Supporting Information

Enantioselective access to multi-cyclic α-amino phosphonates via carbene-catalyzed cycloaddition reactions between enals and six-membered cyclic imines

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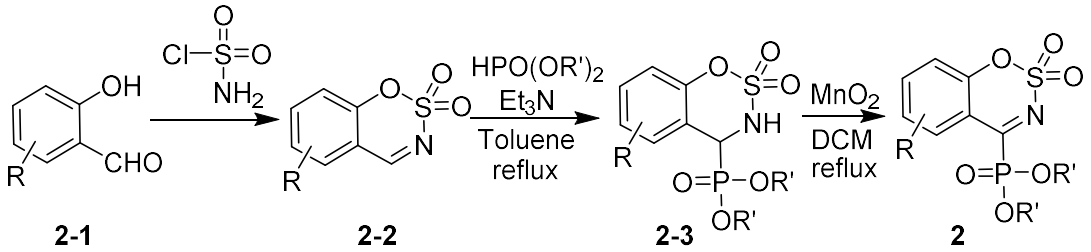
Ⅰ. General information

Commercially available materials purchased from J&K or Aladdin were used as received. THF was distilled over sodium. Unless otherwise specified, all reactions were carried out under an atmosphere of nitrogen in 10 mL dry Schlenk tube. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker (400 MHz) spectrometer or on a JEOL-ECX-500 (500 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker (101 MHz) spectrometer or on a JEOL-ECX-500 (126 MHz) spectrometer. Fluorine (^{19}F) nuclear magnetic resonance (^{19}F NMR) spectra were recorded on a Bruker (376 MHz) spectrometer or on a JEOL-ECX-500 (471 MHz) spectrometer. Phosphorus (^{31}P) nuclear magnetic resonance (^{31}P NMR) spectra were recorded on a Bruker (162 MHz) spectrometer or on a JEOL-ECX-500 (202MHz) spectrometer. The melting points (m.p.) of the title compounds were determined when left untouched on an XT-4-MP apparatus from Beijing Tech. Instrument Co. (Beijing, China). High resolution mass spectral analysis (HRMS) was performed on a quadrupole/electrostatic field orbitrap mass spectrometer. Absolute configuration of the products was determined by X-ray crystallography. HPLC analyses were measured on Waters systems with Empower3 system controller, Alliance column heater, and 2998 Diode Array Waters 2489 UV/Vis detector. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models AD-H, or OD-H in 4.6 x 250 mm size. The racemic products used to determine the er values were synthesized using racemic catalyst. Optical rotations were measured on a Insmark IP-digi Polarimeter in a 1 dm cuvette at 26 ^{o}C. The concentration (c) is given in g/100 mL. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

Ⅱ. Preparation of substrates

α-Iminophosphonates **2** were synthesized from salicylaldehyde by the combination of slightly modified literature procedures.[1]



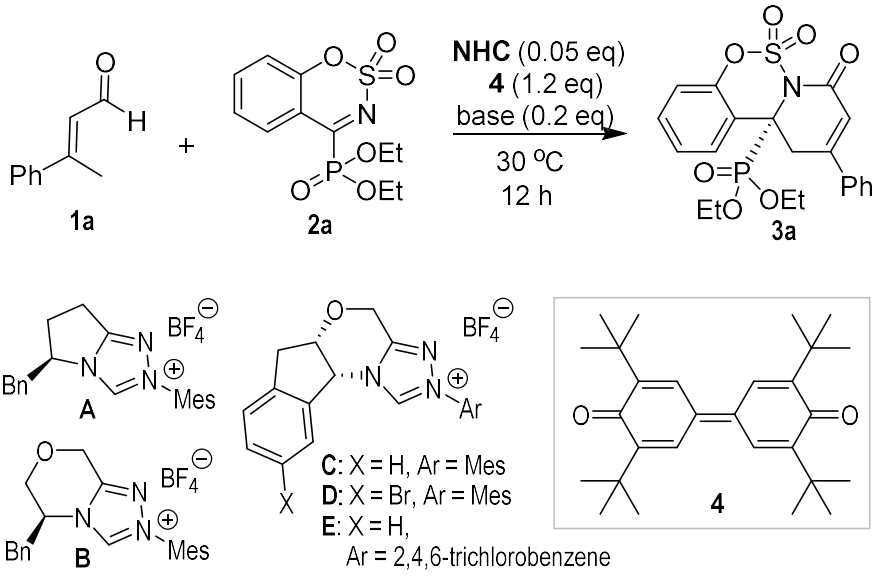
Following a known literature report: to a solution of salicylaldehyde (15 mmol) in dimethylacetamide (100 mL) at 0 °C was carefully added freshly prepared chlorosulfonamide (40 mmol) in small portions and the resulting solution was stirred for 12 h. The reaction was quenched carefully with ice-cold water (100 mL) and the mixture was transferred to a separating funnel containing dichloromethane (200 mL). The aqueous layer was separated and extracted with dichloromethane (3×50 mL), and the combined organic layers were washed with saturated sodium bicarbonate solution (100 mL), dried over sodium sulfate, filtered through a short pad of silica using dichloromethane as eluent and concentrated in vacuo. The residue was heated to 180 °C under vacuum to remove volatile impurities to get benzoxathiazine-2,2-dioxide (**2-2**).

To a suspension of the corresponding benzoxathiazine-2,2-dioxide (25 mmol) and the corresponding dialkylphosphite (30 mmol) in toluene (50 mL) was added triethylamine (2.5mmol). The solution was stirred and refluxed in toluene for 24 h until disappearance of benzoxathiazine-2,2-dioxide. The solution was allowed to cool to room temperature and purification was performed by a silica gel column eluted with dichloromethane to give pure product.

To a solution of the above product (1.0 mmol) in dichloromethane was added freshly prepared manganese dioxide (10 mmol) (the manganese dioxide must be freshly prepared, or the reaction yield will be low). The solution was stirred and refluxed at 50 °C for 4-8 h. The solution was allowed to cool to room temperature and purification was performed by a silica gel column eluted with dichloromethane to give pure product **2**.

Ⅲ. Reaction condition optimization

Table 1. Screening of different carbene catalysts, bases and solvents. [a]



entry	NHC	base	solvent	yield[b]	er[c]
1	**A**	Cs_2CO_3	THF	< 5	--
2	**B**	Cs_2CO_3	THF	< 5	--
3	**C**	Cs_2CO_3	THF	34	98:2
4	**D**	Cs_2CO_3	THF	73	99:1
5	**E**	Cs_2CO_3	THF	< 5	--
6	**D**	K_2CO_3	THF	60	99:1
7	**D**	NaOAc	THF	93	> 99:1
8	**D**	DBU	THF	34	97:3
9	**D**	DMAP	THF	< 5	--
10	**D**	NaOAc	EtOAc	58	> 99:1
11	**D**	NaOAc	CH_2Cl_2	32	99:1

[a]General conditions (unless otherwise specified): **1a** (0.12mmol), **2a** (0.1 mmol), NHC (0.005 mmol), base (0.02 mmol), **4** (0.12 mmol), THF (2.0 mL), 30 °C, 12 h. [b]Isolated yield of **3a**. [c]Er was determined via HPLC on chiral stationary phase.

Ⅳ. Proposed mechanism.

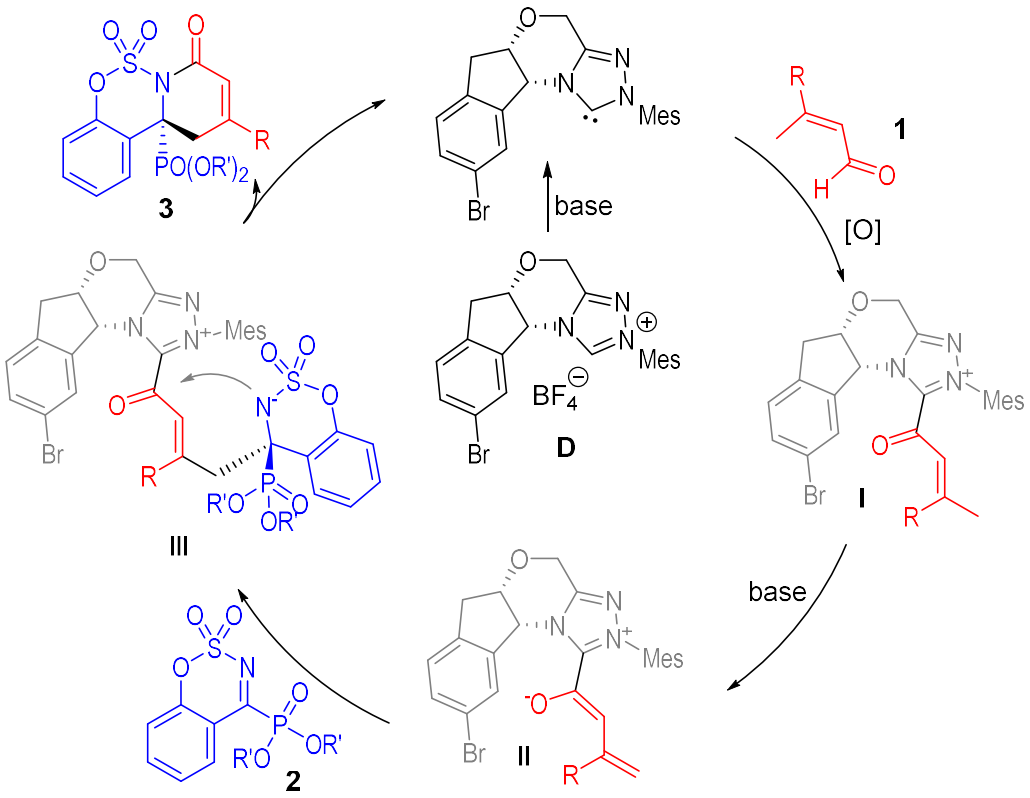
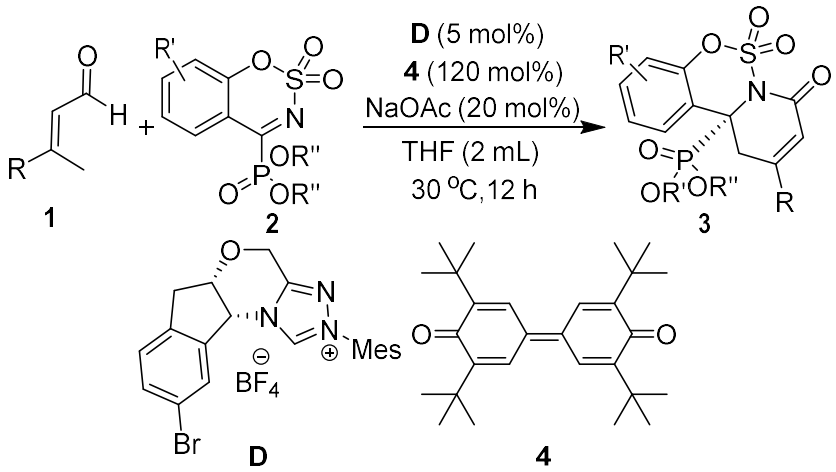


Figure 1. Proposed mechanism

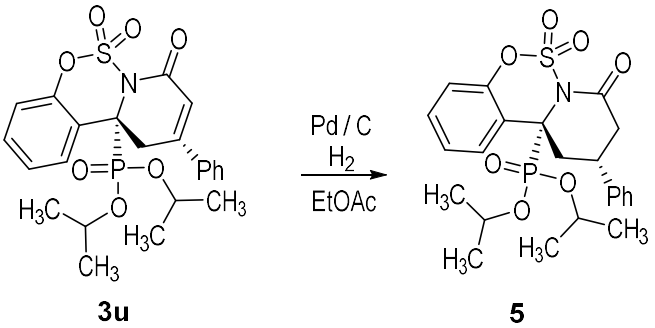
Ⅴ. General procedure.

1. General procedure for the synthesis **3** from cyclic six-membered ring *α*-iminophosphonates substrates **2.**



To a dry Schlenk reaction tube equipped with a magnetic stir bar was added **1** (0.12 mmol), aldehydes **2** (0.1 mmol), triazolium salt **D** (2.5 mg, 0.005 mmol), oxidant **4** (49 mg, 0.12 mmol) and NaOAc (1.6 mg, 0.02 mmol). The schlenk tube was then closed with septum, evacuated and refilled with N_2, freshly distilled anhydrous THF (2 mL) was added. The mixture was stirred at 30 °C for 12 h. After completion of the reaction monitored by TLC, solvent was removed under reduced pressure and the residue was purified via column chromatography on silica gel with Hexane/EtOAc (2: 1) as eluent to afford the products **3**.

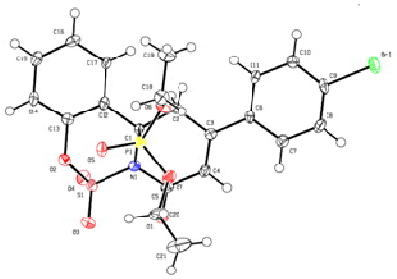
2. General procedure for the synthesis **5.**



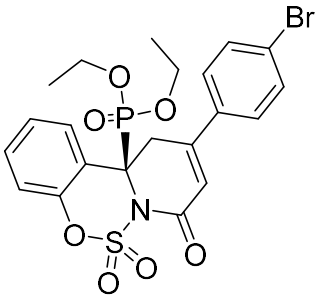
To a solution of **3u** (130 mg) in EtOAc (5 mL) was added Pd/C(5%w, 6 mg), then the mixture was degassed and refilled with H_2(balloon) for 3 times, then the mixture was stirred at rt under H_2(balloon) for 6h, then the mixture was filtered off and the residue was purified via column chromatography on silica gel with Hexane/EtOAc (2: 1) as eluent to afford the product **5** (120 mg).

Ⅵ. Stereochemistry determination via X-ray crystallographic analysis

The absolute stereochemistry of **3e** was determined by the X-ray diffraction. This crystal was deposited in the Cambridge Crystallographic Data Centre and assigned as CCDC: 1854098.



CCDC: 1854098



3e

Refrences:

[1]. Z. Yan, B. Wu, X. Gao, M.-W. Chen, Y.-G. Zhou, *Org. Lett.*, 2016, **18,** 692.

Ⅶ. *In vitro* antibacterial bioassay

The target compounds were dissolved in 150 μL DMSO and diluted with sterile distilled water containing 0.1 % Tween-20 (4 mL) to prepare 1000 and 500 μg/mL stock solution. Their antibacterial activities against *Xanthomonas oryzae pv. oryzae* was evaluated by the turbidimeter test. 1 mL of stock solution was added to 4 mL nutrient broth liquid medium NB (3 g of beef extract, 5 g of peptone, 1 g of yeast powder, 10 g of glucose, and 1000 mL of distilled water, pH 7.0 - 7.2) in tubes. Then, to the tube, 40 μL NB containing bacteria was added and incubated with continuous shaking at 180 rpm for 36 h at 30±1 ^{o}C. The test concentration was fixed at 200 and 100 μg/mL. The data of bacterial growth was reported by measuring the optical density at 600 nm (OD_{600}) with a spectrophotometer.

DMSO in sterile distilled water containing 0.1 % Tween-20 served as the negative control, whereas Bismerthiazol served as positive control. The inhibitory rate of bacterial culture growth was calculated according to the following formula:

$$\text{Inhibition rate (\%)} = (CK\text{-}T)/CK \times 100$$

“CK” means the value of corrected optical density of bacterial growth on untreated NB (negative control), and “T” means the value of corrected optical density of bacterial growth on treated NB.

Table 2. Antibacterial activity

Antibacterial activity of the title compounds

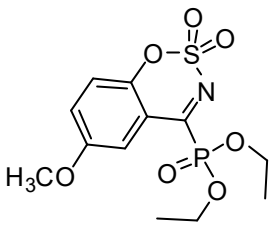
Antibacterial activity of the title compounds

Compound	*X. oryzoe pv. oryzae* inhibition rate [%][a]	
	100 μg/mL	200 μg/mL
3a	10.4±7.2	17.1±4.4
3b	19.2±3.2	32.9±3.8
3c	16.3±6.5	20.9±6.7
3d	17.1±4.8	46.0±1.9
3e	45.6±3.8	80.0±2.5
3f	27.7±6.3	31.7±3.7
3g	22.0±6.3	0
3h	9.7±7.3	2.1±6.4
3i	21.8±6.1	0
3j	6.4±5.7	8.6±3.9
3k	0	0
3l	69.3±3.8	88.8±3.1
3m	0	0
3n	0	o
3o	0	10.6±6.7
3p	23.5±3.6	18.2±4.2
3q	0	6.9±3.9
3r	0	0
3s	0	0
3t	0	0
3u	25.3±2.4	32.6±5.3
Bismerthiazol[b]	45.4±1.9	73.6±1.4
Negative control[c]	0	0

[a]Average of three replicates. [b]Commercial bactericide, used as the positive control. [c]DMSO was used as the negative control.

Ⅷ. Characterization of intermediates & products

Diethyl (6-methoxy-2,2-dioxidobenzo[e][1,2,3]oxathiazin-4-yl)phosphonate (2q)



Light yellow solid, m.p. 45-46 °C 350 mg, 35% yield.

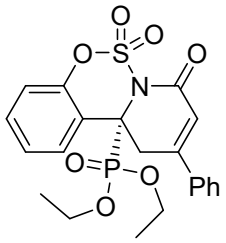
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.9 Hz, 1H), 7.29 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.23 (dd, *J* = 9.1, 1.3 Hz, 1H), 4.43 - 4.30 (m, 4H), 3.88 (s, 3H), 1.42 (td, *J* = 7.1, 0.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5 (d, *J* = 199.1 Hz), 157.0 (s), 148.2 (d, *J* = 8.6 Hz), 125.2 (s), 120.0 (d, *J* = 3.2 Hz), 116.1 (d, *J* = 24.1 Hz), 113.3 (s), 65.5 (d, *J* = 7.0 Hz), 56.1 (s), 16.3 (d, *J* = 6.0 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 0.92 (s).

HRMS (ESI, m/z): Mass calcd for $C_{12}H_{17}O_7NPS$ $[M+H]^+$, 350.0458; found 350.0468.

Diethyl (*R*)-(6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3a)



White solid, m.p. 127-128 °C, 45 mg, 97% yield.

$[\alpha]_D^{28}$ = -31.2 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 - 7.60 (m, 2H), 7.60 - 7.55 (m, 1H), 7.55 - 7.40 (m, 5H), 7.32 - 7.27 (m, 1H), 6.40 (d, *J* = 2.9 Hz, 1H), 4.25 - 4.04 (m, 3H), 4.01 - 3.87 (m, 1H), 3.80 - 3.65 (m, 1H), 3.39 (ddd, *J* = 34.3, 17.2, 2.9 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.10 (t, *J* = 7.0 Hz, 3H).

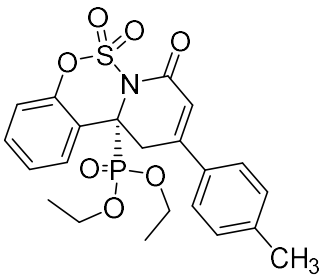
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 150.4 (s), 148.4 (d, *J* = 4.7 Hz), 136.2 (s), 131.3 (d, *J* = 2.8 Hz), 130.8 (s), 129.2 (s), 127.5 (d, *J* = 2.2 Hz), 126.8 (d, *J* = 4.0 Hz), 126.6 (s), 125.4 (s), 119.8 (d, *J* = 2.3 Hz), 118.5 (s), 66.4 (d, *J* = 152.6 Hz), 64.7 (d, *J* = 3.8 Hz), 64.6 (d, *J* = 3.6 Hz), 36.5 (d, *J* = 2.4 Hz), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.57 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{23}O_7NPS$ $[M+H]^+$, 464.0927; found 464.0918.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.8 mL/min, 254 nm), Rt_1 (minor) = 10.5 min, Rt_2 (major) = 17.0 min; er = 99.2:0.8).

Diethyl (*R*)-(6,6-dioxido-8-oxo-10-(p-tolyl)-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3b)



White solid, m.p. 172-173 °C, 46 mg, 96% yield.

$[\alpha]_D^{28}$ = -45.0 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dt, *J* = 17.1, 8.4 Hz, 4H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 8.3, 2.7 Hz, 3H), 6.38 (d, *J* = 2.7 Hz, 1H), 4.22 - 4.02 (m, 3H), 3.99 - 3.89 (m, 1H), 3.72 (ddd, *J* = 16.7, 7.1, 2.2 Hz, 1H), 3.35 (ddd, *J* = 34.4, 17.2, 2.8 Hz, 1H), 2.41 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

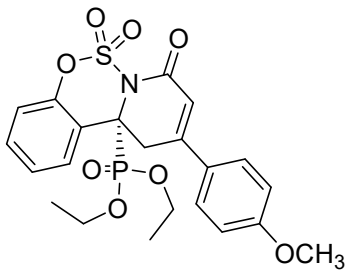
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (s), 150.2 (s), 148.4 (d, *J* = 4.6 Hz), 141.5 (s), 133.1 (s), 131.3 (d, *J* = 2.7 Hz), 129.9 (s), 127.5 (s), 126.8 (d, *J* = 4.0 Hz), 126.5 (s), 125.5 (s), 119.7 (d, *J* = 2.3 Hz), 117.5 (s), 66.3 (d, *J* = 152.8 Hz), 64.6 (d, *J* = 1.8 Hz), 64.6 (d, *J* = 1.6 Hz), 36.2 (s), 21.4 (s), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.62 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_7NPS$ $[M+H]^+$, 478.1084; found 478.1073.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 18.3 min, Rt_2 (minor) = 36.9 min; er = 99:1).

Diethyl (*R*)-(10-(4-methoxyphenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3c)



White solid, m.p. 117-118 °C, 40 mg, 80% yield.

$[\alpha]_D^{28}$ = -37.6 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 - 7.55 (m, 3H), 7.51 (ddd, *J* = 8.0, 4.6, 1.6 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 6.34 (d, *J* = 2.8 Hz, 1H), 4.22 - 4.01 (m, 3H), 3.99 - 3.91 (m, 1H), 3.87 (s, 3H), 3.72 (ddq, *J* = 10.0, 9.1, 7.1 Hz, 1H), 3.33 (ddd, *J* = 34.4, 17.1, 2.8 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.0 Hz, 3H).

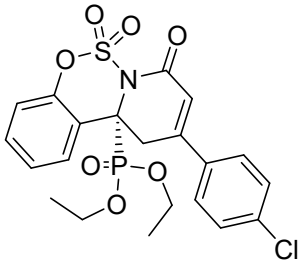
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (s), 161.9 (s), 149.7 (s), 148.4 (d, *J* = 4.6 Hz), 131.3 (d, *J* = 2.7 Hz), 128.2 (s), 128.1 (s), 127.5 (d, *J* = 2.1 Hz), 126.8 (d, *J* = 4.1 Hz), 125.6 (s), 119.7 (d, *J* = 2.3 Hz), 116.4 (s), 114.6 (s), 66.3 (d, *J* = 152.7 Hz), 64.6 (d, *J* = 4.5 Hz), 64.5 (d, *J* = 4.3 Hz), 55.5 (s), 36.2 (s), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.66 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_8NPS$ $[M+H]^+$, 494.1033; found 494.1021.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 30/70, 0.8 mL/min, 254 nm), Rt_1 (major) = 17.0 min, Rt_2 (minor) = 32.9 min; er = 98:2).

Diethyl (*R*)-(10-(4-chlorophenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3d)



White solid, m.p. 116-118 °C, 48 mg, 96% yield.

$[\alpha]_D^{25}$ = -39.8 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (ddd, *J* = 8.2, 5.1, 2.5 Hz, 2H), 7.59 - 7.50 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 8.6 Hz, 2H), 6.34 (d, *J* = 2.8 Hz, 1H), 4.22 - 4.03 (m, 3H), 3.93 (dp, *J* = 10.1, 7.1 Hz, 1H), 3.69 (ddq, *J* = 10.0, 9.2, 7.1 Hz, 1H), 3.36 (ddd, *J* = 34.3, 17.1, 2.8 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.09 (t, *J* = 7.0 Hz, 3H).

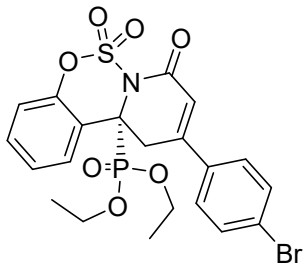
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 252.4 Hz), 162.2 (s), 149.3 (s), 148.3 (d, *J* = 4.6 Hz), 132.3 (d, *J* = 3.3 Hz), 131.4 (d, *J* = 2.7 Hz), 128.8 (s), 128.7 (s), 127.6 (d, *J* = 2.1 Hz), 126.7 (d, *J* = 4.0 Hz), 125.3 (s), 119.8 (d, *J* = 2.2 Hz), 118.3 (s), 116.5 (s), 116.2 (s), 66.4 (d, *J* = 152.3 Hz), 64.7 (dd, *J* = 7.6, 6.7 Hz), 36.5 (d, *J* = 2.0 Hz), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.51 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{22}O_7NClPS$ $[M+H]^+$, 498.0538; found 498.0793.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 20.5 min, Rt_2 (minor) = 41.4 min; er = 98:2).

Diethyl (*R*)-(10-(4-bromophenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3e)



White solid, m.p. 180-182 °C, 49 mg, 91% yield.

$[\alpha]_D^{28}$ = -65.9 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 - 7.59 (m, 2H), 7.58 - 7.48 (m, 4H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 6.37 (d, *J* = 2.8 Hz, 1H), 4.20 - 4.03 (m, 3H), 3.98 - 3.87 (m, 1H), 3.74 - 3.63 (m, 1H), 3.37 (ddd, *J* = 34.2, 17.1, 2.9 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

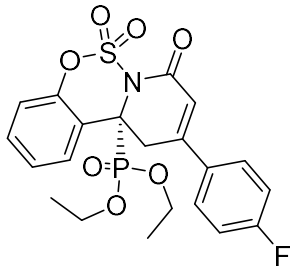
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0 (s), 149.2 (s), 148.4 (d, *J* = 4.6 Hz), 135.1 (s), 132.4 (s), 131.4 (d, *J* = 2.7 Hz), 128.1 (s), 127.6 (d, *J* = 2.2 Hz), 126.6 (d, *J* = 4.1 Hz), 125.4 (s), 125.2 (s), 119.8 (d, *J* = 2.3 Hz), 118.9 (s), 66.4 (d, *J* = 152.3 Hz), 64.7(dd, *J* = 7.9, 5.3 Hz), 36.4 (d, *J* = 2.4 Hz), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.46 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{22}O_7NBrPS$ $[M+H]^+$, 542.0032; found 542.0022.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 24.9 min, Rt_2 (minor) = 54.0 min; er = 99.6:0.4).

Diethyl (*R*)-(10-(4-fluorophenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3f)



White solid, m.p. 132-133 °C, 45 mg, 93% yield.

$[\alpha]_D^{28}$ = -42.9 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 - 7.60 (m, 2H), 7.54 (ddt, *J* = 17.3, 7.9, 1.7 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.33 - 7.28 (m, 1H), 7.21 - 7.13 (m, 2H), 6.35 (d, *J* = 2.8 Hz, 1H), 4.25 - 4.02 (m, 3H), 4.00 - 3.85 (m, 1H), 3.68 (ddq, *J* = 10.0, 9.2, 7.1 Hz, 1H), 3.37 (ddd, *J* = 34.3, 17.1, 2.9 Hz, 1H), 1.25 (dd, *J* = 8.2, 5.9 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 252.4 Hz), 162.2 (s), 149.3 (s), 148.4 (d, *J* = 4.6 Hz), 132.3 (d, *J* = 3.3 Hz), 131.4 (d, *J* = 2.8 Hz), 128.8 (s), 128.7 (s), 127.6 (d, *J* = 2.1 Hz), 126.6 (d, *J* = 4.0 Hz), 125.3 (s), 119.8 (d, *J* = 2.3 Hz), 118.4 (s), 116.5 (s), 116.3 (s), 66.4 (d, *J* = 152.2 Hz), 64.7 (dd, *J* = 7.8, 6.5 Hz), 36.6 (d, *J* = 2.4 Hz), 16.2 (dd, *J* = 20.8, 5.4 Hz).

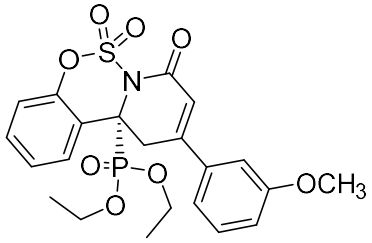
^{19}F NMR (376 MHz, $CDCl_3$) δ -108.90 (s).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.52 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{22}O_7NFPS$ $[M+H]^+$, 482.0833; found 482.0826.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.6 mL/min, 254 nm), Rt_1 (minor) = 29.8 min, Rt_2 (major) = 32.9 min; er = 98:2).

Diethyl (*R*)-(10-(3-methoxyphenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3g)



Colorless oil, 37 mg, 75% yield.

$[\alpha]_D^{25}$ = -43.3 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 - 7.49 (m, 2H), 7.46 - 7.36 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.15 - 7.11 (m, 1H), 7.02 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.39 (d, *J* = 2.8 Hz, 1H), 4.20 - 4.05 (m, 3H), 4.00 - 3.89 (m, 1H), 3.86 (s, 3H), 3.78 - 3.66 (m, 1H), 3.38 (ddd, *J* = 34.3, 17.2, 2.9 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

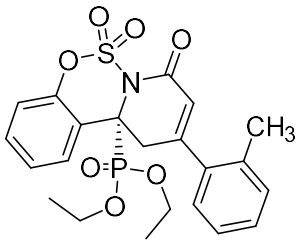
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 160.1 (s), 150.2 (s), 148.4 (d, *J* = 4.6 Hz), 137.5 (s), 131.3 (d, *J* = 2.8 Hz), 130.2 (s), 127.5 (d, *J* = 2.2 Hz), 126.8 (d, *J* = 4.0 Hz), 125.4 (s), 119.8 (d, *J* = 2.4 Hz), 119.0 (s), 118.6 (s), 116.3 (s), 112.2 (s), 66.4 (d, *J* = 152.8 Hz), 64.7 (d, *J* = 4.9 Hz), 64.6 (d, *J* = 4.8 Hz), 55.5 (s), 36.5 (d, *J* = 2.3 Hz), 16.2 (dd, *J* = 20.1, 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.53 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_8NPS$ $[M+H]^+$, 494.1033; found 494.1022.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 34.0 min, Rt_2 (minor) = 57.6 min; er = 98:2).

Diethyl (*R*)-(6,6-dioxido-8-oxo-10-(o-tolyl)-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3h)



Colorless oil, 31 mg, 65% yield.

$[\alpha]_D^{28}$ = -41.4 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.7 Hz, 1H), 7.48 - 7.42 (m, 2H), 7.42 - 7.36 (m, 1H), 7.35 - 7.27 (m, 4H), 6.10 (d, *J* = 2.8 Hz, 1H), 4.30 - 4.16 (m, 2H), 3.92 (ddd, *J* = 17.3, 10.7, 5.9 Hz, 2H), 3.74 - 3.63 (m, 1H), 3.43 (ddd, *J* = 34.4, 17.5, 2.9 Hz, 1H), 2.40 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.10 (t, *J* = 7.0 Hz, 3H).

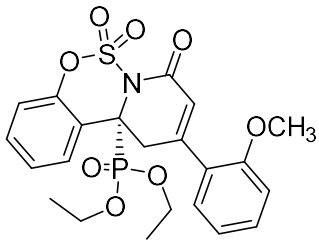
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0 (s), 151.8 (s), 148.3 (d, *J* = 4.6 Hz), 137.4 (s), 134.9 (s), 131.3 (d, *J* = 2.8 Hz), 131.1 (s), 129.4 (s), 127.8 (s), 127.5 (s), 126.7 (d, *J* = 4.0 Hz), 126.4(s), 125.3 (s), 122.0 (s), 119.8 (d, *J* = 2.3 Hz), 66.4 (d, *J* = 152.9 Hz), 64.9 (d, *J* = 8.2 Hz), 64.7 (d, *J* = 7.7 Hz), 39.1 (s), 20.2 (s), 16.4 (d, *J* = 5.6 Hz), 16.2 (d, *J* = 5.2 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.39 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_7NPS$ $[M+H]^+$, 478.1084; found 478.1077.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 15.8 min, Rt_2 (major) = 25.3 min; er = 98:2).

Diethyl (*R*)-(10-(2-methoxyphenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3i)



Colorless, oil, 22 mg, 44% yield.

$[\alpha]_D^{27}$= 7.1 (*c* 0.5 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 - 7.46 (m, 2H), 7.45 - 7.36 (m, 3H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.03 (td, *J* = 7.6, 0.8 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.33 (d, *J* = 2.8 Hz, 1H), 4.25 - 4.09 (m, 2H), 4.04 (dd, *J* = 17.4, 8.4 Hz, 1H), 3.98 - 3.90 (m, 1H), 3.89 (s, 3H), 3.80 - 3.67 (m, 1H), 3.56 (ddd, *J* = 35.0, 17.4, 2.8 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

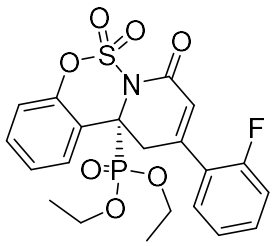
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 157.0 (s), 150.1 (s), 148.3 (d, *J* = 4.5 Hz), 131.5 (s), 131.2 (d, *J* = 2.8 Hz), 129.2 (s), 127.5 (d, *J* = 2.2 Hz), 127.0 (d, *J* = 4.0 Hz), 126.2 (s), 125.7 (s), 121.0 (d, *J* = 14.0 Hz), 120.8 (s), 119.6 (d, *J* = 2.4 Hz), 111.3 (s), 66.3 (d, *J* = 153.8 Hz), 64.5 (d, *J* = 3.8 Hz), 64.4 (d, *J* = 3.6 Hz), 55.5 (s), 37.5 (d, *J* = 2.0 Hz), 16.3 (dd, *J* = 21.4, 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.55 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_8NPS$ $[M+H]^+$, 494.1033; found 494.1021.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 17.0 min, Rt_2 (major) = 32.4 min; er = 97:3).

Diethyl (*R*)-(10-(2-fluorophenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3j)



Colorless oil, 28 mg, 58% yield.

$[\alpha]_D^{28}$ = 17.5 (*c* 0.5 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 - 7.49 (m, 3H), 7.48 - 7.40 (m, 2H), 7.32 - 7.23 (m, 2H), 7.21 - 7.14 (m, 1H), 6.41 (d, *J* = 2.8 Hz, 1H), 4.24 - 4.10 (m, 2H), 4.02 (dd, *J* = 17.2, 8.2 Hz, 1H), 3.97 - 3.88 (m, 1H), 3.79 - 3.67 (m, 1H), 3.55 (ddt, *J* = 34.4, 17.2, 2.5 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (s), 160.1 (d, *J* = 252.1 Hz), 148.3 (d, *J* = 4.6 Hz), 146.1 (s), 132.1 (d, *J* = 8.7 Hz), 131.4 (d, *J* = 2.8 Hz), 129.1 (d, *J* = 2.9 Hz), 127.6 (d, *J* = 2.2 Hz), 126.8 (d, *J* = 4.0 Hz), 125.3 (s), 124.9 (d, *J* = 3.6 Hz), 124.7 (d, *J* = 12.3 Hz), 122.0 (d, *J* = 4.7 Hz), 119.8 (d, *J* = 2.3 Hz), 116.7 (d, *J* = 22.2 Hz), 66.3 (d, *J* = 154.1 Hz), 64.7 (d, *J* = 8.0 Hz), 64.6 (d, *J* = 7.7 Hz), 37.1 (s), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.3 Hz).

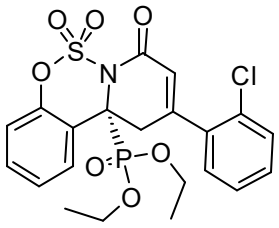
^{19}F NMR (376 MHz, $CDCl_3$) δ -111.92 – -112.00 (m).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.29 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{23}O_7NFPS$ $[M+H]^+$, 482.0833; found 482.0824.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 17.7 min, Rt_2 (major) = 31.6 min; er = 99:1).

Diethyl (*R*)-(10-(2-chlorophenyl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3k)



White solid, m.p. 142-144°C, 44 mg, 88% yield.

$[\alpha]_D^{27}$ = 0.12 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (ddd, *J* = 12.1, 6.3, 1.6 Hz, 2H), 7.48 - 7.43 (m, 2H), 7.43 - 7.38 (m, 1H), 7.37 (dd, *J* = 5.9, 3.5 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 4.31 - 4.18 (m, 2H), 3.96 - 3.80 (m, 2H), 3.76 - 3.58 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H).

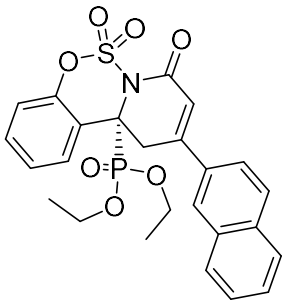
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7 (s), 149.6 (s), 148.3 (d, *J* = 4.5 Hz), 136.8 (s), 131.6 (s), 131.4 (d, *J* = 2.7 Hz), 130.7 (s), 130.3 (s), 129.9 (s), 127.6 (s), 127.4 (s), 126.7 (d, *J* = 4.0 Hz), 125.3 (s), 123.2 (s), 119.8 (d, *J* = 2.3 Hz), 66.6 (d, *J* = 152.9 Hz), 64.8 (d, *J* = 8.1 Hz), 64.6 (d, *J* = 7.7 Hz), 38.2 (s), 16.4 (d, *J* = 5.6 Hz), 16.1 (d, *J* = 5.2 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.19 (s).

HRMS (ESI, m/z): Mass calcd for $C_{21}H_{23}O_7NClPS$ $[M+H]^+$, 498.0538; found 498.0526.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 14.6 min, Rt_2 (major) = 25.2 min; er = 98:2).

Diethyl (*R*)-(10-(naphthalen-2-yl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3l)



White solid, m.p. 182-183 °C, 36 mg, 70% yield.

$[\alpha]_D^{27}$ = -17.7 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.93 (dd, *J* = 9.0, 6.3 Hz, 2H), 7.90 - 7.84 (m, 1H), 7.71 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.65 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.60 - 7.51 (m, 3H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 6.54 (d, *J* = 2.7 Hz, 1H), 4.33 (dd, *J* = 17.1, 8.2 Hz, 1H), 4.20 - 4.01 (m, 2H), 3.96 (dp, *J* = 10.0, 7.2 Hz, 1H), 3.81 - 3.66 (m, 1H), 3.45 (ddd, *J* = 34.3, 17.1, 2.7 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

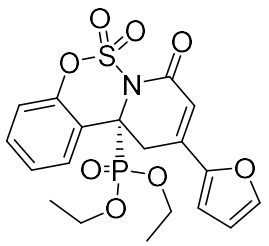
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 150.0 (s), 148.4 (d, *J* = 4.6 Hz), 134.3 (s), 133.2 (s), 133.1 (s), 131.4 (s), 131.3 (s), 129.1 (s), 128.8 (s), 127.8 (s), 127.6 (d, *J* = 2.2 Hz), 127.1 (s), 126.9 (s), 126.8 (s), 125.5 (s), 123.3 (s), 119.8 (d, *J* = 2.2 Hz), 118.7 (s), 66.4 (d, *J* = 152.8 Hz), 64.7 (d, *J* = 3.5 Hz), 64.6 (d, *J* = 3.3 Hz), 36.3 (d, *J* = 2.2 Hz), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.62 (s).

HRMS (ESI, m/z): Mass calcd for $C_{25}H_{25}O_7NPS$ $[M+H]^+$, 514.1084; found 514.1075.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 22.8 min, Rt_2 (major) = 45.5 min; er = 99.2:0.8).

Diethyl (*R*)-(10-(furan-2-yl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e]pyrido [1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3m)



Colorless oil, 23 mg, 51% yield.

$[\alpha]_D^{27}$ = -0.13 (*c* 0.5 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 1.7 Hz, 1H), 7.58 - 7.48 (m, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 3.5 Hz, 1H), 6.58 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.47 (d, *J* = 2.7 Hz, 1H), 4.18 - 3.99 (m, 3H), 3.98 - 3.89 (m, 1H), 3.79 - 3.68 (m, 1H), 3.30 (ddd, *J* = 33.9, 16.8, 2.7 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H).

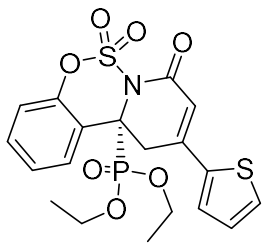
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 149.7 (s), 148.3 (s), 146.1 (s), 137.6 (s), 131.3 (s), 127.5 (s), 126.7 (d, *J* = 4.0 Hz), 125.4 (s), 119.8 (s), 113.8 (s), 113.7 (s), 112.8 (s), 66.2 (d, *J* = 153.2 Hz), 64.7 (d, *J* = 2.9 Hz), 64.6 (d, *J* = 2.6 Hz), 33.6 (s), 16.2 (d, *J* = 5.7 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.22 (s).

HRMS (ESI, m/z): Mass calcd for $C_{19}H_{21}O_8NPS$ $[M+H]^+$, 454.0720; found 454.0709.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 26.1 min, Rt_2 (major) = 27.5 min; er = 99:1).

Diethyl (*R*)-(6,6-dioxido-8-oxo-10-(thiophen-2-yl)-8,11-dihydro-11a*H*-benzo[e]pyrido [1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3n)



White solid, m.p. 138-139 °C, 34 mg, 72% yield.

$[\alpha]_D^{28}$ = -26.0 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 - 7.55 (m, 1H), 7.55 - 7.49 (m, 3H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.32 - 7.27 (m, 1H), 7.16 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.40 (d, *J* = 2.7 Hz, 1H), 4.19 - 4.03 (m, 3H), 4.01 - 3.90 (m, 1H), 3.75 (ddd, *J* = 10.0, 9.1, 7.1 Hz, 1H), 3.40 (ddd, *J* = 33.8, 16.9, 2.7 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H).

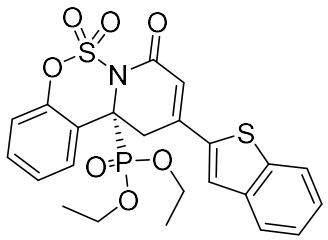
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (s), 148.3 (d, *J* = 4.6 Hz), 143.0 (s), 139.5 (s), 131.3 (d, *J* = 2.7 Hz), 130.0 (s), 128.7 (s), 128.5 (s), 127.5 (d, *J* = 2.2 Hz), 126.7 (d, *J* = 4.0 Hz), 125.3 (s), 119.8 (d, *J* = 2.3 Hz), 115.4 (s), 66.2 (d, *J* = 153.2 Hz), 64.7 (d, *J* = 3.8 Hz), 64.6 (d, *J* = 3.7 Hz), 36.3 (s), 01 MHz, $CDCl_3$) δ 64.7 (d, *J* = 3.8 Hz), 64.6 (d, *J* = 3.7 Hz),

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.32 (s).

HRMS (ESI, m/z): Mass calcd for $C_{23}H_{23}O_7NPS_2$ $[M+H]^+$, 520.0648; found 520.0636.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 28.7 min, Rt_2 (major) = 47.7 min; er = 98:2).

Diethyl (*R*)-(10-(benzo[b]thiophen-2-yl)-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3o)



White solid, m.p. 178-180 °C, 40 mg, 77% yield.

$[\alpha]_D^{28}$ = -11.3 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 6.6, 1.9 Hz, 2H), 7.76 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.50 - 7.38 (m, 3H), 7.30 (d, *J* = 7.8 Hz, 1H), 6.46 (d, *J* = 2.6 Hz, 1H), 4.26 (dd, *J* = 16.8, 8.3 Hz, 1H), 4.17 - 4.03 (m, 2H), 4.00 - 3.91 (m, 1H), 3.80 - 3.69 (m, 1H), 3.43 (ddd, *J* = 33.8, 16.8, 2.7 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

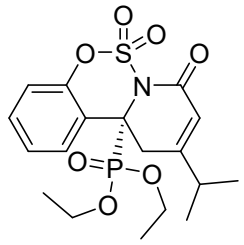
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (s), 148.3 (d, *J* = 4.6 Hz), 143.1 (s), 140.5 (s), 139.6 (s), 139.1 (s), 131.4 (d, *J* = 2.7 Hz), 127.6 (d, *J* = 2.1 Hz), 126.9 (s), 126.8 (d, *J* = 4.0 Hz), 126.2 (s), 125.2 (s), 125.2 (s), 124.9 (s), 122.5 (s), 119.8 (d, *J* = 2.2 Hz), 117.6 (s), 66.2 (d, *J* = 153.3 Hz), 64.8 (d, *J* = 3.5 Hz), 64.7 (d, *J* = 3.6 Hz), 35.6 (s), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.25 (s).

HRMS (ESI, m/z): Mass calcd for $C_{19}H_{21}O_7NPS_2$ $[M+H]^+$, 470.0492; found 470.0482.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 29.9 min, Rt_2 (major) = 36.8 min; er = 99.2:0.8).

Diethyl (*R*)-(10-isopropyl-6,6-dioxido-8-oxo-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3p)



Colorless oil, 23 mg, 53% yield.

$[\alpha]_D^{28}$ = -65.3 (*c* 0.5 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (ddd, *J* = 6.7, 6.2, 5.1 Hz, 2H), 7.42 (d, *J* = 7.1 Hz, 1H), 7.26 - 7.28 (m, 1H), 5.98 - 5.87 (m, 1H), 4.25 - 4.05 (m, 2H), 3.96 - 3.82 (m, 1H), 3.73 - 3.55 (m, 2H), 3.08 (ddd, *J* = 34.5, 17.1, 2.7 Hz, 1H), 2.51 - 2.81 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 6.6 Hz, 6H), 1.10 (t, *J* = 7.1 Hz, 3H).

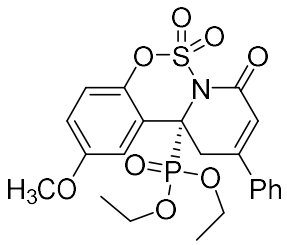
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (s), 160.3 (s), 148.3 (d, *J* = 4.6 Hz), 131.2 (d, *J* = 2.8 Hz), 127.4 (d, *J* = 2.2 Hz), 126.8 (d, *J* = 4.0 Hz), 125.6 (s), 119.7 (d, *J* = 2.4 Hz), 116.9 (s), 66.1 (d, *J* = 153.0 Hz), 64.6 (d, *J* = 6.1 Hz), 64.5 (d, *J* = 5.7 Hz), 36.0 (d, *J* = 2.3 Hz), 34.8 (s), 20.1 (s), 19.8 (s), 16.3 (d, *J* = 5.6 Hz), 16.1 (d, *J* = 5.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.37 (s).

HRMS (ESI, m/z): Mass calcd for $C_{18}H_{25}O_7NPS$ $[M+H]^+$, 430.1084; found 430.1075.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 13.4 min, Rt_2 (major) = 14.2 min; er = 97:3).

Diethyl (*R*)-(2-methoxy-6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3q)



White solid, m.p. 44-47 °C, 32 mg, 65% yield.

$[\alpha]_D^{28}$ = -5.7 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 - 7.60 (m, 2H), 7.48 (dd, *J* = 4.1, 2.4 Hz, 3H), 7.23 (d, *J* = 8.9 Hz, 1H), 7.04 (t, *J* = 2.5 Hz, 1H), 7.01 - 6.96 (m, 1H), 6.38 (d, *J* = 2.9 Hz, 1H), 4.21 - 4.02 (m, 3H), 4.01 - 3.93 (m, 1H), 3.86 (s, 3H), 3.80 - 3.71 (m, 1H), 3.38 (ddd, *J* = 34.3, 17.1, 2.9 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H).

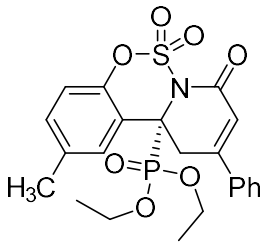
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (s), 158.3 (s), 150.0 (s), 142.2 - 141.4 (m), 136.2 (s), 130.8 (s), 129.2 (s), 126.6 (s), 126.5 (s), 120.6 (s), 118.5 (s), 115.4 (s), 113.0 (s), 66.3 (d, *J* = 152.9 Hz), 64.7 (dd, *J* = 7.4, 5.9 Hz), 56.0 (s), 36.3 (s), 16.3 (d, *J* = 5.2 Hz), 16.2 (d, *J* = 5.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.46 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_8NPS$ $[M+H]^+$, 494.1033; found 494.1024.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 21.5 min, Rt_2 (major) = 22.5 min; er = 99.4:0.6).

Diethyl (*R*)-(2-methyl-6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3r)



White solid, m.p. 139-141 °C, 45 mg, 94% yield.

$[\alpha]_D^{28}$ = -51.5 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 - 7.61 (m, 2H), 7.49 (dd, *J* = 4.0, 2.5 Hz, 3H), 7.36 - 7.28 (m, 2H), 7.17 (d, *J* = 8.2 Hz, 1H), 6.39 (d, *J* = 2.9 Hz, 1H), 4.25 - 4.03 (m, 3H), 4.00 - 3.87 (m, 1H), 3.80 - 3.62 (m, 1H), 3.36 (ddd, *J* = 34.5, 17.2, 2.9 Hz, 1H), 2.44 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

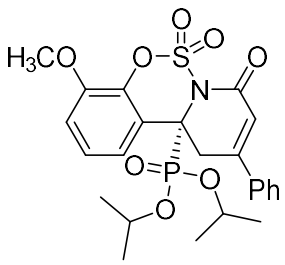
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (s), 150.4(s), 146.3 (d, *J* = 4.6 Hz), 137.7 (d, *J* = 2.2 Hz), 136.2 (s), 131.9 (d, *J* = 2.8 Hz), 130.8 (s), 129.2 (s), 127.0 (d, *J* = 4.1 Hz), 126.6 (s), 125.0 (s), 119.4 (d, *J* = 2.4 Hz), 118.4 (s), 66.3 (d, *J* = 152.5 Hz), 64.6 (dd, *J* = 7.7, 6.6 Hz), 36.3 (d, *J* = 2.3 Hz), 21.3 (s), 16.3 (d, *J* = 5.5 Hz), 16.1 (d, *J* = 5.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.67 (s).

HRMS (ESI, m/z): Mass calcd for $C_{22}H_{25}O_7NPS$ $[M+H]^+$, 478.1084; found 478.1075.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 14.8 min, Rt_2 (minor) = 28.0 min; er = 99:1).

Diisopropyl (*R*)-(4-methoxy-6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3s)



White solid, m.p. 181-183 °C, 48 mg, 92% yield.

$[\alpha]_D^{28}$ = -2.4 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 - 7.60 (m, 2H), 7.48 (dd, *J* = 6.7, 3.6 Hz, 3H), 7.34 (t, *J* = 8.2 Hz, 1H), 7.09 (dd, *J* = 10.2, 5.2 Hz, 2H), 6.36 (d, *J* = 2.9 Hz, 1H), 4.68 (dd, *J* = 12.5, 6.3 Hz, 1H), 4.33 (dd, *J* = 12.4, 6.2 Hz, 1H), 4.20 - 4.11 (m, 1H), 3.94 (s, 3H), 3.35 (ddd, *J* = 34.6, 17.0, 2.9 Hz, 1H), 1.31 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.20 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.2 Hz, 3H).

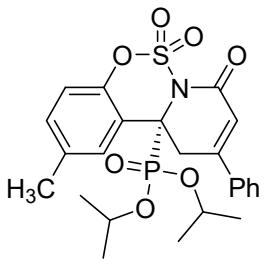
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (s), 150.2 (s), 150.0 (d, *J* = 2.4 Hz), 137.8 (d, *J* = 4.7 Hz), 136.4 (s), 130.6 (s), 129.1 (s), 127.5 (d, *J* = 2.1 Hz), 127.3 (s), 126.6 (s), 118.8 (s), 117.3 (d, *J* = 3.9 Hz), 113.9 (d, *J* = 2.5 Hz), 74.0 (d, *J* = 8.1 Hz), 73.7 (d, *J* = 8.6 Hz), 66.8 (d, *J* = 152.6 Hz), 56.6 (s), 36.6 (s), 24.4 (d, *J* = 2.7 Hz), 23.9 (d, *J* = 2.2 Hz), 23.9 (d, *J* = 0.4 Hz)., 22.6 (d, *J* = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 15.63 (s).

HRMS (ESI, m/z): Mass calcd for $C_{24}H_{29}O_8NPS$ $[M+H]^+$, 522.1346; found 522.1340.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 17.4 min, Rt_2 (major) = 20.1 min; er = 99:1).

Diisopropyl (*R*)-(2-methyl-6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e] pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3t)



Colorless oil, 47 mg, 94% yield.

$[\alpha]_D^{28}$ = -9.3 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, cdcl$_3$) δ 7.69 - 7.58 (m, 2H), 7.53 - 7.43 (m, 3H), 7.35 - 7.27 (m, 2H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.36 (d, *J* = 2.9 Hz, 1H), 4.65 (dq, *J* = 12.5, 6.2 Hz, 1H), 4.34 (dq, *J* = 12.4, 6.2 Hz, 1H), 4.17 (dd, *J* = 17.1, 8.3 Hz, 1H), 3.33 (ddd, *J* = 34.5, 17.1, 2.9 Hz, 1H), 2.43 (s, 3H), 1.31 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.2 Hz, 3H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.82 (d, *J* = 6.2 Hz, 3H).

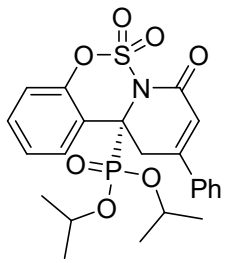
^{13}C NMR (101 MHz, cdcl$_3$) δ 162.6 (s), 150.2 (s), 146.2 (s), 137.5 (s), 136.4 (s), 131.6 (d, *J* = 2.9 Hz), 130.6 (s), 129.1 (s), 126.9 (d, *J* = 4.0 Hz), 126.6 (s), 125.3 (s), 119.5 (d, *J* = 2.4 Hz), 118.8 (s), 74.0 (d, *J* = 8.3 Hz), 73.7 (d, *J* = 8.6 Hz), 66.6 (d, *J* = 153.1 Hz), 36.7 (s), 24.31 (d, *J* = 2.8 Hz), 23.9 (s), 23.8 (d, *J* = 2.3 Hz), 22.7 (d, *J* = 6.3 Hz), 21.2 (s)..

^{31}P NMR (162 MHz, $CDCl_3$) δ 15.72 (s).

HRMS (ESI, m/z): Mass calcd for $C_{24}H_{29}O_7NPS$ $[M+H]^+$, 506.1397; found 506.1394.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; IPA/hexanes = 20/80, 0.8 mL/min, 254 nm), Rt_1 (major) = 9.3 min, Rt_2 (minor) = 18.1 min; er = 99:1).

Diisopropyl (*R*)-(6,6-dioxido-8-oxo-10-phenyl-8,11-dihydro-11a*H*-benzo[e]pyrido [1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (3u)



White solid, m.p. 115-117 ^oC, 37 mg, 75% yield.

$[\alpha]_D^{28}$ = -34.4 (*c* 1.0 $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 2H), 7.57 - 7.42 (m, 6H), 7.29 (d, *J* = 7.8 Hz, 1H), 6.37 (s, 1H), 4.67 (d, *J* = 6.1 Hz, 1H), 4.37 (dd, *J* = 12.1, 6.0 Hz, 1H), 4.18 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.36 (dd, *J* = 34.0, 16.8 Hz, 1H), 1.31 (d, *J* = 5.8 Hz, 3H), 1.24 (d, *J* = 5.8 Hz, 3H), 1.18 (d, *J* = 5.8 Hz, 3H), 0.82 (d, *J* = 5.8 Hz, 3H).

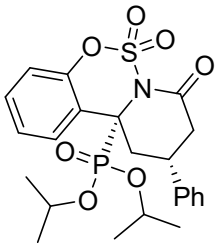
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5 (s), 150.2 (s), 148.5 (d, *J* = 4.4 Hz), 136.3 (s), 131.2 (s), 130.7 (s), 129.1 (s), 127.4 (s), 126.6 (s), 126.5 (s), 125.8 (s), 119.8 (s), 118.8 (s), 74.0 (d, *J* = 8.1 Hz), 73.8 (d, *J* = 8.5 Hz), 66.6 (d, *J* = 153.4 Hz), 36.7 (s), 24.3 (s), 23.9 (d, *J* = 3.6 Hz), 23.8 (d, *J* = 5.1 Hz), 22.8 (d, *J* = 6.2 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 15.59 (dd, *J* = 34.3, 6.8 Hz).

HRMS (ESI, m/z): Mass calcd for $C_{23}H_{27}O_7NPS$ $[M+H]^+$, 492.1240; found 492.1235.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 14.7 min, Rt_2 (major) = 18.4 min; er = 99.2:0.8).

Diisopropyl ((10*R*,11a*R*)-6,6-dioxido-8-oxo-10-phenyl-8,9,10,11-tetrahydro-11a*H*-benzo[e]pyrido[1,2-c][1,2,3]oxathiazin-11a-yl)phosphonate (5)



White solid, m.p.162-164 °C, 120 mg, 92% yield.

$[\alpha]_D^{28}$ = 10.9 (*c* 1.0 $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 - 7.49 (m, 1H), 7.46 - 7.30 (m, 6H), 7.26 - 7.22 (m, 2H), 4.75 (ddd, *J* = 19.2, 12.6, 6.3 Hz, 2H), 3.13 (ddd, *J* = 14.7, 6.4, 3.1 Hz, 1H), 3.05 - 2.90 (m, 2H), 2.90 - 2.83 (m, 1H), 2.83 - 2.68 (m, 1H), 1.32 (dd, *J* = 6.1, 4.9 Hz, 6H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.18 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7 (s), 150.0 (d, *J* = 4.5 Hz), 140.7 (s), 131.3 (d, *J* = 2.7 Hz), 129.3 (s), 127.8 (s), 127.3 (s), 126.6 (s), 125.8 (d, *J* = 5.3 Hz), 125.7 (d, *J* = 2.0 Hz), 120.5 (d, *J* = 2.4 Hz), 74.3 (d, *J* = 7.7 Hz), 73.6 (d, *J* = 8.0 Hz), 67.2 (d, *J* = 159.6 Hz), 41.77 (s), 36.6 (s), 34.2 (d, *J* = 7.1 Hz), 24.3 (d, *J* = 2.8 Hz), 24.0 (d, *J* = 3.7 Hz), 23.8 (d, *J* = 5.3 Hz), 23.3 (d, *J* = 5.9 Hz).

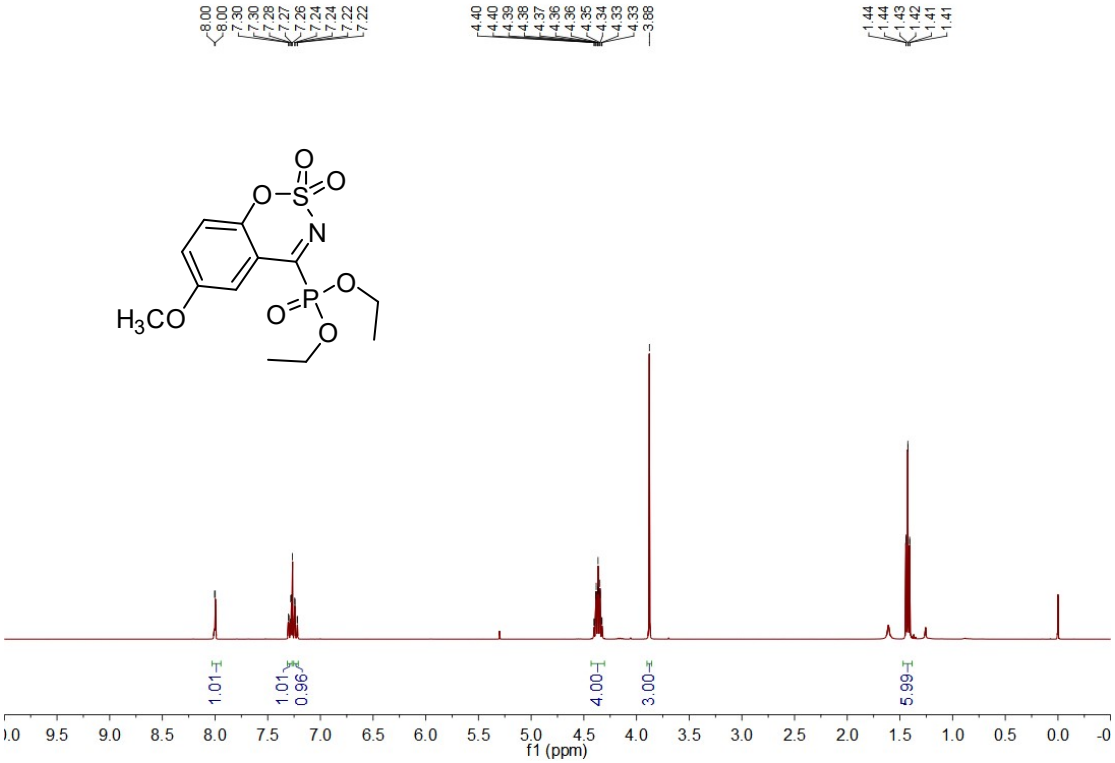
^{31}P NMR (162 MHz, $CDCl_3$) δ 14.78 (s).

HRMS (ESI, m/z): Mass calcd for $C_{23}H_{29}O_7NPS$ $[M+H]^+$, 494.1397; found 494.1390.

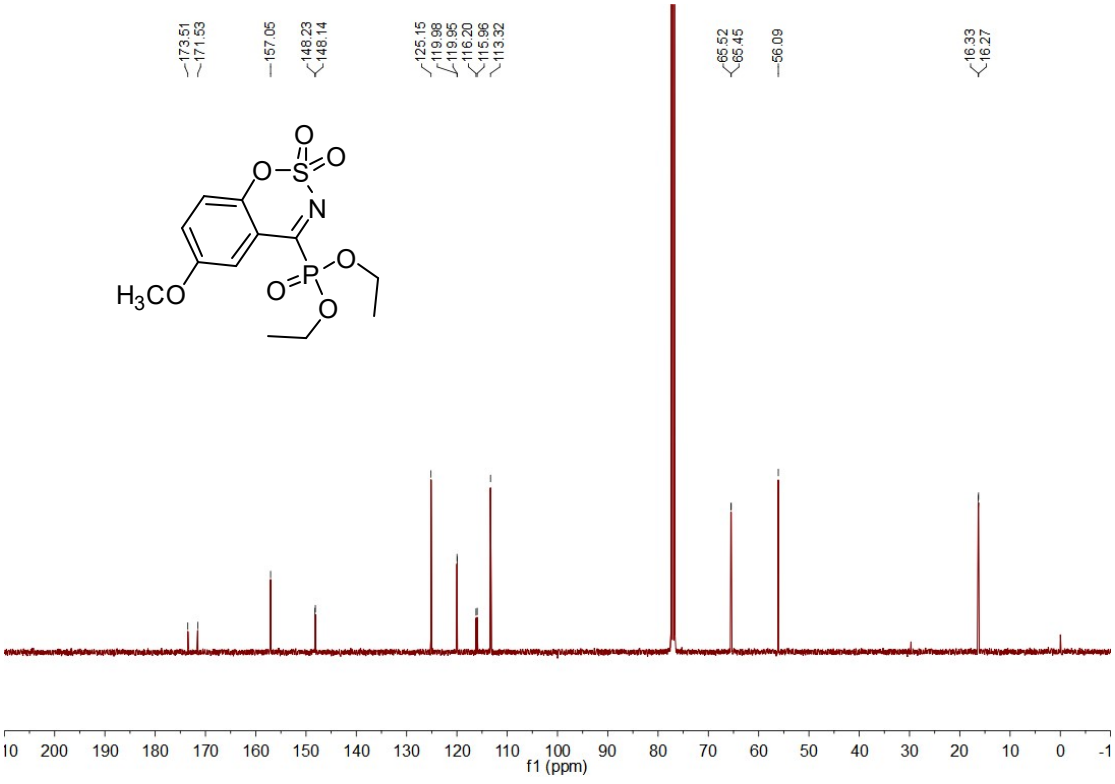
Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; IPA/hexanes = 30/70, 0.4 mL/min, 254 nm), Rt_1 (minor) = 15.7 min, Rt_2 (major) = 17.5 min; er = 98.5:1.5).

Ⅸ. NMR spectra of intermediates & products

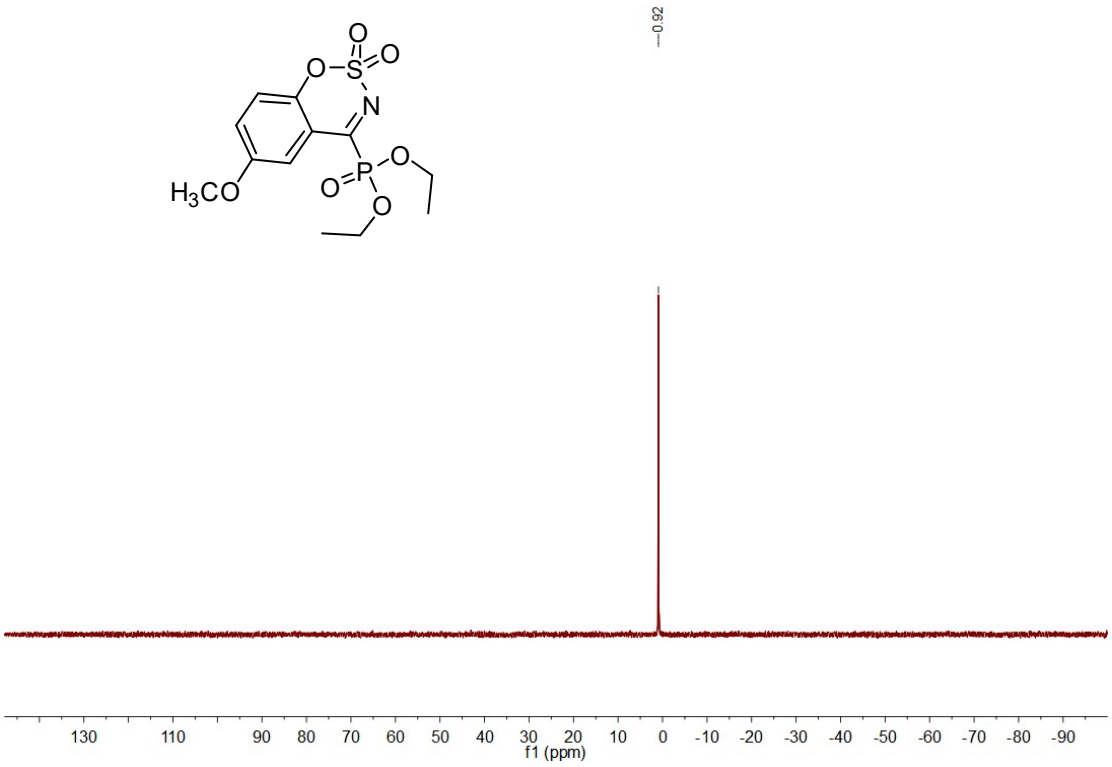
2q: **^{1}H NMR**



^{13}C NMR



^{31}P NMR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110
90
80
70
60
50
40
30
20
10
0
-10
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-30
-40
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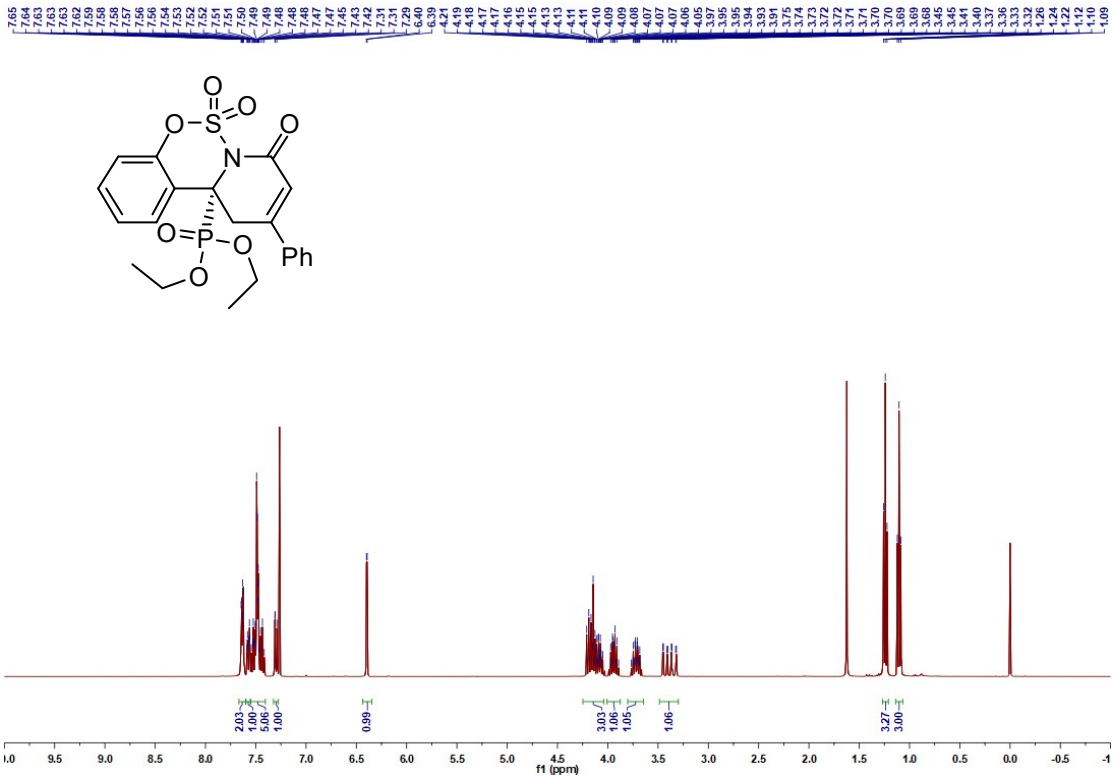
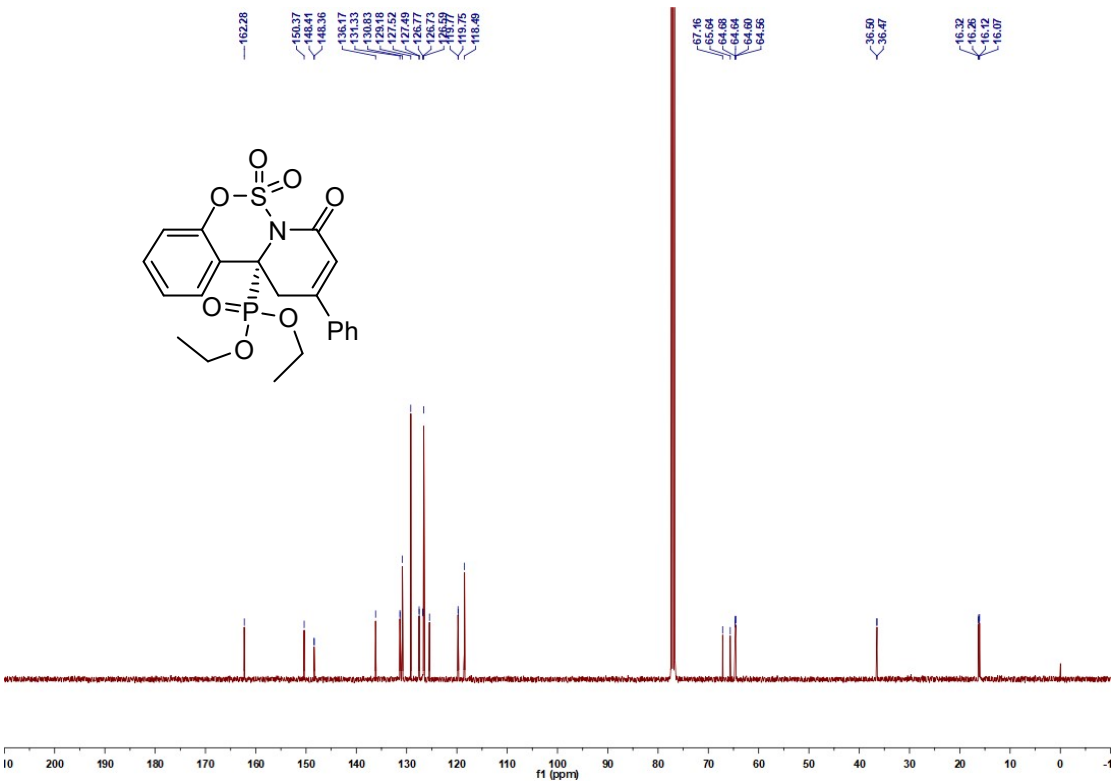
-70
-80
-90
f1 (ppm)

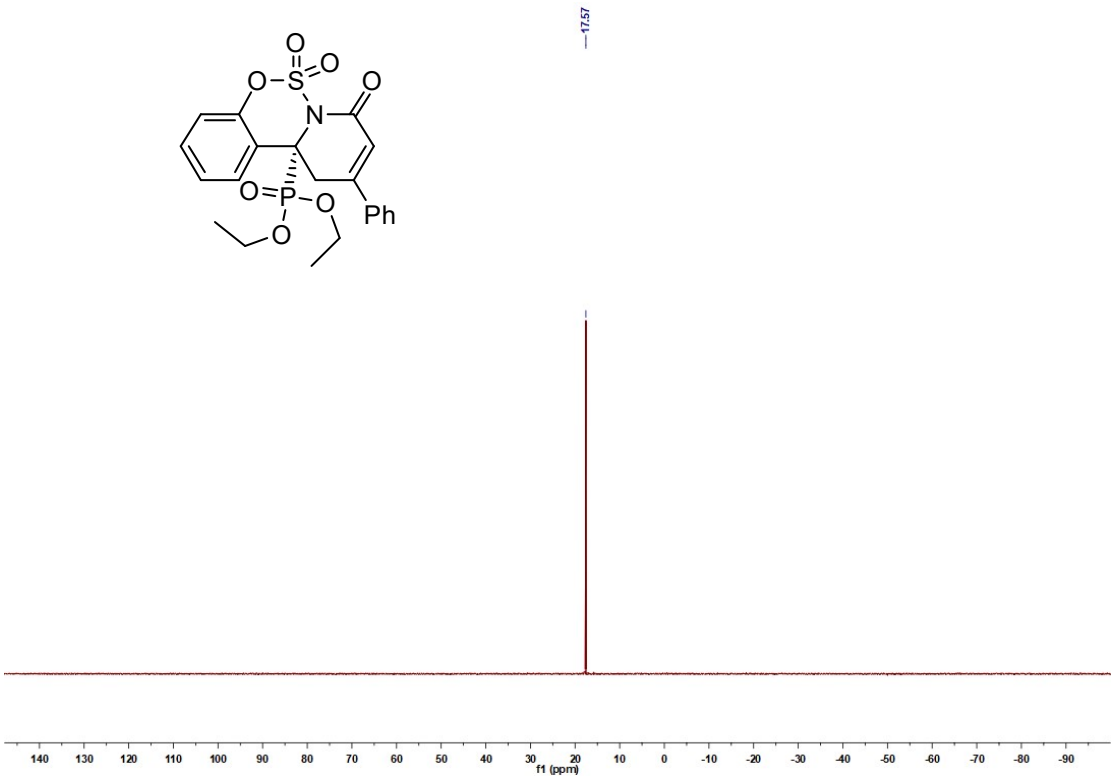
3a: ^{1}H NMR



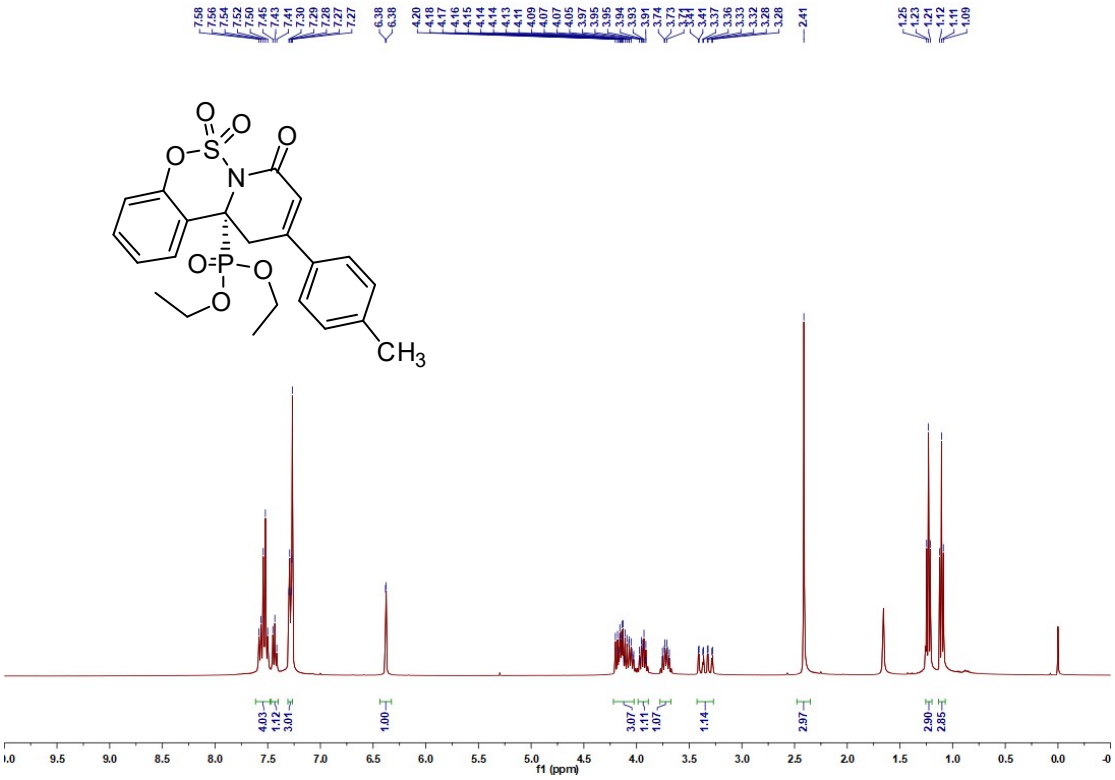
^{13}C NMR



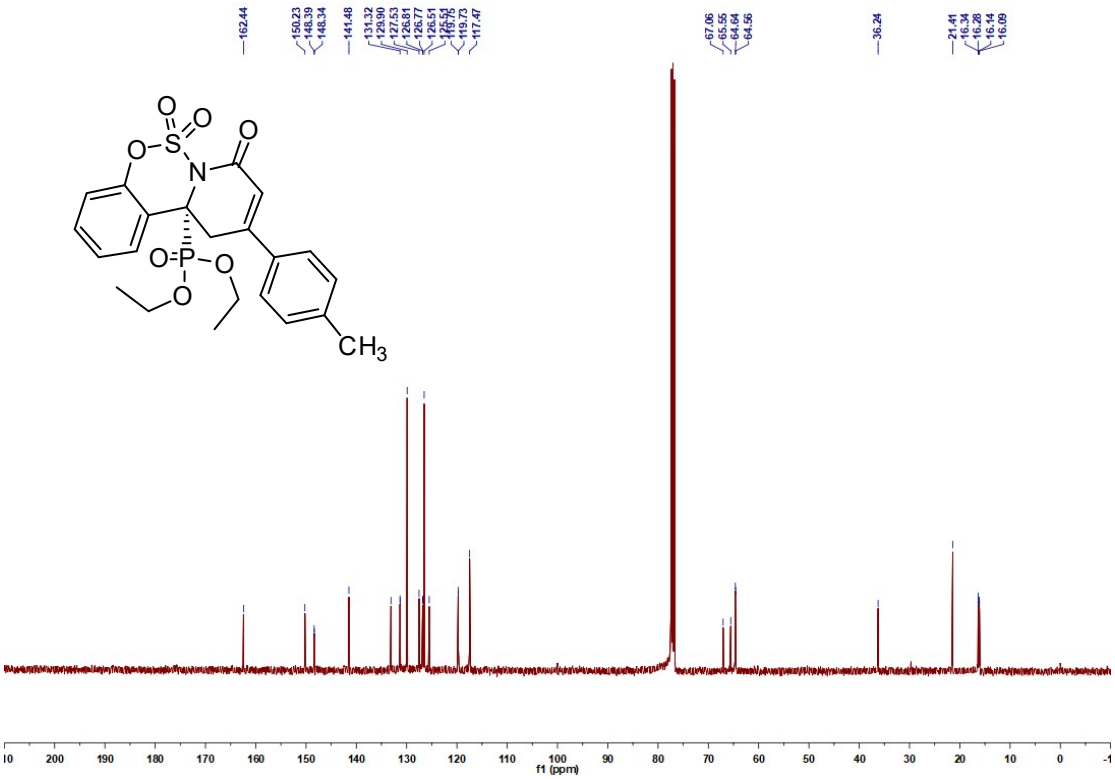
^{31}P NMR


17.57
O
O
O
S
O
N
O
O
P
O
O
Ph
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

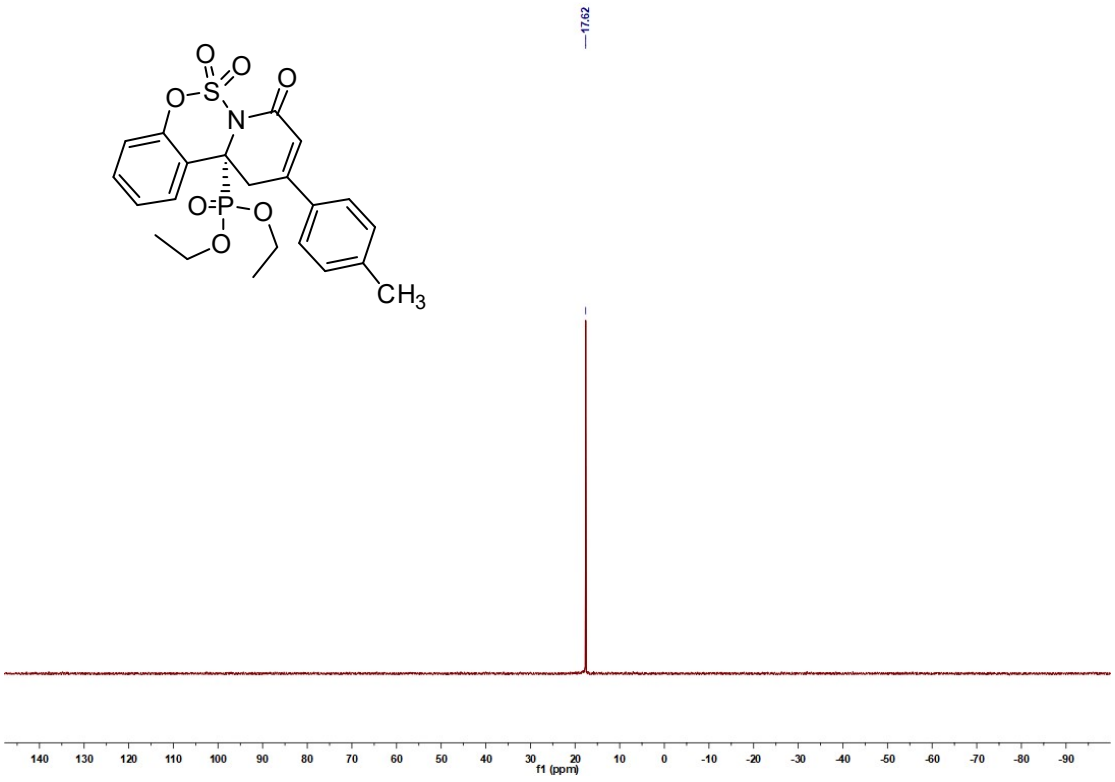
3b: ^{1}H NMR



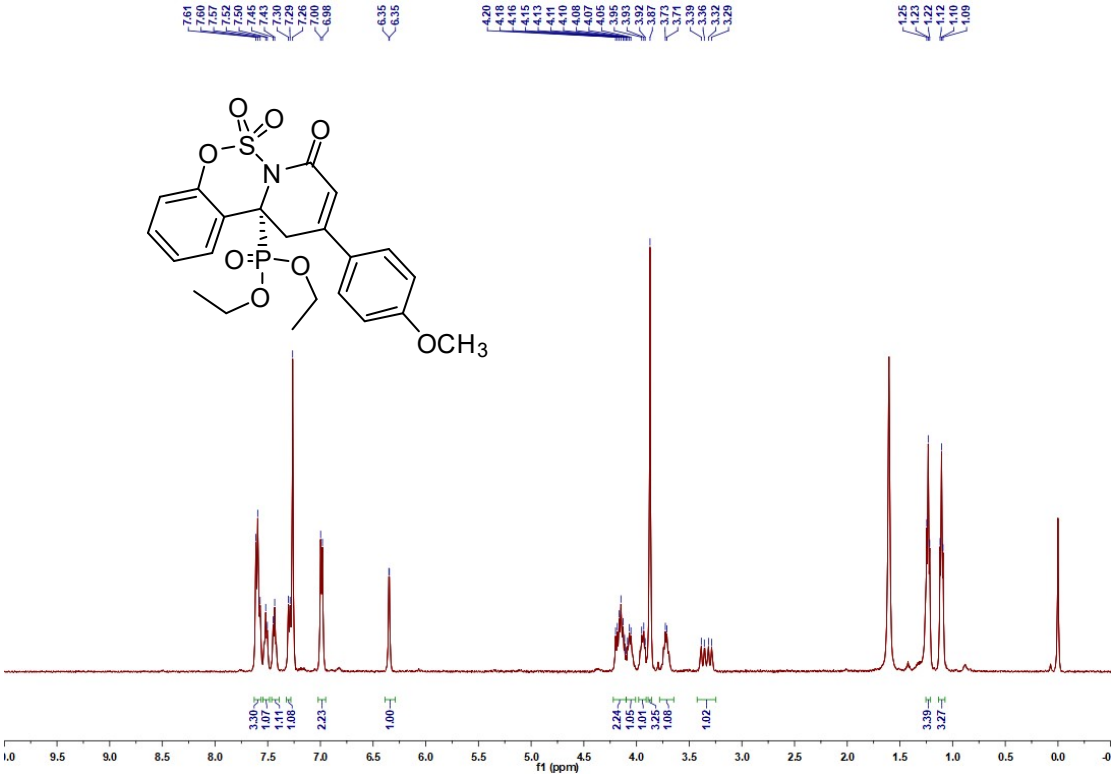
^{13}C NMR



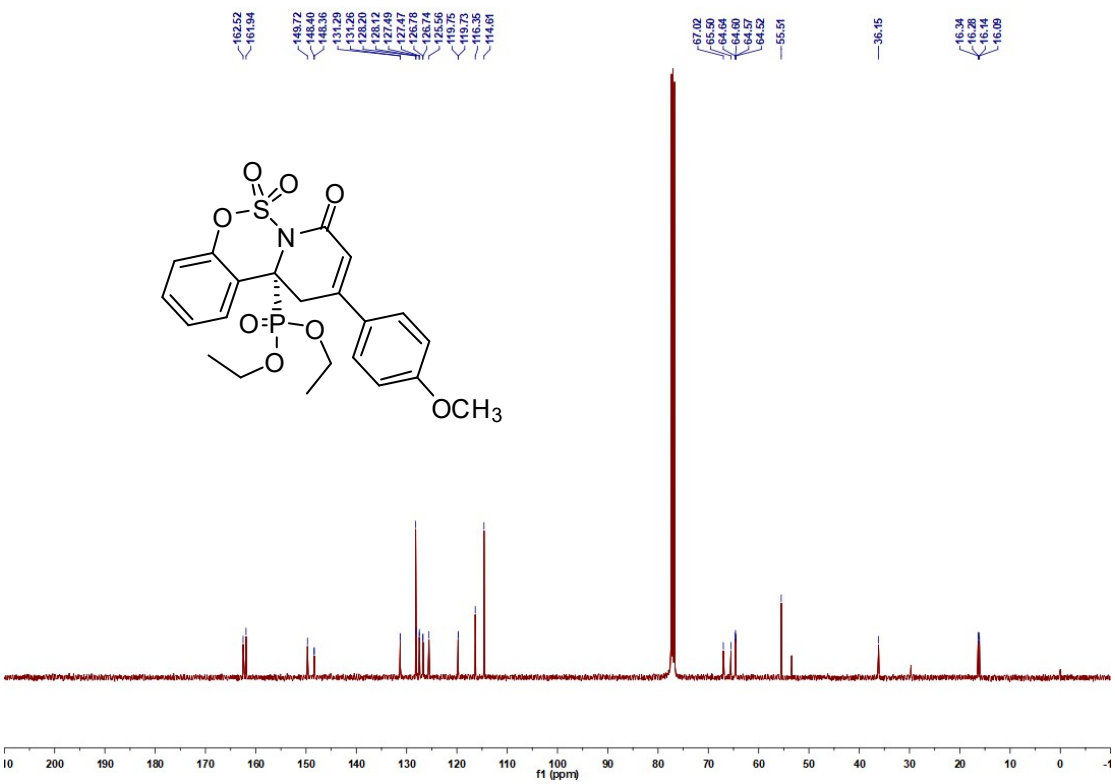
^{31}P NMR


17.62
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

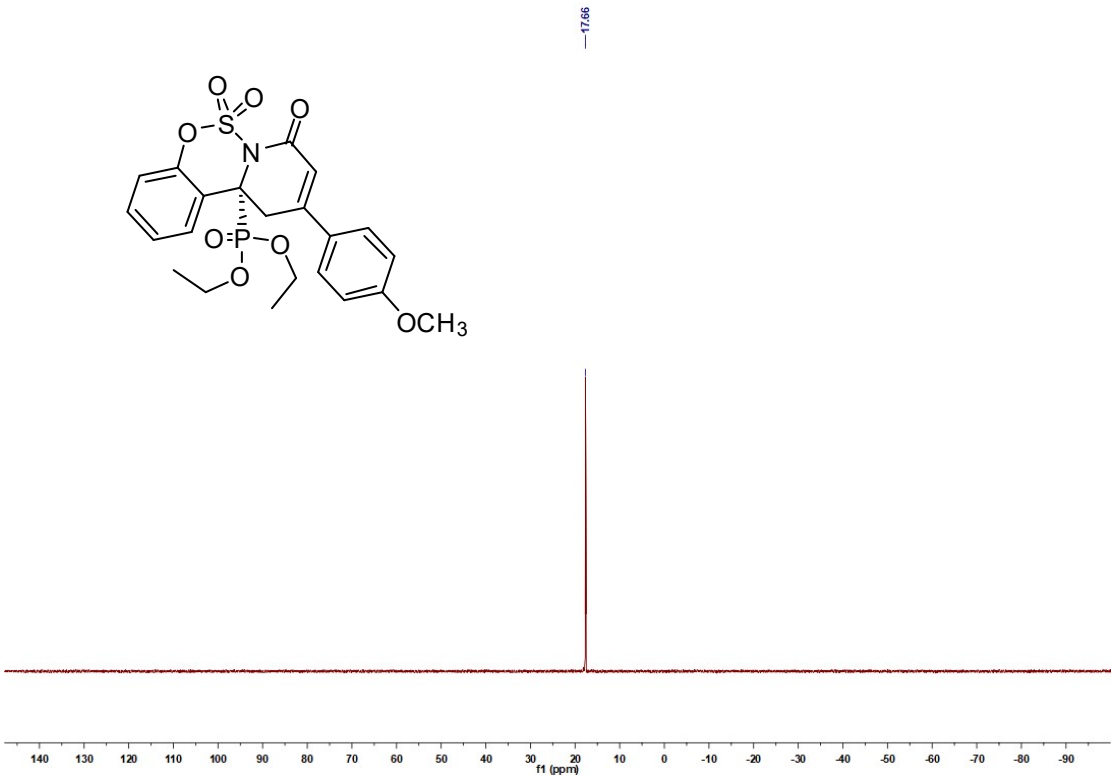
3c: ^{1}H NMR



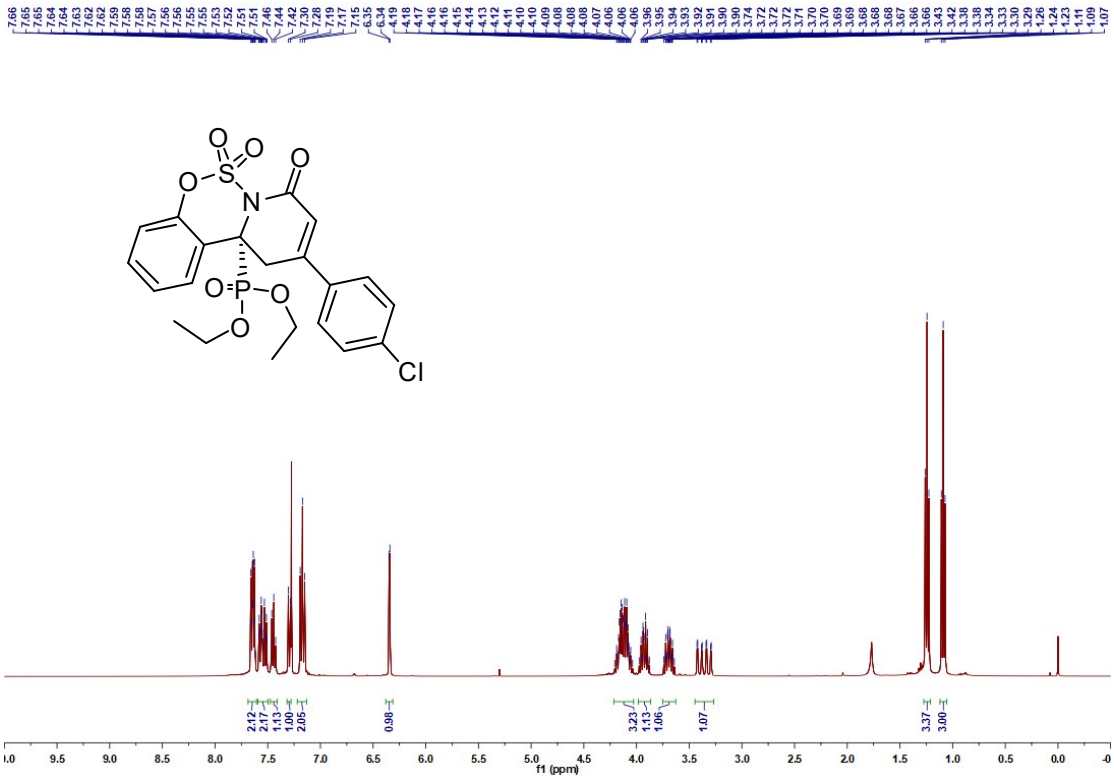
^{13}C NMR



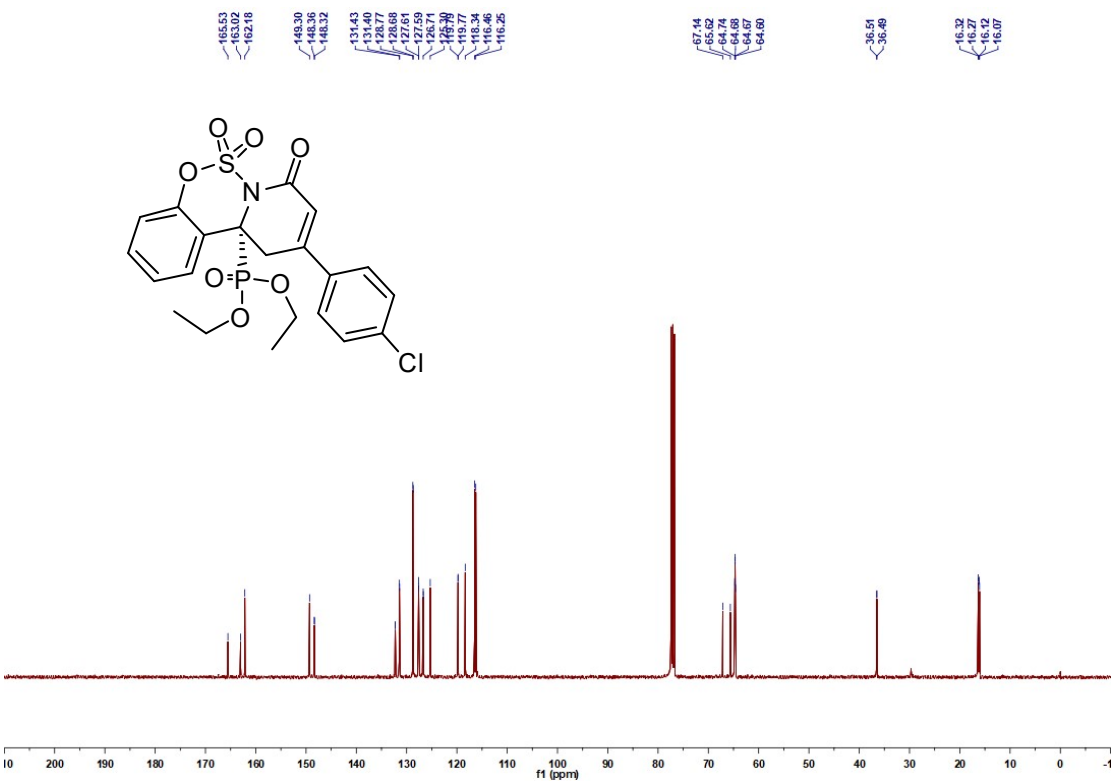
^{31}P NMR


17.66
OCH3
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

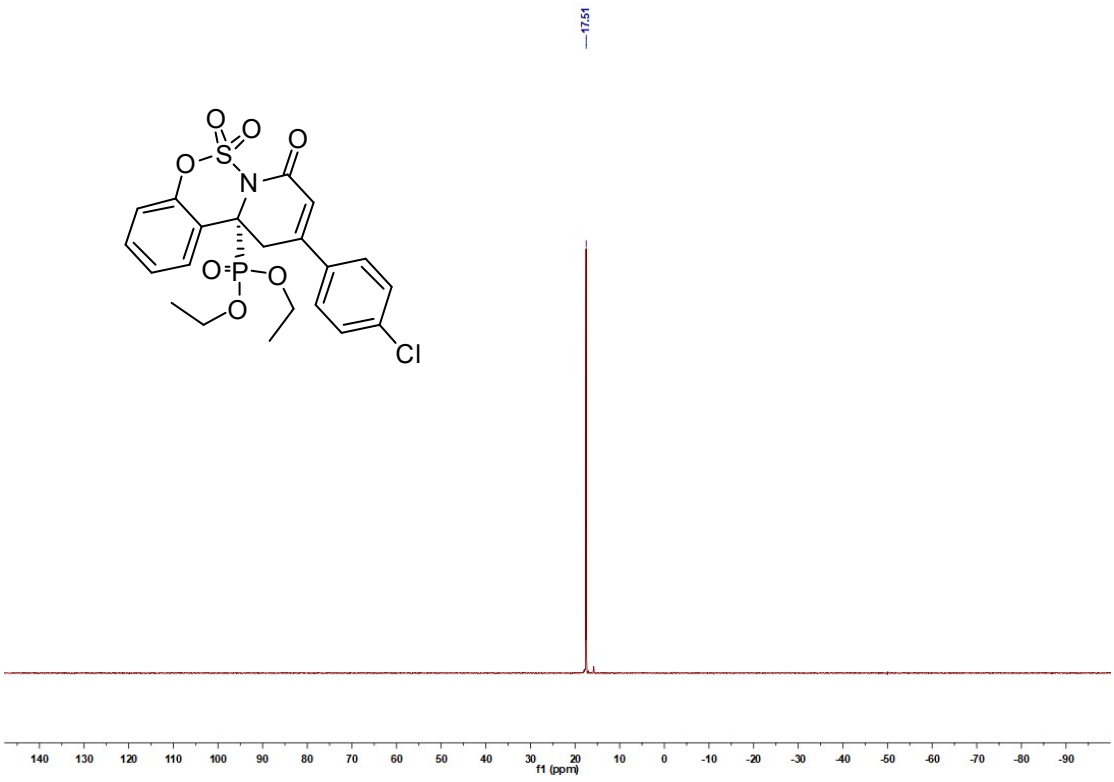
3d: ^{1}H NMR



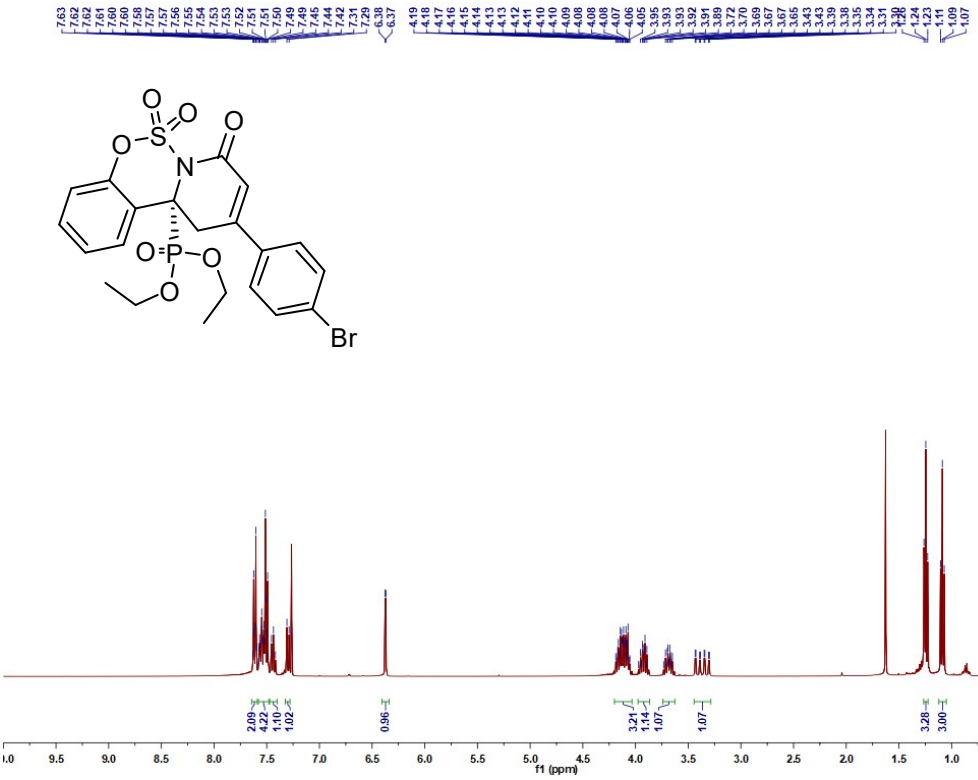
^{13}C NMR



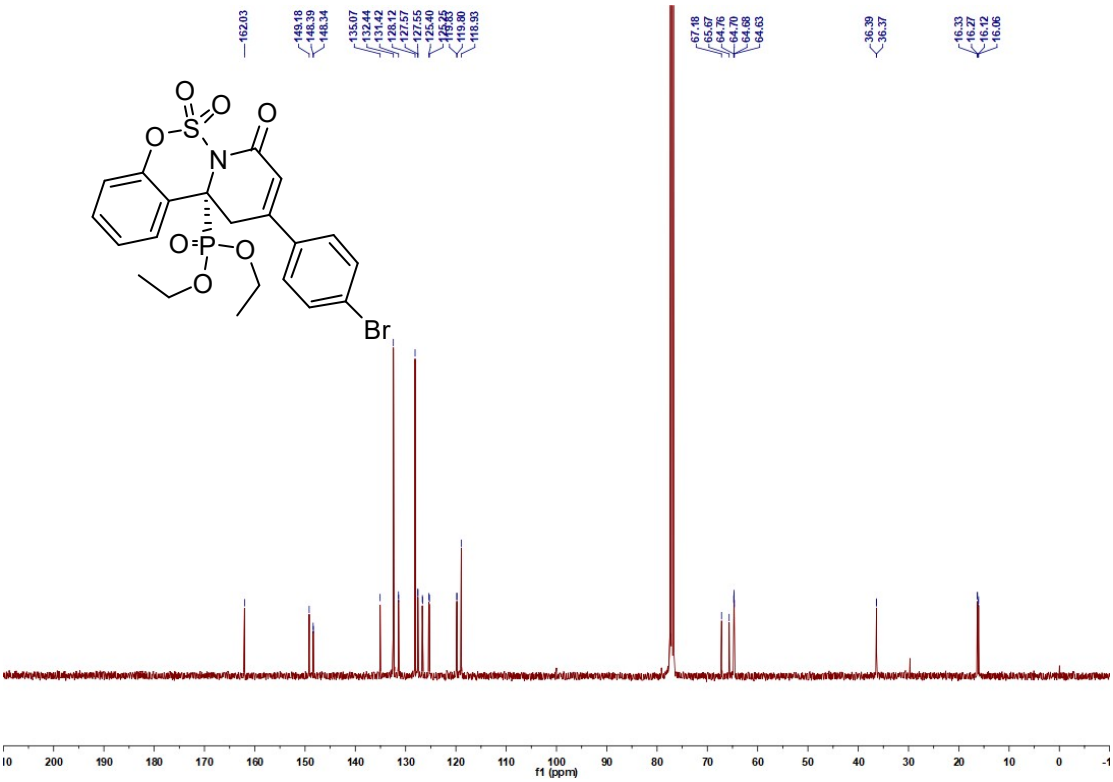
^{31}P NMR


17.51
O
O
S
O
N
O
O
P
O
O
Cl
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

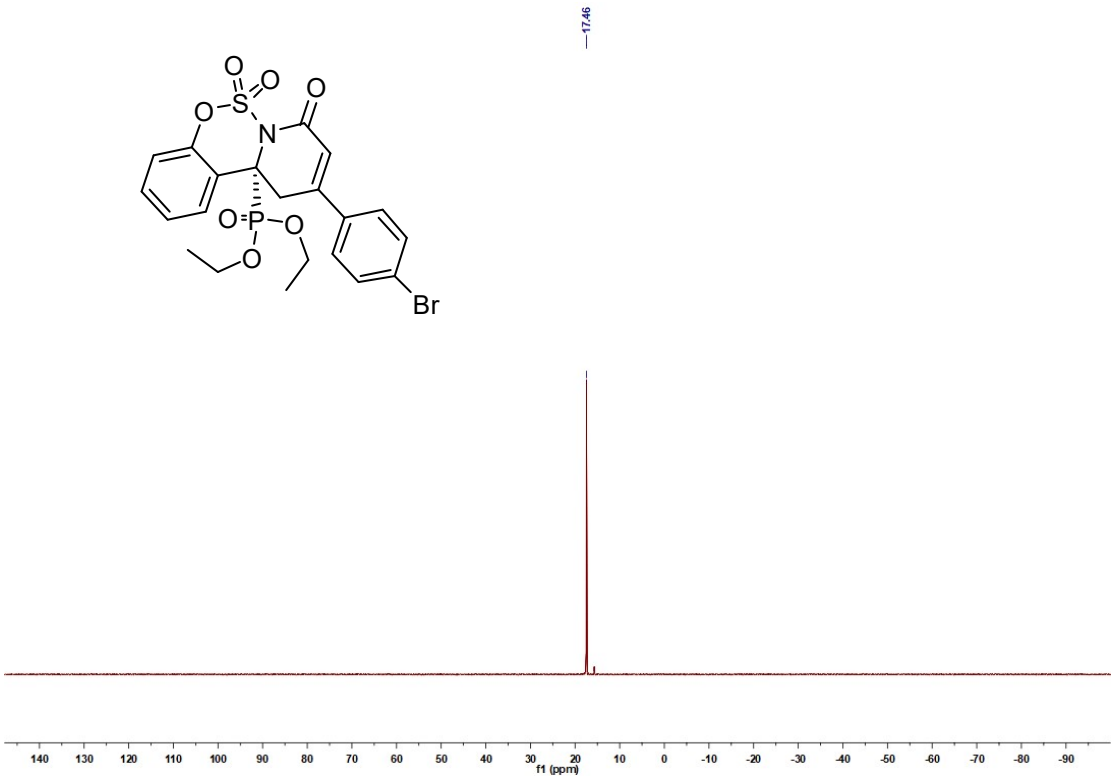
3e: ^{1}H NMR



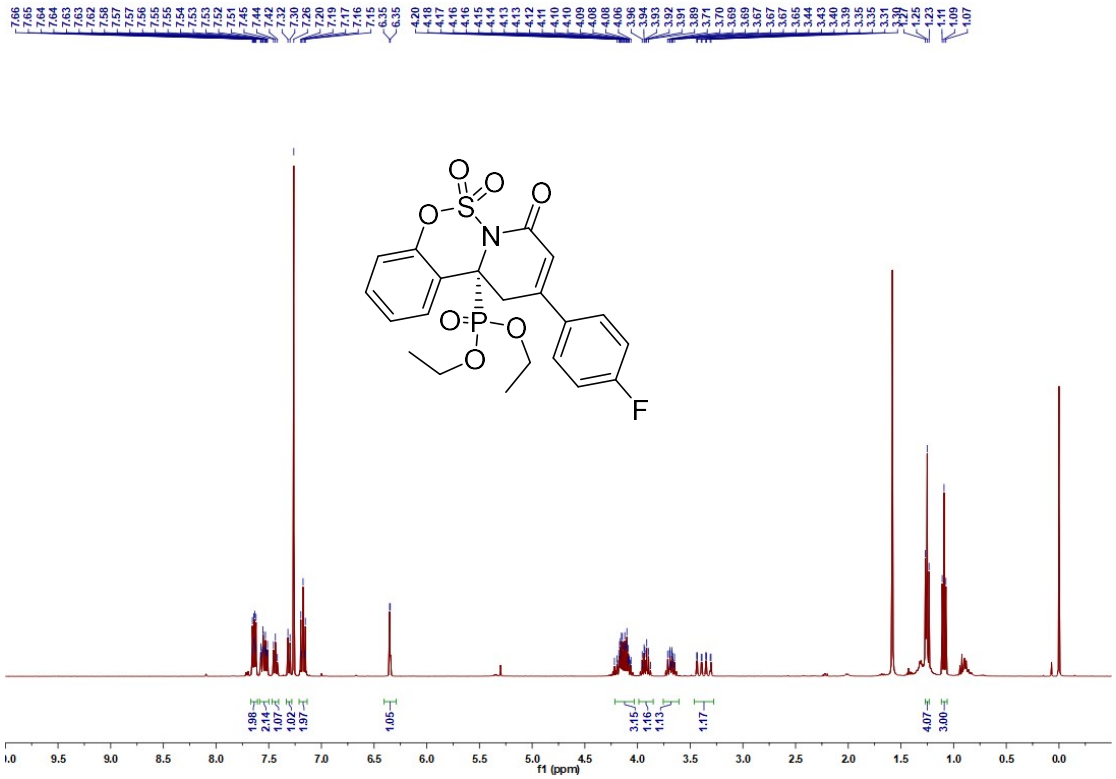
^{13}C NMR



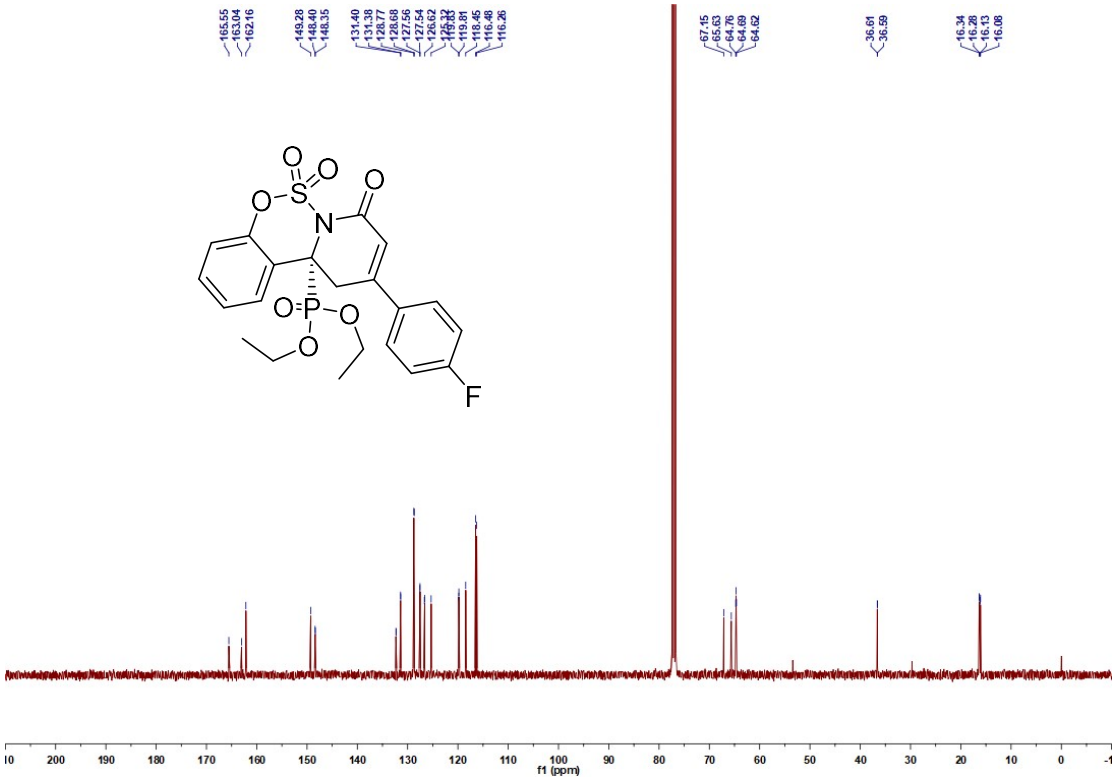
^{31}P NMR


17.46
O
O
S
O
O
N
O
P
O
O
Br
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

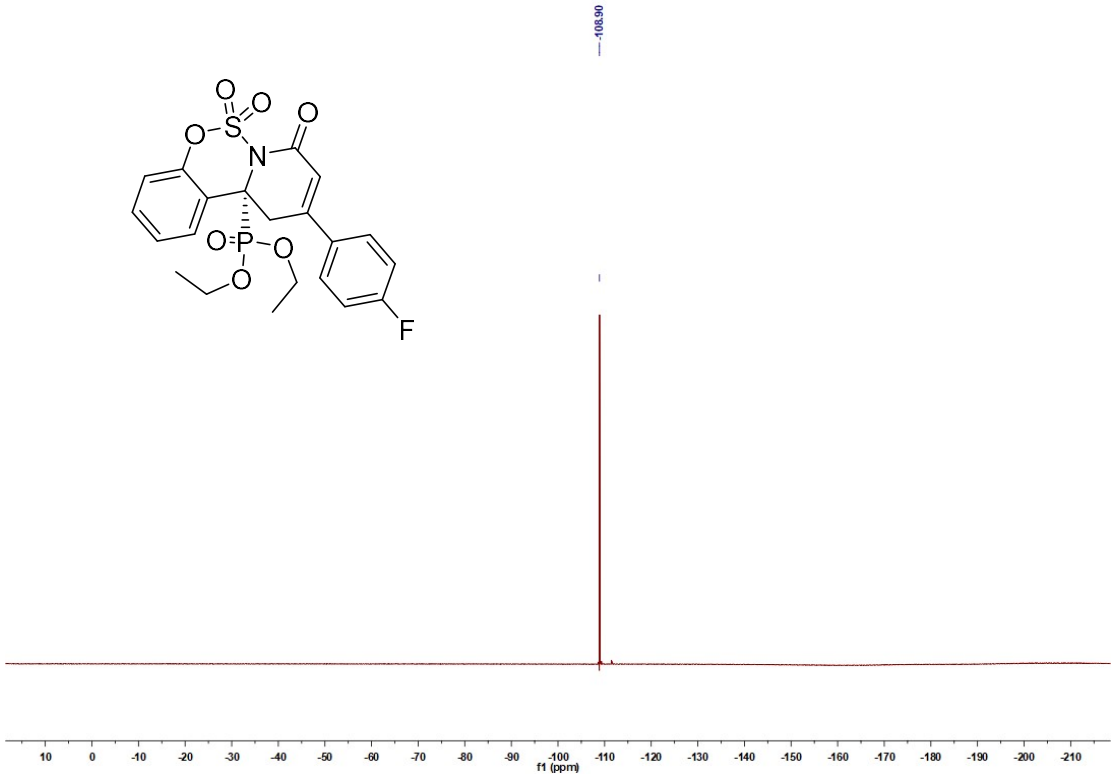
3f: ^{1}**H NMR**



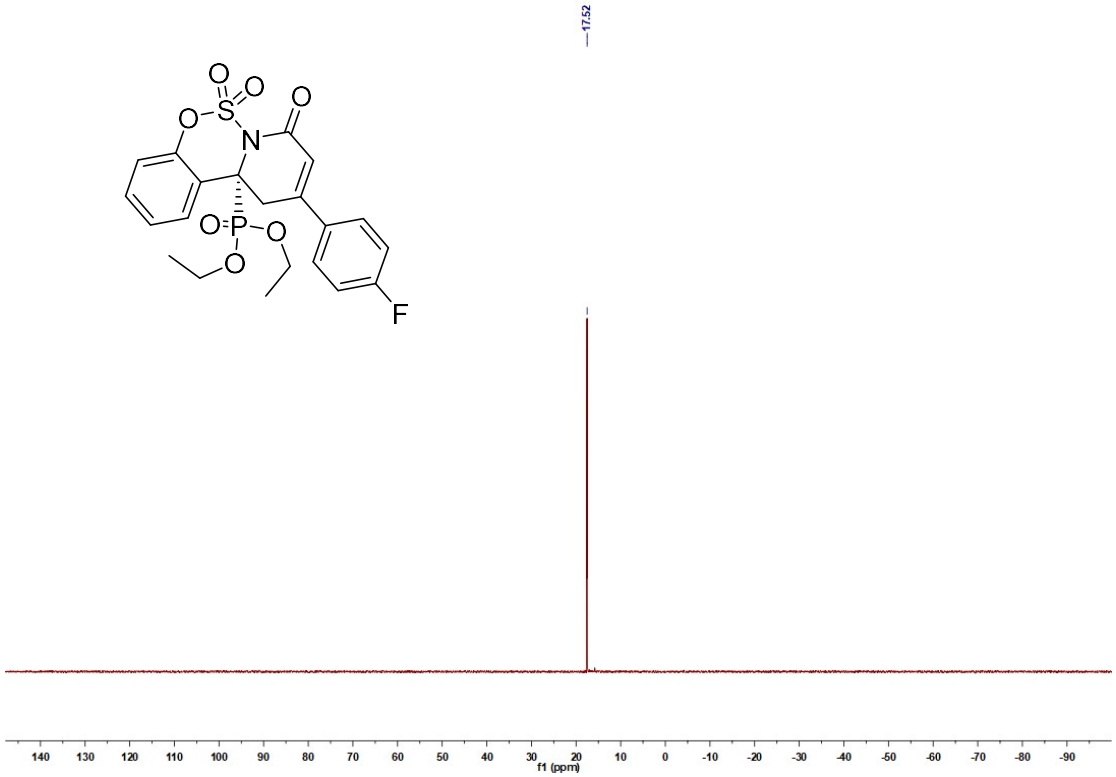
^{13}**C NMR**



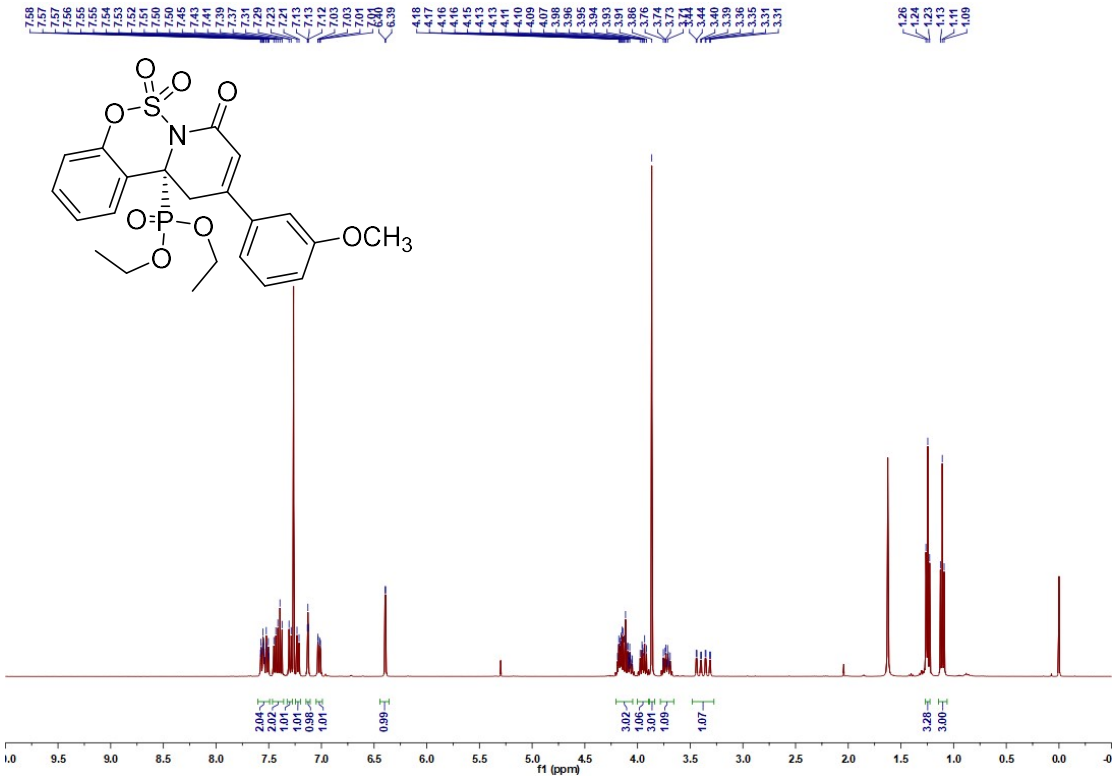
^{19}F NMR



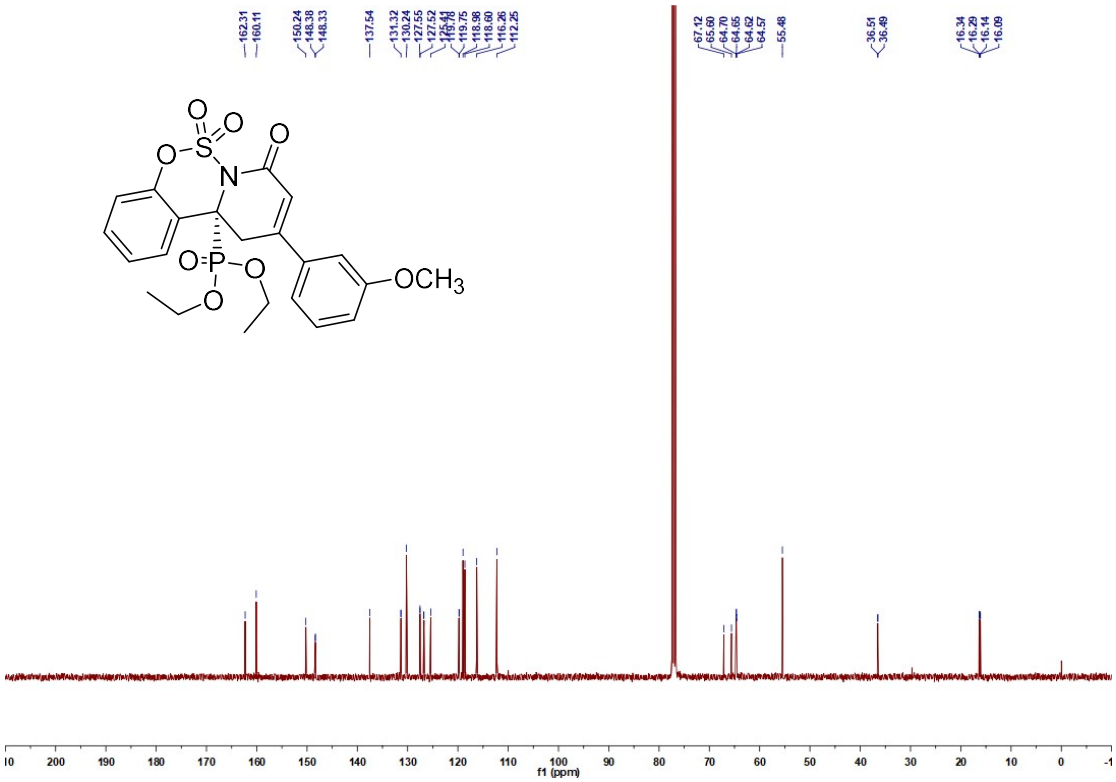
^{31}P NMR



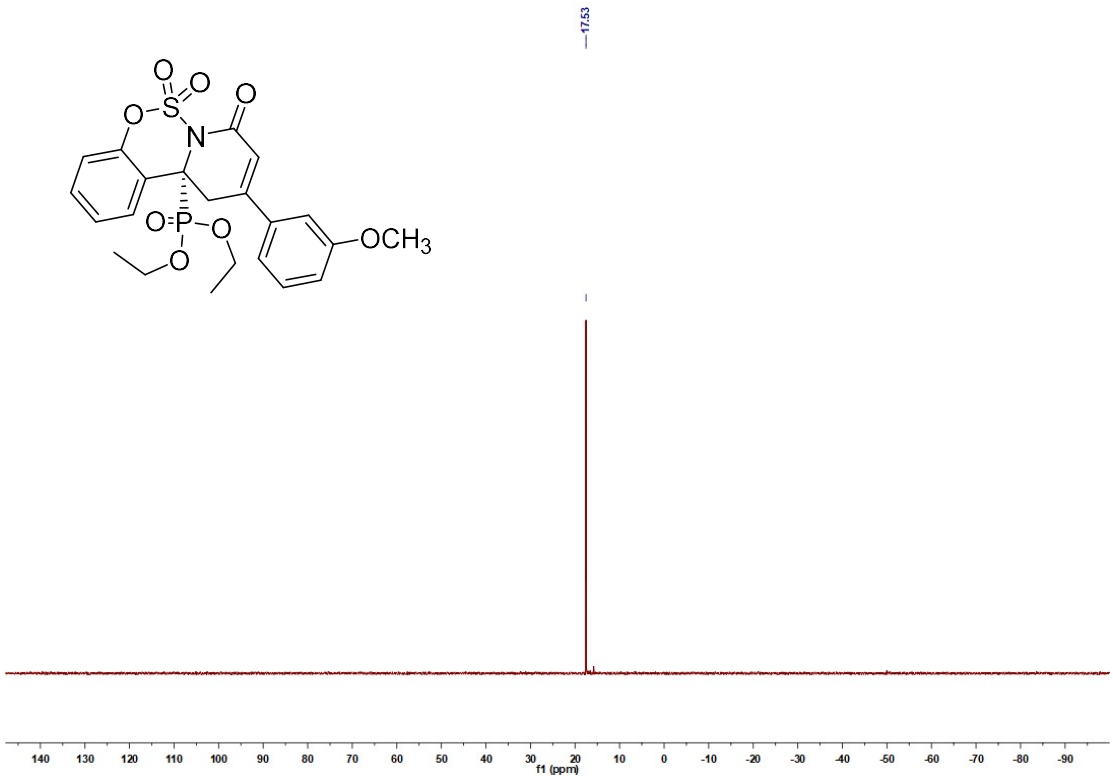
3g: ^{1}H NMR



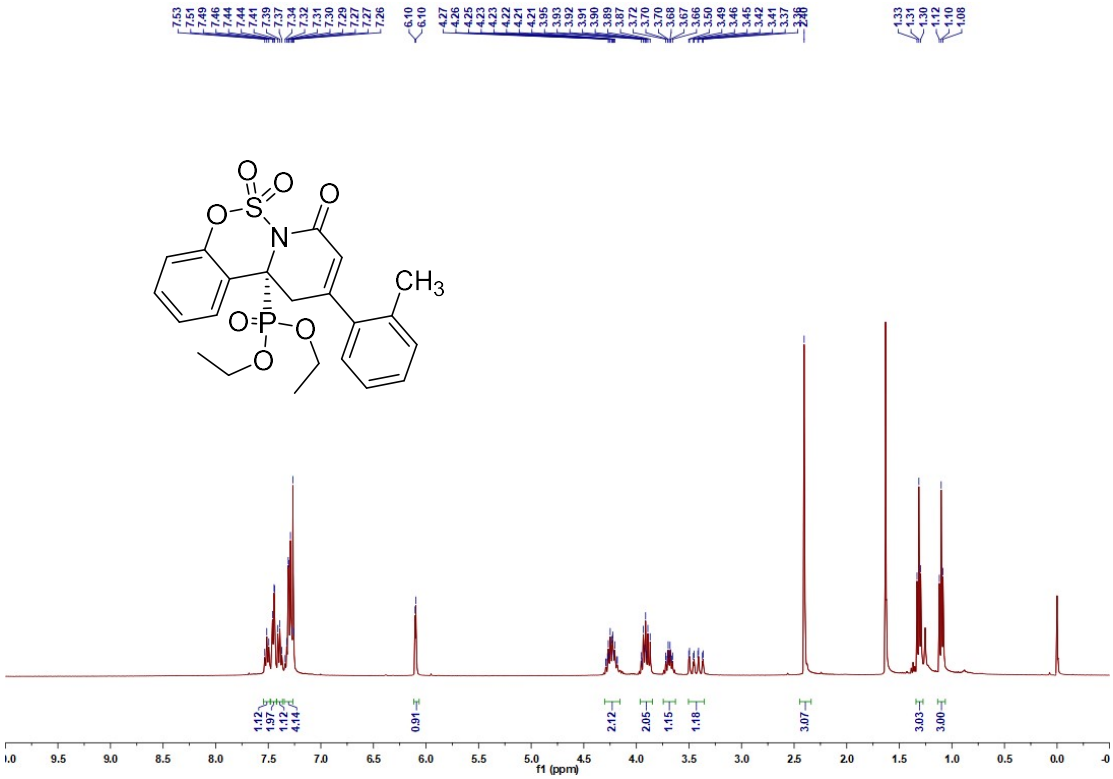
^{13}C NMR



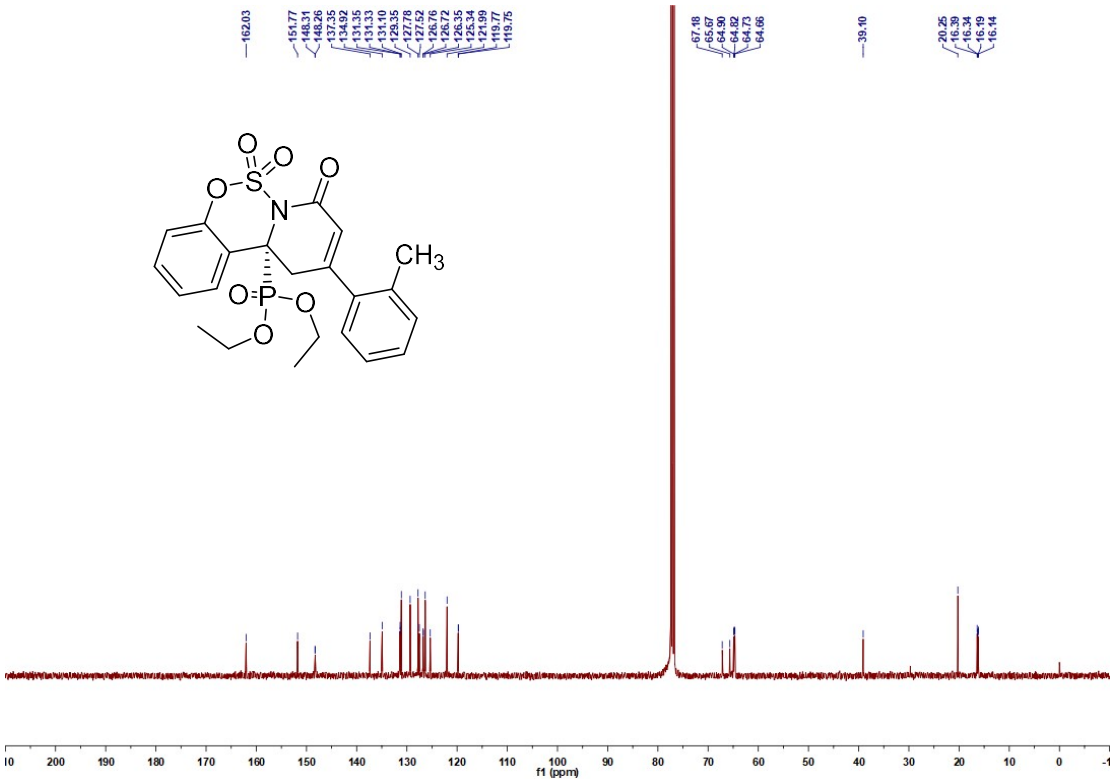
^{31}P NMR


17.53
OCH3
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

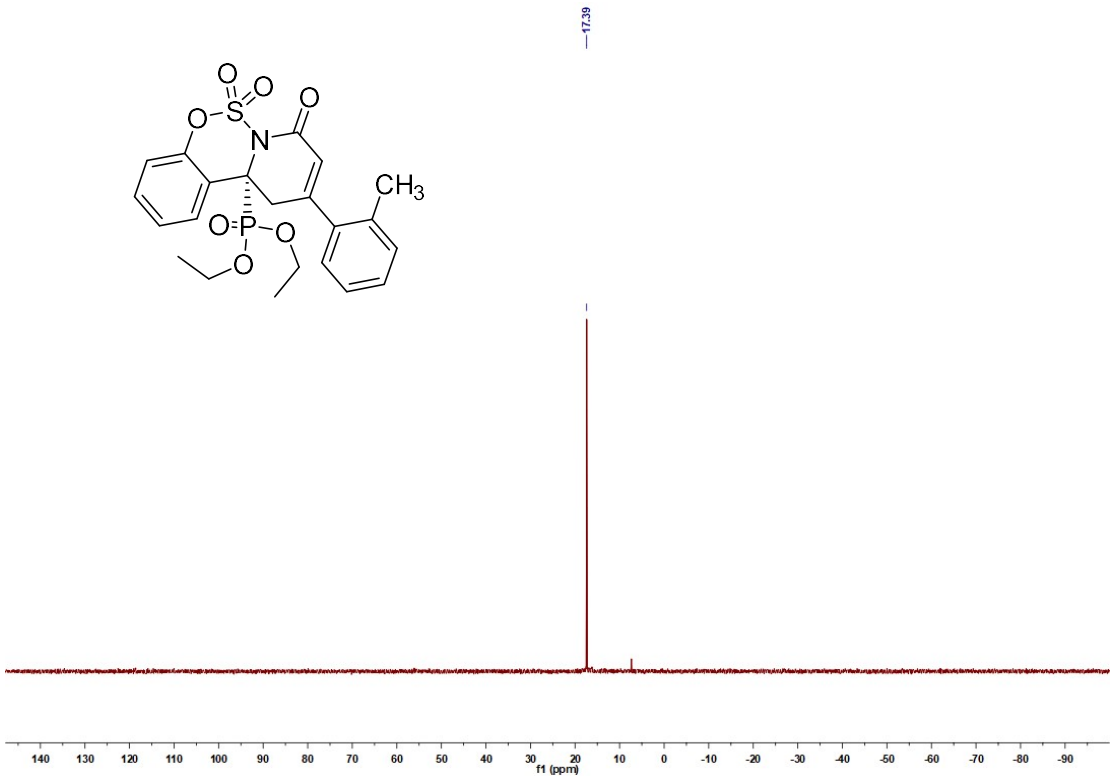
3h: ^{1}**H NMR**



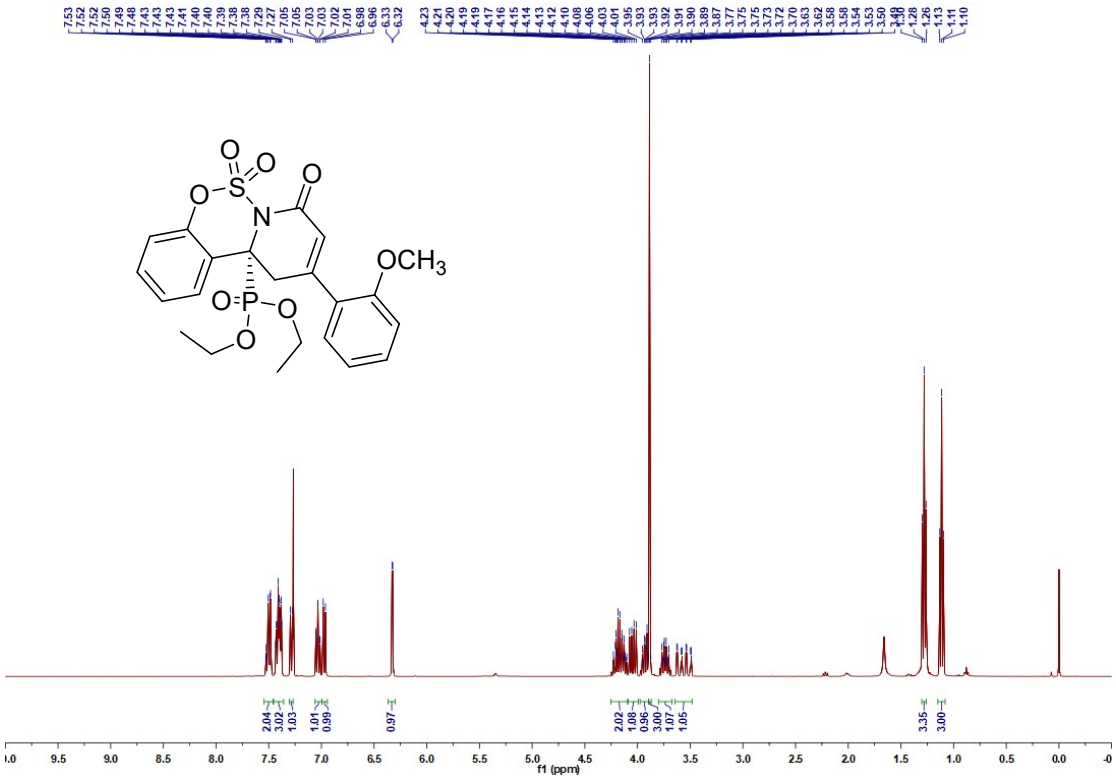
^{13}**C NMR**



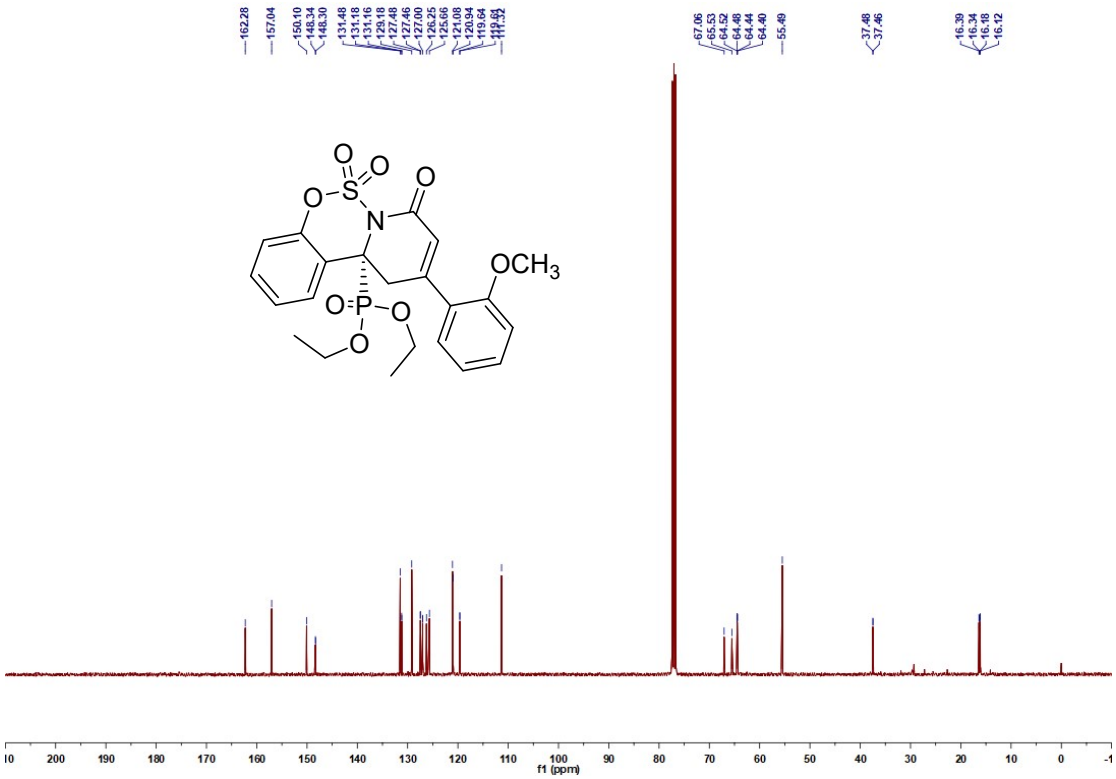
^{31}P NMR


17.39
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

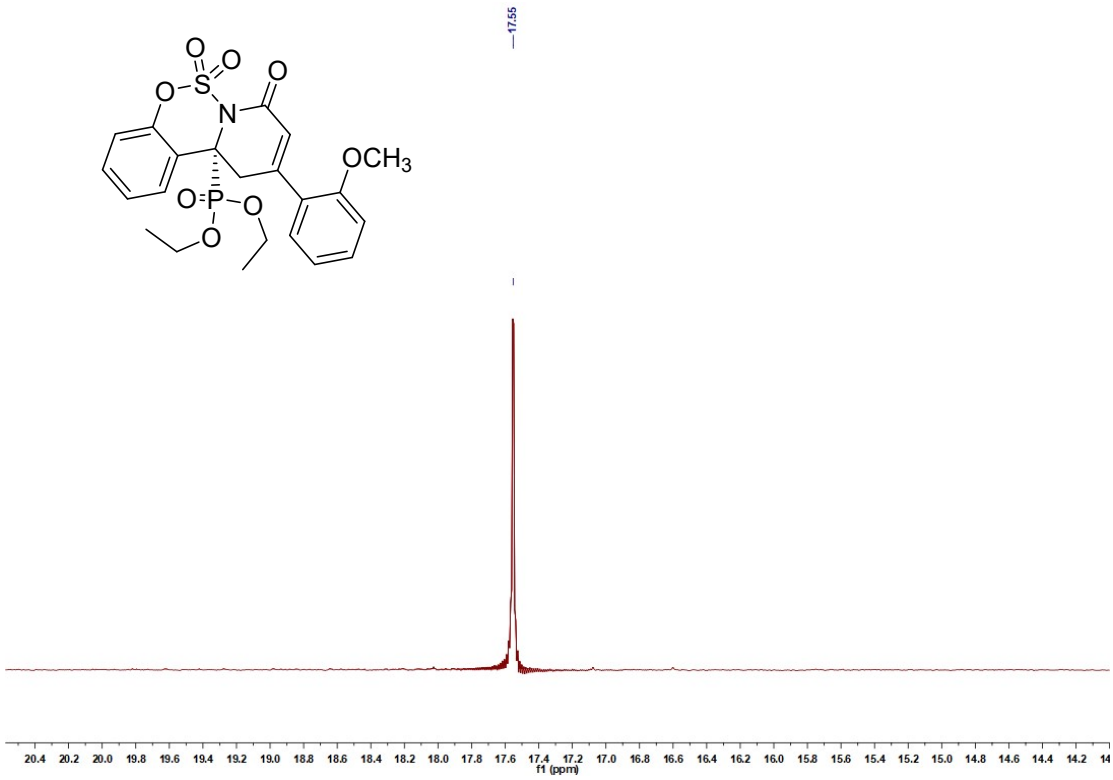
3i: **^{1}H NMR**



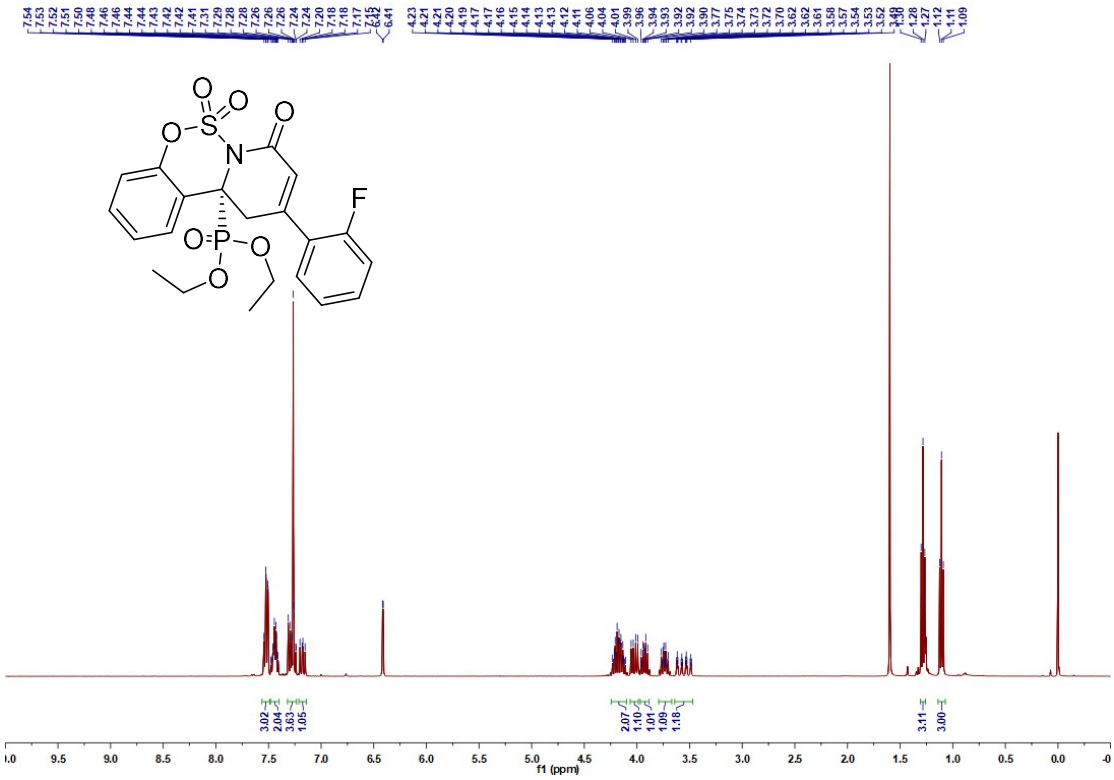
^{13}C NMR



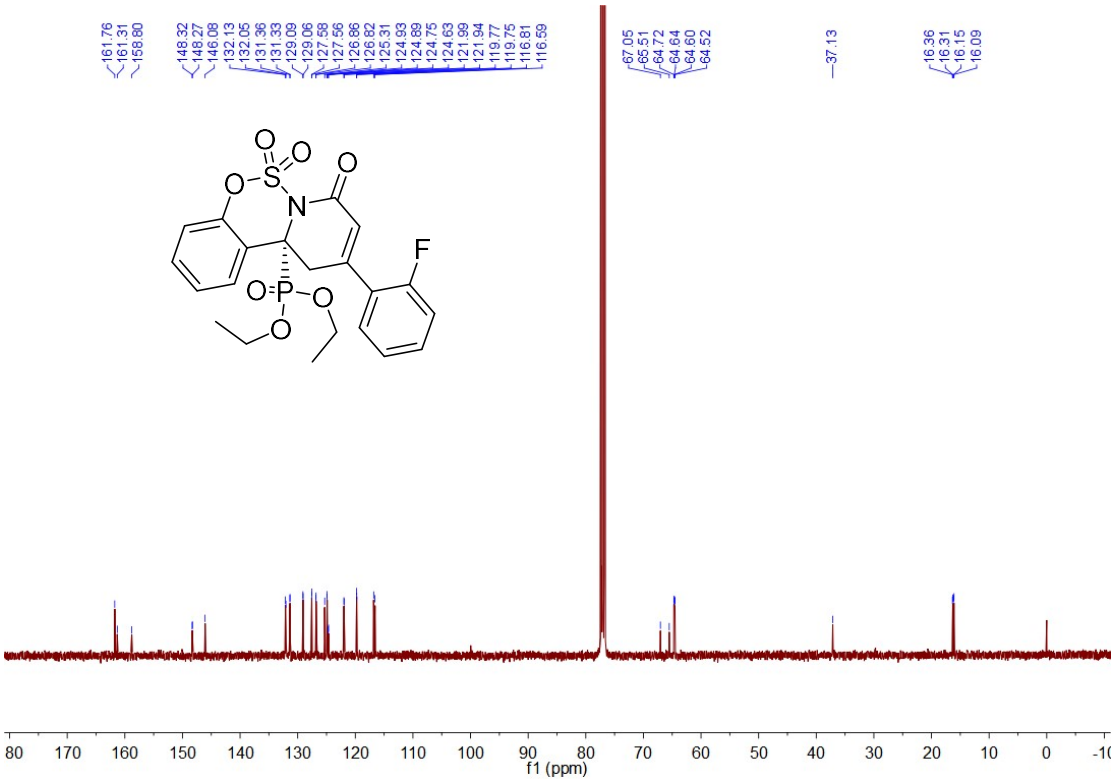
^{31}P NMR


17.55
OCH3
20.4 20.2 20.0 19.8 19.6 19.4 19.2 19.0 18.8 18.6 18.4 18.2 18.0 17.8 17.6 17.4 17.2 17.0 16.8 16.6 16.4 16.2 16.0 15.8 15.6 15.4 15.2 15.0 14.8 14.6 14.4 14.2
f1 (ppm)

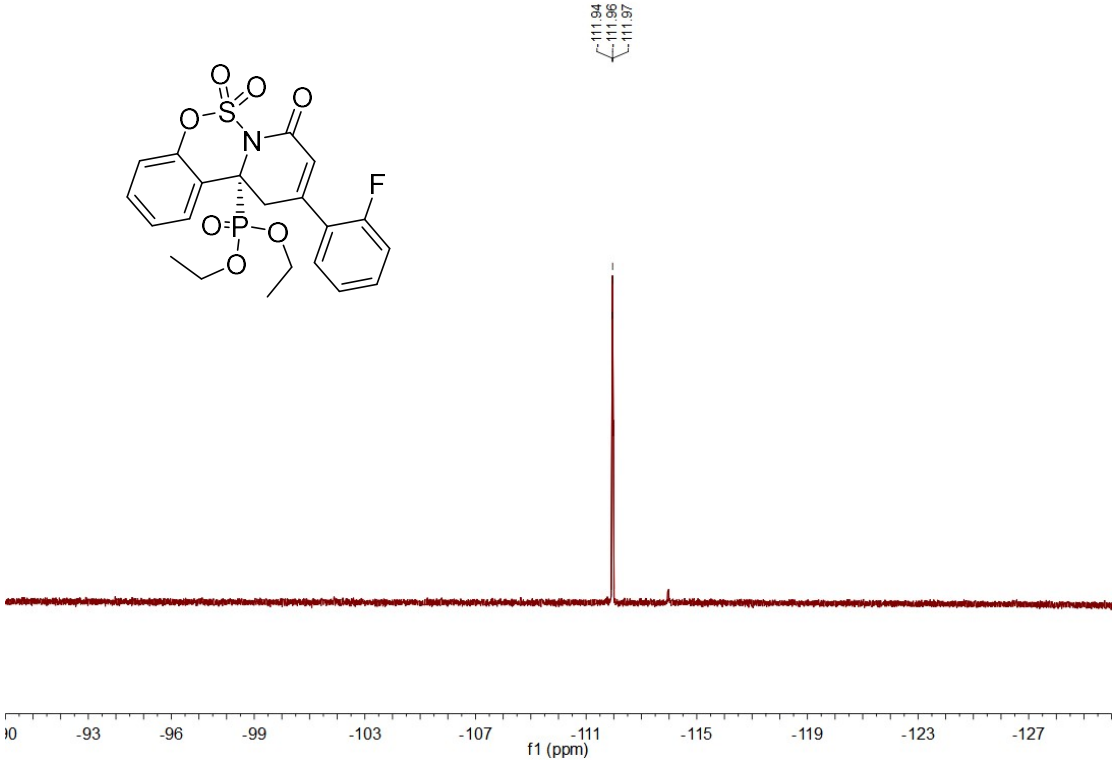
3j: ^{1}**H NMR**



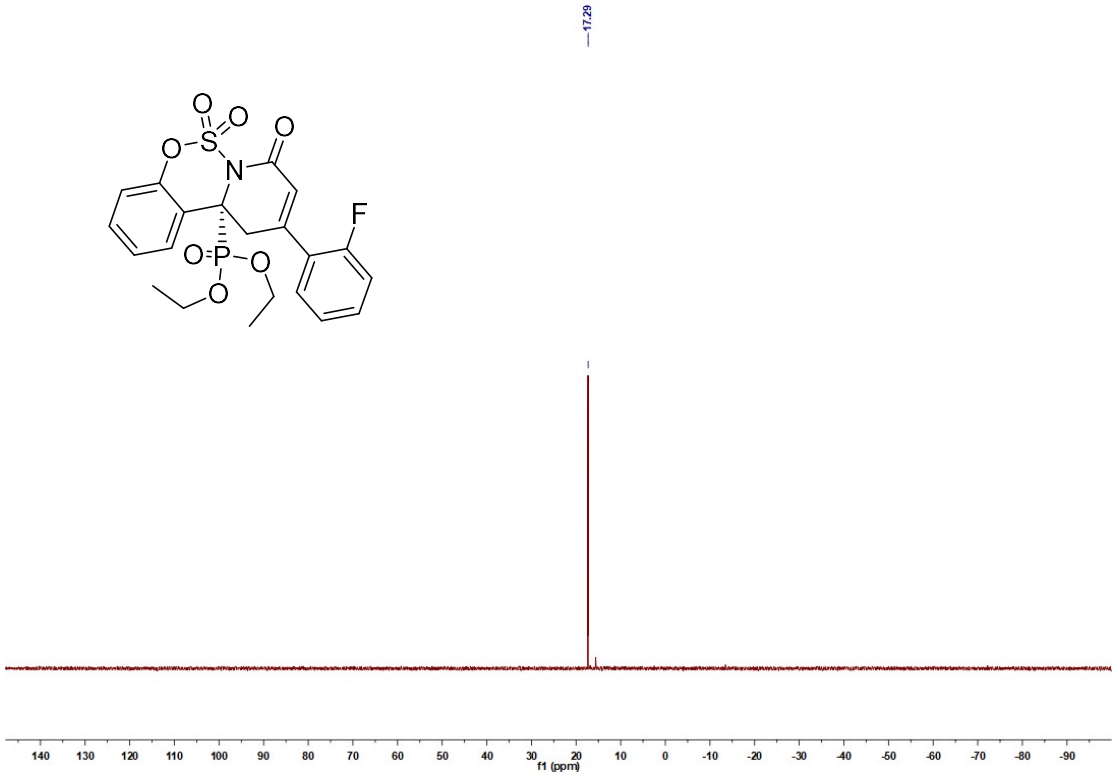
^{13}**C NMR**



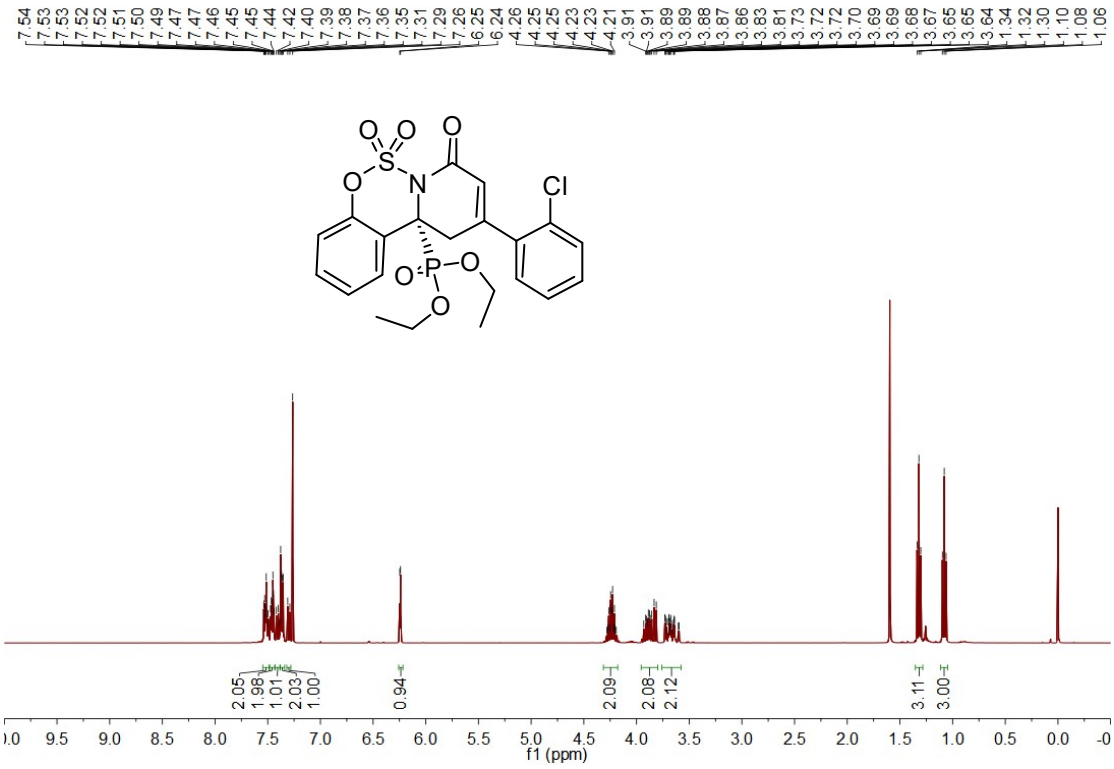
^{19}F NMR



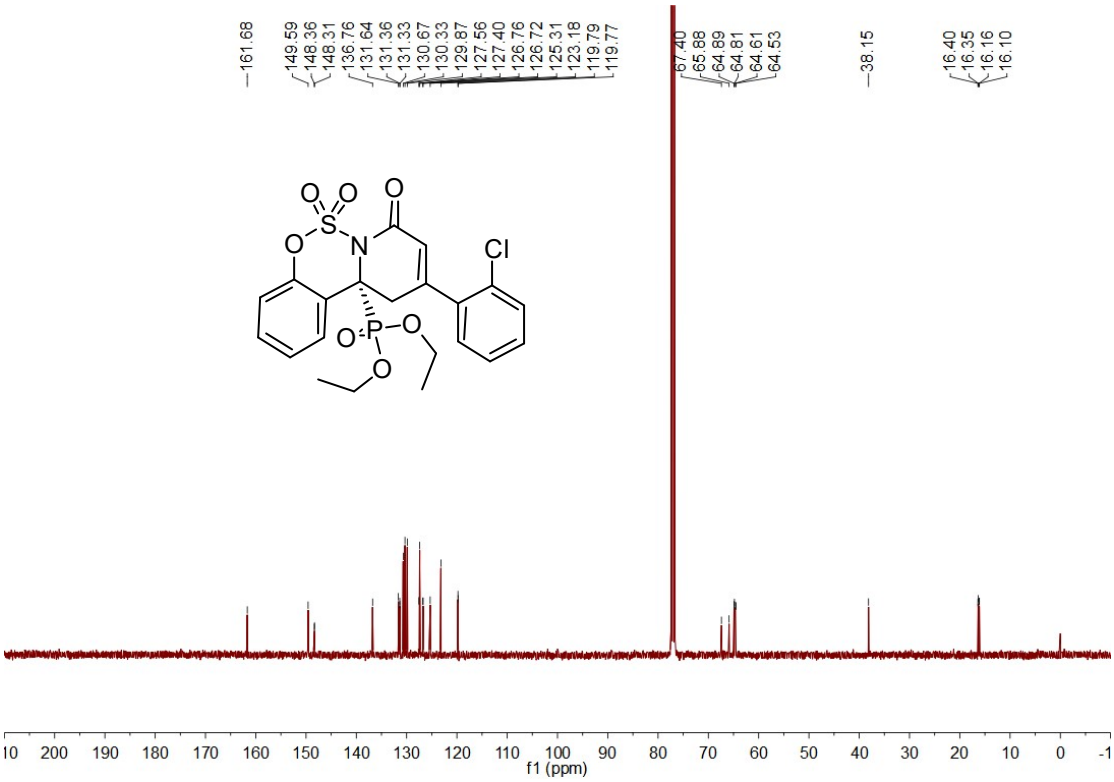
^{31}P NMR



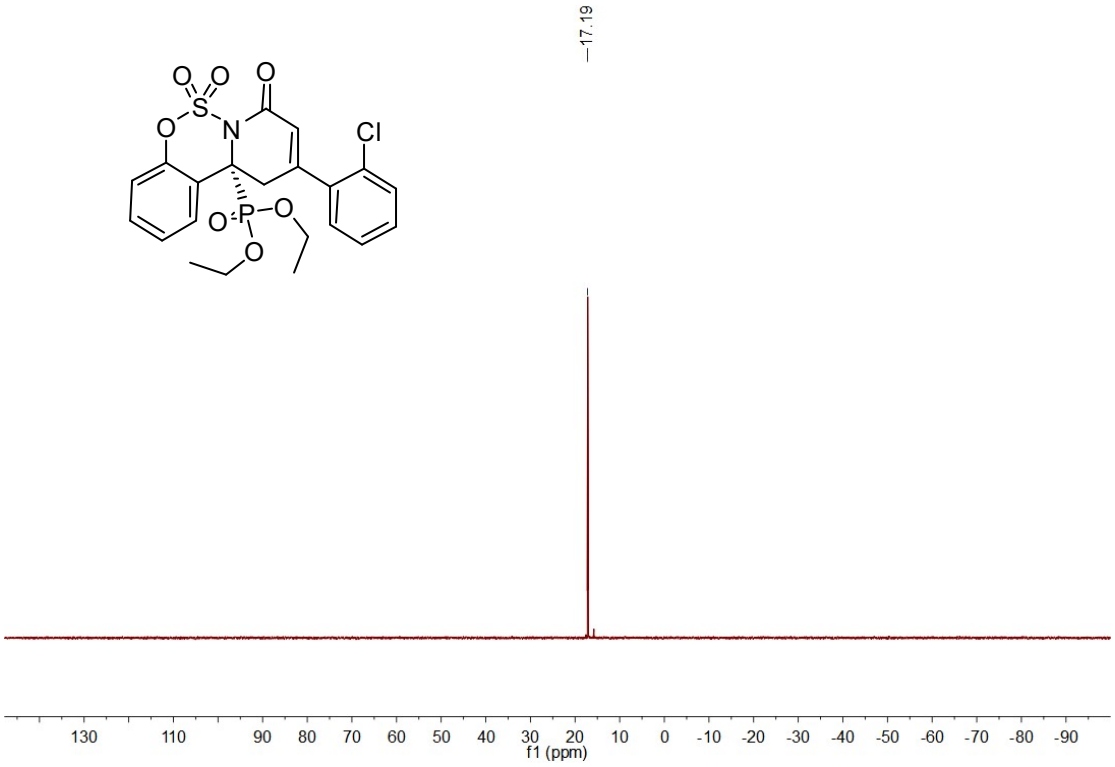
3k: ^{1}H NMR



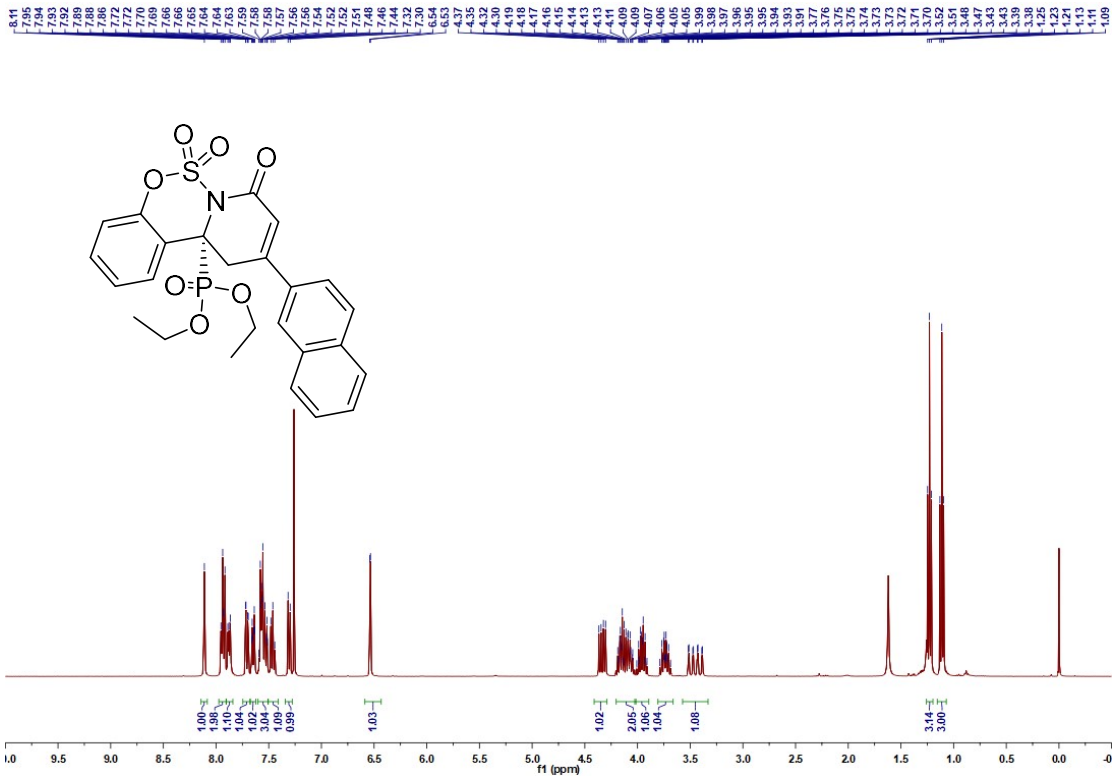
^{13}C NMR



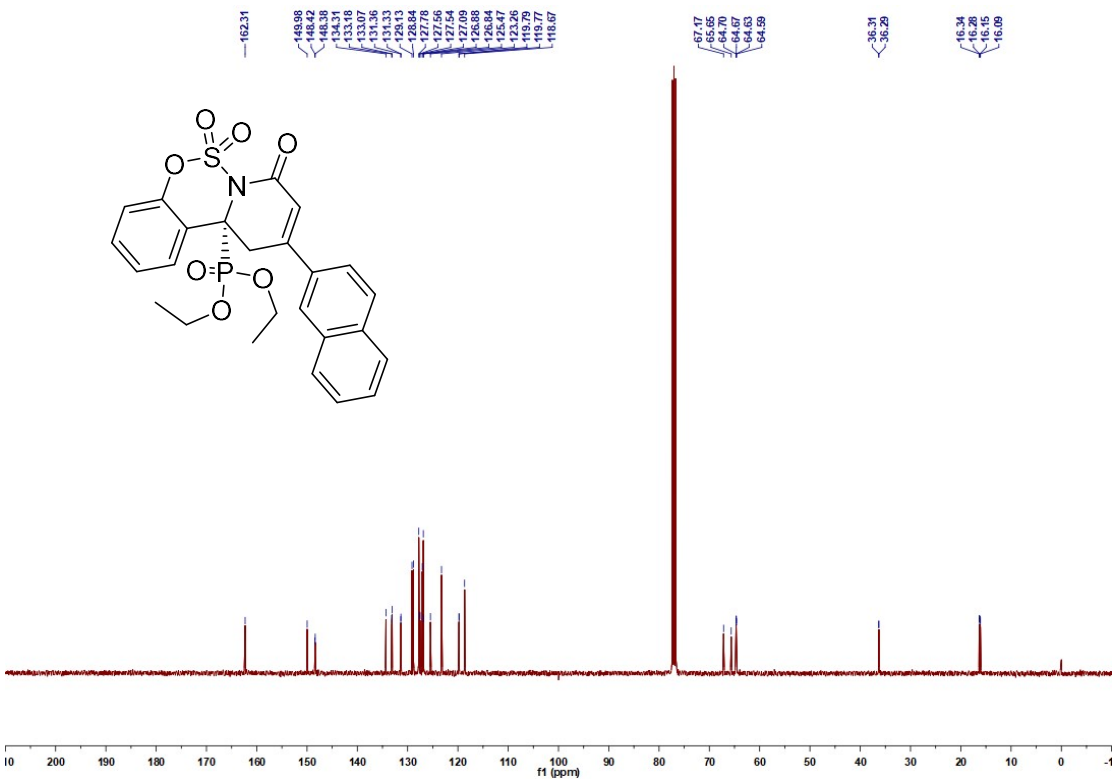
^{31}P NMR


17.19
O
O
O
S
O
N
Cl
O
P
O
O
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

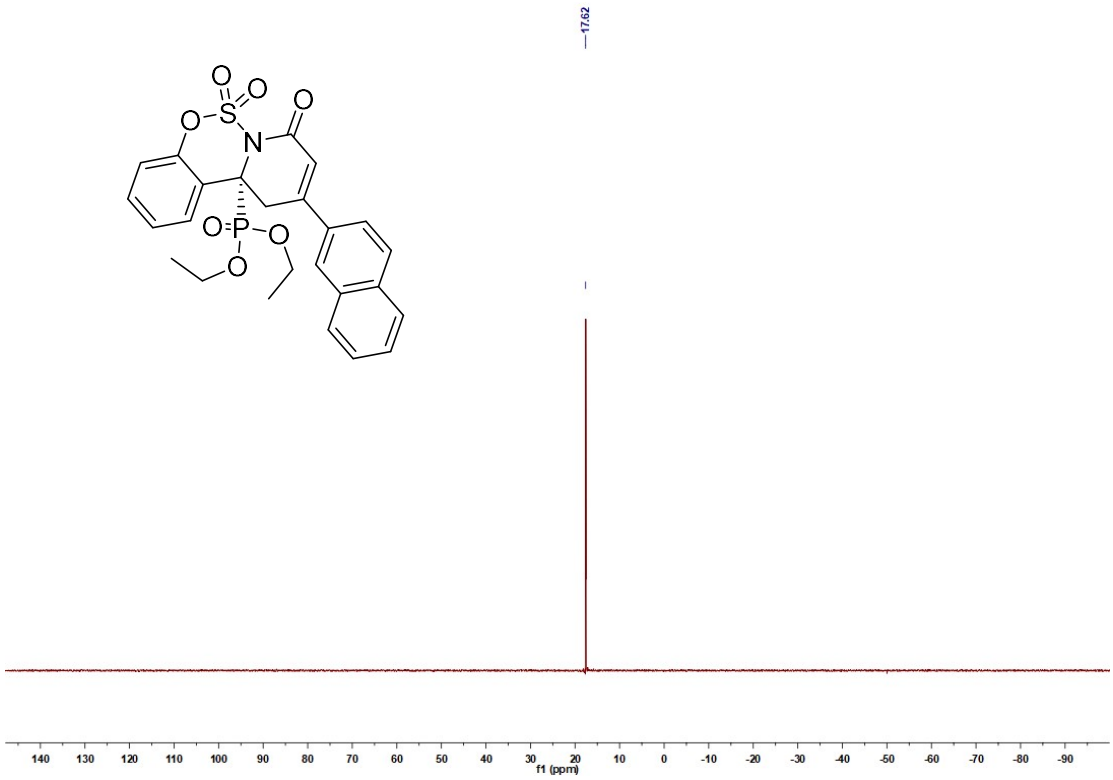
3l: ^{1}**H NMR**



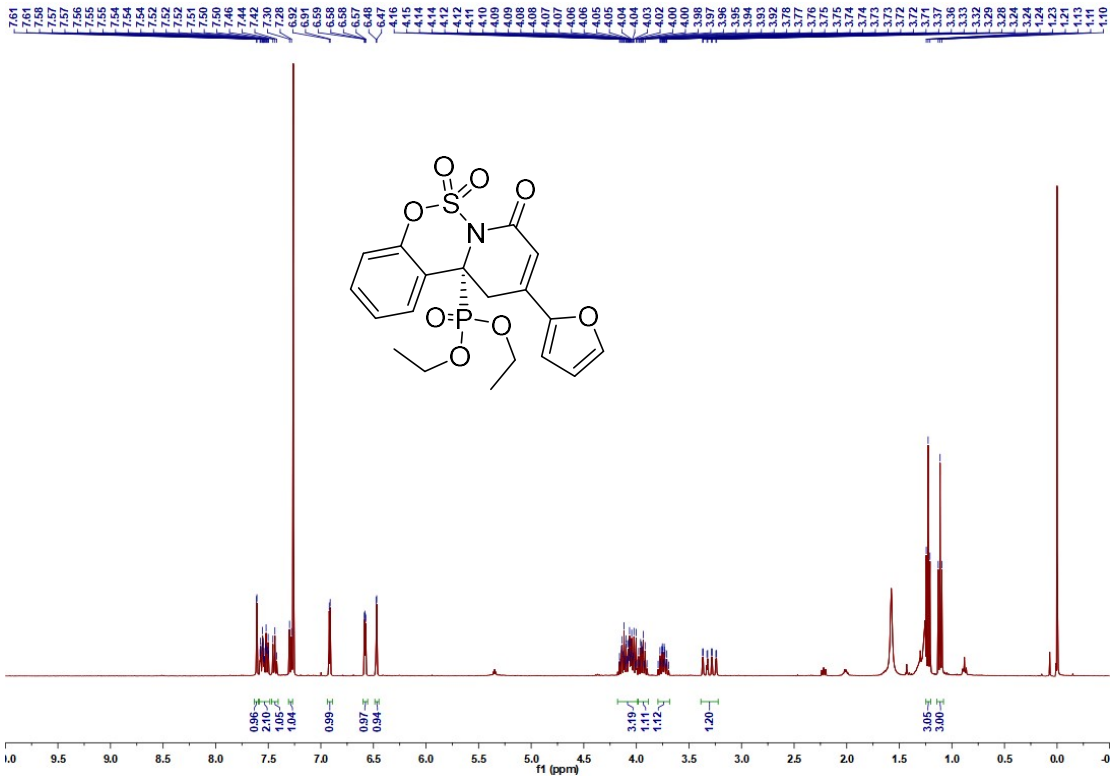
^{13}C NMR



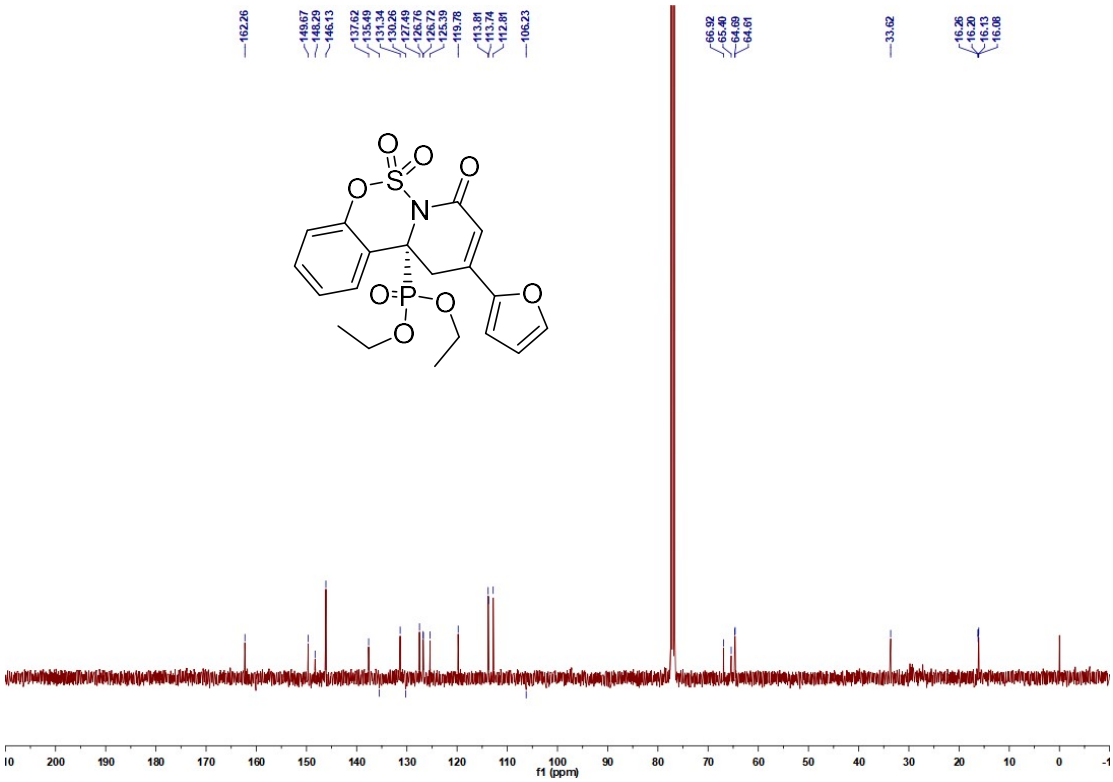
^{31}P NMR


17.62
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

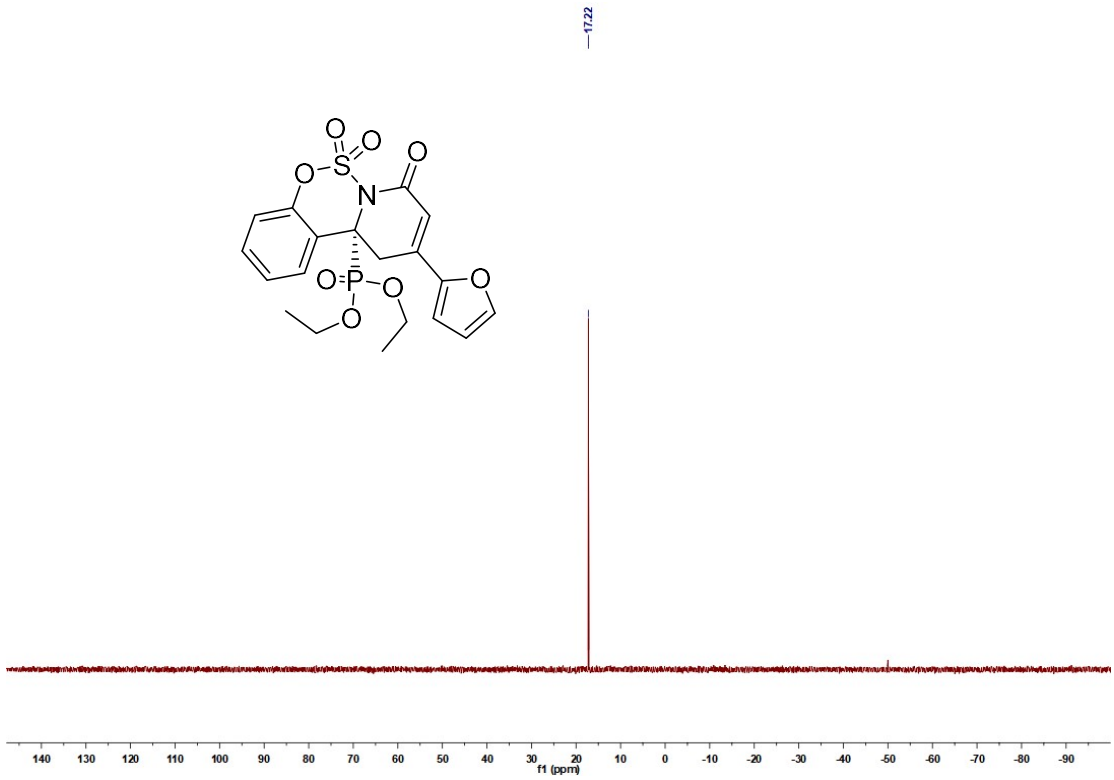
3m: ^{1}H NMR



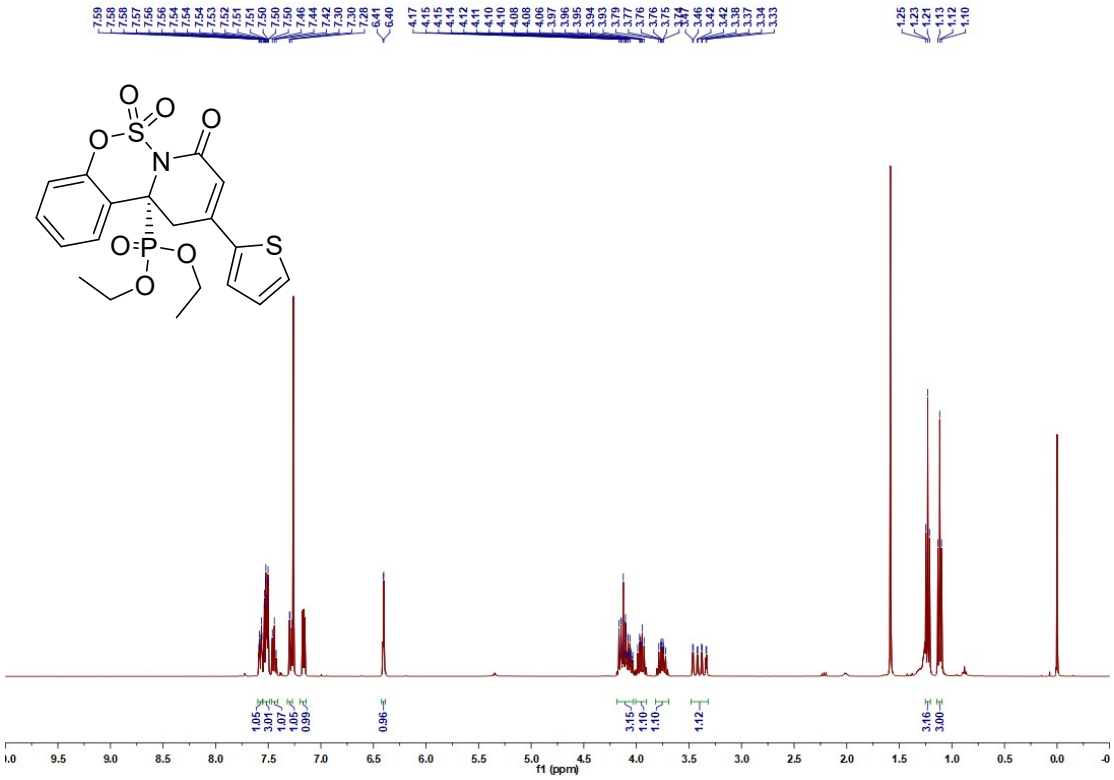
^{13}C NMR



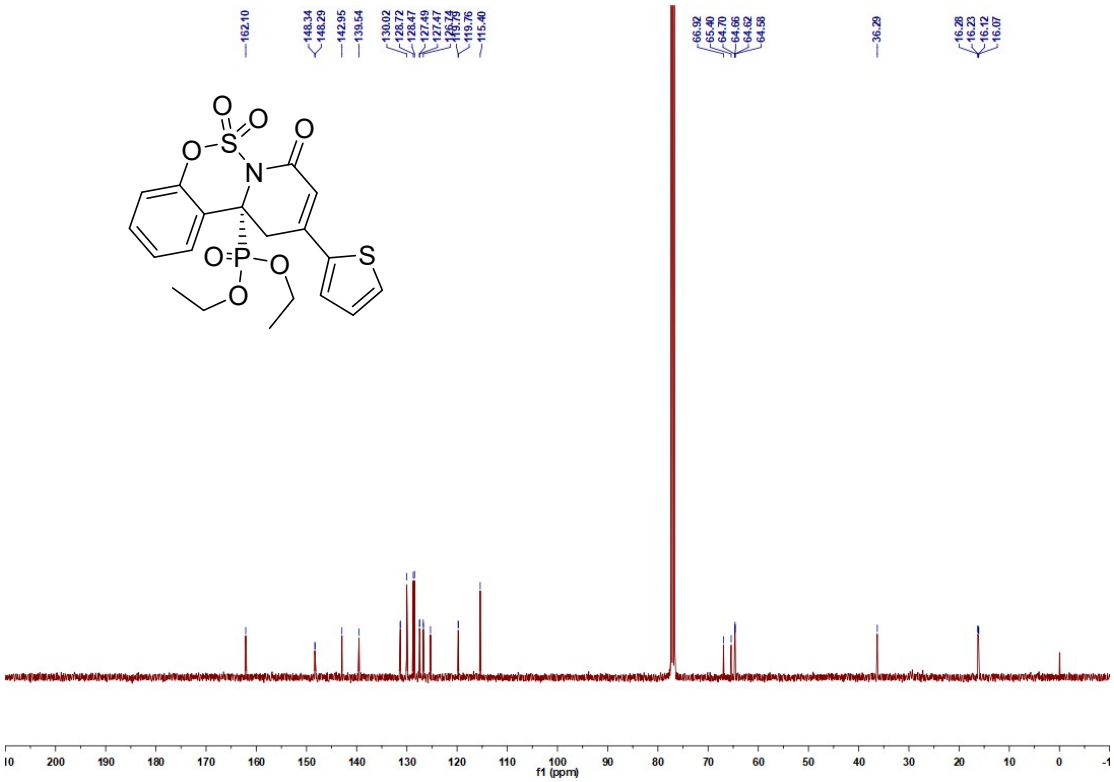
^{31}P NMR


17.22
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

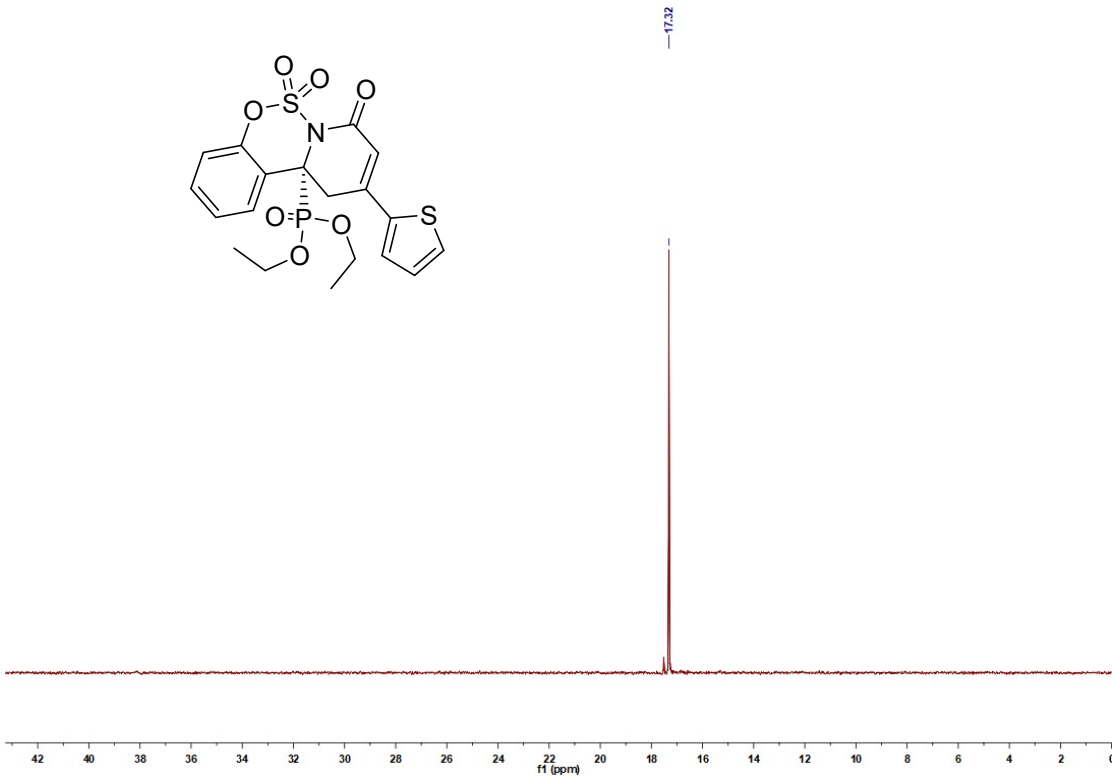
3n: ^{1}H NMR



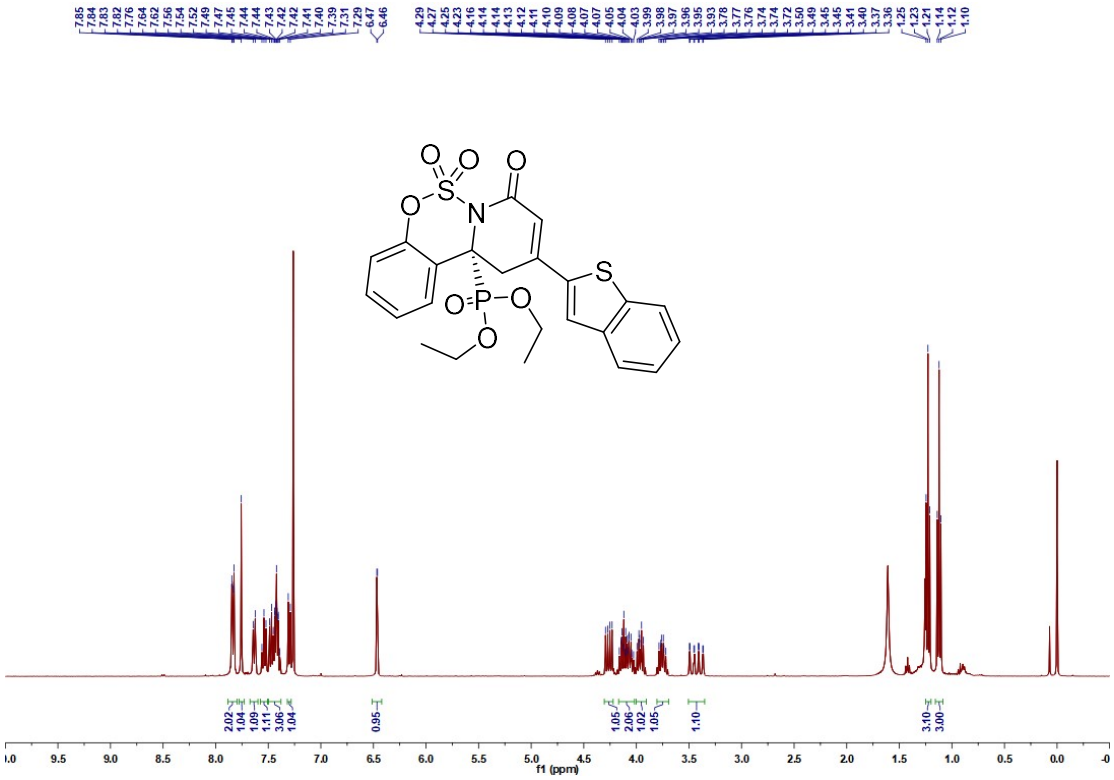
^{13}C NMR



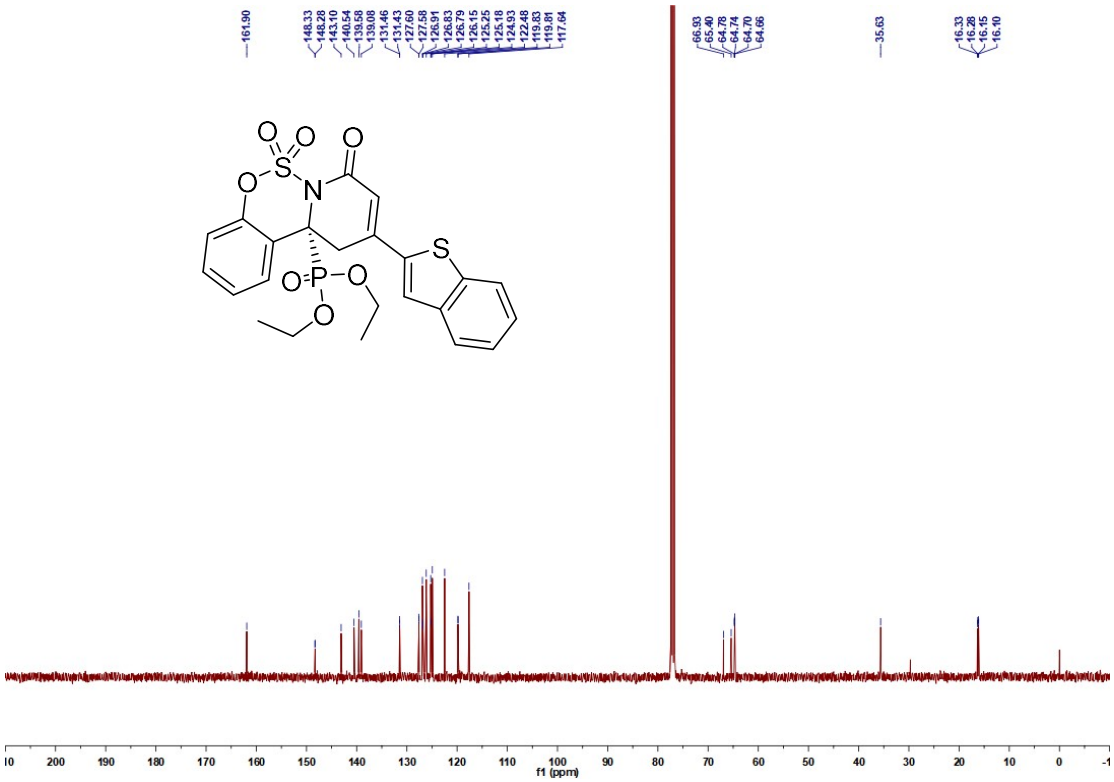
^{31}P NMR



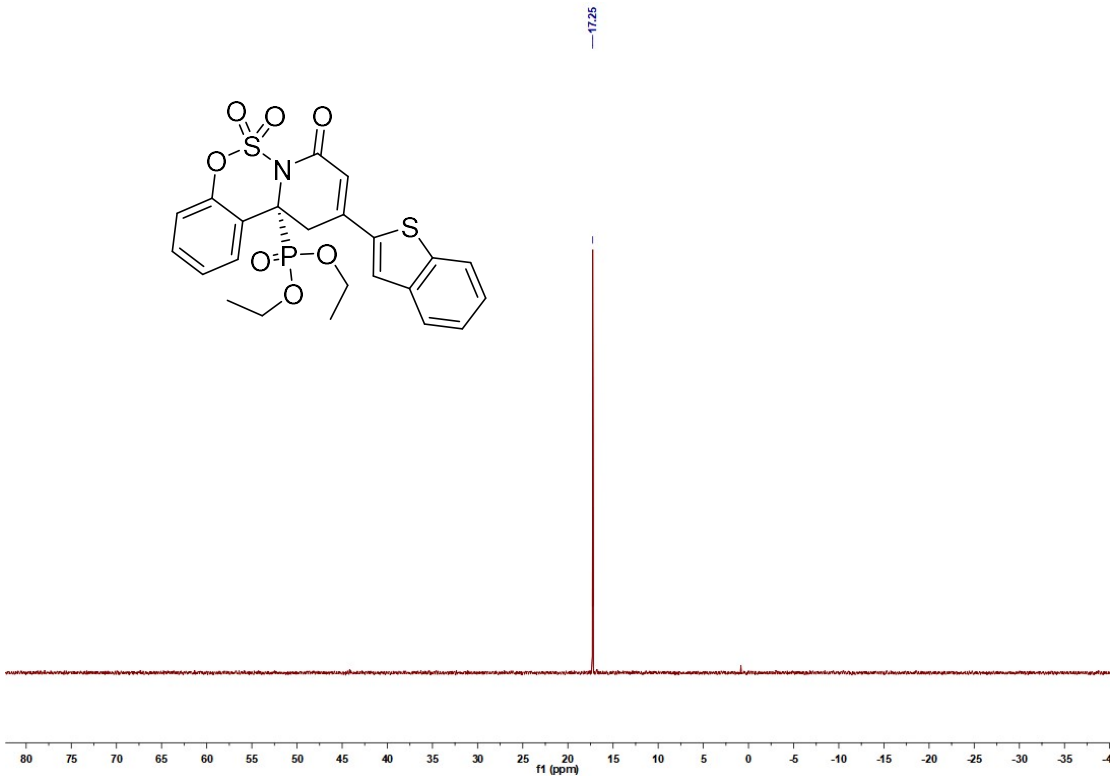
3o: ^{1}H NMR



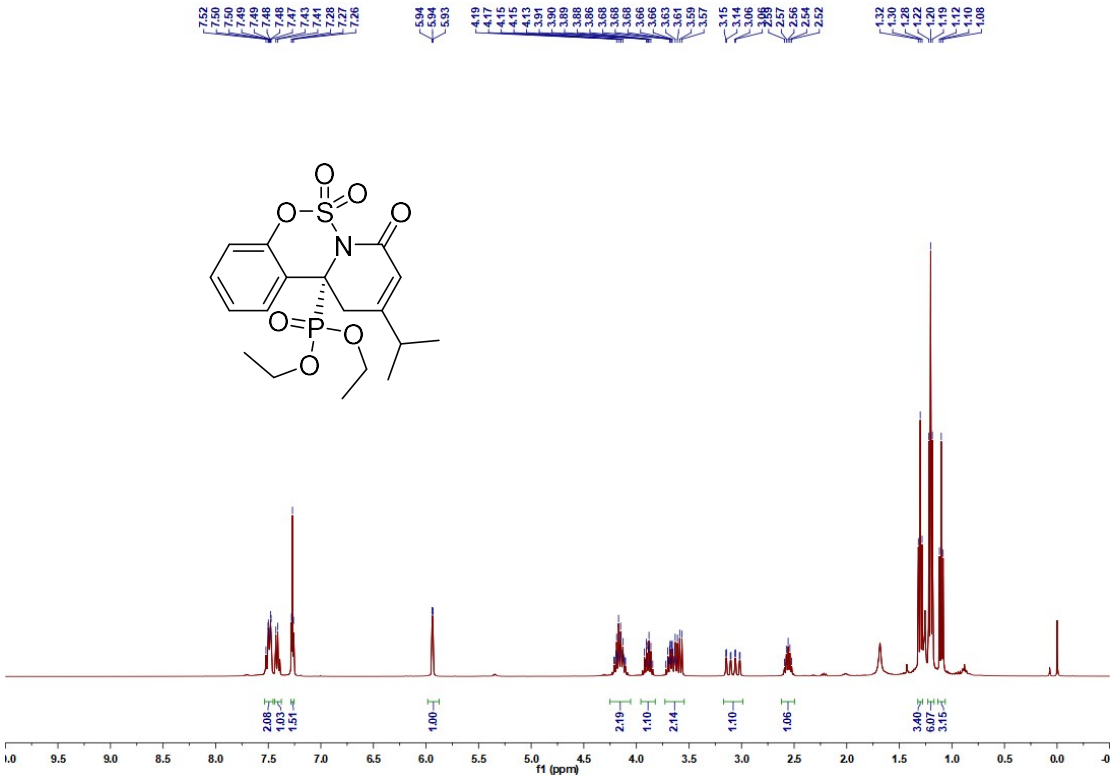
^{13}C NMR



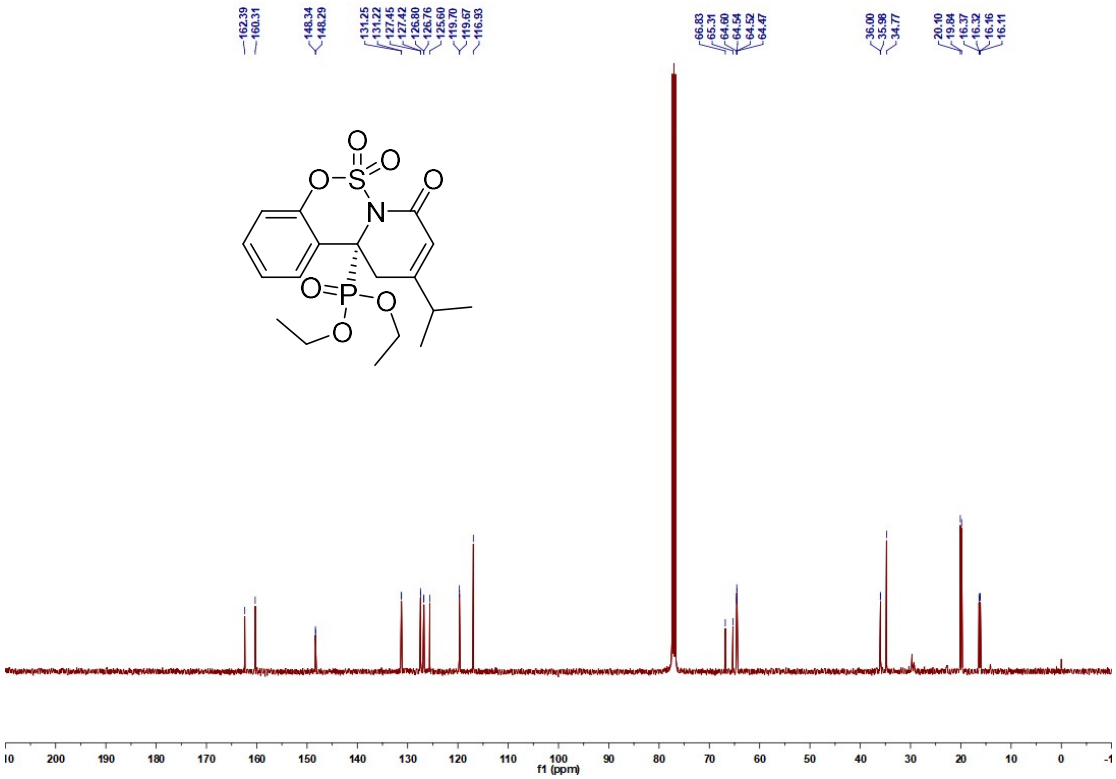
^{31}P NMR


17.25
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
f1 (ppm)

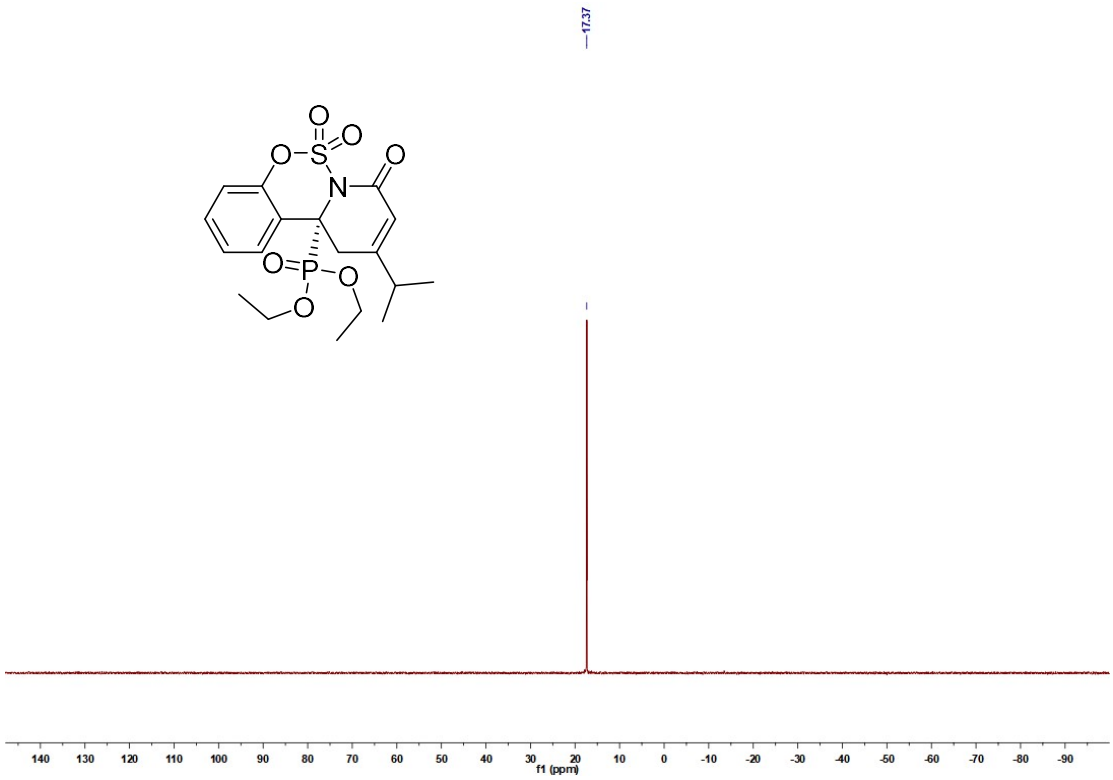
3p: ^{1}H NMR



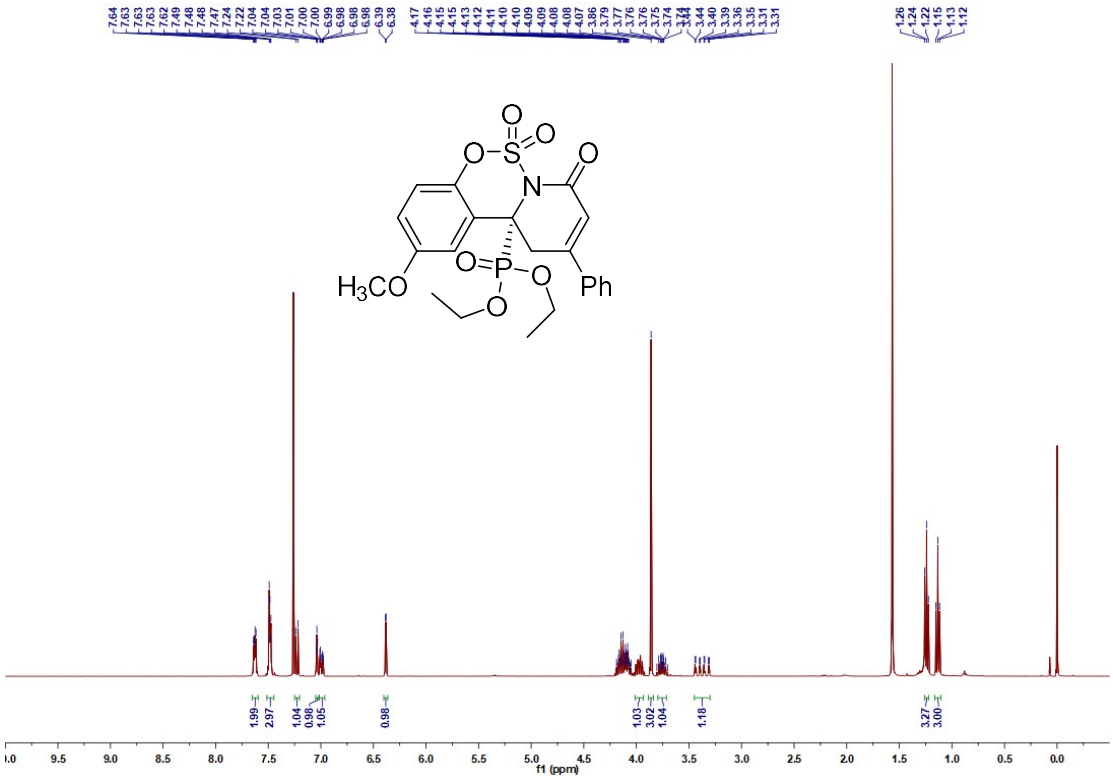
^{13}C NMR



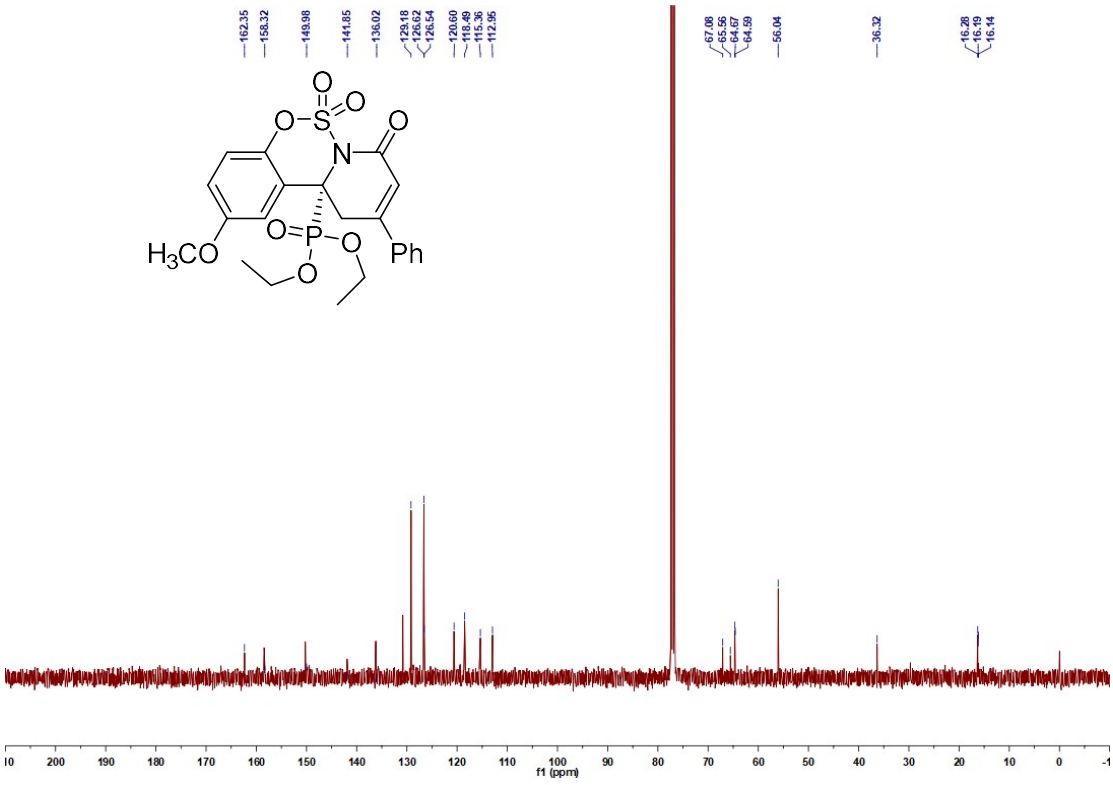
^{31}P NMR


17.37
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

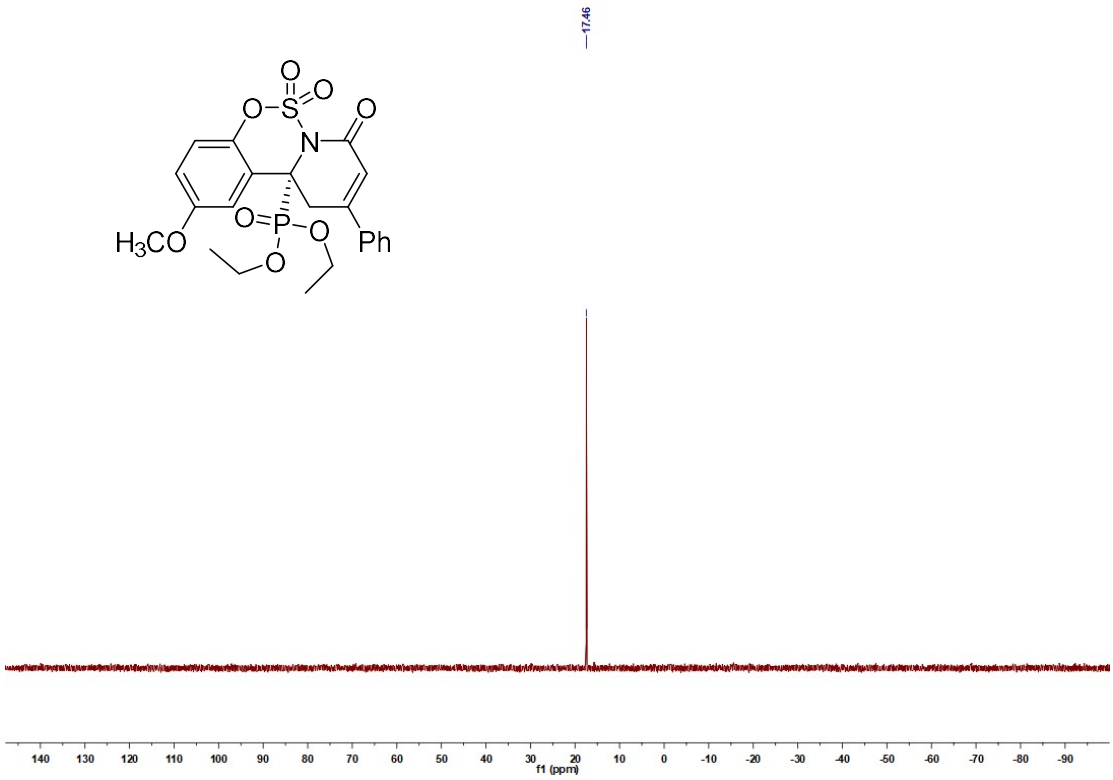
3q: ^{1}H NMR



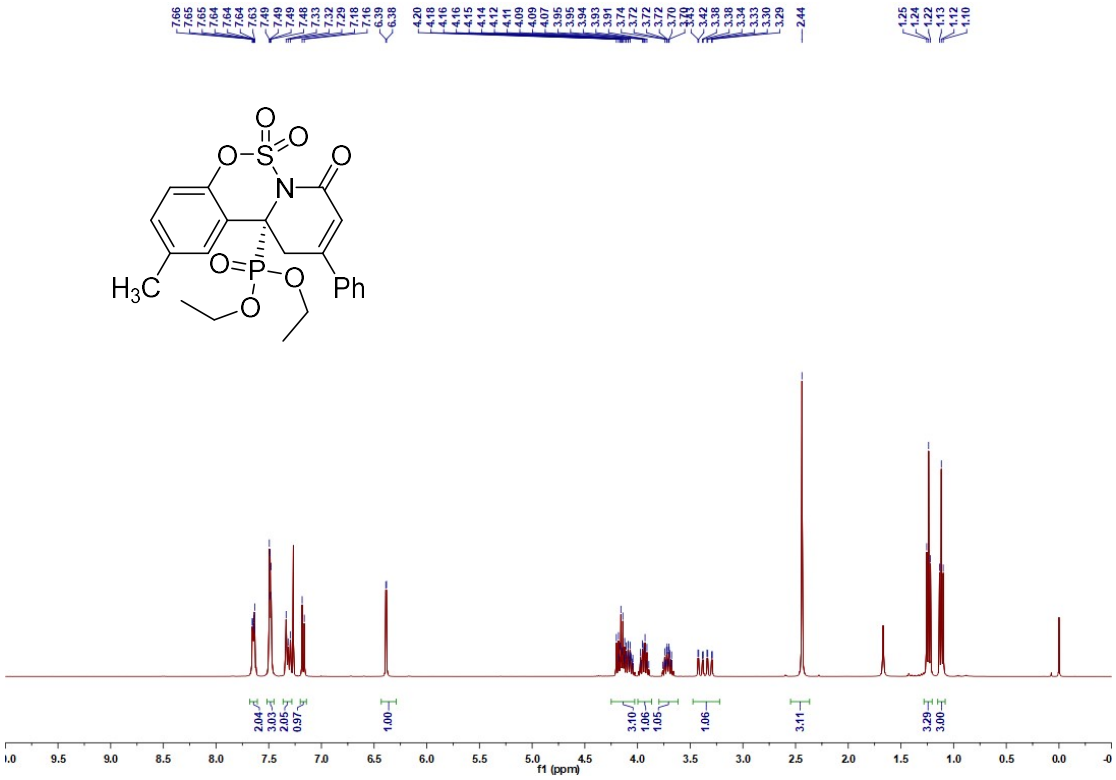
^{13}C NMR



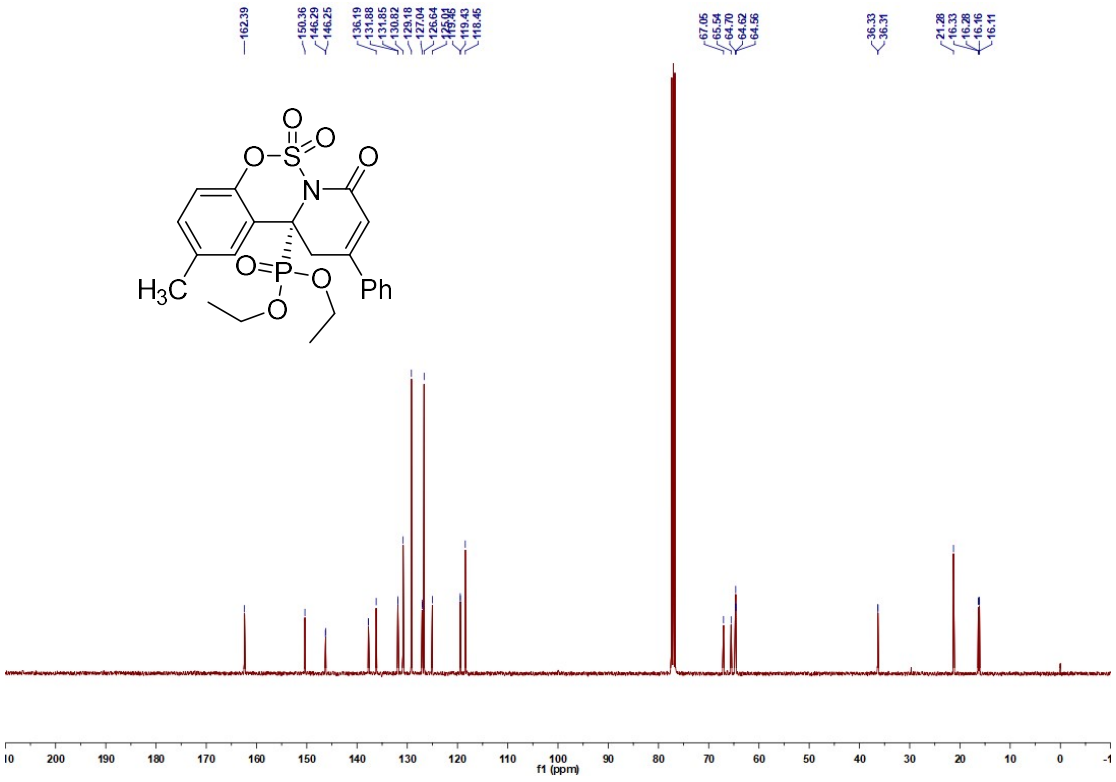
^{31}P NMR


17.46
H3CO
Ph
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

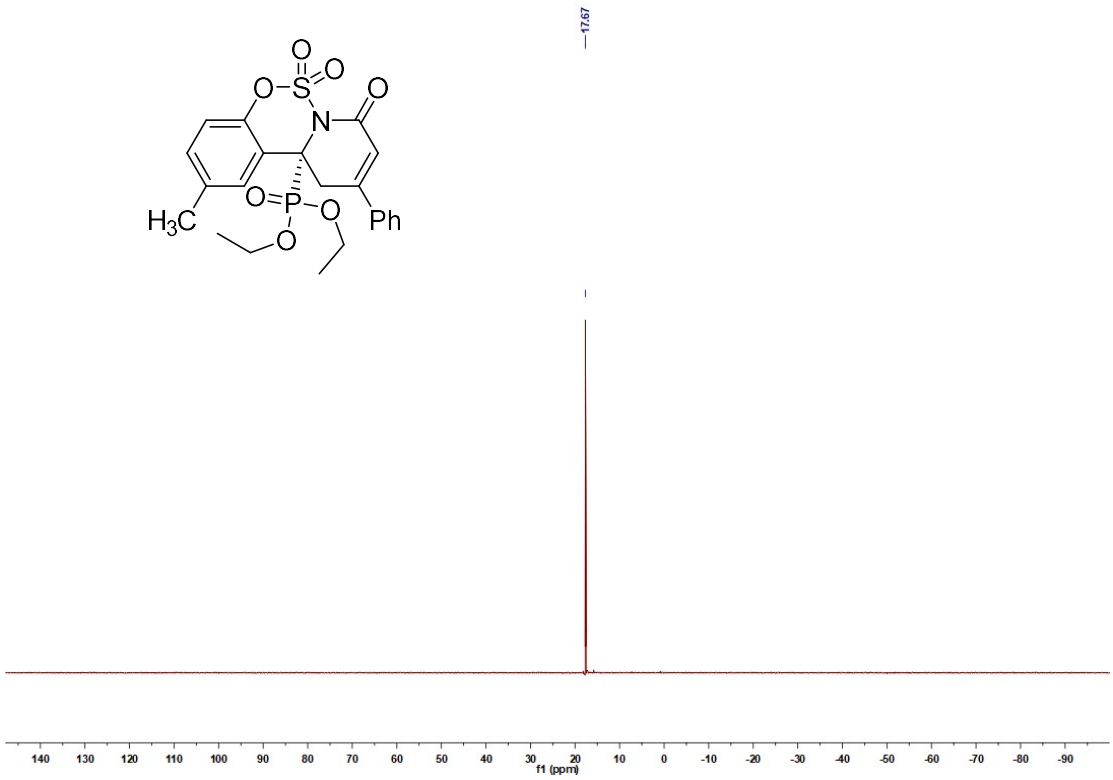
3r: **^{1}H NMR**



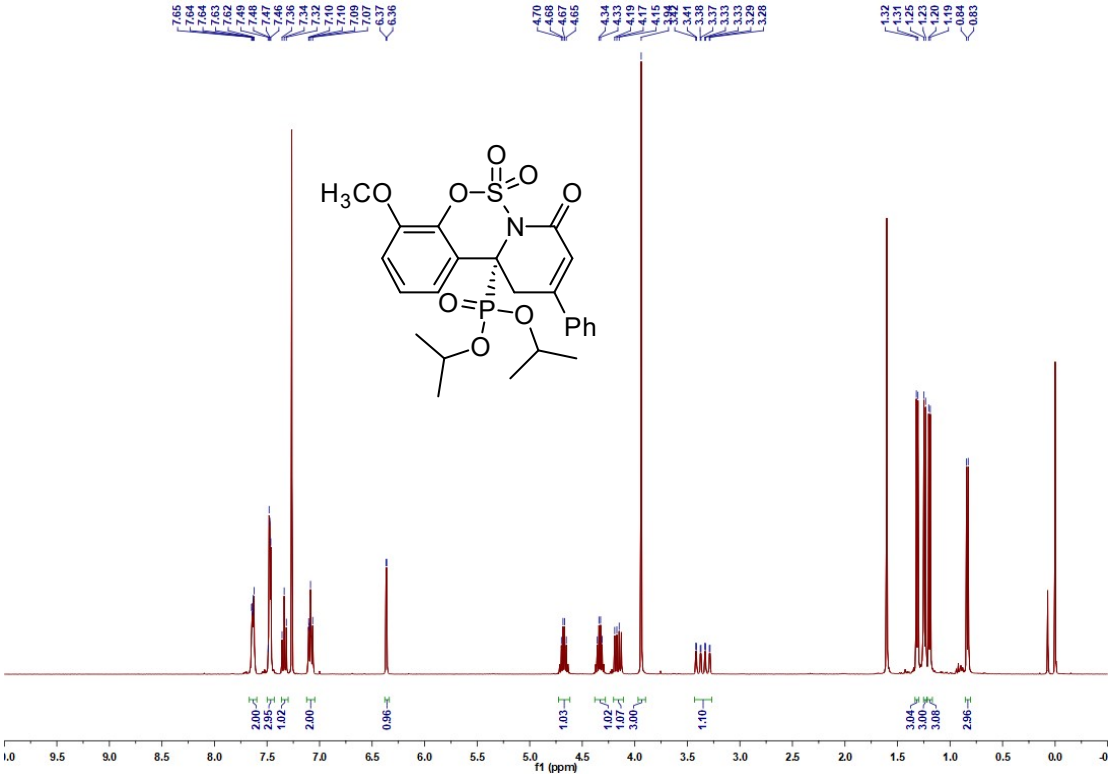
^{13}C NMR



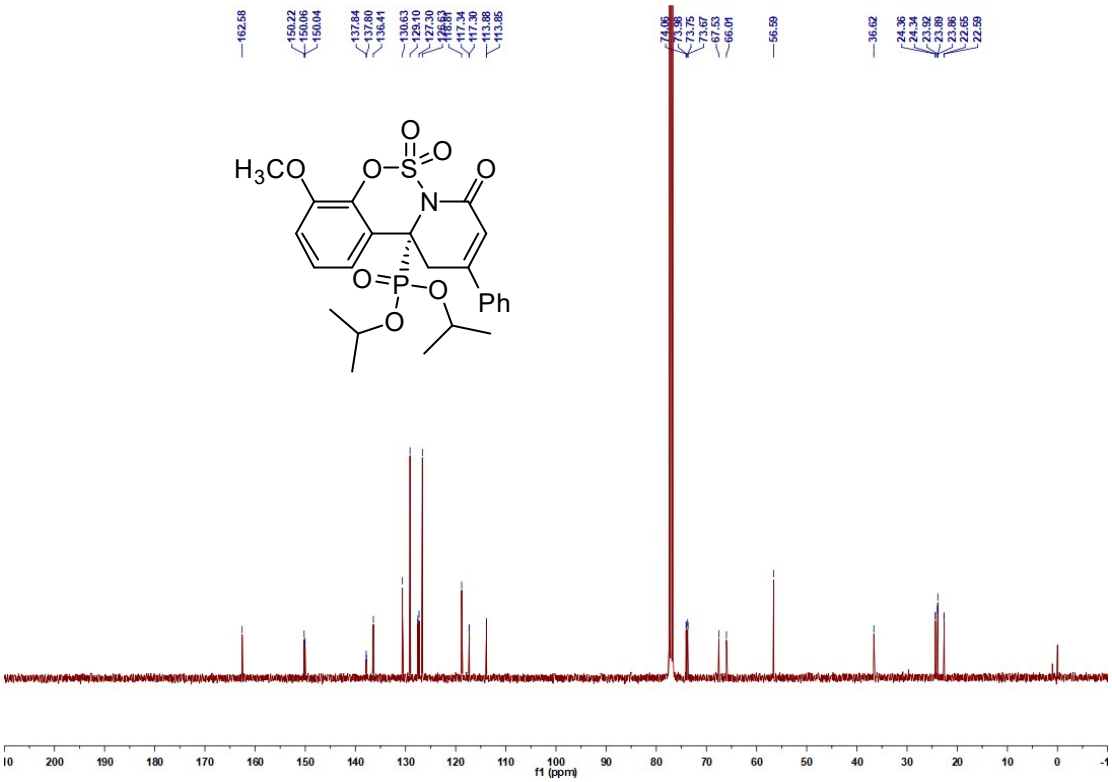
^{31}P NMR


17.67
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

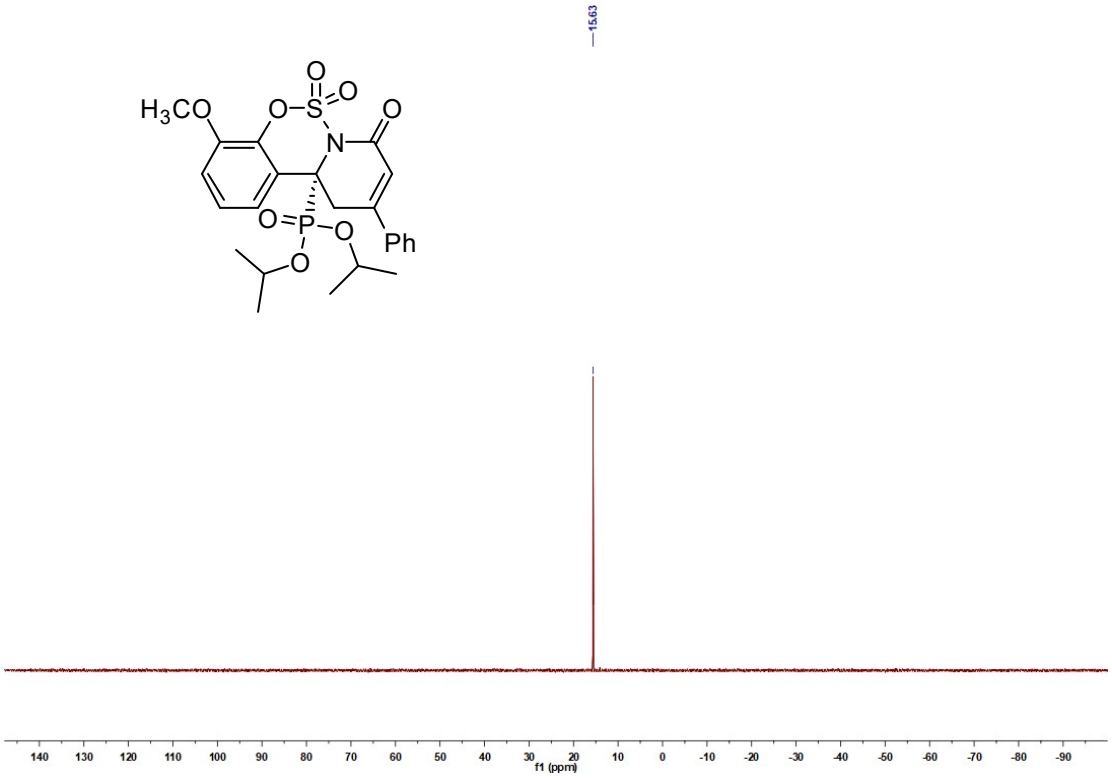
3s: ^{1}H NMR



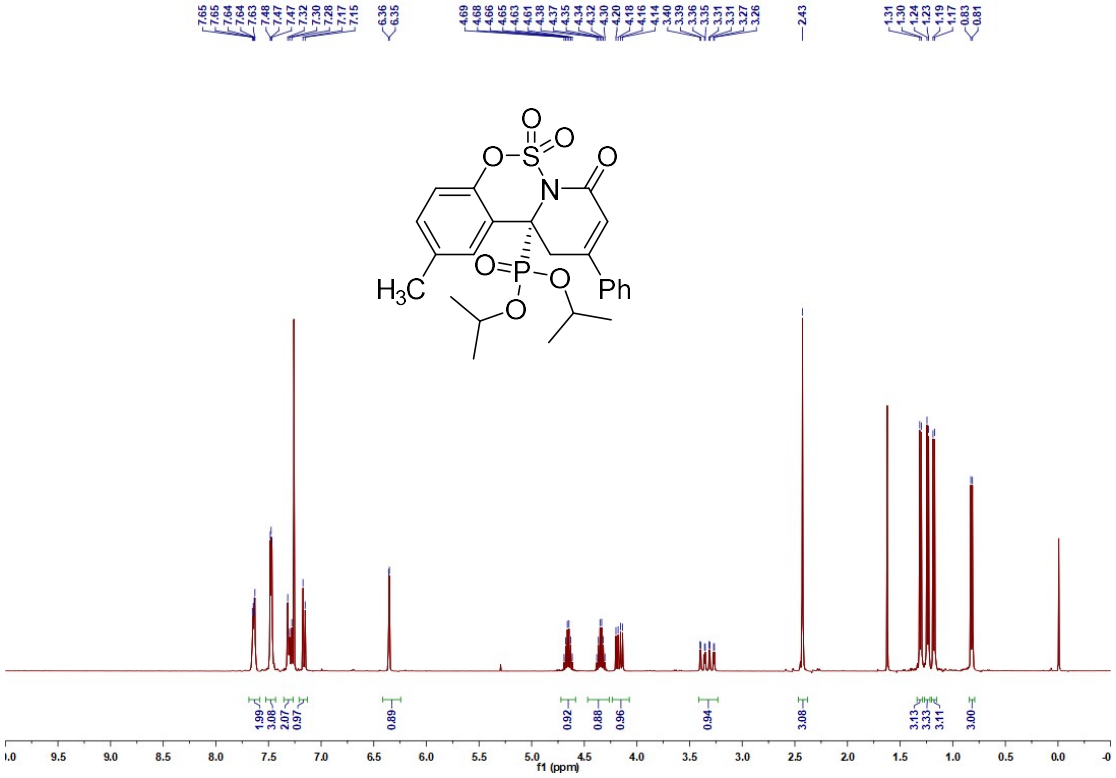
^{13}C NMR



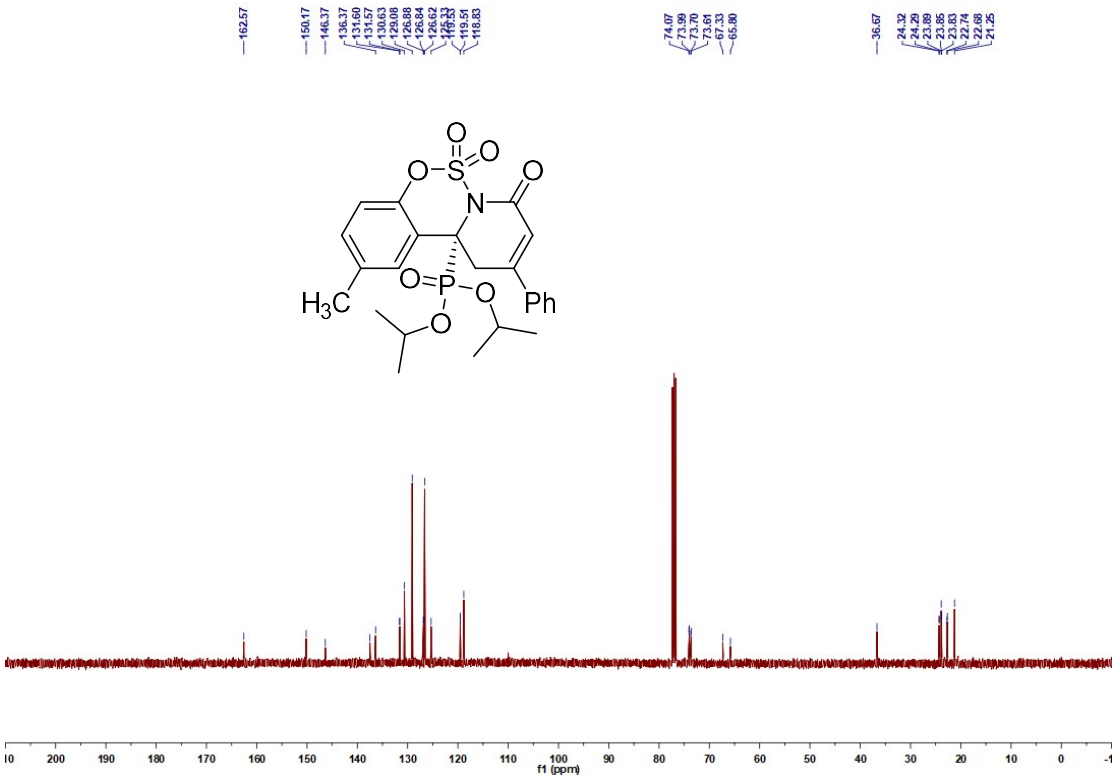
^{31}P NMR


15.63
H3CO
O
S
N
O
O
O
P
O
O
Ph
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

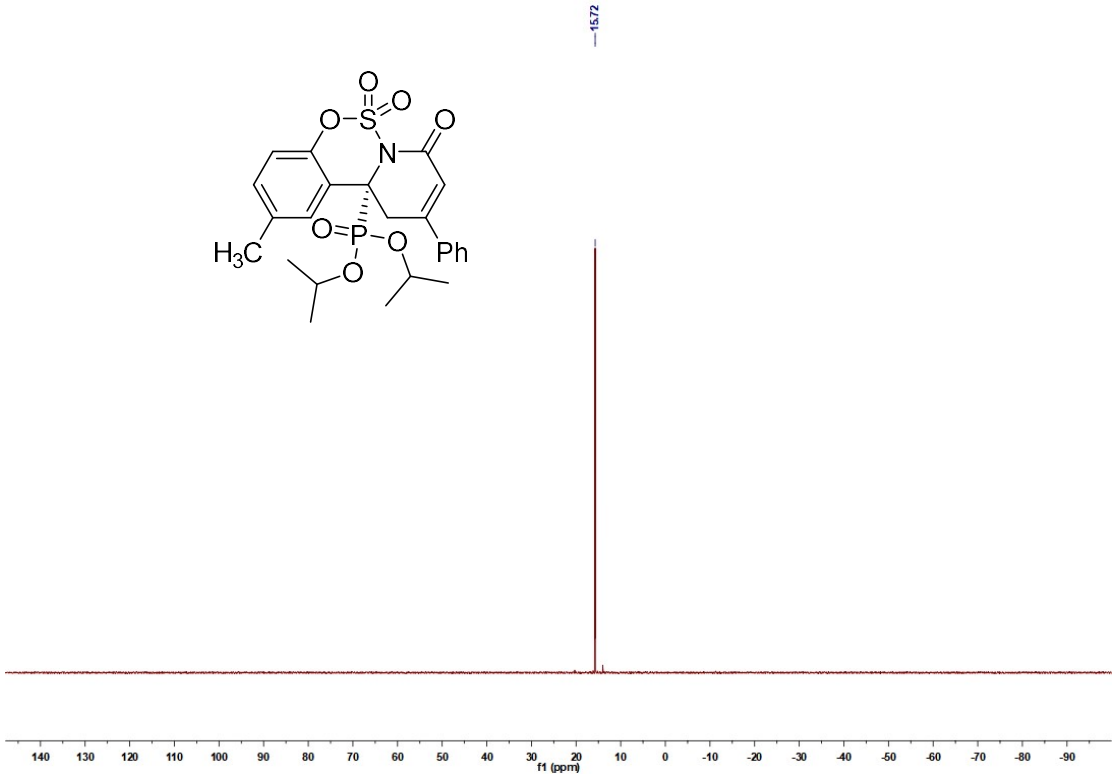
3u: ^{1}H NMR



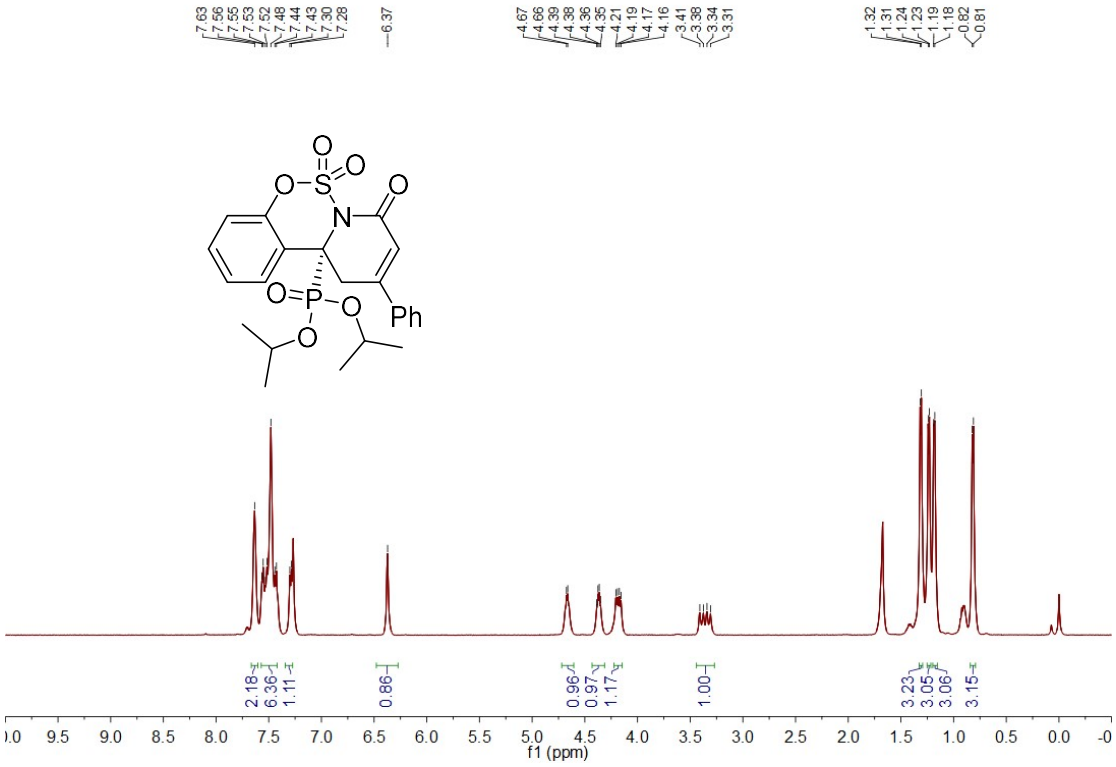
^{13}C NMR



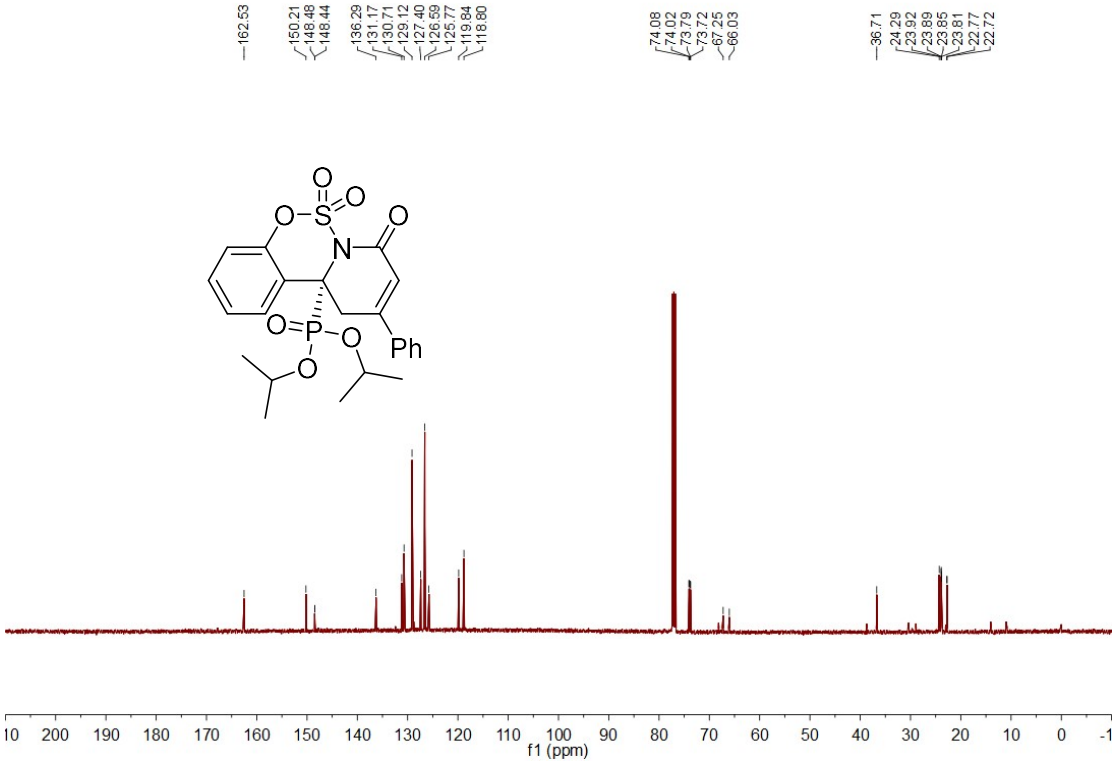
^{31}P NMR


15.72
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

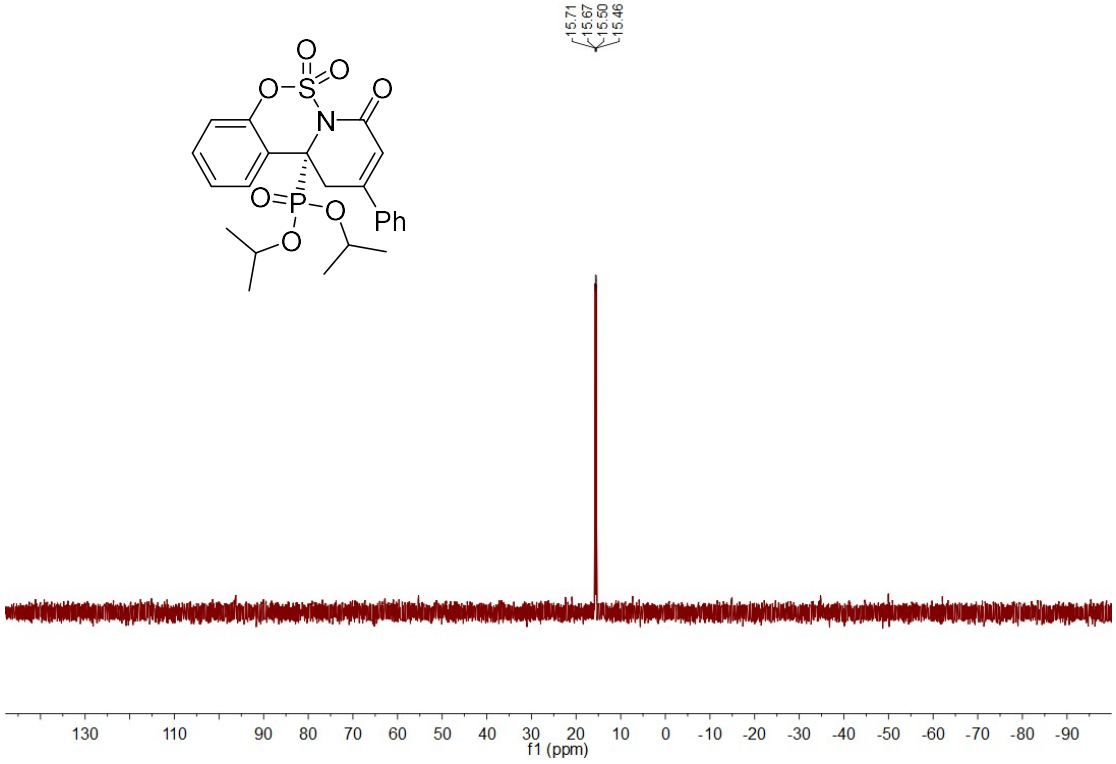
3u: ^{1}H NMR



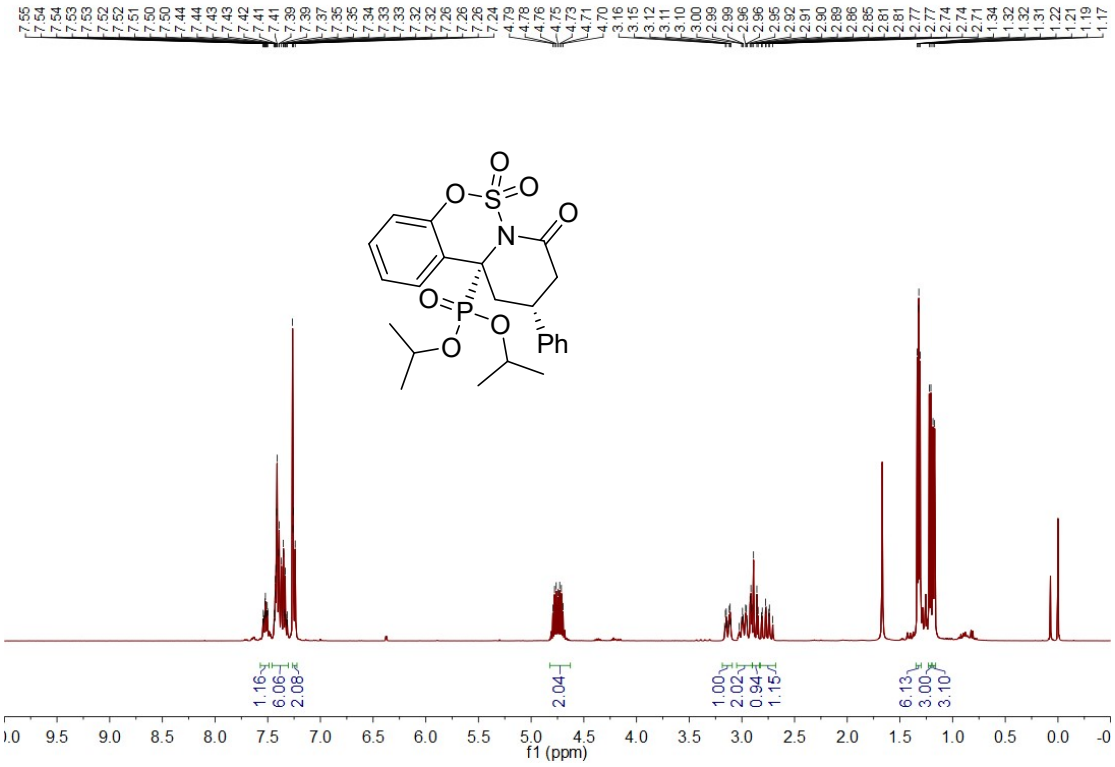
^{13}C NMR



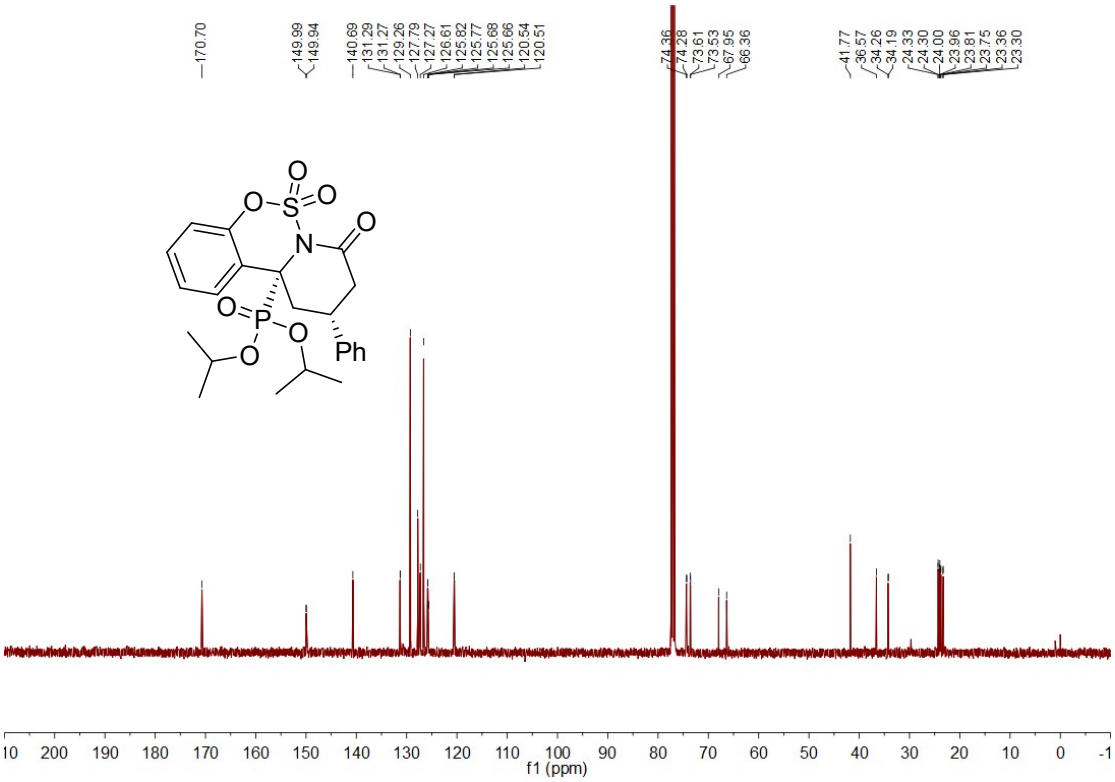
^{31}P NMR


15.71
15.67
15.50
15.46
Ph
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

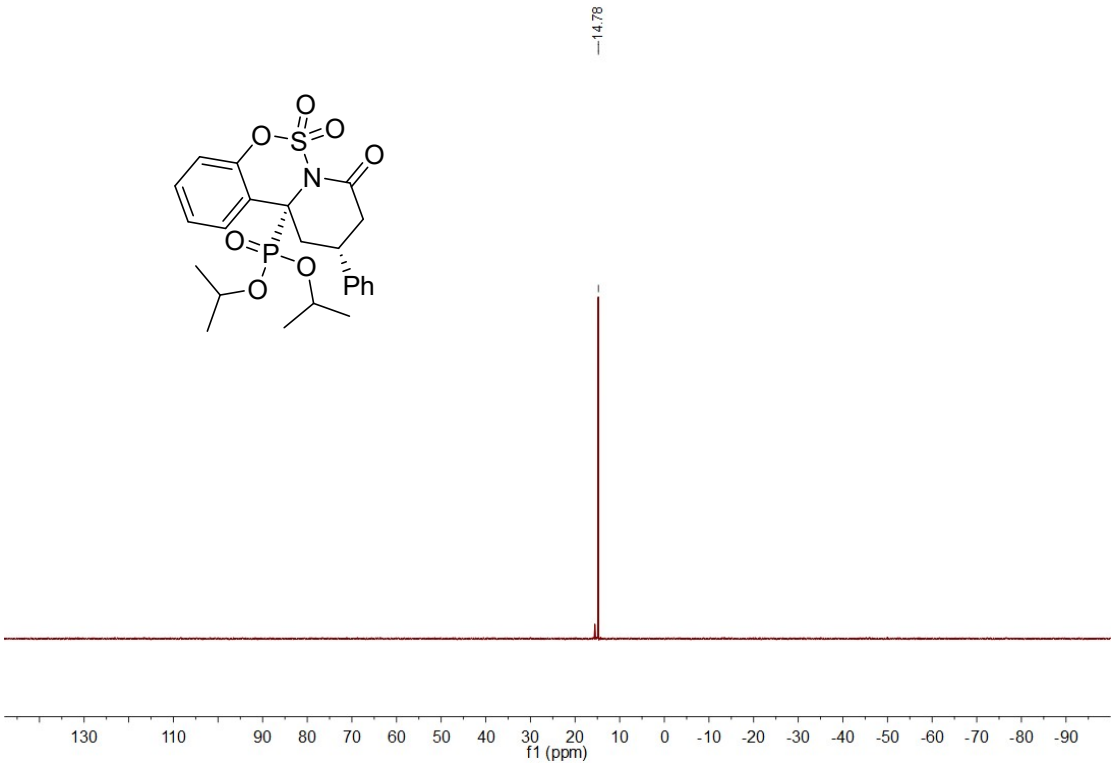
5: **^{1}H NMR**



^{13}C NMR

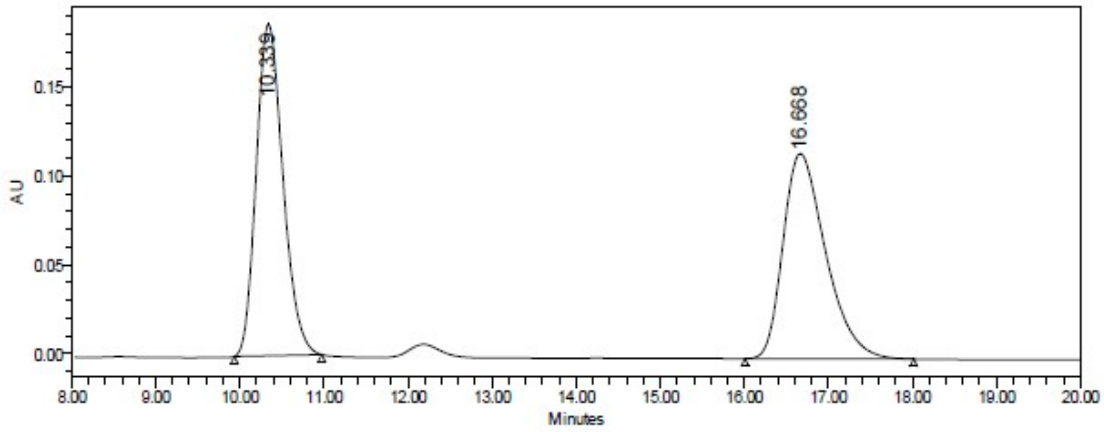


^{31}P NMR


14.78
O
O
S
O
O
N
O
O
P
O
O
Ph
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)

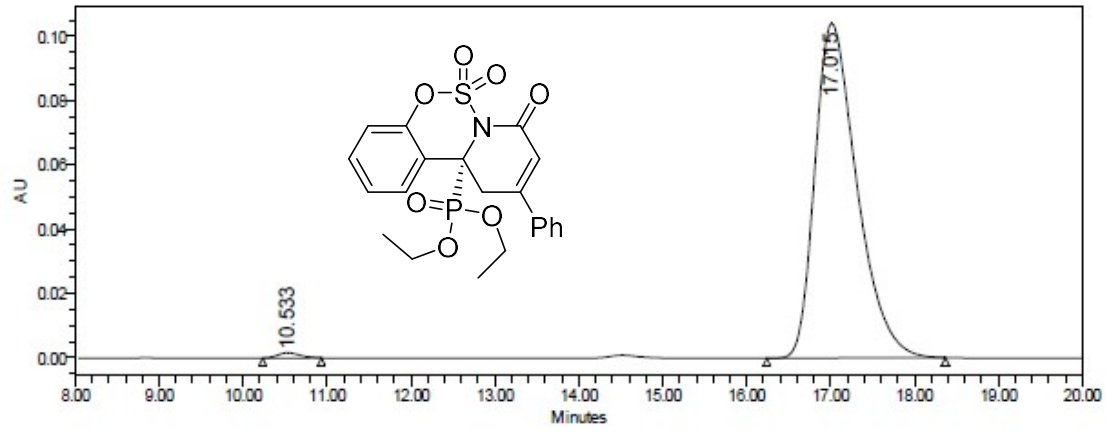
Ⅹ. HPLC spectra of products

Racemic 3a



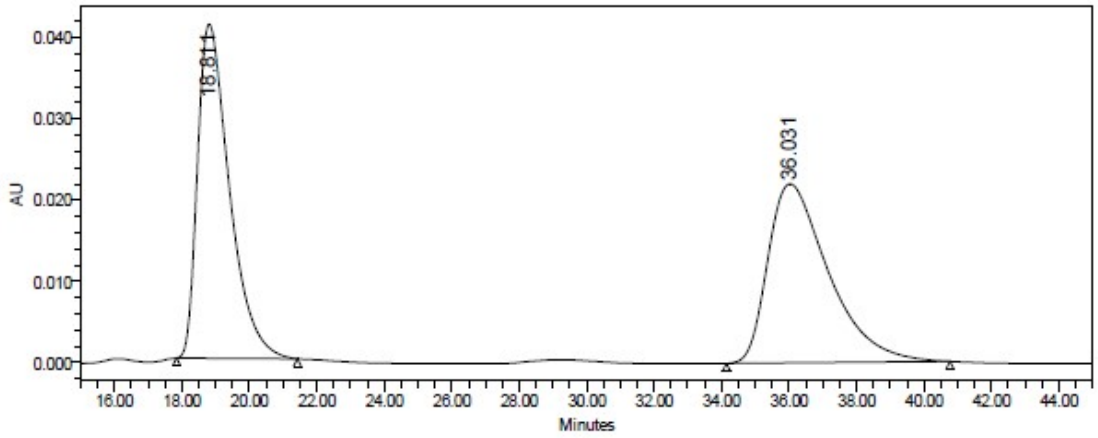
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.339	bb	62.500	4123853	186784	50.38
2	16.668	bb	120.500	4062379	115531	49.62
Sum				8186232.2	302315.4	100.0

Enantioenriched 3a



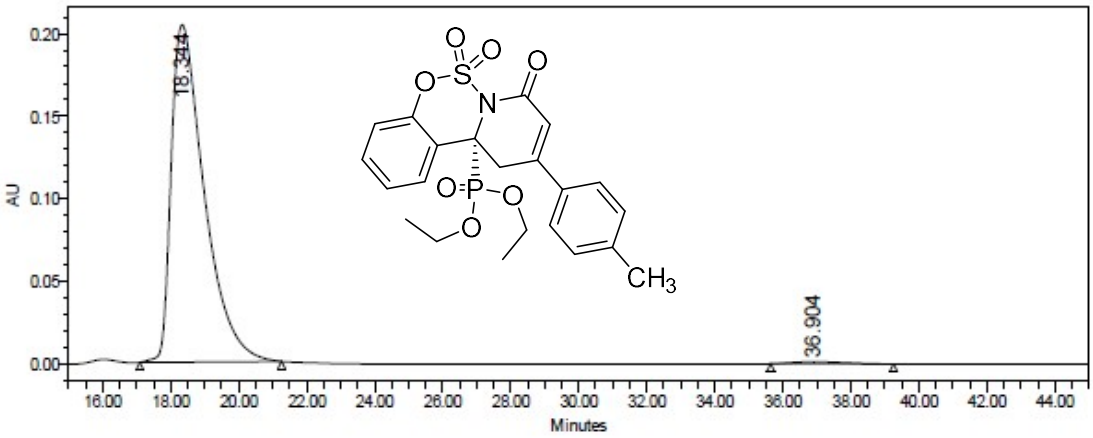
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.533	bb	42.000	29568	1612	0.81
2	17.015	bb	127.500	3626871	104095	99.19
Sum				3656438.5	105706.4	100.0

Racemic 3b



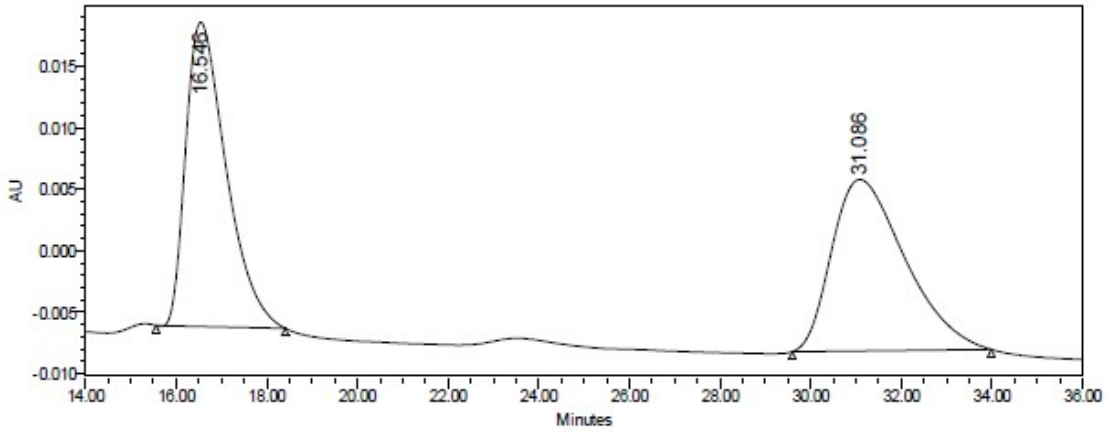
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	18.811	bb	215.000	2705218	41165	49.57
2	36.031	bb	397.500	2752368	22040	50.43
Sum				5457586.1	63204.7	100.0

Enantioenriched 3b



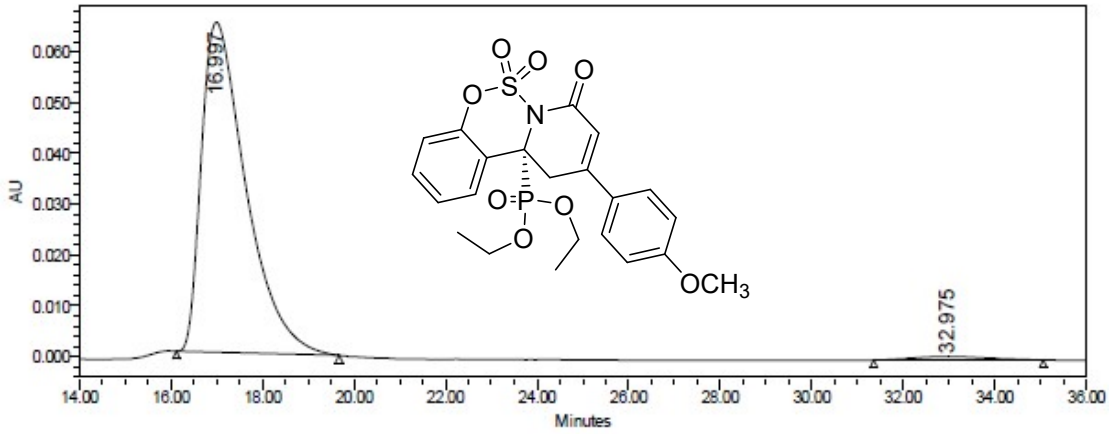
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	18.344	bb	250.000	13773503	204235	99.07
2	36.904	bb	216.500	129675	1196	0.93
Sum				13903178.6	205431.8	100.0

Racemic 3c



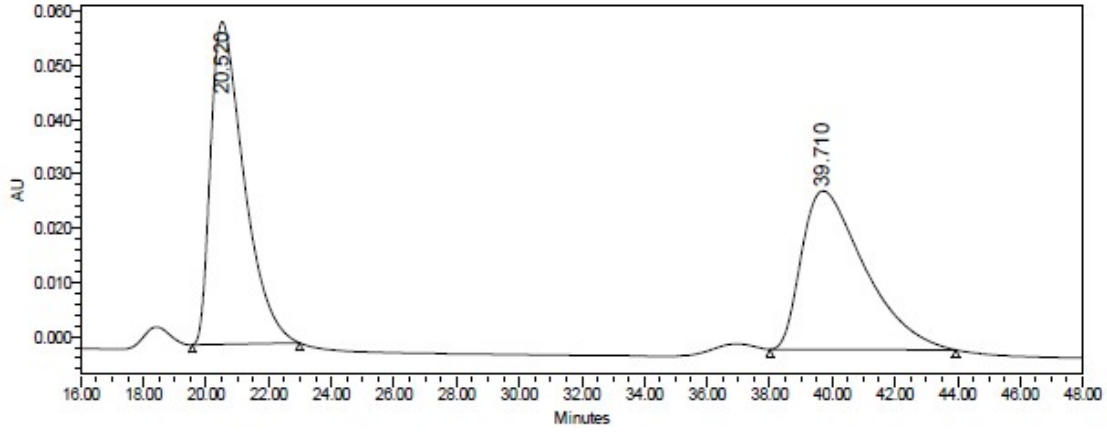
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.546	bb	171.000	1531997	24736	49.49
2	31.086	bb	263.500	1563863	13934	50.51
Sum				3095860.5	38670.0	100.0

Enantioenriched 3c



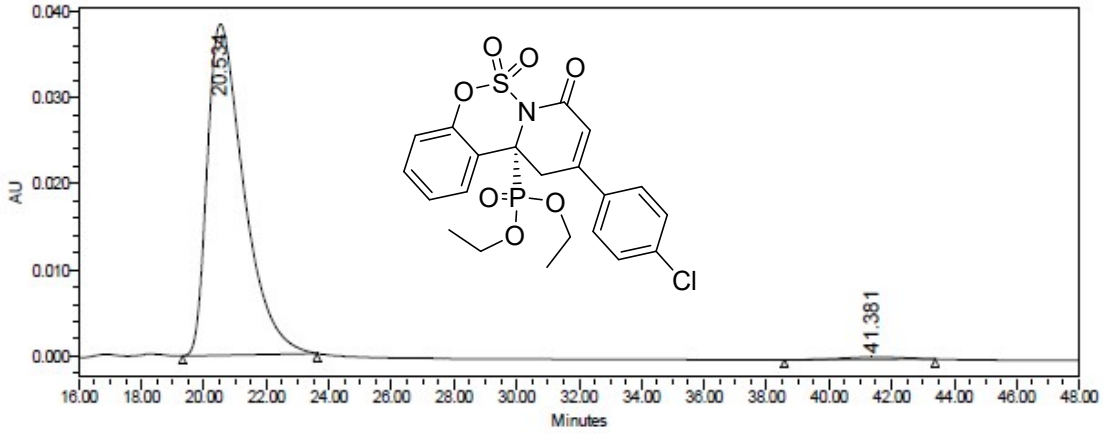
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.997	bb	213.000	4398501	65103	98.29
2	32.975	bb	222.000	76555	682	1.71
Sum				4475056.3	65784.3	100.0

Racemic 3d



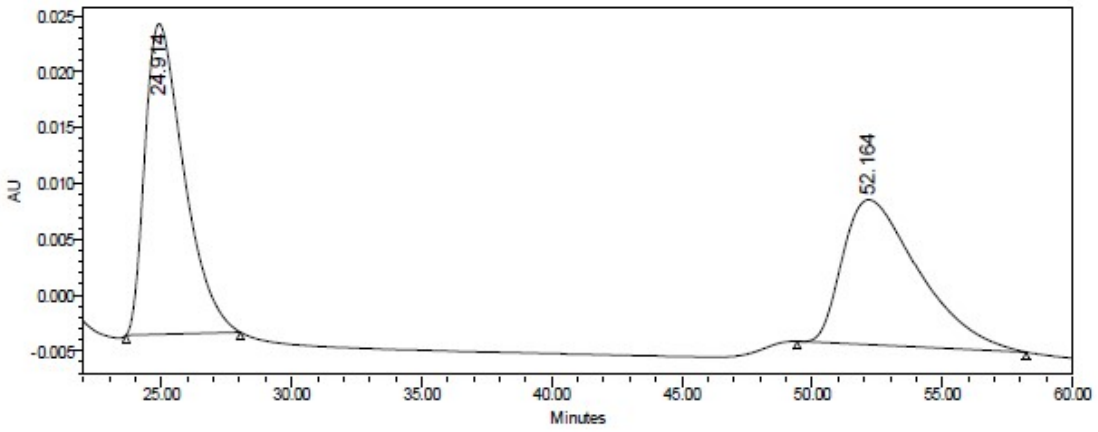
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	20.520	bb	205.500	4408046	59446	51.81
2	39.710	bb	356.500	4099709	29251	48.19
Sum				8507755.0	88697.6	100.0

Enantioenriched 3d



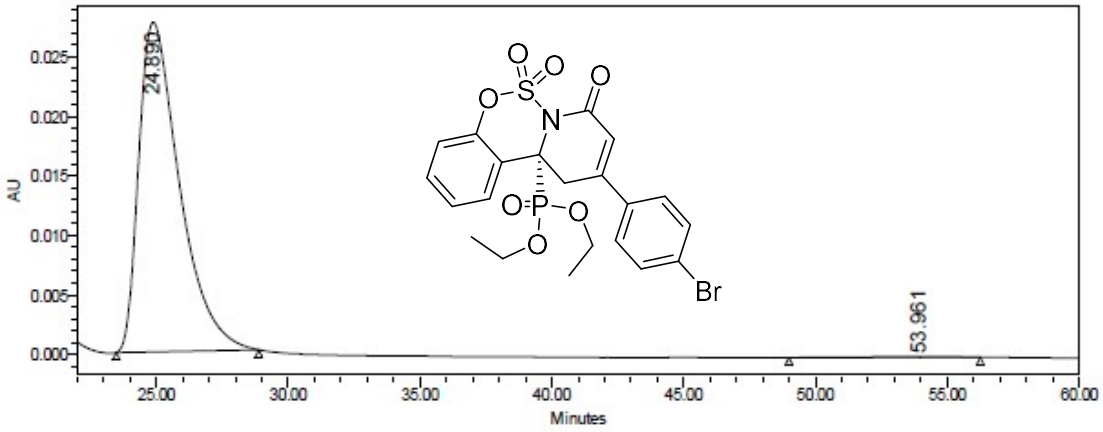
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	20.534	bb	258.500	3112343	38406	98.87
2	41.381	bb	289.000	35412	275	1.13
Sum				3147755.5	38681.3	100.0

Racemic 3e



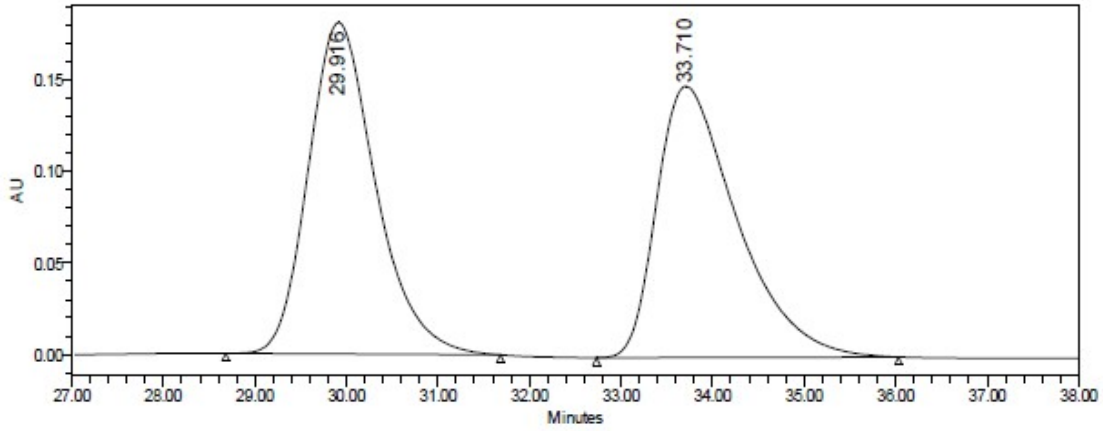
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	24.914	bb	263.500	2895055	27824	52.26
2	52.164	bb	527.500	2644974	13003	47.74
Sum				5540029.5	40826.9	100.0

Enantioenriched 3e



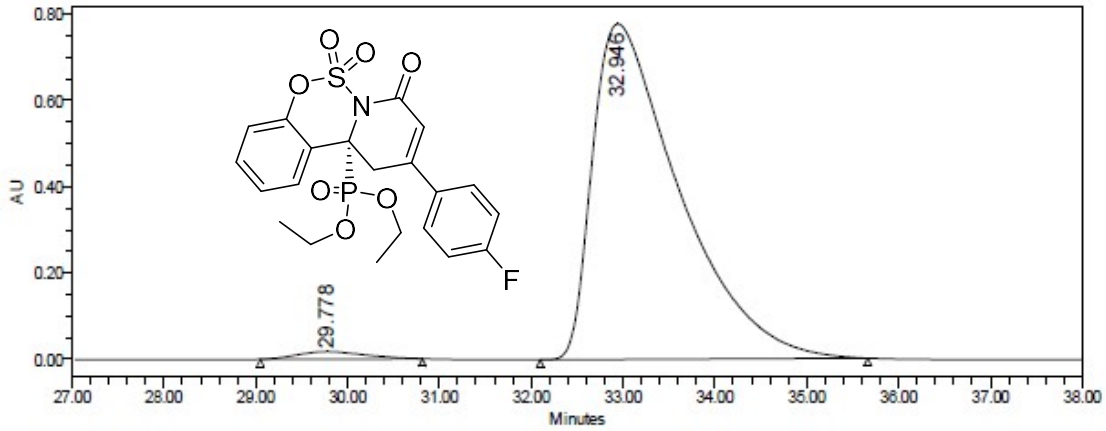
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	24.890	bb	324.000	2970293	27646	99.58
2	53.961	bb	435.500	12436	50	0.42
Sum				2982728.4	27696.1	100.0

Racemic 3f



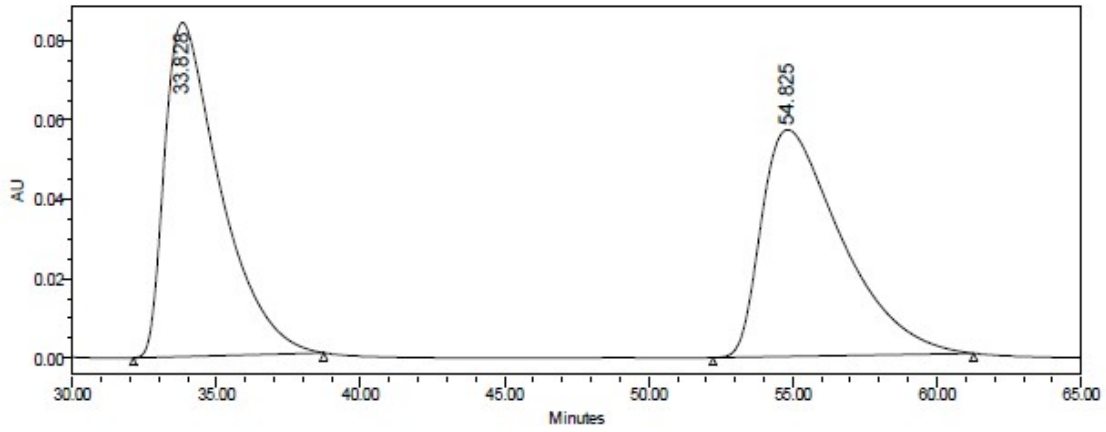
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	29.916	bb	180.000	9270133	181151	50.67
2	33.710	bb	198.000	9025443	148195	49.33
Sum				18295576.6	329346.6	100.0

Enantioenriched 3f



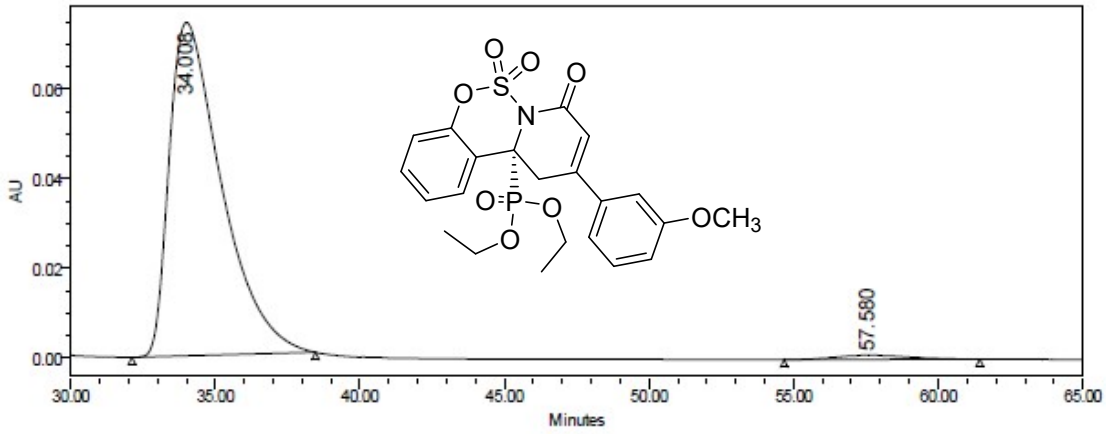
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	29.778	bb	106.000	866761	17001	1.67
2	32.946	bb	214.000	51002259	777292	98.33
Sum				51869019.7	794292.9	100.0

Racemic 3g



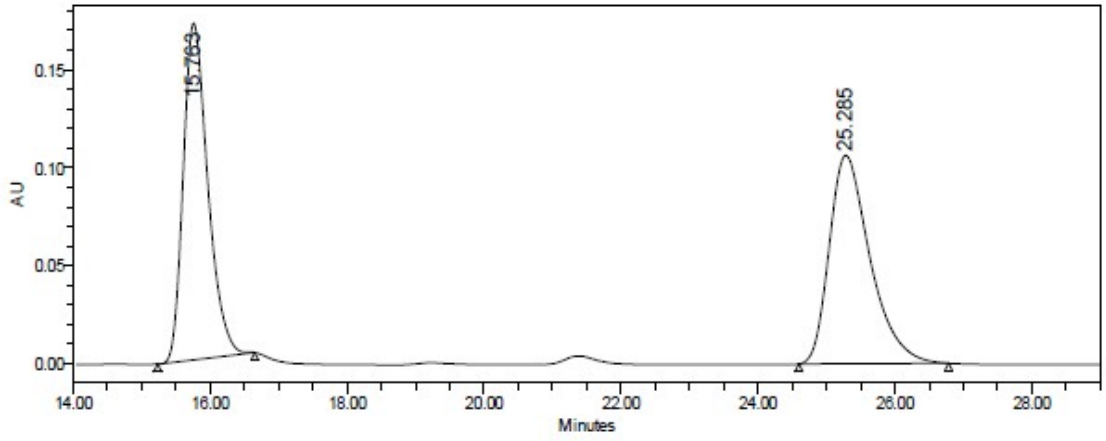
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	33.828	bb	397.000	11317465	84173	50.58
2	54.825	bb	543.000	11057667	57111	49.42
Sum				22375132.3	141283.2	100.0

Enantioenriched 3g



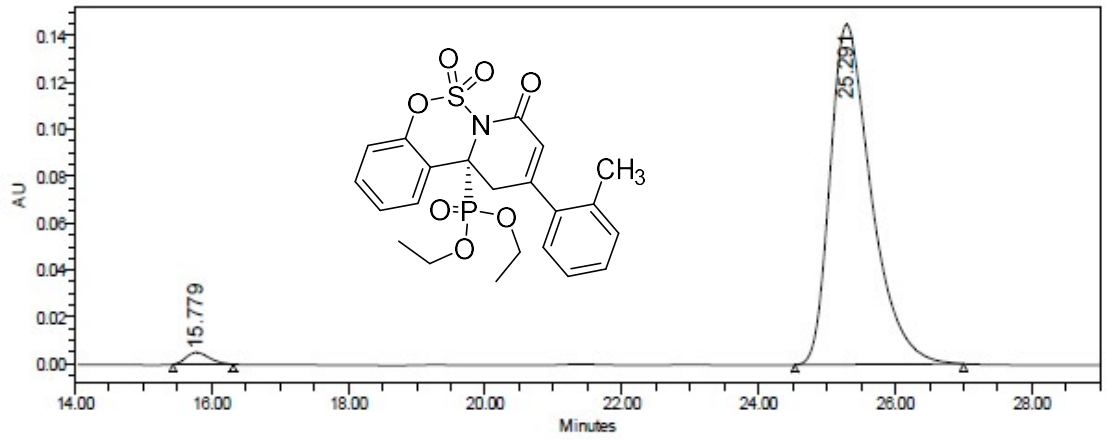
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	34.008	bb	381.000	9365517	74371	98.28
2	57.580	bb	406.500	164303	935	1.72
Sum				9529820.7	75306.6	100.0

Racemic 3h



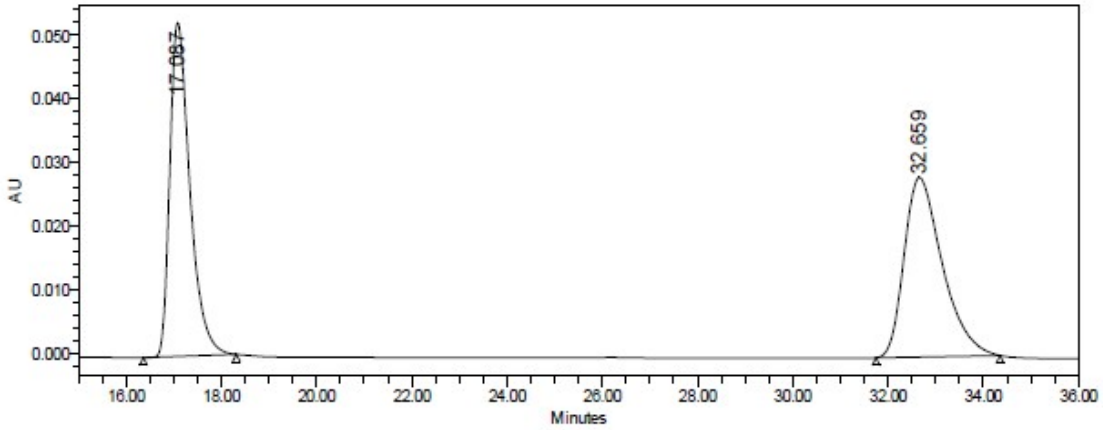
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.763	bb	85.000	4265374	171698	49.23
2	25.285	bb	131.000	4398250	106260	50.77
Sum				8663624.3	277958.1	100.0

Enantioenriched 3h



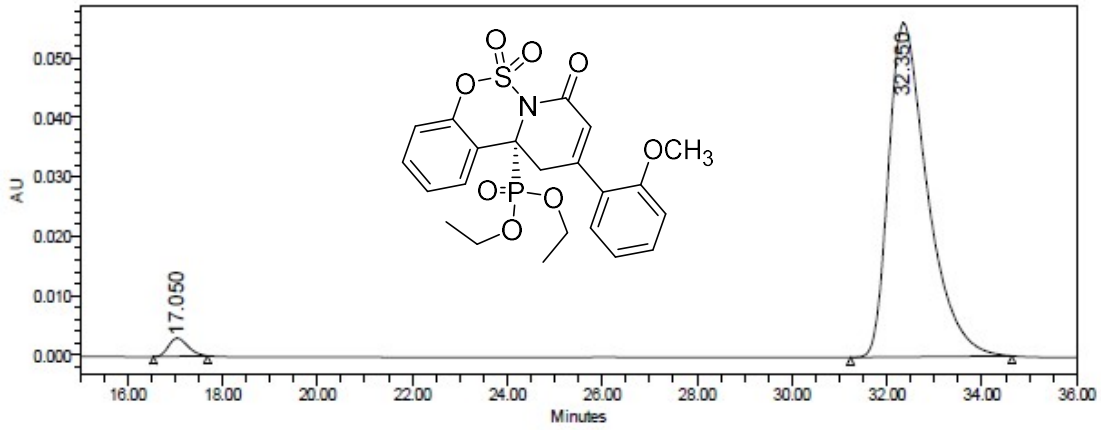
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.779	bb	53.000	118501	5041	1.91
2	25.291	bb	148.000	6075363	145043	98.09
Sum				6193863.8	150084.1	100.0

Racemic 3i



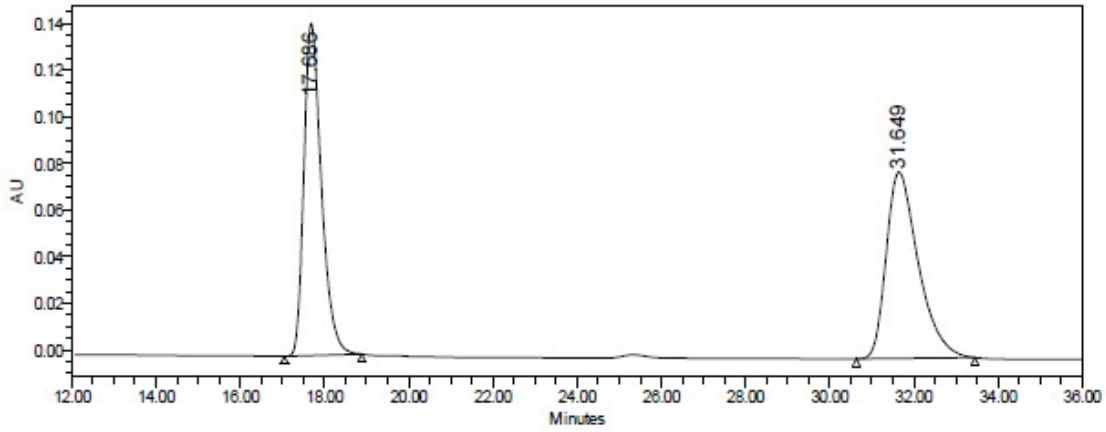
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.087	bb	117.000	1529809	52412	49.38
2	32.659	bb	156.000	1568209	28178	50.62
Sum				3098018.0	80590.1	100.0

Enantioenriched 3i



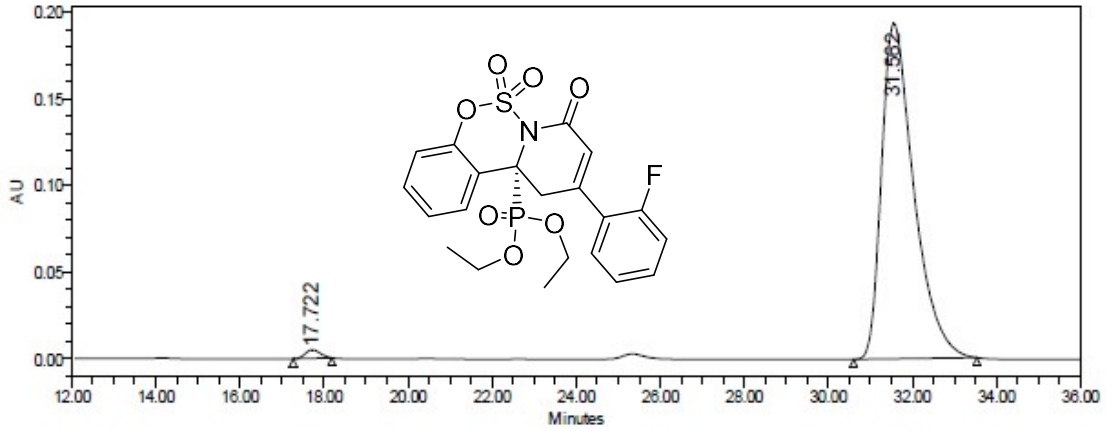
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.050	bb	68.000	86115	3057	2.63
2	32.350	bb	204.000	3194269	56206	97.37
Sum				3280384.4	59262.4	100.0

Racemic 3j



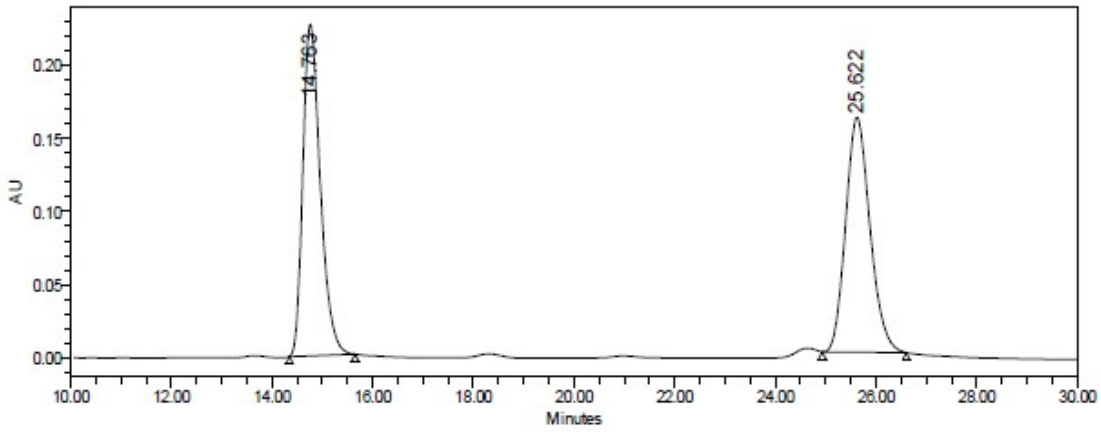
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.686	bb	110.000	4122975	142598	49.34
2	31.649	bb	169.000	4233502	79941	50.66
Sum				8356476.6	222539.2	100.0

Enantioenriched 3j



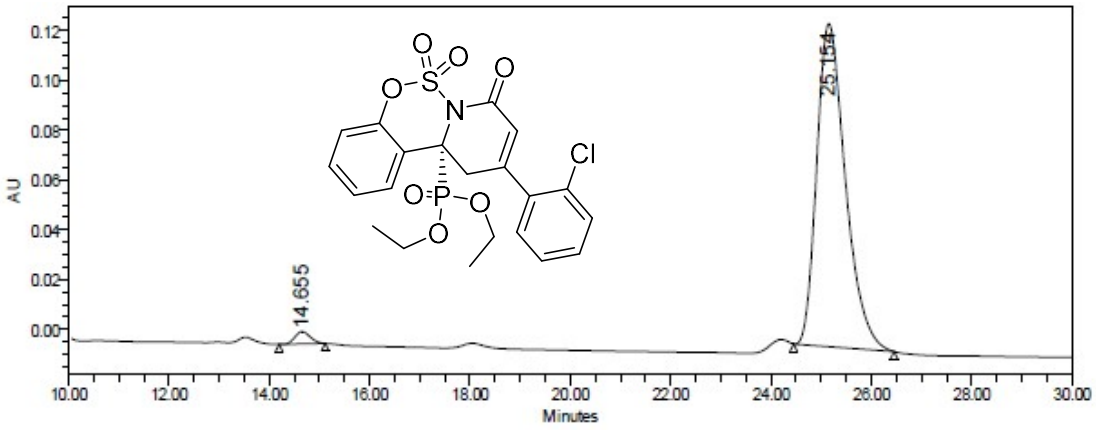
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.722	bb	55.000	121283	4860	1.16
2	31.562	bb	176.000	10338581	193543	98.84
Sum				10459863.7	198403.3	100.0

Racemic 3k



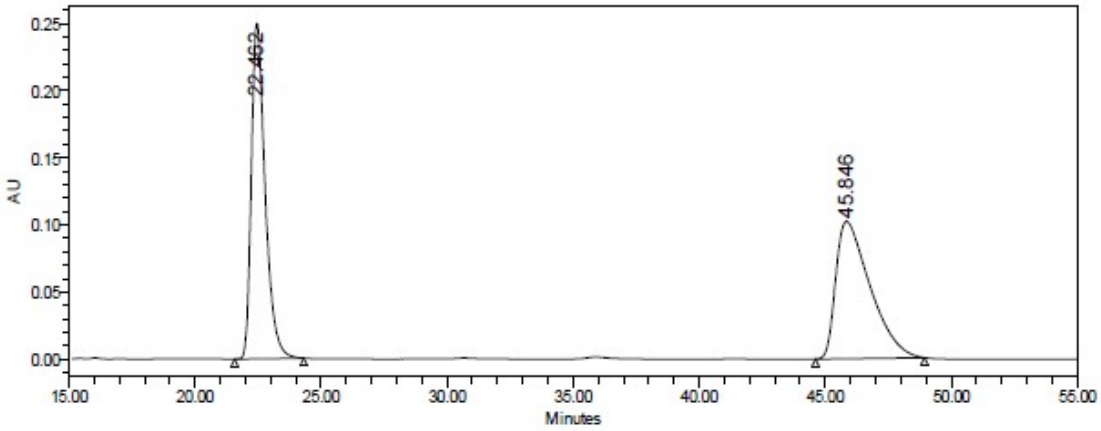
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.763	bb	78.000	5461412	227063	50.26
2	25.622	bb	100.000	5404314	160810	49.74
Sum				10865726.3	387873.0	100.0

Enantioenriched 3k



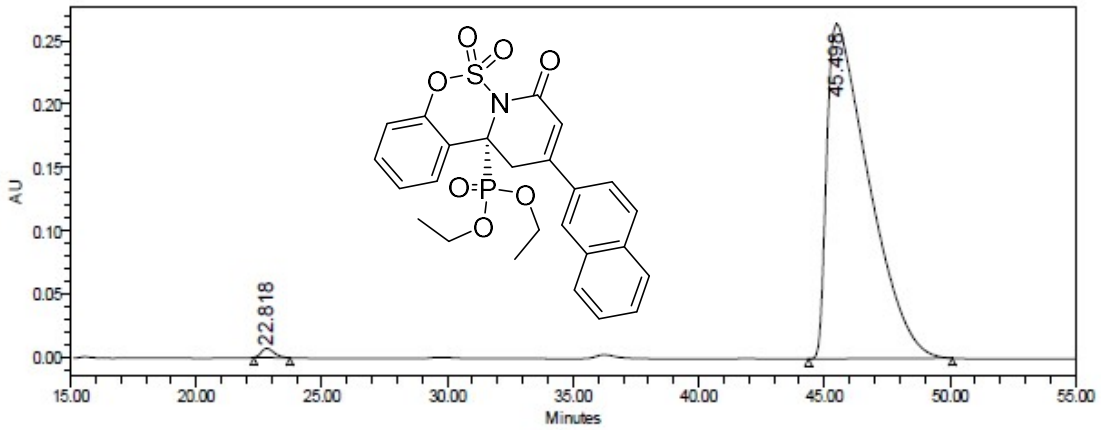
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.655	bb	55.000	102672	4938	1.96
2	25.154	bb	120.000	5146418	129693	98.04
Sum				5249089.8	134630.8	100.0

Racemic 3l



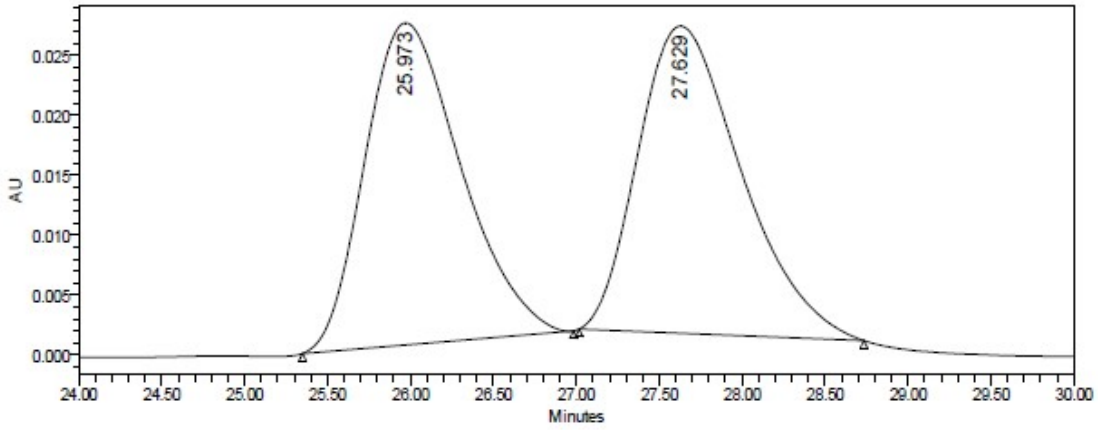
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	22.462	bb	164.000	9485339	249688	49.56
2	45.846	bb	259.000	9653005	102136	50.44
Sum				19138343.3	351823.5	100.0

Enantioenriched 3l



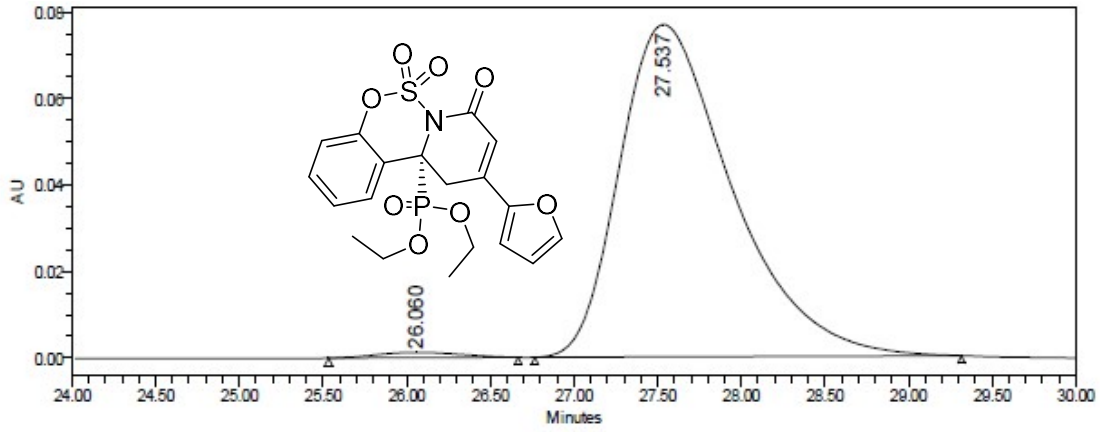
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	22.818	bb	86.000	257853	7206	0.83
2	45.498	bb	343.000	30625425	263557	99.17
Sum				30883278.1	270762.6	100.0

Racemic 3m



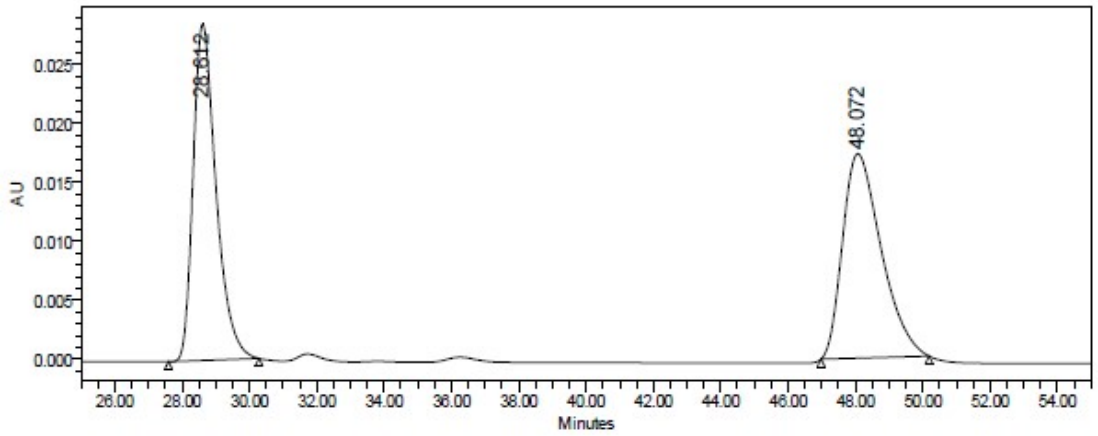
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	25.973	bb	98.000	1079302	26868	49.32
2	27.629	bb	103.000	1108870	25643	50.68
Sum				2188172.2	52511.5	100.0

Enantioenriched 3m



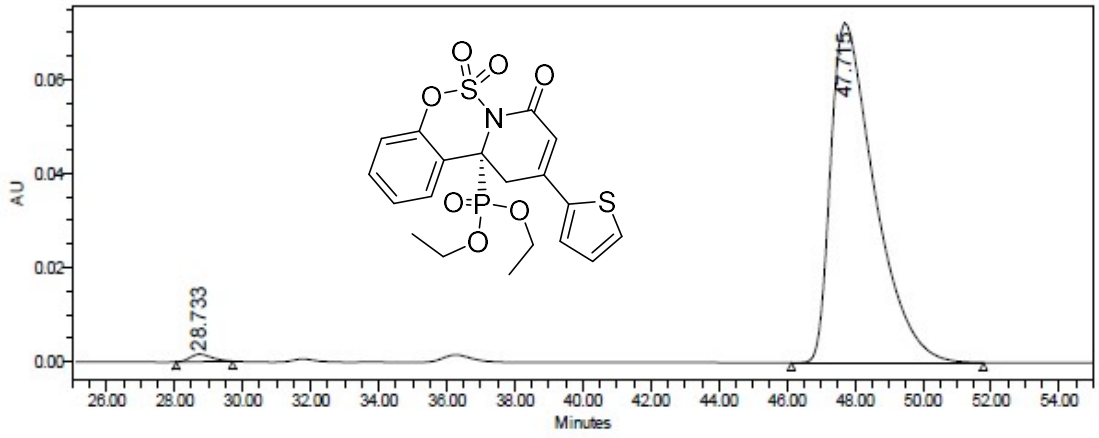
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	26.060	bb	68.000	43607	1248	1.20
2	27.537	bb	153.000	3594569	76881	98.80
Sum				3638176.4	78129.0	100.0

Racemic 3n



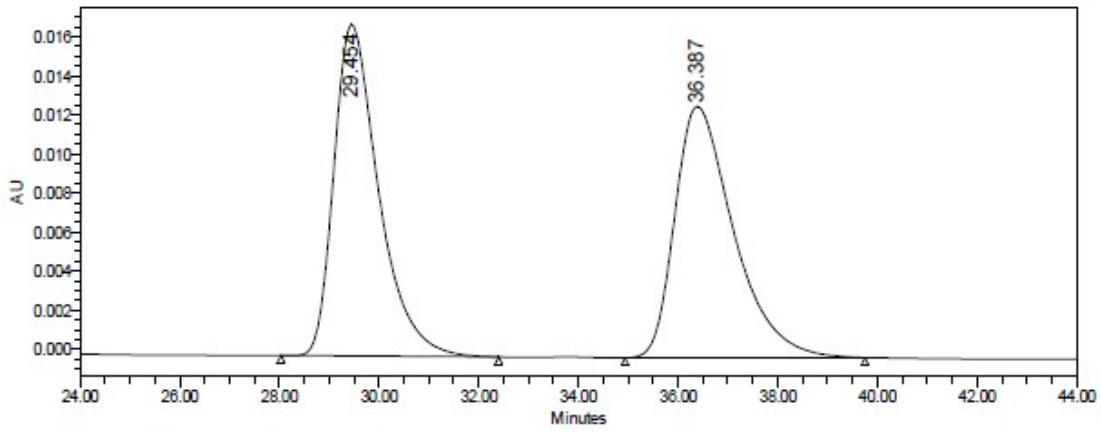
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	28.612	bb	161.000	1349149	28552	49.41
2	48.072	bb	192.000	1381490	17347	50.59
Sum				2730639.2	45898.8	100.0

Enantioenriched 3n



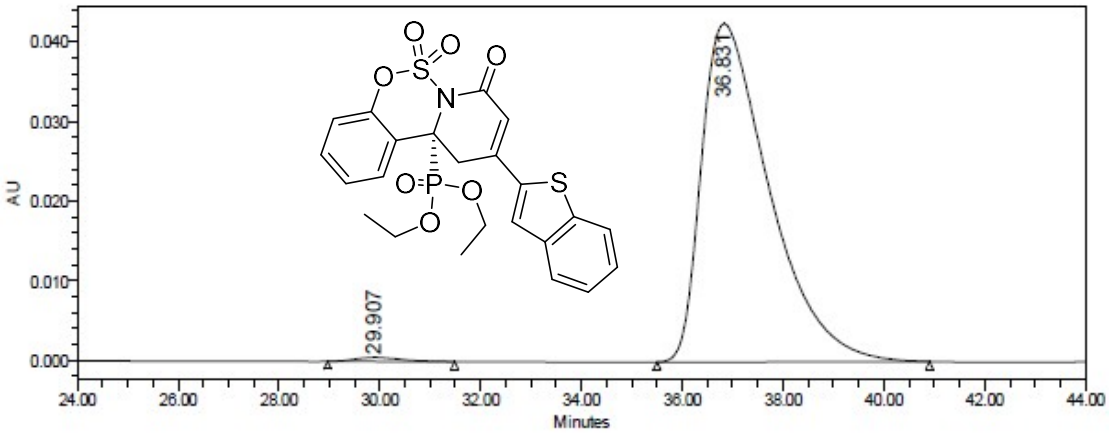
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	28.733	bb	99.000	68272	1550	1.04
2	47.715	bb	339.000	6477785	72103	98.96
Sum				6546057.0	73652.2	100.0

Racemic 3o



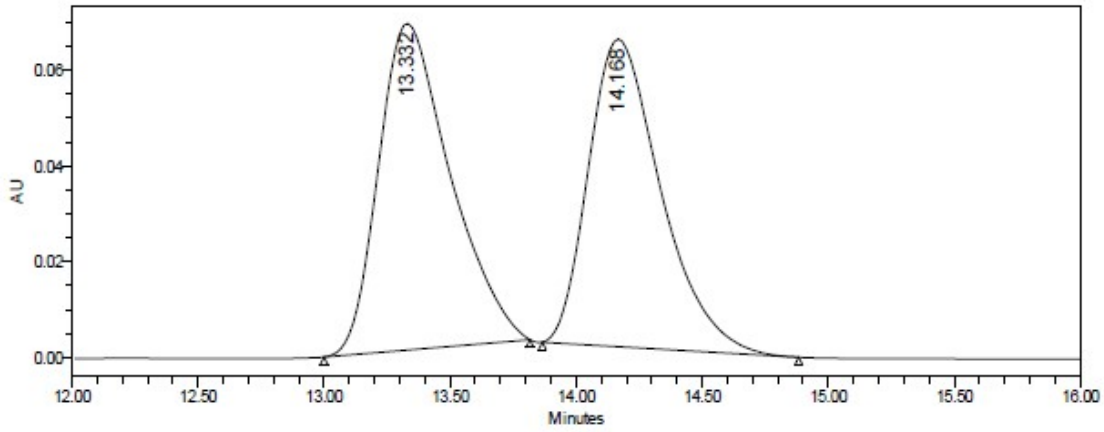
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	29.454	bb	262.000	1058009	16955	50.13
2	36.387	bb	289.000	1052495	12867	49.87
Sum				2110504.6	29821.9	100.0

Enantioenriched 3o



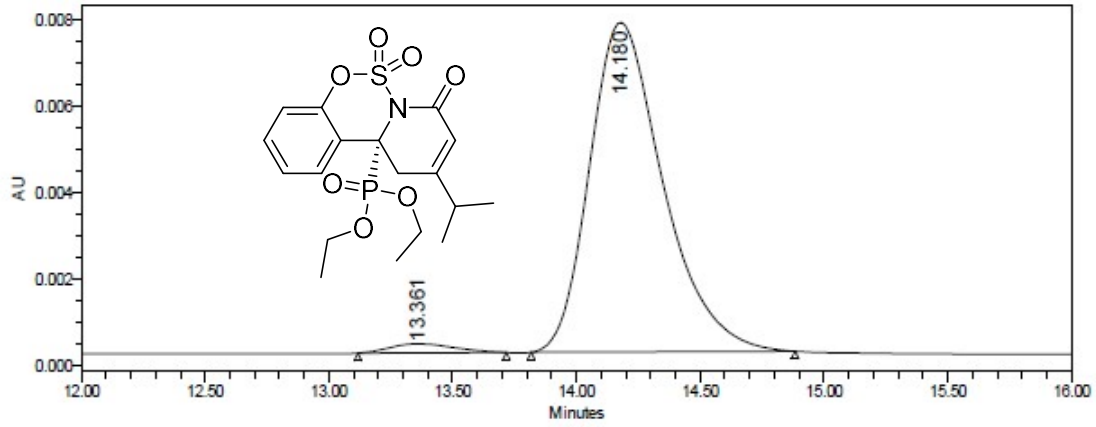
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	29.907	bb	151.000	32730	517	0.82
2	36.831	bb	324.000	3977477	42462	99.18
Sum				4010206.7	42978.8	100.0

Racemic 3p



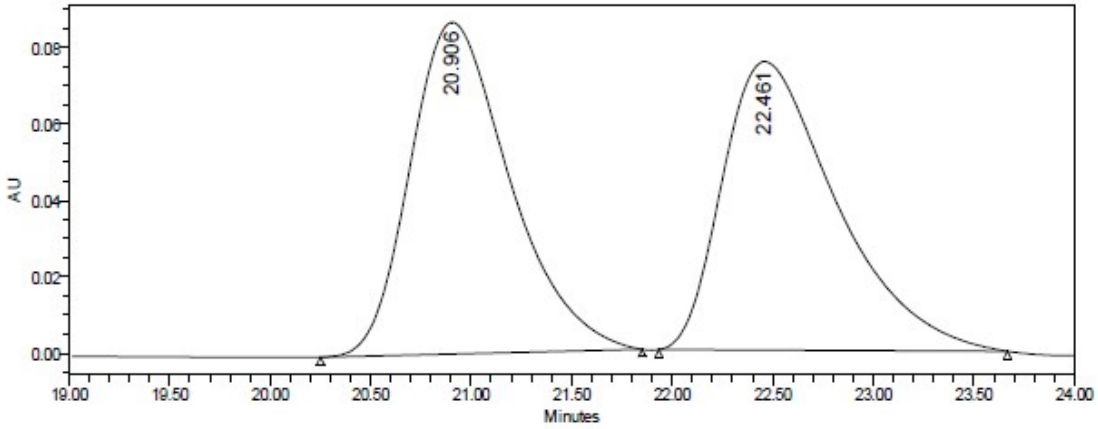
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	13.332	bb	49.000	1348140	68166	51.24
2	14.168	bb	61.000	1282987	64257	48.76
Sum				2631126.4	132423.2	100.0

Enantioenriched 3p



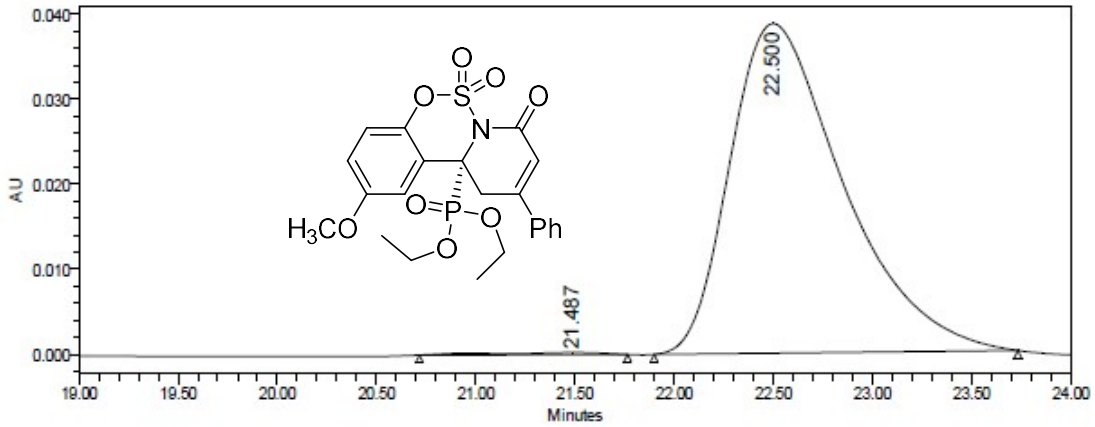
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	13.361	bb	36.000	3774	211	2.34
2	14.180	bb	64.000	157511	7629	97.66
Sum				161285.7	7840.5	100.0

Racemic 3q



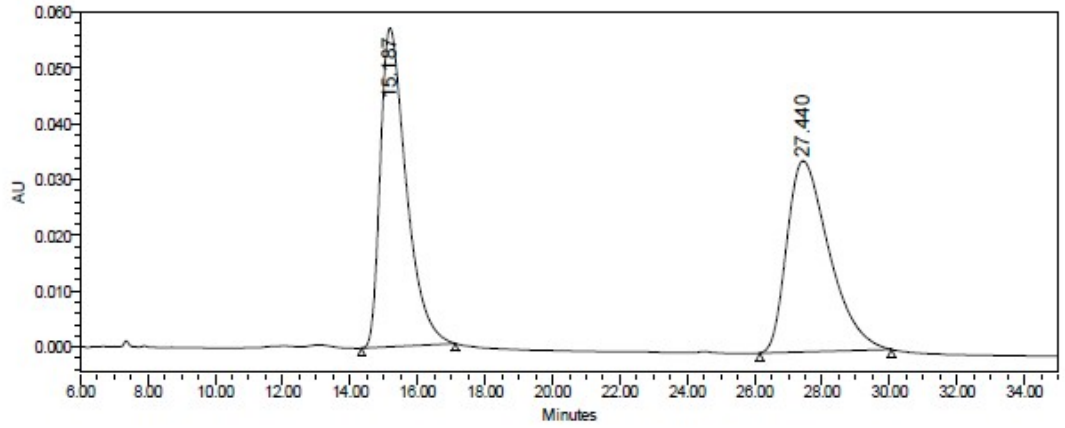
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	20.906	bb	96.000	2987809	86847	50.09
2	22.461	bb	104.000	2977407	75559	49.91
Sum				5965215.8	162406.9	100.0

Enantioenriched 3q



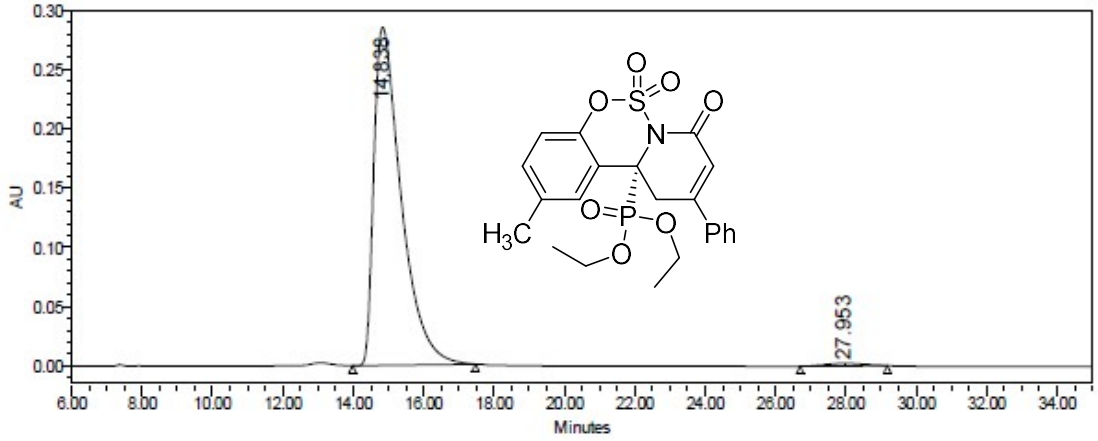
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	21.487	bb	63.000	9666	255	0.62
2	22.500	bb	110.000	1538156	38761	99.38
Sum				1547821.9	39016.3	100.0

Racemic 3r



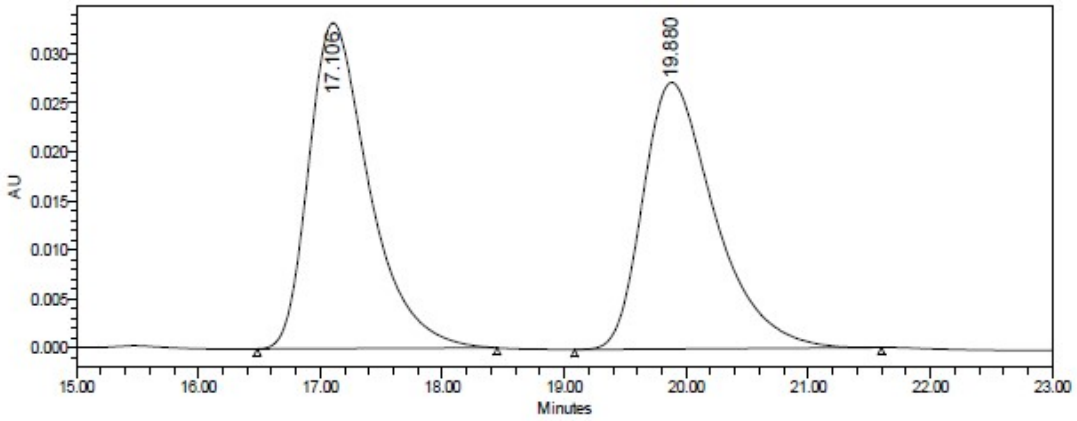
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.187	bb	167.000	3056075	57120	50.61
2	27.440	bb	234.500	2982087	34223	49.39
Sum				6038161.9	91343.6	100.0

Enantioenriched 3r



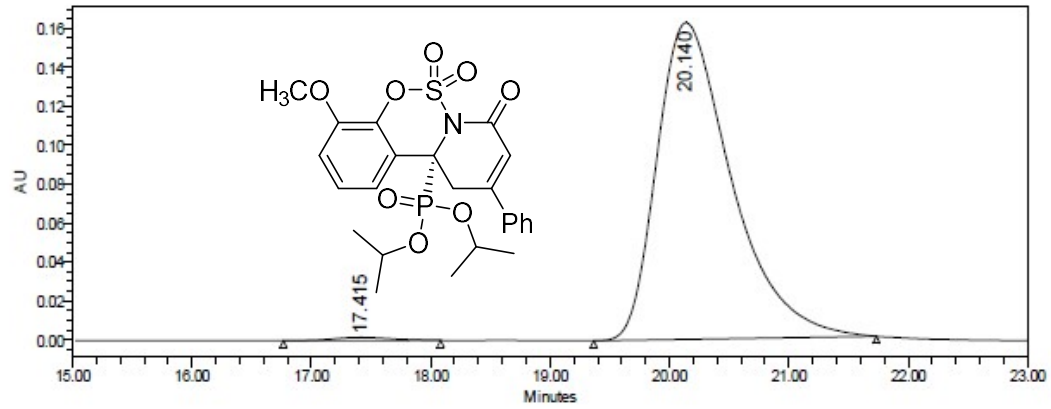
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.838	bb	209.500	15351933	285165	98.91
2	27.953	bb	148.500	169184	2233	1.09
Sum				15521116.5	287397.8	100.0

Racemic 3s



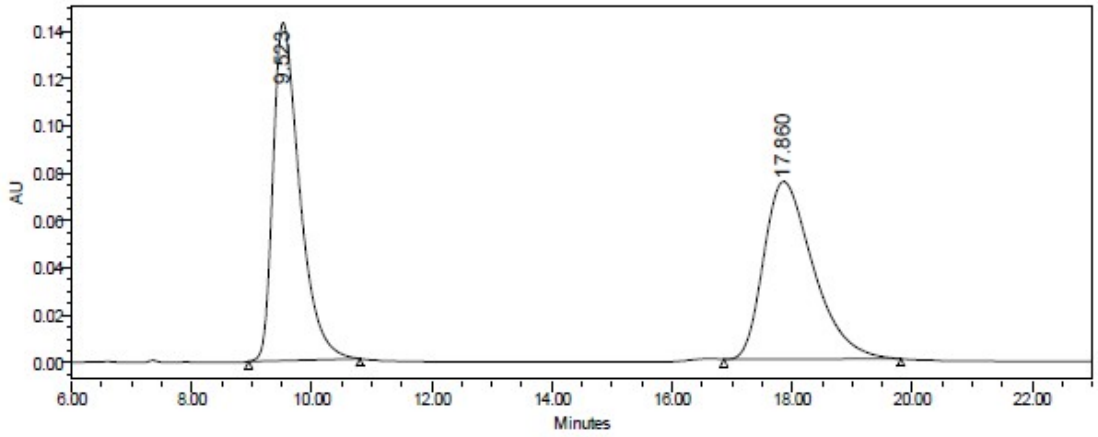
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.106	bb	118.000	1143176	33242	50.68
2	19.880	bb	151.000	1112558	27182	49.32
Sum				2255734.2	60424.3	100.0

Enantioenriched 3s



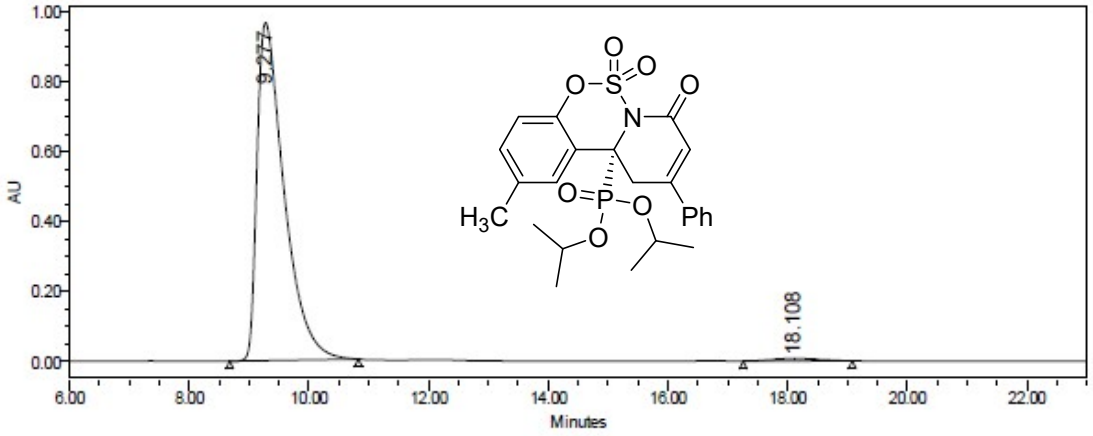
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	17.415	bb	79.000	53410	1587	0.75
2	20.140	bb	142.000	7061206	162605	99.25
Sum				7114615.4	164191.6	100.0

Racemic 3t



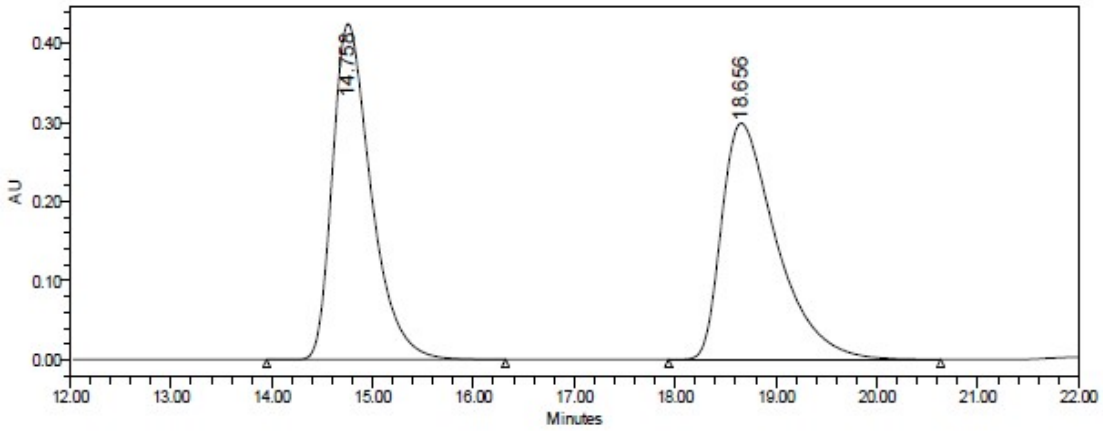
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	9.523	bb	111.000	4398819	142734	50.52
2	17.860	bb	177.000	4308829	74955	49.48
Sum				8707648.6	217688.8	100.0

Enantioenriched 3t



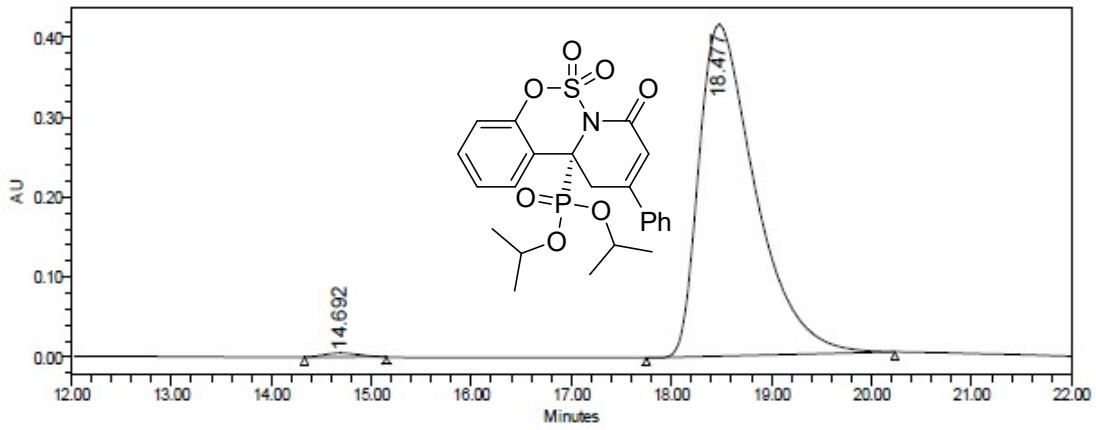
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	9.277	bb	129.000	30446997	966837	98.77
2	18.108	bb	109.500	378081	7128	1.23
Sum				30825077.7	973965.1	100.0

Racemic 3u



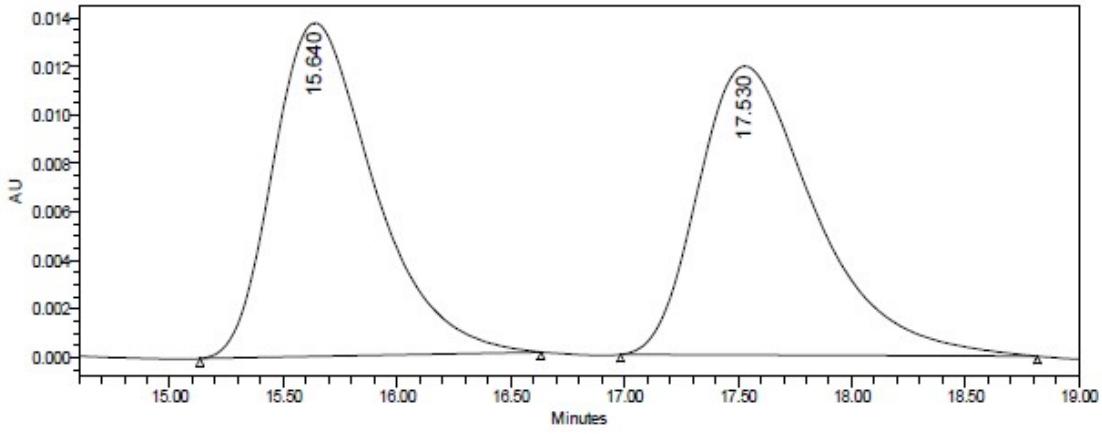
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.758	bb	142.000	11307338	425096	50.00
2	18.656	bb	162.000	11305539	298886	50.00
Sum				22612876.6	723982.1	100.0

Enantioenriched 3u



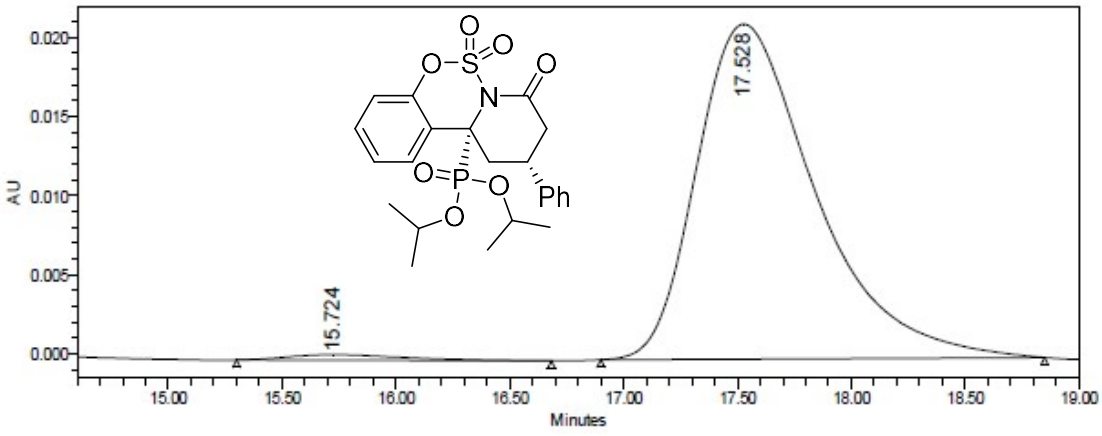
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.692	bb	49.000	122119	4942	0.75
2	18.477	bb	149.000	16245670	414559	99.25
Sum				16367789.1	419501.4	100.0

Racemic 5



	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.640	bb	90.000	424880	13761	49.87
2	17.530	bb	110.000	427022	11924	50.13
Sum				851901.6	25684.4	100.0

Enantioenriched 5



	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.724	bb	83.000	12240	344	1.57
2	17.528	bb	117.000	765964	21149	98.43
Sum				778204.2	21493.0	100.0