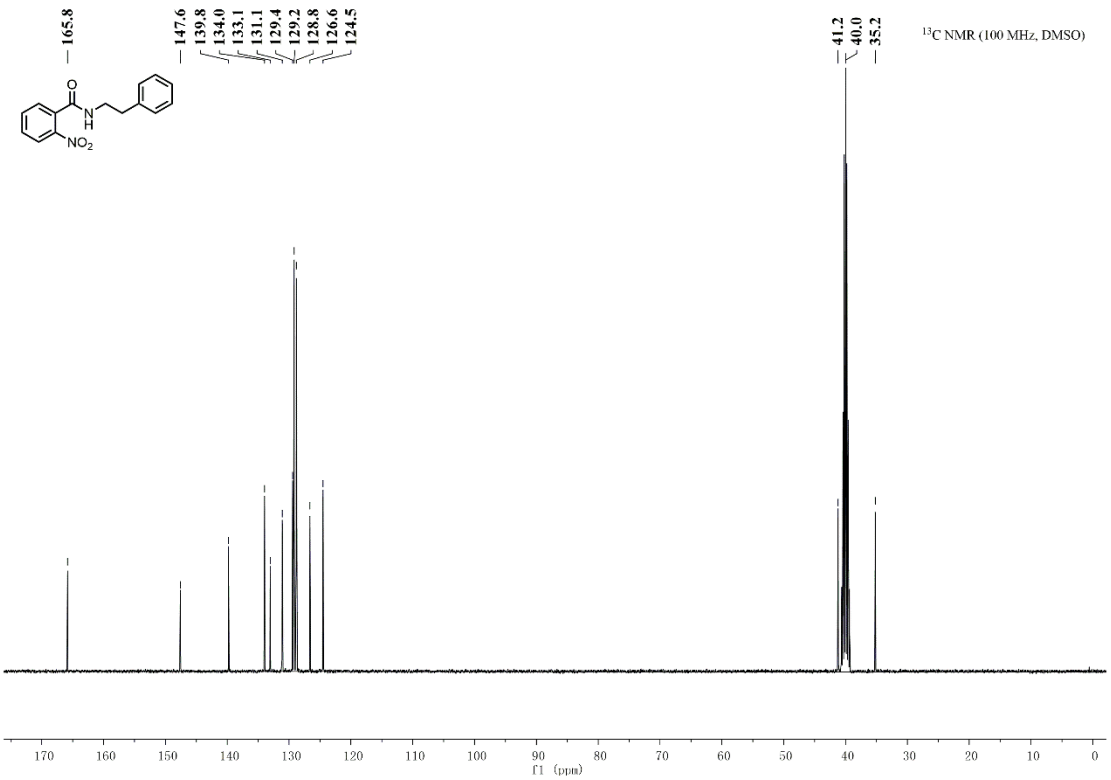


^{13}C NMR (100 MHz, DMSO-*d6*)

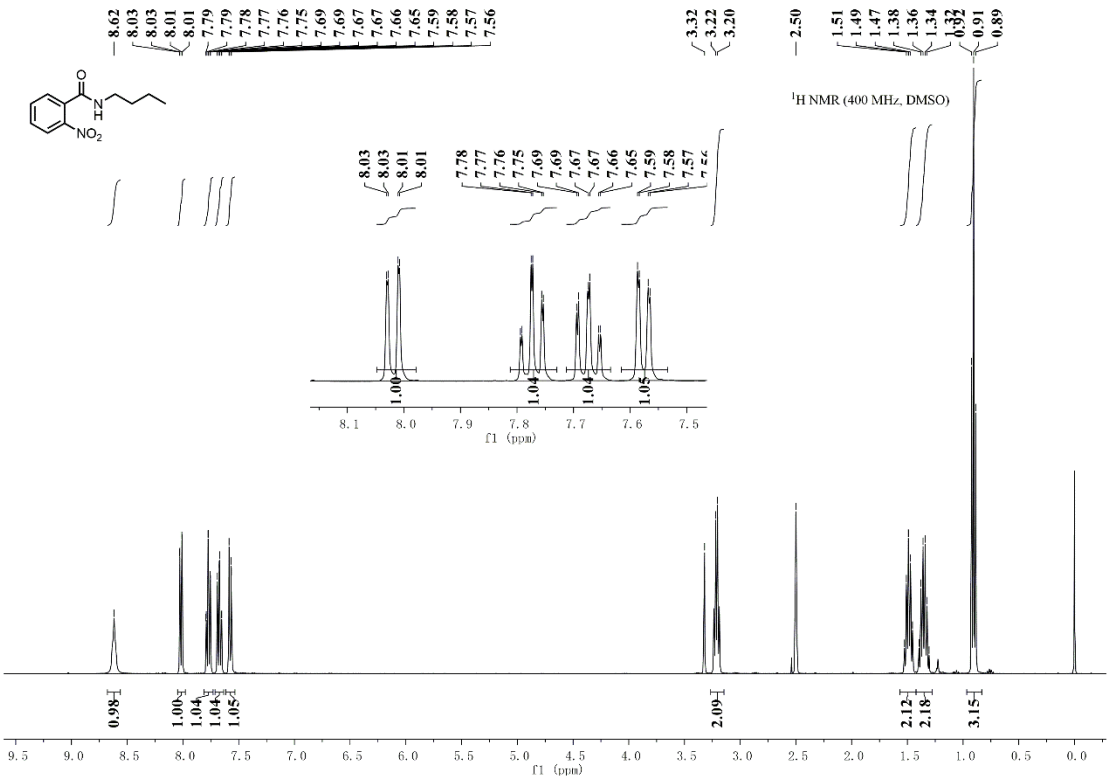


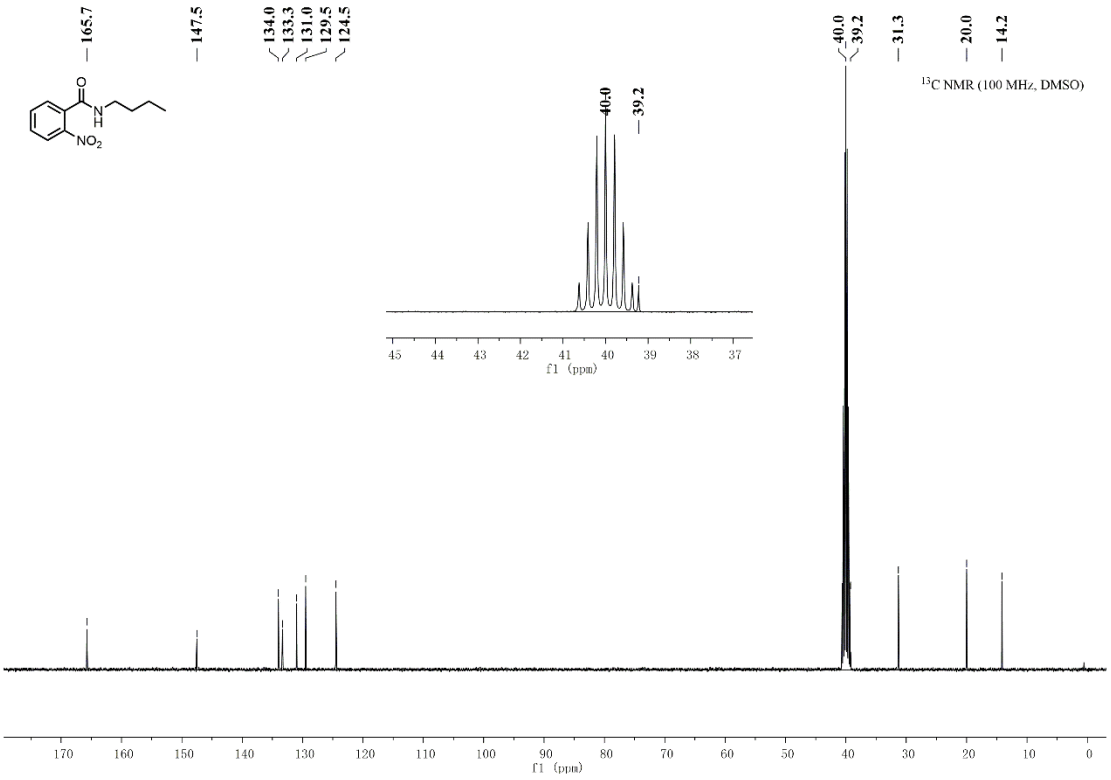
2-nitro-N-phenethylbenzamide (1g)



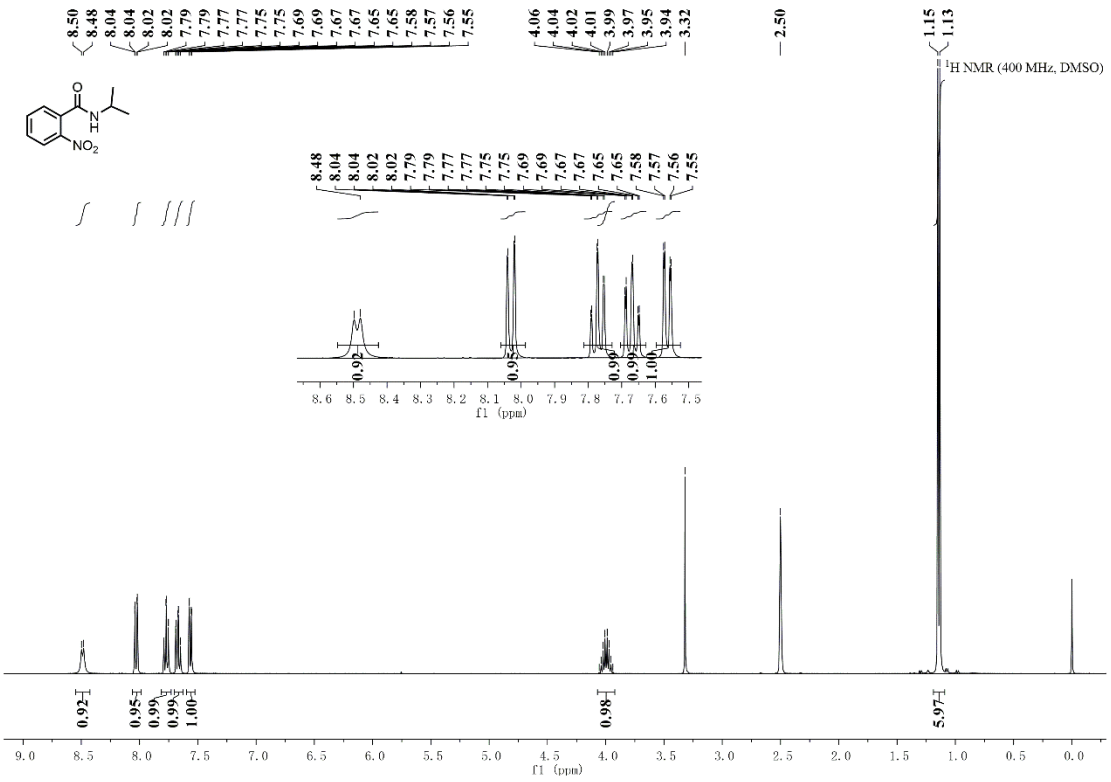


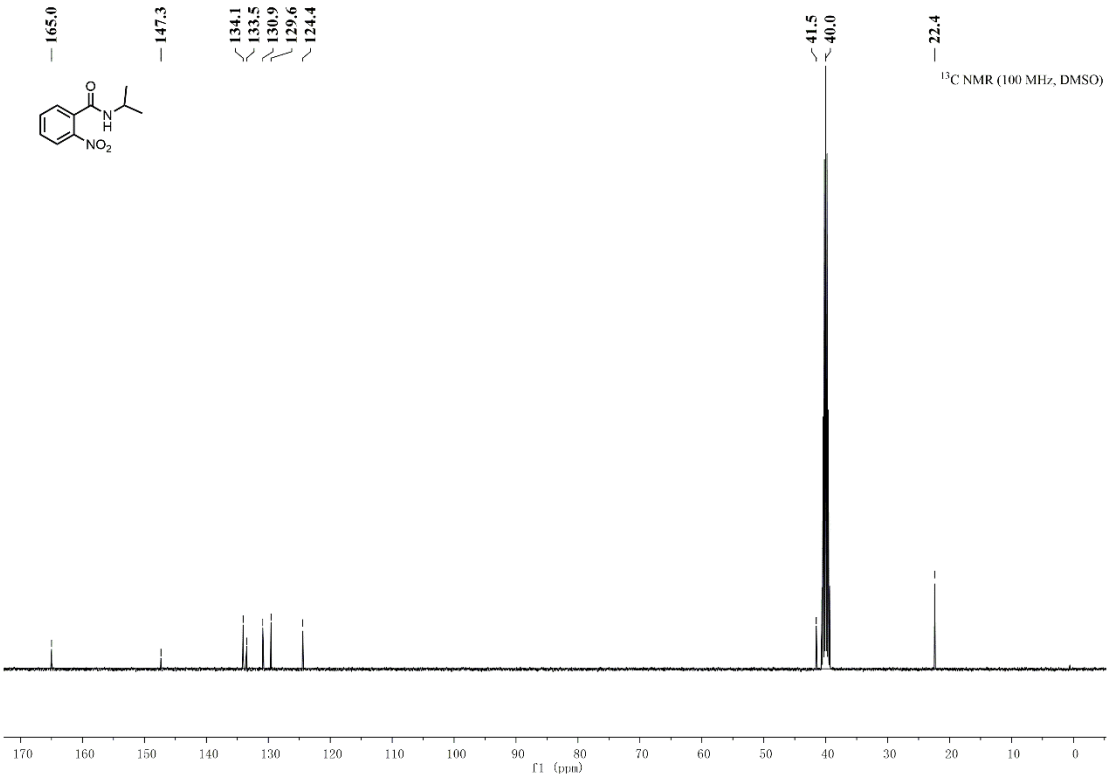
N-butyl-2-nitrobenzamide (1h)



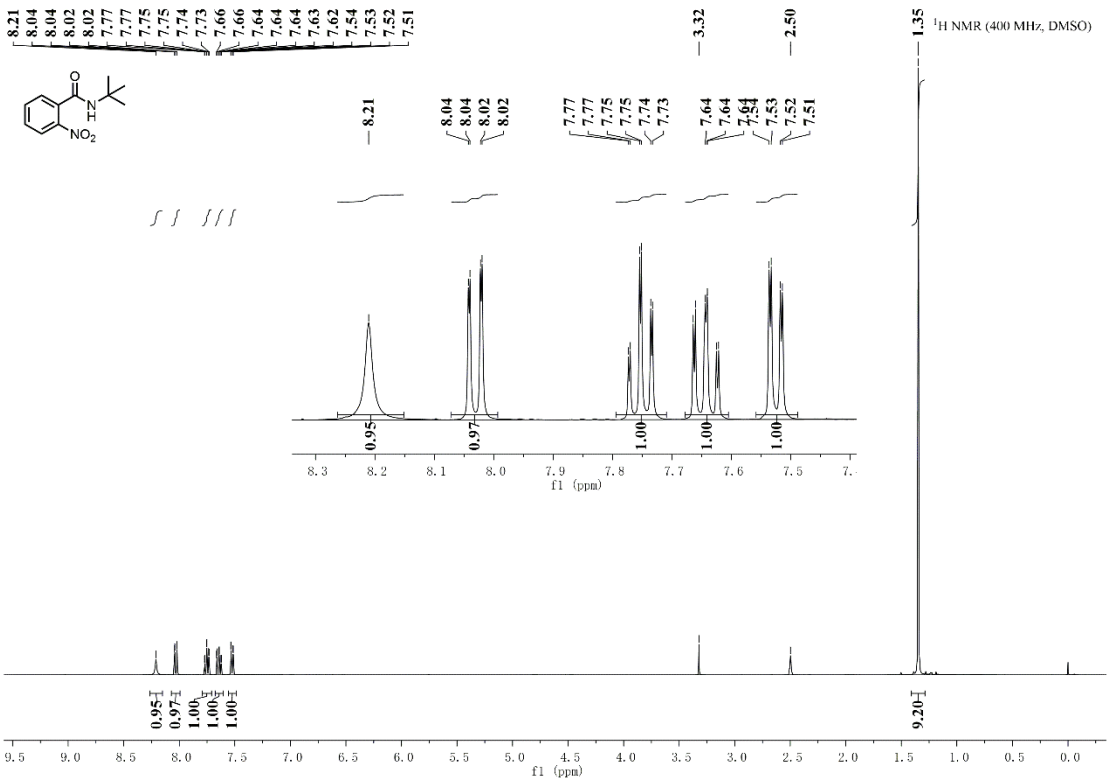


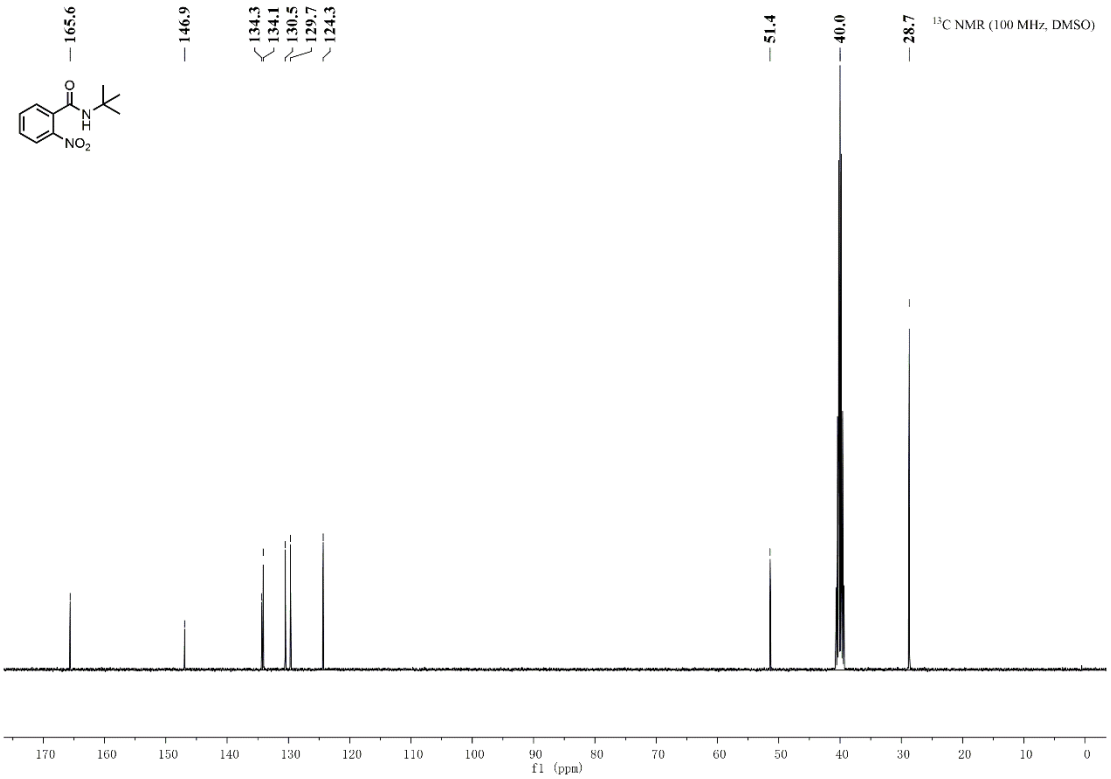
N-isopropyl-2-nitrobenzamide (1i)



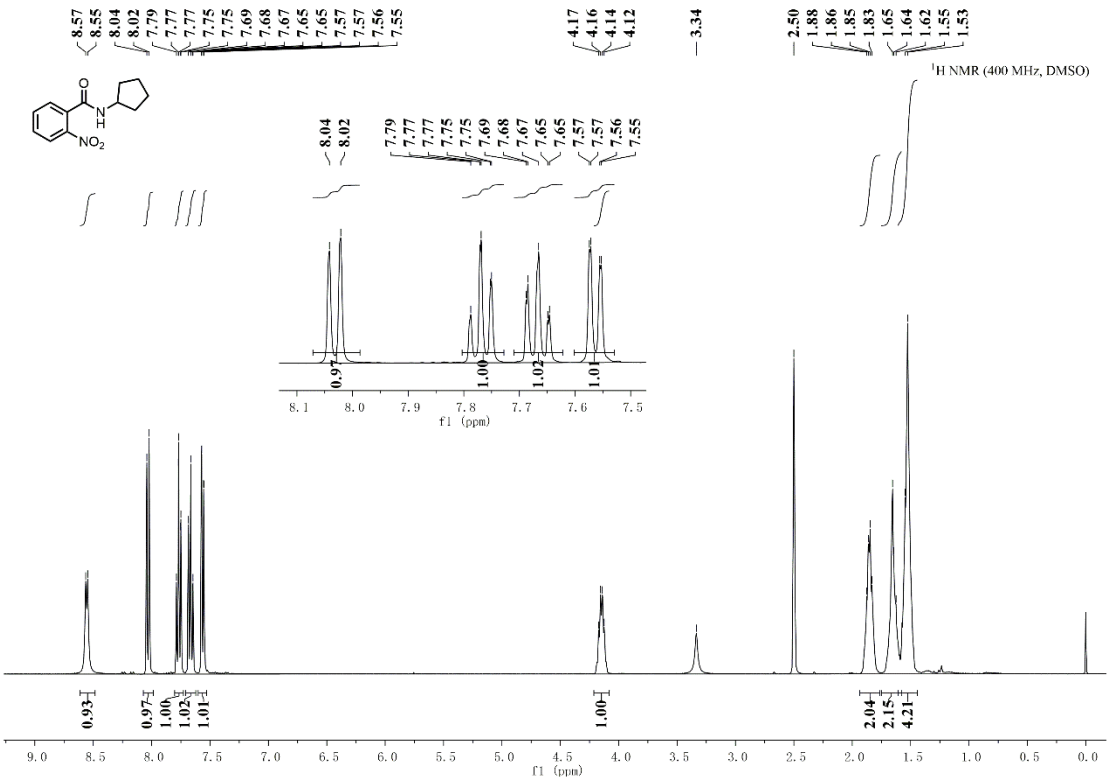


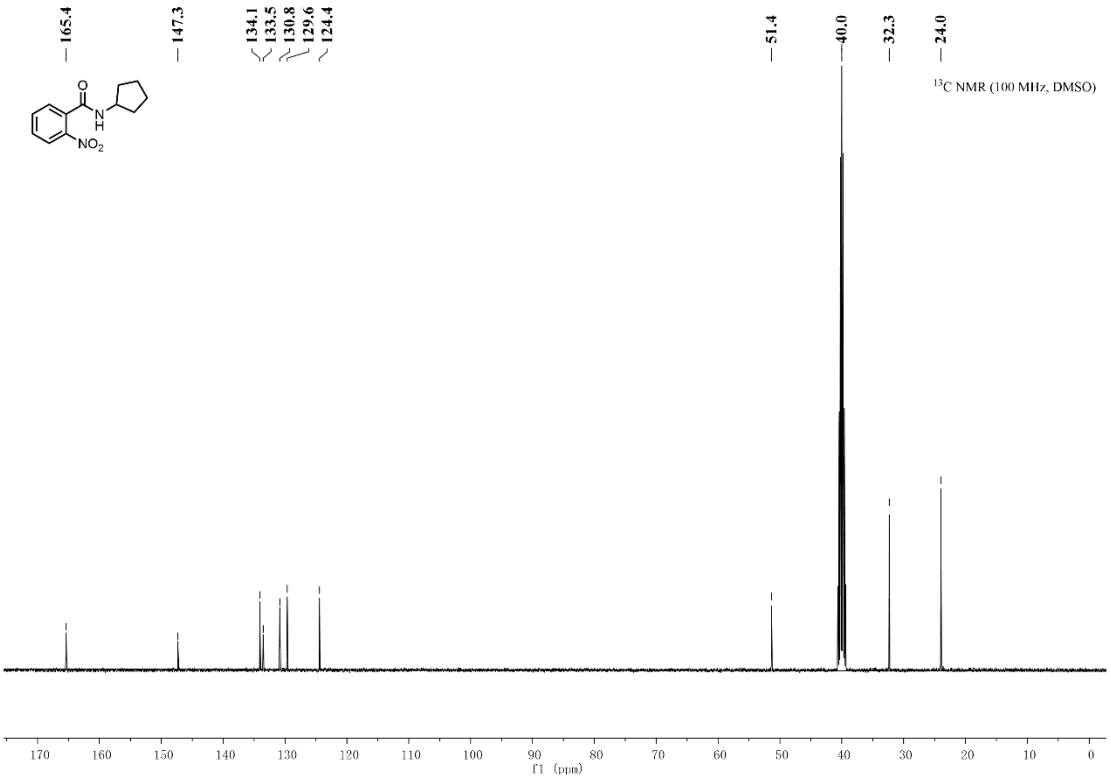
N-(tert-butyl)-2-nitrobenzamide (1j)



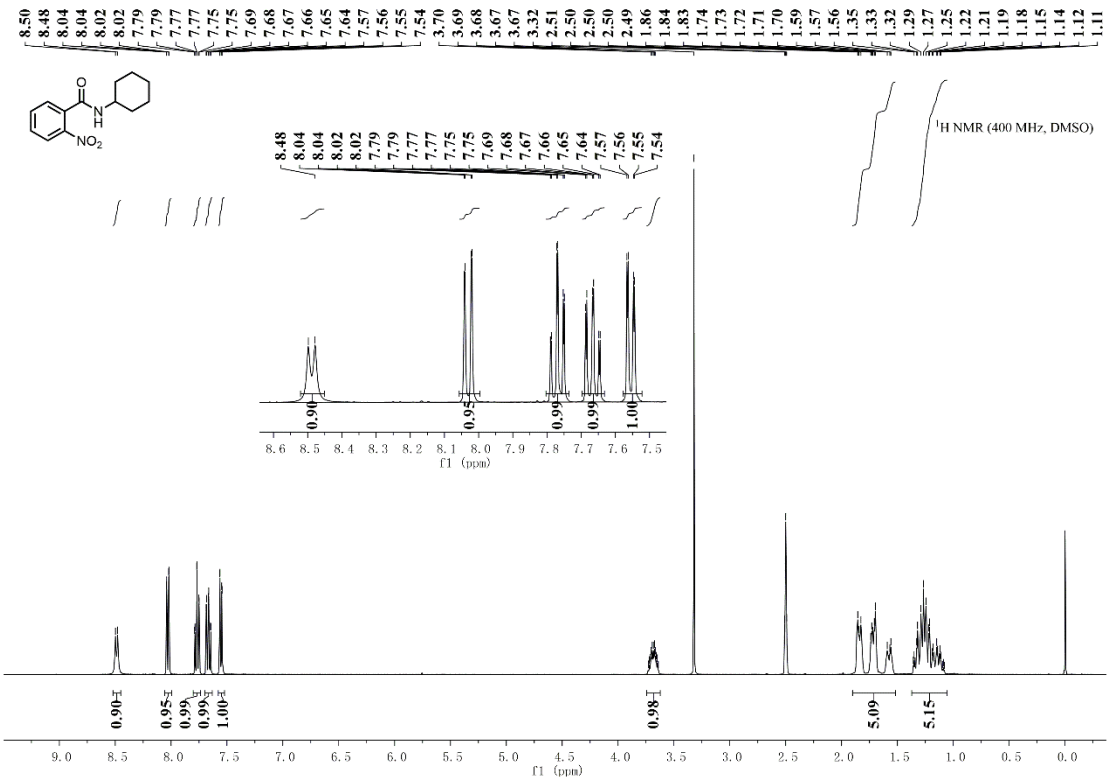


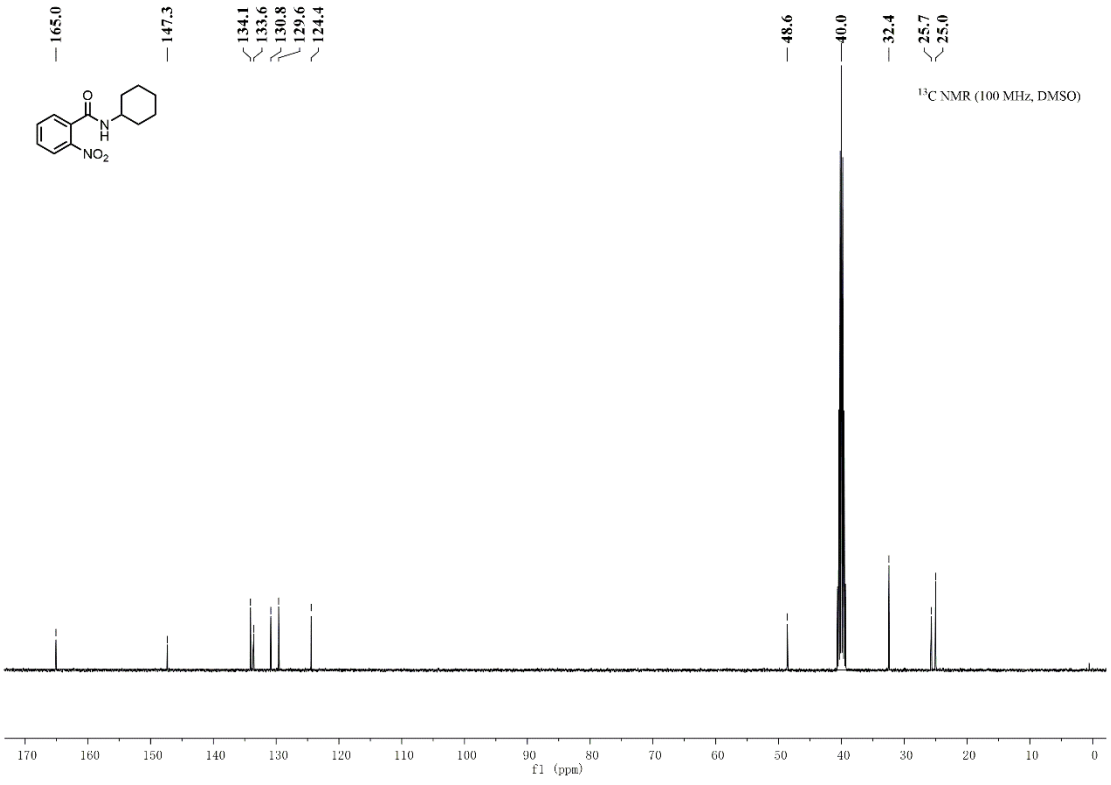
N-cyclopentyl-2-nitrobenzamide (1k)



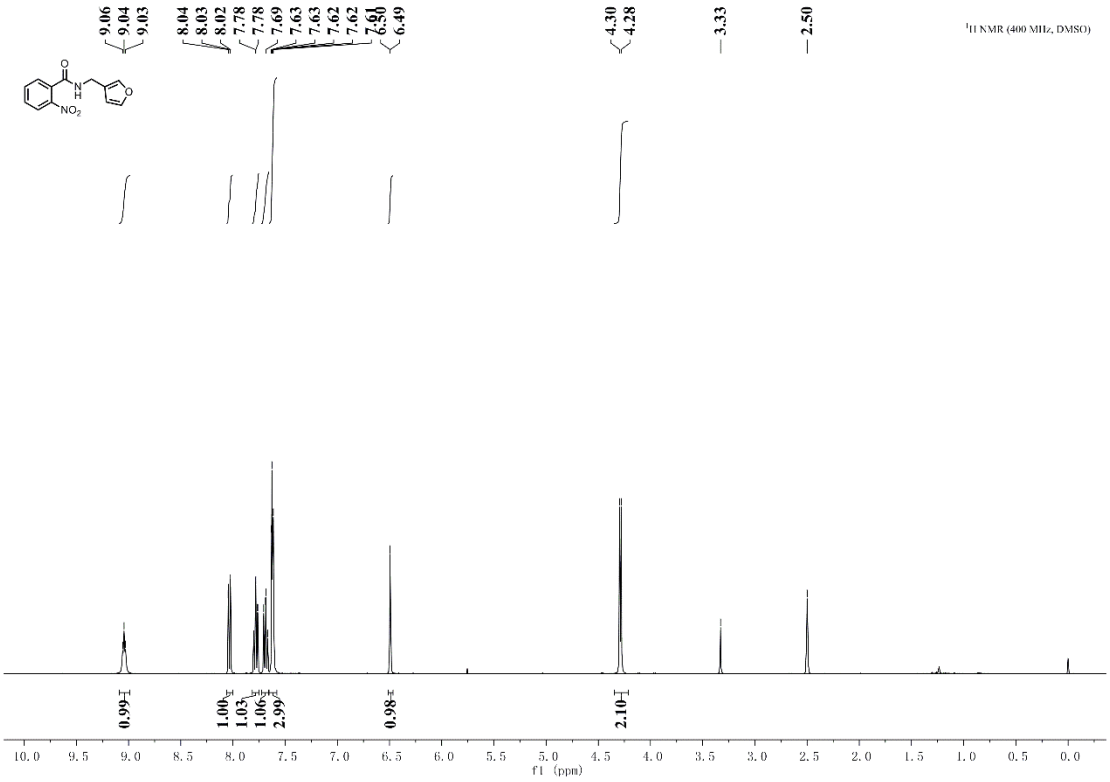


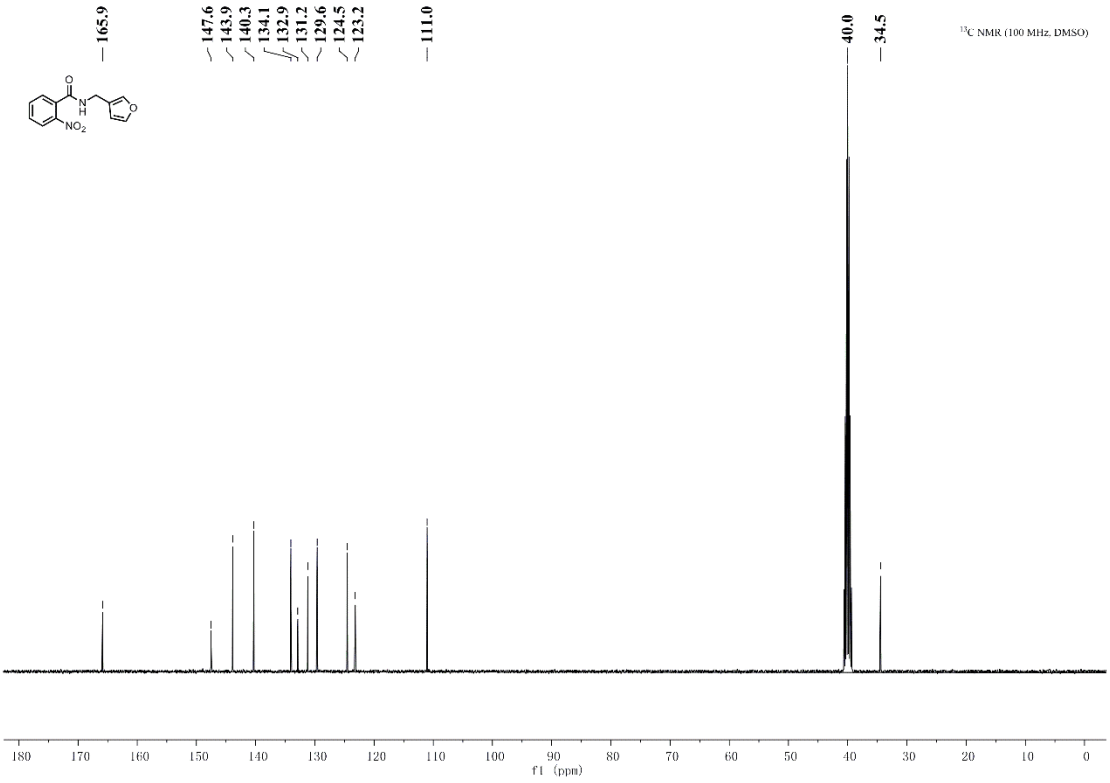
N-cyclohexyl-2-nitrobenzamide (1l)



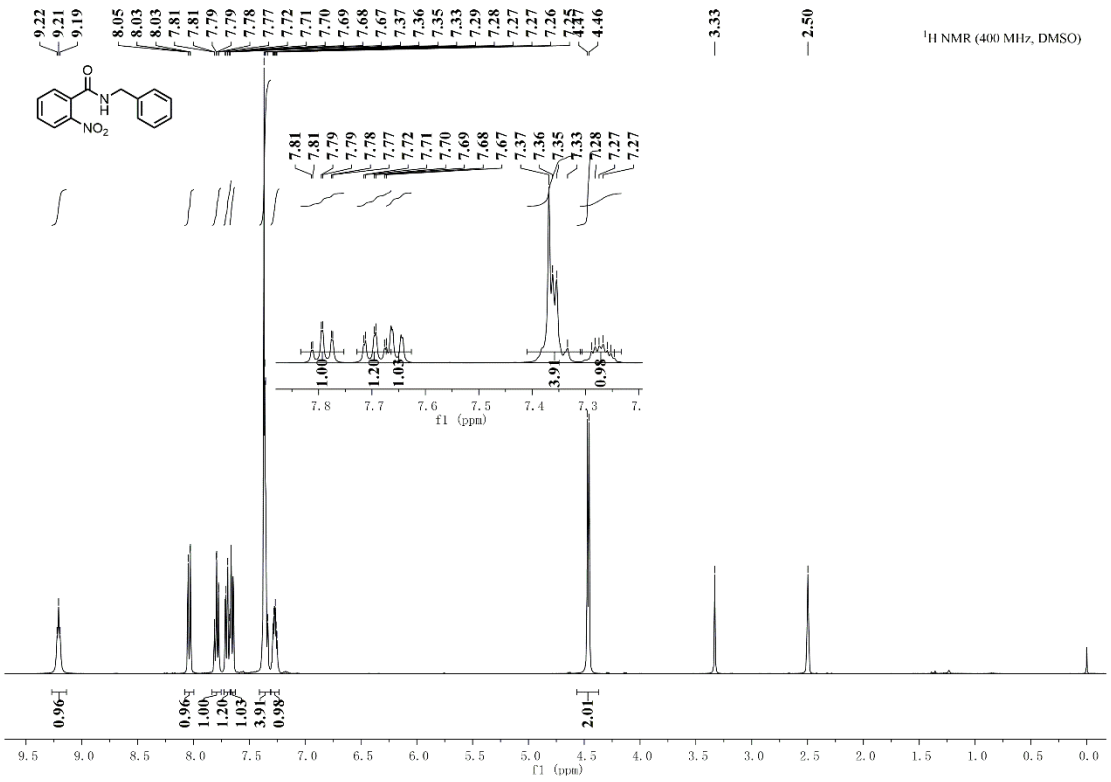


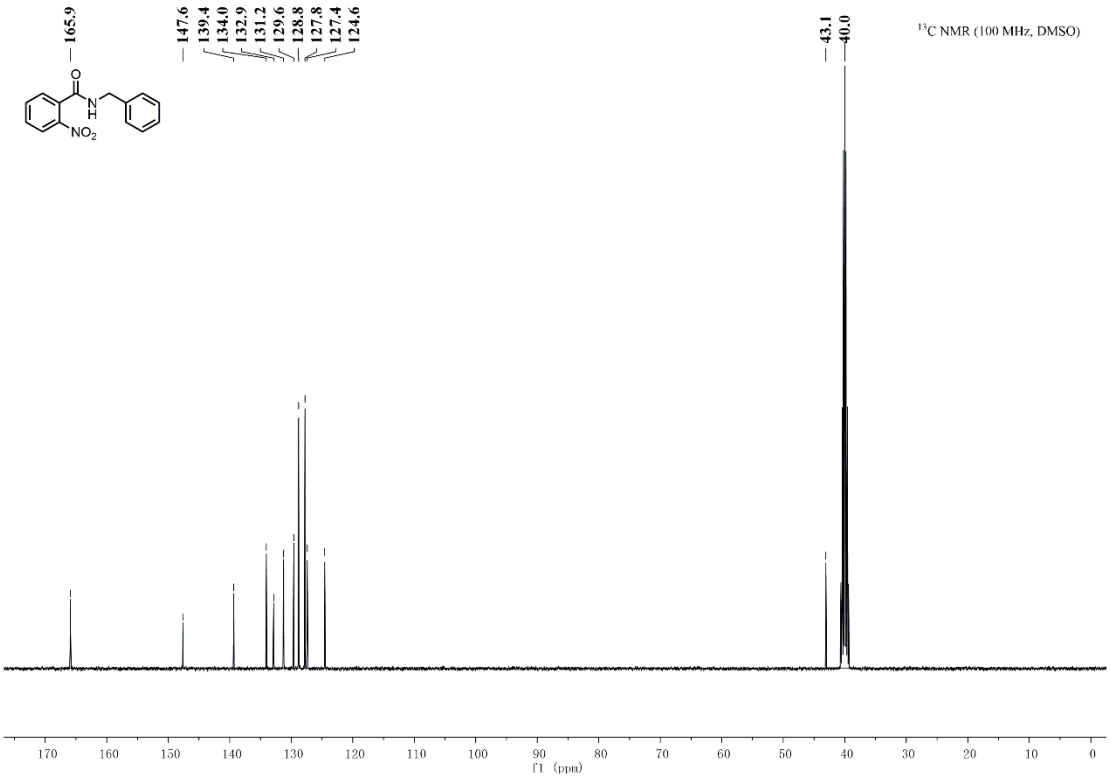
N-(furan-3-ylmethyl)-2-nitrobenzamide (1m)



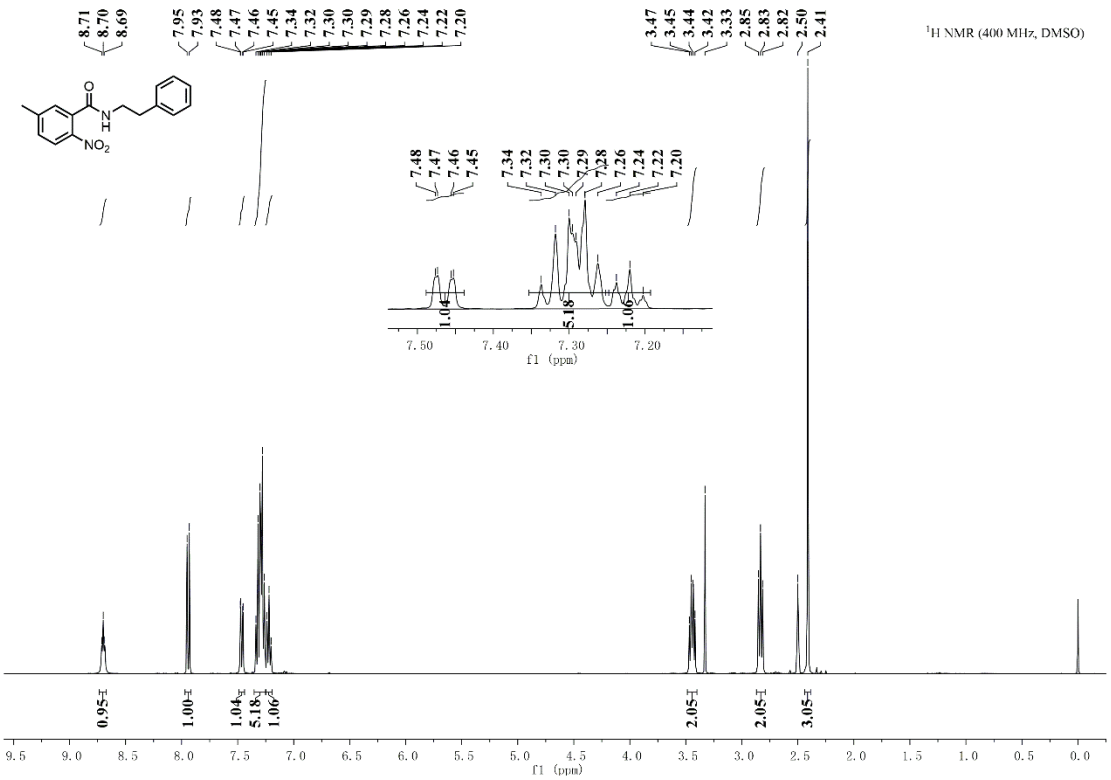


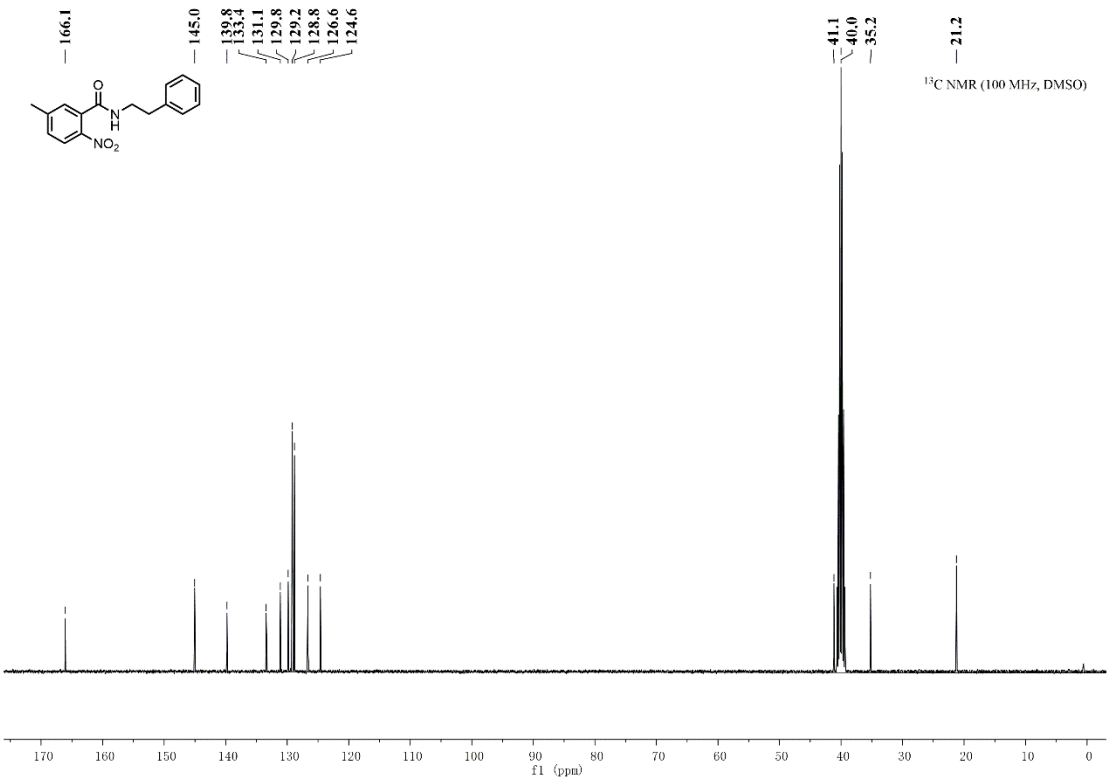
N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1n)



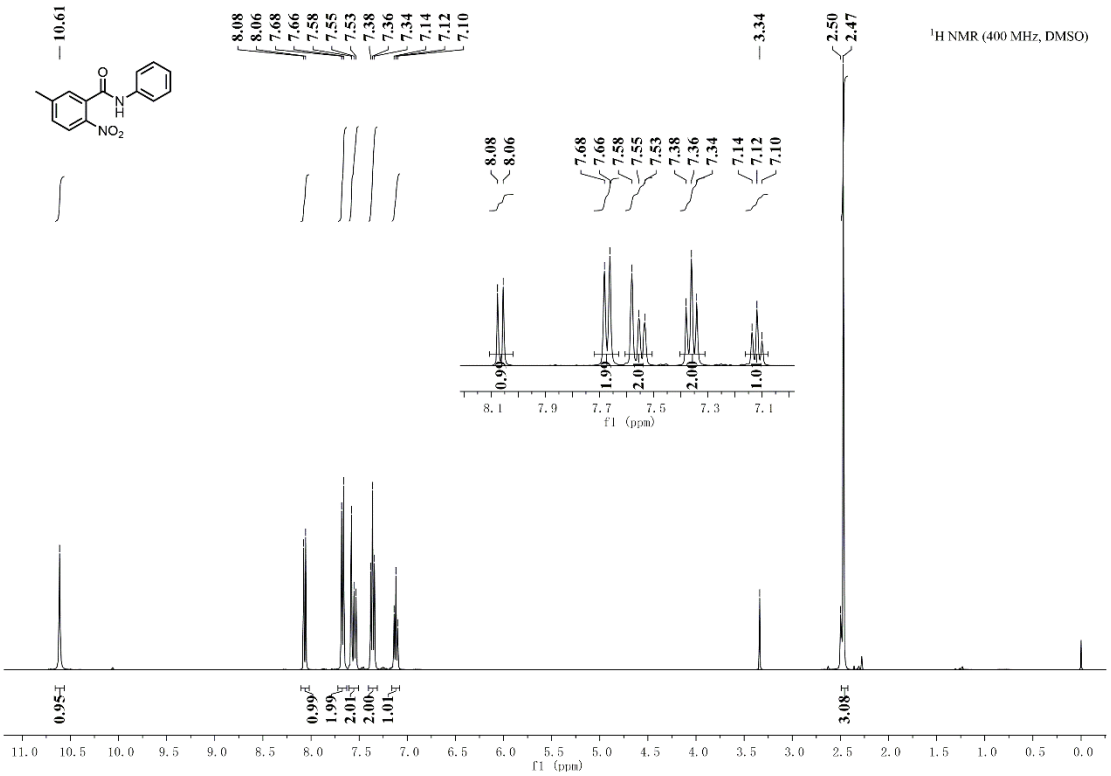


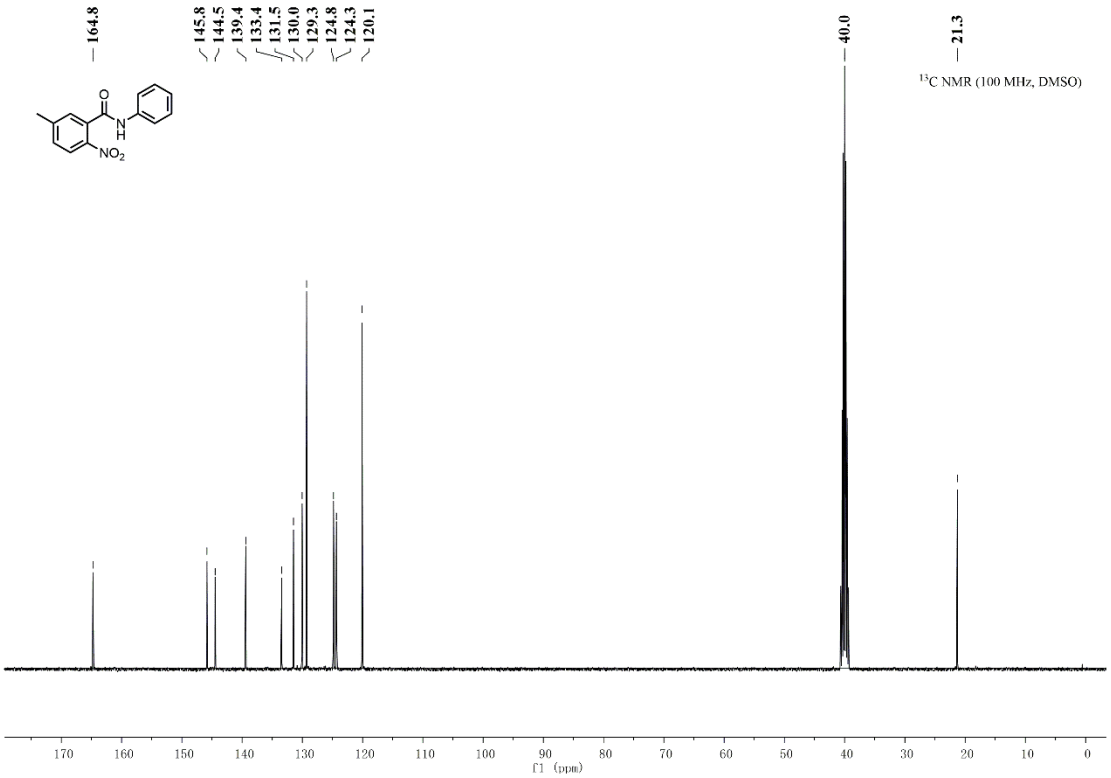
5-methyl-2-nitro-N-phenethylbenzamide (1o)



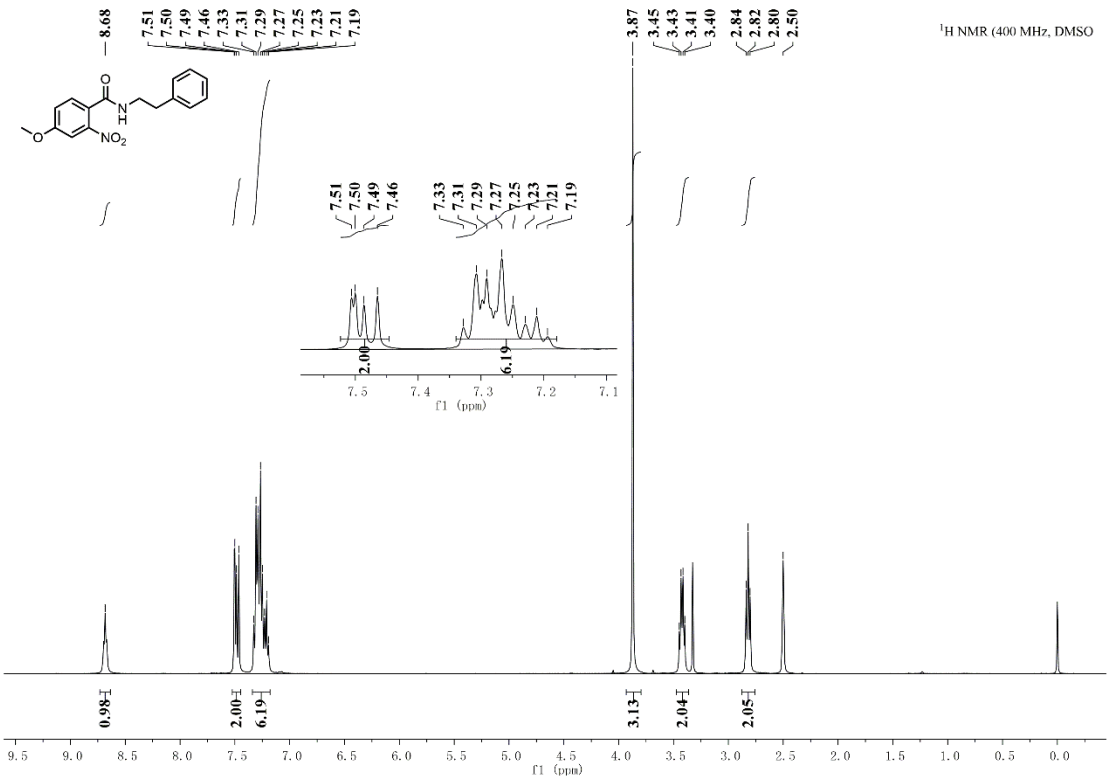


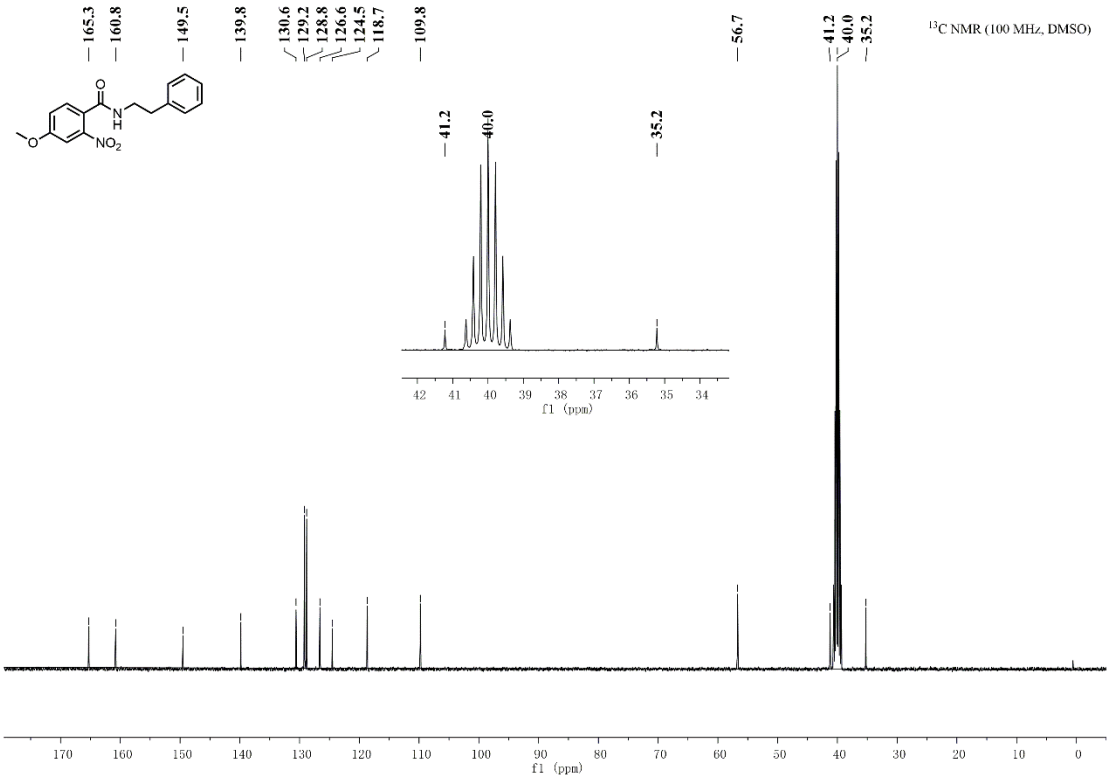
5-methyl-2-nitro-N-phenylbenzamide (1p)





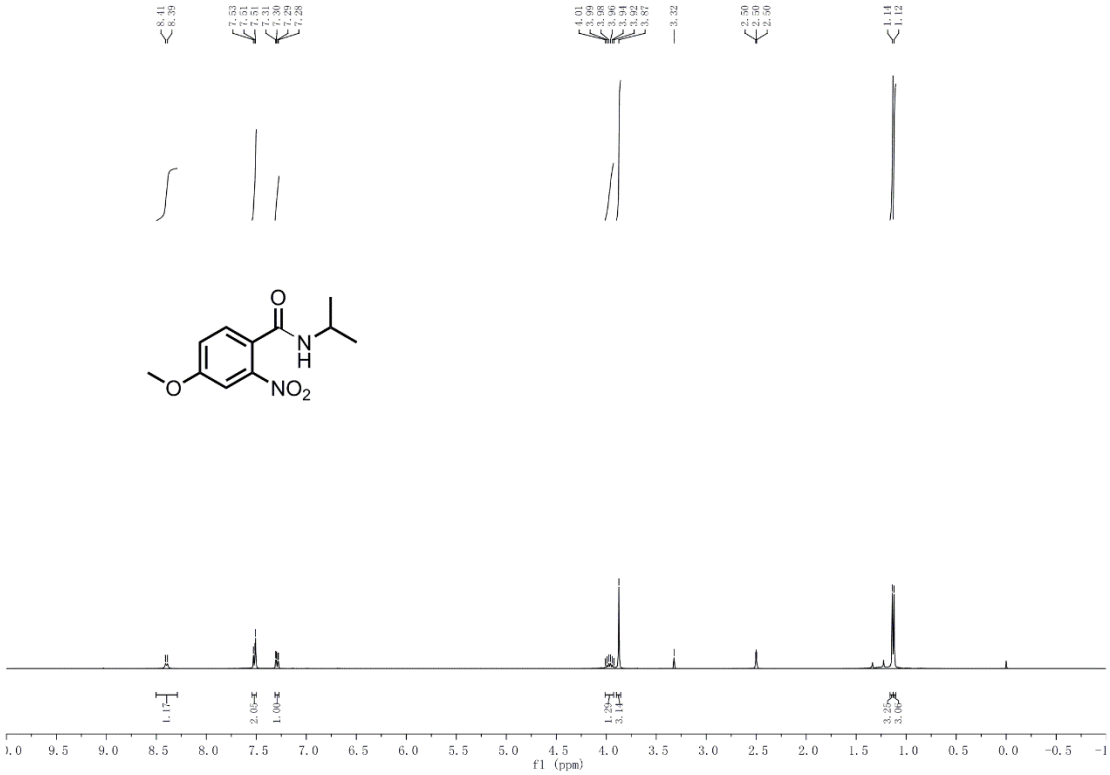
4-methoxy-2-nitro-N-phenethylbenzamide (1q)



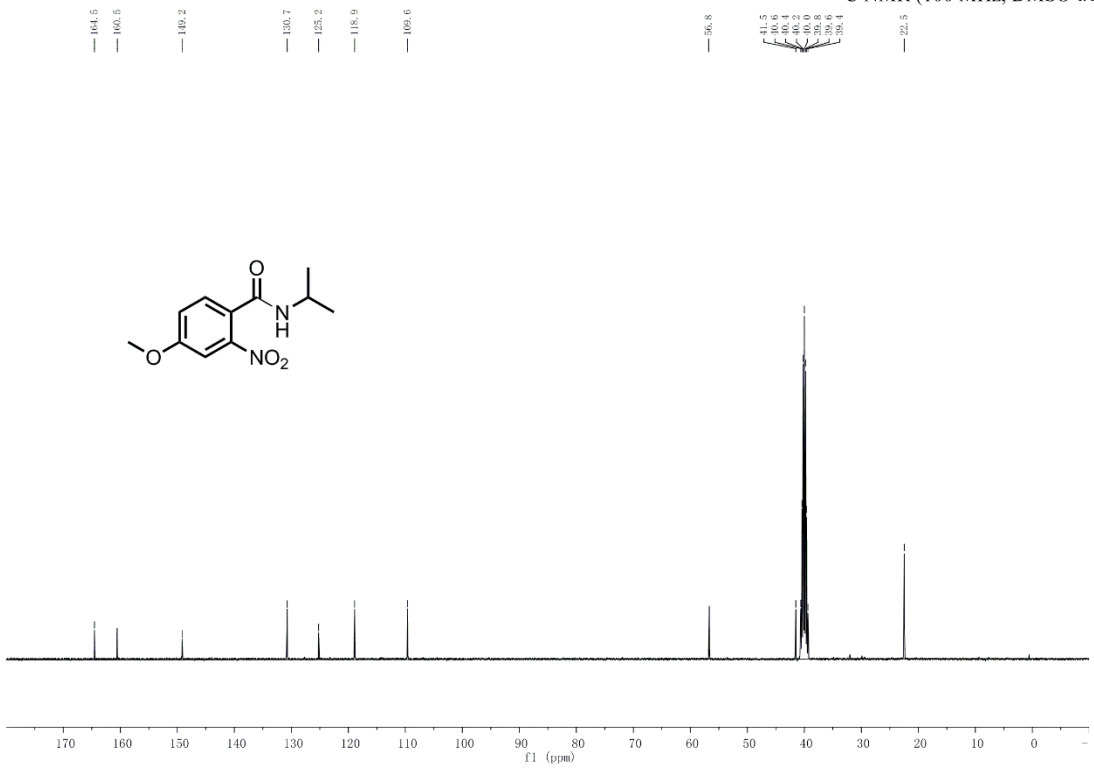


N-isopropyl-4-methoxy-2-nitrobenzamide (1r)

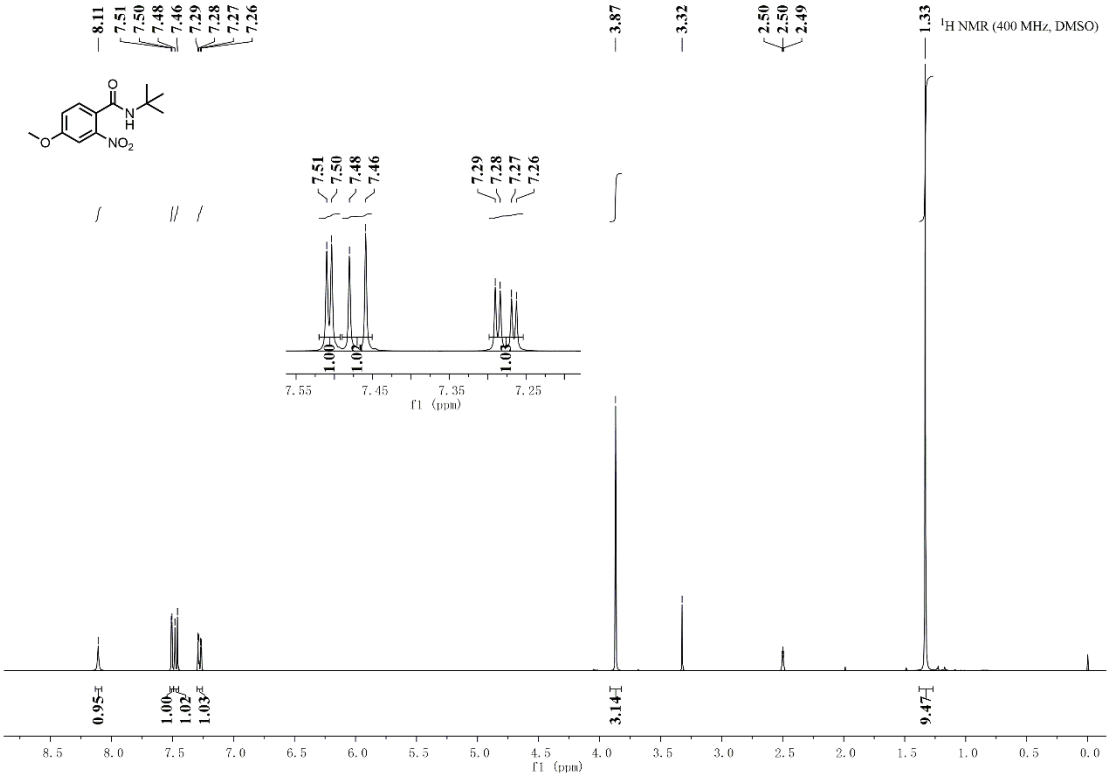
^{1}H NMR (400 MHz, DMSO-*d6)*

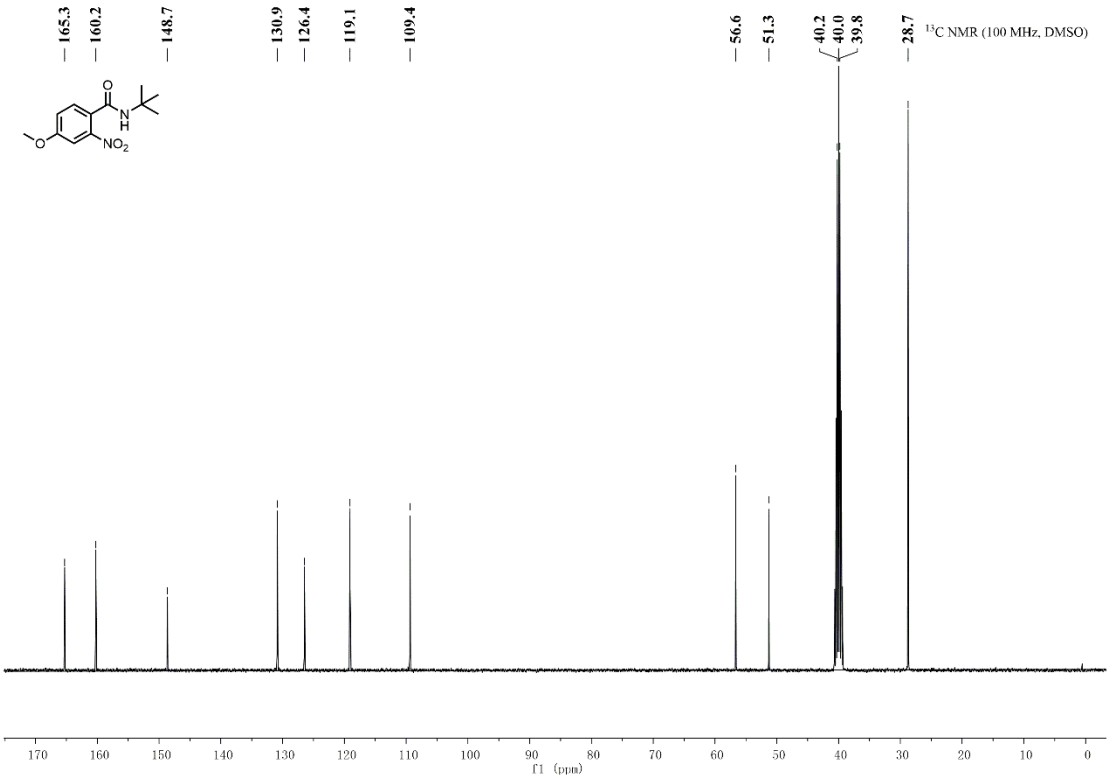


^{13}C NMR (100 MHz, DMSO-*d6)*

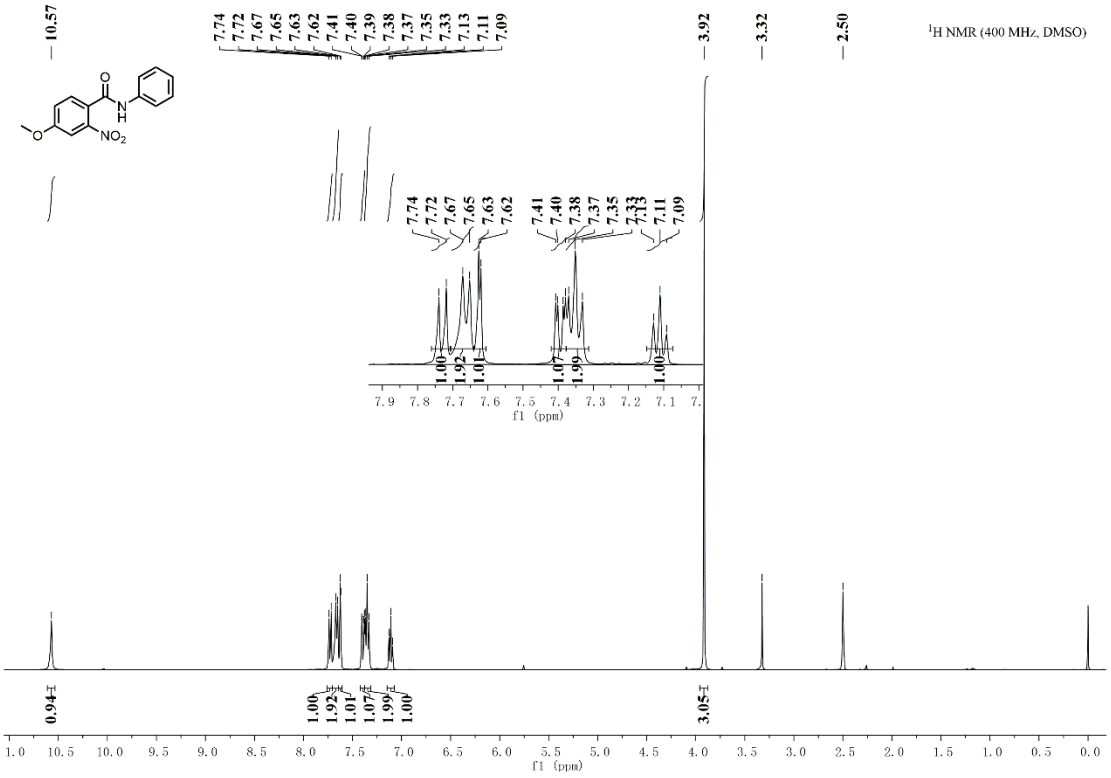


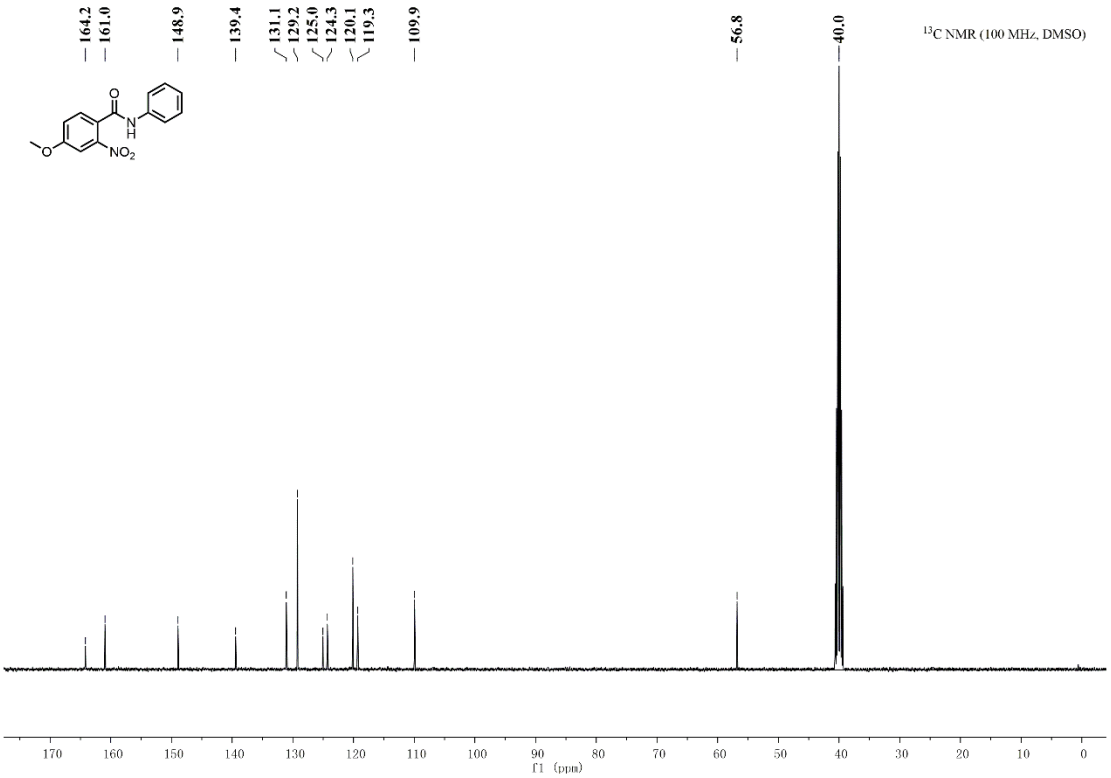
N-(tert-butyl)-4-methoxy-2-nitrobenzamide (1s)



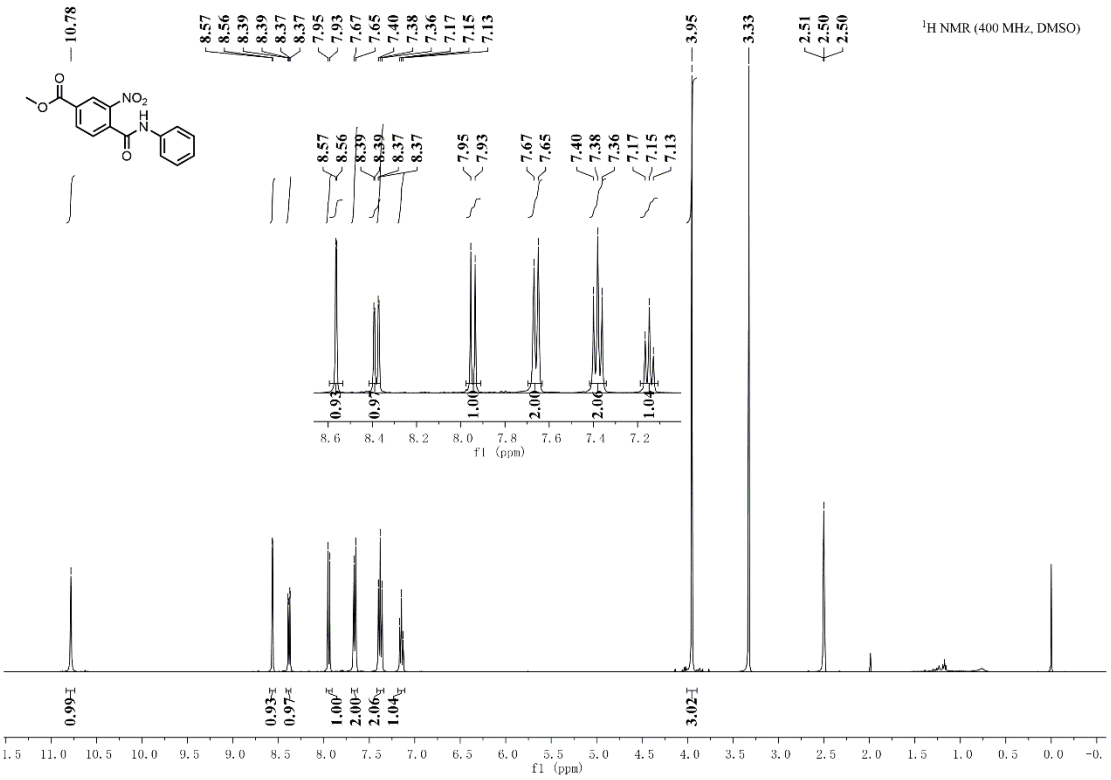


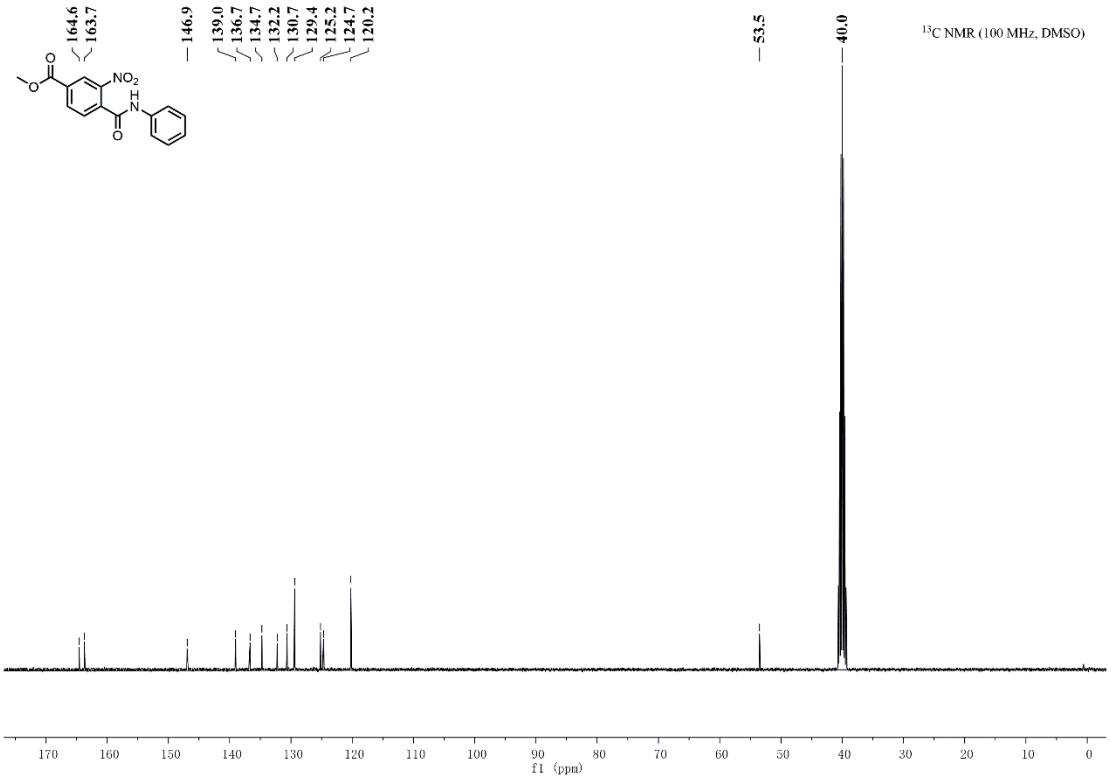
4-methoxy-2-nitro-N-phenylbenzamide (1t)



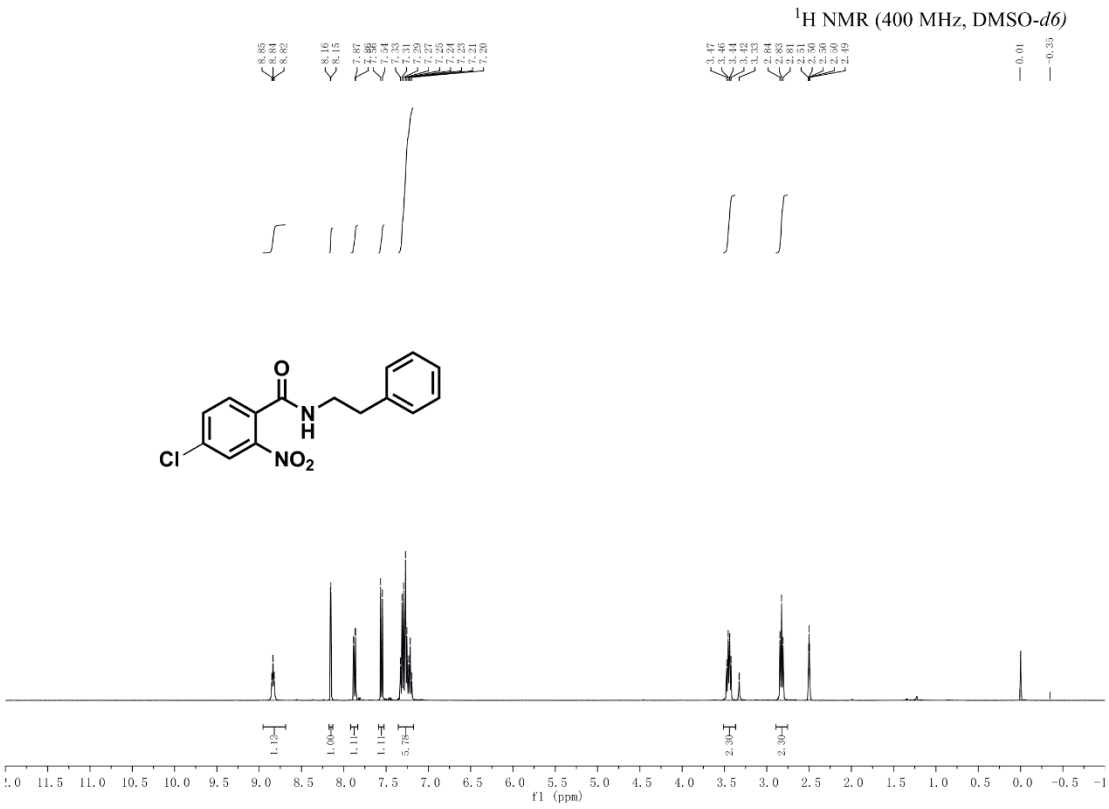


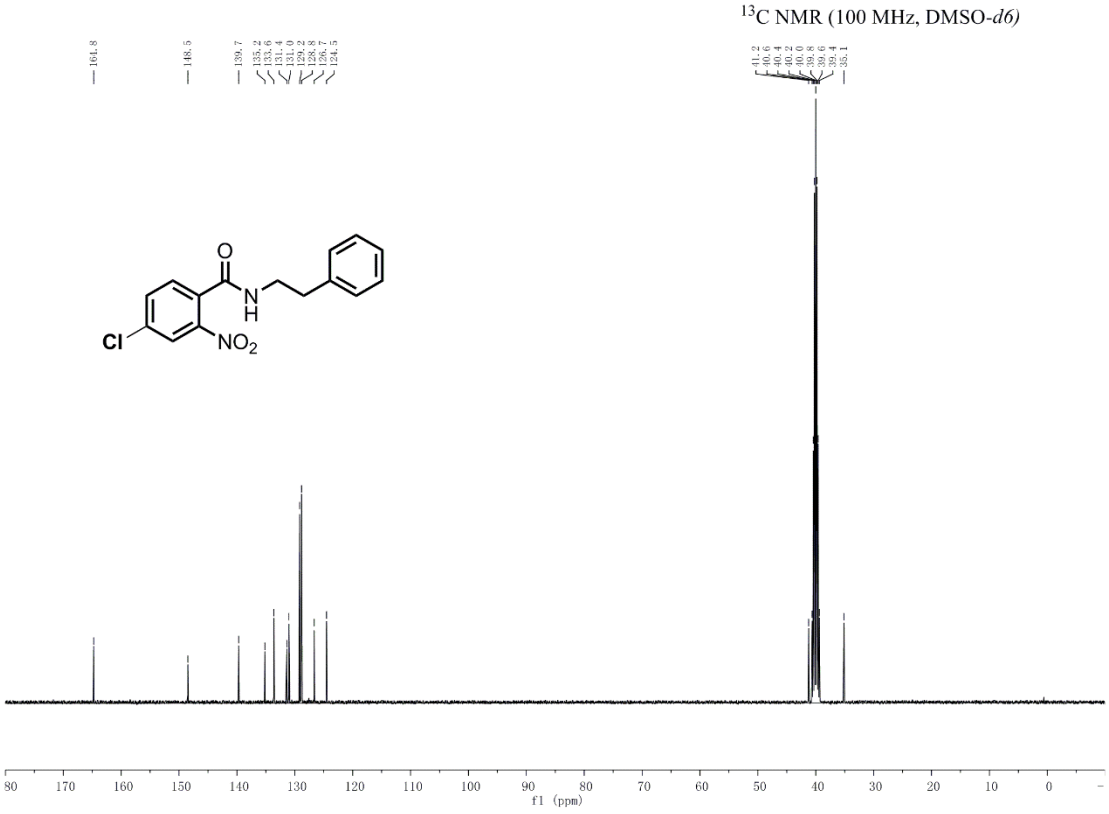
Methyl 3-nitro-4-(phenylcarbamoyl) benzoate (1u)



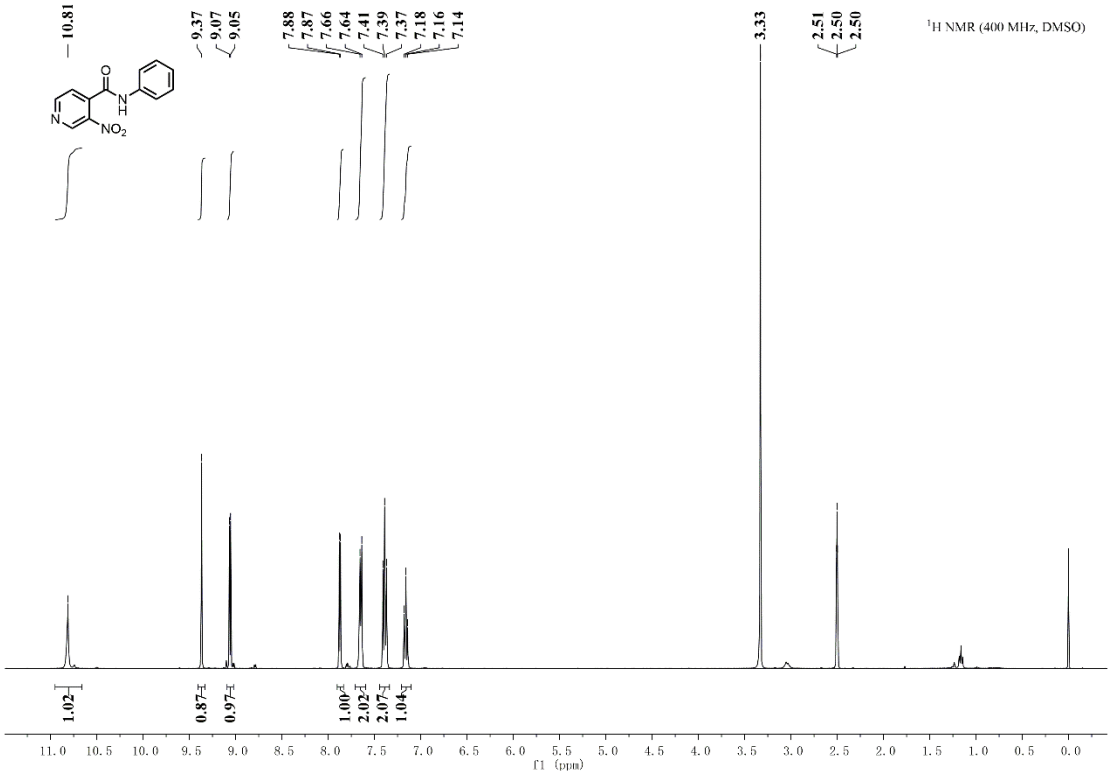


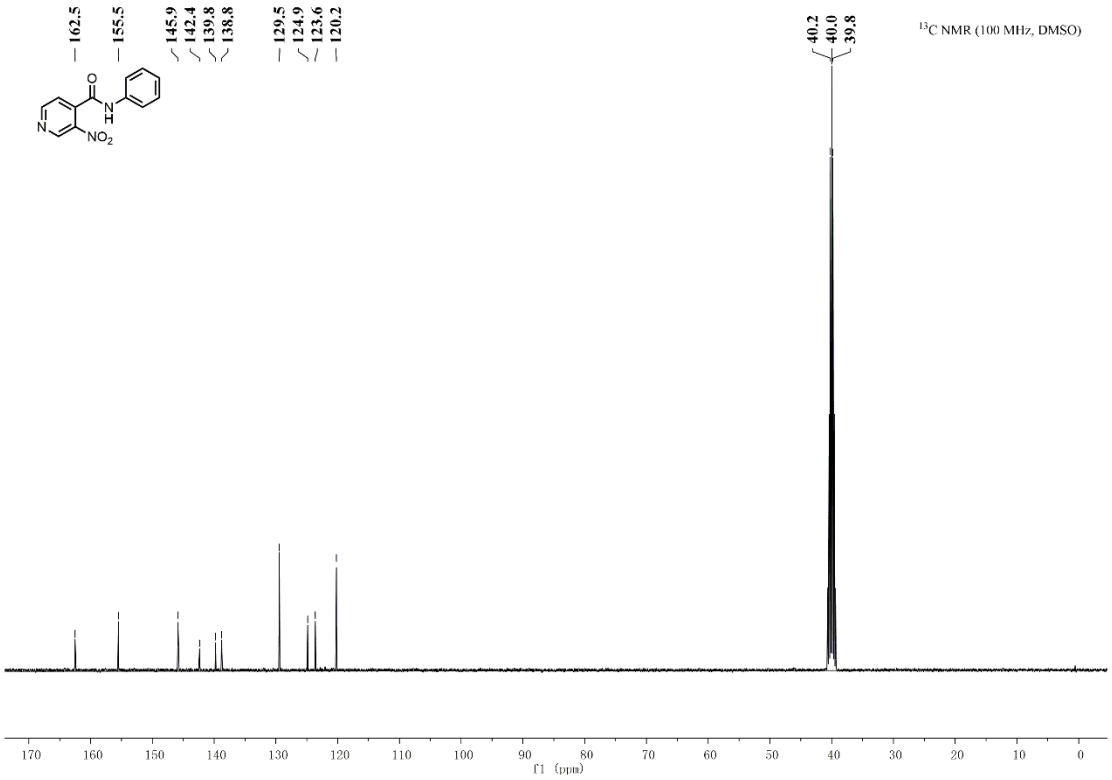
4-chloro-2-nitro-N-phenethylbenzamide (1v)





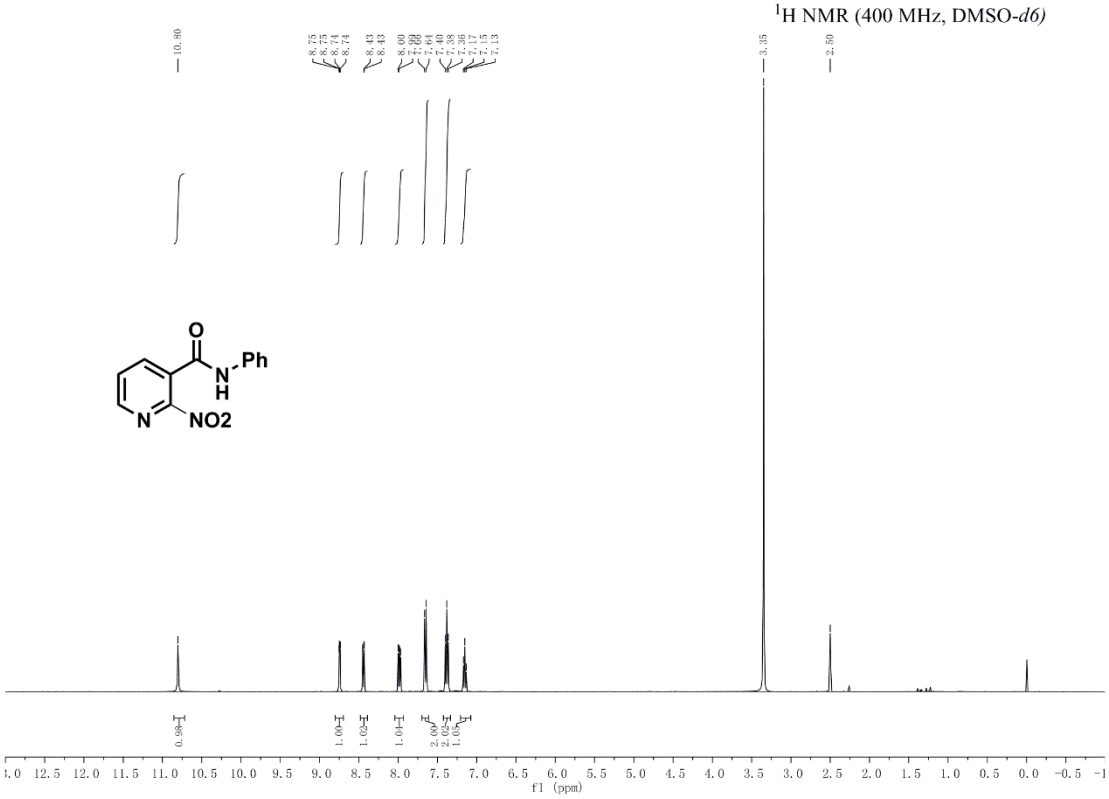
3-nitro-N-phenylisonicotinamide (1w)



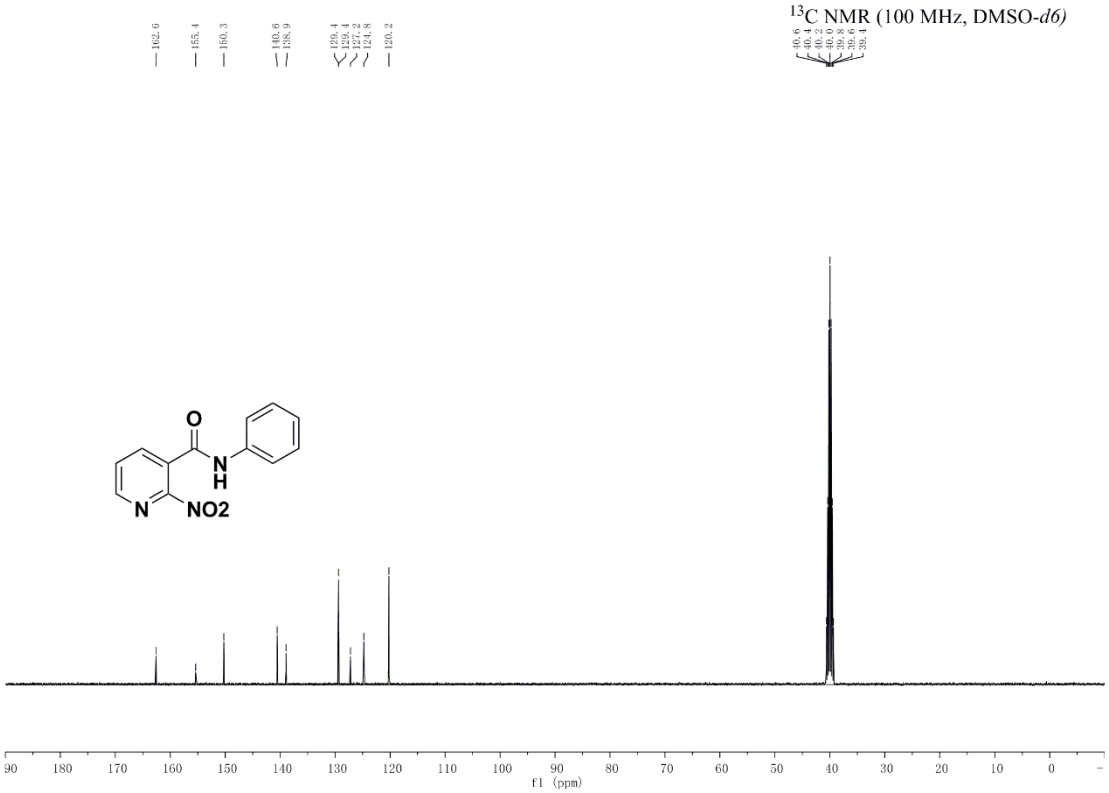


2-nitro-N-phenylnicotinamide (1x)

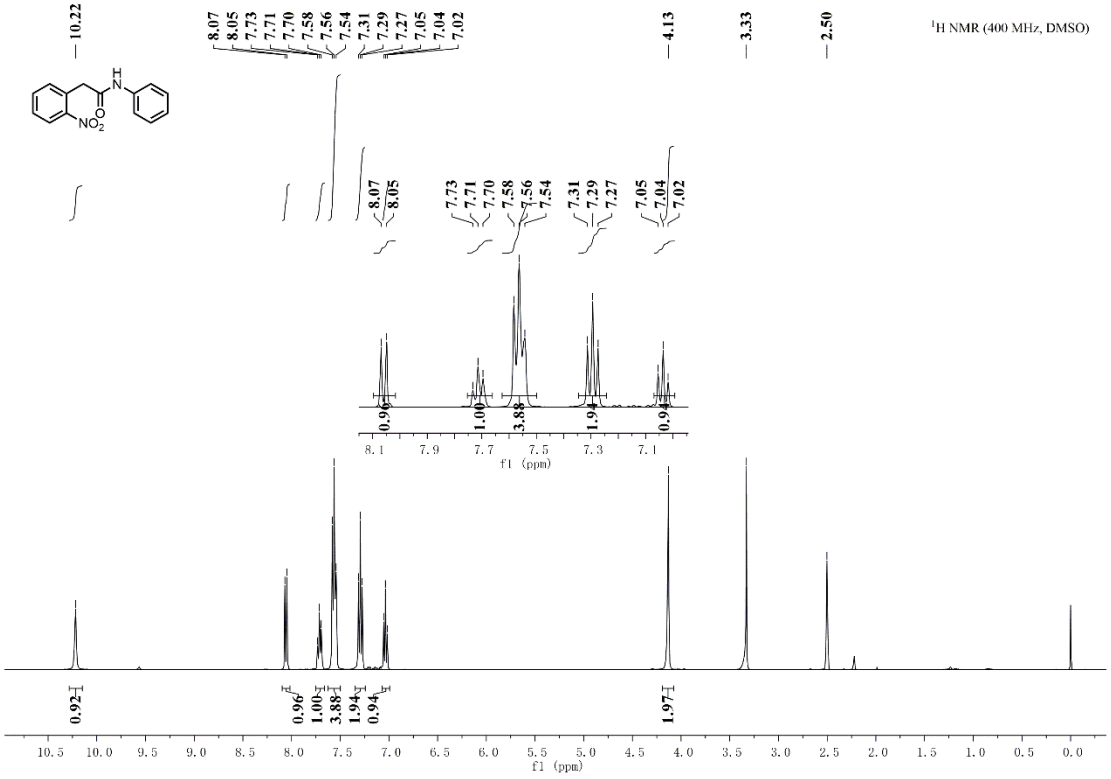
^{1}H NMR (400 MHz, DMSO-*d6)*

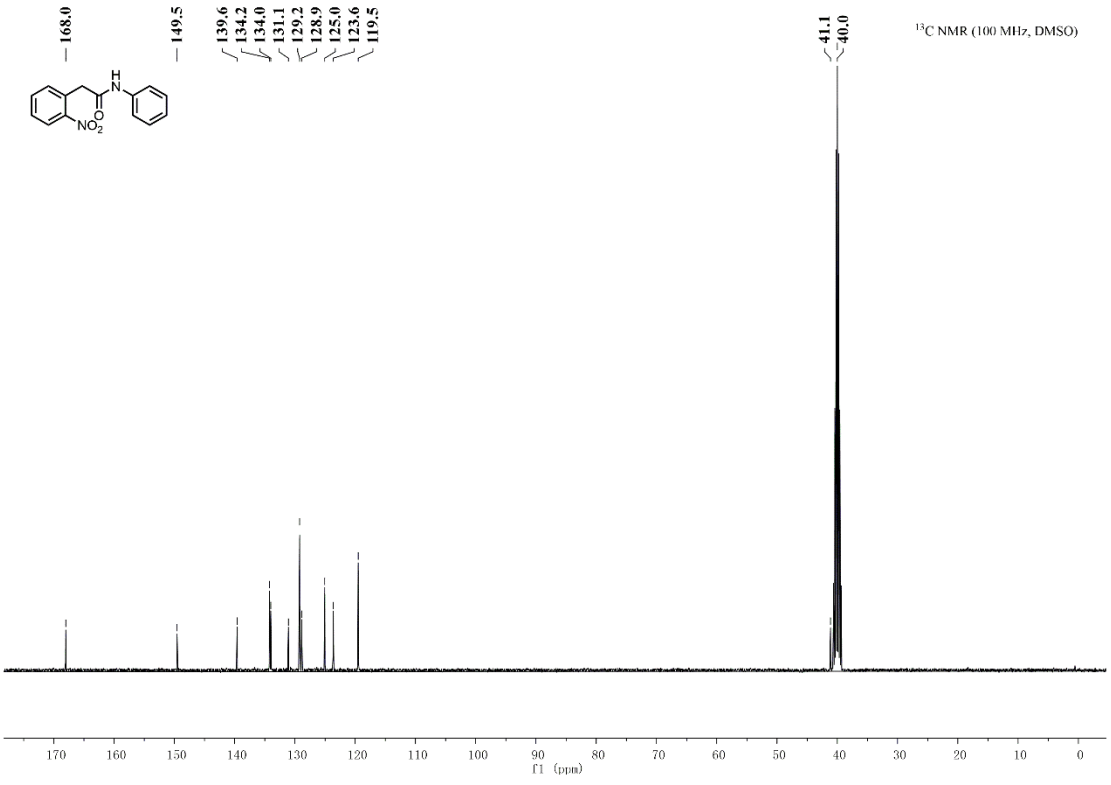


^{13}C NMR (100 MHz, DMSO-*d6)*

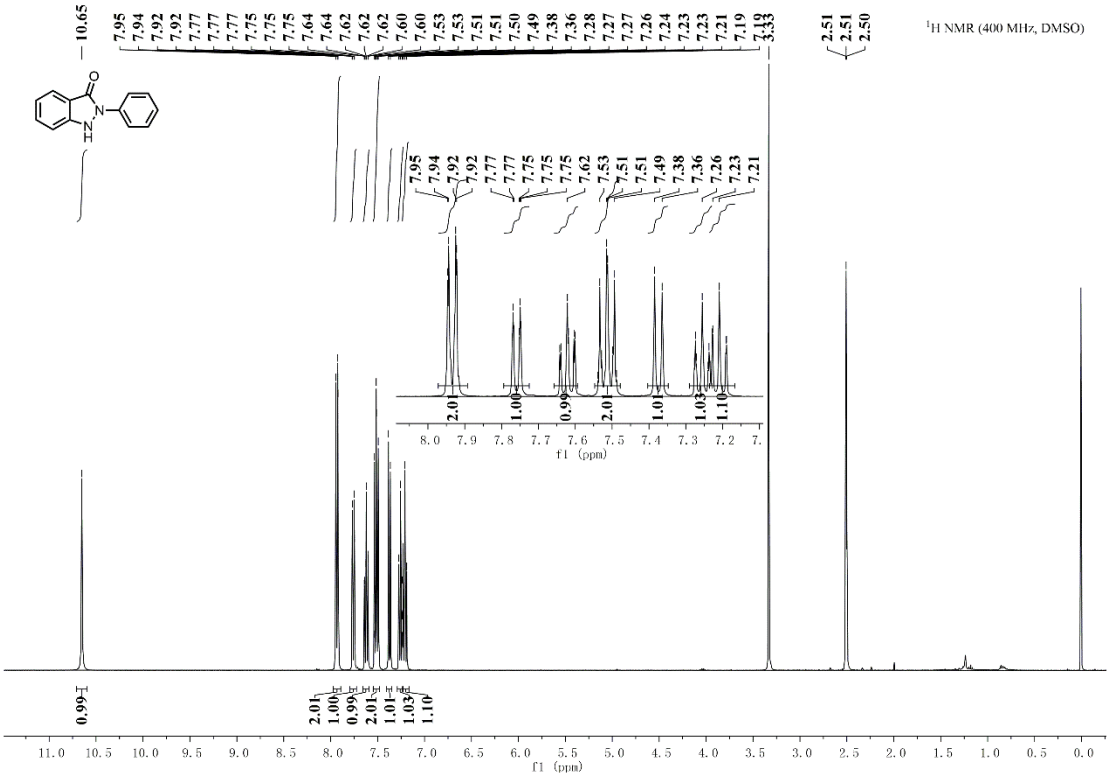


N-(2-methoxy-6-methylpyridin-3-yl)-2-nitrobenzamide (1y)

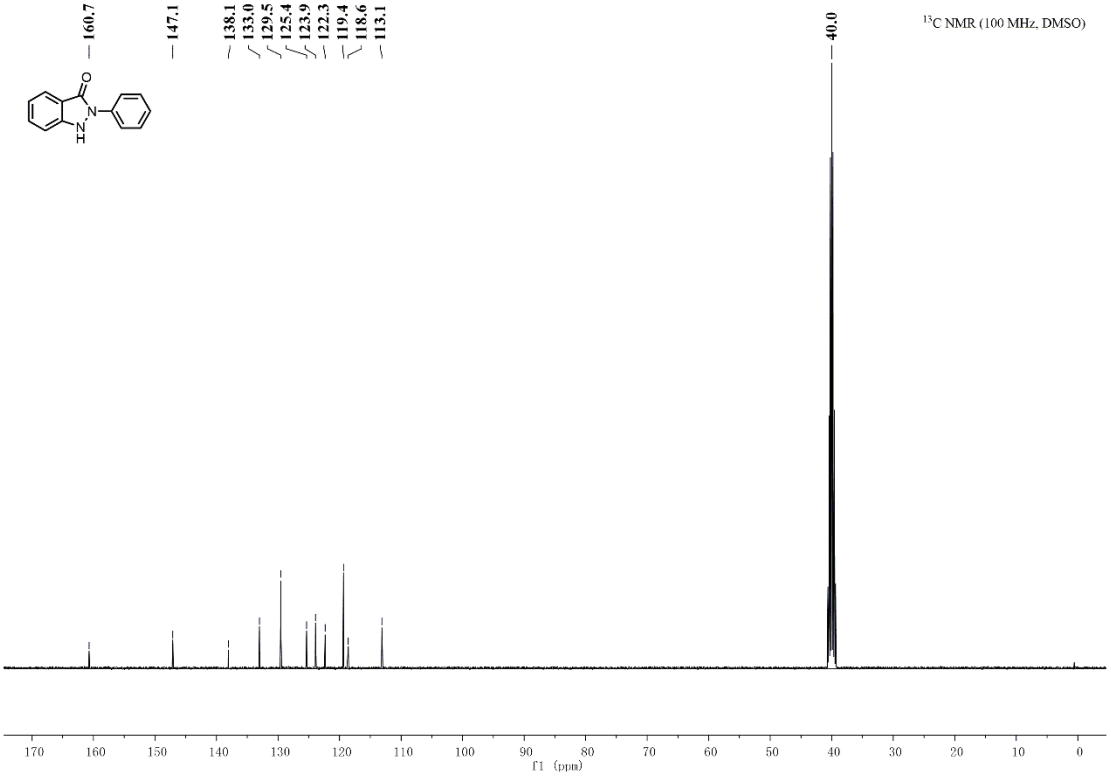




2-phenyl-1,2-dihydro-3H-indazol-3-one (2a)



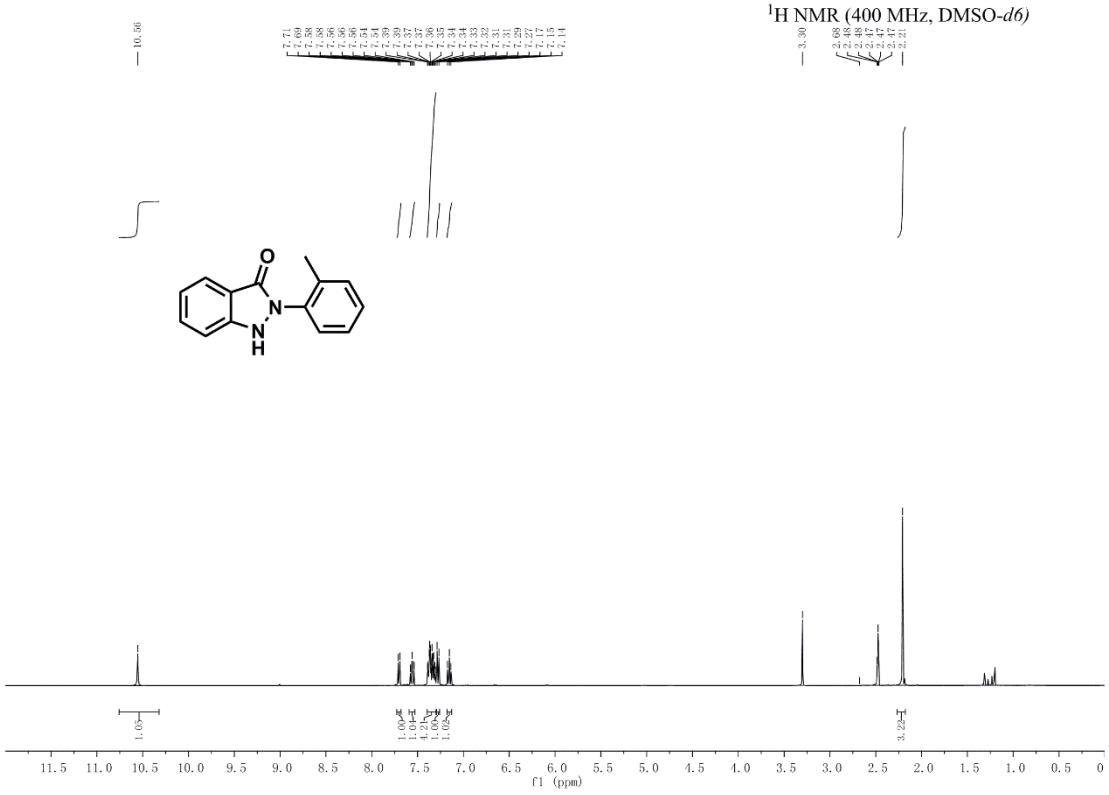
^{1}H NMR (400 MHz, DMSO)



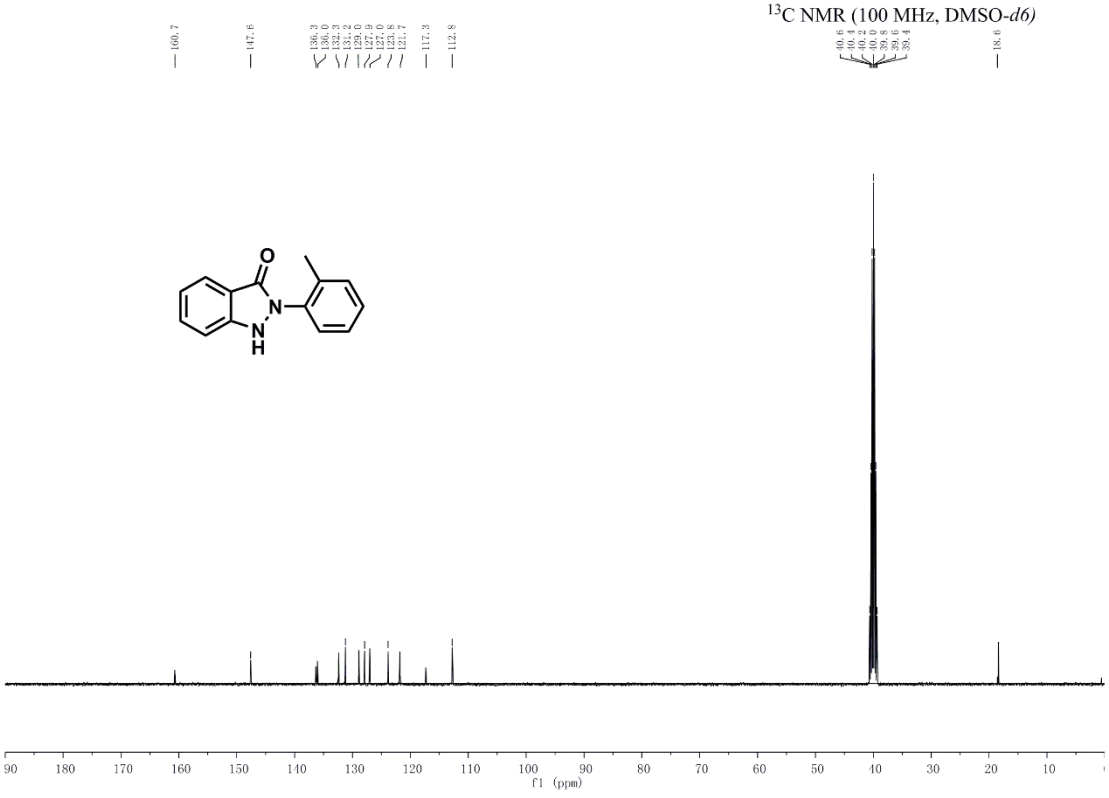
^{13}C NMR (100 MHz, DMSO)

6-methoxy-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2b)

^{1}H NMR (400 MHz, DMSO-*d6)*

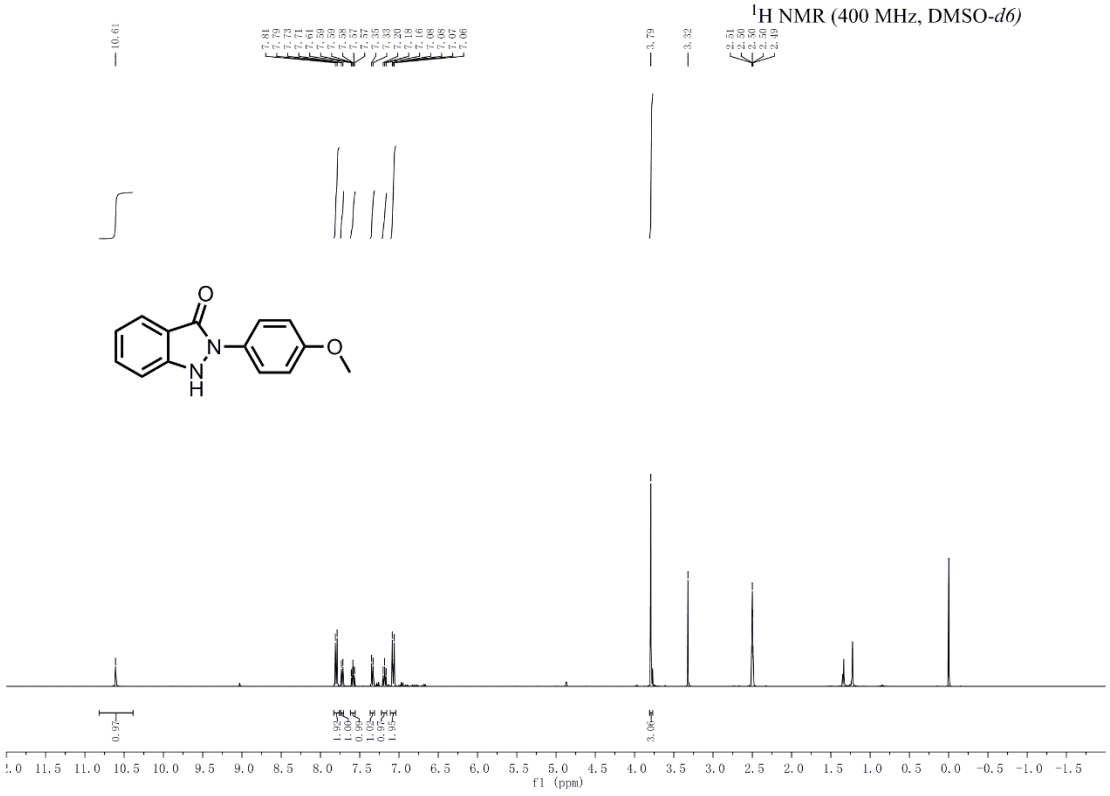


^{13}C NMR (100 MHz, DMSO-*d6)*

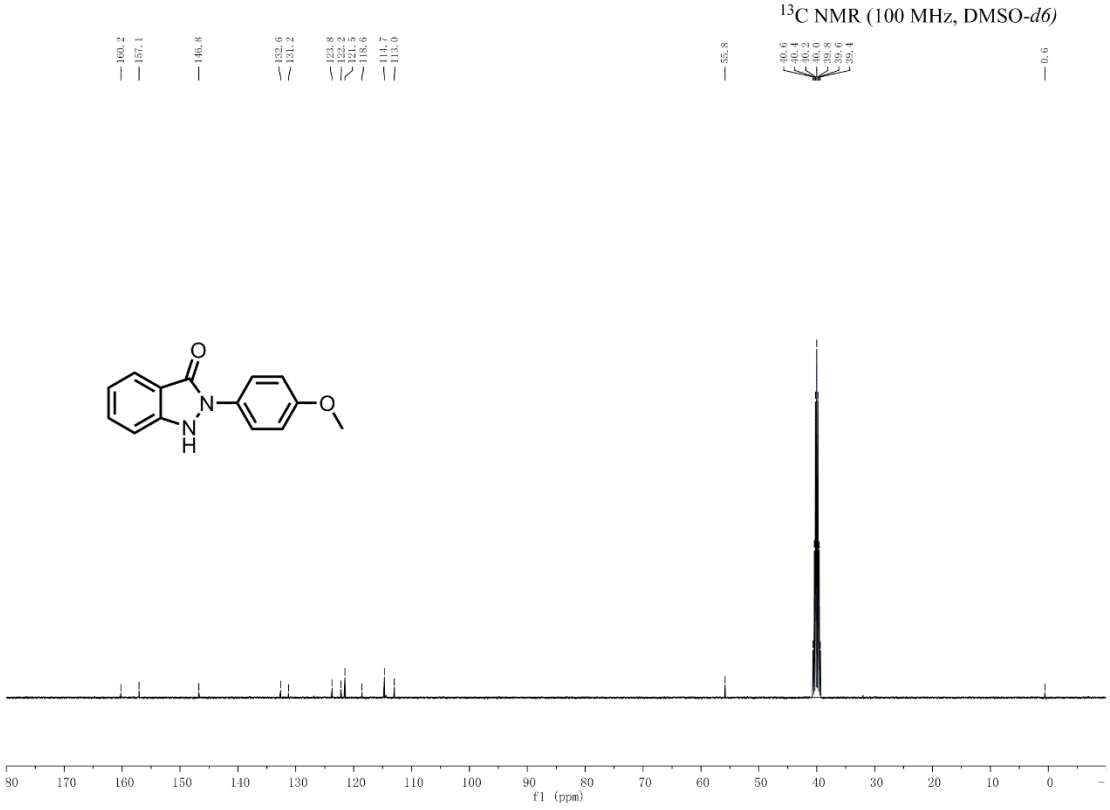


2-(4-methoxyphenyl)-1,2-dihydro-3H-indazol-3-one (2c)

^{1}H NMR (400 MHz, DMSO-*d6)*

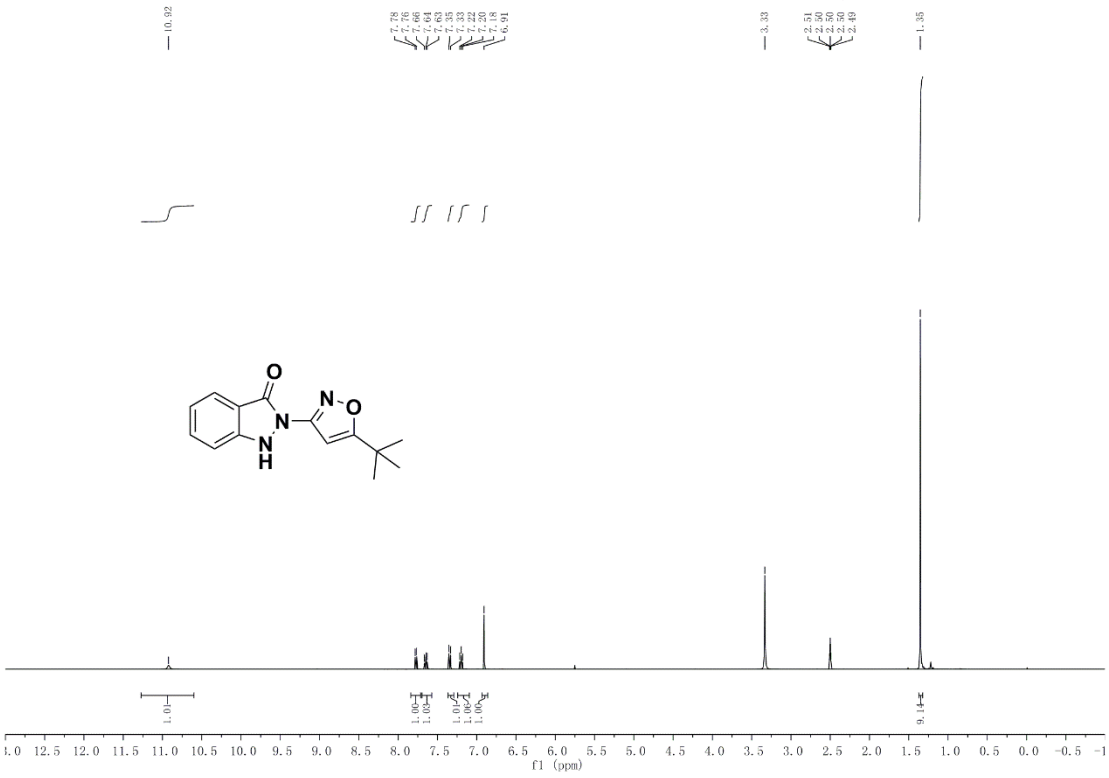


^{13}C NMR (100 MHz, DMSO-*d6)*

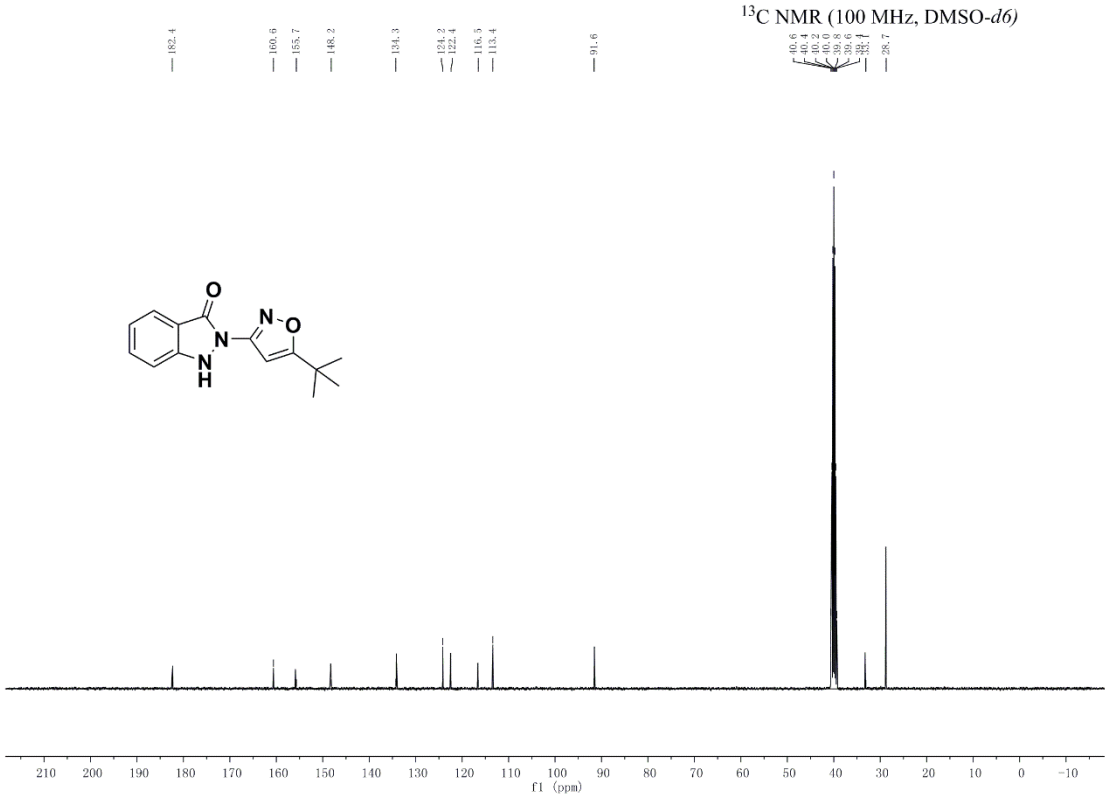


2-(5-(tert-butyl)isoxazol-3-yl)-1,2-dihydro-3H-indazol-3-one (2d)

^{1}H NMR (400 MHz, DMSO-*d6)*

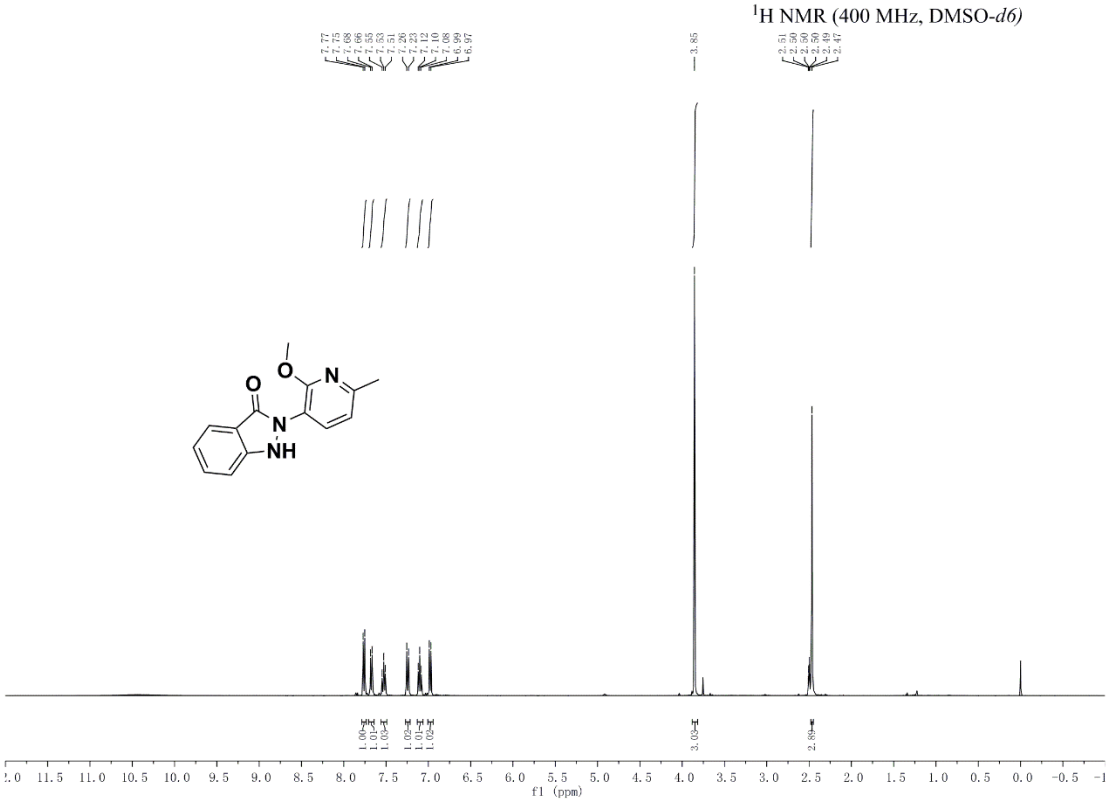


^{13}C NMR (100 MHz, DMSO-*d6)*

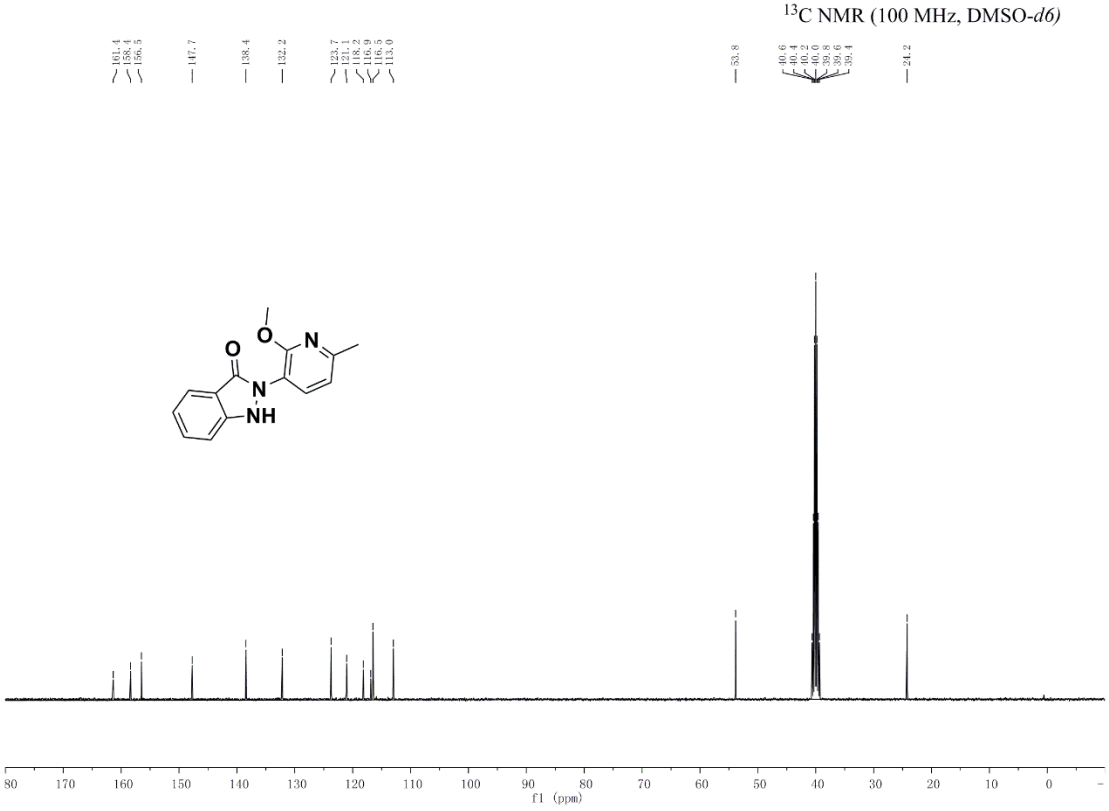


2-(2-methoxy-6-methylpyridin-3-yl)-1,2-dihydro-3H-indazol-3-one (2e)

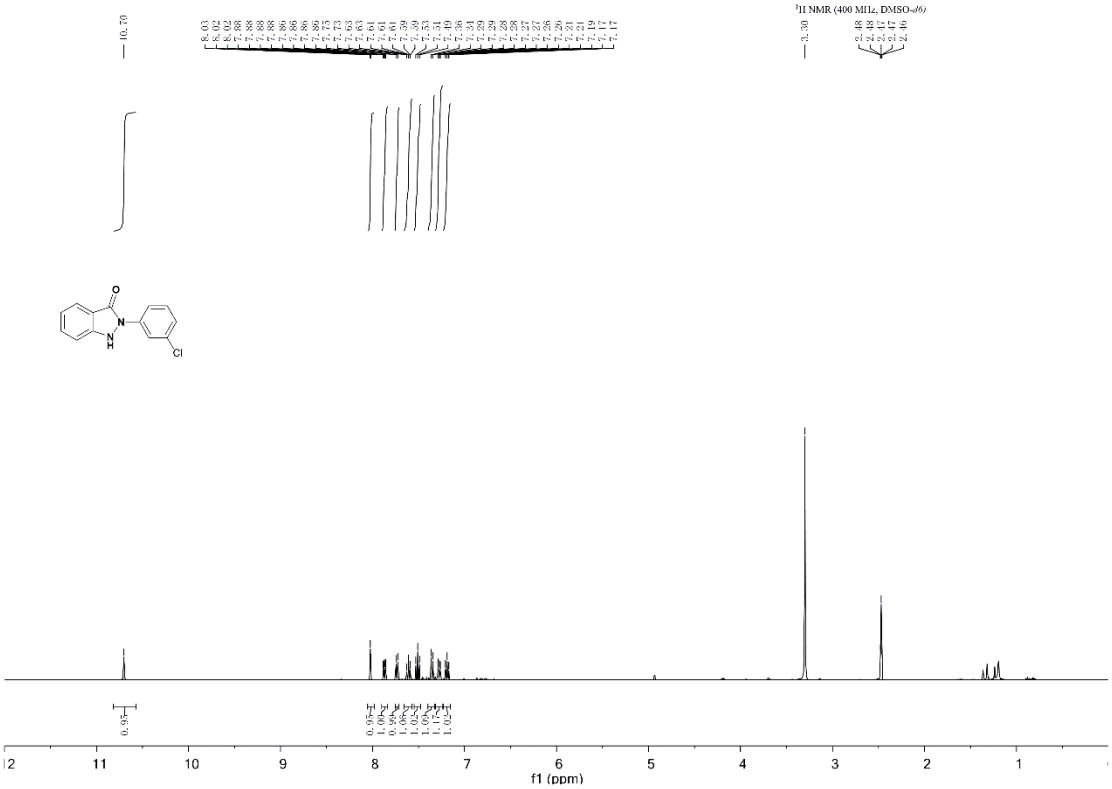
^{1}H NMR (400 MHz, DMSO-*d6)*

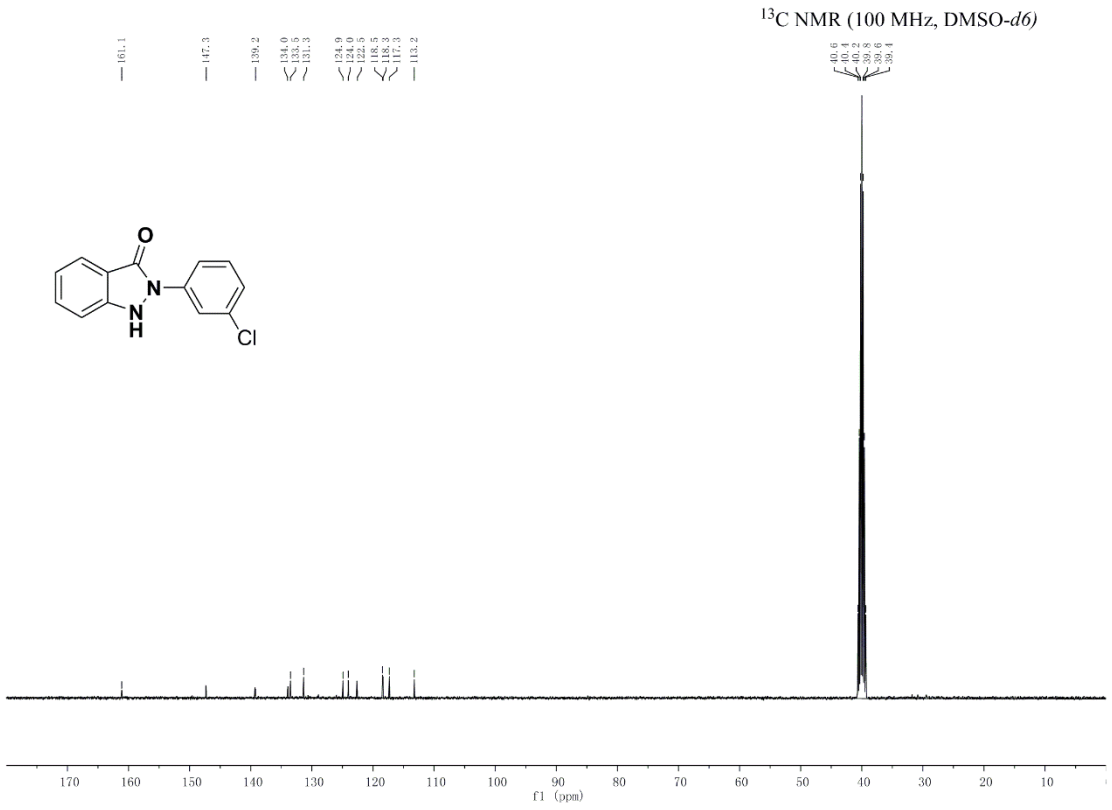


^{13}C NMR (100 MHz, DMSO-*d6)*

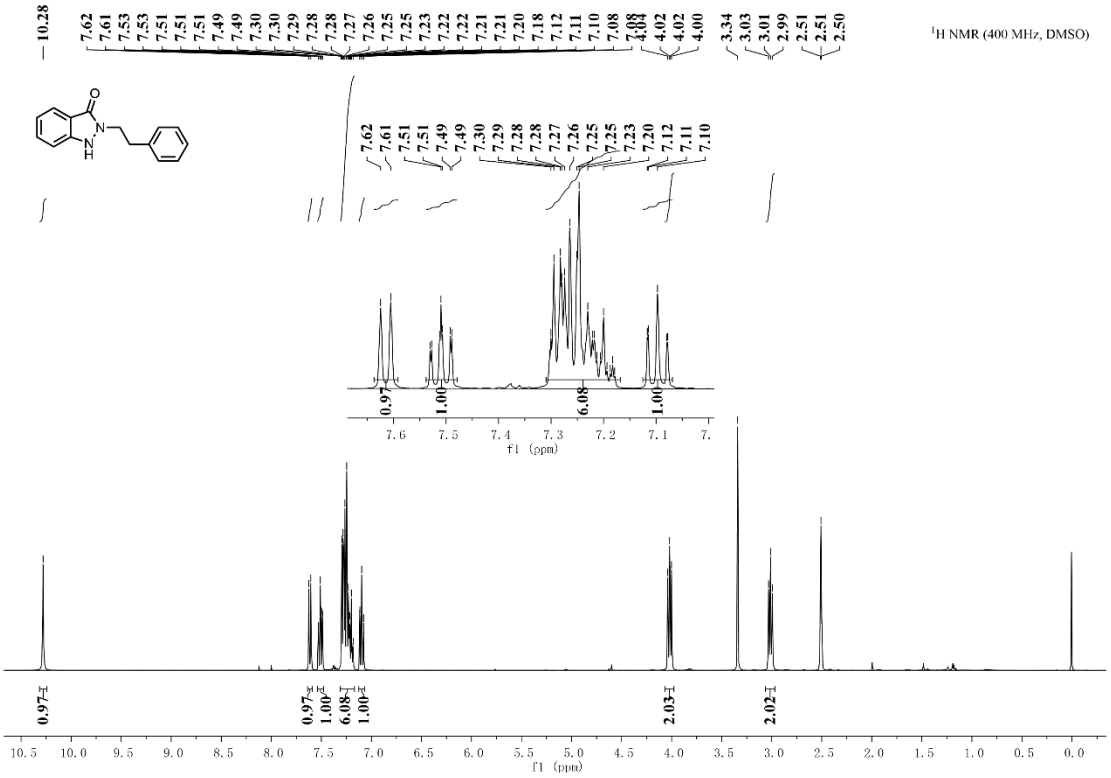


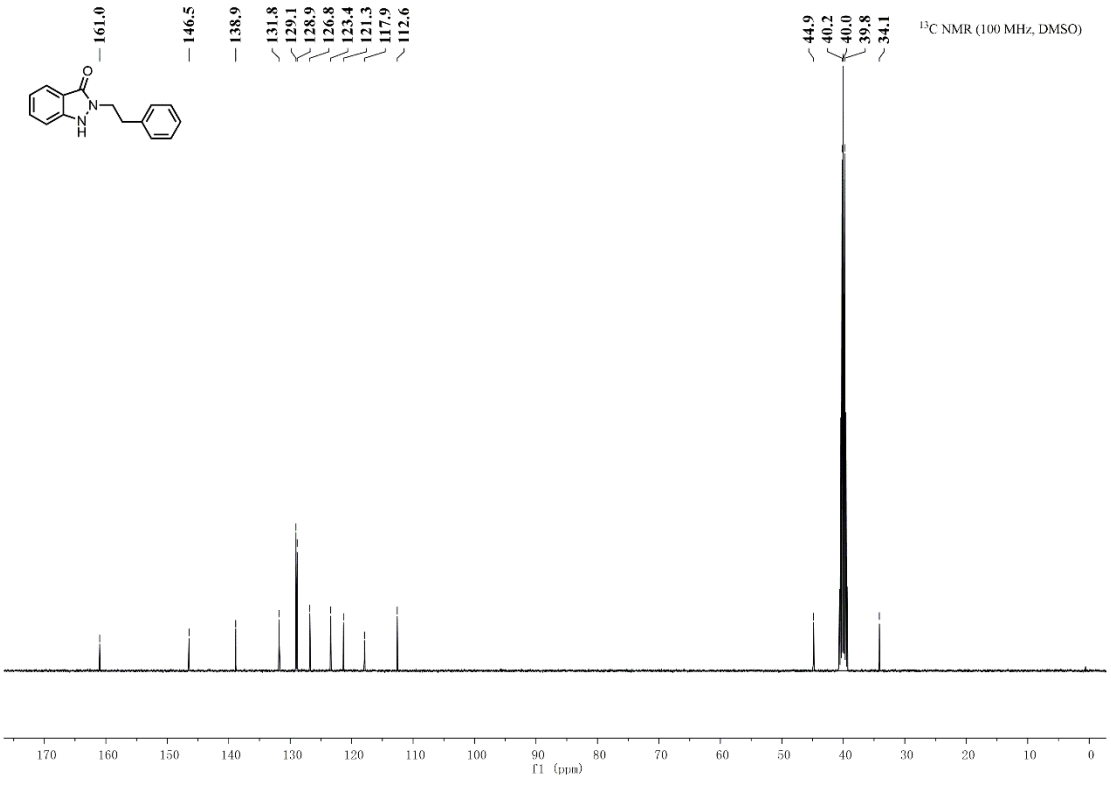
2-(3-chlorophenyl)-1,2-dihydro-3H-indazol-3-one (2f)



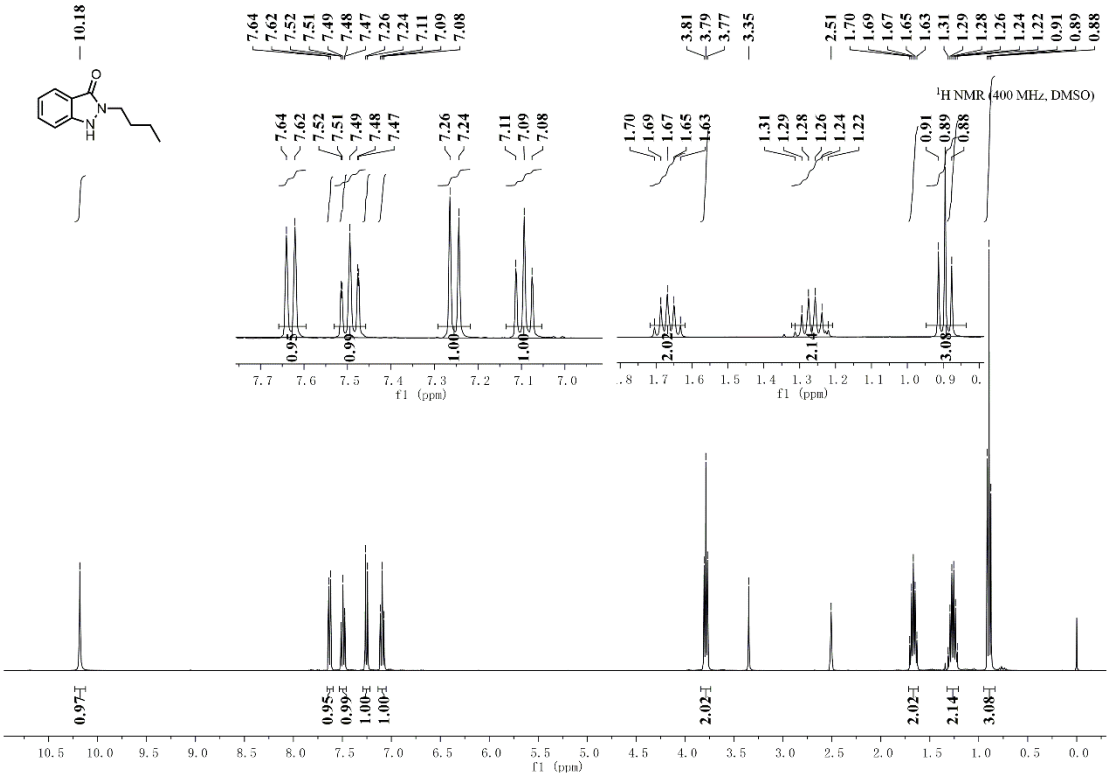


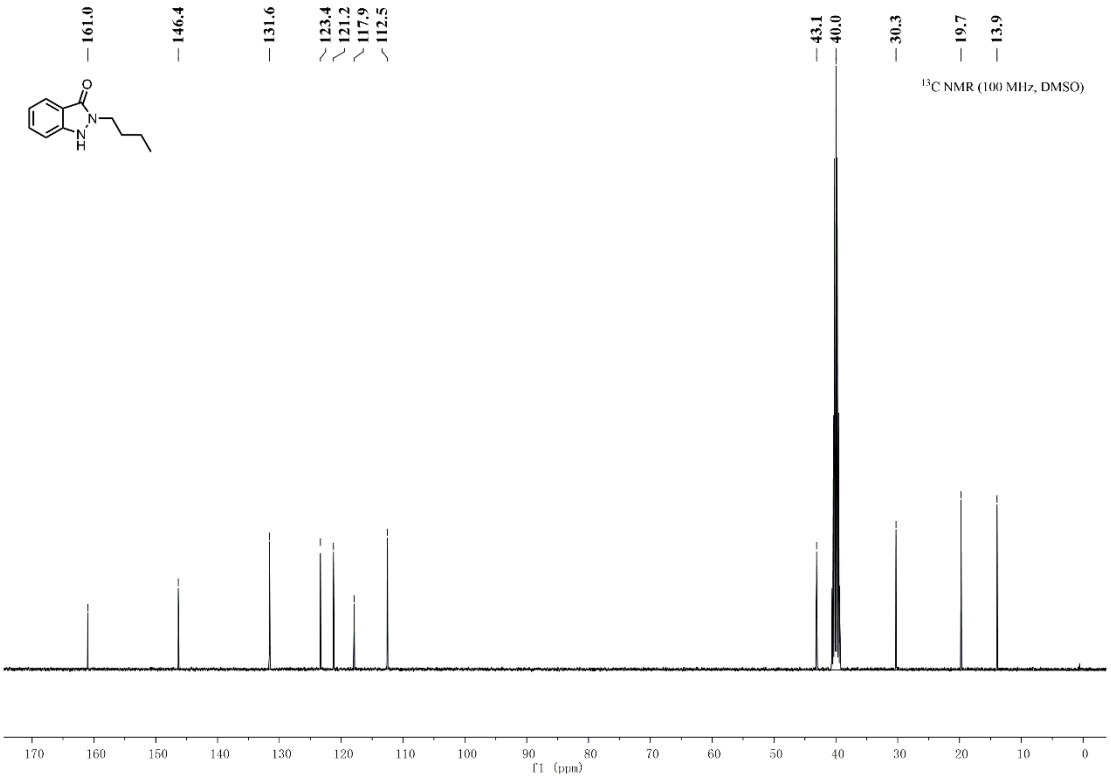
2-phenethyl-1,2-dihydro-3H-indazol-3-one (2g)





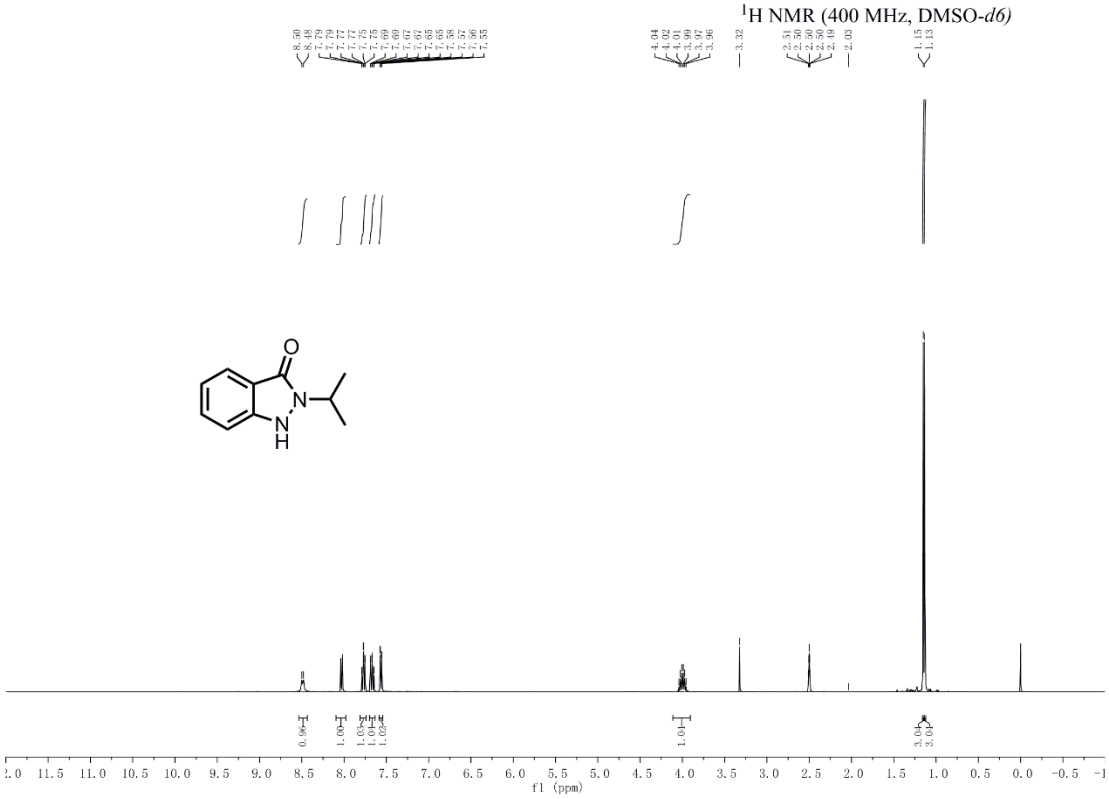
2-butyl-1,2-dihydro-3H-indazol-3-one (2h)[1]



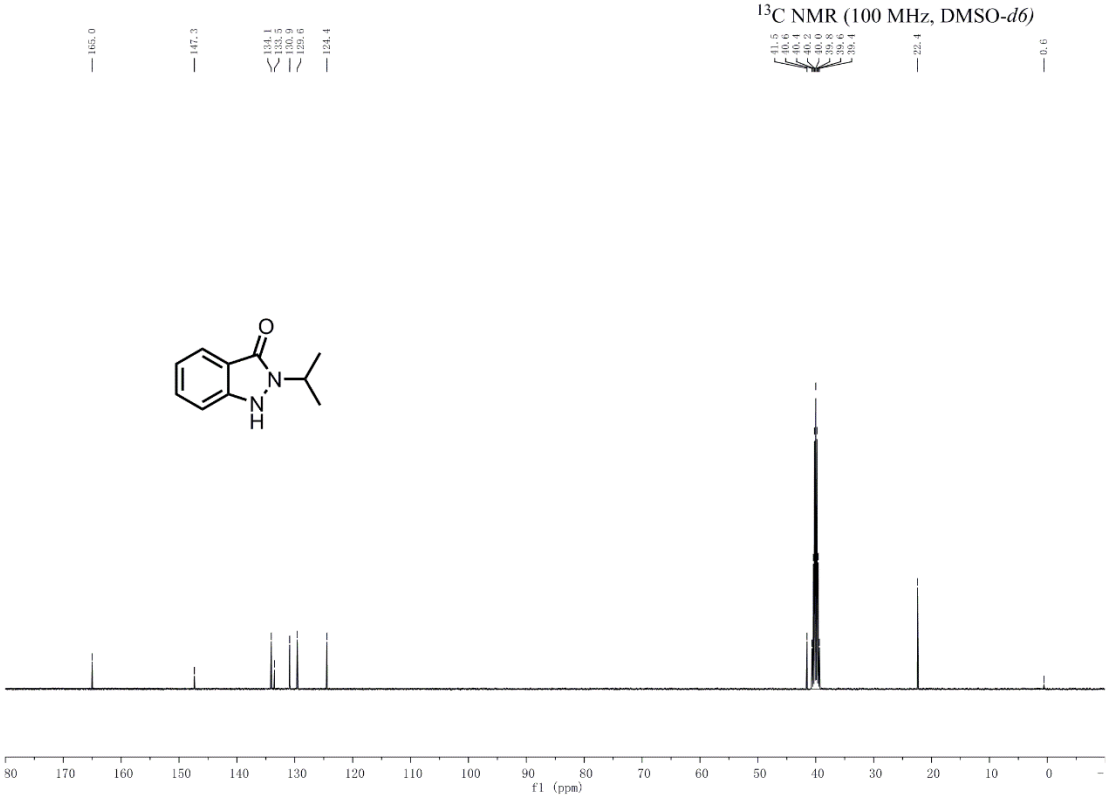


2-isopropyl-1,2-dihydro-3H-indazol-3-one (2i)

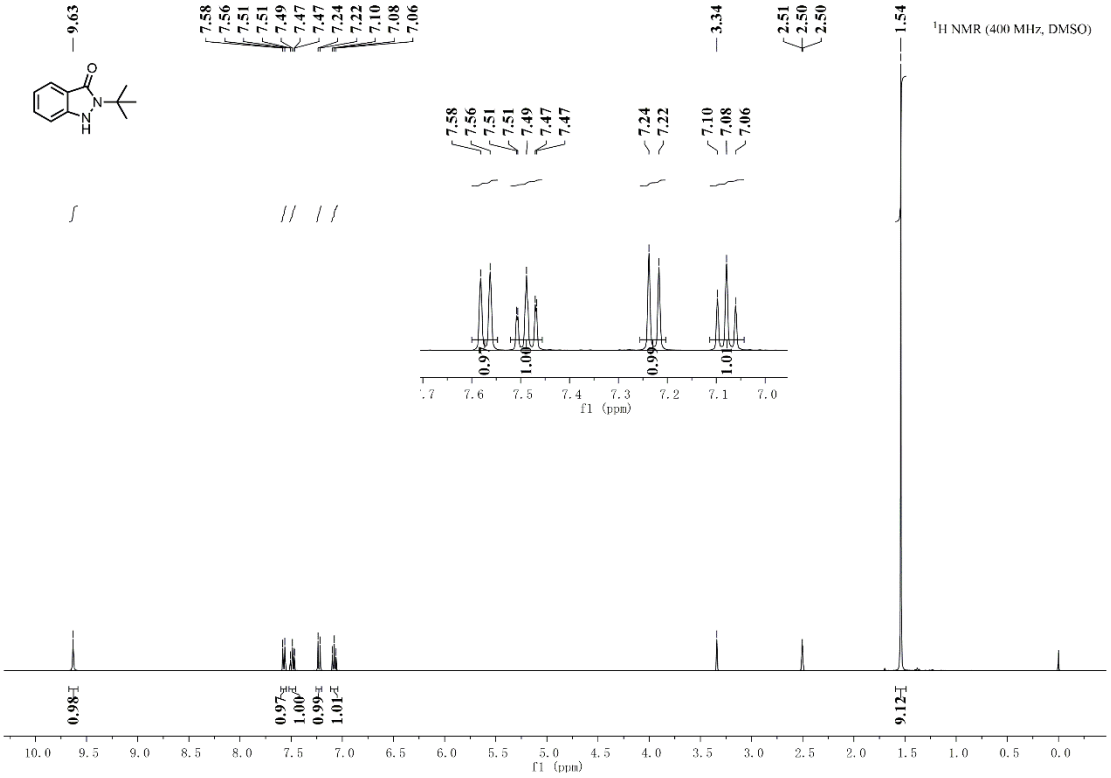
^{1}H NMR (400 MHz, DMSO-*d6)*

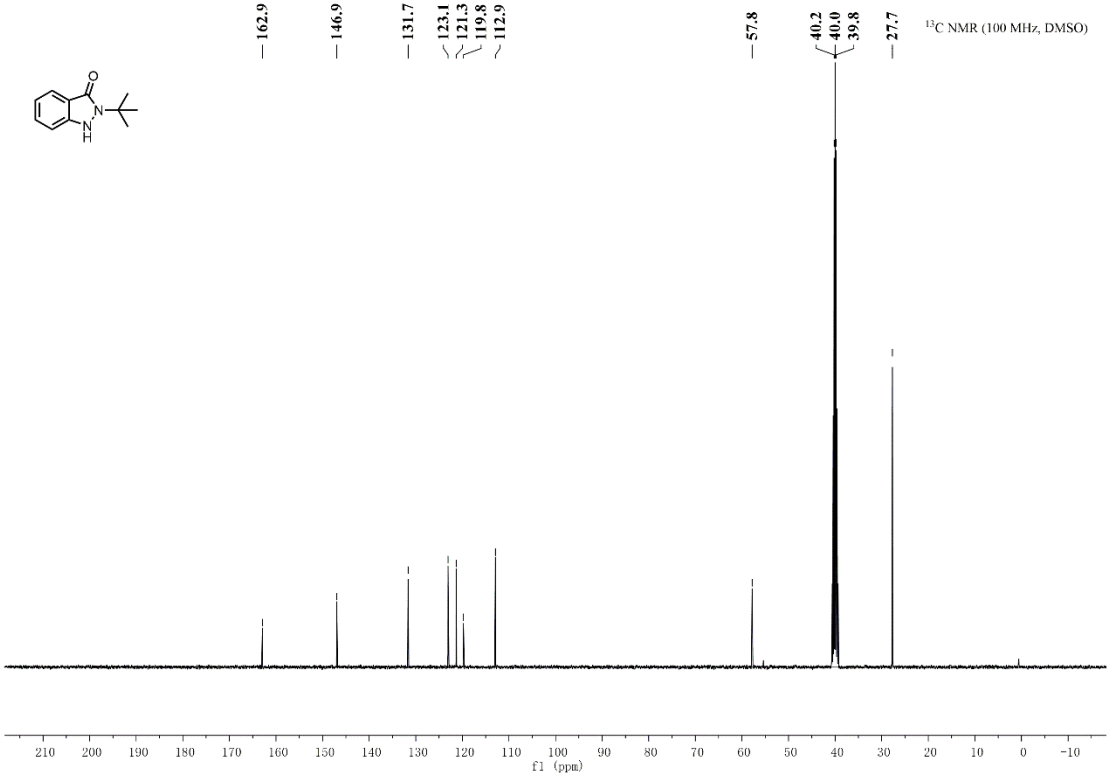


^{13}C NMR (100 MHz, DMSO-*d6)*

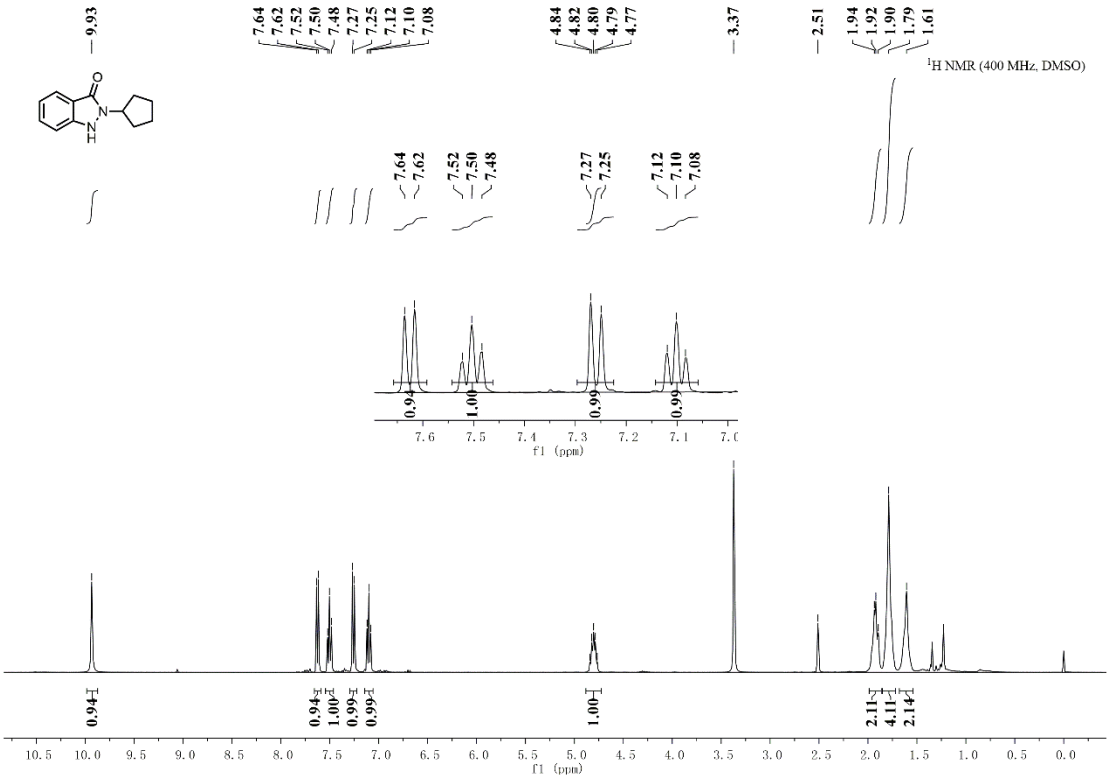


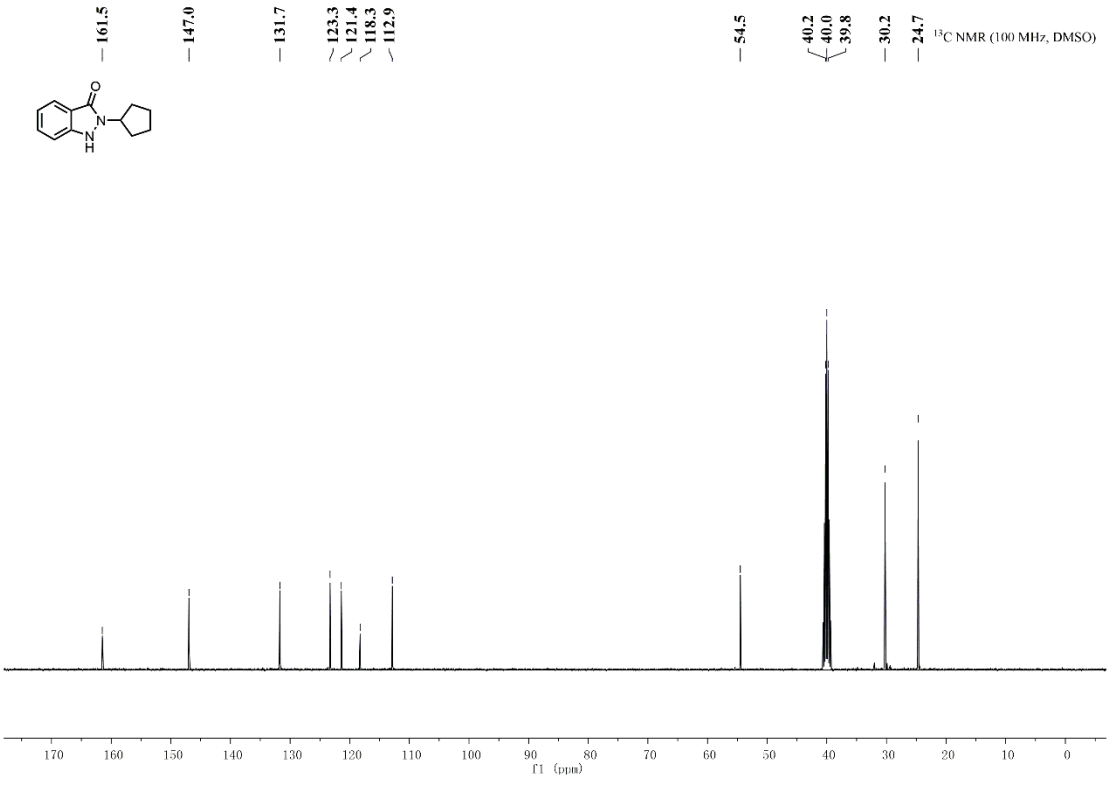
2-(tert-butyl)-1,2-dihydro-3H-indazol-3-one (2j)



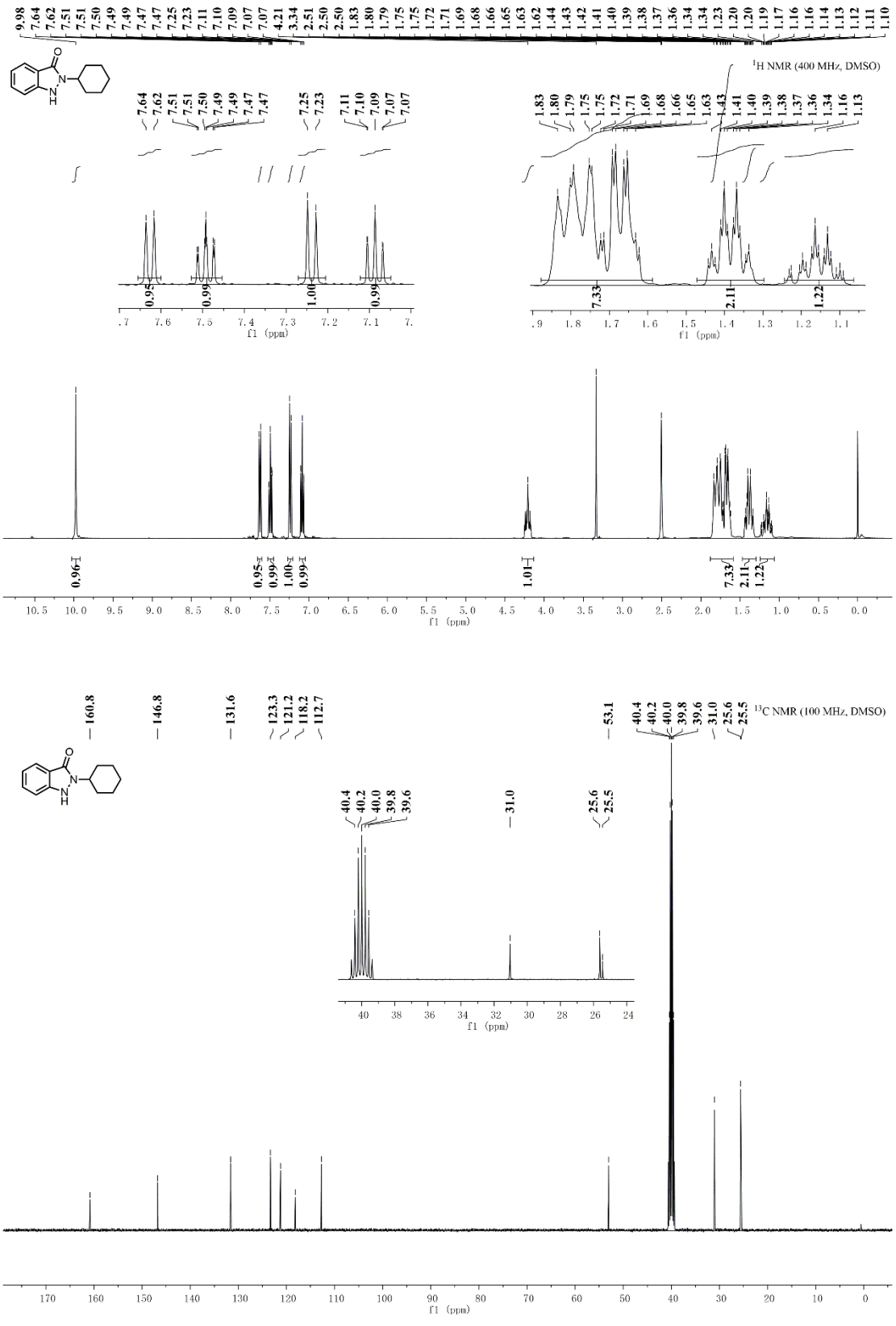


2-cyclohexyl-1,2-dihydro-3H-indazol-3-one (2k)

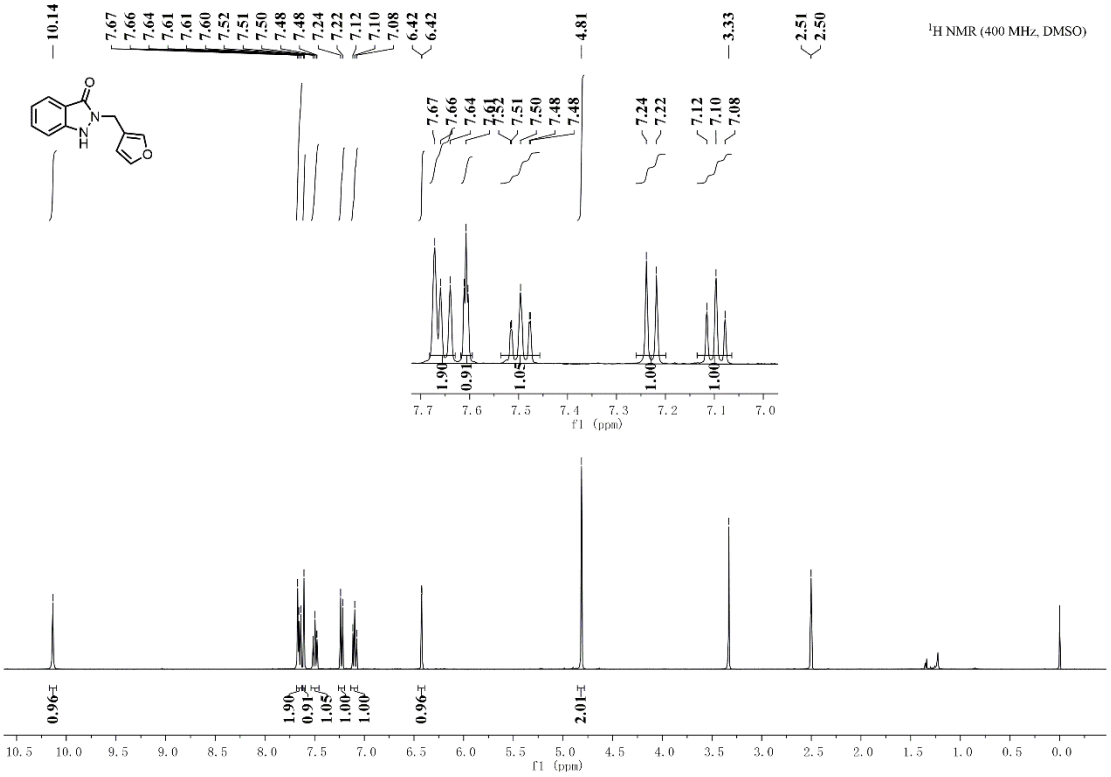


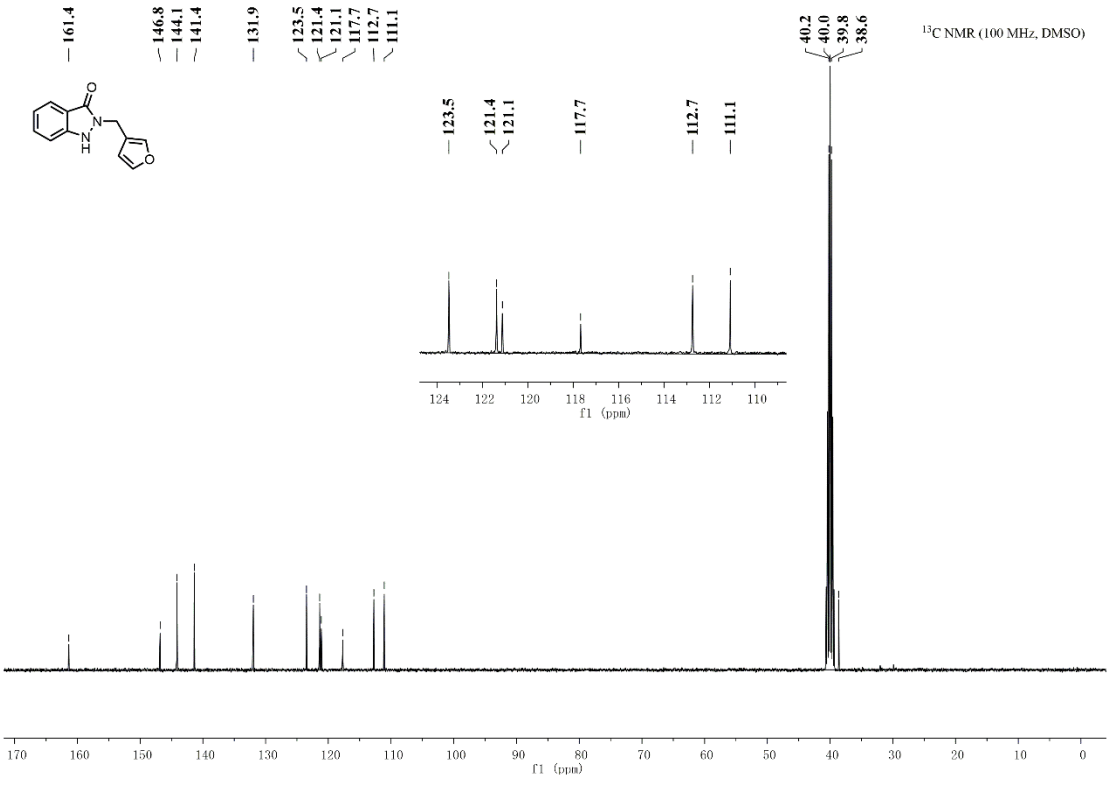


2-cyclohexyl-1,2-dihydro-3H-indazol-3-one (2l)



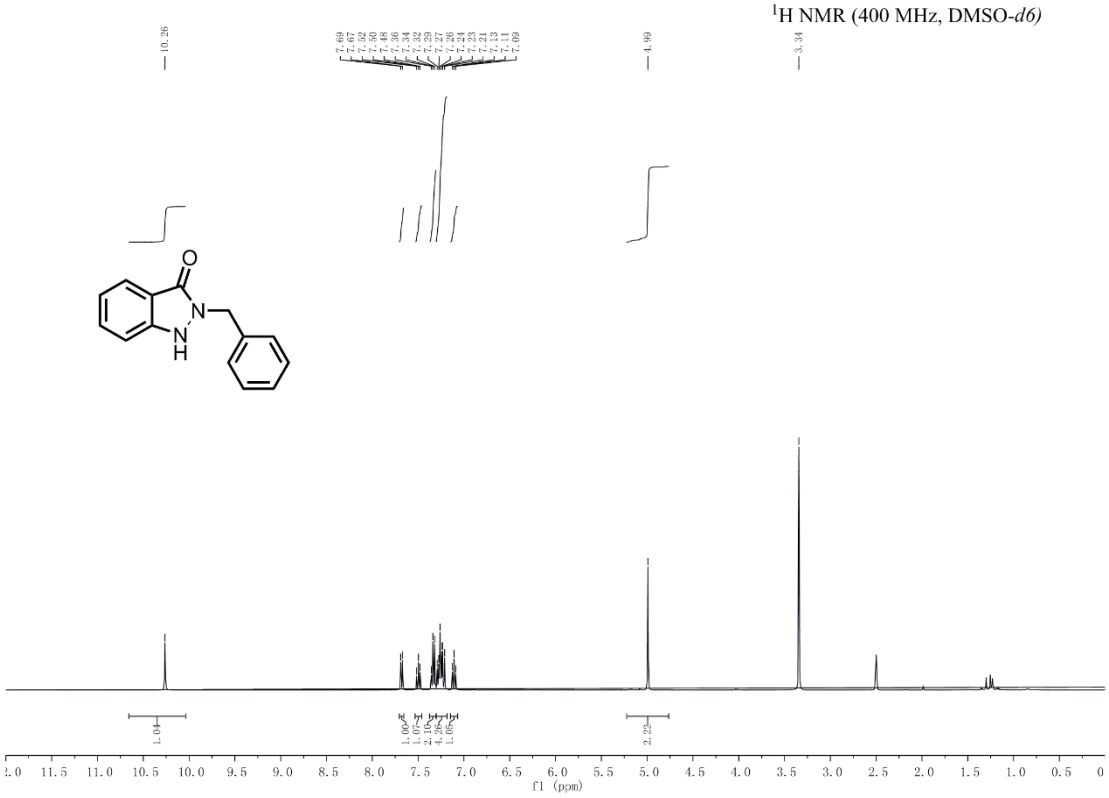
2-(furan-3-ylmethyl)-1,2-dihydro-3H-indazol-3-one (2m)



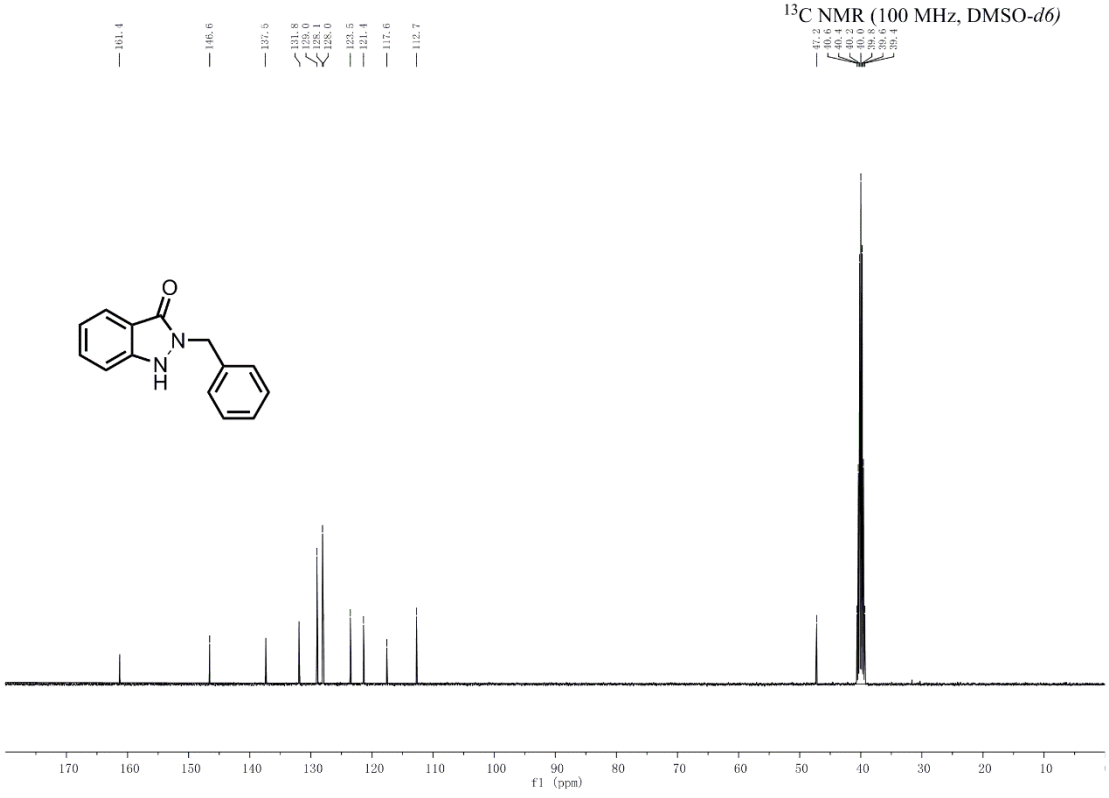


2-benzyl-1,2-dihydro-3H-indazol-3-one (2n)

^{1}H NMR (400 MHz, DMSO-*d6)*

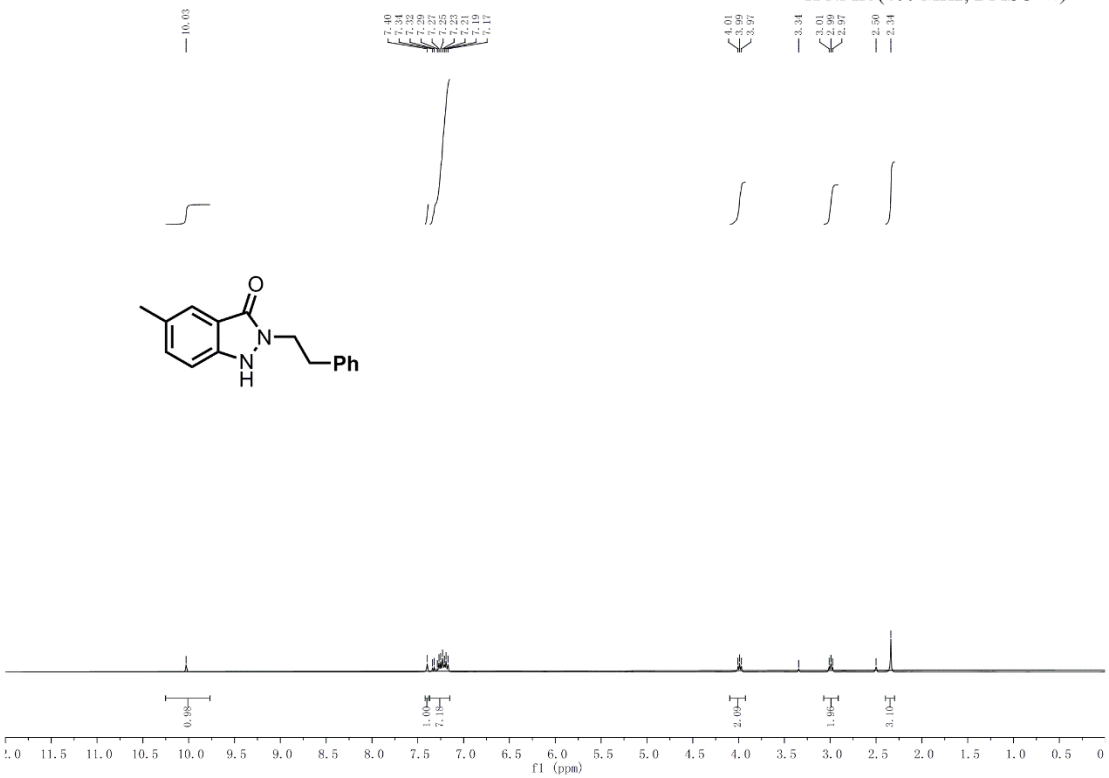


^{13}C NMR (100 MHz, DMSO-*d6)*

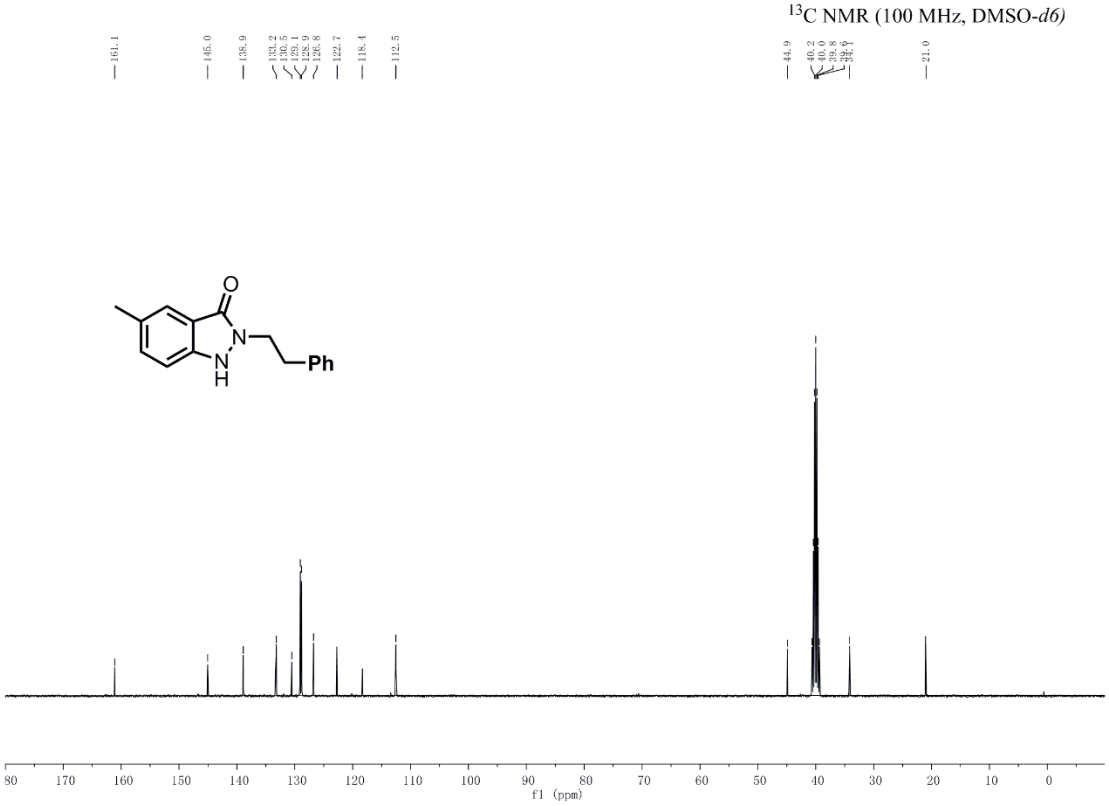


5-methyl-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2o)

^{1}H NMR (400 MHz, DMSO-*d6)*

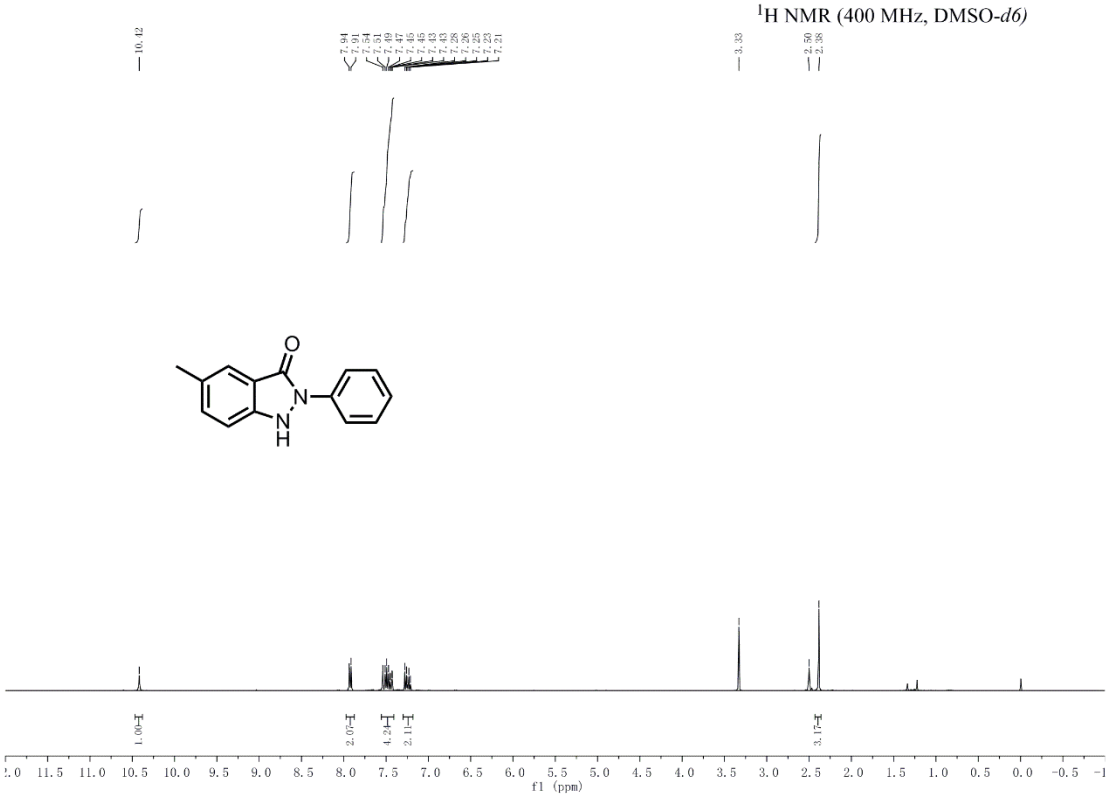


^{13}C NMR (100 MHz, DMSO-*d6)*



5-methyl-2-phenyl-1,2-dihydro-3H-indazol-3-one (2p)

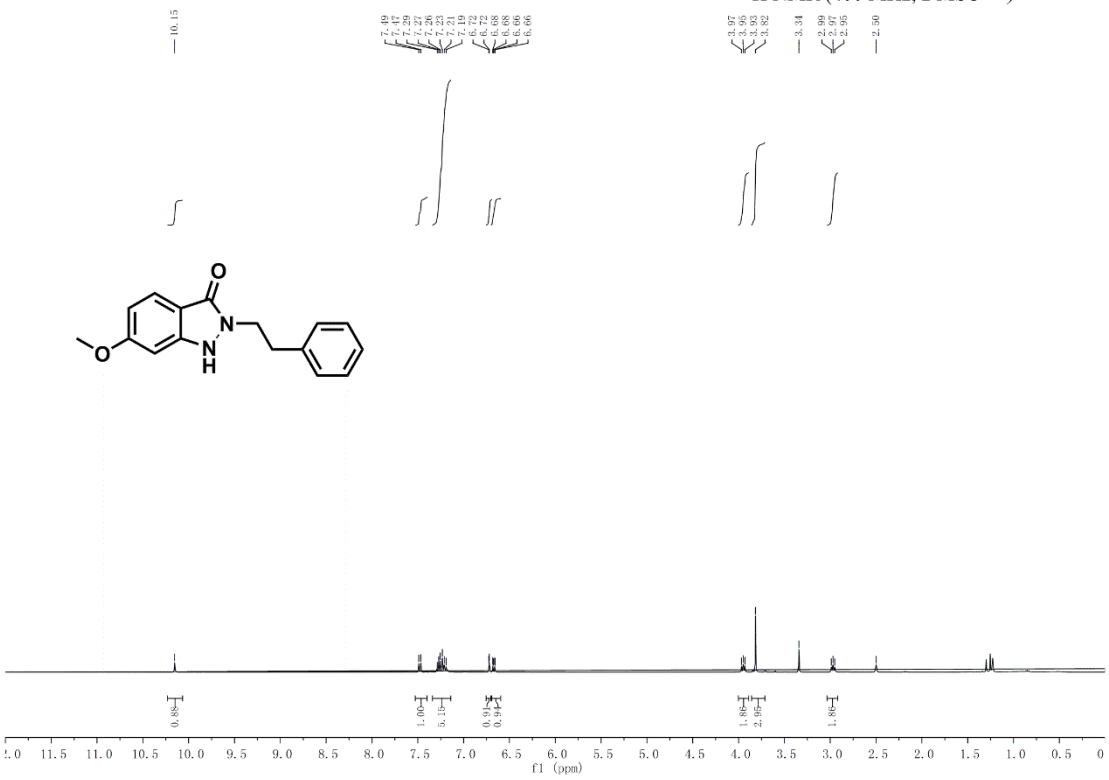
^{1}H NMR (400 MHz, DMSO-*d6*)



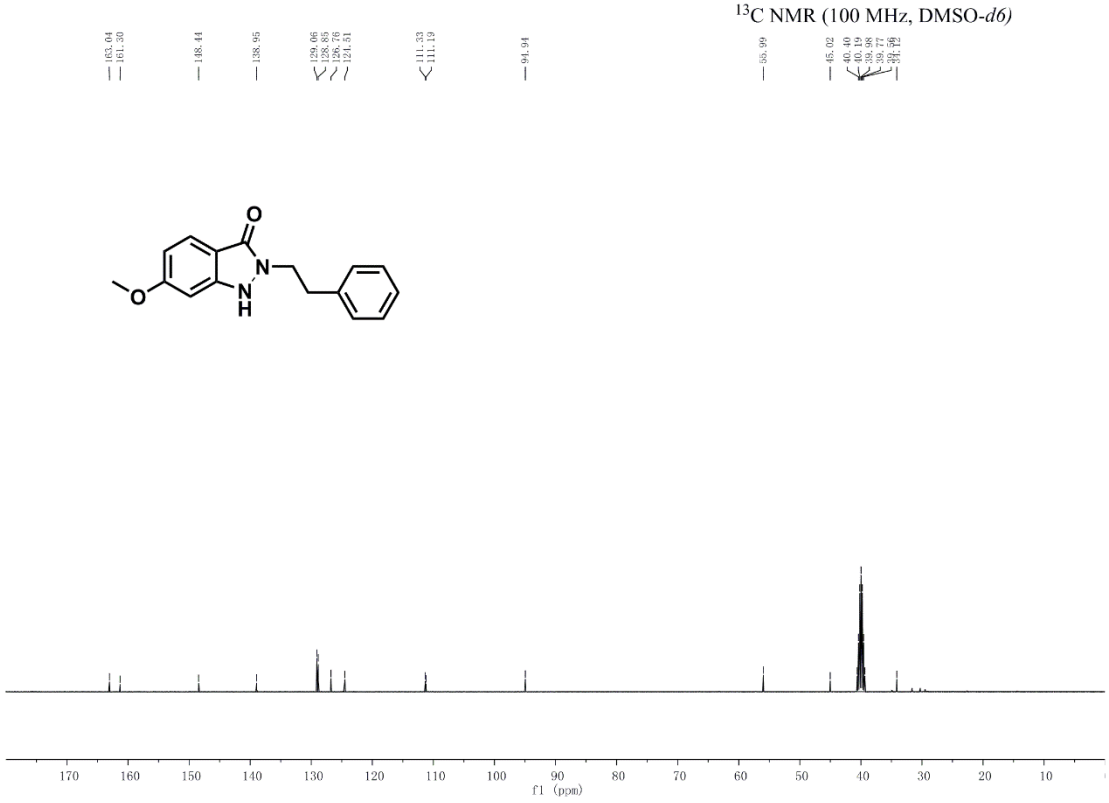
^{13}C NMR (100 MHz, DMSO-*d6*)

6-methoxy-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2q)

^{1}H NMR (400 MHz, DMSO-*d6)*



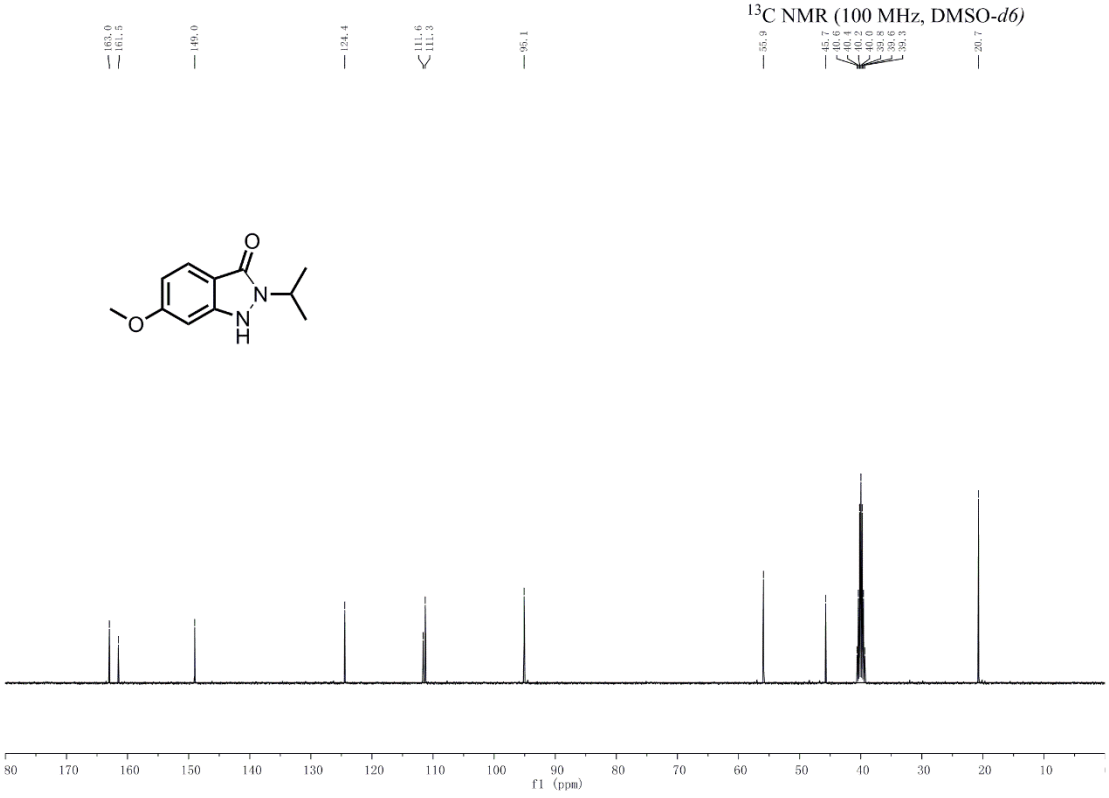
^{13}C NMR (100 MHz, DMSO-*d6)*



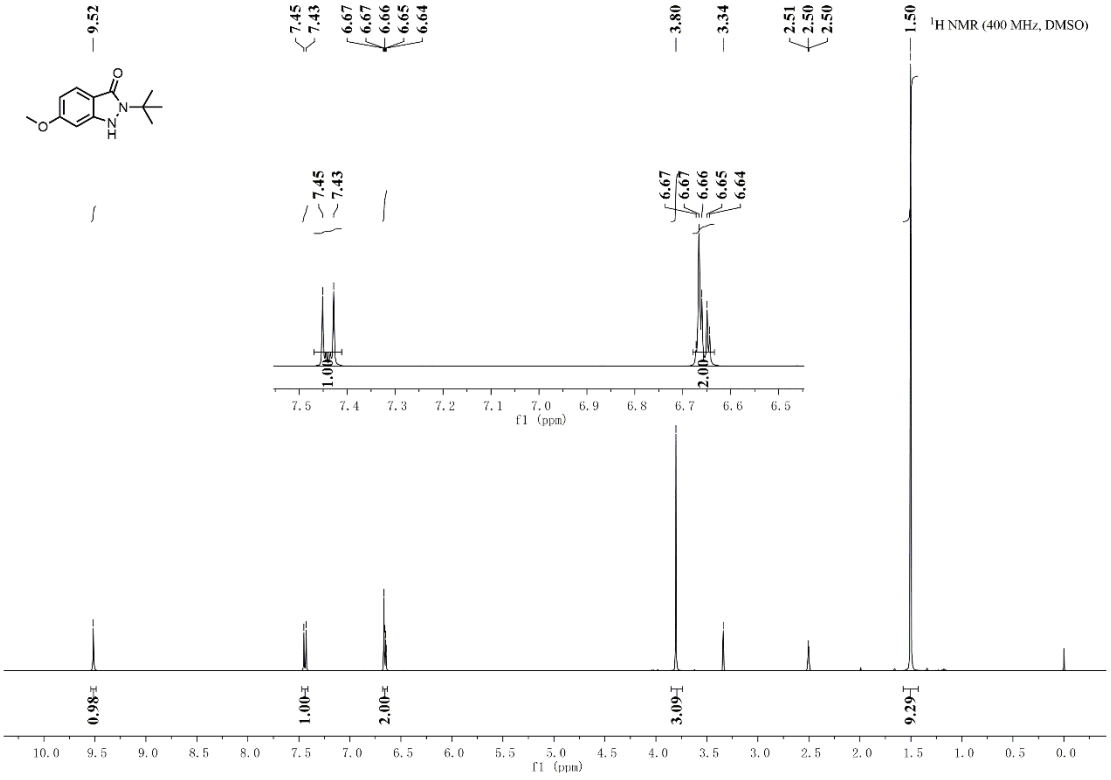
2-isopropyl-6-methoxy-1,2-dihydro-3H-indazol-3-one (2r)

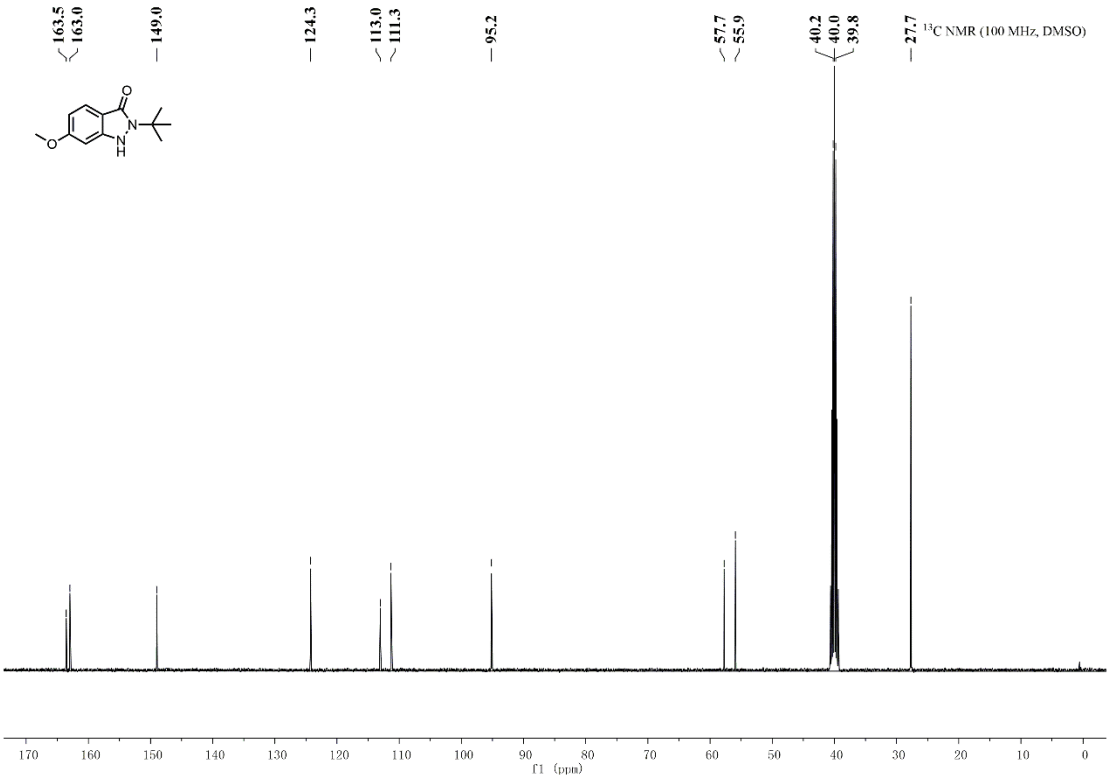
^{1}H NMR (400 MHz, DMSO-*d6)*

^{13}C NMR (100 MHz, DMSO-*d6)*

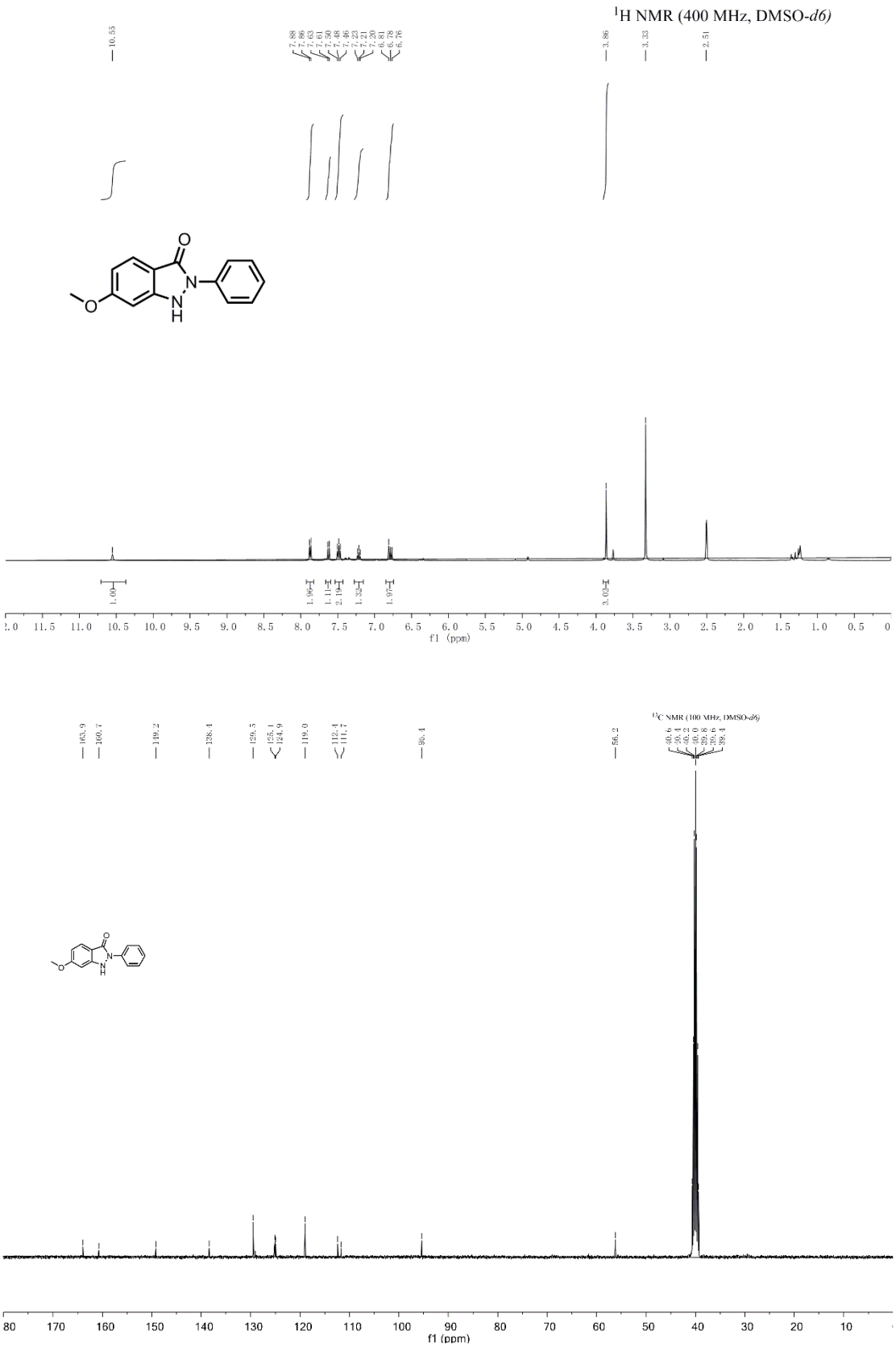


2-(tert-butyl)-6-methoxy-1,2-dihydro-3H-indazol-3-one (2s)

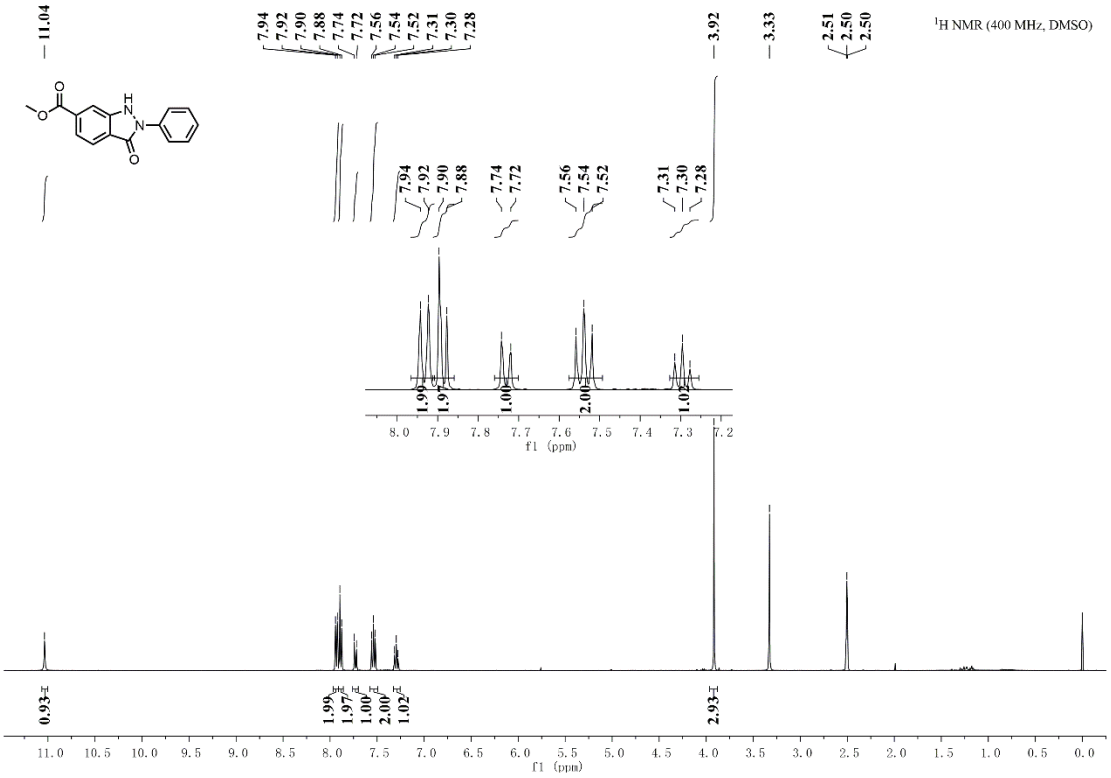


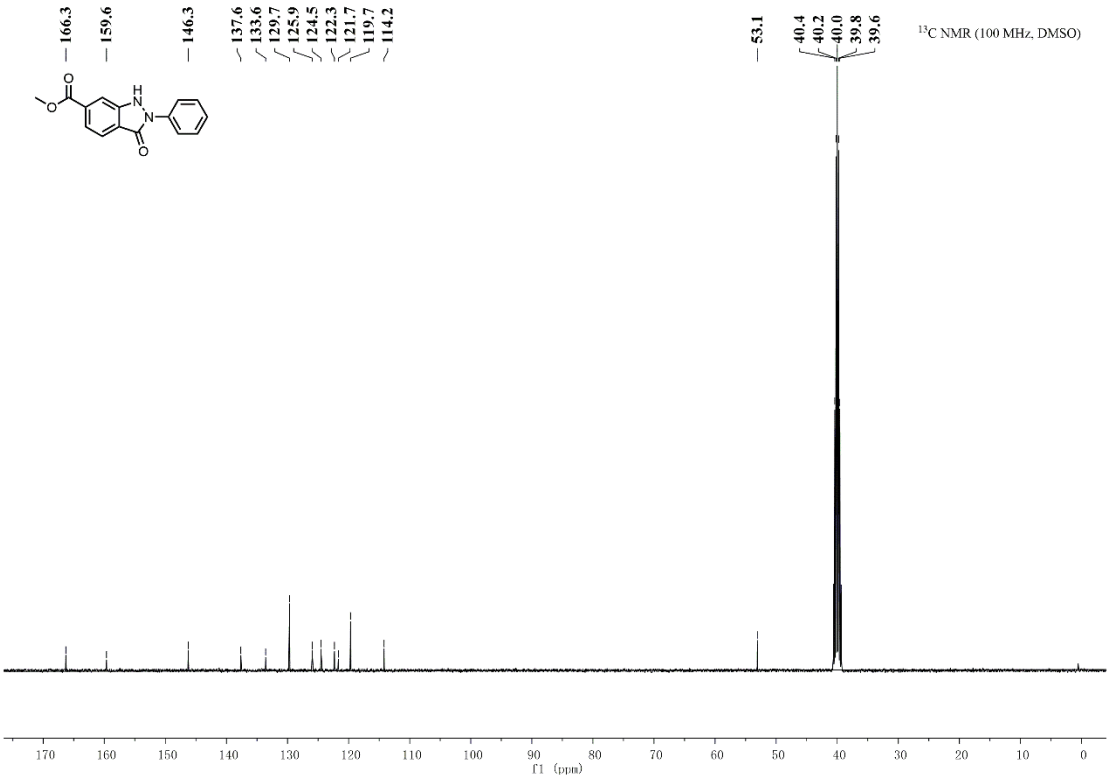


6-methoxy-2-phenyl-1,2-dihydro-3H-indazol-3-one (2t)



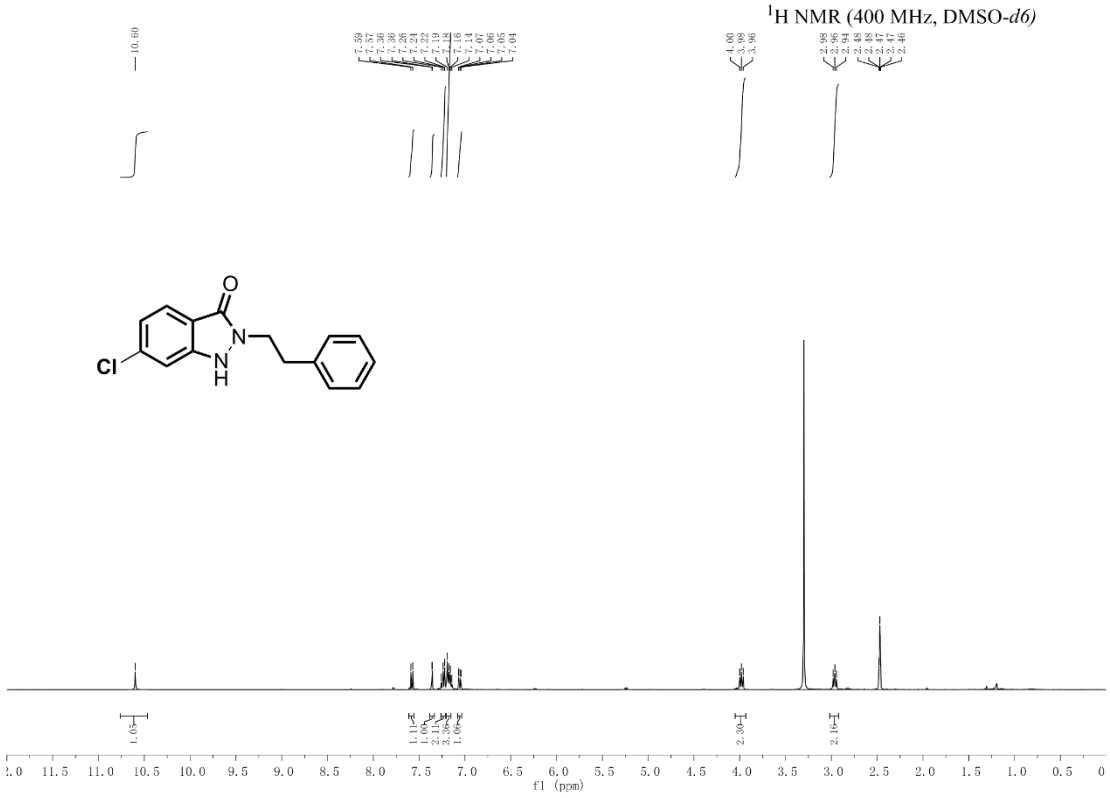
Methyl 3-oxo-2-phenyl-2,3-dihydro-1H-indazole-6-carboxylate (2u)



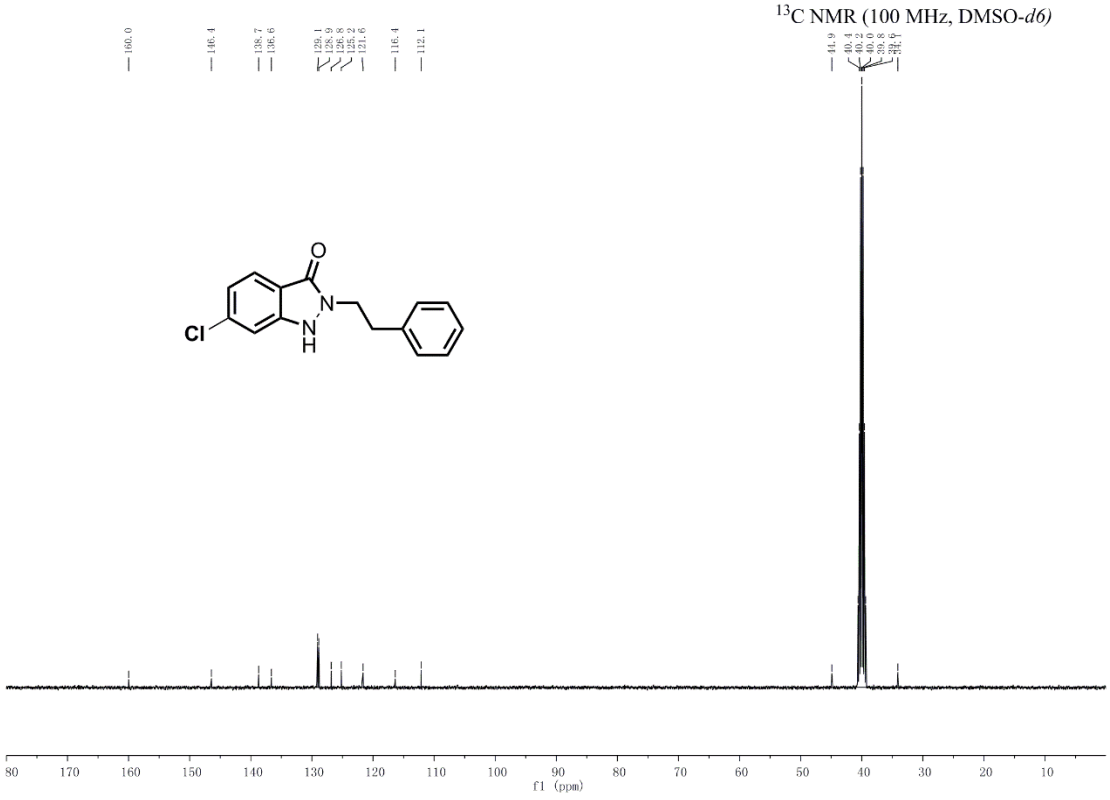


6-chloro-2-phenethyl-1,2-dihydro-3H-indazol-3-one (2v)

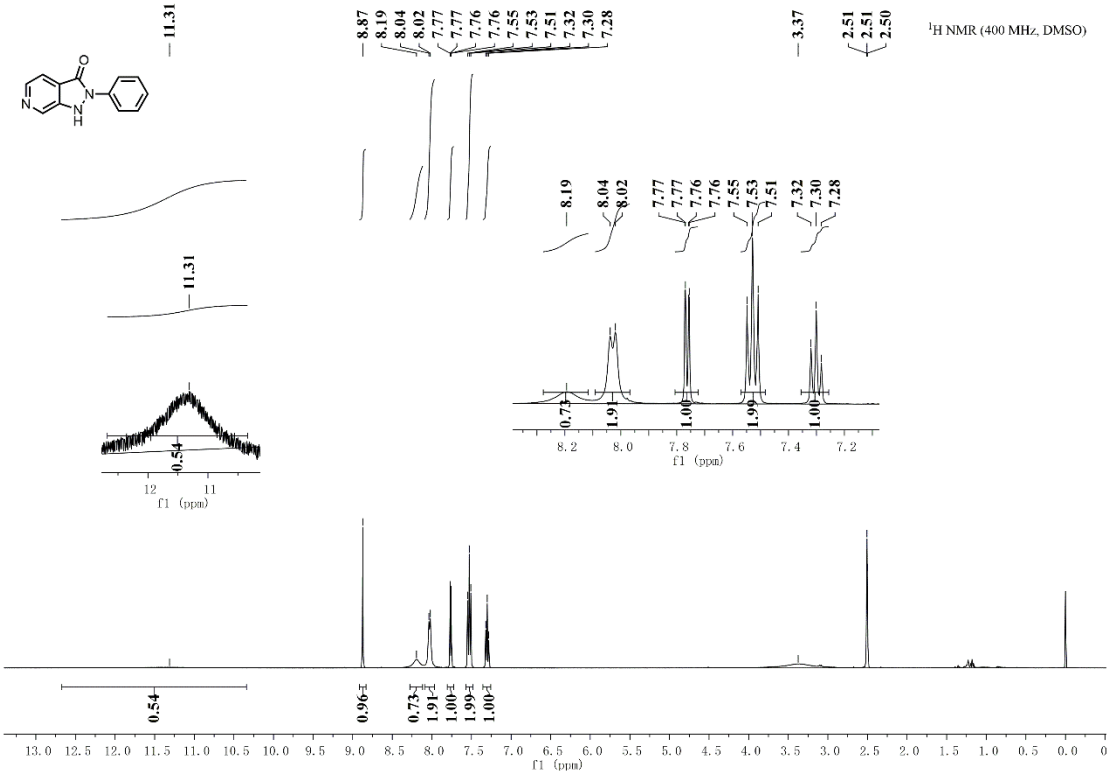
^{1}H NMR (400 MHz, DMSO-*d6)*

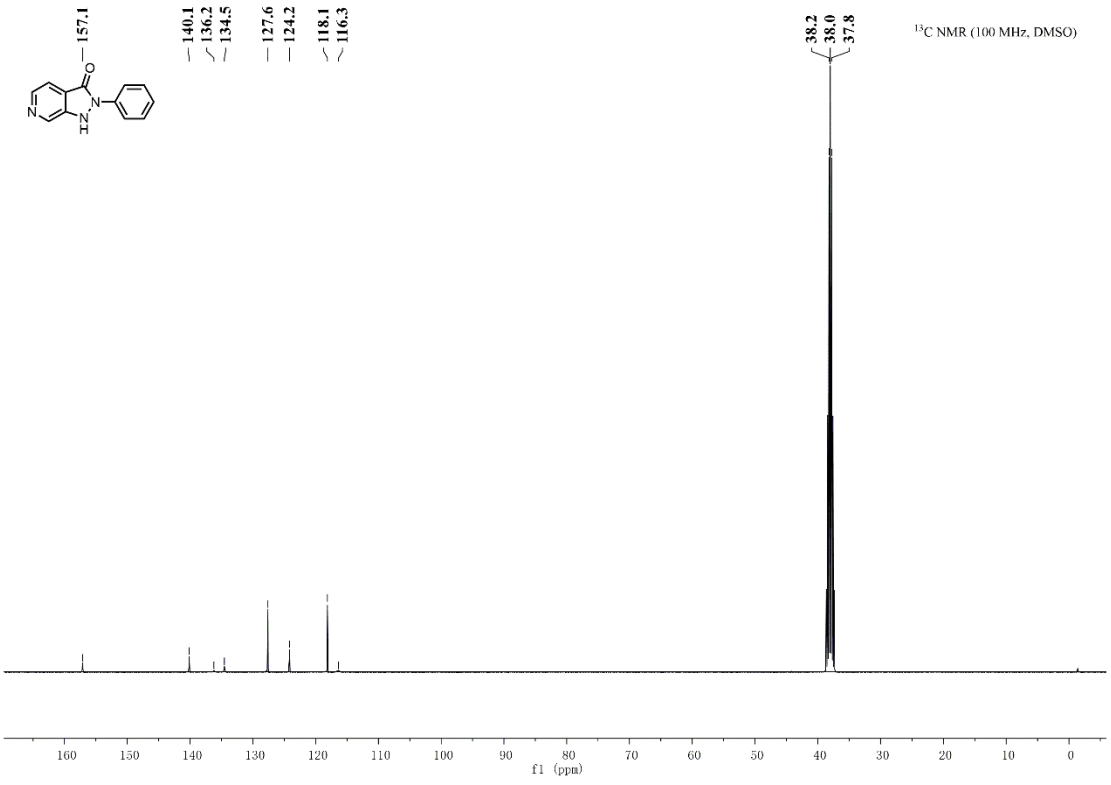


^{13}C NMR (100 MHz, DMSO-*d6)*



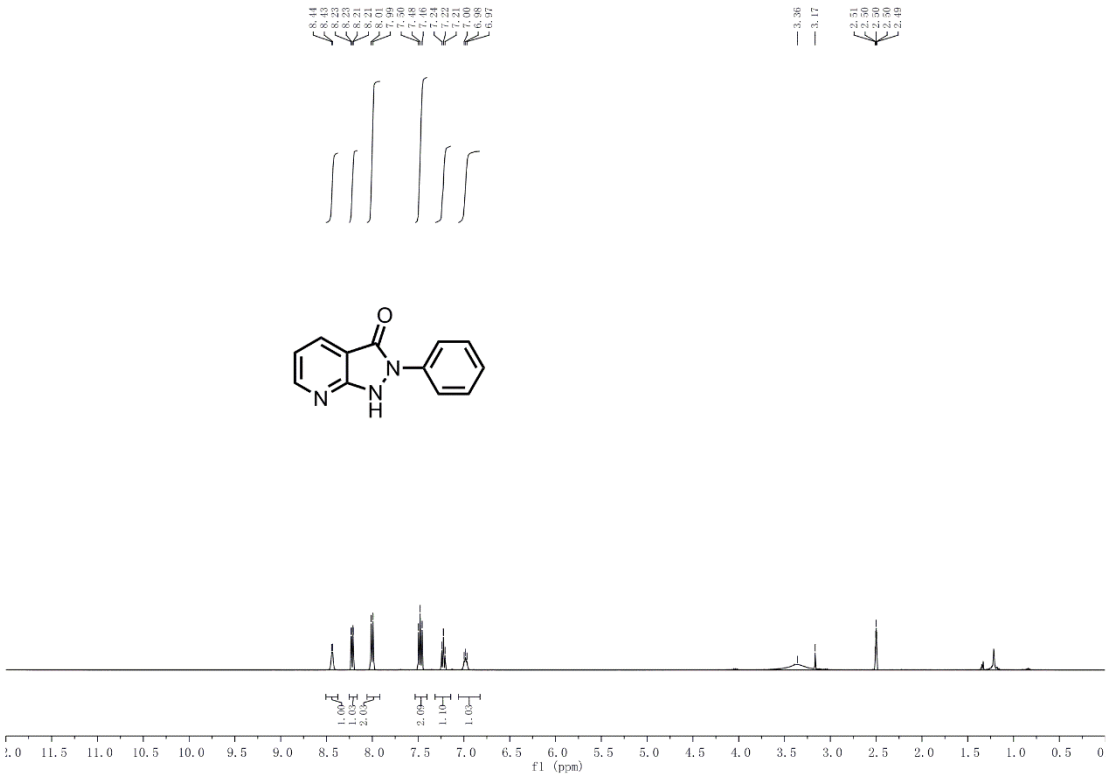
2-phenyl-1,2-dihydro-3H-pyrazolo[3,4-c]pyridin-3-one (2w)





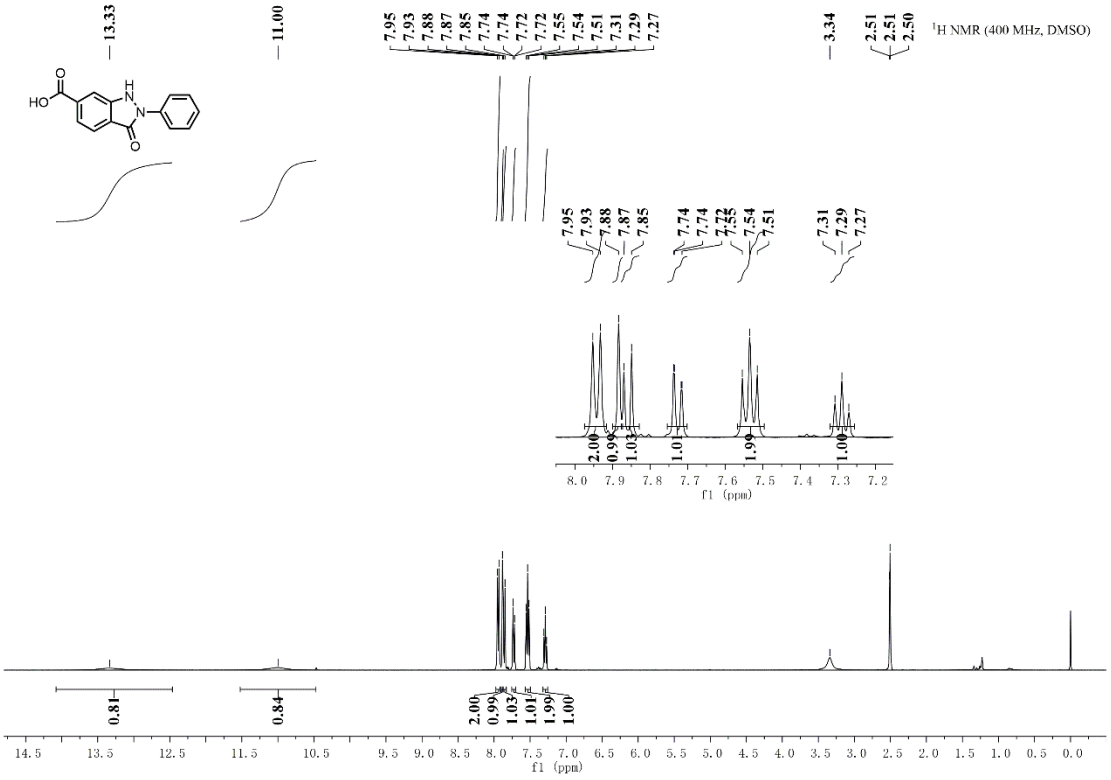
2-phenyl-1,2-dihydro-3H-pyrazolo[3,4-b]pyridin-3-one (2x)

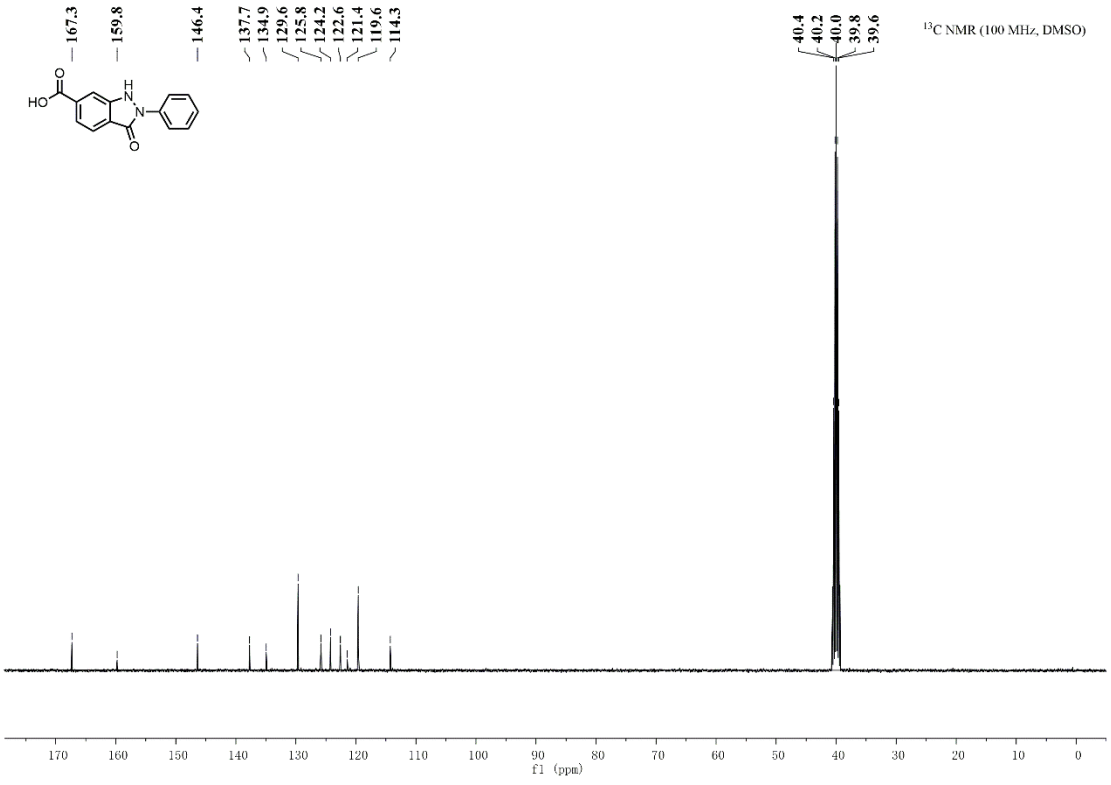
^{1}H NMR (400 MHz, DMSO-*d6)*



^{13}C NMR (100 MHz, DMSO-*d6)*

3-oxo-2-phenyl-2,3-dihydro-1H-indazole-6-carboxylic acid (6)





11. Deconvoluted mass spectra of On-DNA substrates

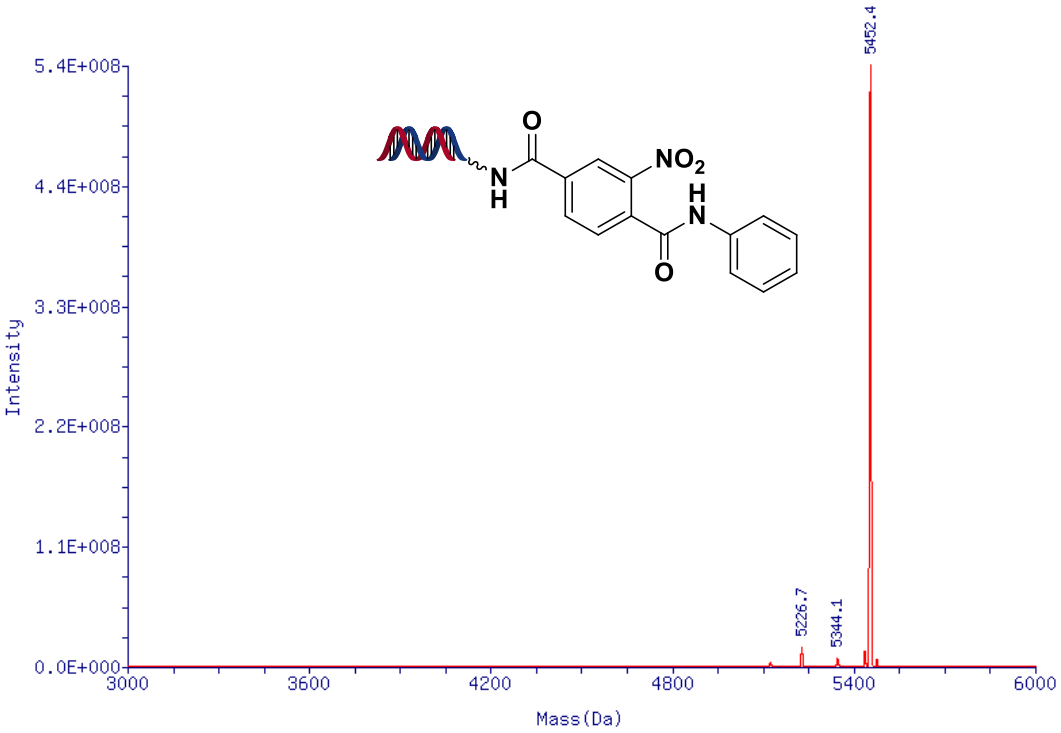


Figure S7. Deconvoluted mass spectrum of conjugate 3a, expected: 5452; observed: 5452.4.

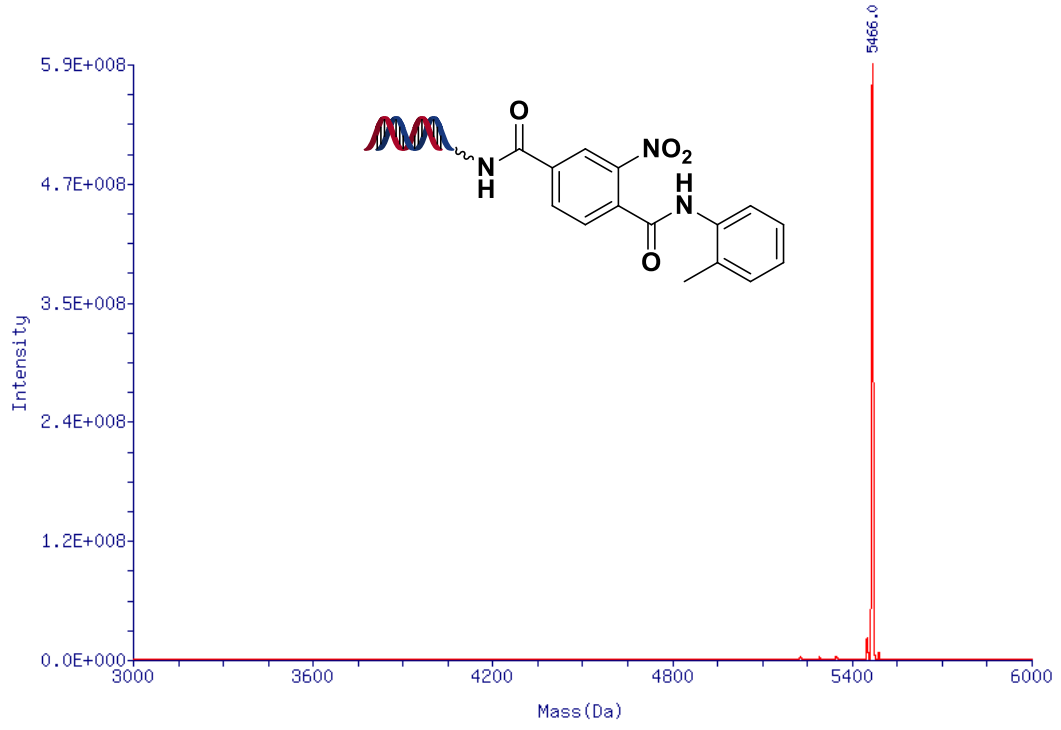


Figure S8. Deconvoluted mass spectrum of conjugate 3b, expected: 5466; observed: 5466.0.

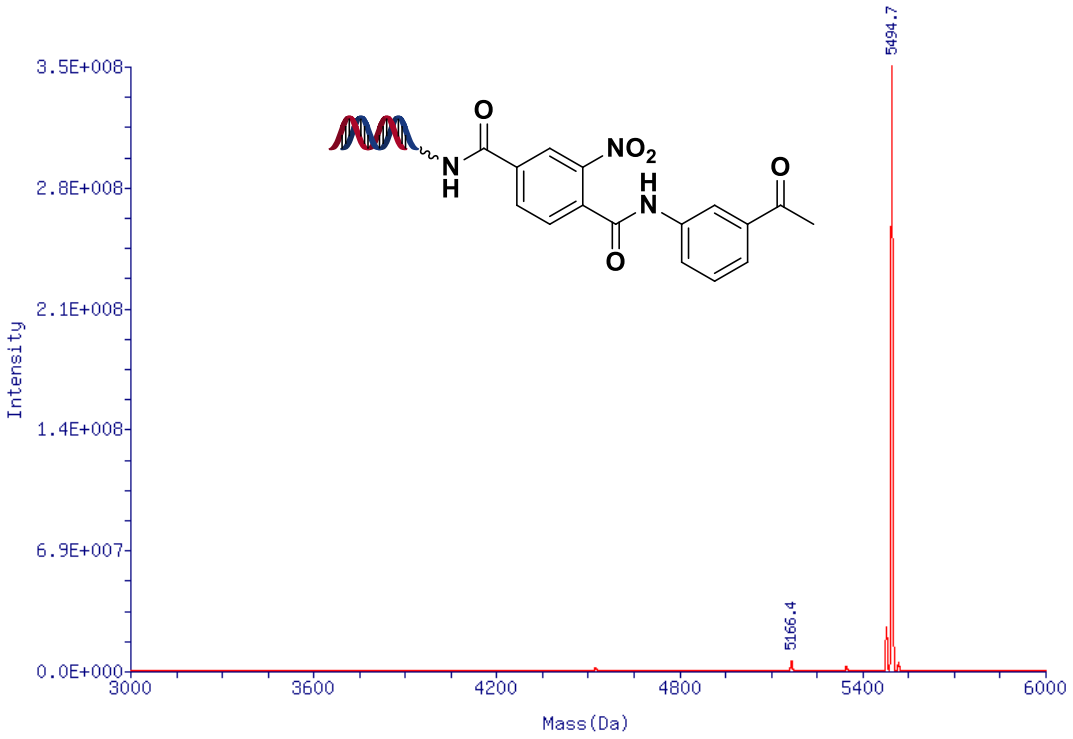


Figure S9. Deconvoluted mass spectrum of conjugate 3c, expected: 5494; observed: 5494.7.

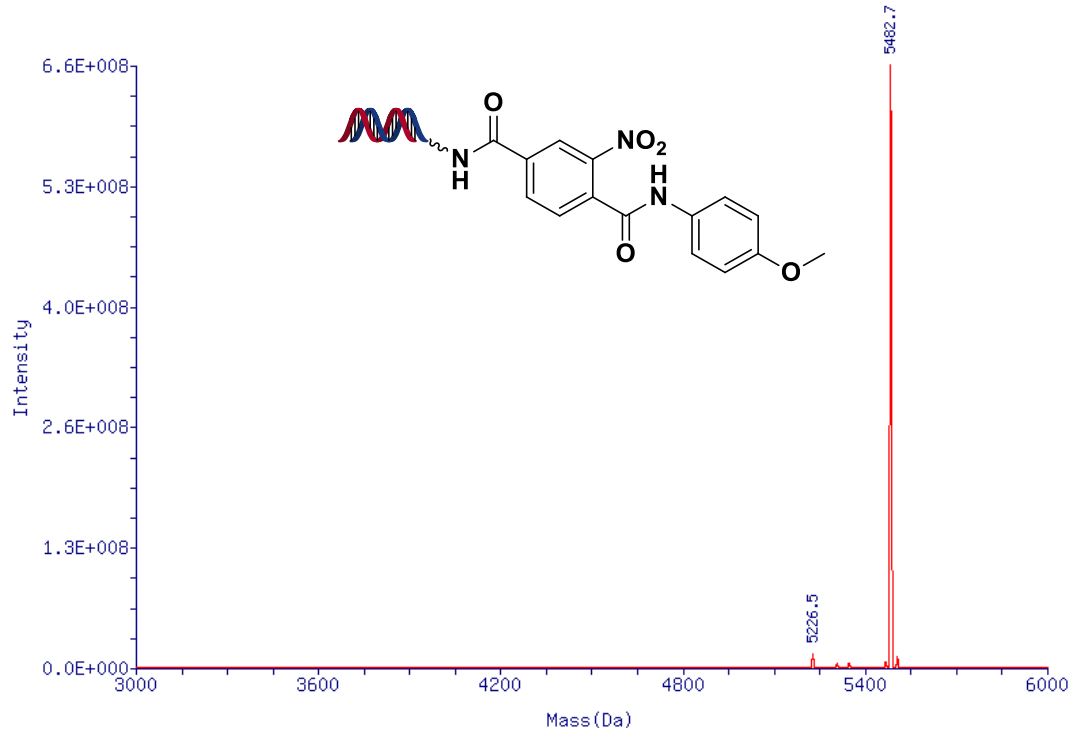


Figure S10. Deconvoluted mass spectrum of conjugate 3d, expected: 5482; observed: 5482.7.

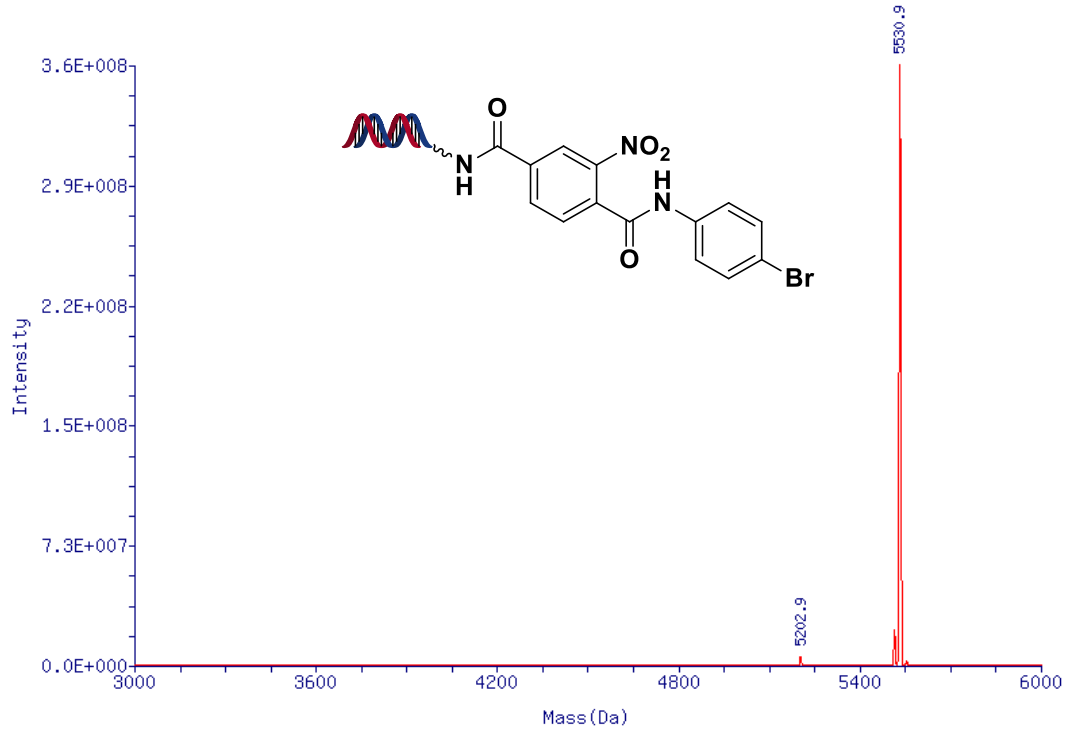


Figure S11. Deconvoluted mass spectrum of conjugate 3e, expected: 5531; observed: 5530.9.

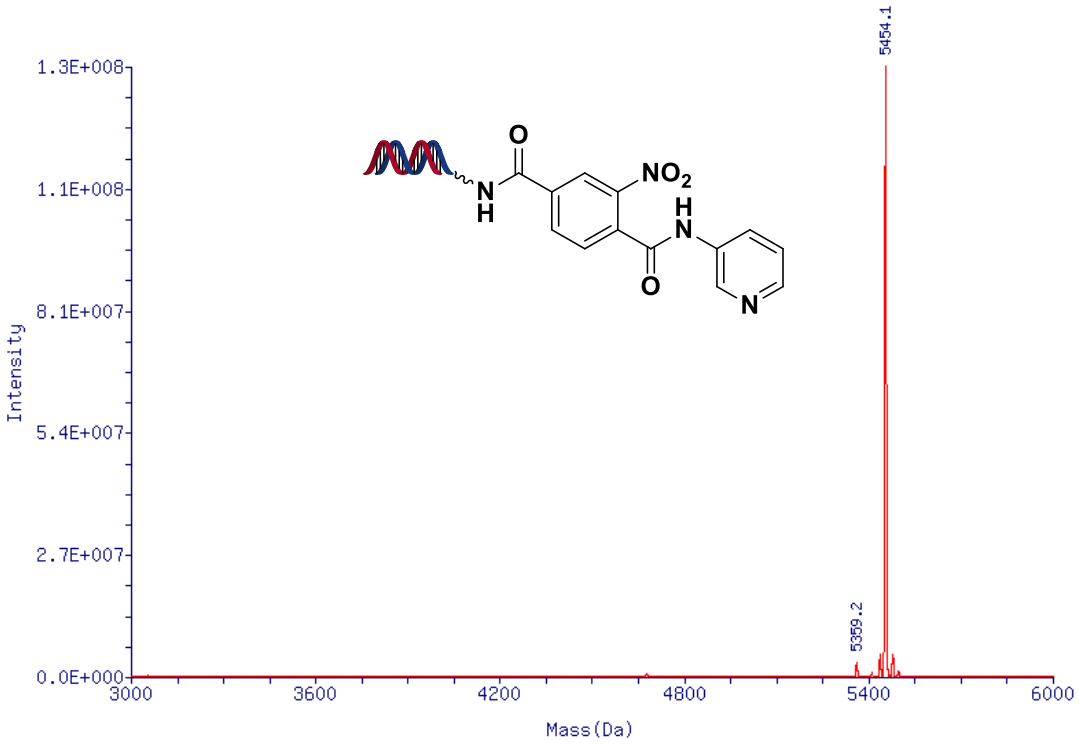


Figure S12. Deconvoluted mass spectrum of conjugate 3f, expected: 5453; observed: 5454.1.

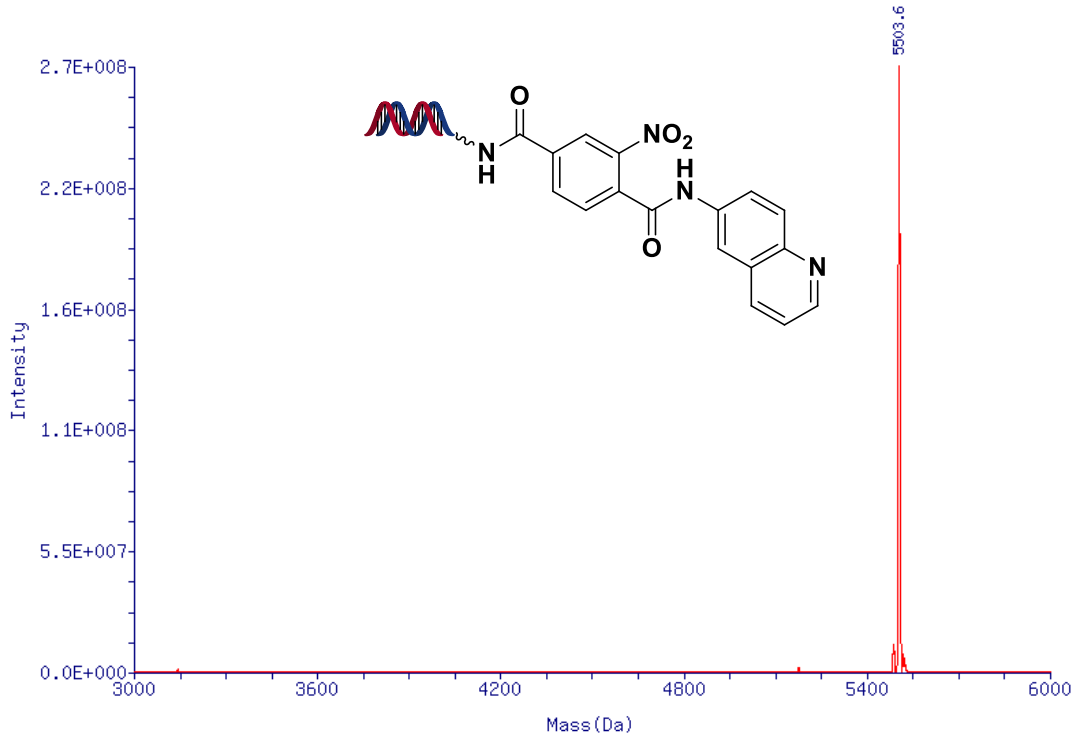


Figure S13. Deconvoluted mass spectrum of conjugate 3g, expected: 5503; observed: 5503.6.

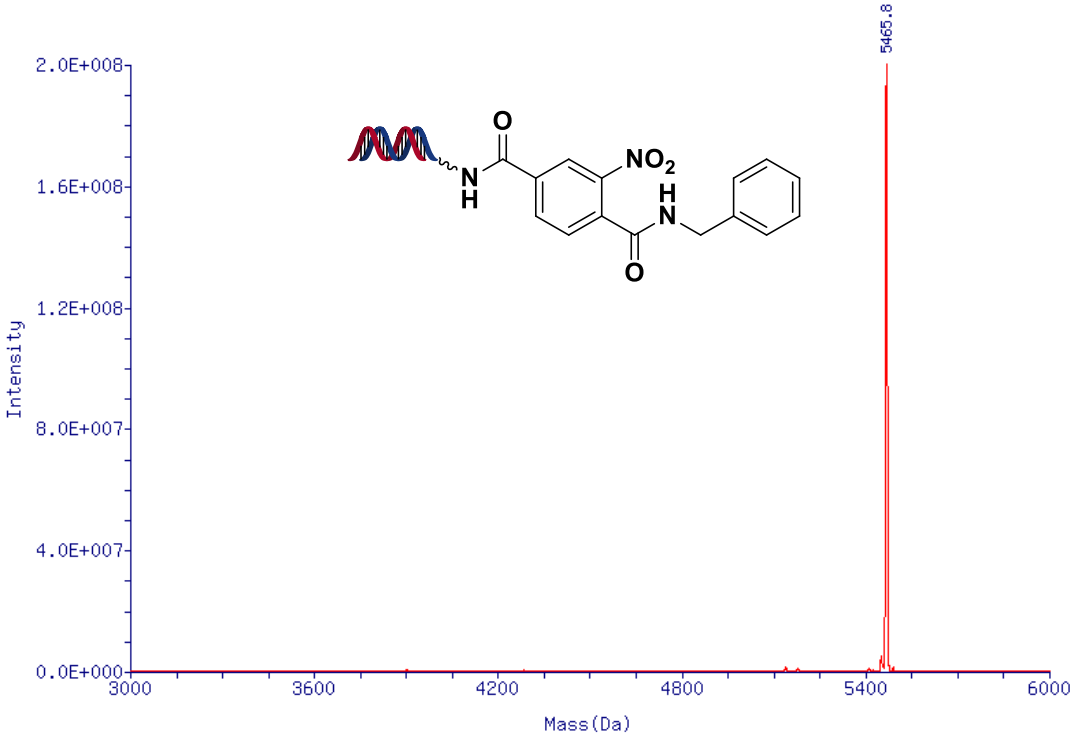


Figure S14. Deconvoluted mass spectrum of conjugate 3h, expected: 5466; observed: 5465.8.

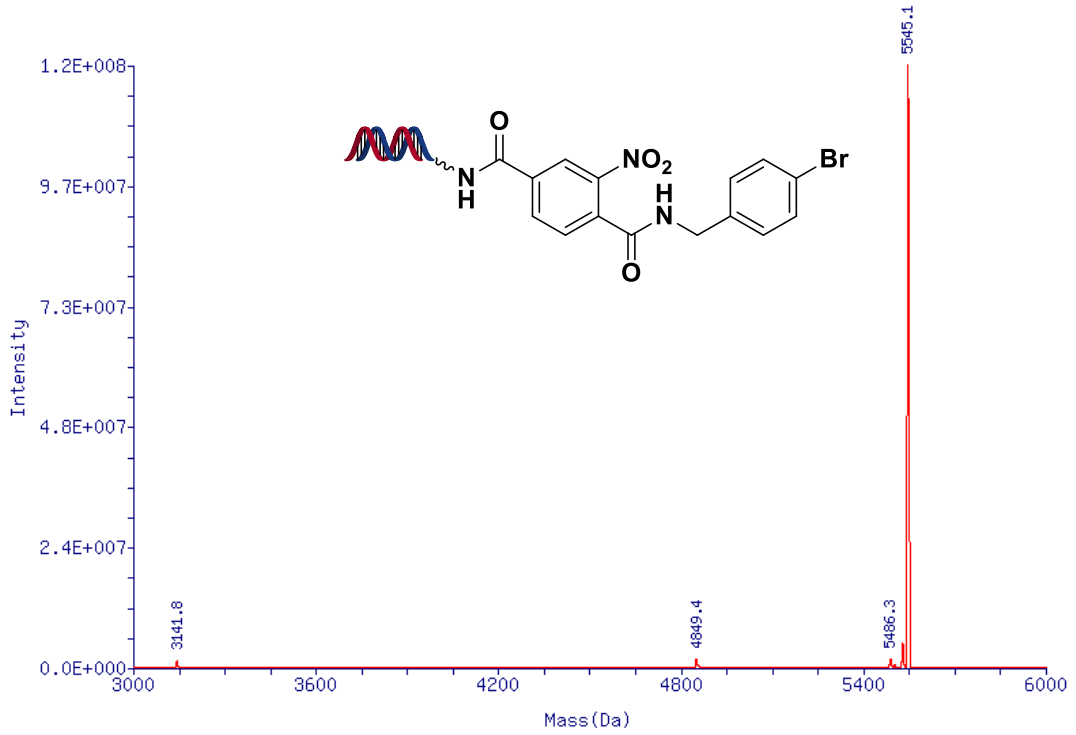


Figure S15. Deconvoluted mass spectrum of conjugate 3i, expected: 5545; observed: 5545.1.

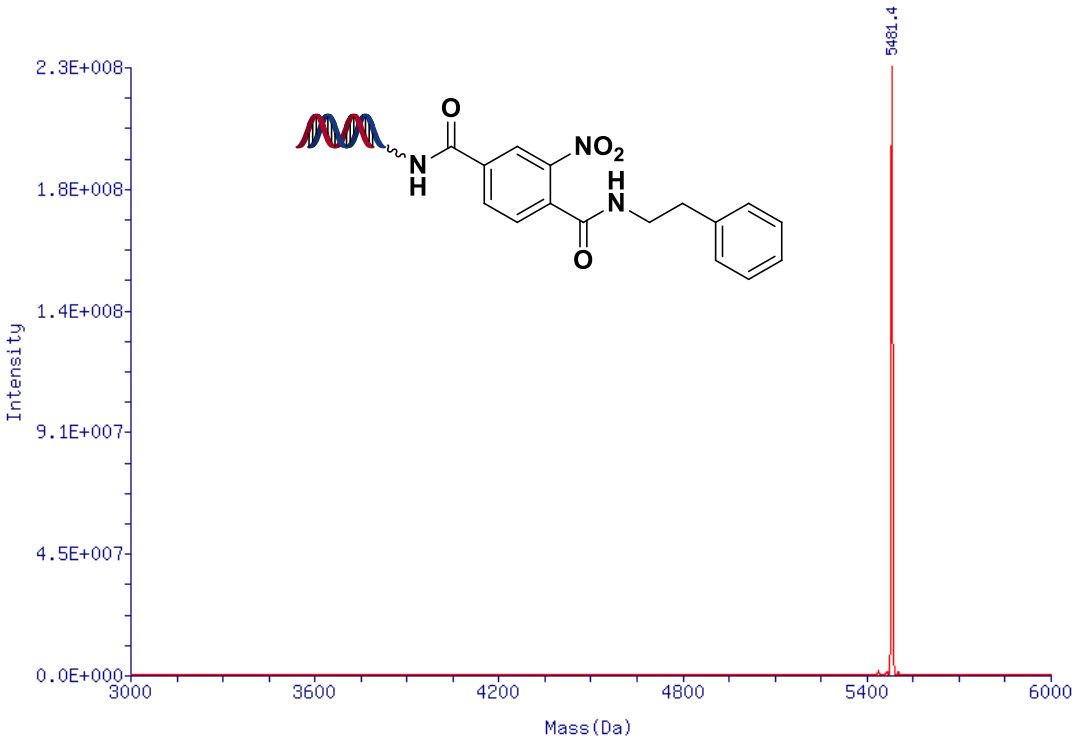


Figure S16. Deconvoluted mass spectrum of conjugate 3j, expected: 5480; observed: 5481.4.

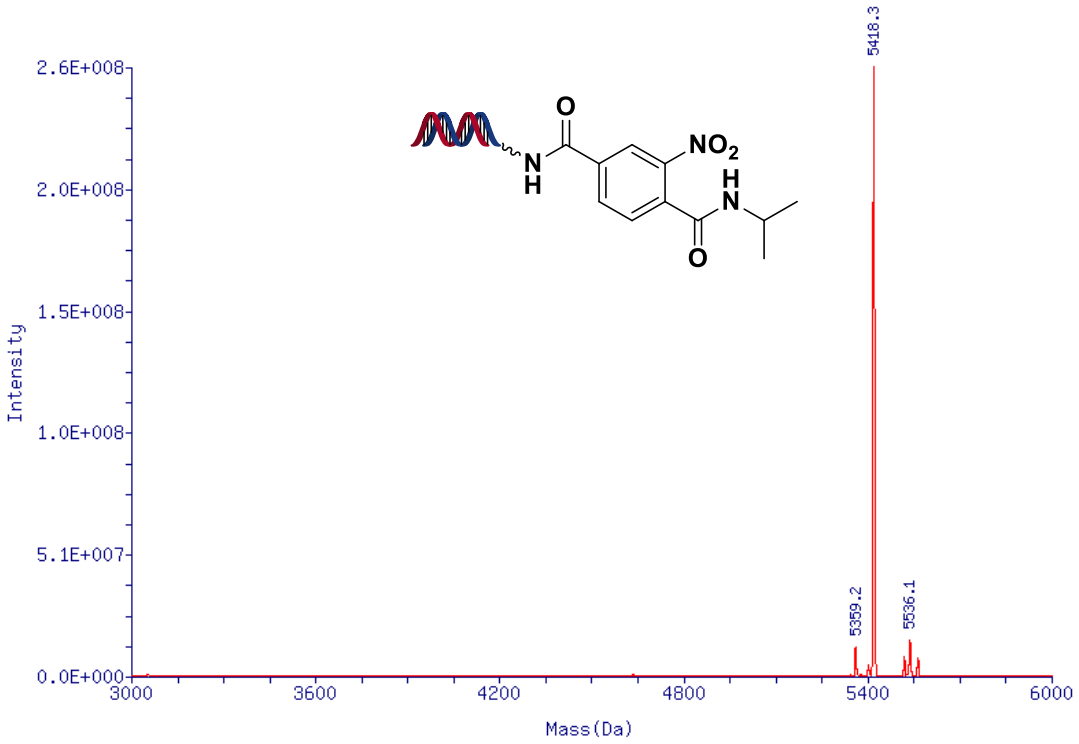


Figure S17. Deconvoluted mass spectrum of conjugate 3k, expected: 5418; observed: 5418.3.

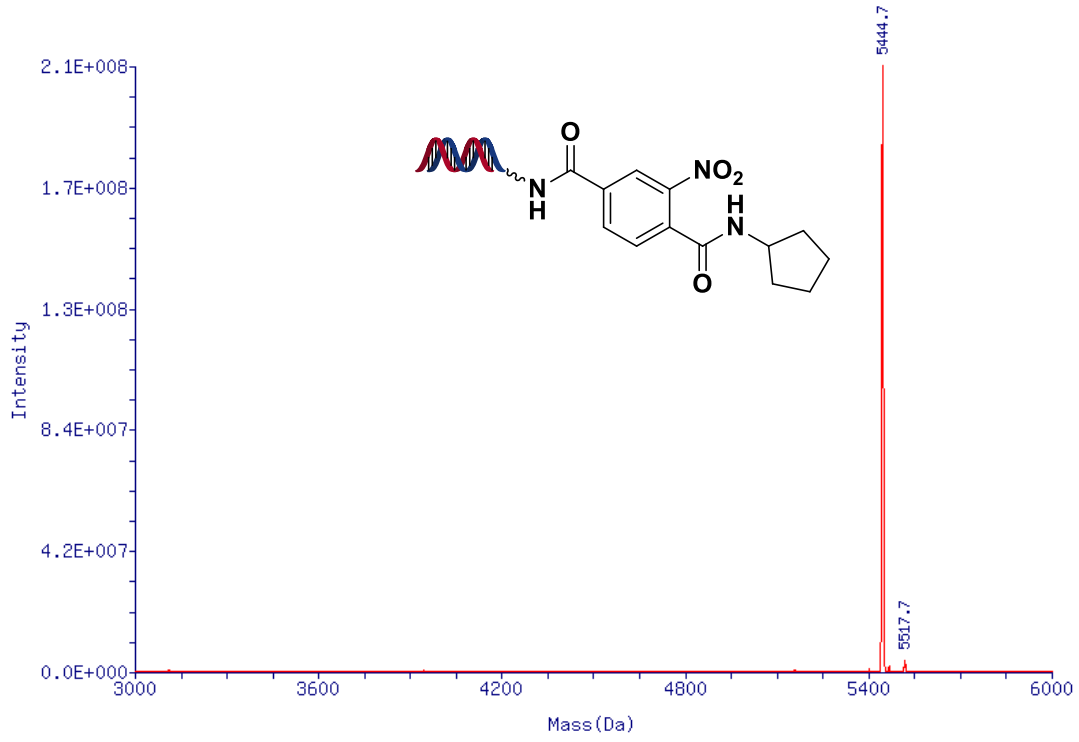


Figure S18. Deconvoluted mass spectrum of conjugate 3l, expected: 5444; observed: 5444.7.

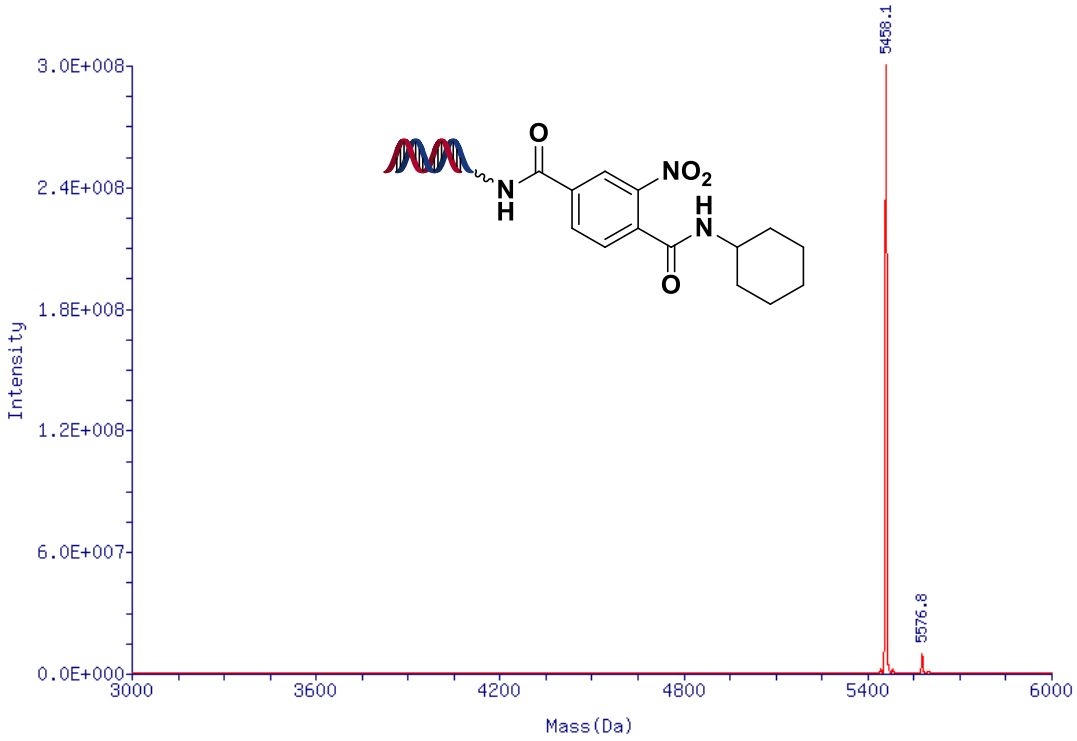


Figure S19. Deconvoluted mass spectrum of conjugate 3m, expected: 5458; observed: 5458.1.

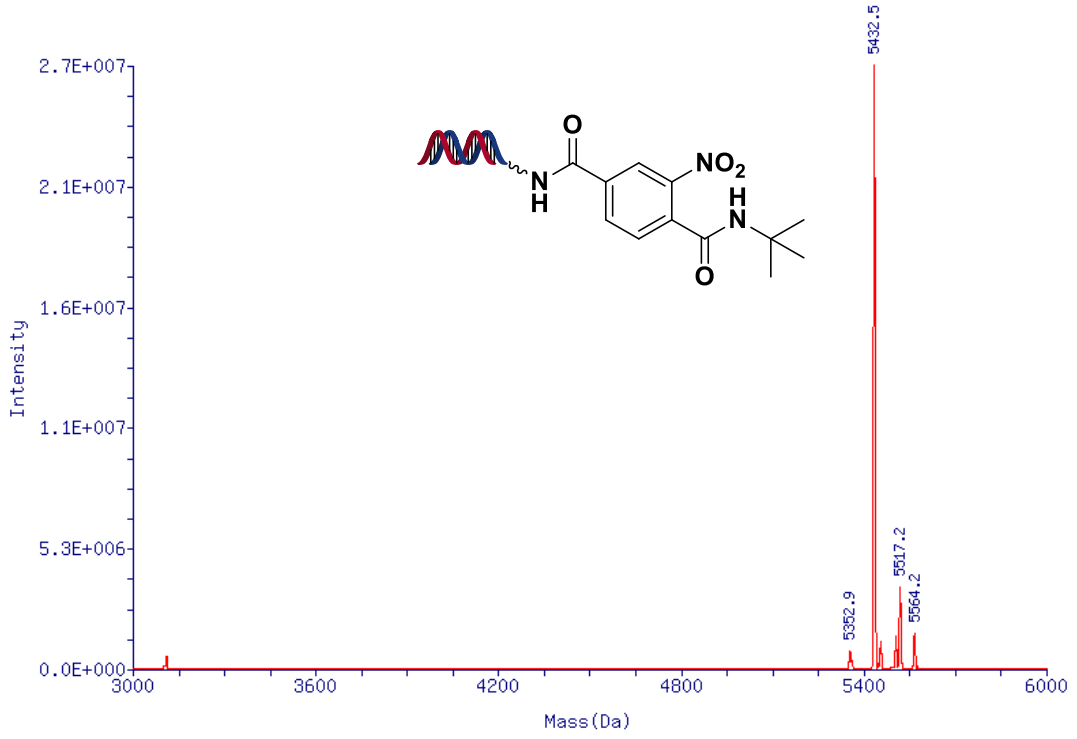


Figure S20. Deconvoluted mass spectrum of conjugate 3n, expected: 5432; observed: 5432.5.

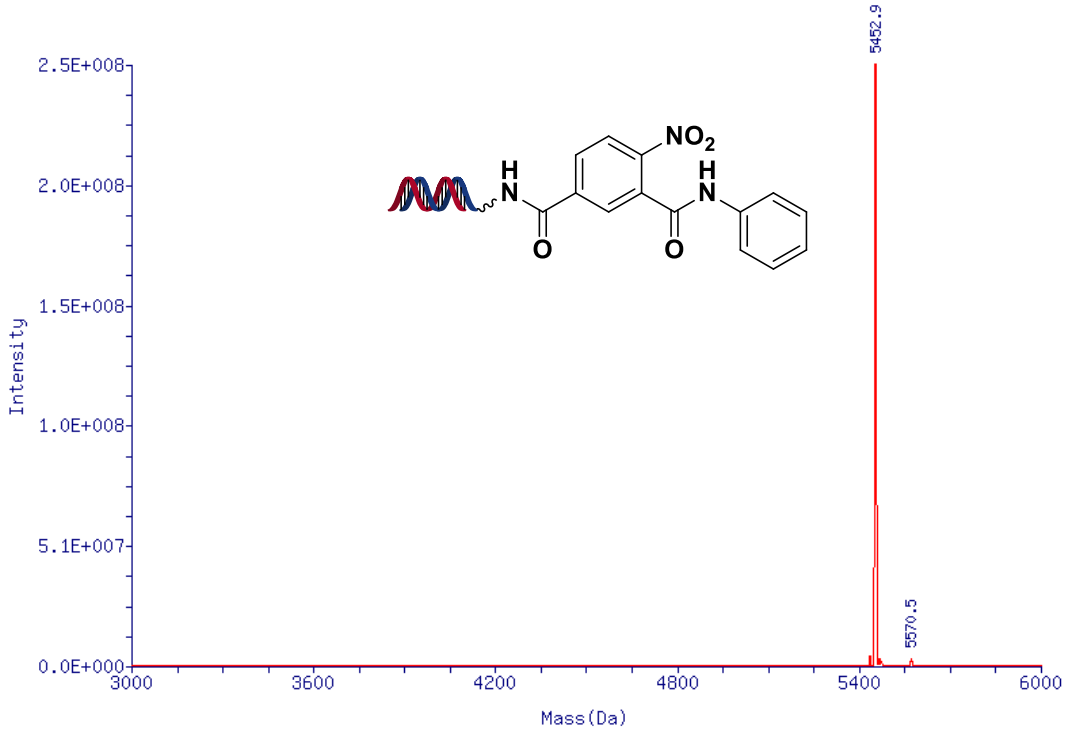


Figure S21. Deconvoluted mass spectrum of conjugate 3aa, expected: 5452; observed: 5452.9.

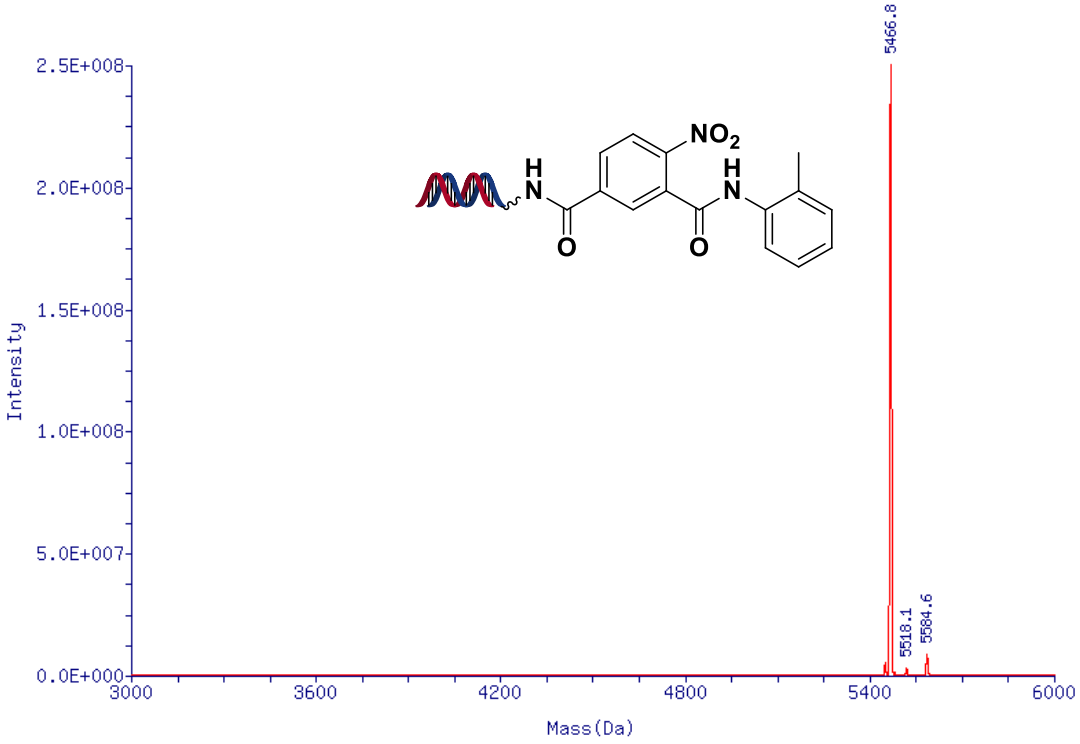


Figure S22. Deconvoluted mass spectrum of conjugate 3bb, expected: 5466; observed: 5466.8.

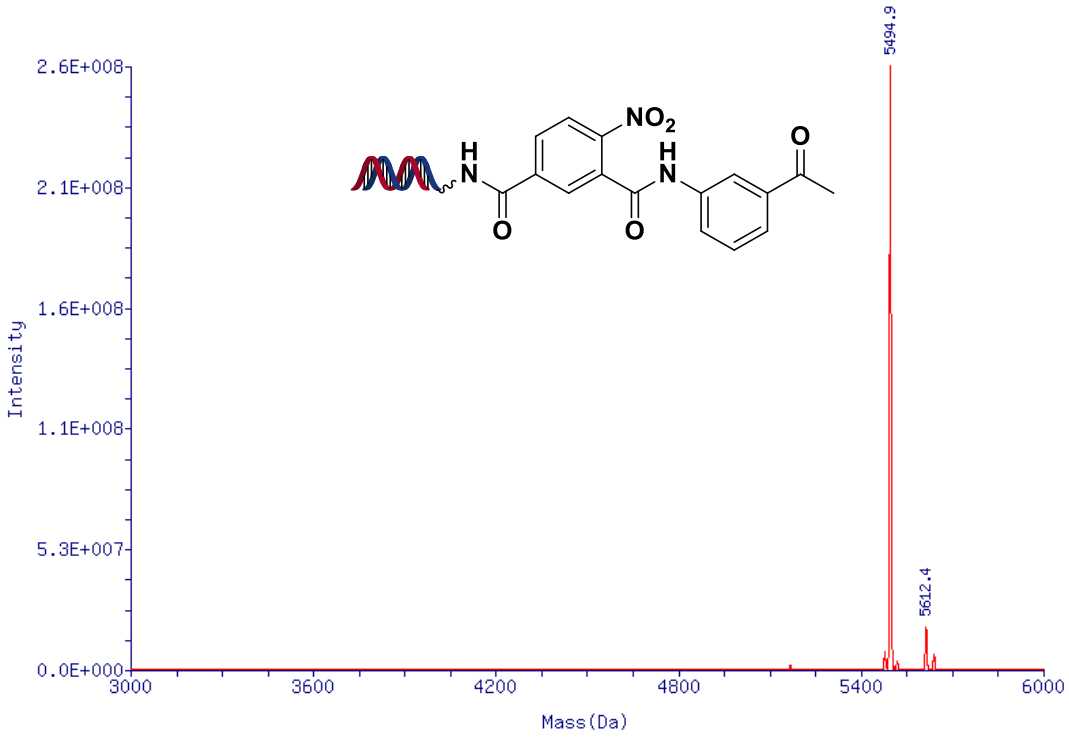


Figure S23. Deconvoluted mass spectrum of conjugate 3cc, expected: 5494; observed: 5494.9.

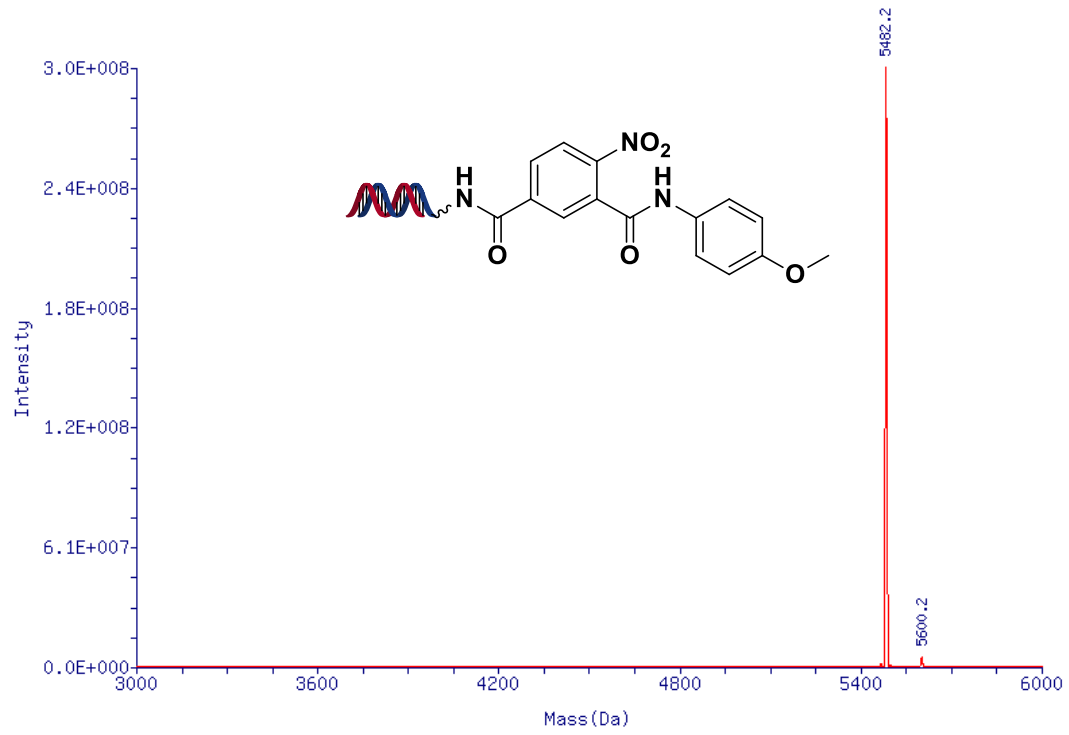


Figure S24. Deconvoluted mass spectrum of conjugate 3dd, expected: 5482; observed: 5482.2.

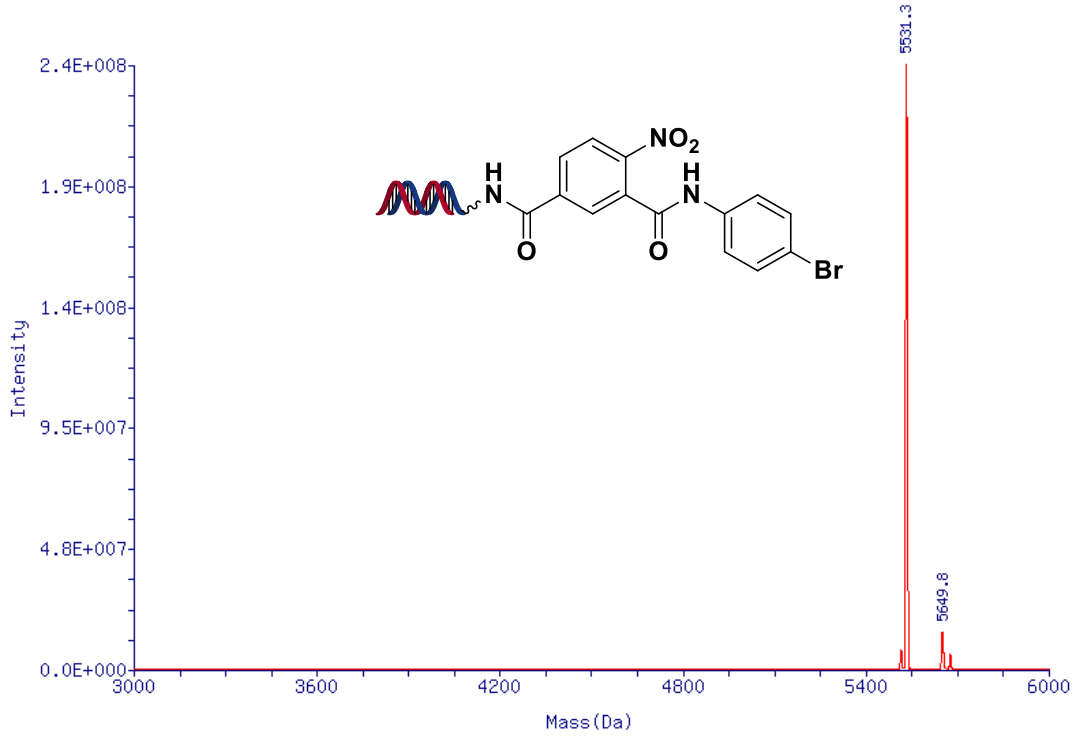


Figure S25. Deconvoluted mass spectrum of conjugate 3ee, expected: 5531; observed: 5531.3.

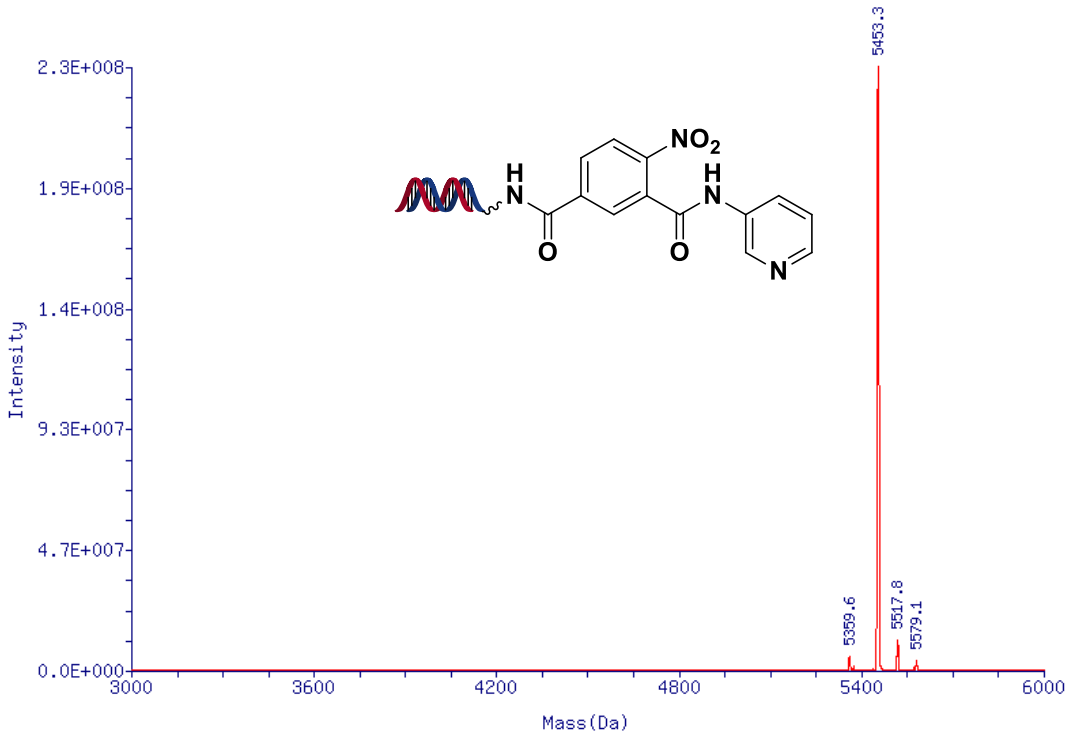


Figure S26. Deconvoluted mass spectrum of conjugate 3ff, expected: 5453; observed: 5453.3.

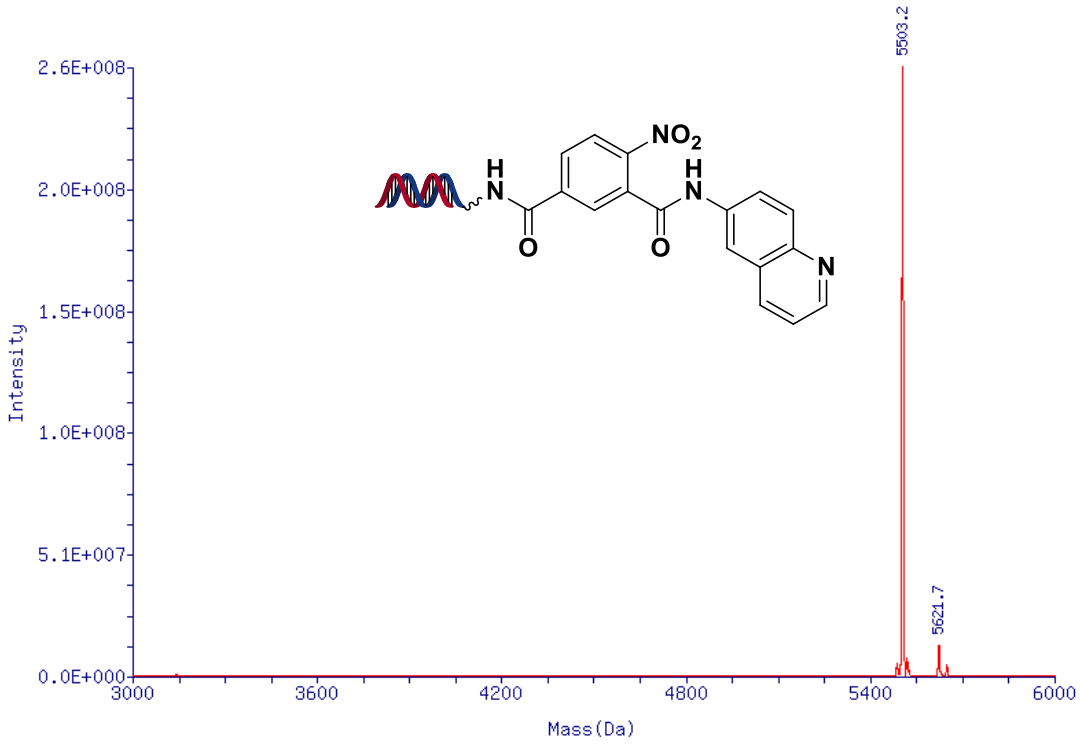


Figure S27. Deconvoluted mass spectrum of conjugate 3gg, expected: 5503; observed: 5503.2.

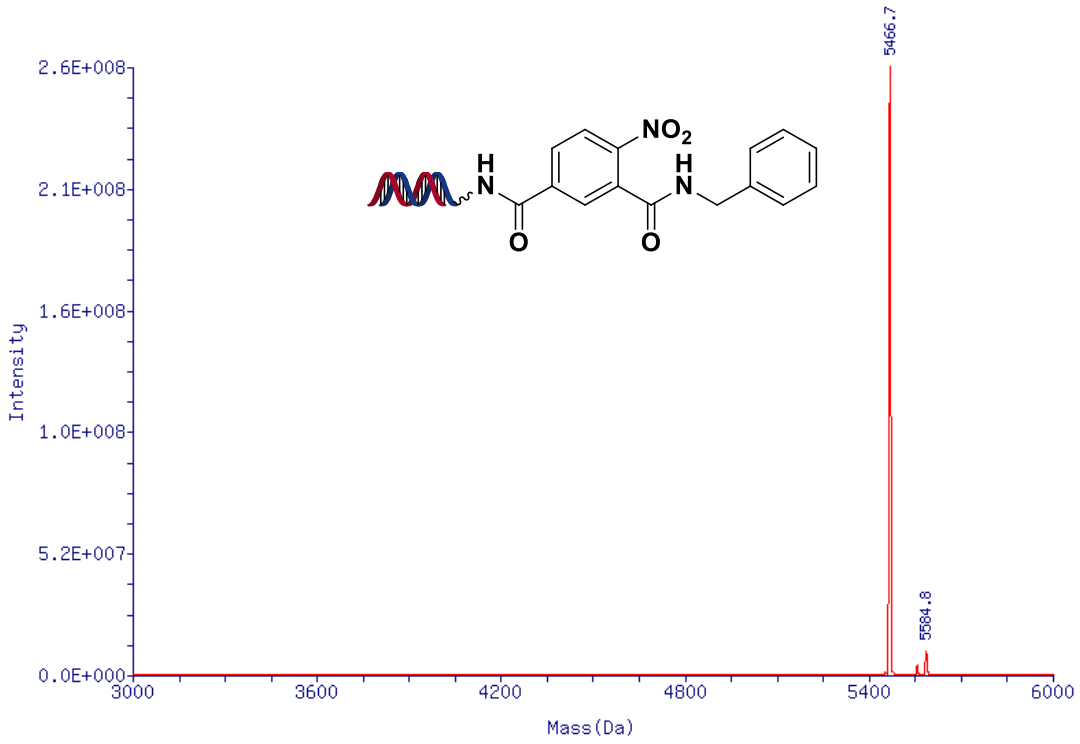


Figure S28. Deconvoluted mass spectrum of conjugate 3hh, expected: 5466; observed: 5466.7.

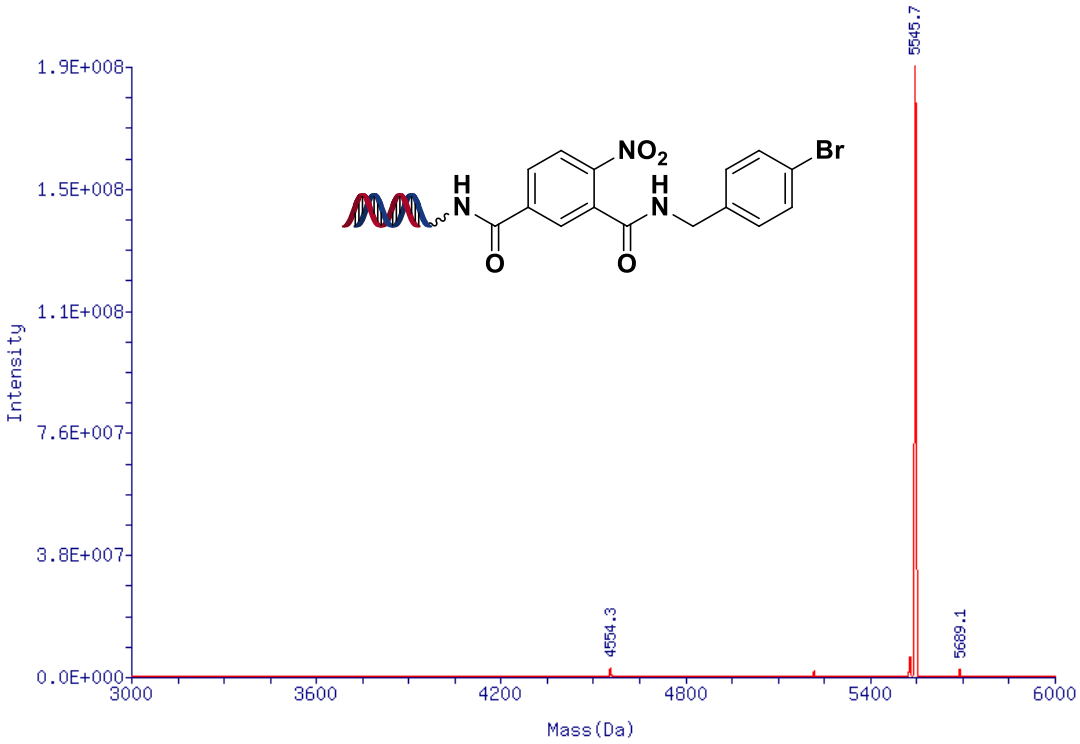


Figure S29. Deconvoluted mass spectrum of conjugate 3ii, expected: 5545; observed: 5545.7.

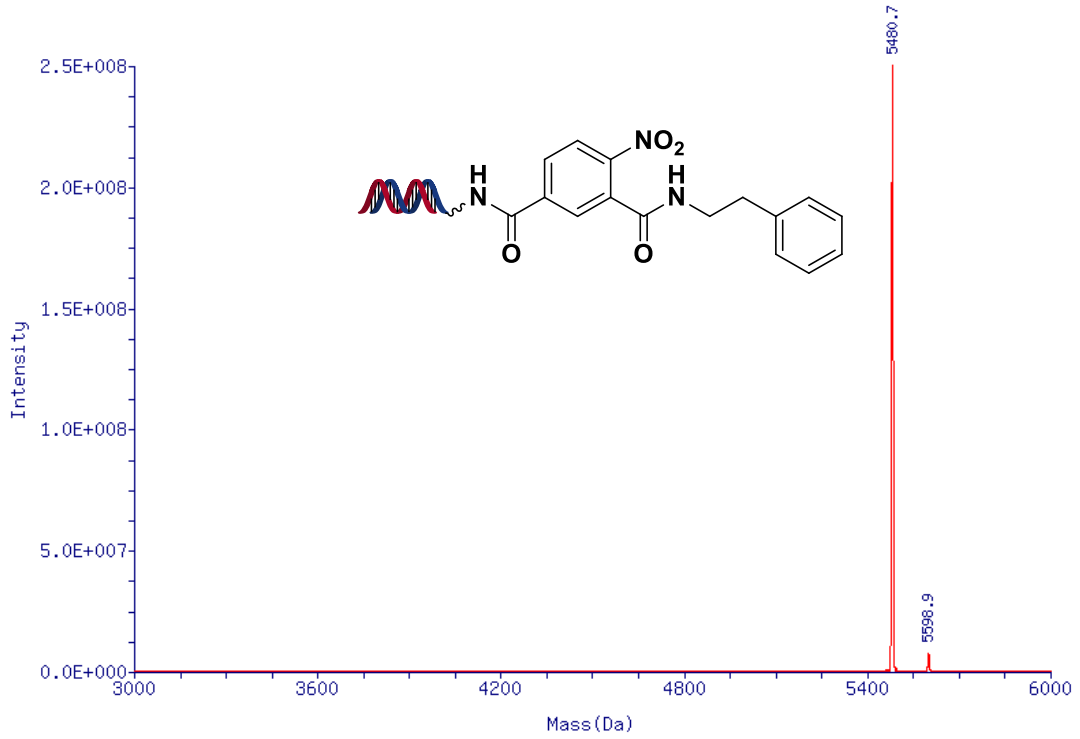


Figure S30. Deconvoluted mass spectrum of conjugate 3jj, expected: 5480; observed: 5480.7.

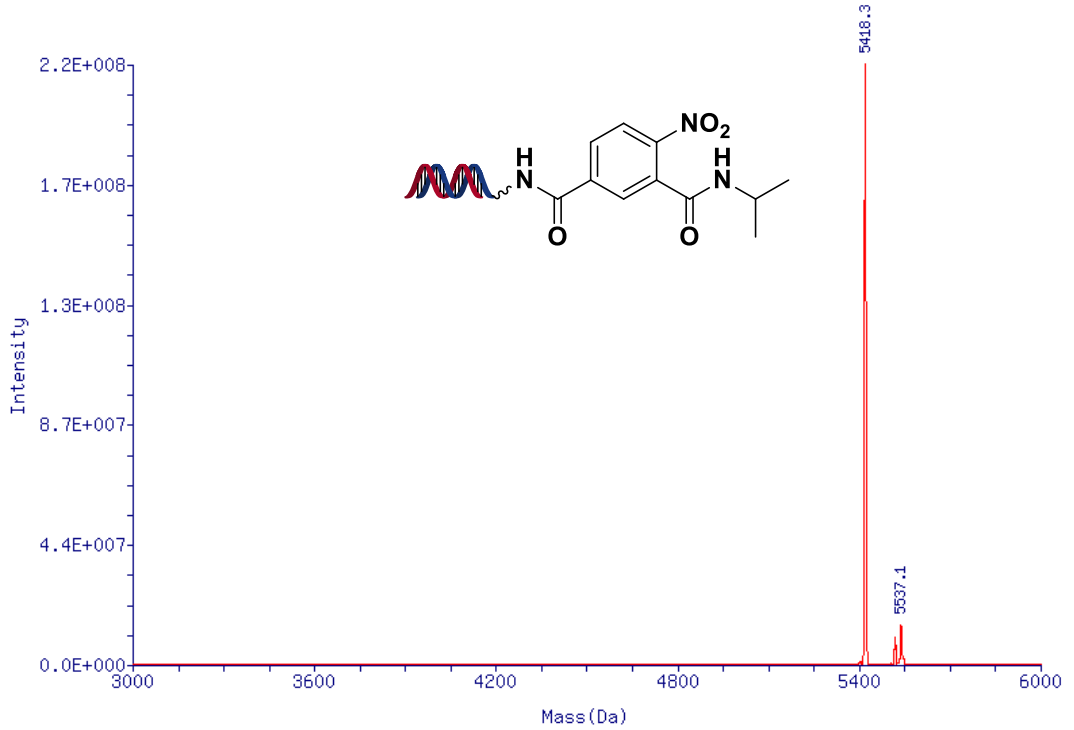


Figure S31. Deconvoluted mass spectrum of conjugate 3kk, expected: 5418; observed: 5418.3.

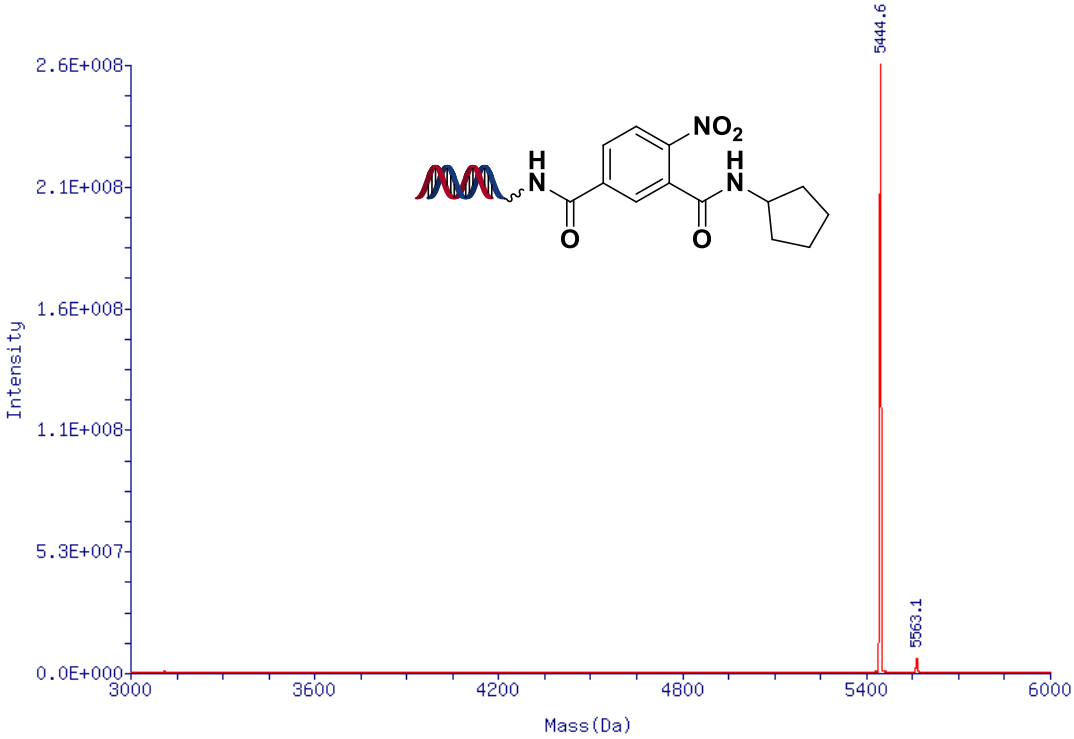


Figure S32. Deconvoluted mass spectrum of conjugate 3ll, expected: 5444; observed: 5444.6.

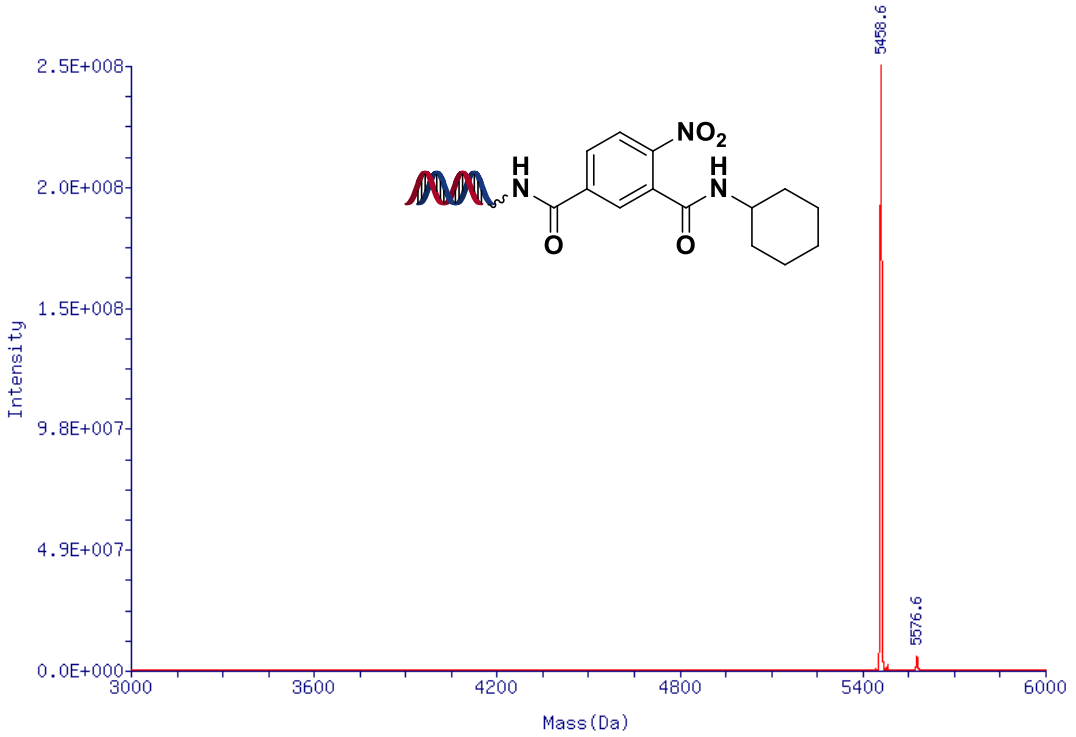


Figure S33. Deconvoluted mass spectrum of conjugate 3mm, expected: 5458; observed: 5458.6.

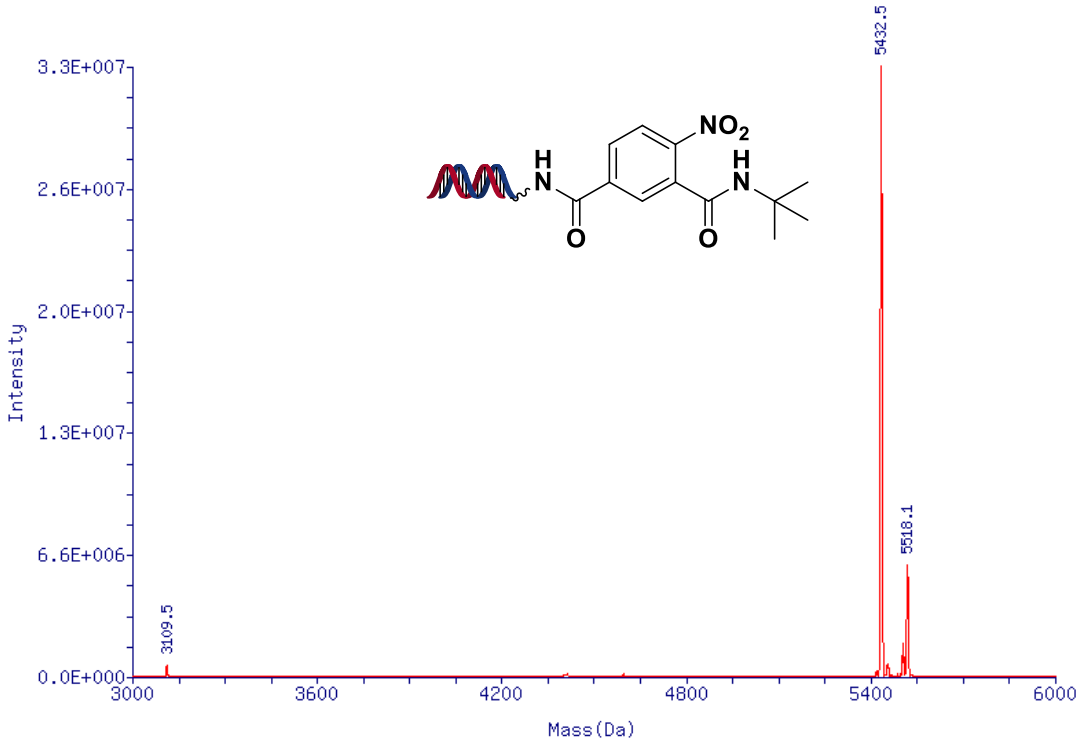


Figure S34. Deconvoluted mass spectrum of conjugate 3nn, expected: 5432; observed: 5432.5.

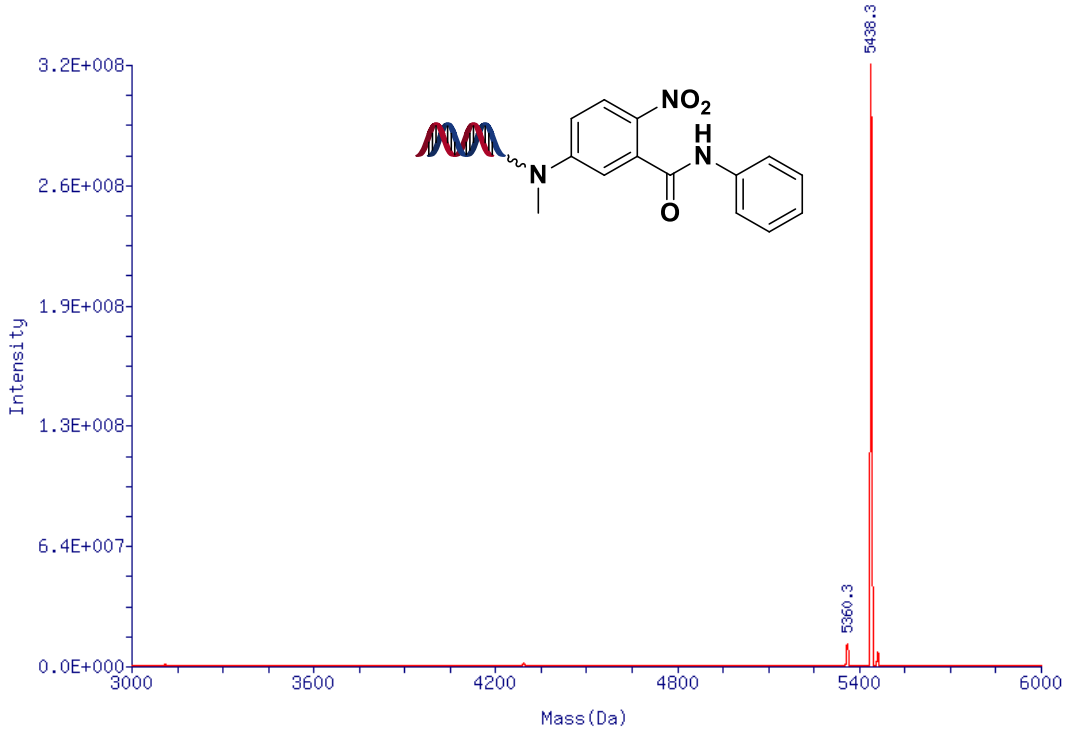


Figure S35. Deconvoluted mass spectrum of conjugate 3oo, expected: 5438.5; observed: 5438.3.

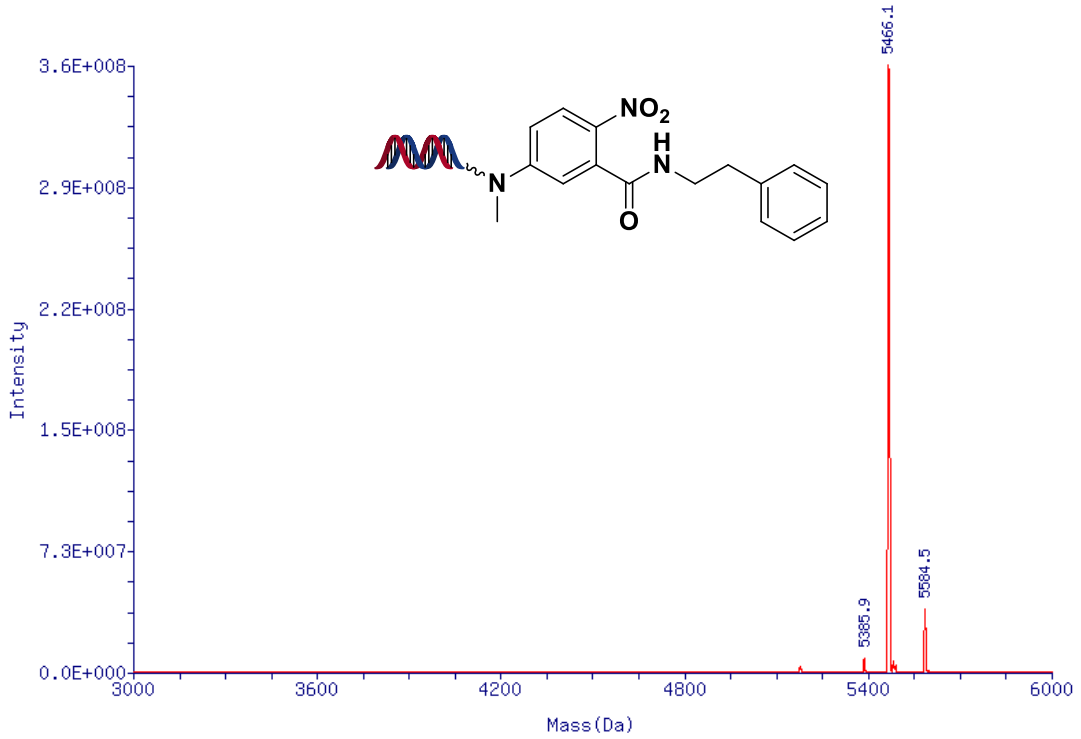


Figure S36. Deconvoluted mass spectrum of conjugate 3pp, expected: 5466.5; observed: 5466.1.

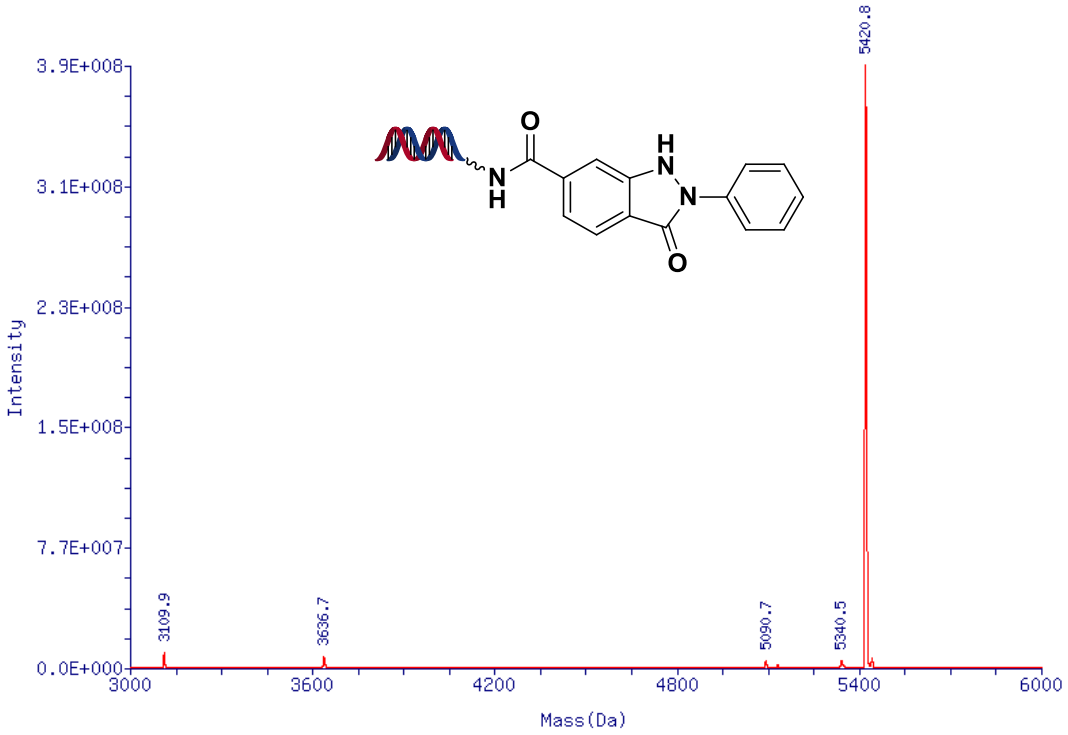


Figure S37. Deconvoluted mass spectrum of conjugate 4a, expected: 5420; observed: 5420.8.

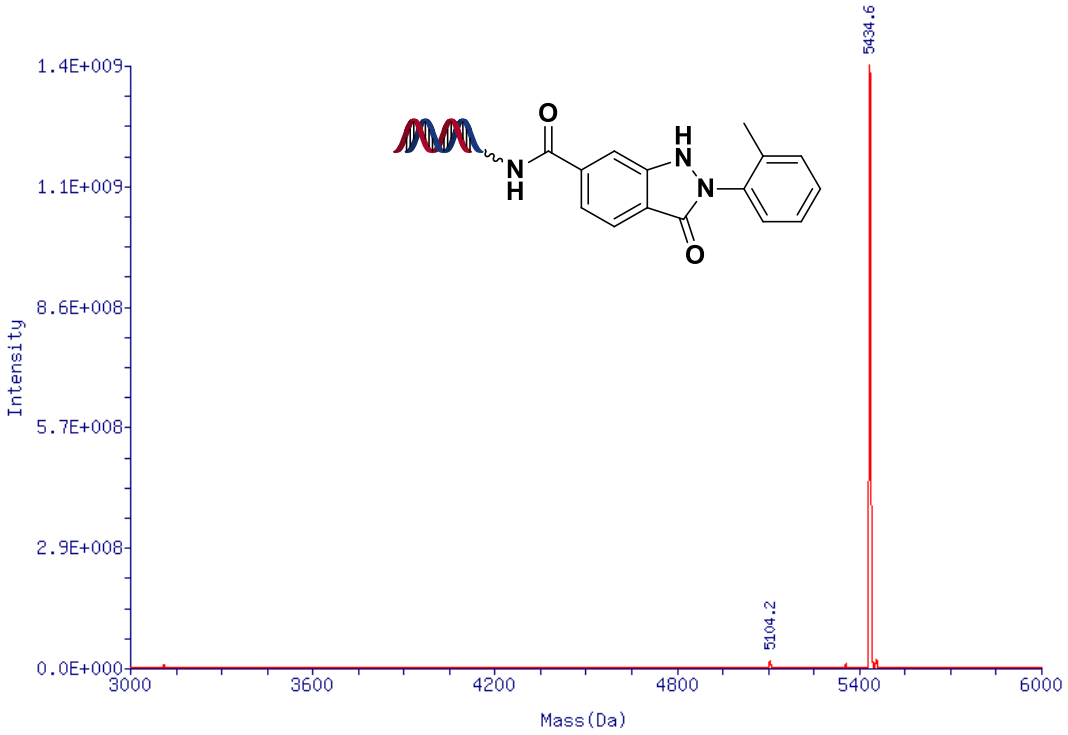


Figure S38. Deconvoluted mass spectrum of conjugate 4b, expected: 5434; observed: 5434.6.

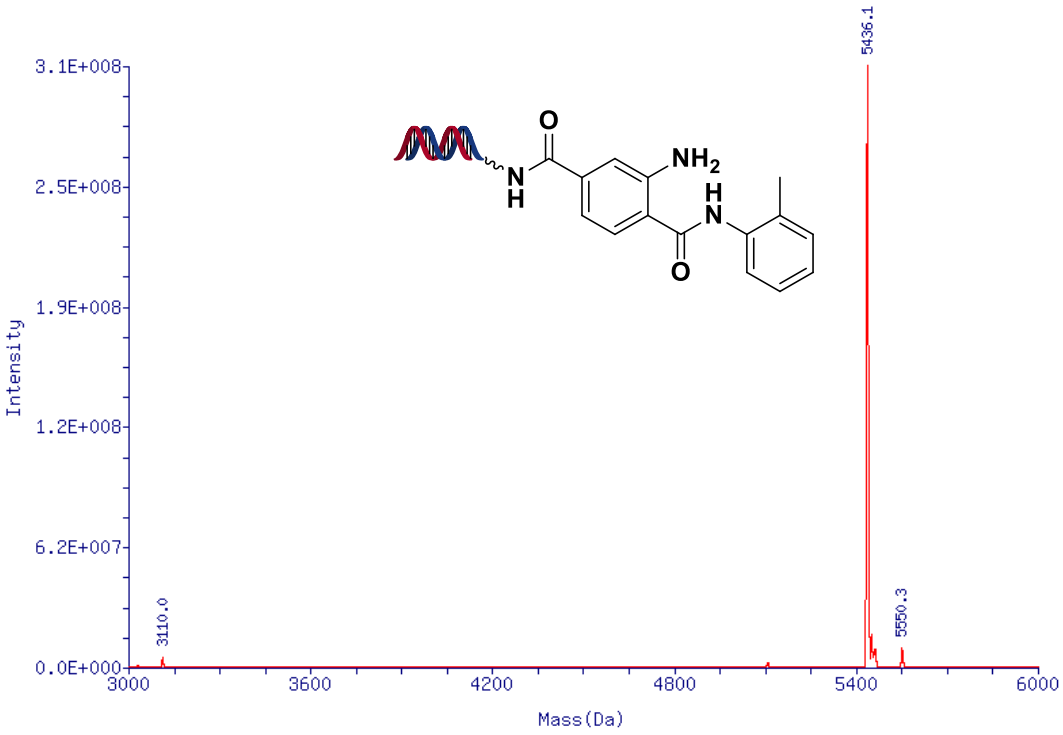


Figure S39. Deconvoluted mass spectrum of conjugate 5b, expected: 5436; observed: 5436.1.

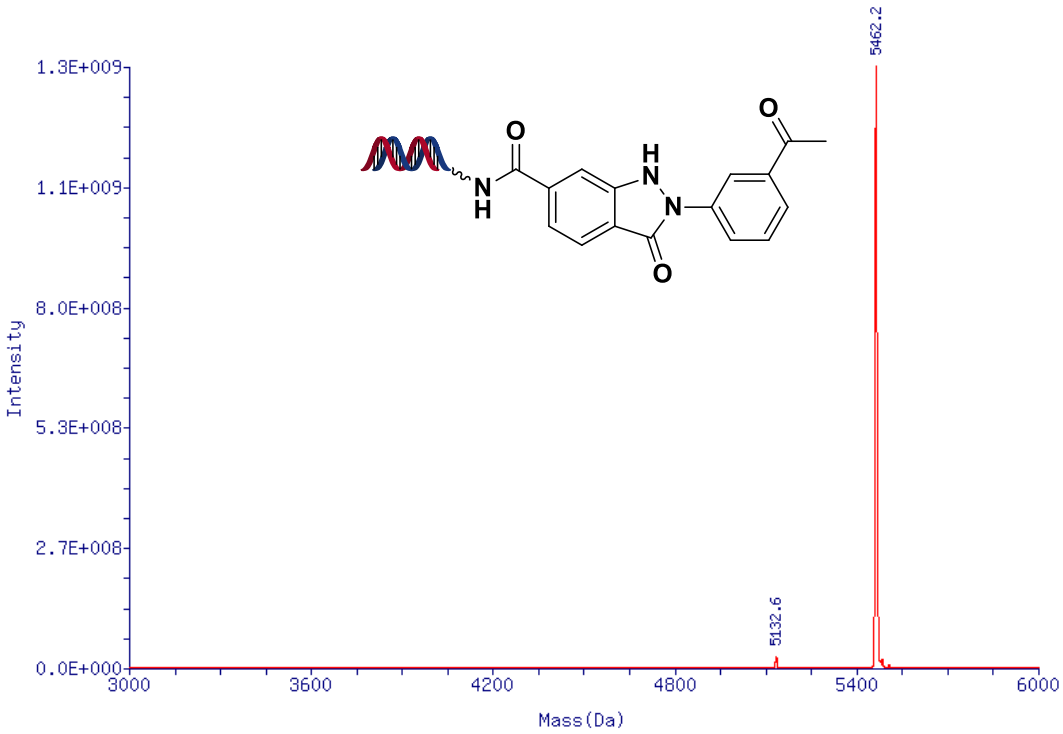


Figure S40. Deconvoluted mass spectrum of conjugate 4c, expected: 5462; observed: 5462.2.

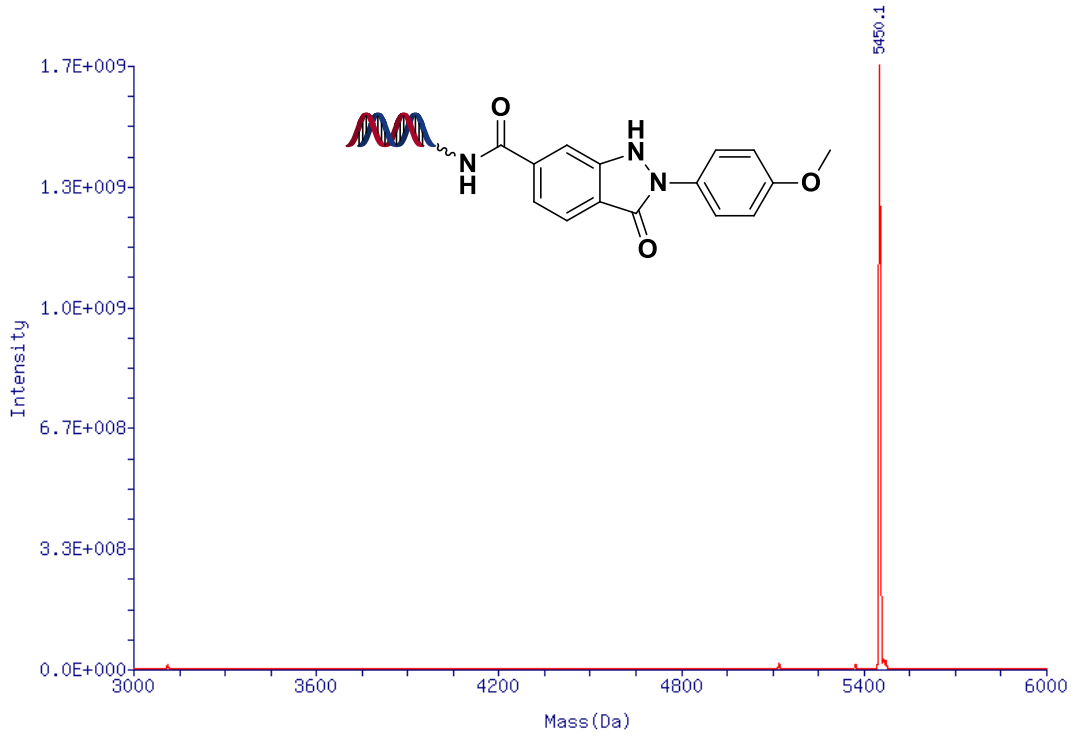


Figure S42. Deconvoluted mass spectrum of conjugate 4d, expected: 5450; observed: 5450.1.

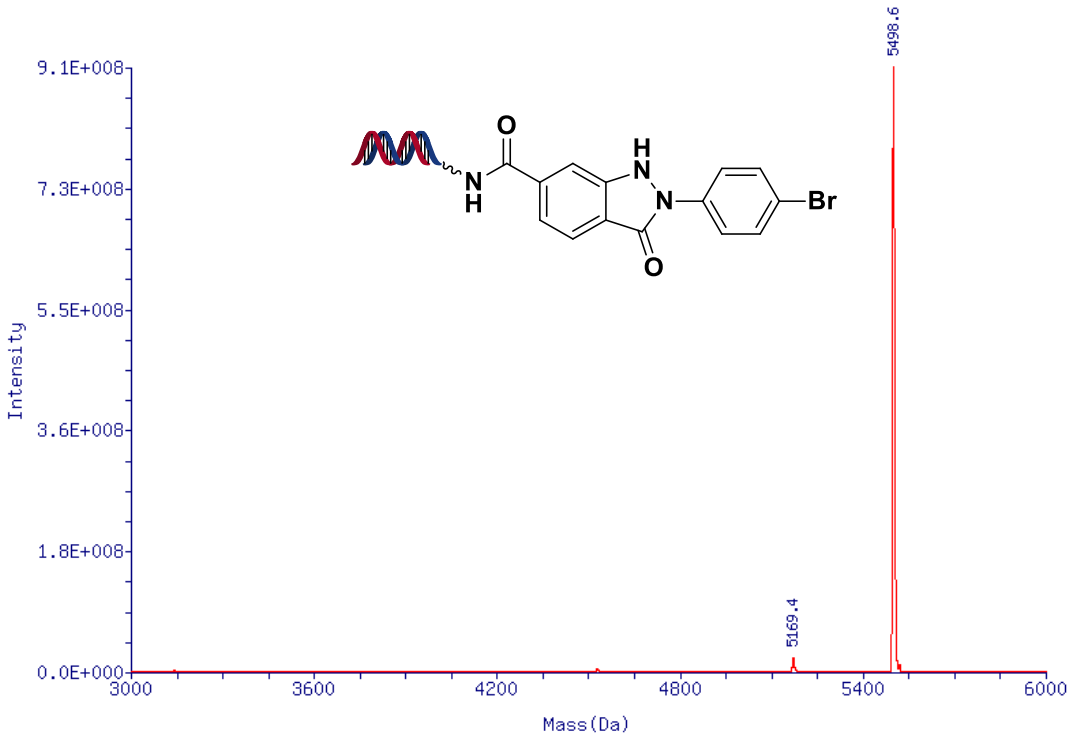


Figure S43. Deconvoluted mass spectrum of conjugate 4e, expected: 5499; observed: 5498.6.

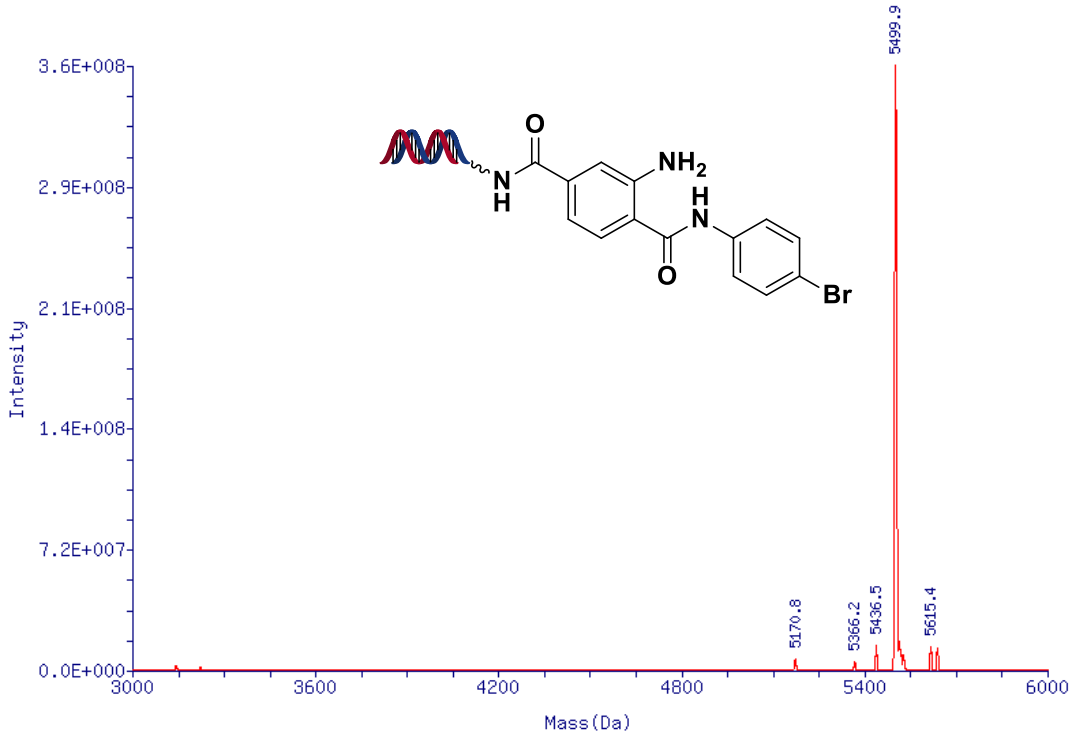


Figure S44. Deconvoluted mass spectrum of conjugate 5e, expected: 5501; observed: 5499.9

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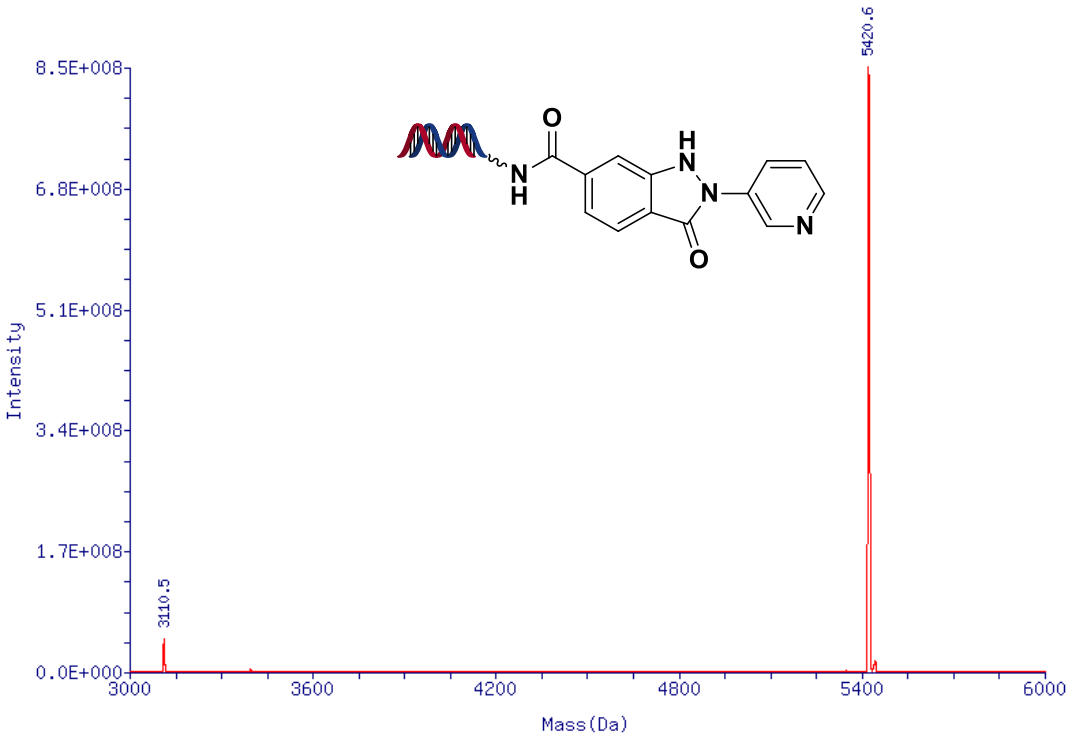

Figure S45. Deconvoluted mass spectrum of conjugate 4f, expected: 5421; observed: 5420.6.

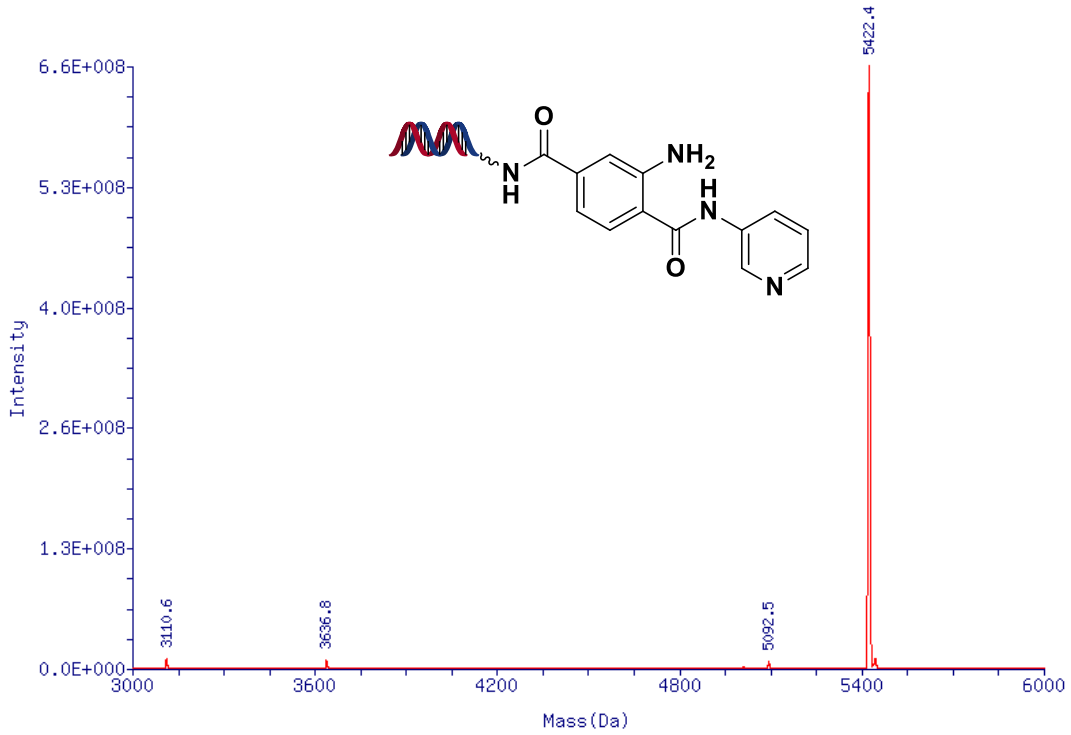

Figure S46. Deconvoluted mass spectrum of conjugate 5f, expected: 5423; observed: 5422.4.

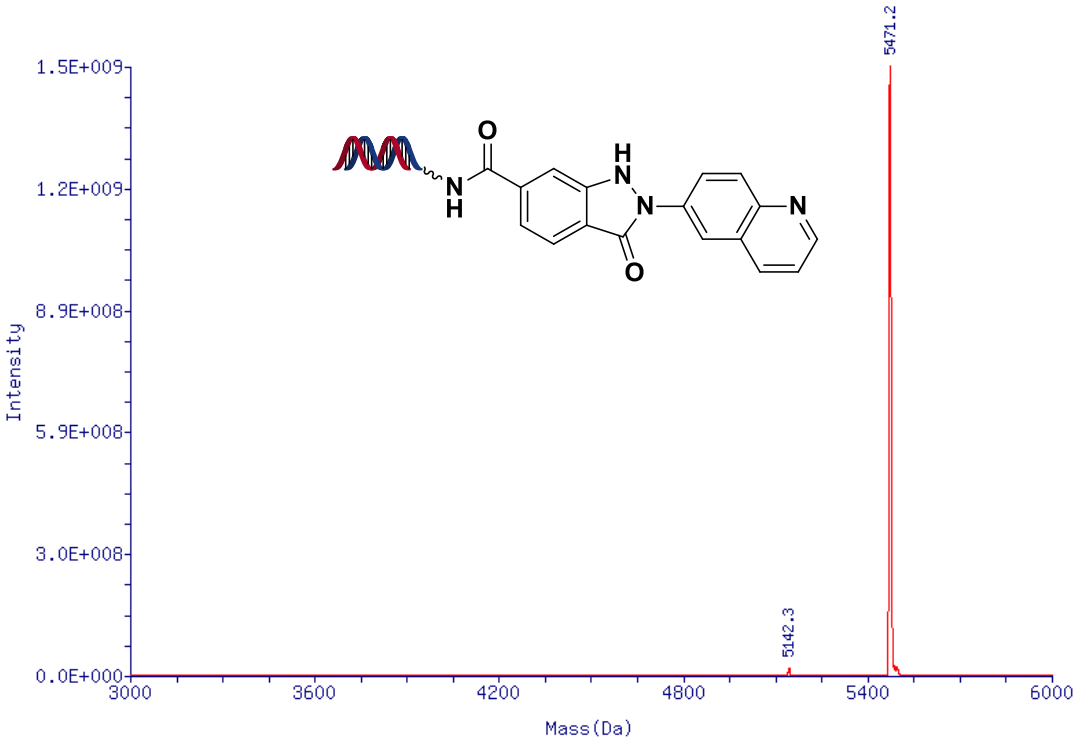

Figure S47. Deconvoluted mass spectrum of conjugate 4g, expected: 5471; observed: 5471.2.

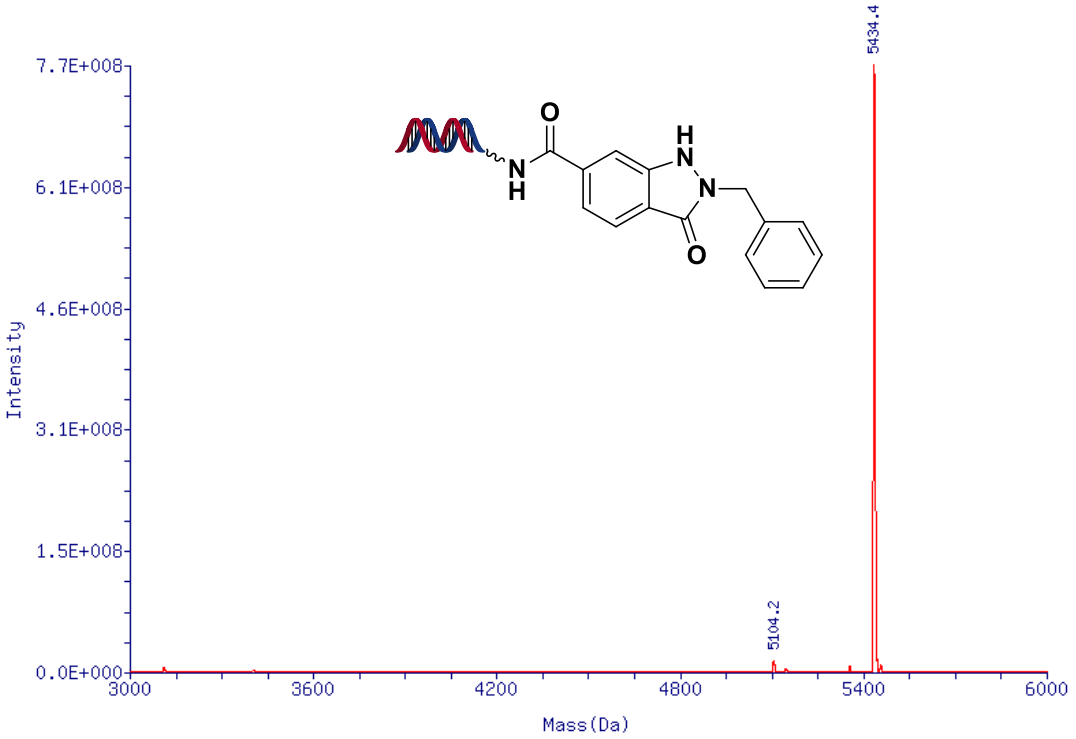

Figure S48. Deconvoluted mass spectrum of conjugate 4h, expected: 5434; observed: 5434.4.

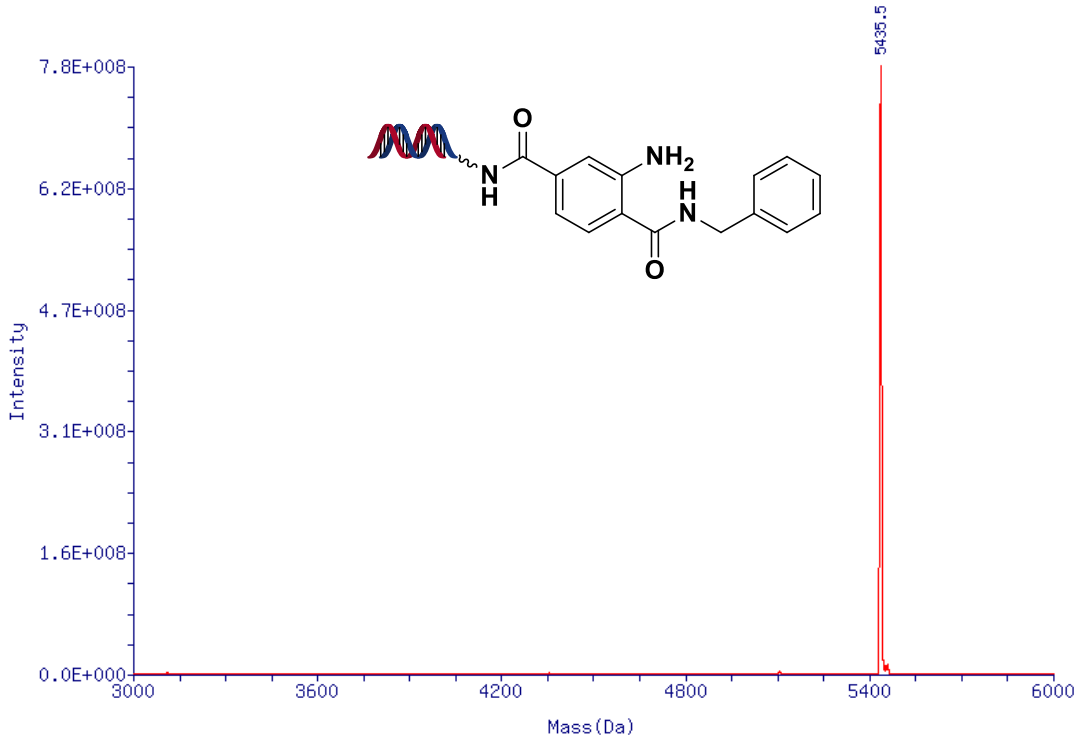

Figure S49. Deconvoluted mass spectrum of conjugate 5h, expected: 5436; observed: 5435.5.

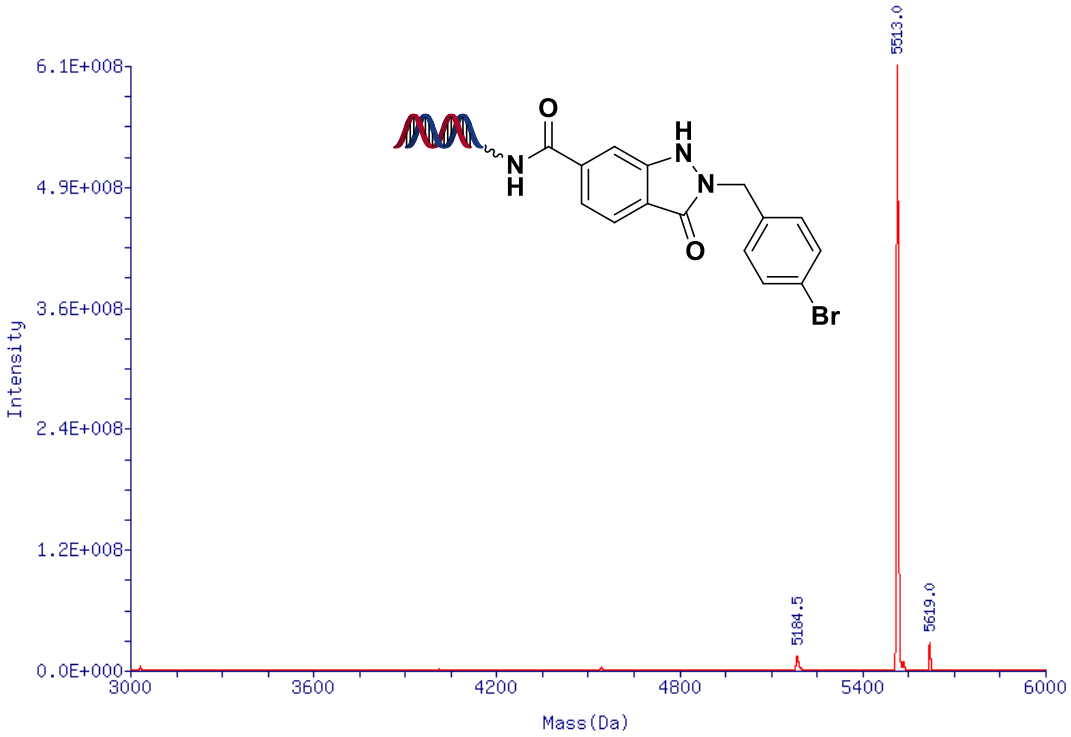

Figure S50. Deconvoluted mass spectrum of conjugate 4i, expected: 5513; observed: 5513.0.

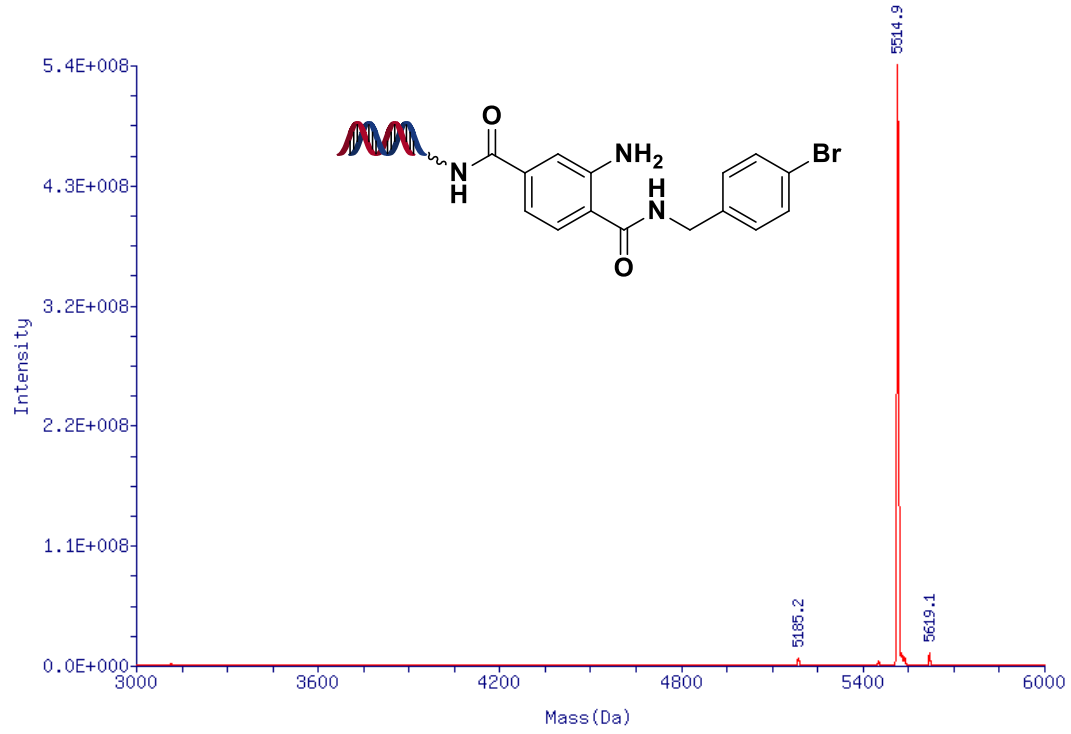

Figure S51. Deconvoluted mass spectrum of conjugate 5i, expected: 5515; observed: 5514.9.

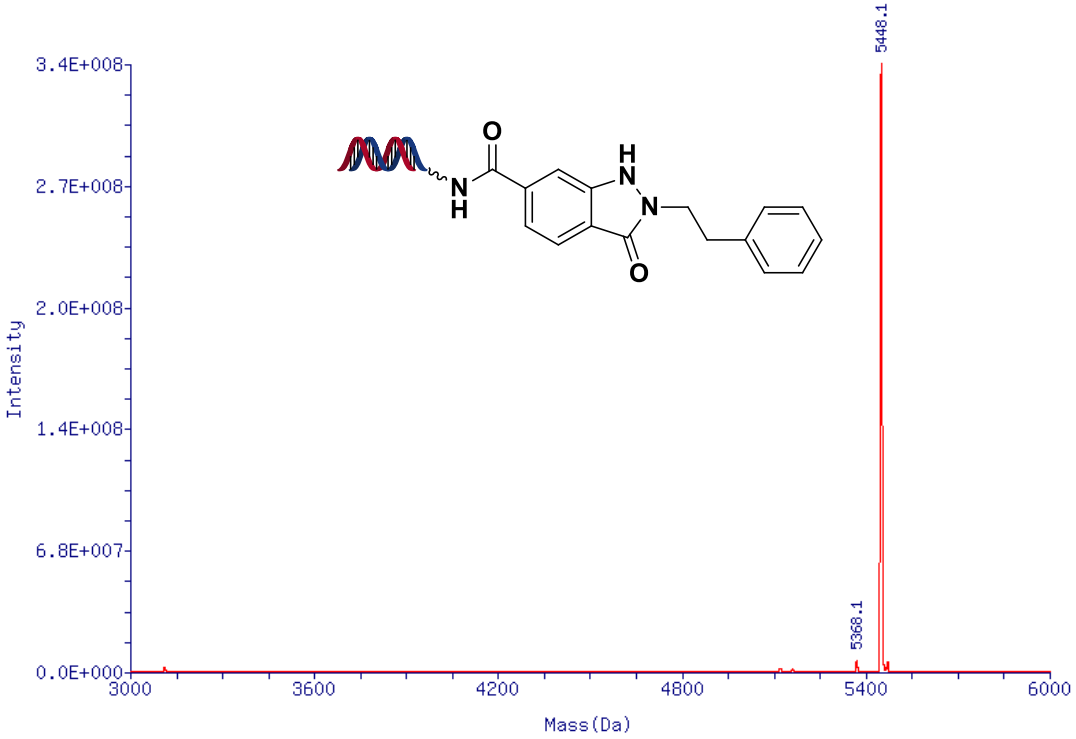

Figure S52. Deconvoluted mass spectrum of conjugate 4j, expected: 5448; observed: 5448.1.

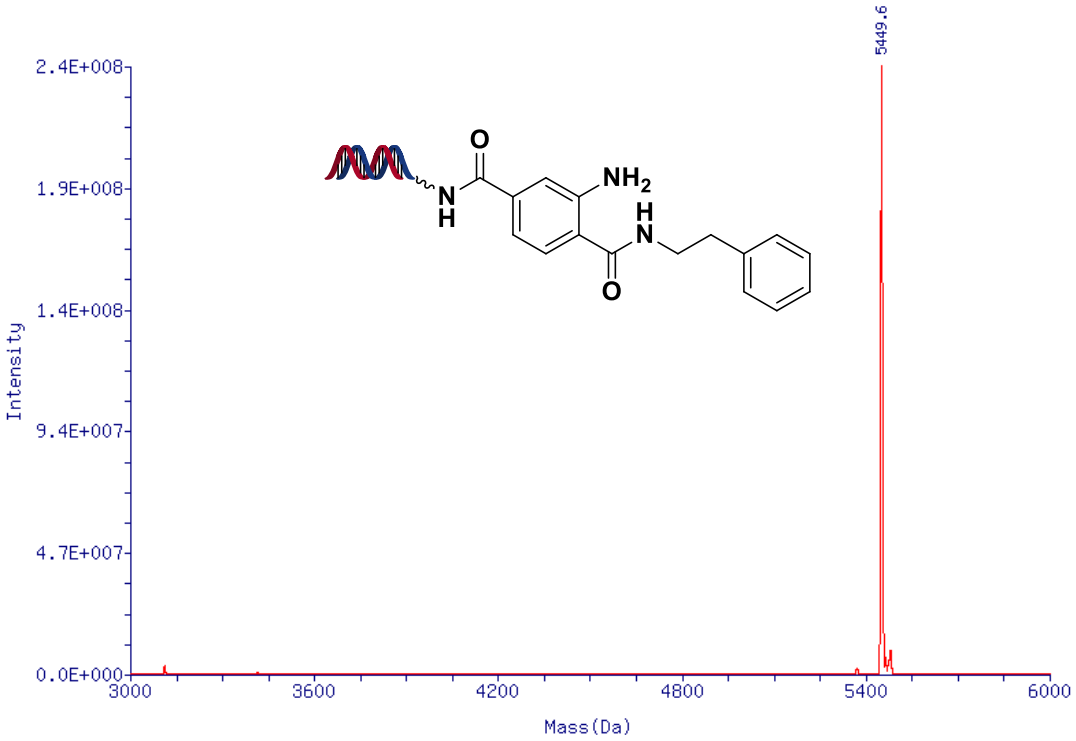

Figure S53. Deconvoluted mass spectrum of conjugate 5j, expected: 5450; observed: 5449.6.

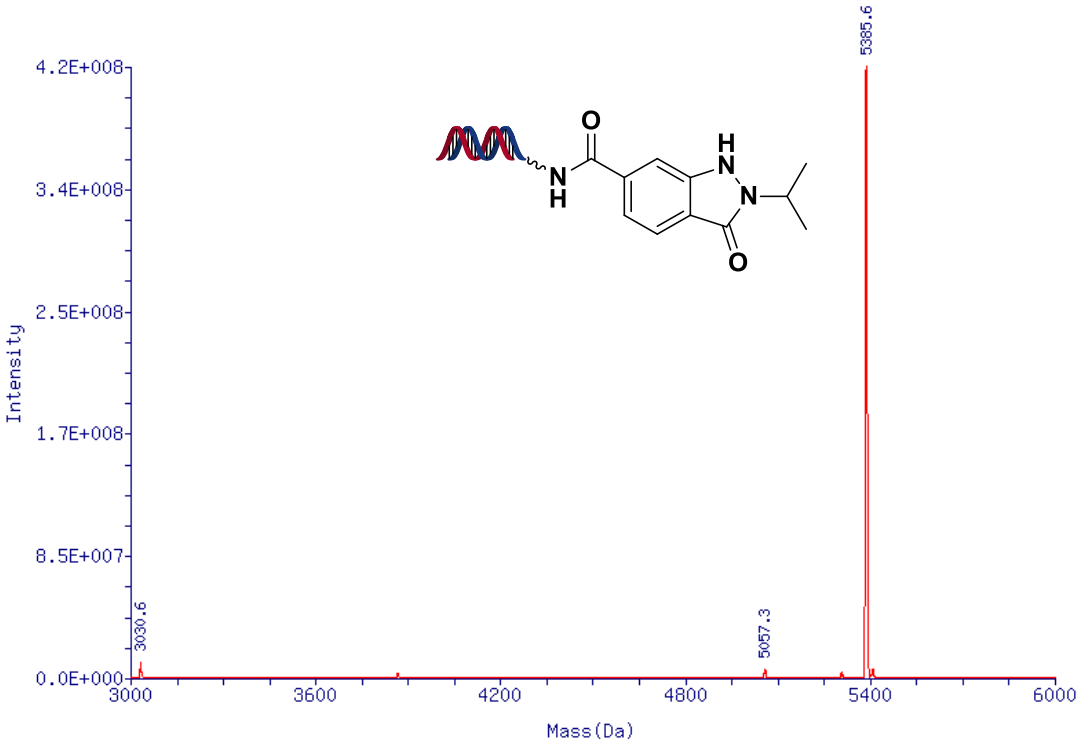

Figure S54. Deconvoluted mass spectrum of conjugate 4k, expected: 5386; observed: 5385.6.

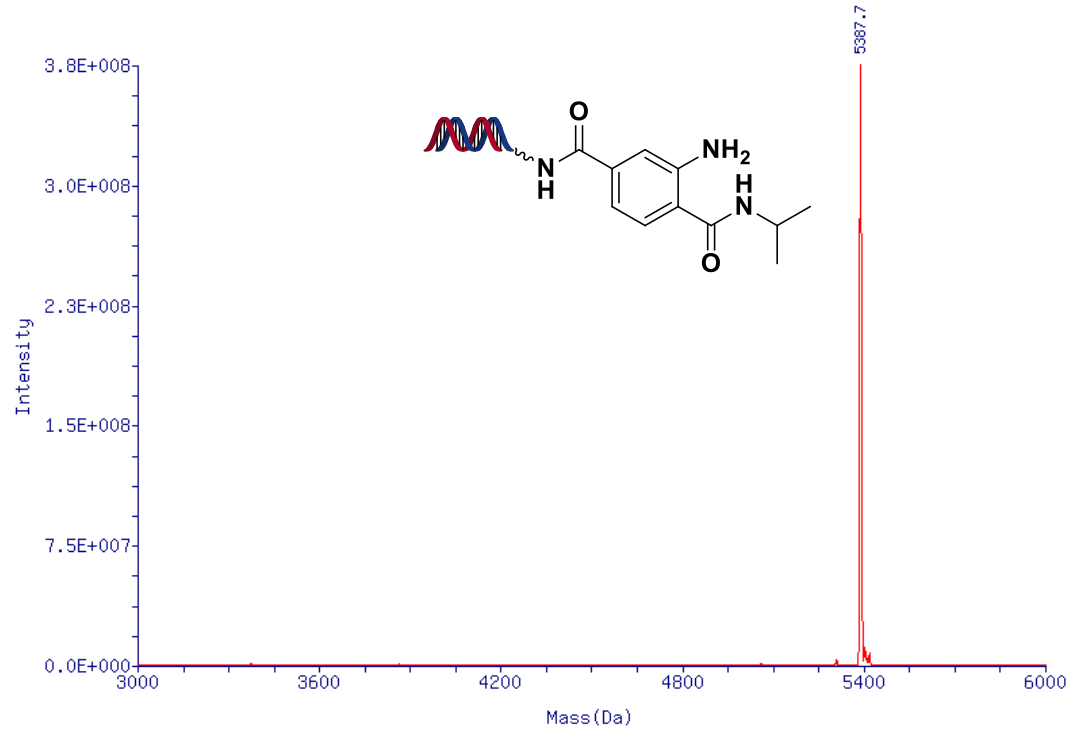

Figure S55. Deconvoluted mass spectrum of conjugate 5k, expected: 5488; observed: 5487.7.

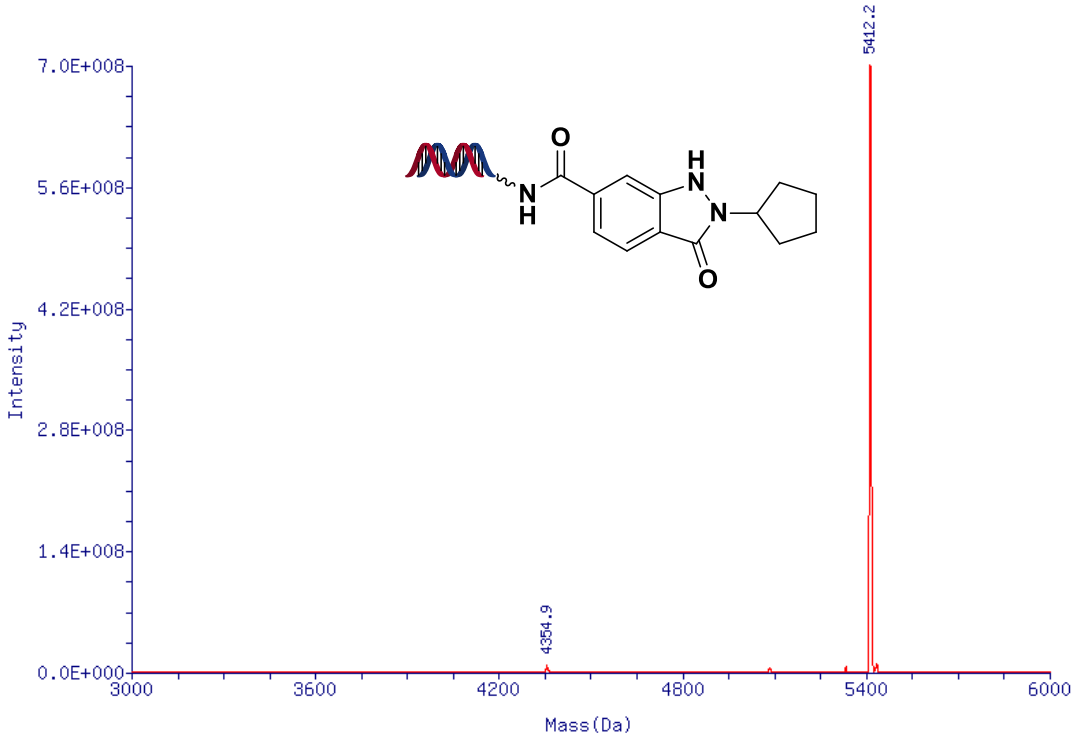

Figure S56. Deconvoluted mass spectrum of conjugate 4l, expected: 5412; observed: 5412.2.

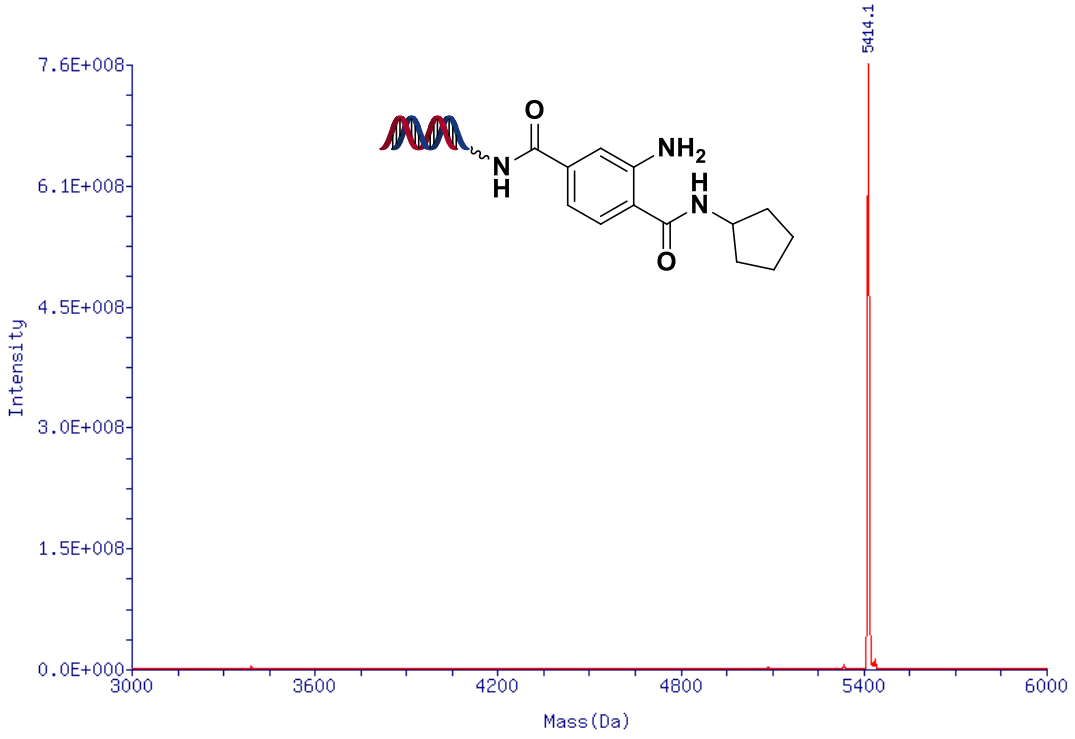

Figure S57. Deconvoluted mass spectrum of conjugate 5l, expected: 5414; observed: 5414.1.

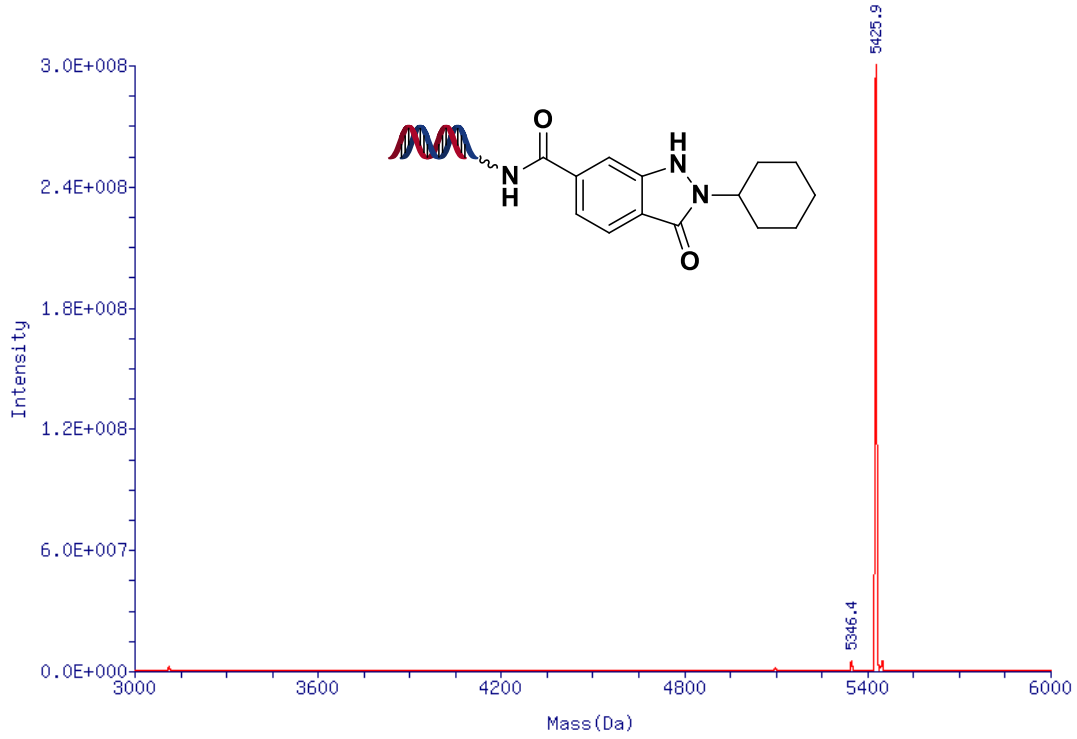

Figure S58. Deconvoluted mass spectrum of conjugate 4m, expected: 5426; observed: 5425.9.

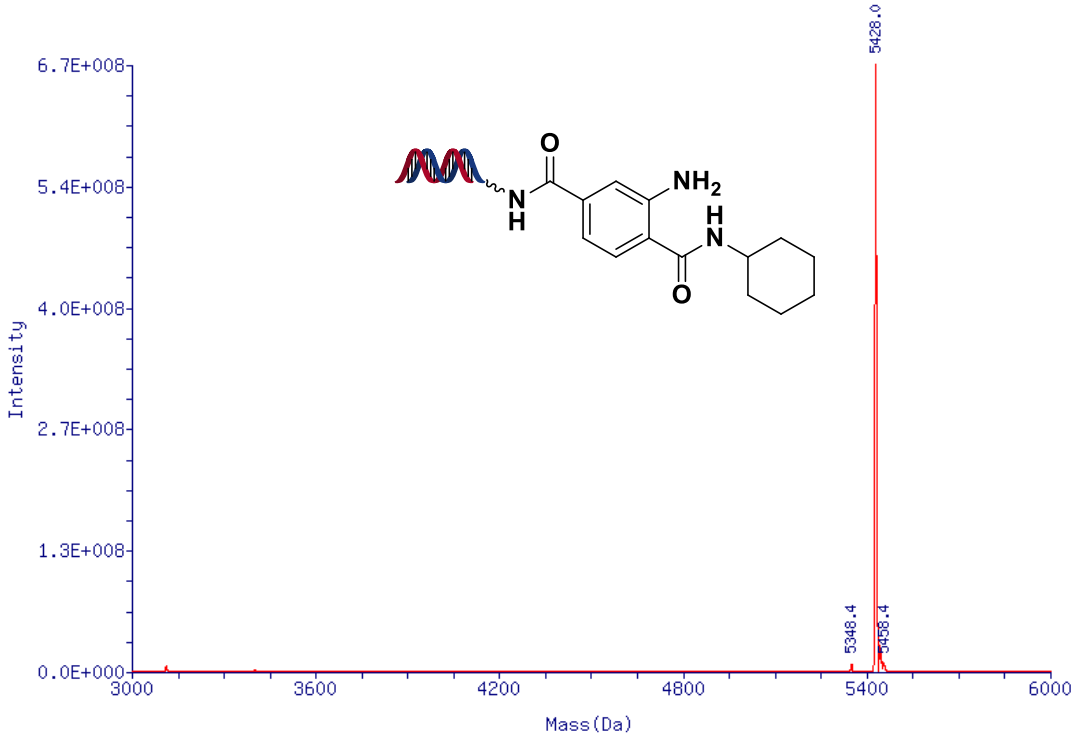

Figure S59. Deconvoluted mass spectrum of conjugate 5m, expected: 5428; observed: 5428.0.

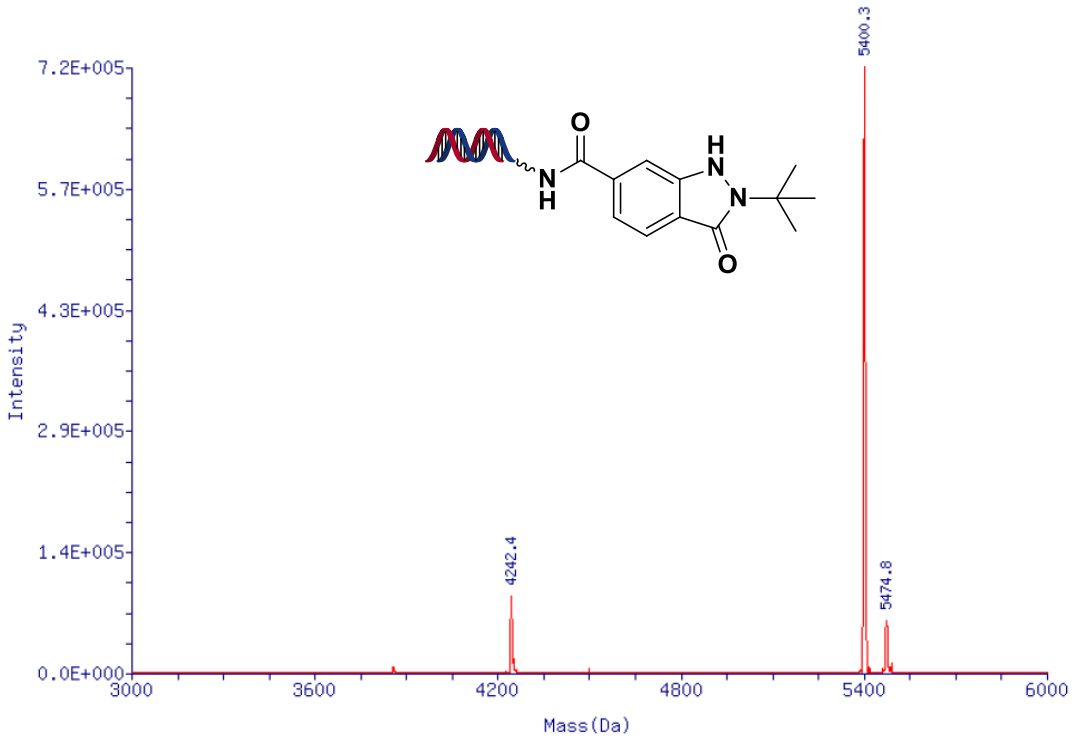

Figure S60. Deconvoluted mass spectrum of conjugate 4n, expected: 5400; observed: 5400.3.

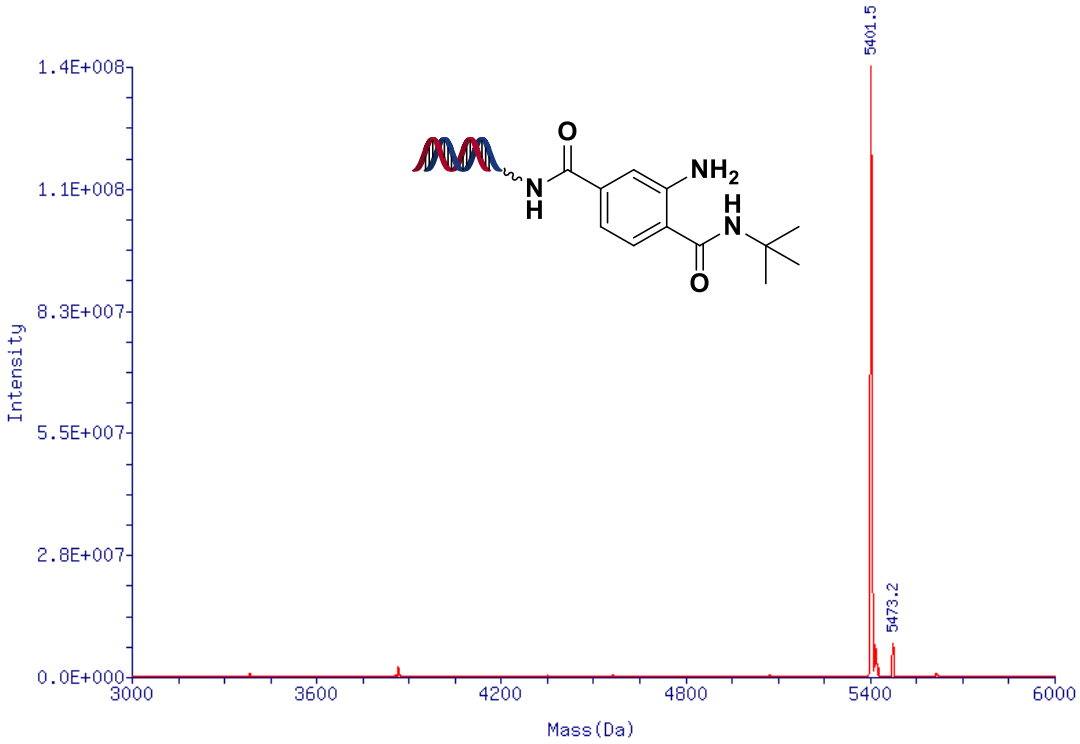

Figure S61. Deconvoluted mass spectrum of conjugate 5n, expected: 5402; observed: 5401.5.

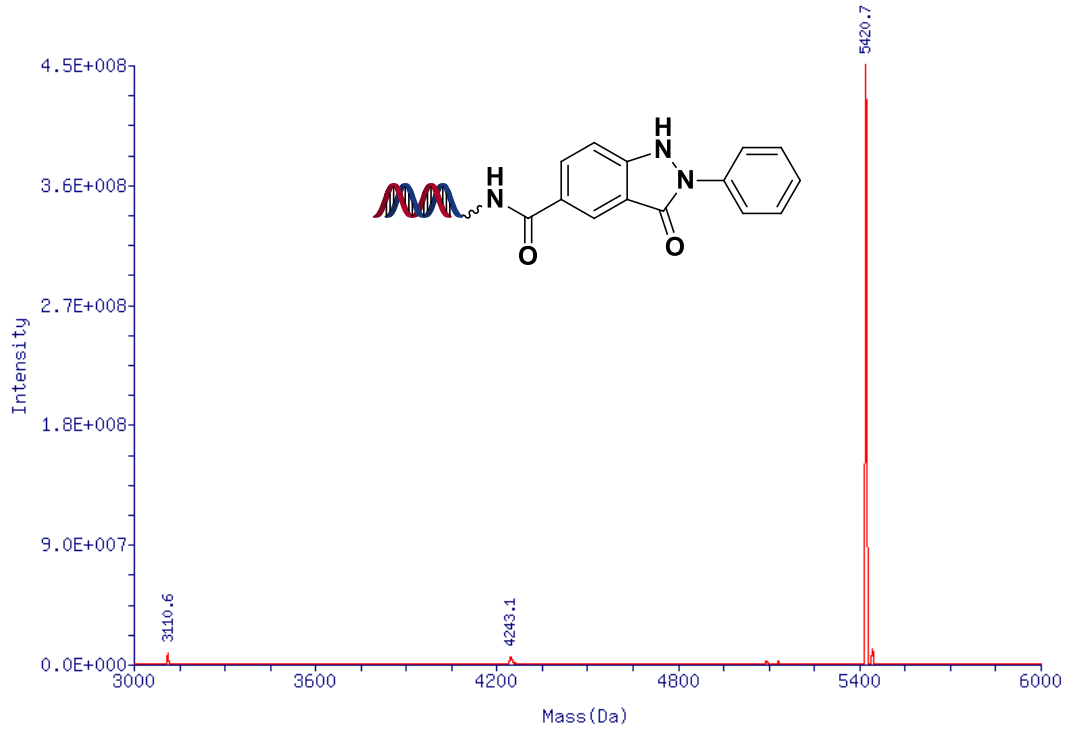

Figure S62. Deconvoluted mass spectrum of conjugate 4aa, expected: 5420; observed: 5420.7.

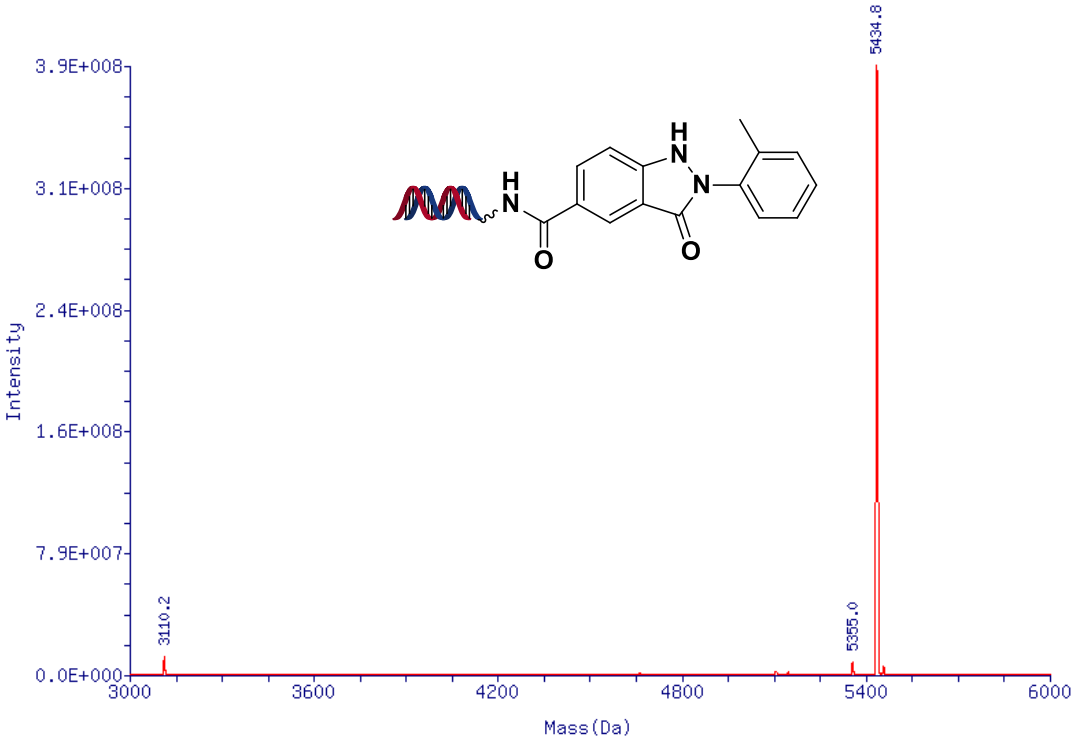

Figure S63. Deconvoluted mass spectrum of conjugate 5bb, expected: 5434; observed: 5434.8.

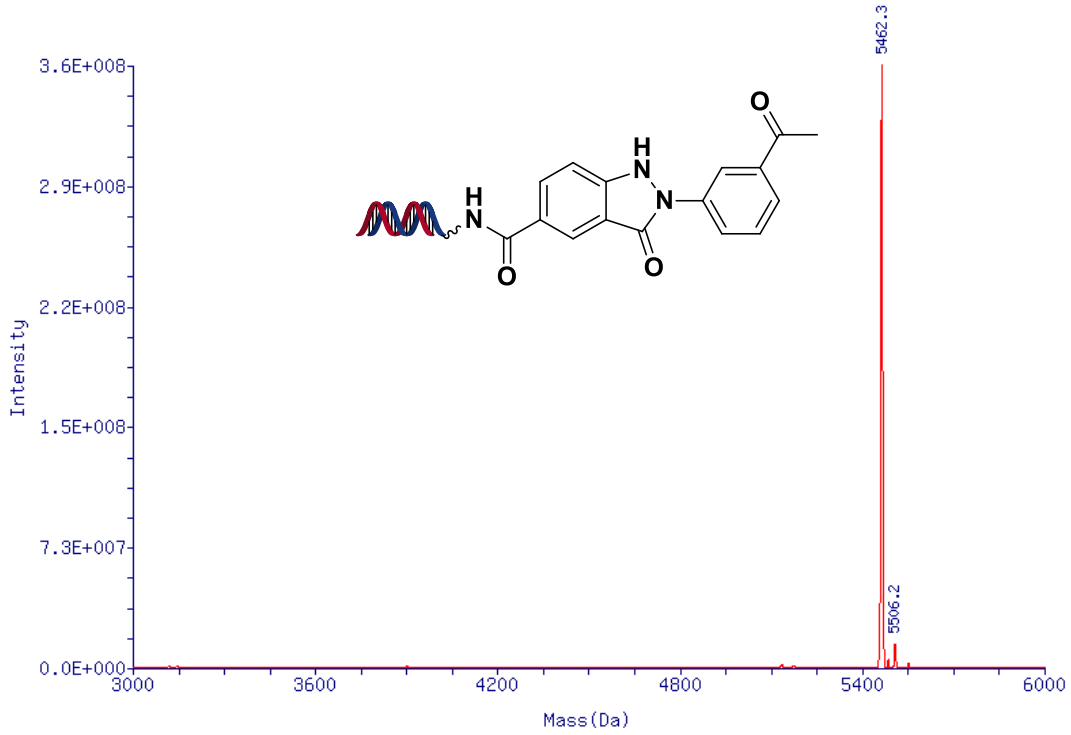

Figure S64. Deconvoluted mass spectrum of conjugate 4cc, expected: 5462; observed: 5462.3.

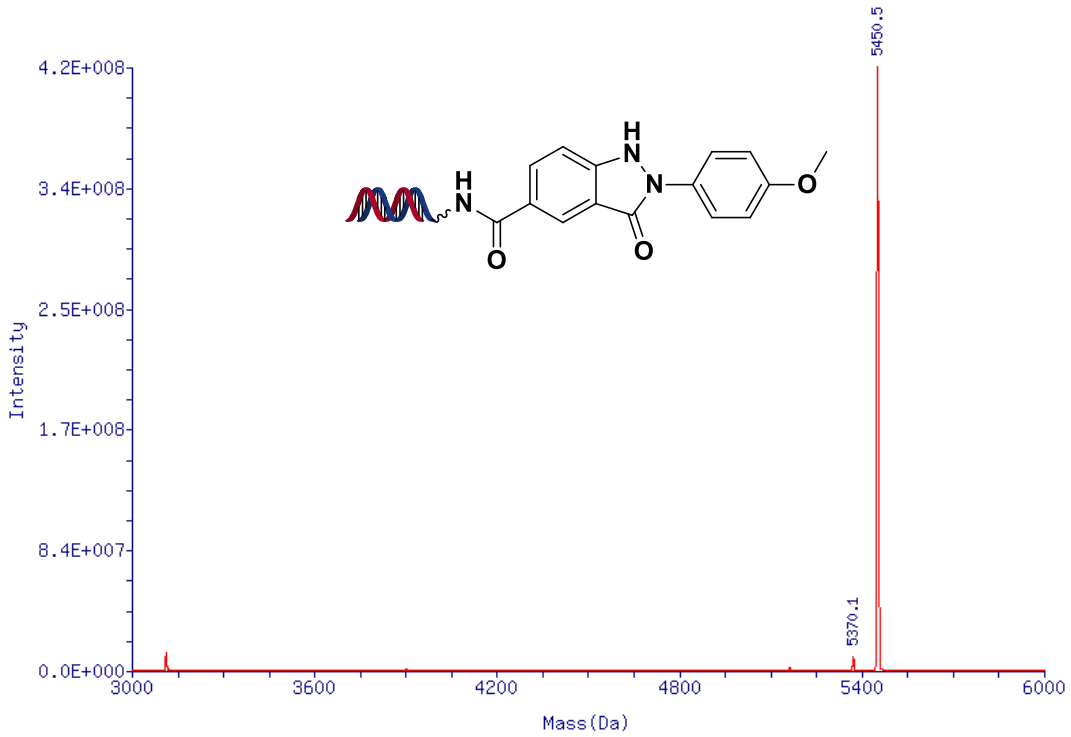

Figure S65. Deconvoluted mass spectrum of conjugate 4dd, expected: 5450; observed: 5450.5

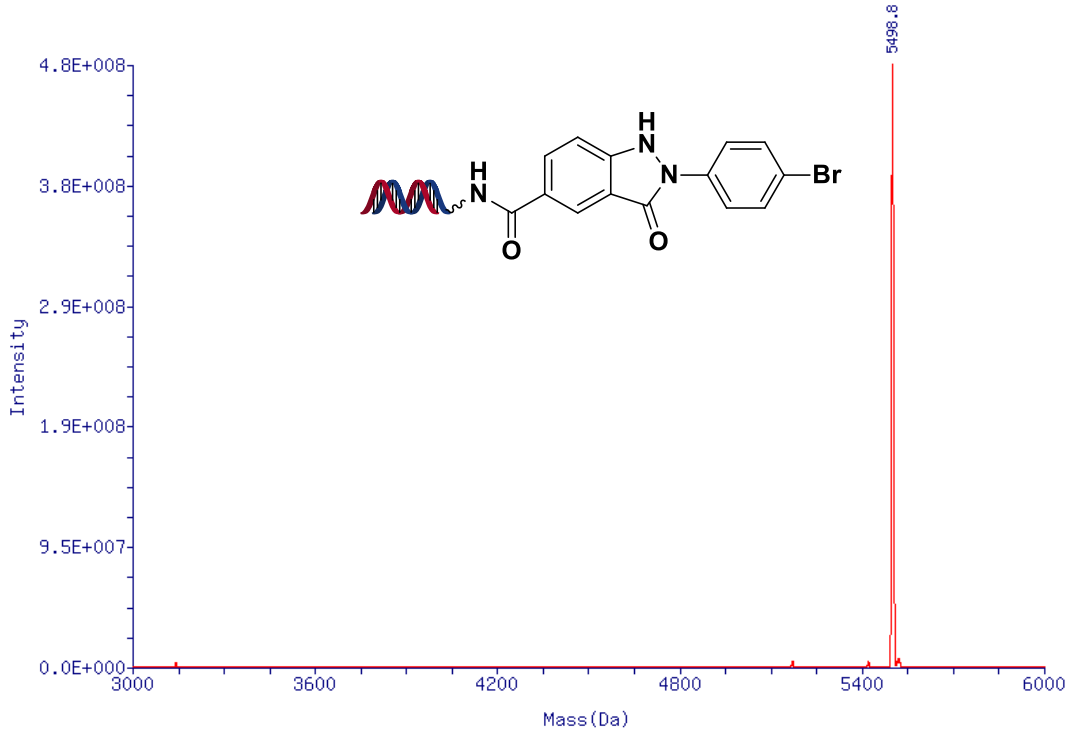

Figure S66. Deconvoluted mass spectrum of conjugate 4ee, expected: 5499; observed: 5498.8.

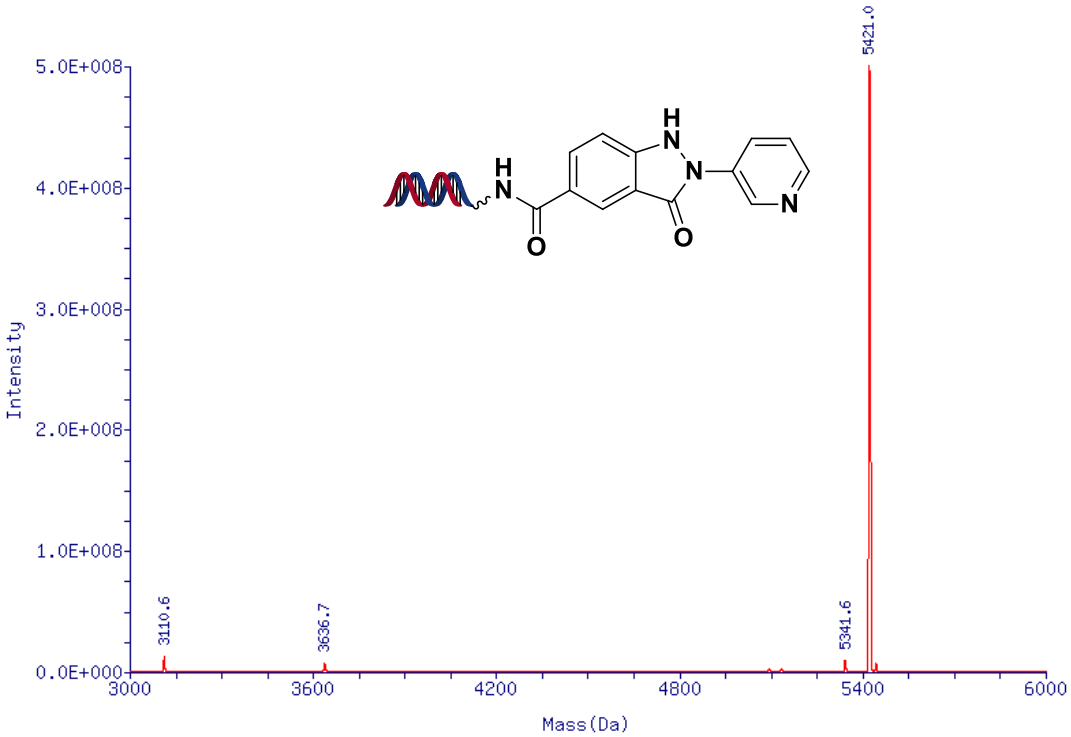

Figure S67. Deconvoluted mass spectrum of conjugate 4ff, expected: 5421; observed: 5421.0.

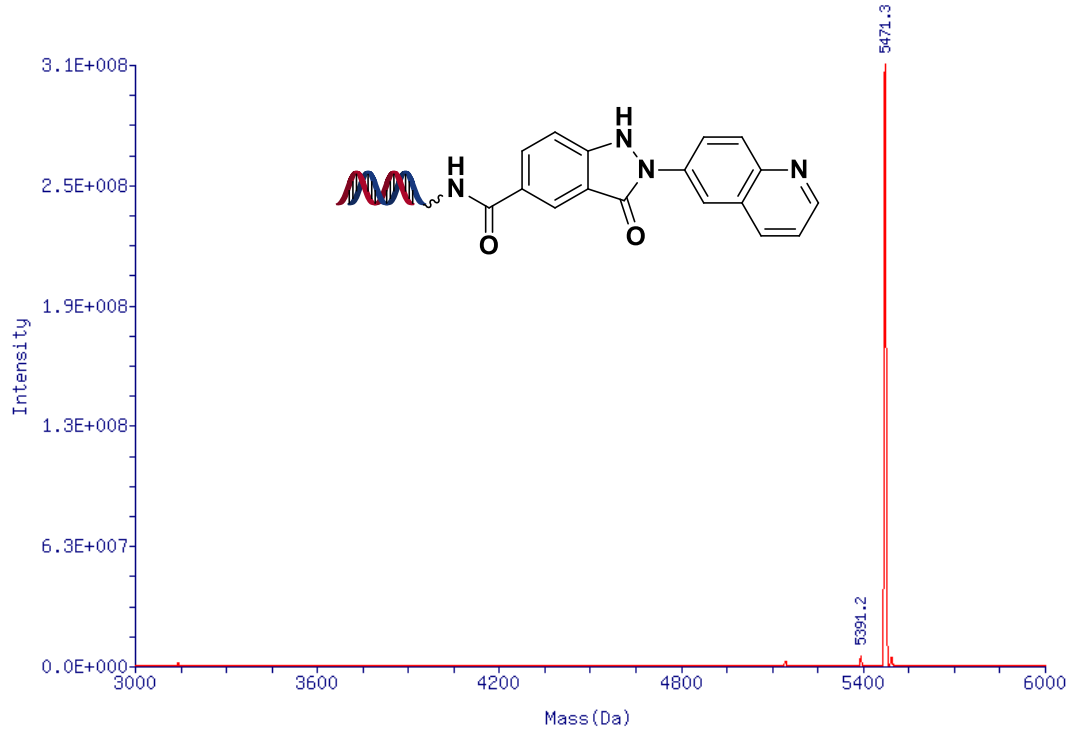

Figure S68. Deconvoluted mass spectrum of conjugate 4gg, expected: 5471; observed: 5471.3.

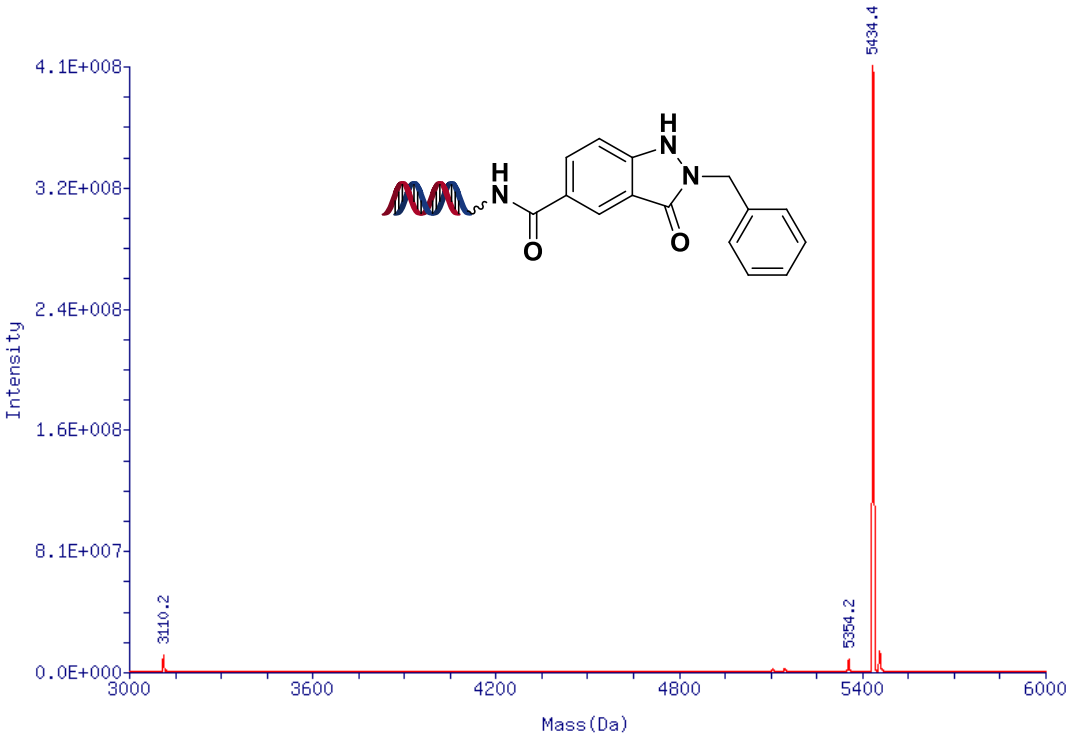

Figure S69. Deconvoluted mass spectrum of conjugate 4hh, expected: 5434; observed: 5434.4.

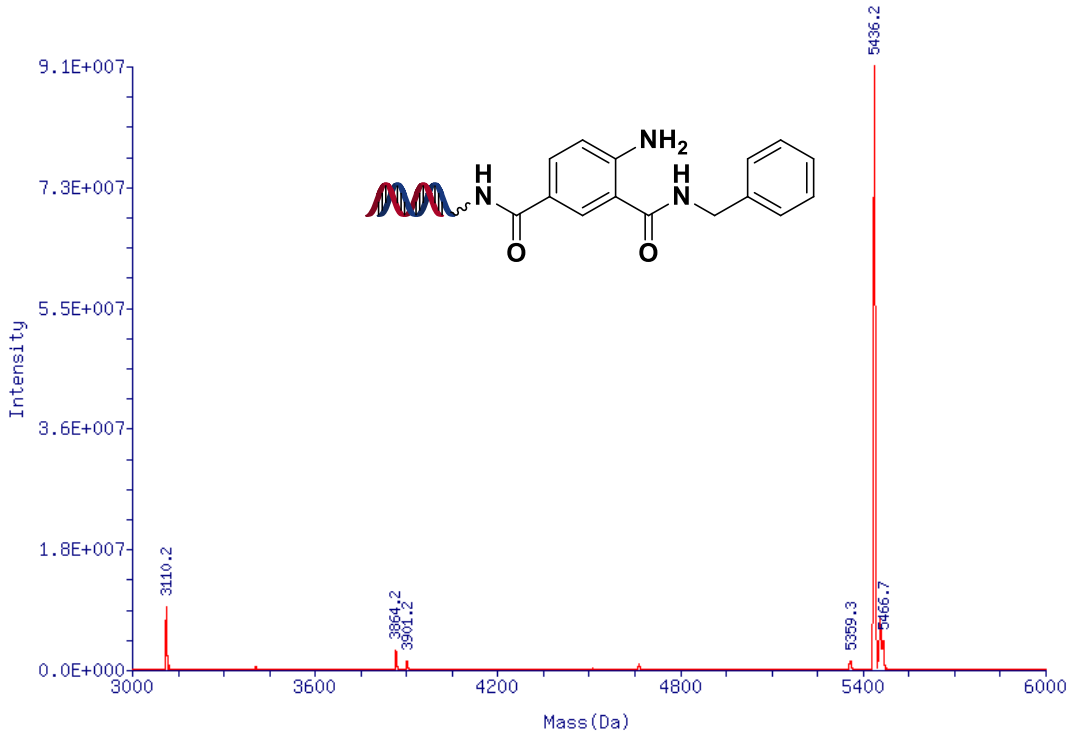

Figure S70. Deconvoluted mass spectrum of conjugate 5hh, expected: 5436; observed: 5436.2.

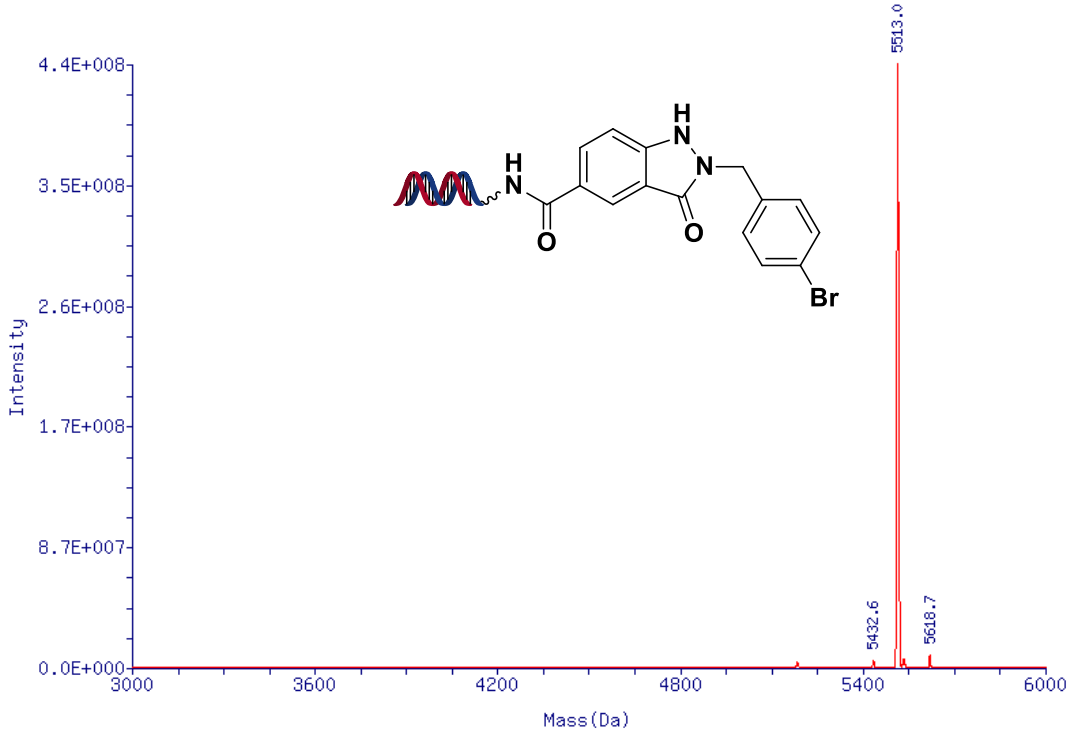

Figure S71. Deconvoluted mass spectrum of conjugate 4ii, expected: 5513; observed: 5513.0.

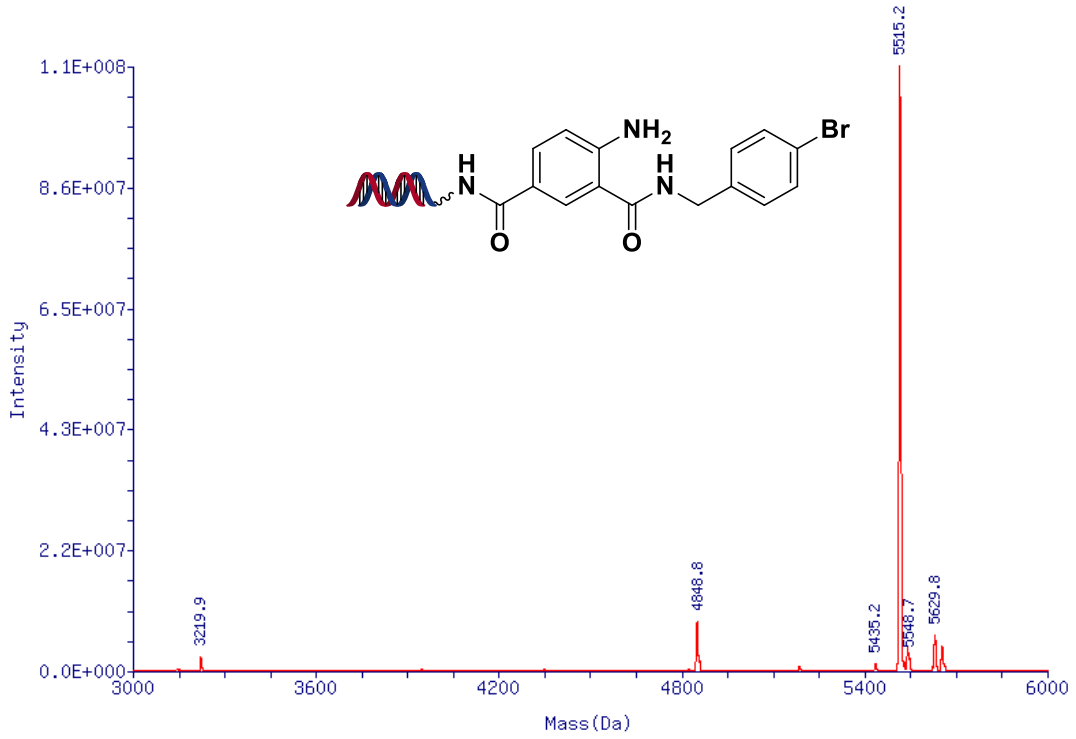

Figure S72. Deconvoluted mass spectrum of conjugate 5ii, expected: 5515; observed: 5515.2.

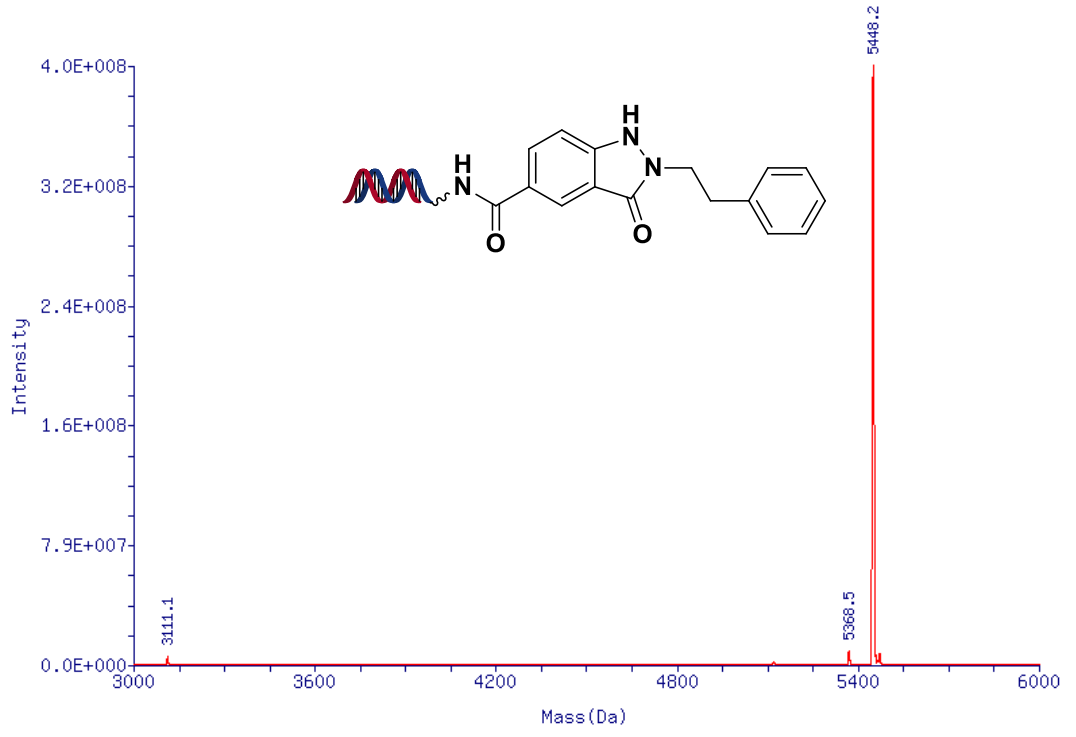

Figure S73. Deconvoluted mass spectrum of conjugate 4jj, expected: 5448; observed: 5448.2.

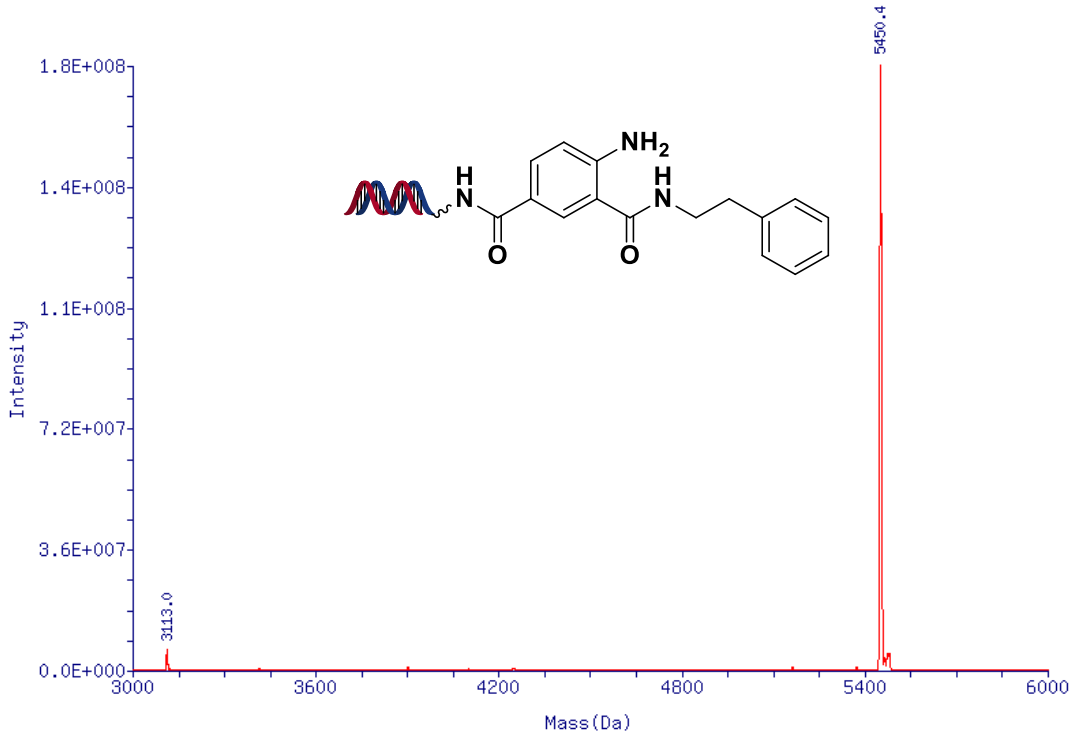

Figure S74. Deconvoluted mass spectrum of conjugate 5jj, expected: 5450; observed: 5450.4.

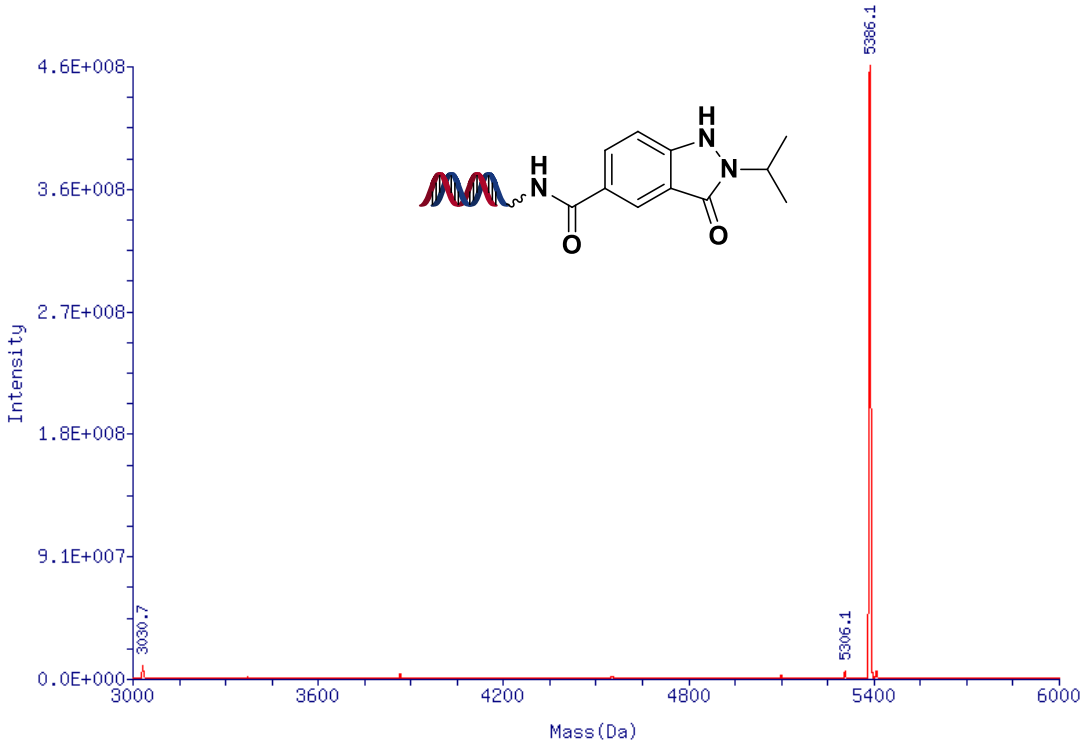

Figure S75. Deconvoluted mass spectrum of conjugate 4kk, expected: 5386; observed: 5386.1.

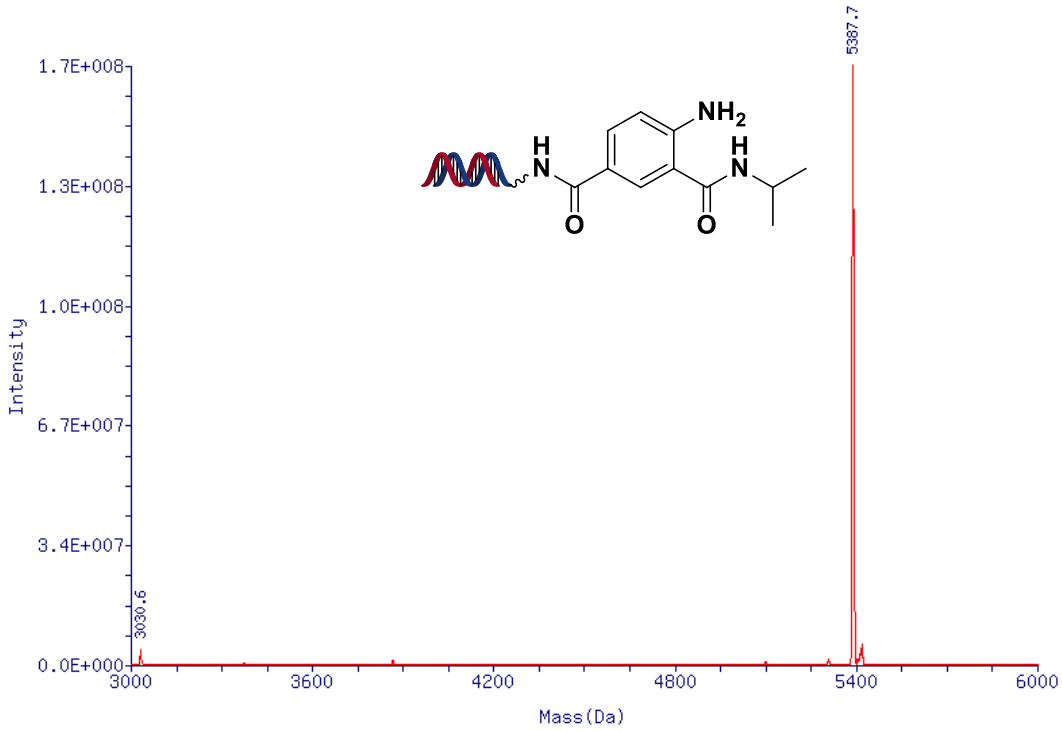

Figure S76. Deconvoluted mass spectrum of conjugate 5kk, expected: 5388; observed: 5387.7.

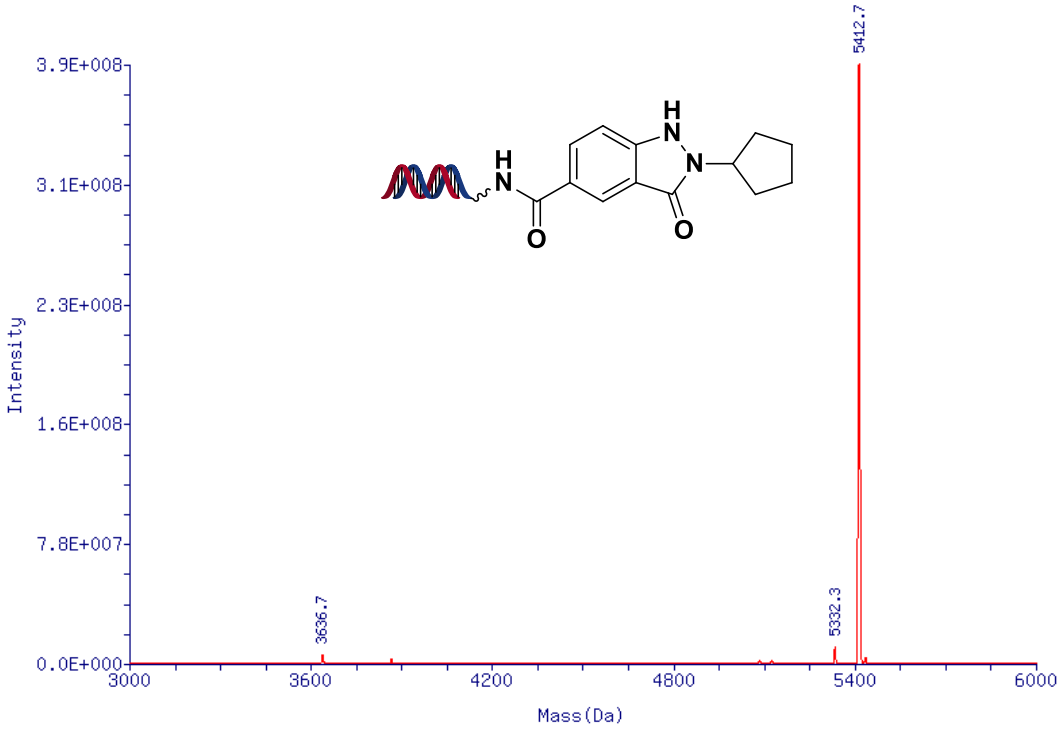

Figure S77. Deconvoluted mass spectrum of conjugate 4ll, expected: 5412; observed: 5412.7.

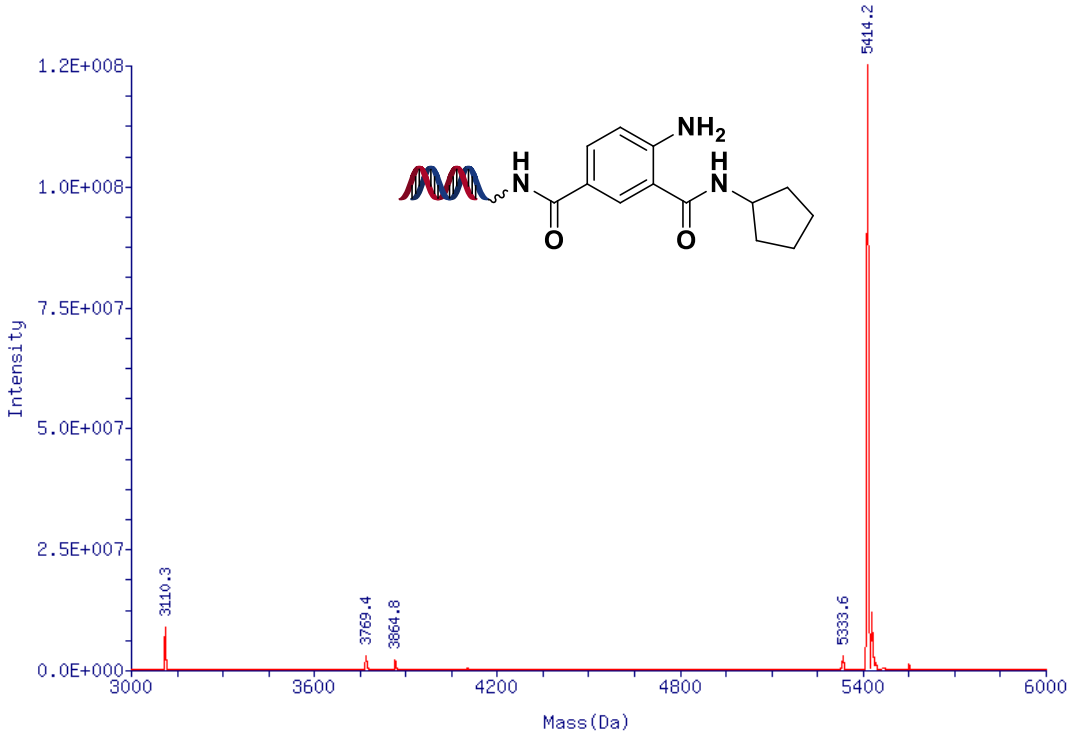

Figure S78. Deconvoluted mass spectrum of conjugate 5ll, expected: 5414; observed: 5414.2.

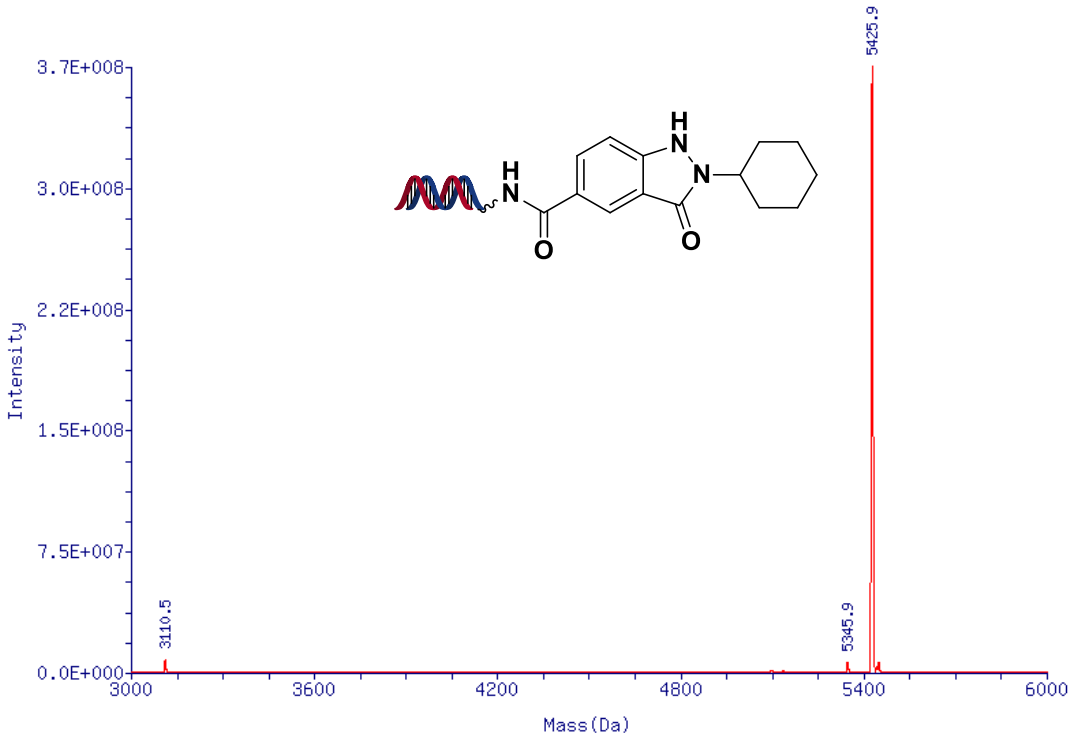

Figure S79. Deconvoluted mass spectrum of conjugate 4mm, expected: 5426; observed: 5425.9.

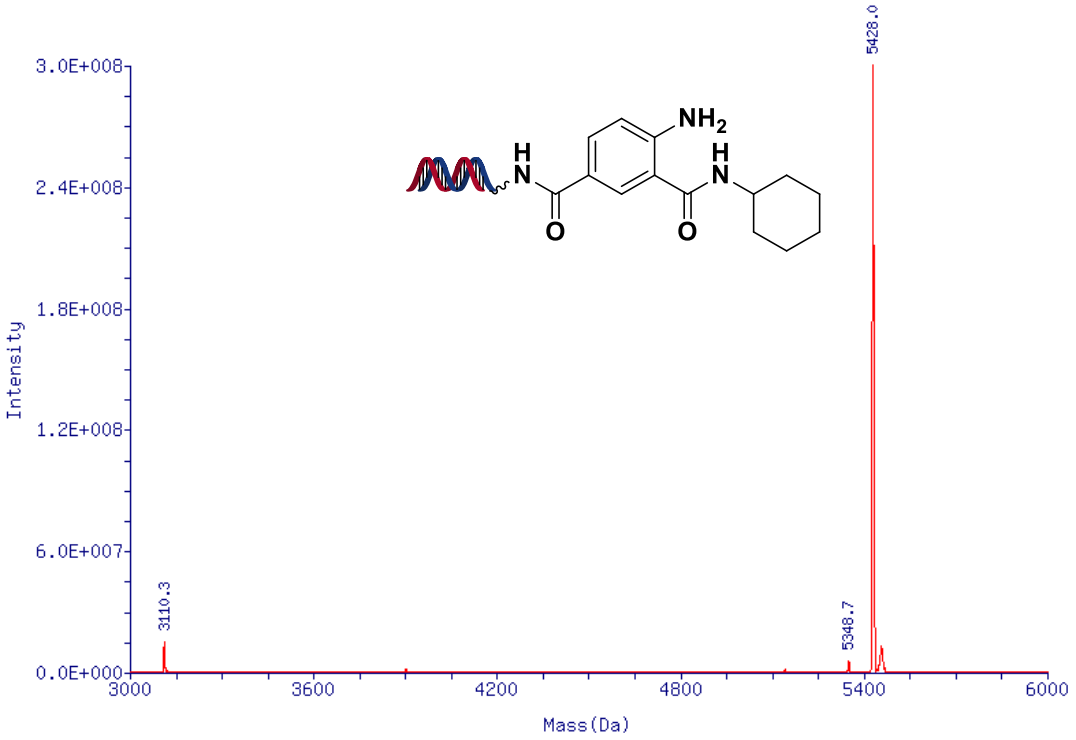

Figure S80. Deconvoluted mass spectrum of conjugate 5mm, expected: 5428; observed: 5428.0.

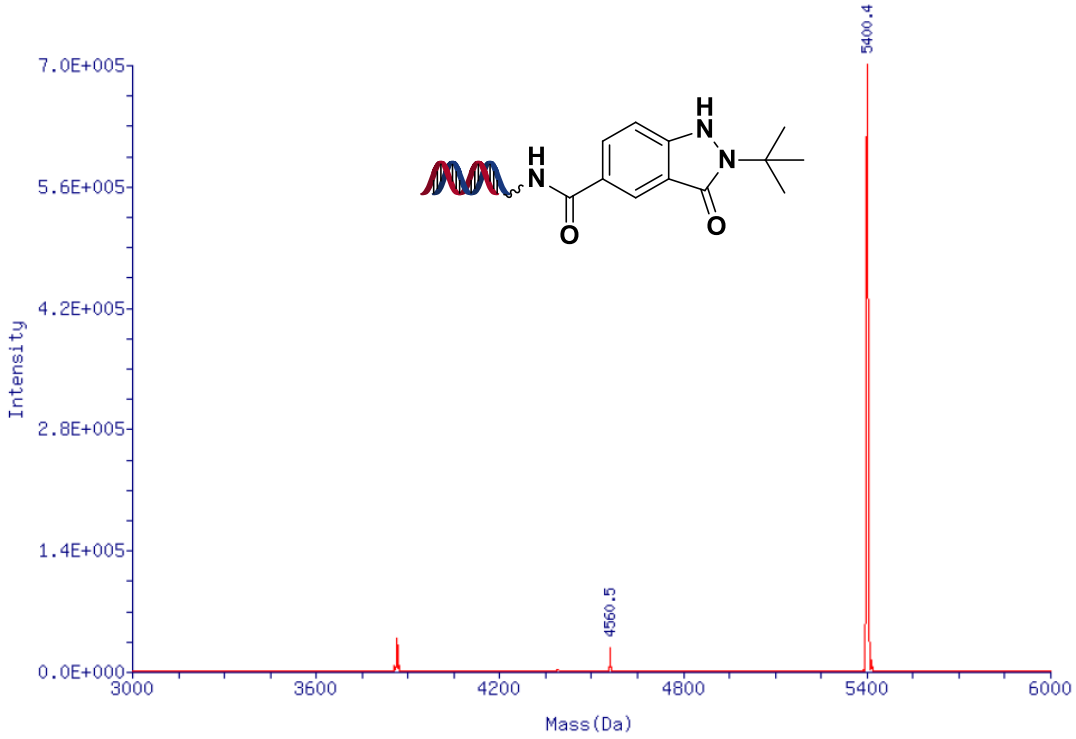

Figure S81. Deconvoluted mass spectrum of conjugate 4nn, expected: 5400; observed: 5400.4.

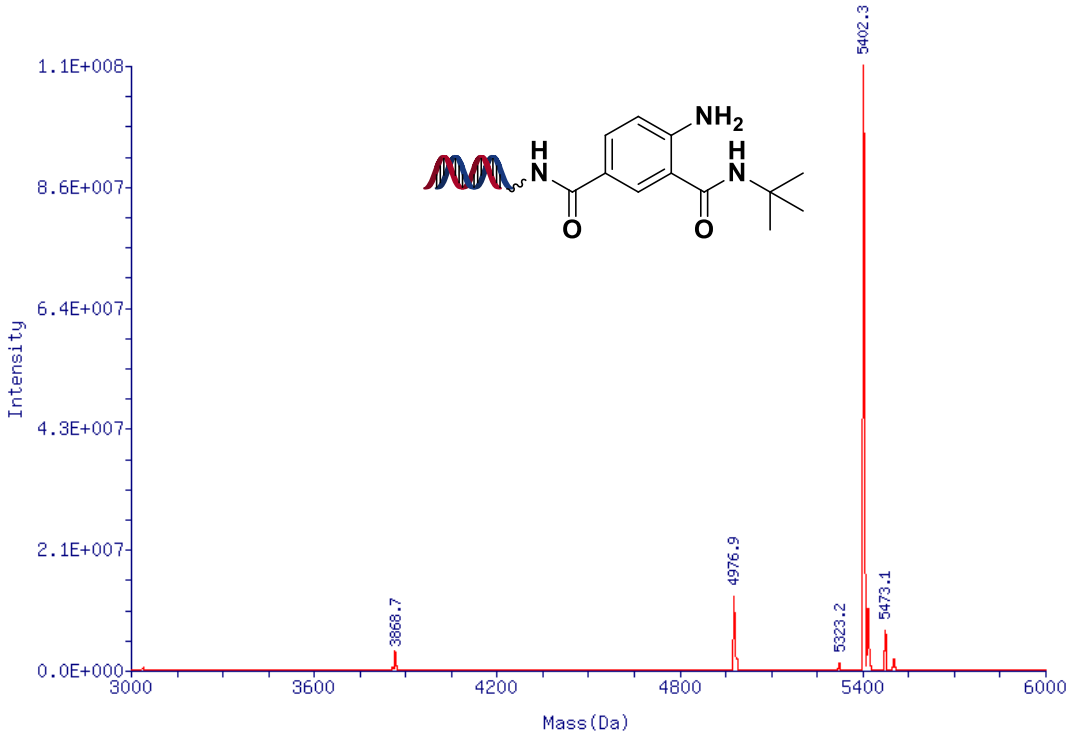

Figure S82. Deconvoluted mass spectrum of conjugate 5nn, expected: 5402; observed: 5402.3.

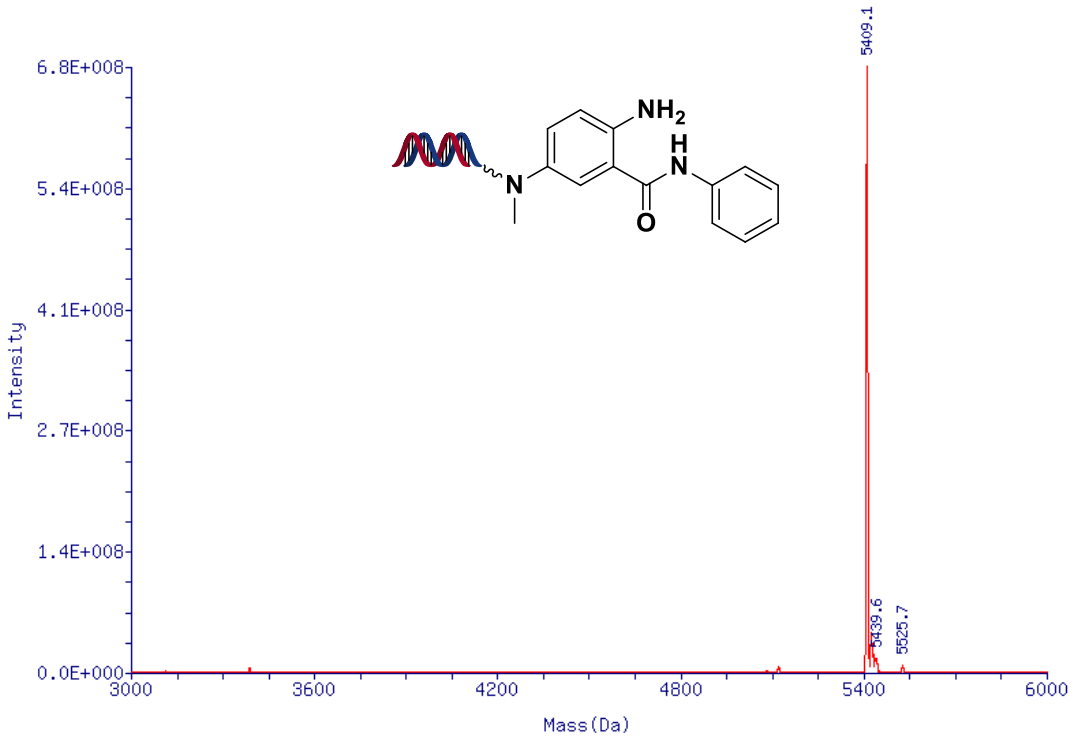

Figure S83. Deconvoluted mass spectrum of conjugate 5oo, expected: 5408; observed: 5409.1.

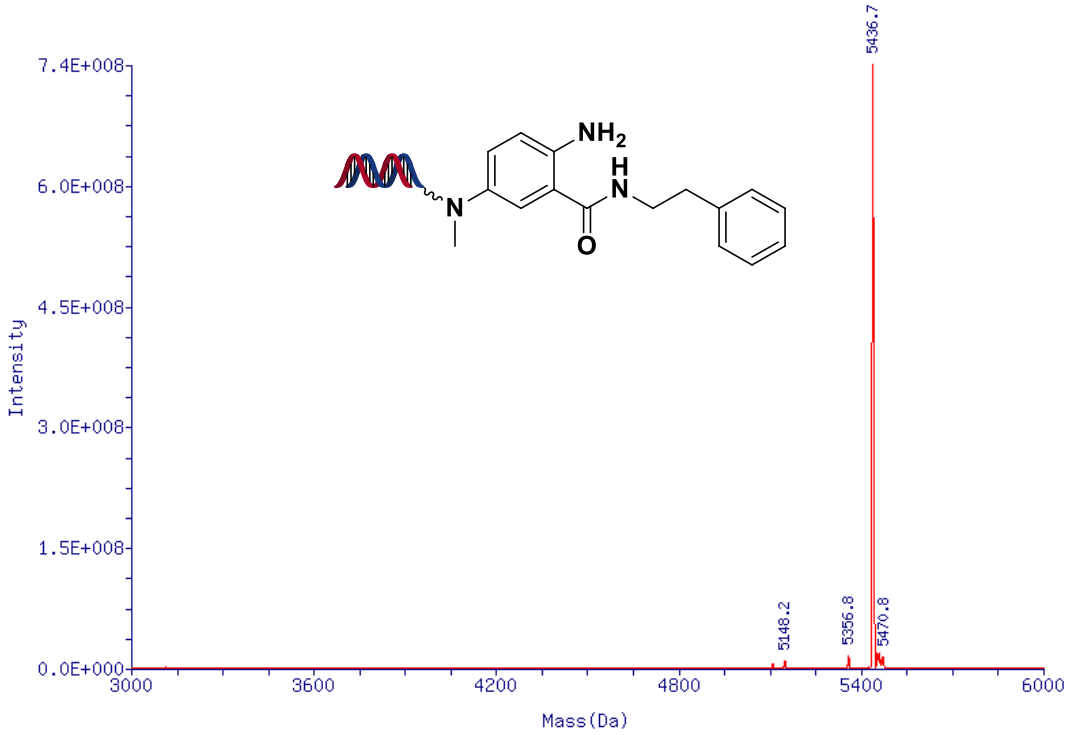

Figure S84. Deconvoluted mass spectrum of conjugate 5pp, expected: 5436; observed: 5436.7.

12. References

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