Umpolung strategy for chemoselective metal-free [4+2] annulations of azlactones: access to tetrahydro β-carbolin 1,3-diketones frameworks

Meng Wang, Ze-Hong Zheng, Mu-Qiu Chen, Gu Zhan, Jie Wang, Qian-Qian Yang * and Wei Huang *

State Key Laboratory of Southwestern Chinese Medicine Resources, Hospital of Chengdu University of Traditional Chinese Medicine, School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu, 611137, China.

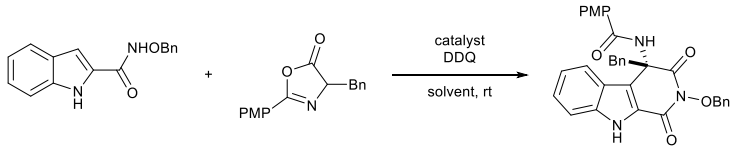
Supporting Information

Table of Contents

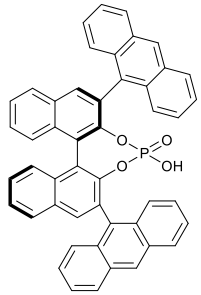
1. General information

Nuclear magnetic resonance (NMR) spectra were recorded in DMSO-d_6 on JEOL 600 NMR instrument. Proton chemical shifts are reported in parts per million (δ scale). The ^{1}H NMR chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as standard. The ^{13}C NMR chemical shifts were given using DMSO-d_6 as the internal standard (DMSO-d_6: δ = 39.50 ppm). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, quin = quintet, m = multiplet, td = triplet doublet, br s = broad singlet), coupling constant(*J*) (Hz), integration]. High-resolution mass spectra (HRMS) were obtained using Agilent P/N G1969-90010 or Waters/Acquity UPLC-Synapt G2HDMS. High-resolution mass spectra were reported for the molecular ion $[M+Na]^{+}$. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained were deposited at the Cambridge Crystallographic Data Centre. UV detection was performed at 254 nm. Column chromatography was performed on silica gel (200-300 mesh) using an eluent of ethyl acetate (EtOAc) and petroleum ether (PE). TLC was performed on glass-backed silica plates; products were visualized using UV light. All reagents and solvents were obtained commercially and used without further purification. *N*-alkoxy indol-2-ylamides **1**[2], azolactones **2**[1] were prepared according to the literature procedures. Melting points were recorded on the BUCHI Melting Point M-565 instrument. Unless otherwise noted, all reagents were obtained commercially and used without further purification.

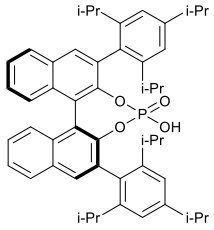
2. Attempt of asymmetric versions



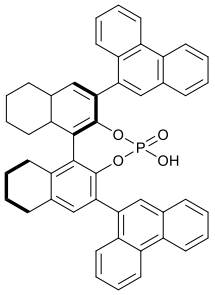
1a 2a 3a



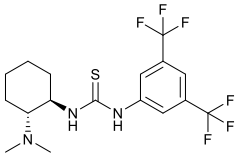
C1



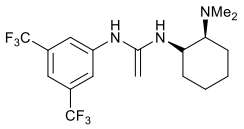
C2



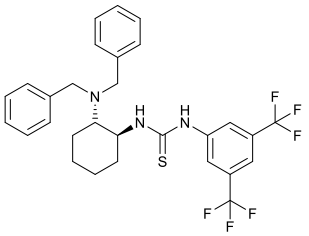
C3



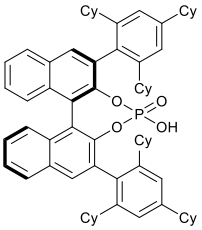
C4



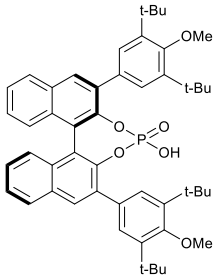
C5



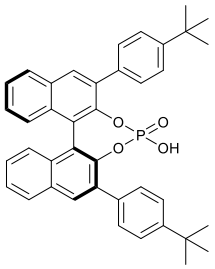
C6



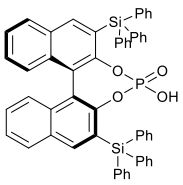
C7



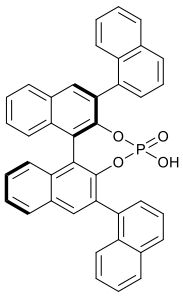
C8



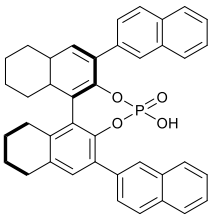
C9



C10



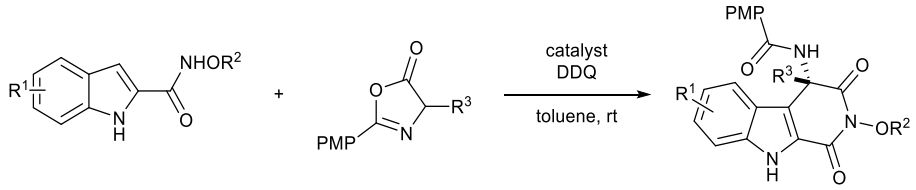
C11



C12

entry[a]	oxidant	catalyst.	solvent	yield (%)[b]	ee (%)[c]
1	DDQ	**C1**	DCM	35	20
2	DDQ	**C2**	DCM	40	25
3	DDQ	**C3**	DCM	45	11
4	DDQ	**C4**	DCM	30	5
5	DDQ	**C5**	DCM	33	<5
6	DDQ	**C6**	DCM	38	<5
7	DDQ	**C7**	DCM	28	<5
8	DDQ	**C8**	DCM	33	7
9	DDQ	**C9**	DCM	40	5
10	DDQ	**C10**	DCM	30	<5
11	DDQ	**C11**	DCM	48	10
12	DDQ	**C12**	DCM	40	10
13	DDQ	**C2**	toluene	46	95
14	DDQ	**C2**	$CHCl_3$	-	-
15	DDQ	**C2**	actone	-	-

[a]Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2a** (0.2 mmol, 2.0 equiv), DDQ (0.2 mmol, 2.0 equiv) and **C** (20 mol%) in 2.0 mL of toluene at rt for 12h. [b]Isolate yield. [c]The ee value determined by HPLC analysis.



1 2 3

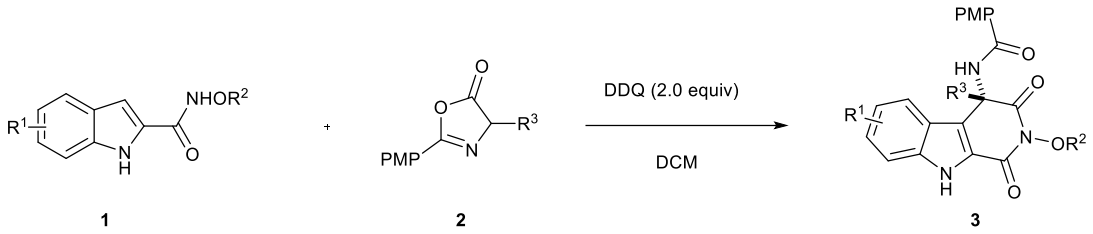
entry[a]	R^1	R^2	R^3	catalyst.	yield (%)[b]	ee (%)[c]
1	5-F	Bn	Bn	**C1**	32	45
2	6-Cl	Bn	Bn	**C1**	34	47
3	5-Me	Bn	Bn	**C1**	30	5
4	6-OMe	Bn	Bn	**C1**	38	17
5	-	Bn	2-Me-Bn	**C1**	35	17
6		Bn	4-Cl-Bn	**C1**	24	21
7		Bn	3-Br-Bn	**C1**	20	7
8		Bn	2-Cl-Bn	**C1**	36	11
9		Bn	2-Me-Bn	**C2**	43	7
10		Bn	3-Br-Bn	**C2**	38	21
11		Bn	2-Cl-Bn	**C2**	30	<5
12	5-F	Bn	Bn	**C2**	28	<5
13	6-Cl	Bn	Bn	**C2**	38	35
14	-	Bn	Bn	**C2**	46	95
15	-	Bn	Ph	**C2**	29	<5
16		Ph	Bn	**C2**	42	9
17	-	Me	Bn	**C2**	38	33
18	-	Bn	4-Cl-Bn	**C2**	34	33

[a]Reaction conditions: **1** (0.1 mmol, 1.0 equiv), **2** (0.2 mmol, 2.0 equiv), DDQ (0.2mmol, 2.0 equiv) and **C** (20 mol%) in 2.0 mL of toluene at rt for 12 h. [b]Isolate yield. [c]The ee value determined by HPLC analysis.

To a mixture of *N*-alkoxy indol-2-ylamides **1** (0.1 mmol), azolactones **2** (0.2 mmol), DDQ (0.2 mmol) in DCM (2.0 mL) was added chiral catalysts (20 mol%) at room temperature for 12 h. By examining several chiral catalyst types, the chiral product **3a**

was created in 46% yield with the highest result being 95% ee. Unfortunately, the reaction might be inhibited by the chiral catalyst, which lowers the reaction yield.

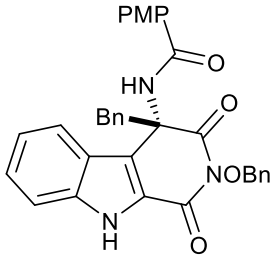
3. General procedure for the synthesis of products 3



General procedure A: To a mixture of *N*-alkoxy indol-2-ylamides **1** (0.1 mmol), azolactones **2** (0.2 mmol) in DCM (2.0 mL) was added DDQ (45.4 mg, 0.2 mmol) at room temperature for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure products **3**.

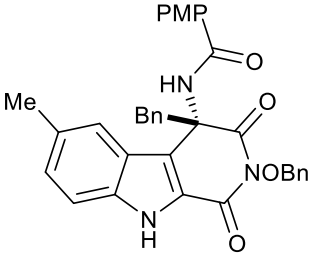
General procedure B: To a mixture of *N*-alkoxy indol-2-ylamides **1** (0.1 mmol), azolactones **2** (0.05mmol each time) in four batches, with an interval of three hours in DCM (2.0 mL) was added DDQ (45.4 mg, 0.2 mmol) at room temperature for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure products **3**.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3a)



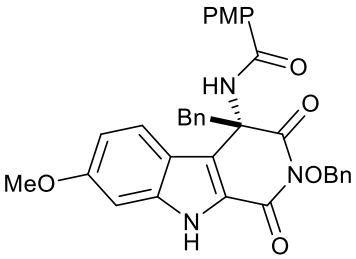
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3a** as a white solid in 75% yield (41.0 mg), m. p. 285.3 – 286.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.12 (s, 1H), 9.80 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 9.0 Hz, 2H), 7.52 – 7.51 (m, 3H), 7.44 – 7.40 (m, 3H), 7.37 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 7.2 Hz, 1H), 7.06 – 7.02 (m, 4H), 6.48 (d, J = 7.8 Hz, 2H), 4.80 (d, J = 9.6 Hz, 1H), 4.61 (s, 1H), 3.83 (d, J = 12.6 Hz, 1H), 3.81 (s, 3H), 3.59 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.1, 165.5, 162.1, 155.7, 138.5, 134.5, 133.0, 129.61, 129.57, 129.3, 128.8, 128.4, 127.9, 127.3, 125.8, 124.9, 123.8, 122.9, 120.8, 120.6, 113.6, 113.4, 77.2, 61.4, 55.4, 44.7. HRMS (ESI-TOF) m/z [M + Na]$^{+}$ Calcd for $C_{33}H_{27}N_3O_5Na^{+}$ 568.1843; found 568.1843.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-6-methyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3b)



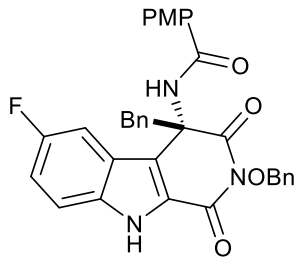
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3b** as a white solid in 82% yield (46.0 mg), m. p. 223.2 – 224.1 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.00 (s, 1H), 9.77 (s, 1H), 7.91 (t, J = 8.4 Hz, 3H), 7.52 (d, J = 6.6 Hz , 2H), 7.43 – 7.39 (m, 4H), 7.20 (d, J = 9.0 Hz, 1H), 7.12 (t, J = 7.2 Hz, 1H), 7.04 (t, J = 7.8 Hz, 4H), 6.49 (d, J = 7.2 Hz, 2H), 4.78 (d, J = 9.0 Hz, 1H), 4.60 (s, 1H), 3.84 (d, J = 12.6 Hz, 1H), 3.82 (s, 3H), 3.57 (d, J = 12.6 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.2, 165.4, 162.1, 155.7, 137.0, 134.5, 133.1, 129.62, 129.60, 129.3, 128.8, 128.4, 127.8, 127.7, 127.3, 125.0, 123.8, 123.2, 119.99, 119.90, 113.6, 113.1, 77.2, 61.4, 55.4, 44.6, 21.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_5Na^+$ 582.1999; found 582.2003.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-7-methoxy-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3c)



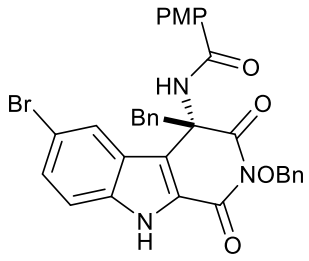
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3c** as a white solid in 73% yield (42.0 mg), m. p. 257.8 – 258.5 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.92 (s, 1H), 9.73 (s, 1H), 7.97 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 5.4 Hz, 2H), 7.43 – 7.39 (m, 3H), 7.12 (t, J = 7.2 Hz, 1H), 7.07 – 7.02 (m, 4H), 6.91 (d, J = 1.8 Hz, 1H), 6.87 (dd, J = 8.4, 2.4 Hz, 1H), 6.50 (d, J = 7.2 Hz, 2H), 4.78 (d, J = 9.6 Hz, 1H), 4.59 (s, 1H), 3.82 (s, 6H), 3.78 (d, J = 13.2 Hz, 1H), 3.56 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.1, 165.4, 162.1, 158.6, 155.4, 139.9, 134.5, 133.0, 129.6, 129.3, 128.8, 128.4, 127.8, 127.3, 125.0, 122.7, 121.7, 121.4, 117.3, 113.6, 112.5, 94.7, 77.2, 61.3, 55.4, 55.2, 44.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_6Na^+$ 598.1949; found 598.1955.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-6-fluoro-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3d)



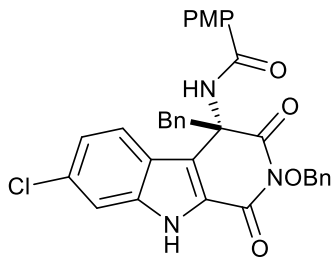
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3d** as a white solid in 60% yield (34.0 mg), m. p. 259.2 – 260.1 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.28 (s, 1H), 9.74 (s, 1H), 7.92 – 7.90 (m, 3H), 7.55 – 7.52 (m, 3H), 7.44 – 7.40 (m, 3H), 7.26 (td, J = 9.0, 2.4 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 7.07 – 7.04 (m, 4H), 6.51 (d, J = 7.2 Hz, 2H), 4.81 (d, J = 9.0 Hz, 1H), 4.63 (s, 1H), 3.87 (d, J = 27.0 Hz, 1H), 3.82 (s, 4H), 3.56 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.9, 165.4, 162.1, 157.3 (d, J = 234.0 Hz), 155.5, 135.2, 134.4, 133.0, 129.6 (d, J = 4.5 Hz), 129.3, 128.8, 128.4, 127.9, 127.4, 125.3, 124.8, 122.8 (d, J = 10.5 Hz), 120.4 (d, J = 6.0 Hz), 115.0 (d, J =10.5 Hz), 114.8 (d, J =27.0 Hz), 113.7, 105.2 (d, J = 22.5 Hz), 77.3, 61.2, 55.4, 44.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}FN_3O_5Na^+$ 586.1749; found 586.1746.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-6-bromo-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3e)



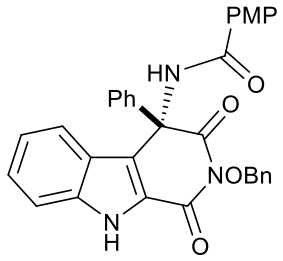
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3e** as a white solid in 45% yield (28.0 mg), m. p. 153.2 – 154.6 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.40 (s, 1H), 9.83 (s, 1H), 8.38 (s, 1H), 7.92 (d, J = 9.0 Hz, 2H), 7.51 (d, J = 5.4 Hz, 2H), 7.49 (d, J = 1.2 Hz, 2H), 7.44 – 7.40 (m, 3H), 7.13 (t, J = 7.8 Hz, 1H), 7.08 – 7.04 (m, 4H), 6.50 (d, J = 7.2 Hz, 2H), 4.80 (d, J = 9.6 Hz, 1H), 4.62 (s, 1H), 3.85 (d, J = 12.6 Hz, 1H), 3.83 (s, 3H), 3.56 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.8, 165.4, 162.2, 155.4, 137.1, 134.4, 132.9, 129.6, 129.3, 128.9, 128.44, 128.37, 127.9, 127.4, 124.9, 124.7, 124.4, 123.0, 119.9, 115.5, 113.7, 113.4, 77.3, 61.2, 55.4, 44.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}BrN_3O_5Na^+$ 646.0948; found 646.0956.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-7-chloro-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3f)



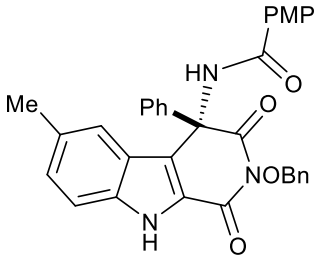
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3f** as a white solid in 59% yield (34.0 mg), m. p. 261.2 – 262.6 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.31 (s, 1H), 9.80 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 9.0 Hz, 2H), 7.52 (d, J = 5.4 Hz, 3H), 7.44 – 7.39 (m, 3H), 7.26 (dd, J = 8.4, 1.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.08 – 7.02 (m, 4H), 6.50 (d, J = 7.8 Hz, 2H), 4.82 (d, J = 9.6 Hz, 1H), 4.63 (s, 1H), 3.82 (s, 3H), 3.80 (d, J = 12.6 Hz, 3H), 3.59 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.0, 165.6, 162.1, 155.4, 138.8, 134.4, 132.9, 130.5, 129.63, 129.58, 129.3, 128.9, 128.4, 127.9, 127.4, 124.8, 124.6, 122.4, 121.7, 121.6, 120.8, 113.6, 112.8, 77.3, 61.3, 55.4, 44.7. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}ClN_3O_5Na^+$ 602.1453; found 602.1454.

Ethyl *N*-(2-(benzyloxy)-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3g)



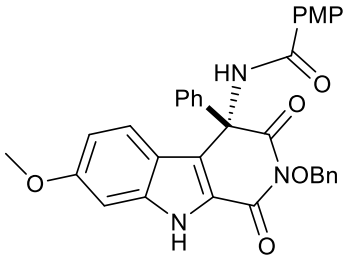
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3g** as a white solid in 94% yield (50.0 mg), m. p. 183.3 – 184.2 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.46 (s, 1H), 9.97 (s, 1H), 7.95 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.40 – 7.38 (m, 5H), 7.36 – 7.35 (m, 2H), 7.33 – 7.29 (m, 4H), 7.02 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 4.98 – 4.94 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.4, 166.2, 162.1, 156.2, 138.8, 137.3, 134.3, 129.9, 129.4, 129.0, 128.8, 128.6, 128.3, 127.7, 125.8, 124.9, 123.9, 123.3, 121.8, 120.9, 120.7, 113.5, 113.3, 77.0, 63.2, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{25}N_3O_5Na^+$ 554.1686; found 554.1687.

Ethyl *N*-(2-(benzyloxy)-6-methyl-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3h)



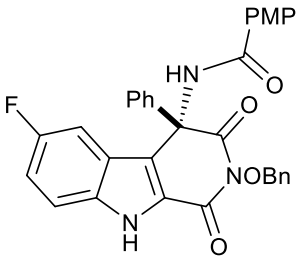
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3h** as a white solid in 97% yield (53.0 mg), m. p. 220.1 – 221.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.34 (s, 1H), 9.95 (s, 1H), 7.96 (d, J = 9.0 Hz, 2H), 7.58 (s, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.40 – 7.38 (m, 5H), 7.37 – 7.35 (m, 2H), 7.33 – 7.31 (m, 3H), 7.13 (d, J = 8.4 Hz, 1H), 6.99 (d, J = 8.4 Hz, 2H), 4.98 – 4.94 (m, 2H), 3.80 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.4, 166.2, 162.1, 156.2, 137.3, 137.2, 134.3, 129.9, 129.42, 129.37, 128.9, 128.7, 128.5, 128.2, 127.75, 127.68, 124.9, 123.8, 123.5, 120.8, 120.2, 113.5, 113.0, 76.9, 63.2, 55.4, 21.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{27}N_3O_5Na^+$ 568.1843; found 568.1839.

Ethyl *N*-(2-(benzyloxy)-7-methoxy-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3i)



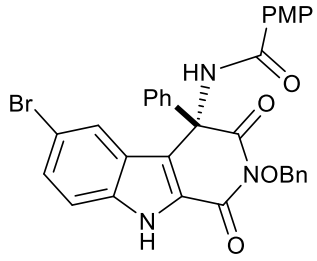
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3i** as a white solid in 93% yield (52.0 mg), m. p. 160.3 – 161.2 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.26 (s, 1H), 9.92 (s, 1H), 7.94 (d, J = 9.0 Hz, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.41 – 7.38 (m, 5H), 7.35 – 7.32 (m, 5H), 6.98 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 1.8 Hz, 1H), 6.69 (dd, J = 9.0, 1.8 Hz, 1H), 4.96 – 4.93 (m, 2H), 3.80 (s, 3H), 3.78(s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.3, 166.1, 162.0, 158.7, 155.9, 140.2, 137.4, 134.4, 129.9, 129.4, 128.9, 128.7, 128.5, 128.2, 127.6, 124.9, 122.7, 122.6, 121.7, 117.7, 113.5, 112.4, 94.5, 76.9, 63.1, 55.4, 55.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{27}N_3O_6Na^+$ 584.1792; found 584.1786.

Ethyl *N*-(2-(benzyloxy)-6-fluoro-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3j)



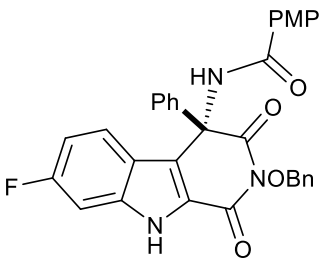
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3j** as a white solid in 91% yield (50.0 mg), m. p. 247.3 – 248.1 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.61 (s, 1H), 9.93 (s, 1H), 7.94 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 9.6 Hz, 1H), 7.56 – 7.54 (m, 1H), 7.42 – 7.38 (m, 5H), 7.35 (d, J = 8.4 Hz, 2H), 7.32 – 7.31 (m, 3H), 7.19 (t, J = 8.4 Hz, 1H), 7.00 (d, J = 7.8 Hz, 2H), 4.98 – 4.93 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.1, 166.2, 162.1, 157.3 (d, J = 234.0 Hz), 156.0, 136.3 (d, J = 237.0 Hz), 134.2, 129.9, 129.4, 129.1, 128.8, 128.6, 128.2, 127.6, 125.5, 124.7, 123.2 (d, J = 12.0 Hz), 120.5 (d, J = 6.0 Hz), 114.9 (d, J = 15.0 Hz), 114.8, 113.6, 105.9 (d, J = 24.0 Hz), 77.0, 62.9, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{24}FN_3O_5Na^+$ 572.1592; found 572.1589.

Ethyl *N*-(2-(benzyloxy)-6-bromo-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3k)



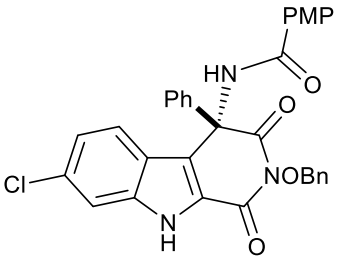
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3k** as a white solid in 90% yield (55.0 mg), m. p. 256.9 – 257.6 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.72 (s, 1H), 10.03 (s, 1H), 8.09 (s, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 1H), 7.43 – 7.39 (m, 6H), 7.36 – 7.31 (m, 5H), 7.01 (d, J = 8.4 Hz, 2H), 4.98 – 4.94 (m, 2H), 3.81 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.9, 166.2, 162.2, 156.0, 137.3, 137.0, 134.2, 129.9, 129.4, 129.1, 128.8, 128.6, 128.5, 128.2, 127.6, 125.1, 124.72, 124.70, 123.7, 120.0, 115.4, 113.6, 113.4, 77.0, 62.9, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{24}BrN_3O_5Na^+$ 632.0792; found 632.0796.

Ethyl *N*-(2-(benzyloxy)-7-fluoro-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3l)



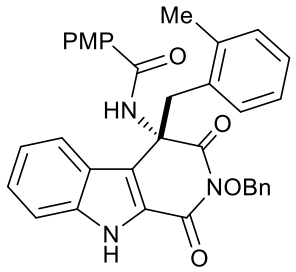
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3l** as a white solid in 91% yield (50.0 mg), m. p. 270.2 – 271.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.59 (s, 1H), 9.98 (s, 1H), 7.94 (d, J = 8.4 Hz, 2H), 7.82 (dd, J = 9.0, 5.4 Hz, 1H), 7.41 – 7.38 (m, 5H), 7.36 – 7.31 (m, 5H), 7.26 (d, J = 12.0 Hz, 1H), 6.99 (d, J = 9.0 Hz, 2H), 6.96 – 6.94 (m, 1H), 4.98 – 4.93 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.2, 166.2, 162.1, 161.1 (d, J = 240.0 Hz), 155.9, 139.0 (d, J = 13.5 Hz), 137.1, 134.2, 129.9, 129.4, 129.1, 128.8, 128.6, 128.2, 127.6, 124.8, 124.6 (d, J = 3.0 Hz), 123.5 (d, J = 9.0 Hz), 121.2, 120.2, 113.5, 110.3 (d, J = 24.0 Hz), 98.8 (d, J = 25.5 Hz), 77.0, 63.1, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{24}FN_3O_5Na^+$ 572.1592; found 572.1595.

Ethyl *N*-(2-(benzyloxy)-7-chloro-1,3-dioxo-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3m)



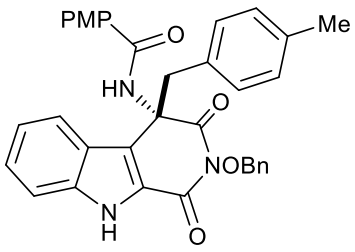
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3m** as a white solid in 80% yield (45.0 mg), m. p. 193.3 – 194.1 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.64 (s, 1H), 9.99 (s, 1H), 7.94 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 1.8 Hz, 1H), 7.42 – 7.38 (m, 5H), 7.36 – 7.31 (m, 5H), 7.09 (dd, J = 8.4, 1.8 Hz, 1H), 6.99 (d, J = 9.0 Hz, 2H), 4.98 – 4.94 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.1, 166.2, 162.1, 156.0, 139.0, 137.0, 134.2, 130.6, 129.9, 129.4, 129.1, 128.8, 128.6, 128.2, 127.6, 124.8, 124.7, 123.3, 122.0, 121.4, 121.0, 113.5, 112.7, 77.0, 63.0, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{24}ClN_3O_5Na^+$ 588.1297; found 588.1305.

Ethyl *N*-(2-(benzyloxy)-4-(2-methylbenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3n)



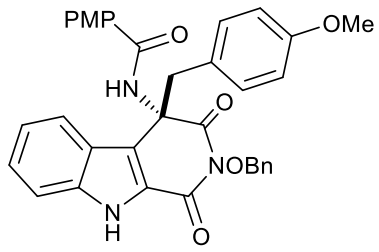
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3n** as a white solid in 95% yield (53.0 mg), m. p. 247.6 – 248.3 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.18 (s, 1H), 9.81 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 9.0 Hz, 2H), 7.51 (t, J = 9.0 Hz, 3H), 7.43 – 7.39 (m, 3H), 7.35 (t, J = 8.4 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.04 – 7.01 (m, 3H), 6.98 (d, J = 7.8 Hz, 1H), 6.84 (t, J = 7.8 Hz, 1H), 6.25 (d, J = 7.8 Hz, 1H), 4.62 (d, J = 40.8 Hz, 2H), 3.82 (s, 3H), 3.76 (s, 1H), 1.88 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.5, 165.4, 162.1, 155.8, 138.5, 137.3, 134.4, 131.6, 130.3, 130.1, 129.7, 129.2, 128.8, 128.4, 127.3, 125.8, 125.1, 125.0, 123.6, 123.2, 121.2, 120.83, 120.79, 113.6, 113.4, 77.2, 61.4, 55.4, 40.9, 19.0. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_5Na^+$ 582.1999; found 582.2008.

Ethyl *N*-(2-(benzyloxy)-4-(4-methylbenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3o)



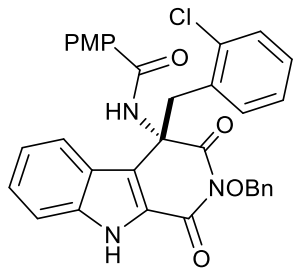
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3o** as a white solid in 71% yield (40.0 mg), m. p. 230.2 – 231.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.11 (s, 1H), 9.77 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.52 (t, J = 4.8 Hz, 3H), 7.44 – 7.40 (m, 3H), 7.36 (t, J = 7.2 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 7.8 Hz, 2H), 6.37 (d, J = 7.8 Hz, 2H), 4.84 (d, J = 9.6 Hz, 1H), 4.66 (s, 1H), 3.81 (s, 3H), 3.79 (s, 1H), 3.55 (d, J = 13.2 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.2, 165.5, 162.1, 155.7, 138.5, 136.4, 134.5, 129.9, 129.6, 129.4, 129.3, 128.8, 128.42, 128.36, 125.7, 124.9, 123.8, 122.9, 120.9, 120.8, 120.6, 113.6, 113.4, 77.3, 61.4, 55.4, 44.3, 20.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_5Na^+$ 582.1999; found 582.1997.

Ethyl *N*-(2-(benzyloxy)-4-(4-methoxybenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3p)



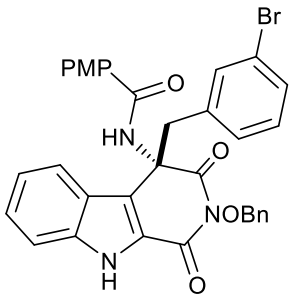
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3p** as a white solid in 83% yield (48.0 mg), m. p. 133.2 – 134.0 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.12 (s, 1H), 9.76 (s, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.91 – 7.89 (m, 2H), 7.54 – 7.51 (m, 3H), 7.44 – 7.39 (m, 3H), 7.38 – 7.35 (m, 1H), 7.21 – 7.19 (m, 1H), 7.03 – 7.00 (m, 2H), 6.61 (d, J = 9.0 Hz, 2H), 6.38 (d, J = 8.4 Hz, 2H), 4.84 (d, J = 9.6 Hz, 1H), 4.67 (s, 1H), 3.81 (s, 3H), 3.77 (d, J = 12.6 Hz, 1H), 3.59 (s, 3H), 3.53 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.3, 165.5, 162.1, 158.4, 155.8, 138.6, 134.5, 130.6, 129.6, 129.3, 128.8, 128.4, 125.8, 125.0, 124.8, 123.8, 122.9, 120.9, 120.8, 120.7, 113.6, 113.5, 113.3, 77.3, 61.6, 55.4, 54.9, 43.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_6Na^+$ 598.1949; found 598.1949.

Ethyl *N*-(2-(benzyloxy)-4-(2-chlorobenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3q)



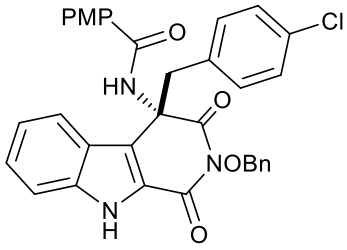
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3q** as a white solid in 90% yield (52.0 mg), m. p. 240.0 – 241.0 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.17 (s, 1H), 9.86 (s, 1H), 7.94 (s, 3H), 7.55 – 7.32 (m, 7H), 7.21 – 7.05 (m, 6H), 6.65 (s, 1H), 4.79 (d, J = 89.4 Hz, 2H), 3.90 (d, J = 32.4 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.0, 165.5, 162.1, 155.8, 138.6, 134.4, 131.9, 131.1, 129.7, 129.4, 129.32, 129.26, 128.9, 128.4, 126.5, 125.7, 124.9, 123.6, 123.3, 121.0, 120.9, 120.6, 113.6, 113.2, 77.3, 61.3, 55.4, 40.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}ClN_3O_5Na^+$ 602.1453; found 602.1450.

Ethyl *N*-(2-(benzyloxy)-4-(3-bromobenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3r)



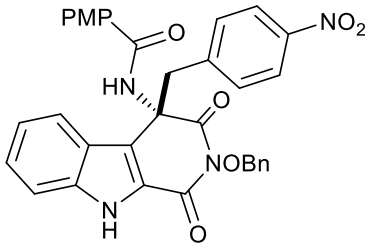
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3r** as a white solid in 58% yield (36.0 mg), m. p. 170.1 – 171.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.22 (s, 1H), 9.84 (s, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 9.0 Hz, 2H), 7.54 (d, J = 7.8 Hz, 3H), 7.45 – 7.41 (m, 3H), 7.39 – 7.34 (m, 2H), 7.21 (t, J = 7.2 Hz, 1H), 7.04 – 7.00 (m, 3H), 6.73 (s, 1H), 6.39 (d, J = 7.8 Hz, 1H), 4.86 (d, J = 9.0 Hz, 1H), 4.61 (d, J = 7.2 Hz, 1H), 3.83 (d, J = 13.2 Hz, 1H), 3.81 (s, 3H), 3.59 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.0, 165.5, 162.1, 155.6, 138.6, 135.8, 134.4, 132.5, 130.2, 130.0, 129.6, 129.1, 128.8, 128.6, 128.4, 125.9, 124.8, 123.7, 122.8, 121.04, 120.97, 120.8, 120.3, 113.6, 113.5, 77.5, 61.2, 55.4, 44.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}BrN_3O_5Na^+$ 646.0948; found 646.0949.

Ethyl *N*-(2-(benzyloxy)-4-(4-chlorobenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3s)



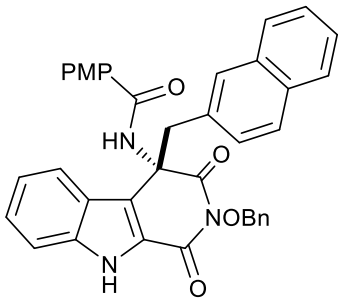
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3s** as a white solid in 83% yield (48.0 mg), m. p. 163.2 – 164.2 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.18 (s, 1H), 9.82 (s, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 9.0 Hz, 2H), 7.53 (t, J = 7.2 Hz, 3H), 7.43 – 7.40 (m, 3H), 7.37 (t, J = 7.2, 1H), 7.20 (t, J = 7.2 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.49 (d, J = 7.8 Hz, 2H), 4.88 (d, J = 9.6 Hz, 1H), 4.70 (d, J = 9.6 Hz, 1H), 3.83 (s, 1H), 3.81 (s, 3H), 3.59 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.1, 165.5, 162.1, 155.6, 138.6, 134.4, 132.2, 132.1, 131.3, 129.6, 129.4, 128.9, 128.4, 127.9, 125.9, 124.9, 123.7, 122.8, 120.9, 120.8, 120.3, 113.6, 113.5, 77.3, 61.3, 55.4, 43.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}ClN_3O_5Na^+$ 602.1453; found 602.1460.

Ethyl *N*-(2-(benzyloxy)-4-(4-nitrobenzyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3t)



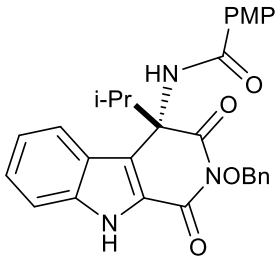
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3t** as a yellow solid in 54% yield (32.0 mg), m. p. 164.0 – 165.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.21 (s, 1H), 9.89 (s, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.54 – 7.52 (m, 3H), 7.44 – 7.37 (m, 4H), 7.21 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 9.0 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 4.90 (d, J = 9.6 Hz, 1H), 4.73 (d, J = 8.4 Hz, 1H), 3.96 (d, J = 12.6 Hz, 1H), 3.81 (s, 3H), 3.73 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.9, 165.6, 162.2, 155.5, 146.8, 141.1, 138.6, 134.4, 131.0, 129.6, 129.4, 128.8, 128.3, 126.0, 124.8, 123.5, 122.9, 122.8, 121.0, 120.8, 119.9, 113.64, 113.55, 77.3, 61.1, 55.4, 44.1. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{33}H_{26}N_4O_7Na^+$ 613.1694; found 613.1690.

Ethyl *N*-(2-(benzyloxy)-4-(naphthalen-2-ylmethyl)-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3u)



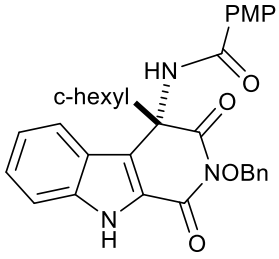
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3u** as a yellow solid in 50% yield (30.0 mg), m. p. 188.0 – 192.5 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.10 (s, 1H), 9.88 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 9.0 Hz, 2H), 7.87 – 7.82 (m, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.41 – 7.36 (m, 7H), 7.25 (t, J = 7.2 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 6.35 (d, J = 10.2 Hz, 1H), 4.76 (d, J = 9.6 Hz, 1H), 4.01 (d, J = 12.6 Hz, 1H), 3.83 (d, J = 6.0 Hz, 3H), 3.79 – 3.76 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.2, 165.5, 162.1, 155.5, 138.6, 134.4, 132.3, 131.9, 130.8, 129.6, 129.0, 128.7, 128.3, 127.4, 127.3, 127.2, 127.1, 126.2, 126.0, 125.9, 124.9, 123.7, 123.0, 120.95, 120.90, 120.7, 113.6, 113.5, 77.2, 61.6, 55.4, 44.9. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{37}H_{29}N_3O_5Na^+$ 618.1999; found 618.1993.f

Ethyl *N*-(2-(benzyloxy)-4-isopropyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3v)



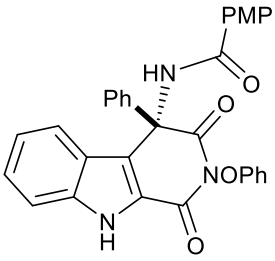
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3v** as a white solid in 52% yield (26.0 mg), m. p. 196.5 – 197.3 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.28 (s, 1H), 9.37 (s, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 6.0 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.45 – 7.39 (m, 3H), 7.28 (t, J = 8.4 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 5.09 (dd, J = 24.6, 9.6 Hz, 2H), 3.80 (s, 3H), 2.78 (quin, J = 6.6 Hz, 1H), 1.09 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.3, 166.0, 162.0, 156.5, 138.6, 134.7, 129.7, 129.3, 128.8, 128.3, 125.5, 125.2, 123.7, 123.0, 121.8, 121.6, 120.3, 113.5, 113.2, 77.3, 64.2, 55.4, 36.3, 17.7, 16.7. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{29}H_{27}N_3O_5Na^+$ 520.1843; found 520.1834.

Ethyl *N*-(2-(benzyloxy)-4-cyclohexyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3w)



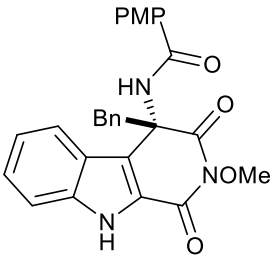
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3w** as a white solid in 37% yield (20.0 mg), m. p. 279.8 – 280.3 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.27 (s, 1H), 9.35 (s, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 6.0 Hz, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.45 – 7.39 (m, 3H), 7.28 (t, J = 8.4 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 5.10 (dd, J = 26.4, 9.6 Hz, 2H), 3.81 (s, 3H), 2.39 (t, J = 12.0 Hz, 1H), 1.99 (d, J = 12.6 Hz, 1H), 1.73 (d, J = 12.6 Hz, 1H), 1.60 (t, J = 11.4 Hz, 2H), 1.53 (d, J = 12.0 Hz, 1H), 1.27 – 1.20 (m, 1H), 1.09 – 1.01 (m, 2H), 0.98 – 0.91 (m, 1H), 0.83 – 0.76 (m, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.8, 166.1, 162.0, 156.6, 138.6, 134.7, 129.7, 129.4, 128.8, 128.3, 125.5, 125.3, 123.6, 123.1, 121.8, 121.6, 120.4, 113.5, 113.1, 77.3, 64.3, 55.4, 46.1, 27.5, 26.2, 26.0, 25.8, 25.5. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{32}H_{31}N_3O_5Na^+$ 560.2156; found 560.2164.

Ethyl *N*-(1,3-dioxo-2-phenoxy-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3x)



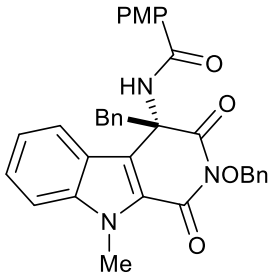
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3x** as a white solid in 97% yield (51.0 mg), m. p. 220.1 – 221.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.60 (s, 1H), 10.08 (s, 1H), 7.97 (d, J = 9.0 Hz, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.44 – 7.38 (m, 6H), 7.34 (t, J = 8.4 Hz, 2H), 7.26 (s, 2H), 7.05 (t, J = 7.8 Hz, 2H), 6.99 (d, J = 9.0 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.9, 166.2, 162.1, 158.3, 139.0, 137.1, 129.9, 129.5, 129.2, 128.7, 127.7, 126.2, 124.7, 123.3, 123.2, 121.8, 121.6, 120.9, 113.5, 113.4, 112.4, 63.6, 55.4. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{31}H_{23}N_3O_5Na^+$ 540.1530; found 540.1534.

Ethyl *N*-(4-benzyl-2-methoxy-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3y)



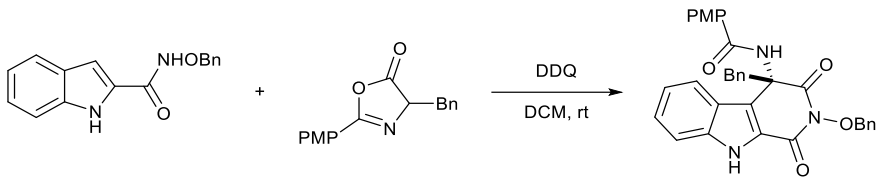
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3y** as a white solid in 83% yield (39.0 mg), m. p. 164.7 – 165.2 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.11 (s, 1H), 9.75 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 7.8 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 7.8 Hz, 1H), 7.05 – 7.01 (m, 4H), 6.44 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H), 3.79 (s, 1H), 3.59 (s, 3H), 3.55 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.8, 165.4, 162.1, 155.4, 138.5, 132.9, 129.6, 129.5, 127.8, 127.3, 125.7, 124.9, 123.8, 122.9, 120.8, 120.5, 113.6, 113.4, 63.0, 61.3, 55.4, 44.7. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{27}H_{23}N_3O_5Na^+$ 492.1530; found 492.1539.

Ethyl *N*-(4-benzyl-2-(benzyloxy)-9-methyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (3z)



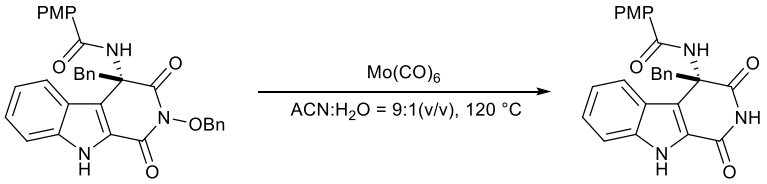
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **3z** as a white solid in 61% yield (28.0 mg), m. p. 147.2 – 148.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 7.8 Hz, 2H), 7.71 (d, J = 9.0 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.47 – 7.41 (m, 4H), 7.26 (t, J = 7.8 Hz, 1H), 7.14 (t, J = 7.2 Hz, 1H), 7.07 – 7.02 (m, 4H), 6.46 (d, J = 7.2 Hz, 2H), 4.78 (d, J = 9.0 Hz, 1H), 4.56 (s, 1H), 4.01 (s, 3H), 3.80 (s, 3H), 3.80 (s, 1H), 3.58 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.6, 165.4, 162.1, 155.9, 140.0, 134.4, 132.9, 129.61, 129.58, 129.3, 128.8, 128.4, 127.9, 127.5, 126.1, 124.8, 122.7, 122.0, 121.6, 121.2, 121.1, 113.6, 111.7, 77.2, 61.2, 55.4, 44.8, 31.2. HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{34}H_{29}N_3O_5Na^+$ 582.1999; found 582.2000.

4. Scale-up reaction and transformations of product 3a



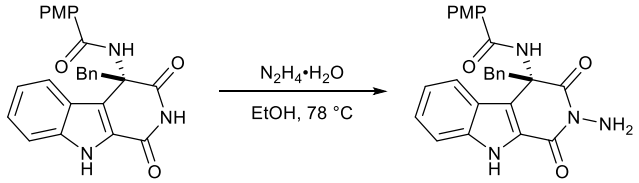
1a 2a 3a

To a mixture of *N*-alkoxy indol-2-ylamides **1a** (266.1 mg, 1.0 mmol, 1.0 equiv), azolactones **2a** (562.2 mg, 2.0 mmol, 2.0 equiv) in DCM (20.0 mL) was added DDQ (454.0 mg, 2.0 mmol, 2.0 equiv) at room temperature for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure product **3a** (480.0 mg, 88% yield) as a white solid.



3a 4a

Compound **4a** was prepared by a modified reported procedure[3]. The corresponding compound **3a** (54.5 mg, 0.1 mmol, 1.0 equiv) was dissolved in acetonitrile/water (9:1 = v/v, 1mL), $Mo(CO)_6$ (29.0 mg, 0.1 mmol, 1.0 equiv) was added. The reaction was refiux at 120 °C for 12 h. After completed (monitored by TLC), the reaction mixture was cooled to room temperature. The reaction mixture was concentrated and purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1) to afford the pure product **4a** (42.0 mg, 95% yield) as a white solid.

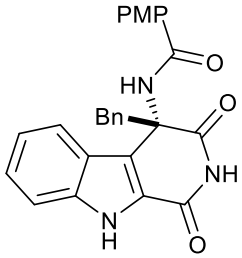


4a 5a

Compound **5a** was prepared by a modified reported procedure[4]. The corresponding

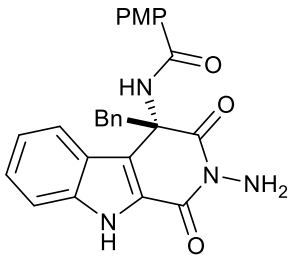
compound **4a** (43.9 mg, 0.1 mmol, 1.0 equiv) was dissolved in EtOH (20.0 mL) was added $N_2H_4 \cdot H_2O$ (10.0 mg, 0.2 mmol, 2.0 equiv) at 78 ℃. After completed (monitored by TLC), cooled down the reaction to room temperature. The reaction mixture was concentrated and purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to afford the pure product **5a** (32.0 mg, 70% yield) as a white solid.

Ethyl *N*-(4-benzyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (4a)



The residue was purified by flash chromatography (PE/EA = 1/1) giving the product **4a** as a white solid in 95% yield (42.0 mg), m. p. 316.2 – 317.0 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.86 (s, 1H), 10.89 (s, 1H), 9.52 (s, 1H), 8.05 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.10 (t, J = 7.2 Hz, 1H), 7.02 (t, J = 7.2 Hz, 4H), 6.45 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H), 3.73 (d, J = 12.6 Hz, 1H), 3.47 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 174.6, 165.1, 161.9, 159.2, 138.2, 133.6, 129.5, 127.7, 127.0, 125.4, 125.3, 125.2, 123.2, 121.7, 120.7, 120.4, 113.5, 113.2, 60.7, 55.4, 44.7. HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{26}H_{21}N_3O_4Na^+$ 462.1424; found 462.1431.

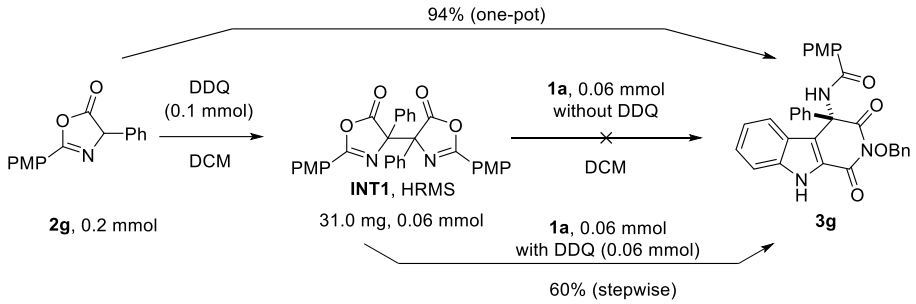
Ethyl *N*-(2-amino-4-benzyl-1,3-dioxo-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-4-yl)-4-methoxybenzamide (5a)



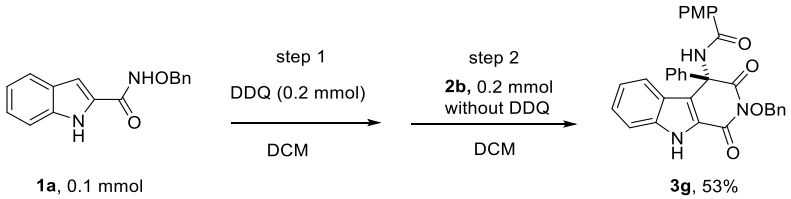
The residue was purified by flash chromatography (PE/EA = 5/1) giving the product **5a** as a white solid in 70% yield (32.0 mg), m. p. 285.0 – 285.8 ℃. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.91 (s, 1H), 9.62 (s, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 1H), 7.31 (t, J = 8.4 Hz, 1H), 7.15 (t, J = 8.4 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 7.8 Hz, 2H), 6.40 (d, J = 7.2 Hz, 2H), 5.20 (s, 2H), 3.81 (s, 3H), 3.71 (d, J = 12.0 Hz, 1H), 3.51 (d, J = 12.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.9, 166.9,

141.43, 141.40, 141.3, 136.8, 130.6, 128.1, 128.0, 127.9, 127.6, 127.1, 126.7, 126.2, 126.0, 125.9, 122.6, 115.0, 57.7, 46.2. HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{26}H_{22}N_4O_4Na^+$ 477.1533; found 477.1539.

5. Control experiments

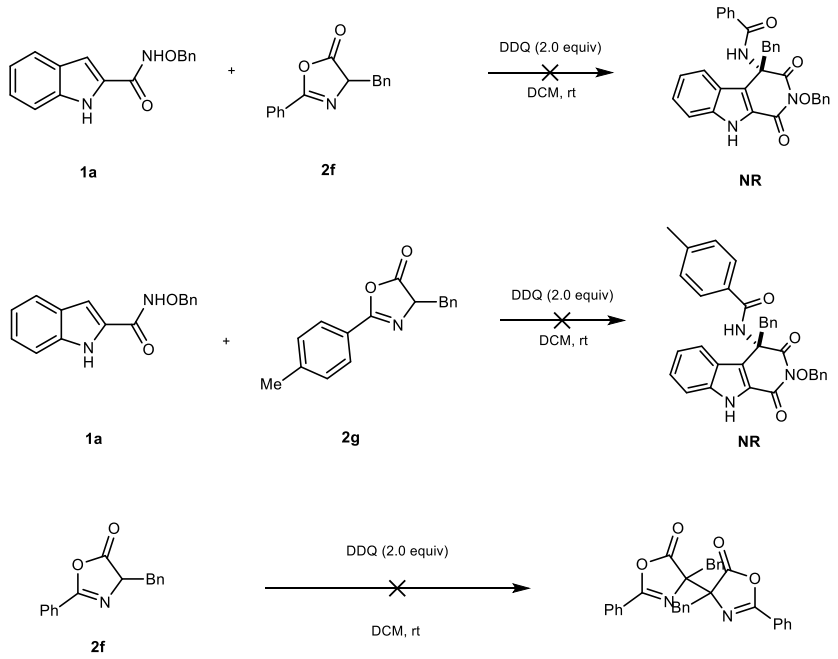


The mixture of **2g** (0.2 mmol), **1a** (0.1 mmol) in DCM (2.0 mL) was added DDQ (0.2 mmol) at room temperature for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure products **3g** (94% yield). Then, we attempted to inject the reaction using the stepwise method: the mixture of **2g** (0.2 mmol) in DCM (2.0 mL) was added DDQ (0.1 mmol) at room temperature for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 25/1) to give the coupling product **INT1** (31.0 mg). The coupling product **INT1** (0.06 mmol) and **1a** (0.06 mmol) was added to the solution for 12 h, no product was detected in the progress at last. The coupling product **INT1** (0.06 mmol), **1a** (0.06 mmol) and DDQ (0.06 mmol) was added to the solution for 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure products **3g** (60% yield).



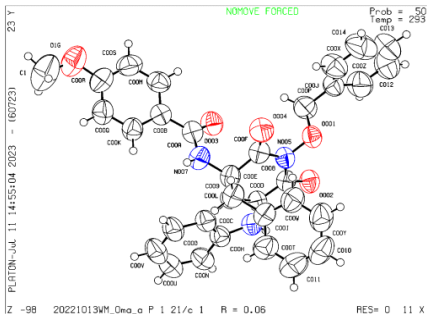
The mixture of **1a** (0.1 mmol) in DCM (2.0 mL) was added DDQ (0.2 mmol) at room temperature for 12 h, no product was detected in the progress at last. Then added **2b**

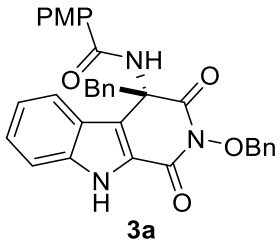
(0.2 mmol) without DDQ in the reaction for another 12 h. After completed (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (PE/EA = 5/1) to give the pure products **3g** (53% yield).



In order to investigate the impact of *p*-methoxyphenyl on azlactones, we conducted experiments where we replaced *p*-methoxyphenyl with either phenyl or *p*-methylphenyl. The results indicated that regardless of the substitution, the azlactones were degraded during the reaction, and no target products were formed. Additionally, we examined the phenyl-substituted azlactones under the presence of oxidant DDQ and observed that no dimeric intermediate was formed. Instead, it underwent destruction, leading to the formation of a polar point. As a result, we propose that the *p*-methoxyphenyl-substituted azlactones may influence the oxidation process of the reaction through electronic effects.

6. Single crystal X-ray diffraction analysis and crystal data





3a

CCDC = 2271201

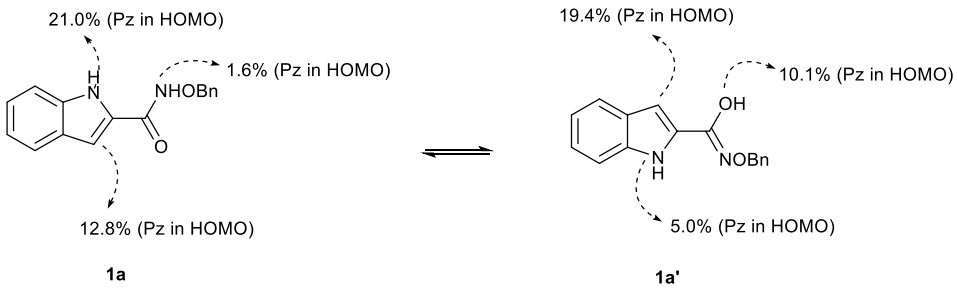
To a 5 mL tube containing **3a** (30 mg) was added a 1:3 mixture of dichloromethane and petroleum ether (4 mL). A clear solution was obtained through ultrasound treatment and was kept at room temperature for 3 day to get crystals of **3a**, which were characterized by single crystal X-ray diffraction. The data were collected by an Agilent Gemini. **3a** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

(Ellipsoid contour probability 50%)

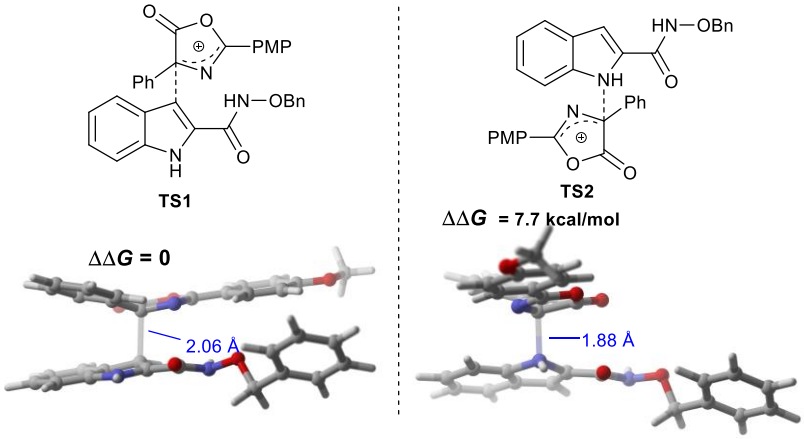
Empirical formula	$C_{33}H_{27}N_3O_5$
Formula weight	545.57
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	18.3523(6)
b/Å	15.4661(6)
c/Å	10.0487(3)
α/°	90
β/°	101.175(2)
γ/°	90
Volume/Å3	2798.13(17)
Z	4
ρcalcg/cm3	1.295

μ/mm-1	0.718
F(000)	1144.0
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.908 to 137.612
Index ranges	-22 ≤ h ≤ 22, -14 ≤ k ≤ 18, -12 ≤ l ≤ 12
Reflections collected	32786
Independent reflections	5117 [Rint =0.0840, Rsigma = 0.0441]
Data/restraints/parameters	5117/1/375
Goodness-of-fit on F^2	1.131
Final R indexes [I>=2σ (I)]	R1 = 0.0575, wR2 = 0.1433
Final R indexes [all data]	R1 = 0.1077, wR2 = 0.1782
Largest diff. peak/hole / e $Å^{-3}$	0.33/-0.19

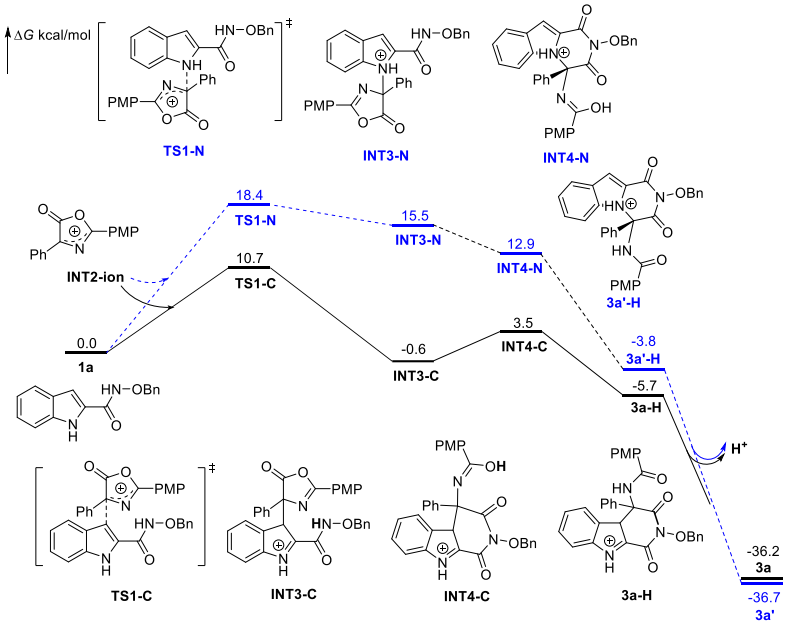
7. DFT calculations



A. Corresponding contribution of $2p_z$ to HOMO



B. Chemoselectivity Investigation



1) Computational Details

In this work, all geometry optimizations and single-point energy calculations were carried out using Gaussian 09.[1] Geometries of minima and transition states were optimized using the M06-2X functional[2] with basis set 6-31G(d) in gas phase. Vibrational frequency calculations were performed for all the stationary points to confirm if each optimized structure is a local minimum or a transition state structure, as well as deriving the thermochemical corrections for the enthalpies and free energies. Solvation energy corrections were calculated in DCM with the continuum solvation model (SMD)[3] based on the gas-phase optimized geometries. To gain more accurate results, the M06-2X functional[4] with basis set 6-311++G(d,p) was used for solvation single-point energy calculations. The integration grids defined by the 'Int=Ultrafine' keyword were used for all calculations.

2) Absolute Calculation Energies, Enthalpies, and Free Energies

Geometry	$E_{(elec\text{-}M06\text{-}2X)}$[1]	$G_{(corr\text{-}M06\text{-}2X)}$[2]	$H_{(corr\text{-}M06\text{-}2X)}$[3]	$E_{(solv,\ M06\text{-}2X)}$[4]	IF[5]
1a	-877.669638	0.227631	0.291562	-877.952347	-
1a'	-877.662470	0.226524	0.291283	-	-
TS-C	-1774.420730	0.457927	0.559982	-1775.007233	*296.91i*
TS-N	-1774.406692	0.457358	0.560144	-1774.994448	*280.10i*
INT3-C	-1774.438099	0.459758	0.562060	-1775.027075	-
INT3-N	-1774.410497	0.457816	0.562008	-1774.999469	-
INT2-ion	-896.730121	0.205716	0.267381	-897.047390	
INT4-C	-1773.909736	0.45818	0.561019	-1775.01899	
INT4-N	-1773.898961	0.459364	0.561357	-1775.00519	
3a-H	-1773.919715	0.459232	0.561597	-1775.03469	
3a′-H	-1773.928195	0.457769	0.56136	-1775.03019	
DDQH	-1485.487026	0.035346	0.088652	-1486.326328	
DDQH2	-1485.988483	0.048591	0.101794	-1486.326328	
3a	-1773.586565	0.446556	0.549322	-1774.6369	
3a′	-1773.596399	0.448095	0.549073	-1774.63917	

[1]The electronic energy calculated by M06-2X in gas phase. [2]The thermal correction to Gibbs free energy calculated by M06-2X in gas phase. [3]The thermal correction to enthalpy calculated by M06-2X in gas phase. [4]The electronic energy calculated by

M06-2X in DCM solvent. [5]The M06-2X calculated imaginary frequencies for the transition states.

3) Geometries for All Optimized Structures

1a

C	-6.26233300	-0.44186500	-0.06342000
C	-6.12374900	0.94767000	0.15290200
C	-4.88182400	1.54483200	0.23801100
C	-3.75947300	0.71617300	0.10119000
C	-3.87485400	-0.68106200	-0.11829600
C	-5.15678400	-1.25628000	-0.19861200
N	-2.42580800	1.01566600	0.14112000
C	-1.69509400	-0.13204100	-0.04544800
C	-2.54482900	-1.19909300	-0.20808900
C	-0.22622200	0.01193100	-0.03749900
O	0.31001600	1.07615800	0.21518000
N	0.47666300	-1.15494000	-0.25747300
O	1.81001100	-0.97292200	-0.57945400
C	3.92072900	-0.37145300	0.28860000
C	5.13977500	-1.02559300	0.44361300
C	6.33369600	-0.36128200	0.16645700
C	6.30731400	0.95688900	-0.27729500
C	5.08647100	1.61255800	-0.44123900
C	3.89670100	0.95323500	-0.15731300
C	2.61736500	-1.05049500	0.60214600
H	-7.25753000	-0.86989900	-0.12331700
H	-7.01498800	1.55851100	0.25473800
H	-4.77583800	2.61187600	0.40470200
H	-5.26890200	-2.32335300	-0.36470900
H	-1.98602400	1.91303900	0.29121200
H	-2.26452300	-2.23393900	-0.34817100
H	0.05908900	-1.84841500	-0.86749600
H	5.15699400	-2.05880300	0.78105300
H	7.28117900	-0.87619000	0.29107200
H	7.23591400	1.47442500	-0.49753700
H	5.06533100	2.64085900	-0.78865800
H	2.93495500	1.44488800	-0.27827500
H	2.76149100	-2.09974700	0.88866000
H	2.09531700	-0.52897900	1.41113700

1a'

C	-6.29606900	-0.82155900	0.23141200
C	-6.35256500	0.54721100	-0.10920100
C	-5.20273100	1.28905000	-0.30356600
C	-3.97780000	0.62858800	-0.14936000
C	-3.89557300	-0.74566000	0.19276200
C	-5.08627600	-1.47003000	0.38323700
N	-2.69592200	1.09716000	-0.27708300
C	-1.81364400	0.06794200	-0.02788500
C	-2.50641400	-1.07798200	0.26430000
C	-0.38112300	0.32001000	-0.10804600
O	-0.05928000	1.59530500	-0.39999800
N	0.46933300	-0.61799200	0.09001600
O	1.75822100	-0.08109500	-0.02306300
C	4.07904000	-0.53966100	-0.00971900
C	5.06186100	-0.89306200	-0.93205000
C	6.34347500	-0.35371300	-0.84056400

C	6.64541800	0.55413200	0.16952500
C	5.66362000	0.91867100	1.09042100
C	4.38845000	0.37179200	1.00330500
C	2.70203300	-1.14195800	-0.08210800
H	-7.22211100	-1.36867500	0.37509200
H	-7.31978400	1.02675900	-0.22069400
H	-5.24583500	2.34157400	-0.56551600
H	-5.04905700	-2.52299400	0.64535300
H	-2.41053100	2.03565300	-0.51263700
H	-2.06142400	-2.03308000	0.50052900
H	4.82285000	-1.59339000	-1.72810400
H	7.10194800	-0.63763000	-1.56329700
H	7.64175200	0.97912100	0.23965200
H	5.89512800	1.62754100	1.87933400
H	3.61942000	0.65175100	1.71756200
H	2.56536800	-1.70932300	-1.01047700
H	2.51291100	-1.81578600	0.76214800
H	0.91375000	1.62801000	-0.45978000

TS-C

C	-5.86322500	0.43289200	-1.83781300
C	-6.14997500	-0.87027500	-1.40136500
C	-5.13902900	-1.75013400	-1.03484700
C	-3.84136800	-1.26317400	-1.12465000
C	-3.52583100	0.03952600	-1.55224800
C	-4.55717700	0.90587300	-1.91755900
N	-2.63264500	-1.89854600	-0.82116000
C	-1.60267400	-1.09923500	-1.03218600
C	-2.08748000	0.20449600	-1.37587200
C	-0.25361000	-1.66955800	-0.70003700
O	-0.19697000	-2.70813600	-0.07080000
N	0.80708600	-1.01741200	-1.23793200
O	2.03899000	-1.33366500	-0.71816800
C	3.87633200	-2.80061400	-0.69040700
C	5.16958600	-2.56893400	-1.15364500
C	6.26688800	-2.96000200	-0.38885600
C	6.07017700	-3.57229700	0.84536000
C	4.77638300	-3.79703500	1.31675800
C	3.68236600	-3.41436200	0.55014600
C	2.67721200	-2.38114800	-1.48638400
H	-6.68140300	1.08465000	-2.12409400
H	-7.18225100	-1.19941200	-1.35497100
H	-5.35202800	-2.75771400	-0.69528700
H	-4.35001200	1.91754100	-2.24724200
H	-2.49876800	-2.83214700	-0.43548600
H	-1.48608700	0.92995000	-1.91462400
H	0.74099700	-0.03529200	-1.48305100
H	5.32013100	-2.08789200	-2.11653700
H	7.27268400	-2.78616400	-0.75696600
H	6.92435200	-3.87803600	1.44085300
H	4.62420000	-4.27653100	2.27825600
H	2.66832100	-3.58369000	0.90379800
H	2.94973500	-1.98985500	-2.47215500
H	1.96103200	-3.20100800	-1.60052700
O	-0.86805400	2.95945100	-0.06096400
C	0.02250800	2.01543400	0.38161000
N	-0.50255900	0.88493100	0.75396400
C	-1.86478600	0.98121700	0.52353100
C	-2.12633400	2.40574800	0.05576700
O	-3.12498000	2.99341600	-0.21499800
C	1.41691600	2.34883500	0.34832100

C	2.36495300	1.36279800	0.69928600
C	3.70734300	1.65045500	0.64122500
C	4.13705500	2.93516000	0.25077100
C	3.19767900	3.92442900	-0.09137400
C	1.84784500	3.62591800	-0.04435900
O	5.45815900	3.11856800	0.23286000
C	5.97002900	4.39309300	-0.13171200
H	2.02891500	0.37644200	1.00097300
H	4.45747500	0.90841100	0.89079800
H	3.51636700	4.91470000	-0.39091900
H	1.11807800	4.38376800	-0.30948200
H	7.05259000	4.30651400	-0.06390700
H	5.68364300	4.64882100	-1.15692200
H	5.61749000	5.16540800	0.55918000
C	-2.81410200	0.26324700	1.37581800
C	-2.37220700	-0.87739200	2.06862200
C	-4.15481700	0.67126200	1.47789000
C	-3.26562000	-1.60474600	2.84399400
H	-1.33133300	-1.17905500	1.99283800
C	-5.03807900	-0.06384500	2.25614900
H	-4.49666000	1.55494300	0.95150800
C	-4.59854300	-1.20205500	2.93330300
H	-2.92198700	-2.48040400	3.38418300
H	-6.07202700	0.25340000	2.33874400
H	-5.29427600	-1.77069100	3.54205700

TS-N

C	3.74427800	-3.87783100	-2.25387000
C	4.03524600	-2.51499900	-2.36844000
C	3.11874800	-1.54088200	-1.96660100
C	1.91076700	-2.00122000	-1.47815400
C	1.58928800	-3.36036700	-1.36633800
C	2.52053500	-4.31949100	-1.75302500
N	0.83548700	-1.24636000	-0.90336500
C	-0.23164500	-2.18253100	-0.67772100
C	0.21529800	-3.43889300	-0.87791900
C	-1.55004500	-1.52227700	-0.47806500
O	-1.65471100	-0.34443300	-0.78678600
N	-2.56268700	-2.31454100	-0.05343800
O	-3.72361700	-1.67786800	0.31473200
C	-5.70862500	-0.63072200	-0.41948400
C	-5.34647400	0.68543800	-0.12046500
C	-6.32057400	1.61195400	0.23011400
C	-7.66194500	1.23108000	0.27703200
C	-8.02510200	-0.07863700	-0.02036100
C	-7.04704700	-1.01053900	-0.36251700
C	-4.63739400	-1.60889800	-0.80107800
H	4.48331200	-4.60561900	-2.57074600
H	4.99122100	-2.20638100	-2.77713800
H	3.34110400	-0.48124100	-2.02781400
H	2.29804200	-5.37842500	-1.67842800
H	0.51032600	-0.40647000	-1.39503500
H	-0.36803400	-4.34545100	-0.77673700
H	-2.37011900	-3.12763100	0.52076500
H	-4.29667100	0.96455700	-0.15919000
H	-6.03858300	2.63347700	0.46442000
H	-8.42259500	1.95658100	0.54705400
H	-9.06734800	-0.37783400	0.01879000
H	-7.32741100	-2.03628400	-0.58696700
H	-5.04407800	-2.60624200	-1.00239800
H	-4.07744200	-1.26238300	-1.67658800

O	0.22120100	1.34246300	1.20188400
C	1.37783000	1.64129000	0.53164600
N	2.14376900	0.62677400	0.23938700
C	1.48934500	-0.50635600	0.69581000
C	0.20589600	-0.01635300	1.38358600
O	-0.63262200	-0.60098700	1.98858900
C	1.62372000	3.02210500	0.24221300
C	2.80879100	3.38816200	-0.43075000
C	3.05656600	4.70776700	-0.71754200
C	2.12665000	5.69900600	-0.33802000
C	0.94560000	5.34234200	0.33456200
C	0.70269000	4.01087500	0.62139800
O	2.45944900	6.94847700	-0.66079200
C	1.58010100	8.00766800	-0.30552800
H	3.51979000	2.61789300	-0.71020400
H	3.95788200	5.02344000	-1.23019700
H	0.22548400	6.09382400	0.63205600
H	-0.20666000	3.72848000	1.14094600
H	2.05652400	8.91831800	-0.66274900
H	0.60747300	7.88396000	-0.79206400
H	1.45297700	8.05827500	0.78038800
C	2.25543300	-1.59572900	1.31938300
C	3.65037600	-1.61390900	1.16861500
C	1.61008400	-2.62635200	2.02066600
C	4.38798800	-2.66465400	1.69361300
H	4.13669800	-0.79555900	0.64950700
C	2.35983100	-3.67285800	2.54503200
H	0.53699900	-2.59591800	2.16819400
C	3.74261800	-3.69717500	2.37529500
H	5.46659200	-2.67713900	1.58046800
H	1.86522400	-4.46523100	3.09632500
H	4.32273500	-4.51540800	2.78970700

INT2-ion

O	-0.06550500	1.76644500	-0.00005900
C	0.29743800	0.47408900	-0.00000300
N	-0.73869500	-0.40257900	-0.00002500
C	-1.83819500	0.31315000	-0.00007600
C	-1.46306100	1.78882500	-0.00008900
O	-2.08873500	2.79217000	-0.00013100
C	1.65029400	0.12460300	-0.00004200
C	2.01861200	-1.25212400	-0.00008800
C	3.33780800	-1.60279800	-0.00008800
C	4.33779400	-0.59460000	-0.00002000
C	3.98334500	0.77828400	-0.00003700
C	2.65671800	1.12670000	-0.00005100
O	5.57734100	-1.03300900	0.00000900
C	6.66819200	-0.10717200	0.00026400
H	1.23884400	-2.00570400	-0.00009400
H	3.66035300	-2.63739500	-0.00010600
H	4.74568100	1.54674400	-0.00006300
H	2.36744800	2.17252200	-0.00005800
H	7.56608600	-0.72029200	0.00058500
H	6.63895100	0.51356400	-0.89901100
H	6.63841300	0.51371100	0.89941700
C	-3.16895500	-0.20178100	-0.00001300
C	-3.35211000	-1.60397700	-0.00012500
C	-4.28626300	0.66286500	0.00017400
C	-4.63029500	-2.12629600	-0.00007500
H	-2.48072000	-2.24981700	-0.00025500
C	-5.56165700	0.12343700	0.00024900

H	-4.14610700	1.73753000	0.00025600
C	-5.73304000	-1.26289800	0.00011700
H	-4.78079500	-3.19991000	-0.00018700
H	-6.42570800	0.77806200	0.00040900
H	-6.73614100	-1.67765300	0.00014700

INT3-C

C	-5.86165900	0.54750900	-1.84293700
C	-6.24000000	-0.77378100	-1.58962600
C	-5.29640700	-1.73041900	-1.22218100
C	-3.99282000	-1.27964900	-1.10831800
C	-3.58650800	0.03978100	-1.32422900
C	-4.53548300	0.97156000	-1.72099500
N	-2.83197300	-2.03103200	-0.81631700
C	-1.75048300	-1.32488400	-0.81812800
C	-2.09107700	0.12686000	-1.08792100
C	-0.48805700	-2.13614300	-0.55703400
O	-0.62375700	-3.33527300	-0.39547000
N	0.65297200	-1.43799800	-0.63343800
O	1.79913100	-2.06852000	-0.21967200
C	3.45234500	-3.68948700	-0.69500900
C	4.79906900	-3.50628100	-0.99935400
C	5.76462200	-4.32810600	-0.42170100
C	5.38305400	-5.32604400	0.46985300
C	4.03559600	-5.50679400	0.78323800
C	3.07228000	-4.69305200	0.20002600
C	2.39360700	-2.82237800	-1.30563100
H	-6.61646100	1.26495300	-2.14562700
H	-7.27948600	-1.06370500	-1.69393400
H	-5.56696000	-2.76538200	-1.04474800
H	-4.27145000	2.00228900	-1.91952600
H	-2.76416900	-3.03788400	-0.62946700
H	-1.54710300	0.48195000	-1.97236200
H	0.64377000	-0.42118000	-0.46374000
H	5.09451800	-2.72340400	-1.69299100
H	6.81225800	-4.18697900	-0.66623100
H	6.13451600	-5.96594500	0.92096700
H	3.73922500	-6.28623400	1.47760200
H	2.01849200	-4.82322700	0.43334300
H	2.80467700	-2.12422500	-2.04260300
H	1.60498500	-3.42409500	-1.76927700
O	-1.00475800	3.22846600	0.06516400
C	0.08569900	2.39435200	0.05720200
N	-0.18018600	1.13892400	0.08148500
C	-1.62126300	0.98637700	0.15126700
C	-2.12558200	2.43735400	0.07262500
O	-3.23026500	2.87976800	0.04620300
C	1.38926300	3.02049900	0.01520300
C	2.54619000	2.22205600	0.08800900
C	3.79094200	2.80591200	0.04658100
C	3.91162500	4.20478500	-0.06602700
C	2.76357300	5.00569500	-0.13367100
C	1.51165100	4.40919900	-0.09102900
O	5.16449100	4.67337900	-0.09671500
C	5.36204600	6.07559700	-0.19385300
H	2.45623900	1.14455800	0.19074100
H	4.69918800	2.21735300	0.10709300
H	2.83844900	6.08252800	-0.21609600
H	0.62145500	5.02709200	-0.14004800
H	6.44027000	6.22346500	-0.19680200
H	4.93400700	6.46666000	-1.12277600

H	4.92157000	6.59181700	0.66545000
C	-2.08674700	0.31685800	1.44772100
C	-1.17358600	-0.40535000	2.22157600
C	-3.43399500	0.36096700	1.81953500
C	-1.61093900	-1.09120900	3.35182800
H	-0.12217200	-0.41852400	1.95334300
C	-3.86081100	-0.32469400	2.95394000
H	-4.14267500	0.94639600	1.24195700
C	-2.95384800	-1.05567100	3.71743800
H	-0.89583500	-1.64613600	3.94970400
H	-4.90480600	-0.27677800	3.24535400
H	-3.29071500	-1.58570000	4.60210300

INT3-N

C	3.21902200	-4.40238400	-2.38348800
C	3.69499000	-3.09039300	-2.44619700
C	2.94285800	-2.01876500	-1.95565800
C	1.71091100	-2.33986300	-1.42842200
C	1.20718400	-3.63915300	-1.35323700
C	1.96918000	-4.69626400	-1.83928900
N	0.73969000	-1.43287000	-0.80344200
C	-0.42862500	-2.28222400	-0.51167600
C	-0.14571400	-3.56014800	-0.80427000
C	-1.67481600	-1.48266700	-0.34416700
O	-1.67974800	-0.34751800	-0.79612000
N	-2.73113900	-2.12808800	0.19863800
O	-3.82793900	-1.35511200	0.49704100
C	-5.77067600	-0.28934200	-0.31810500
C	-5.33021500	1.03285400	-0.21631000
C	-6.24000400	2.05082300	0.04106300
C	-7.59506600	1.75437900	0.19100400
C	-8.03623200	0.43875700	0.08992200
C	-7.12240400	-0.58346100	-0.15847100
C	-4.76888500	-1.36925300	-0.59903100
H	3.83239900	-5.20780000	-2.77225300
H	4.66666300	-2.89549400	-2.88630300
H	3.30074100	-0.99577200	-1.98528600
H	1.60095800	-5.71565500	-1.80274200
H	0.41674400	-0.67785200	-1.43050600
H	-0.84576400	-4.38396900	-0.73557700
H	-2.57639100	-2.85801800	0.88607000
H	-4.27090000	1.24699700	-0.33295800
H	-5.89704300	3.07728300	0.12182700
H	-8.30560500	2.55078700	0.38755400
H	-9.08922700	0.20587000	0.20916400
H	-7.46344800	-1.61289600	-0.22965700
H	-5.23717300	-2.35756300	-0.66438300
H	-4.21550300	-1.16771300	-1.52304300
O	0.42795000	1.30312100	1.21415600
C	1.47510700	1.51726800	0.34234900
N	2.03854800	0.46149400	-0.13712800
C	1.36674300	-0.66094800	0.43569000
C	0.24115000	-0.04226100	1.30176300
O	-0.58762300	-0.56788900	1.97398900
C	1.81283900	2.89391600	0.07564100
C	2.88693100	3.18609900	-0.78636300
C	3.22045500	4.49288000	-1.05335700
C	2.48869800	5.54241500	-0.46296700
C	1.41907700	5.25803600	0.39821500
C	1.08854200	3.93774100	0.66242800
O	2.89229400	6.77574600	-0.78465200

C	2.20559900	7.88437700	-0.22335800
H	3.44785700	2.37173800	-1.23271200
H	4.04259400	4.75025200	-1.71124200
H	0.84851700	6.05344100	0.86046000
H	0.26212200	3.71438700	1.32842100
H	2.70036200	8.76970300	-0.61800700
H	1.15320600	7.88460900	-0.52547000
H	2.27998300	7.87641700	0.86897400
C	2.23198400	-1.59760100	1.24626700
C	3.62165200	-1.47027100	1.18376200
C	1.65280400	-2.58749700	2.04694100
C	4.42911500	-2.34118000	1.90668800
H	4.05871800	-0.68348700	0.57879500
C	2.46870700	-3.45964400	2.76050100
H	0.57466700	-2.65992000	2.13629100
C	3.85456200	-3.33981300	2.68964500
H	5.50780000	-2.23557300	1.86271000
H	2.01937700	-4.22276300	3.38693400
H	4.48633700	-4.01602000	3.25606800

INT4-C

C	-5.65004900	-0.40597800	0.34792600
C	-5.80855300	-1.75799700	0.66910200
C	-4.77100200	-2.66990400	0.48735100
C	-3.59128600	-2.14816000	-0.01489500
C	-3.40284000	-0.79959200	-0.33982300
C	-4.45070300	0.09128300	-0.16767000
N	-2.37264100	-2.82704400	-0.29944400
C	-1.48546900	-2.01602600	-0.76995000
C	-2.01254200	-0.63850200	-0.88850100
C	-0.05754200	-2.40175900	-0.96435100
O	0.28299000	-3.55789500	-1.04174300
N	0.74125400	-1.29097100	-1.07102600
O	2.07081800	-1.52974100	-1.25645800
C	3.78658400	-2.11981600	-2.77606800
C	4.85705200	-1.35190300	-3.22826900
C	6.12752700	-1.91484500	-3.32557400
C	6.32856600	-3.24182700	-2.95832300
C	5.26032700	-4.00999800	-2.49439000
C	3.99143000	-3.45164200	-2.40615400
C	2.41134200	-1.53671700	-2.67098900
H	-6.48161900	0.27312800	0.50223400
H	-6.75671900	-2.10638400	1.06325100
H	-4.88609900	-3.72156600	0.72621600
H	-4.33789300	1.14161200	-0.41651700
H	-2.16270400	-3.80658100	-0.09909700
H	-2.00874000	-0.29752600	-1.93270400
H	4.69739900	-0.31348200	-3.50615000
H	6.95848800	-1.31616700	-3.68406000
H	7.31851900	-3.68051000	-3.03263700
H	5.41901000	-5.04438800	-2.20709800
H	3.15090400	-4.03848500	-2.04327000
H	2.36416600	-0.50985800	-3.04428000
H	1.67137700	-2.15901100	-3.18793300
O	0.72410600	1.01356200	1.82436500
C	-0.04267600	-0.05724300	2.08013500
N	-0.90933000	-0.45788900	1.22317200
C	-0.98792700	0.22403700	-0.06488900
C	0.37308600	0.07258700	-0.80074800
O	1.12201300	0.95040800	-1.10506100
C	0.12787500	-0.74336400	3.37247900

C	-0.22575800	-2.09511100	3.50255900
C	-0.06531000	-2.74879000	4.70473400
C	0.44432300	-2.06118300	5.82018900
C	0.78541300	-0.70912800	5.70770500
C	0.62633500	-0.06487000	4.48582300
O	0.56292600	-2.78550200	6.94373000
C	1.08208700	-2.15099700	8.10111700
H	-0.61400700	-2.62054300	2.63642900
H	-0.31630300	-3.79704900	4.82288100
H	1.16260000	-0.15455700	6.55777400
H	0.85995400	0.99603700	4.43060600
H	1.10083100	-2.91506600	8.87612800
H	2.09815600	-1.78292800	7.92292600
H	0.43748300	-1.32353400	8.41658500
C	-1.48778400	1.65717600	-0.03509000
C	-2.09603900	2.16349600	1.11344300
C	-1.46039200	2.43232000	-1.19769400
C	-2.65841700	3.43765800	1.10325300
H	-2.14427500	1.55703900	2.01210900
C	-2.02408300	3.70353300	-1.20563500
H	-0.98060100	2.05721100	-2.09739500
C	-2.62511400	4.20930000	-0.05447300
H	-3.12473800	3.82498900	2.00334700
H	-1.98753900	4.30157000	-2.11017700
H	-3.06267200	5.20223400	-0.06100200
H	1.46460600	1.06629300	2.44947300

INT4-N

C	3.99047400	-4.00178200	-2.35504800
C	4.09795100	-2.60997100	-2.42240500
C	3.01710300	-1.77805600	-2.11878100
C	1.85121300	-2.41367800	-1.74137600
C	1.71185600	-3.80252900	-1.67512800
C	2.79716500	-4.61707600	-1.98475400
N	0.56266000	-1.80340900	-1.37809100
C	-0.31721300	-2.94634500	-1.11138900
C	0.34178600	-4.10006000	-1.27635400
C	-1.68487900	-2.69095800	-0.62849300
O	-2.55045000	-3.52466500	-0.63348100
N	-1.87765400	-1.38023500	-0.16956700
O	-3.11421500	-1.11169800	0.34639700
C	-5.12706500	0.10520700	0.07841700
C	-4.89108100	1.11579500	1.01431300
C	-5.95480300	1.68654200	1.70171300
C	-7.25803600	1.25509500	1.45283600
C	-7.49463700	0.24766400	0.52284100
C	-6.42757200	-0.33195300	-0.16009300
C	-3.96493400	-0.49522400	-0.65206100
H	4.85228500	-4.61294600	-2.60000400
H	5.04059000	-2.16079000	-2.71539300
H	3.10253000	-0.69814400	-2.15660400
H	2.71278400	-5.69748600	-1.94179200
H	0.19171300	-1.24846100	-2.16729200
H	-0.09441800	-5.07859400	-1.11798400
H	-3.86956700	1.43677000	1.20310300
H	-5.77149600	2.46923300	2.43079800
H	-8.08861800	1.70428700	1.98795700
H	-8.50728600	-0.09272300	0.33285300
H	-6.60746000	-1.12737200	-0.87852600
H	-4.27886800	-1.26086200	-1.36934600
H	-3.37070400	0.27200200	-1.16285900

O -0.20117800 0.71857900 -2.21205300
C 0.88186400 1.11571100 -1.48330600
N 1.33931000 0.35581100 -0.55921300
C 0.58502700 -0.78310000 -0.15702800
C -0.90470800 -0.41606900 0.12019200
O -1.18948000 0.64984900 0.58745000
C 1.51123800 2.38778800 -1.83351700
C 2.30747100 3.04356900 -0.87732500
C 2.90180000 4.24820800 -1.17840900
C 2.72299900 4.82919200 -2.44757000
C 1.94355300 4.17676200 -3.41246100
C 1.34542600 2.96447200 -3.09652200
O 3.33865300 6.00173300 -2.63909500
C 3.18625200 6.65321100 -3.89108000
H 2.42789200 2.59332300 0.10220000
H 3.50722900 4.78052600 -0.45340000
H 1.80935700 4.59779100 -4.40086900
H 0.78007100 2.45573100 -3.87458200
H 3.75181800 7.57978300 -3.81358400
H 3.59348300 6.04040700 -4.70222200
H 2.13297100 6.87981200 -4.08696300
C 1.21411300 -1.48199900 1.03446200
C 2.58968900 -1.34705900 1.24510400
C 0.45387400 -2.26090600 1.91304200
C 3.20002900 -2.00634800 2.30532700
H 3.16688500 -0.70608400 0.58893200
C 1.06973100 -2.91153200 2.97788200
H -0.62332000 -2.34934200 1.80697300
C 2.44257700 -2.79206700 3.17103300
H 4.26746800 -1.89440500 2.46371500
H 0.46974800 -3.50249100 3.66144300
H 2.91925600 -3.29769000 4.00445800
H -0.59739700 1.47230700 -2.68081500

3a-H

C -5.58345700 -0.18379200 0.34282200
C -5.87337200 -1.53346700 0.56367000
C -4.93164200 -2.52931000 0.30500500
C -3.70878500 -2.09333800 -0.17405900
C -3.39386400 -0.74862800 -0.41012800
C -4.34308200 0.22866400 -0.15304400
N -2.55223100 -2.86365100 -0.49794600
C -1.58694600 -2.11131900 -0.90729300
C -1.99441400 -0.68458600 -0.96463500
C -0.19745000 -2.63174000 -1.09906900
O 0.01033700 -3.81522500 -1.22564800
N 0.70295500 -1.60731800 -1.13449100
O 2.00990700 -1.92122100 -1.34368700
C 3.79866200 -2.01984900 -2.89178000
C 4.50236200 -0.86625600 -2.53579500
C 5.88722900 -0.83856000 -2.64040600
C 6.57359900 -1.96027900 -3.10609300
C 5.87497400 -3.11072000 -3.45929900
C 4.48701700 -3.14236600 -3.34587600
C 2.30689100 -2.02837900 -2.76725300
H -6.34116500 0.56120900 0.56011900
H -6.84925700 -1.81520600 0.94323500
H -5.14979000 -3.57856500 0.47192400
H -4.12510400 1.27784900 -0.32739100
H -2.42867100 -3.86964200 -0.36037900
H -1.98480300 -0.32369300 -2.00271900

H	3.95515700	-0.00073000	-2.17065400
H	6.43367900	0.05704900	-2.36310500
H	7.65527700	-1.93580700	-3.19229700
H	6.40870900	-3.98452800	-3.81845500
H	3.93821200	-4.04184400	-3.61237400
H	1.85569300	-1.16291400	-3.26271200
H	1.86669100	-2.95641300	-3.14618200
O	1.35767900	-0.26824300	1.38519200
C	0.30489300	-0.56061200	1.91635700
N	-0.86924700	-0.60556700	1.14773800
C	-0.89429100	0.06953300	-0.14470700
C	0.42720800	-0.21188200	-0.91909000
O	1.12745300	0.61711300	-1.41082500
C	0.16819700	-0.91063400	3.34720100
C	-0.98724500	-1.47914600	3.90732900
C	-1.04113100	-1.77291800	5.25454500
C	0.06464500	-1.50420500	6.07857100
C	1.22554800	-0.94674100	5.52844000
C	1.26725600	-0.66041800	4.17116300
O	-0.08838500	-1.82189000	7.37364500
C	0.99929400	-1.59194400	8.25506400
H	-1.84574600	-1.73297600	3.28997200
H	-1.91891800	-2.22111800	5.70639900
H	2.09079600	-0.73786100	6.14531100
H	2.16046000	-0.23326700	3.72689100
H	0.66157500	-1.92179700	9.23591800
H	1.87702800	-2.17314100	7.95328700
H	1.25451400	-0.52757700	8.29271100
C	-1.19854100	1.55591100	-0.08320100
C	-1.36877900	2.20226300	1.14006300
C	-1.36364600	2.27905600	-1.26977700
C	-1.71075600	3.55327000	1.17724000
H	-1.22294500	1.66933400	2.07472300
C	-1.70727600	3.62426600	-1.23064500
H	-1.19704700	1.80244800	-2.23246100
C	-1.88730400	4.26381000	-0.00430400
H	-1.83386500	4.04712400	2.13531100
H	-1.82485600	4.17644700	-2.15707100
H	-2.15421700	5.31494900	0.02641200
H	-1.73102200	-0.48123200	1.67030400

3a′-H

C	3.79203500	-4.20461000	-2.54884200
C	3.92978900	-2.81748300	-2.65666600
C	2.89433300	-1.95163100	-2.29649300
C	1.74629000	-2.54598600	-1.80910000
C	1.57004900	-3.92992800	-1.72156700
C	2.60927400	-4.77957300	-2.09091100
N	0.49955700	-1.89625400	-1.39717200
C	-0.40869700	-3.00437800	-1.09445300
C	0.20739100	-4.18080000	-1.26889500
C	-1.76287000	-2.70875100	-0.59499100
O	-2.63922500	-3.52781000	-0.53915400
N	-1.93275300	-1.36975000	-0.20791900
O	-3.15720900	-1.03933100	0.29730300
C	-5.16527100	0.16735000	-0.03607800
C	-4.93450300	1.26473900	0.79773600
C	-5.99509500	1.86760500	1.46217200
C	-7.29127600	1.38063200	1.29174400
C	-7.52342200	0.28708700	0.46323300
C	-6.45885800	-0.32350900	-0.19595400

C -4.00585000 -0.47004200 -0.73767400

H 4.61690300 -4.84390100 -2.84403300

H 4.85628000 -2.40104000 -3.03673400

H 2.99575400 -0.87688500 -2.39196100

H 2.49459900 -5.85662500 -2.03485500

H 0.15103200 -1.25380300 -2.16650400

H -0.25753100 -5.14351100 -1.09661300

H -3.91879500 1.63163400 0.92399700

H -5.81538400 2.71943200 2.11016700

H -8.12016900 1.85534200 1.80712700

H -8.53085200 -0.09434100 0.33279500

H -6.63494400 -1.18358100 -0.83654800

H -4.32068700 -1.27372300 -1.41091100

H -3.40867700 0.26643200 -1.28679000

O 0.09260600 0.41914200 -2.51950100

C 0.86975700 0.96482700 -1.72612300

N 1.31946100 0.22553600 -0.64297800

C 0.54232100 -0.89075900 -0.20646900

C -0.93363900 -0.42912800 0.01153900

O -1.15485400 0.68119200 0.40697200

C 1.39095200 2.32033300 -1.91275600

C 1.97834300 3.07045400 -0.87850700

C 2.43981900 4.34585500 -1.11949600

C 2.32532200 4.90681100 -2.40452700

C 1.72853400 4.17243600 -3.43914900

C 1.26247200 2.89269500 -3.18219800

O 2.80762700 6.14786600 -2.53606300

C 2.70039300 6.78759100 -3.79938100

H 2.03826900 2.68646900 0.13641900

H 2.88143800 4.94931300 -0.33469500

H 1.62320000 4.59147700 -4.43202700

H 0.79003400 2.31510200 -3.96994900

H 3.14311900 7.77335900 -3.67018900

H 3.25247100 6.23316300 -4.56542100

H 1.65155900 6.89029200 -4.09622200

C 1.11415700 -1.53837200 1.03712700

C 2.50001800 -1.70677100 1.14675300

C 0.28092200 -1.96549700 2.07593100

C 3.04174500 -2.30563500 2.27839700

H 3.15785800 -1.37493500 0.34930200

C 0.83111100 -2.56209400 3.20624800

H -0.79445600 -1.81942200 2.03401200

C 2.20806500 -2.73642200 3.30774100

H 4.11636200 -2.43146300 2.35619700

H 0.17808200 -2.88283500 4.01053100

H 2.63276800 -3.19970900 4.19214600

H 1.88379300 0.67181900 0.06788700

DDQH

C -0.11330000 0.40940100 0.03158000

C 1.33283600 0.46215400 0.01459700

C 2.05977900 1.67120700 -0.06259900

C 1.42084000 2.90149900 -0.12813400

C 0.01248900 2.90229100 -0.11478500

C -0.72314100 1.73909700 -0.04003100

O 2.17152500 4.04155000 -0.20266800

H 1.56594000 4.79694900 -0.23128500

O -0.77866000 -0.63146200 0.09872400

Cl -0.77372000 4.47069000 -0.19791000

Cl -2.45394300 1.77950000 -0.02562900

C 3.49640600 1.66213400 -0.07541700

C 2.02893500 -0.78128600 0.08062600

N 4.65444200 1.66096900 -0.08598200

N 2.60776900 -1.78577300 0.13385300

DDQH2

C 0.00491400 0.45172900 0.14909400

C 1.40189600 0.46394700 0.07807100

C 2.10048500 1.67375900 -0.06242300

C 1.41272800 2.88971600 -0.13447800

C 0.01391200 2.87241900 -0.06380700

C -0.67944100 1.67170500 0.07602700

O 2.13643900 4.01156100 -0.26864600

H 1.55251000 4.78630000 -0.30597500

O -0.60497100 -0.73579100 0.28381000

H -1.56794700 -0.61745400 0.31947900

Cl -0.82597900 4.38114600 -0.15697000

Cl -2.40623800 1.64468800 0.16329800

C 3.53259000 1.68557100 -0.13557300

C 2.10757100 -0.78229100 0.15094000

N 4.68727300 1.69243900 -0.19447200

N 2.67881700 -1.78584100 0.20902100

3a

C -5.62695700 0.05301100 -0.05922600

C -6.14737200 -1.15570500 -0.57186700

C -5.32062900 -2.19017600 -0.96275600

C -3.94031400 -1.99523800 -0.82596900

C -3.39585200 -0.78719100 -0.30988000

C -4.26769500 0.25075500 0.07384300

N -2.89787200 -2.83741600 -1.13017600

C -1.72659400 -2.20038300 -0.83004100

C -1.97142600 -0.95088100 -0.33320600

C -0.40581700 -2.78627400 -1.06509100

O -0.22209600 -3.90212000 -1.50081900

N 0.62513500 -1.88709200 -0.78442900

O 1.88844400 -2.27287000 -1.14133700

C 3.57279000 -2.10118800 -2.79836300

C 4.27397900 -1.04291500 -2.21349000

C 5.64128700 -0.91499600 -2.42592300

C 6.31581600 -1.83746800 -3.22622100

C 5.62020700 -2.89225900 -3.80821500

C 4.25051300 -3.02612800 -3.58840900

C 2.09287900 -2.21349400 -2.57015000

H -6.31357700 0.84192400 0.22951500

H -7.22249500 -1.27242400 -0.66372700

H -5.72034200 -3.11750100 -1.36036100

H -3.87187300 1.18634200 0.45651700

H -2.94615500 -3.75869000 -1.54181600

H 3.73334400 -0.33464200 -1.59141000

H 6.18397400 -0.09346100 -1.96850400

H 7.38389400 -1.73396000 -3.39230700

H 6.14257100 -3.61586200 -4.42644100

H 3.70548400 -3.85618100 -4.03072300

H 1.57199900 -1.32862700 -2.95176600

H 1.67493400 -3.11492000 -3.02863000

O 1.28660200 0.58822900 1.94325000

C 0.41668000 -0.15215700 2.36312400

N -0.65453800 -0.52467300 1.58847000

C -0.84074200 -0.10590400 0.20001100

C 0.45136200 -0.48994000 -0.58805700

O 1.27206800 0.28909700 -0.98005400

C 0.42640700 -0.69825800 3.75588400

C	-0.27273800	-1.84592700	4.15136700
C	-0.21075900	-2.29129800	5.45946800
C	0.55527000	-1.59391700	6.40235500
C	1.26890700	-0.45588000	6.01639100
C	1.20218700	-0.02473300	4.69592400
O	0.54755800	-2.10411700	7.65645900
C	1.32659900	-1.44958000	8.63570100
H	-0.84053500	-2.42625300	3.42897800
H	-0.73434900	-3.18484500	5.78126700
H	1.87558300	0.09198700	6.72728200
H	1.76031500	0.84735600	4.37058600
H	1.18961000	-2.01495100	9.55692400
H	2.38816000	-1.44777900	8.36221700
H	0.98924400	-0.41746200	8.78706100
C	-1.14137400	1.37921600	0.02862600
C	-1.31007300	2.22779200	1.11791600
C	-1.34301200	1.87350100	-1.26184400
C	-1.68296400	3.55652400	0.91972100
H	-1.15977200	1.85515500	2.12489500
C	-1.71057000	3.19809900	-1.46029100
H	-1.21641700	1.21274700	-2.11589300
C	-1.88523200	4.04444200	-0.36661200
H	-1.81165500	4.20966300	1.77722100
H	-1.86414600	3.56944600	-2.46857100
H	-2.17521600	5.07936700	-0.51888500
H	-1.43320000	-1.00544300	2.01491800

3a′

C	4.07418000	-3.61720400	-2.80770400
C	4.29091300	-2.64329100	-1.80990100
C	3.24204000	-2.07336800	-1.11295700
C	1.94717800	-2.50033400	-1.43886800
C	1.70769200	-3.48198300	-2.43263500
C	2.79866500	-4.04135500	-3.12103000
N	0.72615500	-2.12782700	-0.91569800
C	-0.26015200	-2.84212500	-1.57137200
C	0.29345600	-3.68183300	-2.49551900
C	-1.67729300	-2.66191700	-1.25720700
O	-2.57989600	-3.23470800	-1.81742500
N	-1.91643600	-1.75551100	-0.20871600
O	-3.22578800	-1.53129600	0.11525600
C	-5.01129100	0.01224500	-0.12295100
C	-4.81234200	0.66843900	1.09505800
C	-5.88442800	1.26783700	1.74516600
C	-7.16023300	1.22193000	1.18242900
C	-7.36121500	0.56868600	-0.02919700
C	-6.28797900	-0.04062000	-0.67672900
C	-3.83769000	-0.61247300	-0.82090000
H	4.92679600	-4.03782500	-3.33069600
H	5.30671100	-2.33680900	-1.58096500
H	3.41606600	-1.33878500	-0.33432900
H	2.63276400	-4.79381900	-3.88579700
H	-0.26391500	-4.34983300	-3.13568700
H	-3.81162600	0.69189300	1.51824100
H	-5.72750100	1.77442100	2.69270100
H	-7.99612400	1.69262800	1.69121600
H	-8.35350000	0.52479500	-0.46759900
H	-6.44342200	-0.56333300	-1.61700500
H	-4.13862400	-1.16893200	-1.71347500
H	-3.08975300	0.13984400	-1.09560500
O	-0.51222200	0.36818500	-1.98453200

C 0.50178800 0.80805000 -1.46209300
N 1.08280800 0.15266900 -0.40468800
C 0.50250000 -1.08404600 0.06673100
C -1.02007100 -0.82976000 0.29548500
O -1.36721700 0.11330100 0.96071500
C 1.17166700 2.05722800 -1.91267800
C 2.52710600 2.32426400 -1.68029100
C 3.09531800 3.50324300 -2.12623900
C 2.31426300 4.44116700 -2.81482800
C 0.96424300 4.17708600 -3.06565500
C 0.40845000 2.98401700 -2.61830600
O 2.95796200 5.56537900 -3.20316300
C 2.21753800 6.53524000 -3.91562300
H 3.15666100 1.58879500 -1.18614300
H 4.14523500 3.72452500 -1.96916200
H 0.34637800 4.88558400 -3.60378600
H -0.63460900 2.75504100 -2.81130000
H 2.91287100 7.34577900 -4.13086600
H 1.83022000 6.12621800 -4.85590700
H 1.38440600 6.91808700 -3.31487700
C 1.09664800 -1.44658200 1.43156300
C 1.48960700 -2.75327300 1.71706100
C 1.20151600 -0.46057200 2.41753100
C 2.01028800 -3.06471300 2.97060200
H 1.39600100 -3.52671800 0.96181500
C 1.72481600 -0.77719300 3.66645300
H 0.83296700 0.54144100 2.21904900
C 2.13555500 -2.07878400 3.94412800
H 2.31890100 -4.08333600 3.18224200
H 1.80106100 -0.00632500 4.42660400
H 2.54371300 -2.32463700 4.91933300
H 1.77003900 0.61260100 0.17423600

4) Reference

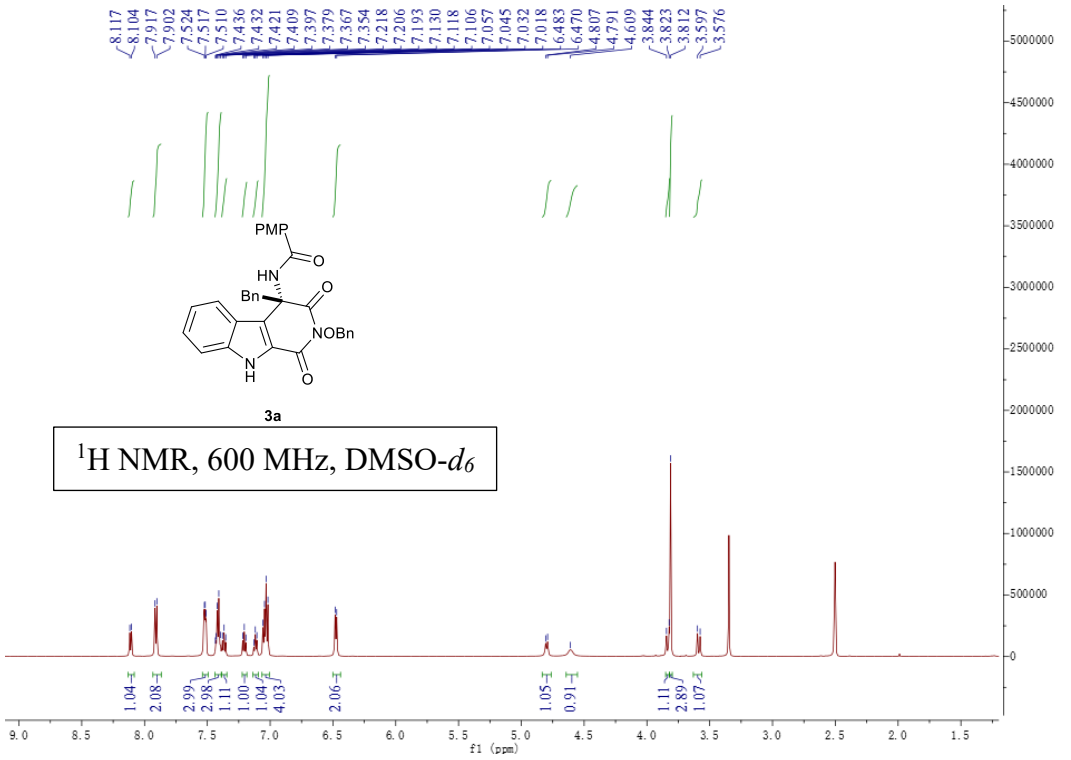
1) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2009.

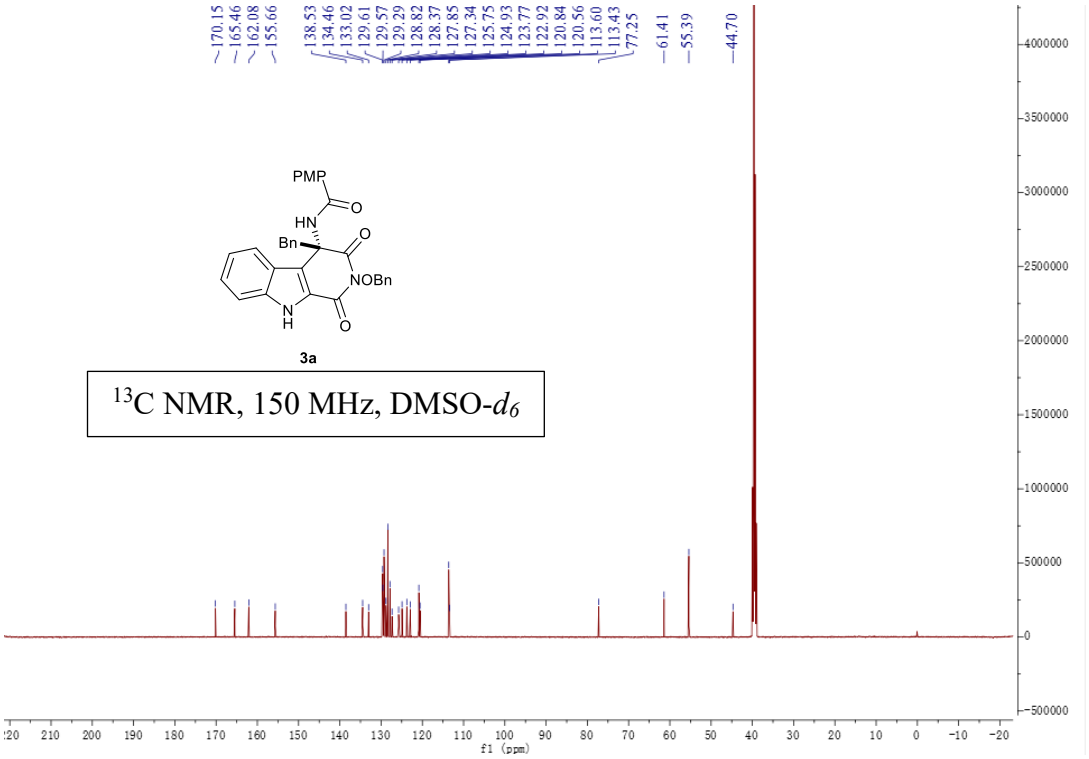
2) a) Becke, A. D., *Phys. Rev. A* **1988,** *38*, 3098-3100; b) Becke, A. D., *J. Chem. Phys.* **1993,** *98*, 5648-5652; c) Grimme, S.; Ehrlich, S.; Goerigk, L., *J. Comput. Chem.* **2011,** *32*, 1456-1465.

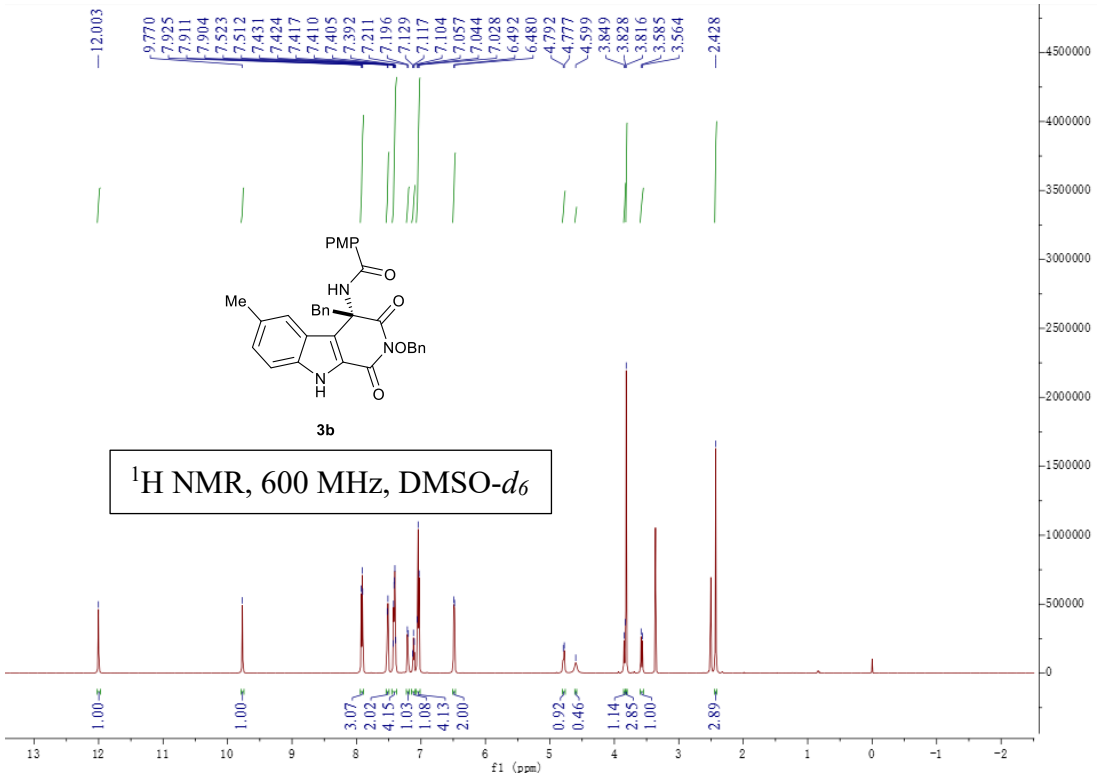
3) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G., *J. Phys. Chem. B* **2009,** *113*, 6378-6396.

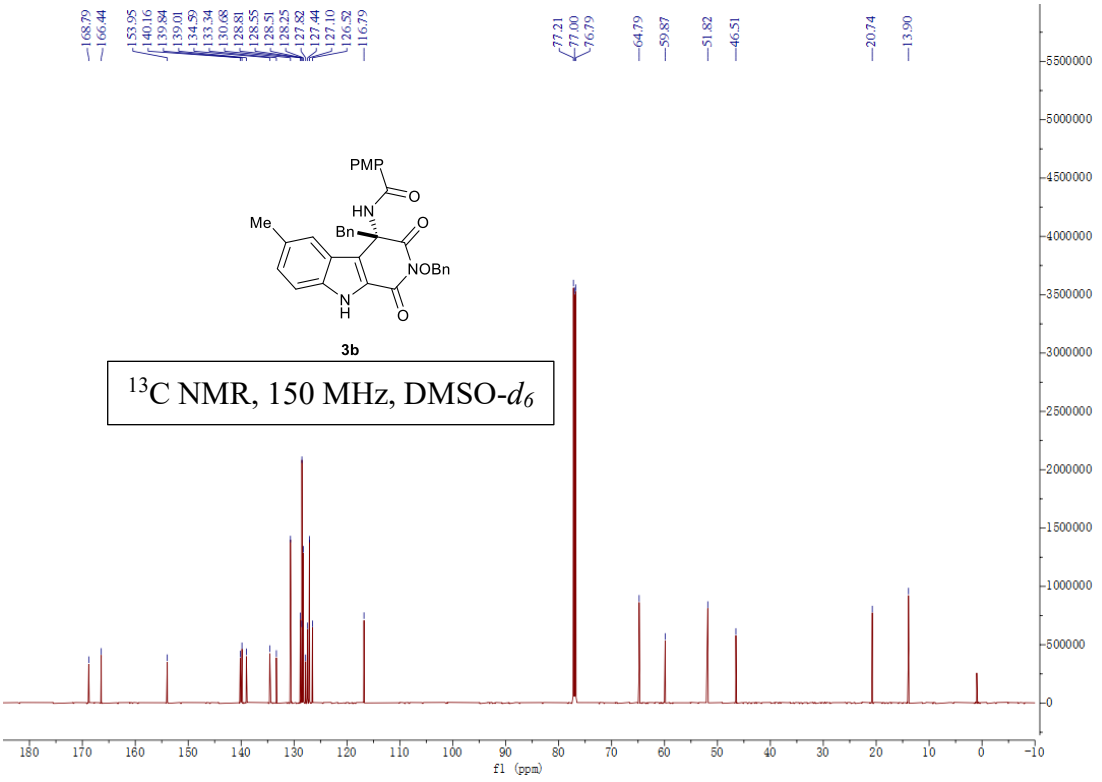
4) Zhao, Y.; Truhlar, D. G., *J. Chem. Phys.* **2006,** *125*, 194101.

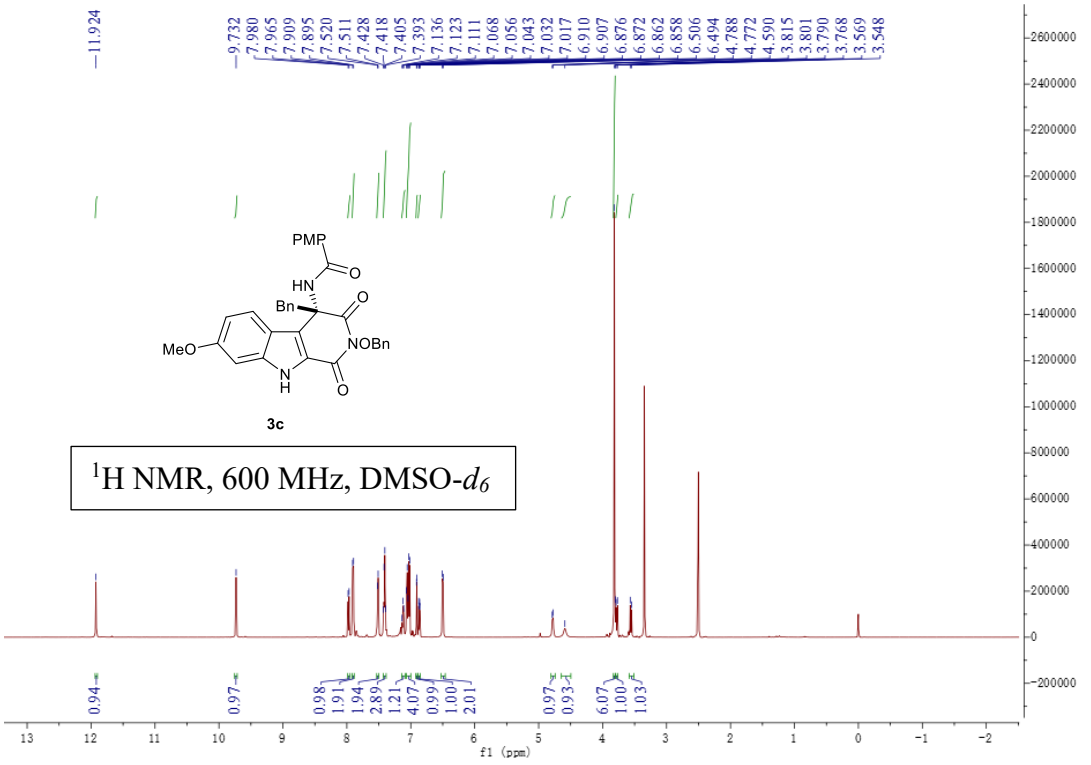
8. ^{1}H NMR and ^{13}C NMR spectra





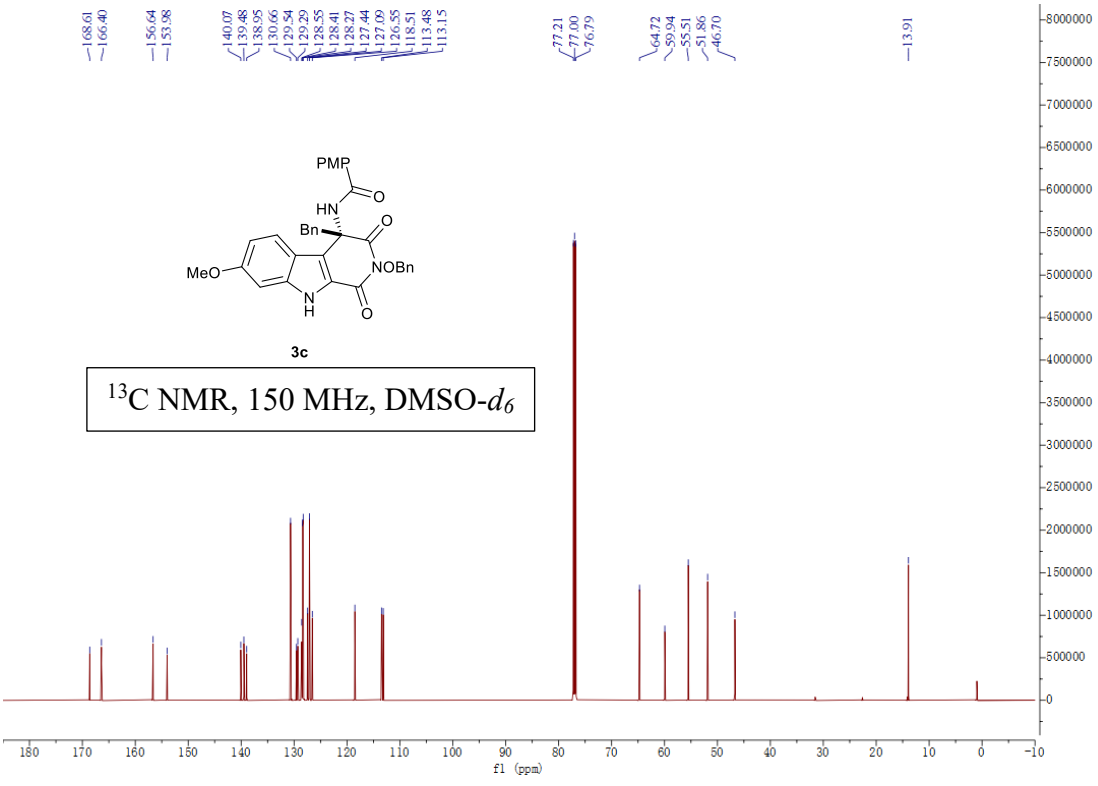

12.003
9.770
7.925
7.911
7.904
7.523
7.512
7.431
7.424
7.417
7.410
7.405
7.392
7.211
7.196
7.129
7.117
7.104
7.057
7.044
7.028
6.492
6.480
4.792
4.777
4.599
3.849
3.828
3.816
3.585
3.564
2.428
PMP
HN
Me
Bn
NOBn
N
H
O
3b
1H NMR, 600 MHz, DMSO-d6
1.00
1.00
3.07
2.02
4.15
1.03
1.08
4.13
2.00
0.92
0.46
1.14
2.85
1.00
2.89
f1 (ppm)


168.79
166.44
153.95
140.16
139.84
139.01
134.59
133.34
130.68
128.81
128.55
128.51
128.25
127.82
127.44
127.10
126.52
116.79
77.21
77.00
76.79
64.79
59.87
51.82
46.51
20.74
13.90
PMP
HN
Me
Bn
NOBn
N
H
O
3b
13C NMR, 150 MHz, DMSO-d6
f1 (ppm)



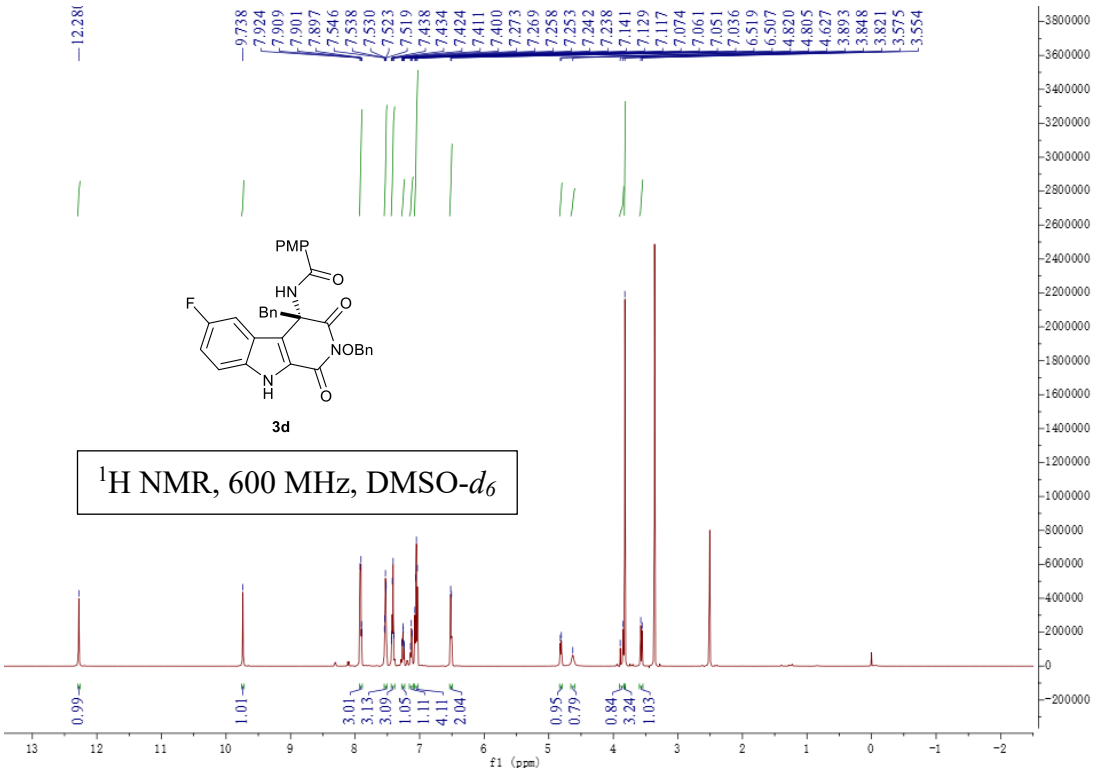
3c

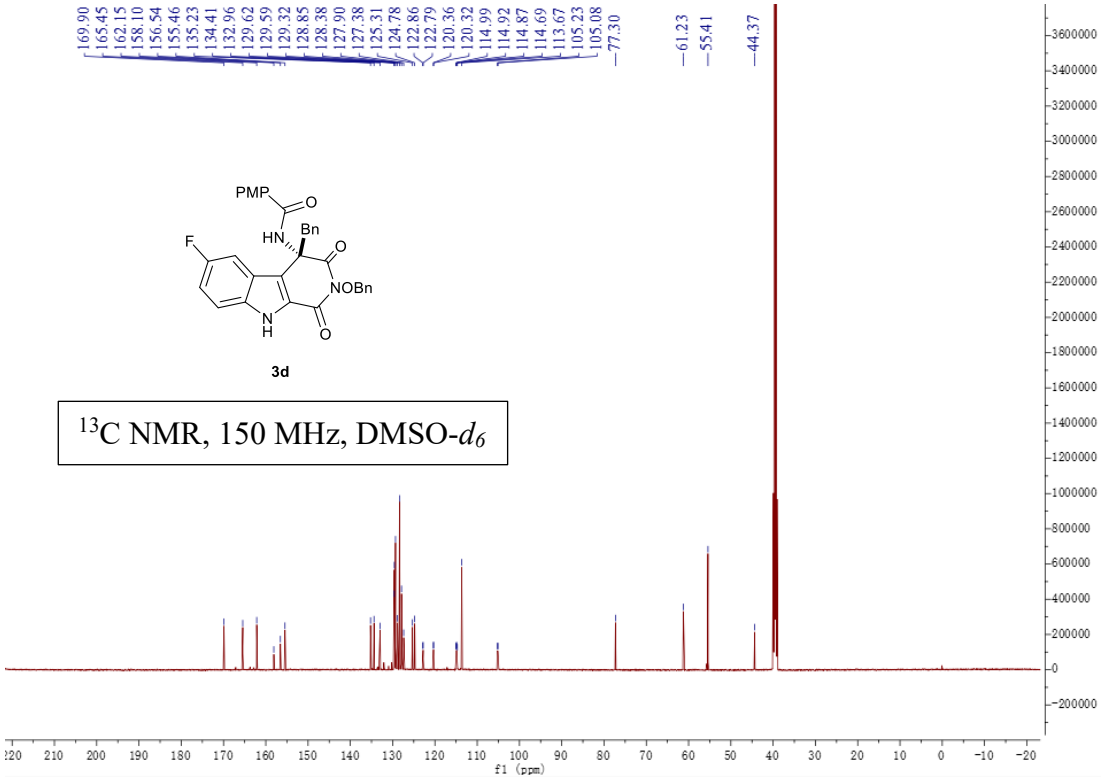
^{1}H NMR, 600 MHz, DMSO-d_6

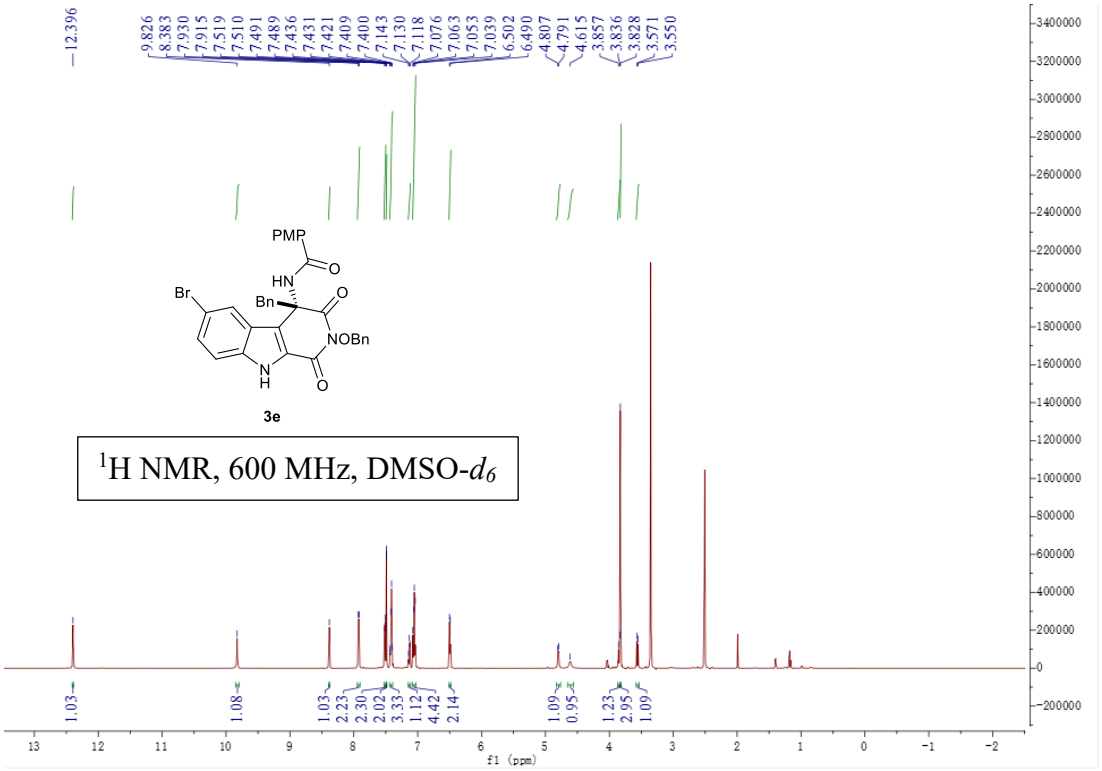


3c

^{13}C NMR, 150 MHz, DMSO-d_6

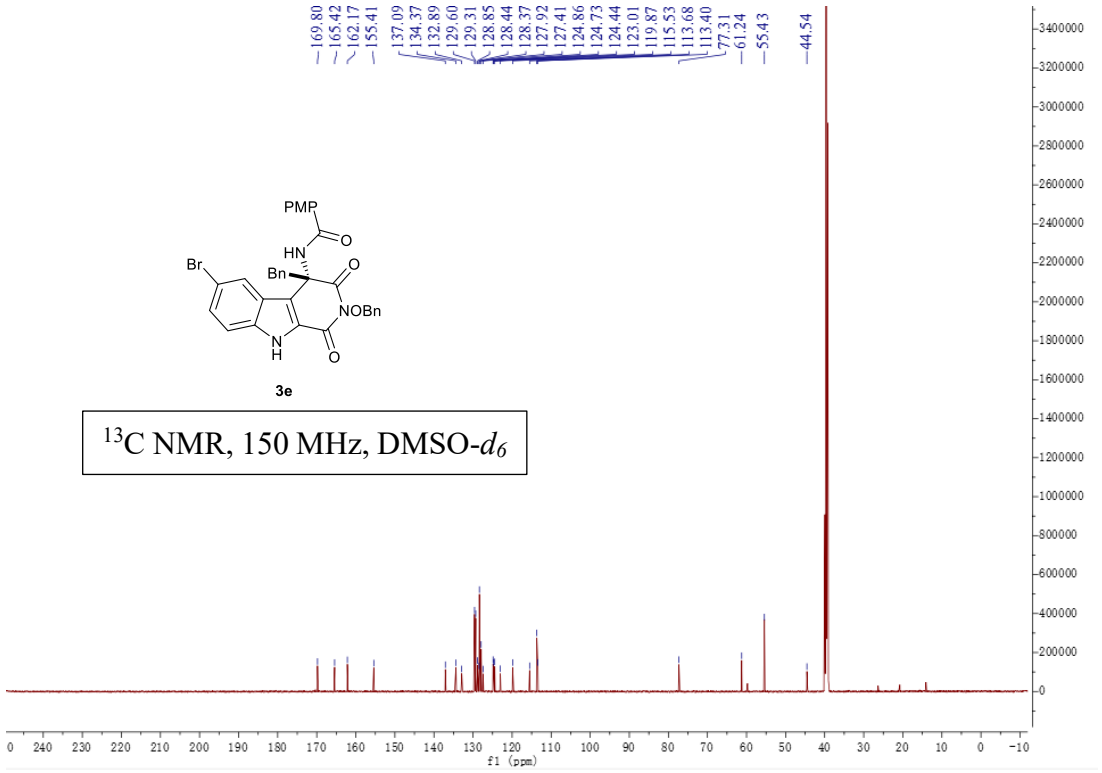

PMP
HN
Bn
F
NOBn
N
H
3d
^{1}H NMR, 600 MHz, DMSO-d_6
f1 (ppm)


PMP
HN
Bn
F
NOBn
N
H
3d
^{13}C NMR, 150 MHz, DMSO-d_6
f1 (ppm)



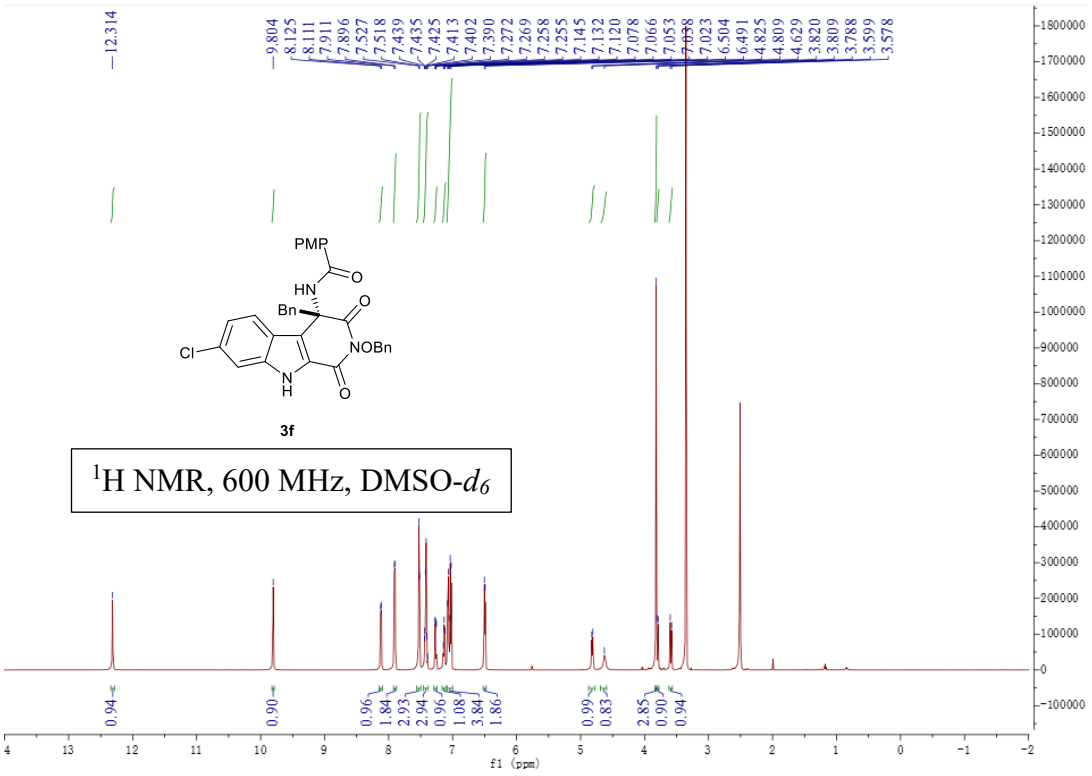
3e

^{1}H NMR, 600 MHz, DMSO-d_6

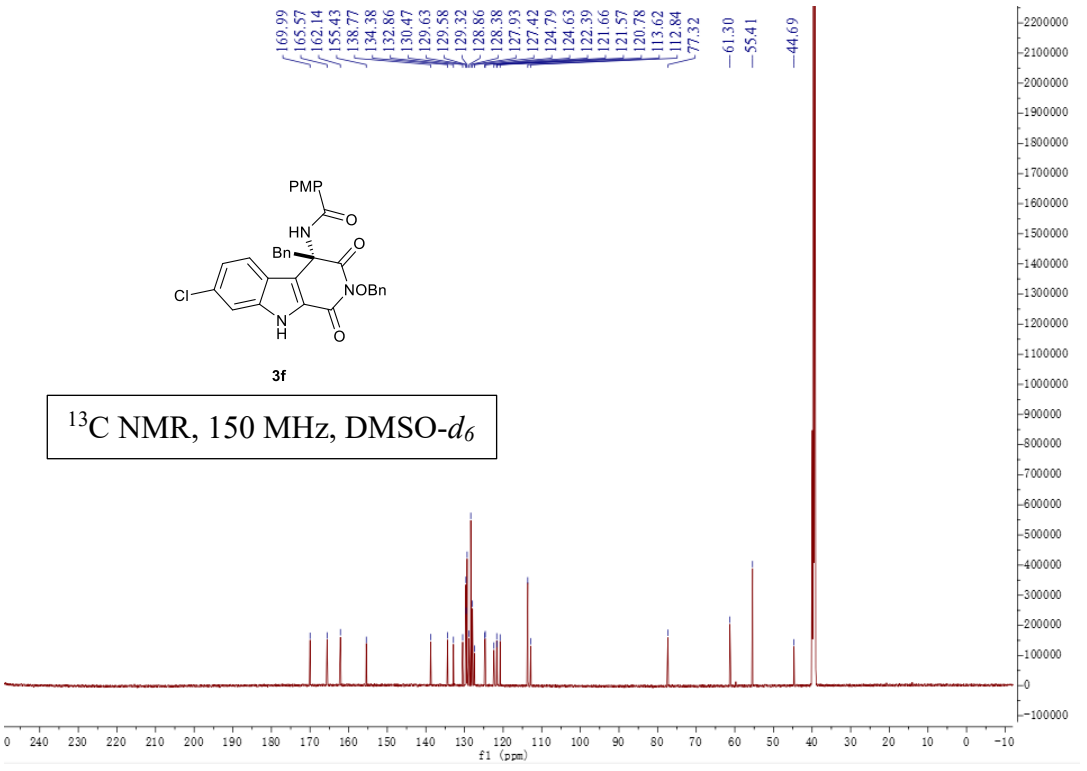


3e

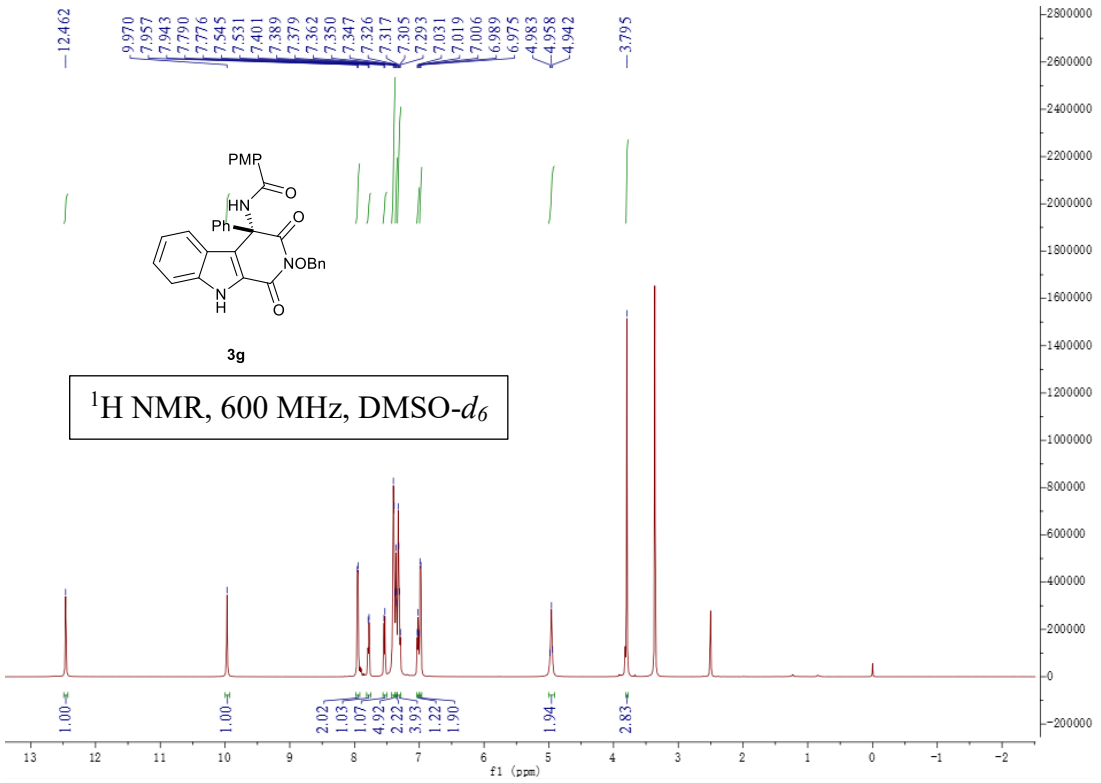
^{13}C NMR, 150 MHz, DMSO-d_6



^{1}H NMR, 600 MHz, DMSO-d_6

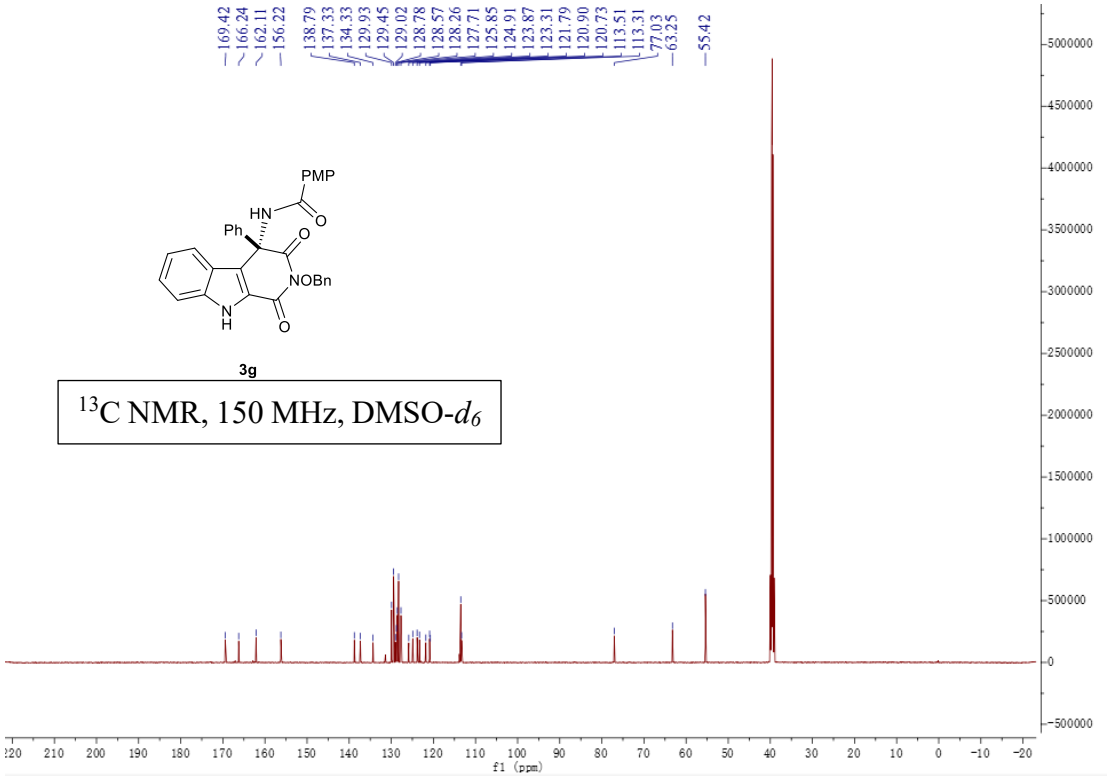


^{13}C NMR, 150 MHz, DMSO-d_6



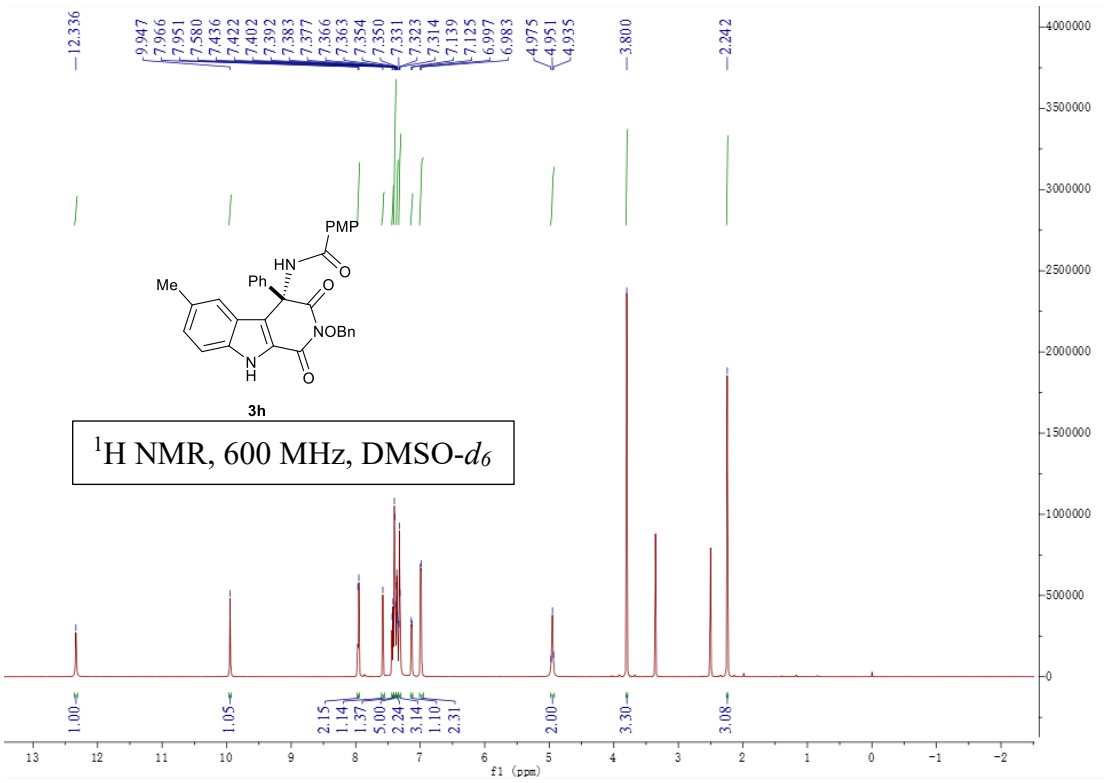
3g

^{1}H NMR, 600 MHz, DMSO-d_6



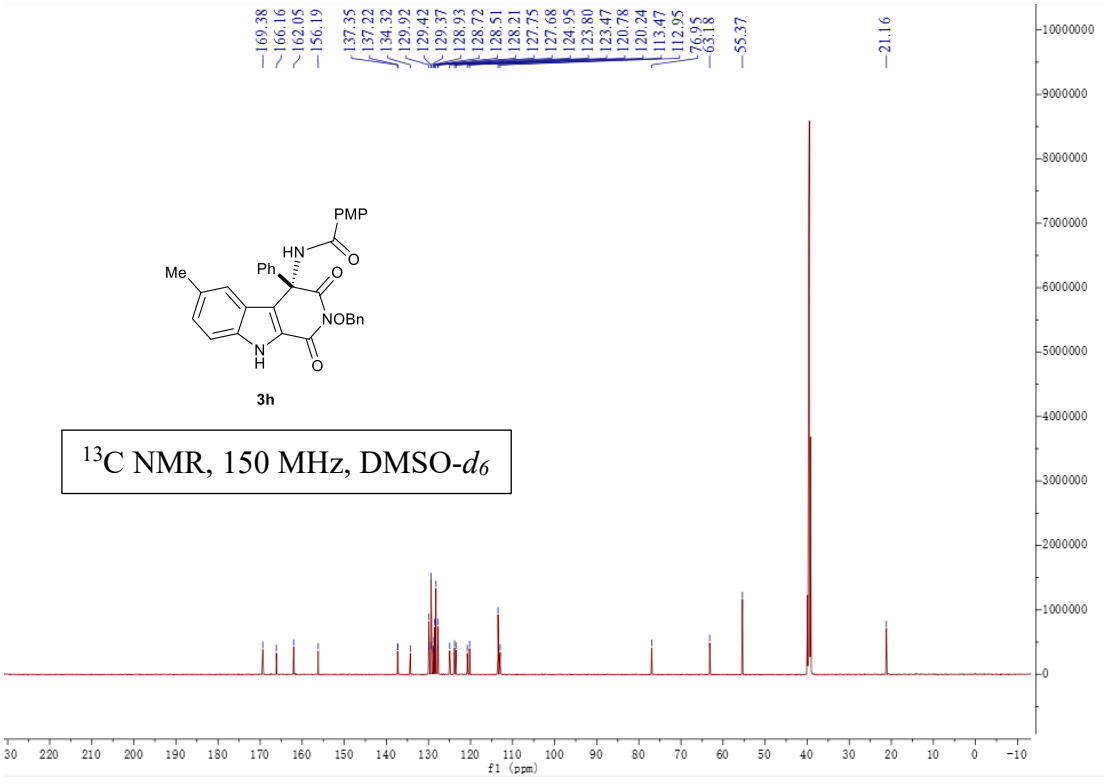
3g

^{13}C NMR, 150 MHz, DMSO-d_6



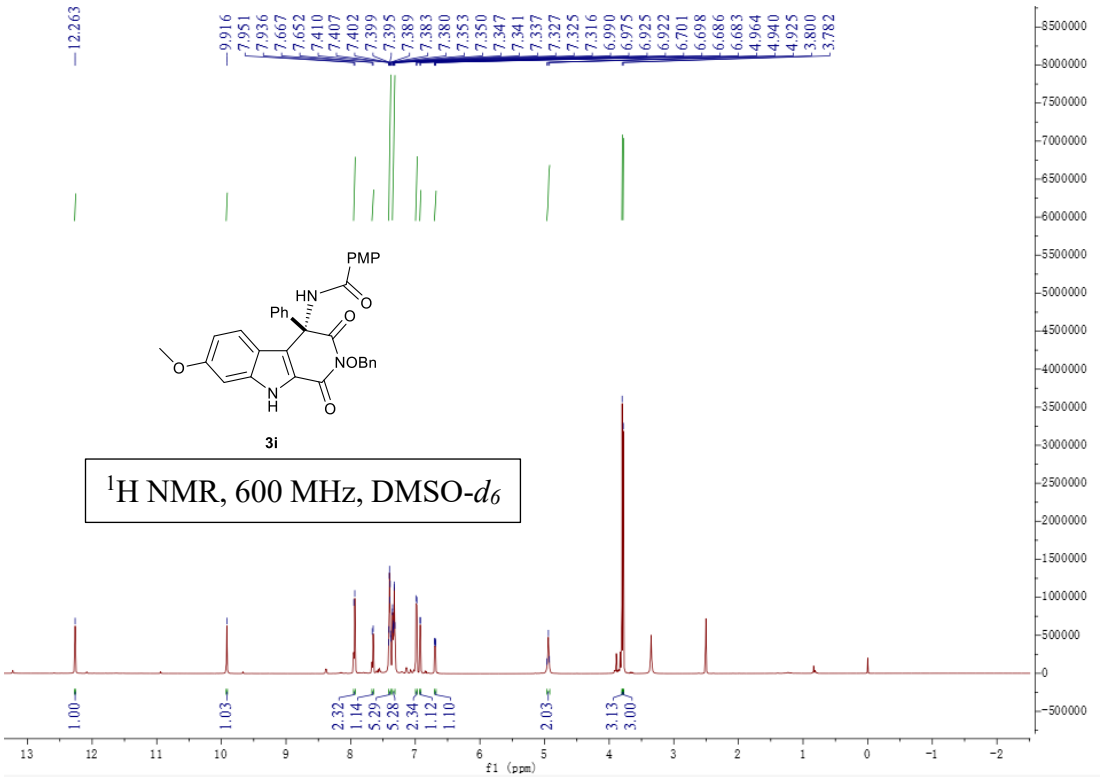
3h

^{1}H NMR, 600 MHz, DMSO-*d*$_6$

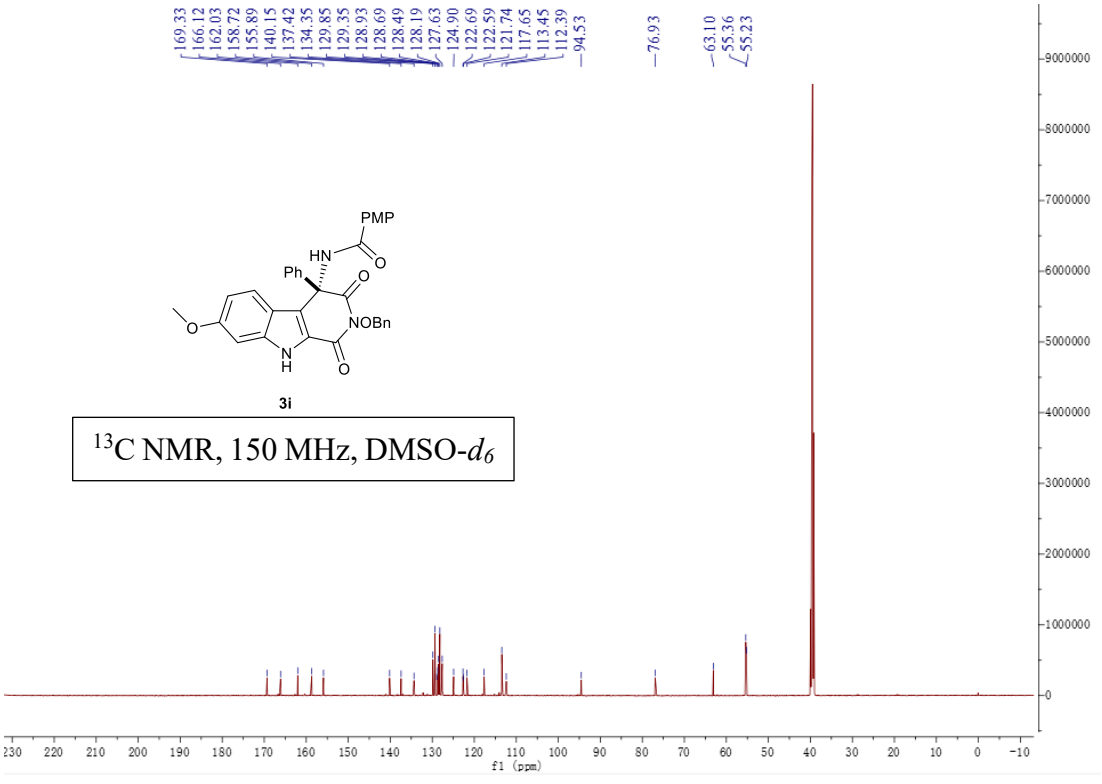


3h

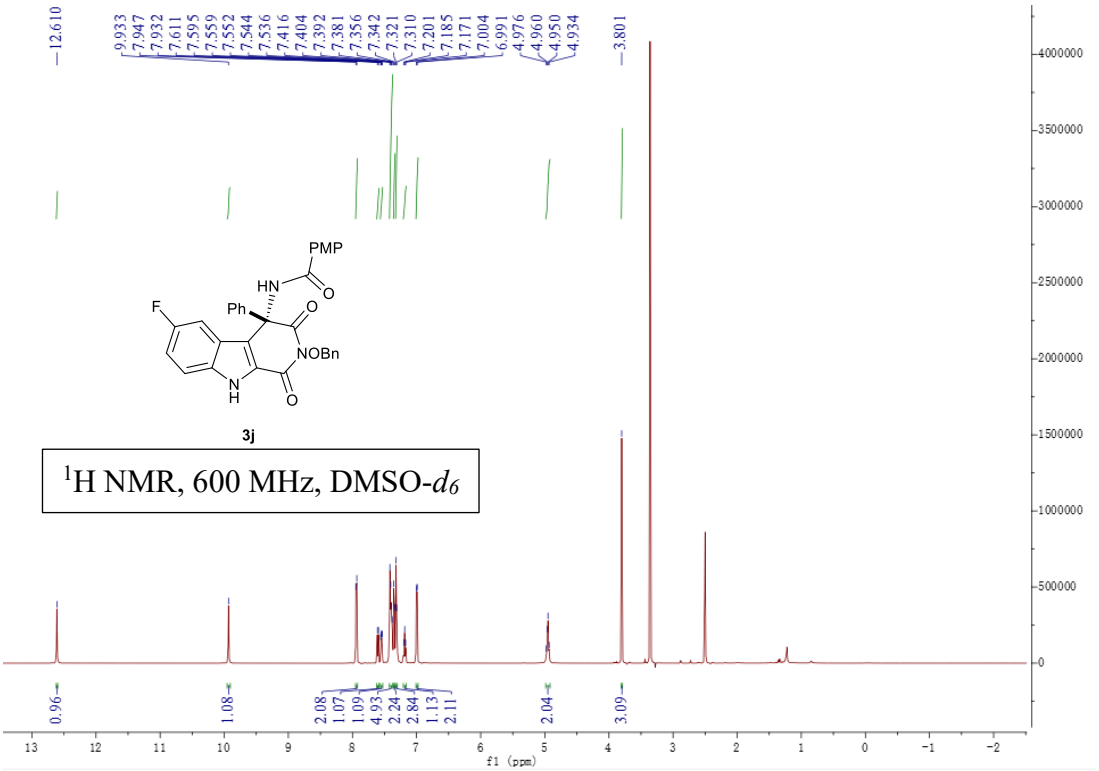
^{13}C NMR, 150 MHz, DMSO-*d*$_6$



^{1}H NMR, 600 MHz, DMSO-d_6

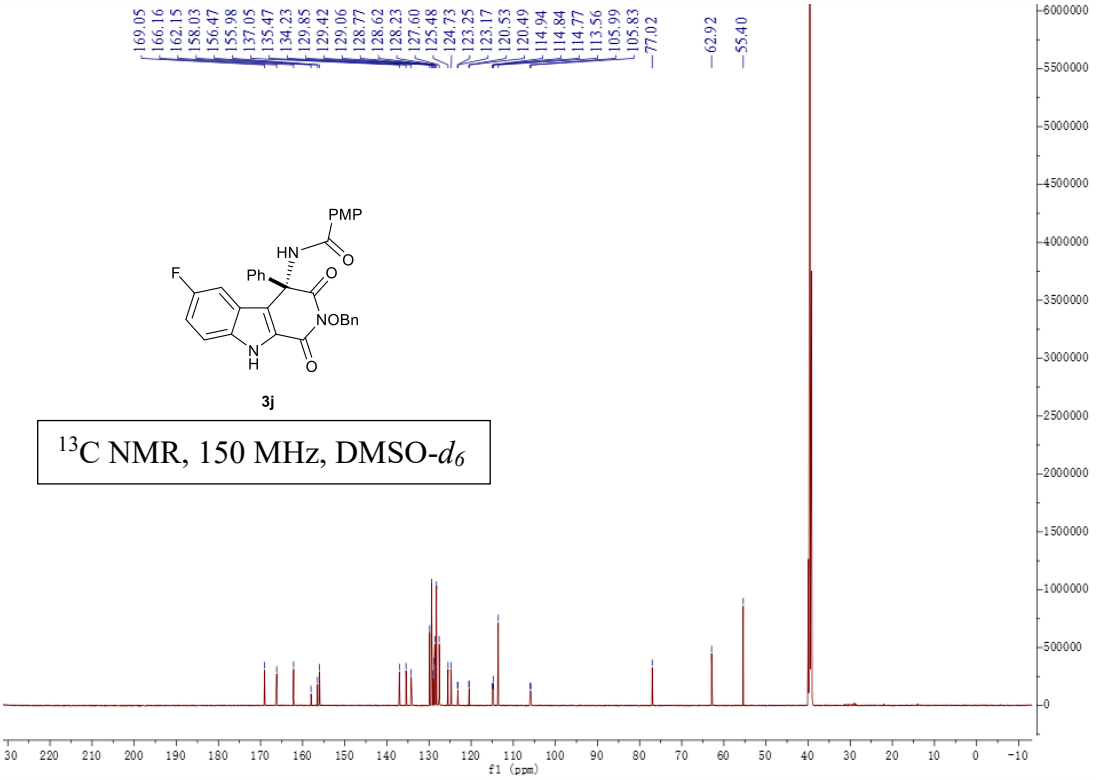


^{13}C NMR, 150 MHz, DMSO-d_6



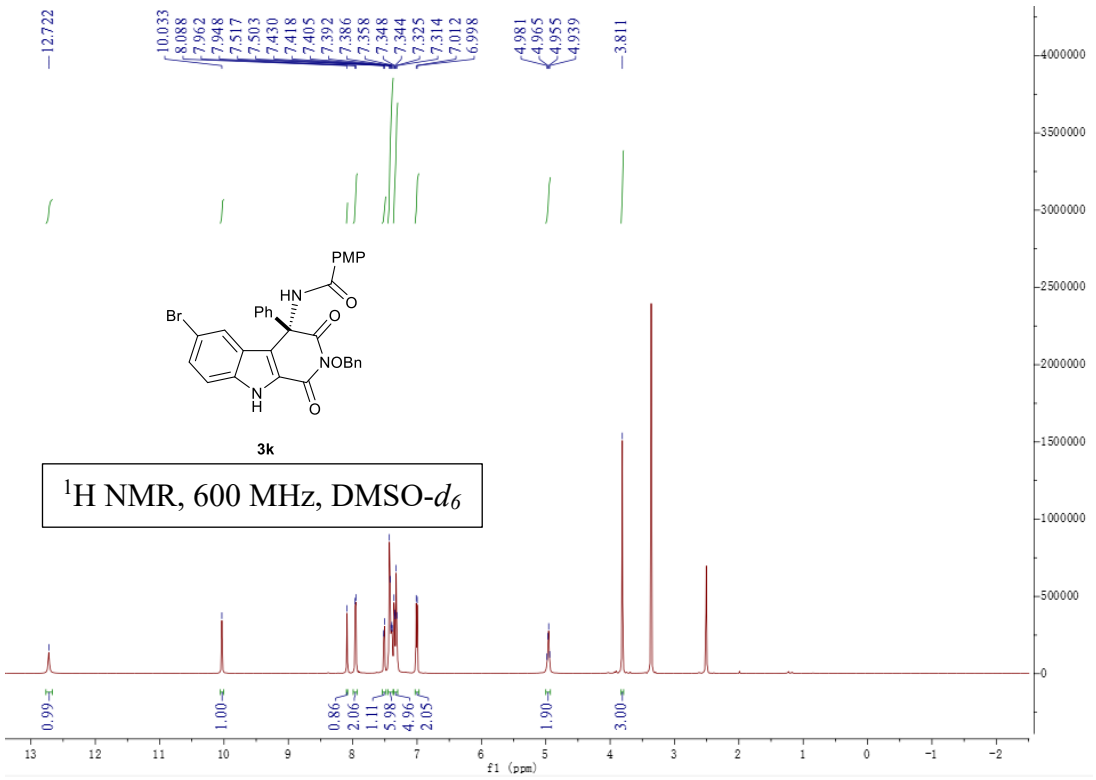
3j

^{1}H NMR, 600 MHz, DMSO-*d*$_6$



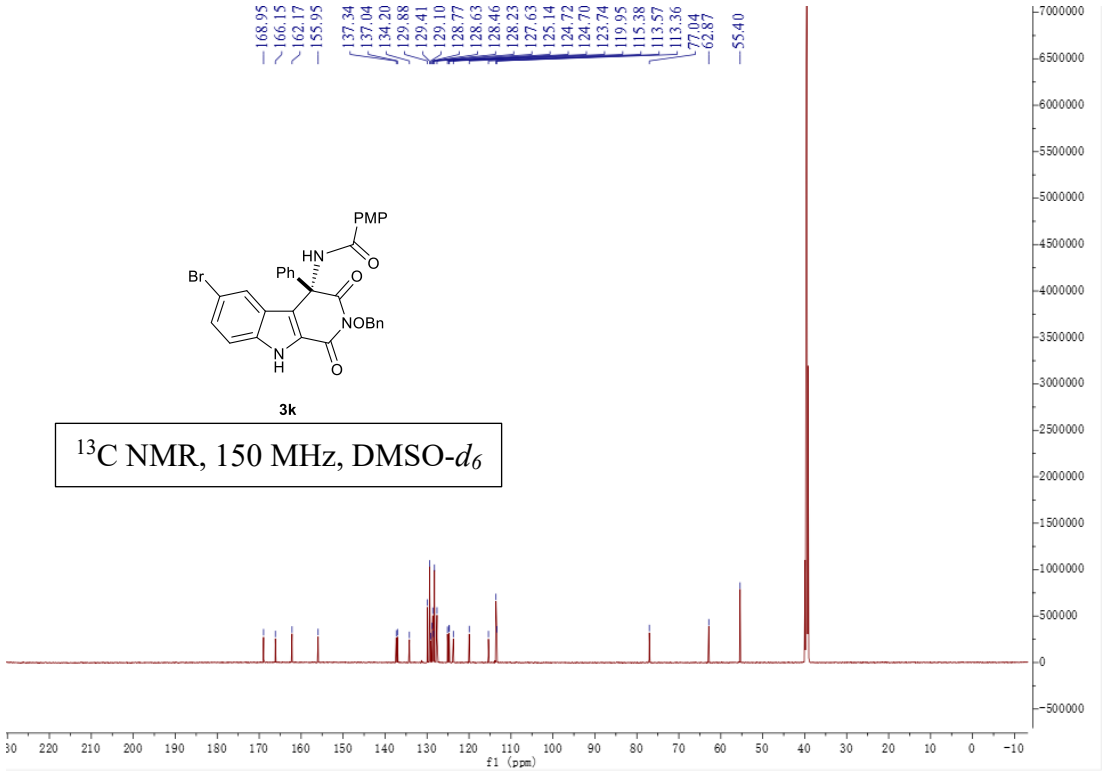
3j

^{13}C NMR, 150 MHz, DMSO-*d*$_6$



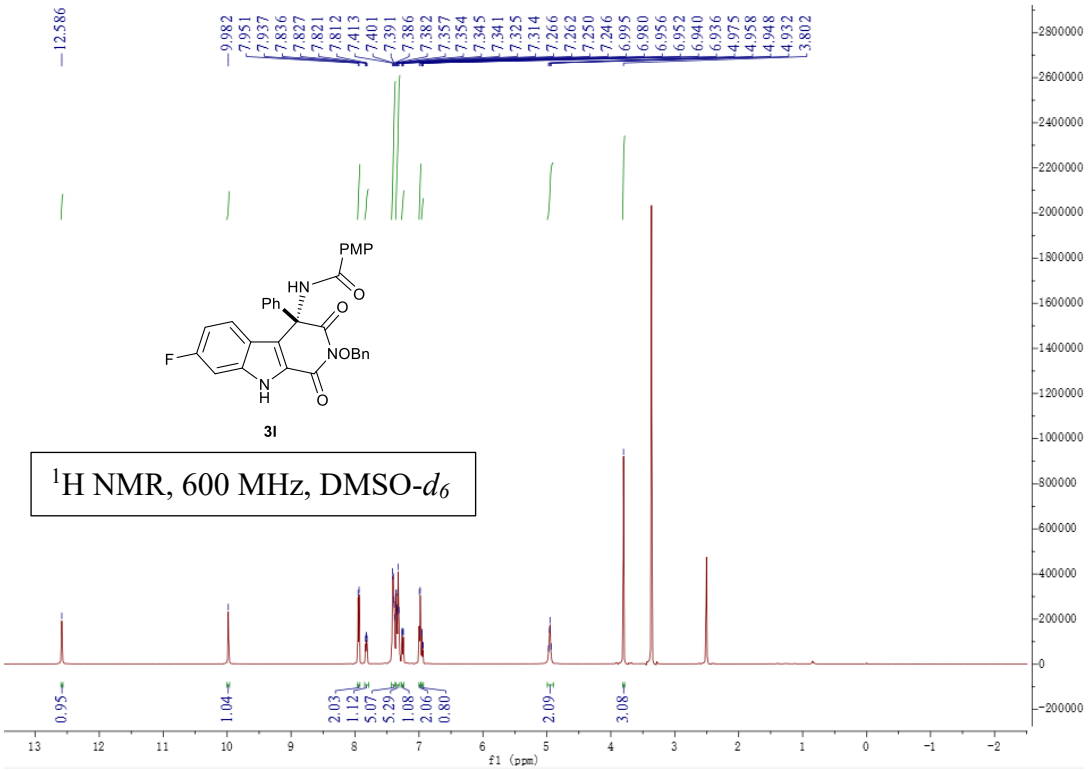
3k

^{1}H NMR, 600 MHz, DMSO-d_6



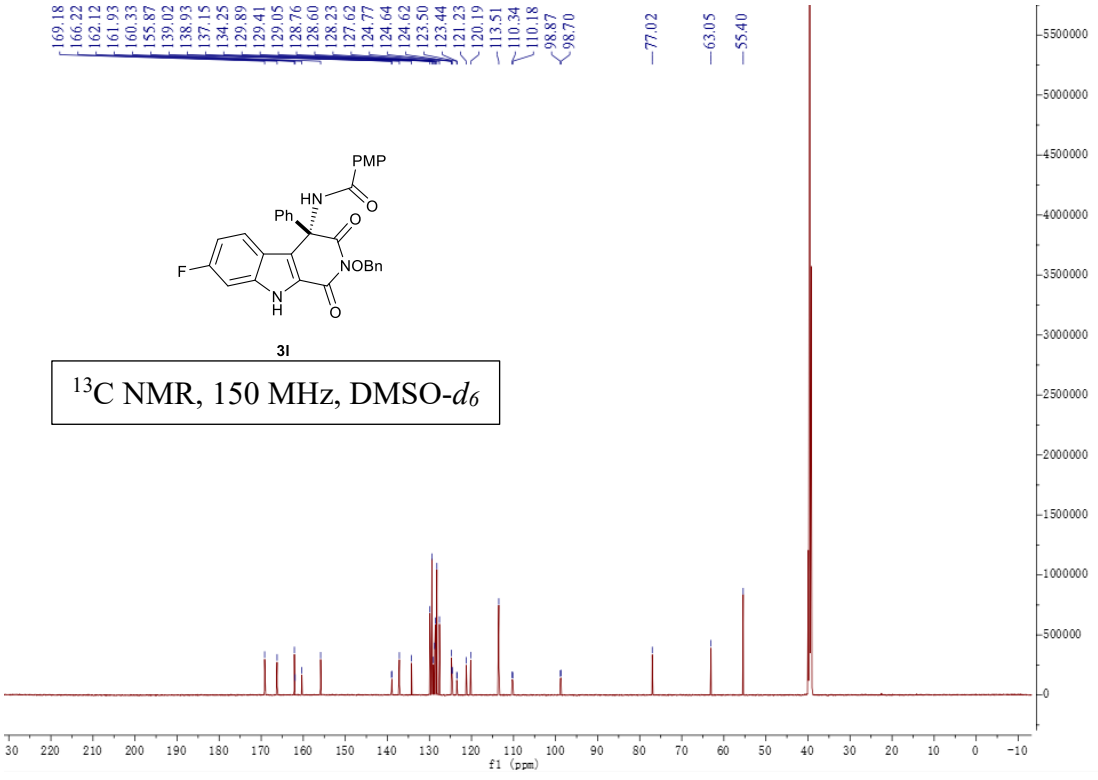
3k

^{13}C NMR, 150 MHz, DMSO-d_6



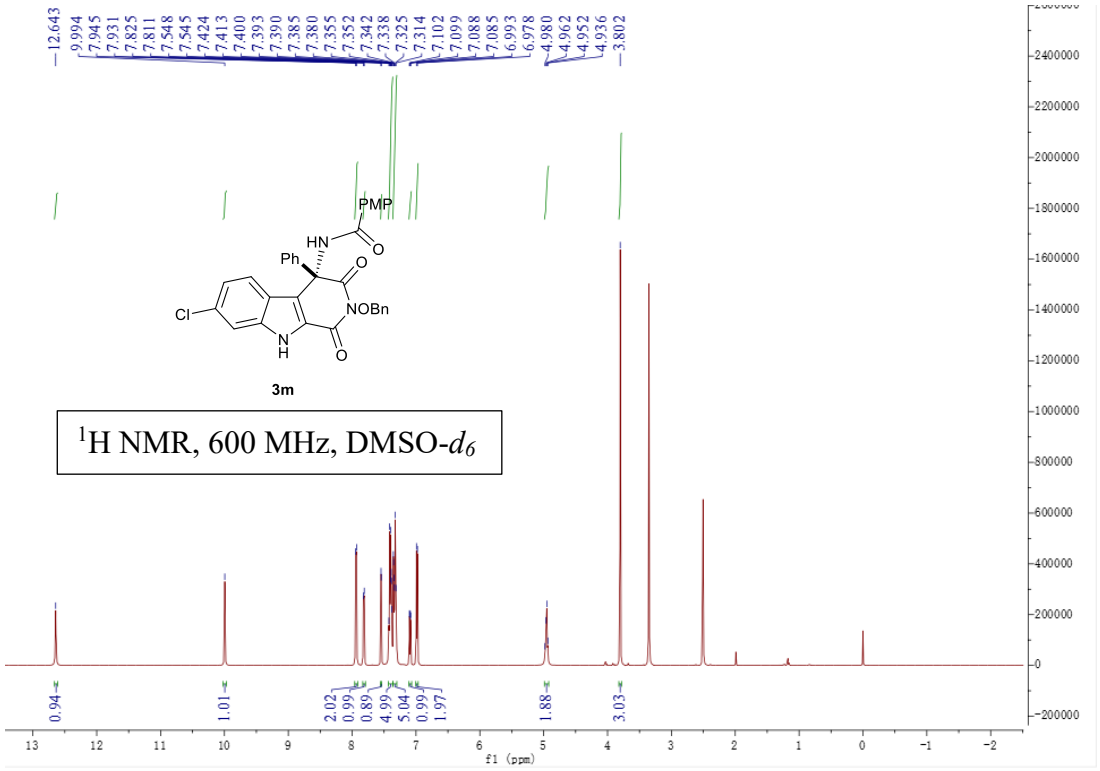
3l

^{1}H NMR, 600 MHz, DMSO-d_6



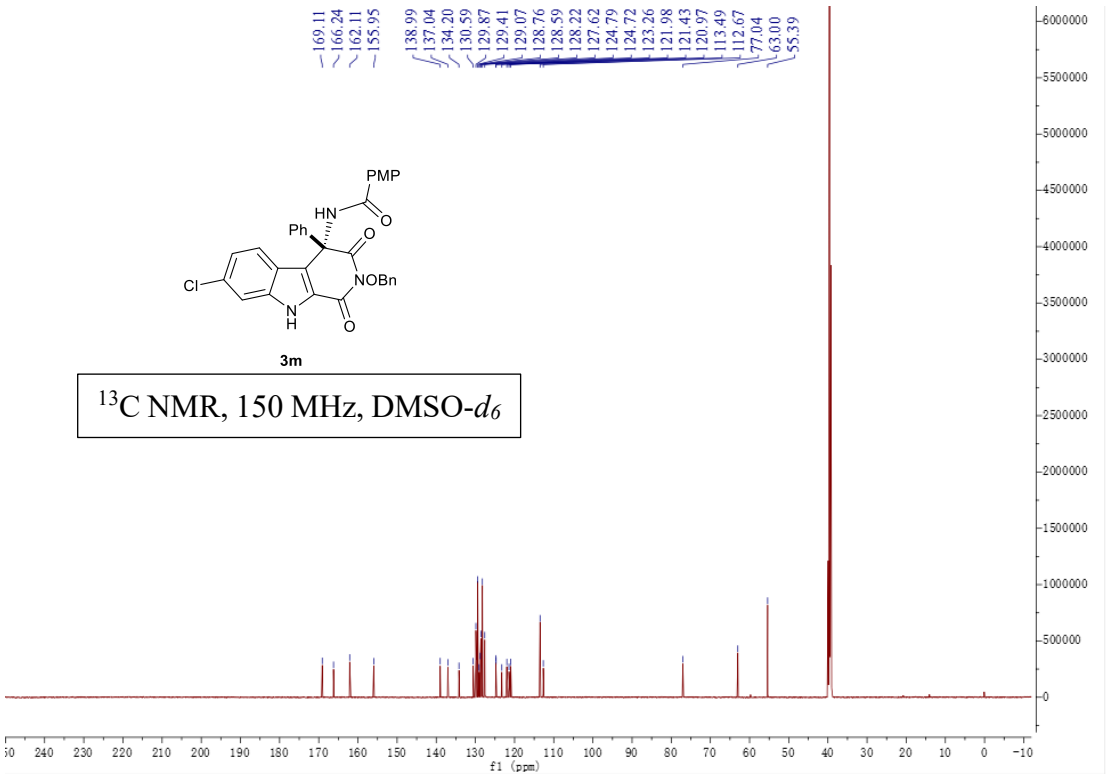
3l

^{13}C NMR, 150 MHz, DMSO-d_6



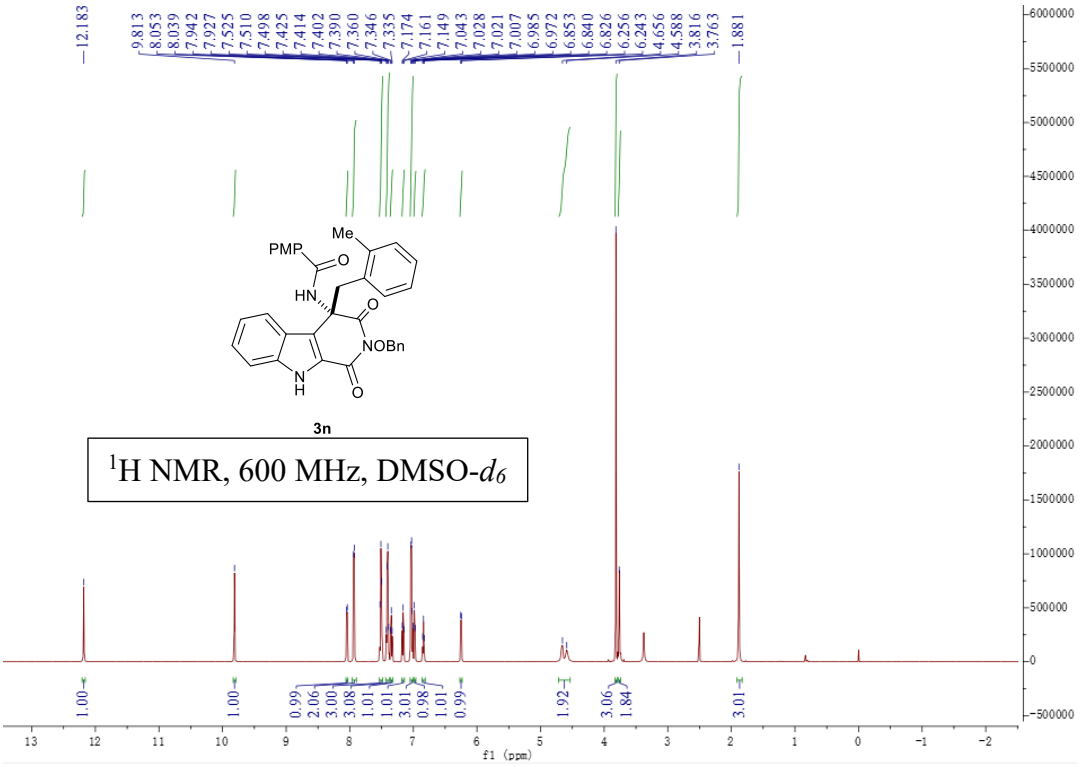
3m

^{1}H NMR, 600 MHz, DMSO-d_6



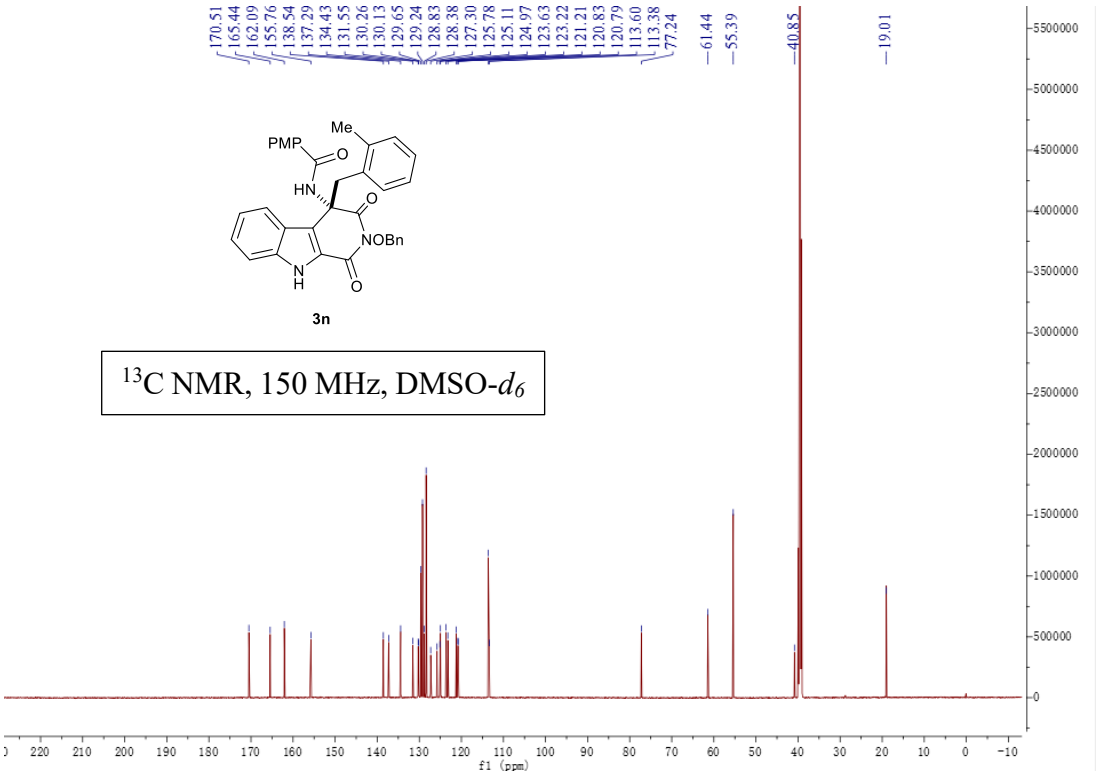
3m

^{13}C NMR, 150 MHz, DMSO-d_6



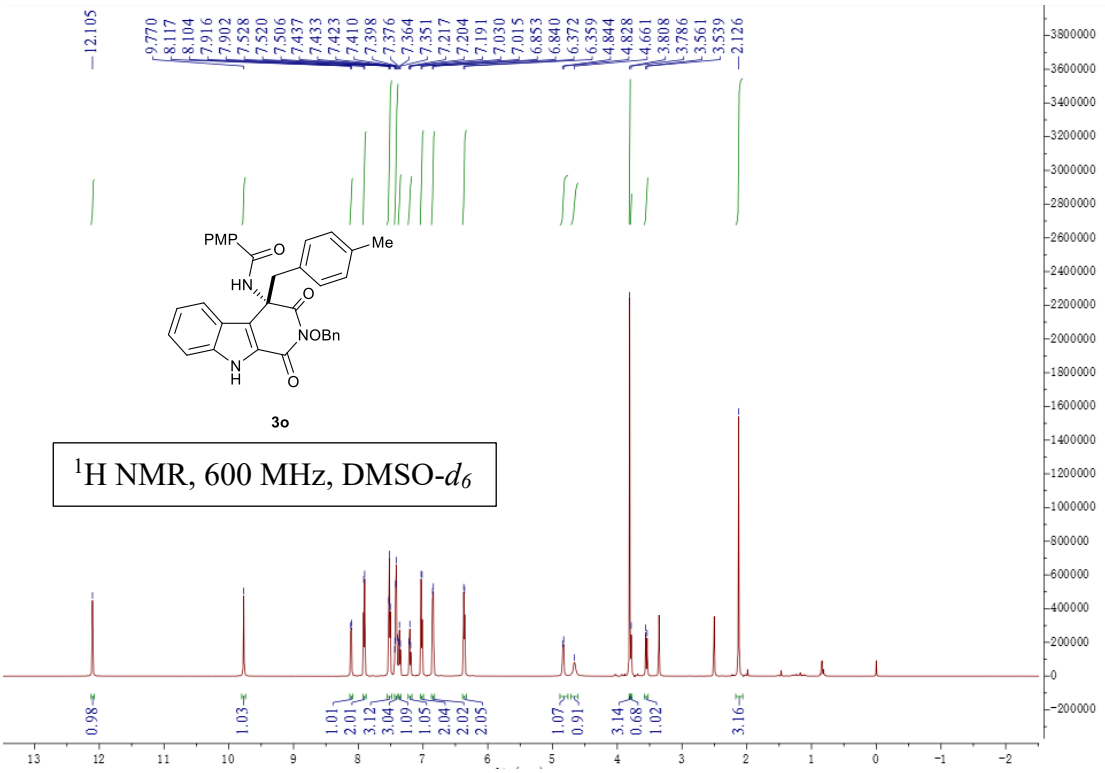
3n

^{1}H NMR, 600 MHz, DMSO-*d*$_6$



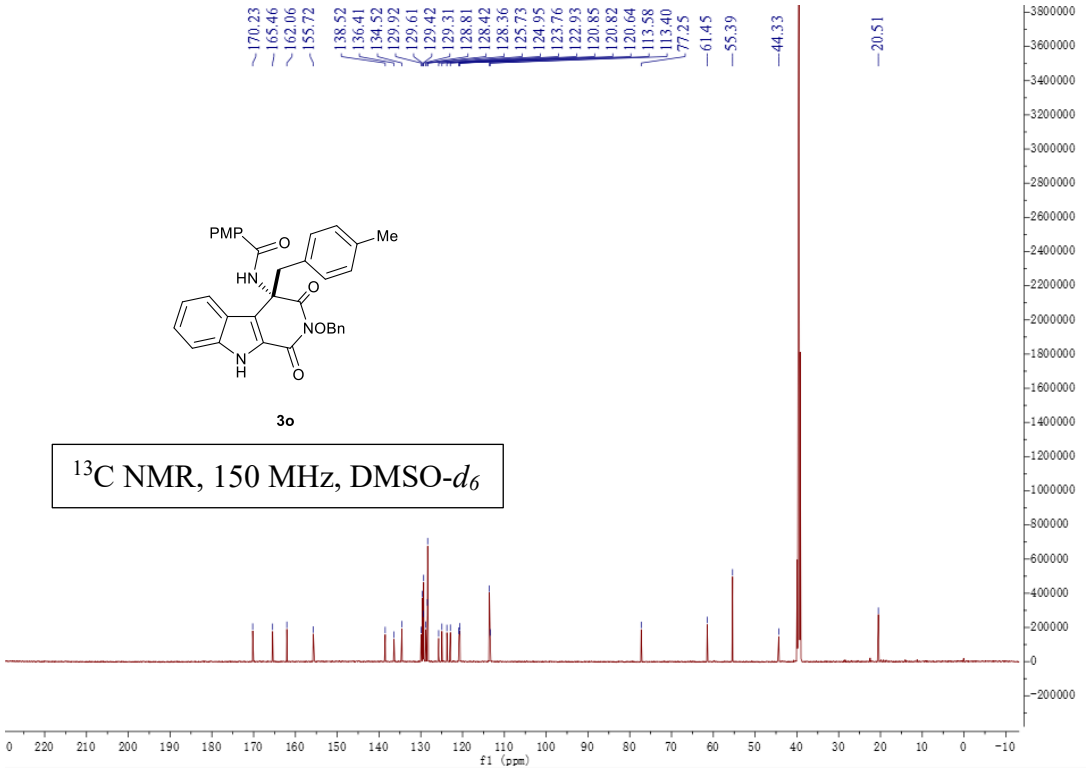
3n

^{13}C NMR, 150 MHz, DMSO-*d*$_6$



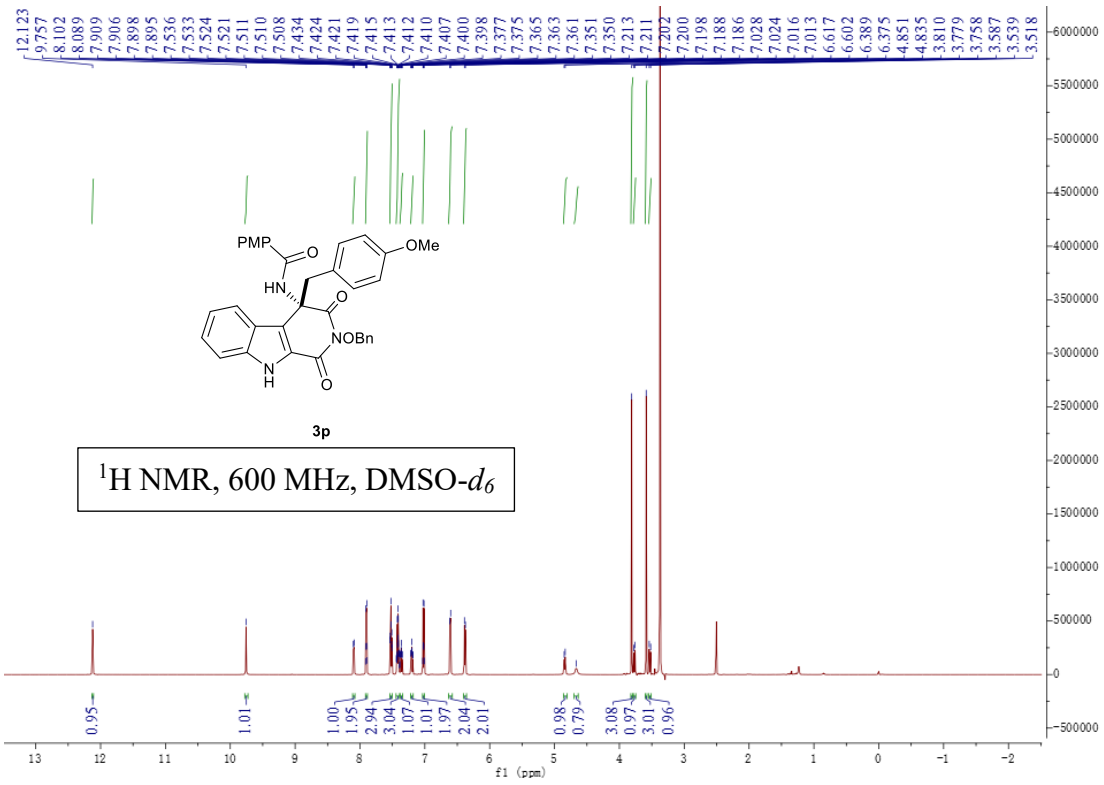
3o

^{1}H NMR, 600 MHz, DMSO-d_6



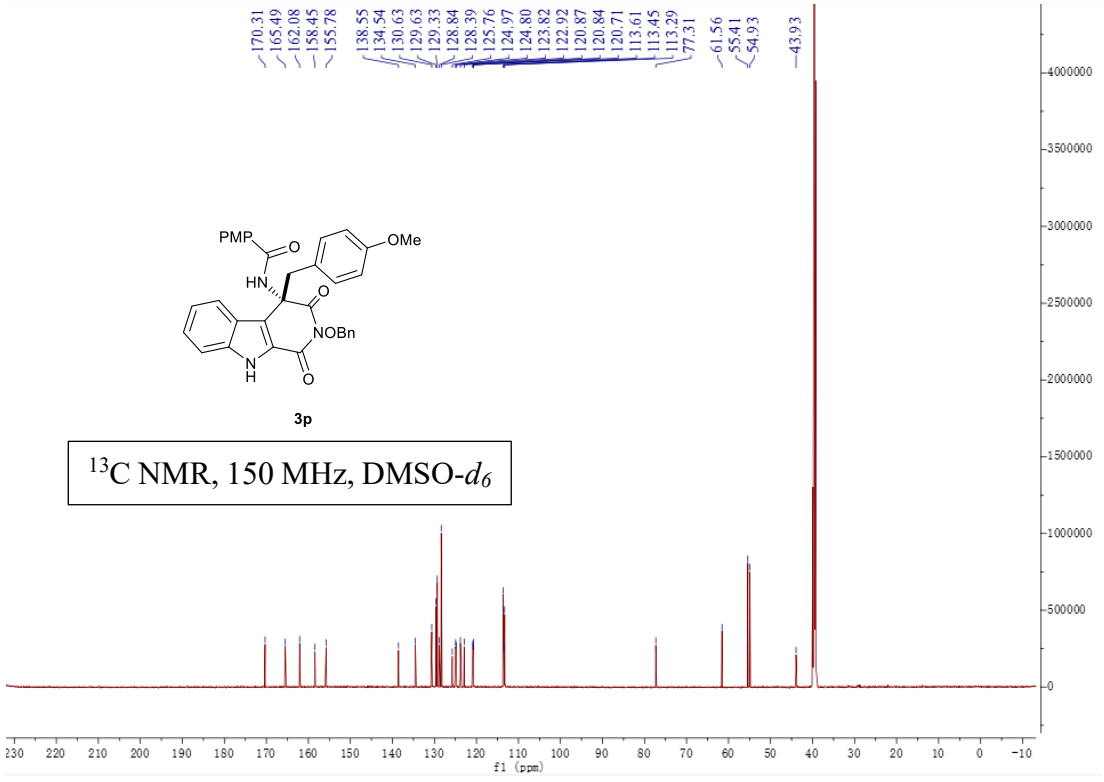
3o

^{13}C NMR, 150 MHz, DMSO-d_6



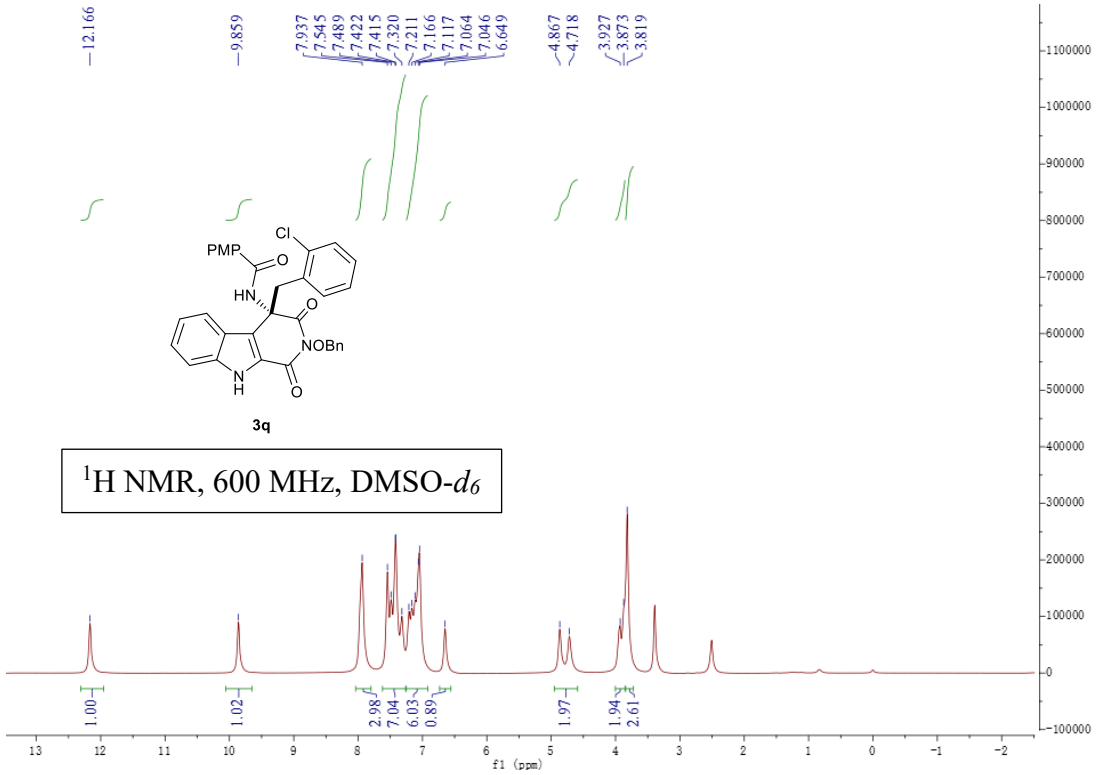
3p

^{1}H NMR, 600 MHz, DMSO-*d*$_6$



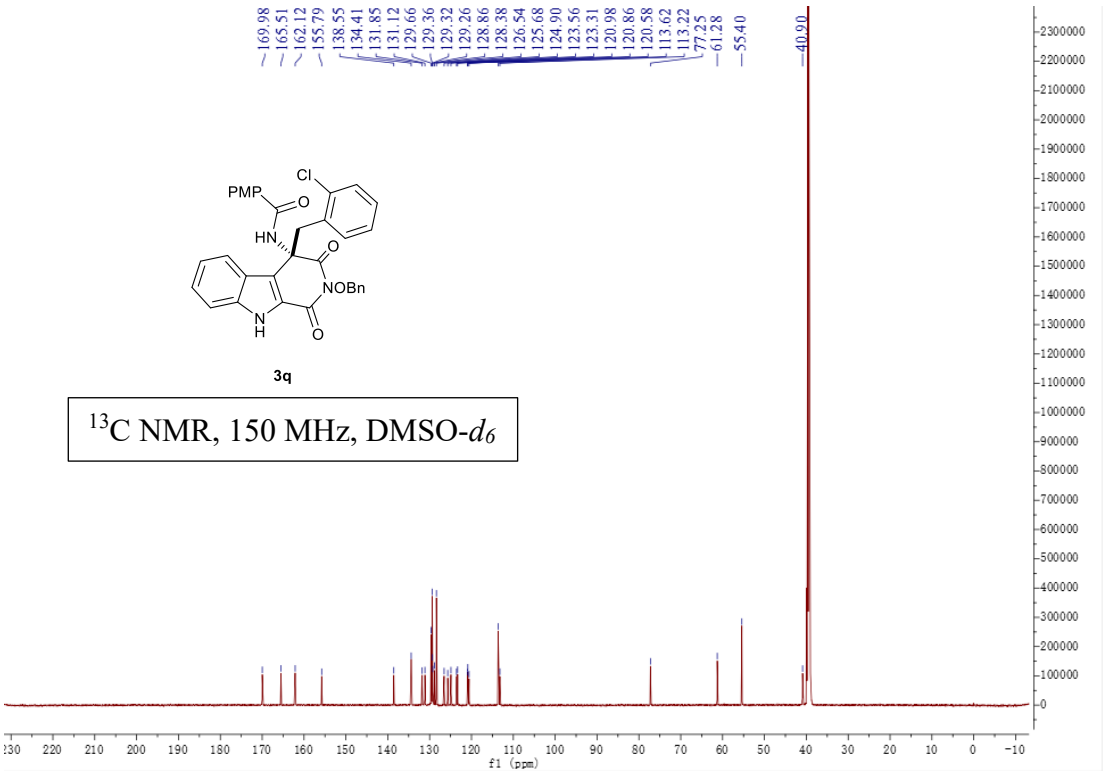
3p

^{13}C NMR, 150 MHz, DMSO-*d*$_6$



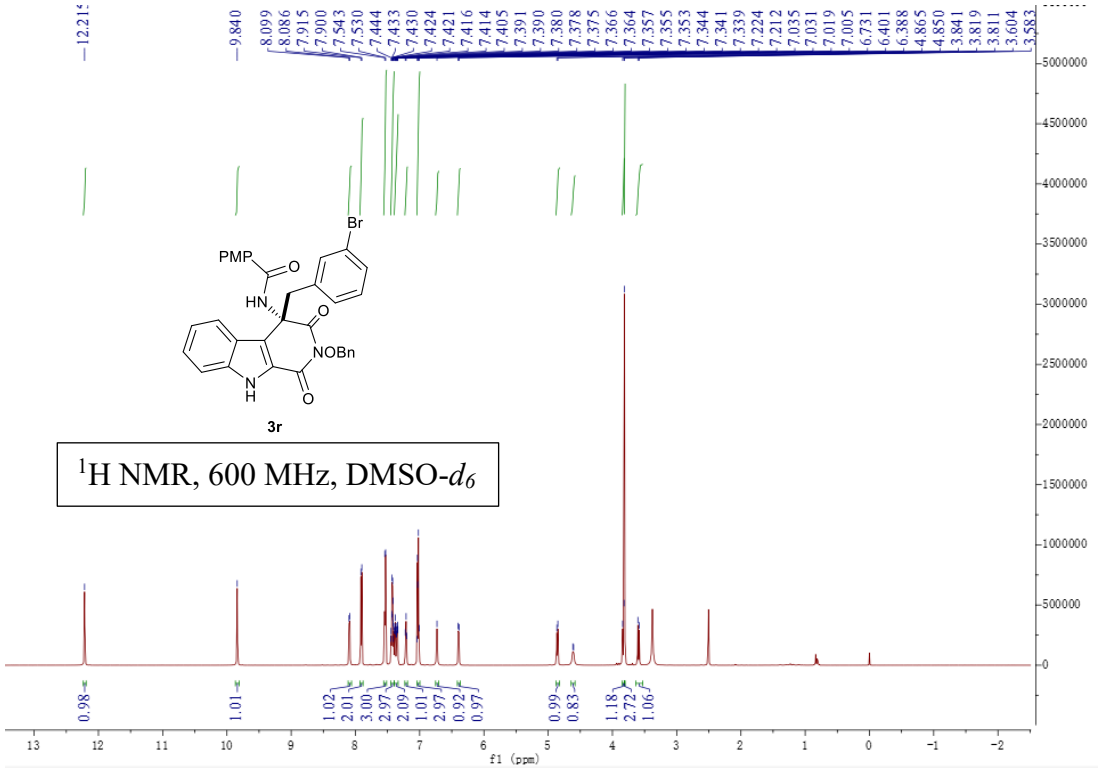
3q

^{1}H NMR, 600 MHz, DMSO-*d*$_6$



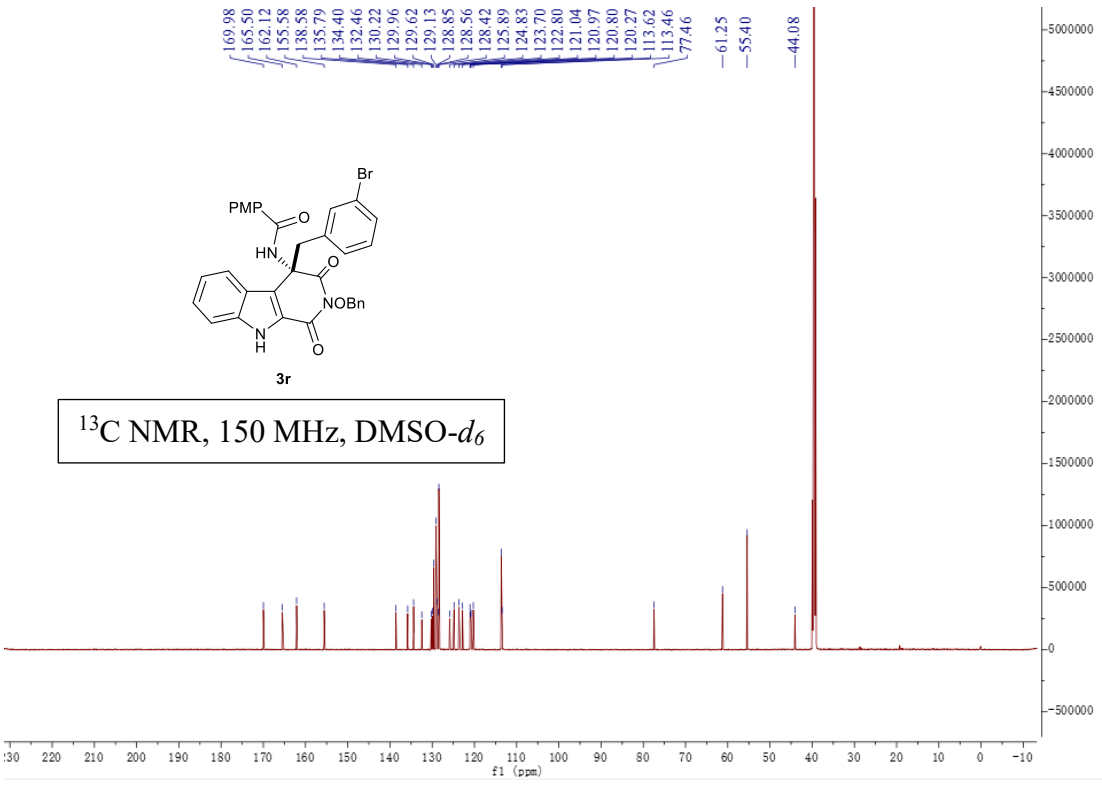
3q

^{13}C NMR, 150 MHz, DMSO-*d*$_6$



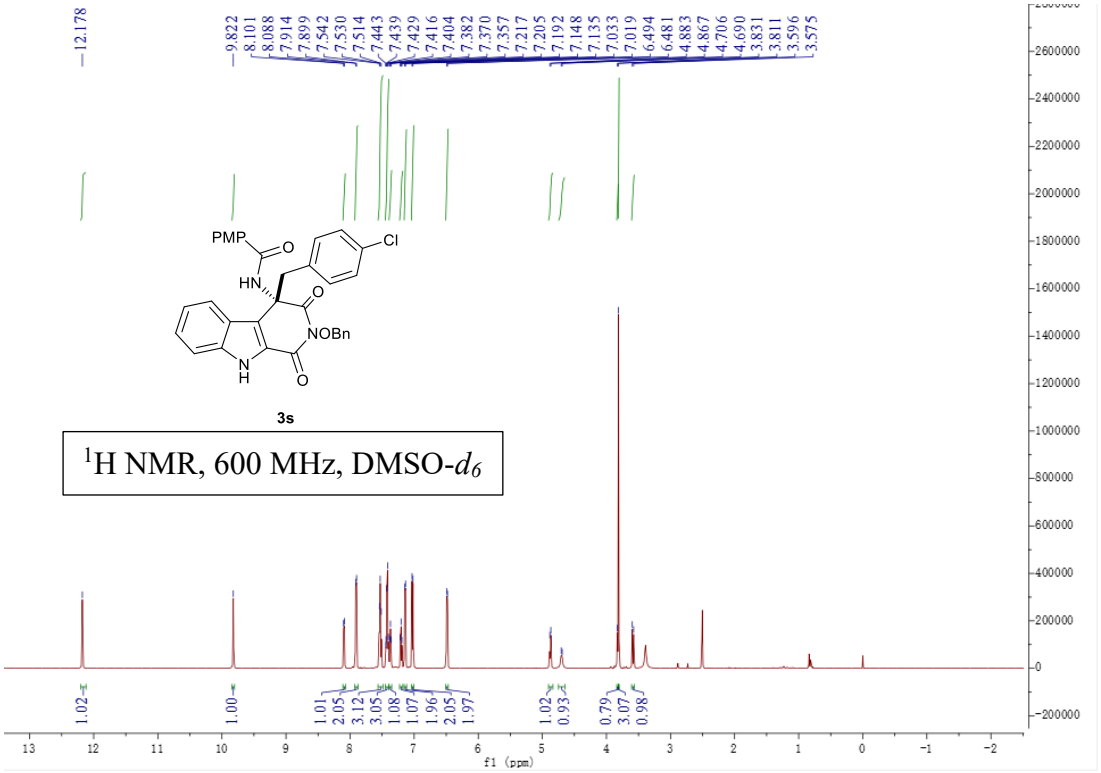
3r

^{1}H NMR, 600 MHz, DMSO-d_6



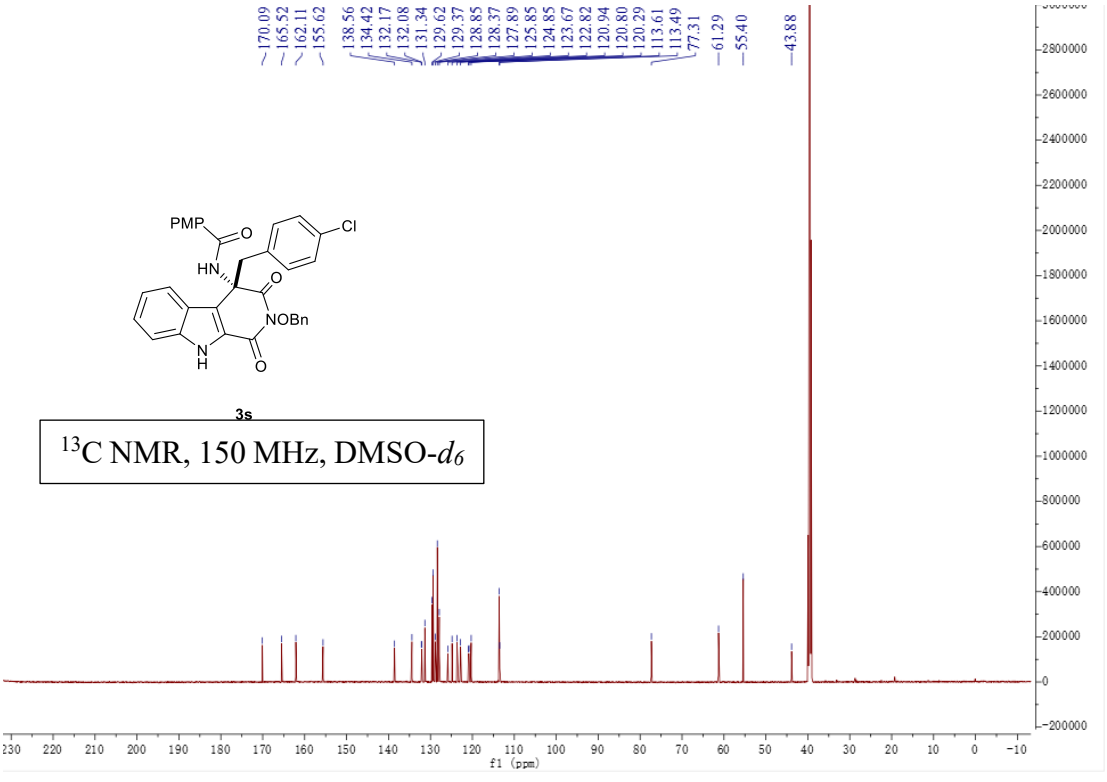
3r

^{13}C NMR, 150 MHz, DMSO-d_6



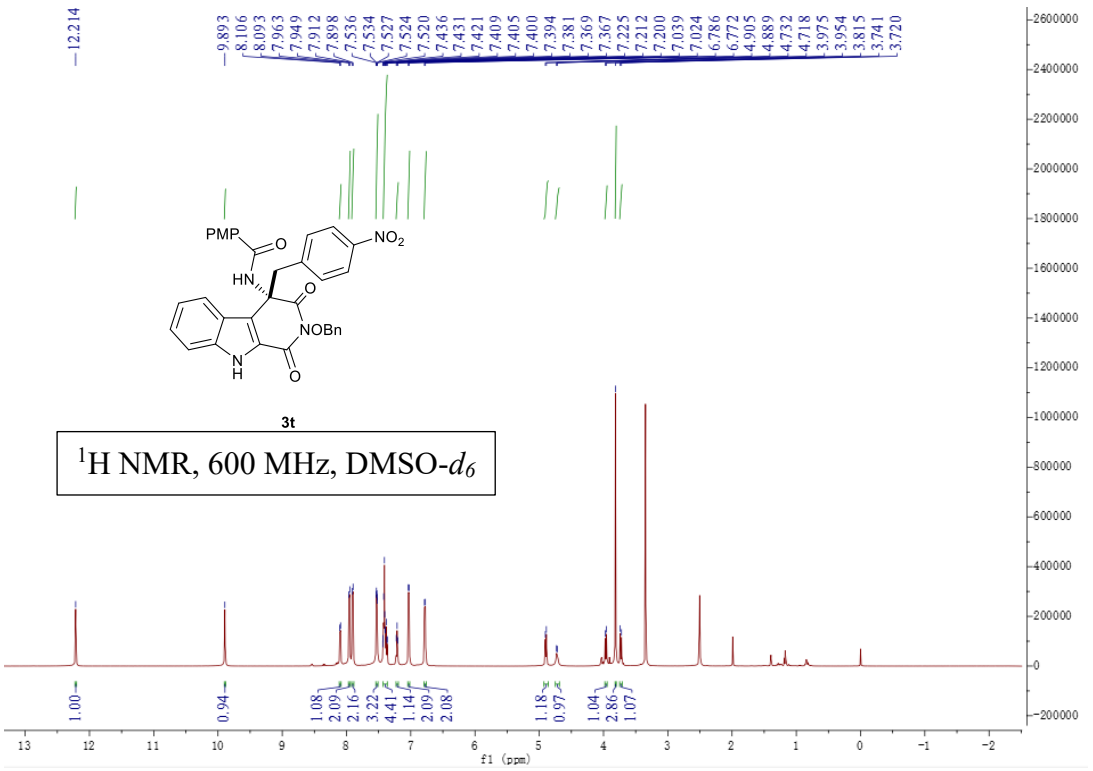
3s

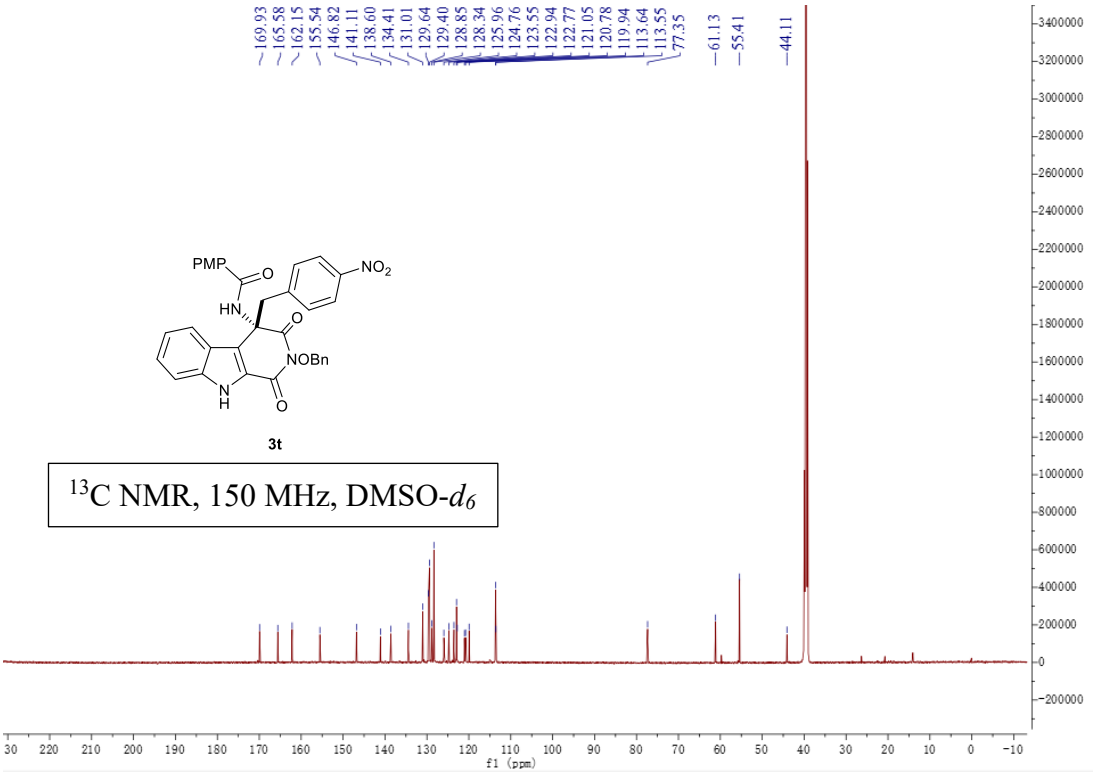
^{1}H NMR, 600 MHz, DMSO-d_6

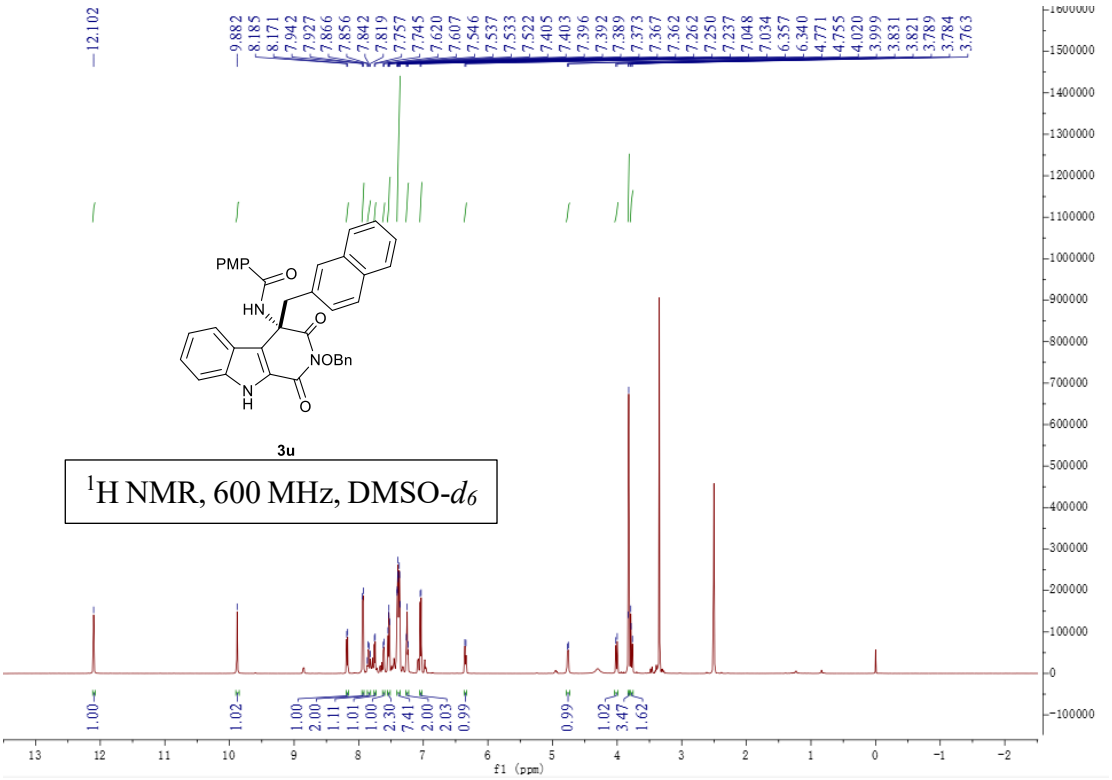


3s

^{13}C NMR, 150 MHz, DMSO-d_6

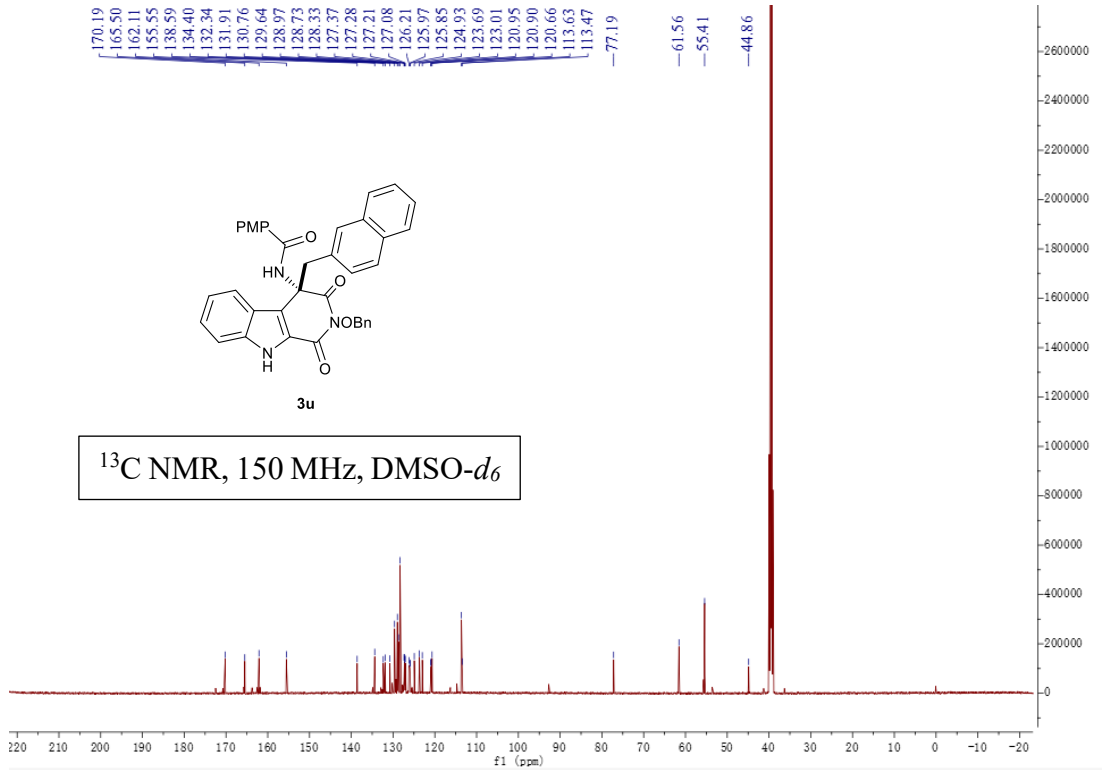

PMP
NO2
HN
O
NOBn
N
H
O
3t
1H NMR, 600 MHz, DMSO-d6


PMP
NO2
HN
O
NOBn
N
H
O
3t
13C NMR, 150 MHz, DMSO-d6



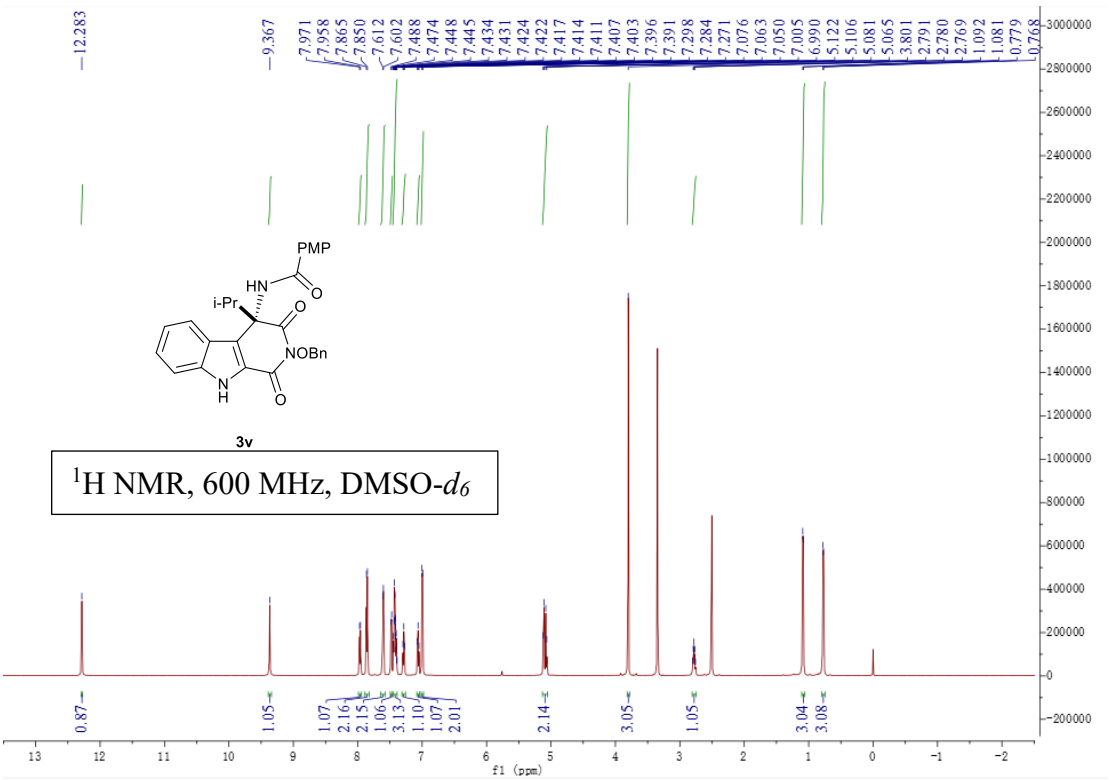
3u

^{1}H NMR, 600 MHz, DMSO-d_6

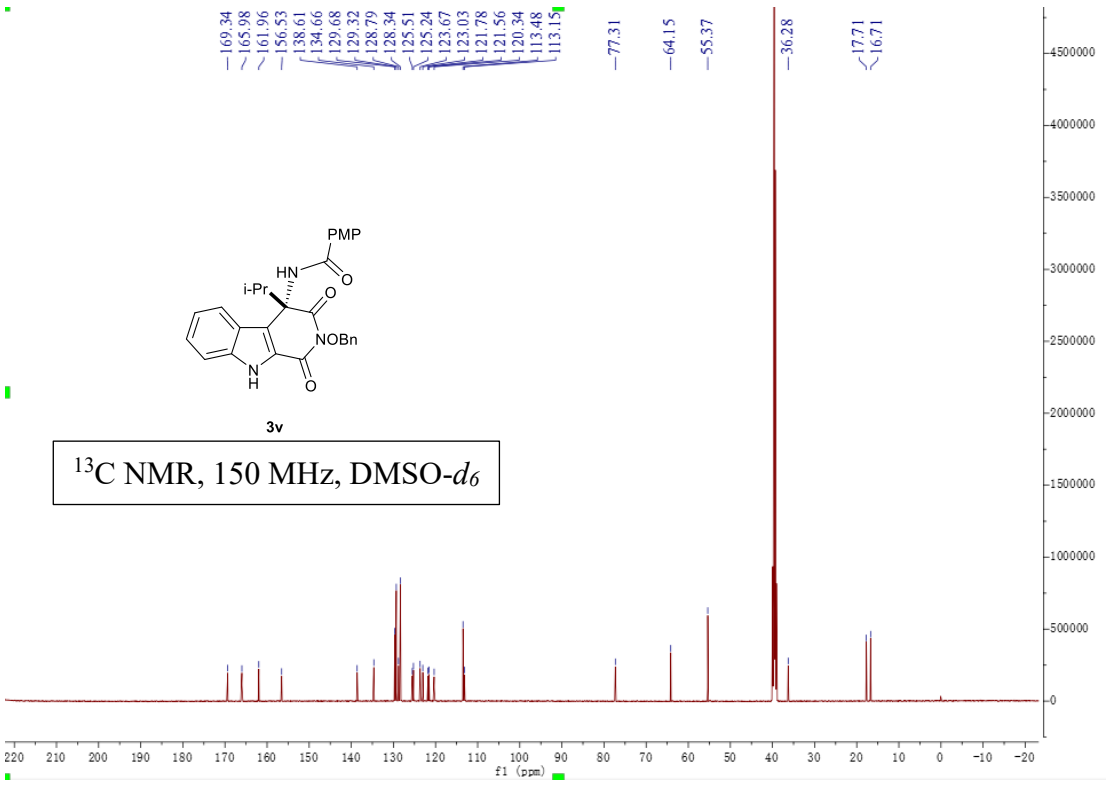


3u

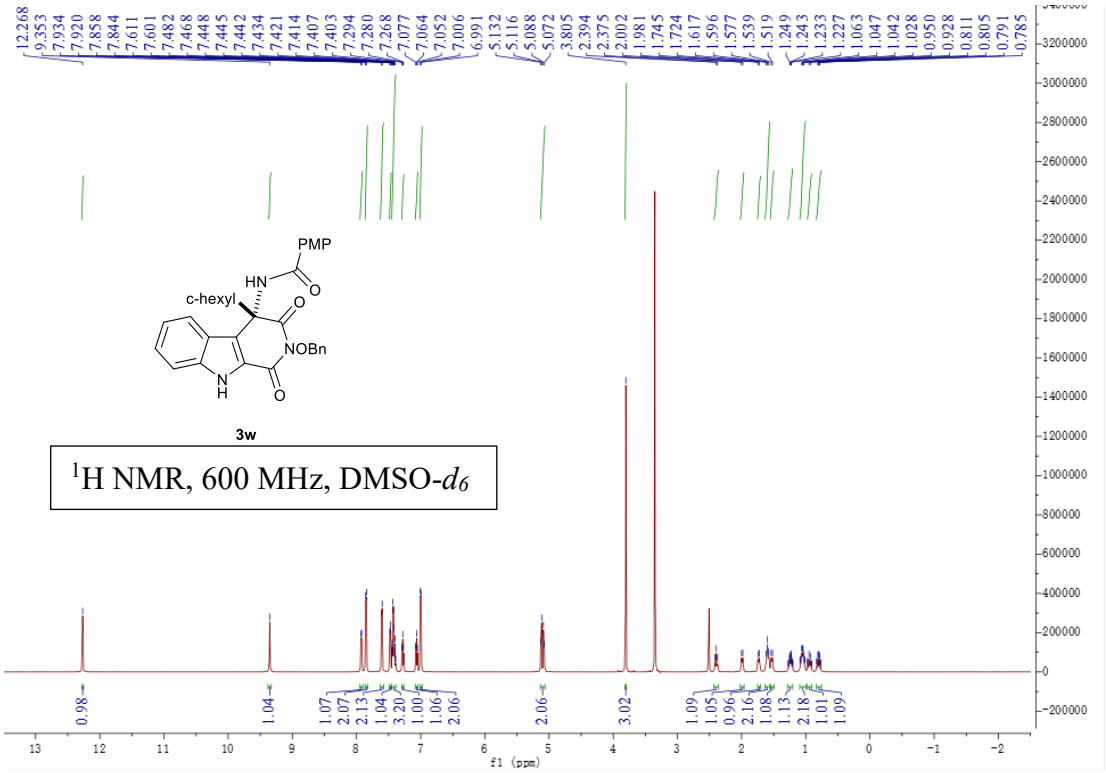
^{13}C NMR, 150 MHz, DMSO-d_6

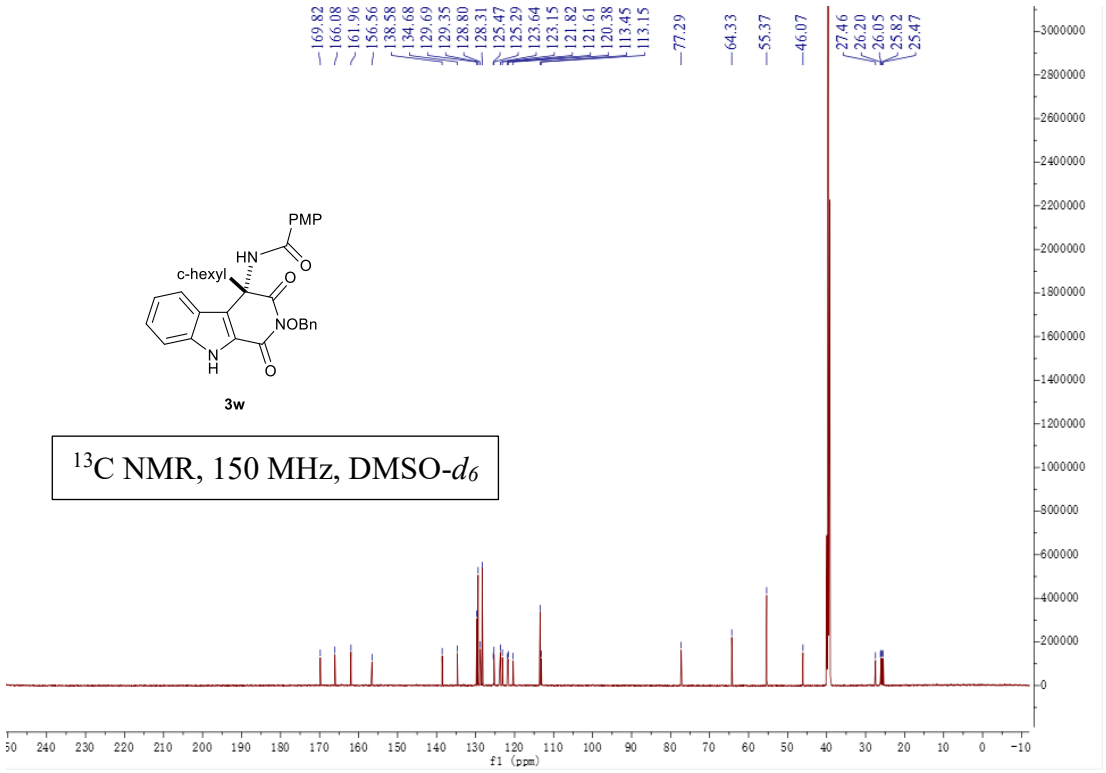


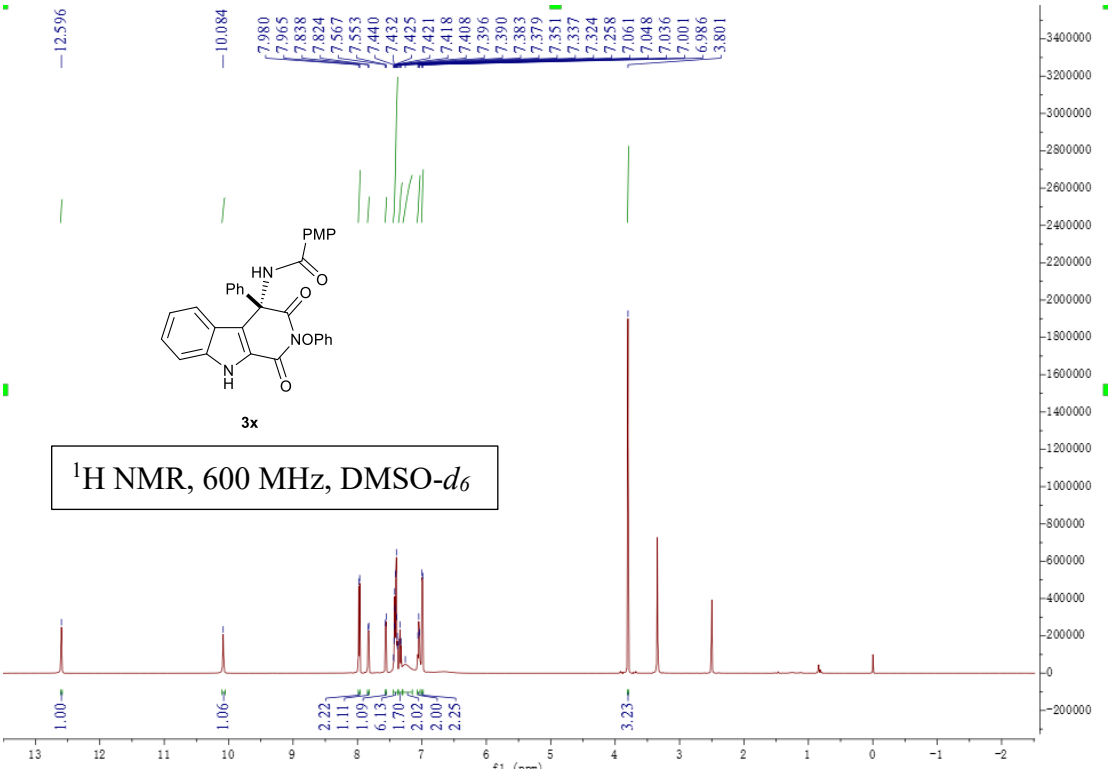
^{1}H NMR, 600 MHz, DMSO-*d*$_6$



^{13}C NMR, 150 MHz, DMSO-*d*$_6$

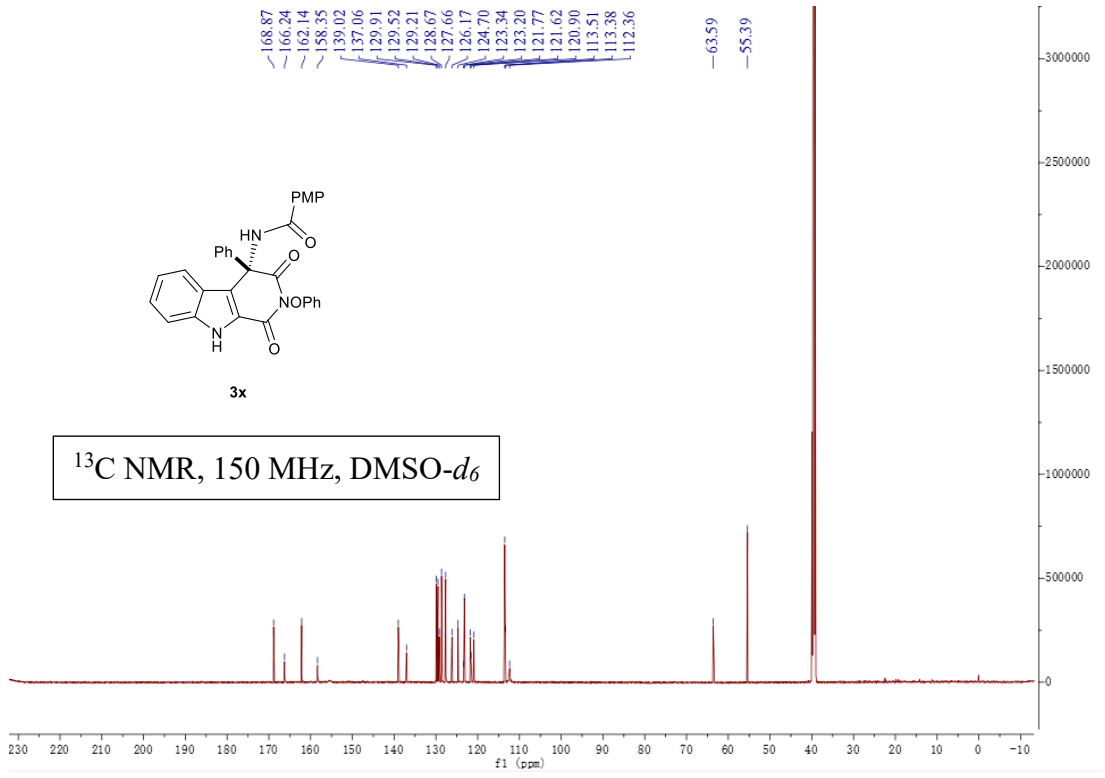

PMP
HN
c-hexyl
O
O
NOBn
N
H
O
3w
1H NMR, 600 MHz, DMSO-d6
f1 (ppm)


PMP
HN
c-hexyl
O
O
NOBn
N
H
O
3w
13C NMR, 150 MHz, DMSO-d6
f1 (ppm)



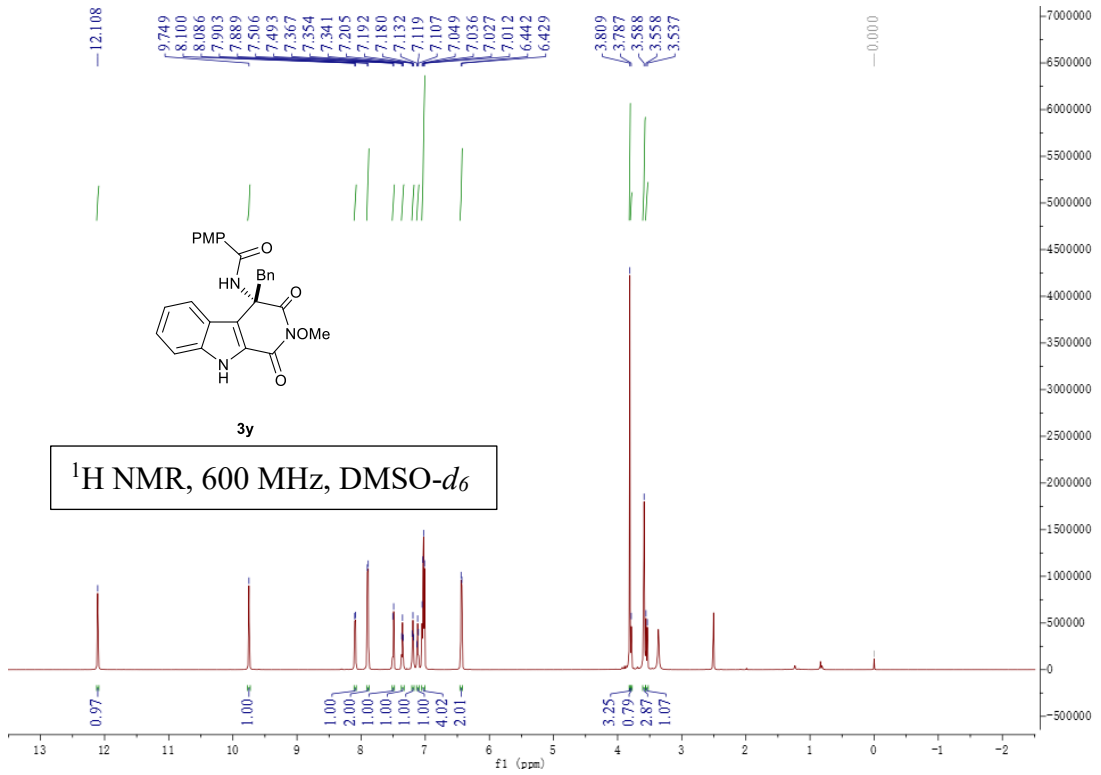
3x

^{1}H NMR, 600 MHz, DMSO-*d*$_6$



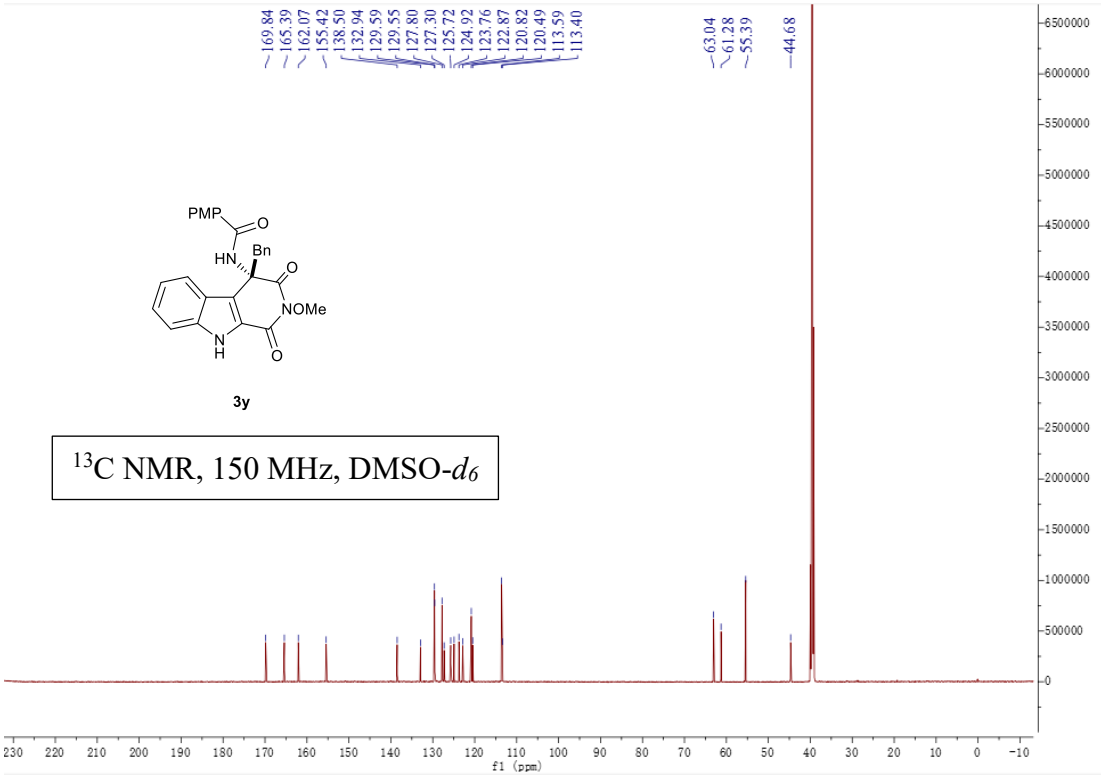
3x

^{13}C NMR, 150 MHz, DMSO-*d*$_6$



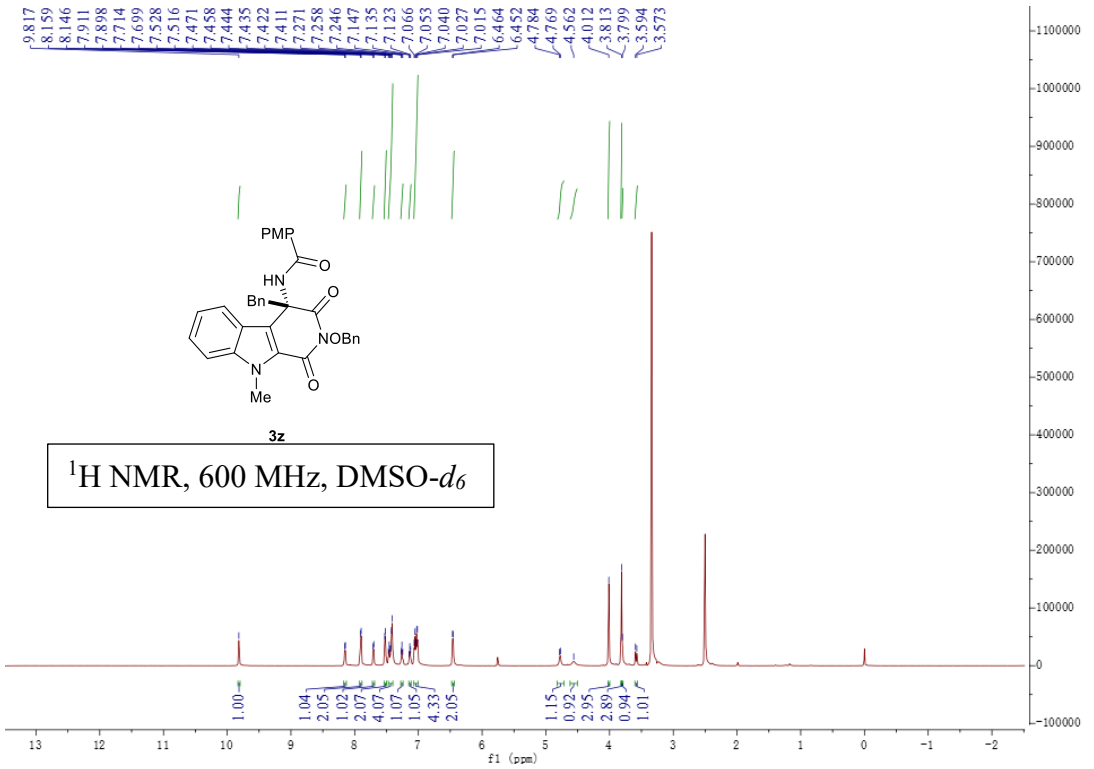
3y

^{1}H NMR, 600 MHz, DMSO-*d*$_6$

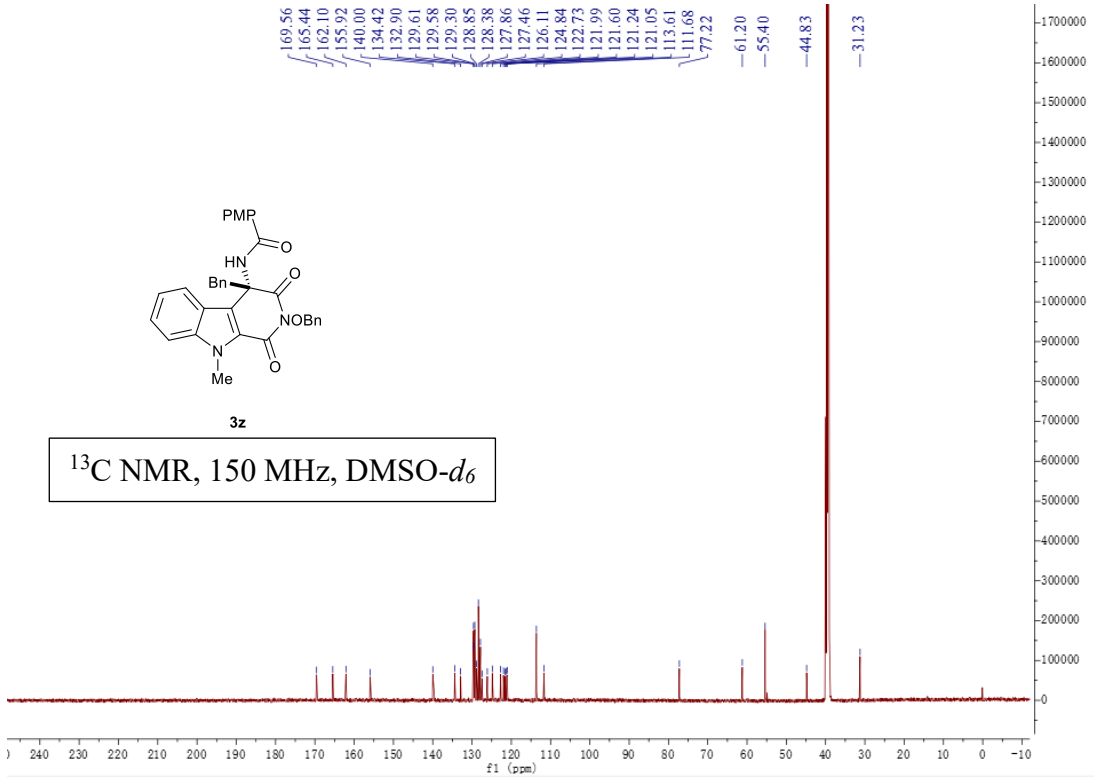


3y

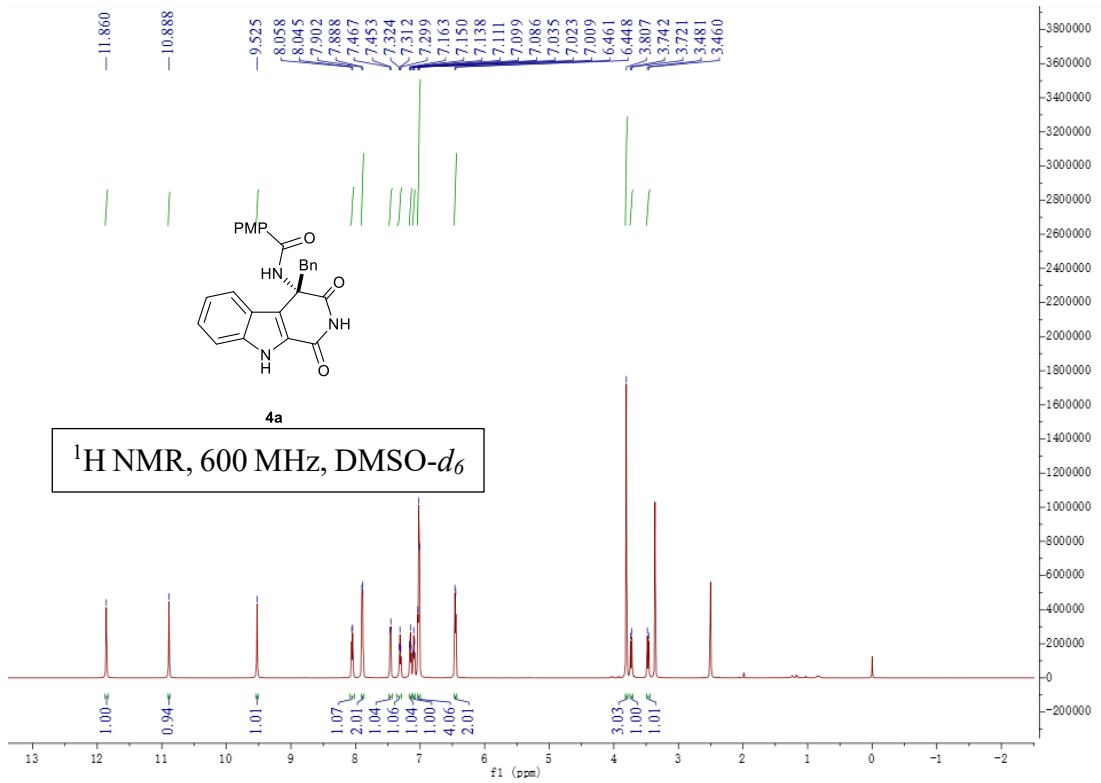
^{13}C NMR, 150 MHz, DMSO-*d*$_6$



^{1}H NMR, 600 MHz, DMSO-*d*$_6$

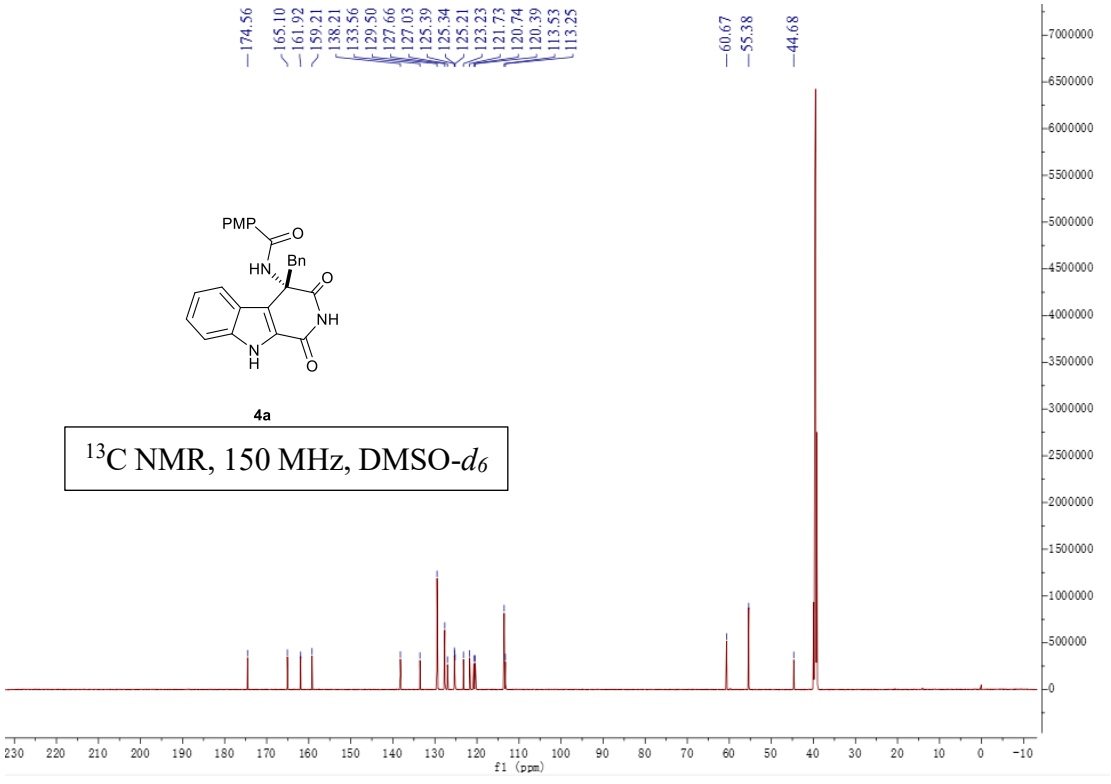


^{13}C NMR, 150 MHz, DMSO-*d*$_6$



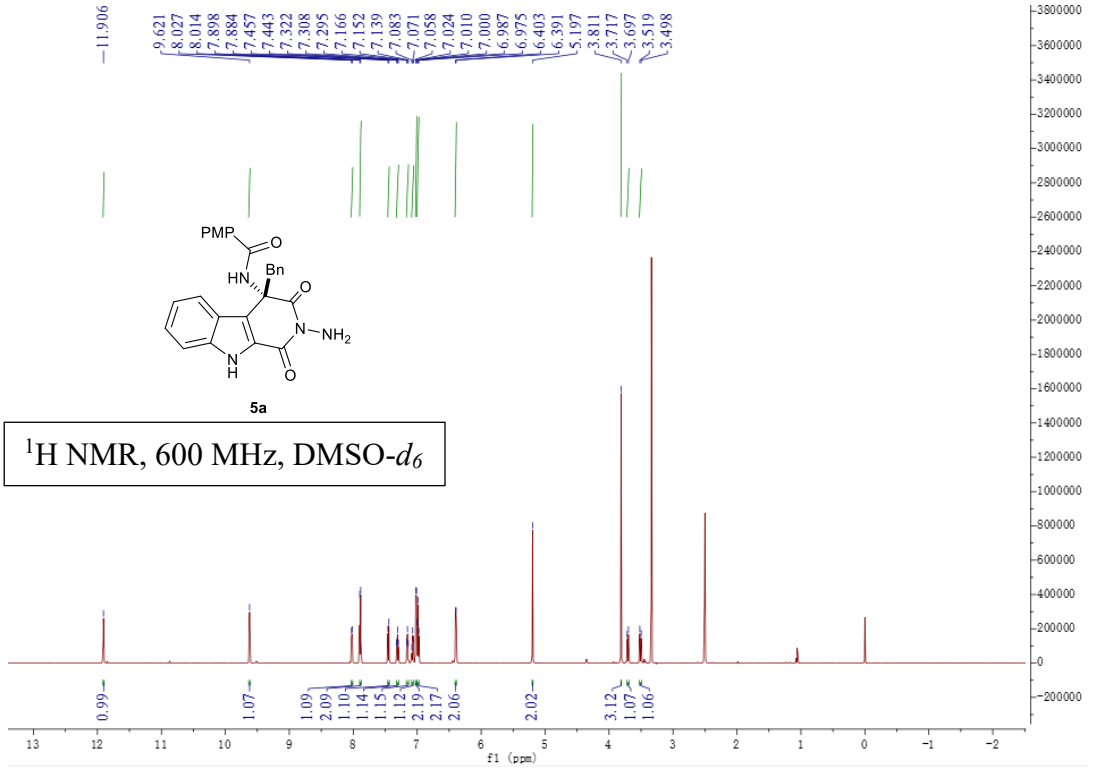
4a

^{1}H NMR, 600 MHz, DMSO-d_6



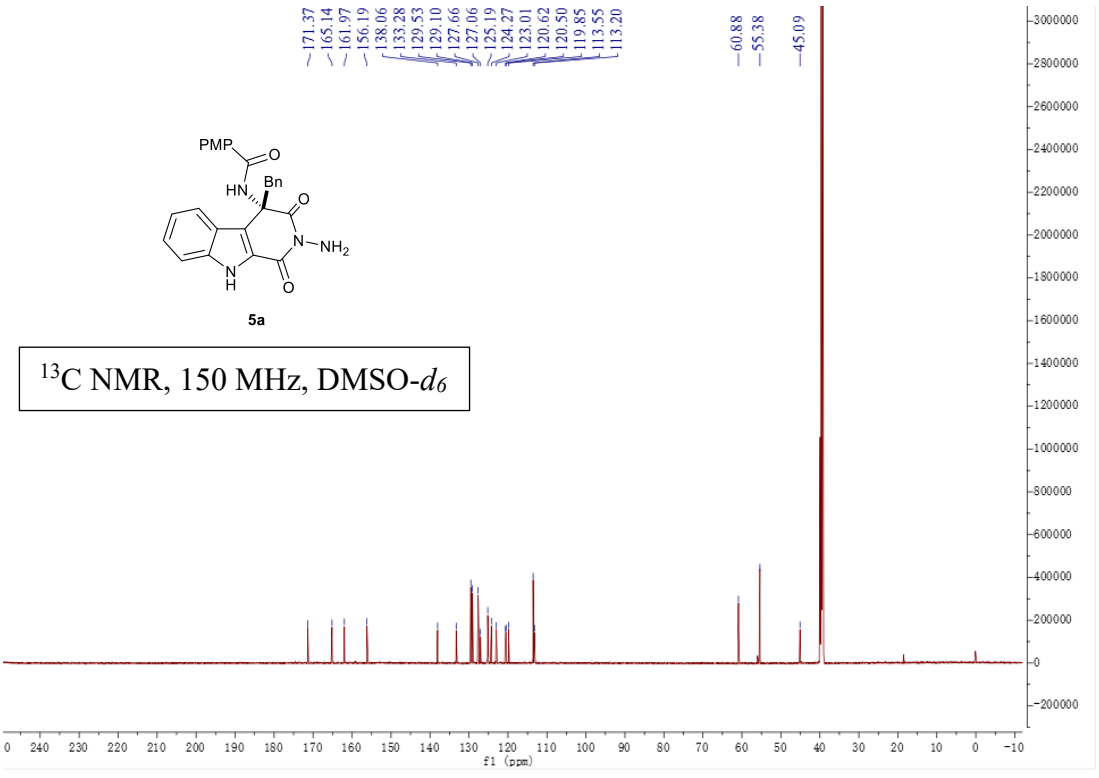
4a

^{13}C NMR, 150 MHz, DMSO-d_6



5a

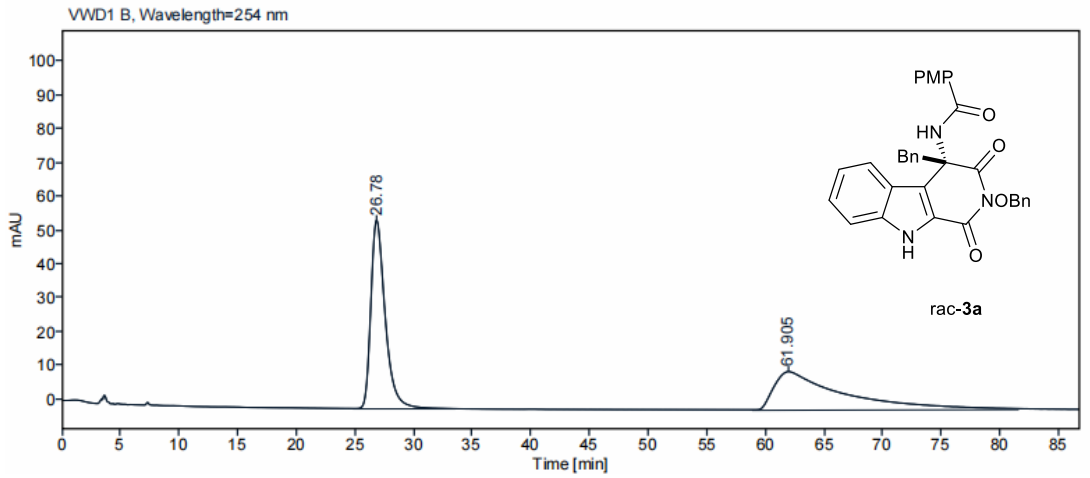
^{1}H NMR, 600 MHz, DMSO-d_6



5a

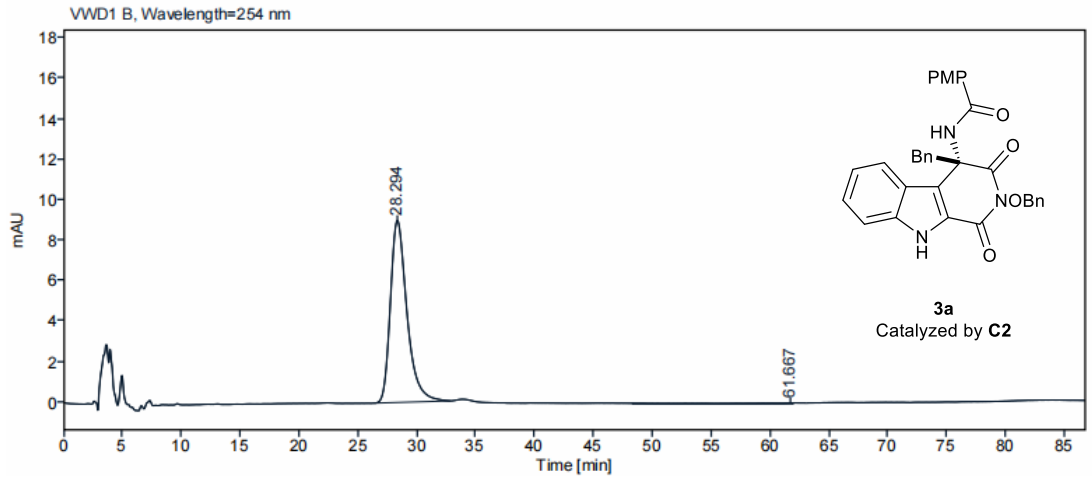
^{13}C NMR, 150 MHz, DMSO-d_6

9. HPLC spectra



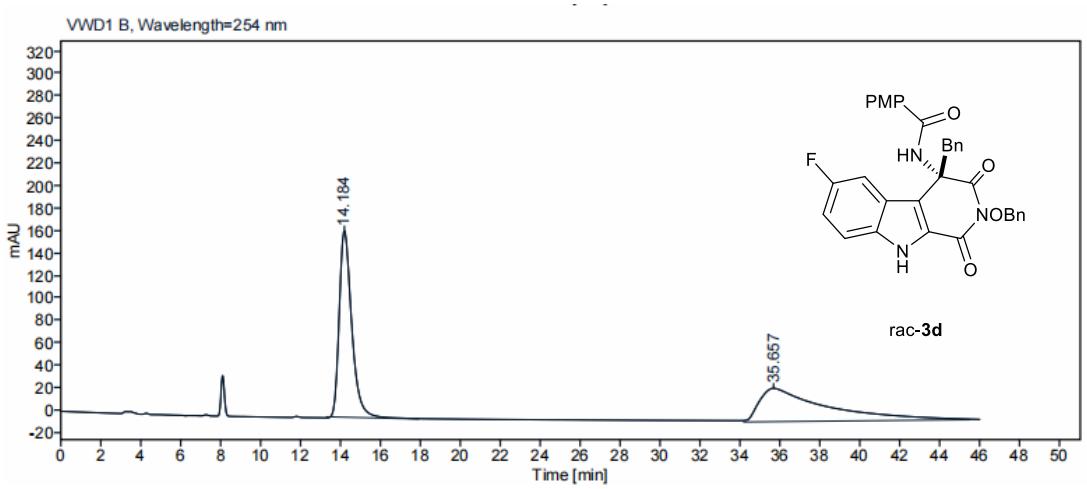
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
26.780	MM	1.4263	4765.9429	55.6917	50.3182	
61.905	MM	6.8683	4705.6704	11.4187	49.6818	
		Sum	9471.6133			



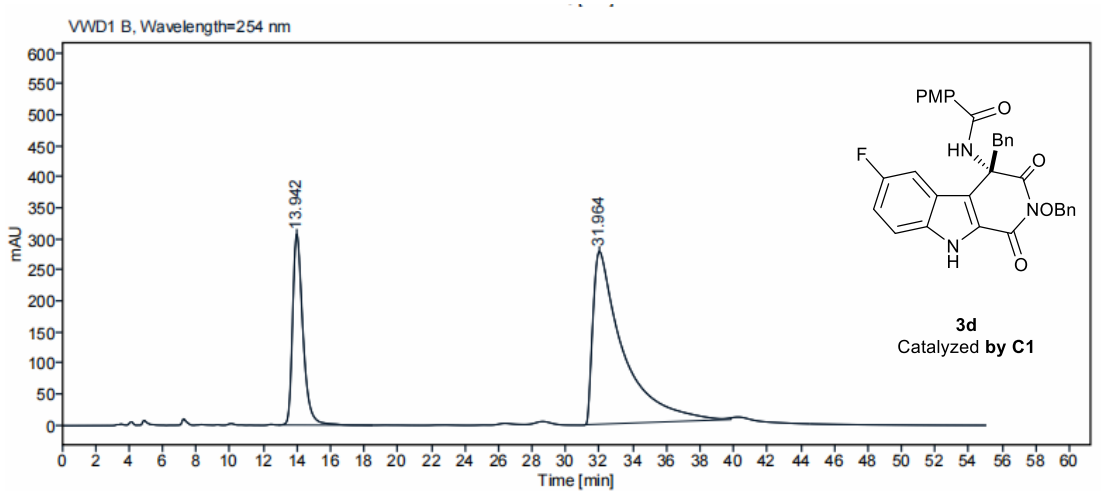
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
28.294	BB	1.4631	879.3219	8.9902	97.2786	
61.667	MM	8.1499	24.5997	0.0503	2.7214	
		Sum	903.9216			



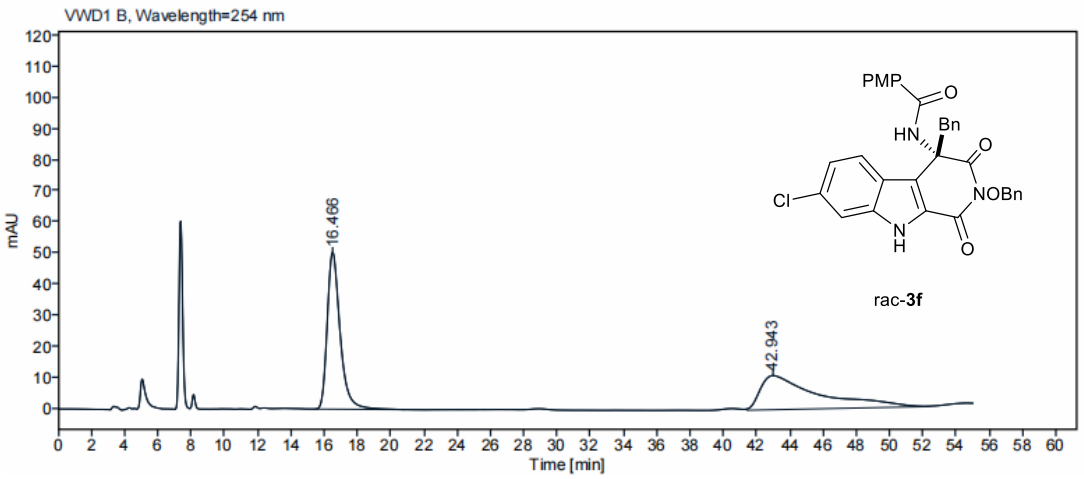
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.184	MM	0.7256	7226.4878	165.9963	51.1808	
35.657	MM	3.8647	6893.0396	29.7262	48.8192	
		Sum	14119.5273			



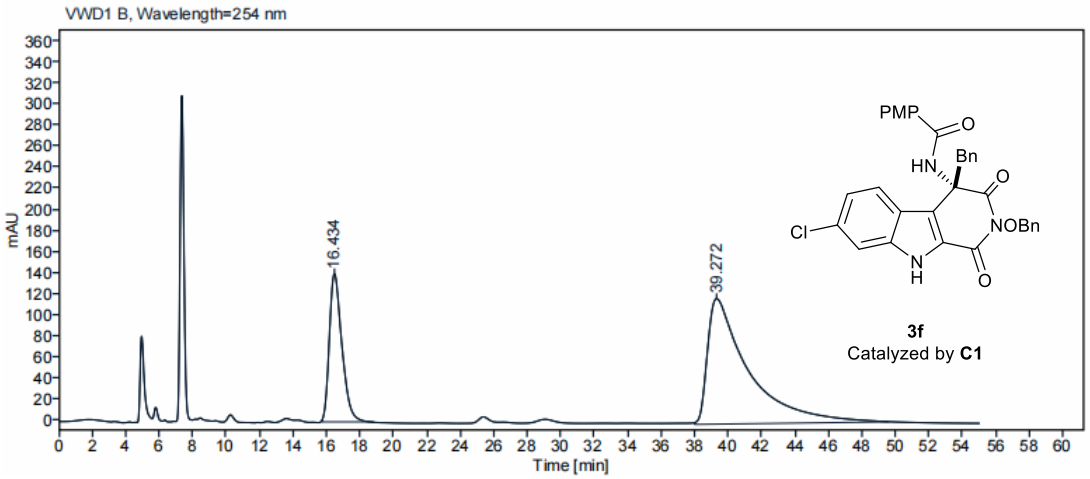
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.942	BB	0.6493	13163.5156	307.5609	27.4507	
31.964	MM	2.0832	34789.7695	278.3318	72.5493	
		Sum	47953.2852			



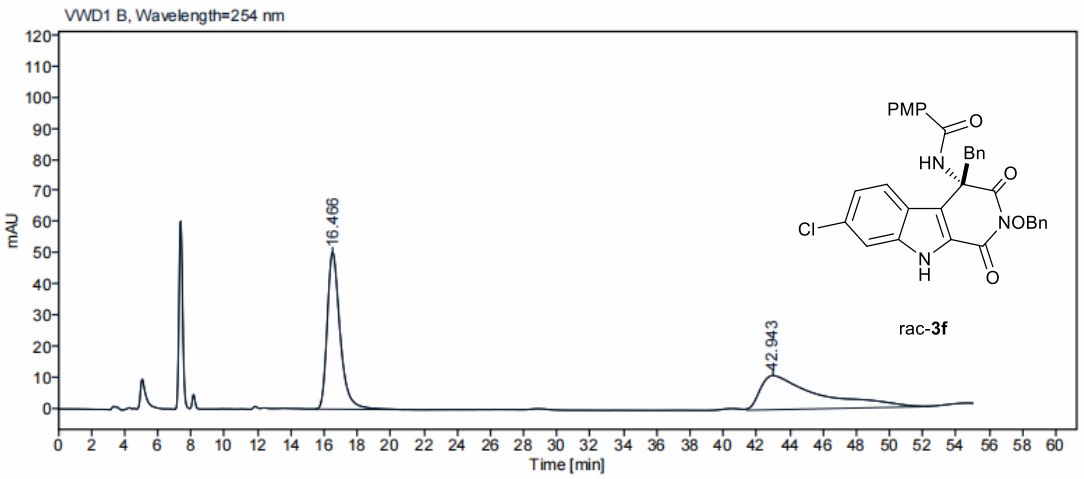
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.466	BB	0.8175	2723.9736	50.4810	50.5319	
42.943	MM	4.0487	2666.6240	10.9773	49.4681	
		Sum	5390.5977			



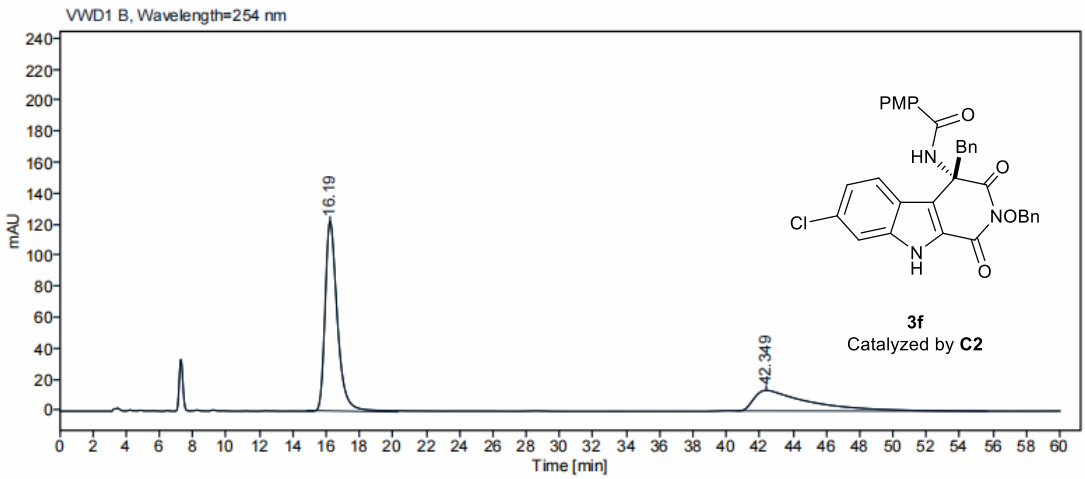
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.434	MM	0.8697	7317.7393	140.2402	26.6525	
39.272	MM	2.8250	20138.3262	118.8110	73.3475	
		Sum	27456.0654			



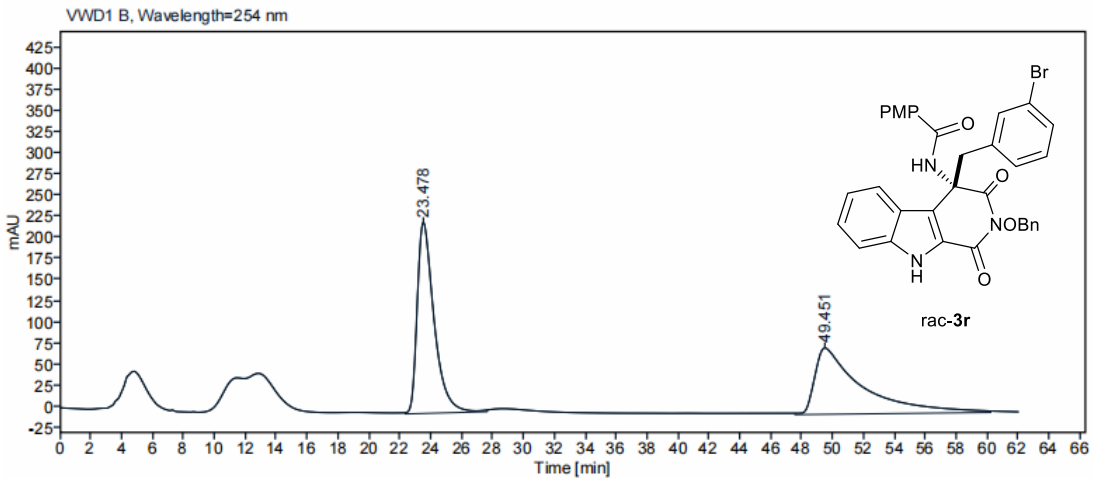
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.466	BB	0.8175	2723.9736	50.4810	50.5319	
42.943	MM	4.0487	2666.6240	10.9773	49.4681	
		Sum	5390.5977			



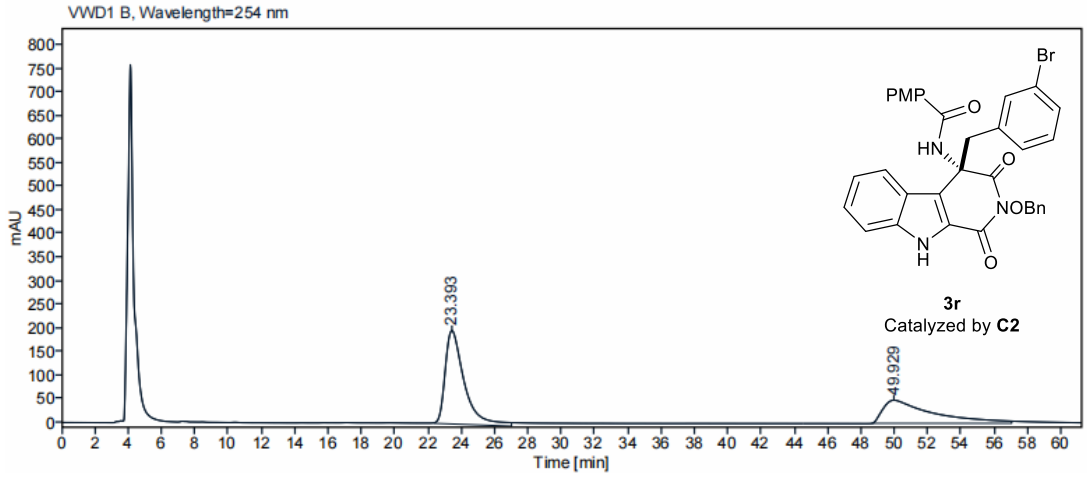
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.190	BB	0.7713	6220.8828	122.3197	67.4182	
42.349	BB	3.0238	3006.4167	13.2270	32.5818	
		Sum	9227.2996			



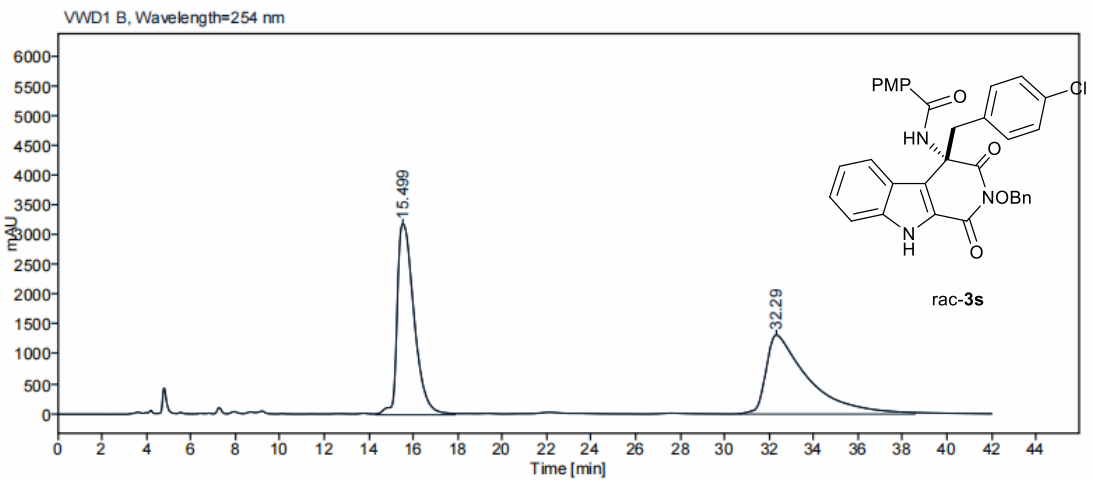
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.478	MM	1.2651	17143.7500	225.8554	50.8053	
49.451	MM	3.5266	16600.2480	78.4535	49.1947	
		Sum	33743.9980			



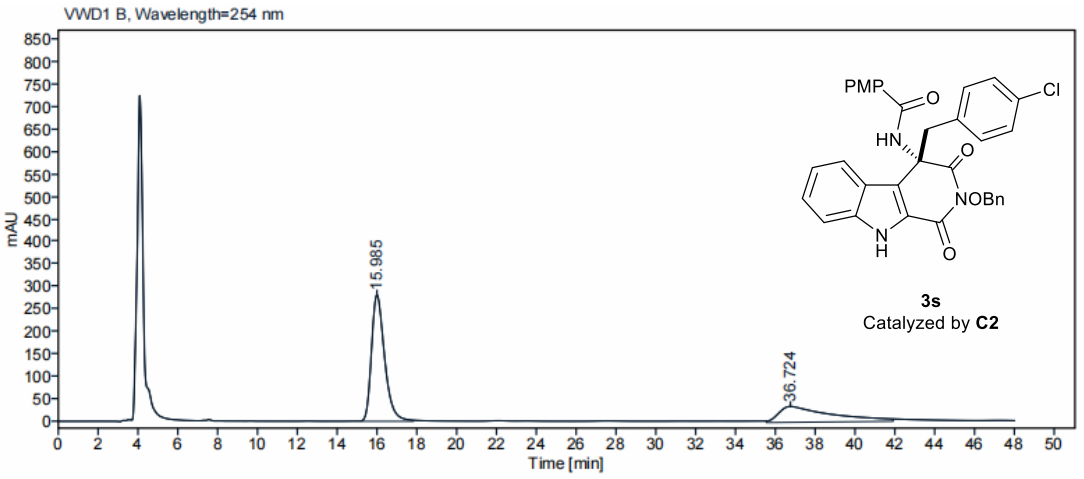
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.393	MM	1.3246	15728.6631	197.9113	60.7606	
49.929	MM	3.4554	10157.6260	48.9946	39.2394	
		Sum	25886.2891			



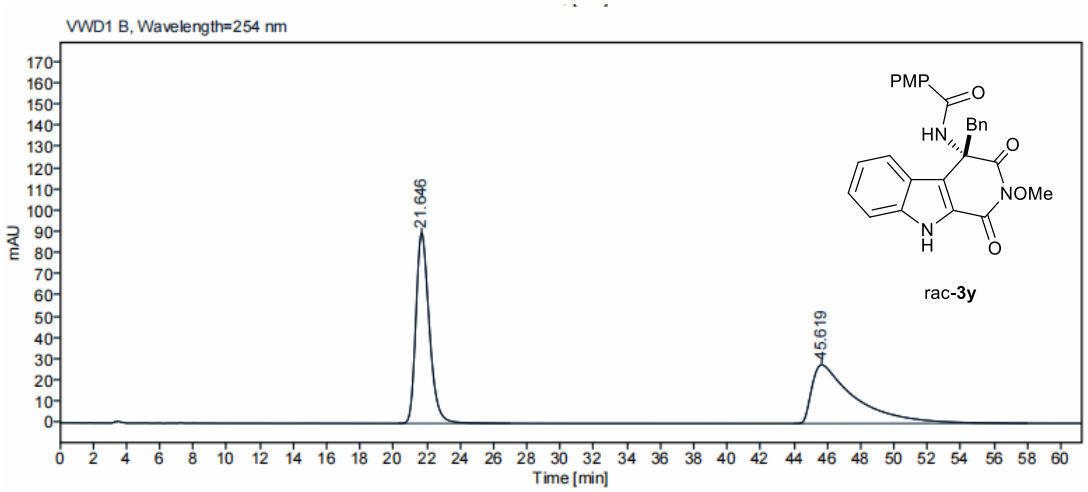
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
15.499	MM	0.8808	169453.9375	3206.2834	49.1076	
32.290	MM	2.2041	175612.9375	1327.9015	50.8924	
		Sum	345066.8750			



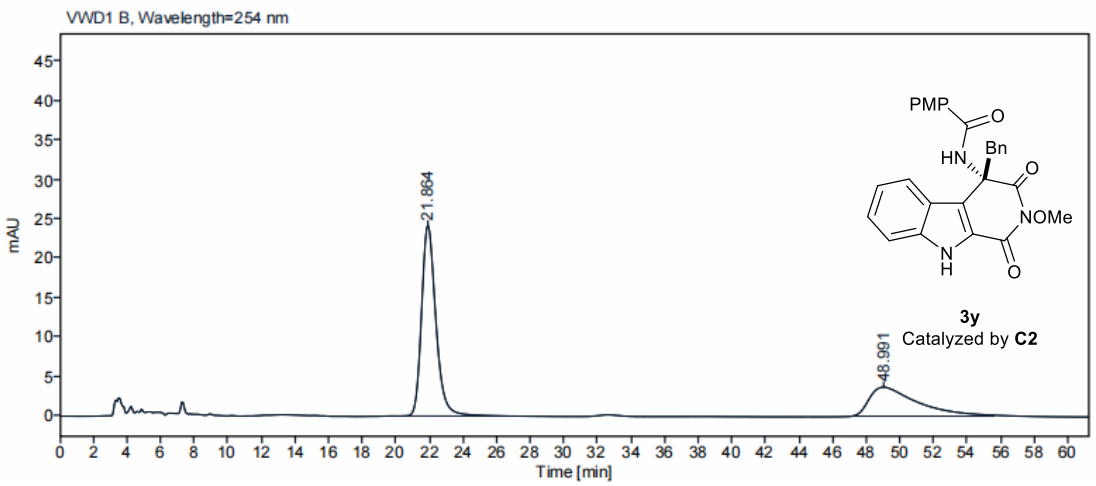
Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
15.985	MM	0.7637	12932.8350	282.2520	66.5276	
36.724	MM	3.0596	6506.9619	35.4454	33.4724	
		Sum	19439.7969			



Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
21.646	BB	0.8591	5027.4756	89.8066	50.3052	
45.619	BB	2.4790	4966.4775	27.6307	49.6948	
		Sum	9993.9531			



Signal: VWD1 B, Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
21.864	BB	0.9020	1431.2595	24.1992	66.0888	
48.991	MM	3.3193	734.4022	3.6876	33.9112	
		Sum	2165.6617			

10. References

[1] S. K. Nimmagadda, M. Liu, M. K. Karunananda, D. W. Gao, O. Apolinar, J. S. Chen, P. Liu and K. M. Engle, Catalytic, Enantioselective alpha-Alkylation of Azlactones with Nonconjugated Alkenes by Directed Nucleopalladation, *Angew. Chem. Int. Ed.*, 2019, **58**, 3923-3927.

[2] M. Schlegel and C. Schneider, Iron(III)-Catalyzed (4 + 2)-Cycloannulation of 2-Hydroxy Ketoxime Ethers with Indol-2-ylamides: Synthesis of Indole-Fused 2-Piperidinones, *J. Org. Chem.*, 2019, **84**, 5886-5892.

[3] A. Acharya, D. Anumandla and C. S. Jeffrey, Dearomative Indole Cycloaddition Reactions of Aza-Oxyallyl Cationic Intermediates: Modular Access to Pyrroloindolines, *J. Am. Chem. Soc.*, 2015, **137**, 14858-14860.

[4] M. A. Kuznetsov, A. N. Shestakov, M. Zibinsky, M. Krasavin, C. T. Supuran, S. Kalinin and M. Tanç, Synthesis, structure and properties of *N* -aminosaccharin – A selective inhibitor of human carbonic anhydrase I, *Tetrahedron Lett.*, 2017, **58**, 172-174.