Supplementary information

Design, Synthesis and Evaluation of the COX-2 Inhibitory Activities of New 1, 3-dihydro-*2H*-indolin-2-one Derivatives

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Relevant spectroscopic data (^{1}H, ^{13}C and HRMS Spectra)

(*Z*)-1-acetyl-6-(trifluoromethyl)-3-(3-(trifluoromethyl)benzylidene)indolin-2-one (4a)

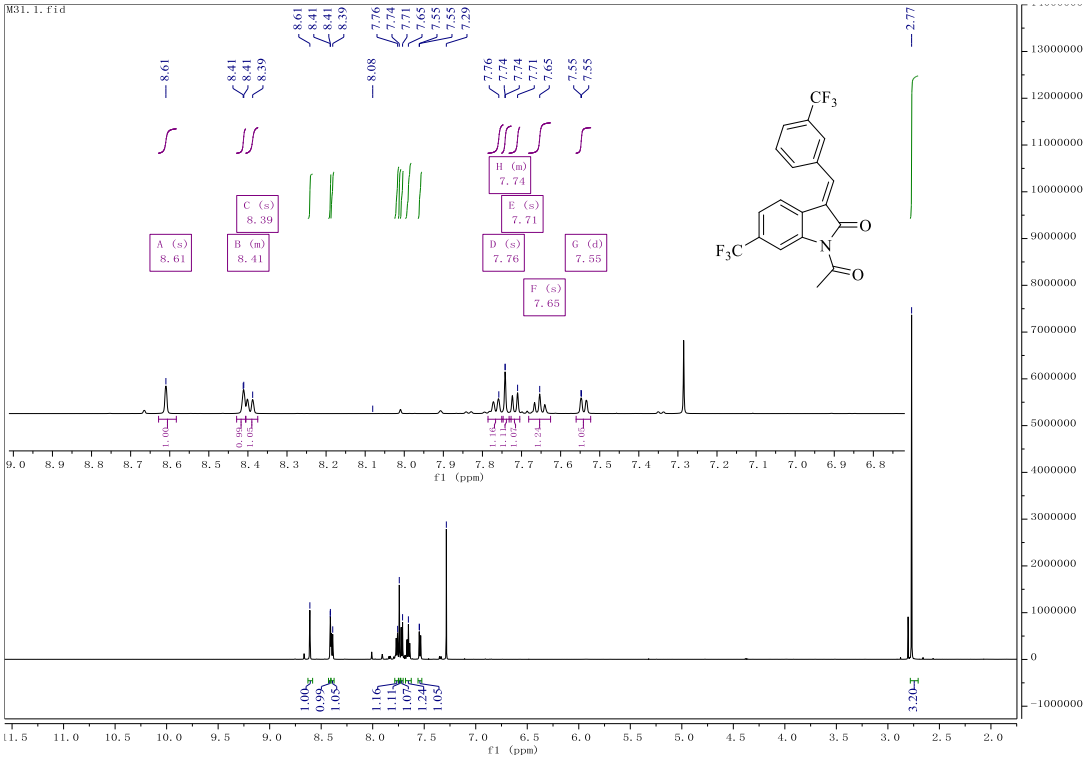


Figure S1-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4a**

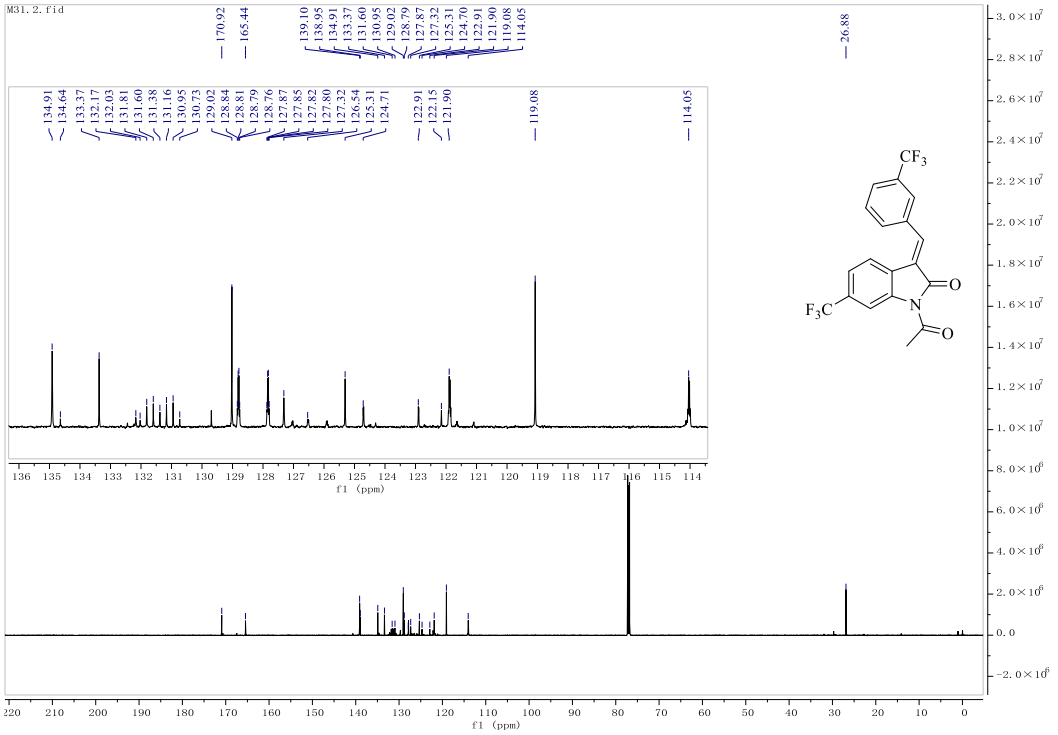


Figure S1-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4a**

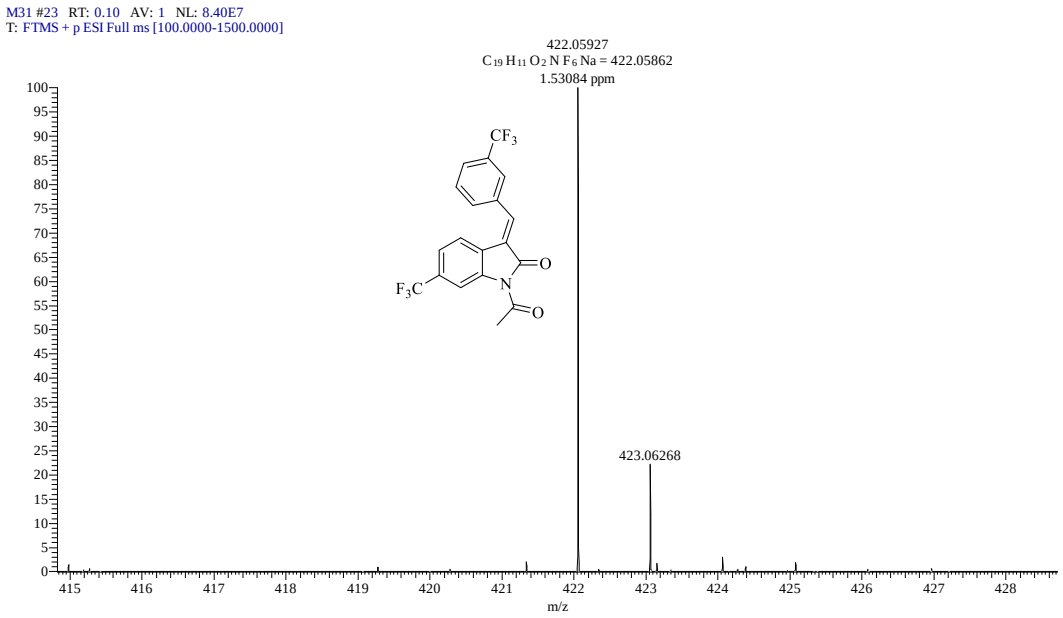


Figure S1-3. HRMS of compound **4a**

(*E*)-1-acetyl-6-(trifluoromethyl)-3-(3-(trifluoromethyl)benzylidene)indolin-2-one (4b)

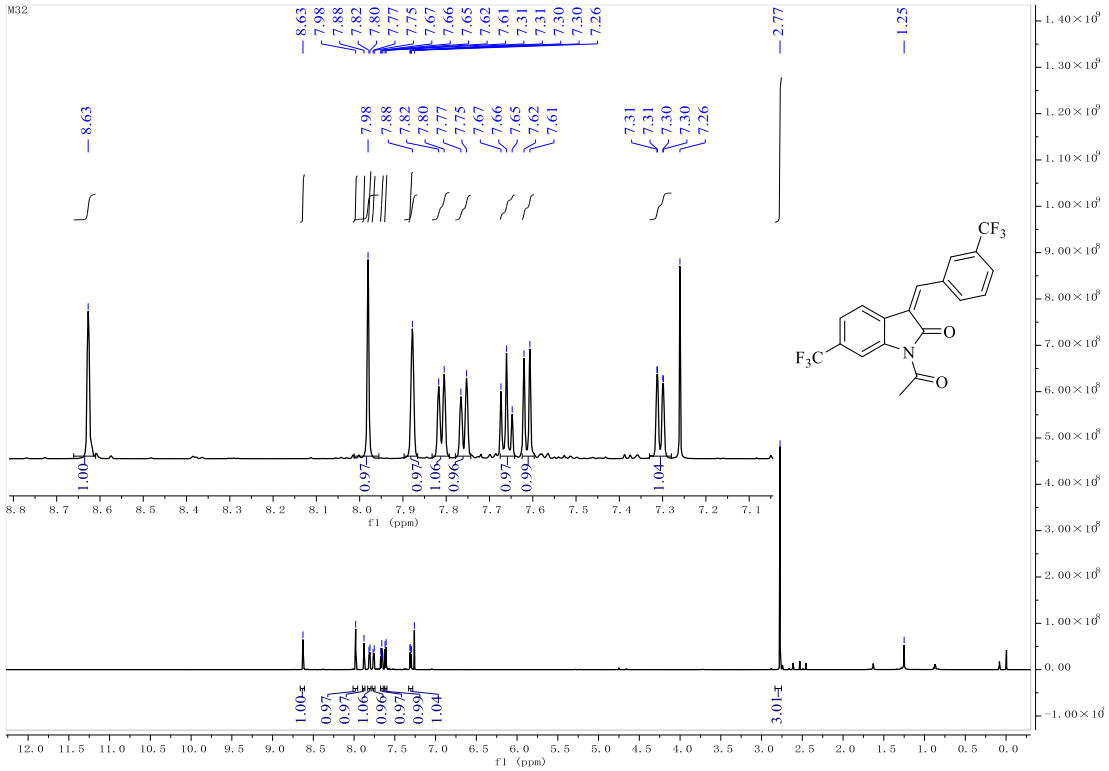


Figure S2-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4b**

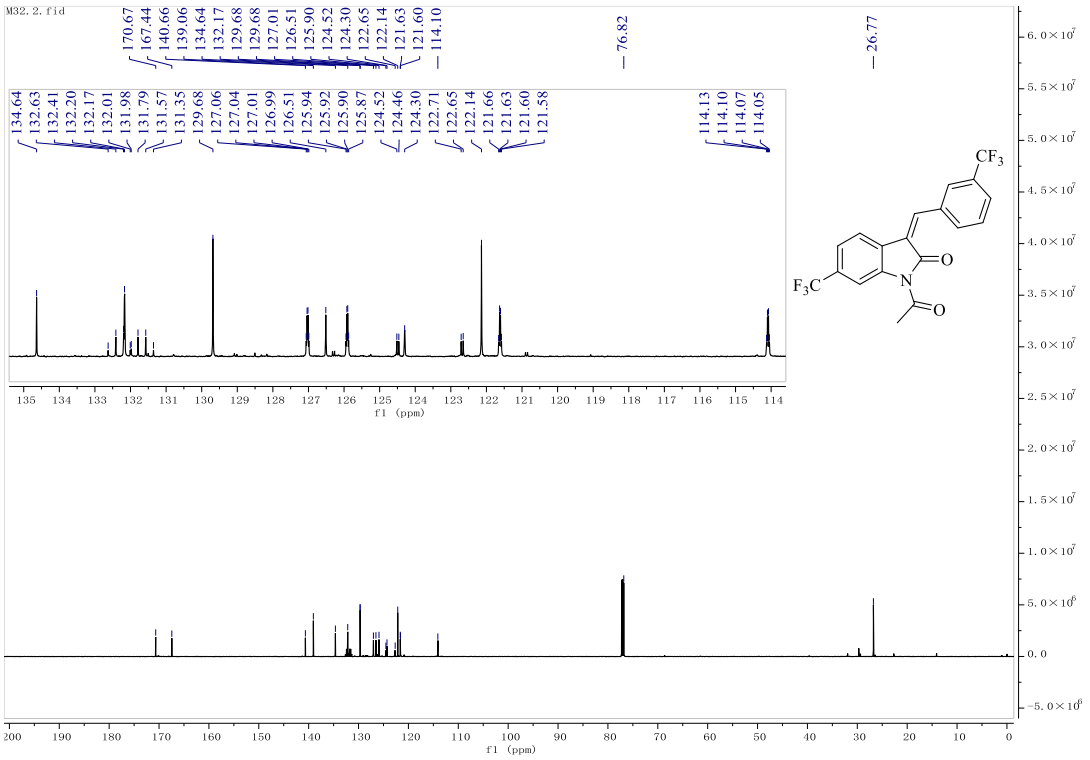


Figure S2-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4b**

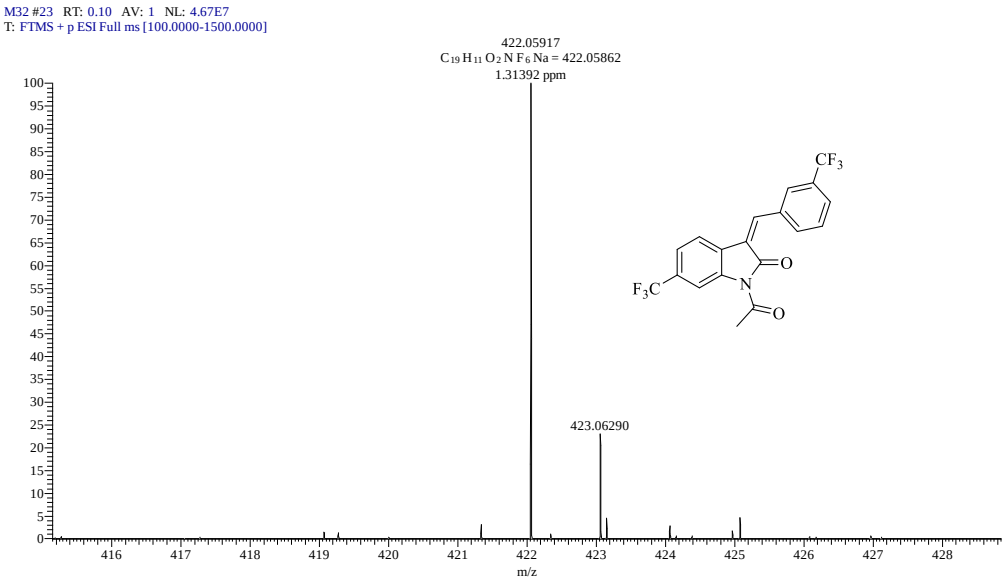


Figure S2-3. HRMS of compound **4b**

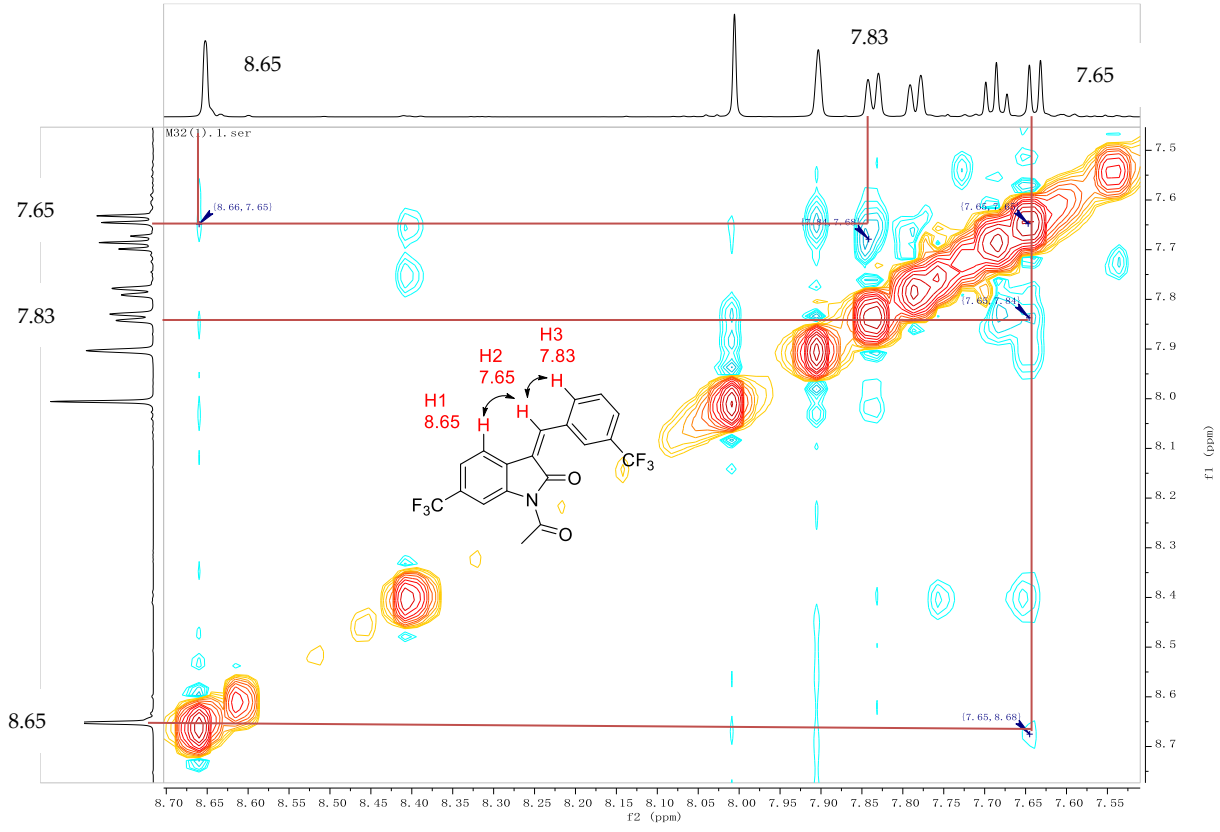


Figure S3-4. 2D-NOEY spectrum (600 Hz, $CDCl_3$) of compound **4b**

1-Acetyl-5-chloro-3-(3-(trifluoromethyl)benzylidene)indolin-2-one(4c)

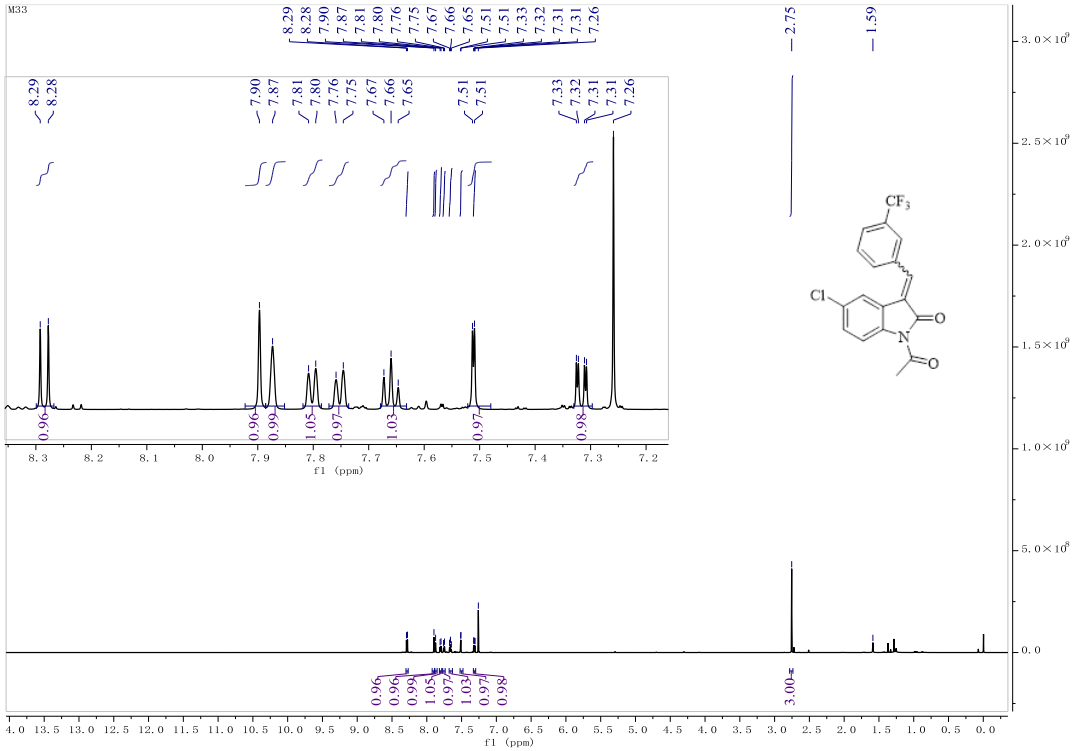


Figure S3-1. ^{1}H, NMR spectrum (600 Hz, $CDCl_3$) of compound **4c**

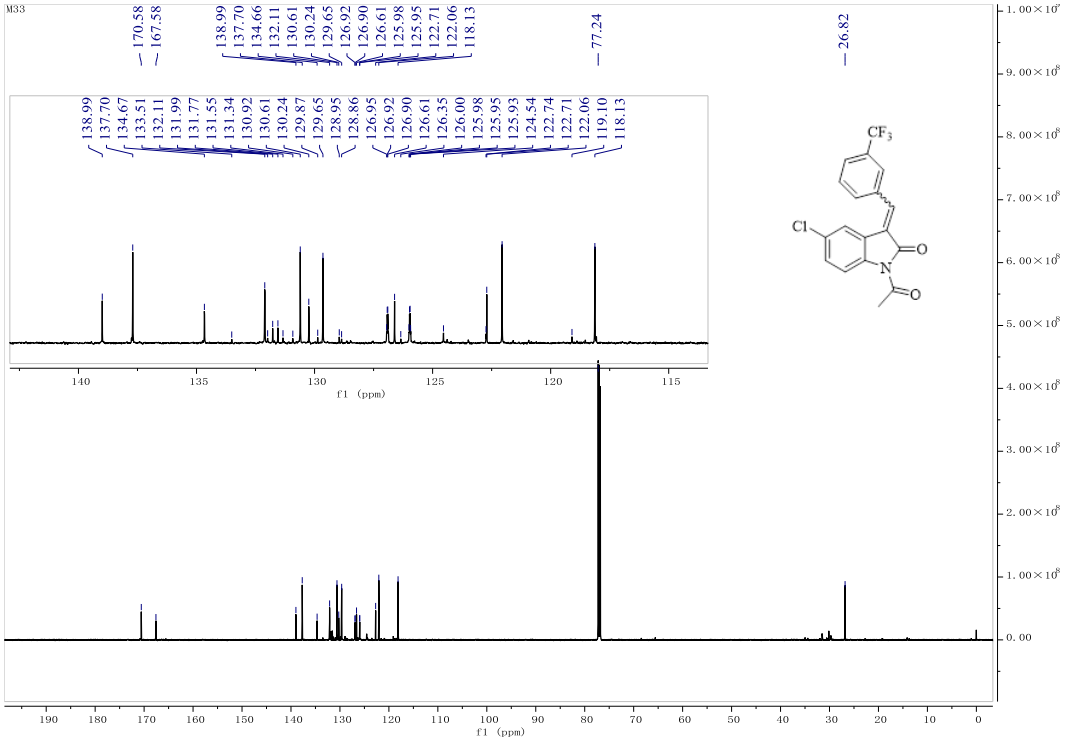


Figure S3-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4c**

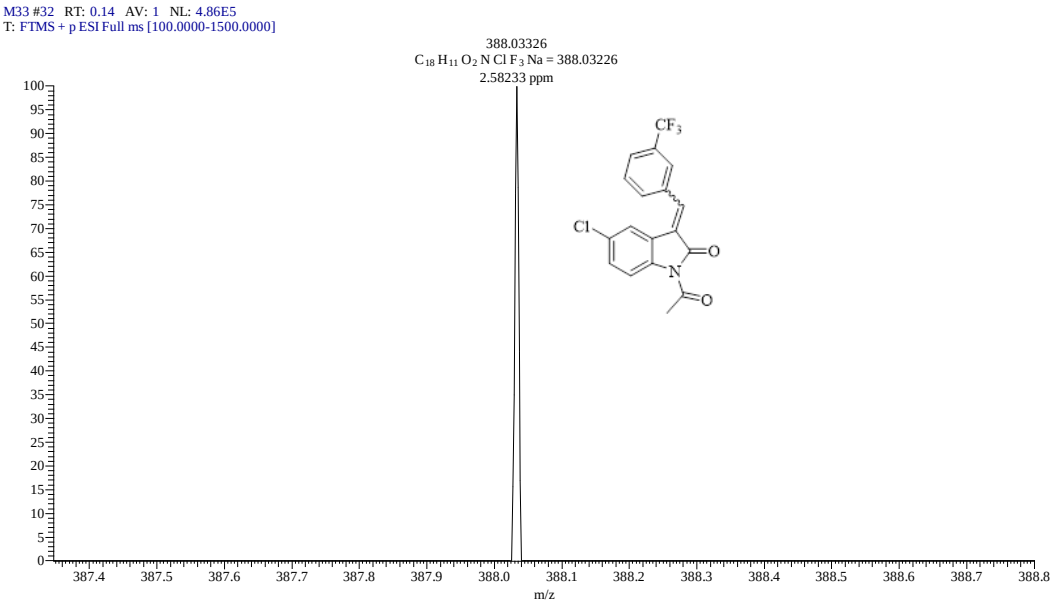


Figure S3-3. HRMS of compound **4c**

1-Acetyl-3-(3, 5-bis(trifluoromethyl)benzylidene)-6-chloroindolin-2-one (4d)

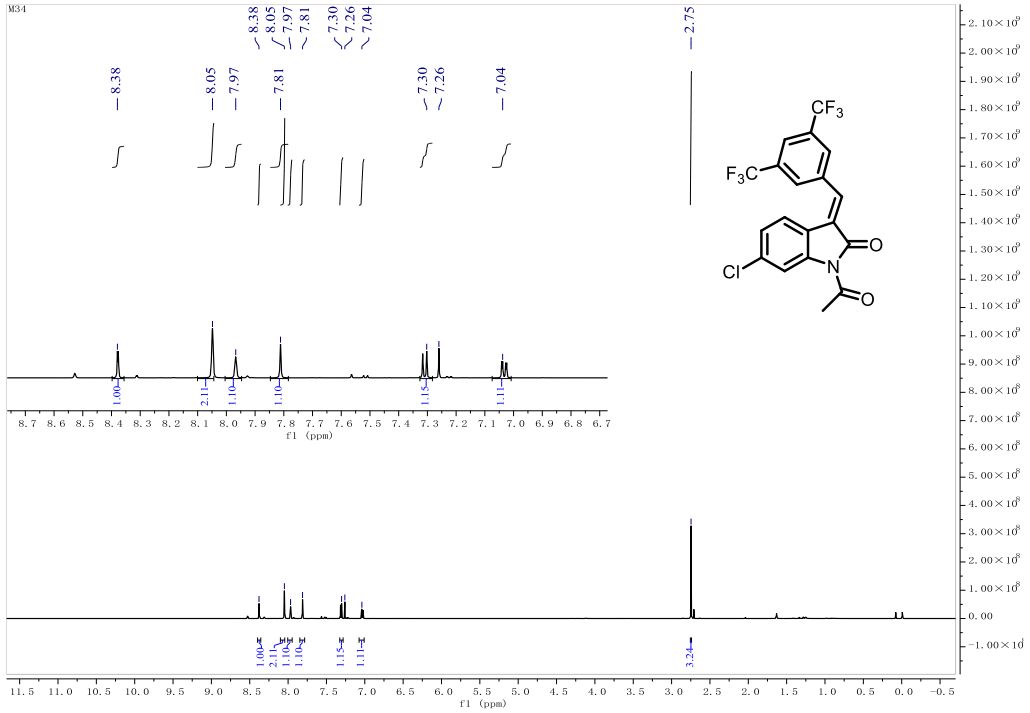


Figure S4-1. ^{1}H, NMR spectrum (600 Hz, $CDCl_3$) of compound **4d**

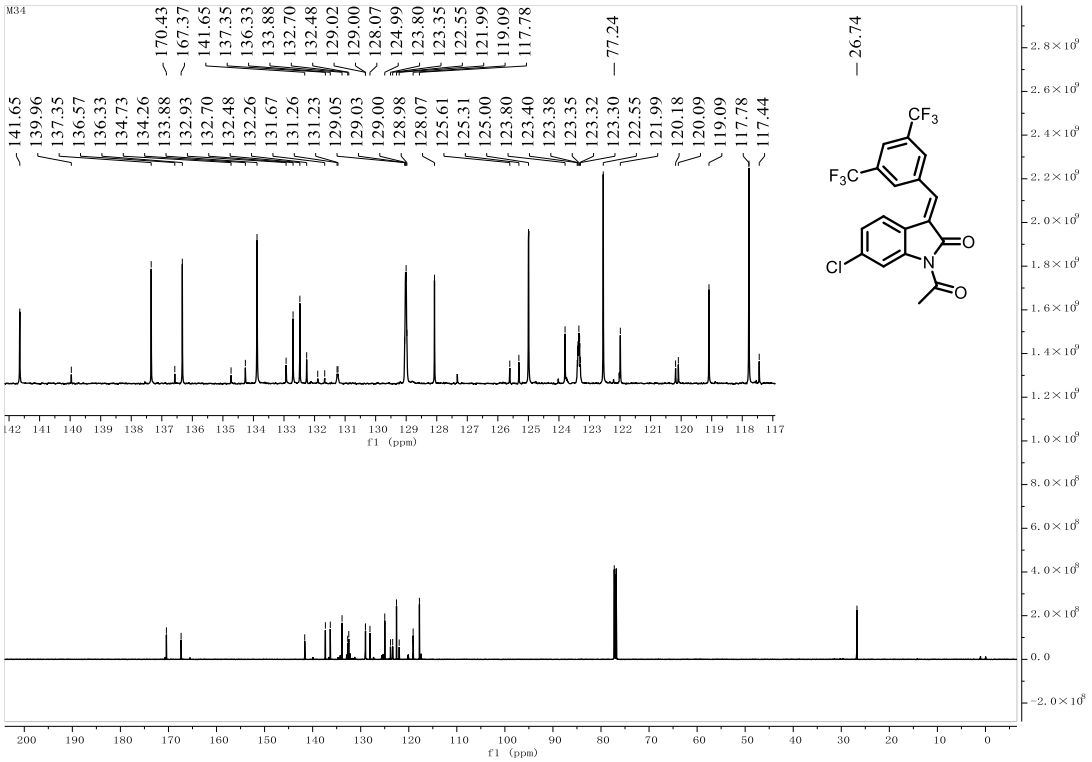


Figure S4-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4d**

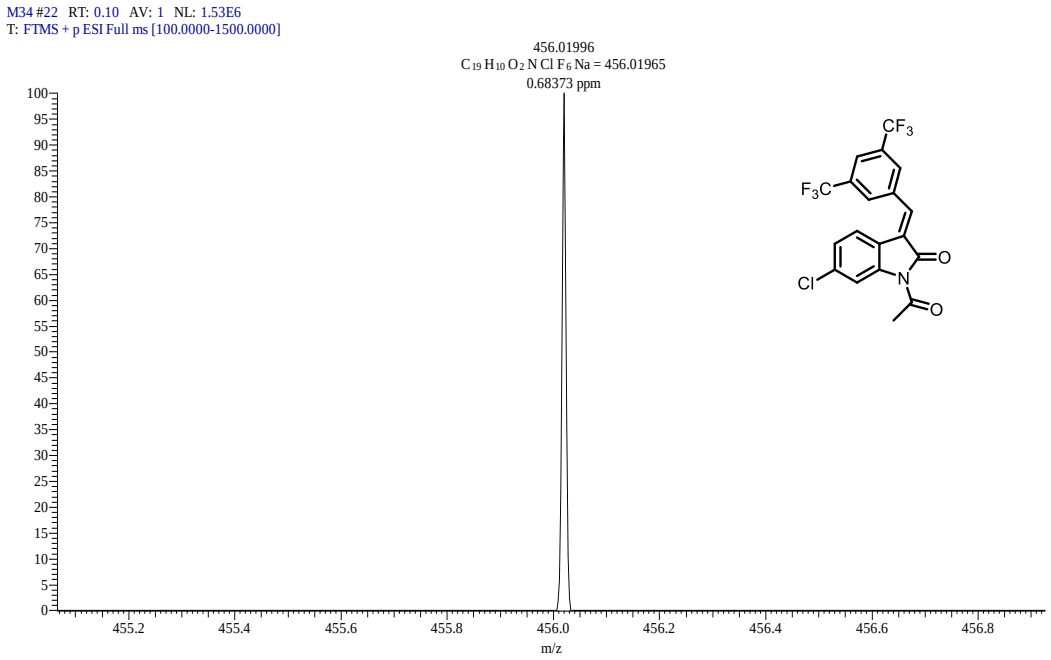


Figure S4-3. HRMS of compound **4d**

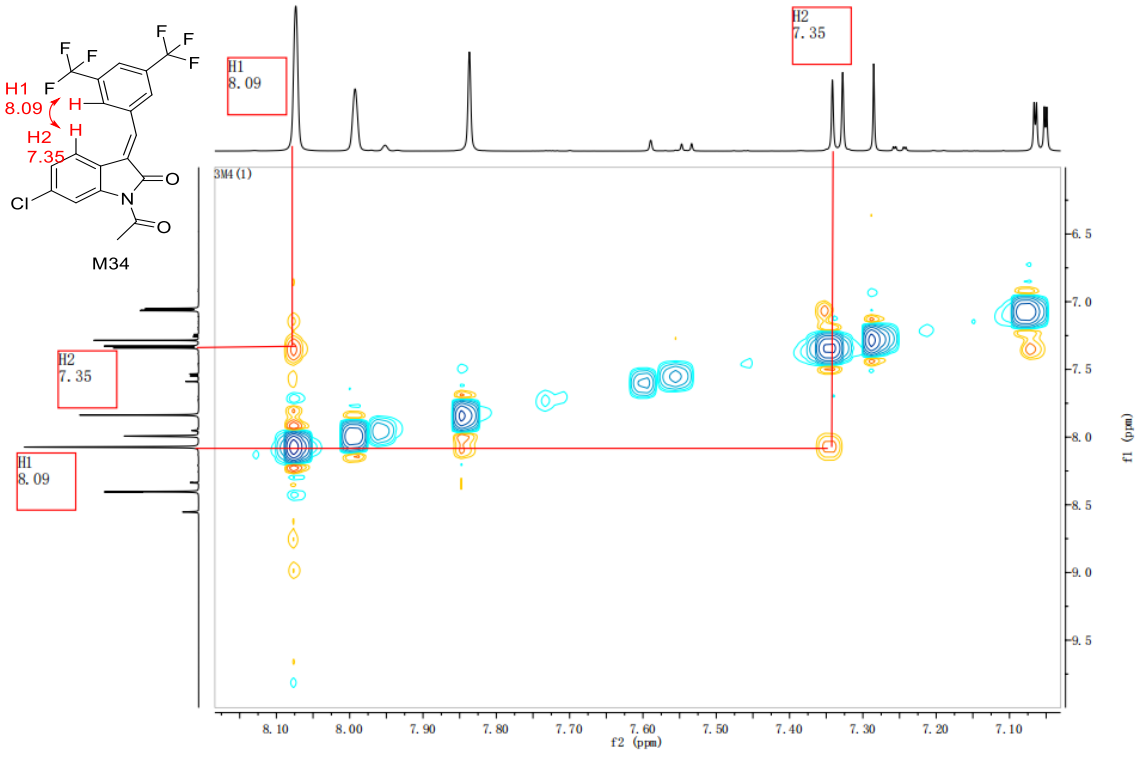


Figure S4-4. 2D-NOEY spectrum (600 Hz, $CDCl_3$) of compound **4d**

(*E*)1-acetyl-5-amino-3-(3-(trifluoromethyl)benzylidene)indolin-2-one (4e)

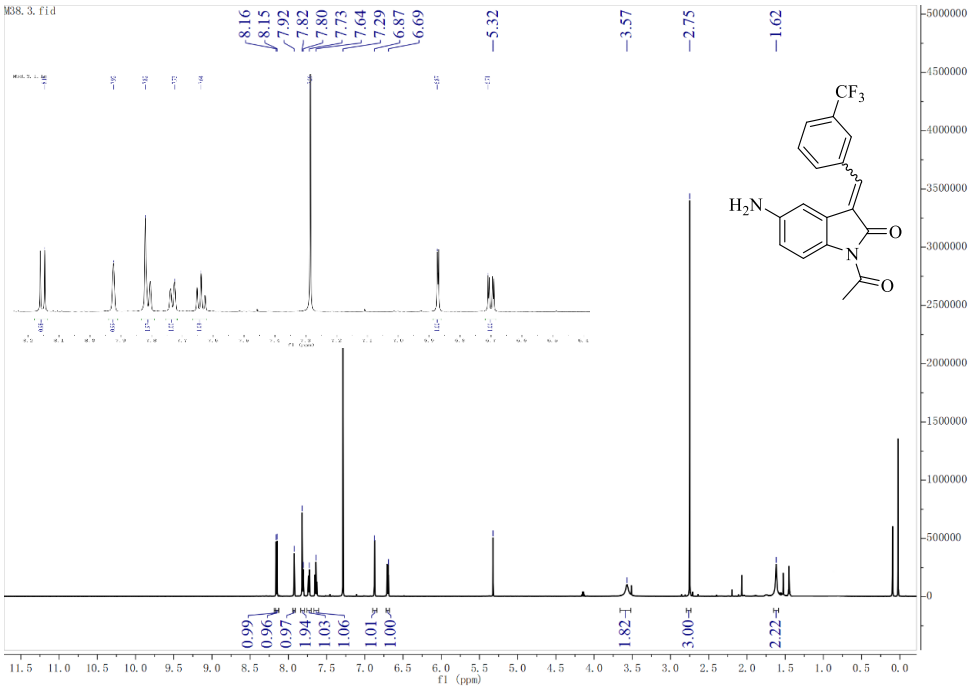


Figure S5-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4e**

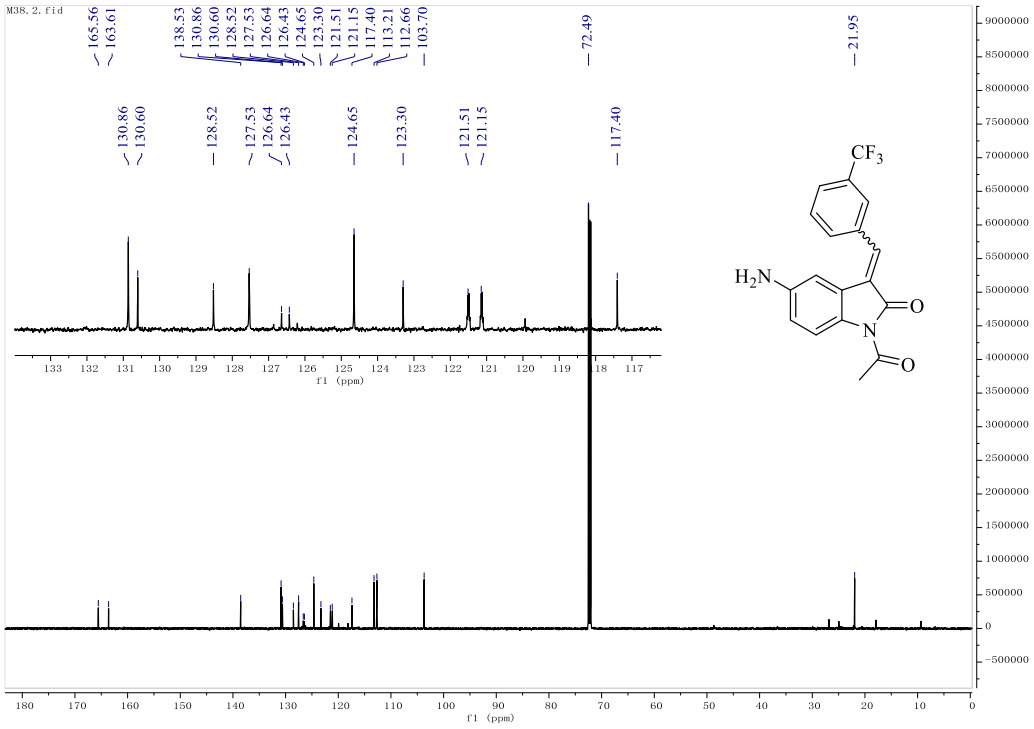


Figure S5-2. ^{1}H, ^{13}C NMR spectrum (150 Hz, DMSO) of compound **4e**

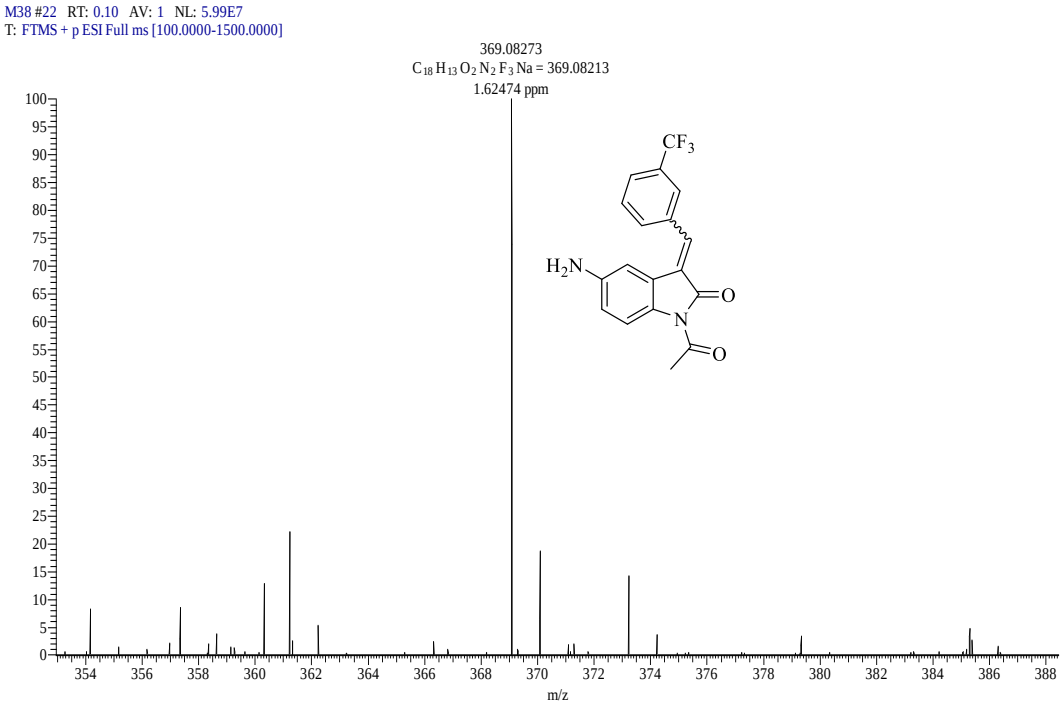


Figure S5-3. HRMS of compound **4e**

(Z)-1-acetyl-3-(3,5-bis(trifluoromethyl)benzylidene)-6-chloroindolin-2-one(4f)

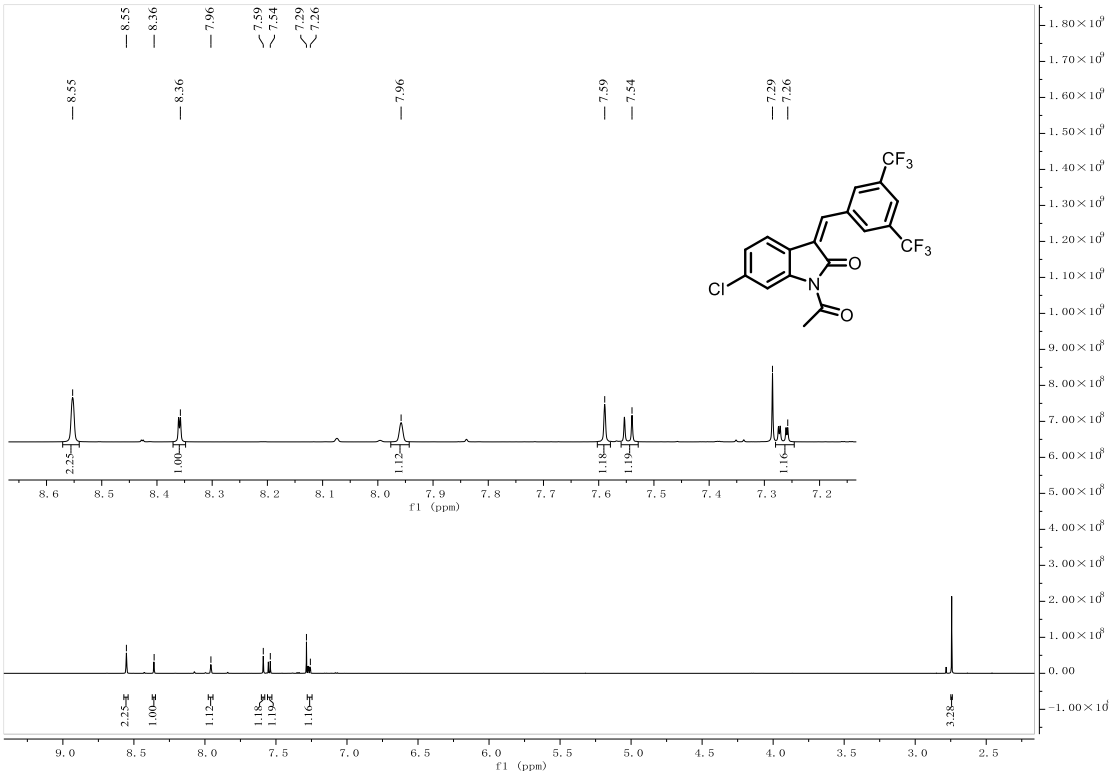


Figure S6-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4f**

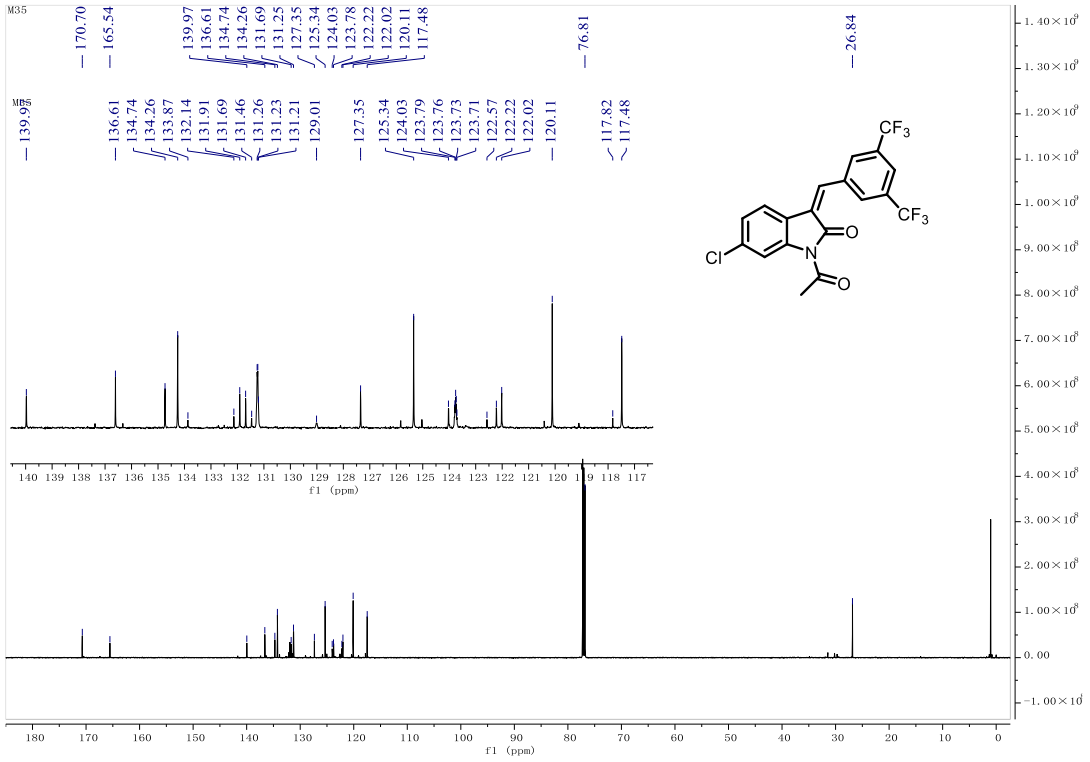


Figure S6-2. ^{1}H, ^{13}C NMR spectrum (600 Hz, 150 Hz, $CDCl_3$) of compound **4f**

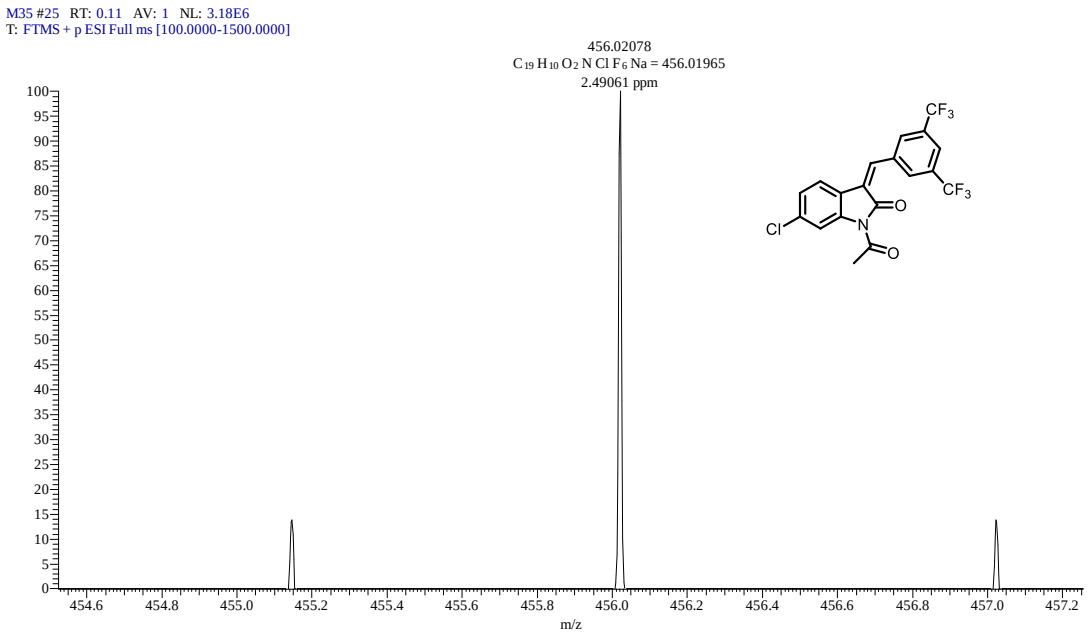


Figure S6-3. HRMS of compound **4f**

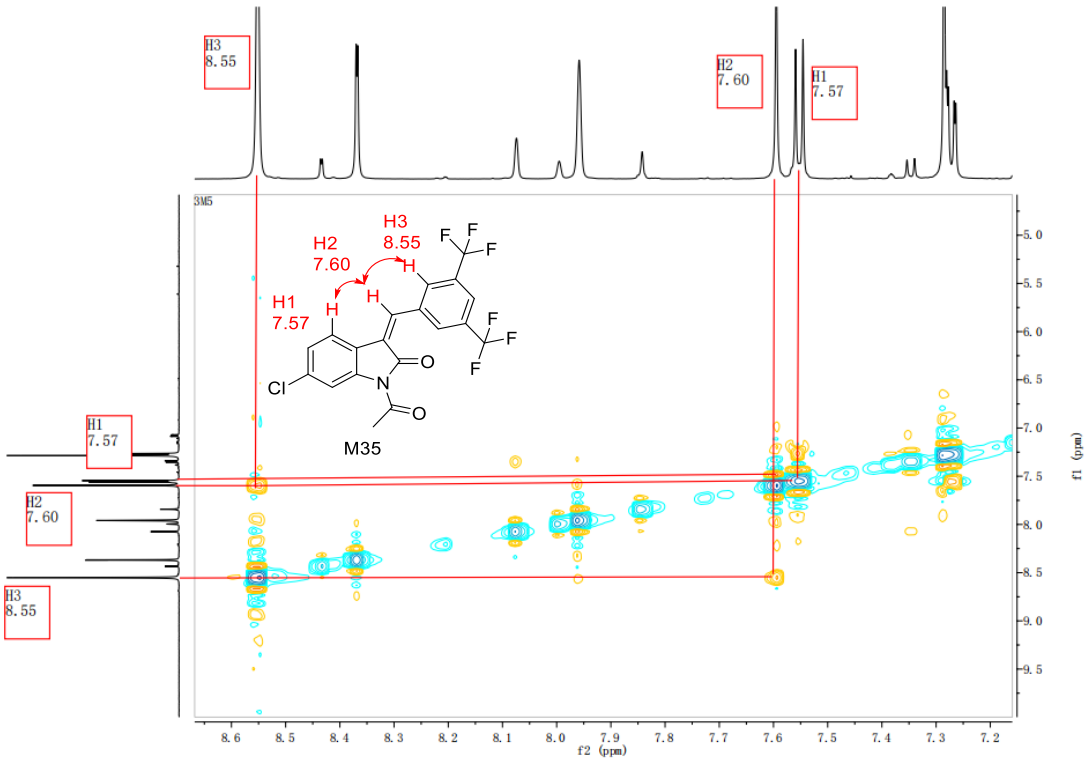


Figure S6-4. 2D-NOEY spectrum (600 Hz, $CDCl_3$) of compound **4f**

1-Acetyl-3-benzylideneindolin-2-one (4g)

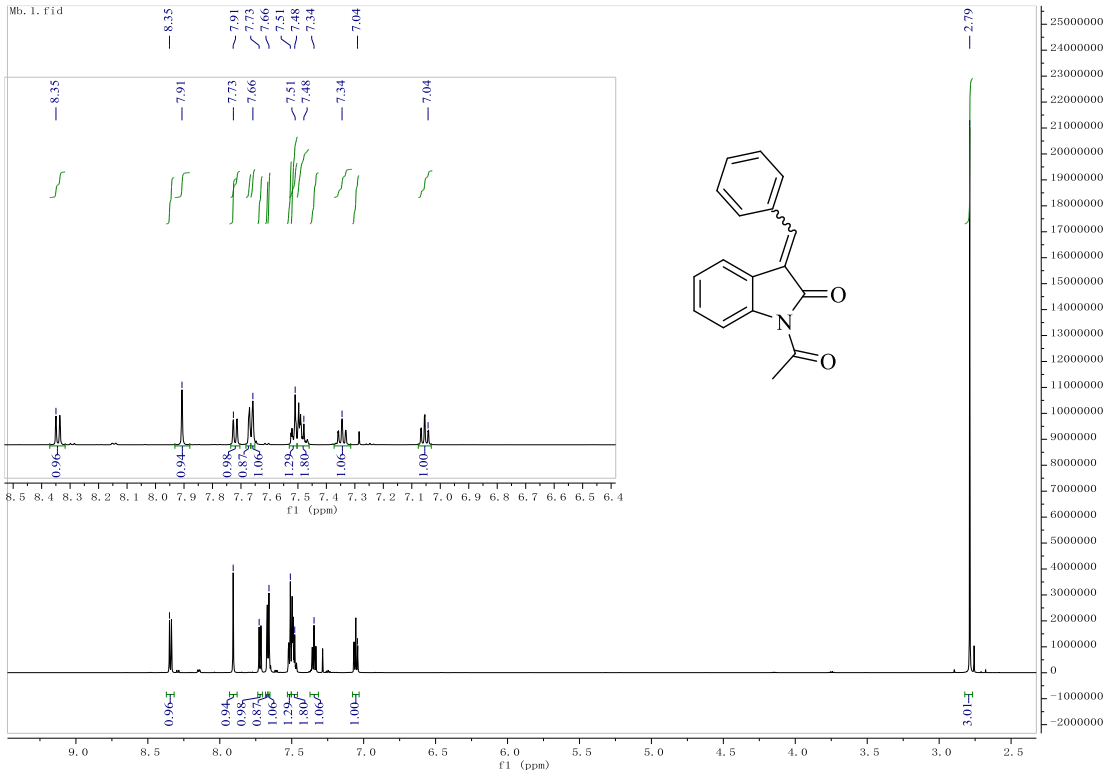


Figure S7-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4g**

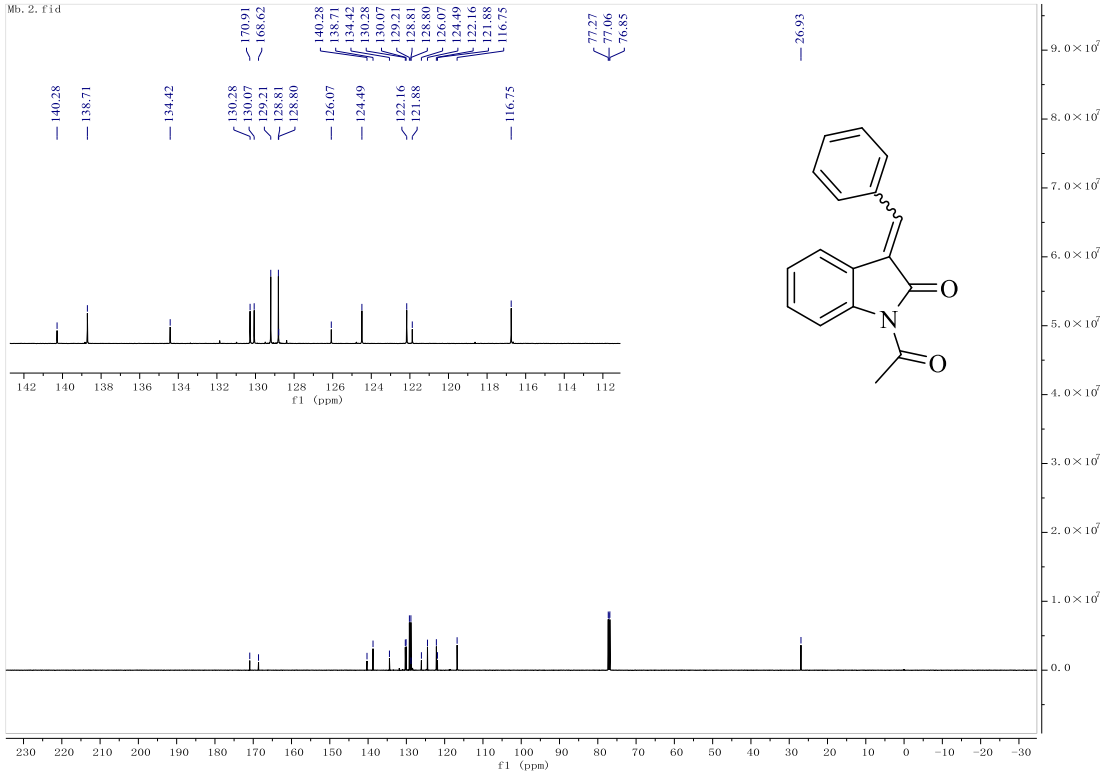


Figure S7-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4g**

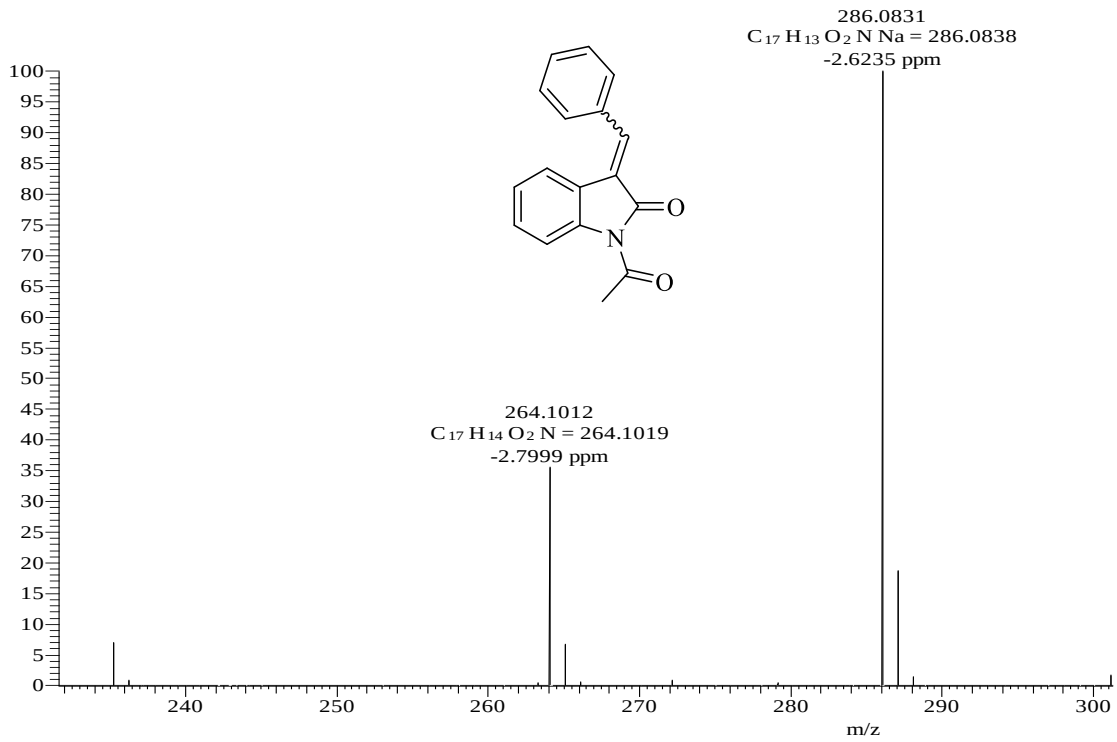


Figure S7-3. HRMS of compound **4g**

1-Acetyl-6-chloro-3-(3-(trifluoromethyl)benzylidene)indolin-2-one(4h)

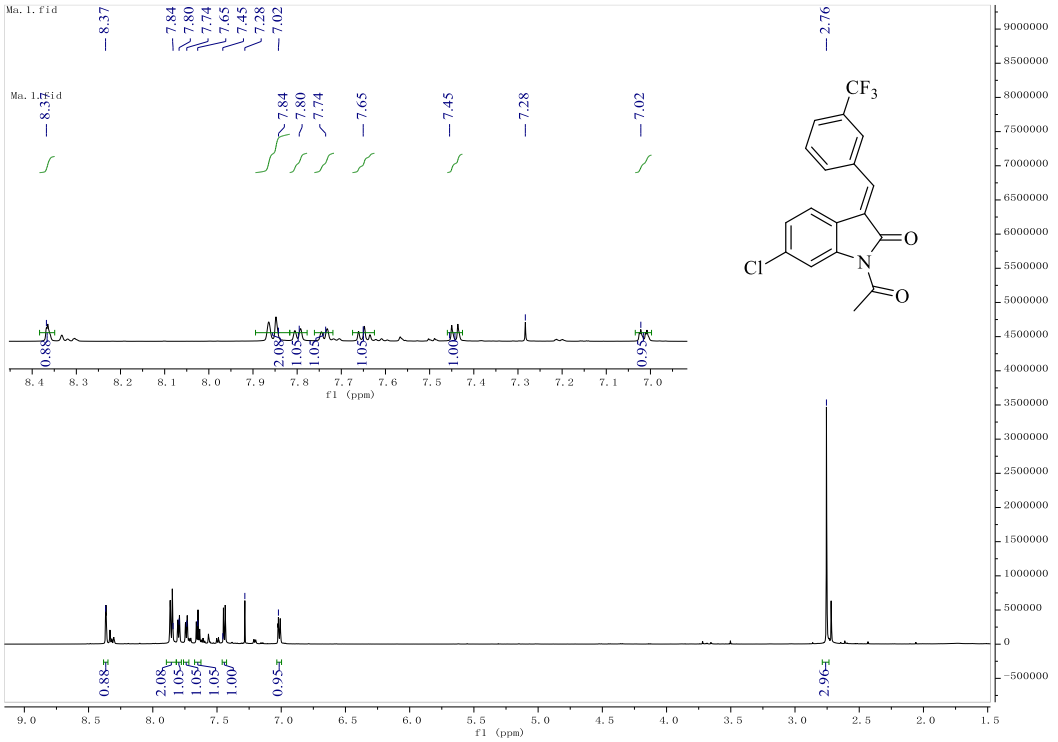


Figure S8-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4h**

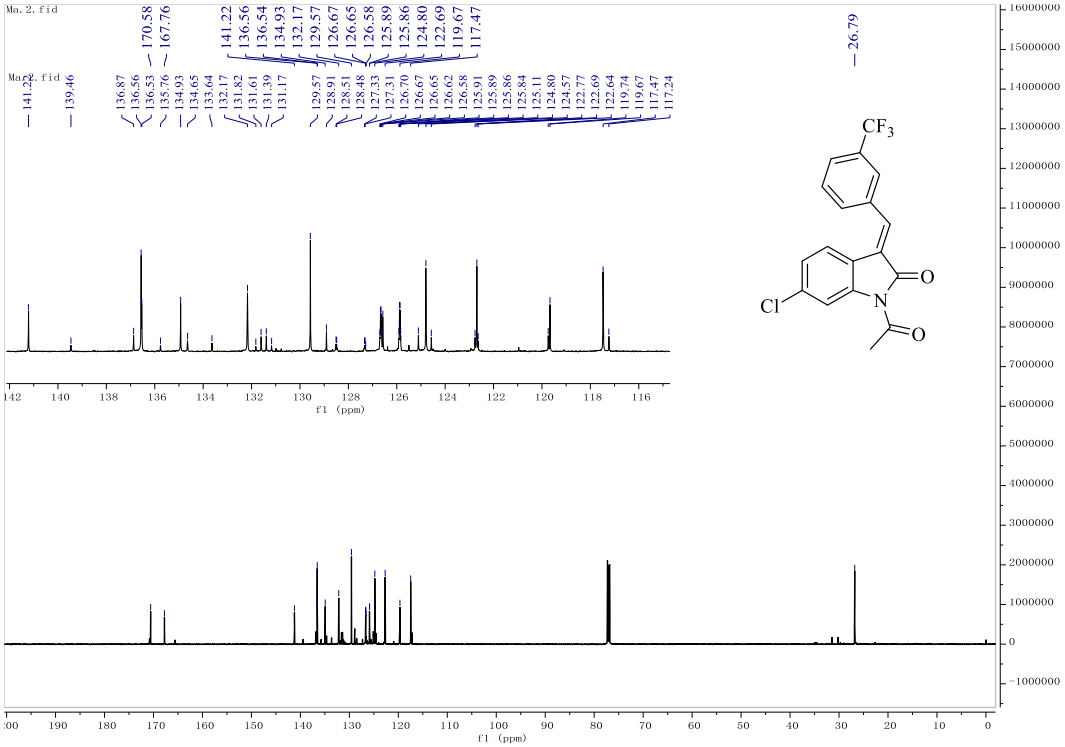


Figure S8-1. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4h**

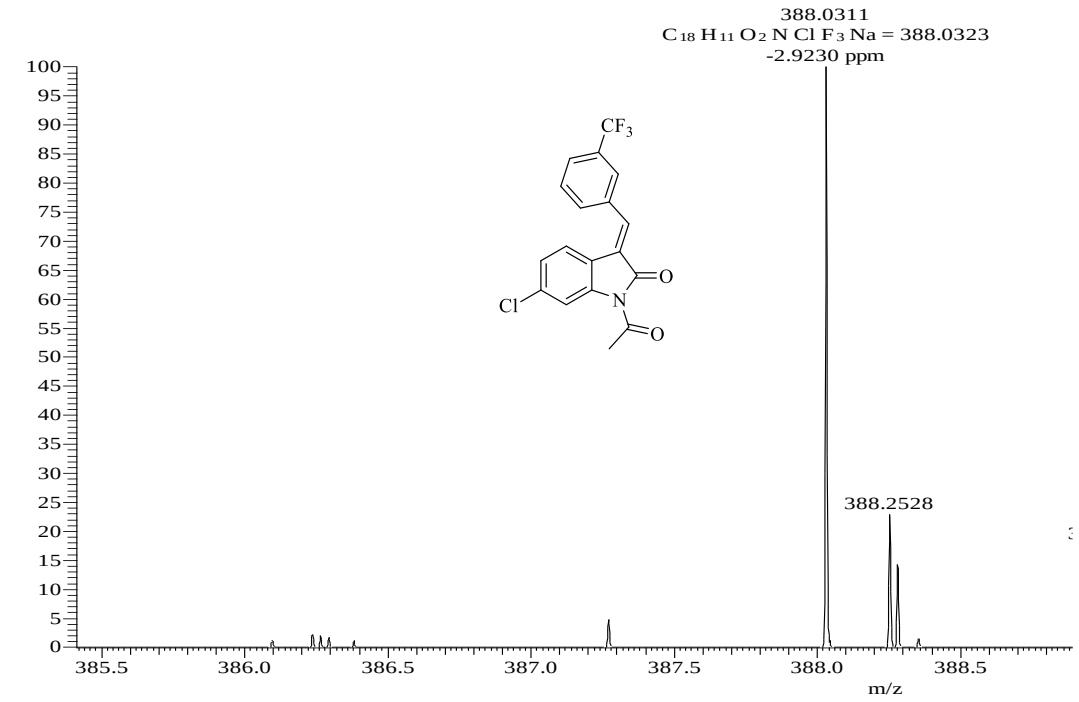


Figure S8-3. HRMS of compound **4h**

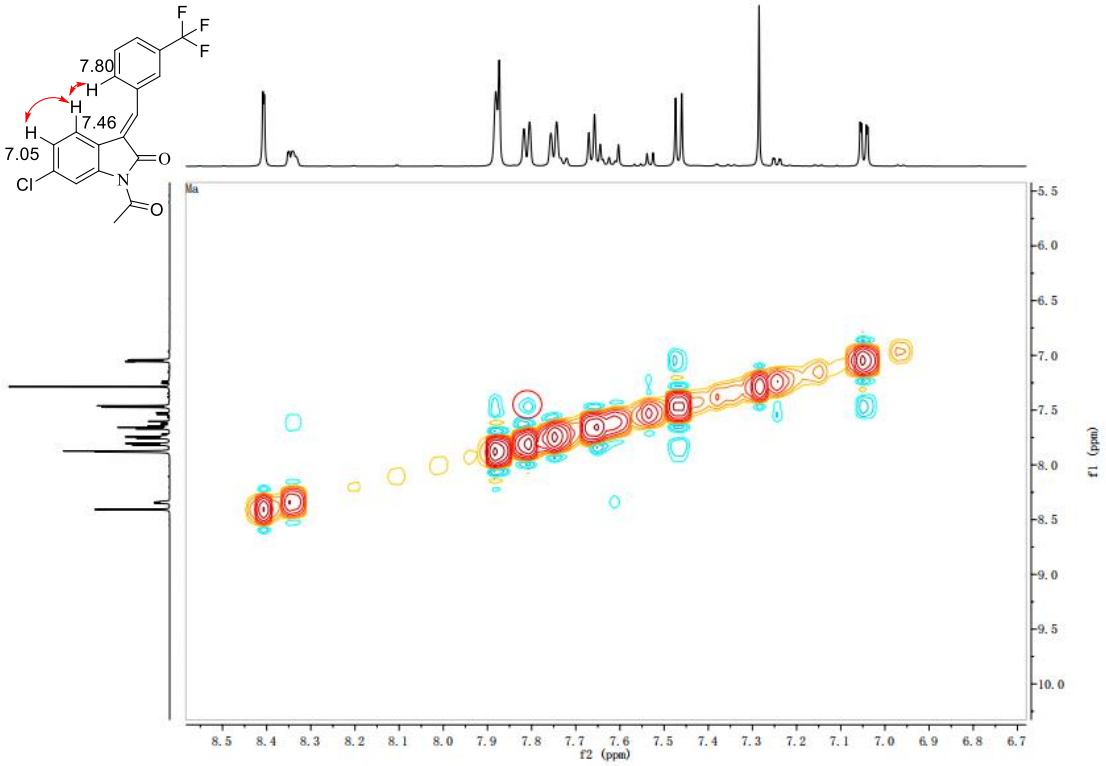


Figure S8-4. 2D-NOEY spectrum (600 Hz, $CDCl_3$) of compound **4h**

1-Acetyl-6-chloro-3-(4-(trifluoromethyl)benzylidene)indolin-2-one(4i)

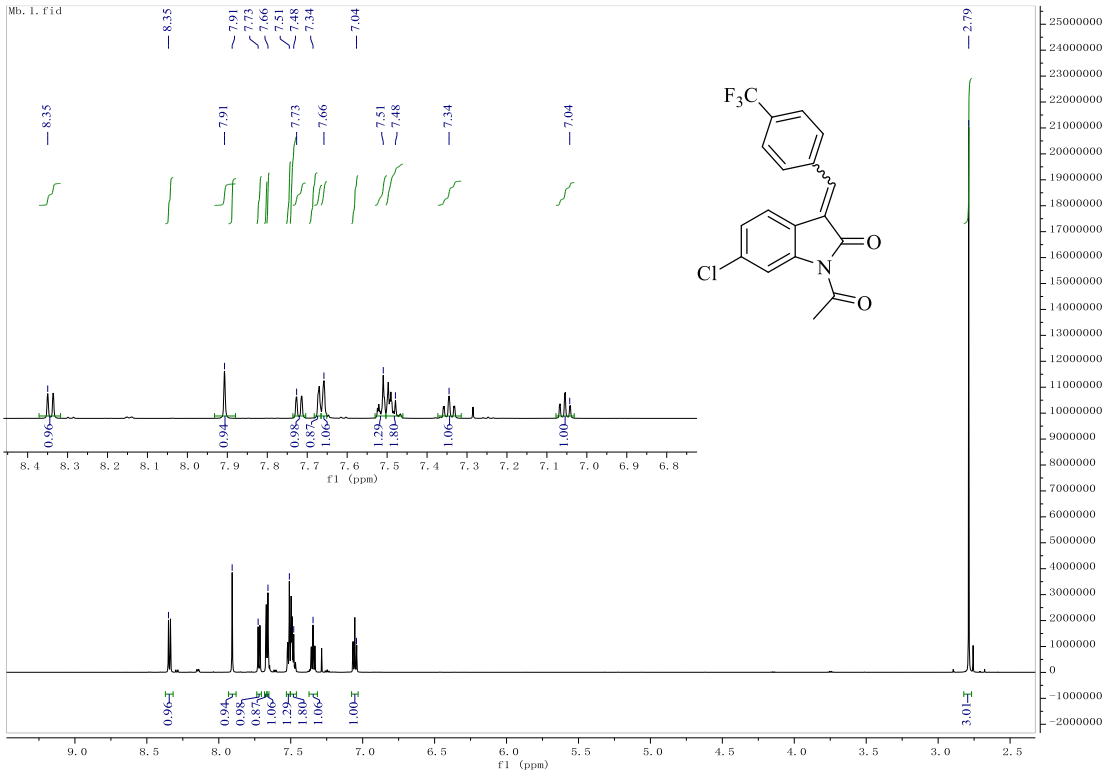


Figure S9-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4i**

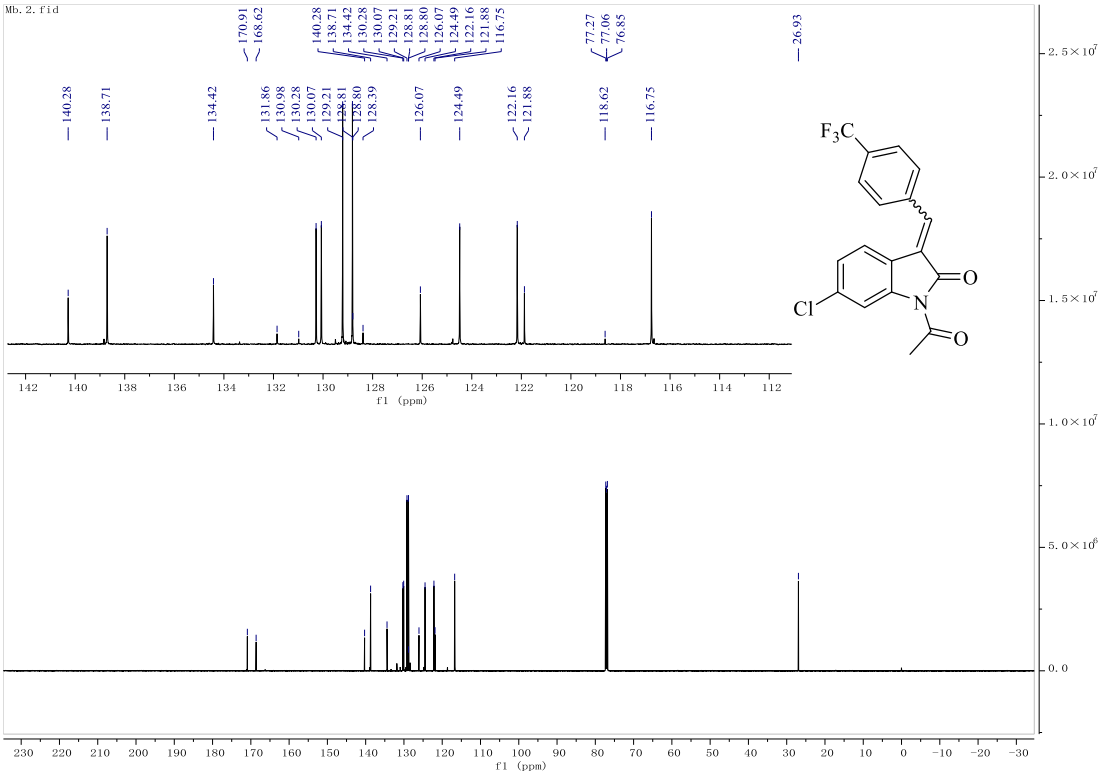


Figure S9-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4i**

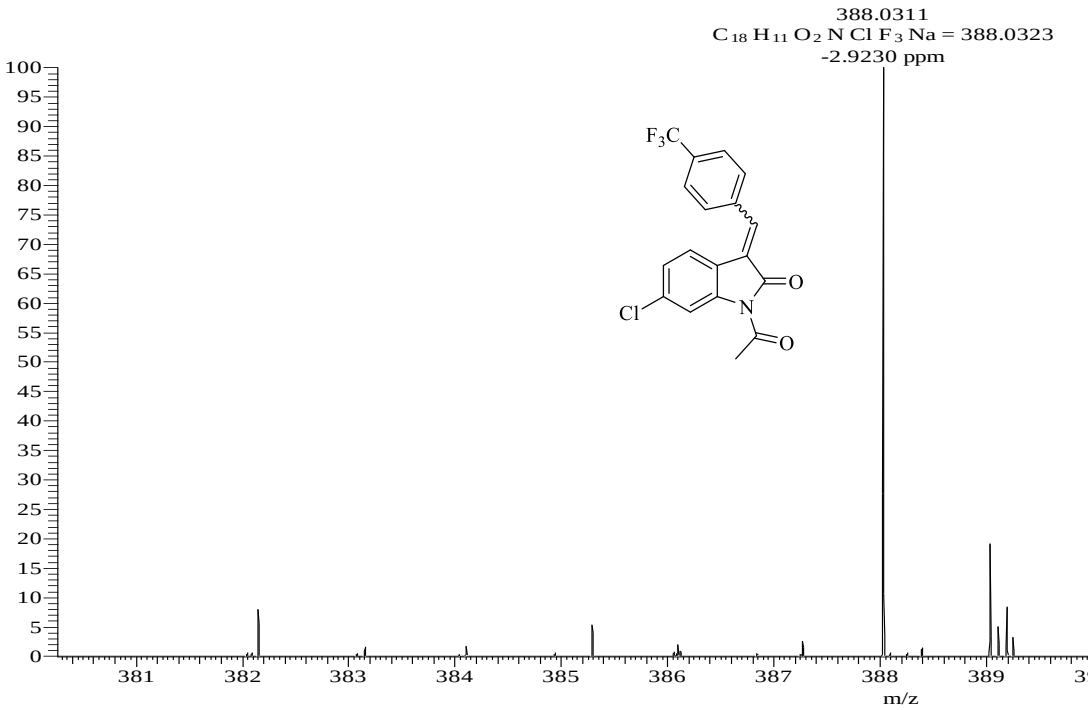


Figure S9-3. HRMS of compound **4i**

1-Acetyl-3-(3-(trifluoromethyl)benzylidene)indolin-2-one(4j)

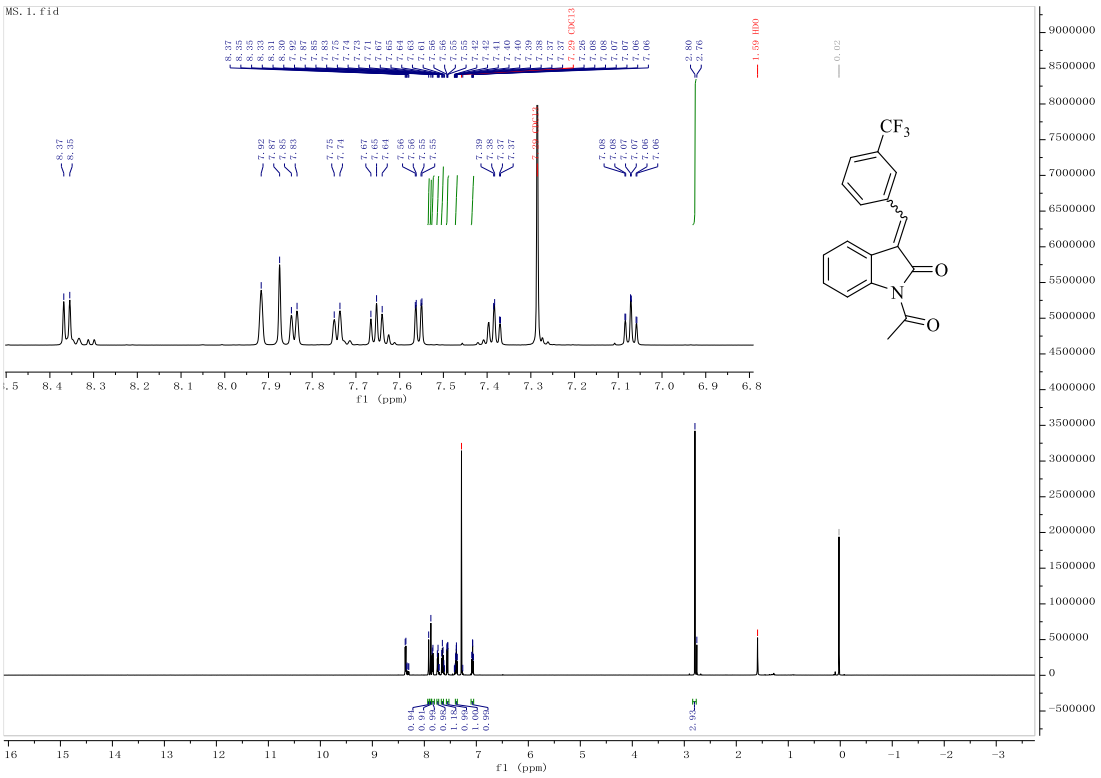


Figure S10-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4j**

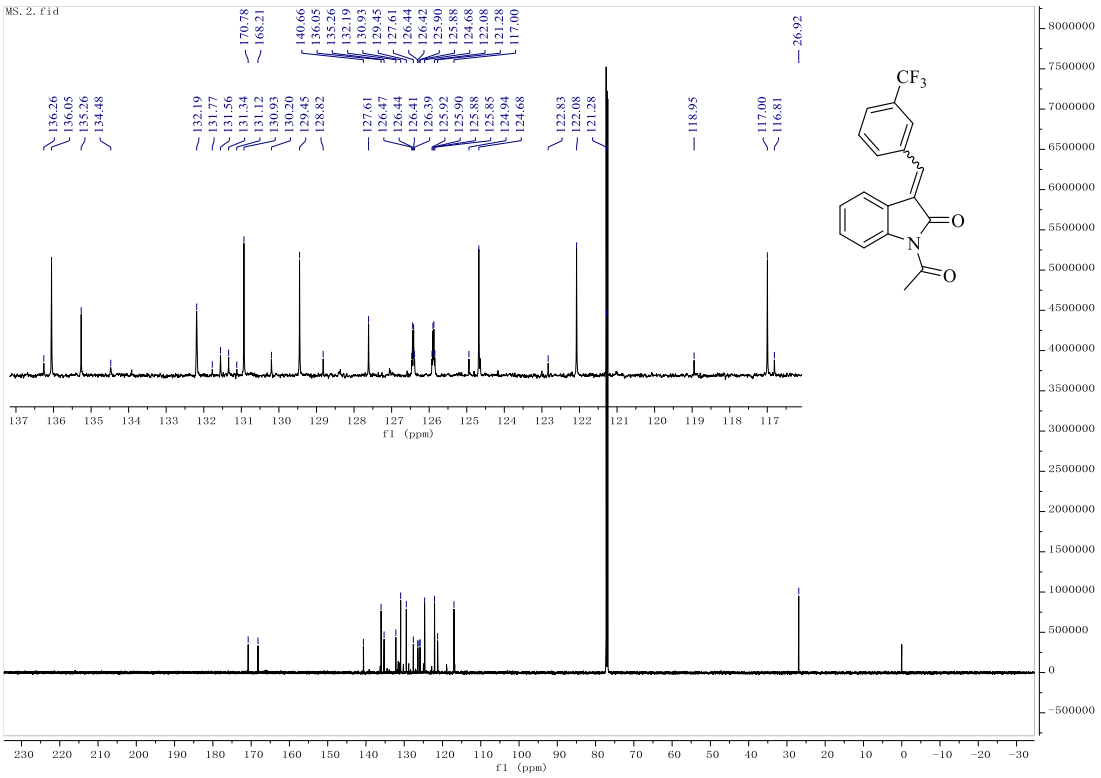


Figure S10-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4j**

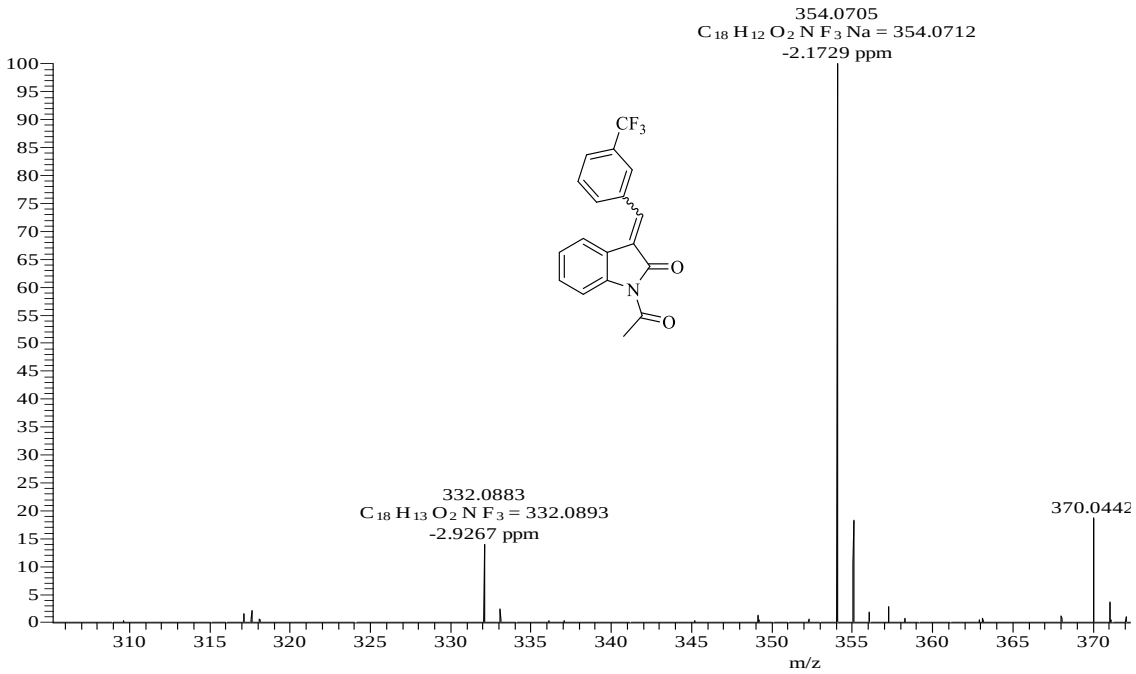


Figure S10-3. HRMS of compound **4j**

1-Acetyl-6-chloro-3-(2-(trifluoromethyl)benzylidene)indolin-2-one(4k)

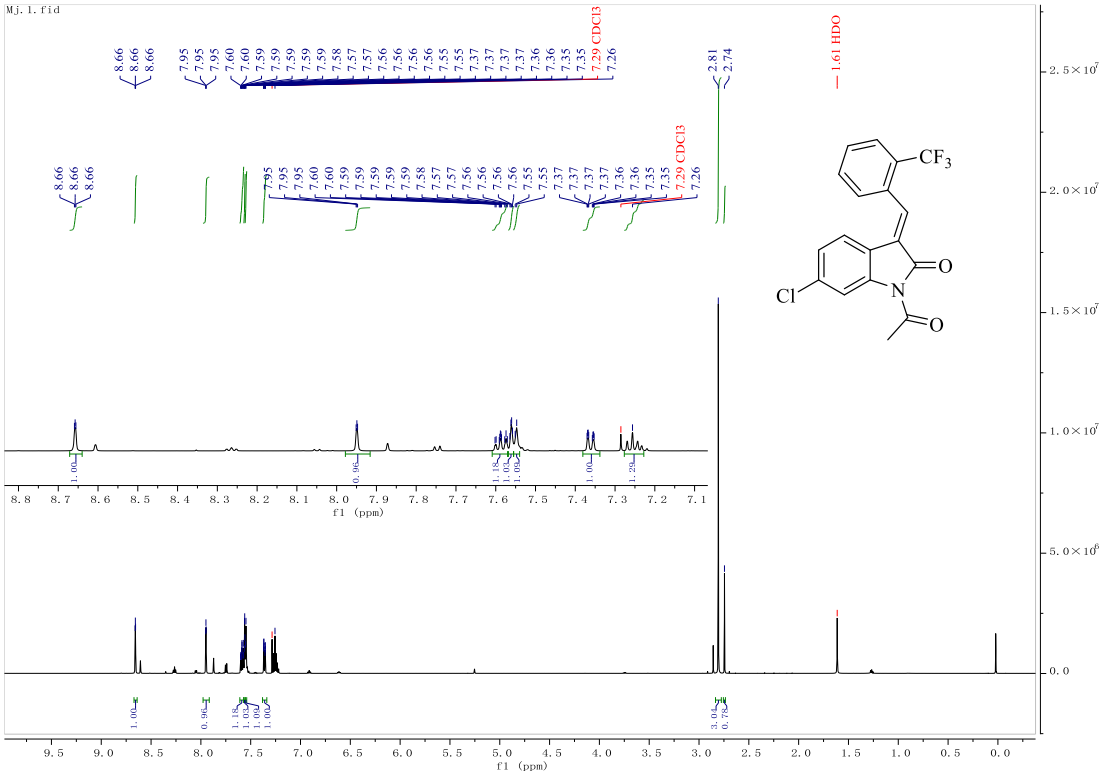


Figure S11-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **4k**

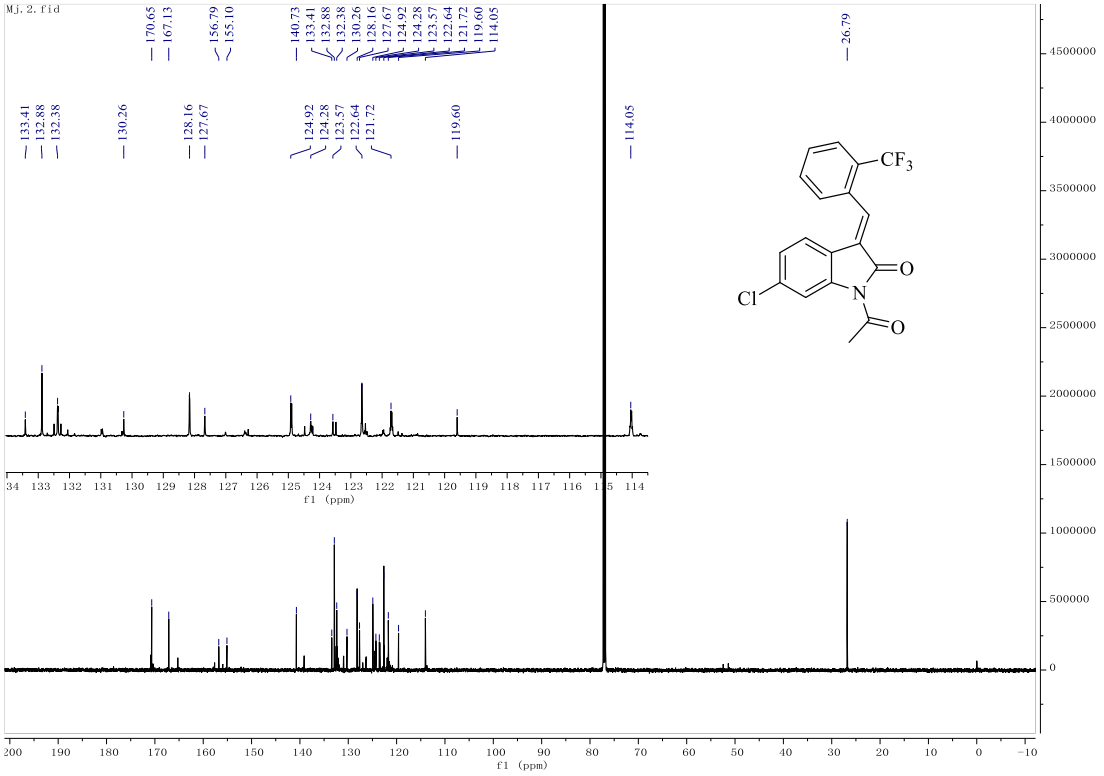


Figure S11-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4k**

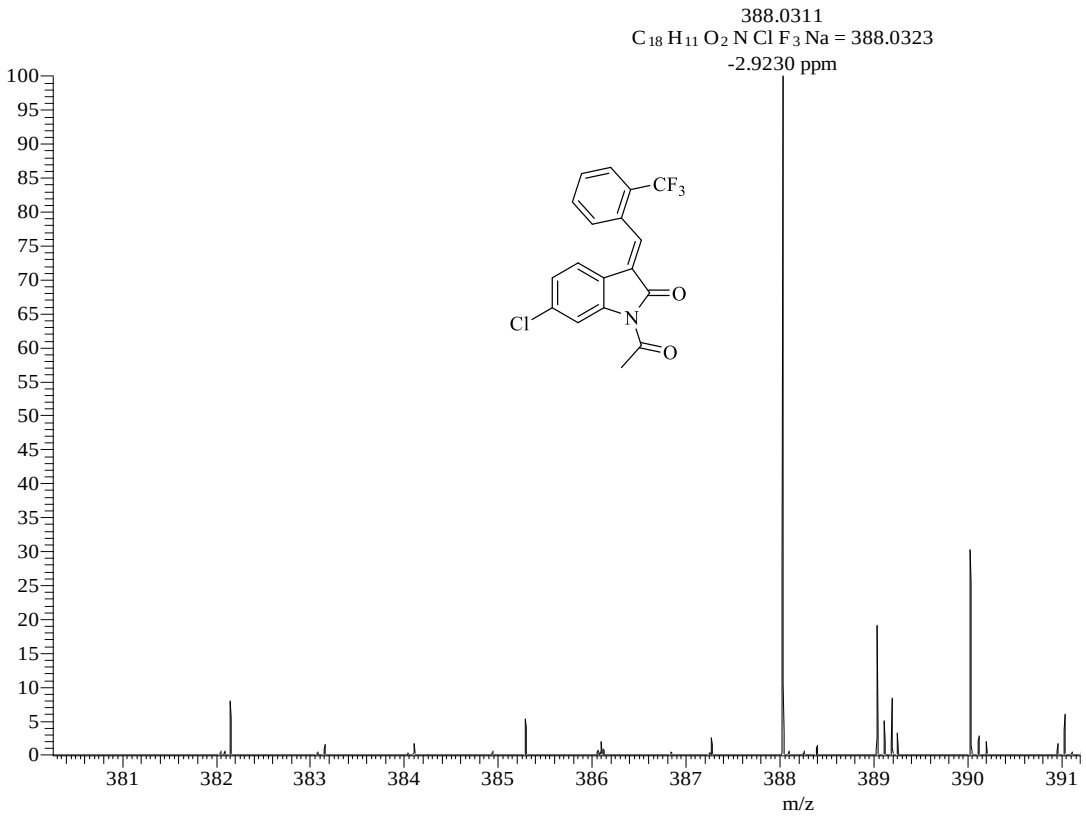


Figure S11-3. HRMS of compound **4k**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.652	BV R	0.1241	92.01453	9.92733	1.0192
2	4.589	BB	0.0961	8936.00000	1406.58325	98.9808
Totals :				9028.01453	1416.51058	

Figure S11-4. HPLC of compound **4k**

1-Acetyl-6-chloro-3-(4-chloro-3-(trifluoromethyl)benzylidene)indolin-2-one(4l)

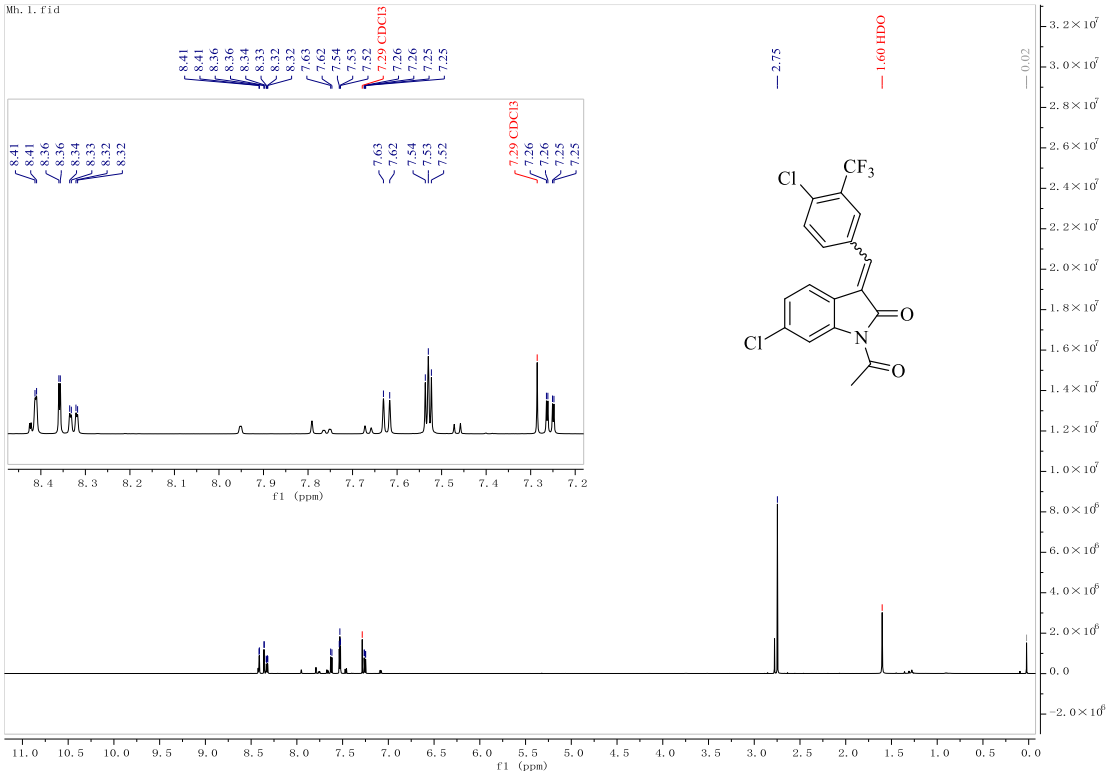


Figure S12-1. ^{1}H, NMR spectrum (600 Hz, $CDCl_3$) of compound **4l**

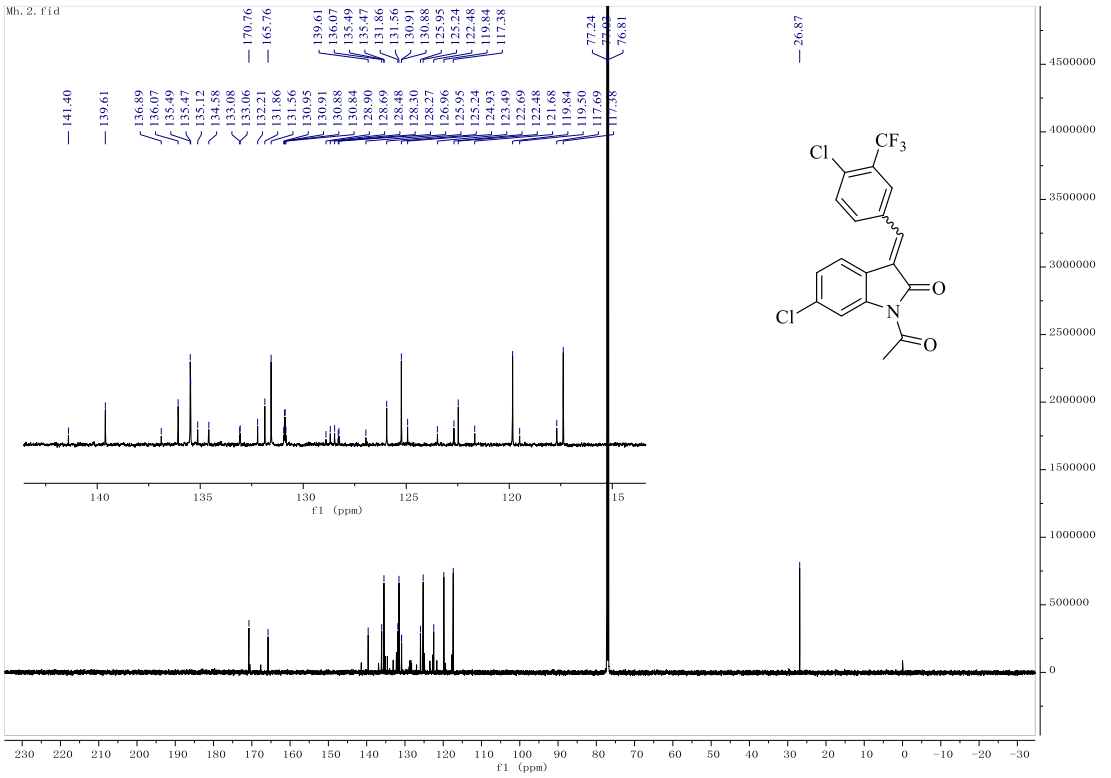


Figure S12-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **4l**

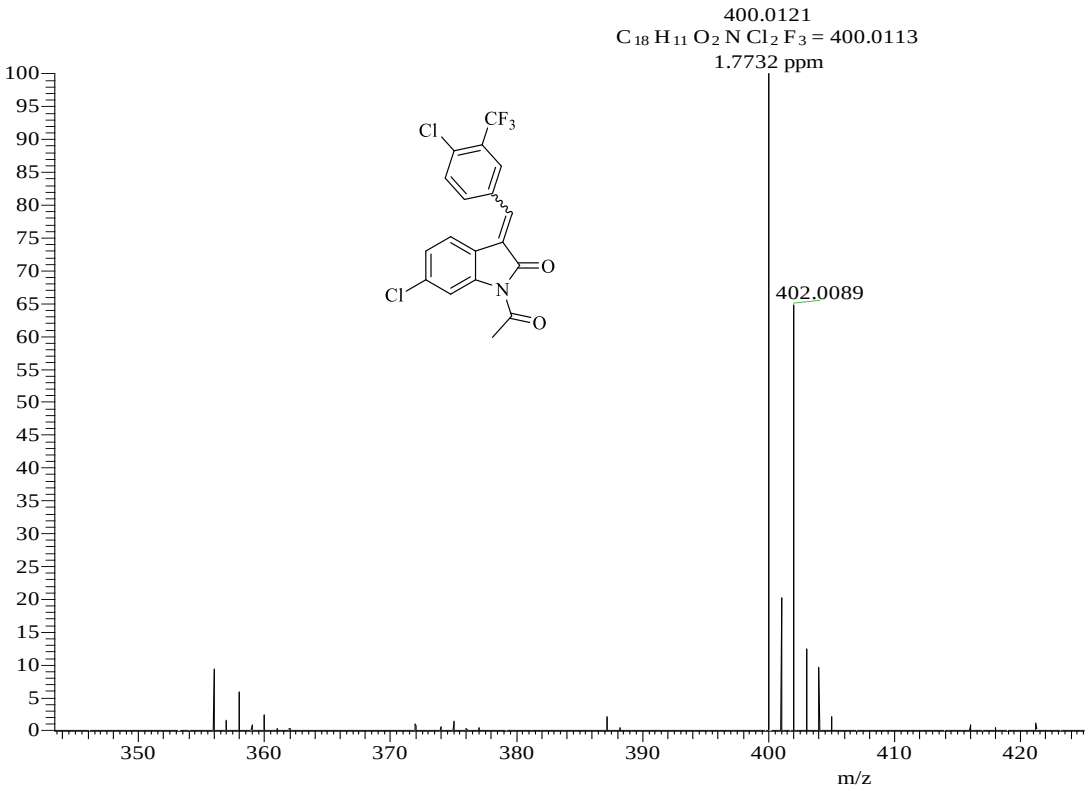
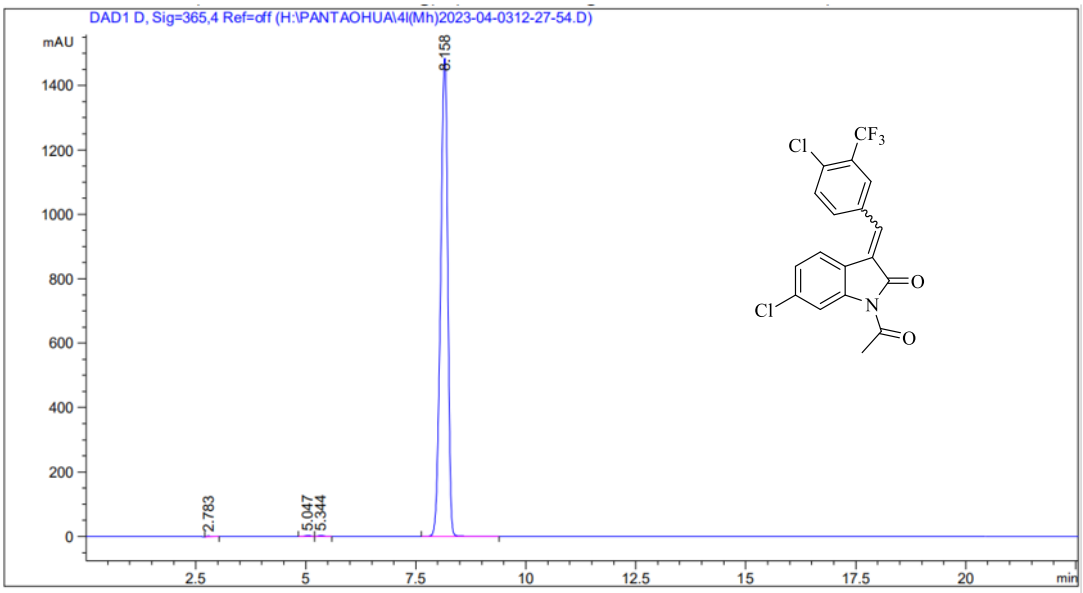


Figure S12-3. HRMS of compound **4l**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.783	BB	0.1095	12.15048	1.65704	0.0717
2	5.047	BV	0.0993	21.11228	3.27005	0.1246
3	5.344	VB	0.1065	20.82145	3.01587	0.1229
4	8.158	BB	0.1807	1.68834e4	1484.52014	99.6807

Figure S12-4. HPLC of compound **4l**

1-Acetyl-6-chloro-3-(4-chloro-3-fluorobenzylidene)indolin-2-one(4m)

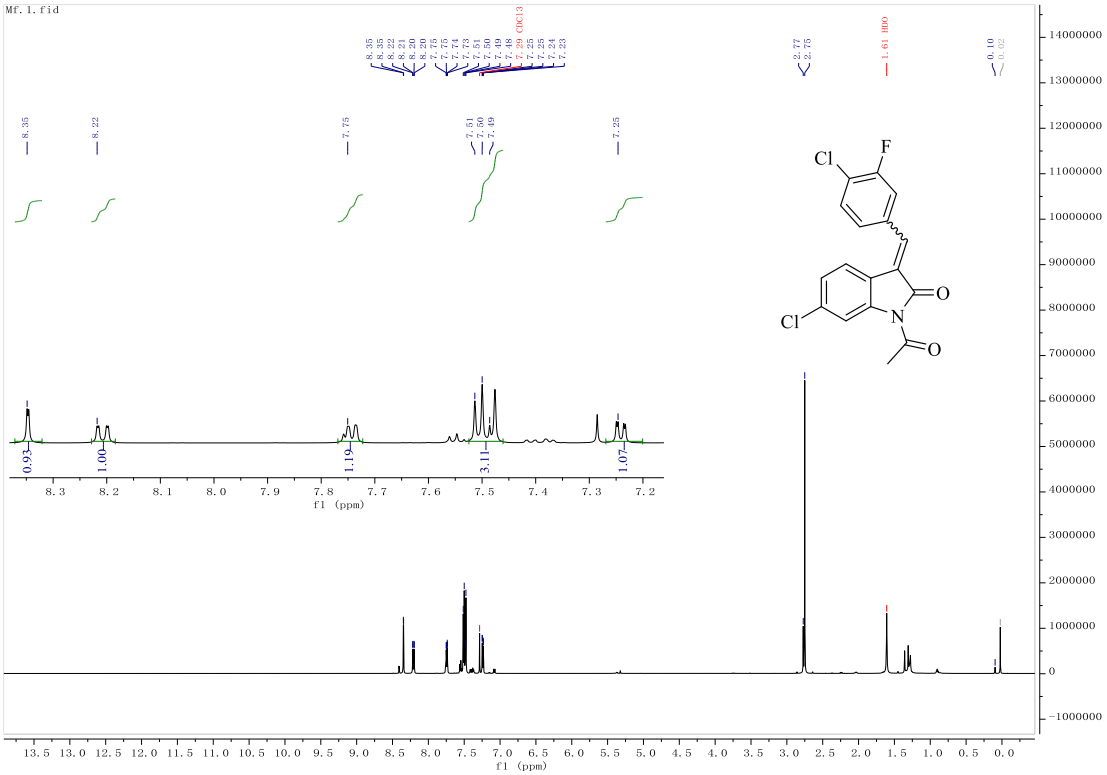


Figure S13-1. ^{1}H NMR spectrum (600 MHz $CDCl_3$) of compound **4m**

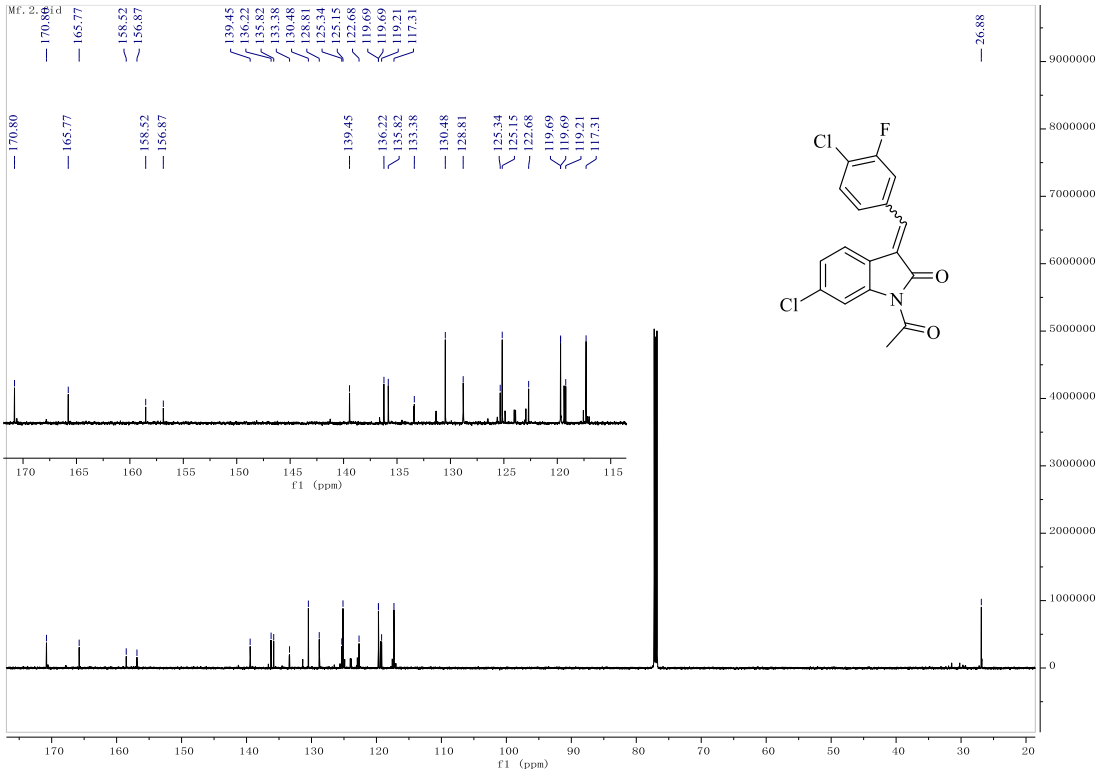


Figure S13-2. ^{13}C NMR spectrum (150 MHz $CDCl_3$) of compound **4m**

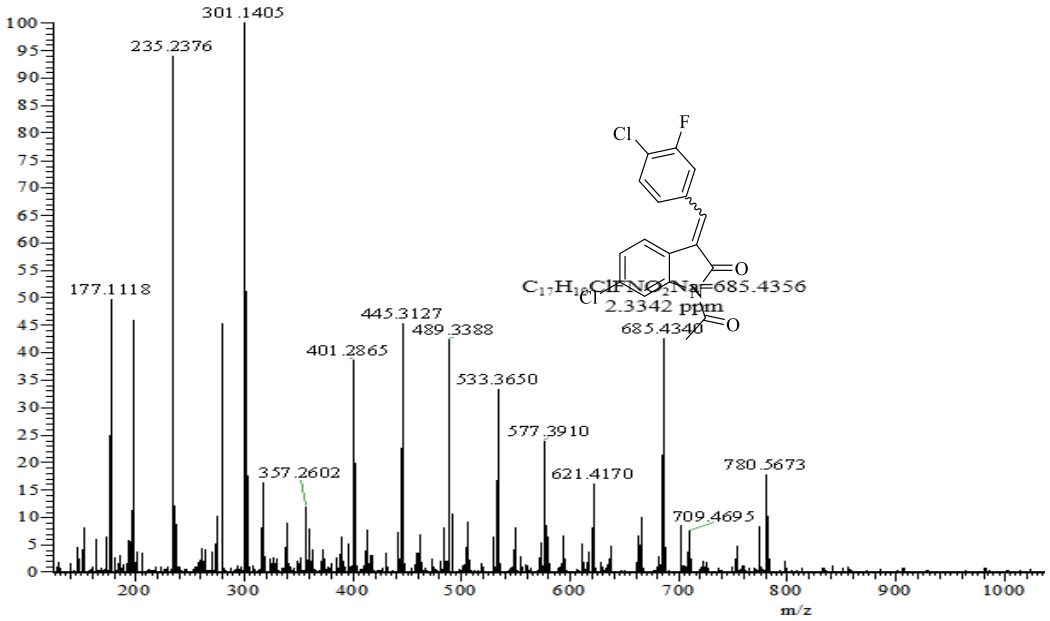


Figure S13-3. HRMS of compound **4m**

1-Acetyl-6-chloro-3-(2, 3-difluorobenzylidene)indolin-2-one(4n)

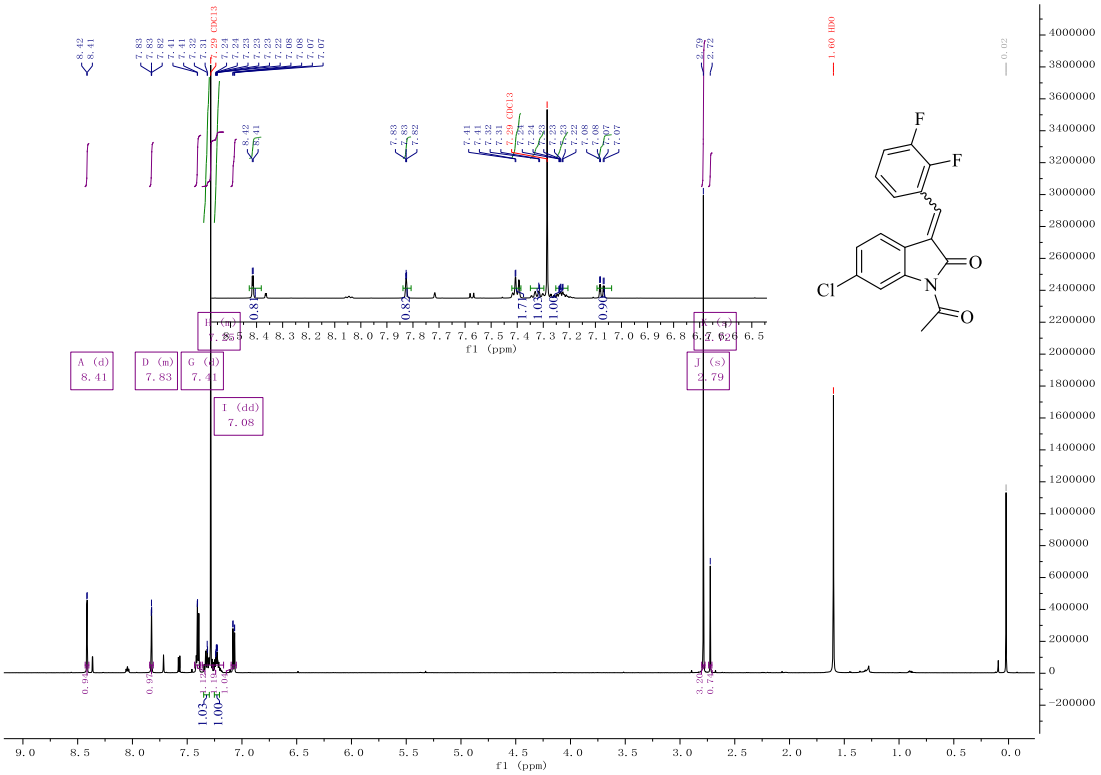


Figure S14-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4n**

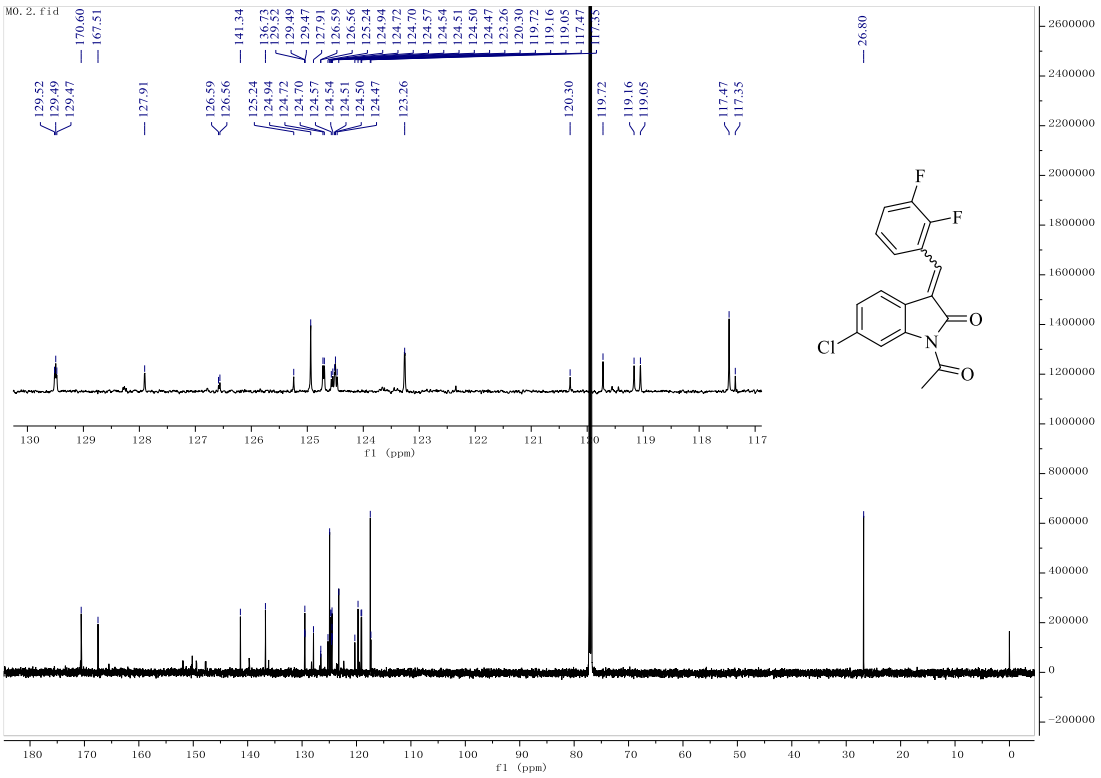


Figure S14-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4n**

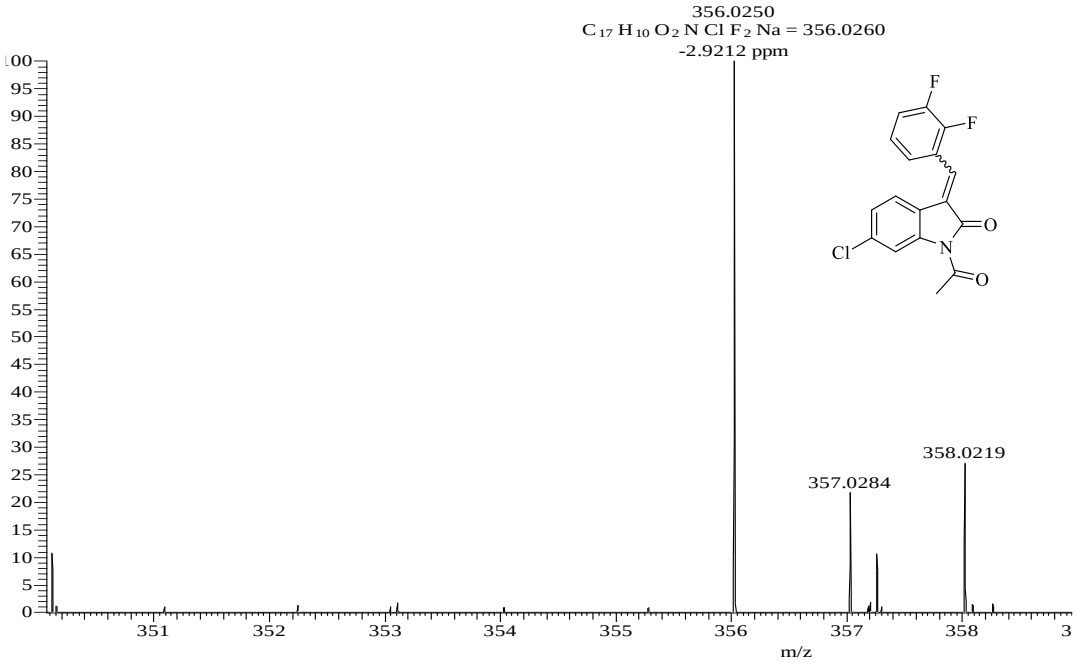


Figure S14-3. HRMS of compound **4n**

1-Acetyl-5-chloro-3-(3-chloro-2-fluorobenzylidene)indolin-2-one(4o)

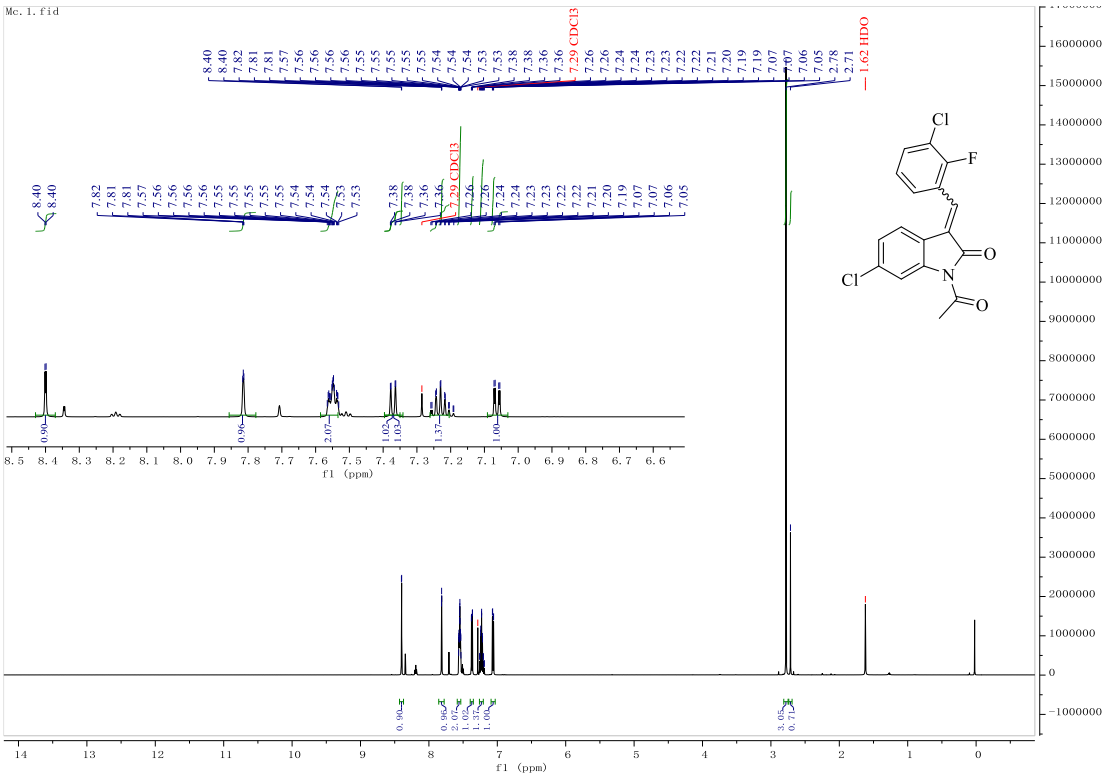


Figure S15-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4o**

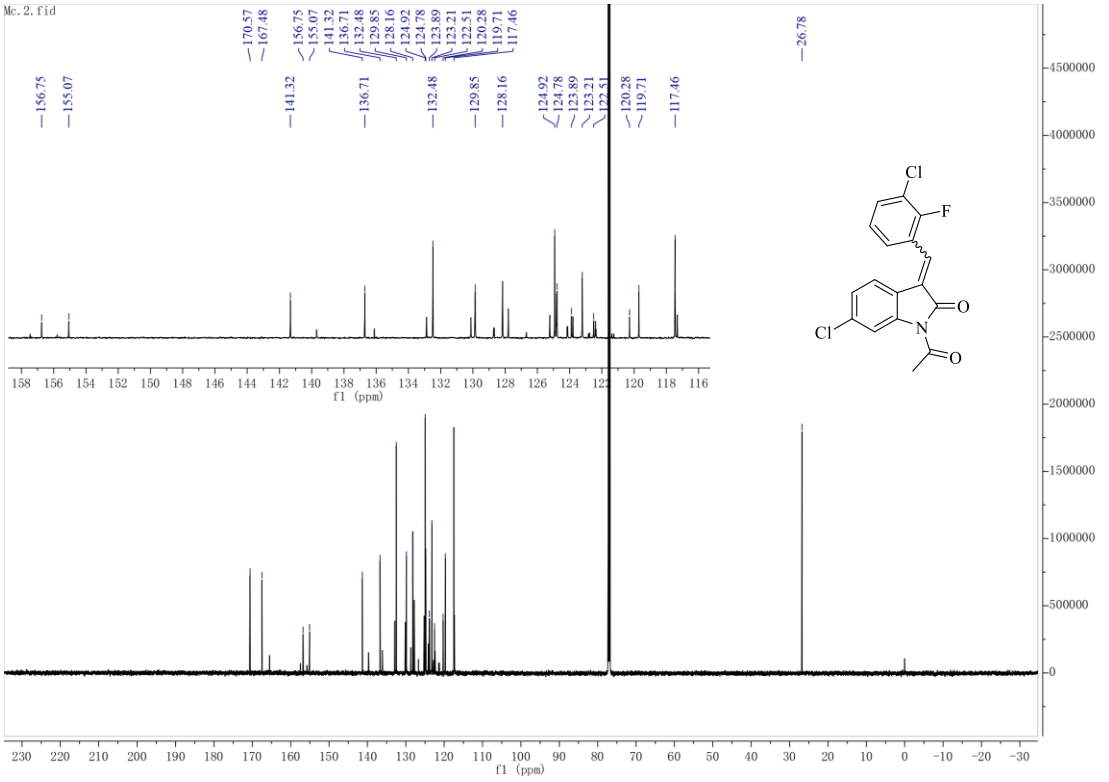


Figure S15-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4o**

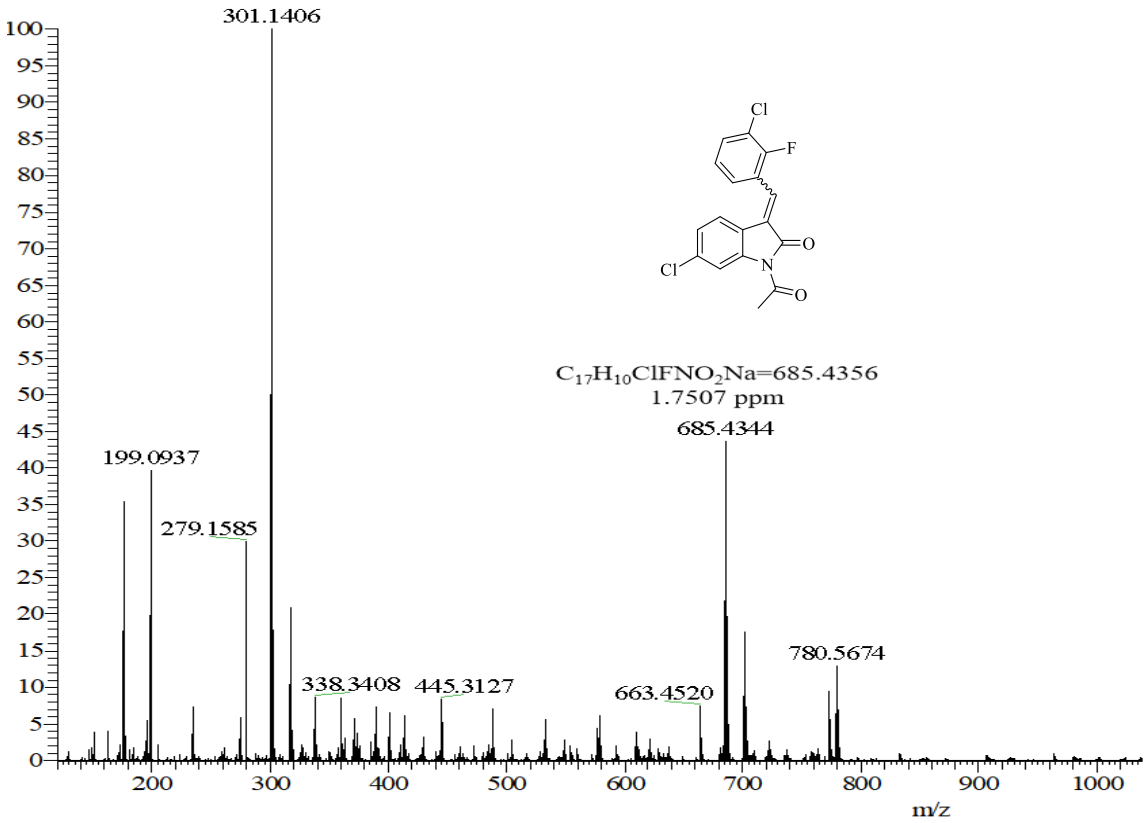


Figure S15-3. HRMS of compound **4o**

1-Acetyl-3-(3-chloro-2-fluorobenzylidene)-6-(trifluoromethyl)indolin-2-one (4p)

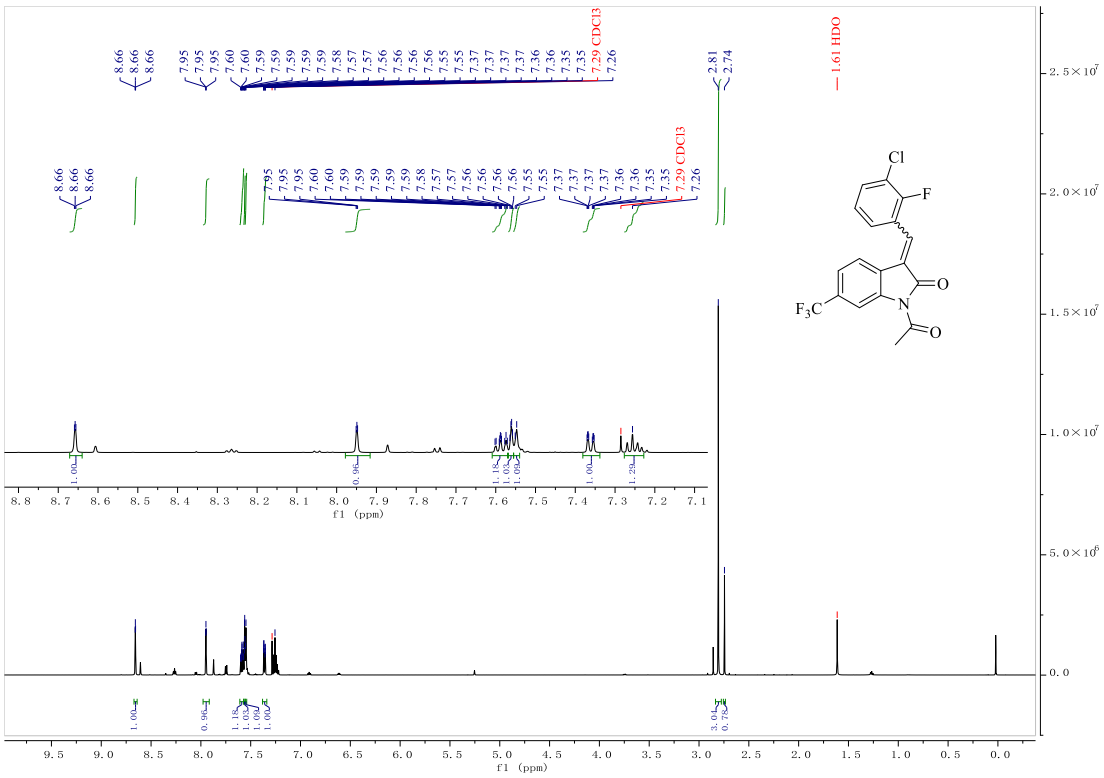


Figure S16-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4p**

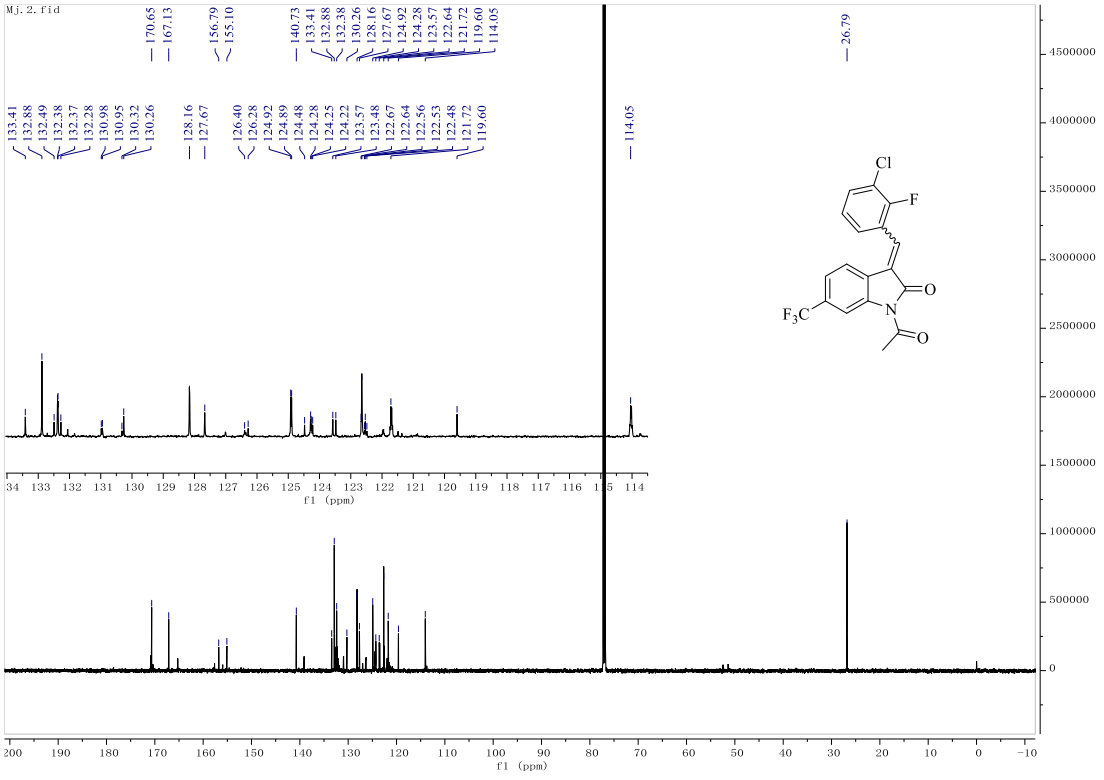


Figure S16-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4p**

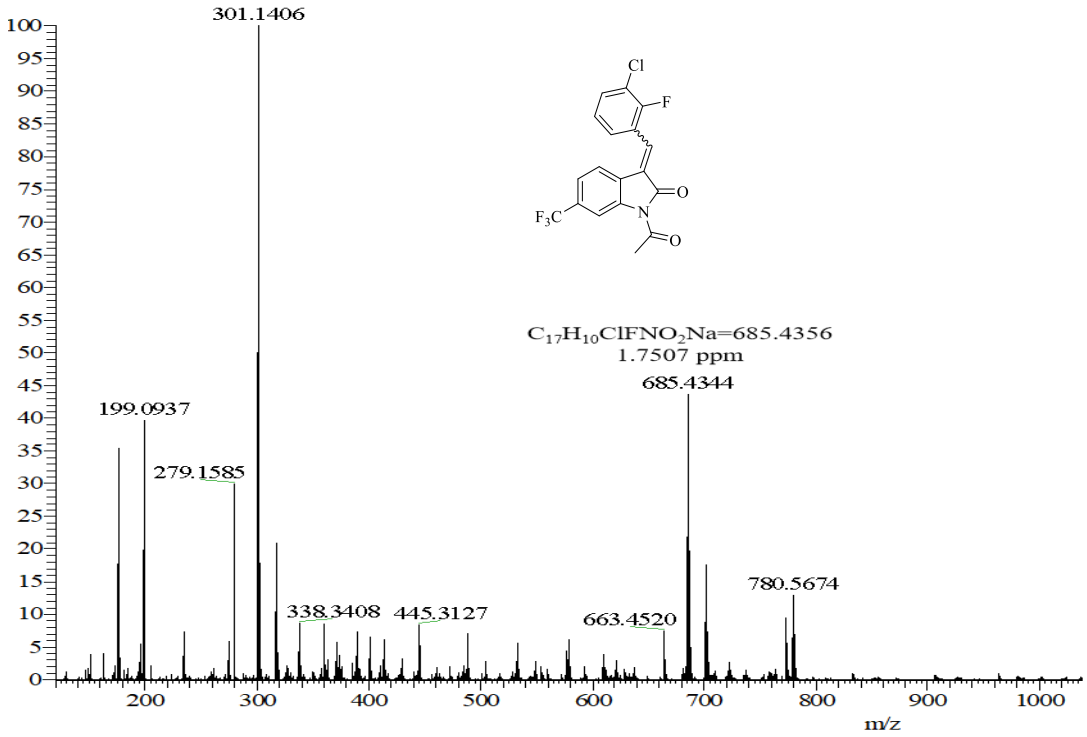


Figure S16-3. HRMS of compound **4p**

1-Acetyl-6-chloro-3-(3-chloro-2-fluorobenzylidene)indolin-2-one(4q)

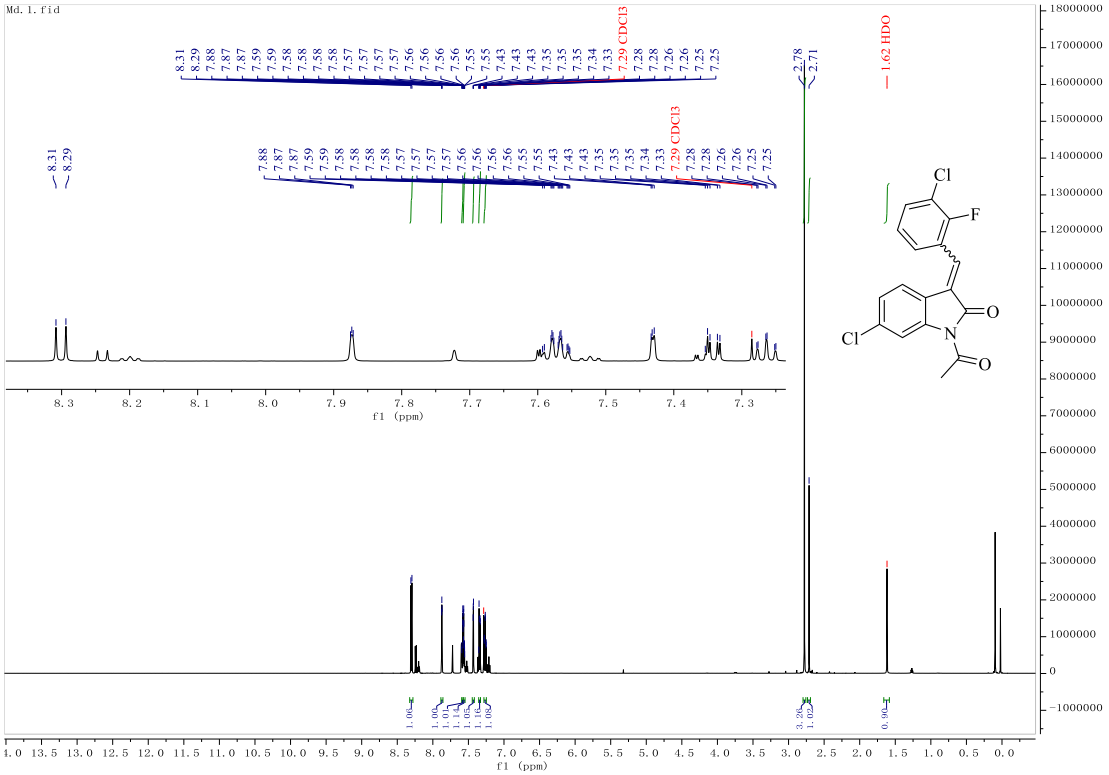


Figure S17-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4q**

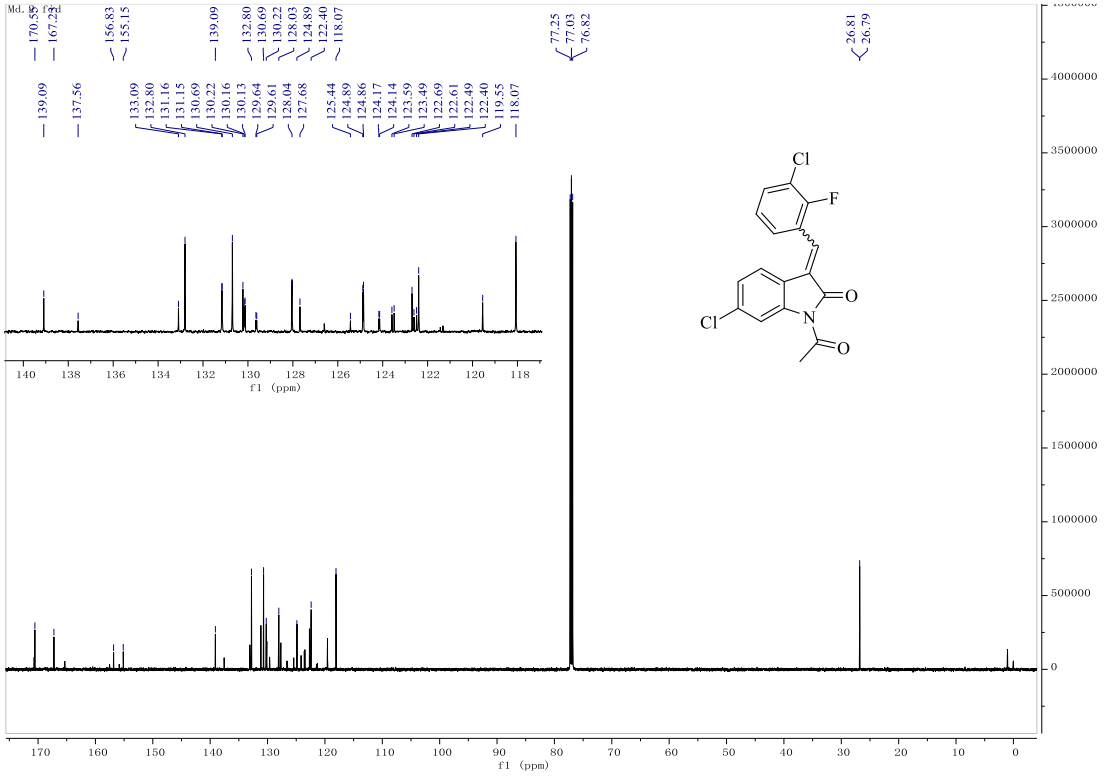


Figure S17-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4q**

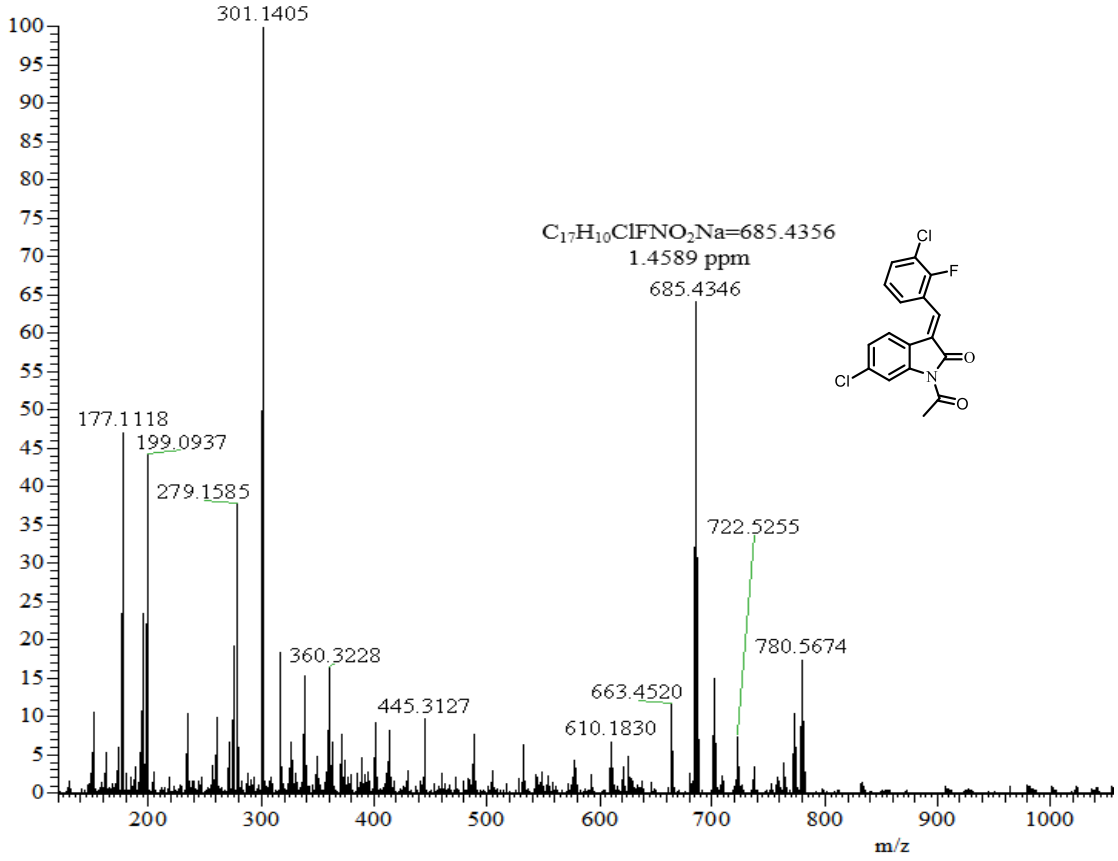


Figure S17-3. HRMS of compound **4q**

1-Acetyl-6-chloro-3-(3-methoxy-5-(trifluoromethyl)benzylidene)indolin-2-one(4r)

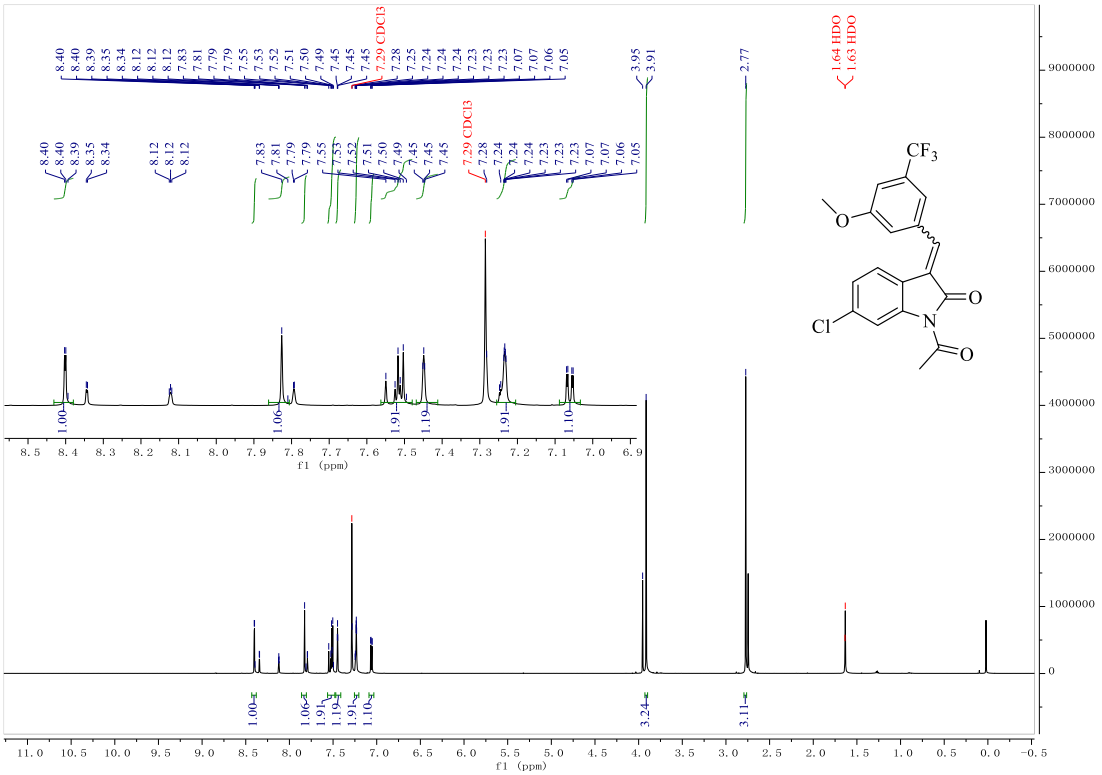


Figure S18-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4r**

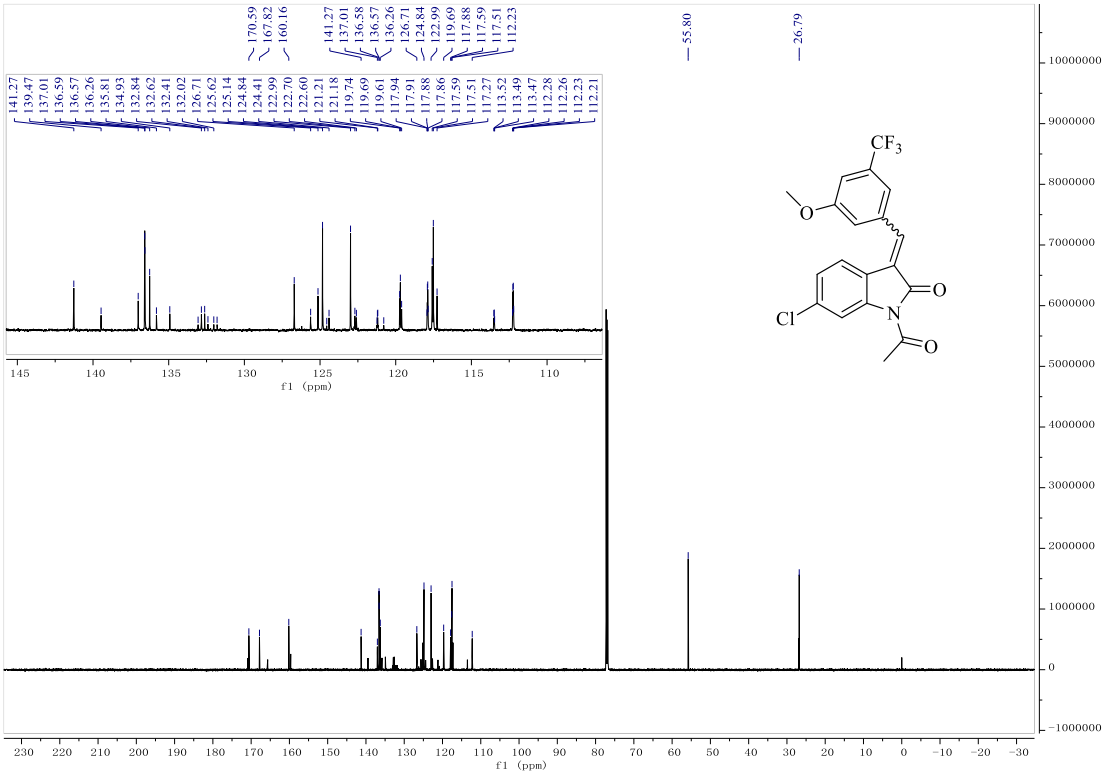


Figure S18-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4r**

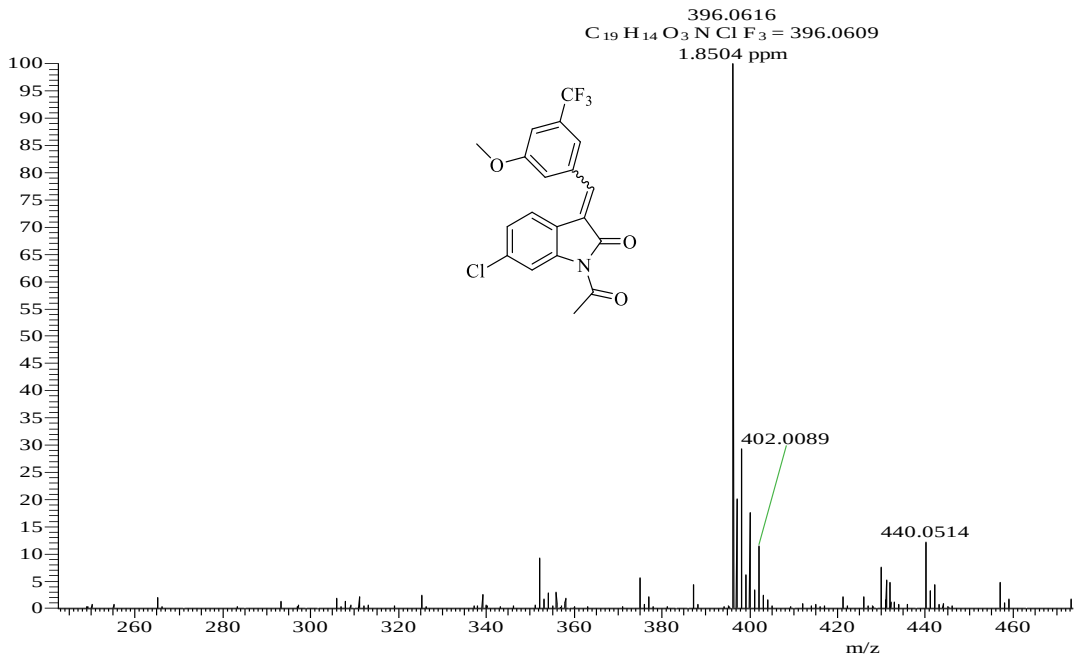


Figure S18-3. HRMS of compound **4r**

1-Acetyl-6-chloro-3-(3-methoxybenzylidene)indolin-2-one(4s)

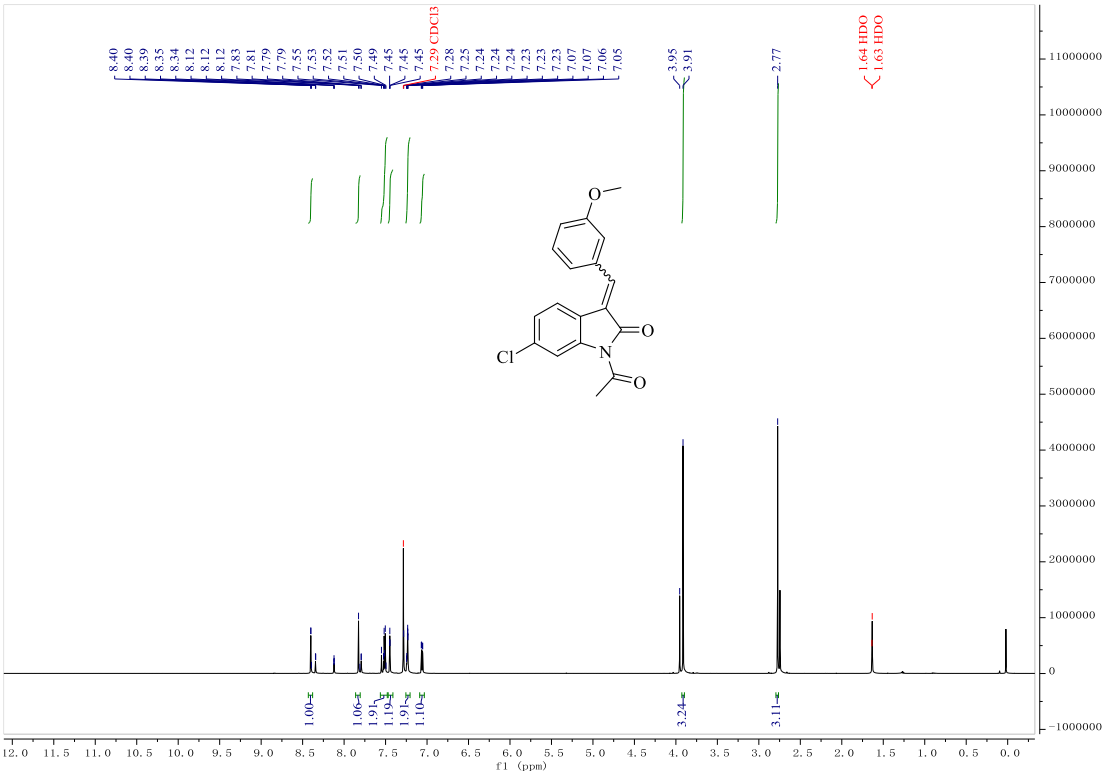


Figure S19-1. ^{1}H NMR spectrum (600 MHz, 150 MHz, $CDCl_3$) of compound **4s**

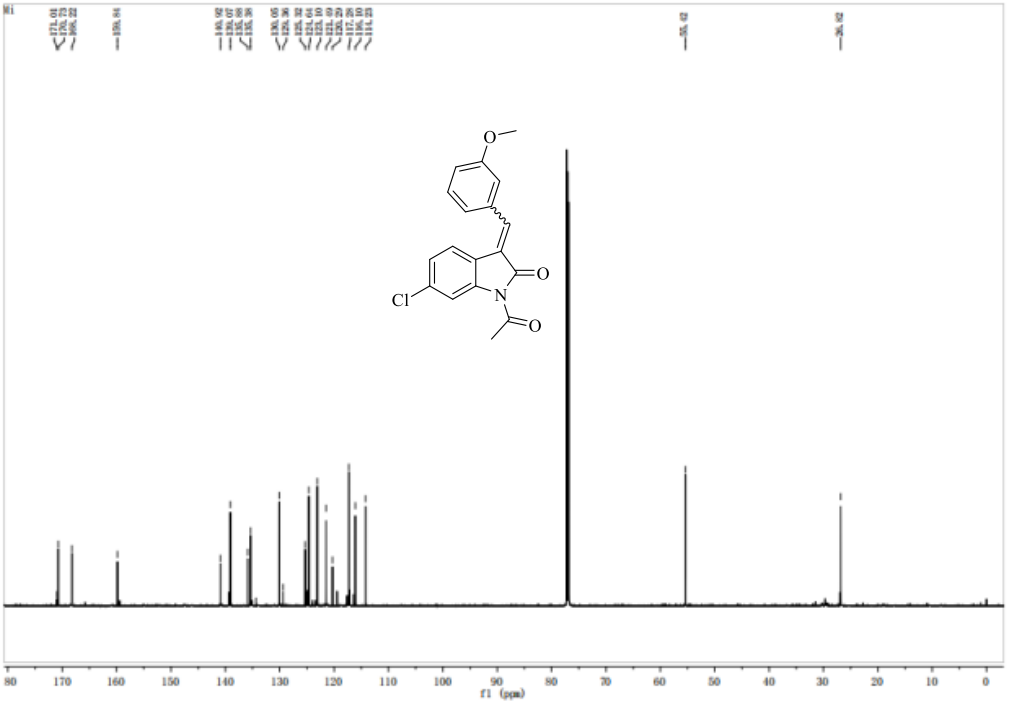


Figure S19-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4s**

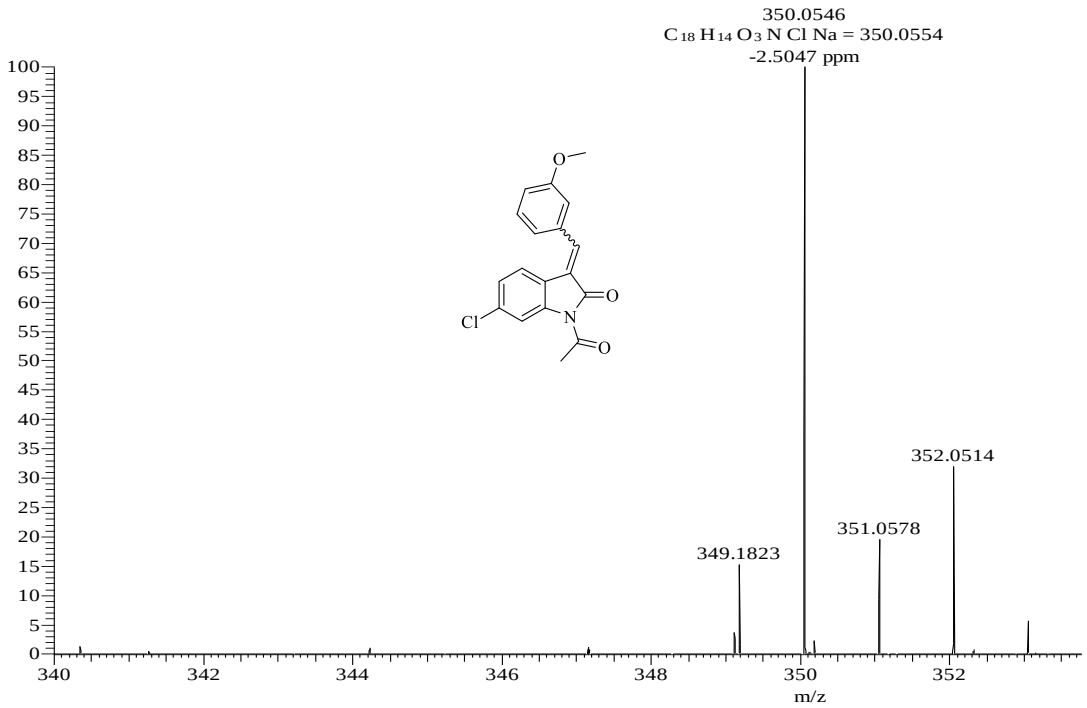


Figure S19-3. HRMS of compound **4s**

Tert-buty-6-chloro-2-oxo-3-(3-(trifluoromethyl)benzylidene)indoline-1-carboxylate(4t)

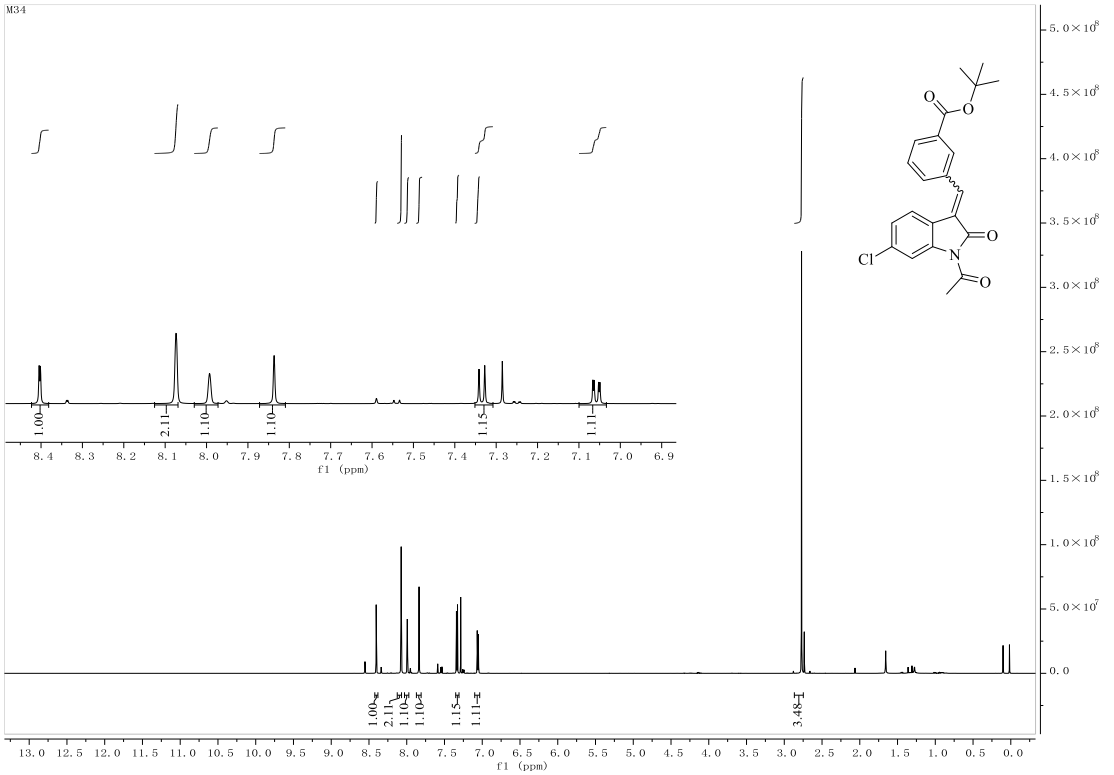


Figure S20-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4t**

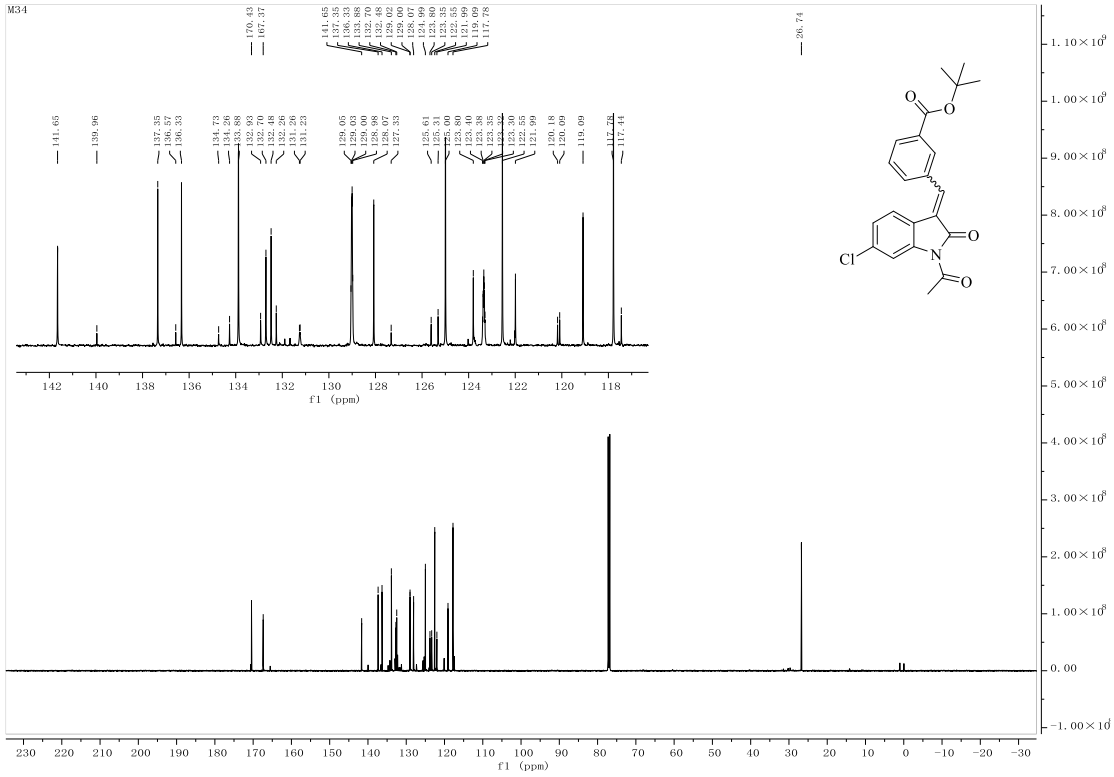


Figure S20-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4t**

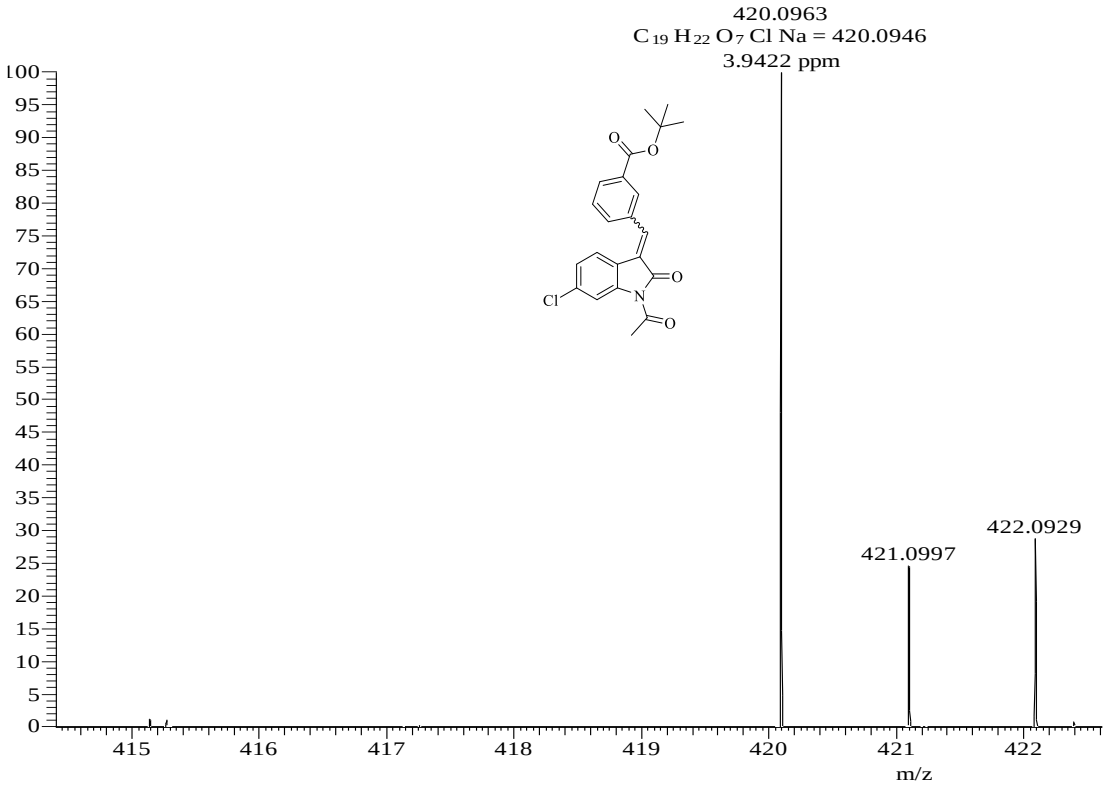


Figure S20-2. HRMS of compound **4t**

1-Acetyl-6-chloro-3-(3-(trifluoromethoxy)benzylidene)indolin-2-one(4u)

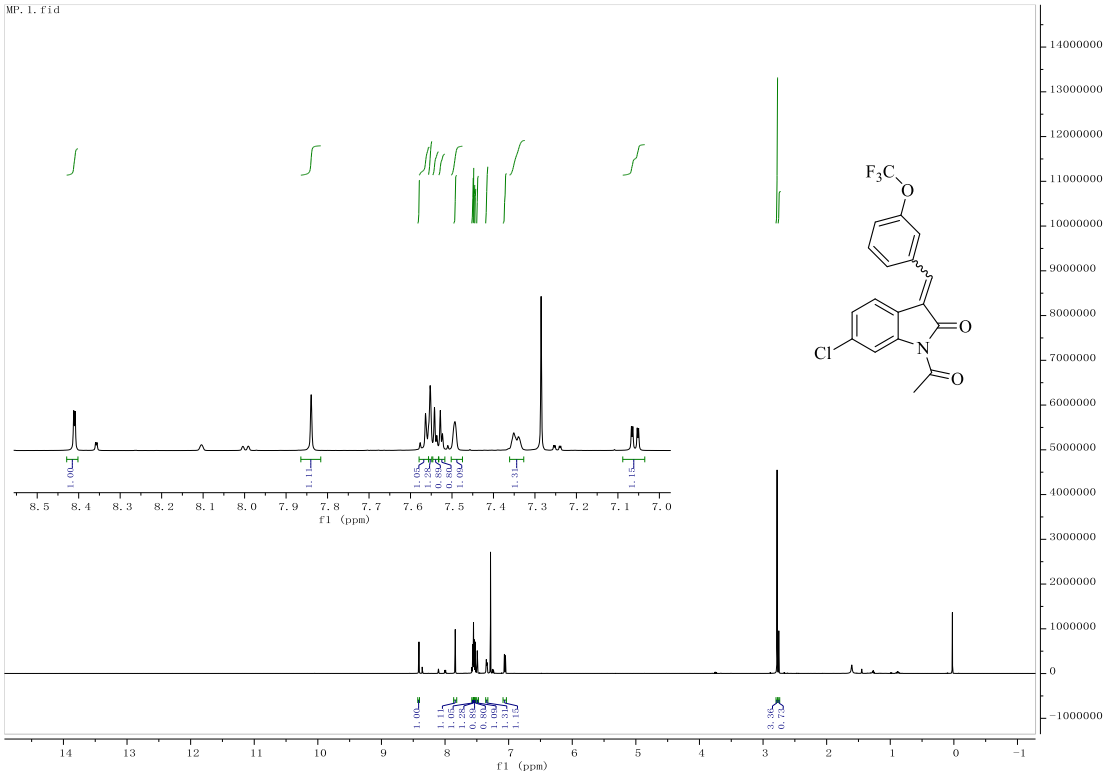


Figure S21-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4u**

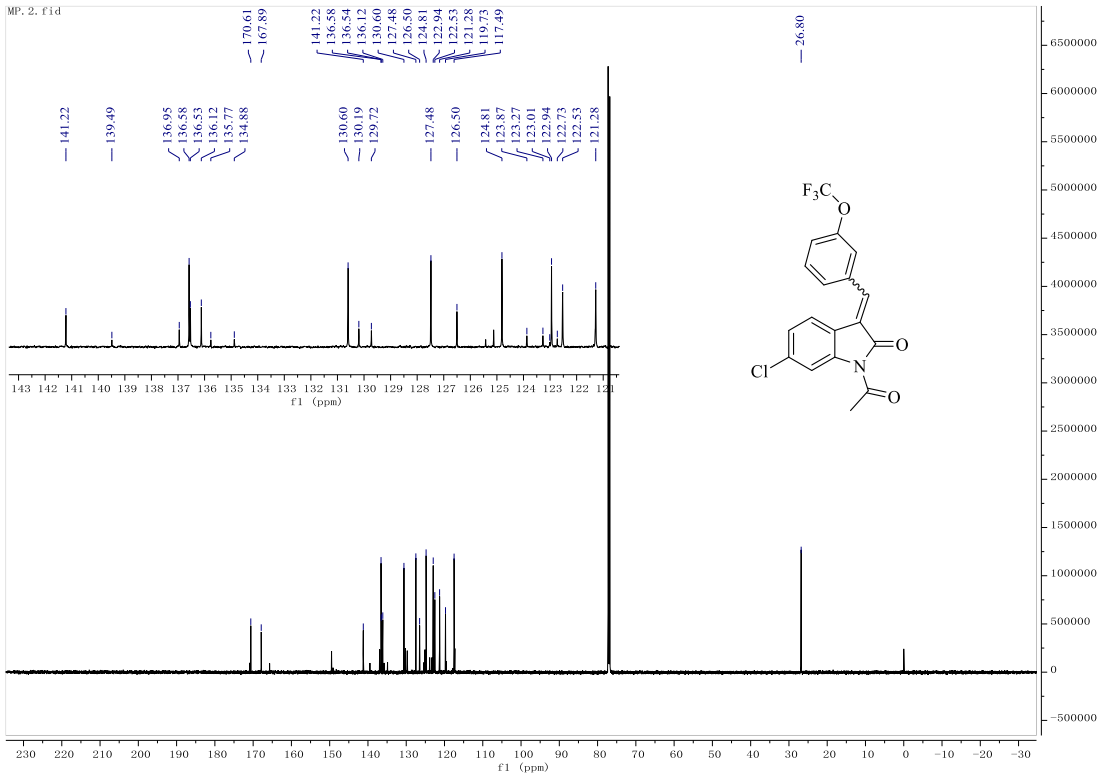


Figure S21-2. ^{13}C NMR spectrum (150 HMz, $CDCl_3$) of compound **4u**

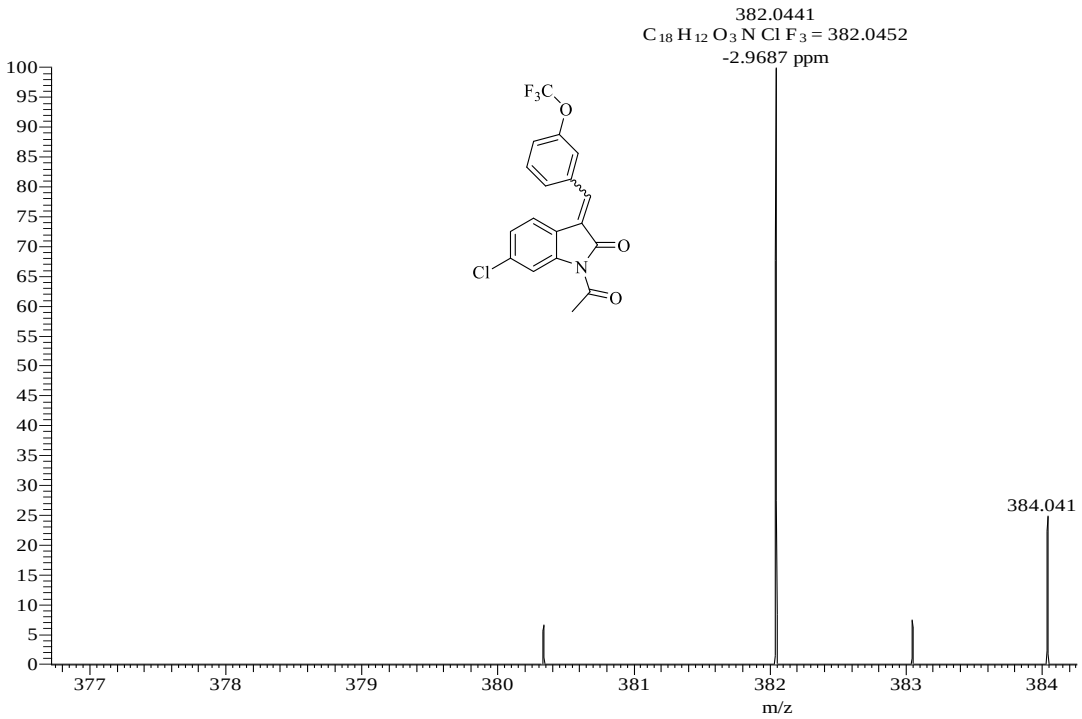


Figure S21-3. HRMS of compound **4u**

1-Acetyl-6-chloro-3-(pyridin-4-ylmethylene)indolin-2-one(4v)

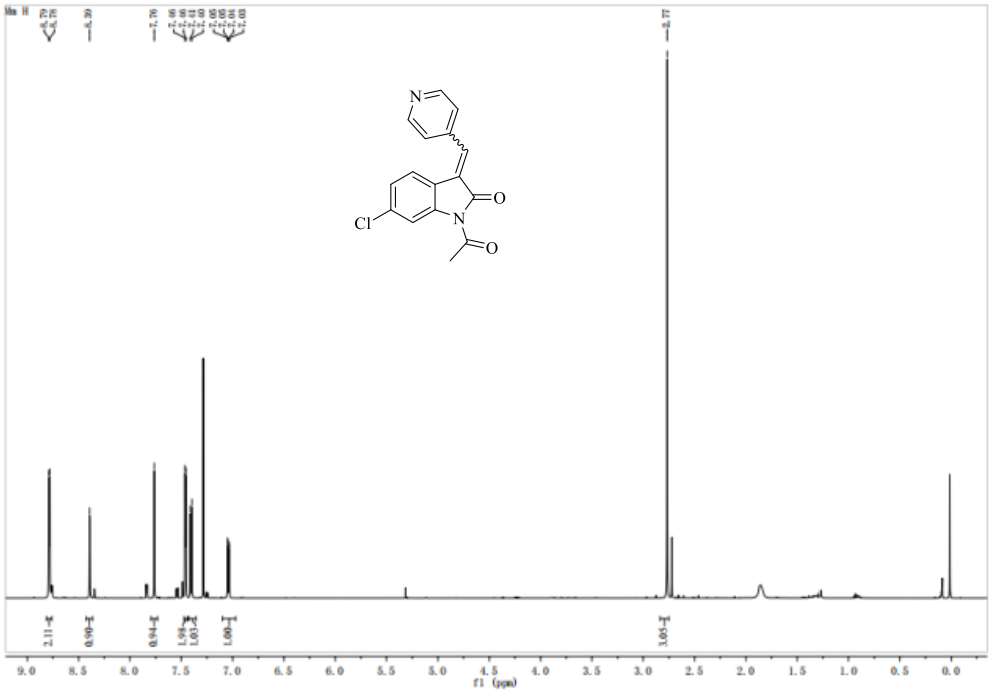


Figure S22-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4v**

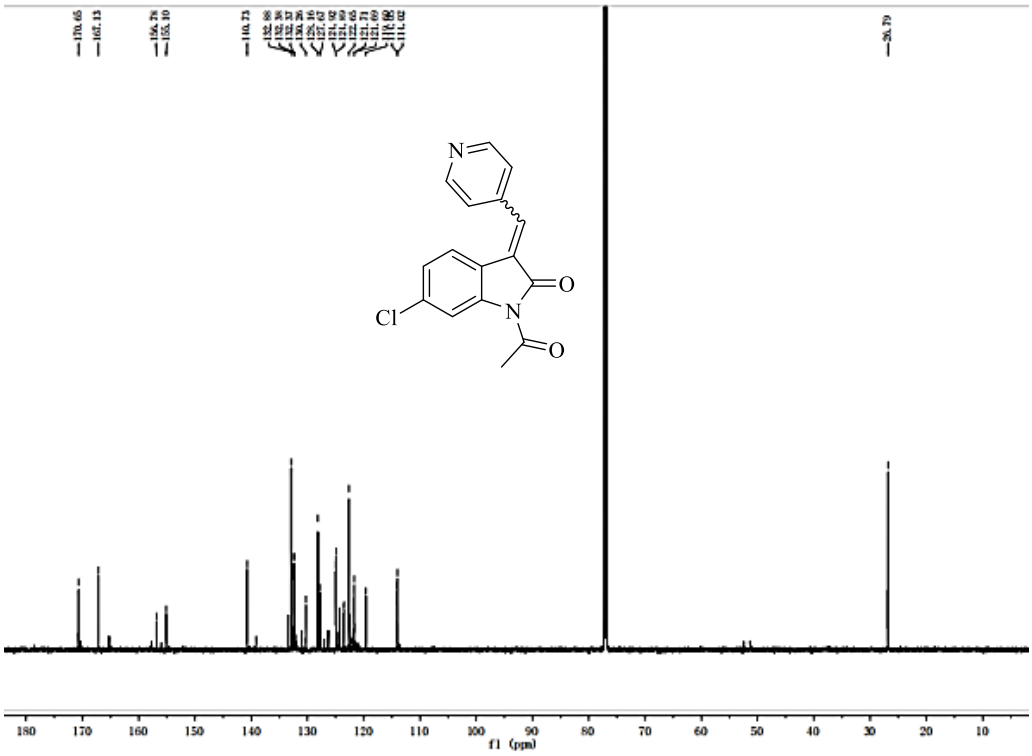


Figure S22-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4v**

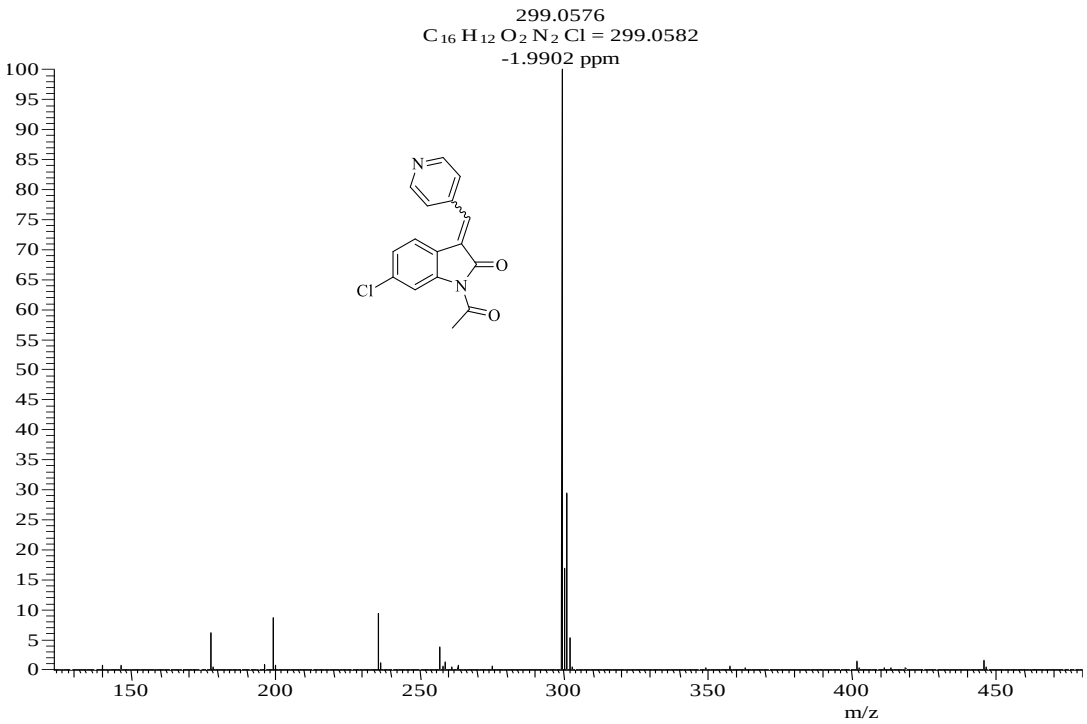


Figure S22-3. HRMS of compound **4v**

1-Acetyl-6-chloro-3-((2-(trifluoromethyl)pyridin-4-yl)methylene)indolin-2-one(4w)

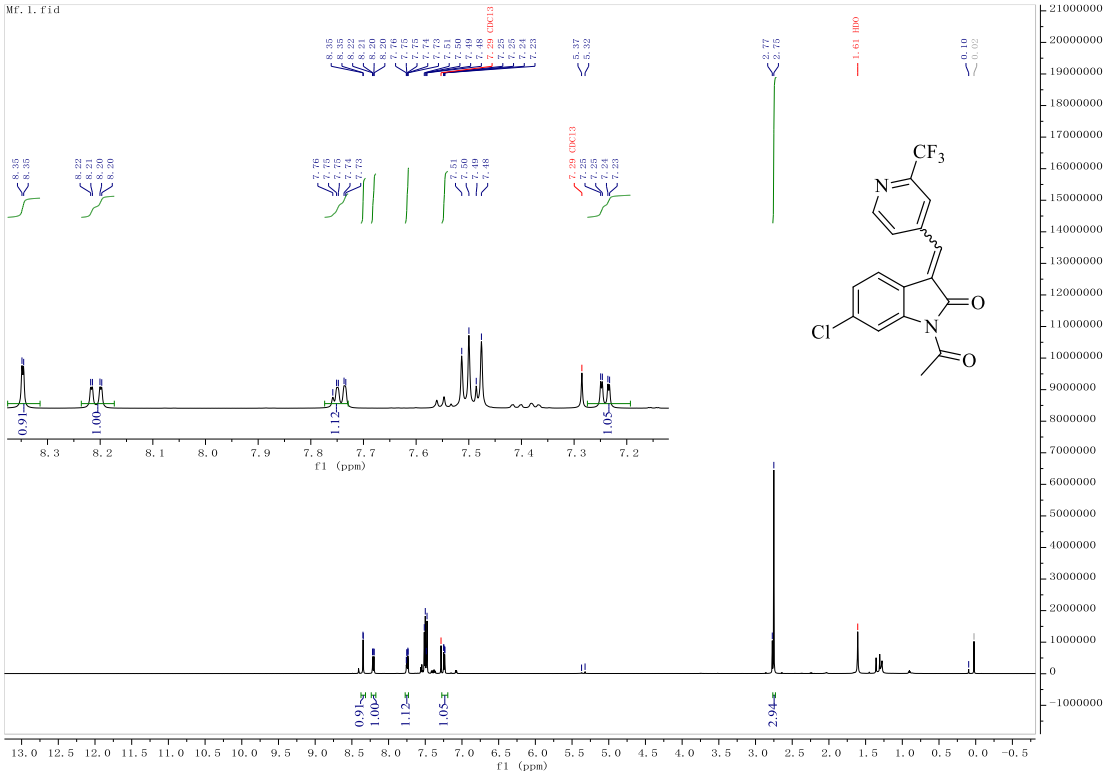


Figure S23-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4w**

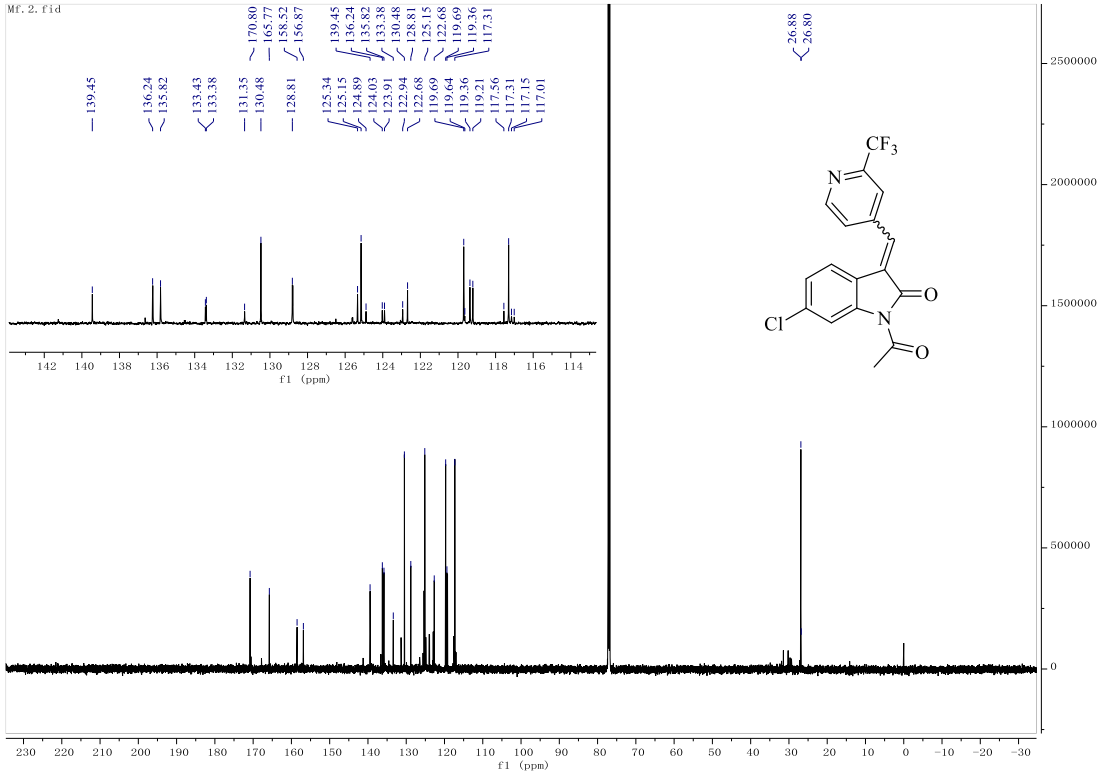


Figure S23-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4w**

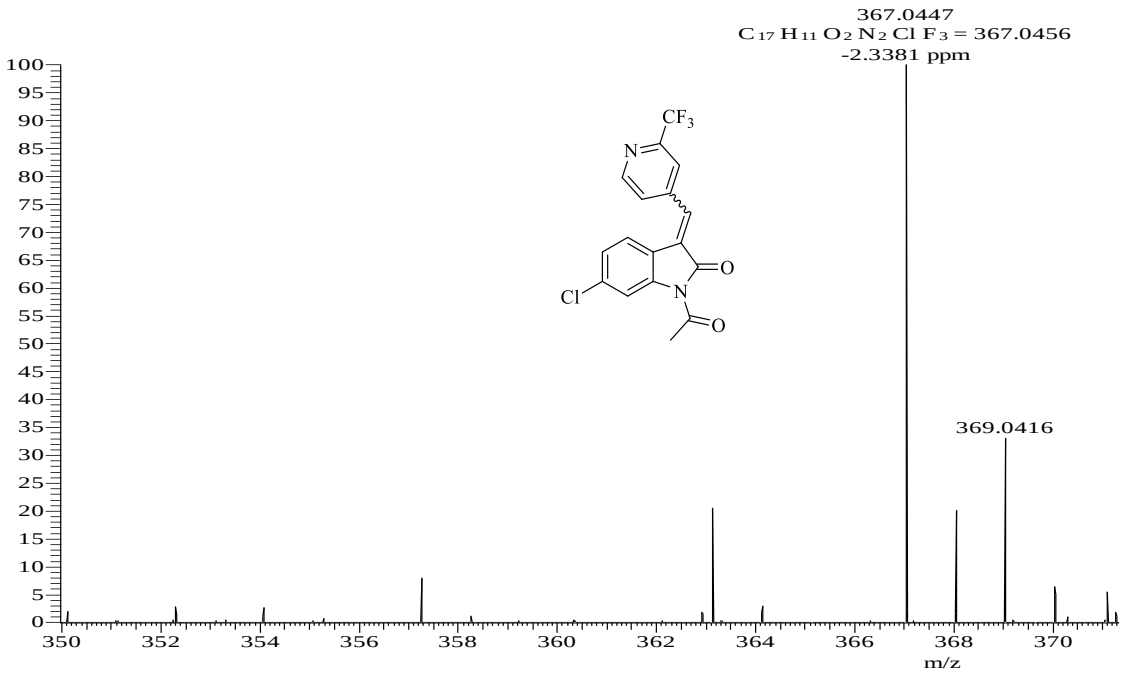


Figure S23-3. HRMS of compound **4w**

***Tert*-butyl -4-((1-acetyl-6-chloro-2-oxoindolin-3-ylidene)methyl)benzoate(4x)**

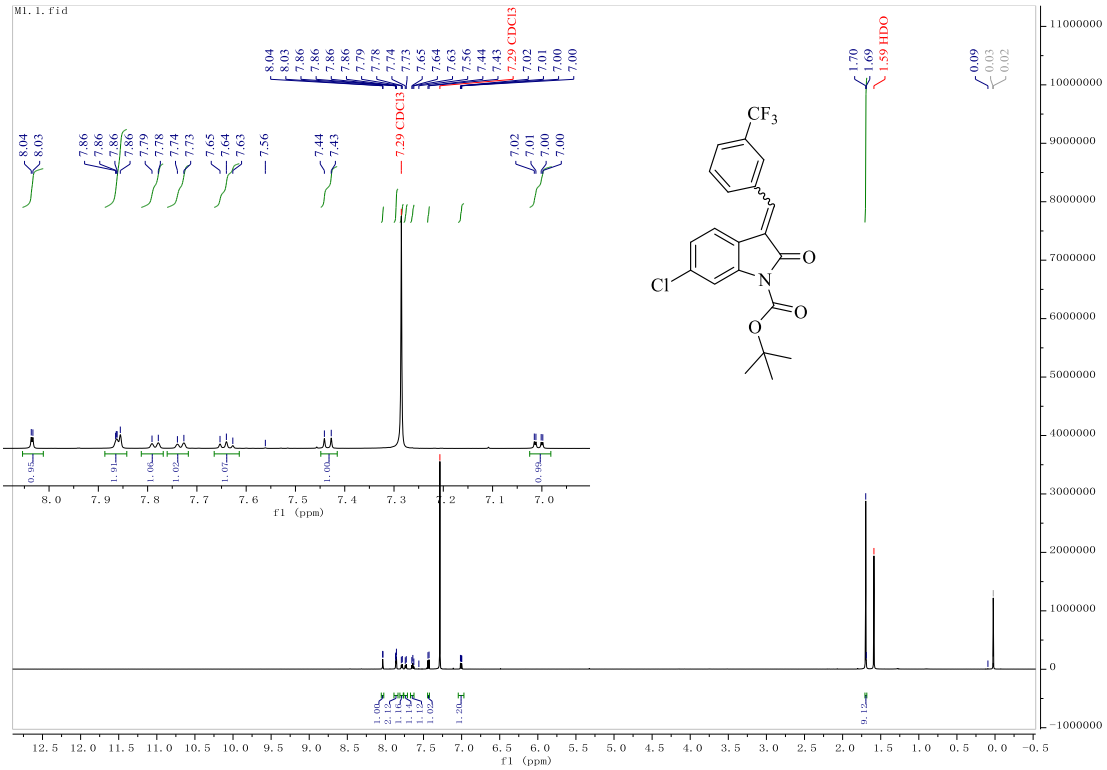


Figure S24-1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **4x**

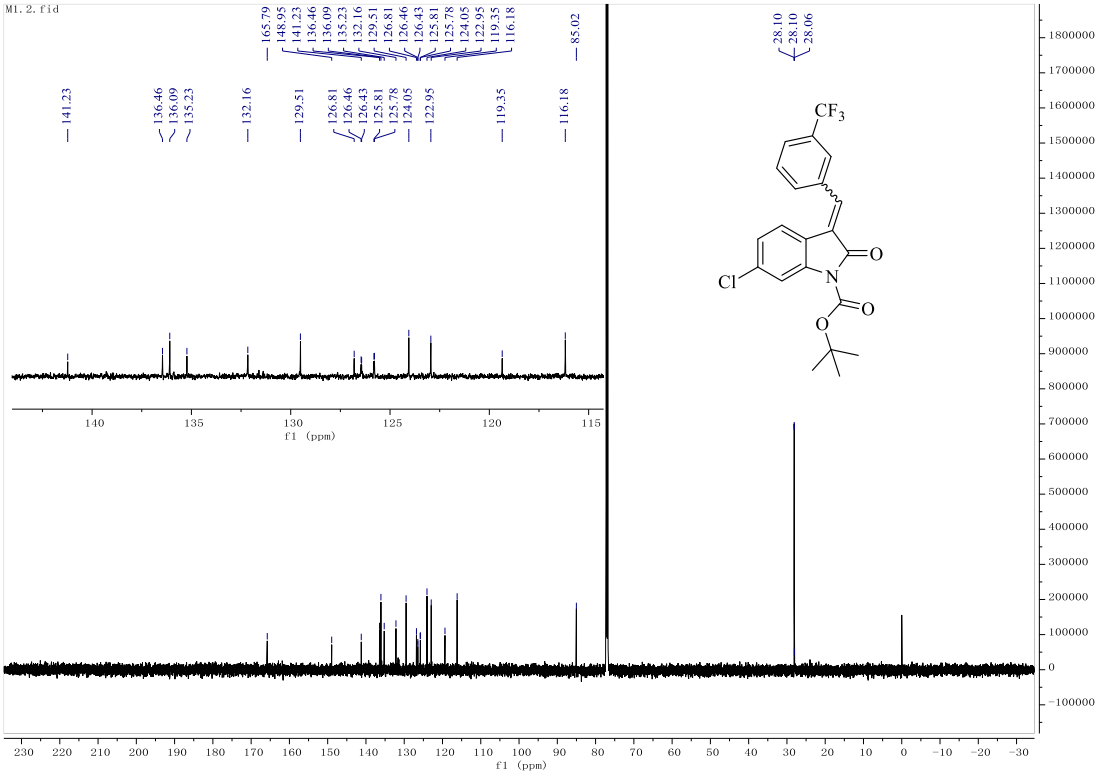


Figure S24-2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **4x**

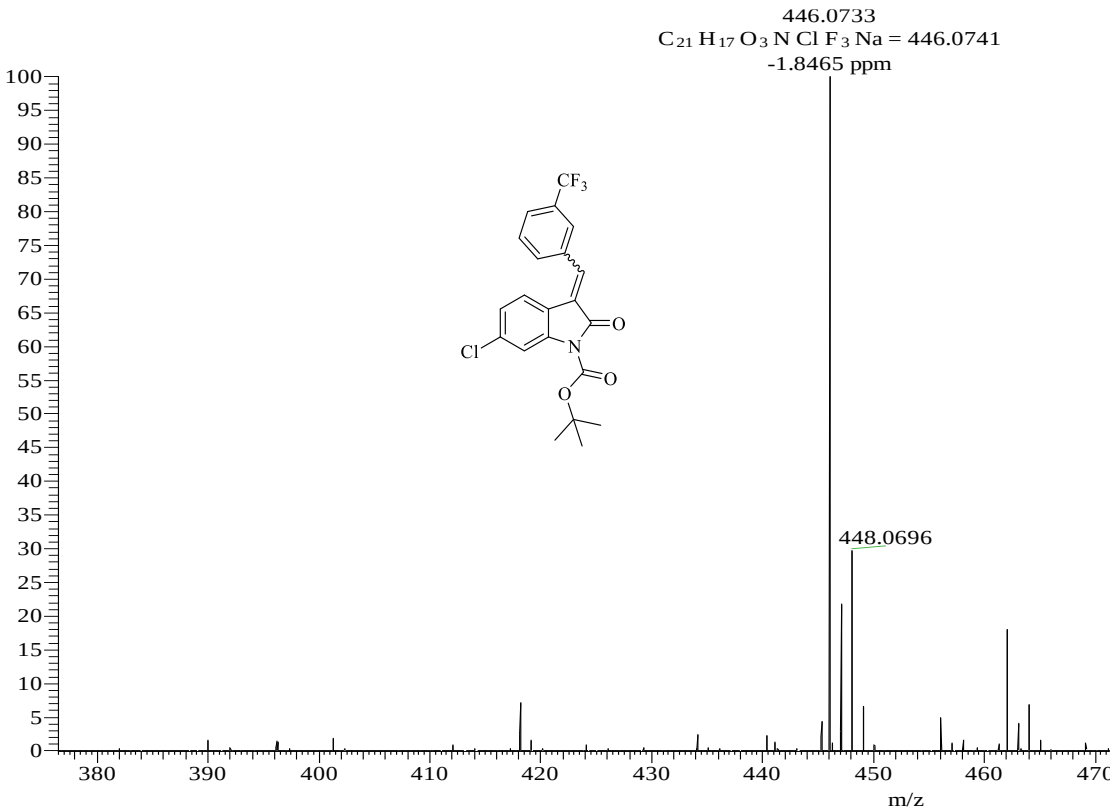


Figure S24-3. HRMS of compound **4x**

4-Nitro-N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)benzenesulfonamide (9d)

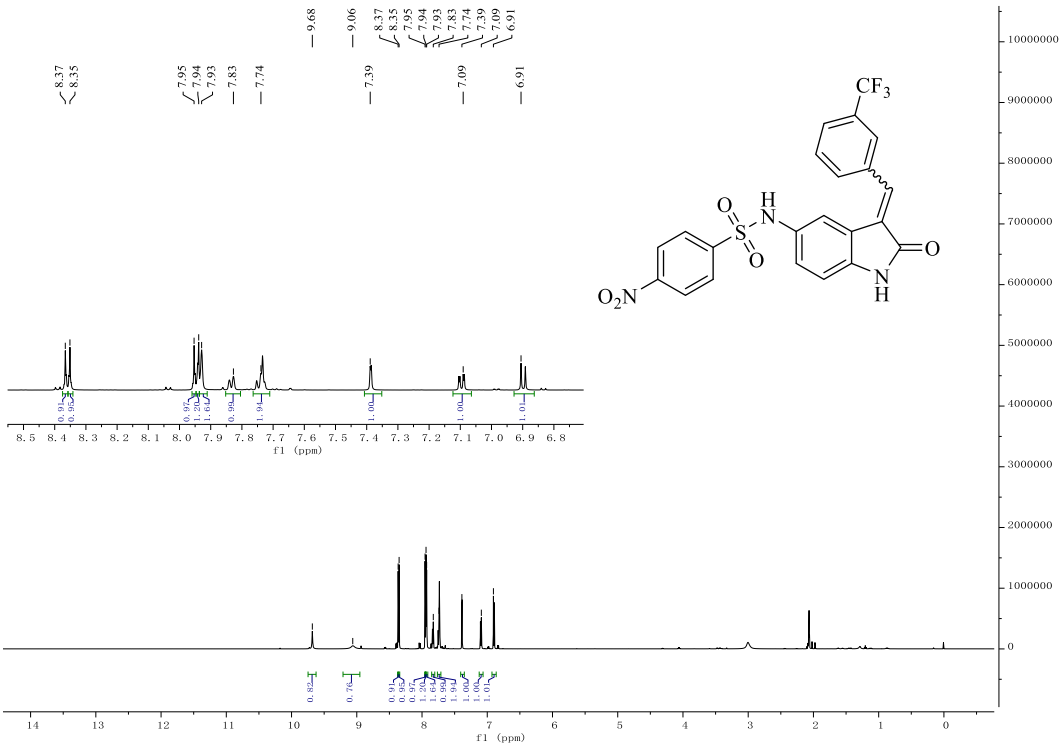


Figure S25-1. ^{1}H NMR spectrum (600 Hz, Acetone) of compound **9d**

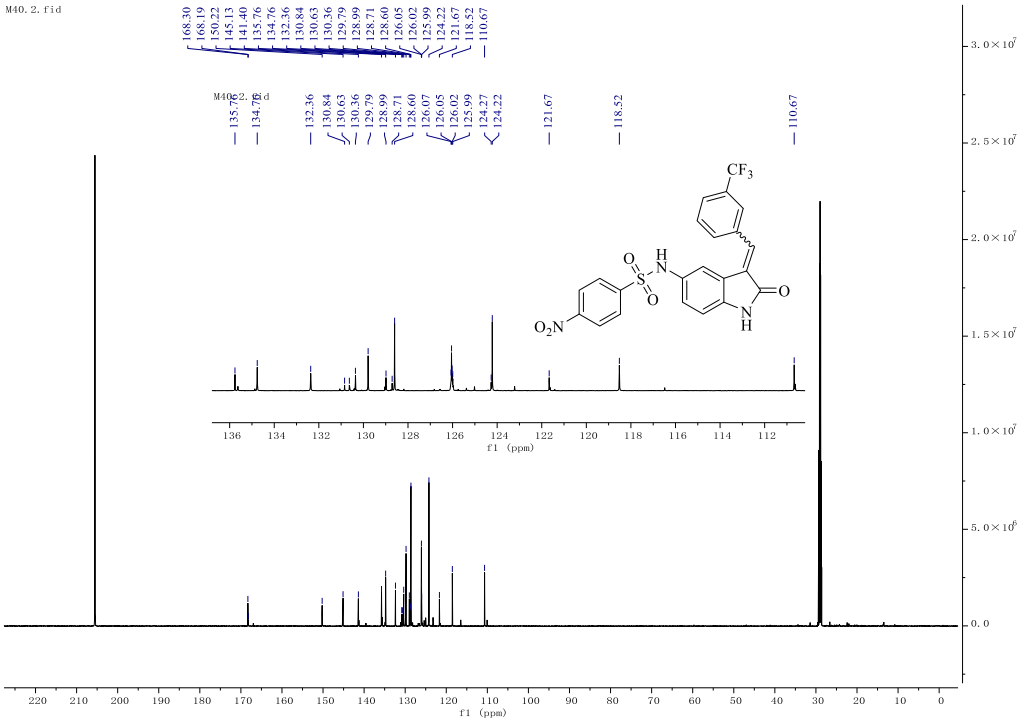


Figure S25-2. ^{13}C NMR spectrum (150 Hz, Acetone) of compound **9d**

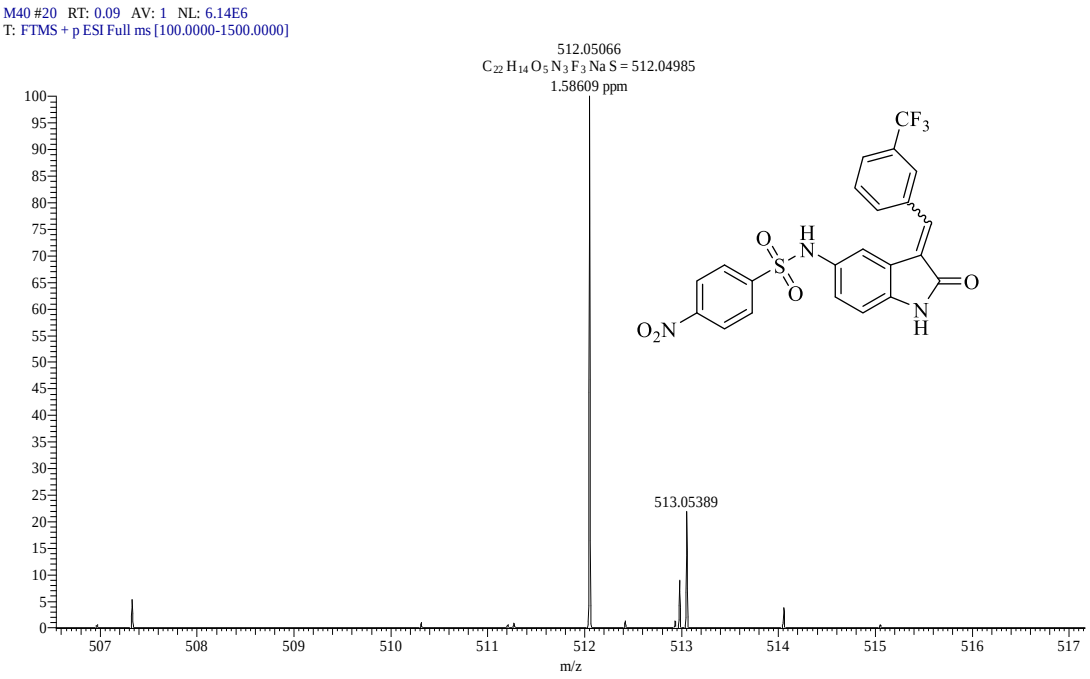


Figure S25-3. HRMS of compound **9d**

nitro-N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)benzenesulfonamide(**9a**)

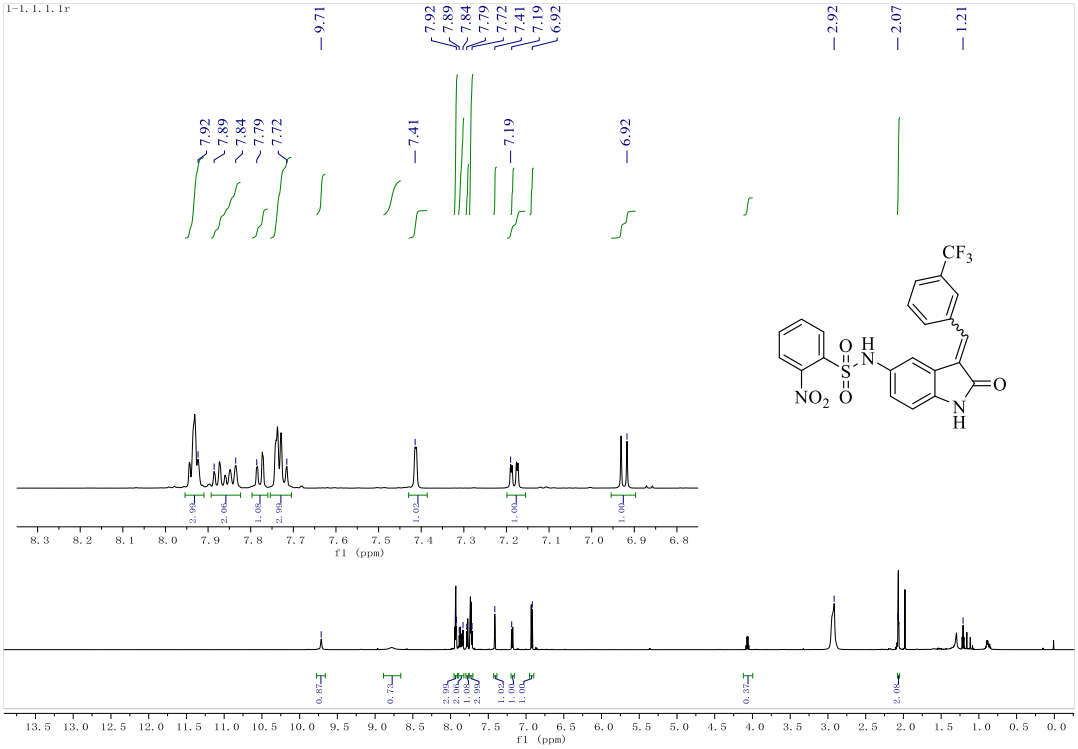


Figure S26-1. ^{1}H NMR spectrum (600 Hz, CD_3COCD_3) of compound **9a**

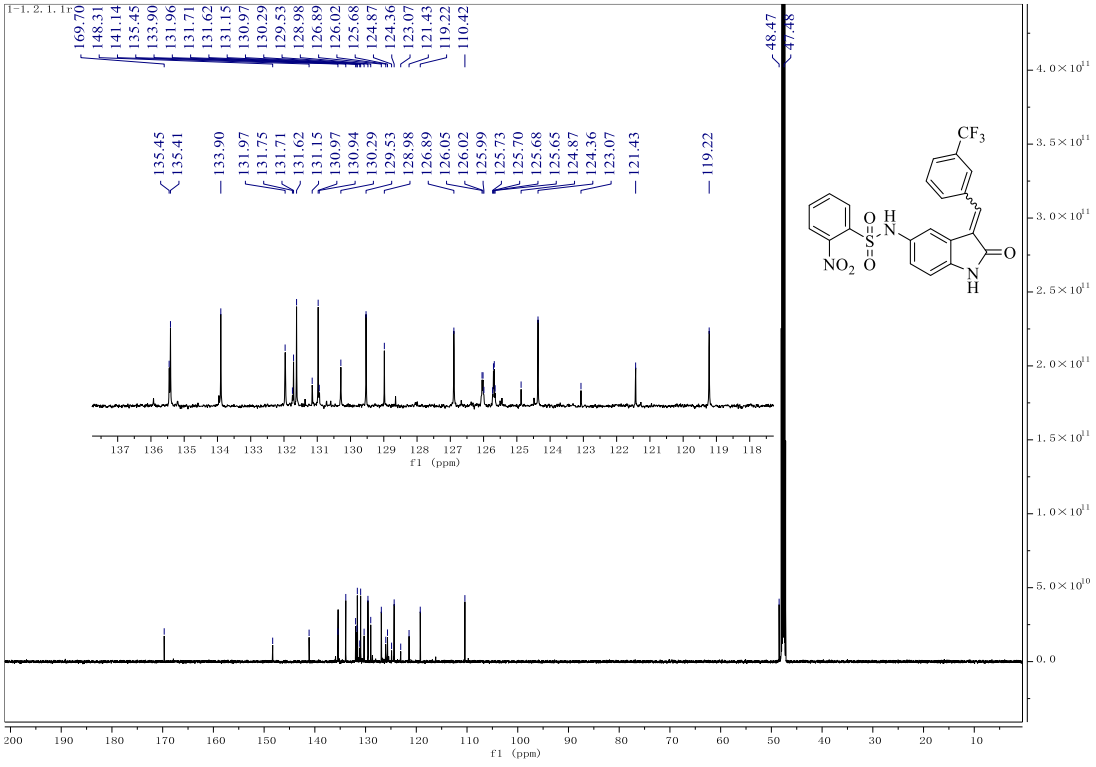


Figure S26-2. ^{13}C NMR spectrum (150 Hz, CD_3OD) of compound **9a**

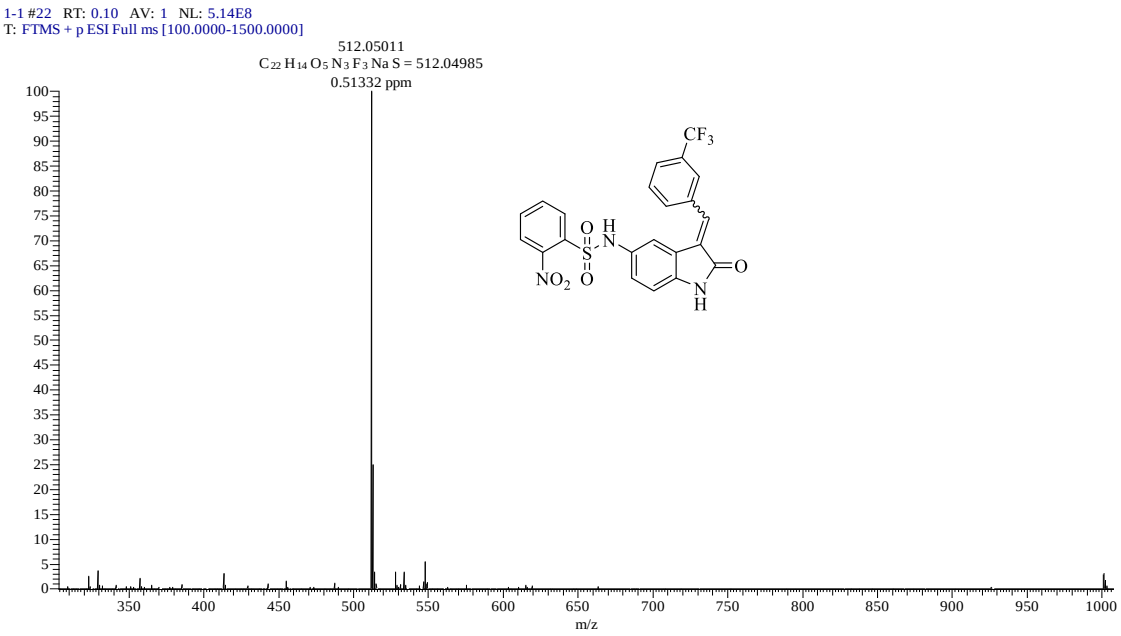


Figure S26-3. HRMS of compound **9a**

2,4-Difluoro-*N*-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)benzenesulfonamide (9b)

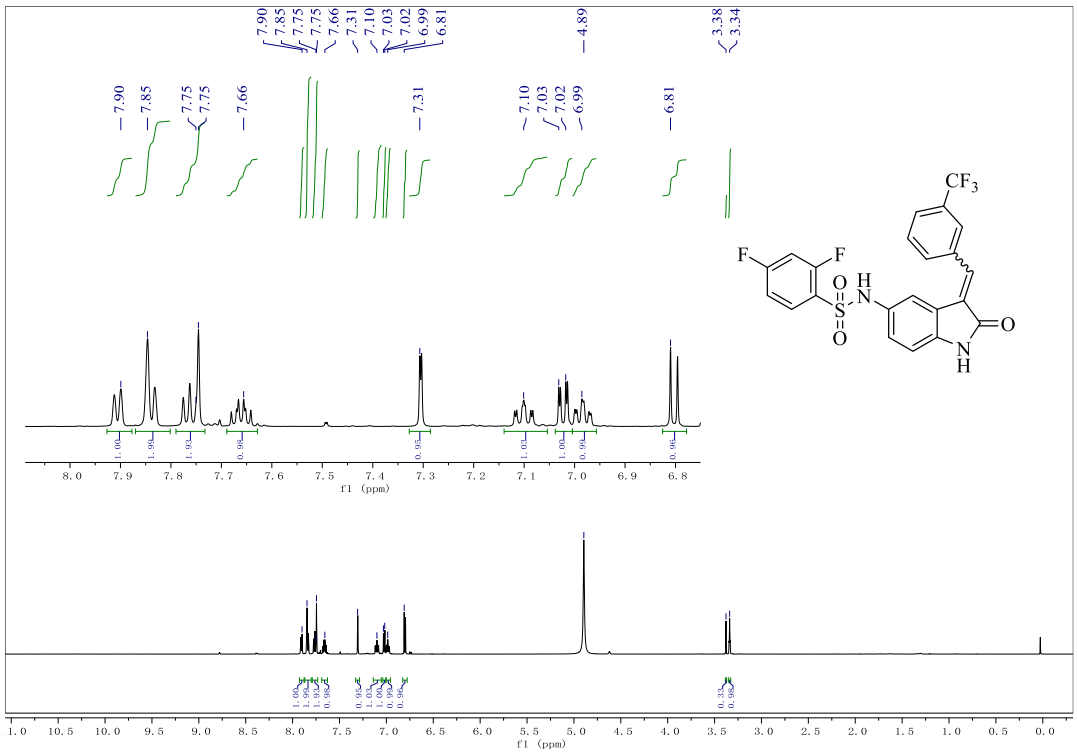


Figure S27-1. ^{1}H, NMR spectrum (150 Hz, CD_3OD) of compound **9b**

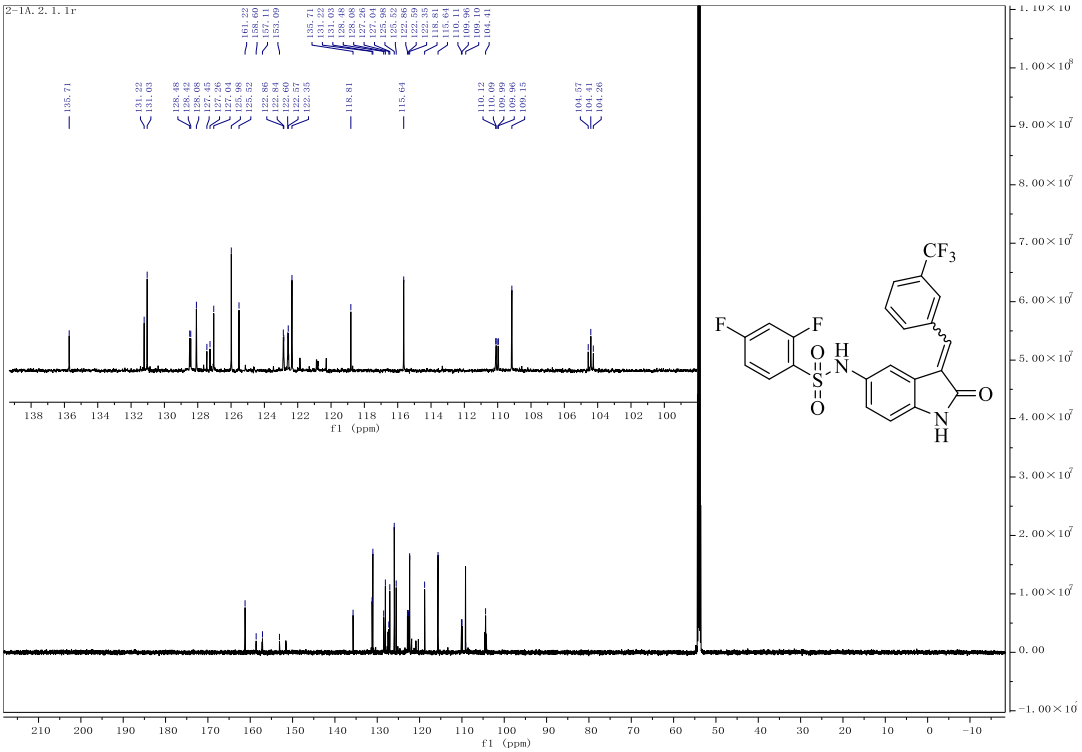


Figure S27-2. ^{13}C NMR spectrum (150 Hz, CD_3OD) of compound **9b**

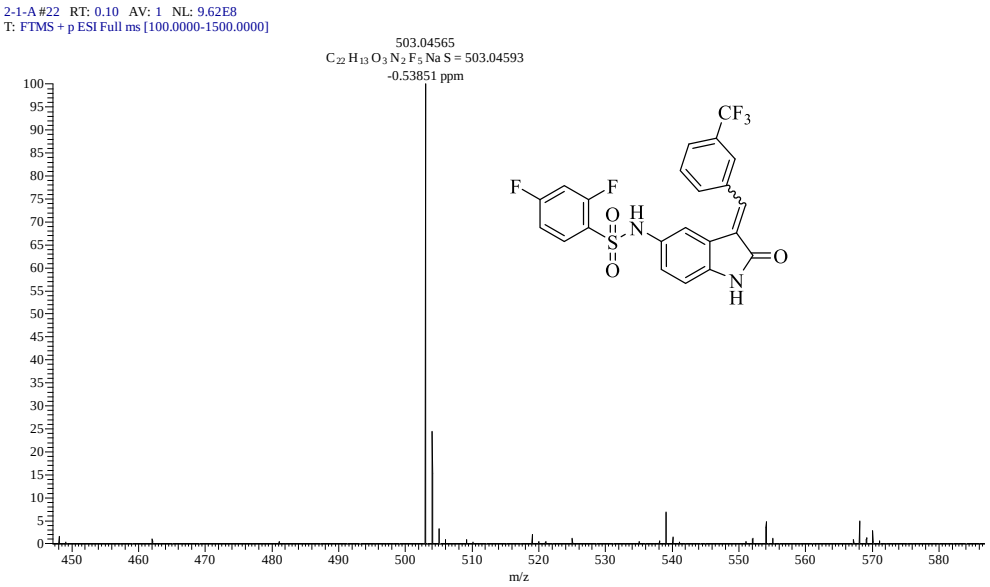


Figure S27-3. HRMS of compound **9b**

N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)ethanesulfonamide (9c)

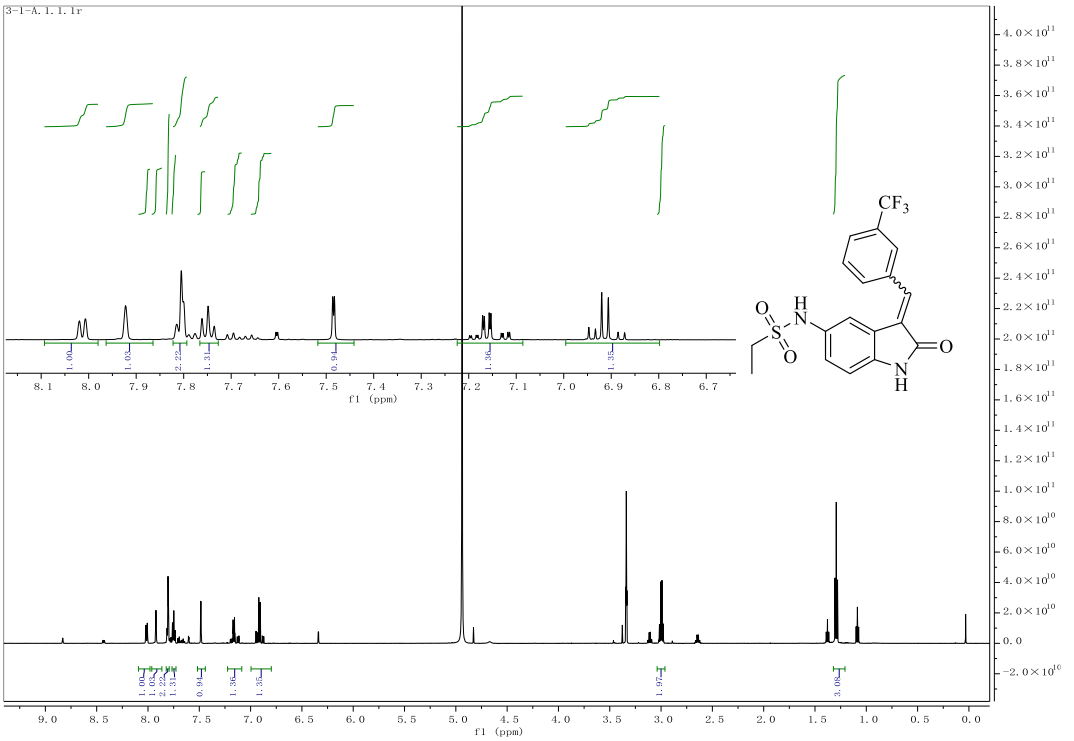


Figure S28-1. ^{1}H NMR spectrum (600 MHz, CD_3OCD_3) of compound **9c**

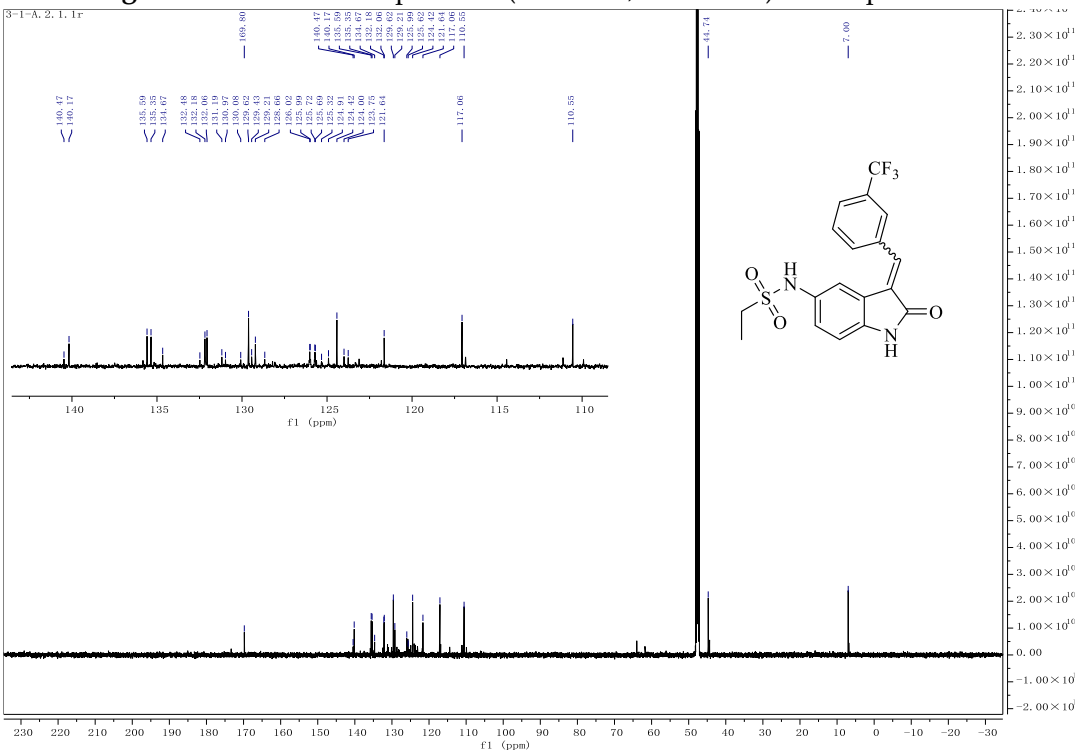


Figure S28-2. ^{13}C NMR spectrum (150 MHz, CD_3OCD_3) of compound **9c**

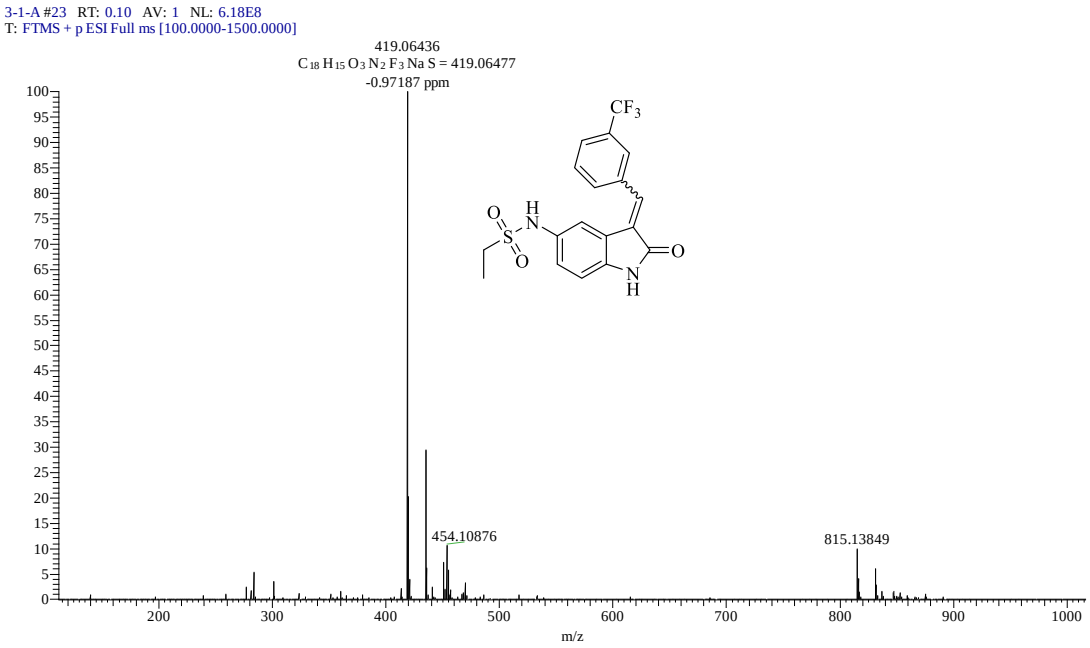


Figure S28-3. HRMS of compound **9c**

N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)-1-phenylmethanesulfonamide **(9e)**

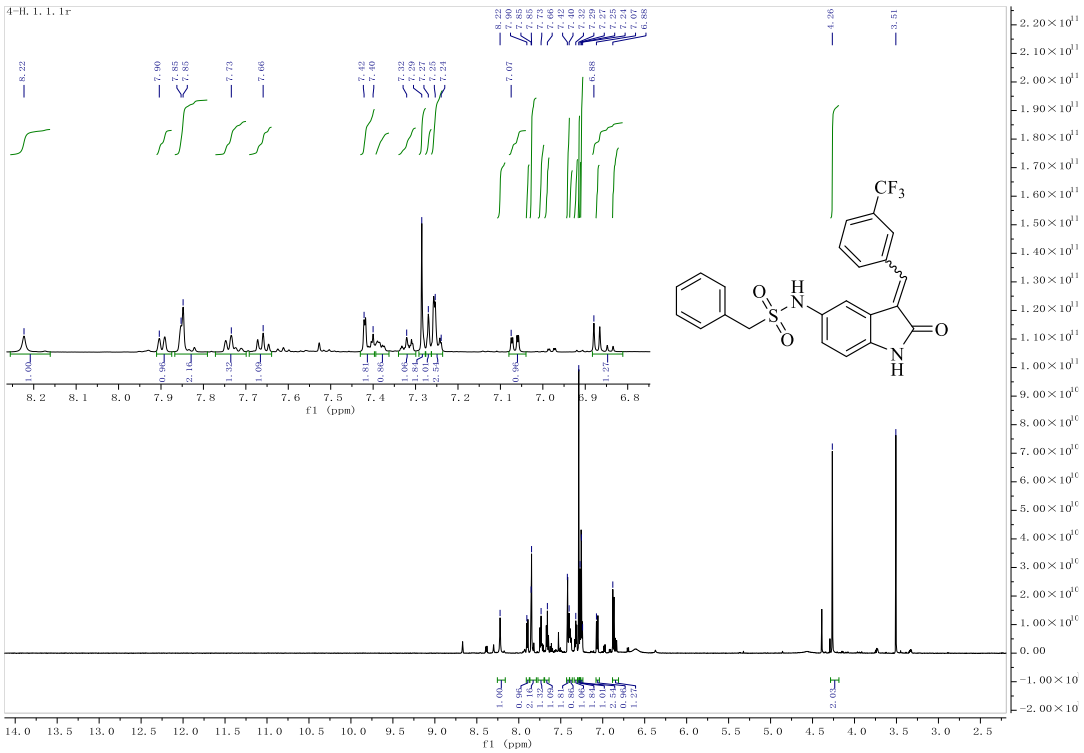


Figure S29-1. ^{1}H NMR spectrum (600 Hz, $CDCl_3$) of compound **9e**

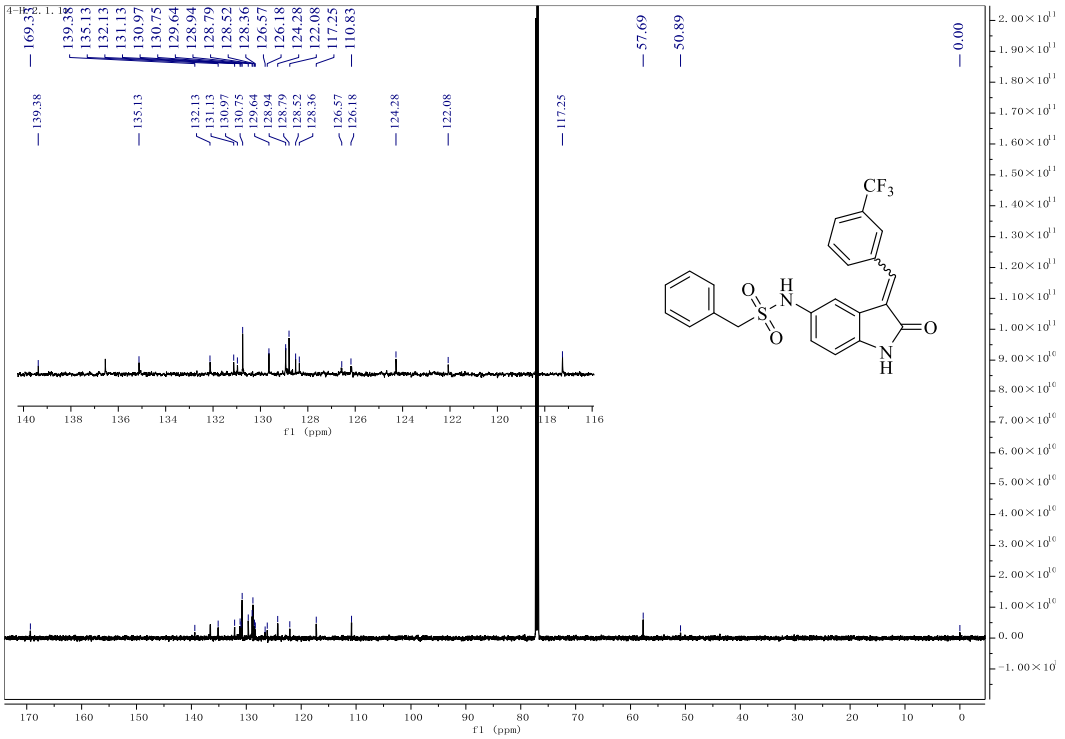


Figure S29-2. ^{13}C NMR spectrum (150 Hz, $CDCl_3$) of compound **9e**

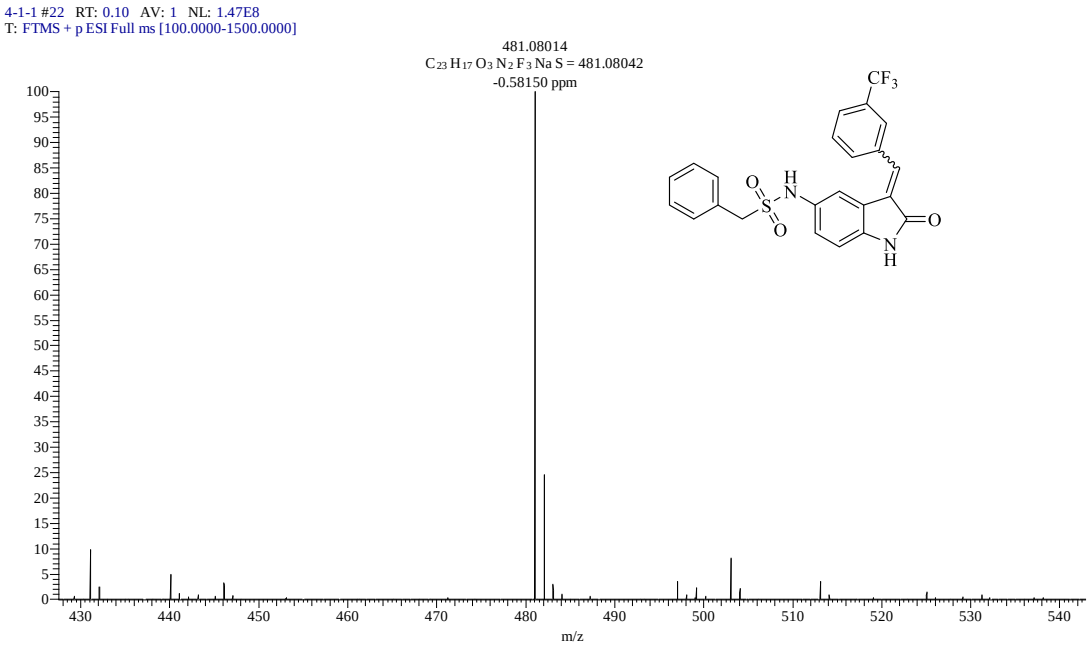


Figure S29-2. HRMS of compound **9e**

(Z)-4-methyl-N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)benzenesulfonamide (9f)

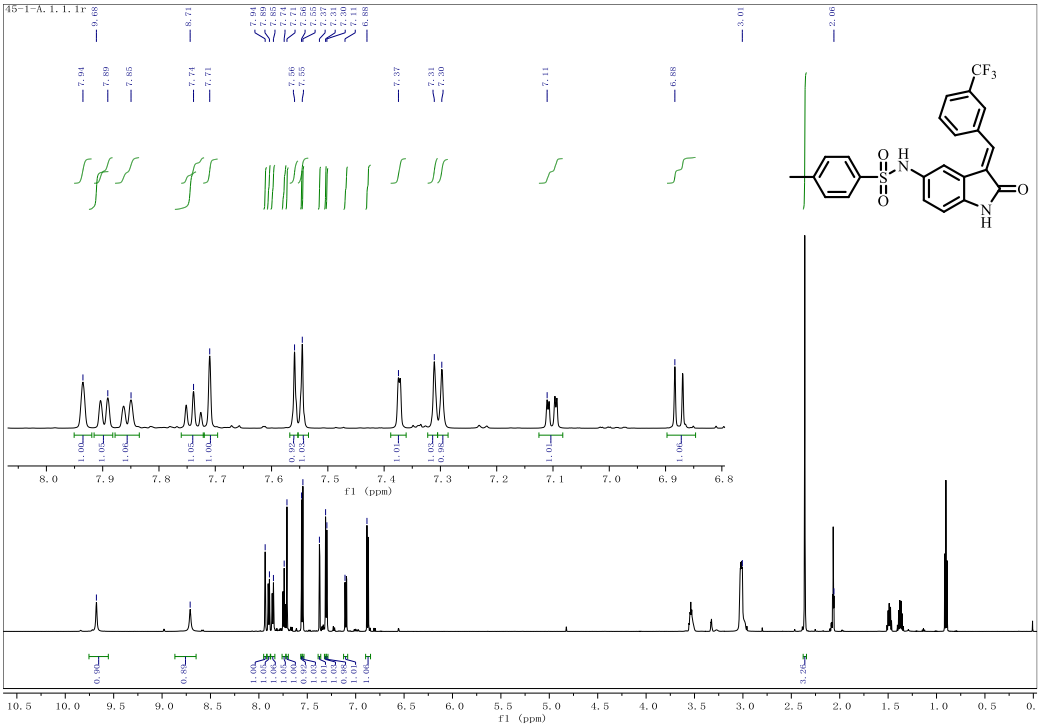


Figure S30-1. ^{1}H NMR spectrum (600 Hz, CD_3OCD_3) of compound **9f**

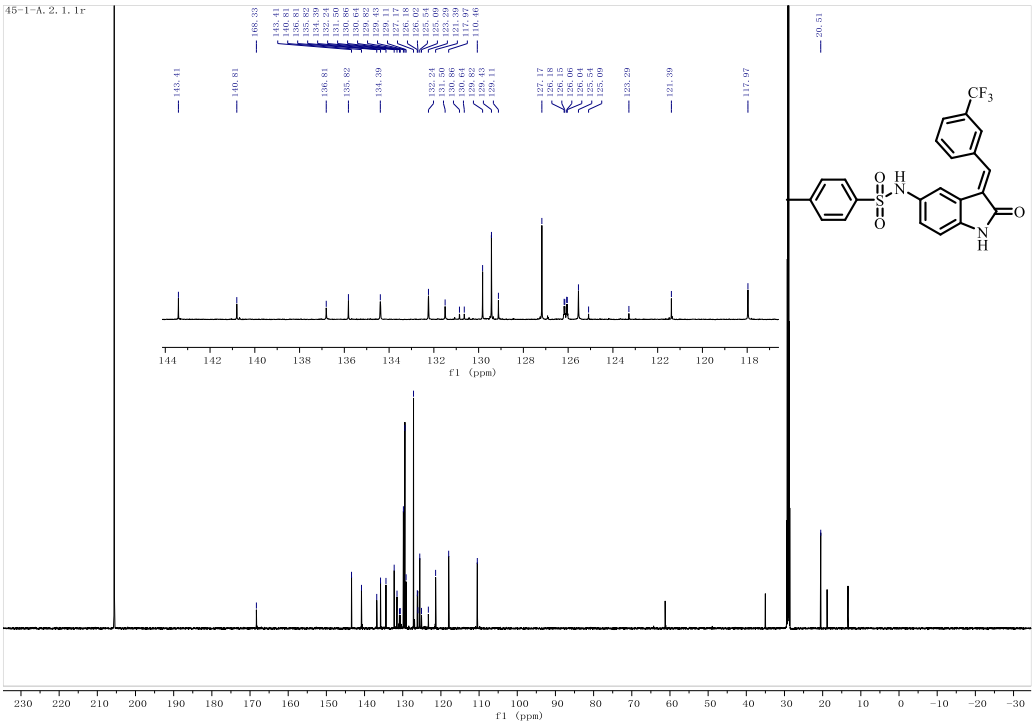


Figure S30-2. ^{13}C NMR spectrum (150 Hz, CD_3OCD_3) of compound **9f**

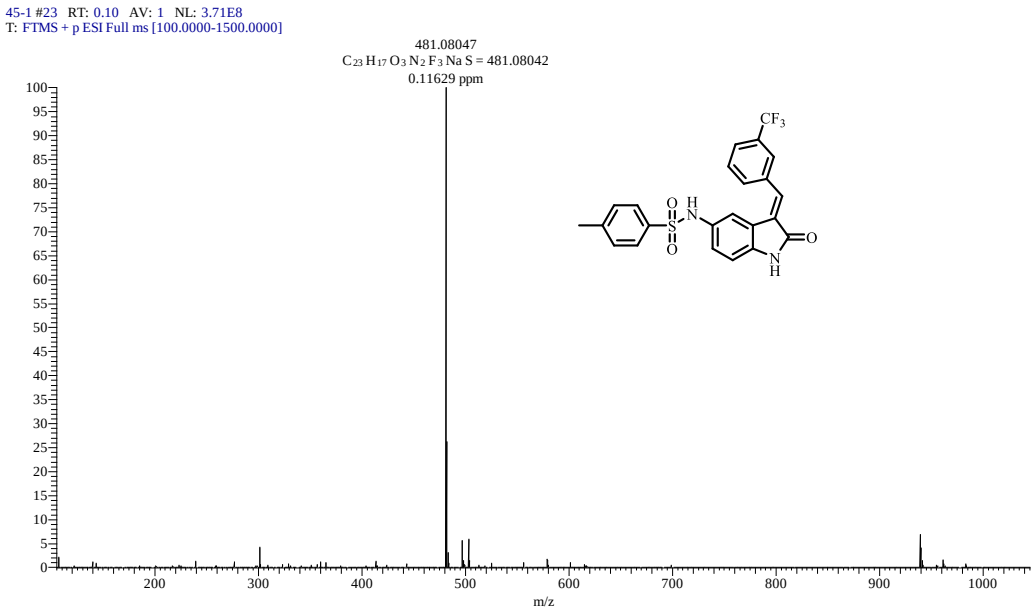


Figure S30-2. HRMS of compound **9f**

(*E*)-4-methyl-N-(2-oxo-3-(3-(trifluoromethyl)benzylidene)indolin-5-yl)benz-enesulfona mide (9g).

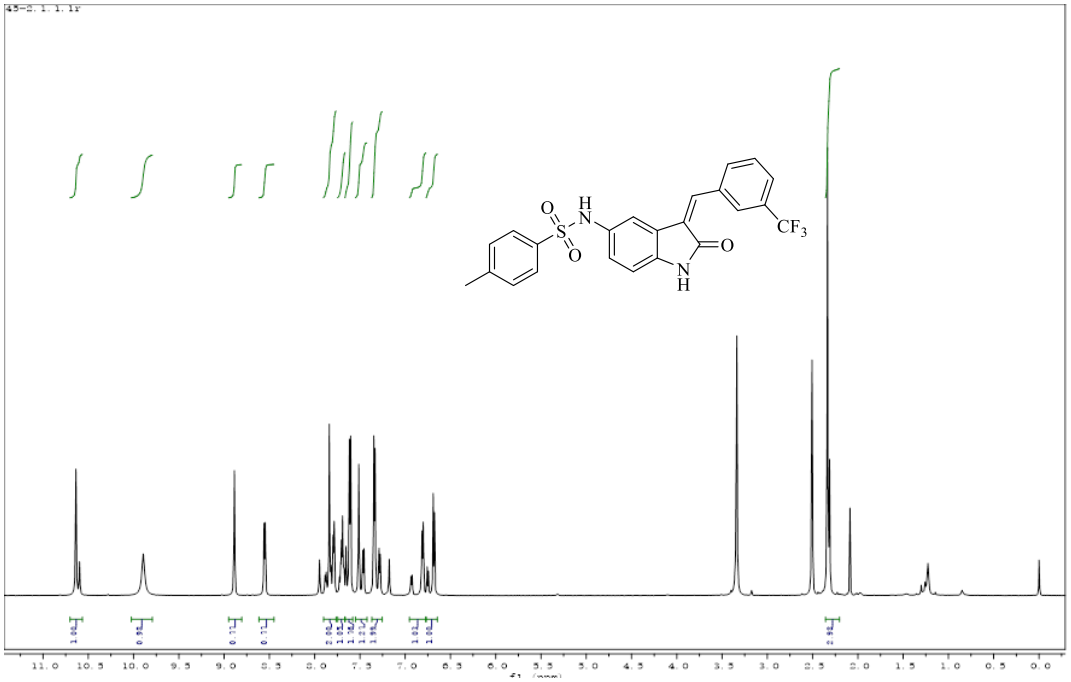


Figure S31-1. ^{1}H NMR spectrum (600 Hz, DMSO) of compound **9g**

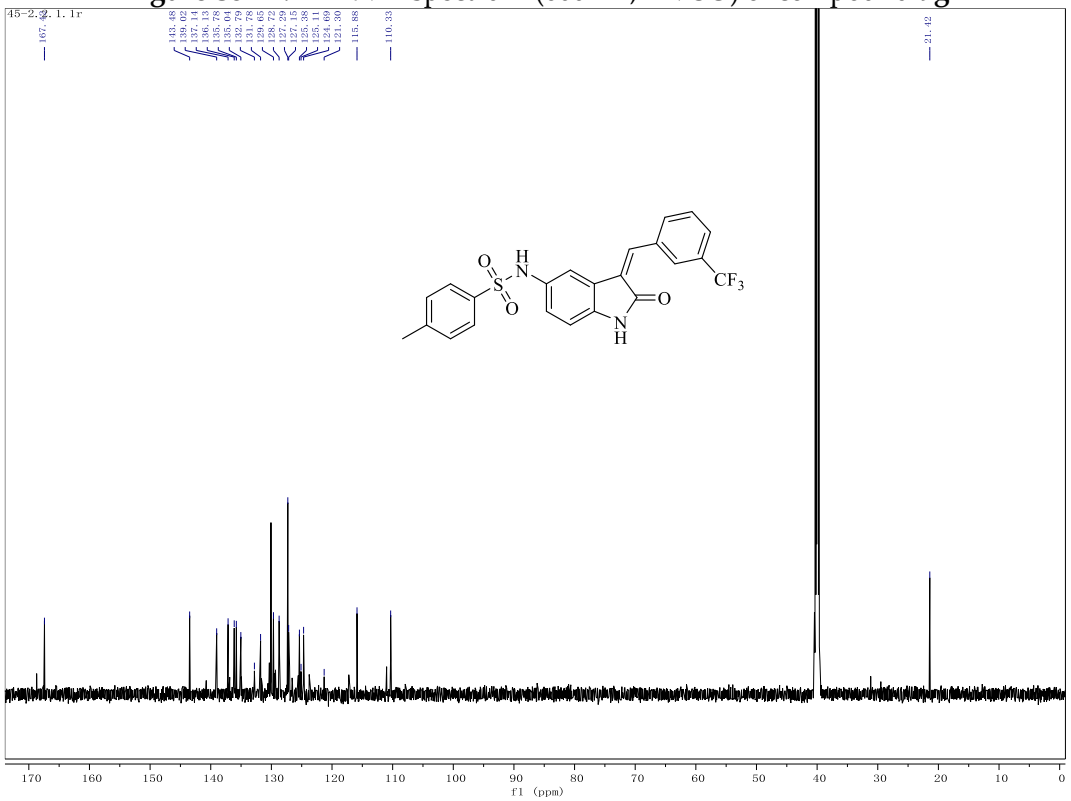


Figure S31-2. ^{13}C NMR spectrum (150 Hz, DMSO) of compound **9g**

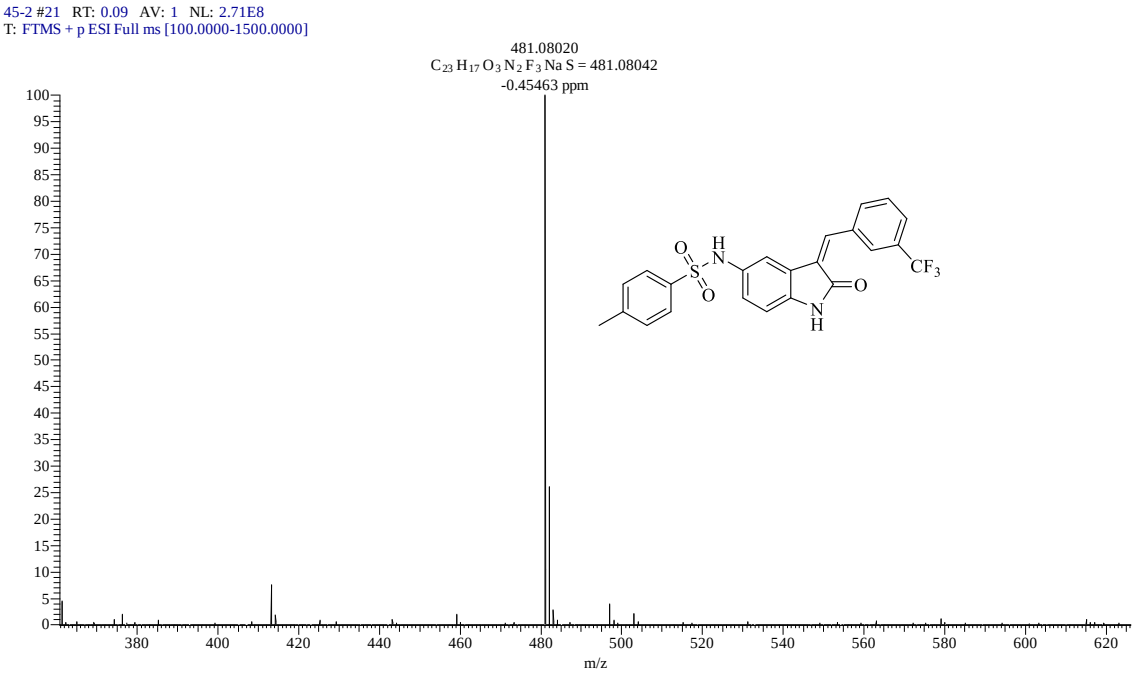


Figure S31-2. HRMS of compound **9g**

5-((3,5-bis(trifluoromethyl)benzylidene)amino)indolin-2-one (9i)

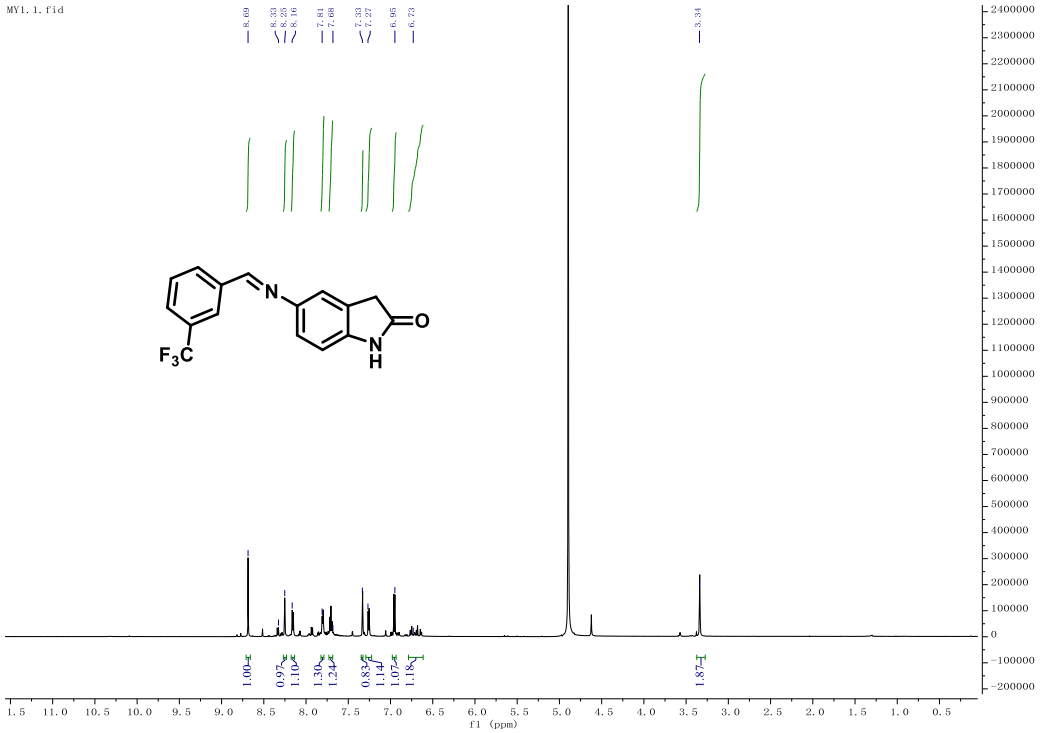


Figure S32-1. ^{1}H NMR spectrum (600 Hz, CD_3OD) of compound **9h**

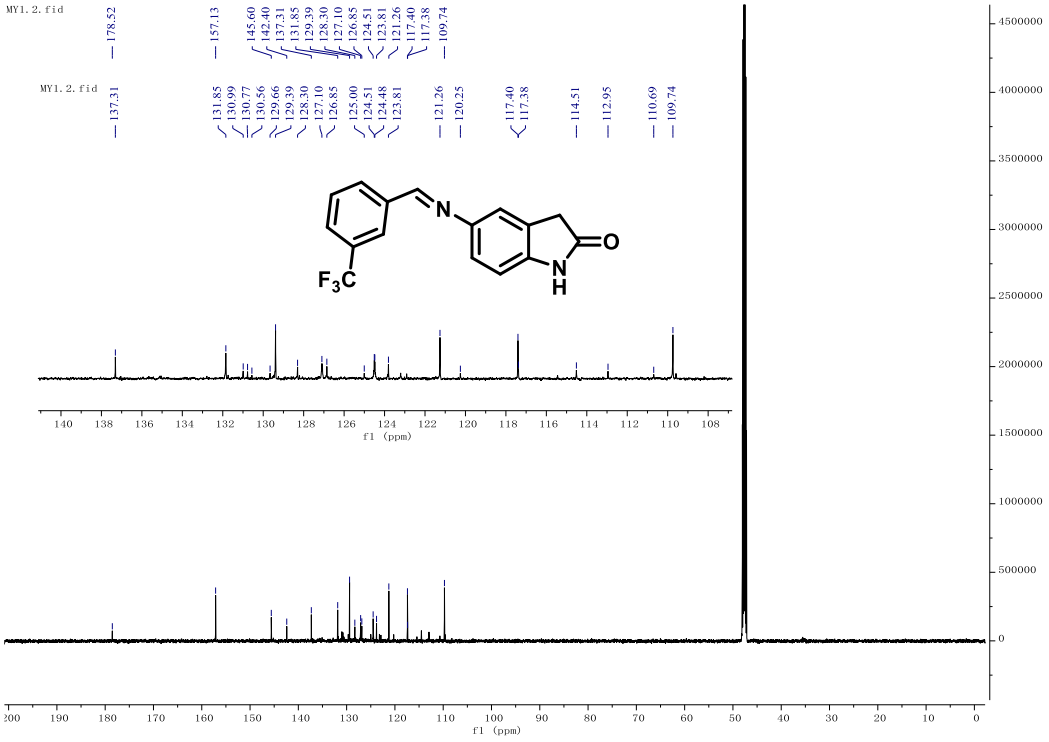


Figure S32-2. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **9h**

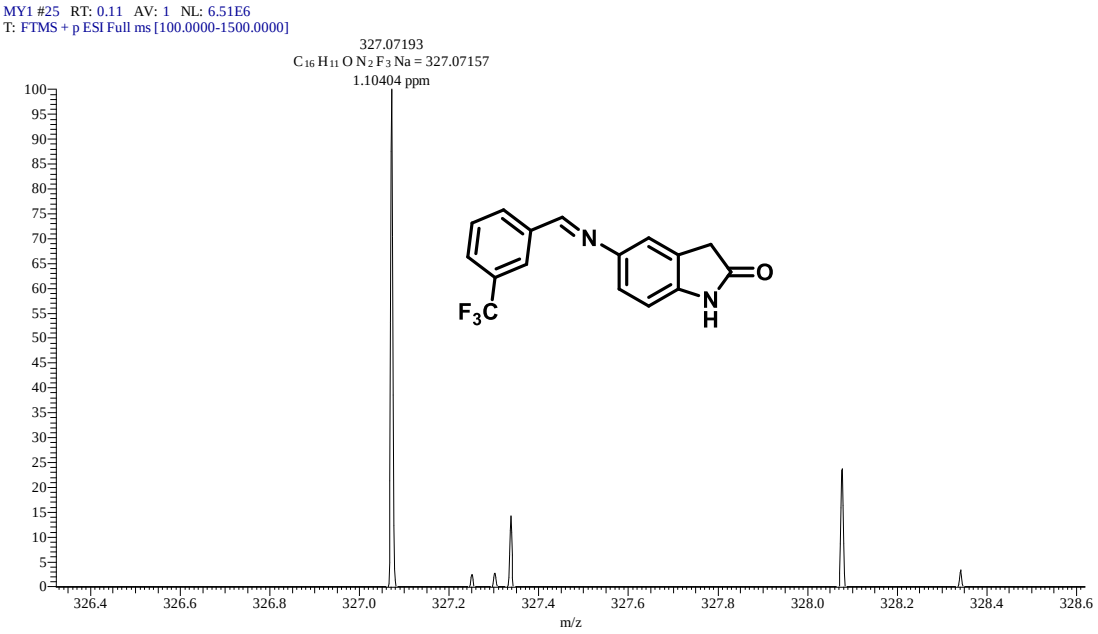


Figure S32-3. HRMS of compound **9h**

5-((3,5-bis(trifluoromethyl)benzylidene)amino)indolin-2-one (9i)

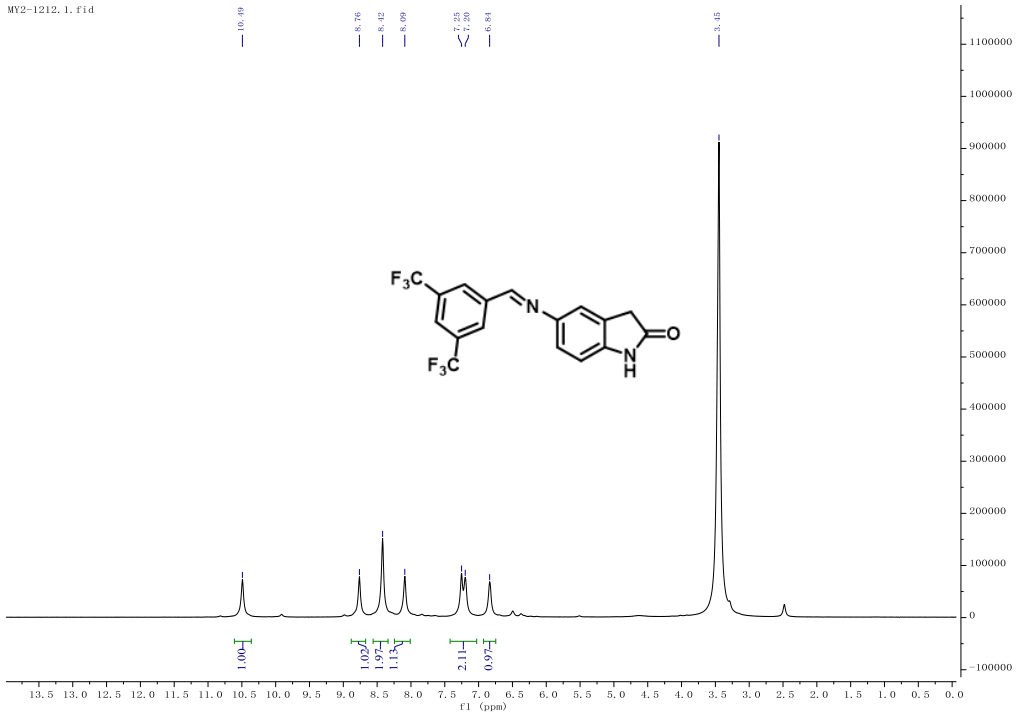


Figure S33-1. [1]H NMR spectrum (600 Hz, DMSO) of compound **9i**

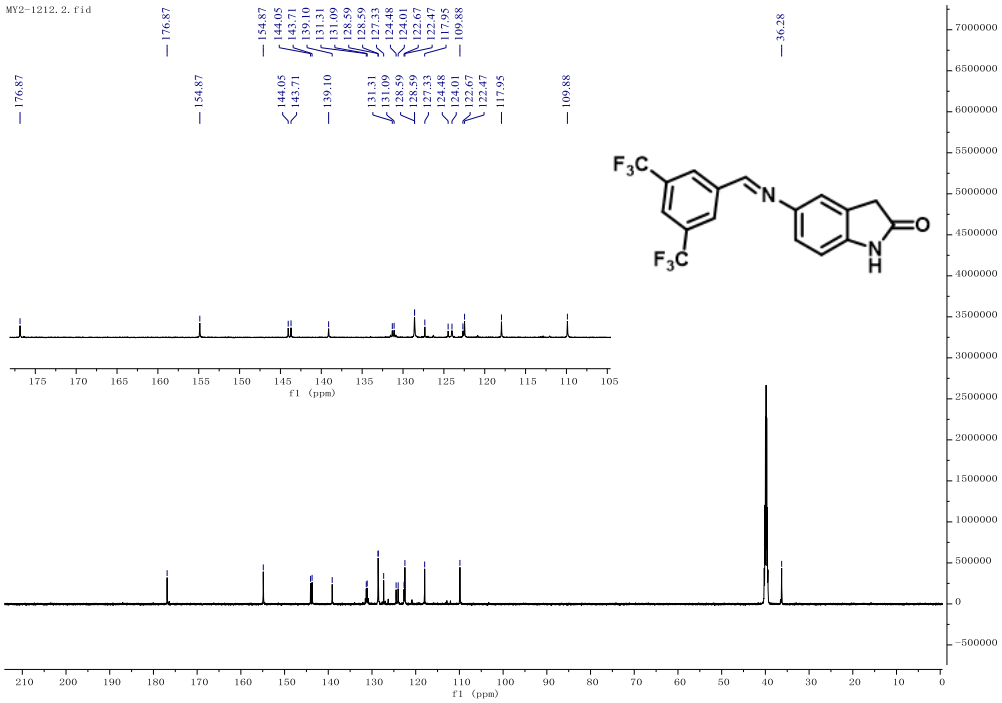


Figure S33-2. [13]C NMR spectrum (150 Hz, DMSO) of compound **9i**

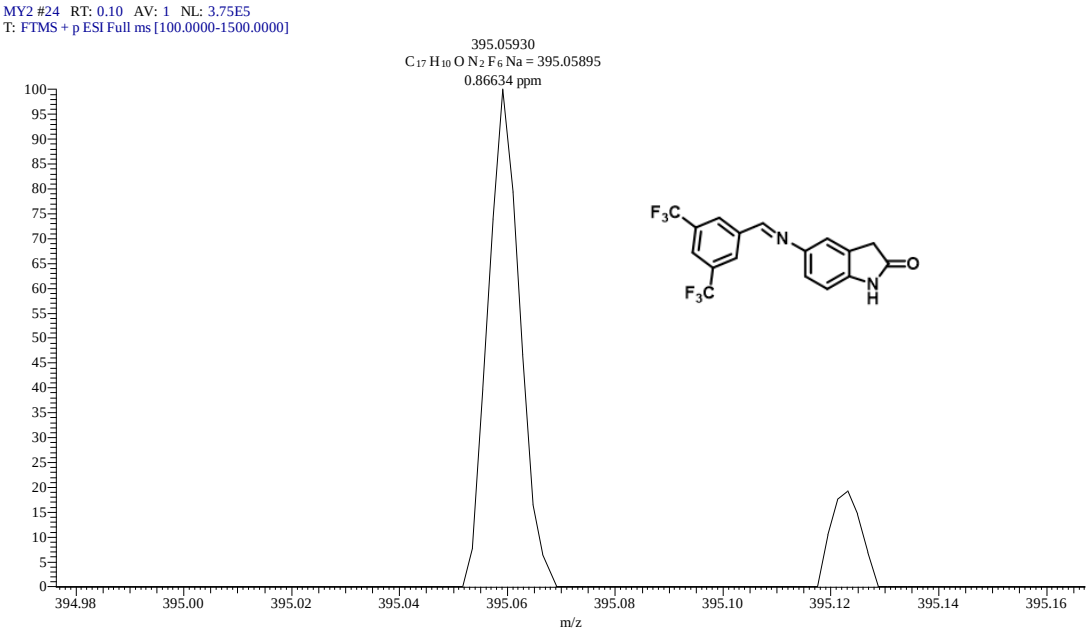


Figure S33-3. HRMS of compound **9i**