Electronic Supplementary Material (ESI) for ChemComm.
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Supplementary information

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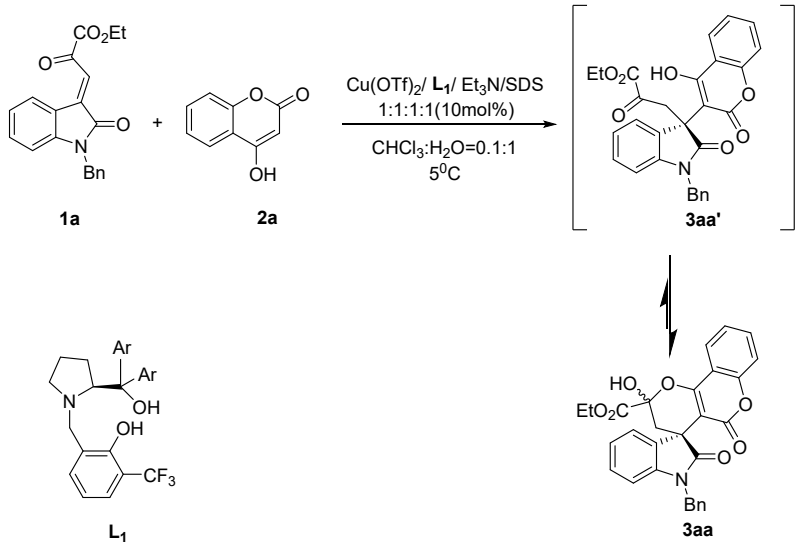
Part I Experiment Section

1.1 General Information

^{1}H NMR and ^{13}C NMR were recorded on Bruker-400 MHz Spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz, ^{19}F NMR: 376 MHz) and Bruker-500 MHz Spectr-ometer (^{1}H NMR: 500 MHz, ^{13}C NMR: 125 MHz, ^{19}F NMR: 470 MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz respectively. UV-Vis Spectrophotometry was carried out on infrared spectrometer. HPLC analysis was carried out on Agilent 1260 series HPLC with a multiple wavelength detector by commercial chiral columns. Chiralpak IC-H, OD-H, AD-H were purchased form Daicel Chemical Industries, LTD. Optical rotations were measured on a PerKinElmer^{TM} Polarimeter (Model 343). HRMS (ESI) were recorded on a Q-TOF Premier. Commercially available compounds were used without further purification. All solvents were purified according to the standard procedures unless otherwise noted. Ligands **L**[1] and isatin-derived β,γ-unsaturated α-ketoesters[2] were prepared according to the literature procedures.

1.2 General working procedure of the Michael/hemiketalization reaction (3aa as an example)

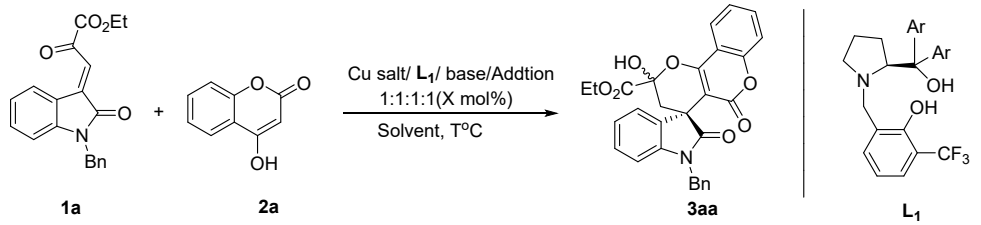


A mixture of Ligand (**L_1**, 4.4 mg, 0.01 mmol), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol), SDS (3.0 mg, 0.01 mmol), Et_3N (1.40 μL, 0.01 mmol) in $CHCl_3/H_2O$ (0.1/1) was stirred for 2h at ambient atmosphere. Then *N*-benzyl isatin-derived β,γ-unsaturated α-ketoester **1a** (33.5 mg, 0.1 mmol) was added and the resulting mixture was cooled to 5 °C. After 10 min, 4-hydroxycoumarin **2a** (20 mg, 0.12 mmol) was added slowly and carried out at 5 °C. After reactions were finished (monitored by TLC), the reaction mixture was extracted with ethyl acetate (3 ×3 mL). The organic phase was dried with Na_2SO_4 and evaporated in vacuum. Purification by flash column chromatograph (petroleum ether:ethyl acetate = 5:1 v/v) afforded **3aa** as a white solid: 93% yield, 46.3 mg, 98% ee.

The Michael addition product was found to exist in rapid equilibrium with a pseudo-diastereomeric hemiketal form in solution. These anomers equilibrate slowly enough that they show up as separate compounds by ^{1}H, ^{19}F and ^{13}C NMR but quickly enough that they do not resolve by chromatography.[3]

1.3 Optimization of reaction conditions

Table S1 Optimization of the reaction conditions



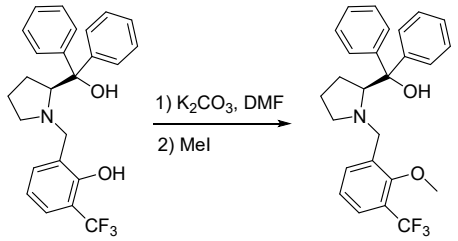
Entry	Solvent	Cu Salt	Addtion	base	T (^{0}C)	X	Yield (%)[b]	ee (%)[c]
1	DCM:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	15	10	86	87
2	DCE :H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	15	10	84	90
3	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	15	10	93	92
4	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	10	10	92	94
5	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	5	10	92	94
6	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	0	10	89	94
7	$CHCl_3$:H_2O =(0.1:1)	$CuBr_2$	SDS	N-ethylmorpholine	5	10	90	95
8	$CHCl_3$:H_2O =(0.1:1)	$Cu(NO_3)_2.5H_2O$	SDS	N-ethylmorpholine	5	10	65	95
9	$CHCl_3$:H_2O =(0.1:1)	$CuSO_4.5H_2O$	SDS	N-ethylmorpholine	5	10	93	90
10	$CHCl_3$:H_2O =(0.1:1)	$Cu(OAc)_2.H_2O$	SDS	N-ethylmorpholine	5	10	85	95
11	$CHCl_3$:H_2O =(0.1:1)	$CuCl_2.2H_2O$	SDS	N-ethylmorpholine	5	10	61	98
12	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	5	10	93	98
13	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	PVP	N-ethylmorpholine	5	10	93	93
14	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	Bu_4NPF_6	N-ethylmorpholine	5	10	92	90
15	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	Bu_4NHSO_4	N-ethylmorpholine	5	10	92	90
16	$CHCl_3$:H_2O =(0.1:1)	$Cu(OTf)_2$	SDS	N-ethylmorpholine	5	5	87	90
17	$CHCl_3$	$Cu(OTf)_2$	SDS	Et_3N	5	10	90	91

[a]Unless otherwise noted, noted, the reaction of **1a** (0.1 mmol) and **2a** (0.12 mmol) was performed in the presence of **L**, base, Addtion and Cu salt in solvent (1.1 mL). [b]Isolated yield. [c]Determined by chiral HPLC analysis.

1.4.1 Procedure of the Michael/hemiketalization reaction on gram scale

A mixture of Ligand (**L_1**, 105.6 mg, 0.24 mmol), $Cu(OTf)_2$ (84 mg, 0.24 mmol), SDS (72 mg, 0.24 mmol), Et_3N (33.4 μL, 0.24 mmol) in $CHCl_3/H_2O$ (2.4/24) was stirred for 5h at ambient atmosphere. Then *N*-benzyl isatin-derived β,γ-unsaturated α-ketoester **1a** (804.3 mg, 2.4 mmol) was added and the resulting mixture was cooled to 5 °C. After 10 min, 4-hydroxycoumarin **2a** (467.0 mg, 2.88 mmol) was added slowly and carried out at 5 °C. After reactions were finished (monitored by TLC), the reaction mixture was extracted with ethyl acetate (3 ×10 mL). The organic phase was dried with Na_2SO_4 and evaporated in vacuum. Purification by flash column chromatograph (petroleum ether:ethyl acetate = 5:1 v/v) afforded **3aa** as a white solid: 90% yield, 1.07g, 94% ee.

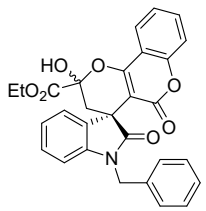
1.4.2 Procedure for the Ligand L_6



A mixture of **L_1** (22 mg, 0.05 mmol) and K_2CO_3 (7.6 mg, 0.055 mmol) in DMF (1.0 mL) was stirred for 4 h at room temperature. MeI (10.6 mg, 0.075 mmol) was added to the mixture and stirred overnight. The mixture was quenched with saturated ammonium chloride solution (1.0 mL), and then extracted with ethyl acetate (3 × 1.0 mL). The organic phase was dried with anhydrous sodium sulfate and evaporated in vacuo. Purification of the residue by column chromatograph (petroleum ether : ethyl acetate =10:1 v/v) to afford **L_6** (21.8 mg, 0.0494 mmol) in 99% yield.

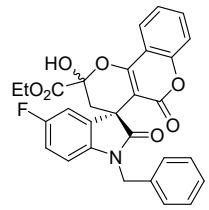
1.5 Experimental date of products

(3*R*)-ethyl 1-benzyl-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3aa)



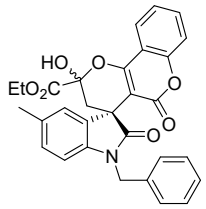
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.3 mg, 93% yield); m.p. 168 - 170 ℃; $[\alpha]_D^{20}$ = -22.3 (*c* = 1.02, $CHCl_3$, 98% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 9.13 min (minor), t_R = 17.0 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.00 (dd, *J* = 7.9, 1.4 Hz, 0.8H), 7.85 – 7.79 (m, 0.2H), 7.67 – 7.56 (m, 1H), 7.54 – 7.42 (m, 2H), 7.41 – 7.33 (m, 3H), 7.31 – 7.28 (m, 2H), 7.24 – 7.13 (m, 1H), 7.11 – 6.92 (m, 2H), 6.79 (d, *J* = 7.9 Hz, 0.8H), 6.71 (d, *J* = 7.8 Hz, 0.2H), 5.18 – 5.07 (m, 1H), 5.03 – 4.92 (m, 1H), 4.51 – 4.35 (m, 2H), 3.18 (d, *J* = 14.0 Hz, 0.2H), 2.89 (d, *J* = 15.0 Hz, 0.8H), 2.66 (d, *J* = 15.0 Hz, 0.8H), 2.30 (d, *J* = 14.0 Hz, 0.2H), 1.41 (dt, *J* = 17.5, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.8, 178.1, 168.5, 166.9, 160.6, 160.0, 159.6, 159.2, 153.0, 152.8, 143.3, 143.2, 135.7, 134.7, 133.0, 132.5, 131.0, 130.4, 129.1, 129.0, 128.8, 128.3, 127.9, 127.5, 127.2, 127.2, 125.8, 124.3, 124.1, 124.1, 123.8, 123.0, 122.3, 122.1, 116.7, 116.6, 115.2, 115.1, 110.4, 109.5, 102.5, 101.4, 97.1, 95.2, 64.1, 62.9, 46.6, 45.5, 44.8, 44.6, 37.5, 36.9, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{29}H_{23}NO_7$ $[M+H]^+$ 498.1547, found 498.1552.

(3*R*)-ethyl 1-benzyl-5-fluoro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indolin-e-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ba)



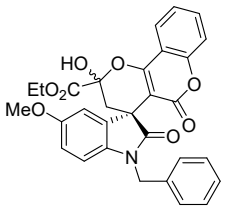
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (47.9 mg, 93% yield); m.p. 200 - 202 ℃; $[\alpha]_D^{20}$ = -41.0 (*c* = 0.53, $CHCl_3$, 94% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 0.8 mL/min, T = 10 ℃, UV = 254 nm, t_R = 12.8 min (minor), t_R = 29.2 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.17 (s, 0.4H), 7.99 (d, *J* = 7.9 Hz, 0.4H), 7.81 (d, *J* = 7.9 Hz, 0.6H), 7.63 – 7.52 (m, 1.7H), 7.49 – 7.27 (m, 7H), 7.04 – 6.97 (m, 0.4H), 6.81 – 6.56 (m, 1H), 6.55 – 6.38 (m, 1H), 5.19 (s, 0.6H), 5.15 – 5.02 (m, 1H), 5.02 – 4.86 (m, 1H), 4.54 – 4.33 (m, 2H), 3.15 (d, *J* = 14.0 Hz, 0.6H), 2.86 (d, *J* = 15.0 Hz, 0.4H), 2.65 (d, *J* = 15.0 Hz, 0.4H), 2.27 (d, *J* = 14.0 Hz, 0.6H), 1.41 (dt, *J* = 14.5, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.2, 178.5, 168.4, 166.8, 163.2 ($^1J_{CF}$ = 246.4 Hz), 163.0 ($^1J_{CF}$ = 245.2 Hz), 160.7, 160.0, 159.6, 159.2, 153.0, 152.7, 144.8 ($^3J_{CF}$ = 11.9 Hz), 144.7 ($^3J_{CF}$ = 11.6 Hz), 135.2, 134.1, 133.1, 132.7, 129.1, 128.9, 128.1, 127.8 ($^3J_{CF}$ = 9.4 Hz), 127.7, 127.2, 127.2, 126.2 ($^4J_{CF}$ = 2.7 Hz), 125.8 ($^4J_{CF}$ = 2.7 Hz), 124.4, 124.2, 123.9, 123.1 ($^3J_{CF}$ = 9.9 Hz), 123.0, 116.7, 116.6, 115.1, 115.0, 110.3 ($^2J_{CF}$ = 22.9 Hz), 108.4 ($^2J_{CF}$ = 21.9 Hz), 102.3, 101.1, 99.4 ($^2J_{CF}$ = 28.3 Hz), 98.1 ($^2J_{CF}$ = 27.7 Hz), 97.0, 95.1, 64.2, 63.0, 46.2, 45.1, 45.0, 44.8, 37.4, 36.9, 14.2, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -110.2, -111.7; HRMS (ESI) m/z calcd for $C_{29}H_{22}FNO_7$ $[M+H]^+$ 516.1453, found 516.1456.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-5-methyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ca)



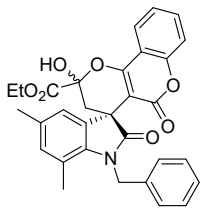
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.0 mg, 90% yield); m.p. 116 - 118 ℃; $[\alpha]_D^{20}$ = -32.8 (*c* = 1.01, $CHCl_3$, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 65:35, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 7.79 min (minor), t_R = 21.5 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.99 (dd, *J* = 8.0, 1.4 Hz, 0.9H), 7.92 – 7.79 (m, 0.1H), 7.58 (ddd, *J* = 8.4, 7.4, 1.6 Hz, 1H), 7.50 – 7.40 (m, 2H), 7.40 – 7.26 (m, 5H), 7.16 – 6.77 (m, 2H), 6.66 (d, *J* = 8.0 Hz, 0.9H), 6.59 (d, *J* = 8.0 Hz, 0.1H), 5.17 – 5.07 (m, 1H), 5.00 – 4.88 (m, 1H), 4.49 – 4.22 (m, 2H), 3.18 (d, *J* = 14.0 Hz, 0.1H), 2.87 (d, *J* = 14.9 Hz, 0.9H), 2.65 (d, *J* = 15.0 Hz, 0.9H), 2.28 (d, *J* = 14.0 Hz, 0.1H), 2.24 (s, 2.5H), 2.22 (s, 0.4H), 1.41 (q, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 178.0, 168.6, 167.0, 160.5, 160.0, 159.6, 1591, 153.0, 152.8, 140.9, 140.8, 135.8, 134.8, 133.9, 132.9, 132.5, 131.7, 130.9, 130.4, 129.4, 128.9, 128.9, 128.8, 127.8, 127.4, 127.2, 127.2, 124.3, 124.1, 123.8, 123.7, 123.0, 122.9, 116.7, 116.6, 115.3, 115.1, 110.1, 109.2, 102.7, 101.5, 97.1, 95.2, 64.1, 62.9, 46.6, 45.5, 44.8, 44.6, 37.6, 37.0, 21.2, 21.2, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_7$ $[M+H]^+$ 512.1704, found 512.1704.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-5-methoxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3da)



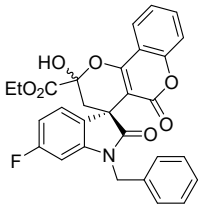
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (45.3 mg, 86% yield); m.p. 186 - 189 ℃; $[\alpha]_D^{20}$ = -49.3 (*c* = 1.06, $CHCl_3$, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 65:35, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 10.8 min (minor), t_R = 27.7 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.00 (dd, *J* = 8.0, 1.5 Hz, 0.8H), 7.82 (dd, *J* = 8.2, 1.3 Hz, 0.2H), 7.65 – 7.52 (m, 1H), 7.44 (dd, *J* = 12.8, 7.5 Hz, 2H), 7.39 – 7.31 (m, 3H), 7.32 – 7.27 (m, 2H), 6.81 – 6.55 (m, 3H), 5.19 – 5.06 (m, 1H), 5.01 – 4.88 (m, 1H), 4.62 – 4.28 (m, 2H), 3.69 (s, 2.6H), 3.67 (s, 0.4H), 3.18 (d, *J* = 14.0 Hz, 0.1H), 2.86 (d, *J* = 14.9 Hz, 0.9H), 2.66 (d, *J* = 14.9 Hz, 0.9H), 2.30 (d, *J* = 14.0 Hz, 0.1H), 1.41 (dt, *J* = 18.7, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.3, 177.7, 168.5, 167.0, 160.6, 160.0, 159.6, 159.1, 157.1, 155.6, 153.0, 152.8, 136.8, 136.4, 135.8, 134.7, 133.0, 132.5, 132.3, 131.8, 129.0, 128.8, 127.8, 127.5, 127.2, 125.9, 124.3, 124.1, 123.8, 123.0, 116.7, 116.6, 115.2, 115.1, 114.2, 113.2, 112.9, 110.8, 109.7, 109.5, 102.6, 101.3, 97.1, 95.2, 64.1, 62.9, 55.7, 55.6, 46.9, 45.9, 44.9, 44.7, 37.6, 36.9, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_8$ $[M+H]^+$528.1653, found 528.1650.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-5,7-dimethyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ea)



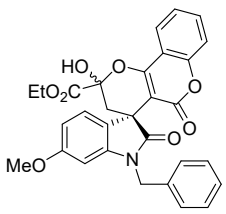
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether= 1:5 v/v) to give the product as white solid (44.1 mg, 84% yield); m.p. 121 - 127 ℃; $[\alpha]_D^{20}$ = -24.6 (*c* = 1.00, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 65:35, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 6.43 min (minor), t_R = 14.2 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.00 (dd, *J* = 7.9, 1.5 Hz, 0.9H), 7.83 (dd, *J* = 8.2, 1.5 Hz, 0.1H), 7.63 – 7.53 (m, 1H), 7.45 – 7.24 (m, 7H), 6.95 – 6.65 (m, 2H), 5.58 – 5.29 (m, 1H), 5.27 – 5.08 (m, 1H), 4.68 – 4.18 (m, 2H), 3.17 (d, *J* = 14.0 Hz, 0.1H), 2.87 (d, *J* = 14.9 Hz, 0.9H), 2.67 (d, *J* = 14.9 Hz, 0.9H), 2.39 (d, *J* = 11.2 Hz, 0.1H), 2.25 (s, 3H), 2.22 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 167.0, 160.5, 159.7, 153.0, 138.8, 136.7, 133.8, 133.6, 132.9, 131.9, 129.0, 127.4, 125.8, 124.2, 123.8, 120.8, 120.6, 116.6, 115.3, 101.7, 97.1, 62.8, 46.1, 46.1, 38.1, 20.8, 18.4, 14.2; HRMS (ESI) m/z calcd for $C_{31}H_{27}NO_7$ $[M+H]^+$526.1860, found 526.1864.

(3*R*)-ethyl 1-benzyl-6-fluoro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3fa)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.9 mg, 91% yield); m.p. 199 - 201 ℃; $[\alpha]_D^{20}$ = -3.9 (*c* = 1.00, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 65:35, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 7.24 min (minor), t_R = 11.7 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.99 (dd, *J* = 7.9, 1.4 Hz, 0.7H), 7.81 (dd, *J* = 7.9, 1.2 Hz, 0.3H), 7.64 – 7.56 (m, 1H), 7.53 – 7.27 (m, 7H), 7.01 (dd, *J* = 8.2, 5.1 Hz, 1H), 6.79 – 6.59 (m, 1H), 6.57 – 6.40 (m, 1H), 5.16 – 5.04 (m, 1H), 5.04 – 4.88 (m, 1H), 4.60 – 4.17 (m, 2H), 3.15 (d, J = 14.0 Hz, 0.3H), 2.86 (d, *J* = 15.0 Hz, 0.7H), 2.65 (d, *J* = 15.0 Hz, 0.7H), 2.27 (d, *J* = 14.0 Hz, 0.3H), 1.41 (dt, *J* = 16.8, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.2, 178.5, 168.4, 166.8, 163.2 ($^1J_{CF}$ = 246.7 Hz), 163.0 ($^1J_{CF}$ = 245.2 Hz), 160.7, 160.0, 159.6, 159.2, 153.0, 152.8, 144.8 ($^3J_{CF}$ = 11.9 Hz), 144.7 ($^3J_{CF}$ = 11.8 Hz), 135.2, 134.2, 133.1, 132.7, 129.1, 128.9, 128.1, 127.7, 127.2, 127.2, 126.2 ($^4J_{CF}$ = 3.1 Hz), 125.8 ($^4J_{CF}$ = 2.8 Hz), 124.4, 124.2, 123.9, 123.2, 123.1, 123.0, 116.7, 116.7, 115.1, 115.0, 110.3 ($^2J_{CF}$ = 22.8 Hz), 108.4 ($^2J_{CF}$ = 22.0 Hz), 102.3, 101.1, 99.4 ($^2J_{CF}$ = 28.1 Hz), 98.1 ($^2J_{CF}$ = 27.6 Hz), 97.0, 95.1, 64.2, 63.0, 46.2, 45.1, 45.0, 44.8, 37.4, 37.0, 14.2, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -110.2, -111.7; HRMS (ESI) m/z calcd for $C_{29}H_{22}FNO_7$ $[M+H]^+$516.1453, found 516.1461.

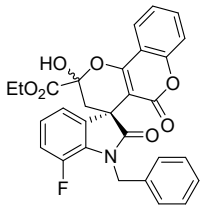
(3*R*)-ethyl 1-benzyl-2'-hydroxy-6-methoxy -2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ga)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (49.0 mg, 85% yield); m.p. 187 - 191 ℃; $[\alpha]_D^{20}$ = -8.3 (*c* = 1.05, $CHCl_3$, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 210

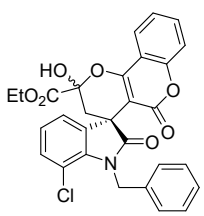
nm, t_R = 9.89 min (minor), t_R = 17.7 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 0.7H), 7.98 (dd, J = 8.0, 1.4 Hz, 0.7H), 7.80 (dd, J = 8.1, 1.5 Hz, 0.3H), 7.62 – 7.50 (m, 1H), 7.49 – 7.40 (m, 2H), 7.40 – 7.27 (m, 5H), 6.96 (d, J = 8.3 Hz, 1H), 6.63 – 6.21 (m, 2H), 5.22 (s, 0.3H), 5.17 – 5.02 (m, 1H), 5.01 – 4.78 (m, 1H), 4.61 – 4.22 (m, 2H), 3.70 (s, 2.2H), 3.68 (s, 0.7H), 3.14 (d, J = 13.9 Hz, 0.3H), 2.86 (d, J = 14.9 Hz, 0.7H), 2.64 (d, J = 15.0 Hz, 0.7H), 2.26 (d, J = 13.9 Hz, 0.3H), 1.49 – 1.35 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.3, 178.6, 168.5, 166.9, 160.6, 160.4, 160.1, 159.9, 159.6, 158.9, 152.9, 152.7, 144.5, 144.4, 135.6, 134.6, 132.8, 132.4, 128.9, 128.7, 127.8, 127.5, 127.2, 127.2, 124.2, 124.0, 123.8, 122.9, 122.6, 122.5, 122.4, 116.6, 116.5, 115.2, 115.0, 107.6, 105.9, 102.7, 101.6, 98.6, 97.4, 97.0, 95.2, 64.0, 62.8, 55.4, 55.3, 46.0, 45.0, 44.8, 44.6, 37.6, 37.1, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_8$ $[M+H]^+$528.1653, found 528.1661.

(3*R*)-ethyl 1-benzyl-7-fluoro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ha)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (43.8 mg, 85% yield); m.p. 62 - 65 ℃; $[\alpha]_D^{20}$ = -8.9 (c = 0.98, $CHCl_3$, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 5.64 min (minor), t_R = 9.45 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.99 (dd, J = 7.9, 1.5 Hz, 0.8H), 7.82 (dd, J = 8.2, 1.4 Hz, 0.2H), 7.64 – 7.53 (m, 1H), 7.44 (d, J = 7.4 Hz, 2H), 7.41 – 7.26 (m, 5H), 7.01 (dd, J = 8.8, 3.3 Hz, 2H), 6.92 – 6.79 (m, 1H), 5.28 – 5.07 (m, 2H), 4.59 – 4.20 (m, 2H), 3.14 (d, J = 14.1 Hz, 0.2H), 2.84 (d, J = 15.0 Hz, 0.8H), 2.64 (d, J = 15.0 Hz, 0.8H), 2.28 (d, J = 14.1 Hz, 0.2H), 1.50 – 1.39 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 177.8, 168.4, 166.7, 160.6, 159.9, 159.5, 159.2, 153.0, 152.8, 147.6 ($^1J_{CF}$ = 246.2 Hz), 147.5 ($^1J_{CF}$ = 243.7 Hz), 137.1, 135.9, 133.9 ($^4J_{CF}$ = 3.1 Hz), 133.3 ($^4J_{CF}$ = 2.7 Hz), 133.1, 132.6, 131.0 ($^2J_{CF}$ = 26.2 Hz), 130.1 ($^3J_{CF}$ = 8.5 Hz), 129.8 ($^3J_{CF}$ = 9.0 Hz), 128.7, 128.5, 127.8, 127.3, 127.2, 124.9 ($^3J_{CF}$ = 6.4 Hz), 124.3, 124.1, 123.8, 123.0, 122.7 ($^3J_{CF}$ = 6.5 Hz), 122.5 ($^4J_{CF}$ = 2.6 Hz), 117.9 ($^4J_{CF}$ = 3.1 Hz), 117.4 ($^2J_{CF}$ = 19.6 Hz), 116.7, 116.6, 115.0 ($^2J_{CF}$ = 18.4 Hz), 102.2, 101.0, 97.0, 95.0, 64.2, 62.9, 46.8, 46.4 ($^4J_{CF}$ = 4.7 Hz), 46.1 ($^4J_{CF}$ = 4.7 Hz), 45.6, 37.4, 37.0, 30.6, 29.7, 14.1, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ -133.1, -134.4; HRMS (ESI) m/z calcd for $C_{29}H_{22}FNO_7$ $[M+H]^+$516.1453, found 516.1450.

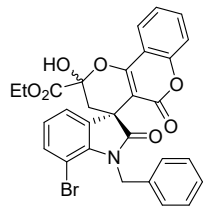
(3*R*)-ethyl 1-benzyl-7-chloro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ia)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (42.6 mg, 80% yield); m.p. 234 - 235 ℃; $[\alpha]_D^{20}$ = -4.2 (c = 1.00, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 8.66 min (minor), t_R = 12.3 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 0.8H), 7.99 (dd, J = 7.9, 1.4 Hz, 0.8H), 7.81 (dd, J = 8.1, 1.5 Hz, 0.2H), 7.72 (dt, J =

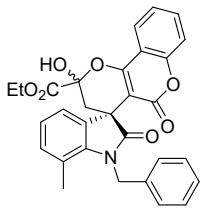
8.7, 4.3 Hz, 0.2H),7.64 – 7.57 (m, 1H), 7.57 – 7.27 (m, 7H), 7.24 – 7.17 (m, 0.8H), 7.17 – 6.78 (m, 2H), 5.60 – 5.33 (m, 2H), 4.54 – 4.34 (m, 2H), 3.91 (s, 0.4H), 3.14 (d, *J* = 14.1 Hz, 0.2H), 2.84 (d, *J* = 14.9 Hz, 0.8H), 2.67 (d, *J* = 15.0 Hz, 0.8H), 2.30 (d, *J* = 14.0 Hz, 0.2H), 1.40 (dt, *J* = 18.6, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.5, 178.7, 168.2, 166.7, 160.7, 159.9, 159.5, 159.3, 153.0, 152.7, 139.4, 139.3, 137.8, 136.5, 134.0, 133.3, 133.1, 132.7, 132.6, 131.7, 131.1, 128.7, 128.5, 127.3, 126.9, 126.3, 126.3, 125.2, 124.9, 124.3, 124.1, 123.8, 123.0, 120.7, 116.7, 116.6, 116.4, 115.0, 114.9, 102.1, 101.0, 97.0, 95.1, 64.2, 62.9, 52.6, 46.2, 46.1, 45.8, 45.2, 37.6, 37.3, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{29}H_{22}ClNO_7$ $[M+H]^+$532.1158, found 532.1165.

(3*R*)-ethyl 1-benzyl-7-bromo-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ja)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (34.6 mg, 60% yield); m.p. 86 - 91 ℃; $[\alpha]_D^{20}$ = +13.4 (*c* = 0.33, $CHCl_3$, 91% ee); HPLC: Daicel Chiralpak IC-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 210 nm, t_R = 13.7 min (minor), t_R = 23.3 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (s, 0.6H), 7.98 (dd, *J* = 7.9, 1.2 Hz, 0.6H), 7.81 (dd, *J* = 8.1, 1.4 Hz, 0.4H), 7.77 – 7.43 (m, 2H), 7.42 – 7.29 (m, 7H), 7.04 (d, *J* = 7.1 Hz, 1H), 6.95 (t, *J* = 7.8 Hz, 0.6H), 6.83 (t, *J* = 7.8 Hz, 0.4H), 5.58 – 5.43 (m, 2H), 5.13 (s, 0.4H), 4.50 – 4.35 (m, 2H), 3.15 (d, *J* = 14.0, 0.4H), 2.84 (d, *J* = 14.9 Hz, 0.6H), 2.67 (d, *J* = 15.0 Hz, 0.6H), 2.30 (d, *J* = 14.0 Hz, 0.4H), 1.41 (dt, *J* = 17.3, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.4, 179.5, 168.3, 166.6, 161.0,159.9,159.6, 159.6, 153.0, 152.8, 141.6, 141.5, 135.4, 134.1, 133.3, 132.8, 130.3, 128.5, 128.3, 127.4, 127.3, 127.1, 126.7, 125.9, 125.8, 125.7, 125.7, 124.4, 124.2, 123.9, 123.8, 123.0, 122.0, 121.7, 116.8, 116.7, 115.0,114.9, 114.1, 113.8, 102.0, 100.7, 96.9, 95.1, 64.3, 63.0, 47.0, 47.0, 45.1, 44.0, 37.5, 37.4, 14.1, 14.1; HRMS (ESI) m/z calcd for $C_{29}H_{22}BrNO_7$ $[M+H]^+$576.0652, found 576.0665.

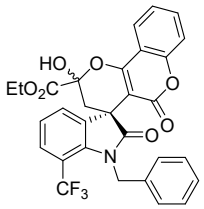
(3*R*)-ethyl 1-benzyl-2'-hydroxy-7-methyl -2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ka)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.5 mg, 91% yield); m.p. 110 - 113 ℃; $[\alpha]_D^{20}$ = -15.9 (*c* = 1.03, $CHCl_3$, 91% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 65:35, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 7.49 min (minor), t_R = 15.4 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.99 (dd, *J* = 7.9, 1.4 Hz, 0.8H), 7.82 (dd, *J* = 8.2, 1.5 Hz, 0.3H), 7.64 – 7.54 (m, 1H), 7.53 – 7.27 (m, 7H), 7.12 – 6.80 (m, 3H), 5.45 – 5.32 (m, 1H), 5.27 – 5.16 (m, 1H), 4.49 – 4.34 (m, 2H), 3.17 (d, *J* = 14.0 Hz, 0.2H), 2.87 (d, *J* = 14.9 Hz, 0.8H), 2.68 (d, *J* = 15.0 Hz, 0.8H), 2.41 (d, *J* = 14.1 Hz, 0.2H), 2.30 (s, 2.5H), 2.28 (s, 0.5H), 1.40 (dt, *J* = 21.0, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.7, 179.1, 168.5, 166.9, 160.5, 159.9, 159.6, 159.1, 152.9, 152.7, 141.3,141.3, 137.9, 136.6, 133.1,

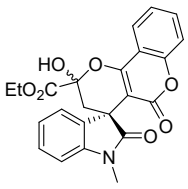
132.9, 132.6, 132.4, 131.8, 131.3, 129.0, 128.8, 127.4, 127.0, 125.8, 125.7, 124.4, 124.2, 124.1, 124.0, 123.8, 123.0, 122.2, 120.9, 120.0, 119.6, 116.6, 116.5, 115.2, 115.1, 102.7, 101.6, 97.1, 95.2, 64.0, 62.8, 46.1, 46.0, 45.9, 44.9, 38.0, 37.5, 18.9, 18.5, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_7$ $[M+H]^+$512.1704, found 512.1707.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-7-trifluoromethyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3la)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (41.8 mg, 74% yield); m.p. 84 - 86 ℃; $[\alpha]_D^{20}$ = -20.6 (*c* = 0.99, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 18.5 min (minor), t_R = 22.5 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 0.5H), 7.99 (dd, *J* = 8.0, 1.5 Hz, 0.5H), 7.89 (d, *J* = 6.7 Hz, 0.5H), 7.85 – 7.70 (m, 0.6H), 7.68 – 7.52 (m, 2H), 7.42 – 7.28 (m, 6.4H), 7.25 – 7.14 (m, 1.4H), 7.14 – 6.95 (m, 0.6H), 5.41 – 5.22 (m, 2H), 5.18 (s, 0.4H), 4.60 – 4.36 (m, 2H), 3.14 (d, *J* = 14.0 Hz, 0.5H), 2.87 (d, *J* = 14.9 Hz, 0.5H), 2.68 (d, *J* = 15.0 Hz, 0.5H), 2.31 (d, *J* = 14.0 Hz, 0.5H), 1.41 (dt, *J* = 16.6, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.3, 180.7, 168.3, 166.7, 161.0, 160.7, 159.9, 159.5, 152.9, 152.7, 140.8, 140.7, 137.7, 136.4, 135.1, 134.3, 133.1, 132.7, 128.7, 128.5, 127.2, 127.1, 126.2, 125.3, 124.8 ($^1J_{CF}$ = 261.9 Hz), 124.4, 124.3, 123.8, 121.2, 116.7, 116.6, 115.0, 114.9, 114.9 ($^3J_{CF}$ = 7.2 Hz), 103.3, 102.3, 100.9, 100.7, 96.9, 96.9, 95.0, 95.0, 64.2, 62.9, 46.1, 45.8, 45.5, 45.1, 37.6, 37.4 ($^2J_{CF}$ = 21.4 Hz), 37.3, 14.1, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ -54.2, -54.6; HRMS (ESI) m/z calcd for $C_{30}H_{22}F_3NO_7$ $[M+H]^+$566.1421, found 566.1423.

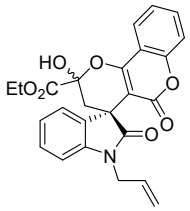
(3*R*)-ethyl 2'-hydroxy-1-methyl -2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ma)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (39.2 mg, 93% yield); m.p. 189 - 191 ℃; $[\alpha]_D^{20}$ = -20.3 (*c* = 0.98, $CHCl_3$, 94% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 9.39 min (minor), t_R = 13.7 min (major);^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.98 (dd, *J* = 8.0, 1.4 Hz, 0.8H), 7.79 (dt, *J* = 7.5, 3.8 Hz, 0.2H), 7.63 – 7.52 (m, 1H), 7.52 – 7.26 (m, 3H), 7.25 – 6.98 (m, 2H), 6.98 – 6.87 (m, 1H), 4.51 – 4.31 (m, 2H), 3.36 (s, 2.5H), 3.34 (s, 0.5H), 3.11 (d, *J* = 14.1 Hz, 0.2H), 2.84 (d, *J* = 14.9 Hz, 0.8H), 2.62 (d, *J* = 14.9 Hz, 0.8H), 2.23 (d, *J* = 14.1 Hz, 0.2H), 1.39 (dt, *J* = 19.6, 7.1 Hz, 3H); ^{1}H NMR (500 MHz, Acetone) δ 9.26 (s, 0.2H), 7.97 (d, J = 7.6 Hz, 0.5H), 7.87 (d, J = 7.7 Hz, 0.5H), 7.71 – 7.60 (m, 1.7H), 7.47 – 7.33 (m, 1.6H), 7.33 – 7.21 (m, 2H), 7.18 – 7.04 (m, 1H), 7.01 (d, J = 7.7 Hz, 0.5H), 6.95 (t, J = 7.4 Hz, 0.5H), 4.44 – 4.26 (m, 2H), 3.84 (s, 0.3H), 3.34 (s, 1.5H), 3.26 (s, 1.5H), 2.87 (t, J = 13.1 Hz, 1H), 2.76 (d, J = 15.0 Hz, 0.5H), 2.36 (d, J = 14.3 Hz, 0.5H), 1.35 – 1.31 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4, 178.1, 168.5, 167.0, 160.5, 159.9, 159.5, 159.0, 152.9, 152.7,

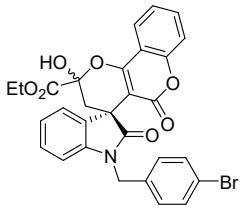
144.3, 144.2, 132.9, 132.5, 130.9, 130.5, 129.2, 129.0, 128.7, 126.6, 124.2, 124.1, 123.8, 123.0, 122.3, 122.1, 116.6, 116.6, 115.3, 115.1, 109.2, 108.3, 102.7, 101.5, 97.1, 95.1, 64.0, 62.8, 46.5, 45.3, 37.1, 36.5, 27.1, 27.0, 14.1, 14.0; ^{13}C NMR (125 MHz, Acetone) δ 209.8, 180.0, 178.1, 168.1, 167.2, 160.7, 159.8, 159.5, 159.4, 153.5, 153.2, 145.3, 145.1, 133.6, 133.2, 132.0, 131.8, 130.3, 129.5, 128.9, 126.9, 124.9, 124.8, 124.1, 123.9, 123.6, 123.0, 122.3, 117.0, 116.9, 115.8, 115.6, 109.8, 108.6, 103.4, 102.3, 97.8, 96.8, 63.1, 62.6, 47.4, 46.1, 38.2, 37.6, 27.0, 26.7, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{23}H_{19}NO_7$ $[M+H]^+$422.1234, found 422.1239.

(3*R*)-ethyl 1-allyl-2'-hydroxy -2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3na)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (39.8 mg, 89% yield); m.p. 203 - 209 ℃; $[\alpha]_D^{20}$ = -10.4 (*c* = 0.48, $CHCl_3$, 94% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 0.9 mL/min, T = 10 ℃, UV = 254 nm, t_R = 6.15 min (minor), t_R = 10.6 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.98 (dd, *J* = 8.0, 1.5 Hz, 0.9H), 7.81 (d, *J* = 7.9 Hz, 0.1H), 7.68-7.51 (m, 1H), 7.49 – 7.26 (m, 3H), 7.23 – 7.00 (m, 2H), 7.00 – 6.87 (m, 1H), 6.06 – 5.71 (m, 1H), 5.59 – 5.35 (m, 1H), 5.32 – 5.13 (m, 1H), 4.63 – 4.48 (m, 1H), 4.46 – 4.38 (m, 2H), 4.38 – 4.31 (m, 1H), 3.13 (d, *J* = 14.1 Hz, 0.2H), 2.86 (d, *J* = 14.9 Hz, 0.8H), 2.63 (d, *J* = 14.9 Hz, 0.8H), 2.25 (d, *J* = 14.0 Hz, 0.2H), 1.47 – 1.35 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4, 177.8, 168.5, 166.9, 160.5, 159.9, 159.5, 159.0, 152.9, 152.7, 143.4, 143.3, 132.9, 132.5, 131.4, 130.9, 130.5, 130.2, 129.1, 129.0, 127.2, 126.6, 124.2, 124.0, 123.8, 123.0, 122.2, 122.1, 118.3, 117.6, 116.6, 116.6, 115.2, 115.0, 110.1, 109.2, 102.7, 101.4, 97.0, 95.2, 64.0, 62.8, 46.5, 45.4, 43.2, 43.1, 37.3, 36.7, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{25}H_{21}NO_7$ $[M+H]^+$ 448.1391, found 448.1403.

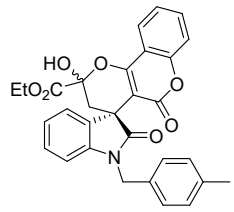
(3*R*)-ethyl 1-(4-bromobenzyl)-2'-hydroxy -2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3oa)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (53.6 mg, 93% yield); m.p. 100 - 103 ℃; $[\alpha]_D^{20}$ = -80.2 (*c* = 1.01, $CHCl_3$, 94% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 9.63 min (minor), t_R = 18.0 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.00 (dd, *J* = 8.0, 1.4 Hz, 0.8H), 7.82 (dd, *J* = 7.9, 1.3 Hz, 0.2H), 7.61 – 7.55 (m, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.38 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 7.13 – 6.87 (m, 2H), 6.80 – 6.59 (m, 1H), 5.16 (dd, *J* = 15.9, 11.0 Hz, 1H), 4.83 (dd, *J* = 15.9, 12.2 Hz, 1H), 4.51 – 4.27 (m, 2H), 3.15 (d, *J* = 14.0 Hz, 0.2H), 2.88 (d, *J* = 15.0 Hz, 0.8H), 2.65 (d, *J* = 15.0 Hz, 0.8H), 2.28 (d, *J* = 14.0 Hz, 0.2H), 1.41 (dt, *J* = 16.6, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.8, 178.1, 168.4, 166.9, 160.7, 160.0, 159.7, 159.2, 153.0, 152.7, 142.9, 142.9, 133.6, 133.0, 132.6, 132.1, 131.9, 130.9, 129.2, 129.1, 129.0, 128.6, 128.5, 128.3, 127.0, 126.8, 126.0,

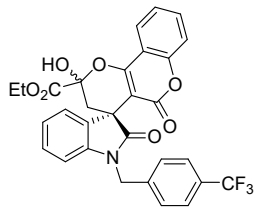
125.8, 124.3, 124.1, 123.9, 122.5, 122.2, 121.9, 116.7, 116.6, 115.2, 115.0, 110.2, 109.3, 102.4, 101.3, 97.0, 95.2, 64.1, 62.9, 46.6, 45.5, 44.2, 44.0, 37.5, 36.9, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{29}H_{22}BrNO_7$ $[M+H]^+$ 576.0652, found 576.0665.

(3*R*)-ethyl 2'-hydroxy -1-(4-methylbenzyl)-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3pa)



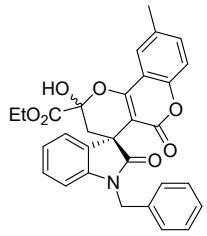
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (47.0 mg, 92% yield); m.p. 229 - 231 ℃; $[\alpha]_D^{20}$ = -5.2 (*c* = 1.00, $CHCl_3$, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 8.51 min (minor), t_R = 17.0 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.00 (dd, *J* = 8.0, 1.5 Hz, 0.8H), 7.82 (dd, *J* = 7.9, 1.3 Hz, 0.2H), 7.61 – 7.50 (m, 1H), 7.37 – 7.27 (m, 4H), 7.24 – 7.14 (m, 3H), 7.11 – 6.91 (m, 2H), 6.85 – 6.65 (m, 1H), 5.18 – 5.02 (m, 1H), 5.01 – 4.88 (m, 1H), 4.58 – 4.31 (m, 2H), 3.17 (d, *J* = 14.0 Hz, 0.2H), 2.88 (d, *J* = 14.9 Hz, 0.8H), 2.65 (d, *J* = 15.0 Hz, 0.8H), 2.33 (s, 3H), 2.28 (d, *J* = 14.0 Hz, 0.2H), 1.41 (dt, *J* = 17.3, 7.1 Hz, 3H); ^{3}C NMR (125 MHz, $CDCl_3$) δ 179.7, 178.0, 168.6, 167.0, 160.6, 159.9, 159.6, 159.1, 153.0, 152.8, 143.4, 143.3, 137.6, 137.1, 132.9, 132.7, 132.5, 131.6, 131.0, 130.5, 129.6, 129.5, 129.1, 128.5, 128.5, 128.3, 127.3, 127.3, 126.0, 125.8, 124.3, 124.1, 123.8, 123.0, 122.2, 122.1, 116.7, 116.6, 115.2, 115.1, 110.4, 109.5, 102.6, 101.4, 97.1, 95.2, 64.1, 62.9, 46.6, 45.6, 44.6, 44.4, 37.5, 21.2, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_7$ $[M+H]^+$ 512.1704, found 512.1704.

(3*R*)-ethyl 2'-hydroxy-1-(4-trifluoromethylbenzyl)-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3qa)



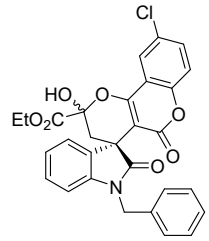
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (52.0 mg, 92% yield); m.p. 118 - 121 ℃; $[\alpha]_D^{20}$ = -39.6 (*c* = 1.03, $CHCl_3$, 95% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 7.65 min (minor), t_R = 15.1 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.00 (dd, *J* = 8.0, 1.5 Hz, 0.8H), 7.83 (dd, *J* = 7.9, 1.4 Hz, 0.2H), 7.70 – 7.54 (m, 5H), 7.39 – 7.28 (m, 2H), 7.25 – 7.13 (m, 1H), 7.12 – 6.92 (m, 2H), 6.85 – 6.61 (m, 1H), 5.42 – 5.15 (m, 1H), 5.03 – 4.78 (m, 1H), 4.56 – 4.20 (m, 2H), 3.16 (d, *J* = 14.0 Hz, 0.2H), 2.90 (d, *J* = 15.0 Hz, 0.8H), 2.68 (d, *J* = 15.0 Hz, 0.8H), 2.30 (d, *J* = 14.0 Hz, 0.2H), 1.41 (dt, *J* = 17.1, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 178.2, 168.4, 166.8, 160.7, 160.1, 159.7, 159.3, 153.0, 152.7, 142.8, 139.8, 138.7, 138.1, 133.1, 132.7, 130.9, 130.4, 130.1 ($^2J_{CF}$ = 32.5 Hz), 129.2, 128.6, 127.5, 127.5, 126.8, 126.0 ($^4J_{CF}$ = 3.6 Hz), 124.4, 124.4, 124.2, 124.0 ($^1J_{CF}$ = 272.1 Hz), 123.9, 123.0, 122.6, 122.3, 116.7, 116.7, 115.2, 115.0, 110.0, 109.2, 102.3, 101.2, 97.0, 95.2, 64.1, 62.9, 46.6, 45.5, 44.3, 44.1, 37.5, 36.9, 14.1, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.5, -62.6; HRMS (ESI) m/z calcd for $C_{30}H_{22}F_3NO_7$ $[M+H]^+$ 566.1421, found 566.1423.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-9'-methyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ab)



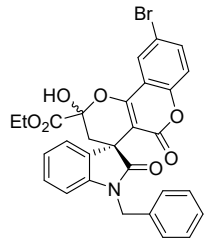
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.0 mg, 90% yield); m.p. 115 - 122 ℃; $[\alpha]_D^{20}$ = -125.5 (*c* = 0.93, $CHCl_3$, 94% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 15.2 min (minor), t_R = 37.7 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.80 – 7.75 (m, 0.8H), 7.67 – 7.61 (m, 0.2H), 7.50 – 7.42 (m, 2H), 7.41 – 7.33 (m, 3H), 7.32 – 7.28 (m, 1H), 7.24 – 7.13 (m, 2H), 7.12 – 7.01 (m, 1.7H), 6.98 – 6.84 (m, 0.3H), 6.81 – 6.75 (m, 0.8H), 6.73 – 6.68 (m, 0.2H), 5.19 – 5.06 (m, 1H), 5.05 – 4.92 (m, 1H), 4.60 – 4.34 (m, 2H), 3.18 (d, *J* = 14.0 Hz, 0.2H), 2.87 (d, *J* = 14.9 Hz, 0.8H), 2.65 (d, *J* = 14.9 Hz, 0.8H), 2.44 (s, 2.4H), 2.43 (s, 0.4H), 2.28 (d, *J* = 14.0 Hz, 0.2H), 1.50 – 1.35 (m, 3H); ^{3}C NMR (125 MHz, $CDCl_3$) δ 179.8, 178.1, 168.7, 167.0, 160.6, 160.1, 159.1, 159.8, 151.1, 150.9, 143.3, 143.2, 135.7, 134.7, 134.1, 134.0, 133.9, 133.6, 131.1, 130.5, 129.1, 129.0, 128.4, 127.9, 127.5, 127.2, 127.2, 126.6, 125.9, 124.1, 123.4, 122.6, 122.1, 116.5, 116.4, 114.9, 114.7, 110.3, 109.4, 102.4, 101.2, 97.0, 95.1, 64.1, 62.9, 53.5, 46.6, 45.5, 44.8, 44.6, 37.5, 37.0, 21.1, 21.0, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_7$ $[M+H]^+$ 512.1704, found 512.1701.

(3*R*)-ethyl 1-benzyl-9'-chloro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ac)



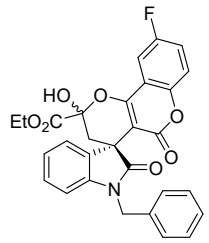
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (47.9 mg, 90% yield); m.p. 255 - 257 ℃; $[\alpha]_D^{20}$ =+62.6 (*c* = 1.02, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 14.3 min (minor), t_R = 25.2 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.96 (d, *J* = 2.5 Hz, 0.8H), 7.78 (d, *J* = 2.5 Hz, 0.2H), 7.59 – 7.50 (m, 1H), 7.47 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 7.25 – 7.13 (m, 2H), 7.10 – 6.91 (m, 2H), 6.85 – 6.68 (m, 1H), 5.18 – 5.06 (m, 1H), 5.04 – 4.92 (m, 1H), 4.56 – 4.31 (m, 2H), 3.17 (d, *J* = 14.0 Hz, 0.2H), 2.88 (d, *J* = 15.0 Hz, 0.8H), 2.66 (d, *J* = 15.0 Hz, 0.8H), 2.30 (d, *J* = 14.0 Hz, 0.2H), 1.46 – 1.35 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 177.8, 168.3, 166.7, 159.6, 159.4, 159.0, 158.1, 151.3, 151.1, 143.3, 143.2, 135.6, 134.6, 132.9, 132.5, 130.7, 130.2, 129.9, 129.7, 129.2, 129.0, 128.8, 128.7, 127.9, 127.5, 127.2, 127.2, 126.6, 124.2, 123.4, 122.6, 122.3, 122.1, 118.2, 118.1, 116.4, 116.2, 110.4, 109.5, 103.5, 102.3, 97.3, 95.4, 64.3, 63.0, 46.6, 45.5, 44.8, 44.6, 37.4, 36.9, 14.1, 14.1; HRMS (ESI) m/z calcd for $C_{29}H_{22}ClNO_7$ $[M+H]^+$ 532.1158, found 532.1161.

(3*R*)-ethyl 1-benzyl-9'-bromo-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ad)



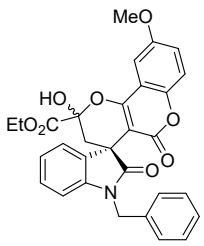
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (51.3 mg, 89% yield); m.p. 243 - 246 ℃; $[\alpha]_D^{20}$ = +3.9 (*c* = 1.03, $CHCl_3$, 95% ee); HPLC: Daicel Chiralpak OD-H, hexane: 2-propanol = 65:35, flow rate = 0.9 mL/min, T = 10 ℃, UV = 254 nm, t_R = 10.7 min (minor), t_R = 22.0 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 0.5H), 8.10 (d, *J* = 2.3 Hz, 0.6H), 7.93 (d, *J* = 2.3 Hz, 0.4H), 7.65 (ddd, *J* = 17.0, 8.6, 2.3 Hz, 1.4H), 7.51 – 7.33 (m, 4H), 7.29 (dd, *J* = 11.8, 7.3 Hz, 1H), 7.25 – 7.11 (m, 2H), 7.06 (dd, *J* = 7.8, 5.3 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 0.4H), 6.84 – 6.67 (m, 1H), 5.25 (s, 0.4H), 5.20 – 5.05 (m, 1H), 5.04 – 4.90 (m, 1H), 4.58 – 4.29 (m, 2H), 3.17 (dd, *J* = 14.0, 1.5 Hz, 0.4H), 2.88 (d, *J* = 15.0 Hz, 0.6H), 2.66 (d, *J* = 15.0 Hz, 0.6H), 2.30 (d, *J* = 14.0 Hz, 0.4H), 1.41 (dt, *J* = 14.2, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 177.8, 168.2, 166.7, 159.5, 159.3, 158.9, 158.0, 151.7, 151.5, 143.2, 143.2, 135.7, 135.6, 135.3, 134.5, 130.6, 130.1, 129.2, 128.9, 128.7, 128.6, 127.9, 127.5, 127.2, 127.1, 126.6, 126.3, 125.5, 124.2, 122.3, 122.0, 118.4, 118.3, 117.1, 116.9, 116.7, 116.6, 110.4, 109.5, 103.4, 102.2, 97.3, 95.3, 77.3, 77.2, 77.0, 76.8, 64.2, 63.0, 46.5, 45.4, 44.8, 44.6, 37.3, 36.8, 14.1, 14.0; HRMS (ESI) m/z calcd for $C_{29}H_{22}BrNO_7$ $[M+H]^+$ 576.0652, found 576.0670.

(3*R*)-ethyl 1-benzyl-9'-fluoro-2'-hydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ae)



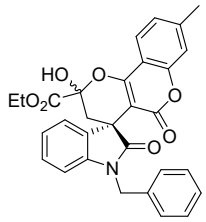
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (46.9 mg, 91% yield); m.p. 97 - 100 ℃; $[\alpha]_D^{20}$ = -15.9 (*c* = 1.03, $CHCl_3$, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 14.6 min (minor), t_R = 17.7 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.65 (td, *J* = 8.6, 1.7 Hz, 1H), 7.44 (dd, *J* = 9.5, 8.2 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.24 – 7.17 (m, 1H), 7.10 – 6.89 (m, 2H), 6.84 – 6.65 (m, 1H), 5.18 – 5.07 (m, 1H), 5.04 – 4.91 (m, 1H), 4.50 – 4.35 (m, 2H), 3.17 (d, *J* = 14.0 Hz, 0.2H), 2.89 (d, *J* = 15.0 Hz, 0.8H), 2.67 (d, *J* = 15.0 Hz, 0.8H), 2.30 (d, *J* = 14.0 Hz, 0.2H), 1.41 (dt, *J* = 16.1, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.6, 177.9, 168.3, 166.8, 159.8 ($^4J_{CF}$ = 2.3 Hz), 159.3, 159.2,158.8 ($^1J_{CF}$ = 244.6 Hz), 158.7 ($^1J_{CF}$ = 235.9 Hz), 158.4 ($^4J_{CF}$ = 2.5 Hz), 149.1 ($^4J_{CF}$ = 1.6 Hz), 148.9 ($^4J_{CF}$ = 1.3 Hz), 143.3, 143.2, 135.6, 134.6, 130.7, 130.2, 129.2, 129.0, 128.8, 128.6, 127.9, 127.5, 127.2, 127.2, 126.6, 126.0, 125.8, 124.2, 122.3, 122.1, 120.5 ($^2J_{CF}$ = 24.6 Hz), 120.0 ($^2J_{CF}$ = 24.6 Hz), 118.4 ($^3J_{CF}$ = 7.9 Hz), 118.3 ($^3J_{CF}$ = 8.2 Hz), 116.2 ($^3J_{CF}$ = 9.1 Hz), 116.0 ($^3J_{CF}$ = 9.2 Hz), 110.4, 109.6 ($^2J_{CF}$ = 25.6 Hz), 108.9 ($^2J_{CF}$ = 25.7 Hz), 103.4, 102.2, 97.3, 95.4, 64.2, 63.0, 46.6, 45.5, 44.8, 44.6, 37.4, 36.9, 14.2, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -116.6, -116.9; HRMS (ESI) m/z calcd for $C_{29}H_{22}FNO_7$ $[M+H]^+$ 516.1453, found 516.1458.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-9'-methoxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3af)



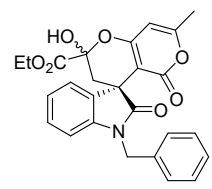
The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (44.3 mg, 84% yield); m.p. 101 - 104 ℃; $[\alpha]_D^{20}$ = -37.1 (*c* = 0.97, $CHCl_3$, 92% ee); HPLC: Daicel Chiralpak OD-H, hexane: 2-propanol = 65:35, flow rate = 0.9 mL/min, T = 10 ℃, UV = 254 nm, t_R = 11.4 min (minor), t_R = 31.5 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.88 (d, *J* = 8.9 Hz, 0.8H), 7.70 (d, *J* = 8.8 Hz, 0.2H), 7.51 – 7.40 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.21 (td, *J* = 7.7, 1.6 Hz, 1H), 7.16 – 7.01 (m, 2H), 6.92 – 6.84 (m, 1H), 6.81 – 6.67 (m, 2H), 5.17 – 5.07 (m, 1H), 5.04 – 4.93 (m, 1H), 4.50 – 4.35 (m, 2H), 3.87 (s, 2.5H), 3.86 (s, 0.4H), 3.15 (d, *J* = 14.0 Hz, 0.2H), 2.85 (d, *J* = 13.2 Hz, 0.8H), 2.63 (d, *J* = 14.9 Hz, 0.8H), 2.27 (d, *J* = 14.0 Hz, 0.2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.0, 178.3, 168.5, 167.0, 163.7, 163.4, 160.9, 160.4, 160.0, 159.4, 154.9, 154.6, 143.3, 143.2, 135.8, 134.7, 131.3, 130.9, 129.0, 129.0, 128.8, 128.5, 128.4, 128.4, 127.8, 127.4, 127.2, 126.6, 126.0, 125.9, 125.0, 124.1, 122.2, 122.1, 112.6, 112.5, 110.3, 109.4, 108.5, 108.3, 100.3, 98.6, 97.0, 95.1, 64.0, 62.8, 55.8, 55.8, 46.5, 45.4, 44.8, 44.6, 37.5, 37.0, 14.1, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_8$ $[M+H]^+$528.1653, found 528.1653.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-8'-methyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3ag)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (47.1 mg, 92% yield); m.p. 93 - 97 ℃; $[\alpha]_D^{20}$ = -24.2 (*c* = 0.99, $CHCl_3$, 92% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 0.8 mL/min, T = 10 ℃, UV = 254 nm, t_R = 22.1 min (minor), t_R = 74.8 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 0.8H), 7.69 (d, *J* = 8.1 Hz, 0.2H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.31 – 7.28 (m, 1H), 7.24 – 7.18 (m, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.11 – 6.90 (m, 3H), 6.80 – 6.69 (m, 1H), 5.20 – 5.05 (m, 1H), 5.04 – 4.92 (m, 1H), 4.47 – 4.35 (m, 2H), 3.16 (d, *J* = 14.0 Hz, 0.2H), 2.87 (d, *J* = 14.9 Hz, 0.8H), 2.65 (d, *J* = 14.9 Hz, 0.8H), 2.46 (s, 2.5H), 2.44 (s, 0.5H), 2.28 (d, *J* = 14.0 Hz, 0.2H), 1.42 (dd, J = 9.2, 5.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 178.2, 168.6, 167.0, 160.8, 160.2, 159.9, 159.3, 153.1, 152.9, 144.3, 143.8, 143.3, 143.2, 135.8, 134.7, 131.2, 130.6, 129.0, 129.0, 128.8, 128.4, 127.8, 127.5, 127.2, 127.2, 125.9, 125.5, 125.3, 124.1, 123.5, 122.7, 122.2, 122.1, 116.8, 116.7, 112.7, 112.6, 110.3, 109.4, 101.5, 100.4, 97.0, 95.0, 64.0, 62.8, 46.6, 45.4, 44.8, 44.6, 37.5, 37.0, 21.9, 21.8, 14.1, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{25}NO_7$ $[M+H]^+$512.1704, found 512.1713.

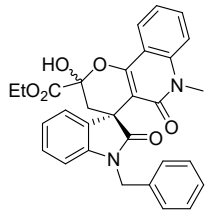
(3*R*)-ethyl 1-benzyl-2'-hydroxy-7'-methyl-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[4,3-b]pyran]-2'-carboxylate (3ah)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid

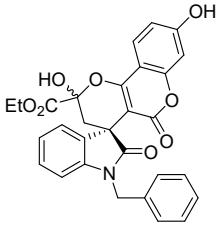
(41.1 mg, 89% yield); m.p. 183 - 186 ℃; $[\alpha]_D^{20}$ = -38.4 (*c* = 0.99, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak OD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 260 nm, t_R = 10.8 min (minor), t_R = 17.7 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.44 – 7.39 (m, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.24 – 7.16 (m, 1H), 7.12 – 6.96 (m, 2H), 6.81 – 6.64 (m, 1H), 6.00 (s, 0.9H), 5.87 (s, 0.1H), 5.12 (d, *J* = 15.9 Hz, 1H), 4.92 (d, *J* = 15.9 Hz, 1H), 4.38 – 4.30 (m, 2H), 3.04 (d, *J* = 14.0 Hz, 0.1H), 2.77 (d, *J* = 15.0 Hz, 0.9H), 2.56 (d, *J* = 15.0 Hz, 0.9H), 2.30 (d, *J* = 14.0 Hz, 0.1H), 2.21 (s, 2.6H), 2.19 (s, 0.4H), 1.41 – 1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8, 178.1, 168.5, 166.9, 164.9, 162.8, 162.0, 161.1, 143.2, 143.1, 135.7, 134.6, 130.8, 130.3, 128.9, 128.9, 128.7, 128.3, 127.8, 127.4, 127.1, 126.5, 126.0, 125.7, 124.0, 123.8, 122.2, 122.0, 110.2, 109.3, 100.7, 100.1, 98.6, 97.0, 96.7, 94.8, 63.9, 62.8, 45.9, 44.8, 44.7, 44.5, 37.2, 36.8, 19.9, 19.9, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{26}H_{23}NO_7$ $[M+H]^+$ 462.1547, found 462.1554.

(3*R*)-ethyl 1-benzyl-2'-hydroxy-6'-methyl-2,5'-dioxo-2',3',5',6'-tetrahydrospiro[indoline-3,4'-pyrano[3,2-c]quinoline]-2'-carboxylate (3ai)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:5 v/v) to give the product as white solid (30.6 mg, 60% yield); m.p. 114 - 117 ℃; $[\alpha]_D^{20}$ = +2.3 (*c* = 1.02, $CHCl_3$, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 260 nm, t_R = 6.74 min (minor), t_R = 15.9 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 0.7H), 8.16 (dd, *J* = 8.0, 1.3 Hz, 0.7H), 8.00 (dd, *J* = 8.0, 1.3 Hz, 0.3H), 7.66 – 7.55 (m, 1H), 7.52 – 7.27 (m, 7H), 7.23 – 7.16 (m, 1H), 7.16 – 6.89 (m, 2H), 6.85 – 6.69 (m, 1H), 5.29 – 5.07 (m, 1H), 5.05 – 4.98 (m, 1H), 4.95 (s, 0.3H), 4.55 – 4.32 (m, 2H), 3.58 (s, 1H), 3.55 (s, 2H), 3.16 (d, *J* = 13.8 Hz, 0.3H), 2.88 (d, *J* = 14.8 Hz, 0.7H), 2.63 (d, *J* = 14.9 Hz, 0.7H), 2.28 (d, *J* = 13.8 Hz, 0.3H), 1.41 (dt, *J* = 21.2, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.7, 179.5, 169.2, 167.5, 160.7, 160.5, 156.9, 155.5, 143.4, 143.3, 139.5, 139.3, 136.2, 135.2, 132.5, 131.8, 131.5, 131.4, 128.9, 128.8, 128.6, 128.2, 127.8, 127.4, 127.3, 127.2, 126.4, 124.1, 123.9, 123.4, 122.1, 122.0, 121.9, 121.8, 115.8, 115.5, 113.9, 113.9, 109.9, 109.2, 107.6, 106.9, 96.3, 94.7, 63.8, 62.7, 47.3, 46.1, 44.7, 44.5, 38.2, 37.1, 29.7, 29.5, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{30}H_{26}N_2O_6$ $[M+H]^+$ 511.1864, found 511.1866.

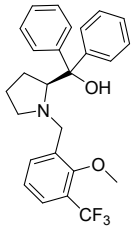
(3*R*)-ethyl 1-benzyl-2',8'-dihydroxy-2,5'-dioxo-2',3'-dihydro-5'*H*-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-2'-carboxylate (3aj)



The title compound was prepared according to general working procedure and purified by column chromatography (ethyl acetate:petroleum ether = 1:2 v/v) to give the product as light yellow solid (25.7 mg, 50% yield); m.p. 150 - 153 ℃; $[\alpha]_D^{20}$ = -8.6 (*c* = 0.50, $CHCl_3$, 91% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 70:30, flow rate = 1.0 mL/min, T = 10 ℃, UV = 254 nm, t_R = 4.86 min (minor), t_R = 6.98 min (major); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 0.6H), 8.96 (s, 0.3H), 8.39 (s, 0.6H), 7.77 – 7.59 (m, 1H), 7.58 – 7.26 (m, 5H), 7.25 – 6.89 (m, 3H), 6.86 – 6.45 (m, 3H), 5.27 (s, 0.3H), 5.21 – 4.89 (m,

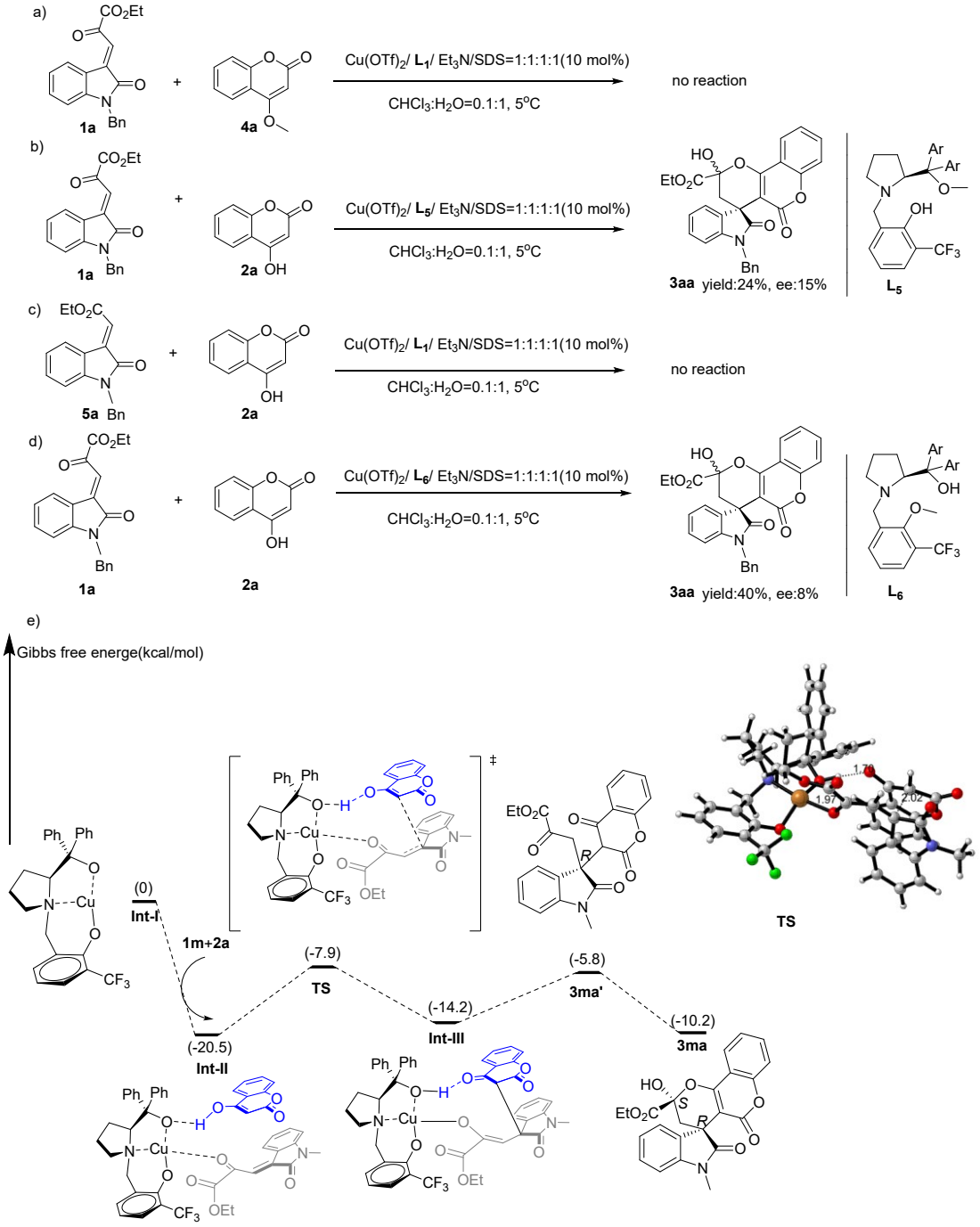
2H), 4.62 – 4.33 (m, 2H), 3.19 (d, J = 13.9, 1.8 Hz, 0.3H), 2.89 (d, J = 15.2 Hz, 0.7H), 2.63 (d, J = 14.6, 0.7H), 2.26 (d, J = 13.9 Hz, 0.3H), 1.47 – 1.37 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.3, 180.1, 168.4, 167.3, 161.5, 161.5, 161.2, 161.1, 161.1, 160.1, 154.5, 154.0, 143.1, 142.6, 135.2, 134.6, 131.2, 131.0, 129.1, 129.0, 128.9, 128.6, 127.9, 127.7, 127.3, 126.7, 125.1, 125.1, 124.3, 124.2, 122.9, 122.1, 113.5, 113.2, 110.4, 109.8, 107.6, 106.9, 102.7, 102.4, 98.2, 97.8, 97.0, 95.1, 64.0, 63.1, 46.4, 45.7, 44.8, 44.8, 37.4,36.4, 14.2, 14.1; HRMS (ESI) m/z calcd for $C_{29}H_{23}NO_8[M+H]^+$ 514.1496, found 514.1502.

(S)-(1-(2-methoxy-3-(trifluoromethyl)benzyl)pyrrolidin-2-yl)diphenylmethanol (L_6)



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether: ethyl acetate = 10:1 v/v) to give the product as a colorless oil (21.8 mg, 99% yield). ^{1}H NMR (500 MHz, $CDCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 7.5 Hz, 2H), 7.66 – 7.57 (m, 2H), 7.52 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 7.7 Hz, 2H), 7.26 – 7.11 (m, 4H), 7.06 (t, J = 7.3 Hz, 1H), 4.85 (s, 1H), 4.05 (dd, J = 9.2, 5.2 Hz, 1H), 3.57 – 3.40 (m, 4H), 3.11 (d, J = 14.2 Hz, 1H), 3.03 – 2.88 (m, 1H), 2.33 (dd, J = 16.8, 9.2 Hz, 1H), 2.05 – 1.93 (m, 1H), 1.85 – 1.74 (m, 1H), 1.74 – 1.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 147.9, 146.4, 134.8, 133.3, 128.20, 128.1, 126.5, 126.4, 125.6, 125.5, 123.9, 77.9, 71.3, 62.5, 55.6, 53.6, 29.6, 24.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ -60.9; HRMS (ESI) m/z calcd for $C_{26}H_{27}F_3NO_2[M+H]^+$ 442.1988, found 442.1996.

1.6 Control experiments and DFT calculations



Scheme S1. Control experiments; Gibbs free energy profiles for the Cu-catalyzed Michael/hemiketalization of **1m** with **2a**; 3D structures were generated by CYLview,[4] key bond distances shown in units of Å.

In order to further understand the reaction mechanism and the coordination with the metal copper in the reaction, several control experiments were carried out. Firstly, when nucleophile 4-hydroxycoumarin was replaced by 4-methoxycoumarin, no desired product was obtained. When the aliphatic hydroxyl group of $\mathbf{L_1}$ was replaced by a methoxy group, both the yield and the enantioselectivity were decreased largely, as shown in scheme S1a-b. This indicated that there maight be a hydrogen bond

between the aliphatic hydroxyl group in $\mathbf{L_1}$ and phenolic hydroxyl of 4-hydroxycoumarin in the reaction. Next, when electrophilic isatin-derived β,γ-unsaturated α-ketoester was replaced by ethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)acetate, the reaction couldn't occur. When the phenol hydroxyl group of $\mathbf{L_1}$ was replaced by a methoxy group, the corresponding product with low yield and poor enantioselectivity was obtained, as shown in scheme S1c-d. According to our previous report, the copper complex developed in our group generally was a four coordination structure.[5] Therefore a plausible reaction mechanism was proposed in SchemeS1e. First, the carbonyl of isatin-derived β,γ-unsaturated α-ketoester coordinates with the copper ions in the catalyst to satisfy the request of square coordination. At the same time, the hydroxyl of 4-hydroxycoumarin binds to the oxygen of the prolinol in the ligand via a hydrogen bond to afford the **Int-II**. Then nucleophilic attack of 4-hydroxycoumarin to the β,γ-unsaturated α-ketoester occurs from *Si* face of the nucleophile acceptor, as shown in **TS**. In contrast, the *Re* attack is hard to occur because of the lack of hydrogen bond. The resulting **Int-III** undergoes a chiral L-Cu complex dissociation to give **3ma'** as the major product and regenerates **Int-I** to restart the catalytic cycle. The product **3ma'** is rapidly converted to hemiketal product **3ma**. The transition state of the reaction was supported by DFT calculation and the solvation effect of water was considered in the calculation. Moreover, we found that the Gibbs free energy of **3ma** was lower than that of **3ma'** which was consistent with the experimental results that **3ma'** was easy to transform to **3ma**.

DFT calculations

All the calculations were performed using Gaussian 16 software packages.[6] The geometry of all reactants and transition states were optimized using the (U)B3LYP[7]-D3(Becke-Johnson damping function)[8] in water (using the SMD solvation model). In these geometry optimizations, a mixed basis set of SDD[9] for Cu, while 6-31G(d)[10] for all the other atoms was used. Vibrational frequency analysis was calculated at the same level of theory to validate each structure as either a minimum or a transition state and to evaluate its zero-point energy and thermal corrections at 298 K. For each transition state, the intrinsic reaction coordinate (IRC) analysis was conducted to ensure that it connects the right reactant and product.[11]

Table 3. Thermal correction of Gibbs free energy (TCG, Hartree) and single point energies (EE + Thermal Free Energy Correction, hartree) in solvent for all species involved in this study.

Compounds	TCG (water)	EE + Thermal Free Energy Correction (water)
2a	0.097003	-572.180924
1m	0.202676	-896.840443
Int-I	0.365571	-1667.817675
Int-II	0.718637	-3136.871662
TS	0.721863	-3136.851507
Int-III	0.719656	-3136.861607
3ma'	0.327467	-1469.057367
3ma	0.331856	-1469.064398

2a (water):

C	2.89613600	0.27055500	-0.00002600
C	1.78308700	1.09816600	0.00002300
C	0.48341600	0.56178300	0.00003900
C	0.33642300	-0.83922800	0.00009100
C	1.45519600	-1.67660600	-0.00003700
C	2.72753300	-1.12087800	-0.00009700
H	3.89216000	0.70087300	0.00001900
H	1.93948400	2.17507300	0.00010500
H	1.29752400	-2.74947500	-0.00011000
H	3.59638400	-1.77190400	-0.00018700
C	-0.73912800	1.34672500	0.00000400
O	-0.70085600	2.69811600	0.00002300
H	0.21648200	3.00950600	-0.00052400
C	-1.94986800	0.73071600	0.00004500
H	-2.86594400	1.30704000	-0.00010400
C	-2.08331800	-0.70749300	0.00000000
O	-3.11117300	-1.34037500	-0.00017700
O	-0.87959000	-1.43943500	0.00022400

1m (water):

C	-3.91925500	2.29740500	-0.09758000
C	-4.12526800	0.91087200	-0.10353700
C	-3.00599900	0.09514100	-0.05291200
C	-1.68819400	0.62422500	0.00346000
C	-1.50967700	2.01049500	0.00774900
C	-2.63370200	2.84014200	-0.04288100
H	-4.78086300	2.95789600	-0.13671700
H	-5.12602100	0.49435800	-0.14633600
H	-0.50902700	2.41751600	0.04989100
H	-2.50307500	3.91758400	-0.03978700
C	-0.77903200	-0.51040800	0.04582100
N	-2.96818300	-1.30179600	-0.04830500
C	-1.65942100	-1.75344600	0.00969600
O	-1.30599900	-2.91841300	0.02773000
C	0.56134300	-0.70101600	0.10618200
H	0.90228500	-1.73160300	0.12159500
C	1.60308000	0.32355100	0.15549700
C	3.03735800	-0.25050700	0.22386500
O	1.43524700	1.53411700	0.14208000
O	3.28231400	-1.43896500	0.17329100
O	3.94090700	0.72372200	0.34433700
C	5.32812700	0.30559900	0.40176800
H	5.39676300	-0.59572100	1.01589500
H	5.83262200	1.13219300	0.90580300
C	5.88499700	0.07067300	-0.99263800
H	5.37550400	-0.76820400	-1.47409200
H	5.76464500	0.96462300	-1.61242100
H	6.95298200	-0.16572000	-0.92894900
C	-4.11759000	-2.17723600	-0.09639200
H	-3.74519900	-3.20248900	-0.07744700

H	-4.77083600	-2.00992300	0.76759400
H	-4.69285200	-2.01456500	-1.01498800

Int-I (Water):

C	0.18820300	0.45661500	1.82873500
C	-1.36577500	-1.02249100	0.75845600
C	-1.79416500	-0.94945500	2.23531800
C	-0.88352400	0.11895100	2.88759400
H	1.20621800	0.45658100	2.21923600
H	-0.00154000	1.42754800	1.37493000
H	-1.37659500	-2.04618400	0.38065200
H	-2.85259900	-0.71499700	2.34756300
H	-1.63026900	-1.92631300	2.70014600
H	-1.44522300	1.01860700	3.15046700
H	-0.42543600	-0.26718200	3.80232800
N	0.07305500	-0.59145900	0.77137600
C	1.00200700	-1.73757300	1.01307000
H	0.76183900	-2.21435600	1.97092400
H	0.80165500	-2.46741100	0.22036400
C	2.45312600	-1.32452300	1.01032700
C	3.00283700	-0.56821500	-0.06340500
C	3.27526700	-1.71082800	2.07002700
C	4.38482400	-0.24763800	-0.00665800
C	4.63578400	-1.39752000	2.10567300
H	2.83346500	-2.27626900	2.88734400
C	5.18523800	-0.66213900	1.05940100
H	5.25345600	-1.71552900	2.93945500
H	6.23777800	-0.40068700	1.06889300
O	2.29789900	-0.15535300	-1.10434500
C	4.97184700	0.55929200	-1.12094800
F	4.38262400	1.77818800	-1.25469100
F	4.86050900	-0.04729300	-2.33157200
F	6.29466600	0.79938000	-0.94050400
C	-2.15341900	-0.17477700	-0.30324900
C	-2.44352800	1.26214200	0.18647200
C	-3.49111800	1.53367900	1.07918600
C	-1.66717300	2.33655100	-0.26494300
C	-3.72448500	2.82908100	1.54288700
H	-4.14453500	0.73046700	1.40376300
C	-1.89766100	3.63539500	0.19428600
H	-0.87198500	2.15333100	-0.97979000
C	-2.92254400	3.88698100	1.10778700
H	-4.54021000	3.01165200	2.23759300
H	-1.27688900	4.45104400	-0.16785900
H	-3.10420600	4.89688000	1.46548600
C	-3.49320800	-0.84516300	-0.65436700
C	-4.24382700	-0.27103800	-1.69332500
C	-4.00269800	-1.98300300	-0.01964000
C	-5.46114400	-0.81820600	-2.08965800
H	-3.86361600	0.61676200	-2.18975000

C	-5.22869900	-2.53323600	-0.41259400
H	-3.46227900	-2.45997500	0.78994400
C	-5.96200500	-1.95563300	-1.44699600
H	-6.02286300	-0.35618300	-2.89741200
H	-5.60516200	-3.41601500	0.09766000
H	-6.91401300	-2.38270500	-1.75053300
O	-1.37949000	-0.15151100	-1.48362000
Cu	0.43307500	-0.09654900	-1.13955200

Int-II (Water):

C	-3.83769200	1.52421500	0.61157600
C	-2.32776900	2.70566400	-0.80888200
C	-3.37214300	3.74142300	-0.35897200
C	-4.25384400	3.00912200	0.68204100
H	-4.67996500	0.83607000	0.55898300
H	-3.22778200	1.24451700	1.46493200
H	-2.09422700	2.78010300	-1.87072300
H	-2.90994600	4.64237400	0.04432500
H	-3.96618800	4.04297400	-1.22528200
H	-4.08715200	3.39513300	1.69023400
H	-5.31368400	3.13255500	0.44615400
N	-3.01004400	1.38131200	-0.62878600
C	-3.88752300	1.08653300	-1.81651700
H	-4.60760500	1.89974600	-1.95266400
H	-3.22725600	1.06479200	-2.68880300
C	-4.61606300	-0.21697400	-1.65290700
C	-3.85802400	-1.40742100	-1.51260900
C	-6.00777300	-0.27132100	-1.60710900
C	-4.55414700	-2.62585300	-1.31808700
C	-6.68456600	-1.48289600	-1.43424200
H	-6.56990900	0.65402600	-1.70636500
C	-5.95080300	-2.65740800	-1.28633700
H	-7.76879200	-1.50783100	-1.40563700
H	-6.45963800	-3.60334200	-1.13695300
O	-2.53431900	-1.39505700	-1.56379500
C	-3.75976600	-3.87718400	-1.12771000
F	-2.94453600	-3.82386900	-0.03369700
F	-2.94617500	-4.15468100	-2.17870600
F	-4.54502500	-4.96601900	-0.95400400
C	-0.96206000	2.76061200	-0.05809900
C	-1.08363100	2.84588700	1.46806700
C	-1.26623200	4.08815100	2.09220600
C	-1.01195600	1.70003300	2.26787900
C	-1.40448600	4.17724900	3.47738500
H	-1.28525500	4.99432300	1.49700300
C	-1.13543900	1.78834600	3.65531900
H	-0.87334900	0.73003200	1.81052700
C	-1.33957800	3.02628600	4.26600500
H	-1.55019800	5.14927700	3.93940300
H	-1.07410000	0.88488300	4.25426300

H	-1.43727800	3.09571400	5.34538100
C	-0.07713000	3.90364600	-0.57759700
C	1.19615000	4.05060200	-0.00365900
C	-0.44813500	4.77286900	-1.60902500
C	2.08381800	5.01811200	-0.46580200
H	1.50049200	3.38416000	0.79587800
C	0.43768300	5.75527100	-2.06440900
H	-1.42582900	4.71127800	-2.07140600
C	1.70649900	5.87844700	-1.50088300
H	3.06958100	5.09967300	-0.01747700
H	0.12749300	6.42157500	-2.86400000
H	2.39476500	6.63733400	-1.86117700
O	-0.31865100	1.51834100	-0.44360100
Cu	-1.56429000	-0.04735200	-0.60658200
C	4.46080700	-1.97664500	-2.97825900
C	5.09935700	-2.49978100	-1.84386100
C	4.33930400	-2.65189100	-0.69873700
C	2.96133800	-2.29959300	-0.64532000
C	2.34839900	-1.78404200	-1.79622000
C	3.10563100	-1.63192400	-2.95859500
H	5.03670000	-1.83597000	-3.88754300
H	6.15086800	-2.76206600	-1.86307000
H	1.30794000	-1.49720800	-1.77521600
H	2.64148500	-1.22067400	-3.84849200
C	2.51313400	-2.57441300	0.70059000
N	4.76472200	-3.14521100	0.54134000
C	3.73923200	-3.09228800	1.44871600
O	3.79662400	-3.40854900	2.63352600
C	1.33639600	-2.52743700	1.39104100
H	1.35568600	-2.90395600	2.40766200
C	0.08643400	-1.99581800	0.93800000
C	-1.11149700	-2.23121100	1.87378400
O	-0.07631700	-1.40680200	-0.14614600
O	-1.08585300	-3.07183600	2.75524400
O	-2.14668900	-1.46878000	1.56027700
C	-3.42138900	-1.72219000	2.23329900
H	-3.52963400	-2.80158000	2.34465700
H	-4.15881500	-1.35506300	1.52033400
C	-3.49675600	-0.99634600	3.55964000
H	-2.72237300	-1.34808400	4.24745500
H	-3.38953800	0.08305600	3.42573400
H	-4.47524600	-1.19401400	4.01125300
C	6.13852700	-3.48729900	0.86246000
H	6.17490700	-3.78743100	1.90940400
H	6.47814200	-4.31547900	0.23403900
H	6.78865400	-2.62205500	0.70944000
C	3.58235800	1.97188600	-2.71742400
C	2.91934600	1.63008400	-1.54621900
C	3.60828300	1.04575600	-0.46950200
C	4.98188300	0.79886700	-0.61930600

C	5.65827700	1.13021300	-1.79535000
C	4.95582600	1.71994300	-2.84100800
H	3.03525000	2.42741500	-3.53673600
H	1.85720300	1.80964000	-1.45532800
H	6.71908400	0.91637300	-1.87139800
H	5.47851500	1.97949400	-3.75659400
C	2.95630000	0.66916700	0.79611300
O	1.70736400	0.86163900	0.99687800
H	0.53239200	1.32524700	0.08986000
C	3.77682200	0.08363900	1.76899200
H	3.34553400	-0.21733400	2.71634600
C	5.15847100	-0.14936600	1.59693400
O	5.94484100	-0.65421400	2.40751800
O	5.73188400	0.21471100	0.37108200

TS (Water):

C	-4.05395700	1.05181300	0.49127300
C	-2.67972000	2.39852400	-0.91114500
C	-3.90924900	3.26320300	-0.58166200
C	-4.73691700	2.43393100	0.43083900
H	-4.75043000	0.21571600	0.44998400
H	-3.45721200	0.94970600	1.39253700
H	-2.39330500	2.46489100	-1.96055500
H	-3.62941600	4.24139000	-0.19115300
H	-4.47779100	3.43421100	-1.49909000
H	-4.73730200	2.89407400	1.42170200
H	-5.77511000	2.34629300	0.10106100
N	-3.13682500	0.98535300	-0.69133600
C	-3.88672800	0.50389100	-1.90777800
H	-4.71402500	1.18777800	-2.12294300
H	-3.17921600	0.55005600	-2.74112000
C	-4.41152200	-0.89043200	-1.72225300
C	-3.47638000	-1.94013600	-1.52518700
C	-5.77759500	-1.16293900	-1.71475800
C	-3.97886800	-3.24867800	-1.30952000
C	-6.25968100	-2.46205400	-1.52226200
H	-6.47564100	-0.34188900	-1.85952800
C	-5.35381400	-3.49977600	-1.31599200
H	-7.32656400	-2.65907100	-1.52389700
H	-5.71167900	-4.51008000	-1.15030300
O	-2.17560500	-1.70718300	-1.53513800
C	-3.00569700	-4.35306700	-1.05430900
F	-2.23191900	-4.13386400	0.04896700
F	-2.13659000	-4.54273300	-2.08088700
F	-3.61766300	-5.54379100	-0.84853500
C	-1.39303100	2.72438800	-0.09601900
C	-1.60250600	2.83245600	1.41894300
C	-2.05129100	4.03519500	1.98322800
C	-1.34277000	1.75119400	2.26891100
C	-2.26286700	4.14314500	3.35756200

H	-2.22009400	4.90002800	1.35133700
C	-1.53799000	1.86278300	3.64664900
H	-1.00462300	0.80877300	1.86039400
C	-2.00552900	3.05655000	4.19668300
H	-2.61579300	5.08274300	3.77228800
H	-1.32633100	1.01030700	4.28475300
H	-2.15970700	3.14344300	5.26814400
C	-0.69105200	3.98510500	-0.62152300
C	0.50075800	4.37841200	0.00946600
C	-1.14281500	4.72868200	-1.71677600
C	1.23414300	5.46572700	-0.45713100
H	0.86612900	3.81511100	0.86188700
C	-0.41465900	5.83085500	-2.17706200
H	-2.06438300	4.47385800	-2.22560100
C	0.77681800	6.19992900	-1.55532900
H	2.16048700	5.74084700	0.03845600
H	-0.78608900	6.39659300	-3.02643800
H	1.34343100	7.05212800	-1.91874200
O	-0.52984100	1.59781400	-0.40348500
Cu	-1.50208300	-0.19925300	-0.47985700
C	4.65188900	-2.02009200	-2.95587100
C	5.29239000	-2.49813900	-1.80443300
C	4.62164000	-2.36287700	-0.59779900
C	3.34919000	-1.76071900	-0.50071400
C	2.72581500	-1.30119800	-1.65919500
C	3.38336500	-1.43921600	-2.88750800
H	5.15420700	-2.10828100	-3.91442900
H	6.27396400	-2.95598800	-1.85596300
H	1.75628600	-0.82946600	-1.59912000
H	2.90691600	-1.07209200	-3.79077600
C	2.99894600	-1.70024800	0.94265400
N	5.05834400	-2.77948000	0.67201400
C	4.13908600	-2.46109700	1.63410400
O	4.22443400	-2.71409400	2.83285500
C	1.71560100	-1.91985200	1.55323500
H	1.75595900	-2.32280500	2.55828800
C	0.46153700	-1.67005700	1.04208100
C	-0.69295600	-2.10362400	1.94063100
O	0.18553500	-1.15566300	-0.10908900
O	-0.58326000	-2.86939800	2.88551600
O	-1.85297000	-1.56606400	1.55138800
C	-3.07837700	-2.02724800	2.19654300
H	-2.98857500	-3.10307400	2.35100400
H	-3.84842300	-1.83328700	1.45029400
C	-3.34206900	-1.28518200	3.49019400
H	-2.54111000	-1.45716600	4.21470900
H	-3.43805100	-0.21038600	3.31717800
H	-4.28122400	-1.65112700	3.92016500
C	6.38562500	-3.29505000	0.95543000
H	6.43923800	-3.52146700	2.02014900

H	6.57244800	-4.20565100	0.38004900
H	7.14063300	-2.54414200	0.70226700
C	3.23204400	2.42251900	-2.70638100
C	2.64444500	2.09636400	-1.49281000
C	3.38708300	1.45666400	-0.48409800
C	4.74000200	1.17390600	-0.73417600
C	5.34188600	1.49525800	-1.94659100
C	4.58089300	2.11572200	-2.93351600
H	2.64498100	2.90723900	-3.47929700
H	1.59773800	2.30554700	-1.32319100
H	6.38759300	1.25351200	-2.09987100
H	5.04219300	2.36179200	-3.88470000
C	2.79511000	1.01596200	0.78107600
O	1.63959700	1.30992400	1.15378400
H	0.28428800	1.58345900	0.17247600
C	3.61719400	0.11420400	1.58493000
H	3.31219000	0.00080700	2.61912400
C	5.07178700	0.17897800	1.43062400
O	5.89174800	-0.14817300	2.27285800
O	5.56205100	0.58337800	0.20807900

Int-III (Water):

C	-4.13716000	0.22734800	0.46524900
C	-3.12900800	1.88427500	-0.90655000
C	-4.53965400	2.41333400	-0.59111400
C	-5.14708400	1.39203600	0.40182100
H	-4.59963900	-0.75728500	0.41804300
H	-3.54013600	0.27670800	1.37038100
H	-2.85017900	2.03301700	-1.95010600
H	-4.51850500	3.42609800	-0.18912600
H	-5.12044100	2.44722600	-1.51617300
H	-5.27952800	1.82687300	1.39535500
H	-6.12409500	1.04812300	0.05313700
N	-3.22347200	0.40006500	-0.70789500
C	-3.82133100	-0.23782700	-1.93430200
H	-4.79094700	0.22051300	-2.15472000
H	-3.14075000	-0.01135600	-2.76042400
C	-3.98513100	-1.71957900	-1.75676000
C	-2.82014100	-2.50405300	-1.55034900
C	-5.24111700	-2.32183500	-1.75636300
C	-2.98498600	-3.89550800	-1.33044500
C	-5.38806500	-3.69914700	-1.56019600
H	-6.11973700	-1.69951600	-1.90841100
C	-4.25502600	-4.47916400	-1.34204600
H	-6.37301400	-4.15402500	-1.56673500
H	-4.35288000	-5.54569800	-1.17136400
O	-1.61717800	-1.95677000	-1.56039000
C	-1.77202100	-4.72451900	-1.05972200
F	-1.09358600	-4.32237700	0.05457000
F	-0.86750700	-4.69186300	-2.07234800

F	-2.07304800	-6.03025600	-0.86042200
C	-1.97881000	2.51077200	-0.06173700
C	-2.23153700	2.56209300	1.44854100
C	-2.97416400	3.61374300	2.00389900
C	-1.71666700	1.58070400	2.30382100
C	-3.22460500	3.66274700	3.37502300
H	-3.34585700	4.40876100	1.36683700
C	-1.95427100	1.63657400	3.67839000
H	-1.14671900	0.75342500	1.90307300
C	-2.71515200	2.67330400	4.21932100
H	-3.80711800	4.48321900	3.78359500
H	-1.54495800	0.86289700	4.32089300
H	-2.90227000	2.71618100	5.28818000
C	-1.58954800	3.90320100	-0.57913000
C	-0.50454000	4.54801600	0.03750500
C	-2.22245300	4.53940800	-1.65191600
C	-0.04735100	5.77957000	-0.42336300
H	-0.00332900	4.07560400	0.87631500
C	-1.77352100	5.78412400	-2.10567600
H	-3.07339600	4.08854600	-2.14763800
C	-0.68302400	6.40528500	-1.49983200
H	0.80227600	6.25220600	0.06048500
H	-2.28214200	6.26201300	-2.93773600
H	-0.33206500	7.36838900	-1.85838700
O	-0.86506600	1.62748500	-0.34504200
Cu	-1.32967100	-0.35372700	-0.48875300
C	4.85234700	-2.28575700	-2.61221000
C	5.45374800	-2.55070100	-1.37505000
C	4.85980900	-2.00387600	-0.24512400
C	3.69901800	-1.21418700	-0.30449900
C	3.11088700	-0.96939500	-1.53994200
C	3.69676800	-1.50728100	-2.69541600
H	5.29509500	-2.69554300	-3.51507900
H	6.35022800	-3.15674300	-1.30338100
H	2.21261600	-0.37411800	-1.61187000
H	3.24281900	-1.31152200	-3.66187600
C	3.36498300	-0.75608200	1.10794100
N	5.29257300	-2.13730600	1.08712300
C	4.49350100	-1.43899300	1.94087100
O	4.61814300	-1.36777400	3.16119800
C	2.07506200	-1.24130900	1.70944400
H	2.16377400	-1.62154900	2.71917000
C	0.84124600	-1.30143600	1.14149000
C	-0.20739400	-1.98396800	2.00480100
O	0.50380600	-0.87420900	-0.05197000
O	0.03600700	-2.67635000	2.98395600
O	-1.45260100	-1.76996900	1.55811300
C	-2.53969400	-2.51767100	2.17692300
H	-2.19127100	-3.53810600	2.34227900
H	-3.31530500	-2.52353000	1.41138200

C	-3.01629000	-1.86633100	3.45958600
H	-2.22220400	-1.84496000	4.21080600
H	-3.36120900	-0.84446300	3.28185300
H	-3.85461300	-2.44811700	3.85929400
C	6.47280000	-2.87957100	1.49362700
H	6.55498400	-2.81581200	2.57849400
H	6.38249000	-3.92773900	1.19449500
H	7.36731100	-2.44939200	1.03308900
C	2.34784700	2.95146400	-2.95753900
C	1.96528100	2.59407000	-1.67328900
C	2.90870200	2.09953600	-0.75330000
C	4.24818000	2.01039100	-1.16423000
C	4.64693300	2.36743800	-2.44691700
C	3.68922400	2.83029300	-3.34527400
H	1.60745400	3.32004700	-3.65945200
H	0.92851300	2.66407100	-1.37969700
H	5.69230100	2.28130800	-2.72088100
H	3.99158400	3.10295600	-4.35128700
C	2.54001900	1.63217700	0.58322300
O	1.44007900	1.82464300	1.11238000
H	-0.08365300	1.81109800	0.23373500
C	3.58564000	0.83028600	1.32380400
H	3.47186500	0.99174400	2.39684500
C	5.00747200	1.18224800	0.95896200
O	5.95114500	1.04995900	1.70702000
O	5.26545900	1.60801000	-0.31302400

3ma' (Water):

C	-4.78352400	-2.22400800	0.57739300
C	-4.84124600	-1.06155000	-0.20117100
C	-3.65264500	-0.37762300	-0.41690900
C	-2.42458300	-0.80273600	0.11628200
C	-2.38458300	-1.96283200	0.87951200
C	-3.57238600	-2.67333000	1.10517200
H	-5.69565200	-2.78310100	0.76340200
H	-5.77665200	-0.71450000	-0.62607400
H	-1.44962100	-2.31896100	1.28909700
H	-3.54447700	-3.58218300	1.69803200
C	-1.35604800	0.19925900	-0.29298100
N	-3.47154300	0.77716200	-1.19851800
C	-2.15382100	1.11851400	-1.27280200
O	-1.67146800	1.97636700	-2.00631800
C	-0.17193400	-0.33741900	-1.11700600
H	-0.57828300	-0.94285700	-1.94177500
C	0.84384600	-1.21836000	-0.45010300
C	2.19413000	-1.30974300	-1.19676600
O	0.67601200	-1.85767400	0.57034000
O	2.51472800	-0.52996400	-2.07574500
O	2.90938500	-2.33648800	-0.75704300
C	4.19198100	-2.58961100	-1.41476000

H	4.05571000	-2.44779600	-2.48887200
H	4.37853500	-3.64371800	-1.20803500
C	5.28567400	-1.70292900	-0.85597400
H	5.11035300	-0.65310900	-1.10189200
H	5.35368300	-1.80803800	0.23120400
H	6.24299800	-2.00648000	-1.29369400
C	-4.51971700	1.40135100	-1.98730600
H	-4.09016800	2.25983200	-2.50284600
H	-4.91692000	0.69400400	-2.72191300
H	-5.33101400	1.73560900	-1.33517300
C	3.72311200	2.17756900	-0.05959700
C	2.39018400	2.55612900	-0.15494500
C	1.41724400	1.90899500	0.62038000
C	1.81360700	0.89260100	1.49763200
C	3.14533200	0.51208100	1.61567100
C	4.09613000	1.16118400	0.82970000
H	4.47391600	2.66739500	-0.67021700
H	2.07344500	3.33857900	-0.83641100
H	3.41912000	-0.27332500	2.31074200
H	5.13718900	0.86812600	0.91028200
C	-0.00712900	2.25180600	0.53414000
O	-0.42160200	3.33783300	0.15137600
C	-0.95967000	1.13253600	0.94383600
C	-0.44319700	0.35883100	2.14580900
O	-1.16489600	-0.14765700	2.97283900
O	0.90807100	0.26053700	2.34047900
H	0.34502800	0.49231800	-1.60343400
H	-1.89275600	1.59014500	1.27852900

3ma (Water):

C	-4.05008600	0.42526400	-2.35546300
C	-4.30751000	-0.30151700	-1.18498100
C	-3.25544300	-0.47269300	-0.29525700
C	-1.98459700	0.07920200	-0.51617400
C	-1.72939900	0.74386000	-1.70497700
C	-2.77501100	0.92643100	-2.62309400
H	-4.85174600	0.57581000	-3.07238300
H	-5.28388500	-0.73376300	-0.99425900
H	-0.73383300	1.10101500	-1.93075100
H	-2.58416900	1.45421200	-3.55248300
C	-1.08324700	-0.30596800	0.65043500
N	-3.24858300	-1.24586800	0.88022200
C	-1.98926200	-1.33281600	1.40075900
O	-1.64590200	-2.02847500	2.35262800
C	-0.83704300	0.79903000	1.71865100
H	-1.65629700	1.52126600	1.71291700
C	0.48556800	1.56308500	1.69367100
C	0.56707400	2.82155400	0.80578800
O	0.76669200	1.94425100	2.99804800
O	1.02222500	3.86684700	1.24065500

O	0.14805100	2.60454700	-0.42249300
C	0.27579700	3.69377000	-1.39353500
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H	-0.50372200	3.47908600	-2.12454900
C	1.65912600	3.68085600	-2.00842300
H	2.42656800	3.87689500	-1.25353900
H	1.86407300	2.71489600	-2.48078700
H	1.71925100	4.46156700	-2.77423200
C	-4.36521200	-2.06401300	1.31839400
H	-5.24313300	-1.43671500	1.49360600
H	-4.60779100	-2.81864500	0.56301700
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C	5.06464000	-1.07408700	-0.19838900
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C	2.65985100	-0.97191000	0.05148300
C	2.55553600	-2.15599300	-0.69169200
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H	6.04811900	-0.65598700	-0.01103600
H	4.02287900	0.48364900	0.86314900
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H	5.82083300	-2.75783900	-1.32155500
C	1.43202700	-0.36497100	0.51608800
O	1.61186900	0.75482700	1.23795000
C	0.21913400	-0.92412000	0.22844400
C	0.15193800	-2.15287500	-0.52206700
O	-0.87992200	-2.75087300	-0.80406500
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H	1.26394500	2.78652500	2.94460800

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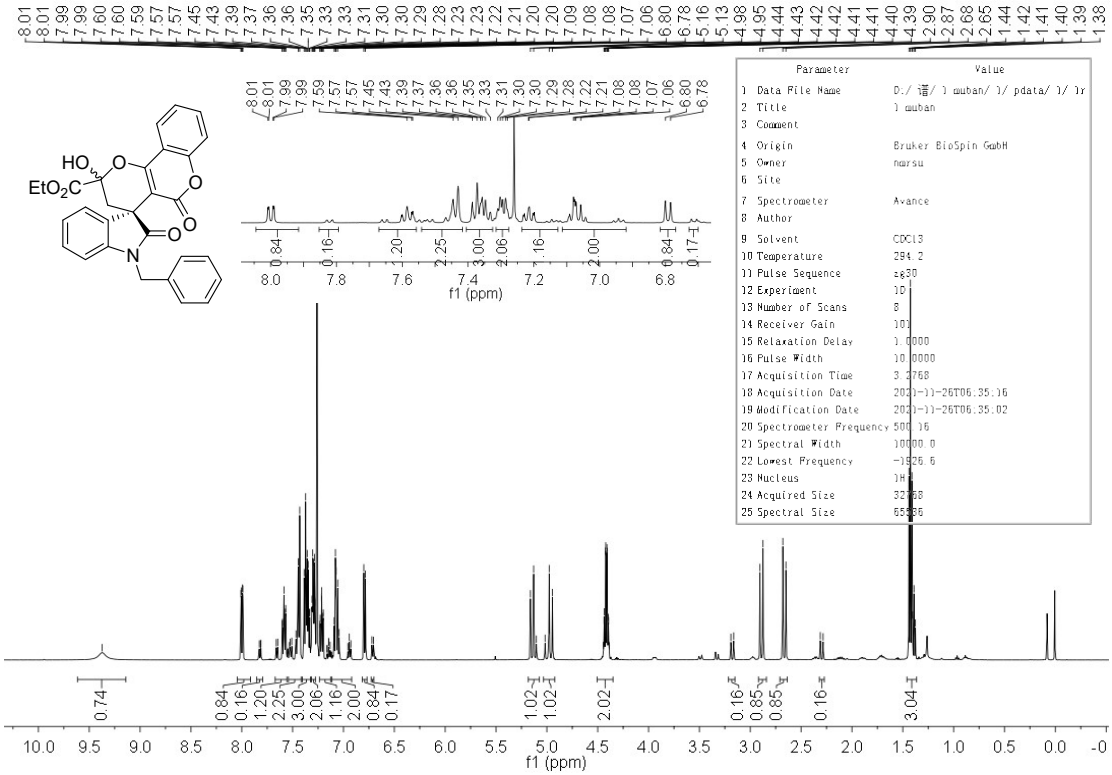
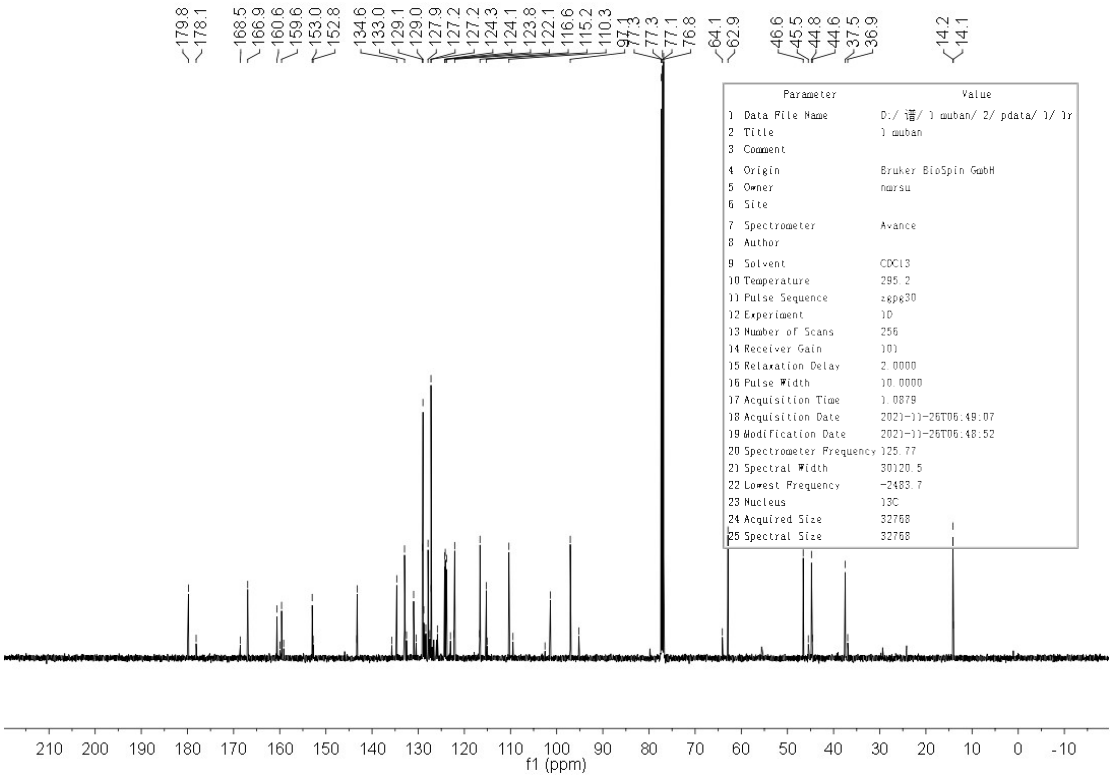
Part Ⅱ ^{1}H NMR & ^{19}F NMR & ^{13}C NMR

^{1}H NMR of **3aa**



^{13}C NMR of **3aa**



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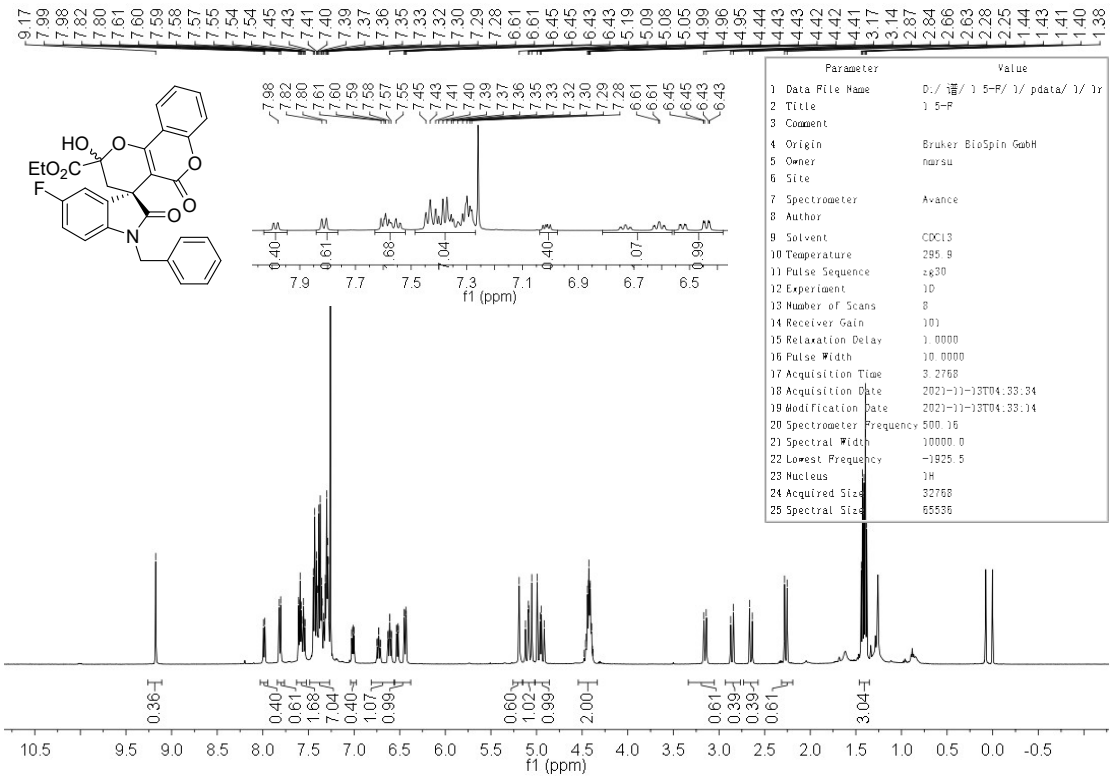
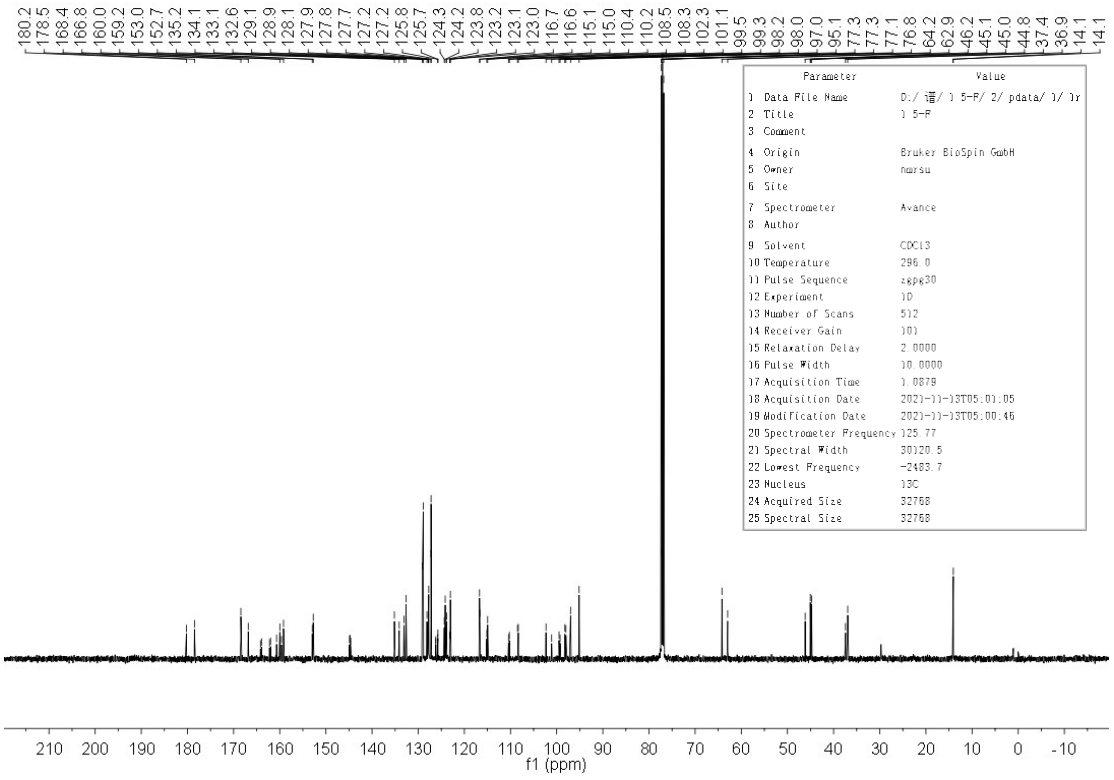
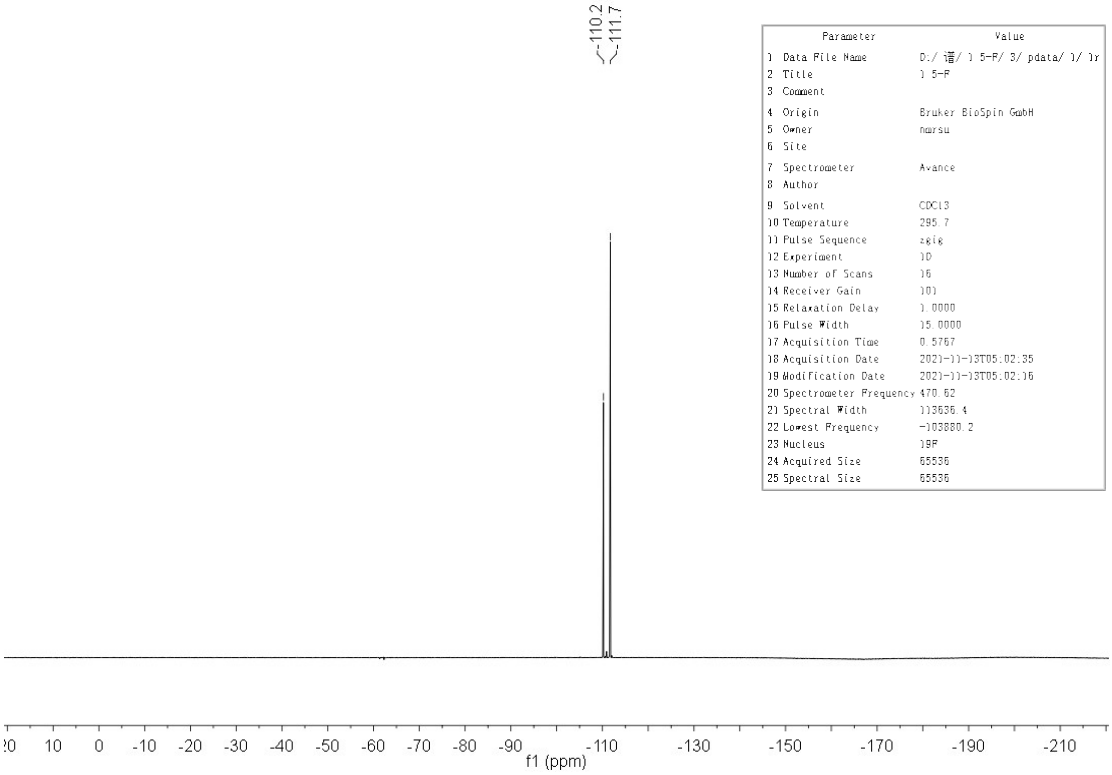


^{13}C NMR of **3ba**



^{19}F NMR of **3ba**



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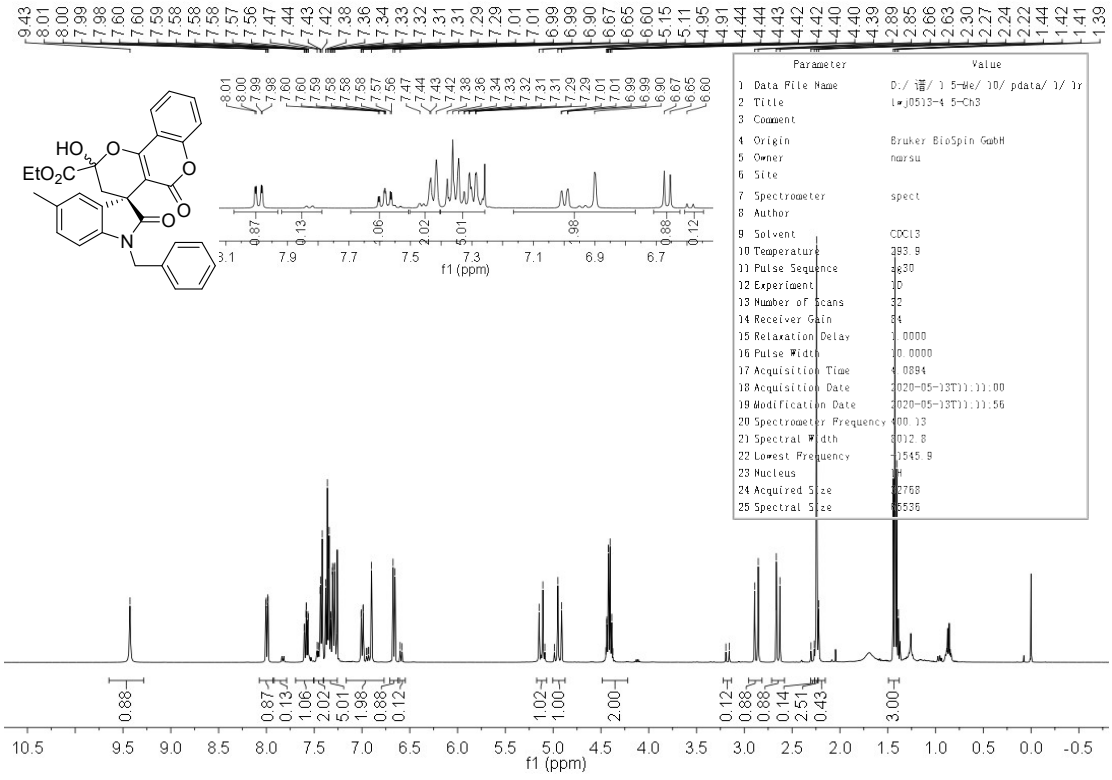
^{1}H NMR of **3ca**



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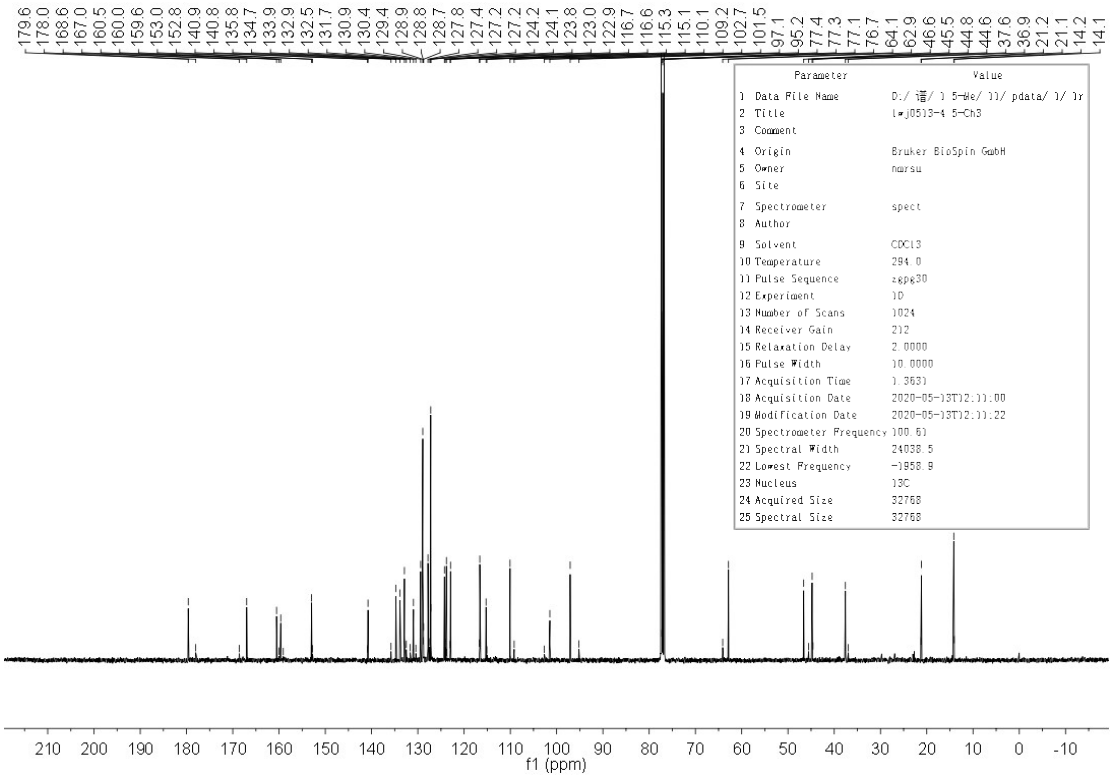
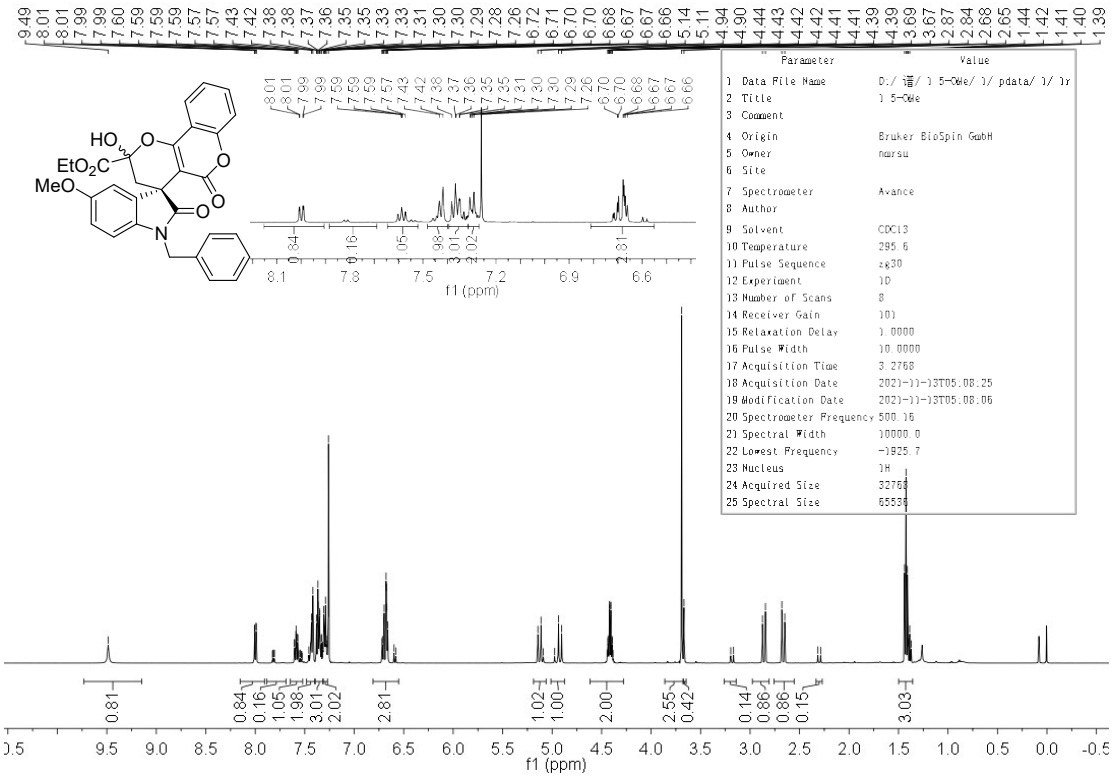
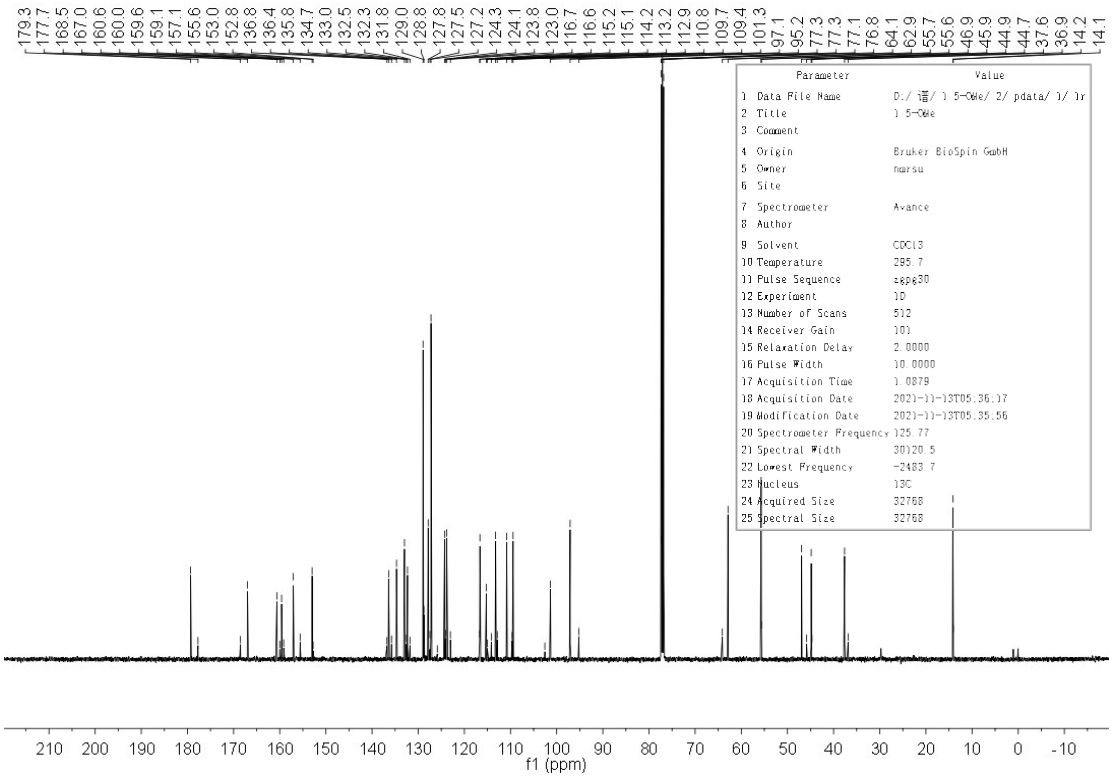
^{13}C NMR of **3ca**



^{1}H NMR of **3da**



^{13}C NMR of **3da**



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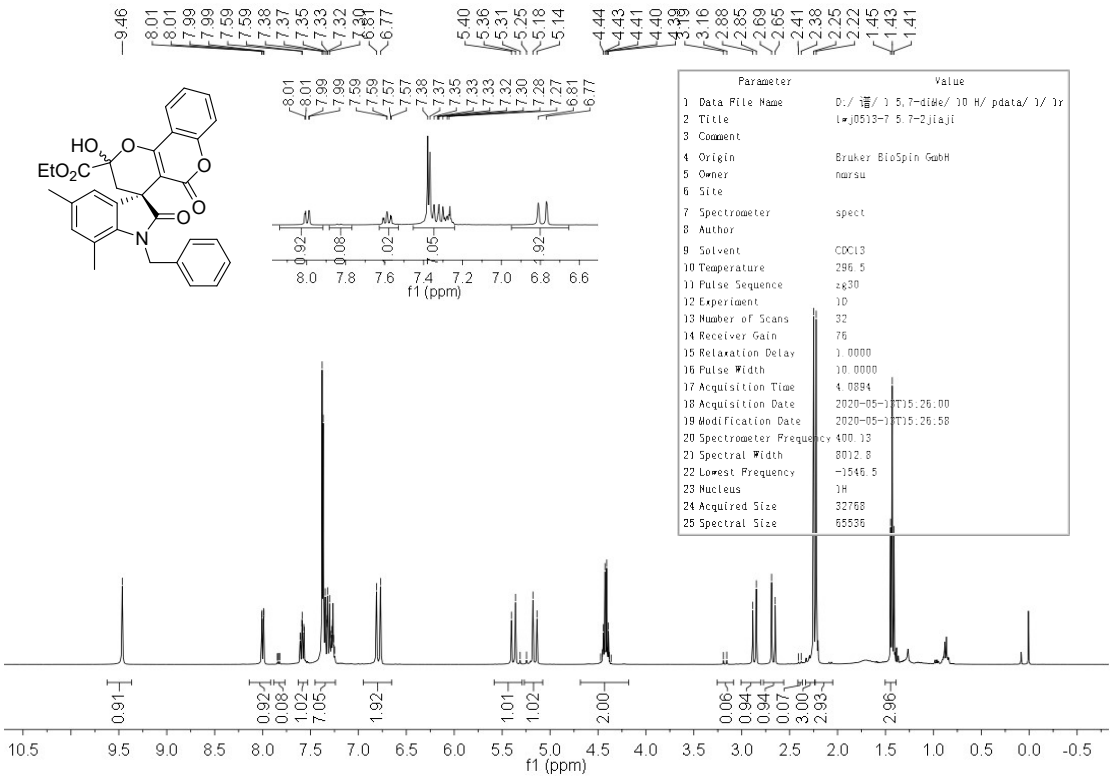

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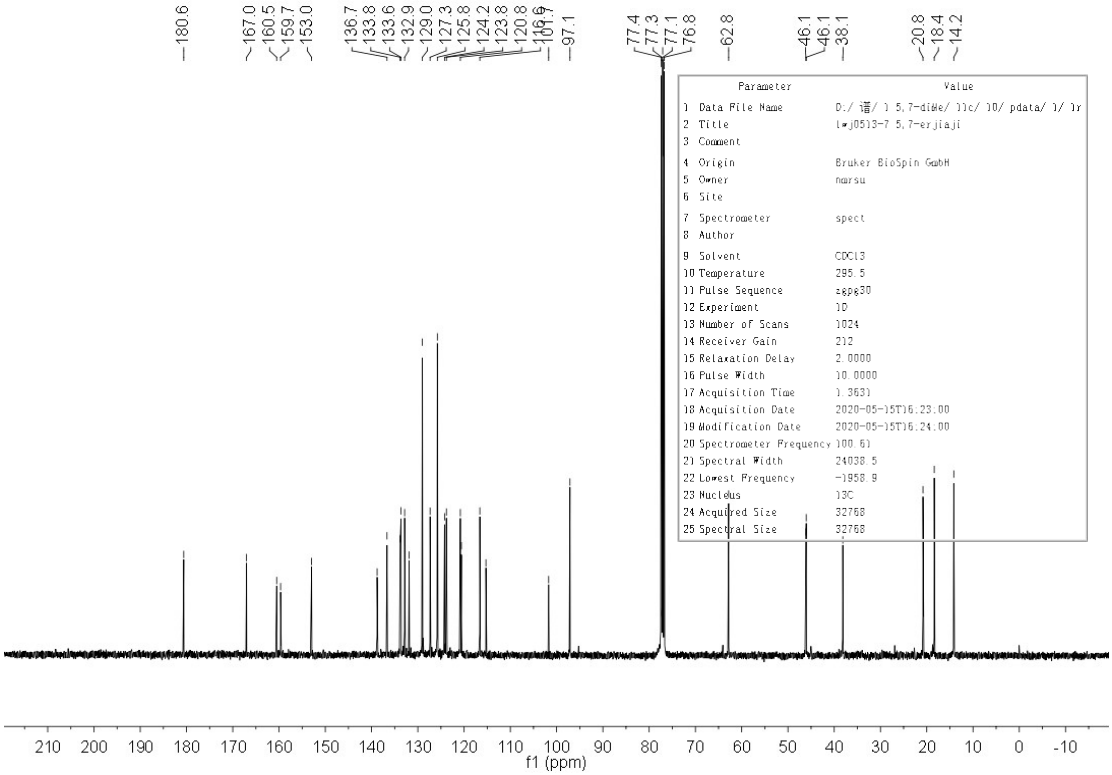

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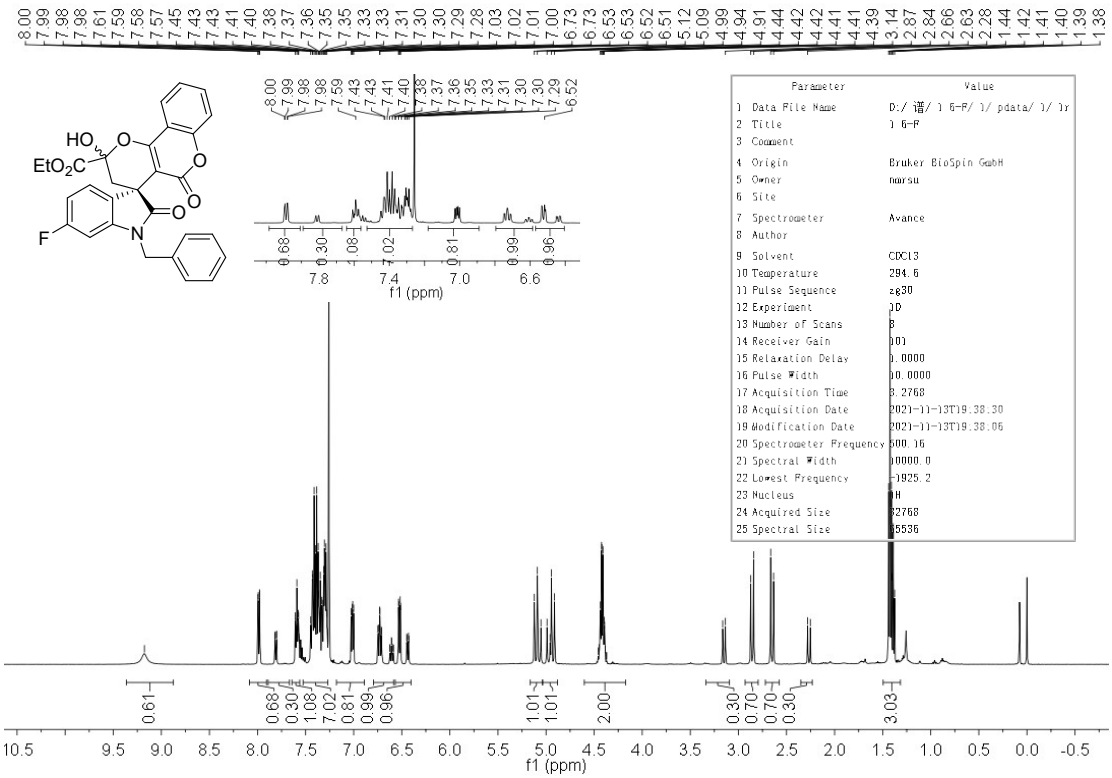
^{1}H NMR of **3fa**



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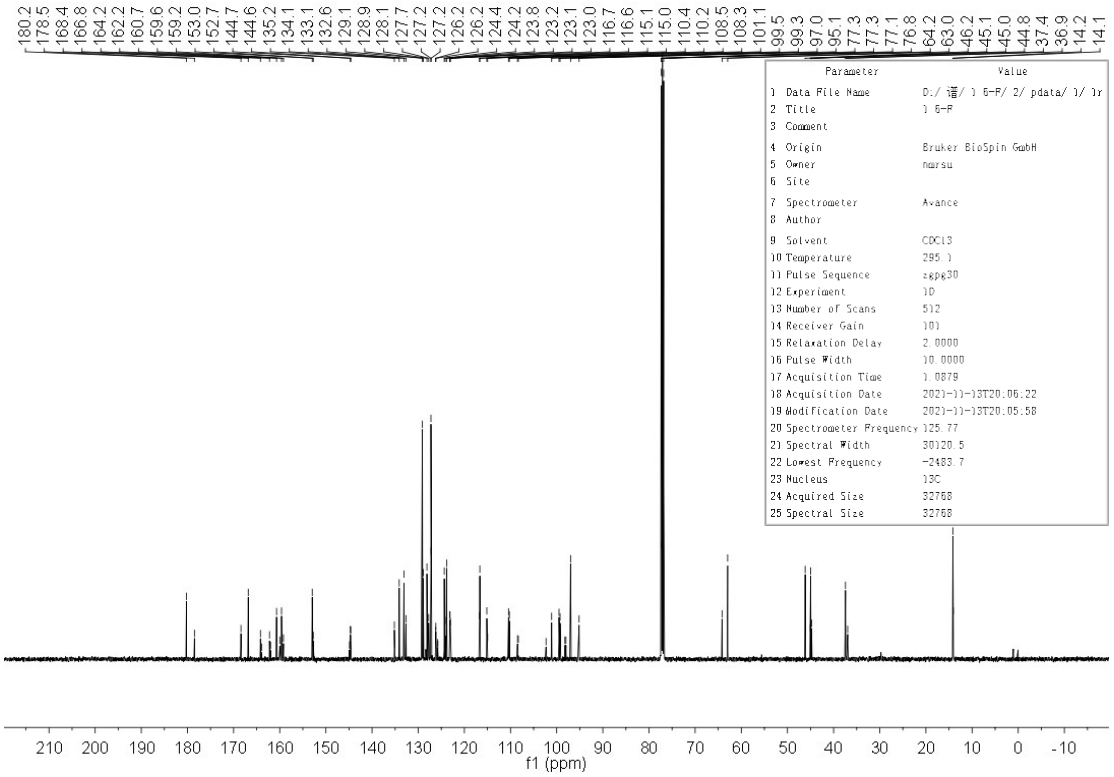
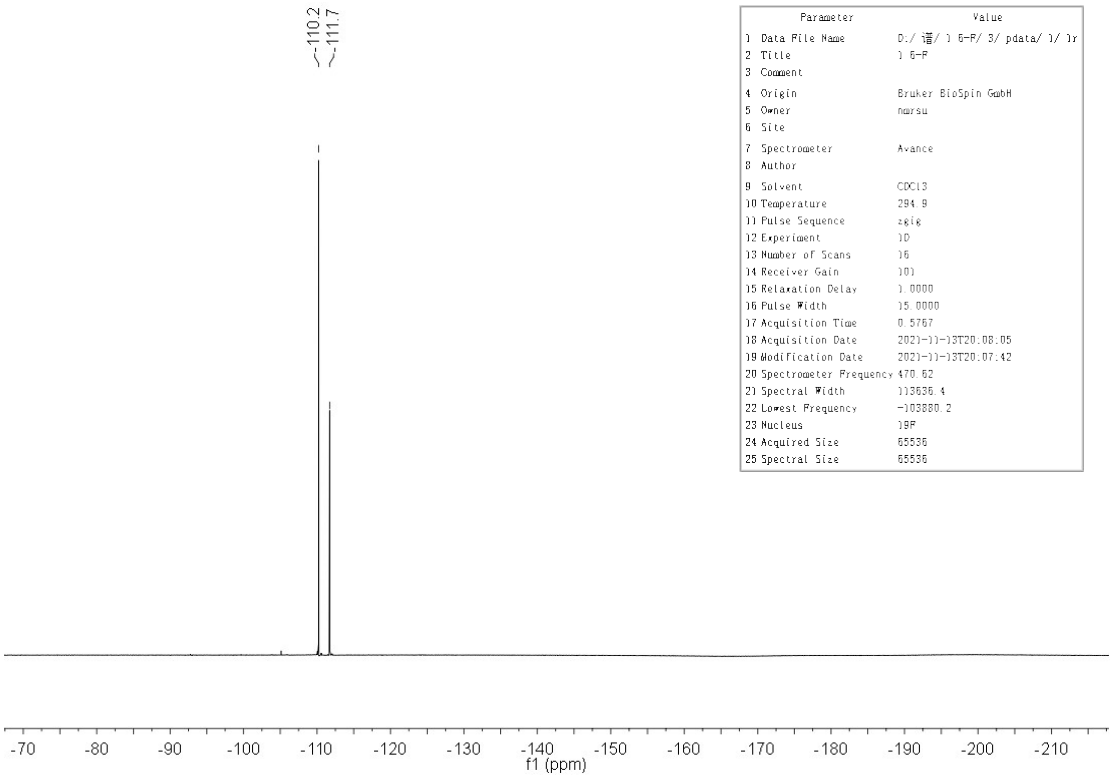
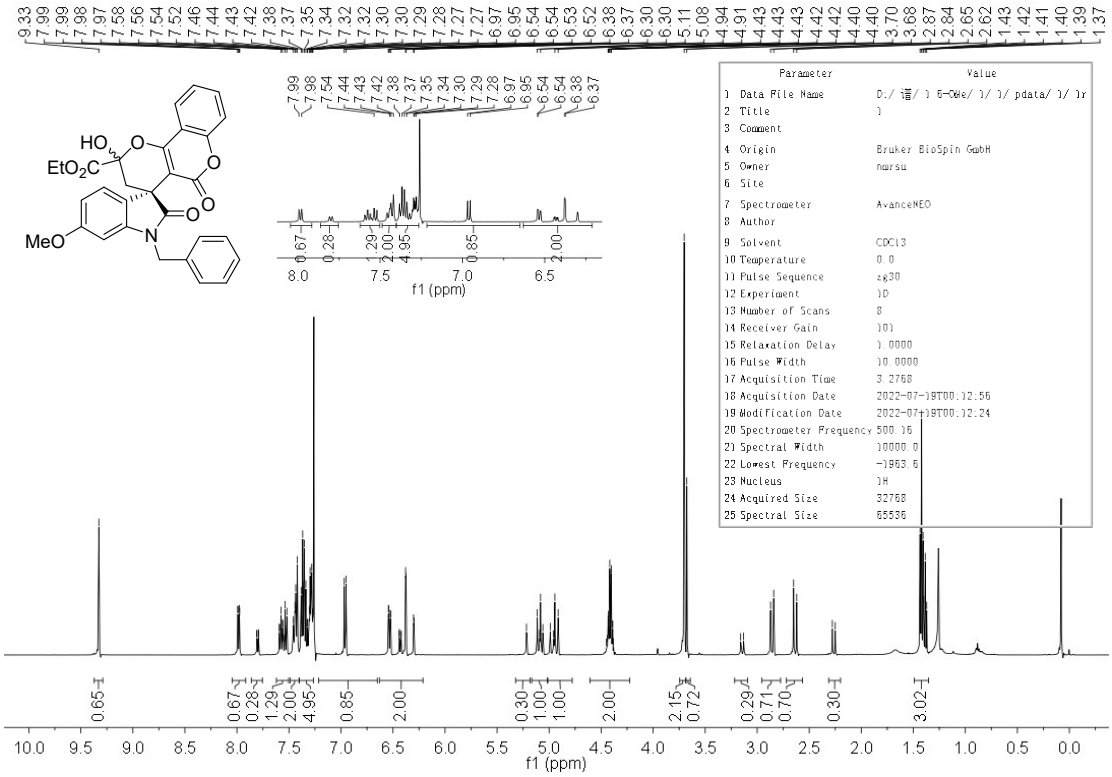
^{13}C NMR of **3fa**



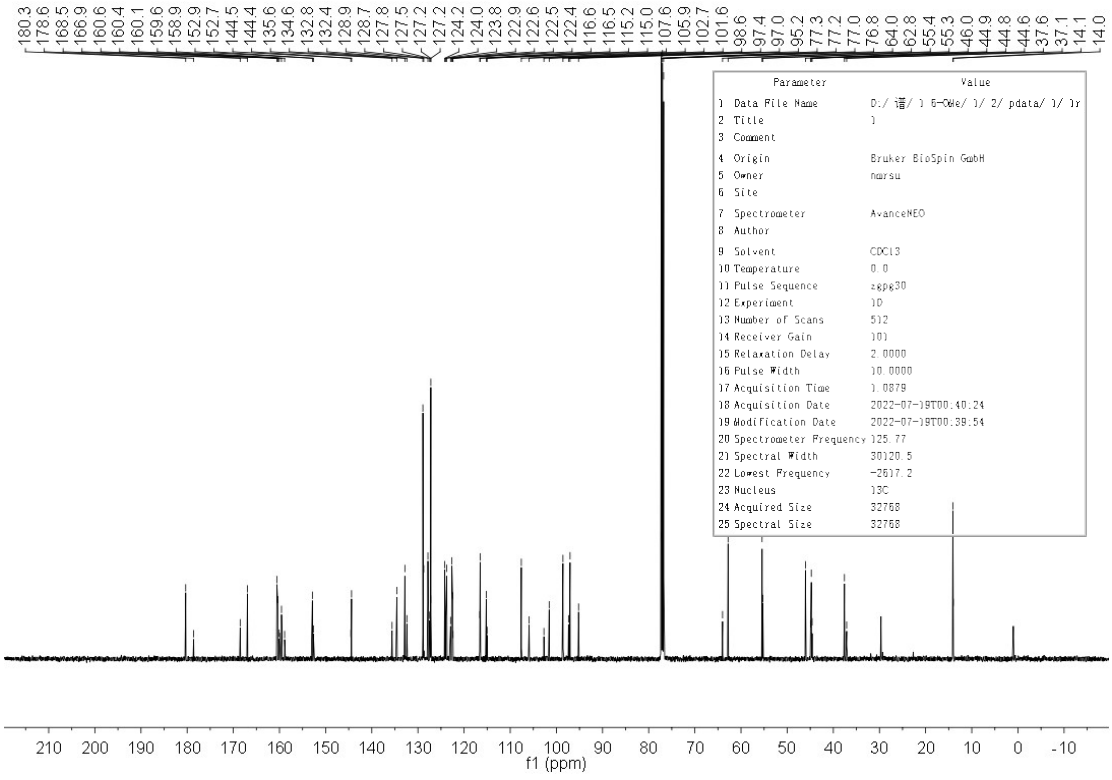
^{19}F NMR of **3fa**



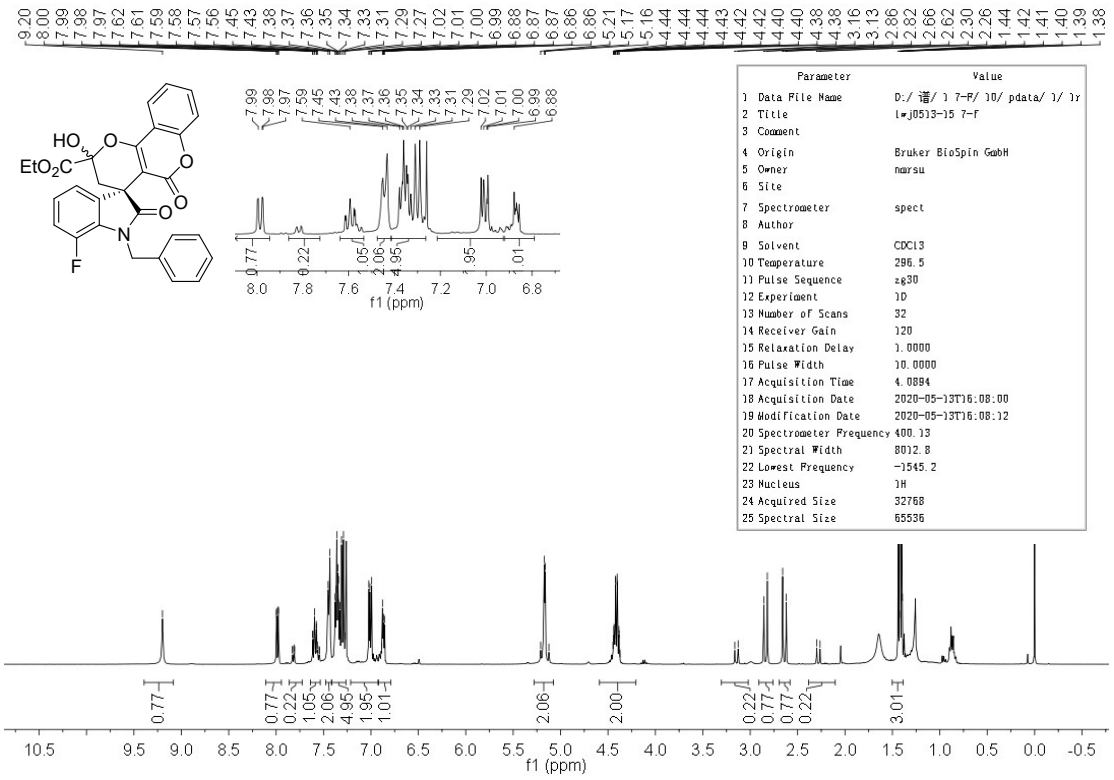
^{1}H NMR of **3ga**



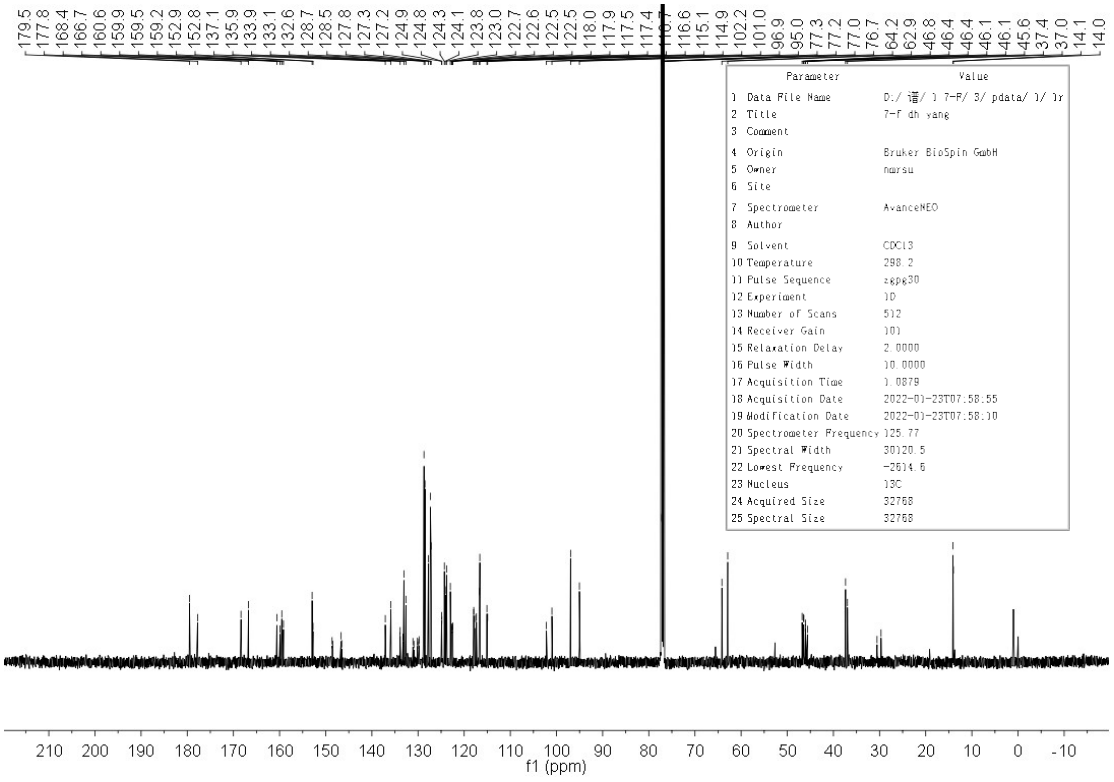
^{13}C NMR of **3ga**



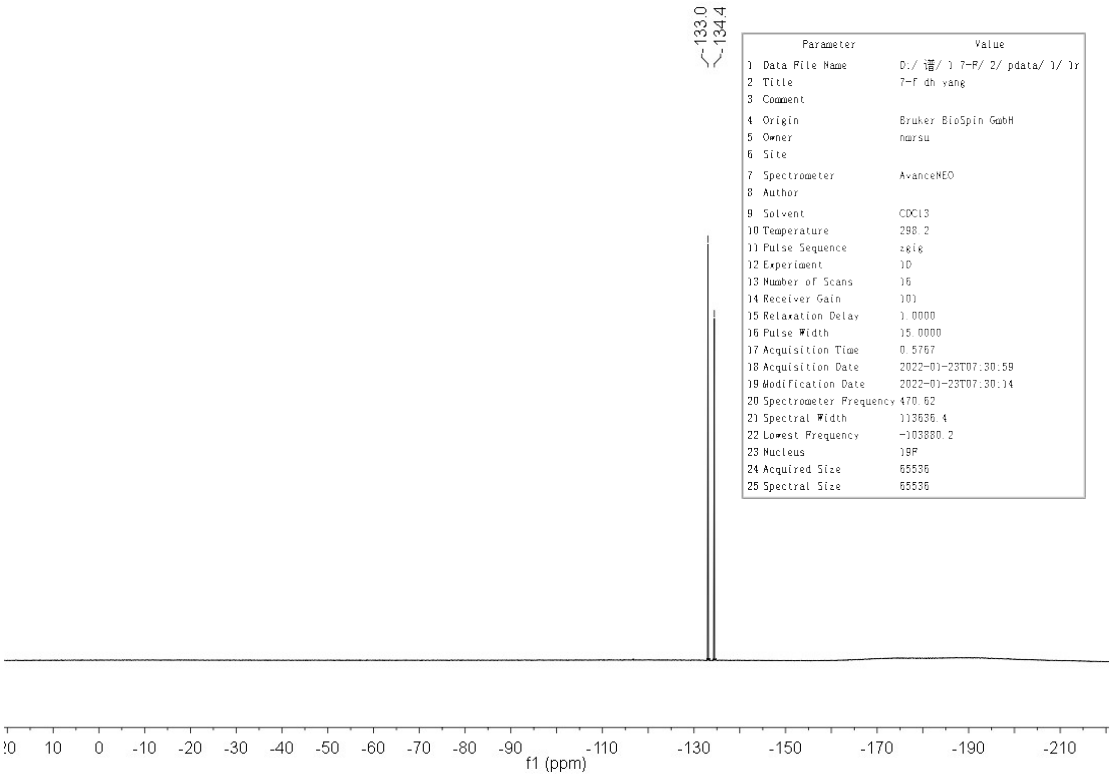
^{1}H NMR of **3ha**



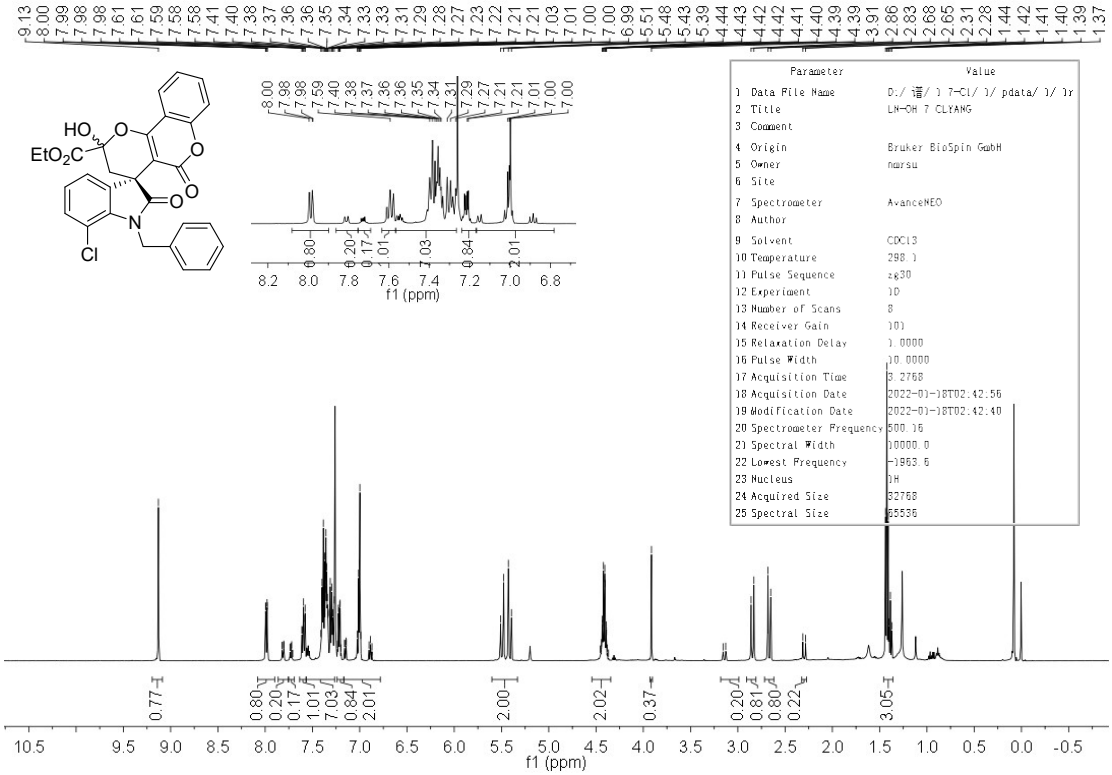
^{13}C NMR of **3ha**



^{19}F NMR of **3ha**



^{1}H NMR of **3ia**



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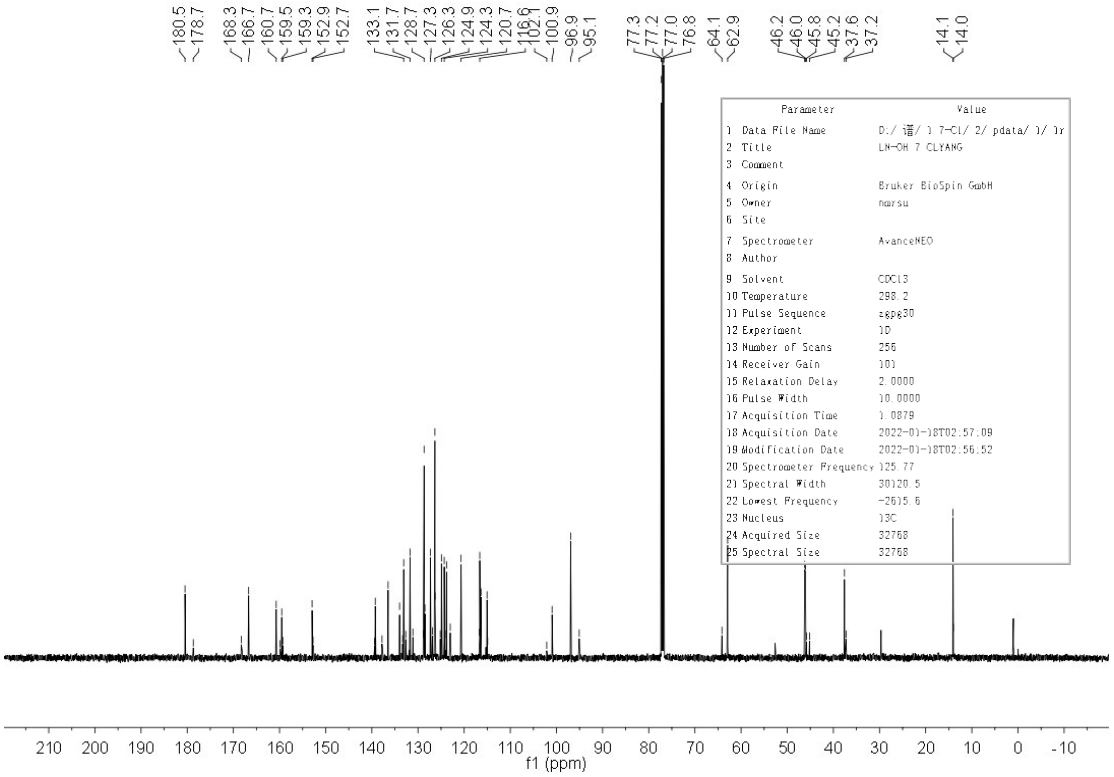

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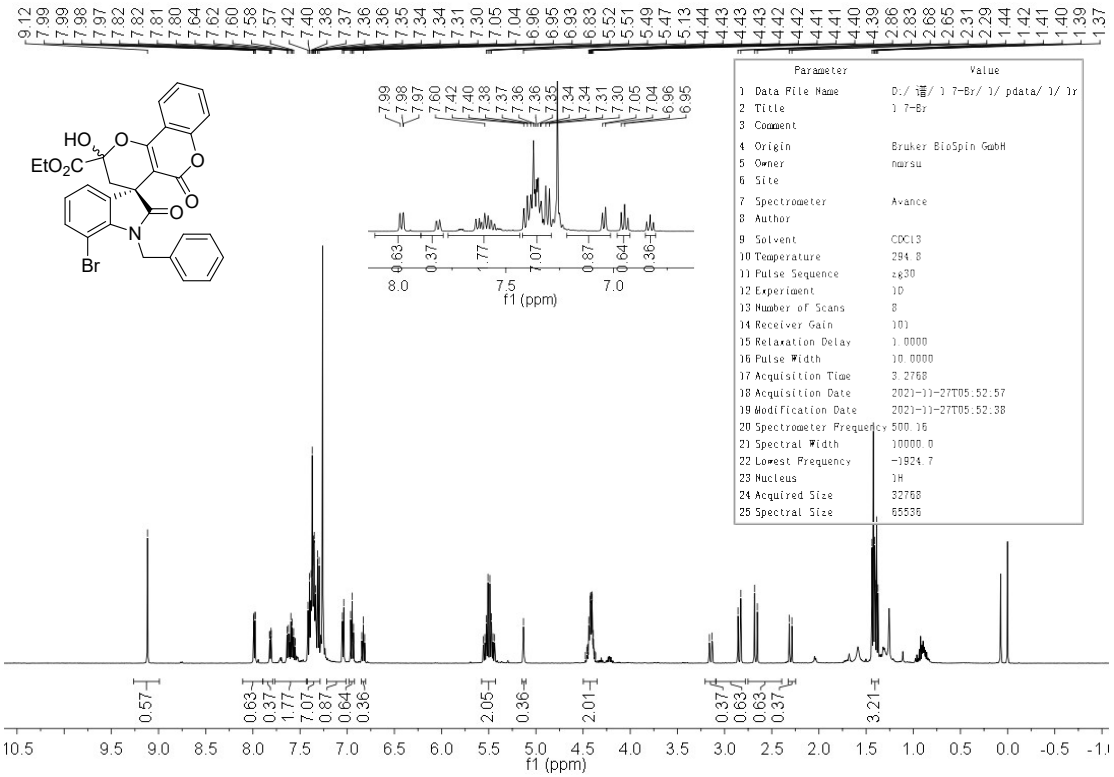
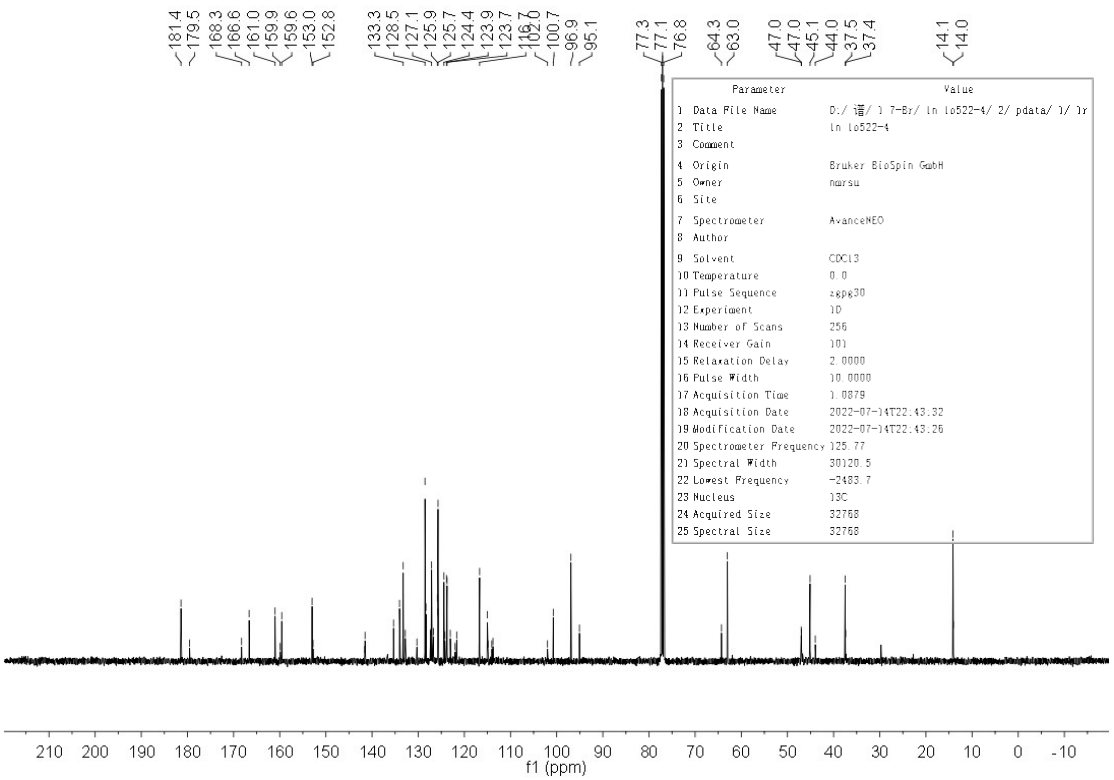
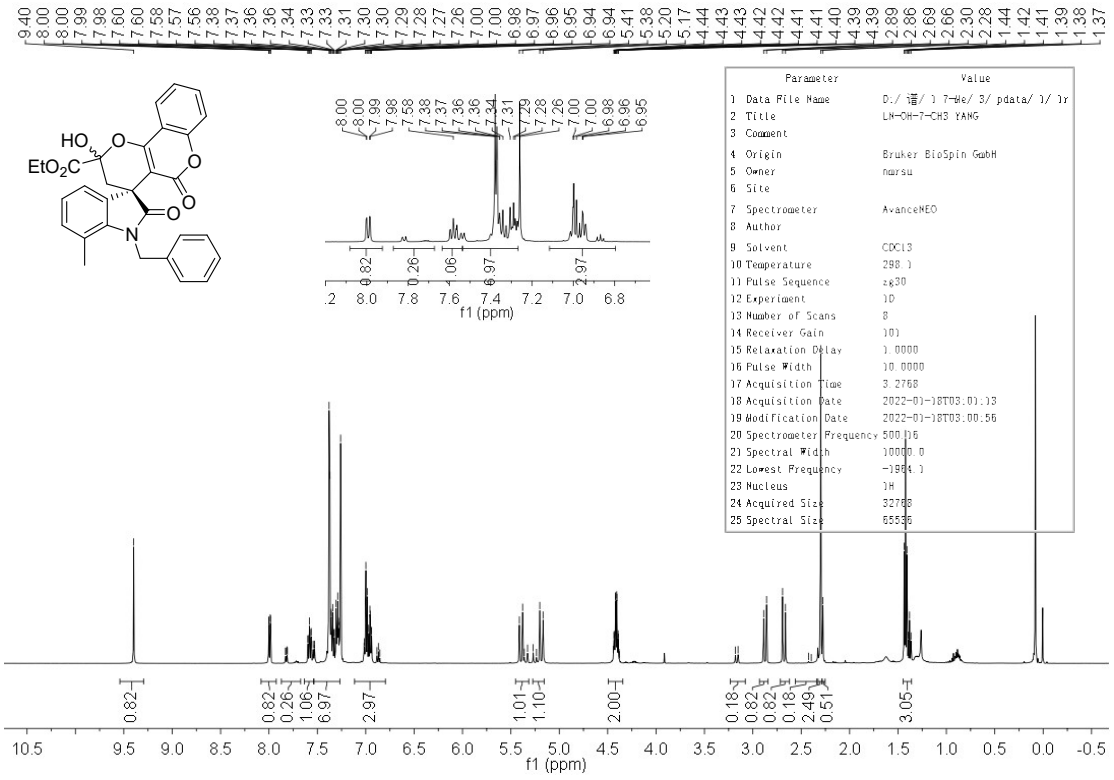


^{13}C NMR of **3ja**



^{1}H NMR of **3ka**



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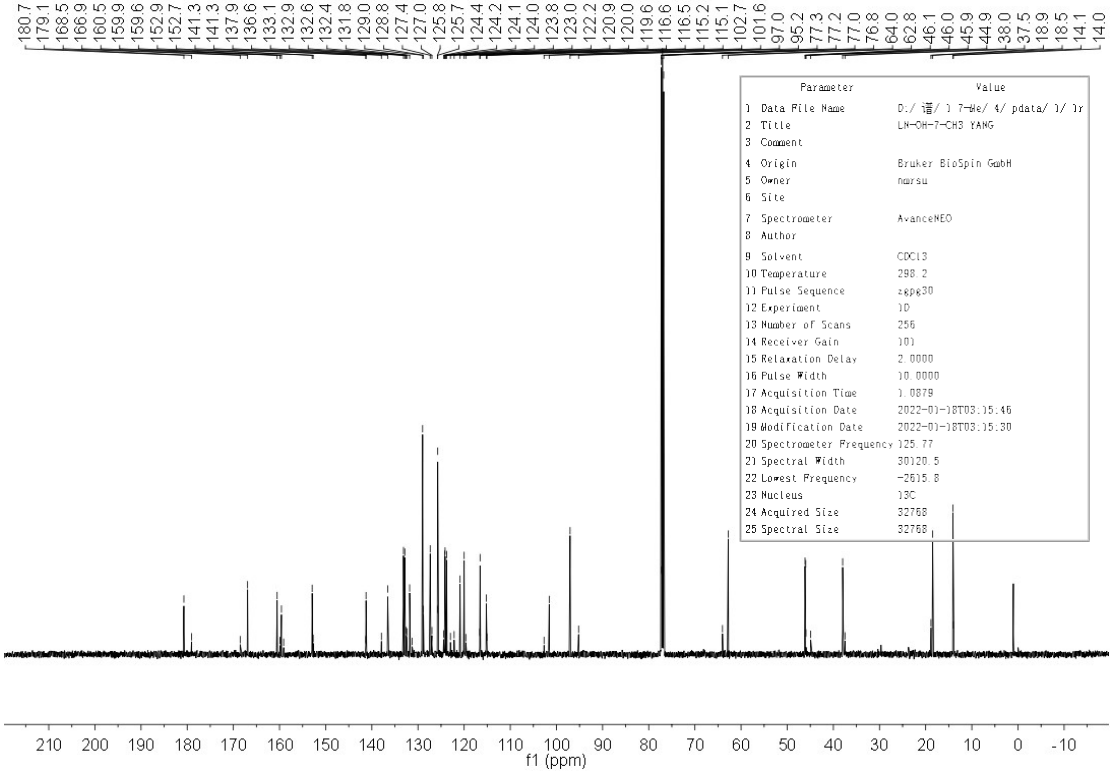
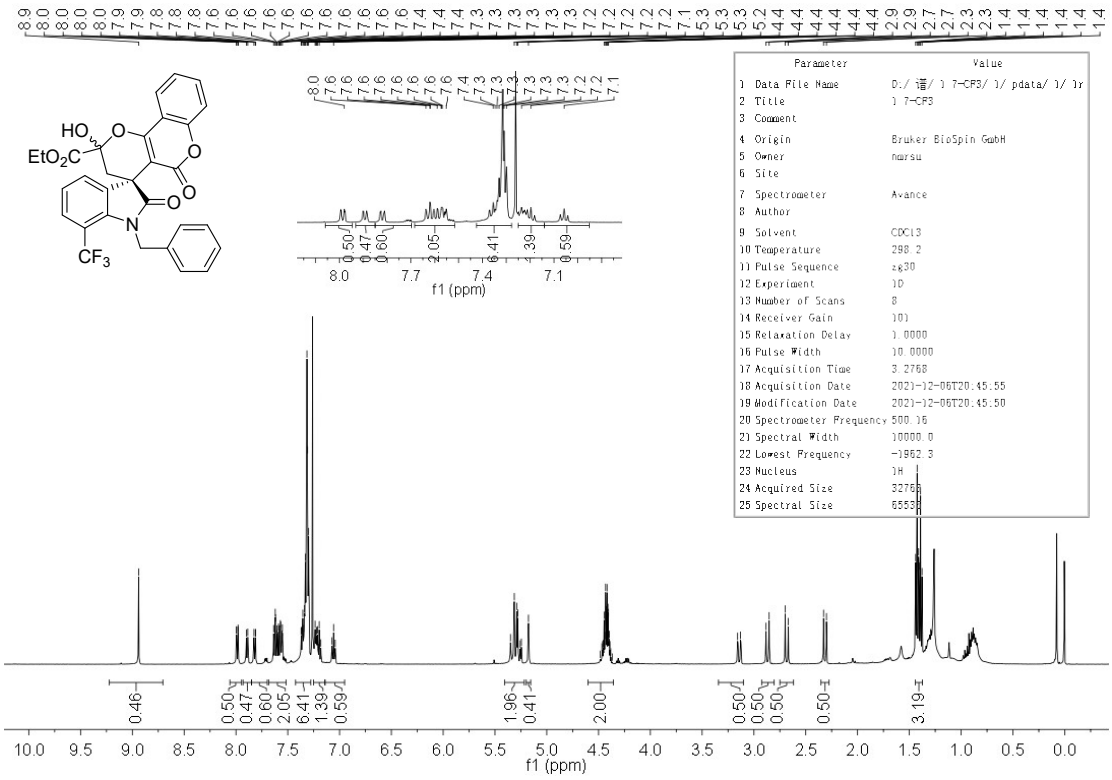
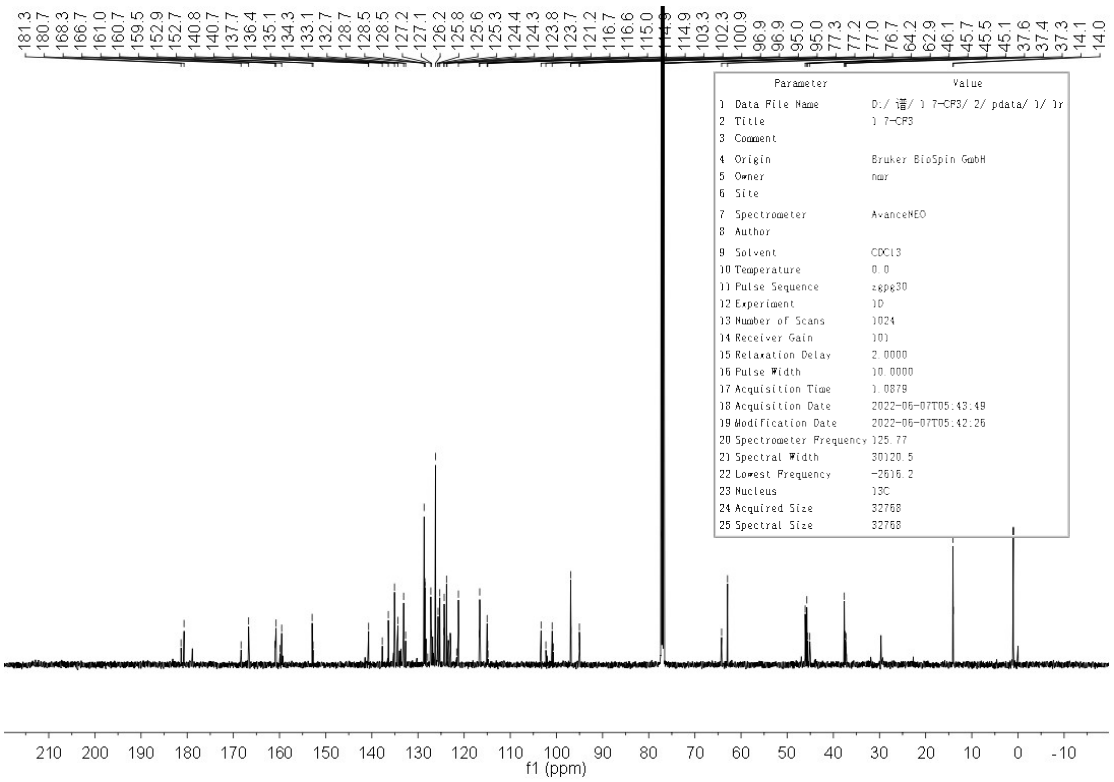


^{1}H NMR of **3la**



^{13}C NMR of **3la**



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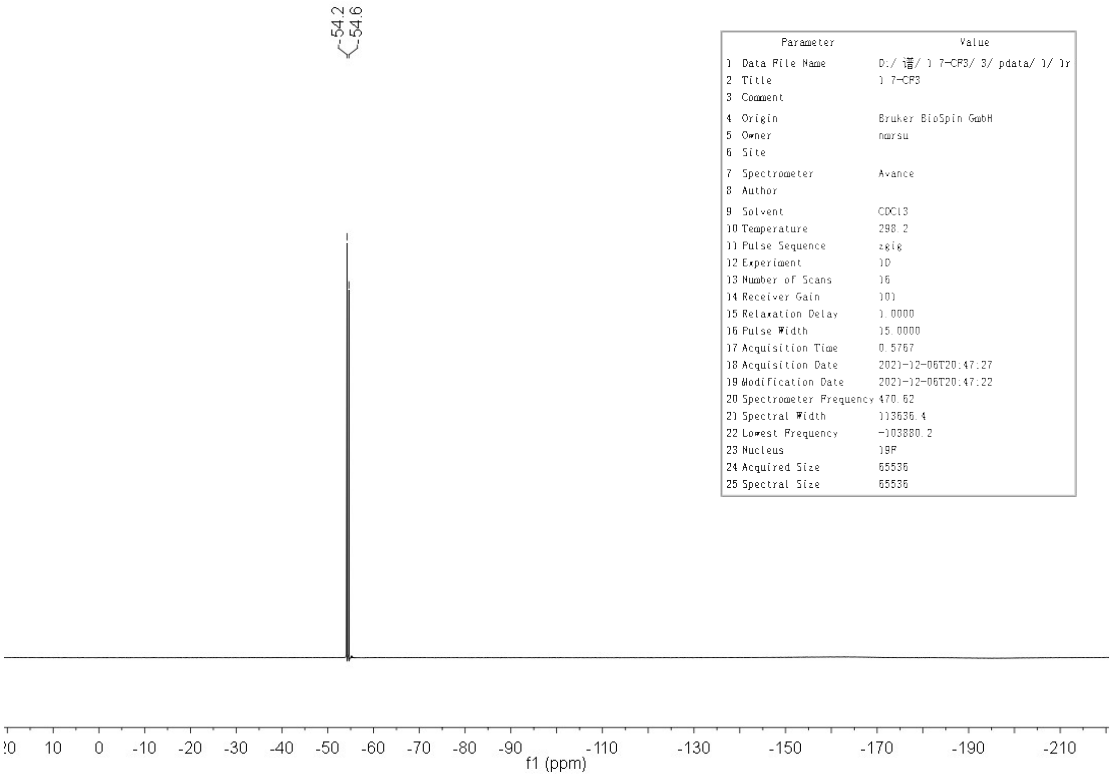
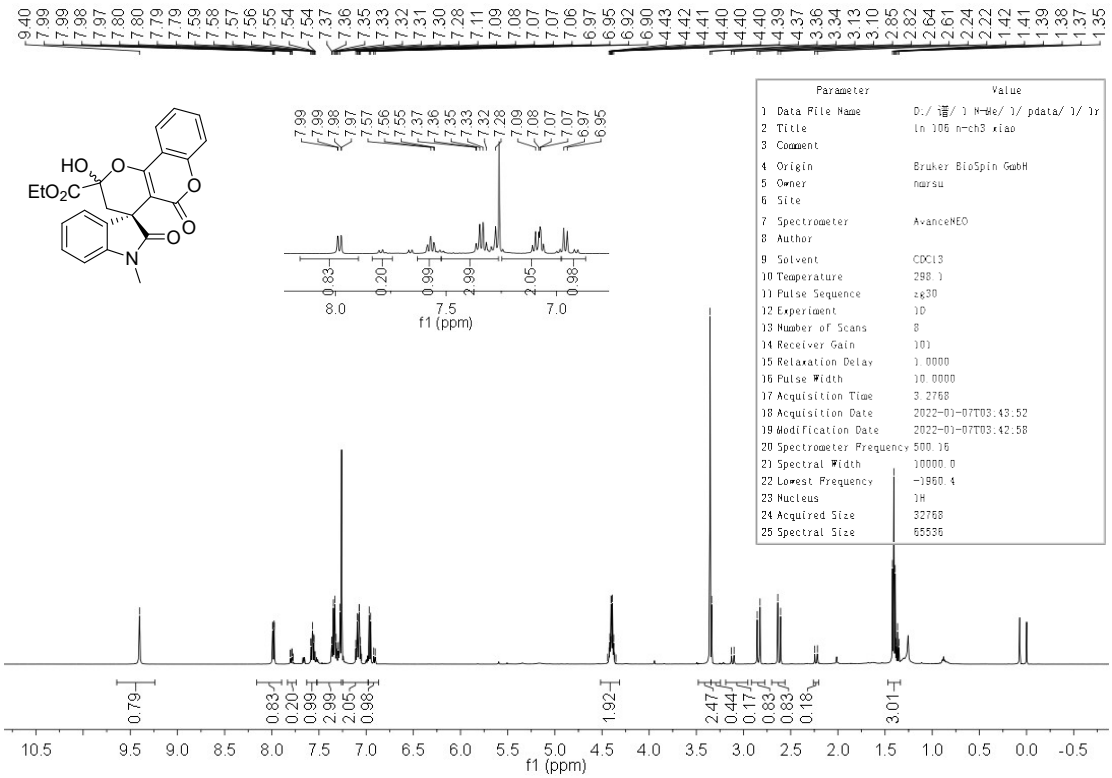


^{1}H NMR of **3ma**



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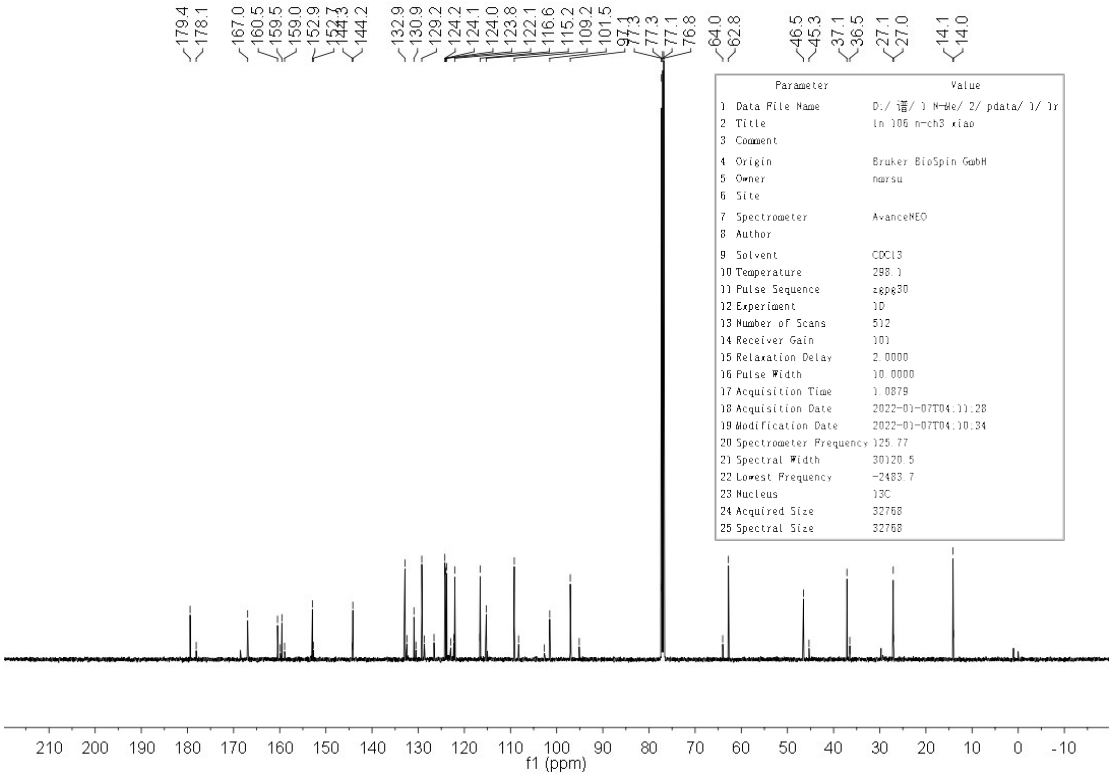
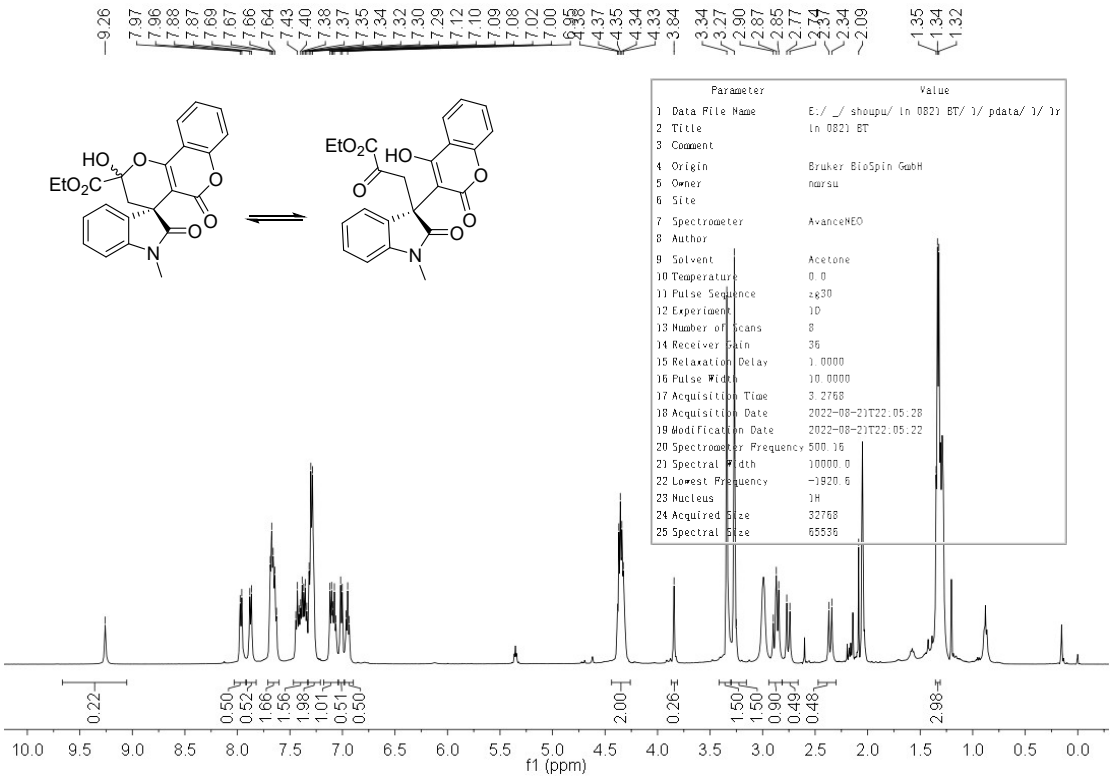
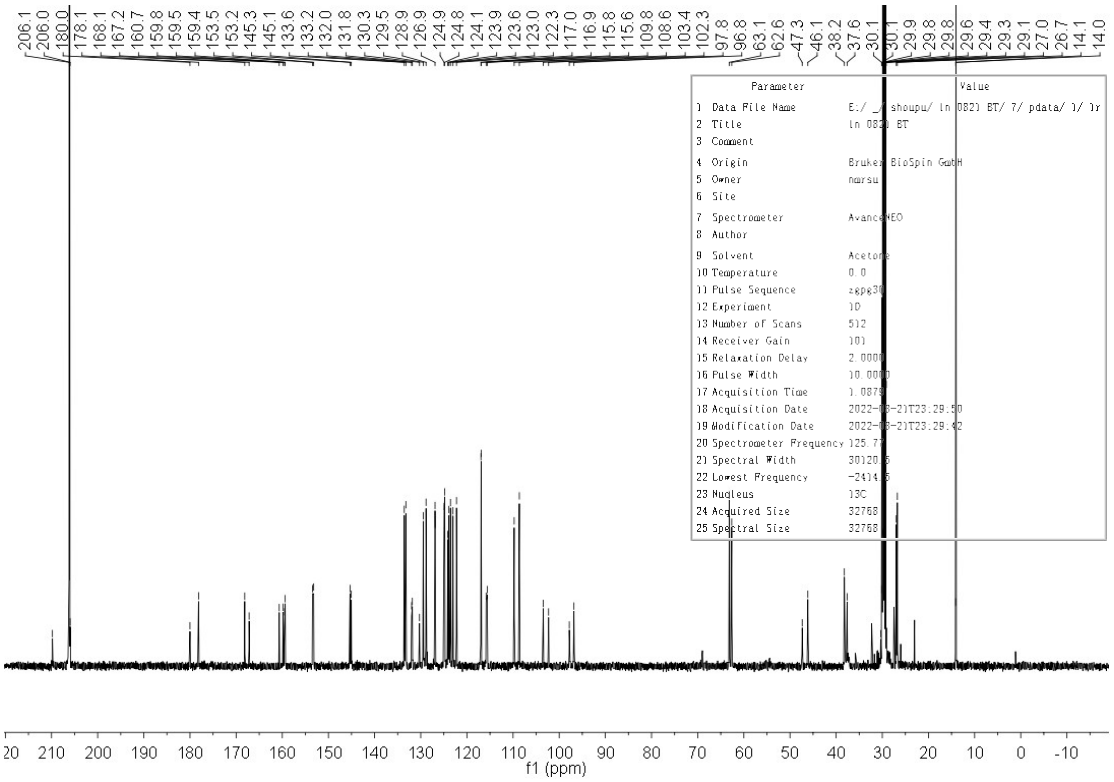


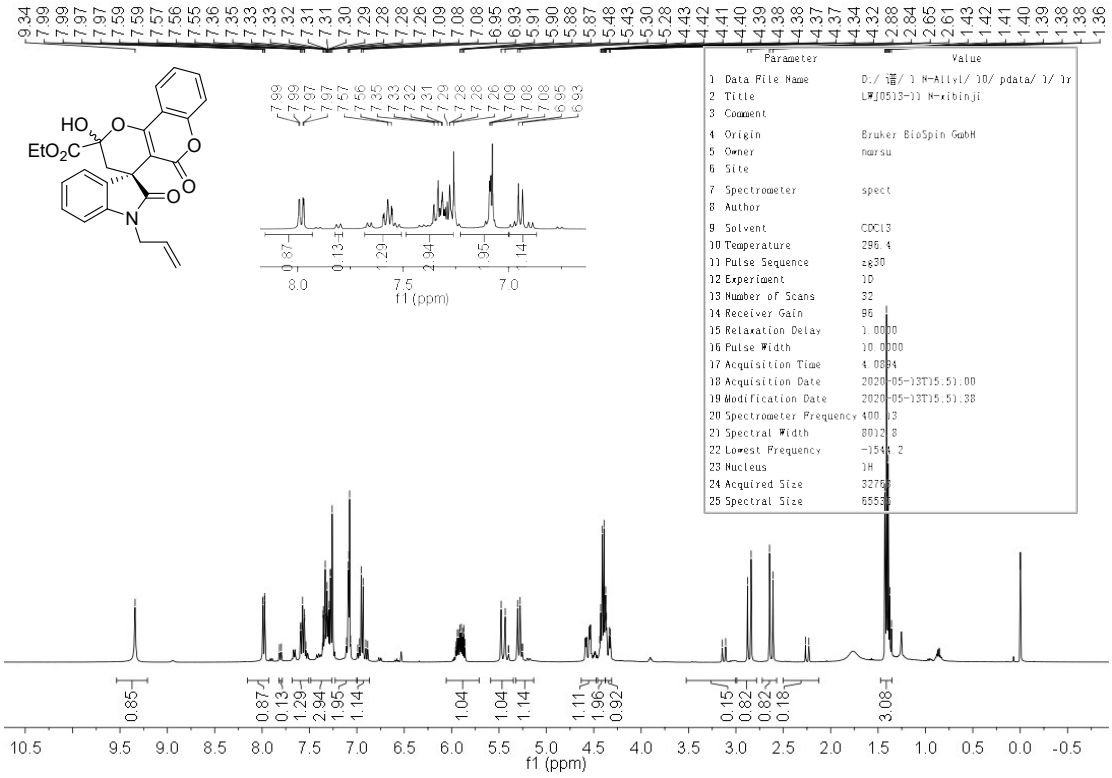
^{1}H NMR of **3ma (acetone-d_6)**



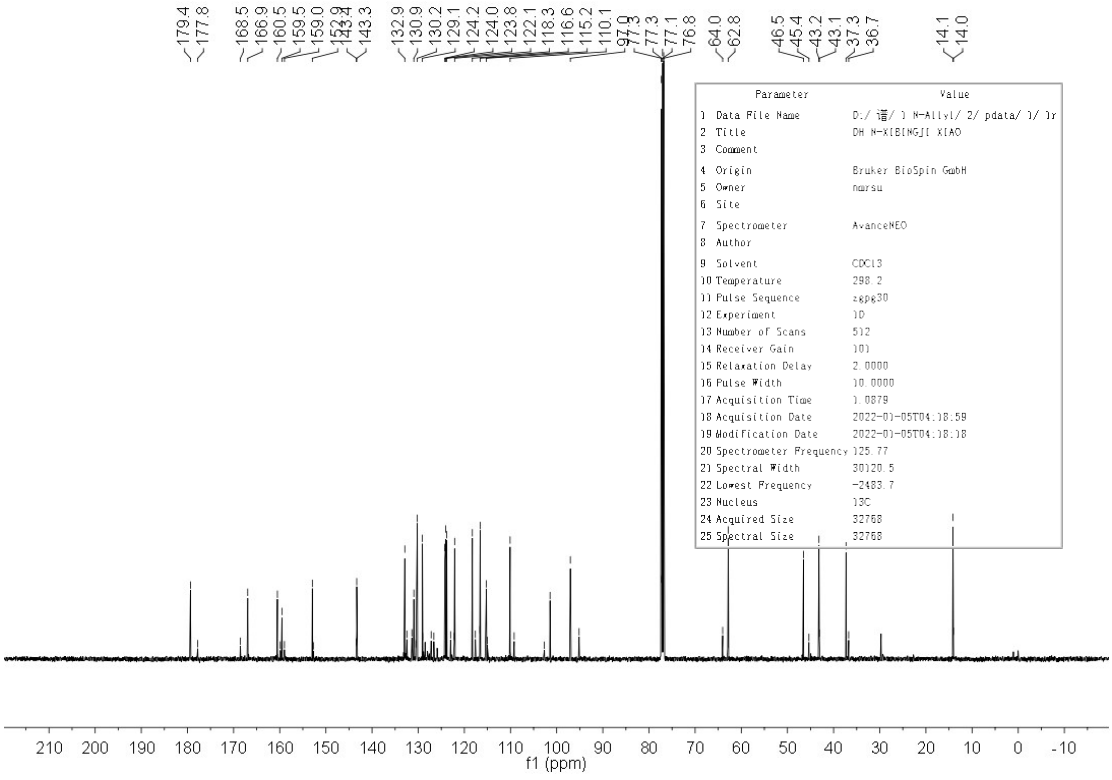
^{13}C NMR of **3ma (acetone-d_6)**



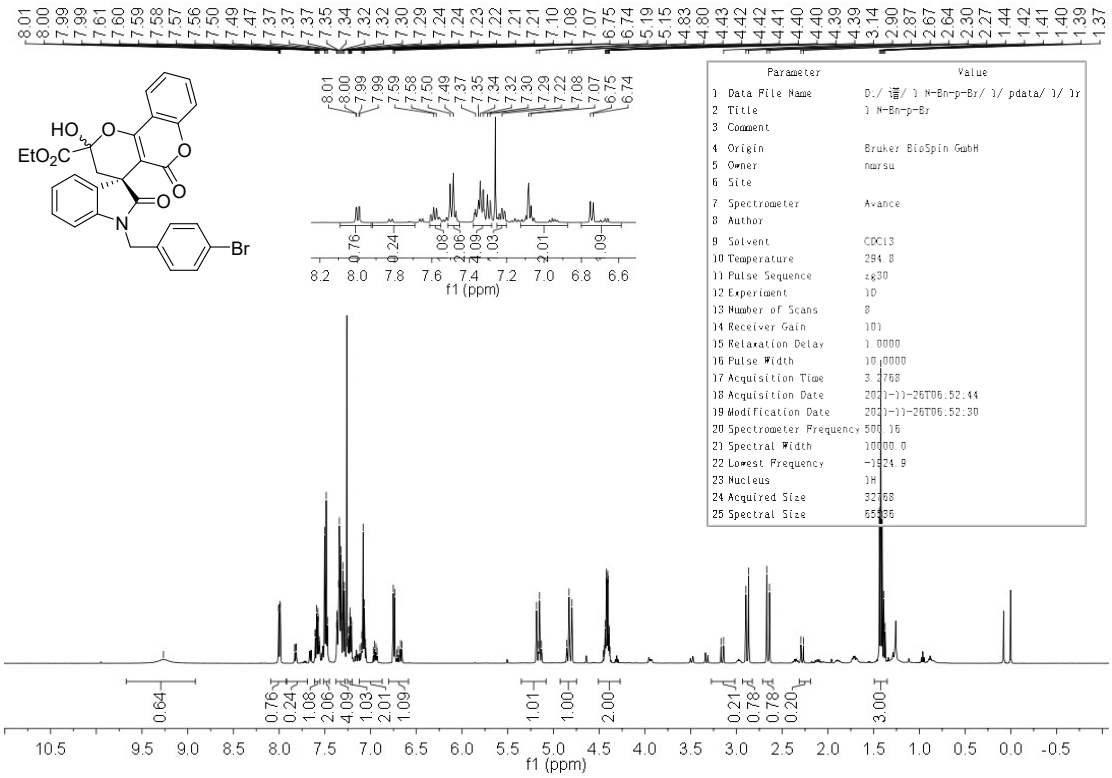
^{1}H NMR of **3na**



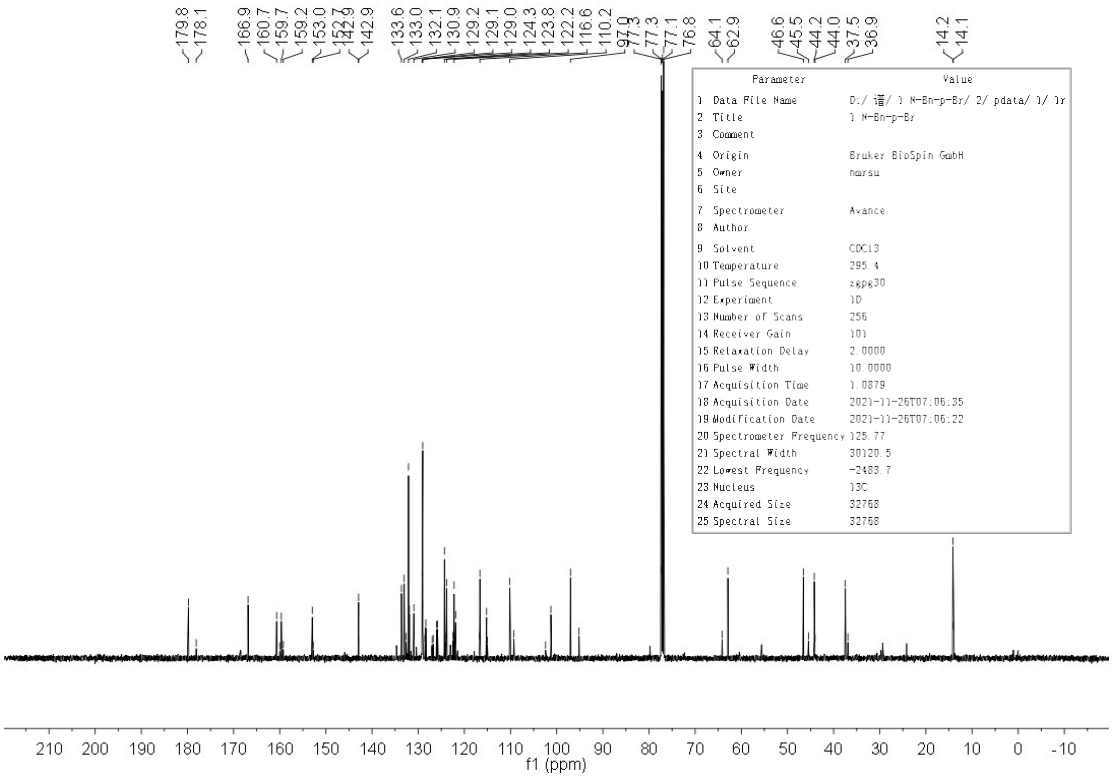
^{13}C NMR of **3na**



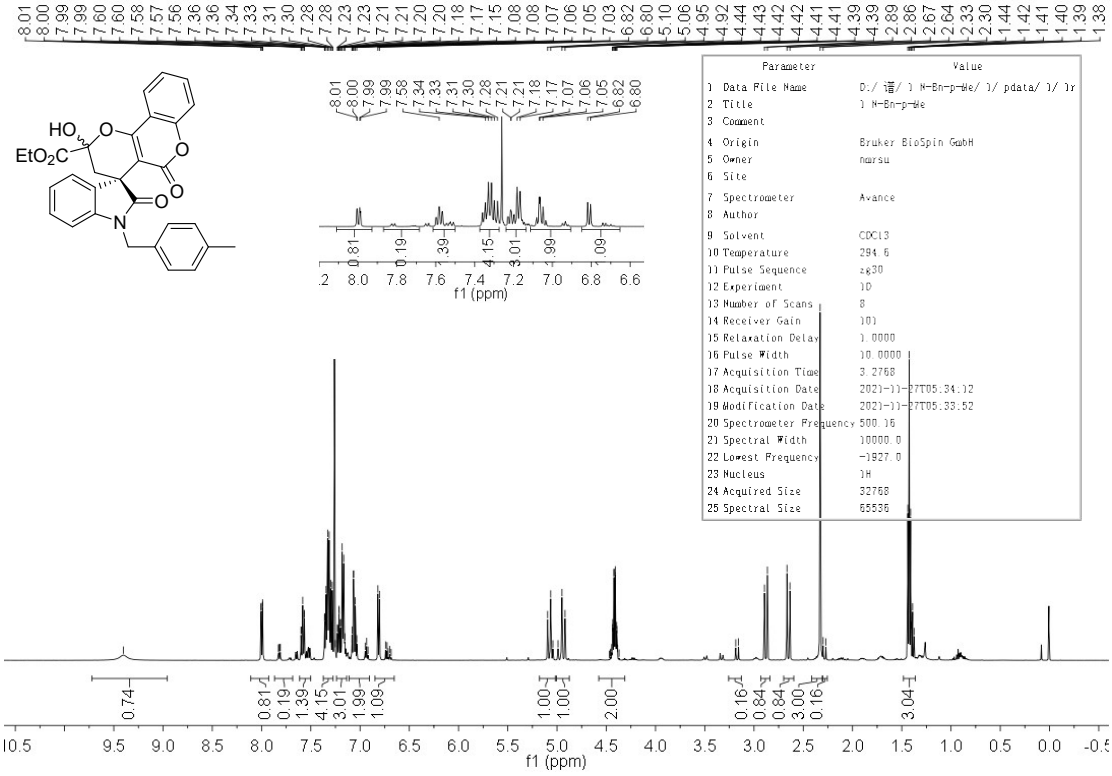
^{1}H NMR of **3oa**



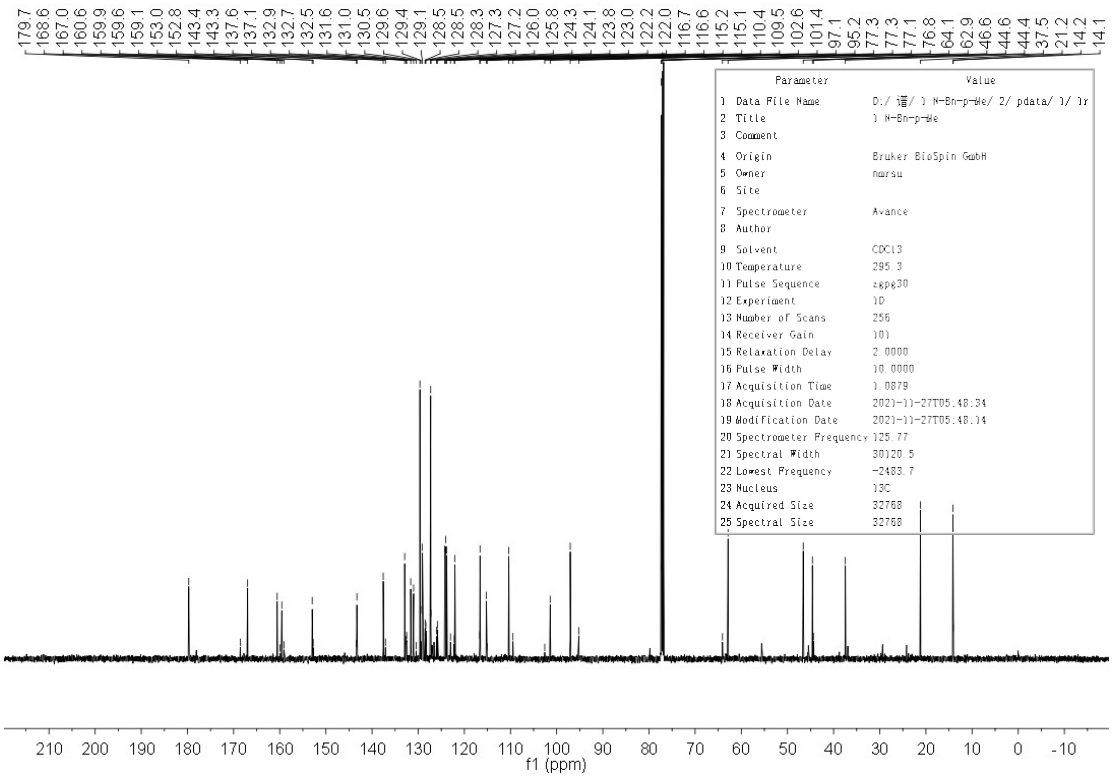
^{13}C NMR of **3oa**



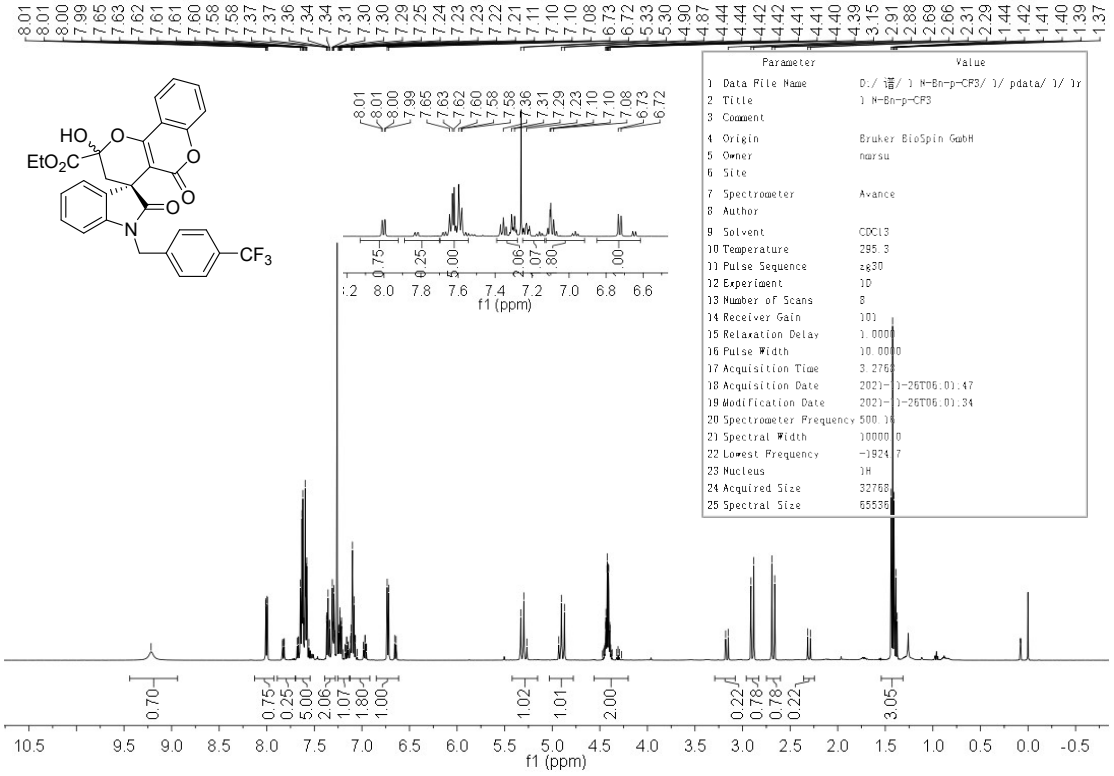
^{1}H NMR of **3pa**



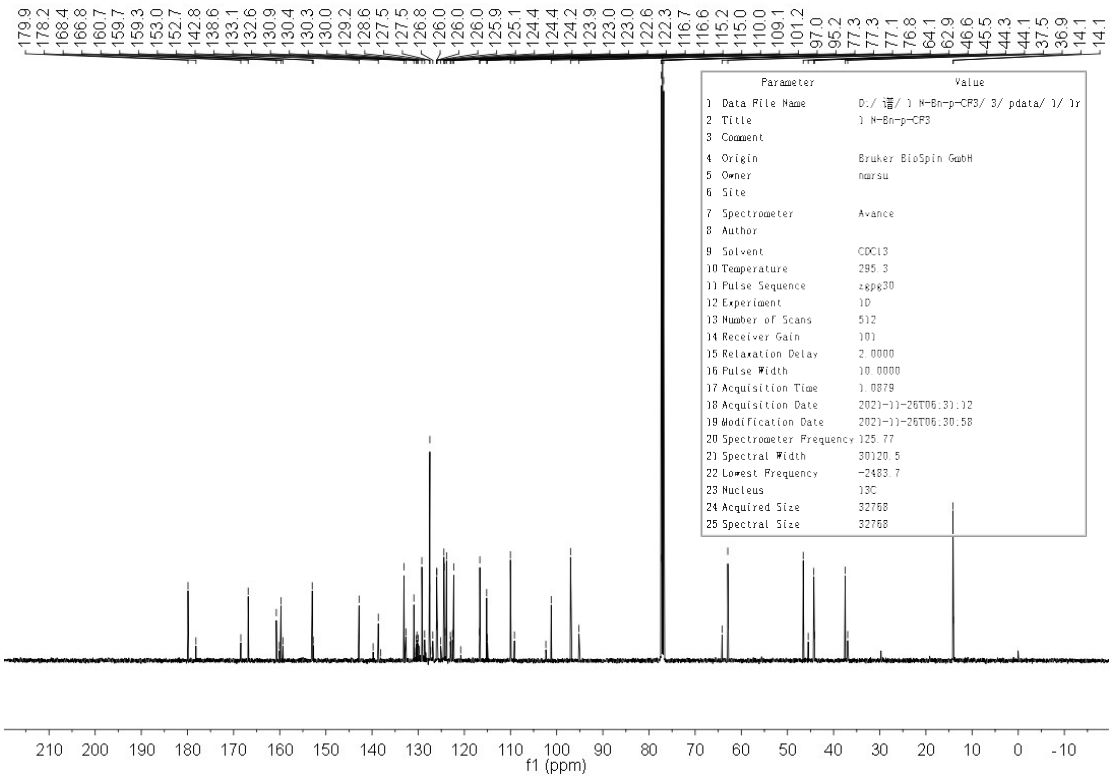
^{13}C NMR of **3pa**



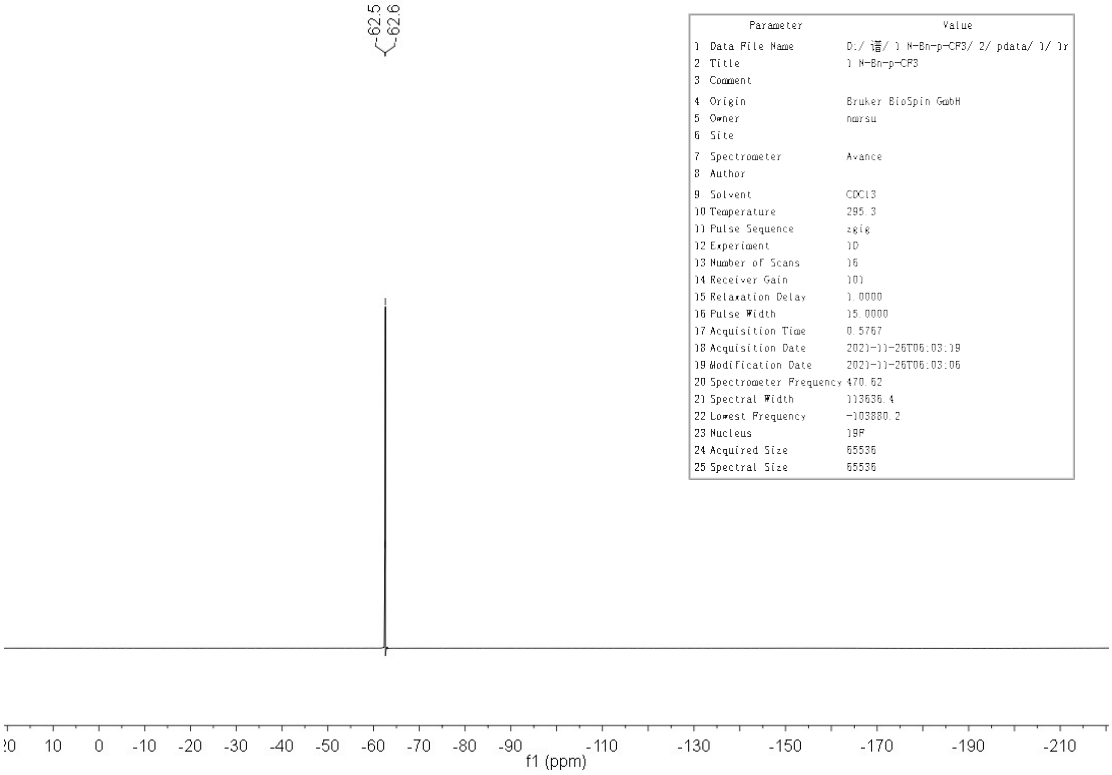
^{1}H NMR of **3qa**



^{13}C NMR of **3qa**



^{19}F NMR of **3qa**



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6 Site	
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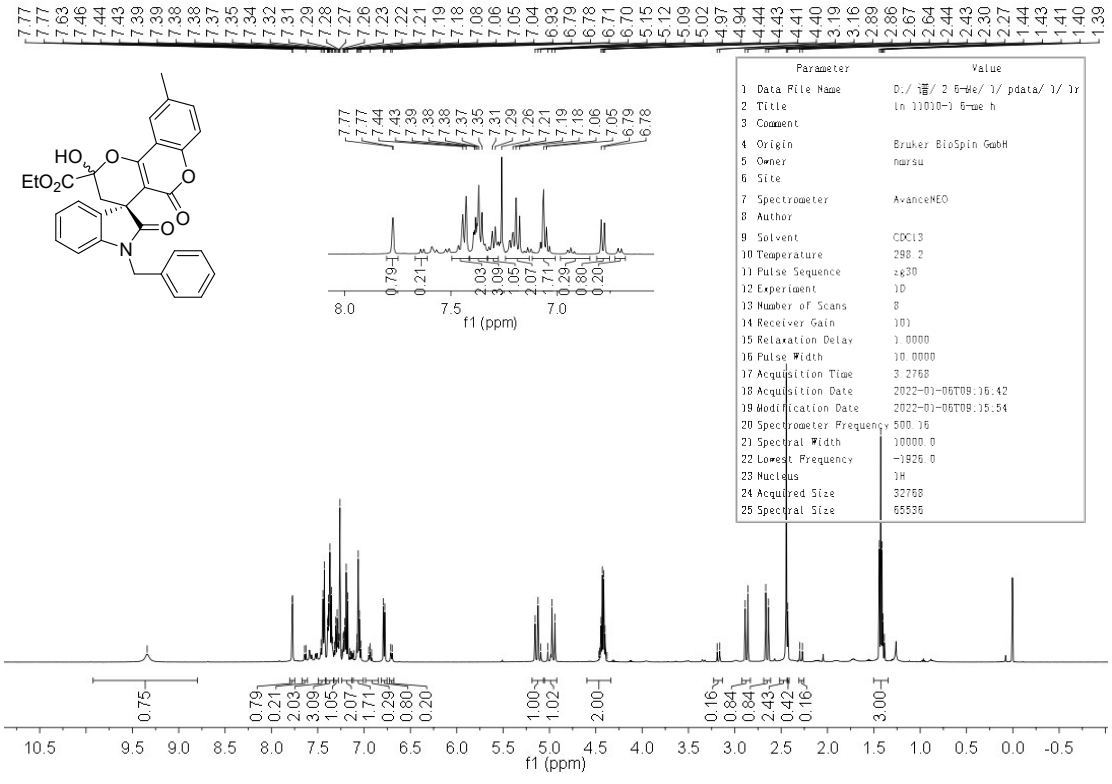
^{1}H NMR of **3ab**



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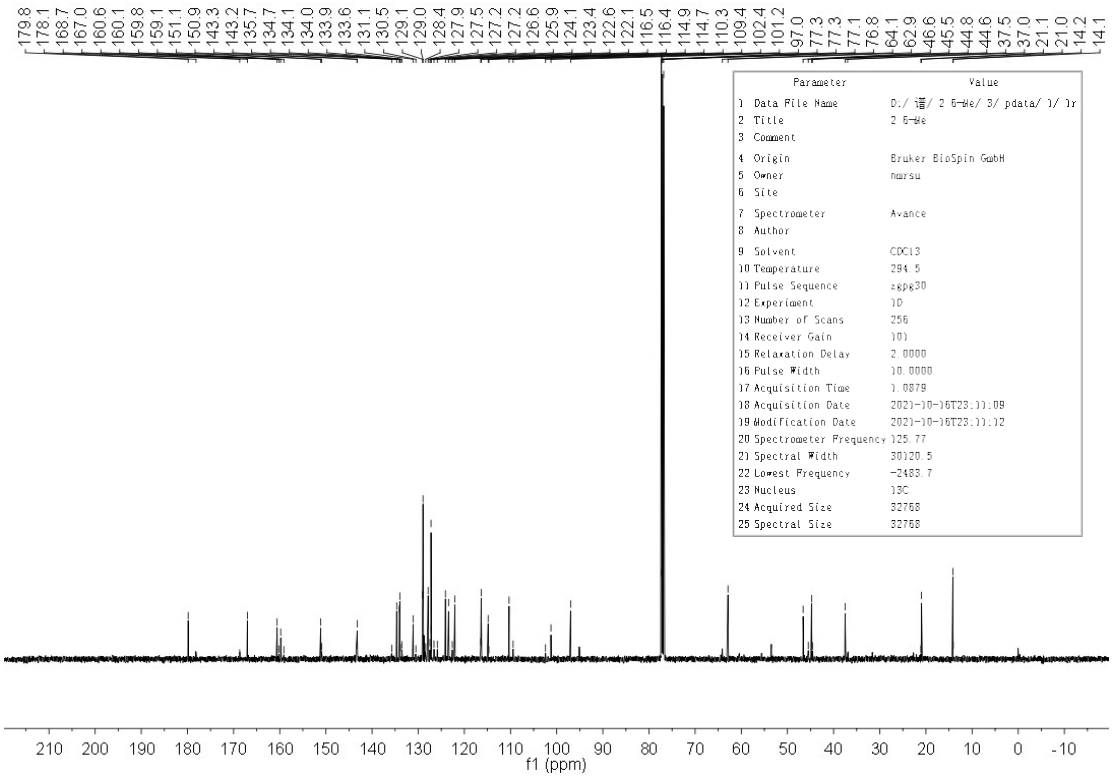
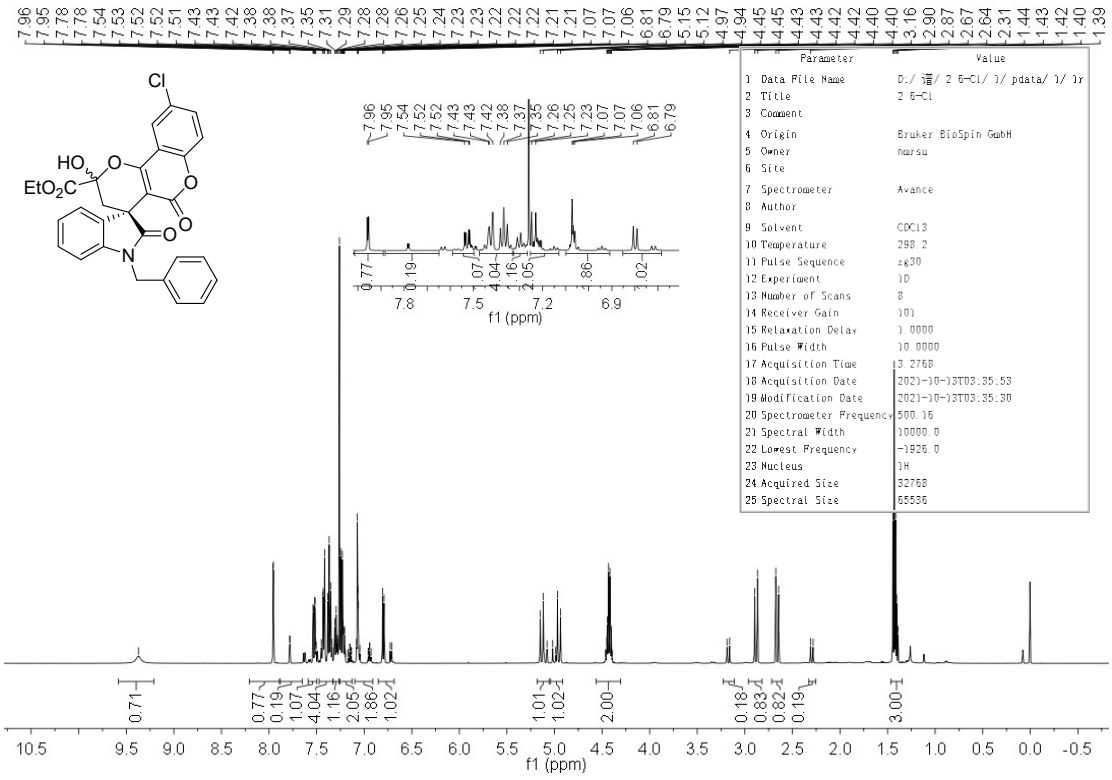
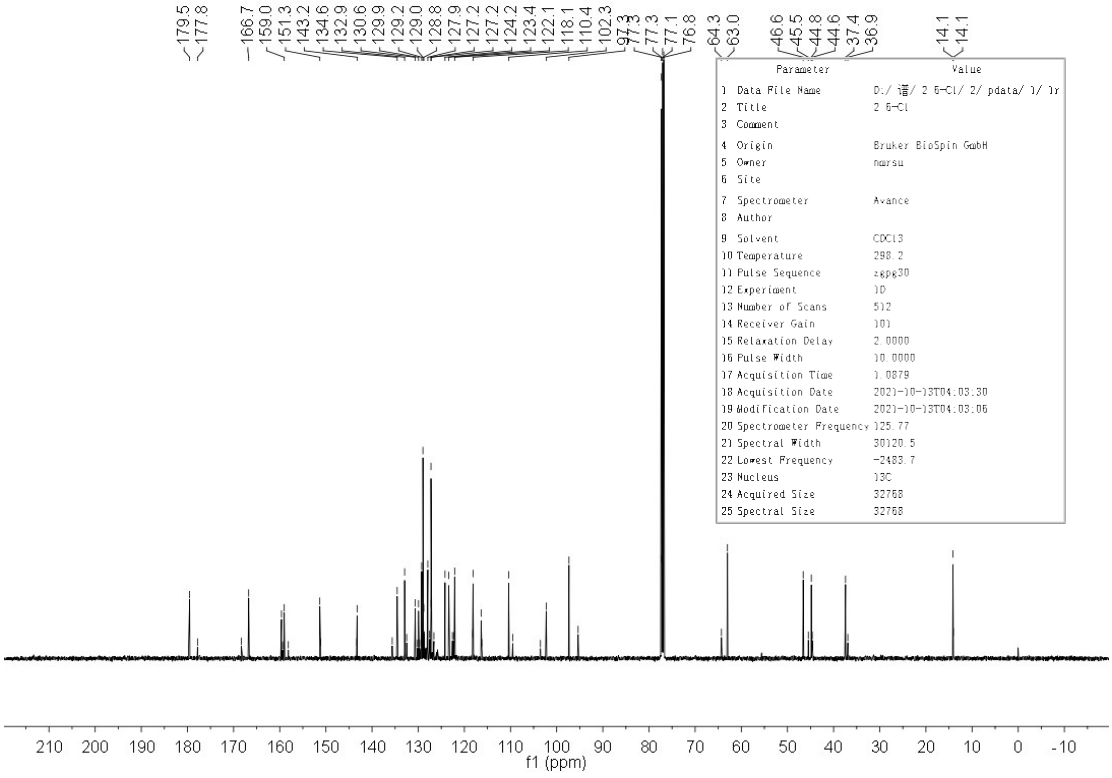
^{13}C NMR of **3ab**



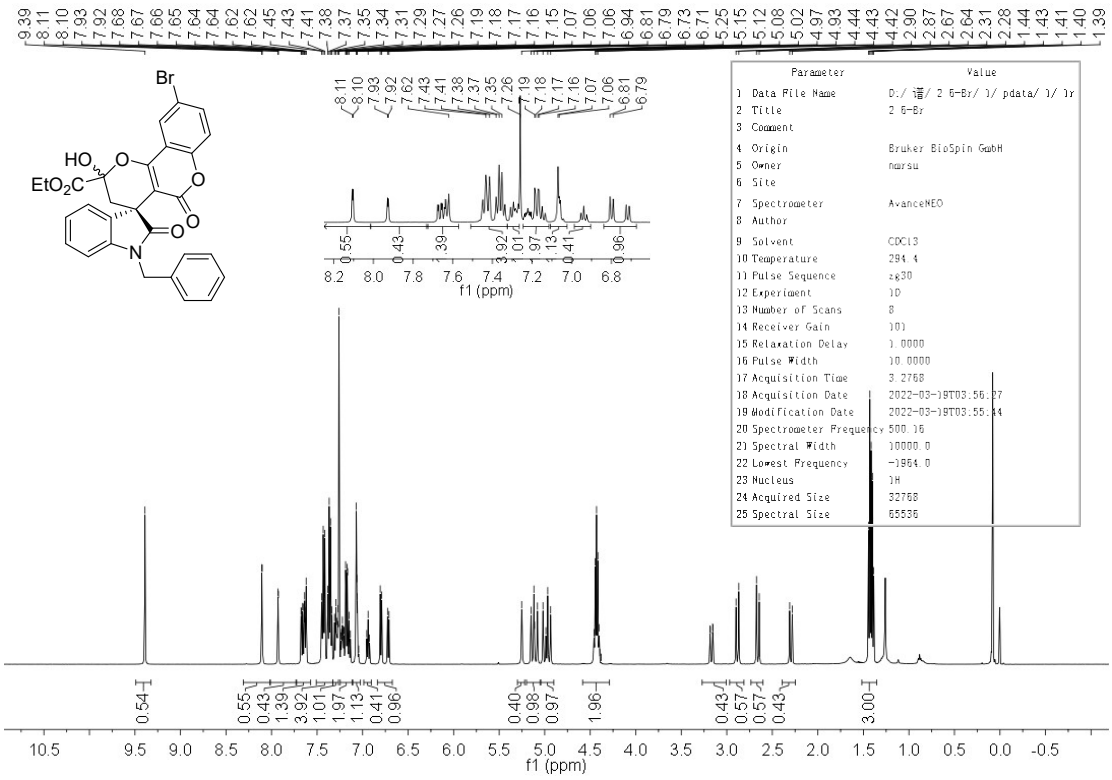
^{1}H NMR of **3ac**



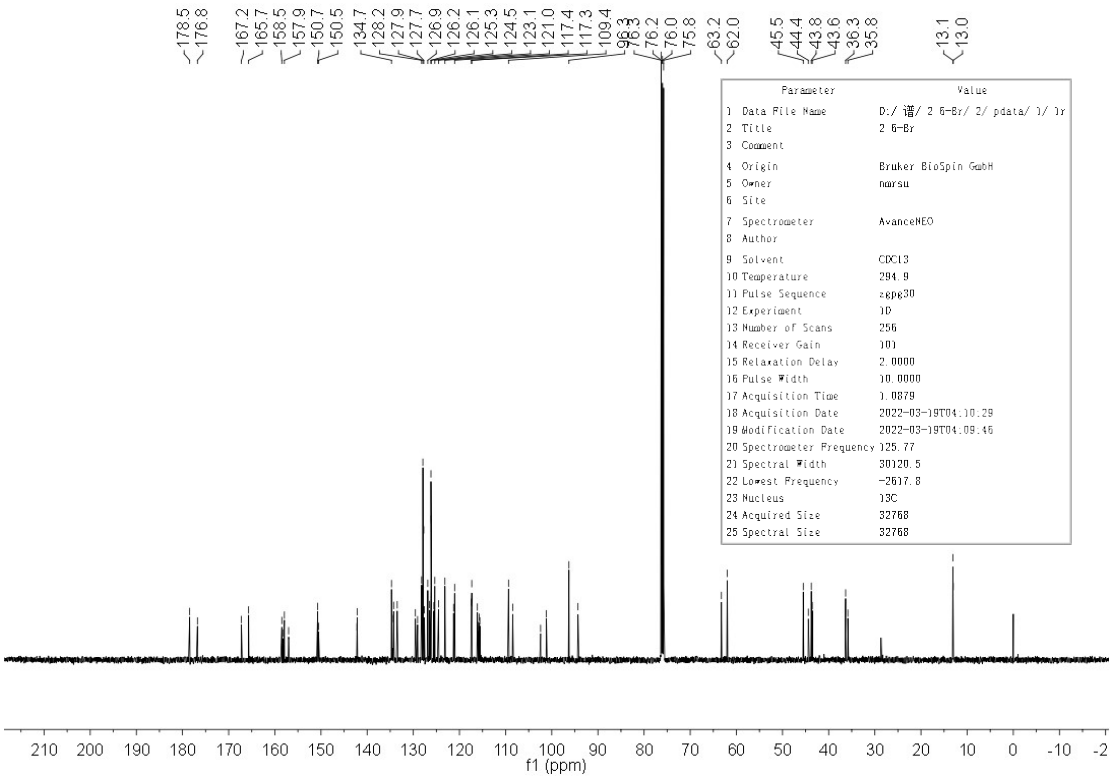
^{13}C NMR of **3ac**



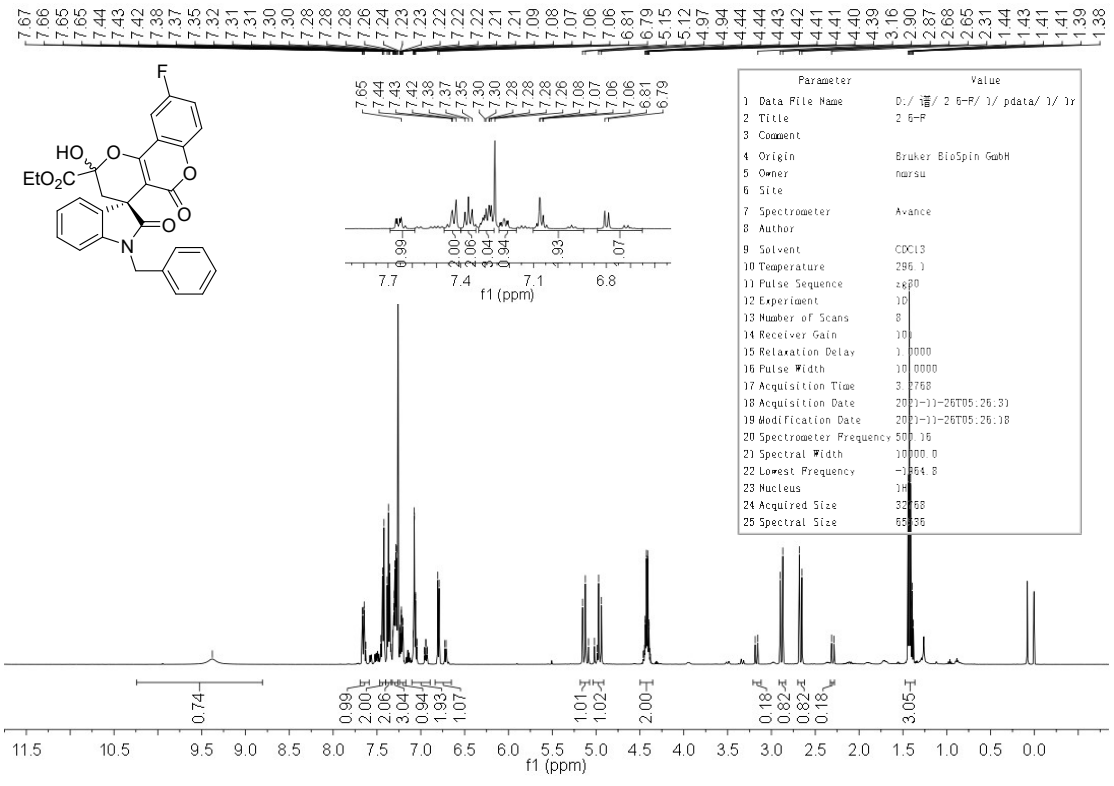
^{1}H NMR of **3ad**



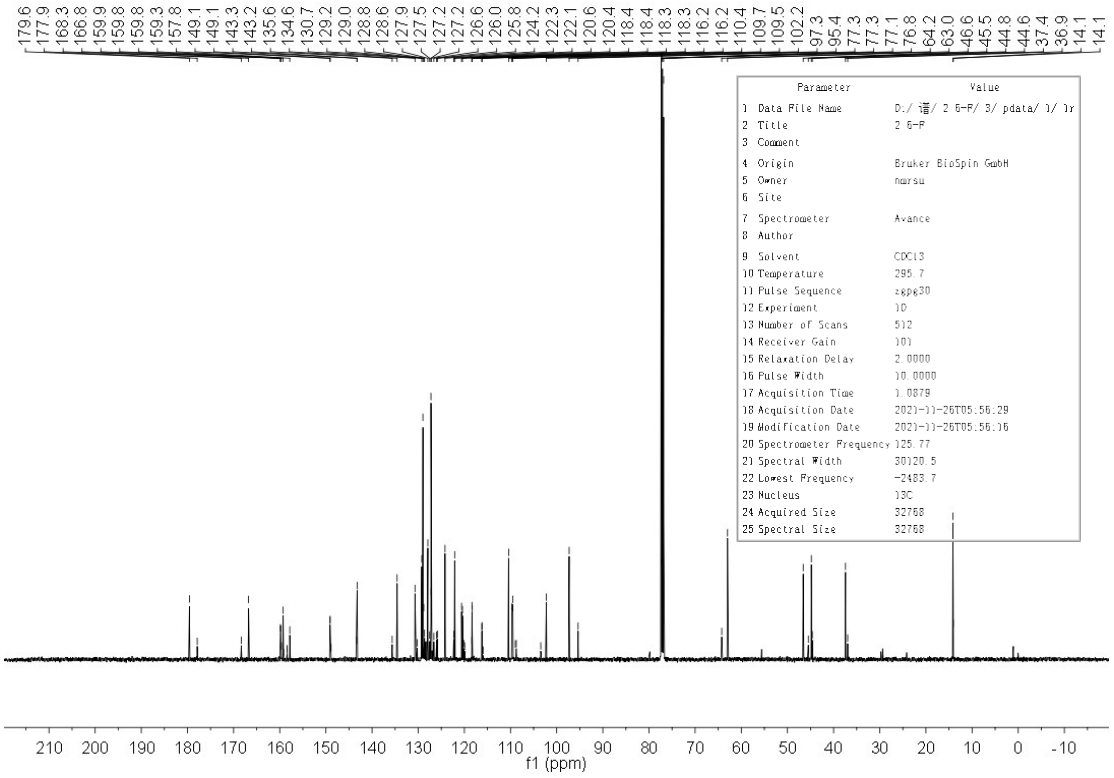
^{13}C NMR of **3ad**



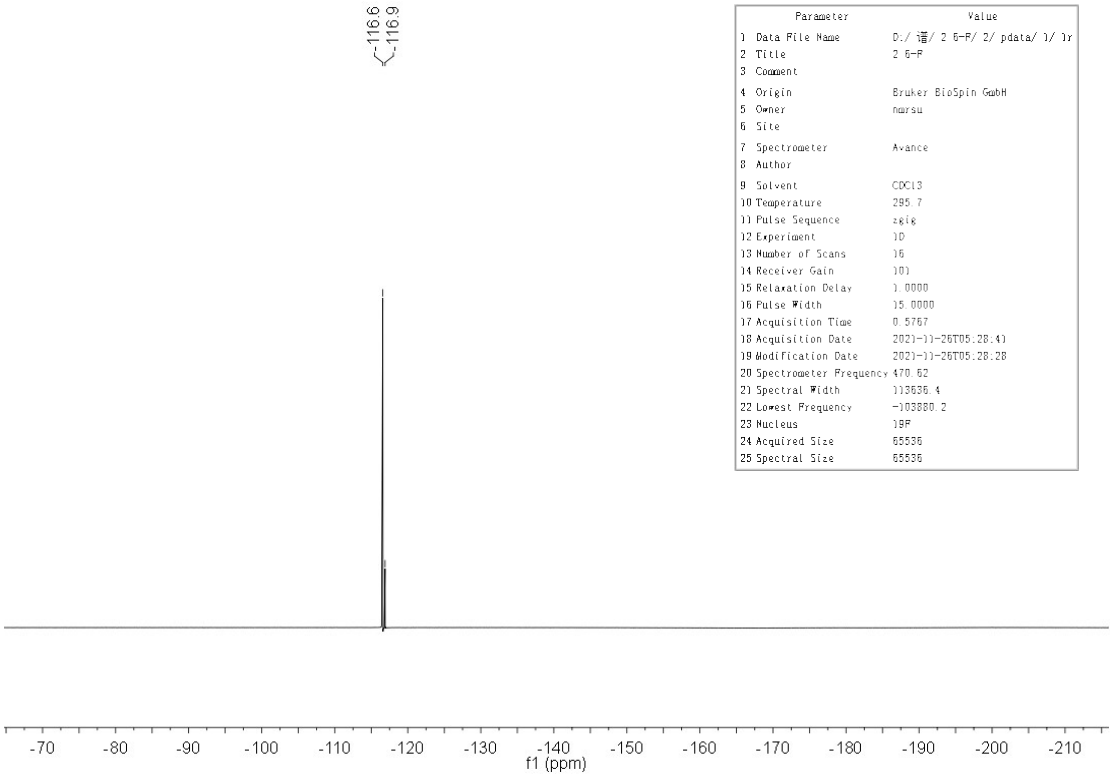
^{1}H NMR of **3ae**



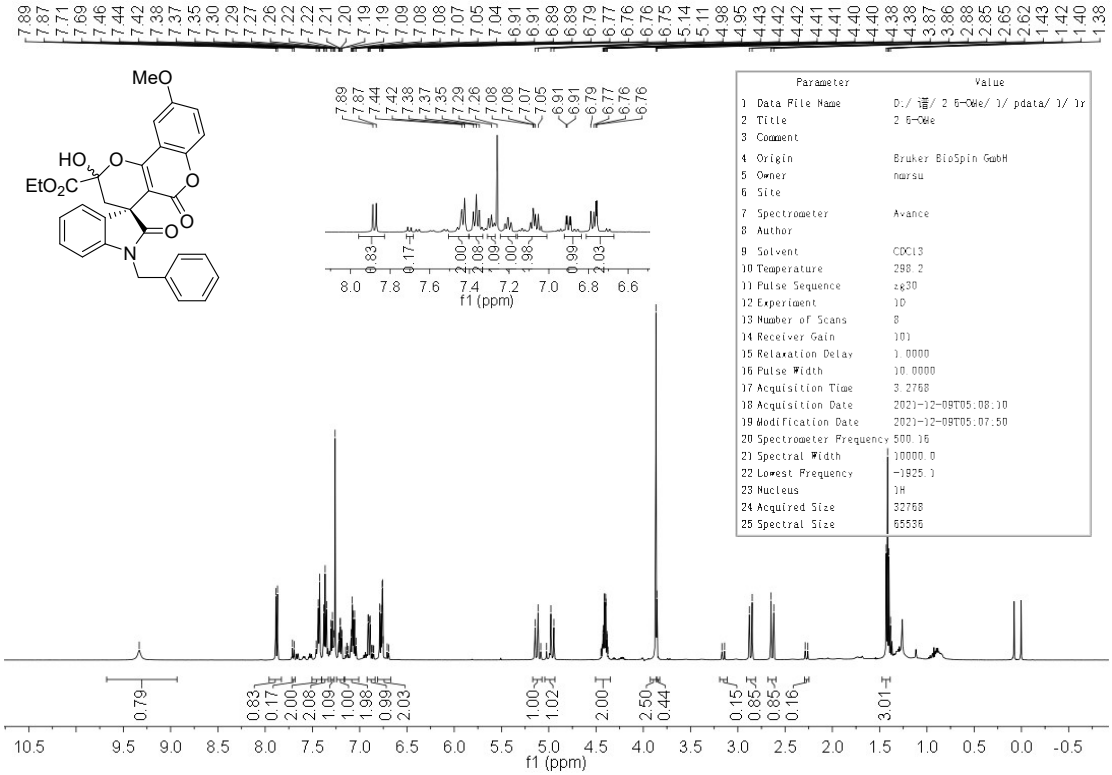
^{13}C NMR of **3ae**



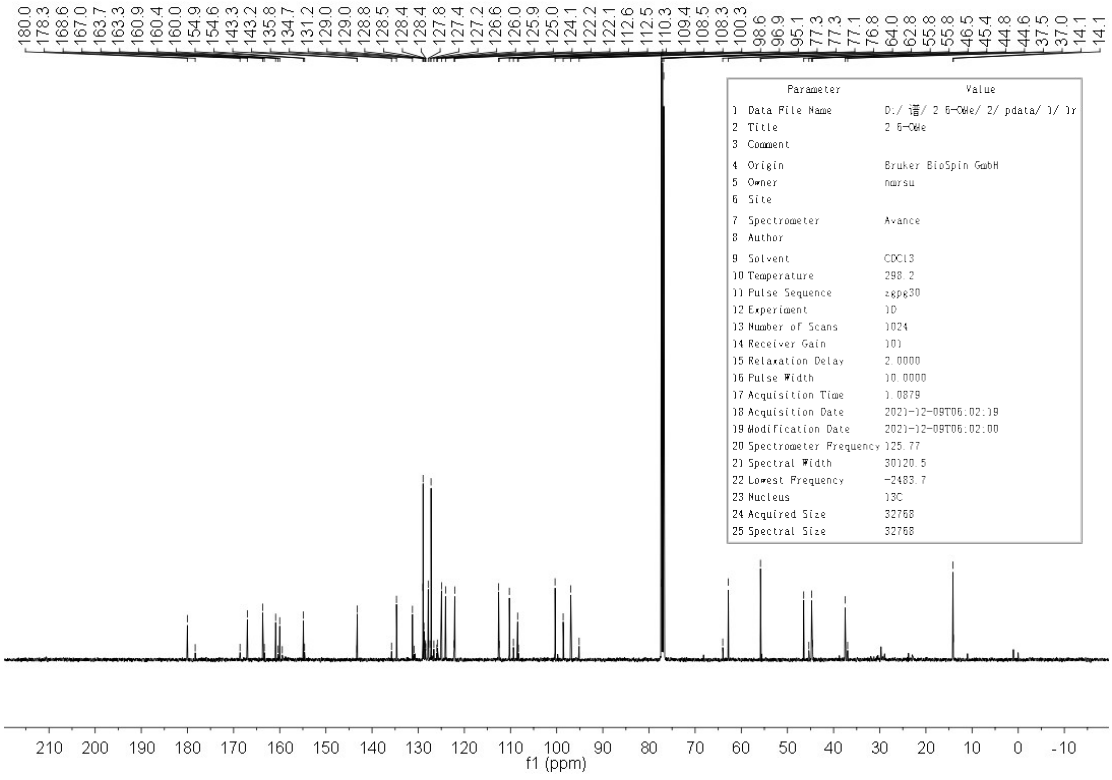
^{19}F NMR of **3ae**



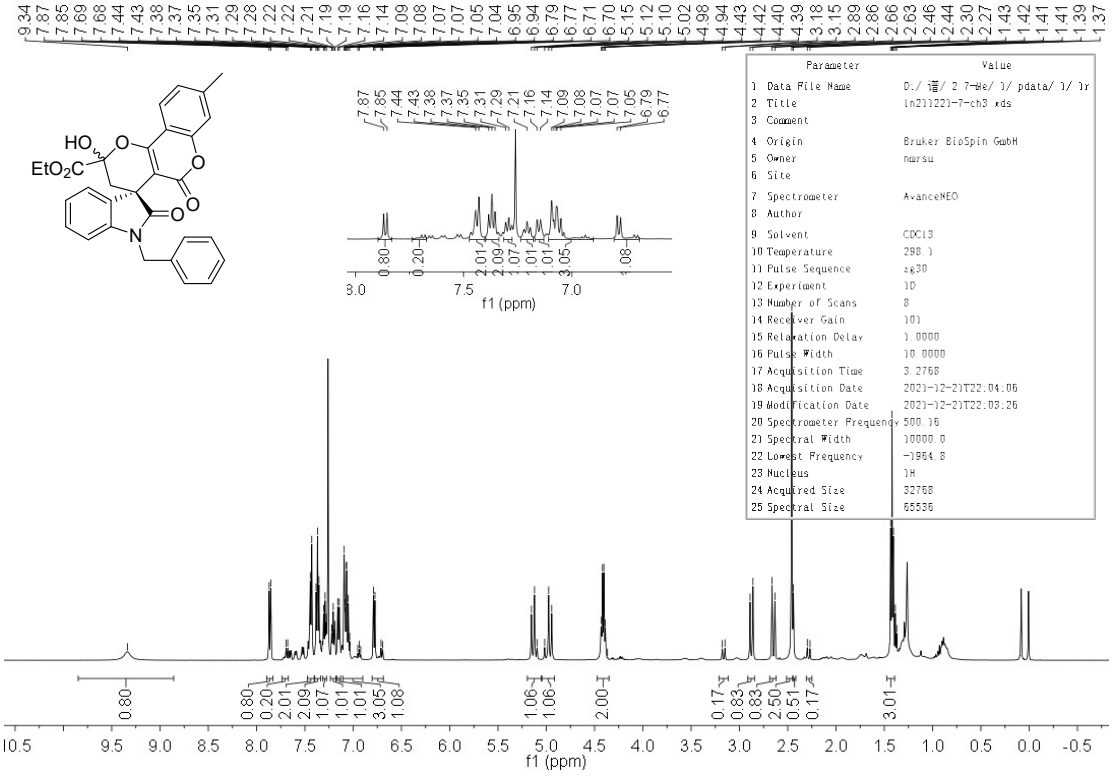
^{1}H NMR of **3af**



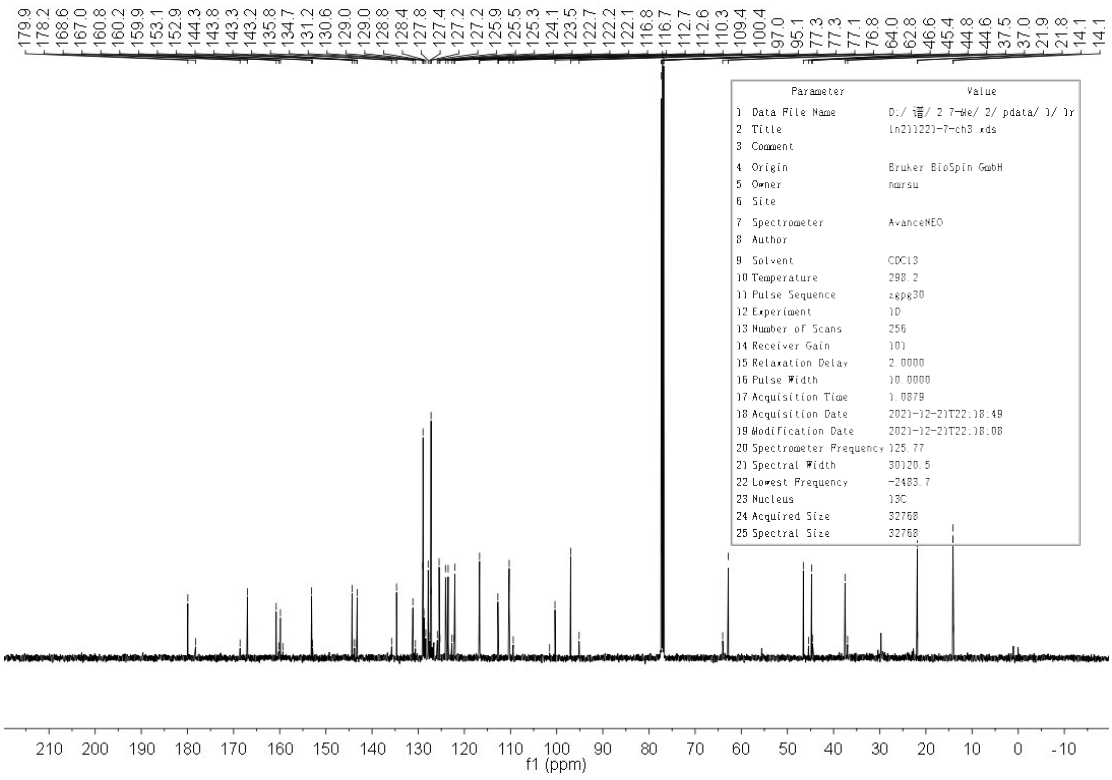
^{13}C NMR of **3af**



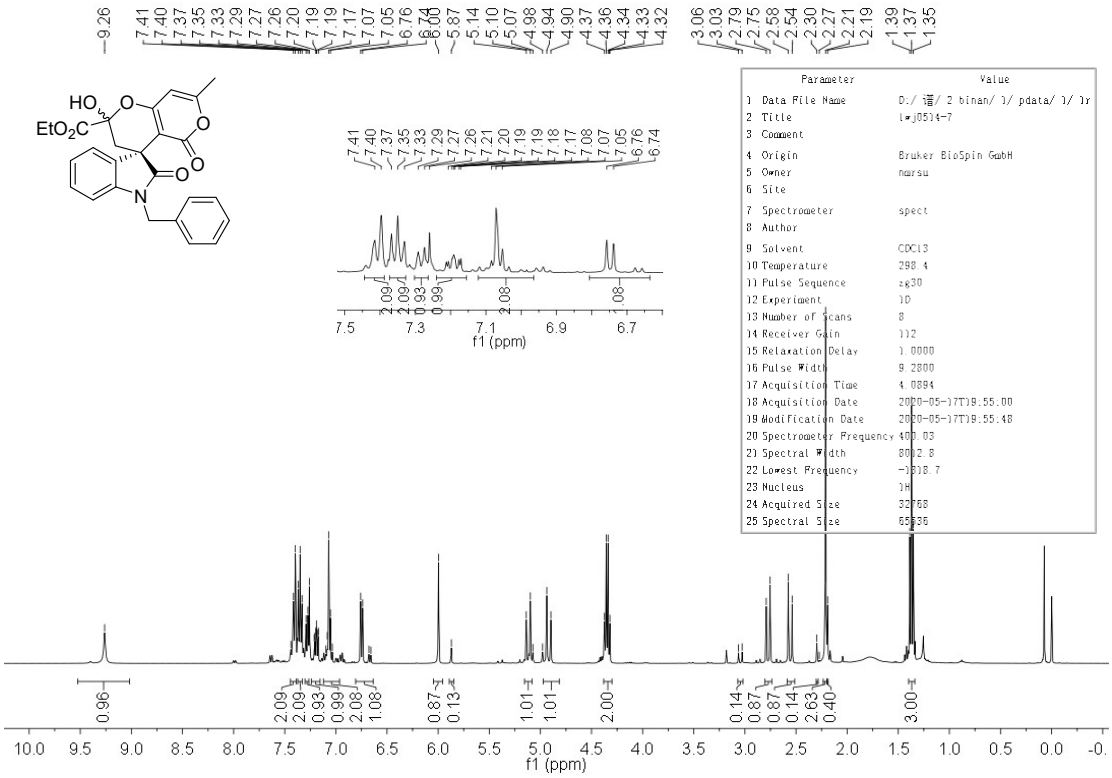
^{1}H NMR of **3ag**



^{13}C NMR of **3ag**



^{1}H NMR of **3ah**



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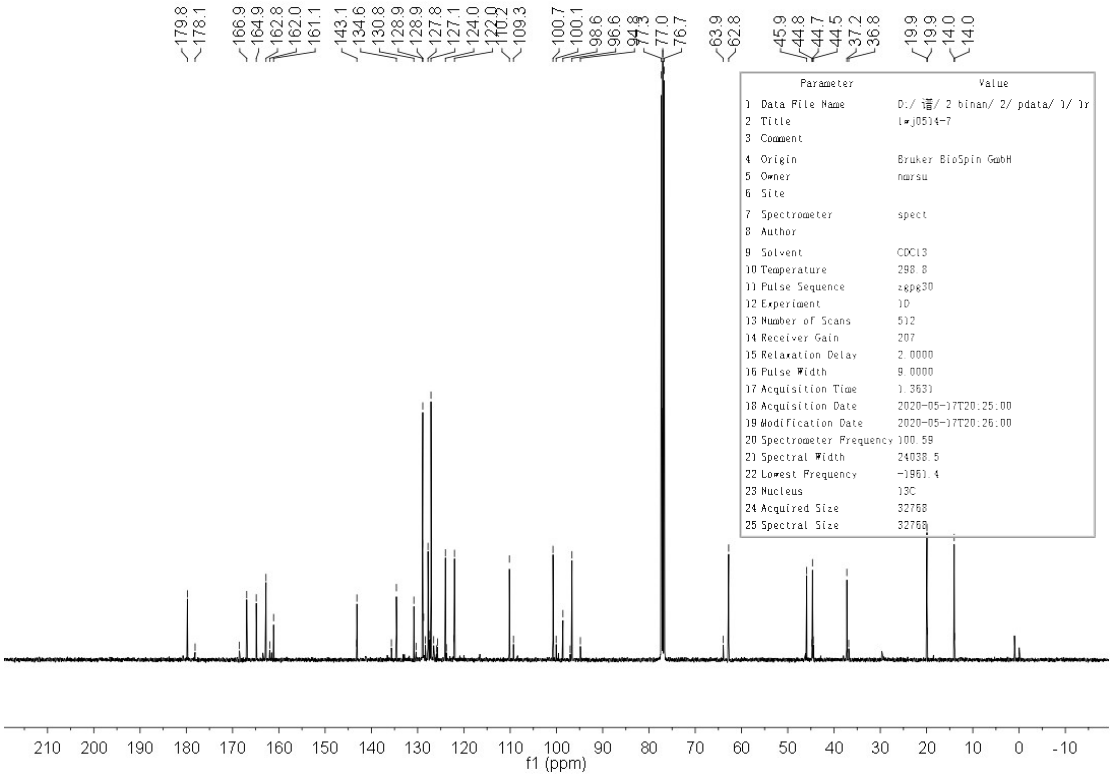

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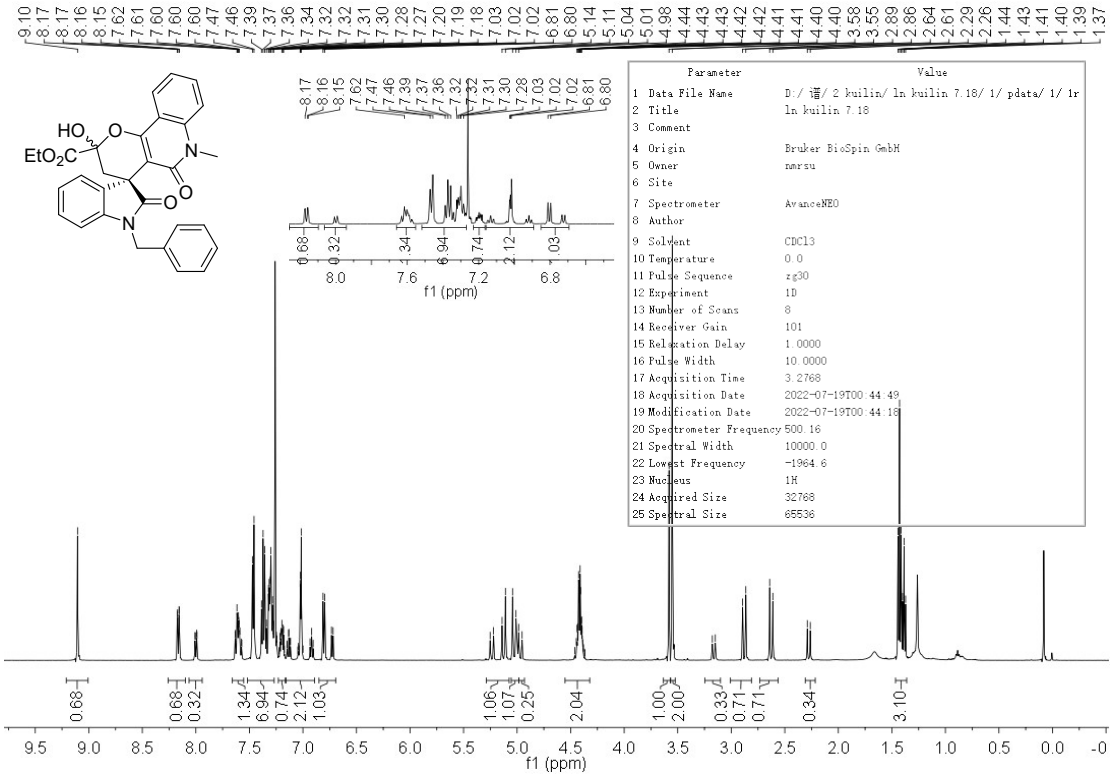
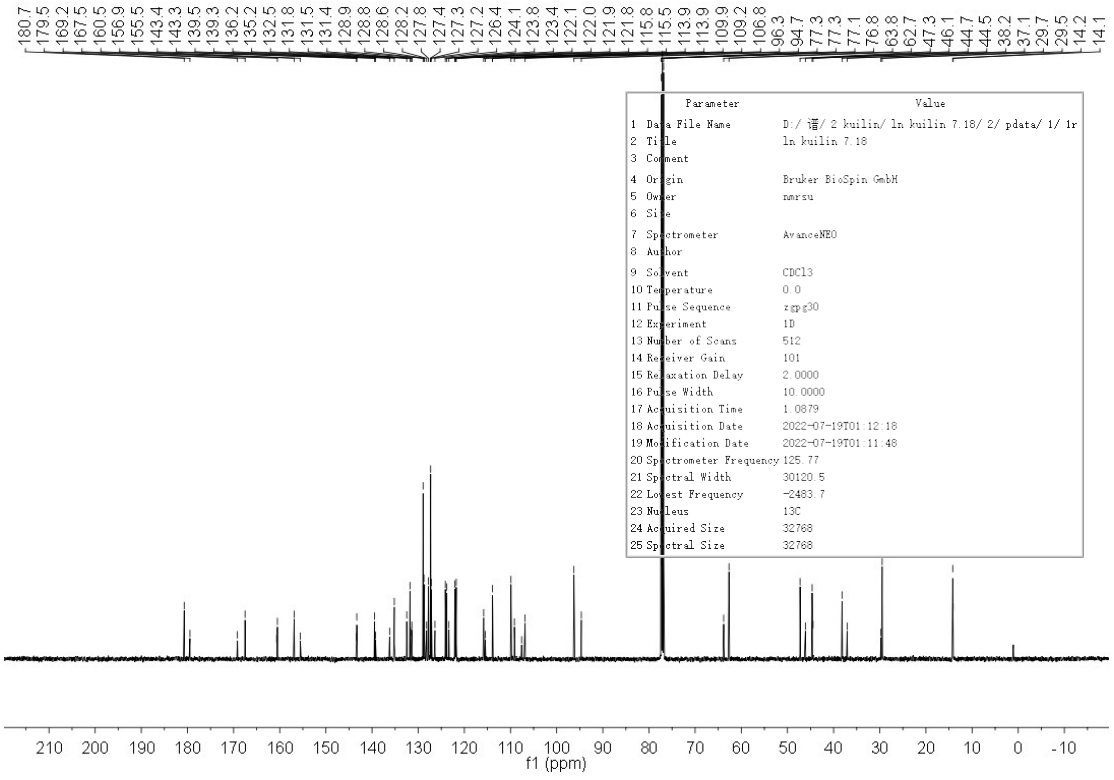


^{13}C NMR of **3ai**



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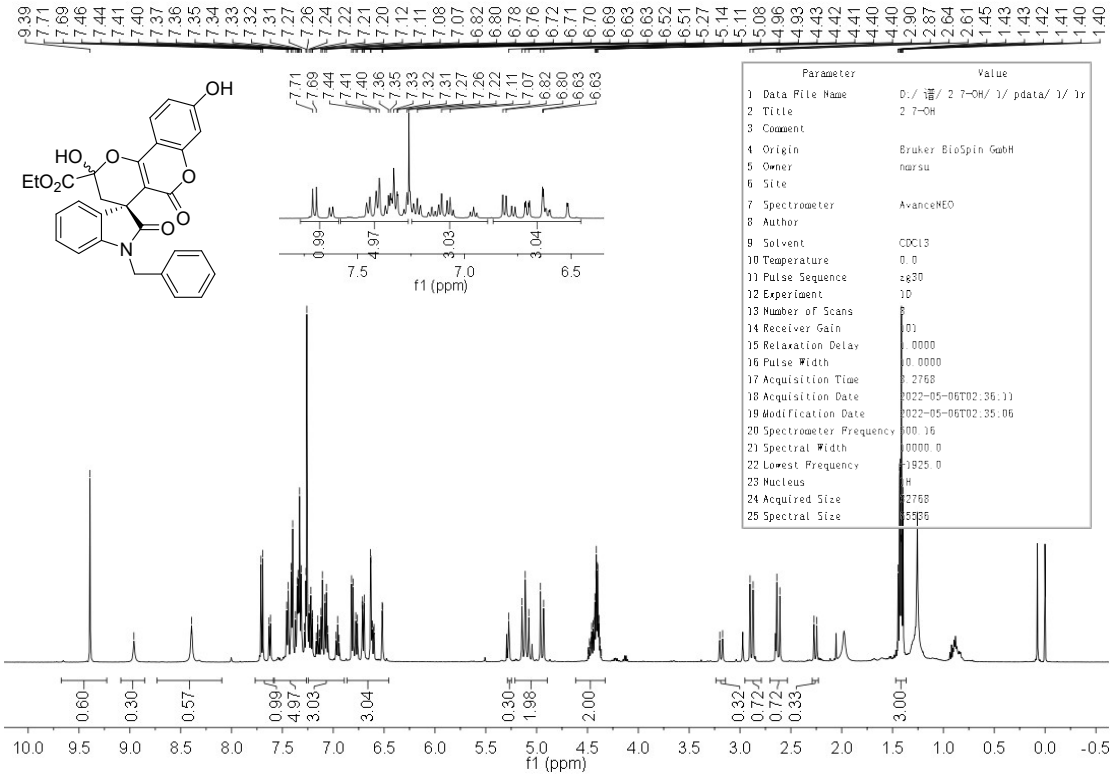

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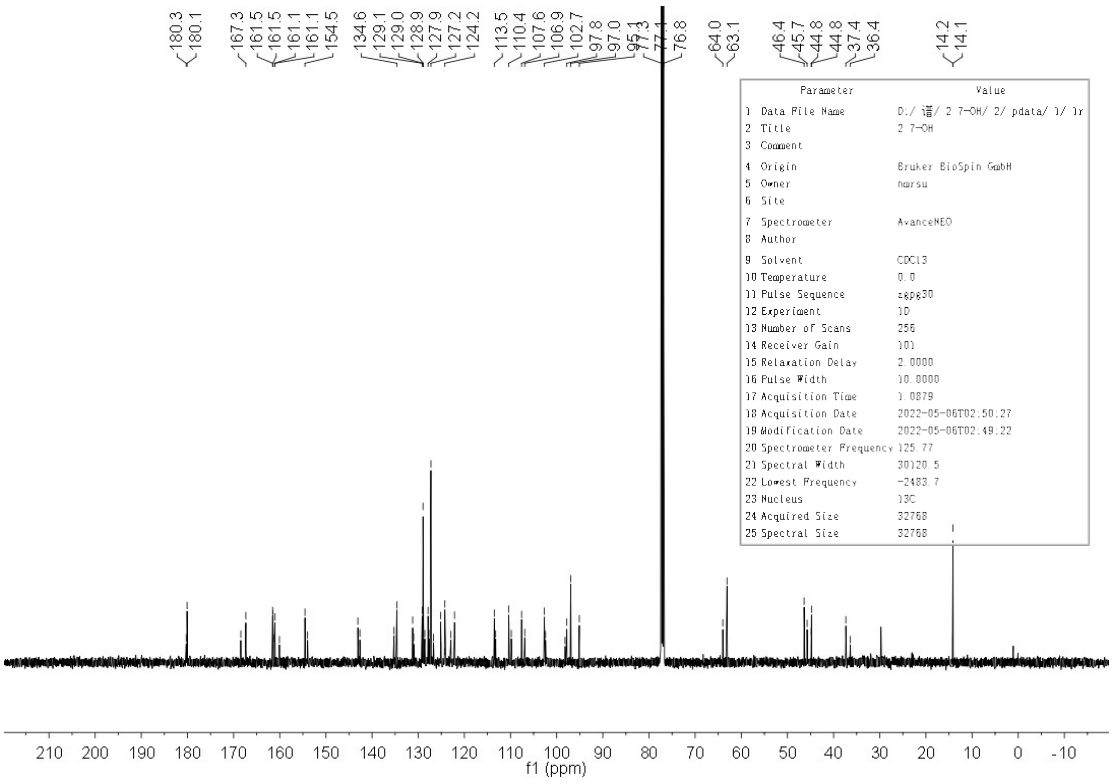
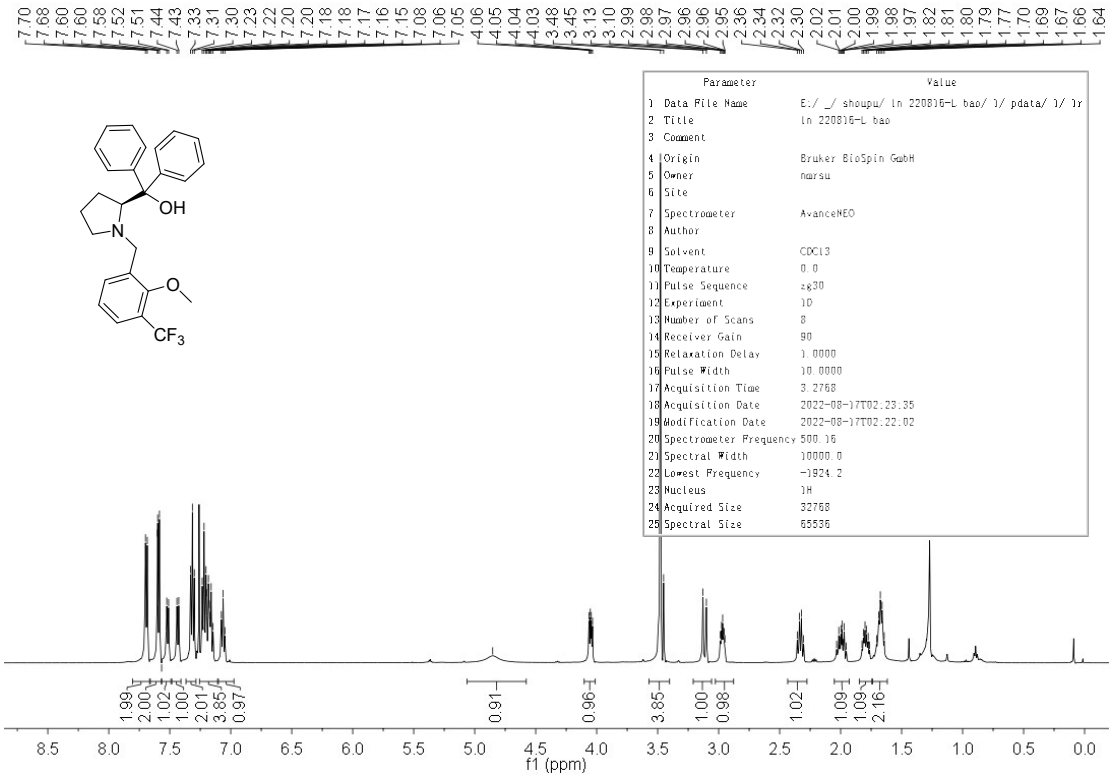
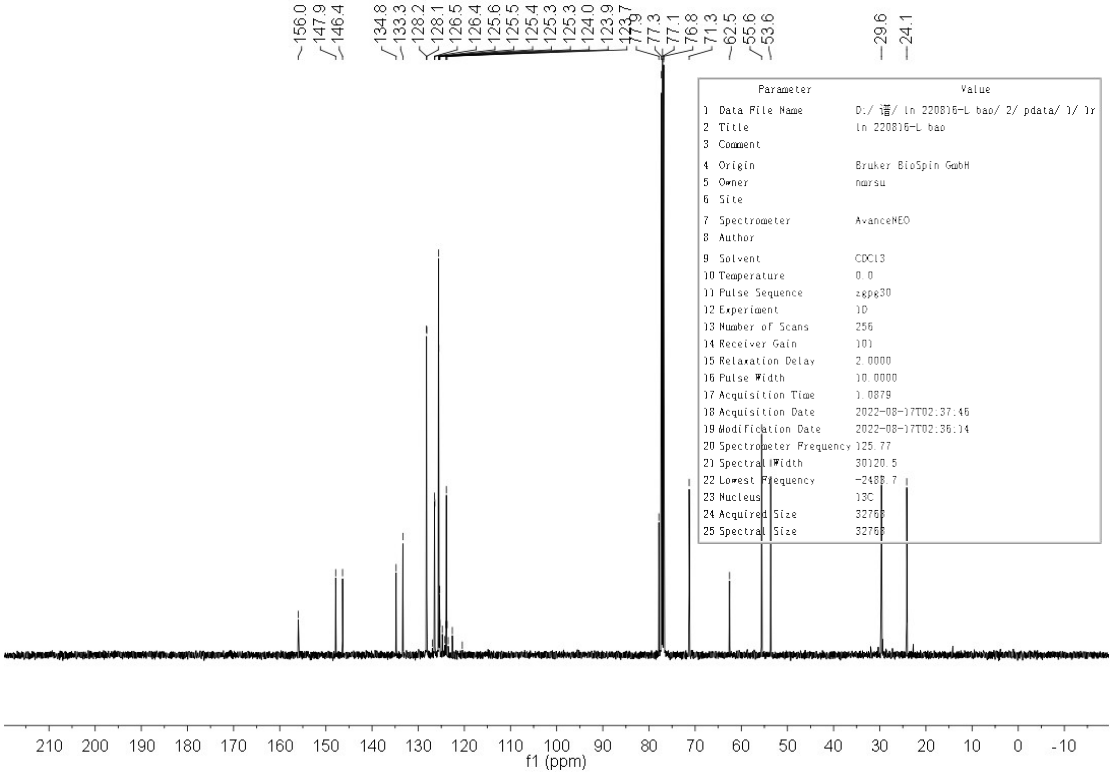


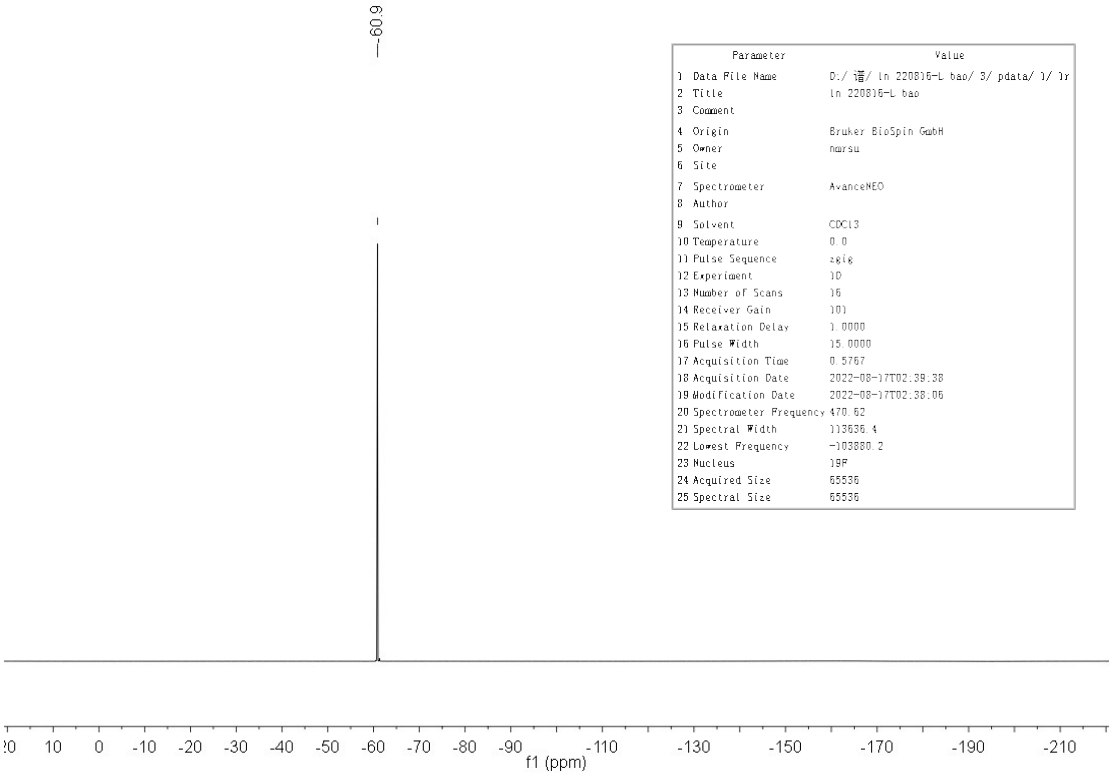
^{1}H NMR of **L_6**



^{13}C NMR of **L_6**



^{19}F NMR of **L_6**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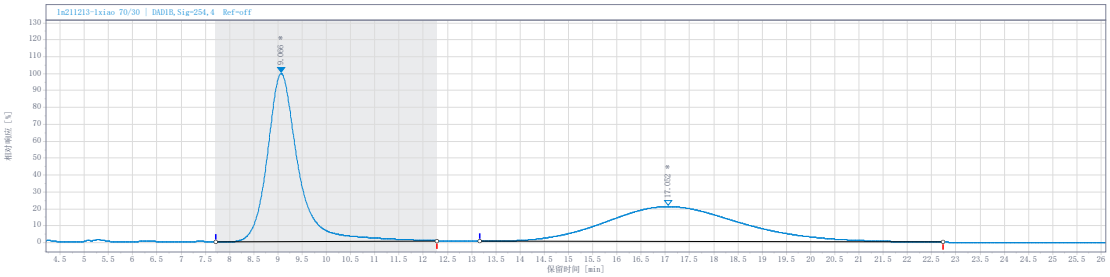
f1 (ppm)

Part III HPLC data

3aa

Racemic sample



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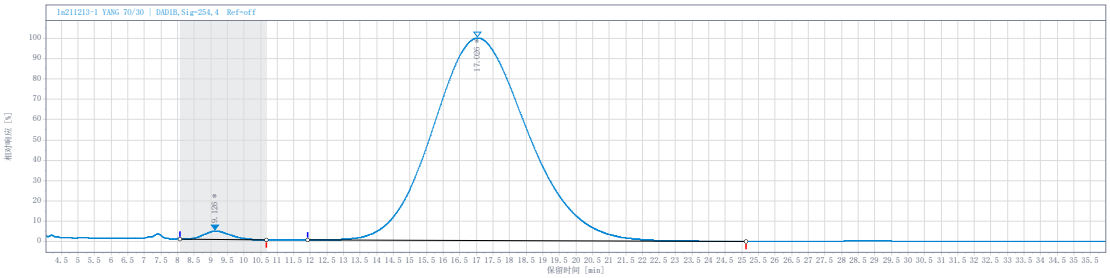
17.1	9.58	25580.86	130.11	48.05

Asymmetric version



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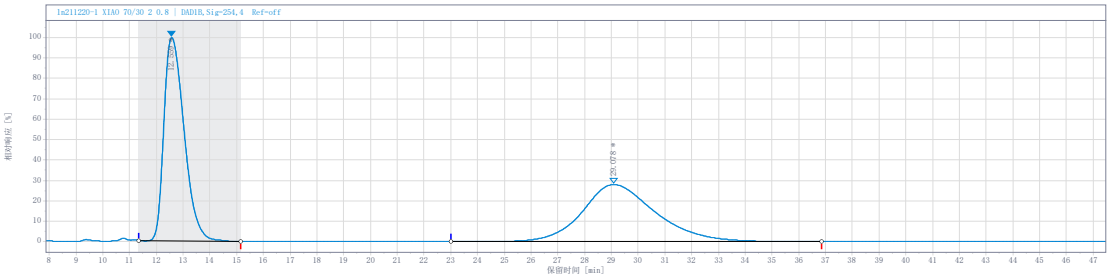
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.13	2.59	162.90	3.02	1.08
17.0	13.22	14944.02	75.48	98.92

3ba

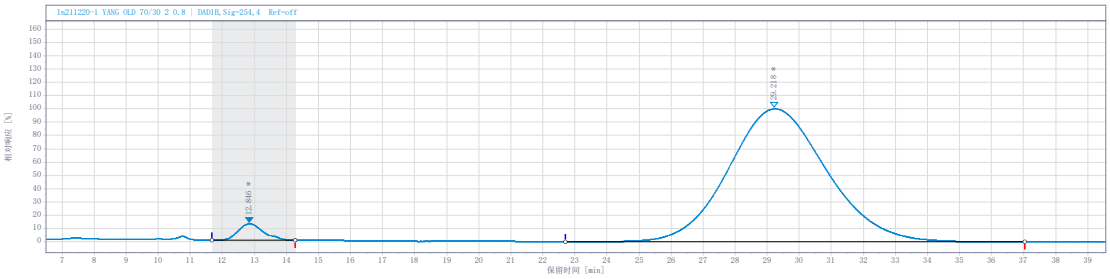
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
12.6	3.80	44962.66	858.52	49.48
29.1	13.86	45903.57	240.80	50.52

Asymmetric version

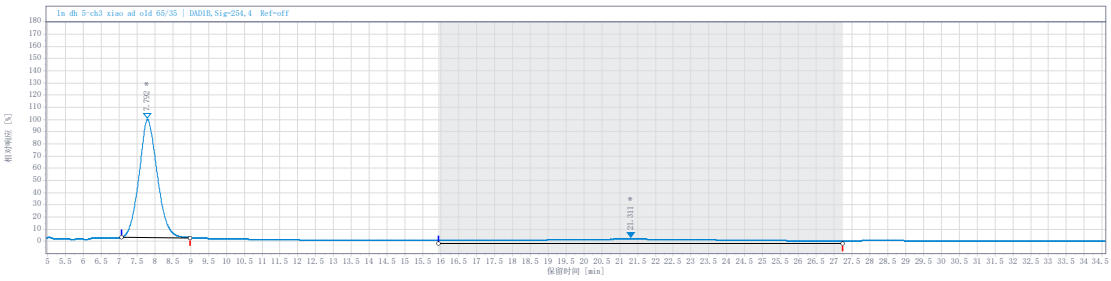


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
12.8	2.59	340.59	6.19	3.12
29.2	14.34	10575.27	49.71	96.88

3ca

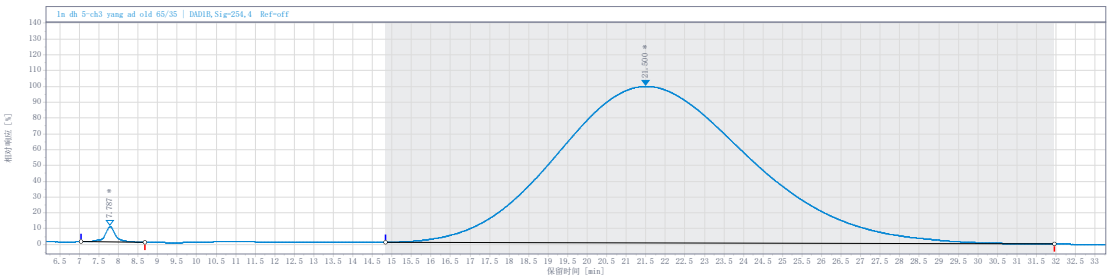
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.79	1.90	2903.38	82.19	65.13
21.3	11.32	1554.32	2.96	34.87

Asymmetric version

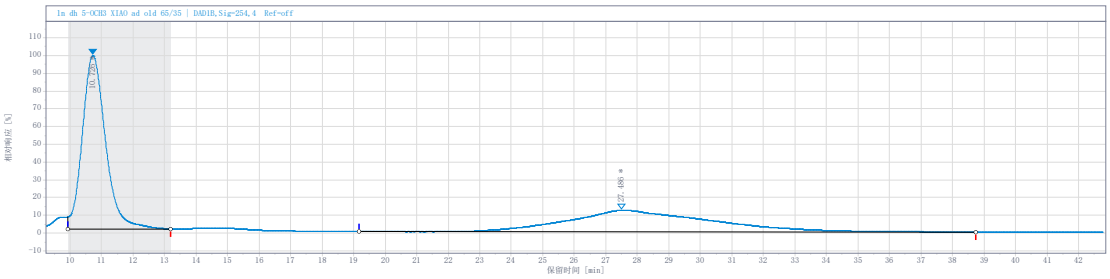


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.79	1.63	193.65	9.98	0.54
21.5	17.12	35407.57	102.68	99.46

3da

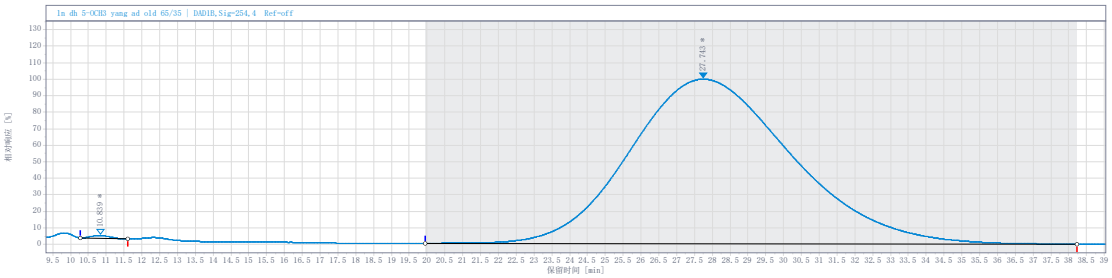
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.7	3.27	1794.75	34.98	57.21
27.5	19.57	1342.62	4.32	42.79

Asymmetric version

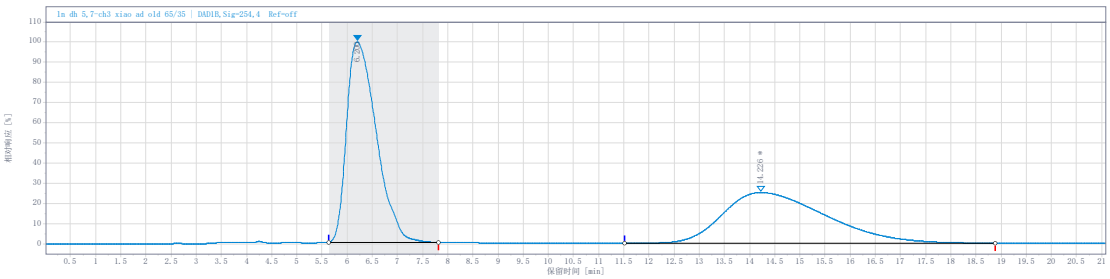


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.8	1.34	42.57	1.15	0.20
27.7	18.28	21030.56	66.22	99.80

3ea

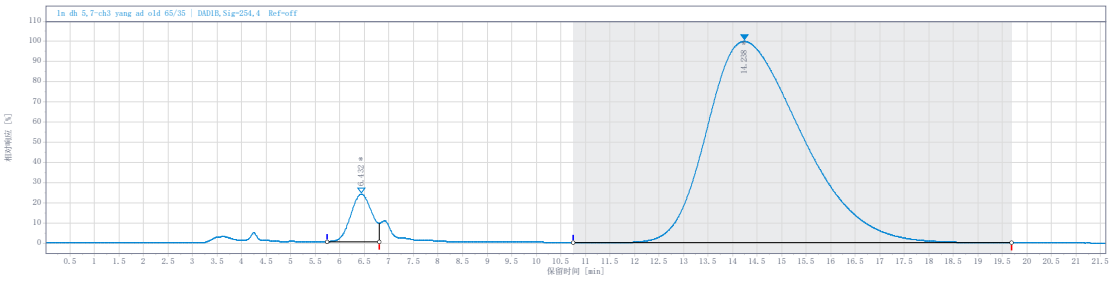
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.20	2.19	36333.83	886.59	53.18
14.2	7.37	31991.48	224.50	46.82

Asymmetric version

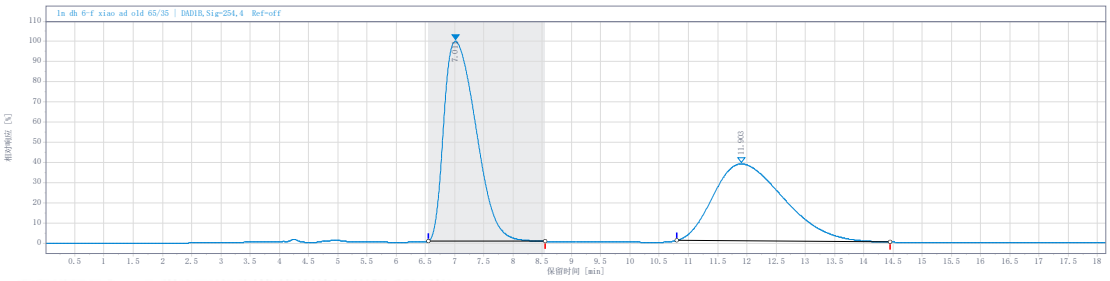


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.43	1.06	1244.93	41.76	4.99
14.2	8.93	23689.57	177.02	95.01

3fa

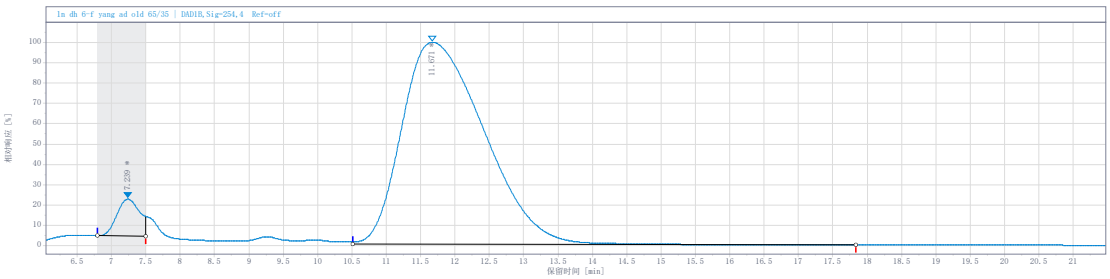
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.01	2.01	25009.58	654.80	54.07
11.9	3.66	21244.62	252.43	45.93

Asymmetric version

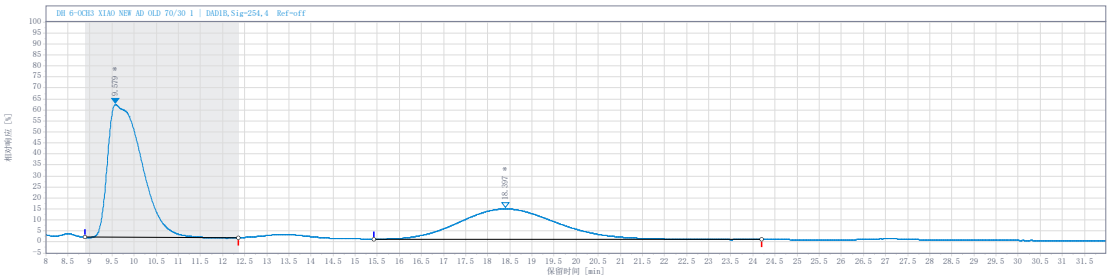


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.24	0.70	1458.50	63.43	4.85
11.7	7.33	28642.86	344.90	95.15

3ga

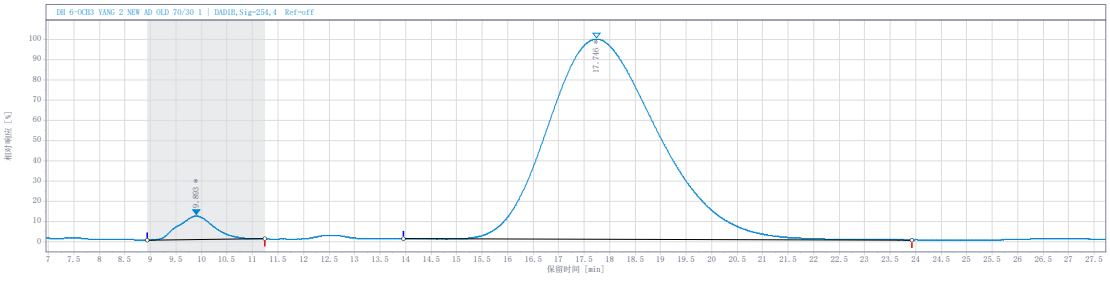
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.58	3.48	2593.98	48.68	60.61
18.4	8.78	1686.04	11.09	39.39

Asymmetric version

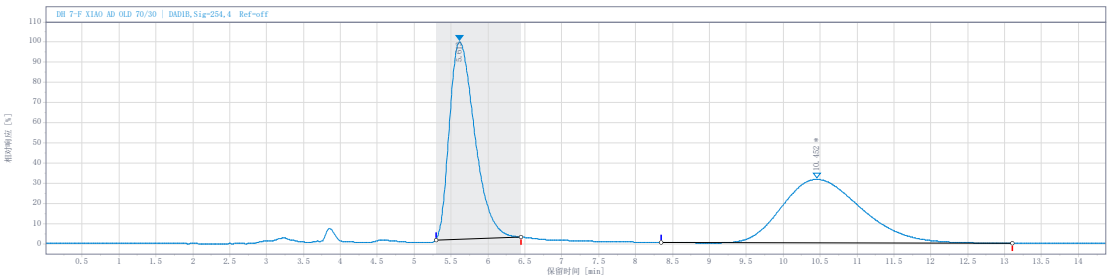


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.89	2.31	195.59	3.99	3.72
17.7	9.97	5056.86	34.09	96.28

3ha

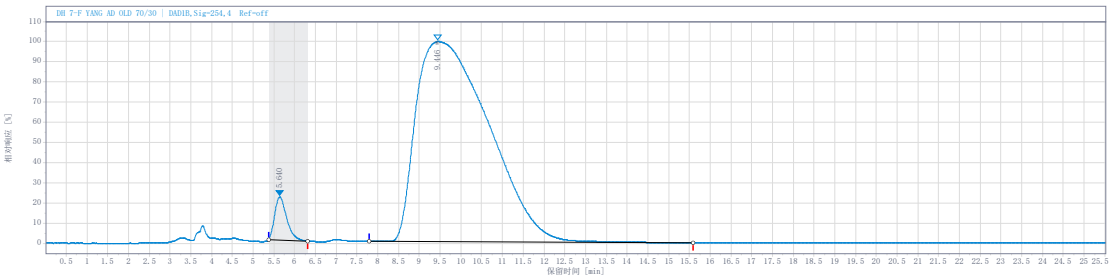
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
5.61	1.15	2734.21	114.54	49.91
10.5	4.76	2743.69	36.89	50.09

Asymmetric version

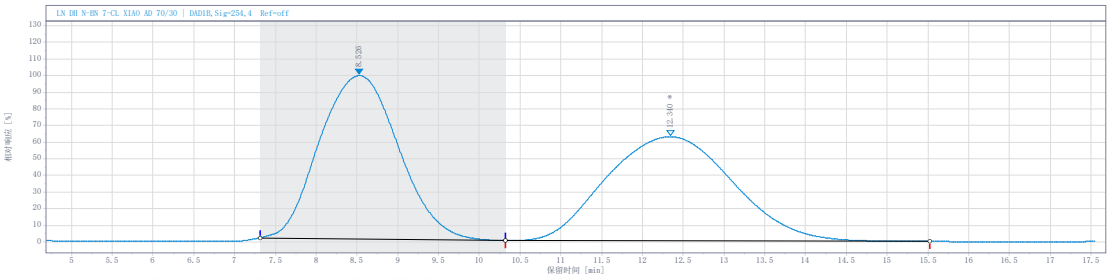


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
5.64	0.95	924.69	46.19	3.40
9.45	7.80	26246.91	215.43	96.60

3ia

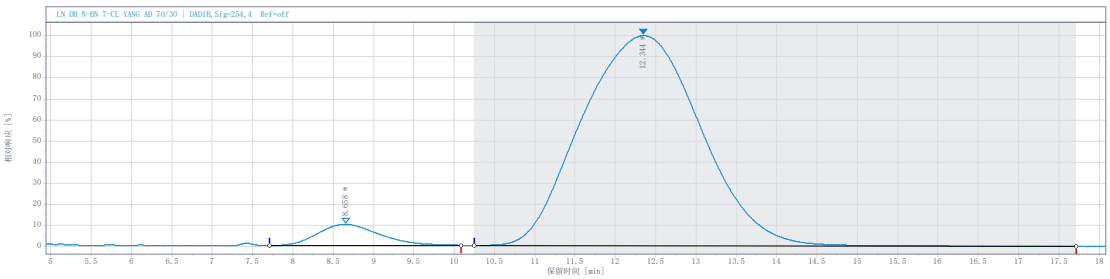
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8.53	3.01	32925.57	488.06	49.49
12.3	5.20	33609.72	311.55	50.51

Asymmetric version

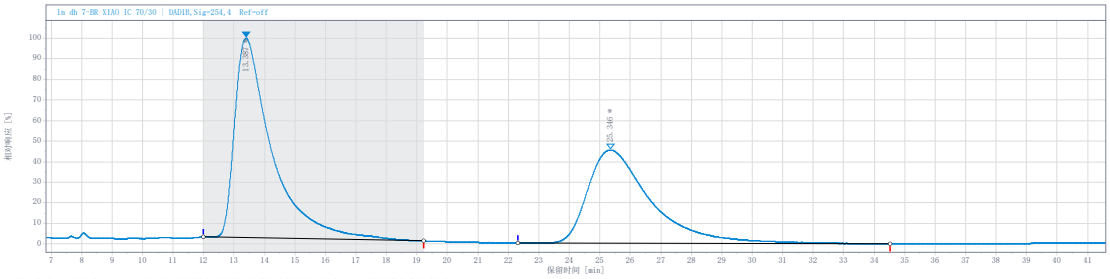


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8.66	2.37	1091.47	20.65	4.96
12.3	7.47	20909.41	204.43	95.04

3ja

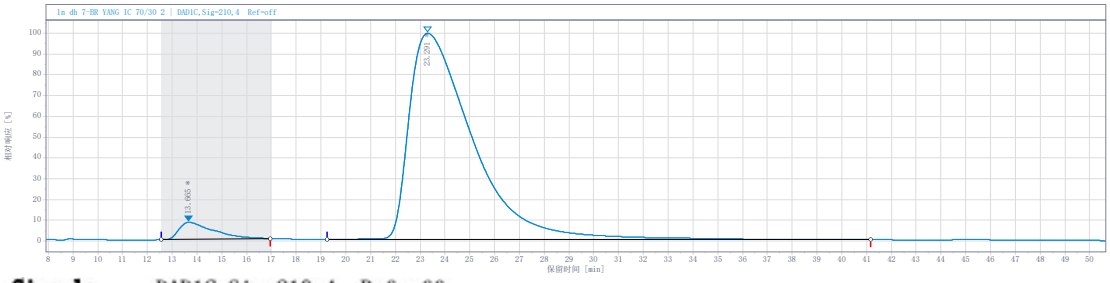
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
13.4	7.24	3103.47	36.49	56.34
25.3	12.22	2405.33	16.98	43.66

Asymmetric version

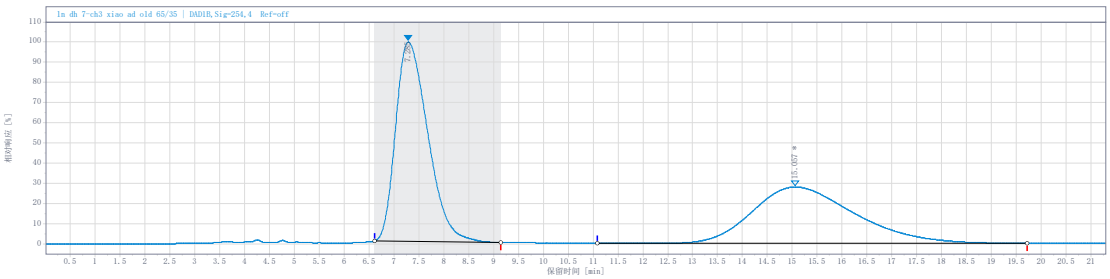


Signal: DAD1C, Sig=210, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
13.7	4.41	10309.70	106.79	4.28
23.3	21.94	230488.13	1291.93	95.72

3ka

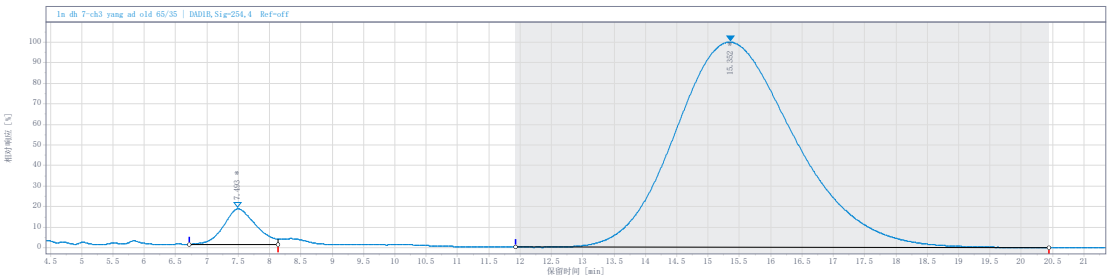
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.29	2.53	30603.33	680.94	52.74
15.1	8.63	27420.64	192.15	47.26

Asymmetric version

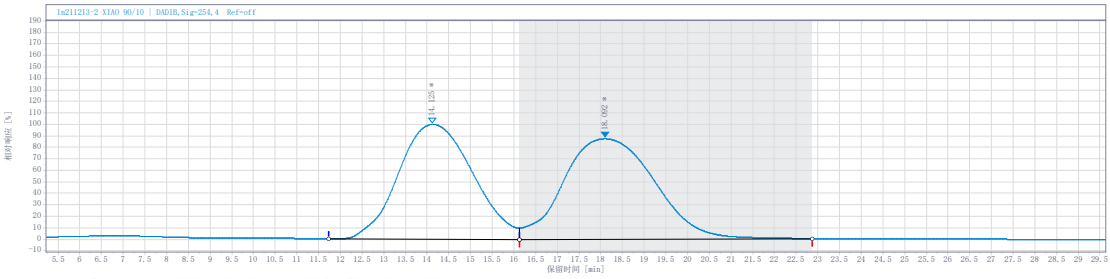


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.49	1.42	394.63	11.03	4.45
15.4	8.51	8472.95	63.81	95.55

3la

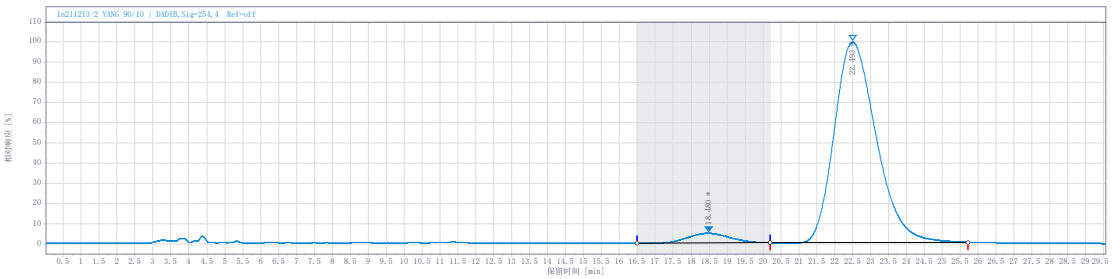
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.1	4.38	32042.27	269.38	48.24
18.1	6.75	34377.23	235.89	51.76

Asymmetric version

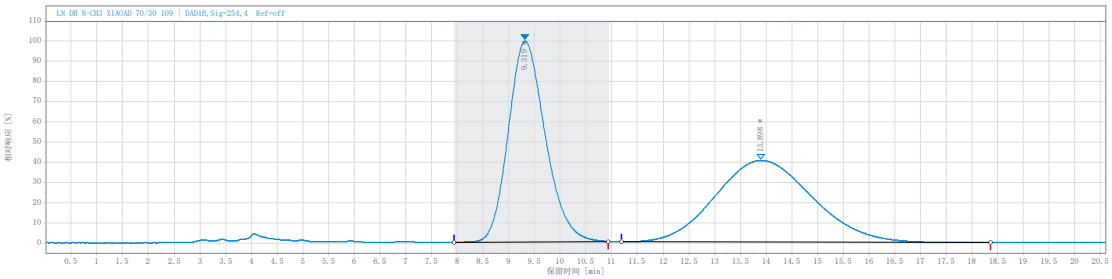


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
18.5	3.71	369.30	4.49	4.71
22.5	5.52	7474.12	92.47	95.29

3ma

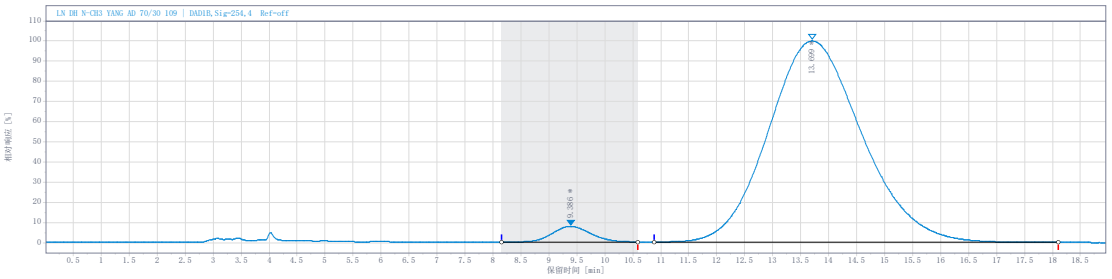
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.32	3.01	8761.38	175.48	48.30
13.9	7.17	9378.44	71.43	51.70

Asymmetric version

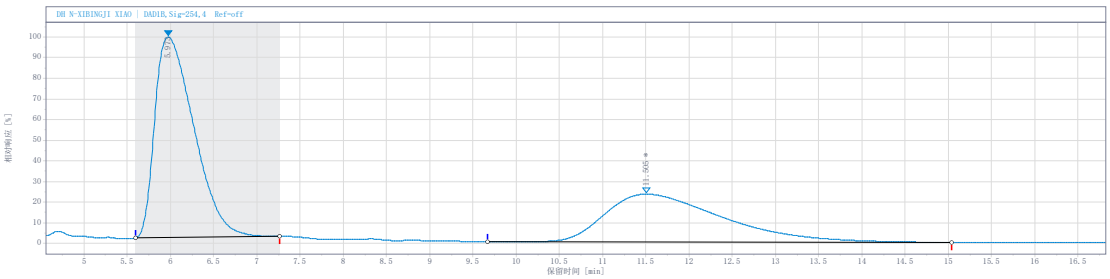


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.39	2.44	711.38	14.86	3.10
13.7	7.22	22267.27	191.16	96.90

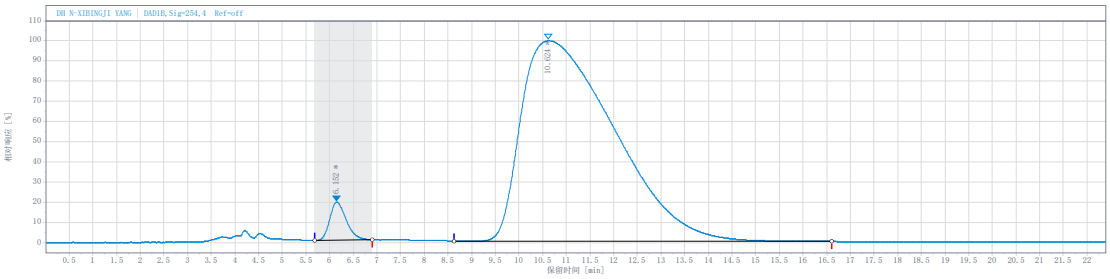
3na

Racemic sample



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
5.97	1.67	12804.93	408.02	58.44
11.5	5.36	9106.15	97.07	41.56

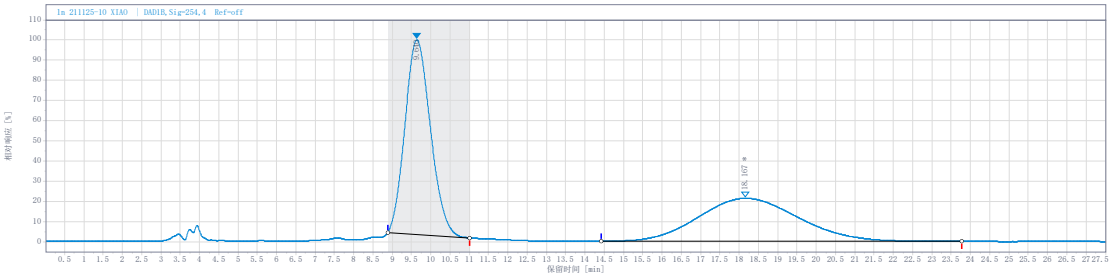
Asymmetric version



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.15	1.22	844.68	35.00	3.26
10.6	7.97	25088.41	184.02	96.74

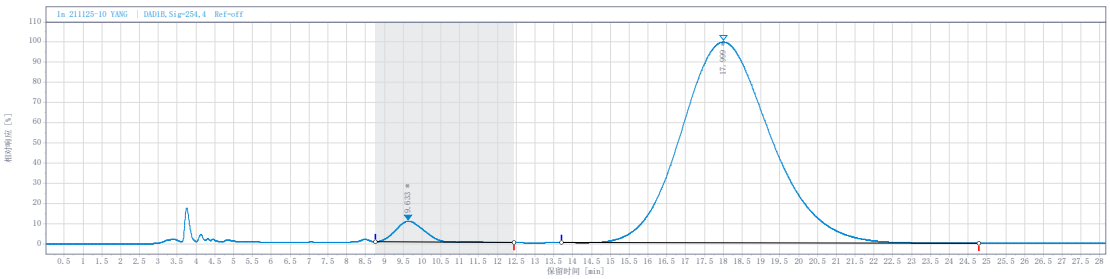
3oa

Racemic sample



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.64	2.12	8091.78	175.92	53.43
18.2	9.35	7054.23	38.93	46.57

Asymmetric version

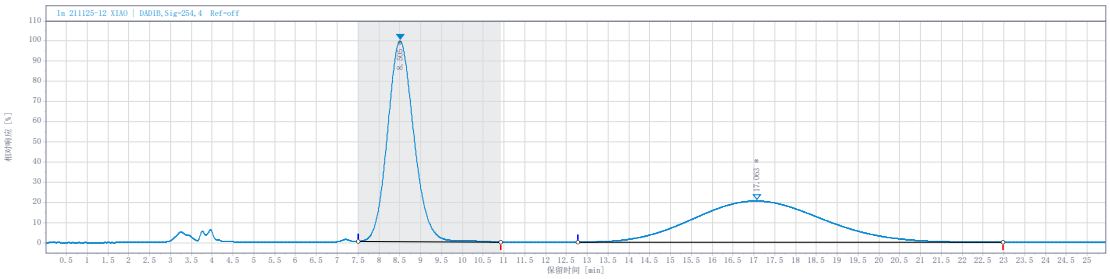


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.63	3.68	1107.13	20.81	3.26
18.0	11.08	32894.06	200.48	96.74

3pa

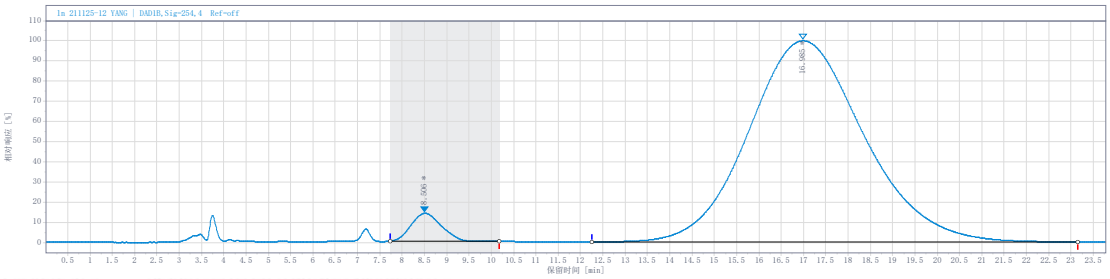
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8.50	3.42	3479.54	79.21	49.60
17.1	10.20	3535.68	16.30	50.40

Asymmetric version

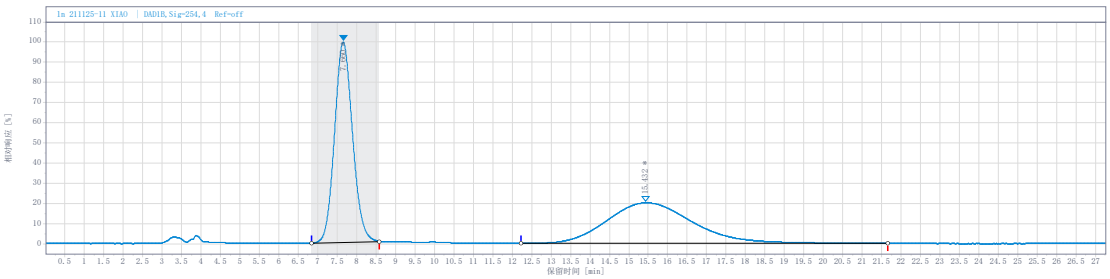


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8.51	2.44	909.93	19.37	3.48
17.0	10.88	25201.32	139.95	96.52

3qa

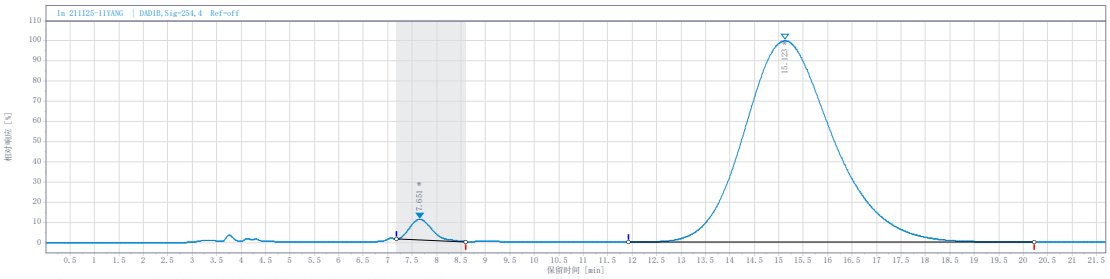
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.66	1.75	3176.57	99.14	50.58
15.4	9.43	3104.17	20.16	49.42

Asymmetric version

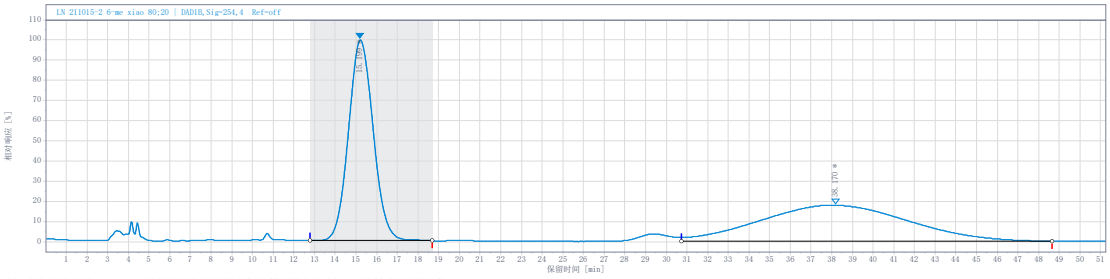


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.65	1.42	1024.59	32.91	2.47
15.1	8.28	40420.89	321.48	97.53

3ab

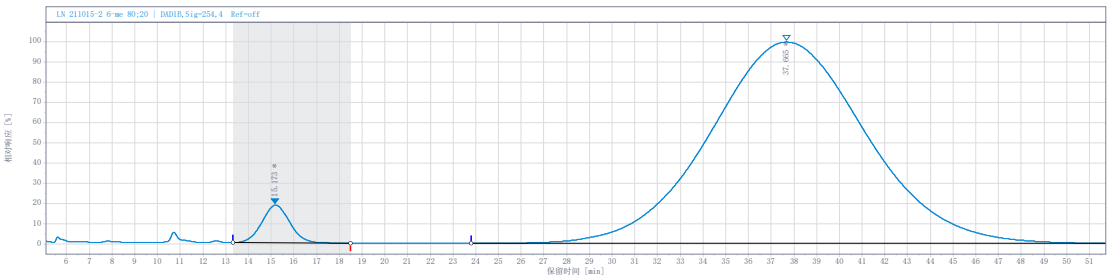
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15.2	5.91	5283.10	63.64	48.31
38.2	17.92	5653.00	11.39	51.69

Asymmetric version

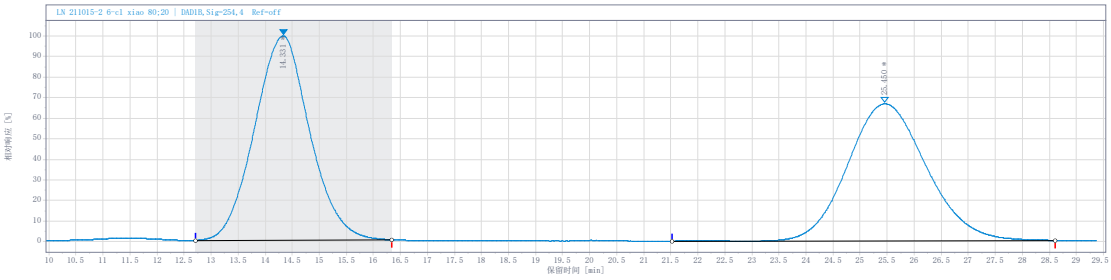


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15.2	5.15	3722.32	44.08	3.19
37.7	28.00	112980.35	235.50	96.81

3ac

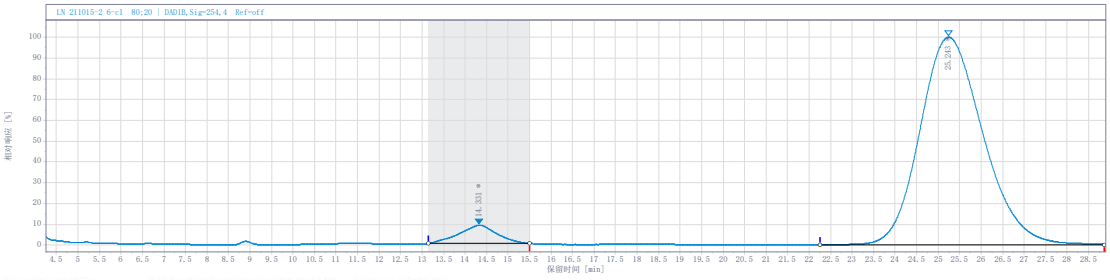
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.3	3.63	2702.86	38.15	51.12
25.4	7.09	2584.14	25.56	48.88

Asymmetric version

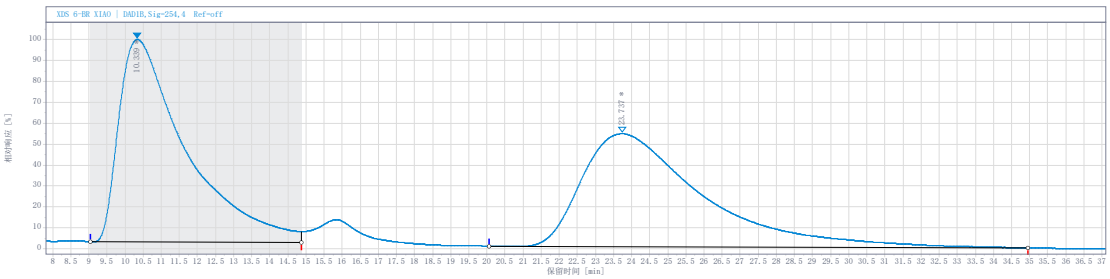


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.3	2.36	525.48	8.57	5.02
25.2	6.62	9936.07	97.93	94.98

3ad

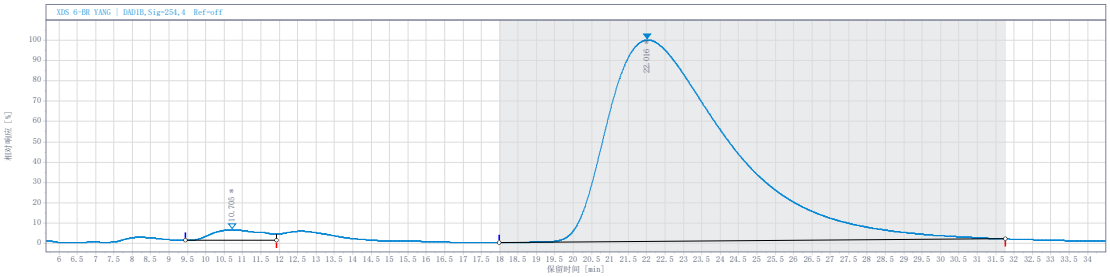
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.3	5.82	4222.53	32.89	50.03
23.7	14.89	4216.95	18.33	49.97

Asymmetric version

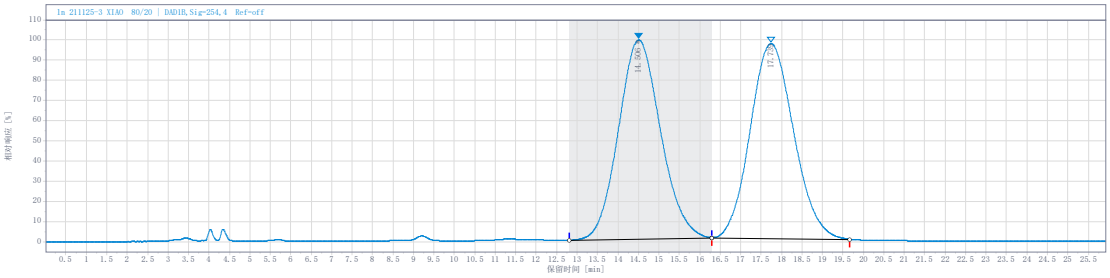


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.7	2.48	503.56	5.17	2.19
22.0	13.77	22508.47	97.87	97.81

3ae

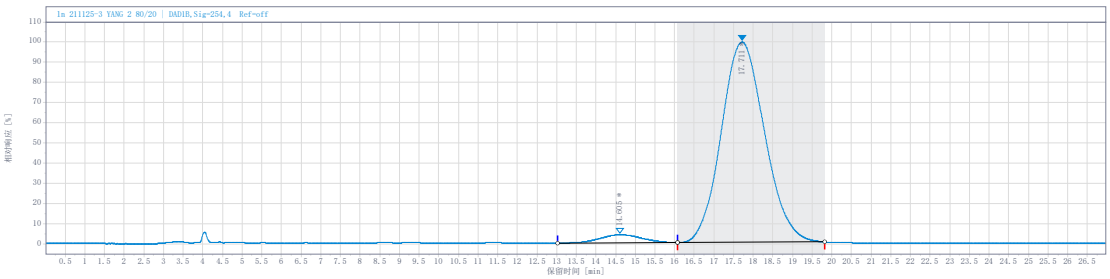
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.5	3.50	14879.70	208.26	49.76
17.7	3.36	15021.79	203.70	50.24

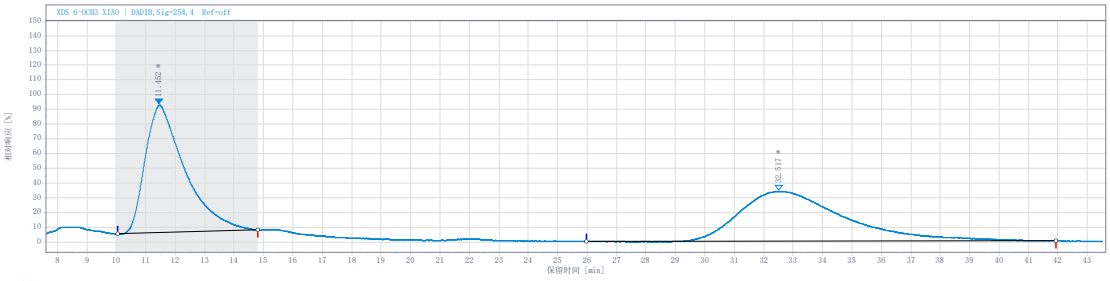
Asymmetric version



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.6	3.05	609.26	8.39	3.68
17.7	3.75	15951.86	208.59	96.32

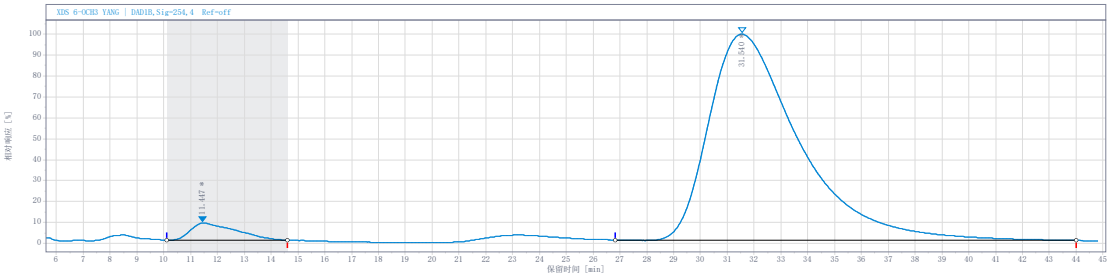
3af

Racemic sample



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
11.5	4.76	801.74	8.59	49.36
32.5	15.95	822.54	3.36	50.64

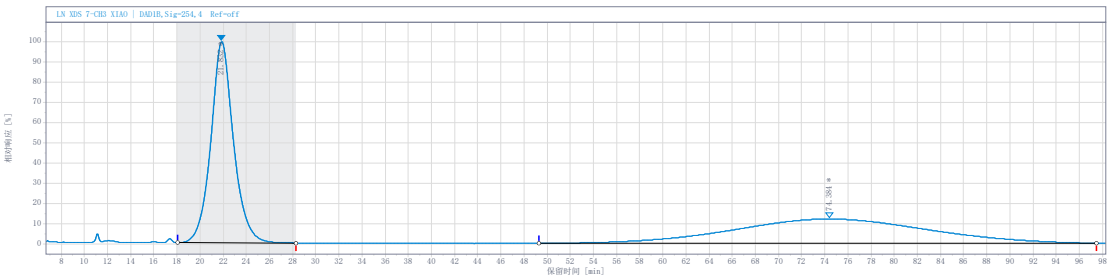
Asymmetric version



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
11.4	4.51	510.96	4.44	4.00
31.5	17.19	12273.75	52.56	96.00

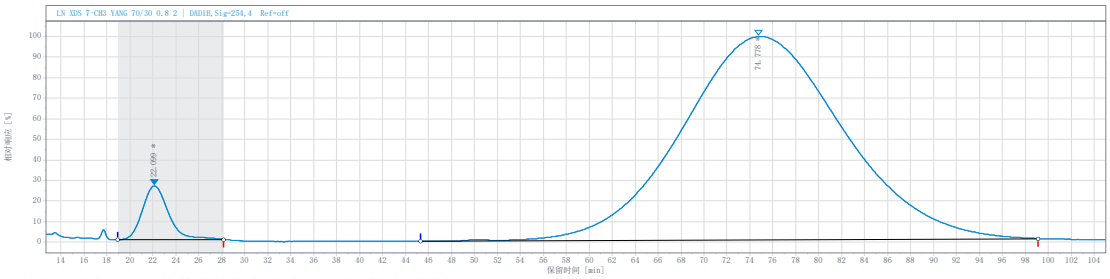
3ag

Racemic sample



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
21.8	10.25	35661.79	262.45	49.21
74.4	48.15	36799.94	31.50	50.79

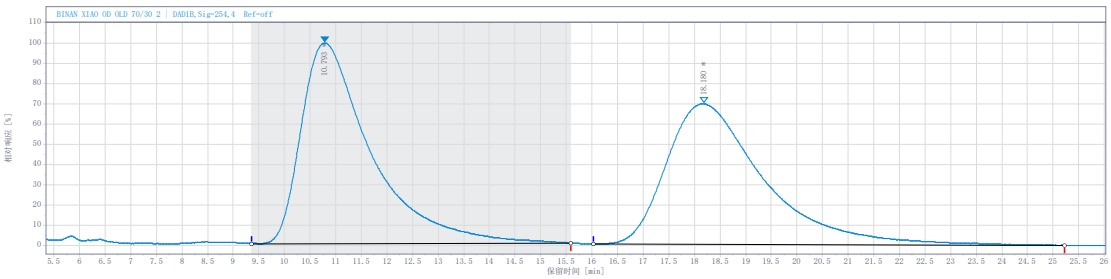
Asymmetric version



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
22.1	9.25	1245.69	7.98	4.04
74.8	53.85	29564.45	30.22	95.96

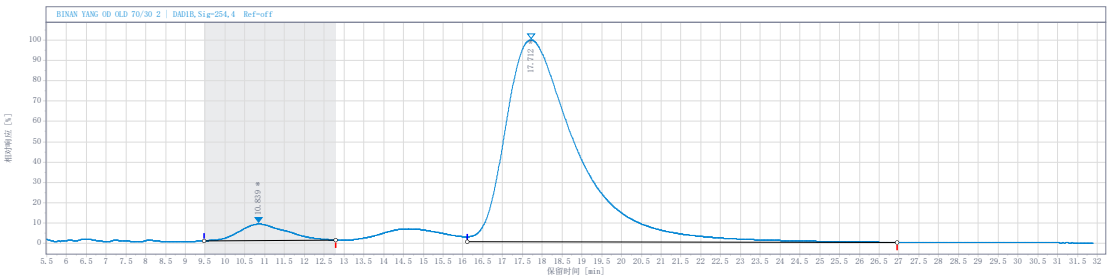
3ah

Racemic sample



Signal:	DAD1B, Sig=254, 4	Ref=off		
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.8	6.23	1483.83	15.72	50.67
18.2	9.19	1444.63	11.00	49.33

Asymmetric version

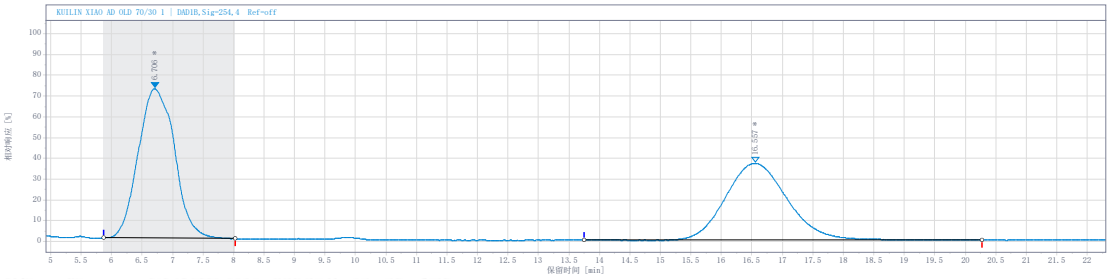


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
10.8	3.33	730.25	8.91	5.09
17.7	10.85	13609.36	108.74	94.91

3ai

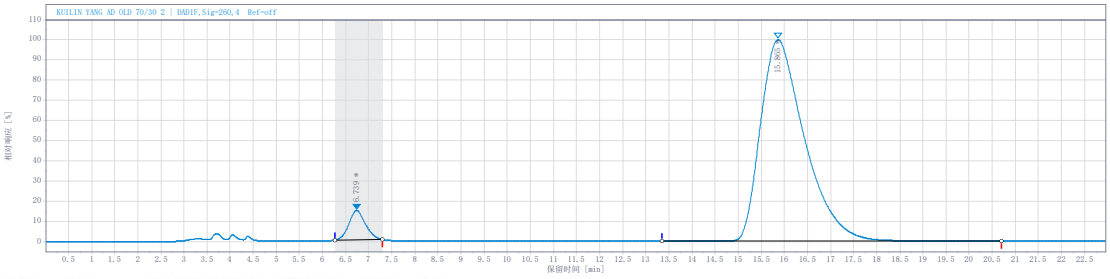
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.71	2.15	619.91	14.97	53.52
16.6	6.52	538.35	7.69	46.48

Asymmetric version

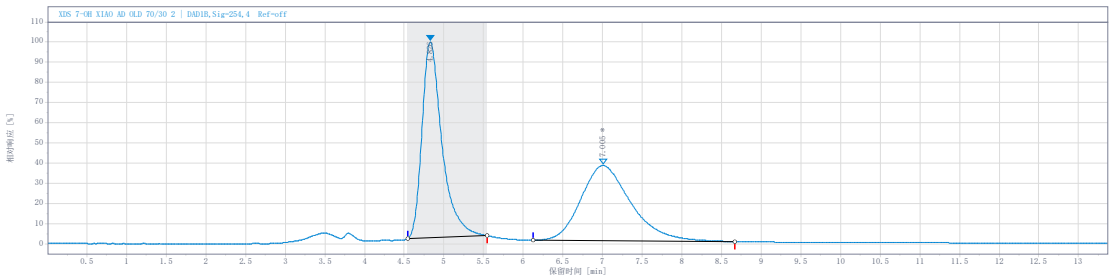


Signal: DAD1F, Sig=260, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.74	1.03	6360.70	258.84	5.16
15.9	7.37	116949.89	1767.38	94.84

3aj

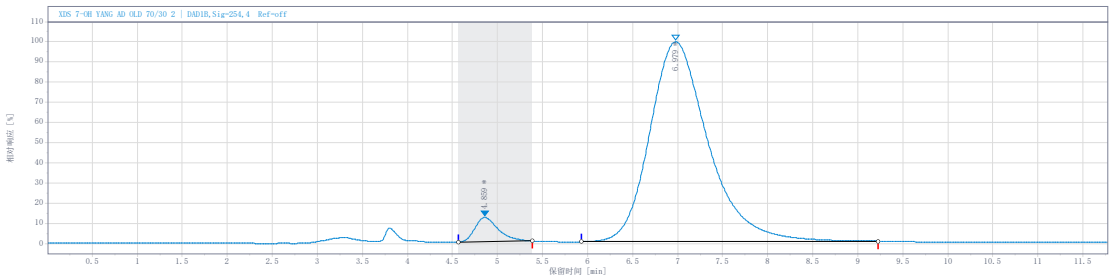
Racemic sample



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.83	1.00	4276.07	243.28	51.11
7.01	2.54	4089.68	93.44	48.89

Asymmetric version

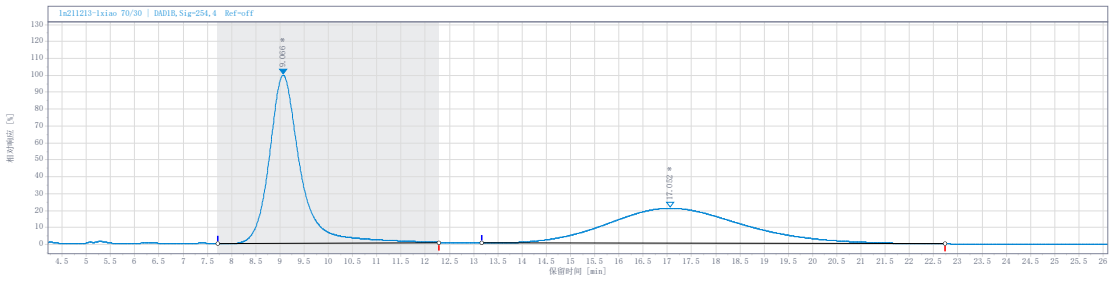


Signal: DAD1B, Sig=254, 4 Ref=off

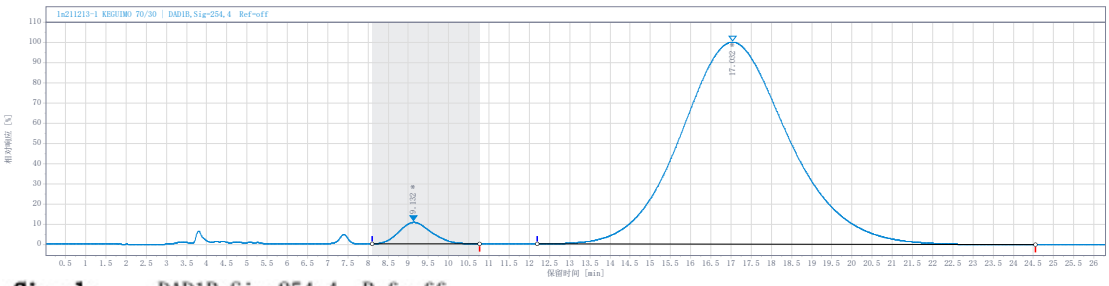
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.86	0.82	267.80	14.87	4.59
6.98	3.29	5561.29	123.34	95.41

3aa (Gram scale)

Racemic sample



Asymmetric version

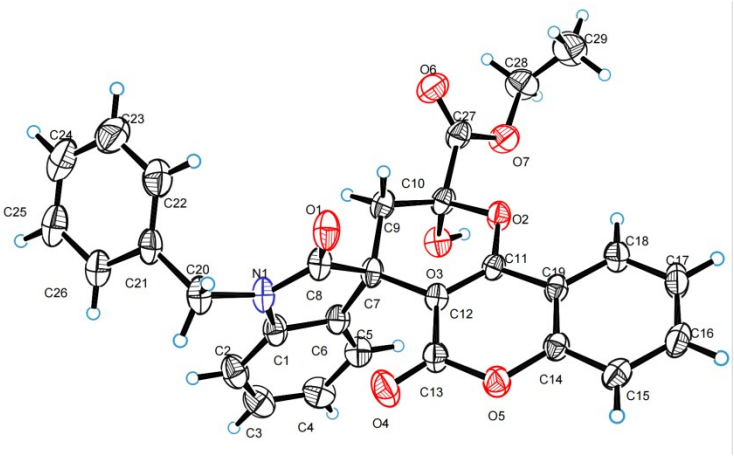


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
9.13	2.66	1139.47	20.33	3.11
17.0	12.35	35518.08	190.52	96.89

Part Ⅳ X-ray data of chiral **3aa**
Crystal data and structure refinement for **3aa:**

Empirical formula	C29H23NO7
Formula weight	497.48
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	11.7964(2)
b/Å	12.7829(2)
c/Å	16.2814(3)
α/°	90
β/°	90
γ/°	90
Volume/Å3	2455.11(7)
Z	4
ρcalcg/cm3	1.346
μ/mm-1	0.802
F(000)	1040.0
Crystal size/mm3	0.2 × 0.18 × 0.15
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.794 to 145.928
Index ranges	-14 ≤ h ≤ 10, -15 ≤ k ≤ 15, -19 ≤ l ≤ 19
Reflections collected	18417
Independent reflections	4814 [Rint = 0.0343, Rsigma = 0.0272]
Data/restraints/parameters	4814/0/336
Goodness-of-fit on F2	1.067
Final R indexes [I>=2σ (I)]	R1 = 0.0450, wR2 = 0.1112
Final R indexes [all data]	R1 = 0.0555, wR2 = 0.1194
Largest diff. peak/hole / e Å-3	0.20/-0.19
Flack parameter	0.01(10)



The crystal was prepared from the solution of **3aa** in toluene. Dissolved 10 mg **3aa** with 1 mL of toluene and volatilized slowly at 0 ℃ for 30 days. CCDC 2171098 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.