

Supporting Information for:

**Efficient Asymmetric Hydrophosphonylation of Unsaturated Amides Catalyzed by Rare-Earth Metal Amides  $[(\text{Me}_3\text{Si})_2\text{N}]_3\text{RE}(m\text{-Cl})\text{Li}(\text{THF})_3$  with Phenoxy-Functionalized Chiral Prolinols**

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## General Methods

All reagents are commercially available, reagent grade, and used as received unless otherwise noted. The reactions involving air and water sensitive components were performed with the standard Schlenk techniques. Solvents, such as THF, toluene and hexane, were degassed and distilled from sodium benzophenone ketyl before use.

Analytical thin layer chromatography (TLC) was performed using F254 pre-coated silica gel plate (0.2 mm thickness). After elution, plates were detected using UV radiation (254 nm) on a UV lamp.

Flash chromatography was performed using 200-300 mesh silica gel with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use.

Nuclear magnetic resonance spectra were obtained on a Bruker AV-400 apparatus ( $\text{CDCl}_3$  as solvent). Chemical shifts for NMR spectra are reported as  $\delta$  in units of parts per million (ppm) downfield from  $\text{SiMe}_4$  ( $\delta$  0.0) and relative to the signal of chloroform-d ( $\delta$  7.26, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); or m (multiplets).

High Resolution Mass (HRMS) spectra were obtained using Bruker ESI-TOF.

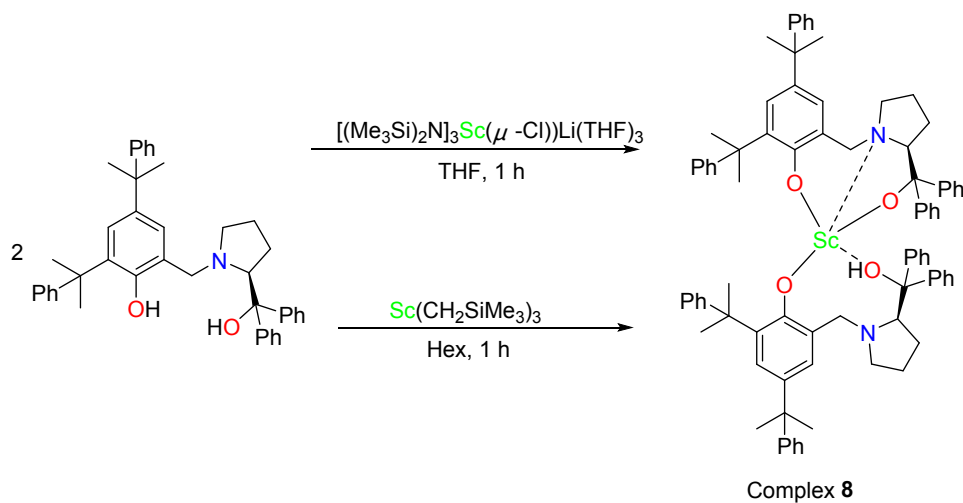
The ee values determination was carried out using HPLC (Agilent Technologies 1200 Series) with Daicel Chiralcel columns at 23-25 °C. Optical rotation was measured using an Autopol IV Polarimeter equipped with a sodium vapor lamp at 589 nm. The absolute configuration of **7a** was determined by the combination of single crystal diffraction, chiral HPLC and the optical rotation analysis. Hence, **7b-7t** were assigned by analogy, assuming the same reaction pathway and the same analysis.

Rare earth metal analysis was performed by EDTA titration with a xylenol orange indicator and a hexamine buffer. Carbon, hydrogen and nitrogen analyses were performed by direct combustion with a Carlo-Erba EA-1110 instrument.

Suitable single crystals of complex **8** was sealed in a thin-walled glass capillary for determining the single-crystal structure. Intensity data were collected with a Rigaku Mercury CCD area detector in  $\omega$  scan mode using Mo- $K\alpha$  radiation ( $\lambda = 0.71075 \text{ \AA}$ ). The diffracted intensities were corrected for Lorentz polarization effects and empirical absorption corrections. Details of the intensity data collection and crystal data are given in Table 1. All the non-hydrogen atoms were refined anisotropically. All the H atoms were held stationary and included in the structure factor calculation in the final stage of full-matrix least-squares refinement. The structures were solved and refined using SHELEXL-97 programs.

## Experimental section:

### General Procedure for the Preparation of the Rare-Earth Metal Complex **8**<sup>1</sup>:

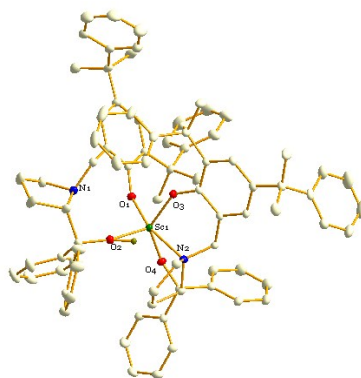


**Table 1 Crystallographic Data for Complex **8****

Compound	<b>8</b>	Compound	<b>8</b>
Formula	$\text{C}_{84}\text{H}_{87}\text{N}_2\text{O}_4\text{Sc}$	$F(000)$	2632
fw	1233.52	$\theta_{\text{max}}/^\circ$	27.50
Crystal system	Orthorhombic	Collected	44528
Crystal size/mm	$0.40 \times 0.20 \times 0.20$	Unique reflns	20922
Space group	P 21 21 21	Obsd reflns, [ $I > 2.0\sigma(I)$ ]	17160
$a/\text{\AA}$	13.546	No. of variables	832
$b/\text{\AA}$	24.517	GOF	1.008
$c/\text{\AA}$	27.817	$R$	0.0651
$V/\text{\AA}^3$	9237.9	wR	0.1600
$Z$	4	$R_{\text{int}}$	0.0466
$D_{\text{calcd}}/\text{g cm}^{-3}$	0.887	Largest diff. peak, hole/ $\text{\AA}^{-3}$	0.384, -0.281
$\mu/\text{mm}^{-1}$	0.119		

### X-Ray Structures of Complex **8** and selected bond lengths and bond angles

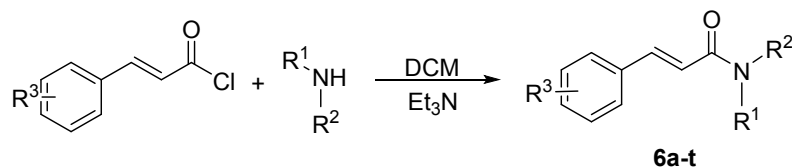
Crystals of complex **8** suitable for X-ray diffraction were obtained in toluene and hexane at room temperature. The definitive structure is shown in Figure 1, and the corresponding selected bond lengths and angles are provided in the figure captions.



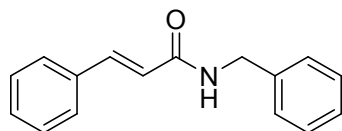
**Figure 1.** Molecular structure of **8** showing 20% probability ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Sc(1)–O(1) 2.0350(16), Sc(1)–O(2) 1.9518(17), Sc(1)–O(3) 2.0141(16), Sc(1)–O(4) 1.9833(16), Sc(1)–N(2) 2.3539(19), O(2)–Sc(1)–O(4) 108.05(7), O(2)–Sc(1)–O(3) 115.27(7), O(4)–Sc(1)–O(3) 132.87(7), O(2)–Sc(1)–O(1) 97.92(7), O(4)–Sc(1)–O(1) 99.48(7), O(2)–Sc(1)–O(1) 92.29(6), O(2)–Sc(1)–N(2) 99.29(7), O(4)–Sc(1)–N(2) 74.83(7), O(3)–Sc(1)–N(2) 80.64(7), O(1)–Sc(1)–N(2) 162.78(7).

### General procedure for the synthesis of the substrates **6a-6t** and their characterization data

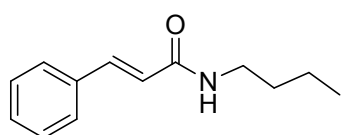
To a dichloromethane solution of 16 mmol substituted amine and 16 mmol Et<sub>3</sub>N, a substituted unsaturated acyl chloride was added dropwise, keeping the reaction temperature at 0 °C. The mixture was continued to stir for 2 h at room temperature, then aqueous NaHCO<sub>3</sub> (25 mL) was added. The crude product was extracted with DCM (3 x 50 mL). The combined organic layers were washed with 1M HCl (3 x 20 mL) and brine (3 x 20 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Solvent was removed in vacuo. then the crude product was purified by column chromatography (ethyl acetate-petroleum ether, 1:10)<sup>2</sup>.



Characterization data as follows:

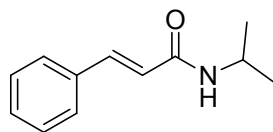


**N-benzylcinnamamide (6a):** White solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.67 (d, *J* = 13.80 Hz, 1H, CH=CH), 7.48 (m, 2H, Ph), 7.34 (m, 8H, Ph), 6.46 (d, *J* = 15.60 Hz, 1H, CH=CH), 5.89 (s, 1H, NH), 4.57 (d, *J* = 5.72 Hz, 2H, CH<sub>2</sub>).

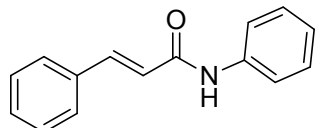


**N-butylcinnamamide (6b):** White solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.61 (d, *J* = 15.60 Hz,

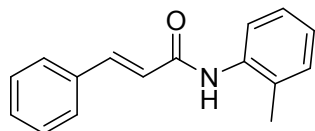
1H, CH=CH), 7.33 (m, 3H, Ph), 6.38 (d,  $J = 15.60$  Hz, 1H, CH=CH), 5.67 (s, 1H, NH), 3.37 (m, 2H, CH<sub>2</sub>), 1.53 (m, 2H, CH<sub>2</sub>), 1.36 (m, 2H, CH<sub>2</sub>), 0.92 (t,  $J = 14.64$  Hz, 3H, CH<sub>3</sub>).



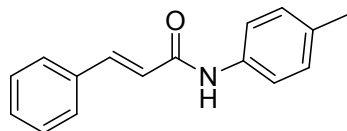
**N-isopropylcinnamamide (6c):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  7.61 (d,  $J = 15.60$  Hz, 1H, CH=CH), 7.45 (m, 2H, Ph), 7.30 (m, 3H, Ph), 6.41 (d,  $J = 15.60$  Hz, 1H, CH=CH), 5.83 (d,  $J = 6.08$  Hz, 1H, NH), 4.21 (m, 1H, CH), 1.18 (d,  $J = 6.56$  Hz, 6H, CH<sub>3</sub>).



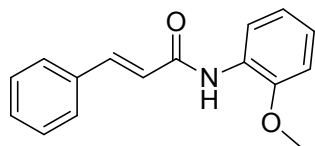
**N-phenylcinnamamide (6d):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  7.92 (s, 1H, NH), 7.74 (d,  $J = 15.52$  Hz, 1H, CH=CH), 7.65 (m, 2H, Ph), 7.45 (m, 2H, Ph), 7.32 (m, 5H, Ph), 7.11 (m, 1H, Ph), 6.63 (d,  $J = 15.52$  Hz, 1H, CH=CH).



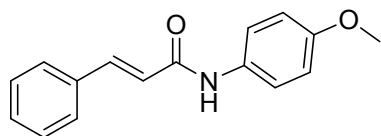
**N-(o-tolyl)cinnamamide (6e):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  7.95 (s, 1H, NH), 7.76 (d,  $J = 15.52$  Hz, 1H, CH=CH), 7.52 (m, 2H, Ph), 7.36 (m, 3H, Ph), 7.19 (m, 2H, Ph), 7.10 (m, 2H, Ph), 6.58 (d,  $J = 15.64$  Hz, 1H, CH=CH).



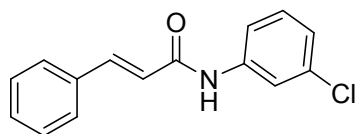
**N-(p-tolyl)cinnamamide (6f):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  8.12 (s, 1H, NH), 7.64 (d,  $J = 15.56$  Hz, 1H, CH=CH), 7.46 (m, 2H, Ph), 7.33 (m, 2H, Ph), 7.20 (m, 3H, Ph), 7.01 (m, 2H, Ph), 6.56 (d,  $J = 15.52$  Hz, 1H, CH=CH), 2.19 (s, 1H, CH<sub>3</sub>).



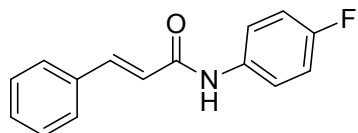
**N-(2-methoxyphenyl)cinnamamide (6g):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  8.51 (m, 1H, Ph), 7.93 (s, 1H, NH), 7.74 (d,  $J = 15.48$  Hz, 1H, CH=CH), 7.55 (m, 2H, Ph), 7.37 (m, 3H, Ph), 7.00 (m, 2H, Ph), 6.87 (m, 1H, Ph), 6.59 (d,  $J = 15.52$  Hz, 1H, CH=CH), 3.90 (s, 3H, CH<sub>3</sub>).



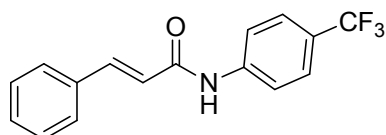
**N-(4-methoxyphenyl)cinnamamide (6h):** White solid. <sup>1</sup>H NMR(400 MHz, CDCl<sub>3</sub>):  $\delta$  7.78 (s, 1H, NH), 7.72 (d,  $J = 15.48$  Hz, 1H, CH=CH), 7.53 (m, 4H, Ph), 7.31 (m, 3H, Ph), 6.82 (m, 2H, Ph), 6.54 (d,  $J = 15.52$  Hz, 1H, CH=CH), 3.75 (s, 3H, CH<sub>3</sub>).



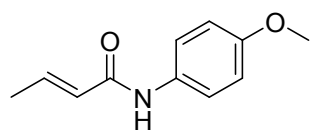
**N-(3-chlorophenyl)cinnamamide (6i):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.85 (s, 1H, NH), 7.76 (m, 2H, Ph, CH=CH), 7.50 (m, 3H, Ph), 7.34 (m, 3H, Ph), 7.23 (m, 1H, Ph), 7.09 (m, 1H, Ph), 6.60 (d,  $J = 15.52$  Hz, 1H, CH=CH).



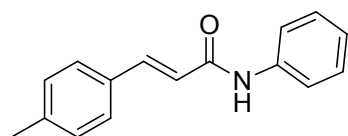
**N-(4-fluorophenyl)cinnamamide (6j):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.75 (d,  $J = 15.48$  Hz, 1H, CH=CH), 7.56 (m, 4H, Ph), 7.37 (m, 3H, Ph), 7.02 (m, 2H, Ph), 6.53 (d,  $J = 15.52$  Hz, 1H, CH=CH).



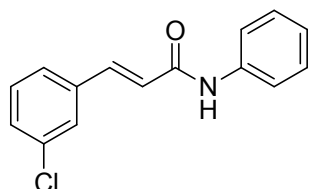
**N-(4-(trifluoromethyl)phenyl)cinnamamide (6k):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.79 (s, 1H, NH), 7.72 (m, 2H, Ph, CH=CH), 7.59 (m, 2H, Ph), 7.49 (m, 3H, Ph), 7.38 (m, 3H, Ph), 6.55 (d,  $J = 15.48$  Hz, 1H, CH=CH).



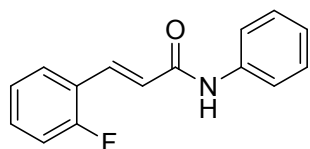
**(E)-N-(4-methoxyphenyl)but-2-enamide (6l):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.55 (m, 3H, Ph, NH), 6.83 (m, 3H, Ph, CH=CH), 5.96 (d,  $J = 15.08$  Hz, CH=CH, 1H), 3.77(s, 3H,  $\text{CH}_3$ ), 1.85 (d,  $J = 5.44$  Hz, 3H,  $\text{CH}_3$ ).



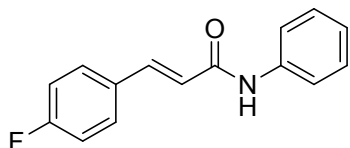
**(E)-N-phenyl-3-(p-tolyl)acrylamide (6m):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.73 (m, d,  $J = 15.48$  Hz, 1H, CH=CH), 7.61 (m, 2H, Ph), 7.43 (s, 1H, NH), 7.38 (m, 2H, Ph), 7.32 (m, 2H, Ph), 7.16 (m, 3H, Ph), 6.52 (d,  $J = 15.48$  Hz, 1H, CH=CH), 2.35 (s, 3H,  $\text{CH}_3$ ).



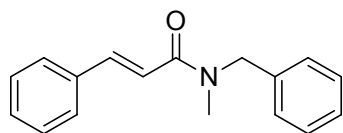
**(E)-3-(3-chlorophenyl)-N-phenylacrylamide (6n):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.68 (m, d,  $J = 15.48$  Hz, 1H, CH=CH), 7.61(m, 2H, NH, Ph), 7.49 (m, 2H, Ph), 7.31 (m, 5H, Ph), 7.12 (m, 1H, Ph), 6.56 (d,  $J = 15.48$  Hz, 1H, CH=CH).



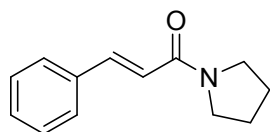
**(E)-3-(2-fluorophenyl)-N-phenylacrylamide (6o):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.82 (m, d,  $J = 15.48$  Hz, 1H, CH=CH), 7.60(m, 2H, NH, Ph), 7.44 (m, 2H, Ph), 7.34 (m, 3H, Ph), 7.14 (m, 3H, Ph), 6.71 (d,  $J = 15.72$  Hz, 1H, CH=CH).



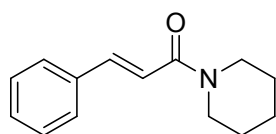
**(E)-3-(4-fluorophenyl)-N-phenylacrylamide (6p):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.72 (m, d,  $J = 15.48$  Hz, 1H, CH=CH), 7.60 (m, 2H, NH, Ph), 7.50 (m, 2H, Ph), 7.33 (m, 3H, Ph), 7.05 (m, 3H, Ph), 6.47 (d,  $J = 15.48$  Hz, 1H, CH=CH).



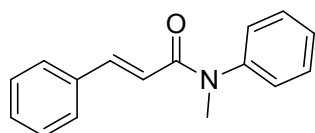
**N-benzyl-N-methylcinnamamide (6q):** White solid.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.67 (m, d,  $J = 15.32$  Hz, 1H, CH=CH), 7.49 (m, 1H, Ph), 7.38 (m, 1H, Ph), 7.25 (m, 8H, Ph), 6.94 (d,  $J = 15.36$  Hz, 1H, CH=CH), 4.84 (m, 2H,  $\text{CH}_2$ ), 2.94 (m, 3H,  $\text{CH}_3$ ).



**(E)-3-phenyl-1-(pyrrolidin-1-yl)prop-2-en-1-one (6r):** White solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.70 (d,  $J = 13.80$  Hz, 1H, CH=CH), 7.52 (m, 2H, Ph), 7.35 (m, 3H, Ph), 6.73 (d,  $J = 15.52$  Hz, 1H, CH=CH), 3.63 (m, 4H,  $\text{CH}_2$ ), 1.99 (m, 2H,  $\text{CH}_2$ ), 1.88 (m, 2H,  $\text{CH}_2$ ).



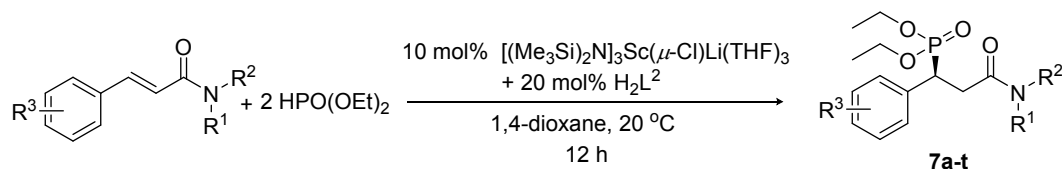
**(E)-3-phenyl-1-(piperidin-1-yl)prop-2-en-1-one (6s):** White solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.61 (d,  $J = 15.48$  Hz, 1H, CH=CH), 7.52 (m, 2H, Ph), 7.34 (m, 3H, Ph), 6.91 (d,  $J = 15.48$  Hz, 1H, CH=CH), 3.66 (m, 4H,  $\text{CH}_2$ ), 1.67 (m, 2H,  $\text{CH}_2$ ), 1.60 (m, 4H,  $\text{CH}_2$ ).



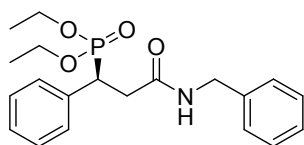
**N-methyl-N-phenylcinnamamide (6t):** White solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.72 (d,  $J = 15.40$  Hz, 1H, CH=CH), 7.23 (m, 10H, Ph), 6.41 (d,  $J = 15.12$  Hz, 1H, CH=CH), 3.38 (s, 3H,  $\text{CH}_3$ ).

### General procedure for the synthesis of the substrates 7a-7t and their characterization data

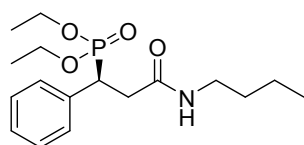
Scandium amide  $[(\text{Me}_3\text{Si})_2\text{N}]_3\text{Sc}(\mu\text{-Cl})\text{Li}(\text{THF})_3$  (0.05 mmol, 39.15 mg) was added to a stirred solution of  $\text{H}_2\text{L}^2$  (0.10 mmol, 59.50 mg) in THF (1 mL) under argon atmosphere. The mixture was stirred at room temperature for 1 h. Then,  $\text{HPO}(\text{OEt})_2$  (1.00 mmol, 129  $\mu\text{L}$ ) was added in the above solution and stirred for 10 min. After that, unsaturated amide (0.5 mmol, 118 mg) was added to the mixture. The reaction system was stirred for further 12 h at room temperature, quenched by water. The crude product was purified by column chromatography (ethyl acetate-petroleum ether, 1:10) to obtain the final hydrophosphonylation product. The enantiomeric excess of hydrophosphonylation was determined by chiral HPLC analysis.



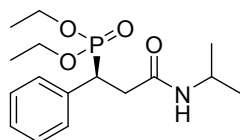
### Characterization data as follows:



**(S)-diethyl (3-(benzylamino)-3-oxo-1-phenylpropyl)phosphonate (7a):** A white powder: yield 99%;  $[\alpha]_{\text{D}}^{24} = 12^\circ$  ( $c$  0.4,  $\text{CH}_3\text{OH}$ );  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.71 (m, 1H, NH), 7.34 (m, 2H, Ph), 7.18 (m, 3H, Ph), 7.02 (m, 3H, Ph), 6.78 (m, 2H, Ph), 4.28 (m, 1H, CH), 4.03 (m, 1H, CH), 3.84 (m, 2H,  $\text{CH}_2$ ), 3.75 (m, 2H,  $\text{CH}_2$ ), 3.62 (m, 1H, CH), 3.44 (m, 1H, CH), 3.06 (m, 2H,  $\text{CH}_2$ ), 1.11 (t,  $J = 14.00$  Hz, 3H,  $\text{CH}_3$ ), 0.85 (t,  $J = 15.30$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  169.65, 137.96, 134.75, 128.99, 127.97, 127.73, 126.85, 126.29, 62.63, 61.55, 42.62, 40.54, 35.97, 15.86;  $^{31}\text{P NMR}$  (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  28.03; 85% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 12.1 min (major), 17.7 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{26}\text{NO}_4\text{P}$   $[\text{M}+\text{H}]^+$  376.1678; found 376.1670.

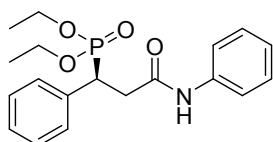


**(S)-diethyl (3-(butylamino)-3-oxo-1-phenylpropyl)phosphonate (7b):** Colorless oil: yield 90%;  $[\alpha]_{\text{D}}^{24} = 15^\circ$  ( $c$  0.5,  $\text{CH}_3\text{OH}$ );  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.40 (m, 2H, Ph), 7.29 (m, 3H, Ph), 4.06 (m, 2H,  $\text{CH}_2$ ), 3.79 (m, 2H,  $\text{CH}_2$ ), 3.62 (m, 1H, CH), 3.13 (m, 1H, CH), 3.01 (m, 3H,  $\text{CH}_2$ ), 1.31 (t,  $J = 13.84$  Hz, 3H,  $\text{CH}_3$ ), 1.25 (m, 2H,  $\text{CH}_2$ ), 1.10 (m, 2H,  $\text{CH}_2$ ), 1.03 (t,  $J = 13.80$  Hz, 3H,  $\text{CH}_3$ ), 0.77 (t,  $J = 14.28$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  169.33, 134.99, 134.92, 128.80, 127.94, 126.81, 62.45, 61.49, 40.58, 38.61, 36.44, 30.87, 19.29, 15.63, 13.15;  $^{31}\text{P NMR}$  (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  28.50; 75% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 7.9 min (major), 8.6 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{17}\text{H}_{28}\text{NO}_4\text{P}$   $[\text{M}+\text{H}]^+$  342.1834; found 342.1847.

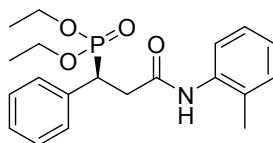




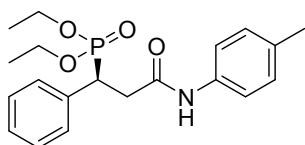
**(S)-diethyl (3-(isopropylamino)-3-oxo-1-phenylpropyl)phosphonate (7c):** Colorless oil : yield 83%;  $[\alpha]_D^{24} = 17^\circ$  (*c* 0.5, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.36 (m, 2H, Ph), 7.27 (m, 2H, Ph), 7.21 (m, 1H, Ph), 5.54 (d, *J* = 7.00 Hz, 1H, NH), 4.07 (m, 2H, CH<sub>2</sub>), 3.88 (m, 2H, CH<sub>2</sub>), 3.69 (m, 2H, CH<sub>2</sub>), 2.92 (m, 1H, CH), 2.69 (m, 1H, CH), 1.28 (d, *J* = 14.00 Hz, 3H, CH<sub>3</sub>), 1.04 (m, 6H, CH<sub>3</sub>), 0.80 (d, *J* = 6.5 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  168.99, 135.36, 129.37, 128.31, 127.21, 63.00, 61.97, 41.15, 39.76, 36.87, 22.30, 16.39; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  28.35; 64% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 8.3 min (major), 10.3 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>16</sub>H<sub>26</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 328.1678; found 328.1669.



**(S)-diethyl (3-oxo-1-phenyl-3-(phenylamino)propyl)phosphonate (7d):** A white powder: yield 98%;  $[\alpha]_D^{24} = 21^\circ$  (*c* 0.2, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.68 (s, 1H, NH), 7.51 (m, 4H, Ph), 7.24 (m, 5H, Ph), 7.00 (m, 1H, Ph), 4.07 (m, 2H, CH<sub>2</sub>), 3.96 (m, 2H, CH<sub>2</sub>), 3.63 (m, 1H, CH), 3.30 (m, 2H, CH<sub>2</sub>), 1.28 (t, *J* = 14.16 Hz, 3H, CH<sub>3</sub>), 1.01 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  167.98, 138.39, 134.86, 134.79, 128.79, 128.12, 127.02, 123.06, 119.10, 62.98, 61.77, 40.09, 36.86, 15.84; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  28.16; 85% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 11.2 min (major), 14.1 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>19</sub>H<sub>24</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 362.1521; found 362.1527.

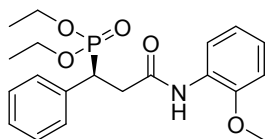


**(S)-diethyl (3-oxo-1-phenyl-3-(*o*-tolylamino)propyl)phosphonate (7e):** A white solid: yield 99%;  $[\alpha]_D^{24} = -22^\circ$  (*c* 0.3, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.77 (s, 1H, NH), 7.46 (m, 3H, Ph), 7.31 (m, 4H, Ph), 7.08 (m, 3H, Ph), 4.07 (m, 2H, CH<sub>2</sub>), 3.81 (m, 2H, CH<sub>2</sub>), 3.62 (m, 1H, CH), 3.19 (m, 2H, CH<sub>2</sub>), 1.94 (s, 3H, CH<sub>3</sub>), 1.27 (d, *J* = 14.10 Hz, 3H, CH<sub>3</sub>), 0.99 (t, *J* = 14.00 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  168.81, 135.70, 135.16, 131.41, 130.23, 129.36, 128.44, 127.38, 126.02, 125.40, 124.73, 63.12, 62.08, 41.15, 36.97, 17.55, 16.35; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  27.68; 81% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 13.4 min (major), 17.3 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>20</sub>H<sub>26</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 376.1678; found 376.1684.

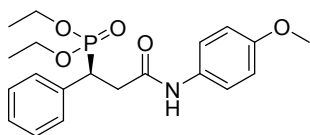


**(S)-diethyl (3-oxo-1-phenyl-3-(*p*-tolylamino)propyl)phosphonate (7f):** A white solid: yield 99%;  $[\alpha]_D^{24} = 28^\circ$  (*c* 0.4, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.96 (s, 1H, NH), 7.46 (m, 2H, Ph), 7.33 (m, 4H, Ph), 7.22 (m, 1H, Ph), 7.00 (m, 2H, Ph), 4.11 (m, 2H, CH<sub>2</sub>), 3.89 (m, 2H, CH<sub>2</sub>), 3.63 (m, 1H, CH), 3.20 (m, 1H, CH), 2.23 (s, 3H, CH<sub>3</sub>), 1.27 (d, *J* = 14.10 Hz, 3H, CH<sub>3</sub>), 1.01 (t, *J* = 14.10 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  167.71, 135.79, 134.94, 132.55, 128.86, 128.62, 128.11, 127.01, 119.08, 62.96, 61.68, 40.16, 36.92, 20.31, 15.94, 15.63; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  28.59; 84% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 11.1 min

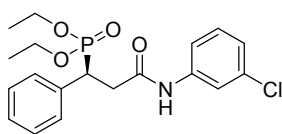
(major), 15.1 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $C_{20}H_{26}NO_4P$   $[M+H]^+$  376.1678; found 376.1689.



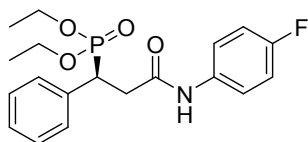
**(S)-diethyl (3-((2-methoxyphenyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7g):** A white solid: yield 99%;  $[\alpha]_D^{24} = -42^\circ$  ( $c$  0.2,  $CH_3OH$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.76 (s, 1H, NH), 7.35 (m, 2H, Ph), 7.23 (m, 4H, Ph), 6.91 (m, 3H, Ph), 3.99 (m, 2H,  $CH_2$ ), 3.79 (m, 2H,  $CH_2$ ), 3.71 (s, 3H,  $CH_3$ ), 3.62 (m, 1H, CH), 3.13 (m, 1H, CH), 2.94 (m, 1H, CH), 1.19 (t,  $J = 13.84$  Hz, 3H,  $CH_3$ ), 0.99 (t,  $J = 13.80$  Hz, 3H,  $CH_3$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  167.28, 147.27, 134.97, 128.69, 128.63, 128.13, 126.92, 123.23, 120.38, 119.32, 109.39, 62.44, 61.57, 55.08, 40.55, 38.06, 15.79;  $^{31}P$  NMR (162 MHz,  $CDCl_3$ ):  $\delta$  27.85; 84% *ee*, HPLC: IA, 90% hexanes, 10%  $iPrOH$ , 1.0 mL/min, 14.8 min (major), 16.6 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $C_{20}H_{26}NO_5P$   $[M+H]^+$  392.1627; found 392.1633.



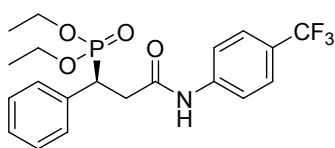
**(S)-diethyl (3-((4-methoxyphenyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7h):** A white solid: yield 99%;  $[\alpha]_D^{24} = 32^\circ$  ( $c$  0.4,  $CH_3OH$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  9.44 (s, 1H, NH), 7.41 (m, 2H, Ph), 7.30 (m, 2H, Ph), 7.15 (m, 3H, Ph), 6.65 (m, 2H, Ph), 3.99 (m, 2H,  $CH_2$ ), 3.87 (m, 2H,  $CH_2$ ), 3.62 (s, 3H,  $CH_3$ ), 3.54 (m, 1H, CH), 3.19 (m, 2H,  $CH_2$ ), 1.21 (t,  $J = 14.00$  Hz, 3H,  $CH_3$ ), 0.941 (t,  $J = 13.80$  Hz, 3H,  $CH_3$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  167.61, 138.08, 130.24, 128.24, 123.27, 119.08, 115.18, 114.97, 63.00, 61.84, 39.39, 37.99, 37.17, 15.91, 15.72;  $^{31}P$  NMR (162 MHz,  $CDCl_3$ ):  $\delta$  28.61; 89% *ee*, HPLC: IA, 90% hexanes, 10%  $iPrOH$ , 1.0 mL/min, 16.5 min (major), 21.5 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $C_{20}H_{26}NO_5P$   $[M+H]^+$  392.1627; found 392.1625.



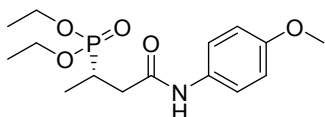
**(S)-diethyl (3-((3-chlorophenyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7i):** A white solid: yield 99%;  $[\alpha]_D^{24} = 55^\circ$  ( $c$  0.3,  $CH_3OH$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  10.00 (s, 1H, NH), 7.45 (m, 4H, Ph), 7.22 (m, 3H, Ph), 7.01 (t,  $J = 14.08$  Hz, 1H, Ph), 6.86 (d,  $J = 8.00$  Hz, Ph), 4.04 (m, 2H,  $CH_2$ ), 3.92 (m, 1H, CH), 3.74 (m, 1H, CH), 3.55 (m, 1H, CH), 3.25 (m, 1H, CH), 1.24 (t,  $J = 14.12$  Hz, 3H,  $CH_3$ ), 0.96 (t,  $J = 14.12$  Hz, 3H,  $CH_3$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  168.09, 136.68, 134.54, 133.62, 129.20, 128.76, 128.70, 128.20, 128.17, 127.15, 63.27, 61.80, 39.88, 38.48, 36.70, 15.93;  $^{31}P$  NMR (162 MHz,  $CDCl_3$ ):  $\delta$  28.40; 81% *ee* HPLC: IA, 90% hexanes, 10%  $iPrOH$ , 1.0 mL/min, 14.3 min (major), 18.0 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $C_{19}H_{23}ClNO_4P$   $[M+H]^+$  396.1131; found 396.1144.



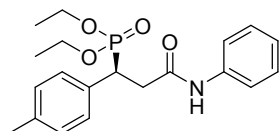
**(S)-diethyl (3-((4-fluorophenyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7j):** A white solid: yield 98%;  $[\alpha]_{\text{D}}^{24} = 36^\circ$  (*c* 0.4, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.30 (s, 1H, NH), 7.46 (m, 4H, Ph), 7.31 (m, 3H, Ph), 6.87 (t, *J* = 17.40 Hz, 2H, Ph), 4.07 (m, 2H, CH<sub>2</sub>), 3.91 (m, 2H, CH<sub>2</sub>), 3.63 (m, 1H, CH), 3.19 (m, 2H, CH), 1.27 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>), 1.01 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  167.81, 159.58, 157.17, 134.73, 134.49, 128.82, 128.14, 127.10, 120.70, 114.74, 114.52, 63.04, 61.78, 39.97, 36.71, 15.90, 0.53; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  27.98; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -118.83; 83% *ee*, HPLC: IA, 90% hexanes, 10% <sup>i</sup>PrOH, 1.0 mL/min, 12.8 min (major), 16.1 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>19</sub>H<sub>23</sub>FNO<sub>4</sub>P [M+H]<sup>+</sup> 380.1427; found 380.1426.



**(S)-diethyl (3-oxo-1-phenyl-3-((4-(trifluoromethyl)phenyl)amino)propyl)phosphonate (7k):** A white solid: yield 92%;  $[\alpha]_{\text{D}}^{24} = 34^\circ$  (*c* 0.4, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.96 (s, 1H, NH), 7.60 (m, 2H, Ph), 7.41 (m, 4H, Ph), 7.31 (m, 3H, Ph), 4.11 (m, 2H, CH<sub>2</sub>), 3.97 (m, 2H, CH<sub>2</sub>), 3.63 (m, 1H, CH), 3.26 (m, 2H, CH), 1.29 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>), 1.02 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  167.49, 138.13, 137.04, 133.92, 129.33, 128.75, 128.23, 127.28, 127.09, 123.29, 119.10, 63.04, 62.01, 39.90, 38.51, 36.65, 15.85; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  28.46; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -62.12; 77% *ee*, HPLC: IA, 90% hexanes, 10% <sup>i</sup>PrOH, 1.0 mL/min, 14.8 min (major), 17.8 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>20</sub>H<sub>23</sub>F<sub>3</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 430.1395; found 430.1396.

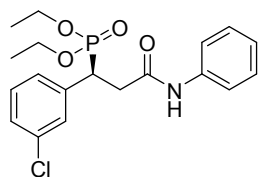


**(S)-diethyl (4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)phosphonate (7l):** A white solid: yield 98%;  $[\alpha]_{\text{D}}^{24} = 21^\circ$  (*c* 0.3, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.28 (s, 1H, NH), 7.53 (m, 2H, Ph), 6.81 (m, 2H, Ph), 4.08 (m, 4H, CH<sub>2</sub>), 3.75 (s, 3H, CH<sub>3</sub>), 2.79 (m, 1H, CH), 2.51 (m, 2H, CH<sub>2</sub>), 1.27 (m, 12H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  168.17, 155.48, 131.48, 120.81, 113.42, 61.76, 61.68, 54.95, 37.05, 27.48, 26.05, 15.92, 13.03; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  34.17; 61% *ee*, HPLC: IA, 95% hexanes, 5% <sup>i</sup>PrOH, 1.0 mL/min, 32.3 min (major), 35.3 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>15</sub>H<sub>24</sub>NO<sub>5</sub>P [M+H]<sup>+</sup> 330.1470; found 330.1478.

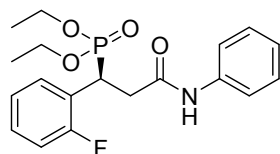


**(S)-diethyl (3-oxo-3-(phenylamino)-1-(*p*-tolyl)propyl)phosphonate (7m):** A white solid: yield 98%;  $[\alpha]_{\text{D}}^{24} = 21^\circ$  (*c* 0.3, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.71 (s, 1H, NH), 7.47 (m, 3H, Ph), 7.31 (m, 3H, Ph), 7.10 (m, 3H, Ph), 4.07 (m, 2H, CH<sub>2</sub>), 3.85 (m, 3H, CH), 3.62 (m, 1H, CH), 3.20 (m, 2H, CH<sub>2</sub>), 1.94 (s, 3H, CH<sub>3</sub>), 1.27 (t, *J* = 14.12 Hz, 3H, CH<sub>3</sub>), 1.00 (t, *J* = 14.08 Hz, 3H, CH<sub>3</sub>);

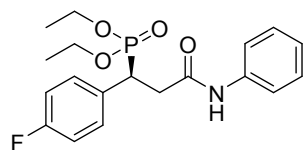
$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.82, 138.31, 136.62, 131.70, 128.85, 128.62, 128.14, 123.07, 119.07, 62.88, 61.67, 39.71, 37.14, 20.61, 15.89;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  28.04; 83% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 8.4 min (major), 17.8 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{23}\text{NO}_4\text{P}$   $[\text{M}+\text{H}]^+$  376.1677; found 376.1676.



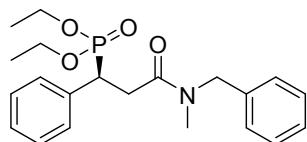
**(S)-diethyl (1-(3-chlorophenyl)-3-oxo-3-(phenylamino)propyl)phosphonate (7n):** A white solid: yield 98%;  $[\alpha]_{\text{D}}^{24} = 29^\circ$  (*c* 0.3,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.01 (s, 1H, NH), 7.55 (m, 2H, Ph), 7.41 (m, 2H, Ph), 7.37 (m, 2H, Ph), 7.23 (m, 3H, Ph), 4.05 (m, 2H,  $\text{CH}_2$ ), 3.90 (m, 1H, CH), 3.76 (m, 1H, CH), 3.57 (m, 1H, CH), 3.25 (m, 2H,  $\text{CH}_2$ ), 1.24 (t,  $J = 14.00$  Hz, 3H,  $\text{CH}_3$ ), 0.97 (t,  $J = 14.00$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.29, 141.52, 134.63, 134.56, 128.76, 128.69, 128.21, 127.25, 125.38, 125.34, 118.58, 63.19, 61.79, 39.84, 36.93, 15.85;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.76; 81% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 10.5 min (major), 11.8 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{23}\text{ClNO}_4\text{P}$   $[\text{M}+\text{H}]^+$  396.1131; found 396.1143.



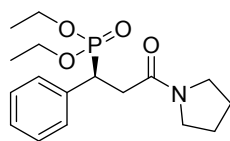
**(S)-diethyl (1-(2-fluorophenyl)-3-oxo-3-(phenylamino)propyl)phosphonate (7o):** A white solid: yield 98%;  $[\alpha]_{\text{D}}^{24} = 29^\circ$  (*c* 0.3,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.14 (s, 1H, NH), 7.46 (m, 3H, Ph), 7.19 (m, 3H, Ph), 7.09 (m, 3H, Ph), 4.27 (m, 13H, CH), 4.11 (m, 2H,  $\text{CH}_2$ ), 3.90 (m, 1H, CH), 3.75 (m, 1H, CH), 3.24 (m, 2H,  $\text{CH}_2$ ), 1.28 (t,  $J = 14.12$  Hz, 3H,  $\text{CH}_3$ ), 1.06 (t,  $J = 14.08$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.64, 138.25, 129.25, 128.64, 128.17, 123.75, 123.14, 122.33, 119.07, 115.29, 62.84, 62.03, 35.88, 30.86, 15.87;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.53;  $^{19}\text{F}$  NMR (MHz,  $\text{CDCl}_3$ ):  $\delta$  -115.75; 73% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 13.1 min (major), 15.1 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{23}\text{FNO}_4\text{P}$   $[\text{M}+\text{H}]^+$  380.1427; found 380.1424.



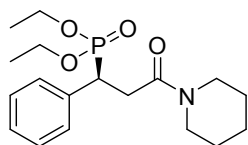
**(S)-diethyl (1-(4-fluorophenyl)-3-oxo-3-(phenylamino)propyl)phosphonate (7p):** A white solid: yield 96%;  $[\alpha]_{\text{D}}^{24} = 29^\circ$  (*c* 0.3,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.23 (s, 1H, NH), 7.44 (m, 4H, Ph), 7.19 (m, 2H, Ph), 6.99 (m, 3H, Ph), 4.08 (m, 2H,  $\text{CH}_2$ ), 3.84 (m, 2H, CH), 3.64 (m, 1H, CH), 3.16 (m, 2H,  $\text{CH}_2$ ), 1.28 (t,  $J = 13.88$  Hz, 3H,  $\text{CH}_3$ ), 1.04 (t,  $J = 13.84$  Hz, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.61, 138.04, 130.31, 130.24, 128.24, 123.33, 119.08, 115.19, 114.97, 63.00, 61.85, 39.39, 37.17, 15.91;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.87;  $^{19}\text{F}$  NMR (MHz,  $\text{CDCl}_3$ ):  $\delta$  -114.65; 87% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 8.6 min (major), 17.9 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{23}\text{FNO}_4\text{P}$   $[\text{M}+\text{H}]^+$  380.1427; found 380.1426.



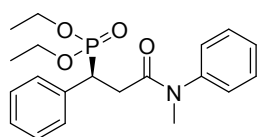
**(S)-diethyl (3-(benzyl(methyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7q):** A white powder: yield 99%;  $[\alpha]_D^{24} = 12^\circ$  (*c* 0.4, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.45 (m, 5H, Ph), 7.18 (m, 2H, Ph), 7.01 (m, 1H, Ph), 6.91 (m, 1H, Ph), 4.63 (m, 1H, CH), 4.33 (m, 1H, CH), 4.02 (m, 2H, CH<sub>2</sub>), 3.85 (m, 2H, CH<sub>2</sub>), 3.65 (m, 1H, CH), 3.06 (m, 2H, CH<sub>2</sub>), 2.87 (m, 3H, CH<sub>3</sub>), 1.29 (m, 3H, CH<sub>3</sub>), 1.04 (m, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 169.64, 136.39, 135.73, 135.57, 128.90, 128.84, 128.36, 127.98, 127.16, 126.68, 125.73, 62.39, 61.39, 52.59, 50.47, 34.45, 33.29, 15.71. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 28.71; 82% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 17.5 min (major), 26.0 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>21</sub>H<sub>28</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 390.1834; found 390.1836.



**(S)-diethyl (3-oxo-1-phenyl-3-(pyrrolidin-1-yl)propyl)phosphonate (7r):** Colorless oil: yield 98%;  $[\alpha]_D^{24} = -12^\circ$  (*c* 0.5, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.41 (m, 2H, Ph), 7.21 (m, 2H, Ph), 7.20 (m, 2H, Ph), 4.06 (m, 2H, CH<sub>2</sub>), 3.90 (m, 2H, CH<sub>2</sub>), 3.71 (m, 1H, CH<sub>2</sub>), 3.46 (m, 2H, CH<sub>2</sub>), 3.29 (m, 2H, CH<sub>2</sub>), 2.93 (m, 2H, CH<sub>2</sub>), 1.77 (m, 4H, CH<sub>2</sub>), 1.27 (t, *J* = 14.00 Hz, 3H, CH<sub>3</sub>), 1.02 (t, *J* = 12.00 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.71, 135.14, 128.77, 127.83, 126.58, 62.11, 61.23, 45.99, 45.09, 40.47, 39.92, 34.94, 25.40, 23.70, 15.84; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 28.57; 83% *ee*, HPLC: IB, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 14.3 min (major), 20.2 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>17</sub>H<sub>26</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 340.1677; found 340.1670.



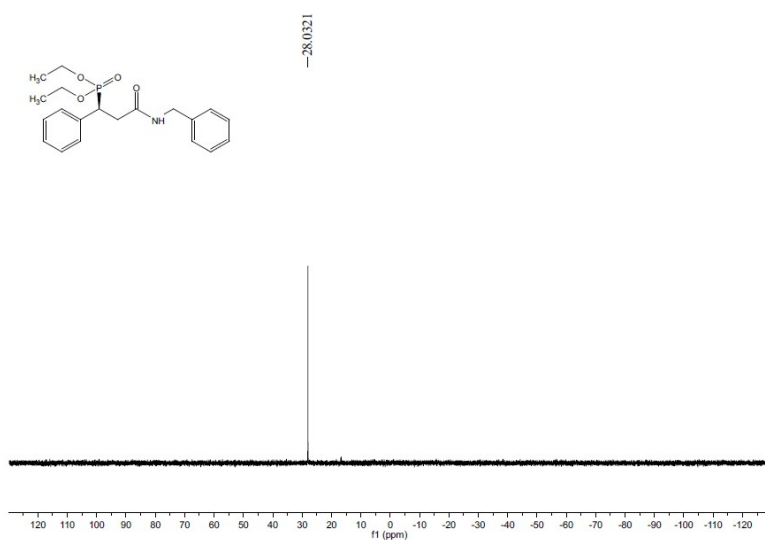
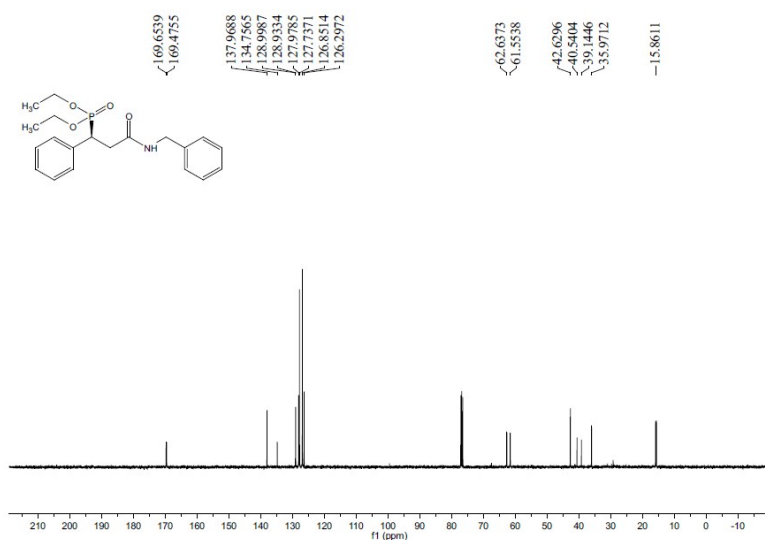
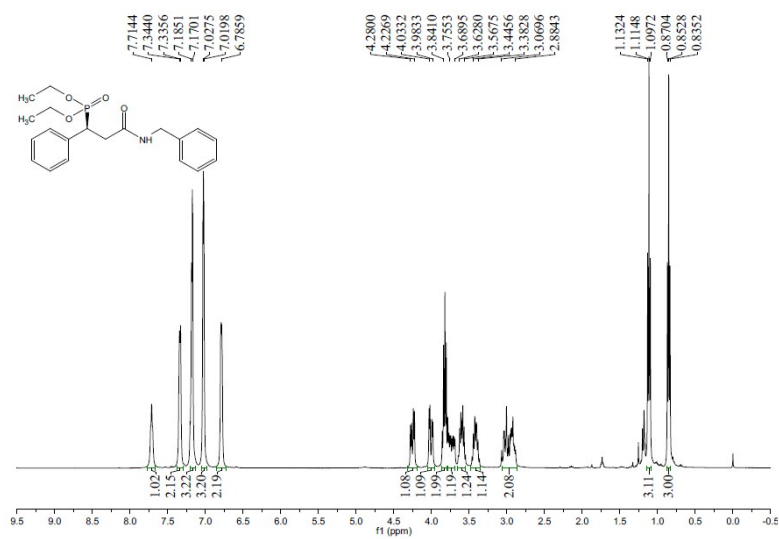
**(S)-diethyl (3-oxo-1-phenyl-3-(piperidin-1-yl)propyl)phosphonate (7s):** Colorless oil: yield 95%;  $[\alpha]_D^{24} = -11^\circ$  (*c* 0.3, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.40 (m, 2H, Ph), 7.29 (m, 2H, Ph), 7.22 (m, 1H, Ph), 4.20 (m, 1H, CH), 4.07 (m, 2H, CH<sub>2</sub>), 3.85 (m, 2H, CH<sub>2</sub>), 3.64 (m, 1H, CH), 3.37 (m, 4H, CH<sub>2</sub>), 3.03 (m, 2H, CH<sub>2</sub>), 1.54 (m, 4H, CH<sub>2</sub>), 1.36 (m, 1H, CH), 1.30 (t, *J* = 14.16 Hz, 3H, CH<sub>3</sub>), 1.05 (t, *J* = 14.16 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.53, 135.64, 128.73, 127.89, 126.65, 62.38, 61.40, 46.09, 42.52, 40.47, 32.98, 25.08, 24.93, 23.89, 15.88; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 28.52; 81% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 12.1 min (major), 17.7 min (minor); HRMS (ESI, positive) *m/z* calcd. for C<sub>20</sub>H<sub>26</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 354.1834.1834; found 354.1832.

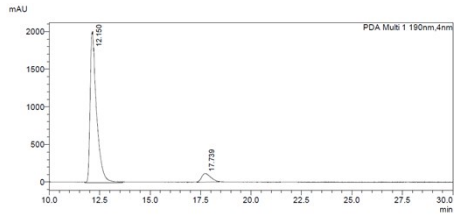
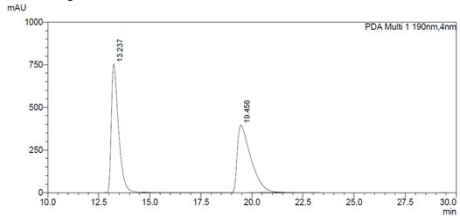


**(S)-diethyl (3-(methyl(phenyl)amino)-3-oxo-1-phenylpropyl)phosphonate (7t):** A white

powder: yield 99%;  $[\alpha]_D^{24} = 13^\circ$  ( $c$  0.3, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.39 (m, 3H, Ph), 7.26 (m, 5H, Ph), 6.98 (m, 2H, Ph), 3.99 (m, 2H, CH<sub>2</sub>), 3.85 (m, 2H, CH<sub>2</sub>), 3.62 (m, 1H, CH), 3.13 (s, 3H, CH<sub>3</sub>), 2.74 (m, 2H, CH<sub>2</sub>), 1.24 (t,  $J = 11.80$ , 3H, CH<sub>3</sub>), 1.00 (t,  $J = 12.64$  Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  169.40, 142.88, 135.27, 129.34, 128.80, 127.84, 127.52, 126.81, 126.70, 62.22, 61.28, 40.76, 39.36, 34.08, 15.62; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>):  $\delta$  28.22; 80% *ee*, HPLC: IA, 90% hexanes, 10% *i*PrOH, 1.0 mL/min, 12.2 min (major), 13.5 min (minor); HRMS (ESI, positive)  $m/z$  calcd. for C<sub>20</sub>H<sub>26</sub>NO<sub>4</sub>P [M+H]<sup>+</sup> 376.1678; found 376.1691.

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7a**





**<Peak Table>**

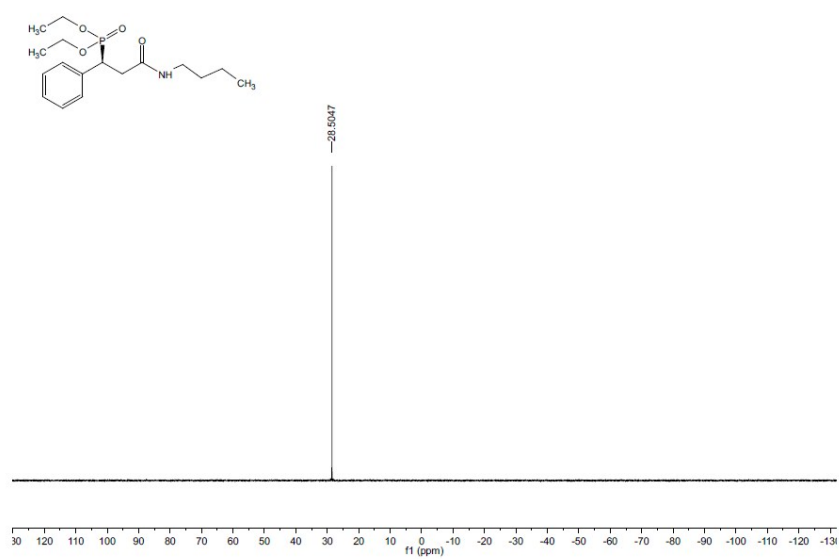
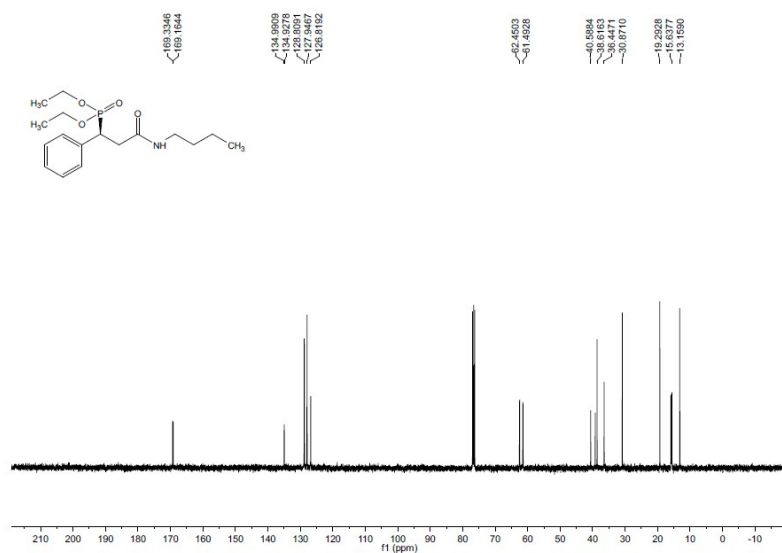
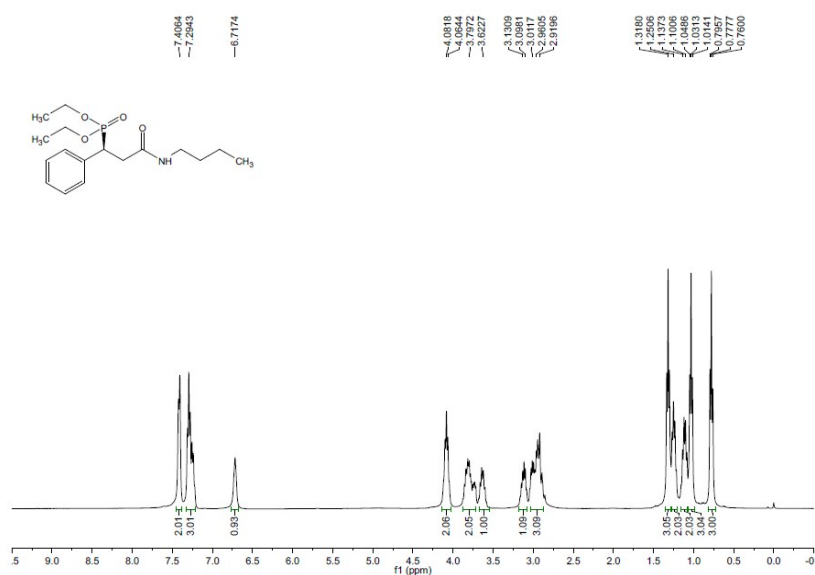
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1	13.237	18754291	756127	50.665
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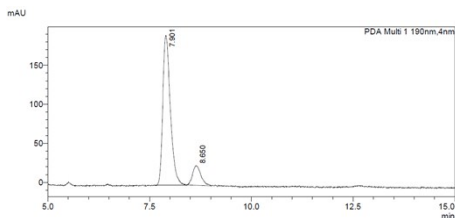
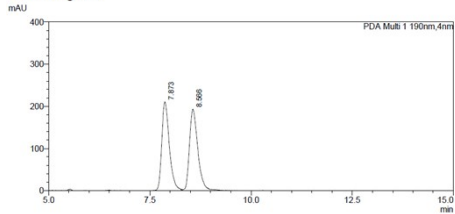
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1	12.150	44417129	2012266	92.432
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Total		48053830	2127109	100.000



The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7b**



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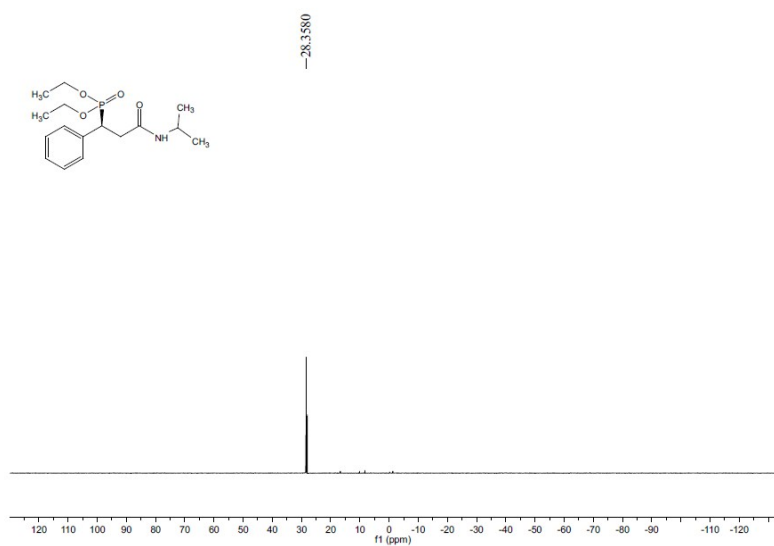
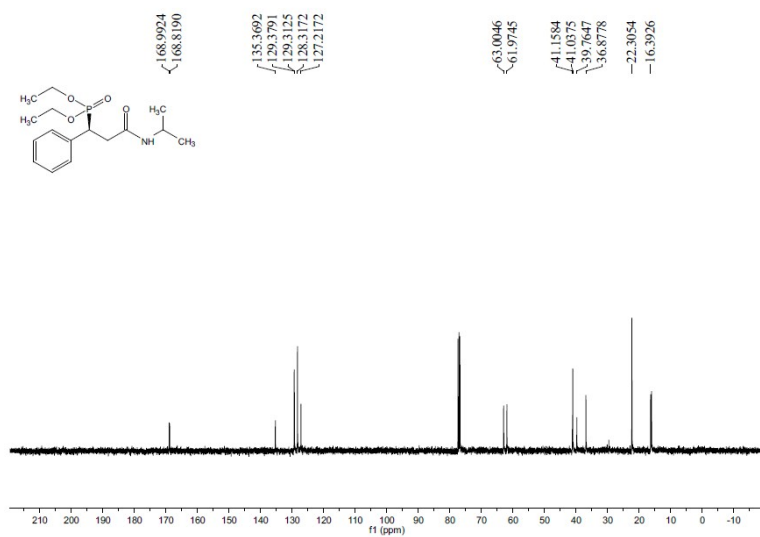
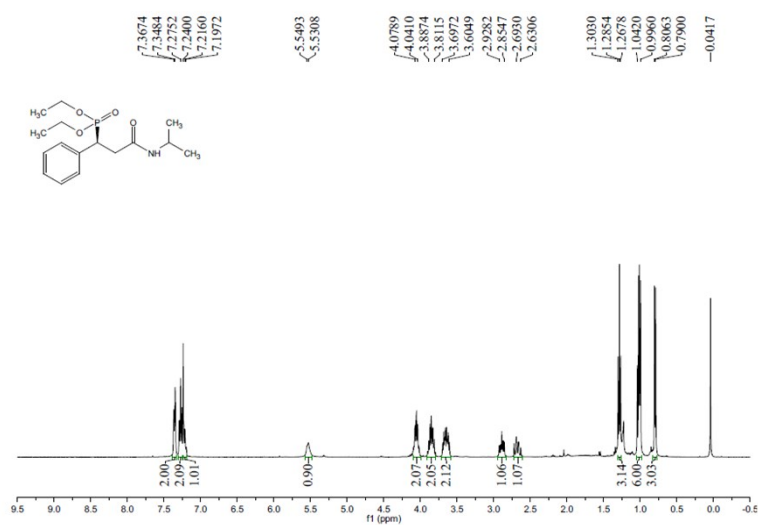
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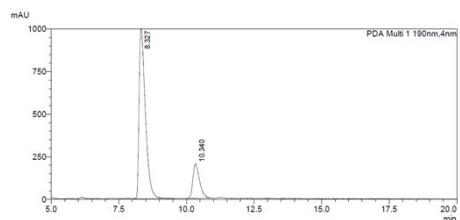
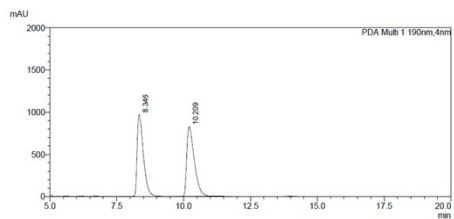
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1	7.873	2767793	211621	49.352
2	8.566	2840521	194689	50.648
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1	7.901	2476822	191862	87.293
2	8.650	360560	25214	12.707
Total		2837382	217076	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7c**





**<Peak Table>**

PDA Ch1 190nm

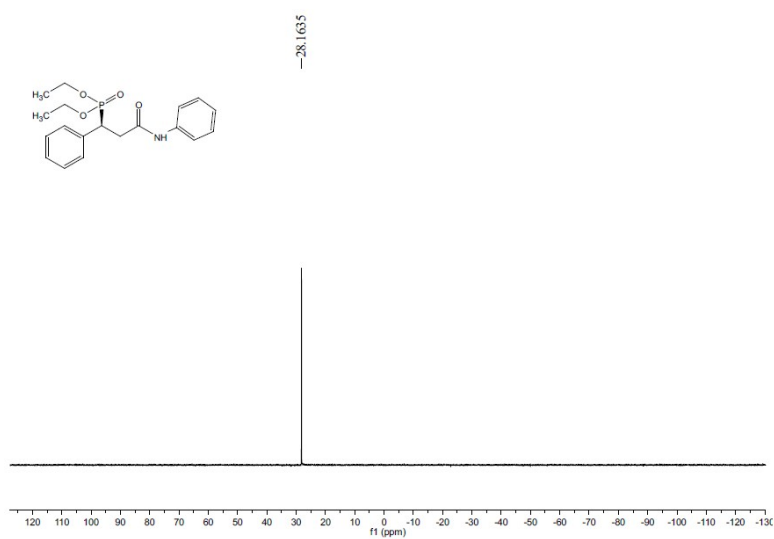
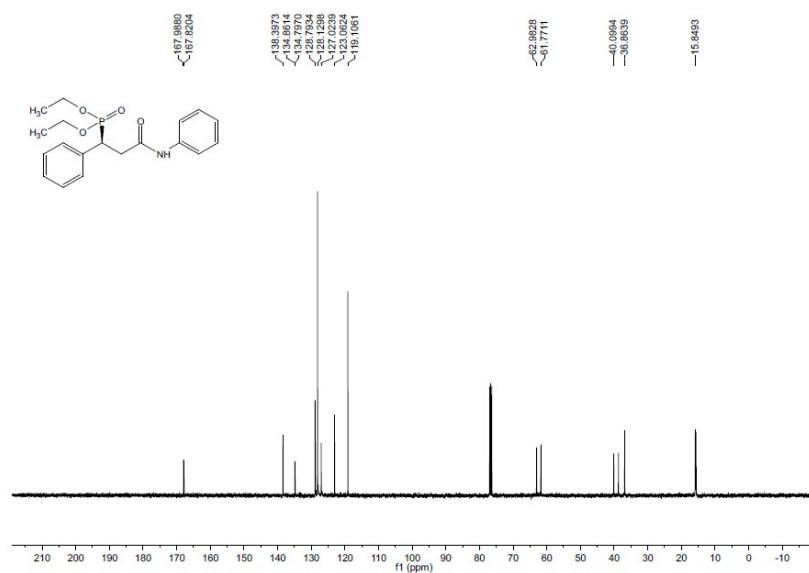
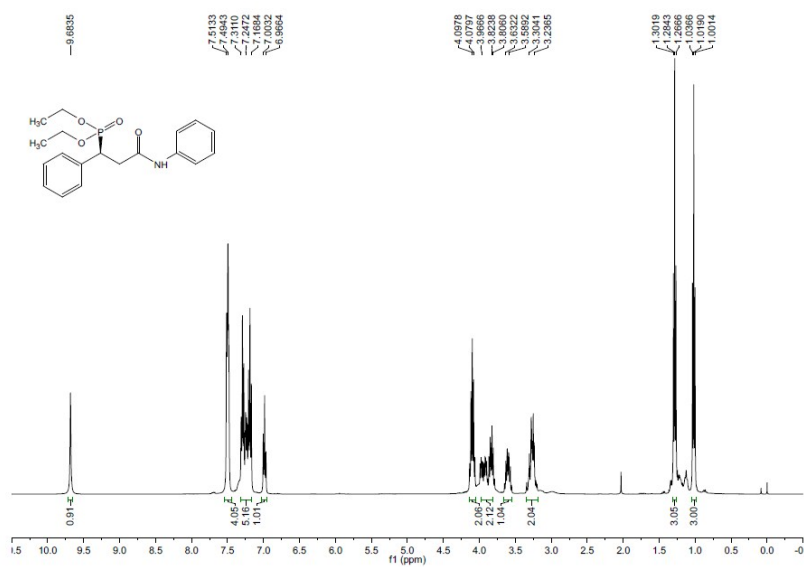
Peak#	Ret. Time	Area	Height	Area%
1	8.346	15749529	970693	49.493
2	10.209	16072338	827254	50.507
Total		31821867	1797947	100.000

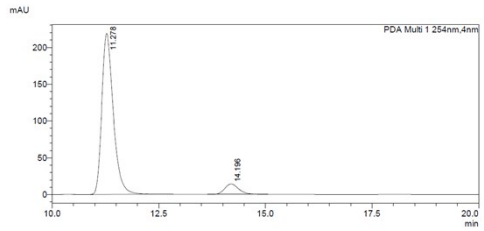
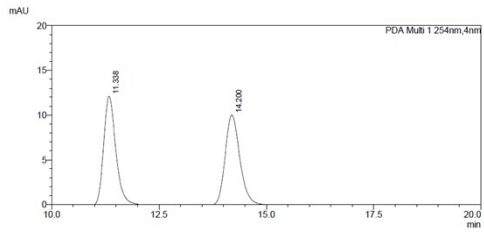
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1	8.327	16058262	995204	82.370
2	10.340	3437024	201272	17.630
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The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7d**





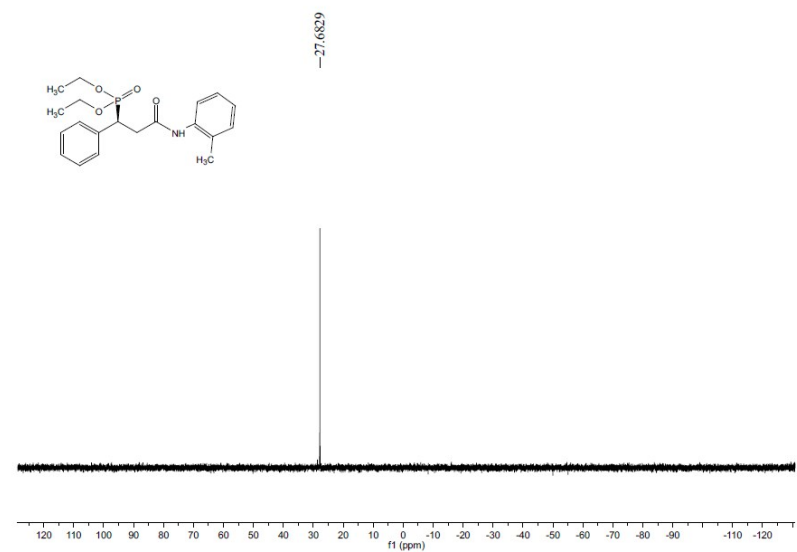
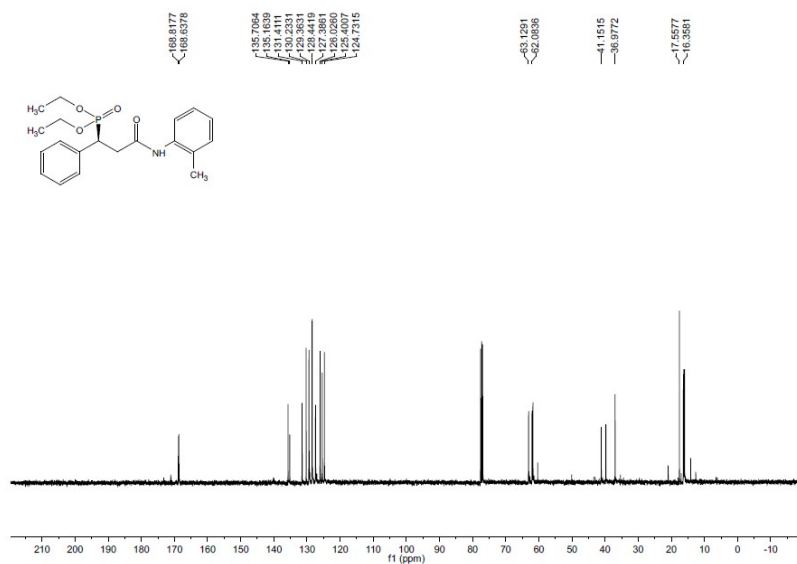
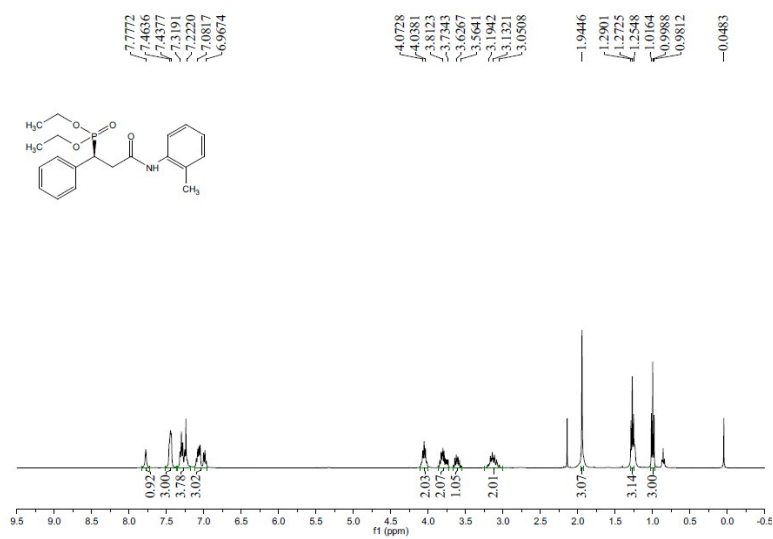
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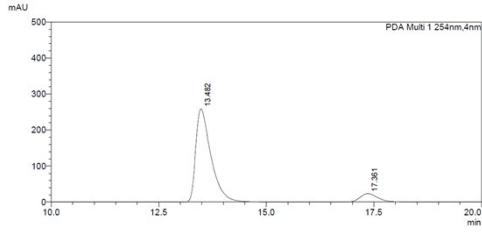
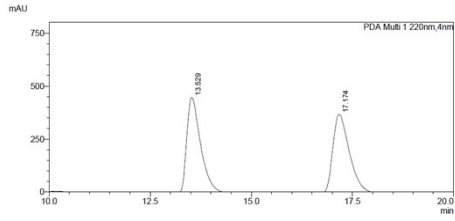
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Peak#	Ret. Time	Area	Height	Area%
1	11.338	245232	12227	50.001
2	14.200	245226	10126	49.999
Total		490458	22353	100.000

**<Peak Table>**

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Peak#	Ret. Time	Area	Height	Area%
1	11.278	4091396	218525	92.499
2	14.196	331795	14287	7.501
Total		4423191	232813	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7e**





**<Peak Table>**

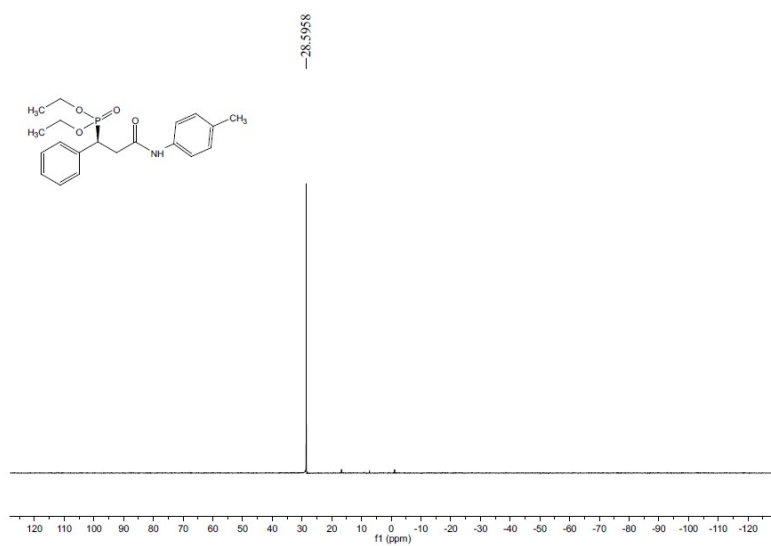
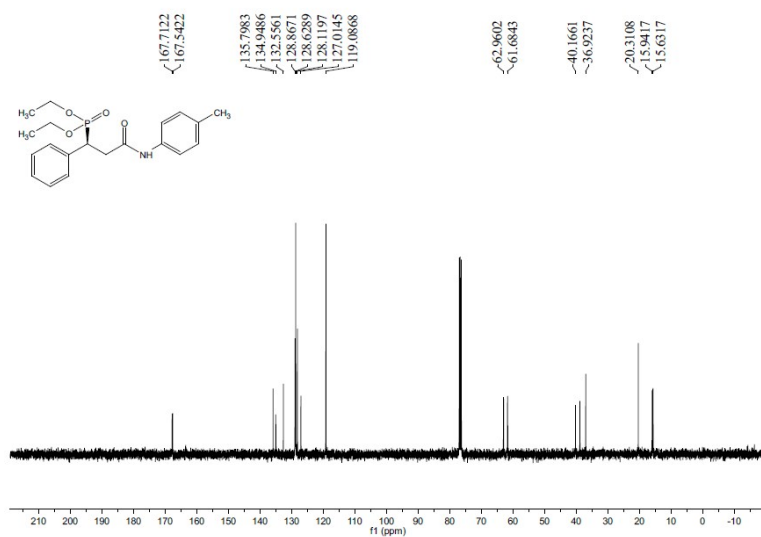
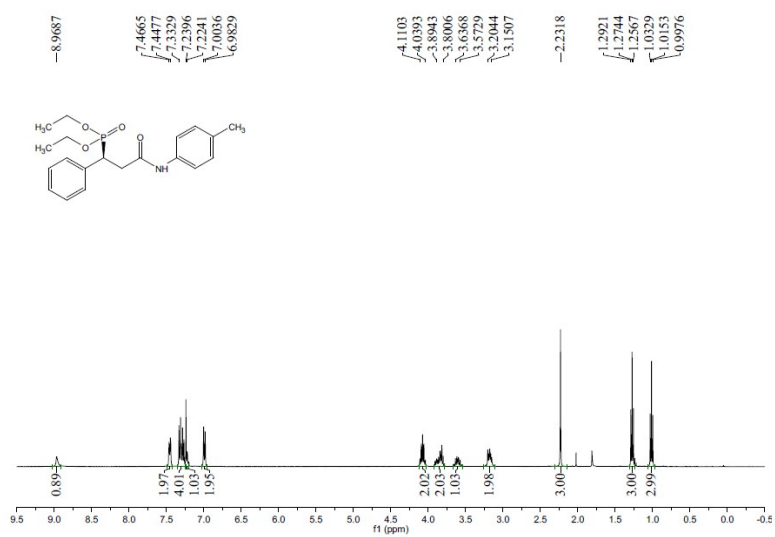
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1	13.529	10988786	454221	50.071
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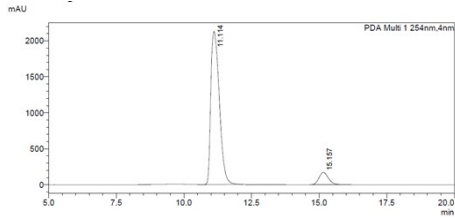
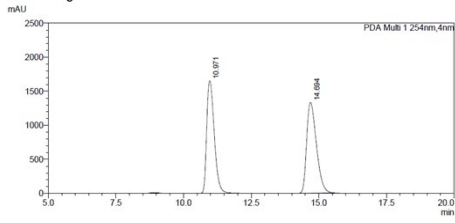
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1	13.482	6389968	259291	90.380
2	17.361	680149	23571	9.620
Total		7070117	282862	100.000



The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7f**





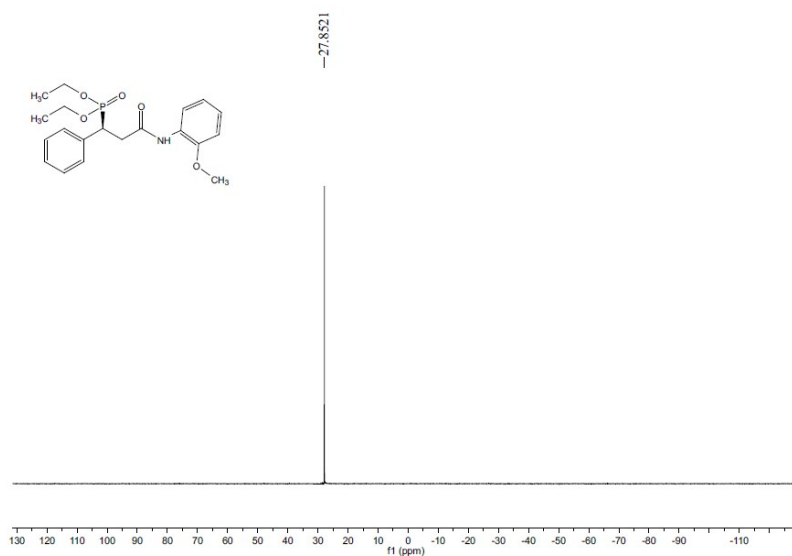
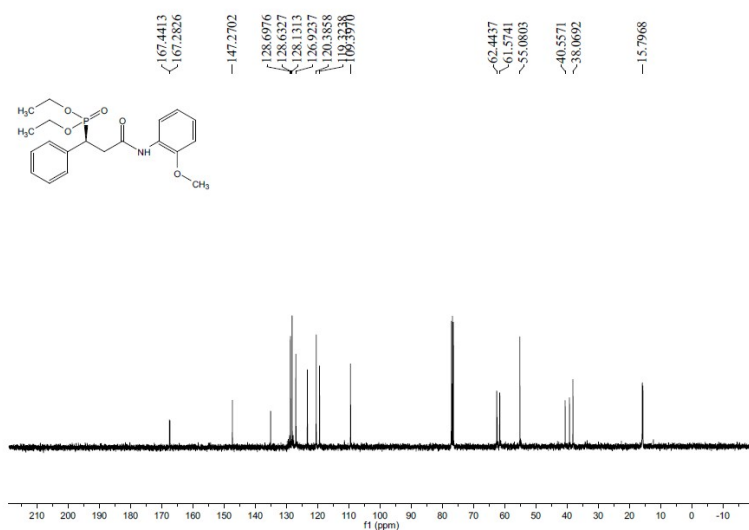
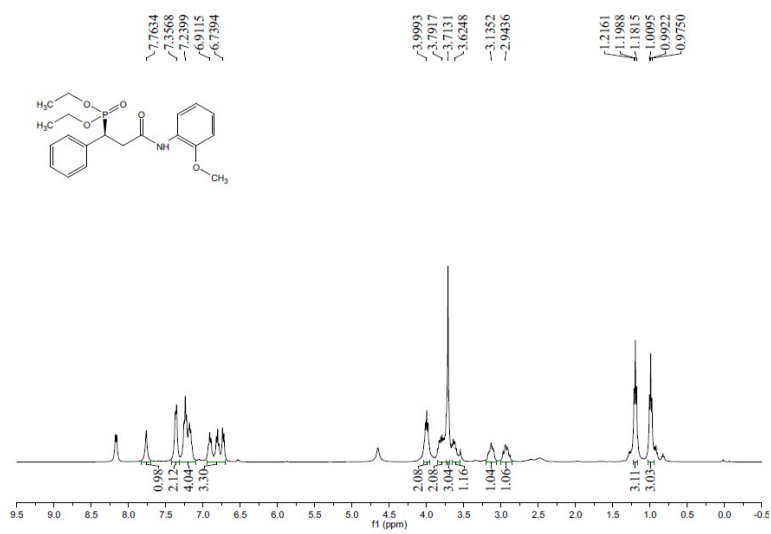
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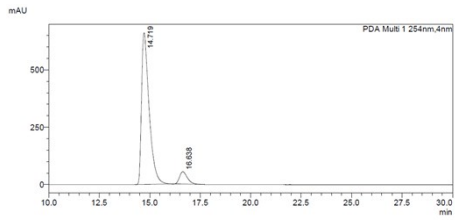
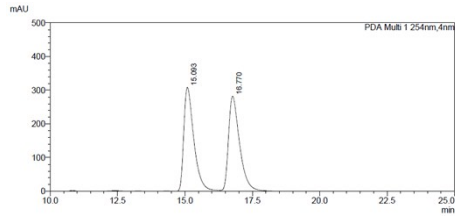
Peak#	Ret. Time	Area	Height	Area%
1	10.971	32233860	1653709	49.053
2	14.694	33478552	1334206	50.947
Total		65712412	2987915	100.000

**<Peak Table>**

Peak#	Ret. Time	Area	Height	Area%
1	11.114	46793676	2126617	92.004
2	15.157	4066915	170506	7.996
Total		50860590	2297123	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7g**





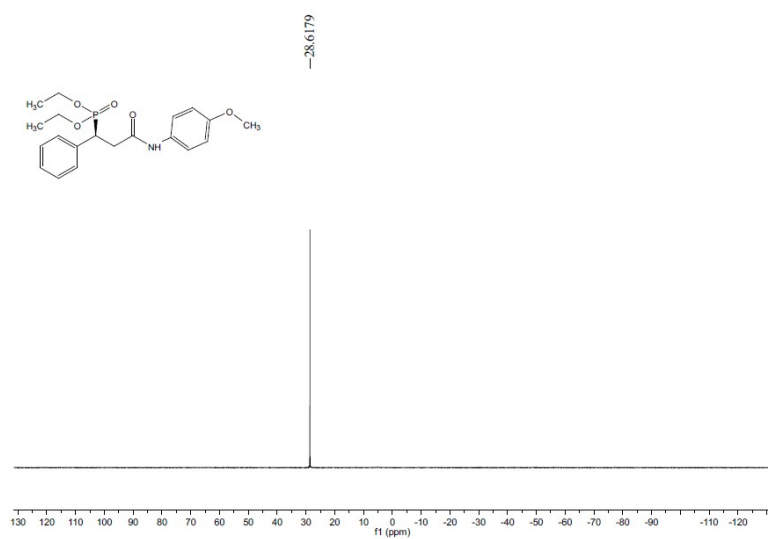
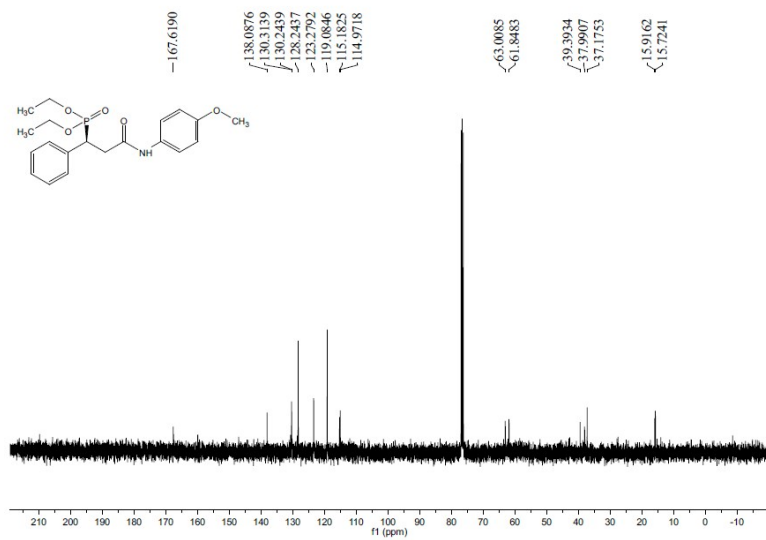
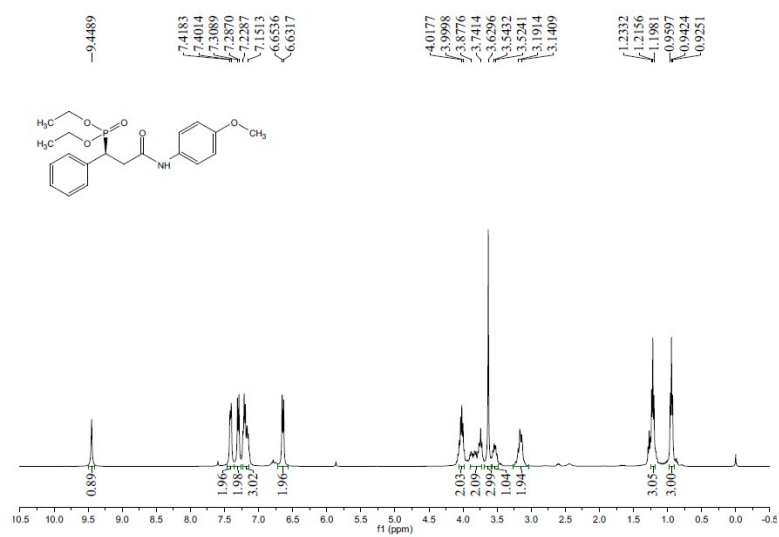
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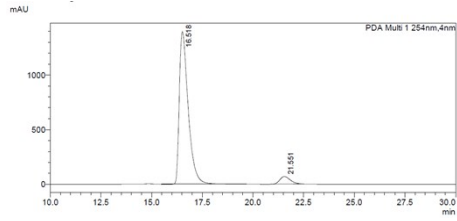
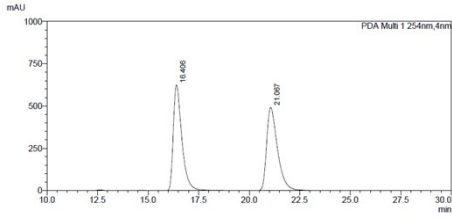
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	15.093	8075670	309046	49.894
2	16.770	8110131	282406	50.106
Total		16185801	591452	100.000

**<Peak Table>**

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	14.719	17279210	661482	92.320
2	16.638	1437375	53621	7.680
Total		18716585	715102	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7h**





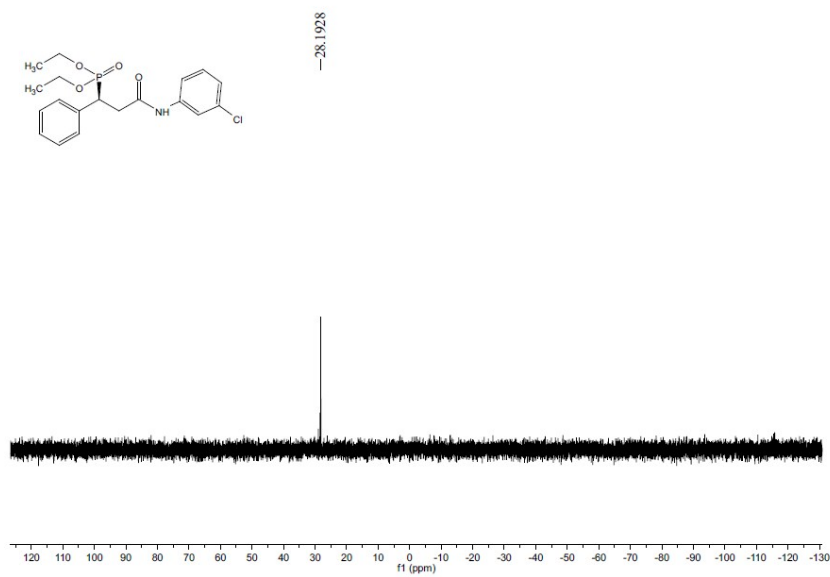
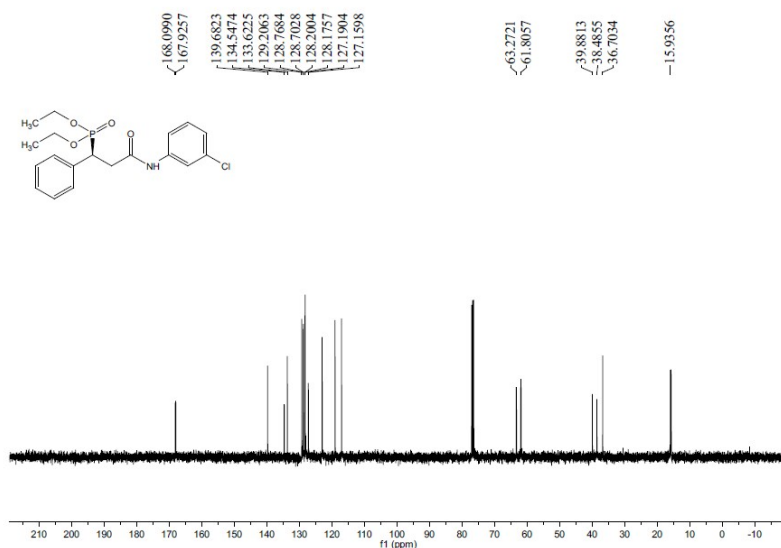
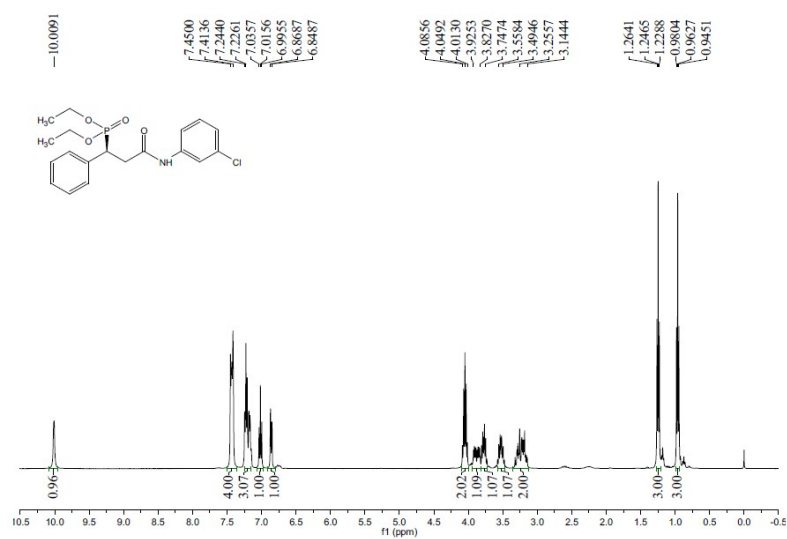
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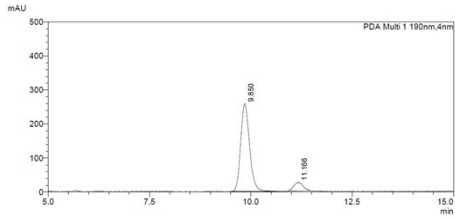
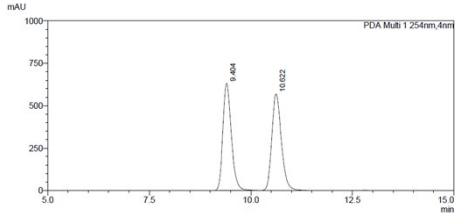
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	16.406	18320092	624710	50.162
2	21.067	18201600	490926	49.838
Total		36521692	1115636	100.000

**<Peak Table>**

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	16.518	42674289	1397341	94.459
2	21.551	2503483	69881	5.541
Total		45177772	1467221	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7i**





<Peak Table>

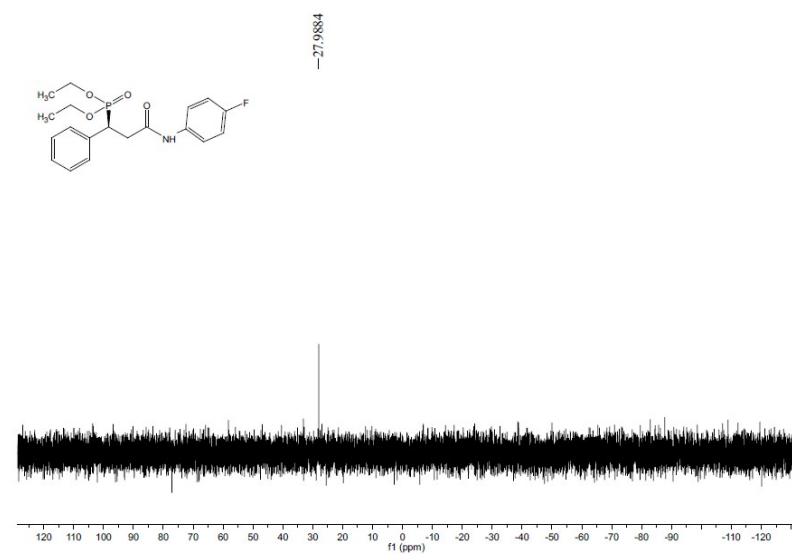
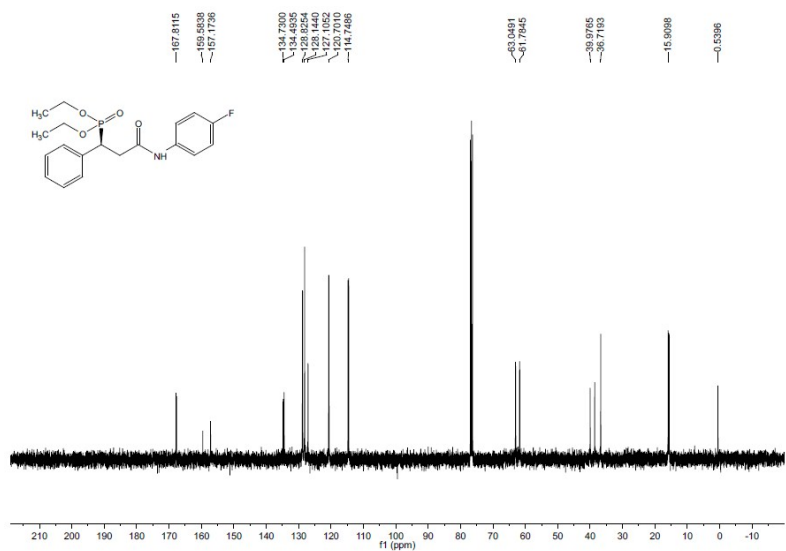
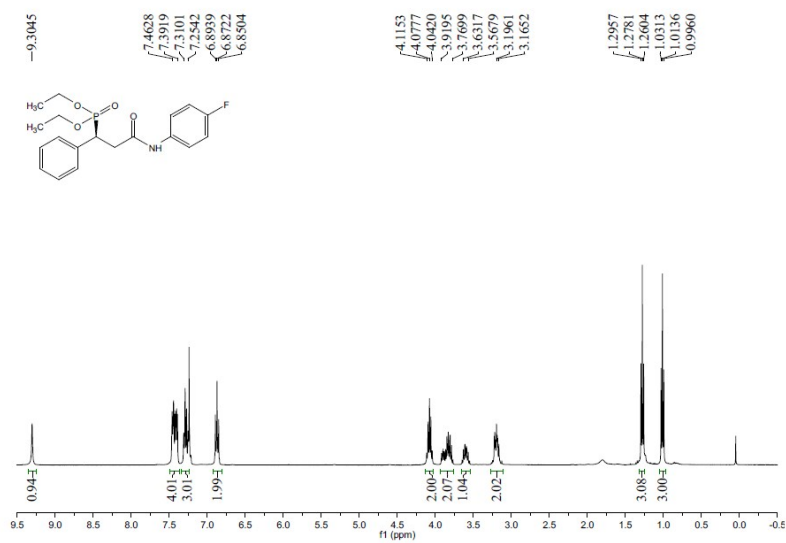
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	9.404	9168567	632358	49.698
2	10.622	9280109	568753	50.302
Total		18448675	1201111	100.000

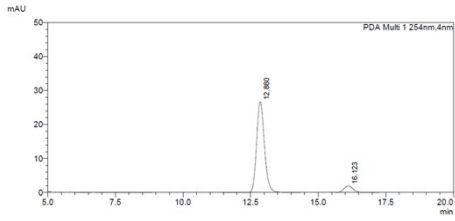
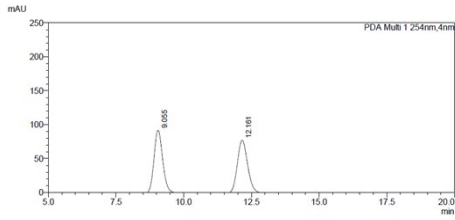
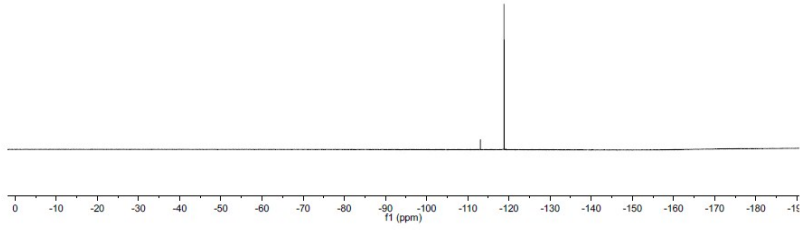
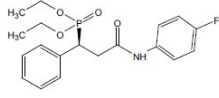
<Peak Table>

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	9.850	3960781	258539	90.991
2	11.166	392137	25305	9.009
Total		4352918	283844	100.000



The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{19}\text{F}$  NMR spectra and HPLC spectrum of compound **7j**





**<Peak Table>**

PDA Ch1 254nm

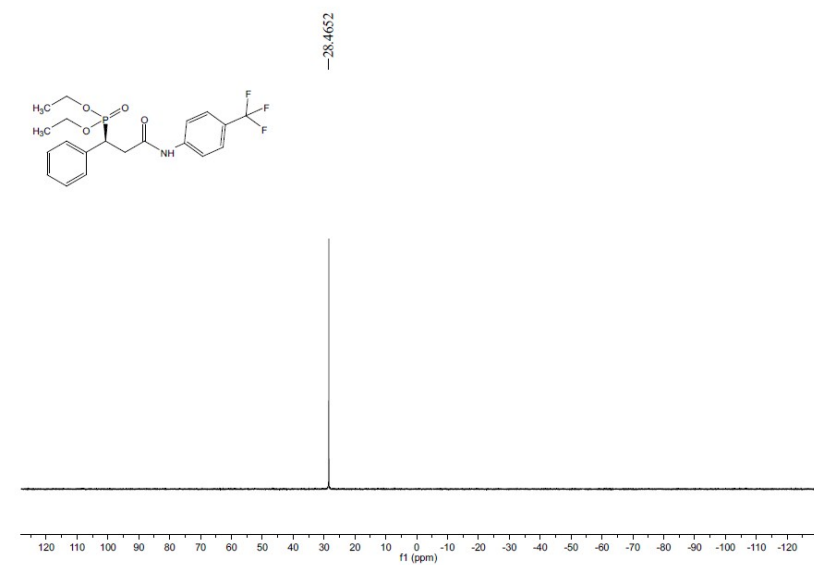
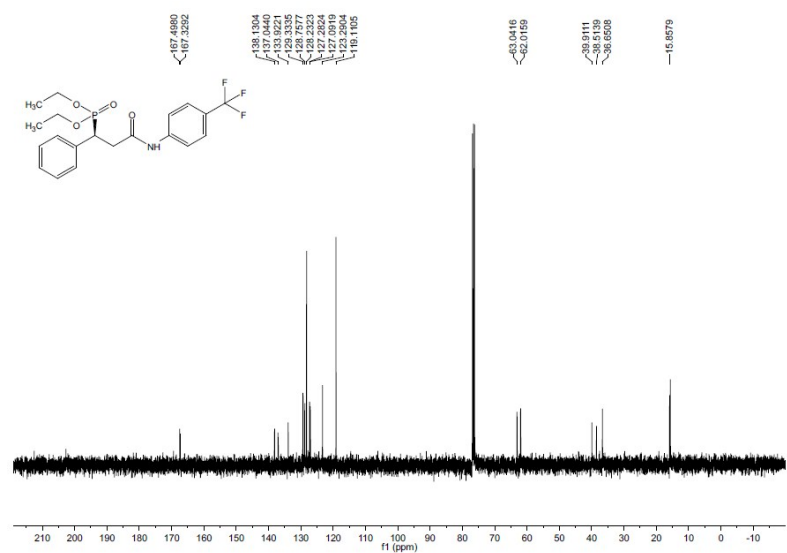
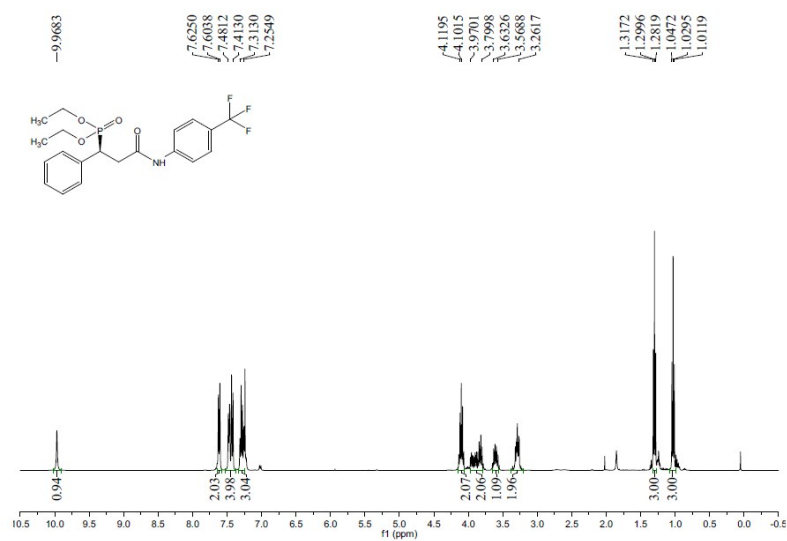
Peak#	Ret. Time	Area	Height	Area%
1	9.055	2108739	93287	49.939
2	12.161	2113896	78597	50.061
Total		4222635	171885	100.000

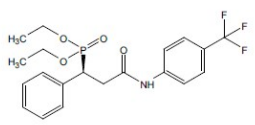
**<Peak Table>**

PDA Ch1 254nm

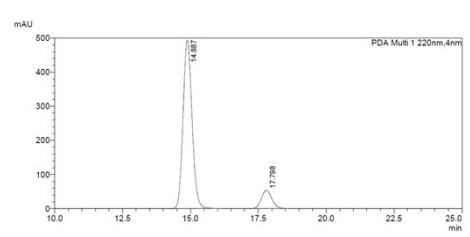
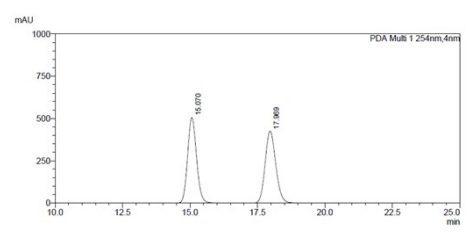
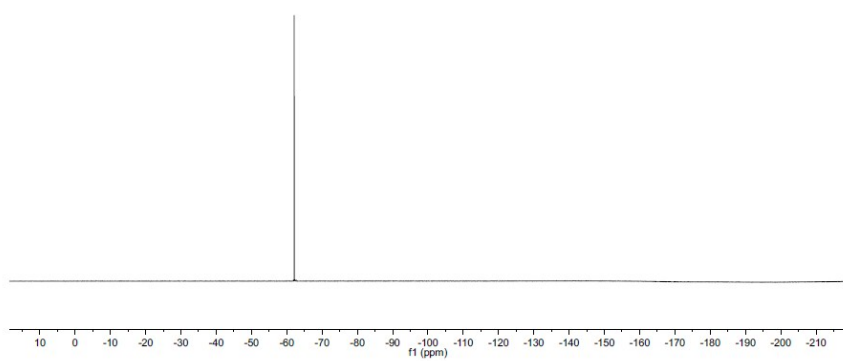
Peak#	Ret. Time	Area	Height	Area%
1	12.860	540350	26782	91.641
2	16.123	49290	2013	8.359
Total		589640	28795	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{19}\text{F}$  NMR spectra and HPLC spectrum of compound **7k**





—62.1251



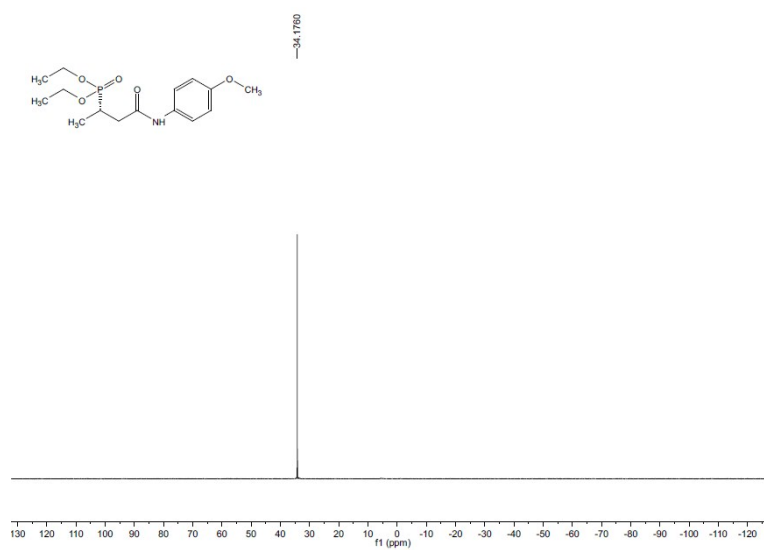
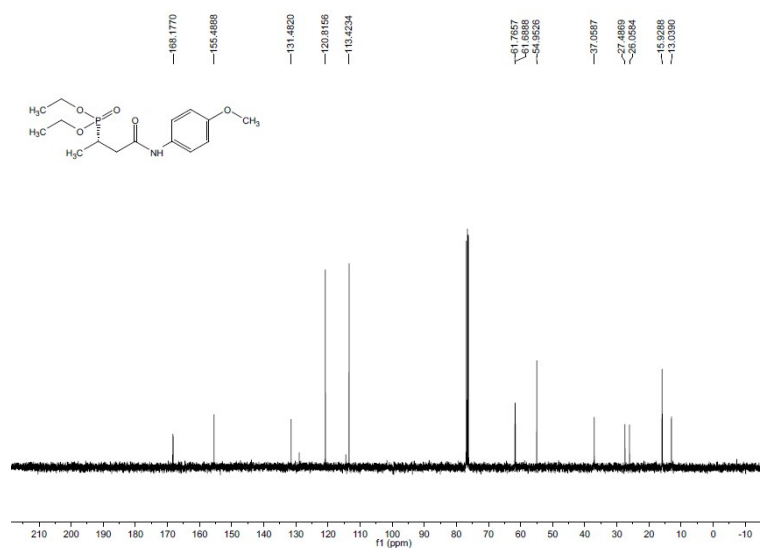
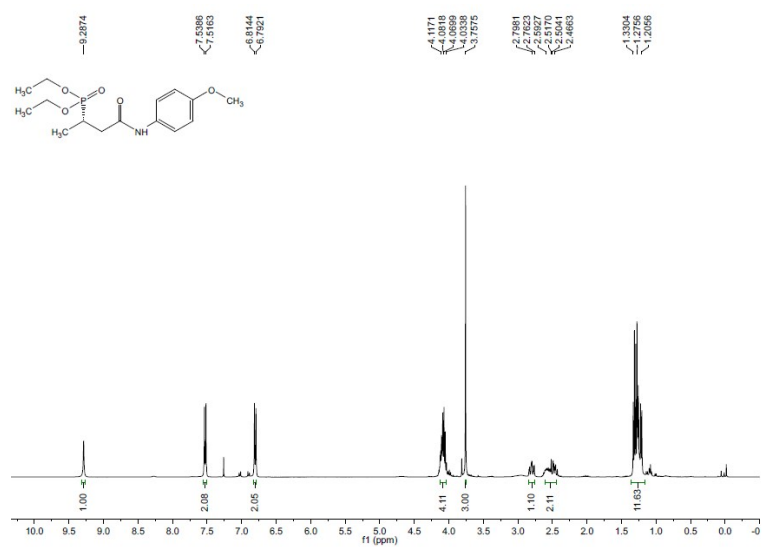
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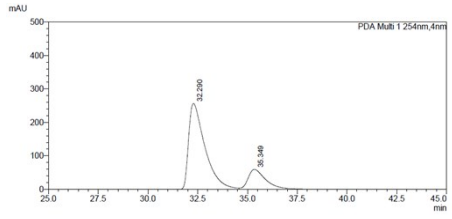
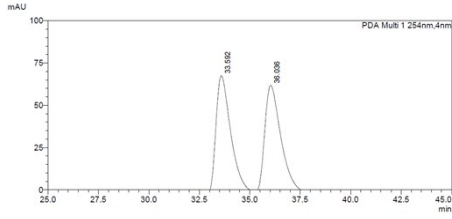
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	15.070	11679986	506366	49.981
2	17.969	11688789	426735	50.019
Total		23368775	933101	100.000

<Peak Table>

PDA Ch1 220nm				
Peak#	Ret. Time	Area	Height	Area%
1	14.887	11364708	493945	88.868
2	17.798	1423556	53374	11.132
Total		12788263	547319	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound 7I





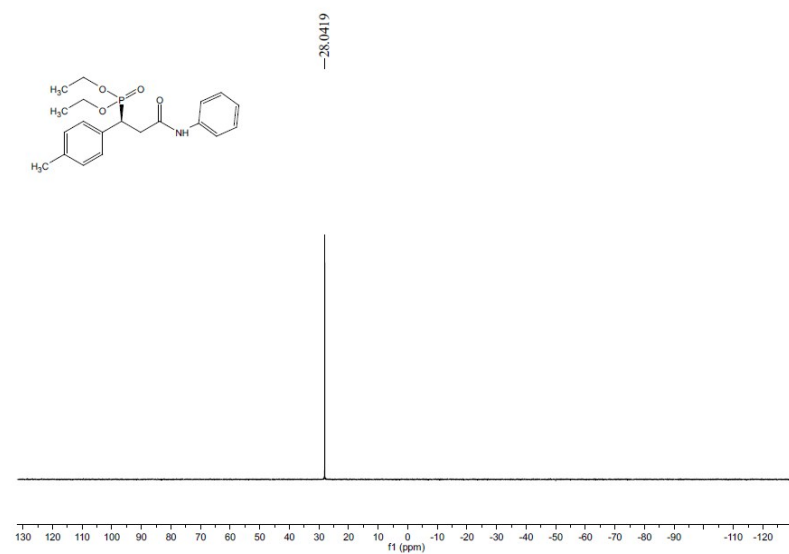
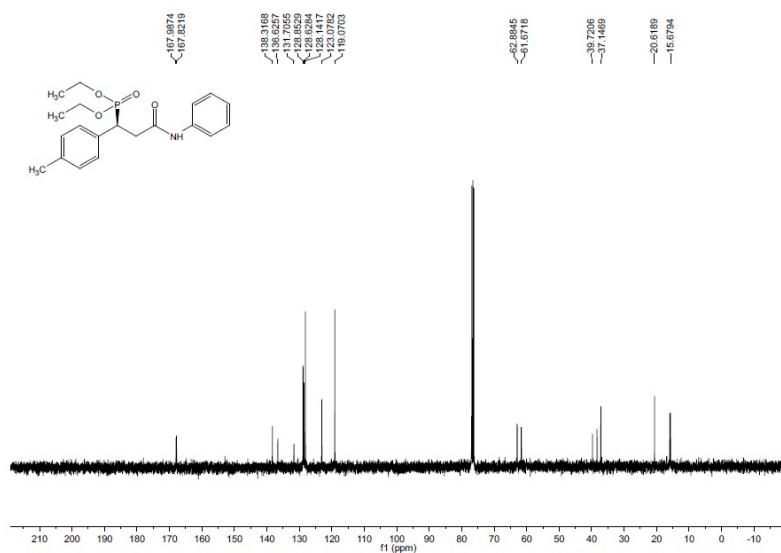
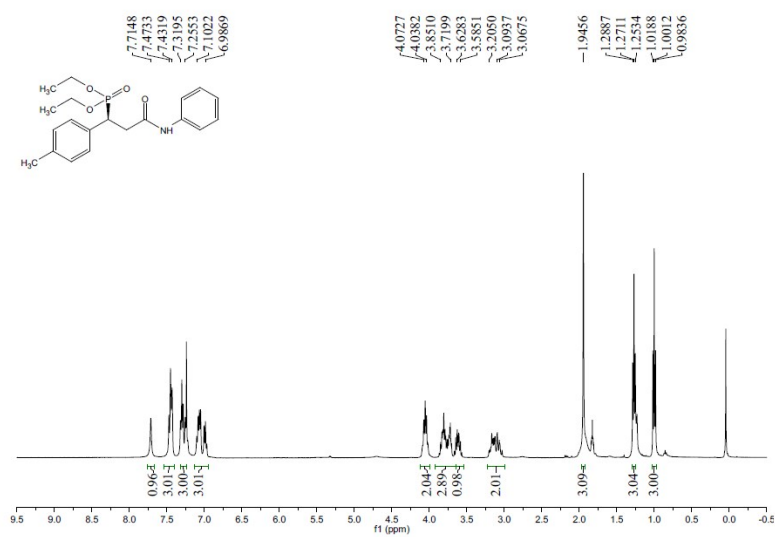
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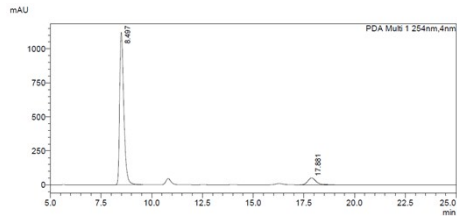
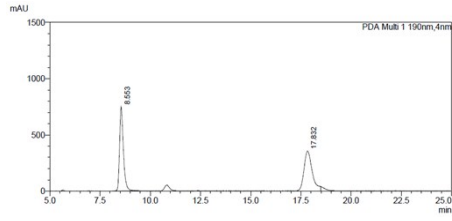
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	33.592	3750953	70784	49.639
2	36.036	3805525	65061	50.361
Total		7556478	135844	100.000

**<Peak Table>**

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	32.290	14634434	256779	80.306
2	35.349	3588956	59035	19.694
Total		18223390	315815	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7m**





**<Peak Table>**

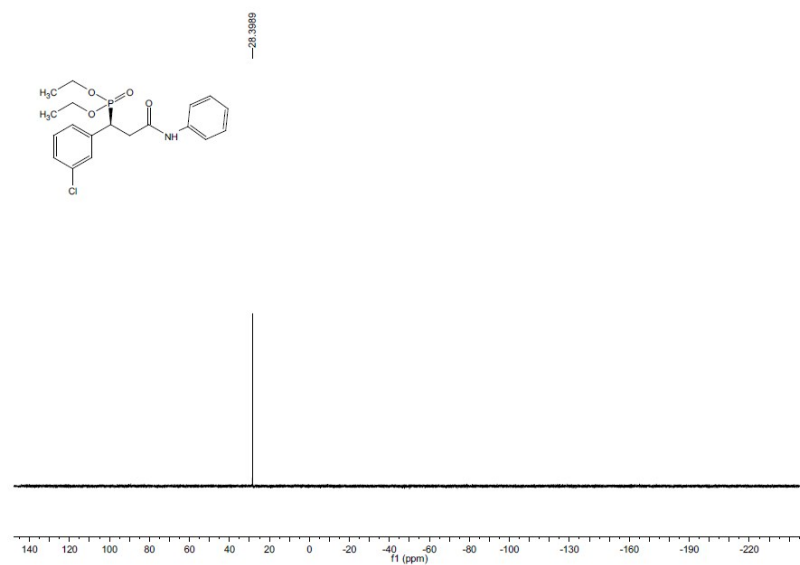
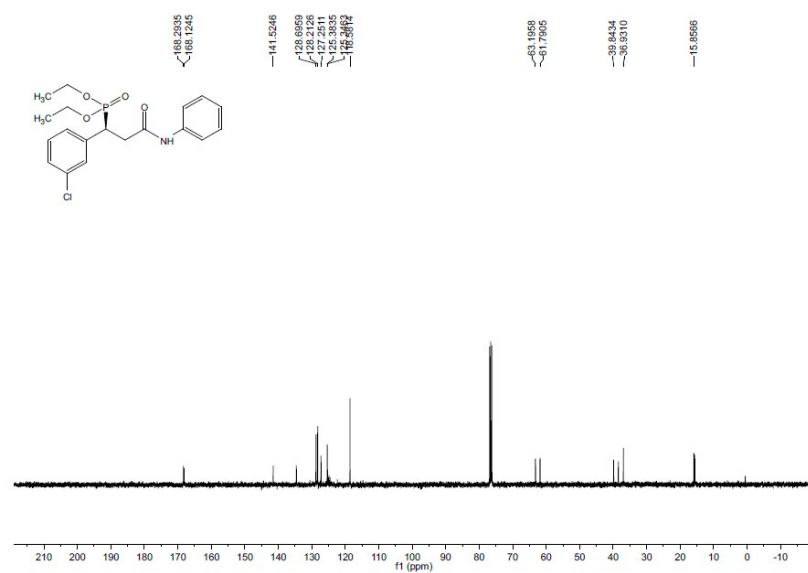
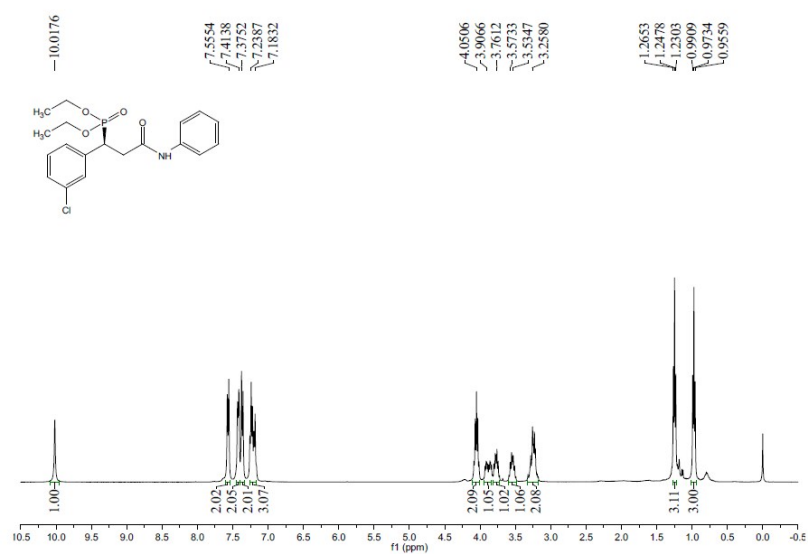
PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	8.553	9967646	751619	49.847
2	17.832	10029018	355304	50.153
Total		19996665	1106922	100.000

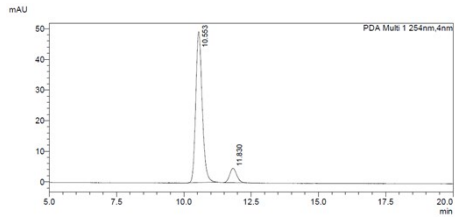
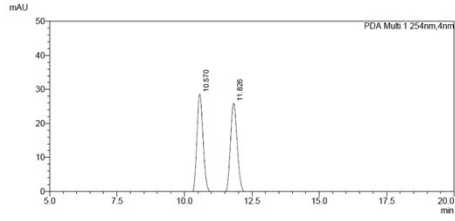
**<Peak Table>**

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	8.497	15986596	1120462	91.595
2	17.881	1466941	50885	8.405
Total		17453537	1171347	100.000



The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7n**





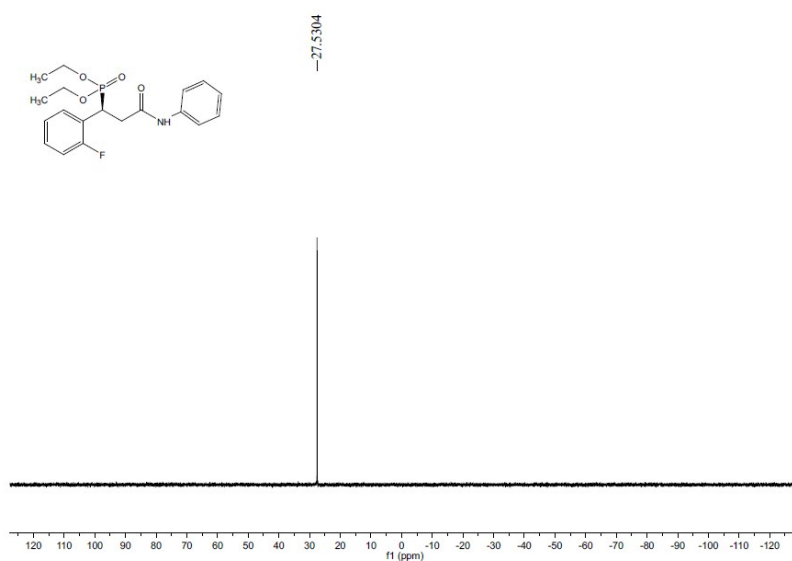
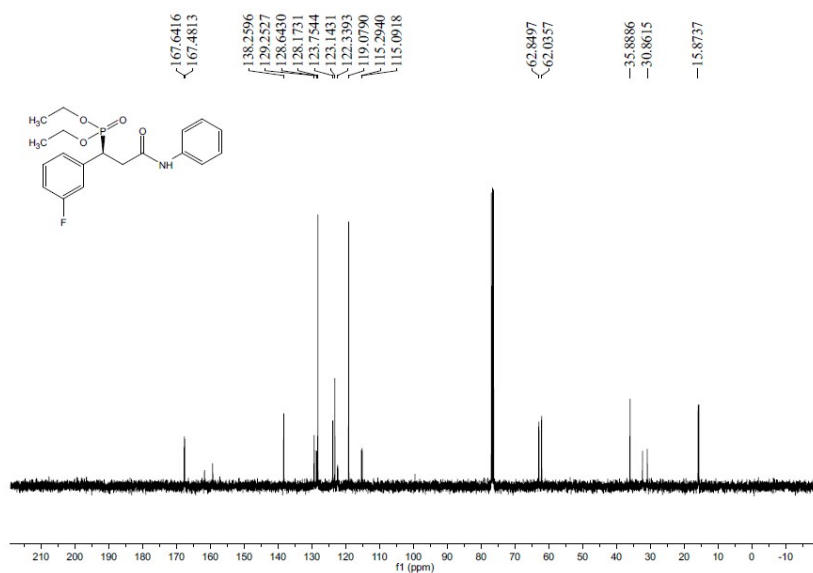
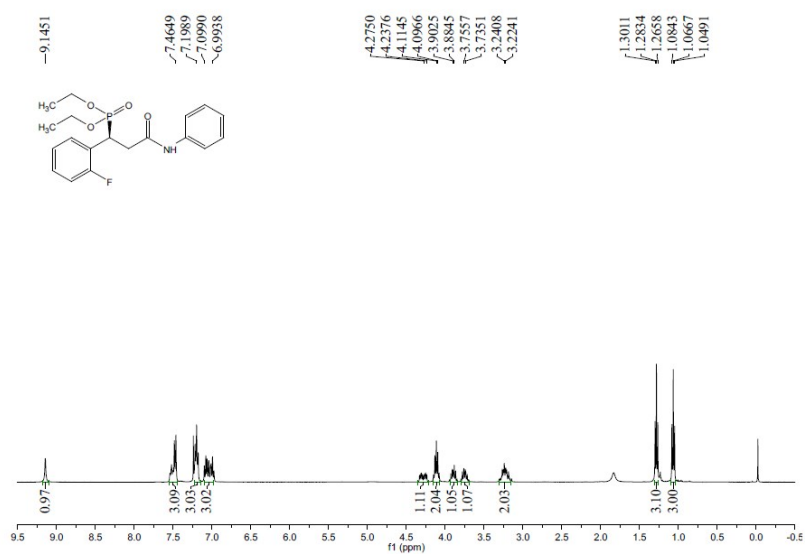
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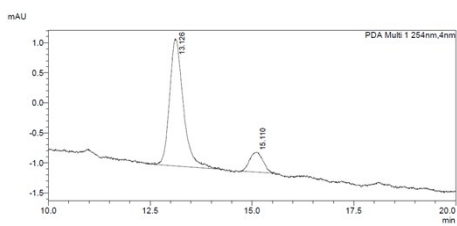
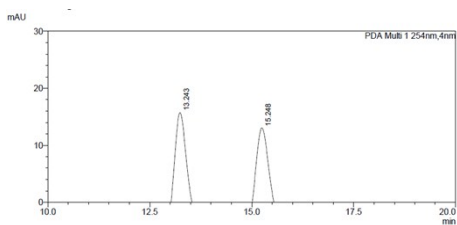
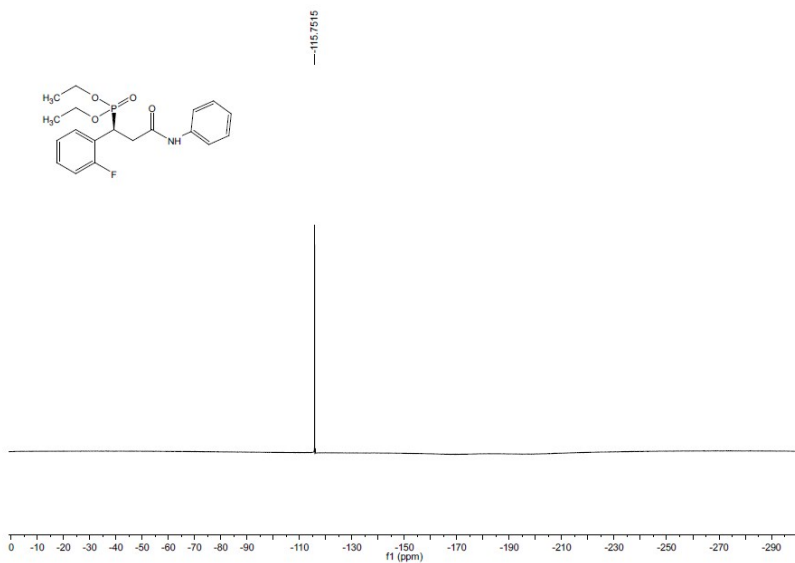
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	10.570	497163	29780	49.652
2	11.826	504137	27173	50.348
Total		1001300	56953	100.000

**<Peak Table>**

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	10.553	822059	49243	90.556
2	11.830	85729	4696	9.444
Total		907789	53939	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{19}\text{F}$  NMR spectra and HPLC spectrum of compound **7o**





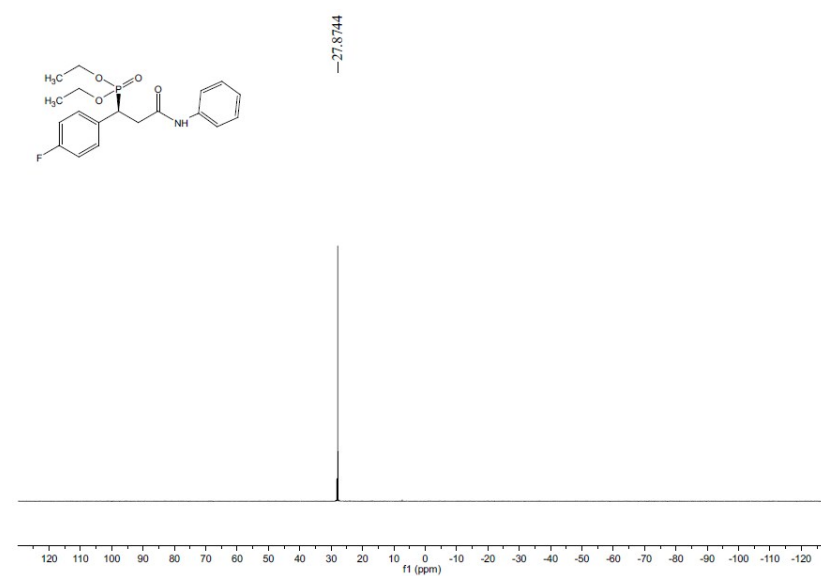
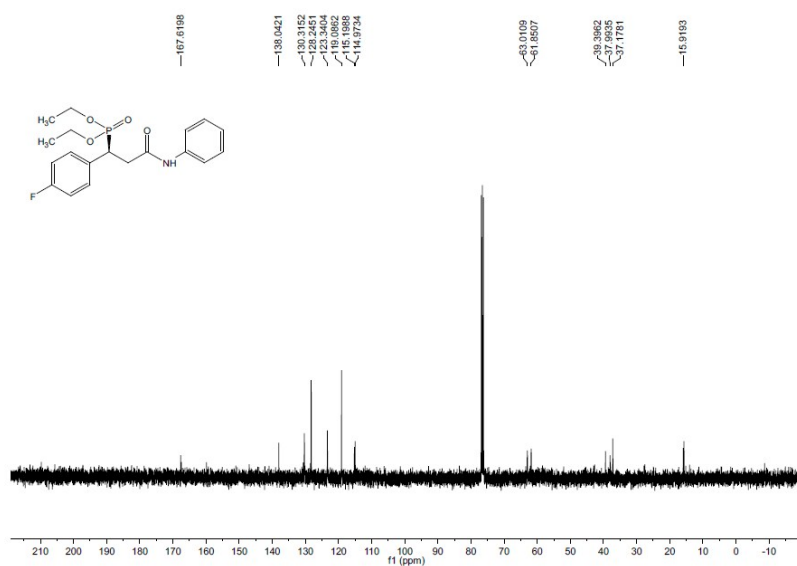
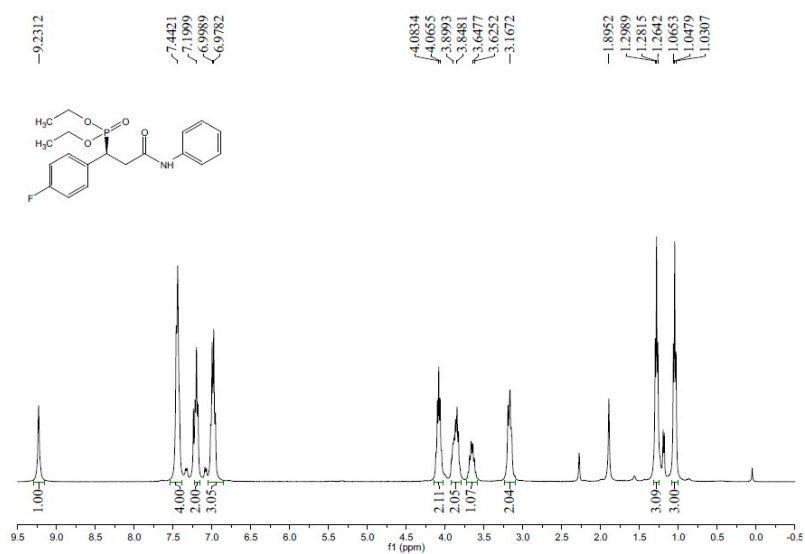
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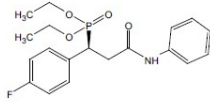
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	13.243	426383	19706	49.877
2	15.248	428490	17530	50.123
Total		854873	37236	100.000

**<Peak Table>**

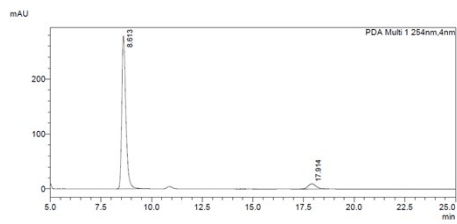
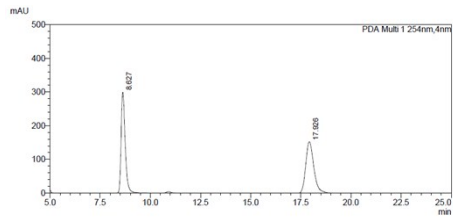
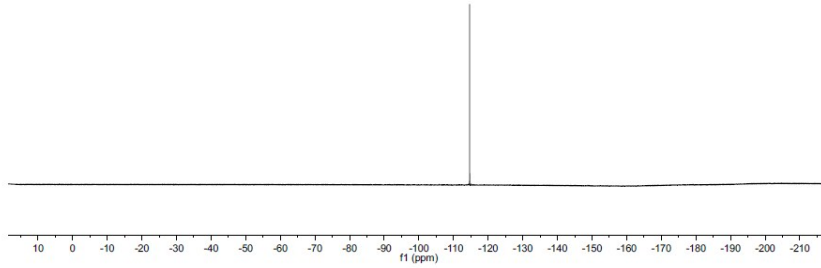
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	13.126	49646	2115	86.850
2	15.110	7517	334	13.150
Total		57163	2449	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{19}\text{F}$  NMR spectra and HPLC spectrum of compound **7p**





—114.6531



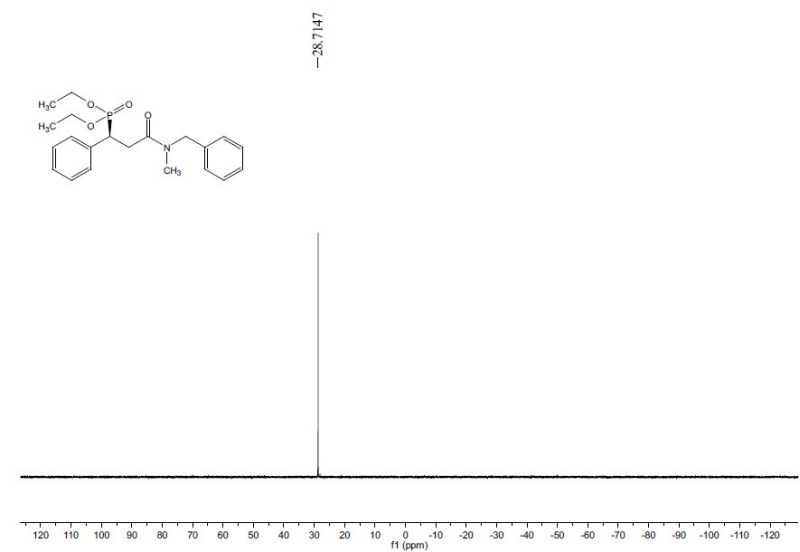
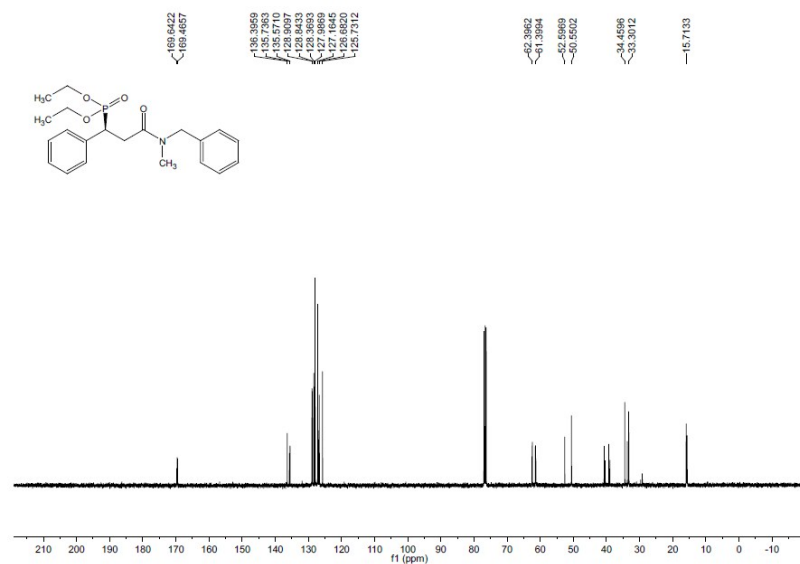
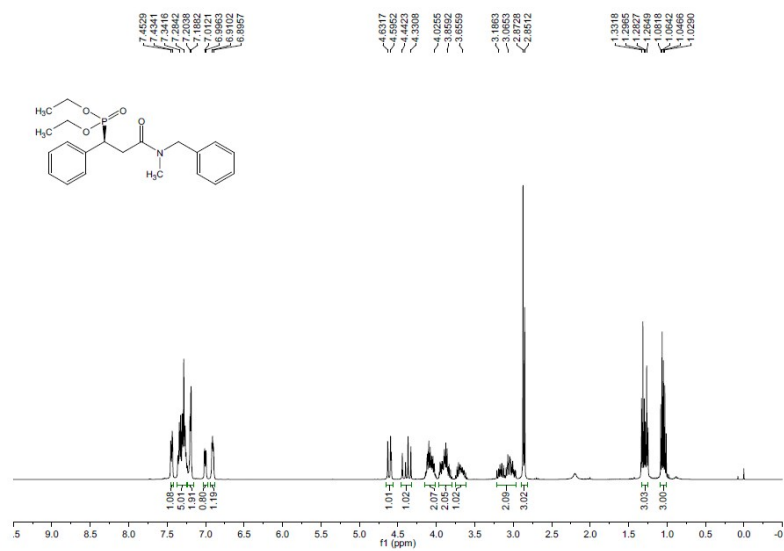
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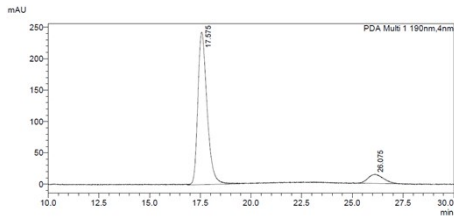
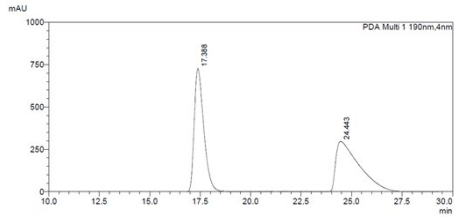
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	8.627	4271617	300672	49.514
2	17.926	4355498	153682	50.486
Total		8627115	454353	100.000

<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	8.613	3905938	278263	93.730
2	17.914	261299	9400	6.270
Total		4167237	287662	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7q**





**<Peak Table>**

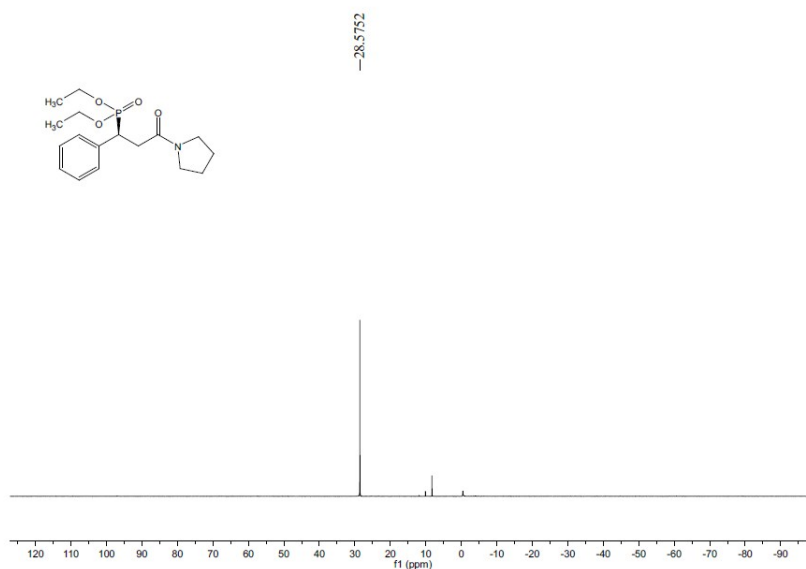
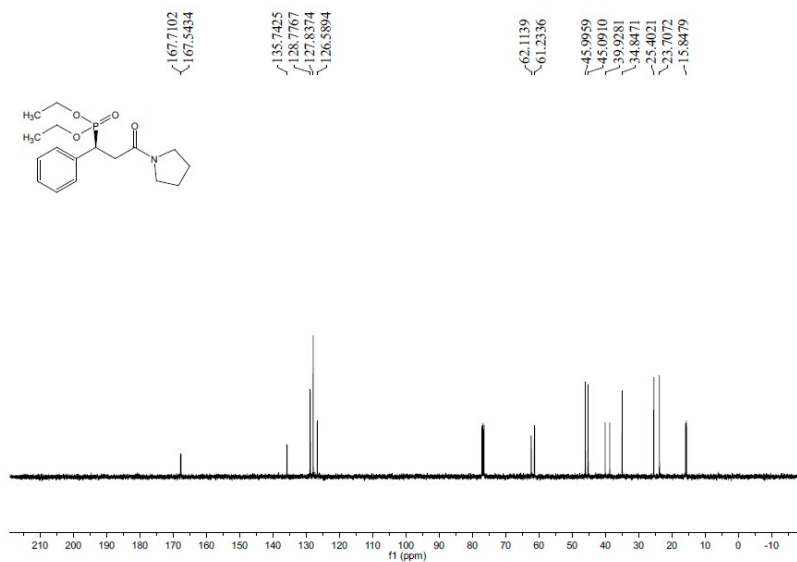
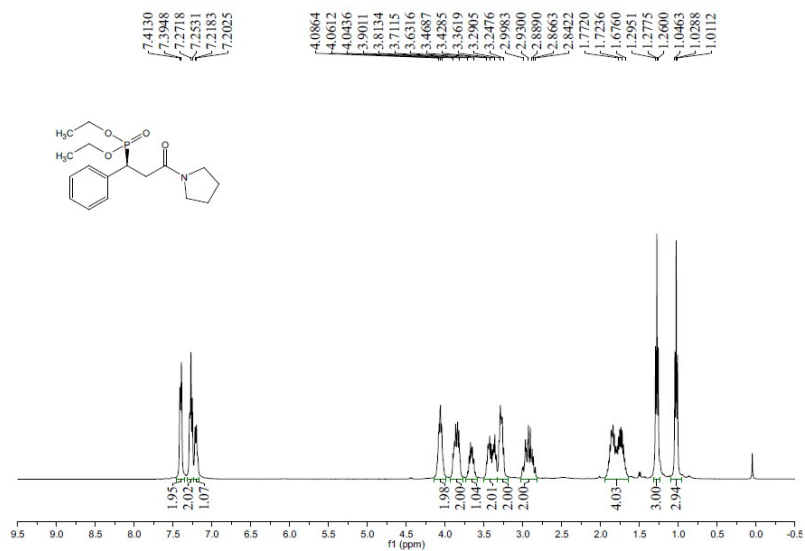
PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	17.388	24219035	730454	49.676
2	24.443	24535241	300211	50.324
Total		48754276	1030665	100.000

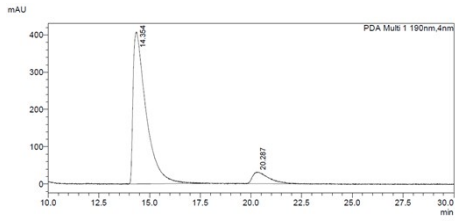
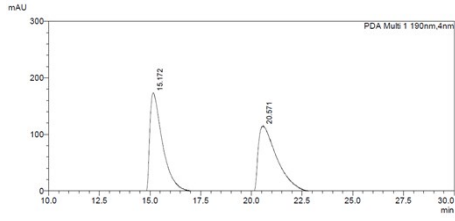
**<Peak Table>**

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	17.575	7672711	242357	91.110
2	26.075	748651	14444	8.890
Total		8421362	256801	100.000



The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7r**





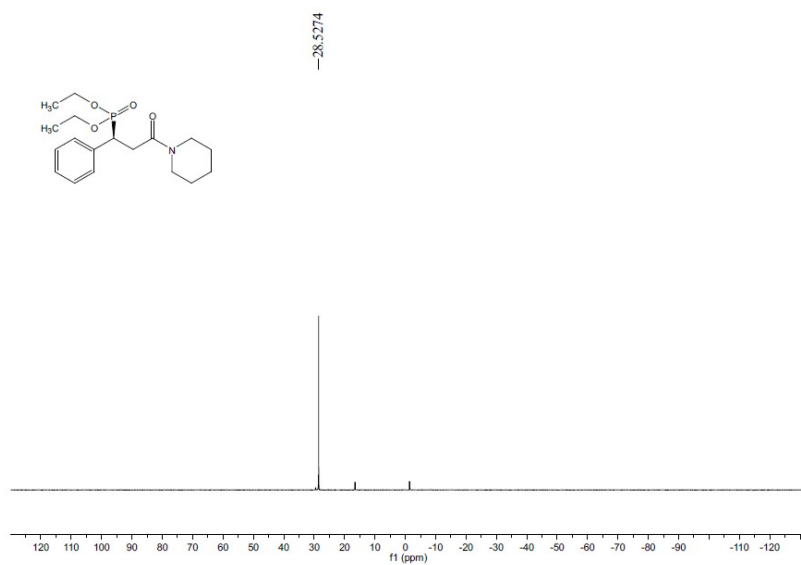
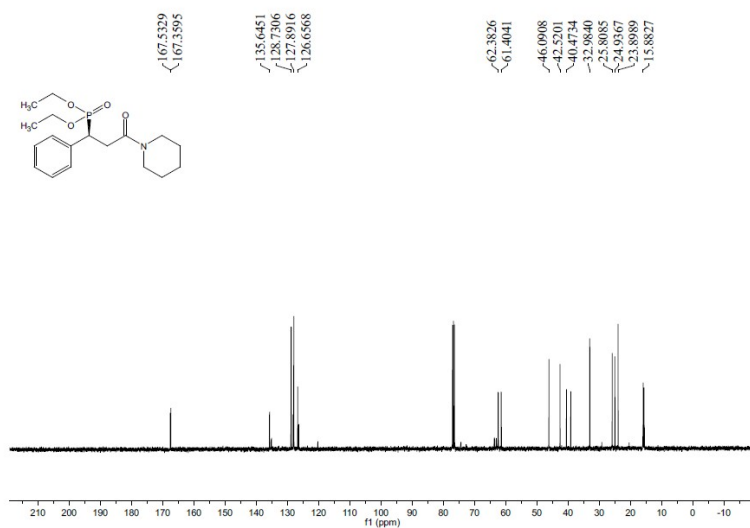
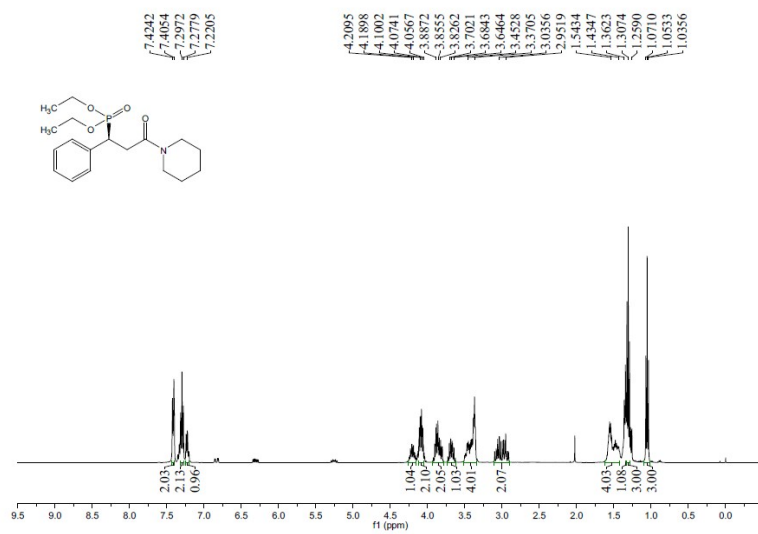
**<Peak Table>**

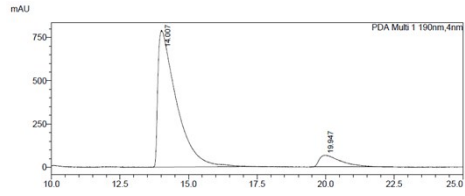
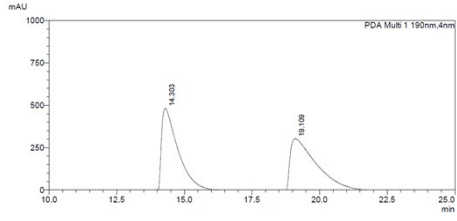
PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	15.172	7938487	177318	49.126
2	20.571	8220883	119456	50.874
Total		16159370	296774	100.000

**<Peak Table>**

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	14.354	18294018	407946	91.515
2	20.287	1696070	30957	8.485
Total		19990088	438903	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7s**





<Peak Table>

PDA Ch1 190nm

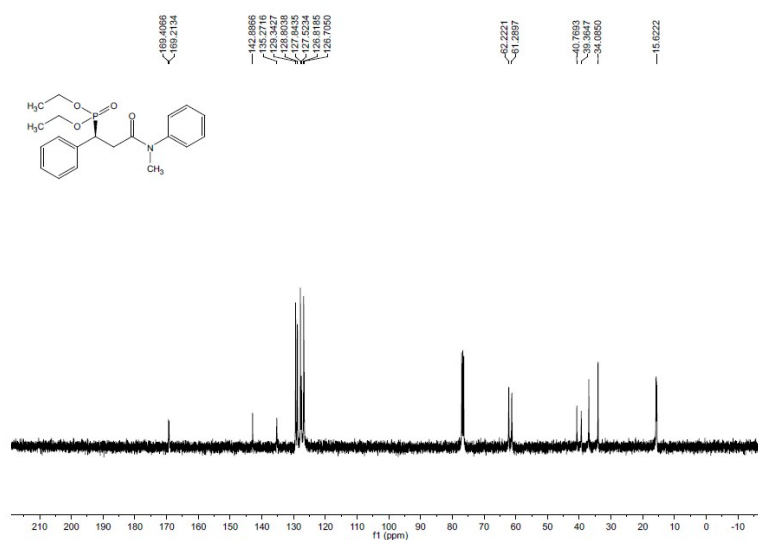
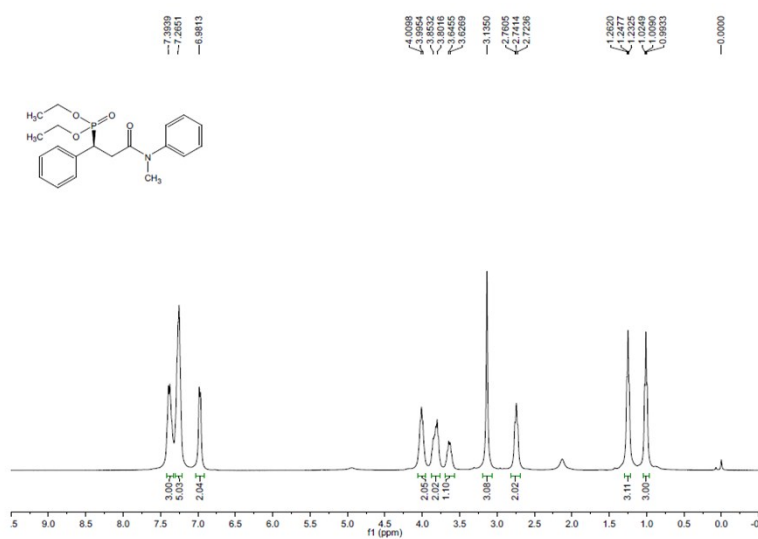
Peak#	Ret. Time	Area	Height	Area%
1	14.303	21516225	490351	49.412
2	19.109	22028437	314112	50.588
Total		43544662	804463	100.000

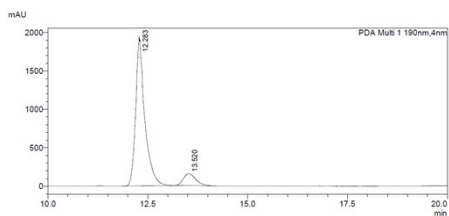
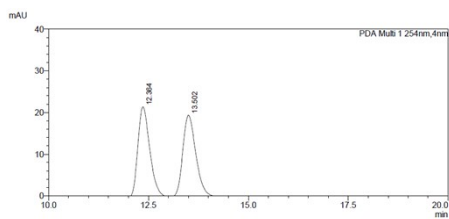
<Peak Table>

PDA Ch1 190nm

Peak#	Ret. Time	Area	Height	Area%
1	14.007	37140563	789874	90.762
2	19.947	3780457	67579	9.238
Total		40921020	857453	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra and HPLC spectrum of compound **7t**





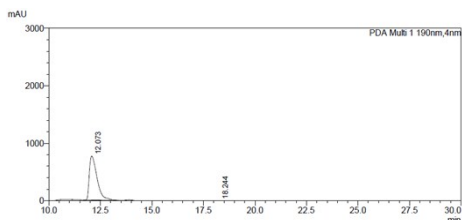
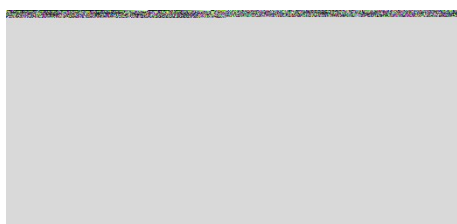
<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	12.364	466019	21929	49.631
2	13.502	472954	19930	50.369
Total		938973	41859	100.000

<Peak Table>

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	12.283	30382339	1944414	90.292
2	13.520	3266483	152046	9.708
Total		33648822	2096460	100.000

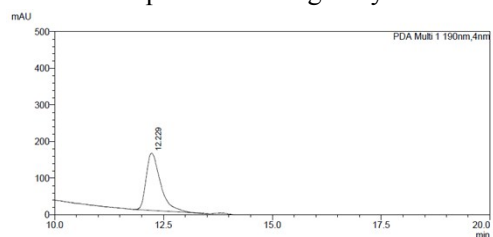
The HPLC spectrum of compound **7a** after recrystallization



<Peak Table>

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	12.073	19809722	762808	98.795
2	18.244	241560	8038	1.205
Total		20051283	770846	100.000

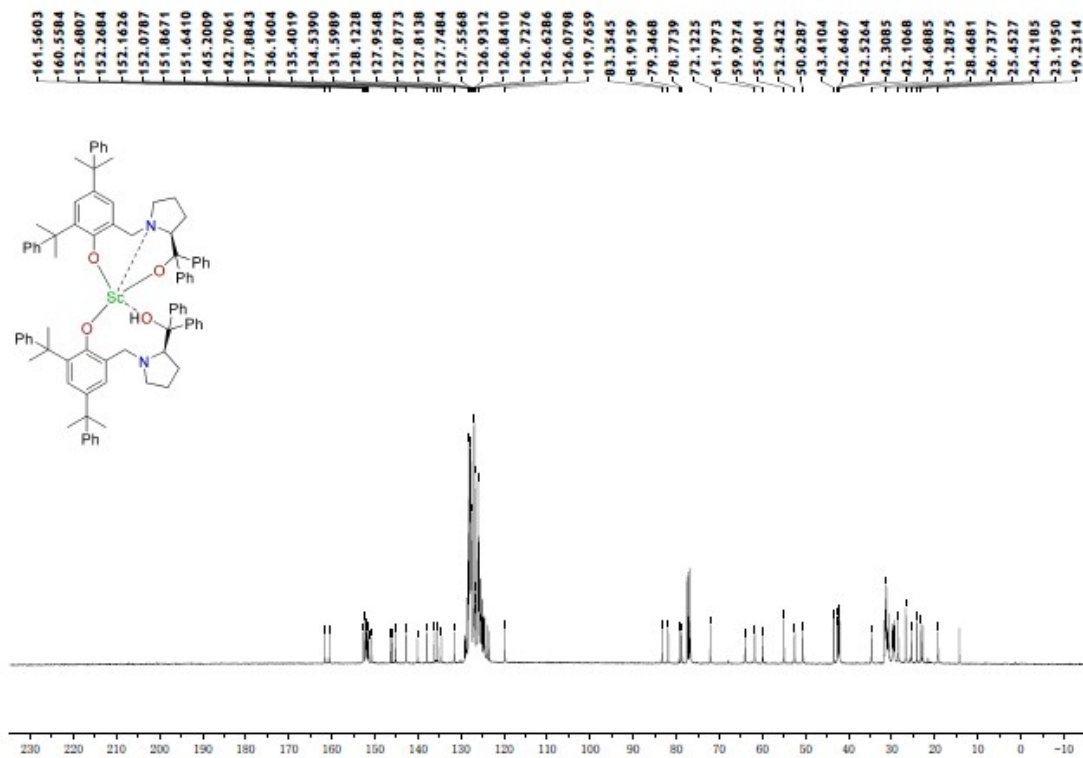
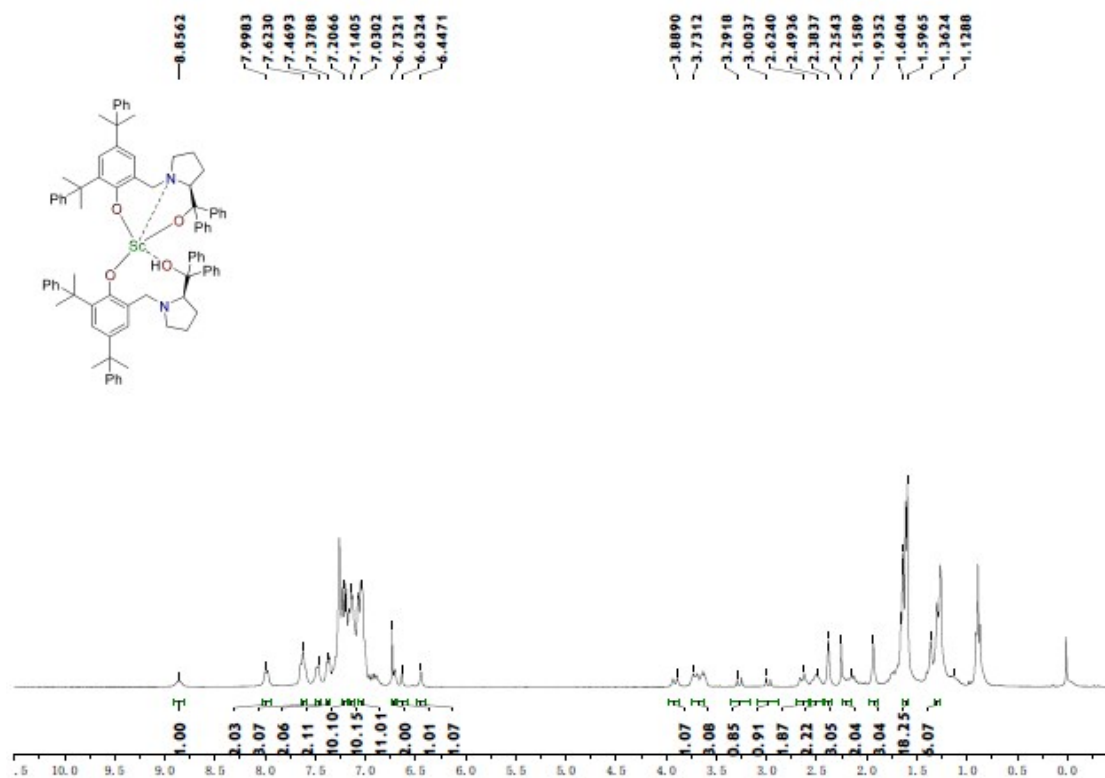
The HPLC spectrum of single crystal of **7a**



<Peak Table>

PDA Ch1 190nm				
Peak#	Ret. Time	Area	Height	Area%
1	12.229	3568854	156292	100.000
Total		3568854	156292	100.000

The  $^1\text{H}$ ,  $^{13}\text{C}$  spectra of compound Complex 8



**Reference:**

- [1] (a) C. Zeng, D. Yuan, B. Zhao, Y. Yao, *Organic Letters*, 2014, **17**(9), 2242-2245.
- [2] (a) S. Yang, T. Kang, C. Rui, X. Yang, Y. Sun, Z. Cui, Y. Ling, *Chin. J. Chem.*, 2011, **29**(11), 2394-2400. (b) S. Ueda, T. Okada, H. Nagasawa, *Chem. Commun.*, 2010, **46**(14), 2462-2464. (c) C.-W. Chan, P.-Y. Lee, W.-Y. Yu, *Tetrahedron Letters*, 2015, **56**(20), 2559-2563. (d) W. Dong, Y. Liu, B. Hu, K. Ren, Y. Li, X. Xie, Y. Jiang, Z. Zhang, *Chem. Commun.*, 2015, **51**(22), 4587-4590.