Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Organocatalytic formal [4+2] cycloaddition of o-quinone-methyl derivatives and 2-isocyanatomalonate diesters for the construction of chroman derivatives with adjacent quaternary chiral centers

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1.General Information

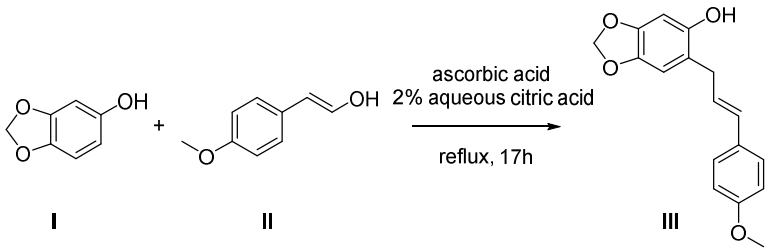
All reactions and manipulations which are sensitive to moisture or air were performed under inert atmosphere of argon. Oil bath was served as the heat source. All commercially available reagents were used without further purification. Chromatography was conducted by using 300-400 mesh silica gel. NMR spectra were recorded on a Bruker Ascend spectrometer at 400 MHz (^{1}H NMR) or 101 MHz or 151 MHz (^{13}C NMR) and 376 MHz (^{19}F NMR). NMR spectra were recorded in deuterated DMSO-*d6* as a solvent with residual DMSO (δ 2.50 ppm. for ^{1}H NMR and δ 39.5 ppm. for ^{13}C NMR) taken as the inert standard and were reported in ppm. Abbreviations for signal coupling are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dq = double quartet, and td = double triplet. Coupling constants were taken from the spectra directly and are uncorrected. Melting points (m.p.) were recorded on an SRS-optic melting point apparatus. Optical rotations were determined using a Rudolph Research Analytical Autopol VI automatic polarimeter. High-resolution mass spectra (HRMS) were recorded on Bruker micrOTOF-Q III, by the ESI method. HPLC analyses were performed using Agilent Technologies 1260 Infinity II with DAICEL Chiralcel AD-H column and DAICEL Chiralcel OD-H column. Single-Crystal X-Ray diffraction was recorded at Bruker APEX-II CCD diffractometer.

2. Experimental Procedures

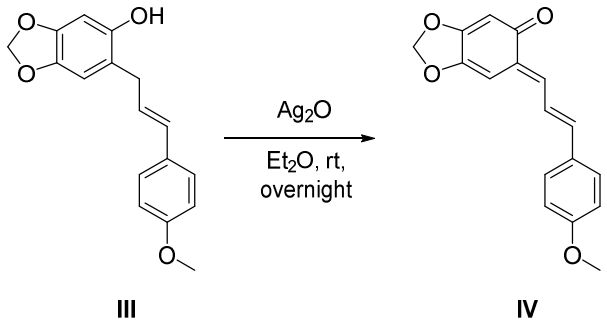
2.1 Synthesis of *o*-quinone methides (o-QMs)[1]

1a-1g were synthesized according to Jurd's procedure.

2.2 General synthesis of vinyl *o*-quinone methides.[2] (4a-4n)



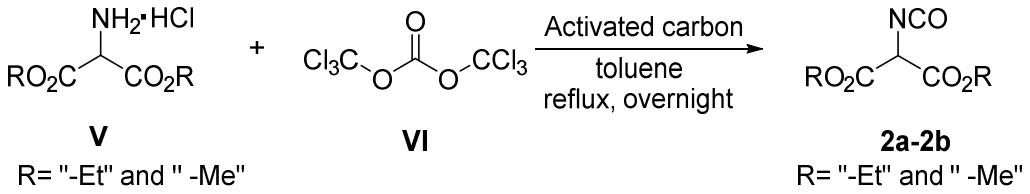
A suspension of sesame phenol **I** (3.00 g, 21.7 mmol) and 4-Methoxybenzyl alcohol **II** (3.00 g, 21.7 mmol) in 2% aqueous citric acid (55 mL) containing ascorbic acid (1.09 g, 6.08 mmol) was refluxed for 17 hours, then cooling to room temperature, The reaction solution was extracted three times with ethyl acetate (30 mL x3). The combined organic extracts were dried over $NaSO_4$, filtered, and concentrated in vacuo. then the oil product was purified by silica gel column chromatography to give **III** which was used in the next step.



Under the argon atmosphere, the solid **III** (1.0 g) was dissolved in dry diethyl ether (50 mL), followed by addition of silver oxide (1.5 g) and reacting at room temperature overnight. Then the reaction solution was filtered, the residue was washed with dichloromethane and diethyl ether until the flowing liquid became colorless. Then the organic solution was concentrated in vacuo to 10 mL and crystals were collected. The products matched the known ^{1}H NMR spectra.

2.3 Synthesis of isocyanatomalonate diester.

2.3.1 Synthesis of 2a-2b[3]



V R= "-Et" and " -Me"

VI

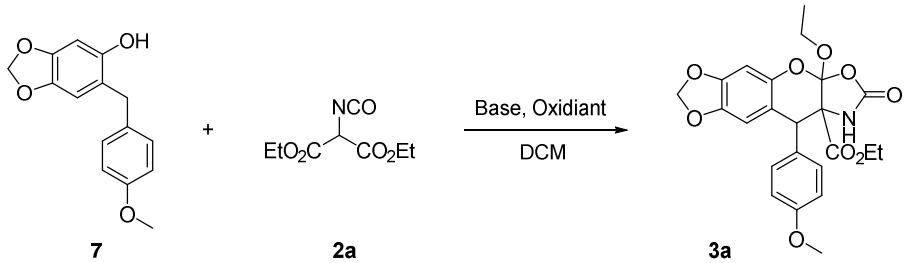
2a-2b R= "-Et" and " -Me"

Diethyl aminomalonate hydrochloride **V** (11.5 g, 54.5 mmol) was dissolved in dry toluene (55 mL) under nitrogen atmosphere, followed by the addition of activated carbon (40 mg), then stirring at 0°C for 10 minutes, Triphosgene **VI** was added in batches within two hours, then the reaction was conducted at 80°C for one hour before stirring at room temperature for five minutes, then refluxed at 115°C overnight, cooled to room temperature, then the reaction solution was filtered quickly through celite, the solvent was removed in vacuo, and the compound **2** (8.8 g, 80% yield) was obtained by distillation under reduced pressure (83°C, 1.0 mmHg). The products matched the known ^{1}H NMR spectra.

2.3.1 Synthesis of 2c.

The **2c** were synthesized according to takemoto's procedure[4].

2.4 Screening conditions for the synthesis of 3a via in-situ oxidation strategy



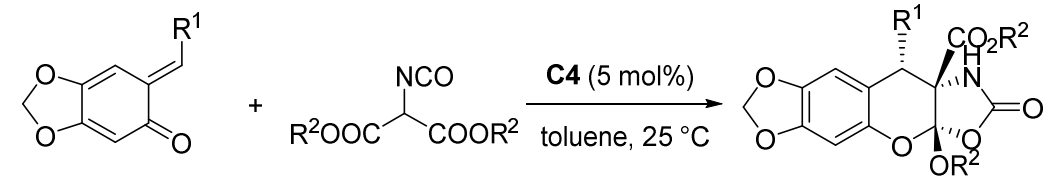
7 **2a** **3a**

Entry	Oxidiant	Base	Solvent	Result
1	Ag_2O	K_2CO_3	DCM	np
2	Ag_2O	Cs_2CO_3	DCM	np
3	$K_3Fe(CN)_6$	Cs_2CO_3	DCM	np
4	$AgNO_3$	Cs_2CO_3	DCM	np
5	DDQ	Cs_2CO_3	DCM	np
6	BPO	Cs_2CO_3	DCM	np
7	PhI(OAc)2	Cs_2CO_3	DCM	np
8	MnO2	**C4**	DCM	np

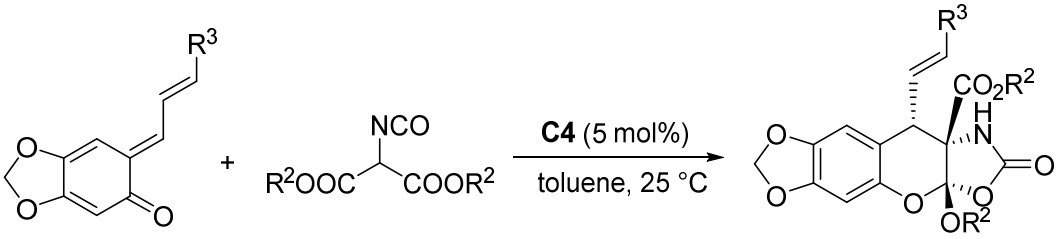
Reaction conditions: **7** (0.12 mmol, 1.2 equiv.), **2** (0.1 mmol, 1.0 equiv.), **Oxidiant** (0.2mmol, 2.0 equiv.), **Base** (0.12mmol, 1.2 equiv.), **C4** (5.0 mol%)

in 1.0 mL dry DCM under an argon atmosphere at room temperature; the reactions were detected by TLC, LCMS and ^{1}H NMR. "np"= "no product".

2.5 General procedure for the formal [4+2] annulation of o-QMs and styryl-substituted o-QMs.



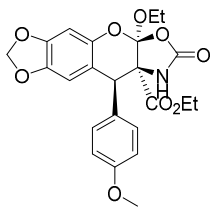
1 **2** **3**



4 **2** **6**

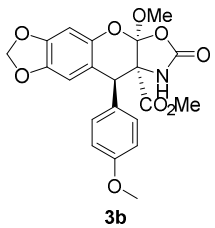
A mixture of **1** or **4** (0.1 mmol) and **C4** (0.005 mmol) in dry toluene (1.0 mL) was stirred for 5 min at 25°C in a Schlenk tube under an atmosphere of argon. Then **2** (30 mg, 0.15 mmol) was added to the above mixtures via microsyringe. The mixture was stirred at 25 ºC until the starting material was completely consumed (determined by thin layer chromatography monitoring). Then, the reaction was quenched with methanol, and the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (PE/EA 8:1) to afford **3** or **6**.

Ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-(4-methoxyphenyl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] Chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (3a)



Prepared by the general procedure, and **3a** was isolated as a white solid, > 20:1 d.r., 93.7% ee. (39.8 mg, 87% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.72 (s, 1H), 7.37 – 7.29 (m, 1H), 7.19 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.06 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.97 – 6.90 (m, 1H), 6.87 (s, 1H), 6.04 (s, 1H), 5.98 (s, 2H), 5.26 (s, 1H), 4.10 – 4.00 (m, 3H), 3.99 – 3.87 (m, 1H), 3.76(s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.3, 157.1, 154.4, 146.7, 144.4, 143.9, 129.1, 129.0, 123.0, 121.4, 120.4, 118.4, 111.0, 106.7, 101.5, 100.9, 73.8, 61.7, 60.2, 55.6, 38.6, 14.8, 13. 7. **HRMS (ESI)** m/z calcd for $C_{23}H_{23}NO_9$ [M + Na] $^+$: 480.1265, found: 480.1264. $[\alpha]_D^{25}$ = -33.26 (c = 0.20, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 16.3 min (major), 21.8 min (minor), mp = 182.8–183.9 ºC.

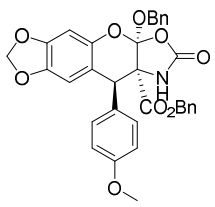
Methyl (3aR,10S,10aR)-3a-methoxy-10-(4-methoxyphenyl)-2-oxo-1,2-dihydro-10H-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3aH)-carboxylate (3b).



3b

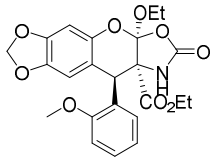
Prepared by the general procedure, and **3b** was isolated as a white solid, > 20:1 d.r., 96% ee. (35.6 mg, 83% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.77 (s, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.88 (s, 1H), 6.27 (s, 1H), 5.99 (s, 2H), 4.71 (s, 1H), 3.77 (s, 3H), 3.64 (s, 3H), 3.62 (s, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.45, 158.86, 153.86, 146.82, 144.27, 143.87, 131.73, 125.40, 120.76, 117.91, 114.02, 107.05, 101.58, 101.00, 74.63, 55.03, 52.92, 51.59, 46.31. **HRMS (ESI)** m/z calcd for $C_{21}H_{19}NO_9$ [M + Na] $^+$: 452.0952, found: 452.0960. $[\alpha]_D^{25}$ = -58.33 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 15.6 min (major), 17.3 min (minor), mp = 162.8–165.4 ºC.

Benzyl (3aR,10S,10aR)-3a-(benzyloxy)-10-(4-methoxyphenyl)-2-oxo-1,2-dihydro-10H-[1,3]dioxolo [4',5':6,7]chromeno[3,2-d]oxazole-10a(3aH)-carboxylate (3c).



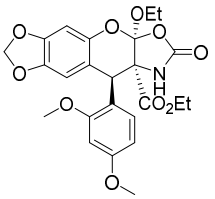
Prepared by the general procedure, and **3c** was isolated as a white solid, > 20:1 d.r., 89% ee. (44.1 mg, 76% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.90 (s, 1H), 7.39 – 7.18 (m, 10H), 7.13 (d, 2H), 6.92 (s, 1H), 6.90 (s, 2H), 6.27 (s, 1H), 6.00 (s, 2H), 5.13 (d, *J* = 12.1 Hz, 1H), 5.01 (s, 2H), 4.98 (d, *J* = 12.2 Hz, 1H), 4.76 (s, 1H), 3.78 (s, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 166.89, 158.87, 153.83, 146.83, 144.27, 143.92, 136.44, 134.78, 131.72, 128.32, 128.24, 128.09, 127.90, 127.79, 127.19, 120.82, 117.84, 114.02, 107.10, 101.59, 101.01, 74.76, 67.48, 65.83, 55.05, 46.42. **HRMS (ESI)** m/z calcd for $C_{33}H_{27}NO_9$ [M + Na] $^+$: 604.1574, found: 604.1580. $[\alpha]_D^{25}$ = -23.33 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL OD-H), n-hexane/2-propanol = 75/25 flow rate 0.8 mL/min, detection at 254 nm, t_R = 17.761 min (major), 10.518 min (minor), mp = 128.4-132.6 ºC.

Ethyl (3aR,10S,10aR)-3a-ethoxy-10-(2-methoxyphenyl)-2-oxo-1,2-dihydro-10H-[1,3]dioxolo [4',5':6,7]chromeno[3,2-d]oxazole-10a(3aH)-carboxylate (3d).



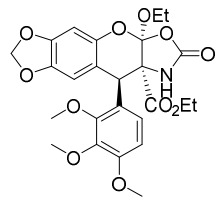
Prepared by the general procedure, and **3d** was isolated as a white solid, > 20:1 d.r., 98% ee. (35.7 mg, 78% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.72 (s, 1H), 7.36 – 7.31. (m, 1H), 7.20 – 7.16 (m, 1H), 7.09 – 7.04 (m, 1H), 6.97 – 6.91 (m, 1H), 6.87 (s, 1H), 6.04 (s, 1H), 5.98 (s, 2H), 5.26 (s, 1H), 4.12 – 4.02 (m, 3H), 3.99 – 3.88 (m, 1H), 3.76 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.3, 157.1, 154.5, 146.7, 144.4, 143.9, 129.1, 129.0, 123.0, 121.4,, 120.4, 118.4, 111.0, 106.7, 101.5, 100.9, 73.7, 61.8, 60.2, 55.6, 38.6, 14.8, 13.7. **HRMS (ESI)** m/z calcd for $C_{23}H_{23}NO_9$ [M + Na] $^+$: 480.1265, found: 480.1263. $[\alpha]_D^{25}$ = -39.33 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 8.3 min (major), 23.8 min (minor), mp = 166.8–167.3 ºC.

ethyl (3a*R*,10*S*,10a*R*)-10-(2,4-dimethoxyphenyl)-3a-ethoxy-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (3e)



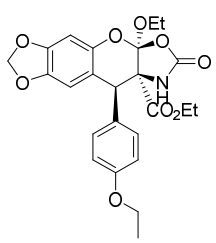
Prepared by the general procedure, and **3e** was isolated as a white solid, > 20:1 d.r., 97 % ee. (36.5 mg, 75% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.71 (s, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 6.85 (s, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 6.51 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.05 (s, 1H), 5.98 (s, 2H), 5.16 (s, 1H), 4.10 – 4.01 (m, 3H), 3.15 – 3.05 (m, 1H), 3.78 (s, 3H), 3.75 (s, 3H),1.17 (t, *J* = 7.2 Hz, 3H),1.09 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.3, 156.0, 158.3, 154.4, 146.6, 144.4, 143.9, 123.0, 121.7, 118.40, 114.84, 106.72, 104.84, 101.48, 100.88, 98.41, 74.04, 61.69, 60.17, 55.63, 55.15, 38.1, 14.8, 13.7. **HRMS (ESI)** m/z calcd for $C_{24}H_{25}NO_{10}$ [M + Na] $^+$: 510.1371, found: 510.1373. $[\alpha]_D^{25}$ = -46.30 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 22.3 min (major), 53.4 min (minor), mp = 181.3–184.9 ºC.

ethyl (3a*R*,10*R*,10a*R*)-3a-ethoxy-2-oxo-10-(2,3,4-trimethoxyphenyl)-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (3f)



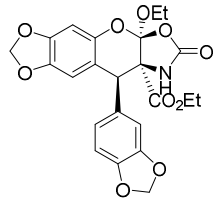
Prepared by the general procedure, and **3f** was isolated as a white solid, > 20:1 d.r., 96 % ee. (41.9mg, 81% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.78 (s, 1H), 7.00 (s, 1H), 6.86 (s, 1H), 6.79 (d, *J* = 3.2 Hz, 1H), 6.01 (s, 1H), 5.98 (s, 2H), 5.13 (s, 1H), 4.16 – 4.03 (m, 3H), 4.02 – 3.87 (m, 1H), 3.82(s, 3H), 3.75 (s, 3H), 3.71 (s,3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.1, 154.4, 153.0, 152.1, 146.6, 144.2, 143.9, 141.6, 123.7, 121.9, 120.3, 118.5, 107.8, 106.6, 101.5, 100.9, 74.2, 61.8, 61.0, 60.3, 60.2, 55.7, 38.7, 14.8, 13.7. **HRMS (ESI)** m/z calcd for $C_{25}H_{27}NO_{11}$ [M + Na] $^+$: 540.1476, found: 540.1479. $[\alpha]_D^{25}$ = -42.56 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n- hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 16.5 min (major), 35.5 min (minor), mp = 191.2–192.6ºC.

ethyl(3a*R*,10*S*,10a*R*)-3a-ethoxy-10-(4-ethoxyphenyl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate(3g)



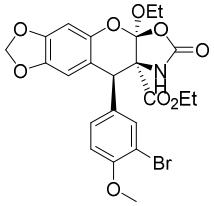
Prepared by the general procedure, and **3g** was isolated as a white solid, > 20:1 d.r., 91 % ee. (42.8mg, 91% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.72 (s, 1H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.86 (s, 1H), 6.23 (s, 1H), 5.99 (s, 2H), 4.70 (s, 1H), 4.15 – 4.06 (m, 3H), 4.06 – 3.99 (q, *J*=7.0 Hz, 2H), 3.94 (dq, *J* = 9.6, 7.1 Hz, 1H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.17 (dt, *J* = 9.0, 7.1 Hz, 6H).**^{13}C NMR** (151 MHz, DMSO-*d6*) 166.9, 158.2, 154.1, 146.7, 144.4, 143.8, 131.8, 125.2, 120.9, 117.9, 114.4, 107.0, 101.5, 101.0, 74.6, 63.0, 61.8, 60.1, 46.1, 14.8, 14.6, 13.8. **HRMS (ESI)** m/z calcd for $C_{24}H_{24}NO_9$ [M + Na] $^+$: 494.1422, found: 494.1428. $[\alpha]_D^{25}$ = -35.63 (c = 0.32, $CDCl_3$). **HPLC** (CHIRALCELAD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 15.2 min (major), 21.1 min (minor), mp = 160.3-161.2 ºC.

ethyl (3a*R*,10*S*,10a*R*)-10-(benzo[d][1,3]dioxol-5-yl)-3a-ethoxy-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (3h)



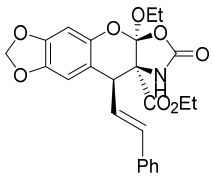
Prepared by the general procedure, and **3h** was isolated as a white solid, > 20:1 d.r., 92 % ee. (42.8 mg, 91% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.78 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.86 (s, 1H), 6.84 (d, *J* = 1.7 Hz, 1H), 6.80 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.30 (s, 1H), 6.05 (s, 2H), 6.00 (s, 2H), 4.70 (s,1H), 4.18 – 4.02 (m, 3H), 3.99 – 3.89 (m, 1H), 1.22 – 1.12 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 166.8, 154.1, 147.2, 147.0, 146.8, 144.3, 143.8, 127.1, 124.3, 120.7, 117.8, 110.7, 108.3, 107.0, 101.6, 101.1, 101.0, 74.5, 61.9, 60.1, 46.5, 14.8, 13.8. **HRMS (ESI)** m/z calcd for $C_{23}H_{21}NO_{10}$ [M + Na] $^+$: 494.1058, found: 494.1056. $[\alpha]_D^{25}$ = -74.50 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 14.9 min (major), 32.5 min (minor), mp = 189.6–190.3 ºC.

ethyl (3a*R*,10*S*,10a*R*)-10-(3-bromo-4-methoxyphenyl)-3a-ethoxy-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5': 6,7]chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (3i)



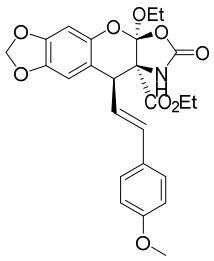
Prepared by the general procedure, and **3i** was isolated as a white solid, > 20:1 d.r., 91 % ee. (49.8mg, 93% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.88 (s, 1H), 7.50 (d, *J* = 2.2 Hz, 1H), 7.30 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.88 (s, 1H), 6.28 (s, 1H), 6.00 (s, 2H), 4.74 (s,1H), 4.20 – 4.03 (m, 3H), 3.99 – 3.89 (m, 1H), 3.86 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 166.8, 155.0, 154.1, 146.9, 144.3, 143.9, 134.9, 131.2, 127.3, 120.4, 117.8, 112.5, 110.5, 106.9, 101.6, 101.0, 74.3, 61.9, 60.1, 56.2, 45.7, 14.8, 13.8. **HRMS (ESI)** m/z calcd for $C_{23}H_{22}BrNO_9$ [M + Na] $^+$: 558.0370 and 560.0350, found: 558.0365 and 560.0345. $[\alpha]_D^{25}$ = -33.17 (c = 0.42, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n- hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 16.3 min (major), 21.6 min (minor), Mp = 151.7–152.6 ºC.

Ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-2-oxo-10-((*E*)-styryl)-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7]chromeno [3,2-d] oxazole-10a(3a*H*)-carboxylate (6a)



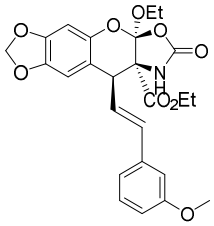
Prepared by the general procedure, and **6a** was isolated as a white solid, > 20:1 d.r., 92% ee. (37.6 mg, 83% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 9.00 (s, 1H), 7.62 – 7.47 (m, 2H), 7.44 – 7.33 (m, 2H), 7.34 – 7.25 (m, 1H), 6.84 (s, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 6.66 (s, 1H), 6.28 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.02 (s, 2H), 4.28 (d, *J* = 9.9 Hz, 1H), 4.27-4.13 (m, 2H), 4.13 – 4.04 (m, 1H), 3.98 – 3.89 (m, 1H), 1.25 – 1.13 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.0, 153.9, 146.9, 144.1, 143.9, 136.7, 136.2, 128.6 128.0, 126.8, 122.2, 120.3, 117.7, 106.8, 101.6, 101.2, 74.1, 61.8, 60.3, 45.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{24}H_{23}NO_8$ [M + Na] $^+$: 476.1316, found: 476.1314. $[\alpha]_D^{25}$ = -35.33 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 10.0 min (major), 21.2 min (minor), mp = 168.3–169.5 ºC.

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-4-methoxystyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6b)



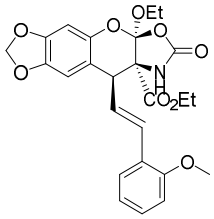
Prepared by the general procedure, and **6b** was isolated as a white solid, >20:1 d.r., 91 % ee, (43.0 mg, 89% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) ^{1}H NMR (400 MHz, DMSO) δ 8.97 (s, 1H), 7.47 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.83 (s, 1H), 6.69 – 6.63 (m, 2H), 6.10 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.01 (s, 2H), 4.30 – 4.13 (m, 3H), 4.13 – 4.03 (m, 1H), 3.99 – 3.87 (m, 1H), 3.77 (s, 3H), 1.19 (td, *J* = 7.0, 6.0 Hz, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.0, 159.2, 153.9, 146.9,144.7, 143.9, 136.2, 128.9, 128.1, 120.5, 119.5, 117.6, 114.0, 106.8, 101.5, 101.2, 74.2, 61.8, 60.3, 55.2, 45.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_9$ [M + Na] $^+$: 506.1422, found: 506.1418. $[\alpha]_D^{25}$ = -41.67 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 16.7 min (major), 26.2 min (minor), mp = 183.8–184.6 ºC.

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-3-methoxystyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6c)



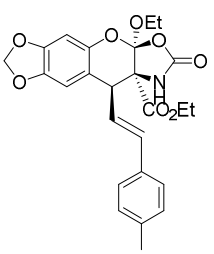
Prepared by the general procedure, and **6c** was isolated as a white solid, > 20:1 d.r., 95% ee. (40.9 mg，83%yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 9.00 (s, 1H), 7.39 – 7.23 (m, 1H), 7.18 – 7.13 (m, 1H), 7.10 – 7.05 (m, 1H), 6.90 – 6.85 (m, 1H), 6.84 (s,1H), 6.71 (d, *J* = 15.7 Hz, 1H), 6.66 (s, 1H), 6.27 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.02 (s, 2H), 4.28 (d, *J* = 9.9 Hz, 1H), 4.25 – 4.15 (m, 2H), 4.13 – 4.04 (m, 1H), 3.99 – 3.88 (m, 1H), 3.73 (s, 3H) 1.26-1.14 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.0, 159.5, 153.9, 146.9, 144.1, 143.9, 137.6, 136.6, 129.6, 122.4, 120.2, 119.6, 117.7, 113.9, 111.7, 106.8, 101.6, 101.2, 74.1, 61.9, 60.3, 55.1, 45.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_9$ [M + Na] $^+$: 506.1422, found: 506.1428. $[\alpha]_D^{25}$ = -29.27 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 10.4 min (major), 31.6 min (minor), mp = 179.7–181.5 ºC.

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-2-methoxystyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6d)



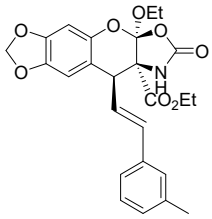
Prepared by the general procedure, and **6d** was isolated as a white solid, > 20:1 d.r., 98 % ee. (4.4 mg, 92% yield)，eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.97 (s, 1H), 7.77 – 7.59 (m, 1H), 7.37 – 7.22 (m, 1H), 7.09 – 6.92 (m, 3H), 6.83 (s,1H), 6.69 (s,1H), 6.18 (dd, *J* = 15.8, 9.9 Hz, 1H), 6.02 (s, 2H), 4.27 (d, *J* = 9.9 Hz, 1H), 4.25 – 4.15 (m, 2H), 4.13 – 4.04 (m, 1H), 3.98 – 3.87 (m, 1H), 3.80 (s, 3H) 1.34 – 1.11 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.0, 156.2, 153.9, 146.9, 144.1, 144.0, 131.2, 129.7, 127.0, 124.9, 122.2, 120.5, 120.4, 117.7, 111.3, 106.7, 101.5, 101.2, 74.2, 61.9, 60.3, 55.5, 45.4, 14.9, 13.8. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_9$ [M + Na] $^+$: 506.1422, found: 506.1418. $[\alpha]_D^{25}$ = -35.86 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 12.2 min (major), 60.3 min (minor), mp = 183.2–184.6 ºC.

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-4-methylstyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6e)



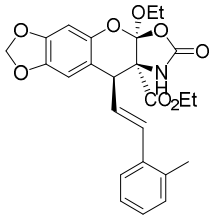
Prepared by the general procedure, and **6e** was isolated as a white solid, > 20:1 d.r., 96 % ee. (40.6 mg, 87% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.98 (s, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 6.83 (s, 1H), 6.69 (d, *J* = 15.7 Hz, 1H), 6.64 (d, *J* = 1.0 Hz, 1H), 6.21 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.08 – 5.95 (m, 2H), 4.26 (d, *J* = 9.9 Hz, 1H), 4.24 – 4.14 (m, 2H), 4.13 – 4.04 (m, 1H), 3.99 – 3.87 (m, 1H), 2.30 (s, 3H), 1.19 (td, *J* = 7.1, 4.8 Hz, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) ^{13}C NMR (101 MHz, DMSO) δ 167.0, 153.9, 146.9, 144.1, 143.9, 137.5, 136.6, 133.5, 129.1, 126.7, 120.9, 120.4, 117.7, 106.7, 101.6, 101.2, 74.1, 61.8, 60.3, 45.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_8$ [M + Na] $^+$: 490.1472, found: 490.1477. $[\alpha]_D^{25}$ = -41.86 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 11.2 min (major), 18.6 min (minor), mp = 166.2–167.1 ºC

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-3-methylstyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6f)



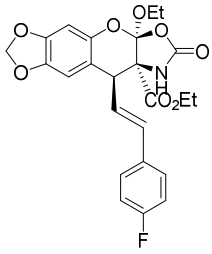
Prepared by the general procedure, and **6f** was isolated as a white solid, > 20:1 d.r., 94 % ee. (47.0 mg, 87% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.97 (s, 1H), 7.46 – 7.36 (m, 1H), 7.34 – 7.29 (m, 1H), 7.29 – 7.21 (m, 1H), 7.16 – 7.08 (m, 1H), 6.83 (s, 1H), 6.70 (d, *J* = 15.7 Hz, 1H), 6.65 (s, 1H), 6.26 (dd, *J* = 15.7, 10.3 Hz, 1H), 6.02 (s, 2H), 4.28 (d, *J* = 10.3 Hz, 1H), 4.24 – 4.13 (m, 2H), 4.09 (dq, *J* = 9.7, 7.0 Hz, 1H), 4.14 – 4.02 (m, 1H), 2.33 (s, 3H), 1.28 – 0.91 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 167.0, 153.9, 146.9, 144.1, 144.0, 137.7, 136.8, 136.2, 128.7, 128.5, 127.2, 124.1, 121.9, 120.3, 117.7, 106.8, 101.6, 101.2, 74.1, 61.8, 60.3, 45.0, 21.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_8$ [M + Na] $^+$: 490.1472, found: 490.1475. $[\alpha]_D^{25}$ = -46.75 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 8.4 min (major), 17.0 min (minor), mp = 174.3–175.6 ºC

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-2-methylstyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6g)



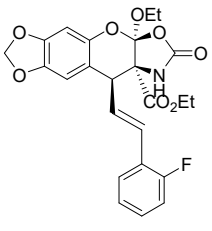
Prepared by the general procedure, and **6g** was isolated as a white solid, > 20:1 d.r., 97 % ee. (37.8 mg, 81% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.97 (s, 1H), 7.75 – 7.54 (m, 1H), 7.37 – 7.14 (m, 3H), 6.94 (d, *J* = 15.7 Hz,1H), 6.83 (s, 1H), 6.70 (s, 1H), 6.13 (dd, *J* = 15.7, 9.8 Hz, 1H), 6.02 (s, 2H), 4.34 (d, *J* = 9.8 Hz, 1H), 4.29 – 4.16 (m, 2H), 4.15 – 4.04 (m, 1H), 3.99 – 3.86 (m, 1H), 2.29 (s, 3H), 1.33 – 0.95 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 167.1, 154.0, 147.0, 144.2, 144.0, 135.4, 135.1, 134.9, 130.2, 128.0, 126.3, 126.1, 123.4, 120.4, 117.8, 106.9, 101.6, 101.3, 74.2, 62.0, 60.4, 45.3, 19.3, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}NO_8$ [M + Na] $^+$: 490.1472, found: 490.1473. $[\alpha]_D^{25}$ = -47.23 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 8.4 min (major), 22.7 min (minor), mp = 167.3–168.8 ºC

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-4-fluorostyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6h)



Prepared by the general procedure, and **6h** was isolated as a white solid, > 20:1 d.r., 97 % ee. (39.1 mg, 83% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.98 (s, 1H), 7.68 – 7.50 (m, 2H), 7.32 – 7.09 (m, 2H), 6.84 (s, 1H), 6.73 (d, *J* = 15.7 Hz, 1H), 6.68 (s, 1H), 6.21 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.02 (s, 2H), 4.27 (d, *J* = 9.9 Hz, 1H), 4.25 – 4.13 (m, 2H), 4.13 – 4.03 (m, 1H), 3.98 – 3.87 (m, 1H), 1.25 – 1.12 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 167.5, 162.4 (d, *J* = 245.0 Hz), 154.4, 147.4, 144.6, 144.4, 135.9, 133.3 (d, *J* = 3.1 Hz), 129.3, 129.2, 122.6, 120.7, 118.2, 116.0, 115.8, 107.3, 102.1, 101.7, 74.6, 62.3, 60.8, 45.4, 15.4, 14.5. **^{19}F NMR** (376 MHz, DMSO-*d6*) δ -113.87. **HRMS (ESI)** m/z calcd for $C_{24}H_{22}FNO_8$ [M + Na] $^+$: 494.1222, found: 494.1220. $[\alpha]_D^{25}$ = -26.73 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n- hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 12.9 min (major), 18.1 min (minor), mp = 191.3–192.7 ºC

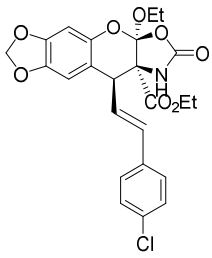
ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-2-fluorostyryl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7] chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6i)



Prepared by the general procedure, and **6i** was isolated as a white solid, > 20:1 d.r., 99 % ee. (41.9 mg, 89% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*), δ 8.99 (s, 1H), 7.92 – 7.72 (m, 1H), 7.43 – 7.29 (m, 1H), 7.29 – 7.16 (m, 2H), 6.87 (d, *J* = 15.8 Hz, 1H), 6.84 (s, 1H), 6.72 (s, 1H), 6.35 (dd, *J* = 15.8, 9.9 Hz, 1H), 6.02 (s, 2H), 4.35 (d, *J* = 9.9 Hz, 1H), 4.29 – 4.14 (m, 2H), 4.14 – 4.04 (m, 1H), 3.99 – 3.88 (m, 1H), 1.33 – 1.08 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 167.0, 159.4 (d, *J* = 247.4 Hz), 153.9, 147.0, 144.2, 143.9, 129.9 (d, *J* = 8.5 Hz), 128.3 (d, *J* = 4.6 Hz), 127.9 (d, J = 3.2 Hz), 125.2 (d, *J* = 3.2 Hz), 124.6 (d, *J* = 3.3 Hz), 123.8 (d, *J* = 12.1 Hz), 120.1, 117.7, 115.6 (d, *J* = 21.7 Hz), 106.8, 101.6, 101.2, 74.1, 61.9, 60.3, 45.3, 14.9, 13.9. **^{19}F NMR** (376 MHz, DMSO-*d6*) δ -119.12, **HRMS (ESI)** m/z calcd for $C_{24}H_{22}FNO_8$ [M + Na] $^+$: 494.1222,

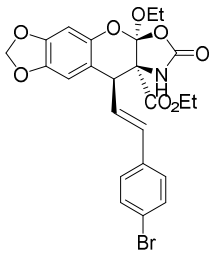
found: 494.1225. $[\alpha]_D^{25}$ = -29.67 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 9.5 min (major), 22.3 min (minor), mp = 183.1–184.9 ºC

ethyl (3a*R*,10*S*,10a*R*)-10-((*E*)-4-chlorostyryl)-3a-ethoxy-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7]chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6j)



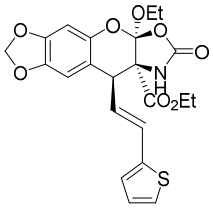
Prepared by the general procedure, and **6j** was isolated as a white solid, > 20:1 d.r., 96 % ee. (44.8 mg, 92% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.97 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 6.67 (s, 1H), 6.30 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.01 (s, 2H), 4.29 (d, *J* = 9.9 Hz, 1H), 4.26 – 4.13 (m, 2H), 4.13 – 4.04 (m, 1H), 3.99 – 3.88 (m, 1H), 1.32 – 1.08 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 166.9, 153.8, 146.9, 144.1, 143.9, 135.4, 135.2, 132.5, 128.5, 128.4, 123.3, 120.1, 117.6, 106.8, 101.6, 101.2, 74.0, 61.8, 60.3, 45.0, 14.8, 14.0. **HRMS (ESI)** m/z calcd for $C_{24}H_{22}ClNO_8$ [M + Na] $^+$: 510.0926 and 512.0897, found: 510.0930 and 512.0898. $[\alpha]_D^{25}$ = -60.50 (c = 0.15, $CDCl_3$). HPLC (CHIRALCEL AD-H), n-Hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 13.5 min (major), 20.030 min (minor), mp = 198.9–200.3 ºC

ethyl (3a*R*,10*S*,10a*R*)-10-((*E*)-4-bromostyryl)-3a-ethoxy-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7]chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6k)



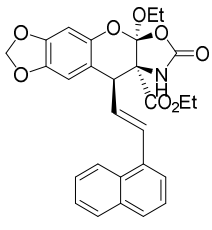
Prepared by the general procedure, and **6k** was isolated as a white solid, > 20:1 d.r., 96 % ee. (48.3 mg, 91% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.97 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 6.67 (s, 1H), 6.30 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.01 (s, 2H), 4.29 (d, *J* = 9.9 Hz, 1H), 4.26 – 4.13 (m, 2H), 4.13 – 4.03 (m, 1H), 3.99 – 3.87 (m, 1H), 1.32 – 1.08 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) δ 167.0, 153.9, 147.0, 144.2, 143.9, 135.5, 135.5, 131.5, 128.8, 123.3, 121.1, 120.1, 117.7, 106.8, 101.6, 101.2, 74.0, 61.9, 60.3, 45.0, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{24}H_{22}BrNO_8$ [M + Na] $^+$: 554.0421 and 556.0401, found: 554.0423 and 556.0403. $[\alpha]_D^{25}$ = -43.86 (c = 0.15, $CDCl_3$). HPLC (CHIRALCEL AD-H), n-Hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 254 nm, t_R = 14.0 min (major), 21.6 min (minor), mp = 201.1–202.7 ºC

ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-2-oxo-10-((*E*)-2-(thiophen-2-yl)vinyl)-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7]chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6l)



Prepared by the general procedure, and **6l** was isolated as a white solid, > 20:1 d.r., 97 % ee. (42.3 mg, 93% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 9.05 (s, 1H), 7.48 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.18 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.05 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.90 (d, *J* = 15.4 Hz, 1H), 6.84 (s,1H), 6.59 (s,1H), 6.11 – 5.96 (m, 3H), 4.26 (d, *J* = 10.1 Hz, 1H), 4.24 – 4.14 (m, 2H), 4.12 – 4.03 (m, 1H), 3.97 – 3.88 (m, 1H), 1.40 – 0.98 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.0, 153.9, 146.9, 144.1, 143.9, 140.8, 129.9, 127.7, 126.8, 125.9, 121.1, 120.3, 117.7, 106.5, 101.6, 101.2, 73.9, 61.9, 60.3, 44.9, 14.9, 14.0. **HRMS (ESI)** m/z calcd for $C_{22}H_{21}NO_8S$ [M + Na] $^+$: 482.0880, found: 482.0880. $[\alpha]_D^{25}$ = -33.33 (c = 0.15, $CDCl_3$). **HPLC** (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 10.4 min (major), 31.0 min (minor), mp = 178.4–179.8 ºC.

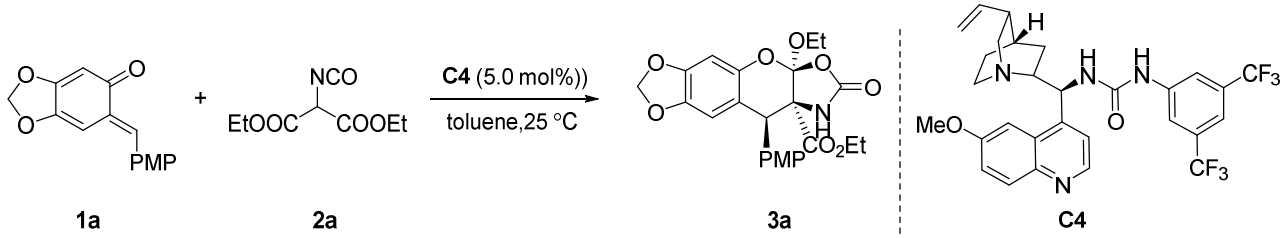
ethyl (3a*R*,10*S*,10a*R*)-3a-ethoxy-10-((*E*)-2-(naphthalen-1-yl)vinyl)-2-oxo-1,2-dihydro-10*H*-[1,3]dioxolo[4',5':6,7]chromeno[3,2-d]oxazole-10a(3a*H*)-carboxylate (6m)



Prepared by the general procedure, and **6m** was isolated as a white solid, > 20:1 d.r., 94 % ee. (41.7 mg, 83% yield), eluent (petroleum ether/ethyl acetate = 8:1). **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 9.05 (s, 1H), 8.18 – 8.10 （m, 1H）, 8.04 – 7.82 (m, 3H), 7.67 – 7.42 (m, 4H) , 6.87 (s,1H), 6.78 (s,1H), 6.30 (dd, *J* = 15.4, 9.9 Hz, 1H), 6.03 (s, 2H), 4.52 (d, *J* = 9.9 Hz, 1H), 4.31 – 4.17 (m, 2H), 4.17 – 4.07 (m, 1H), 4.01 – 3.90 (m, 1H), 1.30 – 1.14 (m, 6H). **^{13}C NMR** (151 MHz, DMSO-*d6*) 167.1, 153.9, 146.9, 144.2, 144.0, 134.1, 133.6, 133.2, 130.5, 128.5, 128.2, 126.4, 125.9, 125.7, 125.1, 124.3, 123.4, 120.4, 117.8, 106.9, 101.6, 101.2, 74.2, 61.9, 60.3, 45.3, 14.9,

14.0. **HRMS (ESI)** m/z calcd for $C_{28}H_{25}NO_8$ [M + Na] $^+$: 526.1472, found: 526.1471. $[\alpha]_D^{25}$ = -38.32 (c = 0.15, $CDCl_3$). HPLC (CHIRALCEL AD-H), n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, detection at 230 nm, t_R = 11.2 min (major), 39.8 min (minor), mp = 191.5–192.8 ºC.

1.5 Tertiary amino-urea catalyzed asymmertic cyclization reaction of QMs and 2-NCO at 1mmol scale.



1a **2a** **3a** **C4**

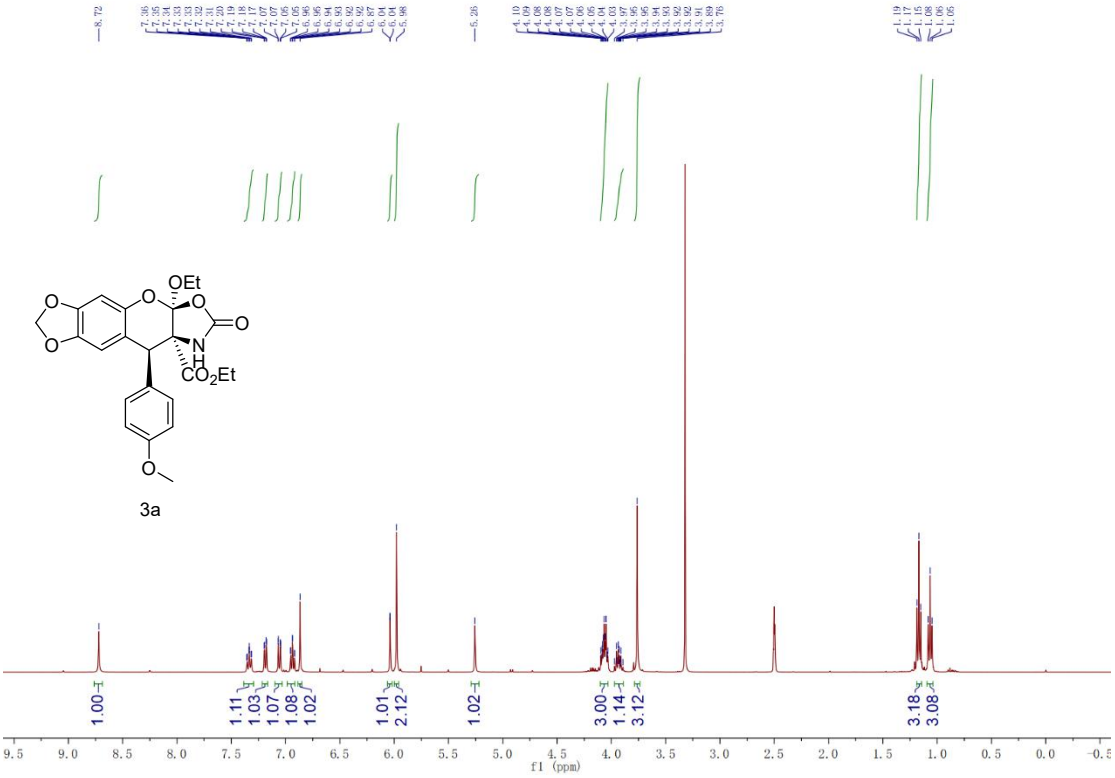
A mixture of **1a** (256 mg, 1.0 mmol) and **C4** (29 mg, 0.05 mmol) in dry toluene (10.0 mL) was stirred for 5 min at 25℃ in a Schlenk tube under an atmosphere of argon. Then diethyl 2-isocyanatomalonate **2a** (30mmg, 1.5mmol) was added to the tube containing the 1 and C4 via microsyringe. When the disappearance of starting material 1 was monitored by TLC plate, the reaction was quenched with methanol, then concentrated in vacuo. The product **3a** (370 mmg, 81 % yield, 91 % ee) was purified by column chromatography on silica gel (PE/EA 8:1).

3. Reference

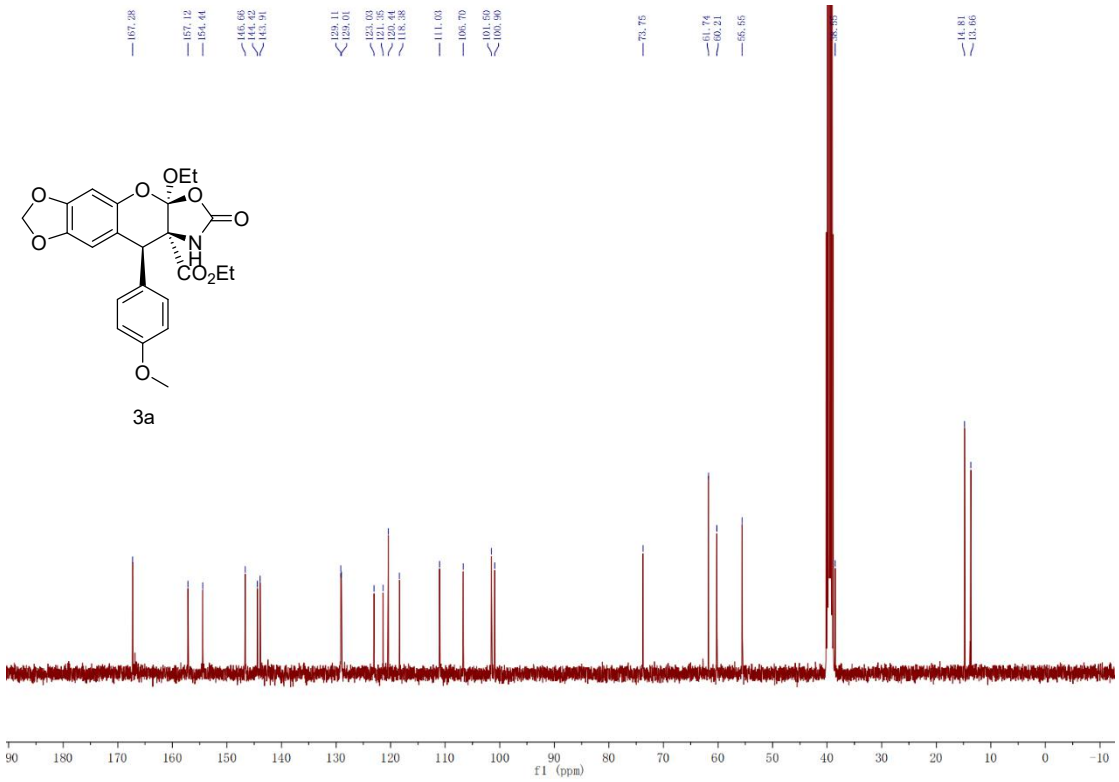
1. Leonard Jurd., *Teterhedron*., **1977**, *33*, 163-168.
2. Alafate Adili, Zhong-Lin Tao, Dian-Feng Chen and Zhi-Yong Han., *Org. Biomol. Chem.*, **2015**, *13*, 2247-2250.
3. Jin-xin Liu, Ya-ling Li, Miao-lin Ke, Min-jie Liu, Ping-ping Zhan,You-Cai Xiao, and Fener Chen., *J. Org. Chem.,* **2020**, *85*, 15360−15367.
4. Sakamoto Shota; Kazumi Naoya; Kobayashi Yusuke; Tsukano Chihiro; Takemoto Yoshiji., *Org. Let.* **2014**, *16*, 4758-4761.

4. Spectral Data

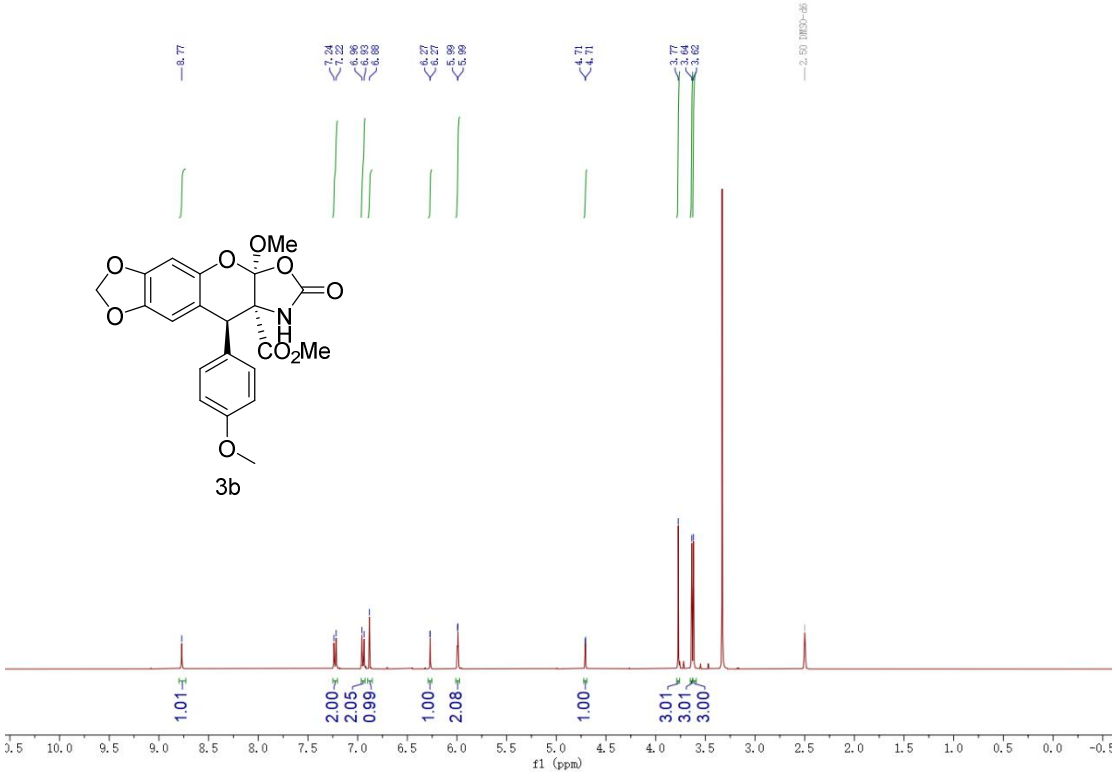
^{1}H NMR Spectrum of Compound 3a (400 MHz, DMSO-*d6*)



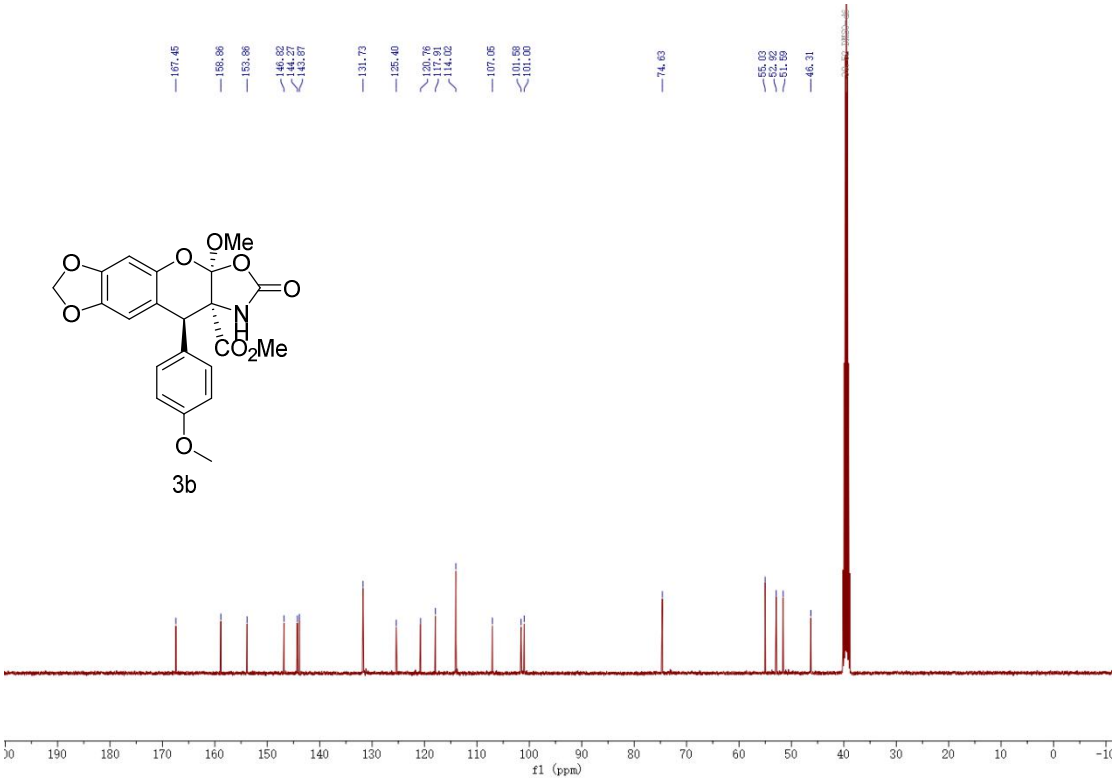
^{13}C NMR Spectrum of Compound 3a (151 MHz, DMSO-*d6*)



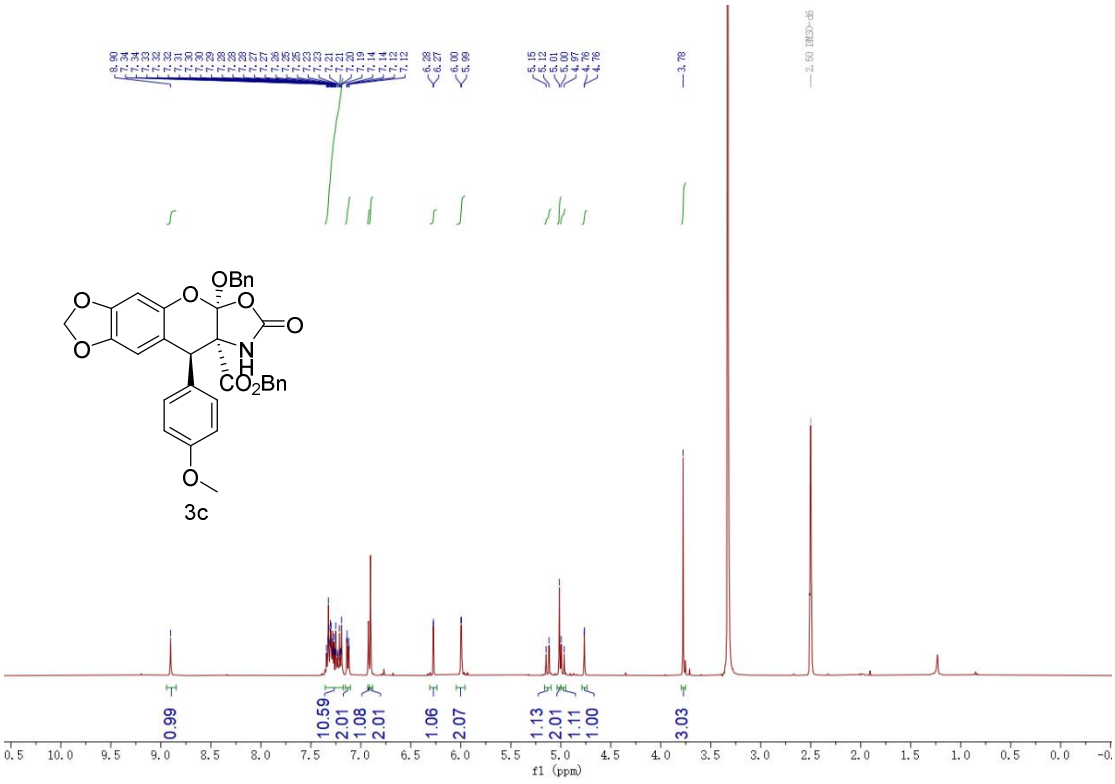
^{1}H NMR Spectrum of Compound 3b (400 MHz, DMSO-*d6*)



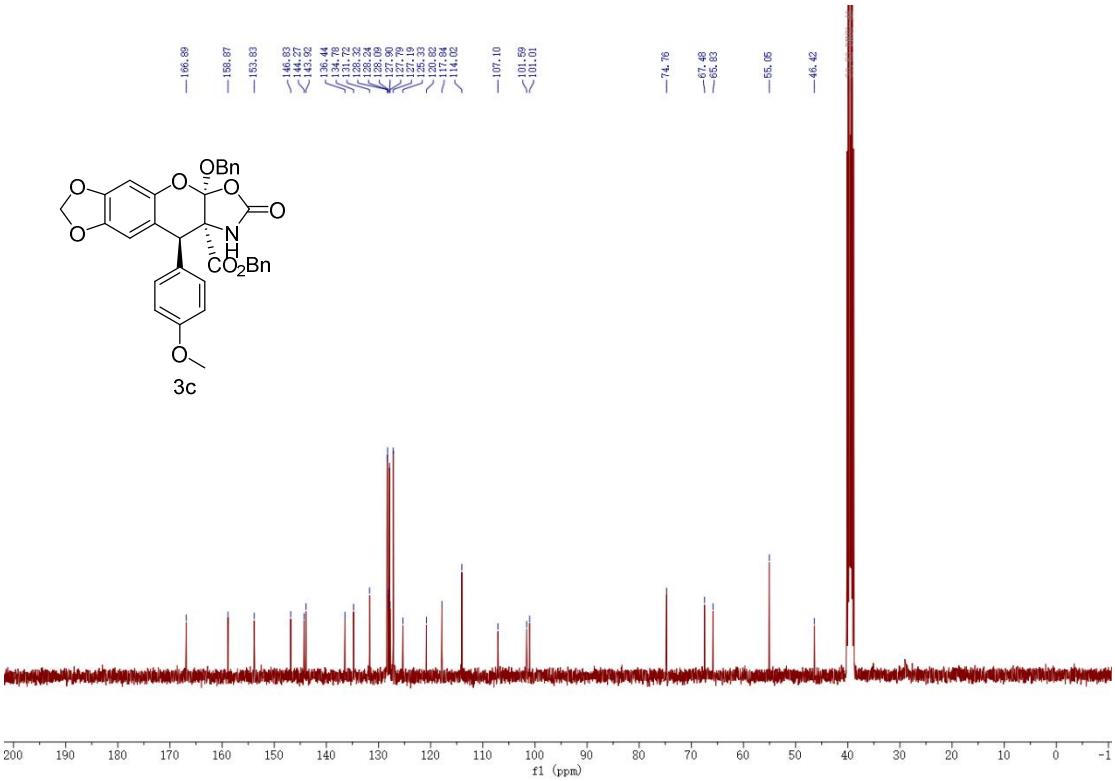
^{13}C NMR Spectrum of Compound 3b (151 MHz, DMSO-*d6*)



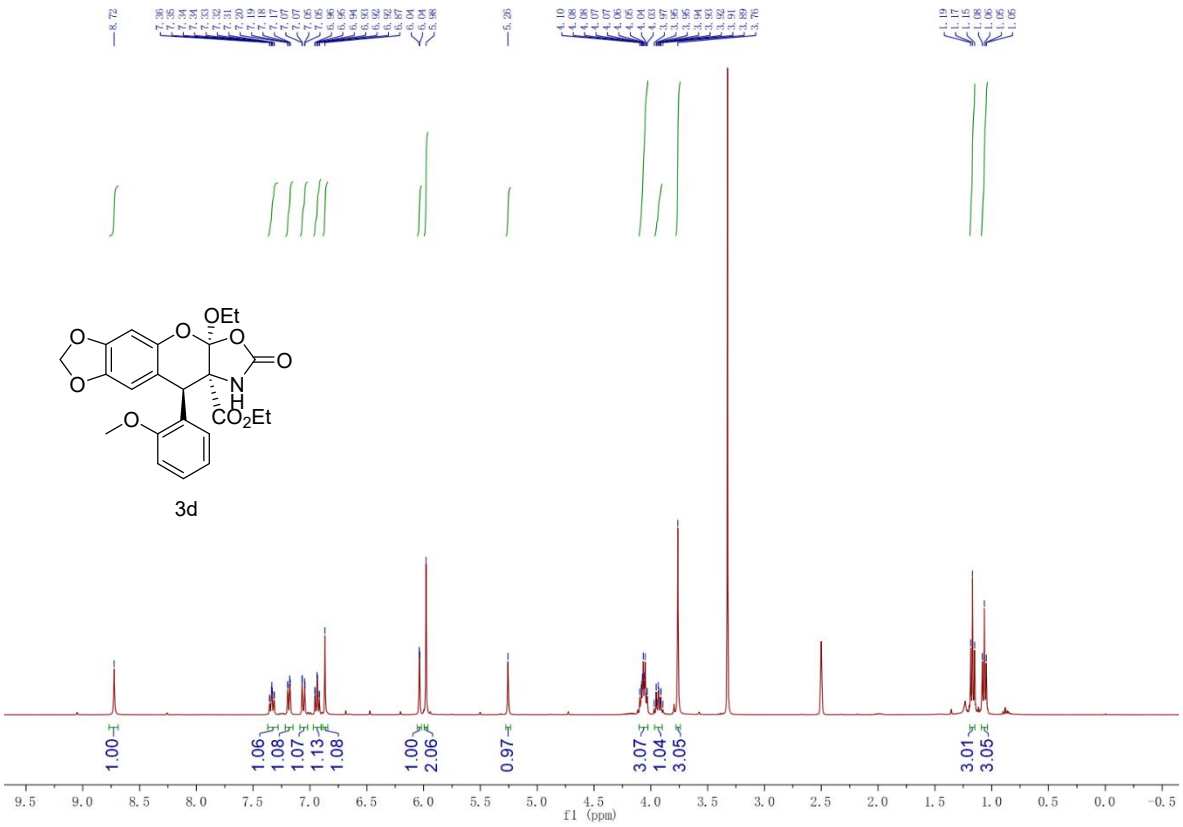
^{1}H NMR Spectrum of Compound 3c (400 MHz, DMSO-*d6*)



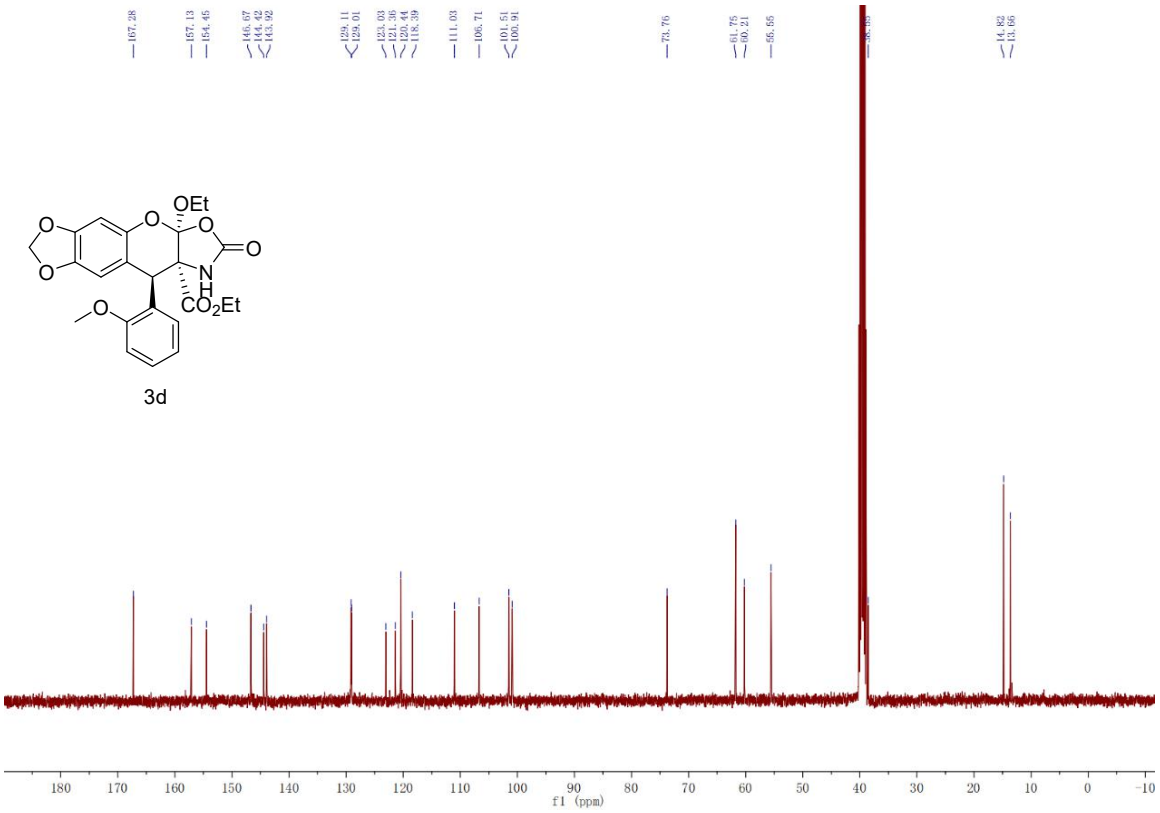
^{13}C NMR Spectrum of Compound 3c (151 MHz, DMSO-*d6*)



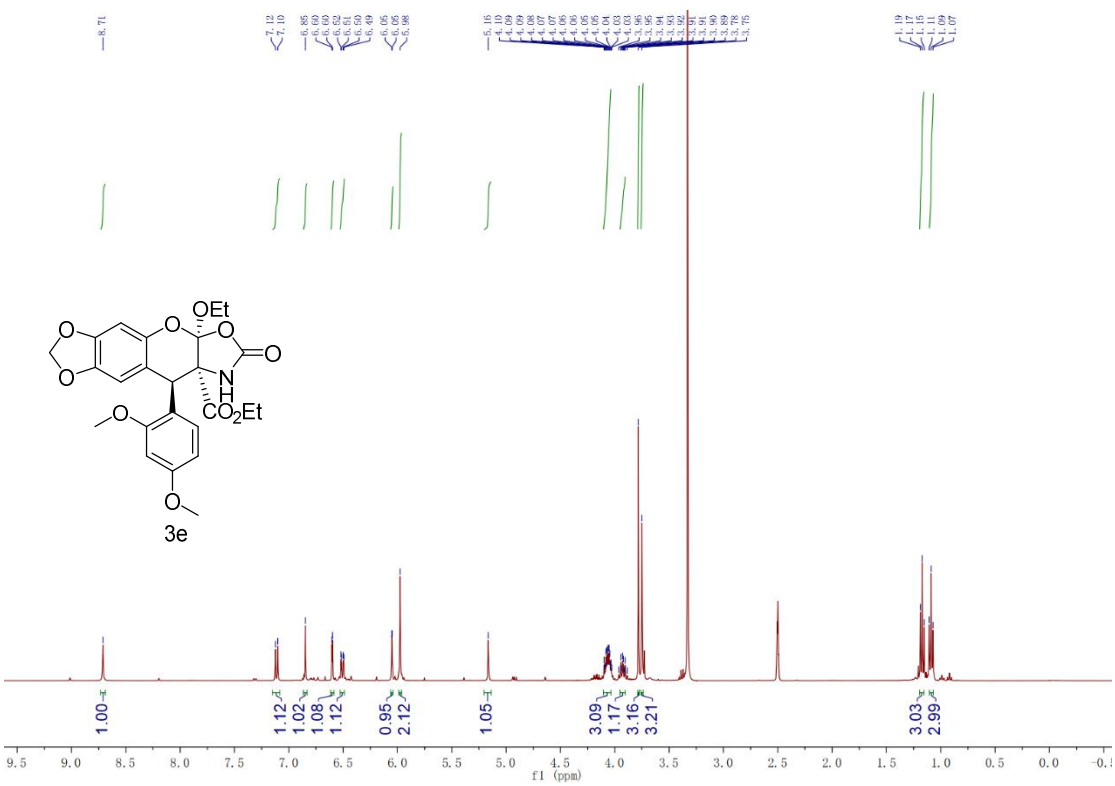
^{1}H NMR Spectrum of Compound 3d (400 MHz, DMSO-*d6*)



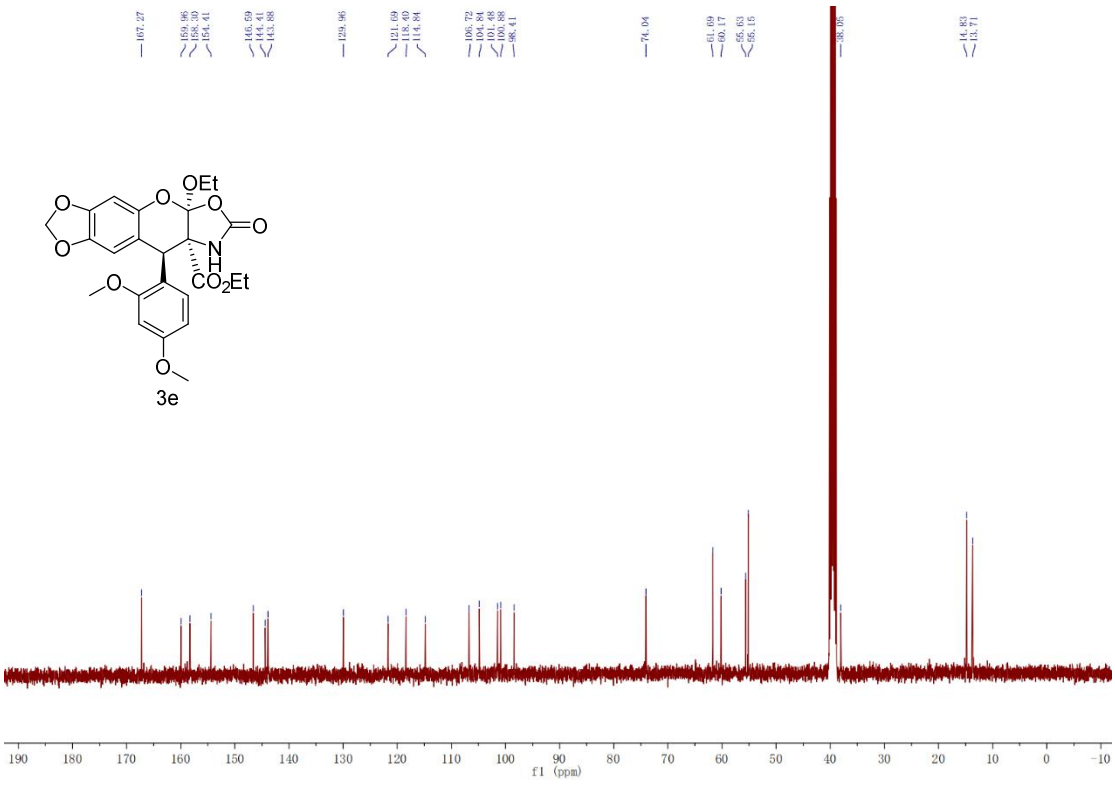
^{13}C NMR Spectrum of Compound 3d (151 MHz, DMSO-*d6*)



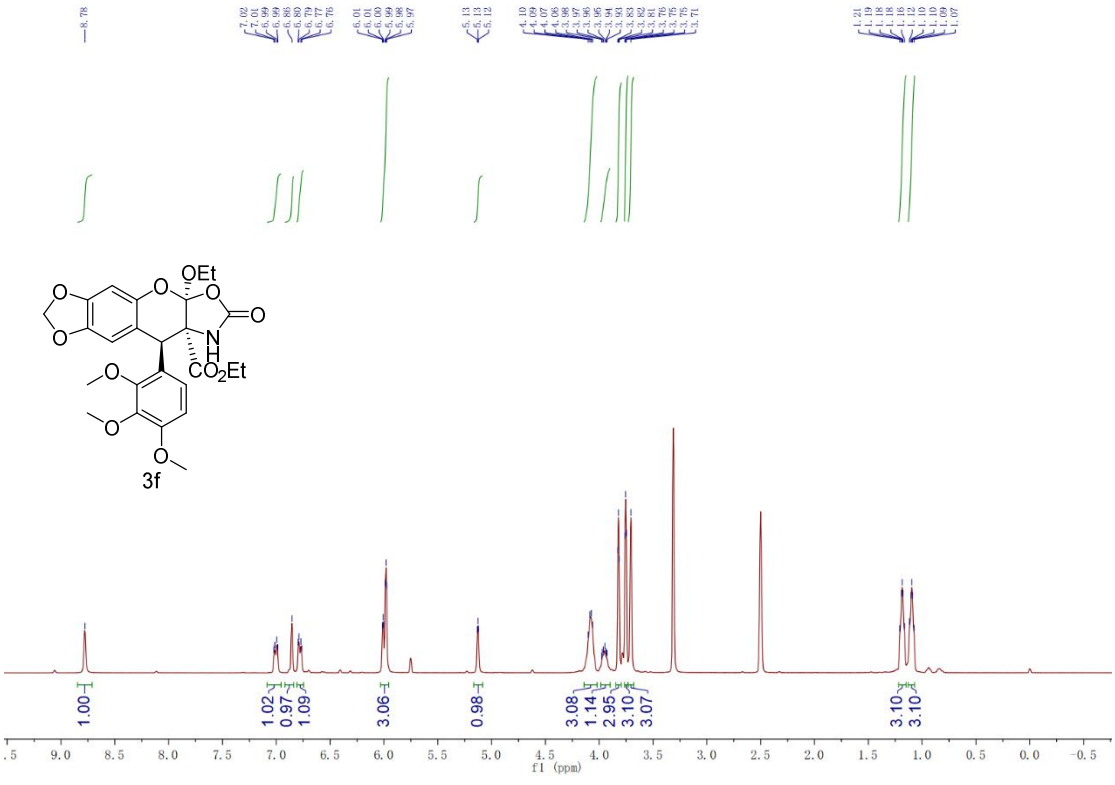
^{1}H NMR Spectrum of Compound 3e (400 MHz, DMSO-*d6*)



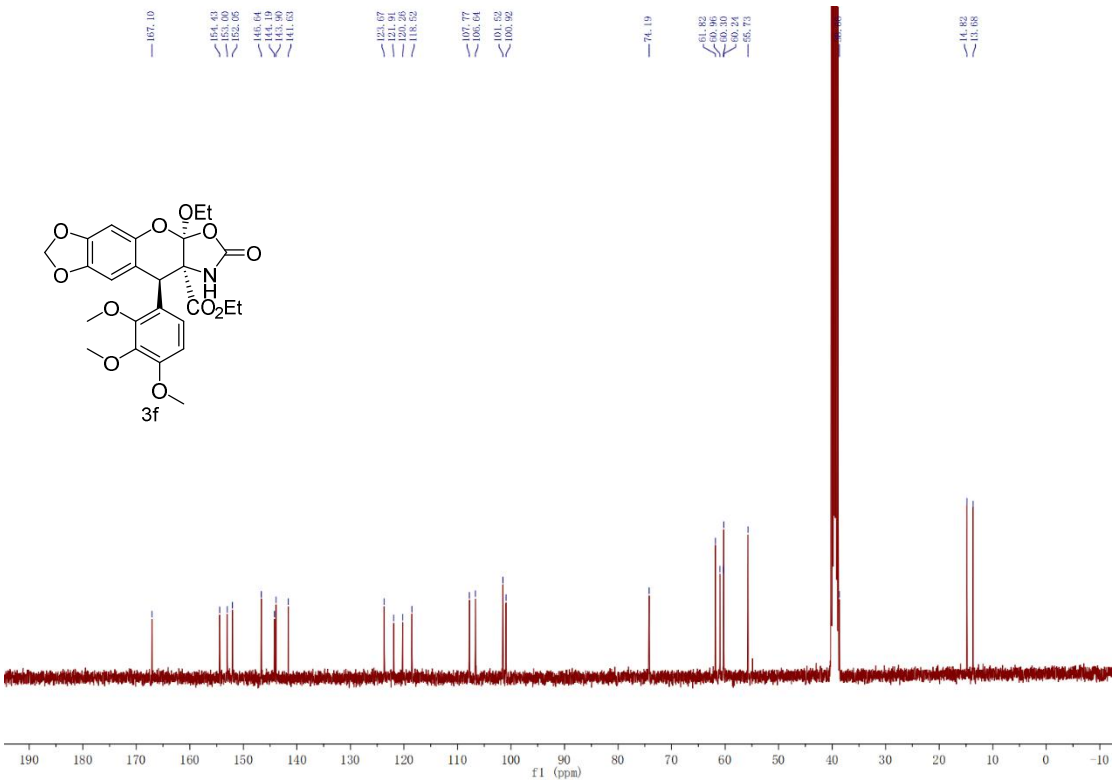
^{13}C NMR Spectrum of Compound 3e (151 MHz, DMSO-*d6*)



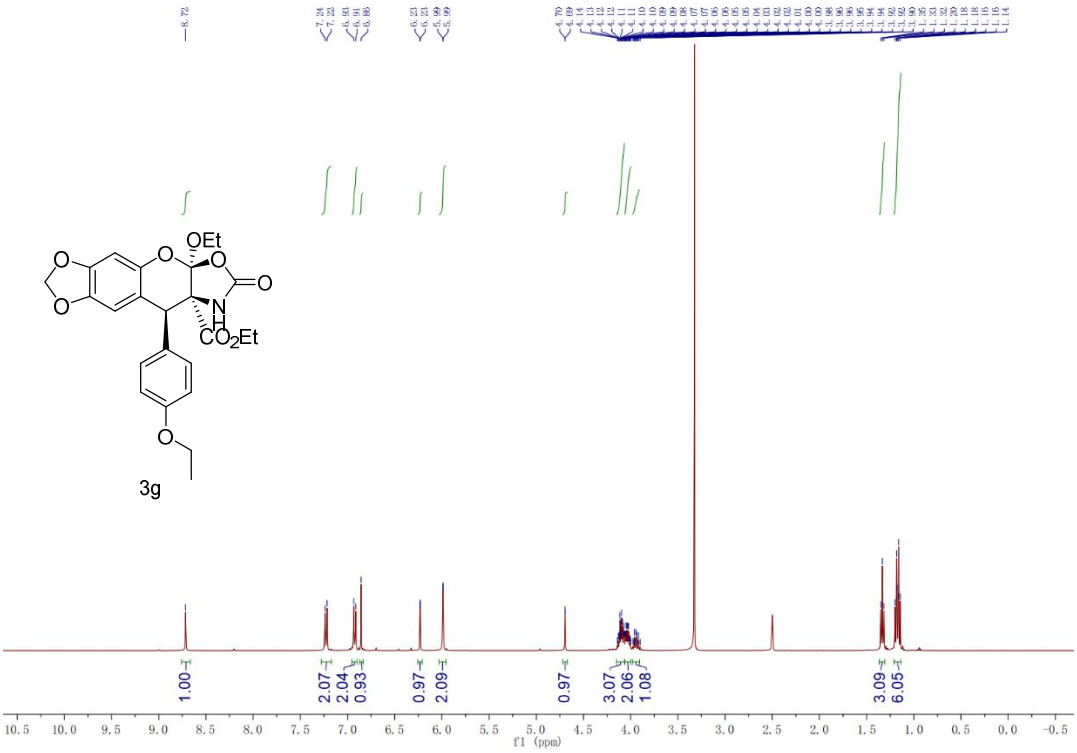
^{1}H NMR Spectrum of Compound 3f (400 MHz, DMSO-*d6*)



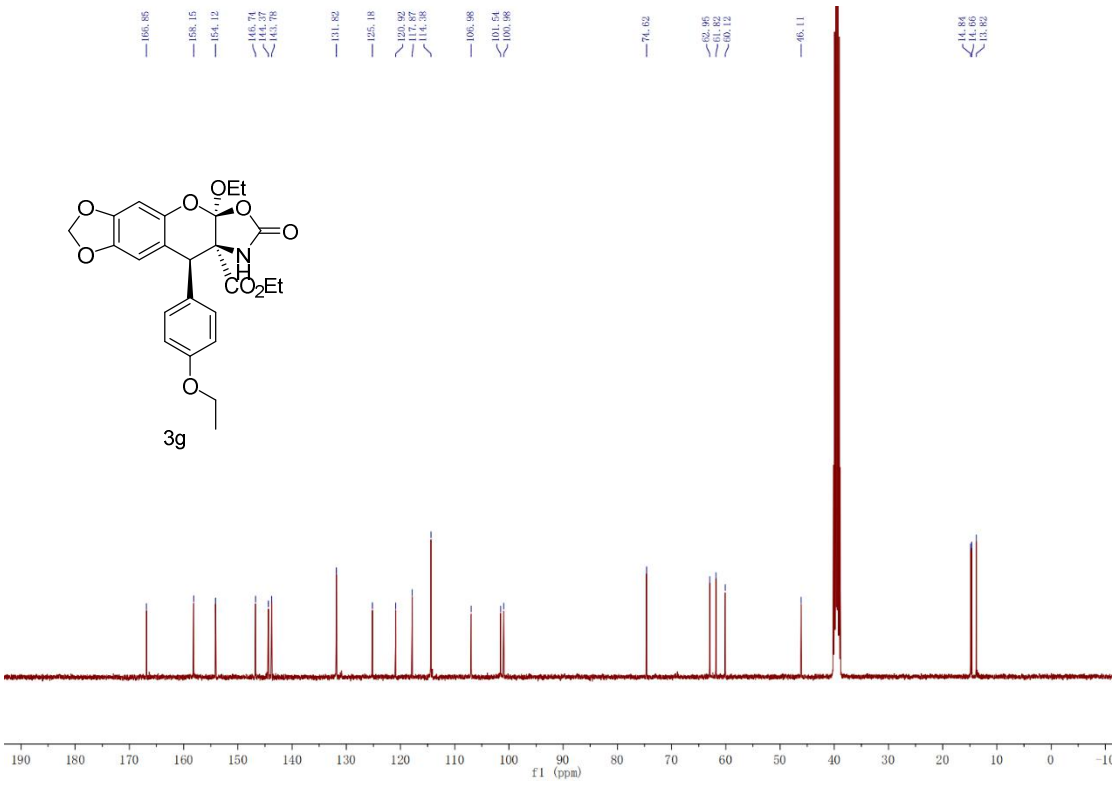
^{13}C NMR Spectrum of Compound 3f (151 MHz, DMSO-*d6*)



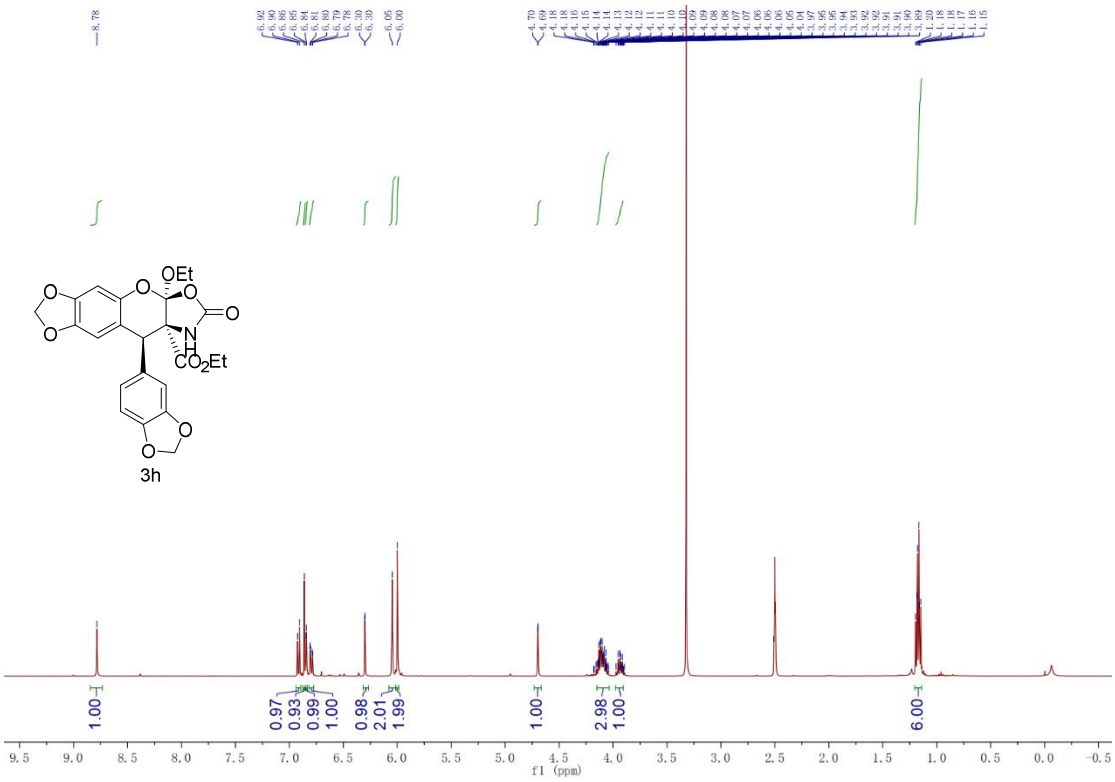
^{1}H NMR Spectrum of Compound 3g (400 MHz, DMSO-*d6*)



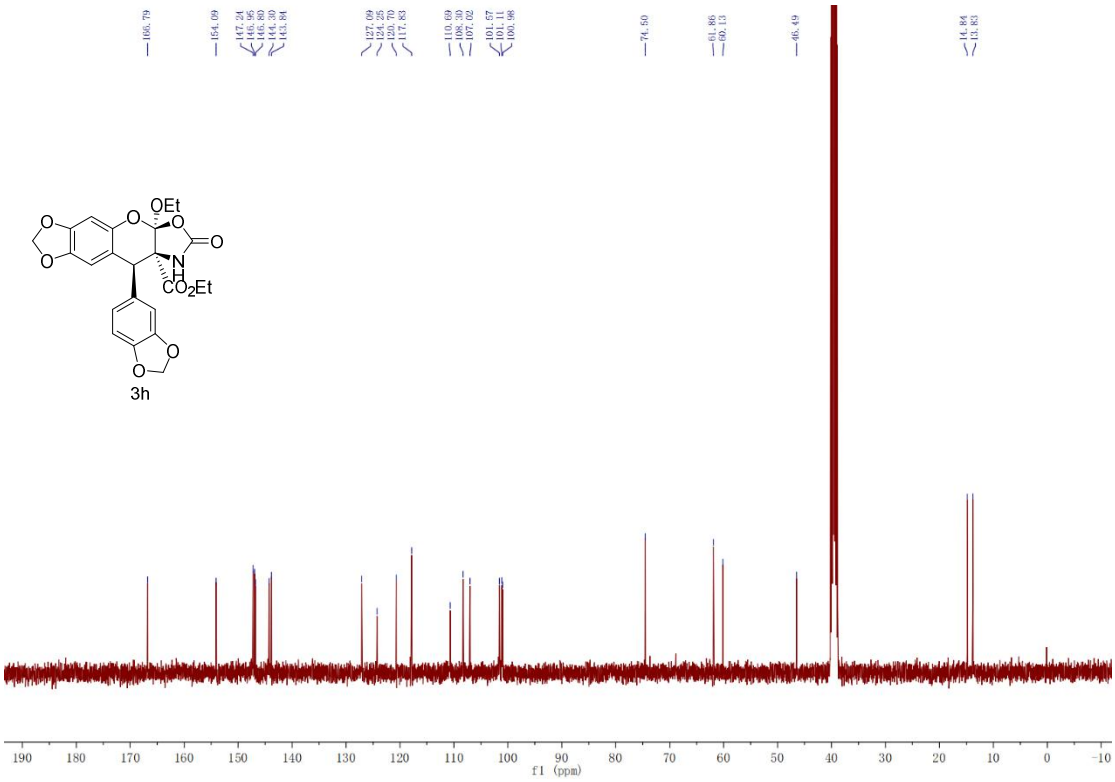
^{13}C NMR Spectrum of Compound 3g (151 MHz, DMSO-*d6*)



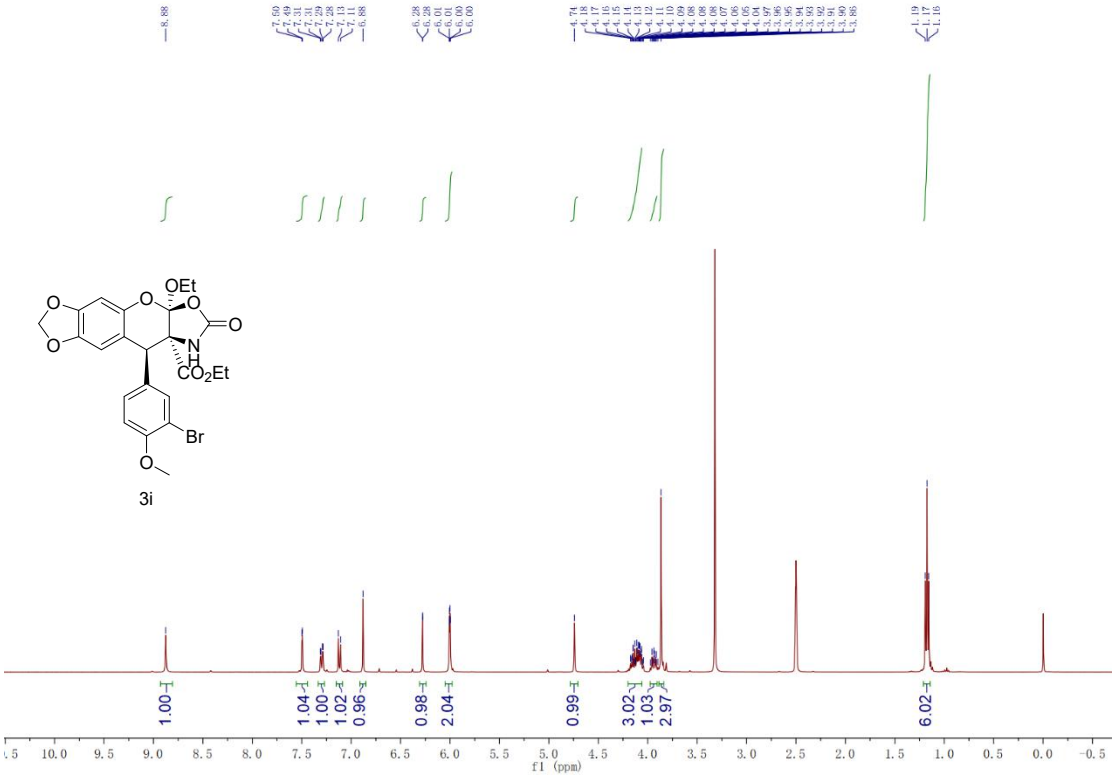
^{1}H NMR Spectrum of Compound 3h (400 MHz, DMSO-*d6*)



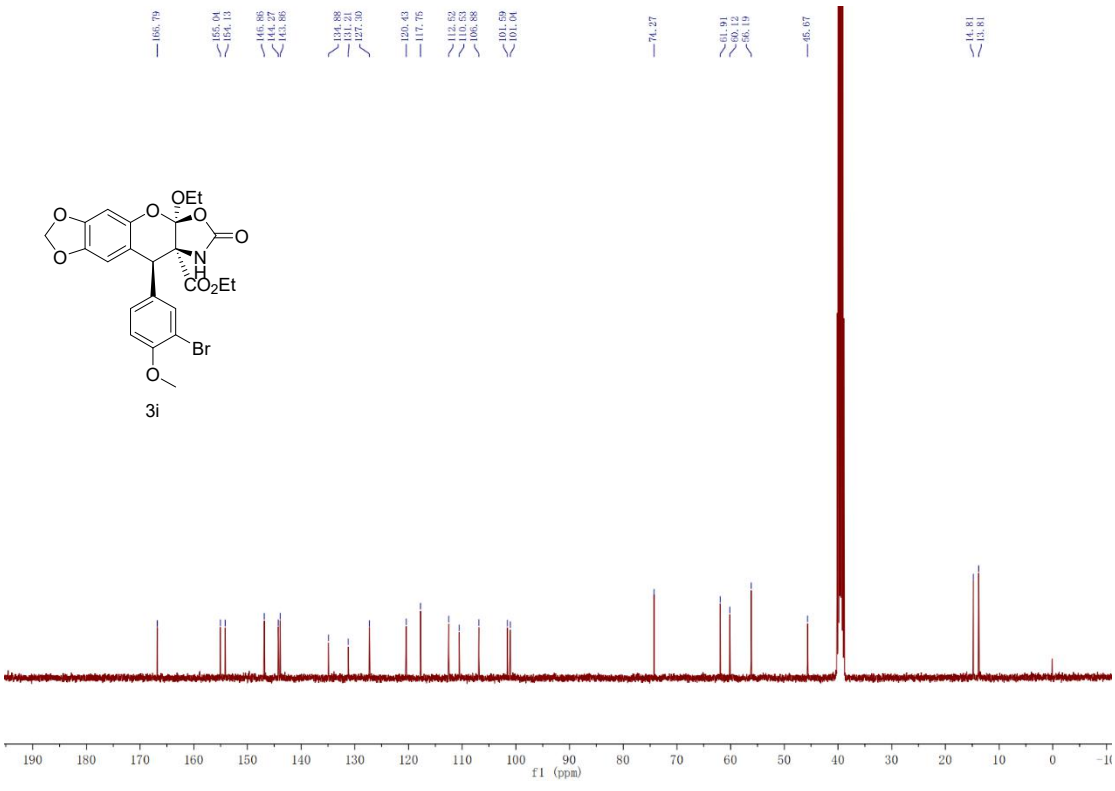
^{13}C NMR Spectrum of Compound 3h (151 MHz, DMSO-*d6*)



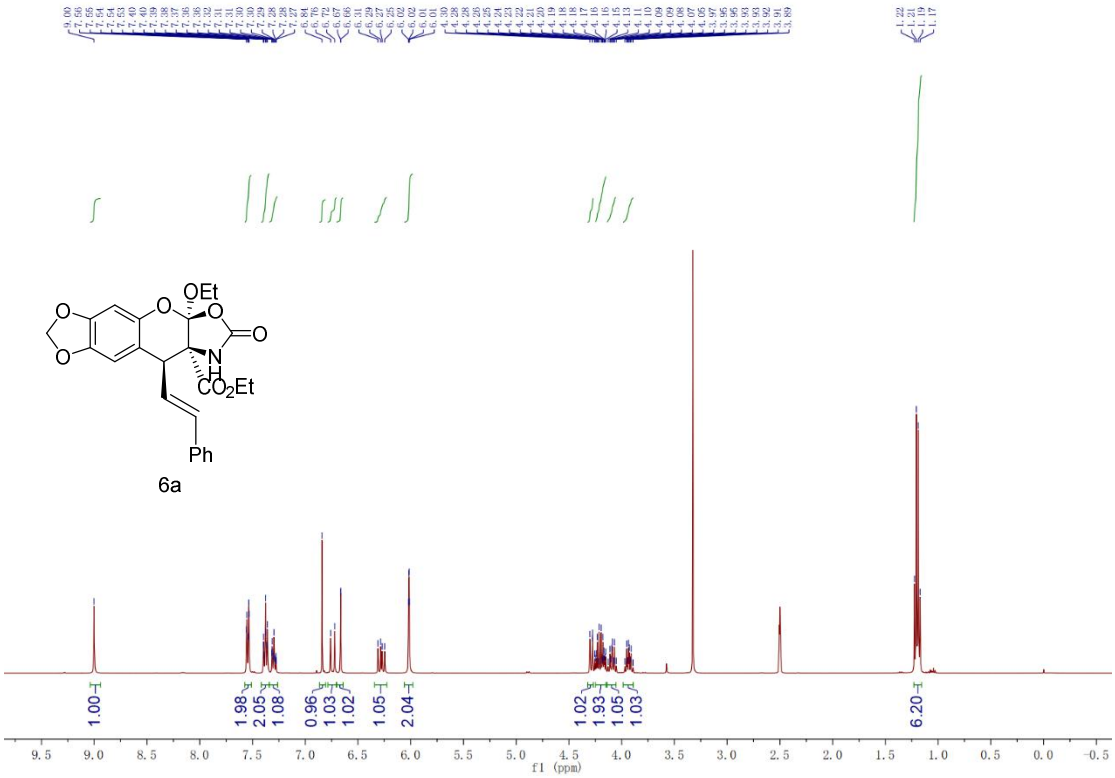
^{1}H NMR Spectrum of Compound 3i (400 MHz, DMSO-*d6*)



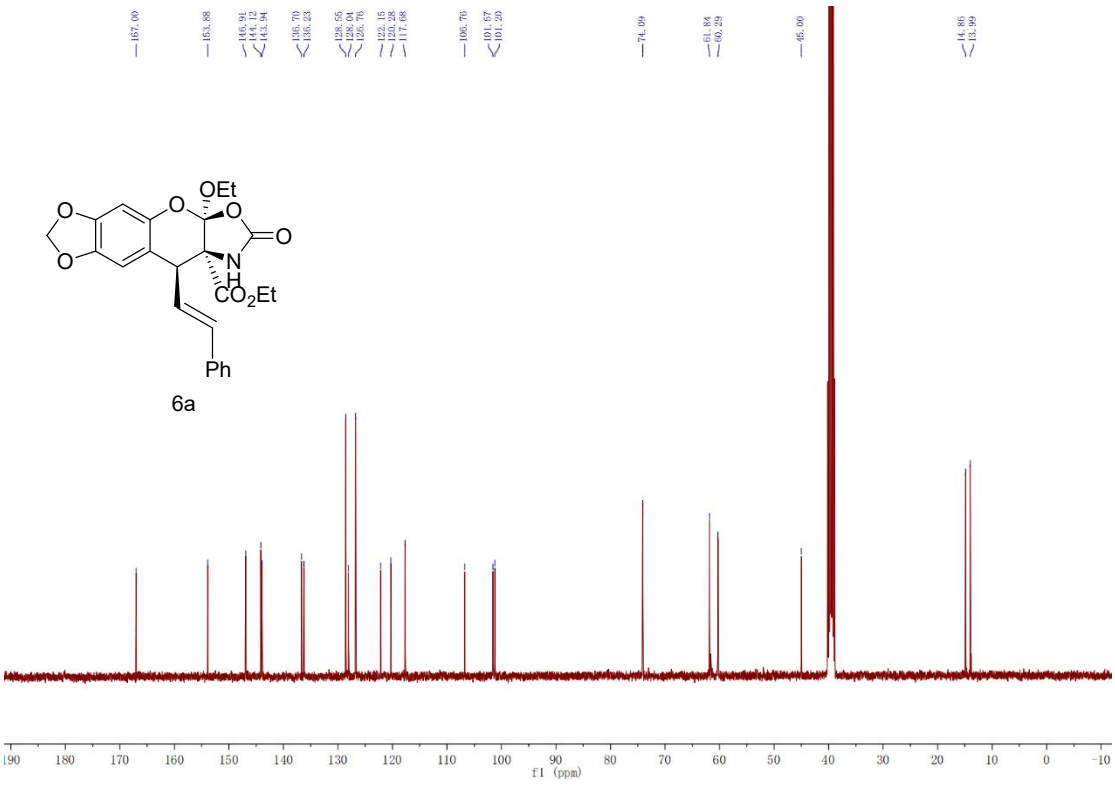
^{13}C NMR Spectrum of Compound 3i (151 MHz, DMSO-*d6*)



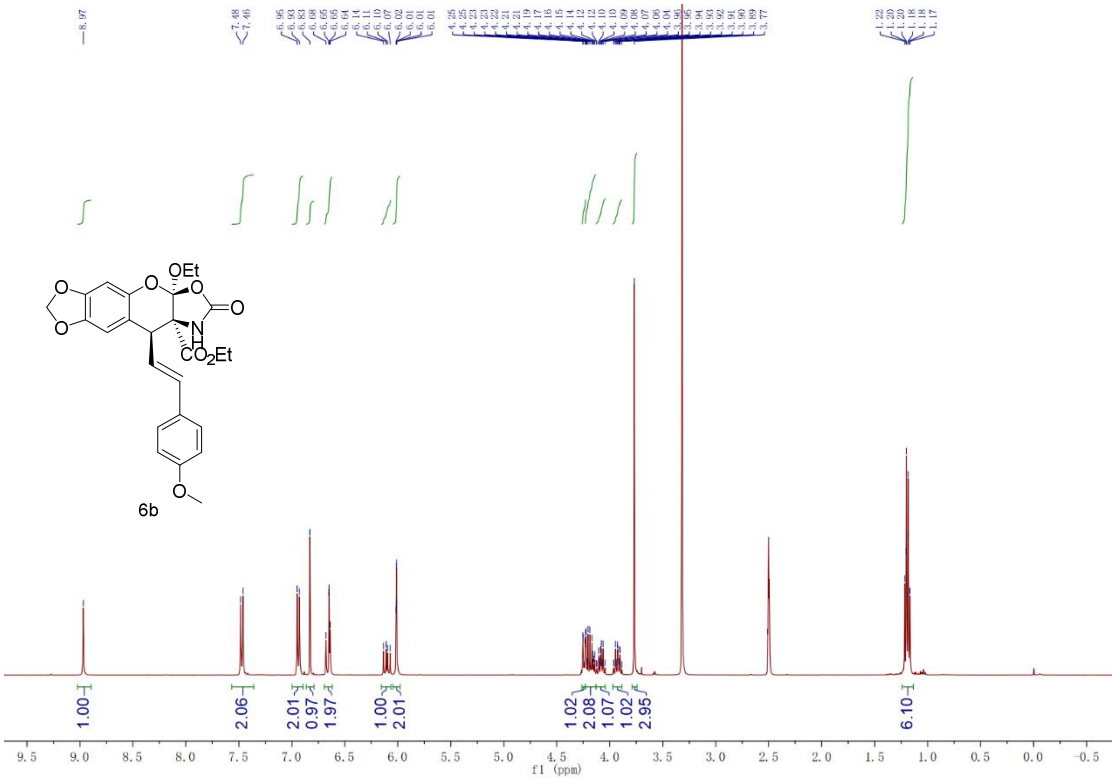
^{1}H NMR Spectrum of Compound 6a (400 MHz, DMSO-*d6*)



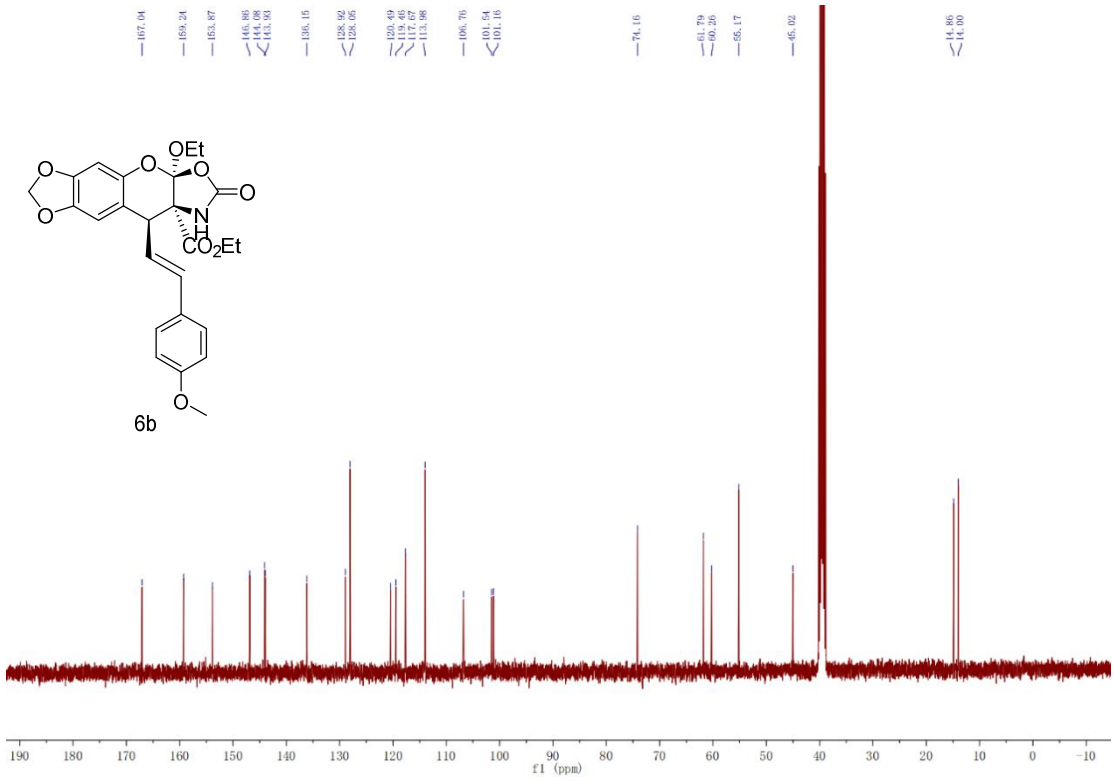
^{13}C NMR Spectrum of Compound 6a (151 MHz, DMSO-*d6*)



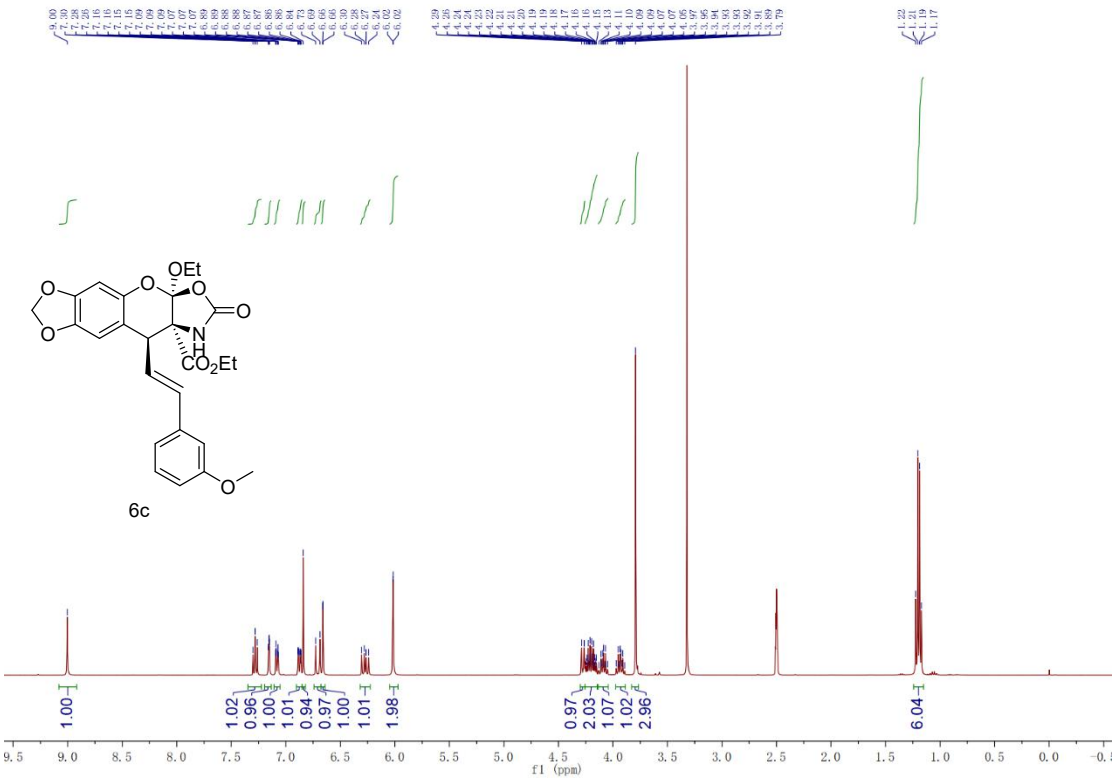
^{1}H NMR Spectrum of Compound 6b (400 MHz, DMSO-*d6*)



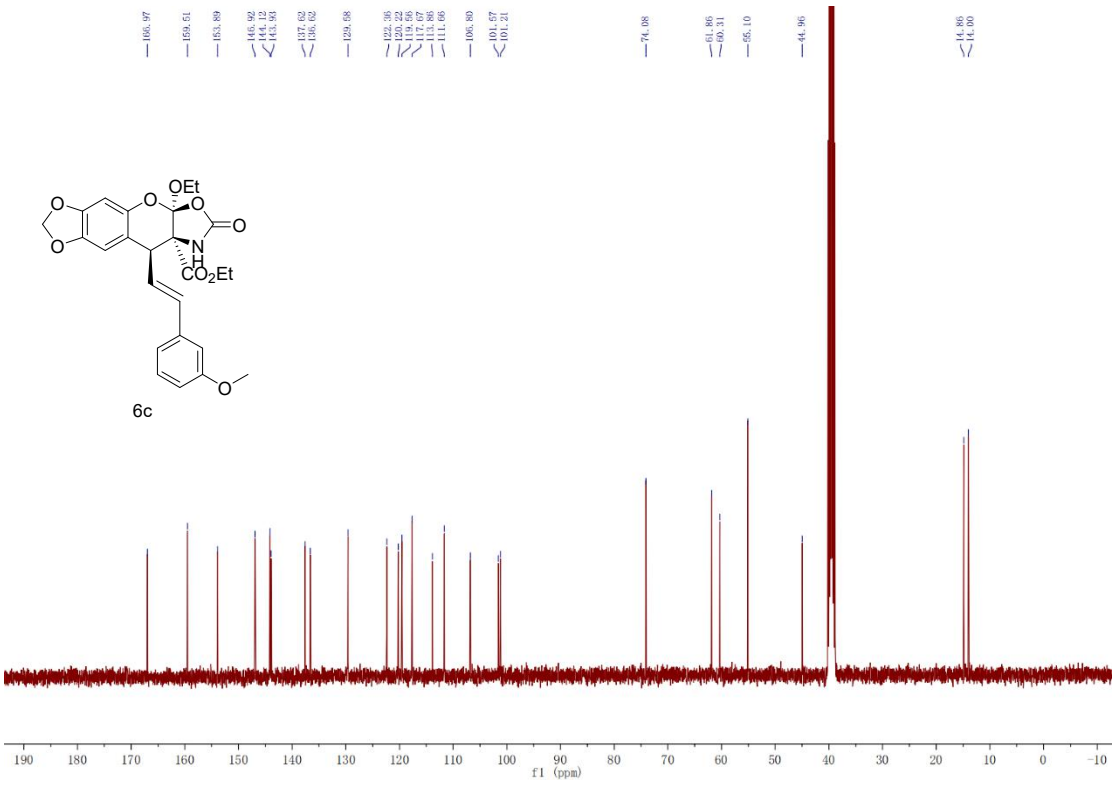
^{13}C NMR Spectrum of Compound 6b (151 MHz, DMSO-*d6*)



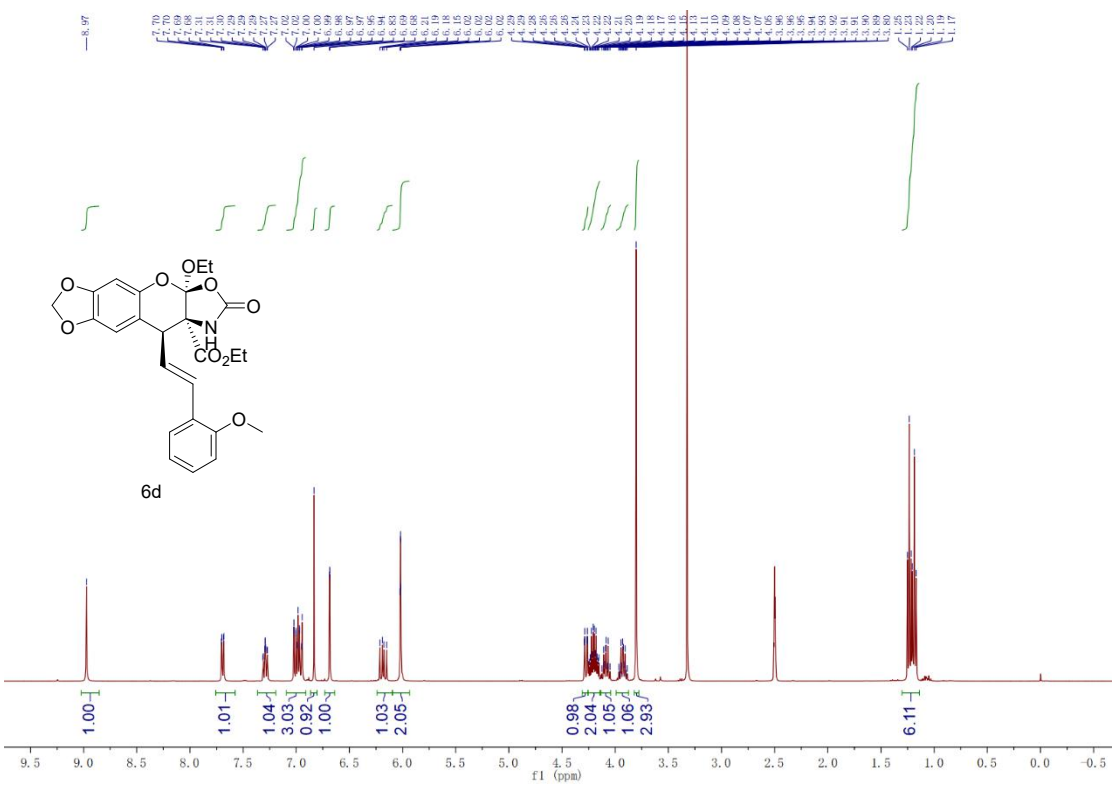
^{1}H NMR Spectrum of Compound 6c (400 MHz, DMSO-*d6*)



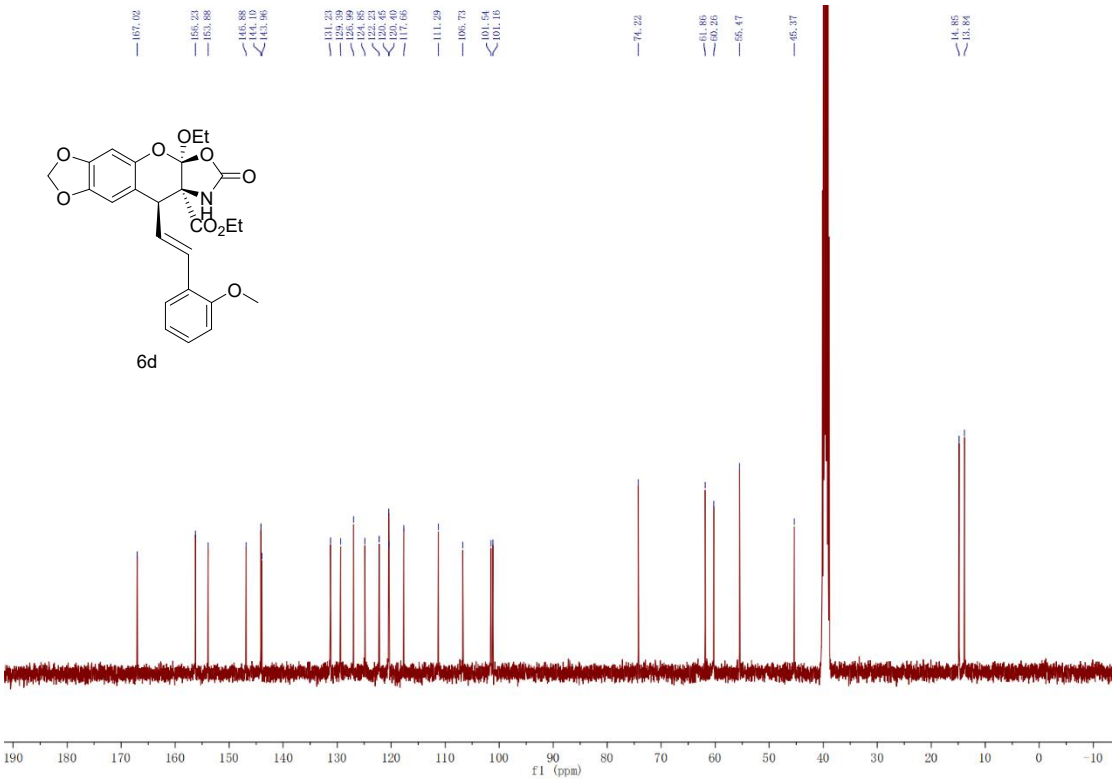
^{13}C NMR Spectrum of Compound 6c (151 MHz, DMSO-*d6*)



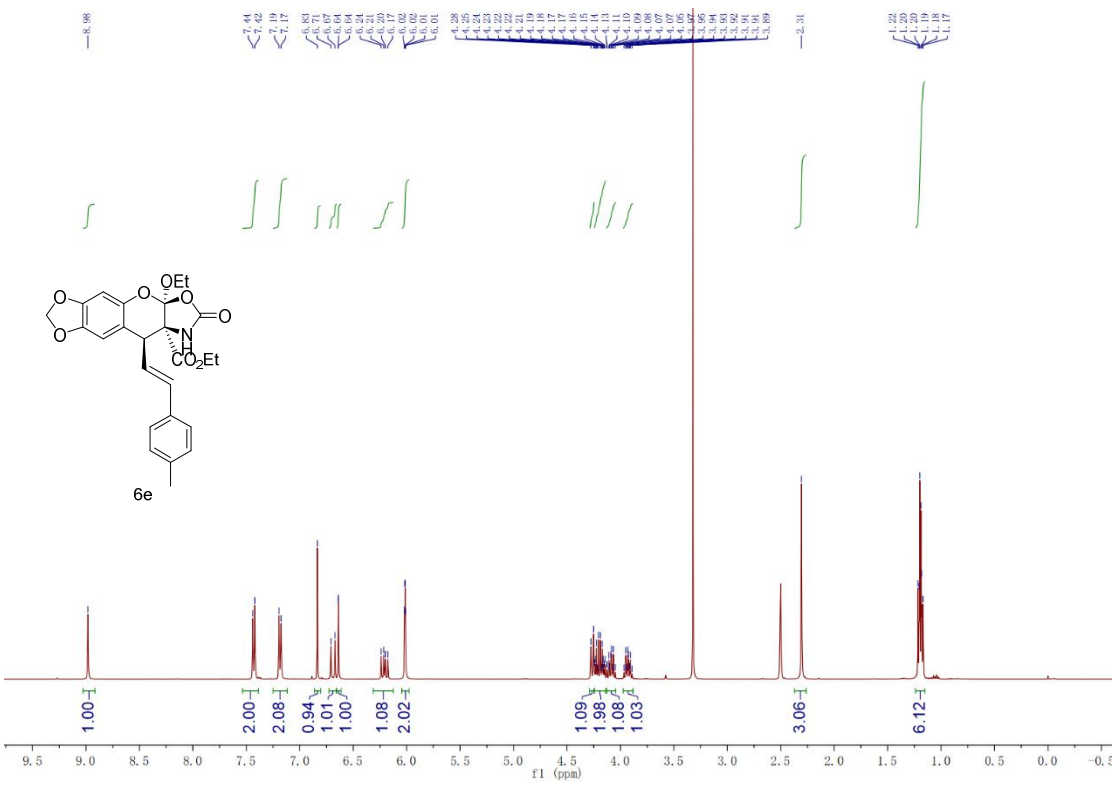
^{1}H NMR Spectrum of Compound 6d (400 MHz, DMSO-*d6*)



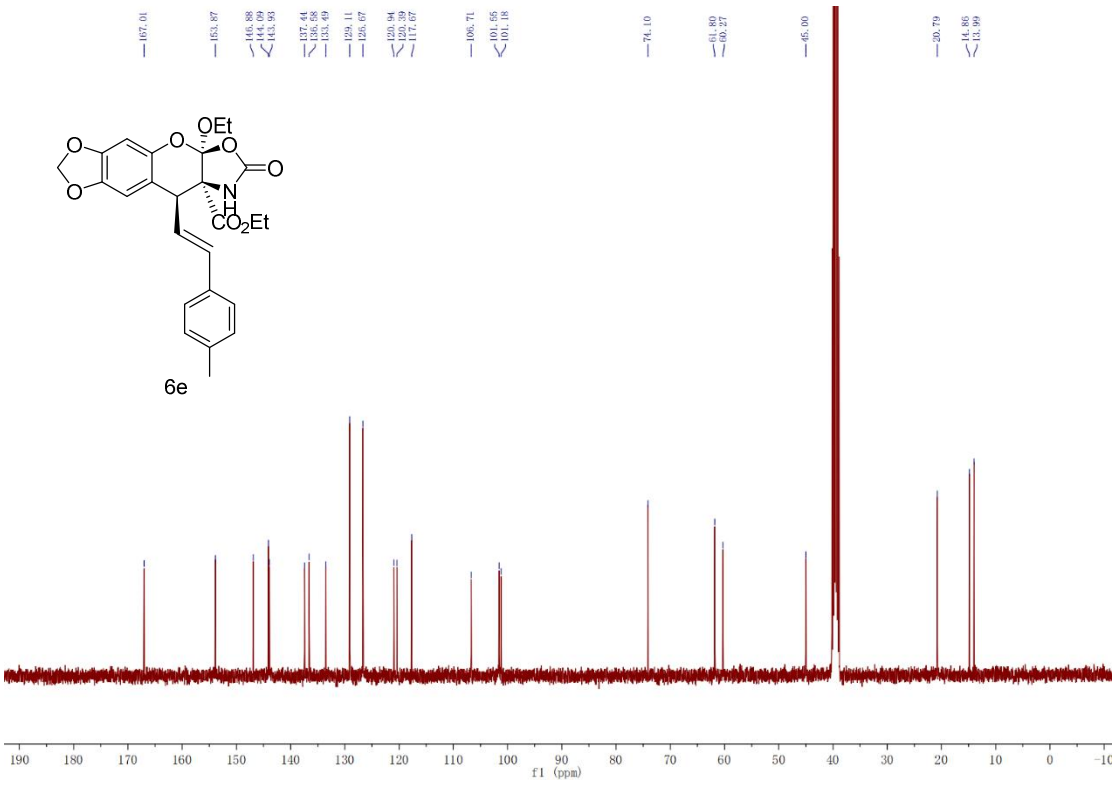
^{13}C NMR Spectrum of Compound 6d (151 MHz, DMSO-*d6*)



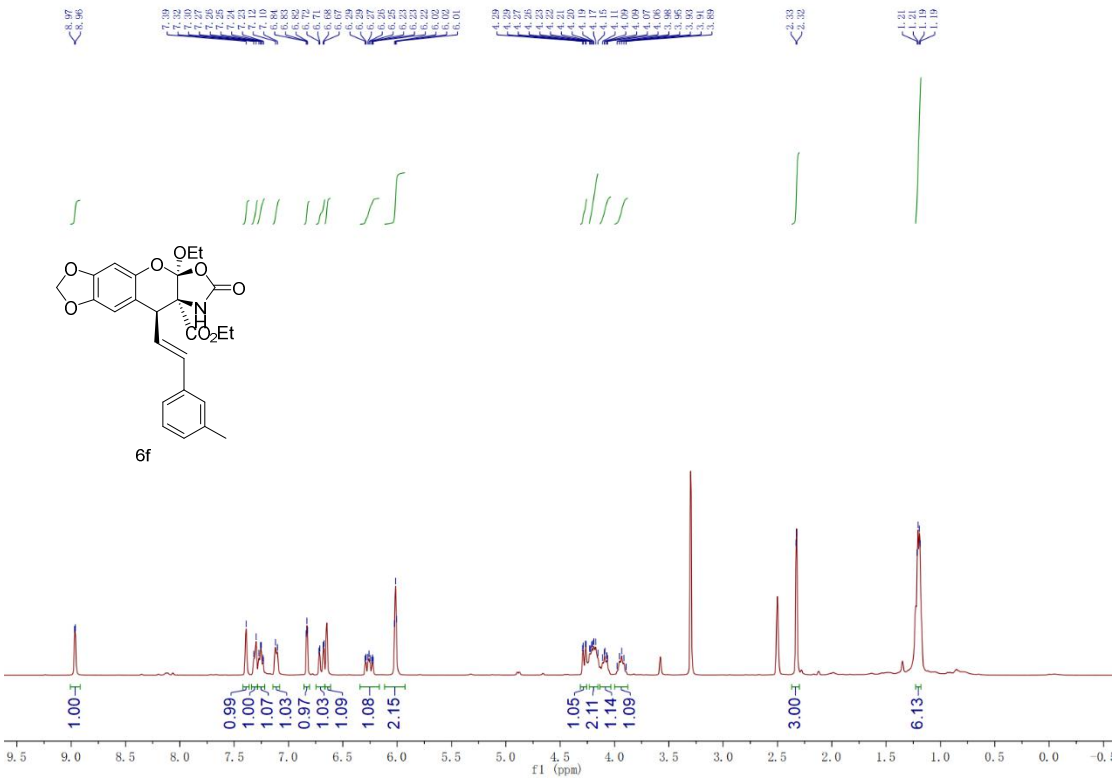
^{1}H NMR Spectrum of Compound 6e (400 MHz, DMSO-*d6*)



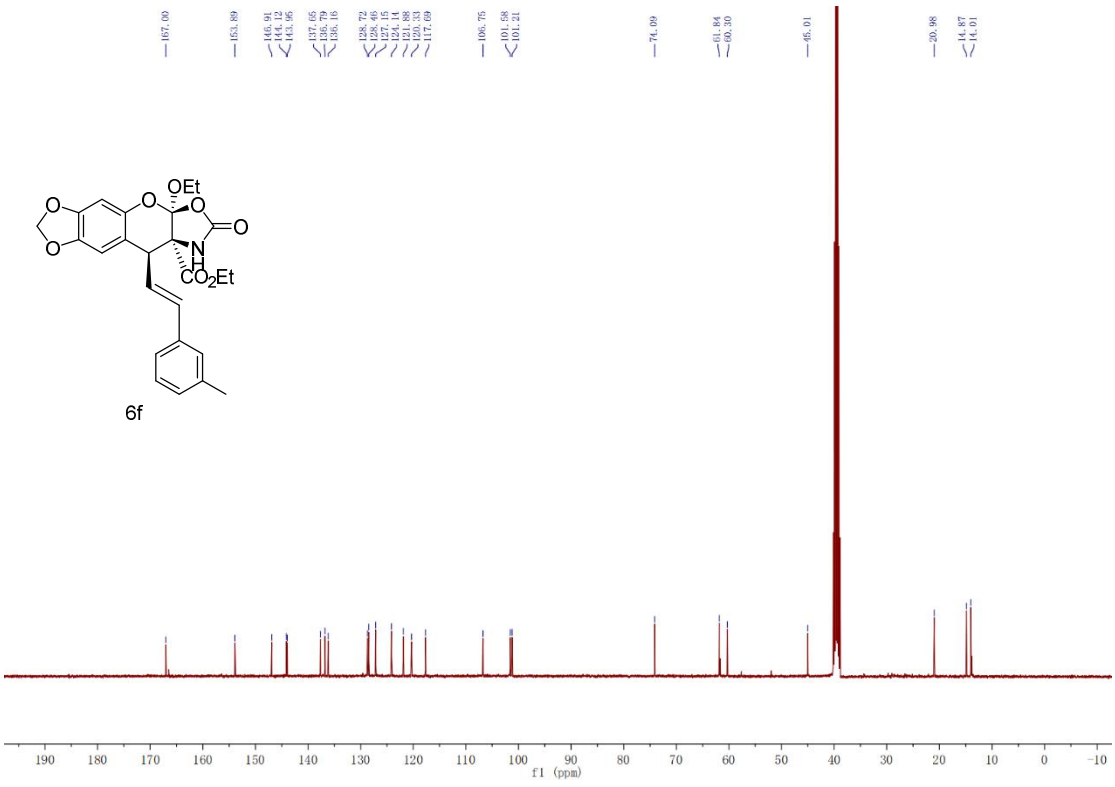
^{13}C NMR Spectrum of Compound 6e (151 MHz, DMSO-*d6*)



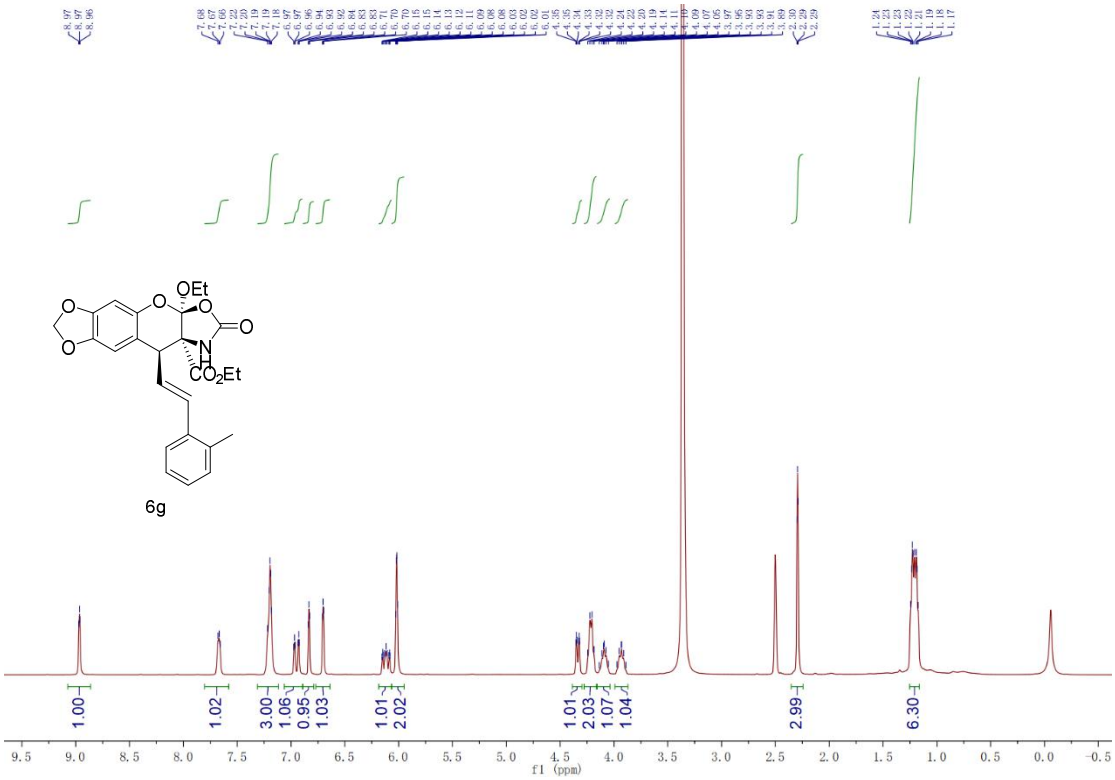
^{1}H NMR Spectrum of Compound 6f (400 MHz, DMSO-*d6*)



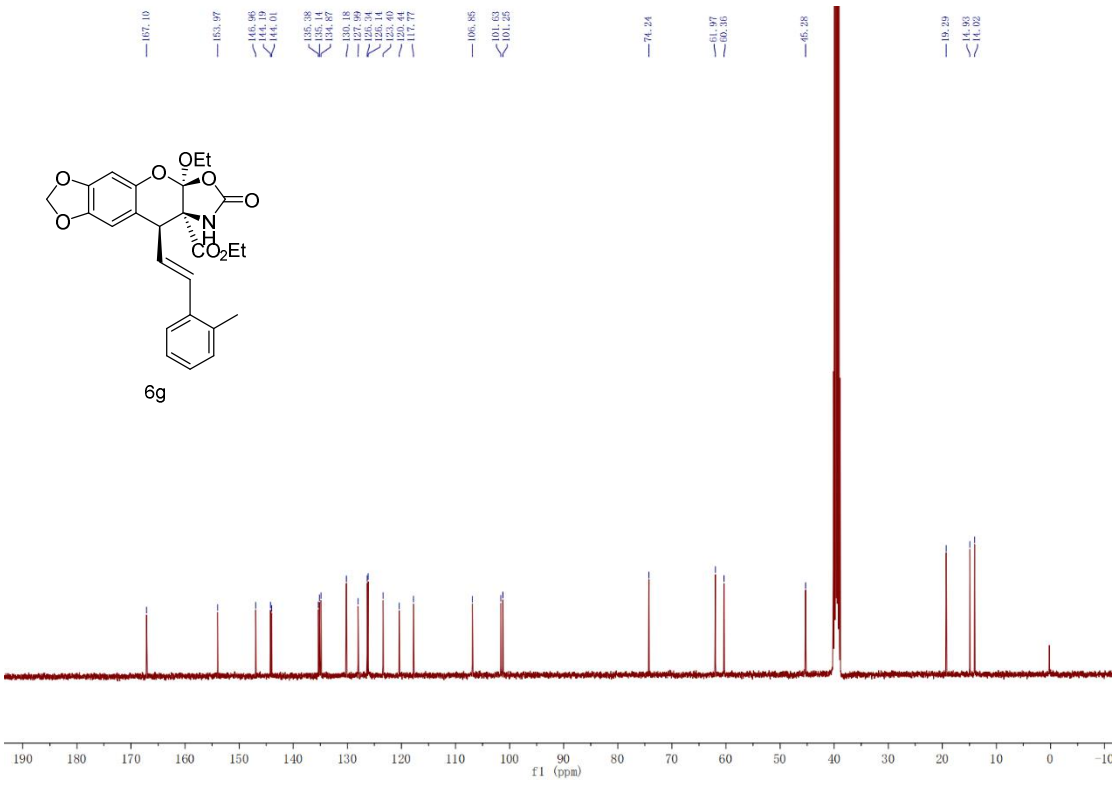
^{13}C NMR Spectrum of Compound 6f (151 MHz, DMSO-*d6*)



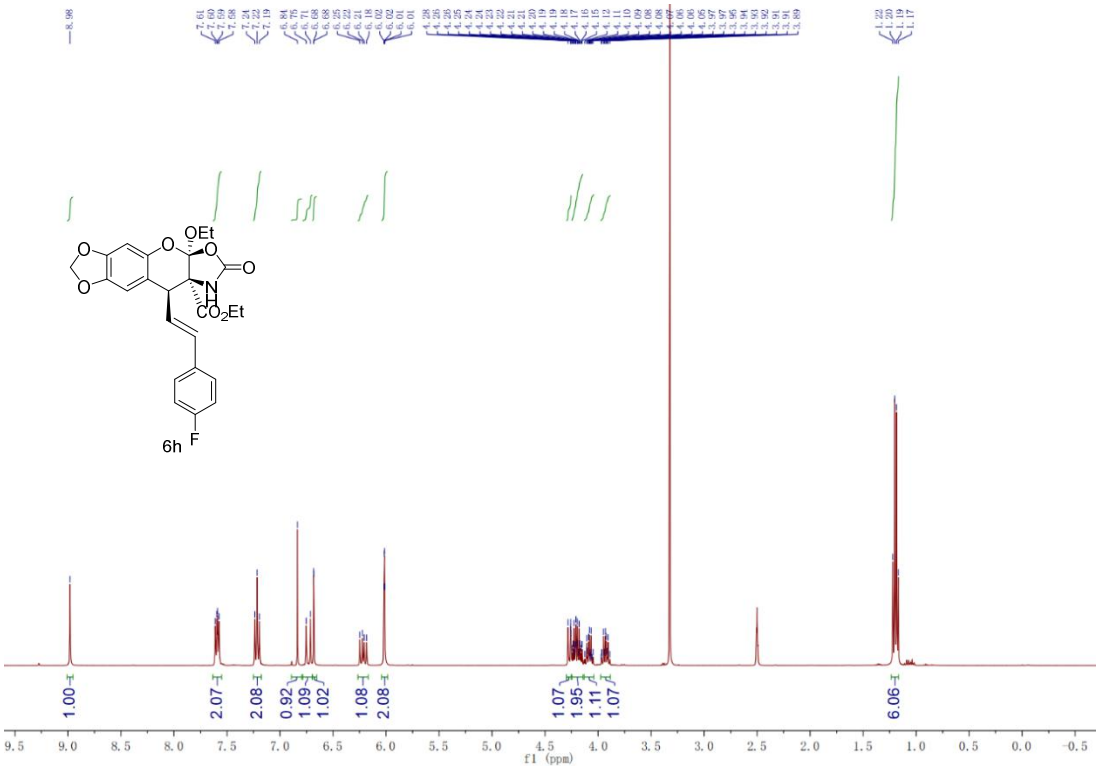
^{1}H NMR Spectrum of Compound 6g (400 MHz, DMSO-*d6*)



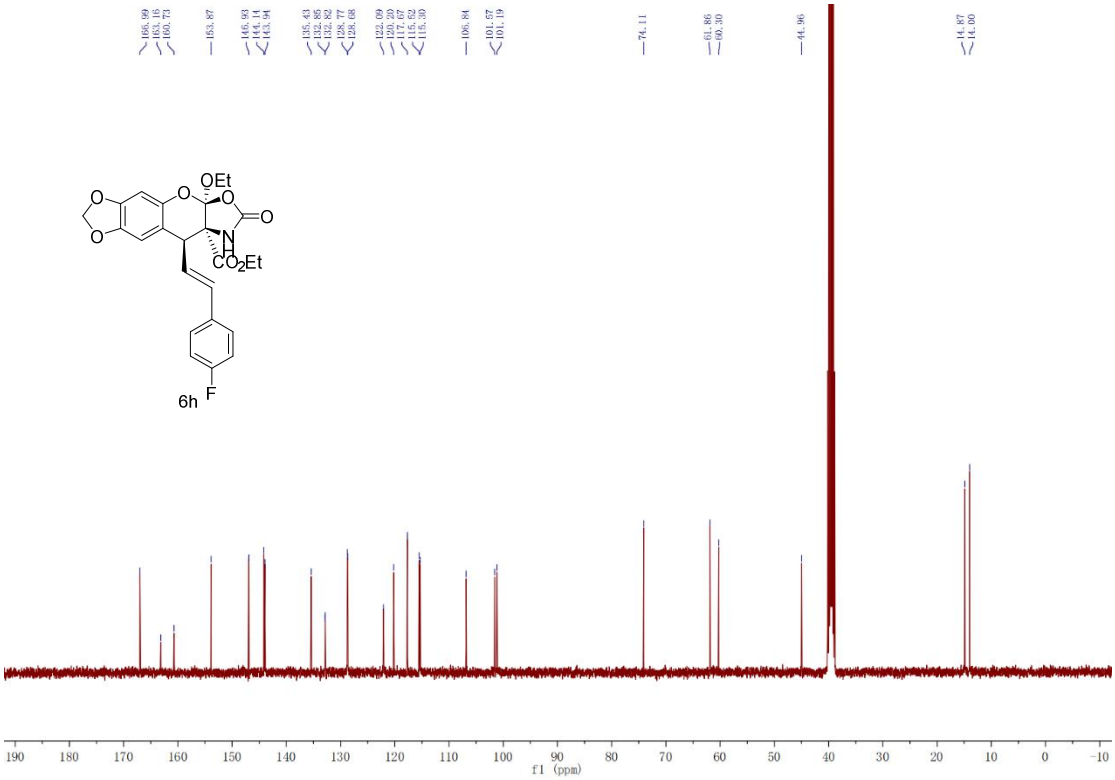
^{13}C NMR Spectrum of Compound 6g (151 MHz, DMSO-*d6*)



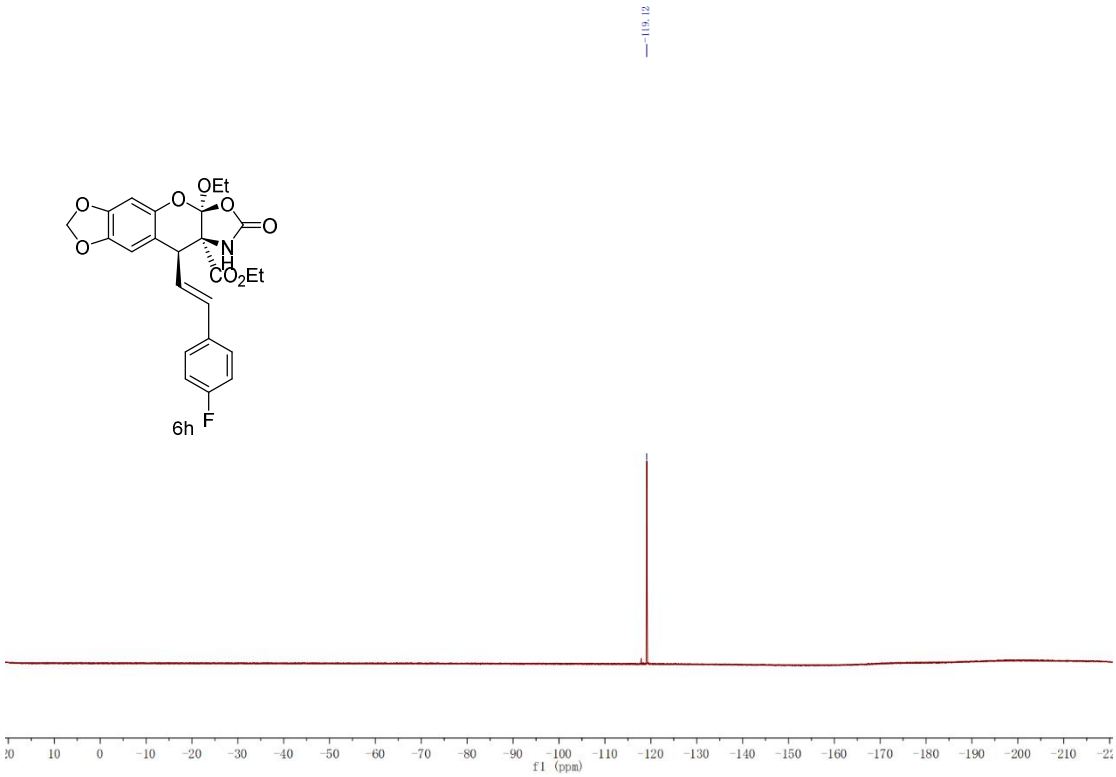
^{1}H NMR Spectrum of Compound 6h (400 MHz, DMSO-*d6*)



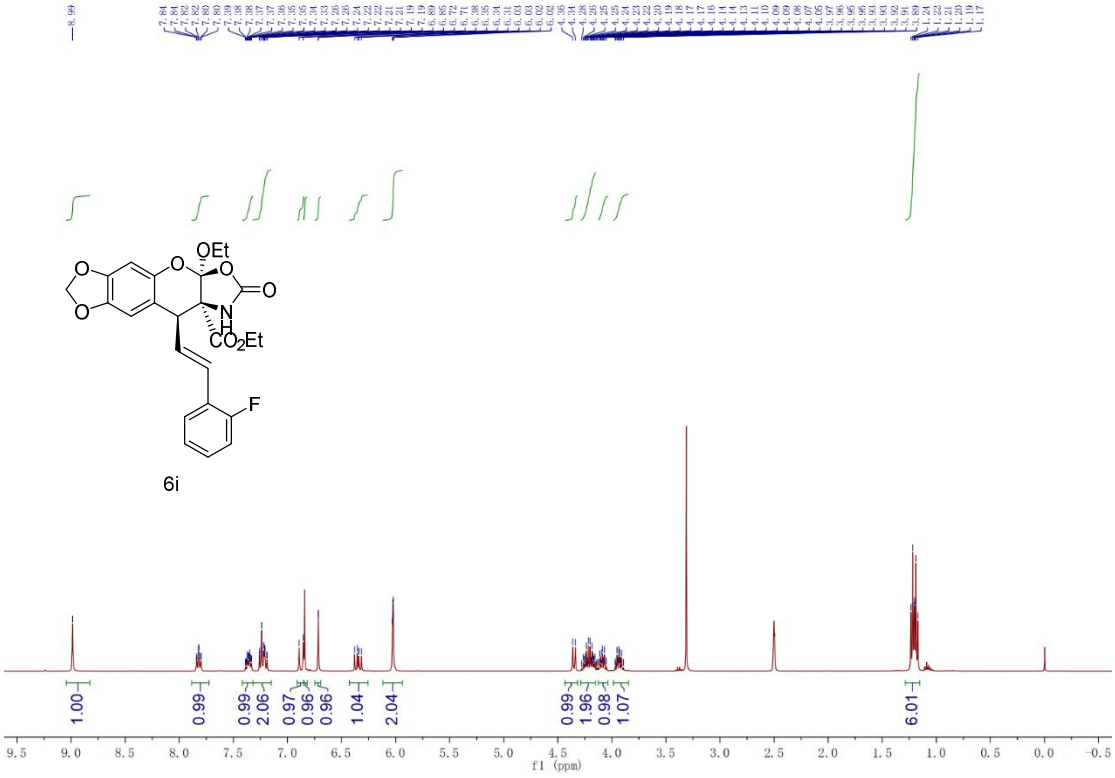
^{13}C NMR Spectrum of Compound 6h (151 MHz, DMSO-*d6*)



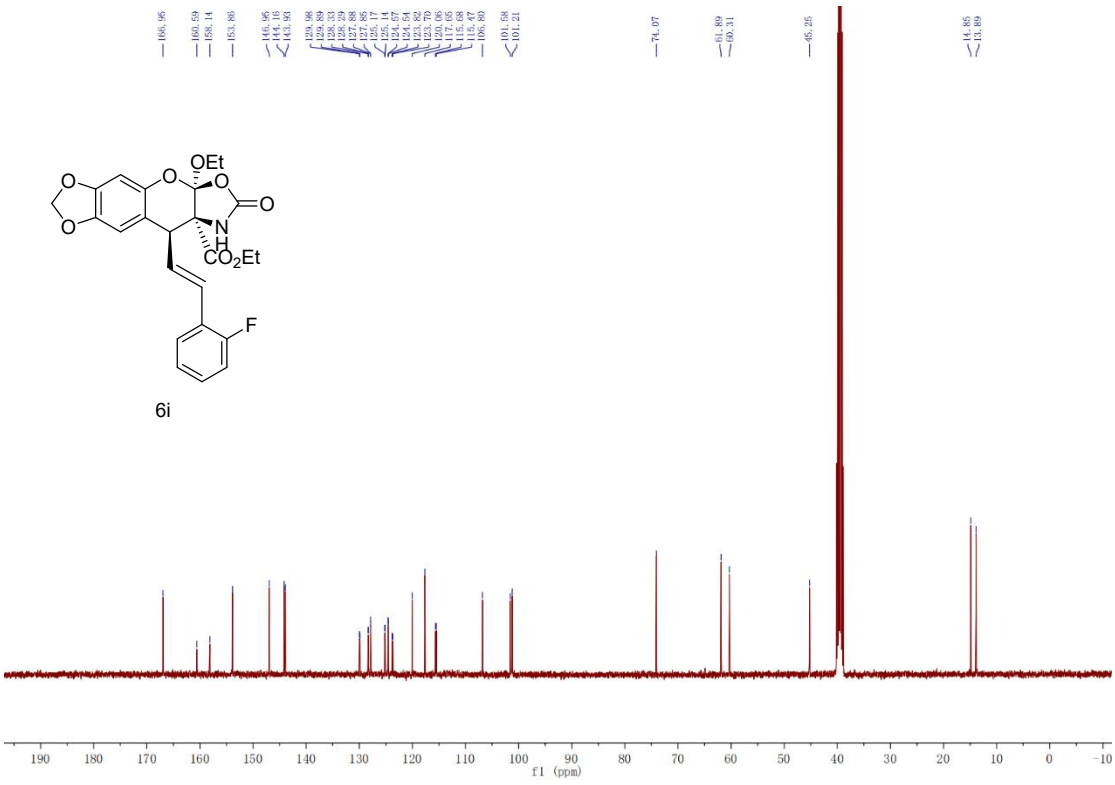
^{19}F NMR Spectrum of Compound 6h (376 MHz, DMSO-*d6*)



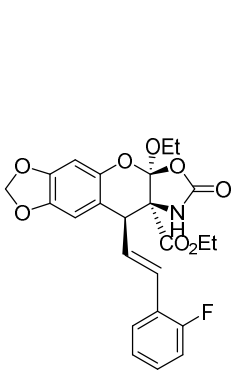
^{1}H NMR Spectrum of Compound 6i (400 MHz, DMSO-*d6*)



^{13}C NMR Spectrum of Compound 6i (151 MHz, DMSO-*d6*)

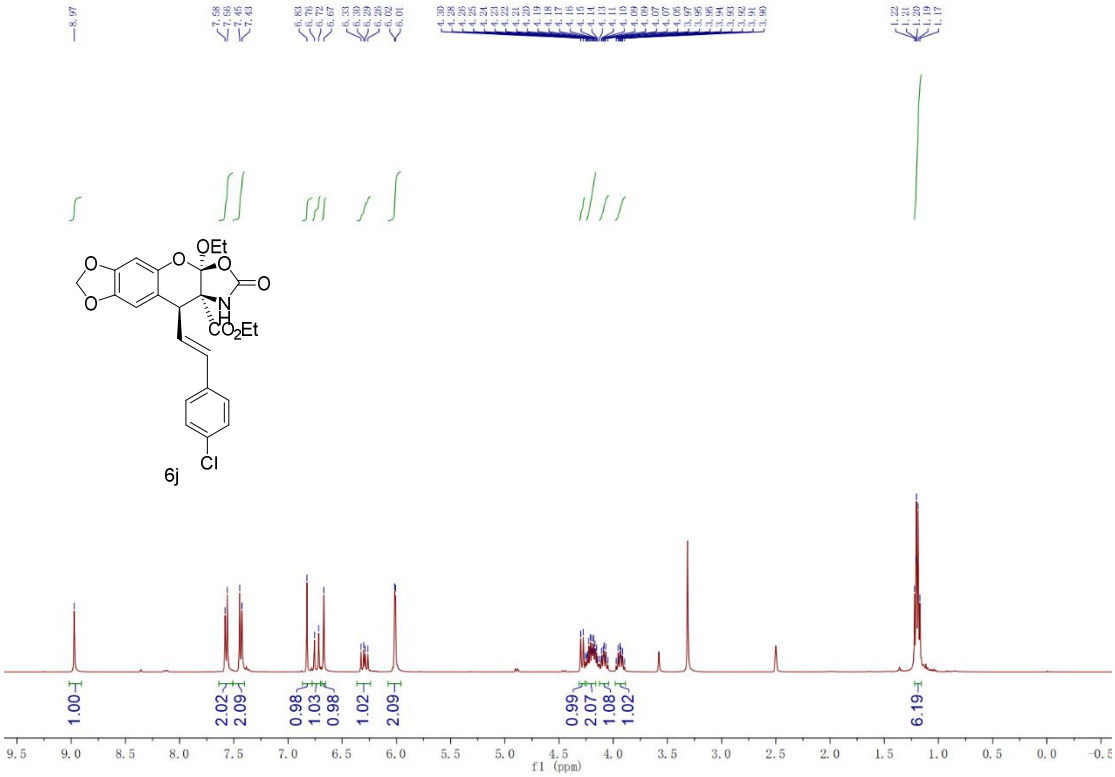


^{19}F NMR Spectrum of Compound 6i (376 MHz, DMSO-*d6*)

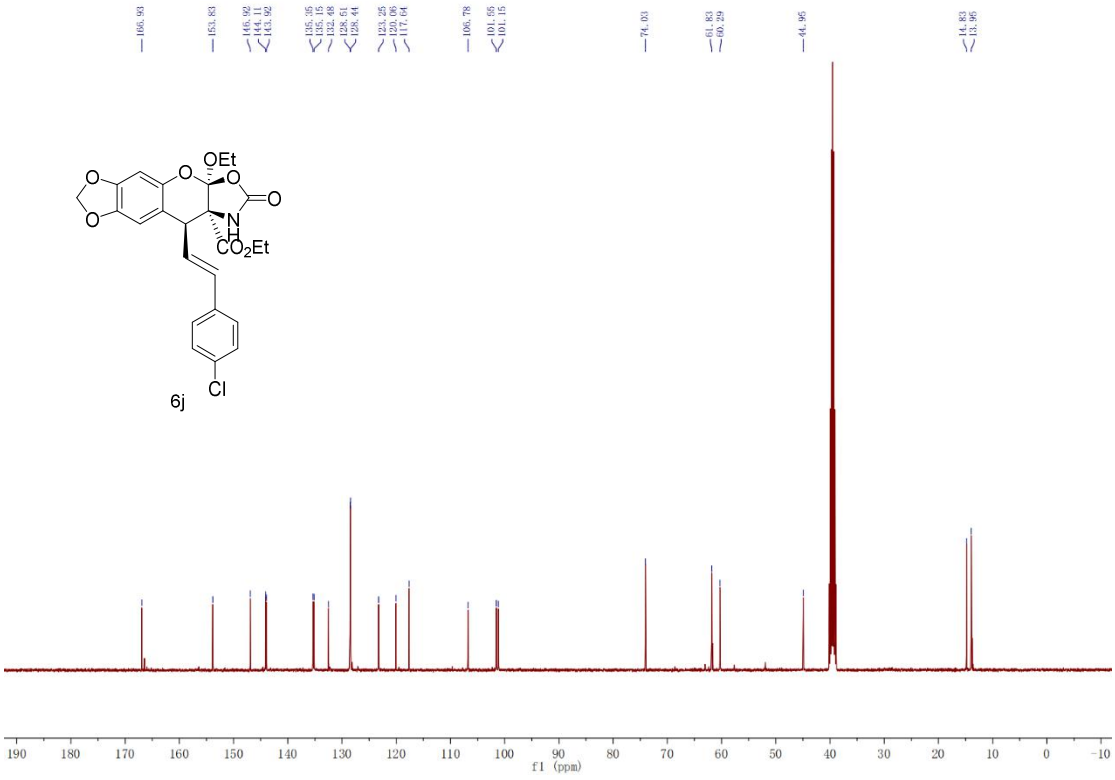


6i

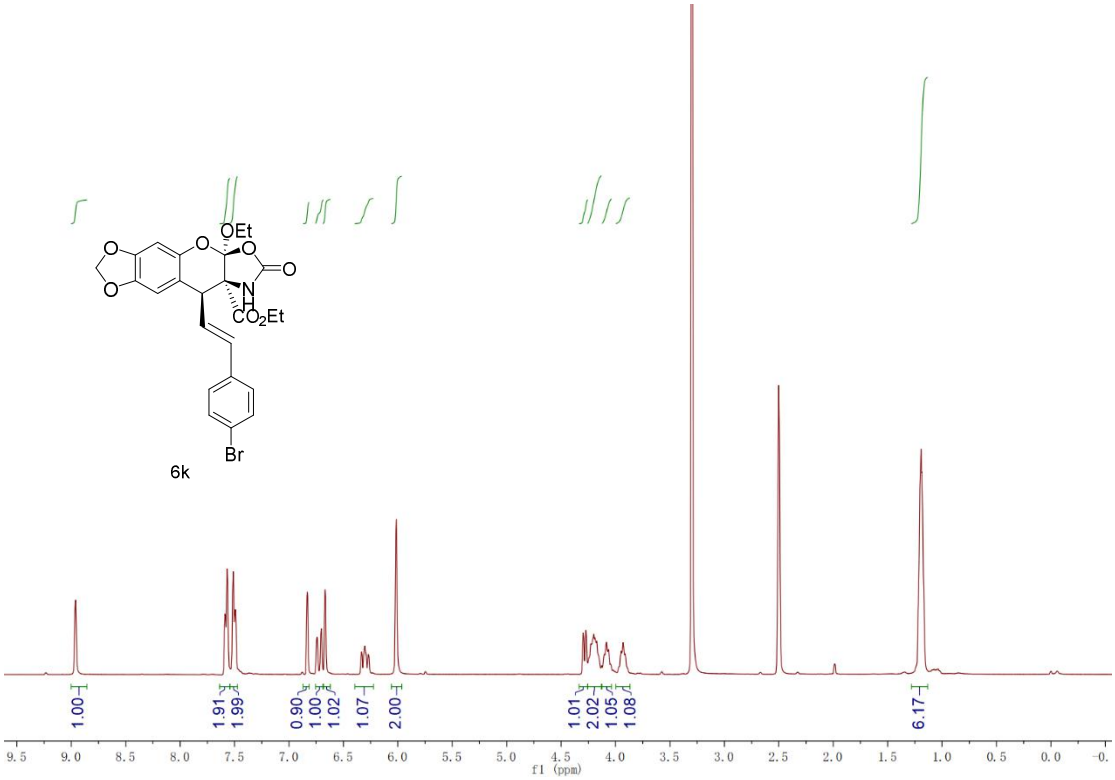
^{1}H NMR Spectrum of Compound 6j (400 MHz, DMSO-*d6*)



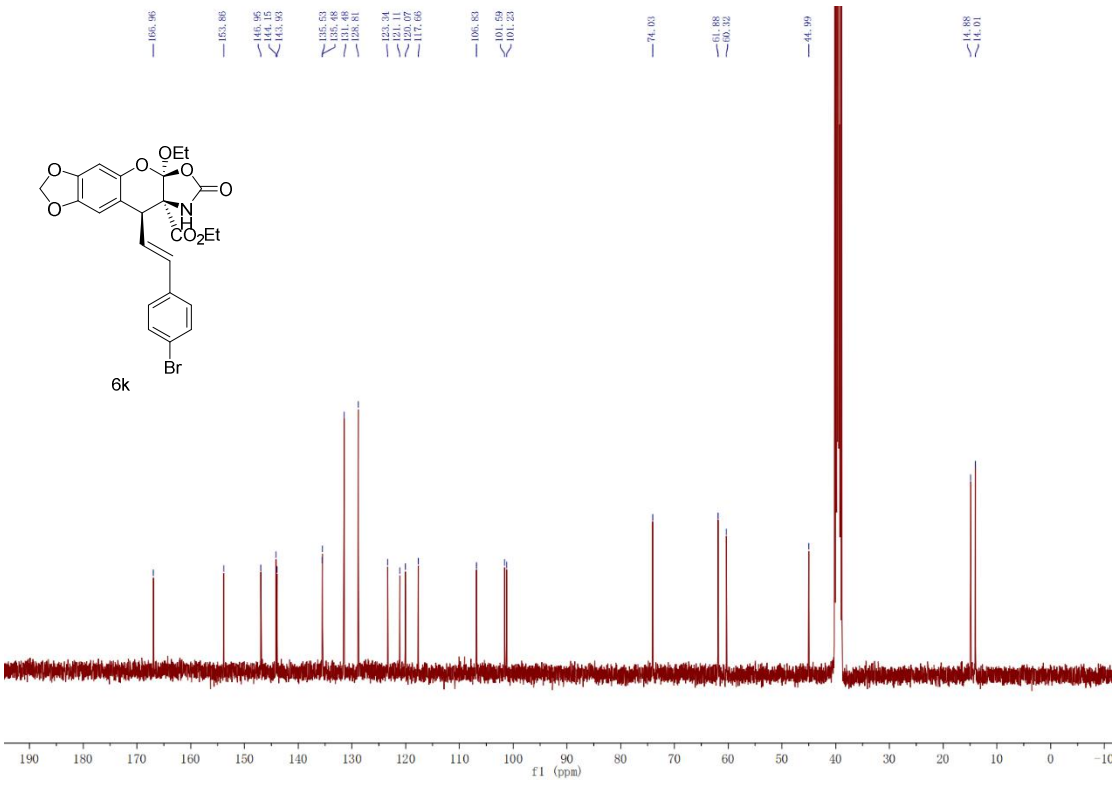
^{13}C NMR Spectrum of Compound 6j (151 MHz, DMSO-*d6*)



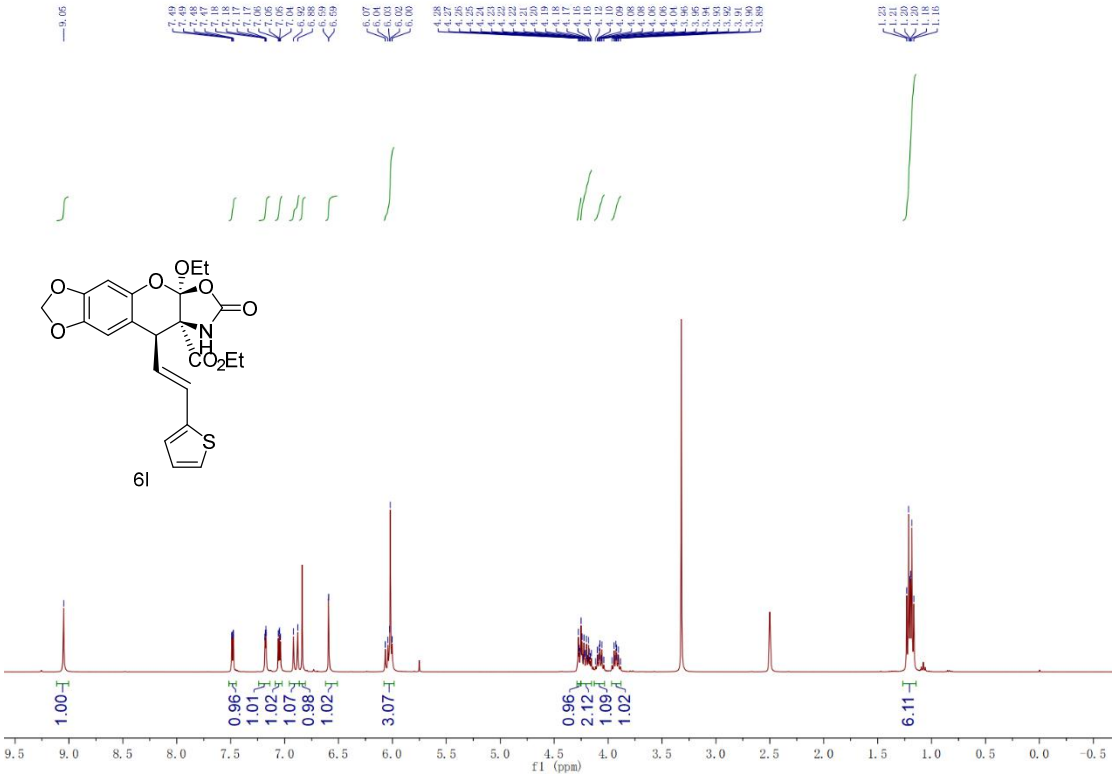
^{1}H NMR Spectrum of Compound 6k (400 MHz, DMSO-*d6*)



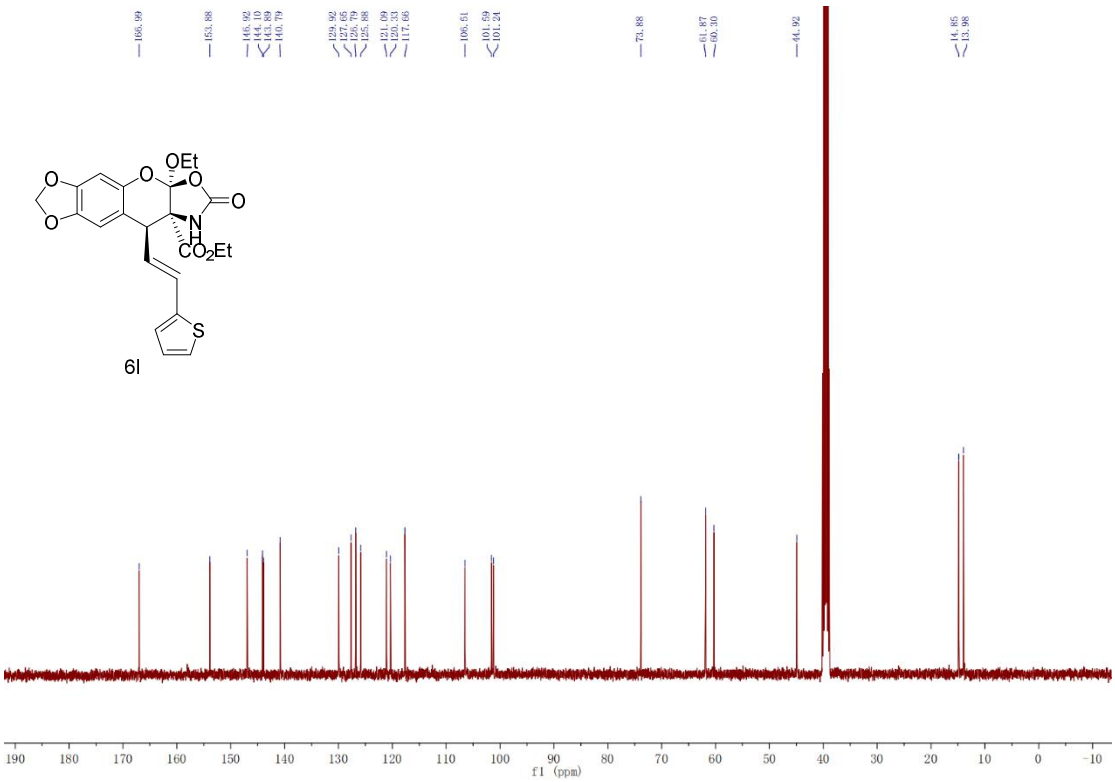
^{13}C NMR Spectrum of Compound 6k (151 MHz, DMSO-*d6*)



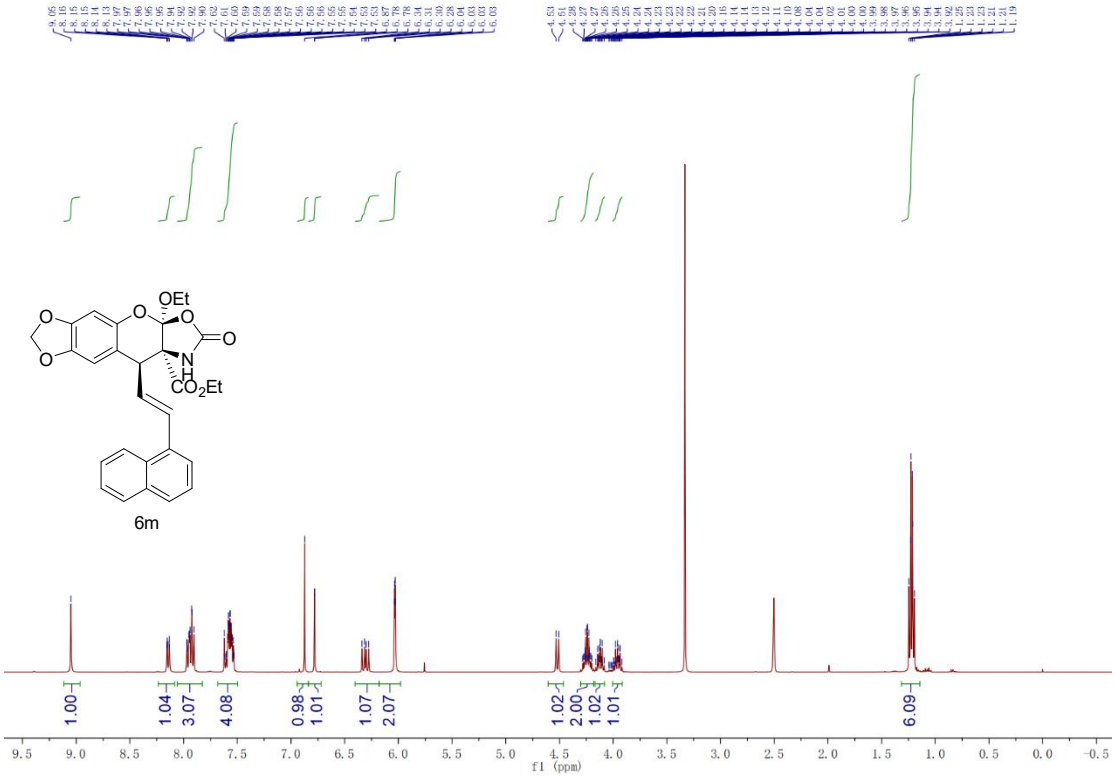
^{1}H NMR Spectrum of Compound 6l (400 MHz, DMSO-*d6*)



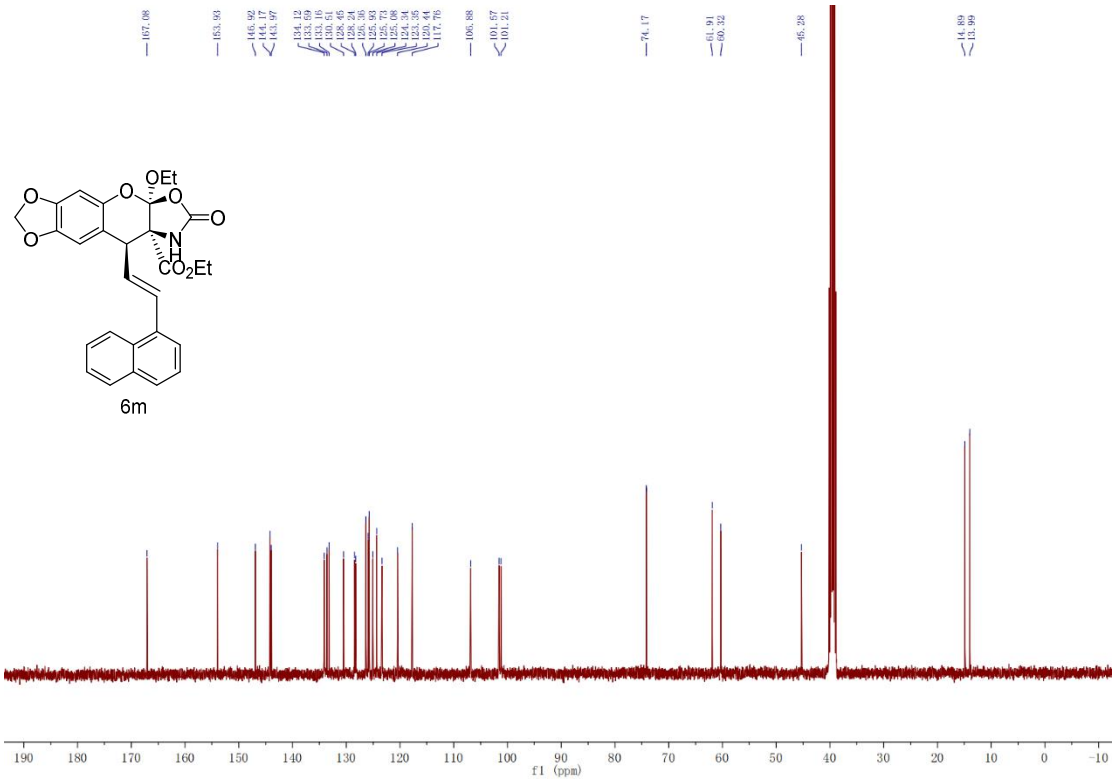
^{13}C NMR Spectrum of Compound 6l (151 MHz, DMSO-*d6*)



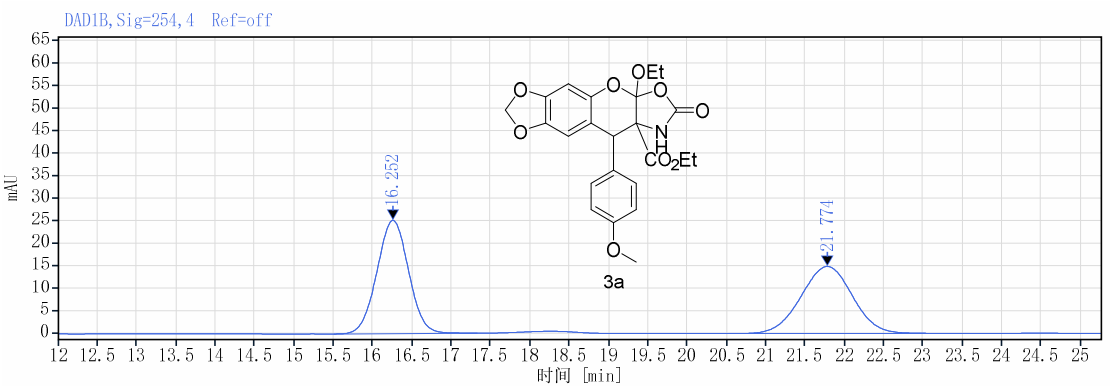
^{1}H NMR Spectrum of Compound 6m (400 MHz, DMSO-*d6*)



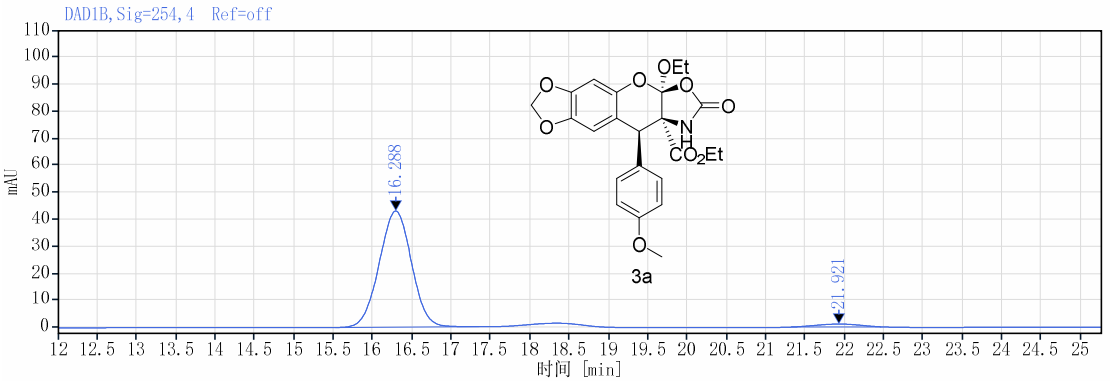
^{13}C NMR Spectrum of Compound 6m (151 MHz, DMSO-*d6*)



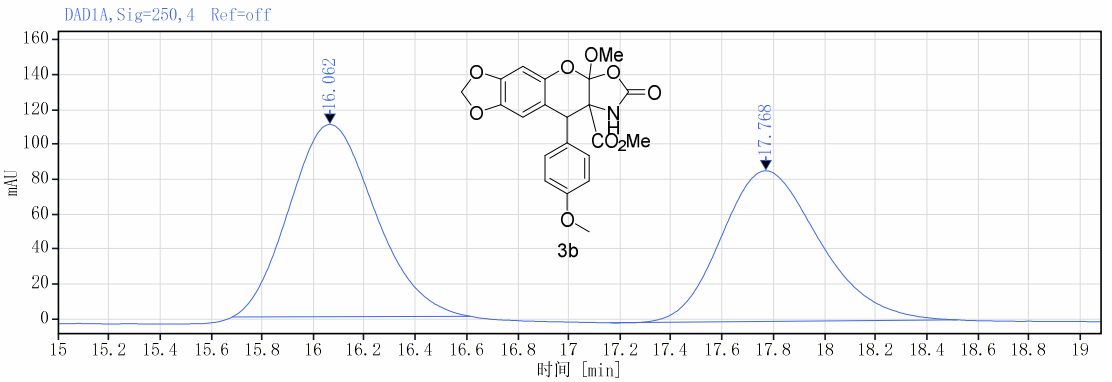
5. HPLC Spectra



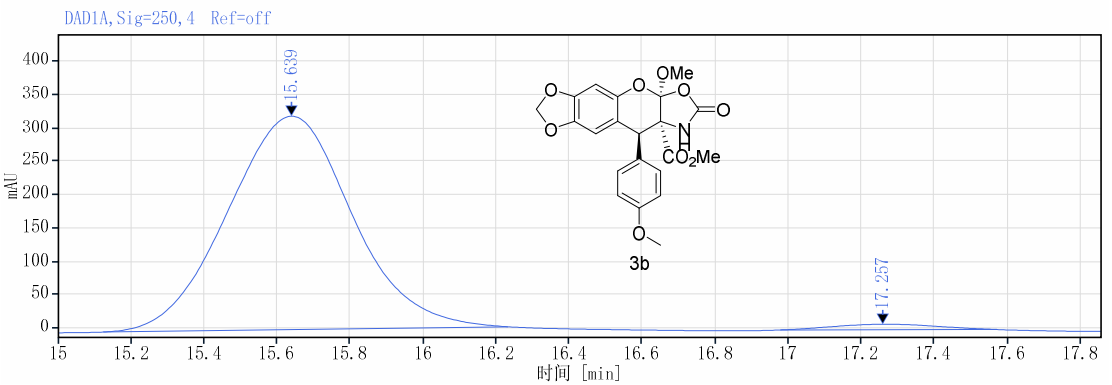
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.252	BB	1.82	703.64	25.19	50.83
21.774	BB	3.07	680.72	14.91	49.17
		Total	1384.36		



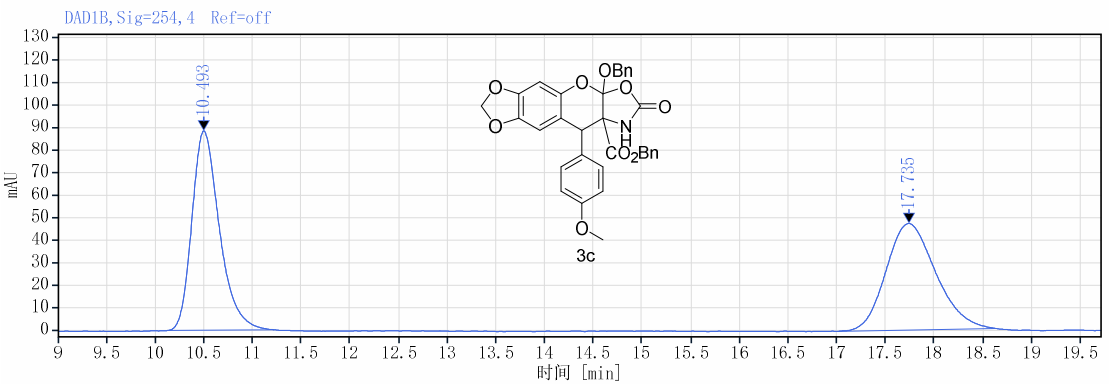
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.288	BB	1.83	1227.73	43.02	96.82
21.921	MM m	0.57	40.38	1.06	3.18
		Total	1268.11		



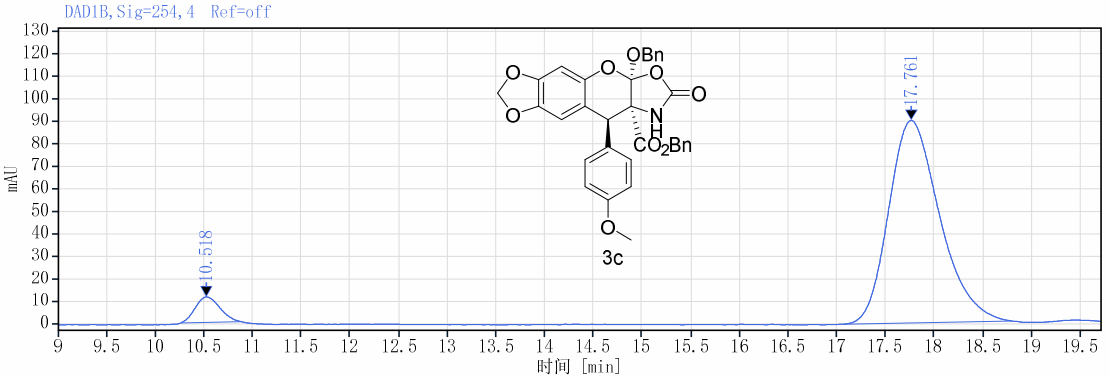
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.062	MM	0.36	2577.28	110.39	52.70
17.768	MM	0.41	2312.77	86.51	47.30
		Total	4890.05		



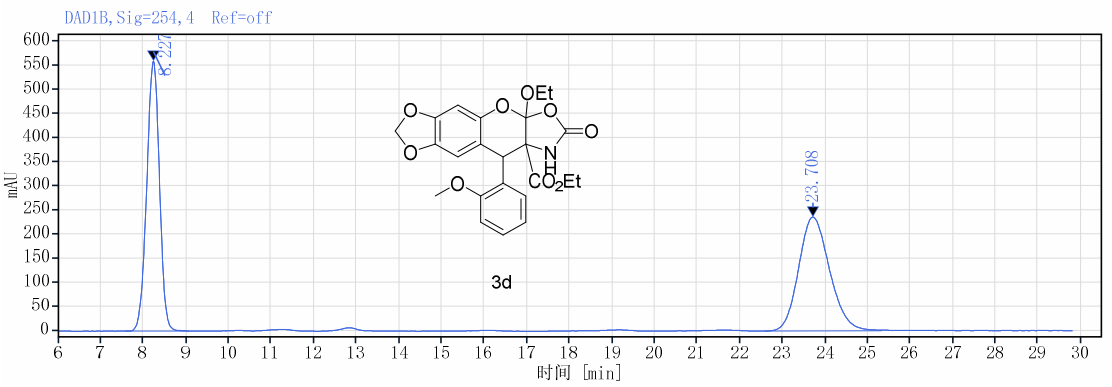
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
15.639	MM	0.37	7575.32	320.00	97.89
17.257	MM	0.30	163.43	8.22	2.11
		Total	7738.75		



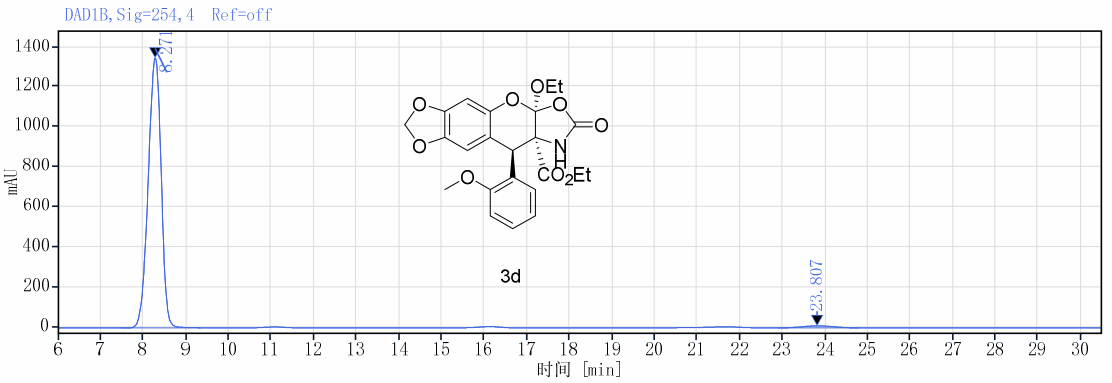
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.493	MM	0.30	1739.07	88.60	50.97
17.735	MM	0.49	1673.21	47.31	49.03
		Total	3412.29		



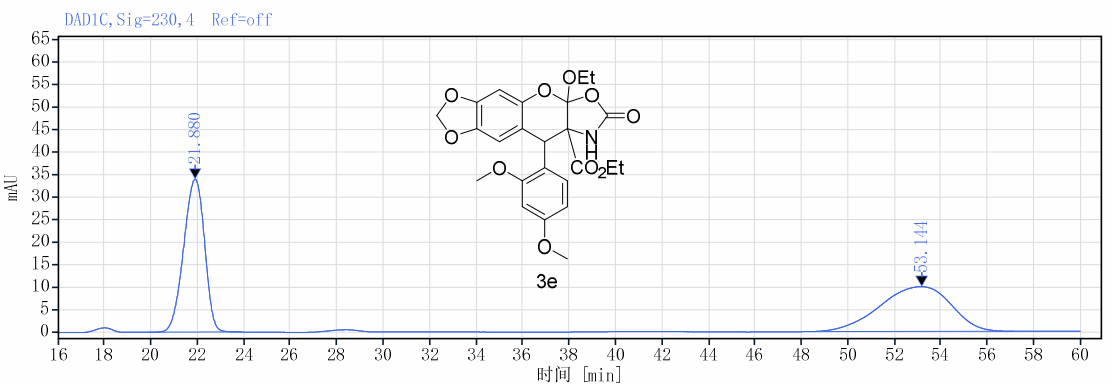
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.518	MM	0.28	197.19	11.30	5.68
17.761	MM	0.55	3272.68	89.97	94.32
		Total	3469.87		



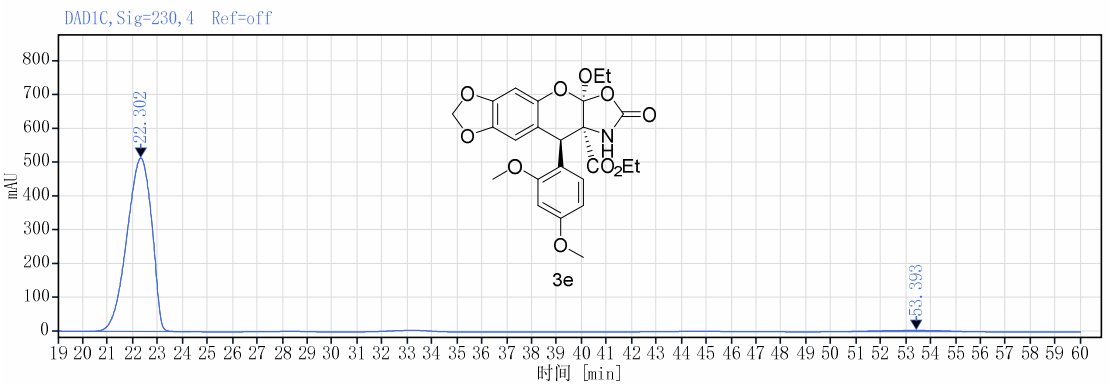
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.227	VV	1.49	11670.59	559.44	49.51
23.708	BV	2.74	11899.39	236.09	50.49
		Total	23569.98		



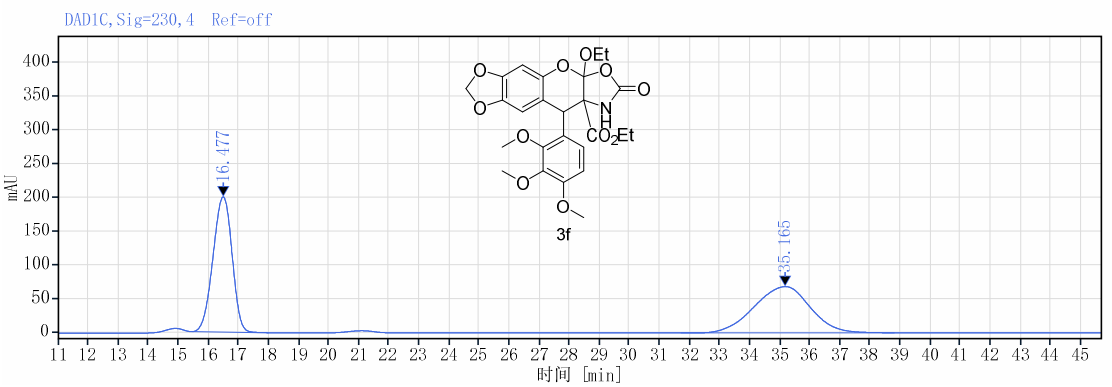
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.271	VV	1.83	28563.15	1345.50	98.22
23.807	BV	1.89	516.46	10.37	1.78
		Total	29079.61		



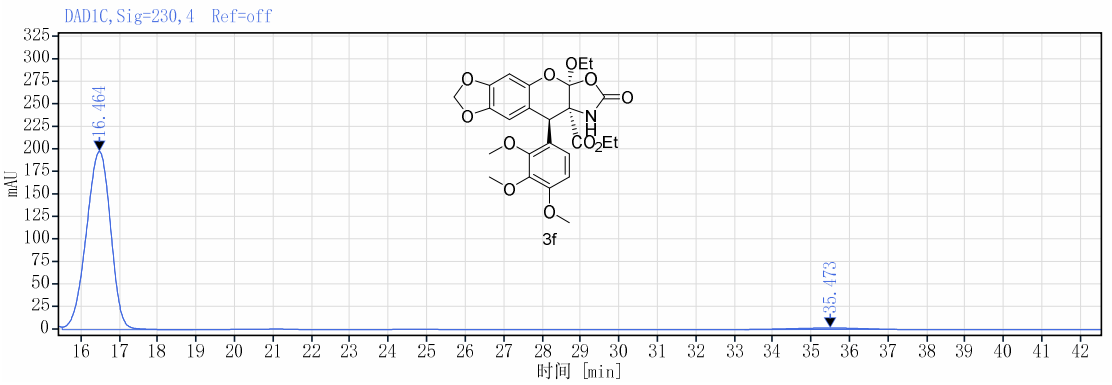
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
21.880	BM m	0.99	2125.96	33.97	50.15
53.144	BB	8.62	2113.01	9.95	49.85
		Total	4238.97		



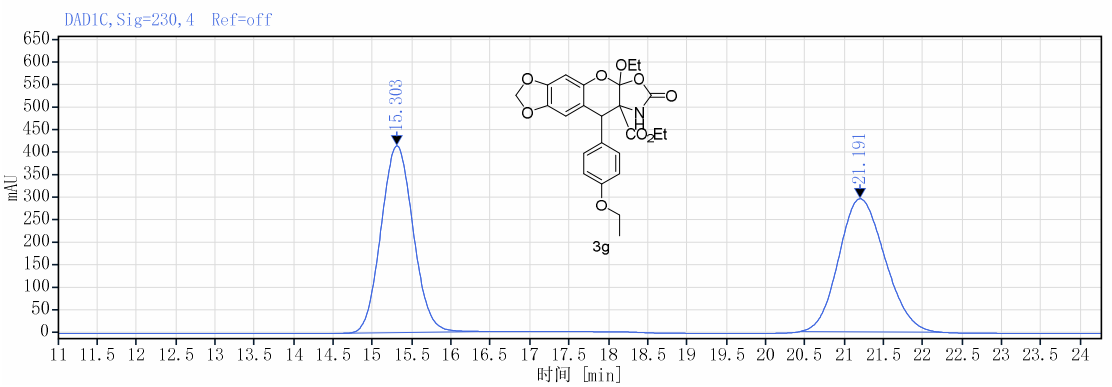
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
22.302	BB	4.04	35442.66	513.81	98.49
53.393	MM m	1.98	543.88	3.24	1.51
		Total	35986.54		



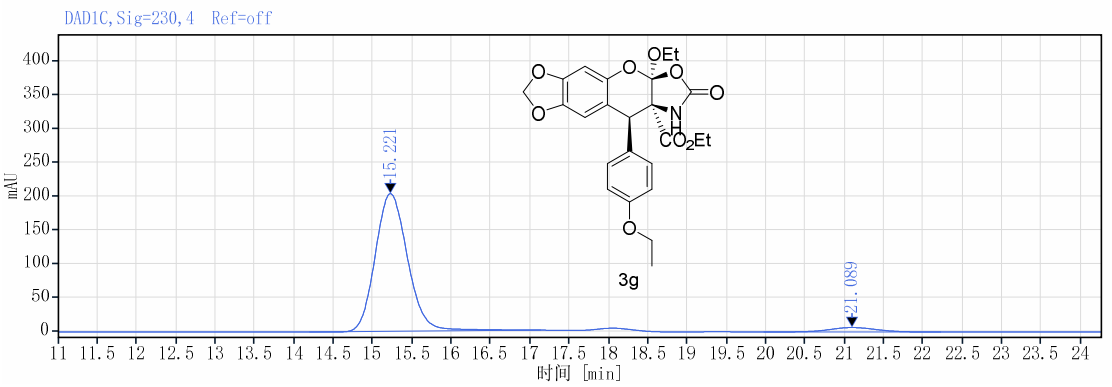
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.477	MM m	0.70	8825.25	200.52	49.82
35.165	BM m	2.04	8887.92	68.56	50.18
		Total	17713.17		



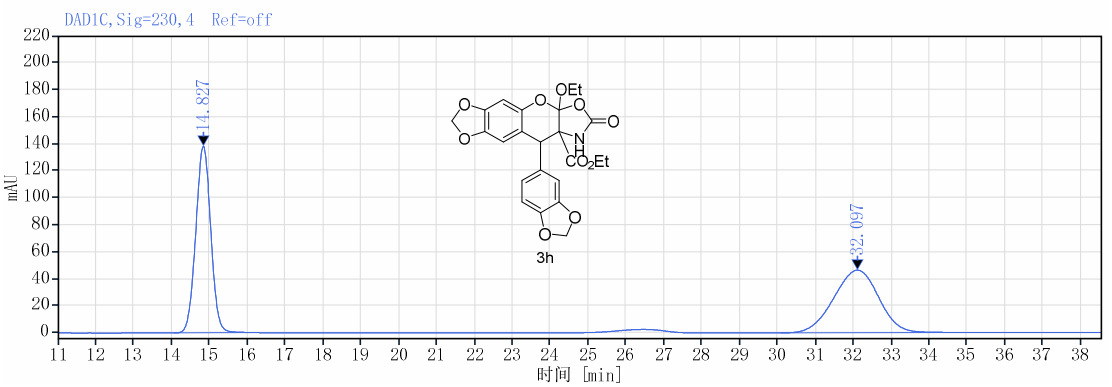
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.464	VB	3.41	8679.48	197.94	97.82
35.473	MM m	1.43	193.33	1.59	2.18
		Total	8872.81		



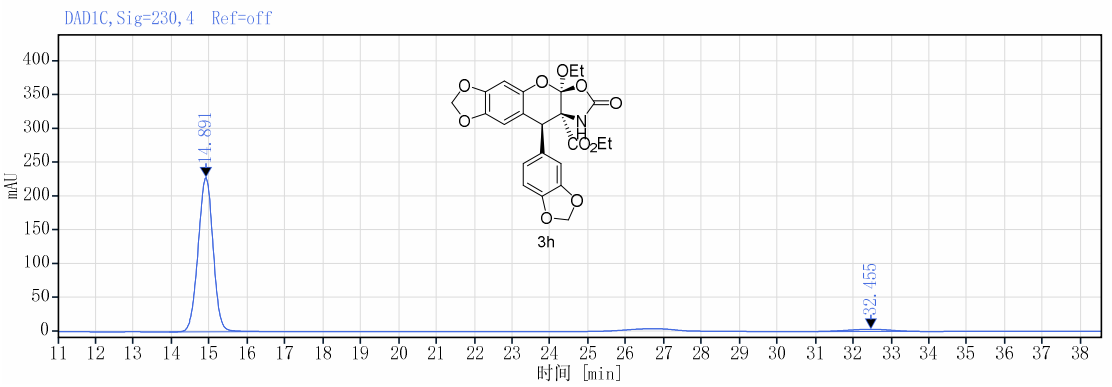
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
15.303	MM m	0.45	11735.12	414.64	49.38
21.191	MM m	0.64	12030.95	295.65	50.62
		Total	23766.07		



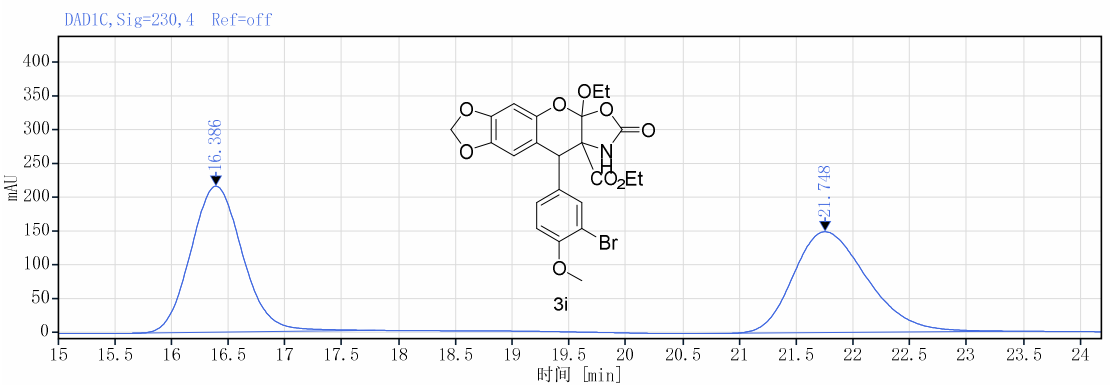
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
15.221	BM m	0.45	5829.52	203.94	95.51
21.089	MM m	0.65	274.12	6.59	4.49
		Total	6103.64		



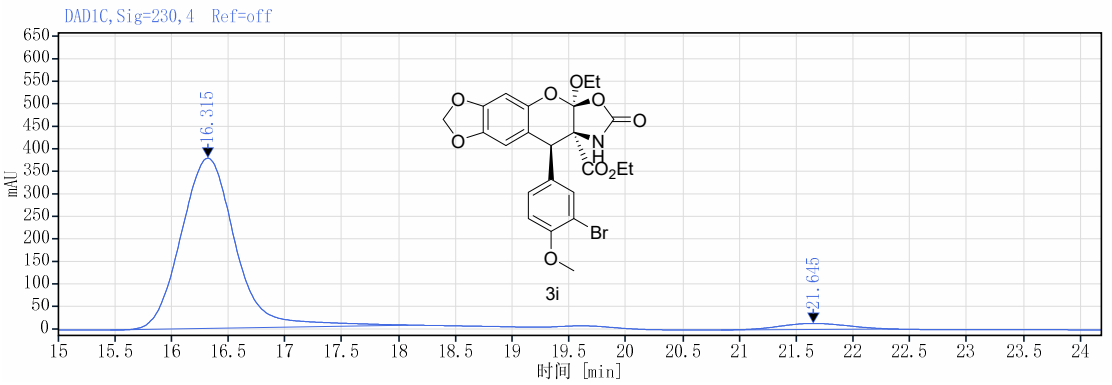
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
14.827	BM	0.43	3805.65	138.24	49.98
32.097	MM m	1.30	3808.44	46.28	50.02
		Total	7614.08		



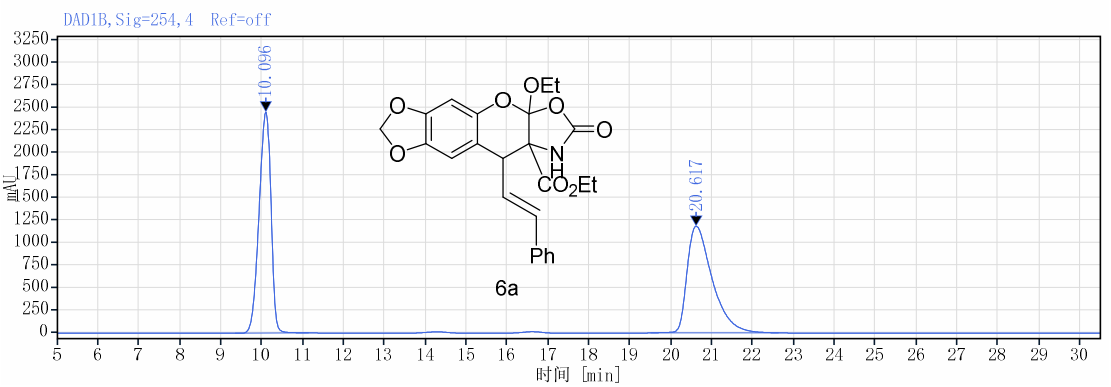
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
14.891	MM m	0.43	6242.00	228.04	96.06
32.455	MM m	1.11	255.99	3.27	3.94
		Total	6497.99		



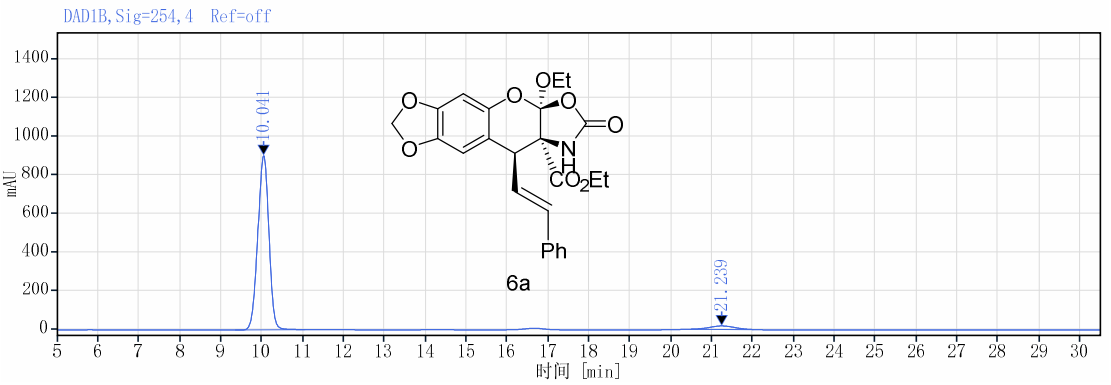
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.386	MM m	0.49	6854.81	216.44	50.47
21.478	BM m	0.70	6726.58	149.38	49.53
		Total	13581.38		



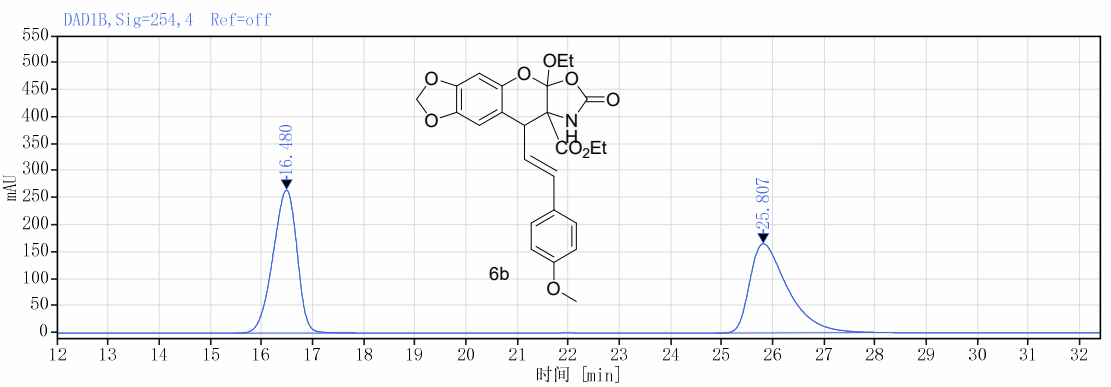
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.315	MM m	0.51	12543.02	378.13	95.69
21.645	MM m	0.66	564.81	13.59	4.31
		Total	13107.83		



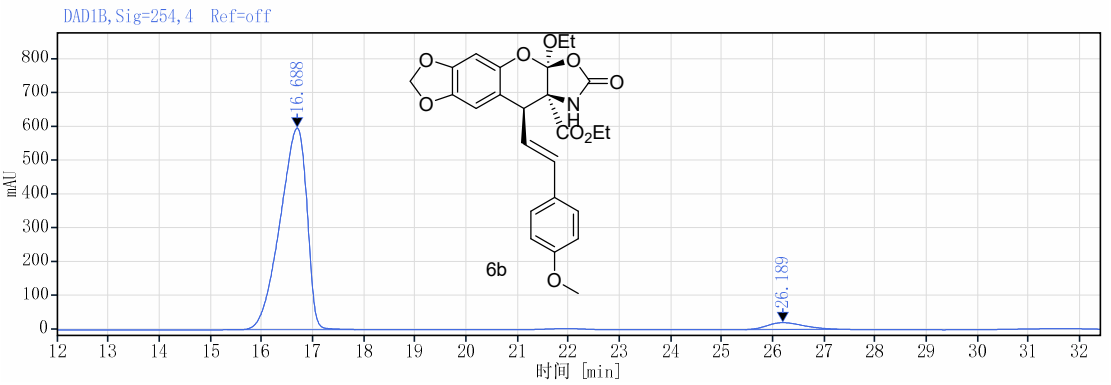
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.096	BM m	0.32	49555.51	2455.07	49.48
20.617	MM m	0.65	50596.08	1185.53	50.52
		Total	100151.58		



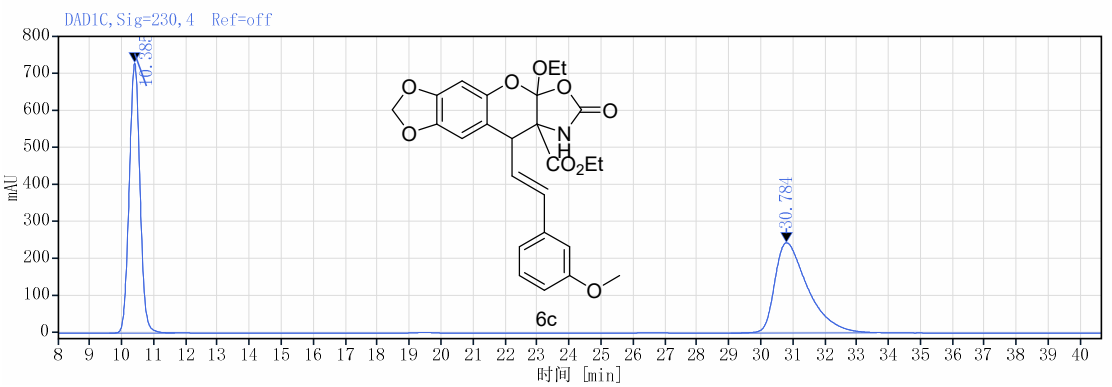
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.041	BM m	0.30	17055.99	903.20	95.75
21.239	MM m	0.65	756.19	17.99	4.25
		Total	17812.17		



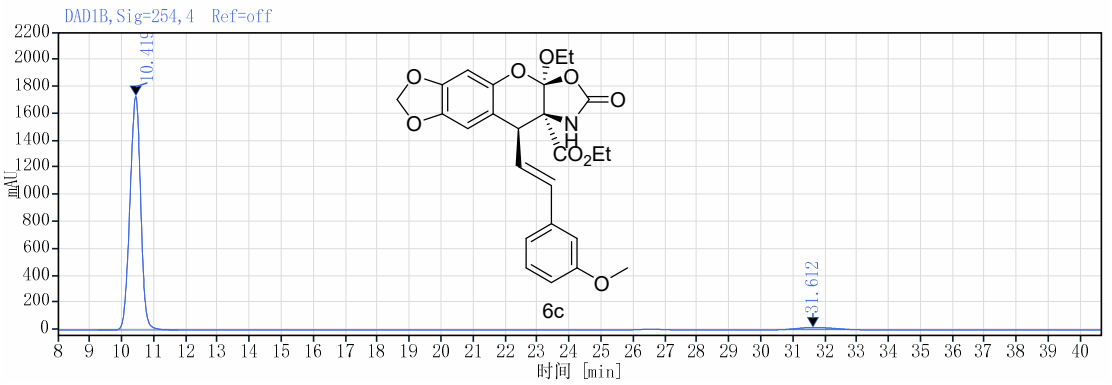
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.480	BM m	0.51	8640.15	264.61	50.22
25.807	BM m	0.78	8564.01	165.23	49.78
		Total	17204.16		



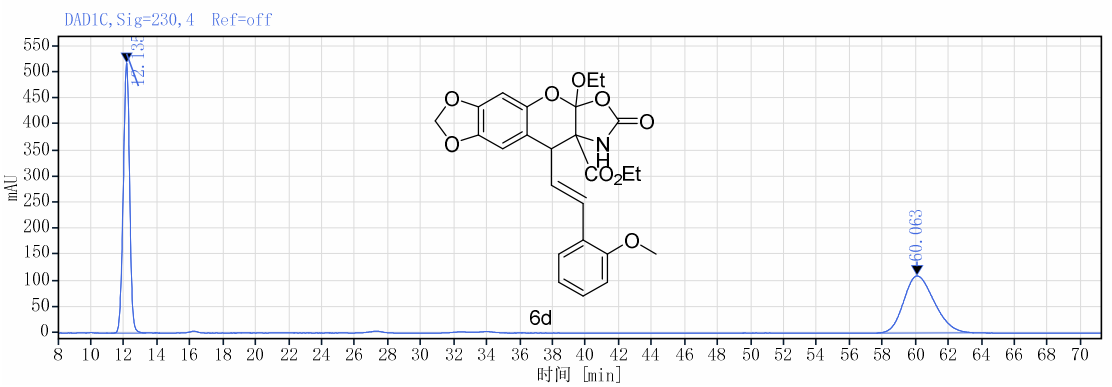
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
16.688	MM m	0.57	21734.81	597.26	95.61
26.189	MM m	0.76	996.80	20.22	4.39
		Total	22731.61		



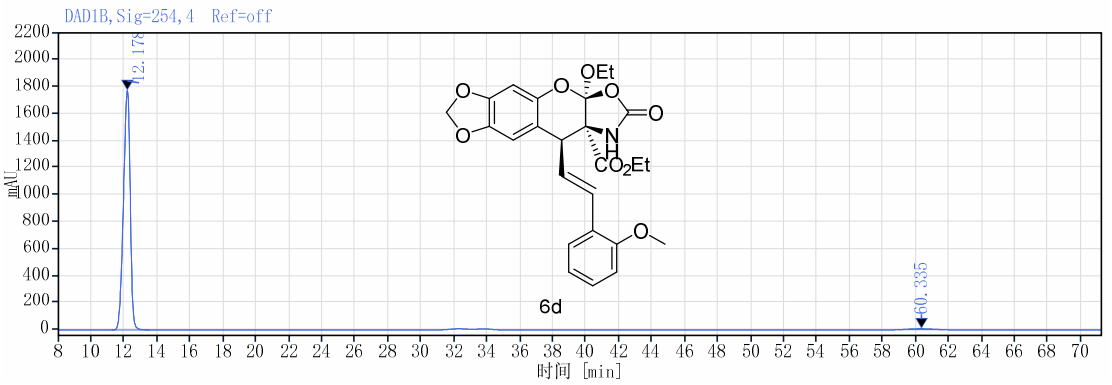
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.385	BV	2.04	17108.17	731.14	49.26
30.784	VV	4.57	17626.89	244.60	50.74
		Total	34735.06		



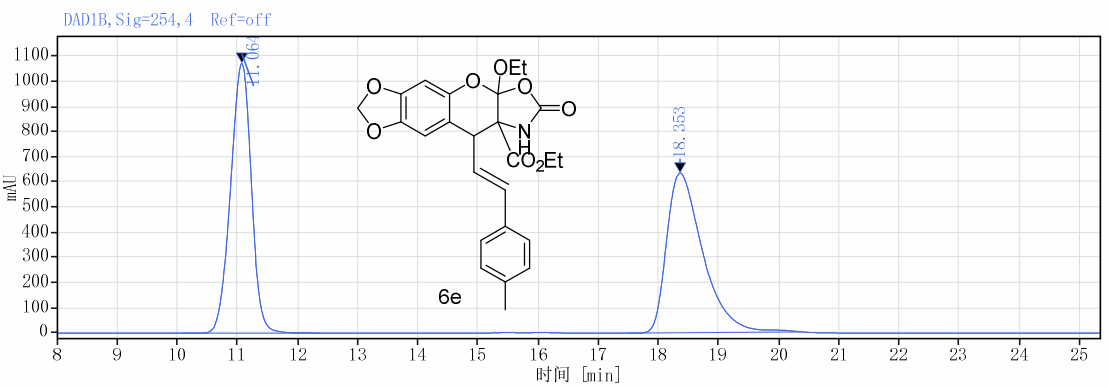
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.419	MB m	0.37	40396.71	1730.12	97.51
31.612	MM m	0.89	1033.49	14.00	2.49
		Total	41430.20		



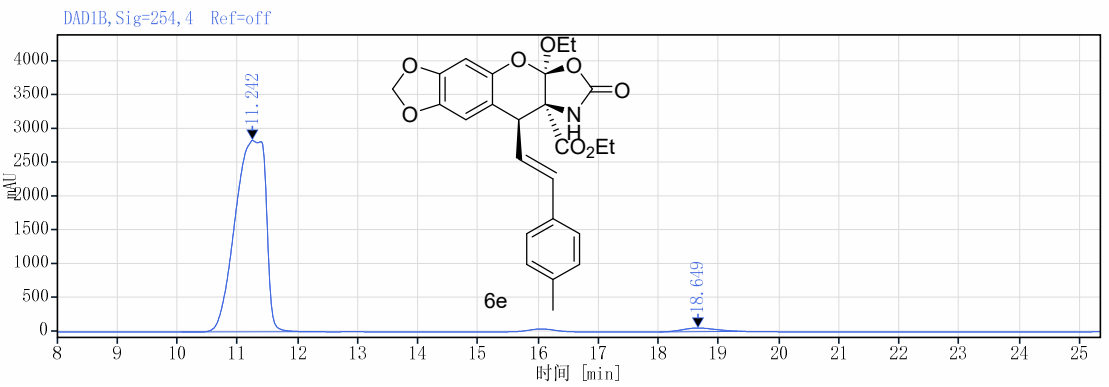
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
12.135	BV	2.12	13835.84	517.63	49.62
60.063	VB	5.92	14046.48	109.38	50.38
		Total	27882.32		



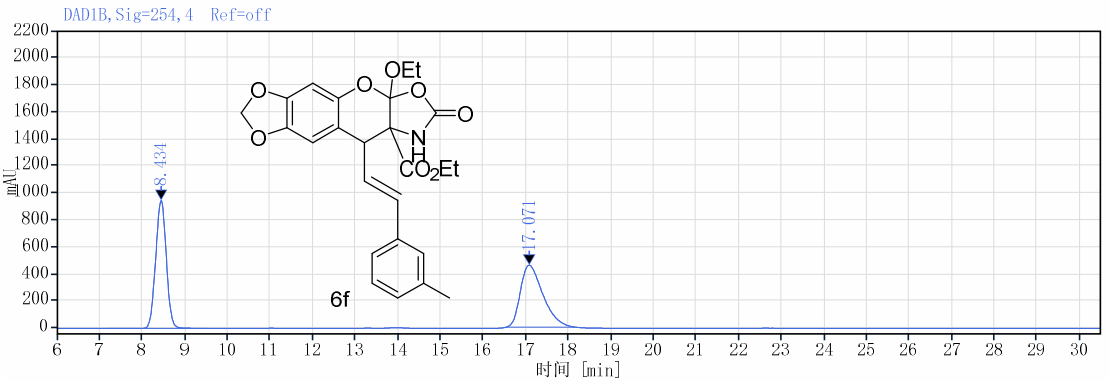
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
12.178	BV	2.29	50639.03	1773.49	98.72
60.335	MM m	1.16	658.03	6.81	1.28
		Total	51297.06		



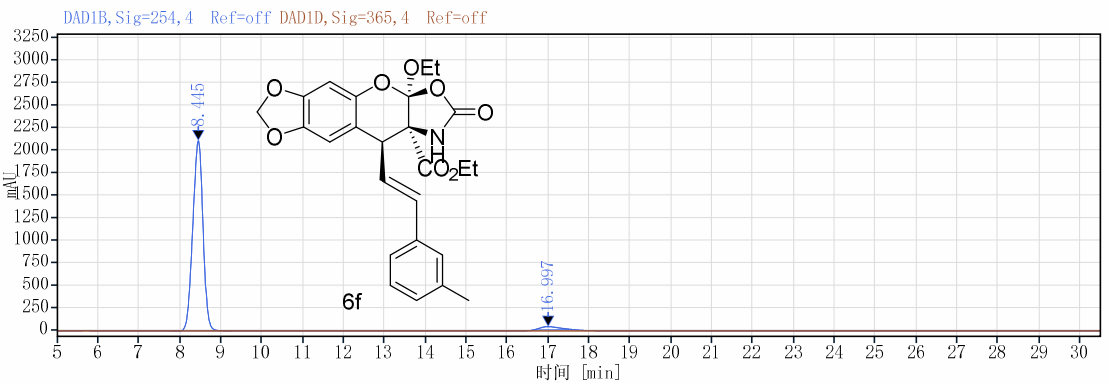
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
11.064	BM m	0.37	25672.83	1073.68	49.20
18.353	BM m	0.64	26510.19	635.43	50.80
		Total	52183.01		



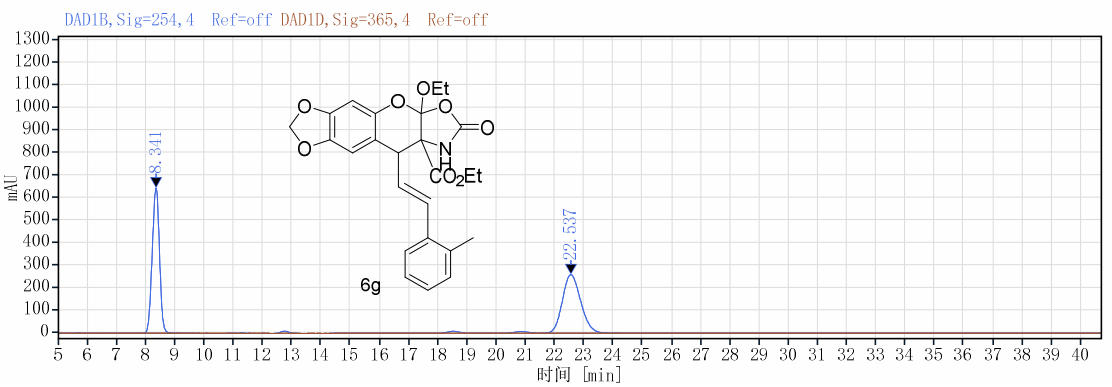
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
11.242	MM m	0.43	100954.77	2838.37	98.00
18.649	MM m	0.61	2060.22	53.38	2.00
		Total	17812.17		



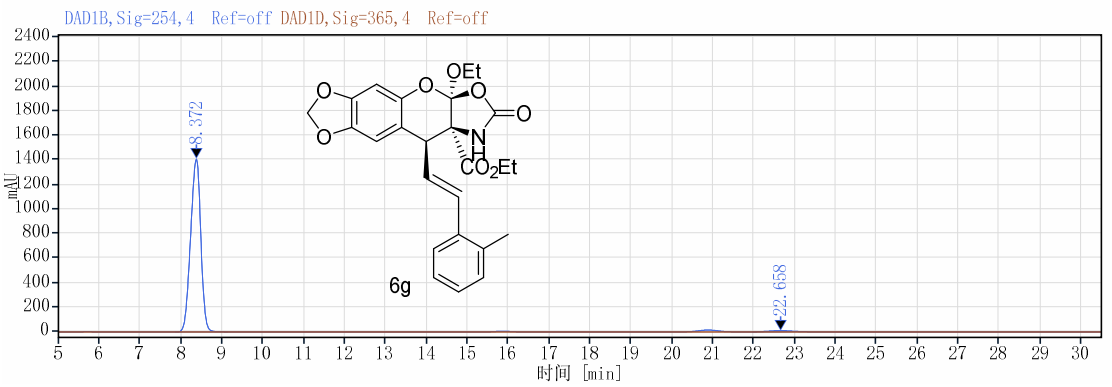
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.434	MM m	0.27	16256.61	947.09	49.23
17.071	MM m	0.57	16866.66	458.97	50.77
		Total	33223.27		



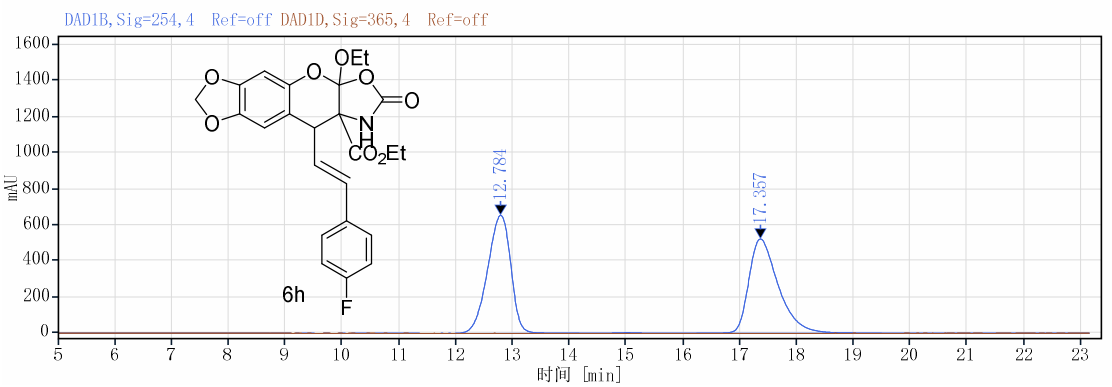
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.445	MM m	0.27	36853.62	2113.71	96.98
16.997	MM m	1.48	1146.30	36.12	3.02
		Total	37999.92		



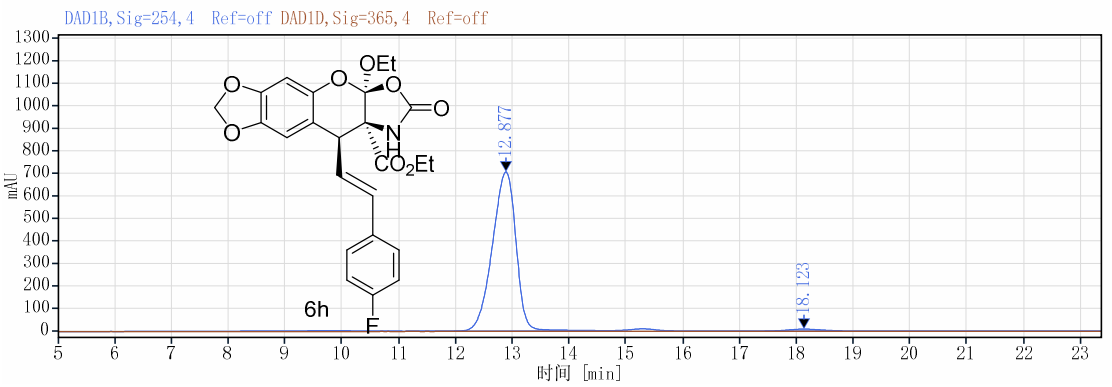
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.341	VV	1.28	11103.81	645.63	49.46
22.537	VV	2.70	11347.46	260.20	50.54
		Total	22451.27		



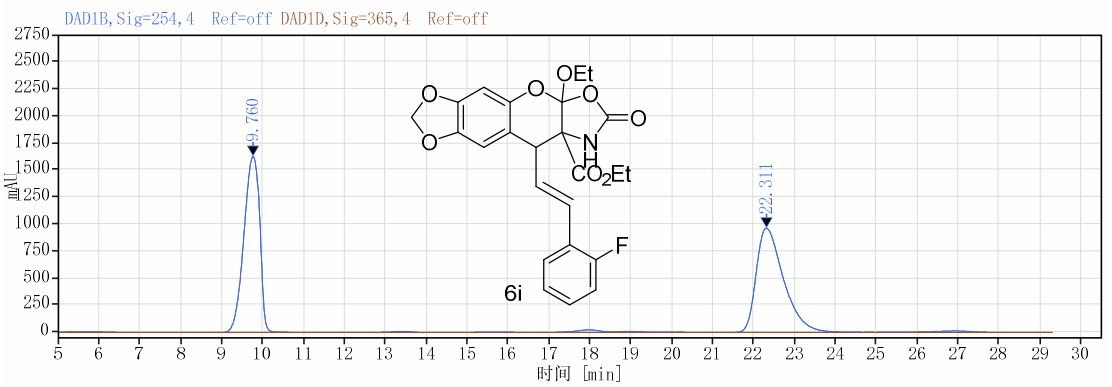
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
8.372	BV	1.29	24515.35	1409.32	98.51
22.658	MM m	0.51	371.12	9.54	1.49
		Total	24886.47		



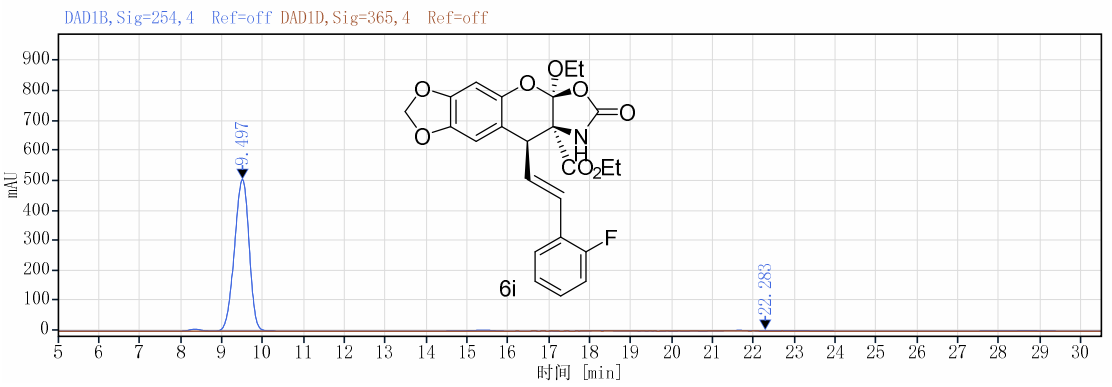
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
12.784	VV	2.22	18595.73	655.75	49.53
17.357	VV	3.27	18950.57	523.56	50.47
		Total	37546.30		



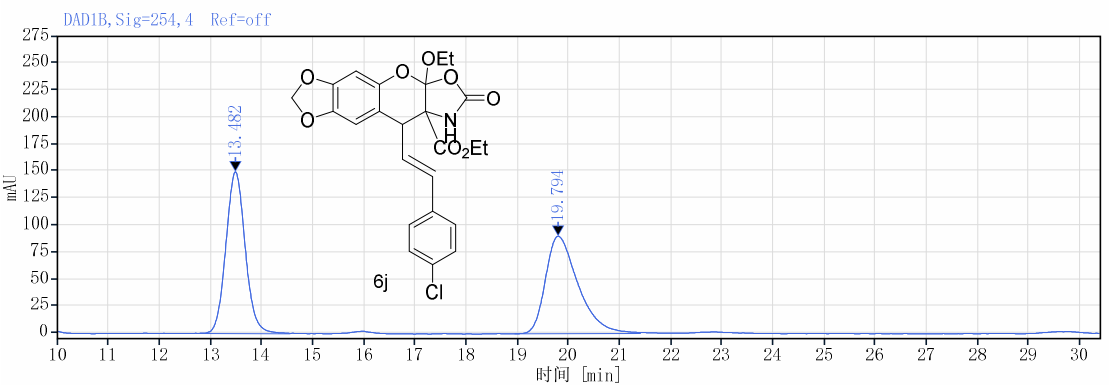
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
12.877	BV	2.29	20341.26	706.93	98.62
18.123	MM m	0.51	284.83	7.91	1..38
		Total	17812.17		



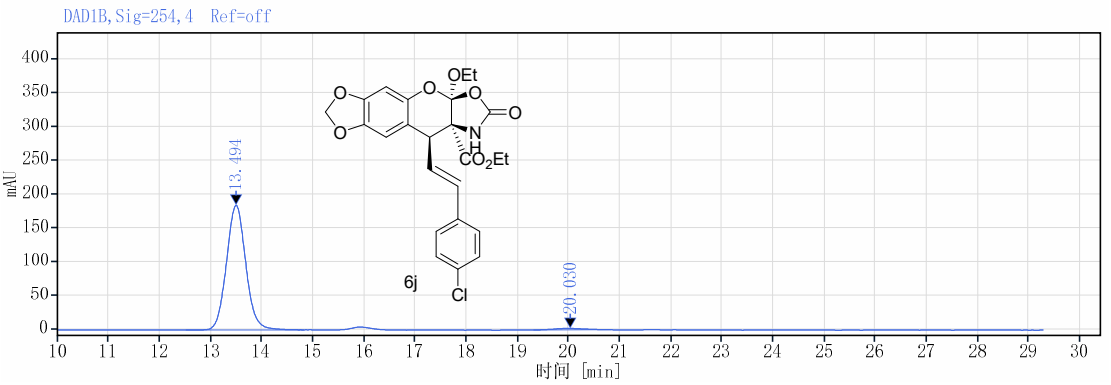
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
9.760	BV	1.91	43665.65	1630.28	49.36
22.311	BV	3.27	44790.70	964.75	50.64
		Total	88456.35		



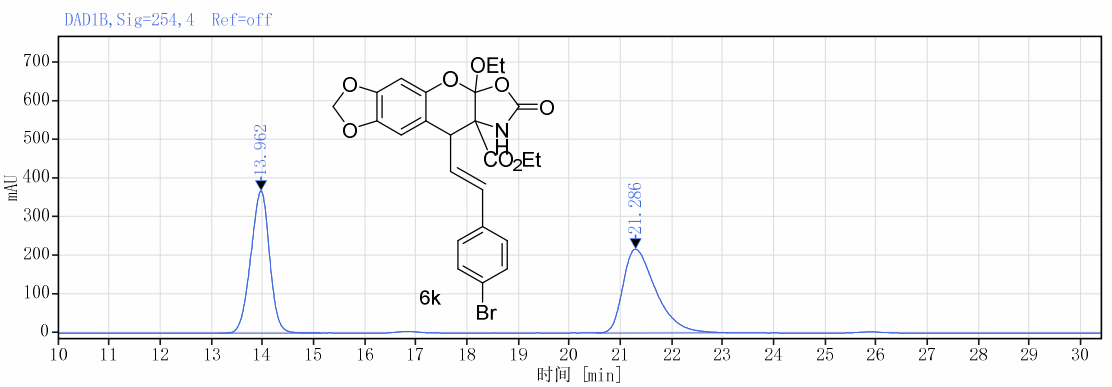
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
9.497	MM m	0.40	12553.33	504.69	99.67
22.283	MM n	0.47	42.10	1.10	0.33
		Total	12595.43		



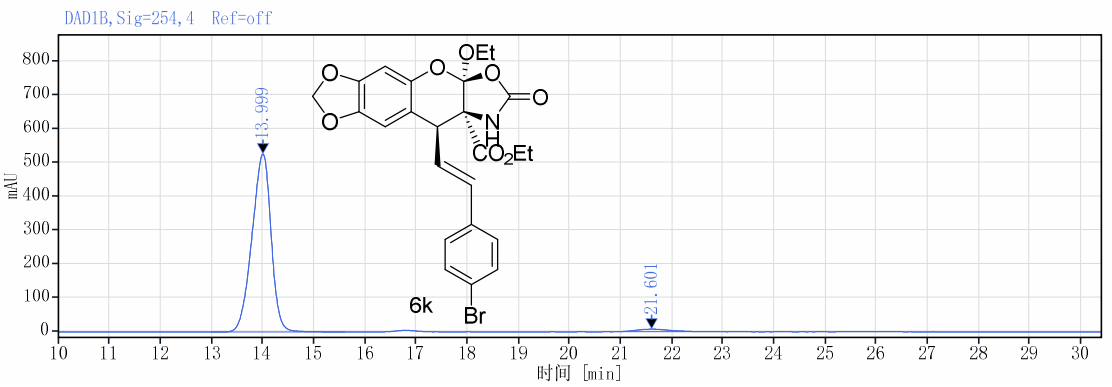
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
13.482	VV	1.80	3944.25	149.84	49.66
19.794	VV	2.46	3998.92	90.28	50.34
		Total	7943.17		



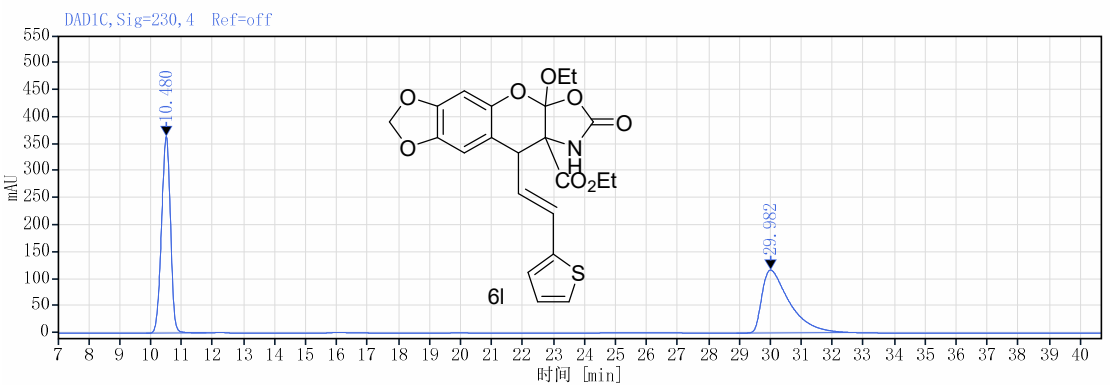
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
13.494	MM m	0.41	4836.43	184.62	98.16
20.030	MM m	0.48	90.72	3.37	1.84
		Total	4927.15		



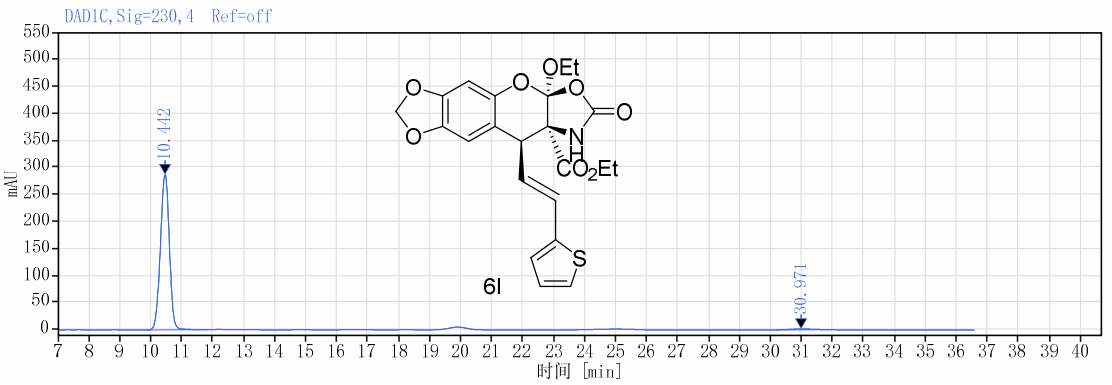
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
13.962	VV	2.01	9411.03	368.43	49.21
21.286	VV	2.58	9712.71	217.48	50.79
		Total	19123.74		



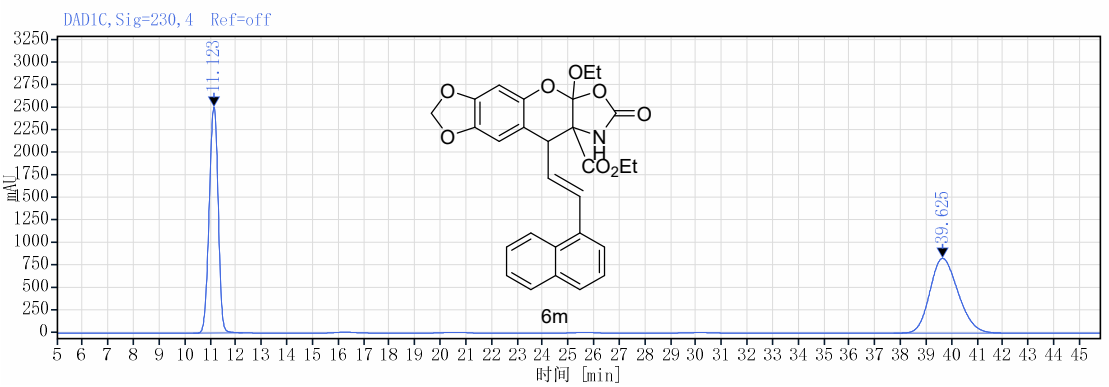
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
13.999	VM m	0.40	13693.97	527.47	97.88
21.601	MM m	0.57	296.79	7.04	2.12
		Total	13990.75		



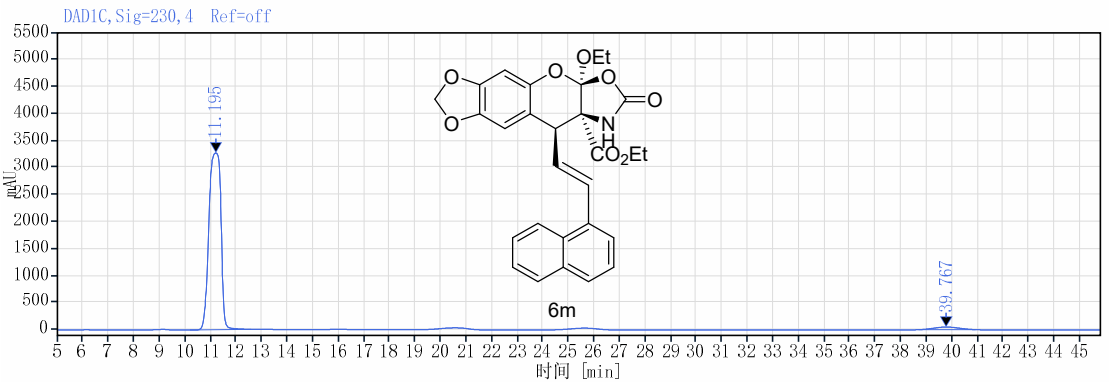
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.480	BB	1.94	7308.38	364.13	50.44
29.982	BM m	0.92	7181.04	116.47	49.56
		Total	17812.17		



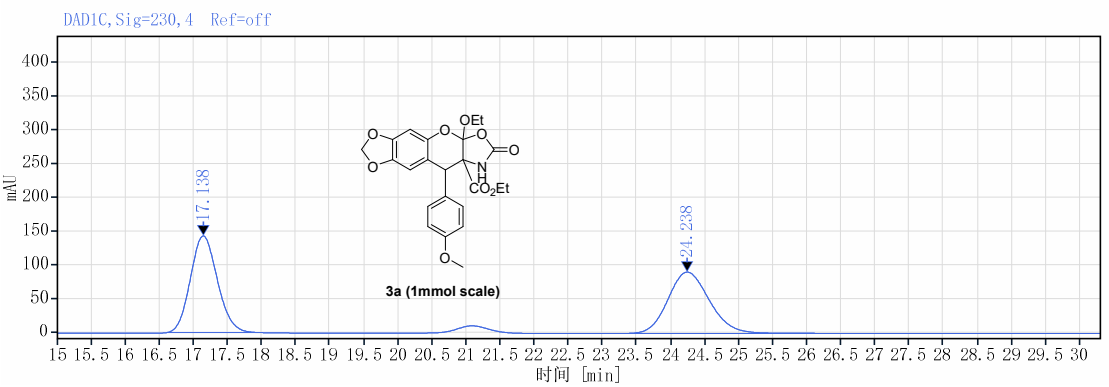
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
10.442	BB	1.98	5769.87	287.29	98.59
30.971	MM m	0.74	82.71	1.49	1.41
		Total	5852.58		



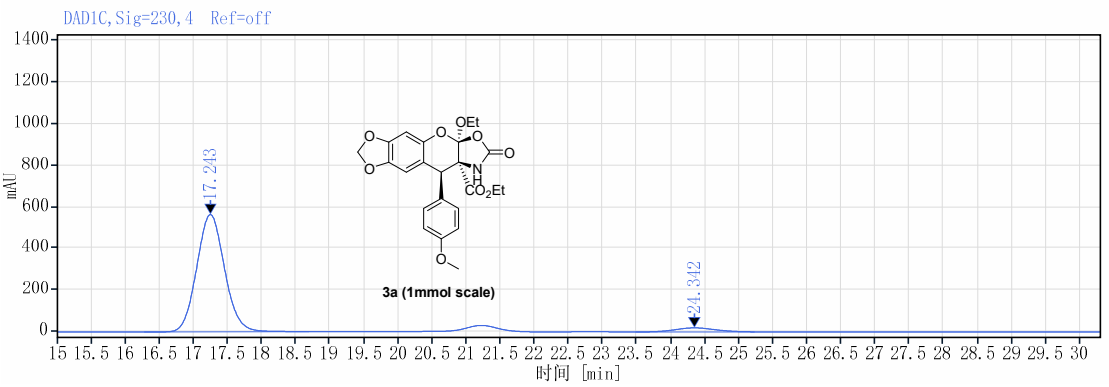
RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
11.123	BM m	0.39	61475.64	2509.77	49.22
39.625	MM m	1.19	63434.90	830.28	50.78
		Total	124910.54		



RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
11.195	MM m	0.53	106298.30	3270.22	97.00
39.767	MM m	1.08	3291.92	48.89	3.00
		Total	109590.22		

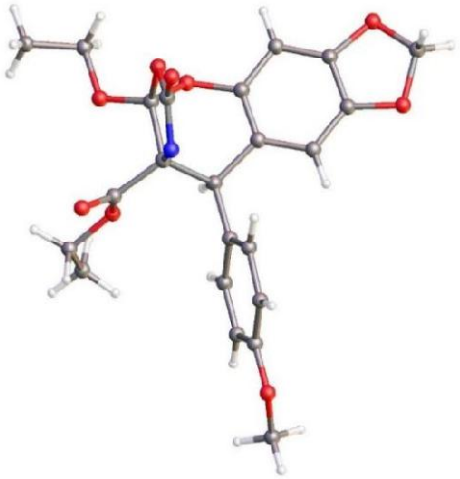


RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
17.138	MM m	0.43	3935.53	142.98	50.70
24.238	MM m	0.66	3827.25	90.83	49.30
		Total	7762.78		



RetTime [min]	Type	Wide [min]	Area[mAu*s]	Height[mAu]	Area%
17.243	MM m	0.44	15983.59	564.33	95.35
24.342	VM m	0.63	778.66	19.34	4.65
		Total	16762.25		

6. Crystallographic Data



The X-ray Single-Crystal Diffraction Analysis of **3a** (CCDC 2203106)

The configuration of the crystal **3a** was first recrystallized and confirmed by chiral HPLC analysis before X-ray crystallography analysis, and the configuration of the crystal is the same compared with the of 3a (99% ee).

The crystals of **3a** were obtained from a solution of ethyl acetate and petroleum ether upon slow volatilization The structure of **3a** ($C_{23}H_{23}NO_9$) was determined by X-ray diffraction. The X-ray intensity data were measured at 168.0 K, on a Bruker APEX-II CCD diffractometer with helios mx multilayer monochrmator Cu Kα radiation (λ = 1.54178 Å). The X-ray data have been deposited at the Cambridge Crystallographic Data Center (CCDC 2203106). The level set for thermal ellipsoids of all atoms is 50%.

Table 1 Crystal data and structure refinement for 3a.

Empirical formula	$C_{23}H_{23}NO_9$
Formula weight	457.13
Temperature/K	180.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	14.647(3)
b/Å	15.996(3)
c/Åq	21.798(4)
α/°	90
β/°	105.457(9)
γ/°	90
Volume/$Å^3$	4922.4(15)
Z	8
pcalcg/cm^3	1.353
μ/mm^{-1}	0.890
F(000)	2112.0
Crystal size/mm^3	0.31 × 0.15 × 0.14
Radiation	CuKα (λ = 1.54178)

2Θ range for data collection/°	4.206 to 146.848
Index ranges	-17 ≤ h ≤ 17, -19 ≤ k ≤ 17, -26 ≤ l ≤ 25
Reflections collected	56578
Independent reflections	17882 [R_{int} = 0.0649, R_{sigma} = 0.0559]
Data/restraints/parameters	17882/1/1313
Goodness-of-fit on F^2	1.049
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.1051
Final R indexes [all data]	R_1 = 0.0458, wR_2 = 0.1084
Largest diff. peak/hole / e $Å^{-3}$	0.38/-0.28
Flack parameter	0.03(5)

These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.