

Supporting Information for

Catalytic Enantioselective and Regioselective Substitution of 2,3-Indolyldimethanols with Enaminones

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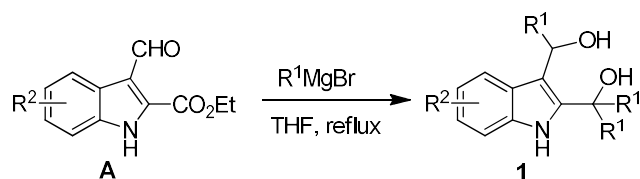
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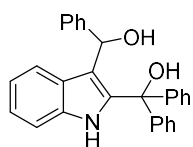
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1. General procedure for the synthesis of substrates 1 and their characteristic data



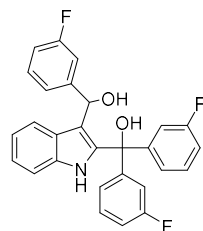
Under argon atmosphere at 0 °C, the solution of starting materials **A** (5 mmol) in THF (40 mL) was added to the Grignard reagents (30 mmol). Then, the reaction mixture was warmed up to 70 °C and stirred overnight. After completing the reaction, saturated NH₄Cl aqueous solution was added to the reaction mixture, which was extracted by EtOAc. The resultant organic layer was dried by anhydrous Na₂SO₄ and purified by flash column chromatography (petroleum ether/ethyl acetate = 6/1) to afford substrates **1**.

(3-(hydroxy(phenyl)methyl)-1H-indol-2-yl)diphenylmethanol (**1a**):



yield: 55% (1.11 g), yellow solid, m.p. 71-72 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.59 (s, 1H), 7.42 – 7.36 (m, 8H), 7.35 – 7.32 (m, 4H), 7.29 (s, 2H), 7.25 – 7.19 (m, 2H), 7.13 – 7.08 (m, 2H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.96 – 6.91 (m, 1H), 6.14 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 146.3, 145.1, 142.7, 140.6, 133.9, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 126.8, 122.2, 120.0, 119.9, 113.8, 111.0, 78.8, 70.4; IR (KBr): 3689, 3005, 2359, 1733, 1684, 1507, 1457, 1275, 1260, 764, 750, 668 cm⁻¹; HRMS (ESI-TOF) *m/z*: [M - H]⁻ Calcd for C₂₈H₂₂NO₂ 404.1651, Found 404.1659.

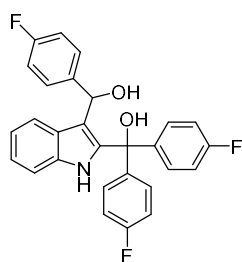
bis(3-fluorophenyl)(3-((3-fluorophenyl)(hydroxy)methyl)-1H-indol-2-yl)methanol (**1b**):



yield: 59% (1.32 g), yellow solid, m.p. 94-95 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.57 (s, 1H), 7.37 – 7.29 (m, 2H), 7.24 (d, *J* = 1.1 Hz, 1H), 7.23 – 7.20 (m, 1H), 7.19 – 7.14 (m, 2H), 7.13 – 7.11 (m, 3H), 7.10 – 7.05 (m, 3H), 7.05 – 6.96 (m, 5H), 6.94 – 6.88 (m, 1H), 6.18 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 162.9(d, *J* = 247.3 Hz), 162.8(d, *J* = 245.4 Hz), 162.7(d, *J* = 247.1 Hz), 148.3(d, *J* = 6.4 Hz), 147.1(d, *J* = 6.6 Hz), 145.0(d, *J* = 6.6 Hz), 139.3, 133.8, 130.0(d, *J* = 3.5 Hz), 129.9(d, *J* = 3.8 Hz), 129.8, 127.2, 123.1(d, *J* = 3.0 Hz), 123.0(d, *J* = 2.9 Hz), 122.7, 122.0(d, *J* = 2.9 Hz), 120.5, 119.4, 115.3(d, *J* = 6.2 Hz), 115.1(d, *J* = 6.1 Hz), 114.8(d, *J* = 2.3 Hz), 114.6(d, *J* = 2.2 Hz),

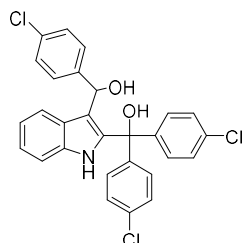
114.3, 113.6(d, $J = 4.6$ Hz), 113.4, 111.3, 78.0, 69.5; IR (KBr): 3689, 3123, 2342, 1733, 1653, 1507, 1446, 1275, 1260, 764, 750, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[M - H]^-$ Calcd for $\text{C}_{28}\text{H}_{19}\text{F}_3\text{NO}_2$ 458.1368, Found 458.1382.

bis(4-fluorophenyl)(3-((4-fluorophenyl)(hydroxy)methyl)-1*H*-indol-2-yl)methanol (1c):



yield: 53% (1.22 g), yellow solid, m.p. 112-113 °C; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.55 – 7.46 (m, 2H), 7.35 – 7.26 (m, 6H), 7.25 – 7.22 (m, 1H), 7.17 – 7.12 (m, 1H), 7.09 – 6.93 (m, 8H), 6.17 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 162.3(d, $J = 246.2$ Hz), 140.4(d, $J = 80.4$ Hz), 138.4, 133.8, 129.4(d, $J = 8.2$ Hz), 129.2(d, $J = 8.1$ Hz), 128.4(d, $J = 8.2$ Hz), 127.3, 122.5, 120.3, 119.5, 115.2(d, $J = 21.4$ Hz), 115.1(d, $J = 21.4$ Hz), 113.7, 111.2, 77.9, 69.8; IR (KBr): 3750, 3123, 2360, 1733, 1653, 1507, 1275, 1260, 764, 750, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[M - H]^-$ Calcd for $\text{C}_{28}\text{H}_{19}\text{F}_3\text{NO}_2$ 458.1368, Found 458.1373.

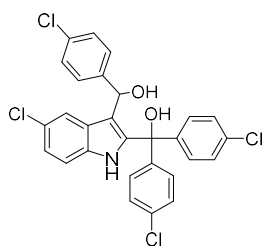
bis(4-chlorophenyl)(3-((4-chlorophenyl)(hydroxy)methyl)-1*H*-indol-2-yl)methanol (1d):



yield: 60% (1.52 g), white solid, m.p. 130-131 °C; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.49 (s, 1H), 7.34 – 7.27 (m, 6H), 7.25 – 7.24 (m, 2H), 7.23 (d, $J = 2.7$ Hz, 3H), 7.21 (s, 1H), 7.19 – 7.10 (m, 3H), 7.05 – 7.00 (m, 1H), 6.18 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 140.8, 134.2, 128.9, 128.8, 128.6, 128.5, 128.4, 127.9, 122.7, 120.5, 119.4, 111.3, 77.9, 69.7; IR (KBr): 3750, 3123, 2360, 1733, 1684, 1507, 1399, 1275, 1260, 764, 750, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[M - H]^-$ Calcd for $\text{C}_{28}\text{H}_{19}\text{Cl}_3\text{NO}_2$ 506.0482, Found 506.0484.

(5-chloro-3-((4-chlorophenyl)(hydroxy)methyl)-1*H*-indol-2-yl)bis(4-chlorophenyl)methanol

(1e):

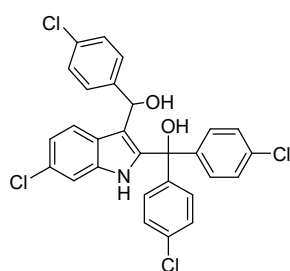


yield: 60% (1.62 g), yellow solid, m.p. 85-86 °C; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.53 (s, 1H), 7.34 – 7.29 (m, 3H), 7.24 (s, 3H), 7.22 (s, 2H), 7.20 (s, 2H), 7.19 – 7.17 (m, 2H), 7.17 – 7.15 (m, 2H), 7.13 – 7.10 (m, 2H), 7.08 – 7.02 (m, 1H), 6.10 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3)

δ (ppm): 144.0, 142.9, 140.8, 140.4, 134.3, 134.2, 133.7, 132.0, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 127.9, 127.8, 126.3, 123.1, 118.8, 113.3, 112.4, 77.9, 69.5; IR (KBr): 3750, 3122, 2359, 1733, 1669, 1521, 1399, 1275, 1260, 764, 750, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^-$ Calcd for $\text{C}_{28}\text{H}_{18}\text{Cl}_4\text{NO}_2$ 540.0092, Found 540.0102.

(6-chloro-3-((4-chlorophenyl)(hydroxy)methyl)-1H-indol-2-yl)bis(4-chlorophenyl)methanol

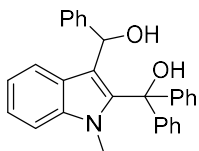
(1f):



yield: 57% (1.54 g), yellow solid, m.p. 92-93 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.50 (s, 1H), 7.35 – 7.30 (m, 3H), 7.28 – 7.27 (m, 2H), 7.25 – 7.23 (m, 4H), 7.22 – 7.17 (m, 7H), 6.97 (d, $J = 1.2$ Hz, 2H), 6.10 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 143.9, 142.9, 140.6, 140.2, 134.4, 134.3, 134.1, 133.6, 128.8, 128.7, 128.6, 128.5,

127.8, 125.7, 121.3, 120.4, 113.8, 111.2, 77.9, 69.5; IR (KBr): 3750, 3005, 2359, 1733, 1683, 1540, 1436, 1275, 1260, 764, 750, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^-$ Calcd for $\text{C}_{28}\text{H}_{18}\text{Cl}_4\text{NO}_2$ 540.0092, Found 540.0091.

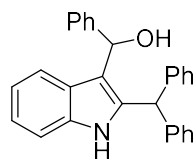
(3-(hydroxy(phenyl)methyl)-1-methyl-1H-indol-2-yl)diphenylmethanol (1g):



yield: 55% (1.15 g), red solid, m.p. 43-44 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.45 (d, $J = 8.0$ Hz, 1H), 7.40 – 7.32 (m, 8H), 7.28 (s, 1H), 7.25 – 7.21 (m, 5H), 7.18 (m, 3H), 7.09 – 7.04 (m, 1H), 5.82 (s, 1H), 3.23 (s, 3H); ^{13}C

NMR (100 MHz, CDCl_3) δ (ppm): 146.5, 143.1, 143.0, 142.5, 140.9, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 121.6, 121.4, 120.0, 119.2, 118.9, 109.9, 88.6, 81.4, 31.0; IR (KBr): 3752, 3415, 2360, 1636, 1617, 1541, 1507, 1275, 1261, 764, 749, 618 cm^{-1} ; HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^-$ Calcd for $\text{C}_{29}\text{H}_{24}\text{NO}_2$ 418.1807, Found 418.1804.

(2-benzhydryl-1H-indol-3-yl)(phenyl)methanol (1h):

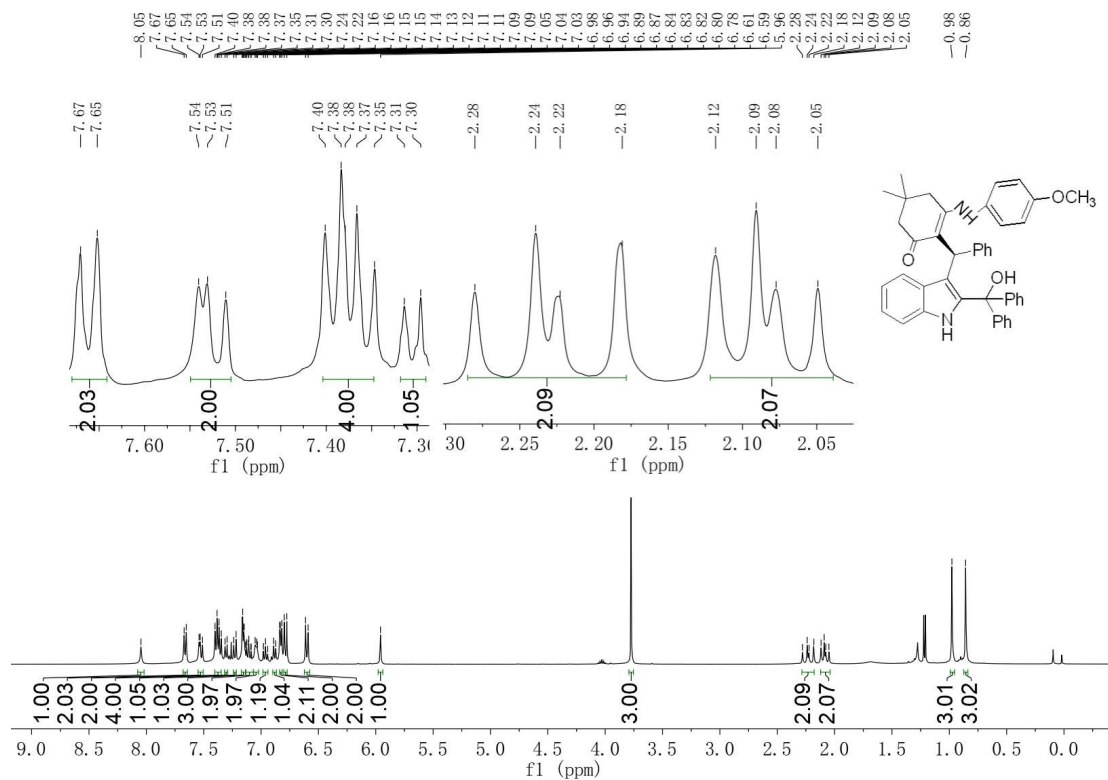


yield: 50% (0.97 g), yellow solid, m.p. 51-52 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.65 (s, 1H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.37 (d, $J = 7.6$ Hz, 2H), 7.34 – 7.28 (m, 6H), 7.25 – 7.18 (m, 4H), 7.15 – 7.09 (m, 5H), 7.00 (m, 1H), 6.21 (d,

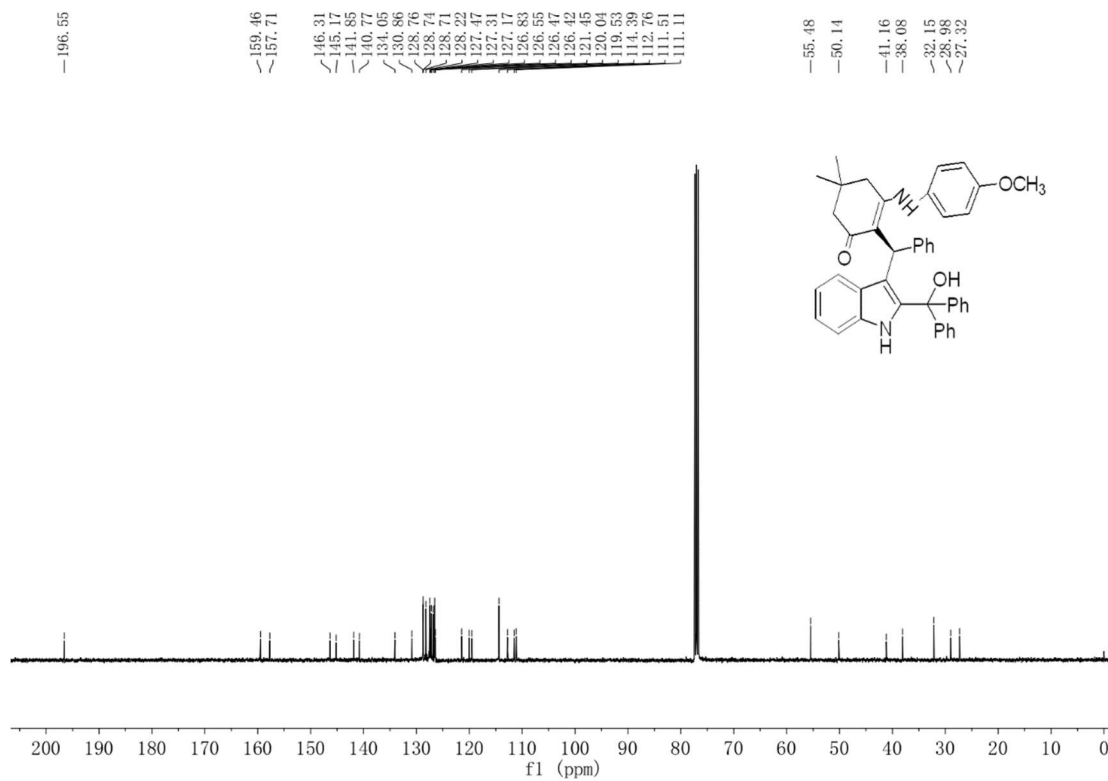
$J = 3.8$ Hz, 1H), 5.91 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 143.3, 141.9, 141.8, 137.3, 128.9, 128.8, 128.7, 128.1, 127.2, 127.1, 126.8, 126.0, 121.8, 119.9, 115.0, 110.8, 68.8, 48.3; IR (KBr): 3415, 2360, 2342, 1636, 1617, 1559, 1430, 1275, 1261, 749, 668 cm^{-1} ; HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^-$ Calcd for $\text{C}_{28}\text{H}_{22}\text{NO}$ 388.1702, Found 388.1699.

2. NMR spectra of products 3

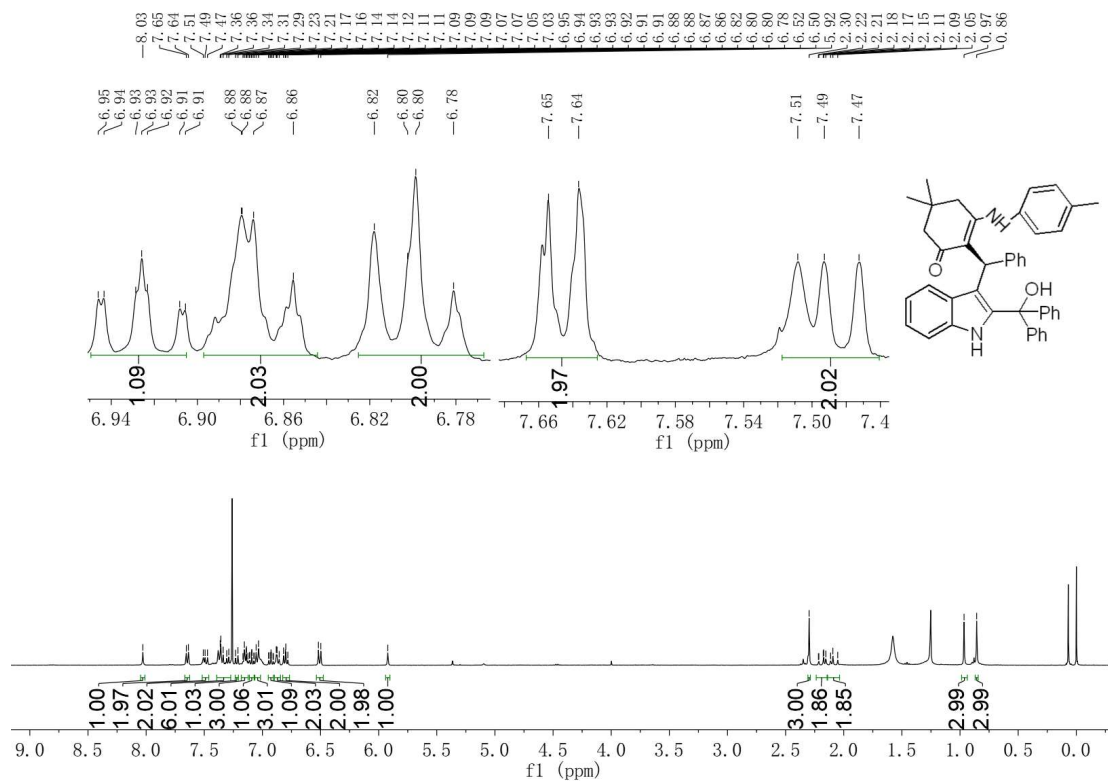
^1H NMR (400 MHz, CDCl_3) of compound **3aa**



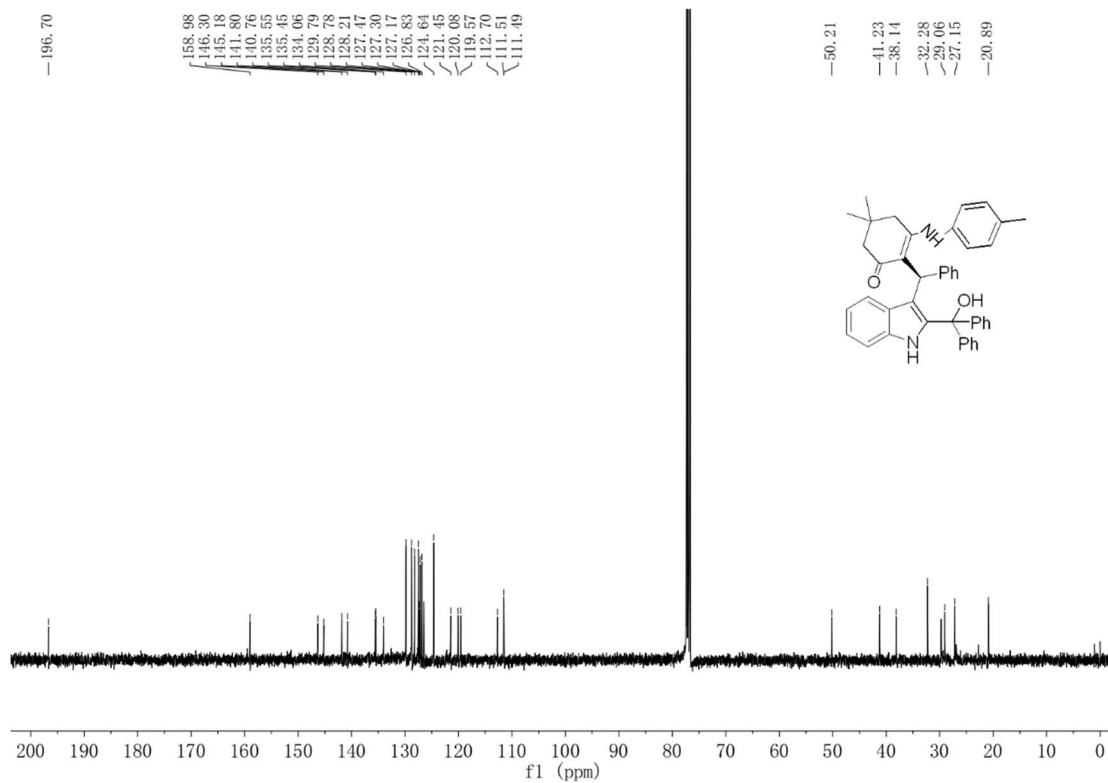
^{13}C NMR (100 MHz, CDCl_3) of compound **3aa**



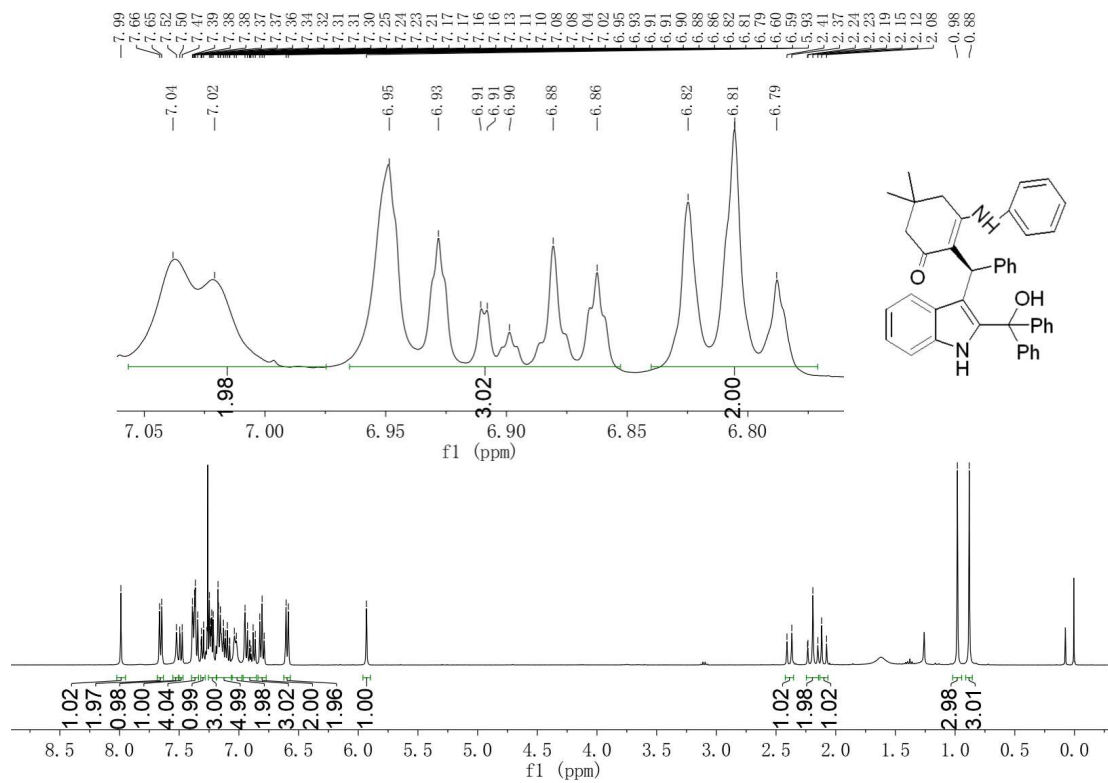
^1H NMR (400 MHz, CDCl_3) of compound **3ab**



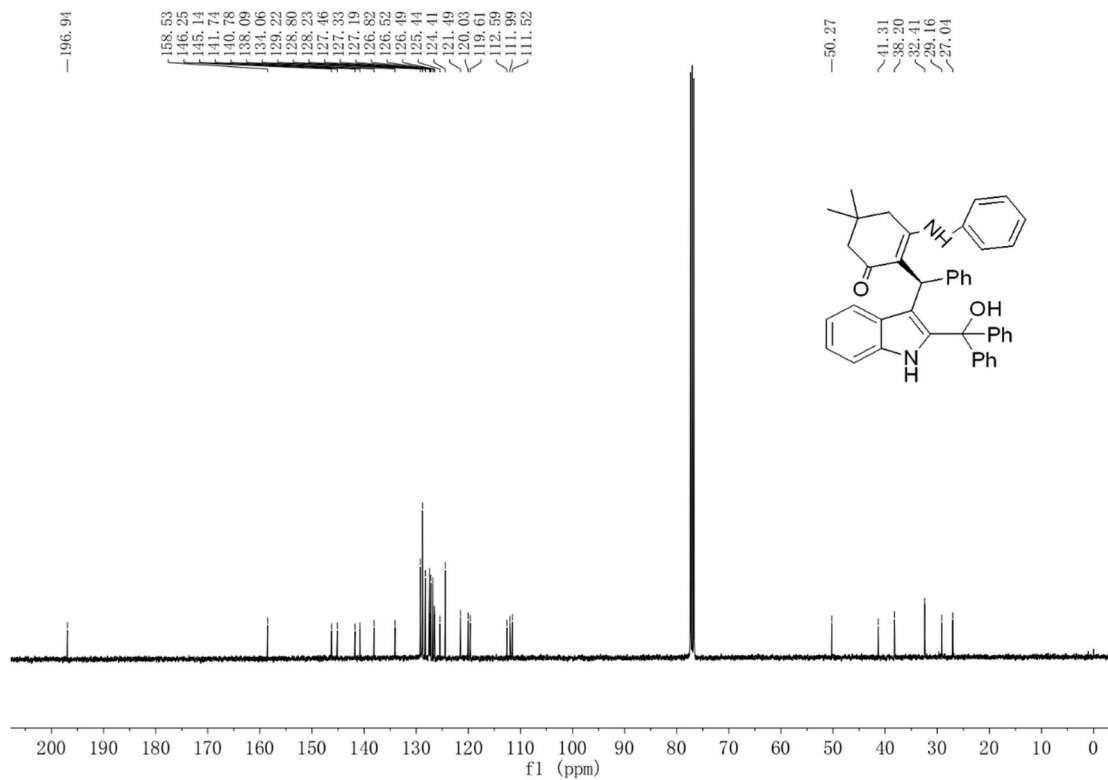
^{13}C NMR (100 MHz, CDCl_3) of compound **3ab**



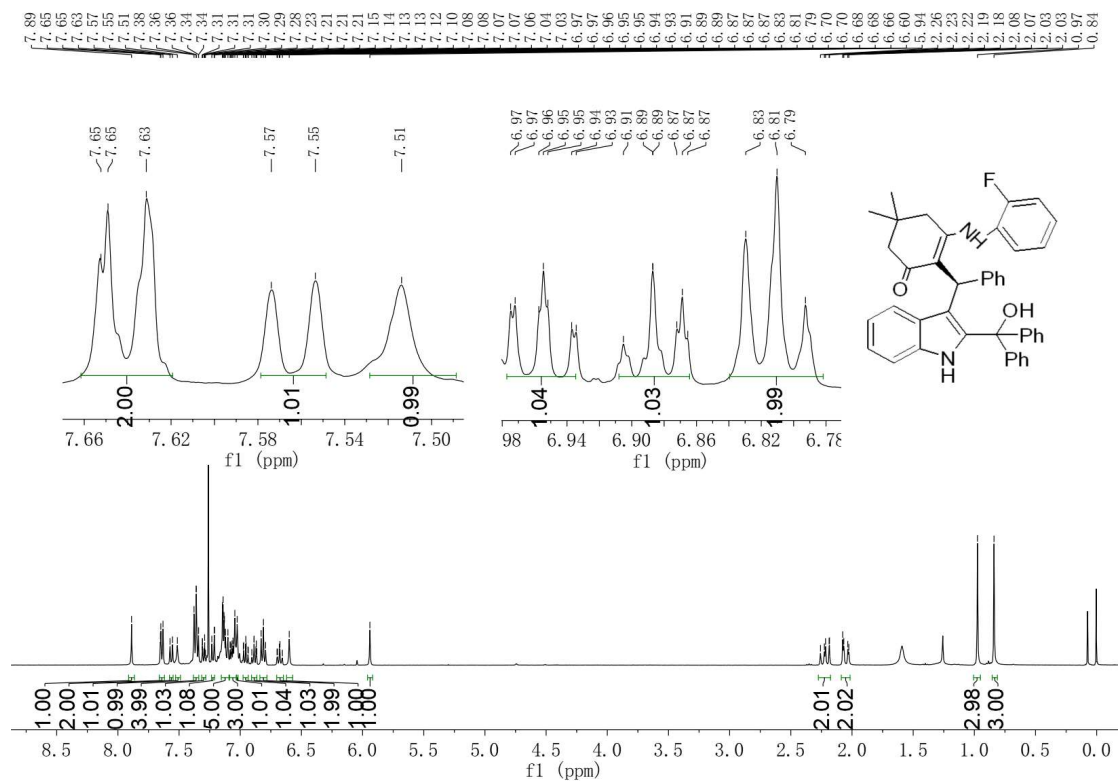
^1H NMR (400 MHz, CDCl_3) of compound **3ac**



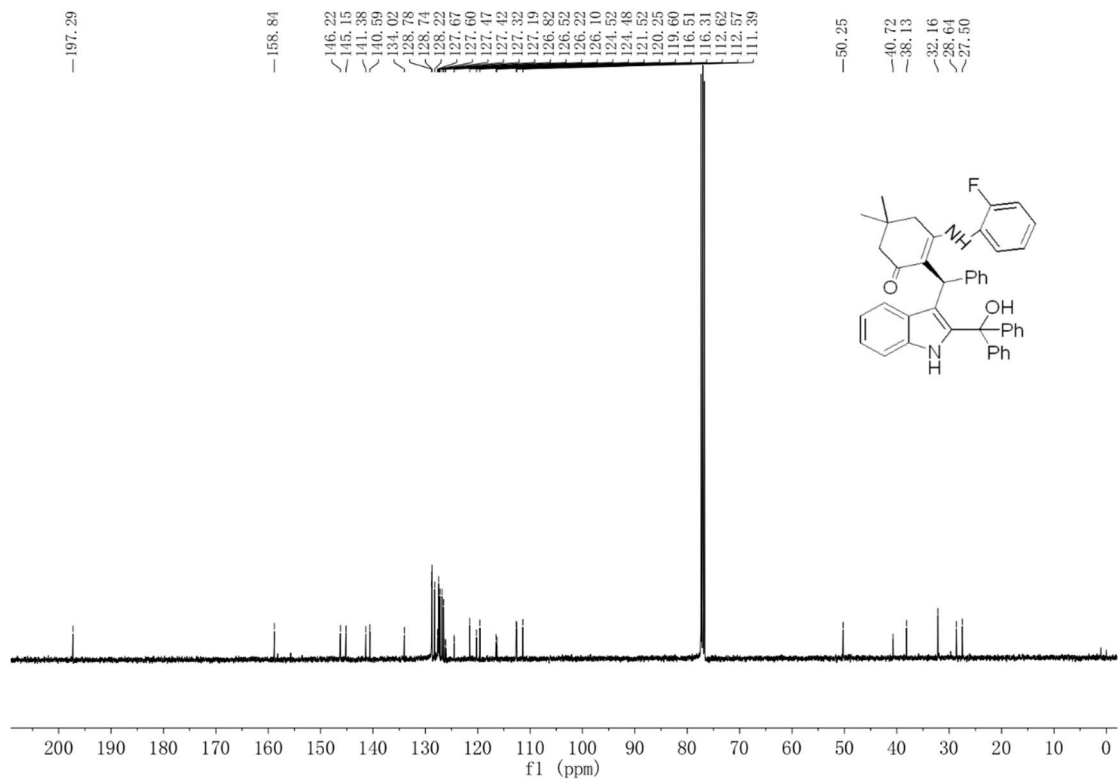
^{13}C NMR (100 MHz, CDCl_3) of compound **3ac**



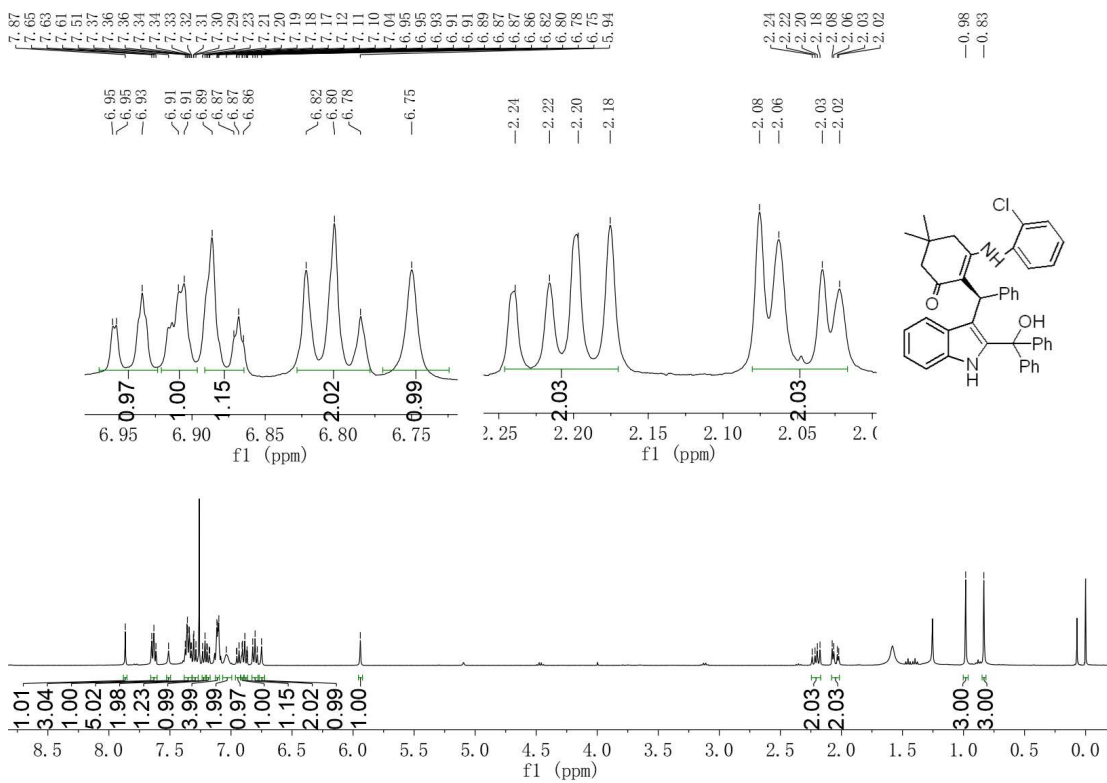
^1H NMR (400 MHz, CDCl_3) of compound **3ad**



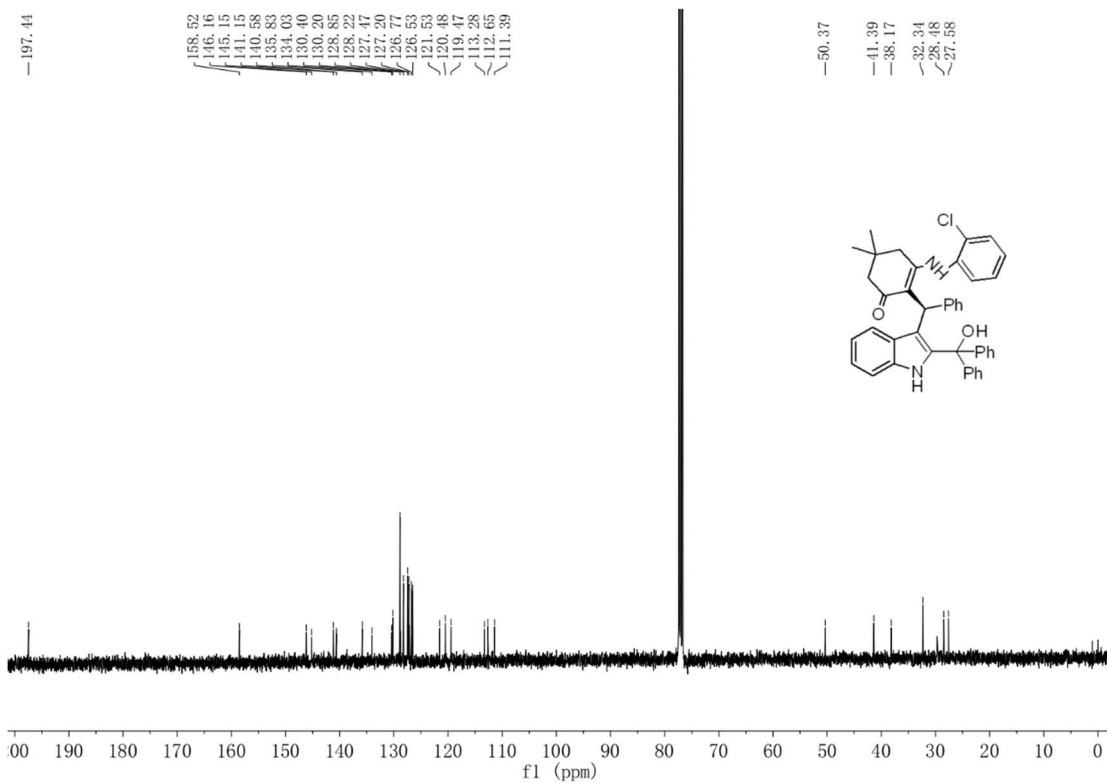
^{13}C NMR (100 MHz, CDCl_3) of compound **3ad**



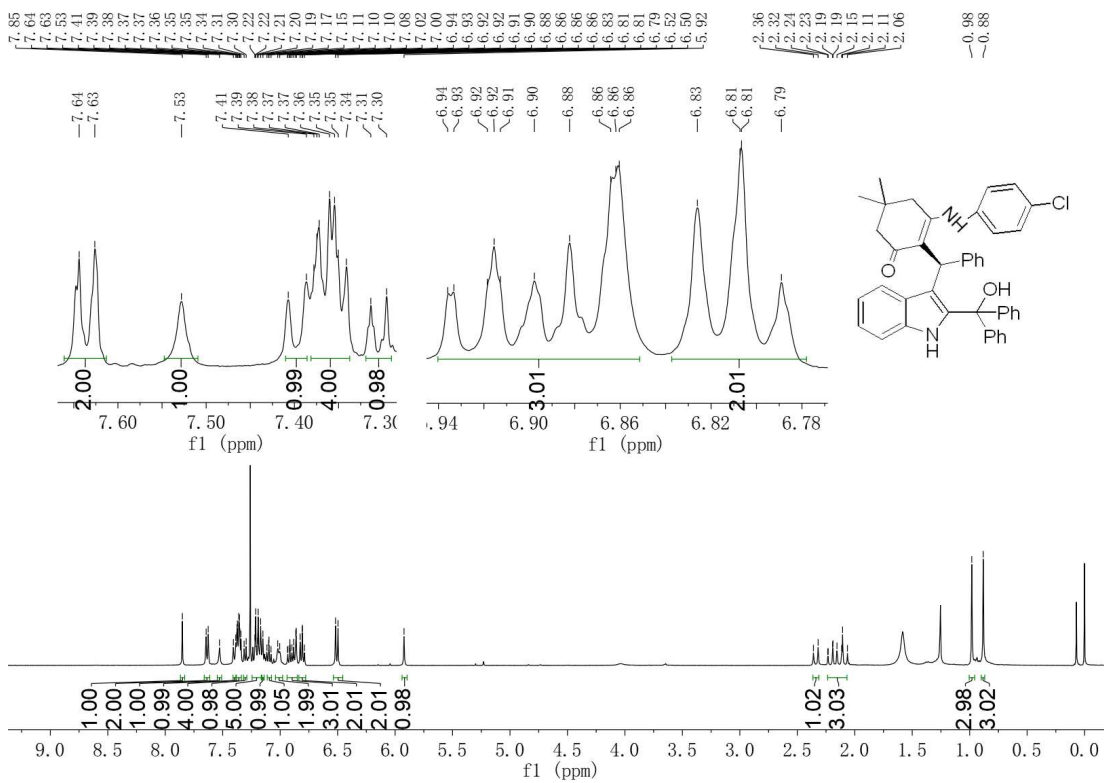
^1H NMR (400 MHz, CDCl_3) of compound **3ae**



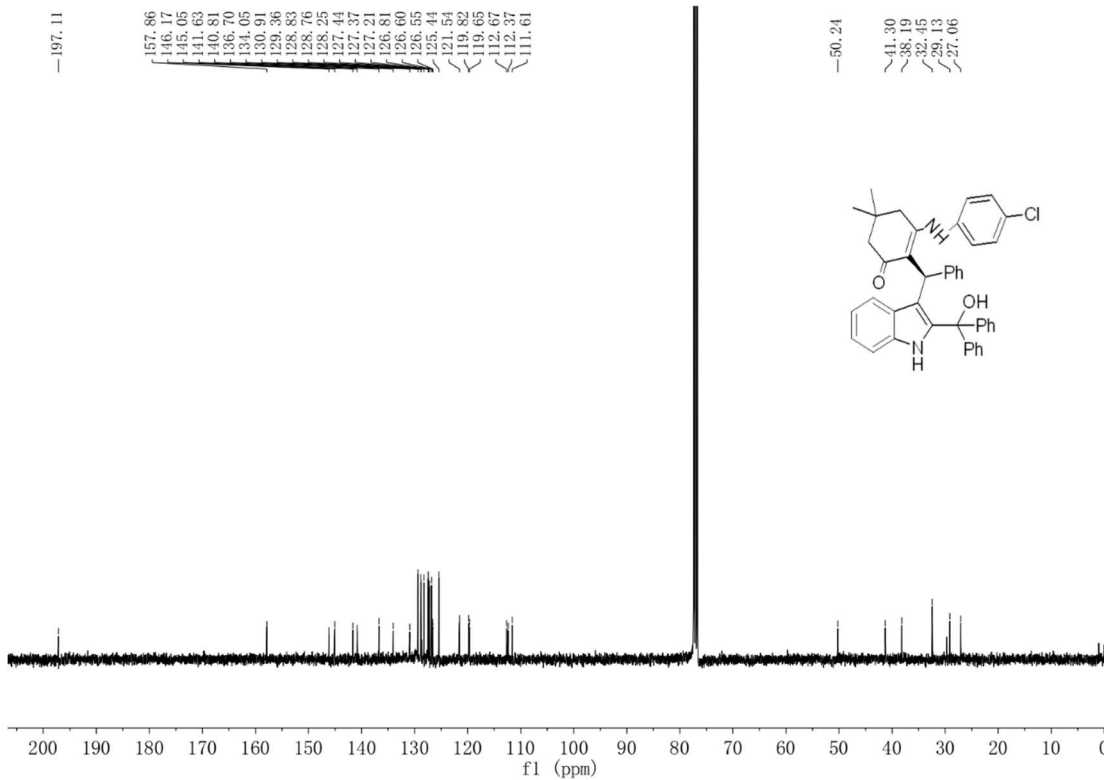
^{13}C NMR (100 MHz, CDCl_3) of compound **3ae**



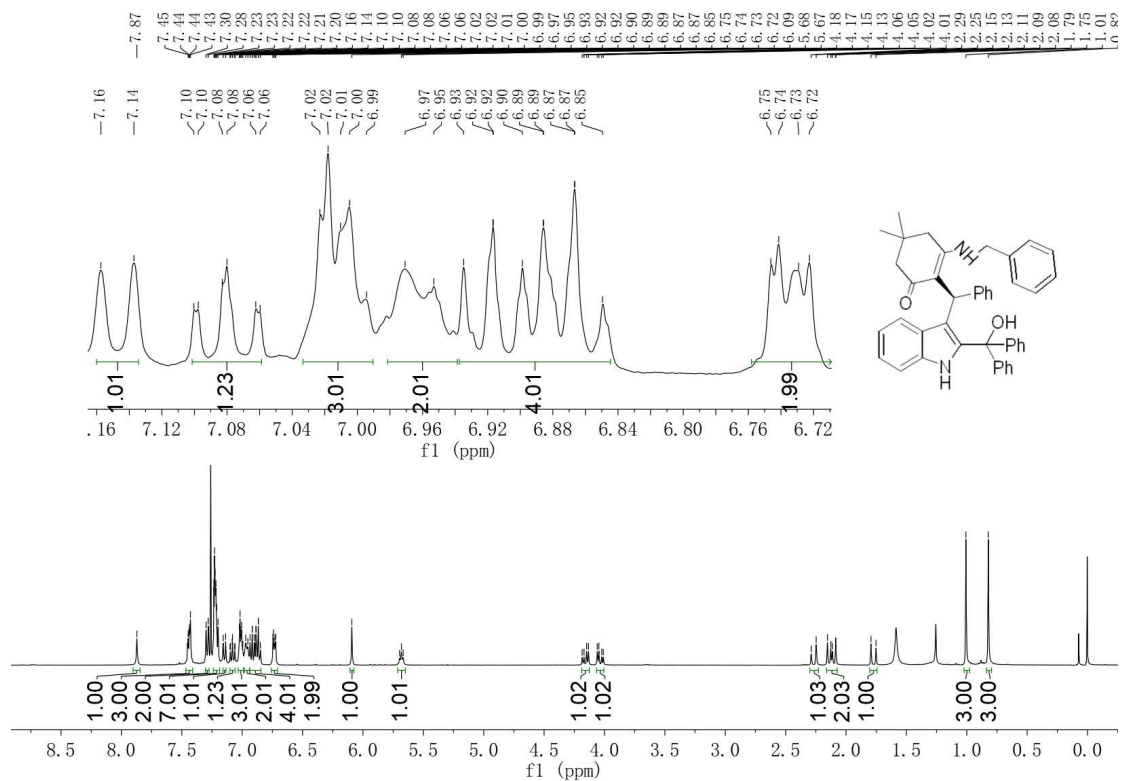
^1H NMR (400 MHz, CDCl_3) of compound **3af**



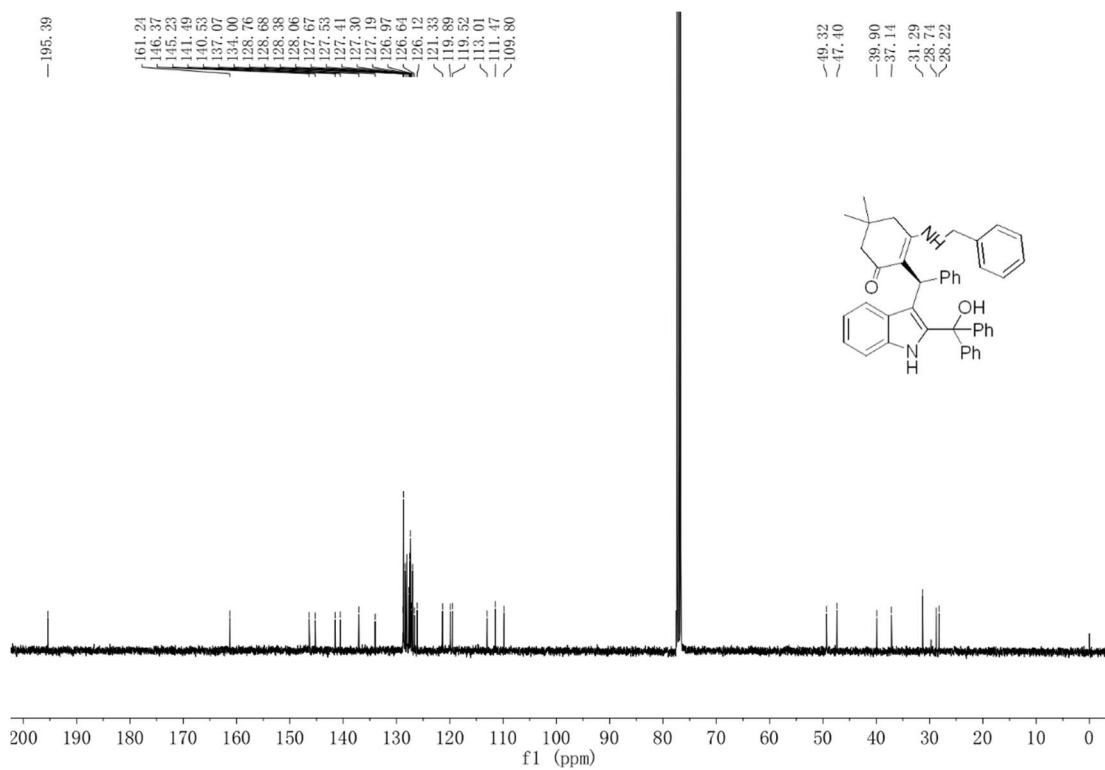
^{13}C NMR (100 MHz, CDCl_3) of compound **3af**



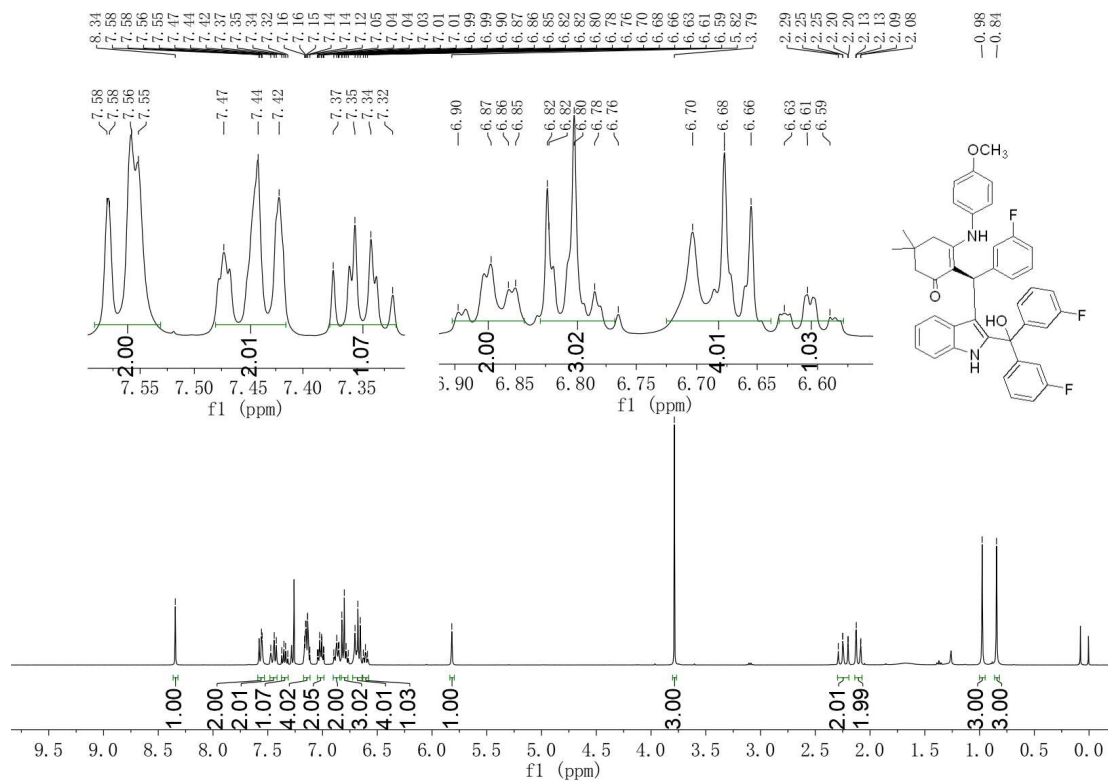
^1H NMR (400 MHz, CDCl_3) of compound **3ag**



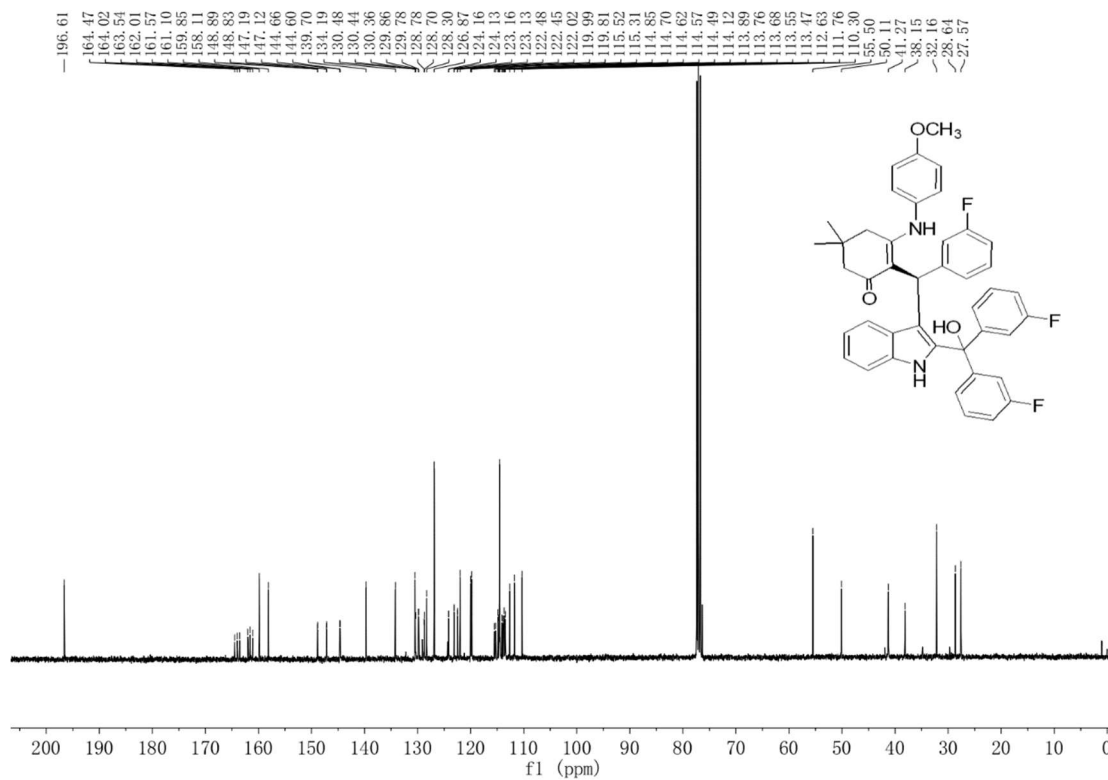
^{13}C NMR (100 MHz, CDCl_3) of compound **3ag**



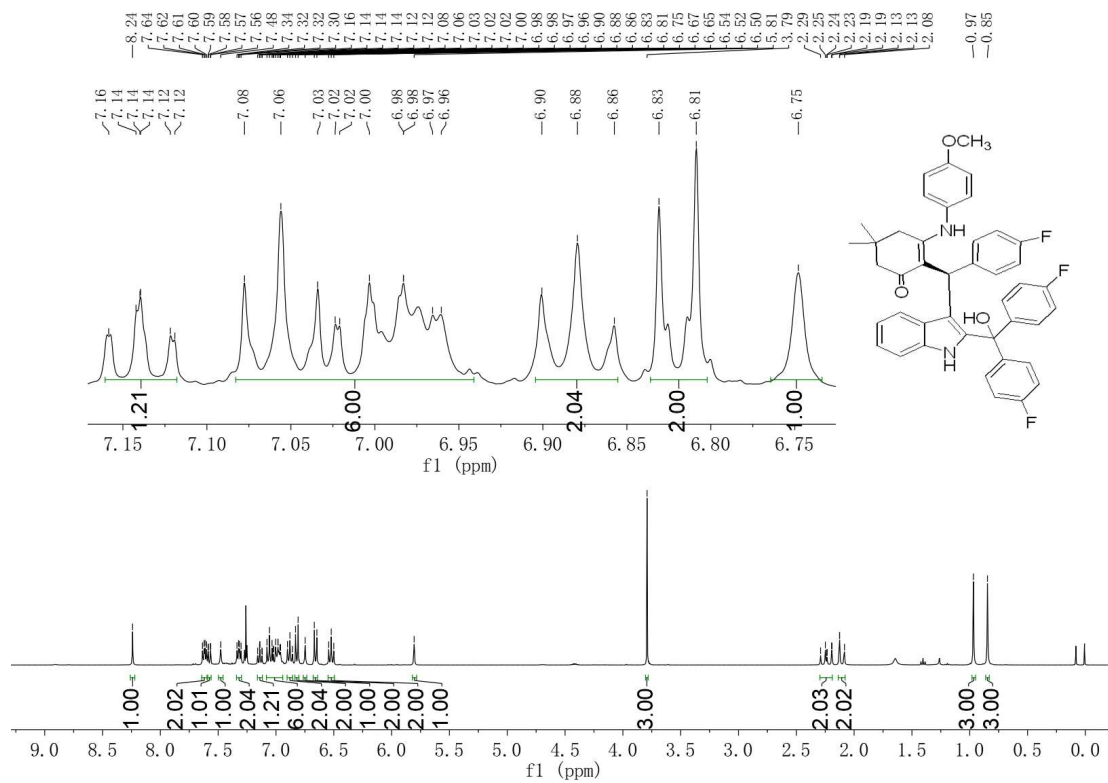
^1H NMR (400 MHz, CDCl_3) of compound **3ba**



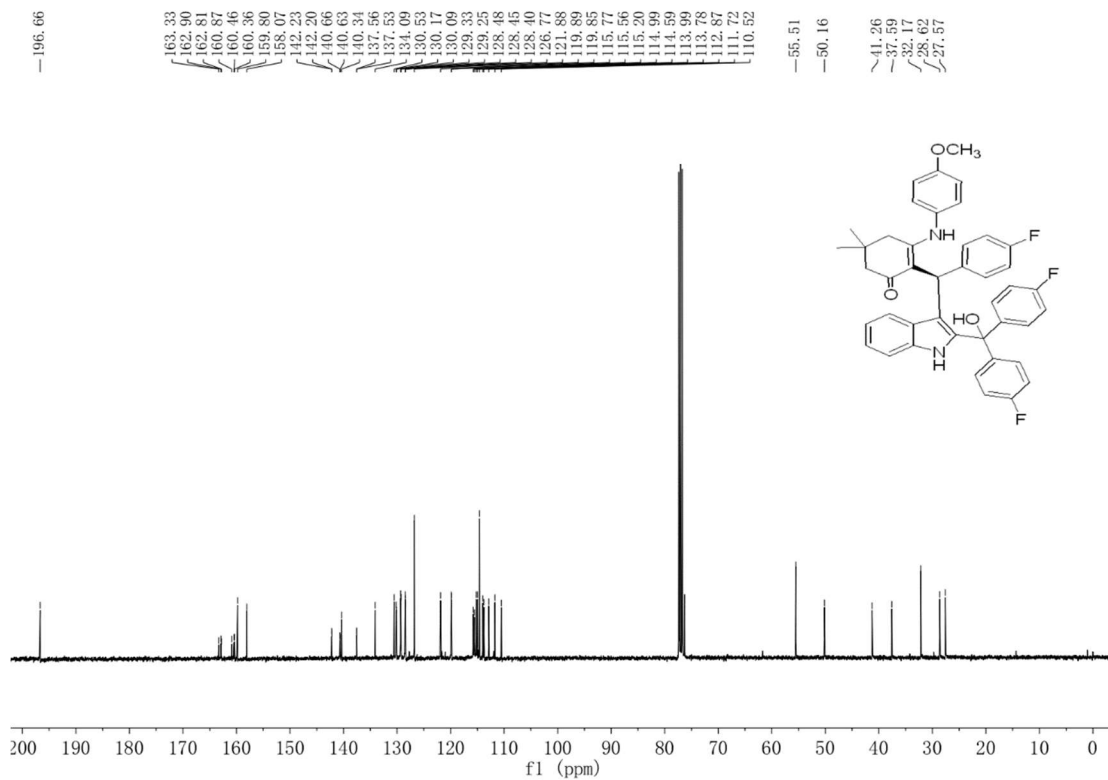
^{13}C NMR (100 MHz, CDCl_3) of compound **3ba**



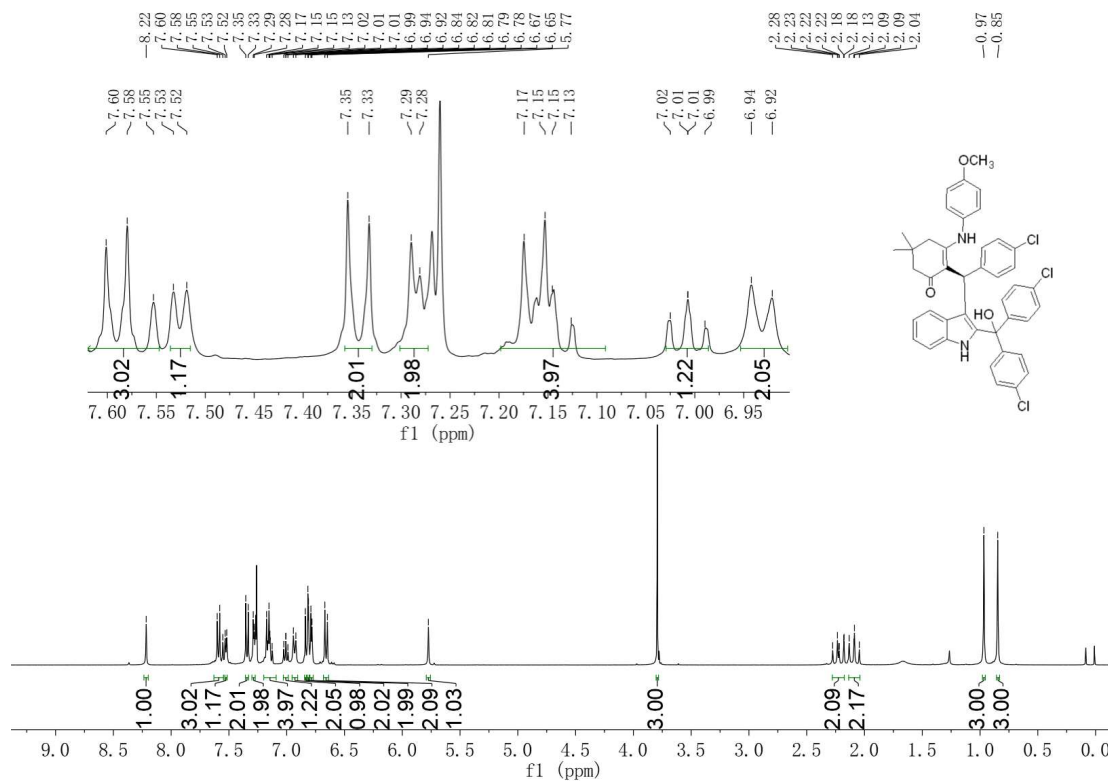
^1H NMR (400 MHz, CDCl_3) of compound **3ca**



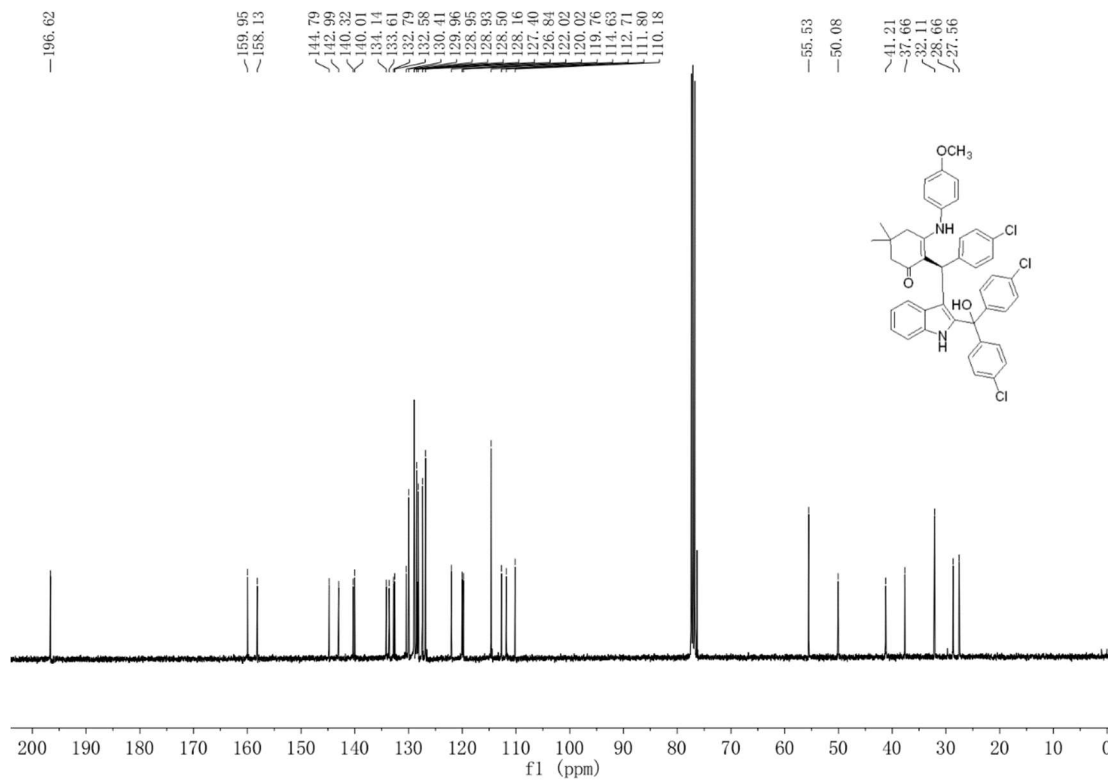
^{13}C NMR (100 MHz, CDCl_3) of compound **3ca**



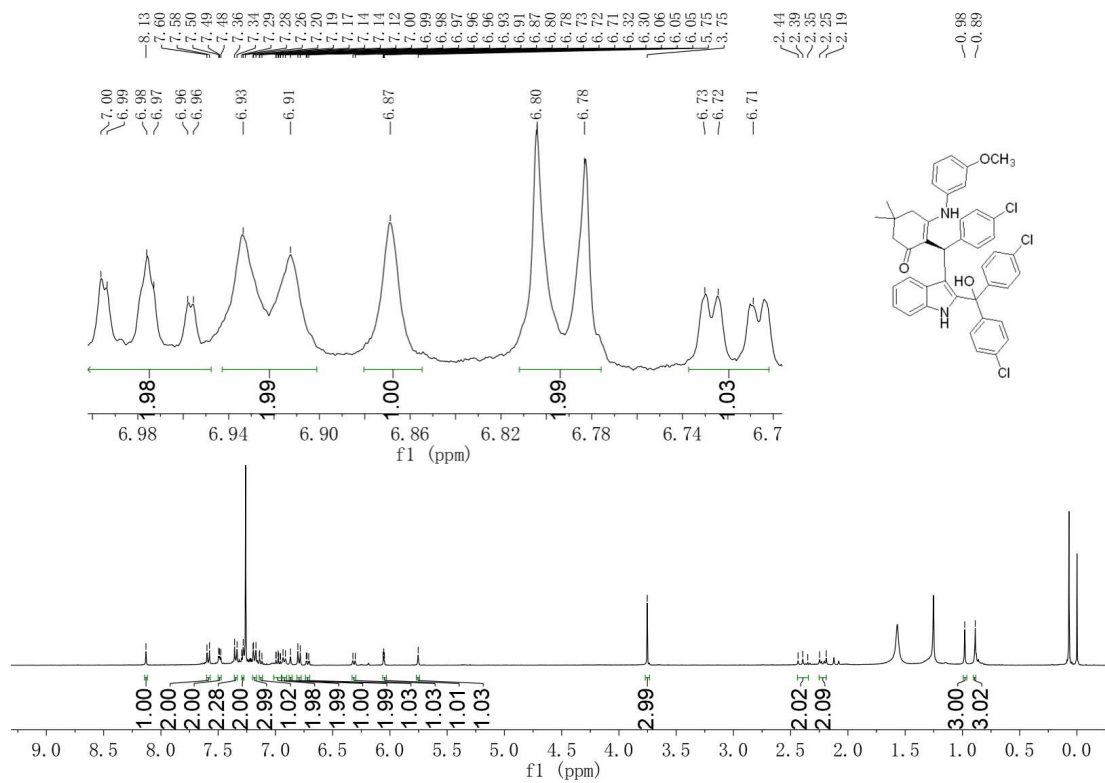
^1H NMR (400 MHz, CDCl_3) of compound **3da**



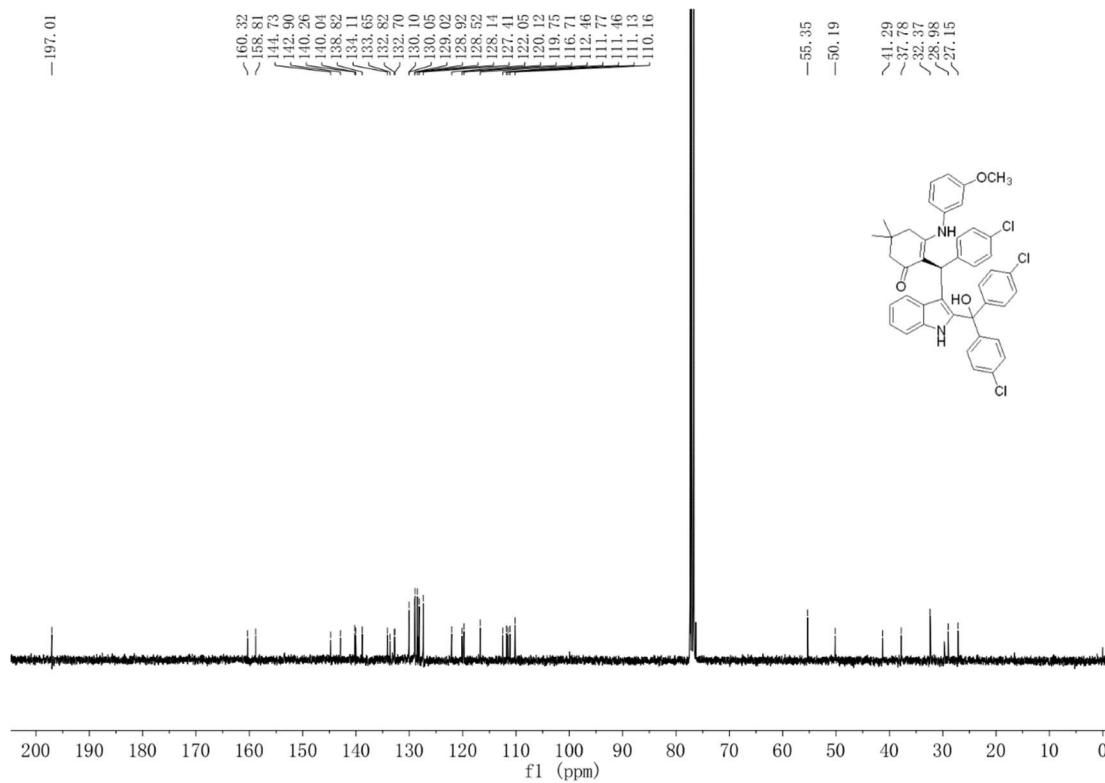
^{13}C NMR (100 MHz, CDCl_3) of compound **3da**



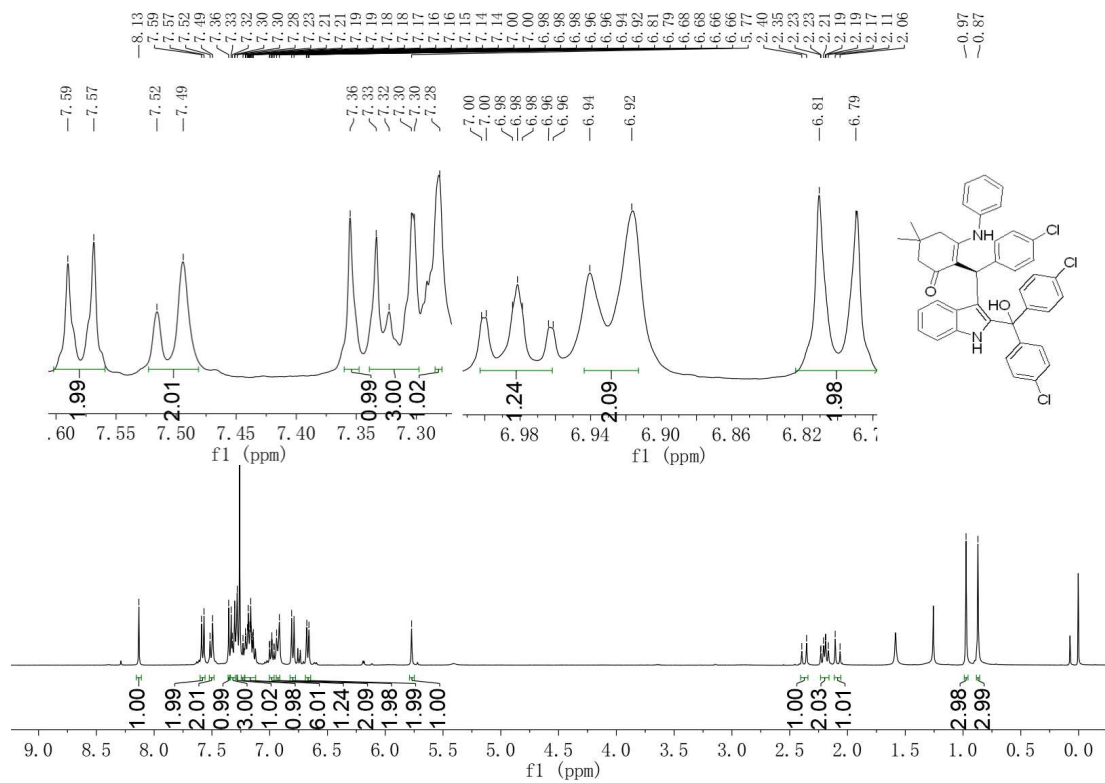
^1H NMR (400 MHz, CDCl_3) of compound **3dh**



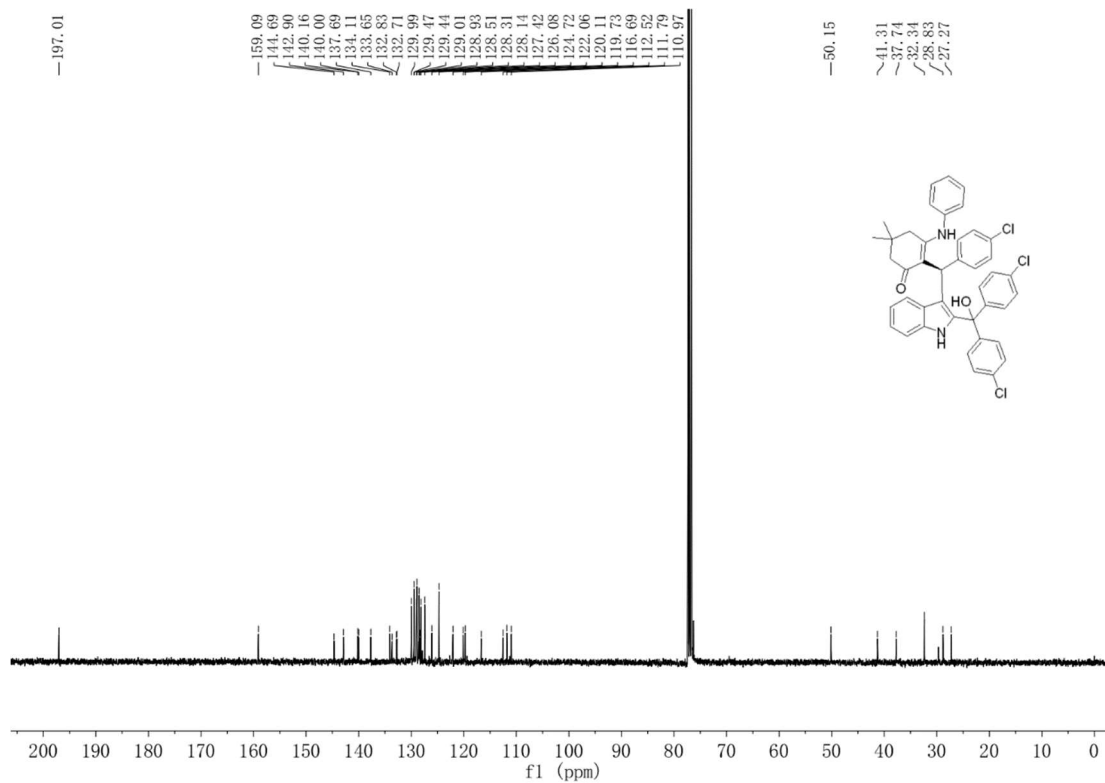
^{13}C NMR (100 MHz, CDCl_3) of compound **3dh**



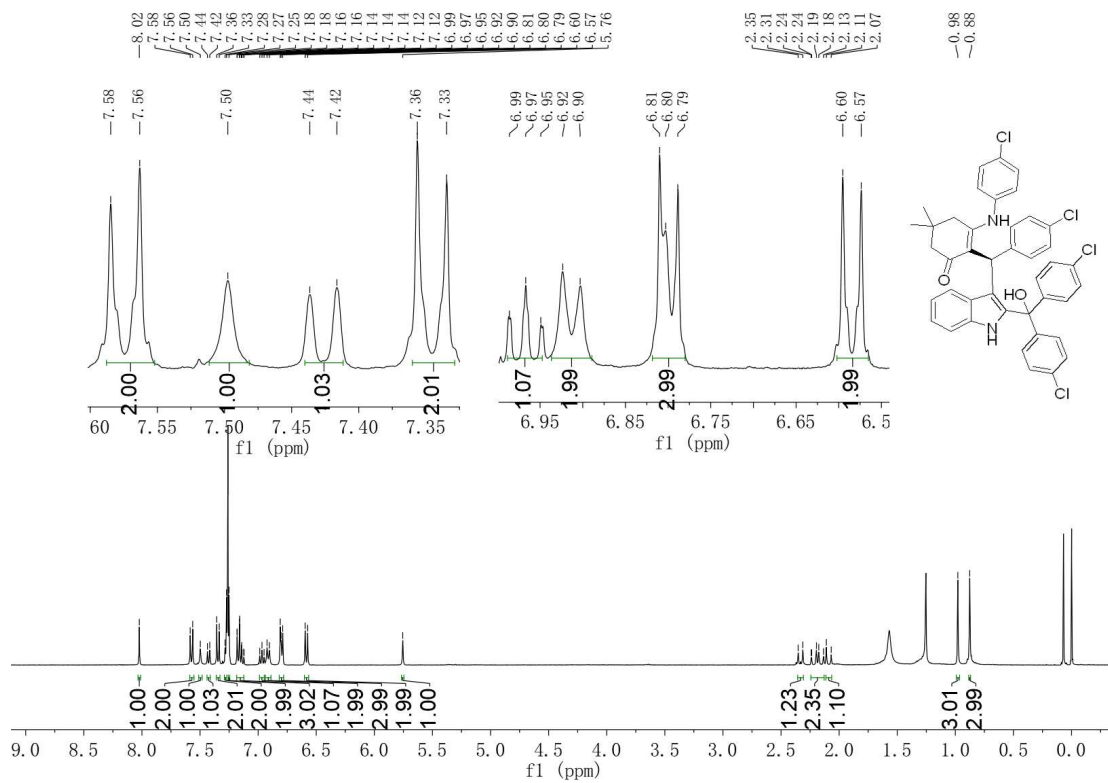
^1H NMR (400 MHz, CDCl_3) of compound **3dc**



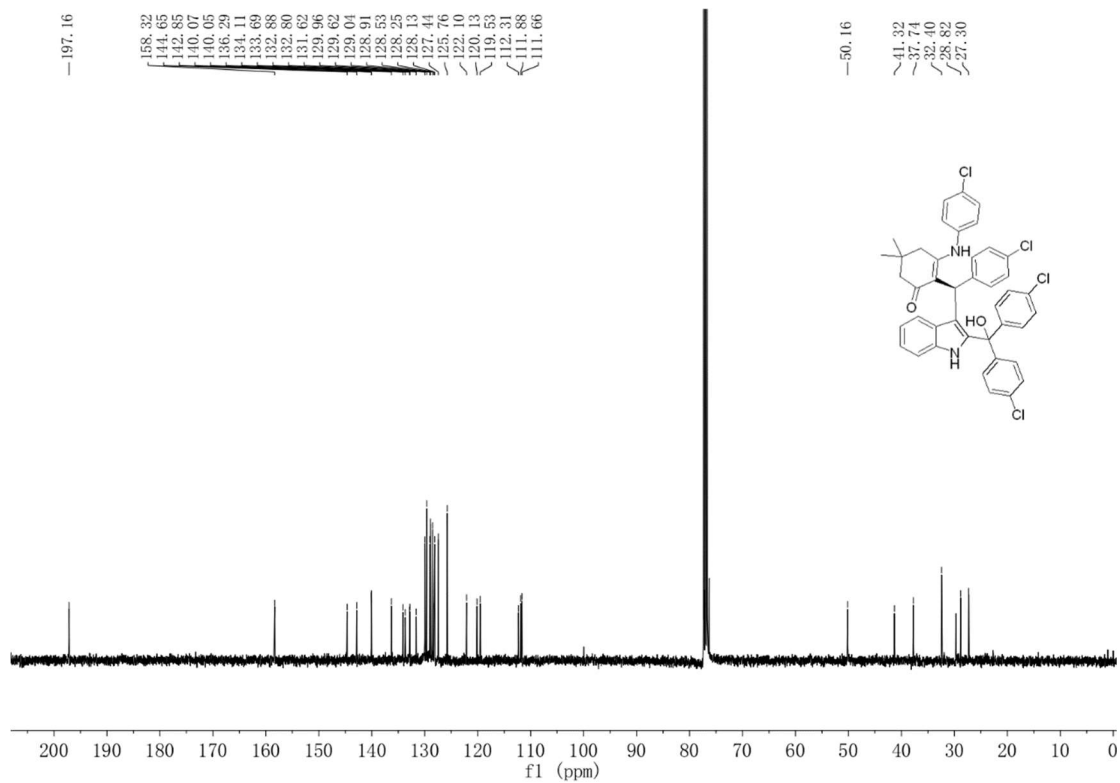
^{13}C NMR (100 MHz, CDCl_3) of compound **3dc**



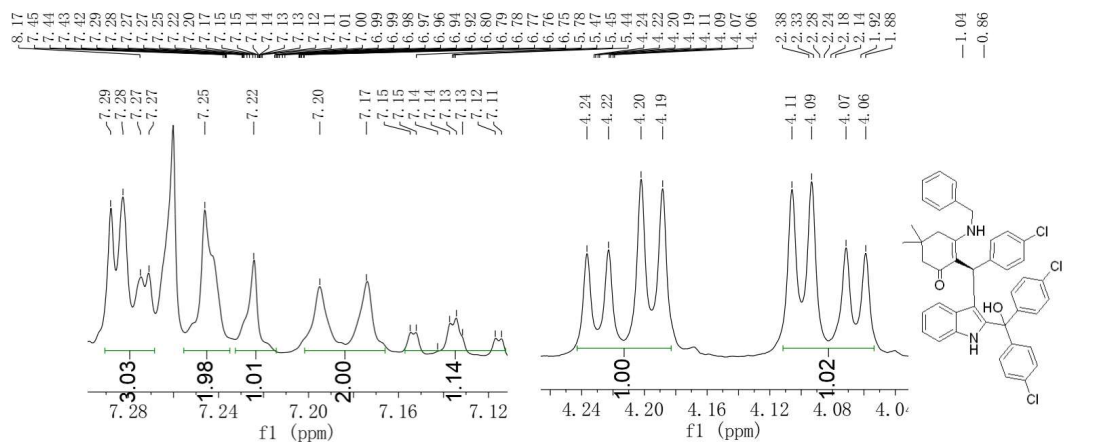
^1H NMR (400 MHz, CDCl_3) of compound **3df**



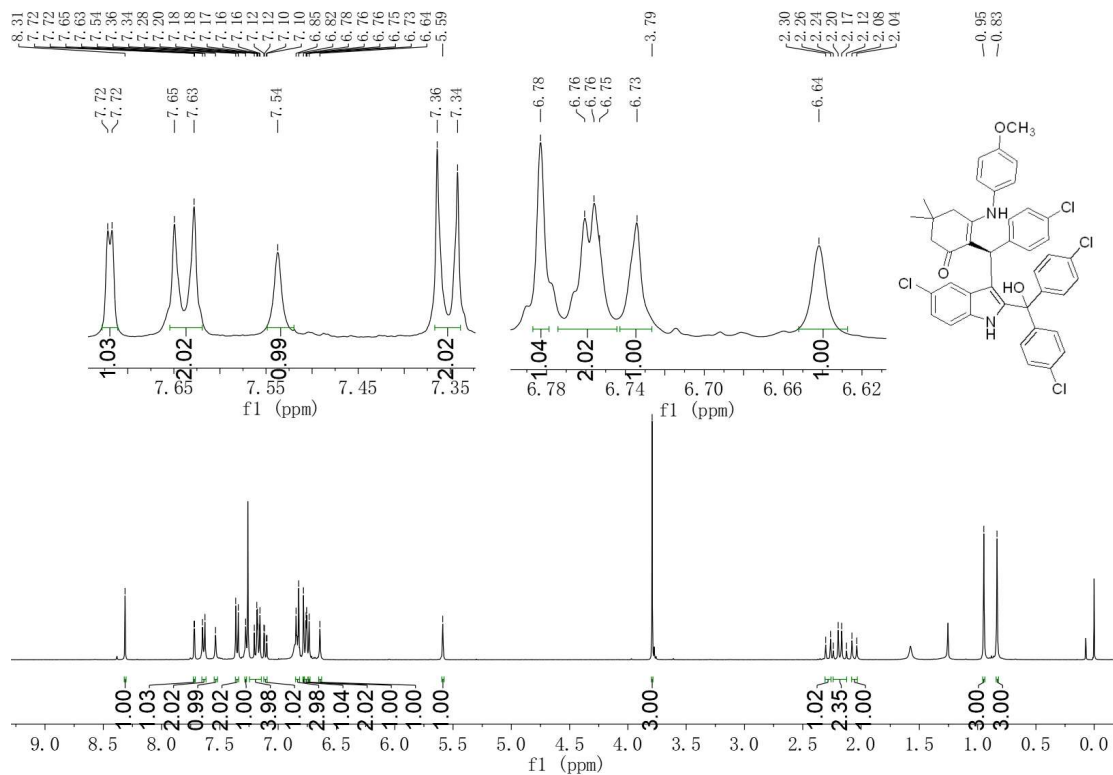
^{13}C NMR (100 MHz, CDCl_3) of compound **3df**



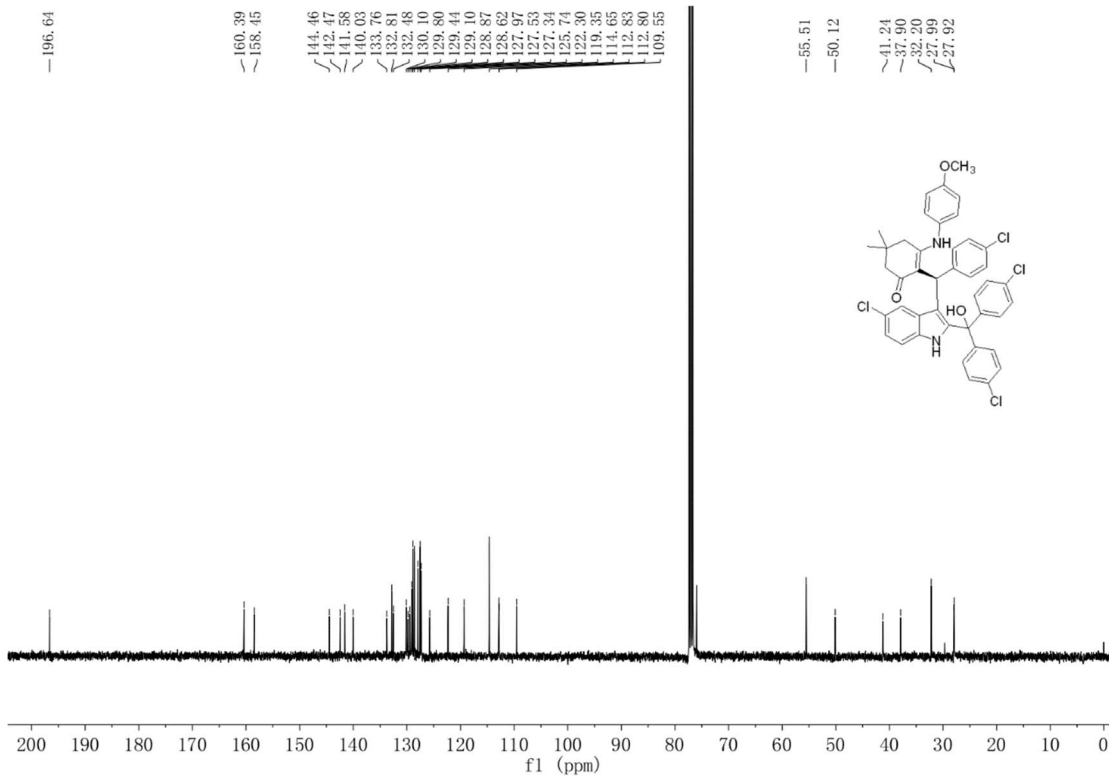
¹H NMR (400 MHz, CDCl₃) of compound **3dg**



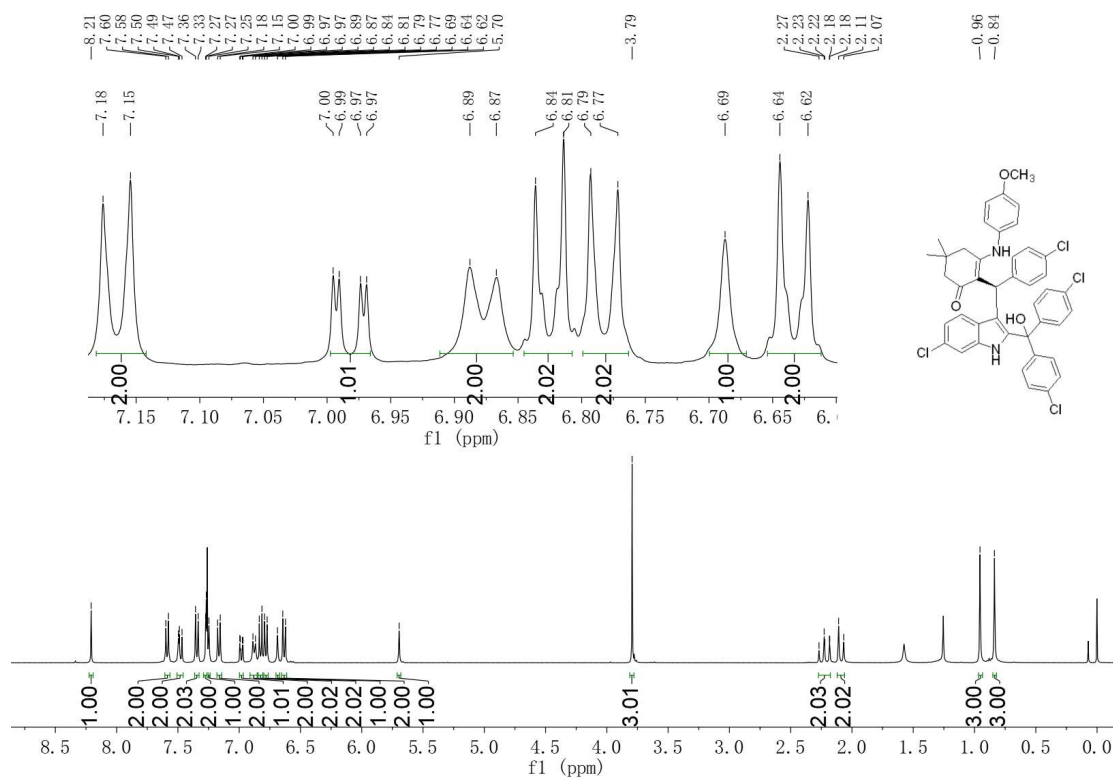
¹H NMR (400 MHz, CDCl₃) of compound **3ea**



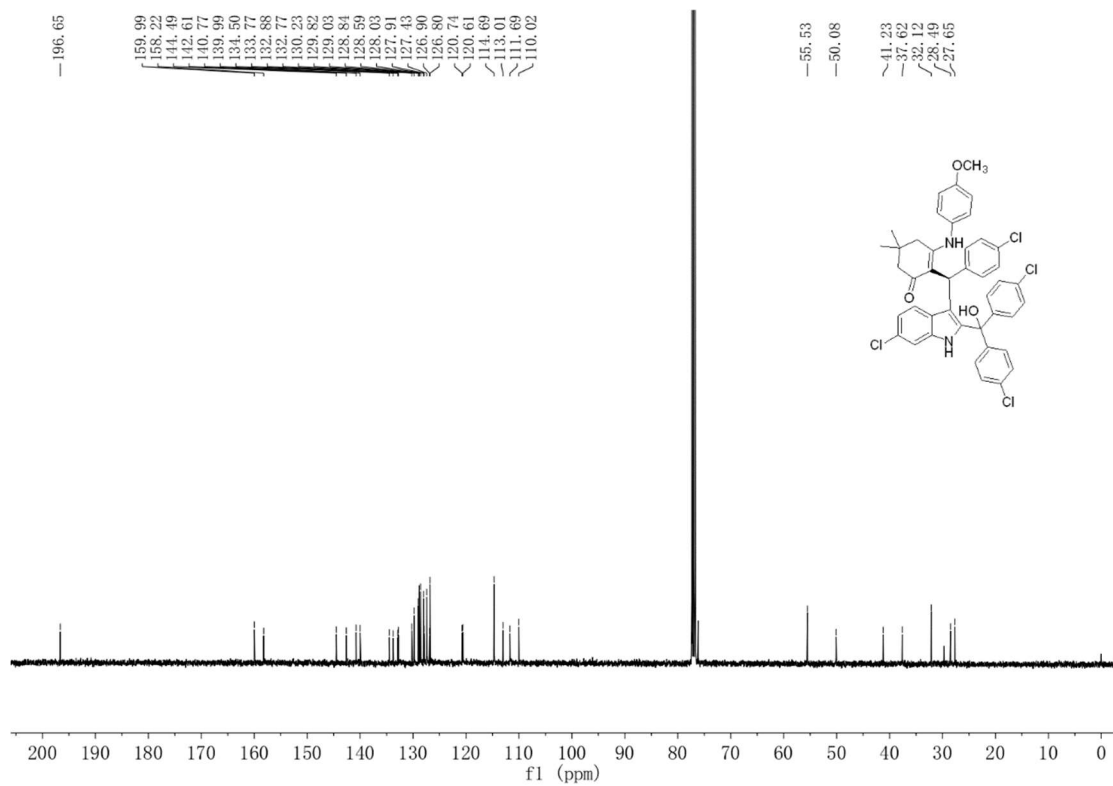
¹³C NMR (100 MHz, CDCl₃) of compound **3ea**



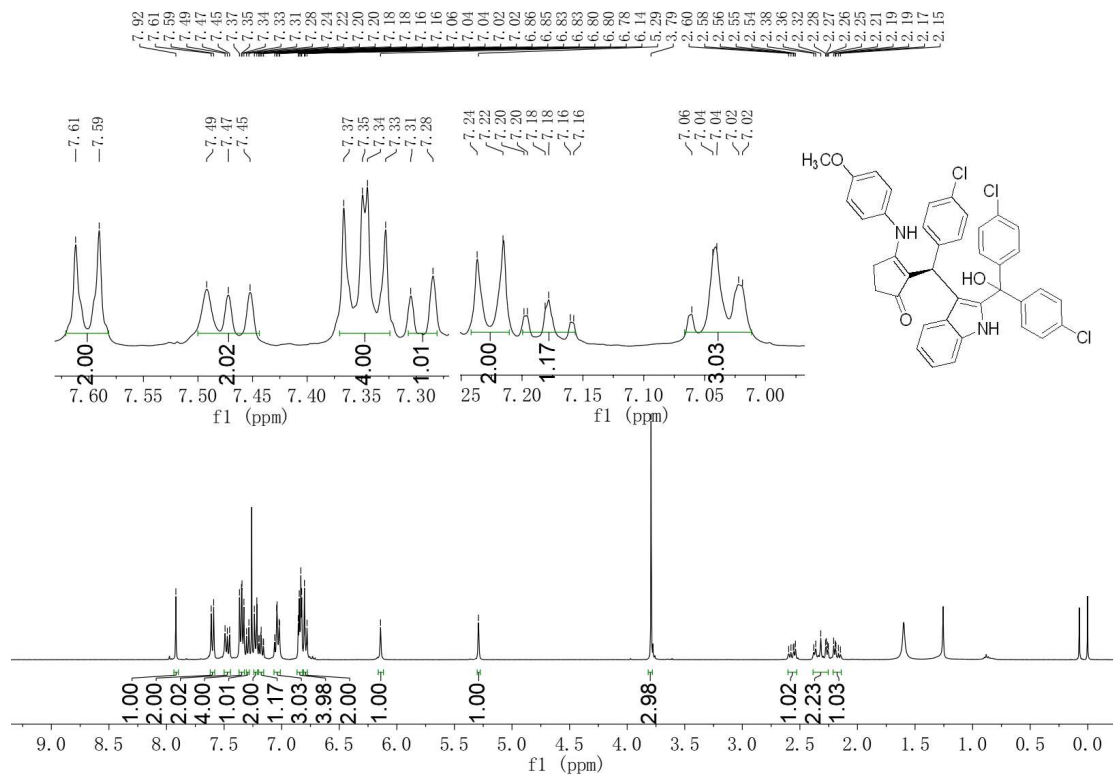
^1H NMR (400 MHz, CDCl_3) of compound **3fa**



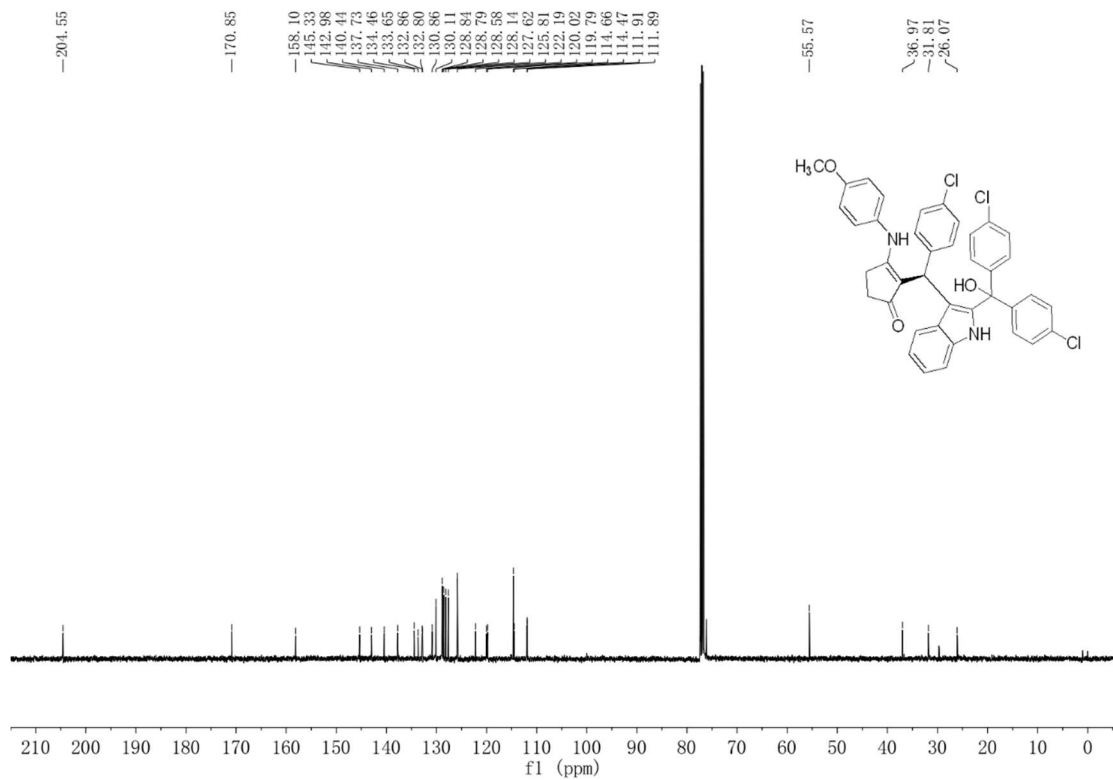
^{13}C NMR (100 MHz, CDCl_3) of compound **3fa**



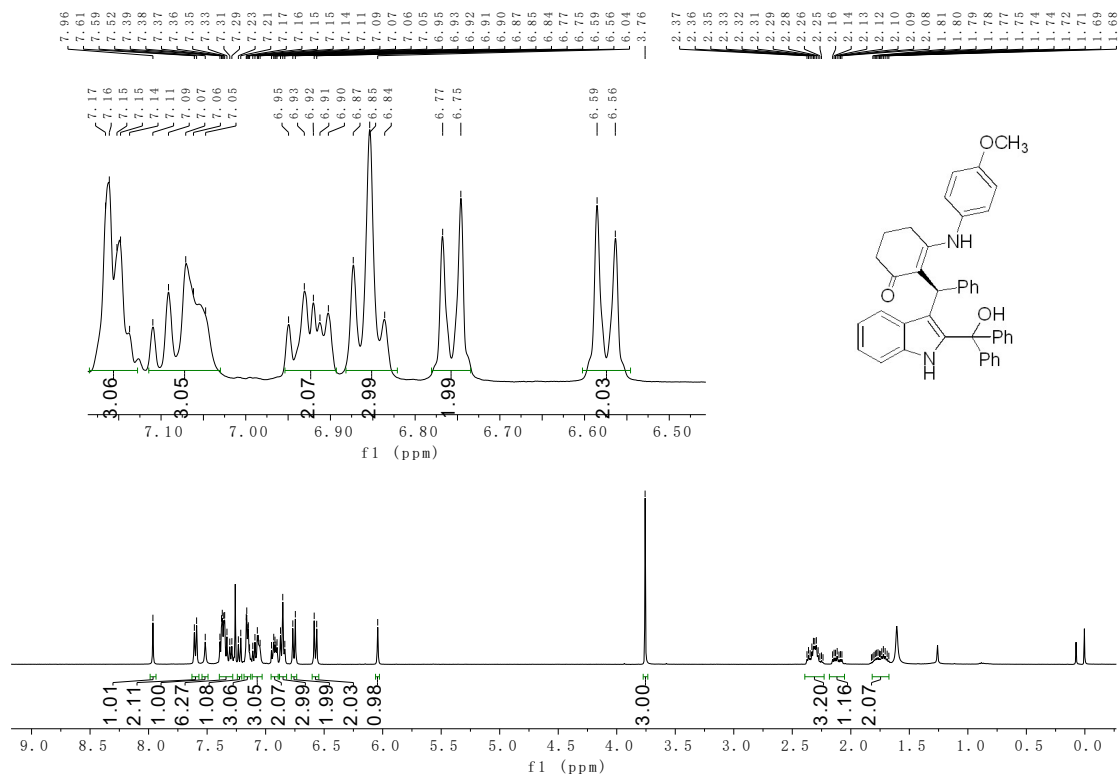
^1H NMR (400 MHz, CDCl_3) of compound **3di**



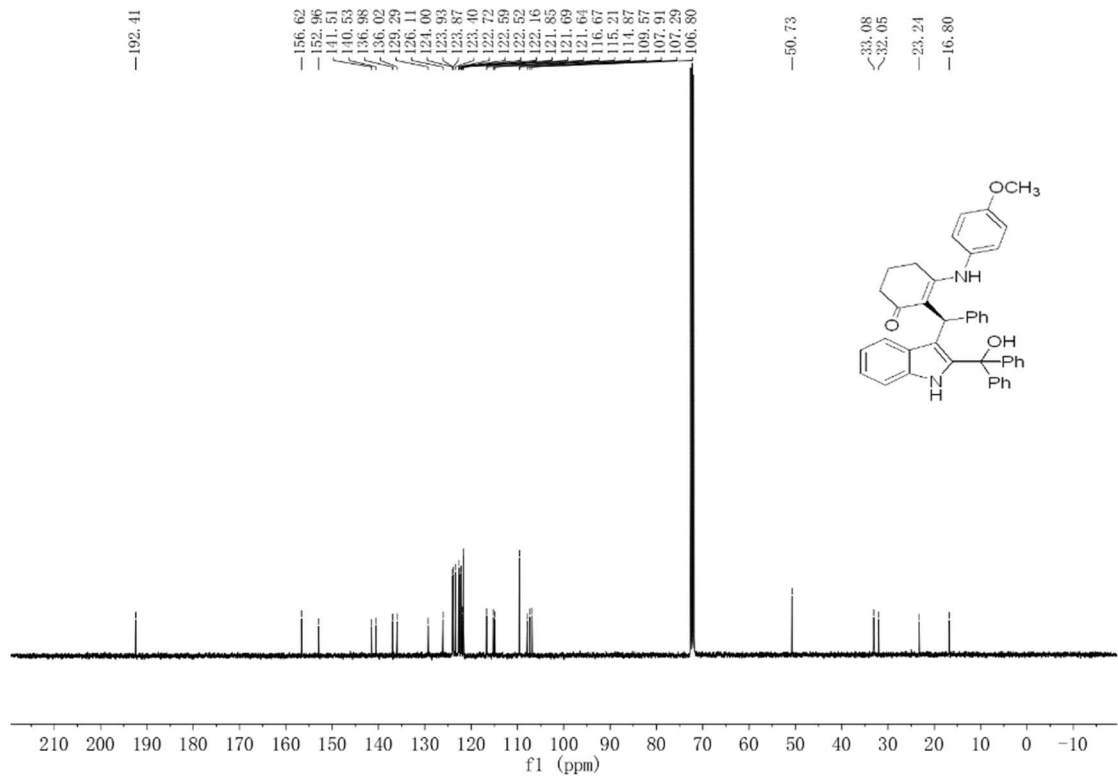
^{13}C NMR (100 MHz, CDCl_3) of compound **3di**



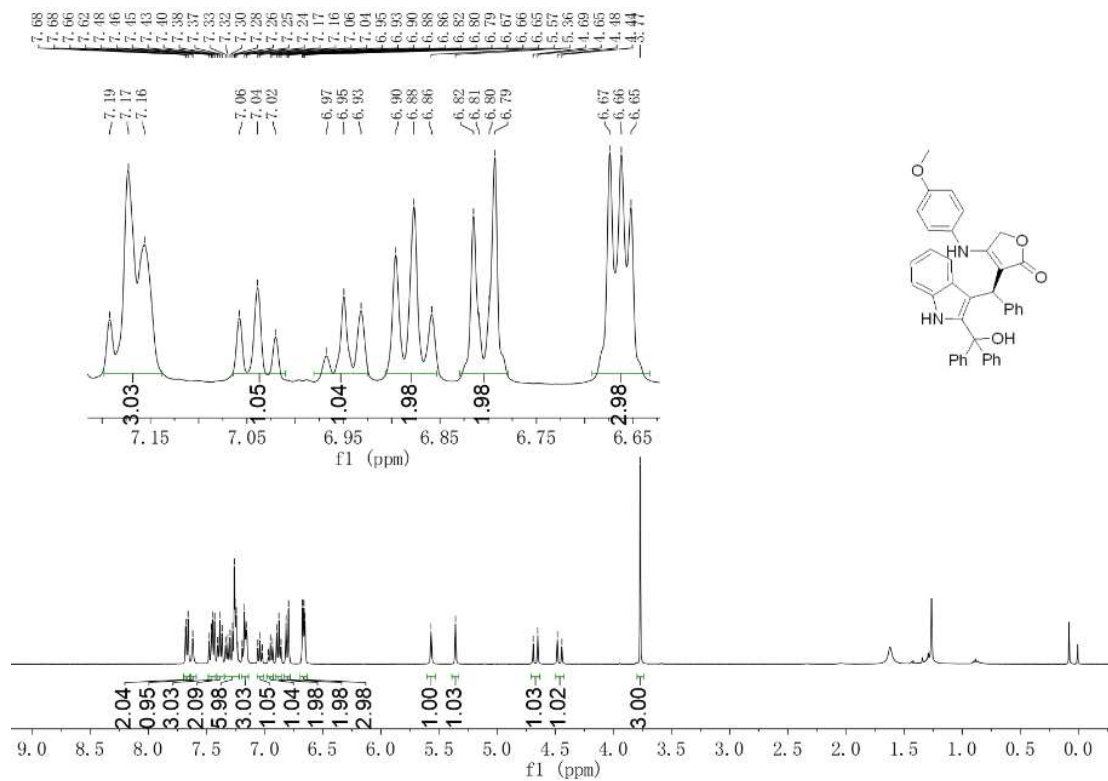
^1H NMR (400 MHz, CDCl_3) of compound **3aj**



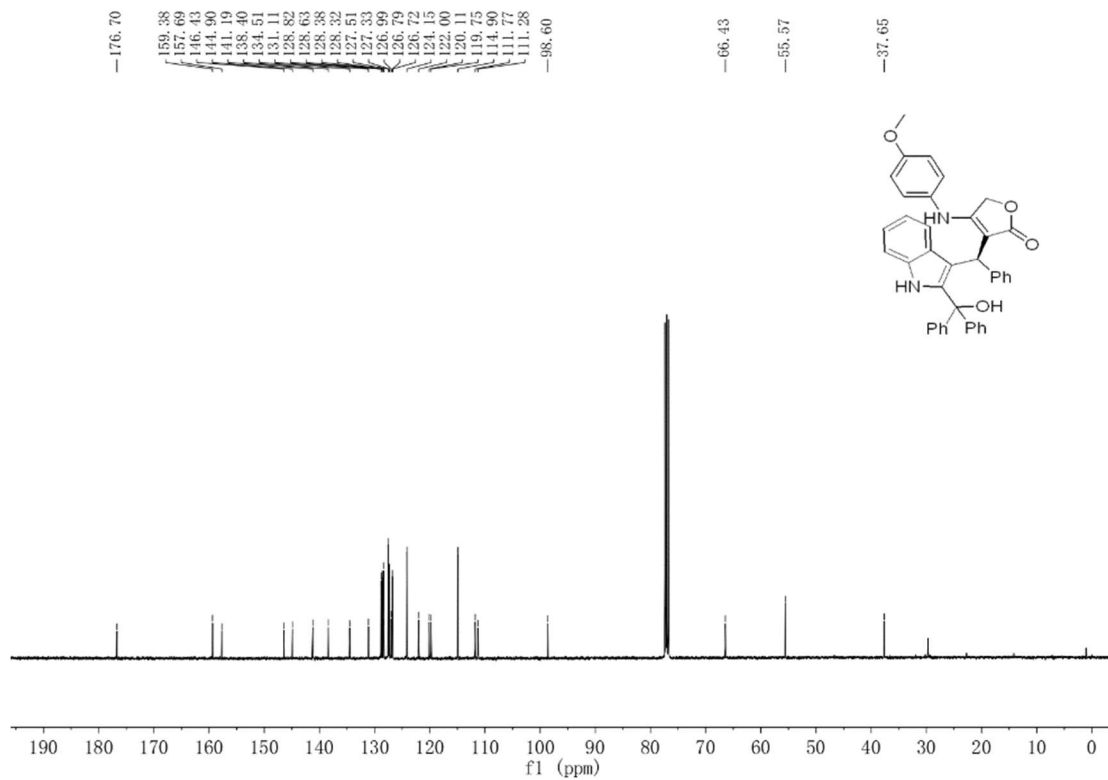
^{13}C NMR (100 MHz, CDCl_3) of compound **3aj**



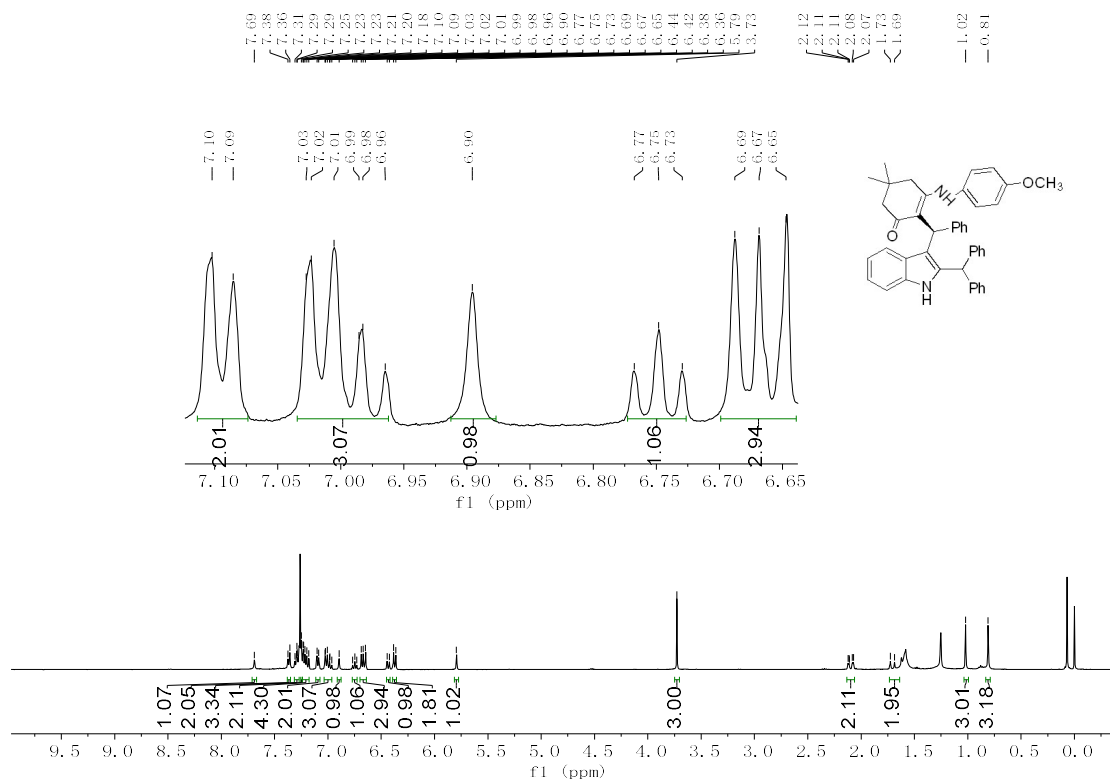
^1H NMR (400 MHz, CDCl_3) of compound **3ak**



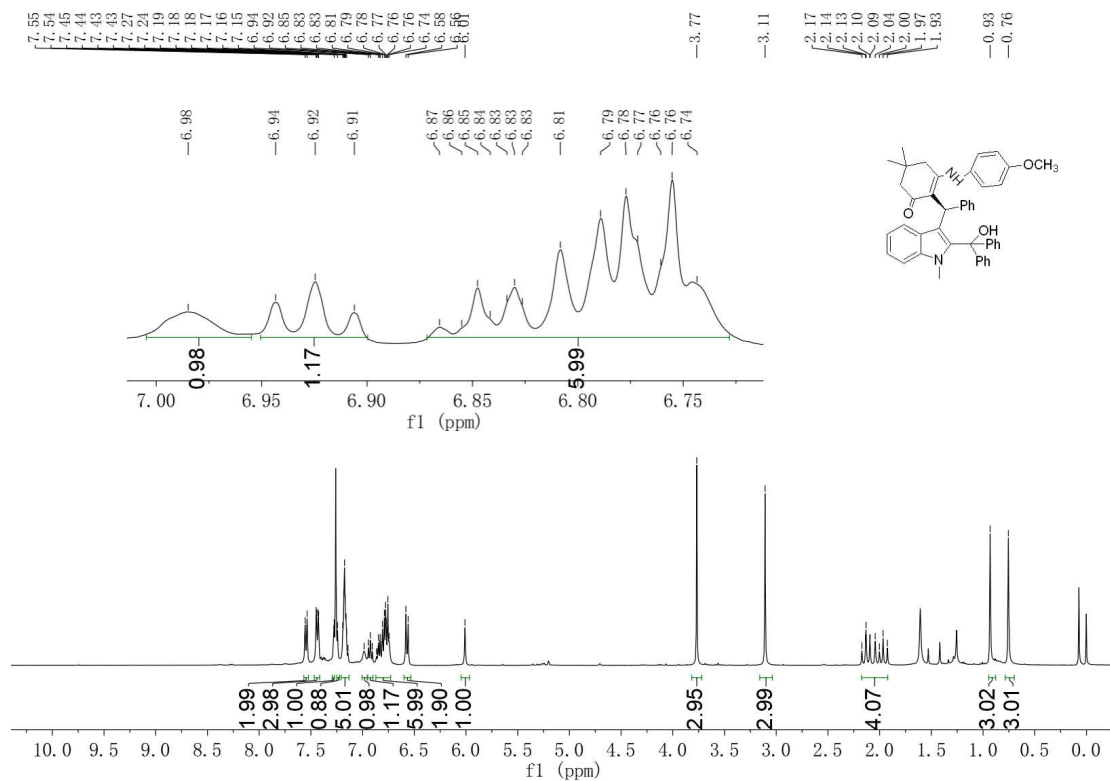
^{13}C NMR (100 MHz, CDCl_3) of compound **3ak**



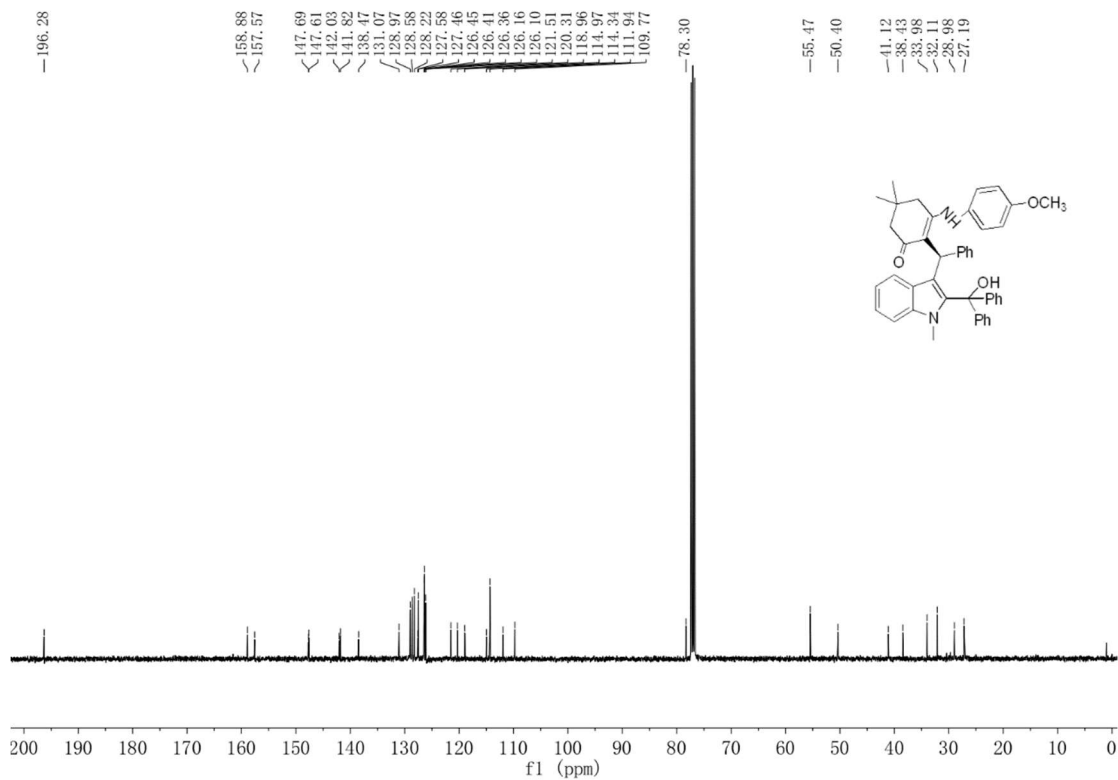
¹H NMR (400 MHz, CDCl₃) of compound **3ha**



¹H NMR (400 MHz, CDCl₃) of compound **3ga**

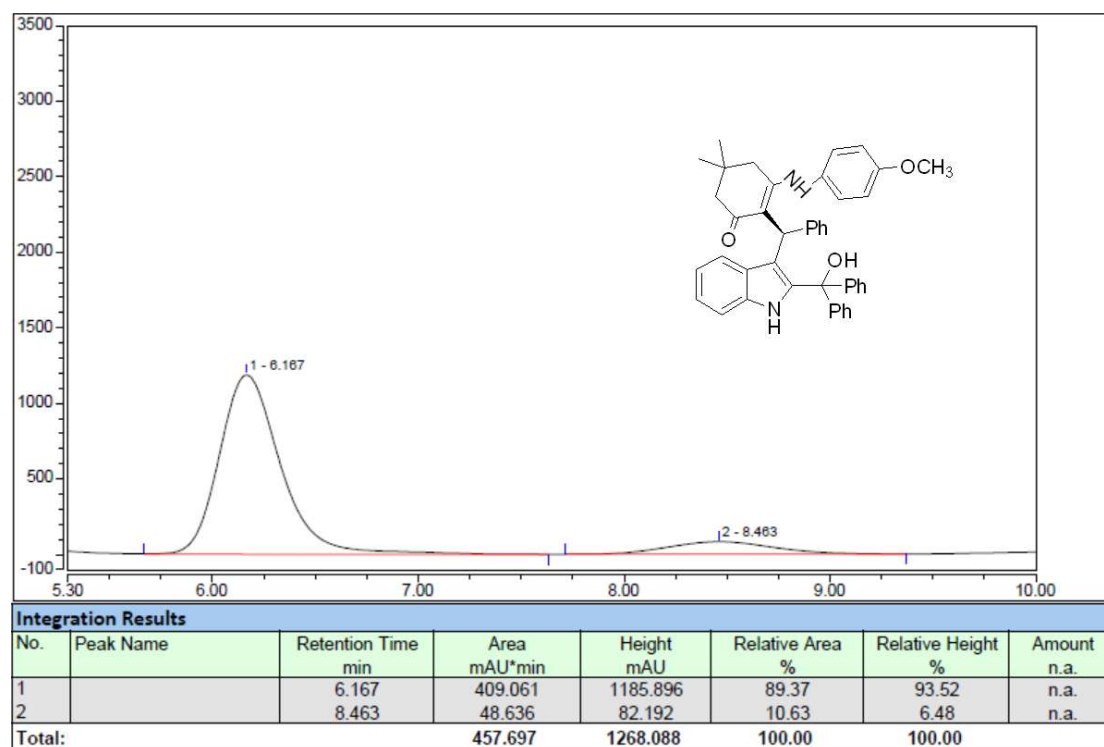
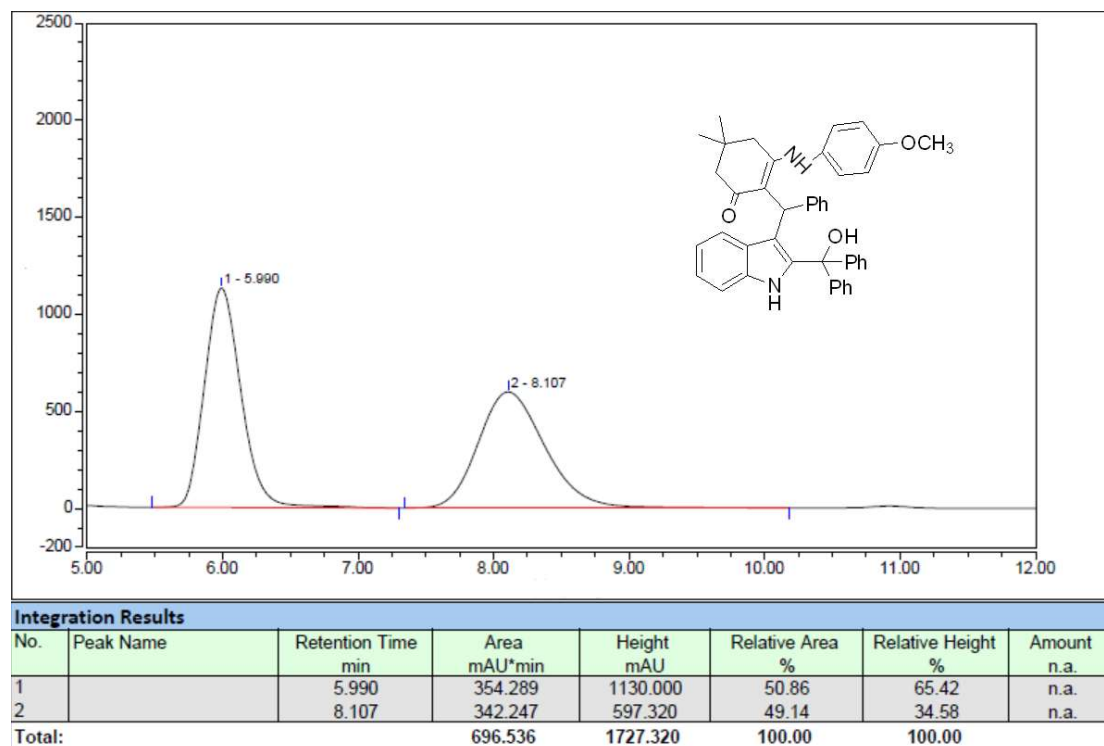


¹³C NMR (100 MHz, CDCl₃) of compound **3ga**

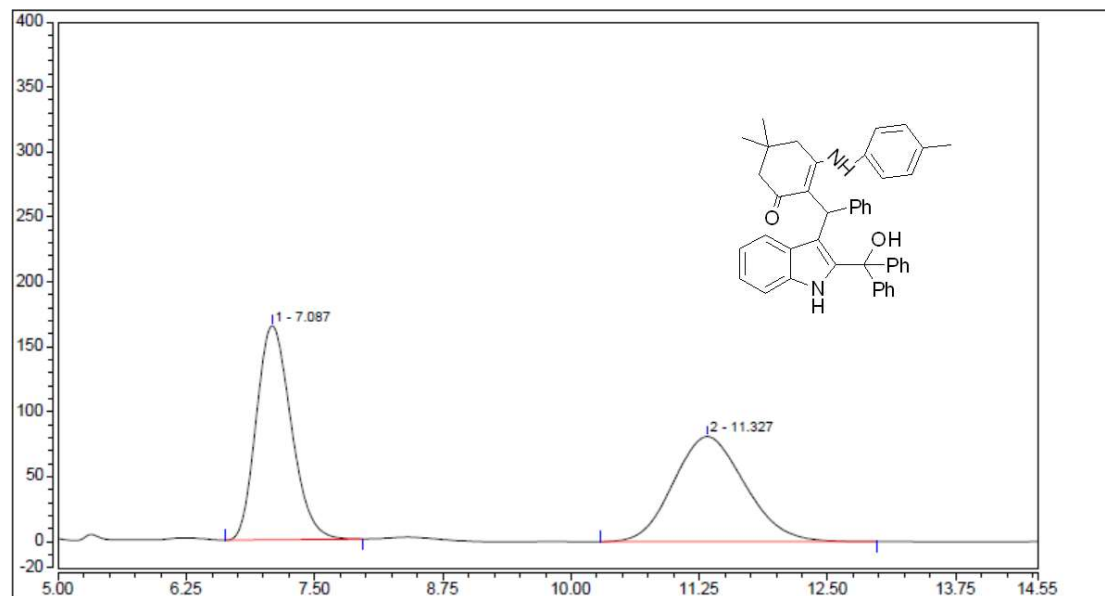


3. HPLC spectra of product 3

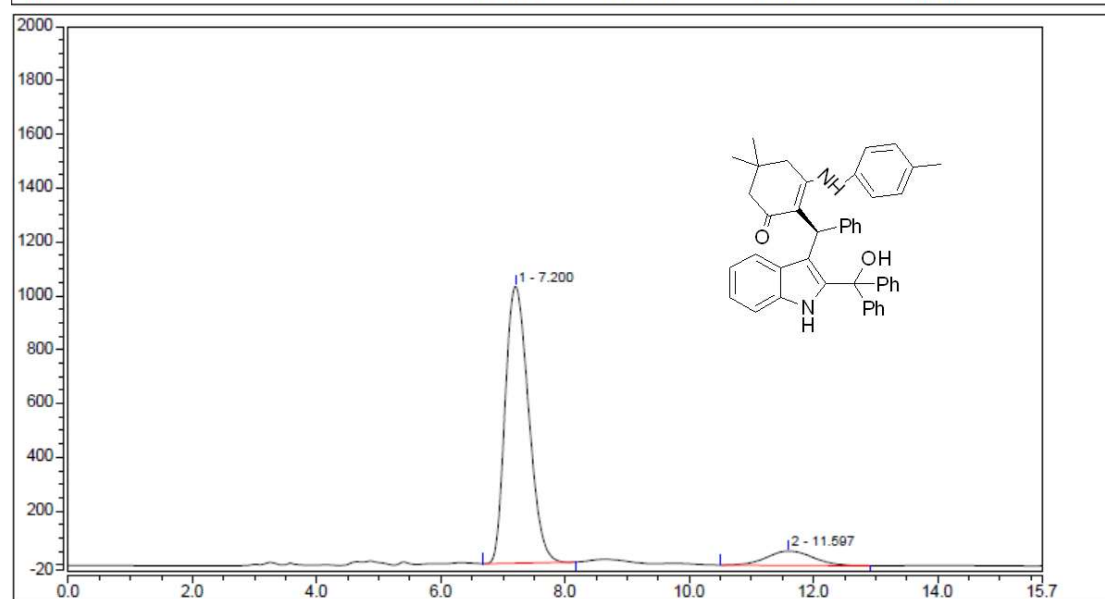
3aa



3ab

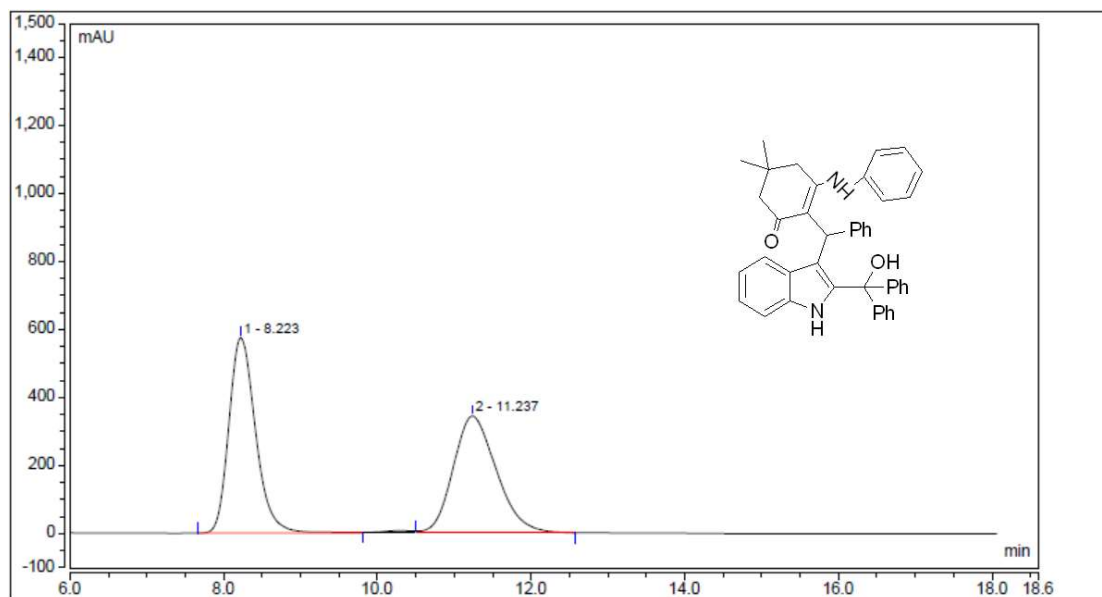


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.087	64.902	164.730	49.92	67.10	n.a.
2		11.327	65.118	80.782	50.08	32.90	n.a.
Total:			130.019	245.512	100.00	100.00	

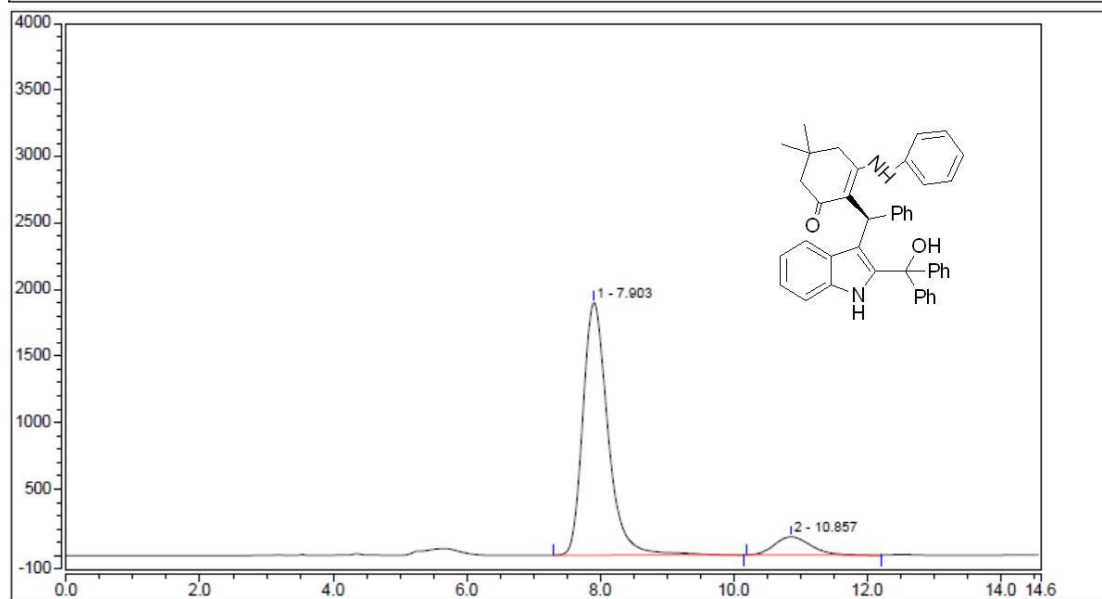


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.200	446.954	1028.282	90.69	95.08	n.a.
2		11.597	45.882	53.197	9.31	4.92	n.a.
Total:			492.836	1081.479	100.00	100.00	

3ac

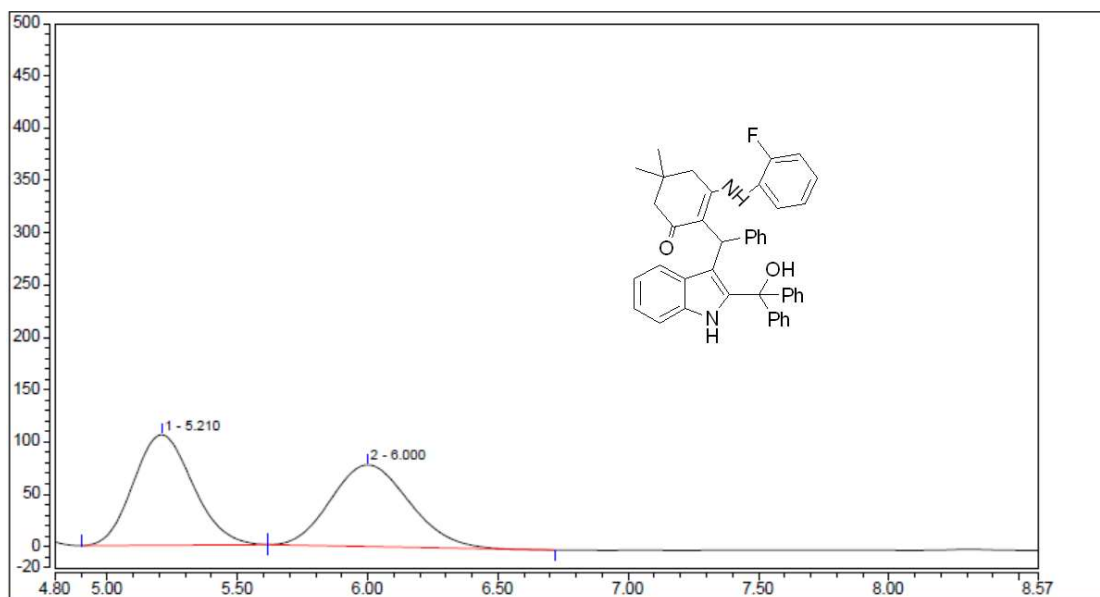


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		8.223	232.392	574.944	50.92	62.61	n.a.
2		11.237	223.976	343.401	49.08	37.39	n.a.
Total:			456.368	918.345	100.00	100.00	

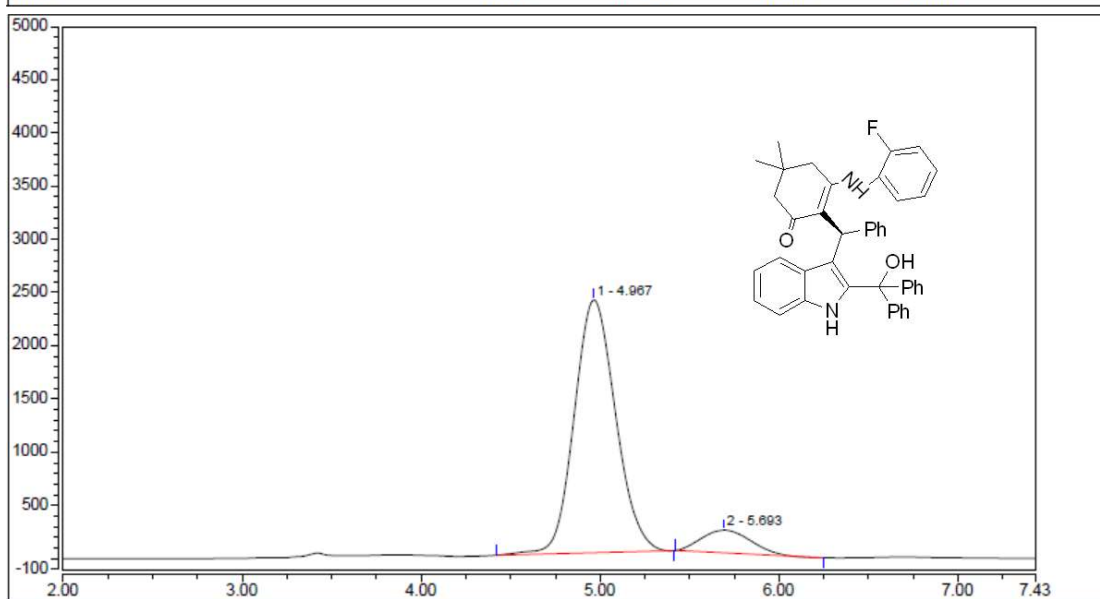


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.903	826.587	1899.577	90.56	93.28	n.a.
2		10.857	86.153	136.762	9.44	6.72	n.a.
Total:			912.740	2036.339	100.00	100.00	

3ad

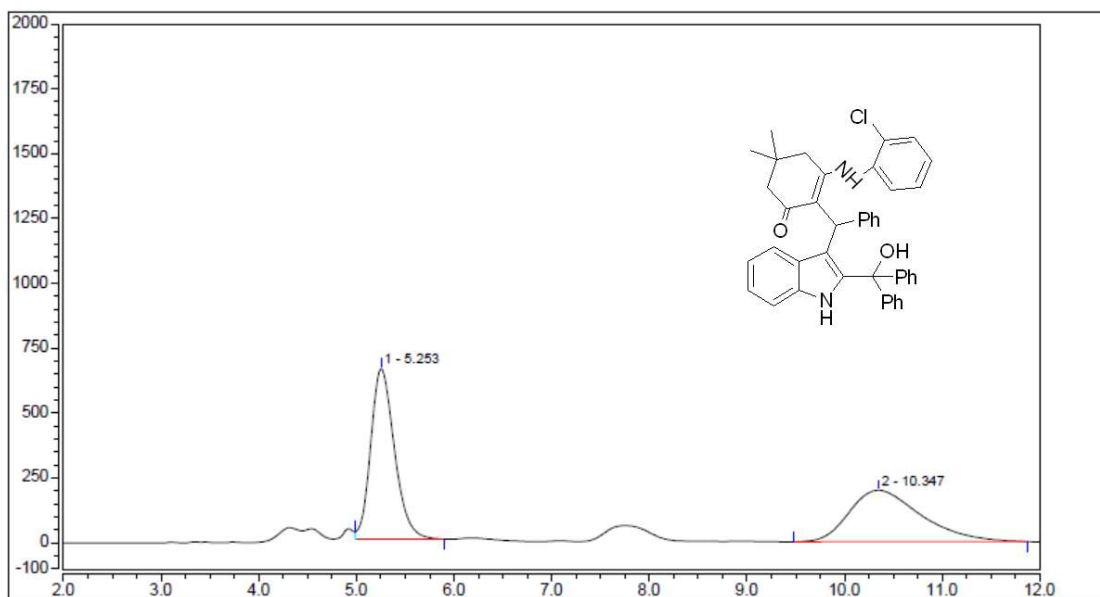


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		5.210	27.946	105.528	50.64	57.51	n.a.
2		6.000	27.241	77.958	49.36	42.49	n.a.
Total:			55.187	183.486	100.00	100.00	

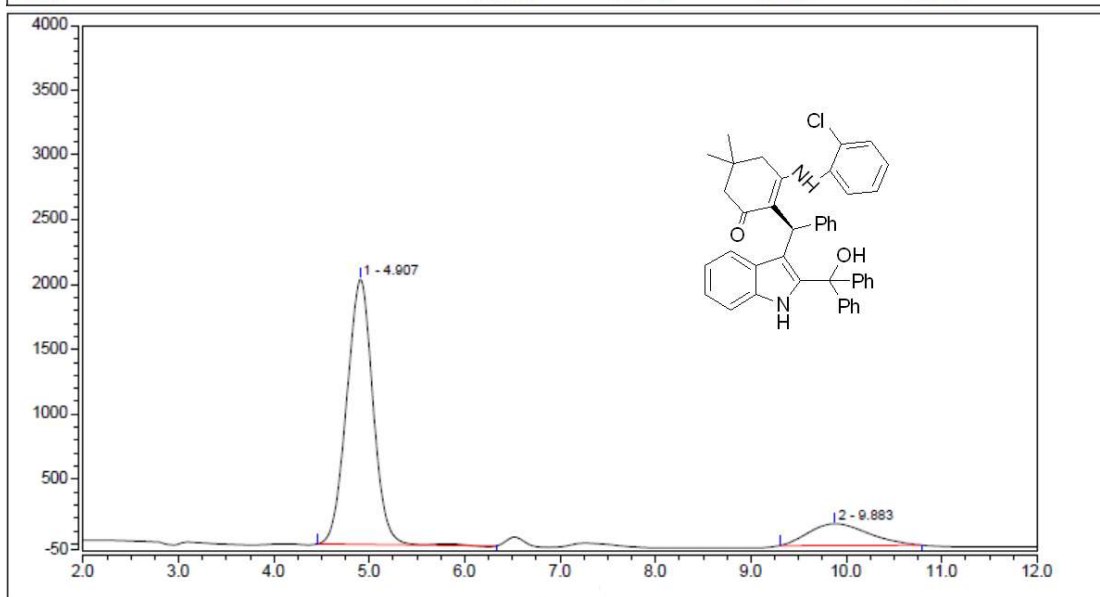


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		4.967	634.891	2375.743	90.36	91.78	n.a.
2		5.693	67.752	212.907	9.64	8.22	n.a.
Total:			702.643	2588.650	100.00	100.00	

3ae

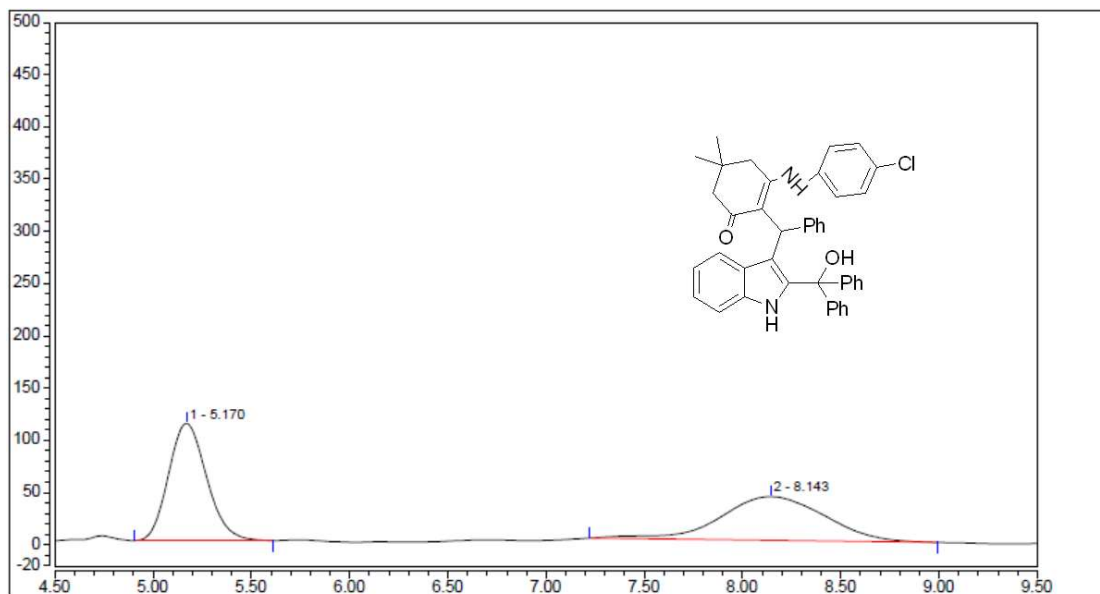


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		5.253	185.692	657.080	52.46	76.85	n.a.
2		10.347	168.308	197.911	47.54	23.15	n.a.
Total:			354.000	854.991	100.00	100.00	

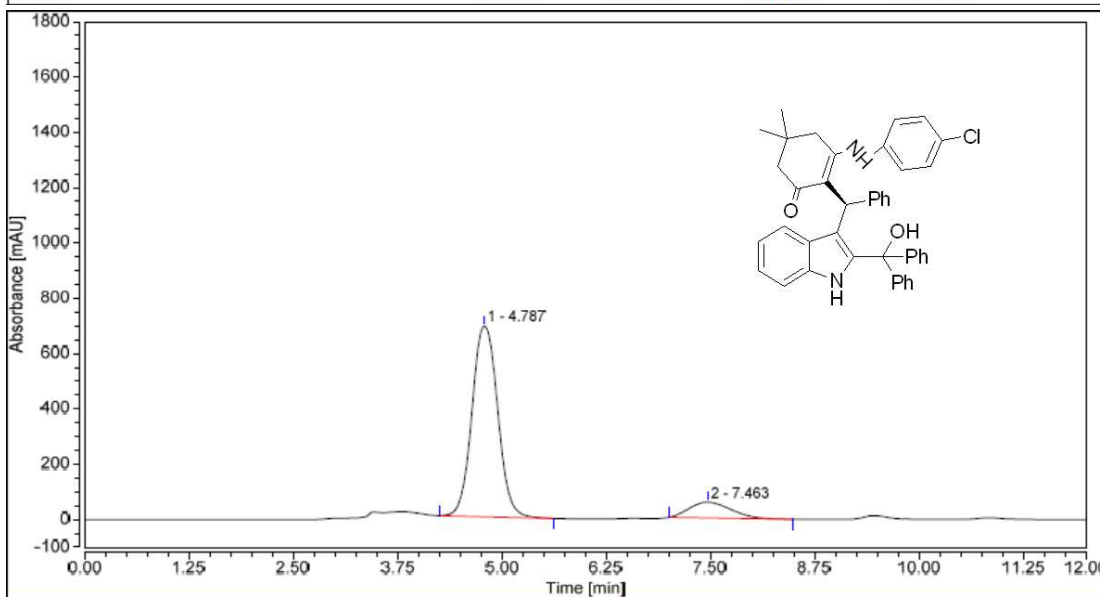


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		4.907	652.552	2045.496	84.32	92.45	n.a.
2		9.883	121.317	166.945	15.68	7.55	n.a.
Total:			773.869	2212.441	100.00	100.00	

3af

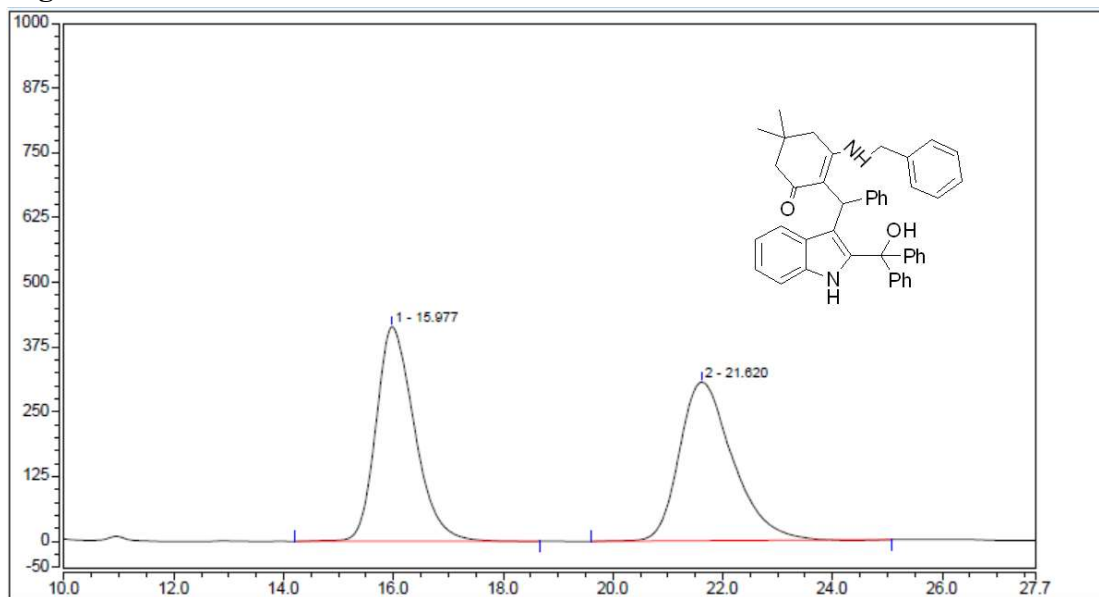


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		5.170	25.190	112.211	49.45	72.85	n.a.
2		8.143	25.746	41.814	50.55	27.15	n.a.
Total:			50.936	154.025	100.00	100.00	

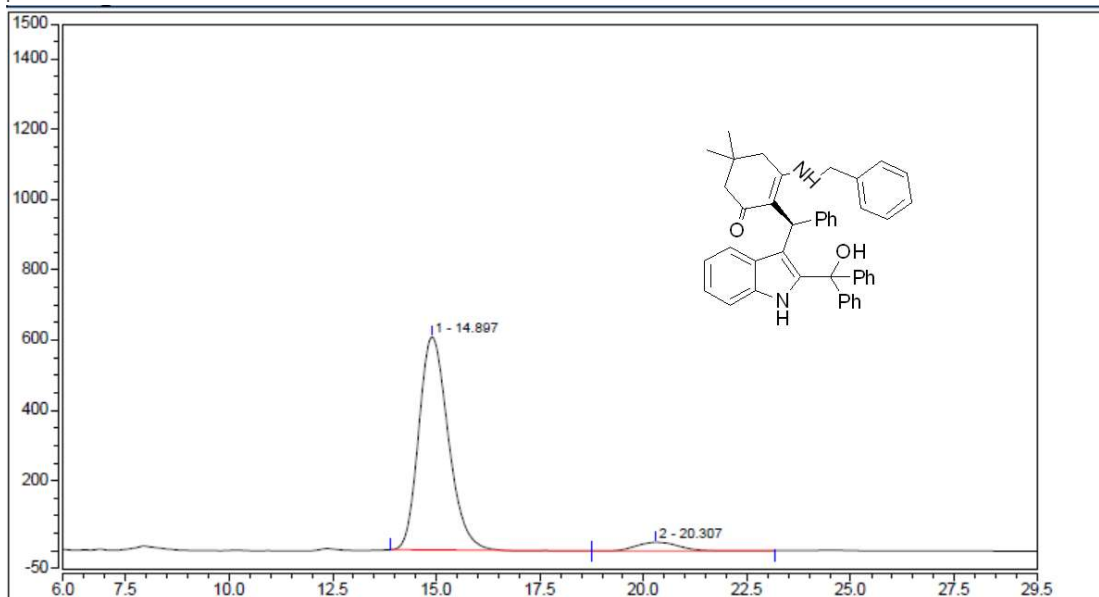


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		4.787	246.712	689.249	88.26	92.35	n.a.
2		7.463	32.820	57.080	11.74	7.65	n.a.
Total:			279.532	746.329	100.00	100.00	

3ag

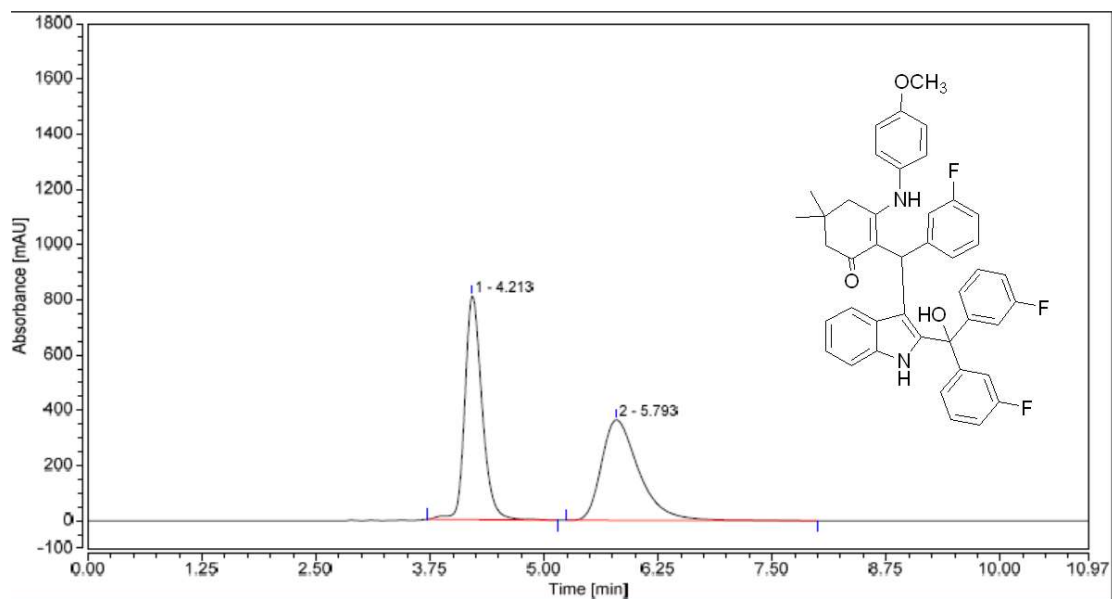


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		15.977	336.070	414.063	49.33	57.51	n.a.
2		21.620	345.218	305.899	50.67	42.49	n.a.
Total:			681.288	719.962	100.00	100.00	

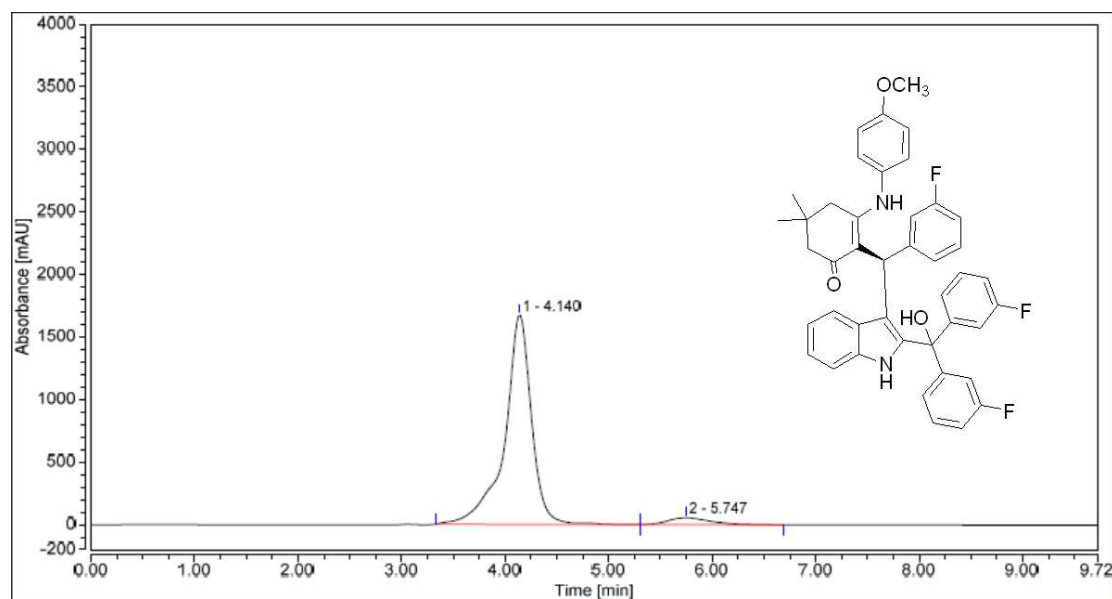


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		14.897	500.728	606.446	94.58	96.04	n.a.
2		20.307	28.706	25.011	5.42	3.96	n.a.
Total:			529.434	631.458	100.00	100.00	

3ba

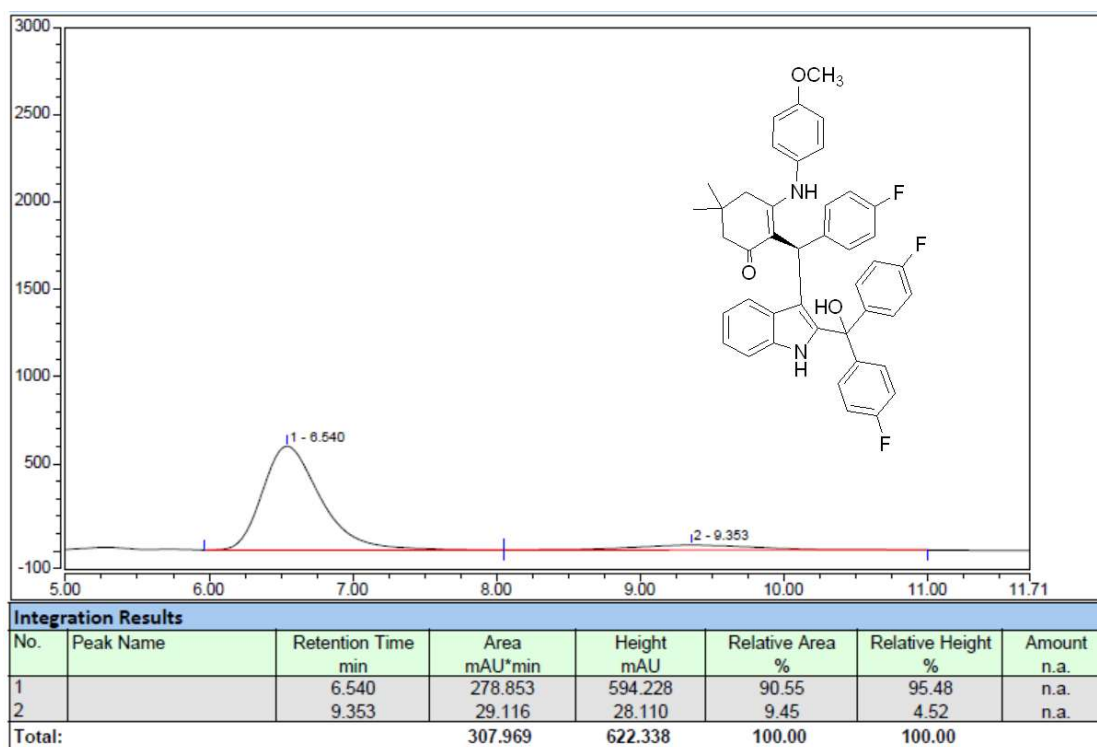
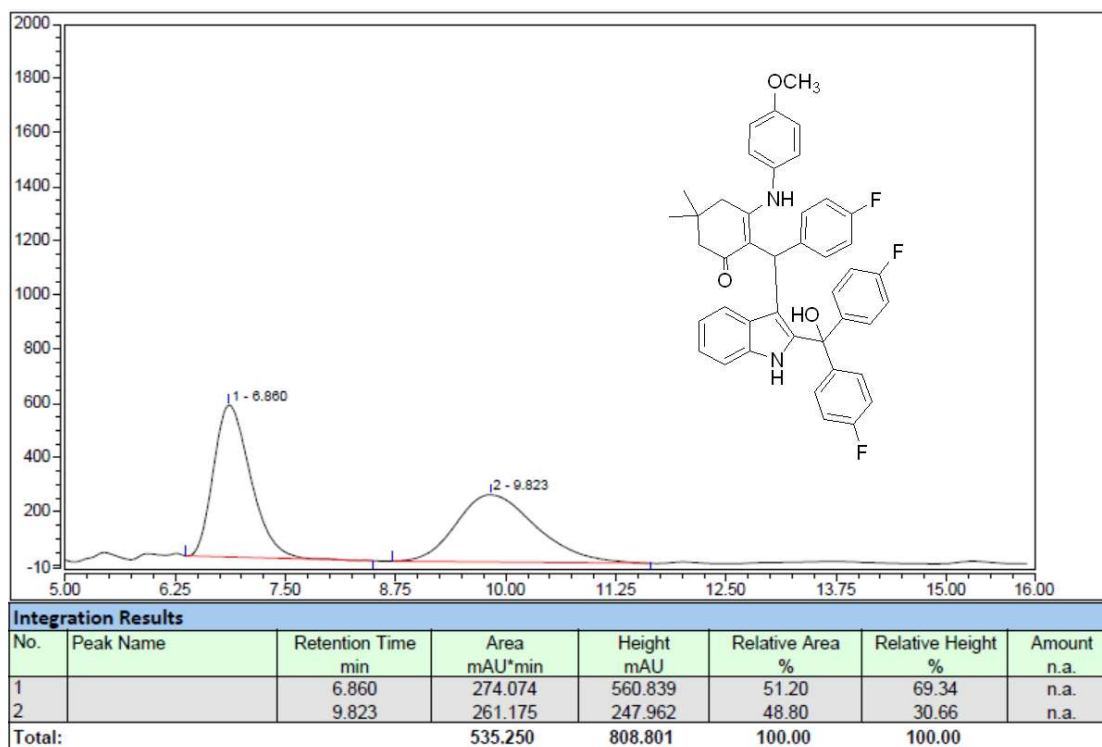


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		4.213	177.623	810.208	50.73	69.03	n.a.
2		5.793	172.493	363.535	49.27	30.97	n.a.
Total:			350.116	1173.743	100.00	100.00	

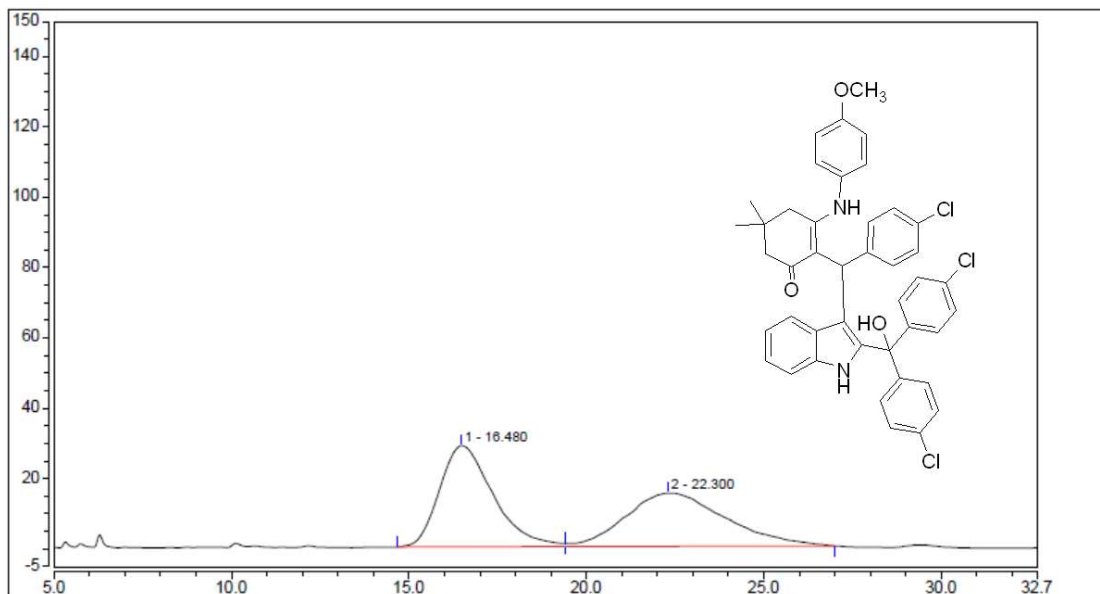


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		4.140	504.963	1674.379	95.20	96.89	n.a.
2		5.747	25.437	53.672	4.80	3.11	n.a.
Total:			530.400	1728.051	100.00	100.00	

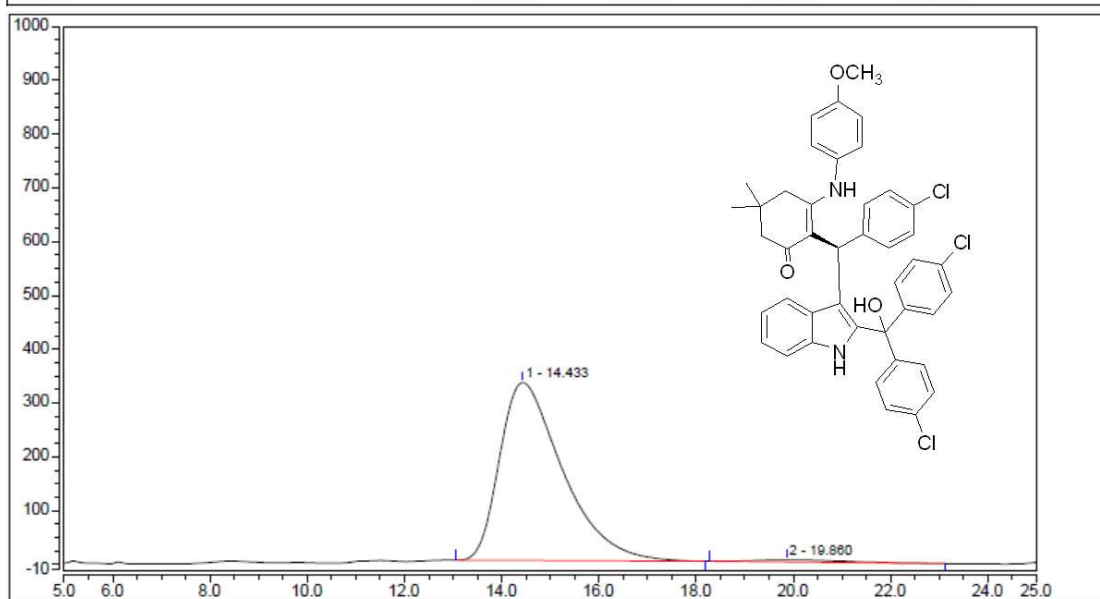
3ca



3da

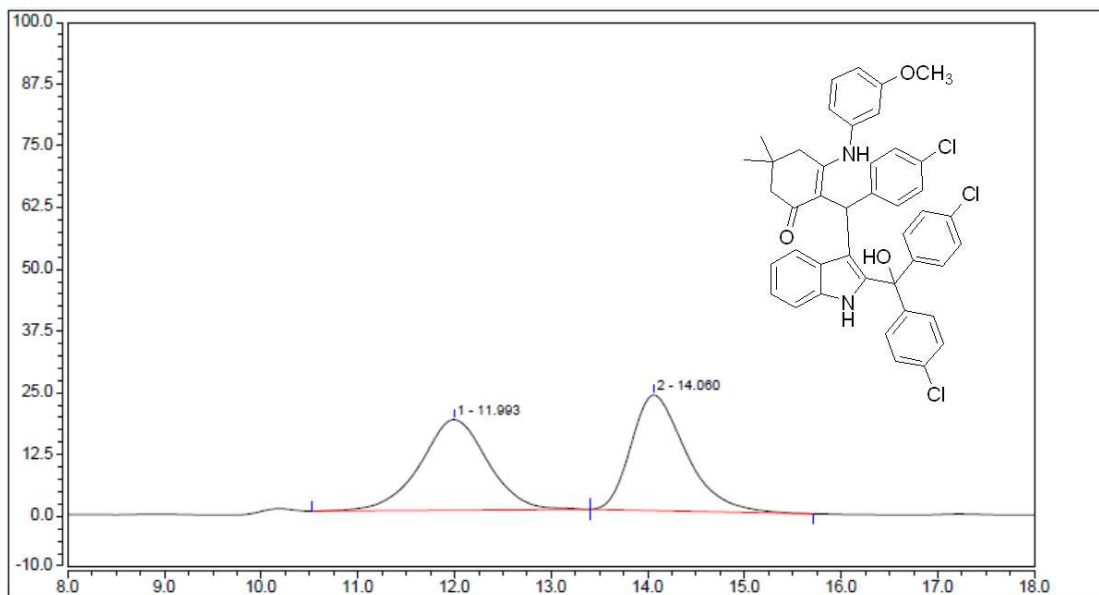


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		16.480	50.393	28.792	50.49	65.56	n.a.
2		22.300	49.405	15.126	49.51	34.44	n.a.
Total:			99.798	43.918	100.00	100.00	

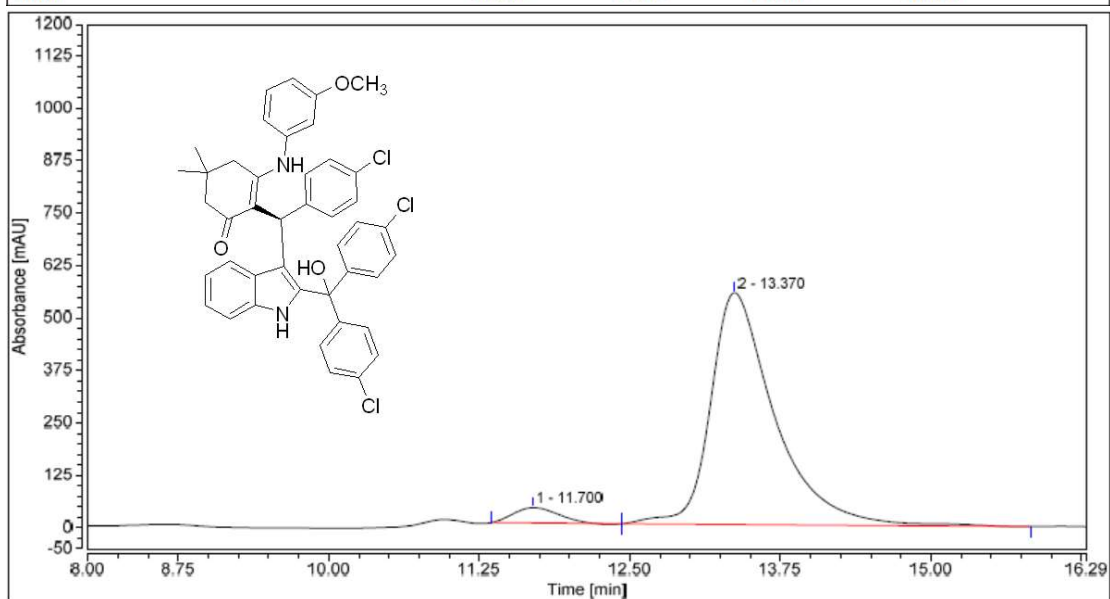


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		14.433	496.004	330.701	98.29	98.89	n.a.
2		19.860	8.630	3.697	1.71	1.11	n.a.
Total:			504.634	334.398	100.00	100.00	

3dh

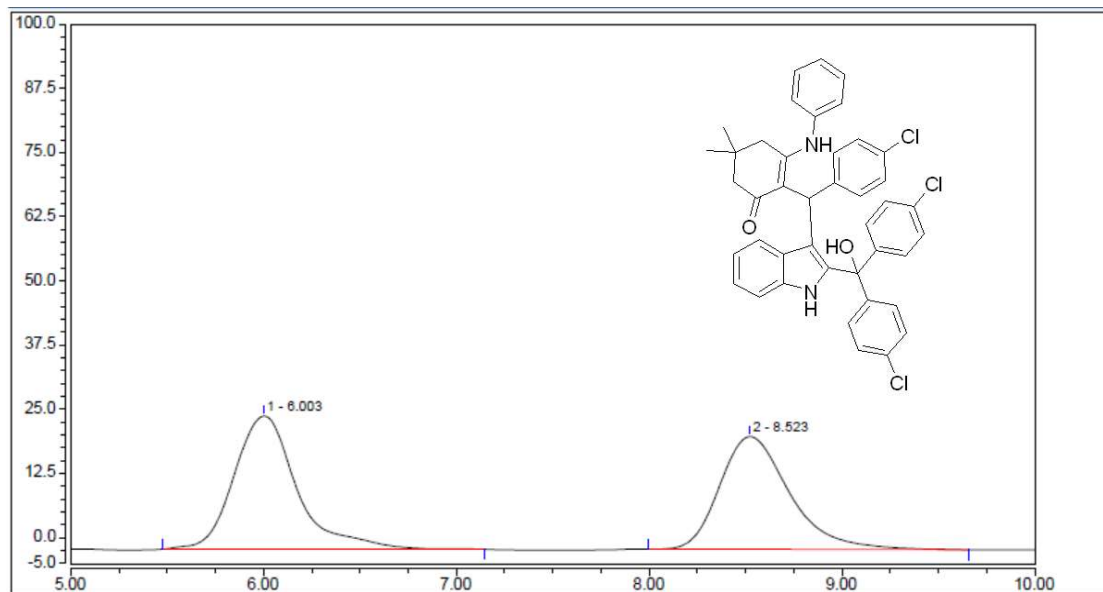


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		11.993	14.877	18.307	49.02	43.91	n.a.
2		14.060	15.473	23.385	50.98	56.09	n.a.
Total:			30.350	41.692	100.00	100.00	

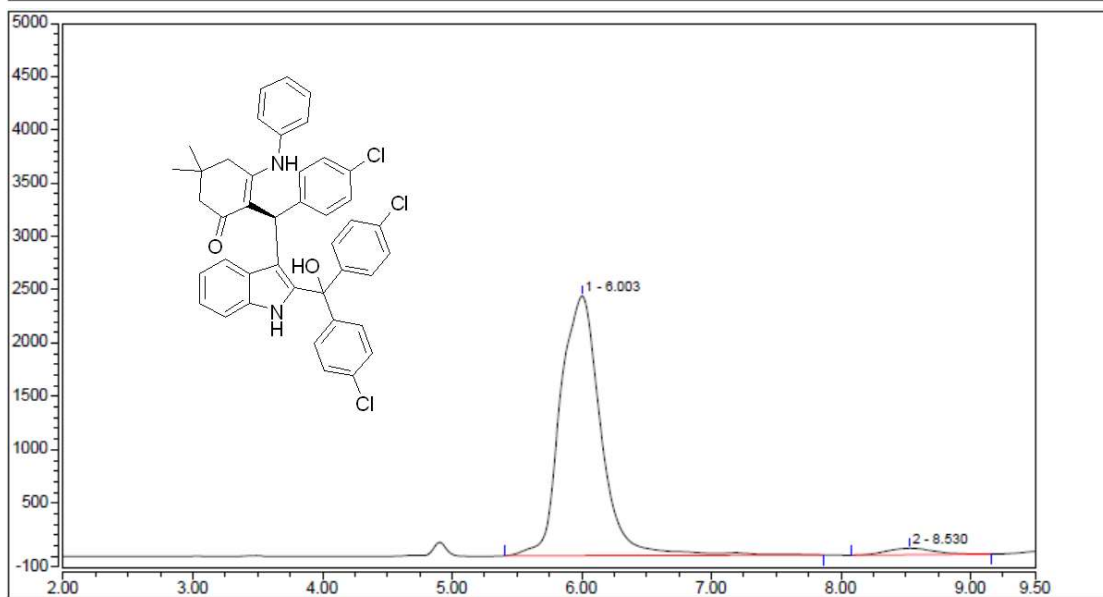


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		11.700	15.357	36.298	4.30	6.16	n.a.
2		13.370	341.959	552.495	95.70	93.84	n.a.
Total:			357.316	588.793	100.00	100.00	

3dc

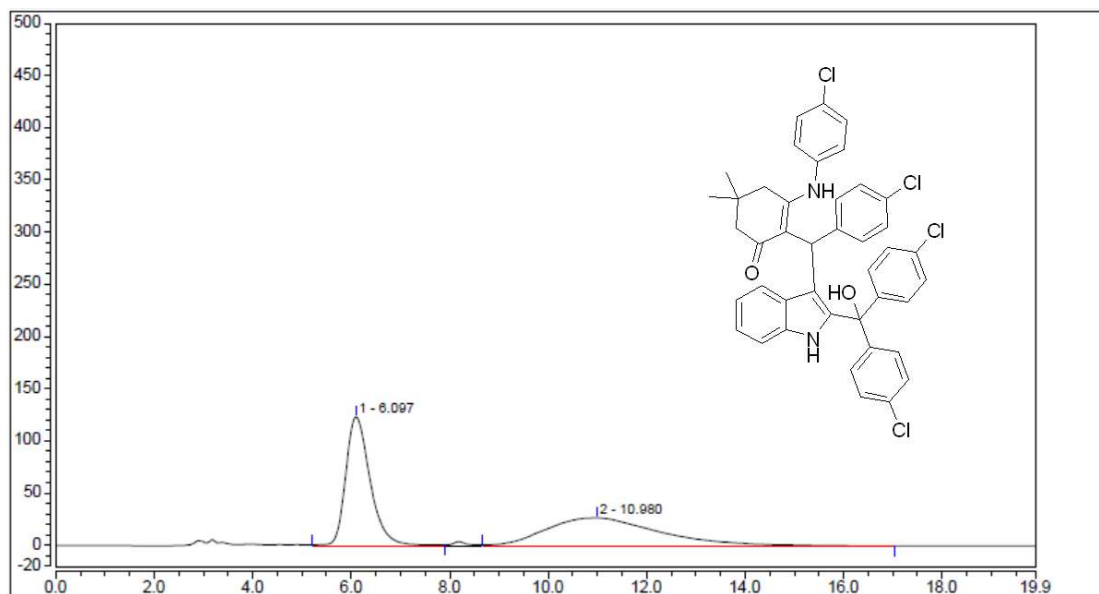


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.003	9.816	25.916	51.63	54.18	n.a.
2		8.523	9.196	21.919	48.37	45.82	n.a.
Total:			19.012	47.834	100.00	100.00	

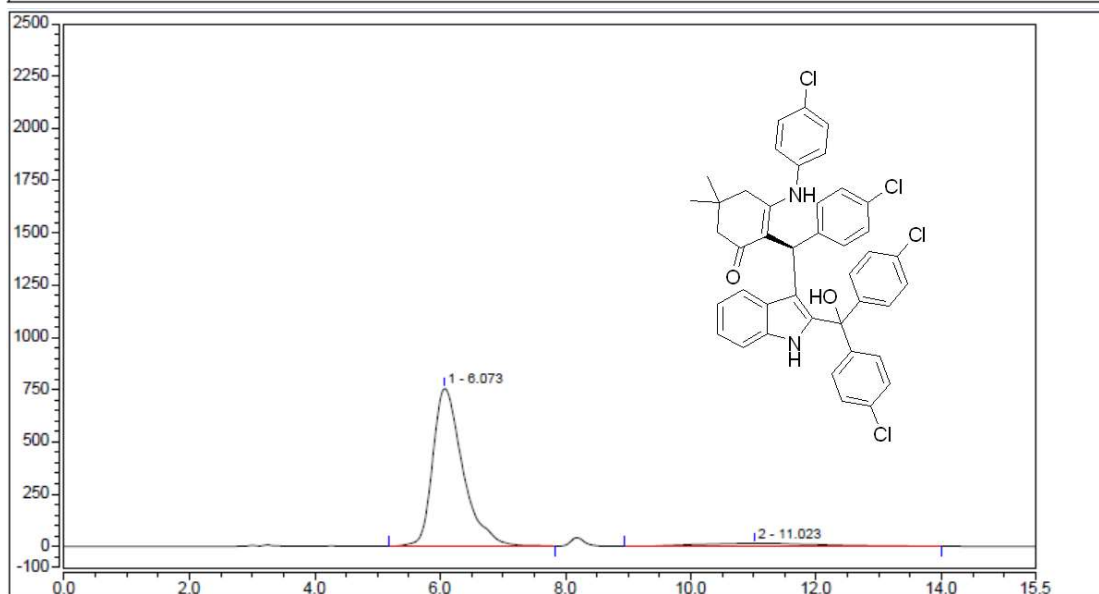


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.003	881.262	2437.382	97.19	97.57	n.a.
2		8.530	25.484	60.820	2.81	2.43	n.a.
Total:			906.746	2498.202	100.00	100.00	

3df

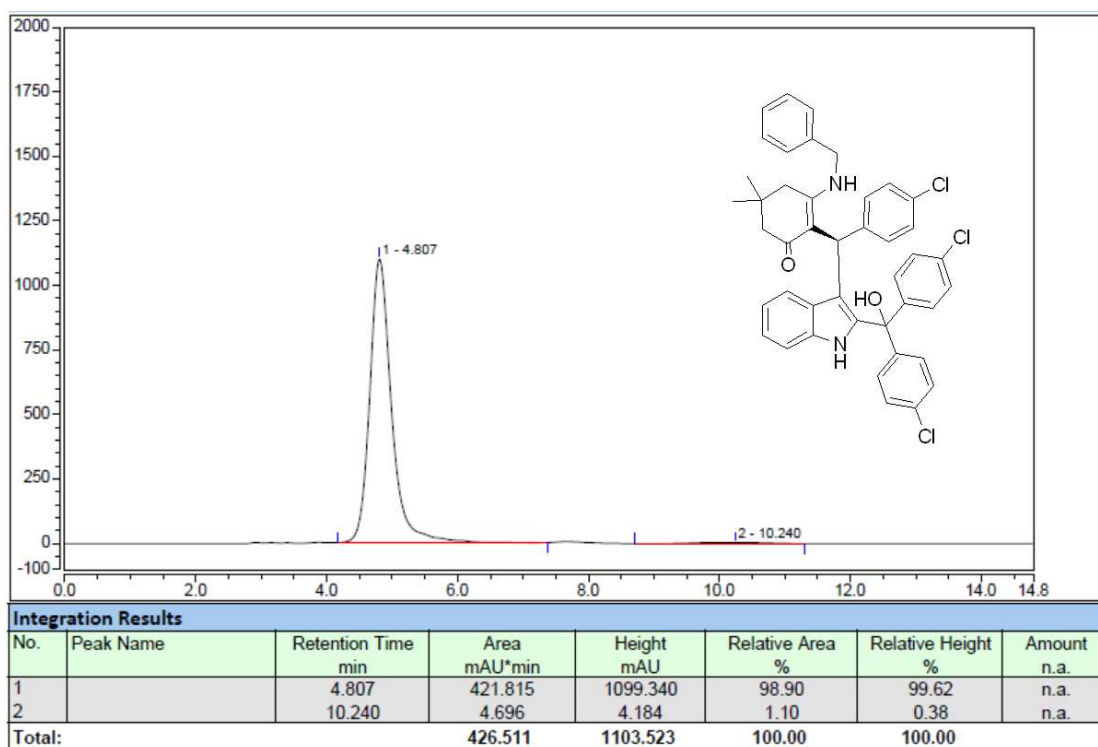
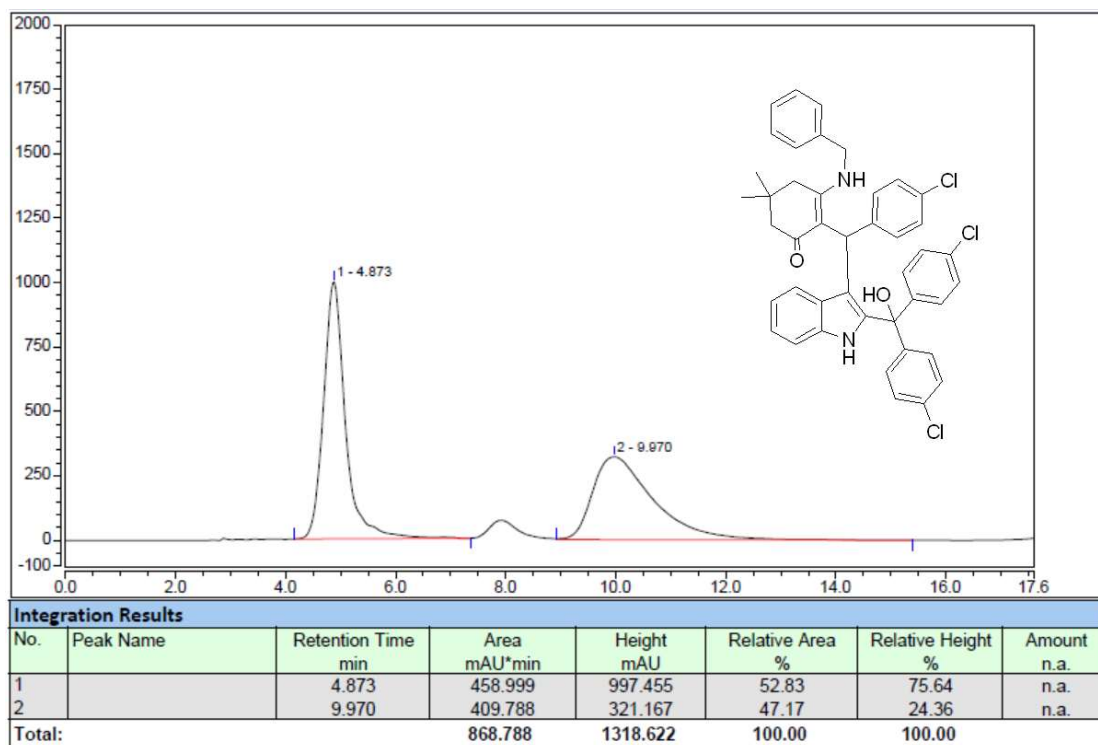


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.097	71.151	123.644	50.14	82.23	n.a.
2		10.980	70.755	26.717	49.86	17.77	n.a.
Total:			141.906	150.361	100.00	100.00	

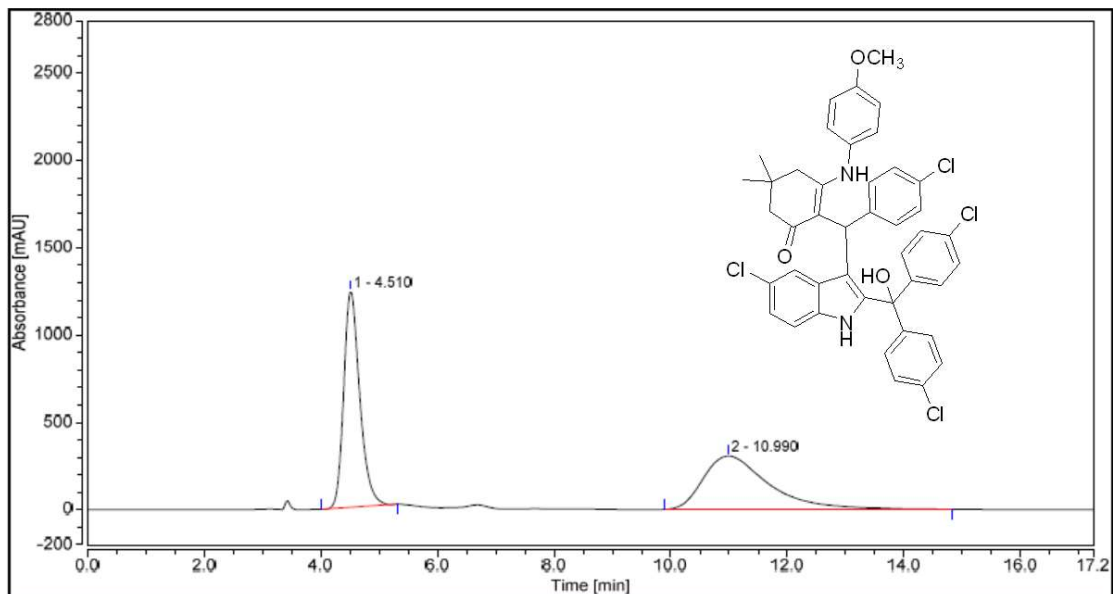


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.073	419.503	753.694	92.81	98.23	n.a.
2		11.023	32.495	13.560	7.19	1.77	n.a.
Total:			451.997	767.254	100.00	100.00	

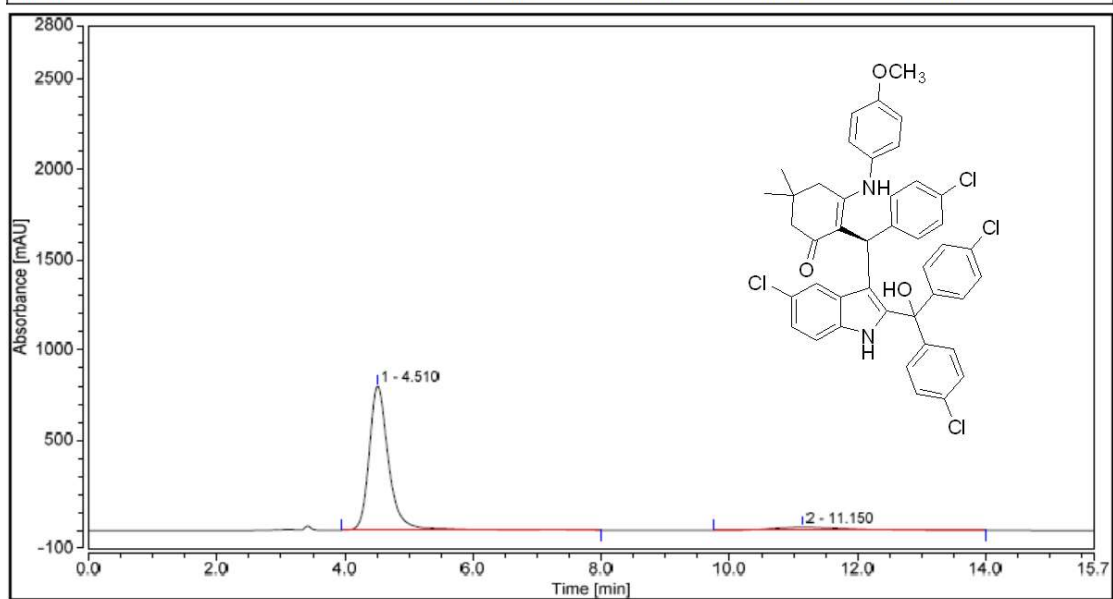
3dg



3ea

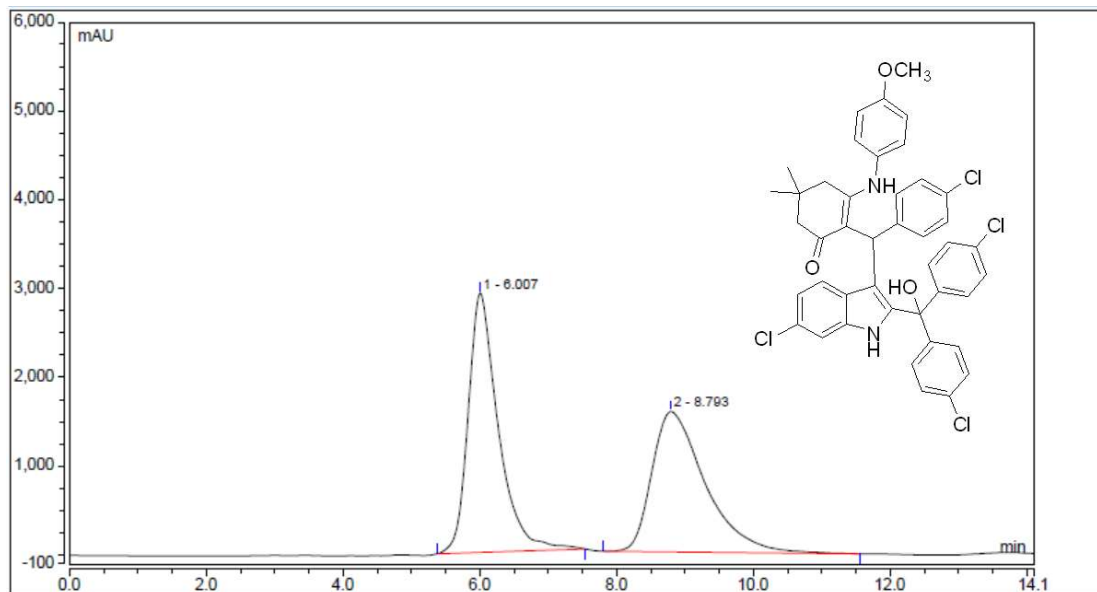


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		4.510	392.159	1235.496	49.67	80.20	n.a.
2		10.990	397.445	305.033	50.33	19.80	n.a.
Total:			789.604	1540.529	100.00	100.00	

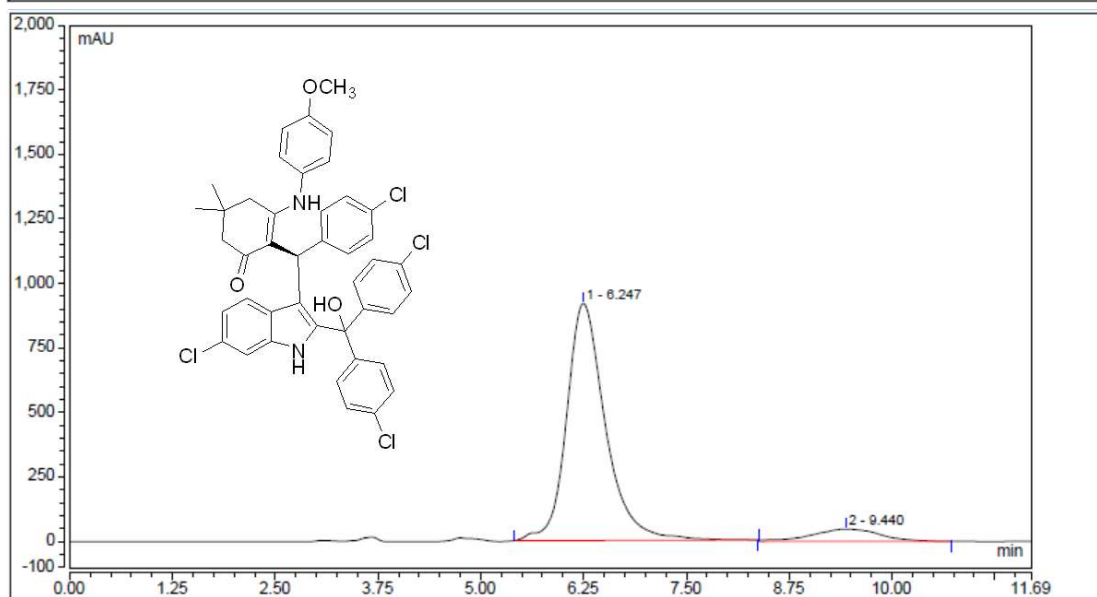


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		4.510	283.527	798.981	92.30	97.87	n.a.
2		11.150	23.655	17.353	7.70	2.13	n.a.
Total:			307.182	816.334	100.00	100.00	

3fa

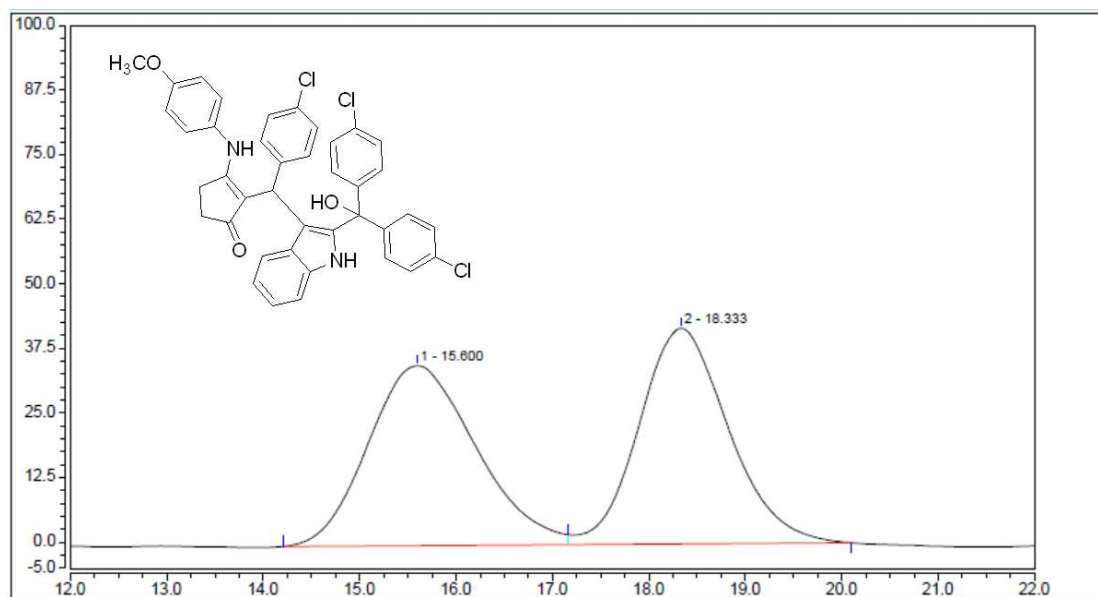


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.007	1488.233	2922.759	51.06	64.90	n.a.
2		8.793	1426.479	1580.963	48.94	35.10	n.a.
Total:			2914.712	4503.722	100.00	100.00	

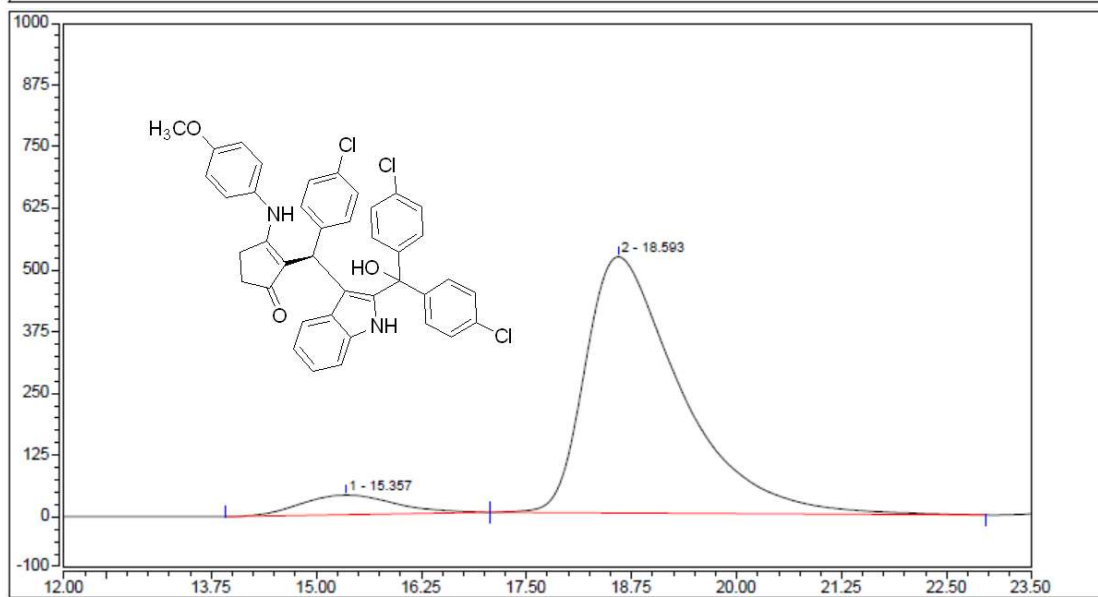


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.247	503.422	918.202	91.69	95.05	n.a.
2		9.440	45.654	47.859	8.31	4.95	n.a.
Total:			549.077	966.061	100.00	100.00	

3di

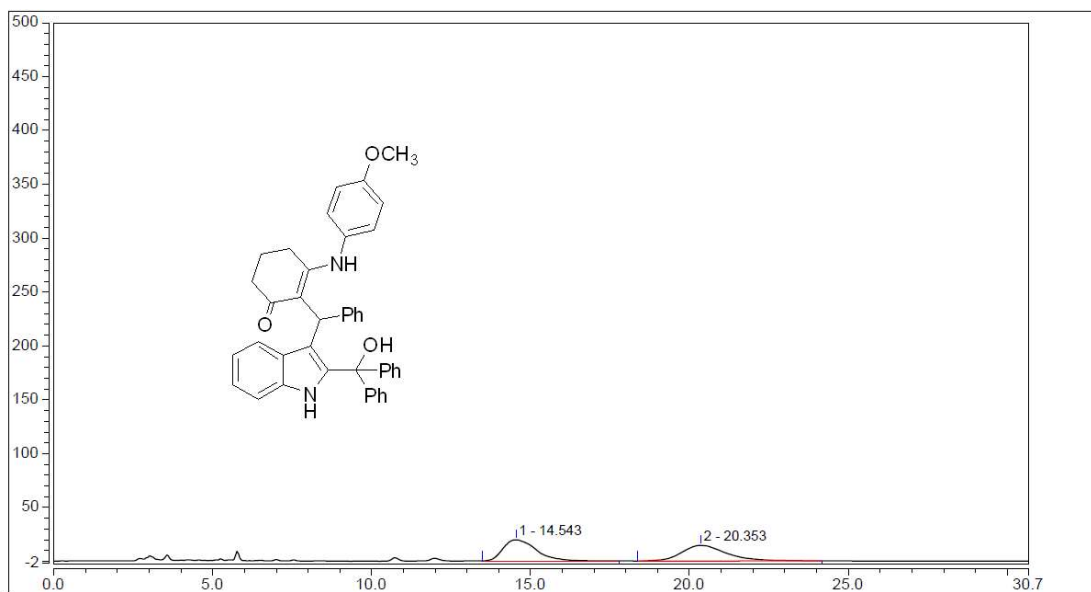


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		15.600	45.064	34.795	50.08	45.49	n.a.
2		18.333	44.913	41.693	49.92	54.51	n.a.
Total:			89.977	76.488	100.00	100.00	

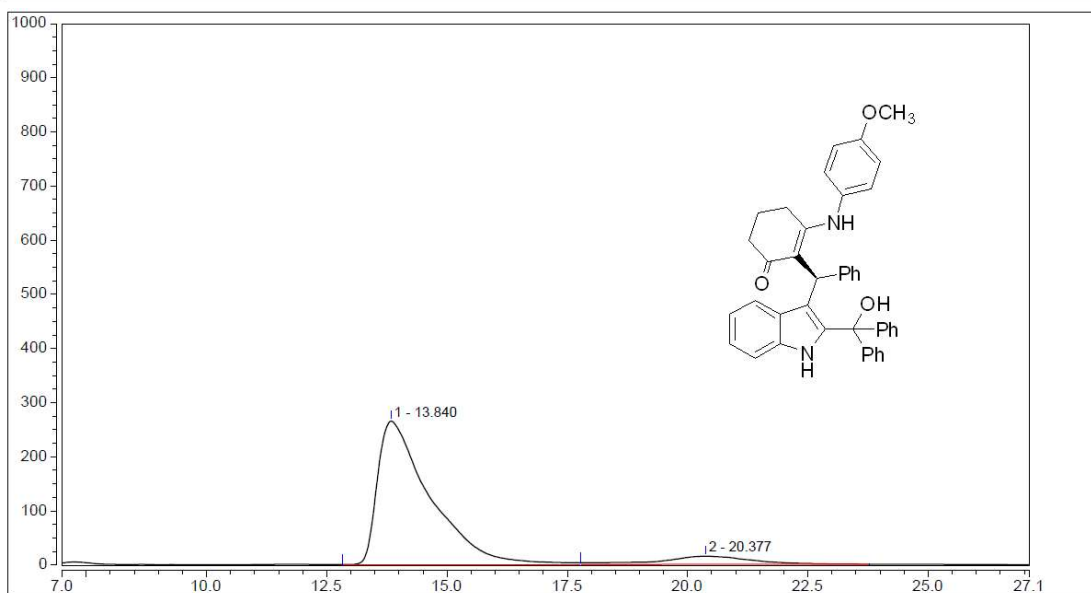


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		15.357	51.216	39.380	6.96	7.05	n.a.
2		18.593	684.561	518.928	93.04	92.95	n.a.
Total:			735.777	558.307	100.00	100.00	

3aj

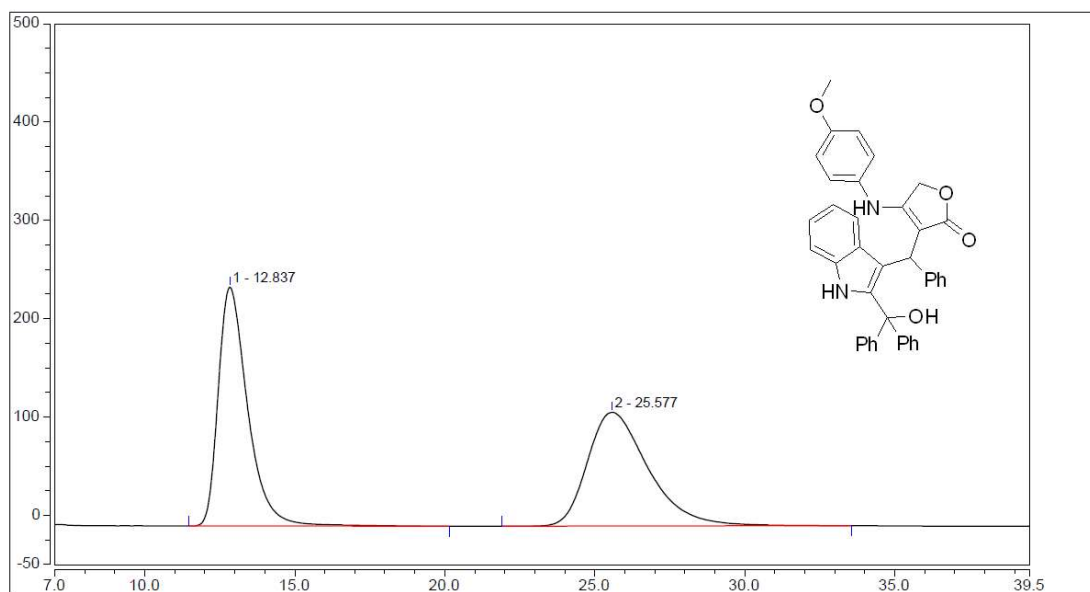


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		14.543	23.443	19.645	49.71	57.56	n.a.
2		20.353	23.712	14.484	50.29	42.44	n.a.
Total:			47.154	34.129	100.00	100.00	

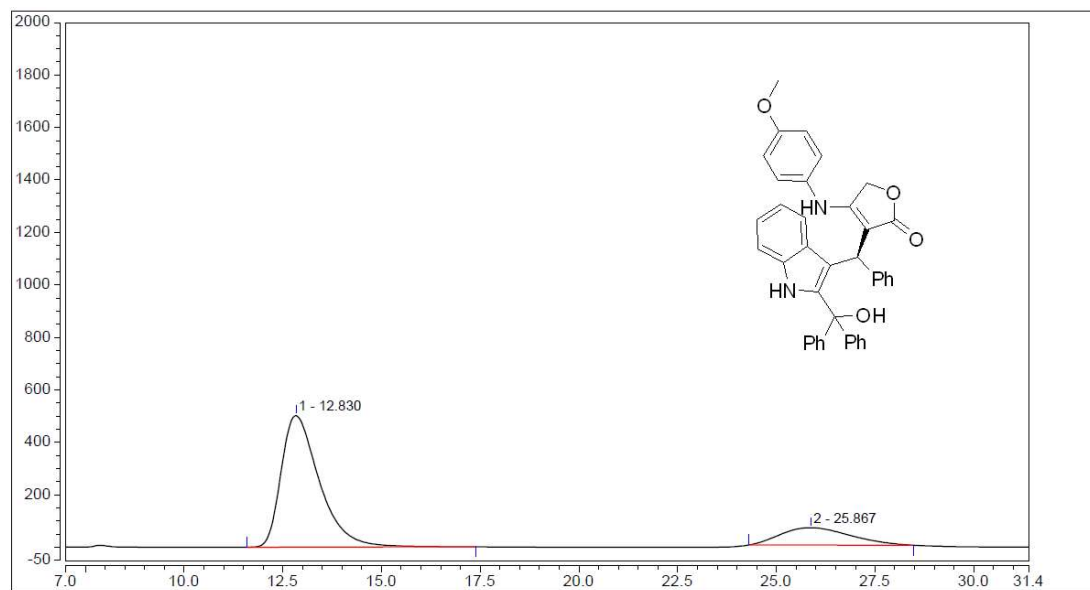


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		13.840	334.593	264.698	91.02	94.59	n.a.
2		20.377	33.026	15.128	8.98	5.41	n.a.
Total:			367.619	279.825	100.00	100.00	

3ak

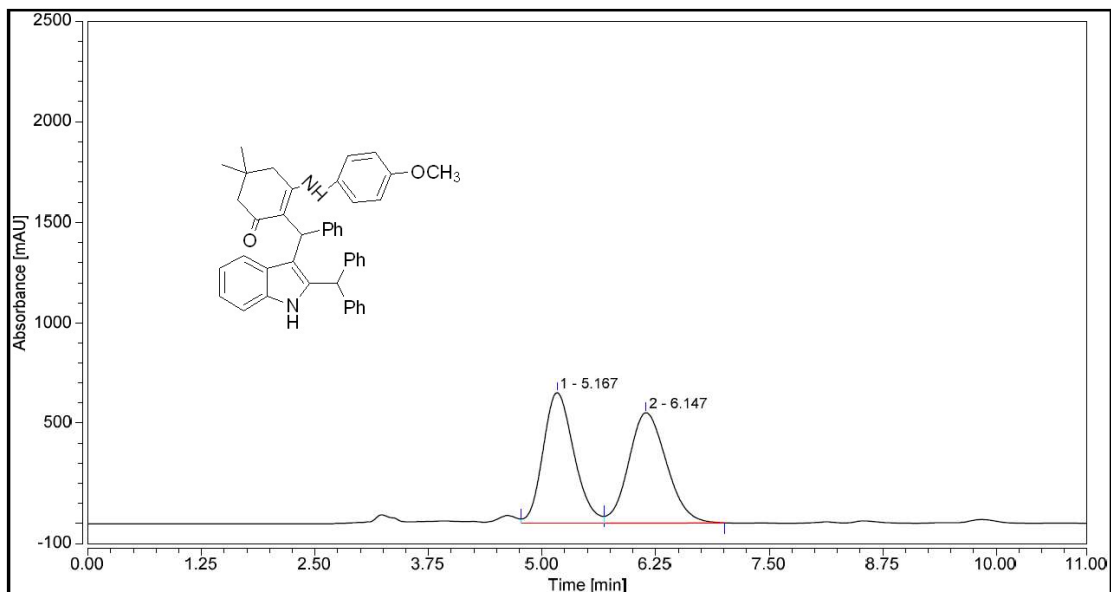


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		12.837	276.938	242.929	50.46	67.73	n.a.
2		25.577	271.871	115.726	49.54	32.27	n.a.
Total:			548.809	358.655	100.00	100.00	

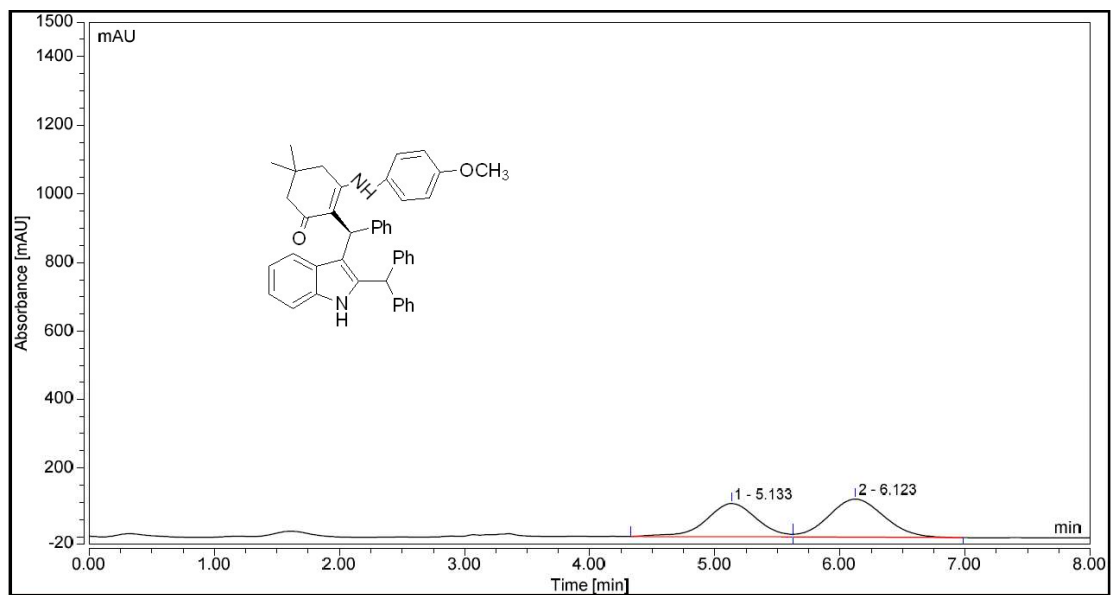


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		12.830	562.644	501.332	80.55	88.34	n.a.
2		25.867	135.878	66.172	19.45	11.66	n.a.
Total:			698.522	567.504	100.00	100.00	

3ha

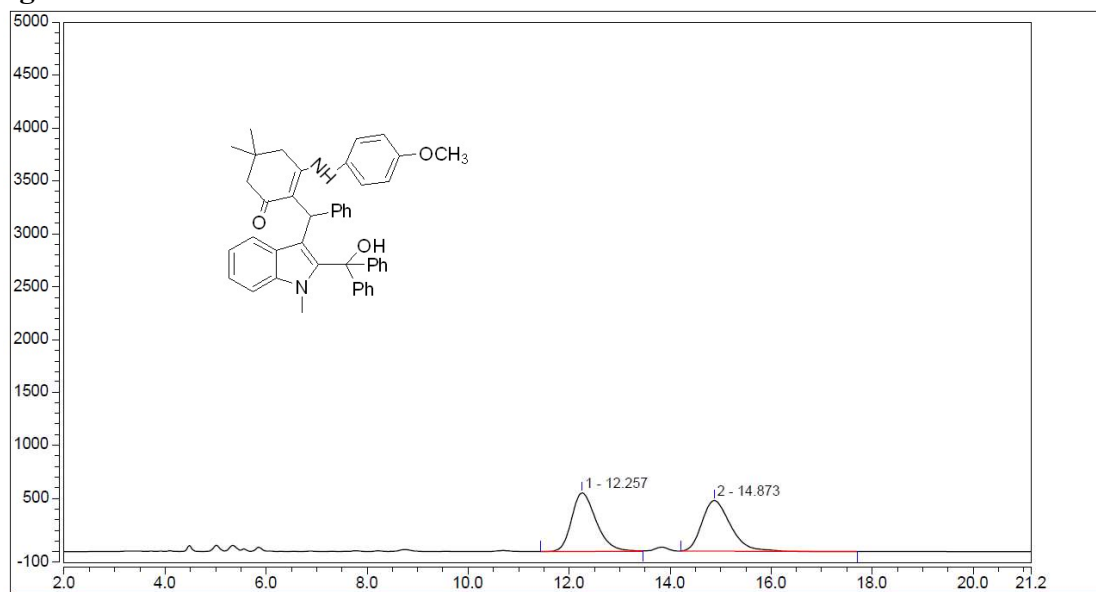


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		5.167	256.003	648.579	49.15	54.19	n.a.
2		6.147	264.898	548.371	50.85	45.81	n.a.
Total:			520.901	1196.950	100.00	100.00	

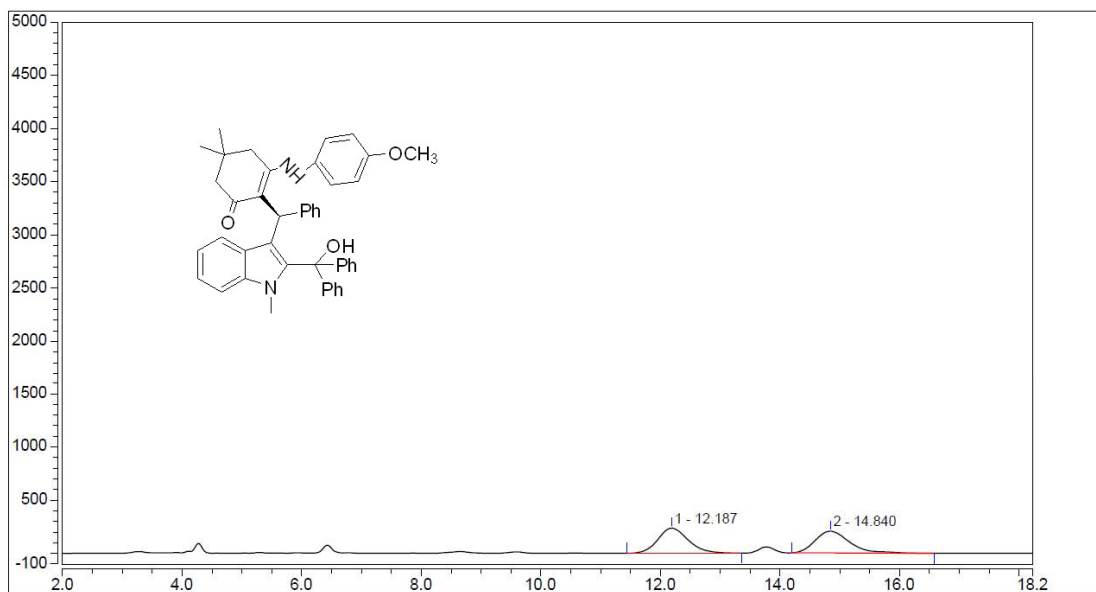


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		5.133	44.958	96.304	44.26	46.60	n.a.
2		6.123	56.625	110.342	55.74	53.40	n.a.
Total:			101.583	206.646	100.00	100.00	

3ga

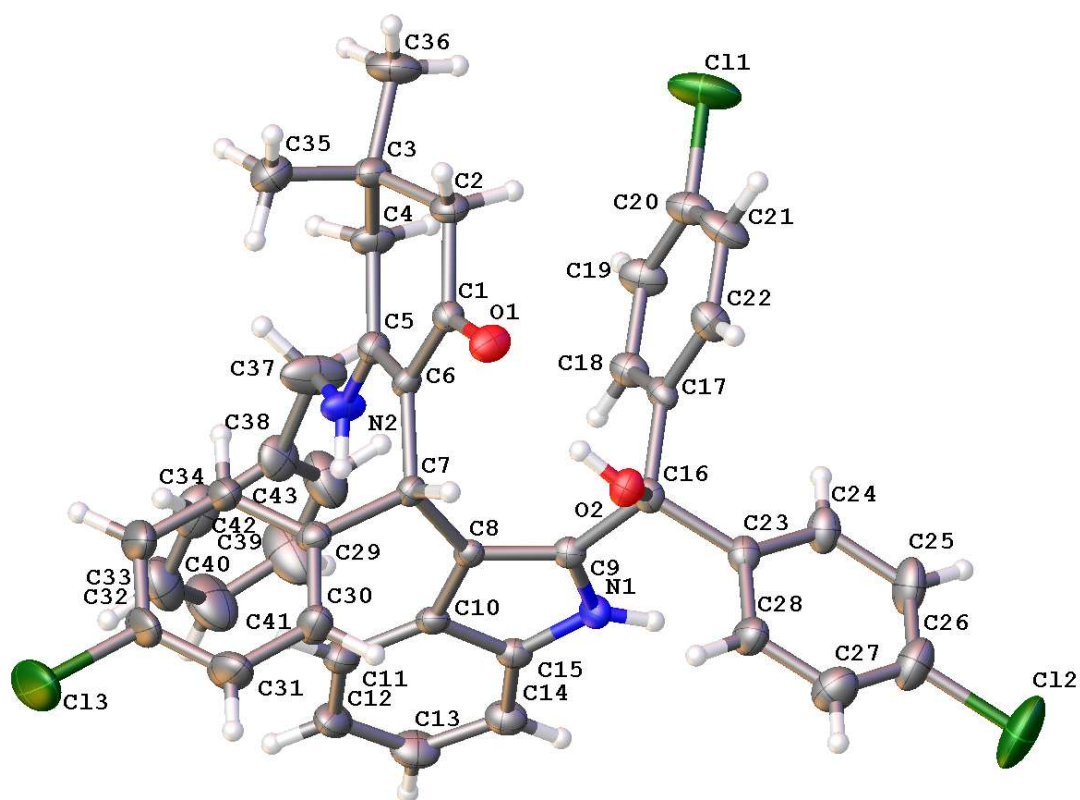
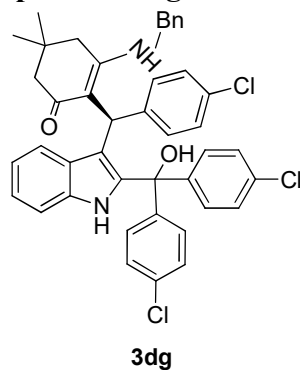


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.257	309.768	549.474	50.02	53.65	n.a.
2		14.873	309.579	474.624	49.98	46.35	n.a.
Total:			619.348	1024.098	100.00	100.00	



Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.187	141.560	236.584	50.80	53.65	n.a.
2		14.840	137.101	204.415	49.20	46.35	n.a.
Total:			278.661	440.998	100.00	100.00	

4. X-ray single-crystal data of product 3dg



The thermal ellipsoid was drawn at the 30% probability level.

Empirical formula	C ₄₃ H ₃₇ Cl ₃ N ₂ O ₂	
Formula weight	720.09	
Temperature	296.15 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 2 ₁ 1	
Unit cell dimensions	a = 10.757(9) Å	α = 90°.
	b = 12.558(10) Å	β = 99.306(10)°.
	c = 14.389(12) Å	γ = 90°.
Volume	1918(3) Å ³	

Z	2
Density (calculated)	1.247 Mg/m ³
Absorption coefficient	0.277 mm ⁻¹
F(000)	752
Crystal size	0.4 x 0.25 x 0.2 mm ³
Theta range for data collection	2.165 to 28.097°.
Index ranges	-12<=h<=14, -14<=k<=16, -18<=l<=18
Reflections collected	13691
Independent reflections	7336 [R(int) = 0.0729]
Completeness to theta = 25.242°	99.1 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7336 / 1 / 454
Goodness-of-fit on F ²	0.988
Final R indices [I>2sigma(I)]	R1 = 0.0663, wR2 = 0.1372
R indices (all data)	R1 = 0.1189, wR2 = 0.1587
Absolute structure parameter	0.00(10)
Extinction coefficient	n/a
Largest diff. peak and hole	0.240 and -0.263 e.Å ⁻³

5. Biological evaluation of compounds **3aa-3ae** and **3ag**

Table S1. Cell viability rate of compounds **3aa-3ae** and **3ag**

Compound	Survival rate on A549 cell line (%)			
	0.01 ug/mL	0.1 ug/mL	1 ug/mL	10 ug/mL
3aa	90.34± 4.72	76.22± 2.59	64.11± 2.88	52.27± 1.20
3ab	91.21±3.53	83.21± 1.87	74.43± 2.07	62.53± 1.38
3ac	99.96± 2.55	89.39± 1.60	78.50± 2.66	72.27± 3.60
3ad	93.55± 1.35	85.03± 1.27	76.58± 1.93	67.14± 1.23
3ae	99.30± 3.17	94.07± 2.34	88.45± 1.87	81.40± 1.71
3ag	97.82± 3.59	90.21± 2.32	80.58± 1.88	71.90± 1.37
Compound	Survival rate on ECA109 cell line (%)			
	0.01 ug/mL	0.1 ug/mL	1 ug/mL	10 ug/mL
3aa	101.49± 1.71	94.44± 3.78	85.20± 1.46	74.49± 1.67
3ab	99.52±1.31	92.41± 2.96	84.29± 1.75	74.38± 1.54
3ac	100.07± 3.00	92.90± 2.14	87.83± 2.51	75.89± 2.69
3ad	101.15± 1.04	96.84± 1.81	89.76± 1.46	82.52± 1.61
3ae	101.56± 3.69	101.04± 2.08	101.22± 1.33	99.47± 0.87
3ag	104.38± 3.56	102.52± 2.83	99.32± 1.57	100.71± 2.67
Compound	Survival rate on MCF-7 cell line (%)			
	0.01 ug/mL	0.1 ug/mL	1 ug/mL	10 ug/mL
3aa	89.19±1.26	71.90±2.03	58.96± 1.79	45.02± 2.07
3ab	90.59±3.08	82.26± 1.95	70.93± 1.61	59.63± 2.10
3ac	98.29± 1.98	85.18± 1.79	73.17± 1.98	65.94± 1.72
3ad	92.59± 1.82	84.56± 1.72	73.91± 1.13	62.52± 1.61
3ae	99.84±1.82	95.33± 1.34	90.19± 1.56	82.10± 1.00
3ag	95.44± 1.58	85.21± 1.31	75.45± 2.75	68.55±1.50