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Support Information

A Mild and Concise Synthesis of Aryloxy Phosphoramidate Prodrug of Alcohols via Transesterification Reaction

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Content

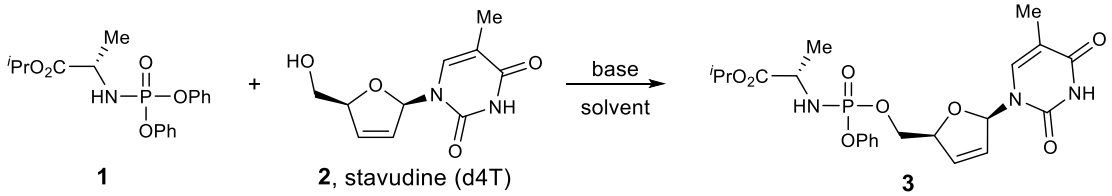
1. General Information

Commercial reagents were purchased from Adamas, Aldrich, Bide, Energy Chemical, and J&K chemical, and were used as received. Chromatographic purification of products was accomplished using flash chromatography on 300-400 mesh silica gel. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker instrument (500 MHz for ^{1}H NMR, 126 MHz for ^{13}C and 202 MHz for ^{31}P) and are internally referenced to chemical shift of residual solvent (for $CDCl_3$, 7.26 and 77.16 ppm, respectively). Data for ^{1}H NMR are reported as follows: chemicals shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant (Hz). ^{13}C spectra were recorded as chemical shifts in ppm and multiplicity where appropriate. ^{31}P NMR data were with complete proton decoupling and the chemical shifts were reported in ppm. High resolution mass spectroscopy (HR-MS) was performed on Thermo Q Exactive Plus (FTMS ESI) mass spectrometer and acetonitrile was used to dissolve the sample.

2. Optimization Experiments

General Procedure and Result

To an oven-dried 8 mL vial equipped with a magnetic stir bar was added stavudine (44.8 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (0.2-0.6 mmol), and anhydrous solvent (1 mL), followed by the addition of base (0.2-0.6 mmol). The reaction mixture was stirred at room temperature for 36 hours. Then the reaction mixture was diluted with EtOAc (5 mL), washed with 1M HCl (2 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 mL×2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to afford the crude product. Then triethyl phosphate (18.2 mg, 0.1 mmol) was added as an internal standard and subjected to ^{31}P NMR. The NMR yield was calculated based on the integration ratio of products and internal standards.



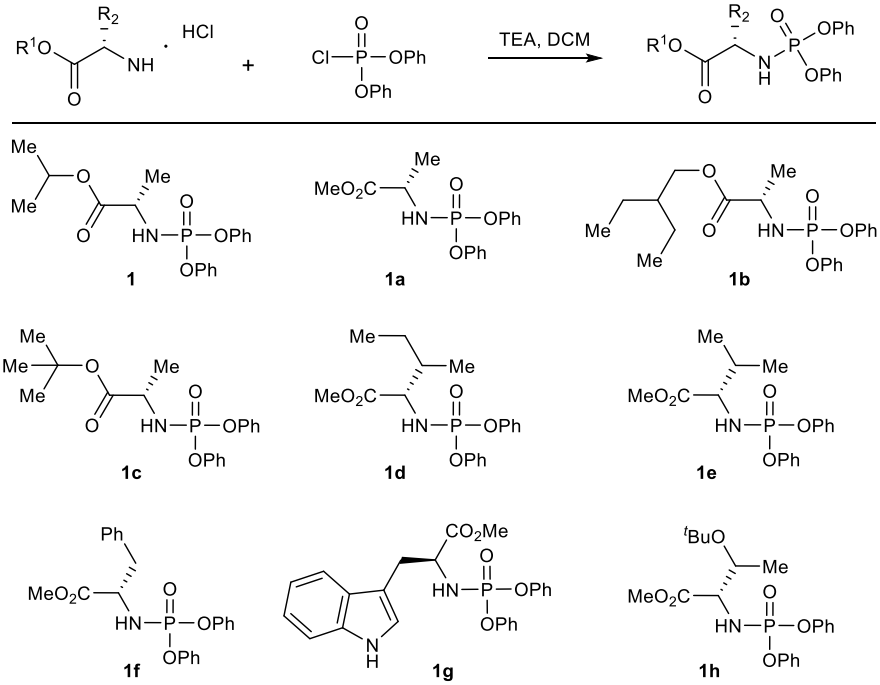
1 **2**, stavudine (d4T) **3**

Entry	**1** (equiv)	**2** (equiv)	base (equiv)	solvent	yield (%) [a]
1	1.5	1.0	DIPEA (2.0)	CH_3CN	--
2	1.5	1.0	DMAP (2.0)	CH_3CN	--
3	1.5	1.0	Pyridine (2.0)	CH_3CN	--
4	1.5	1.0	K_2CO_3 (2.0)	CH_3CN	--
5	1.5	1.0	NaOH (2.0)	CH_3CN	11
6	1.5	1.0	DBU (2.0)	CH_3CN	78
7	2.0	1.0	DBU (2.0)	CH_3CN	91 (88)
8	2.0	1.0	DBU (2.0)	CH_3CN	87[b]
9	2.0	1.0	DBN (2.0)	CH_3CN	77
10	2.0	1.0	TMG (2.0)	CH_3CN	56
11	2.0	1.0	TBD (2.0)	CH_3CN	89
12	3.0	1.0	DBU (2.0)	CH_3CN	92
13	2.0	1.0	DBU (1.0)	CH_3CN	65
14	2.0	1.0	DBU (3.0)	CH_3CN	83
15	2.0	1.0	DBU (2.0)	DCM	71
16	2.0	1.0	DBU (2.0)	DMF	27
17	2.0	1.0	DBU (2.0)	THF	36
18	2.0	1.0	DBU (2.0)	DMSO	15

[a] NMR yield using triethyl phosphate as the internal standard. The yield shown in parentheses is isolated yield, and the product is a ~1:1 mixture of R_P and S_P diastereoisomers. [b] reaction time was 24 hours instead of 36 hours.

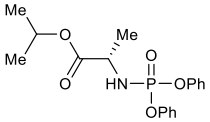
3. Preparation of starting materials

3.1 General procedure for the synthesis of *N*-diphenylphosphoryl amino acid esters



To a 100 mL round bottom flask equipped with a magnetic stir bar was added amino acid ester (10 mmol) and DCM (50 mL), followed by the addition of TEA (4.2 mL, 30 mmol). The reaction mixture was cooled to 0℃ and diphenyl chlorophosphate (2.3 mL, 11 mmol) was added dropwise in 5 mins. After warming to room temperature and stirred for 2 hours, the reaction mixture was diluted with DCM (50 mL), washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was separated and the aqueous layer was extracted with DCM (50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to afford the crude product, which was purified by flash column chromatography to afford the desired product.

3.2 Spectral Characterization of starting materials



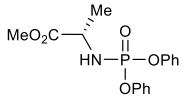
isopropyl (diphenoxyphosphoryl)-*L*-alaninate (1): This compound was prepared according to the General Procedure, using isopropyl *L*-alaninate hydrochloride (1.68 g, 10 mmol), diphenyl

chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a white solid (3.16 g, 87% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 4H), 7.27 – 7.20 (m, 4H), 7.18 – 7.11 (m, 2H), 5.03 – 4.93 (m, 1H), 4.17 – 3.99 (m, 1H), 3.88 (dd, J = 11.8, 9.5 Hz, 1H), 1.36 (d, J = 7.0 Hz, 3H), 1.20 (t, J = 6.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8 (d, $J_{C\text{-}P}$ = 8.2 Hz), 150.9 (d, $J_{C\text{-}P}$ = 7.4 Hz), 150.8 (d, $J_{C\text{-}P}$ = 7.7 Hz), 129.8 (d, $J_{C\text{-}P}$ = 2.7 Hz), 125.2, 120.4 (d, $J_{C\text{-}P}$ = 3.9 Hz), 120.3 (d, $J_{C\text{-}P}$ = 4.3 Hz), 69.4，50.7, 21.8, 21.7, 21.2 (d, $J_{C\text{-}P}$ = 4.5 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.75.

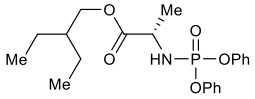


methyl (diphenoxyphosphoryl)-*L*-alaninate (1a): This compound was prepared according to the General Procedure, using *L*-alanine methyl ester hydrochloride (1.40 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 30% EtOAc in Hexanes to 40% EtOAc in PE), the title compound was isolated as a white solid (3.05 g, 91% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 4H), 7.27 – 7.19 (m, 4H), 7.19 – 7.11 (m, 2H), 4.21 – 4.05 (m, 1H), 3.90 – 3.78 (m, 1H), 3.67 (s, 3H), 1.37 (d, J = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8 (d, $J_{C\text{-}P}$ = 7.8 Hz), 150.8 (d, $J_{C\text{-}P}$ = 5.5 Hz), 150.7 (d, $J_{C\text{-}P}$ = 5.6 Hz), 129.8 (d, $J_{C\text{-}P}$ = 3.3 Hz), 125.2, 120.3 (d, $J_{C\text{-}P}$ = 4.8 Hz), 52.6, 50.5, 21.1 (d, $J_{C\text{-}P}$ = 4.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.90.



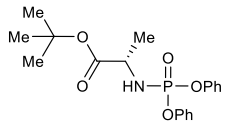
2-ethylbutyl (diphenoxyphosphoryl)-*L*-alaninate (1b): This compound was prepared according to the General Procedure, using *L*-Alanine 2-ethylbutyl ester hydrochloride (2.10 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a colorless oil

(3.85 g, 95% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 4H), 7.27 – 7.20 (m, 4H), 7.19 – 7.13 (m, 2H), 4.20 – 4.08 (m, 1H), 4.08 – 3.96 (m, 2H), 3.83 (dd, *J* = 11.7, 9.4 Hz, 1H), 1.53 – 1.43 (m, 1H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.36 – 1.28 (m, 4H), 0.87 (t, *J* = 7.5 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5 (d, $J_{C\text{-}P}$ = 8.3 Hz), 150.8 (d, $J_{C\text{-}P}$ = 7.1 Hz), 150.7 (d, $J_{C\text{-}P}$ = 7.1 Hz), 129.8 (d, $J_{C\text{-}P}$ = 3.3 Hz), 125.2, 120.4 (d, $J_{C\text{-}P}$ = 4.5 Hz), 120.3 (d, $J_{C\text{-}P}$ = 4.6 Hz), 50.6 (d, $J_{C\text{-}P}$ = 1.5Hz), 40.3, 23.29, 23.26, 21.3 (d, $J_{C\text{-}P}$ = 4.2 Hz), 11.07, 11.05.

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.82.

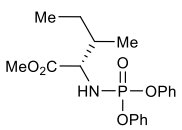


tert-butyl (diphenoxyphosphoryl)-*L*-alaninate (1c): This compound was prepared according to the General Procedure, using methyl *L*-isoleucinate hydrochloride (1.81 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a white solid (3.28 g, 87% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 4H), 7.26 – 7.20 (m, 4H), 7.18 – 7.12 (m, 2H), 4.07 – 3.92 (m, 1H), 3.76 (dd, *J* = 11.9, 9.4 Hz, 1H), 1.42 (s, 9H), 1.34 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5 (d, $J_{C\text{-}P}$ = 8.3 Hz), 150.9 (d, $J_{C\text{-}P}$ = 6.8 Hz), 150.8 (d, $J_{C\text{-}P}$ = 7.0 Hz), 129.8 (d, $J_{C\text{-}P}$ = 1.7 Hz), 125.1, 120.4 (d, $J_{C\text{-}P}$ = 4.6 Hz), 120.3 (d, $J_{C\text{-}P}$ = 4.6 Hz), 82.2, 51.1 (d, $J_{C\text{-}P}$ = 1.3 Hz), 28.0, 21.3 (d, $J_{C\text{-}P}$ = 4.2 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.65.

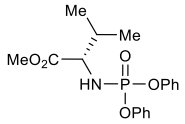


methyl (diphenoxyphosphoryl)-*L*-alloisoleucinate (1d): This compound was prepared according to the General Procedure, using *L*-Alanine tert-butyl ester hydrochloride (1.81 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a white solid (3.36 g, 89% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 7.26 – 7.18 (m, 4H), 7.15 (t, J = 7.4 Hz, 2H), 4.00 – 3.90 (m, 1H), 3.74 (t, J = 10.9 Hz, 1H), 3.62 (s, 3H), 1.80 – 1.66 (m, 1H), 1.48 – 1.36 (m, 1H), 1.19 – 1.04 (m, 1H), 0.86 (t, J = 7.2 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8 (d, $J_{C\text{-}P}$ = 4.6 Hz), 150.8 (d, $J_{C\text{-}P}$ = 6.8 Hz), 129.7 (d, $J_{C\text{-}P}$ = 1.8 Hz), 125.1 (d, $J_{C\text{-}P}$ = 2.1Hz), 120.32 (d, $J_{C\text{-}P}$ = 2.7 Hz), 120.28 (d, $J_{C\text{-}P}$ = 2.8 Hz), 59.3, 52.1, 39.4 (d, $J_{C\text{-}P}$ = 5.4 Hz), 24.8, 15.2, 11.5.

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.16.

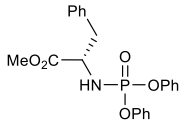


methyl (diphenoxyphosphoryl)-*L*-valinate (1e): This compound was prepared according to the General Procedure, using *L*-Valine methyl ester hydrochloride (1.67 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 40% EtOAc in PE), the title compound was isolated as a white solid (2.87 g, 79% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 4H), 7.27 – 7.19 (m, 4H), 7.15 (t, J = 7.4 Hz, 2H), 3.94 – 3.84 (m, 1H), 3.70 (t, J = 10.7 Hz, 1H), 3.63 (s, 3H), 2.08 – 1.93 (m, 1H), 0.90 (t, J = 6.8 Hz, 6H), 0.86 (t, J = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9 (d, $J_{C\text{-}P}$ = 4.2 Hz), 150.8 (d, $J_{C\text{-}P}$ = 7.4 Hz), 129.8, 125.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 120.34 (d, $J_{C\text{-}P}$ = 2.1 Hz), 120.29 (d, $J_{C\text{-}P}$ = 2.0 Hz), 60.3, 52.2, 32.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 18.9, 17.5.

^{31}P NMR (202 MHz, $CDCl_3$) δ -1.95.

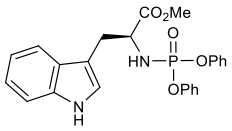


methyl (diphenoxyphosphoryl)-*L*-phenylalaninate (1f): This compound was prepared according to the General Procedure, using *L*-Phenylalanine methyl ester hydrochloride (2.16 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a white solid (3.21g, 78% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 4H), 7.26 – 7.09 (m, 9H), 7.06 – 6.92 (m, 2H), 4.42 – 4.29 (m, 1H), 3.69 (t, J = 11.0 Hz, 1H), 3.60 (s, 3H), 3.10 – 2.88 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 150.8 (d, $J_{C\text{-}P}$ = 4.6 Hz), 150.7 (d, $J_{C\text{-}P}$ = 4.5 Hz), 135.4, 129.8 (d, $J_{C\text{-}P}$ = 1.5 Hz), 129.6, 128.7, 127.3, 125.2, 120.32 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.28 (d, $J_{C\text{-}P}$ = 5.1 Hz), 55.8, 52.3, 40.5 (d, $J_{C\text{-}P}$ = 5.5Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.84.

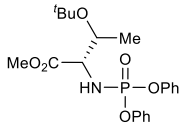


methyl (diphenoxyphosphoryl)-*L*-tryptophanate (1g): This compound was prepared according to the General Procedure, using *L*-tryptophan methyl ester hydrochloride (2.55 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 30% EtOAc in Hexanes to 40% EtOAc in PE), the title compound was isolated as a white solid (3.87 g, 86% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.35 – 7.22 (m, 5H), 7.20 – 7.11 (m, 7H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.85 (s, 1H), 4.47 – 4.28 (m, 1H), 3.73 (t, *J* = 11.2 Hz, 1H), 3.54 (s, 3H), 3.28 (dd, *J* = 14.8, 5.4 Hz, 1H), 3.16 (dd, *J* = 14.7, 5.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8 (d, $J_{C\text{-}P}$ = 5.6 Hz), 150.8 (d, $J_{C\text{-}P}$ = 7.2 Hz), 150.7 (d, $J_{C\text{-}P}$ = 7.2 Hz), 136.3, 129.8 (d, $J_{C\text{-}P}$ = 2.7 Hz), 127.5, 125.2, 123.5, 122.2, 120.3 (d, $J_{C\text{-}P}$ = 5.1 Hz), 120.2 (d, $J_{C\text{-}P}$ = 5.1 Hz), 119.6, 118.6, 111.4, 109.1, 55.2, 52.4, 30.3 (d, $J_{C\text{-}P}$ = 5.8 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ -2.62.



methyl O-(tert-butyl)-N-(diphenoxyphosphoryl)-*L*-allothreoninate (1h): This compound was prepared according to the General Procedure, using O-tert-Butyl-*L*-threonine Methyl ester hydrochloride (2.26 g, 10 mmol), diphenyl chlorophosphate (2.3 mL, 11 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in Hexanes to 30% EtOAc in PE), the title compound was isolated as a white solid (3.33g, 79% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.18 (m, 8H), 7.15 (t, *J* = 7.3 Hz, 2H), 4.14 – 4.05 (m, 1H), 4.05 – 3.85 (m, 2H), 3.61 (s, 3H), 1.13 (d, *J* = 6.2 Hz, 3H), 1.08 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1 (d, $J_{C\text{-}P}$ = 3.2 Hz), 151.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 129.7, 125.0,

120.44 (d, $J_{C\text{-}P}$ = 1.9 Hz), 120.40 (d, $J_{C\text{-}P}$ = 2.1 Hz), 74.1, 68.1 (d, $J_{C\text{-}P}$ = 5.9 Hz), 60.7, 52.2, 28.4, 20.7.

^{31}P NMR (202 MHz, $CDCl_3$) δ -1.83.

4. Transesterification Reaction

4.1 General Procedures

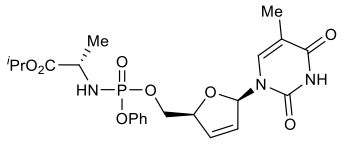
General Procedure A-for primary alcoholic substrates

To an oven-dried 8 mL vial equipped with a magnetic stir bar was added nucleoside or alcohol (0.2 mmol), N-diphenylphosphoryl amino acid esters (0.4 mmol), and anhydrous CH_3CN (1 mL), followed by the addition of DBU (0.4 mmol). The reaction mixture was stirred at room temperature for 36 hours. The reaction mixture was then concentrated under reduced pressure to afford the crude product, which was purified by flash column chromatography to afford desired product.

General Procedure B-for secondary alcoholic substrates

To an oven-dried 8 mL vial equipped with a magnetic stir bar was added nucleoside or alcohol (0.2 mmol), N-diphenylphosphoryl amino acid esters (0.4 mmol), and anhydrous CH_3CN (1 mL), followed by the addition of DBU (0.4 mmol). The reaction mixture was heated to 80℃ and stirred for 36 hours. The reaction mixture was then concentrated under reduced pressure to afford the crude product, which was purified by flash column chromatography to afford desired product.

4.2 Spectral Characterization of the Products



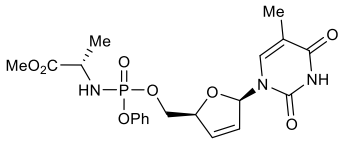
isopropyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (3): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated as a colorless oil (86.8 mg, 88% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.50 – 9.42 (m, 1H), 7.36 – 7.26 (m, 3H), 7.23 – 7.12 (m, 3H), 7.05 – 7.00 (m, 1H), 6.37 – 6.26 (m, 1H), 5.92 – 5.82 (m, 1H), 5.05 – 4.95 (m, 2H), 4.43 – 4.25 (m, 2H), 4.01 – 3.88 (m, 2H), 1.89 – 1.79 (m, 3H), 1.38 – 1.27 (m, 3H), 1.25 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 173.0 (d, $J_{C\text{-}P}$ = 7.8 Hz), 164.1, 164.0, 151.1, 151.0, 150.5 (d, $J_{C\text{-}P}$ = 6.4 Hz), 150.4 (d, $J_{C\text{-}P}$ = 6.1 Hz), 136.0, 135.7, 133.4, 133.2, 129.9, 129.8, 127.6, 127.5, 125.3, 125.2, 120.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 111.5, 111.3, 89.8, 89.6, 84.8 (d, $J_{C\text{-}P}$ = 8.4 Hz), 84.7 (d, $J_{C\text{-}P}$ = 8.7 Hz), 69.5, 69.4, 67.1 (d, $J_{C\text{-}P}$ = 5.3 Hz), 66.6 (d, $J_{C\text{-}P}$ = 4.8 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.7 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.7 Hz), 21.7 , 21.6 (d, $J_{C\text{-}P}$ = 2.8 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.5 Hz), 21.00 (d, $J_{C\text{-}P}$ = 4.7 Hz), 12.5, 12.4.

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.34, 2.76.

HRMS (ESI) *m/z* calcd for $C_{22}H_{29}N_3O_8P^+$ [$(M+H)^+$] 494.1687, found 494.1693.



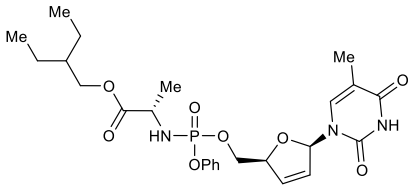
methyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (4): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), methyl (diphenoxyphosphoryl)-*L*-alaninate (134.0 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 5% MeOH in EtOAc), the title compound was isolated as a colorless oil (81.9 mg, 88% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 – 9.57 (m, 1H), 7.36 – 7.24 (m, 3H), 7.22 – 7.10 (m, 3H), 7.06 – 6.97 (m, 1H), 6.38 – 6.20 (m, 1H), 5.94 – 5.79 (m, 1H), 5.07 – 4.93 (m, 1H), 4.43 – 4.20 (m, 2H), 4.17 – 3.87 (m, 2H), 3.74 – 3.59 (m, 3H), 1.89 – 1.75 (m, 3H), 1.38 – 1.27 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0 (d, $J_{C\text{-}P}$ = 7.2 Hz), 173.9 (d, $J_{C\text{-}P}$ = 7.5 Hz), 163.9, 163.8, 150.9, 150.8, 150.4 (d, $J_{C\text{-}P}$ = 6.3 Hz), 150.3 (d, $J_{C\text{-}P}$ = 6.4 Hz), 135.9, 135.7, 133.4, 133.1, 129.8, 129.7, 127.5, 127.4, 125.3, 125.2, 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.0 (d, $J_{C\text{-}P}$ = 4.9 Hz), 111.4, 111.3, 89.8, 89.6, 84.7 (d, $J_{C\text{-}P}$ = 8.7 Hz), 84.6 (d, $J_{C\text{-}P}$ = 9.4 Hz), 67.2, 67.1, 66.6, 66.5, 52.63, 52.61, 50.2 (d, $J_{C\text{-}P}$ = 1.6 Hz), 50.1 (d, $J_{C\text{-}P}$ = 1.7 Hz), 21.0 (d, $J_{C\text{-}P}$ = 4.7 Hz), 20.9 (d, $J_{C\text{-}P}$ = 5.0 Hz), 12.4, 12.3.

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.29, 2.67.

HRMS (ESI) *m/z* calcd for $C_{20}H_{25}N_3O_8P^+$ [$(M+H)^+$] 466.1374, found 466.1377.



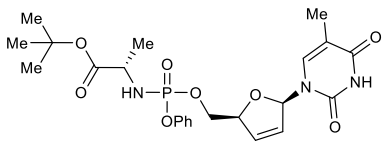
2-ethylbutyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (5): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), 2-ethylbutyl (diphenoxyphosphoryl)-*L*-alaninate (162.2 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated as a colorless oil (97.5 mg, 91% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 – 9.56 (m, 1H), 7.39 – 7.24 (m, 3H), 7.24 – 7.10 (m, 3H), 7.06 – 6.99 (m, 1H), 6.37 – 6.23 (m, 1H), 5.92 – 5.81 (m, 1H), 5.07 – 4.93 (m, 1H), 4.46 – 4.25 (m, 2H), 4.15 – 3.93 (m, 4H), 1.99 – 1.75 (m, 3H), 1.54 – 1.42 (m, 1H), 1.41 – 1.28 (m, 7H), 0.90 – 0.83 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8 (d, $J_{C\text{-}P}$ = 7.6 Hz), 173.7 (d, $J_{C\text{-}P}$ = 7.8 Hz), 164.2, 164.1, 151.08, 151.06, 150.4 (d, $J_{C\text{-}P}$ = 6.2 Hz), 150.3 (d, $J_{C\text{-}P}$ = 5.9 Hz), 135.9, 135.7, 133.3, 133.1, 129.8, 129.7, 127.5, 127.4, 125.22, 125.17, 120.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 111.5, 111.3, 89.8, 89.6, 84.7 (d, $J_{C\text{-}P}$ = 8.5 Hz), 84.6 (d, $J_{C\text{-}P}$ = 8.6 Hz), 67.7, 67.11, 67.07, 66.61, 66.57, 50.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 50.2 (d, $J_{C\text{-}P}$ = 1.8 Hz), 40.3, 40.2, 23.18 (d, $J_{C\text{-}P}$ = 4.1 Hz), 23.16 (d, $J_{C\text{-}P}$ = 4.8 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.6 Hz), 21.0 (d, $J_{C\text{-}P}$ = 4.6 Hz), 12.4, 12.3, 10.98 (d, $J_{C\text{-}P}$ = 3.9 Hz), 10.97 (d, $J_{C\text{-}P}$ = 3.0 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.35, 2.78.

HRMS (ESI) *m/z* calcd for $C_{25}H_{35}N_3O_8P^+$ [$(M+H)^+$] 536.2156, found 536.2162.



tert-butyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (6): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), tert-butyl (diphenoxyphosphoryl)-*L*-alaninate (150.9 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated

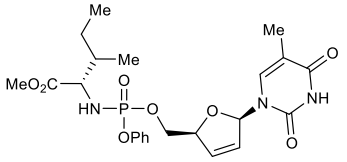
as a colorless oil (93.4 mg, 92% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 – 9.32 (d, J = 12.3 Hz, 1H), 7.38 – 7.24 (m, 3H), 7.24 – 7.11 (m, 3H), 7.07 – 6.97 (m, 1H), 6.39 – 6.22 (m, 1H), 5.99 – 5.73 (m, 1H), 5.11 – 4.85 (m, 1H), 4.45 – 4.20 (m, 2H), 4.01 – 3.75 (m, 2H), 1.92 – 1.75 (m, 3H), 1.50 – 1.35 (m, 9H), 1.35 – 1.23 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8 (d, $J_{C\text{-}P}$ = 7.8 Hz), 172.7 (d, $J_{C\text{-}P}$ = 8.2 Hz), 164.08, 164.05, 151.07, 151.05, 150.5 (d, $J_{C\text{-}P}$ = 6.4 Hz), 150.4 (d, $J_{C\text{-}P}$ = 6.2 Hz), 136.0, 135.7, 133.4, 133.2, 129.84, 129.78, 127.6, 127.4, 125.22, 125.18, 120.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 111.5, 111.3, 89.8, 89.6, 84.8 (d, $J_{C\text{-}P}$ = 8.4 Hz), 84.7 (d, $J_{C\text{-}P}$ = 8.6 Hz), 82.4, 82.3, 67.1, 67.0, 66.6, 66.5, 50.8 (d, $J_{C\text{-}P}$ = 1.5 Hz), 50.7 (d, $J_{C\text{-}P}$ = 1.8 Hz), 28.0, 21.2 (d, $J_{C\text{-}P}$ = 4.4 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.4 Hz), 12.43, 12.42.

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.41, 2.93.

HRMS (ESI) *m/z* calcd for $C_{23}H_{30}N_3NaO_8P^+$ [$(M+Na)^+$] 530.1663, found 530.1656.



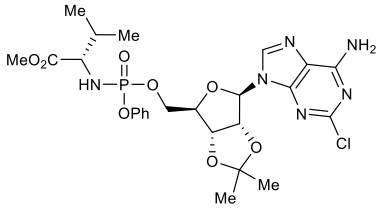
methyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alloisoleucinate (7): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), methyl (diphenoxyphosphoryl)-*L*-alloisoleucinate (150.9 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated as a colorless oil (90.3 mg, 89% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 – 9.43 (m, 1H), 7.43 – 7.08 (m, 6H), 7.07 – 6.96 (m, 1H), 6.42 – 6.16 (m, 1H), 5.94 – 5.81 (m, 1H), 5.08 – 4.93 (m, 1H), 4.47 – 4.20 (m, 2H), 3.98 – 3.75 (m, 2H), 3.74 – 3.59 (m, 3H), 1.92 – 1.64 (m, 4H), 1.51 – 1.00 (m, 2H), 0.96 – 0.70 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.25 (d, $J_{C\text{-}P}$ = 6.8 Hz), 173.16 (d, $J_{C\text{-}P}$ = 5.7 Hz), 164.1, 164.0, 151.1, 150.52, 150.47, 135.9, 135.6, 133.3, 133.1, 129.8, 129.7, 127.51, 127.46, 125.2, 125.1, 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 111.5, 111.4, 89.9, 89.6, 84.7 (d, $J_{C\text{-}P}$ = 8.5 Hz), 84.6 (d, $J_{C\text{-}P}$ = 8.6 Hz), 67.30, 67.26, 66.6, 59.2, 59.0, 52.2, 39.2 (d, $J_{C\text{-}P}$ = 6.8 Hz), 39.1 (d, $J_{C\text{-}P}$ = 5.9 Hz), 24.8, 24.7, 15.3, 12.42, 12.37, 11.5.

^{31}P NMR (202 MHz, CDCl3) δ 3.98, 3.40.

HRMS (ESI) *m/z* calcd for $C_{23}H_{30}N_3NaO_8P^+$ [(M+Na)$^+$] 530.1663, found 530.1658.



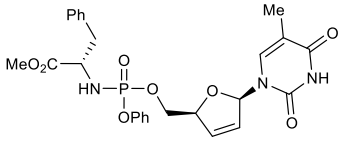
methyl ((((3aR,4R,6R,6aR)-6-(6-amino-2-chloro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro [3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)-*L*-valinate (8): This compound was prepared according to the General Procedure A, using 2-chloro-2',3'-O-isopropylideneadenosine (68.4 mg, 0.2 mmol), methyl (diphenoxyphosphoryl)-*L*-valinate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 10% MeOH in EtOAc), the title compound was isolated as a white solid (96.5 mg, 79% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 1H), 7.22 (t, J = 7.8 Hz, 2H), 7.16 – 7.04 (m, 3H), 6.87 – 6.75 (m, 2H), 6.09 – 6.01 (m, 1H), 5.30 – 4.81 (m, 2H), 4.49 – 4.40 (m, 1H), 4.39 – 4.00 (m, 3H), 3.78 – 3.68 (m, 1H), 3.66 – 3.56 (m, 3H), 2.01 – 1.84 (m, 1H), 1.63 – 1.49 (m, 3H), 1.40 – 1.25 (m, 3H), 0.91 – 0.69 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4 (d, $J_{C\text{-}P}$ = 3.3 Hz), 173.3 (d, $J_{C\text{-}P}$ = 3.4 Hz), 156.61, 156.58, 154.34, 154.29, 150.7 (d, $J_{C\text{-}P}$ = 6.8 Hz), 150.6 (d, $J_{C\text{-}P}$ = 6.6 Hz), 150.3, 150.1, 140.2, 139.9, 129.66, 129.62, 125.0, 124.9, 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 118.86, 118.84, 114.72, 114.65, 90.7, 90.5, 85.7 (d, $J_{C\text{-}P}$ = 8.2 Hz), 85.1 (d, $J_{C\text{-}P}$ = 7.9 Hz), 84.3, 84.1, 81.3, 81.2, 66.5 (d, $J_{C\text{-}P}$ = 5.5 Hz), 66.3 (d, $J_{C\text{-}P}$ = 5.4 Hz), 60.2, 60.1, 52.21, 52.17, 32.3 (d, $J_{C\text{-}P}$ = 6.2 Hz), 32.1 (d, $J_{C\text{-}P}$ = 6.3 Hz), 27.21, 27.16, 25.4, 25.3, 18.89, 18.86, 17.5.

^{31}P NMR (202 MHz, CDCl3) δ 3.63, 3.46.

HRMS (ESI) *m/z* calcd for $C_{25}H_{33}ClN_6O_8P^+$ [(M+H)$^+$] 611.1781, found 611.1779.



methyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-phenylalaninate (9): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), methyl

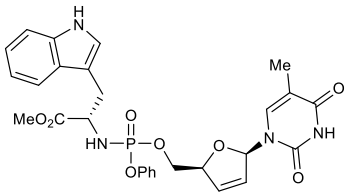
(diphenoxyphosphoryl)-*L*-phenylalaninate (164.6 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated as a colorless oil (94.2 mg, 87% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 – 9.25 (m, 1H), 7.41 – 6.84 (m, 12H), 6.31 – 6.11 (m, 1H), 5.91 – 5.75 (m, 1H), 4.97 – 4.80 (m, 1H), 4.39 – 3.71 (m, 4H), 3.68 – 3.51 (m, 3H), 3.08 – 2.81 (m, 2H), 1.87 – 1.66 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9 (d, $J_{C\text{-}P}$ = 3.7 Hz), 172.8 (d, $J_{C\text{-}P}$ = 5.6 Hz), 160.1, 160.0, 151.1, 151.04, 151.00, 150.4 (d, $J_{C\text{-}P}$ = 6.4 Hz), 150.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 135.9, 135.7, 135.6, 133.3, 133.0, 129.83, 129.79, 129.50, 129.47, 128.72, 128.66, 127.6, 127.4, 127.3, 125.2, 120.2 (d, $J_{C\text{-}P}$ = 4.4 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 111.5, 111.4, 89.8, 89.6, 84.7 (d, $J_{C\text{-}P}$ = 8.3 Hz), 84.6 (d, $J_{C\text{-}P}$ = 8.8 Hz), 67.0, 66.4, 55.8, 55.6, 52.6, 52.4, 40.4 (d, $J_{C\text{-}P}$ = 2.6 Hz), 40.3 (d, $J_{C\text{-}P}$ = 2.5 Hz), 12.38, 12.36.

^{31}P NMR (202 MHz, CDCl3) δ 3.06, 2.68.

HRMS (ESI) *m/z* calcd for $C_{26}H_{28}N_3NaO_8P^+$ [$(M+Na)^+$] 564.1506, found 564.1501.



methyl ((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-tryptophanate (10): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), methyl (diphenoxyphosphoryl)-*L*-tryptophanate (180.2 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 2% MeOH in EtOAc), the title compound was isolated as a white solid (90.8 mg, 78% yield, ~1:1 mixture of two diastereomers).

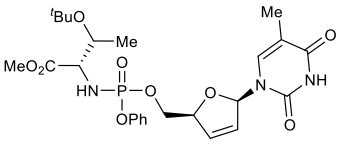
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 – 9.44 (m, 1H), 8.80 – 8.68 (m, 1H), 7.46 – 7.39 (m, 1H), 7.31 – 6.99 (m, 9H), 6.97 – 6.84 (m, 2H), 6.19 – 6.01 (m, 1H), 5.79 – 5.71 (m, 1H), 4.83 –4.76 (m, 1H), 4.32 – 4.13 (m, 2H), 4.03 – 3.84 (m, 2H), 3.61 – 3.52 (m, 3H), 3.23 – 3.05 (m, 2H), 1.77 – 1.70 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5 (d, $J_{C\text{-}P}$ = 3.8 Hz), 173.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 164.2, 164.1, 151.2, 151.1, 150.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 150.4 (d, $J_{C\text{-}P}$ = 5.8 Hz), 136.3, 136.2, 136.0, 135.8, 133.4, 133.1, 129.80, 129.76, 127.5, 127.32, 127.30, 127.1, 125.20, 125.17, 123.59, 123.57, 122.09, 122.07, 120.2

(d, $J_{C\text{-}P}$ = 3.3 Hz), 120.1 (d, $J_{C\text{-}P}$ = 3.3 Hz), 119.56, 119.52, 118.38, 118.36, 111.53, 111.46, 111.38, 109.2, 109.1, 89.9, 89.6, 84.7 (d, $J_{C\text{-}P}$ = 8.3 Hz), 84.6 (d, $J_{C\text{-}P}$ = 9.1 Hz), 67.0 (d, $J_{C\text{-}P}$ = 5.1 Hz), 66.6 (d, $J_{C\text{-}P}$ = 5.0 Hz), 55.3, 55.2, 52.5, 30.2, 30.1, 12.4.

^{31}P NMR (202 MHz, CDCl3) δ 3.35, 2.96.

HRMS (ESI) *m/z* calcd for $C_{28}H_{30}N_4O_8P^+$ [$(M+H)^+$] 581.1796, found 581.1791.



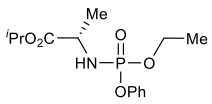
methyl O-(tert-butyl)-N-((((2S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,5-dihydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-allothreoninate (11): This compound was prepared according to the General Procedure A, using stavudine (44.8 mg, 0.2 mmol), methyl O-(tert-butyl)-N-(diphenoxyphosphoryl)-*L*-allothreoninate (168.6 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in Hexanes to 100% EtOAc), the title compound was isolated as a colorless oil (91.6 mg, 83% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 – 9.37 (m, 1H), 7.41 – 7.11 (m, 6H), 7.06 – 6.98 (m, 1H), 6.38 – 6.24 (m, 1H), 5.90 –5.81 (m, 1H), 5.07 – 4.96 (m, 1H), 4.52 – 4.27 (m, 2H), 4.13 – 4.05 (m, 1H), 3.97 – 3.88 (m, 1H), 3.84 – 3.74 (m, 1H), 3.70 – 3.61 (m, 3H), 1.88 – 1.77 (m, 3H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5 (d, $J_{C\text{-}P}$ = 2.3 Hz), 172.1 (d, $J_{C\text{-}P}$ = 2.5 Hz), 164.07, 164.03, 151.1, 151.0, 150.62 (d, $J_{C\text{-}P}$ = 6.4 Hz), 150.58 (d, $J_{C\text{-}P}$ = 6.3 Hz), 136.0, 135.7, 133.5, 133.2, 129.71, 129.67, 127.4, 127.3, 125.13, 125.05, 120.3 (d, $J_{C\text{-}P}$ = 4.8 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 111.44, 111.38, 89.8, 89.6, 84.9 (d, $J_{C\text{-}P}$ = 8.6 Hz), 84.7 (d, $J_{C\text{-}P}$ = 8.8 Hz), 74.2, 74.1, 67.81 (d, $J_{C\text{-}P}$ = 6.3 Hz), 67.79 (d, $J_{C\text{-}P}$ = 6.4 Hz), 67.13, 67.09, 66.73, 66.69, 60.43, 60.36, 52.23, 52.19, 28.3, 20.9, 20.8, 12.4, 12.3.

^{31}P NMR (202 MHz, CDCl3) δ 4.08, 3.72.

HRMS (ESI) *m/z* calcd for $C_{25}H_{34}N_3NaO_9P^+$ [$(M+Na)^+$] 574.1925, found 574.1921.



isopropyl (ethoxy(phenoxy)phosphoryl)-*L*-alaninate (12): This compound was prepared according to the General Procedure A, using ethanol (11.7 μL, 0.2 mmol), isopropyl

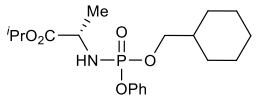
(diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 50% EtOAc in PE), the title compound was isolated as a colorless oil (51.1 mg, 81% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.23 – 7.16 (m, 2H), 7.14 – 7.09 (m, 1H), 5.04 – 4.93 (m, 1H), 4.19 – 4.11 (m, 2H), 4.00 – 3.89 (m, 1H), 3.57 (q, J = 10.3 Hz, 1H), 1.36 – 1.28 (m, 6H), 1.25 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 7.5 Hz), 173.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 151.0 (d, $J_{C\text{-}P}$ = 6.9 Hz), 150.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 129.7, 129.6, 124.8, 124.7, 120.3 (d, $J_{C\text{-}P}$ = 4.8 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 69.3, 69.2, 63.4 (d, $J_{C\text{-}P}$ = 5.5 Hz), 63.3 (d, $J_{C\text{-}P}$ = 5.5 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.5 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.4 Hz), 21.8 (d, $J_{C\text{-}P}$ = 2.7 Hz), 21.7 (d, $J_{C\text{-}P}$ = 3.6 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.5 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 6.1 Hz), 16.11(d, $J_{C\text{-}P}$ = 6.1 Hz).

^{31}P NMR (202 MHz, CDCl3) δ 2.38, 2.25.

HRMS (ESI) *m/z* calcd for $C_{14}H_{22}NNaO_5P^+$ $[(M+Na)^+]$ 338.1128, found 338.1123.



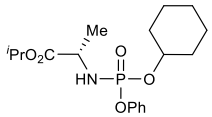
isopropyl ((cyclohexylmethoxy)(phenoxy)phosphoryl)-*L*-alaninate (13): This compound was prepared according to the General Procedure A, using cyclohexylmethanol (22.8 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 40% EtOAc in PE), the title compound was isolated as a colorless oil (59.8 mg, 78% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.23 – 7.17 (m, 2H), 7.15 – 7.09 (m, 1H), 5.05 – 4.94 (m, 1H), 4.00 – 3.81 (m, 3H), 3.57 – 3.48 (m, 1H), 1.76 – 1.56 (m, 6H), 1.34 (d, J = 7.1 Hz, 3H), 1.27 – 1.08 (m, 9H), 0.99 – 0.88 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 7.8 Hz), 173.1 (d, $J_{C\text{-}P}$ = 8.6 Hz), 151.1 (d, $J_{C\text{-}P}$ = 6.9 Hz), 151.0 (d, $J_{C\text{-}P}$ = 7.4 Hz), 129.7, 129.6, 124.8, 124.7, 120.4 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 72.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 72.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 69.2, 50.5 (d, $J_{C\text{-}P}$ = 1.6 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.2 Hz), 38.4 (d, $J_{C\text{-}P}$ = 7.3 Hz), 38.3 (d, $J_{C\text{-}P}$ = 7.3 Hz), 29.3 (d, $J_{C\text{-}P}$ = 5.6 Hz), 29.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 26.4, 25.7, 21.8 (d, $J_{C\text{-}P}$ = 7.4 Hz), 21.7 (d, $J_{C\text{-}P}$ = 9.2 Hz), 21.3 (d, $J_{C\text{-}P}$ = 4.3 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.48, 2.38.

HRMS (ESI) *m/z* calcd for $C_{19}H_{30}NNaO_5P^+$ [$(M+Na)^+$] 406.1754, found 406.1747.



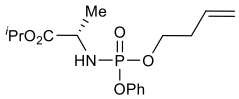
isopropyl ((cyclohexyloxy)(phenoxy)phosphoryl)-*L*-alaninate (14): This compound was prepared according to the General Procedure B, using cyclohexanol (20.0 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 40% EtOAc in PE), the title compound was isolated as a colorless oil (59.1 mg, 80% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.16 (m, 2H), 7.14 – 7.09 (m, 1H), 5.07 – 4.92 (m, 1H), 4.52 – 4.39 (m, 1H), 4.02 – 3.88 (m, 1H), 3.55 – 3.44 (m, 1H), 2.02 – 1.85 (m, 2H), 1.78 – 1.62 (m, 2H), 1.61 – 1.43 (m, 3H), 1.39 – 1.17 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 1.2 Hz), 173.1 (d, $J_{C\text{-}P}$ = 1.3 Hz), 151.2 (d, $J_{C\text{-}P}$ = 7.1 Hz), 151.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 129.7, 129.6, 124.7, 124.6, 120.4 (d, $J_{C\text{-}P}$ = 4.7 Hz), 120.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 77.4, 77.1, 69.2, 50.5 (d, $J_{C\text{-}P}$ = 1.6 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.1 Hz), 33.5 (d, $J_{C\text{-}P}$ = 8.9 Hz), 33.4 (d, $J_{C\text{-}P}$ = 9.1 Hz), 33.3 (d, $J_{C\text{-}P}$ = 3.9 Hz), 33.2 (d, $J_{C\text{-}P}$ = 3.7 Hz), 25.2, 23.6, 23.5, 21.8, 21.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.2 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.4 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 1.46, 1.30.

HRMS (ESI) *m/z* calcd for $C_{18}H_{28}NNaO_5P^+$ [$(M+Na)^+$] 392.1597, found 392.1591.



isopropyl ((but-3-en-1-yloxy)(phenoxy)phosphoryl)-*L*-alaninate (15): This compound was prepared according to the General Procedure A, using 3-buten-1-ol (14.4 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 40% EtOAc in PE), the title compound was isolated as a colorless oil (51.9 mg, 76% yield, ~1:1 mixture of two diastereomers).

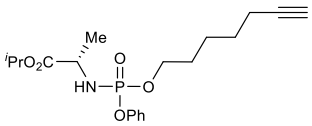
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.22 – 7.16 (m, 2H), 7.15 – 7.09 (m, 1H), 5.81 – 5.69 (m, 1H), 5.13 – 5.03 (m, 2H), 5.03 – 4.94 (m, 1H), 4.19 – 4.05 (m, 2H), 4.02 – 3.87 (m, 1H), 3.58 (q, *J* = 11.2 Hz, 1H), 2.48 – 2.35 (m, 2H), 1.36 – 1.32 (m, 3H), 1.25 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 3.7 Hz), 173.0 (d, $J_{C\text{-}P}$ = 4.1 Hz), 151.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 150.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 133.6, 133.5, 129.7, 129.6, 124.9, 124.8, 120.4 (d, $J_{C\text{-}P}$ = 5.0 Hz),

120.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 117.8, 117.7, 69.2, 66.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 66.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.7 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.4 Hz), 34.7 (d, $J_{C\text{-}P}$ = 5.6 Hz), 34.6 (d, $J_{C\text{-}P}$ = 6.0 Hz), 21.8 (d, $J_{C\text{-}P}$ = 2.8 Hz), 21.7 (d, $J_{C\text{-}P}$ = 3.9 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 21.1 (d, $J_{C\text{-}P}$ = 5.2 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.36, 2.27.

HRMS (ESI) *m/z* calcd for $C_{16}H_{24}NNaO_5P^+$ [$(M+Na)^+$] 364.1284, found 364.1275.



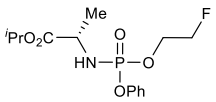
isopropyl ((hept-6-yn-1-yloxy)(phenoxy)phosphoryl)-*L*-alaninate (16): This compound was prepared according to the General Procedure A, using hept-6-yn-1-ol (22.4 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 40% EtOAc in PE), the title compound was isolated as a colorless oil (59.5mg, 78% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.22 – 7.16 (m, 2H), 7.14 – 7.09 (m, 1H), 5.03 – 4.94 (m, 1H), 4.14 – 4.01 (m, 2H), 4.00 – 3.87 (m, 1H), 3.56 (q, *J* = 10.6 Hz, 1H), 2.19 – 2.12 (m, 2H), 1.92 (t, *J* = 2.7 Hz, 1H), 1.72 – 1.62 (m, 2H), 1.56 – 1.41 (m, 4H), 1.36 – 1.31 (m, 3H), 1.25 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 173.0 (d, $J_{C\text{-}P}$ = 5.6 Hz), 151.0 (d, $J_{C\text{-}P}$ = 6.9 Hz), 150.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 129.7, 129.6, 124.8, 124.7, 120.3 (d, $J_{C\text{-}P}$ = 4.7 Hz), 120.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 84.3, 69.2, 68.6, 67.0 (d, $J_{C\text{-}P}$ = 5.8 Hz), 66.9 (d, $J_{C\text{-}P}$ = 5.9 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.5 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.4 Hz), 29.8 (d, $J_{C\text{-}P}$ = 3.7 Hz), 29.7 (d, $J_{C\text{-}P}$ = 3.7 Hz), 28.0, 24.7, 24.6, 21.8 (d, $J_{C\text{-}P}$ = 3.6 Hz), 21.7 (d, $J_{C\text{-}P}$ = 4.1 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.4 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.7 Hz), 21.1.

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.43, 2.34.

HRMS (ESI) *m/z* calcd for $C_{19}H_{28}NNaO_5P^+$ [$(M+Na)^+$] 404.1597, found 404.1591.



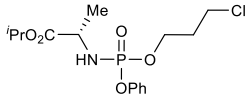
isopropyl ((2-fluoroethoxy)(phenoxy)phosphoryl)-*L*-alaninate (17): This compound was prepared according to the General Procedure A, using 2-fluoroethan-1-ol (12.8 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 50% EtOAc in PE), the title compound was isolated as a colorless oil (50.7 mg, 76% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.24 – 7.18 (m, 2H), 7.17 – 7.11 (m, 1H), 5.05 – 4.92 (m, 1H), 4.66 – 4.58 (m, 1H), 4.56 – 4.48 (m, 1H), 4.41 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H), 3.76 – 3.64 (m, 1H), 1.35 (d, J = 7.2 Hz, 3H), 1.25 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 173.0, 150.8 (d, $J_{C\text{-}P}$ = 6.2 Hz), 150.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 129.8, 129.7, 125.0, 120.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 82.8 (t, $J_{C\text{-}P,C\text{-}F}$ = 7.2 Hz), 81.5 (d, $J_{C\text{-}P,C\text{-}F}$ = 7.1 Hz), 69.4, 69.3, 65.9 (dd, $J_{C\text{-}P,C\text{-}F}$ = 13.8, 5.2 Hz), 65.7 (dd, $J_{C\text{-}P,C\text{-}F}$ = 13.8, 5.3 Hz), 50.5 (d, $J_{C\text{-}P}$ = 1.5 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.2 Hz), 21.8, 21.7 (d, $J_{C\text{-}P}$ = 2.8Hz), 21.0 (d, $J_{C\text{-}P}$ = 4.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.67, 2.57.

HRMS (ESI) *m/z* calcd for $C_{14}H_{21}FNNaO_5P^+$ [$(M+Na)^+$] 356.1034, found 356.1027.



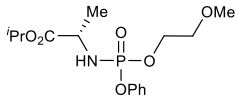
isopropyl ((3-chloropropoxy)(phenoxy)phosphoryl)-*L*-alaninate (18): This compound was prepared according to the General Procedure A, using 3-chloropropan-1-ol (18.9 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 50% EtOAc in PE), the title compound was isolated as a colorless oil (58.2 mg, 80% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.16 (m, 2H), 7.16 – 7.10 (m, 1H), 5.05 – 4.93 (m, 1H), 4.31 – 4.16 (m, 2H), 4.56 – 4.48 (m, 1H), 4.03 – 3.87 (m, 1H), 3.71 – 3.60 (m, 1H), 3.58 (q, J = 7.1 Hz, 2H), 2.16 – 2.04 (m, 2H), 1.37 – 1.32 (m, 3H), 1.25 – 1.18 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 3.2 Hz), 173.0 (d, $J_{C\text{-}P}$ = 3.8 Hz), 150.9 (d, $J_{C\text{-}P}$ = 6.5 Hz), 150.8 (d, $J_{C\text{-}P}$ = 6.9 Hz), 129.8, 129.7, 124.9, 120.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.9 Hz), 69.3, 63.7 (d, $J_{C\text{-}P}$ = 5.5 Hz), 63.6 (d, $J_{C\text{-}P}$ = 5.3 Hz), 50.5 (d, $J_{C\text{-}P}$ = 1.8 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.4 Hz), 40.8, 40.7, 33.1, 33.0, 21.8 (d, $J_{C\text{-}P}$ = 2.9 Hz), 21.7 (d, $J_{C\text{-}P}$ = 3.9 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.5 Hz), 21.0 (d, $J_{C\text{-}P}$ = 5.0 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.45, 2.32.

HRMS (ESI) *m/z* calcd for $C_{15}H_{23}ClNNaO_5P^+$ [$(M+Na)^+$] 386.0895, found 386.0887.



isopropyl ((2-methoxyethoxy)(phenoxy)phosphoryl)-*L*-alaninate (19): This compound was prepared according to the General Procedure A, using 2-methoxyethan-1-ol (15.2 mg, 0.2 mmol),

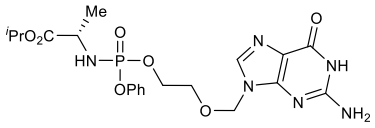
isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 30% EtOAc in PE to 75% EtOAc in PE), the title compound was isolated as a colorless oil (55.9 mg, 81% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.17 (m, 2H), 7.14 – 7.09 (m, 1H), 5.03 – 4.93 (m, 1H), 4.30 – 4.16 (m, 2H), 4.03 – 3.92 (m, 1H), 3.74 (q, J = 8.5 Hz, 1H), 4.62 – 4.53 (m, 1H), 3.38 – 3.31 (m, 3H), 1.37 – 1.31 (m, 3H), 1.23 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 6.5 Hz), 173.0 (d, $J_{C\text{-}P}$ = 6.4 Hz), 151.0 (d, $J_{C\text{-}P}$ = 6.5 Hz), 150.9 (d, $J_{C\text{-}P}$ = 6.5 Hz), 129.7, 129.6, 124.9, 124.8, 120.4 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.3 (d, $J_{C\text{-}P}$ = 5.1 Hz), 71.5 (d, $J_{C\text{-}P}$ = 4.8 Hz), 71.4 (d, $J_{C\text{-}P}$ = 4.7 Hz), 69.2, 69.1, 66.1 (d, $J_{C\text{-}P}$ = 5.5 Hz), 66.0 (d, $J_{C\text{-}P}$ = 5.5 Hz), 59.1, 59.0, 50.4 (d, $J_{C\text{-}P}$ = 1.8 Hz), 50.3 (d, $J_{C\text{-}P}$ = 1.7 Hz), 21.8 (d, $J_{C\text{-}P}$ = 0.8 Hz), 21.7 (d, $J_{C\text{-}P}$ = 1.9 Hz), 21.2 (d, $J_{C\text{-}P}$ = 4.2 Hz), 21.1 (d, $J_{C\text{-}P}$ = 4.3 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.83, 2.69.

HRMS (ESI) *m/z* calcd for $C_{15}H_{24}NNaO_6P^+$ $[(M+Na)^+]$ 368.1233, found 368.1226.



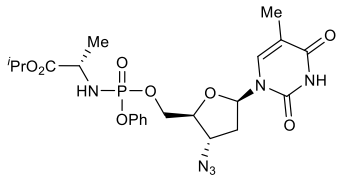
isopropyl ((2-((2-amino-6-oxo-1,6-dihydro-9H-purin-9-yl)methoxy)ethoxy)(phenoxy)phosphoryl)-*L*-alaninate (20): This compound was prepared according to the General Procedure A, using acyclovir (45.0 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% MeOH in EtOAc to 40% MeOH in EtOAc), the title compound was isolated as a white solid (86.0 mg, 87% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.11 (s, 1H), 7.85 (s, 1H), 7.31 – 7.23 (m, 2H), 7.19 (t, J = 7.5 Hz, 2H), 7.13 – 6.98 (m, 3H), 5.41 (s, 2H), 5.03 – 4.86 (m, 1H), 4.46 – 4.08 (m, 3H), 4.06 – 3.89 (m, 1H), 3.85 – 3.61 (m, 2H), 1.46 – 1.28 (m, 3H), 1.23 – 1.09 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 7.2 Hz), 173.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 158.6, 154.7, 151.6, 150.6 (d, $J_{C\text{-}P}$ = 6.1 Hz), 150.7 (d, $J_{C\text{-}P}$ = 6.5 Hz), 137.9, 129.7, 129.6, 125.0, 120.3 (d, $J_{C\text{-}P}$ = 5.2 Hz), 120.2 (d, $J_{C\text{-}P}$ = 5.4 Hz), 116.9, 72.8, 69.3, 69.2, 68.1, 67.9, 65.8, 50.5, 50.4, 21.7 (d, $J_{C\text{-}P}$ = 5.7 Hz), 21.6 (d, $J_{C\text{-}P}$ = 2.9 Hz), 20.9 (d, $J_{C\text{-}P}$ = 5.5 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.3 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.02, 2.98.

HRMS (ESI) *m/z* calcd for $C_{20}H_{28}N_6O_7P^+$ [(M+H)$^+$] 495.1752, found 495.1742.



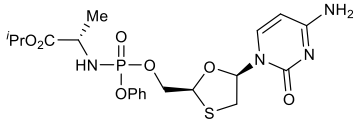
isopropyl ((((2S,3S,5R)-3-azido-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (21): This compound was prepared according to the General Procedure A, using zidovudine (53.4 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 75% EtOAc in PE to 100% EtOAc), the title compound was isolated as a colorless oil (90.1 mg, 84% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 – 9.56 (m, 1H), 7.39 – 7.27 (m, 3H), 7.22 – 7.17 (m, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.22 – 6.11 (m, 1H), 5.03 – 4.93 (m, 1H), 4.40 – 4.19 (m, 3H), 4.17 – 3.85 (m, 3H), 2.41 – 2.26 (m, 1H), 2.22 – 2.04 (m, 1H), 1.93 – 1.80 (m, 3H), 1.38 – 1.28 (m, 3H), 1.26 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 173.0 (d, $J_{C\text{-}P}$ = 7.2 Hz), 164.0, 163.9, 158.6, 154.7, 151.6, 150.6 (d, $J_{C\text{-}P}$ = 6.8 Hz), 150.5, 150.4 (d, $J_{C\text{-}P}$ = 6.3 Hz), 135.4, 135.3, 129.9, 125.4, 125.3, 120.2 (d, $J_{C\text{-}P}$ = 4.7 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 111.6, 111.5, 85.1, 84.7, 82.5 (d, $J_{C\text{-}P}$ = 7.5 Hz), 82.3 (d, $J_{C\text{-}P}$ = 8.0 Hz), 69.6, 65.8 (d, $J_{C\text{-}P}$ = 4.8 Hz), 65.7 (d, $J_{C\text{-}P}$ = 4.7 Hz), 60.6, 60.4, 50.6 (d, $J_{C\text{-}P}$ = 1.5 Hz), 50.4, 37.3, 21.7 (d, $J_{C\text{-}P}$ = 1.8 Hz), 21.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 21.0 (d, $J_{C\text{-}P}$ = 5.0 Hz), 20.9 (d, $J_{C\text{-}P}$ = 5.3 Hz), 12.6, 12.5.

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.06, 2.76.

HRMS (ESI) *m/z* calcd for $C_{22}H_{30}N_6O_8P^+$ [(M+H)$^+$] 537.1857, found 537.1849.



isopropyl ((((2S,5R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-1,3-oxathiolan-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (22): This compound was prepared according to the General Procedure A, using lamivudine (45.9 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 30% MeOH in EtOAc), the title compound was isolated as a white solid (82.7 mg, 83% yield, ~1:1

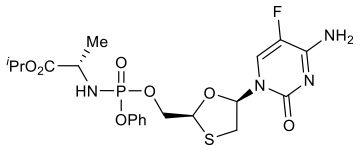
mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.59 (m, 1H), 7.35 – 7.25 (m, 2H), 7.25 – 7.19 (m, 2H), 7.18 – 7.11 (m, 1H), 6.35 – 6.28 (m, 1H), 5.80 – 5.71 (m, 1H), 5.37 – 5.28 (m, 1H), 5.08 – 4.92 (m, 1H), 4.53 – 3.89 (m, 4H), 3.50 – 3.42 (m, 1H), 2.99 – 2.91 (m, 1H), 1.42 – 1.33 (m, 3H), 1.31 – 1.18 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3 (d, $J_{C\text{-}P}$ = 6.9 Hz), 173.2 (d, $J_{C\text{-}P}$ = 7.4 Hz), 166.0, 165.9, 155.6, 150.7 (d, $J_{C\text{-}P}$ = 6.8 Hz), 150.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 140.7, 140.6, 129.9, 129.8, 125.2, 125.1, 120.4 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.7 Hz), 95.2, 95.1, 88.0, 87.9, 82.9 (d, $J_{C\text{-}P}$ = 8.6 Hz), 82.6 (d, $J_{C\text{-}P}$ = 8.5 Hz), 69.4, 67.5 (d, $J_{C\text{-}P}$ = 5.2 Hz), 67.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 50.6 (d, $J_{C\text{-}P}$ = 1.6 Hz), 50.4, 37.5, 37.4, 21.8 (d, $J_{C\text{-}P}$ = 3.6 Hz), 21.7 (d, $J_{C\text{-}P}$ = 3.3 Hz), 21.0 (d, $J_{C\text{-}P}$ = 5.2 Hz), 20.9 (d, $J_{C\text{-}P}$ = 5.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.92, 2.59.

HRMS (ESI) *m/z* calcd for $C_{20}H_{28}N_4O_7PS^+$ [$(M+H)^+$] 499.1411, found 499.1403.



isopropyl ((((2S,5R)-5-(4-amino-5-fluoro-2-oxopyrimidin-1(2H)-yl)-1,3-oxathiolan-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (23): This compound was prepared according to the General Procedure A, using emtricitabine (49.4 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 20% MeOH in EtOAc), the title compound was isolated as a white solid (93.0 mg, 90% yield, ~1:1 mixture of two diastereomers).

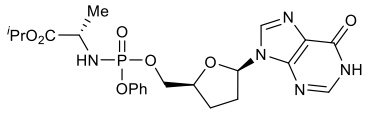
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40, 7.84 – 7.75 (m, 1H), 7.32 – 7.24 (m, 2H), 7.24 – 7.17 (m, 2H), 7.16 – 7.08 (m, 1H), 6.31 – 6.07 (m, 1H), 5.90 (s, 1H), 5.36 – 5.26 (m, 1H), 5.03 – 4.90 (m, 1H), 4.50 – 3.90 (m, 4H), 3.50 – 3.40 (m, 1H), 3.01 – 2.90 (m, 1H), 1.41– 1.32 (m, 3H), 1.22 – 1.14 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3 (d, $J_{C\text{-}P}$ = 6.7 Hz), 173.1 (d, $J_{C\text{-}P}$ = 7.5 Hz), 158.4 (d, $J_{C\text{-}F}$ = 5.9 Hz), 158.3 (d, $J_{C\text{-}F}$ = 5.7 Hz), 153.6, 153.5 150.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 150.6 (d, $J_{C\text{-}P}$ = 6.6 Hz), 137.5, 137.4, 135.6, 135.5, 129.8, 129.7, 125.2, 125.1, 120.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.2 (d, $J_{C\text{-}P}$ = 5.1 Hz), 87.9, 87.7, 83.6 (d, $J_{C\text{-}P}$ = 8.3 Hz), 83.2 (d, $J_{C\text{-}P}$ = 8.2 Hz), 69.4, 69.3, 67.0 (d, $J_{C\text{-}P}$ = 4.6 Hz), 66.6 (d, $J_{C\text{-}P}$ = 4.7 Hz), 50.5 (d, $J_{C\text{-}P}$ = 1.7 Hz), 50.4, 37.9, 37.6, 21.8 (d, $J_{C\text{-}P}$ = 1.6 Hz), 21.7 (d, $J_{C\text{-}$

$_P$ = 3.3 Hz), 20.9 (d, $J_{C\text{-}P}$ = 4.9 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.5 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.04, 2.75.

HRMS (ESI) *m/z* calcd for $C_{20}H_{27}FN_4O_7PS^+$ [$(M+H)^+$] 517.1317, found 517.1309.



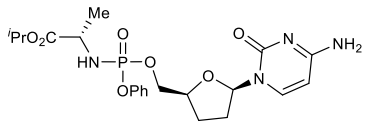
isopropyl ((((2S,5R)-5-(6-oxo-1,6-dihydro-9H-purin-9-yl)tetrahydrofuran-2-yl)methoxy) (phenoxy)phosphoryl)-*L*-alaninate (24): This compound was prepared according to the General Procedure A, using dideoxyinosine (47.2 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 40% MeOH in EtOAc), the title compound was isolated as a white solid (90.0 mg, 89% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.20 (m, 1H), 8.12 – 8.08 (m, 1H), 7.32 – 7.25 (m, 2H), 7.26 – 7.19 (m, 2H), 7.16 – 7.06 (m, 1H), 6.29 – 6.25 (m, 1H), 5.01 – 4.93 (m, 1H), 4.47 – 4.34 (m, 2H), 4.32 – 4.23 (m, 1H), 4.20 – 3.88 (m, 2H), 2.62 – 2.34 (m, 2H), 2.23 – 2.10 (m, 2H), 1.39 – 1.30 (m, 3H), 1.23 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0 (d, $J_{C\text{-}P}$ = 7.4 Hz), 172.9 (d, $J_{C\text{-}P}$ = 7.4 Hz), 158.9, 150.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 148.3, 148.2, 145.3, 138.4, 138.3, 129.7, 125.0, 120.3 (d, $J_{C\text{-}P}$ = 3.6 Hz), 120.2 (d, $J_{C\text{-}P}$ = 3.5 Hz), 85.7, 85.5, 79.9 (d, $J_{C\text{-}P}$ = 6.4 Hz), 79.8 (d, $J_{C\text{-}P}$ = 6.3 Hz), 69.2, 67.6 (d, $J_{C\text{-}P}$ = 5.1 Hz), 67.2 (d, $J_{C\text{-}P}$ = 5.0Hz), 50.5, 50.4, 32.7, 26.0, 25.7, 21.7, 21.6, 21.0 (d, $J_{C\text{-}P}$ = 5.0 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.0 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.12, 3.08.

HRMS (ESI) *m/z* calcd for $C_{22}H_{29}N_5O_7P^+$ [$(M+H)^+$] 506.1799, found 506.1795.



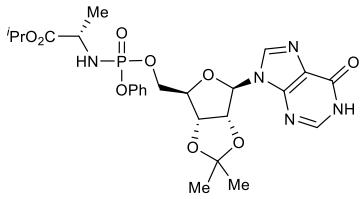
isopropyl ((((2S,5R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methoxy) (phenoxy)phosphoryl)-*L*-alaninate (25): This compound was prepared according to the General Procedure A, using 2',3'-dideoxycytidine (42.2 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 30% MeOH in EtOAc), the title compound was isolated as a white solid (68.2 mg, 71% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.60 (m, 1H), 7.35 – 7.26 (m, 2H), 7.25 – 7.18 (m, 2H), 7.14 (q, J = 7.1 Hz, 1H), 6.09 – 5.99(m, 1H), 5.85 – 5.68 (m, 1H), 5.04 – 4.91 (m, 1H), 4.47 – 4.16 (m, 4H), 4.02 – 3.90 (m, 1H), 2.48 – 2.29 (m, 1H), 2.04 – 1.71 (m, 3H), 1.41 – 1.32 (m, 3H), 1.25 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 173.0, 166.0, 156.1, 156.0, 150.7 (d, $J_{C\text{-}P}$ = 6.5 Hz), 150.6 (d, $J_{C\text{-}P}$ = 6.7 Hz), 140.6, 129.8, 129.7, 125.1, 125.0, 120.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 94.5, 94.4, 87.3, 87.1, 79.2, 79.1, 69.3, 69.2, 67.5 (d, $J_{C\text{-}P}$ = 5.3 Hz), 67.3 (d, $J_{C\text{-}P}$ = 5.4 Hz), 50.5, 50.4, 32.7, 25.4, 25.2, 21.7 (d, $J_{C\text{-}P}$ = 1.8 Hz), 21.6 (d, $J_{C\text{-}P}$ = 2.0 Hz), 20.9 (d, $J_{C\text{-}P}$ = 4.5 Hz), 20.8 (d, $J_{C\text{-}P}$ = 4.7 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.03, 2.98.

HRMS (ESI) *m/z* calcd for $C_{21}H_{30}N_4O_7P^+$ [$(M+H)^+$] 481.1847, found 481.1844.



isopropyl ((((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-oxo-1,6-dihydro-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (26): This compound was prepared according to the General Procedure A, using 9-((3aR,4R,6R,6aR)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-1,9-dihydro-6H-purin-6-one (61.7 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 20% MeOH in EtOAc), the title compound was isolated as a colorless oil (93.6 mg, 81% yield, ~1:1 mixture of two diastereomers).

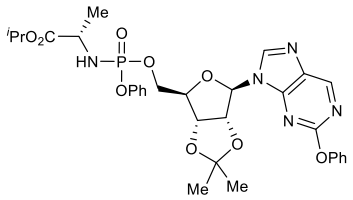
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.00 (s, 1H), 8.24 (s, 1H), 8.09 – 7.99 (m, 1H), 7.34 – 7.17 (m, 3H), 7.17 – 7.03 (m, 2H), 6.13 – 6.09 (m, 1H), 5.31 – 4.78 (m, 3H), 4.61 – 4.45 (m, 1H), 4.45 – 3.83 (m, 4H), 1.65 – 1.56 (m, 3H), 1.41 – 1.29 (m, 6H), 1.24 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 6.9 Hz), 172.9 (d, $J_{C\text{-}P}$ = 7.1 Hz), 158.8, 158.7, 150.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 150.5 (d, $J_{C\text{-}P}$ = 1.8 Hz), 148.4, 148.3, 145.8, 145.7, 139.2, 138.9, 129.8, 129.7, 125.4, 125.2 (d, $J_{C\text{-}P}$ = 8.4 Hz), 125.1 (d, $J_{C\text{-}P}$ = 6.8 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 114.8, 114.5, 91.6, 90.9, 85.3 (d, $J_{C\text{-}P}$ = 8.6 Hz), 85.2 (d, $J_{C\text{-}P}$ = 8.4 Hz), 84.9, 84.6, 81.3, 81.2, 69.3, 69.2, 66.3 (d, $J_{C\text{-}P}$ = 4.9 Hz), 66.2 (d, $J_{C\text{-}P}$ = 5.5 Hz), 50.6, 50.4, 27.2, 27.1, 25.4, 25.2, 21.7 (d,

$J_{C\text{-}P}$ = 8.7 Hz), 21.6 (d, $J_{C\text{-}P}$ = 7.8 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.2 Hz), 20.7 (d, $J_{C\text{-}P}$ = 5.4 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 3.05, 2.83.

HRMS (ESI) *m/z* calcd for $C_{25}H_{33}N_5O_9P^+$ [$(M+H)^+$] 578.2010, found 578.2003.



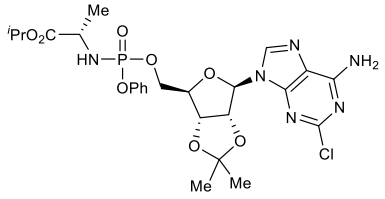
isopropyl ((((3aR,4R,6R,6aR)-2,2-dimethyl-6-(2-phenoxy-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (27): This compound was prepared according to the General Procedure A, using ((3aR,4R,6R,6aR)-6-(2-chloro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (65.3 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 100% EtOAc to 50% MeOH in EtOAc), the title compound was isolated as a colorless oil (90.2 mg, 69% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 – 8.48 (m, 1H), 8.27 – 8.17 (m, 1H), 7.52 – 7.40 (m, 2H), 7.36 – 7.02 (m, 8H), 6.22 – 6.16 (m, 1H), 5.42 – 5.05 (m, 1H), 5.06 – 4.90 (m, 2H), 4.62 – 4.47 (m, 1H), 4.41 – 4.21 (m, 2H), 4.02 – 3.84 (m, 1H), 3.78 – 3.72 (m, 1H), 1.66 – 1.59 (m, 3H), 1.43 – 1.25 (m, 6H), 1.25 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 172.8 (d, $J_{C\text{-}P}$ = 7.5 Hz), 160.4. 160.3, 152.5, 152.4, 152.3, 152.2, 150.6 (d, $J_{C\text{-}P}$ = 6.8 Hz), 150.5 (d, $J_{C\text{-}P}$ = 6.7 Hz), 142.3, 142.0, 129.8, 129.7, 129.6, 125.9, 125.1, 125.0, 122.4, 122.3, 121.9, 120.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 120.0 (d, $J_{C\text{-}P}$ = 5.0 Hz), 114.8, 114.6, 91.8, 91.2, 85.4 (d, $J_{C\text{-}P}$ = 8.4 Hz), 85.3 (d, $J_{C\text{-}P}$ = 8.3 Hz), 84.5, 84.3, 81.4, 81.3, 69.3, 66.3 (d, $J_{C\text{-}P}$ = 5.2 Hz), 66.2 (d, $J_{C\text{-}P}$ = 1.8 Hz), 50.6 (d, $J_{C\text{-}P}$ = 1.8 Hz), 50.3 (d, $J_{C\text{-}P}$ = 5.2 Hz), 27.2, 27.1, 25.4, 25.2, 21.7 (d, $J_{C\text{-}P}$ = 8.3 Hz), 21.6 (d, $J_{C\text{-}P}$ = 7.1 Hz), 21.0 (d, $J_{C\text{-}P}$ = 4.6 Hz), 20.9 (d, $J_{C\text{-}P}$ = 4.9 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.79, 2.57.

HRMS (ESI) *m/z* calcd for $C_{31}H_{37}N_5O_7P^+$ [$(M+H)^+$] 654.2323, found 654.2315.



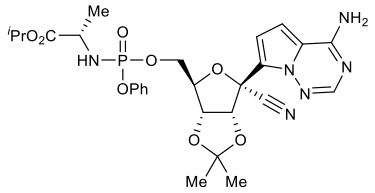
isopropyl ((((3aR,4R,6R,6aR)-6-(6-amino-2-chloro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (28): This compound was prepared according to the General Procedure A, using ((3aR,4R,6R,6aR)-6-(6-amino-2-chloro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (68.4 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 5% MeOH in EtOAc), the title compound was isolated as a colorless oil (96.5 mg, 79% yield, ~1:1 mixture of two diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 – 7.90 (m, 1H), 7.30 – 7.22 (m, 2H), 7.21 – 7.07 (m, 3H), 6.49 (s, 2H), 6.10 – 6.03 (s, 1H), 5.31 – 4.90 (m, 3H), 4.51 – 4.42 (m, 1H), 4.39 – 4.26 (m, 2H), 4.01 – 3.88 (m, 2H), 1.62 – 1.57 (m, 3H), 1.40 – 1.28 (m, 6H), 1.22 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 7.4 Hz), 173.0 (d, $J_{C\text{-}P}$ = 7.7 Hz), 156.5, 156.4, 154.4, 154.3, 150.7 (d, $J_{C\text{-}P}$ = 7.3Hz), 150.5, 150.3, 140.1, 139.9, 129.7, 125.1, 125.0, 120.2 (d, $J_{C\text{-}P}$ = 5.1 Hz), 120.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 119.0, 118.9, 114.9, 114.8, 90.7, 90.5, 85.5 (d, $J_{C\text{-}P}$ = 7.9 Hz), 85.2 (d, $J_{C\text{-}P}$ = 7.9 Hz), 84.3, 84.1, 81.3, 81.2, 69.4, 69.3, 66.3, 66.2, 50.5, 50.4, 27.3, 27.2, 25.5, 25.4, 21.8, 21.7, 21.1 (d, $J_{C\text{-}P}$ = 4.7 Hz), 21.0 (d, $J_{C\text{-}P}$ = 4.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.64, 2.59.

HRMS (ESI) *m/z* calcd for $C_{25}H_{33}ClN_6O_8P^+$ [$(M+H)^+$] 611.1781, found 611.1773.



isopropyl ((((3aR,4R,6R,6aR)-6-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-6-cyano-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (29): This compound was prepared according to the General Procedure A, using (3aR,4R,6R,6aR)-4-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carbonitrile (66.3 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 10% MeOH in EtOAc), the title compound was isolated as a colorless oil (93.7 mg, 78% yield, ~1:1 mixture of two diastereomers).

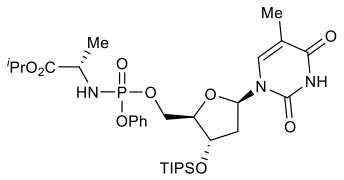
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.90 (m, 1H), 7.31 – 7.08 (m, 5H), 6.91 – 6.83 (m, 1H), 6.62

– 6.56 (m, 1H), 6.37 (s, 2H), 5.43 – 5.24 (m, 1H), 5.02 – 4.85 (m, 2H), 4.66 – 4.55 (m, 1H), 4.44 – 4.23 (m, 3H), 3.98 – 3.87 (m, 1H), 1.75 (s, 3H), 1.39 – 1.33 (m, 3H), 1.32 – 1.26 (m, 3H), 1.22 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 173.0 (d, $J_{C\text{-}P}$ = 7.2 Hz), 155.6, 150.7 (d, $J_{C\text{-}P}$ = 7.0 Hz), 150.6 (d, $J_{C\text{-}P}$ = 7.1 Hz), 147.6, 147.5, 129.8, 129.7, 125.1, 123.0, 122.9, 120.3 (d, $J_{C\text{-}P}$ = 4.7 Hz), 120.2 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.1, 117.0, 115.9, 112.3, 100.4, 83.9, 83.5 (d, $J_{C\text{-}P}$ = 8.5 Hz), 83.4 (d, $J_{C\text{-}P}$ = 7.9 Hz), 82.0, 81.5, 81.4, 69.4, 69.3, 65.7 (d, $J_{C\text{-}P}$ = 5.4 Hz), 65.5 (d, $J_{C\text{-}P}$ = 5.1 Hz), 50.4, 50.3, 26.4, 26.3, 25.5, 25.4, 21.7, 21.6, 20.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.4 Hz).

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.80, 2.66.

HRMS (ESI) *m/z* calcd for $C_{27}H_{34}N_6O_8P^+$ [$(M+H)^+$] 601.2170, found 601.2162.



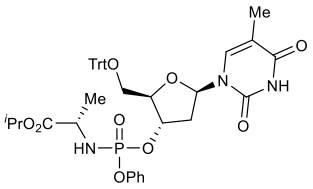
isopropyl ((((2R,3S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)-*L*-alaninate (30): This compound was prepared according to the General Procedure A, using 1-((2R,4S,5R)-5-(hydroxymethyl)-4-((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (79.7 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 100% EtOAc), the title compound was isolated as a colorless oil (53.4 mg, 40% yield, single diastereomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.45 (d, *J* = 1.4 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.22 – 7.12 (m, 3H), 6.30 (dd, *J* = 8.6, 5.5 Hz, 1H), 5.03 – 4.95 (m, 1H), 4.52 – 4.46 (m, 1H), 4.33 – 4.25 (m, 1H), 4.23 – 4.15 (m, 1H), 4.13 – 4.06 (m, 1H), 3.99 – 3.90 (m, 1H), 3.77 (dd, *J* = 11.2, 9.0 Hz, 1H), 2.29 – 2.21 (m, 1H), 1.98 – 1.83 (m, 4H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.23 (s, 3H), 1.22 (s, 3H), 1.08 – 1.01 (m, 18H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0 (d, $J_{C\text{-}P}$ = 8.1 Hz), 163.8, 150.6 (d, $J_{C\text{-}P}$ = 6.6 Hz), 150.3, 135.7, 129.9, 125.3, 120.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 111.3, 86.0 (d, $J_{C\text{-}P}$ = 8.1 Hz), 85.3, 72.7, 69.6, 66.4 (d, $J_{C\text{-}P}$ = 5.5 Hz), 50.5 (d, $J_{C\text{-}P}$ = 1.8 Hz), 41.2, 21.8 (d, $J_{C\text{-}P}$ = 6.9 Hz), 21.3 (d, $J_{C\text{-}P}$ = 4.3 Hz), 18.0, 12.5, 12.1.

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.65.

HRMS (ESI) *m/z* calcd for $C_{31}H_{51}N_3O_9PSi^+$ [(M+H)$^+$] 668.3127, found 668.3121.



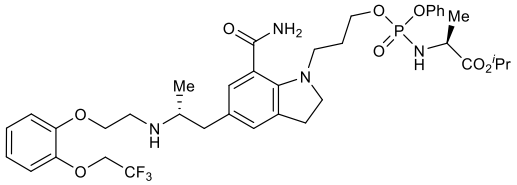
isopropyl ((((2R,3S,5R)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-((trityloxy) methyl)tetrahydrofuran-3-yl)oxy)(phenoxy)phosphoryl)-*L*-alaninate (31): This compound was prepared according to the General Procedure A, using 1-((2R,4S,5R)-4-hydroxy-5-((trityloxy)methyl)tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (96.9 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 100% EtOAc), the title compound was isolated as a white solid (114.6mg, 76% yield, single diastereomer).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.58 – 7.50 (m, 1H), 7.42 – 7.14 (m, 20H), 6.42 (dd, *J* = 9.1, 5.4 Hz, 1H), 5.27 (t, *J* = 6.3 Hz, 1H), 5.00 – 4.94 (m, 1H), 4.32 – 4.28 (m, 1H), 3.99 – 3.88 (m, 1H), 3.73 (t, *J* = 10.1, 1H), 3.51 – 3.41 (m, 2H), 2.59 – 2.49 (m, 1H), 2.44 – 2.33 (m, 1H), 1.36 (d, *J* = 1.2 Hz, 3H), 1.30 (d, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9 (d, $J_{C\text{-}P}$ = 7.3 Hz), 163.8, 150.6 (d, $J_{C\text{-}P}$ = 6.6 Hz), 150.5, 143.2, 135.4, 129.9, 128.8, 128.2, 127.6, 125.3, 120.3 (d, $J_{C\text{-}P}$ = 4.8 Hz), 111.7, 87.9, 84.8 (d, $J_{C\text{-}P}$ = 6.0 Hz), 84.4, 78.5 (d, $J_{C\text{-}P}$ = 5.5 Hz), 69.5, 63.8, 60.5, 50.4, 39.2 (d, $J_{C\text{-}P}$ = 4.2 Hz), 21.8 (d, $J_{C\text{-}P}$ = 8.3 Hz), 21.1 (d, $J_{C\text{-}P}$ = 5.1 Hz), 11.7.

^{31}P NMR (202 MHz, $CDCl_3$) δ 1.79.

HRMS (ESI) *m/z* calcd for $C_{41}H_{44}N_3NaO_9P^+$ [(M+Na)$^+$] 776.2707, found 776.2697.



isopropyl ((3-(7-carbamoyl-5-((R)-2-((2-(2-(2,2,2-trifluoroethoxy)phenoxy)ethyl)amino) propyl)indolin-1-yl)propoxy)(phenoxy)phosphoryl)-*L*-alaninate (32): This compound was prepared according to the General Procedure A, using silodosin (99.1 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 10% MeOH in EtOAc), the title compound was

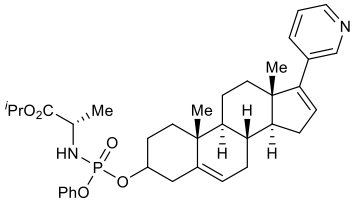
isolated as a colorless oil (125.4 mg, 82% yield, mixture of diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.58 (m, 1H), 7.30 – 7.14 (m, 4H), 7.14 – 7.04 (m, 4H), 6.98 – 6.83 (m, 4H), 5.27 – 4.77 (m, 2H), 4.61 – 3.98 (m, 4H), 3.89 – 3.71 (m, 3H), 3.23 – 3.11 (m, 2H), 2.91 – 2.47 (m, 10H), 2.22 (s, 6H), 1.45 – 1.28 (m, 3H), 1.27 – 1.16 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4 (d, $J_{C\text{-}P}$ = 6.4 Hz), 173.3 (d, $J_{C\text{-}P}$ = 7.8 Hz), 173.2 (d, $J_{C\text{-}P}$ = 6.1 Hz), 173.1 (d, $J_{C\text{-}P}$ = 8.7 Hz), 168.53, 168.51, 168.48, 151.15 (d, $J_{C\text{-}P}$ = 7.3 Hz), 151.08 (d, $J_{C\text{-}P}$ = 7.4 Hz), 151.02 (d, $J_{C\text{-}P}$ = 7.7 Hz), 150.98 (d, $J_{C\text{-}P}$ = 7.4 Hz), 149.8, 149.4, 149.2, 148.0, 147.9, 147.84, 147.77, 134.98, 134.96, 133.61, 133.60, 129.5, 129.40, 129.39, 128.3, 127.21, 127.19, 124.74, 124.70, 124.55, 124.52, 122.1, 122.0, 121.8, 121.6, 121.00, 120.98, 120.9, 120.8, 120.59 (d, $J_{C\text{-}P}$ = 4.6 Hz), 120.49 (d, $J_{C\text{-}P}$ = 4.9 Hz), 120.45 (d, $J_{C\text{-}P}$ = 1.5 Hz), 120.41 (d, $J_{C\text{-}P}$ = 1.7 Hz), 114.62, 114.61, 113.4, 113.1, 112.28, 112.26, 111.7, 74.21 (d, $J_{C\text{-}P}$ = 6.4 Hz), 74.09 (d, $J_{C\text{-}P}$ = 6.4 Hz), 74.06 (d, $J_{C\text{-}P}$ = 6.5 Hz), 74.03 (d, $J_{C\text{-}P}$ = 5.8 Hz), 70.24, 70.20, 70.10, 70.06, 70.02, 69.02, 68.98, 68.8, 61.7, 61.6, 59.9 (d, $J_{C\text{-}P}$ = 4.7 Hz), 59.8 (d, $J_{C\text{-}P}$ = 4.4 Hz), 59.4 (d, $J_{C\text{-}P}$ = 3.7 Hz), 59.3 (d, $J_{C\text{-}P}$ = 4.4 Hz), 55.87, 55.84, 55.6, 55.5, 54.05, 54.00, 53.91, 53.82, 53.77, 53.74, 53.63, 50.6 (d, $J_{C\text{-}P}$ = 1.9 Hz), 50.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 50.3 (d, $J_{C\text{-}P}$ = 2.2 Hz), 50.2 (d, $J_{C\text{-}P}$ = 2.2 Hz), 21.8, 21.7, 21.69, 21.67, 21.3 (d, $J_{C\text{-}P}$ = 4.0 Hz), 21.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.4 Hz), 20.7 (d, $J_{C\text{-}P}$ = 5.4 Hz), 18.7.

^{31}P NMR (202 MHz, $CDCl_3$) δ 2.91, 2.82, 2.36, 2.08.

HRMS (ESI) *m/z* calcd for $C_{37}H_{49}F_3N_4O_8P^+$ [$(M+H)^+$] 765.3235, found 765.3229.



isopropyl ((((8R,9S,10R,13S,14S)-10,13-dimethyl-17-(pyridin-3-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)(phenoxy)phosphoryl)-*L*-alaninate (33): This compound was prepared according to the General Procedure B, using abiraterone (69.9 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 20% EtOAc in PE to 50% EtOAc in PE), the title compound was isolated as a white solid (107.7mg, 87% yield, mixture of diastereomers).

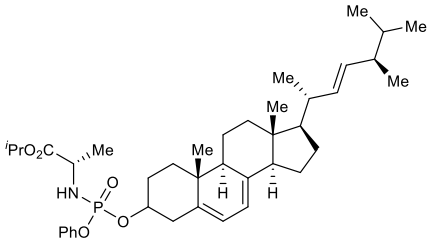
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.45 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.37 – 7.27 (m, 2H), 7.26 – 7.18 (m, 3H), 7.16 – 7.09 (m, 1H), 6.02 – 5.94 (m, 1H), 5.48 – 5.34 (m, 1H),

5.09 – 4.93 (m, 1H), 4.39 – 4.24 (m, 1H), 4.03 – 3.91 (m, 1H), 3.75 – 3.59 (m, 1H), 2.57 – 2.36 (m, 2H), 2.31 – 2.19 (m, 1H), 2.12 – 1.94 (m, 4H), 1.90 – 1.80 (m, 1H), 1.81 – 1.53 (m, 6H), 1.52 – 1.42 (m, 1H), 1.40 – 1.32 (m, 3H), 1.29 – 1.17 (m, 6H), 1.17 – 0.99 (m, 8H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 173.0, 151.6, 151.1 (d, $J_{C\text{-}P}$ = 7.1 Hz), 151.0 (d, $J_{C\text{-}P}$ = 7.4 Hz), 147.8, 147.7, 141.4, 139.9, 139.8 (d, $J_{C\text{-}P}$ = 3.7 Hz), 133.8, 133.0, 129.6, 129.5, 129.3, 129.2, 124.7, 124.6, 123.1, 122.7, 122.6, 121.1, 120.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 120.3 (d, $J_{C\text{-}P}$ = 1.8 Hz), 120.3, 120.2, 77.96, 77.92, 77.88, 77.84, 71.4, 69.1, 57.6, 57.5, 50.4, 50.2, 47.3, 42.4, 40.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 40.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 40.0 (d, $J_{C\text{-}P}$ = 4.1 Hz), 39.9 (d, $J_{C\text{-}P}$ = 3.6 Hz), 37.3, 36.9, 36.8, 36.7, 36.6, 35.3, 35.2, 31.8, 31.6, 31.5, 30.5, 30.4, 29.8 (d, $J_{C\text{-}P}$ = 4.6 Hz), 29.7 (d, $J_{C\text{-}P}$ = 4.8 Hz), 29.6 (d, $J_{C\text{-}P}$ = 4.3 Hz), 29.5 (d, $J_{C\text{-}P}$ = 4.1 Hz), 21.8 (d, $J_{C\text{-}P}$ = 1.5 Hz), 21.73, 21.69, 21.65, 21.19, 21.17, 21.15, 21.13, 21.12, 21.10, 20.9, 20.8, 19.4, 19.3, 16.6.

^{31}P NMR (202 MHz, $CDCl_3$) δ 1.41, 1.37, 1.21, 1.18.

HRMS (ESI) *m/z* calcd for $C_{36}H_{48}N_2O_5P^+$ [$(M+H)^+$] 619.3295, found 619.3291.



isopropyl ((((3S,9S,10R,13R,14R,17R)-17-((2R,5R,E)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)(phenoxy)phosphoryl)-*L*-alaninate (34): This compound was prepared according to the General Procedure B, using ergosterol (79.3 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 15% EtOAc in PE to 40% EtOAc in PE), the title compound was isolated as a white solid (58.6 mg, 44% yield, mixture of diastereomers).

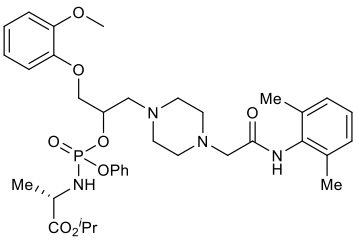
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.21 (t, *J* = 8.6 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 5.59 – 5.47 (m, 1H), 5.40 – 5.30 (m, 1H), 5.29 – 5.09 (m, 2H), 5.05 – 4.94 (m, 1H), 4.45 – 4.30 (m, 1H), 4.02 – 3.89 (m, 1H), 3.62 – 3.48 (m, 1H), 2.71 – 2.31 (m, 2H), 2.12 – 1.44 (m, 14H), 1.37 – 1.20 (m, 13H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.95 – 0.88 (m, 5H), 0.82 (t, *J* = 7.2 Hz, 6H), 0.62 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 173.1, 151.1 (d, $J_{C\text{-}P}$ = 6.9 Hz), 151.0 (d, $J_{C\text{-}P}$ =6.9 Hz), 141.8, 141.7, 138.37, 138.34, 135.7, 132.1, 129.71, 129.69, 129.67, 124.8, 120.60, 120.57, 120.43, 120.39,

120.37, 120.33, 116.41, 116.37, 69.25, 69.23, 55.8, 54.6, 50.5, 46.1, 42.95, 42.94, 40.6, 39.1, 37.0, 33.2, 28.4, 23.1, 21.87, 21.85, 21.83, 21.79, 21.74, 21.27, 21.23, 21.17, 20.1, 19.8, 17.7, 16.3, 12.2.

^{31}P NMR (202 MHz, $CDCl_3$) δ 1.35, 1.32, 1.18, 1.16.

HRMS (ESI) *m/z* calcd for $C_{40}H_{60}NNaO_5P^+$ [$(M+Na)^+$] 688.4101, found 688.4097.



isopropyl (((1-(4-(2-((2,6-dimethylphenyl)amino)-2-oxoethyl)piperazin-1-yl)-3-(2-methoxy phenoxy)propan-2-yl)oxy)(phenoxy)phosphoryl)-*L*-alaninate (35): This compound was prepared according to the General Procedure B, using ranolazine (85.5 mg, 0.2 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (145.3 mg, 0.4 mmol). After purification by column chromatography (SiO_2, 50% EtOAc in PE to 5% MeOH in EtOAc), the title compound was isolated as a white solid (110.1 mg, 79% yield, mixture of diastereomers).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.60 (m, 1H), 7.31 – 7.14 (m, 4H), 7.14 – 7.02 (m, 4H), 6.99 – 6.82 (m, 4H), 5.23 – 4.81 (m, 2H), 4.58 – 4.35 (m, 1H), 4.33 – 3.99 (m, 3H), 3.86 – 3.73 (m, 3H), 3.21 – 3.13 (m, 2H), 2.89 – 2.45 (m, 10H), 2.22 (s, 6H), 1.44 – 1.28 (m, 3H), 1.24 – 1.15 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4 (d, $J_{C\text{-}P}$ = 6.6 Hz), 173.3 (d, $J_{C\text{-}P}$ = 7.8 Hz), 173.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 173.1 (d, $J_{C\text{-}P}$ = 8.6 Hz), 168.53, 168.51, 168.48, 151.15 (d, $J_{C\text{-}P}$ = 7.4 Hz), 151.08 (d, $J_{C\text{-}P}$ = 7.3 Hz), 151.02 (d, $J_{C\text{-}P}$ = 7.8 Hz), 150. 97 (d, $J_{C\text{-}P}$ = 7.3 Hz), 149.8, 149.4, 149.2, 148.0, 147.9, 147.84, 147.77, 134.98, 134.96, 133.61, 133.60, 129.5, 129.40, 129.39, 128.3, 127.21, 127.19, 124.74, 124.70, 124.55, 124.52, 122.1, 122.0, 121.8, 121.6, 121.00, 120.98, 120.93, 120.8, 120.58 (d, $J_{C\text{-}P}$ = 4.7 Hz), 120.49 (d, $J_{C\text{-}P}$ = 5.0 Hz), 120.45 (d, $J_{C\text{-}P}$ = 1.4 Hz), 120.41 (d, $J_{C\text{-}P}$ = 1.7 Hz), 114.62, 114.61, 113.4, 113.1, 112.28, 112.26, 111.7, 74.24, 74.19, 74.11, 74.09, 74.06, 74.01, 70.24, 70.20, 70.10, 70.06, 70.02, 69.02, 68.98, 68.8, 61.7, 61.6, 59.9 (d, $J_{C\text{-}P}$ = 4.7 Hz), 59.8 (d, $J_{C\text{-}P}$ = 4.5 Hz), 59.4 (d, $J_{C\text{-}P}$ = 3.6 Hz), 59.3 (d, $J_{C\text{-}P}$ = 4.6 Hz), 55.9, 55.8, 55.6, 55.5, 54.05, 54.00, 53.91, 53.82, 53.77, 53.74, 53.63, 50.6 (d, $J_{C\text{-}P}$ = 1.8 Hz), 50.4 (d, $J_{C\text{-}P}$ = 2.1 Hz), 50.3 (d, $J_{C\text{-}P}$ = 2.2 Hz), 50.2 (d, $J_{C\text{-}P}$ = 2.1 Hz), 21.77, 21.74, 21.69, 21.67, 21.3 (d, $J_{C\text{-}P}$ = 4.1 Hz), 21.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 20.8 (d, $J_{C\text{-}P}$ = 5.8 Hz), 20.7 (d, $J_{C\text{-}P}$ = 5.5 Hz), 18.7.

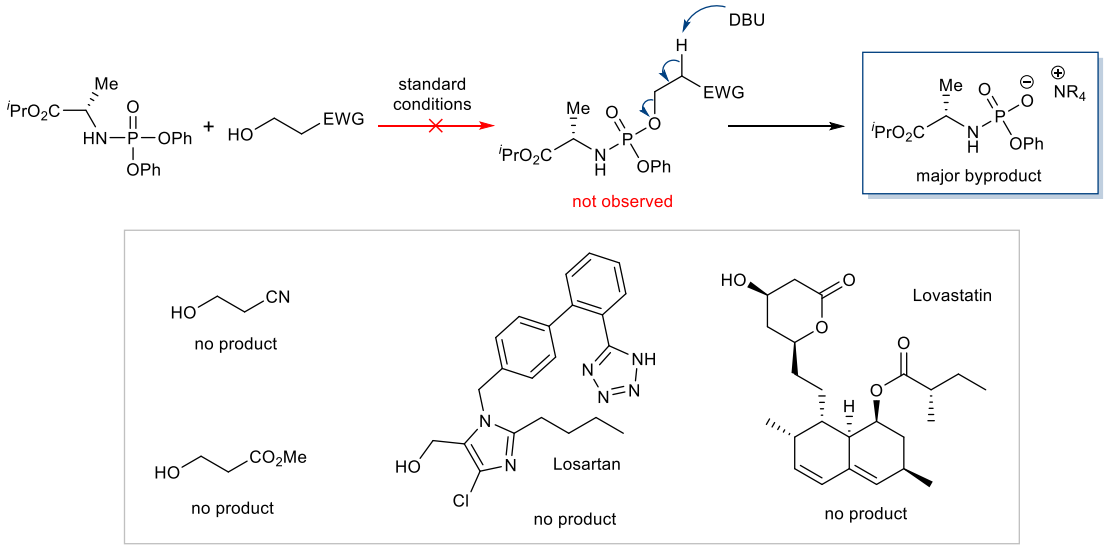
^{31}P NMR (202 MHz, $CDCl_3$) δ 2.91, 2.81, 2.36, 2.08.

HRMS (ESI) *m/z* calcd for $C_{36}H_{50}N_4O_8P^+$ [$(M+H)^+$] 697.3361, found 697.3354.

5. Limitation of this method

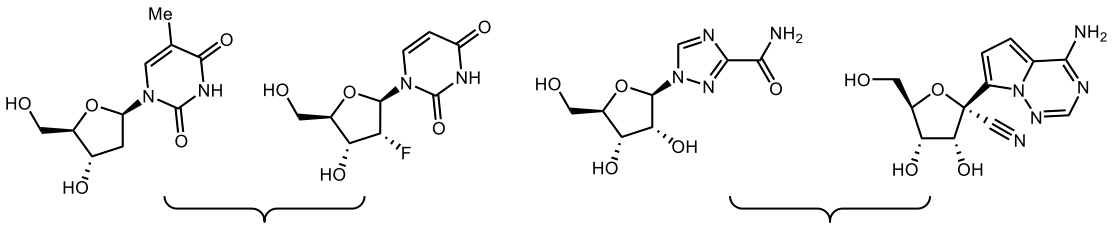
a) unsuccessful substrates

Alcoholic compounds bearing acidic β-protons were not compatible substrates for this reaction. We hypothesize that the transesterification processes proceeded in high yield, but the product was not stable in the reaction condition. We observed high yielding mono-phosphate byproducts in those unsuccessful reactions, likely generated from DBU mediated elimination of products.

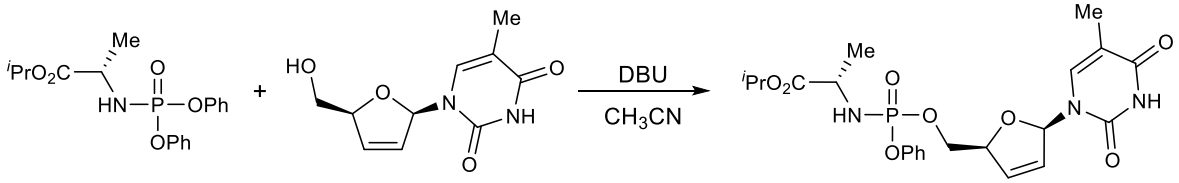


b) substrates with low yielding or poor regioselectivity

Nucleosides with multiple hydroxy groups gave unsatisfactory result. Substrates bearing unprotected 3',5'-hydroxyl groups proceeded smoothly under the standard reaction condition, but gave a mixture of regioisomers. Substrates containing 2',3'-hydroxyl groups only gave low conversion, likely due to poor solubility of this type of substrates in CH_3CN.



6. Scalability of the reaction

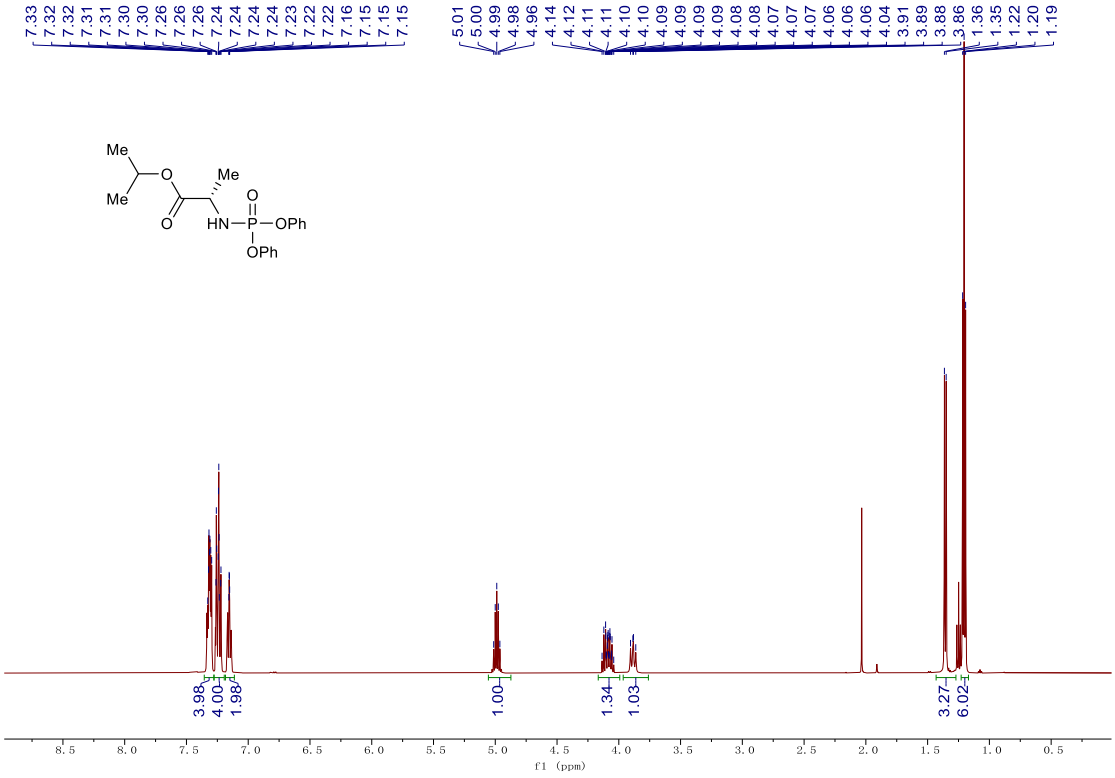


1.09 g, 3.0 mmol 0.336 g, 1.5 mmol **3**

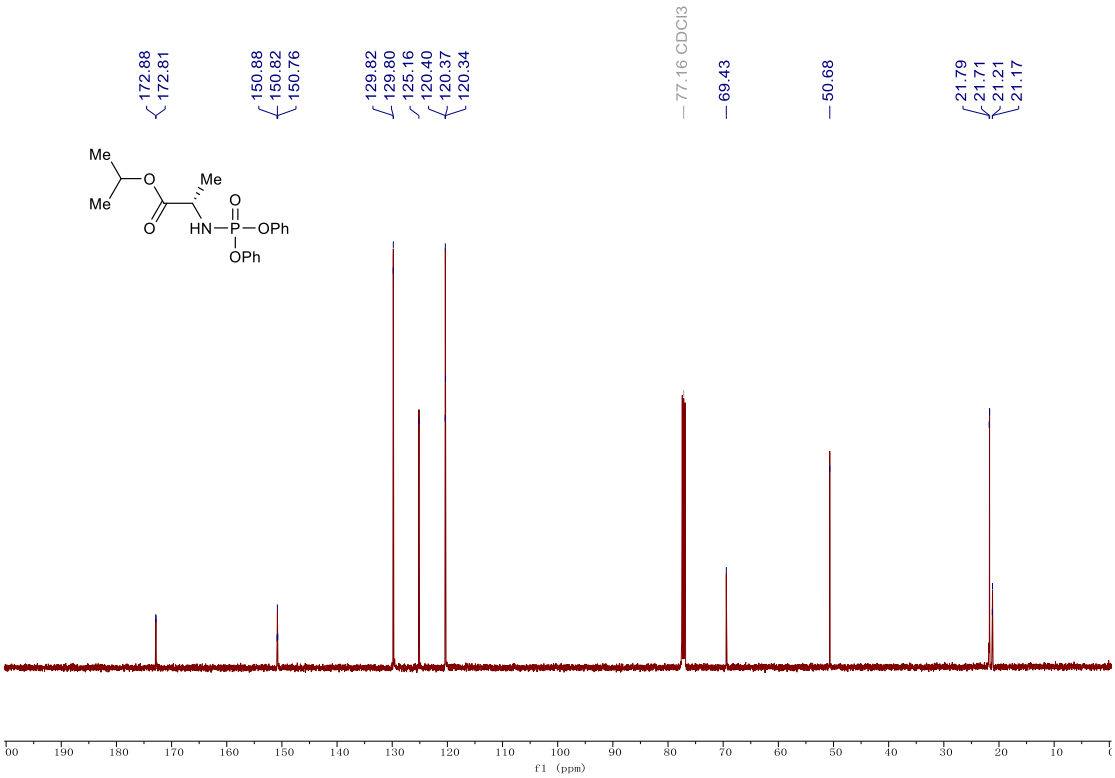
To an oven-dried 50 mL round bottom flask equipped with a magnetic stir bar was added stavudine (0.336 g, 1.5 mmol), isopropyl (diphenoxyphosphoryl)-*L*-alaninate (1.09 g, 3.0 mmol), and anhydrous CH_3CN (8 mL), followed by the addition of DBU (0.45 mL, 3.0 mmol). The reaction mixture was stirred at 25 ℃ for 36 hours. Then the reaction was concentrated under reduced pressure to afford the crude product. The crude products was purified by flash column chromatography on silical gel (50% EtOAc in PE to 5% MeOH in EtOAc) to afford desired product as colorless oil (0.626 g, 85% yield). The purity was confirmed by ^{1}H and ^{31}P NMR spectrum.

NMR Data

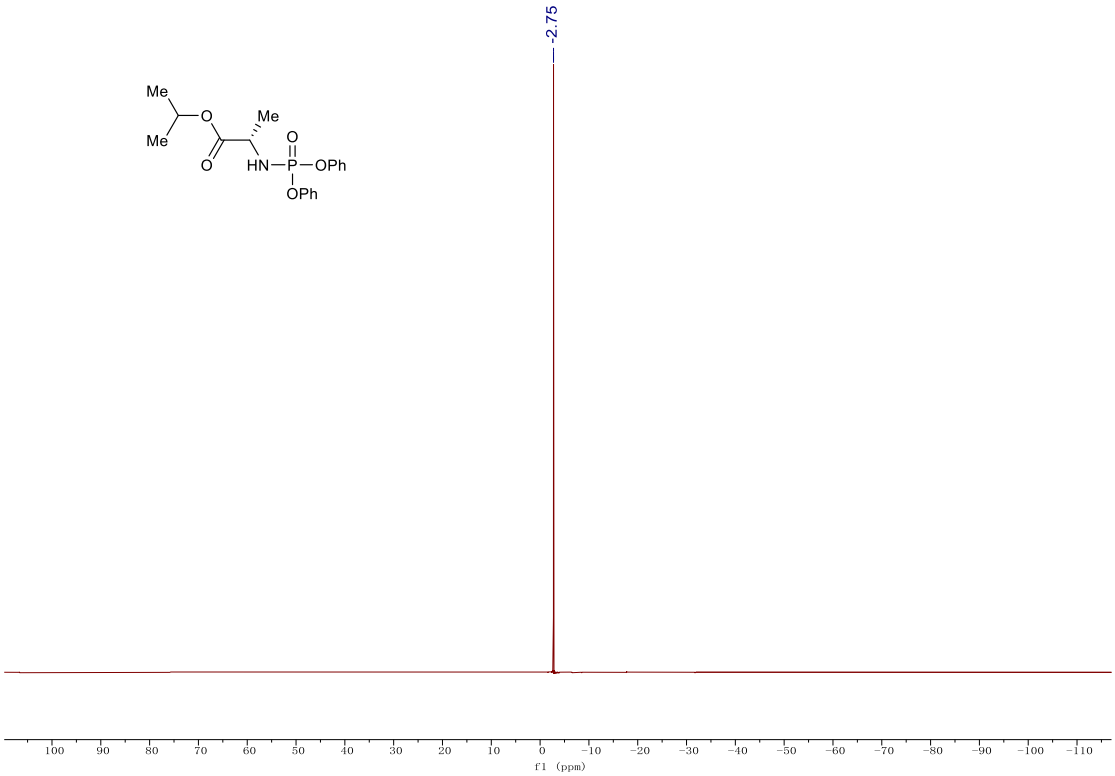
1, ^{1}H NMR (500 MHz, $CDCl_3$)



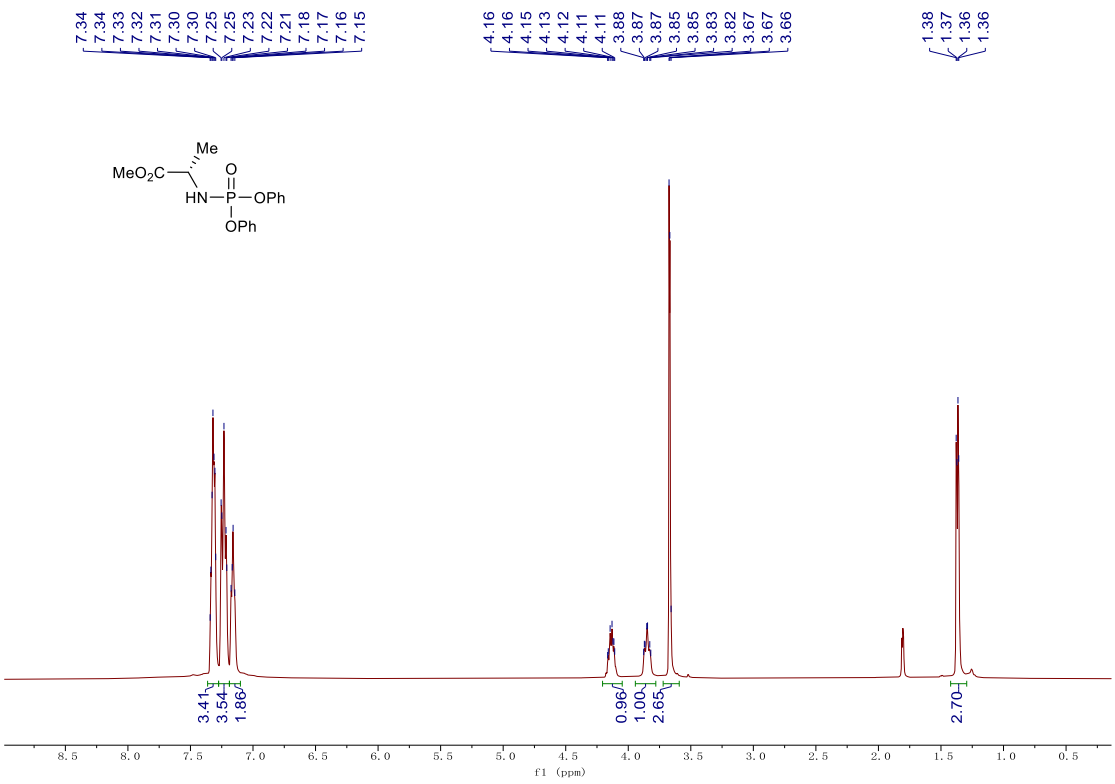
1, ^{13}C NMR (126 MHz, $CDCl_3$)



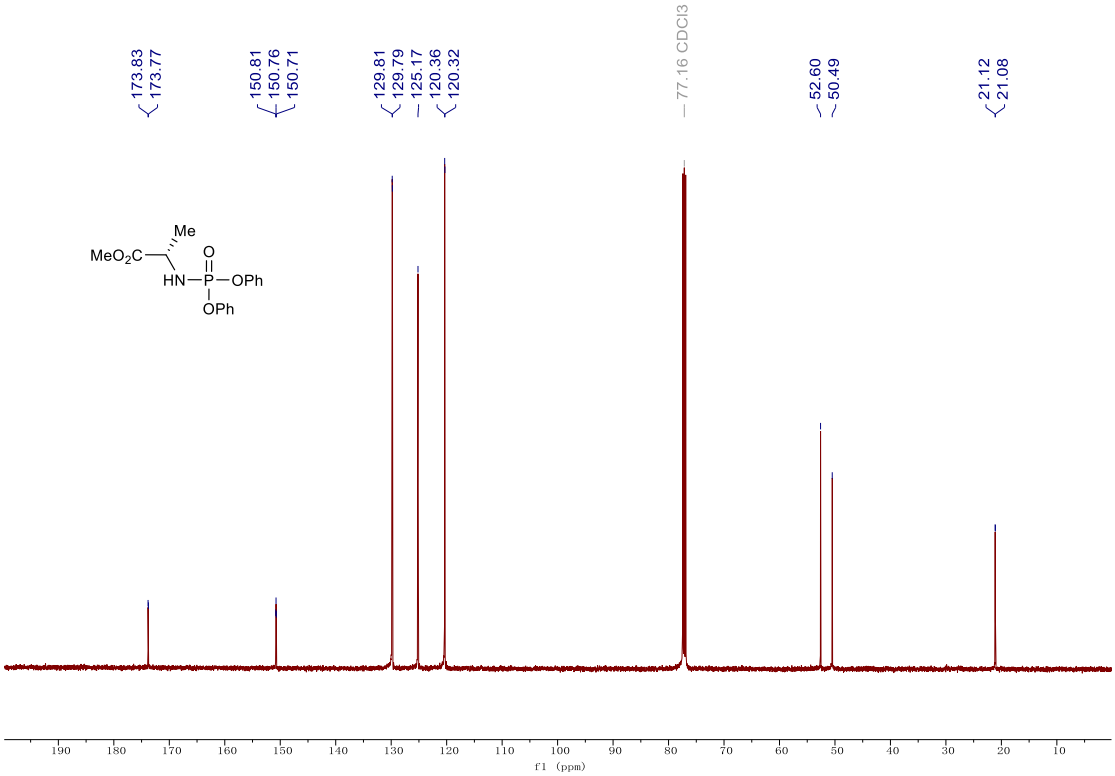
1, ^{31}P NMR (202 MHz, $CDCl_3$)



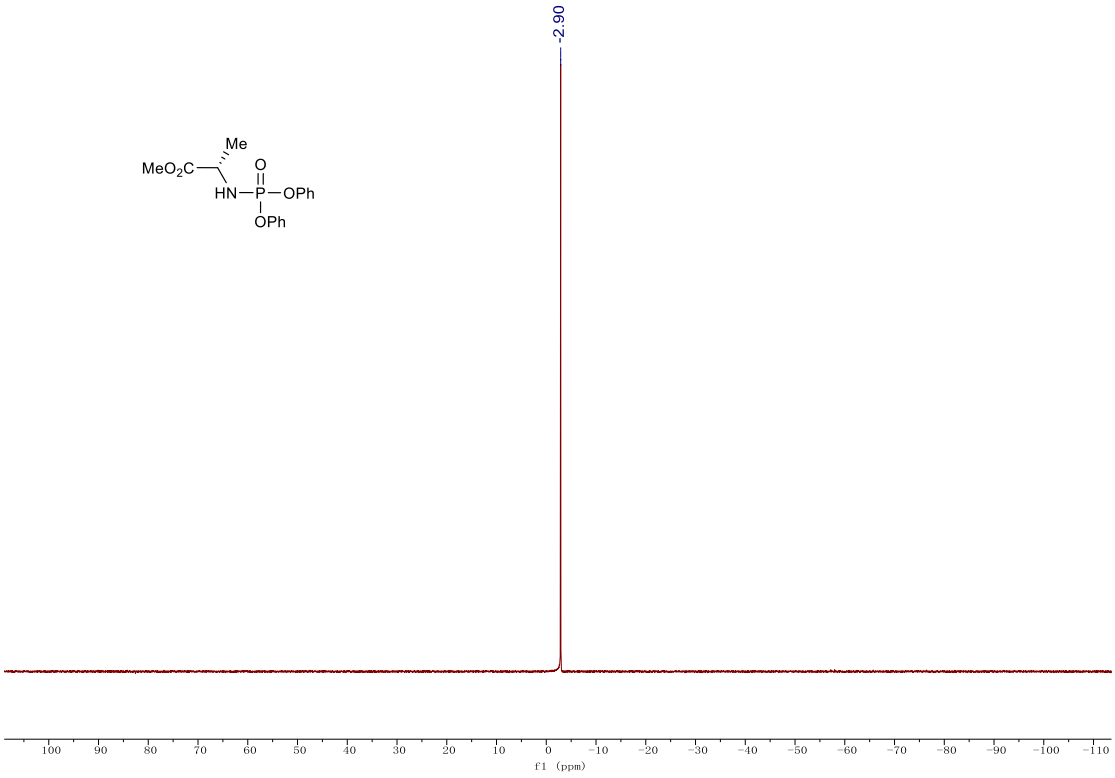
1a, ^{1}H NMR (500 MHz, $CDCl_3$)



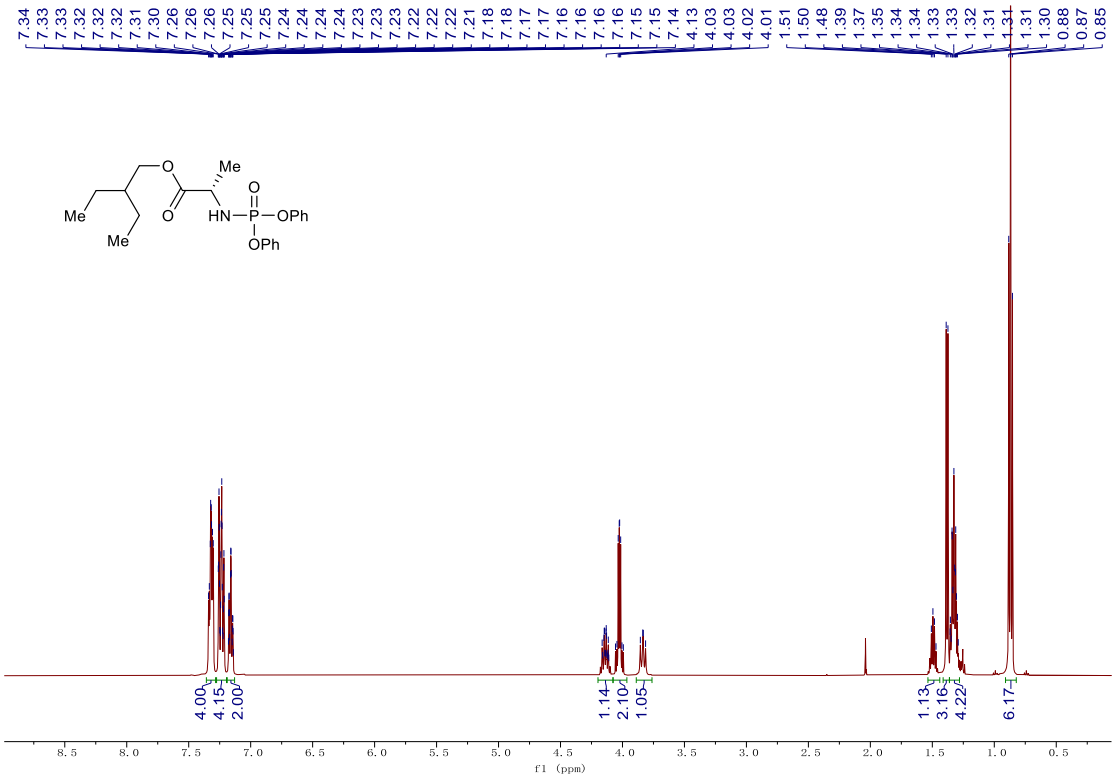
1a, ^{13}C NMR (126 MHz, $CDCl_3$)



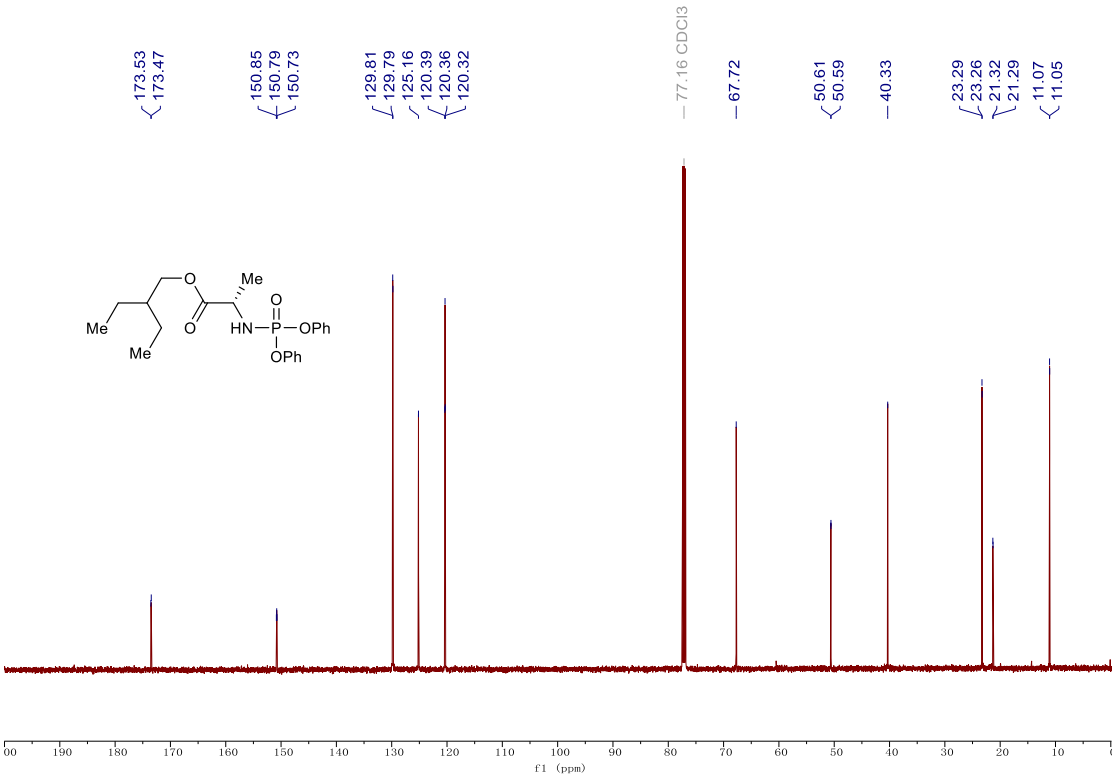
1a, ^{31}P NMR (202 MHz, $CDCl_3$)



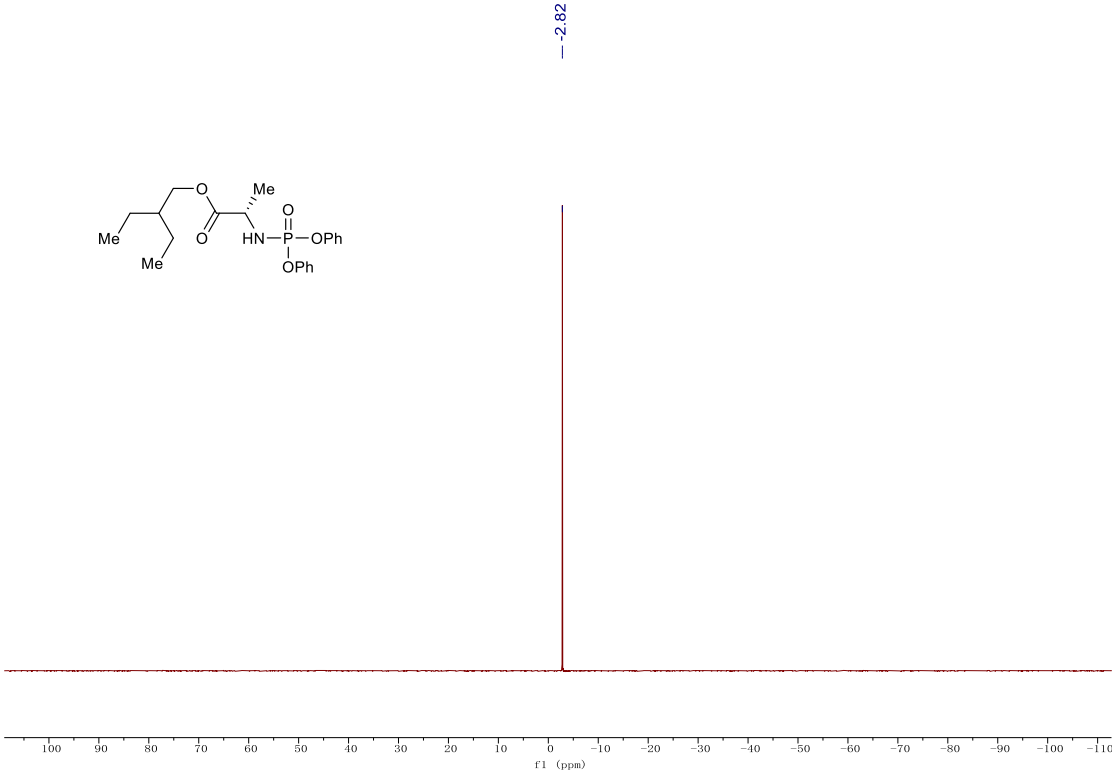
1b, ^{1}H NMR (500 MHz, $CDCl_3$)



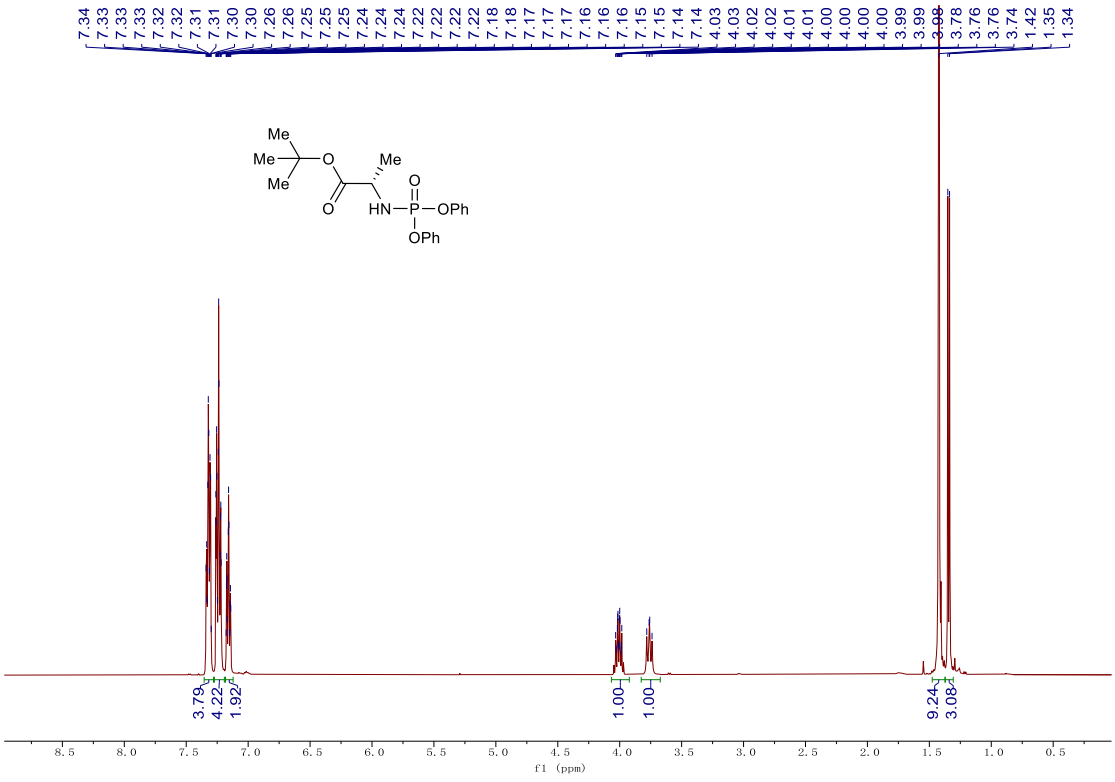
1b, ^{13}C NMR (126 MHz, $CDCl_3$)



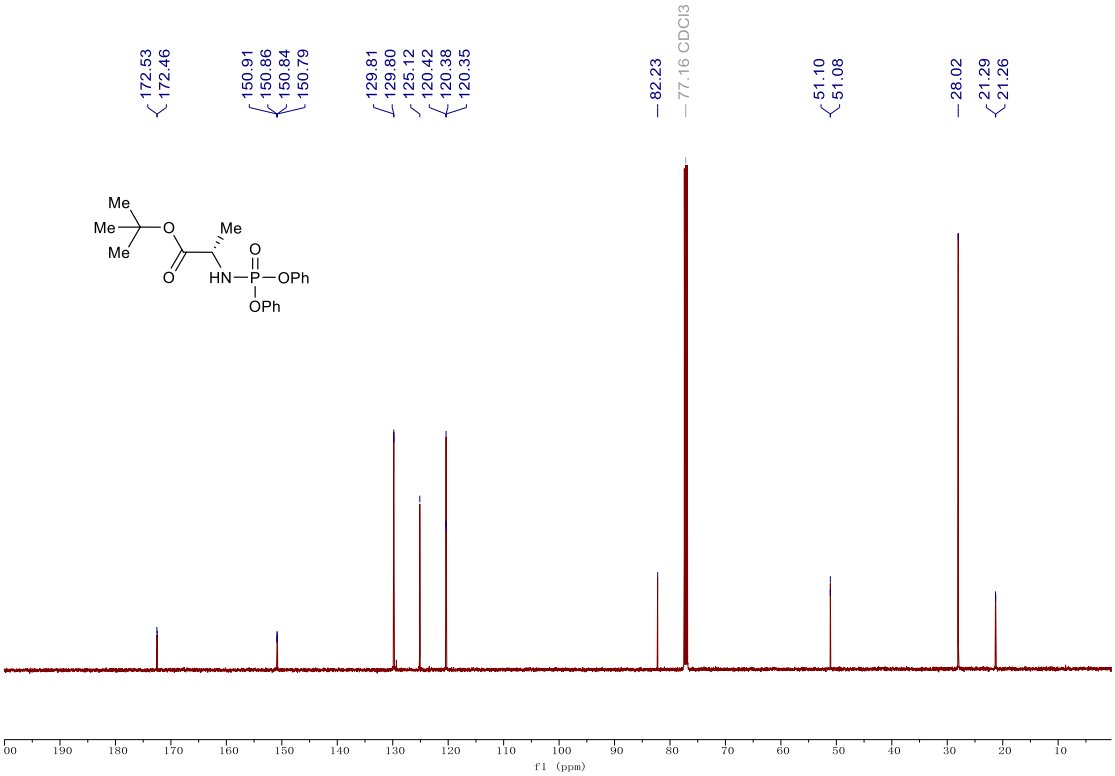
1b, ^{31}P NMR (202 MHz, $CDCl_3$)



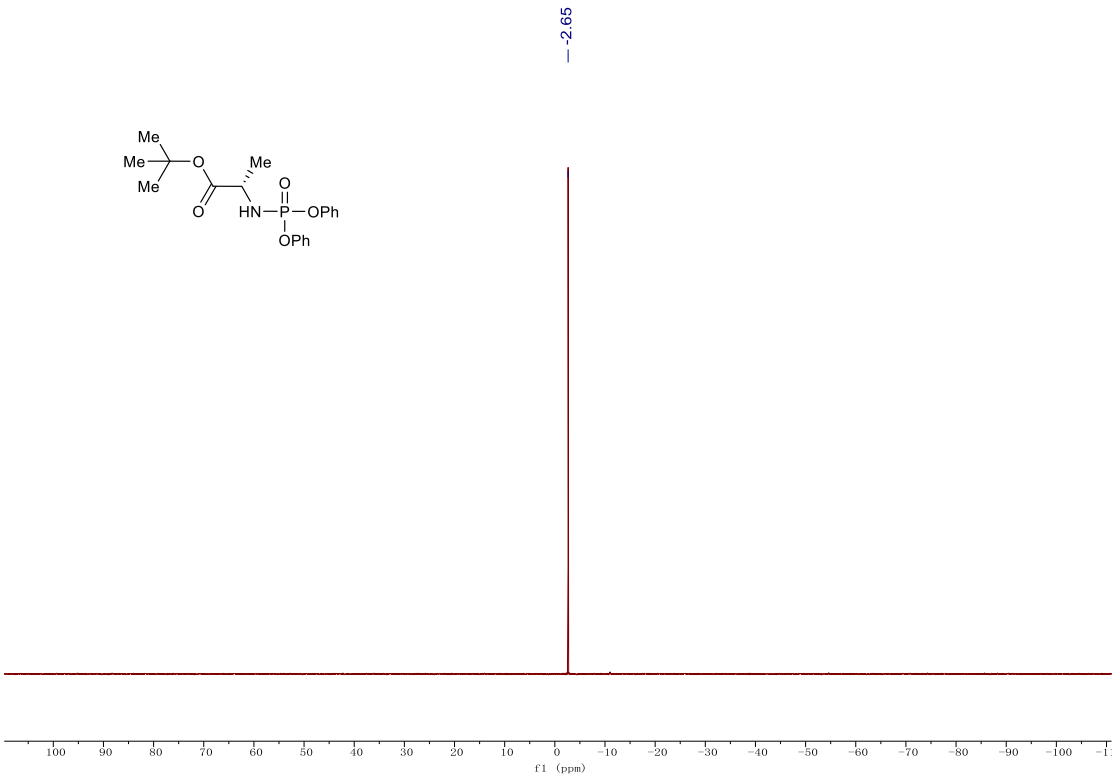
1c, ^{1}H NMR (500 MHz, $CDCl_3$)



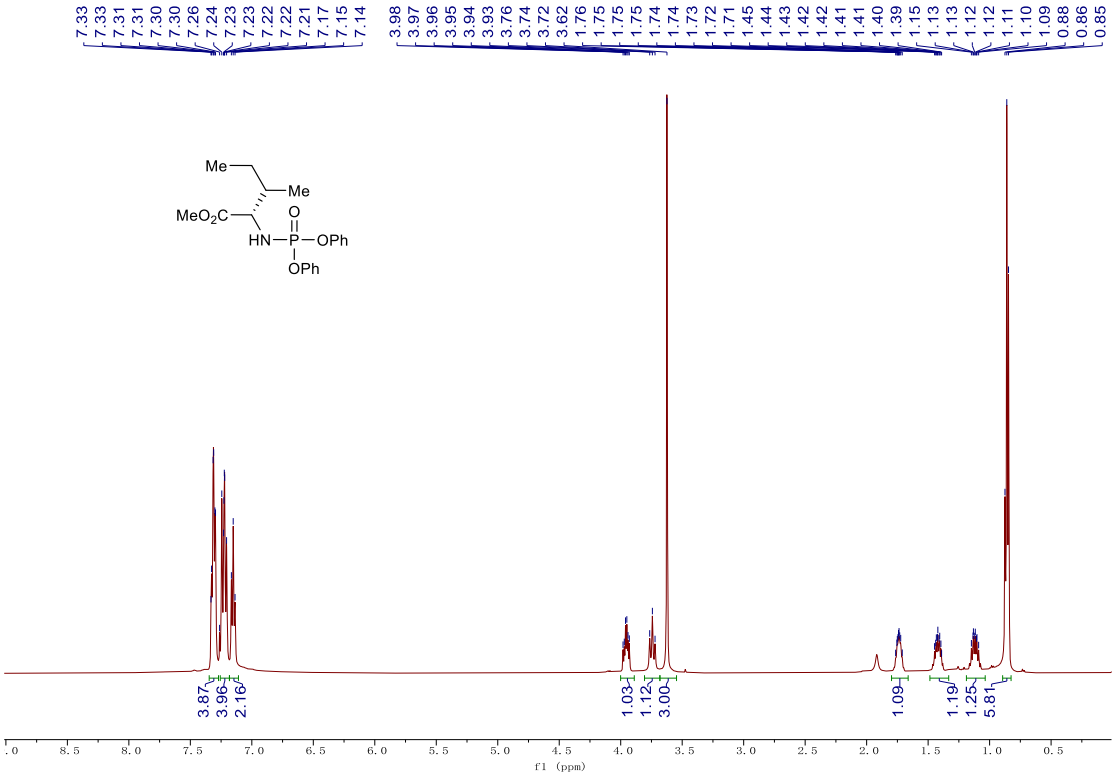
1c, ^{13}C NMR (126 MHz, $CDCl_3$)



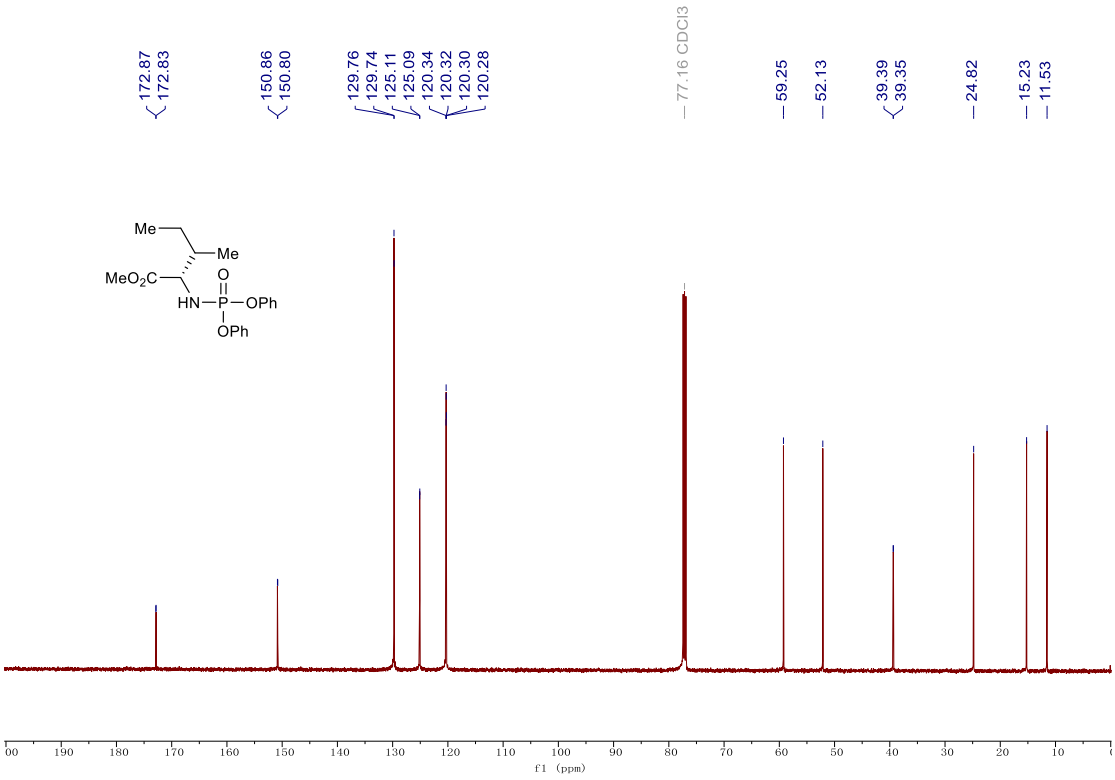
1c, ^{31}P NMR (202 MHz, $CDCl_3$)



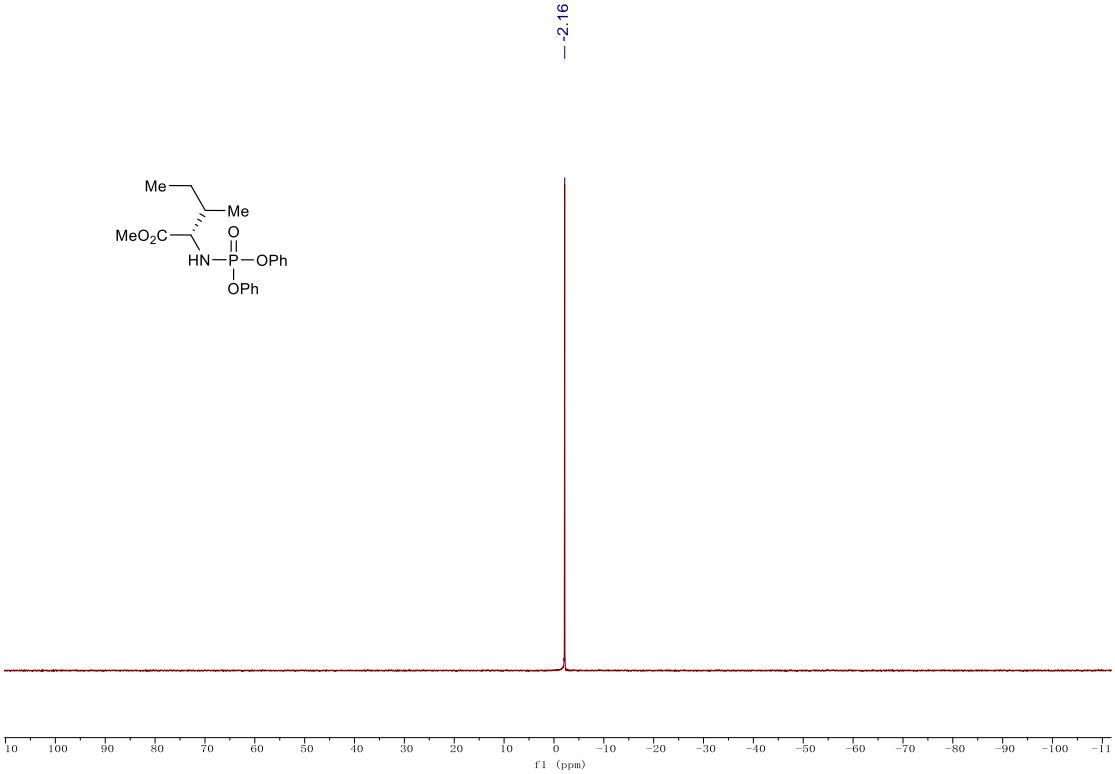
1d, ^{1}H NMR (500 MHz, $CDCl_3$)



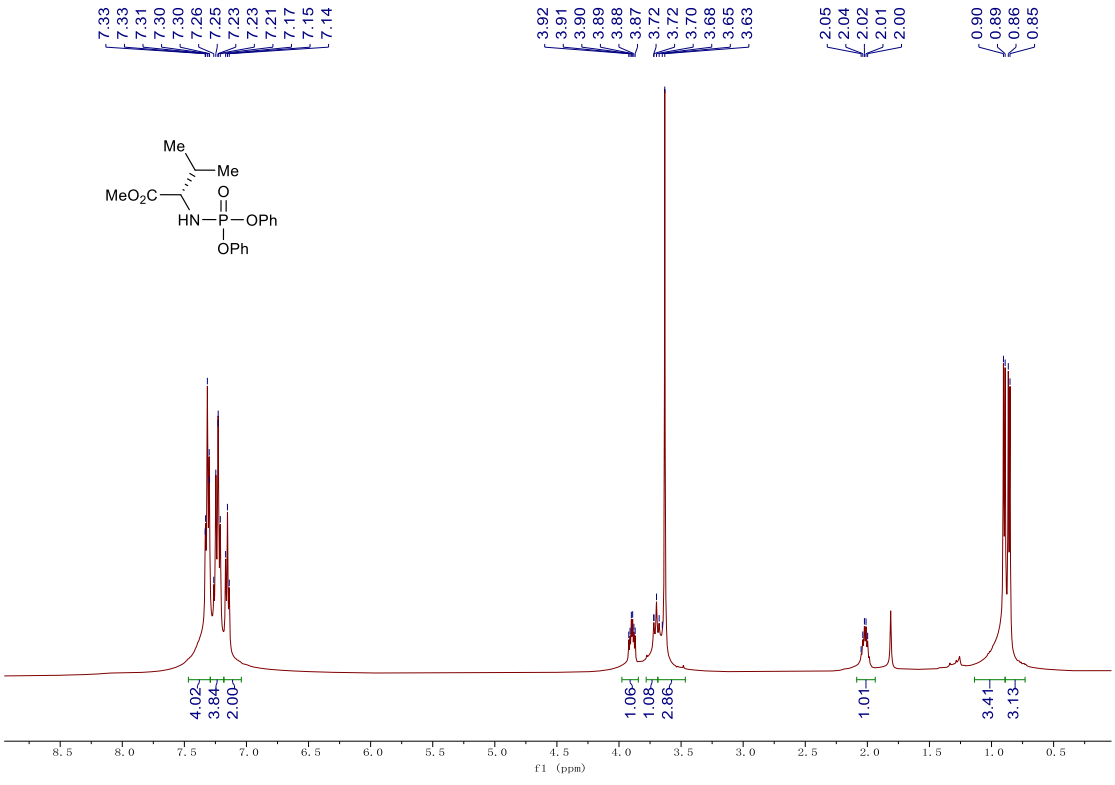
1d, ^{13}C NMR (126 MHz, $CDCl_3$)



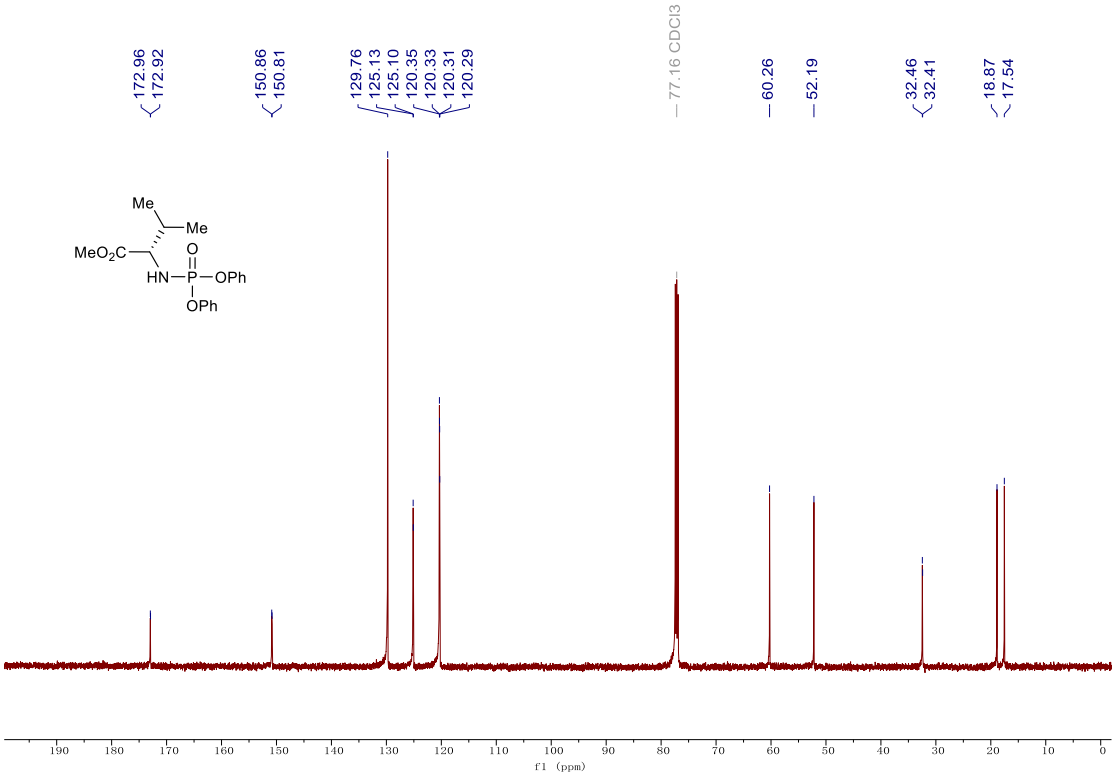
1d, ^{31}P NMR (202 MHz, $CDCl_3$)



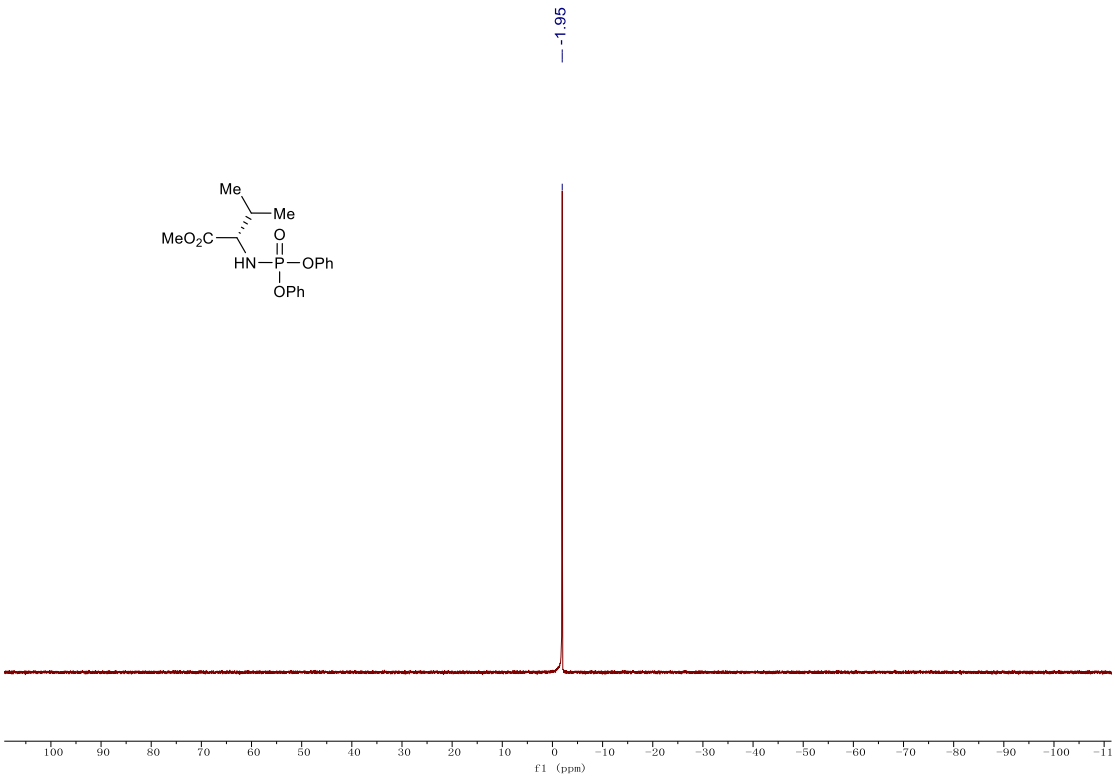
1e, ^{1}H NMR (500 MHz, $CDCl_3$)



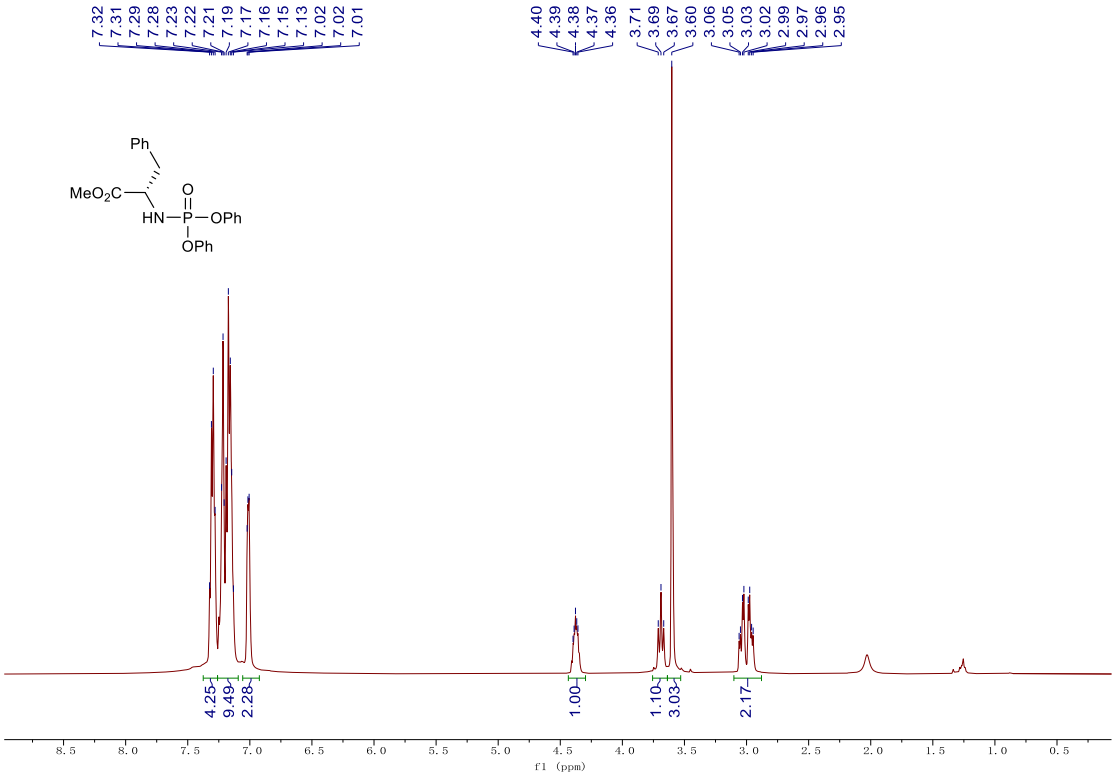
1e, ^{13}C NMR (126 MHz, $CDCl_3$)



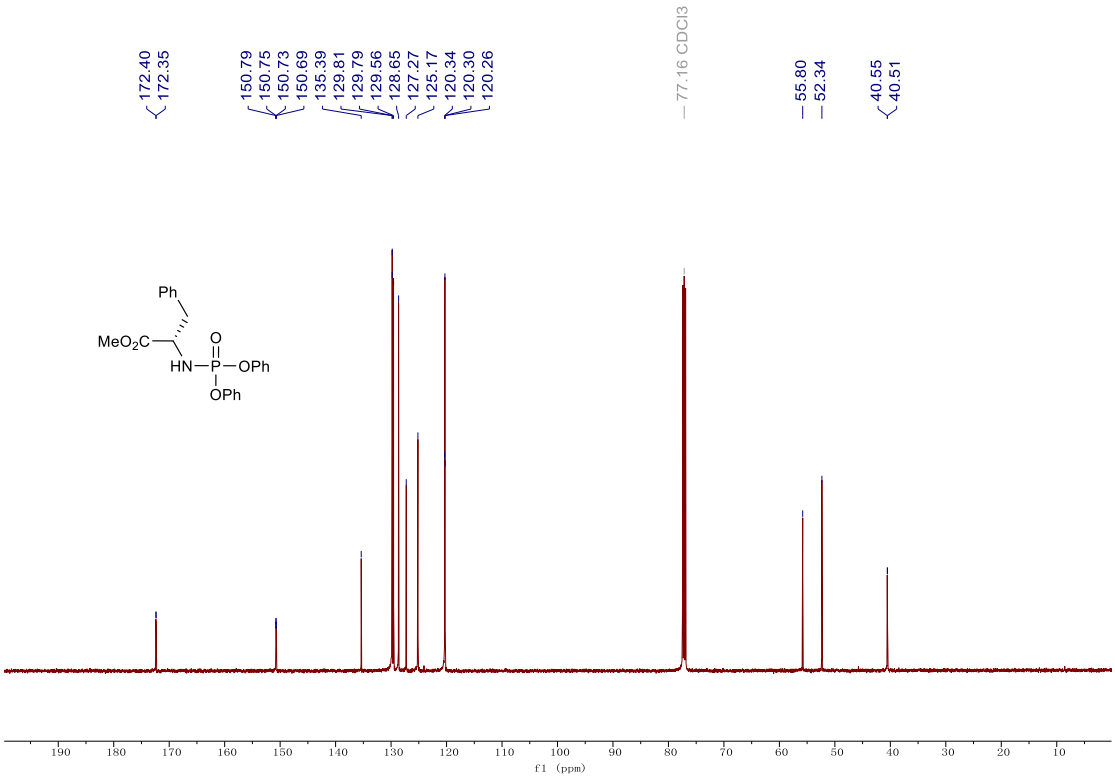
1e, ^{31}P NMR (202 MHz, $CDCl_3$)



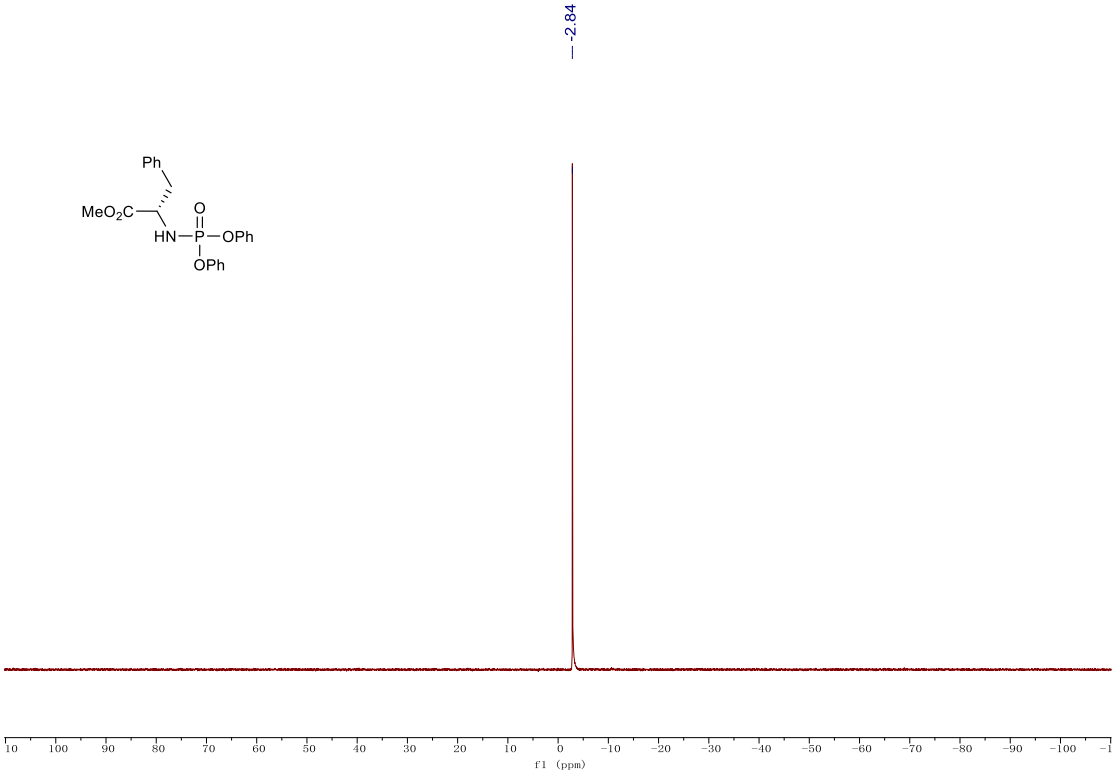
1f, ^{1}H NMR (500 MHz, $CDCl_3$)



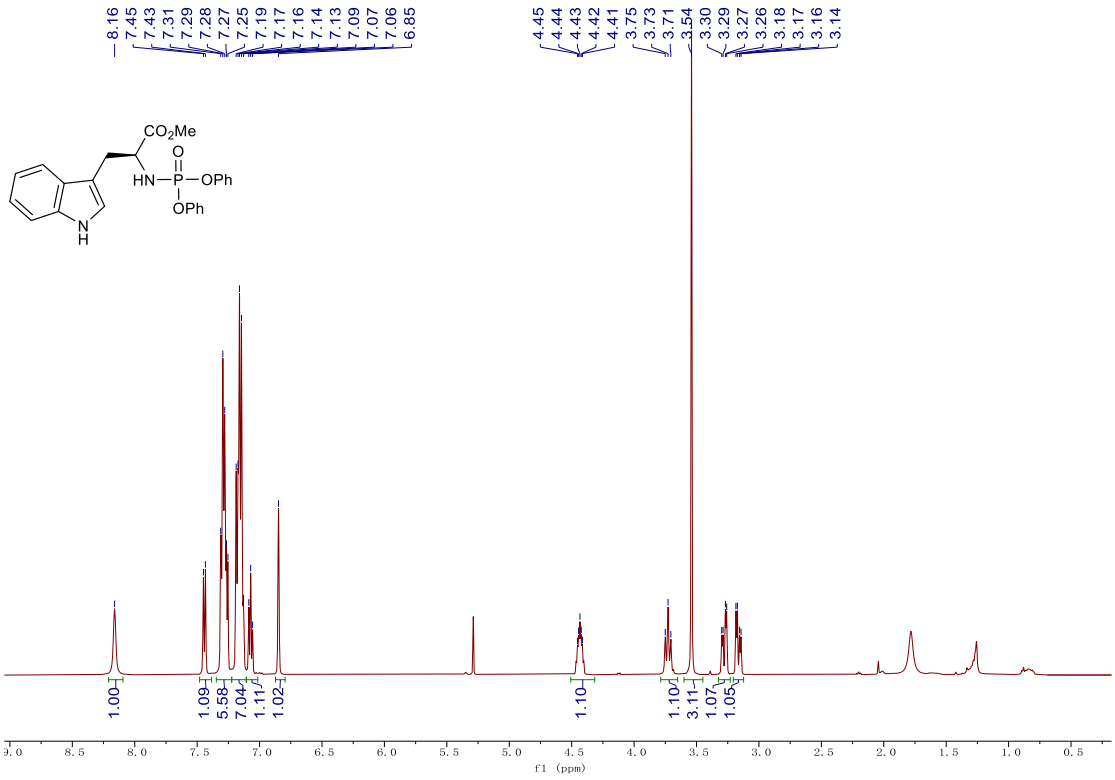
1f, ^{13}C NMR (126 MHz, $CDCl_3$)



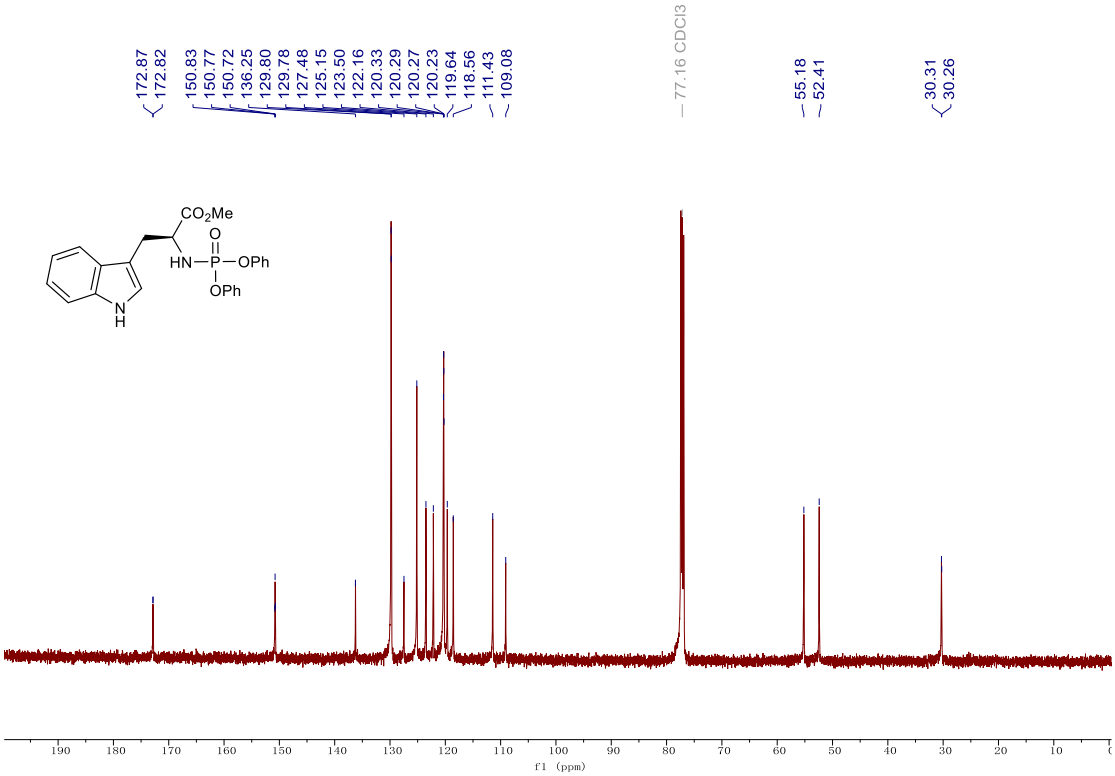
1f, ^{31}P NMR (202 MHz, $CDCl_3$)



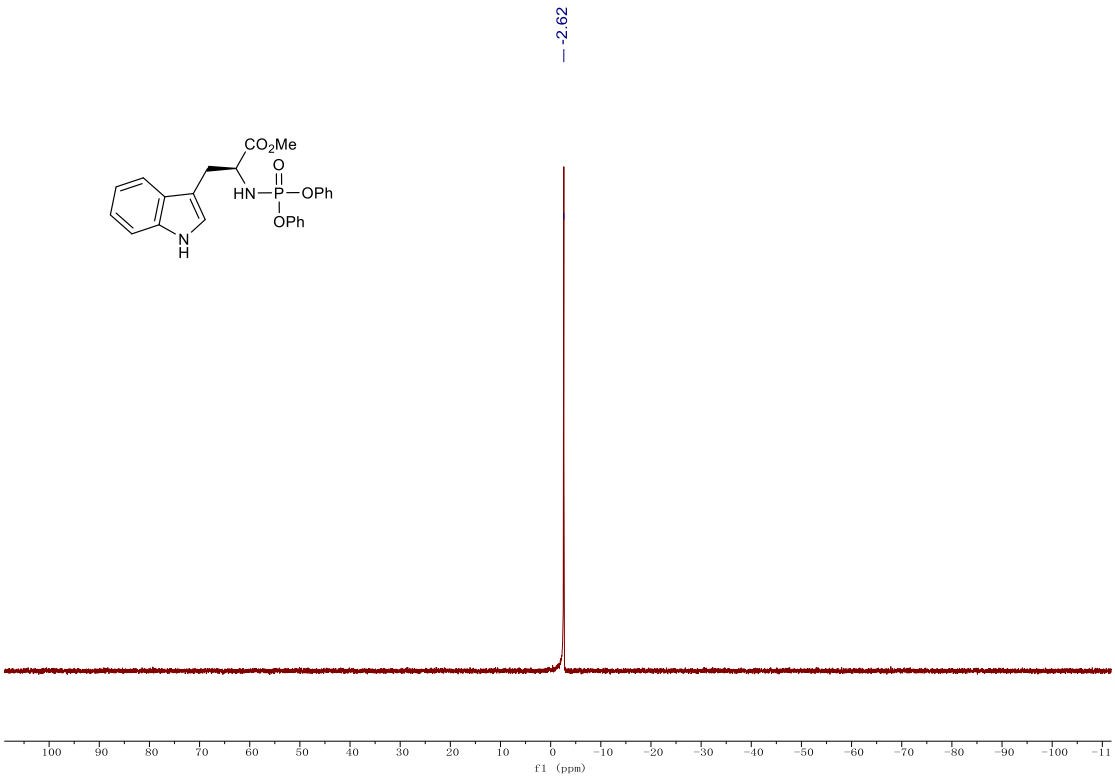
1g, ^{1}H NMR (500 MHz, $CDCl_3$)



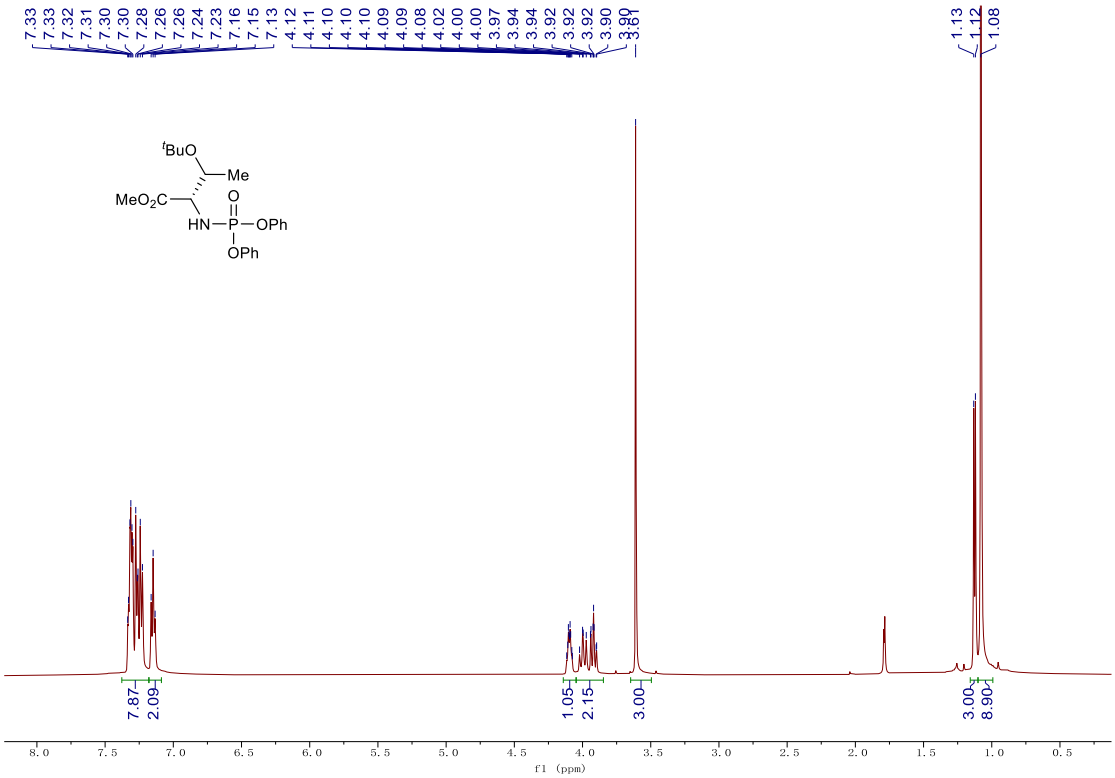
1g, ^{13}C NMR (126 MHz, $CDCl_3$)



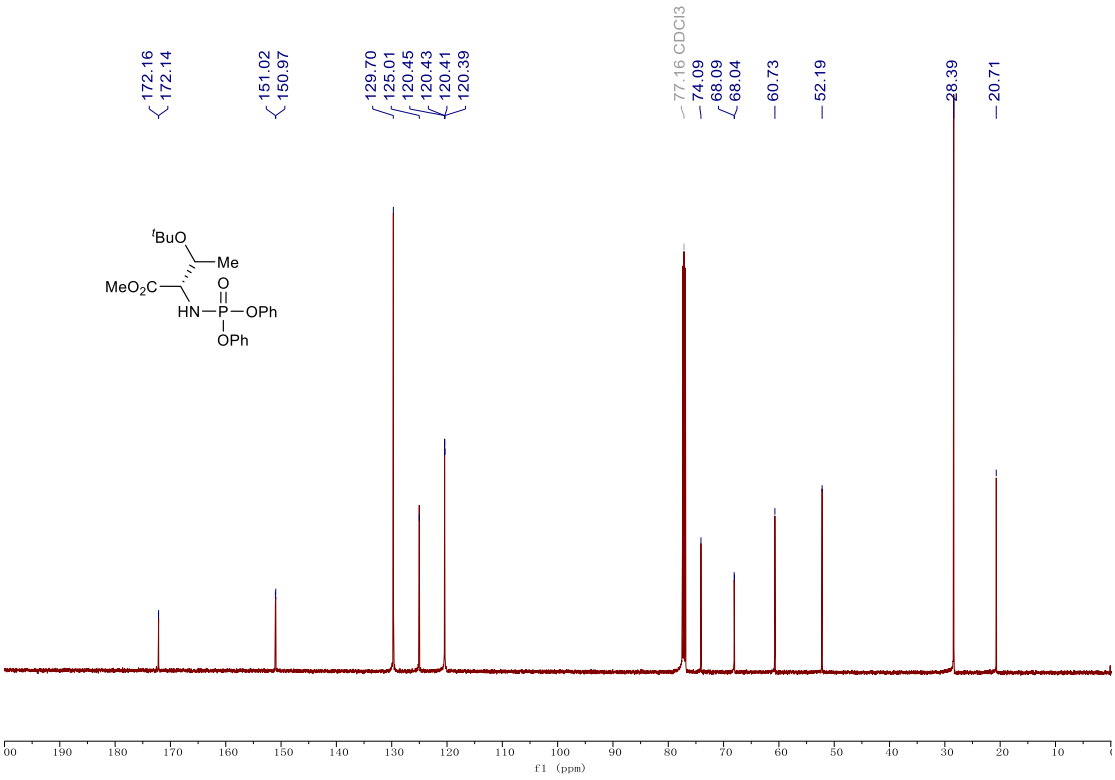
1g, ^{31}P NMR (202 MHz, $CDCl_3$)



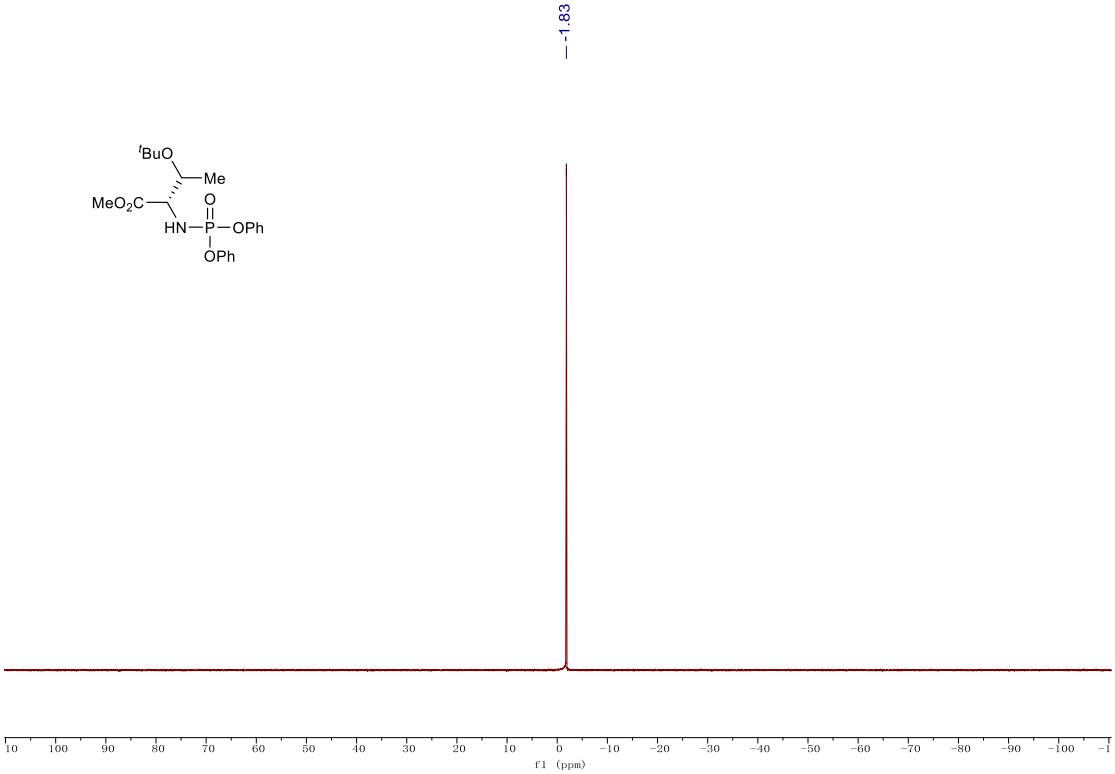
1h, ^{1}H NMR (500 MHz, $CDCl_3$)



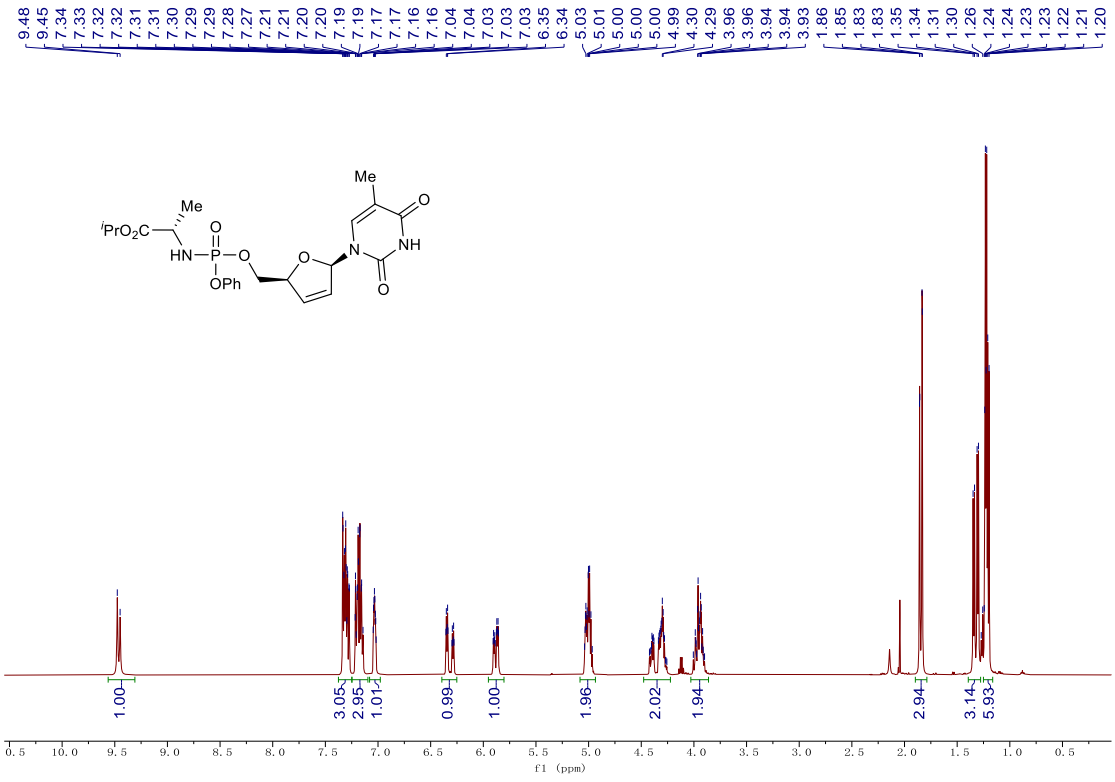
1h, ^{13}C NMR (126 MHz, $CDCl_3$)



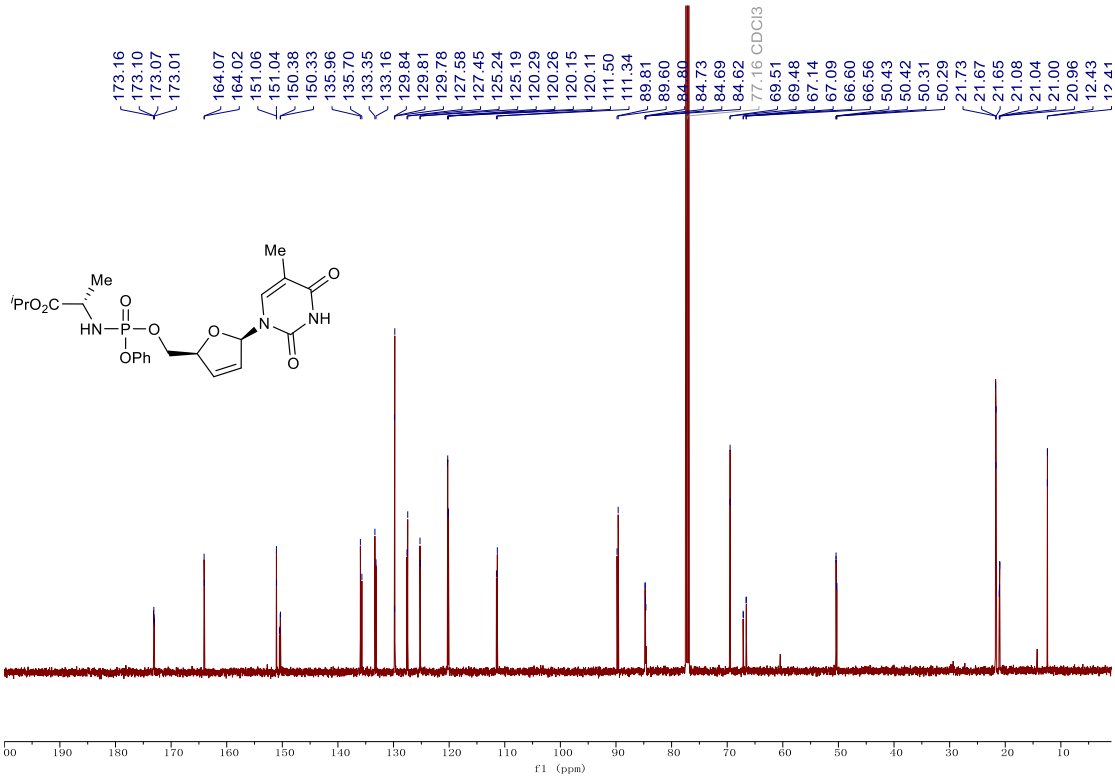
1h, ^{31}P NMR (202 MHz, $CDCl_3$)



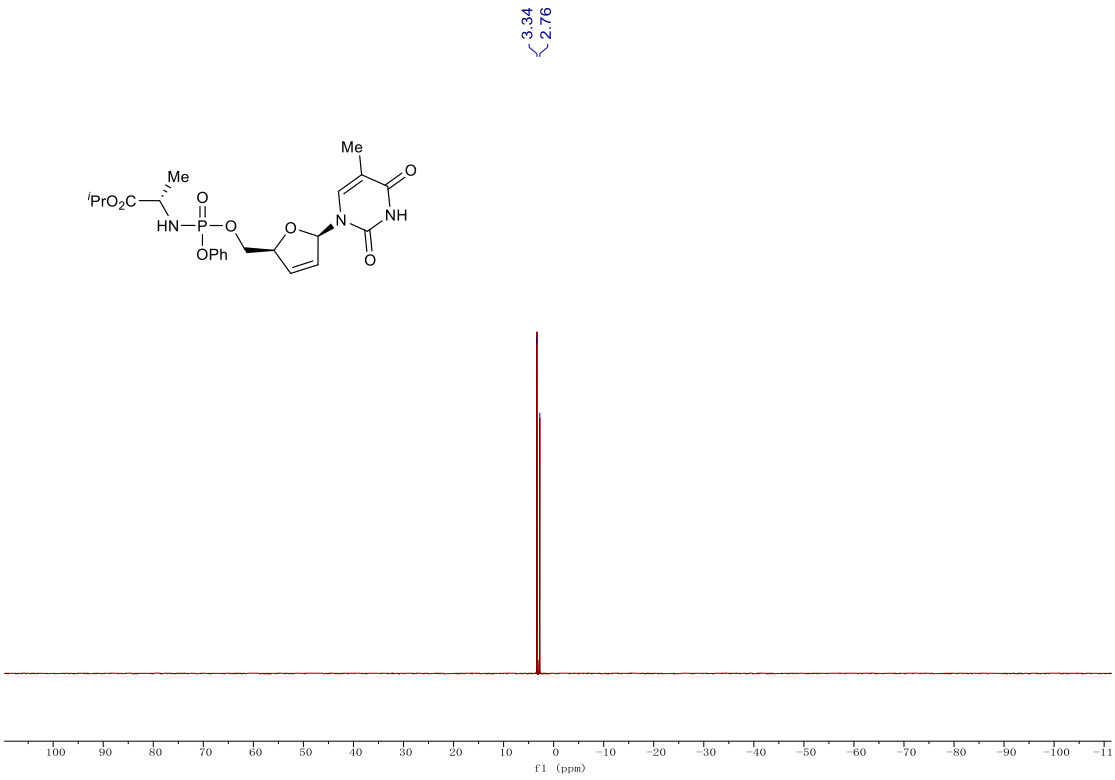
3, ^{1}H NMR (500 MHz, $CDCl_3$)



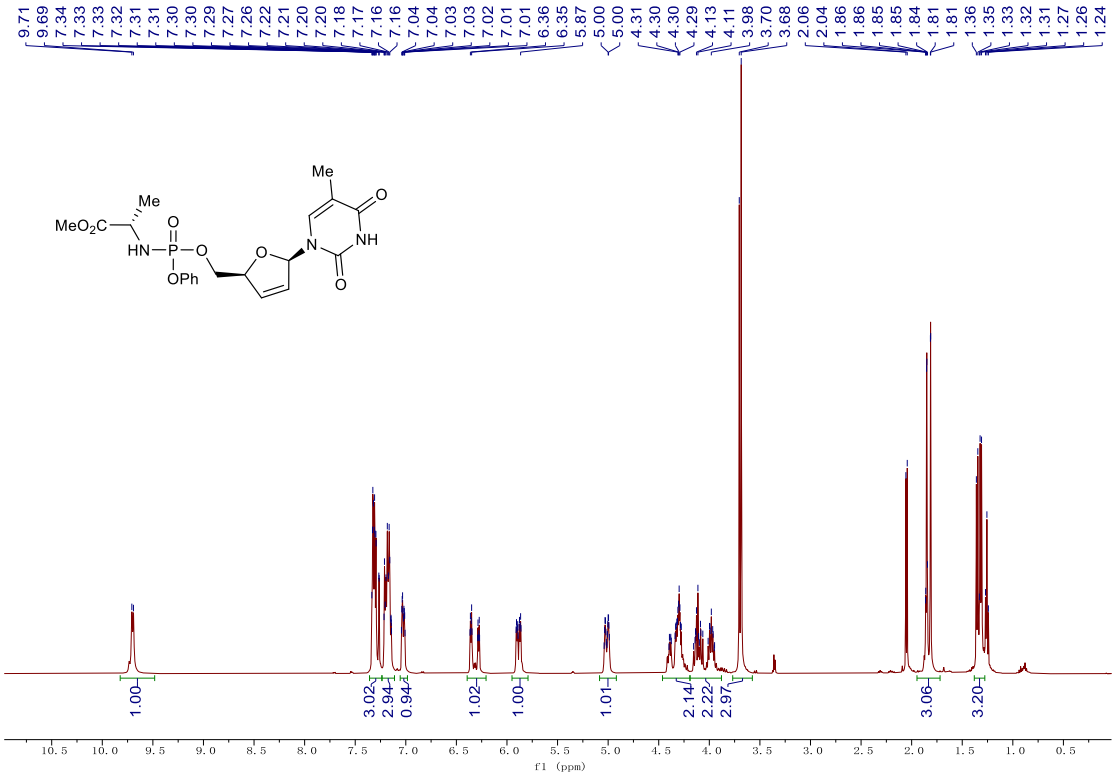
3, ^{13}C NMR (126 MHz, $CDCl_3$)



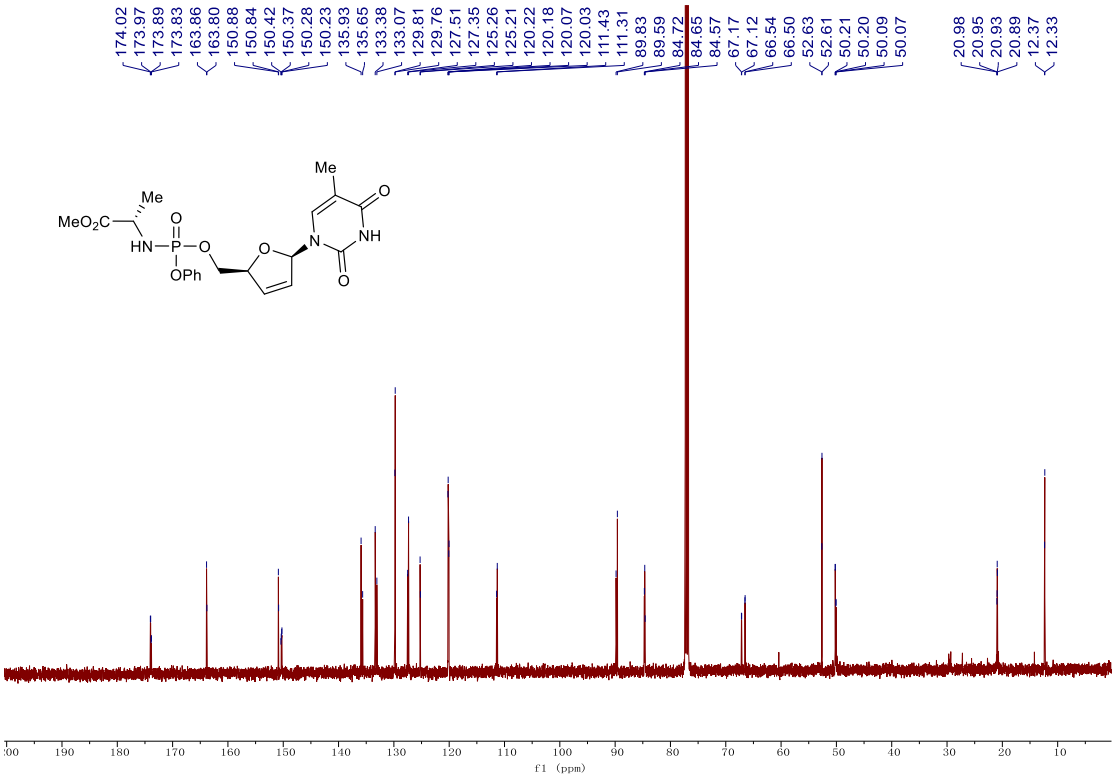
3, ^{31}P NMR (202 MHz, $CDCl_3$)



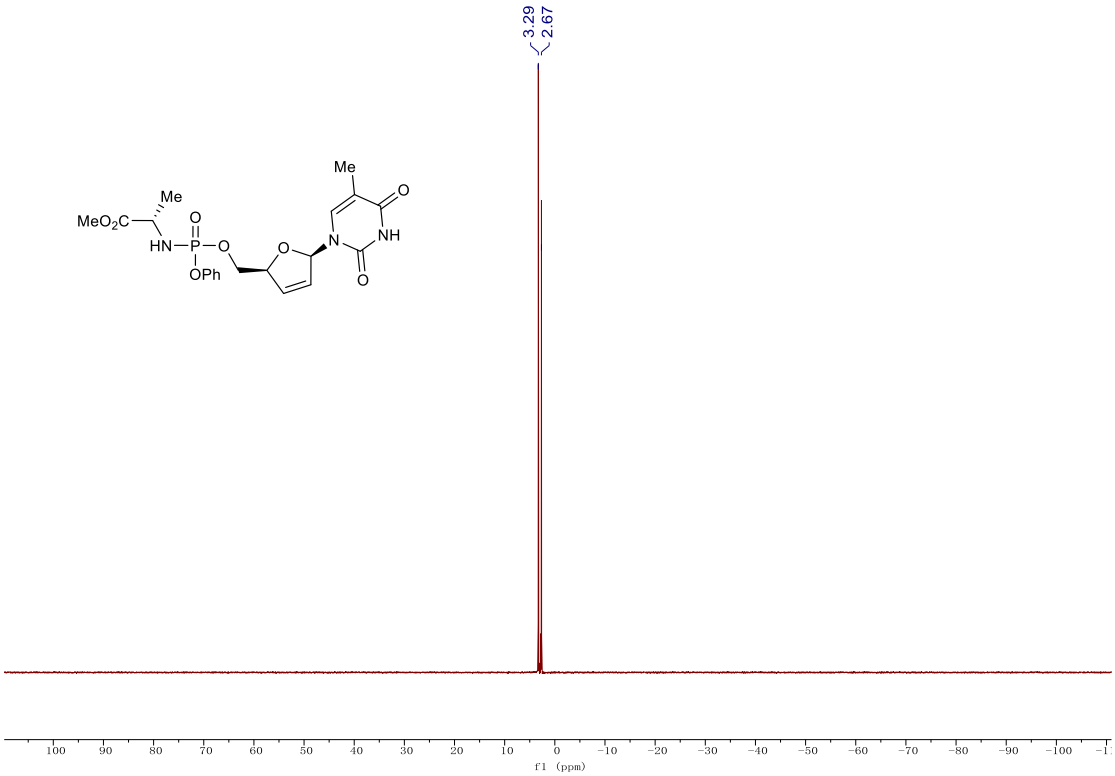
4, ^{1}H NMR (500 MHz, $CDCl_3$)



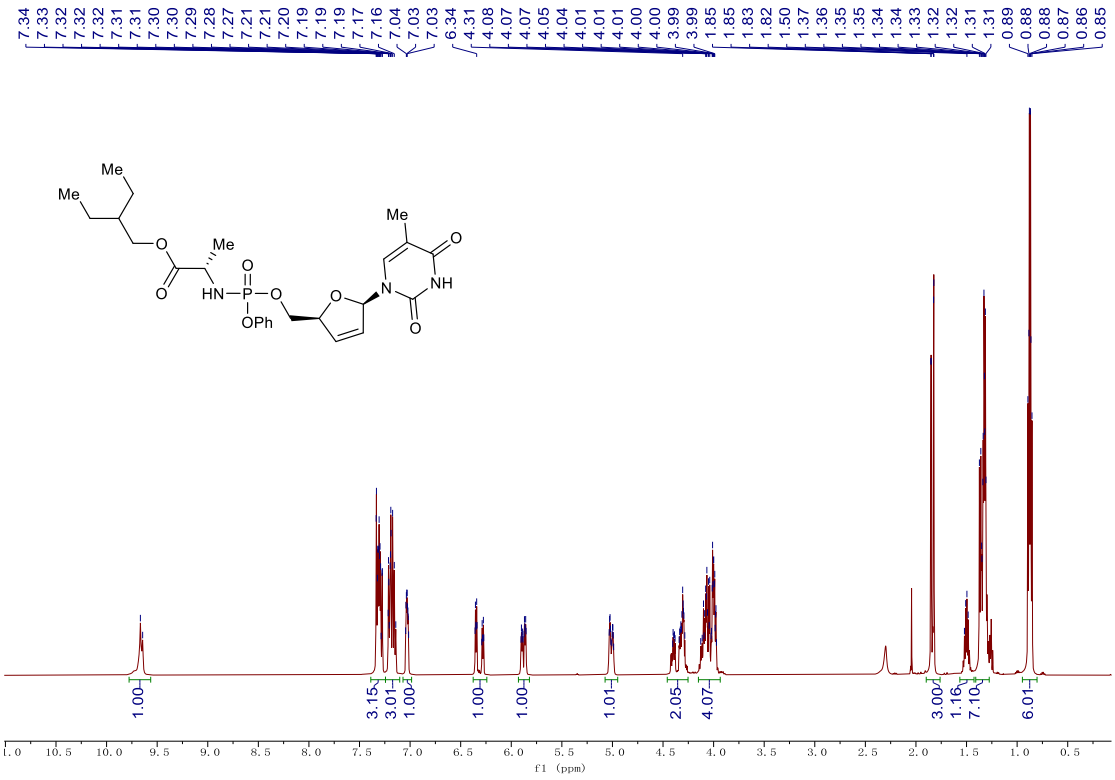
4, ^{13}C NMR (126 MHz, $CDCl_3$)



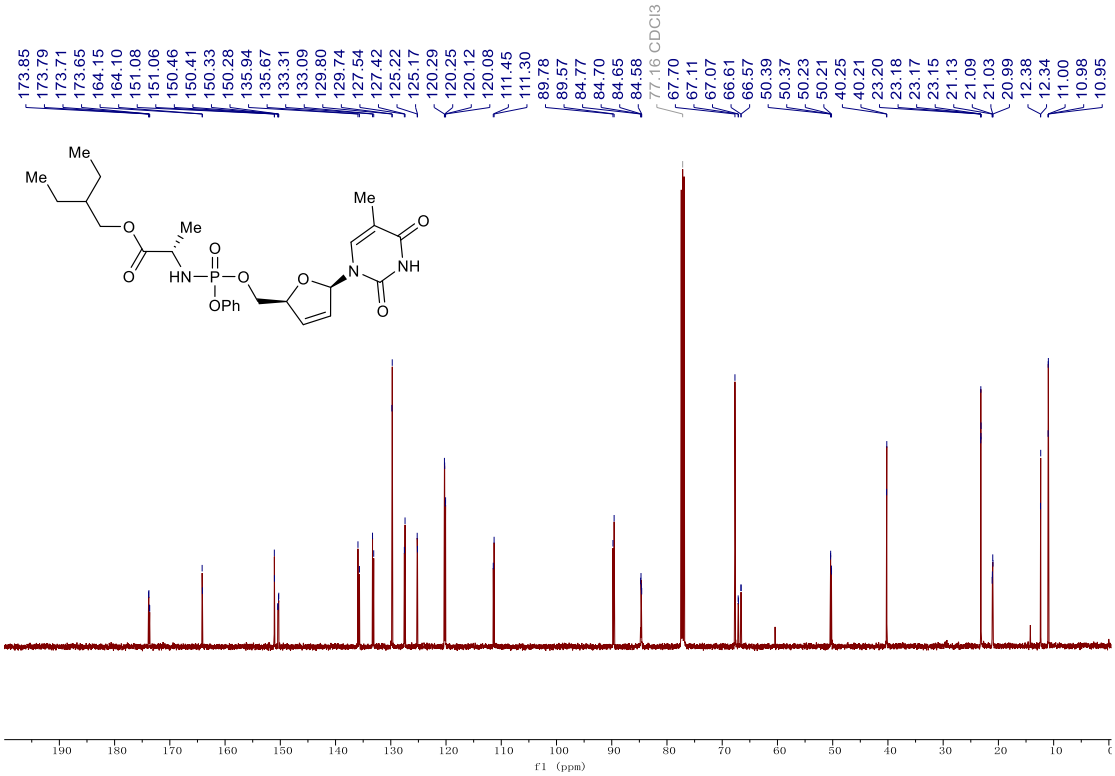
4, ^{31}P NMR (202 MHz, $CDCl_3$)



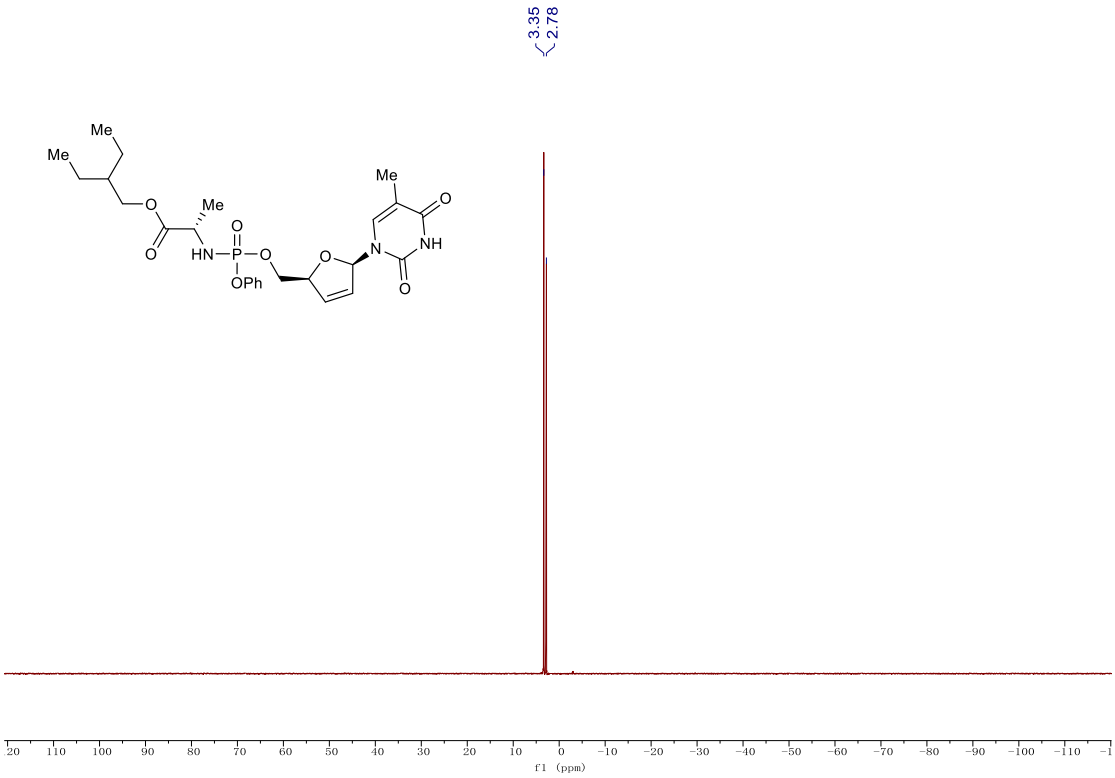
5, ^{1}H NMR (500 MHz, $CDCl_3$)



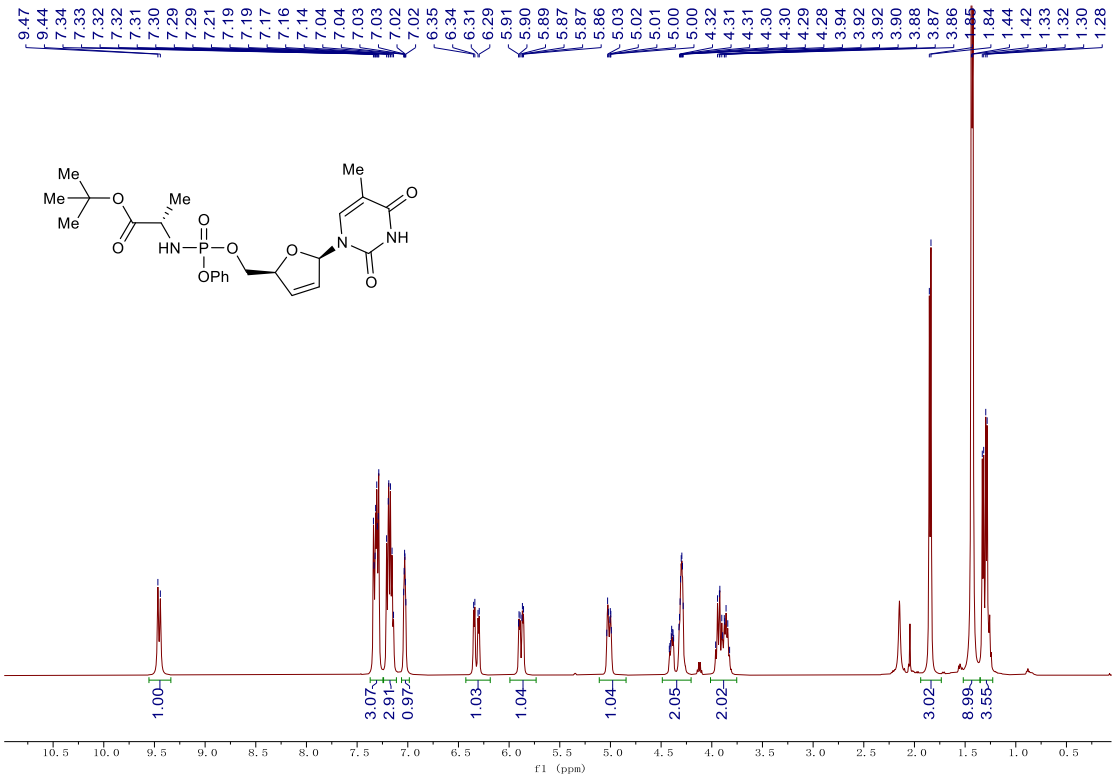
5, ^{13}C NMR (126 MHz, $CDCl_3$)



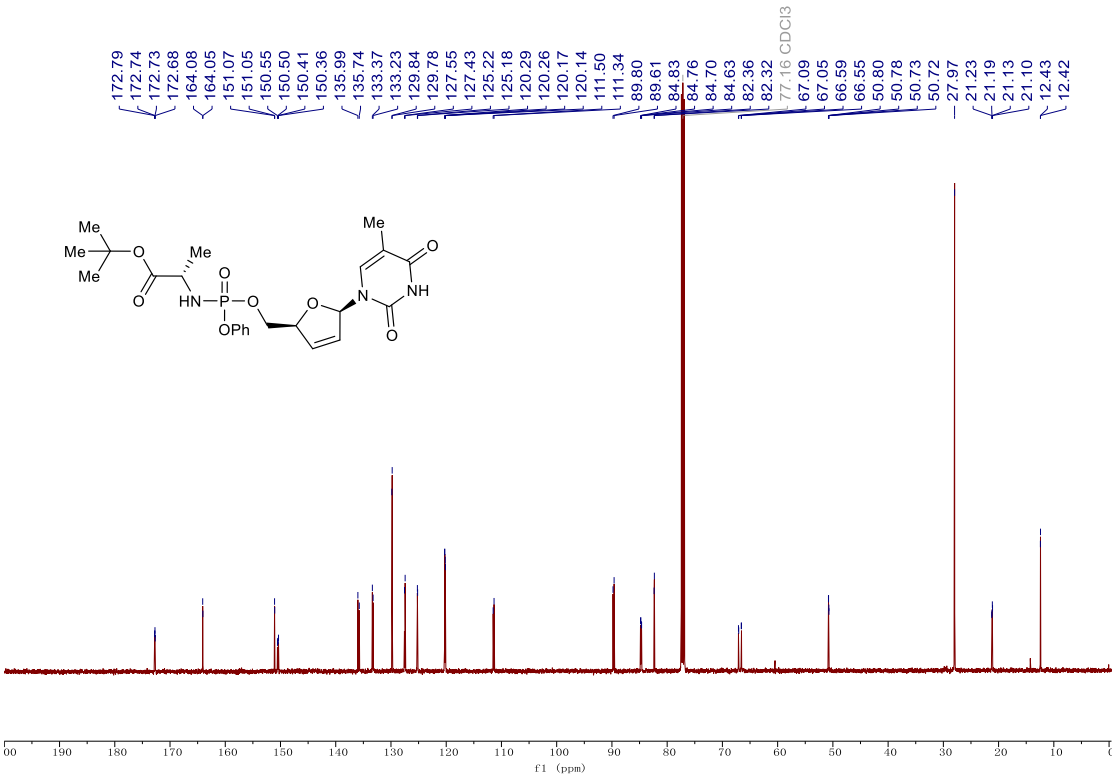
5, ^{31}P NMR (202 MHz, $CDCl_3$)



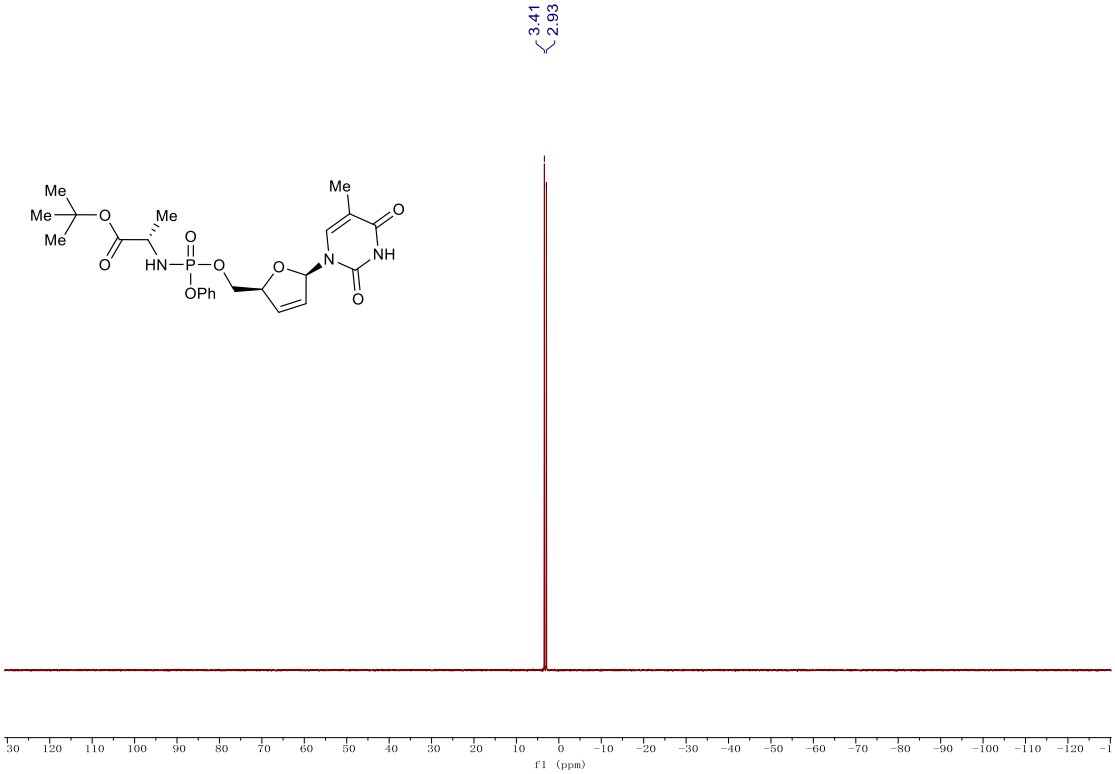
6, ^{1}H NMR (500 MHz, $CDCl_3$)



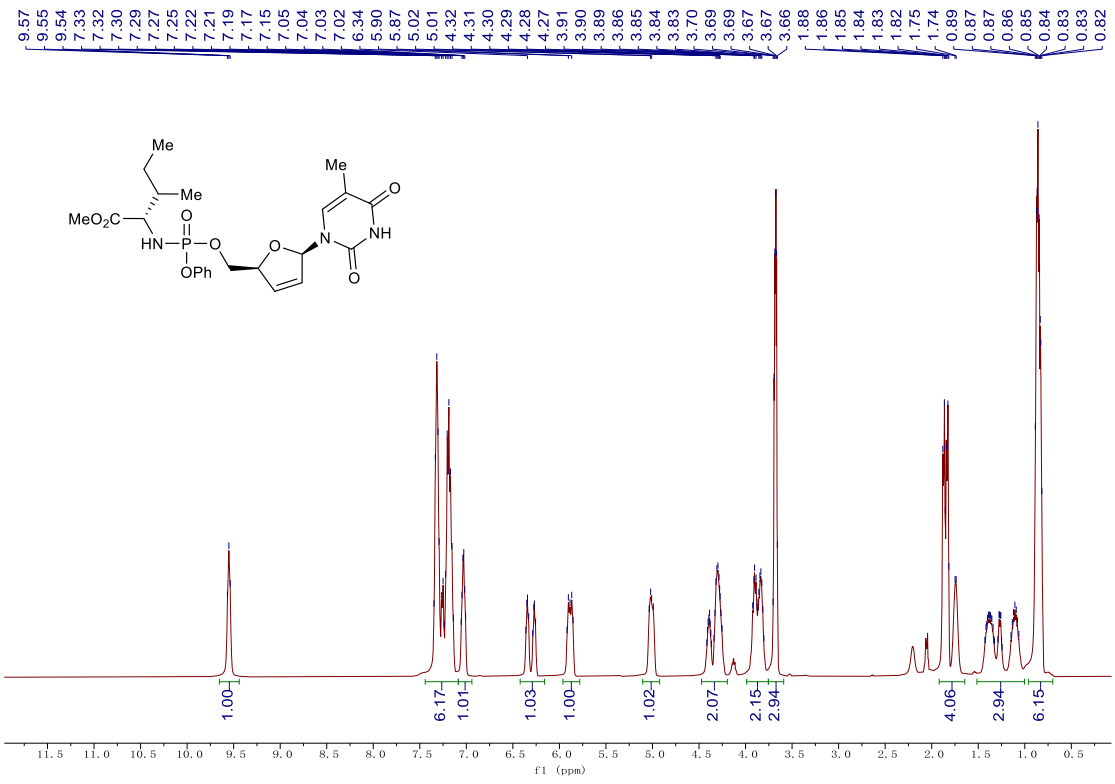
6, ^{13}C NMR (126 MHz, $CDCl_3$)



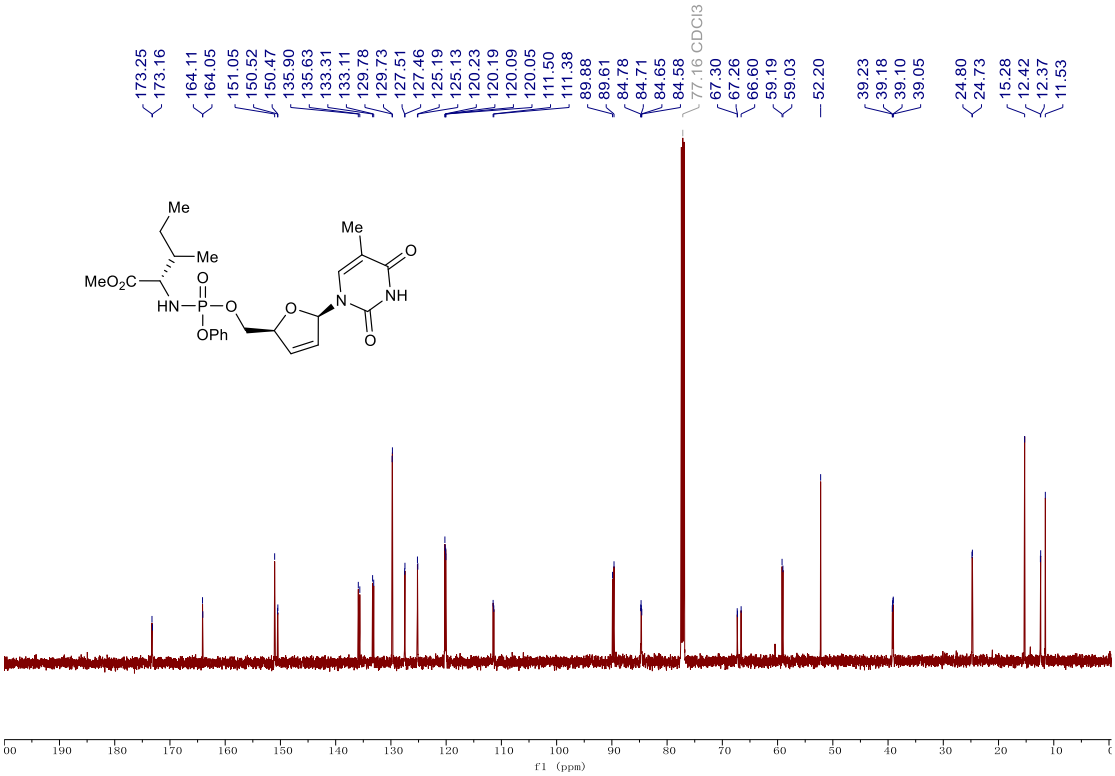
6, ^{31}P NMR (202 MHz, $CDCl_3$)



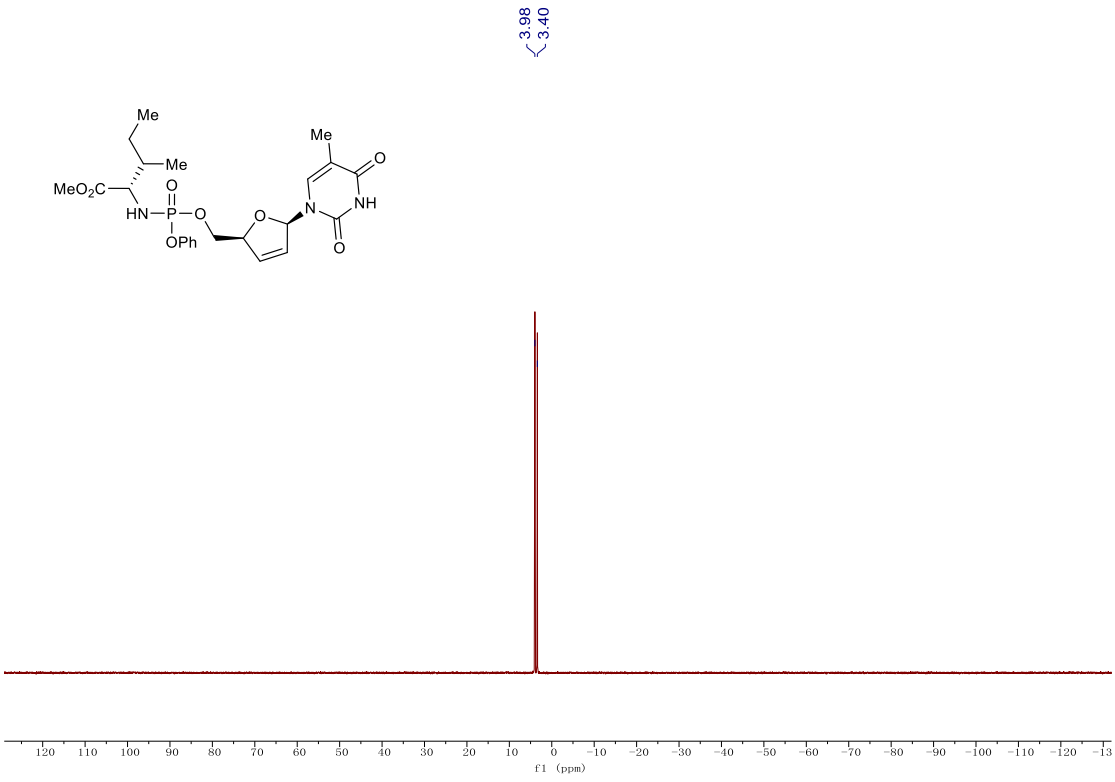
7, ^{1}H NMR (500 MHz, $CDCl_3$)



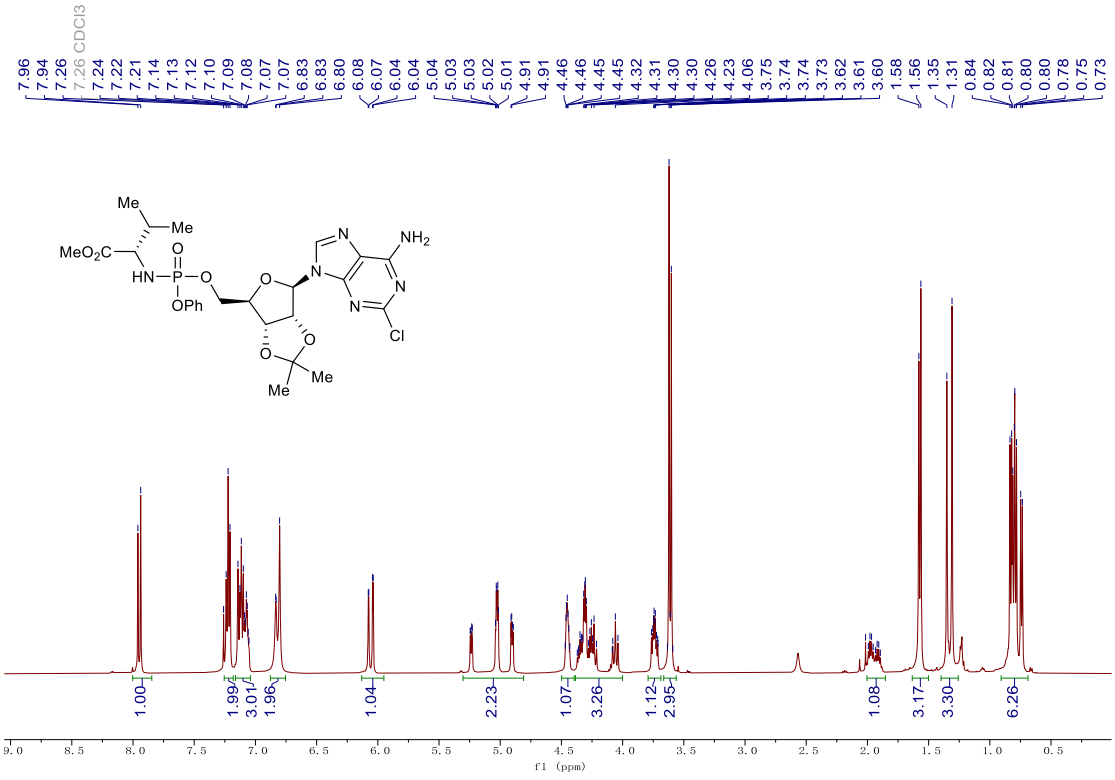
7, ^{13}C NMR (126 MHz, $CDCl_3$)



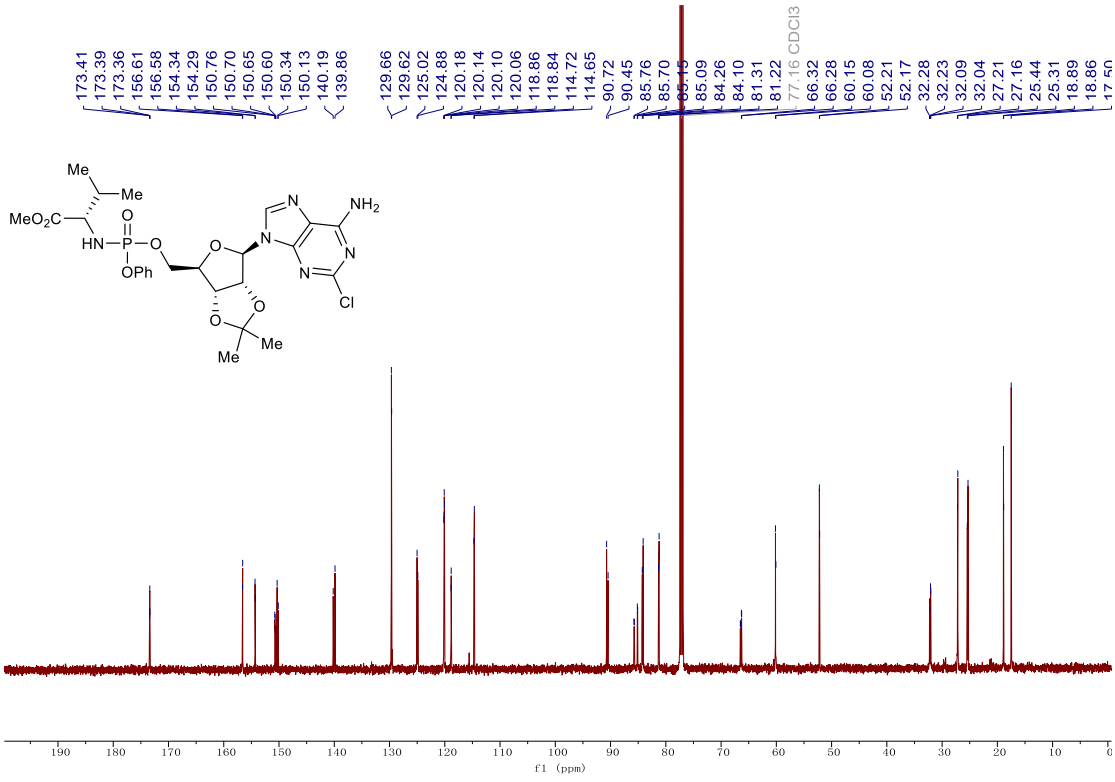
7, ^{31}P NMR (202 MHz, $CDCl_3$)



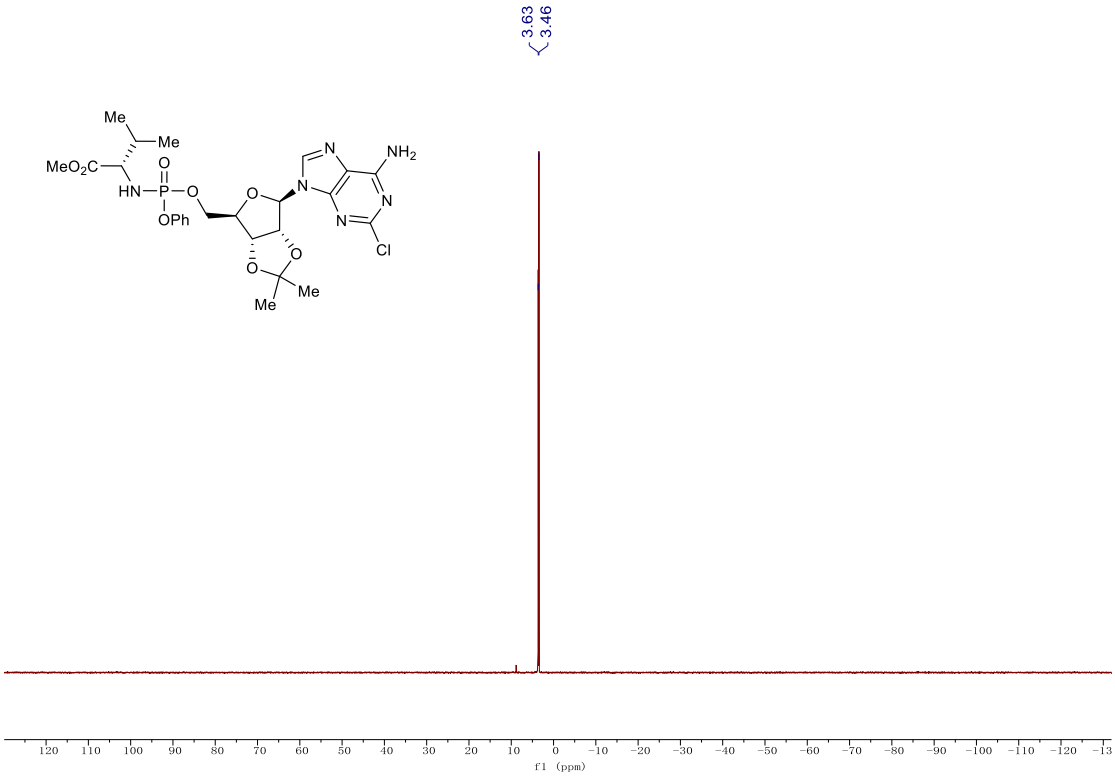
8, ^{1}H NMR (500 MHz, $CDCl_3$)



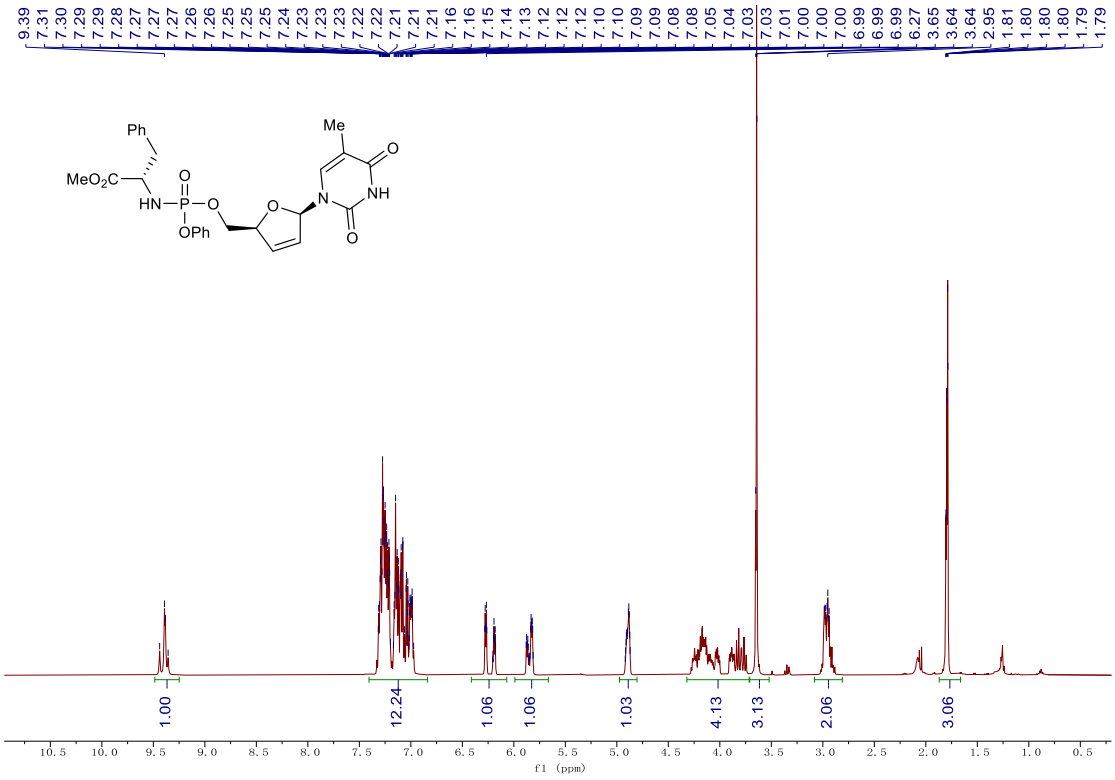
8, ^{13}C NMR (126 MHz, $CDCl_3$)



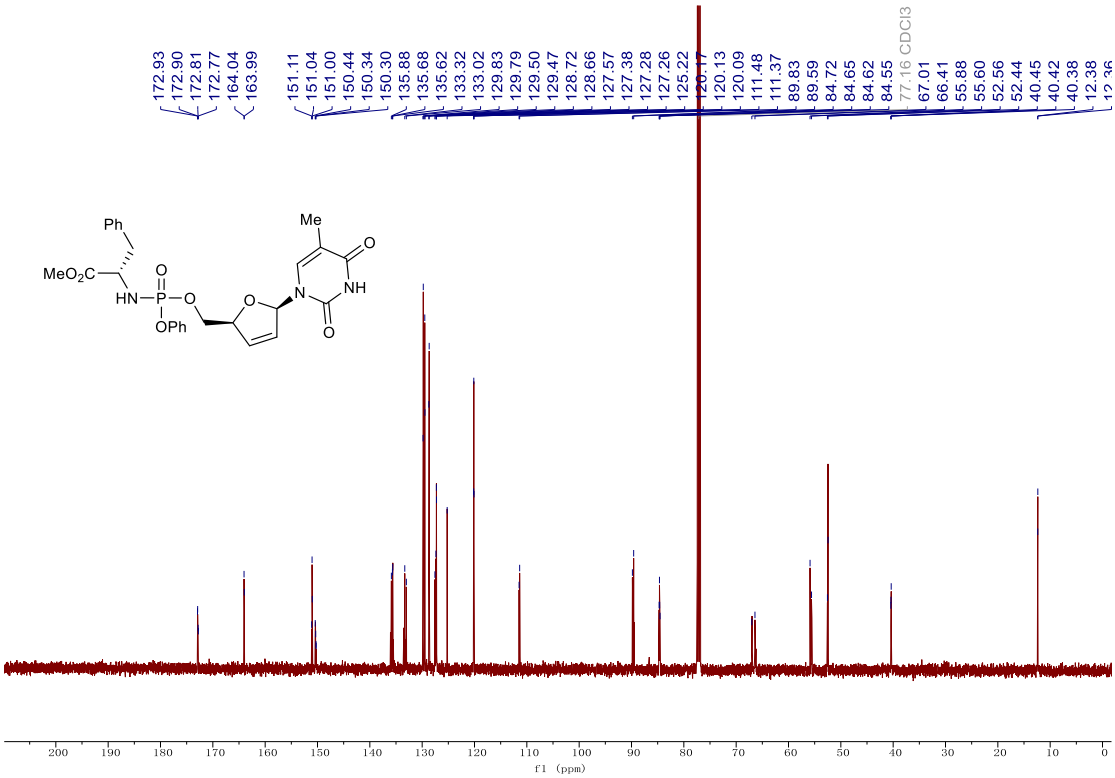
8, ^{31}P NMR (202 MHz, $CDCl_3$)



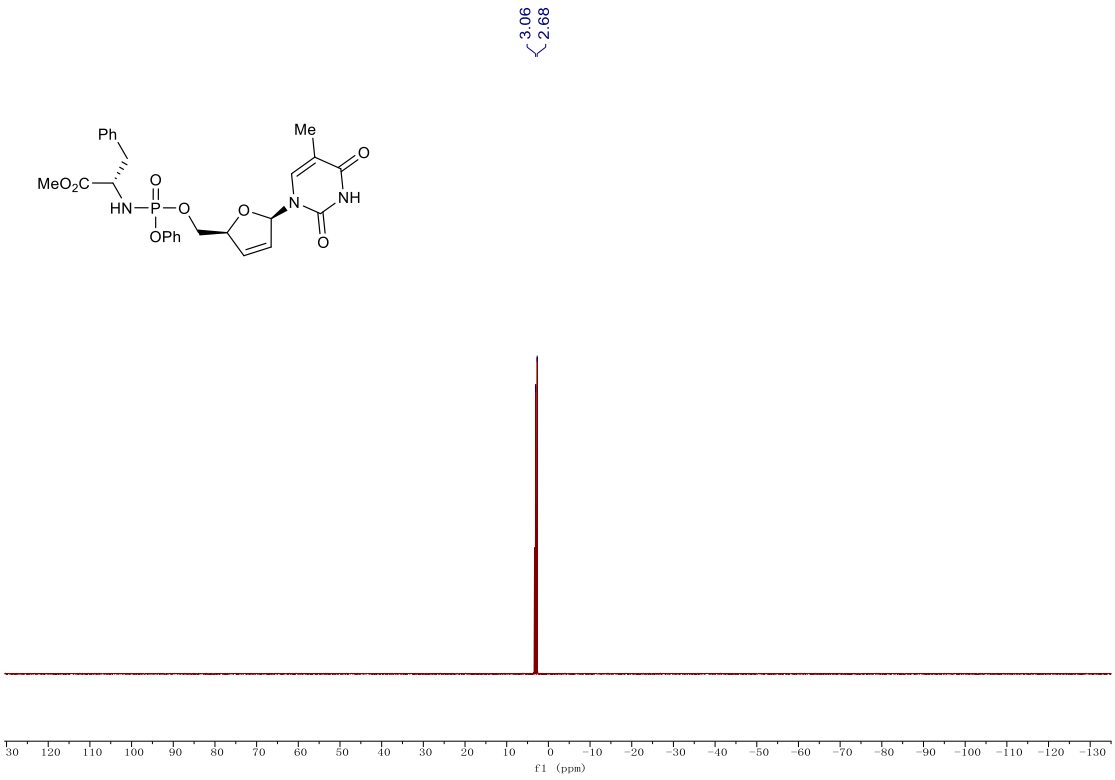
9, ^{1}H NMR (500 MHz, $CDCl_3$)



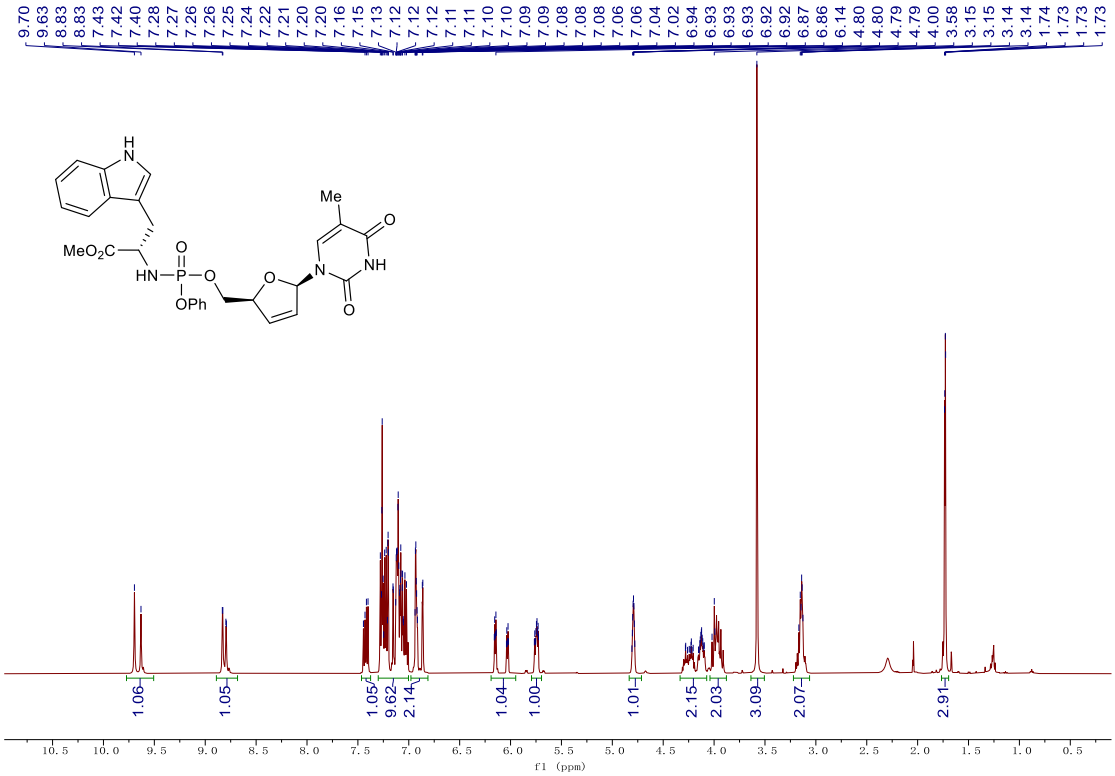
9, ^{13}C NMR (126 MHz, $CDCl_3$)



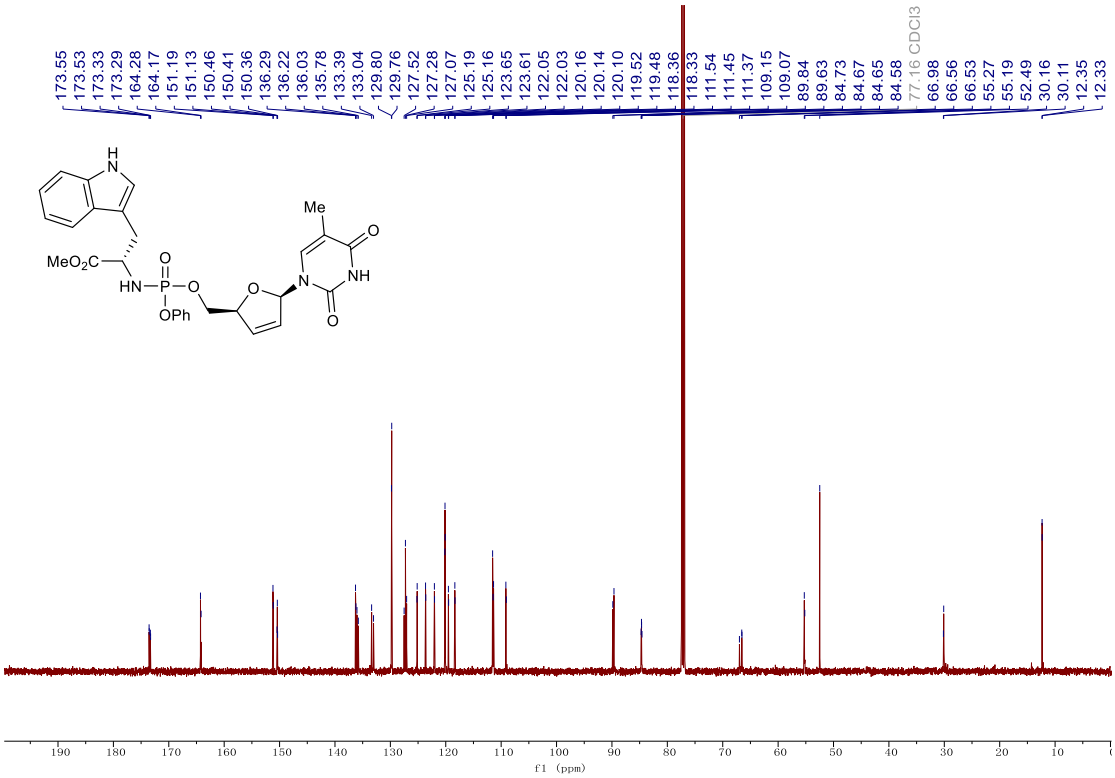
9, ^{31}P NMR (202 MHz, $CDCl_3$)



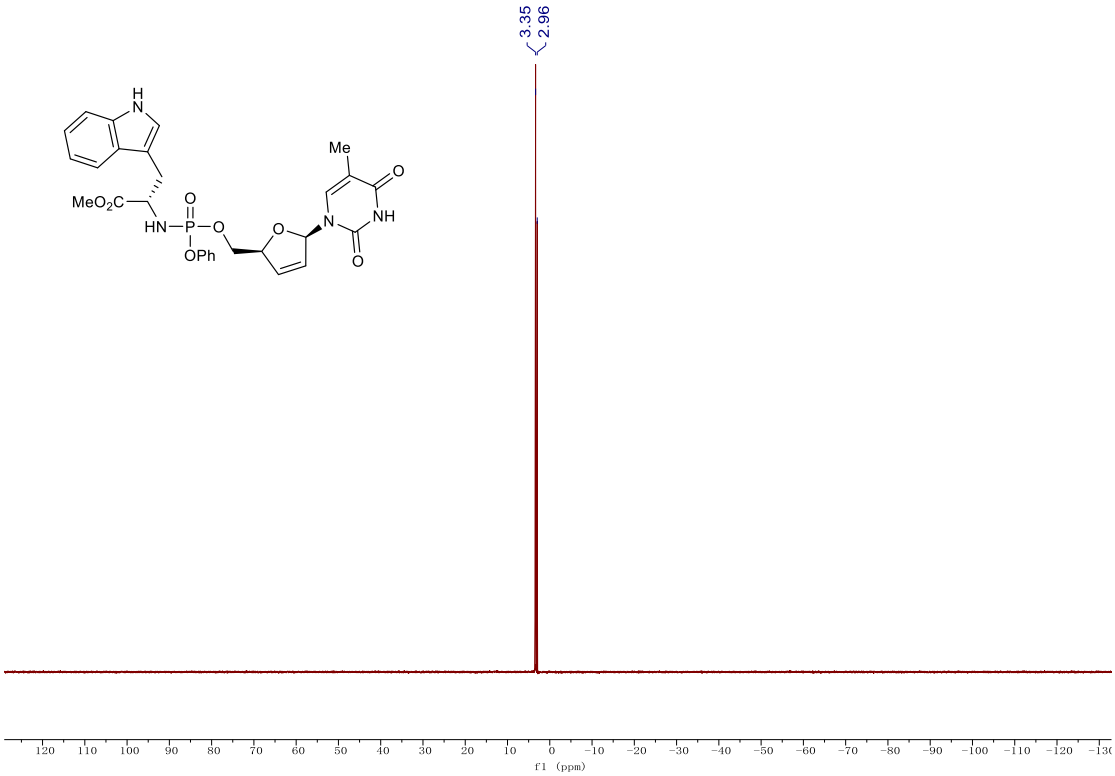
10, ^{1}H NMR (500 MHz, $CDCl_3$)



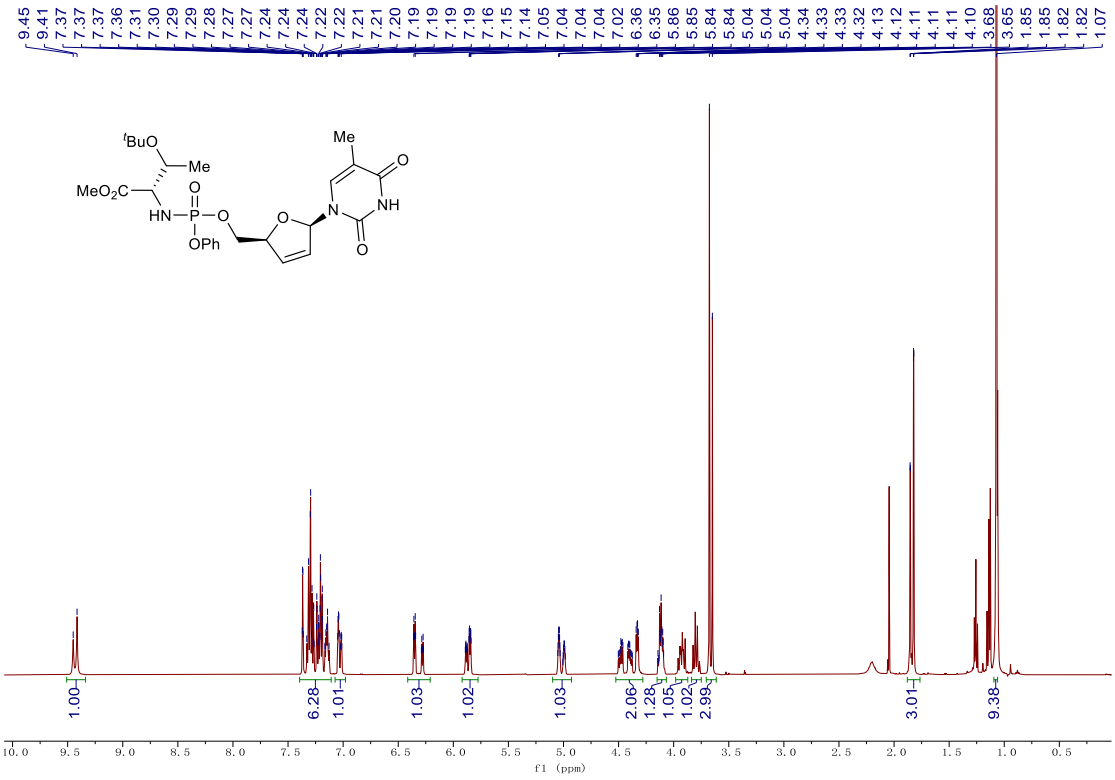
10, ^{13}C NMR (126 MHz, $CDCl_3$)



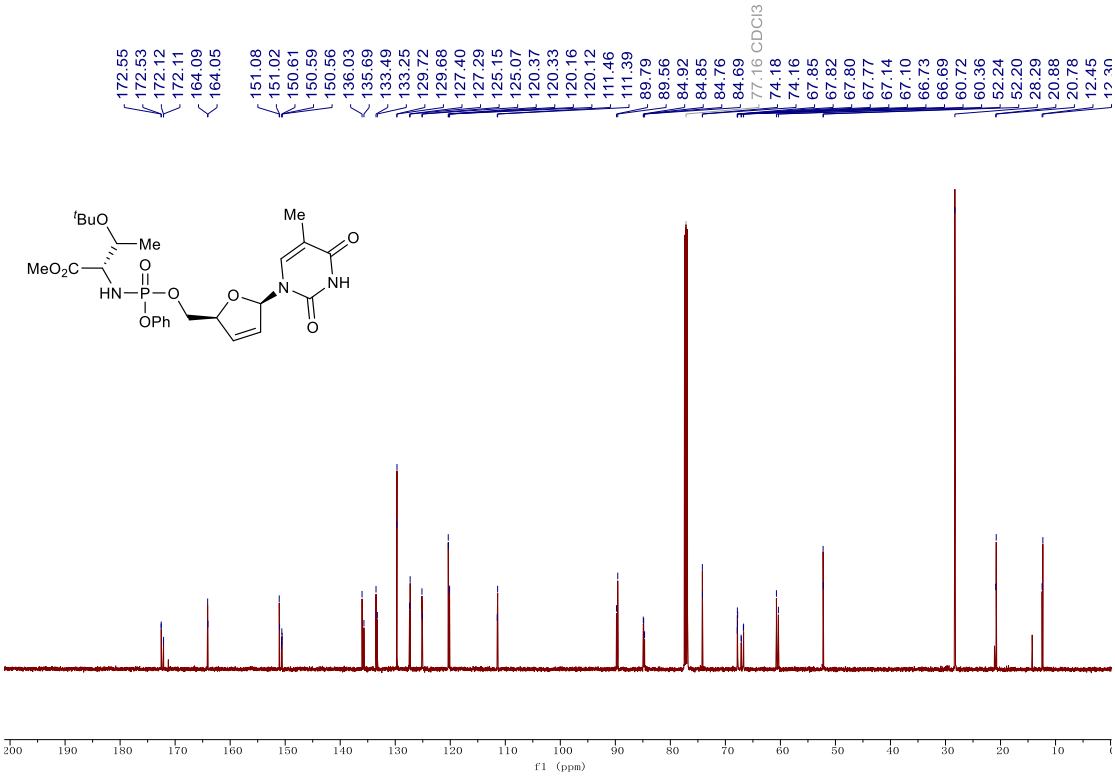
10, ^{31}P NMR (202 MHz, $CDCl_3$)



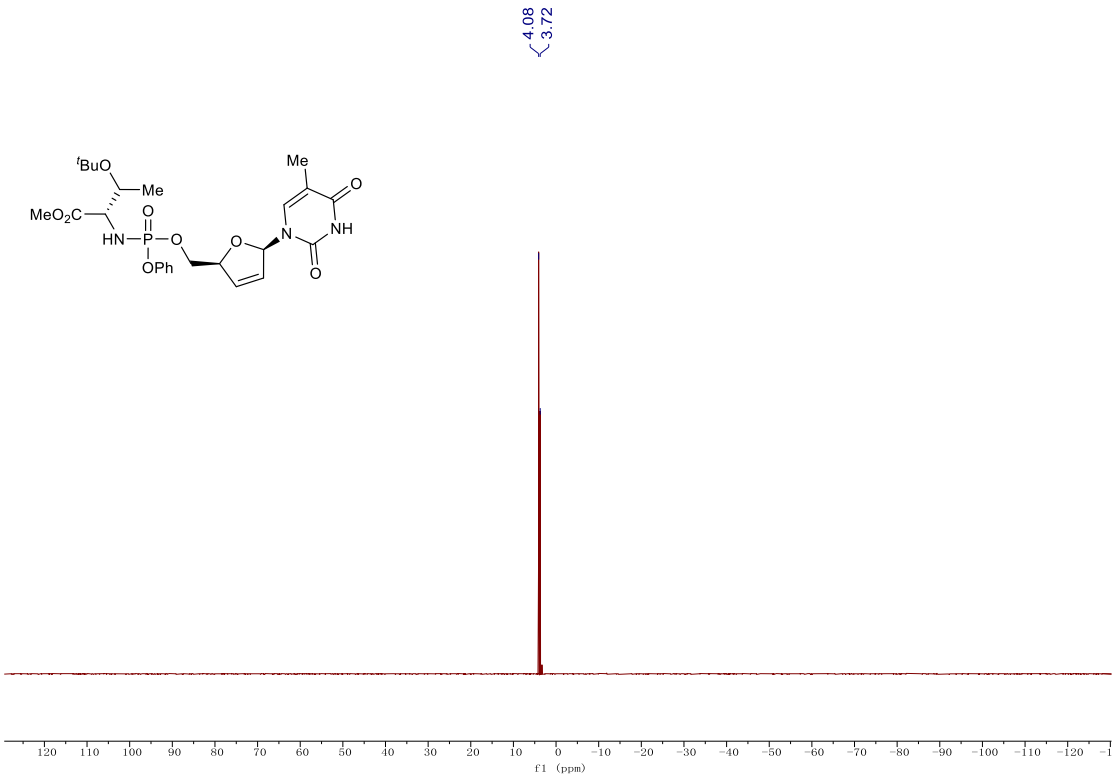
11, ^{1}H NMR (500 MHz, $CDCl_3$)



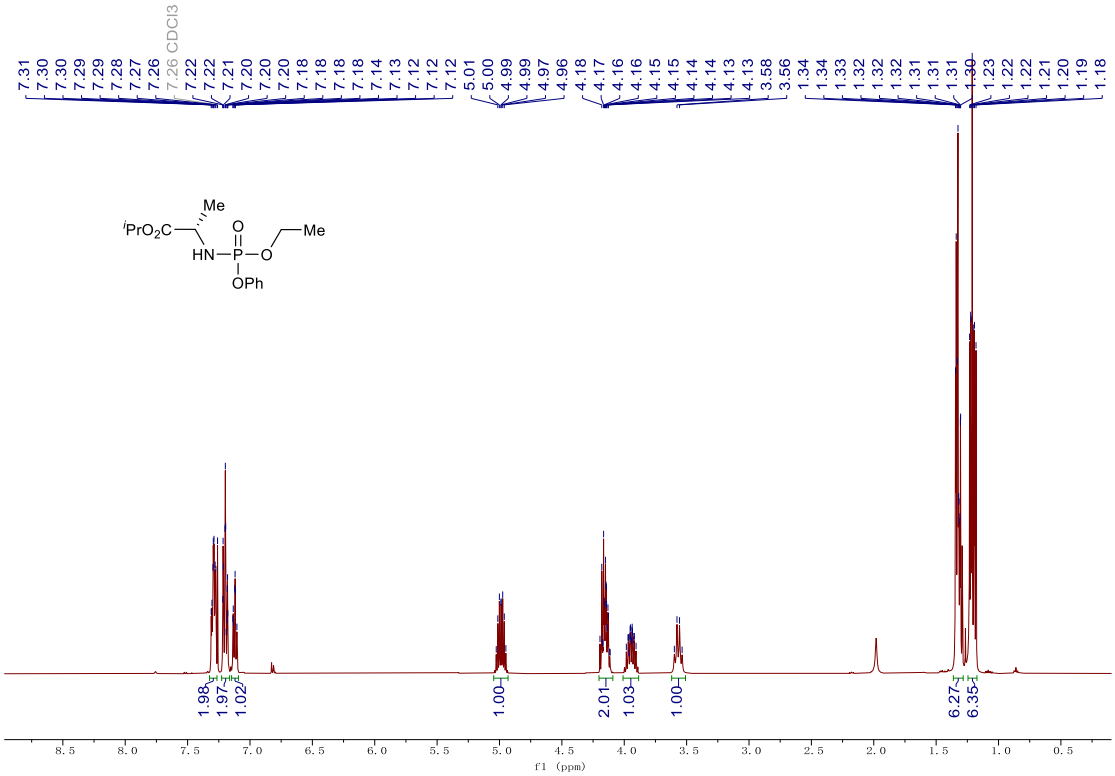
11, ^{13}C NMR (126 MHz, $CDCl_3$)



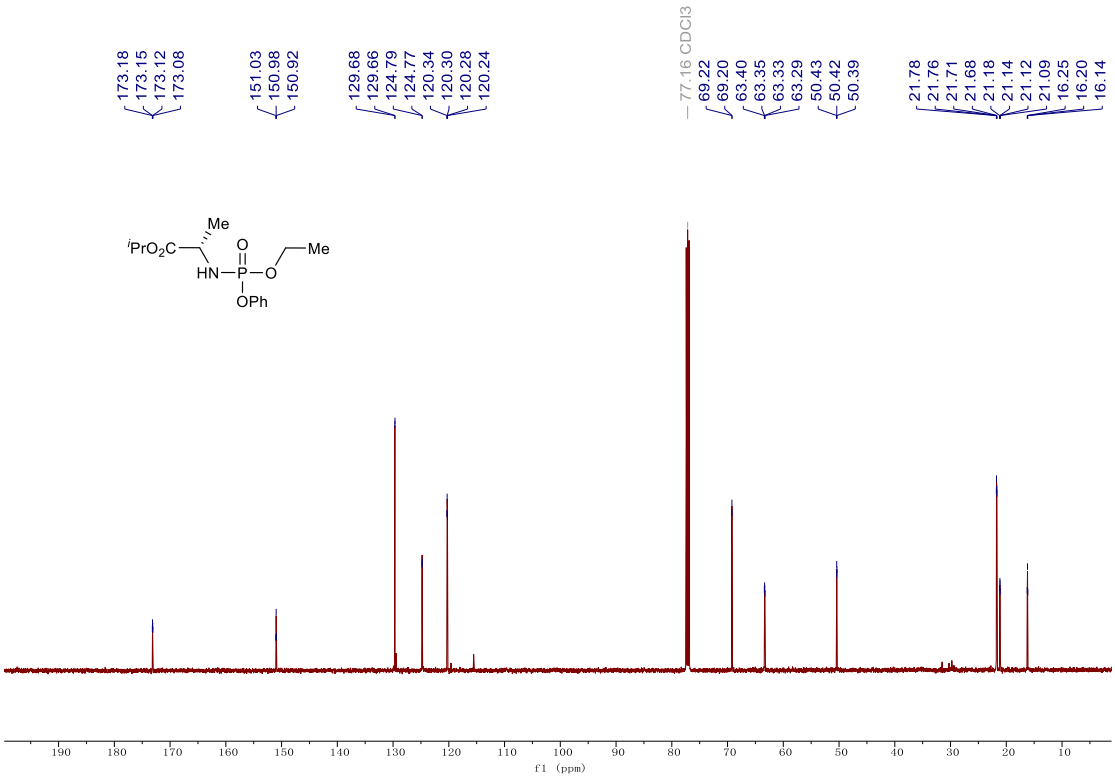
11, ^{31}P NMR (202 MHz, $CDCl_3$)



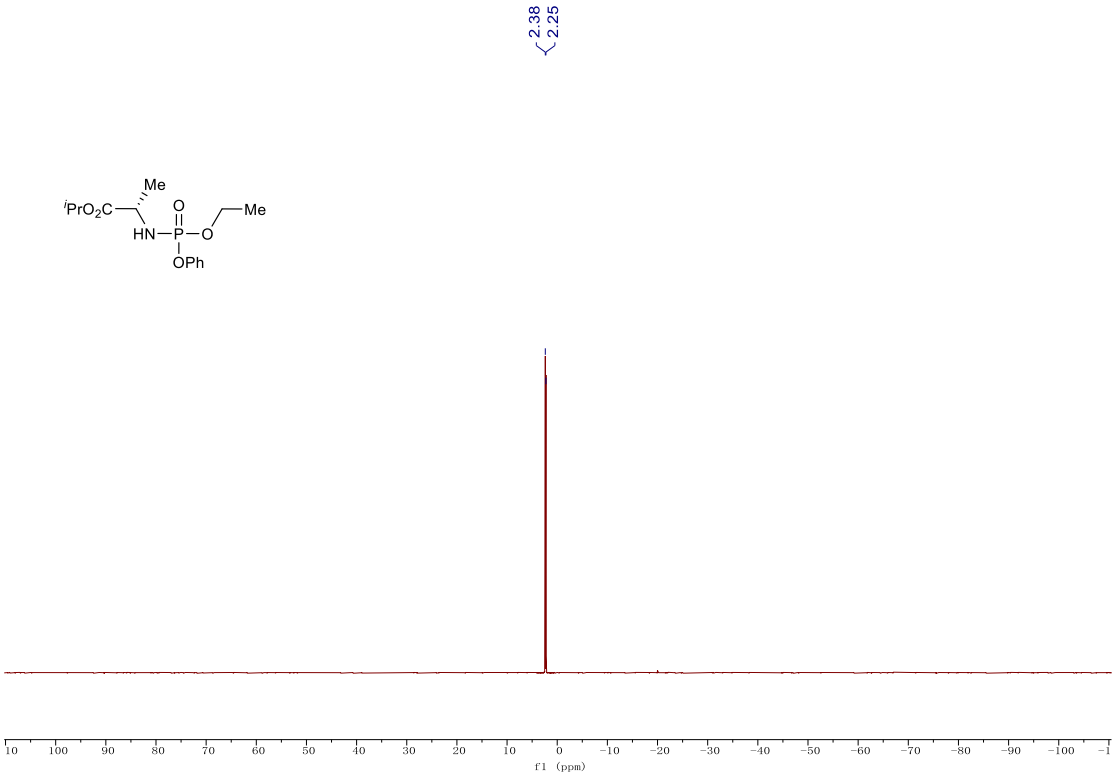
12, ^{1}H NMR (500 MHz, $CDCl_3$)



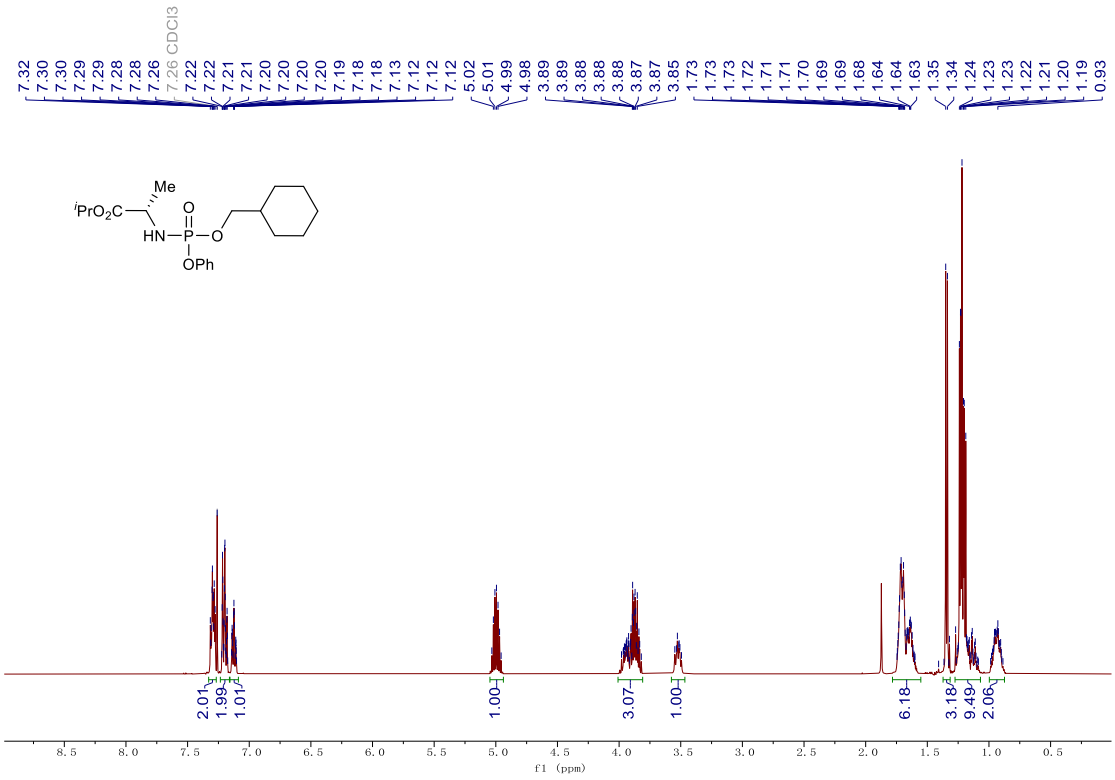
12, ^{13}C NMR (126 MHz, $CDCl_3$)



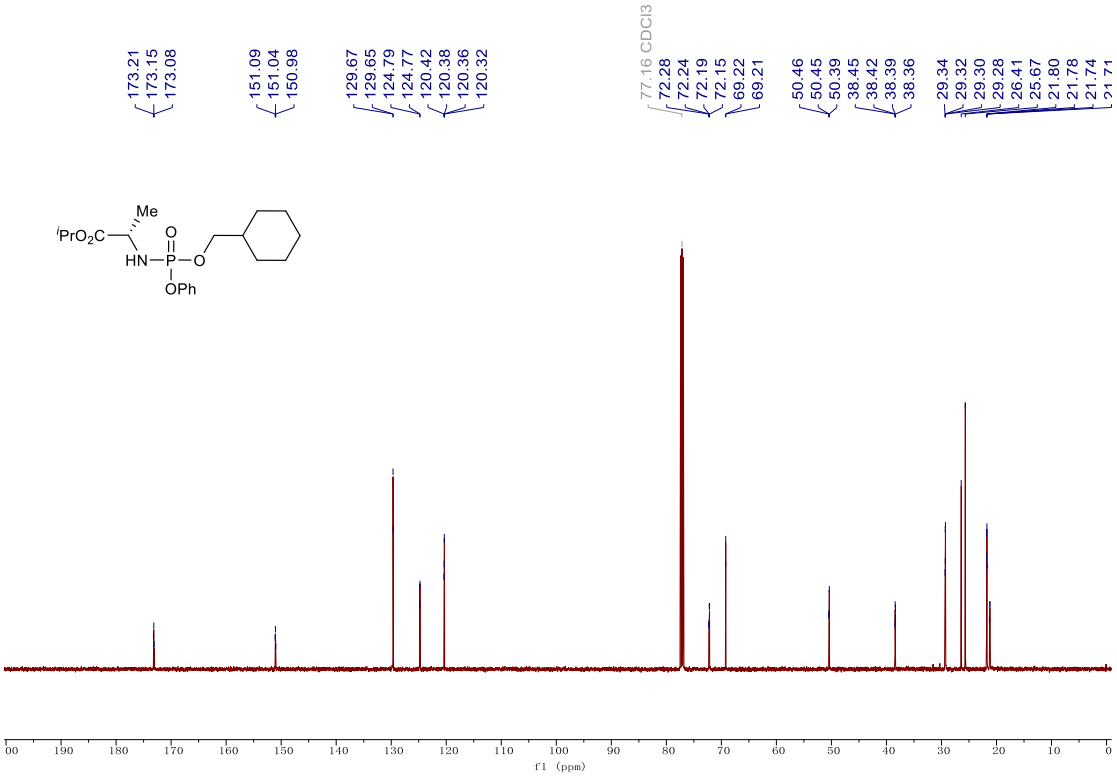
12, ^{31}P NMR (202 MHz, $CDCl_3$)



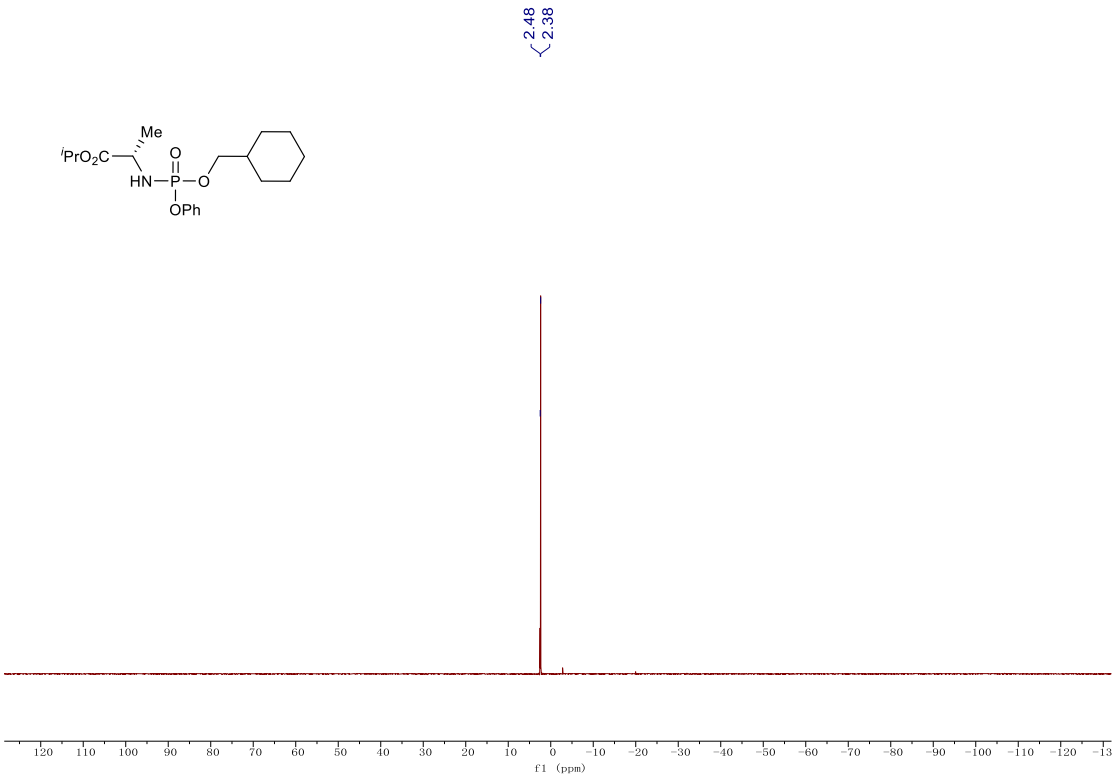
13, ^{1}H NMR (500 MHz, $CDCl_3$)



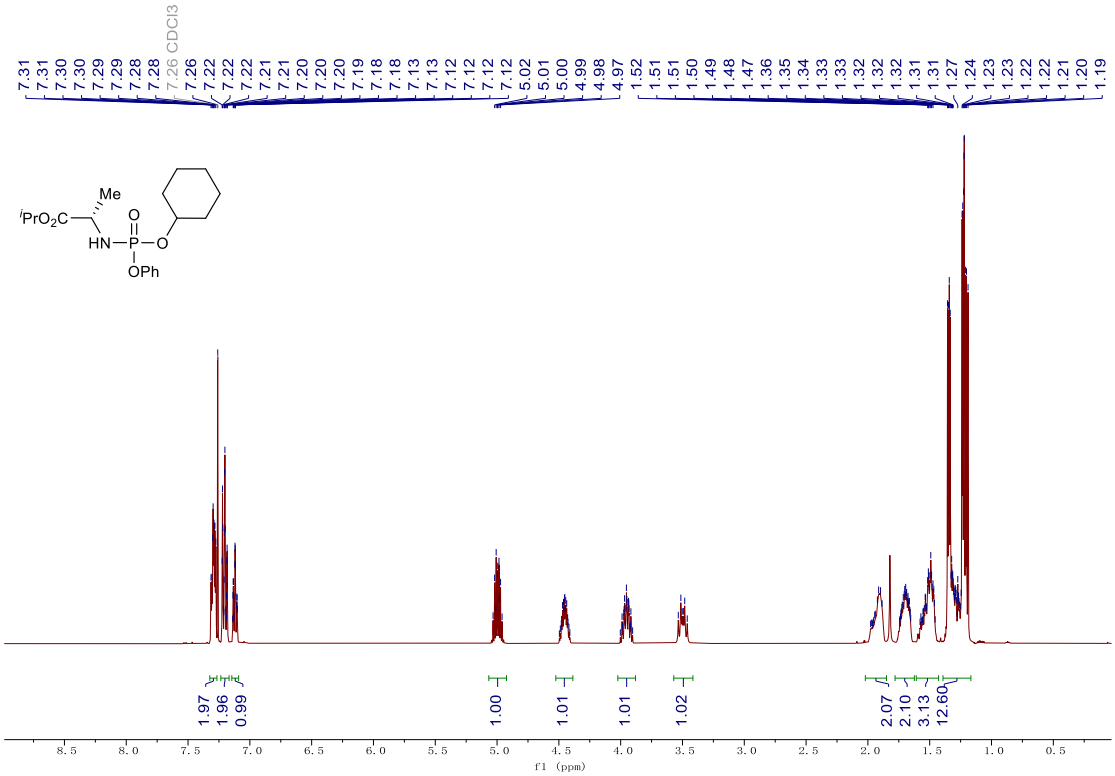
13, ^{13}C NMR (126 MHz, $CDCl_3$)



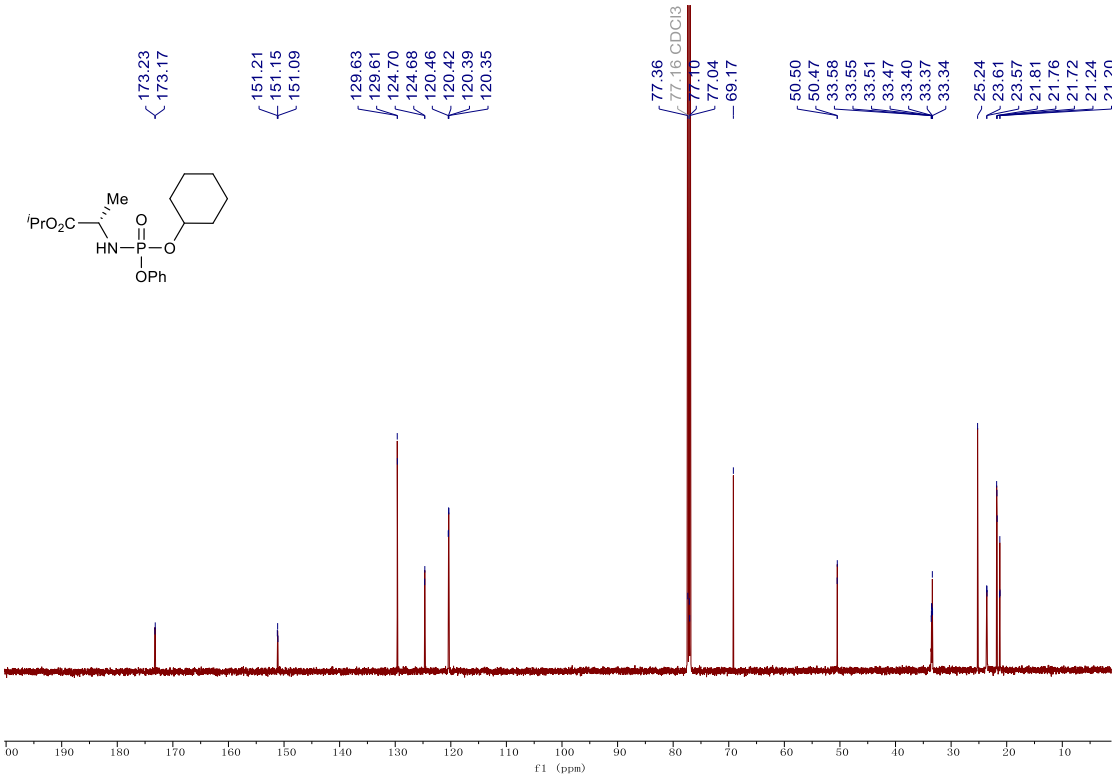
13, ^{31}P NMR (202 MHz, $CDCl_3$)



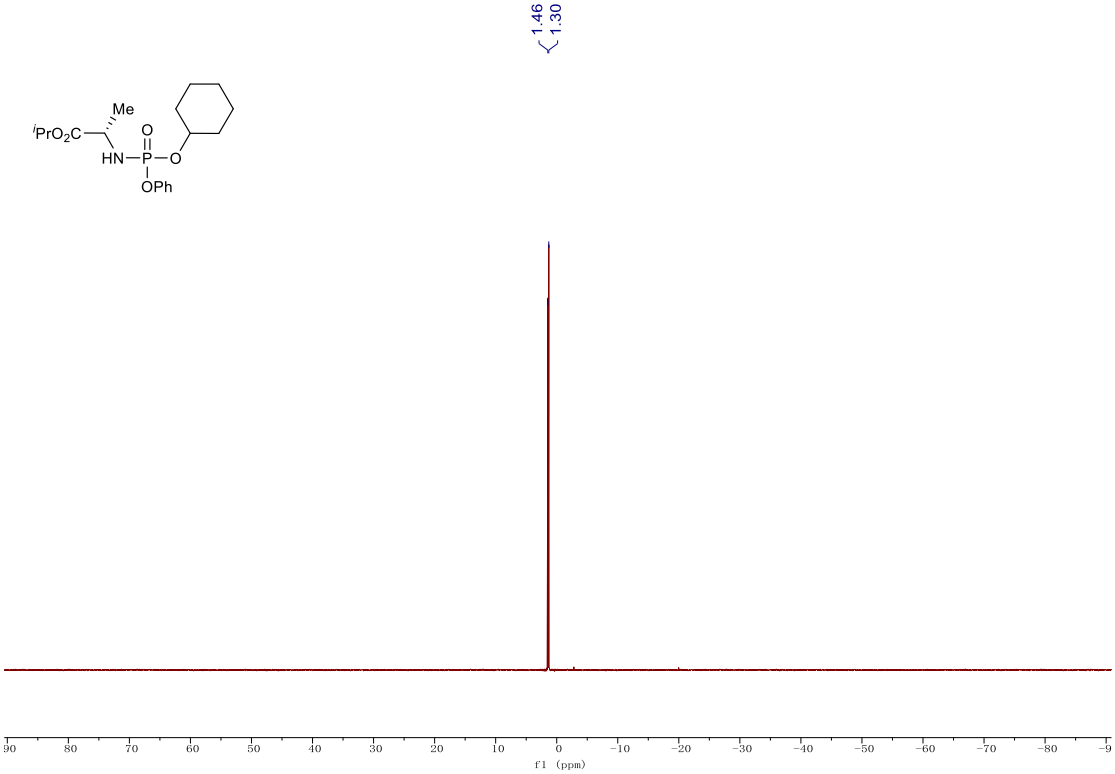
14, ^{1}H NMR (500 MHz, $CDCl_3$)



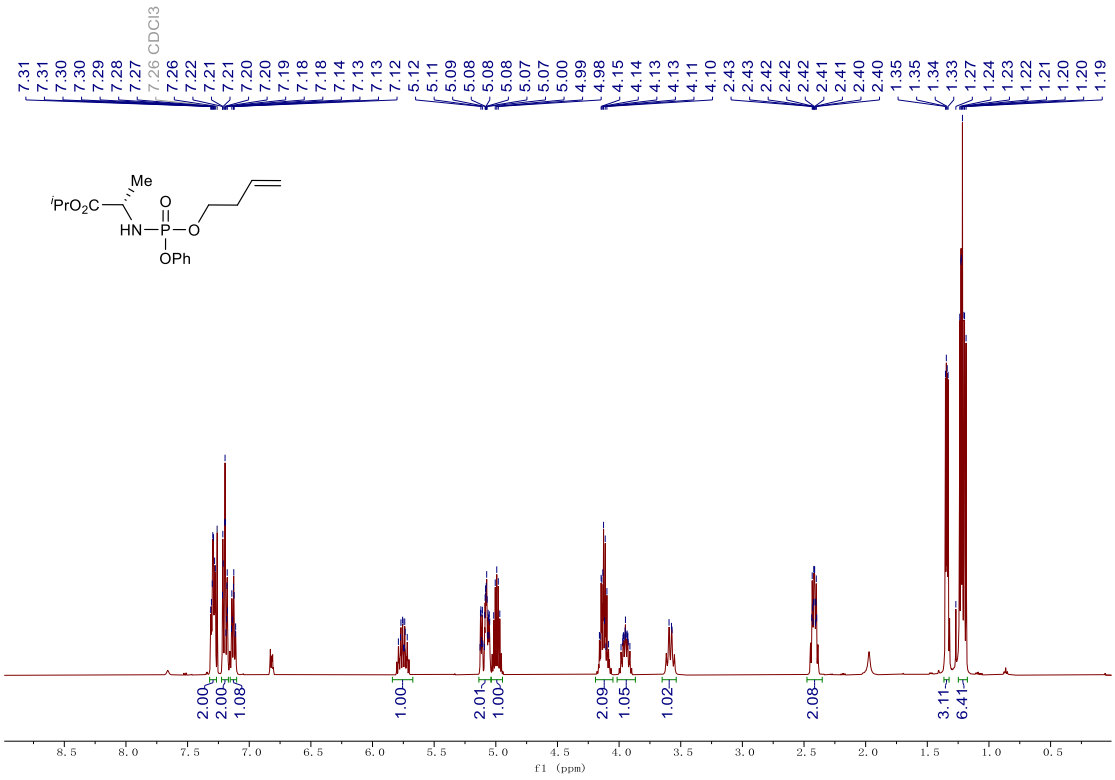
14, ^{13}C NMR (126 MHz, $CDCl_3$)



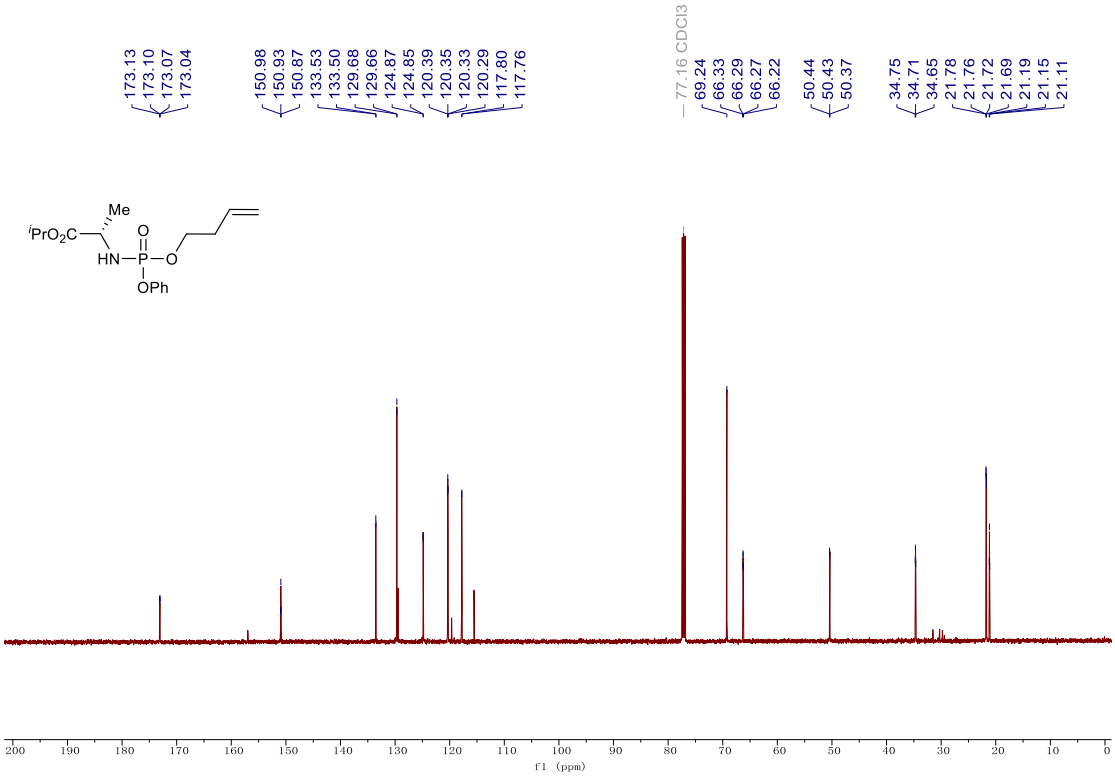
14, ^{31}P NMR (202 MHz, $CDCl_3$)



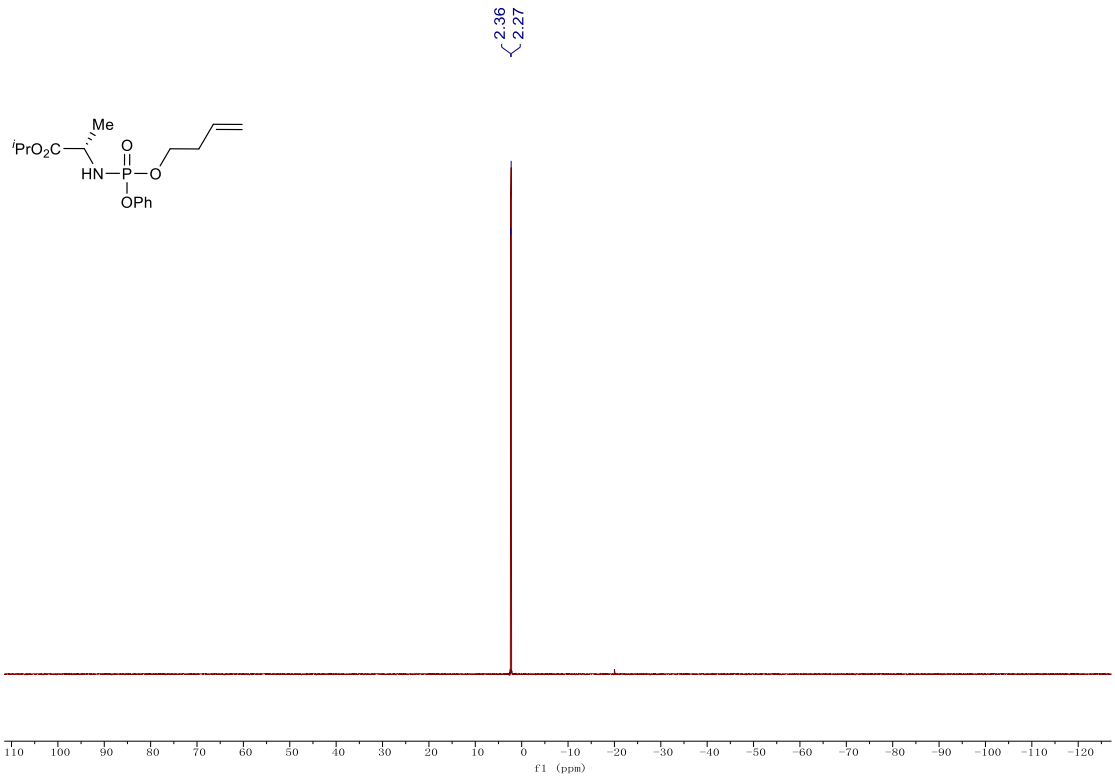
15, ^{1}H NMR (500 MHz, $CDCl_3$)



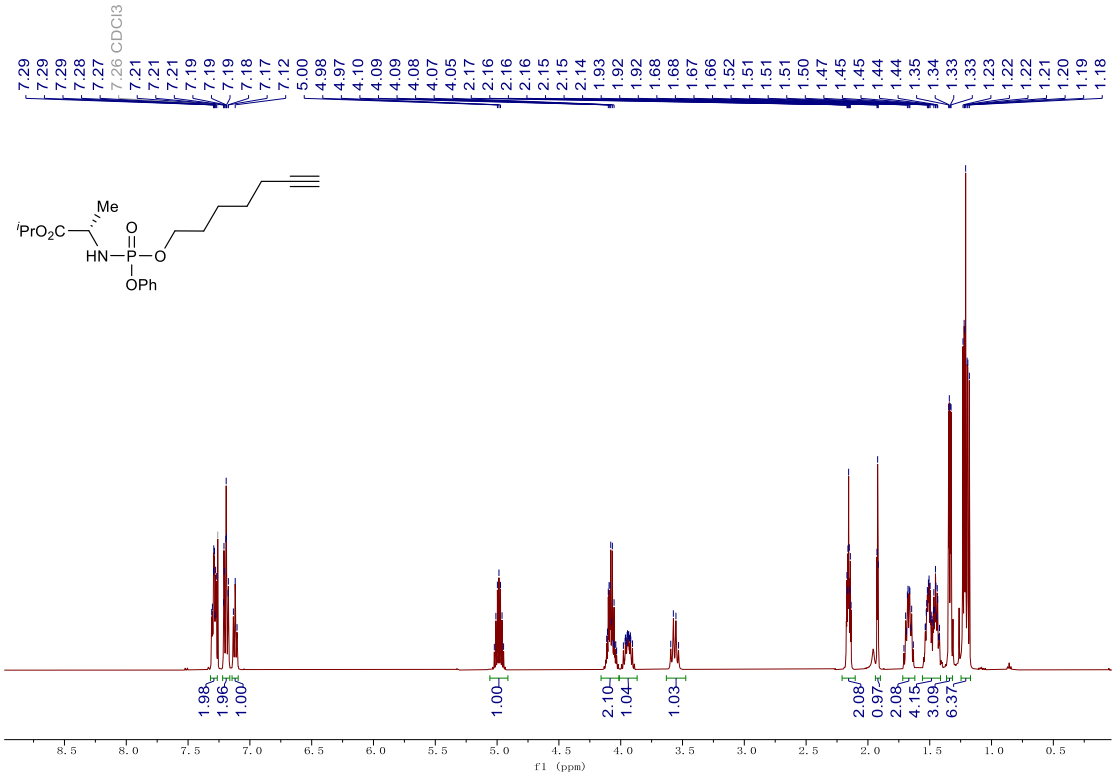
15, ^{13}C NMR (126 MHz, $CDCl_3$)



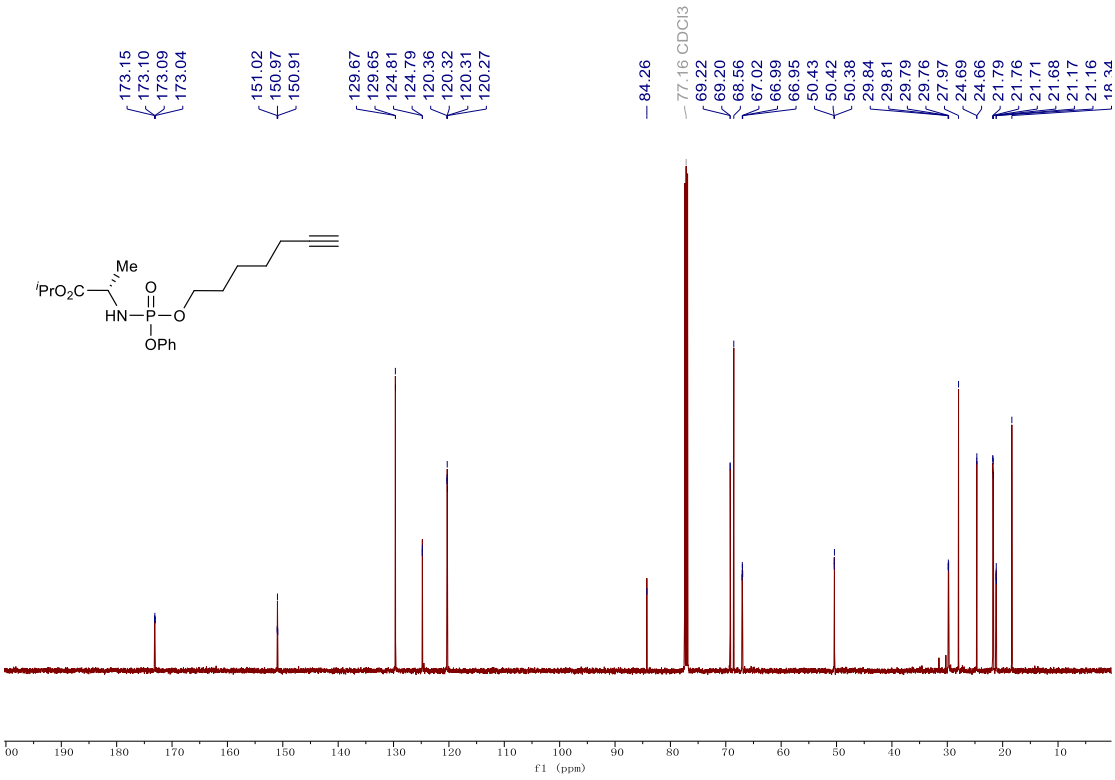
15, ^{31}P NMR (202 MHz, $CDCl_3$)



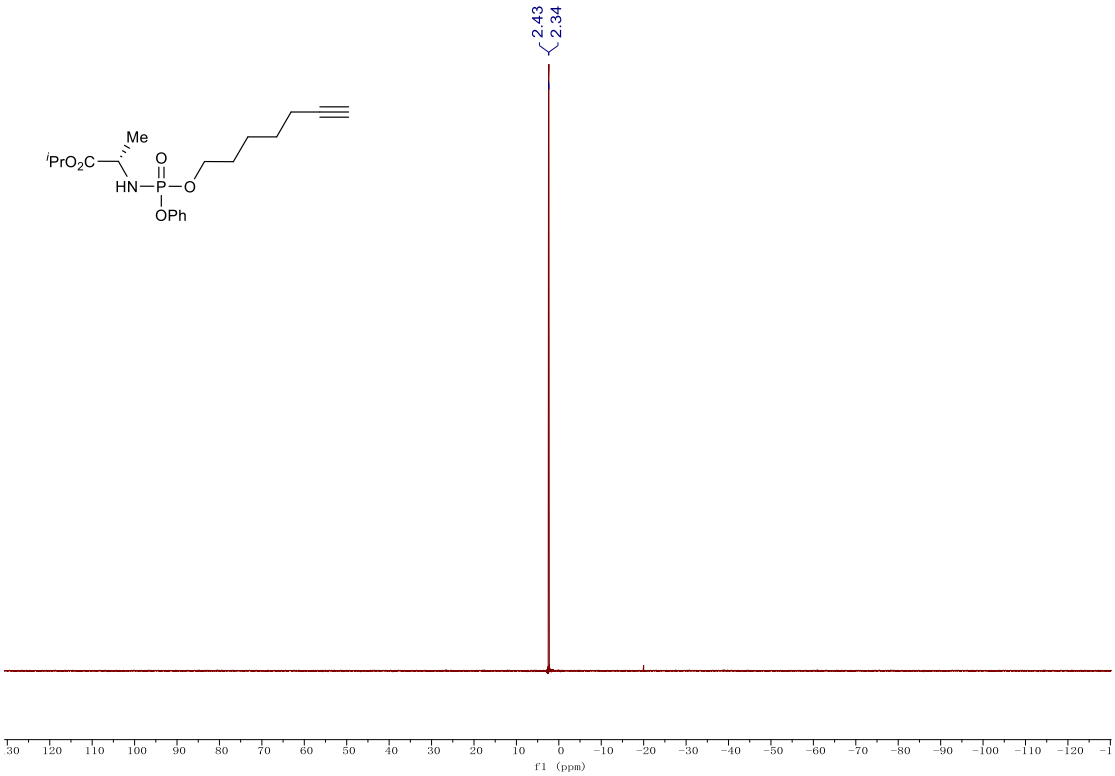
16, ^{1}H NMR (500 MHz, $CDCl_3$)



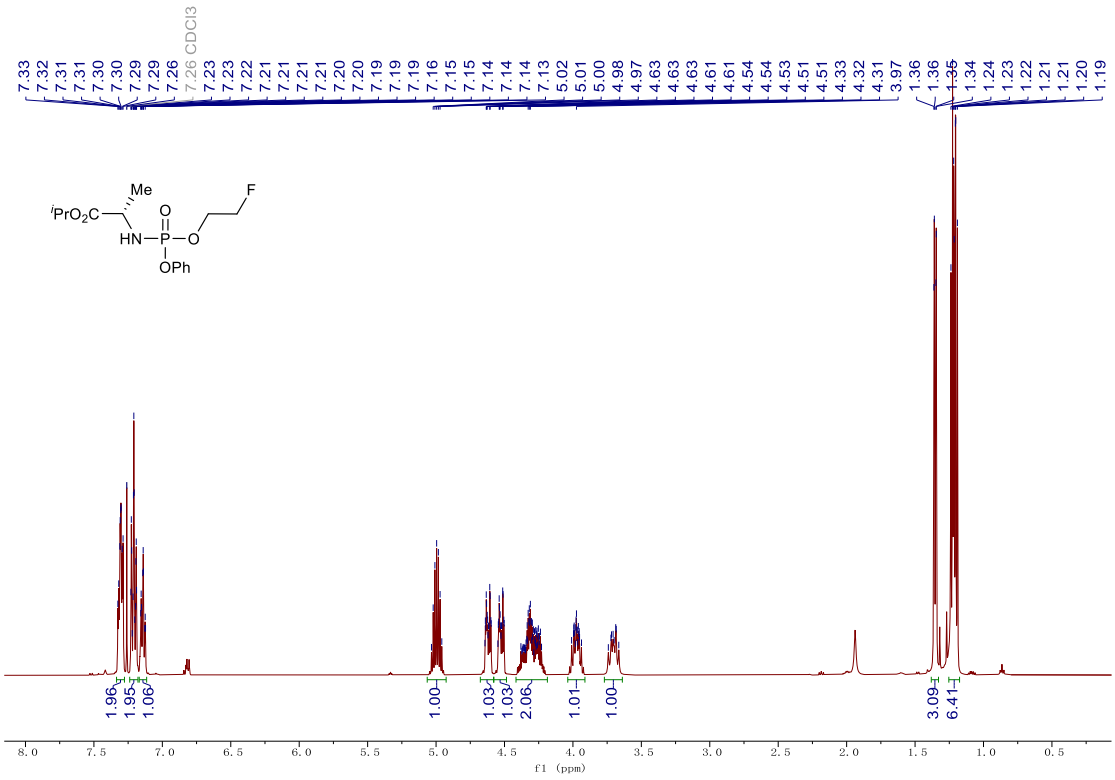
16, ^{13}C NMR (126 MHz, $CDCl_3$)



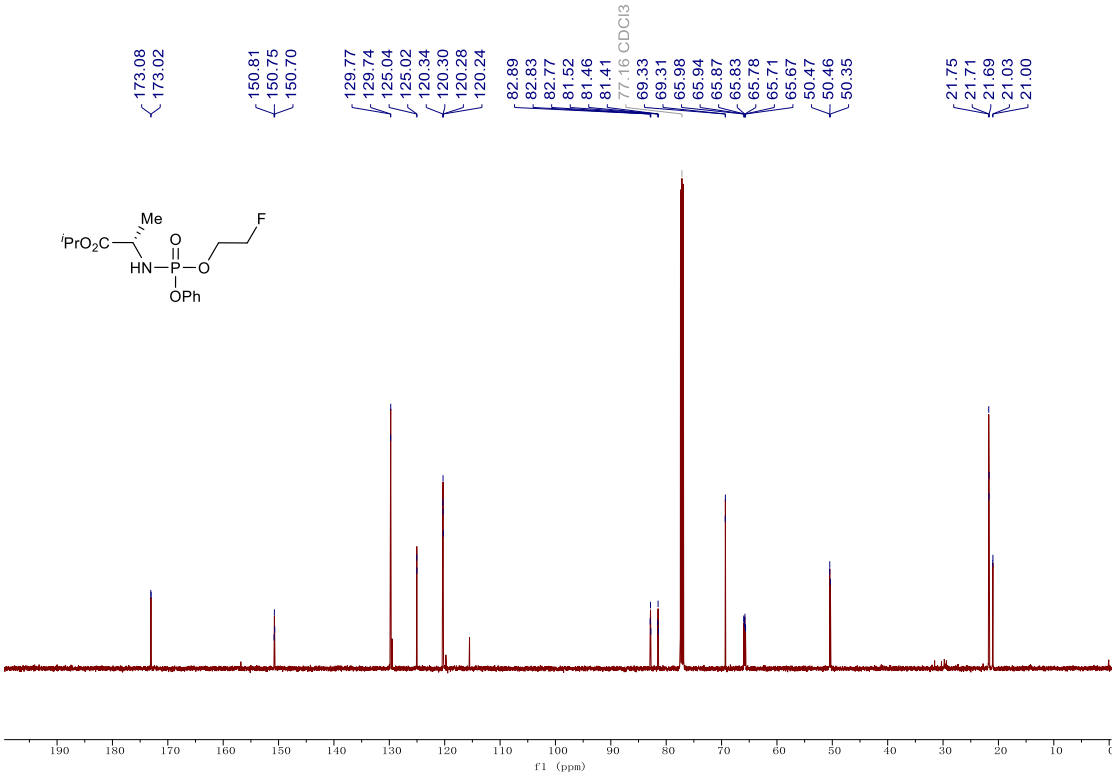
16, ^{31}P NMR (202 MHz, $CDCl_3$)



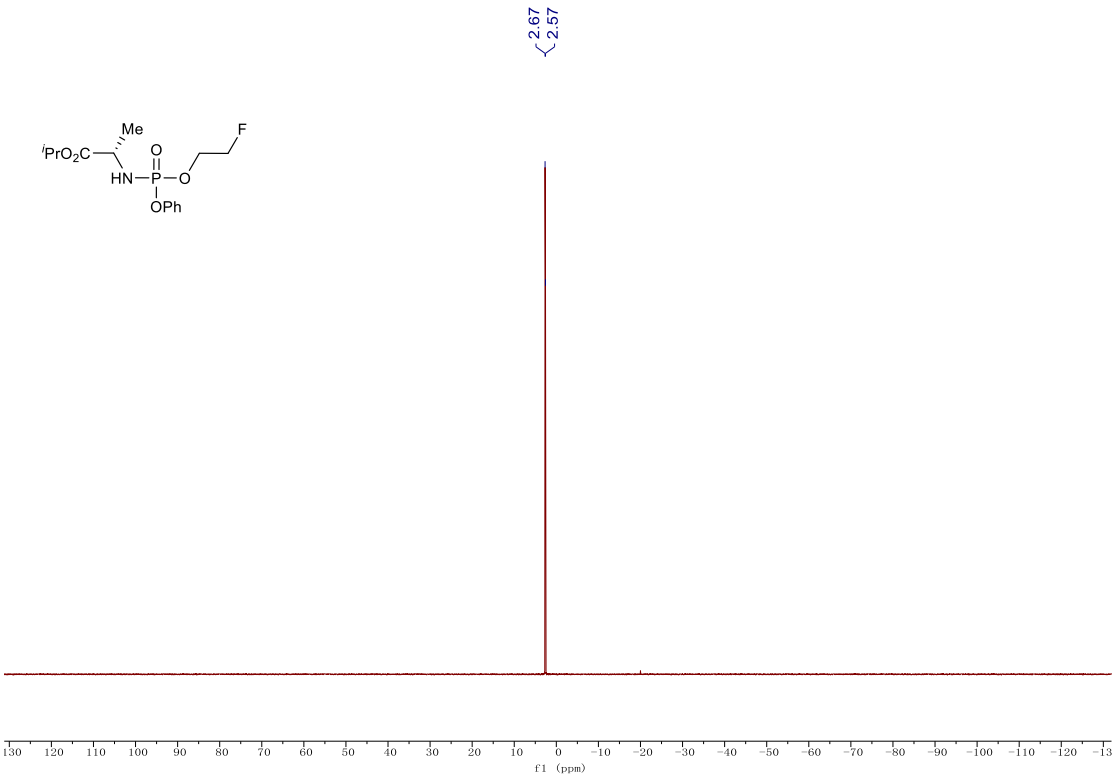
17, ^{1}H NMR (500 MHz, $CDCl_3$)



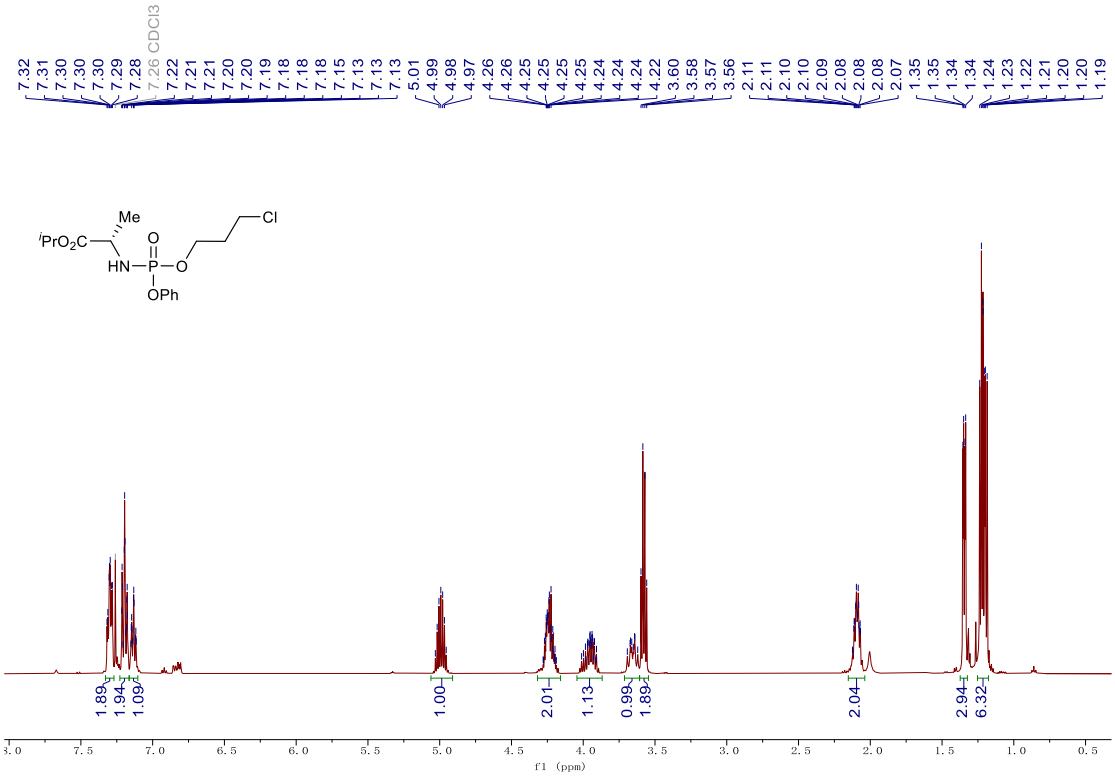
17, ^{13}C NMR (126 MHz, $CDCl_3$)



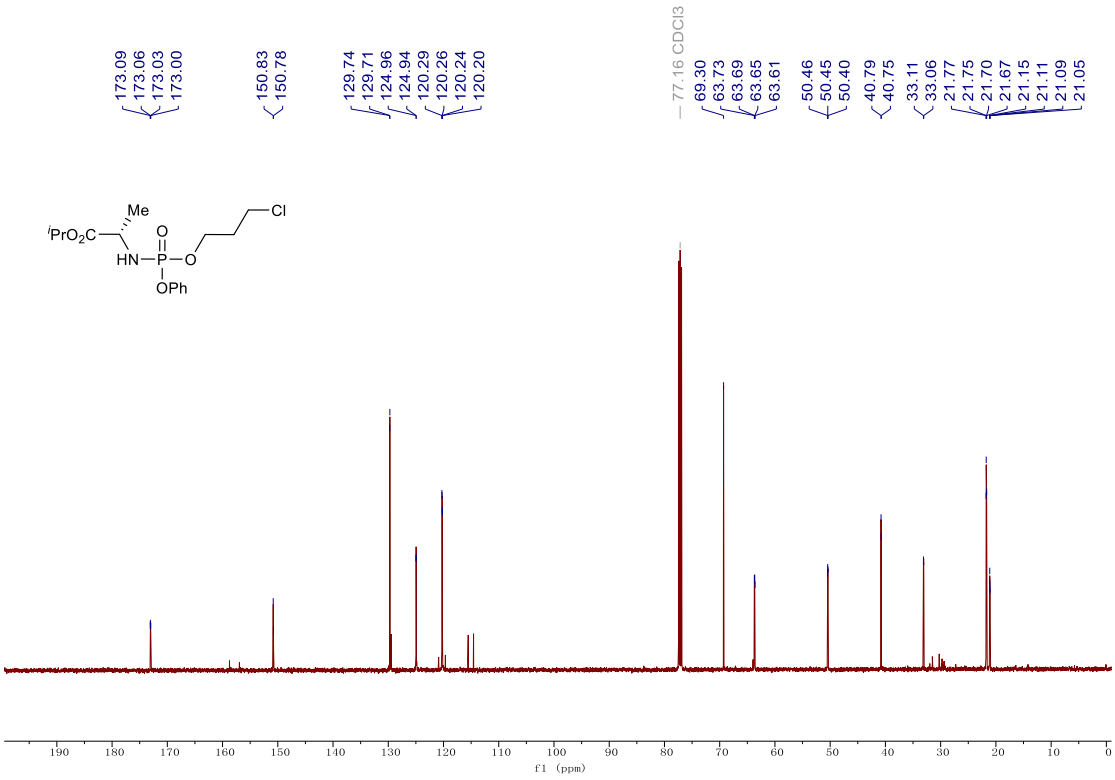
17, ^{31}P NMR (202 MHz, $CDCl_3$)



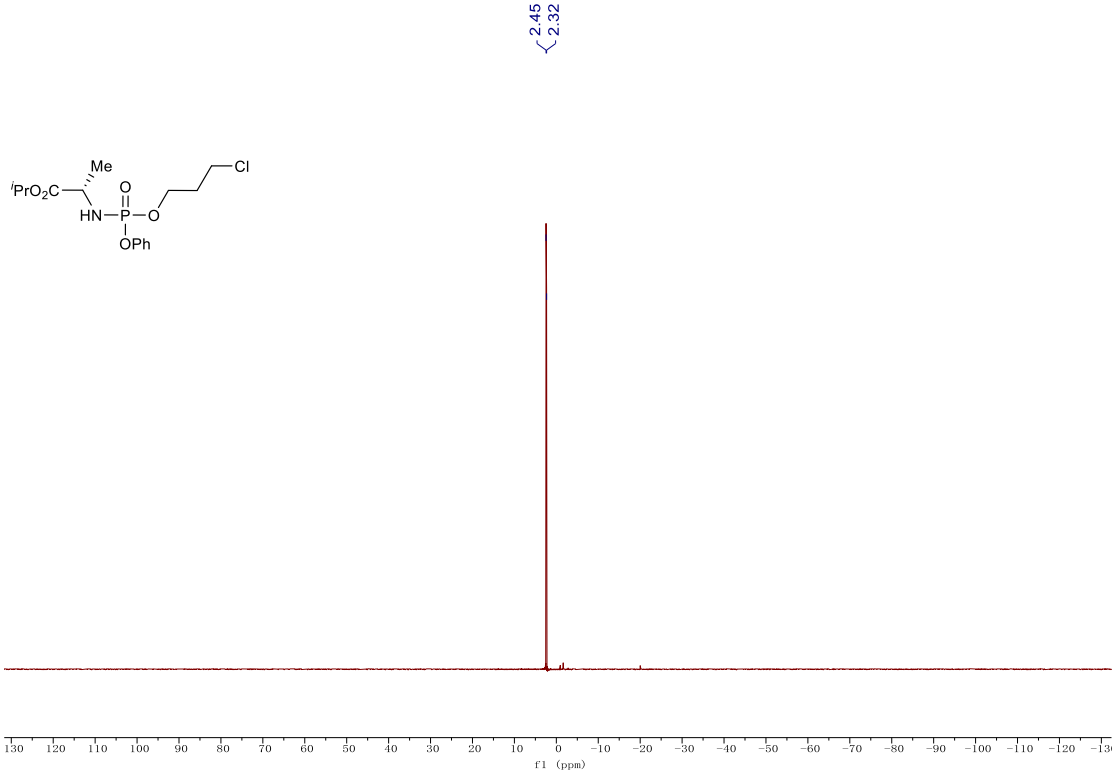
18, ^{1}H NMR (500 MHz, $CDCl_3$)



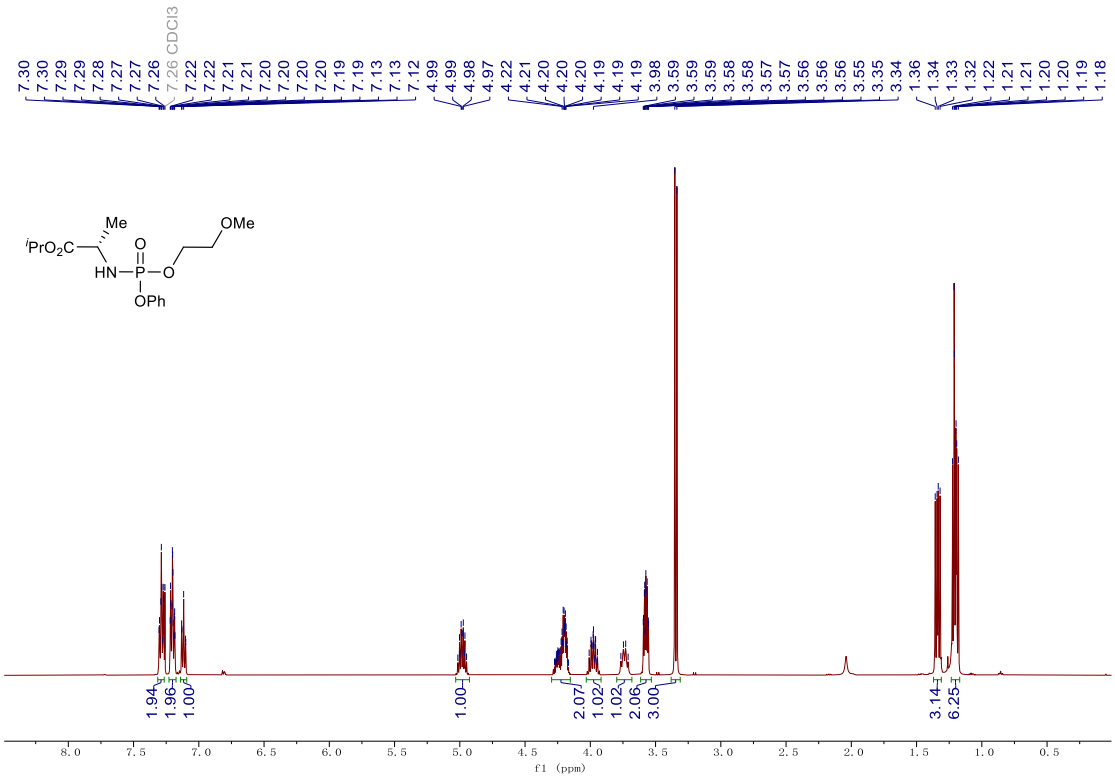
18, ^{13}C NMR (126 MHz, $CDCl_3$)



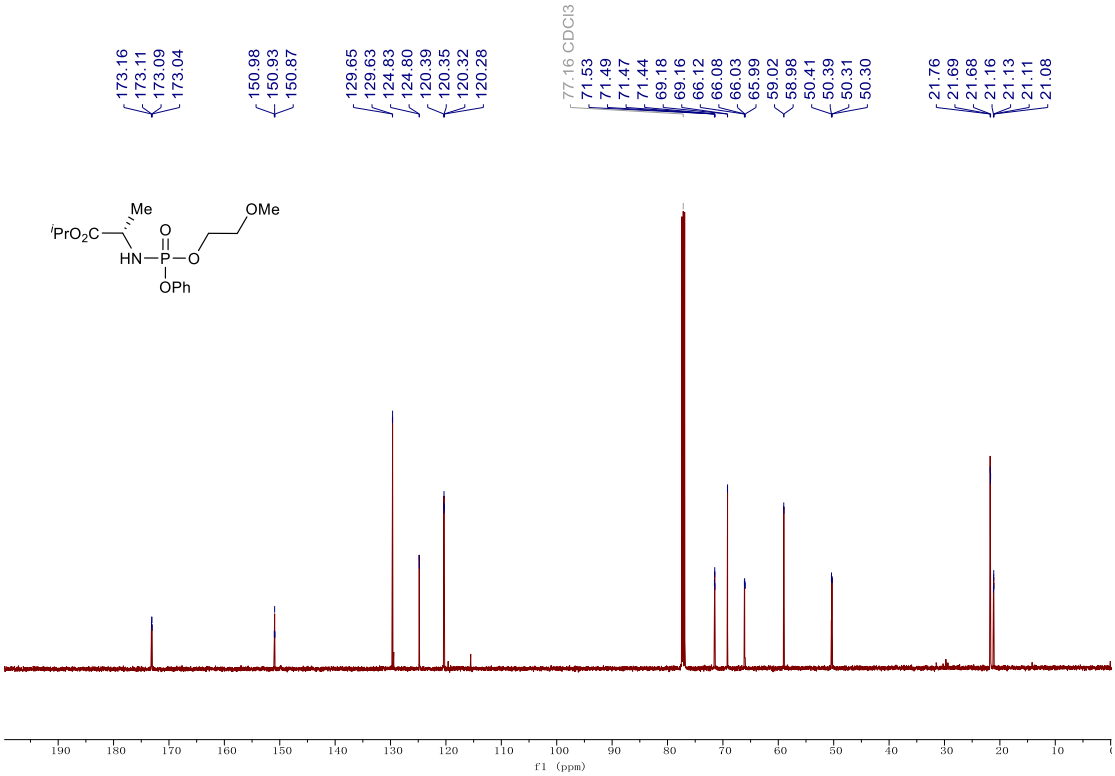
18, ^{31}P NMR (202 MHz, $CDCl_3$)



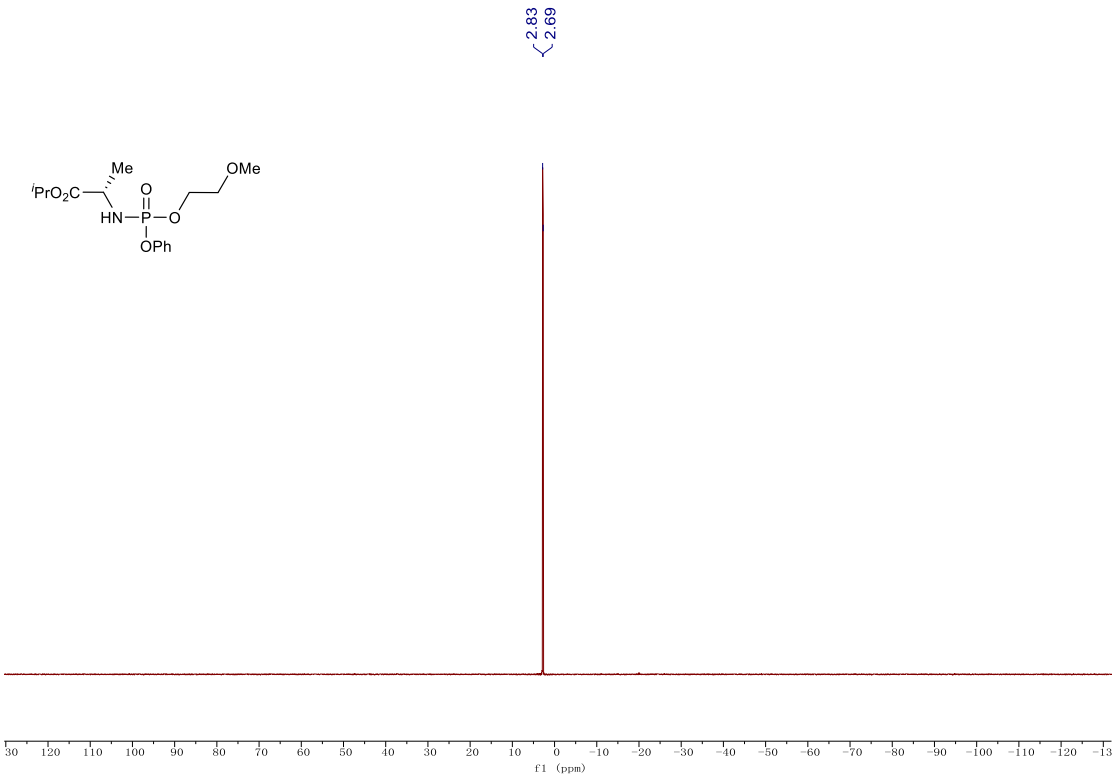
19, ^{1}H NMR (500 MHz, $CDCl_3$)



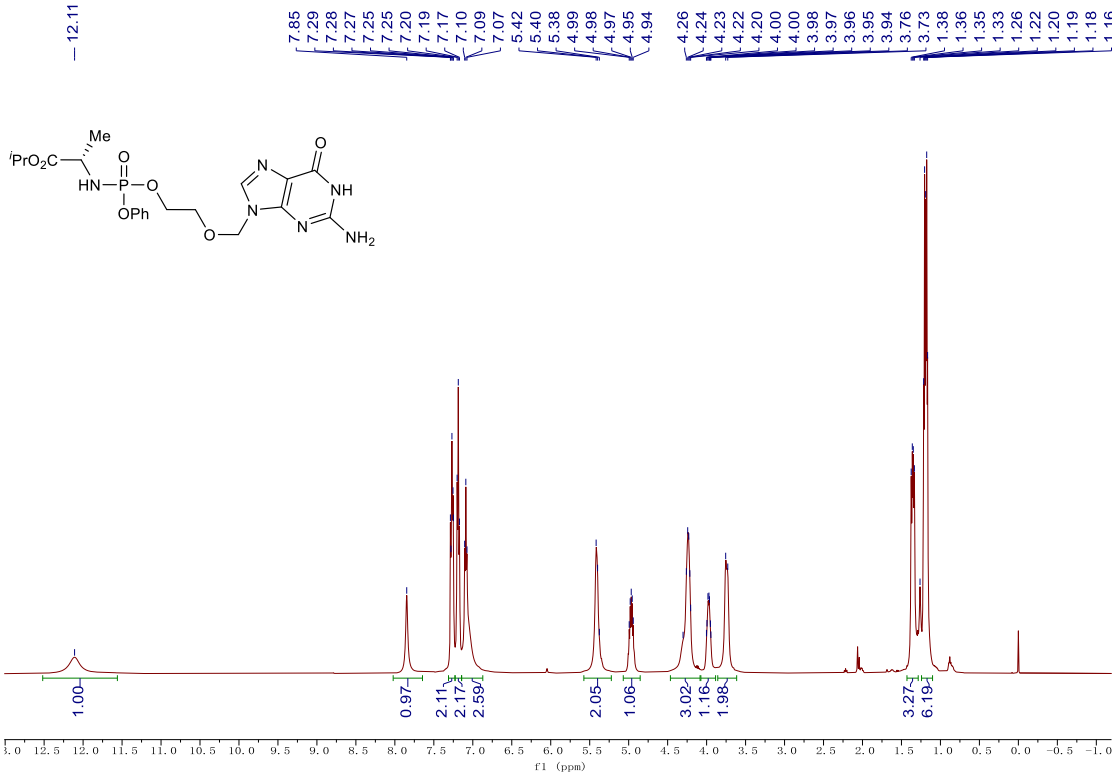
19, ^{13}C NMR (126 MHz, $CDCl_3$)



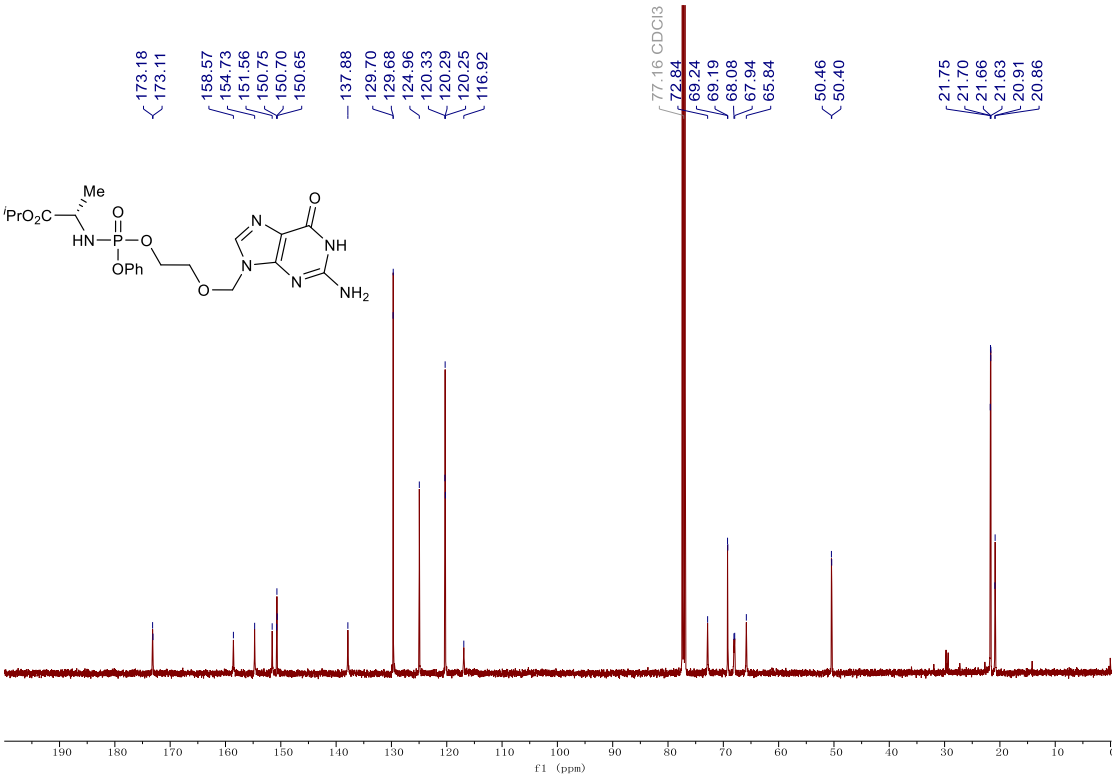
19, ^{31}P NMR (202 MHz, $CDCl_3$)



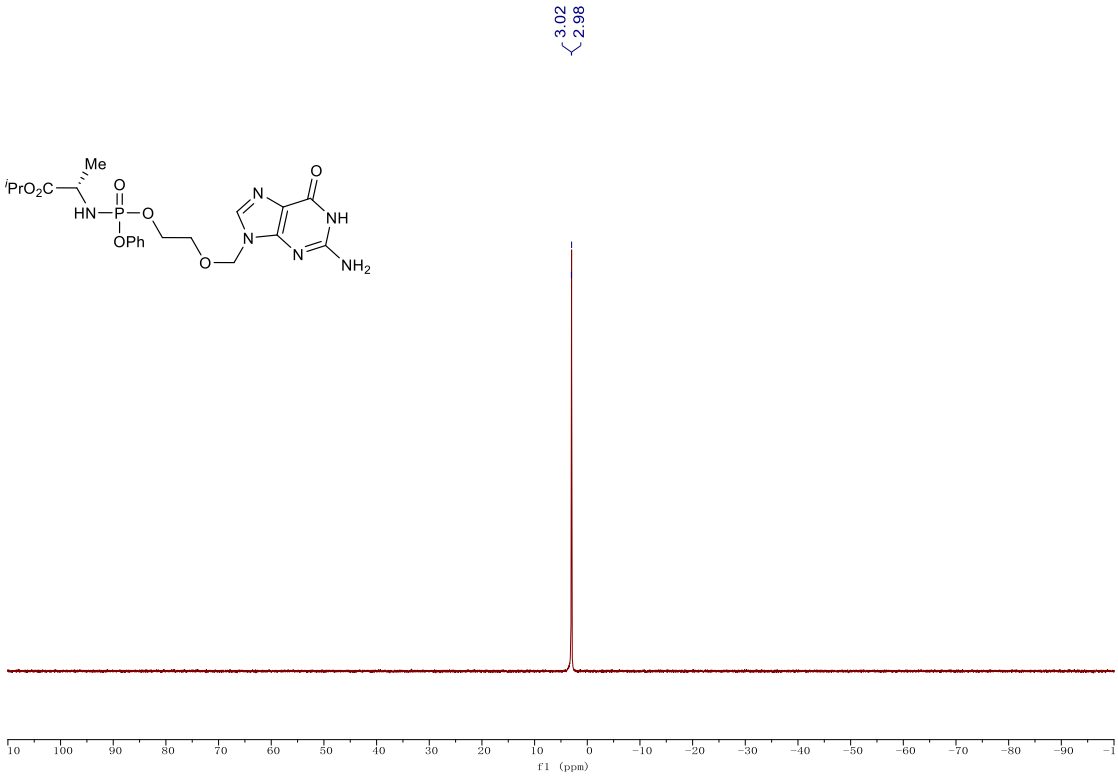
20, ^{1}H NMR (500 MHz, $CDCl_3$)



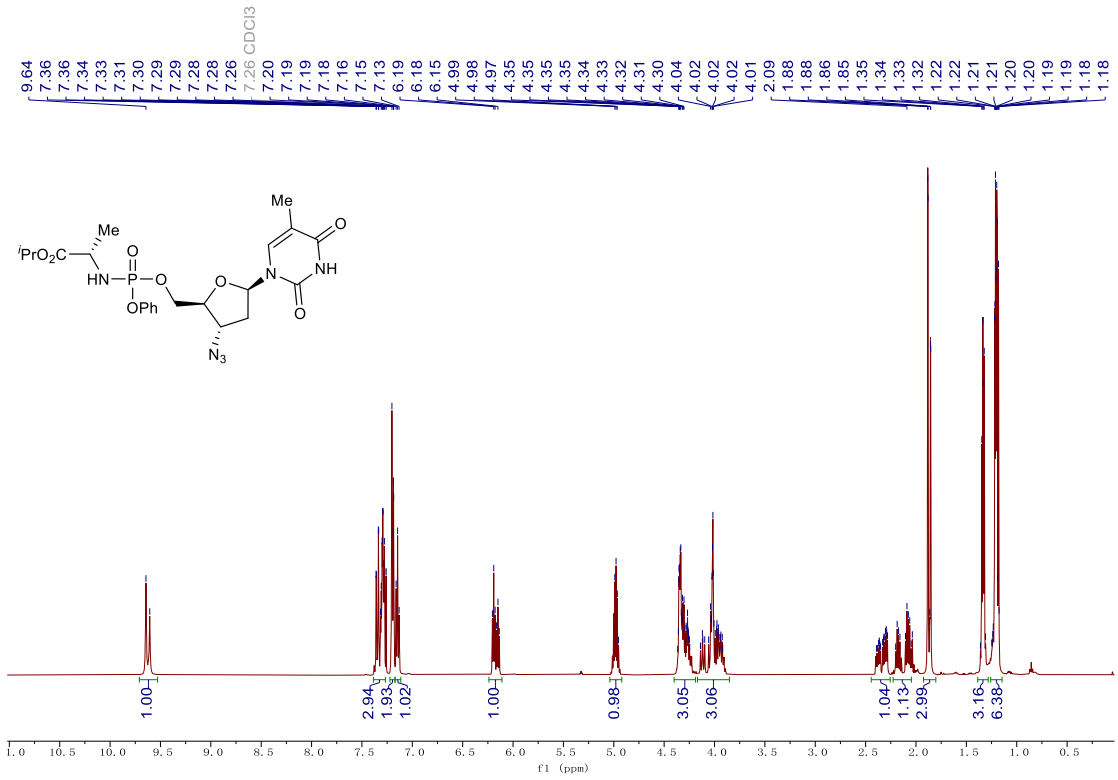
20, ^{13}C NMR (126 MHz, $CDCl_3$)



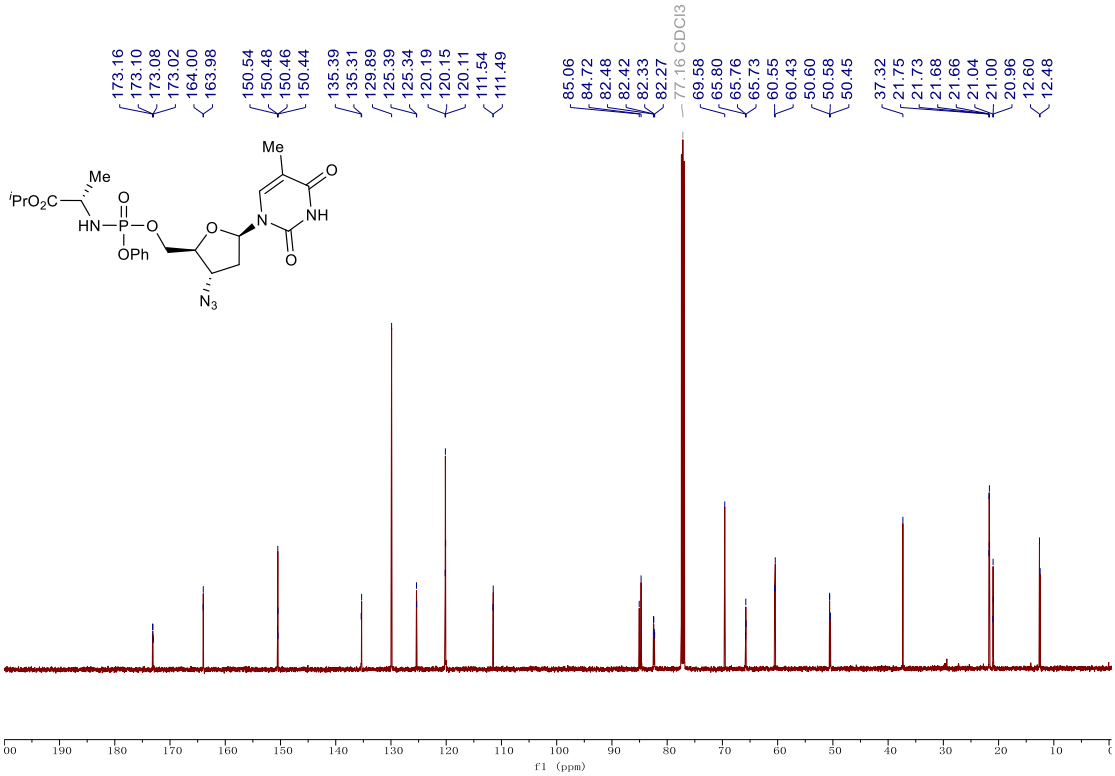
20, ^{31}P NMR (202 MHz, $CDCl_3$)



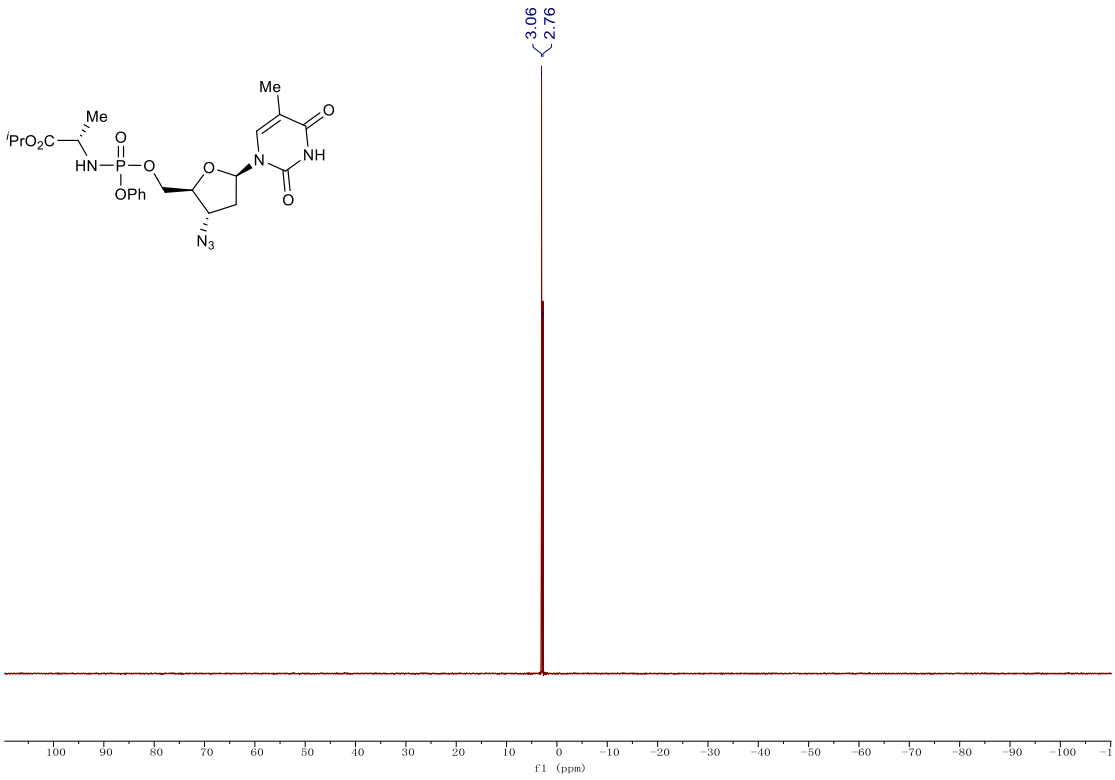
21, ^{1}H NMR (500 MHz, $CDCl_3$)



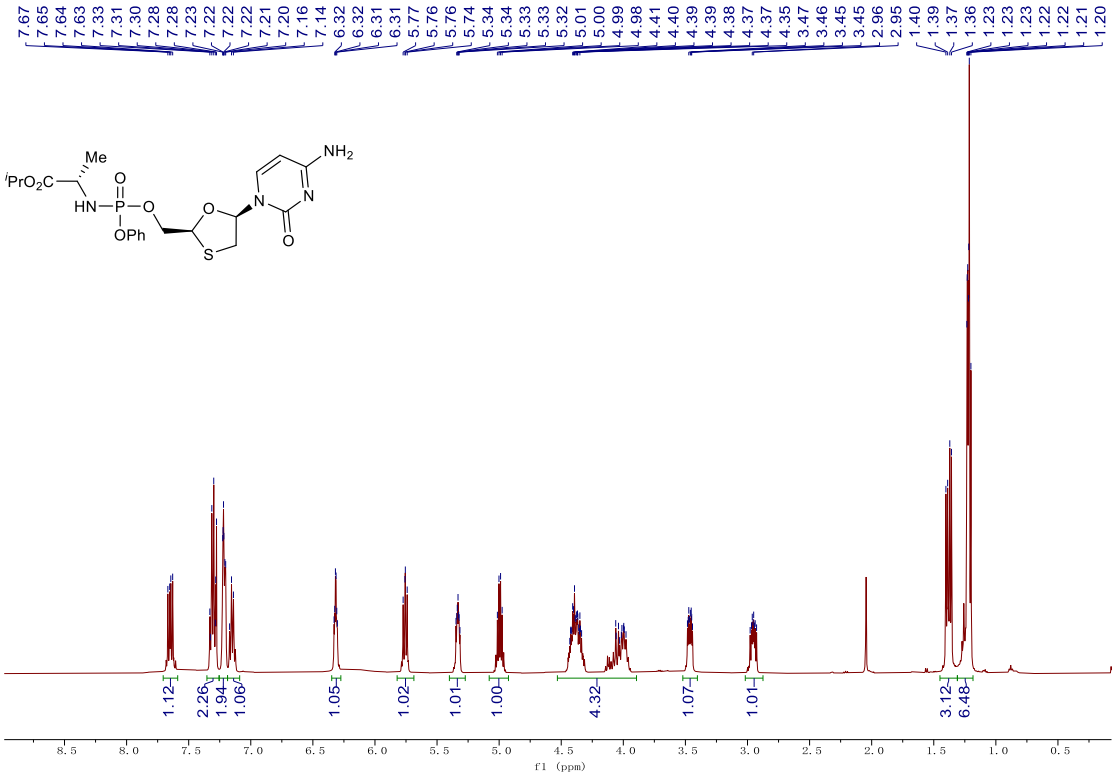
21, ^{13}C NMR (126 MHz, $CDCl_3$)



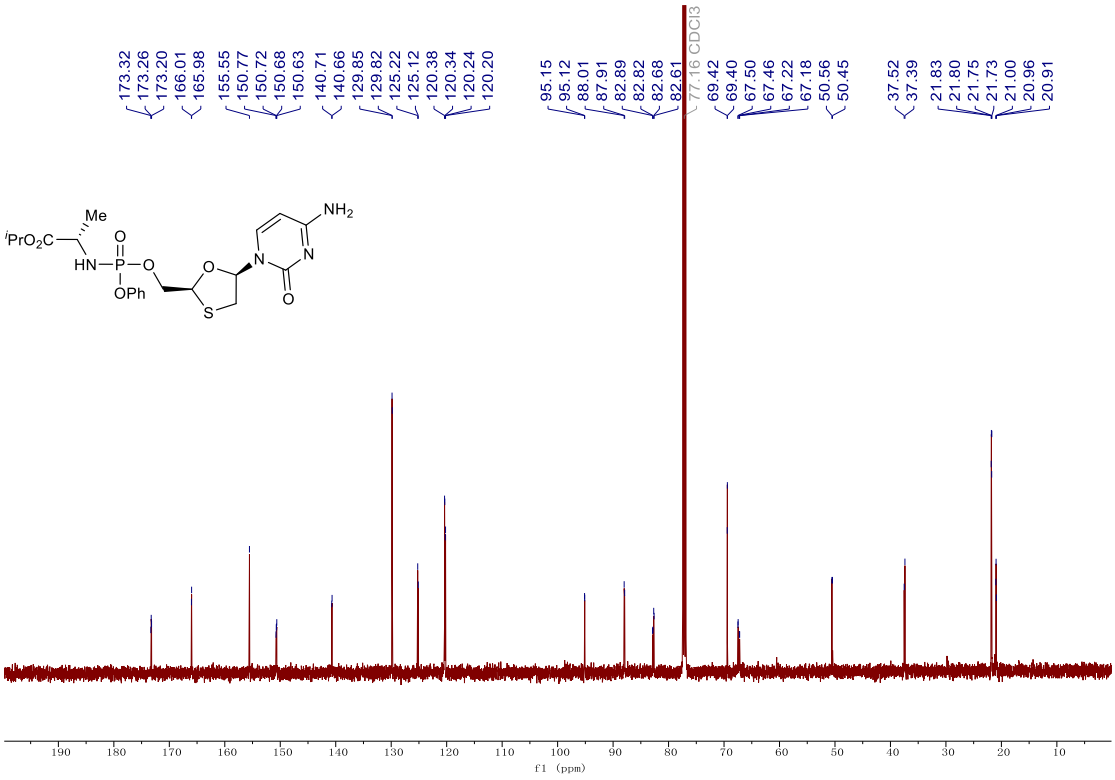
21, ^{31}P NMR (202 MHz, $CDCl_3$)



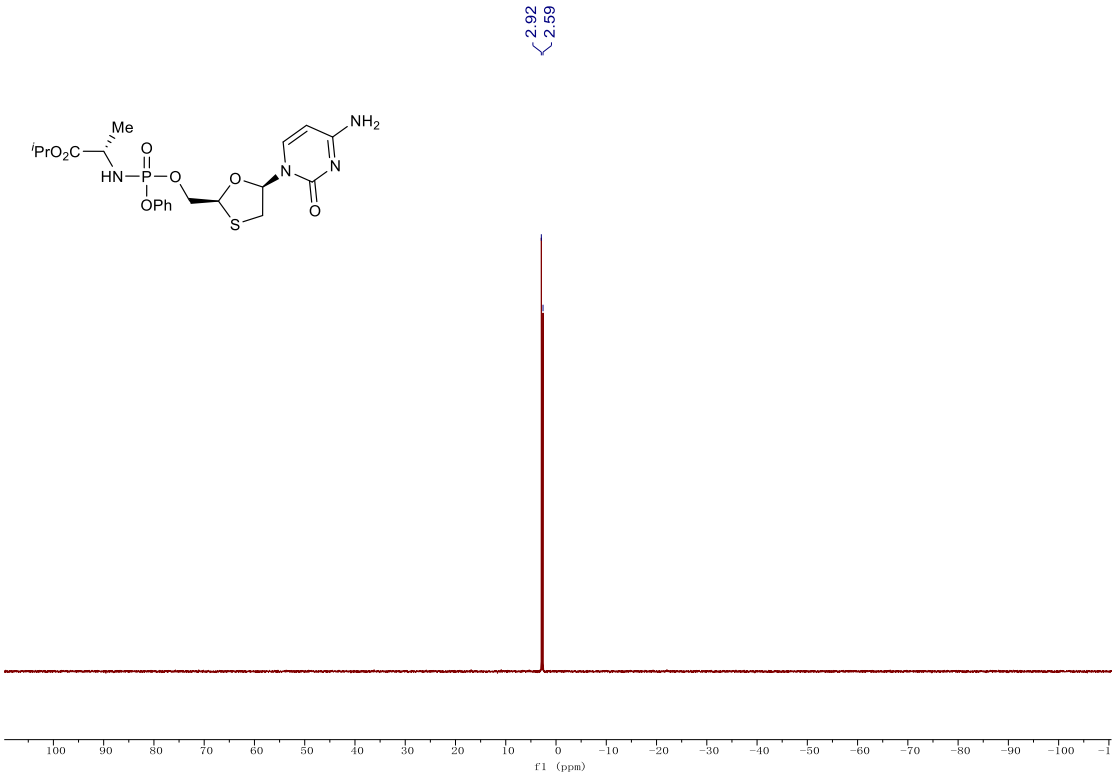
22, ^{1}H NMR (500 MHz, $CDCl_3$)



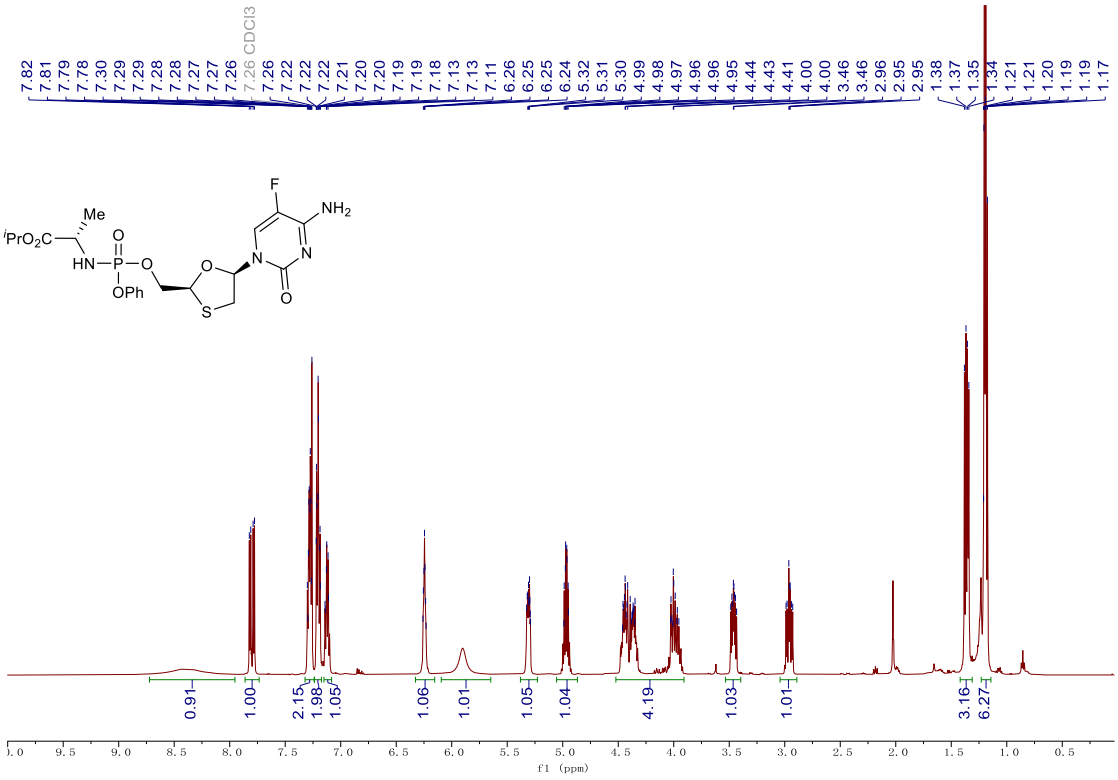
22, ^{13}C NMR (126 MHz, $CDCl_3$)



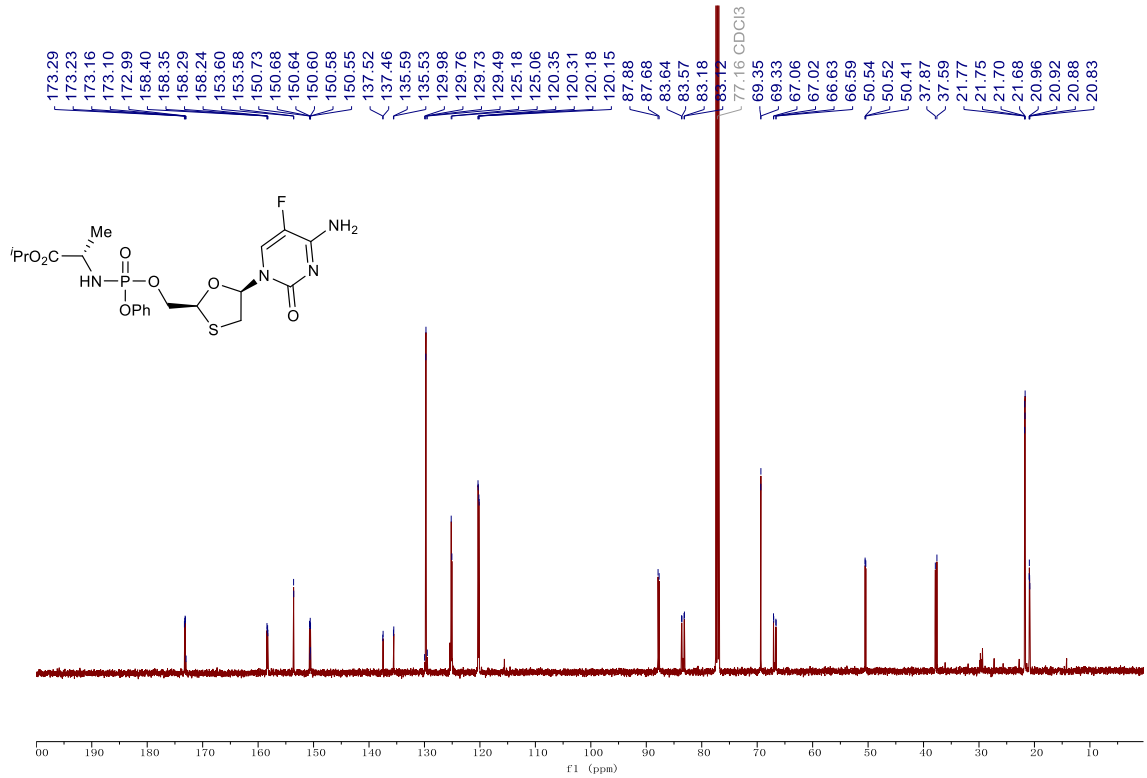
22, ^{31}P NMR (202 MHz, $CDCl_3$)



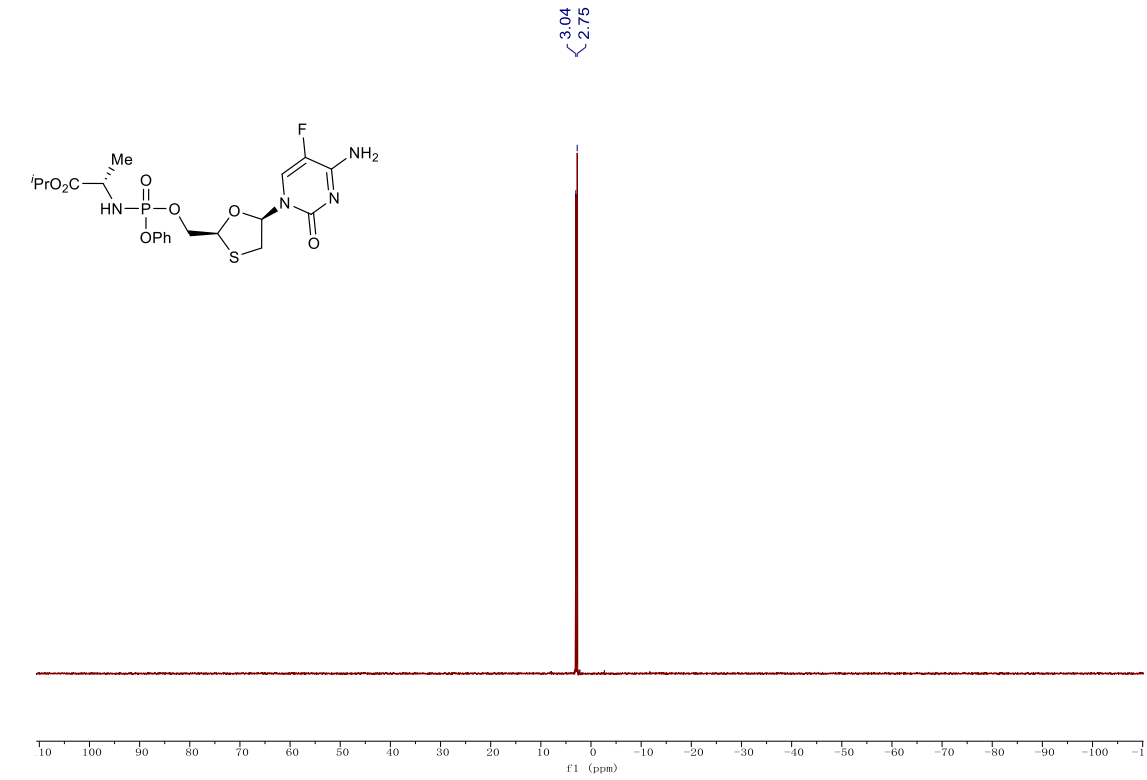
23, ^{1}H NMR (500 MHz, $CDCl_3$)



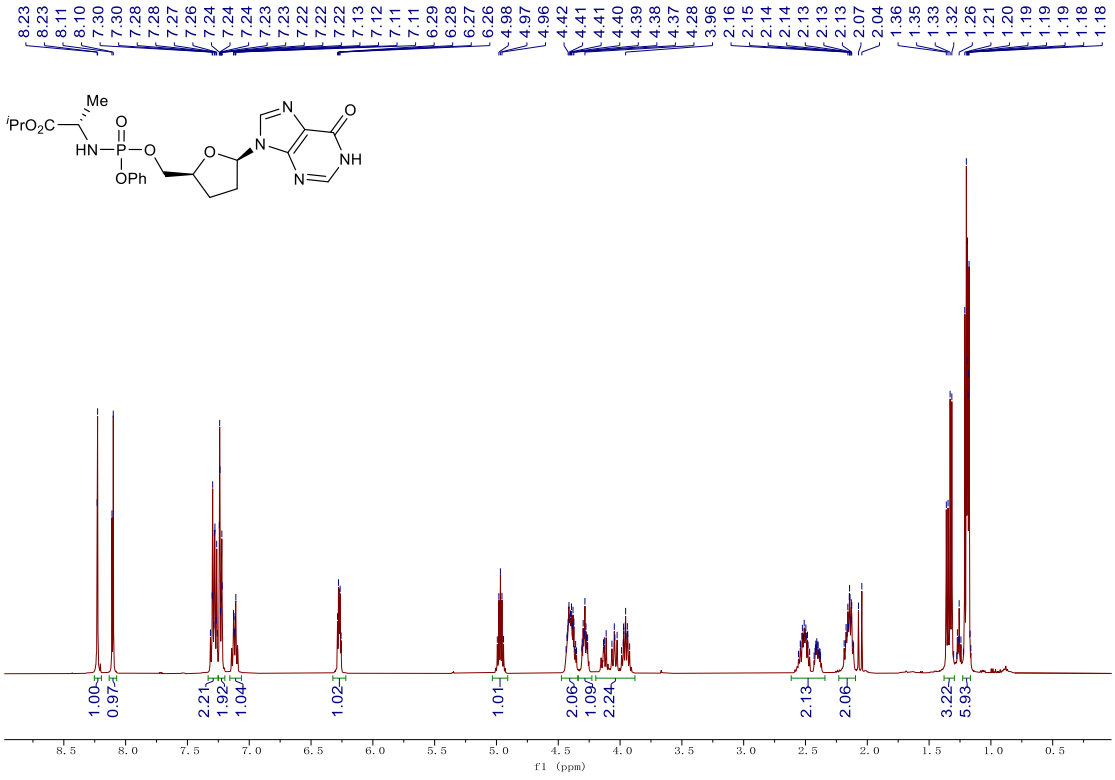
23, ^{13}C NMR (126 MHz, $CDCl_3$)



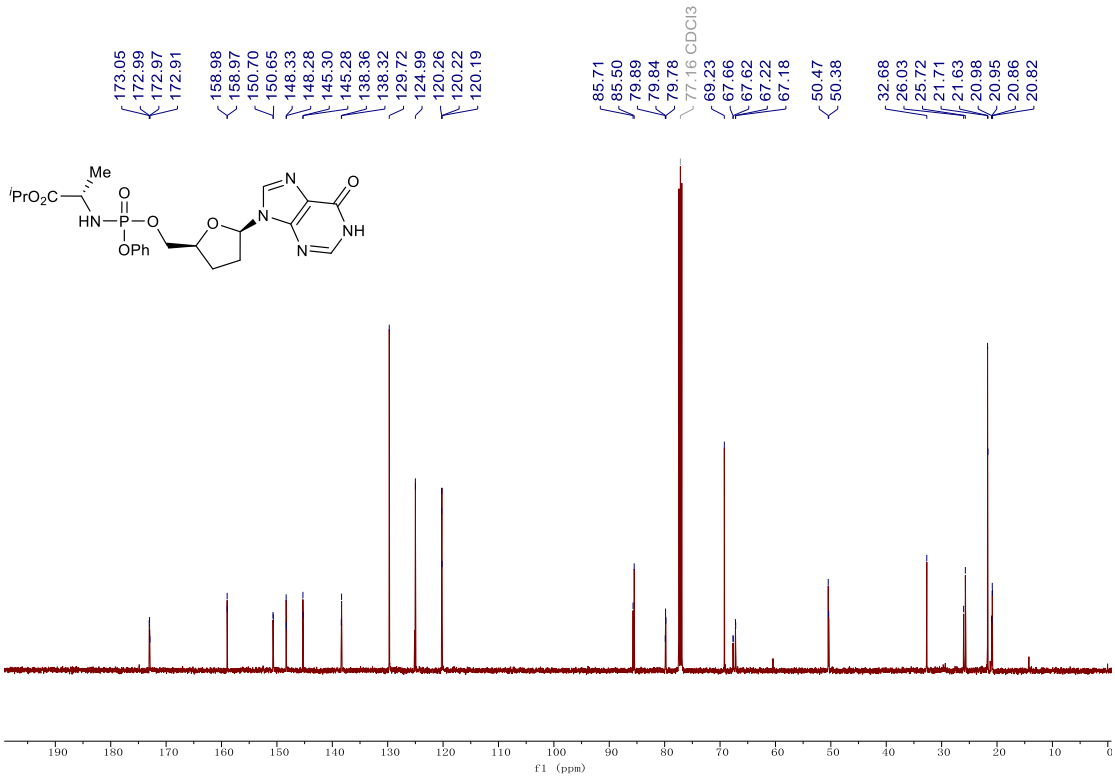
23, ^{31}P NMR (202 MHz, $CDCl_3$)



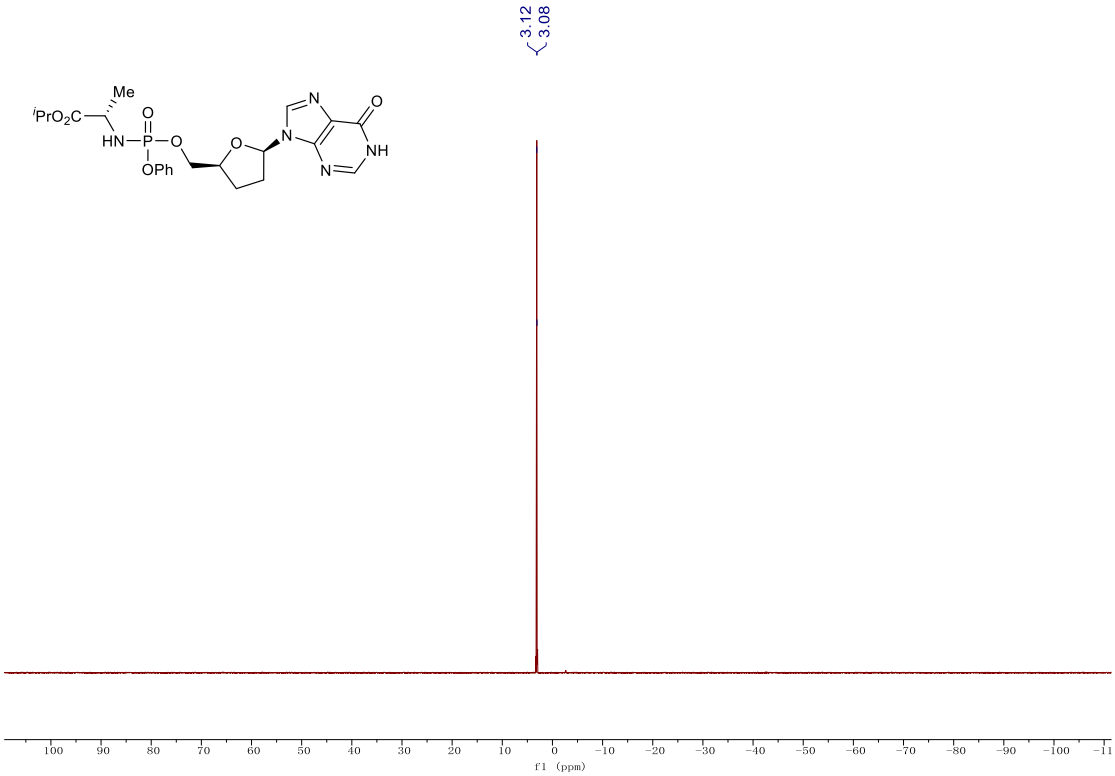
24, ^{1}H NMR (500 MHz, $CDCl_3$)



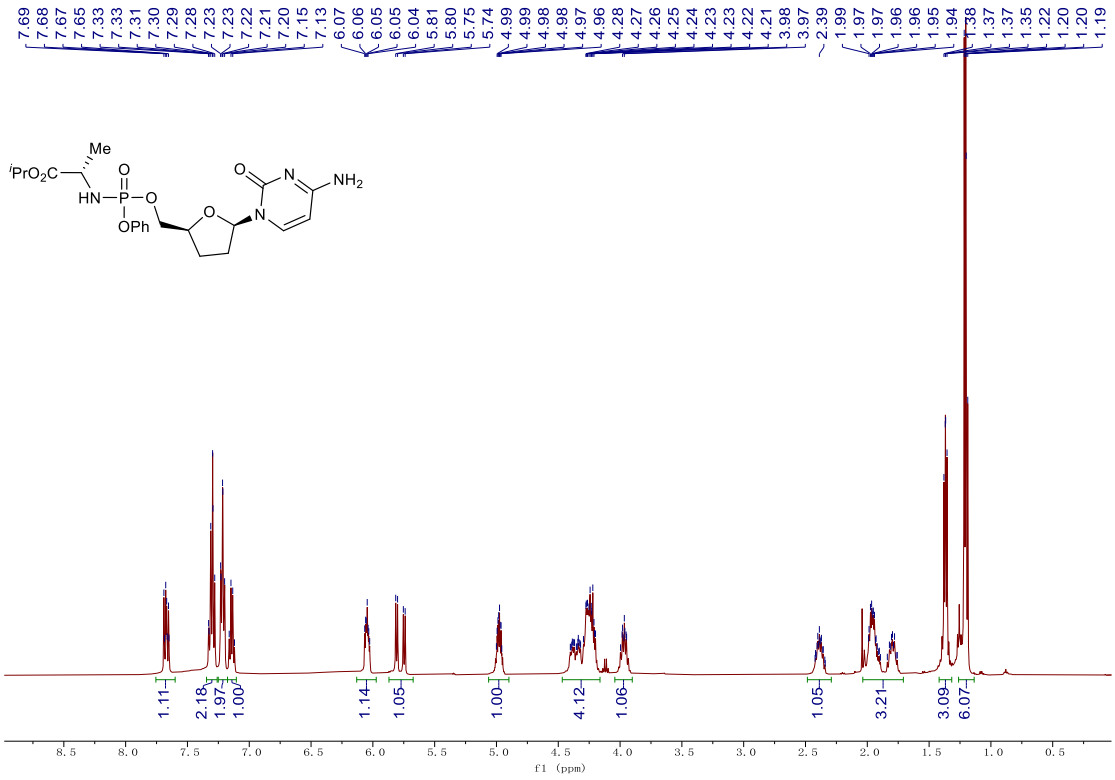
24 ^{13}C NMR (126 MHz, $CDCl_3$)



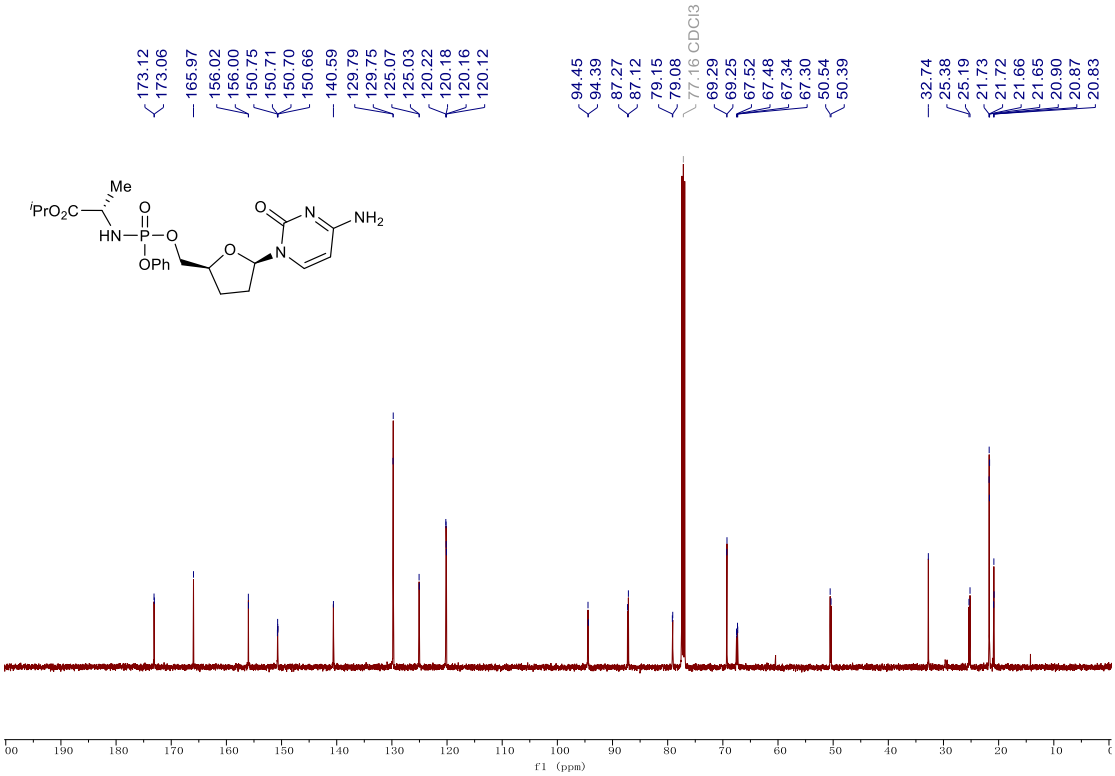
24, ^{31}P NMR (202 MHz, $CDCl_3$)



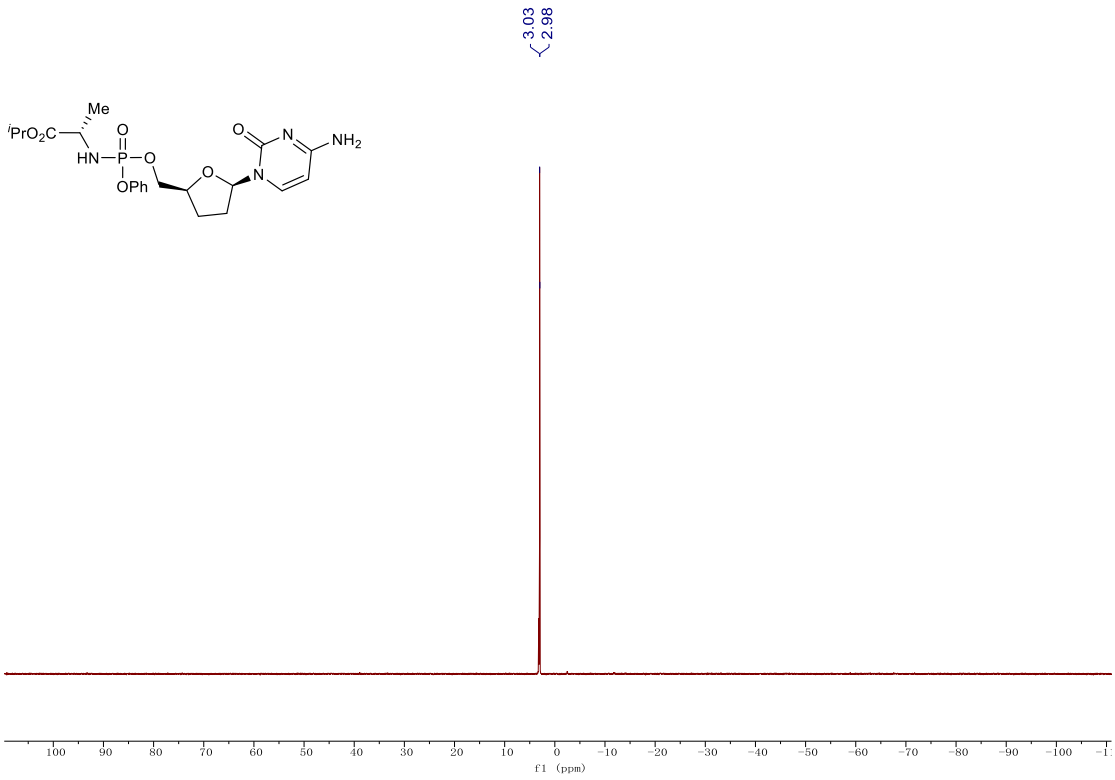
25, ^{1}H NMR (500 MHz, $CDCl_3$)



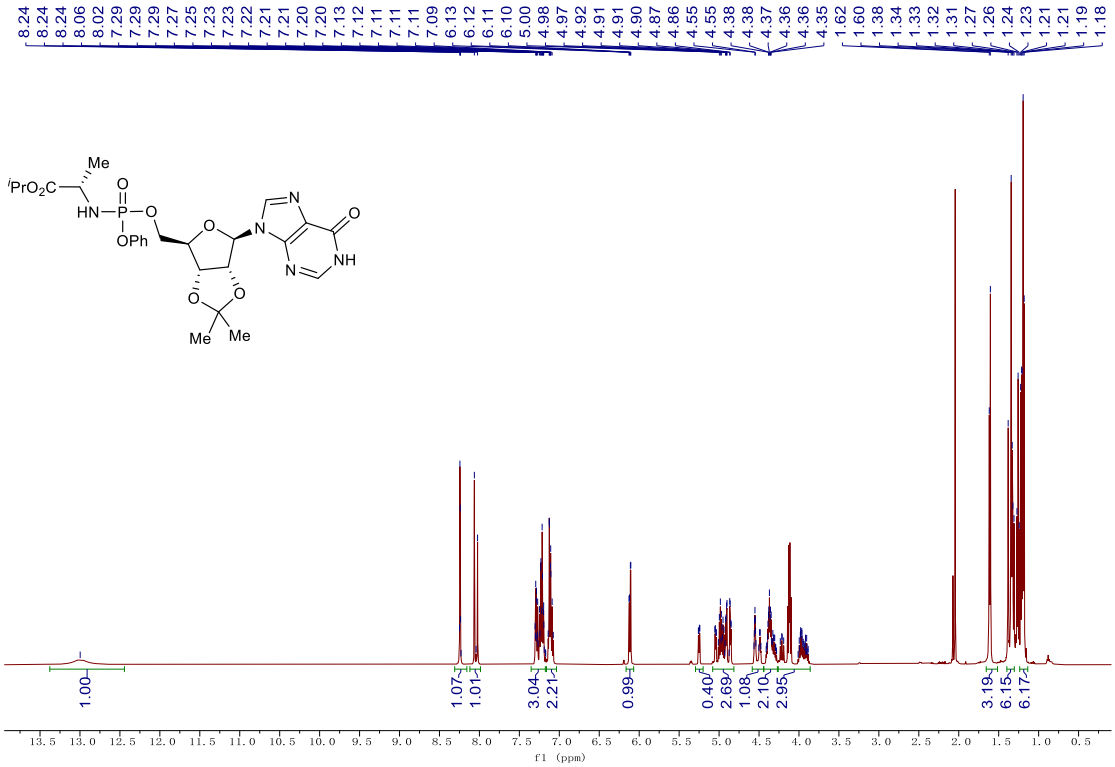
25, ^{13}C NMR (126 MHz, $CDCl_3$)



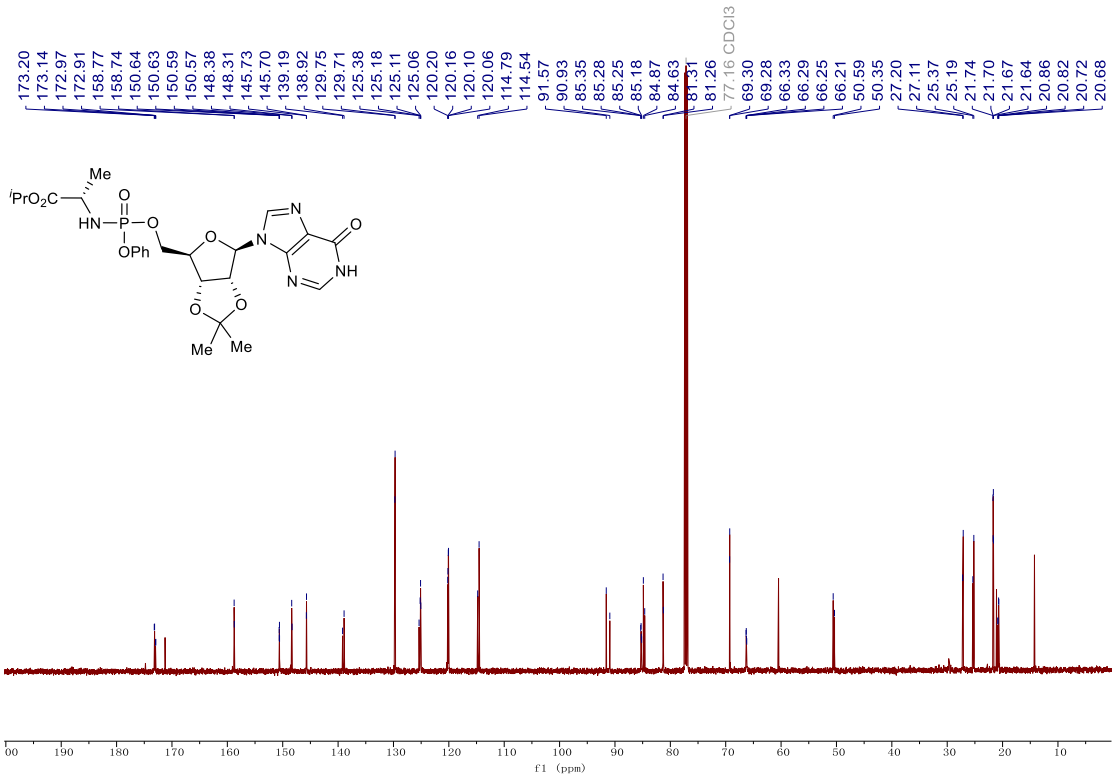
25, ^{31}P NMR (202 MHz, $CDCl_3$)



26, ^{1}H NMR (500 MHz, $CDCl_3$)

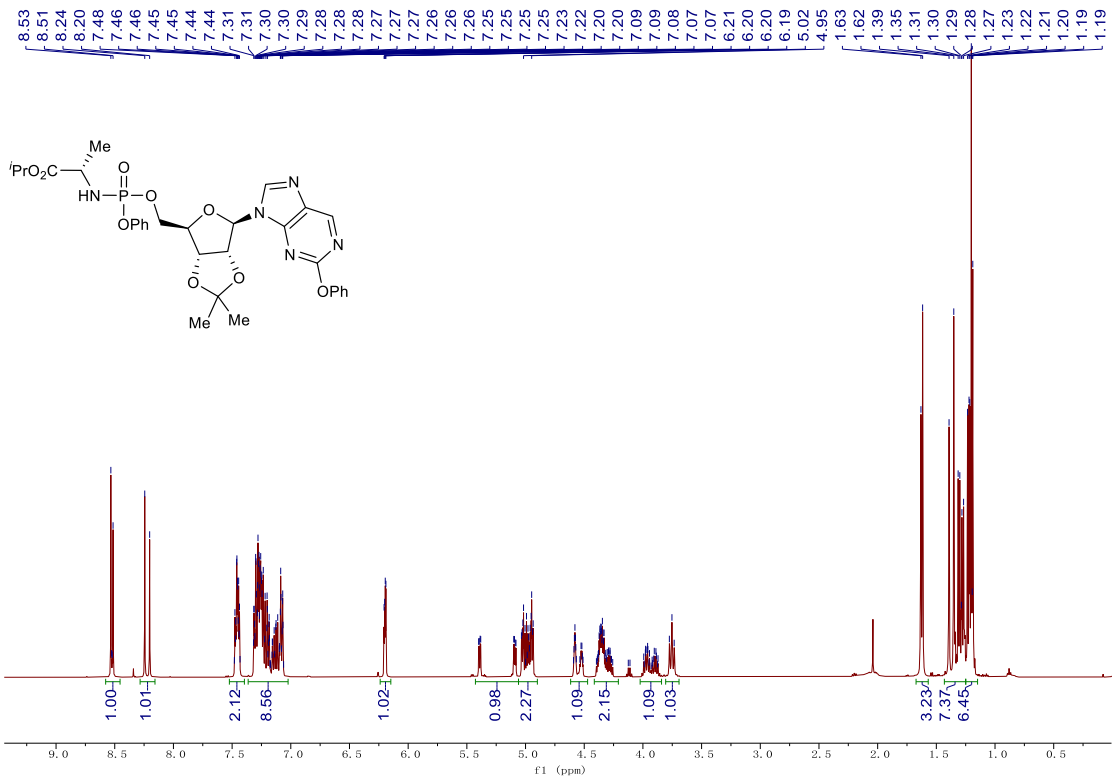


26, ^{13}C NMR (126 MHz, $CDCl_3$)

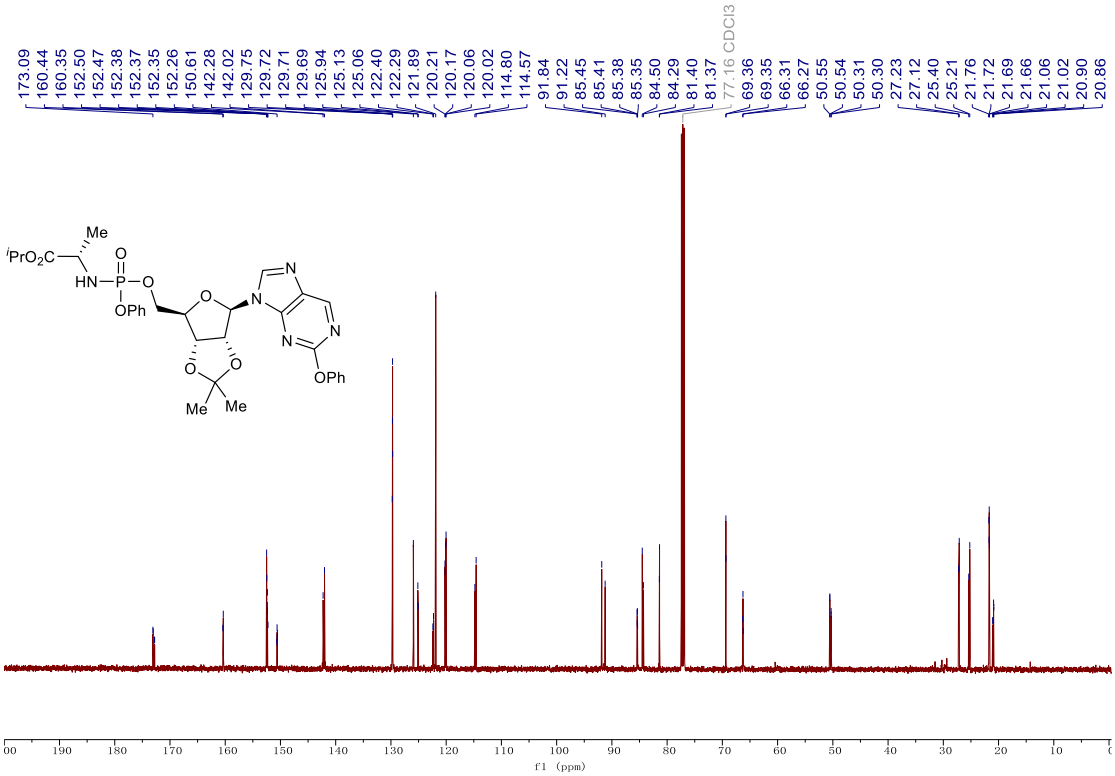


26, ^{31}P NMR (202 MHz, $CDCl_3$)

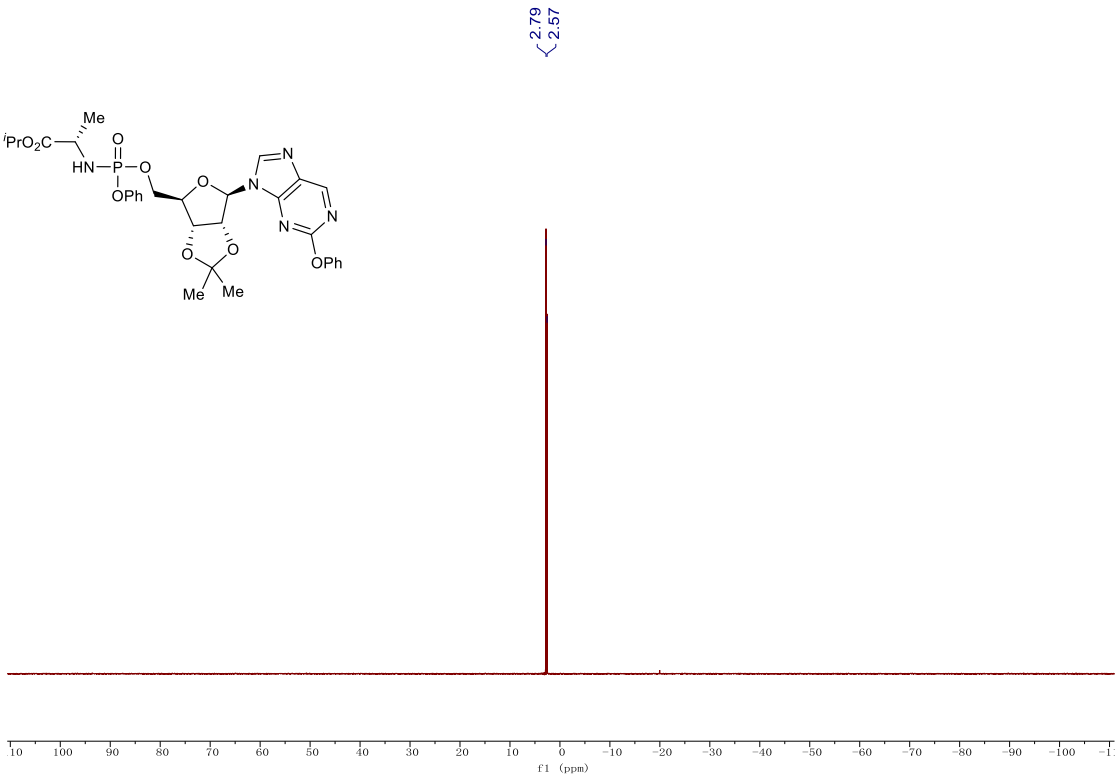
27, ^{1}H NMR (500 MHz, $CDCl_3$)



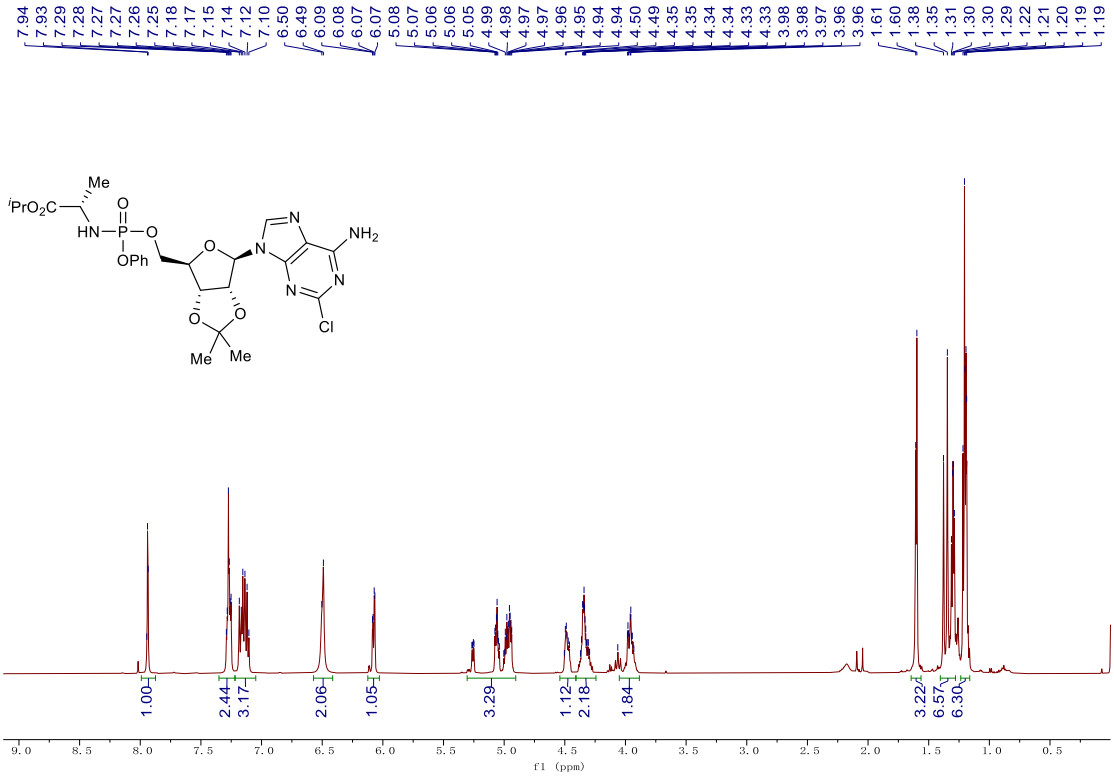
27, ^{13}C NMR (126 MHz, $CDCl_3$)



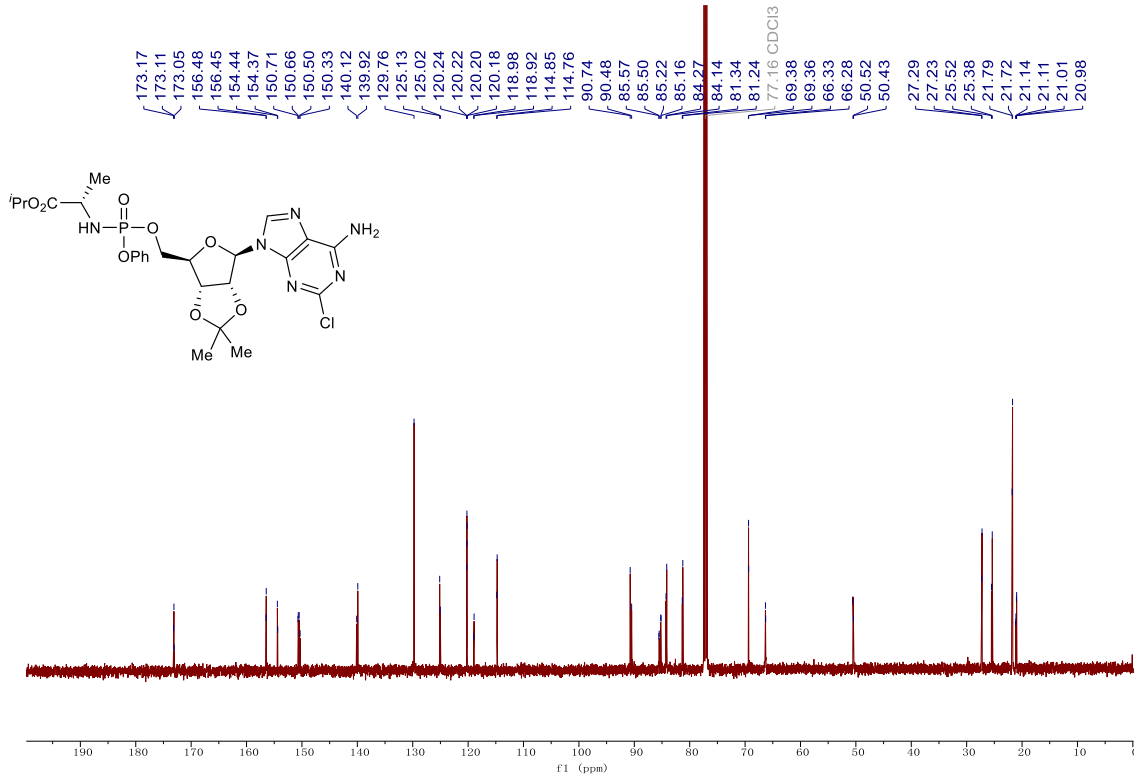
27, ^{31}P NMR (202 MHz, $CDCl_3$)



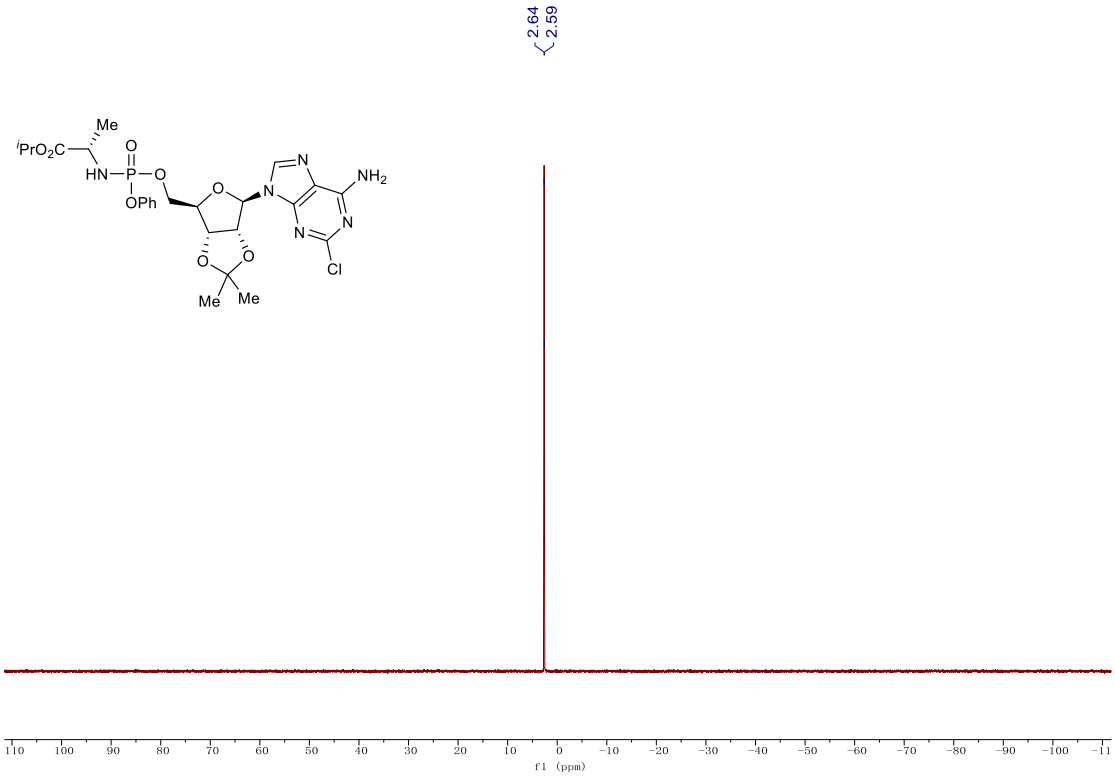
28, ^{1}H NMR (500 MHz, $CDCl_3$)



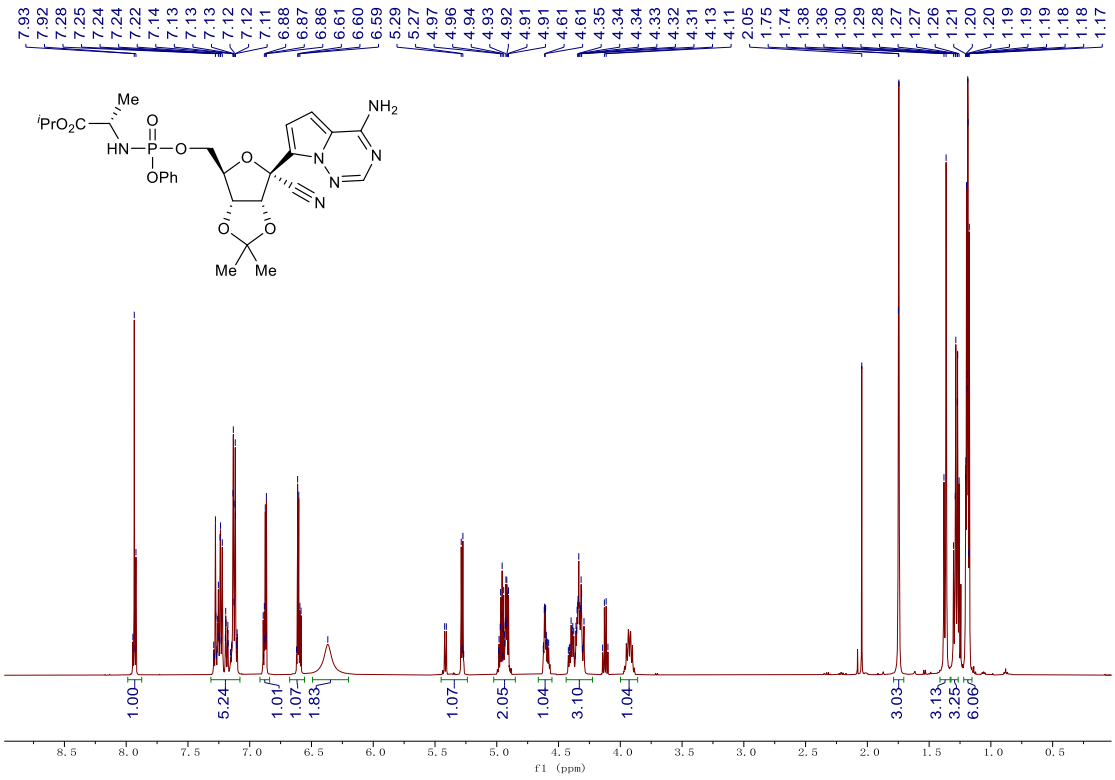
28, ^{13}C NMR (126 MHz, $CDCl_3$)



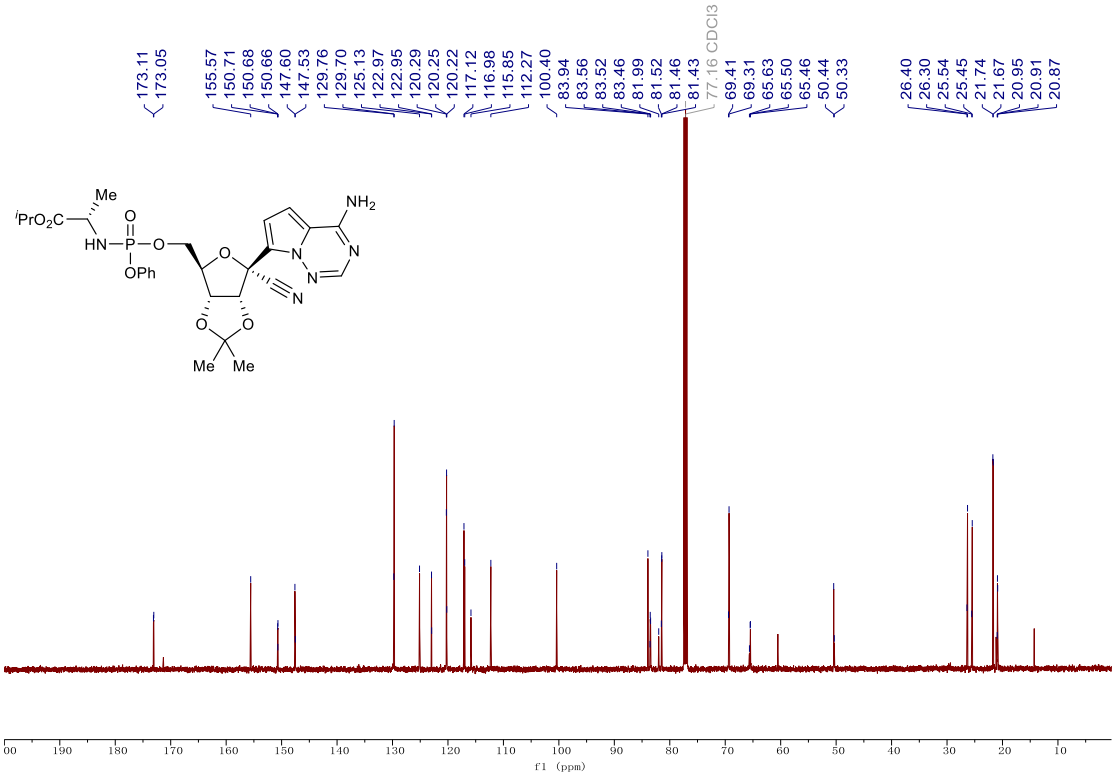
28, ^{31}P NMR (202 MHz, $CDCl_3$)



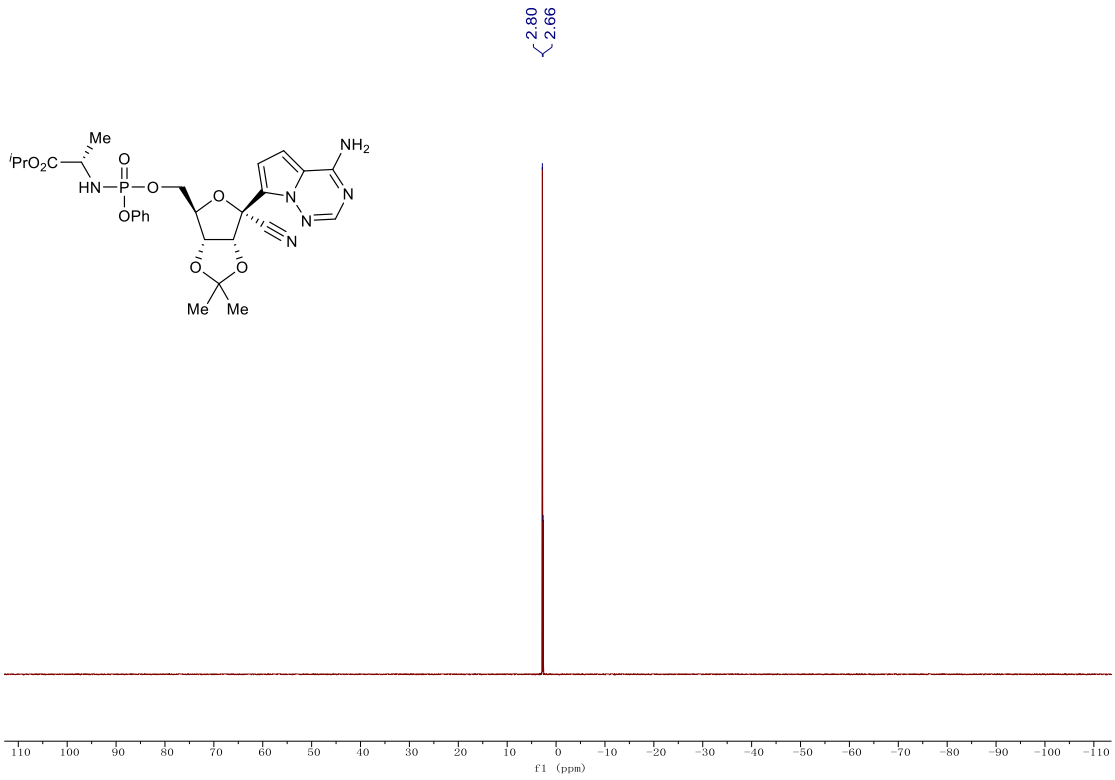
29, ^{1}H NMR (500 MHz, $CDCl_3$)



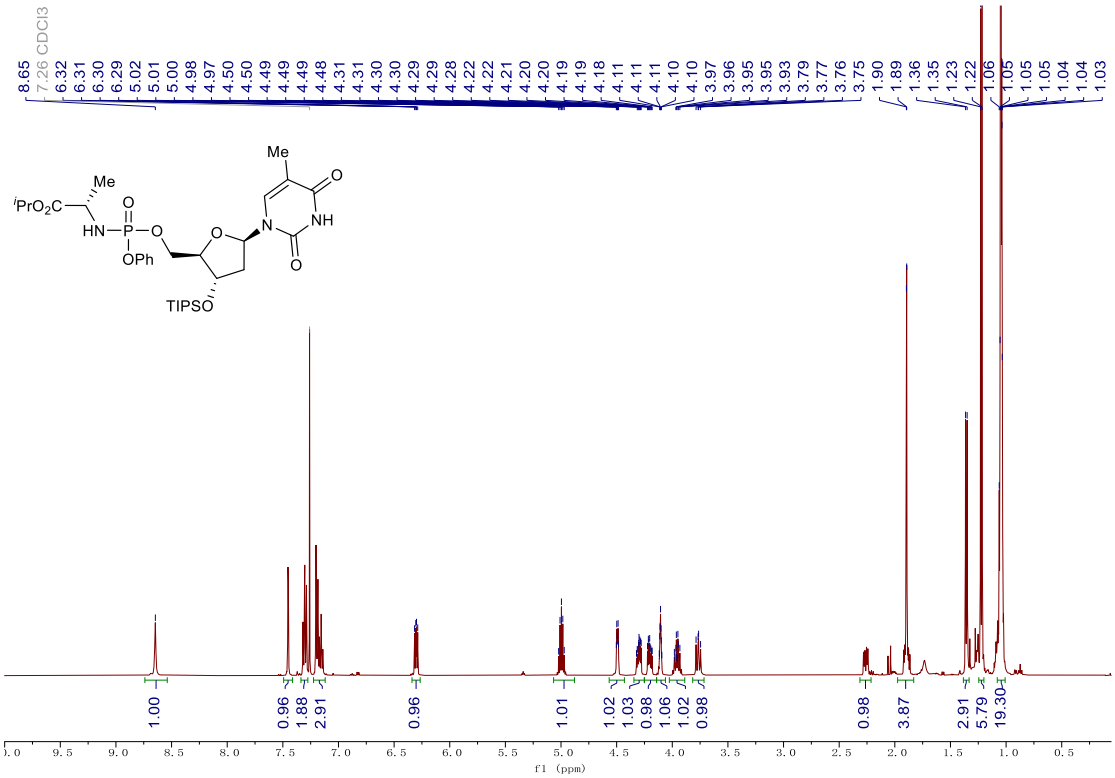
29, ^{13}C NMR (126 MHz, $CDCl_3$)



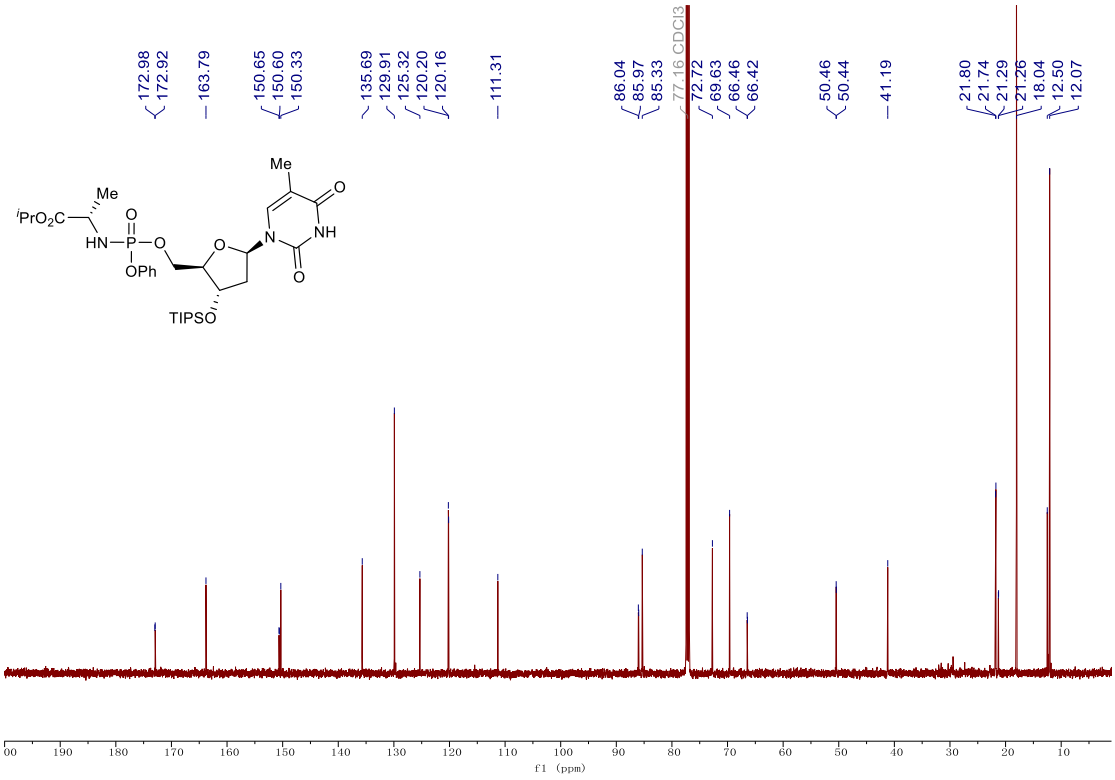
29, ^{31}P NMR (202 MHz, $CDCl_3$)



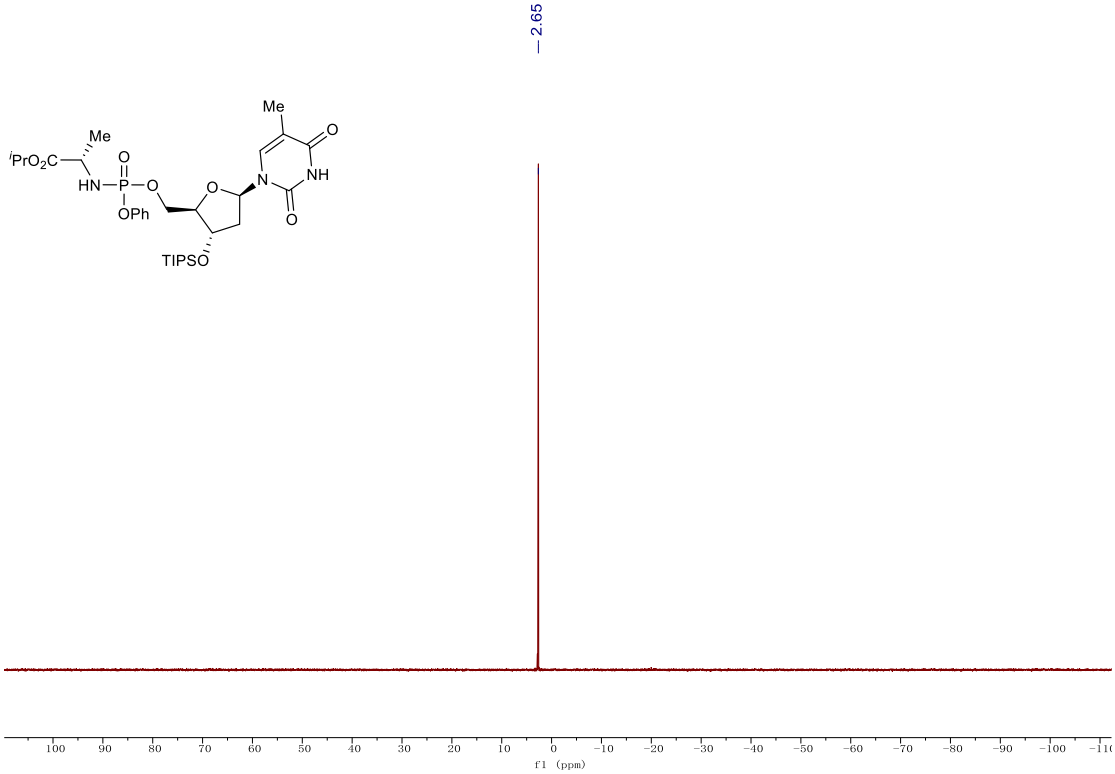
30, ^{1}H NMR (500 MHz, $CDCl_3$)



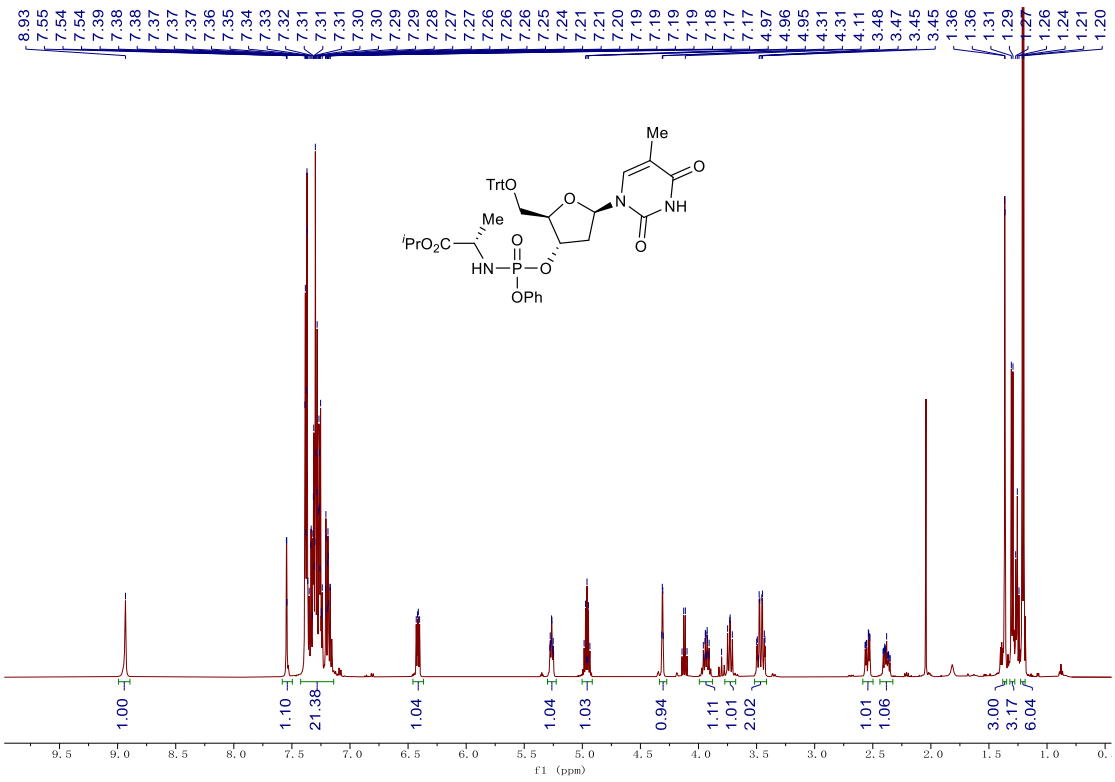
30, ^{13}C NMR (126 MHz, $CDCl_3$)



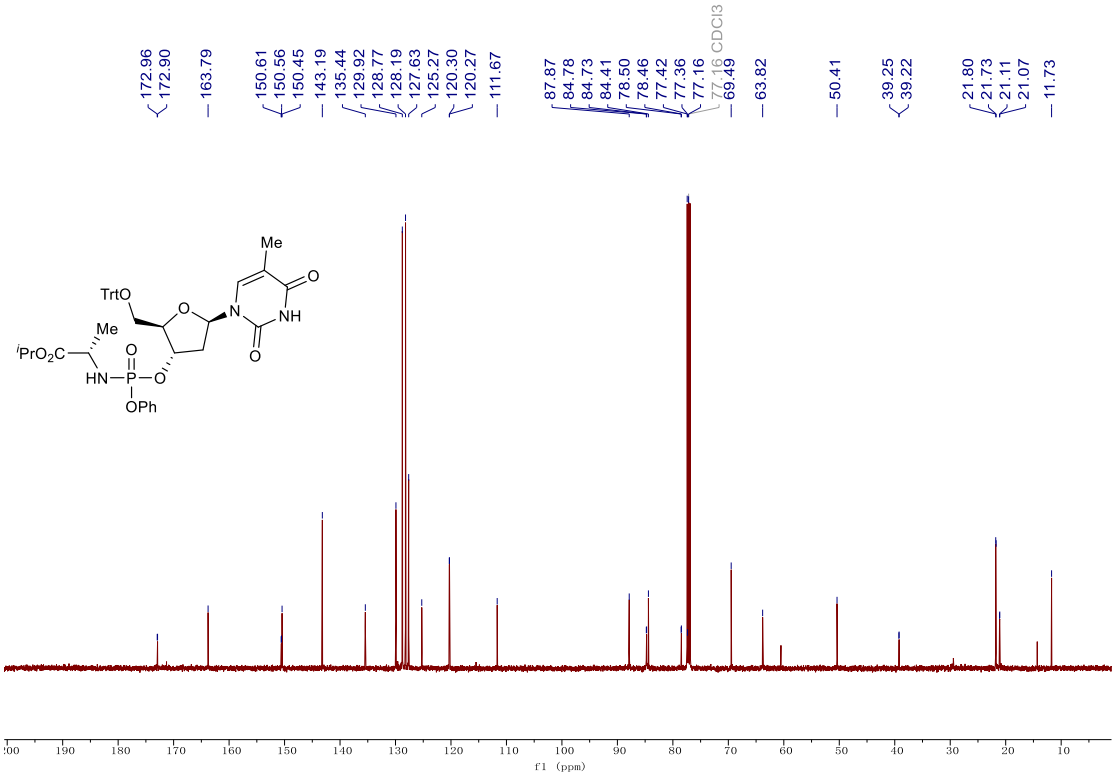
30, ^{31}P NMR (202 MHz, $CDCl_3$)



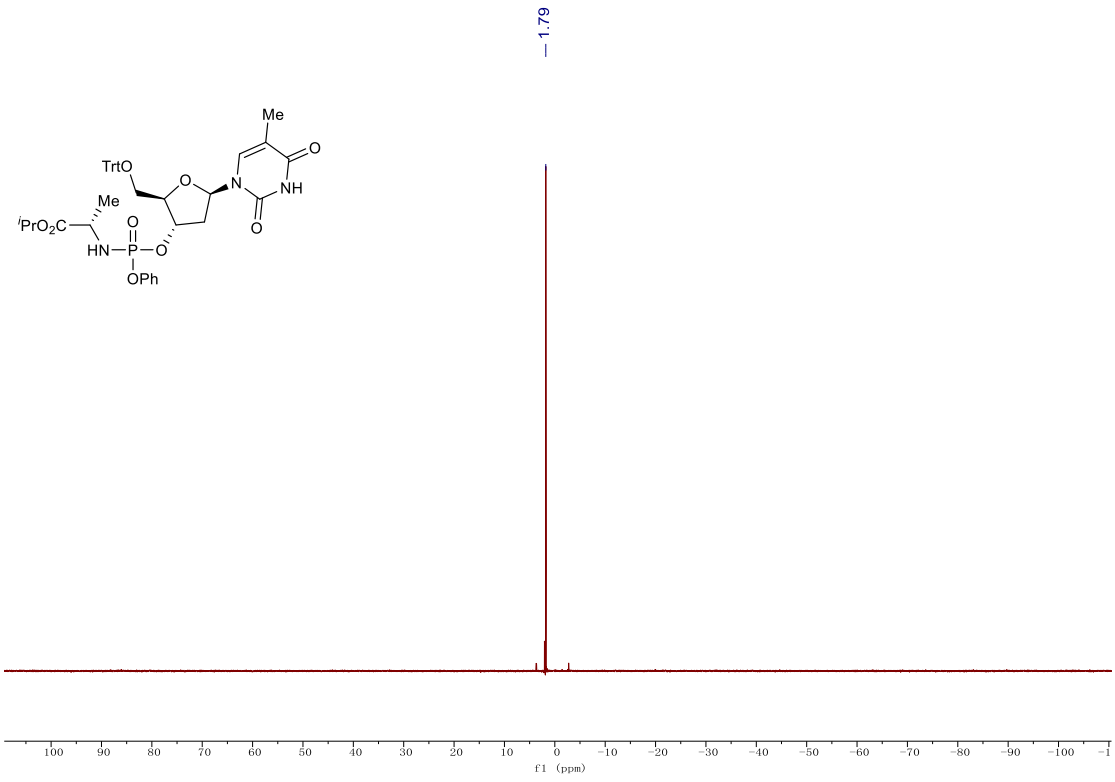
31, ^{1}H NMR (500 MHz, $CDCl_3$)



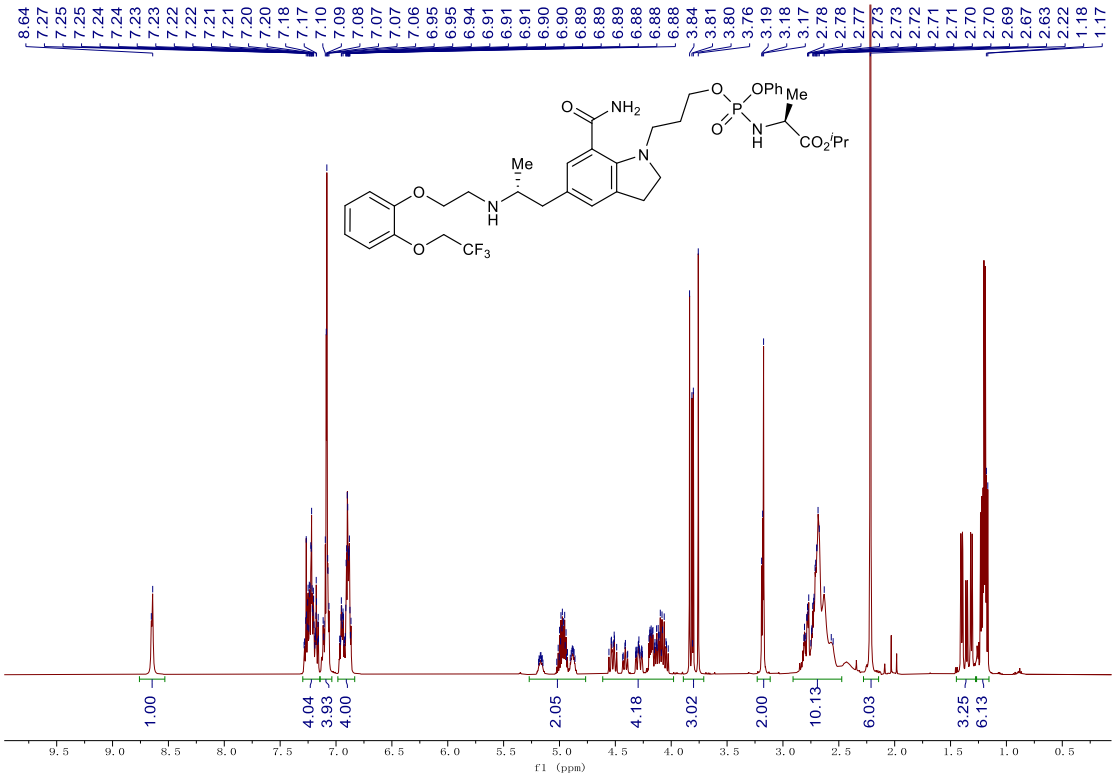
31, ^{13}C NMR (126 MHz, $CDCl_3$)



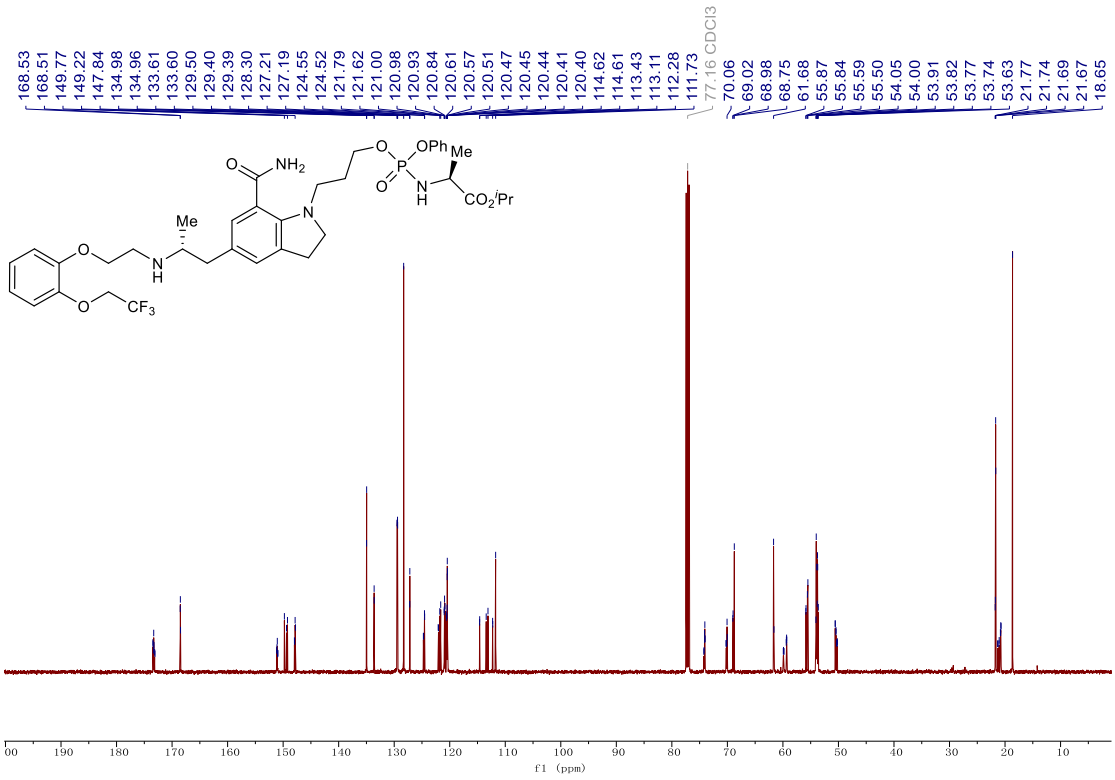
31, ^{31}P NMR (202 MHz, $CDCl_3$)



32, ^{1}H NMR (500 MHz, $CDCl_3$)

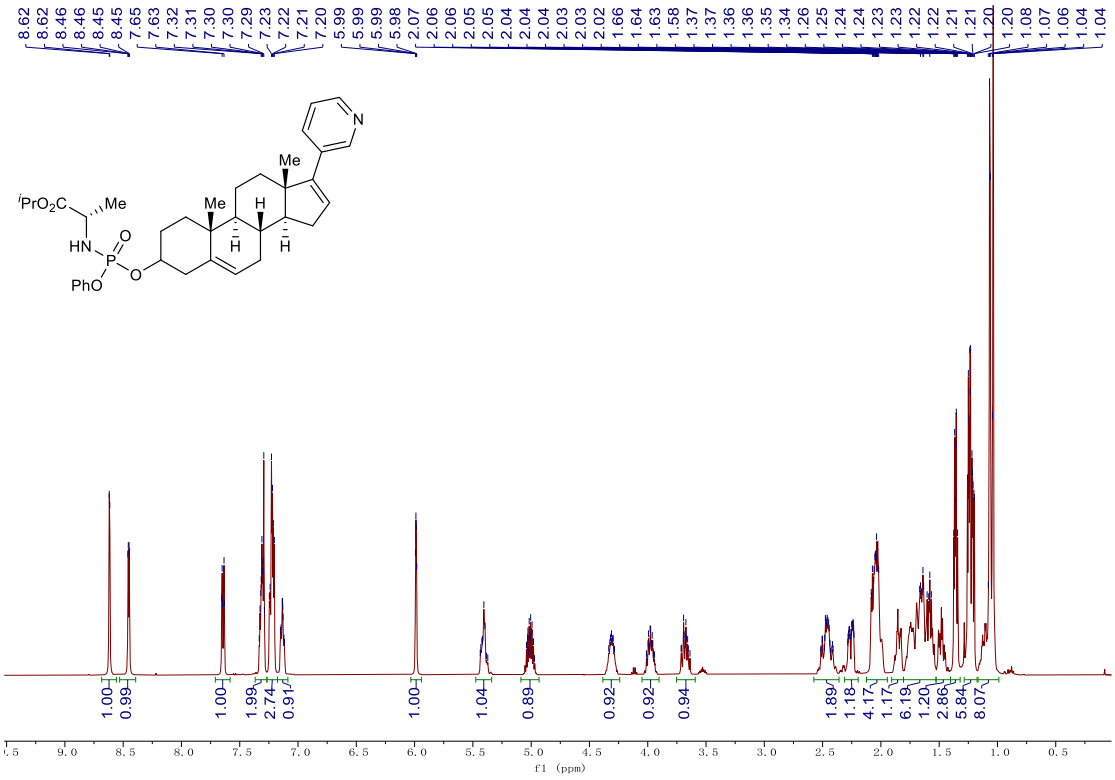


32, ^{13}C NMR (126 MHz, $CDCl_3$)

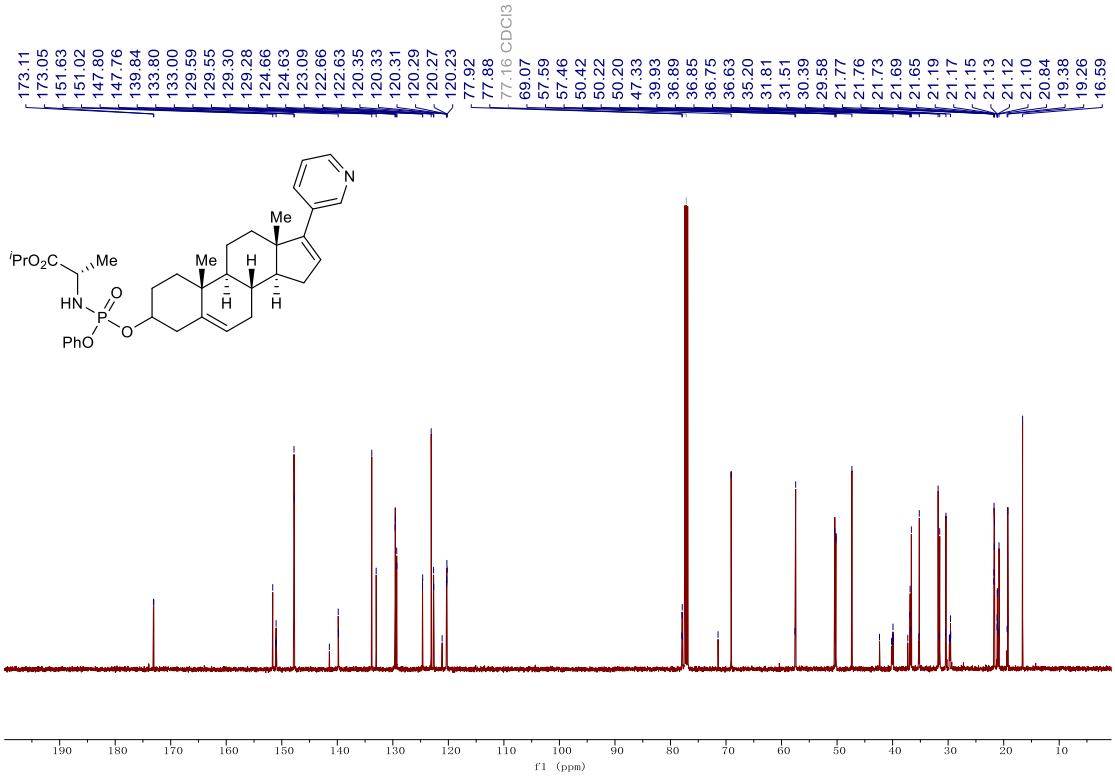


32, ^{31}P NMR (202 MHz, $CDCl_3$)

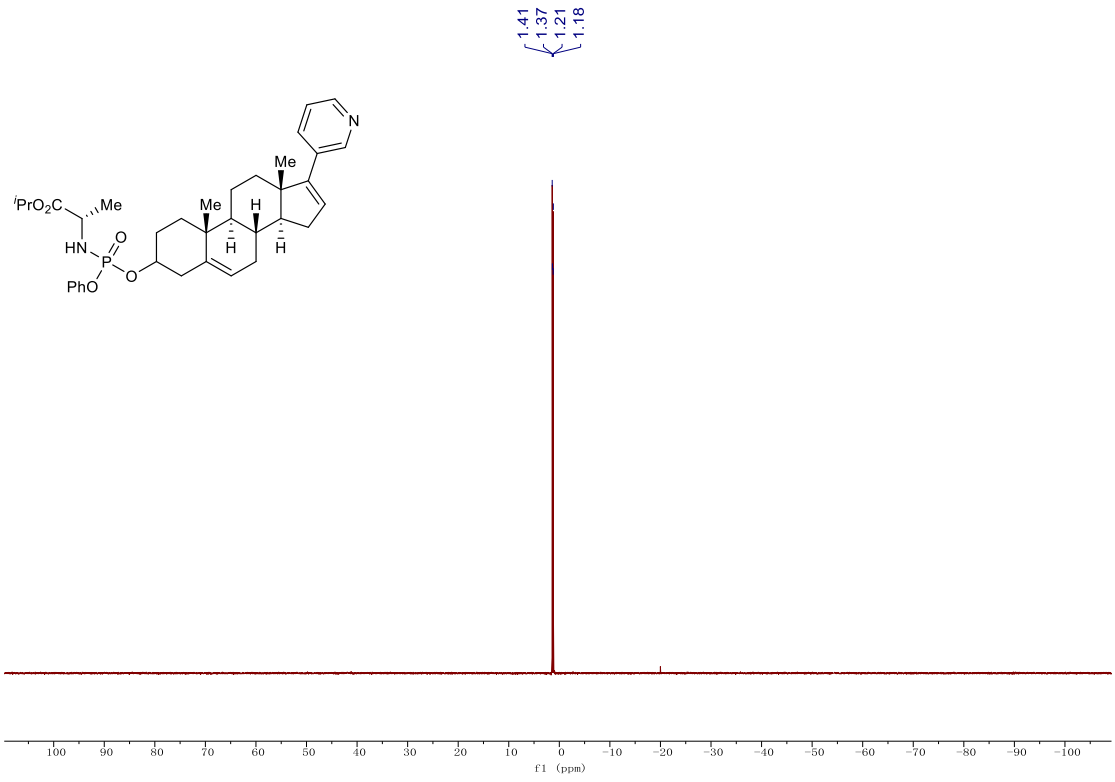
33, ^{1}H NMR (500 MHz, $CDCl_3$)



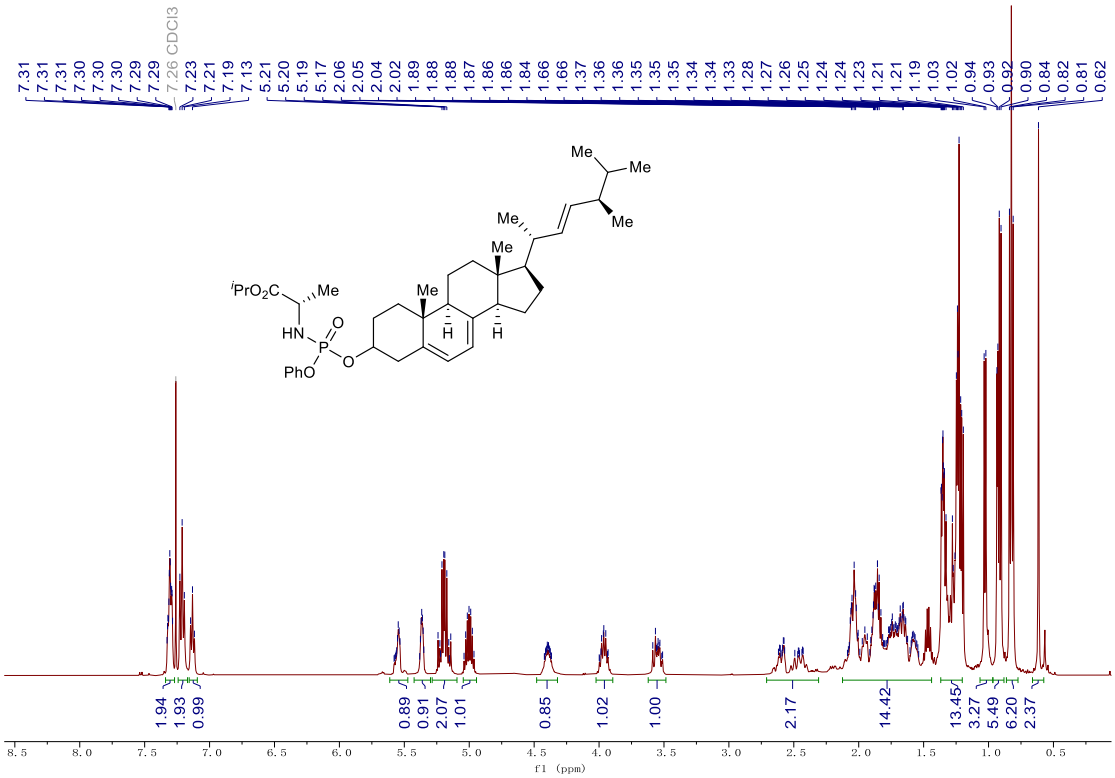
33, ^{13}C NMR (126 MHz, $CDCl_3$)



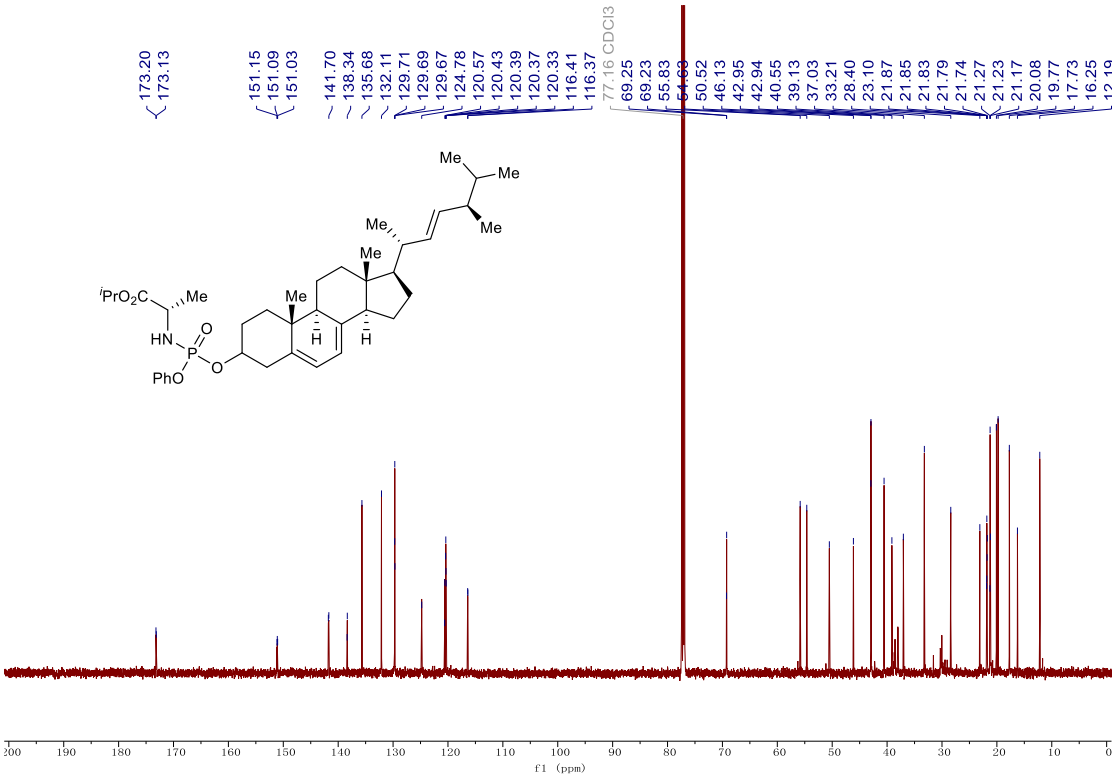
33, ^{31}P NMR (202 MHz, $CDCl_3$)



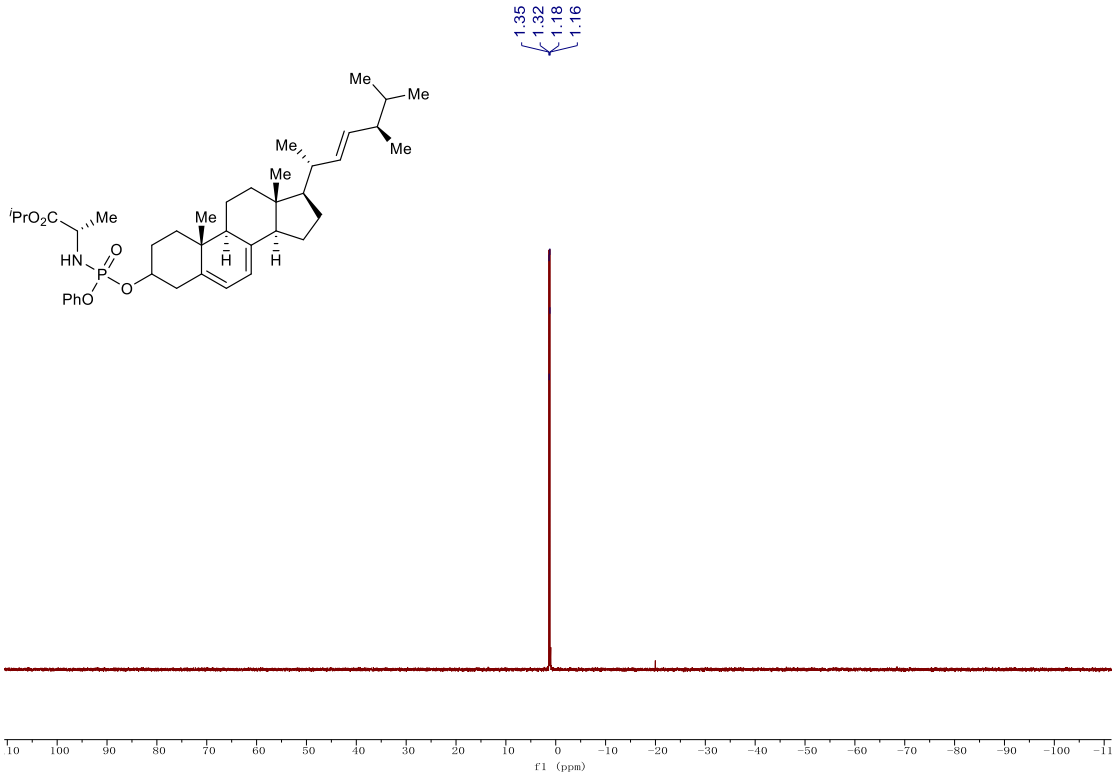
34, ^{1}H NMR (500 MHz, $CDCl_3$)



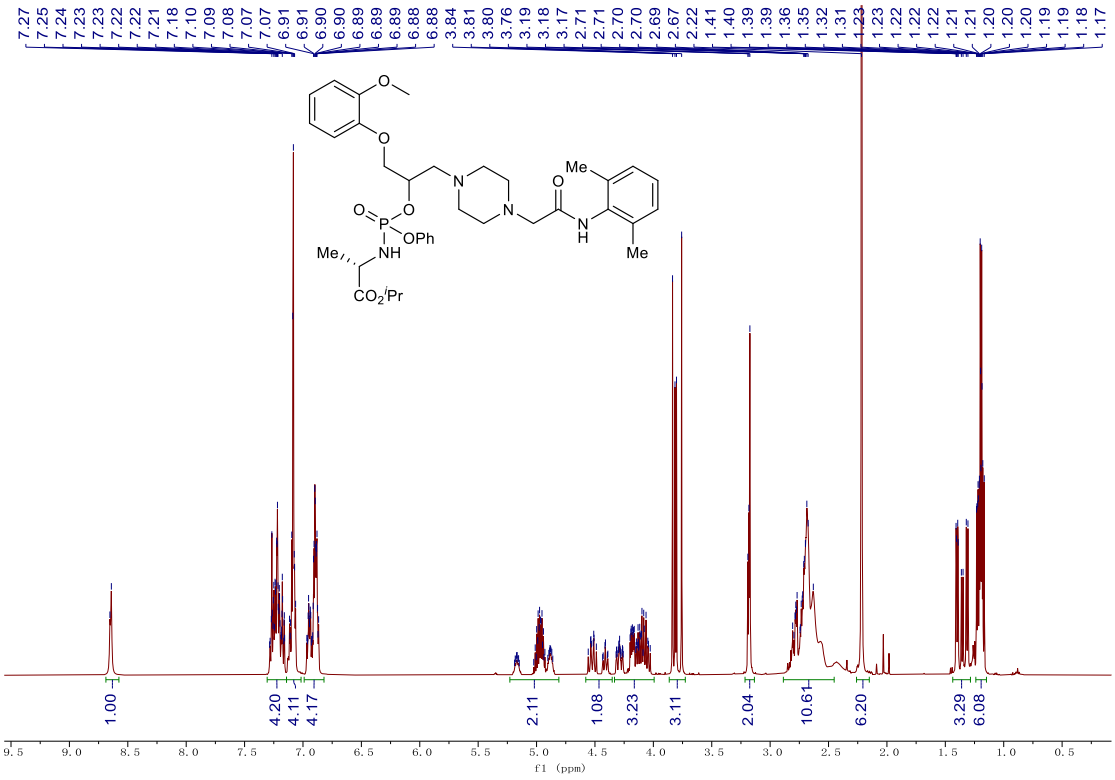
34, ^{13}C NMR (126 MHz, $CDCl_3$)



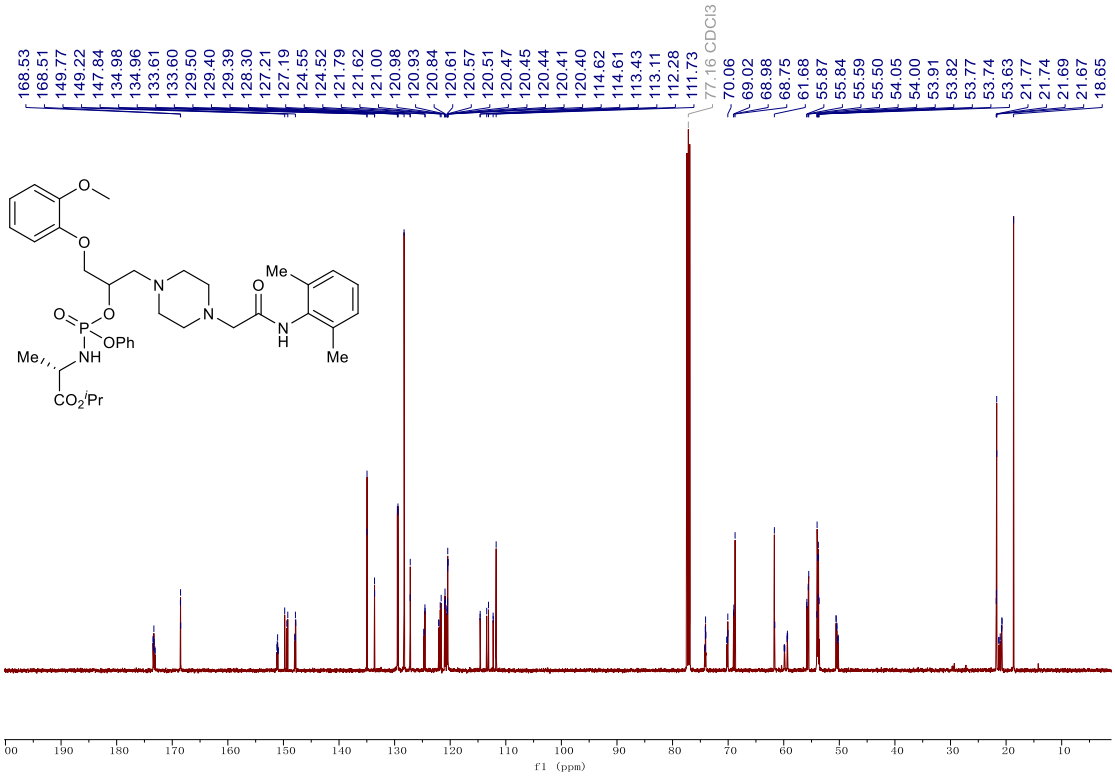
34, ^{31}P NMR (202 MHz, $CDCl_3$)



35, ^{1}H NMR (500 MHz, $CDCl_3$)



35, ^{13}C NMR (126 MHz, $CDCl_3$)



35, ^{31}P NMR (202 MHz, $CDCl_3$)