Supporting Information

Carbene-catalyzed enal γ-carbon addition to α-ketophosphonates for enantioselective access to bioactive 2-Pyranylphosphonates

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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.

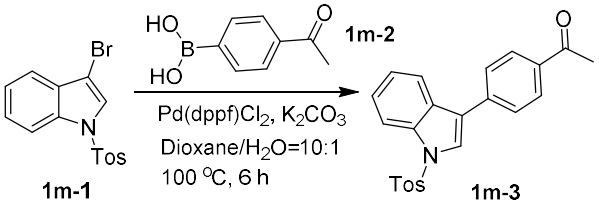
Ⅱ. Preparation of substrates

1. General procedure for the preparation of acyl phosphonate substrates

2-1 **2**

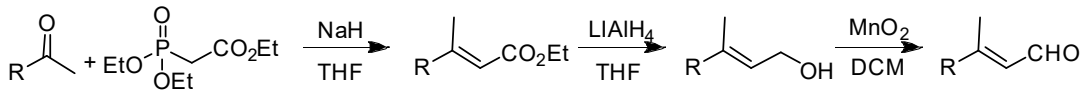
All acyl phophonates were synthesized using a published Arbuzov reaction procedure.[1] Into an dried 100 mL round bottom flask equipped with a magnetic stir bar, the benzoyl chloride derivative (7 mmol, 1 equiv) was dissolved in CH_2Cl_2 (45 mL). Then, the reaction was purged with N_2 and triethylphosphite (7.7 mmol, 1.1 equiv) was added dropwise. After 24 h stirring, the reaction was concentrated under reduced pressure. The oil obtained was purified by vacuum distillation and stocked in a nitrogen-filled drybox.

2. Preparation of 1-(4-(1-tosyl-1H-indol-3-yl)phenyl)ethan-1-one (1m-3)



To a solution of **1m-1** (3.6 g, 10.3 mmol) and **1m-2** (2.0 g, 12.3 mmol) in Dioxane/H_2O (10: 1, 40 mL) was added K_2CO_3 (2.85 g, 25.6 mmol) and Pd(dppf)Cl_2 (400 mg, 0.55 mmol), the mixture was evacuated and refilled with N_2, then the mixture was stirred at 100 ^oC for 6 h. monitored by TLC, the mixture was filtered and the filtrate was removed under reduced pressure and the residue was purified via column chromatography on silica gel with Hexane/EtOAc (10: 1) as eluent to afford the product **1m-3**.

3. Preparation of enal substrates



1-1 **1-2** *step 1* **1-3** *step 2* **1-4** *step 3* **1**

The enal substrates were prepared and characterized according to the known procedure as briefed below:[2,3]

Step 1: To a 100 mL round bottom flask containing NaH (20 mmol, 60% mineral dispersion) and anhydrous THF (40 mL) at 0 ^oC was added triethyl phosphonoacetate (21.5 mmol) dropwise via an addition funnel. The reaction mixture was naturally warmed to rt, followed by a dropwise addition of a acetophenone solution (13 mmol, in 20 mL

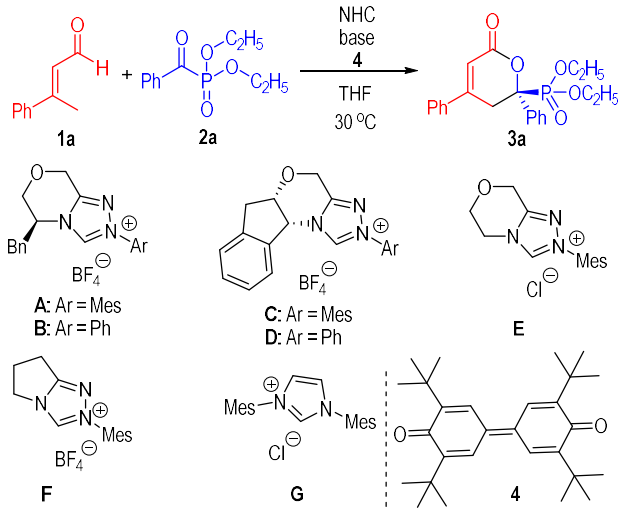
anhydrous THF). The reaction mixture was stirred for 12 h, and then poured into a separating funnel containing water. The organic layer was collected, and the aqueous layer was extracted with diethyl ether (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude esidue was subjected to flash chromatography (Hexanes/EtOAc: 95/5) to afford the corresponding α,β-unsaturated ester as a light yellow oil.

Step 2: To a 100 mL round bottom flask containing the unsaturated ester (20 mmol) obtained above and anhydrous THF (40 mL) was carefully added $LiAlH_4$ (25 mmol) in a few portions at 0 ^oC. The reaction mixture was gradually warmed to room temperature and stirred overnight. The reaction mixture was then cooled to 0 ^oC and quenched with 1 M aqueous HCl. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was subjected to flash chromatography (Hexanes/EtOAc: 50/50) to afford the corresponding allylic alcohol as a light yellow oil.

Step 3: To a 100 mL round bottom flask containing the allylic alcohol (20 mmol) obtained above was added activated MnO_2 (100 mmol) and anhydrous CH_2Cl_2 (40 mL) at rt. The reaction mixture was then stirred at 60 ^oC. After complete consumption of the starting material (as indicated by TLC analysis), the reaction mixture was filtered through a pad of celite. The resulting filtrate was concentrated under reduced pressure. The crude residue was subjected to flash chromatography (Hexanes/EtOAc: 95/5) to afford the corresponding β,β-disubstituted enal as a light yellow oil.

Ⅲ. Reaction conditions optimization

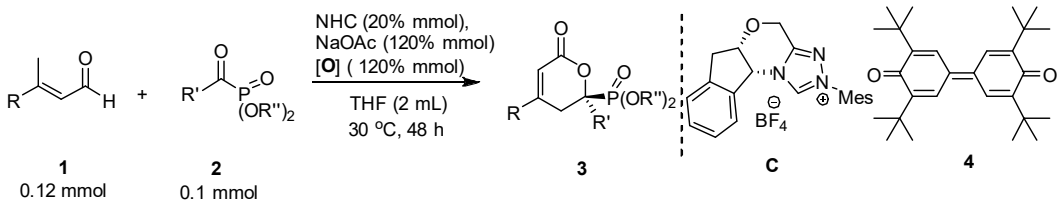
Table 1. Screening of different carbene catalysts, bases and solvents[a].



Entry	Cat.	Base	Solvent	Time [h]	Yield [%][b]	*e.r.*[c]
1	**A**	Cs_2CO_3	THF	24	n.r.	--
2	**B**	Cs_2CO_3	THF	24	<5	--
3	**C**	Cs_2CO_3	THF	24	10	90:10
4	**D**	Cs_2CO_3	THF	24	<5	--
5	**E**	Cs_2CO_3	THF	24	n.r.	--
6	**F**	Cs_2CO_3	THF	24	n.r.	--
7	**G**	Cs_2CO_3	THF	24	36	50:50
8	**C**	Na_2CO_3	THF	48	33	n.d
9	**C**	K_3PO_4	THF	48	<10	n.d
10	**C**	K_2CO_3	THF	48	26	89:11
11	**C**	Et_3N	THF	48	42	97:3
12	**C**	DMAP	THF	48	31	97:3
13	**C**	DABCO	THF	48	38	97:3
14	**C**	NaOAc	THF	48	63	97:3
15	**C**	NaOAc	THF	24	51	97:3
16	**C**	NaOAc	toluene	48	23	95:5
17	**C**	NaOAc	EA	48	40	96:4
18	**C**	NaOAc	CH_3CN	48	<10	n.d.

[a] Reaction conditions: **1a** (0.12 mmol), **2a** (0.1 mmol), NHC (0.02 mmol), base (0.12 mmol), **4** (0.12 mmol), THF (2 mL), 30 °C, 48 h. [b]Yields were isolated yields after column chromatography; n.r. = no reaction. [c]e.r. was determined *via* HPLC using a chiral stationary phase, n.d. = no determined.

Ⅳ. General procedure.

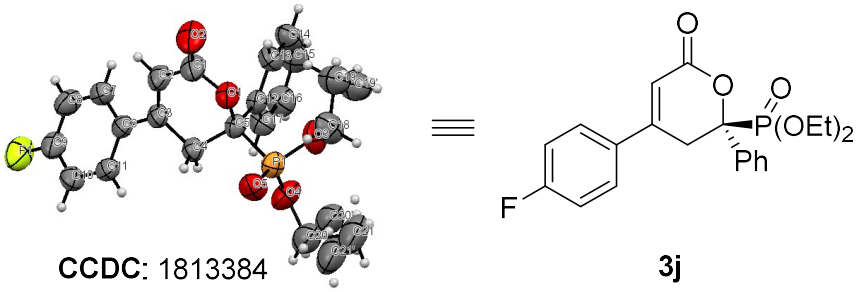


1 0.12 mmol　　**2** 0.1 mmol　　**3**　　**C**　　**4**

To a dry Schlenk reaction tube equipped with a magnetic stir bar was added α-ketophosphonates **2** (0.1 mmol), aldehydes **1** (0.12 mmol), triazolium salt **C** (8.4 mg, 0.02 mmol), oxidant **4** (49 mg, 0.12 mmol) and NaOAc (9.9 mg, 0.12 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 48 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 (3: 1) as eluent to afford the products **3**.

Ⅴ. Stereochemistry determination via X-ray crystallographic analysis

The absolute stereochemistry of **3j** was determined by the X-ray diffraction. This crystal was deposited in the Cambridge Crystallographic Data Centre and assigned as CCDC: 1813384.



CCDC: 1813384　　**3j**

Ⅵ. *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 24 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.

Ⅶ. Antiviral biological assay

1. Purification of tobacco mosaic virus: Using Gooding's method,[4] the upper leaves of *Nicotiana tabacum* L. inoculated with TMV were selected and ground in phosphate buffer and then filtered through double-layer pledget. The filtrate was centrifuged at 10000 g treated with PEG twice, and centrifuged again. The whole experiment was processed at 4 °C. Absorbance value was estimated at 260 nm by ultraviolet spectrophotometer

$$\text{virus concn} = (A_{260} \times \text{dilution ratio}) / \mathrm{E}_{1\mathrm{cm}}^{0.1\%,260\mathrm{nm}}$$

2. Inhibition effect of compound on TMV *in vivo*: The virus was inhibited by mingling with the compound solution at the same volume for 30 min. The mixture was then inoculated on the left side of the leaves of *N. tabacum* L., whereas the right side of the leaves was inoculated with the mixture of solvent and the virus for control. The local lesion numbers were recorded 3 - 4 days after inoculation.[5] Three repetitions were conducted for each compound.

***3.* Cure effect of compound on TMV *in vivo*:** The leaves of *N. tabacum* L. growing at the same ages were selected. TMV at a concentration of 6 x 10^{-3} mg/mL was dipped and

inoculated on the whole leaves. Then the leaves were washed with water and dried. The compound solution was smeared on the left side, and the solvent was smeared on the right side for control. The local lesion numbers were then recorded 3 - 4 days after inoculation.[5] For each compound, three repetitions were conducted to ensure the reliability of the results.

4. Inactivation activities of compounds against TMV *in vivo*: The virus was inhibited by mixing with the compound solution at the same volume for 30 min and inoculated on the left side of *N. tabacum* L. leaves, and the solvent and virus mixture was smeared on the right side of the leaves as the control. The number of local lesions was recorded 3 - 4 days after inoculation.[6,7] Every experiment for each compound was conducted in triplicate. The *in vivo* inhibiton rates of the compounds were calculated using the following formula ("av" means average).

Inhibition rate ＝ [(av number of local lesionsincontrol av number of local lesions smeared with drugs)/ av number of local lesions of control]×100%.

Refrences:

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Table 2. Antibacterial activity

Antibacterial activity of the title compounds

Compound	*X. oryzoe pv. oryzae* inhibition rate [%][a]	
	100 μg/mL	200 μg/mL
3a	3.5±1.8	5.3±3.5
3b	10.8±3.0	45.8±1.5
3c	7.9±3.9	3.0±0.5
3d	*1.9*±6.7	26.8±4.1
3e	8.1±3.8	22.1±1.3
3f	54.2±2.0	60.8±1.2
3h	4.9±2.7	0
3i	21.8±6.1	13.8±2.9
3j	35.0±3.4	39.8±5.4
3k	0	28.1±6.8
3l	18.5±4.5	27.4±1.8
3n	23.2±1.5	31.2±3.8
3o	36.4±1.2	29.2±7.8
3p	0	8.6±3.6
3q	42.0±3.8	44.7±4.4
3s	10.7±4.2	13.4±5.4
3t	0	28.0±4.4
3u	44.4±4.2	59.9±4.4
Bismerthiazol[b]	47.1±4.7	72.7±5.8
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.

Table 3. Inhibitory effect against TMV

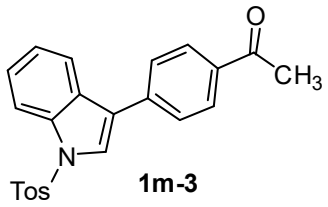
Inhibitory effect of the title compounds against TMV *in vivo* at 500 μg/mL

Compound	curative effect(%)[a]	protective effect(%)[a]	inactivation effect(%)[a]
3a	31.6±1.4	17.5±2.9	80.1±3.9
3b	36.7±2.7	3.4±1.5	61.4±3.3
3c	41.9±6.3	5.6±2.4	57.4±5.3
3d	23.8±3.2	25.7±2.2	41.7±3.3
3e	19.0±3.0	17.8±4.1	58.3±4.2
3f	7.5±3.7	19.8±2.0	31.2±5.4
3g	47.6±4.4	3.9±1.9	78.4±5.0
3h	42.1±2.0	4.6±1.5	17.6±2.3
3i	44.8±2.9	24.3±3.5	59.7±7.2
3j	43.0±3.4	8.0±1.2	72.9±6.0
3k	22.2±1.3	-9.9±1.8	86.9±5.7
3l	31.7±1.9	7.8±1.3	51.8±1.8
3n	23.3±1.8	14.7±1.8	48.8±5.1
3o	43.1±4.4	24.1±2.9	42.3±3.7
3p	30.4±3.4	44.8±2.7	45.7±4.2
3q	14.8±4.5	12.6±3.9	37.0±3.2
3r	27.6±5.6	44.4±7.9	20.4±2.1
3s	-74.1±2.1	6.4±2.8	68.1±2.0
3t	-21.3±2.1	17.5±1.1	31.1±6.6
3u	50.4±3.2	23.6±1.8	35.0±6.5
Ningnanmycin[b]	45.5±2.3	44.6±1.3	90.1±1.2

[a]Average of three replicates. [b]Ningnanmycin was used as the control.

Ⅷ. Characterization of intermediates & products

1-(4-(1-tosyl-1*H*-indol-3-yl)phenyl)ethan-1-one (1m-3):



1m-3

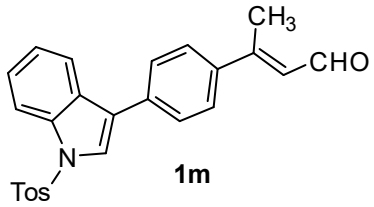
White solid. 2.4 g, 67% yield, m.p. 131 - 133 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 - 8.03 (m, 3H), 7.85 - 7.77 (m, 4H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.42 - 7.36 (m, 1H), 7.34 - 7.29 (m, 1H), 7.26 - 7.25 (m, 1H), 7.24 (s, 1H), 2.65 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.56 (s), 145.29 (s), 138.11 (s), 135.98 (s), 135.53 (s), 135.11 (s), 130.05 (s), 129.04 (s), 128.74 (s), 127.81 (s), 127.47 (s), 126.97 (s), 125.20 (s), 123.84 (d, *J* = 2.7 Hz), 122.71 (s), 120.29 (s), 113.94 (s), 26.64 (s), 21.61 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{23}H_{20}O_3NS$ $[M+H]^+$, 390.1158; found 390.1159.

(*E*)-3-(4-(1-tosyl-1*H*-indol-3-yl)phenyl)but-2-enal (1m):



1m

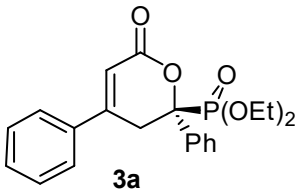
Yellow solid, 500 mg, 39% yield for 3 steps, m.p. 65 - 67 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21 (d, *J* = 7.7 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.83 - 7.73 (m, 4H), 7.66 (s, 4H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.24 (d, *J* = 8.3 Hz, 2H), 6.46 (d, *J* = 7.6 Hz, 1H), 2.61 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 191.27 (s), 156.86 (s), 145.28 (s), 139.50 (s), 135.62 (s), 135.23 (s), 130.08 (s), 129.06 (d, *J* = 20.6 Hz), 128.12 (s), 127.87 (s), 127.16 (s,), 127.02 (s), 126.96 (s), 125.19 (s), 123.81 (s), 123.53 (s), 122.96 (s), 120.39 (s), 114.01 (s), 21.67 (s), 16.36 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{25}H_{22}O_3NS$ $[M+H]^+$, 416.1315; found 146.1314.

Diethyl (*R*)-(6-oxo-2,4-diphenyl-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3a):



3a

Light yellow oil, 24.7 mg, yield: 63%.

[α]$_D^{26}$ = 115.7 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 2H), 7.43 (dd, *J* = 4.8, 2.9 Hz, 2H), 7.39 - 7.33 (m, 3H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.25 (t, *J* = 3.4 Hz, 1H), 6.17 (s, 1H), 4.28 - 4.14 (m, 2H), 3.86 (ddd, *J* = 10.1, 8.3, 7.0 Hz, 1H), 3.71 - 3.59 (m, 2H), 3.55 (dd, *J* = 17.8, 7.0 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H).

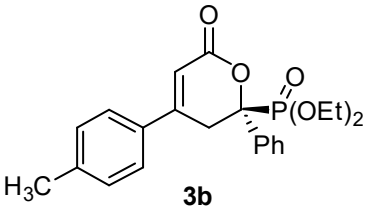
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.14 (d, *J* = 9.2 Hz), 152.72 (d, *J* = 13.1 Hz), 136.61 (s), 136.06 (s), 130.91 (s), 129.09 (s), 128.59-128.57 (m), 126.27 (d, *J* = 3.8 Hz), 126.14 (s), 115.07 (s), 82.22 (d, *J* = 170.1 Hz), 64.51 (d, *J* = 7.5 Hz), 64.37 (d, *J* = 7.5 Hz), 32.11 (s), 16.54 (d, *J* = 5.0 Hz), 16.28 (d, *J* = 6.8 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 16.92 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{24}O_5P$ $[M+H]^+$, 387.1356; found 387.1349.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H, 25 °C, IPA / Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 15.8 min, Rt_2 (major) = 22.9 min; er = 97:3).

Diethyl (*R*)-(6-oxo-2-phenyl-4-(p-tolyl)-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3b):



3b

Light yellow oil, 29 mg, yield: 70%.

$[\alpha]_D^{26}$ = 126.4 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 - 7.56 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.32 - 7.28 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 6.21 (d, *J* = 2.0 Hz, 1H), 4.31 - 4.21 (m, 2H), 3.91 - 3.88 (m, 1H), 3.72 - 3.63 (m, 2H), 3.59 (dd, *J* = 17.8, 6.6 Hz, 1H), 2.38 (s, 3H), 1.35 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H).

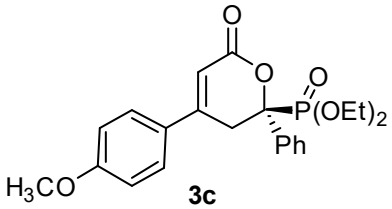
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.46 (d, *J* = 9.4 Hz), 152.63 (d, *J* = 13.4 Hz), 141.56 (s), 136.61 (s), 133.14 (s), 129.82 (s), 128.58 (s), 128.54 (d, *J* = 2.2 Hz), 126.31 (d, *J* = 3.7 Hz), 126.12 (s), 114.06 (s), 82.22 (d, *J* = 170.1 Hz), 64.56 (d, *J* = 7.5Hz), 64.44 (d, *J* = 7.5 Hz), 31.93 (s), 21.46 (s), 16.57 (d, *J* = 5.4 Hz), 16.31 (d, *J* = 5.5 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 17.00 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_5P$ $[M+H]^+$, 401.1512; found 401.1504.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 16.2 min, Rt_2 (major) = 20.6 min; er = 97:3).

Diethyl (*R*)-(4-(4-methoxyphenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3c):



3c

Light yellow oil, 30 mg, yield: 72%;

$[\alpha]_D^{26}$ = 111.9 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 - 7.54 (m, 2H), 7.48 (d, *J* = 8.9 Hz, 2H), 7.38 - 7.28 (m, 3H), 6.96 - 6.90 (m, 2H), 6.16 (d, *J* = 1.8 Hz, 1H), 4.32 - 4.22 (m, 2H), 3.95 - 3.84 (m, 1H), 3.84 (s, 3H), 3.70 - 3.60 (m, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

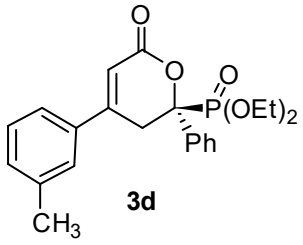
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.53 (d, *J* = 9.4 Hz), 161.91 (s), 152.03 (d, *J* = 13.5 Hz), 136.57 (s), 128.51 (d, *J* = 3.8 Hz), 128.46 (d, *J* = 3.8 Hz), 128.09 (d, *J* = 2.1 Hz), 127.77 (s), 126.22 (d, *J* = 4.2 Hz), 114.43 (s), 112.67 (s), 82.04 (d, *J* = 211.6 Hz), 64.50 (d, *J* = 7.6 Hz), 64.39 (d, *J* = 7.6 Hz), 55.46 (s), 31.70 (s), 16.49 (d, *J* = 5.6 Hz), 16.22 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.38 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_6P$ $[M+H]^+$, 417.1461; found 417.1451.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^{o}C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 21.4 min, Rt_2 (major) = 25.3 min; er = 97:3).

Diethyl (*R*)-(6-oxo-2-phenyl-4-(m-tolyl)-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3d):



3d

Light yellow oil, 33 mg, yield: 82%.

$[\alpha]_D^{26}$ = 113.0 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 - 7.52 (m, 2H), 7.39 - 7.28 (m, 6H), 7.25 (ddd, *J* = 6.0, 4.2, 2.9 Hz, 1H), 6.22 (d, *J* = 2.1 Hz, 1H), 4.34 - 4.21 (m, 2H), 3.90 (dt, *J* = 10.1, 7.1 Hz, 1H), 3.75 - 3.64 (m, 2H), 3.58 (dd, *J* = 17.8, 6.9 Hz, 1H), 2.38 (s, 3H), 1.36 (td, *J* = 7.1, 0.6 Hz, 3H), 1.11 (td, *J* = 7.1, 0.6 Hz, 3H).

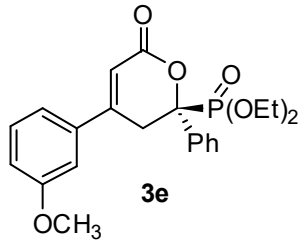
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.22 (d, *J* = 9.2 Hz), 152.80 (d, *J* = 13.2 Hz), 138.80 (s), 136.55 (s), 135.99 (d, *J* = 2.0 Hz), 131.66 (s), 128.90 (s), 128.52 (d, *J* = 2.6 Hz), 128.47 (d, *J* = 3.0 Hz), 126.73 (s), 126.25 (d, *J* = 4.1 Hz), 123.23 (s), 114.79 (s), 82.16 (d, *J* = 211.6 Hz), 64.49 (d, *J* = 7.6 Hz), 64.36 (d, *J* = 7.6 Hz), 32.07 (s), 21.42 (s), 16.48 (d, *J* = 5.6 Hz), 16.21 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.36 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_5P$ $[M+H]^+$,401.1512; found 401.1504.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^{o}C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 8.2 min, Rt_2 (major) = 12.6 min; er = 96:4).

Diethyl (*R*)-(4-(3-methoxyphenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3e):



3e

Light yellow oil, 35 mg, yield: 84%.

$[\alpha]_D^{26}$ = 107.3 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 - 7.53 (m, 2H), 7.41 - 7.28 (m, 4H), 7.11 - 7.06 (m, 1H), 7.01 - 6.94 (m, 2H), 6.22 (d, *J* = 2.1 Hz, 1H), 4.33 - 4.19 (m, 2H), 3.96 - 3.86 (m, 1H), 3.82 (s, 3H), 3.75 - 3.64 (m, 2H), 3.62 - 3.53 (m, 1H), 1.36 (td, *J* = 7.0, 0.5 Hz, 3H), 1.12 (td, *J* = 7.0, 0.5 Hz, 3H).

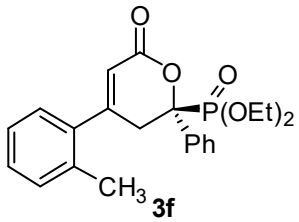
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.14 (d, *J* = 9.3 Hz), 159.97 (s), 152.61 (d, *J* = 13.2 Hz), 137.49 (d, *J* = 2.1 Hz), 136.48 (s), 130.06 (s), 128.54 (d, *J* = 2.7 Hz), 128.51 (d, *J* = 3.2 Hz), 126.25 (d, *J* = 4.1 Hz), 118.51 (s), 116.27 (s), 115.26 (s), 111.71 (s), 82.21 (d, *J* = 211.6 Hz), 64.48 (d, *J* = 7.6 Hz), 64.36 (d, *J* = 7.6 Hz), 55.42 (s), 32.14 (s), 16.48 (d, *J* = 5.6 Hz), 16.22 (d, *J* = 5.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 16.92 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_6P$ $[M+H]^+$, 417.1461; found 417.1454.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 11.6 min, Rt_2 (major) = 16.0 min; er = 97.5:2.5).

Diethyl (*R*)-(6-oxo-2-phenyl-4-(o-tolyl)-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3f):



3f

Light yellow oil, 16 mg, yield: 40%;

$[\alpha]_D^{26}$ = -6.3 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 - 7.51 (m, 2H), 7.43 - 7.30 (m, 3H), 7.24 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.22 - 7.16 (m, 2H), 7.04 - 6.94 (m, 1H), 5.87 (d, *J* = 2.1 Hz, 1H), 4.27 (dq, *J* = 14.2, 7.1 Hz, 2H), 3.94 - 3.88 (m, 1H), 3.76 - 3.66 (m, 2H), 3.28 (dd, *J* = 17.9, 7.5 Hz, 1H), 2.11 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

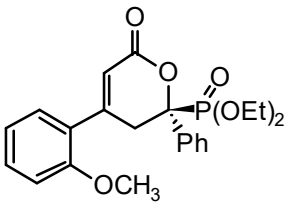
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.59 (d, *J* = 8.8 Hz), 155.26 (d, *J* = 12.7 Hz), 137.83 (d, *J* = 1.8 Hz), 136.67 (s), 134.59 (s), 131.00 (s), 129.08 (s), 128.52 (d, *J* = 1.9 Hz), 128.50 (d, *J* = 2.4 Hz), 126.94 (s), 126.37 (s), 126.33 (s), 119.10 (s), 82.52 (d, *J* = 170.1 Hz), 64.40 (d, *J* = 2.1 Hz), 64.33 (d, *J* = 5.6 Hz), 35.25 (s), 19.94 (s), 16.48 (d, *J* = 5.6 Hz), 16.22 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.28 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_5P$ $[M+H]^+$, 401.1512; found 401.1507.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 10.6 min, Rt_2 (major) = 14.1 min; er = 99:1).

Diethyl (*R*)-(4-(2-methoxyphenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3g):



3g

Light yellow oil, 17 mg, yield: 41%.

$[\alpha]_D^{26}$ = 58.4 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.36 - 7.26 (m, 4H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.93 - 6.84 (m, 2H), 6.05 (d, *J* = 1.9 Hz, 1H), 4.23 (p, *J* = 7.1 Hz, 2H), 3.91-3.85 (m, 1H), 3.79 (s, 3H), 3.74 - 3.63 (m, 2H), 3.58 (dd, *J* = 17.9, 6.5 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H).

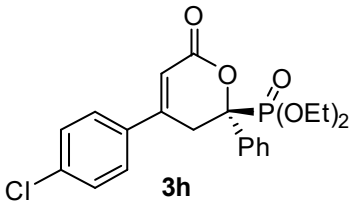
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.18 (d, *J* = 9.3 Hz), 157.15 (s), 153.92 (d, *J* = 14.0 Hz), 136.53 (s), 131.38 (s), 128.94 (s), 128.33 (d, *J* = 3.0 Hz), 128.23 (d, *J* = 2.6 Hz), 126.61 (s), 126.57 (s), 120.89 (s), 117.77 (s), 111.23 (s), 82.59 (d, *J* = 170.1 Hz), 64.35 (d, *J* = 7.6 Hz), 64.16 (d, *J* = 7.6 Hz), 55.36 (s), 33.43 (s), 16.47 (d, *J* = 5.6 Hz), 16.21 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.45 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_6P$ $[M+H]^+$, 417.1461; found 417.1451.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^{o}C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 12.1 min, Rt_2 (major) = 14.6 min; er = 98:2).

Diethyl (*R*)-(4-(4-chlorophenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3h):



3h

Light yellow oil, 32 mg, yield: 76%.

$[\alpha]_D^{26}$ = 111.2 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.47 (dt, *J* = 8.9, 4.0 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.31 - 7.26 (m, 1H), 7.07 (t, *J* = 8.6 Hz, 2H), 6.15 (d, *J* = 1.8 Hz, 1H), 4.23 (pd, *J* = 7.1, 1.2 Hz, 2H), 3.94 - 3.80 (m, 1H), 3.65 (dddd, *J* = 17.2, 8.5, 5.7, 1.4 Hz, 2H), 3.52 (dd, *J* = 17.8, 7.1 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H).

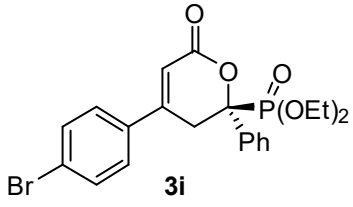
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.25 (d, *J* = 252.5 Hz), 163.13 - 162.84 (m), 151.45 (d, *J* = 13.1 Hz), 136.45 (s), 132.17 (dd, *J* = 3.3, 2.1 Hz), 128.57 (d, *J* = 2.5 Hz), 128.18 (d, *J* = 8.7 Hz), 126.15 (d, *J* = 4.1 Hz), 116.32 (s), 116.11 (s), 114.85 (s), 82.11 (d, *J* = 184.8 Hz), 64.53 (d, *J* = 7.6 Hz), 64.38 (d, *J* = 7.6 Hz), 32.15 (s), 16.46 (d, *J* = 5.6 Hz), 16.20 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.23 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{23}ClO_5P$ $[M+H]^+$, 421.0966; found 421.1088.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^{o}C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 16.0 min, Rt_2 (major) = 25.2 min; er = 98:2).

Diethyl (*R*)-(4-(4-bromophenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3i):



3i

Light yellow oil, 35 mg, yield: 75%.

$[\alpha]_D^{26}$ = 127.6 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.6 Hz, 4H), 7.39 - 7.32 (m, 4H), 7.30 (dd, *J* = 7.2, 1.6 Hz, 1H), 6.20 (d, *J* = 2.1 Hz, 1H), 4.29 - 4.19 (m, 2H), 3.88 (dt, *J* = 10.0, 7.0 Hz, 1H), 3.72 - 3.59 (m, 2H), 3.51 (dd, *J* = 17.8, 7.1 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

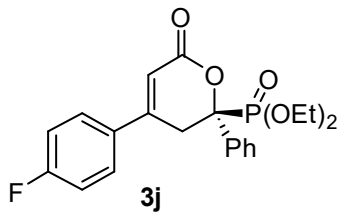
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.93 (d, *J* = 9.3 Hz), 151.48 (d, *J* = 13.1 Hz), 136.44 (s), 134.99 (s), 132.38 (s), 128.67 (d, *J* = 1.7 Hz), 127.64 (s), 126.25 (s), 126.22 (s), 125.48 (s), 115.51 (s), 82.22 (d, *J* = 170.1 Hz), 64.64 (d, *J* = 7.5 Hz), 64.49 (d, *J* = 7.5 Hz), 32.06 (s), 16.55 (d, *J* = 5.6 Hz), 16.28 (d, *J* = 5.3 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 16.79 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{23}BrO_5P$ $[M+H]^+$, 465.0461; found 465.0451.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 19.1 min, Rt_2 (major) = 27.4 min; er = 96:4).

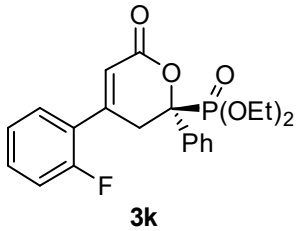
Diethyl (*R*)-(4-(4-fluorophenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3j):



3j

Light yellow crystal, m.p. 111 - 112°C. 25.6 mg, yield: 63%.
$[\alpha]_D^{26}$ = 97.6 (*c* 1.0 $CHCl_3$).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 - 7.55 (m, 2H), 7.53 - 7.48 (m, 2H), 7.40 - 7.29 (m, 3H), 7.15 - 7.07 (m, 2H), 6.19 (d, *J* = 2.1 Hz, 1H), 4.34 - 4.19 (m, 2H), 3.90 (dt, *J* = 10.1, 7.1 Hz, 1H), 3.76 - 3.60 (m, 2H), 3.56 (dd, *J* = 17.8, 7.0 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.30 (d, *J* = 246.4 Hz), 163.00 (*J* = 2.0 Hz), 151.48 (d, *J* = 13.2 Hz), 136.42 (s), 132.14 (d, *J* = 3.3 Hz), 128.59 (d, *J* = 2.5 Hz), 128.19 (d, *J* = 8.7 Hz), 126.17 (d, *J* = 4.1 Hz), 116.34 (s), 116.12 (s), 114.84 (s), 82.11 (d, *J* = 184.8 Hz), 64.57 (d, *J* = 7.6 Hz), 64.42 (d, *J* = 7.6 Hz), 32.14 (s), 16.48 (d, *J* = 5.6 Hz), 16.21 (d, *J* = 5.6 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ 16.22 (s).
^{19}F NMR (376 MHz, $CDCl_3$) δ -108.89 (s).
HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{23}FO_5P$ $[M+H]^+$, 405.1261; found 405.1254.
Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 19.1 min, Rt_2 (major) = 31.1 min; er = 97:3).

Diethyl (*R*)-(4-(2-fluorophenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3k):



3k

Light yellow oil, 33 mg, yield: 81%.
$[\alpha]_D^{26}$ = 82.4 (*c* 1.0 $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 - 7.52 (m, 2H), 7.40 - 7.33 (m, 3H), 7.32 - 7.28 (m, 1H), 7.25 (td, *J* = 7.9, 1.7 Hz, 1H), 7.18 - 7.05 (m, 2H), 6.19 (d, *J* = 2.2 Hz, 1H), 4.27 - 4.20 (m, 2H), 3.94 - 3.85 (m, 1H), 3.77 - 3.64 (m, 2H), 3.55 (dd, *J* = 18.0, 7.5 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.66 (d, *J* = 9.0 Hz), 160.27 (d, *J* = 253.3 Hz), 149.35 (d, *J* = 13.4 Hz), 136.41 (s), 132.06 (d, *J* = 8.7 Hz), 128.85 (s), 128.56 (s), 126.46 (d, *J* = 3.8 Hz), 124.93 (d, *J* = 12.2 Hz), 124.81 (d, *J* = 2.6 Hz), 119.03 (d, *J* = 5.2 Hz), 116.80 (s), 116.62 (s), 82.47 (d, *J* = 170.1 Hz), 64.55 (d, *J* = 7.5 Hz), 64.40 (d, *J* = 7.5 Hz), 33.21 (s), 16.52 (d, *J* = 5.6 Hz), 16.29 (d, *J* = 5.6 Hz).

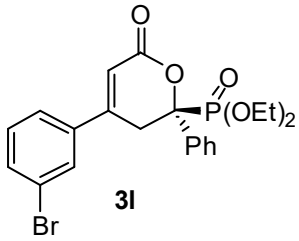
^{31}P NMR (202 MHz, $CDCl_3$) δ 16.83 (s).

^{19}F NMR (471 MHz, $CDCl_3$) δ -111.45 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{23}FO_5P$ $[M+H]^+$, 405.1261; found 405.1252.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1(minor) = 12.4 min, Rt_2 (major) = 17.4 min; er = 98:2).

Diethyl (*R*)-(4-(3-bromophenyl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3l):



3l

Light yellow oil, 30 mg, yield: 64%.

[α]$_D^{26}$ = 99.3 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (t, *J* = 1.7 Hz, 1H), 7.56 - 7.51 (m, 3H), 7.40 - 7.32 (m, 3H), 7.32 - 7.28 (m, 1H), 7.25 (s, 1H), 6.19 (d, *J* = 2.0 Hz, 1H), 4.29 - 4.16 (m, 2H), 3.94 - 3.80 (m, 1H), 3.74 - 3.58 (m, 2H), 3.49 (dd, *J* = 17.8, 7.2 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H).

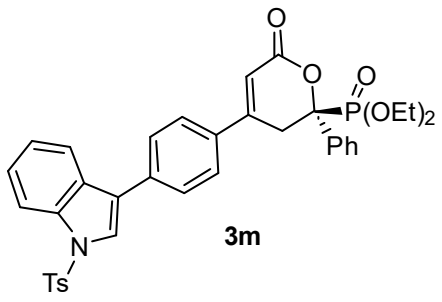
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.66 (d, *J* = 9.1 Hz), 151.04 (d, *J* = 13.1 Hz), 138.15 (d, *J* = 2.1 Hz), 136.34 (s), 133.66 (s), 130.54 (s), 129.09 (s), 128.63 (s), 128.60 (s), 126.17 (d, *J* = 4.1 Hz), 124.64 (s), 123.27 (s), 116.16 (s), 82.20 (d, *J* = 184.8 Hz) (s), 64.55 (d, *J* = 7.6 Hz), 64.38 (d, *J* = 7.6 Hz), 32.11 (s). 16.48 (d, *J* = 5.6 Hz), 16.21 (d, *J* = 5.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 16.77 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{23}BrO_5P$ $[M+H]^+$, 465.0461; found 465.0455.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 10.3 min, Rt_2 (major) = 18.4 min; er = 96:4).

Diethyl (*R*)-(6-oxo-2-phenyl-4-(4-(1-tosyl-1H-indol-3-yl)phenyl)-3,6-dihydro-2*H*-pyran -2-yl)phosphonate (3m):



3m

Light yellow solid, m.p. 105 - 106 °C. 37 mg, yield: 57%.

[α]$_D^{21}$ = 108.4 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.76 - 7.74 (m, 2H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.60 - 7.58 (m, 4H), 7.39 - 7.35 (m, 3H), 7.33 - 7.29(m, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 6.29 (d, *J* = 1.9 Hz, 1H), 4.32 - 4.24 (m, 2H), 3.91 - 3.89 (m, 1H), 3.73 - 3.63 (m, 3H), 2.34 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.32 (d, *J* = 9.3 Hz), 152.07 (d, *J* = 13.3 Hz), 145.38 (s), 136.50 (s), 136.04 (s), 135.54 (s), 135.06 (s), 134.86 (s), 130.13 (s), 128.80 (s), 128.68(s),

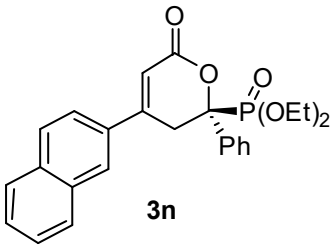
128.33 (s), 127.04(s), 126.80 (s), 126.34 (s), 126.31 (s), 125.27 (s), 123.89 (s), 123.67 (s), 122.67 (s), 120.34 (s), 114.84 (s), 114.01 (s), 82.27(d, *J* = 170.1 Hz), 64.66 (d, *J* = 7.4 Hz), 64.54(d, *J* = 7.4 Hz), 31.92 (s), 21.72 (s), 16.62 (d, *J* = 5.6 Hz), 16.35 (d, *J* = 5.4 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 16.91 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{36}H_{35}O_7NPS$ $[M+H]^+$, 656.1866; found 656.1869.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^oC, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 46.8 min, Rt_2 (major) = 60.8 min; er = 96:4).

Diethyl (*R*)-(4-(naphthalen-2-yl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3n):



3n

Light yellow oil, 30 mg, yield: 69%.

[α]$_D^{26}$ = 196.9 (*c* 1.0 $CHCl_3$).

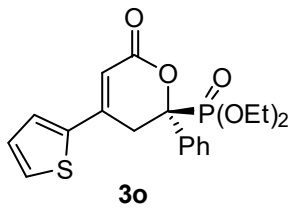
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.89 (dd, *J* = 8.1, 4.7 Hz, 1H), 7.83 (dd, *J* = 9.0, 3.3 Hz, 2H), 7.63 - 7.58 (m, 2H), 7.57 - 7.51 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (dd, *J* = 7.8, 6.2 Hz, 1H), 6.38 (d, *J* = 1.9 Hz, 1H), 4.35 - 4.21 (m, 2H), 3.91 (dt, *J* = 10.1, 7.1 Hz, 1H), 3.86 - 3.72 (m, 2H), 3.71 - 3.61 (m, 1H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.30 (d, *J* = 9.2 Hz), 152.28 (d, *J* = 13.3 Hz), 136.58 (s), 134.38 (s), 133.10 (d, *J* = 9.8 Hz), 128.95 (s), 128.94 (s), 128.64 (d, *J* = 1.9 Hz), 128.61 - 128.56 (m), 127.84 (s), 127.79 (s), 127.12 (s), 126.67 (s), 126.37 (s), 126.34 (s), 122.74 (s), 115.20 (s), 82.28 (d, *J* = 170.1 Hz), 64.65 (d, *J* = 7.6 Hz),64.45 (d, *J* = 7.6 Hz), 31.97 (s), 16.59 (d, *J* = 5.6 Hz), 16.31 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 16.34 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{25}H_{26}O_5P$ $[M+H]^+$, 437.1510; found 437.1512. Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^oC, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 16.0 min, Rt_2 (major) = 24.3 min; er = 96:4).

Diethyl (*R*)-(6-oxo-2-phenyl-4-(thiophen-2-yl)-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3o):



3o

Light yellow oil, 21 mg, yield: 54%.

[α]$_D^{24}$ = 167.7 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 - 7.53 (m, 2H), 7.45 - 7.39 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.30 - 7.27 (m, 1H), 7.08 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.13 (d, *J* = 2.0 Hz, 1H), 4.26 - 4.22 (m, 2H), 3.89 - 3.86 (m, 1H), 3.68 - 3.63 (m, 2H), 3.61 - 3.56 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H).

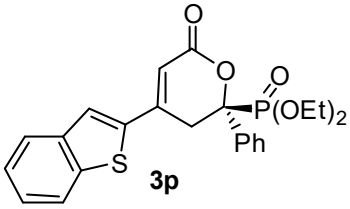
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.14 (d, *J* = 9.5 Hz), 145.76 (d, *J* = 14.1 Hz), 140.15 (d, *J* = 2.8 Hz), 136.29 (d, *J* = 0.7 Hz), 129.87 (s), 128.57 (d, *J* = 2.6 Hz), 128.54 (d, *J* = 2.4 Hz), 128.26 (s), 126.21 (s), 126.17 (s), 111.99 (s), 81.97 (d, *J* = 170.6 Hz), 64.58 (d, *J* = 7.6 Hz), 64.44 (d, *J* = 7.6 Hz), 32.14 (s), 16.46 (d, *J* = 5.7 Hz), 16.21 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 15.98 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{19}H_{22}O_5PS$ $[M+H]^+$, 393.0920; found 393.0910.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 14.8 min, Rt_2 (major) = 21.1 min; er = 95:5).

Diethyl (*R*)-(4-(benzo[b]thiophen-2-yl)-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3p):



3p

Light yellow solid, m.p. 136 - 138 °C, 30 mg, yield: 68%.

[α]$_D^{22}$ = 179.1 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 - 7.76 (m, 2H), 7.68 (s, 1H), 7.59 (dd, *J* = 7.6, 1.9 Hz, 2H), 7.40 - 7.33 (m, 4H), 7.32 - 7.28 (m, 1H), 6.22 (d, *J* = 1.9 Hz, 1H), 4.31 - 4.18 (m, 2H), 3.96 - 3.85 (m, 1H), 3.80 - 3.61 (m, 3H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H).

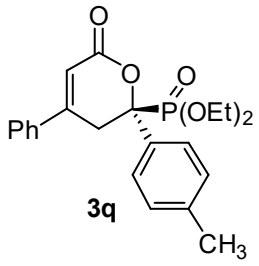
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.85 (d, *J* = 9.3 Hz), 145.93 (d, *J* = 13.8 Hz), 140.40 (s), 139.78 (d, *J* = 2.9 Hz), 139.41 (s), 136.25 (s), 128.62 (d, *J* = 2.4 Hz), 126.81 (s), 126.22 (s), 126.18 (s), 125.79 (s), 125.16 (s), 124.86 (s), 122.43 (s), 114.42 (s), 82.13 (d, *J* = 169.6 Hz), 64.61 (d, *J* = 7.4 Hz), 64.44 (d, *J* = 7.8 Hz), 31.75 (s), 16.49 (d, *J* = 5.6 Hz), 16.23 (d, *J* = 5.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ 15.99 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{23}H_{24}O_5PS$ $[M+H]^+$, 443.1076; found 443.1070.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 12.7 min, Rt_2 (major) = 17.7 min; er = 95:5).

Diethyl (*R*)-(6-oxo-4-phenyl-2-(p-tolyl)-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3q):



3q

Light yellow oil, 34 mg, yield: 84%;

[α]$_D^{26}$ = 119.2 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 - 7.46 (m, 2H), 7.42 (ddd, *J* = 9.3, 8.0, 3.8 Hz, 5H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.21 (d, *J* = 2.2 Hz, 1H), 4.30 - 4.17 (m, 2H), 3.97 - 3.84 (m, 1H), 3.73 - 3.63 (m, 2H), 3.60 - 3.53 (m, 1H), 2.30 (d, *J* = 1.2 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.32 (d, *J* = 9.5 Hz), 152.78 (d, *J* = 13.3 Hz), 138.44 (s), 136.16 (s), 133.42 (s), 130.89 (s), 129.32 (s), 129.09 (s), 126.22 (d, *J* = 4.6 Hz), 126.19 (s),

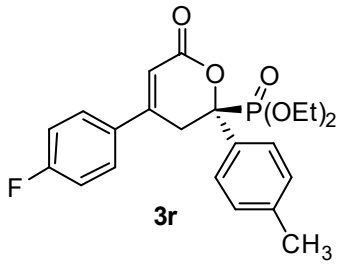
115.12 (s), 82.93 (s), 81.57 (s), 64.45 (dd, *J* = 21.5, 7.4 Hz), 32.04 (s), 21.12 (s), 16.46 (dd, *J* = 27.5, 5.3 Hz), 16.31 - 16.20 (m).

^{31}P NMR (202 MHz, $CDCl_3$) δ 17.05 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{26}O_5P$ $[M+H]^+$, 401.1512; found 401.1502.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^oC, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 13.9 min, Rt_2 (major) = 23.9 min; er = 96:4).

Diethyl (*R*)-(4-(4-fluorophenyl)-6-oxo-2-(p-tolyl)-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3r):



3r

Light yellow oil, 29 mg, yield: 69%.

[α]$_D^{25}$ = 115.5 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 - 7.43 (m, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.07 (td, *J* = 8.7, 2.1 Hz, 2H), 6.14 (s, 1H), 4.22 (dd, *J* = 14.2, 7.1 Hz, 2H), 3.93 - 3.84 (m, 1H), 3.71 -3.58 (m, 2H), 3.53 - 3.48 (m, 1H), 2.28 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.28 (d, *J* = 239.6 Hz), 162.98 (d, *J* = 3.3 Hz), 151.46 (d, *J* = 13.4 Hz), 138.42 (d, *J* = 3.1 Hz), 133.30 (d, *J* = 0.9 Hz), 132.22 (dd, *J* = 3.2, 2.3 Hz), 129.27 (d, *J* = 2.6 Hz), 128.17 (d, *J* = 8.6 Hz), 126.08 (d, *J* = 4.1 Hz), 116.18 (d, *J* = 21.9 Hz), 114.86 (s), 82.94 (s), 81.24 (s), 64.39 (dd, *J* = 18.6, 7.5 Hz), 32.04 (s), 21.01 (s), 16.35 (dd, *J* = 22.5, 5.6 Hz).

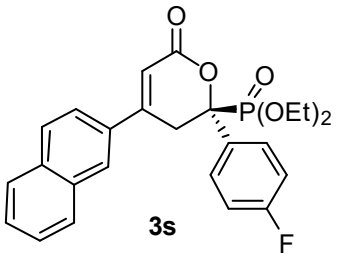
^{31}P NMR (162 MHz, $CDCl_3$) δ 16.34 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.89 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{22}H_{25}FO_5P$ $[M+H]^+$, 419.1418; found 419.1408.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 ^oC, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 19.1 min, Rt_2 (major) = 38.3 min; er = 96:4).

Diethyl (*R*)-(2-(4-fluorophenyl)-4-(naphthalen-2-yl)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl) phosphonate (3s):



3s

Light yellow oil, 40 mg, yield: 88%.

[α]$_D^{26}$ = 214.2 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.5 Hz, 1H), 7.94 - 7.88 (m, 1H), 7.85 - 7.82 (m, 2H), 7.59 - 7.51 (m, 3H), 7.48 (dd, *J* = 8.4, 2.2 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.36 (dd, *J* = 12.1, 1.5 Hz, 1H), 4.35 - 4.22 (m, 2H), 3.97 - 3.91(m, 1H), 3.80 - 3.68 (m, 3H), 2.30 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H).

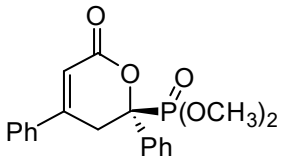
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.02 (d, *J* = 9.0 Hz), 162.79 (d, *J* = 248.5 Hz), 152.24 (d, *J* = 13.7 Hz), 138.42 (d, *J* = 3.1 Hz), 134.29 (s), 133.14 (dd, *J* = 17.7, 15.5 Hz), 129.29 (d, *J* = 2.6 Hz), 128.86 (s), 127.73 (d, *J* = 2.6 Hz), 127.03 (s), 126.59 (s), 126.21 (d, *J* = 4.1 Hz), 122.70 (s), 115.14 (s), 82.19 (d, *J* = 170.6 Hz), 64.56 (d, *J* = 7.6 Hz), 64.47 (d, *J* = 7.6 Hz), 31.78 (s), 21.04 (s), 16.62 (d, *J* = 5.6 Hz), 16.29 (d, *J* = 5.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 17.09 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{26}H_{28}O_5P$ $[M+H]^+$, 451.1669; found 451.1658.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 16.1 min, Rt_2 (major) = 22.3 min; er = 96:4).

Dimethyl (*R*)-(6-oxo-2,4-diphenyl-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3t):



3t

Light yellow oil, 18 mg, yield: 50%.

$[\alpha]_D^{26}$ = 114.1 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.50 - 7.45 (m, 2H), 7.43 - 7.33 (m, 5H), 7.33 - 7.28 (m, 1H), 6.22 (d, *J* = 2.1 Hz, 1H), 3.88 (d, *J* = 10.4 Hz, 3H), 3.73 - 3.66 (m, 1H), 3.62 - 3.55 (m, 1H), 3.46 (d, *J* = 10.4 Hz, 3H).

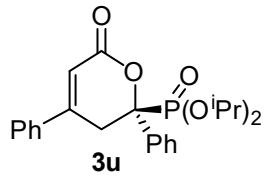
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.92 (d, *J* = 9.3 Hz), 152.64 (d, *J* = 13.3 Hz), 136.24 (s), 135.93 (d, *J* = 2.1 Hz), 130.93 (s), 129.07 (s), 128.70 (d, *J* = 2.7 Hz), 128.67 (d, *J* = 3.4 Hz), 126.17 (d, *J* = 4.2 Hz), 126.10 (s), 114.96 (s), 82.29 (d, *J* = 170.0 Hz), 54.95 (d, *J* = 7.3 Hz), 54.76 (d, *J* = 7.7 Hz), 31.98 (s).

^{31}P NMR (162 MHz, $CDCl_3$) δ 18.52 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{19}H_{20}O_5P$ $[M+H]^+$, 359.1043; found 359.1037.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.8 mL/min, 254 nm), Rt_1 (minor) = 15.2 min, Rt_2 (major) = 23.8 min; er = 97:3).

Diisopropyl (*R*)-(6-oxo-2,4-diphenyl-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3u):



3u

Light yellow oil, 25.2 mg, yield: 61%.

$[\alpha]_D^{26}$ = 100.0 (*c* 1.0 $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.47 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.43 - 7.37 (m, 3H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.30 - 7.27 (m, 1H), 6.21 (d, *J* = 2.1 Hz, 1H), 4.82 (dq, *J* = 12.5, 6.3 Hz, 1H), 4.36 (dq, *J* = 12.5, 6.3 Hz, 1H), 3.68 (ddd, *J* = 17.8, 11.1, 2.2 Hz, 1H), 3.55 (dd, *J* = 17.8, 6.5 Hz, 1H), 1.35 (d, *J* = 6.2 Hz, 3H), 1.33 (d, *J* = 6.1 Hz, 3H), 1.22 (d, *J* = 6.1 Hz, 3H), 0.95 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.39 (d, *J* = 9.2 Hz), 152.72 (d, *J* = 13.2 Hz), 136.90 (s), 136.26 (s), 130.81 (s), 129.07 (s), 128.42 (d, *J* = 1.6 Hz), 128.38 (d, *J* = 2.1 Hz), 126.48 (d,

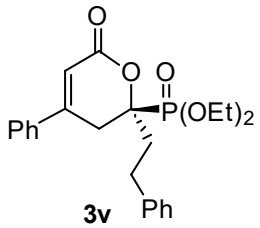
J = 4.1 Hz), 126.16 (s), 115.20 (s), 82.27 (d, *J* = 171.1 Hz), 73.45 (d, *J* = 7.5 Hz), 73.15 (d, *J* = 7.9 Hz), 32.41 (s), 24.32 (d, *J* = 2.1 Hz), 24.07 (d, *J* = 3.8 Hz), 23.26 (d, *J* = 5.9 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 15.34 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{23}H_{28}O_5P$ $[M+H]^+$, 415.1669; found 415.1657.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel OD-H; 25 °C, IPA/Hexane = 20/80, 0.6 mL/min, 254 nm), Rt_1 (major) = 8.0 min, Rt_2 (minor) = 9.4 min; er = 97: 3).

Diethyl (*S*)-(6-oxo-2-phenethyl-4-phenyl-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3v):



3v

Light yellow oil, 8 mg, yield: 19%.

$[\alpha]_D^{26}$ = 84.2 (*c* 0.5 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 - 7.52 (m, 2H), 7.48 - 7.43 (m, 3H), 7.31 - 7.26 (m, 2H), 7.19 (dd, *J* = 5.2, 2.4 Hz, 3H), 6.37 (d, *J* = 1.4 Hz, 1H), 4.29 - 4.16 (m, 4H), 3.46 - 3.36 (m, 1H), 3.02 (ddd, *J* = 20.2, 18.5, 1.6 Hz, 1H), 2.93 - 2.83 (m, 2H), 2.45 - 2.23 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

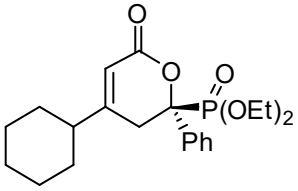
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.19 (d, *J* = 4.5 Hz), 152.43 (d, *J* = 6.6 Hz), 140.87 (s), 136.01 (s), 130.88 (s), 129.09 (s), 128.61 (s), 128.40 (s), 126.25 (s), 126.13 (s), 114.33 (s), 81.18 (d, *J* = 168.0 Hz), 63.85 (d, *J* = 7.2 Hz), 63.76 (d, *J* = 7.6 Hz), 38.02 (d, *J* = 2.3 Hz), 30.37 (d, *J* = 3.1 Hz), 29.81 (d, *J* = 5.3 Hz), 16.55 (s), 16.50 (s).

^{31}P NMR (202 MHz, $CDCl_3$) δ 21.06 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{23}H_{28}O_5P$ $[M+H]^+$, 415.1669; found 415.1656.

Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.6 mL/min, 254 nm), Rt_1 (minor) = 19.6 min, Rt_2 (major) = 32.5 min; er = 97:3).

Diethyl (*R*)-(4-cyclohexyl-6-oxo-2-phenyl-3,6-dihydro-2*H*-pyran-2-yl)phosphonate (3w):



Colorless oil, 7 mg, yield: 17%.

$[\alpha]_D^{26}$ = 294.0 (*c* 1.0 $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 - 7.48 (m, 2H), 7.41 - 7.30 (m, 3H), 5.68 (s, 1H), 4.29 - 4.20 (m, 2H), 4.16 (ddd, *J* = 14.2, 9.0, 7.1 Hz, 1H), 3.92 - 3.78 (m, 1H), 3.61 (ddd, *J* = 10.1, 8.1, 7.1 Hz, 1H), 3.29 (ddd, *J* = 17.8, 11.2, 2.1 Hz, 1H), 3.06 (dd, *J* = 17.8, 6.6 Hz, 1H), 2.00 (dd, *J* = 15.7, 7.3 Hz, 1H), 1.84 - 1.73 (m, 2H), 1.73 - 1.60 (m, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.29 - 1.23 (m, 2H), 1.22 - 1.15 (m, 2H), 1.08 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.25 (d, *J* = 8.9 Hz), 162.81 (d, *J* = 12.4 Hz), 136.61 (s), 128.35 (s), 128.33 (s), 126.20 (d, *J* = 4.1 Hz), 114.11 (s), 81.99 (d, *J* = 168.9 Hz), 64.31 (t,

J = 7.1 Hz), 44.87 (d, J = 1.6 Hz), 32.23 (s), 30.19 (s), 29.91 (s), 26.15 - 25.50 (m), 16.46 (d, J = 5.6 Hz), 16.18 (d, J = 5.6 Hz).

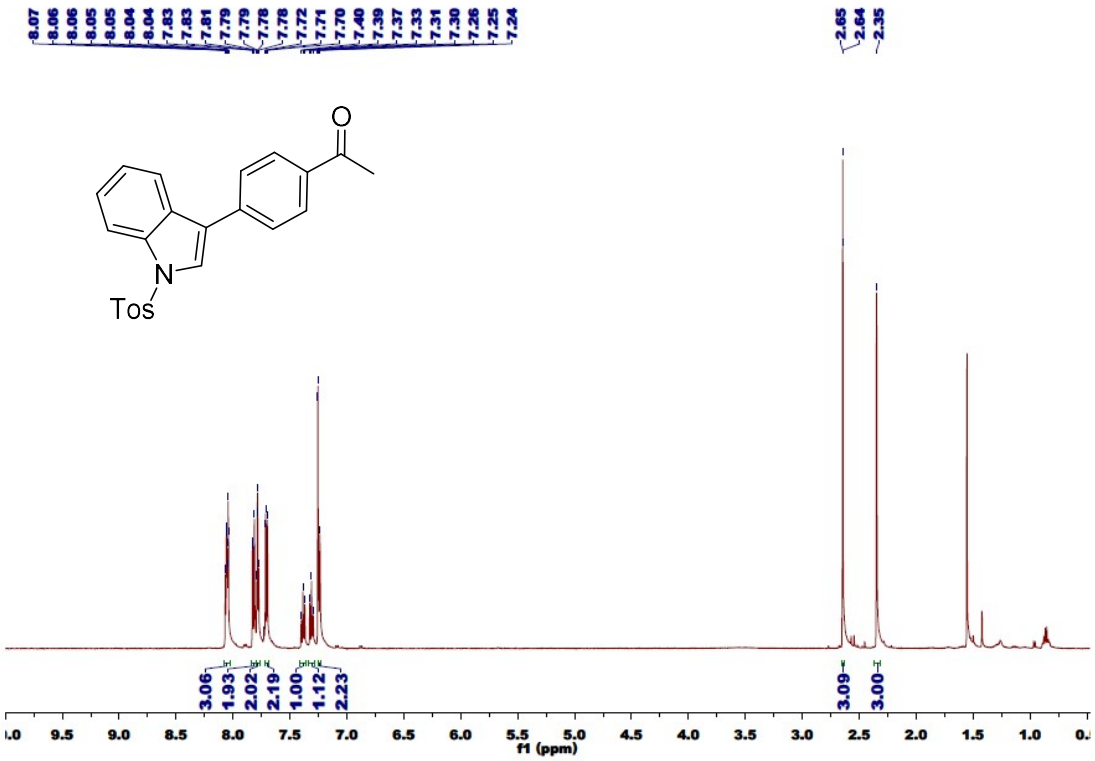
^{31}P NMR (162 MHz, $CDCl_3$) δ 16.46 (s).

HRMS (ESI, m/z): Mass calcd. for $C_{21}H_{30}O_5P$ $[M+H]^+$, 393.1825; found 393.1813.

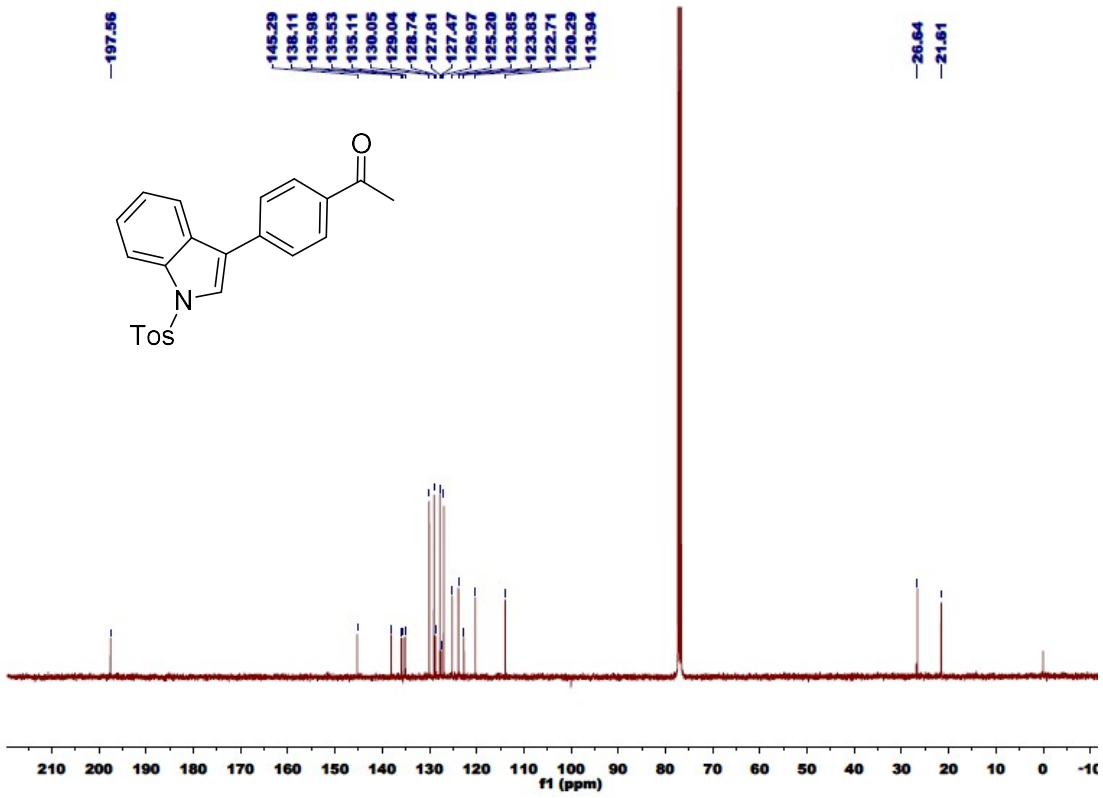
Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel AD-H; 25 °C, IPA/Hexane = 20/80, 0.6 mL/min, 254 nm), Rt_1 (minor) = 10.8 min, Rt_2 (major) = 14.0 min; er = 98:2).

Ⅸ. NMR spectra of intermediates & products

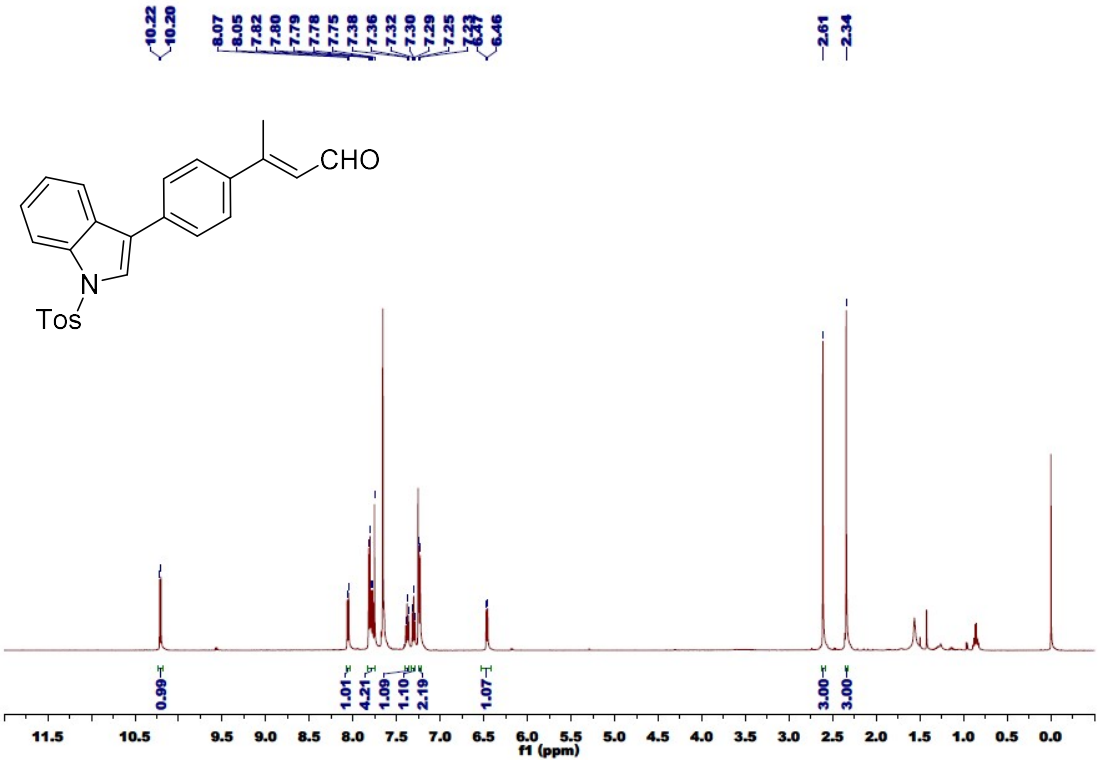
1m-3 ^{1}H NMR



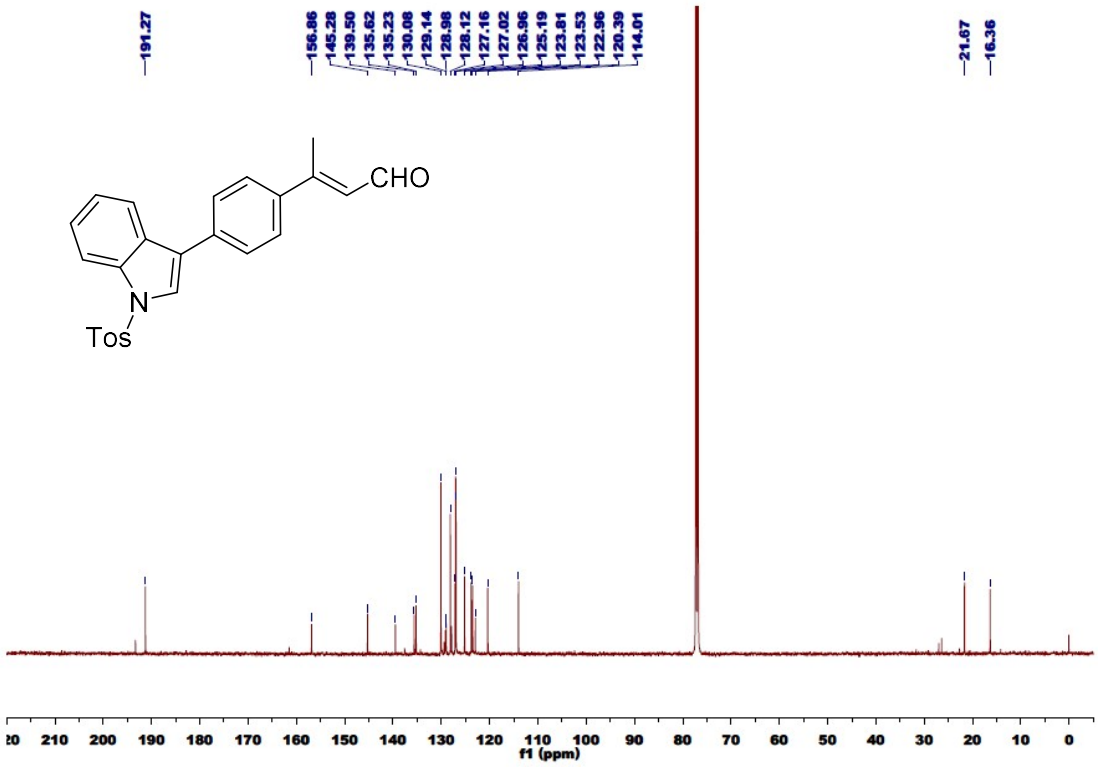
1m-3 ^{13}C NMR



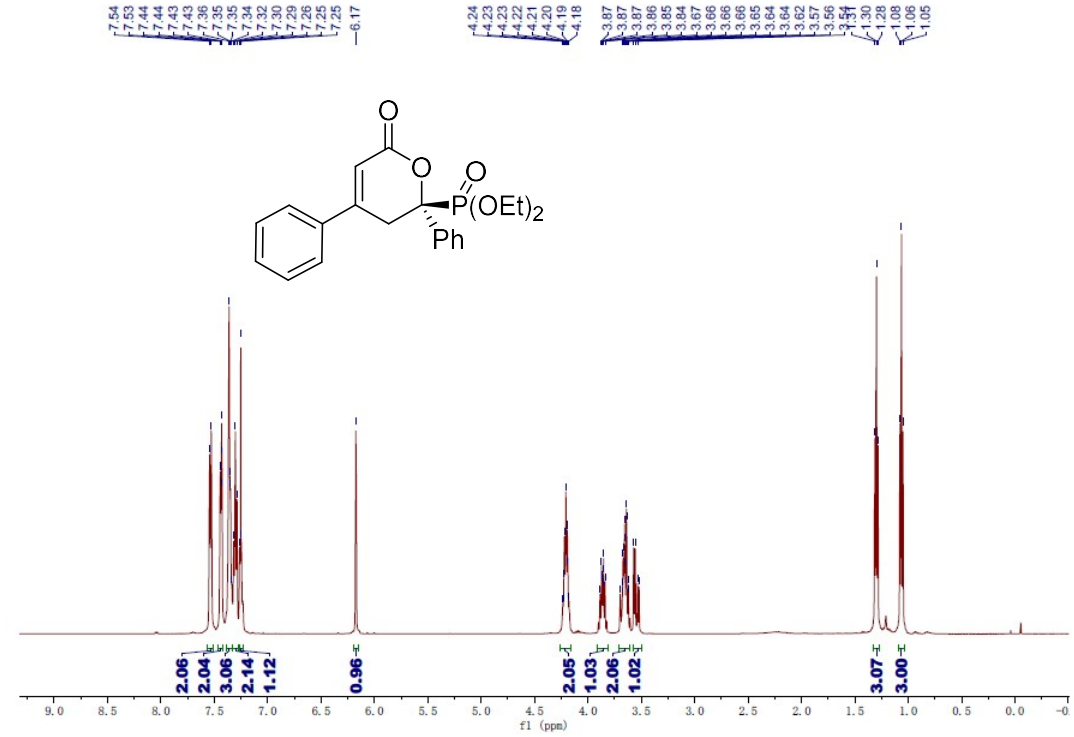
1m ^{1}H NMR



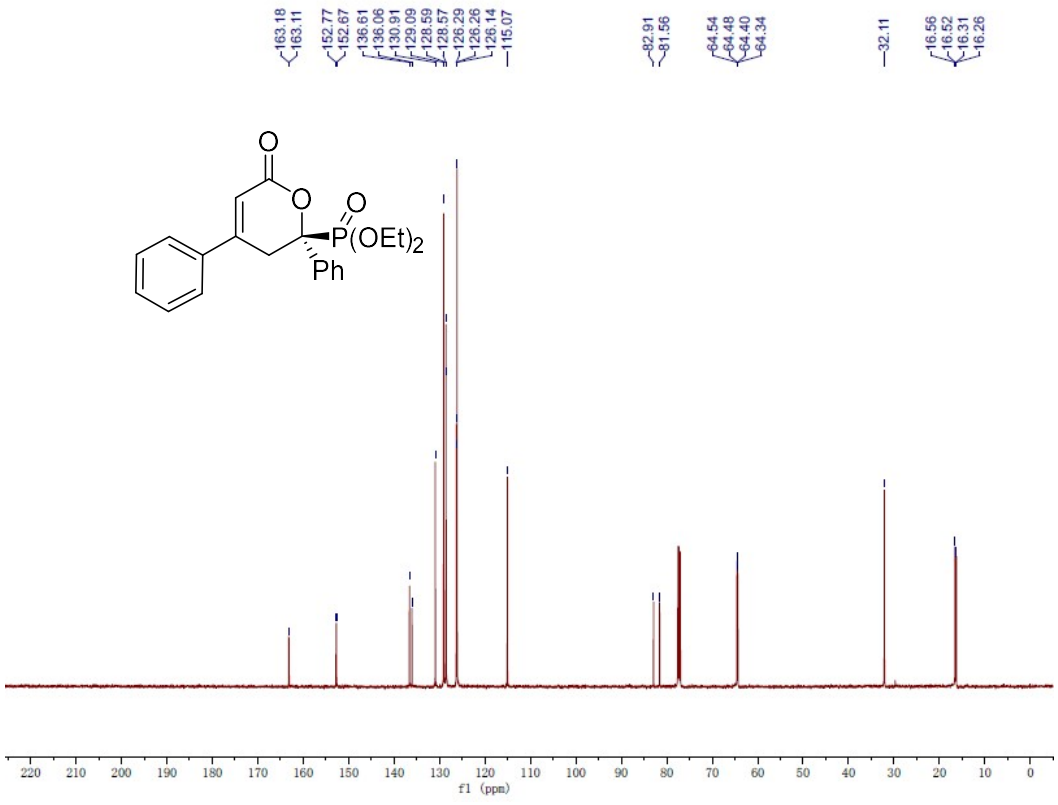
1m ^{13}C NMR



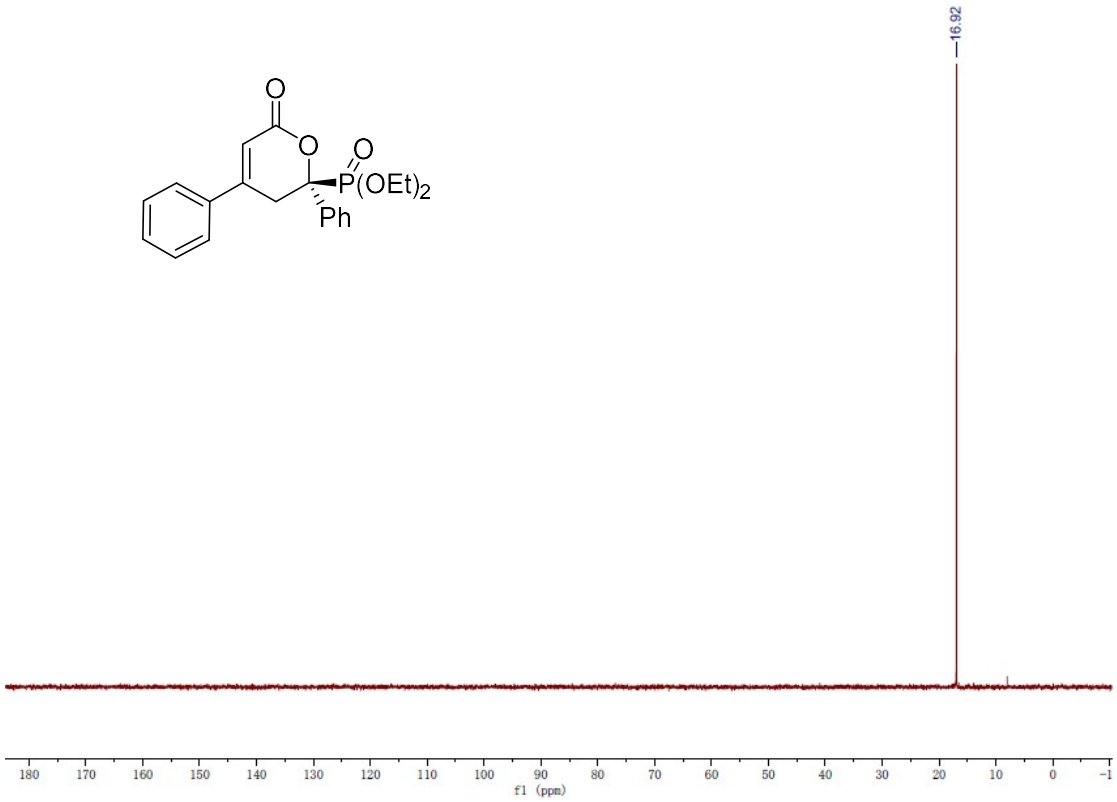
3a ^{1}H NMR



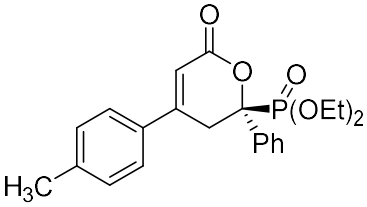
3a ^{13}C NMR

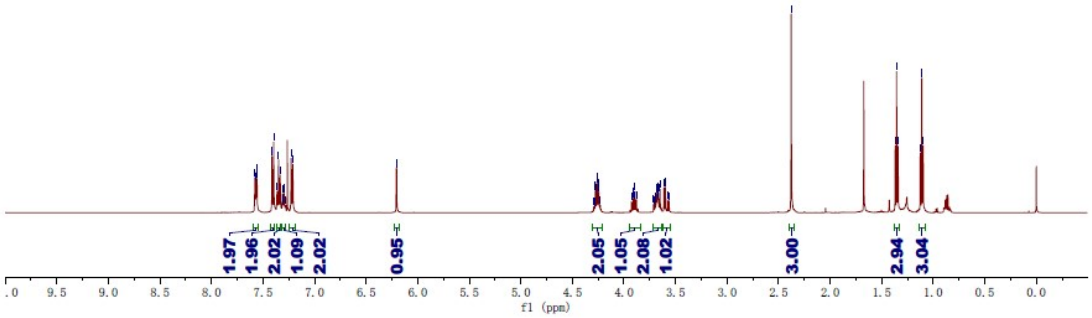


3a ^{31}P NMR

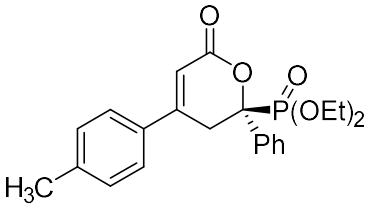

16.92
O
O
O
P(OEt)2
Ph
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

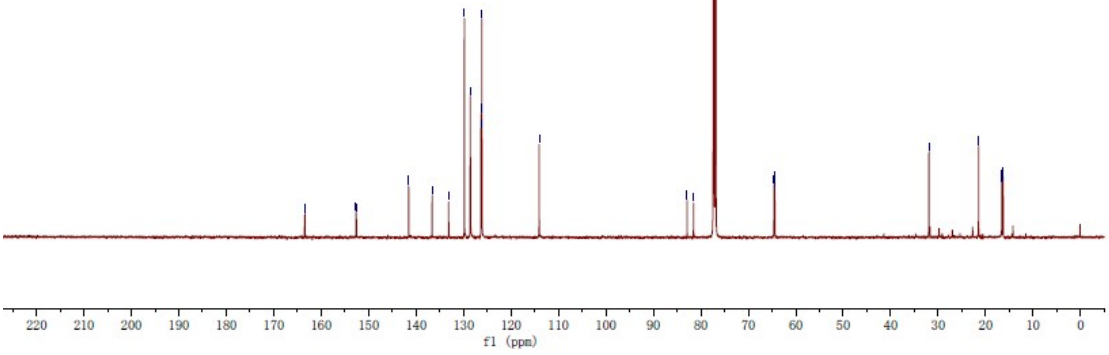
3b ^{1}H NMR



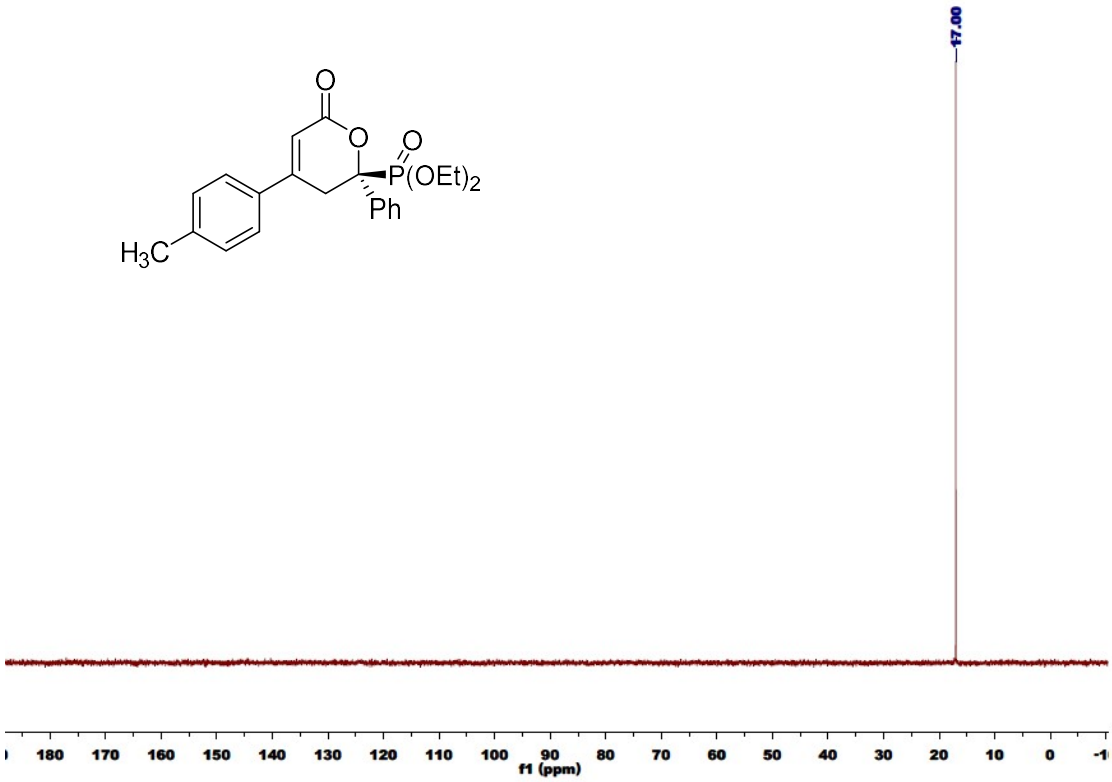


3b ^{13}C NMR

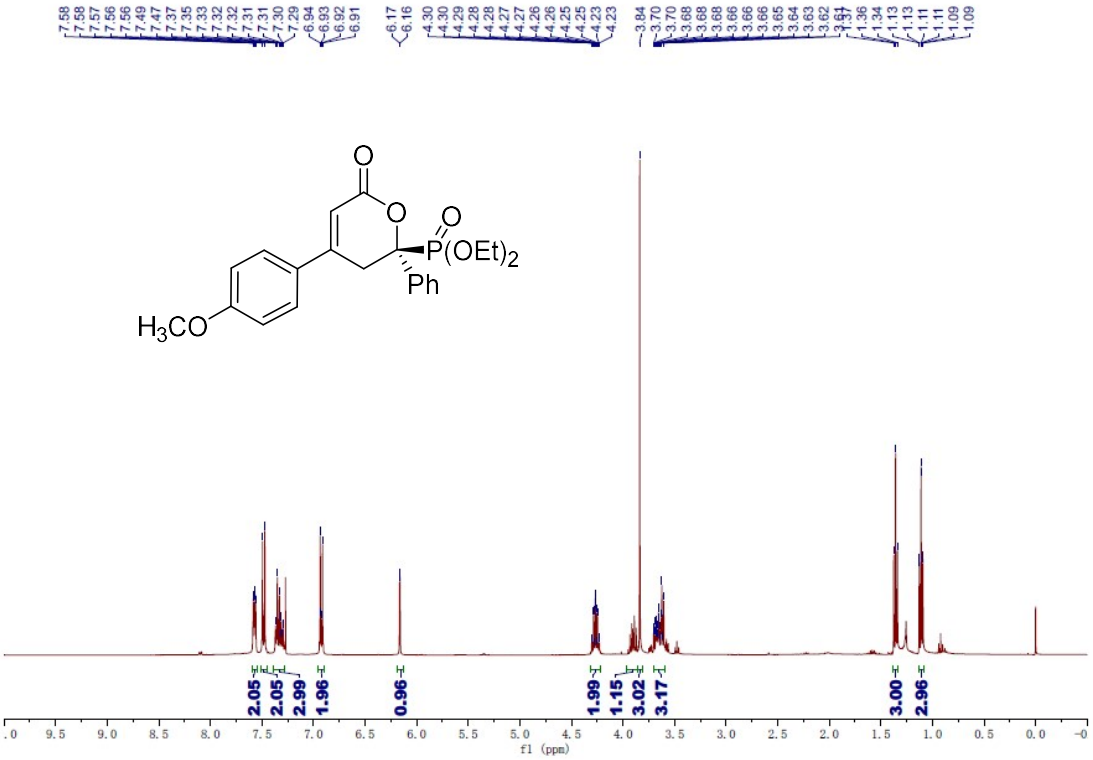




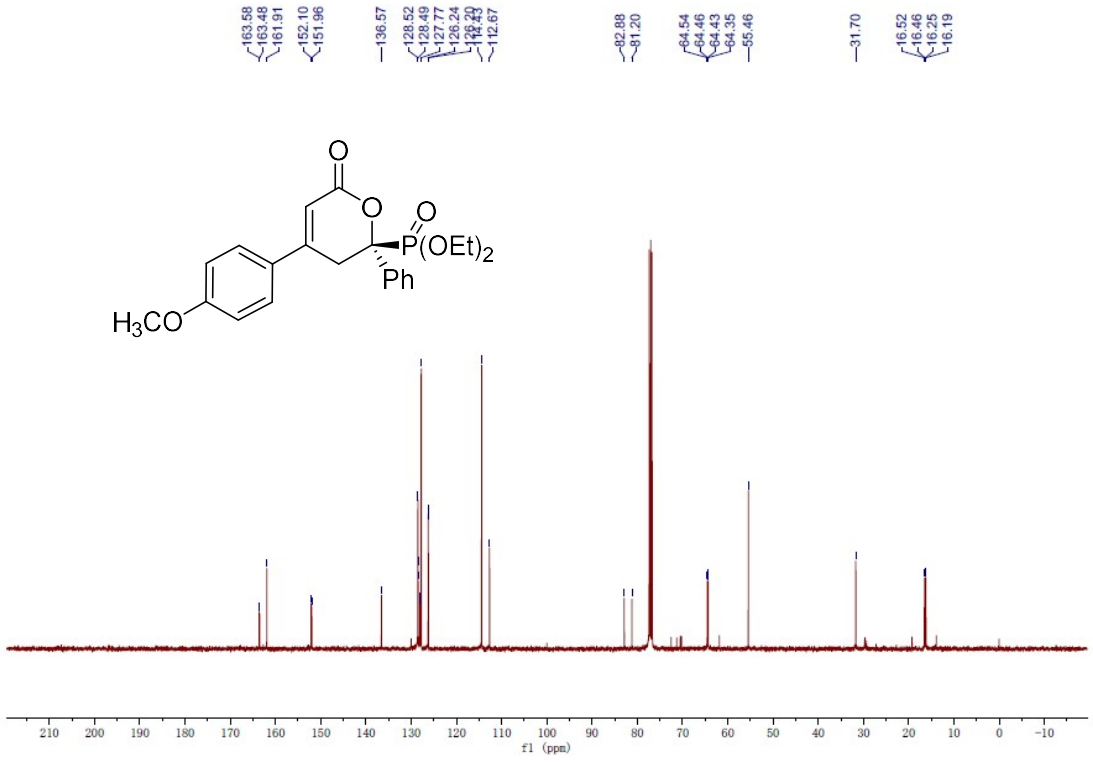
3b ^{31}P NMR


17.00
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

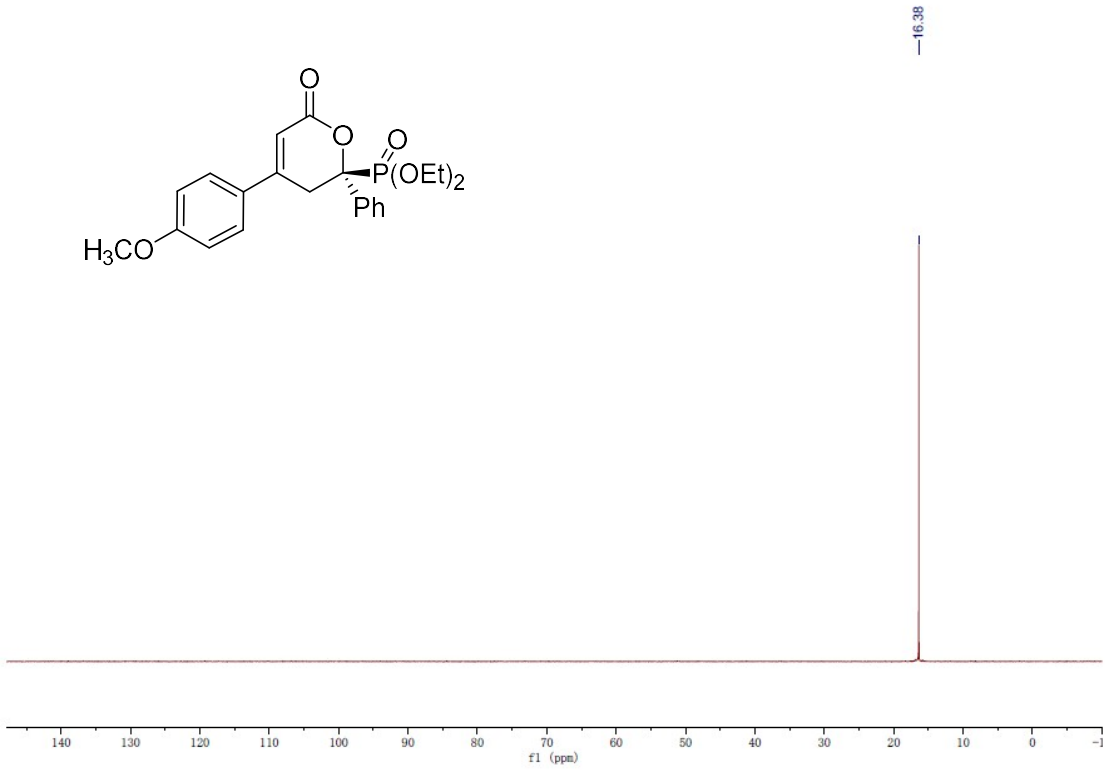
3c ^{1}H NMR



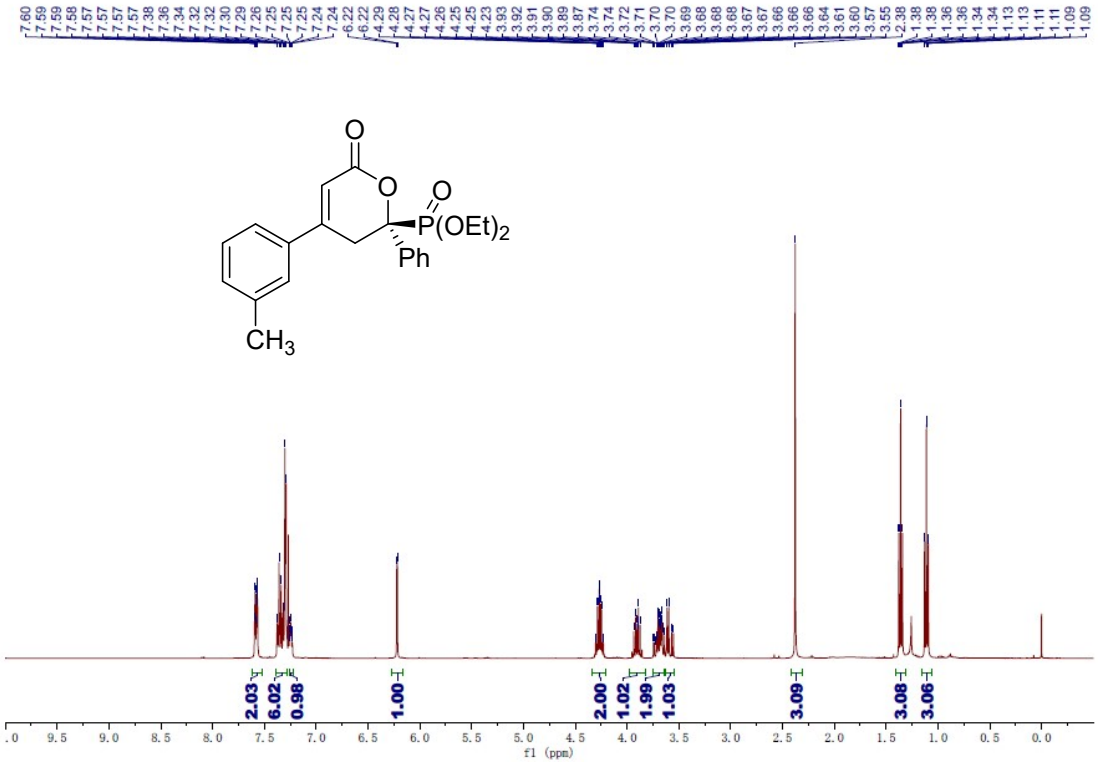
3c ^{13}C NMR



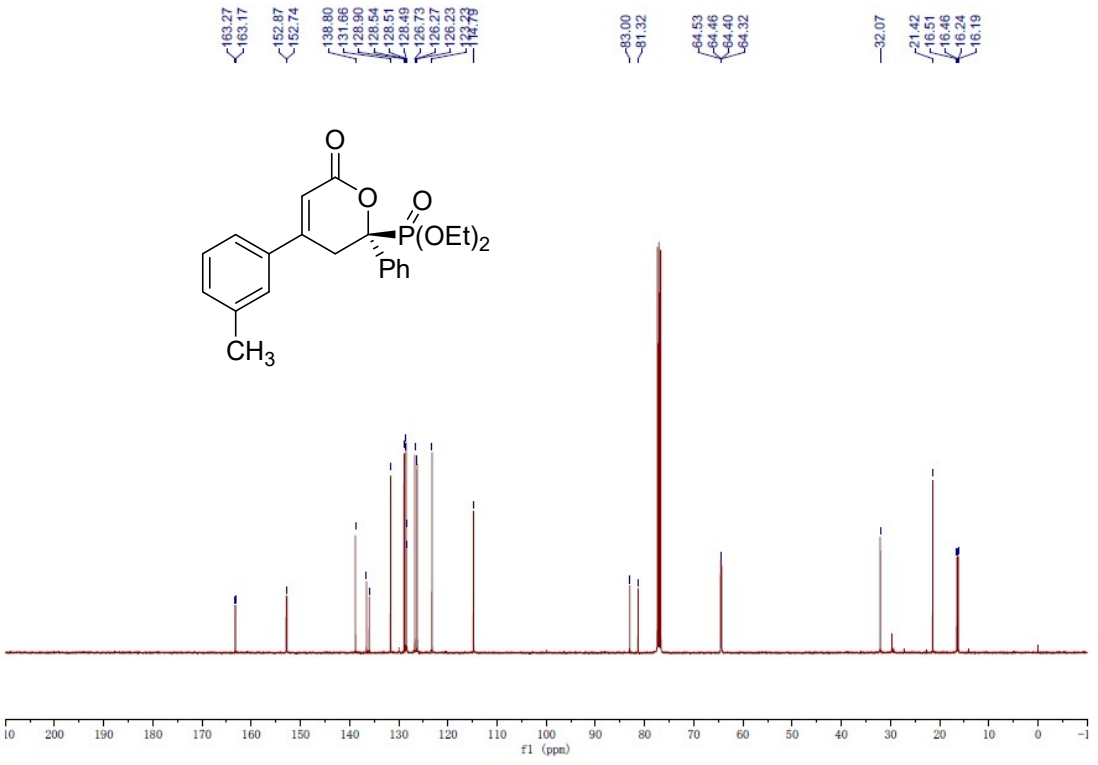
3c ^{31}P NMR


16.38
O
O
O
P(OEt)2
Ph
H3CO
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

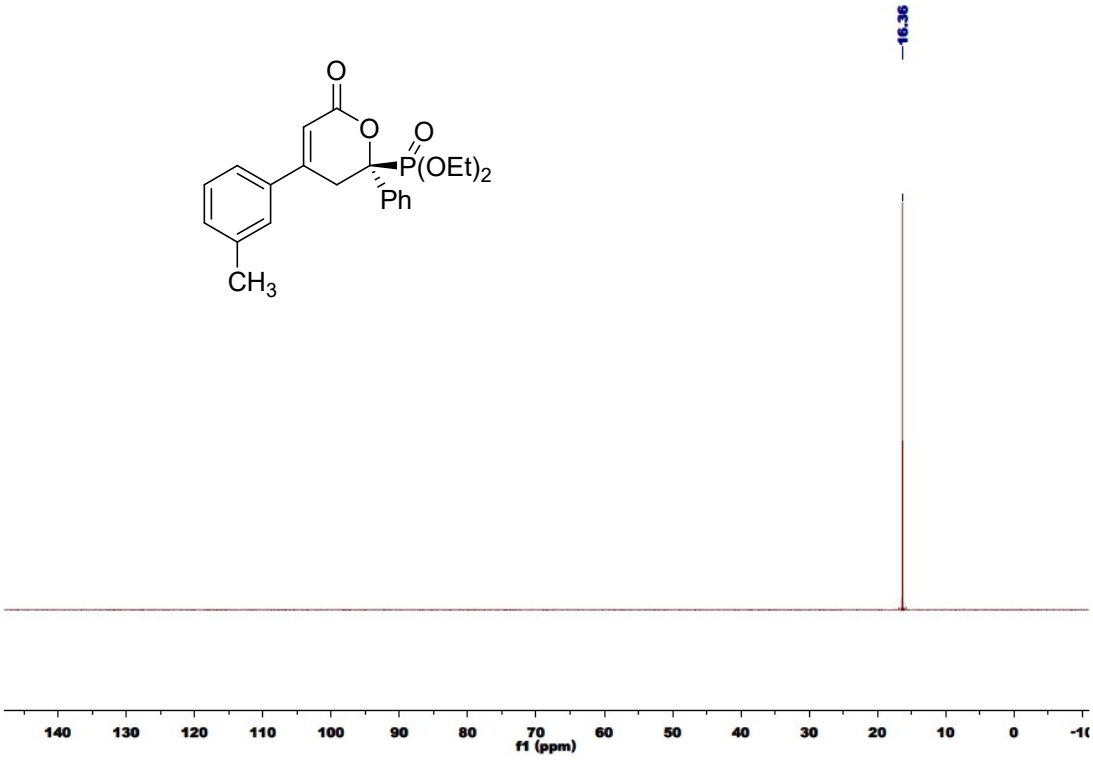
3d ^{1}H NMR



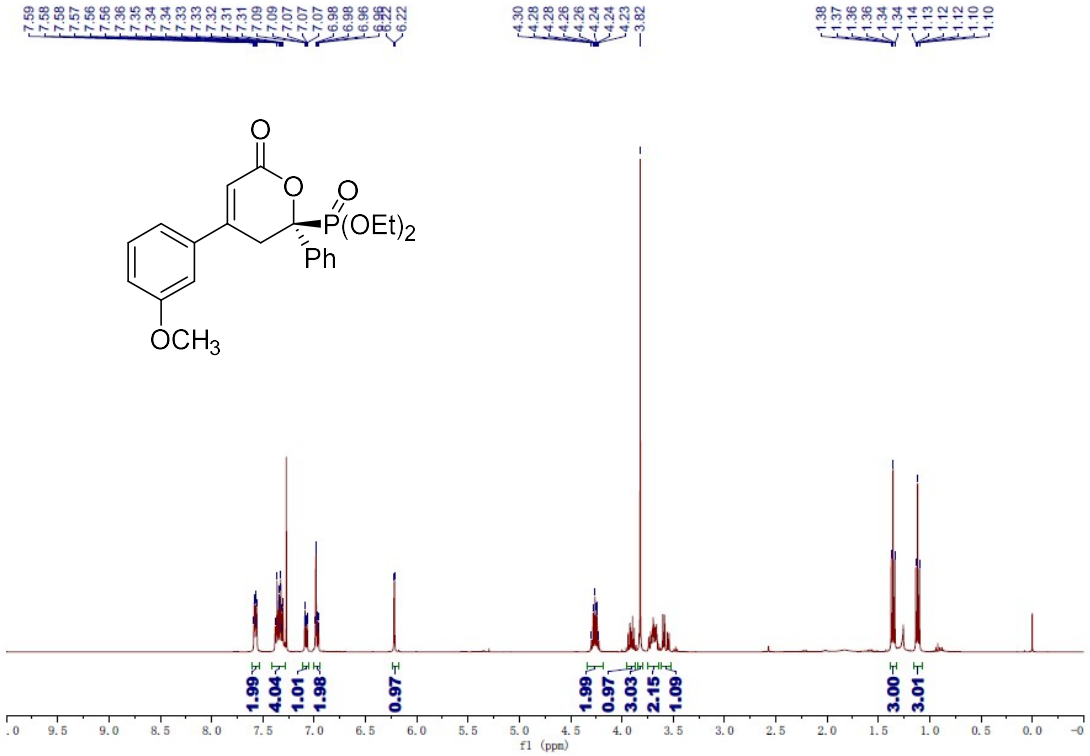
3d ^{13}C NMR



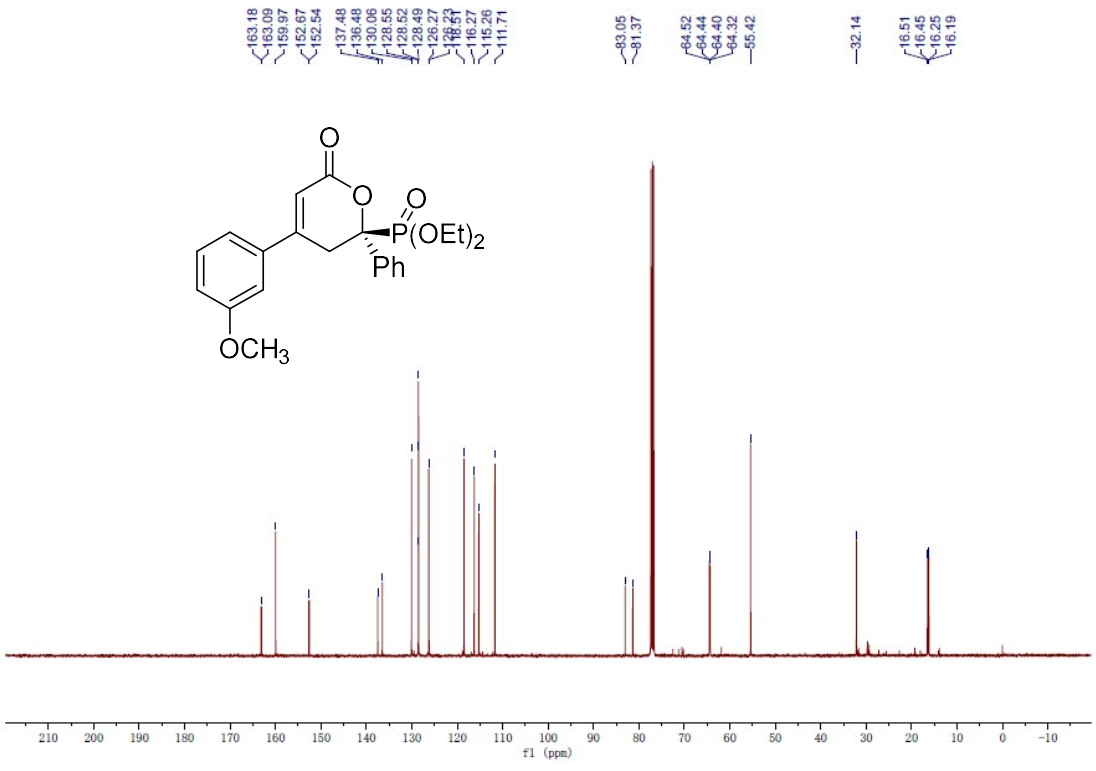
3d ^{31}P NMR


16.36
O
O
O
P(OEt)2
Ph
CH3
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

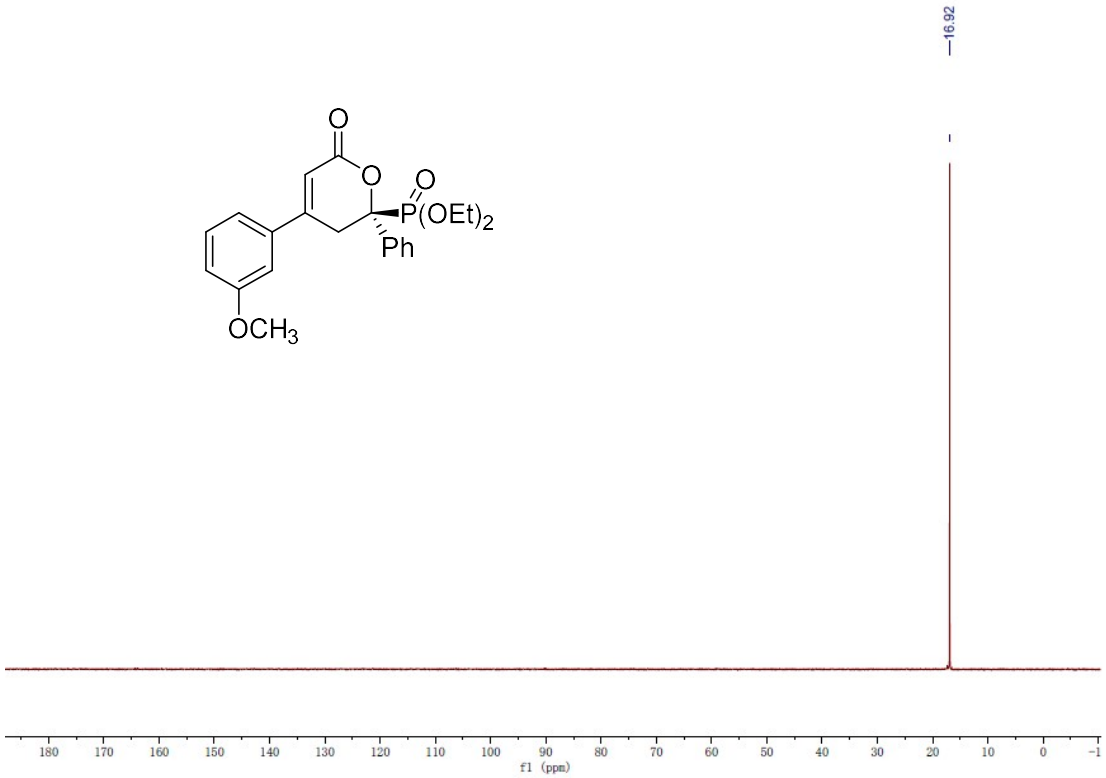
3e ^{1}H NMR



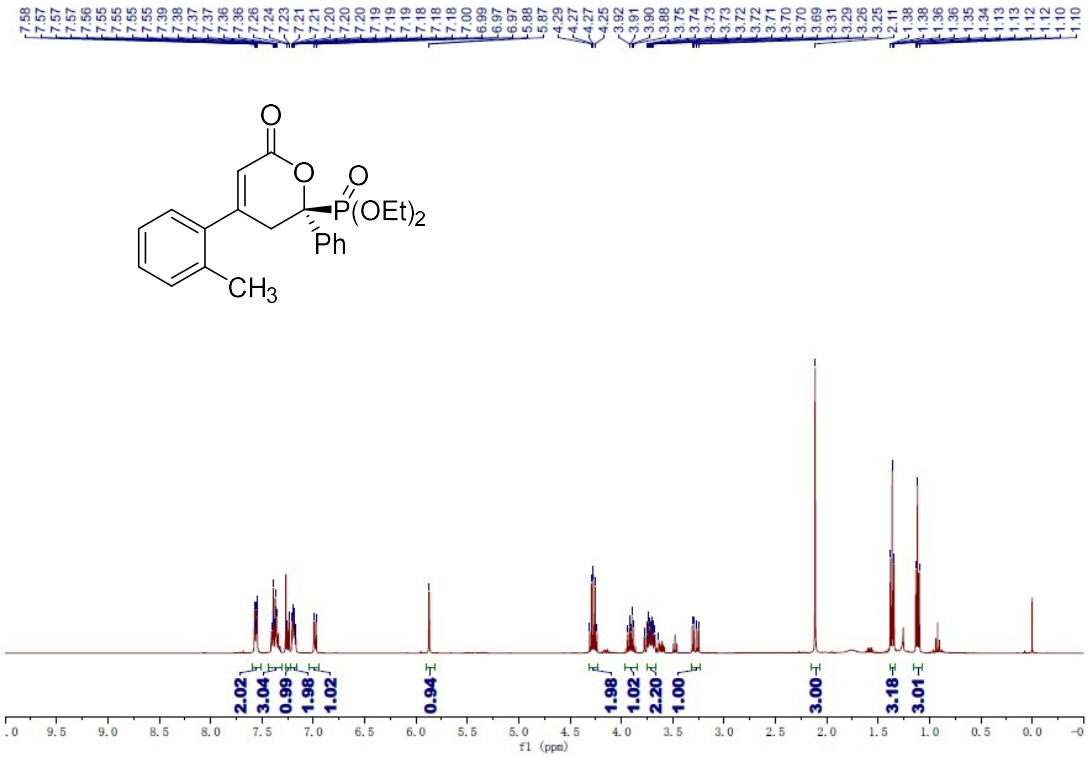
3e ^{13}C NMR



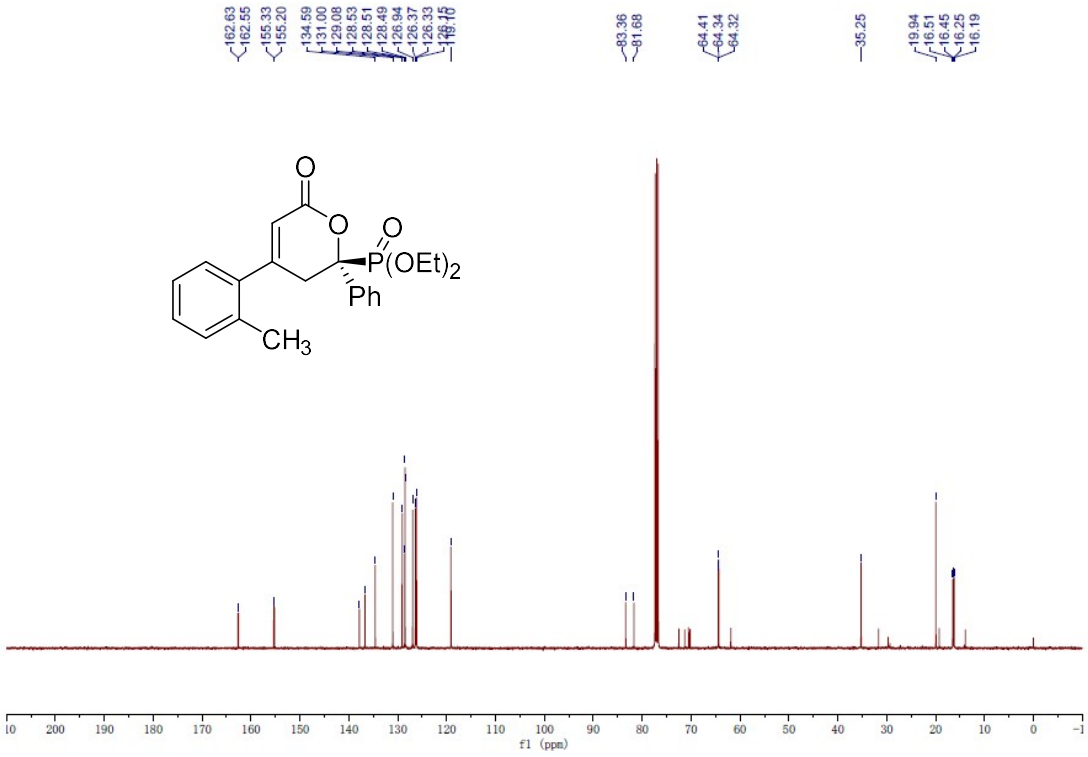
3e ^{31}P NMR


16.92
O
O
O
P(OEt)2
Ph
OCH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

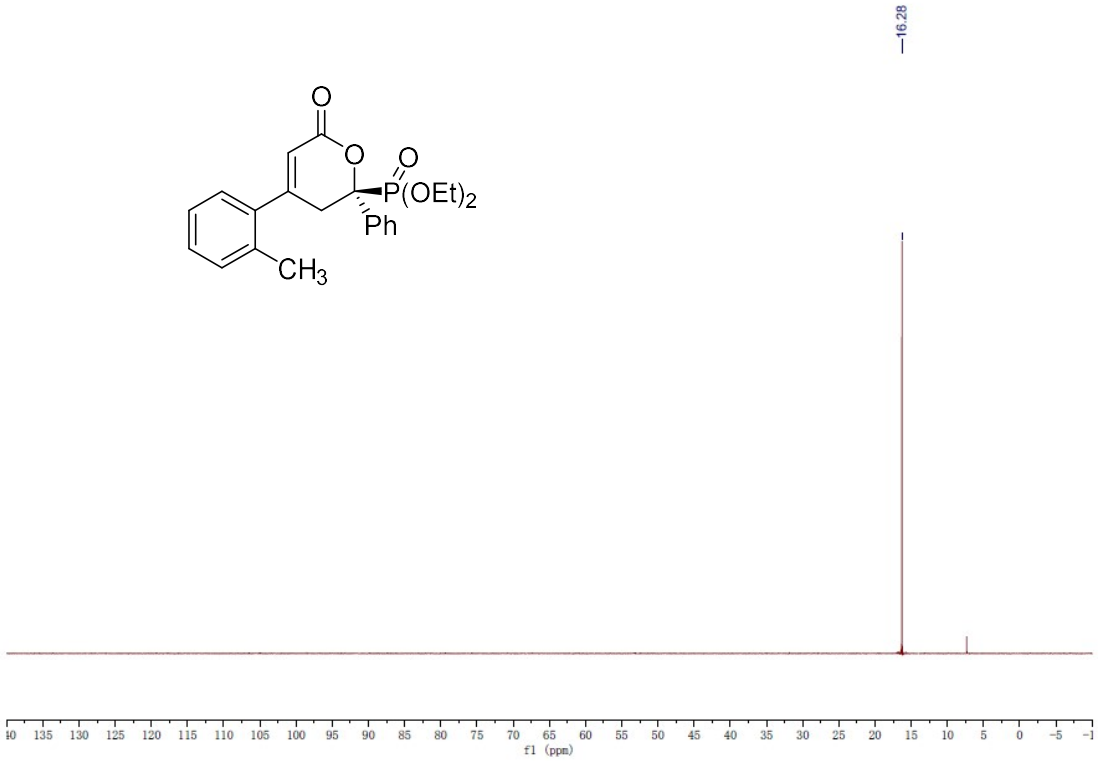
3f ^{1}H NMR



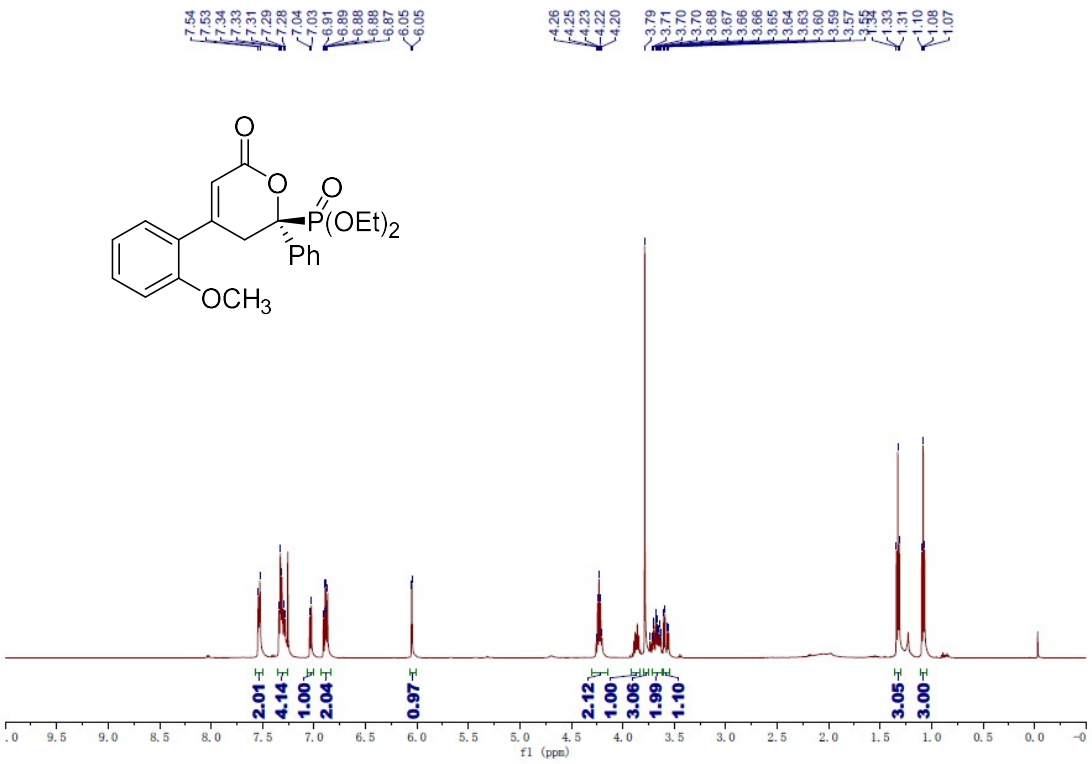
3f ^{13}C NMR



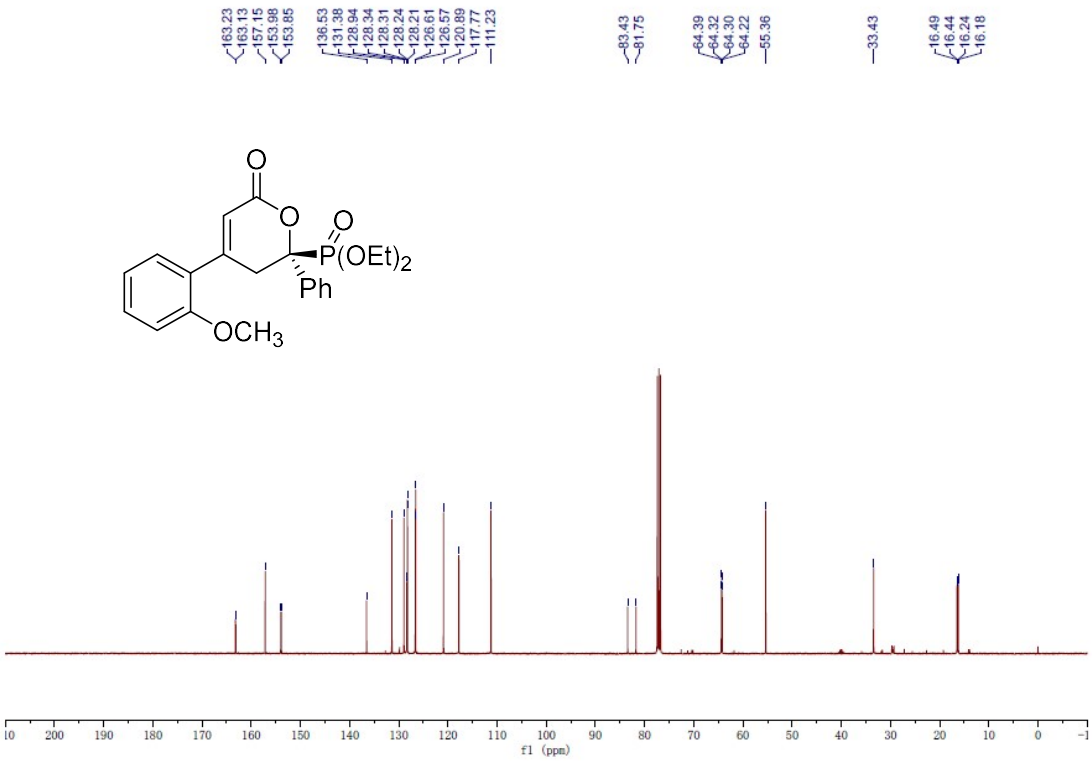
3f ^{31}P NMR


16.28
O
O
O
P(OEt)2
Ph
CH3
40 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 −5 −1
f1 (ppm)

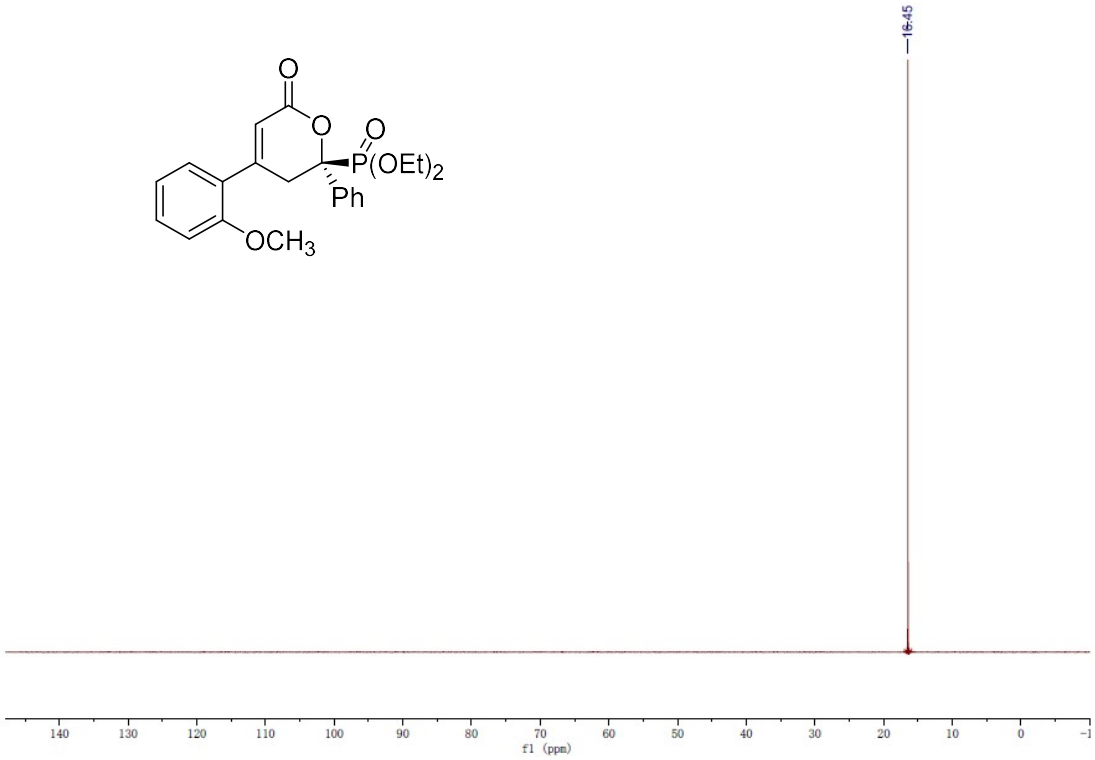
3g ^{1}H NMR



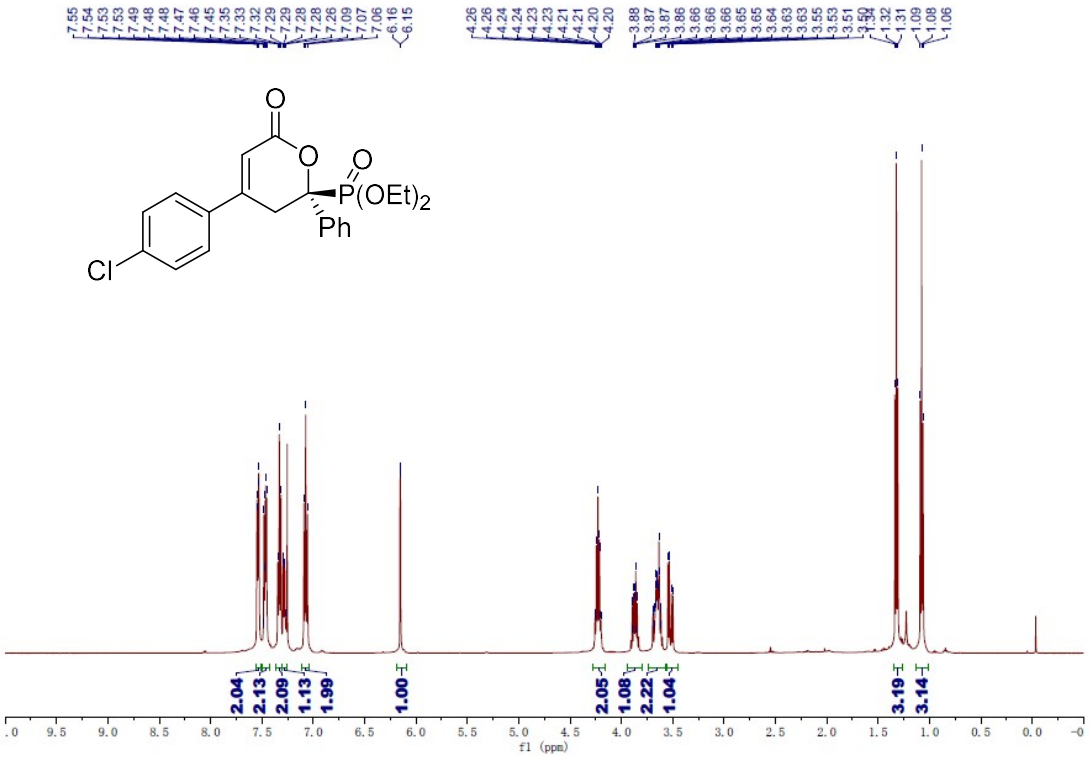
3g ^{13}C NMR



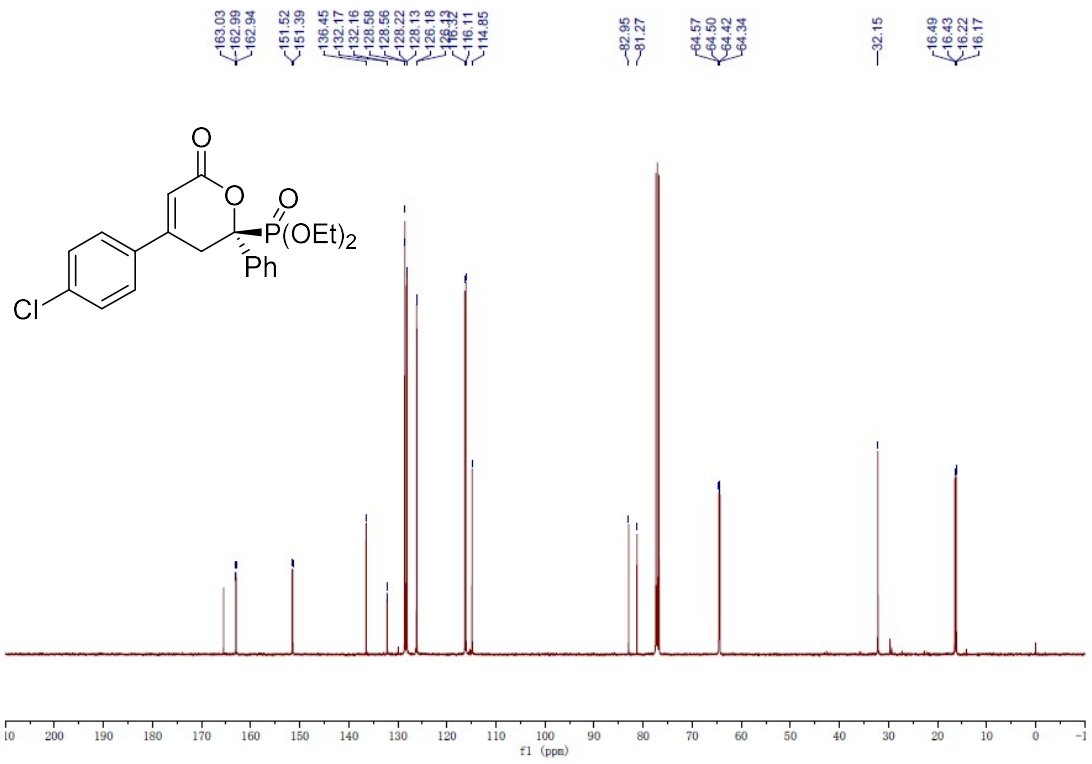
3g ^{31}P NMR


16.45
O
O
O
P(OEt)2
Ph
OCH3
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

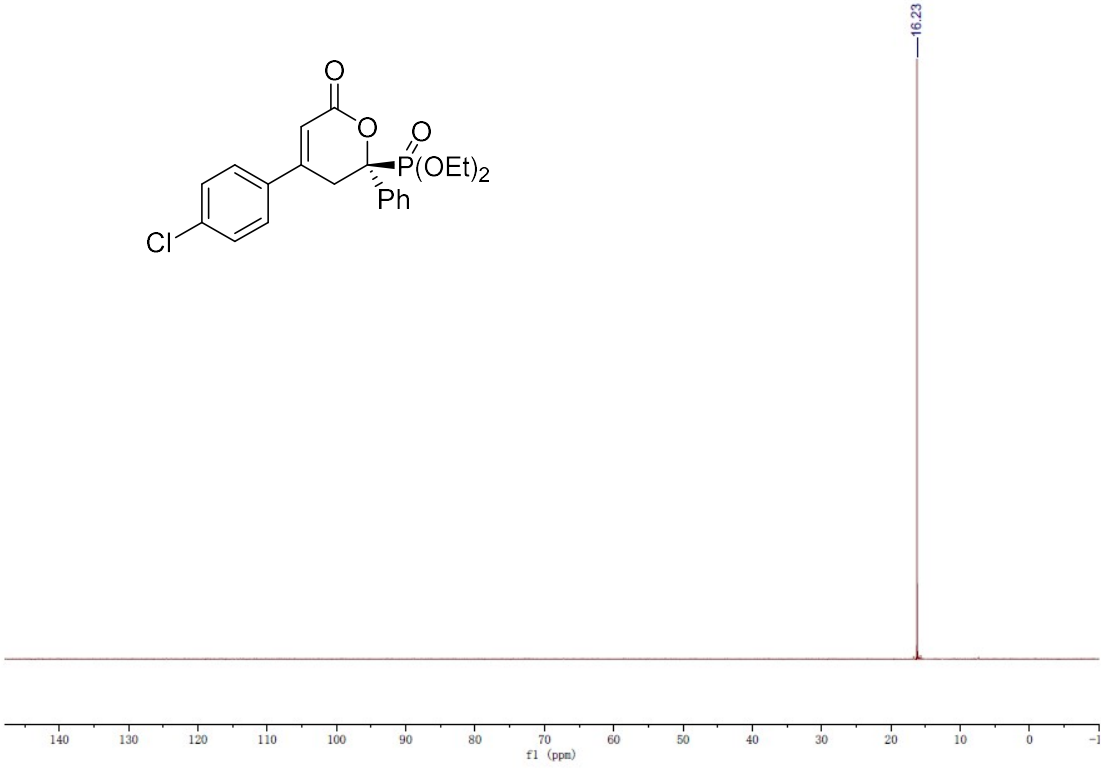
3h ^{1}H NMR



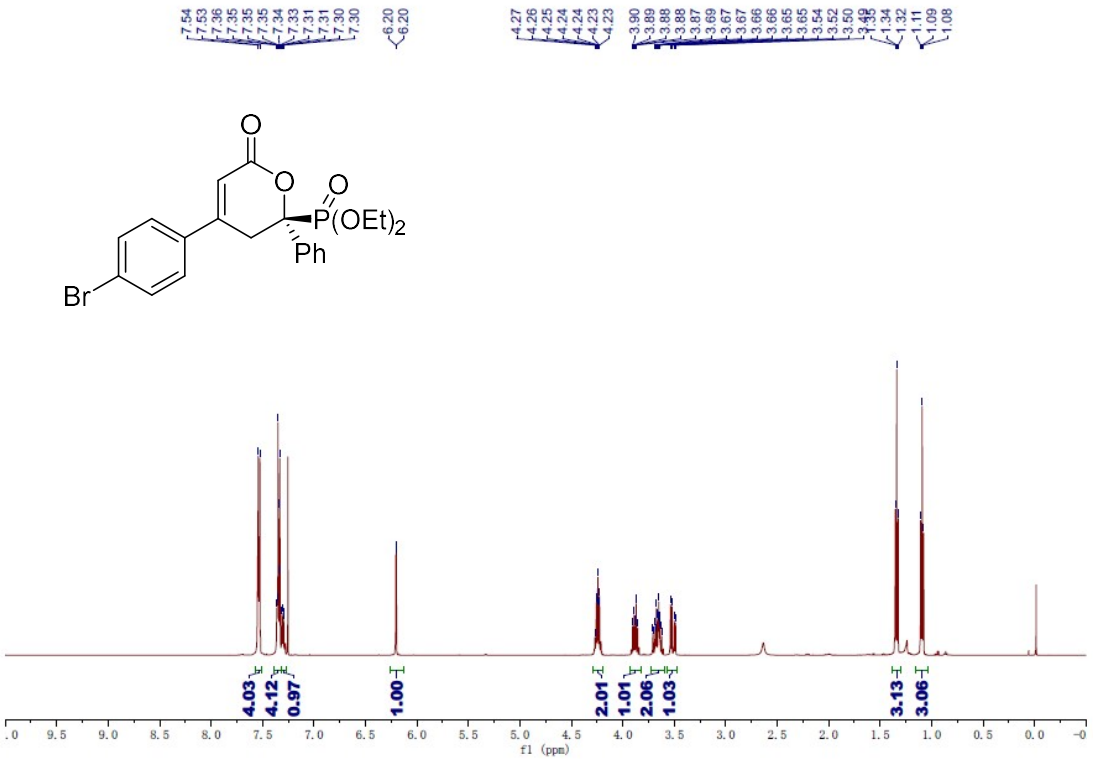
3h ^{13}C NMR



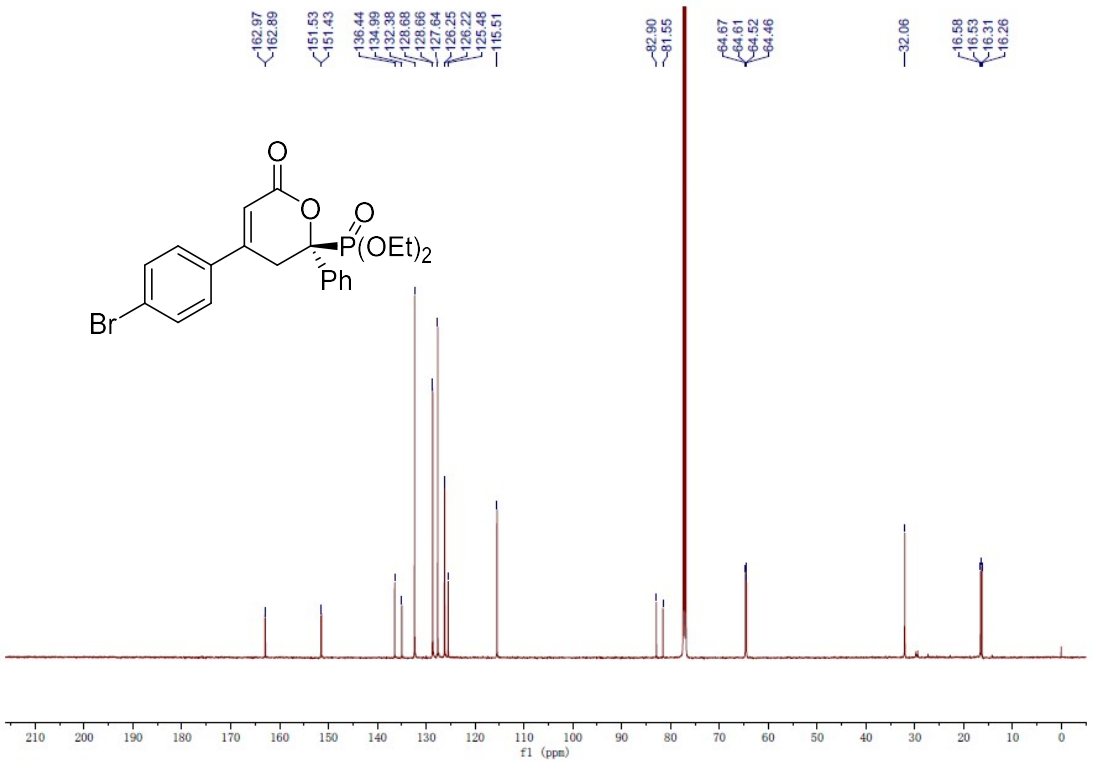
3h ^{31}P NMR


16.23
O
O
O
P(OEt)2
Ph
Cl
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

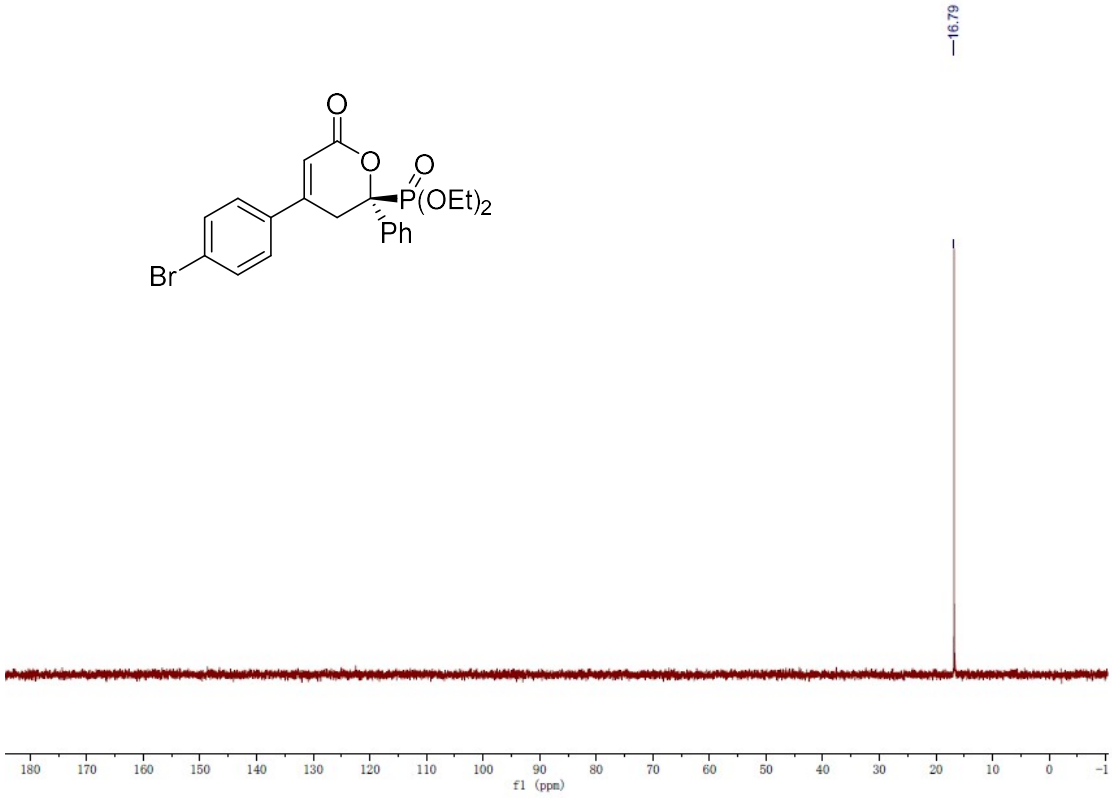
3i ^{1}H NMR



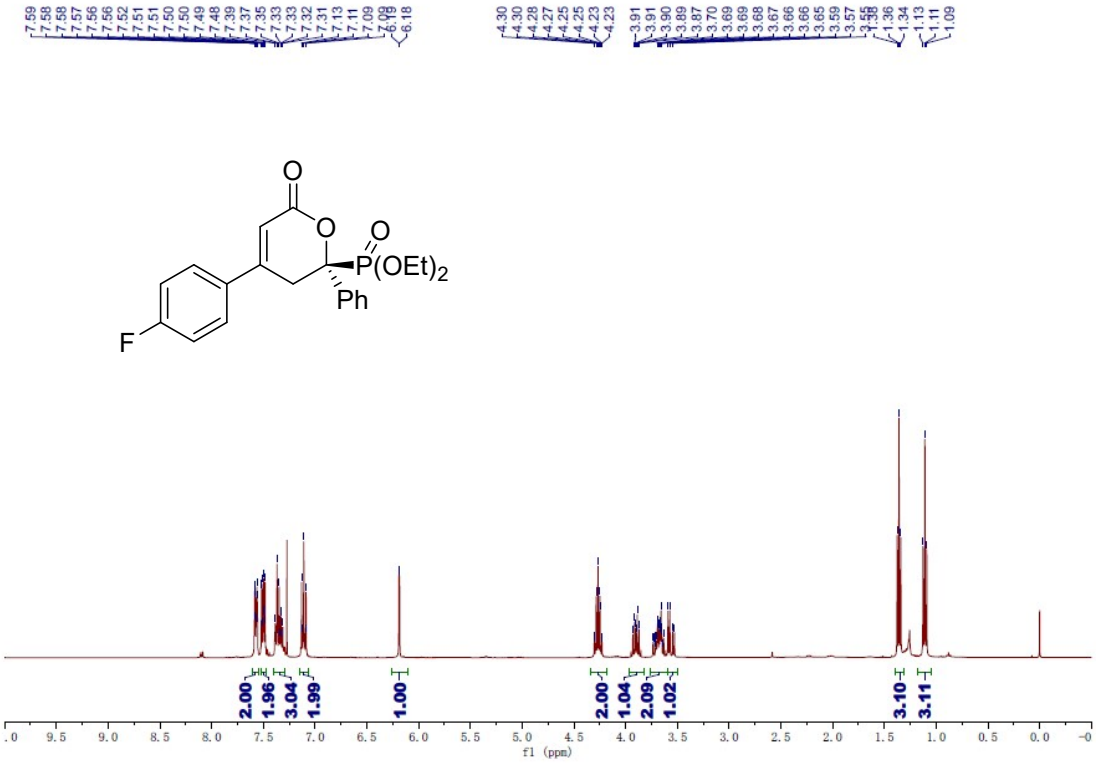
3i ^{13}C NMR



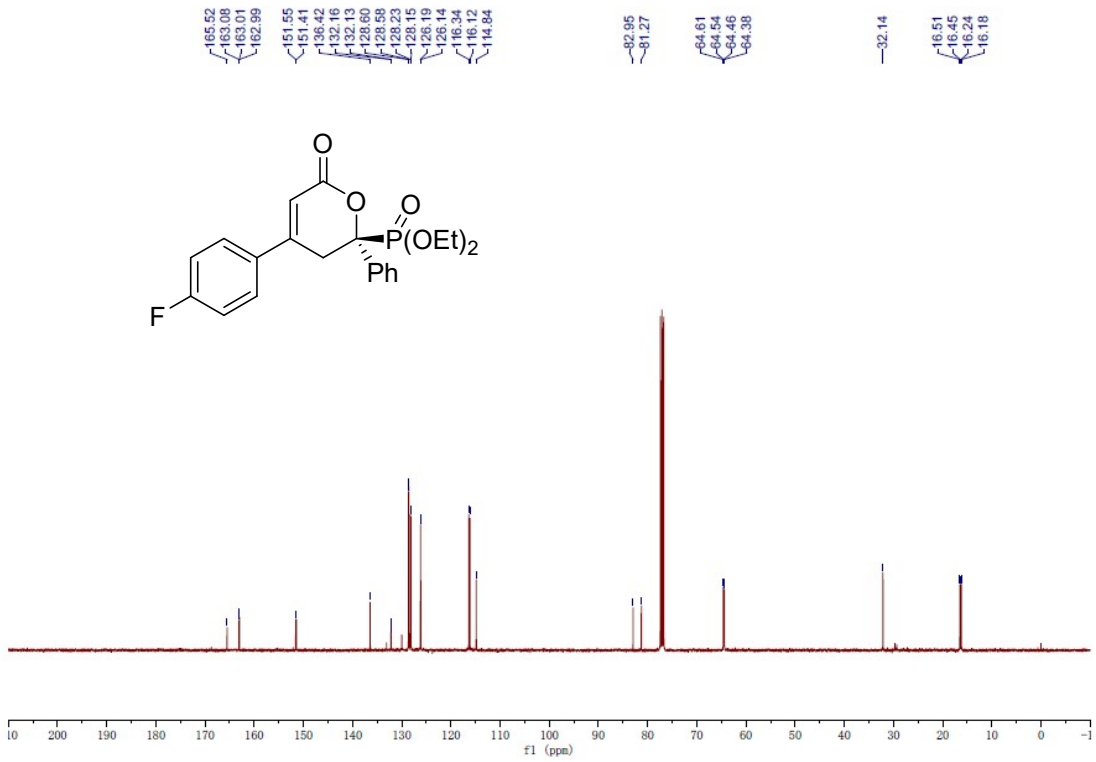
3i ^{31}P NMR


16.79
O
O
O
P(OEt)2
Ph
Br
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

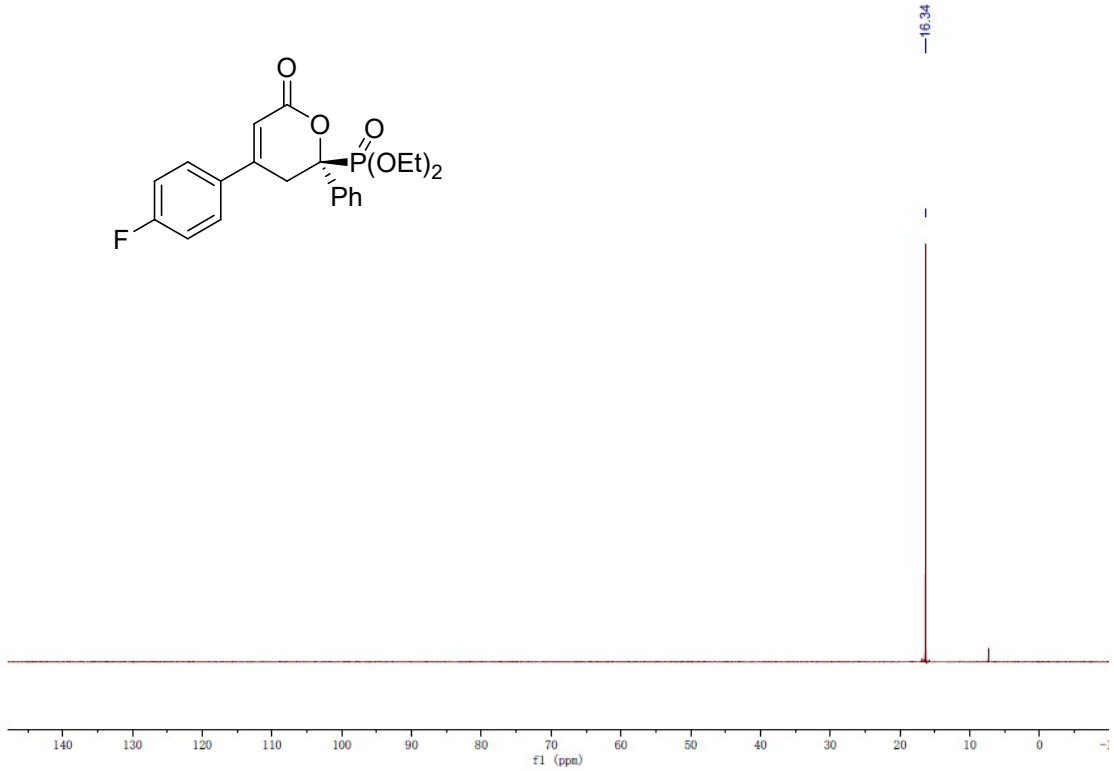
3j ^{1}H NMR



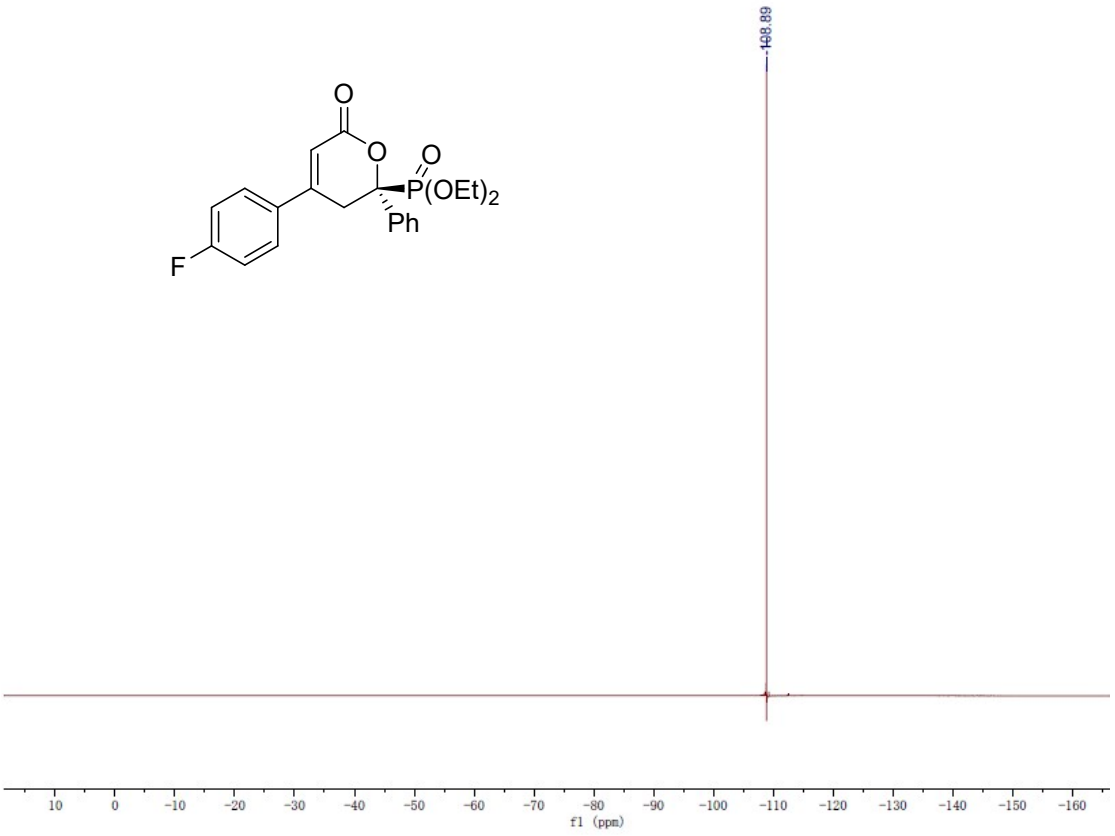
3j ^{13}C NMR



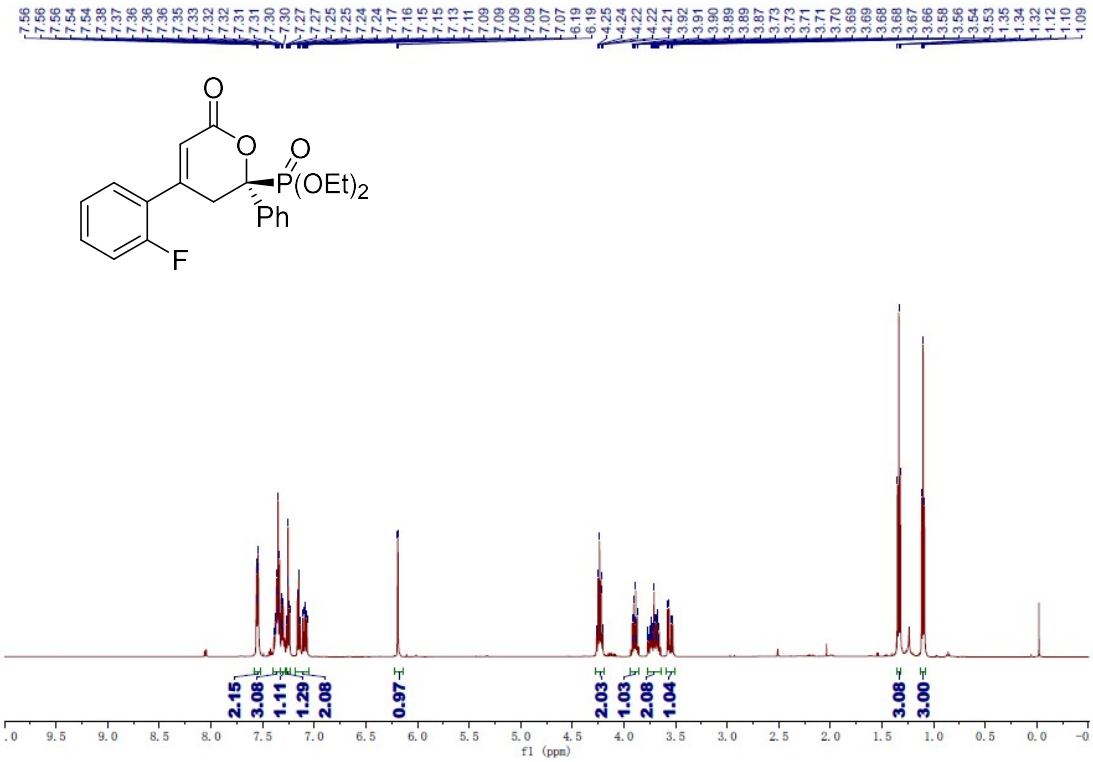
3j ^{31}P NMR



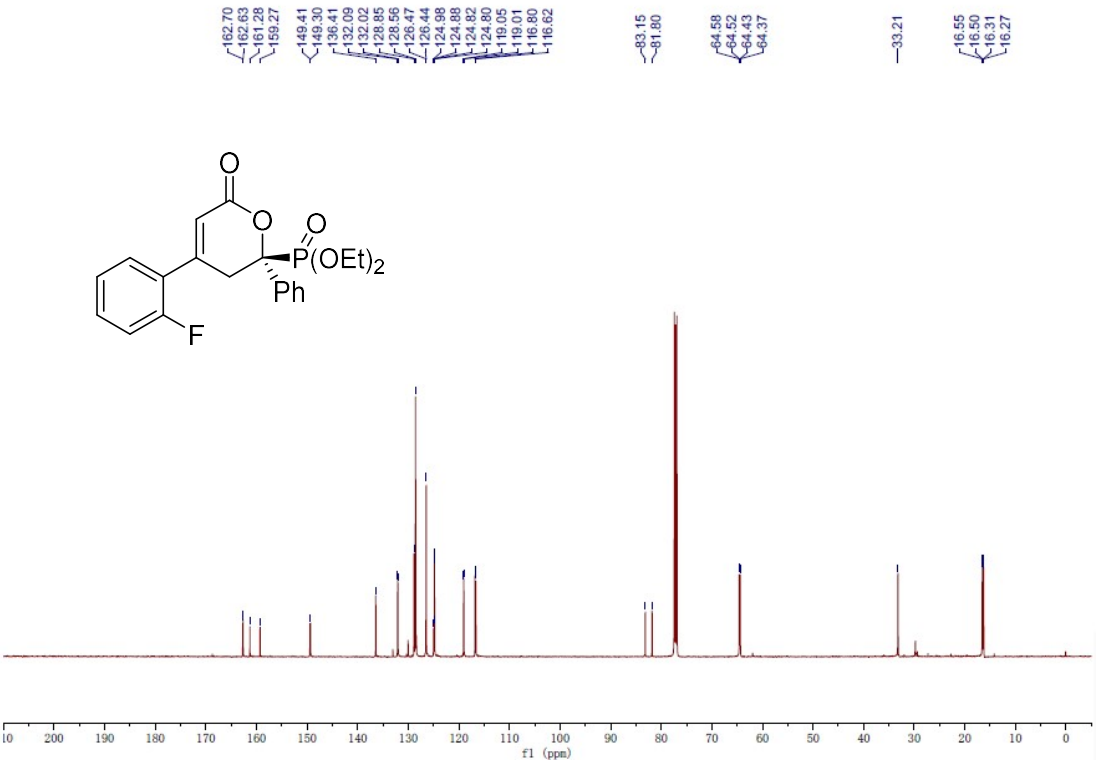
3j ^{19}F NMR



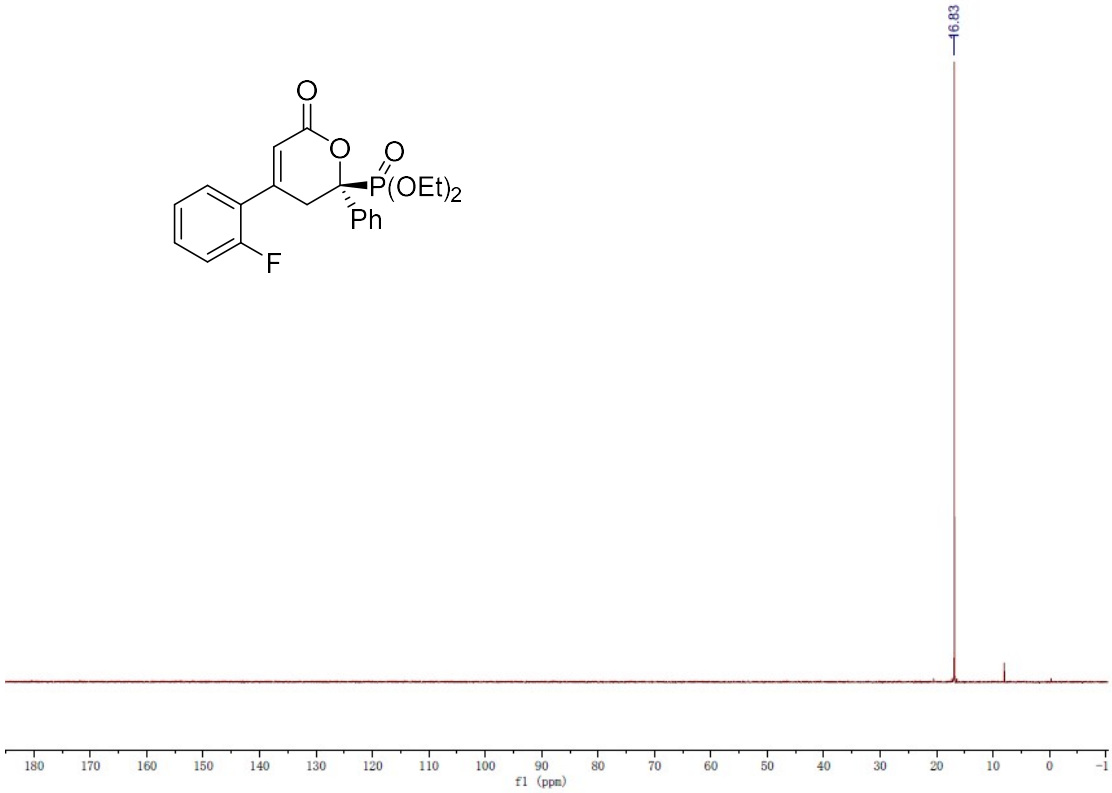
3k ^{1}H NMR



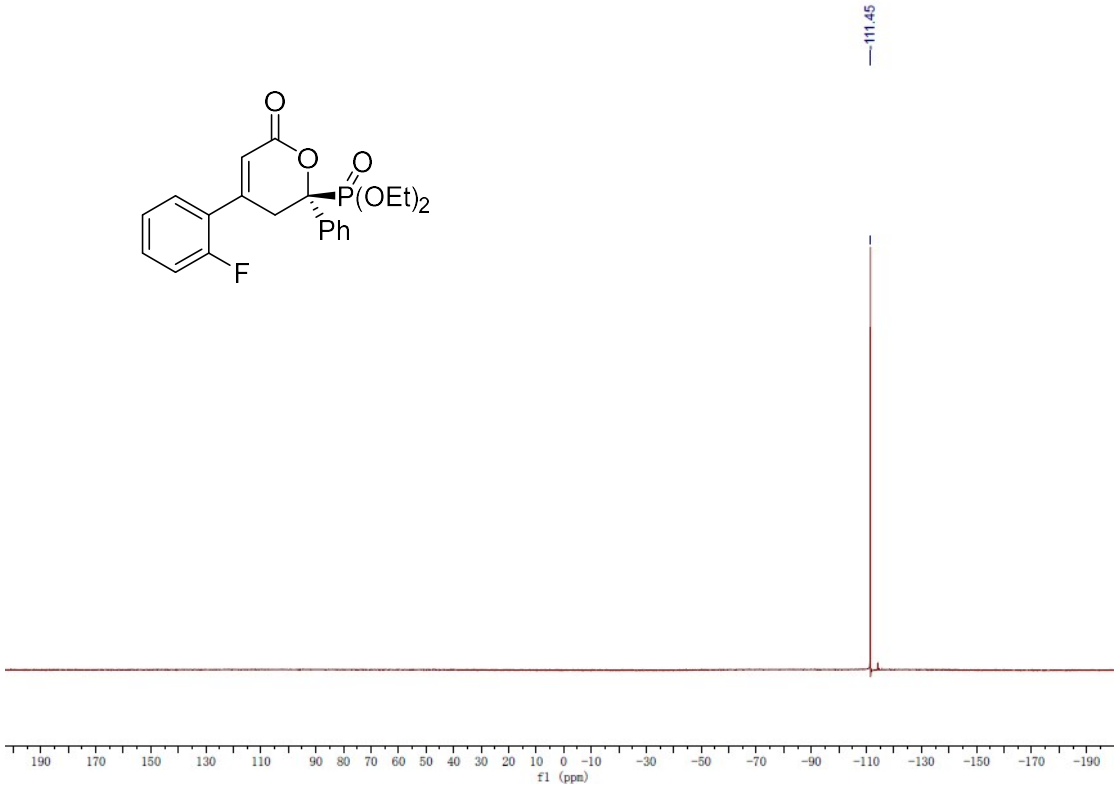
3k ^{13}C NMR



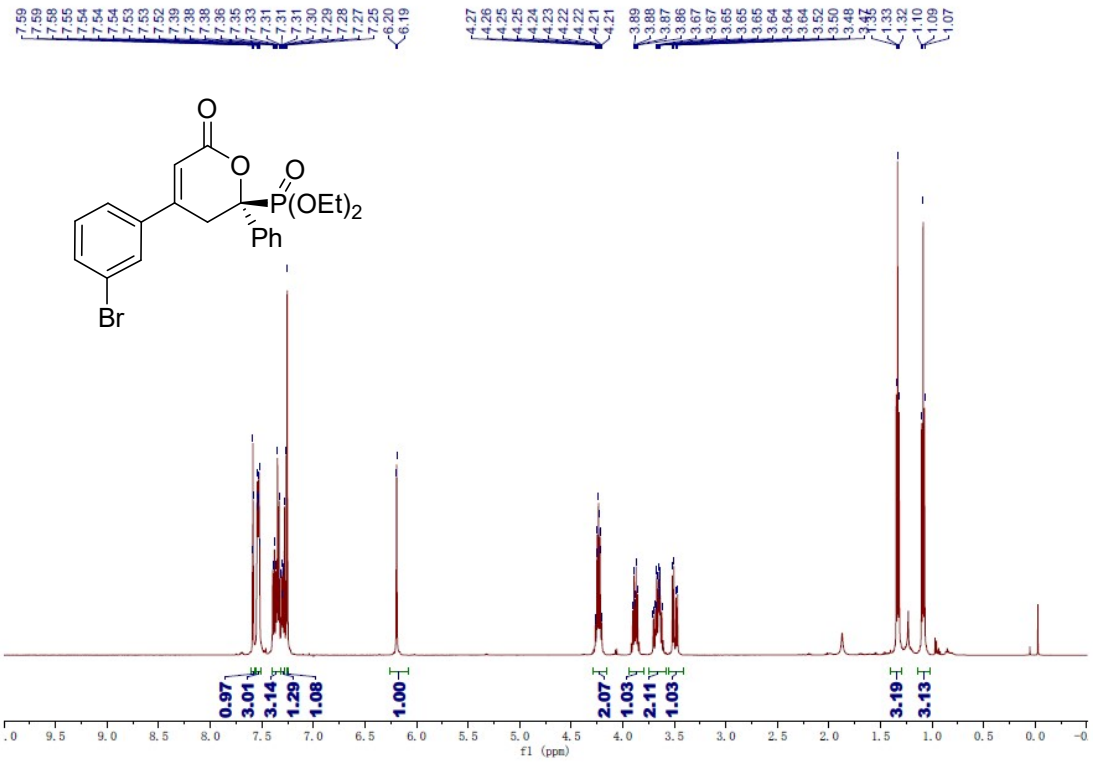
3k ^{31}P NMR



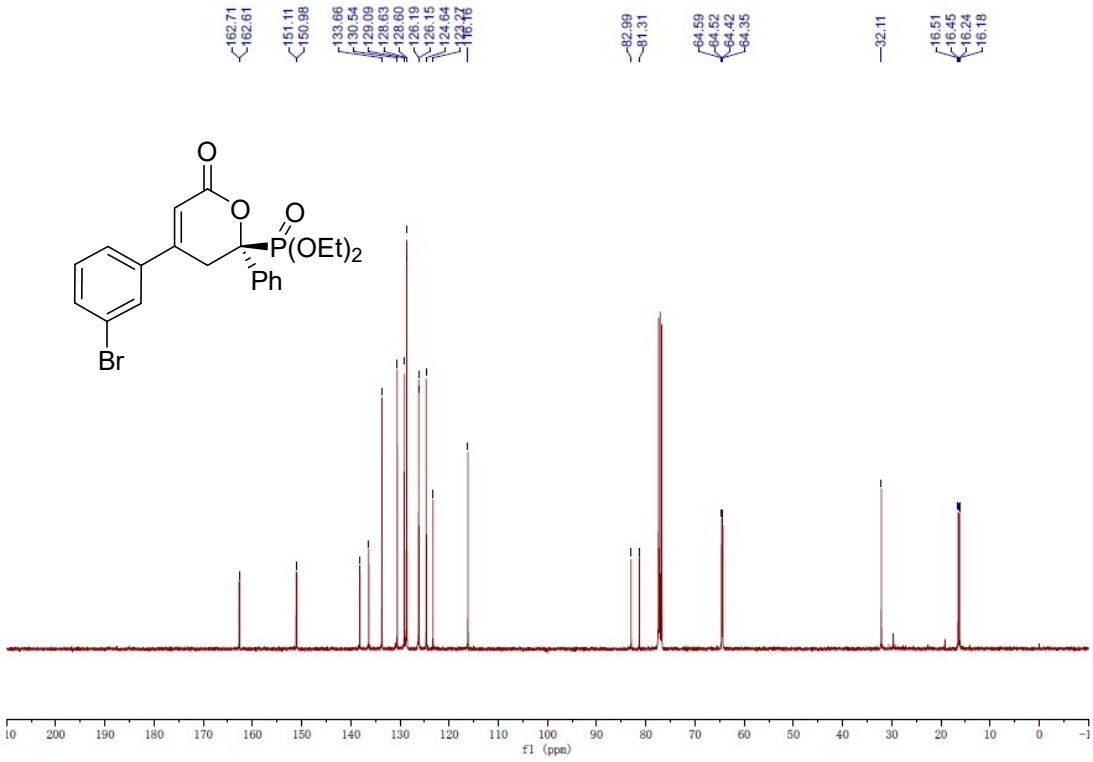
3k ^{19}F NMR



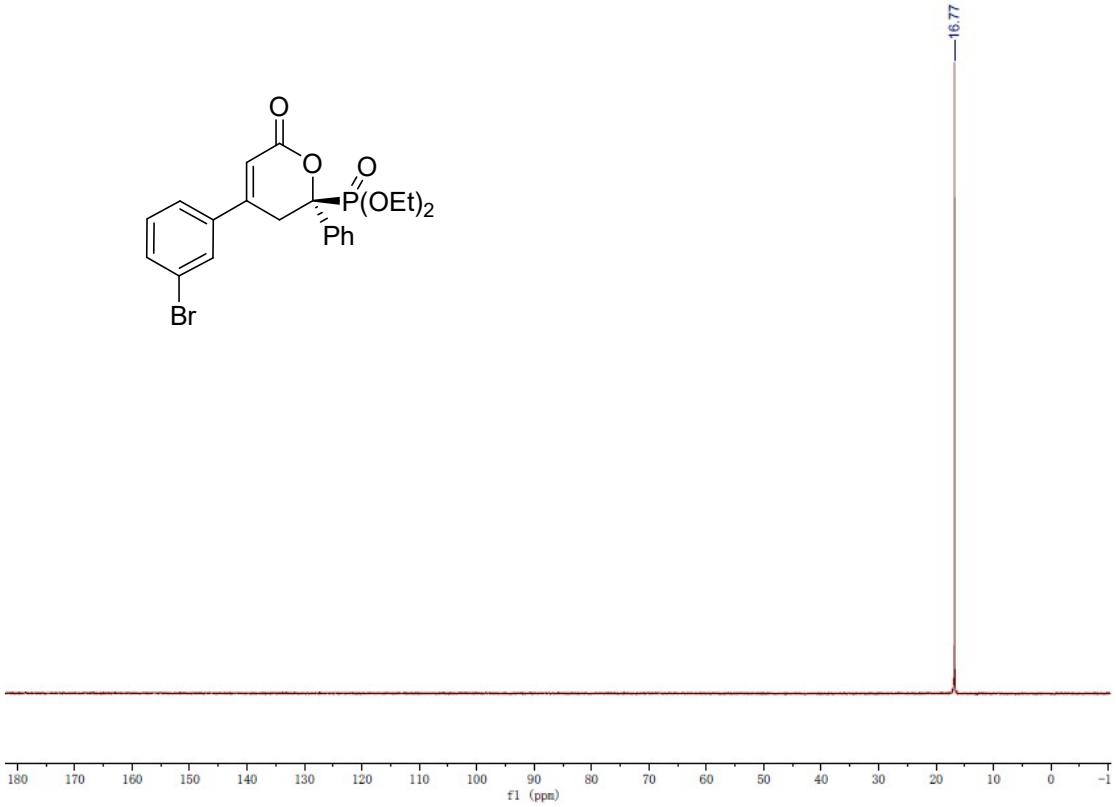
3l ^{1}H NMR



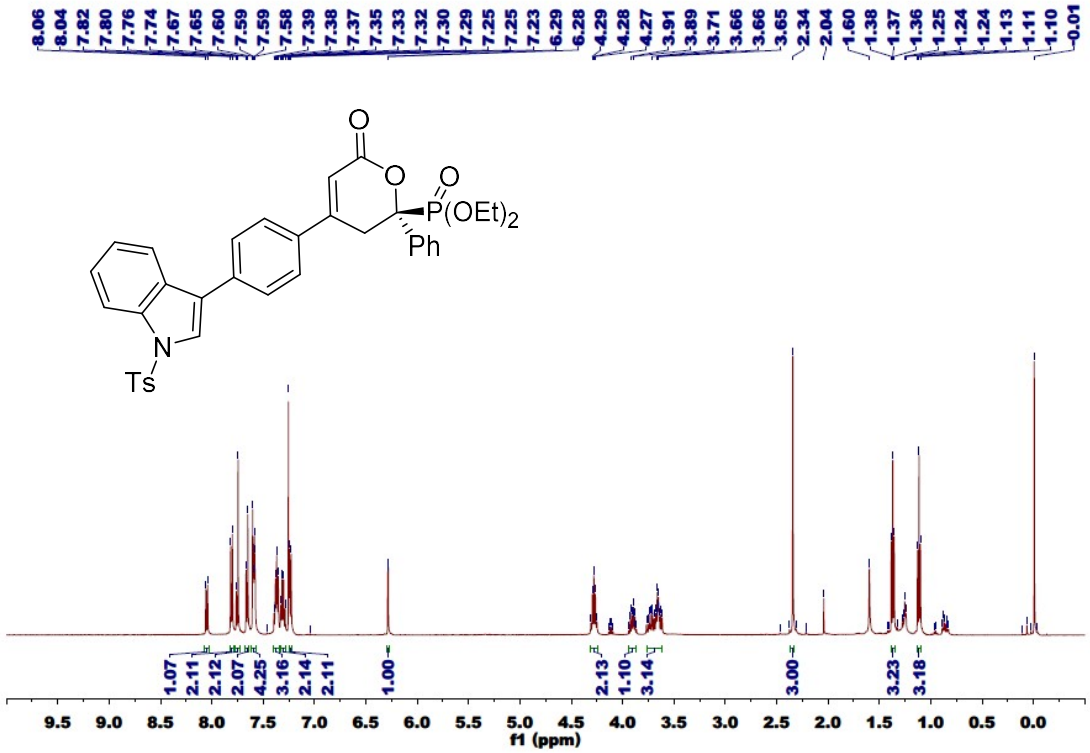
3l ^{13}C NMR



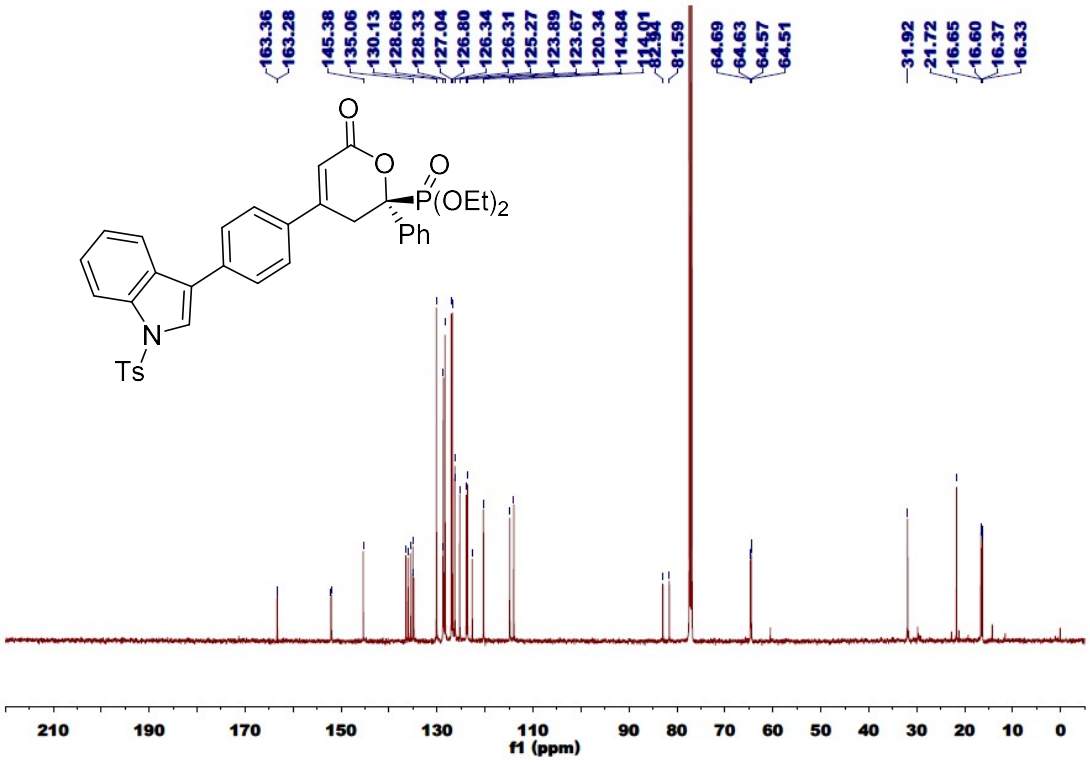
3l ^{31}P NMR


16.77
O
O
O
P(OEt)2
Ph
Br
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

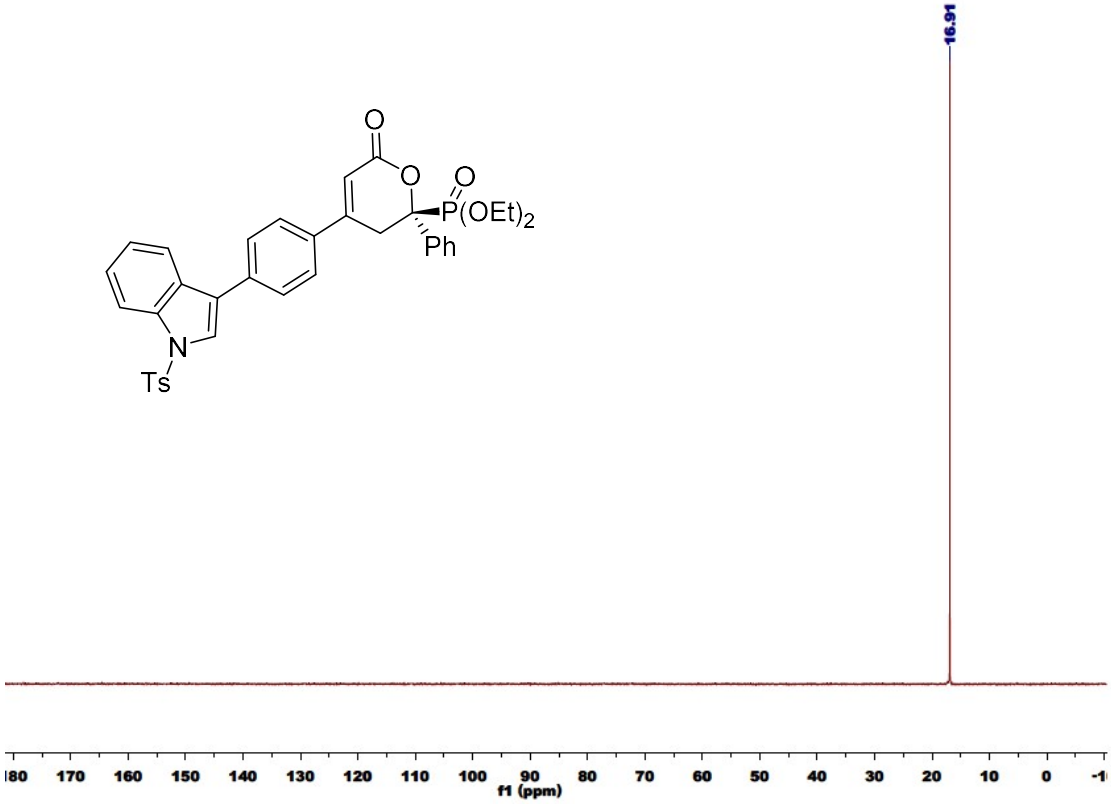
3m ^{1}H NMR



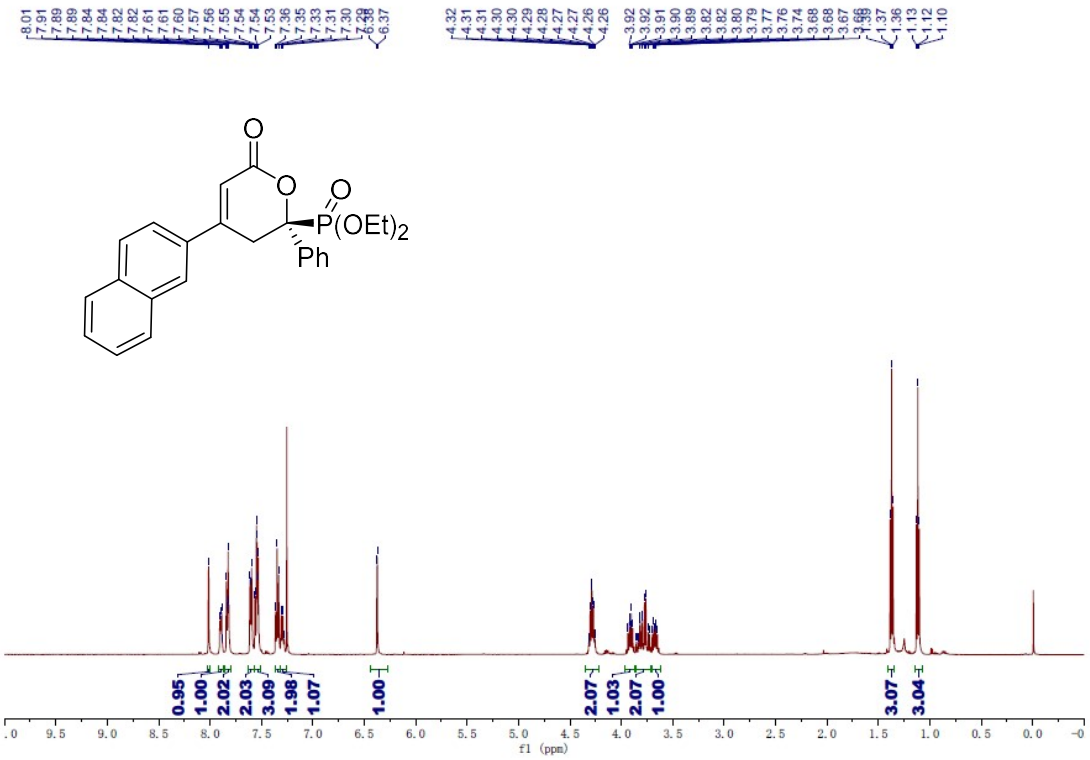
3m ^{1}C NMR



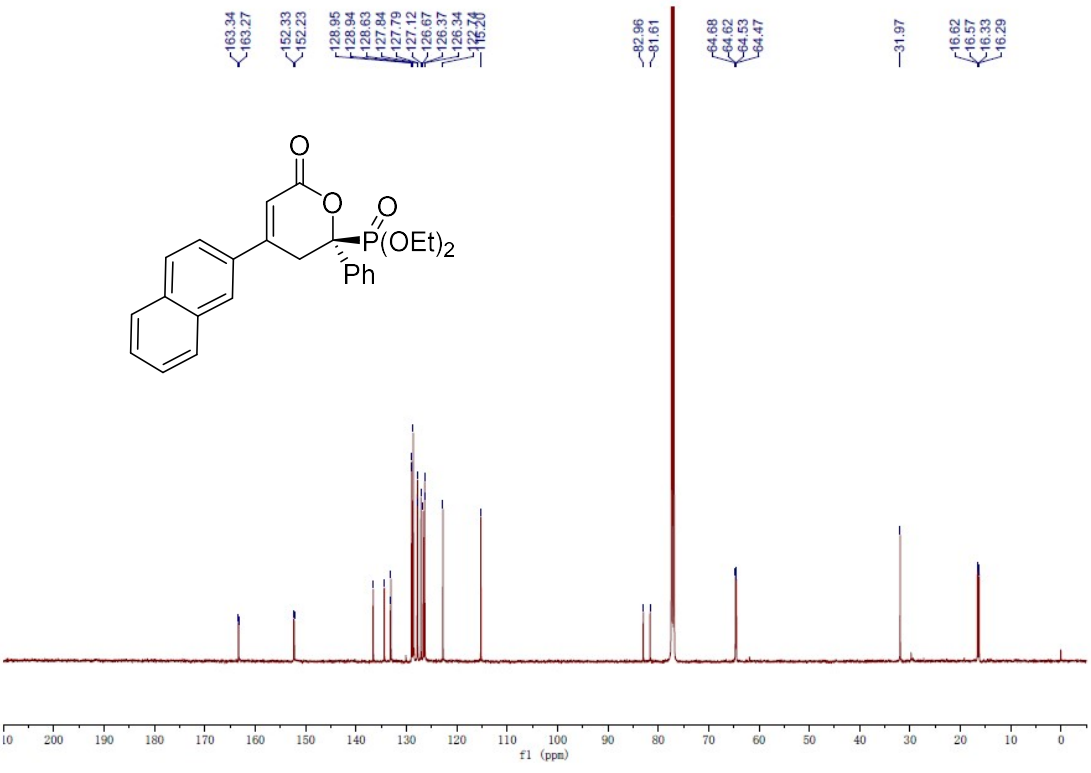
3m ^{31}P NMR


16.91
O
O
O
P(OEt)2
Ph
N
Ts
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

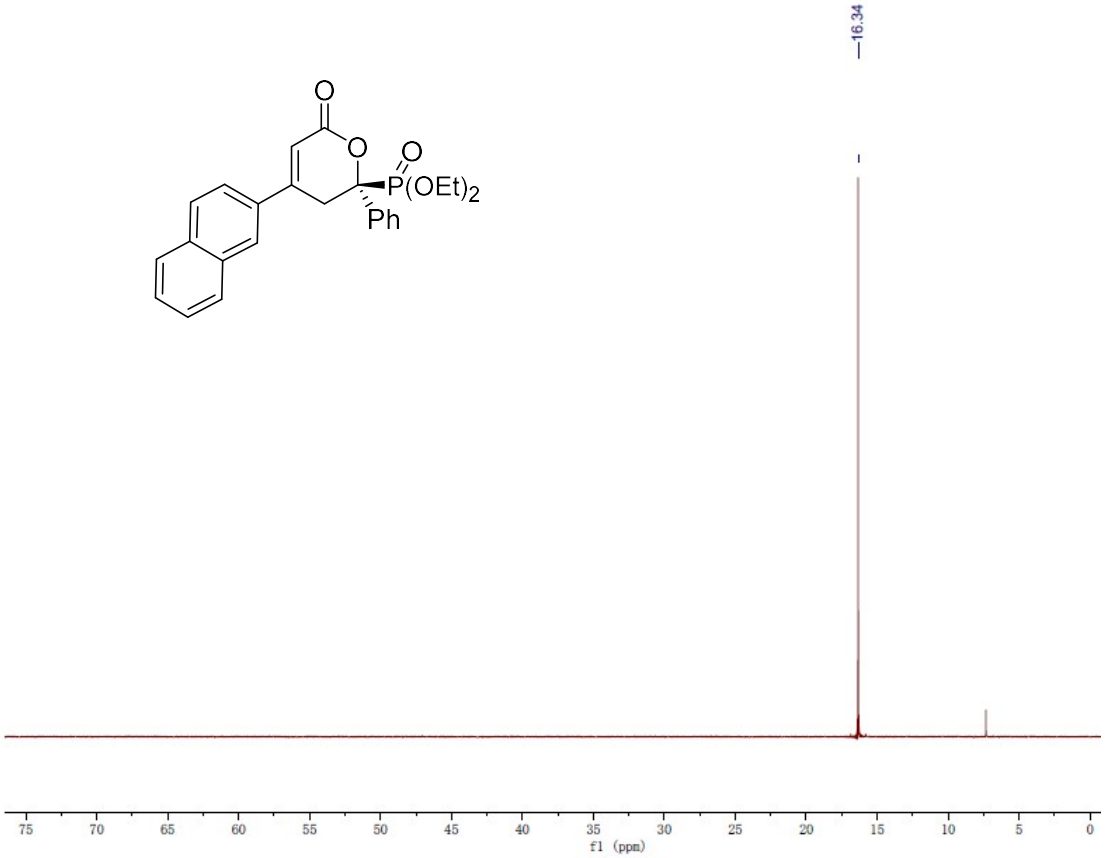
3n ^{1}H NMR



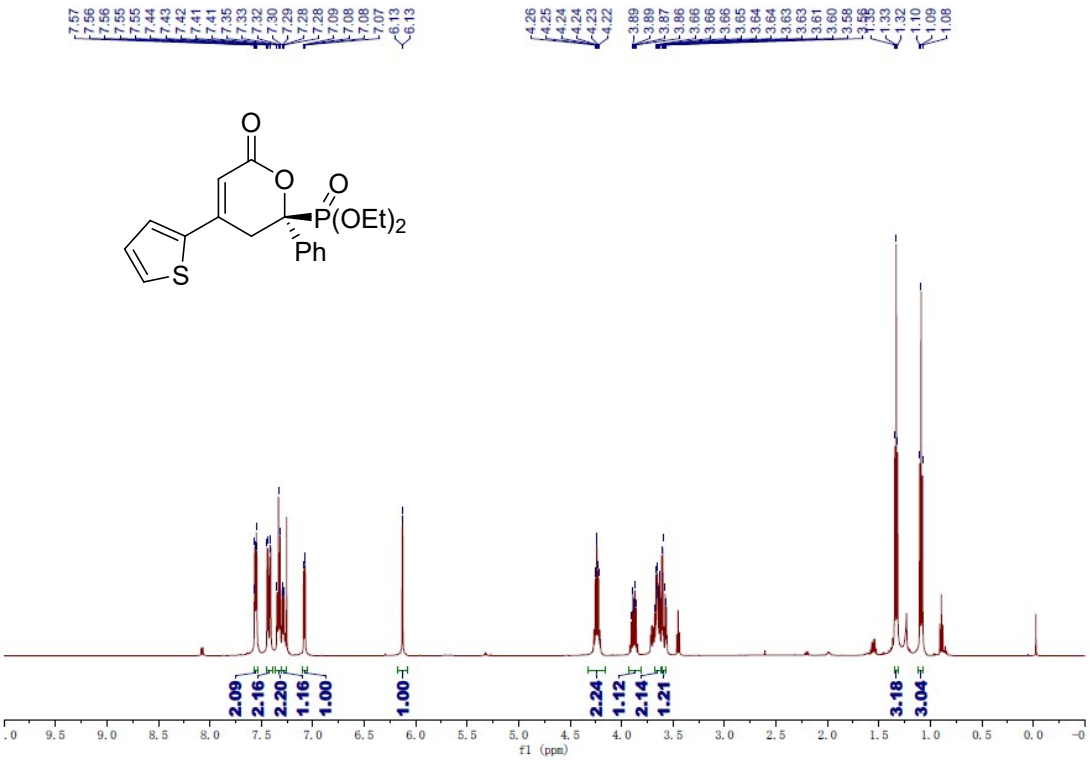
3n ^{13}C NMR



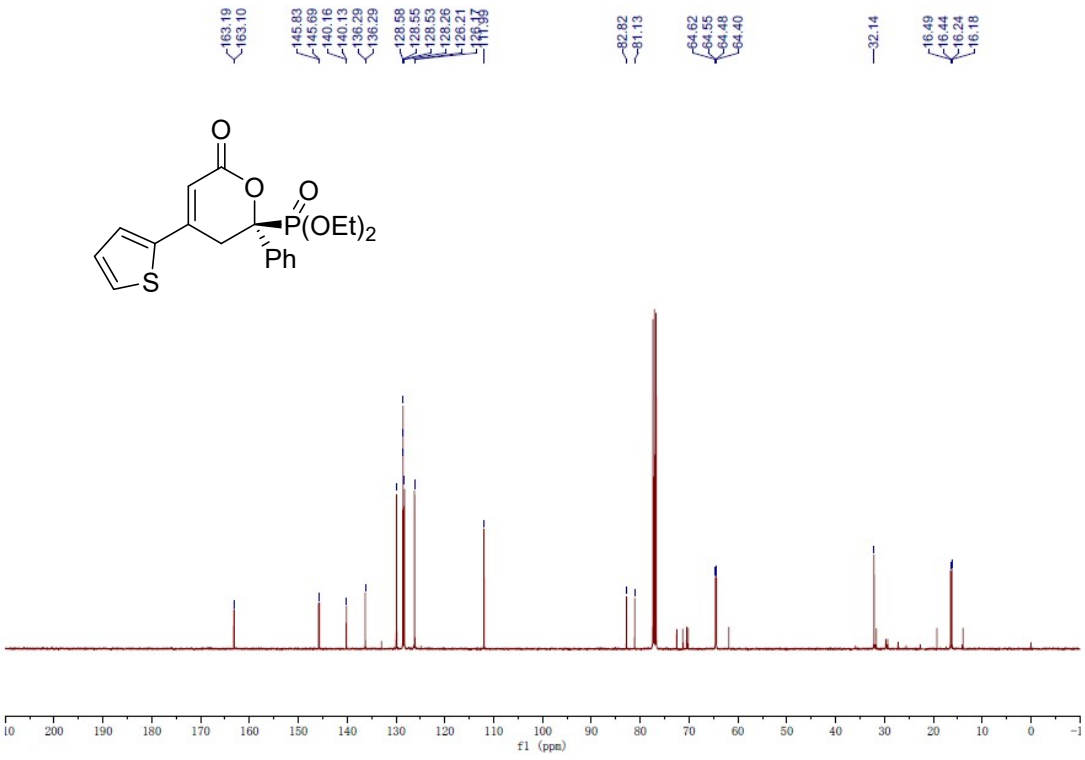
3n ^{31}P NMR



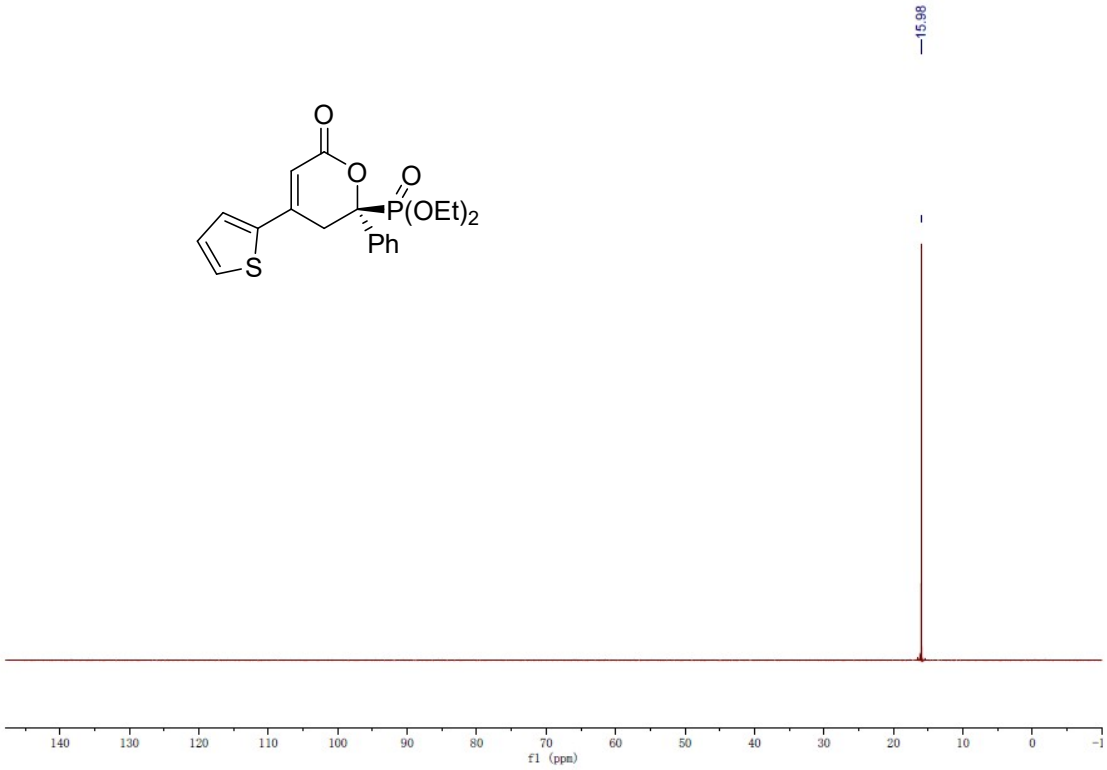
3o ^{1}H NMR



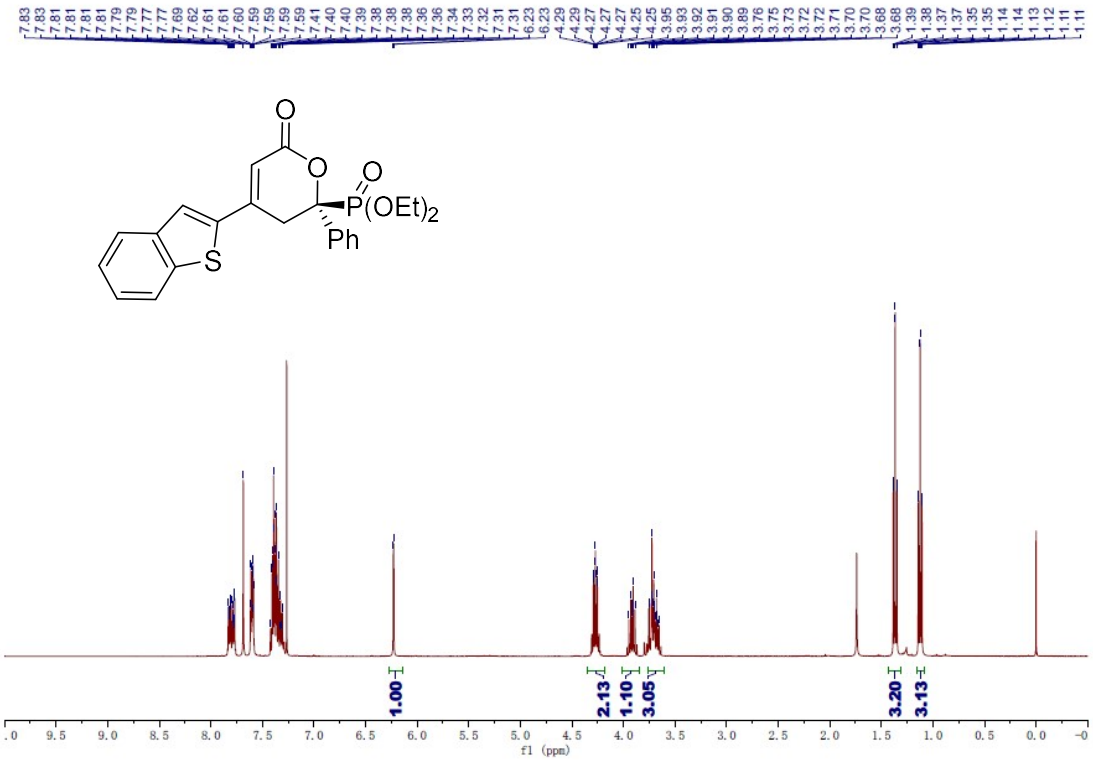
3o ^{13}C NMR



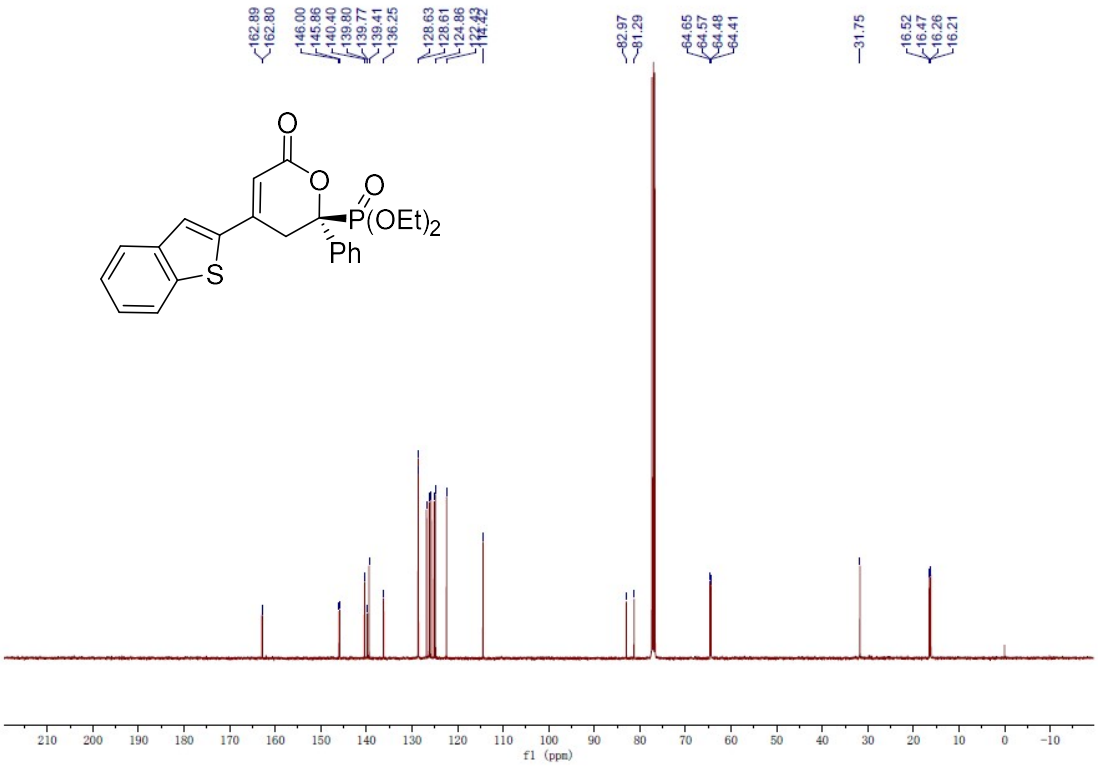
3o ^{31}P NMR


15.98
O
O
O
P(OEt)2
Ph
S
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

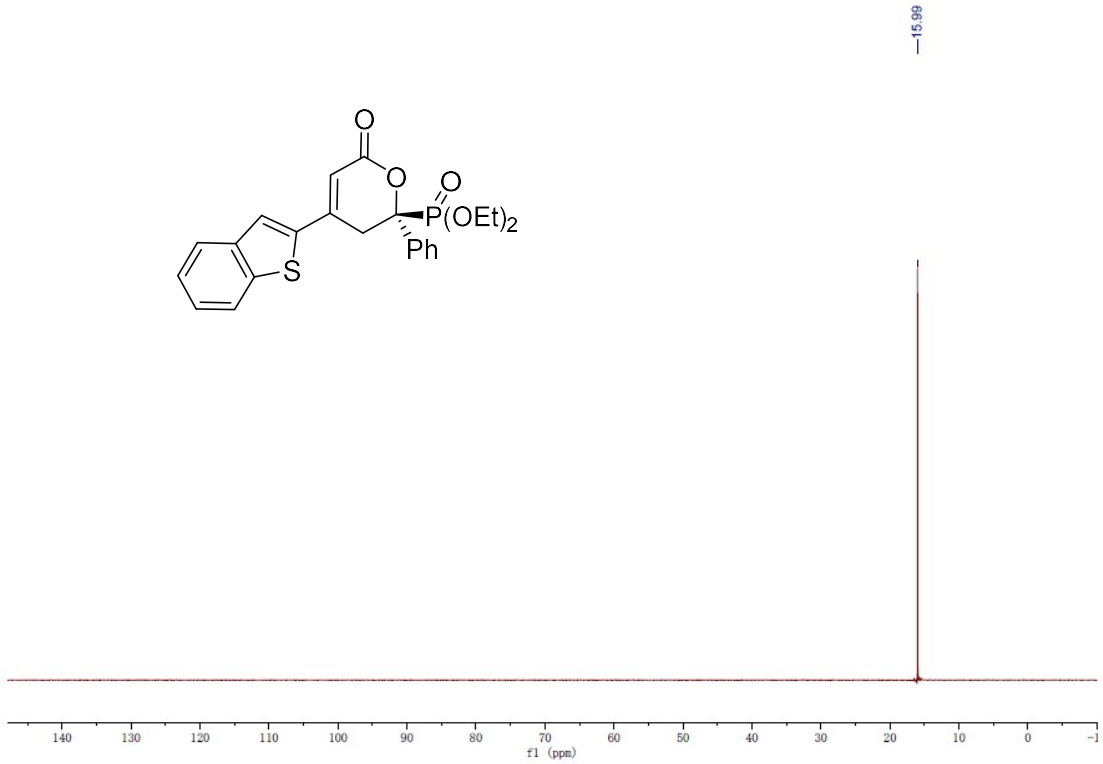
3p ^{1}H NMR



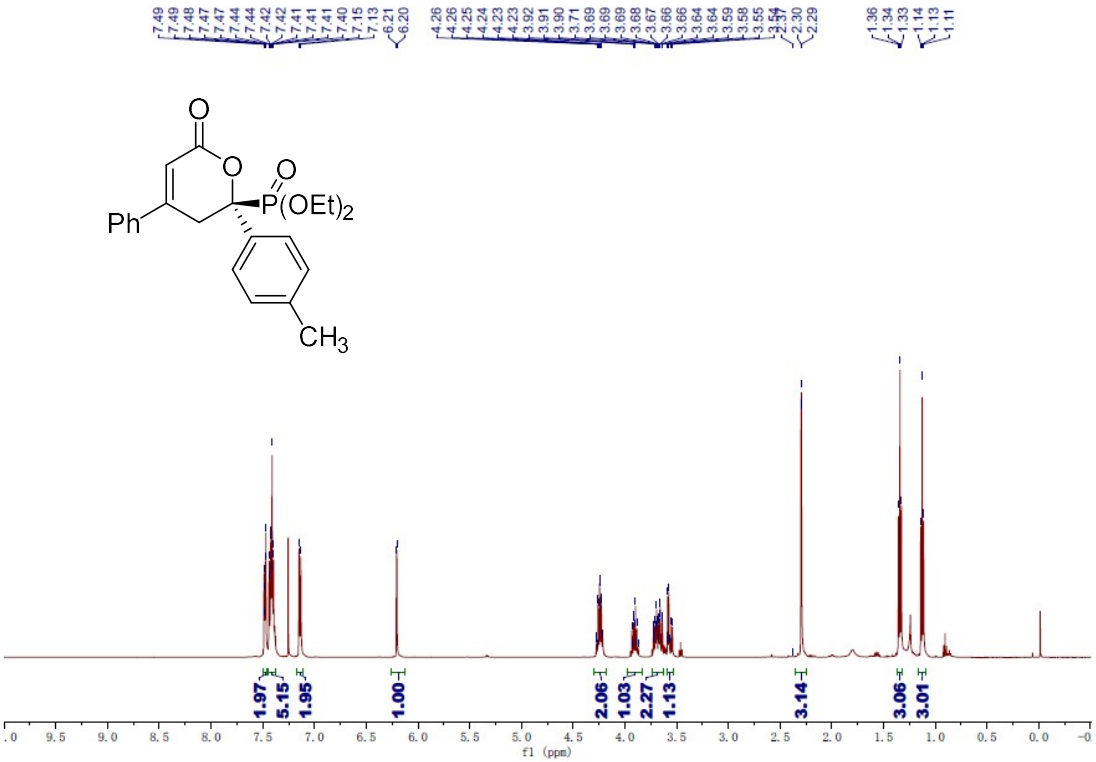
3p ^{13}C NMR



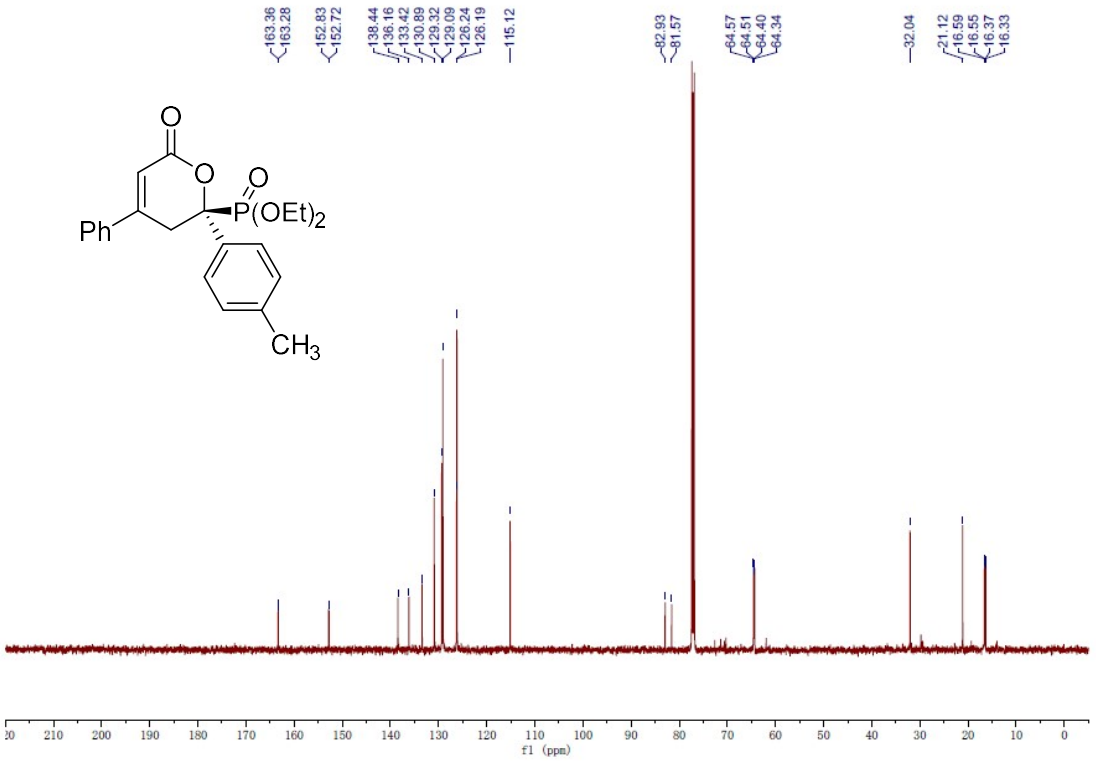
3p ^{31}P NMR


15.99
O
O
O
P(OEt)2
Ph
S
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

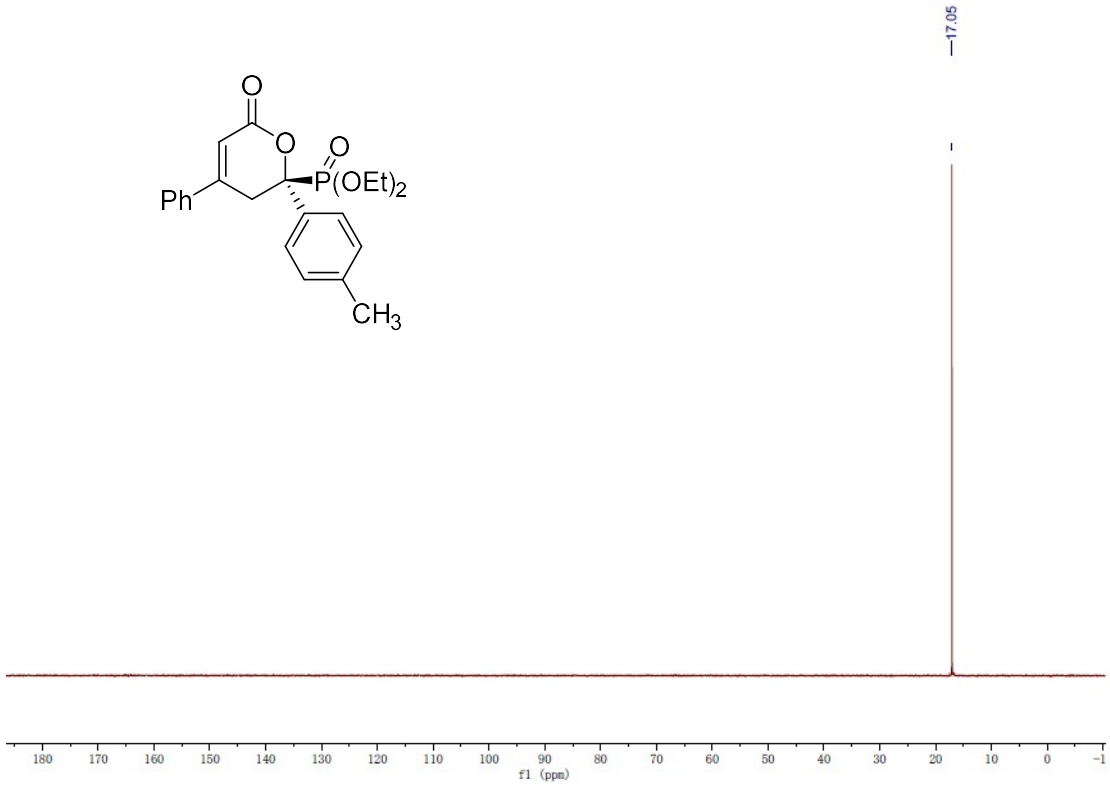
3q ^{1}H NMR



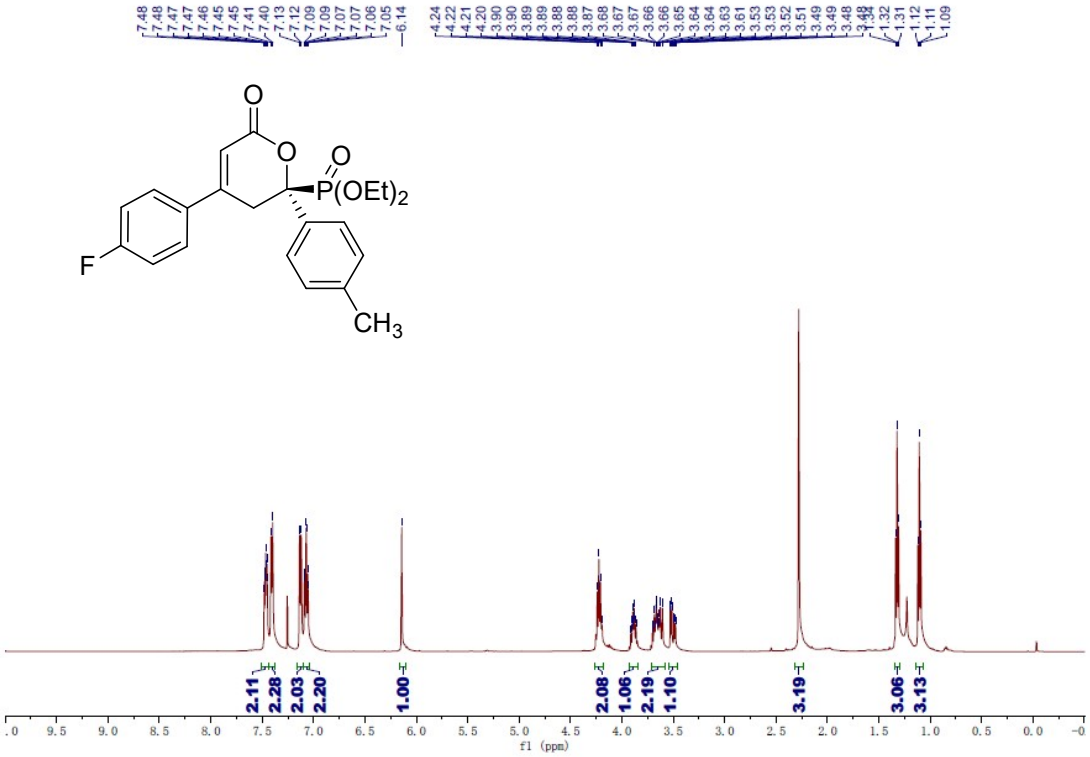
3q ^{13}C NMR



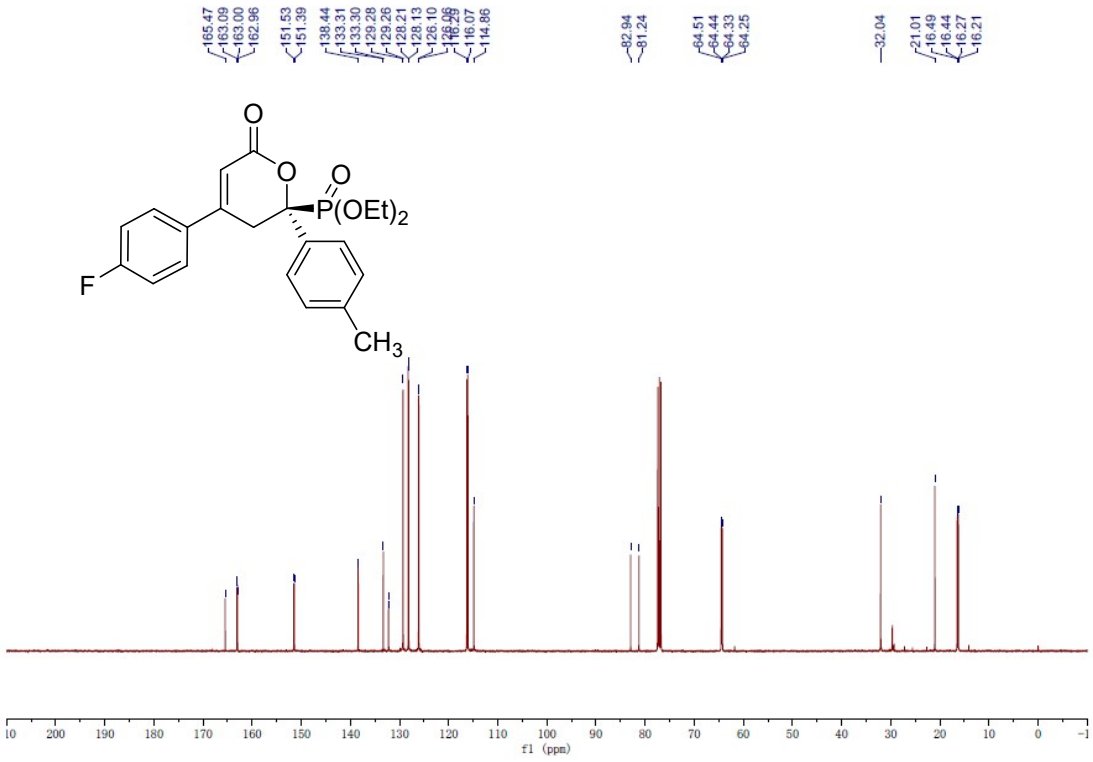
3q ^{31}P NMR


17.05
O
O
O
P(OEt)2
Ph
CH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

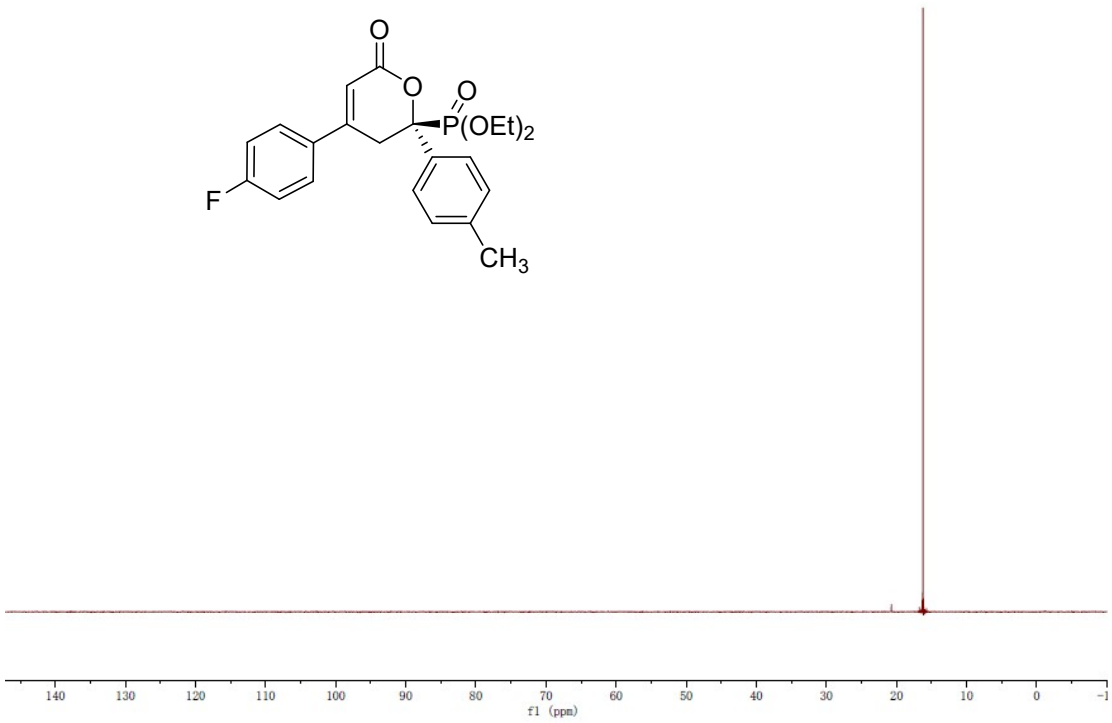
3r ^{1}H NMR



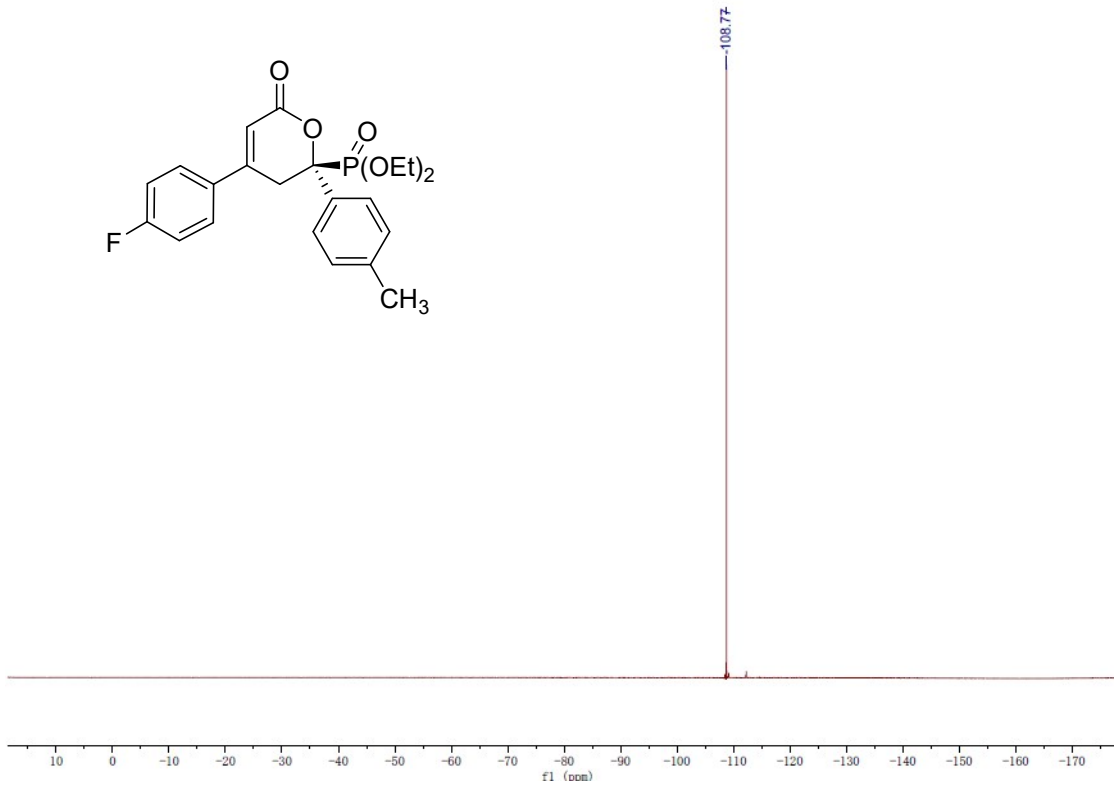
3r ^{13}C NMR



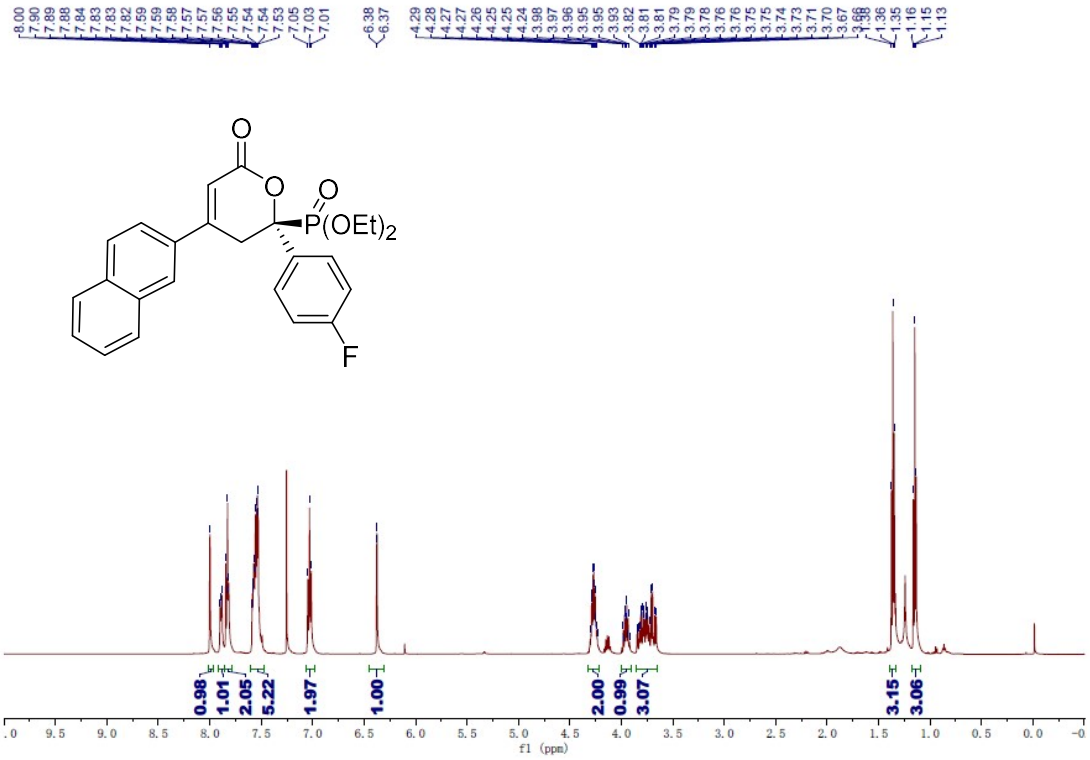
3r ^{31}P NMR



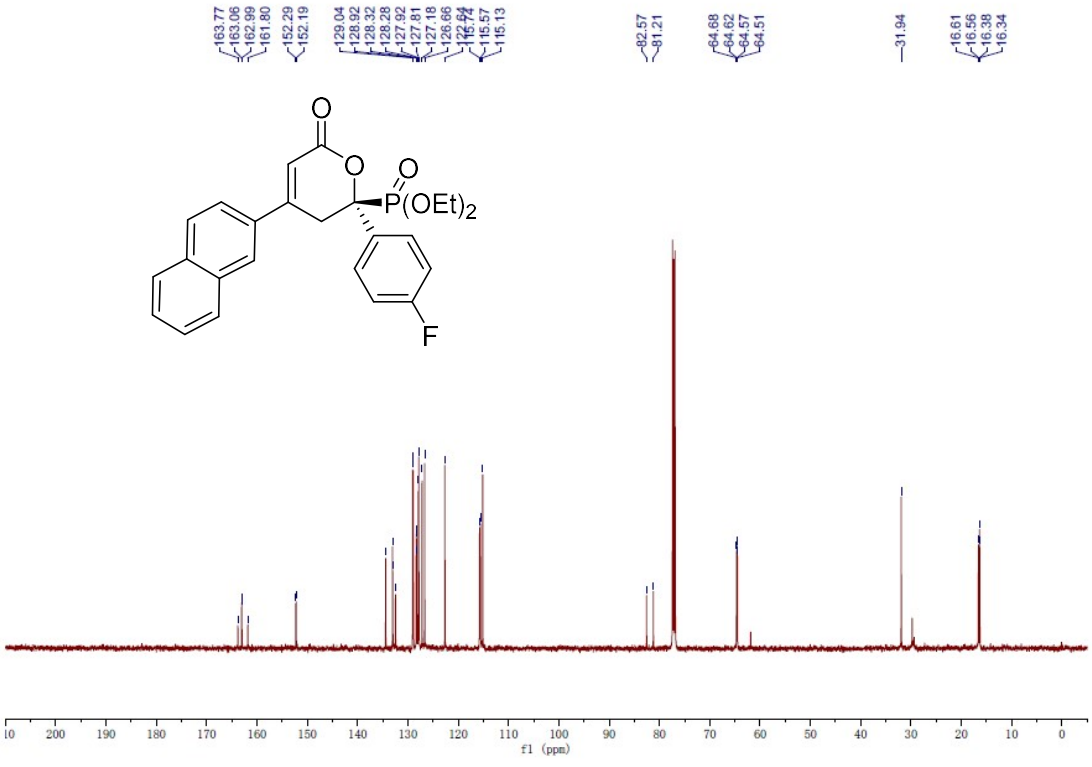
3r ^{19}F NMR



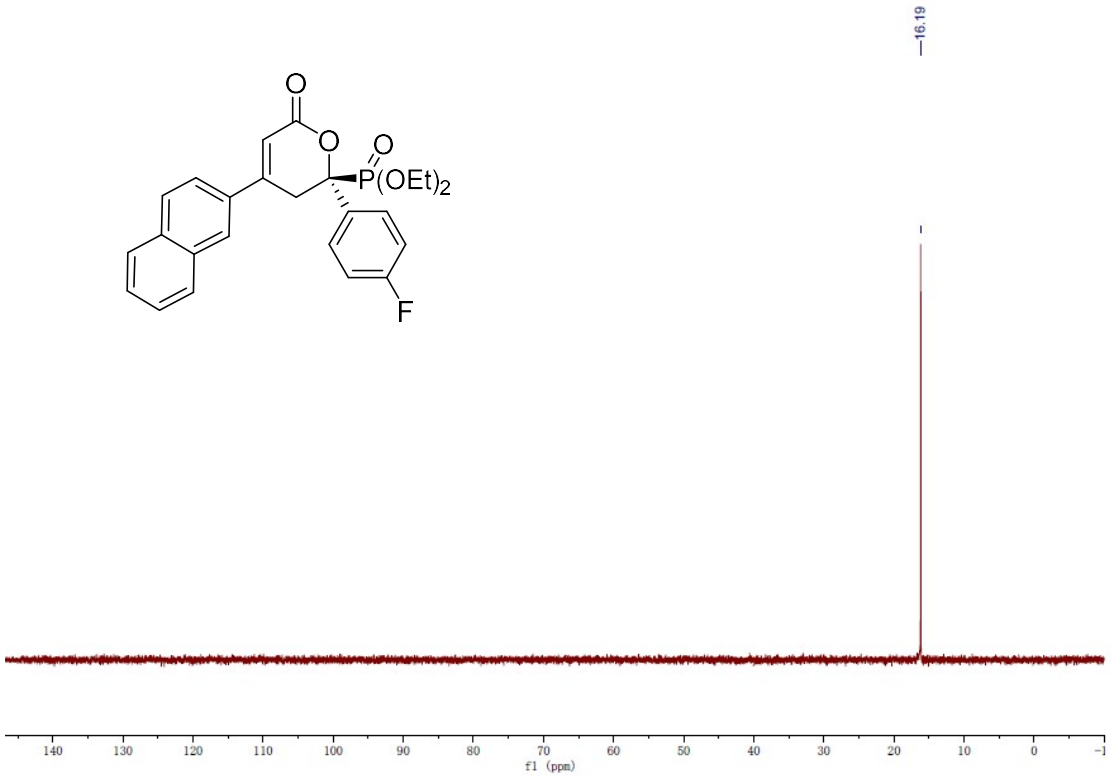
3s ^{1}H NMR



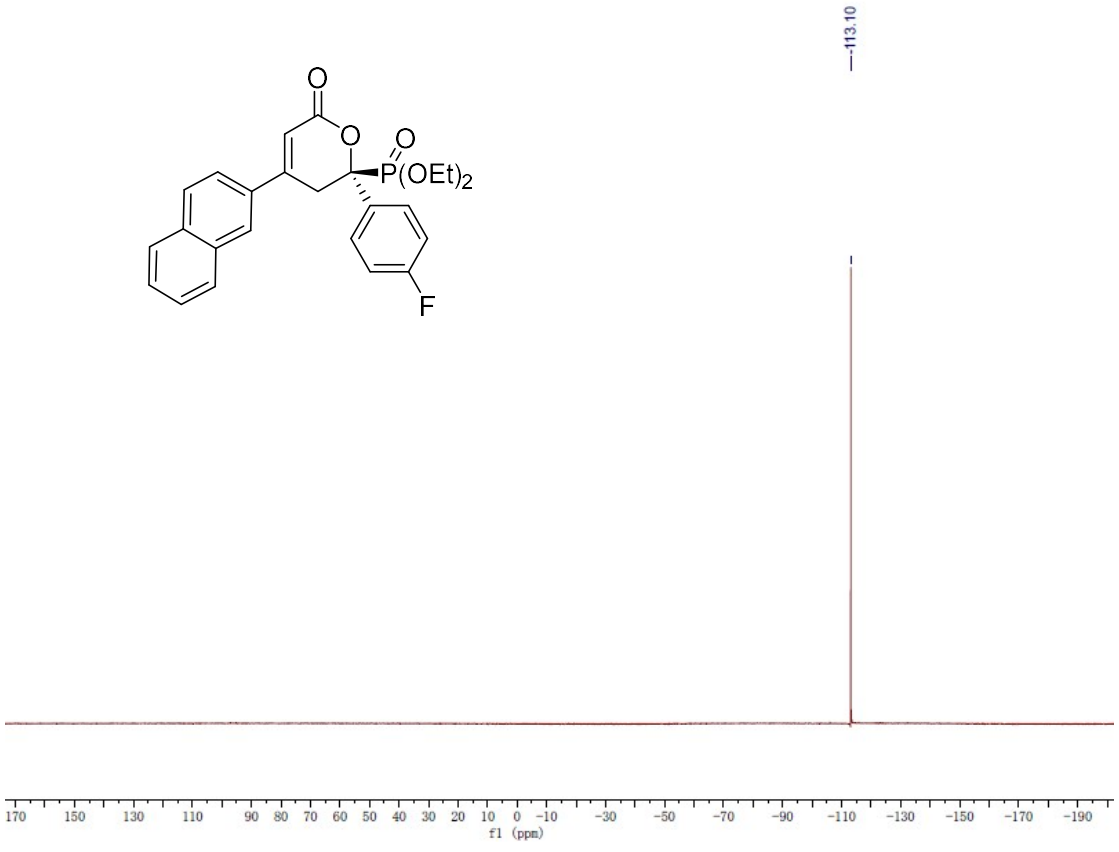
3s ^{13}C NMR



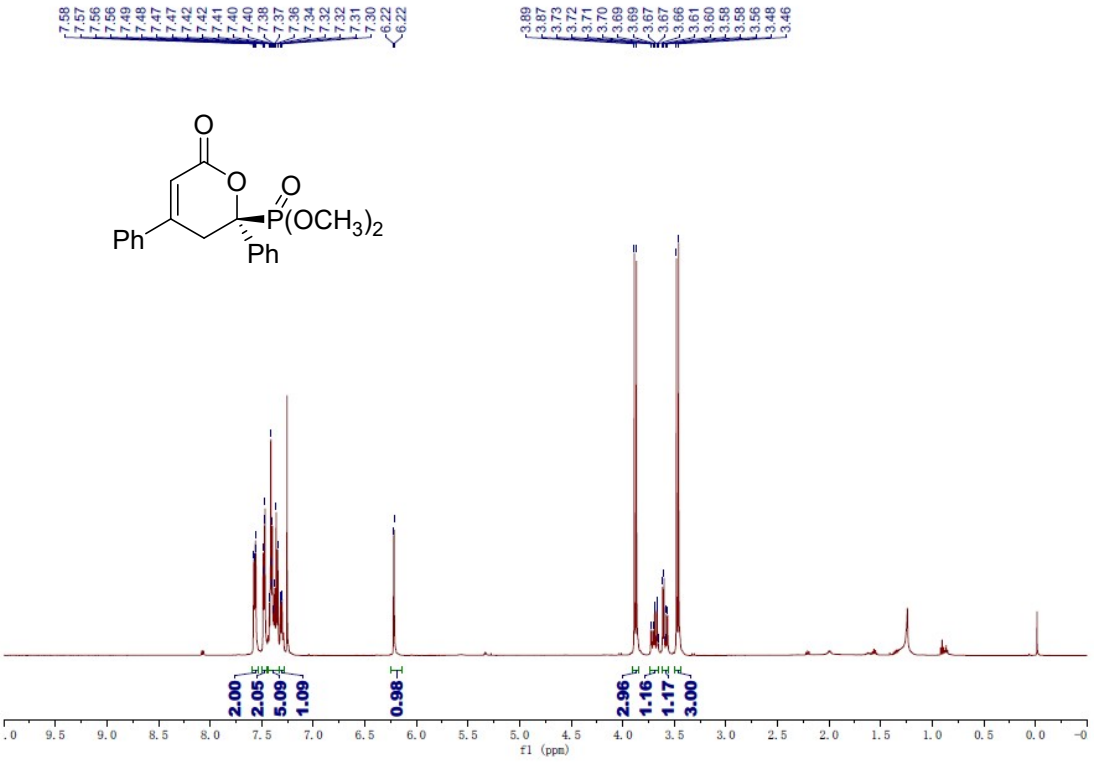
3s ^{31}P NMR



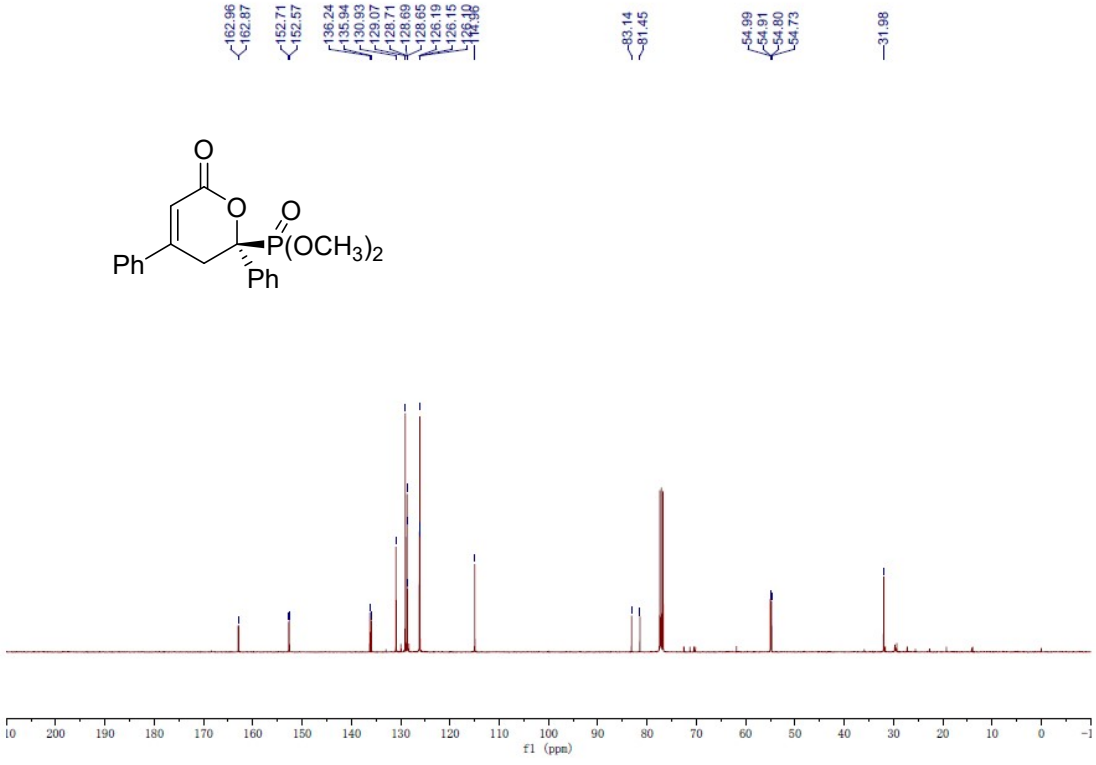
3s ^{19}F NMR



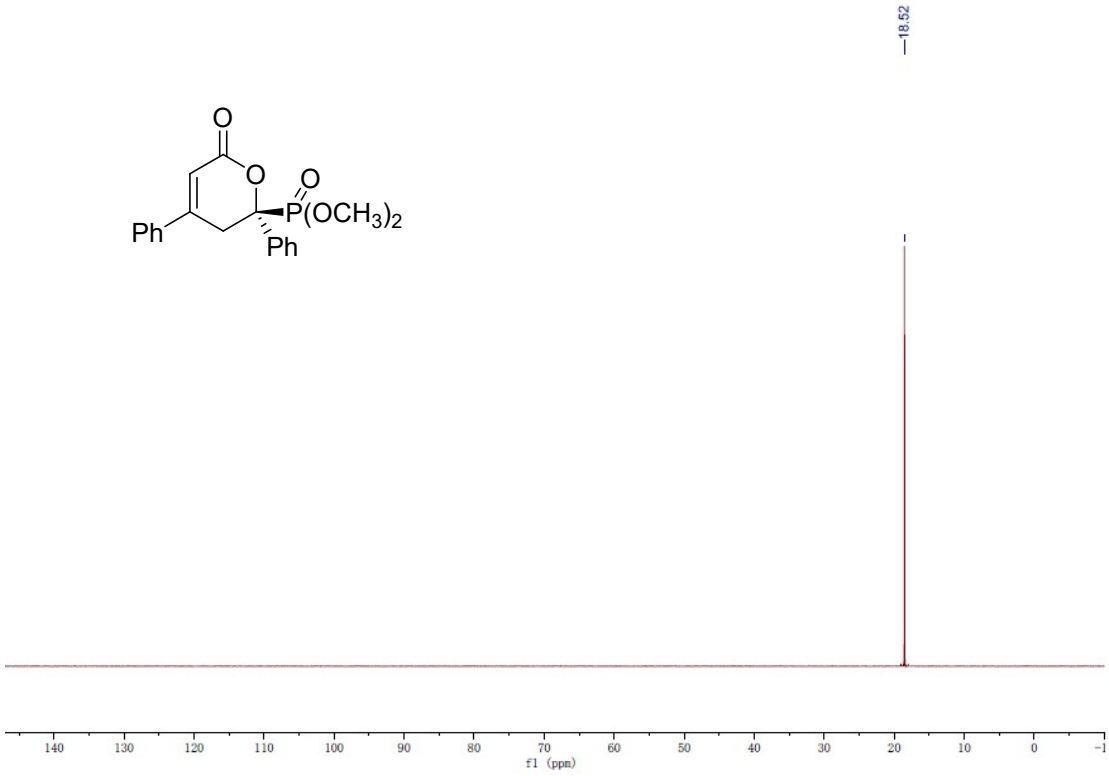
3t ^{1}H NMR



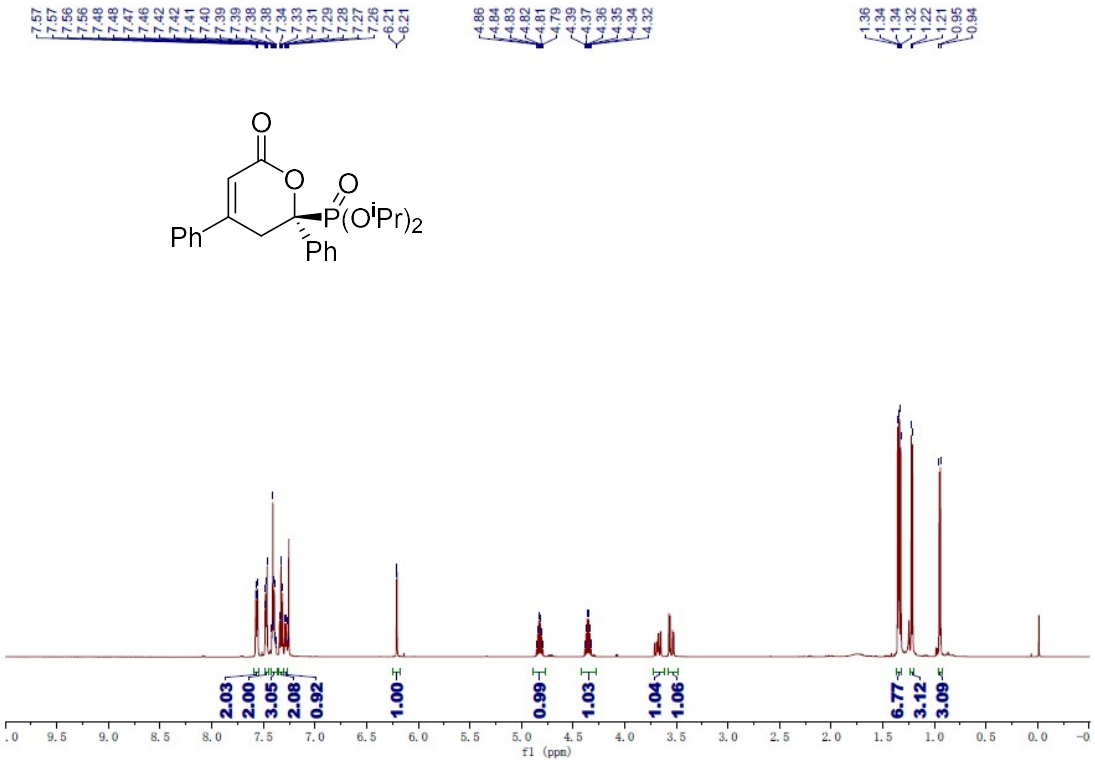
3t ^{13}C NMR



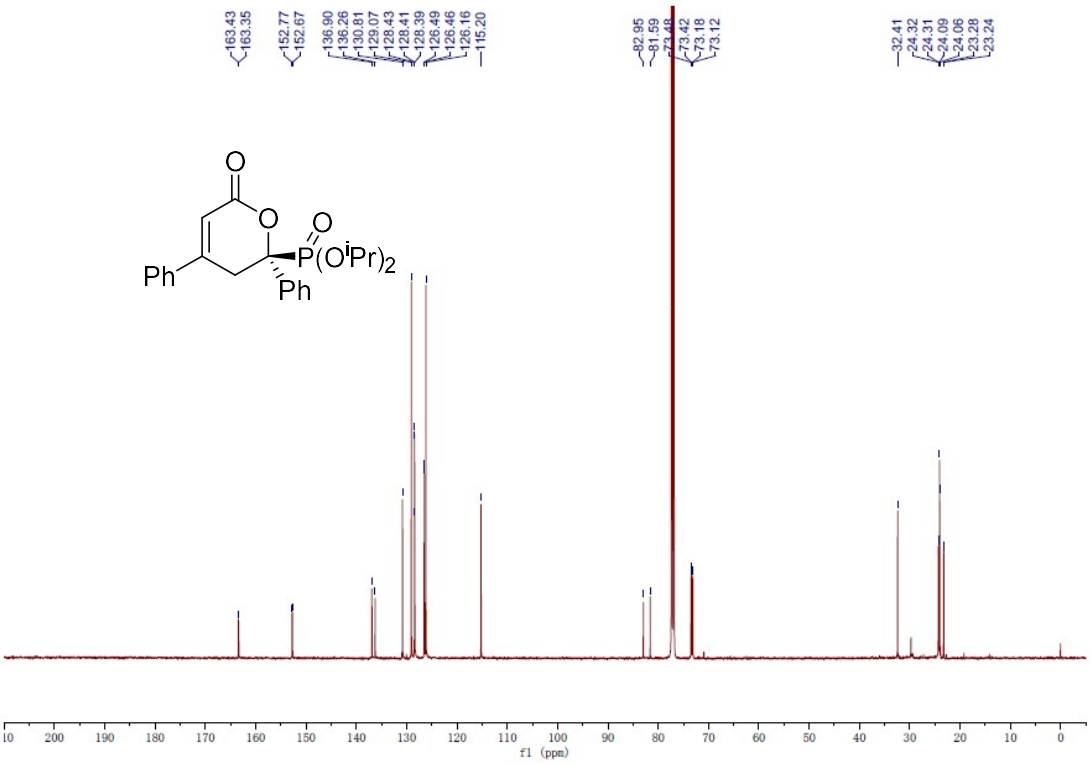
3t ^{31}P NMR


18.52
O
O
O
P(OCH3)2
Ph
Ph
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

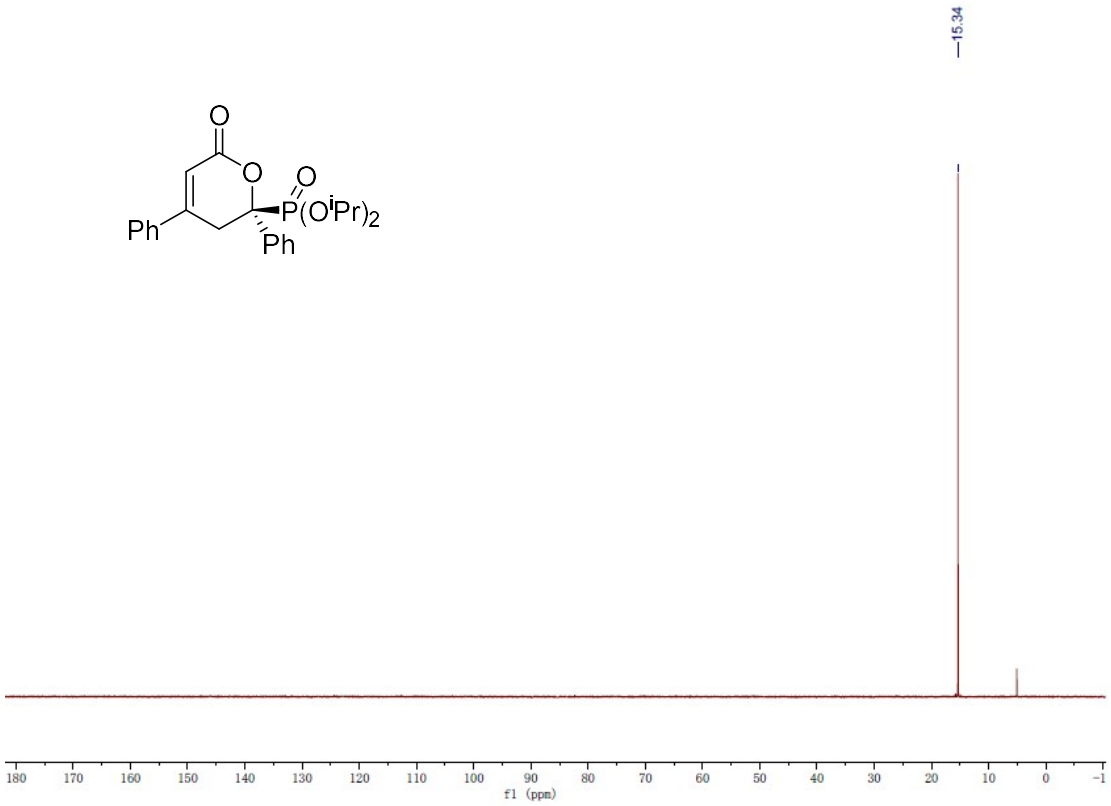
3u ^{1}H NMR



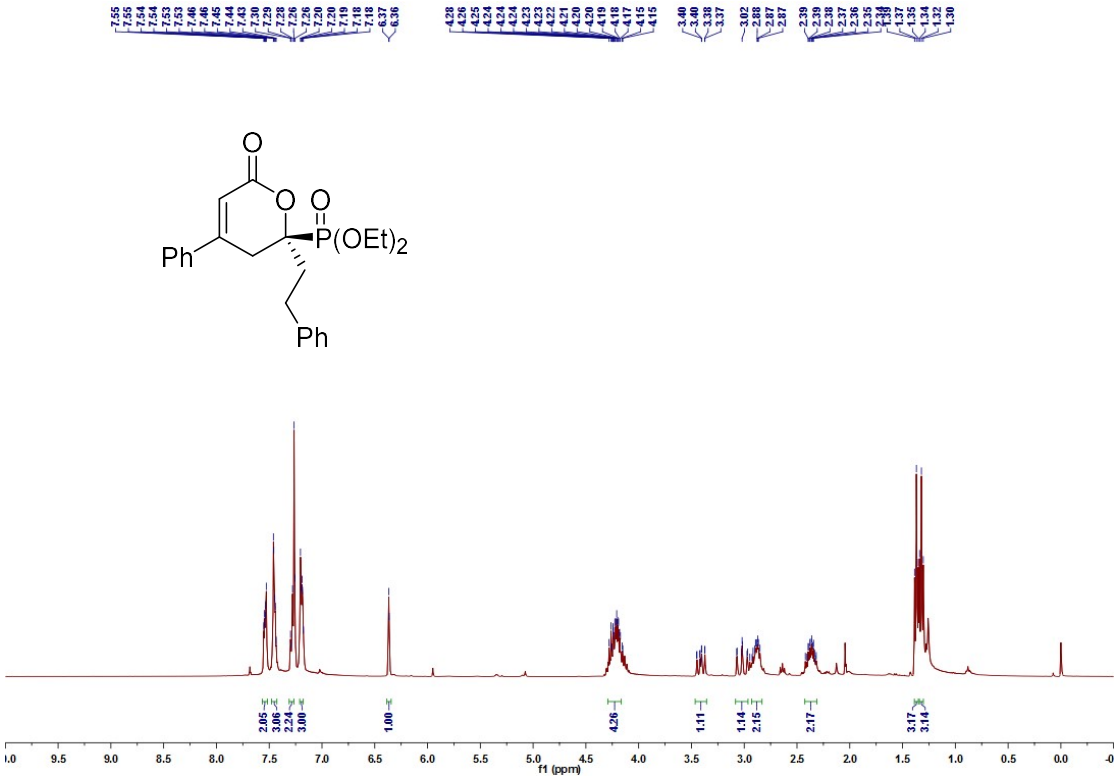
3u ^{13}C NMR



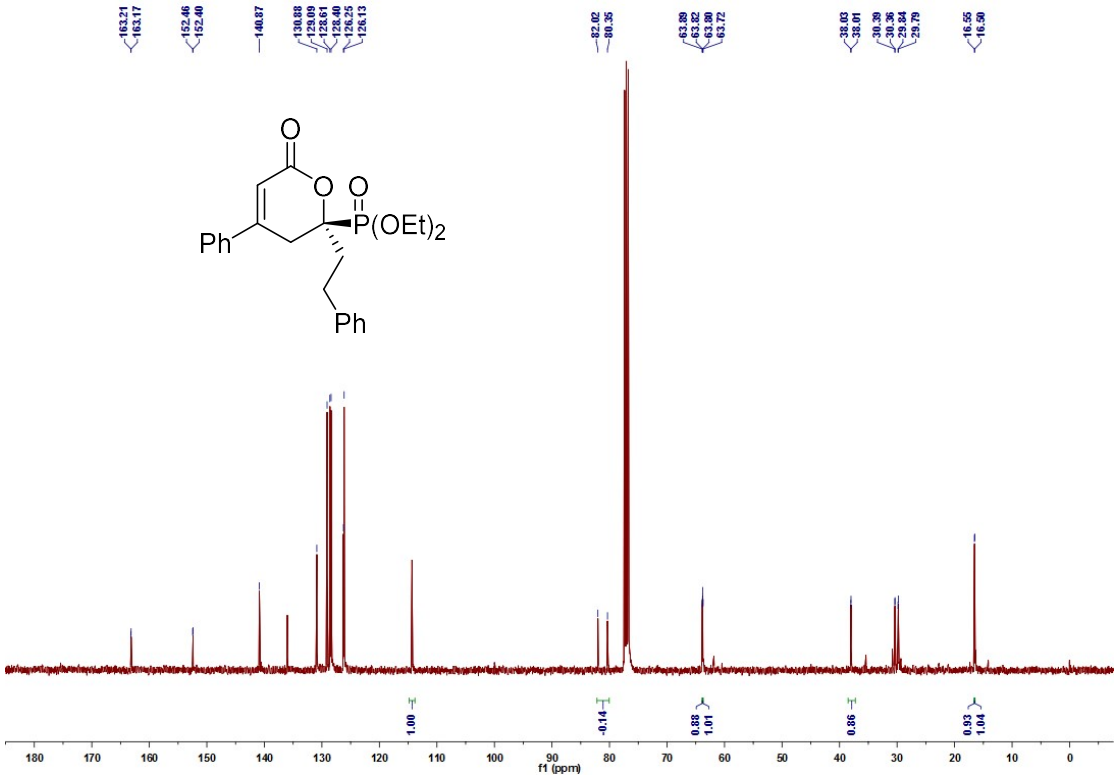
3u ^{31}P NMR


15.34
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

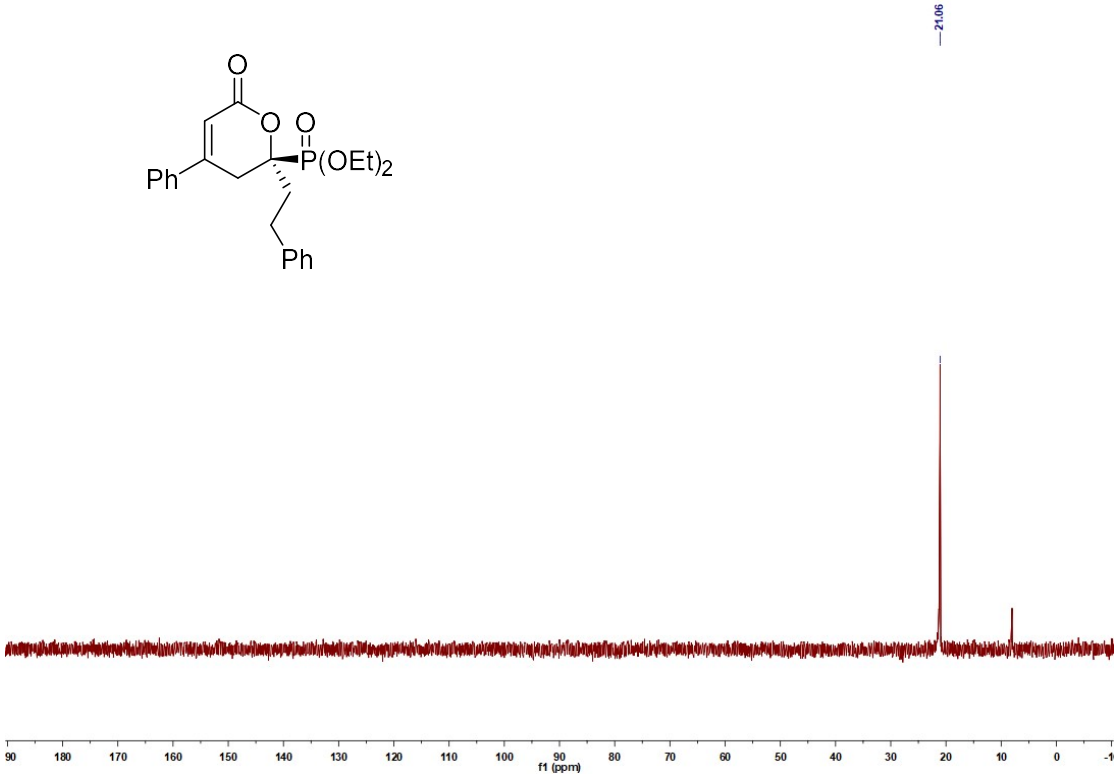
3v ^{1}H NMR



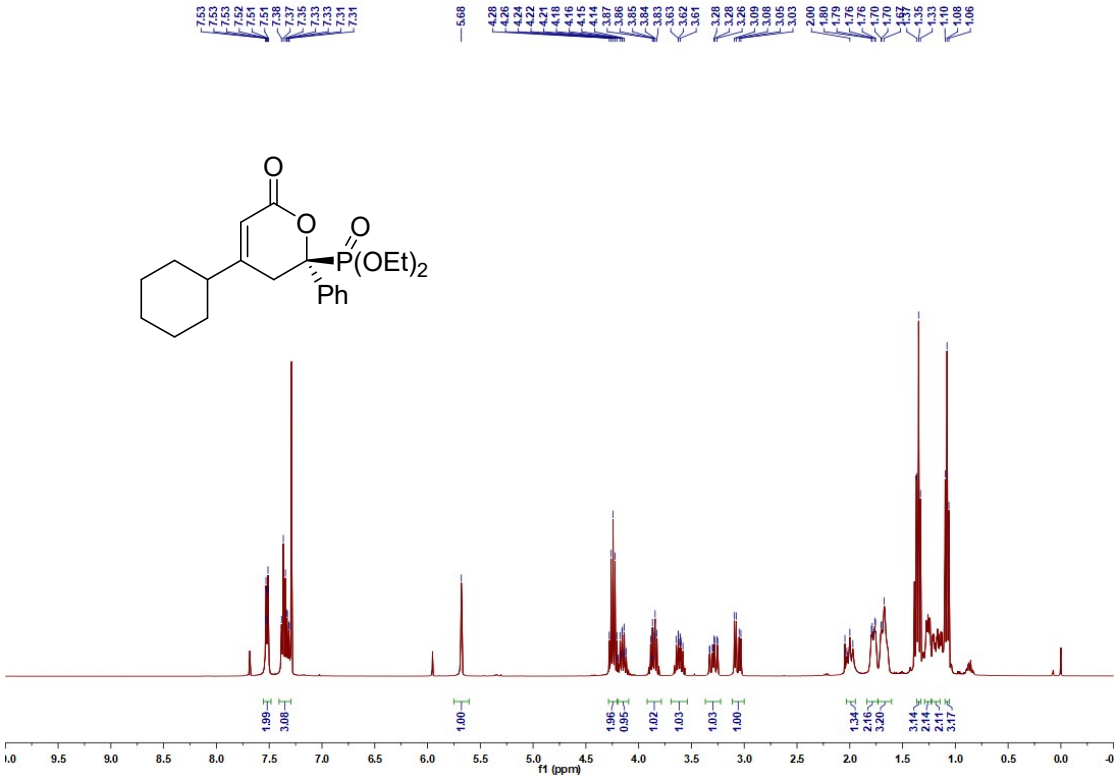
3v ^{13}C NMR



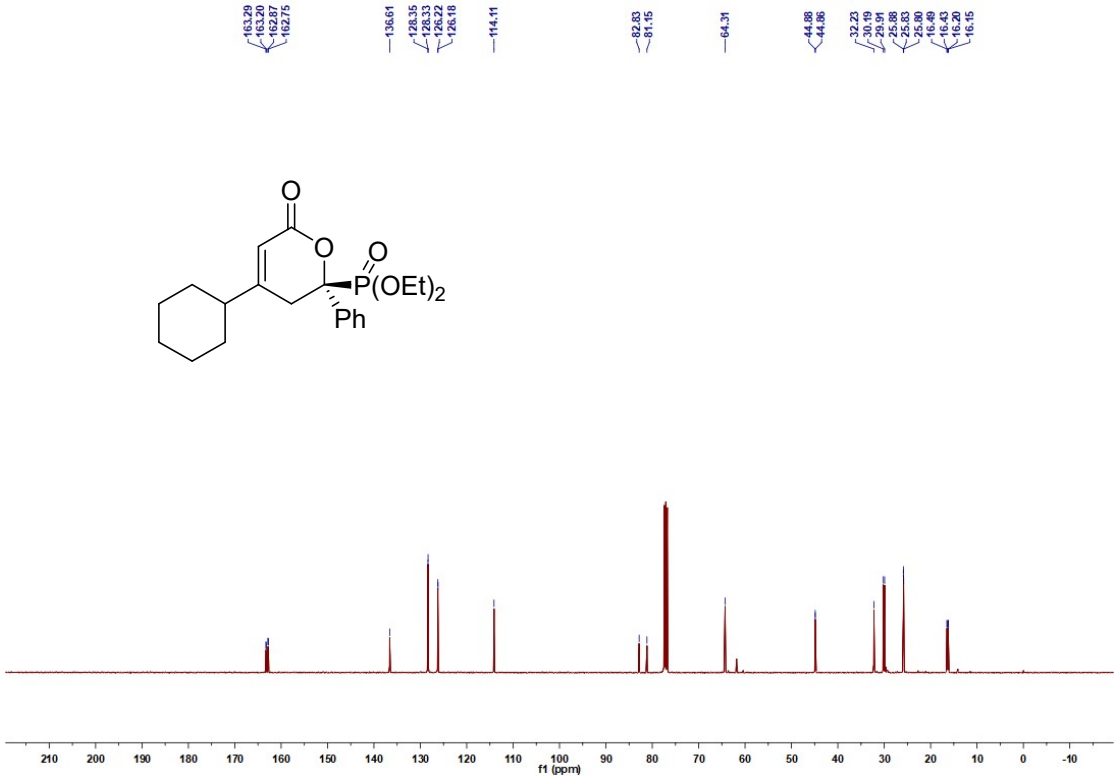
3v ^{31}P NMR


21.06
O
O
O
P(OEt)2
Ph
Ph
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

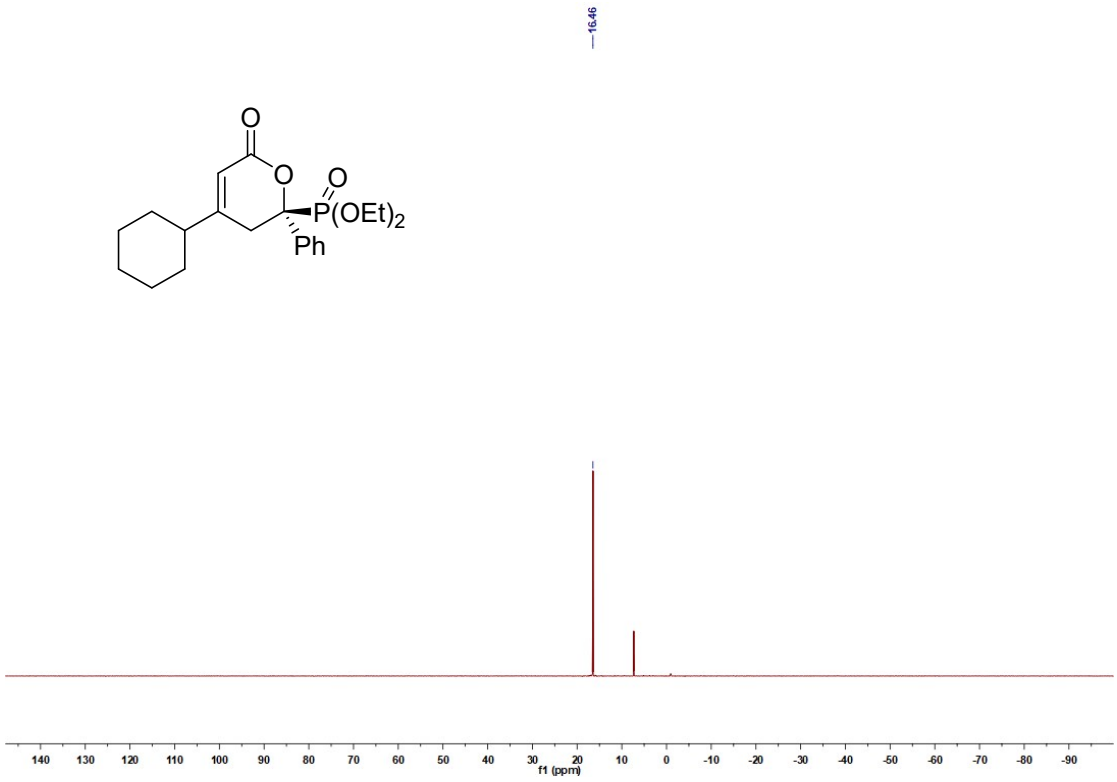
3w ^{1}H NMR



3w ^{13}C NMR

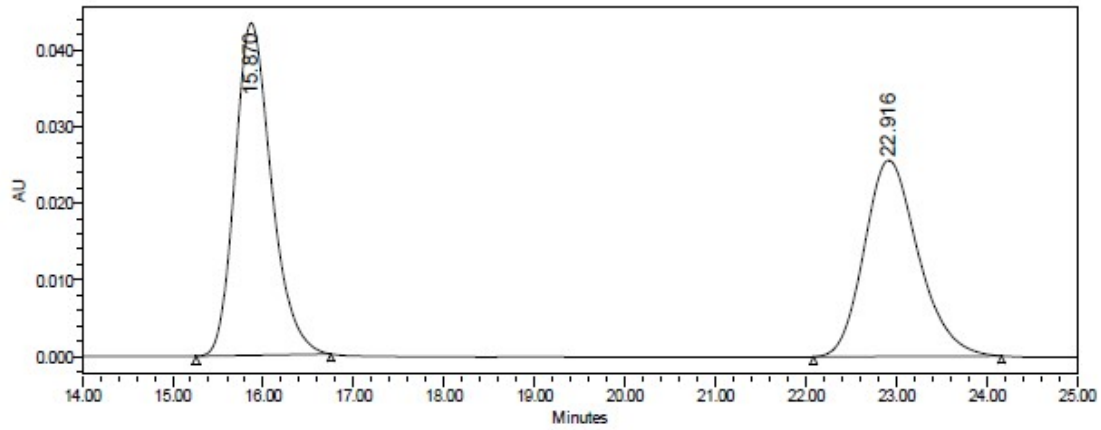


3w ^{31}P NMR


16.46
O
O
O
P(OEt)2
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)

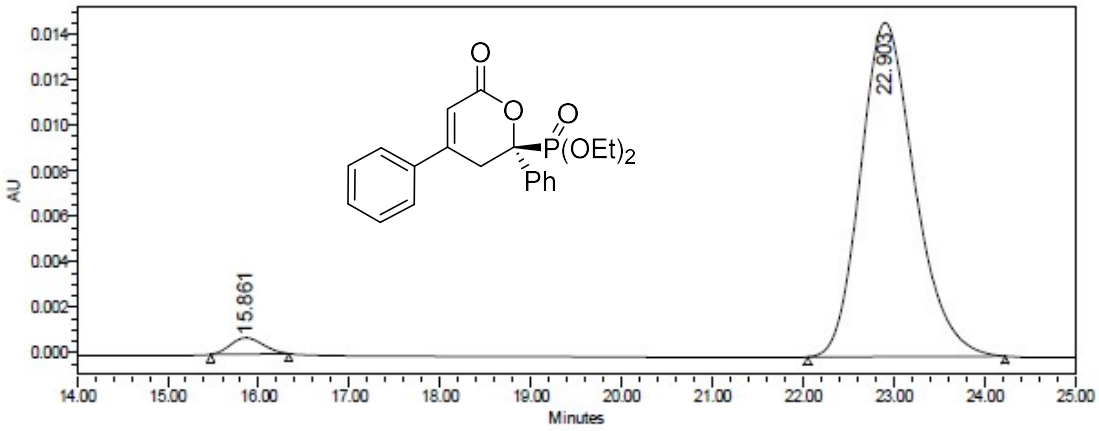
Ⅹ. HPLC spectra of products

Racemic 3a



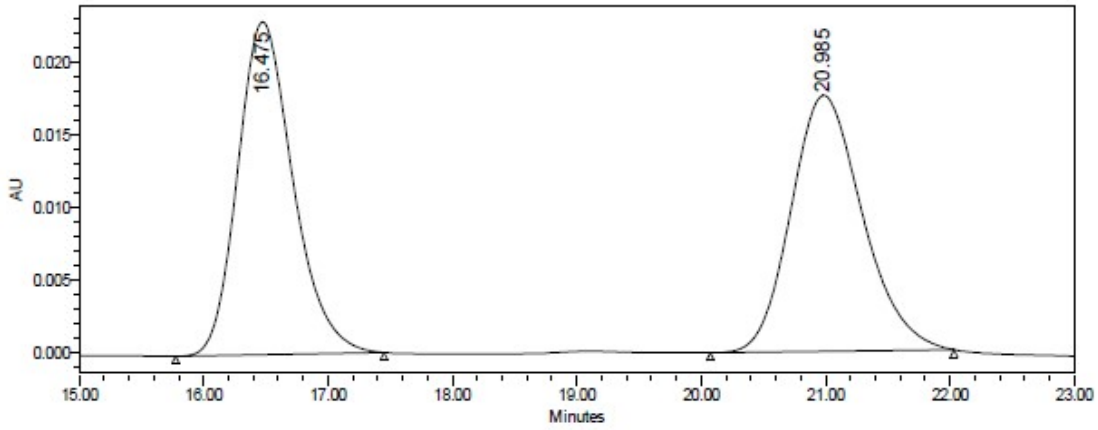
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.870	bb	89.500	1216502	43391	53.38
2	22.916	bb	124.500	1062435	25612	46.62
Sum				2278937.1	69003.4	100.0

Enantioenriched 3a



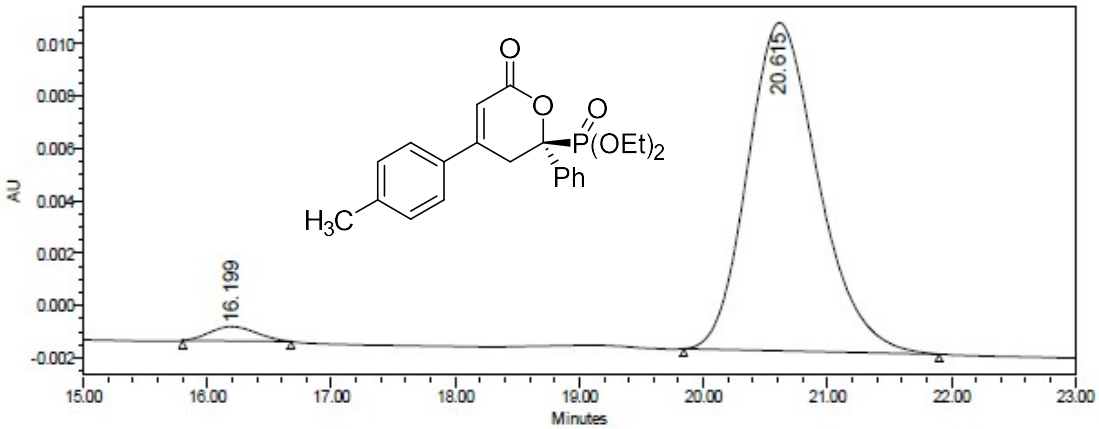
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.861	bb	51.500	17652	712	2.81
2	22.903	bb	130.500	609800	14687	97.19
Sum				627451.6	15398.6	100.0

Racemic 3b



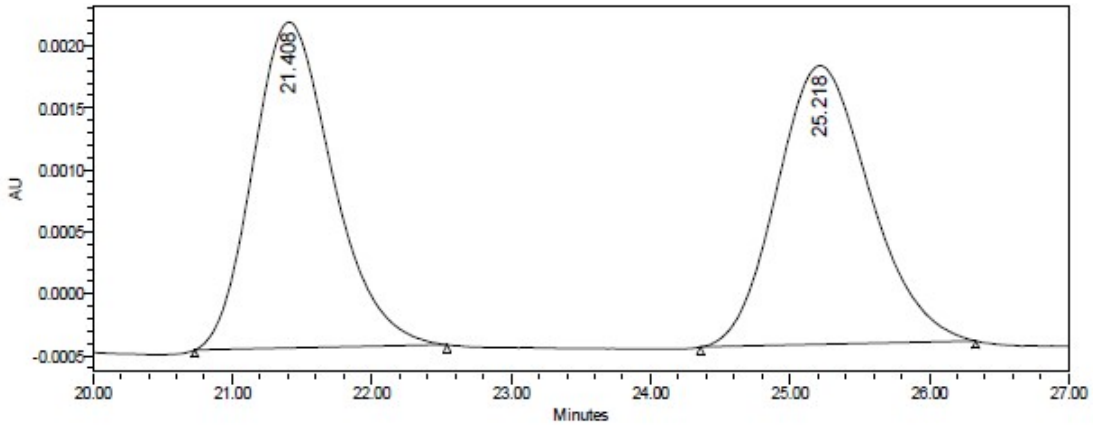
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.475	bb	100.500	709110	22961	50.11
2	20.985	bb	117.500	705856	17658	49.89
Sum				1414965.8	40619.8	100.0

Enantioenriched 3b

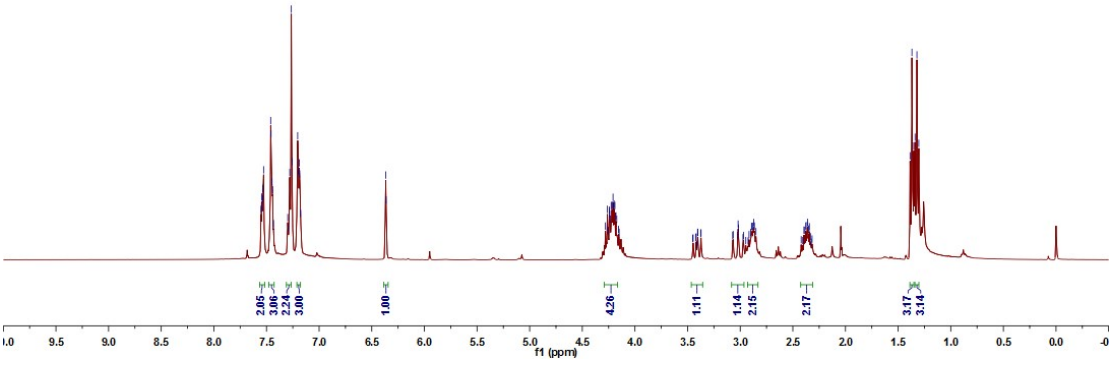


	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.199	bb	52.500	14468	552	2.82
2	20.615	bb	123.500	497879	12543	97.18
Sum				512347.3	13094.7	100.0

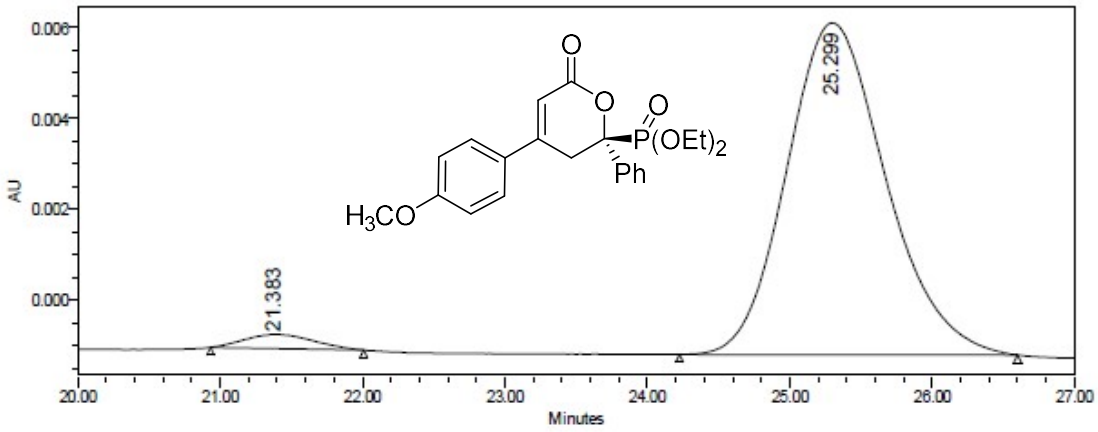
Racemic 3c



	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	21.408	bb	108.500	104627	2631	50.04
2	25.218	bb	118.500	104443	2250	49.96
Sum				209070.5	4880.5	100.0

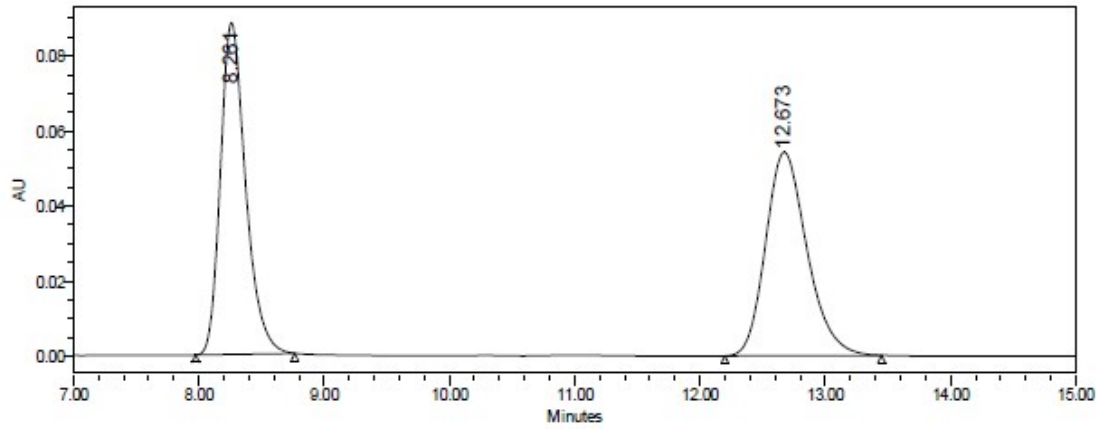


Enantioenriched 3c



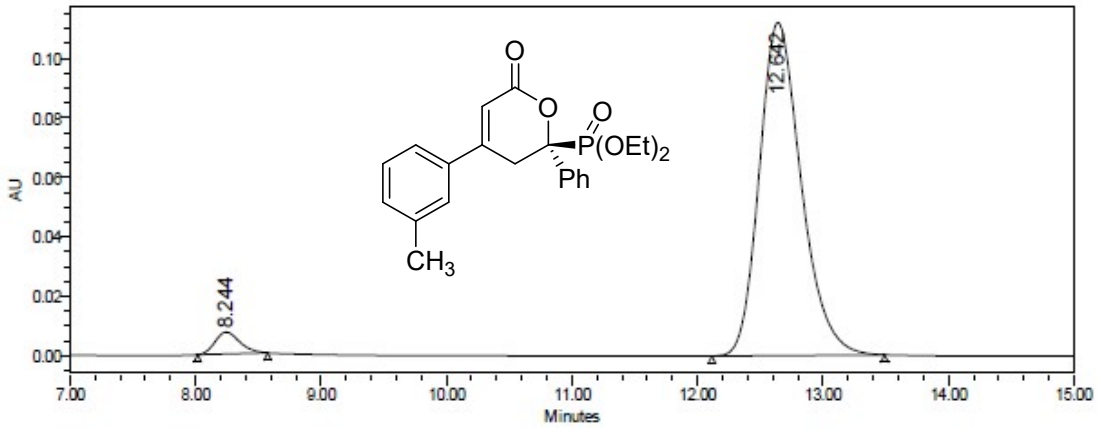
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	21.383	bb	64.500	10372	309	2.85
2	25.299	bb	142.500	353100	7303	97.15
Sum				363472.6	7612.5	100.0

Racemic 3d



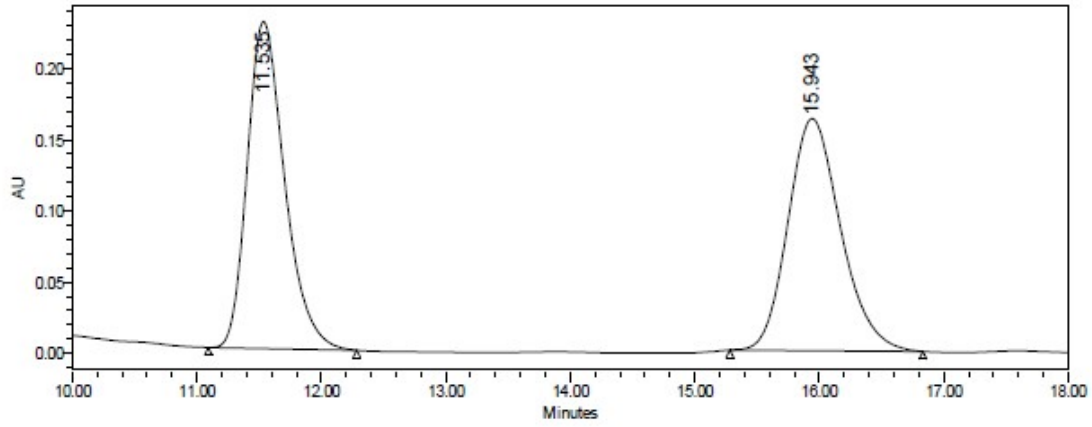
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	8.261	bb	47.500	1234277	88511	49.80
2	12.673	bb	75.000	1244169	54275	50.20
Sum				2478445.5	142785.6	100.0

Enantioenriched 3d



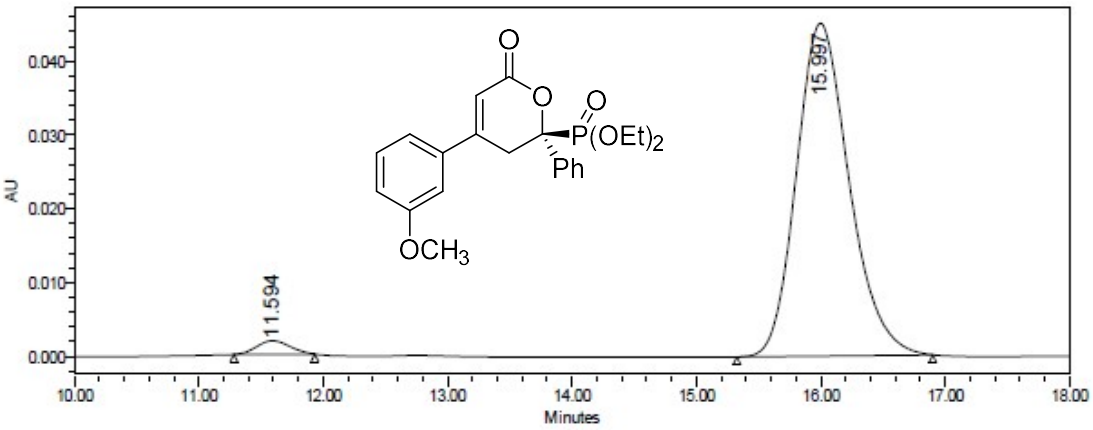
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	8.244	bb	33.500	101053	7371	3.74
2	12.642	bb	82.500	2598137	111991	96.26
Sum				2699189.9	119362.1	100.0

Racemic 3e



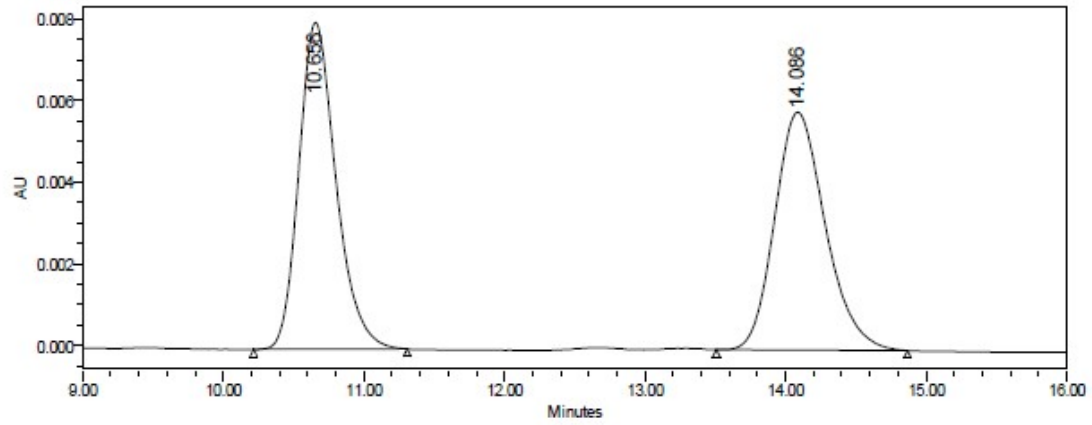
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	11.535	bb	71.500	4811559	230009	50.06
2	15.943	bb	93.000	4799359	163162	49.94
Sum				9610917.2	393171.2	100.0

Enantioenriched 3e



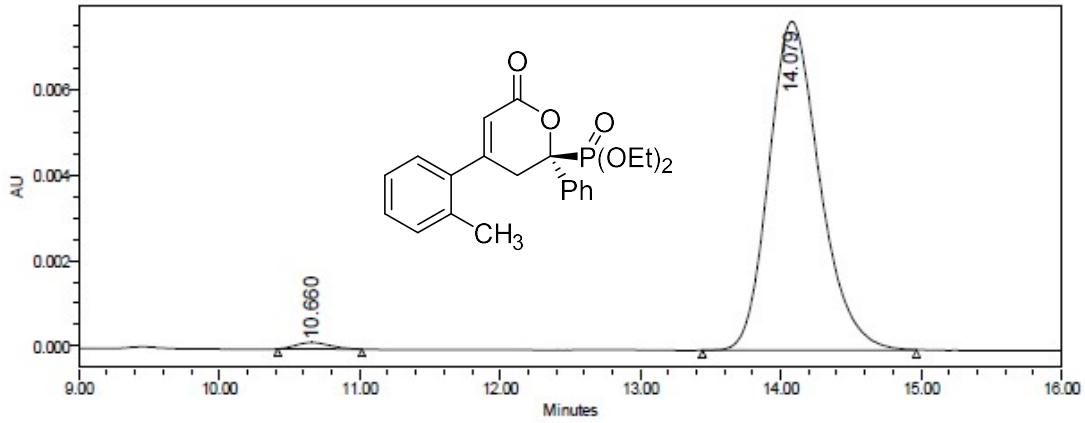
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	11.594	bb	39.000	33834	1833	2.49
2	15.997	bb	94.500	1327362	45081	97.51
Sum				1361195.6	46913.8	100.0

Racemic 3f



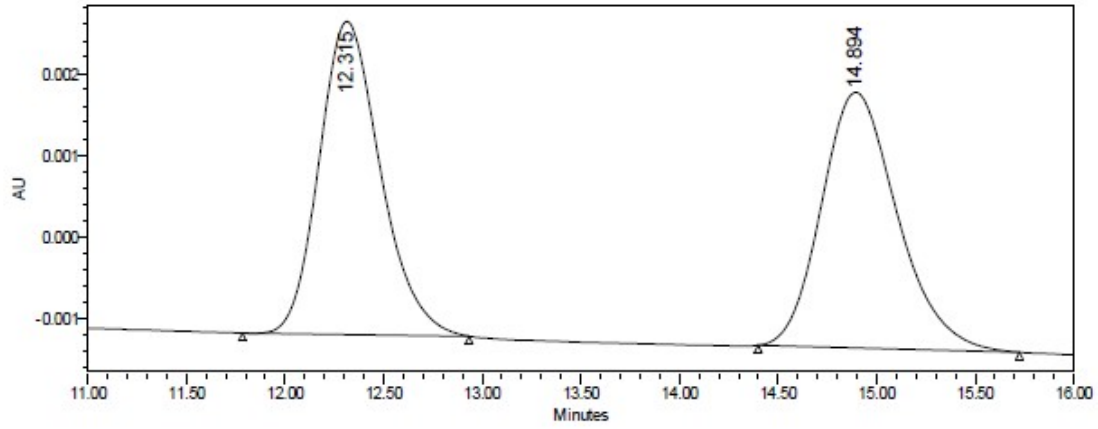
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.656	bb	65.500	146572	7998	50.14
2	14.086	bb	81.500	145750	5825	49.86
Sum				292322.1	13822.9	100.0

Enantioenriched 3f



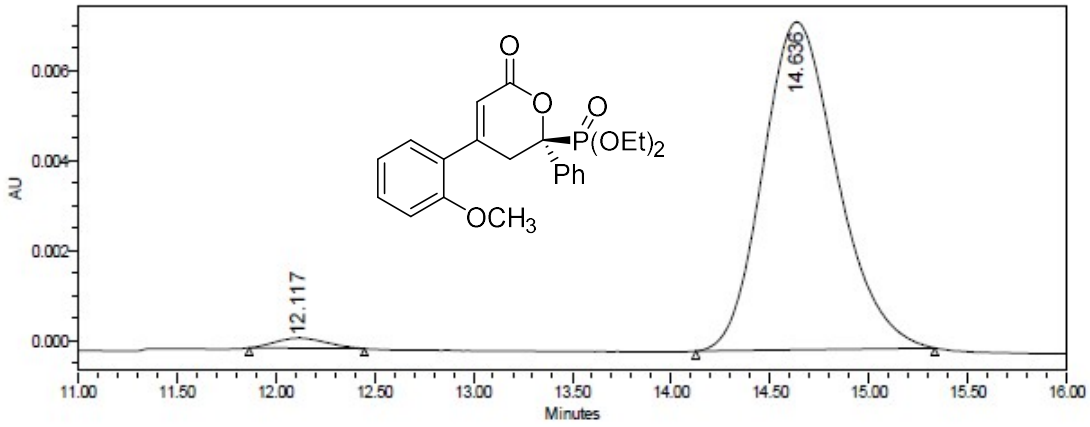
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.660	bb	36.000	2538	152	1.29
2	14.079	bb	91.500	193592	7689	98.71
Sum				196129.5	7841.7	100.0

Racemic 3g



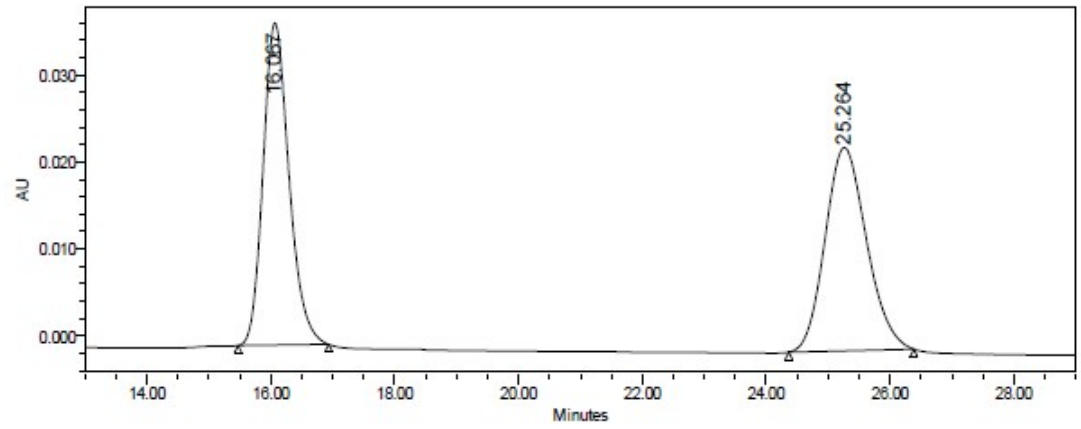
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.315	bb	69.000	83057	3842	49.78
2	14.894	bb	79.500	83787	3136	50.22
Sum				166843.2	6977.8	100.0

Enantioenriched 3g



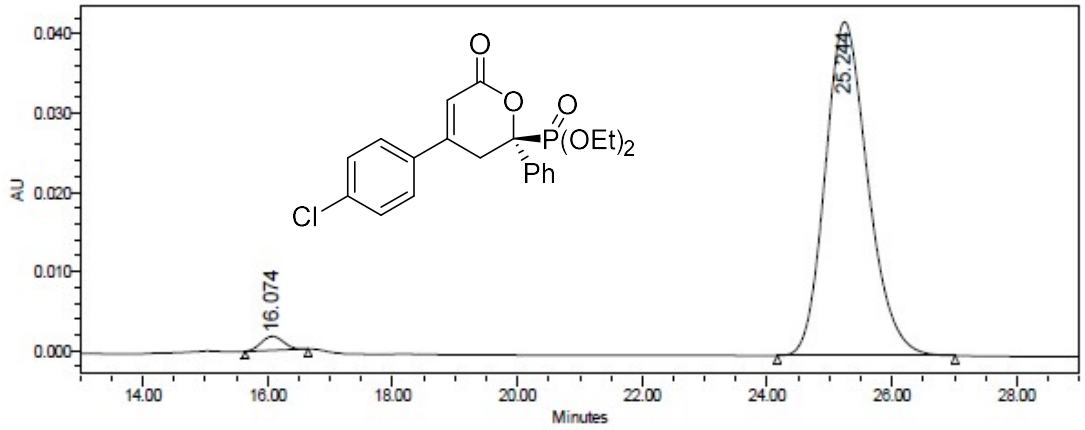
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.117	bb	35.000	3976	222	2.05
2	14.636	bb	72.500	190319	7281	97.95
Sum				194294.9	7503.5	100.0

Racemic 3h



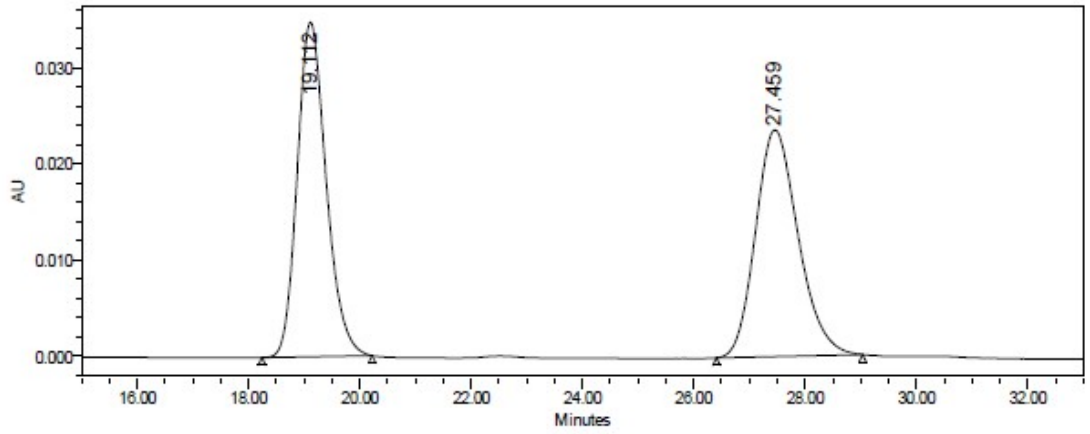
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.067	bb	87.500	1076200	37001	49.81
2	25.264	bb	121.000	1084412	23338	50.19
Sum				2160612.1	60338.8	100.0

Enantioenriched 3h



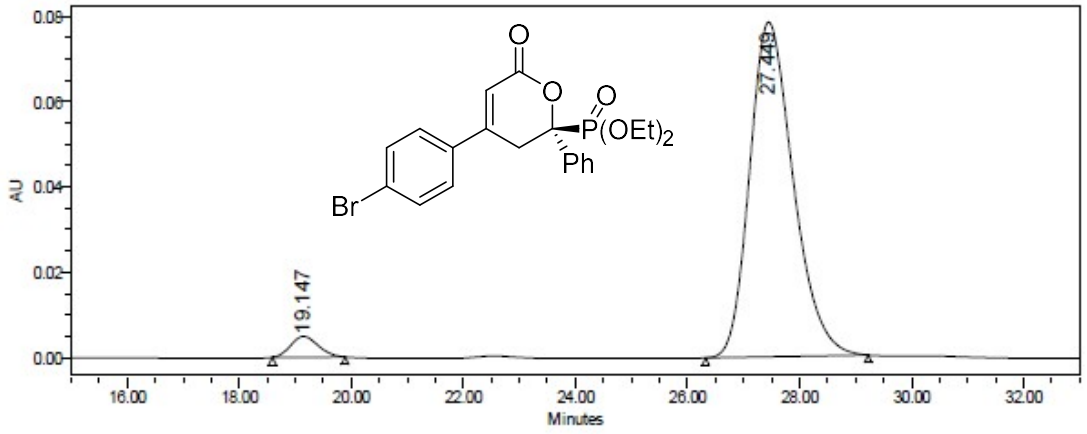
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.074	bb	60.500	43345	1760	2.12
2	25.244	bb	171.000	2003099	42129	97.88
Sum				2046444.0	43889.1	100.0

Racemic 3i



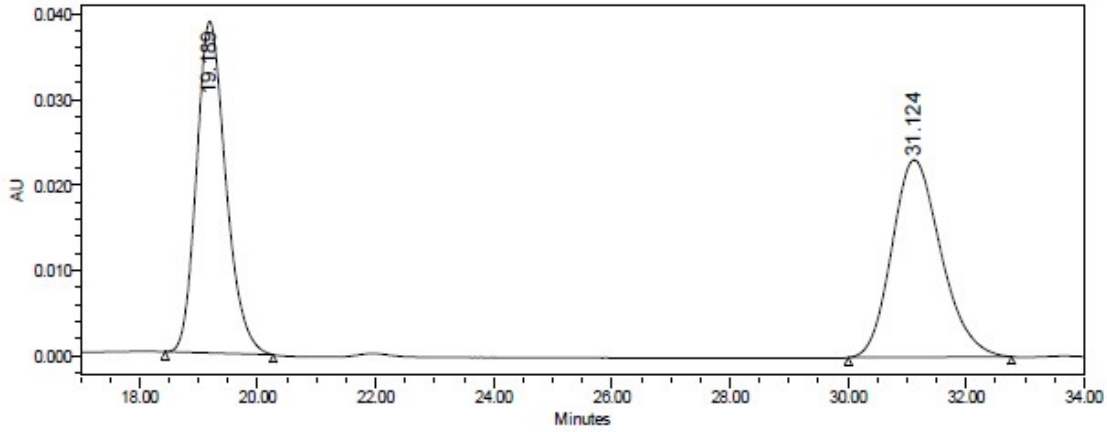
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.112	bb	118.500	1254169	34745	50.01
2	27.459	bb	157.500	1253623	23564	49.99
Sum				2507791.9	58309.2	100.0

Enantioenriched 3i



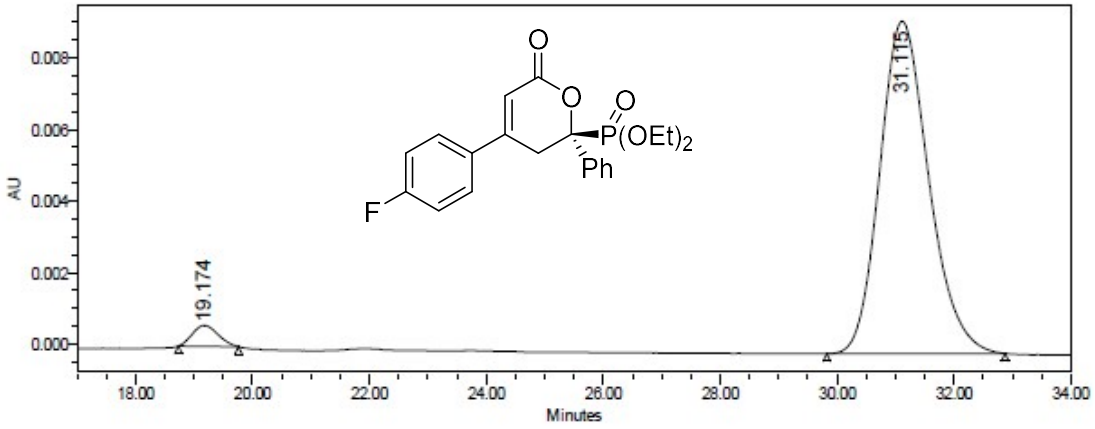
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.147	bb	78.000	167356	4894	3.79
2	27.449	bb	174.000	4242566	78444	96.21
Sum				4409922.7	83337.2	100.0

Racemic 3j



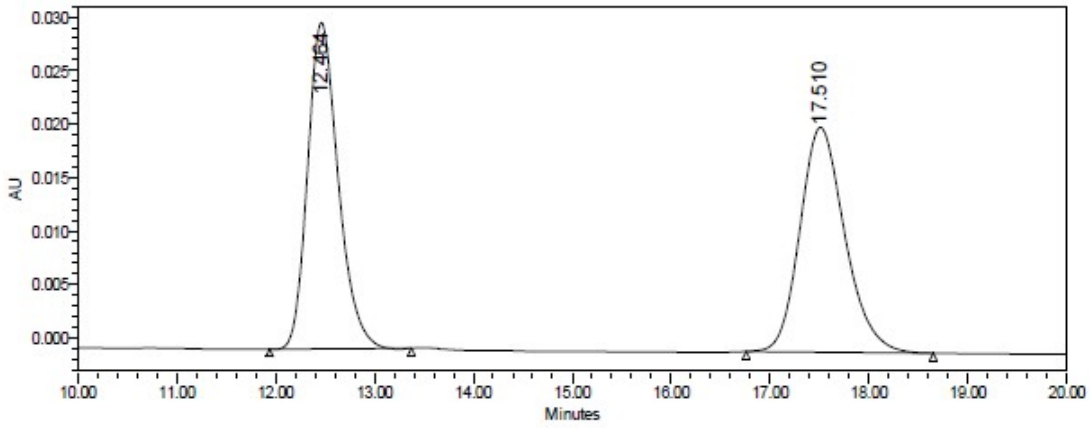
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.189	bb	110.000	1341899	38803	50.10
2	31.124	bb	166.000	1336772	23107	49.90
Sum				2678670.6	61910.9	100.0

Enantioenriched 3j



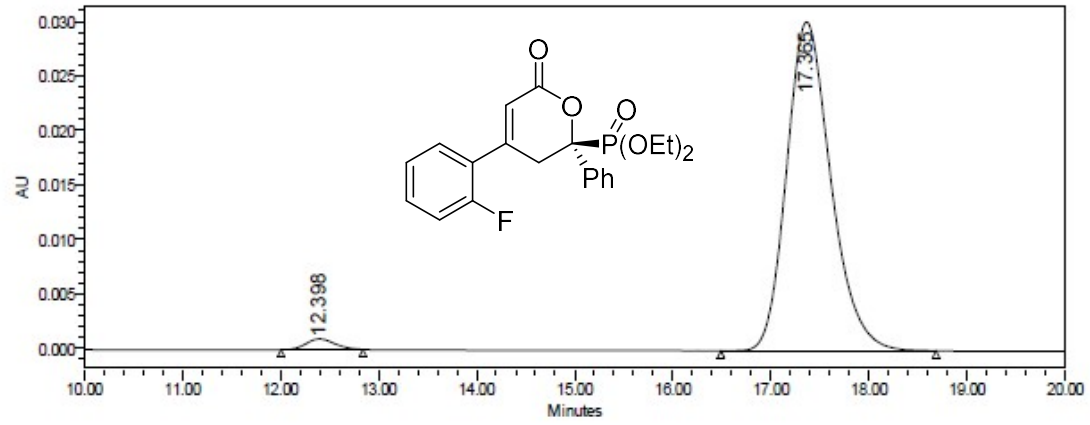
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.174	bb	61.500	17817	584	3.19
2	31.115	bb	183.000	540604	9295	96.81
Sum				558420.9	9878.9	100.0

Racemic 3k



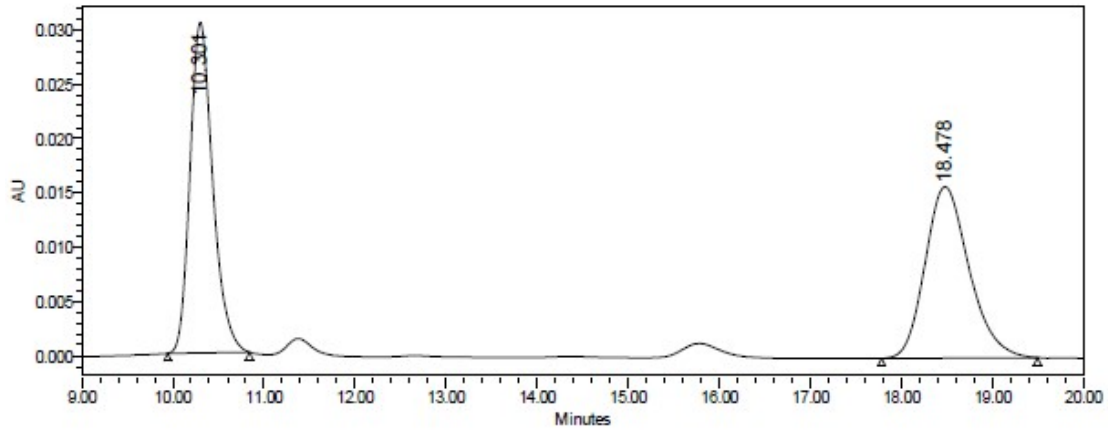
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.464	bb	86.000	656910	30480	49.77
2	17.510	bb	113.500	662919	21007	50.23
Sum				1319829.6	51486.4	100.0

Enantioenriched 3k



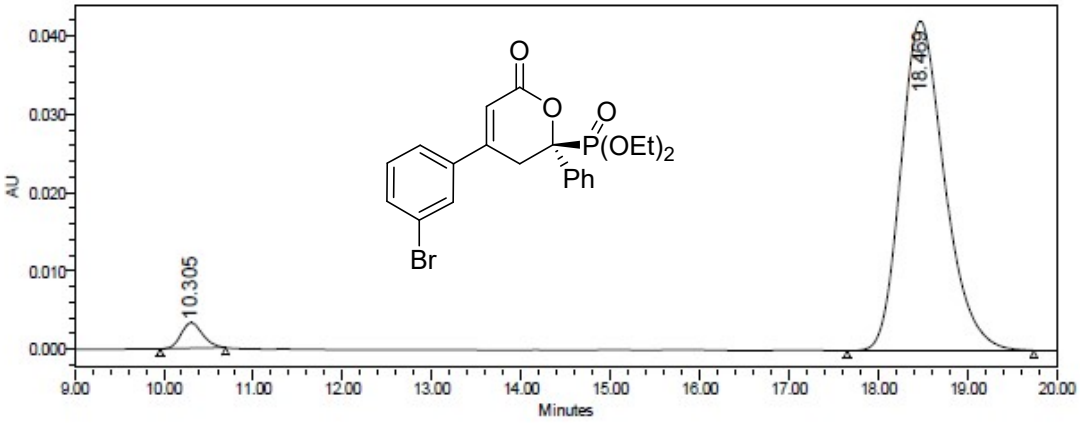
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.398	bb	50.000	19801	983	2.05
2	17.365	bb	131.500	947072	30172	97.95
Sum				966873.1	31154.5	100.0

Racemic 3l



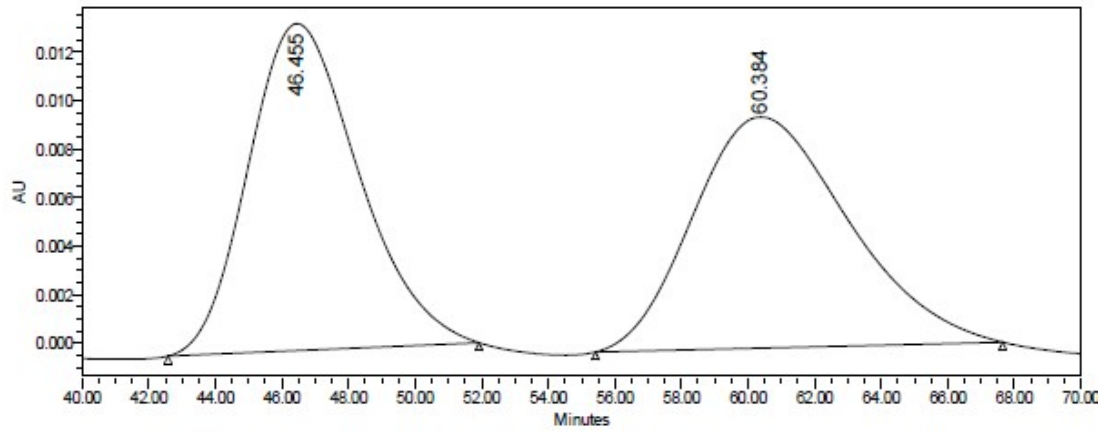
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.301	bb	54.000	528010	30418	50.00
2	18.478	bb	102.500	528017	15766	50.00
Sum				1056026.9	46184.9	100.0

Enantioenriched 3l



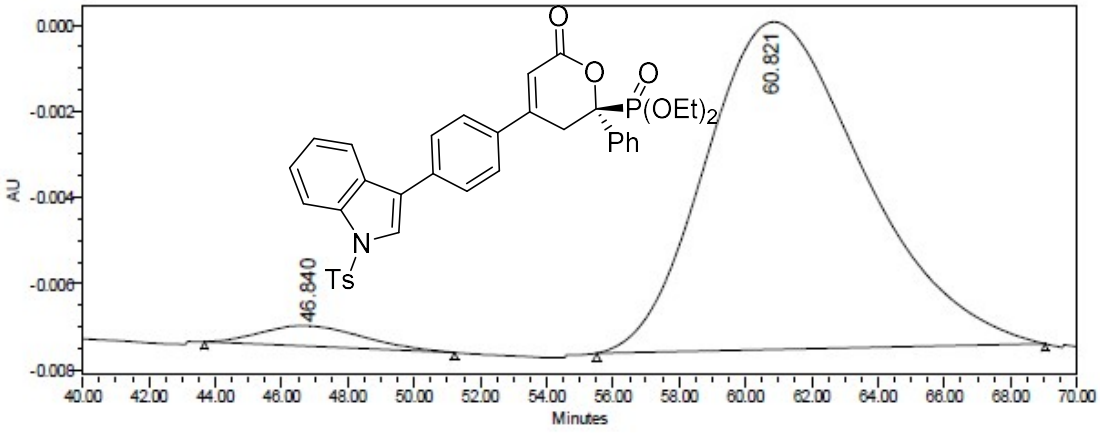
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.305	bb	44.000	54480	3248	3.68
2	18.469	bb	125.500	1426690	42026	96.32
Sum				1481170.5	45273.9	100.0

Racemic 3m



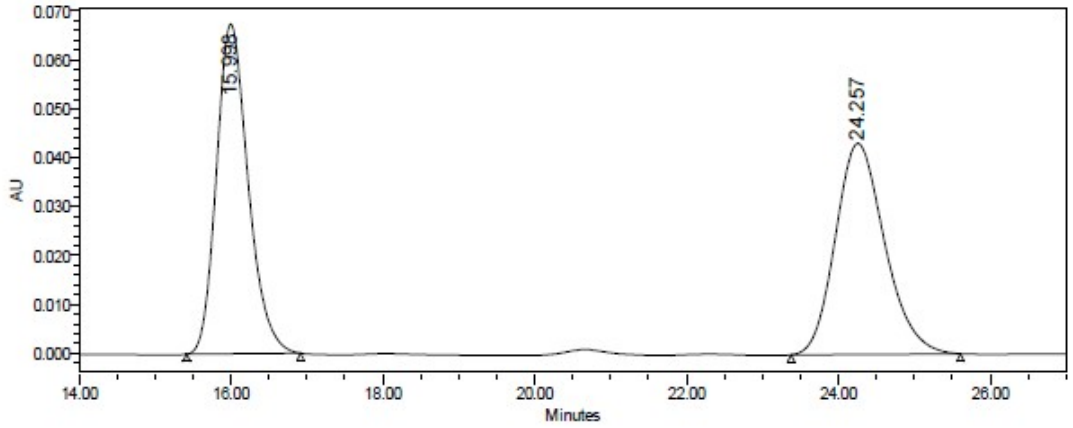
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	46.455	bb	560.500	3091829	13471	50.12
2	60.384	bb	734.000	3077422	9514	49.88
Sum				6169250.2	22985.8	100.0

Enantioenriched 3m



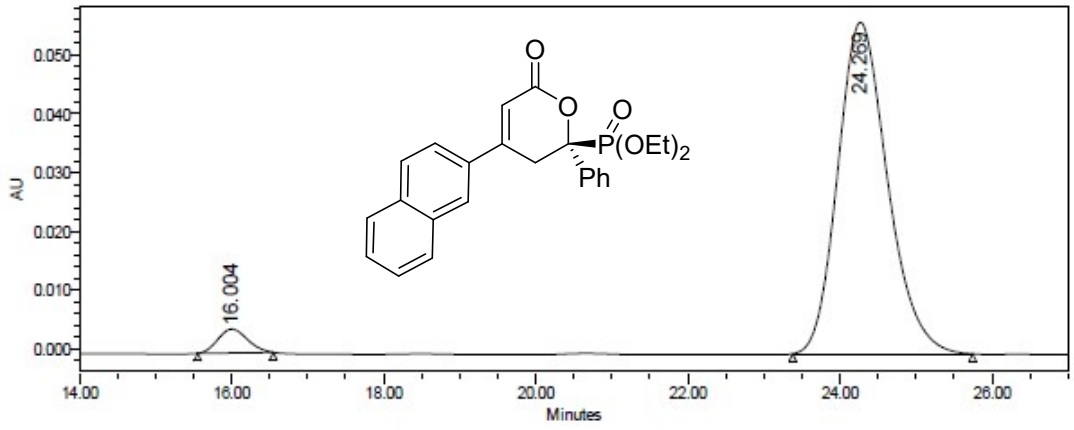
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	46.840	bb	453.000	101939	475	3.86
2	60.821	bb	811.500	2536772	7601	96.14
Sum				2638710.9	8076.1	100.0

Racemic 3n



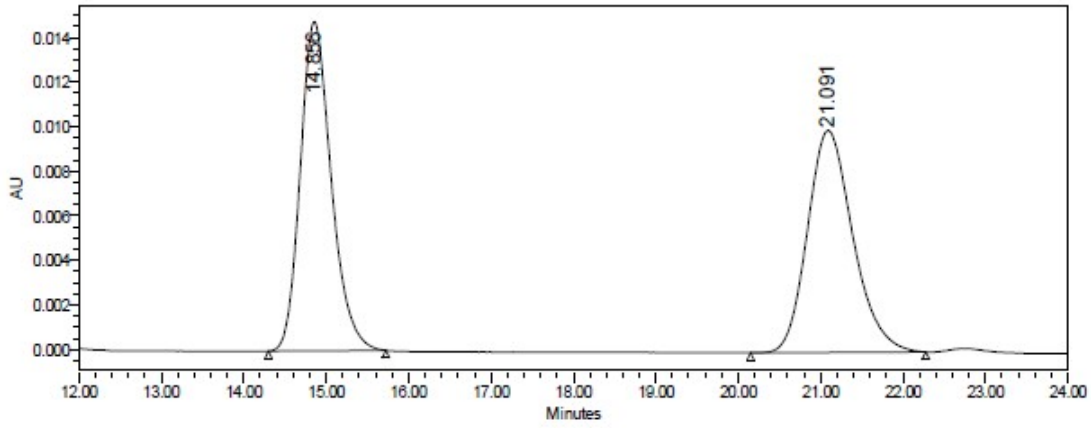
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.998	bb	90.000	1956543	67459	50.11
2	24.257	bb	134.000	1947890	43159	49.89
Sum				3904433.5	110617.5	100.0

Enantioenriched 3n



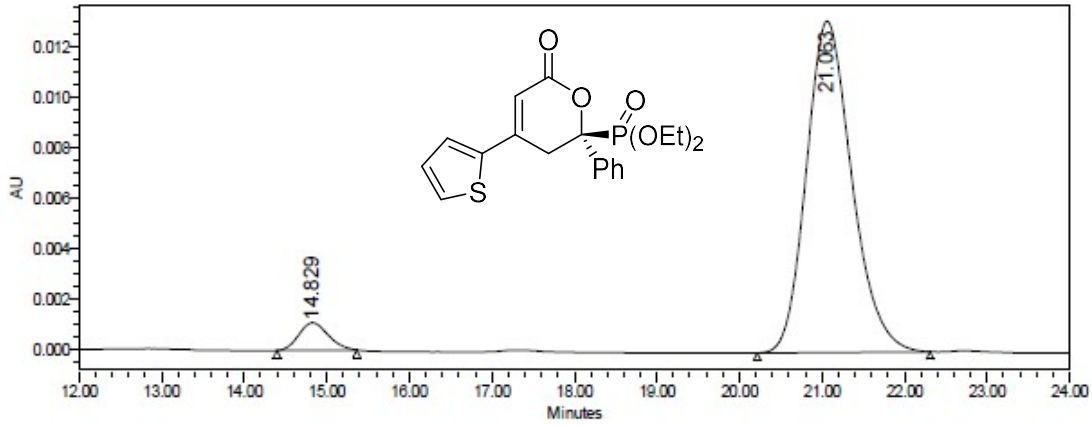
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.004	bb	59.500	109207	4064	4.09
2	24.269	bb	142.000	2560075	56371	95.91
Sum				2669282.4	60434.7	100.0

Racemic 3o



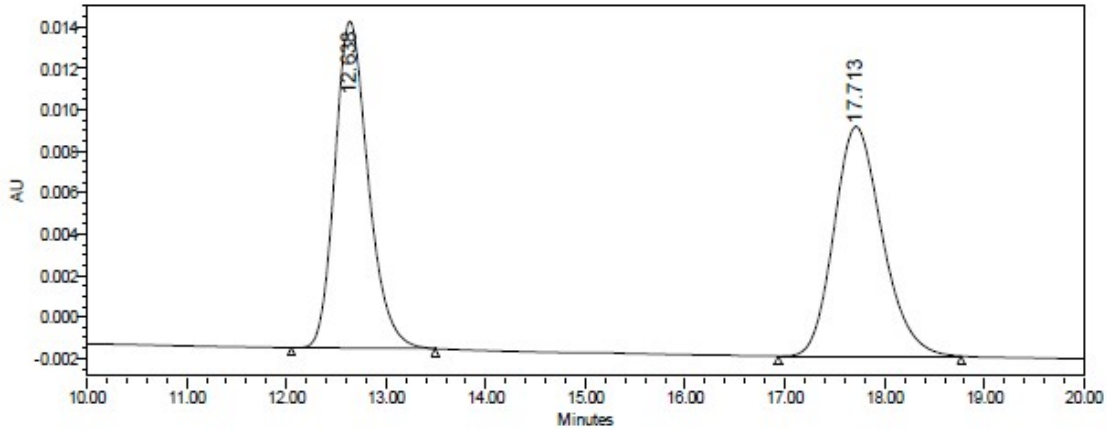
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.856	bb	85.500	385535	14776	50.25
2	21.091	bb	127.500	381706	9965	49.75
Sum				767240.9	24741.2	100.0

Enantioenriched 3o



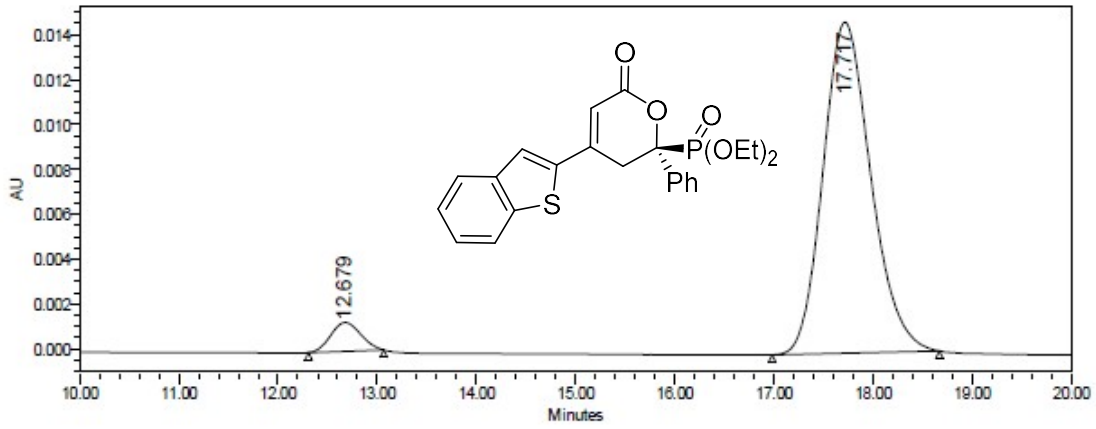
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.829	bb	58.000	26834	1088	5.07
2	21.063	bb	125.500	502442	13104	94.93
Sum				529275.4	14191.8	100.0

Racemic 3p



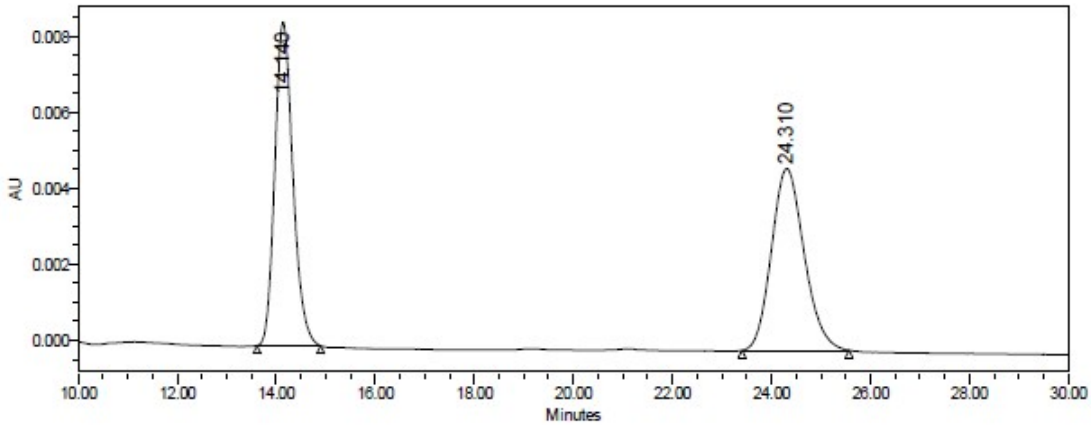
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.638	bb	86.500	366562	15771	49.62
2	17.713	bb	110.000	372138	11080	50.38
Sum				738700.2	26850.0	100.0

Enantioenriched 3p



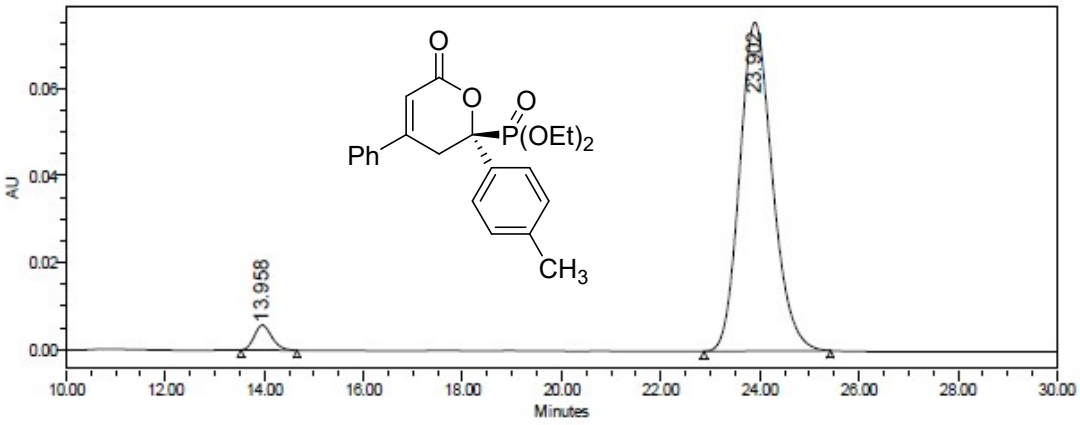
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	12.679	bb	45.500	26936	1288	5.17
2	17.717	bb	101.000	494349	14758	94.83
Sum				521285.5	16046.0	100.0

Racemic 3q



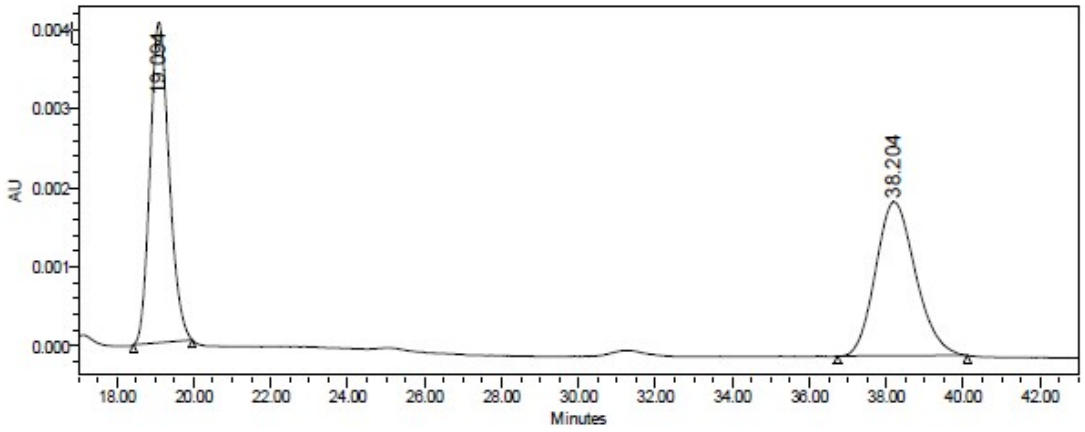
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	14.140	bb	77.500	216526	8527	49.64
2	24.310	bb	129.500	219625	4785	50.36
Sum				436151.4	13311.4	100.0

Enantioenriched 3q



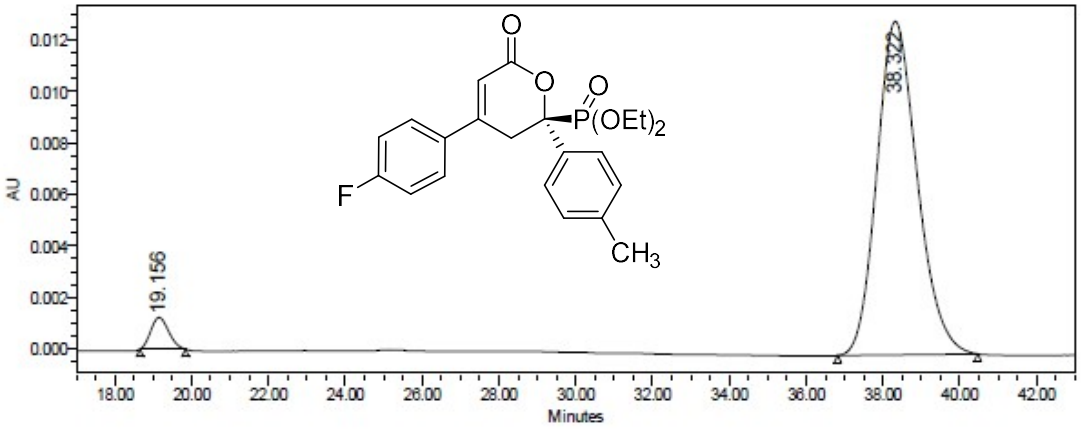
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	13.958	bb	68.000	141488	5736	3.93
2	23.902	bb	153.000	3463041	75443	96.07
Sum				3604529.7	81178.3	100.0

Racemic 3r



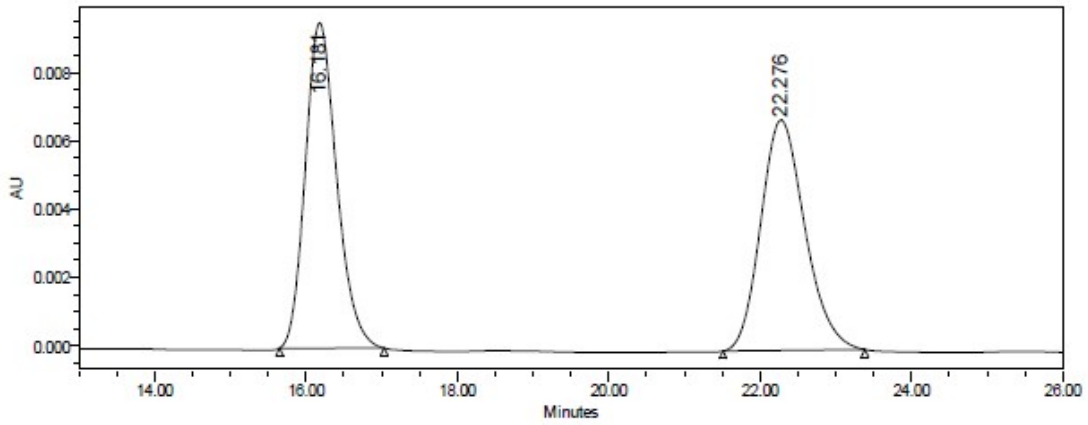
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.094	bb	91.500	139634	4053	49.87
2	38.204	bb	202.500	140380	1946	50.13
Sum				280014.1	5999.5	100.0

Enantioenriched 3r



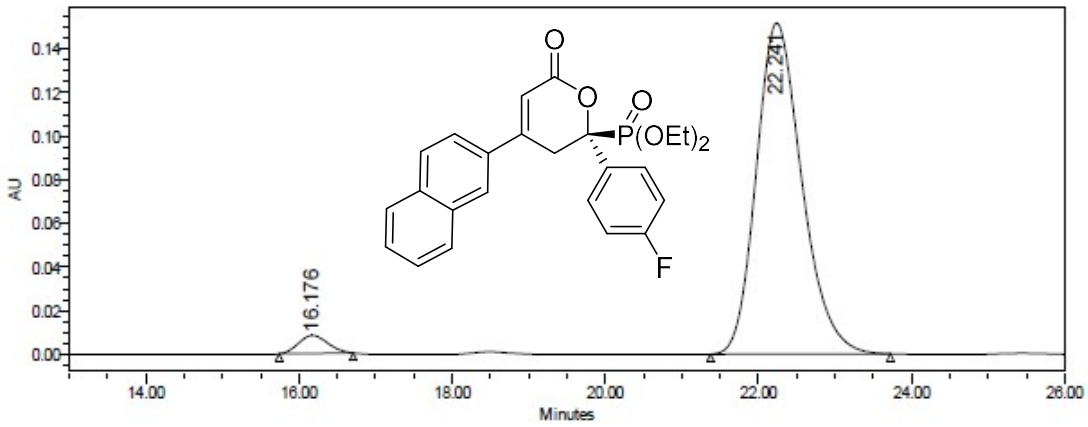
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.156	bb	71.000	40162	1239	4.06
2	38.322	bb	218.500	949971	12976	95.94
Sum				990133.1	14215.6	100.0

Racemic 3s



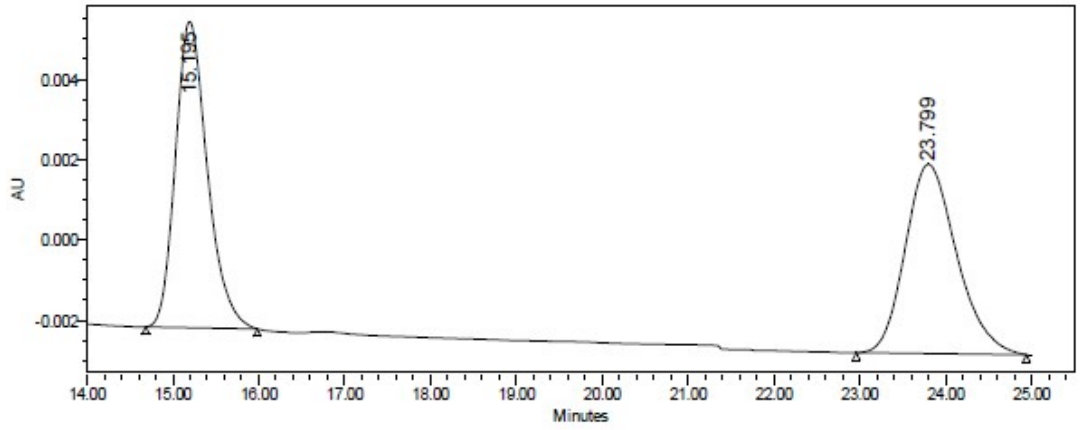
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.181	bb	83.000	274608	9530	50.09
2	22.276	bb	112.500	273571	6746	49.91
Sum				548178.9	16276.2	100.0

Enantioenriched 3s



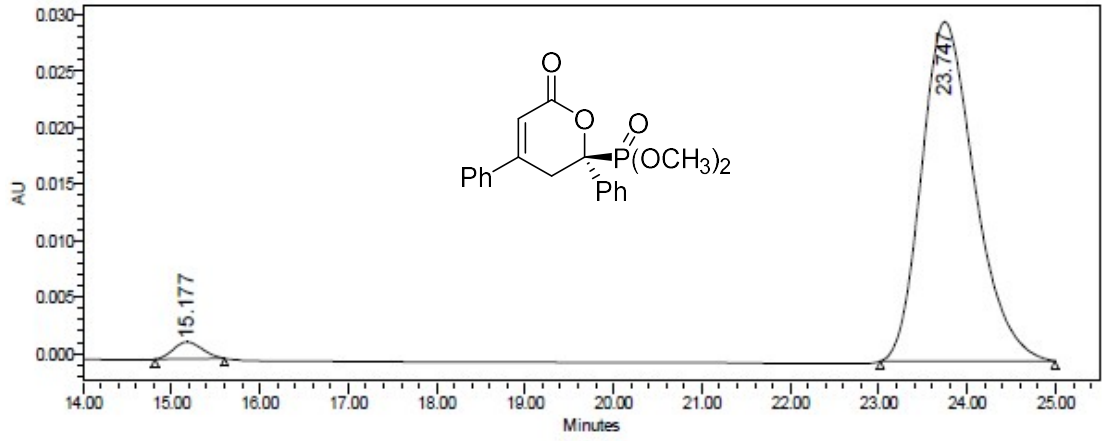
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	16.176	bb	58.000	220445	8285	3.39
2	22.241	bb	141.000	6282591	151784	96.61
Sum				6503035.8	160069.1	100.0

Racemic 3t



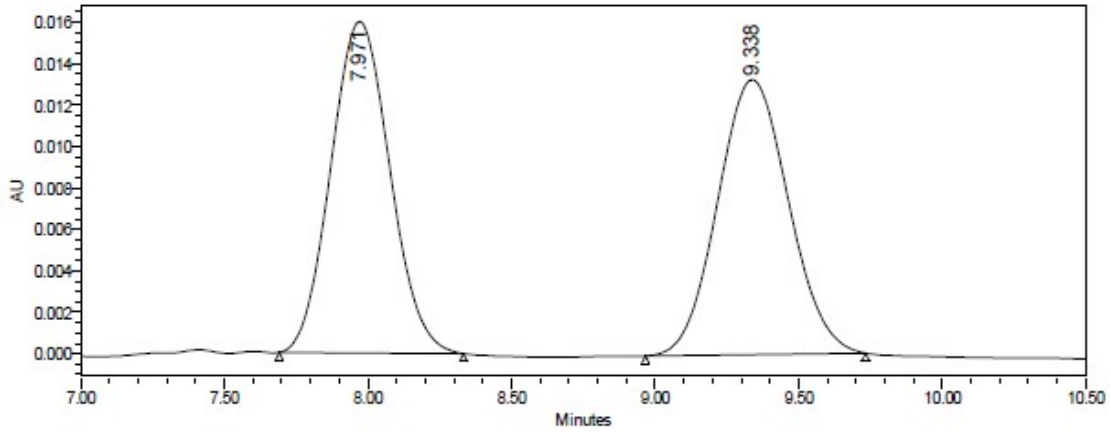
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.195	bb	78.000	196905	7621	50.08
2	23.799	bb	119.000	196261	4714	49.92
Sum				393165.7	12335.0	100.0

Enantioenriched 3t



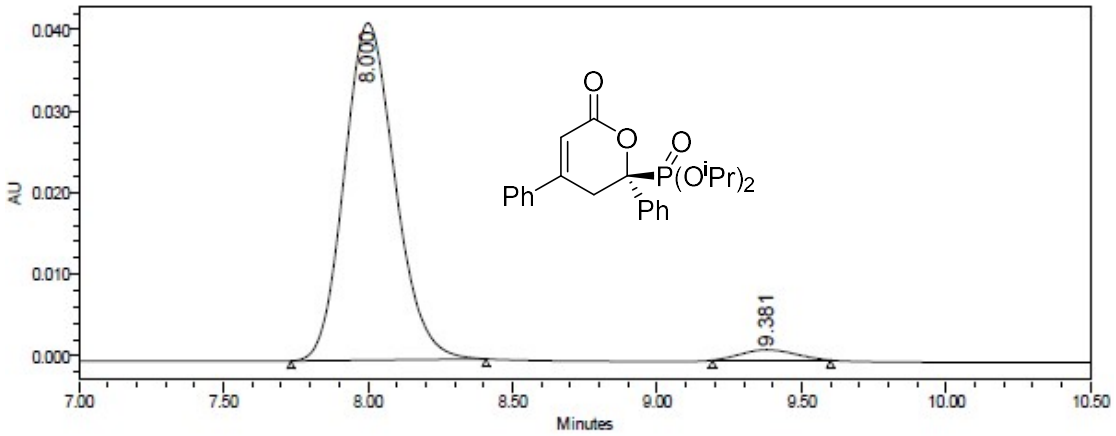
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	15.177	bb	47.000	33748	1488	2.62
2	23.747	bb	118.500	1256295	30059	97.38
Sum				1290043.5	31546.7	100.0

Racemic 3u



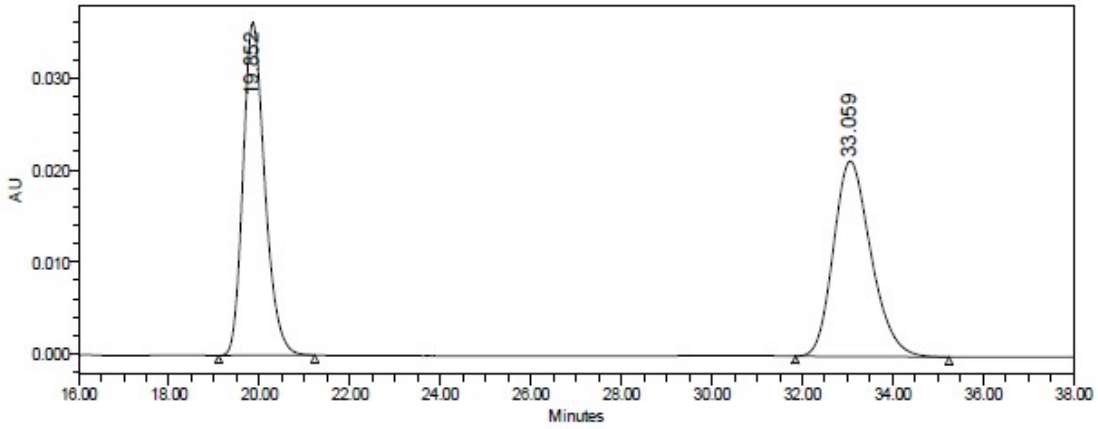
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	7.971	bb	38.500	228907	15991	50.19
2	9.338	bb	46.000	227138	13264	49.81
Sum				456045.7	29255.3	100.0

Enantioenriched 3u



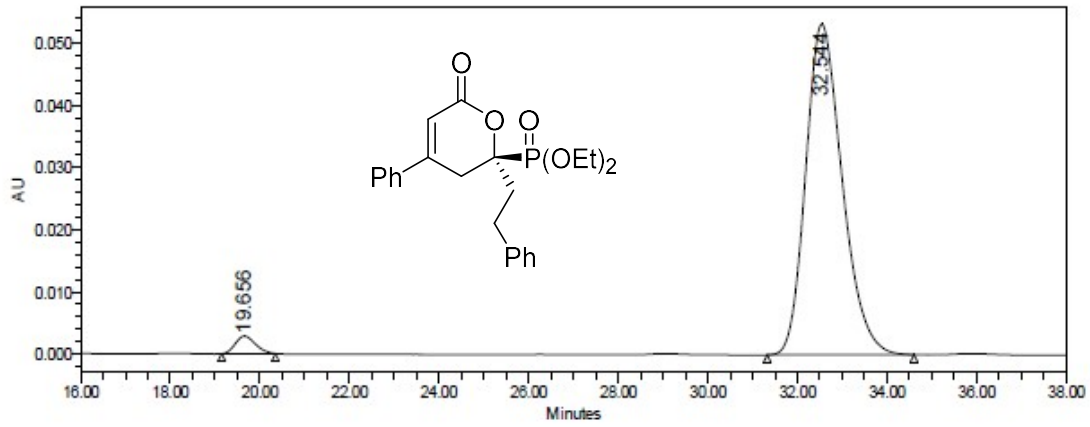
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	8.000	bb	40.500	503389	41316	96.83
2	9.381	bb	24.500	16496	1271	3.17
Sum				519885.7	42587.6	100.0

Racemic 3v



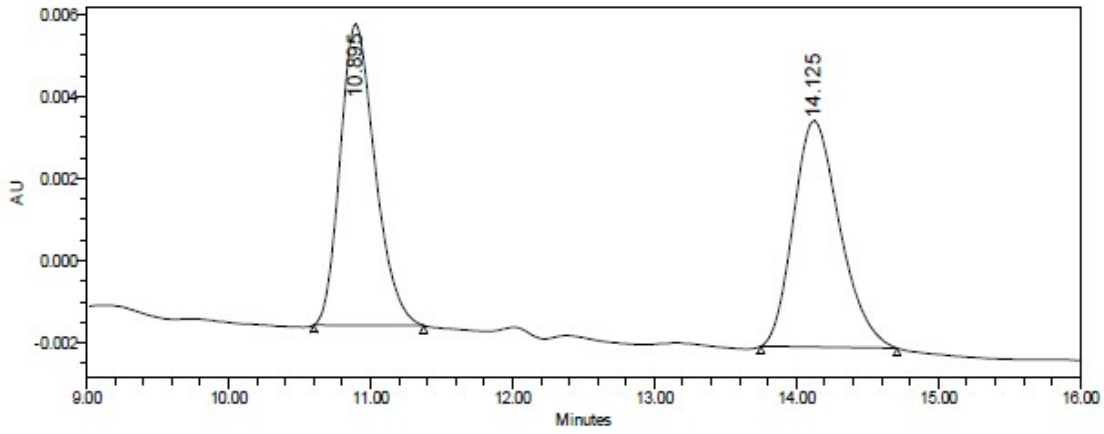
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.852	bb	127.500	1206278	36178	49.61
2	33.059	bb	203.500	1225281	21253	50.39
Sum				2431559.3	57431.8	100.0

Enantioenriched 3v



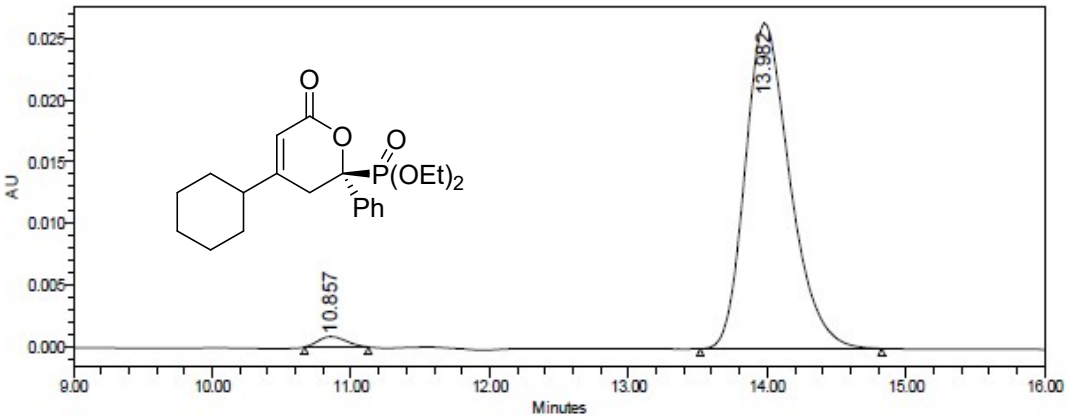
	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	19.656	bb	72.000	87135	2824	2.81
2	32.544	bb	196.500	3019153	53252	97.19
Sum				3106288.5	56075.9	100.0

Racemic 3w



	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.895	bb	46.500	125342	7324	50.09
2	14.125	bb	57.500	124907	5500	49.91
Sum				250249.6	12824.2	100.0

Enantioenriched 3w



	RT(min)	Int Type	Width (sec)	Area	Height	% Area
1	10.857	bb	27.500	11721	843	1.93
2	13.982	bb	78.500	594232	26431	98.07
Sum				605953.1	27274.0	100.0