Assembly of Fluorinated Chromanones via Enantioselective Tandem Reaction

Mengxue Lu,[a] Zongli Xiong,[a] Yuqiao Zhou,[b] Xin Wang,[a] Xiaoyi Li,[a] Jingxiang Duan,[a] Weijun Yao,[c] Yi Xia,*[a] Zhen Wang*[a]

[a] School of Pharmaceutical Sciences and Chongqing Key Laboratory of Natural Drug Research, Chongqing University, Chongqing 401331, P.R. China.
E-mail: wangz1114@cqu.edu.cn; yixia@cqu.edu.cn

[b] Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, P. R. China.

[c] Department of Chemistry, Zhejiang Sci-Tech University, Hangzhou, 310018, P. R. China.

21 May 2021
Note added after first publication: this supplementary information file replaces that originally published on 06 April 2021, in which the structure of compound **3an** was incorrect. This does not affect any of the conclusions or discussion in the main article.

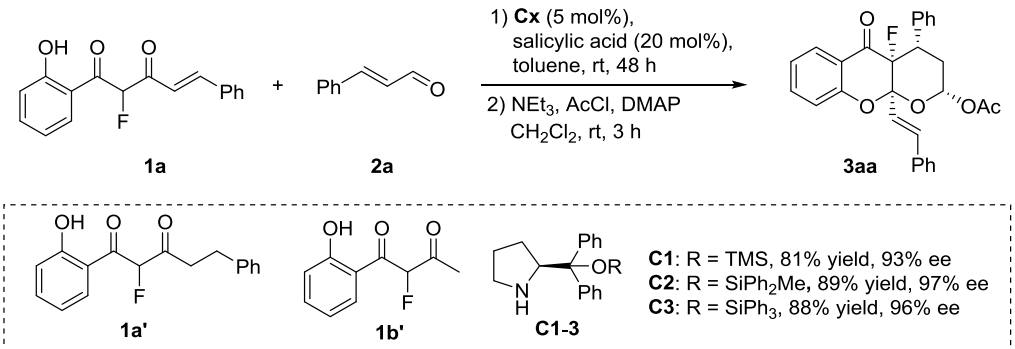
Contents

1. General Information:

^{1}H NMR spectra were recorded at 400 or 600 Hz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 or 150 MHz with complete proton decoupling. ^{19}F NMR data of compunds **3aa-3fa**, **3ia-3ka**, **3ma**, **3pa, 3ad, 3af, 3ai-3ak** and **3an** were collected at 565 MHz with complete proton decoupling.

Enantiomeric excesses (*ee*'s) were determined by chiral HPLC analysis on Daicel Chiralcel IA, IC, ID, and IF columns in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]_D^T$ (c: g/100 mL, in solvent CH_2Cl_2). ESI-HRMS spectra were recorded on a commercial apparatus and methanol or acetonitrile was used to dissolve the sample. Unless noted, solvent and commercial reagents were used without further purification. Vinyl and aryl substituted 2-F-1-(2-hydroxyaryl)-1,3-diketone **1** derivatives were prepared according to the literature.[1] α,β-Unsaturated aldehydes **2** were prepared according to the literature.[2,3,4]

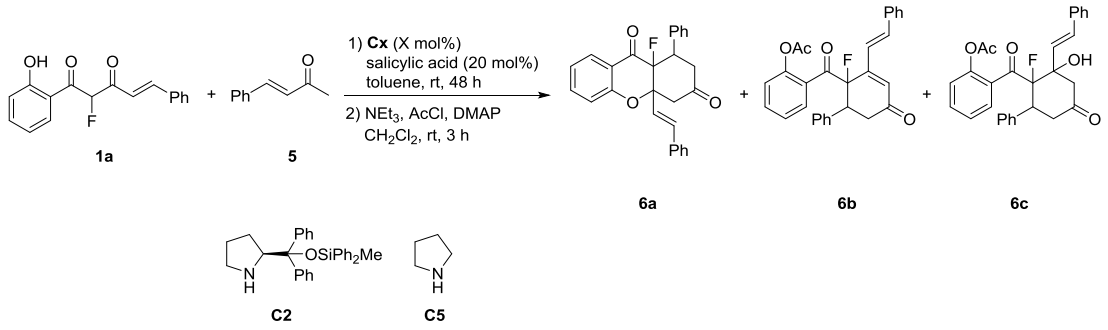
2. The catalytic condition screening



Entry[a]	Solvent	Substrate	Catalyst	d.r. (**3aa**)[b]	yield (**3aa**)[c]	ee (**3aa**)[d]
1	Toluene	**1a'**	**C1**	-	NR	-
2	Toluene	**1b'**	**C1**	-	NR	-
3	Toluene	**1a**	**C1**	> 19:1	81%	93%
4	Toluene	**1a**	**C2**	> 19:1	89%	97%
5	Toluene	**1a**	**C3**	> 19:1	88%	96%
6	Toluene	**1a**	**L-proline**	> 19:1	76%	0%

[a] Reactions were carried out with **1a** (0.1 mmol), **2a** (0.12 mmol), chiral amine **C1-3** (5 mol%) and acid additive (20 mol%) in toluene (0.1 M) at 20-23 ^{o}C for 48 hours, followed by the acylation in the presence of NEt_3 (2.0 equiv.), acetyl chloride (1.5 equiv.) and DMAP (0.1 equiv.) in CH_2Cl_2 (4.0 mL) for 3 h. [b] d.r. was determined by ^{1}H NMR and ^{19}F NMR analysis of crude products. [c] Isolated yield. [d] Determined by chiral HPLC analysis.

The reaction with (*E*)-4- phenylbut-3-en-2-one 5

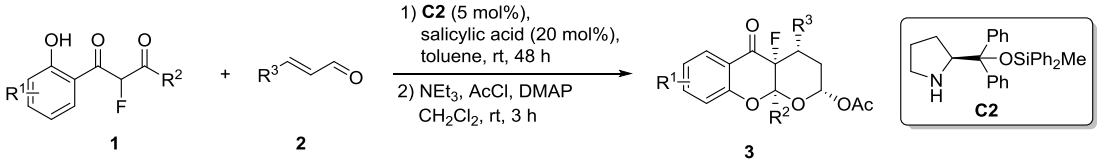


entry[a]	Cat.	yield[b] (**6a**)	yield[b] (**6b**)	yield[b] (**6c**)
1	**C2** (5 mol%)	——————No reaction——————		
2	**C5** (20 mol%)	13% (>19:1 d.r.)[c]	24% (>19:1 d.r.)[c]	10% (>19:1 d.r.)[c]

[a] Reactions were carried out with **1a** (0.1 mmol), **5** (0.12 mmol), amine **Cx** (5-20 mol%) and salicylic acid (20 mol%) in toluene (0.1 M) at 20-23 °C for 24 hours, followed by the acylation in the presence of NEt_3 (2.0 equiv.), acetyl chloride (1.5 equiv.) and DMAP (0.1 equiv.) in CH_2Cl_2 (4.0 mL) for 3 h. [b] Isolated yield. [c] >19:1 d.r. was determined by ^1H NMR and ^{19}F NMR analysis of products.

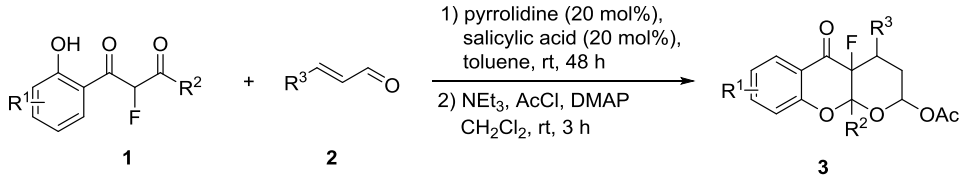
3. Typical experimental procedure for the synthesis of fluorinated chromanones

Synthesis of enantioselective product 3



To a dried test tube containing a solution of vinyl substituted 2-F-1-(2-hydroxyaryl) -1,3-diketone **1** (0.2 mmol, 1 equiv.), salicylic acid (0.04 mmol, 0.2 equiv.) and **C2** (0.01 mmol, 0.05 equiv.) dissolved in toluene (2.0 mL, 0.1 M) was added α,β-unsaturated aldehydes **2** (0.24 mmol, 1.2 equiv.) at room temperature. The reaction was stirred at 20-23 °C for 48 hours, and monitored by TLC. The mixture was simply purified by short column chromatography on silica gel with CH_2Cl_2, and then followed by the acylation reaction. NEt_3 (0.4 mmol, 2 equiv) and DMAP (0.02 mmol, 0.1 equiv.) were added into the solution of crude products in CH_2Cl_2 (4.0 mL, 0.5 M), then the acetyl chloride (0.3 mmol, 1.5 equiv.) was added dropwise at room temperature, and the mixture was stirred for further 3 hours. The solvent was evaporated, and the residue was purified by fast column chromatography on silica gel with petroleum ether/ethyl acetate (8/1) to obtain the crude products **3** with >19:1 d.r. determined by ^1H NMR and ^{19}F NMR analysis. The ee values were determined by HPLC analysis on a chiral stationary phase.

Synthesis of racemic product 3



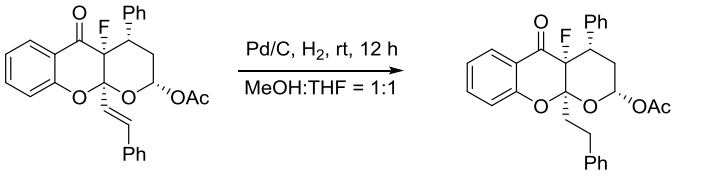
To a dried test tube containing a solution of vinyl substituted 2-F-1-(2-hydroxyaryl) -1,3-diketone **1** (0.05 mmol, 1 equiv.), salicylic acid (0.01 mmol, 0.2 equiv.) dissolved in toluene (0.5 mL, 0.1 M) was added α,β-unsaturated aldehydes **2** (0.06 mmol, 1.2 equiv.) and pyrrolidine (0.01 mmol, 0.2 equiv.) at room temperature. The reaction was stirred at 20-23 ^{o}C for 48 hours, and monitored by TLC. The mixture was simply purified by short column chromatography on silica gel with CH_2Cl_2, and then followed by the acylation reaction. NEt_3 (0.1 mmol, 2 equiv) and DMAP (0.005 mmol, 0.1 equiv.) were added into the solution of crude products in CH_2Cl_2 (1.0 mL, 0.5 M), then the acetyl chloride (0.075 mmol, 1.5 equiv.) was added dropwise at room temperature, and the mixture was stirred for further 3 hours. The solvent was evaporated, and the residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (8/1) to obtain the racemic products **3**.

4. The procedure for scaled-up reaction

To a dried round bottom flask containing 2-fluoro-1-(2-hydroxyphenyl)-5-phenylpent -4-ene-1,3-dione **1a** (1.0 g, 3.5 mmol), salicylic acid (0.7 mmol, 96.6 mg) and **C2** (0.175 mmol, 78.6 mg) dissolved in 6.0 mL of toluene was added cinnamaldehyde **2a** (4.2 mmol, 528 μL) at room temperature. The reaction mixture was stirred at 20-23^{o}C for 48 hours, the mixture was filtered through a pad of silica gel and washed with 10.0 mL DCM, the solution was evaporated under reduced pressure. After that, NEt_3 (7.0 mmol, 972 μL) and DMAP (0.35 mmol, 42.7 mg) were added to the solution of crude product, and cooled to 0 ^{o}C. Then the acetyl chloride (5.25 mmol, 374 μL) was added dropwise, and the mixture was warmed to room temperature and stirred for further 3 hours. >19:1 d.r. was determined by ^{1}H NMR and ^{19}F NMR analysis by taking about 1.0 mL of the reaction solution. The solution was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1-3:1) to obtain the product **3aa** (1.31 g, 82% yield, 97% ee, >19:1 d.r.) .

5. The procedure for further transformation of products

Synthesis of 4a

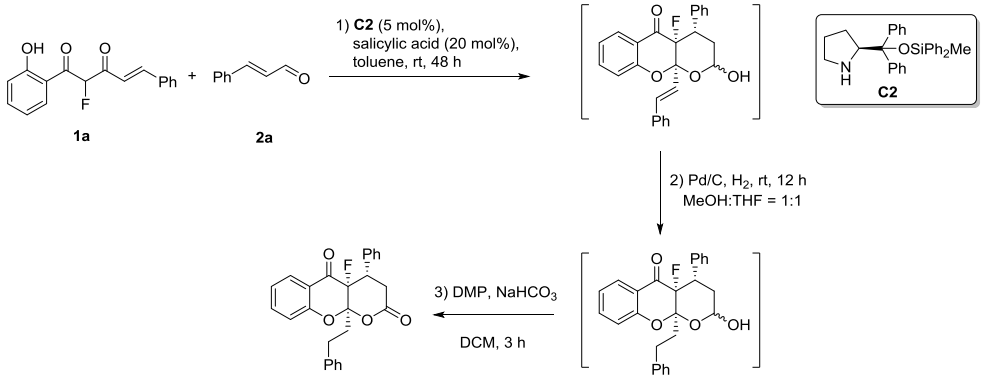


3aa, 97% ee

4a, 92% yield, 97% ee

To a solution of **3aa** (1.0 equiv., 68.7 mg) in 3 mL MeOH/THF (1:1, v/v) was added Pd/C (5% mmol), the reaction was stirred under the hydrogen atmosphere for 12 hours at room temperature, and monitored by TLC. After a simple filtration, the solvent was evaporated under reduced pressure and purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1-8:1) to obtain the product **4a** (63.5 mg, 92% yield, 97% ee) as white solid**.**

Synthesis of 4b

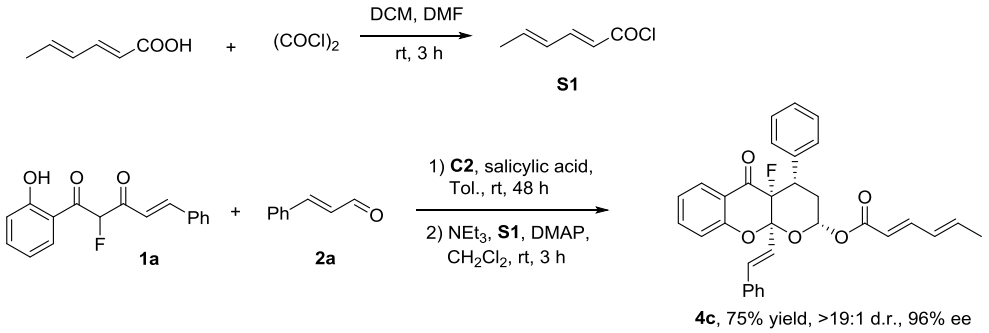


4b, 71% yield, 97% ee

To a dried round bottom flask containing 2-fluoro-1-(2-hydroxyphenyl)-5-phenylpent -4-ene-1,3-dione **1a** (56.8 mg, 0.2 mmol), salicylic acid (0.04 mmol, 5.52 mg) and **C2** (0.01 mmol, 4.5 mg) dissolved in 2.0 mL of toluene was added cinnamaldehyde **2a** (0.24 mmol, 30.2 μL) at room temperature. The reaction mixture was stirred at 20-23 ^{o}C for 48 hours, and the mixture was filtered through a pad of silica gel and washed with 10.0 mL DCM, the solution was evaporated under reduced pressure. The crude product was redissolved in 3 mL MeOH/THF (1:1, v/v), then Pd/C (5% mmol) was added subsequently. The reaction was stirred under the hydrogen atmosphere for 12 hours at room temperature, and monitored by TLC. After a simple filtration, the solvent was evaporated under reduced pressure, $NaHCO_3$ (0.4 mmol, 84 mg) and DMP (0.4 mmol, 170 mg) were added to the DCM (4 mL) solution of crude product directly at room temperature. The mixture was further stirred for 3 hours, followed by the filtration and washed with 10.0 mL DCM. The filtrate was evaporated under reduced pressure and the residue was purified by column chromatography on silica

gel with petroleum ether/ethyl acetate (20:1-10:1) to obtain the product **4b** (59.4 mg, 71% yield, 97% ee, >19:1 d.r.) as white solid.

Synthesis of 4c

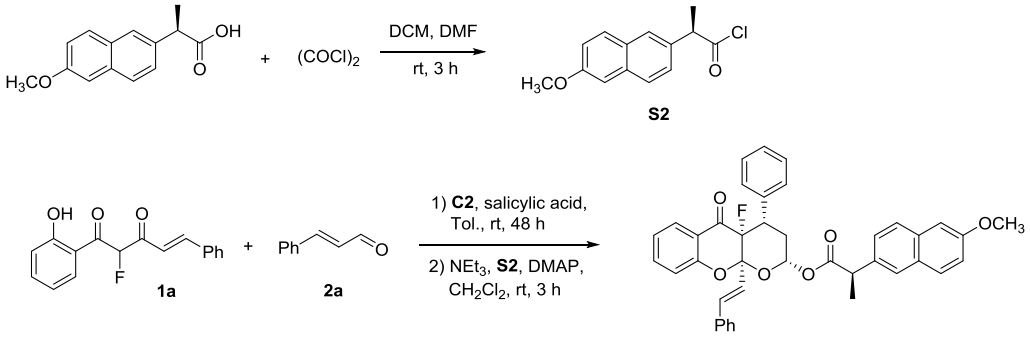


4c, 75% yield, >19:1 d.r., 96% ee

To a solution of sorbic acid (44.8 mg, 0.4 mmol) in dichloromethane (2.0 mL) was added DMF (3 μL) and oxalyl chloride (36 μL, 0.42 mmol) at room temperature, and the mixture was stirred for 2 hours to afford the acyl chloride **S1** without further purification.

To a dried round bottom flask containing 2-fluoro-1-(2-hydroxyphenyl)-5-phenylpent -4-ene-1,3-dione **1a** (0.2 mmol, 56.8 mg), salicylic acid (0.04 mmol, 5.52 mg) and **C2** (0.01 mmol, 4.5 mg) dissolved in 2.0 mL of toluene was added cinnamaldehyde **2a** (0.24 mmol, 30.2 μL) at room temperature. The reaction mixture was stirred at 20-23 ^{o}C for 48 hours, and then filtered through a pad of silica gel and washed with 10.0 mL DCM. The organosolvent was evaporated under reduced pressure with the addition of NEt_3 (0.6 mmol, 83 μL) and DMAP (0.02 mmol, 2.44 mg) in 2.0 mL DCM. After that, the mixture was added into the solution of **S1**, the mixture was stirred for 3 hours at room temperature, and monitored by TLC. The solvent was evaporated under reduced pressure and purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1-10:1) to obtain the product **4c** (76.5 mg, 75% yield, >19:1 d.r., 96% ee) as white solid.

Synthesis of 4d



4d, 90% yield, >19:1 d.r., > 99% ee

To a solution of naproxen (92 mg, 0.4 mmol) in dichloromethane (2.0 mL) was added DMF (3.0 μL) and oxalyl chloride (36 μL, 0.42 mmol) at room temperature and the

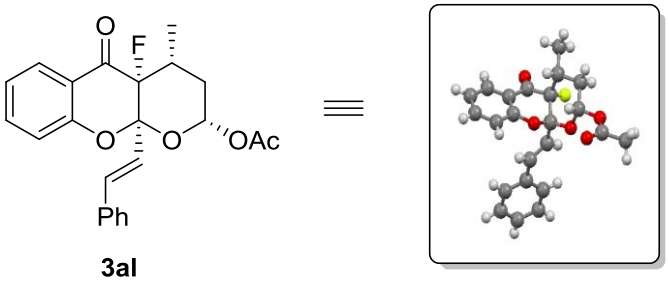
reaction mixture was stirred for 2 hours to afford the acyl chloride **S2** without further purification.

To a dried round bottom flask containing 2-fluoro-1-(2-hydroxyphenyl)-5-phenylpent -4-ene-1,3-dione **1a** (0.2 mmol, 56.8 mg), salicylic acid (0.04 mmol, 5.52 mg) and **C2** (0.01 mmol, 4.5 mg) dissolved in 2.0 mL of toluene was added cinnamaldehyde **2a** (0.24 mmol, 30.2 μL) at room temperature. The reaction mixture was stirred at 20-23 ^{o}C for 48 hours, and the mixture was filtered through a pad of silica gel and washed with 10.0 mL DCM. The solvent was evaporated under reduced pressure, followed by the addition of NEt_3 (0.6 mmol, 83 μL) and DMAP (0.02 mmol, 2.44 mg) in 2.0 mL DCM. After that, the mixture was added into the solution of **S2** at 0 ^{o}C, the mixture was stirred for 3 hours at room temperature, and monitored by TLC. Then, the solvent was evaporated under reduced pressure and purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1-10:1) to obtain the product **4d** (113.5 mg, 90% yield, > 19:1 d.r., >99% ee) as white solid.

6. X-ray crystal structure for 3al

The colourless crystal in triangle-shape, with approximate dimensions of 0.311 × 0.135 × 0.097 mm^3, was selected and mounted for the single-crystal X-ray diffraction. The data set was collected by Bruker D8 Venture Photon II diffractometer at 145(2)K equipped with micro-focus Cu radiation source (K_α = 1.54178Å). Applied with face-indexed numerical absorption correction, the structure solution was solved and refinement was processed by SHELXTL (version 6.14) program package[5-8]. The structure was analyzed by ADDSYM routine implemented in PLATON suite and no higher symmetry was suggested[9].

CCDC 2067319 (**3al**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



3al

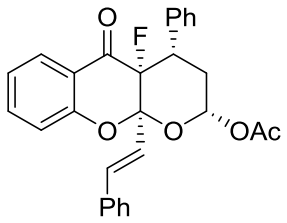
Crystallographic Data for C23 H21 F O5

Formula	C23 H21 F O5
Formula mass (amu)	396.40
Space group	P 21 21 21
a (Å)	8.5243(2)
b (Å)	14.7793(4)

c (Å)	15.8032(4)
α (deg)	90
β (deg)	90
γ (deg)	90
V (Å^3)	1990.94(9)
Z	4
λ (Å)	1.54178
T (K)	145 K
ρ_{calcd} (g cm^{-3})	1.322
μ (mm^{-1})	0.824
Transmission factors	0.858,0.954
$2\theta_{max}$ (deg)	80.744
No. of unique data, including $F_o^2 < 0$	4317
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	4148
No. of variables	262
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0331
$R_w(F_o^2)$ [b]	0.0874
Goodness of fit	1.089

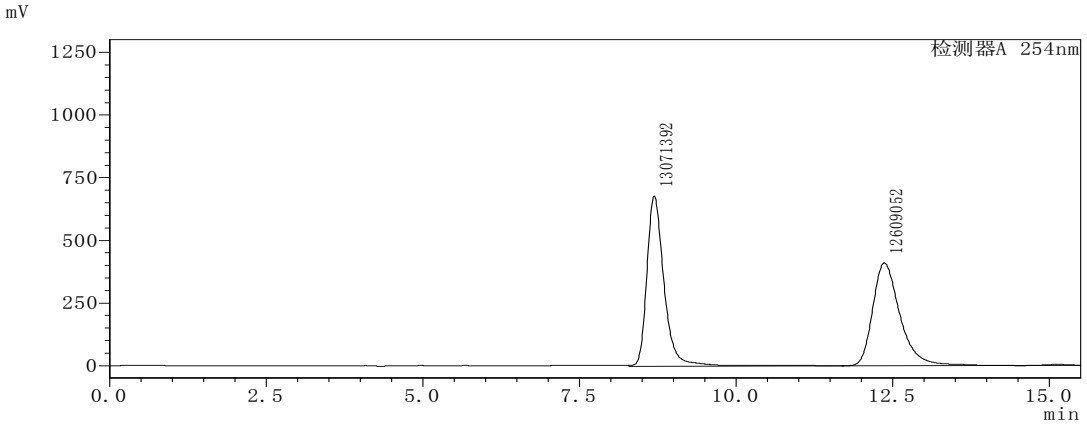
7. The analytical and spectral characterization data for the products

(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3aa)



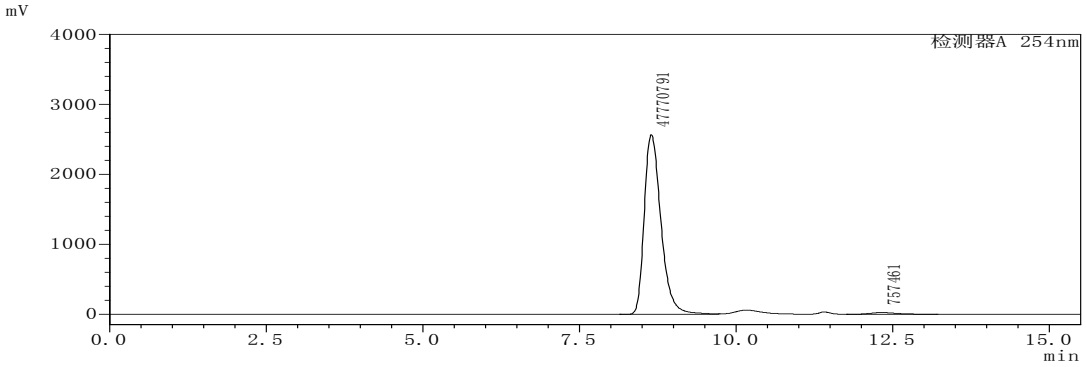
Compound **3aa**: Prepared in 0.2 mmol scale at 20-23 ^oC for 48 h. 89% yield (81.5 mg), white solid; Mp: 198.2-199.3 ^oC; >19:1 d.r., 97% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 8.65 min, *t*r (minor) = 12.33 min.
$[\alpha]^{25}_D$ = - 53.7 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.44 – 7.15 (m, 9H), 7.17 – 7.04 (m, 3H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.75 (d, *J* = 9.2 Hz, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 3.65 (ddd, *J* = 31.2, 13.6, 3.2 Hz, 1H), 2.59 (dd, *J* = 24.0, 13.2 Hz, 1H), 2.21 (s, 3H), 2.12 (d, *J* = 13.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.98 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (d, *J* = 19.5 Hz), 169.1, 157.2, 137.3, 136.8, 135.5, 135.0, 129.0, 128.7, 128.6, 128.4, 127.7, 127.3, 123.0, 119.7, 119.5, 118.2, 104.6 (d, *J* = 22.9 Hz), 92.9 (d, *J* = 204.3 Hz), 91.1, 42.6, 42.4, 29.8, 21.2. HRMS (ESI), m/z calcd for $C_{28}H_{23}FNaO_5^+$ ($[M + Na]^+$) 481.1422, found 481.1417.



racemic

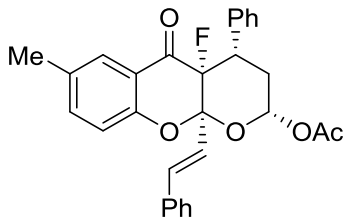
	Retention Time	Area	%Area
1	8.697	13071392	50.900
2	12.370	12609052	49.100



enantio-enriched

	Retention Time	Area	%Area
1	8.651	47770791	98.439
2	12.330	757461	1.561

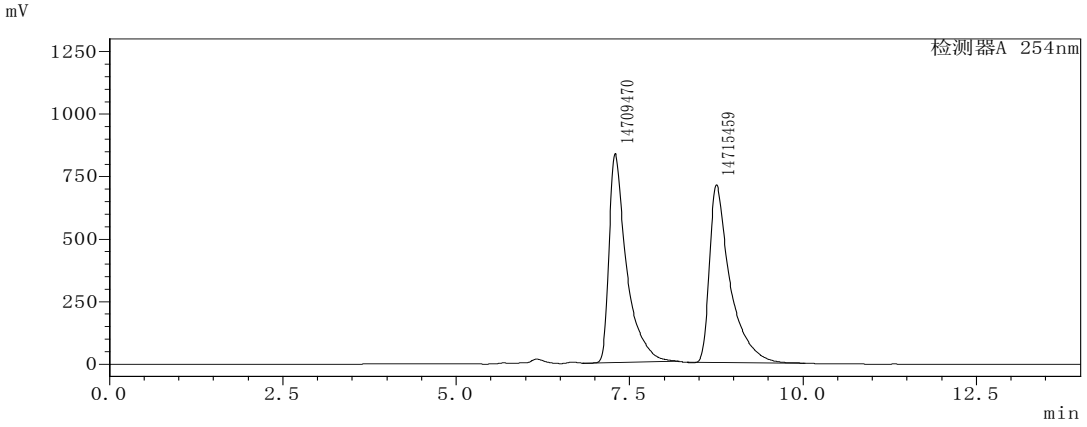
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-7-methyl-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ba)



Compound **3ba**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 83% yield (78.4 mg), white solid; Mp: 178.0-178.3 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 7.29 min, *t*r (major) = 8.73 min. $[\alpha]^{25}_{D}$ = - 36.6 (c = 1.0 in CH_2Cl_2).

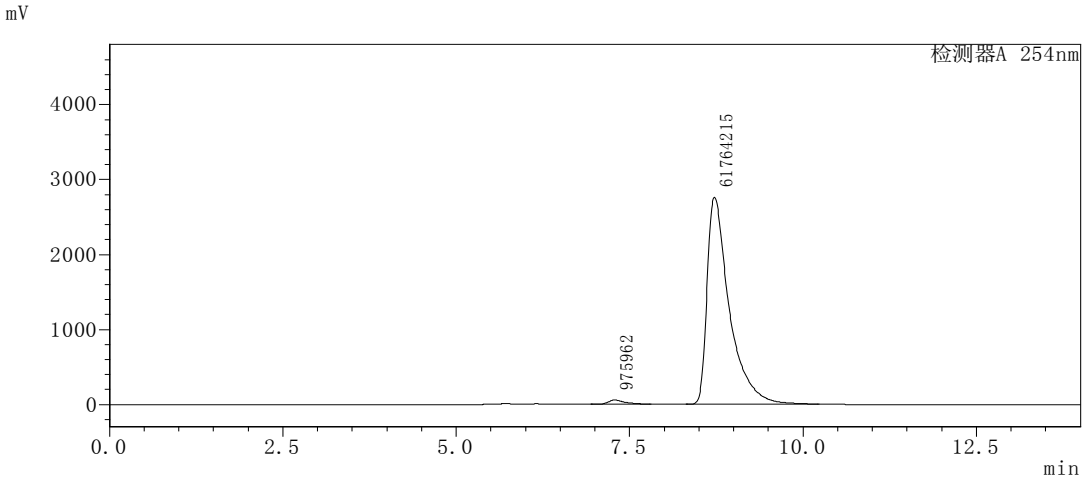
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.27 – 7.20 (m, 3H), 7.19 – 7.13 (m, 5H), 7.08 – 6.98 (m, 3H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.66 (dd, *J* = 10.4, 1.6 Hz, 1H), 6.17 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.56 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.49 (td, *J* = 13.2, 10.8 Hz, 1H), 2.23 (s, 3H), 2.12 (s, 3H), 2.05 – 2.00 (m, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.04 (s, 1F). ^{13}C NMR (150 MHz,$CDCl_3$) δ 189.0 (d, *J* = 17.2 Hz), 169.2, 155.2, 138.4, 136.7 (d, *J* = 1.9 Hz), 135.6, 135.1, 132.7, 129.0, 128.7, 128.6, 128.4, 127.3, 127.2, 119.9 (d, *J* = 4.5 Hz), 119.1, 118.0, 104.5 (d,

J = 22.6 Hz), 93.0 (d, *J* = 203.9 Hz), 91.1, 91.1, 42.5 (d, *J* = 15.3 Hz), 29.9, 21.2 (d, *J* = 5.1 Hz), 20.5 (d, *J* = 5.2 Hz). HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_5^+$ ([M + Na]$^+$) 495.1578, found 495.1586.



racemic

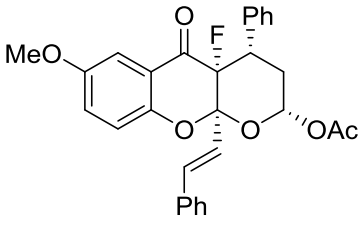
	Retention Time	Area	%Area
1	7.293	14709470	49.990
2	8.754	14715459	50.010



enantio-enriched

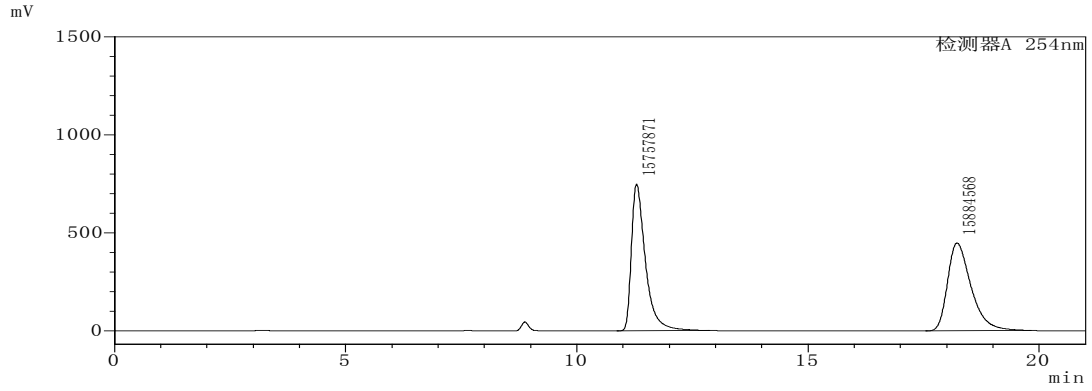
	Retention Time	Area	%Area
1	7.285	975962	1.556
2	8.725	61764215	98.444

(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-7-methoxy-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ca)



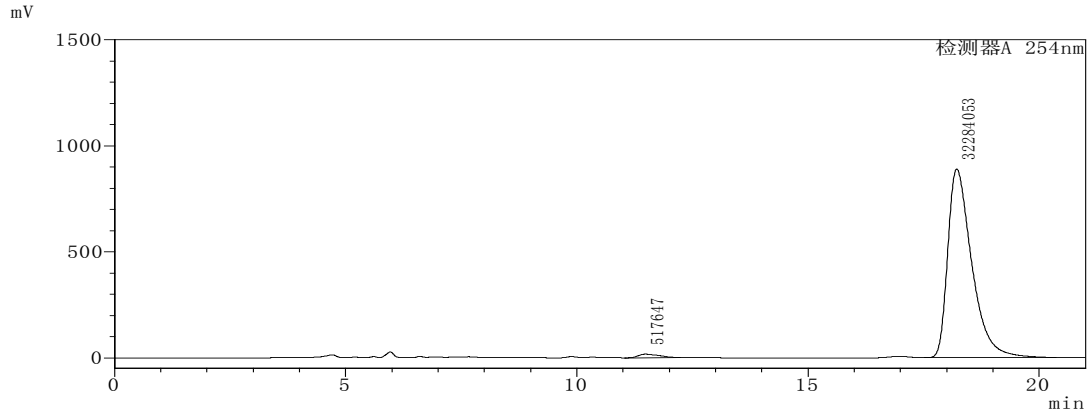
Compound **3ca**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 77% yield (75.2 mg), white solid; Mp: 196.2-197.0 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 11.48 min, *t*r (major) = 18.22 min. $[\alpha]^{25}_D$ = - 34.3 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.8 Hz, 1H), 7.19 (m, 8H), 7.03 (d, *J* = 1.6 Hz, 2H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.65 (dd, *J* = 10.4, 2.0 Hz, 1H), 6.62 – 6.53 (m, 2H), 6.19 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.83 (s, 3H), 3.53 (ddd, *J* = 31.2, 13.6, 3.6 Hz, 1H), 2.50 (td, *J* = 13.2, 10.8 Hz, 1H), 2.13 (s, 3H), 2.01 (dt, *J* = 13.2, 3.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.17 (s, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.3 (d, *J* = 17.5 Hz), 169.2, 167.1, 159.3, 136.6, 135.7, 135.1, 129.3, 129.0, 128.8, 128.7, 128.6, 128.3, 127.3, 120.1 (d, *J* = 5.7 Hz), 112.9, 111.4, 104.6 (d, *J* = 22.7 Hz), 101.5 (d, *J* = 6.6 Hz), 92.5 (d, *J* = 203.2 Hz), 91.0 (d, *J* = 6.0 Hz), 56.1 (d, *J* = 6.9 Hz), 42.7 (d, *J* = 42.0 Hz), 29.9, 21.2 (d, *J* = 4.7 Hz). HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_6^+$ ([M + Na]$^+$) 511.1527, found 511.1516.



racemic

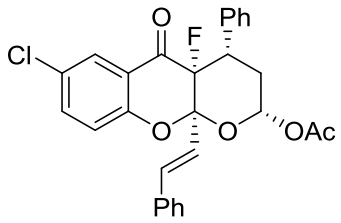
	Retention Time	Area	%Area
1	11.295	15757871	49.800
2	18.225	15884568	50.200



enantio-enriched

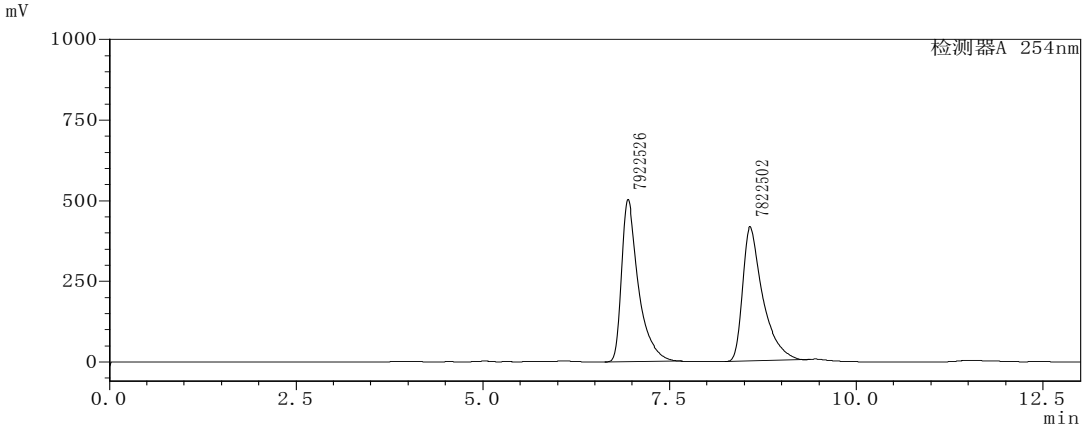
	Retention Time	Area	%Area
1	11.483	517647	1.578
2	18.219	32284053	98.422

(2S,4S,4aS,10aR)-7-chloro-4a-fluoro-5-oxo-4-phenyl-10a-((E)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3da)



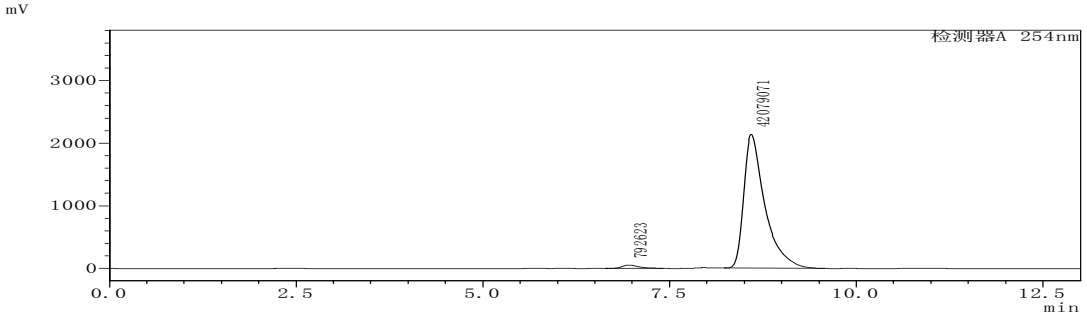
Compound **3da**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 75% yield (73.8 mg), white solid; Mp: 215.8-216.3 ^{o}C; >19:1 d.r., 96% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 6.96 min, *t*r (major) = 8.60 min.
$[\alpha]^{25}_{D}$ = - 96.4 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz,$CDCl_3$) δ 7.69 (d, *J* = 2.2 Hz, 1H), 7.56 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.32 (t, *J* = 2.8 Hz, 3H), 7.28 - 7.20 (m, 6H), 7.10 (m, 2H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.73 (d, *J* = 8.8 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 3.61 (ddd, *J* = 31.2, 13.6, 3.6 Hz, 1H), 2.59 (dd, *J* = 24.0, 13.2 Hz, 1H), 2.21 (s, 3H), 2.18 – 1.99 (m, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.78 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.8 (d, *J* = 17.9 Hz) , 169.0, 155.6, 137.0, 135.0, 134.7, 129.1, 128.7, 128.6, 128.5, 128.4, 127.2, 126.8, 120.2, 119.8, 119.1, 104.8 (d, *J* = 22.6 Hz), 92.7 (d, *J* = 204.4 Hz), 90.8, 42.3 (d, *J* = 20.5 Hz), 29.6, 21.1. HRMS (ESI), m/z calcd for $C_{28}H_{22}ClFNaO_5^+$ ($[M + Na]^+$) 515.1032, found 515.1036.



racemic

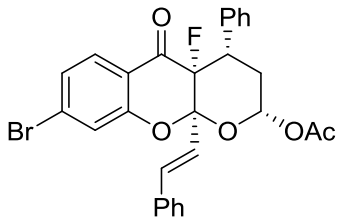
	Retention Time	Area	%Area
1	6.942	7922526	50.318
2	8.578	7822502	49.682



enantio-enriched

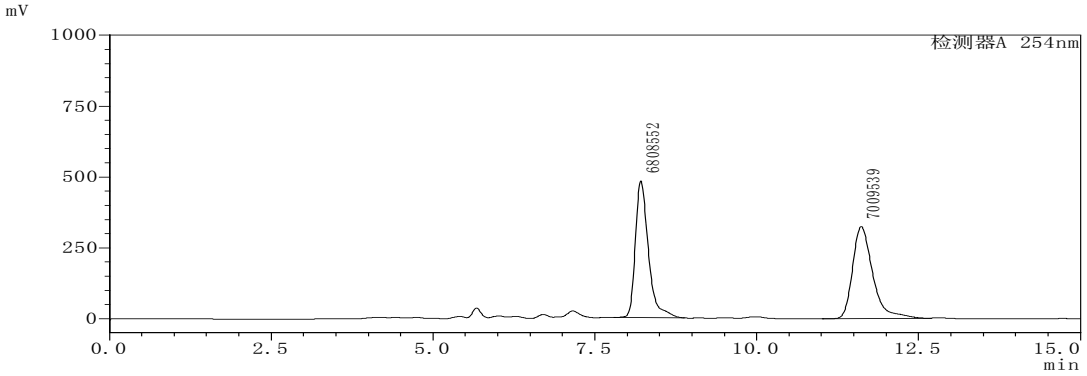
	Retention Time	Area	%Area
1	6.956	792623	1.849
2	8.596	42079071	98.151

(2*S*,4*S*,4a*S*,10a*R*)-8-bromo-4a-fluoro-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ea)



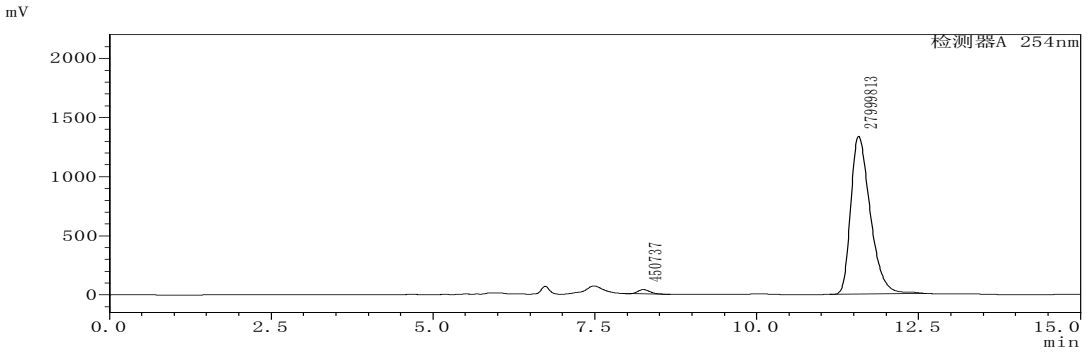
Compound **3ea**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 71% yield (76.1 mg), white solid; Mp: 188.4-189.2 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 8.25 min, *t*r (major) = 11.58 min.
$[\alpha]^{25}_{D}$ = -13.5 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.3 Hz, 1H), 7.46 (s, 1H), 7.30 (d, *J* = 3.2 Hz, 9H), 7.08 (d, *J* = 2.0 Hz, 2H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.70 (d, *J* = 9.6 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 3.70 – 3.48 (m, 1H), 2.58 (dd, *J* = 24.0, 12.8 Hz, 1H), 2.21 (s, 3H), 2.11 (d, *J* = 13.0 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.66 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.1 (d, *J* = 17.7 Hz), 169.1, 157.4, 137.1, 135.2, 134.8, 131.9, 129.2, 128.8, 128.7, 128.5, 127.4, 126.8, 126.8, 121.6, 121.5, 119.3, 119.2, 118.3, 105.0 (d, *J* = 22.7 Hz), 92.7 (d, *J* = 204.4 Hz), 91.0 (d, *J* = 8.9 Hz), 42.5 (d, *J* = 23.5 Hz), 29.8, 29.8, 21.3, 21.3. HRMS (ESI), m/z calcd for $C_{28}H_{22}BrFNaO_5^+$ ([M + Na]$^+$) 559.0527 (561.0506 for Br^{81}), found 559.0529 (561.0508 for Br^{81}).



racemic

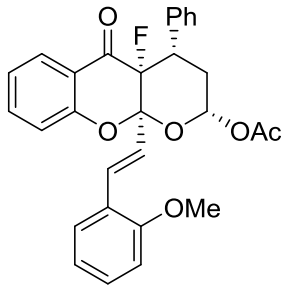
	Retention Time	Area	%Area
1	8.210	6808552	49.273
2	11.614	7009539	50.727



enantio-enriched

	Retention Time	Area	%Area
1	8.247	450737	1.584
2	11.575	2799983	98.416

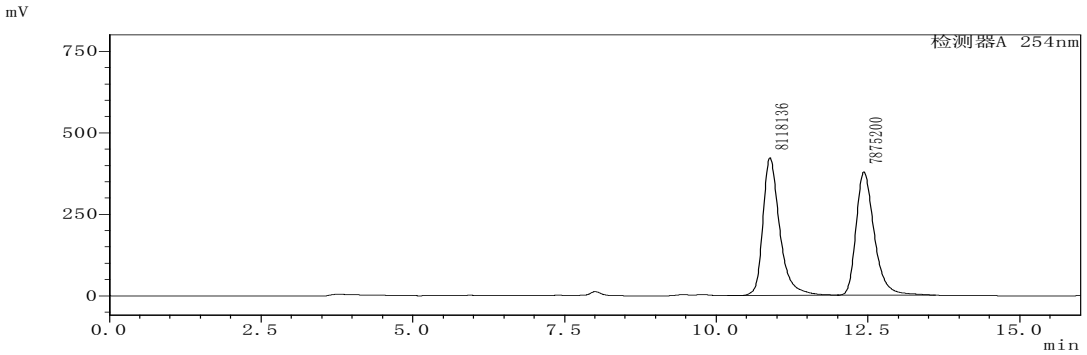
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-10a-((*E*)-2-methoxystyryl)-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3fa)



Compound **3fa**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 77% yield (75.2 mg), white solid; Mp: 169.9- 170.9 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IF column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) =10.96 min, *t*r (major) = 12.45 min.

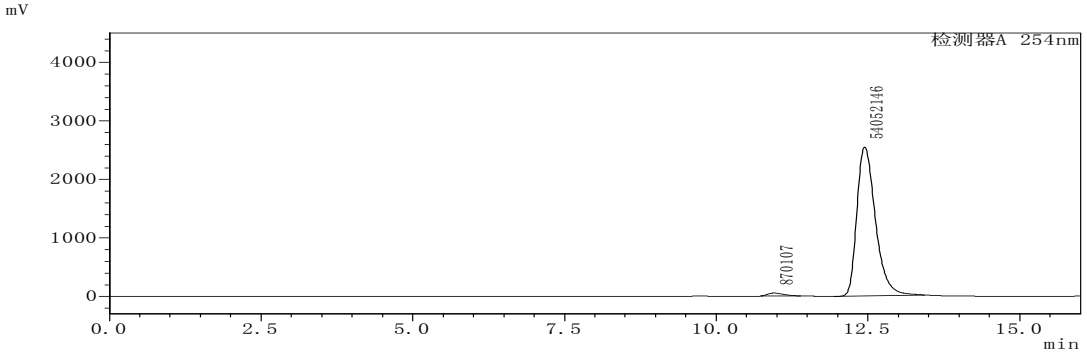
$[\alpha]^{25}_{D}$ = - 48.1 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.30 (s, 3H), 7.20 (dd, *J* = 20.2, 9.6 Hz, 4H), 7.10 (s, 3H), 6.92 – 6.68 (m, 3H), 6.35 (d, *J* = 16.2 Hz, 1H), 3.71 (s, 3H), 3.62 (dd, *J* = 13.2, 2.8 Hz, 1H), 2.59 (dd, *J* = 24.0, 12.8 Hz, 1H), 2.20 (s, 3H), 2.12 (d, *J* = 12.8 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.22 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (d, *J* = 17.3 Hz), 169.2, 157.5, 157.4, 137.1, 135.6, 132.2, 130.1, 128.7, 128.3, 127.9, 127.6, 124.1, 122.8, 120.5, 119.9, 119.5, 118.2, 111.0, 104.9 (d, *J* = 22.2 Hz), 93.0 (d, *J* = 204.0 Hz), 91.1 (d, *J* = 5.0 Hz), 55.5 (d, *J* = 8.1 Hz), 42.3 (d, *J* = 21.0 Hz), 29.8, 21.3. HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_6^+$ ([M + Na]$^+$) 511.1527, found 511.1524.



racemic

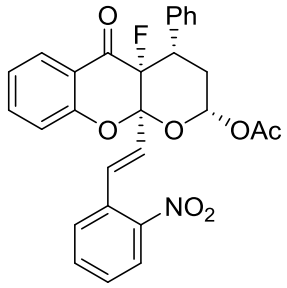
	Retention Time	Area	%Area
1	10.866	8118136	50.759
2	12.433	7875200	49.241



enantio-enriched

	Retention Time	Area	%Area
1	10.955	870107	1.584
2	12.446	54052146	98.416

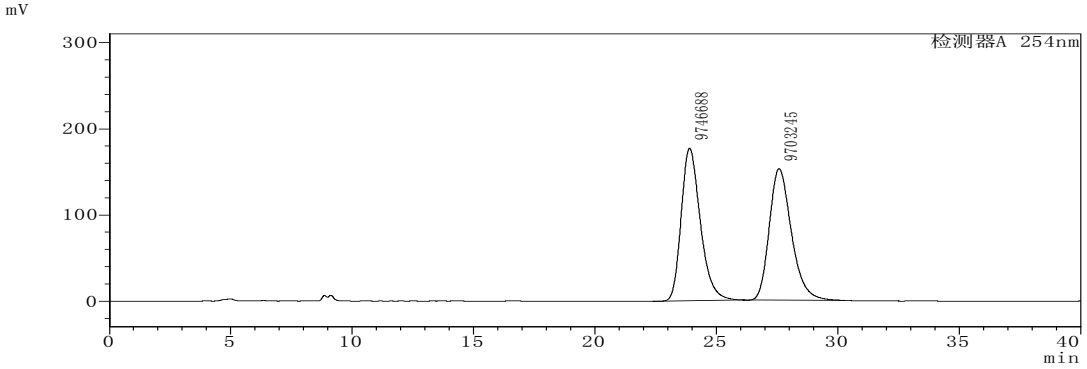
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-10a-((*E*)-2-nitrostyryl)-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ga)



Compound **3ga**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 67% yield (67.4 mg), white solid; Mp: 202.4- 204.3 ^{o}C; >19:1 d.r., 94% *ee*. HPLC (chiral IC column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 24.27 min, *t*r (minor) = 28.27 min.

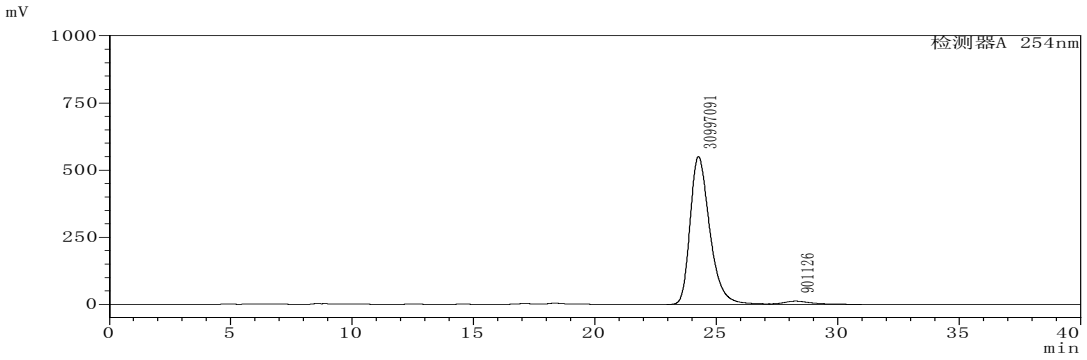
$[\alpha]^{25}_{D}$ = - 21.7 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.57 – 7.35 (m, 4H), 7.28 (d, *J* = 8.8 Hz, 4H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.09 (s, 2H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.25 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.68 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.59 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.21 (s, 3H), 2.13 (dd, *J* = 10.0, 3.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.15 (d, *J* = 6.7 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (d, *J* = 17.2 Hz), 169.0, 157.1, 147.8, 137.6, 135.3, 133.5, 132.8, 131.1, 129.4, 129.1, 128.7, 128.7, 128.4, 127.6, 124.8, 124.6, 123.3, 119.3, 118.3, 104.1 (d, *J* = 17.3 Hz), 92.8 (d, *J* = 203.8 Hz), 91.1, 42.4 (d, *J* = 20.6 Hz), 29.8, 21.2. HRMS (ESI), m/z calcd for $C_{28}H_{22}FNNaO_7^+$ ([M + Na]$^+$) 526.1273, found 526.1273.



racemic

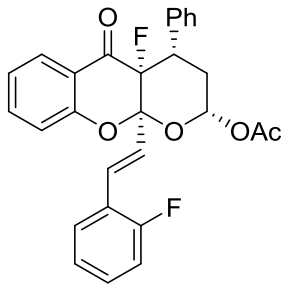
	Retention Time	Area	%Area
1	23.900	9746688	50.112
2	27.585	9703245	49.888



enantio-enriched

	Retention Time	Area	%Area
1	24.267	30997091	97.175
2	28.268	901126	2.825

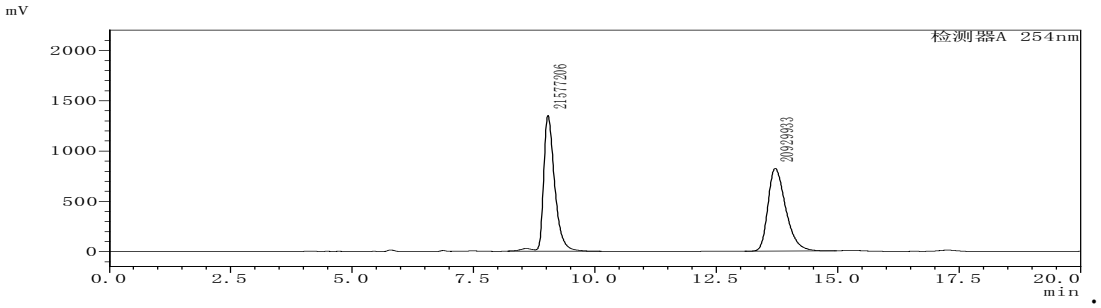
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-10a-((*E*)-2-fluorostyryl)-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ha)



Compound **3ha**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 83% yield (81.9 mg), white solid; Mp: 181.1- 182.2 ^{o}C; >19:1 d.r., 96% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 9.16 min, *t*r (major) = 13.76 min.

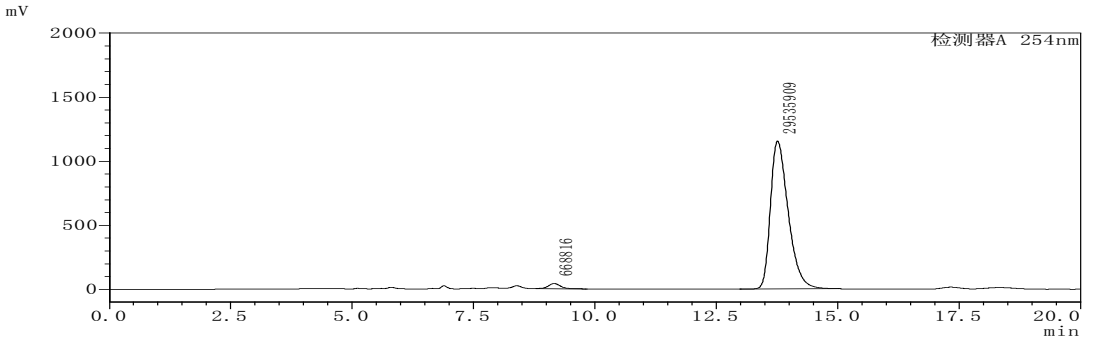
$[\alpha]^{25}_{D}$ = - 59.2 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.37 – 7.04 (m, 10H), 6.97 (dt, *J* = 18.8, 8.4 Hz, 2H), 6.74 (d, *J* = 10.0 Hz, 1H), 6.35 (d, *J* = 16.2 Hz, 1H), 3.64 (ddd, *J* = 31.2, 13.2, 2.8 Hz, 1H), 2.57 (dd, *J* = 24.0, 12.8 Hz, 1H), 2.19 (s, 3H), 2.10 (d, *J* = 13.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -116.50 (d, *J* = 4.6 Hz, 1F), -191.07 (d, *J* = 4.7 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (d, *J* = 17.4 Hz), 169.1, 160.7 (d, *J* = 251.7 Hz), 157.2, 137.4, 135.5, 130.5 (d, *J* = 8.7 Hz), 129.5, 128.8, 128.4, 128.0, 128.0, 127.7, 124.2 (d, *J* =3.3 Hz), 123.1, 122.9 (d, *J* = 17.4 Hz), 121.9, 119.4, 118.2, 116.1, 115.8, 104.5 (d, *J* = 22.6 Hz), 92.8 (d, *J* = 202.9 Hz), 91.1 (d, *J* = 4.6 Hz), 42.5 (d, *J* = 20.6 Hz), 29.8, 21.2 (d, *J* = 3.8 Hz). HRMS (ESI), m/z calcd for $C_{28}H_{22}F_2NaO_5^+$ ($[M + Na]^+$) 499.1328, found 499.1322



racemic

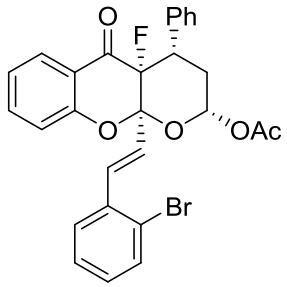
	Retention Time	Area	%Area
1	9.035	21577206	50.761
2	13.716	20929933	49.239



enantio-enriched

	Retention Time	Area	%Area
1	9.157	668816	2.214
2	13.763	29535909	97.786

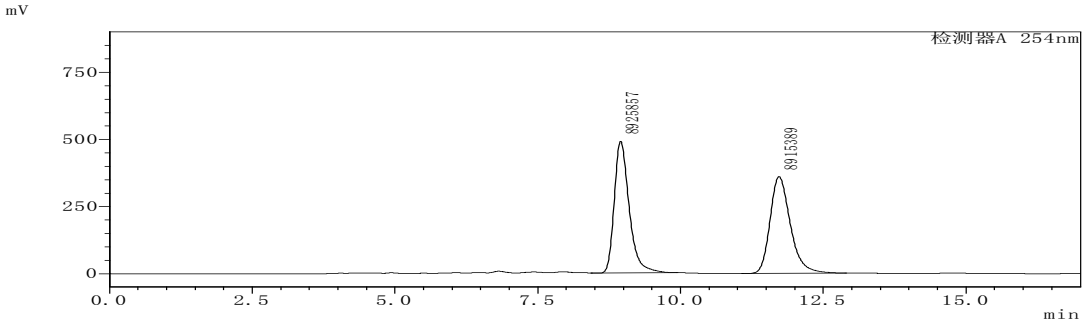
(2*S*,4*S*,4a*S*,10a*R*)-10a-((*E*)-2-bromostyryl)-4a-fluoro-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ia)



Compound **3ia**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 91% yield (97.6 mg), white solid; Mp: 232.3- 234.3 ^{o}C; >19:1 d.r., 95% *ee*. HPLC (chiral IC column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 8.87 min, *t*r (minor) = 11.62 min.

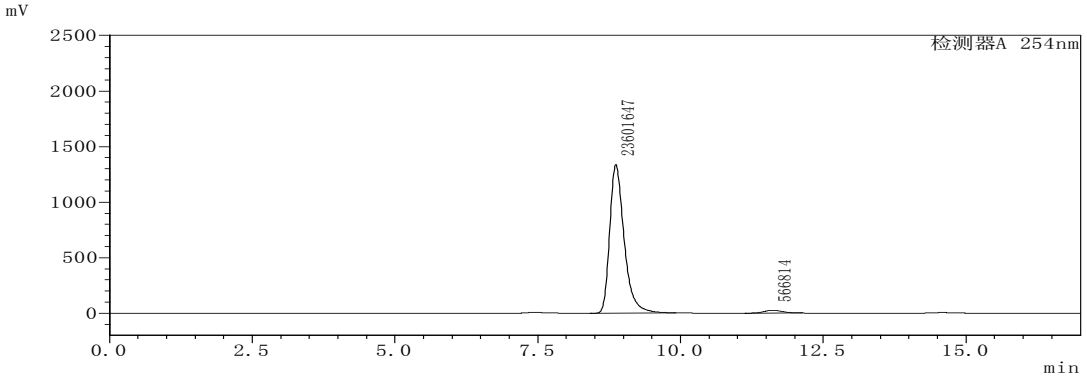
$[\alpha]^{25}_{D}$ = -57.7 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.41 (dd, *J* = 21.6, 7.6 Hz, 2H), 7.35 – 7.24 (m, 5H), 7.23 – 7.01 (m, 5H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.21 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.68 (ddd, *J* = 31.6, 13.6, 3.2 Hz, 1H), 2.60 (dd, *J* = 24.0, 13.2 Hz, 1H), 2.21 (s, 3H), 2.13 (dd, *J* = 10.0, 2.8 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.25 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7 (d, *J* = 17.3 Hz), 169.1, 157.3, 137.3, 135.8, 135.5, 135.1, 133.0, 130.2, 128.8, 128.4, 127.7, 127.6, 127.5, 124.5, 123.2, 122.2, 119.5, 118.3, 104.5 (d, *J* = 22.4 Hz), 92.9 (d, *J* = 203.8 Hz), 91.2, 91.1, 42.5 (d, *J* = 22.5 Hz), 29.9, 21.2 (d, *J* = 4.4 Hz). HRMS (ESI), m/z calcd for $C_{28}H_{22}BrFNaO_5^+$ ($[M + Na]^+$) 559.0527 (561.0506 for Br^{81}), found 559.0528 (561.0511 for Br^{81}).



racemic

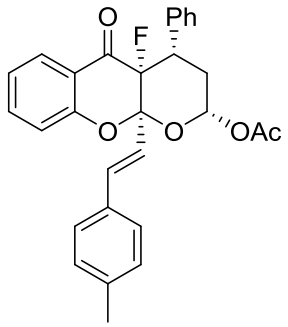
	Retention Time	Area	%Area
1	8.952	8925857	50.029
2	11.725	8915389	49.971



enantio-enriched

	Retention Time	Area	%Area
1	8.867	23601647	97.655
2	11.615	566814	2.345

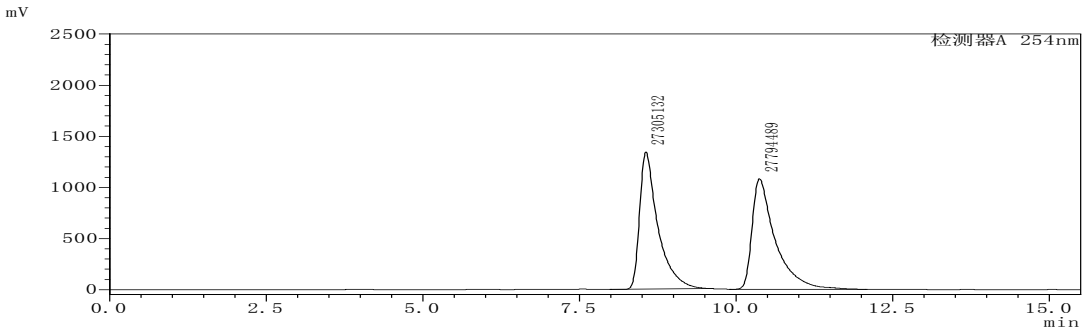
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-10a-((*E*)-4-methylstyryl)-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ja)



Compound **3ja**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 70% yield (66.1 mg), white solid; Mp: 212.8- 213.3 ^{o}C; >19:1 d.r., 98% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 8.57 min, *t*r (major) = 10.37 min.

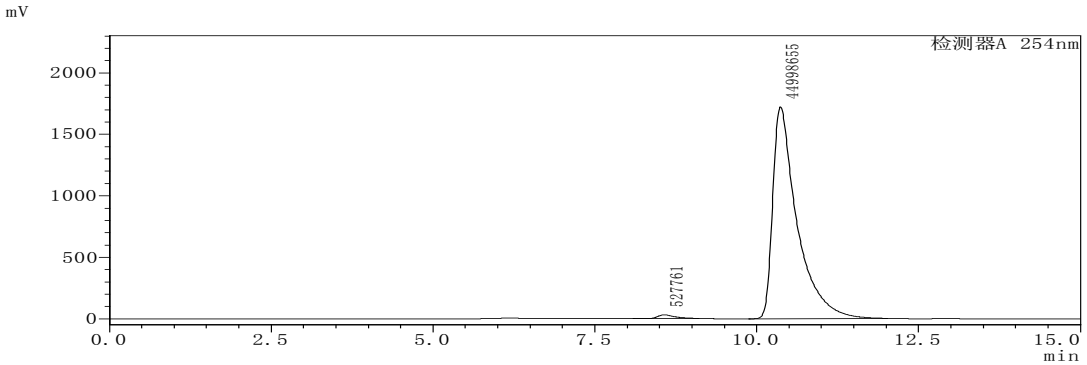
$[\alpha]^{25}_{D}$ = - 42.8 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.63 (m, 1H), 7.36 – 7.21 (m, 4H), 7.20 – 7.01 (m, 7H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.82 – 6.68 (m, 1H), 6.22 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.65 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.58 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.28 (s, 3H), 2.21 (s, 3H), 2.15 – 2.05 (m, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -191.02 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (d, *J* = 17.3 Hz), 169.2, 157.2, 139.1, 137.2, 136.7, 136.7, 135.5, 132.2, 129.3, 128.7, 128.4, 127.6, 127.2, 123.0, 119.4, 118.4, 118.2, 104.7 (d, *J* = 22.6 Hz), 92.9 (d, *J* = 203.9 Hz), 91.1, 42.5 (d, *J* = 20.5 Hz), 29.8, 21.4, 21.2. HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_5^+$ ([M + Na]$^+$) 495.1578, found 495.1576.



racemic

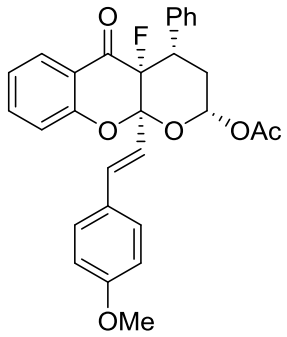
	Retention Time	Area	%Area
1	8.565	27305132	49.556
2	10.378	27794489	50.444



enantio-enriched

	Retention Time	Area	%Area
1	8.573	527761	1.159
2	10.367	44998655	98.841

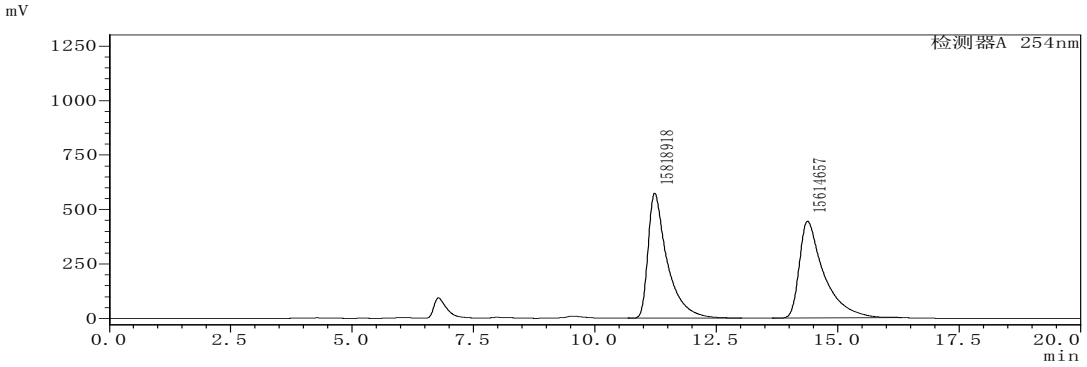
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-10a-((*E*)-4-methoxystyryl)-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ka)



Compound **3ka**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 82% yield (80.0 mg), white solid; Mp: 103.1- 104.3 ^{o}C; >19:1 d.r., 98% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 11.28 min, *t*r (major) = 14.43 min.

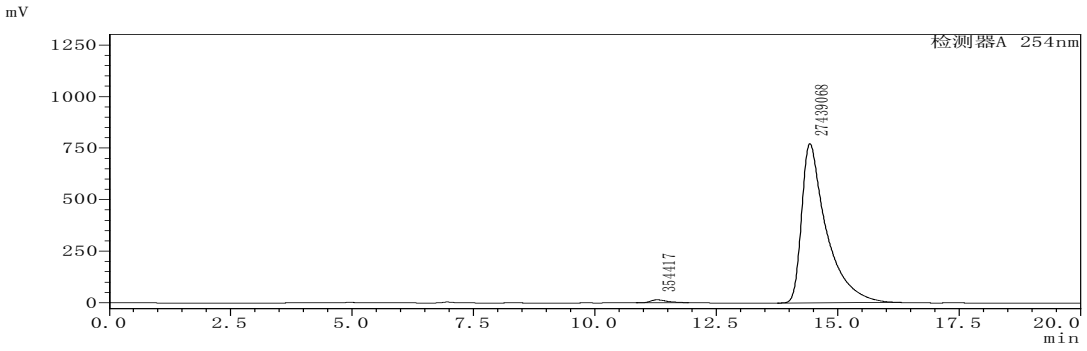
$[\alpha]^{25}_{D}$ = -33.9 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.2 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.38 – 7.16 (m, 6H), 7.12 (d, *J* = 7.6 Hz, 3H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.75 (m, 3H), 6.13 (d, *J* = 16.0 Hz, 1H), 3.75 (m, 3H), 3.64 (ddd, *J* = 31.2, 13.6, 3.2 Hz, 1H), 2.58 (dd, *J* = 24.0, 13.2 Hz, 1H), 2.21 (s, 3H), 2.11 (d, *J* = 13.2 Hz, 1H). ^{19}F NMR (565 MHz,) δ -191.05 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (d, *J* = 17.4 Hz), 169.0, 160.2, 157.1, 137.1, 136.2 (d, *J* = 1.9 Hz), 135.4, 128.6, 128.6, 128.2, 127.6, 127.5, 122.8, 119.3, 118.0, 117.1, 113.9, 104.6 (d, *J* = 22.8 Hz), 93.0 (d, *J* = 203.8 Hz), 91.1, 55.2, 42.5 (d, *J* = 20.6 Hz), 29.7, 21.1. HRMS (ESI), m/z calcd for $C_{29}H_{26}FO_6^+$ ($[M + H]^+$) 489.1708, found 489.1698.



racemic

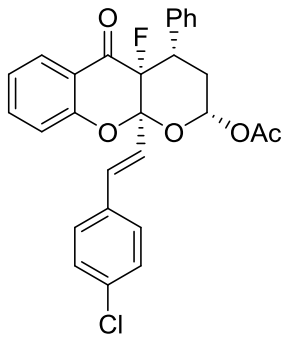
	Retention Time	Area	%Area
1	11.233	15818918	50.325
2	14.382	15614657	49.675



enantio-enriched

	Retention Time	Area	%Area
1	11.279	354417	1.275
2	14.428	27439068	98.725

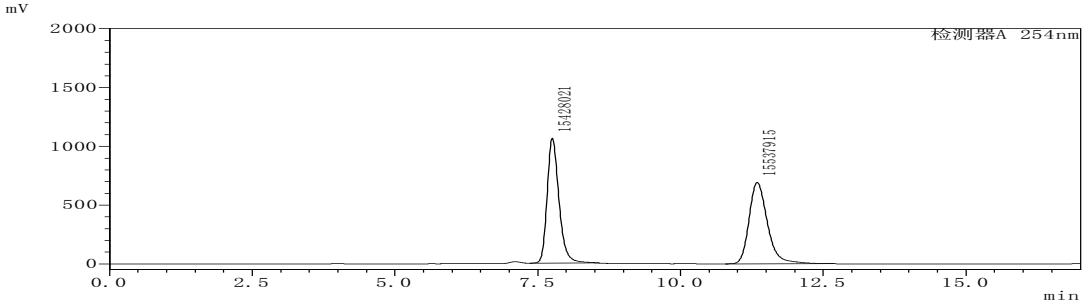
(2*S*,4*S*,4a*S*,10a*R*)-10a-((*E*)-4-chlorostyryl)-4a-fluoro-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3la)



Compound **3la**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 76% yield (74.8 mg), white solid; Mp: 220.0- 202.3 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IC column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 7.77 min, *t*r (minor) = 11.40 min.

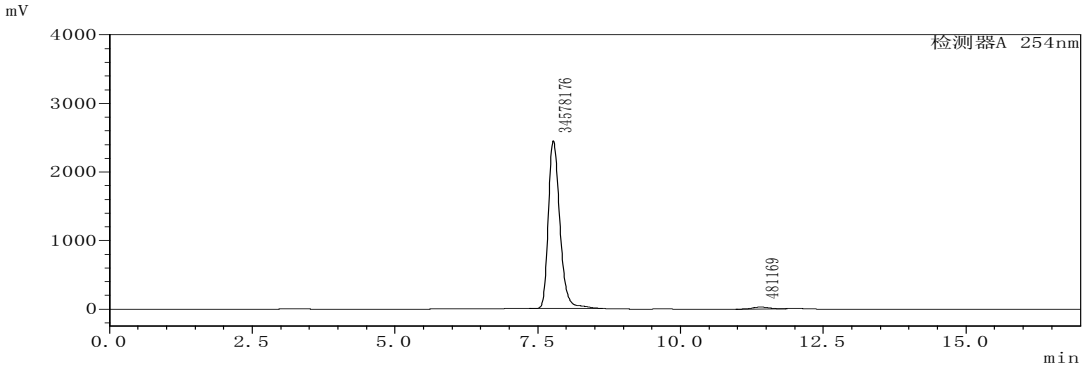
$[\alpha]^{25}_{D}$ = - 39.6 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.62 (m, 1H), 7.60 – 7.48 (m, 1H), 7.26 – 7.19 (m, 3H), 7.20 – 7.08 (m, 5H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.00 (m , 2H), 6.81 (d, *J* = 16.1 Hz, 1H), 6.70 – 6.63 (m, 1H), 6.15 (dd, *J* = 16.1, 1.1 Hz, 1H), 3.56 (ddd, *J* = 31.4, 13.5, 3.6 Hz, 1H), 2.50 (dd, *J* = 23.8, 13.2 Hz, 1H), 2.13 (s, 3H), 2.06 – 2.00 (m, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.99 (d, *J* = 105.7 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (d, *J* = 17.4 Hz), 169.1, 157.1, 137.4, 135.6, 135.4, 134.8, 133.5, 128.8, 128.8, 128.7, 128.5, 128.5, 127.7, 123.1, 120.4 (d, *J* = 4.0 Hz), 119.4, 118.2, 104.5 (d, *J* = 22.6 Hz), 92.8 (d, *J* = 204.1 Hz), 91.1 (d, *J* = 5.6 Hz), 42.5 (d, *J* = 21.3 Hz), 29.8, 21.2 (d, *J* = 4.9 Hz). HRMS (ESI), m/z calcd for $C_{28}H_{22}ClFNaO_5^+$ ([M + Na]$^+$) 515.1032, found 515.1041.



racemic

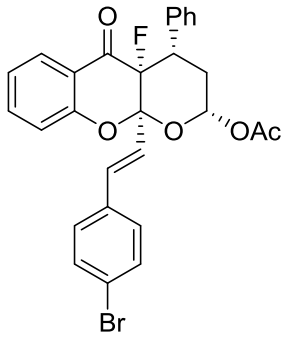
	Retention Time	Area	%Area
1	7.756	15428021	49.823
2	11.343	15537915	50.177



enantio-enriched

	Retention Time	Area	%Area
1	7.774	34578176	98.628
2	11.403	481169	1.372

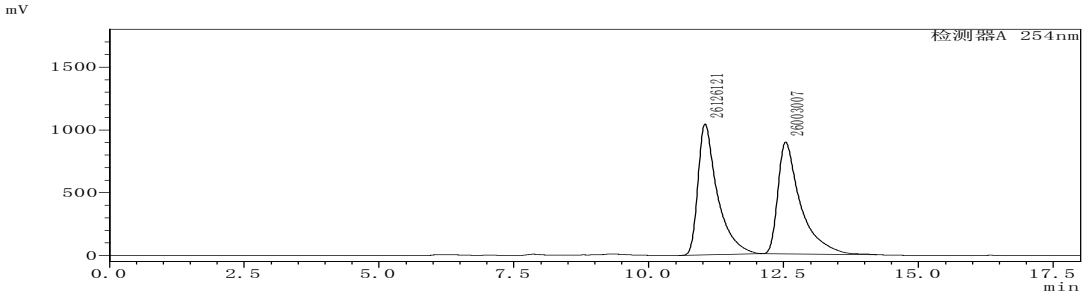
(2*S*,4*S*,4a*S*,10a*R*)-10a-((*E*)-4-bromostyryl)-4a-fluoro-5-oxo-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ma)



Compound **3ma**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 76% yield (64.3 mg), white solid; Mp: 234.0- 235.3 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 11.02 min, *t*r (major) = 12.50 min.

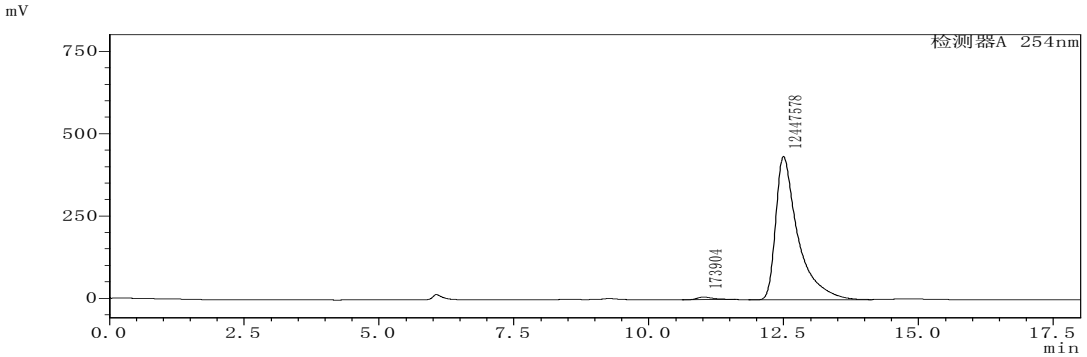
$[\alpha]^{25}_{D}$ = - 46.2 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.29 (m, 3H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.17 – 7.03 (m, 5H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.74 (d, *J* = 9.6 Hz, 1H), 6.24 (d, *J* = 16.0 Hz, 1H), 3.64 (ddd, *J* = 31.2, 13.2, 3.2 Hz, 1H), 2.58 (dd, *J* = 23.9, 13.2 Hz, 1H), 2.21 (s, 3H), 2.11 (d, *J* = 13.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.88 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (d, *J* = 17.3 Hz), 169.1, 157.1, 137.4, 135.7, 135.7, 135.4, 134.0, 131.8, 128.8, 128.8, 128.7, 128.5, 127.7, 123.2, 123.1, 120.5, 119.4, 118.2, 104.5 (d, *J* = 22.7 Hz), 92.8 (d, *J* = 203.9 Hz), 91.6, 42.5 (d, *J* = 20.6 Hz), 29.8, 21.2. HRMS (ESI), m/z calcd for $C_{28}H_{22}BrFNaO_5^{+}$ ([M + Na]$^{+}$) 559.0527 (561.0506 for Br^{81}), found 559.0535 (561.0519 for Br^{81}).



racemic

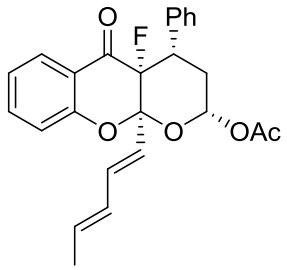
	Retention Time	Area	%Area
1	11.043	26126121	50.118
2	12.537	26003007	49.882



enantio-enriched

	Retention Time	Area	%Area
1	11.018	173904	1.378
2	12.498	12447578	98.622

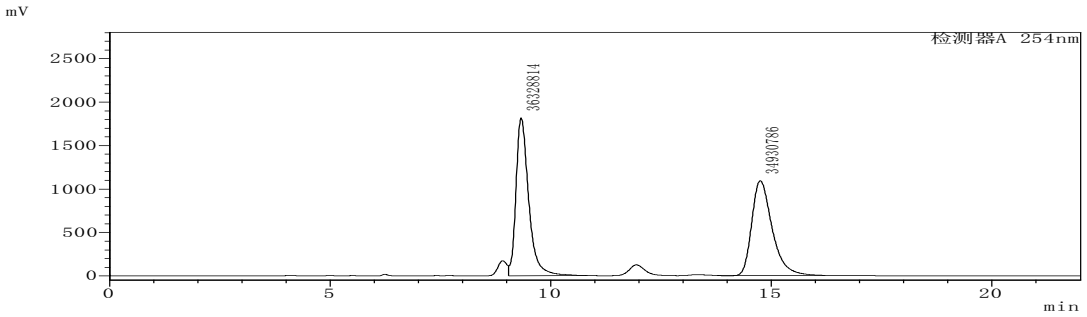
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-10a-((1*E*,3*E*)-penta-1,3-dien-1-yl)-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3na)



Compound **3na**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 60% yield (54.2 mg), white solid; Mp: 78.5-80.3 ^{o}C, >19:1 d.r., 97% *ee*. HPLC (chiral IC column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 9.35 min, *t*r (minor) = 14.73 min.

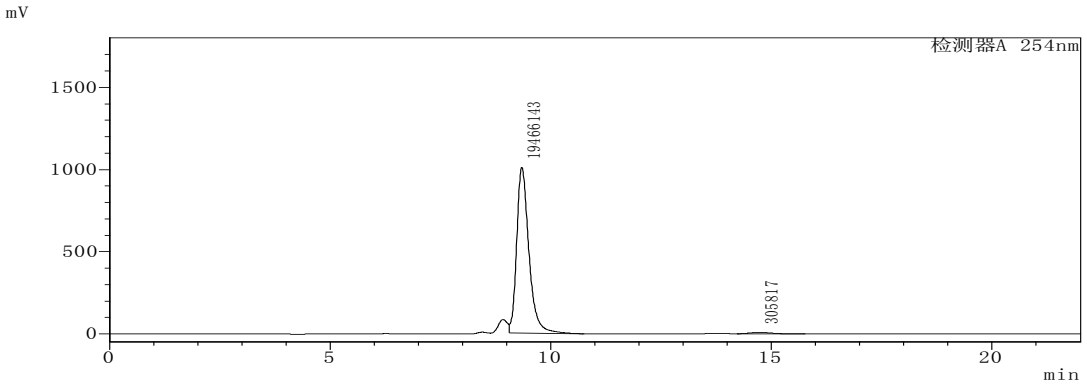
$[\alpha]^{25}_{D}$ = -240.2 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.66 – 7.50 (m, 1H), 7.27 (dd, *J* = 6.8, 2.8 Hz, 3H), 7.18 (d, *J* = 8.2 Hz, 1H), 7.15 – 6.98 (m, 3H), 6.68 (dd, *J* = 10.2, 1.6 Hz, 1H), 6.49 (dd, *J* = 15.6, 10.4 Hz, 1H), 5.98 – 5.83 (m, 1H), 5.73 (td, *J* = 13.6, 6.8 Hz, 1H), 5.61 (d, *J* = 15.6 Hz, 1H), 3.59 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.62 – 2.44 (m, 1H), 2.19 (s, 3H), 2.14 – 2.00 (m, 1H), 1.68 (d, *J* = 6.8 Hz, 3H). ^{19}F NMR (564 MHz,$CDCl_3$) δ -191.65 (d, *J* = 31.6 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.0 (d, *J* = 17.3 Hz), 169.1, 157.3, 137.1 (d, *J* = 2.4 Hz), 137.1, 135.6, 134.8, 130.0, 128.7, 128.3, 127.6 (d, *J* = 1.5 Hz), 122.9, 120.2 (d, *J* = 1.3 Hz), 119.5 (d, *J* = 1.5 Hz), 118.2, 104.6 (d, *J* = 22.5 Hz), 92.8 (d, *J* = 203.9 Hz), 91.0, 42.4 (d, *J* = 20.6 Hz), 29.8 (d, *J* = 2.1 Hz), 21.2, 18.3. HRMS (ESI), m/z calcd for $C_{25}H_{24}FO_5^+$ ($[M + H]^+$) 423.1602, found 423.1612.



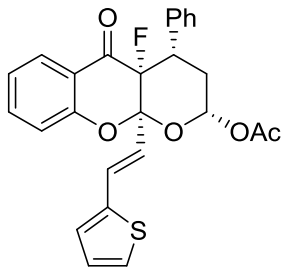
racemic

	Retention Time	Area	%Area
1	9.330	36328844	50.981
2	14.748	34930786	49.019



	Retention Time	Area	%Area
1	9.345	19466143	98.453
2	14.733	305817	1.547

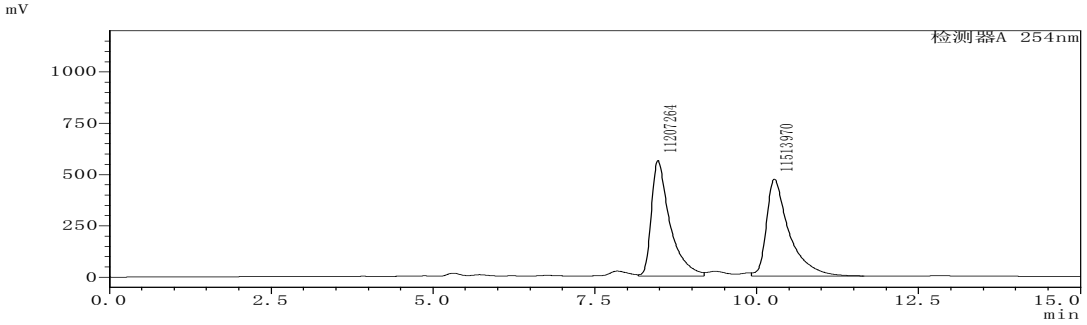
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-4-phenyl-10a-((*E*)-2-(thiophen-2-yl)vinyl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3oa)



Compound **3oa**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 61% yield (56.6 mg), white solid; Mp: 205.7- 206.3 ^{o}C; >19:1 d.r., 94% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 9.39 min, *t*r (major) = 10.26 min.

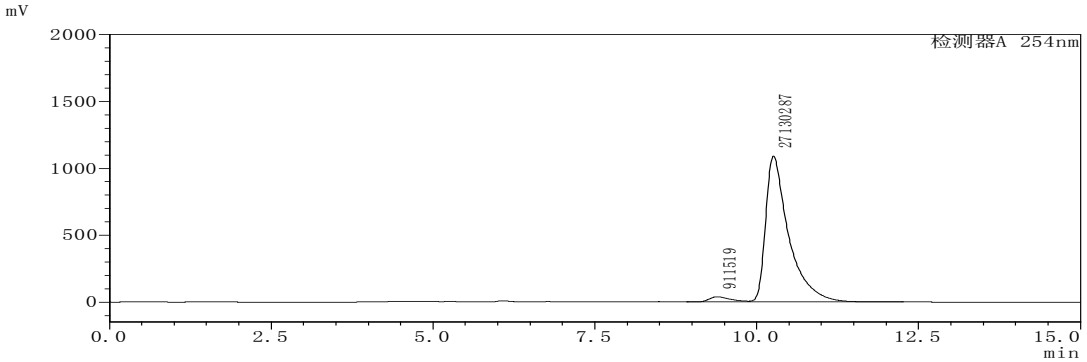
$[\alpha]^{25}_{D}$ = - 56.8 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 3.2 Hz, 3H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.19 – 6.98 (m, 5H), 6.96 – 6.84 (m, 2H), 6.72 (d, *J* = 9.0 Hz, 1H), 6.08 (d, *J* = 16.0 Hz, 1H), 3.62 (ddd, *J* = 31.6, 13.6, 3.2 Hz, 1H), 2.57 (dd, *J* = 24.0, 13.2 Hz, 1H), 2.21 (s, 3H), 2.10 (d, *J* = 13.0 Hz, 1H). ^{19}F NMR (564 MHz,$CDCl_3$) δ -190.96 (d, *J* = 31.4 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.8 (d, *J* = 17.4 Hz), 168.1, 156.1, 139.0, 136.3, 134.5, 128.8 (d, *J* = 2.4 Hz), 127.8, 127.7, 127.5, 127.4, 126.7 (d, *J* = 1.5 Hz), 126.5, 125.5, 122.1, 118.4 (d, *J* = 1.4 Hz), 117.8 (d, *J* = 1.6 Hz), 117.2, 103.4 (d, *J* = 22.7 Hz), 91.8 (d, *J* = 204.0 Hz), 90.1, 41.5 (d, *J* = 20.5 Hz), 28.8 (d, *J* = 2.0 Hz), 20.2. HRMS (ESI), m/z calcd for $C_{26}H_{21}FNaO_5S^+$ ($[M + Na]^+$) 487.0986, found 487.0986.



racemic

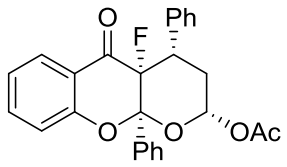
	Retention Time	Area	%Area
1	8.475	11207624	49.325
2	10.273	11513970	50.675



enantio-enriched

	Retention Time	Area	%Area
1	9.393	911519	3.251
2	10.259	27130287	96.749

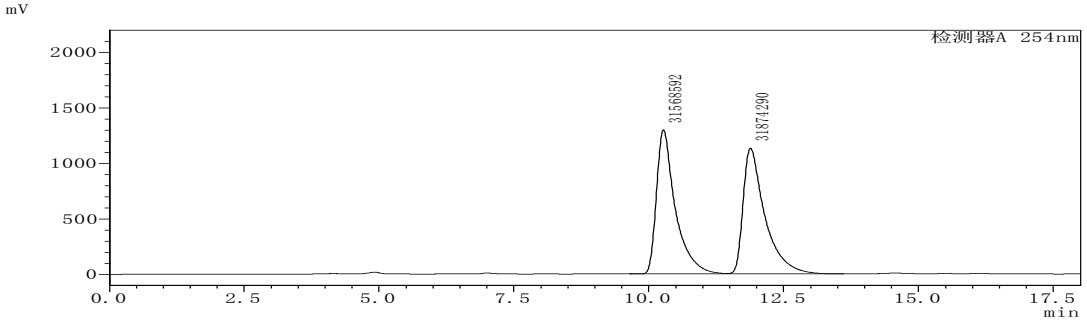
(2S,4S,4aS,10aR)-4a-fluoro-5-oxo-4,10a-diphenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3pa)



Compound **3pa**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 70% yield (60.5 mg), brown solid; Mp: 117.5-118.3 ^{o}C; >19:1 d.r., 99% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 90/10, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 10.28 min, *t*r (major) = 11.88 min.

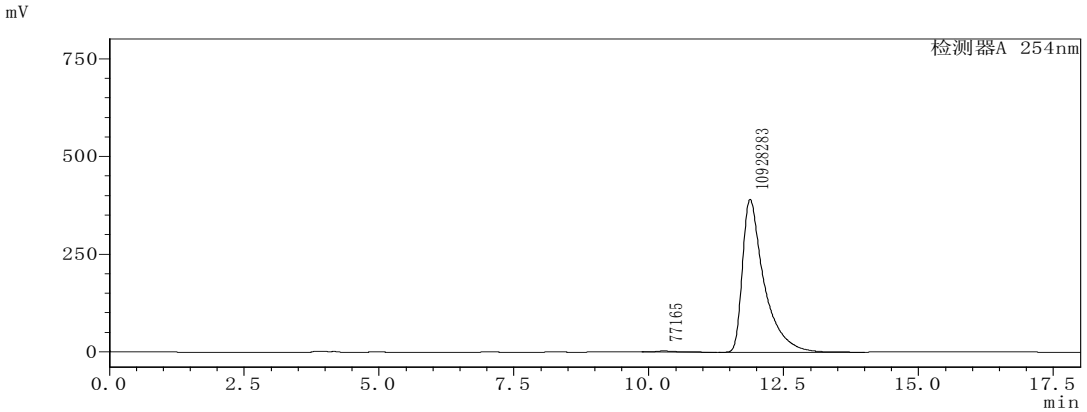
$[\alpha]^{25}_{D}$ = - 108.9 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 5.6 Hz, 3H), 7.37 – 7.16 (m, 7H), 7.14 – 7.00 (m, 3H), 6.86 (d, *J* = 10.0 Hz, 1H), 3.77 (dd, *J* = 31.2, 13.6 Hz, 1H), 2.68 (dd, *J* = 24.4, 12.0 Hz, 1H), 2.18 (d, *J* = 1.6 Hz, 3H), 2.15 (s, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -188.20 (s, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.0 (d, *J* = 16.9 Hz), 169.2, 157.5, 137.3, 135.5, 134.8 (d, *J* = 1.8 Hz), 129.9, 128.8 (d, *J* = 1.6 Hz), 128.4, 128.3, 127.7, 127.7, 127.5 (d, *J* = 1.4 Hz), 123.0, 119.9 (d, *J* = 1.4 Hz), 118.2, 105.7 (d, *J* = 21.9 Hz), 93.3 (d, *J* = 206.4 Hz), 91.1, 43.4 (d, *J* = 20.8 Hz), 29.8 (d, *J* = 2.3 Hz), 21.2. HRMS (ESI), m/z calcd for $C_{26}H_{21}FNaO_5^{+}$ ($[M + Na]^{+}$) 455.1265, found 455.1268.



acemic

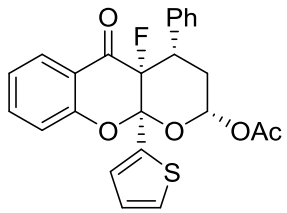
	Retention Time	Area	%Area
1	10.272	31568592	49.759
2	11.885	31874290	50.241



enantio-enriched

	Retention Time	Area	%Area
1	10.275	77165	0.701
2	11.877	10928283	99.299

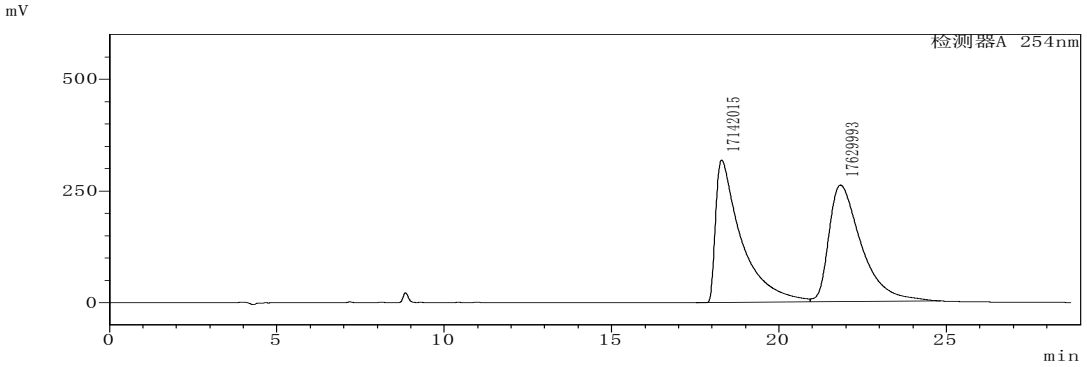
(2*S*,4*S*,4a*S*,10a*S*)-4a-fluoro-5-oxo-4-phenyl-10a-(thiophen-2-yl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3qa)



Compound **3qa**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 49% yield (42.9 mg), colorless oil; >19:1 d.r., 99% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 19.24 min, *t*r (major) = 21.02 min.

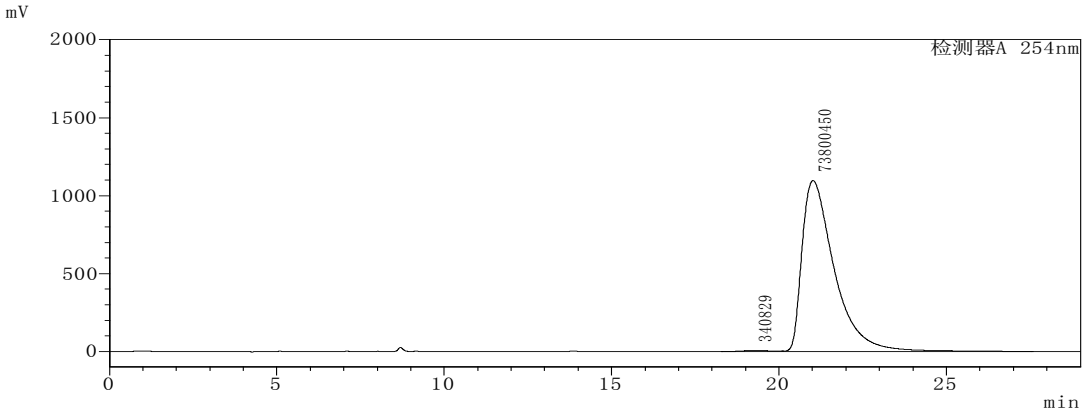
$[\alpha]^{25}_{D}$ = - 121.2 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 1H), 7.61 (dd, *J* = 11.2, 4.4 Hz, 1H), 7.35 – 7.28 (m, 3H), 7.24 (dd, *J* = 13.6, 6.0 Hz, 3H), 7.10 (m, 3H), 6.87 – 6.75 (m, 2H), 3.73 (ddd, *J* = 31.2, 13.6, 3.6 Hz, 1H), 2.65 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.28 – 2.07 (m, 4H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -188.00 (d, *J* = 31.2 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5 (d, *J* = 17.4 Hz), 169.1, 157.0, 137.2, 135.3, 129.0, 129.0, 128.8, 128.5, 128.0, 127.5, 126.5, 123.3, 119.6, 118.4, 104.2 (d, *J* = 23.1 Hz), 93.3 (d, *J* = 203.0 Hz), 91.2, 42.6 (d, *J* = 20.6 Hz), 29.7, 21.2. HRMS (ESI), m/z calcd for $C_{24}H_{19}FNaO_5S^{+}$ ($[M + Na]^{+}$) 461.0829, found 461.0824.



racemic

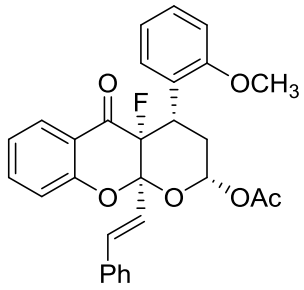
	Retention Time	Area	%Area
1	18.289	17142015	49.298
2	21.837	17629993	50.702



enantio-enriched

	Retention Time	Area	%Area
1	19.241	340829	0.460
2	21.016	73800450	99.540

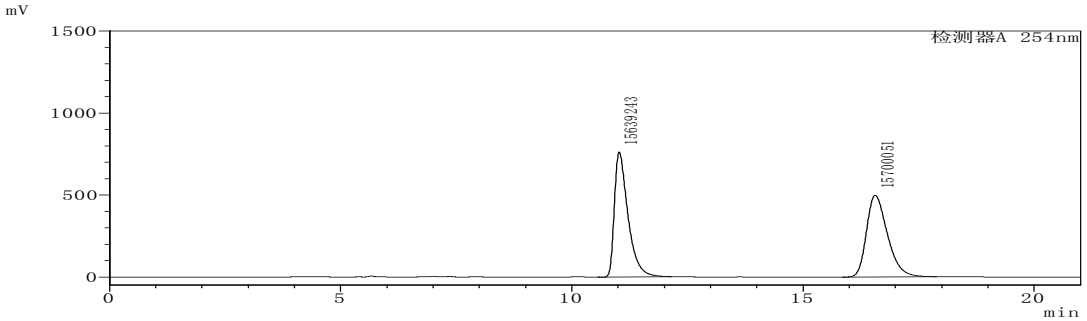
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-4-(2-methoxyphenyl)-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ab)



Compound **3ab**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 68% yield (66.4 mg), white solid; Mp: 158.7-159.9 ^{o}C, >19:1 d.r., 92% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 11.15 min, *t*r (major) = 16.47 min.

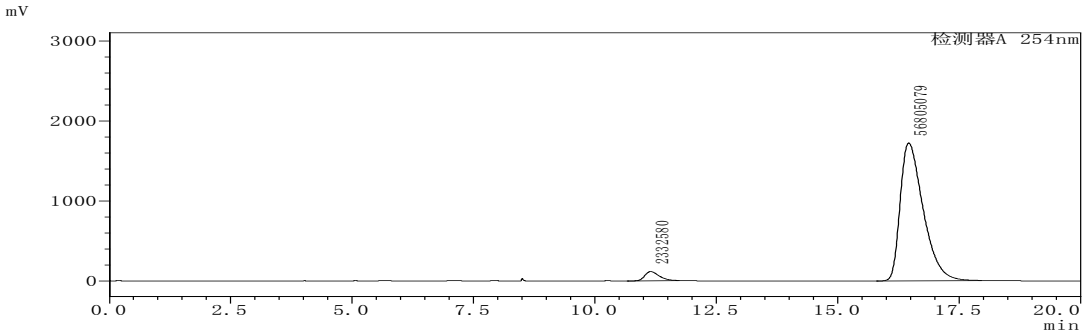
$[\alpha]^{25}_{D}$ = - 35.8 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.64 – 7.54 (m, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.19 (m, 7H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.84 – 6.66 (m, 2H), 6.27 (dd, *J* = 16.0, 1.6 Hz, 1H), 4.41 (ddd, *J* = 32.2, 13.6, 3.6 Hz, 1H), 3.29 (s, 3H), 2.59 (dt, *J* = 13.2, 8.0 Hz, 1H), 2.21 (s, 3H), 2.07 – 1.92 (m, 1H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -189.53 (d, *J* = 32.3 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.5 (d, *J* = 17.3 Hz), 169.2, 157.1, 156.3, 136.8 (d, *J* = 2.4 Hz), 136.6, 135.2, 129.4 (d, *J* = 1.8 Hz), 129.2, 128.9, 128.6, 127.3, 127.3, 123.5, 122.3, 120.9, 120.2 (d, *J* = 1.4 Hz), 120.2, 118.2, 109.9, 104.6 (d, *J* = 22.9 Hz), 92.8 (d, *J* = 202.8 Hz), 91.4, 54.7, 33.3 (d, *J* = 21.6 Hz), 28.9, 21.3. HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_6^+$ ($[M + Na]^+$) 511.1527, found 511.1524.



racemic

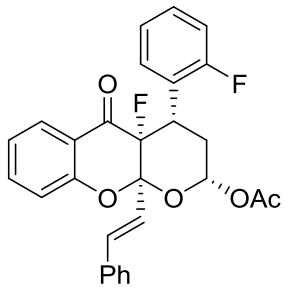
	Retention Time	Area	%Area
1	11.027	15639243	49.903
2	16.564	15700051	50.097



enantio-enriched

	Retention Time	Area	%Area
1	11.151	2332580	3.944
2	16.466	56805079	96.056

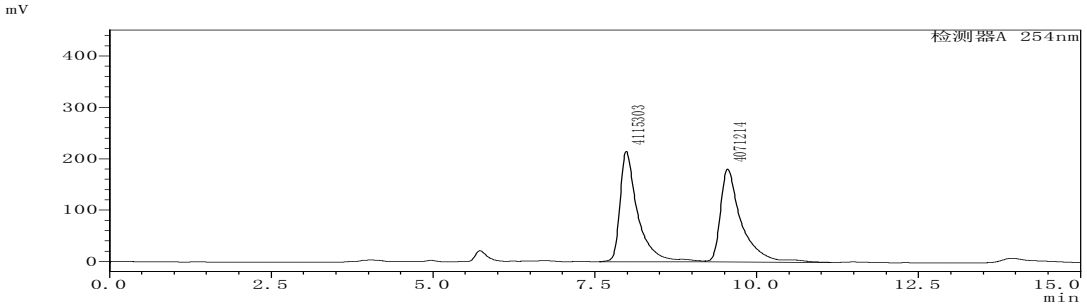
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-4-(2-fluorophenyl)-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ac)



Compound **3ac**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 55% yield (52.3 mg), white solid; Mp: 153.3-154.9 ^{o}C, >19:1 d.r., 95% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 7.97 min, *t*r (major) = 9.50 min.

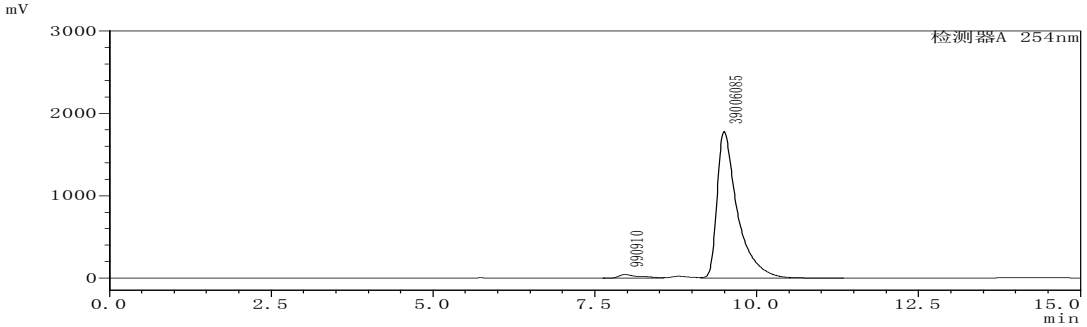
$[\alpha]^{25}_{D}$ = - 106.5 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.35 – 7.13 (m, 8H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.00 – 6.89 (m, 2H), 6.84 – 6.70 (m, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 4.17 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.58 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.21 (s, 3H), 2.06 (dd, *J* = 10.0, 3.0 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -116.44 (dd, *J* = 22.4, 19.1 Hz, 1F), -189.94 (d, *J* = 2.7 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.6 (d, *J* = 17.2 Hz), 169.1, 160.2 (d, *J* = 246.1 Hz), 157.2, 137.2, 137.0 (d, *J* = 2.5 Hz), 135.1, 130.1, 130.1, 130.1, 129.9 (d, *J* = 8.5 Hz), 129.0, 128.6, 127.9 (d, *J* = 1.3 Hz), 127.3, 124.6 (d, *J* = 3.4 Hz), 123.0, 122.4 (d, *J* = 14.1 Hz), 119.7 (d, *J* = 1.8 Hz), 119.4, 118.1, 115.3 (d, *J* = 22.8 Hz), 104.5 (d, *J* = 22.7 Hz), 92.4 (d, *J* = 203.9 Hz), 90.9, 33.8 (d, *J* = 23.8 Hz), 29.1 (d, *J* = 1.3 Hz), 21.2. HRMS (ESI), m/z calcd for $C_{28}H_{22}F_2NaO_5^+$ ([M + Na]$^+$) 499.1328, found 499.1328.



racemic

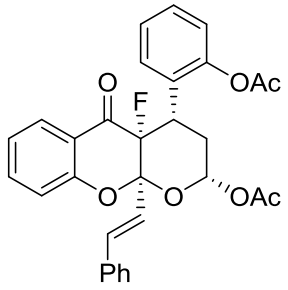
	Retention Time	Area	%Area
1	7.985	4115303	50.269
2	9.551	4071214	49.731



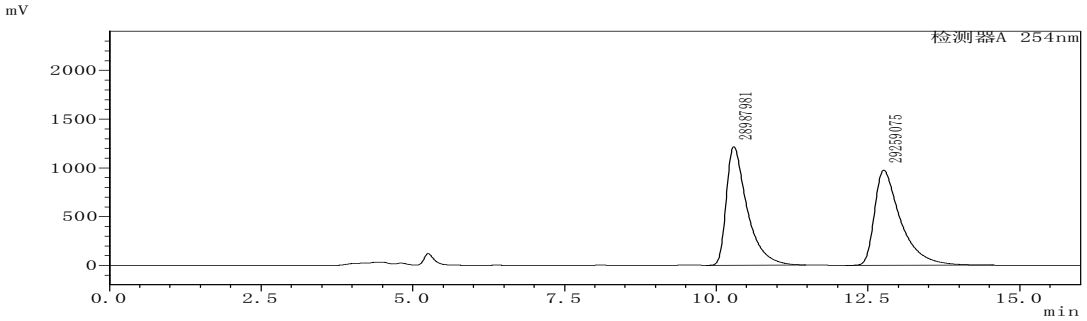
enantio-enriched

	Retention Time	Area	%Area
1	7.967	990910	2.477
2	9.497	39006985	97.523

2-((2*S*,4*S*,4a*S*,10a*R*)-2-acetoxy-4a-fluoro-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-4-yl)phenyl acetate (3ad)

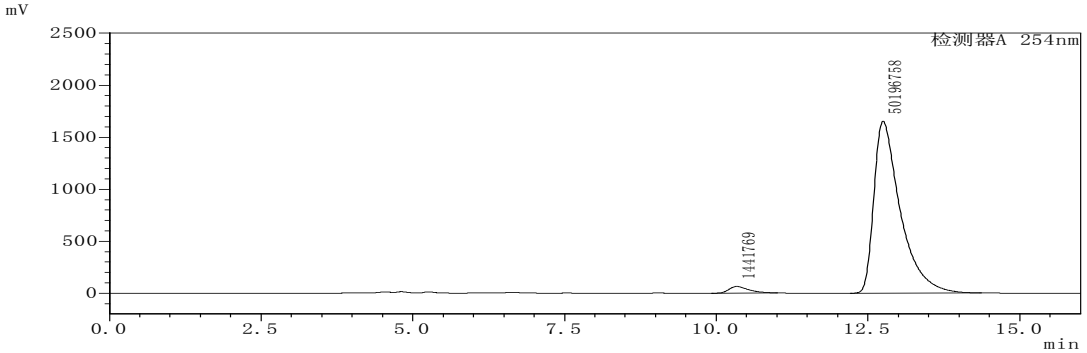


Compound **3ad**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 58% yield (56.8 mg), white solid; Mp: 195.4-196.3 ^{o}C; >19:1 d.r., 94% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 10.38 min, *t*r (major) = 12.75 min.
$[\alpha]^{25}_{D}$ = - 19.8 (c = 1.0 in CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.6 Hz, 1H), 7.91 (m, 2H), 7.59 (m, 8H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.27 (dd, *J* = 19.6, 11.6 Hz, 2H), 7.07 (d, *J* = 9.6 Hz, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 4.25 (dd, *J* = 31.2, 13.2 Hz, 1H), 2.88 (dd, *J* = 24.2, 12.0 Hz, 1H), 2.52 (d, *J* = 1.2 Hz, 3H), 2.34 (d, *J* = 12.8 Hz, 1H), 1.81 (s, 3H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -189.97 (s. 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.2 (d, *J* = 17.3 Hz), 169.1, 168.7, 157.3, 148.1, 137.1 (d, *J* = 2.4 Hz), 137.0, 135.0, 129.9 (d, *J* = 3.3 Hz), 129.2, 129.1, 128.6, 128.4 (d, *J* = 1.4 Hz), 127.3, 127.1, 126.5, 122.9, 122.2, 119.7 (d, *J* = 1.4 Hz), 119.6 (d, *J* = 1.6 Hz), 118.1, 104.6 (d, *J* = 22.7 Hz), 92.3 (d, *J* = 202.0 Hz), 90.8, 34.4 (d, *J* = 20.0 Hz), 29.2, 21.2, 19.9. HRMS (ESI), m/z calcd for $C_{30}H_{25}FNaO_7^+$ ([M + Na]$^+$) 539.1477, found 539.1476.



racemic

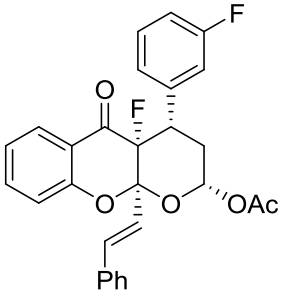
	Retention Time	Area	%Area
1	10.290	28987981	49.767
2	12.762	29259075	50.233



enantio-enriched

	Retention Time	Area	%Area
1	10.377	1441769	2.792
2	12.750	50196758	97.208

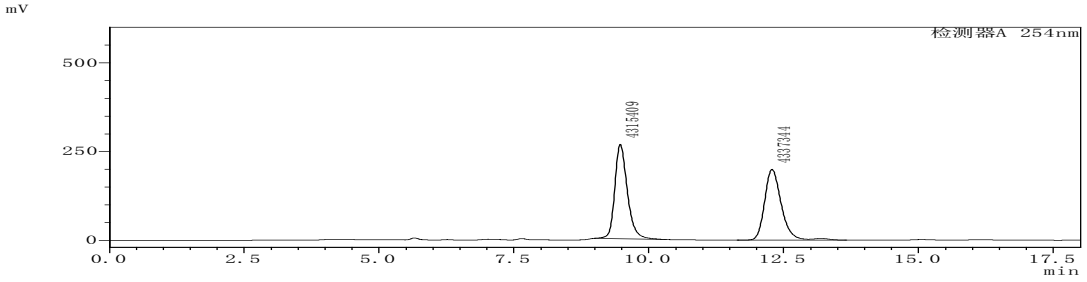
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-4-(3-fluorophenyl)-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ae)



Compound **3ae**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 70% yield (66.6 mg), white solid, Mp: 231.6-232.9 ^{o}C; >19:1 d.r., 91% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 9.59 min, *t*r (major) = 12.39 min.

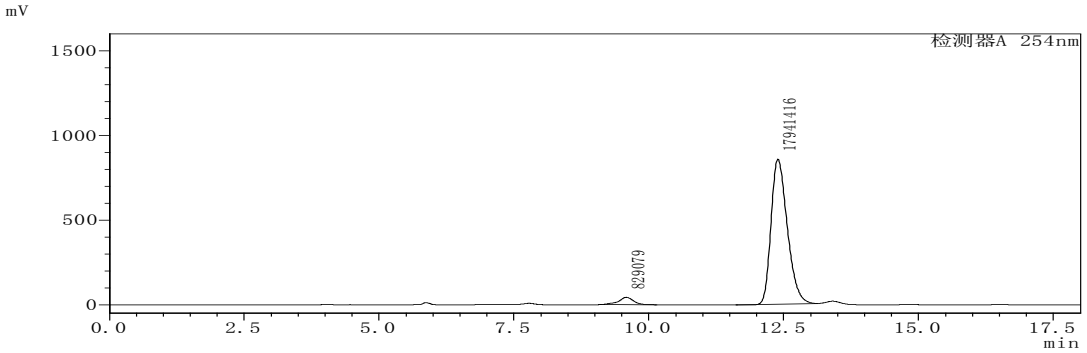
$[\alpha]^{25}_{D}$ = - 54.0 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 8.4 Hz, 1H), 7.33 – 7.20 (m, 7H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.05 – 6.90 (m, 2H), 6.85 (t, *J* = 10.0 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 1H), 6.26 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.65 (ddd, *J* = 30.8, 13.6, 3.2 Hz, 1H), 2.53 (dd, *J* = 23.6, 13.0 Hz, 1H), 2.21 (s, 3H), 2.11 (dd, *J* = 10.0, 3.2 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -112.16 (d, *J* = 3.6 Hz, 1F), -190.90 (d, *J* = 4.6 Hz,1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (d, *J* =17.4 Hz), 169.1, 162.7 (d, *J* = 246.6 Hz), 157.2, 137.8 (d, *J* = 7.2 Hz), 137.4 (d, *J* = 7.6 Hz), 137.0, 134.9, 130.2 (d, *J* = 7.8 Hz), 129.1, 128.6, 127.7 (d, *J* = 9.3 Hz), 127.3, 124.5, 123.2, 119 (d, *J* = 9.0 Hz), 119.3, 118.2, 115.8 (d, *J* = 22.6 Hz), 115.5, 115.3, 104.5 (d, *J* =22.5 Hz), 92.6 (d, *J* =204.4 Hz), 91.6, 90.9 (d, *J* = 8.1 Hz), 42.2 (dd, *J* = 20.4, 6.5 Hz), 29.7 (d, *J* = 6.3 Hz), 21.2 (d, *J* = 8.1 Hz). HRMS (ESI), m/z calcd for $C_{28}H_{22}F_2NaO_5^+$ ($[M + Na]^+$) 499.1328, found 499.1318.



racemic

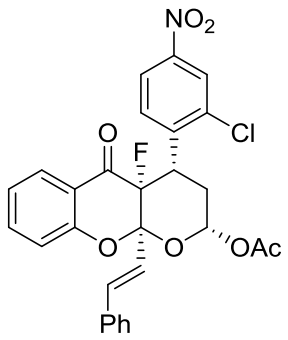
	Retention Time	Area	%Area
1	9.471	4315409	49.873
2	12.284	4337344	50.127



enantio-enriched

	Retention Time	Area	%Area
1	9.585	829079	4.417
2	12.394	17941416	95.583

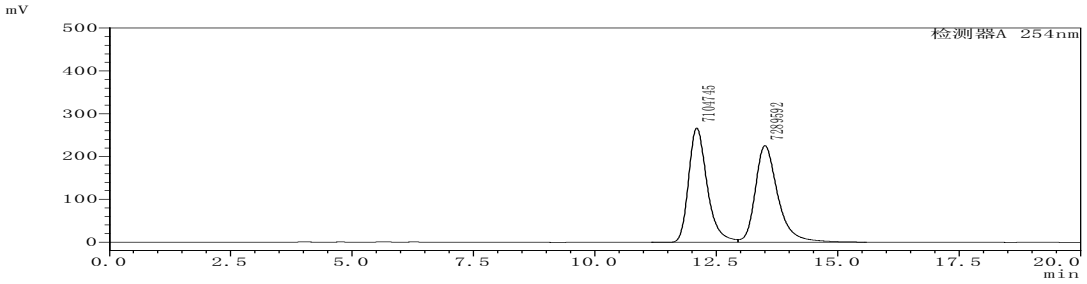
(2*S*,4*S*,4a*S*,10a*R*)-4-(2-chloro-4-nitrophenyl)-4a-fluoro-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3af)



Compound **3af**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 89% yield (96.6 mg), yellow solid; Mp: 235.2-236.3 ^{o}C; >19:1 d.r., 90% *ee*. HPLC (chiral IC column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 12.07 min, *t*r (major) = 13.45 min.

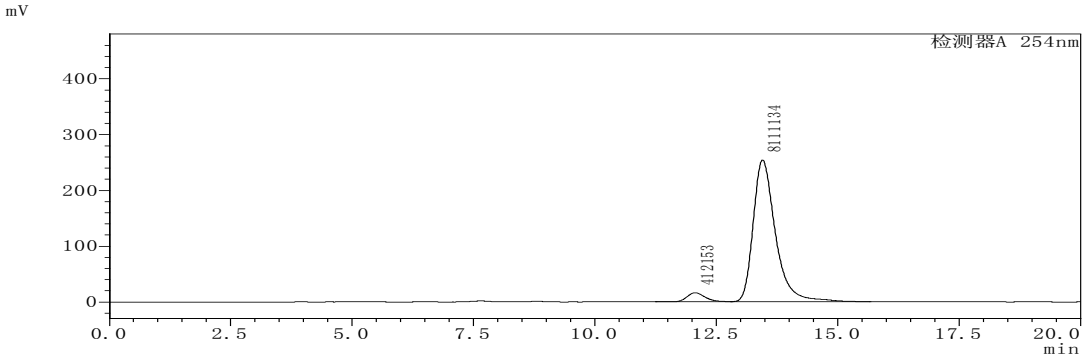
$[\alpha]^{25}_{D}$ = -7.3 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 – 8.47 (m, 1H), 8.11 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.73 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.68 – 7.56 (m, 1H), 7.46 (d, *J* = 8.8 Hz, 1H), 7.34 – 7.16 (m, 6H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.80 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.25 (dd, *J* = 16.0, 1.6 Hz, 1H), 4.49 (ddd, *J* = 30.4, 13.6, 4.0 Hz, 1H), 2.58 (td, *J* = 13.2, 10.8 Hz, 1H), 2.22 (s, 3H), 2.16 – 2.06 (m, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -189.12 (s, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.0 (d, *J* =17.4 Hz), 169.1, 157.4, 146.9, 140.7, 137.7, 137.5 (d, *J* = 2.4 Hz), 135.1, 134.9, 130.5, 129.2, 128.7, 128.0, 128.0, 127.3, 125.9 (d, *J* = 4.6 Hz), 124.2, 123.2, 119.4 (d, *J* = 0.9 Hz), 119.2 (d, *J* = 1.2 Hz), 118.3, 104.4 (d, *J* =22.6 Hz), 92.6 (d, *J* =204.5 Hz), 90.5, 37.6 (d, *J* = 20.3 Hz), 29.7 (d, *J* = 0.6 Hz), 21.2. HRMS (ESI), m/z calcd for $C_{28}H_{21}ClFNNaO_7^+$ ([M + Na]$^+$) 560.0883 (562.0853 for Cl^{37}), found 560.0884 (562.0874 for Cl^{37}).



racemic

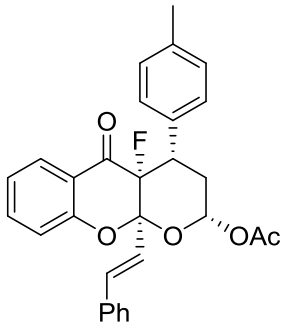
	Retention Time	Area	%Area
1	12.099	7104745	49.358
2	13.504	7289592	50.642



enantio-enriched

	Retention Time	Area	%Area
1	12.066	412153	4.836
2	13.454	8111134	95.164

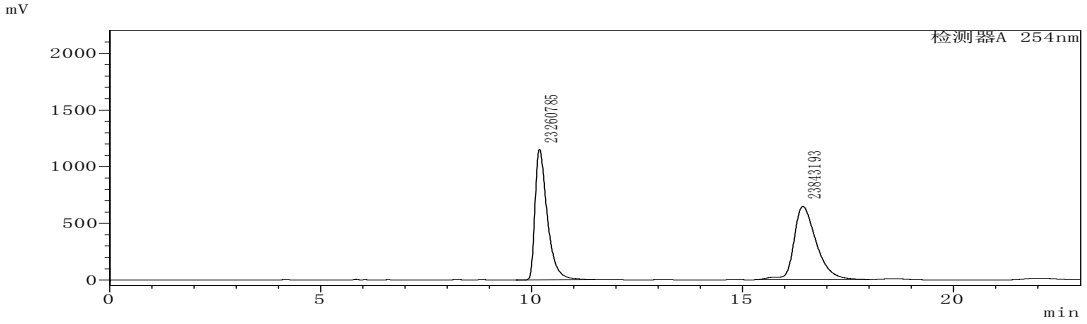
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-10a-((*E*)-styryl)-4-(p-tolyl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ag)



Compound **3ag**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 84% yield (79.3 mg),white solid; Mp: 188.9-189.9 ^{o}C >19:1 d.r., 97% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 10.40 min, *t*r (major) = 16.57 min.

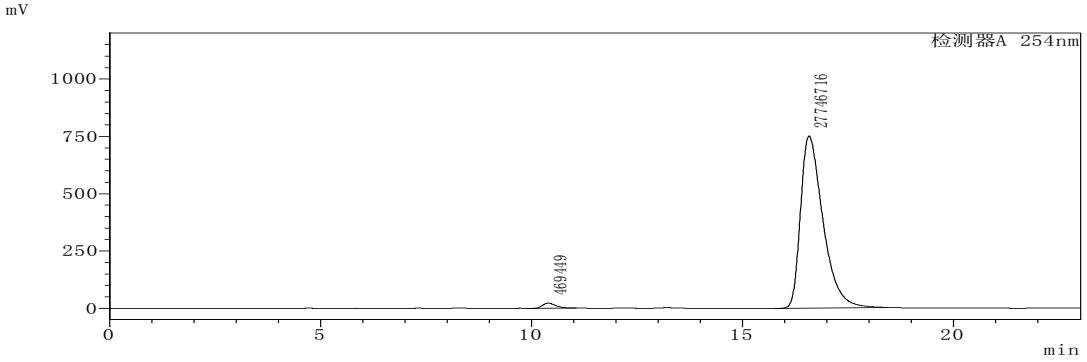
$[\alpha]^{25}_{D}$ = - 134.4 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.67 – 7.57 (m, 1H), 7.32 – 7.20 (m, 6H), 7.12 (t, *J* = 7.2 Hz, 3H), 6.97 (dd, *J* = 16.2, 12.0 Hz, 3H), 6.81 – 6.71 (m, 1H), 6.28 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.63 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.58 (dd, *J* = 23.6, 13.0 Hz, 1H), 2.33 (s, 3H), 2.21 (s, 3H), 2.14 – 2.05 (m, 1H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -191.08 (d, *J* = 31.4 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.9 (d, *J* =17.3 Hz), 169.1, 157.2, 138.0, 137.2, 136.7 (d, *J* = 2.4 Hz), 135.0, 132.5, 129.4, 129.0, 128.6, 128.5 (d, *J* = 1.5 Hz), 127.6 (d, *J* = 1.3 Hz), 127.3, 123.0, 119.8 (d, *J* = 1.3 Hz), 119.4 (d, *J* = 1.3 Hz), 118.1, 104.6 (d, *J* =22.6 Hz), 92.9 (d, *J* =203.7 Hz), 91.1, 42.1 (d, *J* =20.6 Hz), 29.9 (d, *J* =1.9 Hz), 21.2, 21.2. HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_5^+$ ([M + Na]$^+$) 495.1578, found 495.1578.



racemic

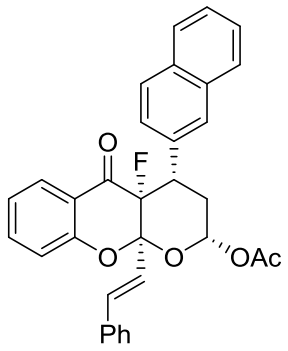
	Retention Time	Area	%Area
1	10.189	23260785	49.382
2	16.428	23843193	50.418



enantio-enriched

	Retention Time	Area	%Area
1	10.395	469449	1.664
2	16.574	27746716	98.336

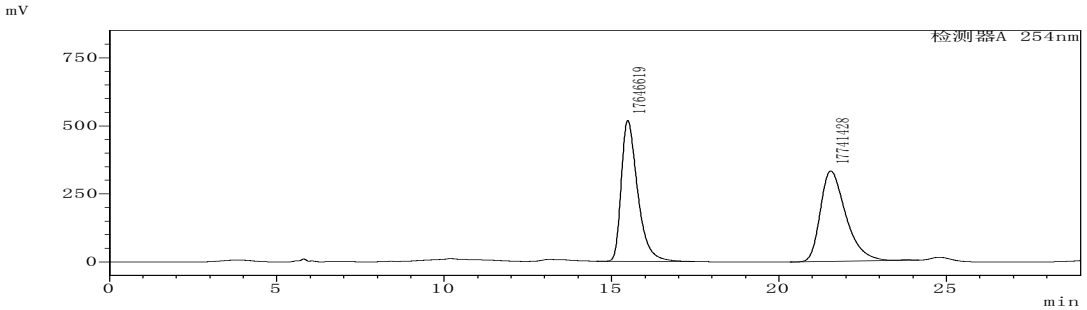
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-4-(naphthalen-2-yl)-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ah)



Compound **3ah**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 73% yield (74.2 mg), white solid; Mp: 220.6-222.3 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 15.78 min, *t*r (major) = 21.59 min.

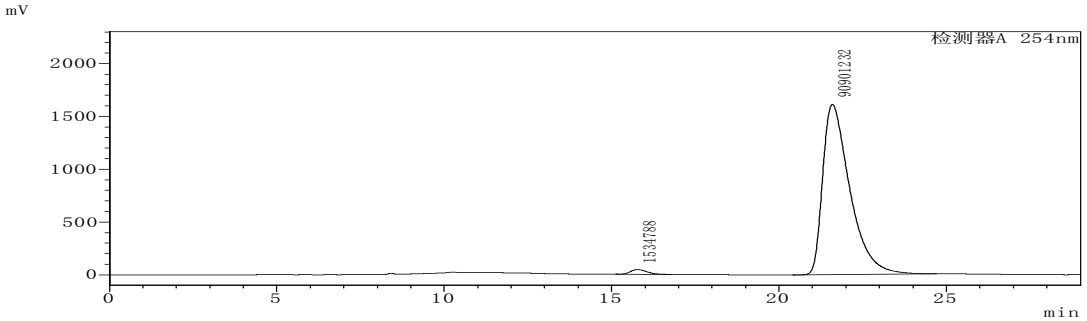
$[\alpha]^{25}_{D}$ = - 158.4 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (ddd, *J* = 19.6, 11.2, 6.4 Hz, 4H), 7.70 – 7.61 (m, 1H), 7.56 (s, 1H), 7.48 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.36 – 7.18 (m, 7H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 16.0 Hz, 1H), 6.83 (d, *J* = 9.0 Hz, 1H), 6.33 (d, *J* = 16.0 Hz, 1H), 3.85 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.73 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.24 (s, 3H), 2.22 – 2.15 (m, 1H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -190.76 (d, *J* = 31.4 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.8 (d, *J* = 17.3 Hz), 169.1, 157.2, 137.3, 136.9 (d, *J* = 2.2 Hz), 135.0, 133.3, 133.1 (d, *J* = 12.2 Hz), 129.0, 128.6, 128.4, 128.1, 127.9, 127.8, 127.6 (d, *J* = 7.0 Hz), 127.3, 126.4 (d, *J* = 2.5 Hz), 126.3, 123.1, 119.7 (d, *J* = 1.4 Hz), 119.5 (d, *J* =1.0 Hz), 118.2, 104.6 (d, *J* = 22.5 Hz), 93.0 (d, *J* = 204.0 Hz), 91.07, 42.6 (d, *J* = 20.5 Hz), 30.1 (d, *J* =1.6 Hz), 21.2. HRMS (ESI), m/z calcd for $C_{32}H_{25}FNaO_5^+$ ([M + Na]$^+$) 531.1578, found 531.1578.



racemic

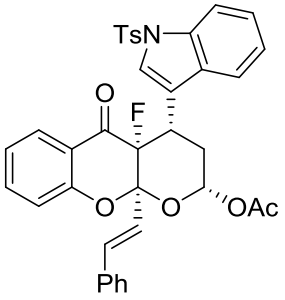
	Retention Time	Area	%Area
1	15.483	17646619	49.866
2	21.547	17741428	50.134



enantio-enriched

	Retention Time	Area	%Area
1	15.776	1534788	1.660
2	21.594	90901232	98.340

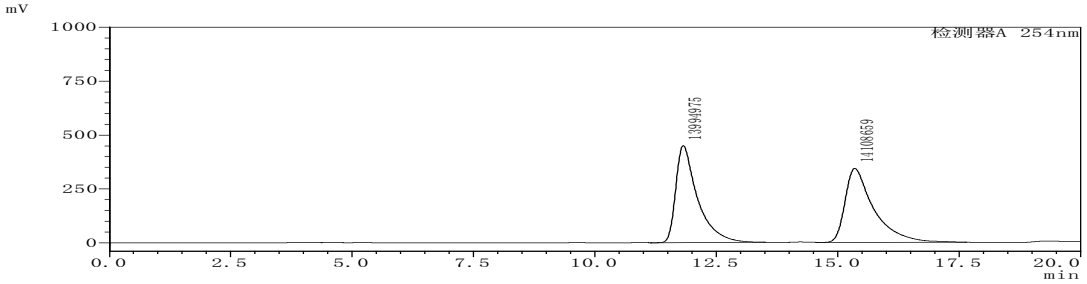
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-10a-((*E*)-styryl)-4-(1-tosyl-1H-indol-3-yl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ai)



Compound **3ai**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 63% yield (82.0 mg), white solid; Mp: 195.5-196.9 ^{o}C >19:1 d.r., 95% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 80/20, flow rate 0.8 ml/min, λ = 254 nm, *t*r (major) = 11.90 min, *t*r (minor) = 15.51 min.

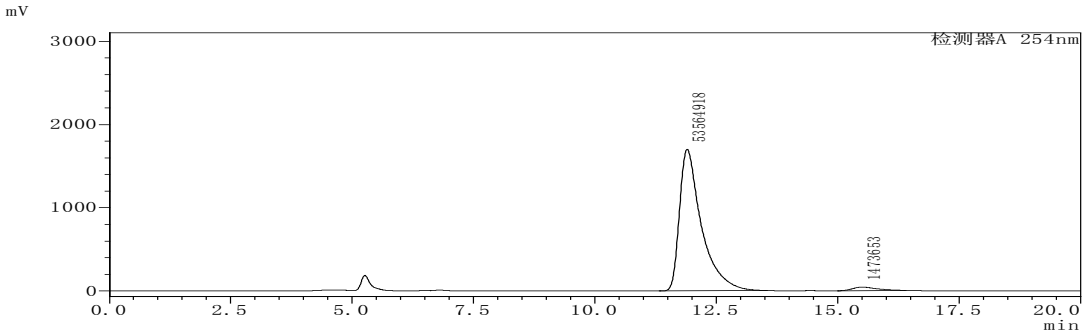
$[\alpha]^{25}_{D}$ = - 82.8 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.66 – 7.57 (m, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.14 (m, 9H), 7.07 (t, *J* = 7.6 Hz, 2H), 6.98 (dd, *J* = 17.6, 12.0 Hz, 2H), 6.77 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.29 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.94 (ddd, *J* = 31.2, 13.6, 3.6 Hz, 1H), 2.61 – 2.40 (m, 1H), 2.36 (s, 3H), 2.26 – 2.12 (m, 4H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -188.76 (s, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.2 (d, *J* = 17.5 Hz), 169.2, 157.2, 145.0, 137.4, 137.1 (d, *J* = 2.2 Hz), 135.3, 135.0, 134.8, 130.1, 129.7, 129.1, 128.7, 127.8 (d, *J* = 1.2 Hz), 127.4, 127.0, 126.3 (d, *J* = 3.9 Hz), 124.9, 123.2, 123.0, 119.5 (d, *J* = 1.3 Hz), 119.2 (d, *J* = 1.4 Hz), 118.9, 118.2, 116.6, 113.9, 104.5 (d, *J* = 22.4 Hz), 92.3 (d, *J* = 203.5 Hz), 90.8, 33.9 (d, *J* = 21.9 Hz), 30.4 (d, *J* = 1.5 Hz), 21.7, 21.2. HRMS (ESI), m/z calcd for $C_{37}H_{30}FNNaO_7S^+$ ($[M + Na]^+$) 674.1619, found 674.1626.



racemic

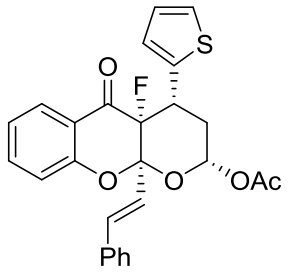
	Retention Time	Area	%Area
1	11.821	13994975	49.798
2	15.354	14108659	50.202



enantio-enriched

	Retention Time	Area	%Area
1	11.901	53564918	97.323
2	15.505	1473653	2.677

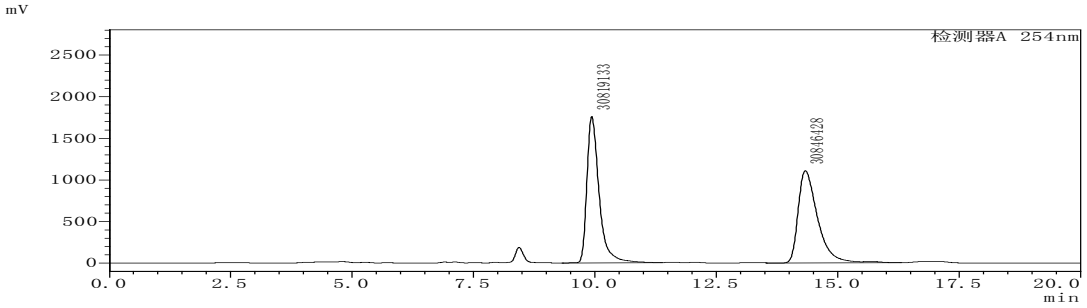
(2*S*,4*R*,4a*S*,10a*R*)-4a-fluoro-5-oxo-10a-((*E*)-styryl)-4-(thiophen-2-yl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3aj)



Compound **3aj**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 94% yield (87.2 mg), yellow solid; Mp: 164.3-165.9 ^{o}C >19:1 d.r., 97% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 10.04 min, *t*r (major) = 14.43 min.

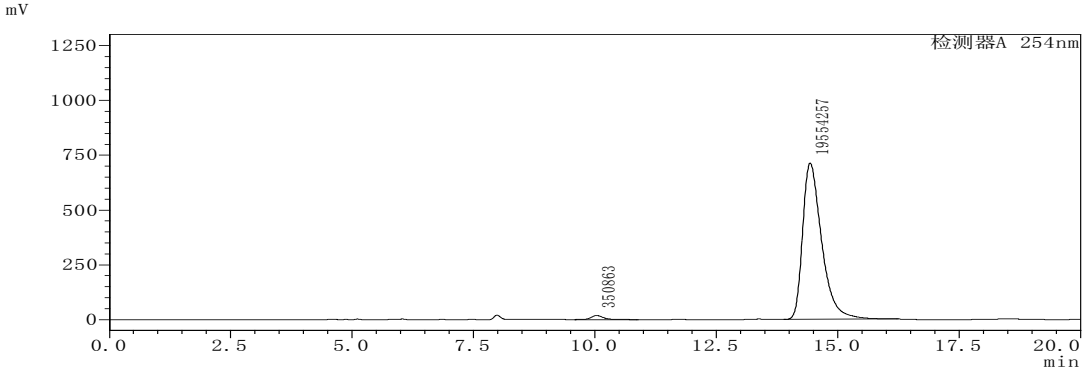
$[\alpha]^{25}_{D}$ = - 55.6 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.69 – 7.54 (m, 1H), 7.34 – 7.16 (m, 7H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.98 – 6.86 (m, 2H), 6.80 (d, *J* = 3.2 Hz, 1H), 6.71 (dd, *J* = 10.4, 1.6 Hz, 1H), 6.27 (dd, *J* = 16.0, 1.6 Hz, 1H), 4.01 (ddd, *J* = 30.2, 13.6, 4.0 Hz, 1H), 2.61 – 2.40 (m, 1H), 2.30 – 2.11 (m, 4H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -189.63 (d, *J* = 3.6 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.4 (d, *J* = 12.8 Hz), 169.0, 157.1, 137.4, 137.3, 136.9 (d, *J* = 2.4 Hz), 135.0, 129.1, 128.6, 127.8 (d, *J* = 1.5 Hz), 127.3, 126.8, 125.6, 123.1, 119.6 (d, *J* = 0.9 Hz), 119.2 (d, *J* = 1.5 Hz), 118.2, 104.3 (d, *J* = 22.4 Hz), 92.3 (d, *J* = 204.1 Hz), 90.6, 38.2 (d, *J* = 21.5 Hz), 31.7 (d, *J* = 2.1 Hz), 21.1. HRMS (ESI), m/z calcd for $C_{26}H_{21}FNaO_5S^+$ ($[M + Na]^+$) 487.0986, found 487.0994.



racemic

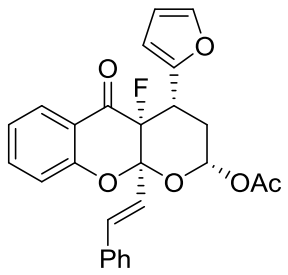
	Retention Time	Area	%Area
1	9.936	30819133	49.978
2	14.219	30846428	50.022



enantio-enriched

	Retention Time	Area	%Area
1	10.037	350863	1.763
2	14.433	19554257	98.237

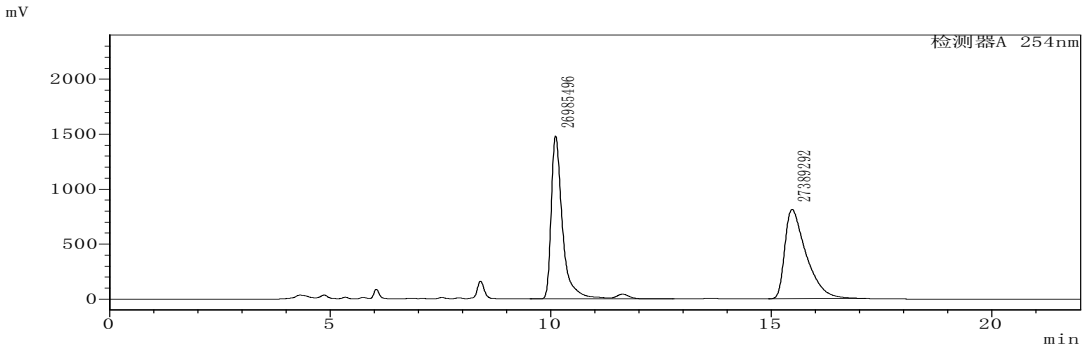
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-4-(furan-2-yl)-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3ak)



Compound **3ak**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 78% yield (69.9 mg), white solid; Mp: 142.1-143.9 ^{o}C >19:1 d.r., 93% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 10.20 min, *t*r (major) = 15.42 min.

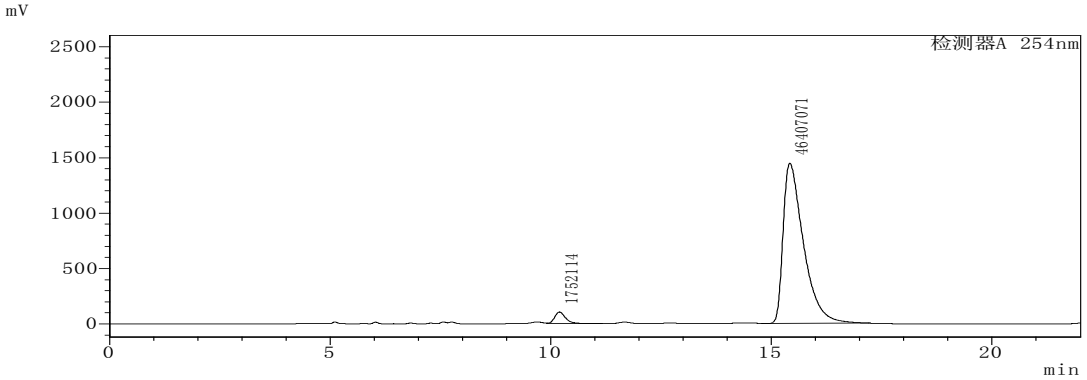
$[\alpha]^{25}_{D}$ = - 86.6 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.68 – 7.57 (m, 1H), 7.30 (d, *J* = 1.0 Hz, 1H), 7.29 – 7.19 (m, 6H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.70 (dd, *J* = 10.4, 1.8 Hz, 1H), 6.38 – 6.30 (m, 1H), 6.28 – 6.19 (m, 2H), 3.85 (ddd, *J* = 29.6, 13.6, 3.6 Hz, 1H), 2.54 – 2.39 (m, 1H), 2.25 – 2.14 (m, 4H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -190.23 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7 (d, *J* = 17.3 Hz), 169.1, 157.1, 149.3, 142.4, 137.3, 137.0, 135.0, 129.1, 128.6, 127.8, 127.3, 123.1, 119.4, 119.3, 118.1, 110.7, 108.8, 104.3 (d, *J* = 22.2 Hz), 91.5 (d, *J* = 204.3 Hz), 90.5, 36.6 (d, *J* = 21.7 Hz), 28.3, 21.2. HRMS (ESI), m/z calcd for $C_{26}H_{21}FNaO_6^{+}$ ($[M + Na]^{+}$) 471.1214, found 471.1218.



racemic

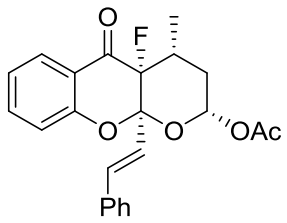
	Retention Time	Area	%Area
1	10.110	26985496	49.629
2	15.469	27389292	50.371



enantio-enriched

	Retention Time	Area	%Area
1	10.198	1752114	3.638
2	15.420	46407071	96.362

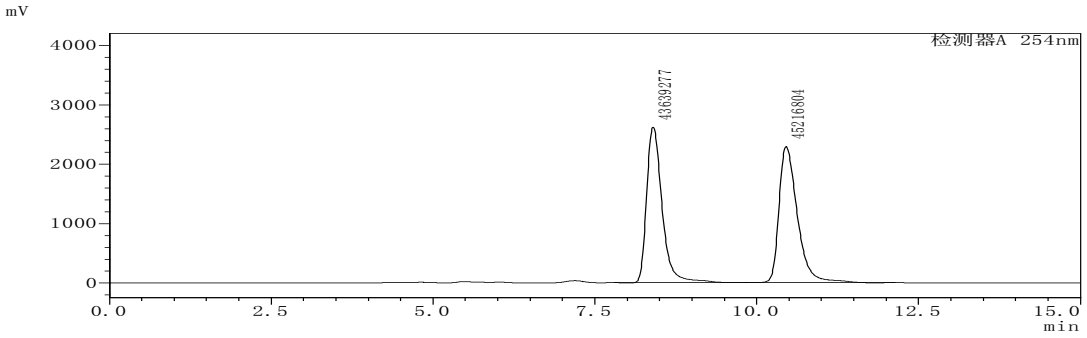
(2*S*,4*R*,4a*S*,10a*R*)-4a-fluoro-4-methyl-5-oxo-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3al)



Compound **3al**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 64% yield (50.7 mg), white solid; Mp: 156.5-157.9 ^{o}C >19:1 d.r., 90% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 8.58 min, *t*r (major) = 10.66 min.

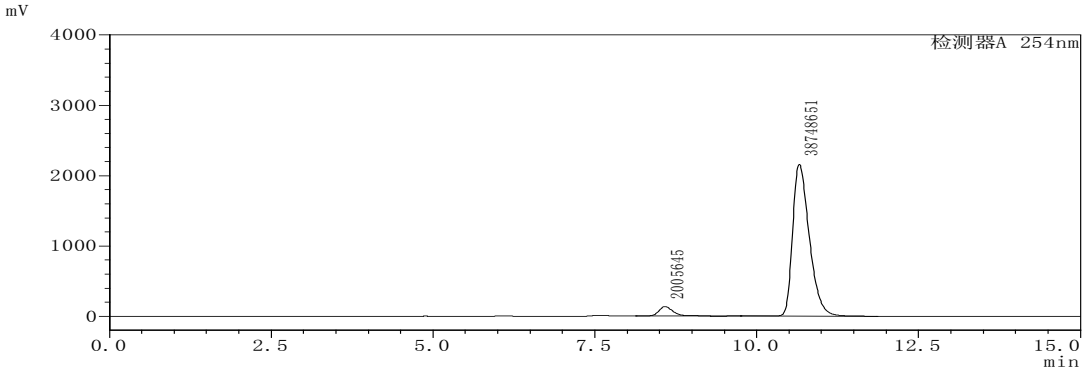
$[\alpha]^{25}_{D}$ = - 38.7 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.50 (m, 1H), 7.30 – 7.19 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.57 (dd, *J* = 7.2, 6.4 Hz, 1H), 6.23 (dd, *J* = 16.0, 1.6 Hz, 1H), 2.59 – 2.39 (m, 1H), 2.17 (s, 3H), 1.94 – 1.83 (m, 2H), 1.02 (d, *J* = 6.8 Hz, 3H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -195.92 (d, *J* = 29.6 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0 (d, *J* = 17.2 Hz), 169.2, 157.5, 137.3, 136.6, 135.1, 129.0, 128.6, 127.6, 127.3, 122.8, 119.8, 119.1, 118.1, 104.3 (d, *J* =22.8 Hz), 92.7 (d, *J* = 201.6 Hz), 90.8, 31.1, 30.8 (d, *J* = 22.2 Hz), 21.2, 13.8 (d, *J* = 3.9 Hz). HRMS (ESI), m/z calcd for $C_{23}H_{21}FNaO_5^+$ ([M + Na]$^+$) 419.1265, found 419.1261.



racemic

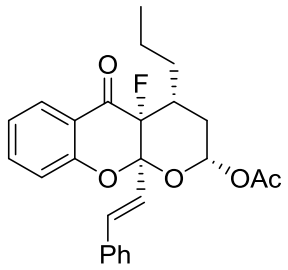
	Retention Time	Area	%Area
1	8.400	43639277	49.112
2	10.455	45216804	50.888



enantio-enriched

	Retention Time	Area	%Area
1	8.584	2005645	4.921
2	10.658	38748651	95.079

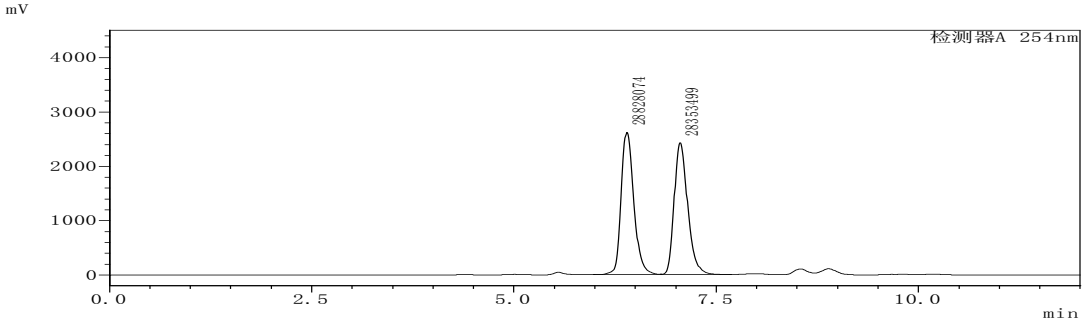
(2*S*,4*R*,4a*S*,10a*R*)-4a-fluoro-5-oxo-4-propyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (3am)



Compound **3am**: Prepared in 0.2 mmol scale at 20-23 ^{o}C for 48 h. 70% yield (59.4 mg), white solid; Mp: 116.2-117.9 ^{o}C >19:1 d.r., 95% *ee*. HPLC (chiral IF column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 6.39 min, *t*r (major) = 7.04 min.

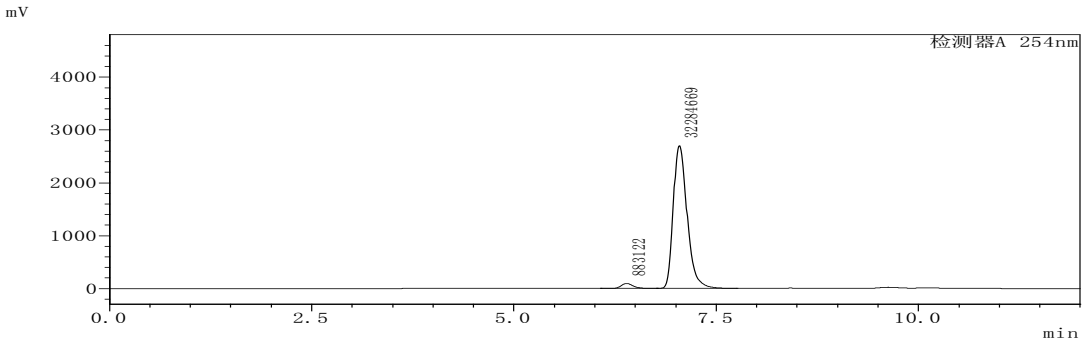
$[\alpha]^{25}_{D}$ = - 71.0 (c = 1.0 in CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.67 – 7.52 (m, 1H), 7.33 – 7.20 (m, 5H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 16.0 Hz, 1H), 6.58 (dd, *J* = 10.4, 2.4 Hz, 1H), 6.24 (dd, *J* = 16.0, 1.6 Hz, 1H), 2.50 – 2.23 (m, 1H), 2.18 (s, 3H), 2.05 (dt, *J* = 13.2, 3.6 Hz, 1H), 1.80 (dd, *J* = 23.6, 12.8 Hz, 1H), 1.49 – 1.31 (m, 3H), 1.17 – 1.00 (m, 1H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -193.33 (d, *J* = 30.2 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.4 (d, *J* =17.3 Hz), 169.2, 157.4, 137.3, 136.7 (d, *J* = 2.2 Hz), 135.1, 129.0, 128.6, 127.7 (d, *J* = 1.5 Hz), 127.3, 122.8, 119.9 (d, *J* = 1.9 Hz), 119.2 (d, *J* = 1.1 Hz), 118.1, 104.4 (d, *J* = 22.7 Hz), 93.1 (d, *J* =201.6 Hz), 91.2, 35.6 (d, *J* =21.8 Hz), 29.8 (d, *J* =2.5 Hz), 28.5, 21.2, 19.7, 14.0. HRMS (ESI), m/z calcd for $C_{25}H_{25}FNaO_5^+$ ([M + Na]$^+$) 447.1578, found 447.1584.



racemic

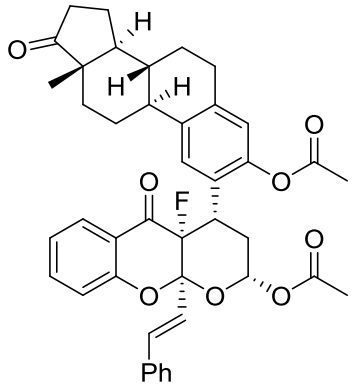
	Retention Time	Area	%Area
1	6.395	28828074	50.415
2	7.054	28357499	49.585



enantio-enriched

	Retention Time	Area	%Area
1	6.392	883122	2.663
2	7.044	32284669	97.337

(2*S*,4*S*,4a*S*,10a*R*)-4-((3a*R*,5a*R*,11b*S*,11c*R*)-9-acetoxy-3a-methyl-3-oxo-2,3,3a,4,5,5a,6,7,11b,11c-decahydro-1H-cyclopenta[c]phenanthren-10-yl)-4a-fluoro-5-oxo-10a-styryl-2,3,4,4a,5,10a-hexahydropyrano[2,3-b]chromen-2-yl acetate (3an)

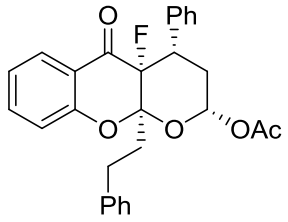


Compound **3an**: Prepared in 0.1 mmol scale at 20-23 ^{o}C for 48 h. 88% yield (60.9 mg), white solid; Mp: 161.7-163.3 ^{o}C; >19:1 d.r.

$[\alpha]^{25}_{D}$ = - 4.3 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.65 – 7.55 (m, 1H), 7.43 (s, 1H), 7.30 – 7.18 (m, 6H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.67 (s, 1H), 6.24 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.84 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.98 – 2.78 (m, 2H), 2.65 – 2.41 (m, 3H), 2.32 – 2.23 (m, 1H), 2.20 (s, 3H), 2.18 – 1.91 (m, 5H), 1.74 – 1.57 (m, 4H), 1.52 (dd, *J* = 11.6, 6.8 Hz, 1H), 1.48 (s, 3H), 1.40 (ddd, *J* = 18.4, 9.2, 5.6 Hz, 1H), 0.94 (s, 3H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -189.12 (s,1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.3 (d, *J* = 17.3 Hz), 169.1 (d, *J* =6.8 Hz), 157.3, 145.9, 137.9 (d, *J* =1.4 Hz), 137.0, 137.0, 135.0, 129.1, 128.6, 128.4 (d, *J* = 0.7 Hz), 127.3, 126.9 (d, *J* = 3.4 Hz), 124.0, 122.9, 122.0, 119.7, 119.5 (d, *J* = 1.3 Hz), 118.0, 104.6 (d, *J* = 22.7 Hz), 93.3 (d, *J* = 203.7 Hz), 90.8, 50.6, 48.1, 44.4, 37.9, 36.0, 31.7, 29.4, 29.2, 26.4, 25.9, 21.7, 21.2, 19.9, 14.0. HRMS (ESI), m/z calcd for $C_{42}H_{41}FNaO_8^+$ ([M + Na]$^+$) 715.2678, found 715.2661.

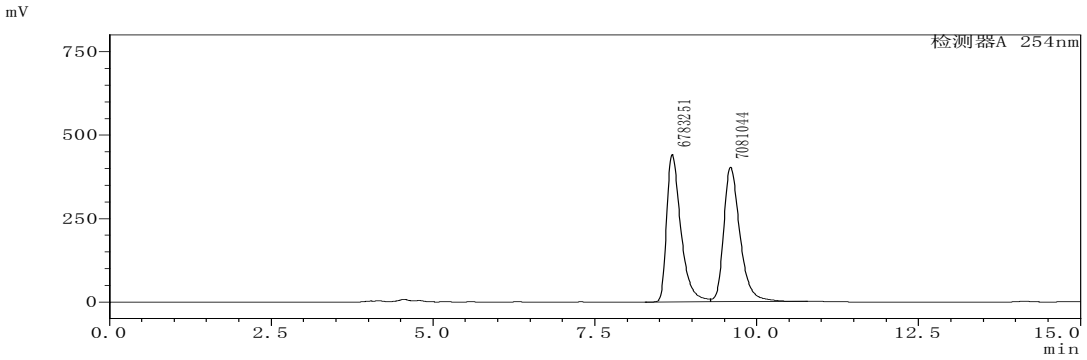
(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-10a-phenethyl-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl acetate (4a)



Compound **4a**: Prepared in 0.15 mmol scale at 20-23 ^{o}C for 48 h. 92% yield (63.5 mg), white solid; Mp: 188.9-190.3 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 8.70 min, *t*r (major) =9.45 min.

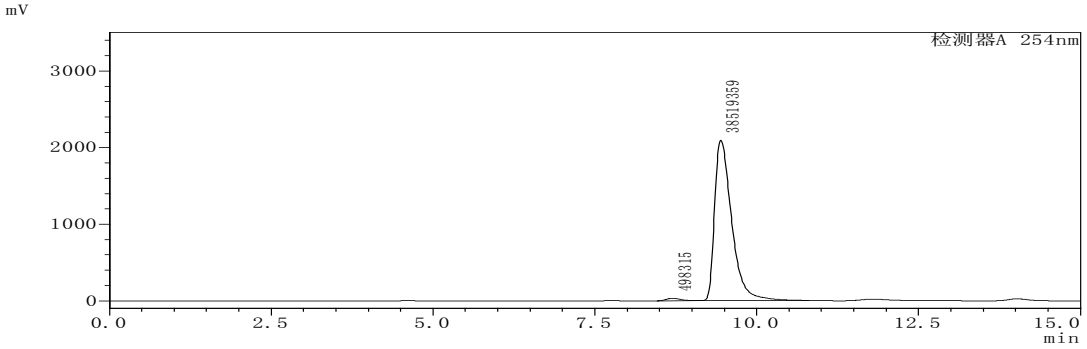
$[\alpha]^{25}_{D}$ = - 50.0 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.67 – 7.54 (m, 1H), 7.37 – 7.26 (m, 3H), 7.25 – 6.94 (m, 9H), 6.67 (dd, *J* = 10.4, 1.6 Hz, 1H), 3.59 (ddd, *J* = 31.6, 13.6, 3.6 Hz, 1H), 2.97 (ddd, *J* = 16.0, 11.2, 5.2 Hz, 1H), 2.84 – 2.70 (m, 1H), 2.52 (td, *J* = 13.0, 10.8 Hz, 1H), 2.43 – 2.27 (m, 1H), 2.23 (s, 3H), 2.16 – 1.88 (m, 2H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -192.71 (d, *J* = 31.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3 (d, *J* =17.7 Hz), 189.2, 169.1, 156.8, 141.0, 137.2, 135.5, 128.7, 128.4, 128.4, 128.3, 127.5, 126.0, 122.9, 119.3, 118.4, 106.4 (d, *J* =23.6 Hz), 106.3, 93.3 (d, *J* =203.2 Hz), 90.7, 42.2 (d, *J* =20.4 Hz), 32.7, 29.9, 27.7, 21.3. HRMS (ESI), m/z calcd for $C_{28}H_{25}FNaO_5^+$ ([M + Na]$^+$) 483.1578, found 483.1588.



racemic

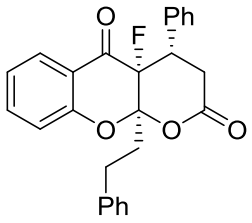
	Retention Time	Area	%Area
1	8.695	6783251	48.926
2	9.596	7081004	51.074



enantio-enriched

	Retention Time	Area	%Area
1	8.700	498315	1.377
2	9.446	38519359	98.623

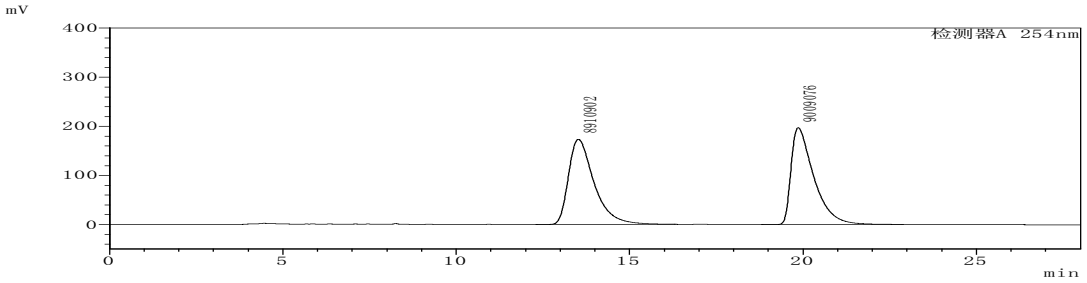
(4*S*,4a*S*,10a*R*)-4a-fluoro-10a-phenethyl-4-phenyl-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromene-2,5-dione (4b)



Compound **4b**: Prepared in 0.15 mmol scale at 20-23 ^{o}C for 48 h. 71% yield (59.4 mg), white solid; Mp: 227.1-230.1 ^{o}C; >19:1 d.r., 97% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 13.48 min, *t*r (major) = 19.33 min.

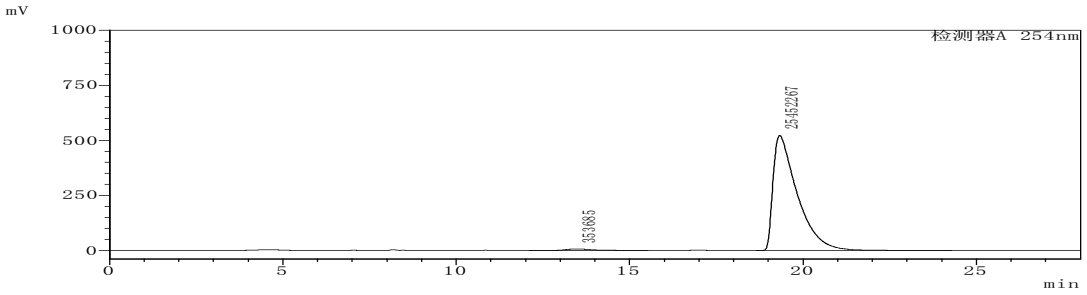
$[\alpha]^{25}_{D}$ = - 5.7 (c = 1.0 in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 4.44 Hz, 3H), 7.24 – 7.11 (m, 4H), 7.06 (t, *J* = 9.6 Hz, 5H), 3.92 (ddd, *J* = 32.2, 13.2, 6.0 Hz, 1H), 3.29 (dd, *J* = 17.6, 13.2 Hz, 1H), 3.16 – 2.99 (m, 2H), 2.92 – 2.73 (m, 1H), 2.48 (ddd, *J* = 14.8, 7.6, 3.6 Hz, 1H), 2.24 – 2.05 (m, 1H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -195.47 (d, *J* = 32.2 Hz). ^{13}C NMR (100MHz, $CDCl_3$) δ 187.4 (d, *J* = 17.7 Hz), 166.2, 155.6, 140.2, 137.6, 133.8, 128.9, 128.8, 128.5, 128.3, 128.3, 128.3, 127.5, 126.2, 123.6, 119.0, 118.1, 107.1 (d, *J* = 24.4 Hz), 93.2 (d, *J* = 203.6 Hz), 40.5 (d, *J* =19.9 Hz), 32.4 (d, *J* = 4.7 Hz), 32.4, 27.4. HRMS (ESI), m/z calcd for $C_{26}H_{21}FNaO_4^+$ ([M + Na]$^+$) 439.1316, found 439.1314.



racemic

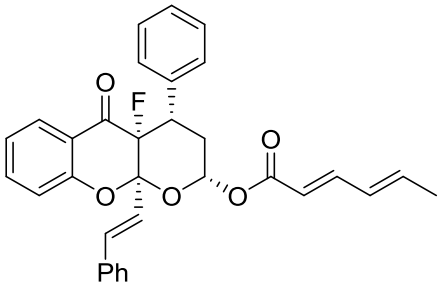
	Retention Time	Area	%Area
1	13.526	8910902	49.726
2	19.865	9009076	50.274



enantio-enriched

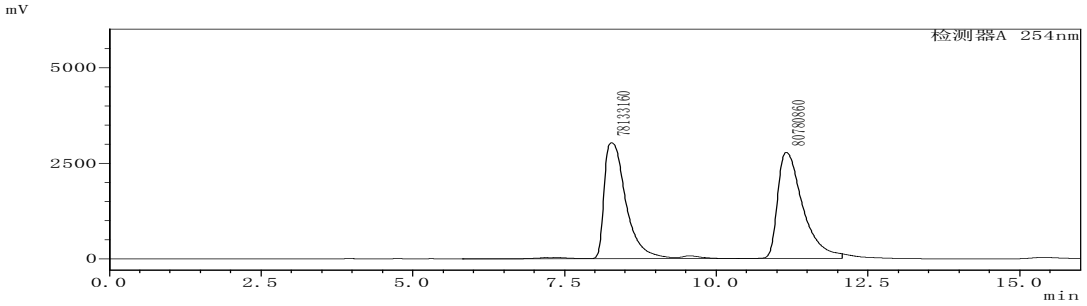
	Retention Time	Area	%Area
1	13.479	353685	1.371
2	19.331	25452267	98.629

(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl (2E,4E)-hexa-2,4-dienoate (4c)



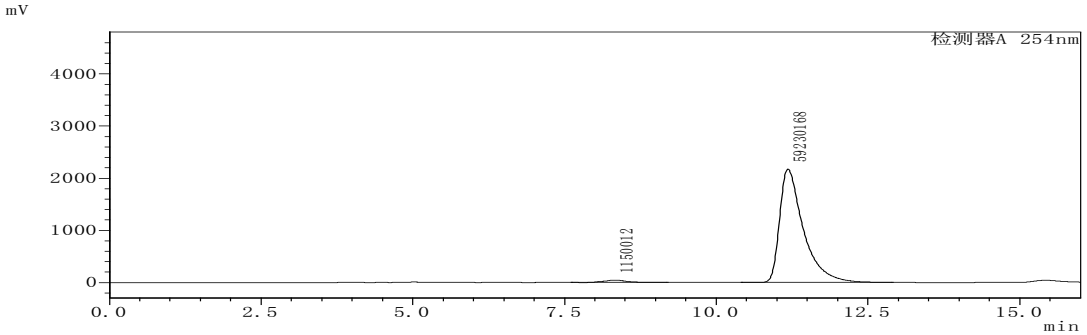
Compound **4c**: Prepared in 0.1 mmol scale at 20-23 ^{o}C for 48 h. 75% yield (38.3 mg), white solid; Mp: 135.6-136.9 ^{o}C >19:1 d.r., 96% *ee*. HPLC (chiral IA column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 8.33 min, *t*r (major) = 11.18 min. $[\alpha]^{25}_{D}$ = - 15.0 (c = 1.0 in CH_2Cl_2). ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.50 – 7.36 (m, 1H), 7.34 – 7.17 (m, 9H), 7.12 (t, *J* = 7.2 Hz, 3H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.37 – 6.13 (m, 3H), 5.86 (d, *J* = 15.2 Hz, 1H), 3.67 (ddd, *J* = 31.2, 13.6, 3.2 Hz, 1H), 2.63 (dd, *J* = 23.6, 13.2 Hz, 1H), 2.15 (dd, *J* = 10.0, 2.8 Hz, 1H), 1.89 (d, *J* = 4.4 Hz, 3H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -190.91 (d, *J* = 31.5 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.0 (d, *J* =17.3 Hz), 165.2, 157.3, 147.4, 141.1, 137.3, 136.8 (d, *J* = 2.3 Hz), 135.6, 135.1, 129.8, 129.0, 128.8, 128.8, 128.7, 128.6, 128.4, 127.7 (d, *J* = 1.3 Hz), 127.3, 123.0, 119.9 (d, *J* = 1.6 Hz), 119.5 (d, *J* = 1.4 Hz), 118.2, 117.7, 104.7 (d, *J* =22.6 Hz), 93.0

(d, *J* =203.9 Hz), 91.1, 42.6 (d, *J* = 20.5 Hz), 30.0 (d, *J* = 2.1 Hz), 18.9. HRMS (ESI), m/z calcd for $C_{32}H_{27}FNaO_5^+$ ($[M + Na]^+$) 533.1735, found 533.1735.



racemic

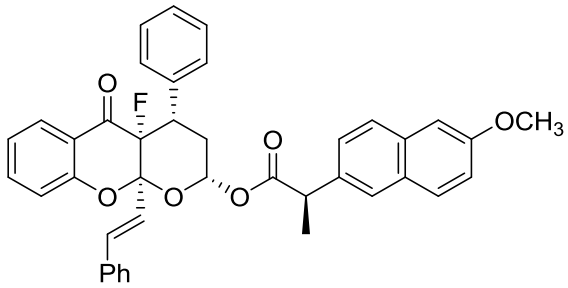
	Retention Time	Area	%Area
1	8.275	78133160	49.167
2	11.156	80780860	50.833



enantio-enriched

	Retention Time	Area	%Area
1	8.326	1150012	1.905
2	11.182	59230168	98.095

(2*S*,4*S*,4a*S*,10a*R*)-4a-fluoro-5-oxo-4-phenyl-10a-((*E*)-styryl)-3,4,4a,10a-tetrahydro-2H,5H-pyrano[2,3-b]chromen-2-yl (R)-2-(6-methylnaphthalen-2-yl)propanoate (4d)

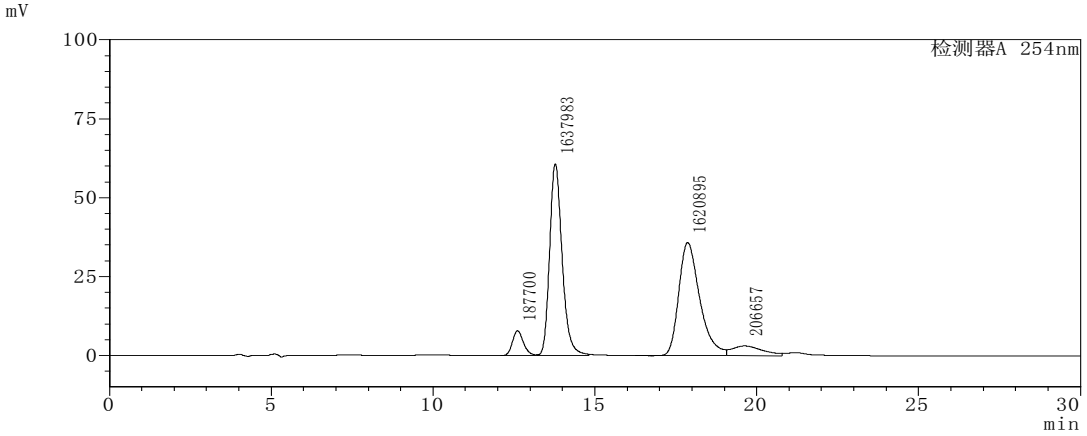


Compound **4d**: Prepared in 0.2 mmol scale at 20-23 ^oC for 48 h. 90% yield (113.0 mg), white solid; Mp: 137.2-138.9 ^oC, >19:1 d.r, >99% *ee*. HPLC (chiral ID column), hexane/*i*-PrOH = 70/30, flow rate 0.8 ml/min, λ = 254 nm, *t*r (minor) = 13.40 min, *t*r (major) = 17.71 min.

$[\alpha]^{25}_D$ = - 7.9 (c = 1.0 in CH_2Cl_2).

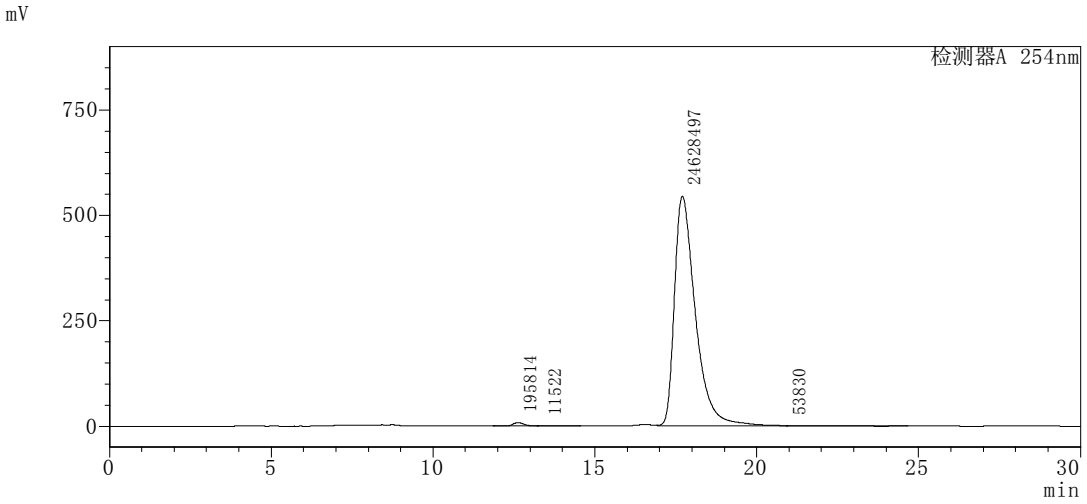
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.66 (m, 4H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.41 – 6.99 (m, 14H), 6.82 (m, 2H), 6.19 (dd, *J* = 16.0, 0.7 Hz, 1H), 4.02 (dd, *J* = 13.6, 6.6 Hz, 1H), 3.91 (s, 3H), 3.74 – 3.40 (m, 1H), 2.58 (dd, *J* = 23.9, 12.9 Hz, 1H), 2.11 (d, *J* = 12.8 Hz, 1H), 1.68 (d, *J* = 6.9 Hz, 3H). ^{19}F NMR (564 MHz,

$CDCl_3$) δ -190.75 (d, *J* = 31.5 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (d, *J* =17.5 Hz), 173.0, 157.8, 157.2, 137.3, 136.7, 135.5, 135.0, 134.8, 133.8, 129.5, 129.0, 128.9, 128.7, 128.5, 128.3, 127.6, 127.3, 127.2, 126.4, 126.2, 122.9, 119.5, 119.3, 119.1, 118.2, 105.6, 104.6 (d, *J* =22.8 Hz), 92.8 (d, *J* =203.7 Hz), 91.2, 55.4 (d, *J* = 3.1 Hz), 45.4, 42.5 (d, *J* = 20.5 Hz), 29.6, 18.7. HRMS (ESI), m/z calcd for $C_{40}H_{33}FNaO_6^+$ ([M + Na]$^+$) 651.2153, found 651.2162.



racemic

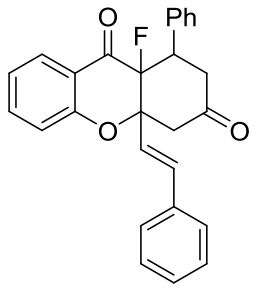
	Retention Time	Area	%Area
1	12.611	187700	5.138
2	13.776	1637983	44.837
3	17.868	1620895	44.369
4	19.625	206657	5.657



enantio-enriched

	Retention Time	Area	%Area
1	12.628	195814	0.787
2	13.400	11522	0.046
3	17.707	24722908	99.005
4	20.863	41085	0.165

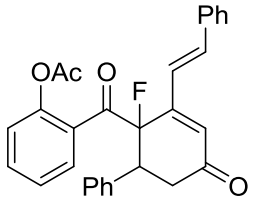
(*E*)-9a-fluoro-1-phenyl-4a-styryl-1,4,4a,9a-tetrahydro-3H-xanthene-3,9(2H)-dion e (6a)



Compound 6a: was prepared in 0.4 mmol scale catalyzed by 20 mol% pyrrolidine at 20-23 ^{o}C for 22 h in the presence of 20 mol% salicylic acid. 13% yield (21.5 mg), >19:1 d.r., White solid, Mp: 223.2- 224.9 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.53 (m, 2H), 7.39 – 7.18 (m, 9H), 7.18 – 6.97 (m, 3H), 6.66 (d, *J* = 16.2 Hz, 1H), 6.33 (dd, *J* = 16.2, 1.7 Hz, 1H), 3.79 (ddd, *J* = 32.9, 13.9, 4.3 Hz, 1H), 3.36 – 3.05 (m, 2H), 2.89 (d, *J* = 15.5 Hz, 1H), 2.69 (dd, *J* = 14.5, 2.5 Hz, 1H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -192.7(d, *J* =33.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.3, 188.3 (d, *J* =17.1 Hz), 157.3, 137.1, 135.4 (d, *J* =40.7 Hz), 134.2 (d, *J* =4.1 Hz), 128.9, 128.8, 128.7, 128.5, 128.5, 128.5, 127.5 (d, *J* =1.6 Hz), 126.9, 122.9 (d, *J* =23.9 Hz), 120.6 (d, *J* =1.6 Hz), 118.2, 94.9 (d, *J* =203.3 Hz), 86.6(d, *J* =22.3 Hz), 48.6, 44.9 (d, *J* =20.0 Hz), 42.8 (d, *J* =3.5 Hz). HRMS (ESI), m/z calcd for $C_{27}H_{21}FNaO_3^+$ ($[M + Na]^+$) 435.1367, found 435.1359.

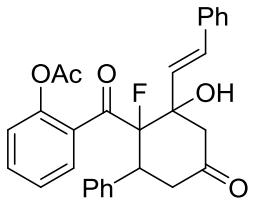
(*E*)-2-(2-fluoro-5-oxo-3-styryl-1,2,5,6-tetrahydro-[1,1'-biphenyl]-2-carbonyl)phen yl acetate (6b)



Compound 6b was prepared in 0.4 mmol scale catalyzed by 20 mol% pyrrolidine at 20-23 ^{o}C for 22 h in the presence of 20 mol% salicylic acid. 24% yield (43 mg), >19:1 d.r., colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 13H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.72 (dd, *J* = 16.0, 2.8 Hz, 1H), 6.38 (s, 1H), 3.96 (ddd, *J* = 26.8, 12.0, 4.0 Hz, 1H), 3.29 (dd, *J* = 16.8, 12.0 Hz, 1H), 2.81 (dd, *J* = 17.0, 4.0 Hz, 1H), 2.27 (s, 3H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -162.7 (d, *J* = 28.3 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.1 (d, *J* =2.7 Hz), 196.5 (d, *J* =27.1 Hz), 169.2, 150.7 (d, *J* =16.2 Hz), 147.4, 145.1 (d, *J* =2.3 Hz), 136.4, 134.3, 133.8 (d, *J* =6.0 Hz), 131.1, 130.4, 129.8, 129.5 (d, *J* =1.4 Hz), 129.4, 128.9, 128.8, 128.7, 128.3, 126.2, 123.5, 119.7 (d, *J* =2.0 Hz), 98.1 (d, *J* =196.6 Hz), 48.2 (d, *J* =21.2 Hz), 39.2 (d, *J* =3.7 Hz), 21.2. HRMS (ESI), m/z calcd for $C_{29}H_{24}FO_4^+$ ($[M + H]^+$) 455.1653, found 455.1661.

(*E*)-2-(1-fluoro-2-hydroxy-4-oxo-6-phenyl-2-styrylcyclohexane-1-carbonyl)pheny l acetate (6c)



Compound 6c: was prepared in 0.4 mmol scale catalyzed by 20 mol% pyrrolidine at 20-23 ^{o}C for 22 h in the presence of 20 mol% salicylic acid. 10% yield (19.1 mg), >19:1 d.r., colorless oil.

^{1}H NMR (400 .12 (m, 11H), 7.00 – 6.86 (m, 2H), 6.80 (d, *J* = 16.0 Hz, 1H), 6.60 – 6.45 (m, 1H), 6.31 (d, *J* = 16.0 Hz, 1H), 4.31 (ddd, *J* = 34.4, 13.2, 4.8 Hz, 1H), 4.10 (s, 1H), 3.17 (t, *J* = 14.2 Hz, 1H), 3.05 (d, *J* = 14.8 Hz, 1H), 2.69 (dd, *J* = 14.8, 4.2 Hz, 1H), 2.49 (d, *J* = 14.8 Hz, 1H), 1.91 (s, 3H). ^{19}F NMR (565 MHz, $CDCl_3$) δ -175.87 (d, *J* = 34.5 Hz, 1F). ^{13}C NMR (150

MHz, CDCl3) δ 205.3, 204.4 (d, *J* =28.3 Hz), 169.2, 148.5, 136.5, 136.0, 133.2, 132.0, 129.7 (d, *J* =11.4 Hz), 129.5, 129.3, 128.7, 128.6, 128.3, 128.2 (d, *J* =2.8 Hz), 127.6, 126.9, 124.9, 124.9, 124.3, 102.2 (d, *J* =205.9 Hz), 79.8 (d, *J* =22.6 Hz) , 48.6 (d, *J* =1.8 Hz), 46.0 (d, *J* =19.1 Hz), 42.2 (d, *J* =3.8 Hz), 20.5. HRMS (ESI), m/z calcd for $C_{29}H_{25}FNaO_5^+$ ($[M + Na]^+$) 495.1578, found 495.1581.

8. Reference

[1] S. W. Leong, S. M . Faudzi, F. Abas, M. F. Aluwi, K. Rullah, L. K. Wai, M. N. Bahari, S. Ahmad, C. L. Tham, K. Shaari, N. H. Lajis, *Molecules*, **2014,** *19* (10), 16058-16081.

[2] E. Kim, S. Park, S. Chang, *Chemistry*, **2018**, *24*, 5765.

[3] H. Watanabe, T. Ariyoshi, A. Ozaki, M. Ihara, M. Ono, H. Saji, *Bioorg. Med. Chem*., **2017**, *25*, 6398.

[4] M. Lu, X. Wang, Z. Xiong, J. Duan, W. Ren, W. Yao, Y. Xia and Z. Wang, *Adv. Synth. Catal*., 2020, **362**, 5524-5528.

[5] G. M. Sheldrick, *Acta Cryst.*, **2008**, *A64*, 112–122.

[6] G. M. Sheldrick, *Acta Cryst.*, **2015**, *A71*, 3–8.

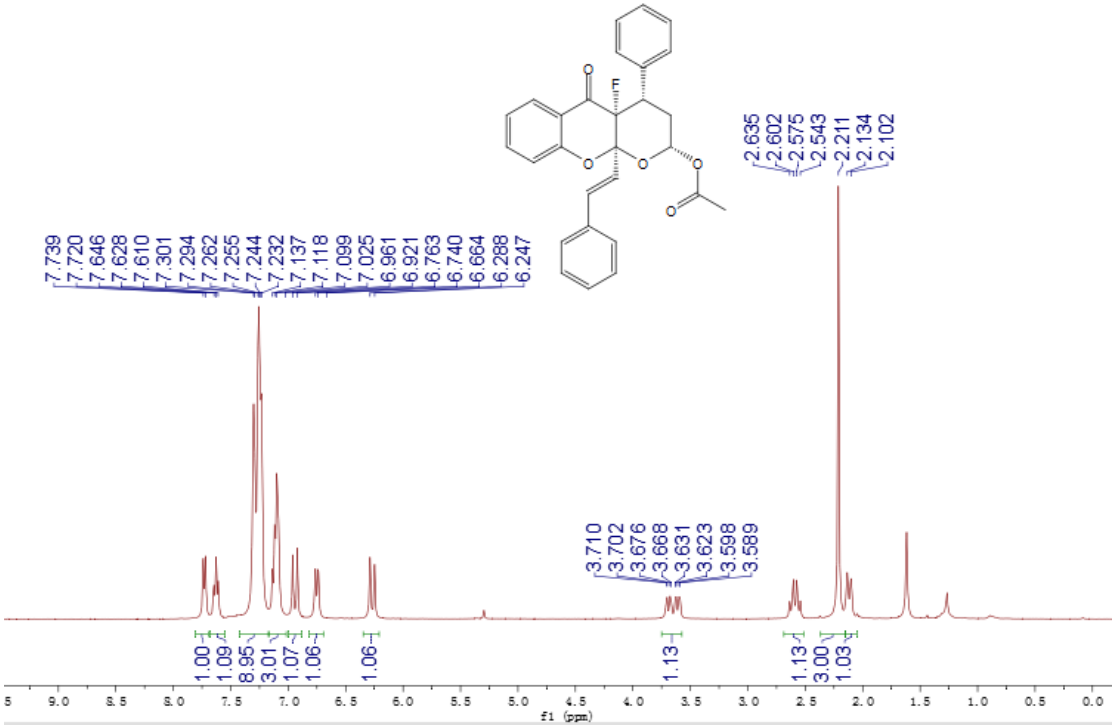
[7] G. M. Sheldrick, *Acta Cryst*., **2015**, *C71*, 3–8.

[8] O.V. Dolomanov, L. J. Bourhis, R.J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Cryst*., **2009**, *42*, 339-341.

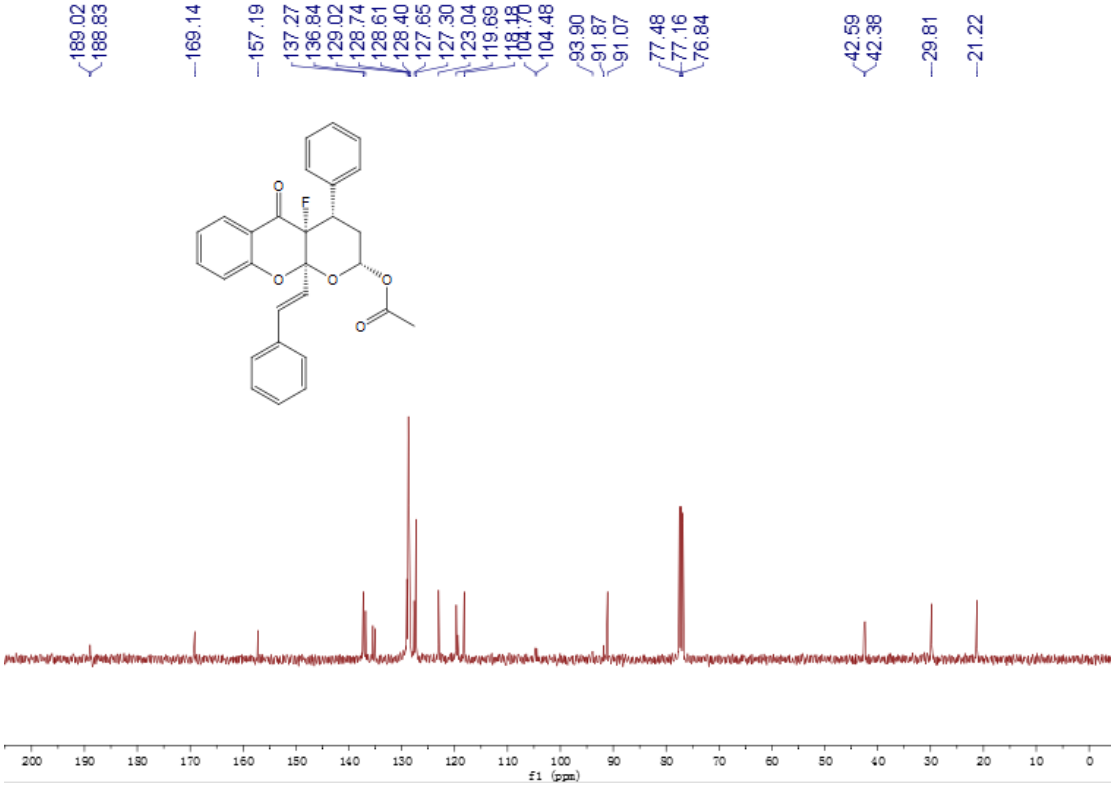
[9] A. L. Spek, *J. Appl. Cryst.*, **2003**, *36*, 7–13.

9. Copies of NMR spectra

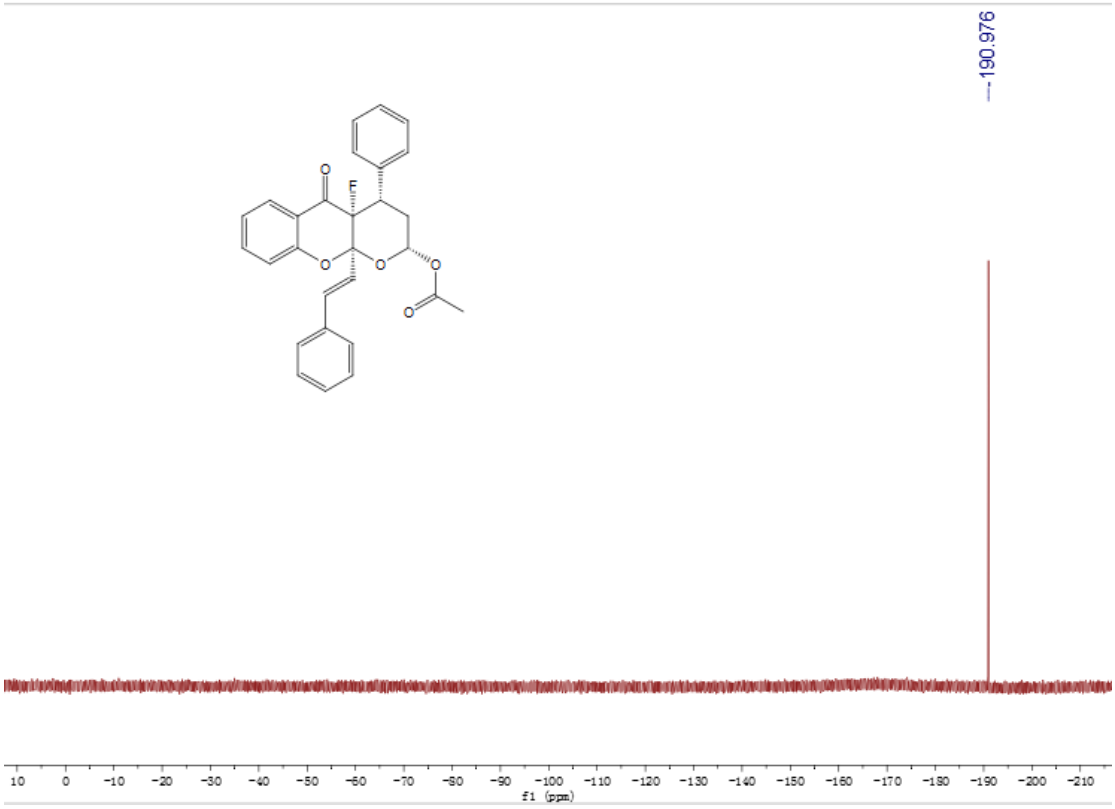
3aa-^{1}H NMR (400 MHz, $CDCl_3$)



3aa-^{13}C NMR (100 MHz, $CDCl_3$)



3aa-^{19}F NMR (565 MHz, $CDCl_3$)



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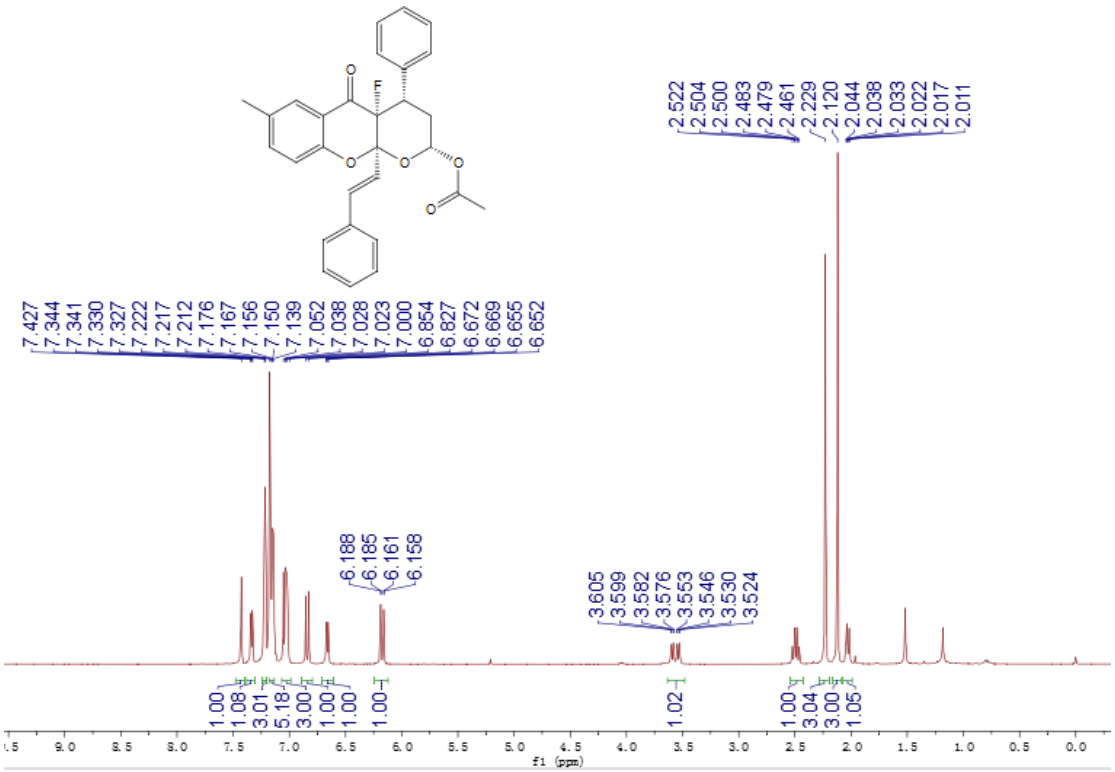
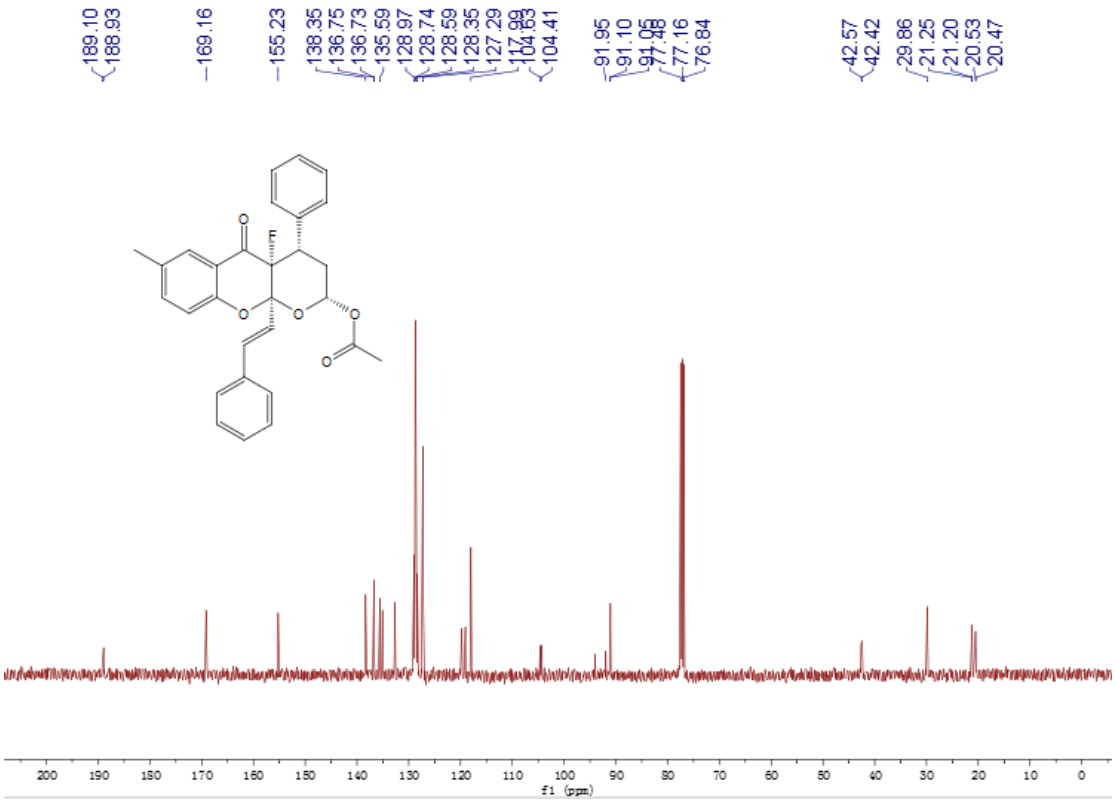
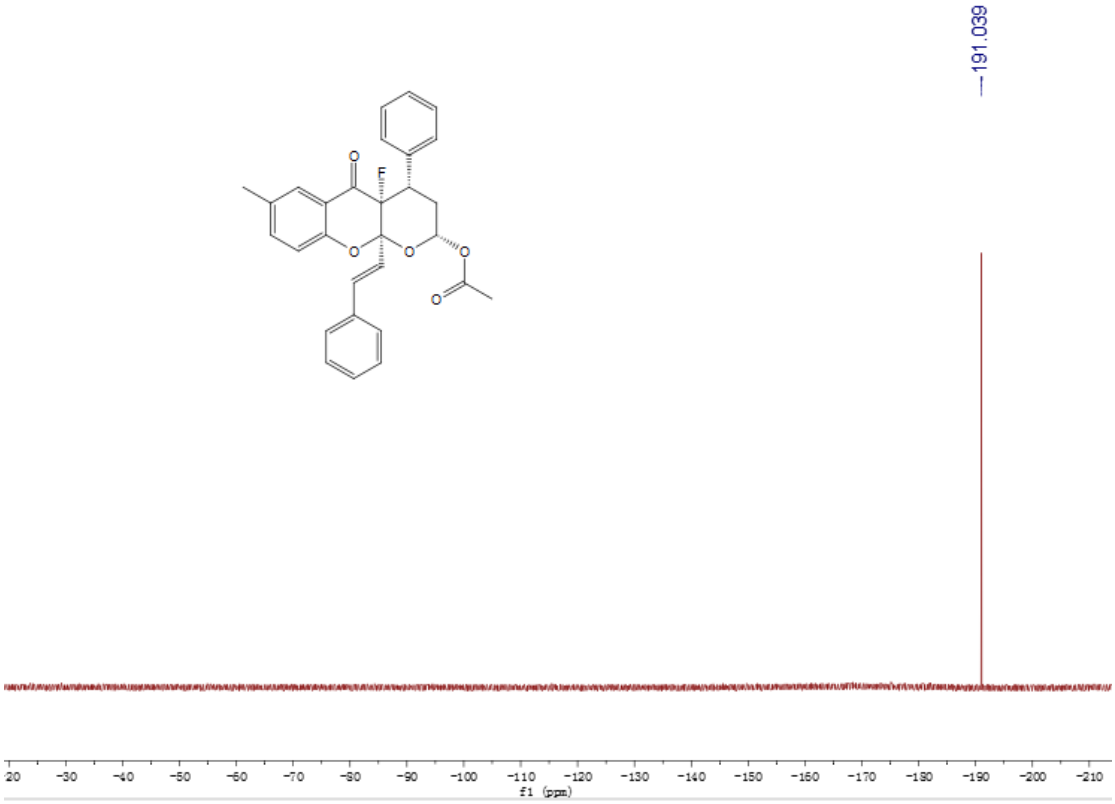


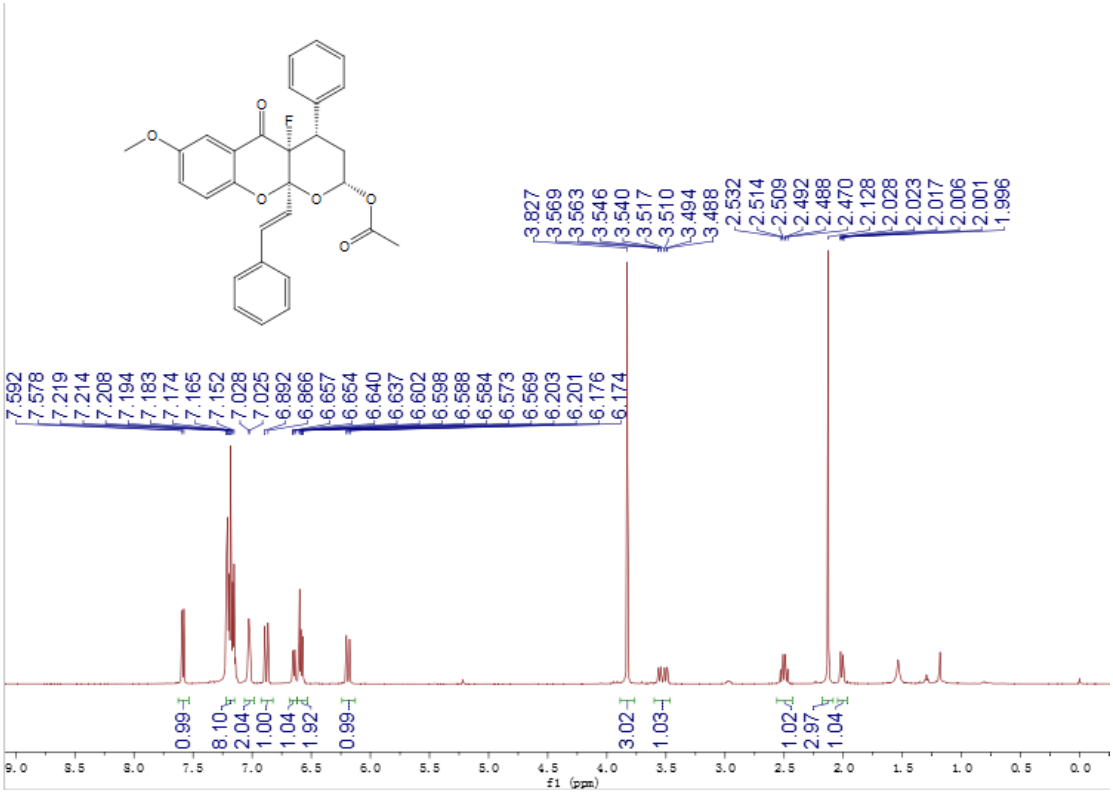
3ba-^{13}C NMR (150 MHz, $CDCl_3$)



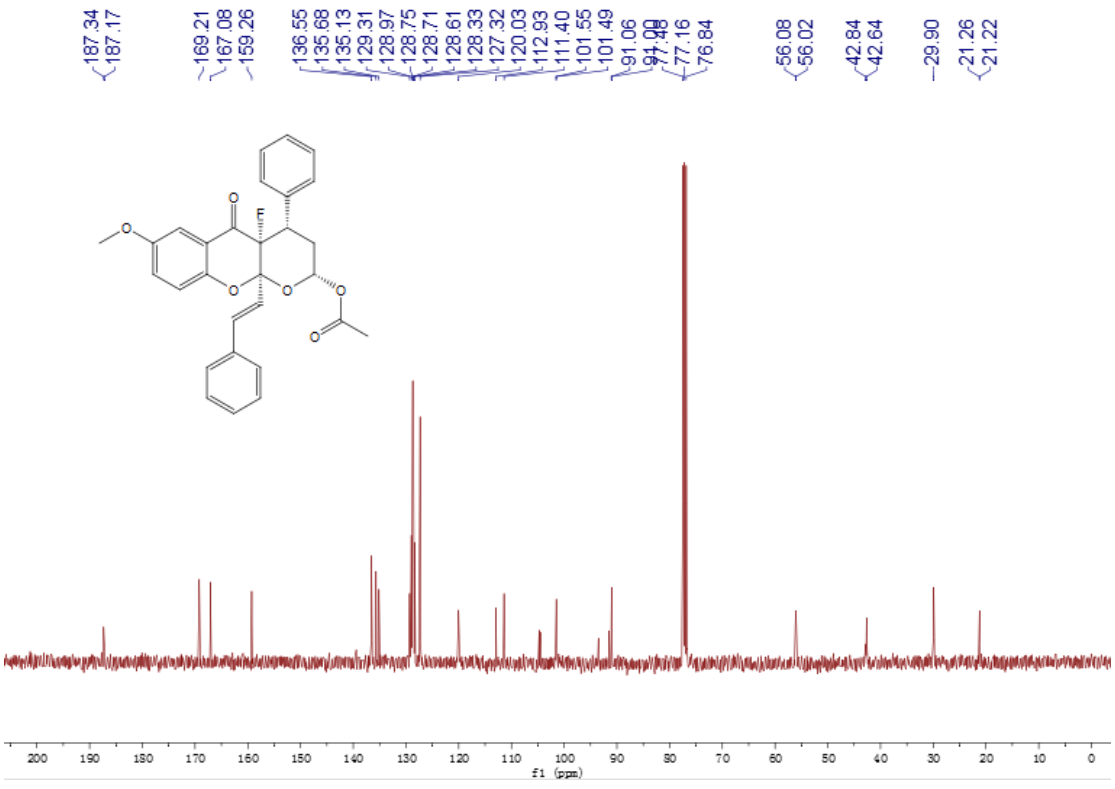
3ba-^{19}F NMR (565 MHz, $CDCl_3$)



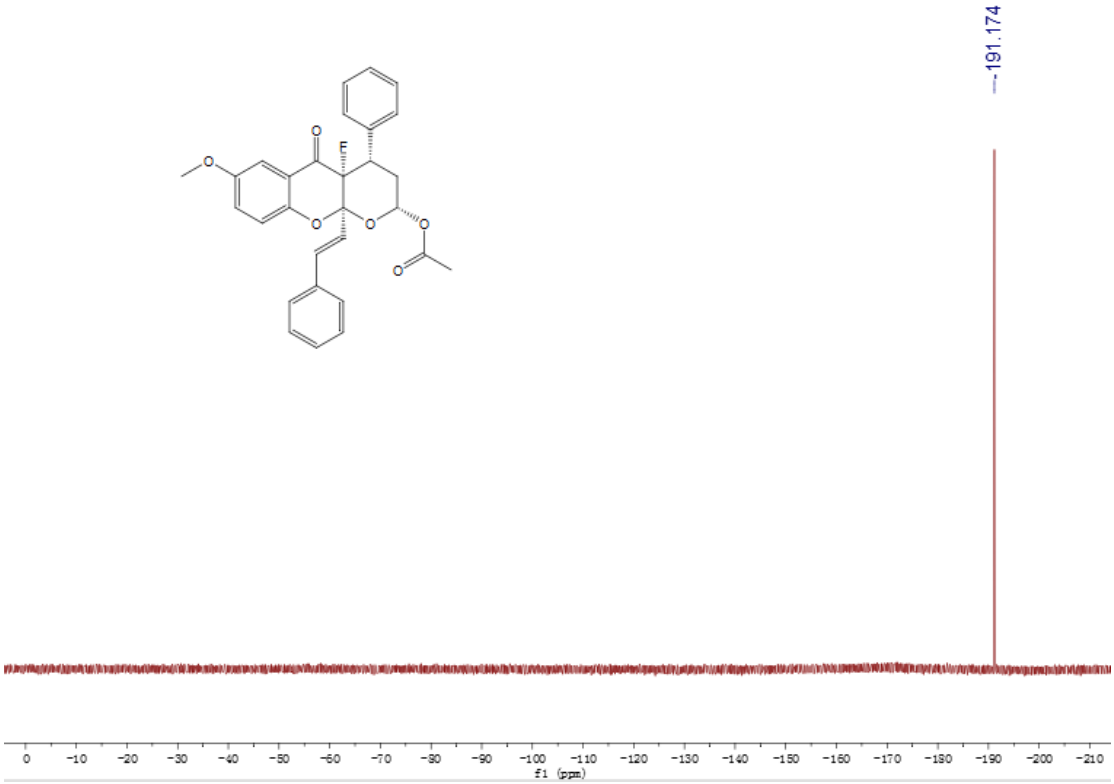
3ca-^{1}H NMR (400 MHz, $CDCl_3$)



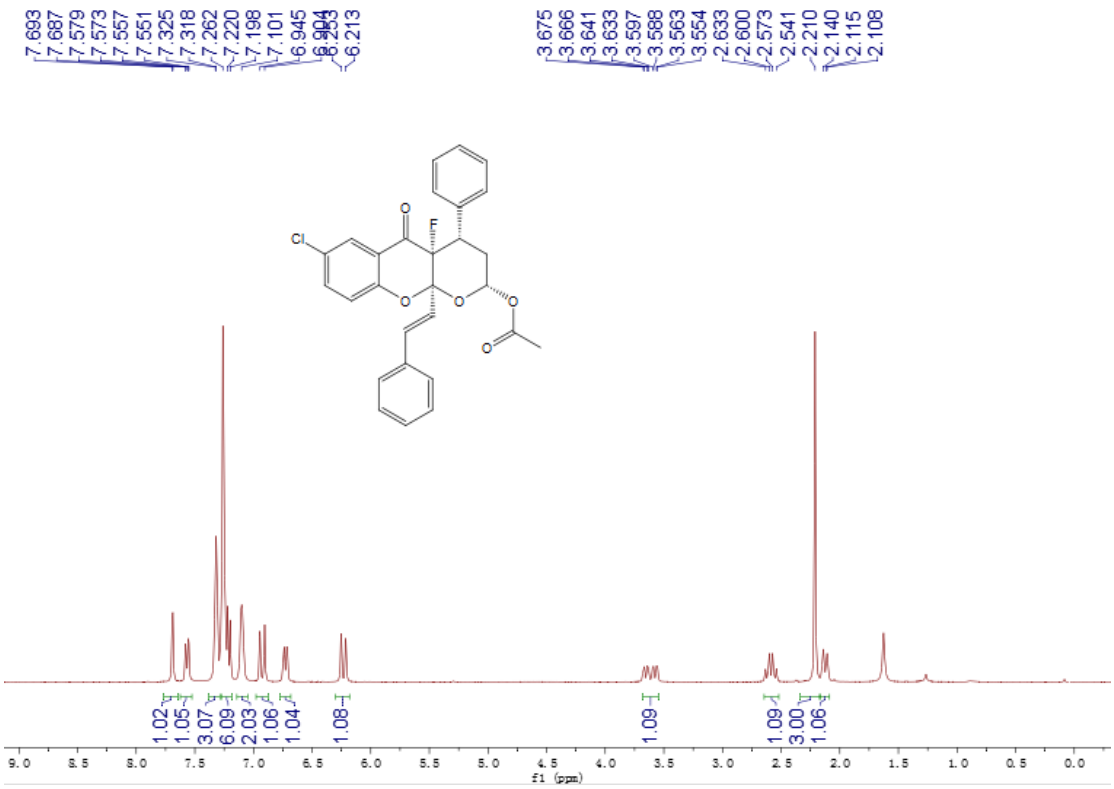
3ca-^{13}C NMR (150 MHz, $CDCl_3$)



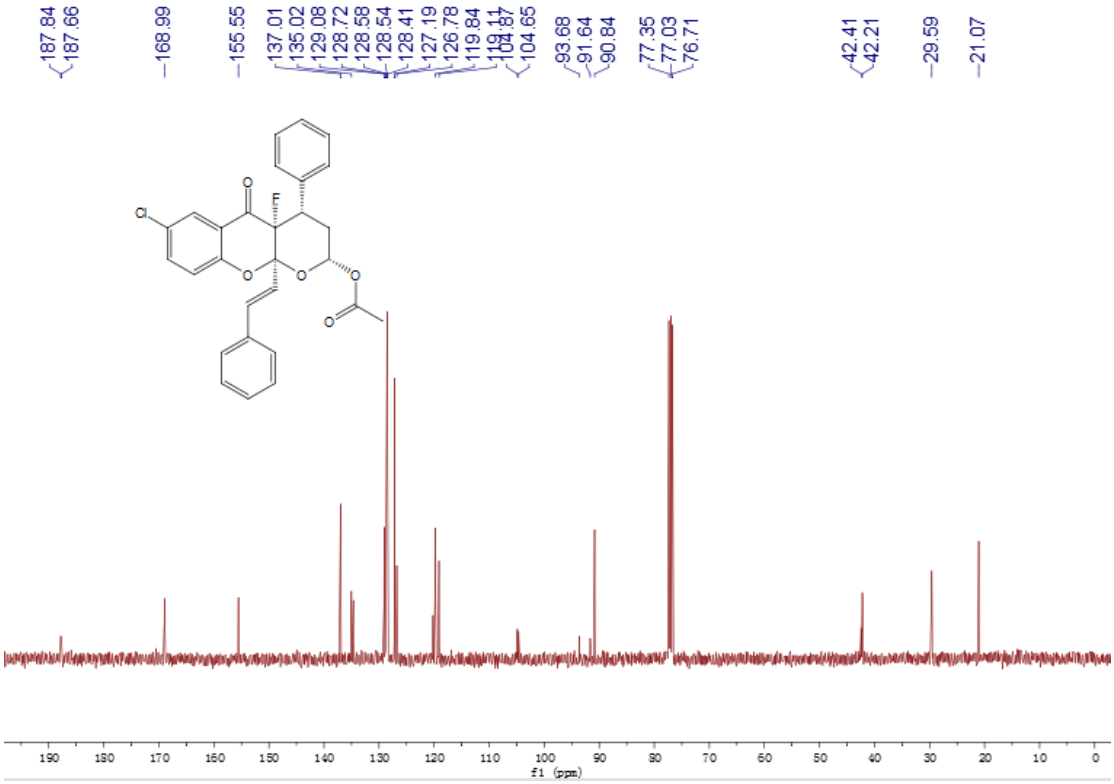
3ca-^{19}F NMR (565 MHz, $CDCl_3$)



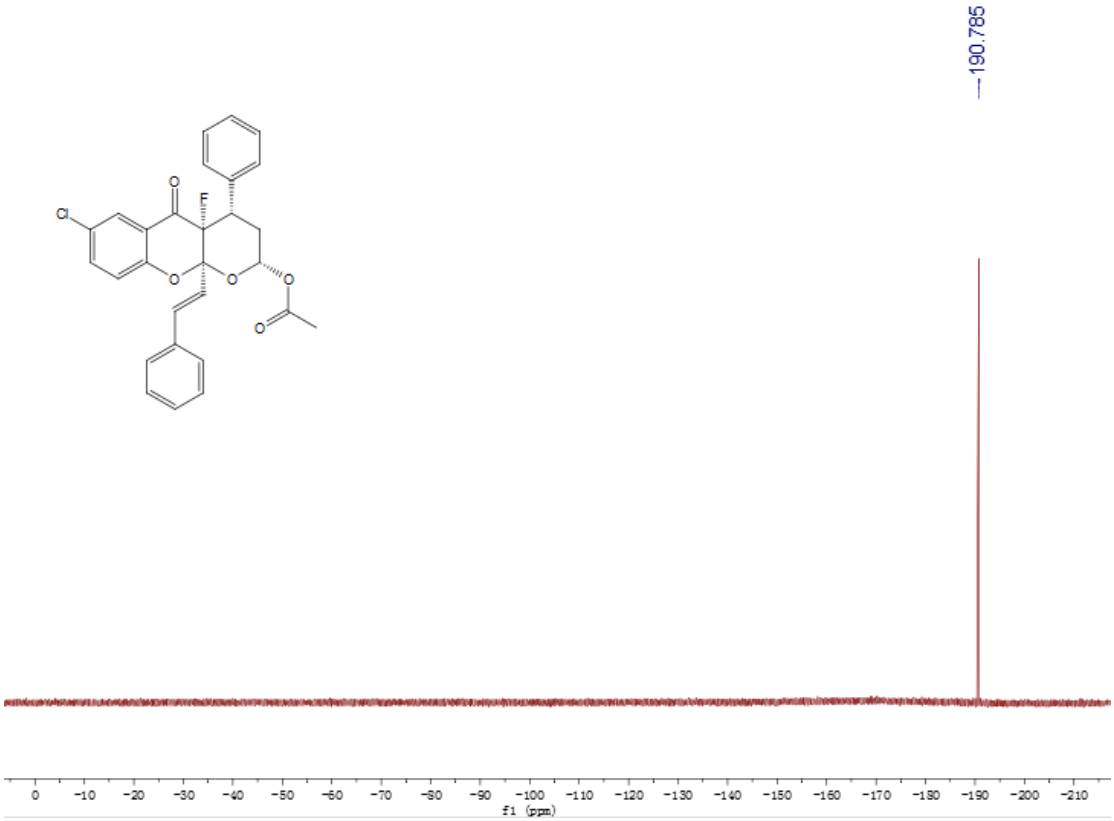
3da-^{1}H NMR (400 MHz, $CDCl_3$)



3da-^{13}C NMR (100 MHz, $CDCl_3$)



3da-^{19}F NMR (565 MHz, $CDCl_3$)



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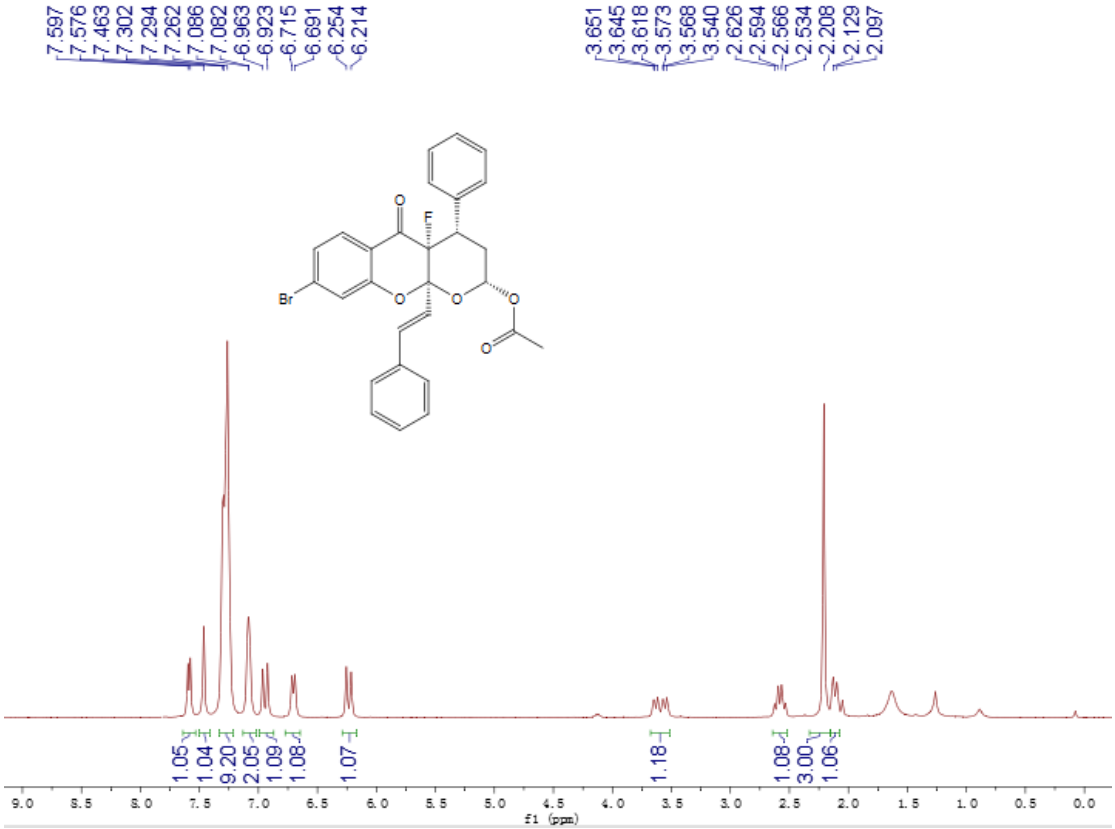

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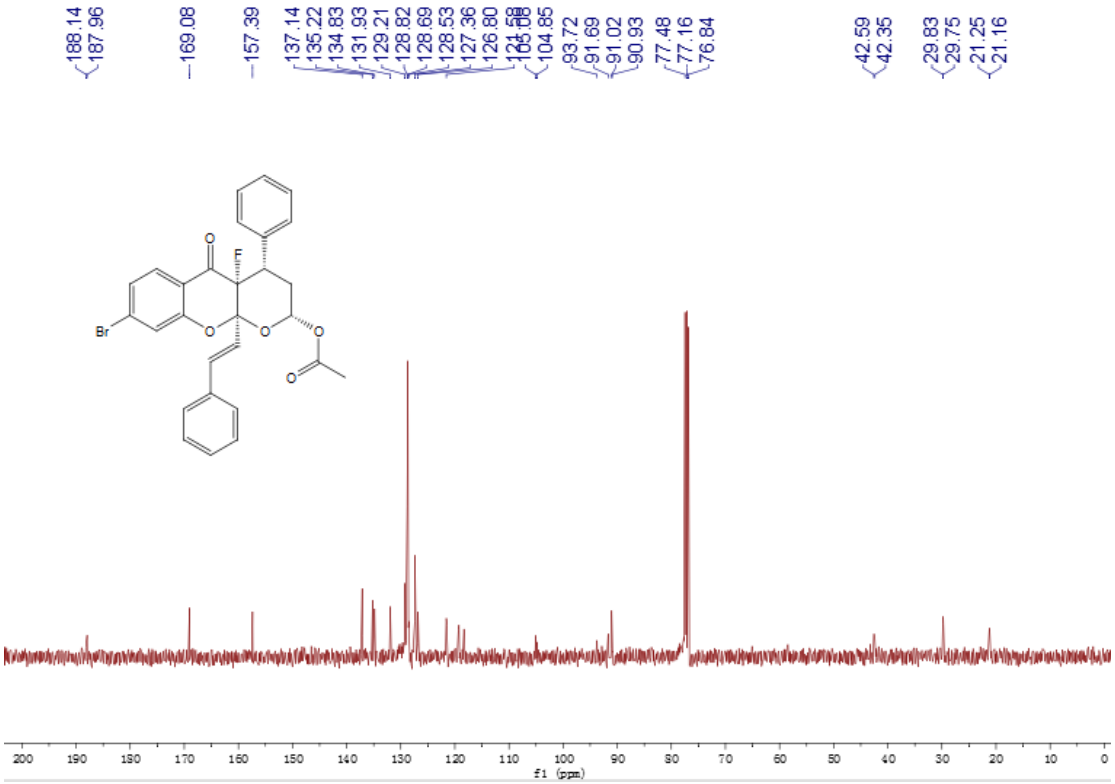
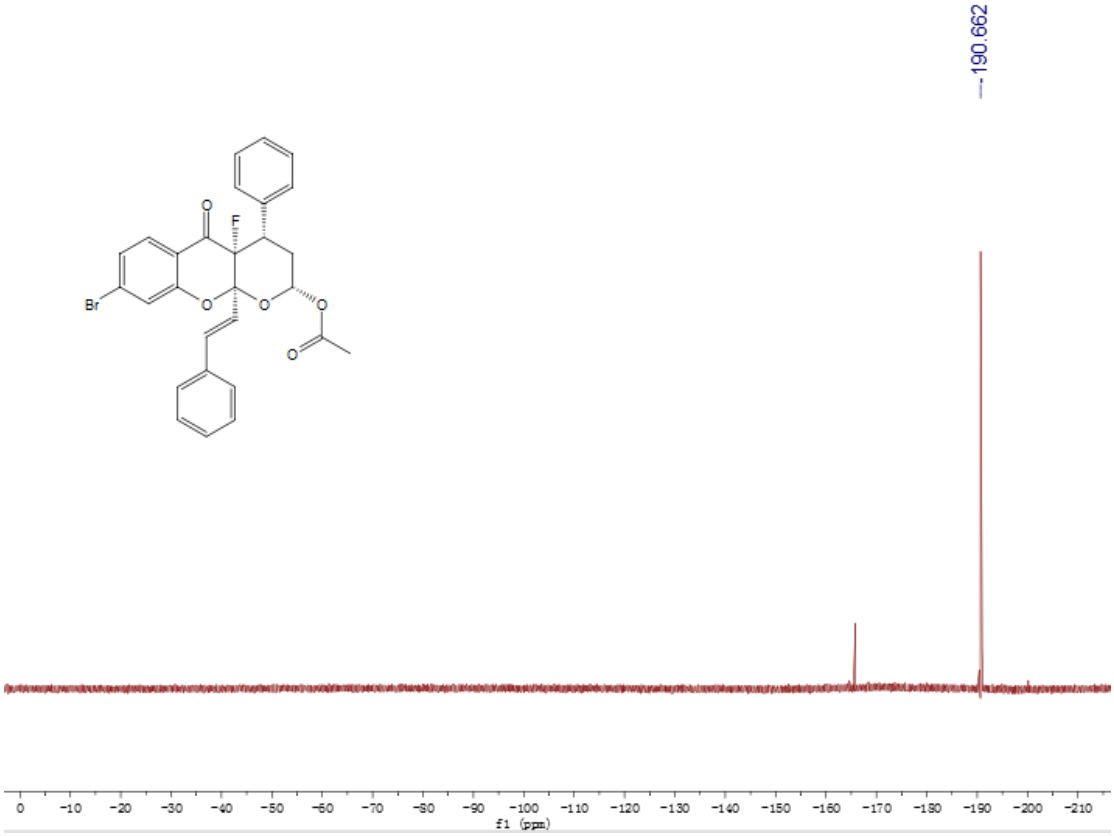
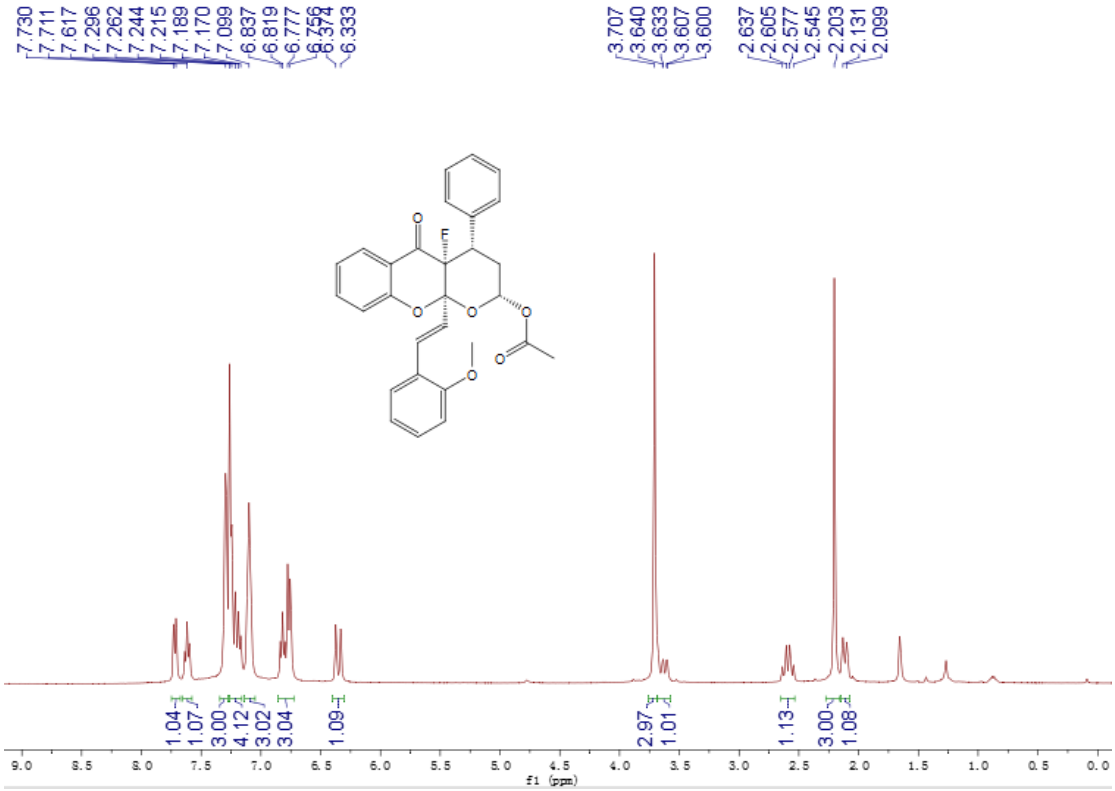


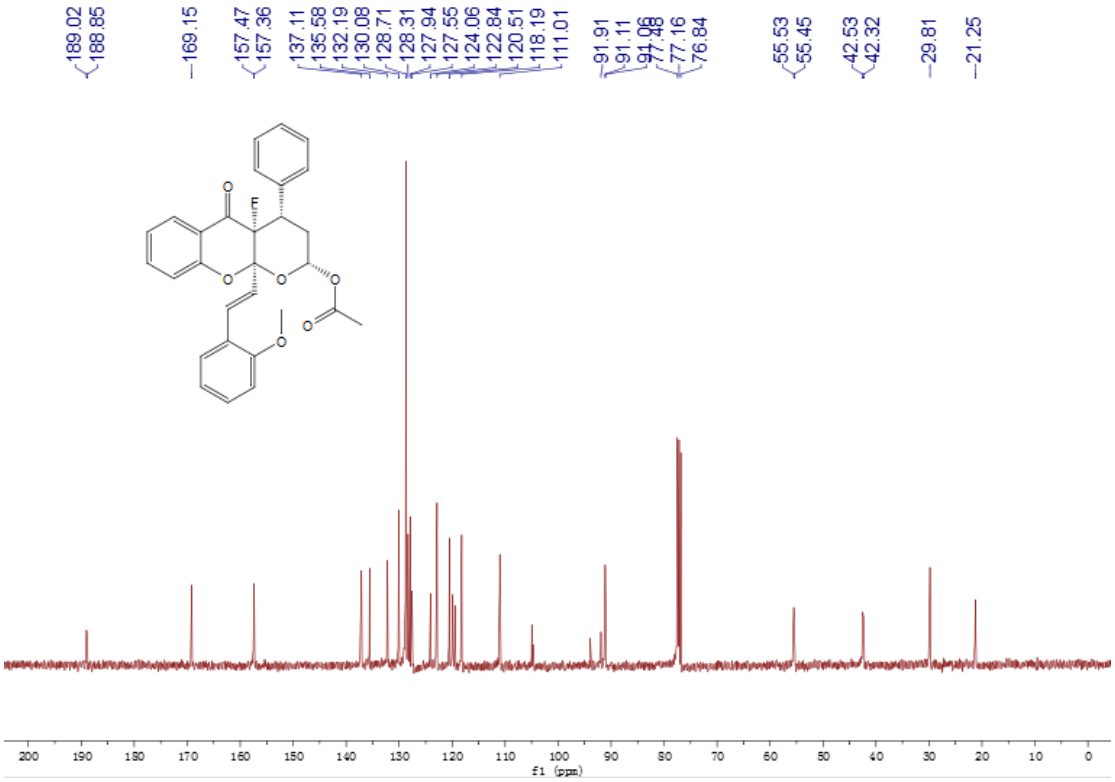
3ea-^{19}F NMR (565 MHz, $CDCl_3$)



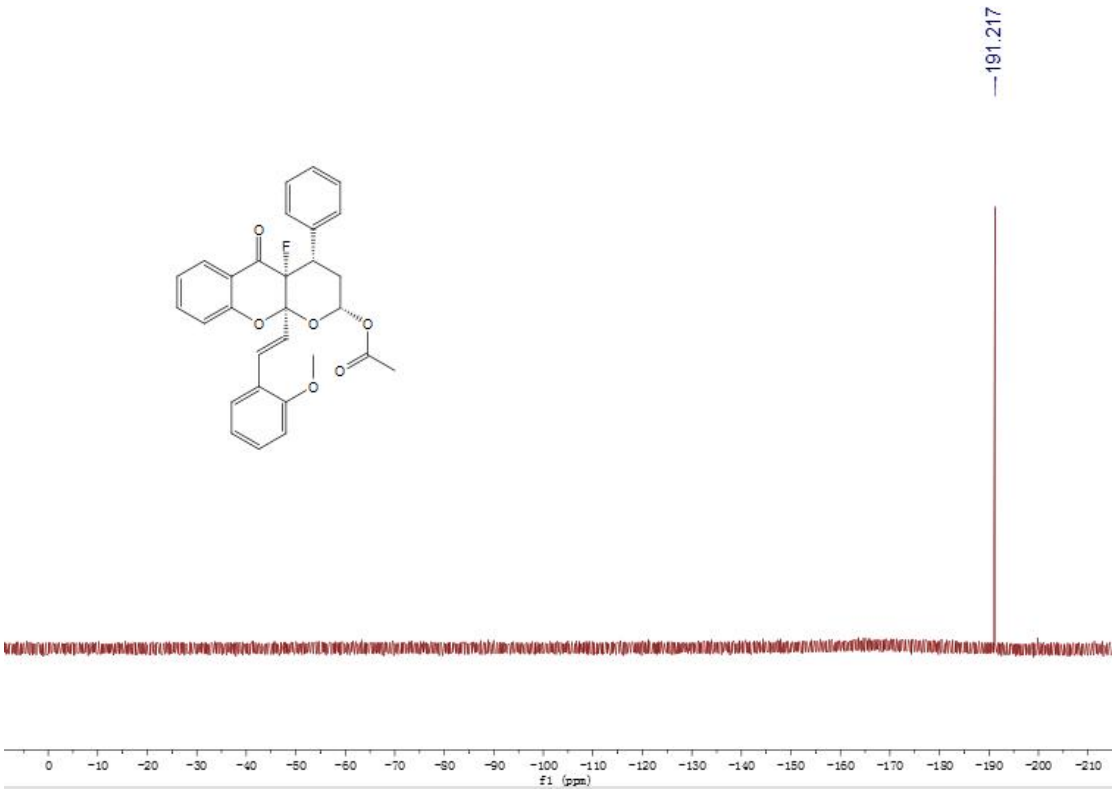
3fa-^{1}H NMR (400 MHz, $CDCl_3$)



3fa-^{13}C NMR (100 MHz, $CDCl_3$)



3fa-^{19}F NMR (565 MHz, $CDCl_3$)



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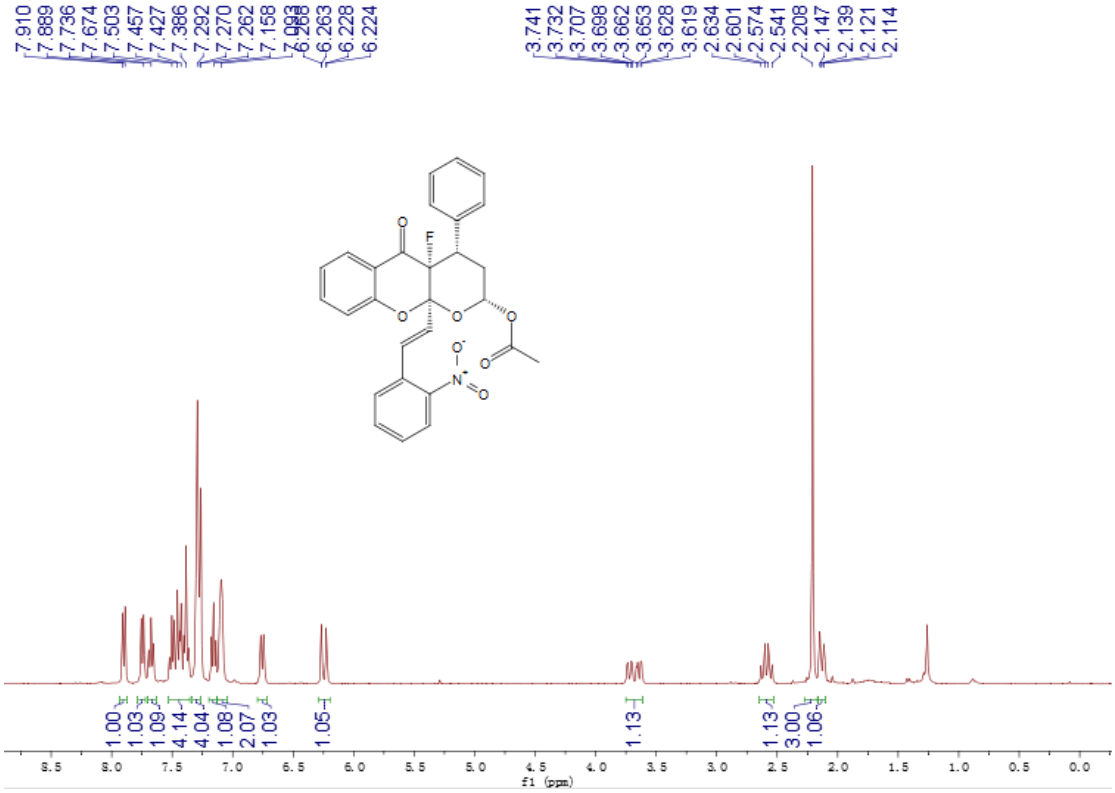

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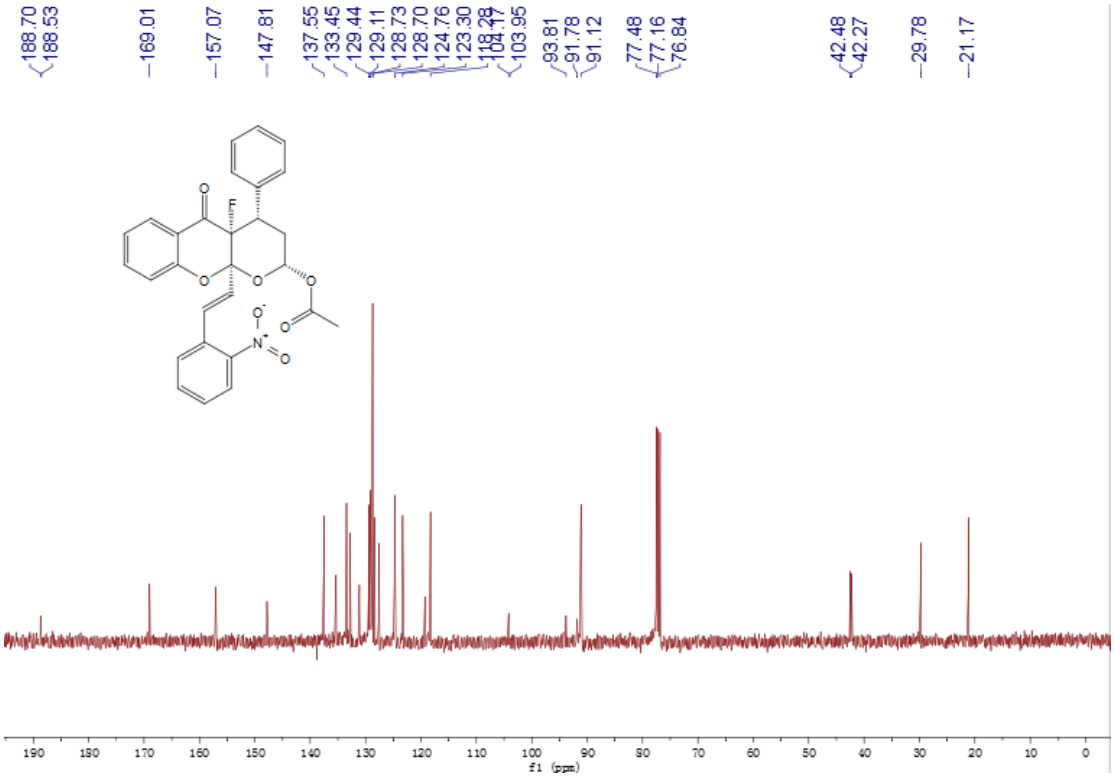
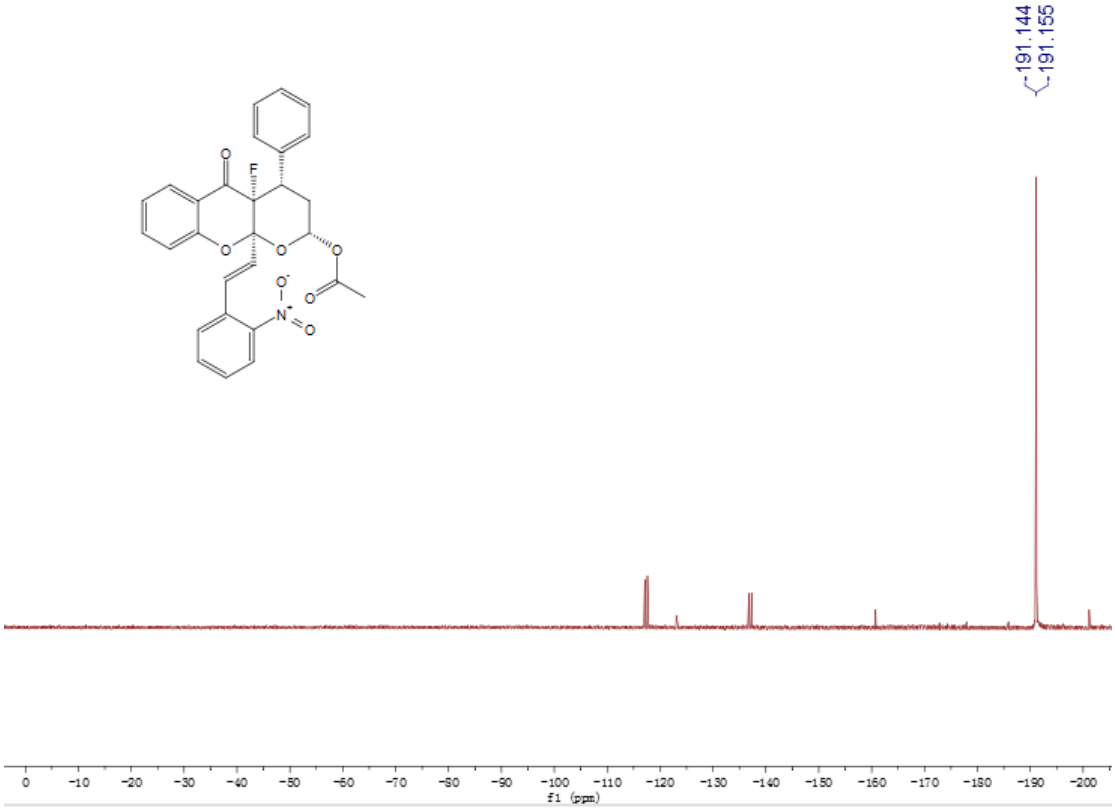
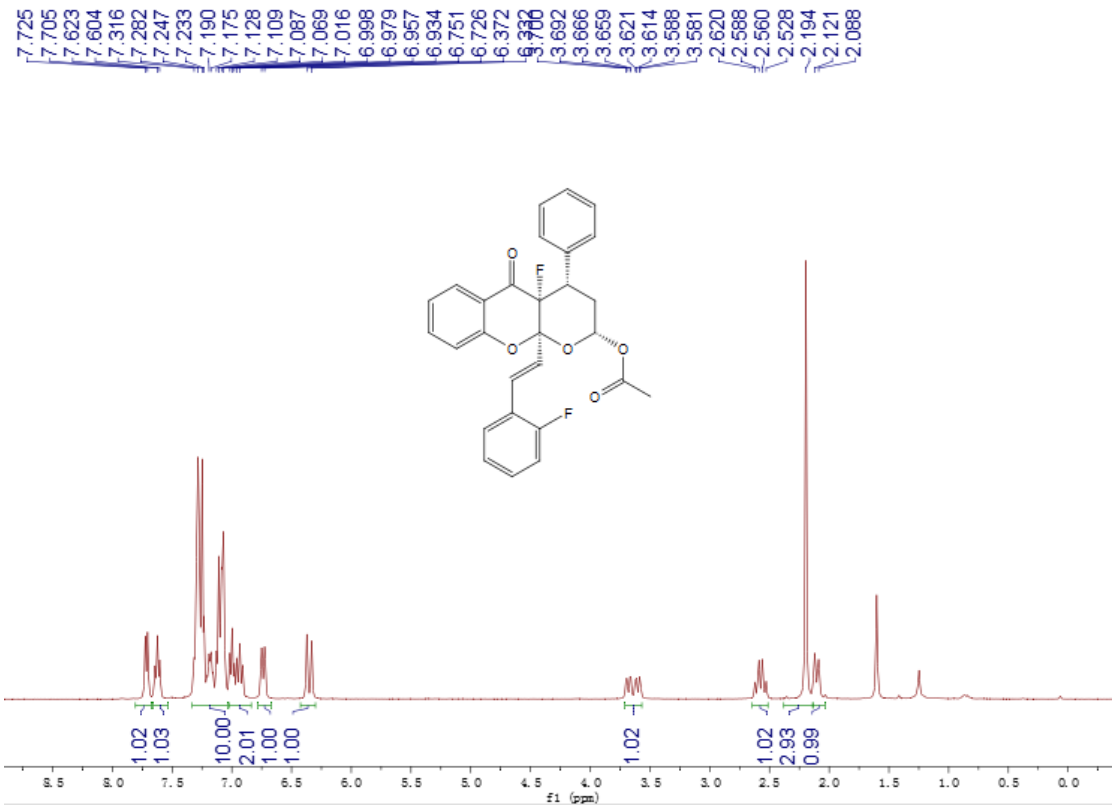


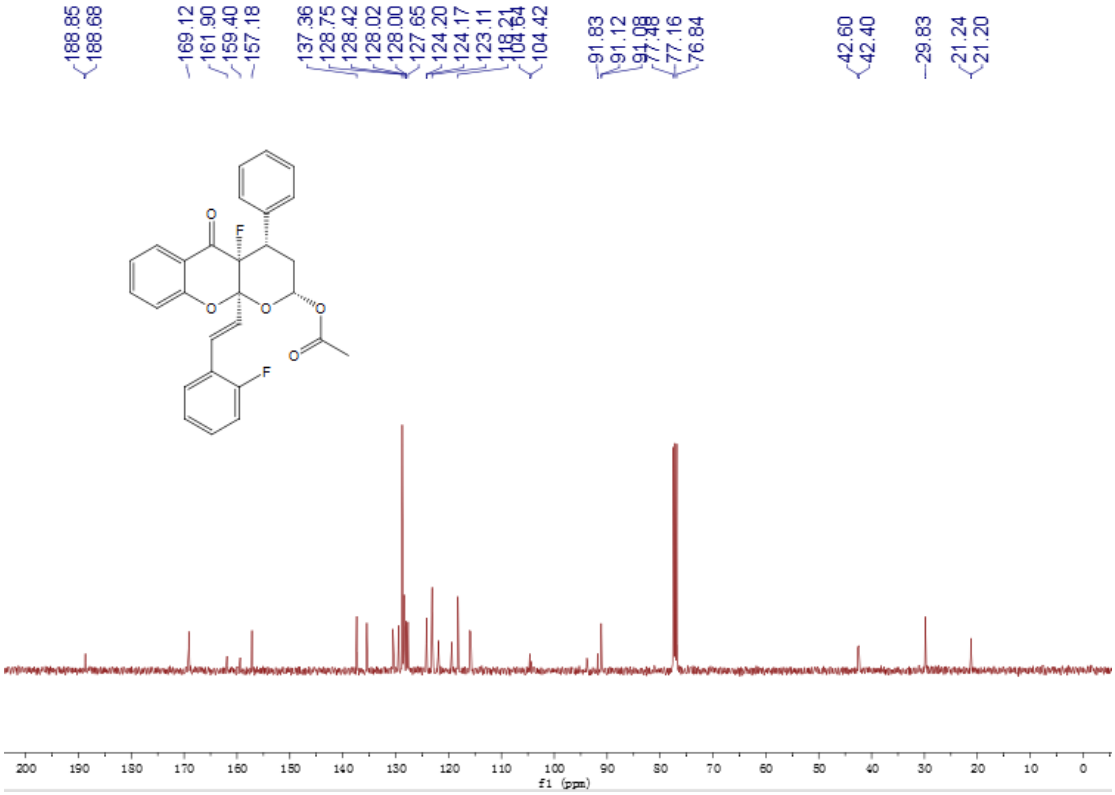
3ga-^{19}F NMR (565 MHz, $CDCl_3$)



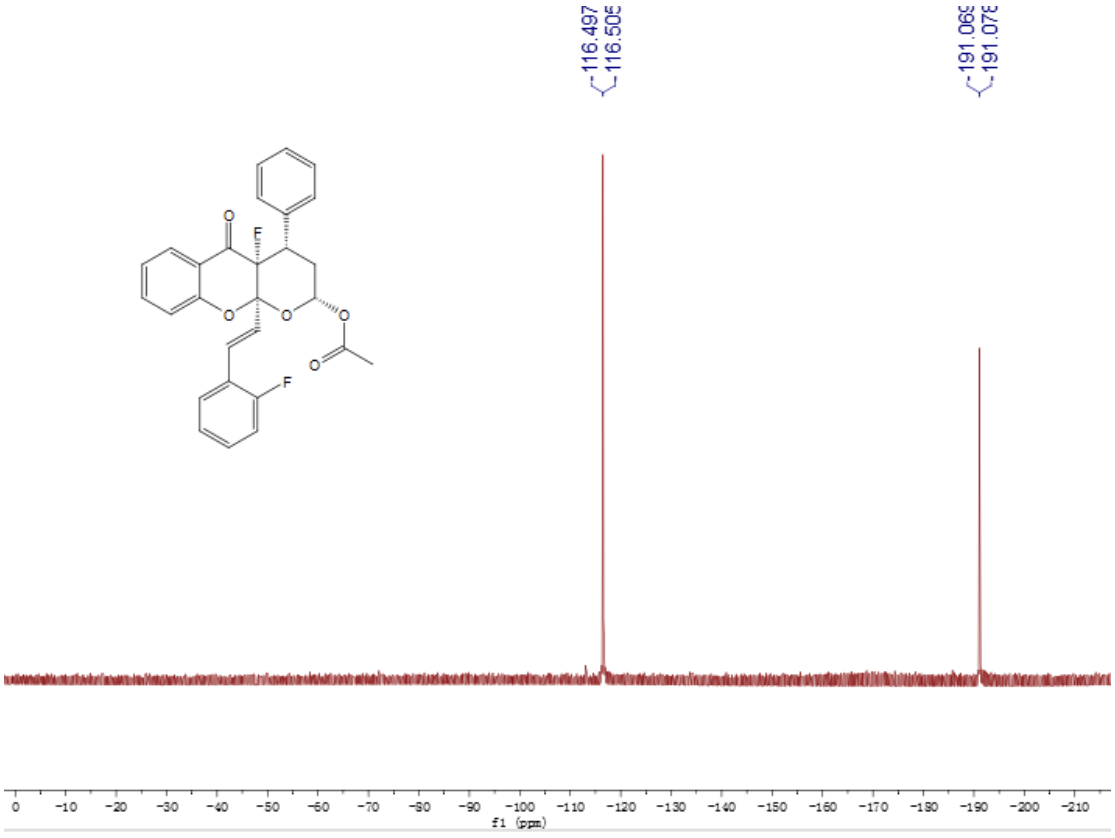
3ha-^{1}H NMR (400 MHz, $CDCl_3$)



3ha-^{13}C NMR (100 MHz, $CDCl_3$)



3ha-^{19}F NMR (565 MHz, $CDCl_3$)



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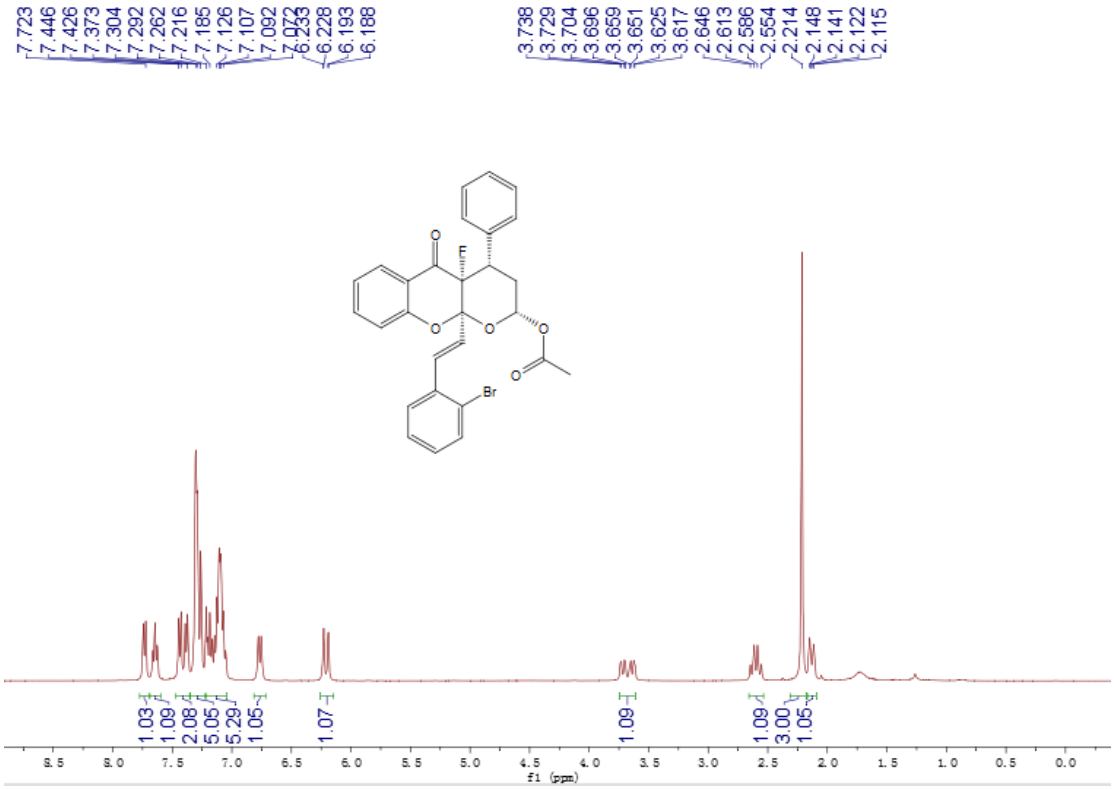
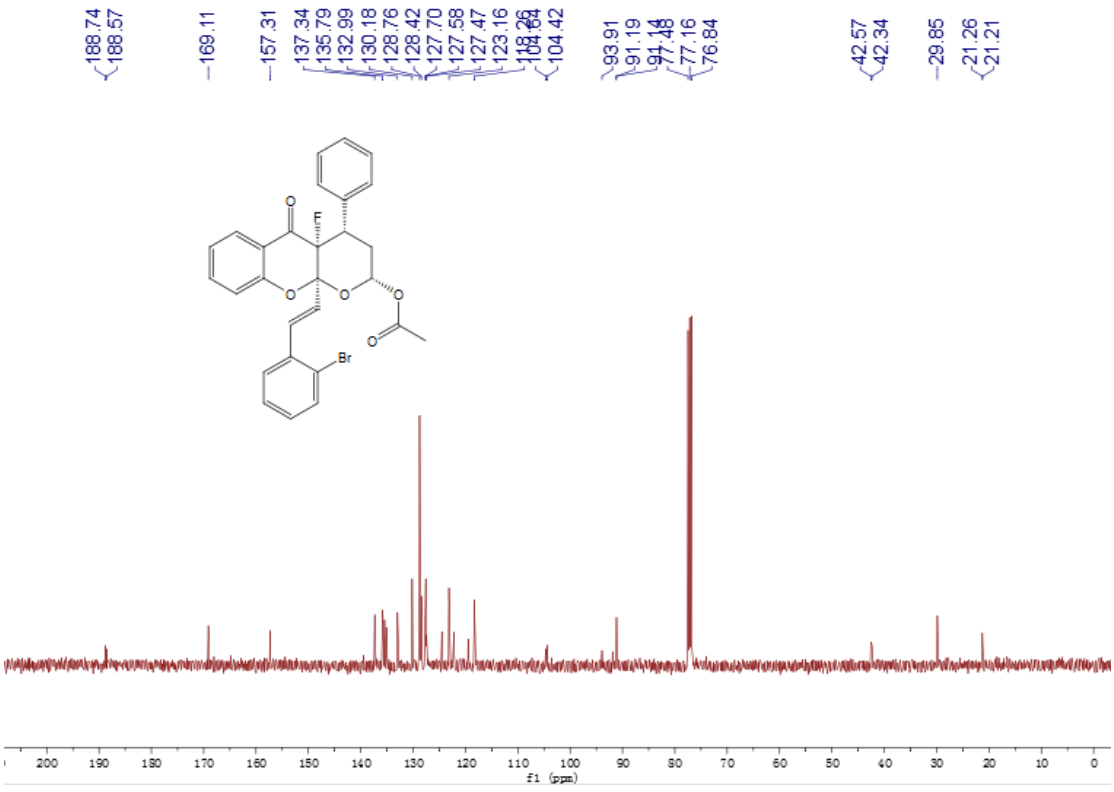
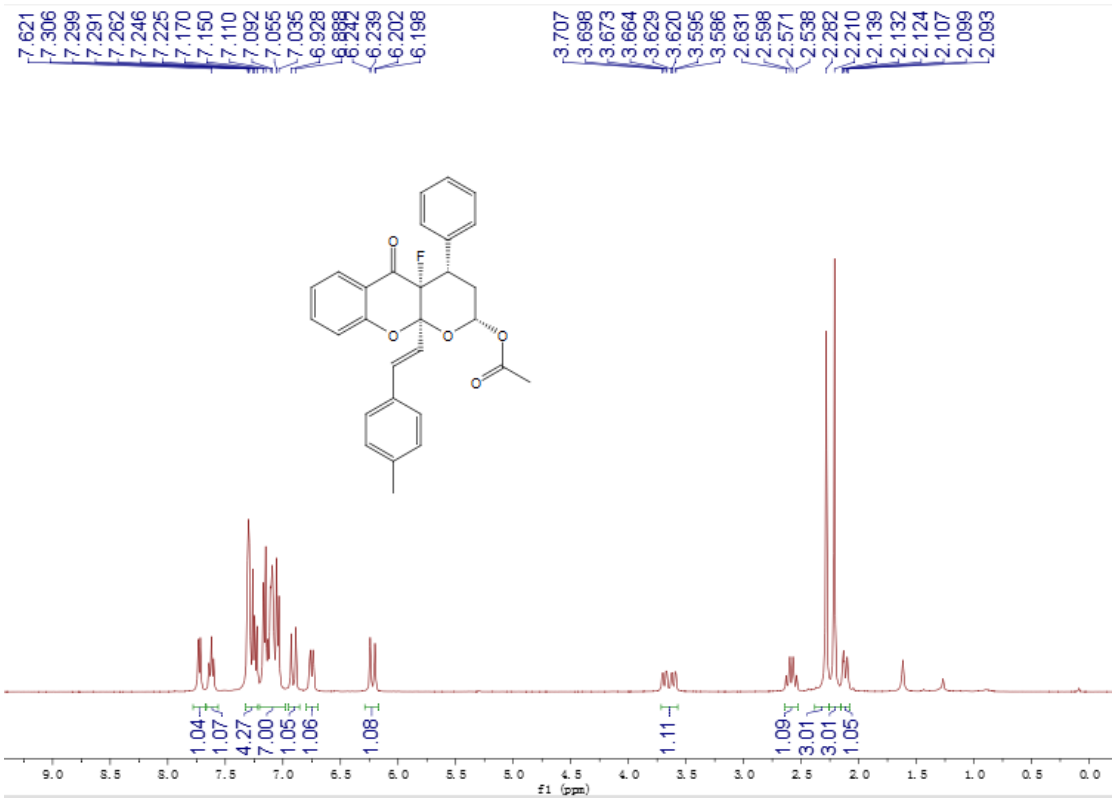


3ia-^{13}C NMR (100 MHz, $CDCl_3$)



3ia-^{19}F NMR (565 MHz, $CDCl_3$)

3ja-^{1}H NMR (400 MHz, $CDCl_3$)



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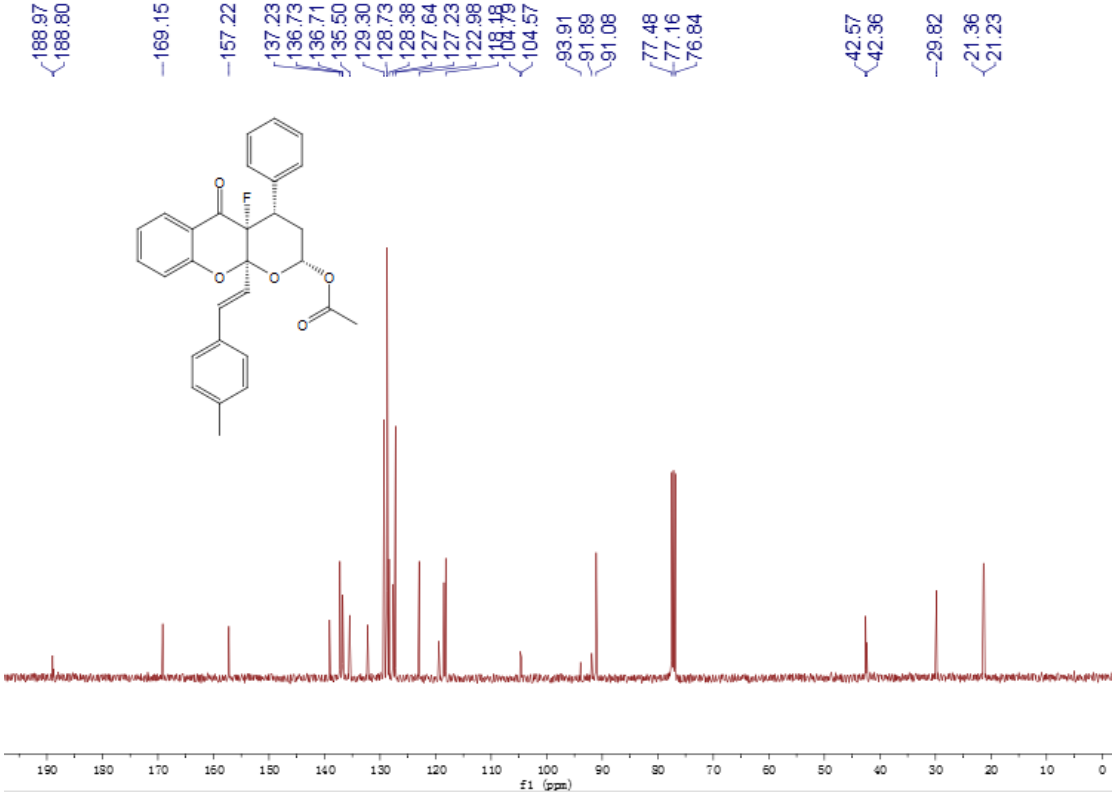
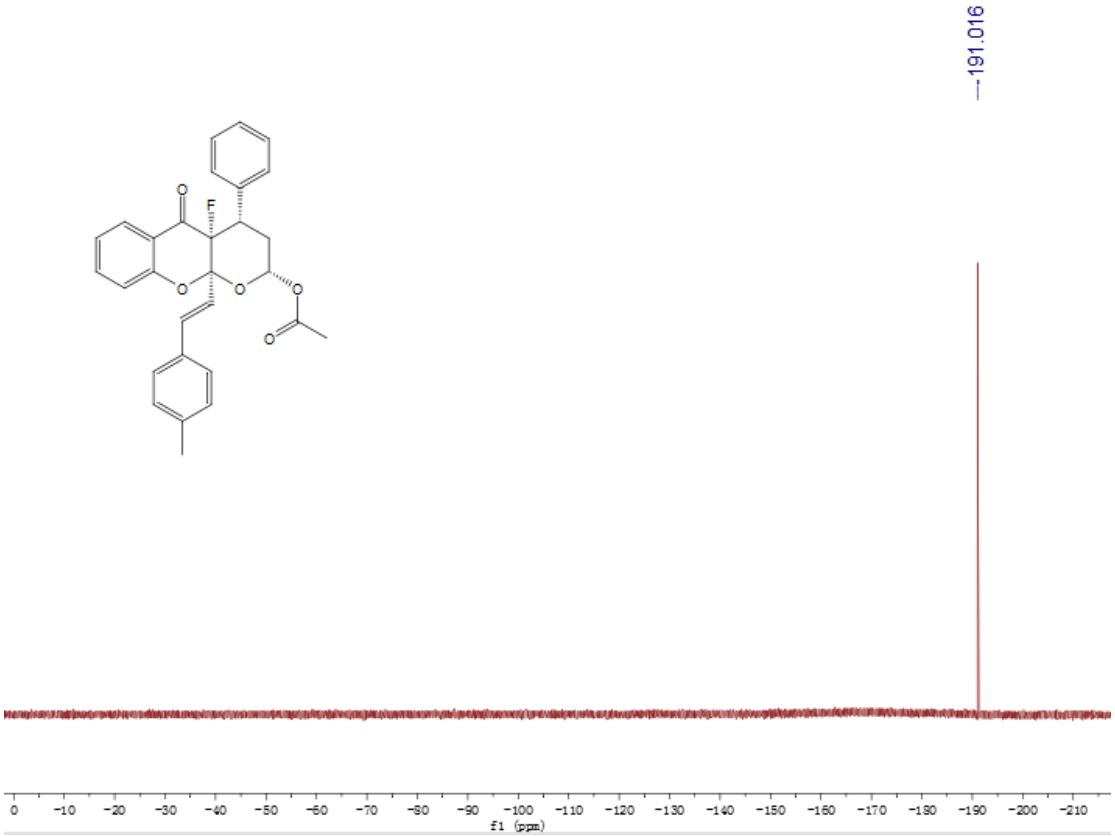
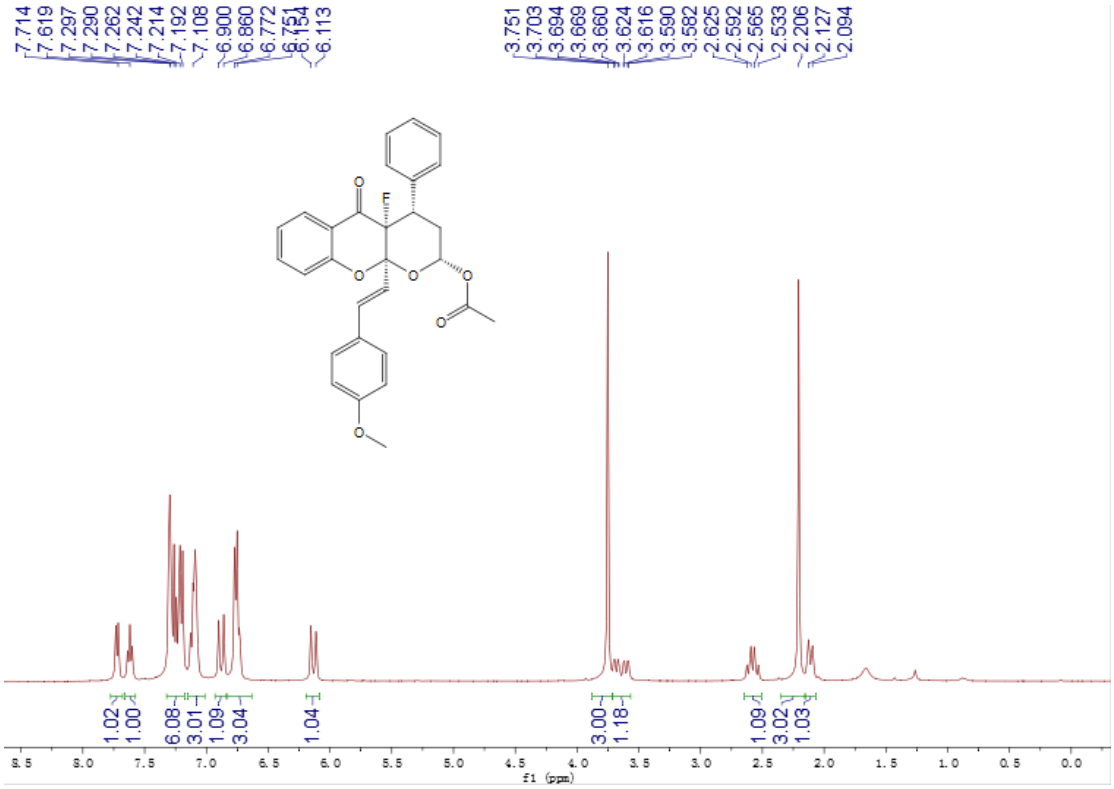


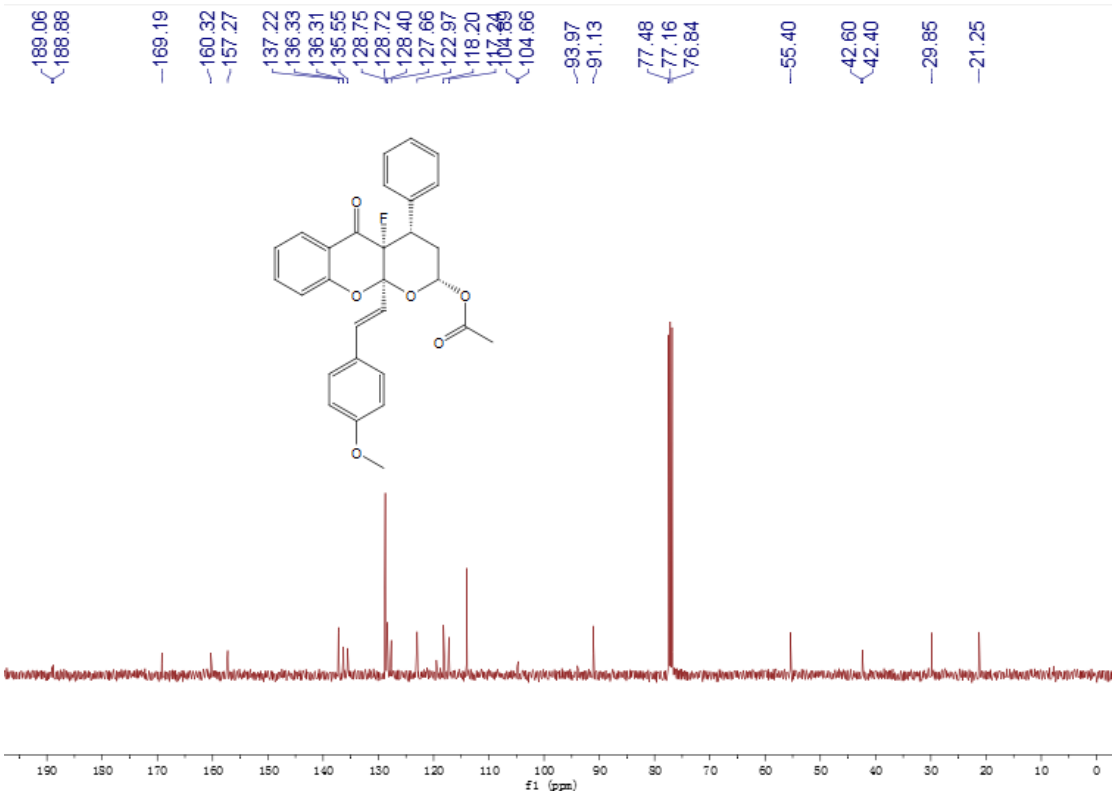
3ja-^{19}F NMR (565 MHz, $CDCl_3$)



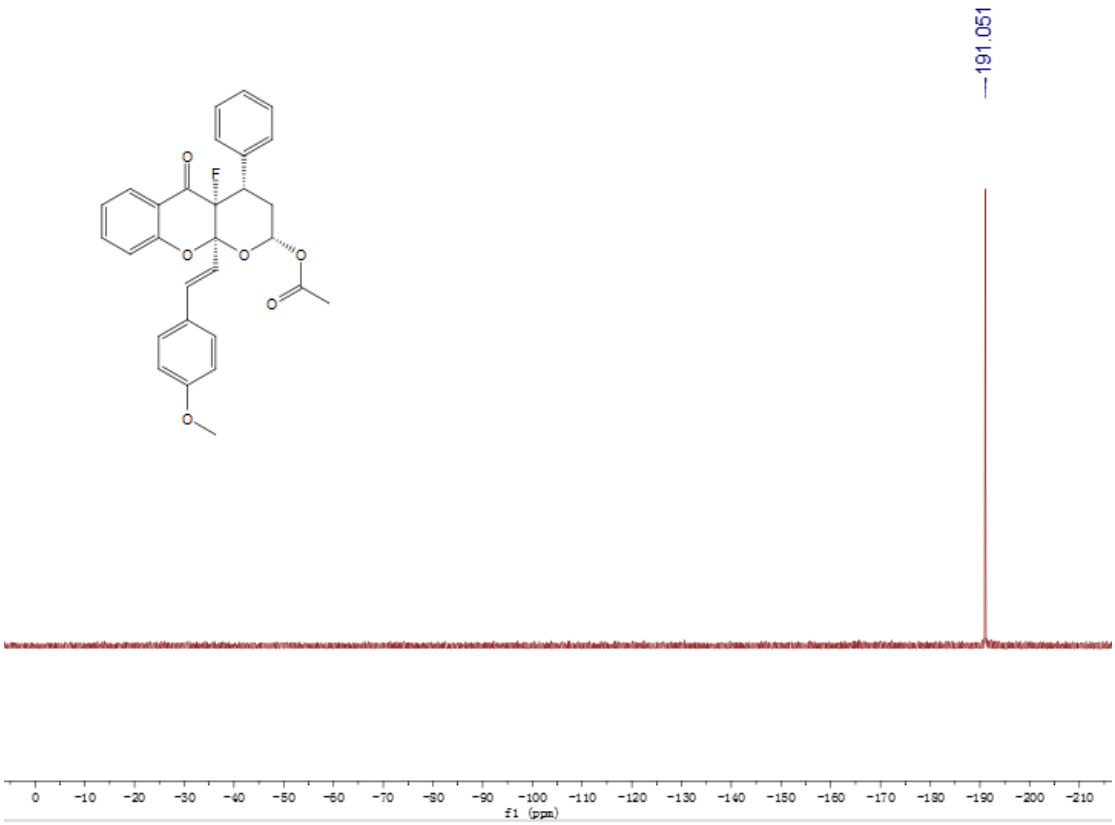
3ka-^{1}H NMR (400 MHz, $CDCl_3$)



3ka-^{13}C NMR (100 MHz, $CDCl_3$)



3ka-^{19}F NMR (565 MHz, $CDCl_3$)



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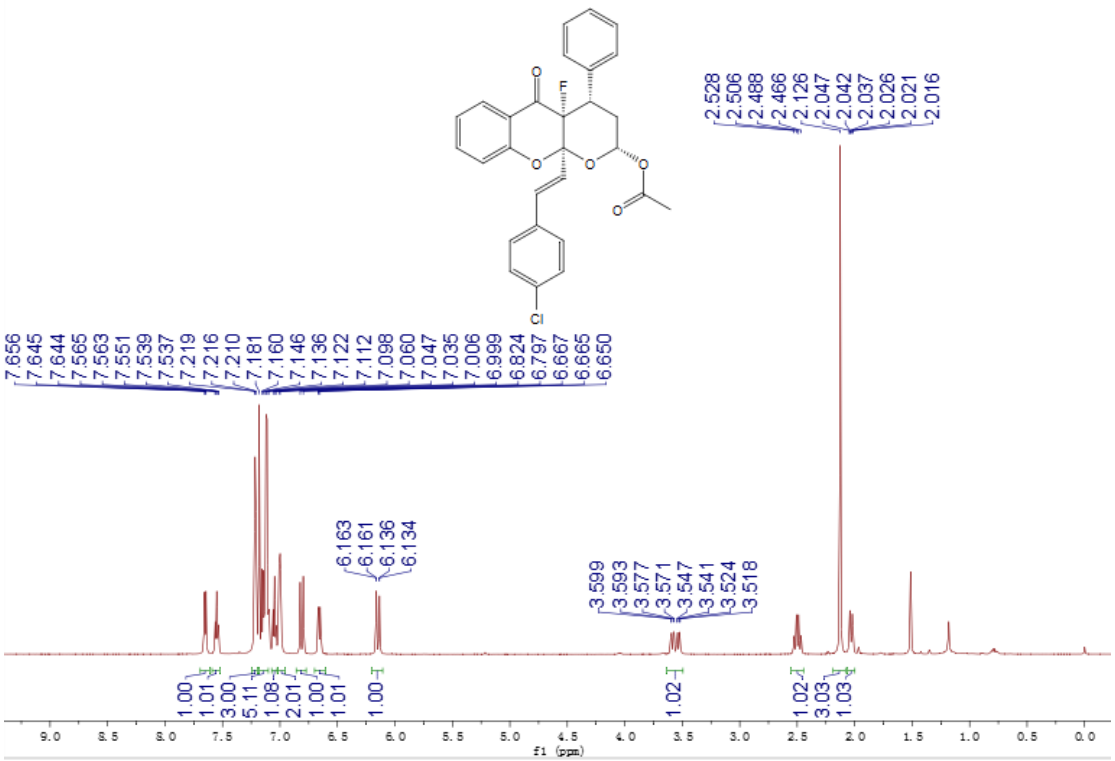
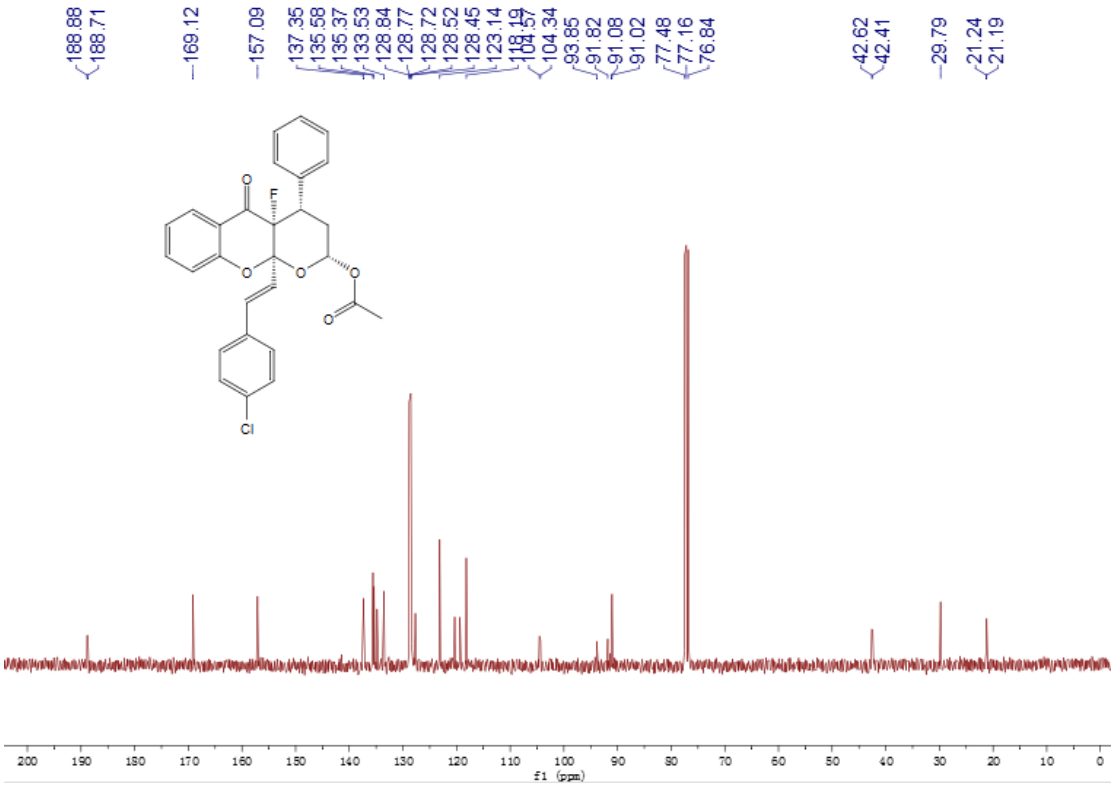
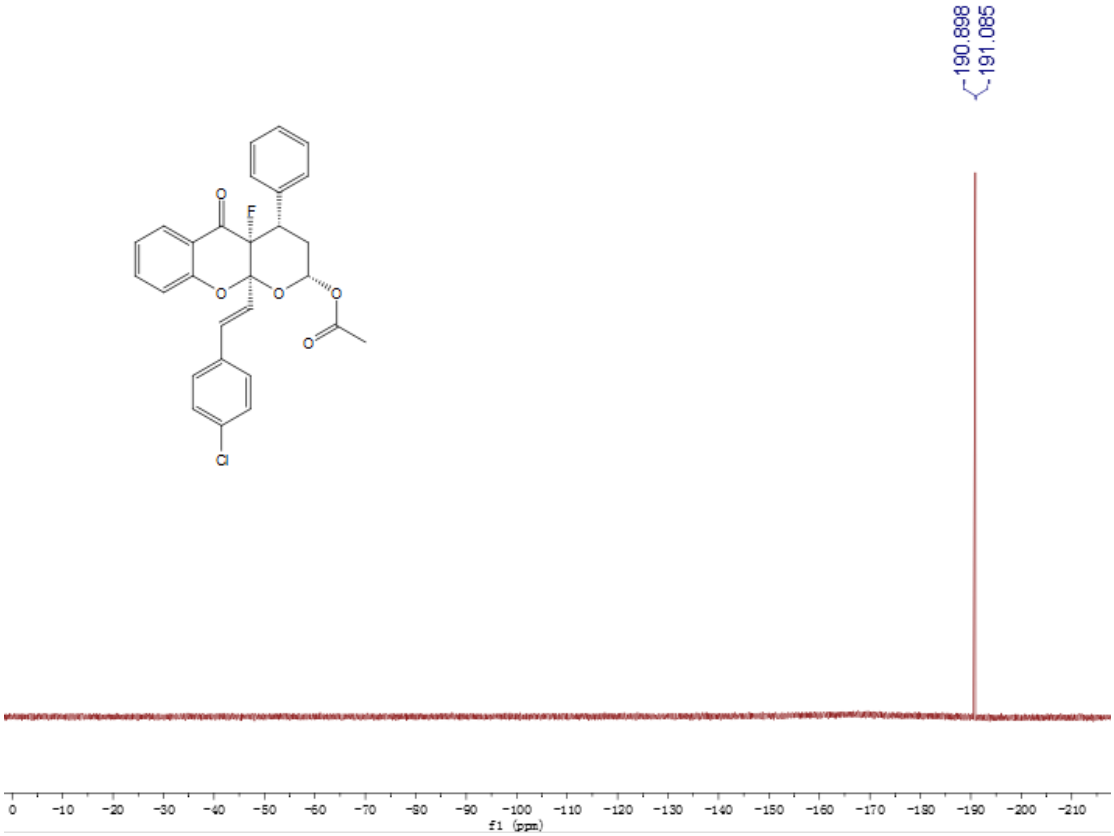


3la-^{13}C NMR (100 MHz, $CDCl_3$)



3la-^{19}F NMR (565MHz, $CDCl_3$)



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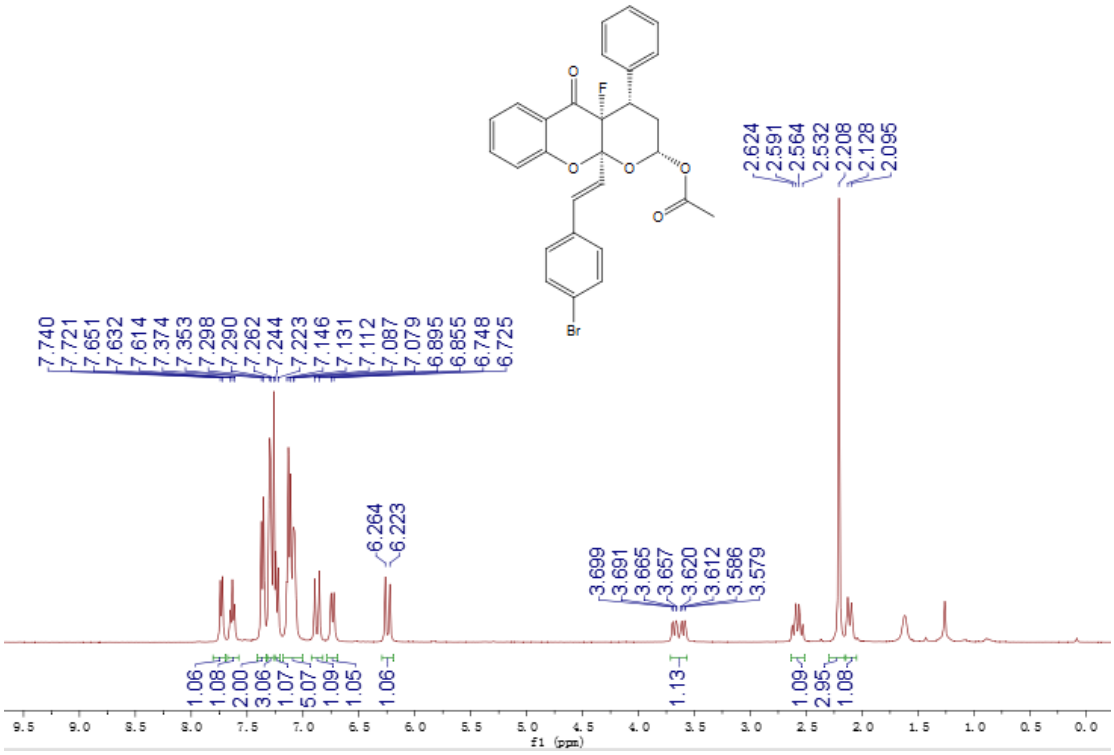
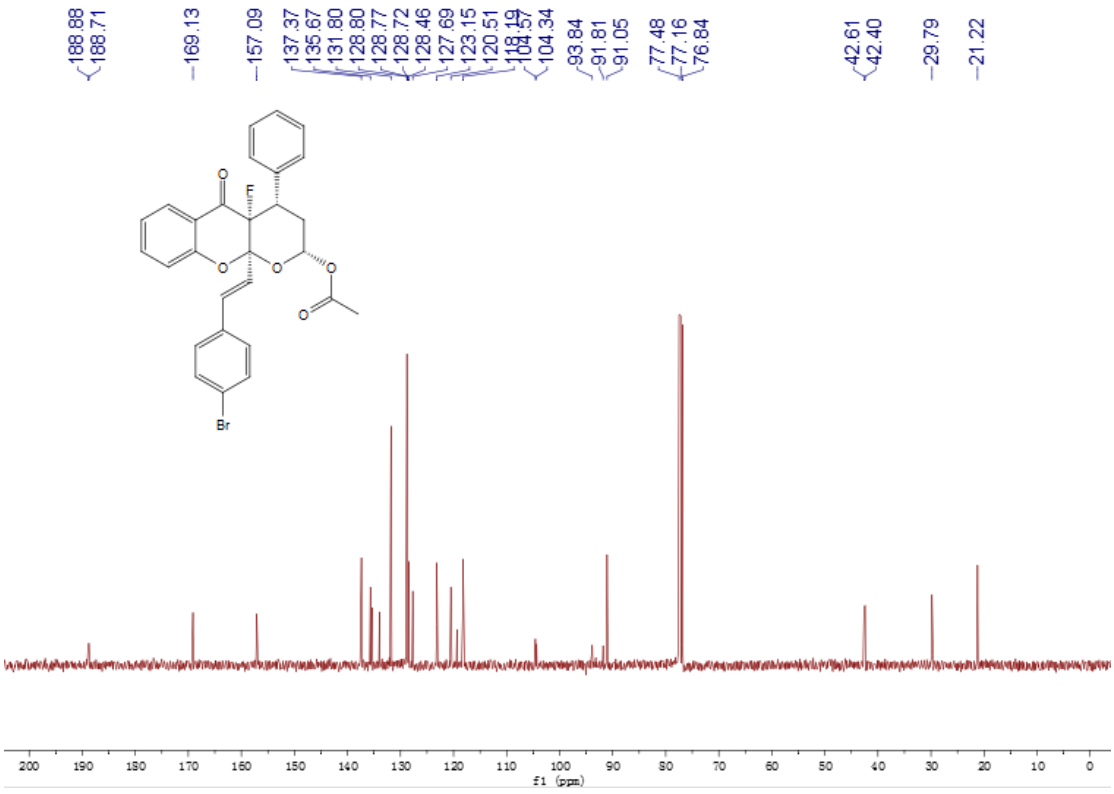
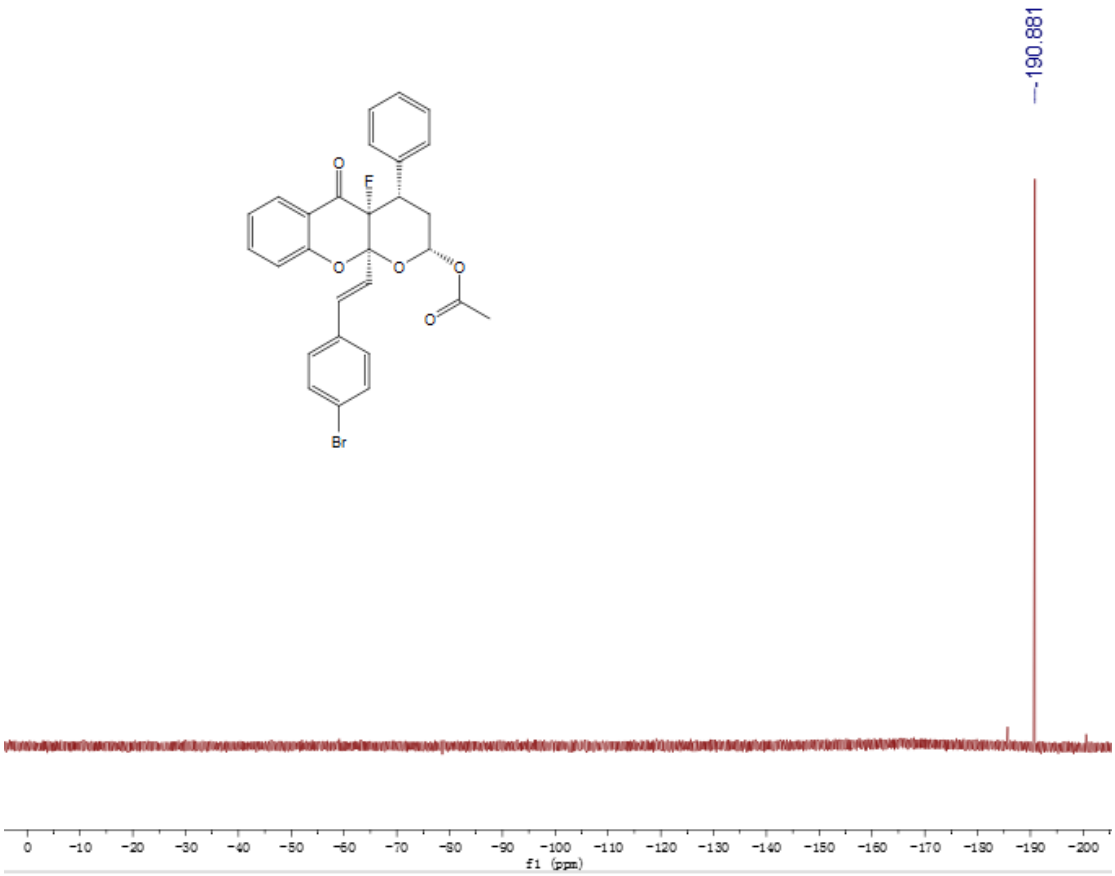


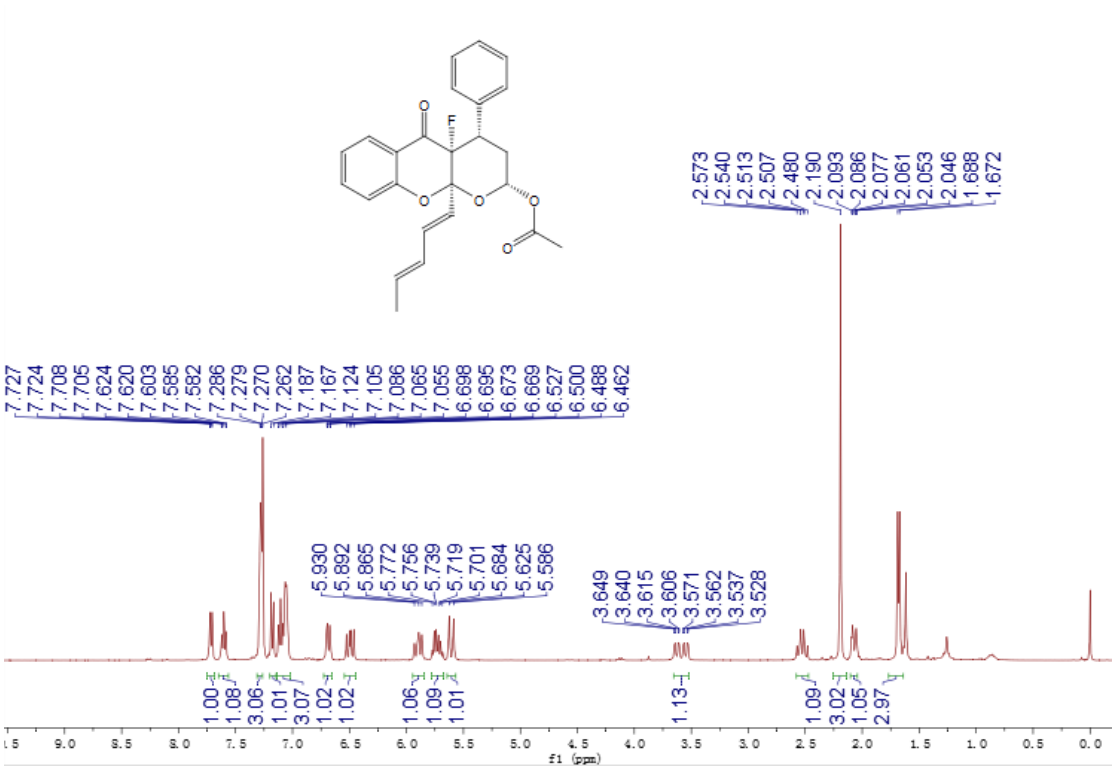
3ma-^{13}C NMR (100 MHz, $CDCl_3$)



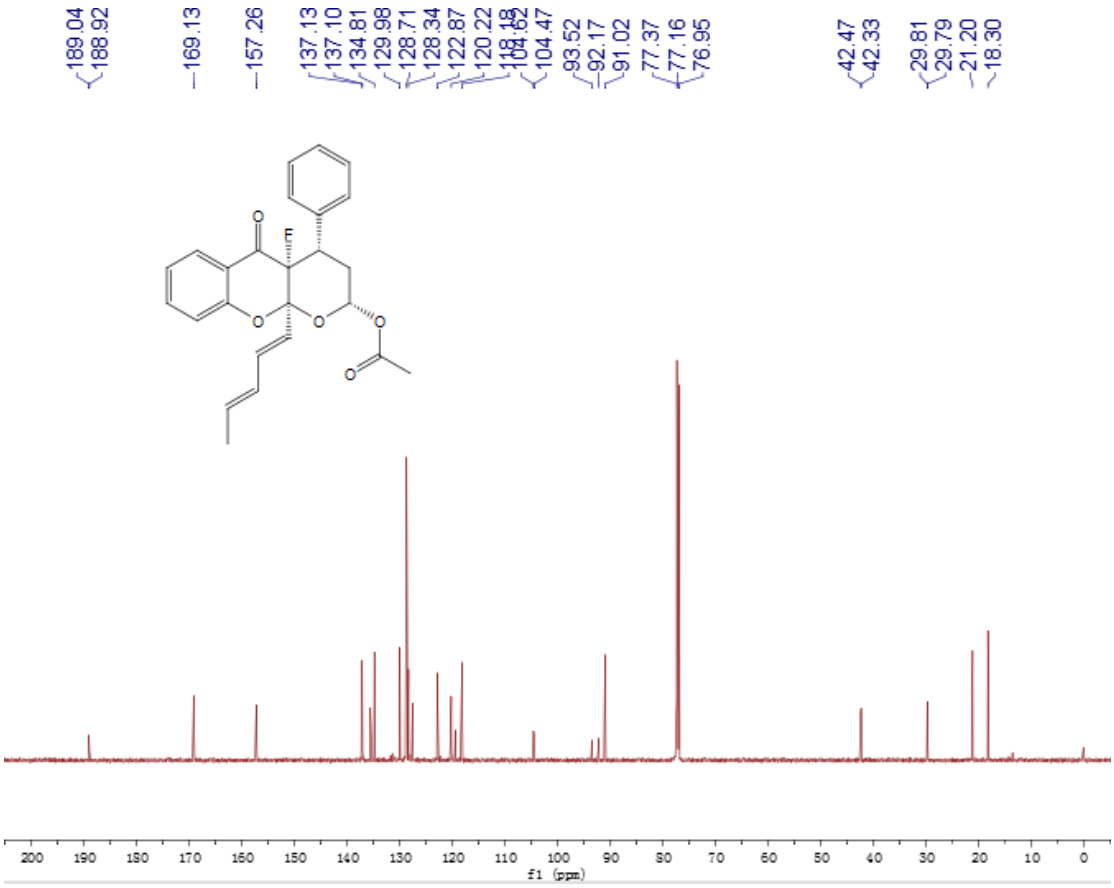
3ma-^{19}F NMR (565 MHz, $CDCl_3$)



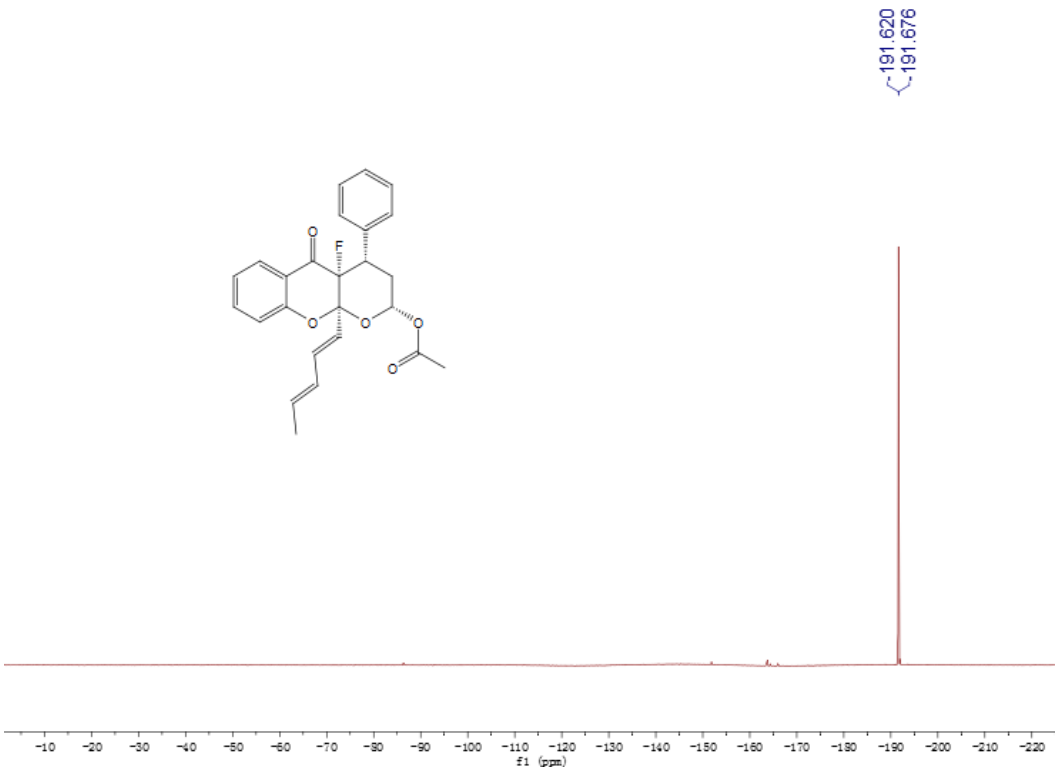
3na-^{1}H NMR (400 MHz, $CDCl_3$)



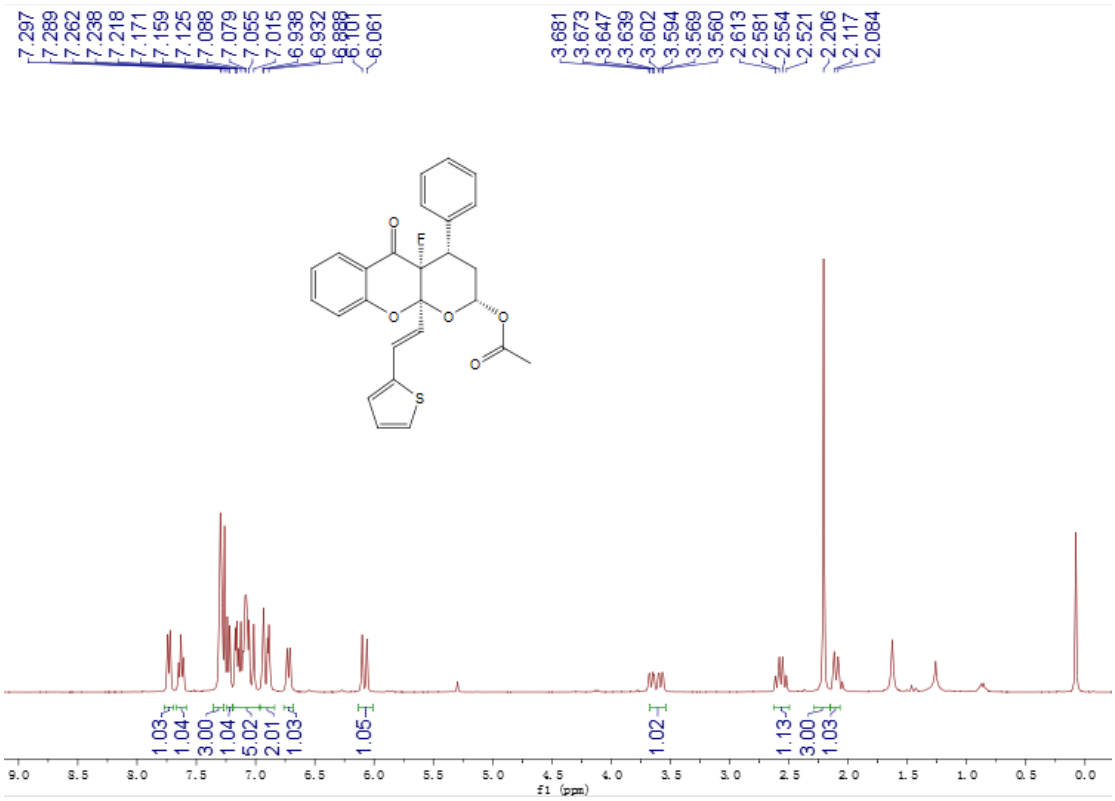
3na-^{13}C NMR (150 MHz, $CDCl_3$)



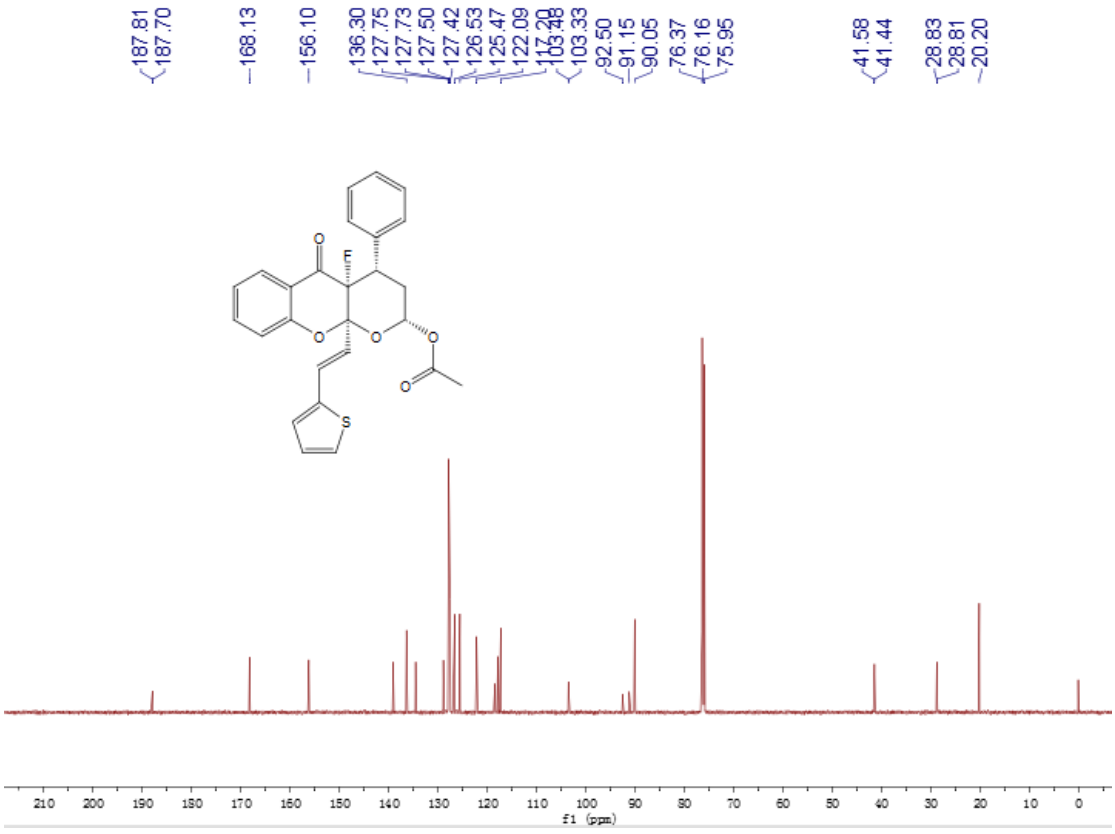
3na-^{19}F NMR (565 MHz, $CDCl_3$)



3oa-^{1}H NMR (400 MHz, $CDCl_3$)

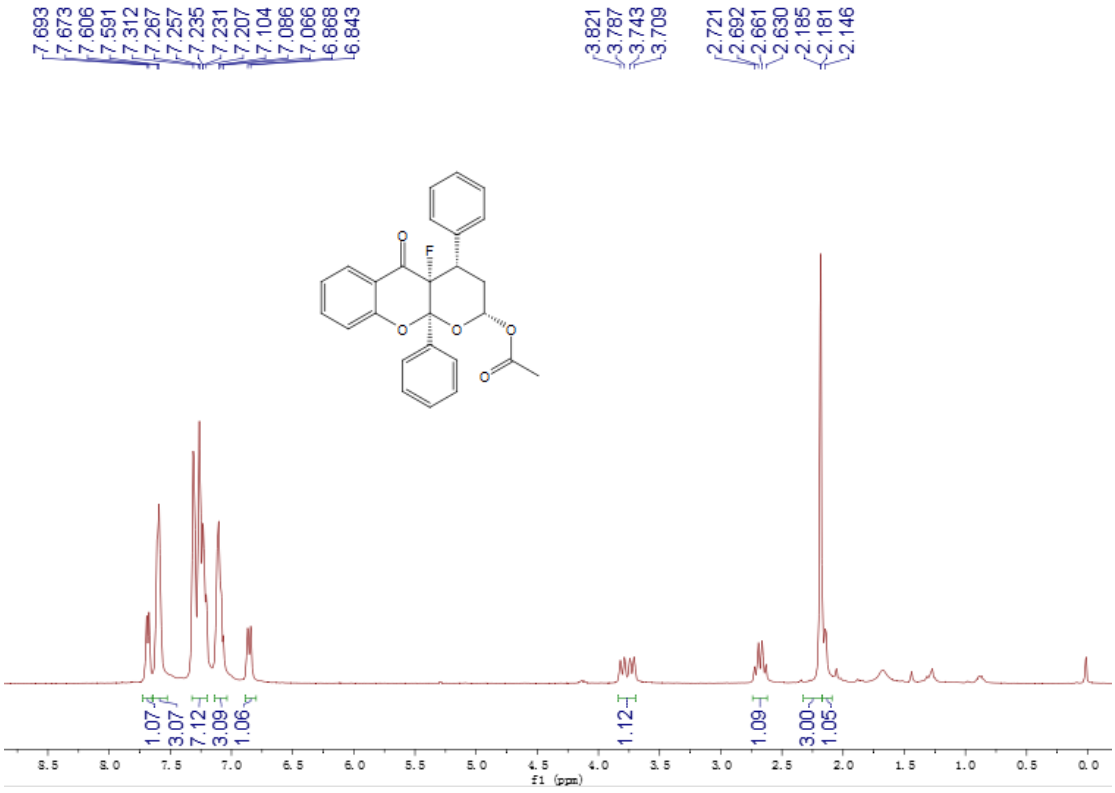


3oa-^{13}C NMR (150 MHz, $CDCl_3$)

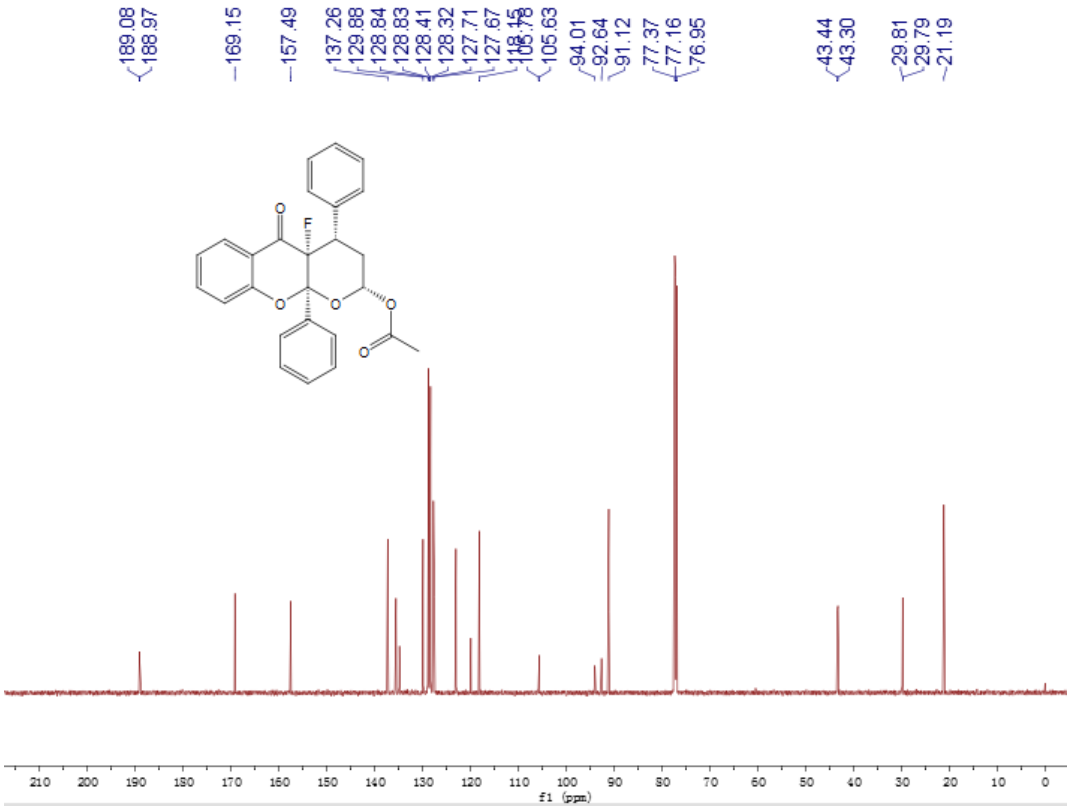


3oa-^{19}F NMR (565 MHz, $CDCl_3$)

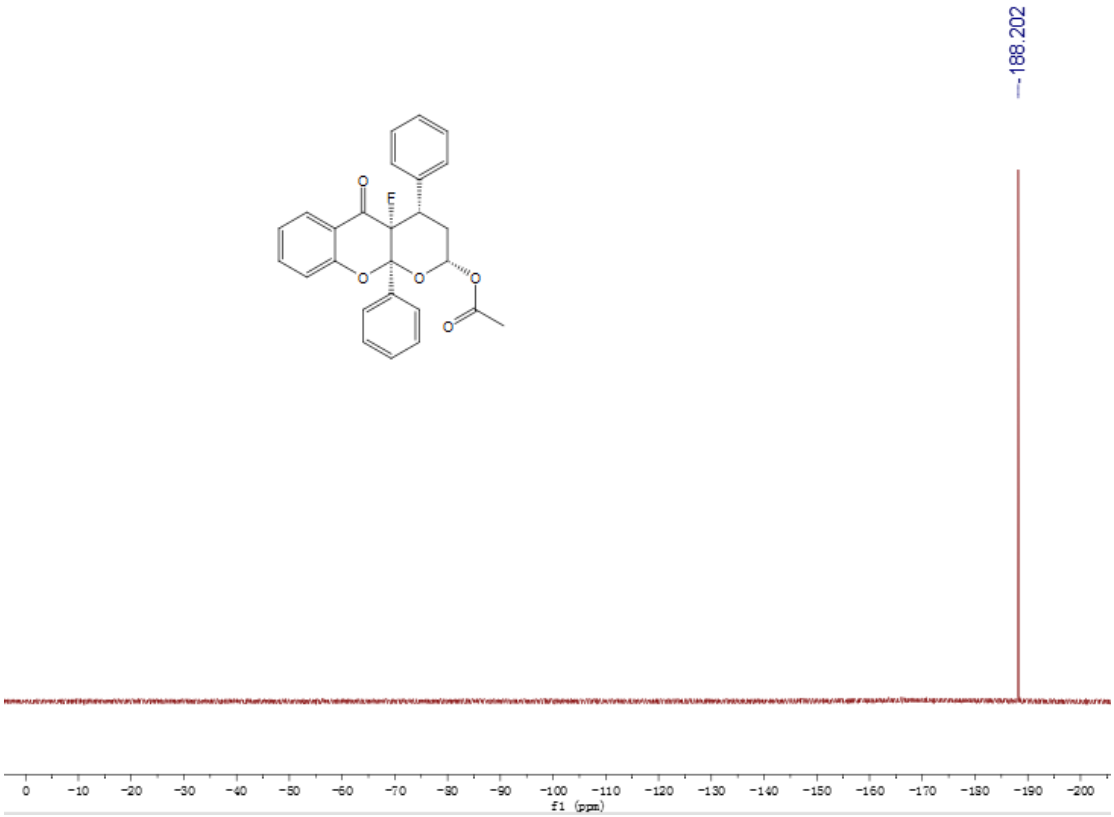
3pa-^{1}H NMR (400 MHz, $CDCl_3$)



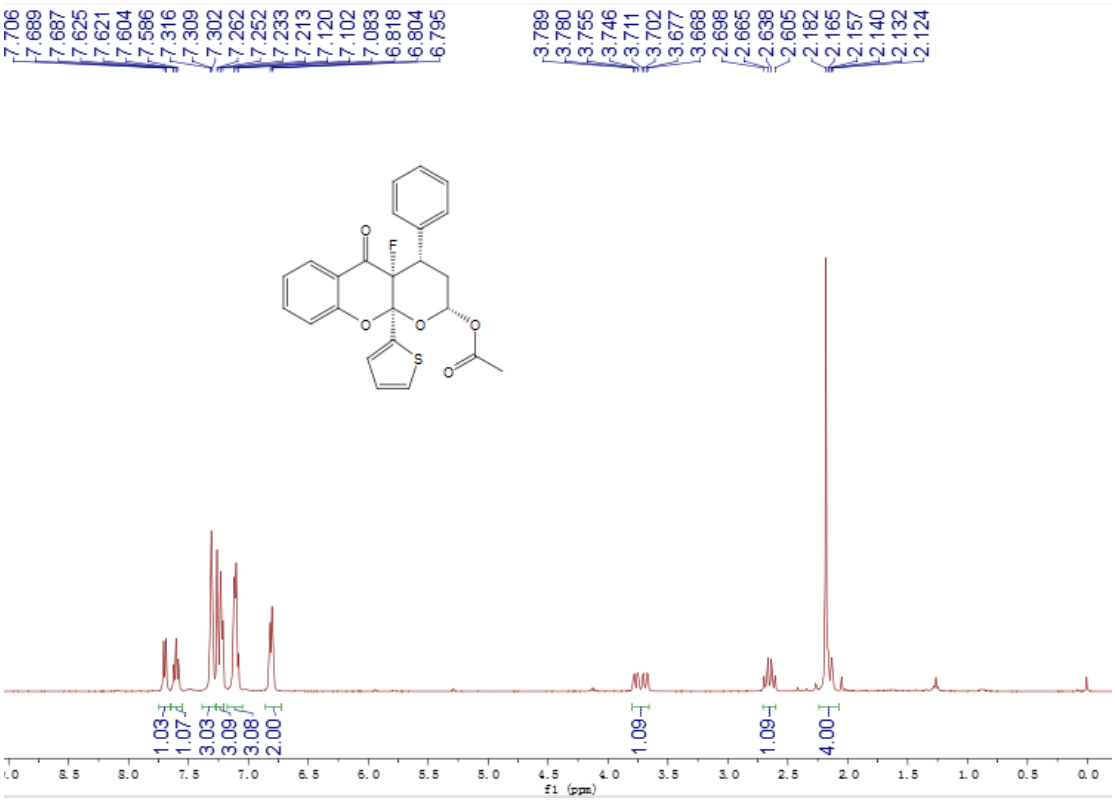
3pa-^{13}C NMR (150 MHz, $CDCl_3$)



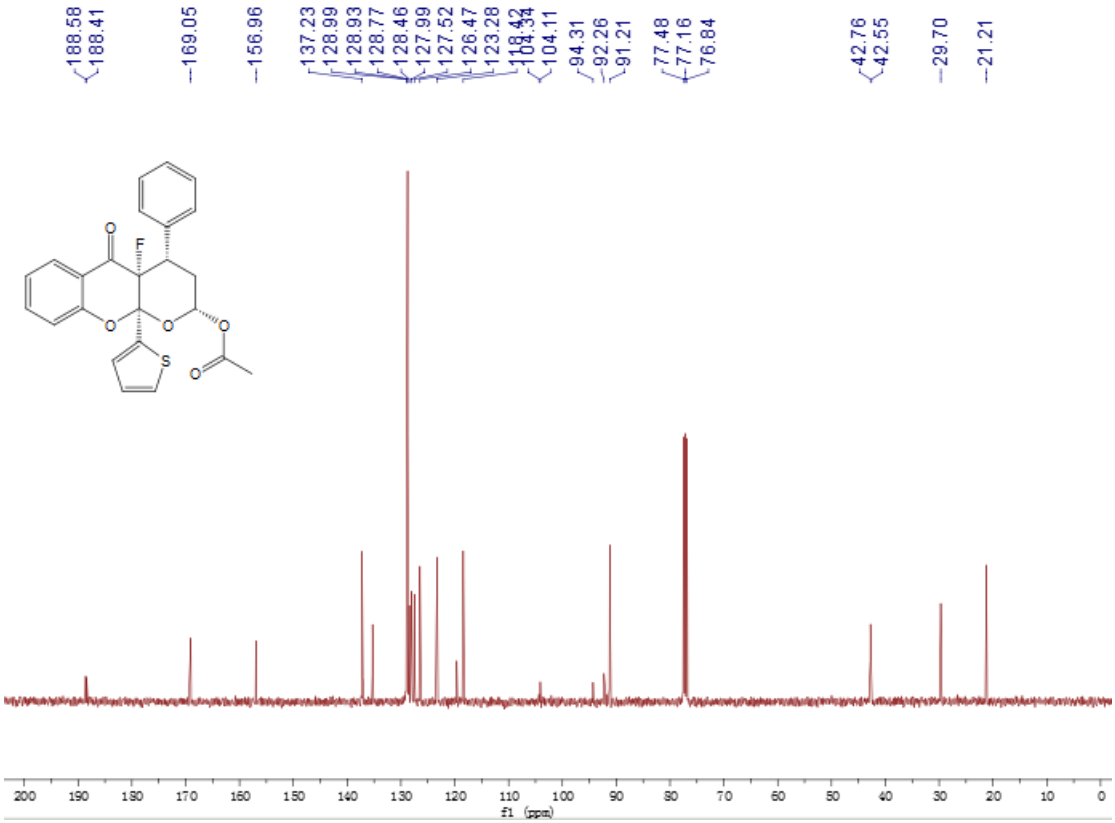
3pa-^{19}F NMR (565 MHz, $CDCl_3$)



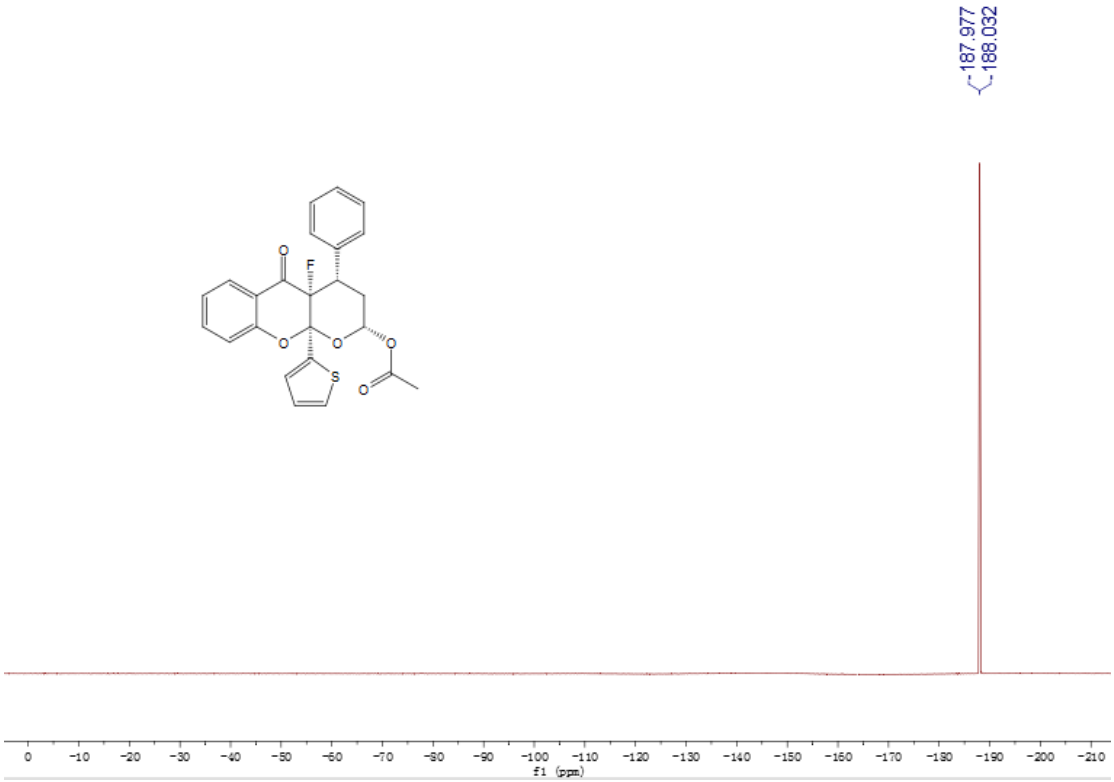
3qa-^{1}H NMR (400 MHz, $CDCl_3$)



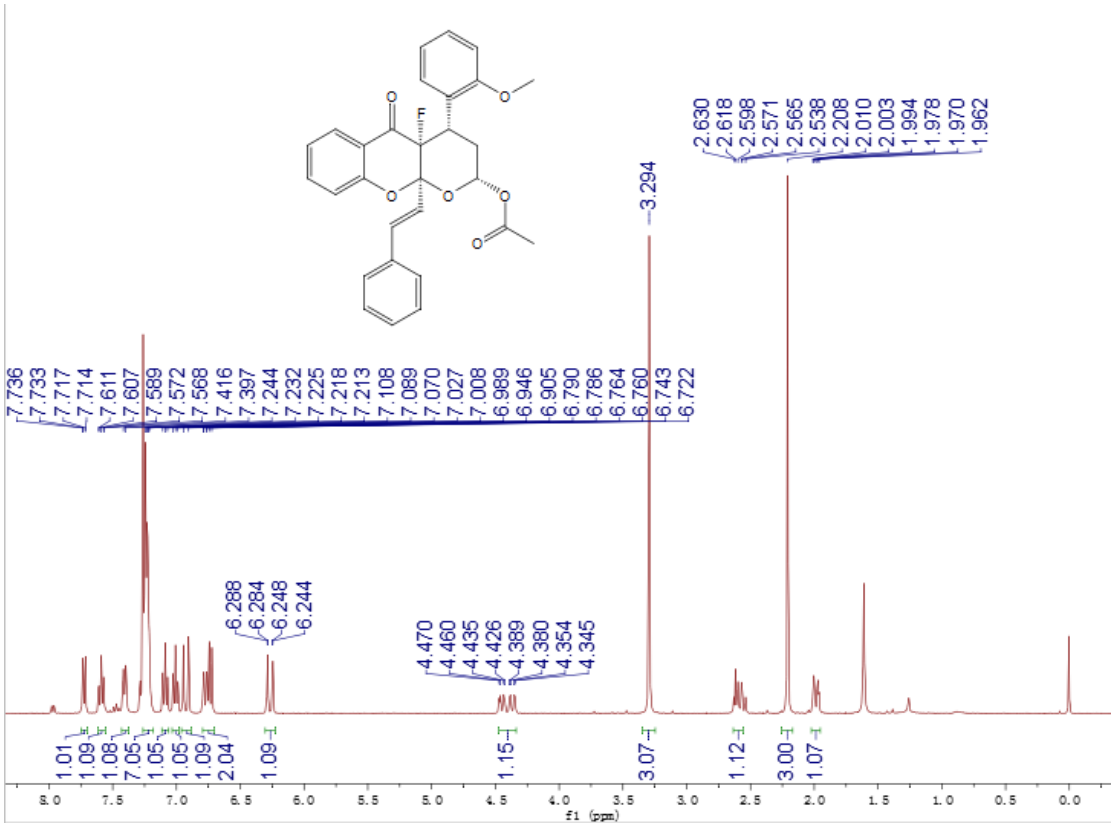
3qa-^{13}C NMR (100 MHz, $CDCl_3$)



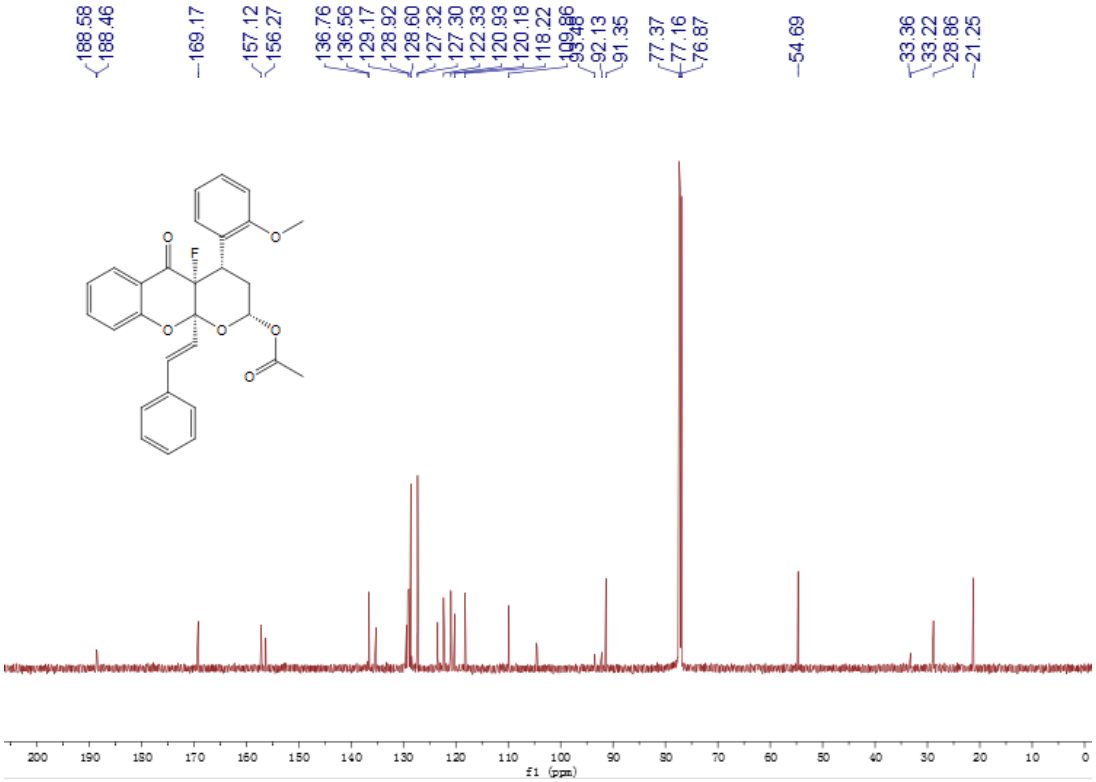
3qa-^{19}F NMR (565 MHz, $CDCl_3$)



3ab-^{1}H NMR (400 MHz, $CDCl_3$)

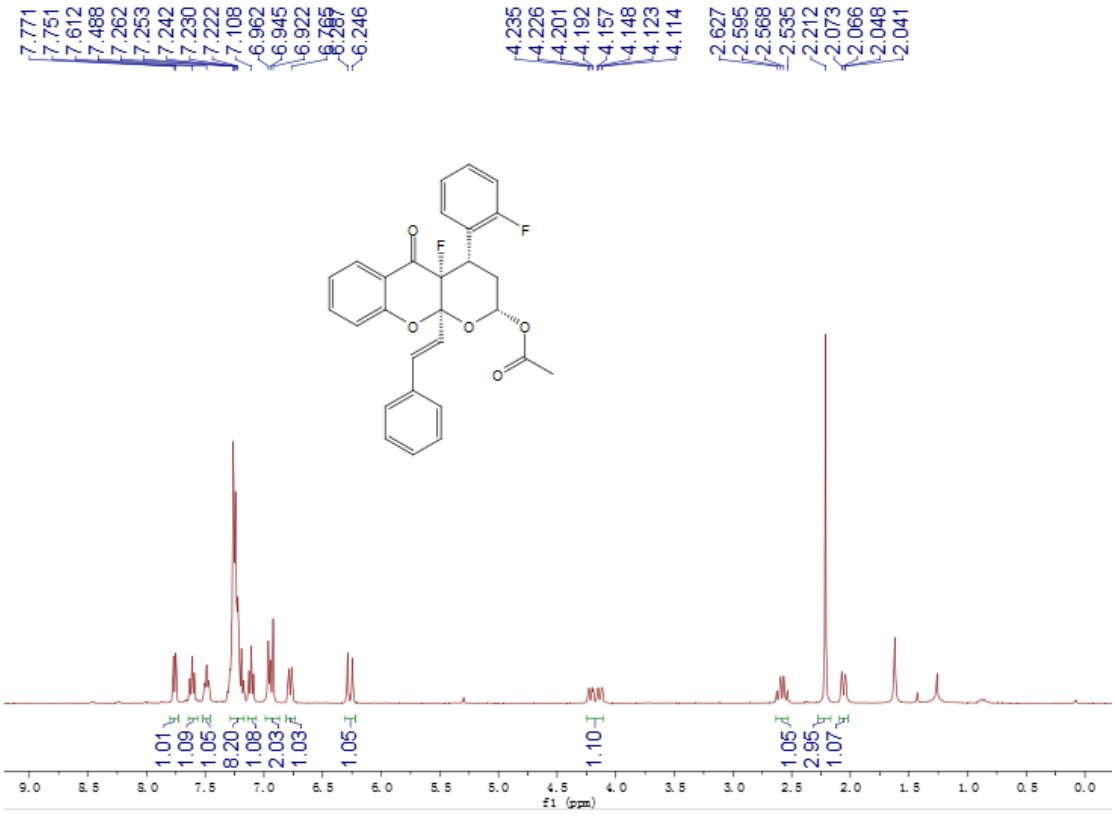


3ab-^{13}C NMR (150 MHz, $CDCl_3$)

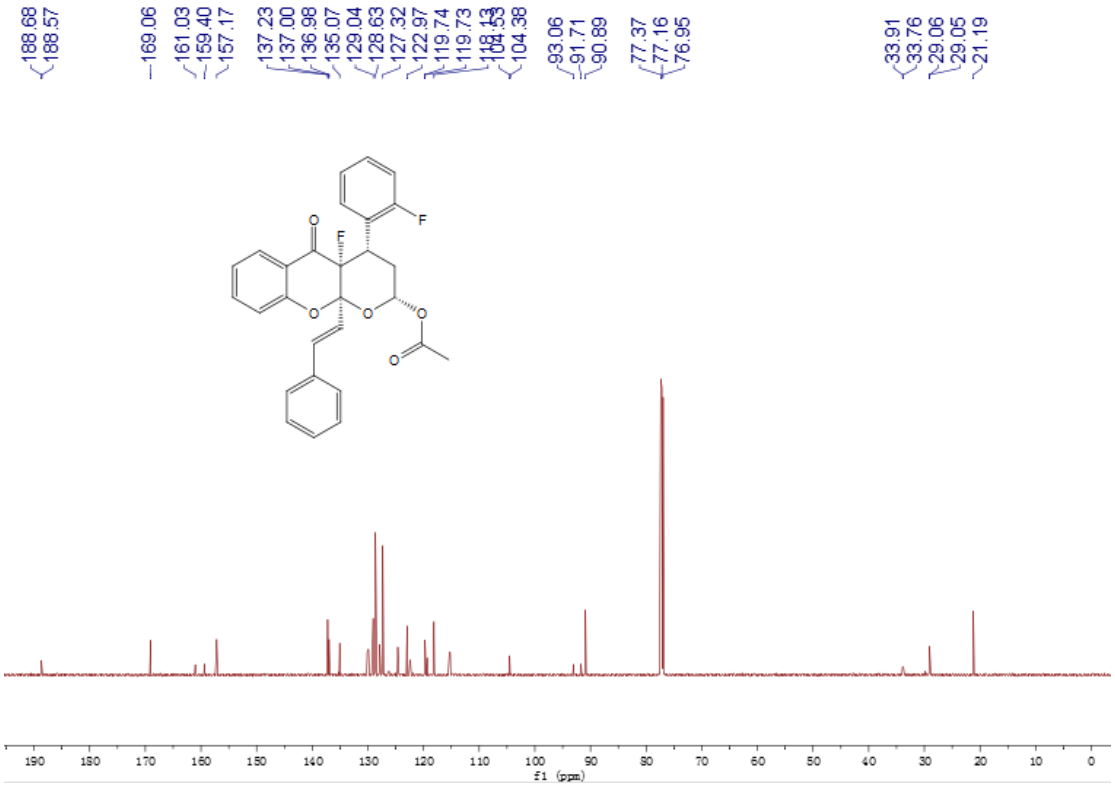


3ab-^{19}F NMR (565 MHz, $CDCl_3$)

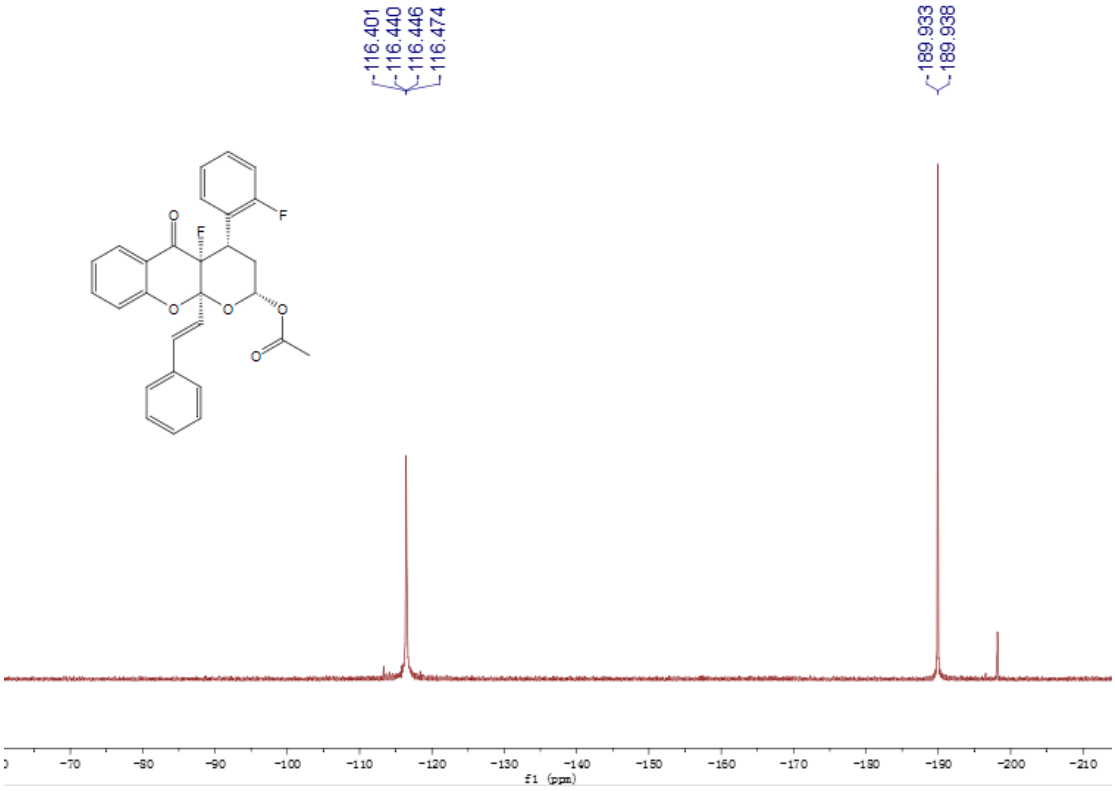
3ac-^{1}H NMR (400 MHz, $CDCl_3$)



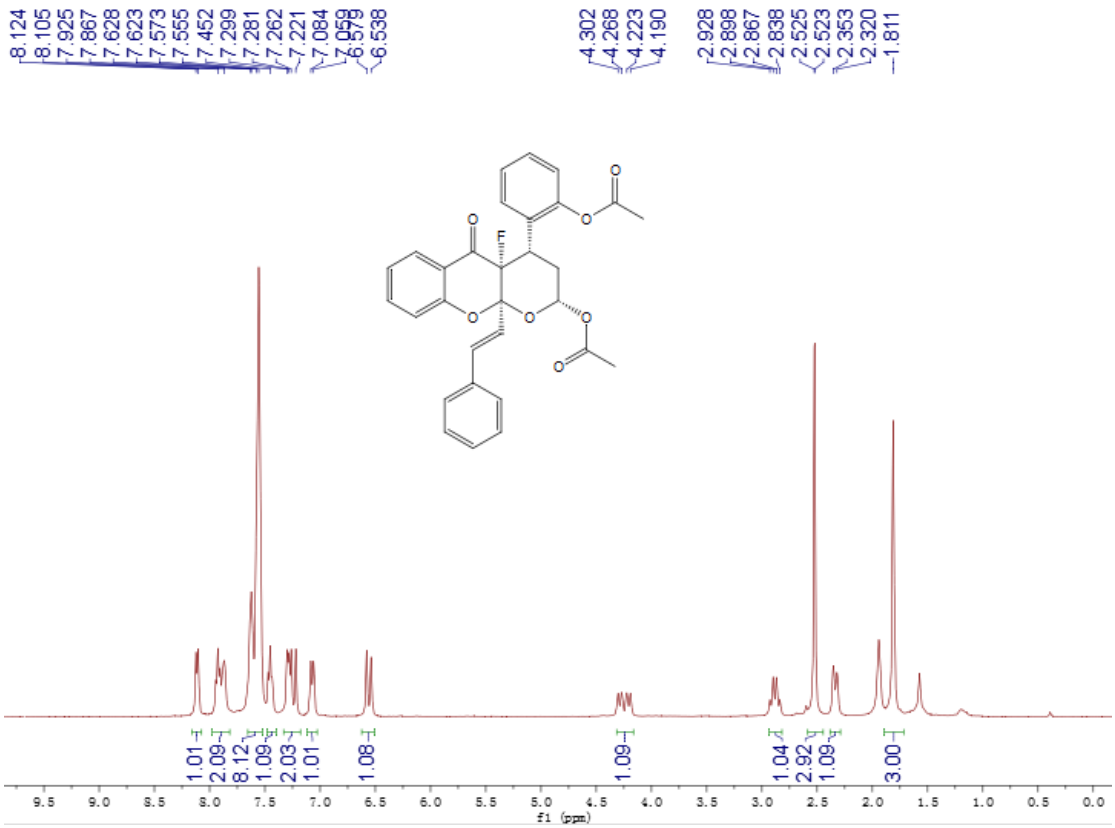
3ac-^{13}C NMR (150 MHz, $CDCl_3$)



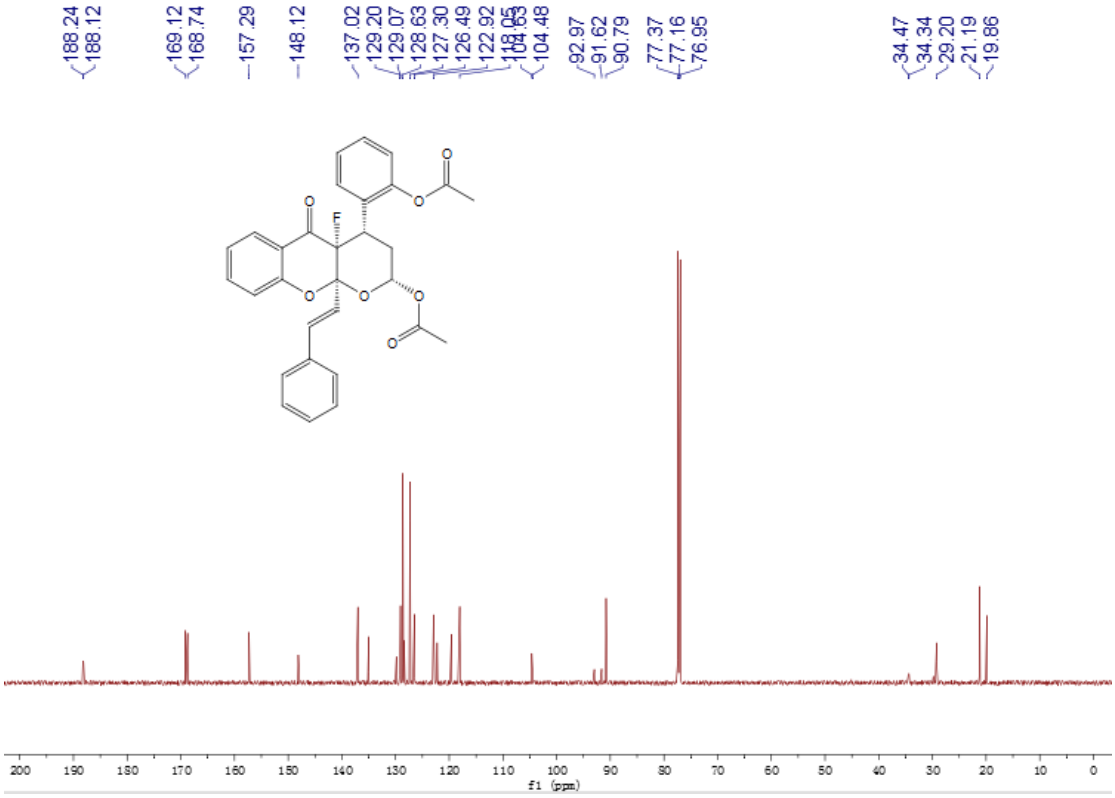
3ac-^{19}F NMR (565 MHz, $CDCl_3$)



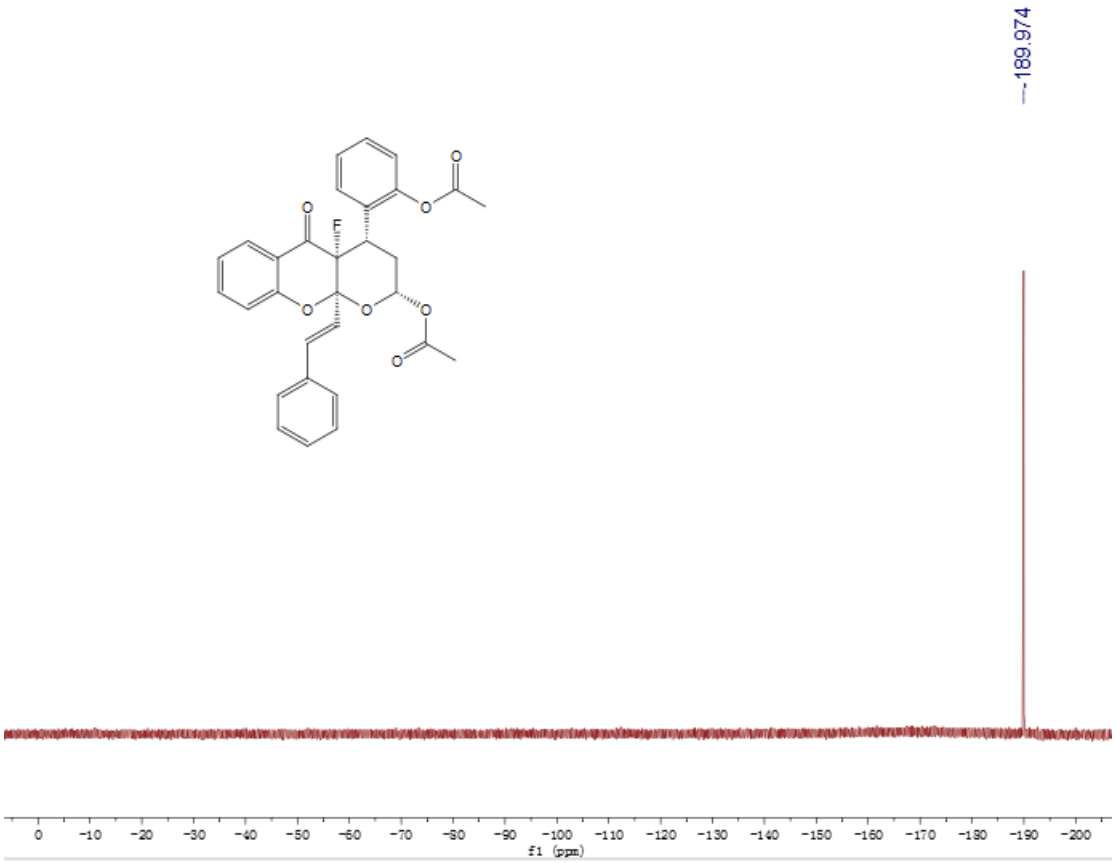
3ad-^{1}H NMR (400 MHz, $CDCl_3$)



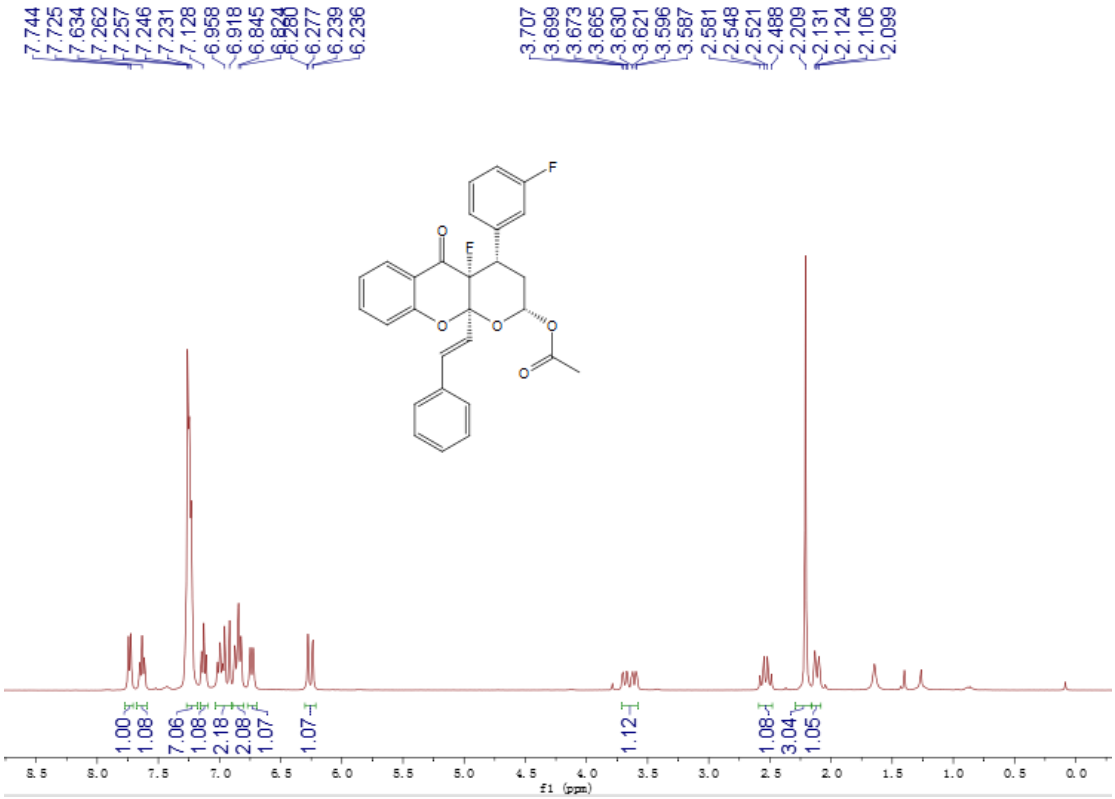
3ad-^{13}C NMR (150 MHz, $CDCl_3$)



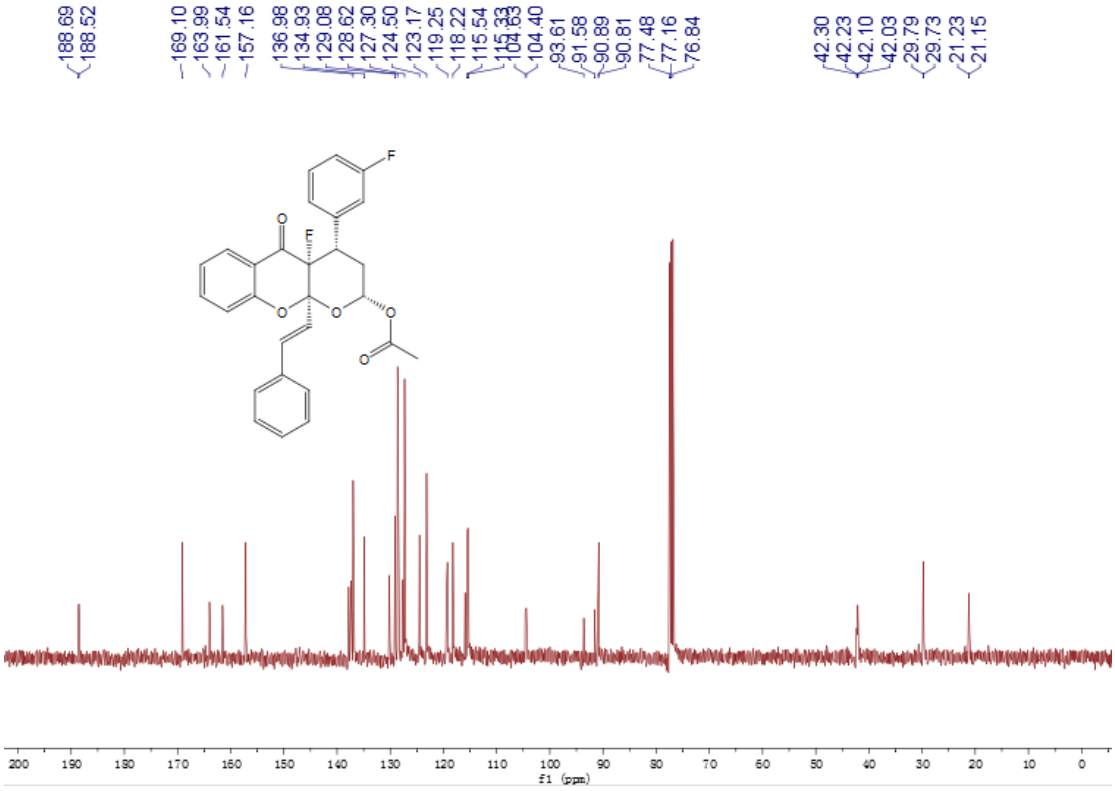
3ad-^{19}F NMR (565 MHz, $CDCl_3$)



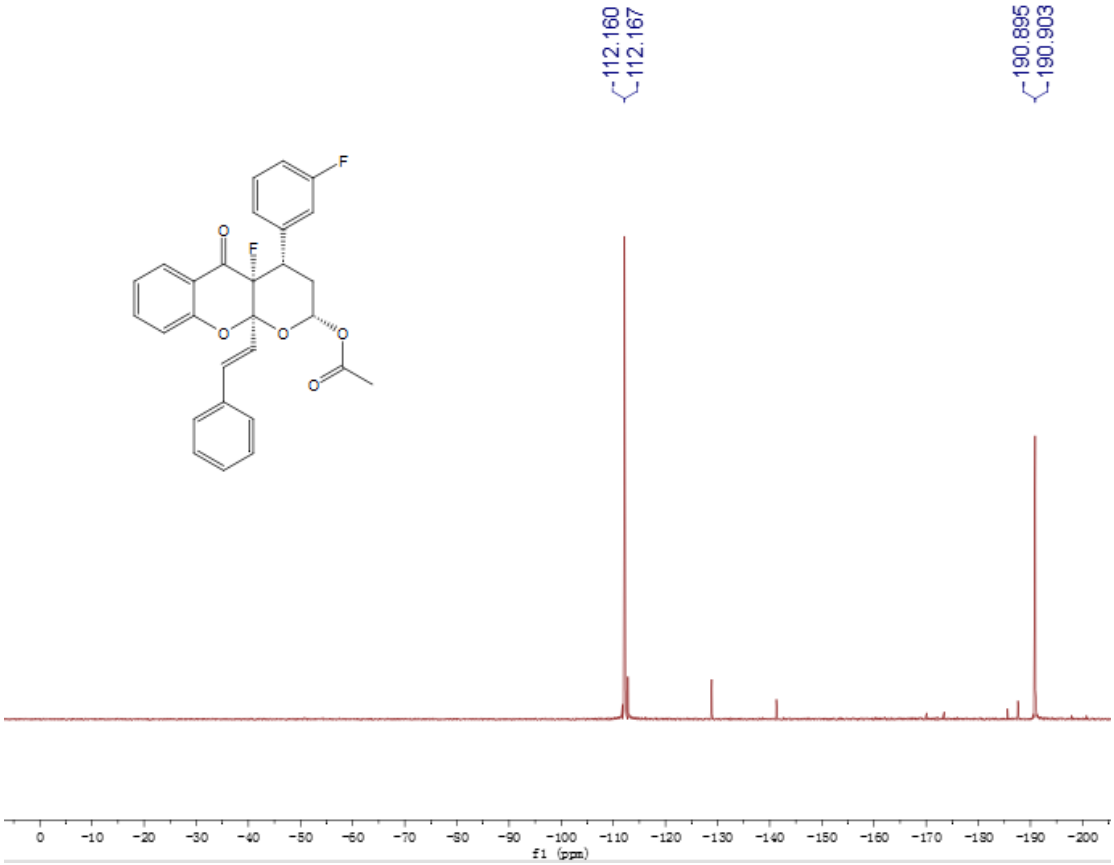
3ae-^{1}H NMR (400 MHz, $CDCl_3$)



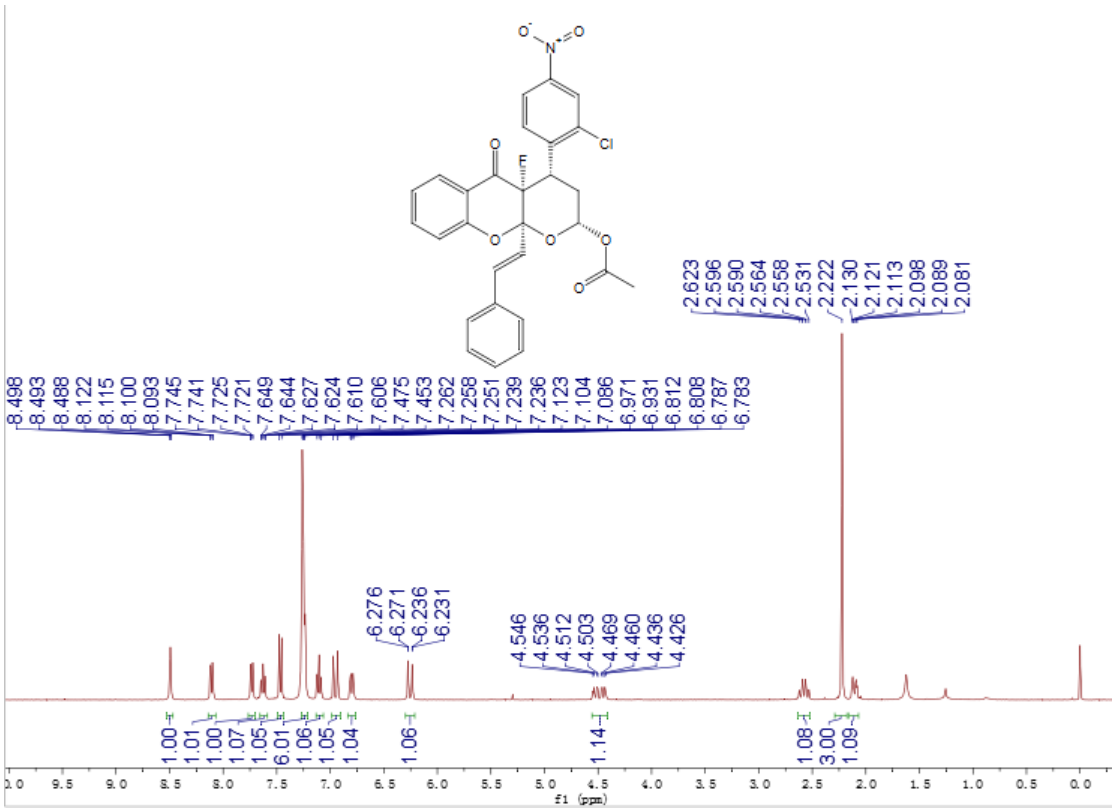
3ae-^{13}C NMR (100 MHz, $CDCl_3$)



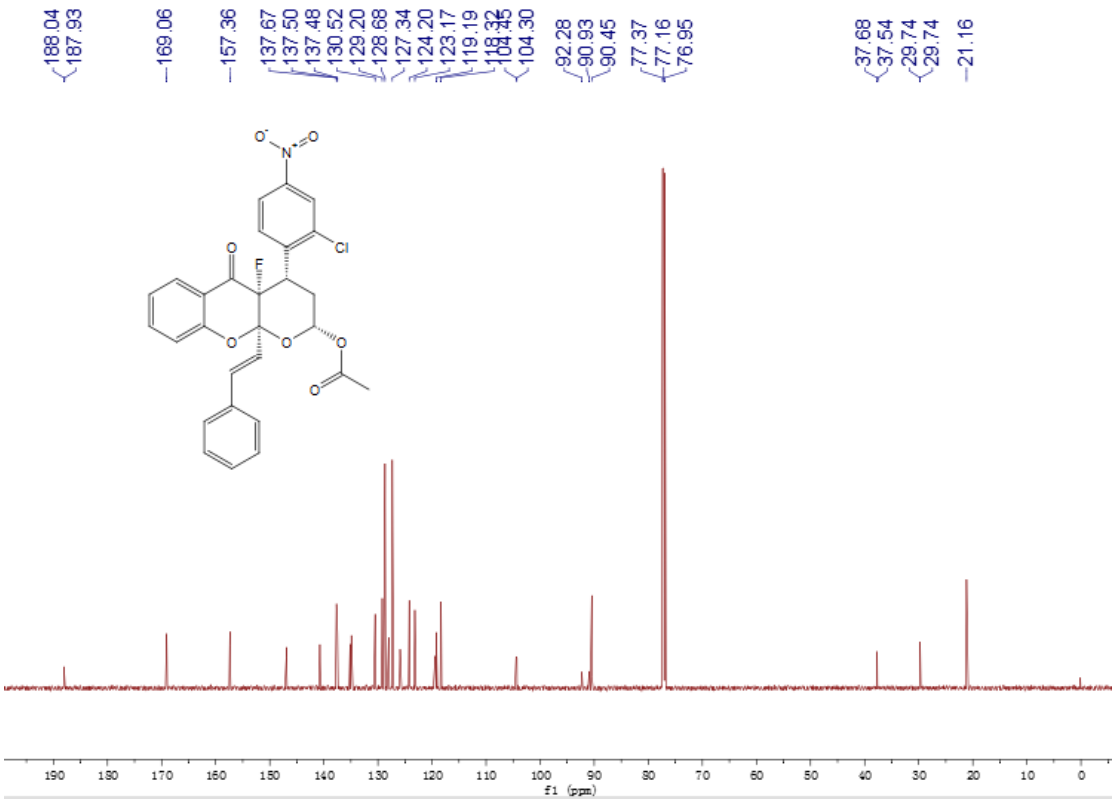
3ae-^{19}F NMR (565 MHz, $CDCl_3$)



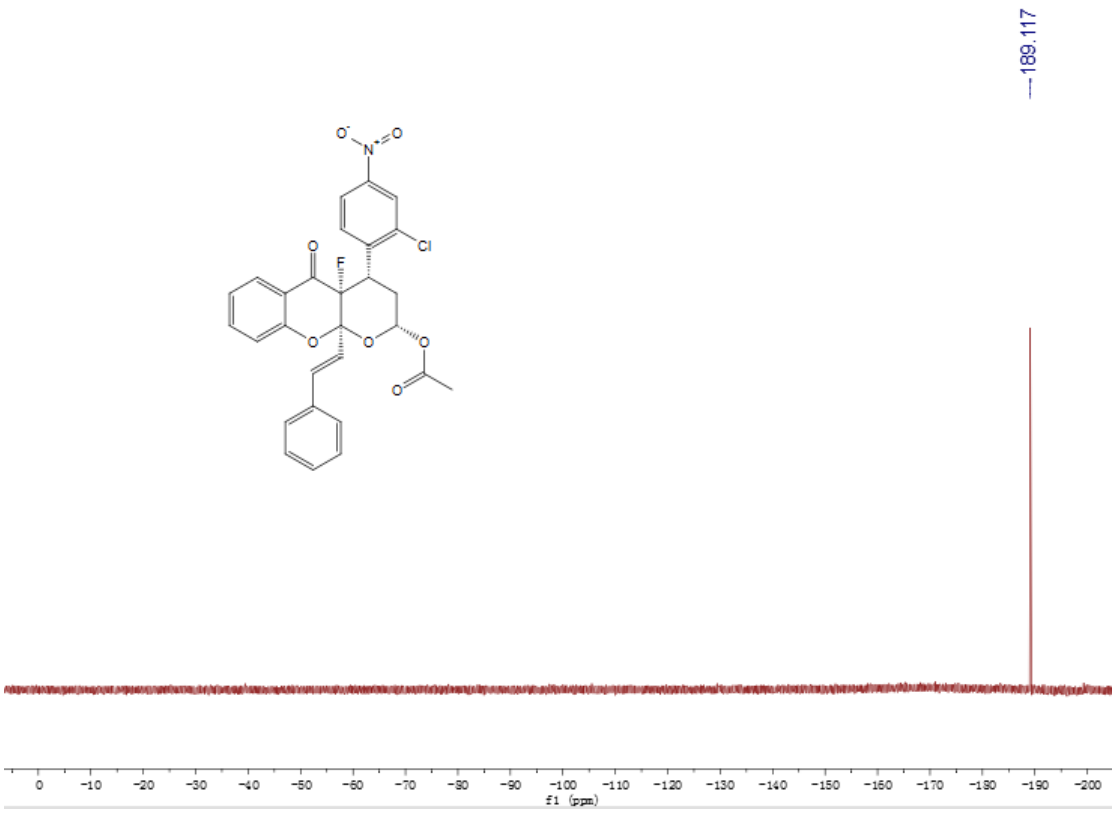
3af-^{1}H NMR (400 MHz, $CDCl_3$)



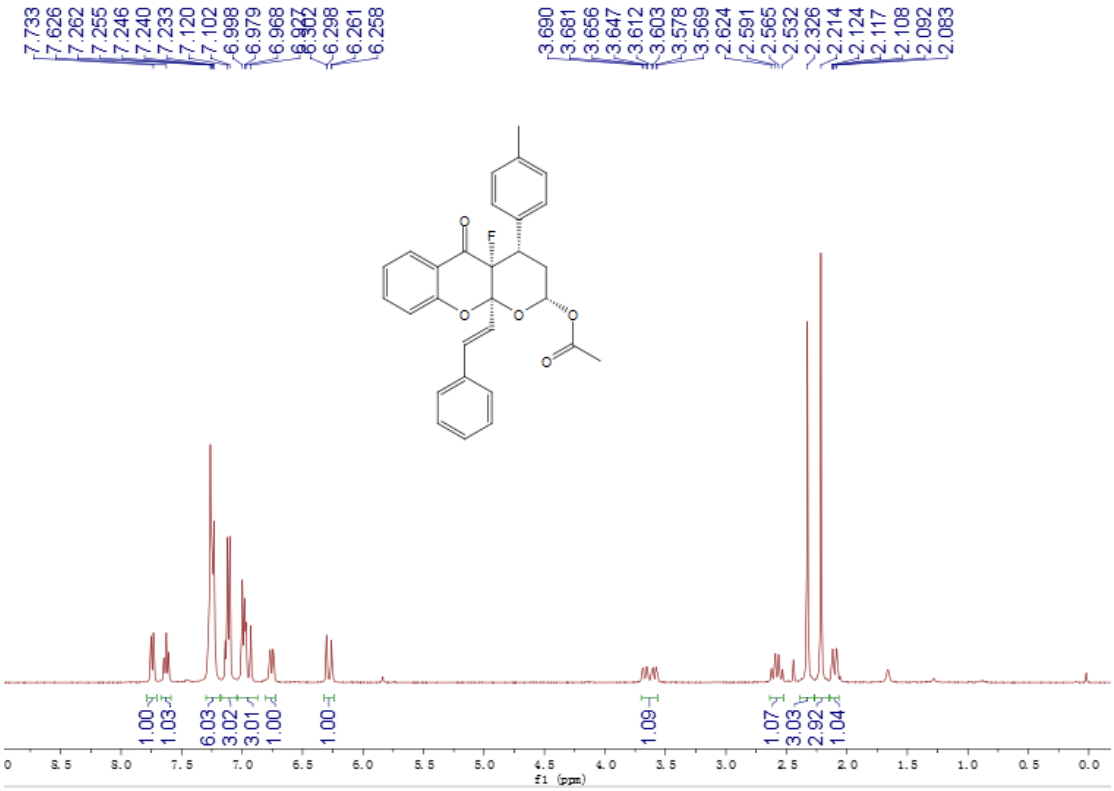
3af-^{13}C NMR (150 MHz, $CDCl_3$)



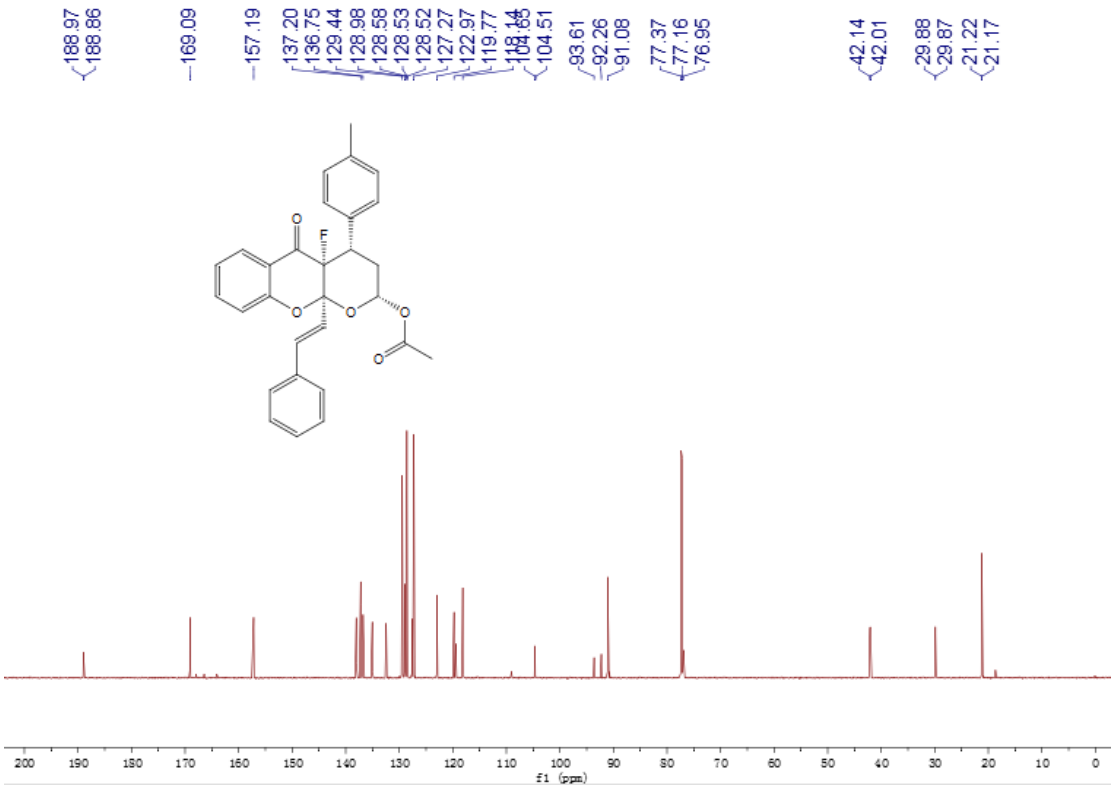
3af-^{19}F NMR (565 MHz, $CDCl_3$)



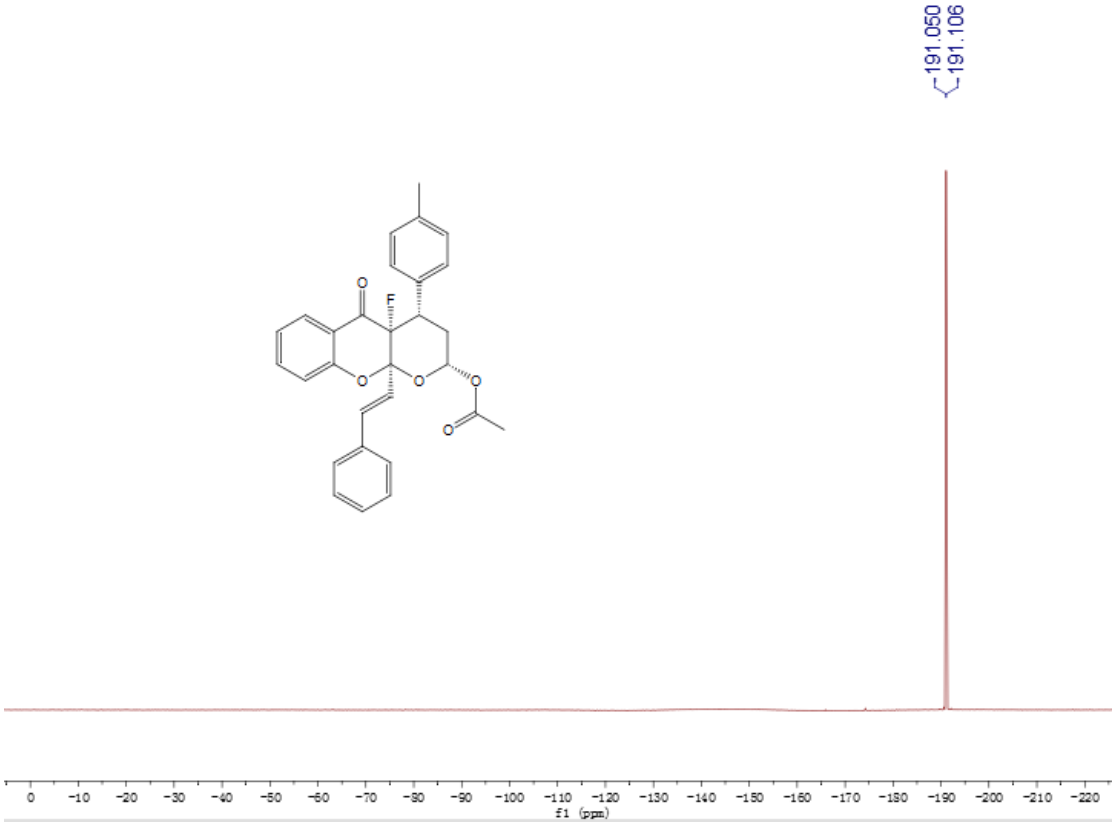
3ag-^{1}H NMR (400 MHz, $CDCl_3$)



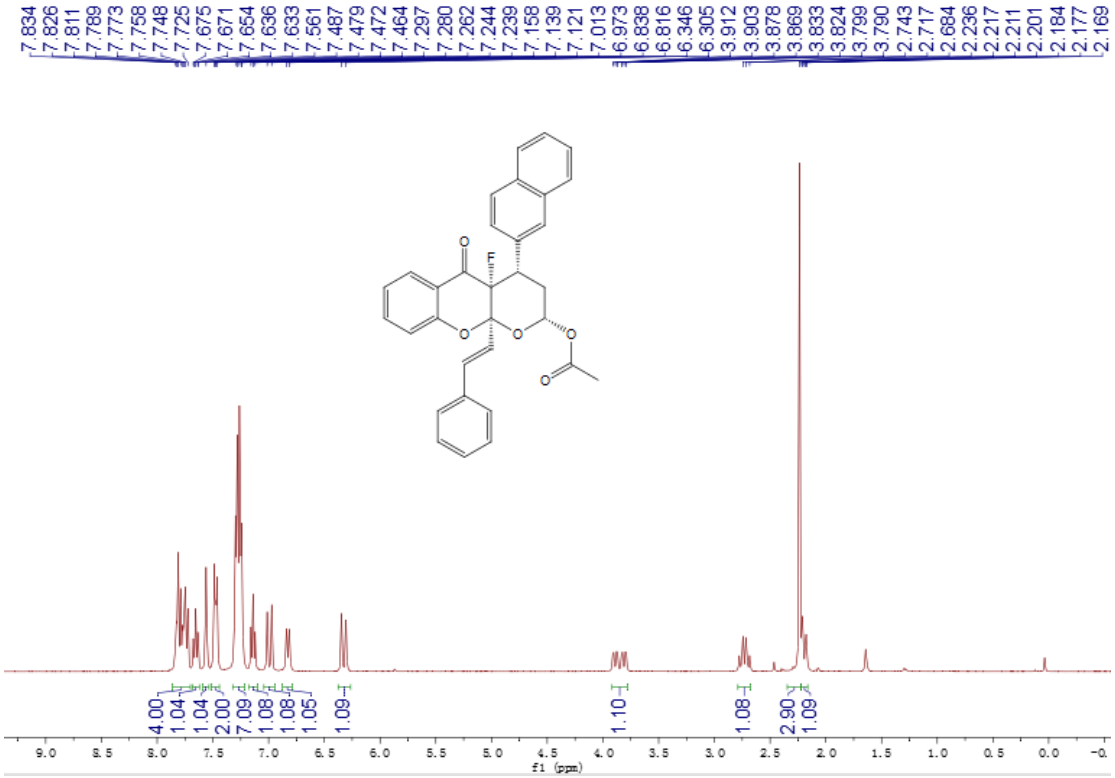
3ag-^{13}C NMR (150 MHz, $CDCl_3$)



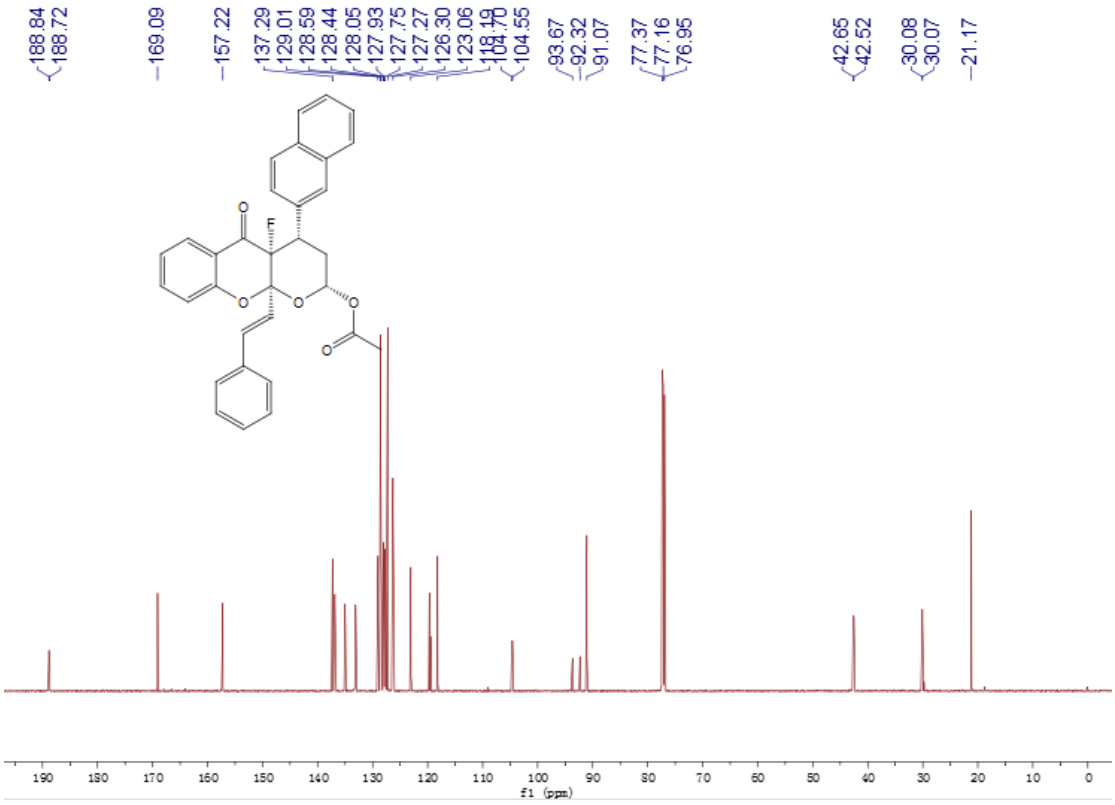
3ag-^{19}F NMR (565 MHz, $CDCl_3$)



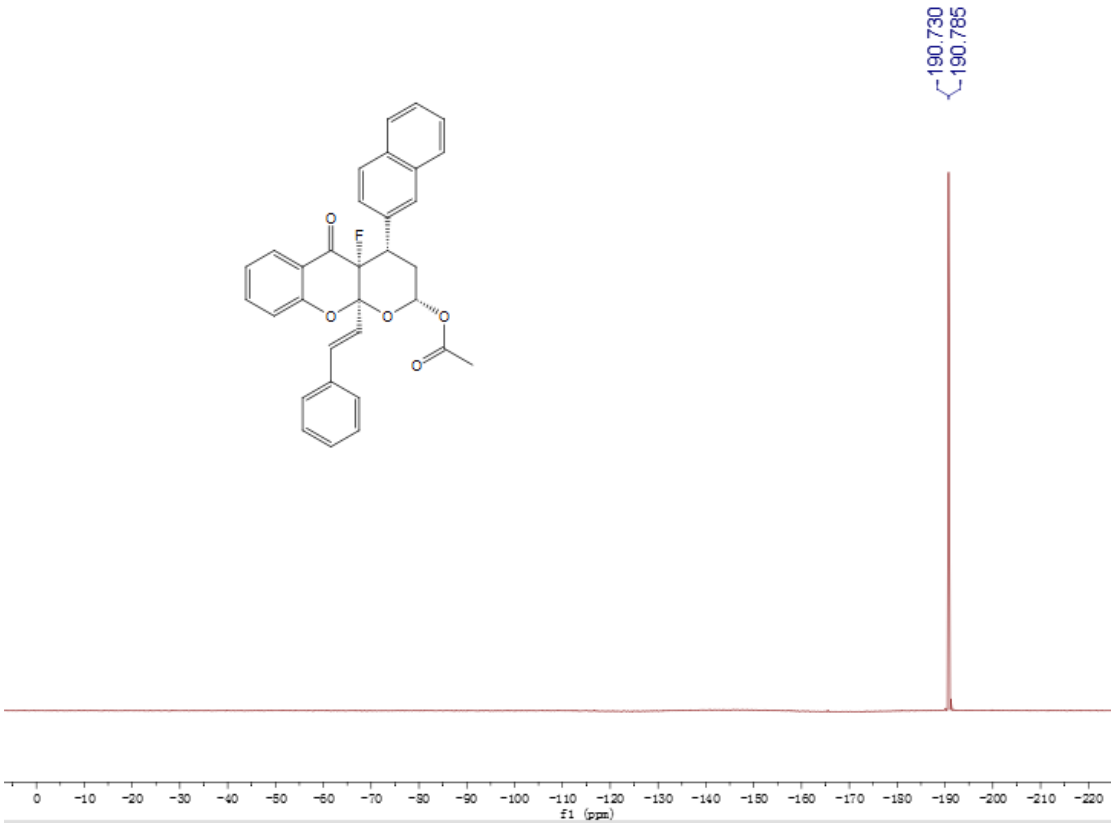
3ah-^{1}H NMR (400 MHz, $CDCl_3$)



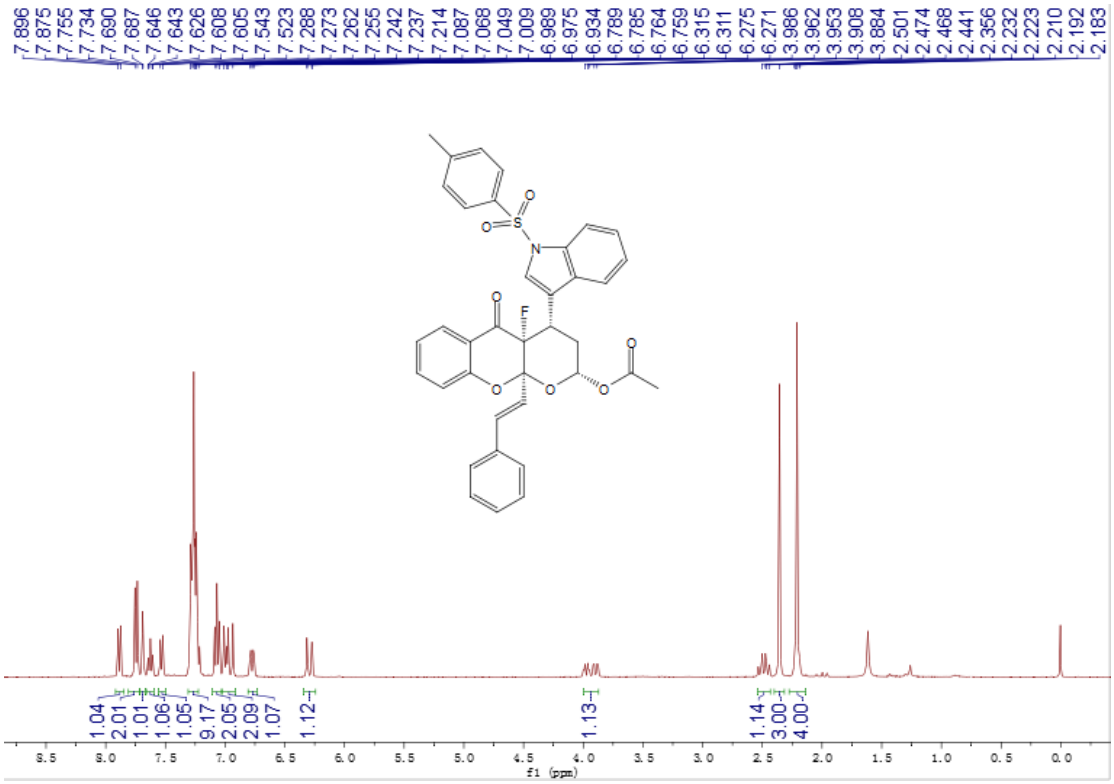
3ah-^{13}C NMR (150 MHz, $CDCl_3$)



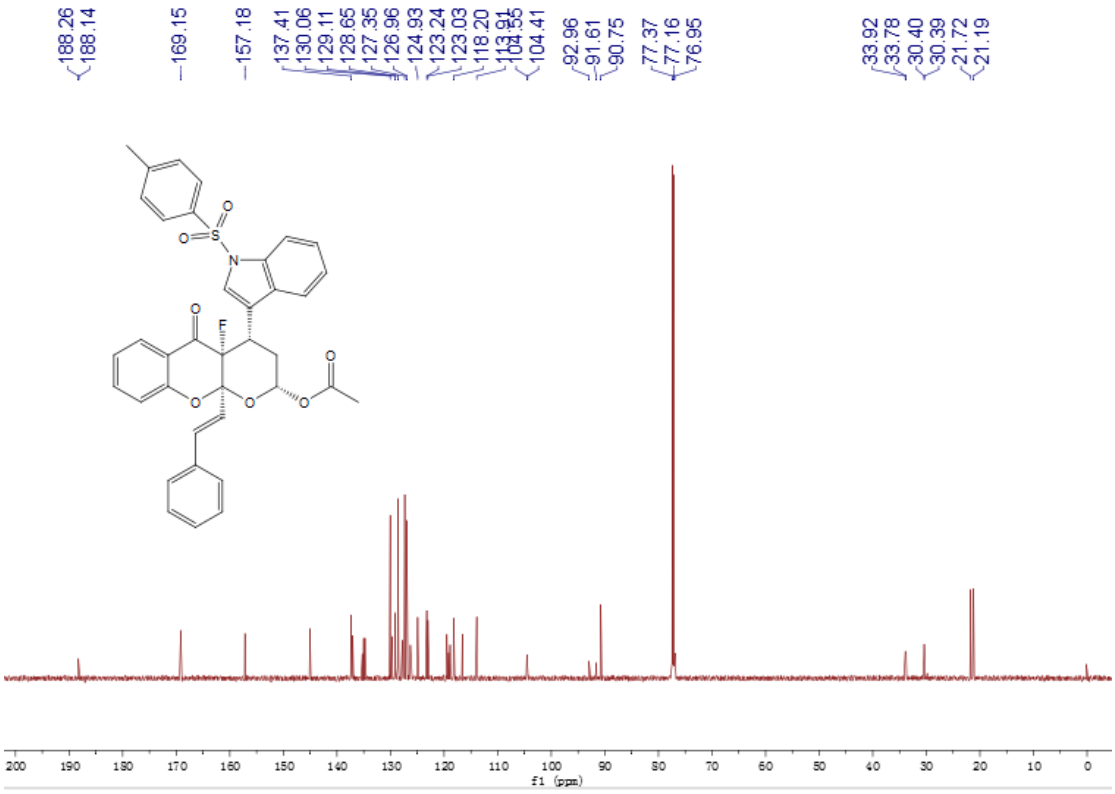
3ah-^{19}F NMR (565 MHz, $CDCl_3$)



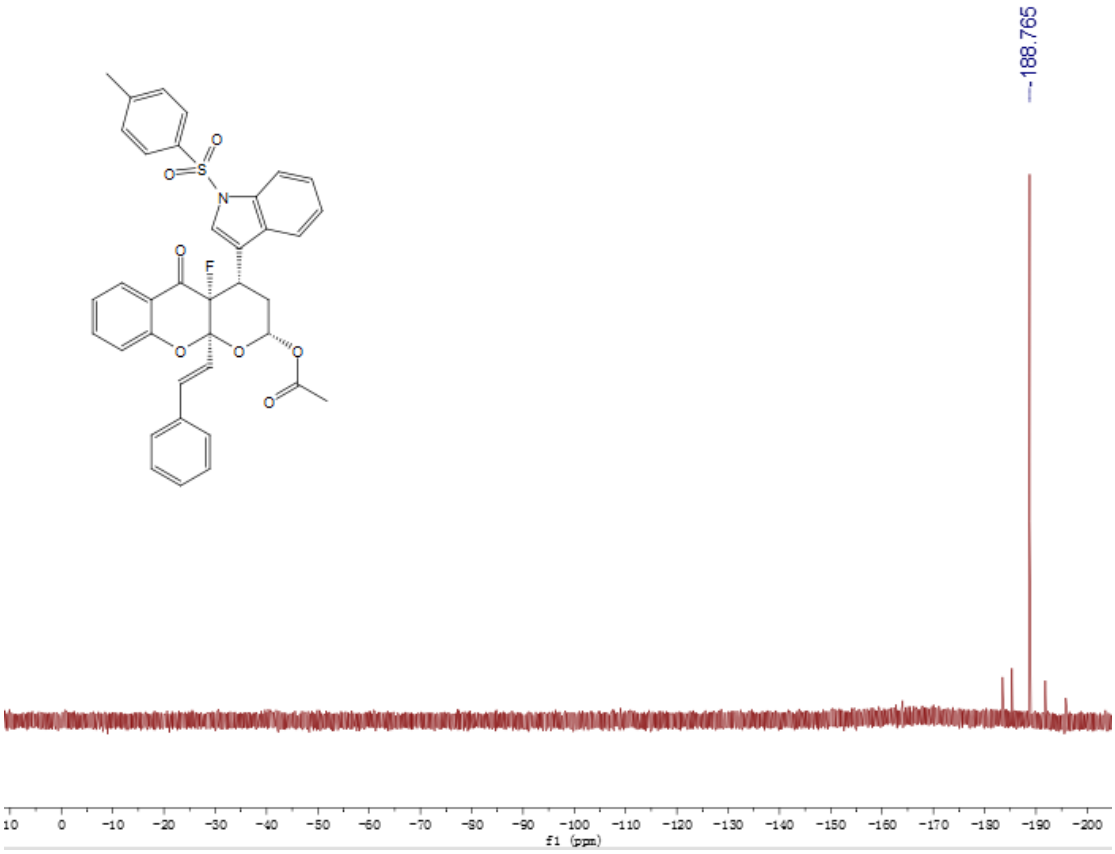
3ai-^{1}H NMR (400 MHz, $CDCl_3$)



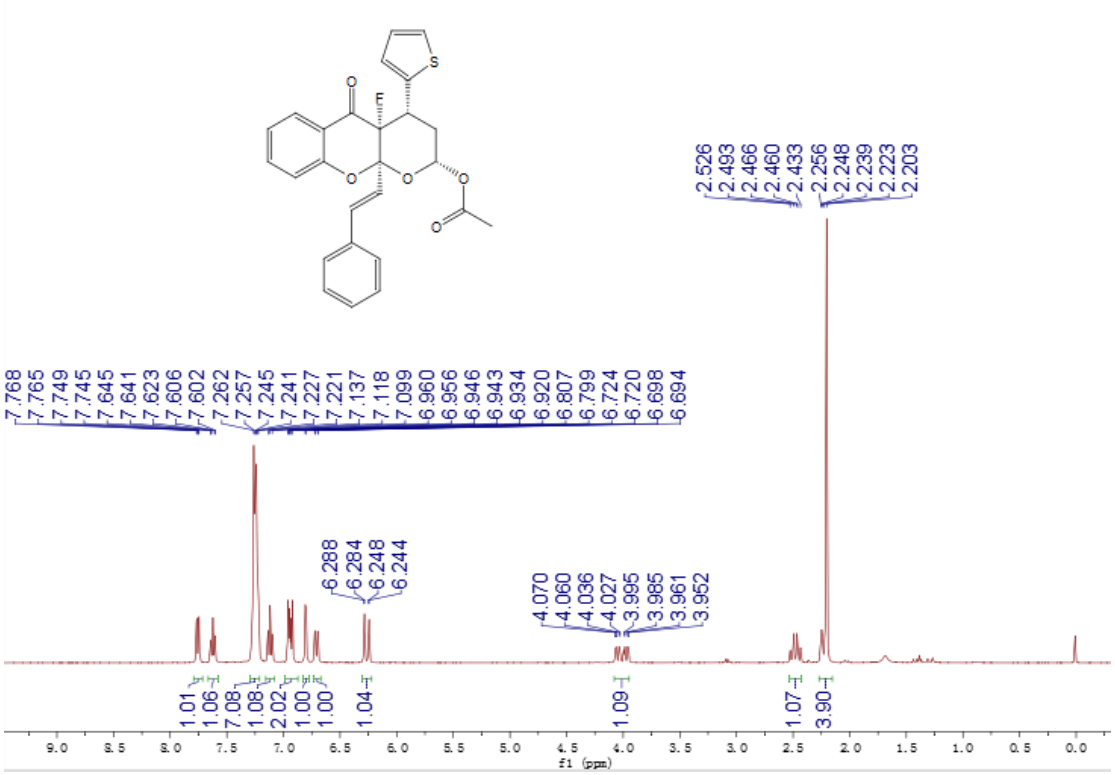
3ai-^{13}C NMR (150 MHz, $CDCl_3$)



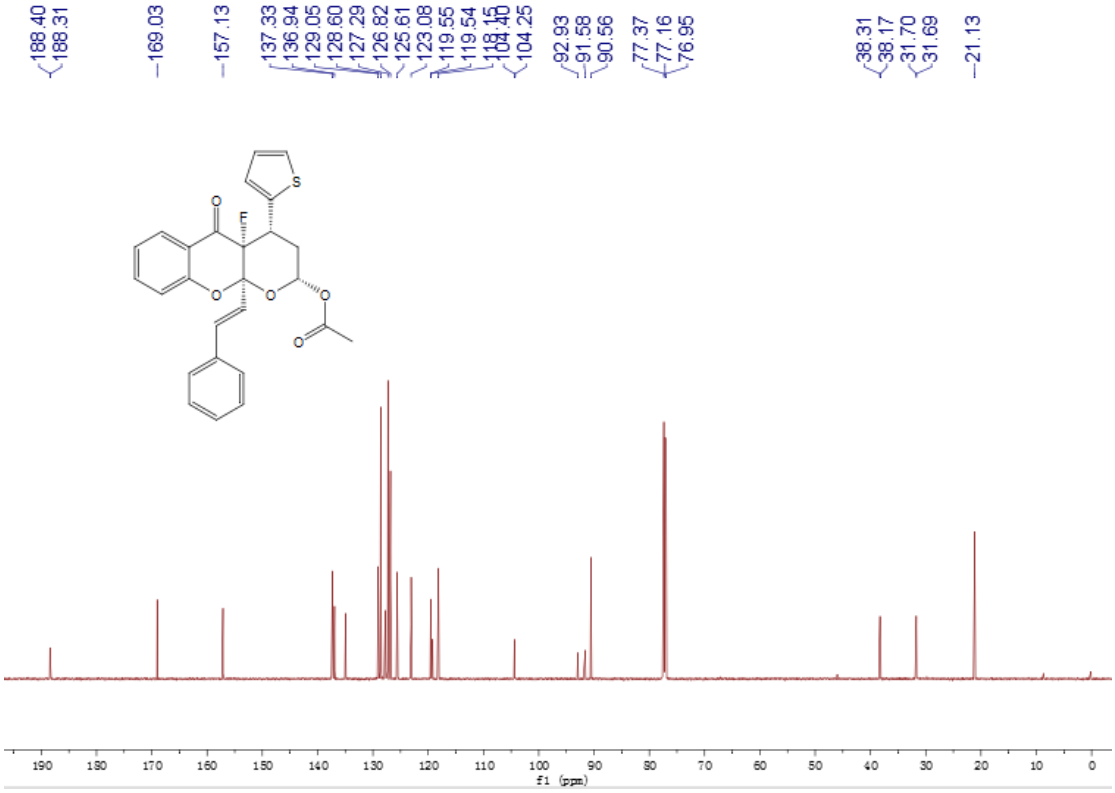
3ai-^{19}F NMR (565 MHz, $CDCl_3$)



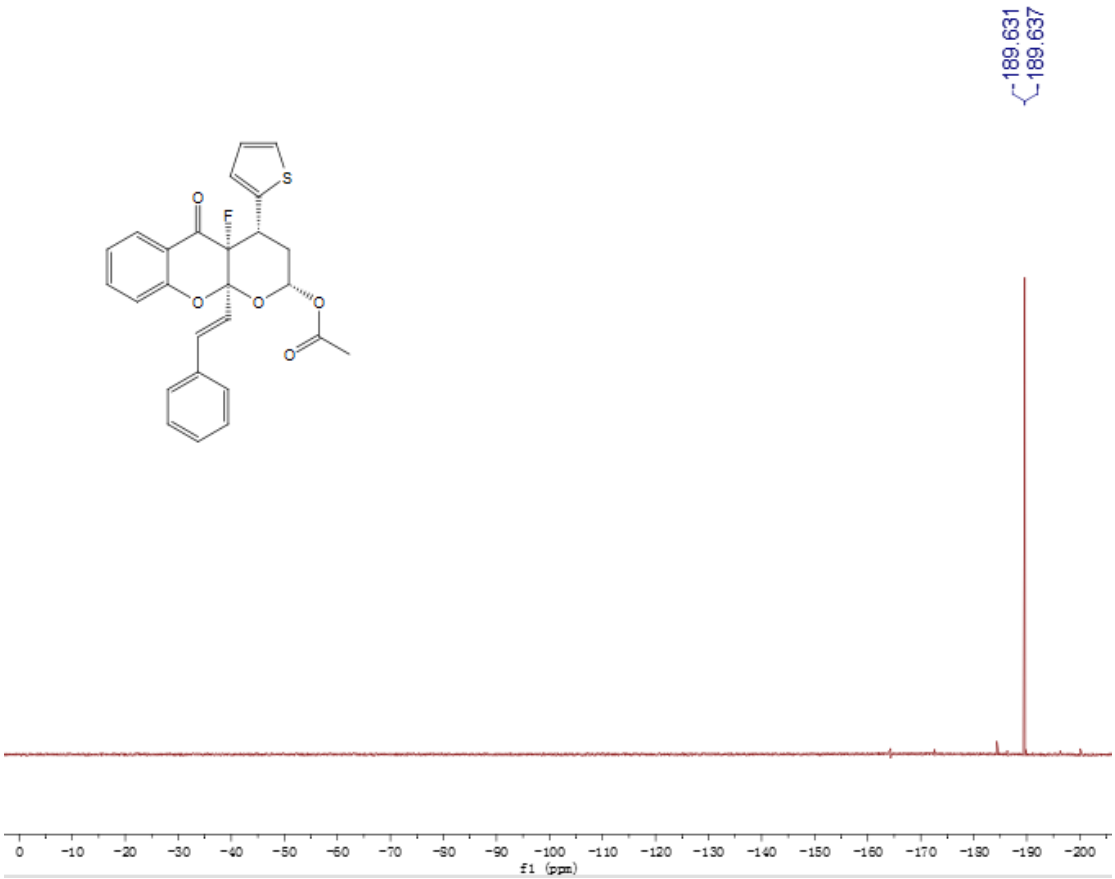
3aj-^{1}H NMR (400 MHz, $CDCl_3$)



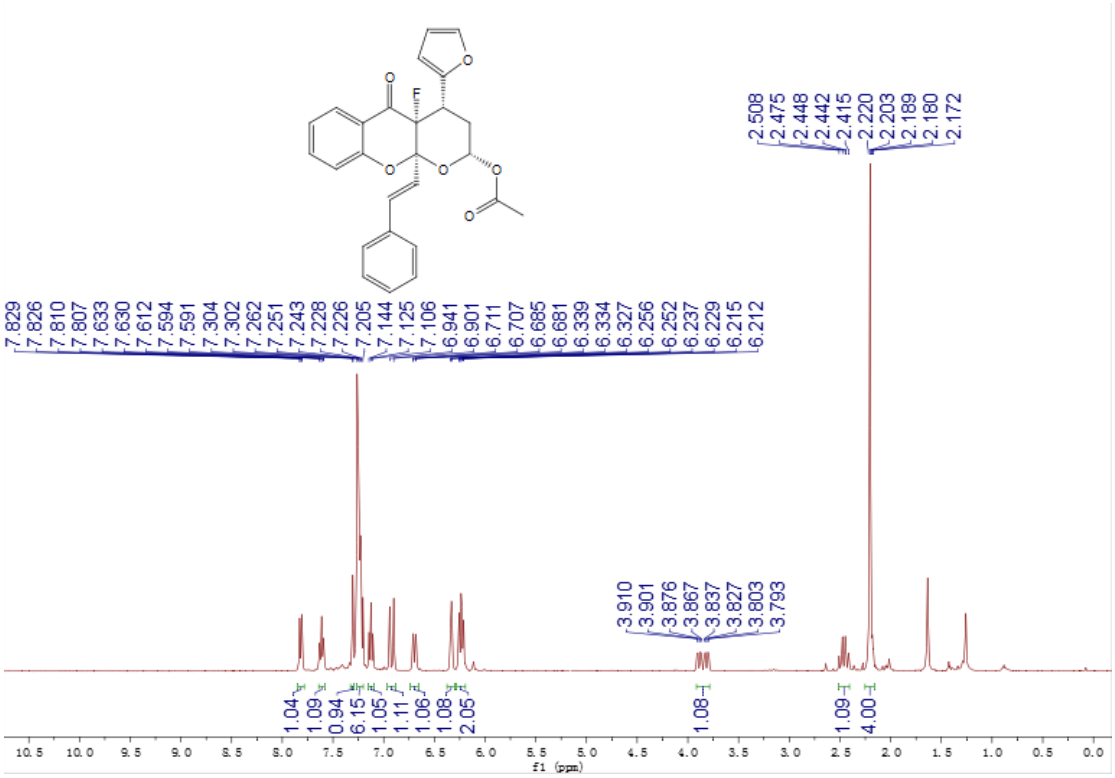
3aj-^{13}C NMR (150 MHz, $CDCl_3$)



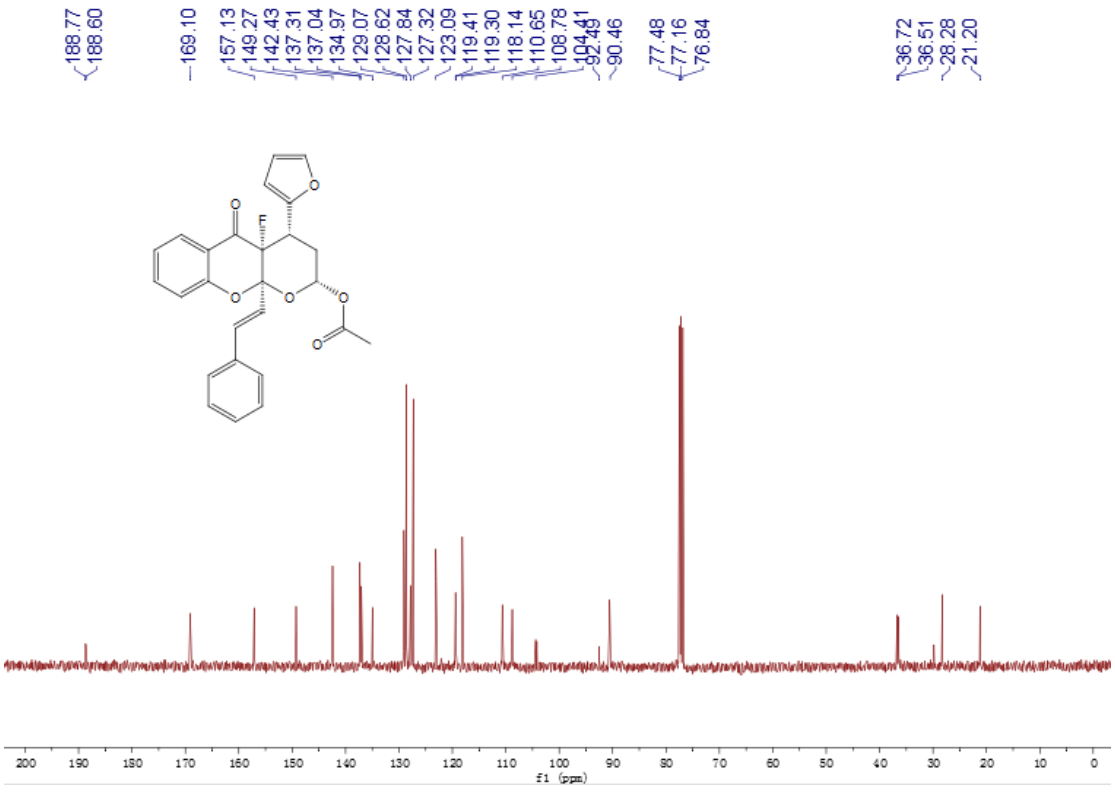
3aj-^{19}F NMR (565 MHz, $CDCl_3$)



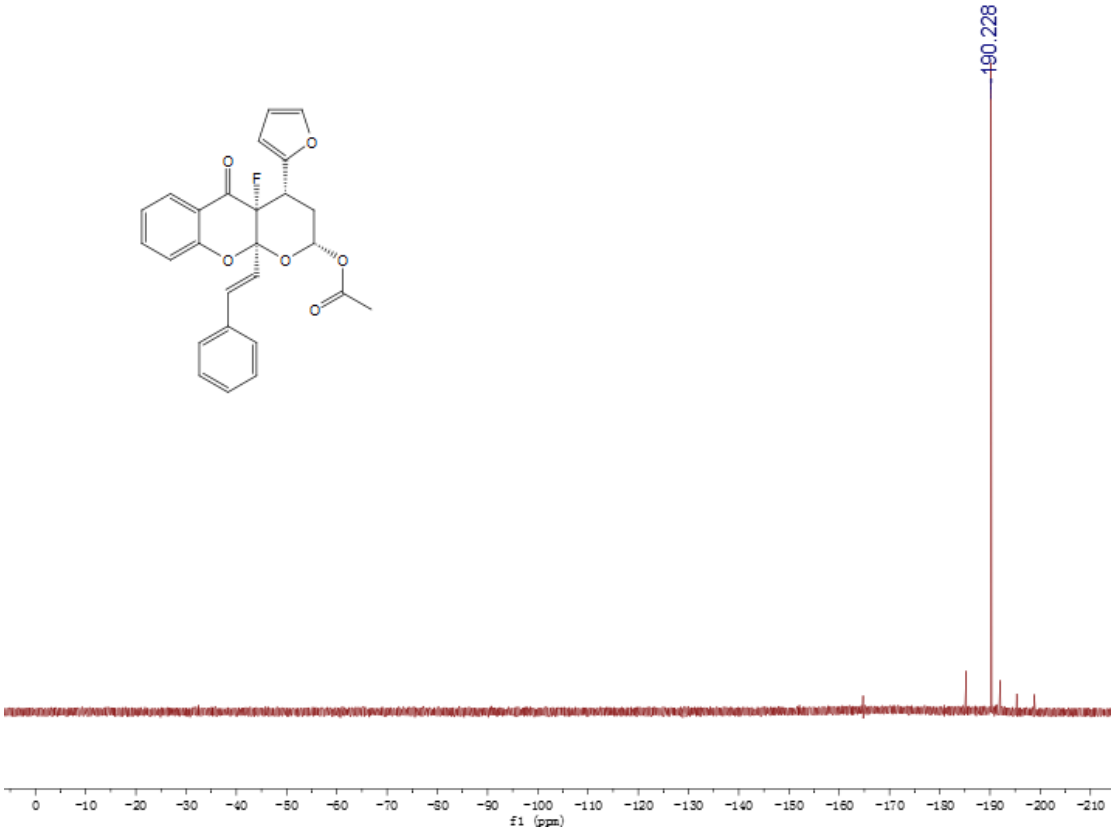
3ak-^{1}H NMR (400 MHz, $CDCl_3$)



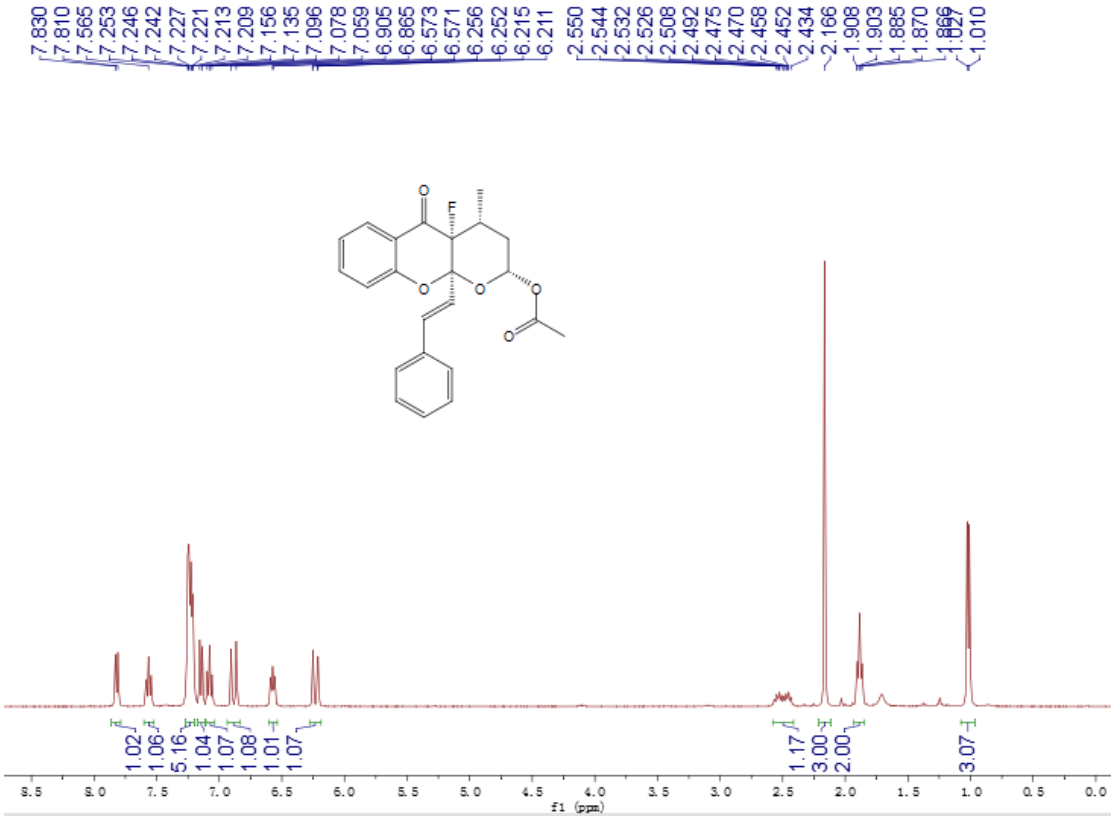
3ak-^{13}C NMR (100 MHz, $CDCl_3$)



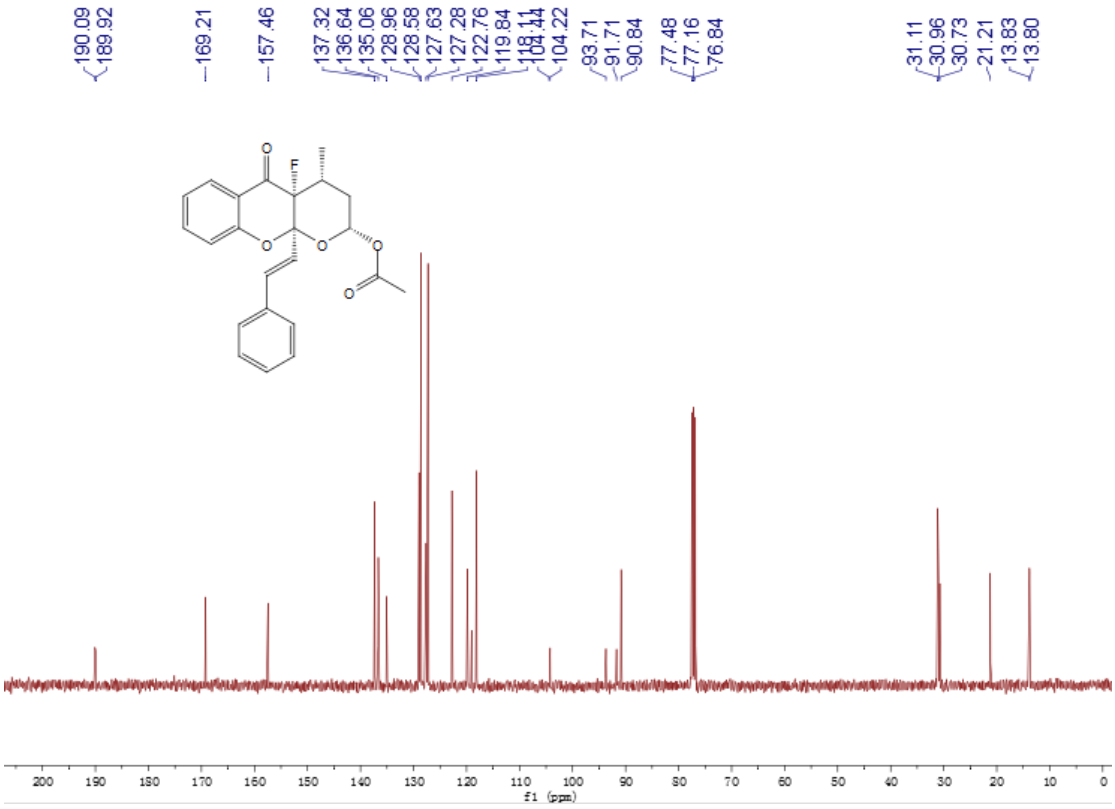
3ak-^{19}F NMR (565MHz, $CDCl_3$)



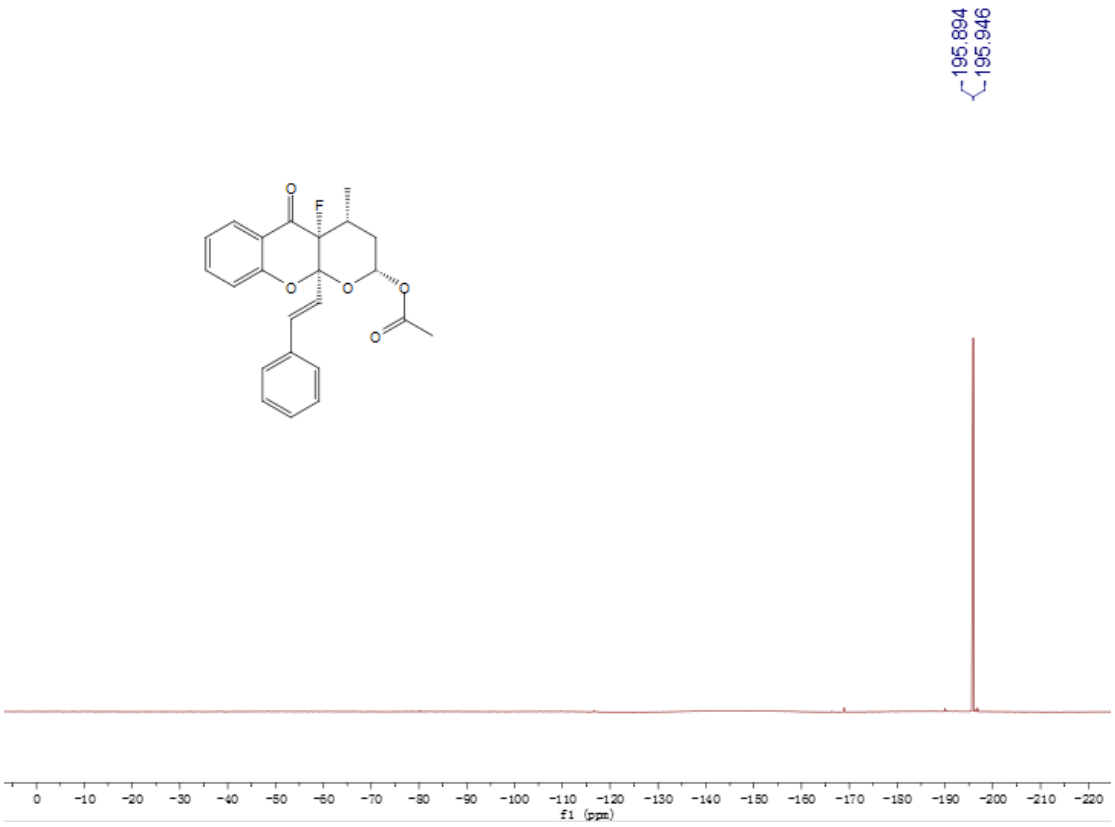
3al-^{1}H NMR (400 MHz, $CDCl_3$)



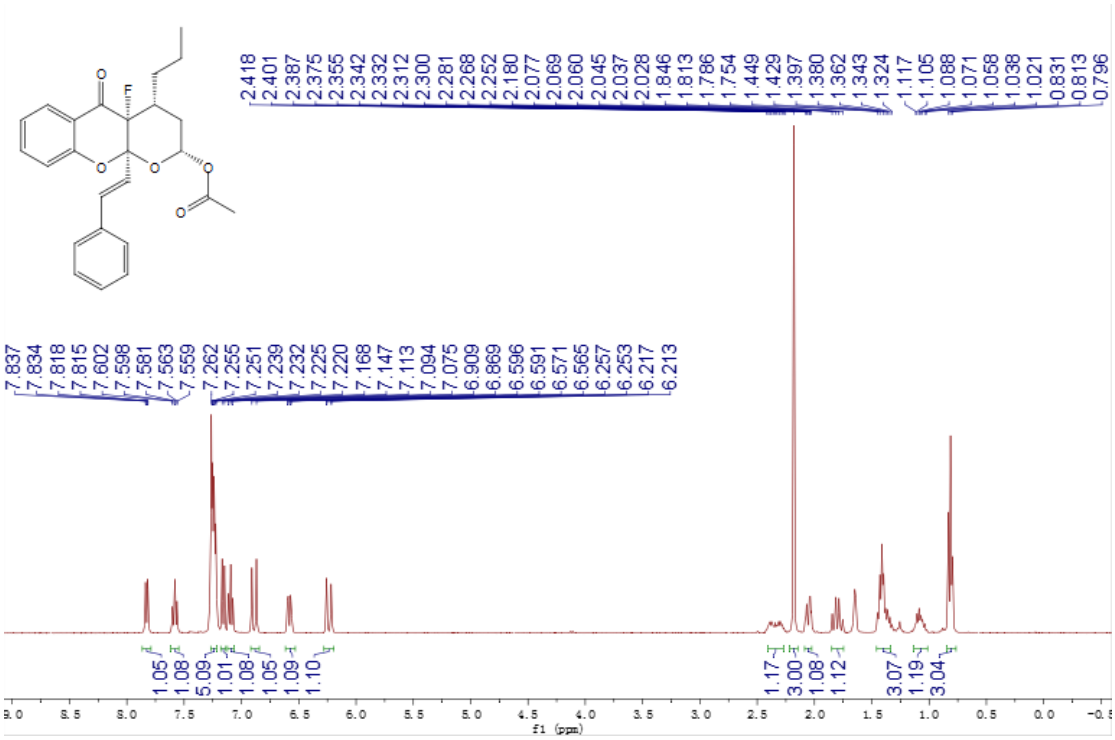
3al-^{13}C NMR (100 MHz, $CDCl_3$)



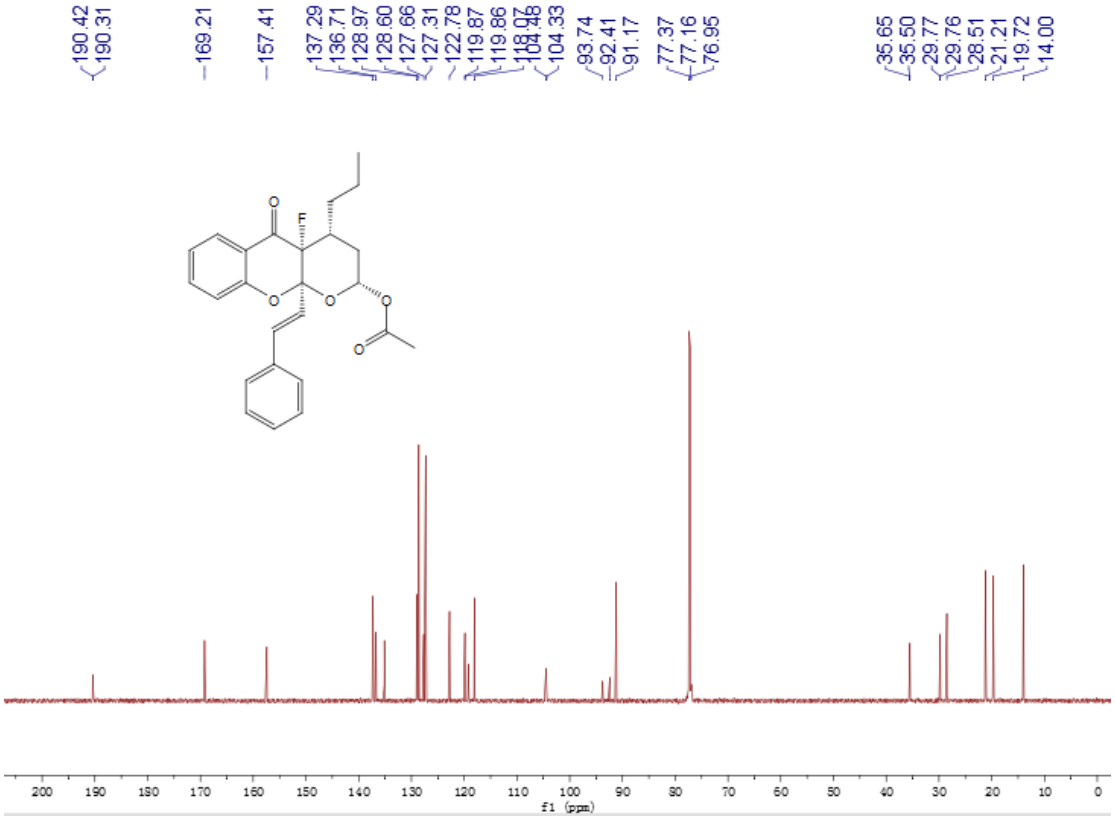
3al-^{19}F NMR (565 MHz, $CDCl_3$)



3am-^{1}H NMR (400 MHz, $CDCl_3$)

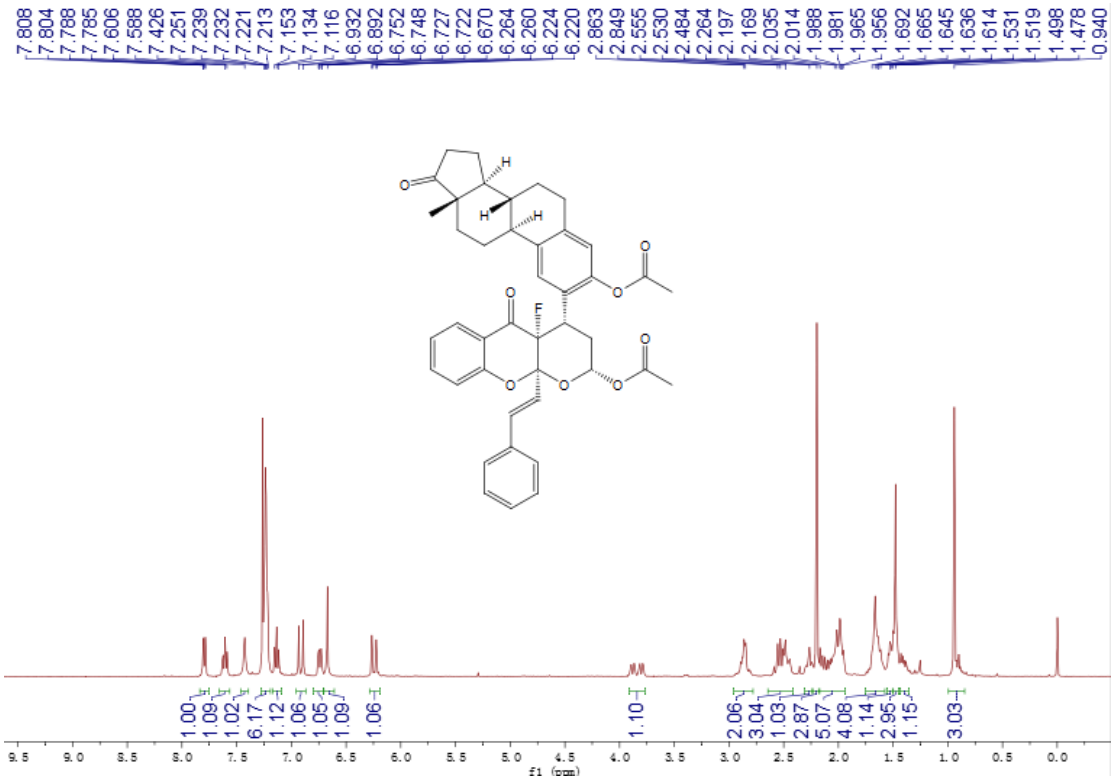


3am-^{13}C NMR (150 MHz, $CDCl_3$)

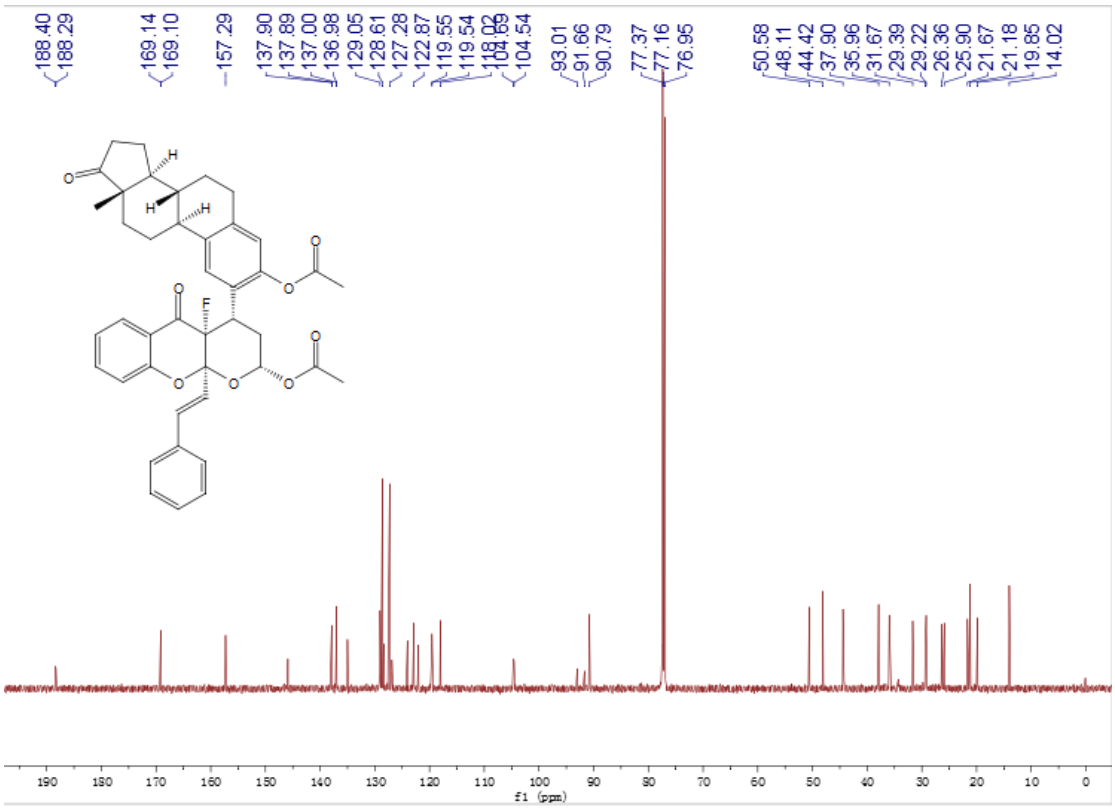


3am-^{19}F NMR (565 MHz, $CDCl_3$)

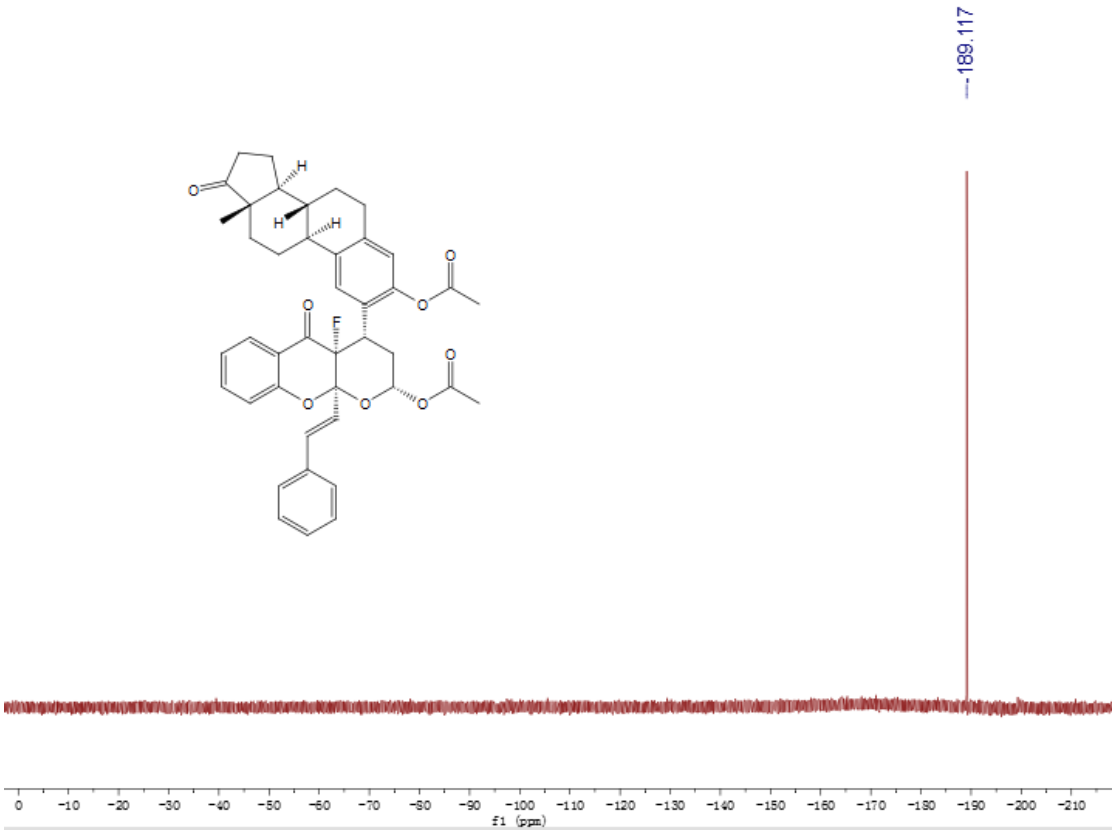
3an-^{1}H NMR (400 MHz, $CDCl_3$)



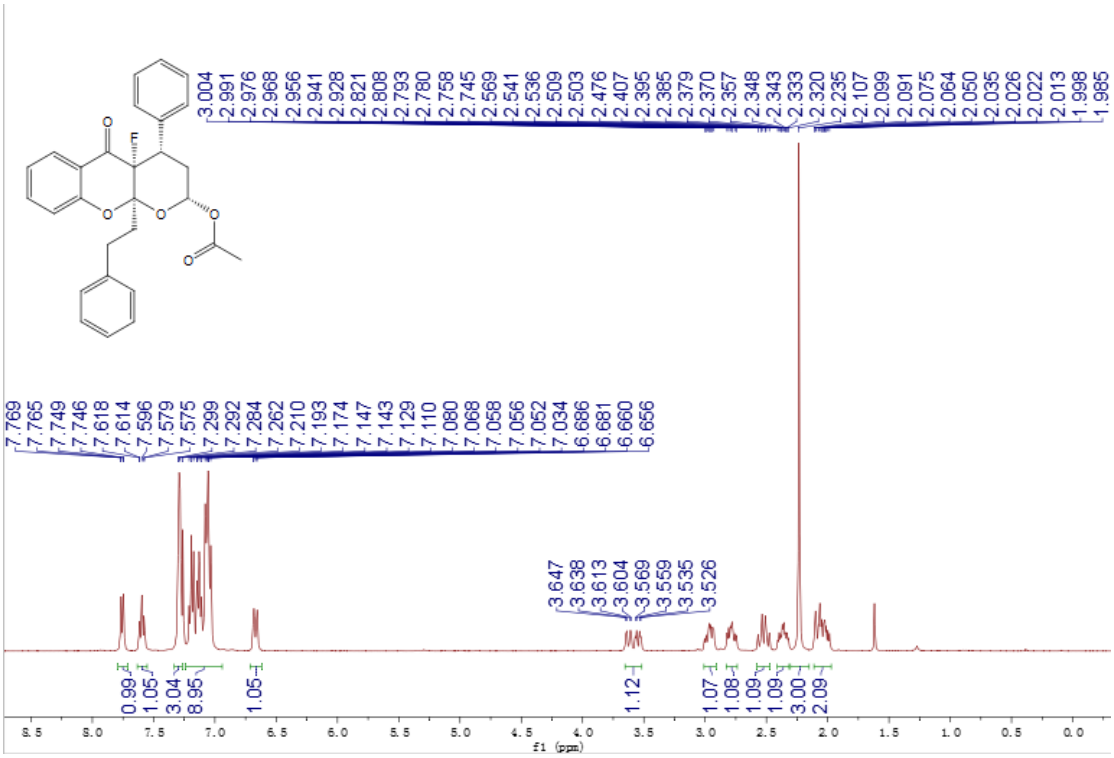
3an-^{13}C NMR (150 MHz, $CDCl_3$)



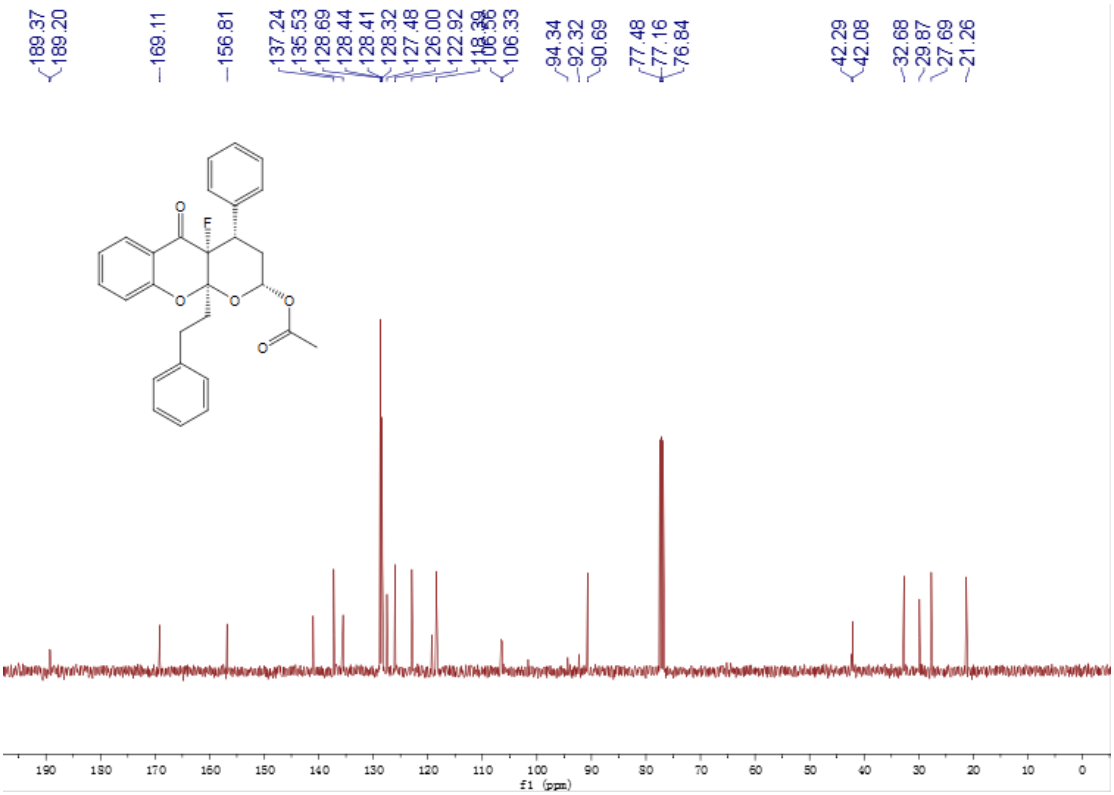
3an-^{19}F NMR (565 MHz, $CDCl_3$)



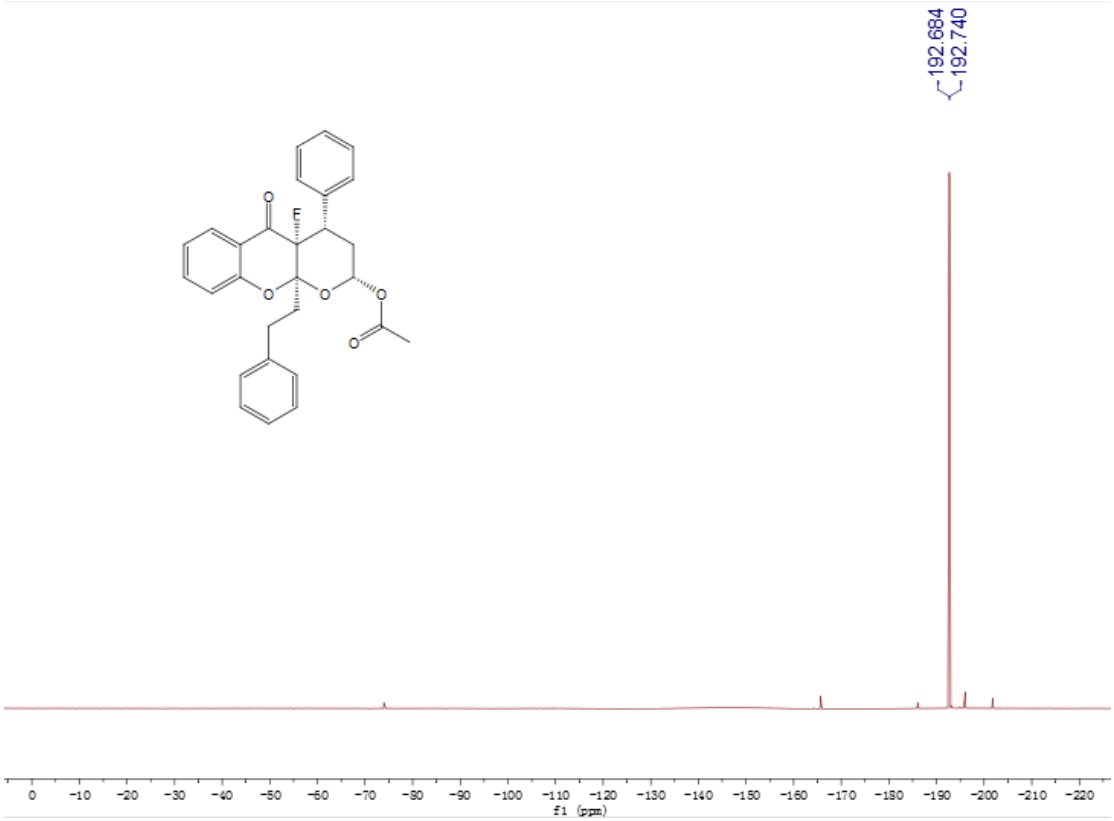
4a-^{1}H NMR (400 MHz, $CDCl_3$)



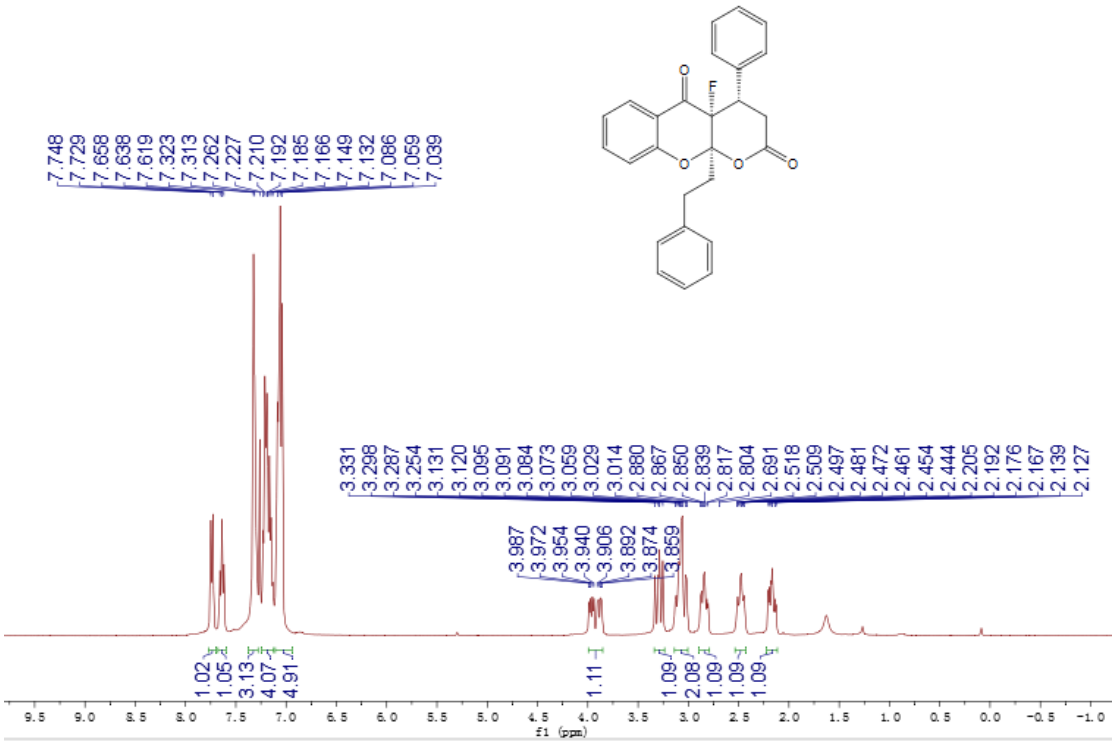
4a-^{13}C NMR (100 MHz, $CDCl_3$)



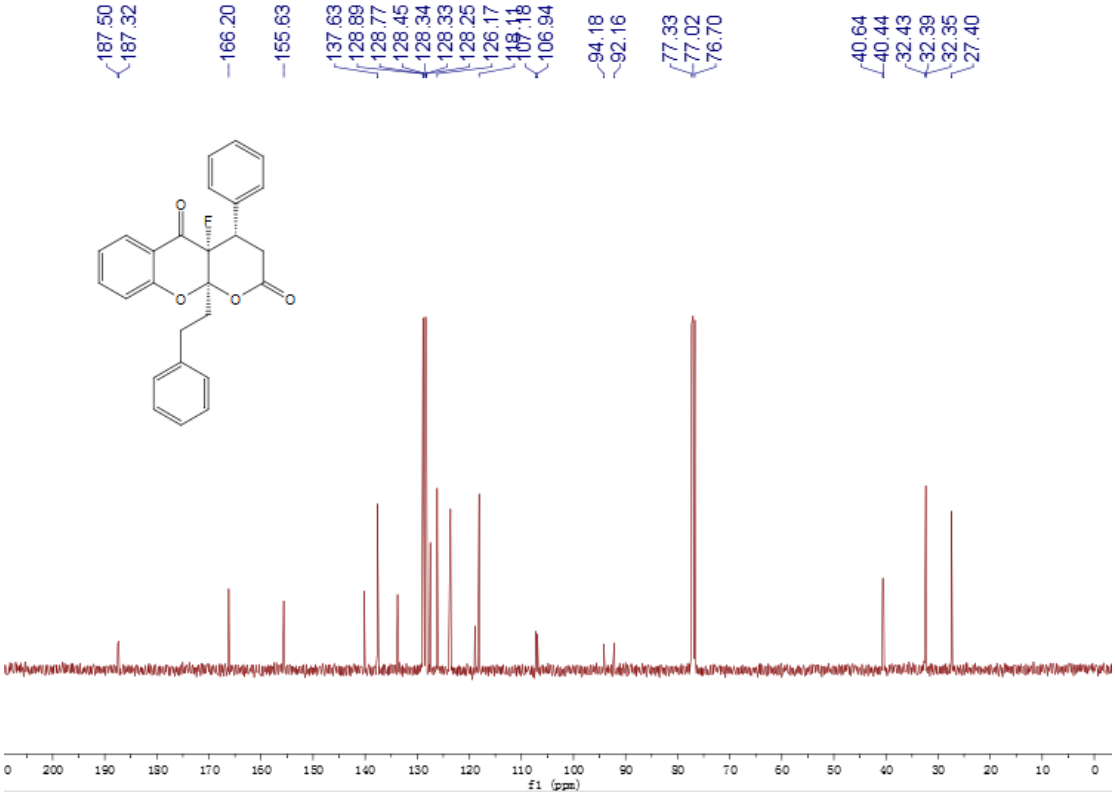
4a-^{19}F NMR (565 MHz, $CDCl_3$)



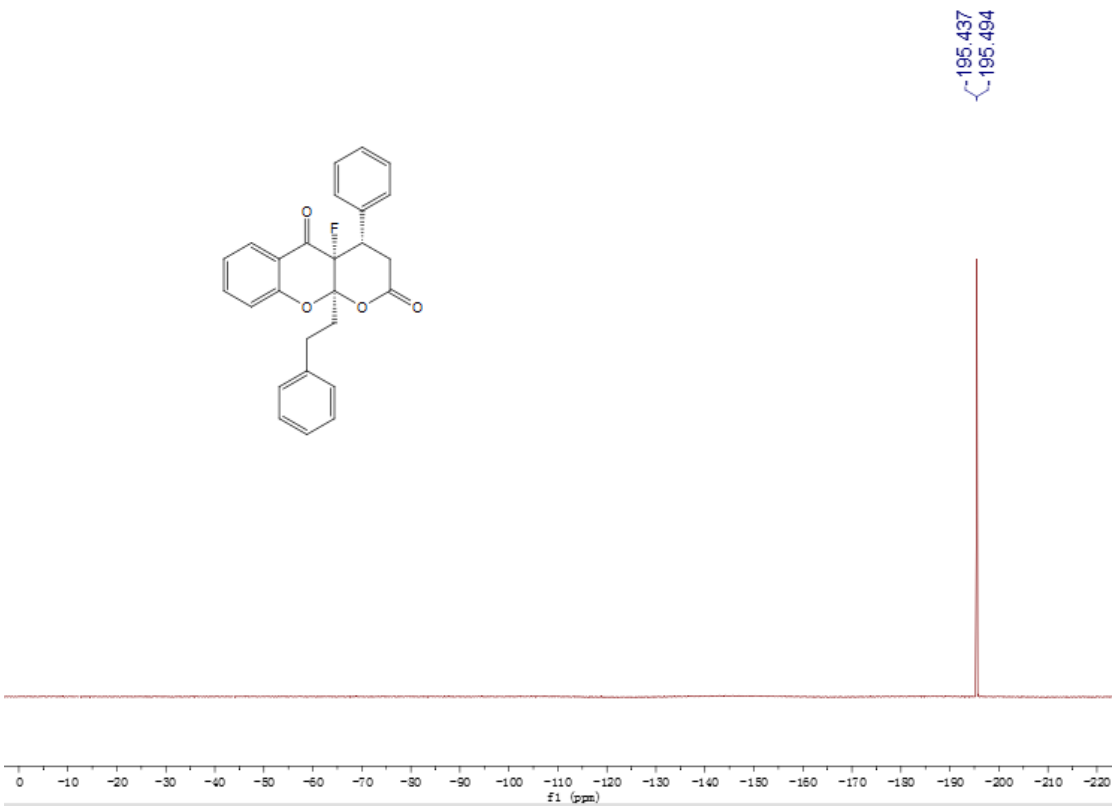
4b-^{1}H NMR (400 MHz, $CDCl_3$)



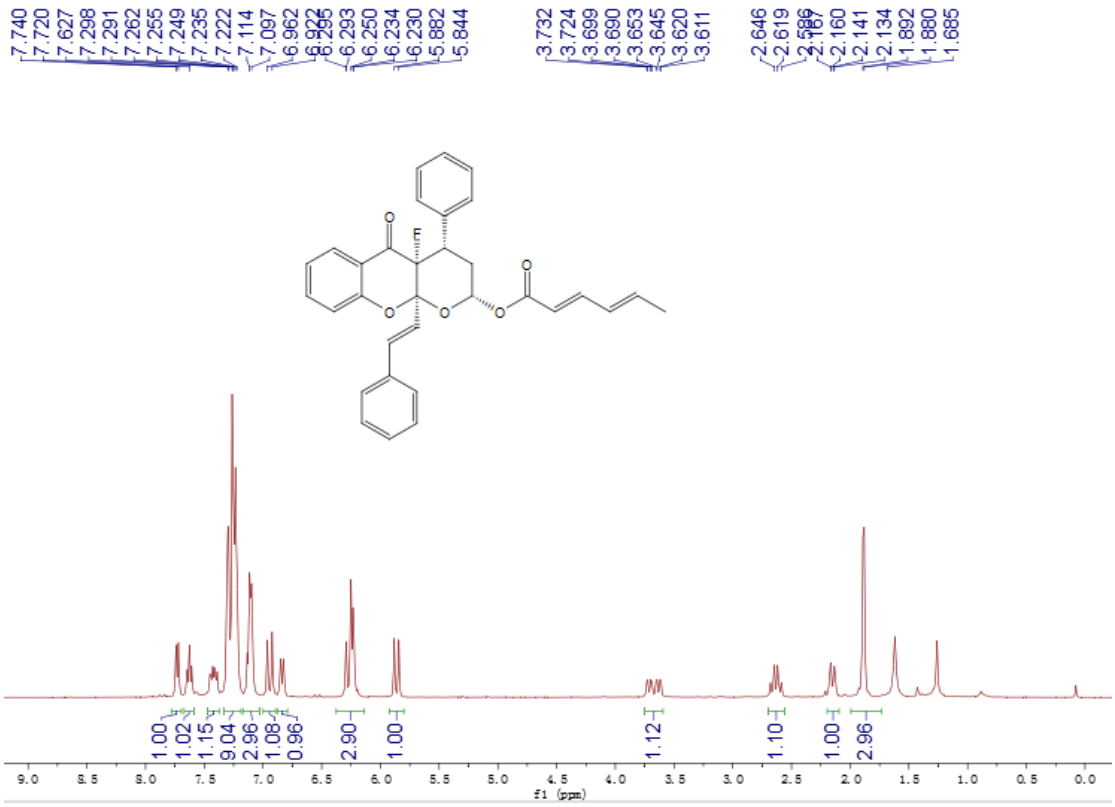
4b-^{13}C NMR (150 MHz, $CDCl_3$)



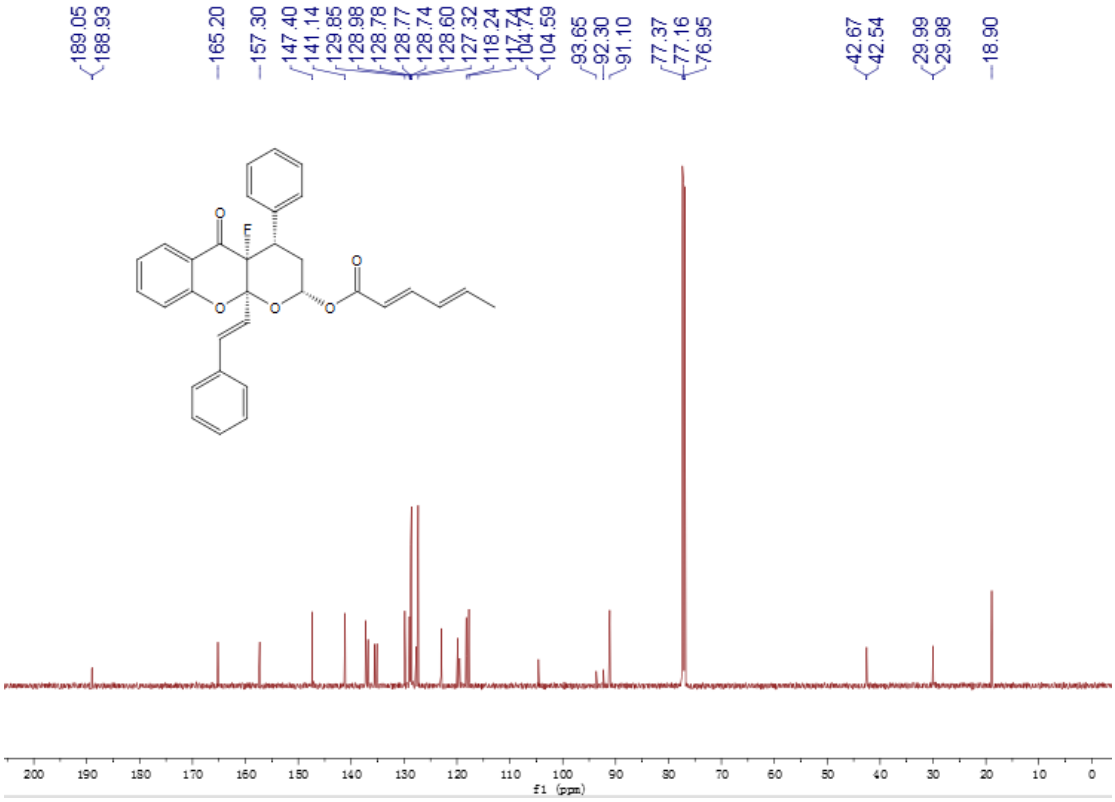
4b-^{19}F NMR (565 MHz, $CDCl_3$)



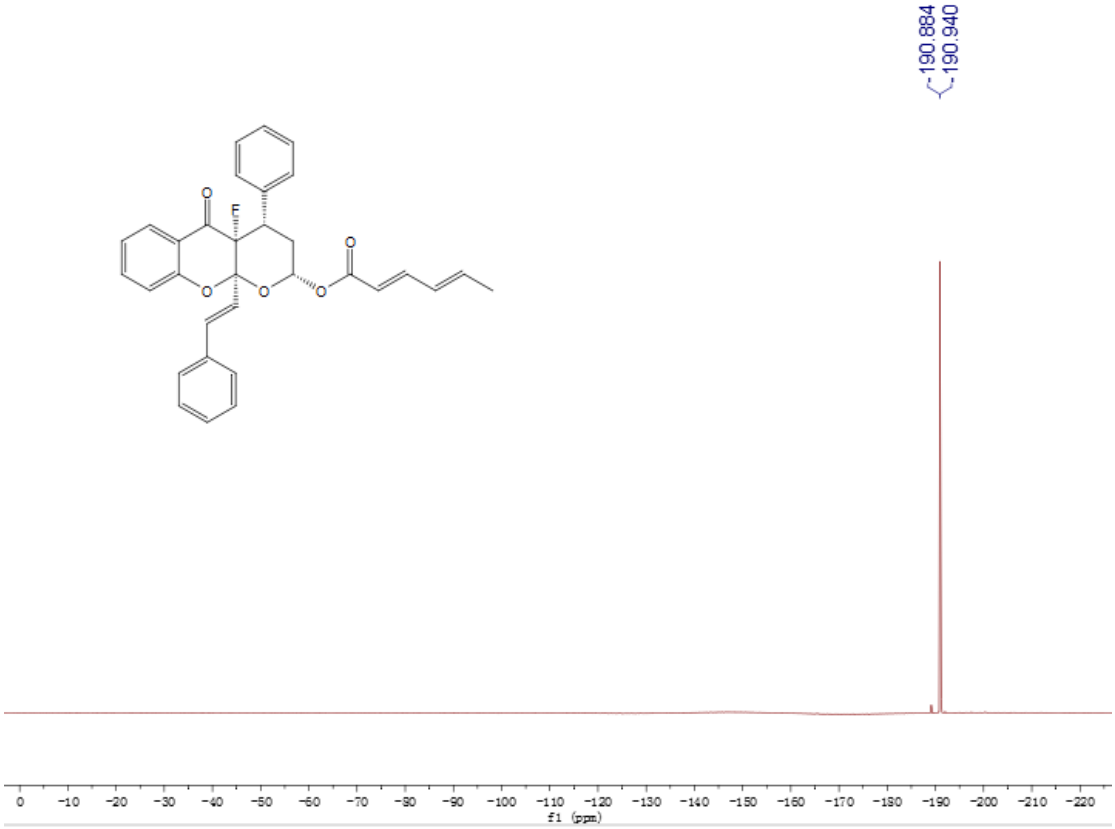
4c-^{1}H NMR (400 MHz, $CDCl_3$)



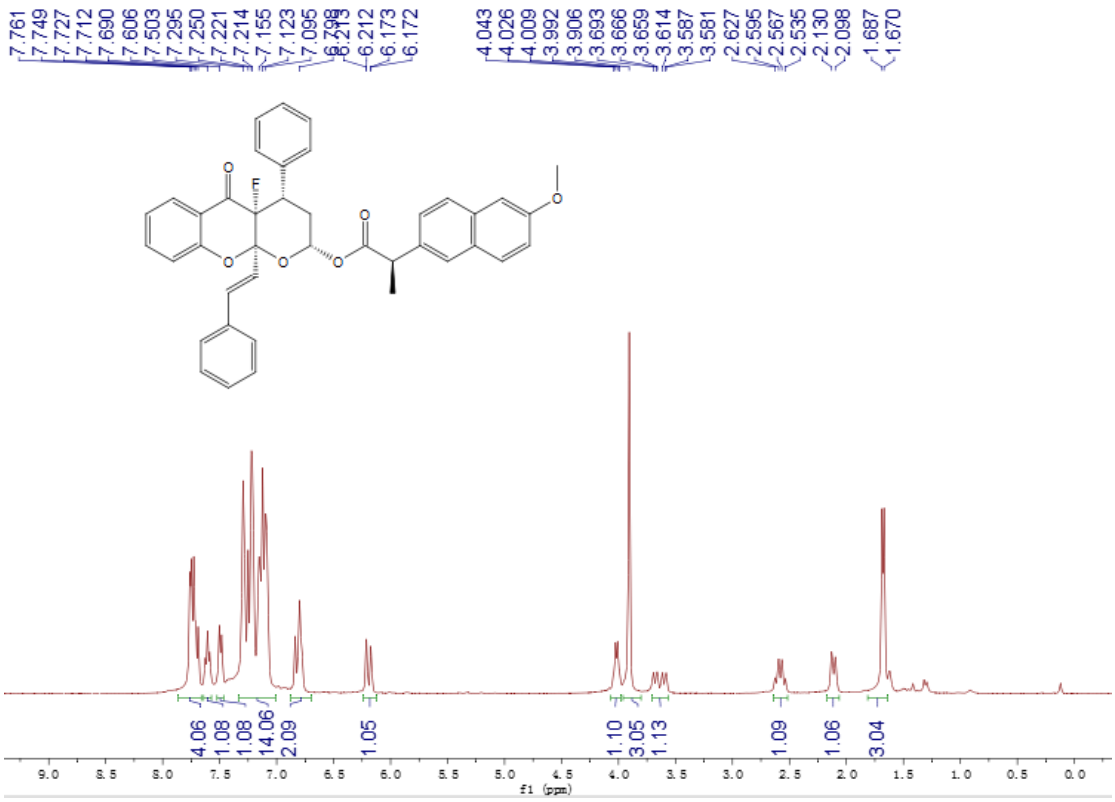
4c-^{13}C NMR (150 MHz, $CDCl_3$)



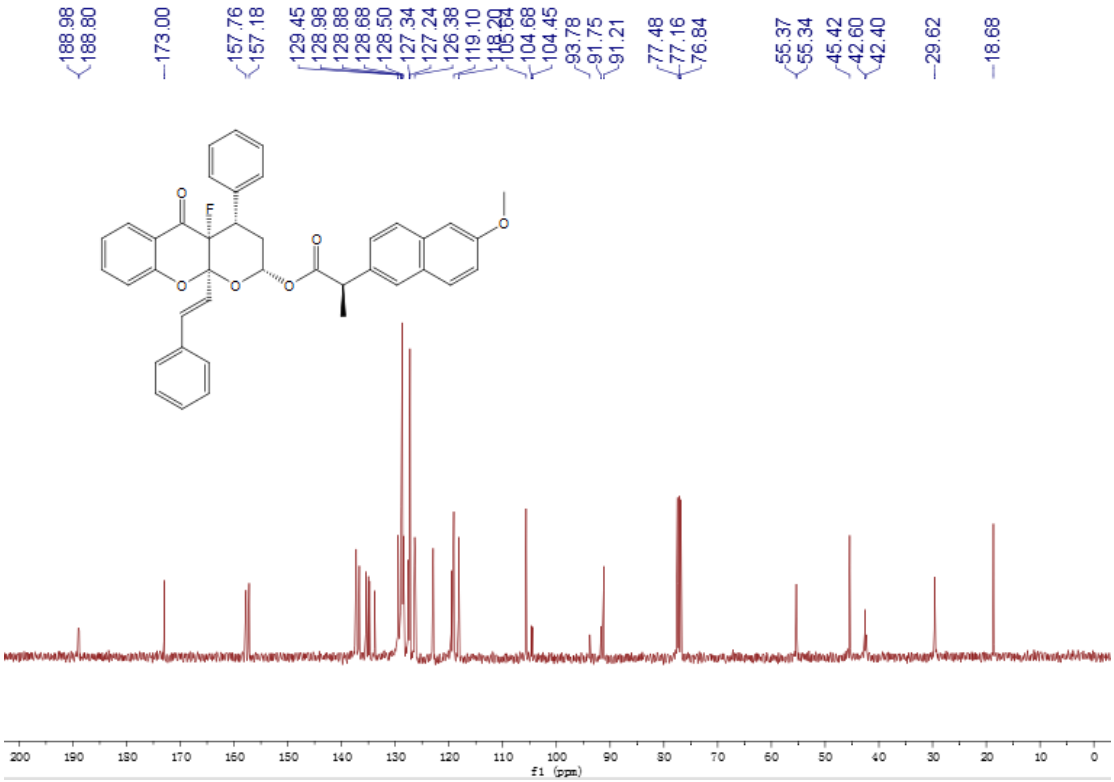
4c-^{19}F NMR (565 MHz, $CDCl_3$)



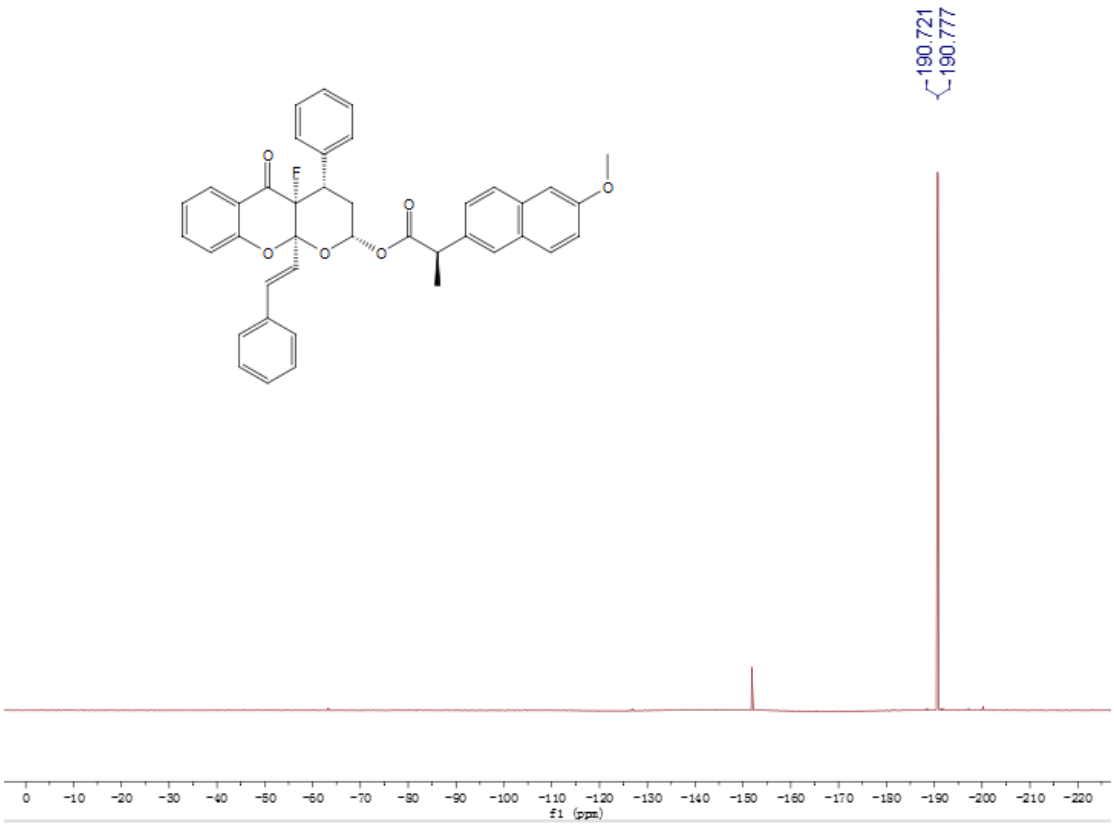
4d-^{1}H NMR (400 MHz, $CDCl_3$)



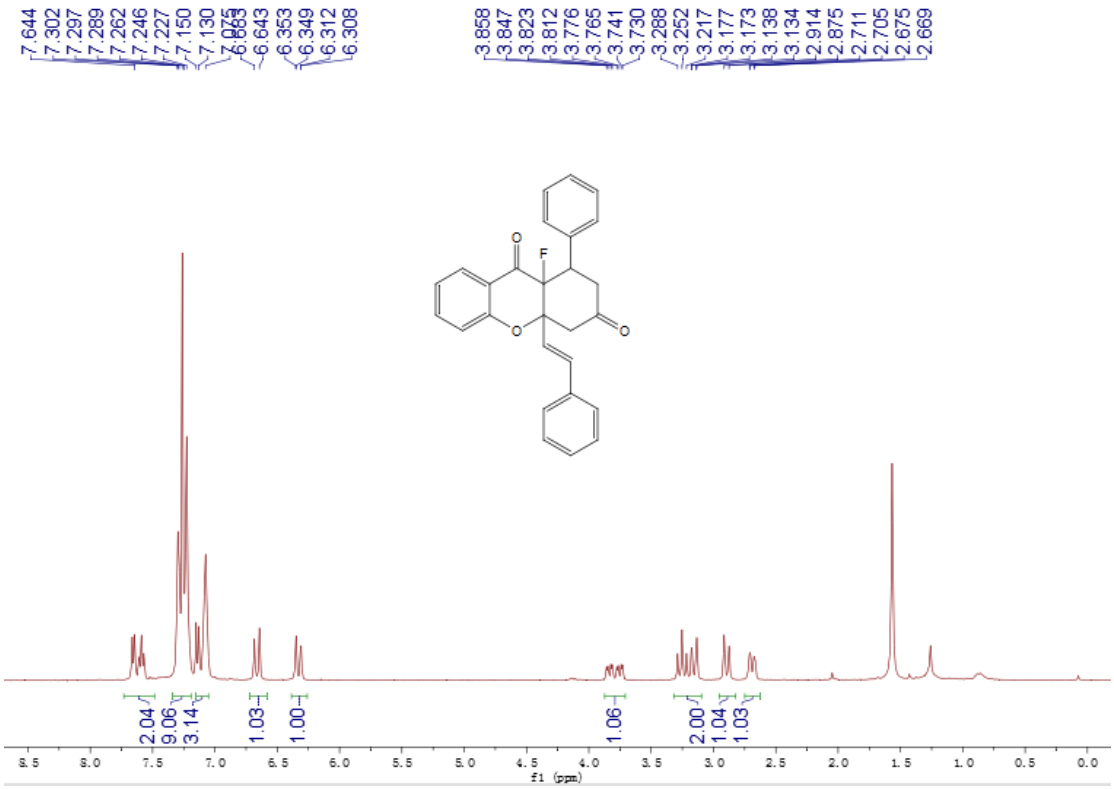
4d-^{13}C NMR (150 MHz, $CDCl_3$)



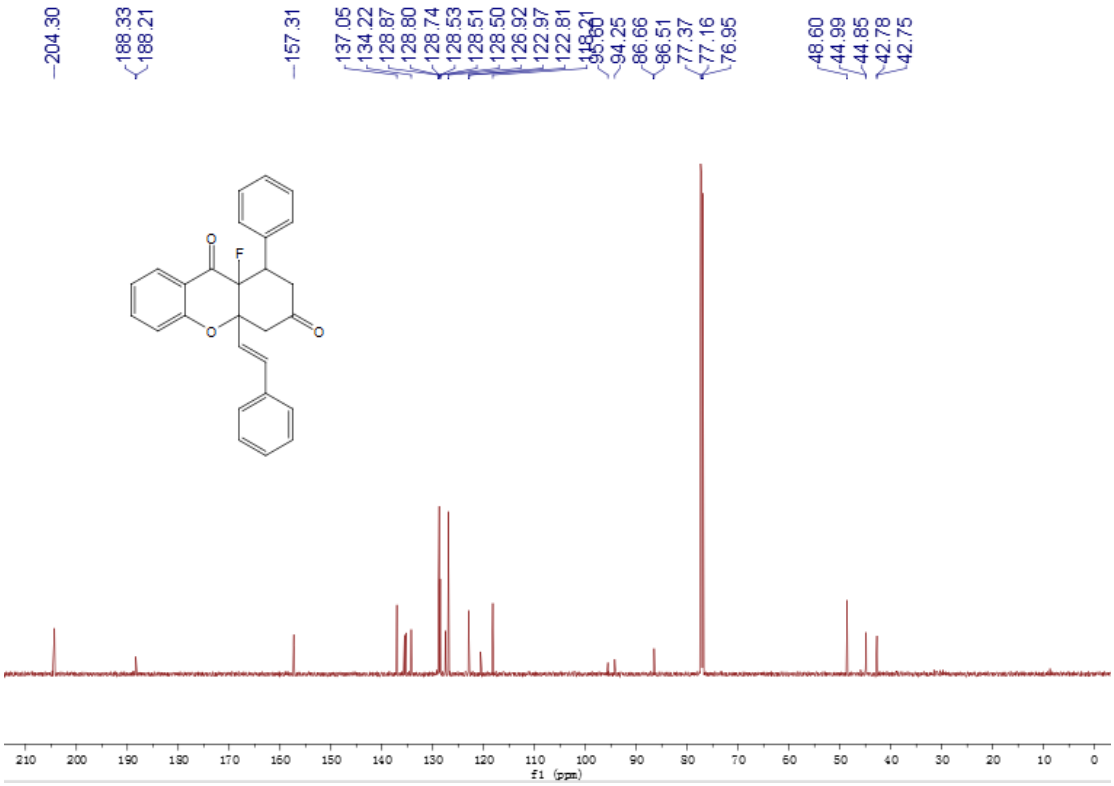
4d-^{19}F NMR (565 MHz, $CDCl_3$)



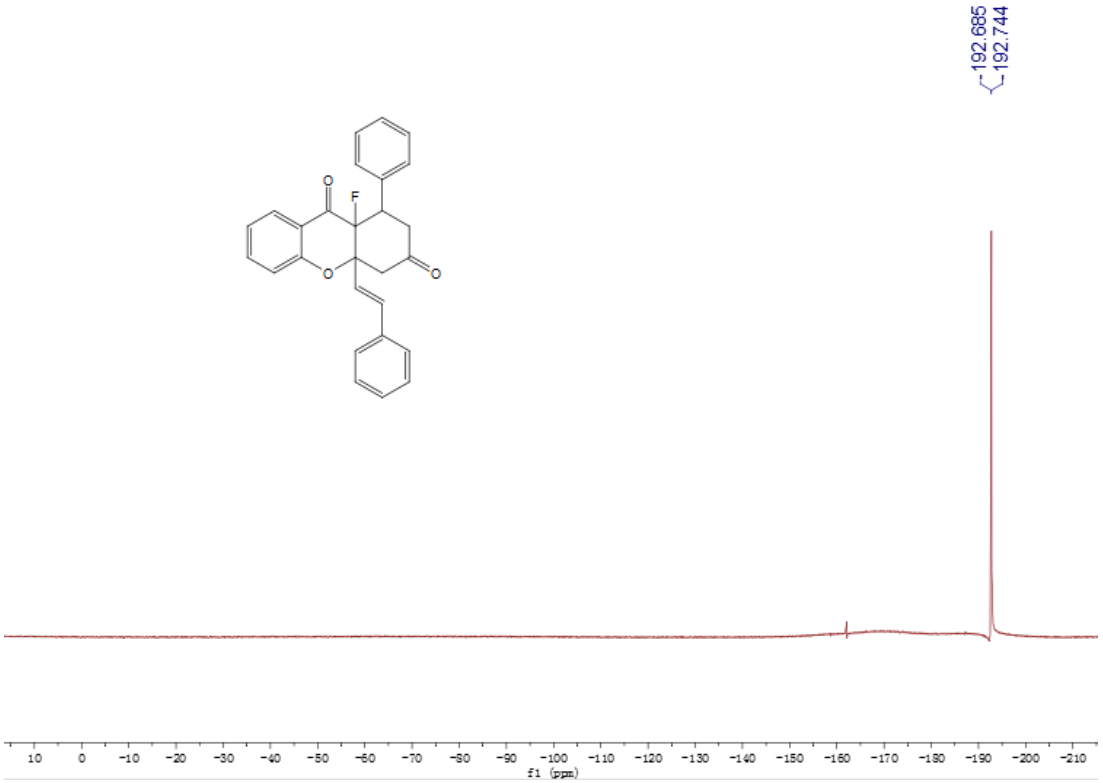
6a-^{1}H NMR (400 MHz, $CDCl_3$)



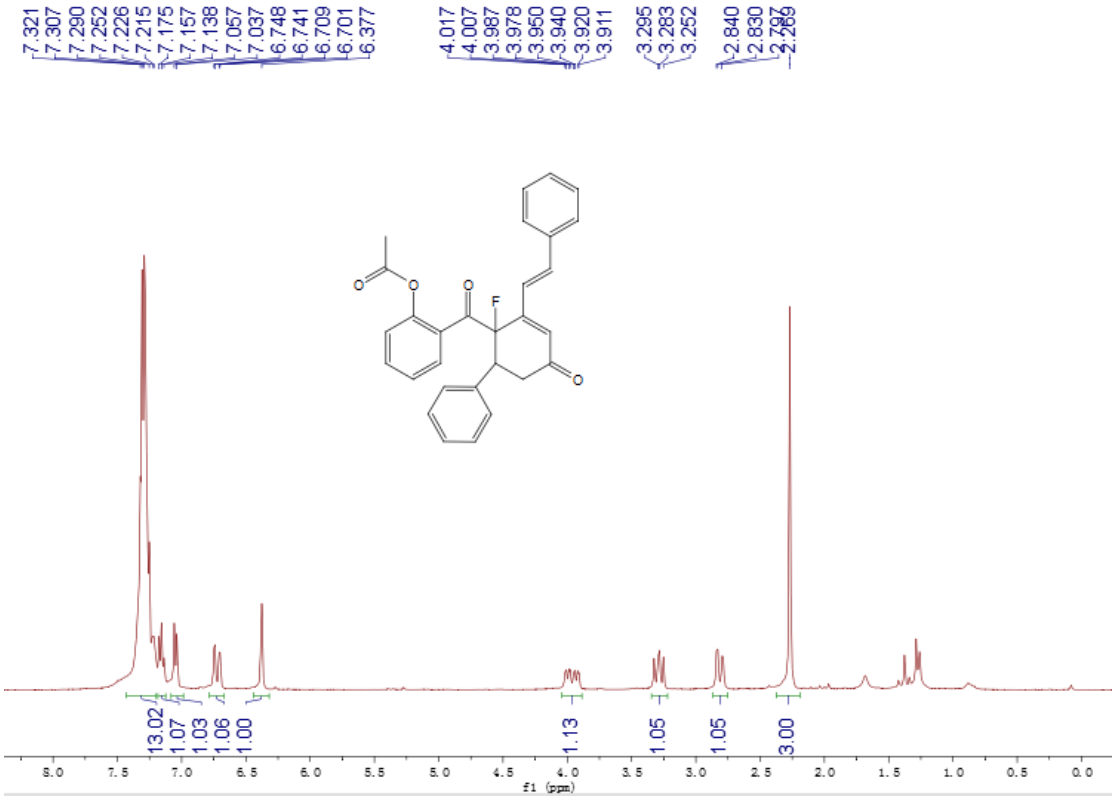
6a-^{13}C NMR (150 MHz, $CDCl_3$)



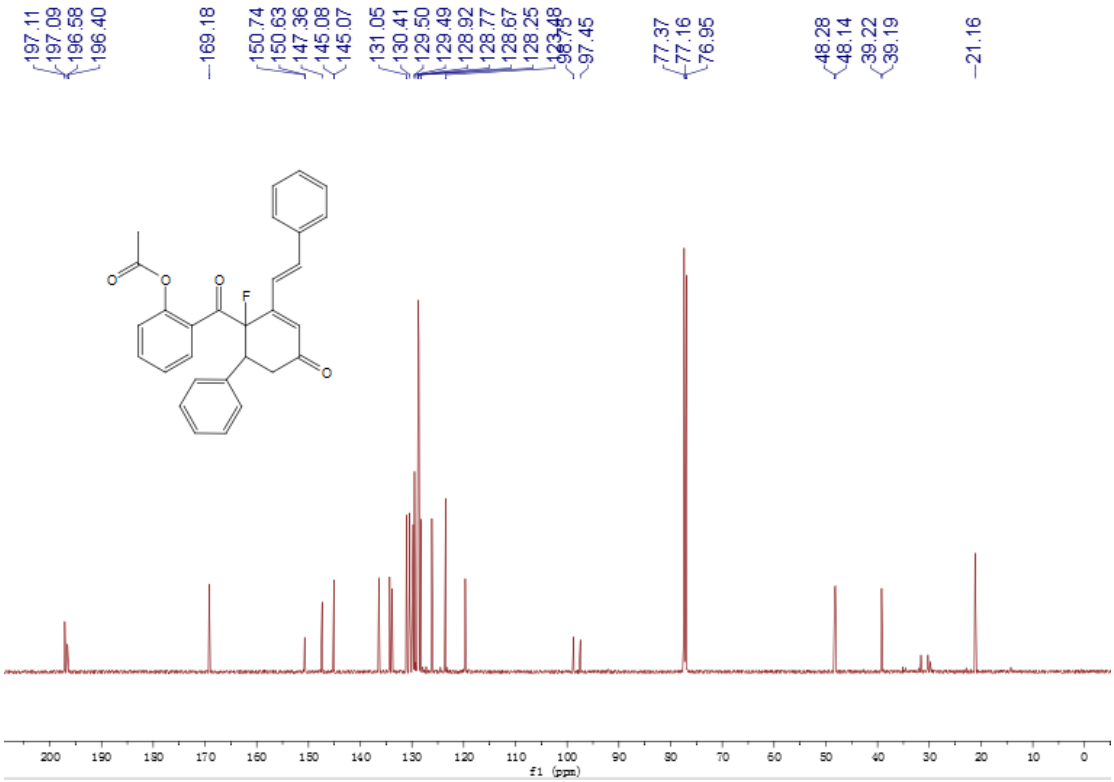
6a-^{19}F NMR (565 MHz, $CDCl_3$)



6b-^{1}H NMR (400 MHz, $CDCl_3$)

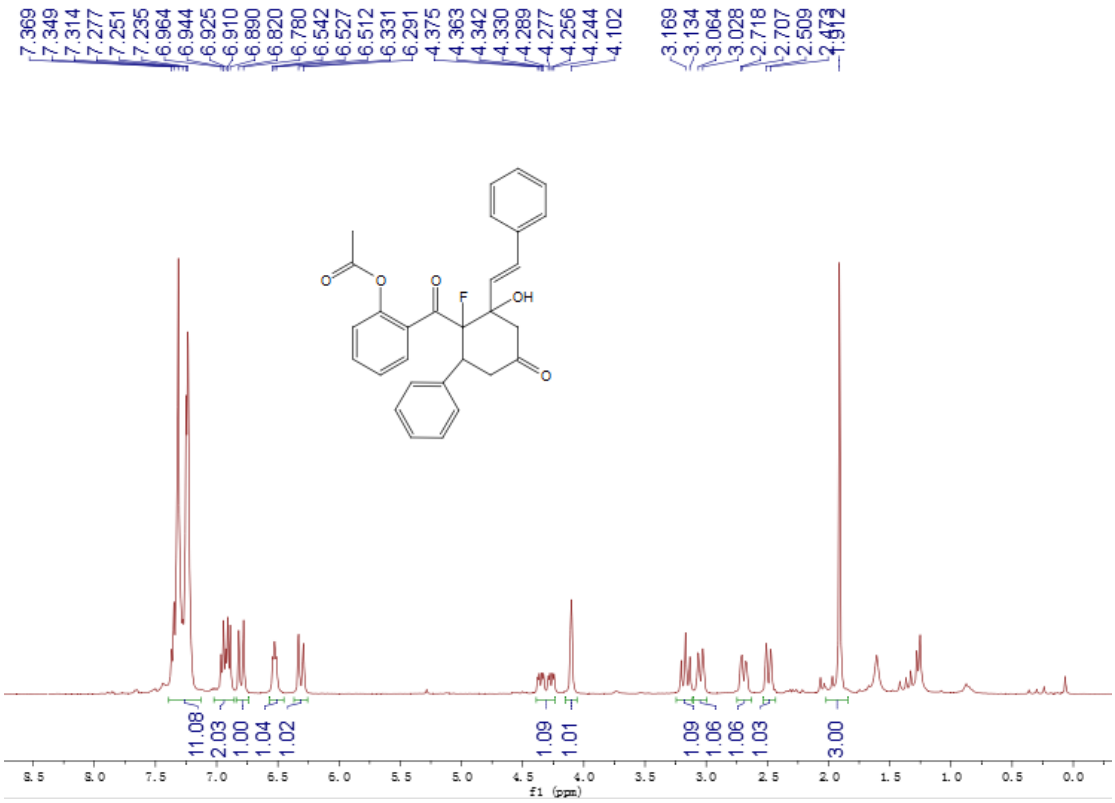


6b-^{13}C NMR (150 MHz, $CDCl_3$)

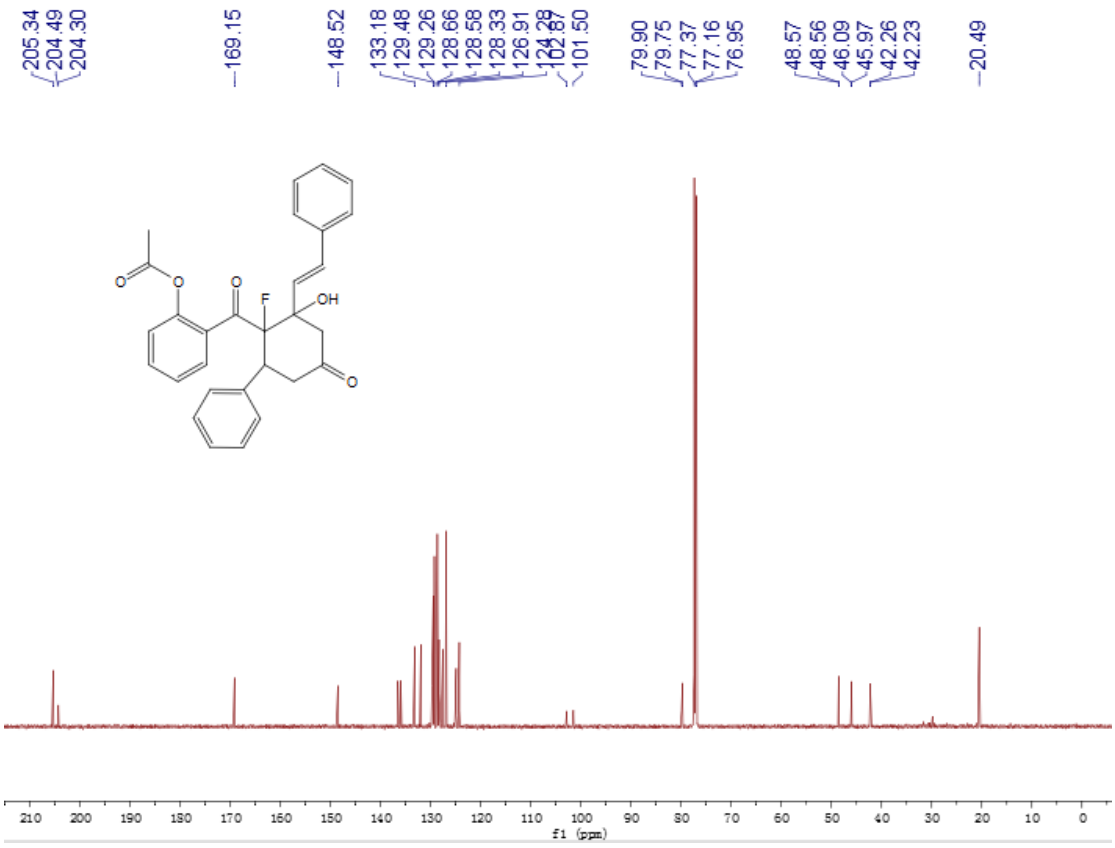


6b-^{19}F NMR (565 MHz, $CDCl_3$)

6c-^{1}H NMR (400 MHz, $CDCl_3$)



6c-^{13}C NMR (150 MHz, $CDCl_3$)



6c-^{19}F NMR (565 MHz, $CDCl_3$)