A Highly Efficient Catalytic Method for the Synthesis of Phosphite Diesters

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Supporting Information

Contents

1. General

· JEOL JNM-ECZ 500R/M3 or ECX 600 spectrometers were used for NMR measurement. Tetramethyl silane was used as an internal standard for ^{1}H NMR (δ = 0 ppm), and $CDCl_3$ or DMSO-d_6 was used for ^{13}C NMR ($CDCl_3$: δ = 77.00 ppm, DMSO-d_6: δ = 39.50 ppm). Structures of known compounds were confirmed by comparing them with data shown in the literature.

· IR spectra were measured using Shimazu IRSpirit spectrometer.

· DART and ESI mass spectra were recorded on JEOL JMS-T100TD mass spectrometer.

· APCI mass spectra were recorded on Shimadzu LCMS-IT-TOF mass spectrometer.

· Solvents were purchased in anhydrous grade from FUJIFILM Wako Pure Chemical Corporation and Kanto Chemical Co. Inc. and used as received.

· MS 5A was purchased from Sigma-Aldrich as a powder form and dried at 100 ºC under vacuum before use.

· $Zn(acac)_2$, $Zn(OAc)_2$, and $Zn(TMHD)_2$ were purchased from Tokyo Chemical Industry Co., Ltd. and FUJIFILM Wako Pure Chemical Corporation and used as received. $Zn(OPiv)_2$ was prepared from commercially available starting materials by following the reported methods.[1]

· Alcohols **1** except for **1aa, 1ad** were purchased from Tokyo Chemical Industry Co., Ltd. and FUJIFILM Wako Pure Chemical Corporation or prepared from commercially available starting materials by following reported methods.[2-10] All of them were purified by distillation or recrystallization before use.

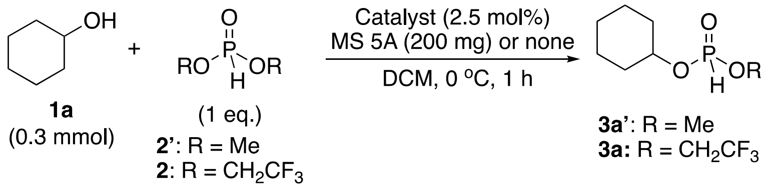
· Phosphite **2** was prepared by following reported methods[11] and phosphite **2'** was purchased from Tokyo Chemical Industry Co., Ltd. Both of them were purified by distillation before use.

· All commercially available reagents, unless otherwise stated, were used without further purification.

· All reactions, unless otherwise stated, were carried out under an argon atmosphere.

2. Additional data for comparison with previous study

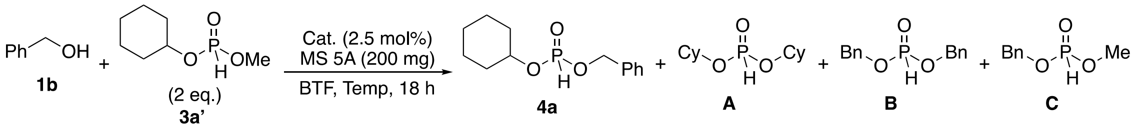
Table S0. Comparison of the previous method and the new method (reactivity)



R	Catalyst	MS	Yield (%)[a]	Comment
Me	$Zn(acac)_2$	+	<5	Previous method[b]
Me	$Zn(acac)_2$	–	<5	Previous method[b]
CH_2CF_3	$Zn(acac)_2$	–	42	New method
CH_2CF_3	$Zn(TMHD)_2$	–	97	New method

[a] Yield was determined by ^1H NMR analysis using 1,3,5-trimethoxylbenzene as an internal standard. [b] *Org. Lett.* **2020**, *22*, 3171.

Table S1. Optimization of consecutive phosphonylation of **3a'** (Scheme 2)

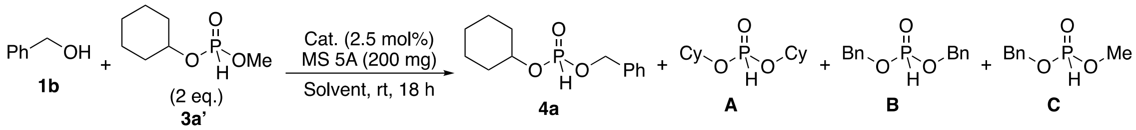


Entry	Catalyst	Temp.	Yield[a] (%)			
			4a	**A**	**B**	**C**
1	$Zn(acac)_2$	rt	78(75)	14(13)	11(9)	5(5)
2	$Zn(TMHD)_2$	rt	76	19	12	9
3	$Zn(acac\text{-}F_6)_2$	rt	5	0	0	0
4	$Zn(OTf)_2$	rt	21	0	0	3
5	$Zn(OAc)_2$	rt	84	9	7	2
6	$Zn(OBz)_2$	rt	71	4	6	3
7	$ZnEt_2$	rt	2(5)	0(0)	0(0)	0(0)
8	$ZnBr_2$	rt	1(3)	0(0)	0(0)	0(0)
9	$Zn(OMe)_2$	rt	0	0	0	0
10	$Zn(TFA)_2$	rt	51(58)	2(2)	3(4)	3(3)
11	$Zn(OPiv)_2$	rt	73	6	8	3
12	Zinc isobutyrate	rt	77	5	8	3

13	$Zn(acac)_2$	0 °C	65	9	7	5
14	$Zn(TMHD)_2$	0 °C	52	9	7	7
15	$Zn(OAc)_2$	0 °C	39	1	3	2
16	Zinc propionate	rt	4	7	3	89
17	Zinc formate	rt	8	11	8	2
18	Zinc methoxy acetate	rt	6	0	0	0
19	$Zn(2\text{-}Hydroxypyridine)_2$	rt	11	1	0	2
20	$Co(acac)_2$	rt	19	0	0	0
21	$Co(OAc)_2$	rt	71	4	8	3

[a] Yield was determined by ^1H NMR analysis using 1,2,4,5-tetramethylbenzene as an internal standard. Yield in parenthesis is the result of the second trial.

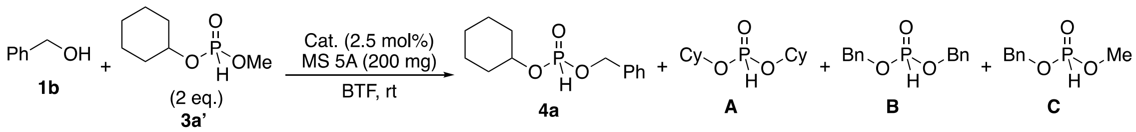
Table S2. Optimization of consecutive phosphonylation of **3a'** (Scheme 2)

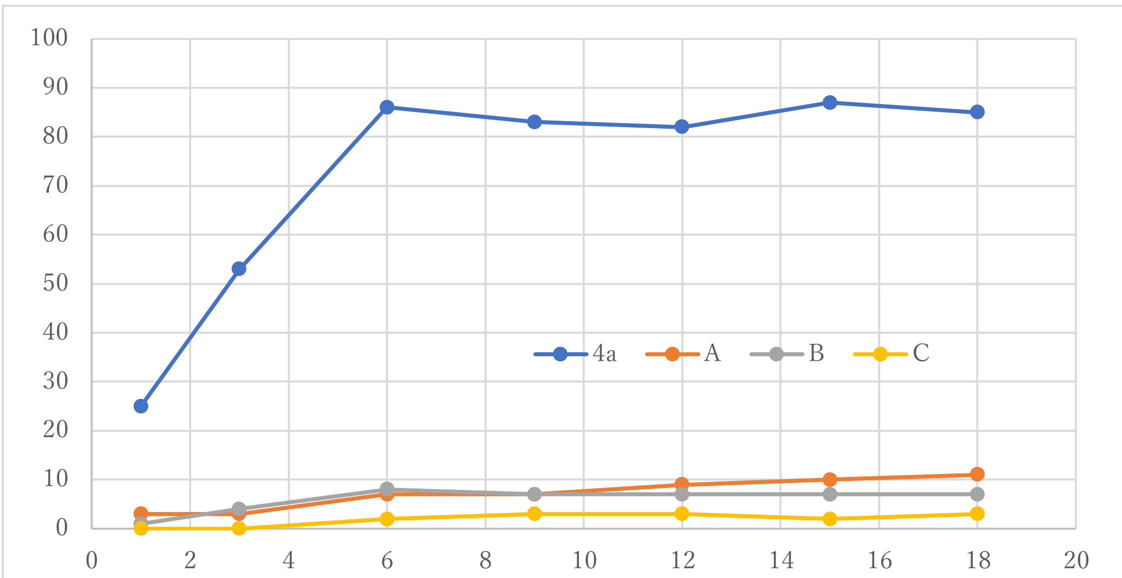


Entry	Solvent	MS		Yield[a] [%]				Conv.[%]
		Size	Amount	**4a**	**A**	**B**	**C**	
1	BTF	5A	200 mg	84(88)	9(10)	7(7)	2(2)	>99(99)
2	Toluene	5A	200 mg	85	11	7	3	99
3	DCM	5A	200 mg	79	8	8	5	92
4	THF	5A	200 mg	77	4	7	5	79
5	BTF	4A	200 mg	23	4	1	4	31
6	BTF	3A	200 mg	51	1	4	3	59
7	Toluene	5A	300 mg	82	9	7	3	99
8[b]	BTF	5A	200 mg	64	2	5	2	80

[a]Yield was determined by ^{1}H NMR analysis using 1,2,4,5-tetramethylbenzene as an internal standard. Yield in parenthesis is the result of the second trial. [b]Reaction was performed at 10 °C.

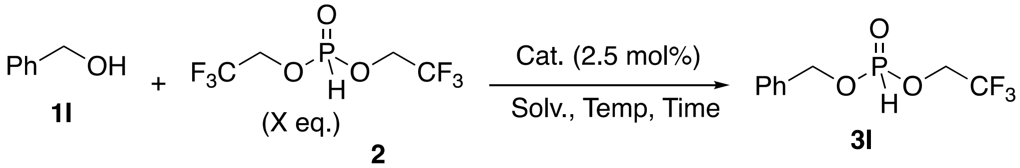
Figure S1. Reaction Profile of consecutive phosphonylation of **3a'** (Scheme 2)





3. Additional optimizations

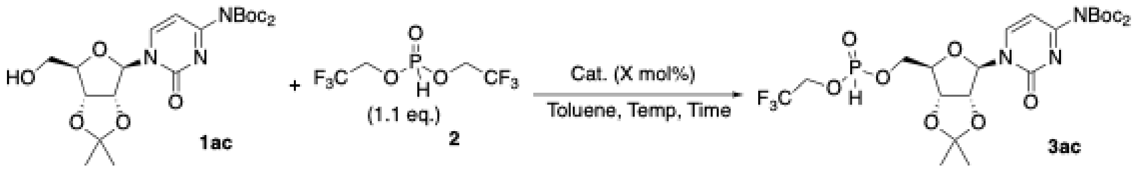
Table S3. Optimization of phosphonylation of **2l** with **2** (Scheme 3, Conditions B)



Entry	X (eq.)	Catalyst	Solvent	Temp. (°C)	Time (h)	Yield[a] (%)
1	2	Zn(TMHD)2	Toluene	0	2	93
2	1.5	Zn(TMHD)2	Toluene	0	2	89
3	1.1	Zn(TMHD)2	Toluene	0	2	82
4	2	Zn(OPiv)2	Toluene	0	2	95
5	2	Zn(TMHD)2	DCM	0	2	93
6	1.1	Zn(TMHD)2	Toluene	-20	22	86
7	1.1	Zn(OPiv)2	Toluene	-20	22	94
8	1.1	Zn(OPiv)2	Toluene	-20	12	94

[a]Yield was determined by ^{1}H NMR analysis using 1,2,4,5-tetramethylbenzene as an internal standard.

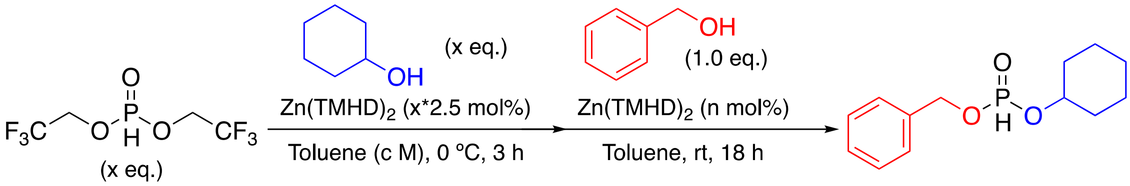
Table S4. Optimization of consecutive phosphonylation of **1ac** with **2** (Scheme 3, Conditions D)



Entry	Catalyst	Temp. (°C)	X (mol%)	Time (h)[a]	Results
1	Zn(TMHD)2	rt	5	3	Messy crude ^{1}H & ^{31}P NMR, significant overreaction
2	Zn(OPiv)2	rt	5	8	Messy crude ^{1}H & ^{31}P NMR, significant overreaction
3[b]	Zn(OPiv)2	0	2.5	17	Low conversion
4[b]	Zn(OPiv)2	0	5	19	96% target yield

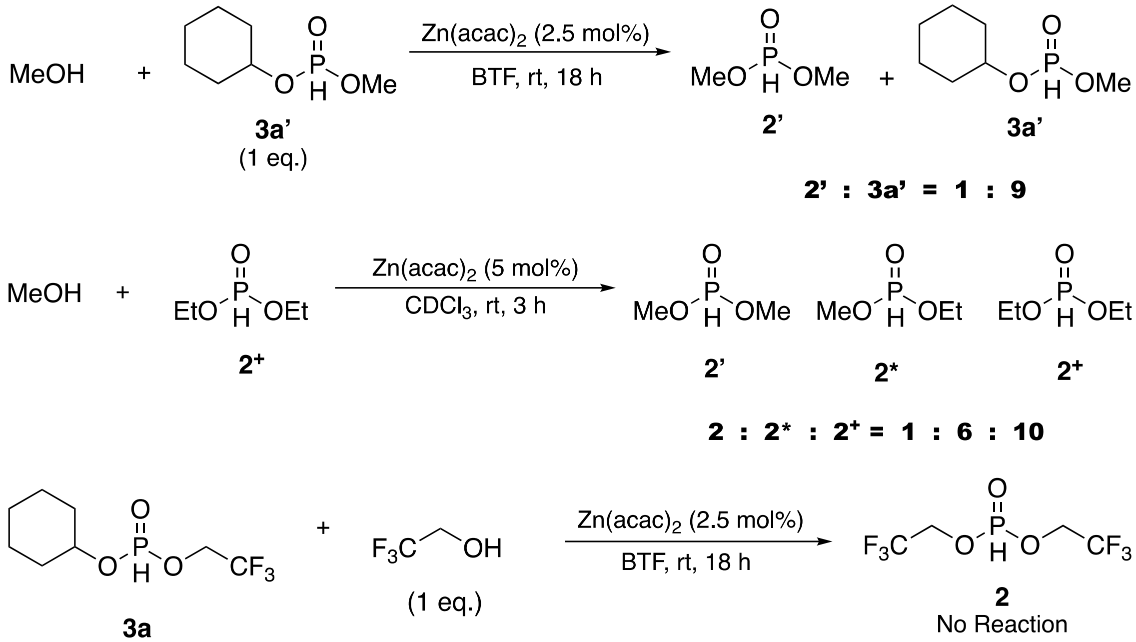
[a]Reaction monitored by TLC, quenched at full conversion.[b]Reaction conducted in DCM instead of Toluene

Table S5. Optimization of One-pot Reaction (Scheme 4)



Entry	x (eq.)	c (M)	n (mol%)	Yield (%)
1	1	0.3	0	15
2	1.2	0.3	0	49
3	1.2	0.3	2.5	85
4	1.3	0.3	2.5	76
5	1.3	0.38	2.5	85
6	1.5	0.38	2.5	89
7[a]	1.5	0.38	2.5	89

4. Mechanistic study



Scheme S1. Reversibility Experiments using **2** and **2'** as phosphonylation reagents

5. Data and discussion for NMR experiments

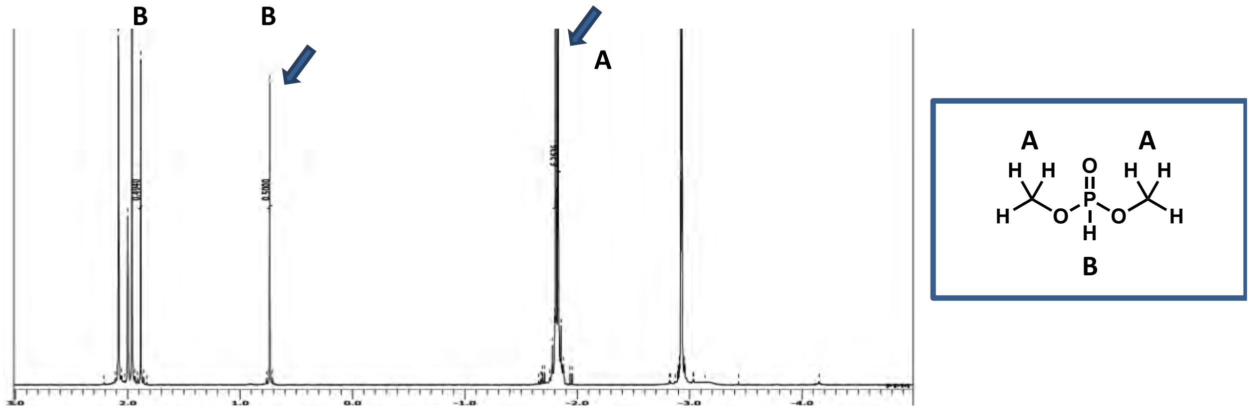


Figure S2-1. ^{1}H NMR spectrum of Dimethyl Phosphite in Toluene-d_8

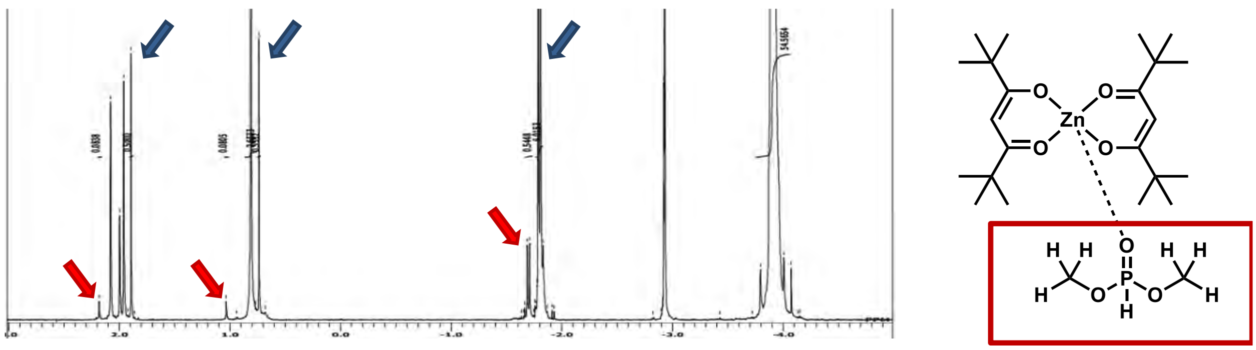


Figure S2-2. ^{1}H NMR spectrum of Dimethyl Phosphite + $Zn(TMHD)_2$ 1 equiv. in Toluene-d_8

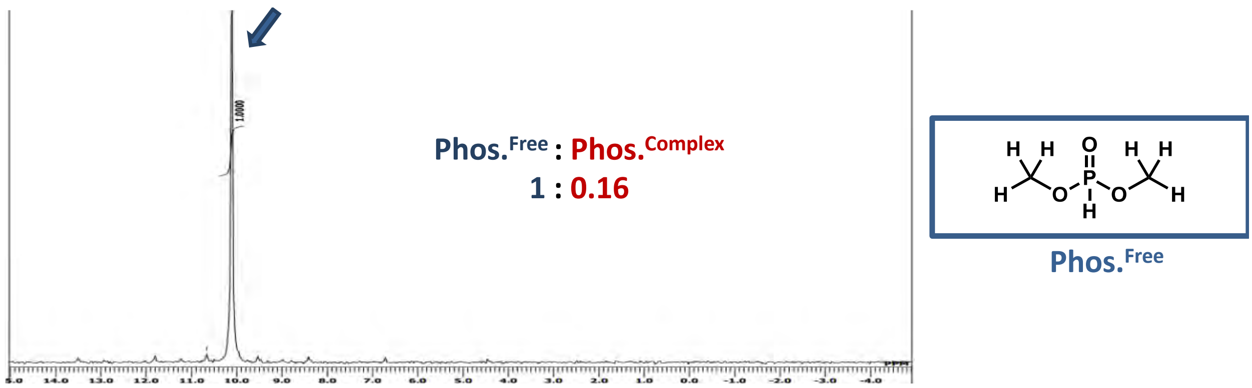


Figure S3-1. ^{31}P NMR spectrum of Dimethyl Phosphite in Toluene-d_8

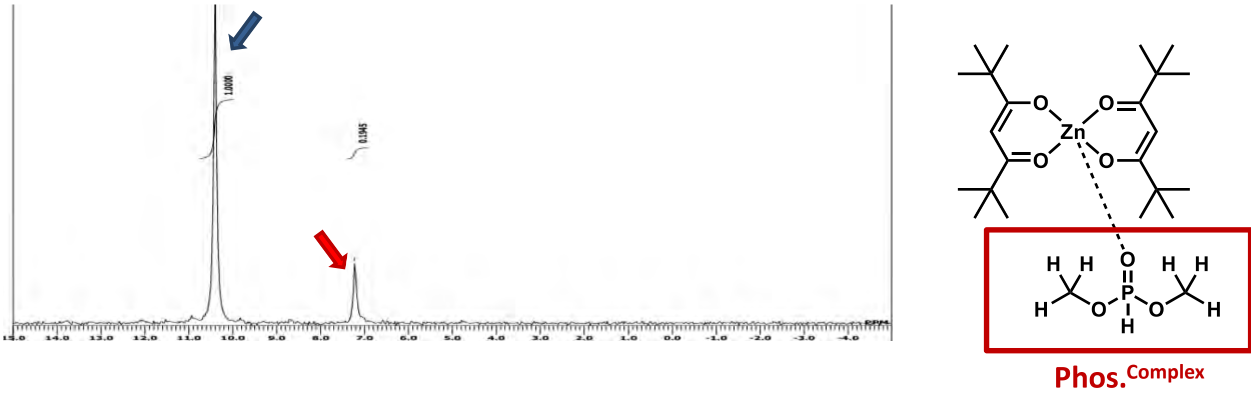


Figure S3-2. ^{31}P NMR spectrum of Dimethyl Phosphite + $Zn(TMHD)_2$ 1 equiv. in Toluene-d_8

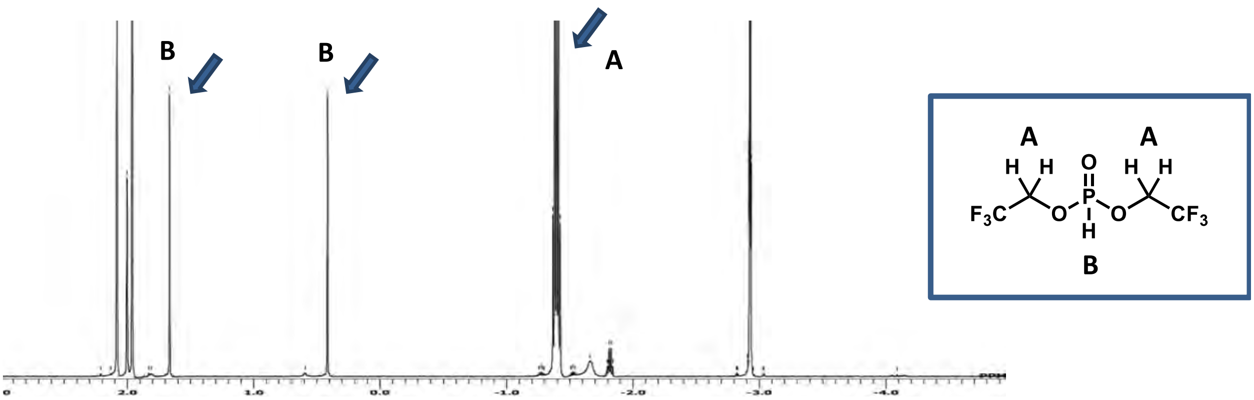


Figure S4-1. ^{1}H NMR spectrum of $(CF_3CH_2O)_2(H)P{=}O$ in Toluene-d_8 (Reference)

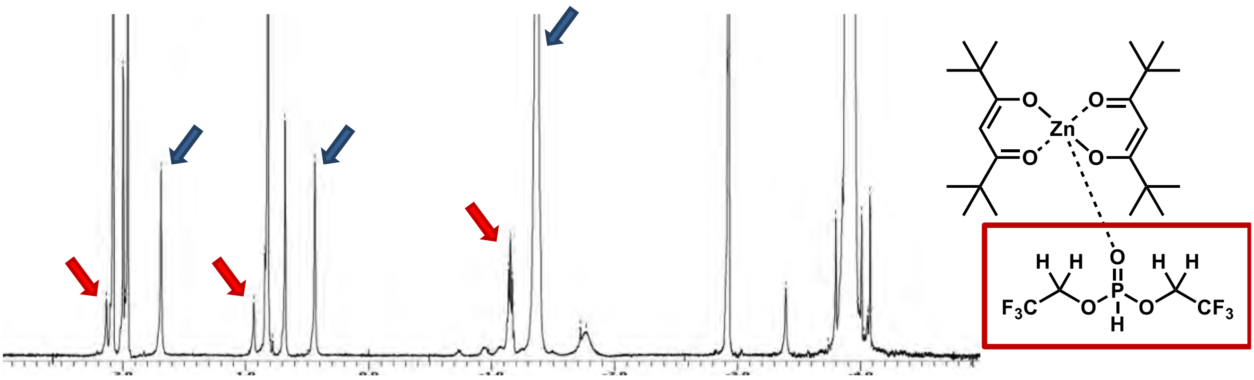


Figure S4-2. ^{1}H NMR spectrum of $(CF_3CH_2O)_2(H)P{=}O$ + $Zn(TMHD)_2$ 1 equiv. in Toluene-d_8

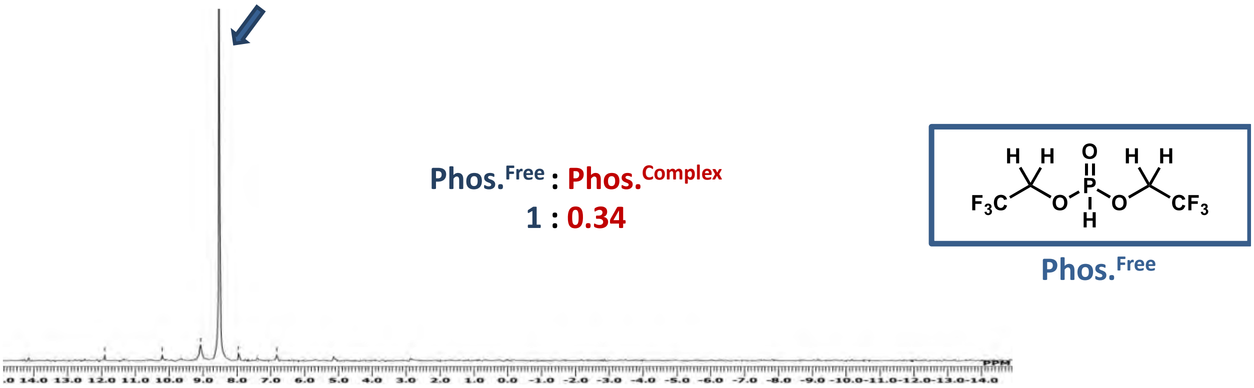


Figure S5-1. ^{31}P NMR spectrum of $(CF_3CH_2O)_2(H)P{=}O$ in Toluene-d_8 (Reference)

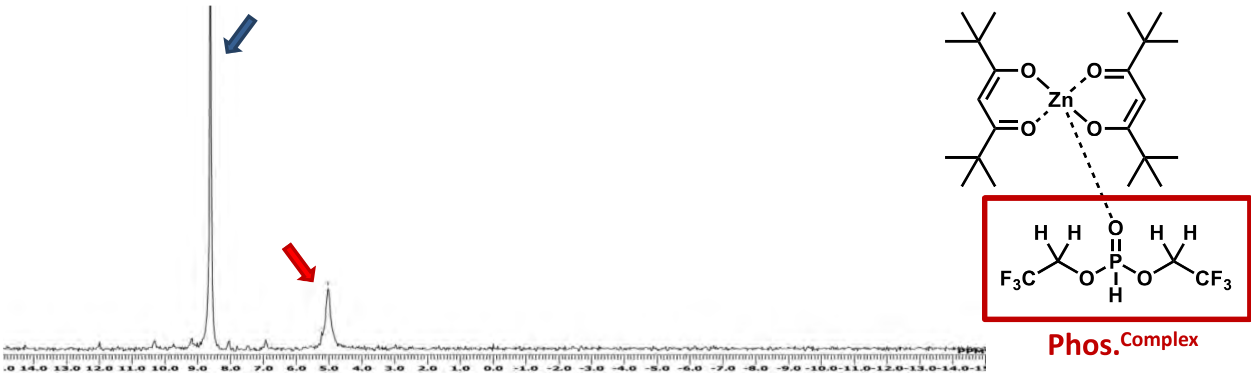
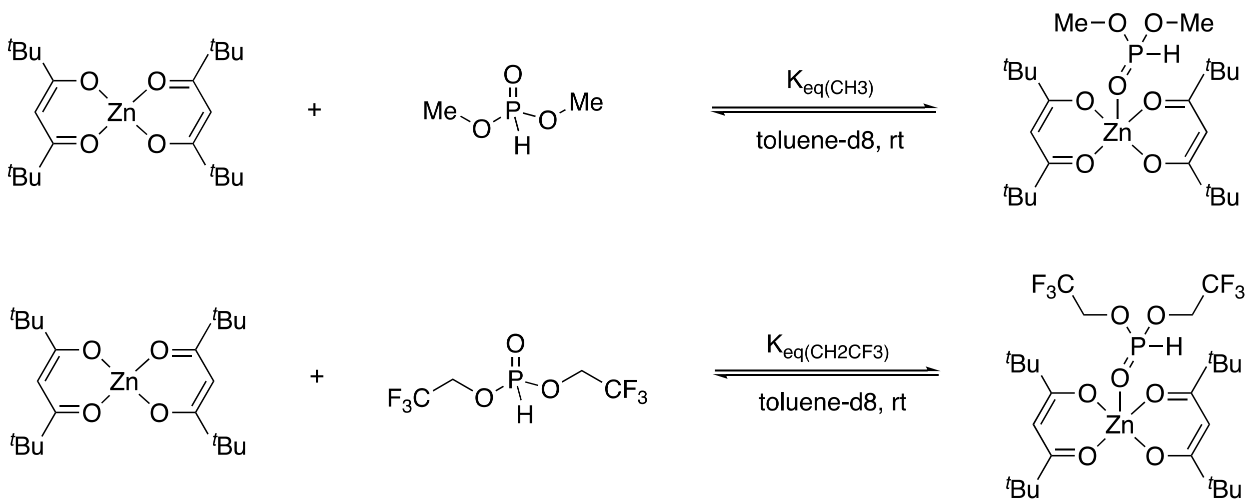


Figure S5-2. ^{31}P NMR spectrum of $(CF_3CH_2O)_2(H)P{=}O$ + $Zn(TMHD)_2$ 1 equiv. in Toluene-d_8



Based on the results of NMR experiments, we hypothesized that $Zn(TMHD)_2$ and phosphite formed complexes by the coordination of P=O to the Zn center.

Equilibrium constants $\boldsymbol{Keq(CH_3)}$ and $\boldsymbol{Keq(CH_2CF_3)}$ were calculated by the following equation. The concentration of each species was calculated based on ^{1}H NMR.

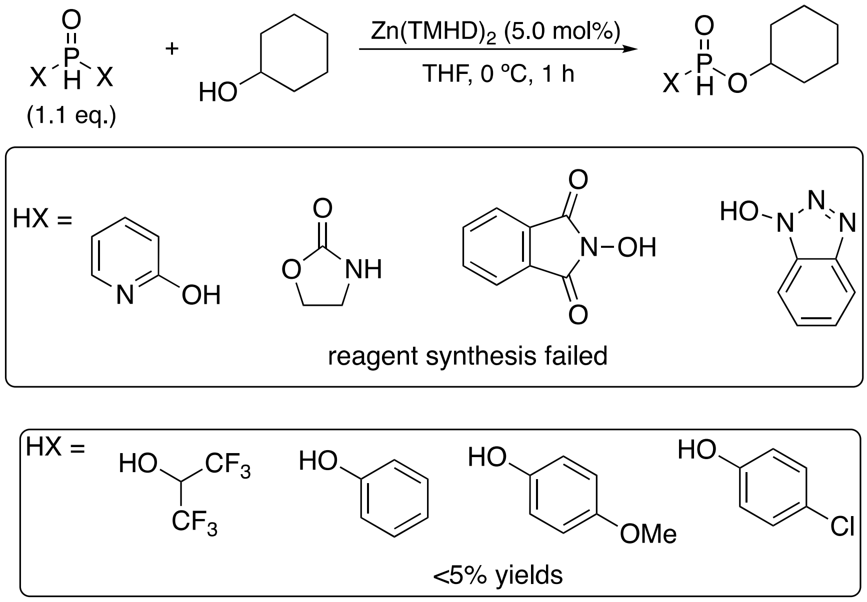
$$Keq(CH_3) = \frac{[Phos. Complex]}{[Free\ Zn(TMHD)_2][Free\ 2']} = 0.33\ M^{-1}$$

$$Keq(CH_2CF_3) = \frac{[Phos. Complex]}{[Free\ Zn(TMHD)_2][Free\ 2]} = 1.24\ M^{-1}$$

Table S6. Summary of the phosphite-catalyst interaction parameters

Phosphite	K_{eq} (M^{-1})	ΔShifts[Complex-Free Phosphite] (ppm)
Dimethyl phosphite (2’)	0.33	0.29
Bis(trifluoroethyl) phosphite (2)	1.24	0.45

These observations lead us to hypothesize that the greater reactivity observed for bis(trifluoroethyl) phosphite when compared to dimethyl phosphite is due not solely to the leaving group ability of the substituents, but also to the favourable interaction parameters with the catalyst they bring about. Interestingly, the phosphite that would be expected to be the weakest Lewis base, with two electron-withdrawing trifluoroethyl substituents, is showing the strongest interaction with the Lewis acid, suggesting some additional interaction between BTP and the metal complex. While no such interaction can be observed or proposed presently, this matter is still under ongoing investigation.



Scheme S2. Investigation of other leaving groups

6. Experimental Procedure

6-0. Synthesis of bis(2,2,2-trifluoroethyl) phosphite) 2 in a large scale[11]

To an oven-dried 3-neck flask equipped with a magnetic stirring bar and a dropping funnel was added PCl_3 (20 mL, 229 mmol) under an Ar atmosphere. DCM (45 mL) was added and the flask was cooled in a water-ice bath. A solution of ^{t}BuOH (21.5 mL, 229 mmol) in DCM (22.5 mL) was added dropwise. The solution was stirred for 1 h at 0 ^{o}C and a solution of trifluoroethanol (33.3 mL, 457 mmol) in DCM (22.5 mL) was added at once. The solution was stirred for 12 h at room temperature. The solution was then stirred under reflux for 3 h. After cooling to room temperature, the solvent was removed by distillation at ambient pressure. The target compound was purified by distillation (2 mmHg, 40 ^{o}C) to obtain as a colorless oil (39.0 g, 69%).

6-1. A typical procedure of optimization of consecutive phosphonylation using 3a' (Scheme 1)

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(OAc)_2$ (1.4 mg, 0.0075 mmol) and powdered MS 5A (200 mg). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. toluene (1.0 mL) was added to the tube, followed by the addition of cyclohexyl methyl phosphite **3a'** (106.9 mg, 0.60 mmol) and alcohol **1b** (32.4 mg, 0.30 mmol) by syringe. The reaction mixture was stirred for 18 h at room temperature. Then, the reaction mixture was diluted with ethyl acetate (5 mL). The solid material was removed by filtration and washed with ethyl acetate (5 mL*2). The combined organic phase was evaporated and connected to a vacuum line. The ^{1}H NMR was recorded with 1,3,5-trimethoxy benzene as an internal standard in DMSO-d_6. The yield of product **4a** was determined to be 85% by ^{1}H NMR analysis.

6-2. A typical procedure of optimization of reaction conditions between phosphite 2 and cyclohexanol 1a (Table 1, entry 10)

To an oven-dried test tube equipped with a magnetic stirring bar was added Zn(TMHD)$_2$ (3.2 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube which was cooled down to 0 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (73.8 mg, 0.3 mmol) and cyclohexanol **1a** (30.0 mg, 0.3 mmol) by syringe. The solution was stirred for 3 h at 0 °C. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5- trimethoxybenzene as the internal standard and the yield of **3a** was calculated.

6-3. A general procedure of substrate scope of mono-phosphonylation using Zn(TMHD)$_2$ (Scheme 2, Conditions A)

[For liquid alcohols]

To an oven-dried test tube equipped with a magnetic stirring bar was added Zn(TMHD)$_2$ (3.2 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube which was cooled down to 0 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite) **2** (73.8 mg, 0.3 mmol) and alcohol **1** (0.3 mmol) by syringe. The solution was stirred for 3 h at 0 °C. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5-trimethoxybenzene as internal standard and the yield was calculated.

[For solid alcohols]

To an oven-dried test tube equipped with a magnetic stirring bar was added Zn(TMHD)$_2$ (3.2 mg, 0.0075 mmol) and alcohol **1** (0.3 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube which was cooled down to 0 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (73.8 mg, 0.3 mmol) by syringe. The solution was stirred for 3 h at 0 °C. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5- trimethoxy as the internal standard and the yield was calculated.

6-4. A general procedure of substrate scope of mono-phosphonylation using $Zn(OPiv)_2$ (Scheme 2, Conditions B)

[For liquid alcohols]

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(OPiv)_2$ (2.0 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. Toluene (1.0 mL) was added to the tube which was cooled down to -20 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (81.2 mg, 0.33 mmol) and alcohol **1** (0.3 mmol) by syringe. The solution was stirred for 22 h at -20 °C, after which full consumption of the alcohol was confirmed by TLC. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5- trimethoxybenzene as the internal standard and the yield was calculated.

[For solid alcohols]

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(OPiv)_2$ (2.0 mg, 0.0075 mmol)) and alcohol **1** (0.3 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. Toluene (1.0 mL) was added to the tube which was cooled down to -20 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (81.2 mg, 0.33 mmol) by syringe. The solution was stirred for 22 h at -20 °C, after which full consumption of the alcohol was confirmed by TLC. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5- trimethoxybenzene as the internal standard and the yield was calculated.

6-5. A general procedure of substrate scope of mono-phosphonylation using $Zn(TMHD)_2$ (Scheme 2, Conditions C)

[For liquid alcohols]

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(TMHD)_2$ (3.2 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (11.7 mg, 0.45 mmol) and alcohol **1** (0.3 mmol) by syringe. The solution was stirred for 3 h at rt. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5-trimethoxybenzene as the internal standard and the yield was calculated.

[For solid alcohols]

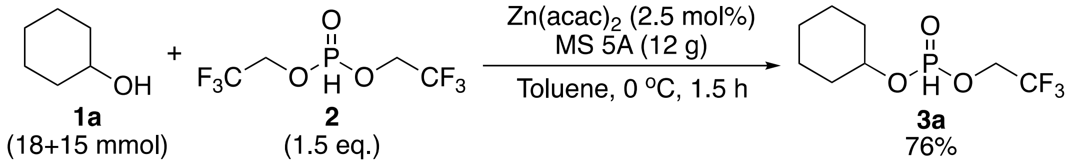
To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(TMHD)_2$ (3.2 mg, 0.0075 mmol) and alcohol **1** (0.3 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (110.7 mg, 0.45 mmol) by syringe. The solution was stirred for 3 h at rt. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5-trimethoxy as internal standard and the yield was calculated.

6-6. A general procedure of substrate scope of mono-phosphonylation using $Zn(OPiv)_2$ (Scheme 2, Conditions D)

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(OPiv)_2$ (4.0 mg, 0.015 mmol) and alcohol **1** (0.3 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. DCM (1.0 mL) was added to the tube which was cooled down to 0 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (81.2 mg, 0.33 mmol by syringe. The solution was stirred for

19 h at 0 °C, after which full consumption of the alcohol was confirmed by TLC. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,3,5- trimethoxybenzene as the internal standard and the yield was calculated.

6-7. A procedure of synthesis of 3a in a large scale



To an oven-dried 2-neck round bottom flask (200 mL) equipped with a magnetic stirring bar was added powdered MS 5A (12 g). The flask was connected to a vacuum line, heated by a heat gun, then an Ar balloon was equipped. A solution of $Zn(acac)_2$ (237.2 mg, 0.9 mmol) in toluene (60 mL) was added to the flask, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite **2** (6.64 g, 27 mmol) and cyclohexanol **1a** (1.80 g, 18 mmol) by syringe. The reaction mixture was stirred for 1.5 h at room temperature. The solid material was removed by filtration and washed with ethyl acetate (20 mL*3). The combined organic phase was evaporated and connected to a vacuum line. The ^{1}H NMR was recorded. The same reaction was performed in a 15 mmol scale for 3 h and combined crude was carefully purified by column chromatography using DCM/ethyl acetate = 9/1 as eluent. The product **3a** was isolated as a colorless oil. (6.18 g, 25.1 mmol, 76% yield)

6-8. A typical procedure of optimization of second substitution reaction conditions (Table 2, entry 5)

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(TMHD)_2$ (2.0 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. Toluene (1.0 mL) was added to the tube, followed by the addition of cyclohexyl (2,2,2-trifluoroethyl) phosphite **3a** (81.2 mg, 0.33 mmol) and benzyl alcohol **1l** (32.4 mg, 0.30 mmol) by syringe. The reaction mixture was stirred for 3 hours at room temperature after which full consumption of the alcohol was confirmed by TLC. Then, the reaction mixture was concentrated under reduced pressure. The ^{1}H NMR was recorded with 1,2,4,5- tetramethyl benzene as the internal standard and the yield of **4a** was calculated. The product could be isolated by column chromatography in 92% yield.

6-9. A typical procedure of substrate scope of the one-pot phosphonylation reaction (Scheme 3)

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(TMHD)_2$ (4.9 mg, 0.01125 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. Toluene (1.2 mL) was added to the tube which was cooled down to 0 °C, followed by the addition of bis(2,2,2-trifluoroethyl) phosphite) **2** (110.7 mg, 0.45 mmol) and secondary **1** (0.45 mmol) by syringe. The solution was stirred for 3 h at 0 °C. This solution was then transferred to a separate test tube containing primary alcohol **1** (0.30 mmol) and $Zn(TMHD)_2$ (3.2 mg, 0.0075 mmol) by syringe and the syringe was rinsed with toluene (2*0.15 mL). The solution was stirred for 3 h at 0 °C, after which full consumption of the primary alcohol **1** was confirmed by TLC. Then, the reaction mixture was put to a pad of silica gel and the product **4** was purified by column chromatography.

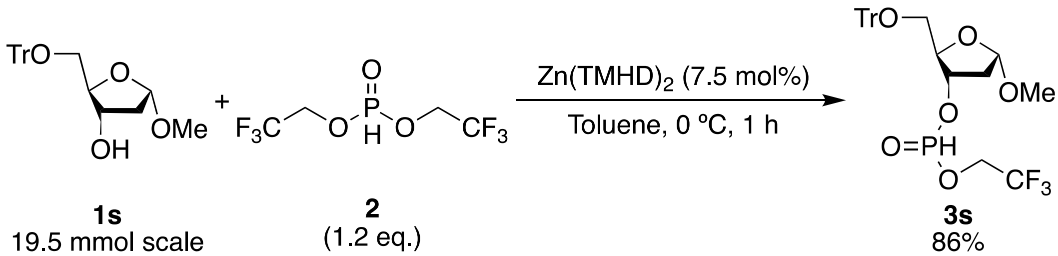
6-10. A procedure of the one-pot phosphonylation reaction and oxidation reaction with carbohydrates (Scheme 4a)

To a flame-dried test tube was added alcohol **1s** (117.1 mg, 0.3 mmol) in a grove box. The tube was put in a dry chamber for 10 minutes and to the tube was added $Zn(TMHD)_2$ (9.7 mg, 0.0225 mmol). The tube was equipped with a stir bar capped with a septum and taken out from the grove box. An argon balloon was equipped. THF (1.0 mL) was added to the tube and it was cooled down to 0 °C, followed by the addition of bis(trifluoroethyl) phosphite **2** (81.2 mg, 0.33 mmol) by syringe. The solution was stirred at 0 °C for 2.5 h.

Zn(TMHD)$_2$ (12.9 mg, 0.03 mmol) in THF (0.3 mL) was transferred by cannulation with THF (2*0.1 mL), followed by the addition of alcohol **1t** (110.3 mg, 0.54 mmol). The solution was stirred at 0 °C for 15 h. Then, the reaction mixture was diluted with hexane (5 mL) and put on a pad of silica gel. The fractions containing Zn(TMHD)$_2$ were removed with the elution of ethyl acetate/hexane (1:4) (15 mL) and the remaining compounds were collected with the elution of ethyl acetate (70 mL). The latter was concentrated under reduced pressure and the reaction crude was analyzed by ^{1}H NMR with durene as an internal standard.

To a 20 mL, 2-neck round bottom flask was transferred the crude with DCM and the solvent was removed under reduced pressure. The flask was equipped with a stir bar and capped with a septum. An argon balloon was equipped, followed by the addition of anhydrous alcohol (3 mL) and DCM (1 mL). To the flask anhydrous pyridine (71.3 mg, 0.9 mmol) was added by syringe, followed by the immediate addition of I_2 (91.3 mg, 0.36 mmol). The solution was stirred at room temperature for 40 min. Then, the reaction mixture was quenched by saturated $Na_2S_2O_3$ aq. (2 mL) and extracted by DCM (10 mL*3). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The reaction crude was purified by column chromatography and PTLC.

6-11. A procedure of the preparation of phosphite 3s in a large scale

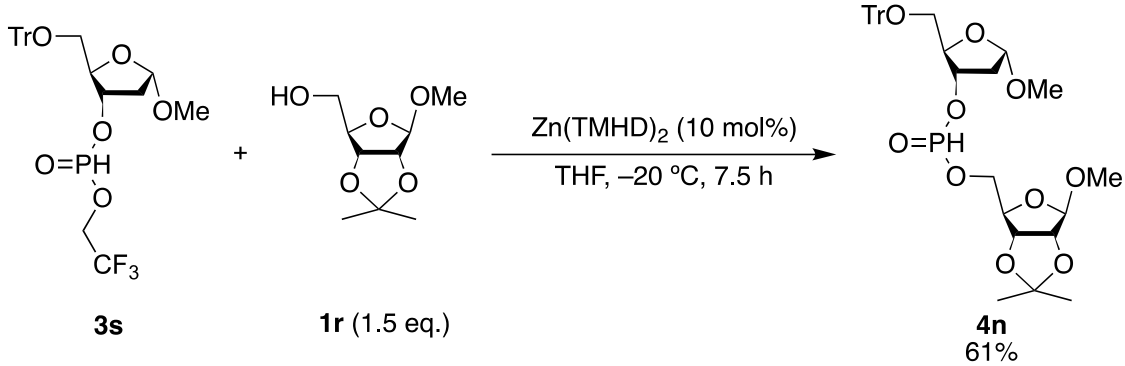


1s 19.5 mmol scale; **2** (1.2 eq.); **3s** 86%

To an oven-dried 300 mL 2-neck round bottom flask was added alcohol **1s** (7.61 g, 19.5 mmol). This flask was put into a grove box and was added Zn(TMHD)$_2$ (631.3 mg, 1.46 mmol). The flask was equipped with a stir bar, capped with a septum and a three-way cock, and taken out from the grove box. An argon balloon was equipped. Toluene

(65 mL) was added to the flask and it was cooled down to 0 °C, followed by the addition of bis(trifluoroethyl) phosphite **2** (5.75 g, 23.4 mmol) by syringe. The solution was stirred at 0 °C for 1 h. The reaction mixture was concentrated under reduced pressure, and the crude was purified by silica gel column chromatography (ethyl acetate/hexane (5:2 to 2:1)) to afford **3s** (4.61 g, 86%) as a white gum.

6-12. A procedure of the synthesis of phosphite 4n as an authentic sample



To a flame-dried test tube was added phosphite **3s** (171.1 mg, 0.3 mmol) in a grove box. The tube was put in a dry chamber for 10 minutes and to the tube was added Zn(TMHD)$_2$ (12.9 mg, 0.03 mmol). The tube was equipped with a stir bar and capped with a septum and taken out from the grove box. An argon balloon was equipped. THF (1.0 mL) was added to the tube and it was cooled down to –20 ºC, followed by the addition of alcohol **1r** (91.9 mg, 0.45 mmol). The solution was stirred at –20 °C for 7.5 h. Then, the reaction mixture was diluted with hexane (5 mL) and put on a pad of silica gel. The fractions containing Zn(TMHD)$_2$ were removed with the elution of ethyl acetate/hexane (1:4) (15 mL) and the remaining compounds were collected with the elution of ethyl acetate (70 mL). The latter was concentrated under reduced pressure and the reaction crude was analyzed by ^{1}H NMR with durene as an internal standard. Then, the crude was purified by silica gel column chromatography (ethyl acetate/hexane (3:1 to 1:1)) to afford **4n** (116.6 mg, 61%) as a white gum.

6-13. A procedure of the one-pot phosphonylation reaction (Scheme 4b)

To a flame-dried test tube was added Zn(TMHD)$_2$ (3.2 mg, 0.0075 mmol) and alcohol **1ad** (75.7 mg, 0.3 mmol) in a grove box. The tube was equipped with a stir bar and capped with a septum and taken out from the grove box. An argon balloon was equipped. THF (0.6 mL) was added to the tube and it was cooled down to 0 °C, followed by the addition of bis(trifluoroethyl) phosphite **2** (81.2 mg, 0.33 mmol) by syringe. The solution was stirred at 0 °C for 3 h. $Zn(TMHD)_2$ (3.2 mg, 0.0075 mmol) in THF (0.2 mL) was transferred by cannulation with THF (2*0.1 mL), followed by the addition of alcohol **1ae** (49.2 mg, 0.36 mmol). The solution was stirred at rt for 6 h. Then, the reaction mixture was diluted with hexane (5 mL) and put on a pad of silica gel. The fractions containing $Zn(TMHD)_2$ were removed with the elution of ethyl acetate/hexane (1:4) (15 mL) and the remaining compounds were collected with the elution of ethyl acetate (70 mL). The latter was concentrated under reduced pressure and the reaction crude was analyzed by ^{1}H NMR with durene as an internal standard. The crude material was purified by pTLC (Hex: EA = 1:1) to afford target compound **4o** as white foam (114.7 mg, 87% yield).

6-14. A procedure of the oxidation with benzyl alcohol (Scheme 4b)

To a 10 mL, 2-neck round bottom flask was transferred **4o** (114.0 mg, 0.25 mmol) with THF and the solvent was removed under reduced pressure. The flask was equipped with a stir bar and capped with a septum. An argon balloon was equipped, followed by the addition of a solution of I_2 (78.7 mg, 0.31 mmol), pyridine (40.8 mg, 0.516 mmol), and benzyl alcohol (164.7 mg, 1.548 mmol) in THF (0.7 mL). The solution was stirred at room temperature for 6 h. Then, the reaction mixture was quenched by saturated $Na_2S_2O_3$ aq. (2 mL) and extracted by DCM (10 mL*3). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The reaction crude was purified by column chromatography and PTLC (Hex: EA = 1:1) to afford the target compound **5c** as a white foam (88.1 mg, 64% yield).

6-15. A procedure of the hydrogenolysis of benzylphosphate (Scheme 4b)

To a 10 mL, the 2-neck round bottom flask was transferred **5d** (88.0 mg, 0.16 mmol) with Ethyl Acetate (0.5 mL). The flask was equipped with a stir bar and capped with a septum. An argon balloon was equipped, followed by the addition of Pd/C (10 mg). The atmosphere was purged with H_2 and the solution was stirred at room temperature for 18 h. Then, the reaction mixture was filtered through Celite and washed with MeOH. The combined organic layer was concentrated under reduced pressure to afford the target compound **5e** as a white foam (65.9 mg, 91% yield).

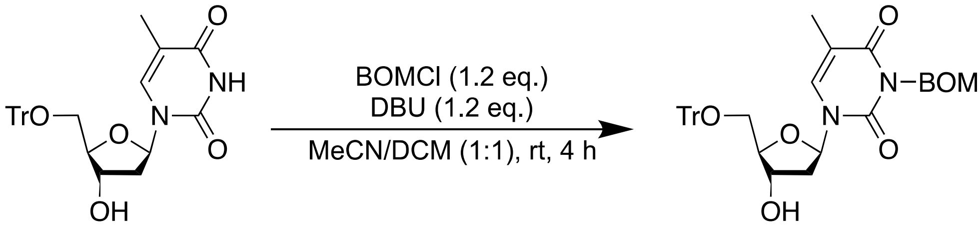
6-16. A procedure of the hydrolysis of methyl ester (Scheme 4b)

To a 10 mL, 2-neck round bottom flask was transferred **5c** (88.0 mg, 0.16 mmol) with THF (0.5 mL) and the solvent was removed under reduced pressure. The flask was equipped with a stir bar and capped with a septum. An argon balloon was equipped, followed by the addition of a solution of LiOH (11.7 mg, 0.32 mmol) in water (0.7 mL). The solution was stirred at room temperature for 18 h. Then, the reaction mixture was quenched by 0.5 N HCl aq. and extracted by DCM (10 mL*3). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford the target compound **5c** as a white foam (70.4 mg, 82% yield).

6-17. A procedure of the one-pot phosphonylation reaction and phosphorthioate synthesis (Scheme 4c)

To an oven-dried test tube equipped with a magnetic stirring bar was added $Zn(TMHD)_2$ (2.0 mg, 0.0075 mmol). The tube was capped with a septum, and connected to a vacuum line, then an Ar balloon was equipped. Toluene (1.0 mL) was added to the tube, followed by the addition of cyclohexyl (2,2,2-trifluoroethyl) phosphite **3a** (81.2 mg, 0.33 mmol) and benzyl alcohol **1l** (32.4 mg, 0.30 mmol) by syringe. The reaction mixture was stirred for 3 hours at room temperature after which full consumption of the alcohol was confirmed by TLC. A solution of S_8 (10.6 mg, 0.36 mmol) in EtOAc (2.0 mL) was added to the reaction mixture. After the addition of NEt_3 (91.1 mg, 0.9 mmol), the reaction mixture was stirred for 12 h. The reaction mixture was concentrated under reduced pressure. The product could be isolated by column chromatography in 81% yield (93.4 mg).

6-18. A procedure of the synthesis of thymidine derivative 1ad



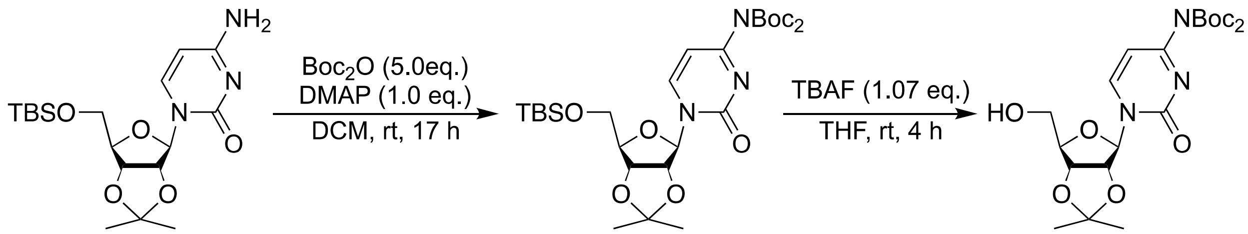
1ad
74%

To a 200 mL two-neck round bottom flask equipped with a stir bar and an argon balloon, 5'-O-Tr-thymidine[12] (4.21 g, 7.91 mmol), acetonitrile (25 mL), and DCM (25 mL) were added. DBU (1.45 g, 1.42 mL 9.49 mmol) was added to the suspension to form a clear solution. The solution was cooled by a water bath, and benzyl chloromethyl ether (BOMCl, 1.49 g, 1.30 mL, 9.49 mmol) was added over 5 minutes and stirred for 4 h. The reaction mixture was diluted with ethyl acetate (120 ml) and washed with water (2*40 ml) and saturated $NaHCO_3$ aq. (40 ml). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude was purified by column chromatography (diethyl ether/hexane (4:1)) to afford **1ad** (3.65 g, 74%) as a white solid.

Mp: 139-141 ºC; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53 (1H, s), 7.42 (6H, d, J = 7.6 Hz), 7.39 (2H, d, J = 7.6 Hz), 7.33 (8H, t, J = 7.6 Hz), 7.29 (6H, t, J = 6.9 Hz), 6.42 (1H, t, J = 6.9 Hz), 5.51 (2H, s), 4.72 (2H, s), 4.57 (1H, td, J = 6.5, 3.2 Hz), 4.05 (1H, q, J = 3.2 Hz), 3.50 (1H, dd, J = 10.3, 3.4 Hz), 3.40 (1H, dd, J = 10.7, 3.1 Hz), 2.42 (1H, ddd, J = 13.7, 6.2, 3.4 Hz), 2.30 (1H, quintet, J = 6.9 Hz), 1.90 (1H, d, J = 4.1 Hz), 1.52 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5, 150.9, 143.2, 137.9, 134.4, 128.6, 128.2, 128.0, 127.61, 127.58, 127.4, 110.4, 87.4, 85.9, 85.3, 72.1(*2), 70.5, 63.6, 41.0, 12.5; HRMS (DART): m/z calcd. for $C_{37}H_{37}N_2O_6$ ($[M+H]^+$): 605.26516; found: 605.26761; IR (neat):

3443, 3062, 3032, 2926, 1707, 1645, 1490, 1467, 1450, 1362, 1278, 1154, 1091, 1028, 901, 773, 747, 700, 633, 568, 426 cm^{-1}.

6-19. A procedure of the synthesis of cytidine derivative 1aa

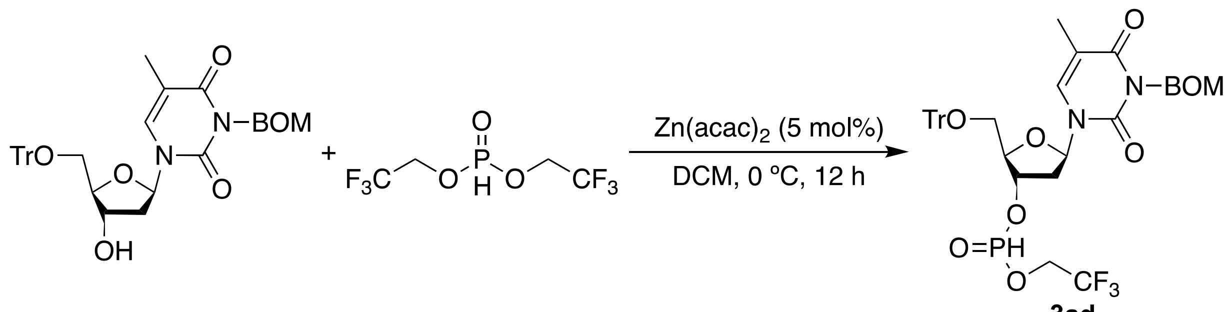


To a 300 mL two-neck round bottom flask equipped with a stir bar, 5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-*O*-isopropylidene cytidine[13] (2.05 g, 5.15 mmol) and DMAP (635.3 mg, 5.2 mmol) was added and the flask was connected to a vacuum line. To the flask was equipped an argon balloon and was added DCM (100 mL). Boc_2O (5.67 g, 26.0 mmol) was added and the mixture was stirred at room temperature for 17 h. It was quenched with water (10 mL) and extracted with DCM (50 mL*2). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude was purified by column chromatography (ethyl acetate/hexane (1:4)) and a white solid (2.35 g) was obtained.

To a 300 mL two-neck round bottom flask equipped with a stir bar, obtained white solid (2.35 g) was added and the flask was connected to a vacuum line. To the flask was equipped an argon balloon and was added THF (100 mL). TBAF (1.0 M THF solution, 4.23 mL, 4.23 mmol) was added and stirred at room temperature for 4 h. The reaction mixture was diluted with ethyl acetate (100 ml) and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude was purified by column chromatography (ethyl acetate/hexane (1:1)) to afford cytidine derivative **1aa** (1.70 g, 67% in two steps) as a white solid.

Mp: 94-100 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (1H, d, *J* = 7.4 Hz), 7.11 (1H, d, *J* = 7.4 Hz), 5.43 (1H, d, *J* = 2.6 Hz), 5.21 (1H, dd, *J* = 6.4, 2.6 Hz), 5.07 (1H, q, *J* = 3.3 Hz), 4.32 (1H, dd, *J* = 5.9, 3.3 Hz), 3.90 (1H, dd, *J* = 12.2, 2.3 Hz), 3.79 (1H, dd, *J* = 12.2, 3.4 Hz), 3.60-3.30 (1H, br), 1.55 (3H, s) 1.54 (18H, s), 1.32 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 154.3, 149.3, 147.1, 114.0, 99.5, 96.4, 88.3, 85.3, 83.5, 80.4, 62.9, 27.7, 27.2, 25.2; HRMS (DART): m/z calcd. for $C_{22}H_{34}N_3O_9$ ($[M+H]^+$): 484.23621; found: 484.23136; IR (neat): 2982, 2938, 1778, 1743, 1652, 1624, 1527, 1457, 1395, 1371, 1320, 1260, 1214, 1157, 1117, 1083, 958, 850, 788, 744, 591, 513, 403 cm^{-1}.

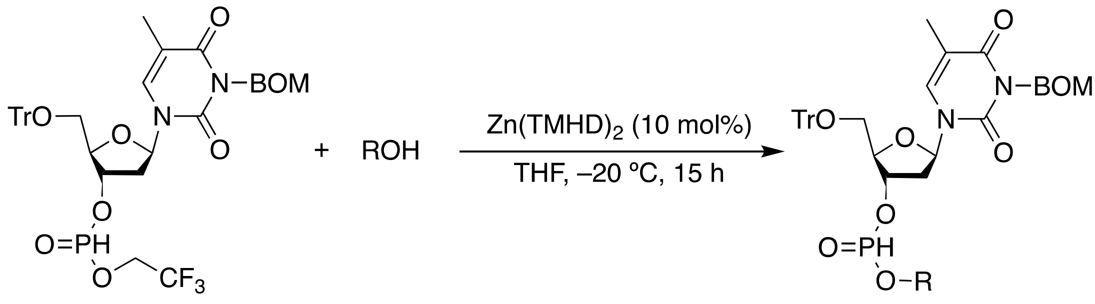
6-20. A procedure of the preparation of phosphite 3ad in a large scale



1ad **2** (1.2 eq.) **3ad** 74%

To a flame-dried 20 mL round bottom flask was added alcohol **1af** (614.3 mg, 1.0 mmol) in a grove box. The tube was put in a dry chamber for 10 minutes and to the tube was added $Zn(acac)_2$ (13.2 mg, 0.05 mmol). The tube was equipped with a stir bar and capped with a septum and taken out from the grove box. An argon balloon was equipped. DCM (1.0 mL) was added to the tube and it was cooled down to 0 °C, followed by the addition of bis(trifluoroethyl) phosphite **2** (295.8 mg, 0.36 mmol) by syringe. The solution was stirred at 0 °C for 12 h. The solution was diluted with DCM (20 mL). Then, the reaction mixture was concentrated under reduced pressure. The reaction crude was analyzed by ^{1}H NMR with durene as an internal standard. Then, the crude was purified by silica gel column chromatography (ethyl acetate/hexane (4:1 to 1:1)) to afford **3af** (576.0 mg, 74% yield) as a white solid.

6-21. A procedure of the synthesis of phosphites 6 as authentic samples



To a flame-dried test tube was added phosphite **3af** (248.8 mg, 0.3 mmol) and nucleoside **1ae** (217.6 mg, 0.45 mmol) or **1aa** (202.7 mg, 0.45 mmol) in the grove box. The tube was put into a dry chamber for 10 minutes and to the tube was added $Zn(TMHD)_2$ (13.0 mg, 0.03 mmol). The tube was equipped with a stir bar and capped with a septum and taken out from the grove box. An argon balloon was equipped. The tube was stirred for 1 min at room temperature and was cooled down to –20 °C. THF (1.0 mL) was added to the tube and was stirred at –20 °C for 15 h. Then, the reaction mixture was diluted with hexane (5 mL) and put on a pad of silica gel. The fractions containing $Zn(TMHD)_2$ were removed with the elution of ethyl acetate/hexane (1:4) (15 mL) and the remaining compounds were collected with the elution of ethyl acetate (80 mL). The latter was concentrated under reduced pressure and the reaction crude was analyzed by ^{1}H NMR with durene as an internal standard. Then, the crude was purified by silica gel column chromatography to afford **6**.

6-22. A procedure of the one-pot phosphonylation reaction and oxidation reaction with nucleosides (Scheme 4d)

To a flame-dried test tube A was added nucleoside **1af** (183.9 mg, 0.3 mmol) in a grove box. The tube A was put in a dry chamber for 10 minutes and to the tube was added $Zn(acac)_2$ (4.0 mg, 0.015 mmol). The tube A was equipped with a stir bar and capped with a septum and taken out from the grove box. An argon balloon was equipped. THF (1.0 mL) was added to the tube A and it was cooled down to 0 °C, followed by the addition of bis(trifluoroethyl) phosphite **2** (88.6 mg, 0.36 mmol) by syringe. The solution was stirred at 0 °C for 15 h. To another flame-dried test tube B was added nucleoside **1ae** or

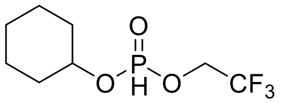
1aa (0.6 mmol) in the grove box. The tube B was put in a dry chamber for 10 minutes, followed by the addition of $Zn(TMHD)_2$ (12.9 mg, 0.03 mmol). The tube B was equipped with a stir bar, capped with a septum, and taken out from the grove box, then an argon balloon was equipped. The solution in the tube A was transferred to the tube B by cannulation with THF (4*0.125 mL). The solution was stirred at rt for 24 h. Then, the reaction mixture was diluted with DCM (1 mL) and hexane (1 mL) and put on a pad of silica gel. The fractions containing $Zn(TMHD)_2$ were removed with the elution of ethyl acetate/hexane (1:6) (15 mL) and the remaining compounds were collected with the elution of ethyl acetate (80 mL). The latter was concentrated under reduced pressure and the reaction crude was analyzed by ^{1}H NMR with durene as an internal standard.

To a 20 mL, 2-neck round bottom flask was transferred the crude with DCM and the solvent was removed under reduced pressure. The flask was equipped with a stir bar and capped with a septum. An argon balloon was equipped, followed by the addition of DCM (1 mL) and anhydrous ethanol (3 mL). To the flask anhydrous pyridine (71.3 mg, 0.9 mmol) was added by syringe, followed by the immediate addition of I_2 (91.3 mg, 0.36 mmol). The solution was stirred at room temperature for 40 min. Then, the reaction mixture was quenched by saturated $Na_2S_2O_3$ aq. (2 mL) and extracted by DCM (10 mL*3). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The reaction crude was analyzed by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. Then, the crude was purified by silica gel column chromatography and PTLC.

7. Product data

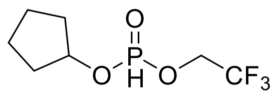
Due to the difficulty of isolation, the NMR spectra of **3b-3r, 3t-3z** and **3aa-3ac** were recorded in the crude product state, and 1,3,5-trimethoxybenzene (^{1}H NMR: δ 6.11 (3H, s), 3.79 (9H, s); ^{13}C NMR: δ 161.7, 93.2, 55.5 in DMSO-*d*$_6$) or durene (^{1}H NMR: δ 6.89 (2H, s), 2.18 (12H, s); ^{13}C NMR: δ 133.6, 131.1, 19.0 in $CDCl_3$) was added as an internal standard.

Cyclohexyl (2,2,2-trifluoroethyl) phosphonate (**3a**)



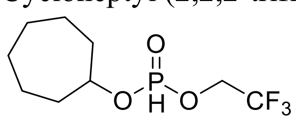
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.96 (1H, d, $J_{P\text{-}H}$ = 720.3 Hz), 4.60-4.50 (1H, m), 4.47-4.35 (2H, m), 2.01-1.88 (2H, m), 1.82-1.70 (2H, m), 1.68-1.48 (3H, m), 1.42-1.21 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 122.6 (qd, *J* = 277.4, 7.2 Hz), 77.0 (d, *J* = 5.8 Hz), 61.6 (qd, *J* = 38.3, 5.8 Hz), 33.5 (d, *J* = 4.3 Hz), 33.4 (d, *J* = 4.3 Hz), 24.84, 24.83, 23.3; ^{19}F NMR (565 MHz, $CDCl_3$): δ -75.25 (s); ^{31}P NMR (240 MHz, $CDCl_3$): δ 6.77; HRMS (APCI-) calcd for $C_8H_{13}F_3O_3P$ ($[M\text{-}H]^-$): 245.0554; found: 245.0647; IR (neat): 2940, 2863, 2445, 1452, 1256, 1171, 1110, 981, 657 cm^{-1}.

Cyclopentyl (2,2,2-trifluoroethyl) phosphonate (**3b**)



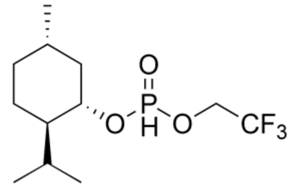
^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ 6.98 (1H, d, $J_{P\text{-}H}$ = 721.7 Hz), 4.96-4.93 (1H, m), 4.68-4.61 (2H, m), 1.82-1.74 (4H, m), 1.71-1.63 (2H, m), 1.61-1.52 (2H, m); ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 123.3 (qd, *J* = 278.0, 8.4 Hz), 79.5 (d, *J* = 6.0 Hz), 60.9 (qd, *J* = 35.6, 3.6 Hz), 33.5 (d, *J* = 4.8 Hz), 33.4 (d, *J* = 6.0 Hz), 22.5; ^{19}F NMR (565 MHz, DMSO-*d*$_6$): δ -74.04; ^{31}P NMR (243 MHz, DMSO-d$_6$): δ 8.61; HRMS (APCI-) calcd for $C_7H_{11}F_3O_3P$ ($[M\text{-}H]^-$): 231.0398; found: 231.0403; IR (neat): 3046, 2716, 2158, 1344, 1205, 1128, 1087, 1011, 885, 700 cm^{-1}.

Cycloheptyl (2,2,2-trifluoroethyl) phosphonate (**3c**)



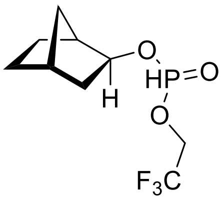
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 6.91 (1H, d, $J_{P\text{-}H}$ = 720.4 Hz), 4.65-4.58 (1H, m), 4.52-4.45 (2H, m), 1.93-1.90 (2H, m), 1.78-1.70 (2H, m), 1.63-1.58 (6H, m), 1.39-1.36 (2H, m); ^{13}C NMR (151 MHz, DMSO-*d*$_6$): δ 123.4 (qd, *J* = 277.4, 8.4 Hz), 78.3 (d, *J* = 7.2 Hz), 61.0 (qd, *J* = 36.1, 4.3 Hz), 35.2 (d, *J* = 4.3 Hz), 35.1 (d, *J* = 4.3 Hz), 27.51, 27.49, 21.6; ^{19}F NMR (565 MHz, DMSO-*d*$_6$): δ -74.04; ^{31}P NMR (243 MHz, DMSO-d$_6$): δ 7.47; HRMS (APCI-) calcd for $C_9H_{15}F_3O_3P$ ($[M\text{-}H]^-$): 259.0711; found: 259.0733; IR (neat): 2932, 2863, 2430, 1462, 1284, 1260, 1171, 1111, 970, 868, 838, 753, 560 cm^{-1}.

(1*S*,2*R*,5*S*)-2-Isopropyl-5-methylcyclohexyl (2,2,2-trifluoroethyl) phosphonate (**3d**)



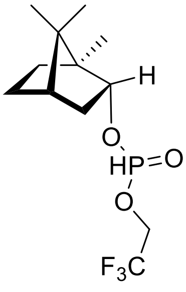
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.03 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 722.6 Hz), 7.01 (1H for the other diastereomer, d, J = 724.6 Hz), 4.67-4.61 (2H, m), 4.26-4.21 (1H, m), 2.11-1.97 (2H, m), 1.61 (2H, d, J = 11.7 Hz), 1.48-1.33 (1H, m), 1.32 (1H, t, J = 11.3 Hz), 1.16 (2H, q, J = 13.5 Hz), 0.98 (1H, q, J = 12.0 Hz), 0.88 (6H, d, J = 6.9 Hz), 0.75 (3H, q, J = 3.4 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.3 (qd, J = 278.2, 9.4 Hz), 77.84, 77.79, 77.6, 77.5, 61.5, 61.3, 61.22, 61.20, 61.10, 61.08, 60.99, 60.96, 60.86, 60.84, 60.74, 60.72, 60.62, 60.58, 47.7, 47.6, 42.5, 42.3, 33.33, 33.31, 30.88, 30.86, 26.96, 25.30, 25.2, 22.4, 21.7, 20.6, 20.5, 15.5, 15.4; ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.04; ^{31}P NMR (243 MHz, DMSO-d_6): δ 8.53, 8.34; HRMS (APCI-) calcd for $C_{12}H_{21}F_3O_3P$ ($[M\text{-}H]^-$): 301.1180; found:301.1036; IR (neat): 2925, 1649, 1280, 1207, 1144, 1051, 1044, 1207, 933, 823, 760, 613 cm^{-1}.

(1*S*,2*S*,4*R*)-Bicyclo[2.2.1]heptan-2-yl (2,2,2-trifluoroethyl) phosphonate (**3e**)



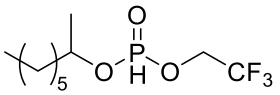
^{1}H NMR (600 MHz, DMSO-d_6): δ 6.98 (1H, d, $J_{P\text{–}H}$ = 722.5 Hz), 4.70-4.58 (2H, m), 4.42-4.40 (1H, m), 2.35-2.33 (1H, m), 2.25 (1H, s), 1.71-1.68 (1H, m), 1.50-1.44 (3H, m), 1.41-1.30 (1H, m), 1.18-1.08 (2H, m), 1.05-0.95 (2H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.3 (qd, J = 277.8, 9.3 Hz), 79.29, 79.26, 61.3, 61.1, 61.04, 61.02, 60.84, 60.81, 60.78, 60.6, 60.5, 42.5, 42.4, 42.33, 42.31, 40.04, 40.01, 39.98, 34.82, 34.81, 34.40, 34.38, 27.4, 25.6, 23.2; ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.98; ^{31}P NMR (243 MHz, DMSO-d_6): δ 8.23; HRMS (APCI-) calcd for $C_9H_{13}F_3O_3P$ ($[M\text{-}H]^-$): 257.0554; found: 257.0502; IR (neat): 2909, 1665, 1402, 1345, 1280, 1207, 1142, 1053, 1024, 1005, 931, 821, 758, 613 cm^{-1}.

2,2,2-Trifluoroethyl ((1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) phosphonate (**3f**)



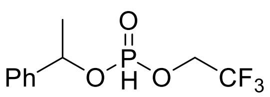
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.018 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 726.8 Hz), 7.031 (1H for the other diastereomer, d, J = 724.6 Hz), 4.70-4.58 (3H, m), 2.27-2.26 (1H, m), 1.83-1.79 (1H, m), 1.71-1.66 (2H, m), 1.27-1.12 (3H, m), 0.84-0.80 (9H, m); ^{13}C NMR (151 MHZ, DMSO-d_6): δ 123.3 (qd, J = 277.4, 8.7 Hz), 82.2, 82.1, 82.03, 81.99, 61.0 (q, J = 36.1 Hz), 49.2, 47.3, 44.57, 44.2, 36.4, 27.5, 19.6, 18.4, 12.89, 12.76; ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.01; ^{31}P NMR (243 MHz, DMSO-d_6): δ 9.85, 9.69; HRMS (APCI-) calcd for $C_{12}H_{19}F_3O_3P$ ($[M\text{-}H]^-$): 299.1024; found: 299.0938; IR (neat): 2532, 2333, 1654, 1397, 1341, 1278, 1207, 1134, 1050, 1025, 824, 761cm^{-1}.

Octan-2-yl (2,2,2-trifluoroethyl) phosphonate (**3g**)



^{1}H NMR (600 MHz, DMSO-d_6) δ: 7.00 (1H, d, J = 721.70 Hz), 4.68-4.62 (2H, m), 4.59-4.55 (1H, m), 1.58-1.53 (2H, m), 1.30-1.22 (11H, m), 0.87-0.85(3H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.3 (qd, J = 278.2, 9.4 Hz), 74.8 (for one diastereomer, d, J = 7.2 Hz), 74.7 (for the other diastereomer, d, J = 7.2 Hz), 61.00 (for one diastereomer, qd, J = 36.1, 4.3 Hz), 60.95 (for the other diastereomer, qd, J = 36.1, 2.9 Hz), 36.8 (for one diastereomer, d, J = 4.3 Hz), 36.7 (for the other diastereomer, d, J = 5.8 Hz), 31.1 (for both diastereomers), 28.4 (for both diastereomers), 24.5 (for one diastereomer), 24.4 (for the other diastereomer), 21.6 (for one diastereomer, d, J = 2.9 Hz), 21.5 (for the other diastereomer, d, J = 2.9 Hz), 14.0 (for both diastereomers); ^{19}F NMR (565 MHz, DMSO-d_6) δ: -74.10; ^{31}P NMR (243 MHz, DMSO-d_6) δ: 8.53, 8.47; HRMS (APCI-) calcd for $C_{10}H_{19}F_3O_3P$ ($[M-H]^-$): 275.1024; found: 275.0966; IR (neat): 2912, 2823, 2255, 1730, 1278, 1207, 1134, 1024, 1007, 823, 760, 624 cm^{-1}.

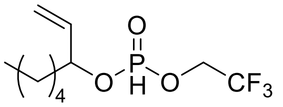
1-Phenylethyl (2,2,2-trifluoroethyl) phosphonate (**3h**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 7.42-7.32 (5H, m), 7.04 (1H for one diastereomer, d, J_{P-H}= 727.9 Hz), 7.03 (1H for one diastereomer, d, J_{P-H}= 727.2 Hz), 5.76-5.67 (1H, m), 4.73-4.59 (1H, m), 4.59-4.50 (1H, m), 1.59 (3H for one diastereomer, d, J= 6.2 Hz), 7.03 (3H for one diastereomer, d, J= 6.2 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 141.02 (d, J = 4.3 Hz), 128.5, 128.29 (for one diastereomer), 128.25 (for the other diastereomer), 125.8 (d, J = 2.9 Hz), 123.2 (qd, J = 276.7, 9.4 Hz), 75.11 (for one diastereomer, d, J = 2.9 Hz), 75.07 (for the other diastereomer, d, J = 2.9 Hz), 60.95 (for one diastereomer, qd, J = 36.9, 3.6 Hz), 60.92 (for the other diastereomer, qd, J = 36.1, 4.3 Hz), 24.0 (for one diastereomer, d, J = 4.3 Hz), 23.8 (for the other diastereomer, d, J = 4.3 Hz); ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.04; ^{31}P NMR (243 MHz, DMSO-d_6): δ 8.66, 8.54; HRMS (APCI-) calcd for $C_{10}H_{11}F_3O_3P$ ($[M-H]^-$): 267.0398; found: 267.0315; IR (neat): 2913, 2826, 2255,1401, 1280, 1134, 1023, 1005, 823, 761 cm^{-1}.

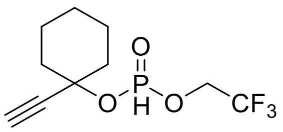
Oct-1-en-3-yl (2,2,2-trifluoroethyl) phosphonate (**3i**)

^{1}H NMR (600 MHz, DMSO-d_6): δ 7.02 (1H for one diastereomer, d, J_{P-H} = 724.5 Hz), 7.01 (1H for one diastereomer, d, J_{P-H} = 726.5 Hz), 5.90-5.84 (1H, m), 5.31 (1H, d, J = 17.2 Hz), 5.22 (1H, d, J = 10.3 Hz), 4.87-4.83 (1H, m), 4.68-4.61 (m, 2H), 1.65-1.57 (2H, m), 1.29-1.25 (6H, m), 0.86-0.84 (3H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 136.72 (for one diastereomer, d, J = 2.9 Hz), 136.61 (for the other diastereomer, d, J = 2.9 Hz), 123.2 (qd, J = 277.4, 8.7 Hz), 117.34 (for one diastereomer), 117.31 (for the other diastereomer), 78.2 (for one diastereomer, d, J = 5.8 Hz), 78.1 (for the other diastereomer, d, J = 5.8 Hz), 61.00 (for one diastereomer, qd, J = 36.1, 4.3 Hz), 60.95 (for the other diastereomer, qd, J = 36.1, 5.8 Hz), 35.1 (for one diastereomer, d, J = 4.3 Hz), 35.0 (for the other diastereomer, d, J = 7.2 Hz), 30.8, 23.9 (for one diastereomer), 23.8 (for the other diastereomer), 21.9, 13.73 (for one diastereomer), 13.72 (for the other diastereomer); ^{19}F



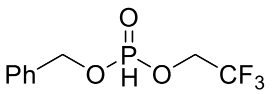
NMR (565 MHz, DMSO-d_6): δ -74.07; ^{31}P NMR (243 MHz, DMSO-d_6): δ 8.66, 8.61; HRMS (APCI-) calcd for $C_{10}H_{17}F_3O_3P$ ($[M-H]^-$): 273.0867; found: 273.0563; IR (neat): 2913, 2824, 2255, 1280, 1207, 1147, 1024, 1005, 823, 760, 616 cm^{-1}.

1-Ethynylcyclohexyl (2,2,2-trifluoroethyl) phosphonate (**3j**)



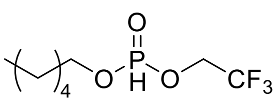
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.18 (1H, d, $J_{P\text{-}H}$ = 725.82 Hz), 4.67-4.62 (2H, m), 3.97 (1H, s), 2.03-1.92 (2H, m), 1.92-1.80 (2H, m), 1.67-1.60 (2H, m), 1.51-1.38 (3H, m), 1.34-1.24 (1H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.2 (qd, J = 277.4, 10.1 Hz), 82.2 (d, J = 5.8 Hz), 79.7, 77.8 (d, J = 5.8 Hz), 61.1 (qd, J = 36.1, 4.3 Hz), 38.7 (d, J = 2.9 Hz), 38.6 (d, J = 4.3 Hz), 23.9, 22.13, 22.11; ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.89; ^{31}P NMR (243 MHz, DMSO-d_6): δ 5.16; HRMS (APCI-) calcd for $C_{10}H_{13}F_3O_3P$ ($[M-H]^-$): 269.0554; found: 269.0531; IR (neat): 2943, 2829, 1448, 1414, 1023, 824, 763, 628 cm^{-1}.

Benzyl (2,2,2-trifluoroethyl) phosphonate (**3k**)



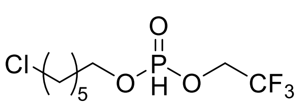
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.43-7.36 (5H, m), 7.12 (1H, d, $J_{P\text{-}H}$ = 731.3 Hz), 5.13 (2H, dd, J = 9.3, 2.4 Hz), 4.68 (2H, qd, J = 8.6, 8.6 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 135.7 (d, J = 5.8 Hz), 128.55, 128.54, 128.50, 123.2 (qd, J = 277.4, 8.7 Hz), 66.8 (d, J = 4.3 Hz), 61.1 (qd, J = 36.1, 4.3 Hz); ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.95; ^{31}P NMR (243 MHz, DMSO-d_6): δ 10.18; HRMS (APCI-) calcd for $C_9H_9F_3O_3P$ ($[M-H]^-$): 253.0241; found: 253.0367; IR (neat): 2948, 2833, 1457, 1420, 1155, 1174, 1111, 1020, 656 cm^{-1}.

Hexyl (2,2,2-trifluoroethyl) phosphonate (**3l**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 6.98 (1H, d, $J_{P\text{-}H}$ = 725.1 Hz), 4.66 (2H, qd, J = 8.9, 8.9 Hz), 4.04 (2H, dt, J = 8.9, 6.5 Hz), 1.61 (2H, tt, J = 7.2, 7.2 Hz), 1.29-1.27 (6H, m), 0.85 (3H, t, J = 6.9 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.3 (qd, J = 277.4, 8.7 Hz), 65.7 (d, J = 5.8 Hz), 61.0 (qd, J = 36.1, 2.9 Hz), 30.7, 29.6 (d, J = 7.2 Hz), 24.5, 22.0, 13.7; ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.10; ^{31}P NMR (243 MHz, DMSO-d_6): δ 9.91; HRMS (APCI-) calcd for $C_8H_{15}F_3O_3P$ ($[M-H]^-$): 247.0711; found 247.0488; IR (neat): 2956, 2841, 2360, 2160, 1970, 1868, 1652, 1541, 1064, 1030, 1013, 665 cm^{-1}.

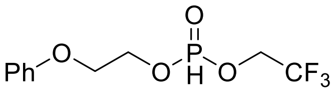
6-Chlorohexyl (2,2,2-trifluoroethyl) phosphonate (**3m**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 6.99 (1H, d, $J_{P\text{-}H}$ = 725.1 Hz), 4.66 (2H, qd, J = 8.9, 8.9 Hz), 4.05 (2H, td, J = 8.3, 6.5 Hz), 3.61 (2H, t, J = 6.5 Hz), 1.75-1.57 (4H, m), 1.45-1.27 (4H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 125.1 (qd, J = 277.4, 8.7 Hz), 65.55 (d, J = 7.22 Hz), 61.0 (qd, J = 36.1, 4.3 Hz), 45.2, 31.9, 29.5 (d, J = 5.8 Hz), 25.7, 24.1; ^{19}F NMR

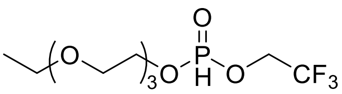
(565 MHz, DMSO-d_6): δ -74.07; ^{31}P NMR (243 MHz, DMSO-d_6): δ 9.94; HRMS (APCI-) calcd for $C_8H_{14}ClF_3O_3P$ ([M-H]$^-$): 281.0321; found 281.0148; IR (neat): 2941, 2829, 2356, 2161, 1654, 1023, 995, 825, 763 cm^{-1}.

2,2,2-Trifluoroethyl (2-phenoxyethyl) phosphonate (**3n**)



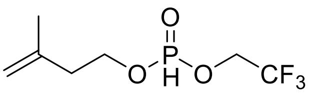
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.29 (2H, t, J = 7.9 Hz), 7.10 (1H, d, $J_{P\text{-}H}$ = 740.9 Hz), 7.00-6.90 (3H, m), 4.69 (2H, qd, J = 8.9, 8.9 Hz), 4.45-4.32 (2H, m), 4.22-4.17 (2H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 158.0, 129.5, 123.3 (qd, J = 277.4, 8.7 Hz), 120.9, 114.5, 66.6 (d, J = 5.8 Hz), 64.5 (d, J = 5.8 Hz), 60.9 (qd, J = 36.1, 4.3 Hz); ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.98; ^{31}P NMR (243 MHz, DMSO-d_6): δ 10.45; HRMS (APCI-) calcd for $C_{10}H_{11}F_3O_4P$ ([M-H]$^-$): 283.0347; found 283.2507; IR (neat): 2359, 2159, 1652,1047, 1024, 993, 824, 761 cm^{-1}.

2-Ethoxy-1-(2-ethoxyethoxy)ethyl (2,2,2-trifluoroethyl) phosphonate (**3o**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 7.03 (1H, d, $J_{P\text{-}H}$ = 733.4 Hz), 4.66 (2H, qd, J = 8.9, 8.9 Hz), 4.23-4.12 (2H, m), 3.62 (2H, t, J = 4.5 Hz), 3.58-3.48 (6H, m), 3.46-3.44 (2H, m), 3.41 (2H, q, J = 6.9 Hz), 1.09 (3H, t, J = 7.2 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 123.3 (qd, J = 277.4, 8.7 Hz), 69.8, 69.70, 69.68, 69.3 (d, J = 5.8 Hz), 69.2, 65.5, 65.2 (d, J = 5.8 Hz), 60.7 (qd, J = 36.1, 4.3 Hz), 15.0; ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.04; ^{31}P NMR (243 MHz, DMSO-d_6): δ 10.40; HRMS (APCI-) calcd for $C_{10}H_{19}F_3O_6P$ ([M-H]$^-$): 323.0871; found 323.0659; IR (neat): 2361, 2159, 1677, 1652, 1048, 1024, 993, 824, 761 cm^{-1}.

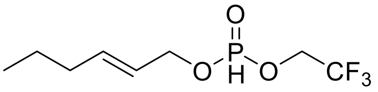
3-Methylbut-3-en-1-yl (2,2,2-trifluoroethyl) phosphonate (**3p**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 7.00 (1H, d, $J_{P\text{-}H}$ = 727.2 Hz), 4.81 (1H, s), 4.76 (1H, s), 4.66 (2H, qd, J = 8.9, 8.9 Hz), 4.22-4.12 (2H, m), 2.35 (2H, t, J = 6.5 Hz), 1.71 (3H, s); ^{13}C NMR (151 MHz, DMSO-d_6): δ 141.0, 123.3 (qd, J = 277.4, 8.7 Hz), 112.7, 63.7 (d, J = 5.8 Hz), 60.9 (qd, J = 36.9, 3.6 Hz), 33.7 (d, J = 5.8 Hz), 21.9; ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.01; ^{31}P NMR (243 MHz, DMSO-d_6): δ 9.83; HRMS (APCI-) calcd for $C_7H_{11}F_3O_3P$ ([M-H]$^-$): 231.0398; found 231.0162; IR (neat): 2943, 2829, 2361, 2165, 1662, 1024, 1001, 824, 761 cm^{-1}.

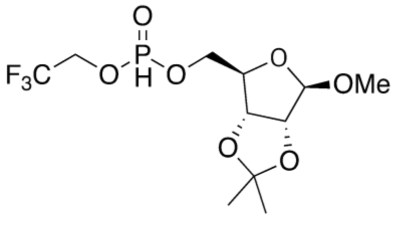
(*E*)-Hex-2-en-1-yl (2,2,2-trifluoroethyl) phosphonate (**3q**)

^{1}H NMR (600 MHz, DMSO-d_6): δ 7.01 (1H, d, $J_{P\text{–}H}$ = 726.5 Hz), 5.83 (1H, td, J = 7.2, 14.4 Hz), 5.63-5.54 (1H, m), 4.66 (2H, qd, J = 8.9, 8.9 Hz), 4.52 (2H, dd, J = 6.9, 9.6 Hz), 2.00 (2H, q, J = 6.9 Hz), 1.36 (2H, td, J = 7.3, 7.3 Hz), 0.86 (3H, t, J = 7.6 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 136.2, 124.4 (d, J = 5.8 Hz), 123.3 (qd, J = 278.2, 9.4 Hz), 66.1 (d, J = 5.8 Hz), 60.9 (qd, J = 36.1, 4.3 Hz), 33.5, 21.4, 13.4; ^{19}F NMR (565 MHz, DMSO-



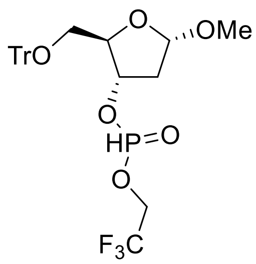
*d*6): δ -74.04; ^{31}P NMR (243 MHz, DMSO-*d*6): δ 9.91; HRMS (APCI-) calcd for $C_8H_{13}F_3O_3P$ ([M-H]$^-$): 245.0554; found 245.0310; IR (neat): 2942, 2829, 2358, 2164, 1654, 1023, 824, 763 cm^{-1}.

((3a*R*,4*R*,6*R*,6a*R*)-6-Methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl (2,2,2-trifluoroethyl) phosphonate (**3r**)



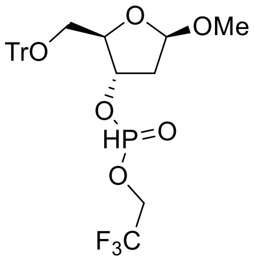
^{1}H NMR (600 MHz, DMSO-*d*6): δ 7.07 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 736.1 Hz), 7.06 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 737.5 Hz), 4.95 (1H, s), 4.77-4.67 (3H, m), 4.57 (1H, d, *J* = 6.2 Hz), 4.25 (1H, t, *J* = 6.9 Hz), 4.08-3.96 (2H, m), 3.24 (3H, d, *J* = 5.2 Hz), 1.38 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (151 MHz, DMSO-*d*6): δ 123.3 (qd, *J* = 277.4, 8.7 Hz), 111.71, 111.69, 108.81, 108.78, 84.4, 84.24, 84.19, 84.1, 80.7, 80.6, 61.03 (for one diastereomer, qd, *J* = 36.1, 4.3 Hz), 61.01 (for the other diastereomer, qd, *J* = 36.1, 4.3 Hz), 54.5, 54.4, 26.2, 24.6; ^{19}F NMR (565 MHz, DMSO-*d*6): δ -74.04; ^{31}P NMR (243 MHz, DMSO-*d*6): δ 10.21; HRMS (APCI-) calcd for $C_{11}H_{17}F_3O_7P$ ([M-H]$^-$): 349.0664; found: 349.0300; IR (neat): 2915, 2825, 1665, 1280, 1207, 1144, 1050, 1024, 1004, 823, 761, 616 cm^{-1}.

(2*R*,3*S*,5*S*)-2-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-5-methoxytetrahydrofuran-3-yl (2,2,2-trifluoroethyl) phosphonate (**3s**)



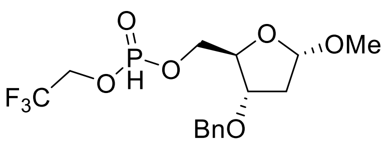
^{1}H NMR (600 MHz, CDCl3): δ 7.40 (6H, d, *J* = 8.3 Hz), 7.29 (6H, t, *J* = 7.6 Hz), 7.22 (3H, t, *J* = 6.9 Hz), 6.88 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 734.0 Hz), 6.87 (1H for the other diastereomer, d, $J_{P\text{-}H}$ = 732.7 Hz), 5.18 (1H, d, *J* = 4.1 Hz), 5.06-4.95 (1H, m), 4.45-4.20 (2H and 1H for one diastereomer, m), 4.13-4.01 (1H for the other diastereomer, m), 3.41 (3H for one diastereomer, s), 3.40 (3H for the other diastereomer, s), 3.31 (1H for one diastereomer, dd, *J* = 10.3, 4.1 Hz), 3.30 (1H for the other diastereomer, dd, *J* = 10.3, 4.8 Hz), 3.19 (1H for one diastereomer, dd, *J* = 10.3, 3.4 Hz), 3.15 (1H for the other diastereomer, dd, *J* = 10.3, 3.4 Hz), 2.49-2.38 (1H, m), 2.23 (1H for one diastereomer, d, *J* = 14.4 Hz), 2.20 (1H for the other diastereomer, d, *J* = 14.4 Hz); ^{13}C NMR (151 MHz, CDCl3): δ 143.6 (for one diastereomer), 143.5 (for the other diastereomer), 128.6 (for both diastereomers), 127.9 (for both diastereomers), 127.1 (for both diastereomers), 122.5 (qd, *J* = 277.4, 7.2 Hz), 105.1 (for one diastereomer), 105.0 (for the other diastereomer), 86.9 (for one diastereomer), 86.8 (for the other diastereomer), 83.43 (for one diastereomer, d, *J* = 5.8 Hz), 83.42 (for the other diastereomer, d, *J* = 7.2 Hz), 76.7 (d, *J* = 7.2 Hz), 63.3 (for one diastereomer), 63.1 (for the other diastereomer), 61.71 (for one diastereomer, qd, *J* = 37.6, 2.9 Hz), 61.68 (for the other diastereomer, qd, *J* = 37.6, 5.8 Hz), 55.2 (for one diastereomer), 55.1 (for the other diastereomer), 40.5 (for one diastereomer, d, *J* = 4.3 Hz), 40.3 (for the other diastereomer, d, *J* = 4.3 Hz); ^{19}F NMR (565 MHz, $CDCl_3$): δ -75.09; ^{31}P NMR (243 MHz, $CDCl_3$): δ 7.72, 7.34; HRMS (APCI-) calcd for $C_{27}H_{27}F_3O_6P$ ([M-H]$^-$): 535.1497; found: 535.1733; IR (neat): 2903, 2255, 1655, 1491, 1450, 1280, 1295, 1134, 1050, 1024, 1005, 824, 761 cm^{-1}.

(2*R*,3*S*,5*R*)-2-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-5-methoxytetrahydrofuran-3-yl (2,2,2-trifluoroethyl) phosphonate (**3t**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 7.44-7.17 (15H, m), 7.04 (d, 1H, $J_{P\text{-}H}$ = 735.5 Hz), 5.14-5.10 (1H, m), 5.05-5.02 (1H, m), 4.70-4.48 (2H, m), 4.26-4.14 (1H, m), 3.21 (3H, s), 3.19-3.11 (1H, m), 3.11-3.00 (1H, m), 2.34-2.24 (1H, m), 2.24-2.12 (1H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 143.6, 128.3, 127.9, 127.1, 123.2 (qd, *J* = 260.0, 5.8 Hz), 104.7, 86.2, 82.8, 76.64 (for one diastereomer, d, *J* = 5.8 Hz), 76.57 (for the other diastereomer, d, *J* = 5.8 Hz), 63.65, 63.60, 61.42, 61.36, 61.32, 61.30, 61.23, 61.21, 61.17, 61.1, 61.0, 60.91, 60.88, 60.85, 60.7, 60.6, 54.8; ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.98; ^{31}P NMR (243 MHz, DMSO-d_6): δ 9.37; HRMS (APCI-) calcd for $C_{26}H_{26}F_3O_5P$ ([M-CH_3]$^-$): 506.1470; found: 506.5250; IR (neat): 2900, 2255, 2116, 1659, 1280, 1207, 1135, 1050, 1024, 1005, 823, 761, 626 cm^{-1}.

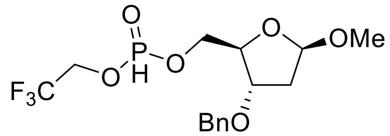
((2*R*,3*S*,5*S*)-3-(Benzyloxy)-5-methoxytetrahydrofuran-2-yl)methyl (2,2,2-trifluoroethyl) phosphonate (**3u**)



^{1}H NMR (600 MHz, DMSO-d_6): δ 7.35-7.26 (5H, m), 7.04 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 734.8 Hz), 7.03 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 736.1 Hz), 5.04-5.02 (1H, m), 4.70-4.64 (2H, m), 4.50-4.44 (2H, m), 4.24-4.17 (1H, m), 4.15-4.08 (2H, m), 4.00-3.96 (1H, m), 3.25 (3H, s), 2.29-2.20 (1H, m), 1.89 (d, 1H, *J* = 14.4 Hz); ^{13}C NMR (151 MHz, DMSO-d_6): δ 138.2, 128.2, 127.6, 127.5, 124.2, 124.1, 122.4, 122.3, 104.7, 81.0, 80.9, 78.0, 70.8, 65.72, 65.68, 61.3, 61.02, 61.00, 60.98, 60.95, 60.78, 60.76, 60.74, 60.71, 54.4, 38.1; ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.98; ^{31}P NMR (243 MHz, DMSO-d_6): δ 10.72, 10.53; HRMS (APCI-) calcd for $C_{15}H_{19}F_3O_6P$ ([M-H]$^-$): 383.0871; found: 383.0530; IR (neat): 2909, 2825, 2255, 1637, 1280, 1207, 1134, 1050, 1023, 1004, 823, 760, 616 cm^{-1}.

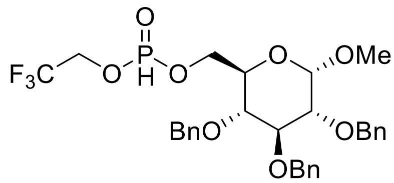
((2*R*,3*S*,5*R*)-3-(Benzyloxy)-5-methoxytetrahydrofuran-2-yl)methyl (2,2,2-trifluoroethyl) phosphonate (**3v**)

^{1}H NMR (600 MHz, DMSO-d_6): δ 7.35-7.27 (5H, m), 7.08 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 734.1 Hz), 7.06 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 734.8 Hz), 5.09-5.07 (1H, m), 4.72-4.66 (2H, m), 4.47 (2H, s), 4.18-3.99 (4H, m), 3.24 (3H for one diastereomer, s), 3.23 (3H for the other diastereomer, s), 2.20-2.15 (1H, m), 2.10-2.03 (1H, m); ^{13}C NMR (151 MHz, DMSO-d_6): δ 138.0, 128.2, 127.6, 127.5, 124.21, 124.15, 122.3, 122.2, 105.3, 81.83, 81.79, 81.77, 81.7, 78.63, 78.60, 70.7, 70.6, 66.7, 66.6, 66.41, 66.37, 61.33, 61.3,



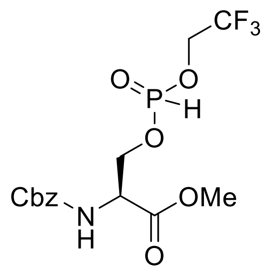
61.08, 61.05, 60.84, 60.81, 60.59, 60.56, 54.5, 38.71, 38.68; ^{19}F NMR (565 MHz, DMSO-d$_6$): δ: -74.01; ^{31}P NMR (243 MHz, DMSO-*d*$_6$): δ 10.29, 10.12; HRMS (APCI-) calcd for $C_{15}H_{19}F_3O_6P$ ([M-H]$^-$): 383.0871; found: 383.0918; IR (neat): 2920, 2826, 2255, 1654, 1280, 1207, 1134, 1050, 1024, 1004, 823, 761, 626 cm^{-1}.

2,2,2-Trifluoroethyl (((2*R*,3*R*,4*S*,5*R*,6*S*)-3,4,5-tris(benzyloxy)-6-methoxytetrahydro-2H-pyran-2-yl)methyl) phosphonate (**3w**)



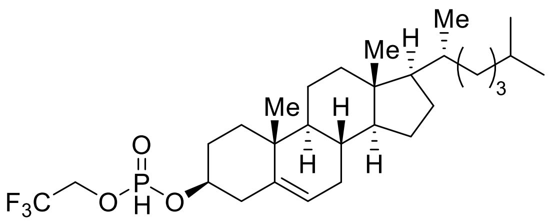
^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ 7.36-7.27 (15H, m), 7.06 (1H for one diastereomer, d, 1H, $J_{P\text{-}H}$ = 737.5 Hz), 7.05 (1H for one diastereomer, d, 1H, $J_{P\text{-}H}$ = 737.5 Hz), 4.88-4.86 (2H, m), 4.80-4.59 (8H, m), 4.32-4.19 (2H, m), 3.81 (1H, t, *J* = 9.28 Hz), 3.53-3.44 (2H, m), 3.32 (s, 3H); ^{13}C NMR (151 MHz, DMSO-*d*$_6$): δ 138.6, 138.42, 138.38, 138.1, 128.2, 128.1, 127.72, 127.66, 127.62, 127.59, 127.57, 127.55, 127.51, 127.4, 124.2, 124.1, 122.33, 122.27, 97.0, 80.9, 79.5, 79.4, 76.73, 76.67, 74.5, 74.0, 71.5, 68.9, 61.3, 61.2, 61.02, 61.00, 60.78, 60.76, 60.6, 60.5, 54.70, 54.67; ^{19}F NMR (565 MHz, DMSO-*d*$_6$) δ: -73.95; ^{31}P NMR (243 MHz, DMSO-*d*$_6$): δ 10.69, 10.58; HRMS (APCI-) calcd for $C_{30}H_{33}F_3O_8P$ ([M-H]$^-$): 609.1865; found: 609.1949; IR (neat): 2943, 2832, 1450, 1418, 1112, 1023, 620 cm^{-1}.

Methyl N-((benzyloxy)carbonyl)-O-((2,2,2-trifluoroethyl) phosphonate)-L-serinate (**3x**)



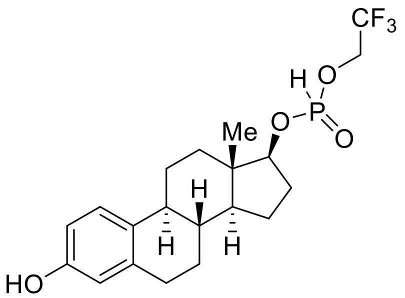
^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ 8.00 (1H, d, *J* = 8.3 Hz), 7.33-7.30 (m, 5H), 7.04 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 740.9 Hz) 7.02 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 738.9 Hz), 5.07 (2H, s), 4.71-4.62 (2H, m), 4.55-4.50 (1H, m), 4.37-4.22 (2H, m), 3.67 (3H, s); ^{13}C NMR (151 MHz, DMSO-*d*$_6$): δ 169.7, 169.6, 156.1, 136.8, 128.4, 128.0, 127.9, 127.8, 124.2, 124.1, 122.4, 122.3, 120.54, 120.46, 65.9, 64.70, 64.67, 64.6, 61.1, 60.9, 54.10, 54.05, 54.0, 52.35, 52.33; ^{19}F NMR (565 MHz, DMSO-*d*$_6$): δ -74.07; ^{31}P NMR (243 MHz, DMSO-*d*$_6$): δ 10.31, 10.26; HRMS (APCI-) calcd for $C_{14}H_{16}F_3NO_7P$ ([M-H]$^-$): 398.0616; found: 398.0363; IR (neat): 2937, 2831, 1717, 1541, 1457,1345, 1278, 1214, 1130, 1025, 883, 698cm^{-1}.

(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl (2,2,2-trifluoroethyl) phosphonate (**3y**)



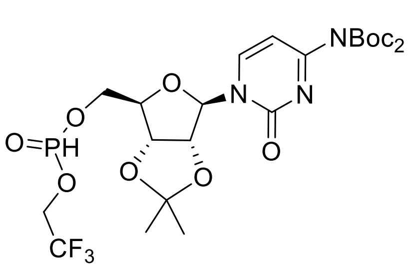
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.87 (1H, d, $J_{P\text{-}H}$ = 721.7 Hz), 5.32 (1H, br), 4.34-4.25 (3H, m), 2.44-2.32 (2H, m), 1.95-1.90 (3H, m), 1.82-1.66 (3H, m), 1.53-1.13 (10H, m), 1.10-0.87 (12H, m), 0.84 (4H, d, J = 6.9 Hz), 0.795 (d, 3H, J = 6.9 Hz), 0.792 (d, 3H, J = 6.9 Hz), 0.60 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.79, 138.77, 123.5, 123.1, 121.73, 121.69, 78.02, 77.98, 62.02, 62.00, 61.8, 61.7, 61.53, 61.50, 61.48, 61.3, 61.25, 61.23, 56.6, 56.1, 49.9, 42.3, 40.12, 40.09, 40.03, 40.00, 39.6, 39.5, 36.8, 36.3, 36.1, 35.7, 31.8, 31.7, 29.9, 29.83, 29.79, 29.76, 28.2, 28.0, 27.3, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 14.1, 11.8; ^{19}F NMR (565 MHz, $CDCl_3$): δ -75.13 (s); ^{31}P NMR (243 MHz, $CDCl_3$) δ: 6.78; HRMS (APCI-) calcd for $C_{29}H_{47}F_3O_3P$ ([M-H]$^-$): 531.3215; found: 531.3165; IR (neat): 3033, 2493, 2355, 1384, 1341, 1278, 1205, 1134, 1068, 884, 677cm^{-1}.

(8*R*,9*S*,13*S*,14*S*,17*S*)-3-Hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-17-yl (2,2,2-trifluoroethyl) phosphonate (**3z**)



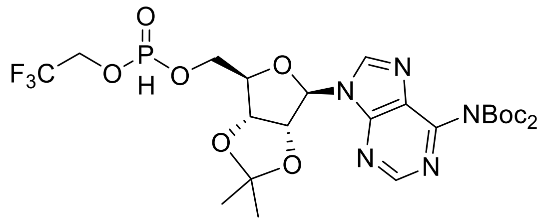
^{1}H NMR (600 MHz, DMSO-d_6): δ 7.01 (d, 1H, J = 8.9 Hz), 6.82 (d, 1H, J = 677.7 Hz), 6.49 (dd, 1H, J = 8.6, 2.4 Hz), 6.42 (d, 1H, J = 2.1 Hz), 4.52-4.46 (m, 1H), 4.03-3.99 (m, 1H), 3.50 (t, 1H, J = 8.3 Hz), 2.70-2.65 (m, 2H), 2.20 (dd, 1H, J = 13.4, 3.1 Hz), 2.03 (dd, 1H, J = 15.1, 6.9 Hz), 1.88-1.85 (m, 1H), 1.74 (dt, 1H, J = 12.1, 2.9 Hz), 1.55 (t, 1H, J = 4.1 Hz), 1.37 (q, 1H, J = 4.1 Hz), 1.30-1.15 (m, 7H), 0.65 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 155.0, 137.2, 130.5, 126.1, 125.4, 125.3, 124.65, 124.59, 115.0, 112.8, 80.2, 61.02, 61.00, 60.78, 60.77, 60.55, 60.53, 60.32, 60.29, 59.8, 49.6, 43.6, 42.9, 38.8, 36.7, 30.0, 29.3, 27.1, 26.2, 22.9, 20.8, 14.1, 11.3; ^{19}F NMR (565 MHz, DMSO-d_6): δ -73.98; ^{31}P NMR (243 MHz, DMSO-d_6): δ: 4.73; HRMS (APCI-) calcd for $C_{20}H_{25}F_3O_4P$ ([M-H]$^-$): 417.1443; found: 417.1604; IR (neat): 2923, 2833, 1501, 1448, 1401, 1207, 1132, 1023, 871, 617cm^{-1}.

Tert-butyl (tert-butoxycarbonyl)(1-((3a*R*,4*R*,6*R*,6a*R*)-6-(((2,2,2-trifluoroethyl) phosphonate) methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)carbamate methyl phosphonate (**3aa**)



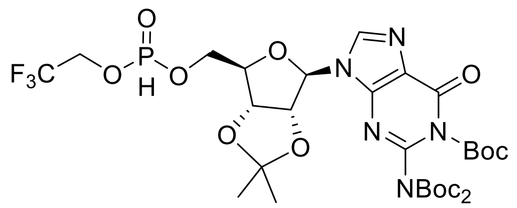
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.56 (dd, 1H, J = 7.22, 2.41 Hz), 7.04 (q, 1H, J = 3.67 Hz), 6.86 (dd, 1H, J = 736.16, 13.60 Hz), 5.50 (d, 1H, J = 13.75 Hz), 5.10-5.07 (m, 1H), 4.89-4.87 (m, 1H), 4.38-4.29 (m, 5H), 1.48 (d, 21H, J = 9.62 Hz), 1.25 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.04, 162.99, 153.9, 153.8, 149.2, 149.1, 146.9, 146.7, 125.22, 125.17, 123.4, 123.3, 121.54, 121.49, 119.7, 114.1, 114.0, 98.2, 98.1, 96.3, 87.45, 87.40, 87.37, 87.3, 85.13, 85.11, 84.6, 84.5, 81.5, 81.3, 65.9, 65.82, 65.78, 62.03, 61.99, 61.8, 61.7, 61.53, 61.49, 61.3, 61.2, 27.5, 26.82, 26.79, 24.93, 24.91; ^{19}F NMR (565 MHz, $CDCl_3$): δ -75.16; ^{31}P NMR (243 MHz, $CDCl_3$): δ 8.88; HRMS (APCI-) calcd for $C_{24}H_{34}F_3N_3O_{11}P$ ($[M-H]^-$): 628.1883; found: 628.1440; IR (neat): 2982, 2361, 2164, 1777, 1744, 1678, 1457, 1321, 1264, 1157, 1058, 1015, 787 cm^{-1}.

Tert-butyl (tert-butoxycarbonyl)(9-((3a*R*,4*R*,6*R*,6a*R*)-6-(((2,2,2-trifluoroethyl) phosphonate) methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-9H-purin-6-yl)carbamate (**3ab**)



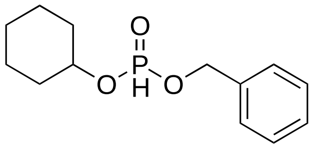
^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.80 (d, 1H, J = 3.44 Hz), 8.17 (s, 1H), 6.76 (dd, 1H, J = 750.22, 5.84 Hz), 5.38 (dd, 1H, J = 6.53, 1.72 Hz), 5.07 (q, 1H, J = 3.44 Hz), 4.42-4.22 (m, 6H), 1.56 (s, 3H), 1.39 (s, 18H), 1.33 (s, 3H). ^{31}P NMR (243 MHz, $CDCl_3$): δ 8.99, 8.82. Phosphonylated nucleosides (**8ab**) was too unstable, and therefore not able to take ^{13}C NMR, IR, and HRMS.

Tert-butyl 2-(bis(tert-butoxycarbonyl)amino)-9-((3a*R*,4*R*,6*R*,6a*R*)-6-(((2,2,2-trifluoroethyl) phosphonate) methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-6-oxo-6,9-dihydro-1H-purine-1-carboxylate (**3ac**)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, 1H, J = 2.75 Hz), 6.79 (dd, 1H, J = 737.85, 17.53 Hz), 6.05 (dd, 1H, J = 10.31, 1.37 Hz), 5.35-5.32 (m, 1H), 5.05 (td, 1H, J = 6.19, 3.44 Hz), 4.38-4.18 (m, 5H), 1.64-1.57 (m, 11H), 1.51 (s, 3H), 1.42 (s, 16H), 1.29 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.0, 160.9, 151.3, 151.01, 150.98, 150.7, 150.6, 141.7, 121.0, 120.9, 114.6, 114.5, 113.9, 93.3, 90.34, 90.29, 86.8, 86.6, 86.4, 86.12, 86.09, 85.91, 85.88, 84.9, 84.4, 84.3, 84.2, 84.1, 83.7, 83.4, 83.24, 83.22, 81.5, 81.2, 81.0, 65.5, 62.8, 61.8, 61.72, 61.69, 61.65, 61.51, 61.5, 61.47, 61.44, 61.4, 30.29, 30.27, 28.2, 28.1, 27.80, 27.79, 27.75, 27.67, 27.61, 27.58, 27.5, 27.4, 27.1, 26.9, 25.3, 25.11, 25.09, 25.06, 25.0; ^{19}F NMR (565 MHz, $CDCl_3$): δ -75.19; ^{31}P NMR (243 MHz, $CDCl_3$): δ 8.99, 8.88; HRMS (APCI-) calcd for $C_{30}H_{42}F_3N_5O_{13}P$ ($[M-H]^-$): 768.2469; found: 768.2492; IR (neat): 2945, 2833, 2362, 2162, 1652, 1454, 1420, 1112, 1020, 733 cm^{-1}.

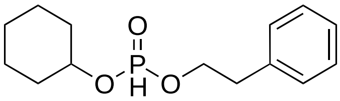
Benzyl cyclohexyl phosphite (**4a**)



Colorless oil, 67.0 mg (90%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33- 7.20 (5H, m), 6.80 (1H, d, $J_{P\text{-}H}$ = 697.6 Hz), 5.00 (2H, d, J = 9.60 Hz), 4.38-4.30 (1H, m), 1.95-1.85 (2H, m), 1.65-1.59 (2H, m), 1.49-1.38 (3H, m), 1.25-1.10 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 135.7 (d, J = 7.2 Hz), 128.6, 128.4, 127.8, 76.0 (d, J = 5.8 Hz), 66.9 (d, J = 5.8 Hz), 33.5 (d, J = 4.3 Hz), 33.4 (d, J = 4.3 Hz), 24.9, 23.4; ^{31}P NMR (240 MHz, $CDCl_3$): δ 6.74; HRMS (DART): m/z calcd. for $C_{26}H_{39}O_6P_2$ ($[2M+H]^+$): 509.22219; found: 509.22349; IR (neat): 2936, 2859, 2425, 1498, 1455, 1255, 969 cm^{-1}.

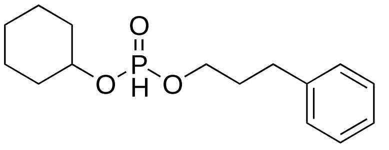
Cyclohexyl phenethyl phosphite (**4b**)



Colorless oil, 56.9 mg (70%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25-7.03 (5H, m), 6.69 (1H, d, $J_{P\text{-}H}$ = 690.0 Hz), 4.32-4.29 (1H, m), 4.23-4.12 (2H, m), 2.93 (2H, t, J = 6.9 Hz), 1.85-1.70 (2H, m), 1.70-1.55 (2H, m), 1.47-1.42 (3H, m), 1.26-1.13 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.0, 128.9, 128.5, 126,7, 75.9 (d, J = 5.8 Hz), 65.8 (d, J = 7.2 Hz), 36.9, 36.8, 33.6 (d, J = 4.3 Hz), 33.4 (d, J = 4.3 Hz), 24.9, 23.4; ^{31}P NMR (243 MHz, $CDCl_3$): δ 6.71; HRMS (APCI-) calcd. for $C_{14}H_{20}O_3P$ ($[M-H]^-$): 267.1150; found: 267.1092; IR (neat): 2935, 2829, 2366, 1654, 1404, 1345, 1278, 1207, 1132, 1050, 1024, 824, 761, 607cm^{-1}.

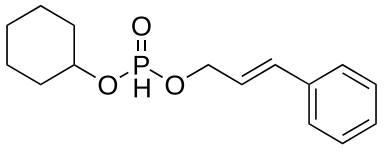
Cyclohexyl (3-phenylpropyl) phosphite (**4c**)



Pale yellow oil, 70.9 mg (85%)

^{1}H NMR (495 MHz, $CDCl_3$): δ 7.29 (2H, t, J = 7.4 Hz), 7.22-7.13 (3H, m), 6.85 (1H, d, $J_{P\text{-}H}$ = 691.5 Hz), 4.52-4.42 (1H, m), 4.12-4.02 (2H, m), 2.73 (2H, t, J = 7.6 Hz), 2.01 (2H, quin., J = 7.1 Hz), 1.98-1.90 (2H, m), 1.80-1.72 (2H, m), 1.62-1.48 (3H, m), 1.40-1.21 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 128.40, 128.36, 126.0, 75.9 (d, J = 6.0 Hz), 64.5 (d, J = 6.0 Hz), 33.7 (d, J = 3.6 Hz), 33.4 (d, J = 4.8 Hz), 31.9 (d, J = 7.2 Hz), 31.6, 25.0, 23.4; ^{31}P NMR (200 MHz, $CDCl_3$): δ 6.85 (s); HRMS (DART): m/z calcd. for $C_{30}H_{47}O_6P_2$ ($[2M+H]^+$): 565.28479; found: 565.28511; IR (neat): 2935, 2859, 1454, 1254, 1077, 741, 701 cm^{-1}.

Cinnamyl cyclohexyl phosphite (**4d**)

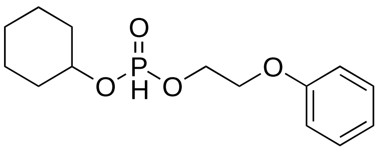


Pale yellow oil, 70.4 mg (82%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (2H, d, J = 7.4 Hz), 6.98 (2H, dd, J = 6.8, 7.9 Hz), 7.22-7.14 (1H, m), 6.96 (1H, d, $J_{P\text{-}H}$ = 695.5 Hz), 6.62 (2H, d, J = 15.8 Hz), 6.24 (2H, dt, J = 15.8, 6.2 Hz), 4.65 (2H, ddd, J = 9.6, 6.2, 1.1 Hz), 4.46-4.36 (1H, m), 1.93-1.80 (2H, m), 1.72-1.62 (2H, m), 1.55-1.38 (3H, m), 1.30-1.11 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ135.8, 134.1, 128.5, 128.1, 126.6, 127.6 (d, J = 5.7 Hz), 76.0 (d, J = 5.7

Hz), 65.8 (d, J = 5.7 Hz), 33.6 (d, J = 4.3 Hz), 33.4 (d, J = 4.3 Hz), 24.9, 23.4; ^{31}P NMR (243 MHz, $CDCl_3$): δ6.82; HRMS (DART): m/z calcd. for $C_{30}H_{43}O_6P_2$ ($[2M+H]^+$): 561.25349; found: 561.25415; IR (neat): 2935, 2858, 1450, 1260, 741, 693 cm^{-1}.

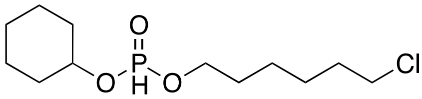
Cyclohexyl (2-phenoxyethyl) phosphite (**4e**)



Colorless oil, 74.7 mg (88%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (2H, dd, J = 8.2, 7.6 Hz), 6.98 (1H, dd, J = 8.3, 7.6 Hz), 6.95 (1H, d, J_{P-H} = 701.7 Hz), 6.91 (2H, d, J = 8.9 Hz), 4.53-4.33 (3H, m), 4.18 (2H, dd, J = 4.8, 4.1 Hz), 1.98-1.88 (2H, m), 1.78-1.68 (2H, m), 1.60-1.47 (3H, m), 1.37-1.20 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ158.1, 129.4, 121.2, 114.5, 76.0 (d, J = 7.2 Hz), 66.8 (d, J = 5.7 Hz), 63.8 (d, J = 5.7 Hz), 33.5 (d, J = 4.3 Hz), 33.4 (d, J = 4.3 Hz), 24.9, 23.4; ^{31}P NMR (243 MHz, $CDCl_3$): δ7.47; HRMS (DART): m/z calcd. for $C_{28}H_{43}O_8P_2$ ($[2M+H]^+$): 569.24331; found: 561.24802; IR (neat): 2935, 2859, 1598, 1497, 1457, 1245, 971, 755, 693 cm^{-1}.

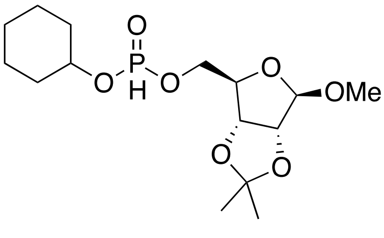
6-Chlorohexyl cyclohexyl phosphite (**4f**)



Pale yellow oil, 51.6 mg (61%)

^{1}H NMR (600 MHz, $CDCl_3$):δ 6.85 (1H, d, J_{P-H} = 690.8 Hz), 4.50-4.38 (1H, m), 4.11-4.01 (2H, m), 3.54 (2H, t, J = 6.5 Hz), 1.99-1.88 (2H, m), 1.82-1.65 (6H, m), 1.65-1.15 (10H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 75.9 (d, J = 5.8 Hz), 65.2 (d, J = 5.8 Hz), 44.8, 33.7 (d, J = 4.3 Hz), 33.4 (d, J = 4.3 Hz), 32.3, 30.1 (d, J = 7.2 Hz), 26.3, 25.0, 24.8, 23.4. ^{31}P NMR (243 MHz, $CDCl_3$) δ 6.82; HRMS (DART) calcd. for $C_{12}H_{25}ClO_3P$ ($[M+H]^+$): 283.12298; found: 283.12293: IR (neat): 2938, 2860, 1450, 1254, 970 cm^{-1}.

Cyclohexyl (((3a*R*,4*R*,6*R*,6a*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl) phosphite (**4g**)

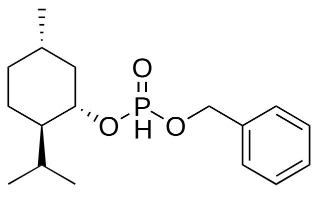


Colorless oil, 72.3 mg (69%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.83 (1H for one diastereomer, d, J = 700.39 Hz), 6.82 (1H for one diastereomer, d, J = 701.08 Hz), 4.91 (1H, s), 4.65 (1H, d, J = 6.19 Hz), 4.53 (1H, d, J = 5.50 Hz), 4.45-4.41 (1H, m), 4.29 (1H, t, J = 6.87 Hz), 4.06-3.93 (2H, m), 3.27 (3H for one diastereomer, d, J = 1.37 Hz), 3.26 (3H for one diastereomer, s), 1.89-1.87 (2H, m), 1.70-1.68 (2H, m), 1.53-1.36 (6H, m), 1.32-1.15 (6H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 112.55, 109.33, 84.94, 84.92, 84.90, 81.42, 81.35, 76.25, 76.21, 65.06, 65.02, 64.78, 64.74, 55.04, 55.01, 33.64, 33.61, 33.42, 26.32, 24.93, 24.84, 23.41; ^{31}P NMR (243 MHz, $CDCl_3$) δ 6.77, 6.69; HRMS (APCI-): calcd. for $C_{15}H_{26}O_7P$ ($[M-H]^-$):

349.1416; found: 349.1379; IR (neat): 3016, 2935, 2359, 1559, 1395, 1340, 1278, 1207, 1132, 1065, 1065, 881, 636 cm^{-1}.

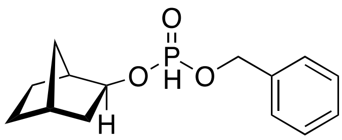
Benzyl ((1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl) phosphite (**4h**)



Pale yellow oil, 87.8 mg (91%), dr = 47:53

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.23 (5H, m), 6.86 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 697.6 Hz), 6.83 (1H for the other diastereomer, d, *J* = 698.4 Hz), 5.08-4.98 (2H, m), 4.23-4.13 (1H, m), 2.09-1.95 (2H, m), 1.62-1.55 (2H, m), 1.40-1.25 (2H, m), 1.15-1.05 (1H, m), 0.95-0.65 (11H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ135.73, 135.69, 128.55, 128.48, 127.90, 127.88 , 78.37, 78.31, 78.14, 78.08, 67.02, 66.98, 66.92, 66.88, 48.20, 48.19, 48.16, 48.13, 43.1, 42.8, 33.8, 31.5, 25.7, 25.5, 22.80, 22.78, 21.8, 20.8, 20.7, 15.6, 15.4; ^{31}P NMR (243 MHz, $CDCl_3$): δ7.45, 6.85; HRMS (DART): m/z calcd. for $C_{34}H_{55}O_6P_2$ ([2M+H]$^+$): 621.34739; found: 621.34711; IR (neat): 2953, 2916, 2870, 2427, 1457, 1371, 1255, 985, 964, 737, 697 cm^{-1}.

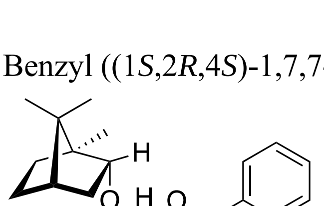
Benzyl ((1*S*,2*S*,4*R*)-bicyclo[2.2.1]heptan-2-yl) phosphite (**4i**)



Pale yellow oil, 77.1 mg (90%), dr = 50:50

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.24 (5H, m), 6.79 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 694.0 Hz), 6.79 (1H for the other diastereomer, d, *J* = 697.0 Hz), 5.03 (2H for one diastereomer, d, *J* = 9.6 Hz), 5.02 (2H for the other diastereomer, d, *J* = 9.6 Hz), 4.31 (1H, t, *J* = 6.9 Hz), 2.31 (1H for one diastereomer, d, *J* = 4.8 Hz), 2.28 (2H for the other diastereomer, d, *J* = 4.8 Hz), 2.21 (1H, d, *J* = 2.8 Hz), 1.62 (1H for one diastereomer, ddd, *J* = 14.3, 6.9 ,2.8 Hz), 1.60 (1H for the other diastereomer, ddd, *J* = 14.3, 6.9, 2.8 Hz), 1.56-1.46 (2H, m), 1.46-1.38 (1H, m), 1.38-1.28 (1H, m), 1.12-1.08 (1H, m), 1.00-0.90 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 135.8, 135.7, 128.6, 128.5, 127.9, 79.75, 79.71, 79.67, 67.1, 67.0, 43.0, 42.8, 40.63, 40.60, 40.56, 35.3, 34.7, 27.9, 23.78, 23.76; ^{31}P NMR (243 MHz, $CDCl_3$): δ6.85; HRMS (DART): m/z calcd. for $C_{28}H_{39}O_6P_2$ ([2M+H]$^+$): 533.22219; found: 533.22205; IR (neat): 2959, 2873, 1457, 1255, 971, 734, 697 cm^{-1}.

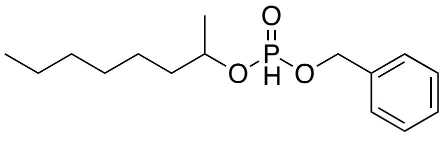
Benzyl ((1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) phosphite (**4j**)



Pale yellow oil, 90.8 mg (99%), dr = 49:51

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45-7.32 (5H, m), 6.90 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 699.7 Hz), 6.90 (1H for the other diastereomer, d, *J* = 699.7 Hz), 5.11 (2H for one diastereomer, d, *J* = 9.6 Hz), 5.11 (2H for the other diastereomer, d, *J* = 9.7 Hz), 4.68-4.61 (1H for one diastereomer, m), 4.61-4.54 (1H for one diastereomer, m), 2.30-2.21 (1H, m), 1.95-1.87 (1H, m), 1.77-1.69 (1H, m), 1.35-1.15 (3H, m), 0.88-0.80 (9H, m): ^{13}C NMR (150 MHz, $CDCl_3$): δ 135.8, 135.7, 128.6, 128.5, 127.9, 82.7, 82.66, 82.64, 67.03, 66.99, 49.5, 47.62, 47.59, 44.8, 37.05, 37.03, 36.97, 36.95, 27.9, 26.4, 26.3, 19.8, 18.6, 13.2, 13.1; ^{31}P NMR (243 MHz, $CDCl_3$): δ 8.42, 8.28; HRMS (DART): m/z calcd. for $C_{17}H_{25}O_3P$ ($[M+H]^+$): 309.16196; found: 309.16232; IR (neat): 2953, 2878, 1457, 1255, 1040, 967, 735, 697 591, 540 cm^{-1}.

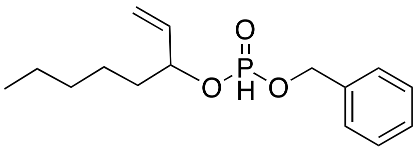
Benzyl octan-2-yl phosphite (**4k**)



Pale yellow oil, 81.2 mg (95%), dr = 50:50

^{1}H NMR (600 MHz, $CDCl_3$): δ7.43-7.30 (5H, m), 6.90 (1H, d, $J_{P\text{-}H}$ = 697.0 Hz), 5.13-5.05 (2H, m), 4.62-4.52 (1H, m), 1.68-1.58 (1H, m),1.55-1.45 (1H, m), 1.40-1.20 (11H, m), 0.92-0.83 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.75 (for one diastereomer, d, J = 6.0 Hz), 135.71 (for the other diastereomer, d, J = 7.1 Hz), 128.6, 128.5, 127.8, 74.9 (d, J = 6.0 Hz), 67.0 (for one diastereomer, d, J = 6.0 Hz), 66.9 (for the other diastereomer, d, J = 6.0 Hz), 37.5 (for one diastereomer, d, J = 4.8 Hz), 37.4 (for the other diastereomer, d, J = 6.0 Hz), 31.6, 30.8, 28.9, 25.2 (for one diastereomer), 25.0 (for the other diastereomer), 22.0 (for one diastereomer, d, J = 2.4 Hz), 21.7 (for the other diastereomer, d, J = 3.6 Hz), 14.0; ^{31}P NMR (243 MHz, $CDCl_3$): δ7.18, 6.91; HRMS (DART): m/z calcd. for $C_{34}H_{55}O_6P_2$ ($[2M+H]^+$): 621.34739; found: 621.34711; IR (neat): 2953, 2916, 2870, 2427, 1457, 1371, 1255, 985, 964, 737, 697 cm^{-1}.

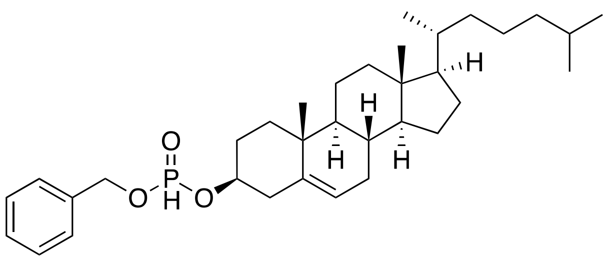
Benzyl oct-1-en-3-yl phosphite (**4l**)



Yellow oil, 50.0 mg (59%), dr = 49:51

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45-7.31 (5H, m), 6.911 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 700.4 Hz), 6.905 (1H for the other diastereomer, d, J = 703.1 Hz), 5.87-5.77 (1H, m), 5.30 (1H, t, J = 16.8 Hz), 5.21 (1H, dd, J = 14.8, 10.7 Hz), 5.16-5.03 (2H, m), 4.82 (1H, dt, J = 13.8, 6.9 Hz), 1.74-1.66 (1H, m), 1.64-1.56 (1H, m), 1.43-1.10 (6H, m), 0.88 (3H, t, J = 6.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ 136.80, 136.77, 136.51, 136.49, 135.7, 128.6, 128.5, 127.89, 127.87, 117.7, 117.5, 78.85, 78.80, 78.7, 78.6, 66.98, 66.96, 66.94, 66.91, 35.9, 35.84, 35.80, 35.76, 31.4, 24.5, 24.4, 22.4, 13.9; ^{31}P NMR (243 MHz, $CDCl_3$): δ 7.26, 7.15; HRMS (DART): m/z calcd. for $C_{30}H_{47}O_6P_2$ ($[2M+H]^+$): 565.28479; found: 565.28167; IR (neat): 2929, 2859, 1457, 1255, 1058, 965, 737, 697 cm^{-1}.

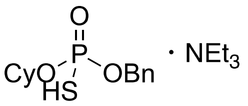
benzyl ((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl) phosphite (**4m**)



White solid, 136.1 mg (84%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.24 (5H, m), 6.83 (1H, d, $J_{P\text{-}H}$ = 698.4 Hz), 5.30-5.24 (1H, m), 5.03 (2H, d, J = 8.9 Hz), 4.24-4.10 (1H, m), 2.41-2.24 (2H, m), 1.98-1.80 (3H, m), 1.80-1.70 (2H, m), 1.70-1.57 (1H, m), 1.57-1.14 (10H, m), 1.14-0.87 (12H, m), 0.87-0.70 (10H, m), 0.60 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 139.1, 135.72, 135.68, 128.6, 128.5, 127.9, 123.1, 77.07, 77.05, 77.03, 67.06, 67.04, 67.00, 56.6, 56.1, 49.9, 42.2, 40.2, 40.1, 40.04, 40.01, 39.6, 39.4, 36.8, 36.3, 36.1, 35.7, 31.8, 31.7, 29.89, 29.86, 29.77, 29.74, 28.1, 27.9, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 11.8; ^{31}P NMR (243 MHz, $CDCl_3$): δ 6.69; HRMS (DART): m/z calcd. for $C_{34}H_{54}O_3P$ ($[M+H]^+$): 541.38106; found: 541.38290; IR (neat): 2936, 1457, 1382, 1238, 1070, 967, 734, 697, 593, 548, 478 cm^{-1}.

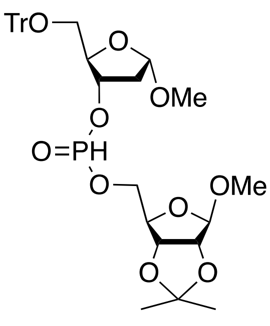
O-benzyl O-cyclohexyl S-hydrogen phosphorothioate-triethylamine salt (**4a-S**)



Pale yellow oil, 93.4 mg (81%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.25 (s, 1H), 7.36 (d, J = 7.3 Hz, 2H), 7.25 (t, J = 7.4 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 4.97 (ddd, J = 33.8, 12.3, 8.1 Hz, 2H), 4.34-4.30 (m, 1H), 3.02 (qd, J = 7.3, 4.4 Hz, 6H), 1.93 (dd, J = 15.4, 11.7 Hz, 2H), 1.68-1.63 (m, 2H), 1.47-1.36 (m, 3H), 1.28-1.20 (m, 11H), 1.15-1.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.7 (d, J = 9.1 Hz), 128.1, 127.5, 127.3, 75.3 (d, J = 6.3 Hz), 67.6 (d, J = 5.1 Hz), 45.5, 33.9, 33.9, 33.7 (d, J = 4.2 Hz), 25.6, 24.2, 8.6; ^{31}P NMR (243 MHz, CDCl3): δ 57.66; HRMS (DART): m/z calcd. for C13H18O3PS ($[M\text{-}HNEt_3]^-$): 285.07198; found: 285.07188; IR (neat): 2932, 2856, 1453, 1116, 1020, 990, 865, 792, 744, 698, 460 cm^{-1}.

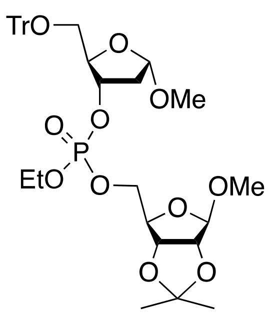
((3a*R*,4*R*,6*R*,6a*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl ((2*R*,3*S*,5*S*)-5-methoxy-2-((trityloxy)methyl)tetrahydrofuran-3-yl) phosphonate (**4n**)



White gum, 116.6 mg (61%), *dr* =59:41

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 (6H, d, J = 7.6 Hz), 7.23 (6H, t, J = 7.6 Hz), 7.16 (3H, t, J = 7.2 Hz), 6.86 (1H for one diastereomer, d, $J_{P\text{-}H}$ = 711.4 Hz), 6.81 (1H for the other diastereomer, d, $J_{P\text{-}H}$ = 713.4 Hz), 5.12 (1H for one diastereomer, d, J = 4.8 Hz), 5.10 (1H for the other diastereomer, d, J = 5.5 Hz), 5.04-4.93 (1H, m), 4.96 (1H for one diastereomer, s), 4.94 (1H for the other diastereomer, s), 4.69 (1H for one diastereomer, d, J = 6.2 Hz), 4.58 (1H, t, J = 5.5 Hz), 4.54 (1H for the other diastereomer, d, J = 5.5 Hz), 4.37-4.24 (2H, m), 4.08-3.98 (1H and 1H for one diastereomer, m), 3.91-3.85 (1H for the other diastereomer, m), 3.42 (3H for one diastereomer, s), 3.41 (3H for the other diastereomer, s), 3.34-3.29 (1H, m), 3.29 (3H for one diastereomer, s), 3.27 (3H for the other diastereomer, s), 3.23-3.16 (1H, m), 2.51-2.41 (1H, m), 2.24 (1H for one diastereomer, d, J = 11.0 Hz), 2.21 (1H for the other diastereomer, d, J = 10.3 Hz), 1.47 (3H for one diastereomer, s), 1.46 (3H for the other diastereomer, s), 1.31 (3H for one diastereomer, s), 1.27 (3H for the other diastereomer, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.6, 128.6, 127.81, 127.76, 127.1, 112.5, 109.3, 105.1, 105.0, 86.8, 86.7, 84.93, 84.88, 84.80, 84.75, 84.64, 84.58, 83.61, 83.57, 83.21, 83.17, 81.4, 81.2, 76.6, 76.5, 76.32, 76.28, 65.49, 65.45, 65.03, 64.99, 63.4, 63.3, 55.09, 55.07, 55.0, 40.64, 40.62, 40.22, 40.19, 26.3, 24.85, 24.83; ^{31}P NMR (243 MHz, $CDCl_3$): δ 7.72, 7.58; HRMS (ESI): m/z calcd. for $C_{34}H_{42}O_{10}P$ ($[M+H]^+$): 641.25156; found: 641.24924; IR (neat): 3059, 2989, 2935, 2835, 1598, 1491, 1450, 1372, 1260, 1090, 1047, 961, 901, 868, 823, 764, 748, 735, 704, 643, 633, 577, 516, 461 cm^{-1}.

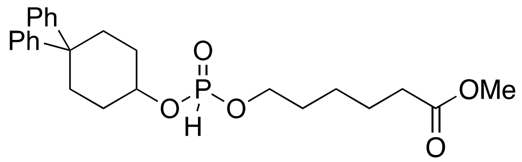
Ethyl (((3a*R*,4*R*,6*R*,6a*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl) ((2*R*,3*S*,5*S*)-5-methoxy-2-((trityloxy)methyl)tetrahydrofuran-3-yl) phosphate (**5a**)



White gum, 129.9 mg (63%), *dr* =59:41

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (6H, d, J = 8.3 Hz), 7.30 (6H, t, J = 7.2 Hz), 7.23 (3H, t, J = 7.2 Hz), 5.19 (1H for one diastereomer, d, J = 4.8 Hz), 5.18 (1H for the other diastereomer, d, J = 5.5 Hz), 4.95 (1H for one diastereomer, s), 4.94 (1H for the other diastereomer, s), 4.92-4.84 (1H, m), 4.69 (1H for one diastereomer, d, J = 6.2 Hz), 4.61 (1H for the other diastereomer, d, J = 5.5 Hz), 4.57 (1H for one diastereomer, d, J = 6.2 Hz), 4.53 (1H for the other diastereomer, d, J = 5.5 Hz), 4.40-4.25 (2H, m), 4.20-3.93 (3H and 1H for one diastereomer, m), 3.93-3.84 (1H for the other diastereomer, m), 3.40 (3H, s), 3.35-3.20 (1H, m), 3.28 (3H for one diastereomer, s), 3.26 (3H for the other diastereomer, s), 3.17 (1H for one diastereomer, d, J = 4.1 Hz), 3.15 (1H for the other diastereomer, d, J = 3.4 Hz), 2.47-2.38 (1H, m), 2.28-2.22 (1H, m), 1.47 (3H for one diastereomer, s), 1.45 (3H for the other diastereomer, s), 1.33-1.18 (6H, m); ^{13}C NMR (126 MHz, $CDCl_3$): δ 143.71, 143.70, 128.6, 127.8, 127.0, 112.5, 109.3, 105.11, 105.06, 86.7, 84.99, 84.96, 84.64, 84.56, 84.51, 83.52, 83.47, 83.42, 83.38, 81.5, 81.4, 78.2, 78.1, 76.8, 67.03, 66.98, 64.2, 64.1, 64.0, 63.7, 55.0, 54.9, 40.2, 26.3, 24.9, 24.83,16.02, 15.97; ^{31}P NMR (202 MHz, $CDCl_3$): δ -1.65, -1.76; HRMS (ESI): m/z calcd. for $C_{36}H_{46}O_{11}P$ ($[M+H]^+$): 685.27777; found: 685.27634; IR (neat): 2982, 2936, 2833, 1598, 1491, 1450, 1372, 1267, 1210, 1161, 1093, 1047, 1013, 963, 901, 868, 827, 765, 748, 704, 643, 633, 580, 516, 423 cm^{-1}.

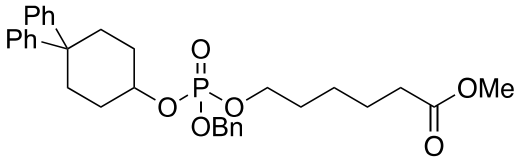
methyl 6-((((4,4-diphenylcyclohexyl)oxy)phosphoryl)oxy)hexanoate (**4o**)



White foam, 114.7 mg (87%)

^{1}H NMR (500 MHz, $CDCl_3$): 7.28-7.11 (m, 10H), 6.82 (d, $J_{P\text{-}H}$ = 690 Hz, 1H), 4.61 (tt, J = 11.6, 3.8 Hz, 1H), 4.07-3.98 (m, 2H), 3.64 (s, 3H), 2.56 (t, J = 9.2 Hz, 2H), 2.30 (t, J = 7.4 Hz, 2H), 2.24-2.19 (m, 2H), 1.93-1.88 (m, 2H), 1.84-1.78 (m, 2H), 1.71-1.61 (m, 4H), 1.43-1.36 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$):δ 173.9, 147.3, 128.6, 128.5, 127.1, 126.8, 126.0, 125.9, 74.9, 65.4, 65.4, 51.6, 45.5, 33.9, 32.8, 30.2, 30.1, 30.0, 29.9, 29.7, 29.7, 25.2, 24.5; ^{31}P NMR (203 MHz, $CDCl_3$): δ 6.93; HRMS (DART): m/z calcd. for $C_{25}H_{34}O_5P$ ($[M+H]^+$): 445.21439; found: 445.21422; IR (neat): cm^{-1}.

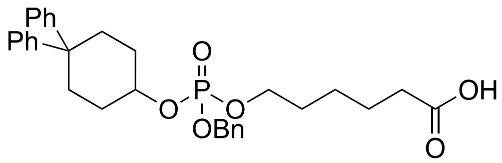
methyl 6-(((benzyloxy)((4,4-diphenylcyclohexyl)oxy)phosphoryl)oxy)hexanoate (**5b**)



White foam, 88.1 mg (64%)

^{1}H NMR (500 MHz, $CDCl_3$):δ 7.37-7.12 (m, 15H), 5.04 (d, J = 8.3 Hz, 2H), 4.51-4.48 (m, 1H), 3.97 (qd, J = 6.5, 2.0 Hz, 2H), 3.64 (s, 3H), 2.52 (t, J = 4.9 Hz, 2H), 2.29 (dt, J = 23.6, 7.5 Hz, 2H), 2.17 (dd, J = 20.8, 10.1 Hz, 2H), 1.90-1.73 (m, 4H), 1.67-1.57 (m, 4H), 1.39-1.32 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 136.2, 136.2, 128.6, 128.5, 128.5, 127.9, 127.1, 126.9, 125.9, 125.9, 69.1, 69.1, 67.5, 67.4, 51.6, 45.5, 33.9, 32.8, 30.0, 30.0, 29.5, 29.4, 25.1, 24.5; ^{31}P NMR (203 MHz, $CDCl_3$): δ -0.92; HRMS (DART): m/z calcd. for $C_{32}H_{40}O_6P$ ($[M+H]^+$): 551.25570; found: 551.25599; IR (neat): cm^{-1}.

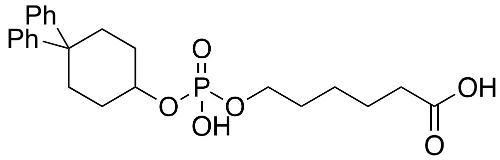
6-(((benzyloxy)((4,4-diphenylcyclohexyl)oxy)phosphoryl)oxy)hexanoic acid (**5c**)



White foam, 70.4 mg (82%)

^{1}H NMR (500 MHz, $CDCl_3$):δ7.37-7.12 (m, 15H), 5.04 (d, J = 8.4 Hz, 2H), 4.52-4.49 (m, 1H), 3.97 (qd, J = 6.7, 1.8 Hz, 2H), 2.52-2.48 (m, 2H), 2.30 (t, J = 7.4 Hz, 2H), 2.20-2.14 (m, 2H), 1.87-1.75 (m, 4H), 1.65-1.58 (m, 4H), 1.40-1.34 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.3, 136.2, 136.1, 128.6, 128.5, 128.5, 128.5, 127.9, 127.1, 126.9, 125.9, 125.9, 69.2, 69.2, 67.6, 67.5, 45.5, 33.8, 30.0, 29.9, 29.4, 29.4, 25.0, 24.3; ^{31}P NMR (203 MHz, $CDCl_3$): δ -1.05; HRMS (DART): m/z calcd. for $C_{31}H_{38}O_6P$ ($[M+H]^+$): 537.24005; found: 537.23991; IR (neat): cm^{-1}.

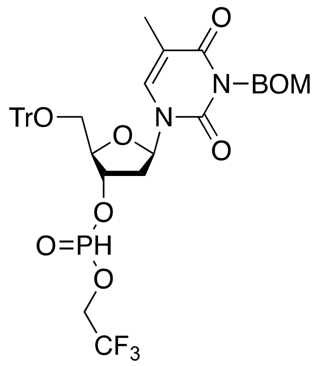
6-((((4,4-diphenylcyclohexyl)oxy)(hydroxy)phosphoryl)oxy)hexanoic acid (**5d**)



White foam, 65.9 mg (91%)

^{1}H NMR (500 MHz, MeOH-d_4) δ 7.30-7.19 (m, 8H), 7.08 (dd, J = 16.7, 7.4 Hz, 2H), 4.34 (d, J = 7.0 Hz, 1H), 3.90 (s, 2H), 2.56 (s, 2H), 2.28-2.19 (m, 4H), 1.86 (s, 2H), 1.72-1.57 (m, 6H), 1.40 (s, 2H); ^{13}C NMR (126 MHz, MeOH-d4) δ 176.2, 128.0, 127.9, 126.9, 126.6, 125.3, 73.8, 65.4, 45.3, 33.6, 32.8, 32.7, 30.1, 29.6, 25.1, 24.4; ^{31}P NMR (203 MHz, MeOH-d4): δ 0.09 (br)

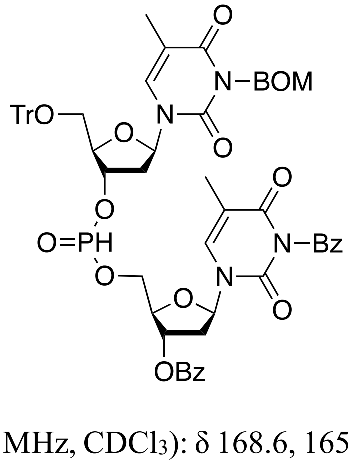
(2*R*,3*S*,5*R*)-5-(3-((benzyloxy)methyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((trityloxy)methyl)tetrahydrofuran-3-yl (2,2,2-trifluoroethyl) phosphonate (**3af**)



White solid, 576.0 mg (74%), *dr*: ca 1:1

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 (1H, s), 7.48-7.10 (20H, m), 6.94 (1H for one diastereomer, d, J_{P-H} = 738.9 Hz), 6.93 (1H for the other diastereomer, d, J_{P-H} = 727.2 Hz), 6.53-6.40 (1H, m), 5.49 (2H, s), 5.30-5.20 (1H, m), 4.71 (2H, s), 4.47-4.18 (3H, m), 3.60-3.50 (1H, m), 3.40 (1H, d, *J* = 9.6, 21.6 Hz), 3.38 (1H for the other diastereomer, d, *J* = 10.3 Hz), 2.69-2.55 (1H, m), 2.47-2.35 (1H, m), 1.464 (3H for one diastereomer, s), 1.456 (3H for the other diastereomer, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.2, 150.9, 142.9, 142.8, 137.9, 133.70, 137.68, 128.5, 128.2, 128.0, 127.6, 127.51, 125.2, 125.13, 125.09, 125.0, 123.33, 123.30, 123.26, 123.2, 121.49, 121.45, 121.42, 121.37, 119.7, 119.61, 119.58, 119.5, 110.94, 110.88, 87.7, 84.9, 84.8, 84.34, 84.30, 84.28, 72.1, 70.5, 63.97, 62.91, 62.4, 62.32, 62.28, 62.25, 62.10, 62.07, 62.03, 62.00, 61.85, 61.82, 61.78, 61.75, 61.60, 61.57, 61.53, 61.50, 39.3, 39.24, 39.19, 39.17, 12.39. 12.36 ; ^{31}P NMR (243 MHz, $CDCl_3$): δ 7.77; ^{19}F NMR (565 MHz, $CDCl_3$): δ –74.9, –75.0; HRMS (DART): m/z calcd. for $C_{39}H_{39}F_3N_2O_8P$ ($[M+H]^+$): 751.23961; found: 751.23647; IR (neat): 3059, 3032, 2359, 1709, 1652, 1491, 1465, 1448, 1362, 1275, 1175, 1074, 1028, 970, 903, 773, 747, 698, 633, 563, 467 cm^{-1}.

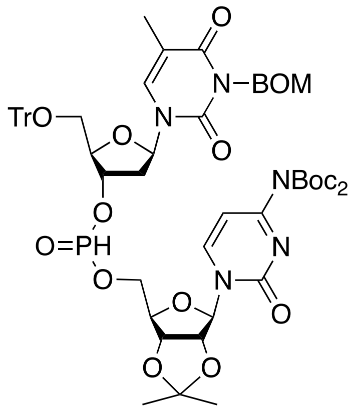
(2*R*,3*S*,5*R*)-5-(3-benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((((((2*R*,3*S*,5*R*)-5-(3-((benzyloxy)methyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((trityloxy)methyl)tetrahydrofuran-3-yl)oxy)(hydroxy)phosphaneyl)oxy)methyl)tetrahydrofuran-3-yl benzoate (**6a**)



White solid, 232.1 mg (70%), *dr* = 61:39

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04-7.97 (2H, m), 7.97-7.90 (2H, m), 7.68-7.20 (28H and 0.5H for P-H bond, m), 6.51-6.34 (2H and 0.5H for P-H bond, m), 5.59-5.34 (3H, m), 5.33-5.23 (1H, m), 4.71 (2H for one diastereomer, s), 4.68 (2H for the other diastereomer, s), 4.60-4.20 (4H, m), 3.63-3.51 (1H, m), 3.47-3.38 (1H, m), 2.71-2.57 (2H, m), 2.50-2.26 (2H, m), 2.00 (3H for one diastereomer, s), 1.98 (3H for the other diastereomer, s), 1.47 (3H for one diastereomer, s), 1.46 (3H for the other diastereomer, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6, 165.7, 165.6, 163.0, 162.3, 150.7, 149.09, 149.05, 142.72, 142.68, 137.7, 134.8, 133.6, 133.50, 133.47, 131.2, 130.1, 129.4, 128.9, 128.3, 127.99, 127.97, 127.8, 127.5, 127.3, 111.7, 111.6, 111.44, 111.42, 110.6, 87.52, 87.49, 85.2, 85.0, 84.9, 84.8, 84.7, 84.41, 84.37, 84.1, 84.0, 82.70, 82.65, 82.6, 82.5, 76.6, 76.5, 73.9, 73.8, 71.9, 71.8, 70.3, 70.2, 65.43, 65.39, 65.0, 64.9, 62.9, 53.3, 39.2, 39.03, 39.00, 36.9, 36.7, 12.3, 12.21, 12.19; ^{31}P NMR (243 MHz, $CDCl_3$): δ 9.29, 7.69; HRMS (ESI): m/z calcd. for $C_{61}H_{58}N_4O_{14}P$ ($[M+H]^+$): 1101.36871; found: 1101.37185; IR (neat): 3062, 1749, 1705, 1664, 1600, 1491, 1450, 1364, 1317, 1270, 1180, 1097, 1037, 1027, 968, 907, 773, 763, 708, 633, 563, 426, 403 cm^{-1}.

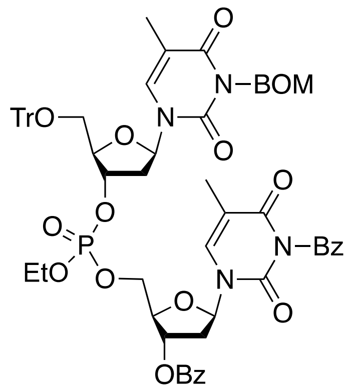
Tert-butyl (1-((3a*R*,4*R*,6*R*,6a*R*)-6-((((((2*R*,3*S*,5*R*)-5-(3-((benzyloxy)methyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((trityloxy)methyl)tetrahydrofuran-3-yl)oxy)(hydroxy)phosphaneyl)oxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)(*tert*-butoxycarbonyl)carbamate (**6b**)



White solid, 166.5 mg (49%), *dr* = 51:49

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.56-7.50 (2H, m), 7.48-7.20 (22H and 0.5H for P-H bond, m), 7.04 (1H for one diastereomer, d, *J* = 7.6 Hz), 7.03 (1H for the other diastereomer, d, *J* = 7.6 Hz), 6.46-6.40 (1H, m), 6.28 (0.5H for P-H bond of one diastereomer, s), 6.22 (0.5H for P-H bond of the other diastereomer, s), 5.52 (1H, d, *J* = 17.9 Hz), 5.49 (2H, s), 5.27-5.19 (1H, m), 5.16 (1H for one diastereomer, d, *J* = 6.2 Hz), 5.13 (1H for the other diastereomer, d, *J* = 6.2 Hz), 4.98-4.92 (1H for one diastereomer, m), 4.91-4.86 (1H for the other diastereomer, m), 4.71 (2H, s), 4.42-4.31 (2H and 1H for one diastereomer, m), 4.29-4.18 (1H and 1H for the other diastereomer, m), 3.55-3.45 (1H, m), 3.44-3.30 (1H, m), 2.65-2.55 (1H, m), 2.44-2.34 (1H, m), 1.553 (18H for one diastereomer, s), 1.546 (18H for the other diastereomer, s), 1.54 (3H, s), 1.454 (3H for one diastereomer, s), 1.448 (3H for the other diastereomer, s), 1.314 (3H for one diastereomer, s), 1.310 (3H for the other diastereomer, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.27, 163.25, 162.9, 153.7, 150.8, 149.2, 146.9, 146.7, 142.94, 142.92, 137.9, 133.94, 133.86, 128.5, 128.2, 128.0, 127.9, 127.6, 127.54, 127.50, 127.44, 127.42, 114.1, 114.0, 110.7, 110.6, 98.2, 98.1, 96.2, 87.6, 87.5, 85.1, 84.88, 84.86, 84.6, 84.50, 84.48, 84.3, 81.48, 81.45, 76.24, 76.21, 76.16, 76.1, 72.1, 70.5, 66.2, 66.1, 65.89, 65.85, 62.9, 60.3, 39.29, 39.27, 27.7, 27.6, 26.91, 26.89, 25.02, 24.97, 20.9, 14.1, 12.3; ^{31}P NMR (243 MHz, $CDCl_3$): δ 8.37, 8.12; HRMS (ESI): m/z calcd. for $C_{59}H_{68}N_5O_{16}P$ ($[M+H]^+$): 1134.44769; found: 1134.45125; IR (neat): 2985, 2929, 1777, 1744, 1709, 1668, 1560, 1491, 1450, 1395, 1370, 1318, 1260, 1211, 1155, 1074, 1037, 1028, 960, 904, 857, 787, 773, 747, 698, 633, 563, 418 cm^{-1}.

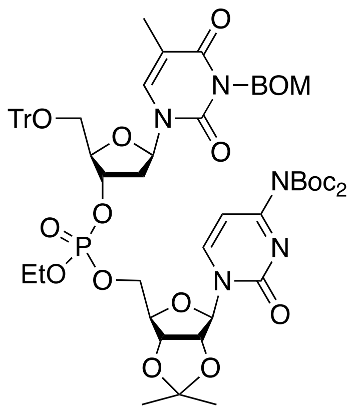
(2*R*,3*S*,5*R*)-5-(3-benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-(((((2*R*,3*S*,5*R*)-5-(3-((benzyloxy)methyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((trityloxy)methyl)tetrahydrofuran-3-yl)oxy)(ethoxy)phosphoryl)oxy)methyl)tetrahydrofuran-3-yl benzoate **(7a)**



White solid, 150.8 mg (44%), *dr* = 56:44

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (2H for one diastereomer, d, *J* = 6.9 Hz), 7.99 (2H for the other diastereomer, d, *J* = 6.9 Hz), 7.94 (2H for one diastereomer, d, *J* = 6.9 Hz), 7.93 (2H for the other diastereomer, d, *J* = 6.9 Hz), 7.66-7.20 (28H, m), 6.52-6.43 (2H, m), 5.60-5.40 (3H, m), 5.25-5.18 (1H, m), 4.71 (2H for one diastereomer, s), 4.68 (2H for the other diastereomer, s), 4.49-4.07 (6H, m), 3.59-3.52 (1H, m), 3.46-3.39 (1H, m), 2.72-2.67 (2H, m), 2.64 (1H for one diastereomer, dd, *J* = 5.5, 14.4 Hz), 2.59 (1H for the other diastereomer, dd, *J* = 5.5, 14.4 Hz), 2.49-2.40 (1H, m), 2.40-2.29 (1H, m), 2.004 (3H for one diastereomer, s), 1.995 (3H for the other diastereomer, s), 1.45 (3H, s), 1.38 (3H for one diastereomer, t, *J* = 6.9 Hz), 1.30 (3H for the other diastereomer, t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.65, 168.62, 165.8, 165.7, 163.13, 163.11, 162.44, 162.42, 150.8, 149.3, 149.2, 142.81, 142.80, 137.8, 134.9, 134.7, 133.72, 133.67, 133.6, 131.4, 130.3, 129.5, 129.0, 128.7, 128.6, 128.5, 128.4, 128.10, 128.09, 127.9, 127.5, 127.44, 127.42, 111.8, 111.6, 110.8, 110.7, 87.6, 84.9, 84.81, 84.80, 84.7, 84.4, 84.30, 84.29, 84.2, 82.9, 82.83, 82.80, 82.77, 78.83, 78.79, 78.73, 78.69, 77.3, 77.0, 76.7, 74.4, 72.02, 72.00, 70.4, 67.24, 67.21, 67.20, 67.17, 64.74, 64.69, 64.68, 64.6, 63.3, 63.2, 39.1, 39.03, 38.97, 38.9, 37.3, 37.0, 30.7, 16.1, 16.05, 16.01, 16.00, 12.4, 12.3; ^{31}P NMR (243 MHz, $CDCl_3$): δ -1.19, -1.57; HRMS (ESI): m/z calcd. for $C_{63}H_{62}N_4O_{15}P$ ($[M+H]^+$): 1145.39493; found: 1145.39645; IR (neat): 2982, 2938, 1749, 1705, 1652, 1600, 1491, 1448, 1395, 1364, 1317, 1268, 1180, 1158, 1097, 1070, 1033, 1015, 904, 823, 773, 763, 747, 698, 633, 558, 487 cm^{-1}.

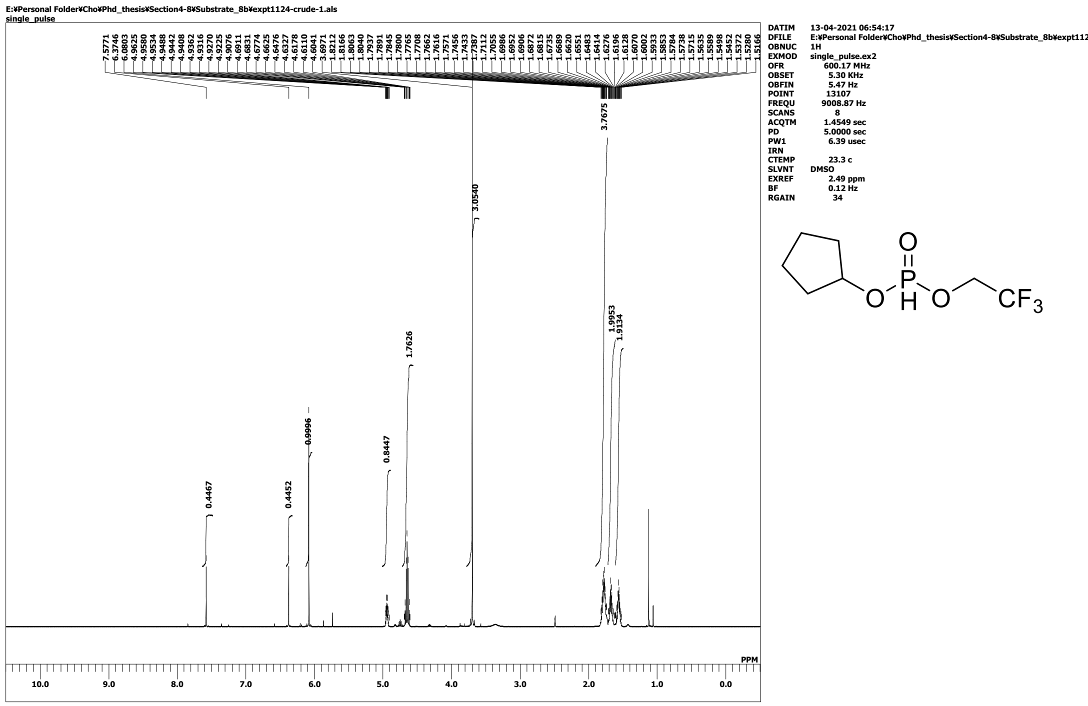
Tert-butyl (1-((3a*R*,4*R*,6*R*,6a*R*)-6-((((((2*R*,3*S*,5*R*)-5-(3-((benzyloxy)methyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-((trityloxy)methyl)tetrahydrofuran-3-yl)oxy)(ethoxy)phosphoryl)oxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)(*tert*-butoxycarbonyl)carbamate (**7b**)



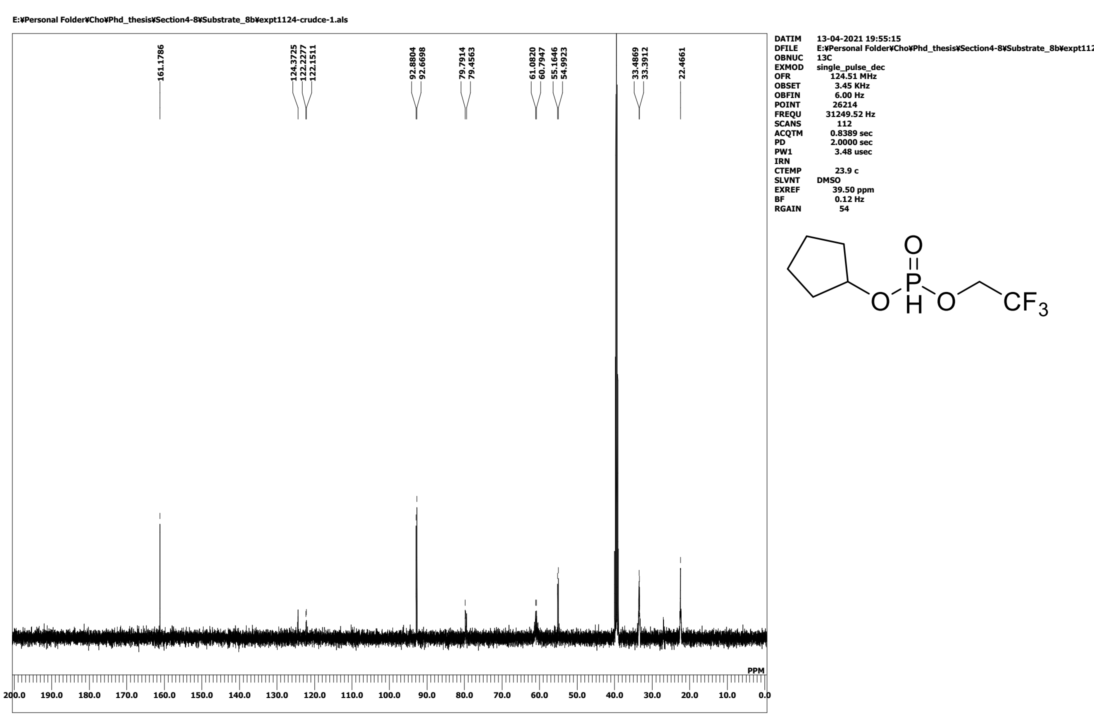
White solid, 136.7 mg (37%), *dr* = 61:39

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (1H for one diastereomer, d, *J* = 7.9 Hz), 7.53 (1H for one diastereomer, d, *J* = 6.4 Hz), 7.52 (1H for the other diastereomer, d, *J* = 6.9 Hz), 7.42-7.36 (9H, m), 7.35-7.22 (12H, m), 7.04 (1H for one diastereomer, d, *J* = 7.3 Hz), 6.99 (1H for the other diastereomer, d, *J* = 7.3 Hz), 6.47-6.40 (1H, m), 5.57 (1H for one diastereomer, s), 5.52 (1H for the other diastereomer, s), 5.49 (2H, s), 5.19-5.06 (2H, m), 4.91 (1H for one diastereomer, d, *J* = 6.4, 4.1 Hz), 4.87 (1H for the other diastereomer, d, *J* = 6.4, 4.1 Hz), 4.71 (2H, s), 4.43-4.23 (4H, m), 4.14-3.98 (4H, m), 3.52-3.43 (1H,m), 3.43-3.35 (1H, m), 2.71-2.58 (1H, m), 2.42-2.32 (1H, m), 1.55 (21H, s), 1.45-1.20 (9H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4, 162.95, 162.92, 153.80, 153.77, 150.9, 149.28, 149.27, 146.5, 146.4, 143.1, 143.0, 138.0, 134.0, 128.6, 128.3, 128.0, 127.65, 127.58, 127.5, 114.11, 114.09, 110.74, 110.70, 97.8, 97.7, 96.15, 96.09, 87.6, 87.5, 87.4, 85.18, 85.16, 85.01, 84.97, 84.70, 84.66, 84.42, 84.38, 81.48, 81.45, 78.31, 78.26, 78.2, 78.1, 77.2, 72.2, 70.5, 69.5, 67.84, 67.79, 67.7, 64.61, 64.56, 64.5, 64.4, 63.3, 53.7, 39.3, 39.24, 39.16, 39.1, 31.7, 30.9, 29.2, 27.8, 27.6, 27.0, 25.12, 25.10, 16.07, 16.06, 16.02, 16.00, 12.38, 12.36; ^{31}P NMR (202 MHz, $CDCl_3$): δ -1.44, -1.62; HRMS (ESI): m/z calcd. for $C_{61}H_{73}N_5O_{17}P$ ($[M+H]^+$): 1178.47390; found: 1178.47235; IR (neat): 2026, 2856, 1779, 1744, 1711, 1527, 1491, 1450, 1371, 1321, 1261, 1212, 1157, 1127, 1093, 1067, 1023, 963, 858, 788, 773, 747, 700, 633, 567, 513 cm^{-1}.

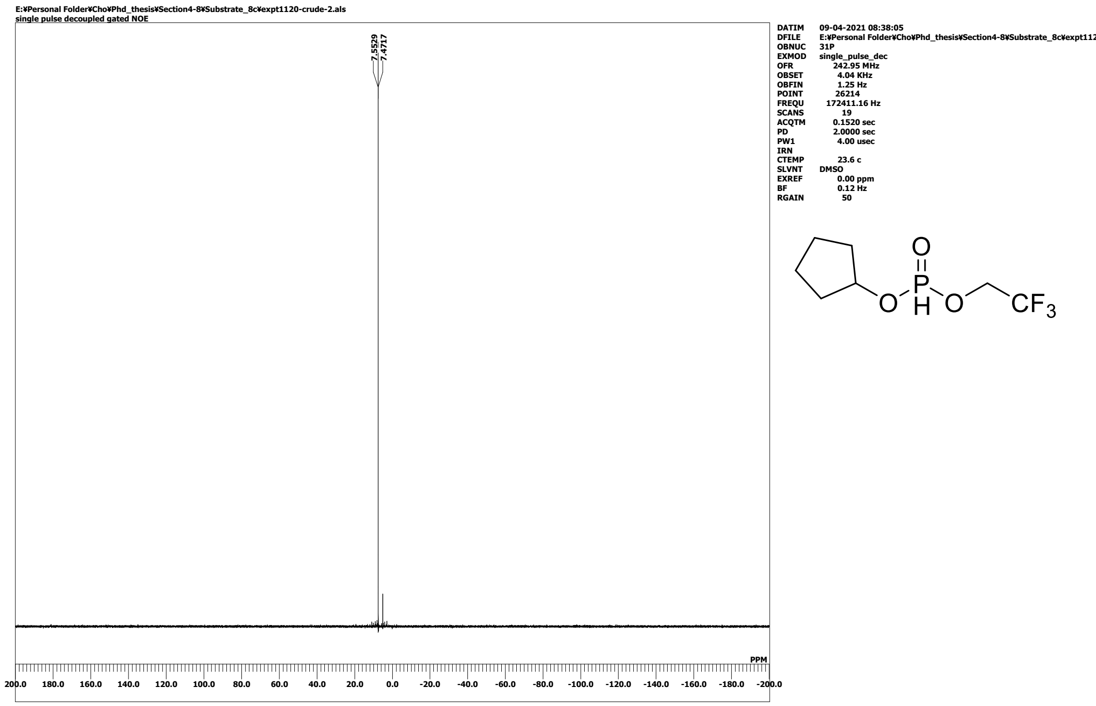
^{1}H NMR (600 MHz, DMSO-d_6) of **3b**



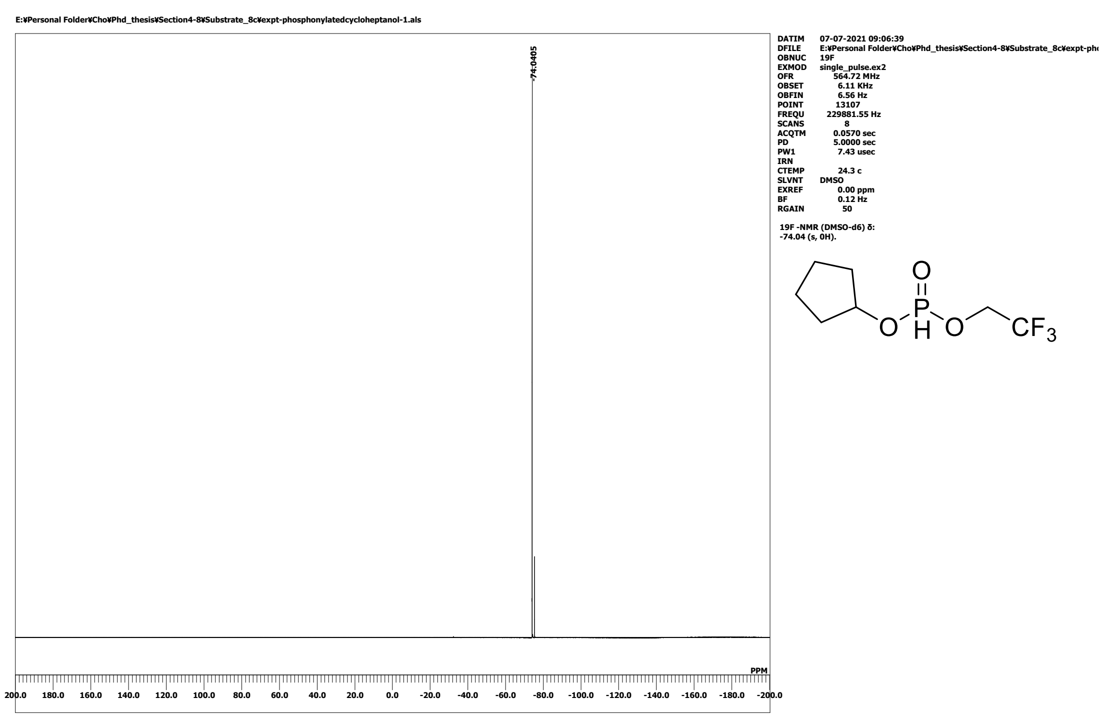
^{13}C NMR (150 MHz, DMSO-d_6) of **3b**



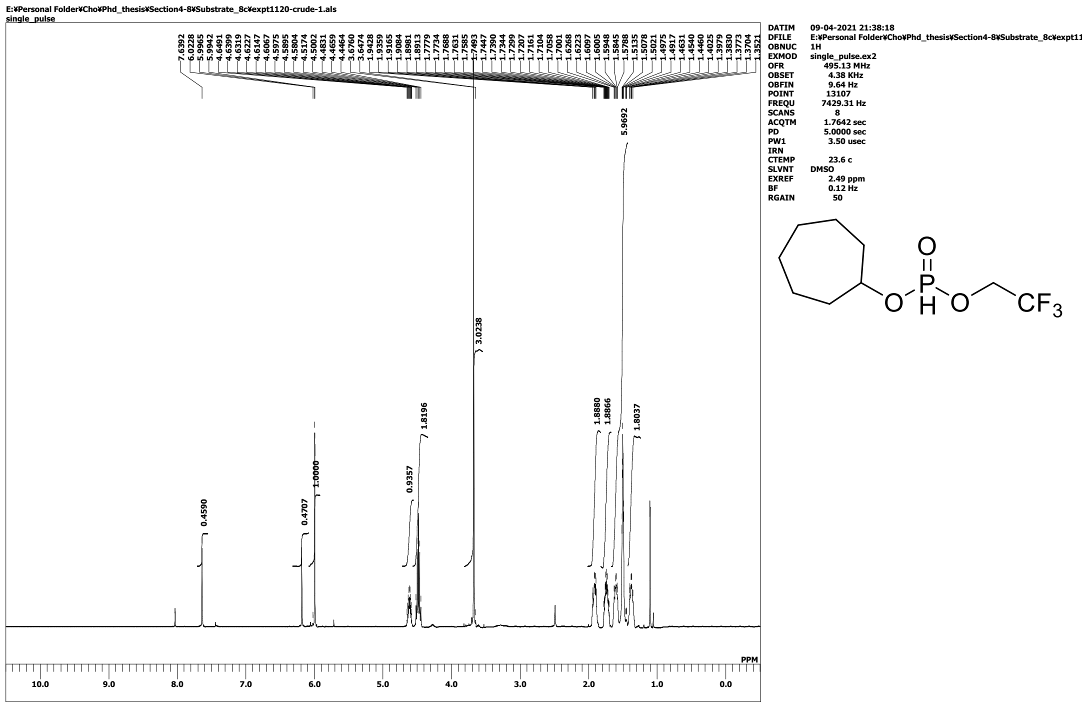
^{31}P NMR (243 MHz, DMSO-d_6) of **3b**



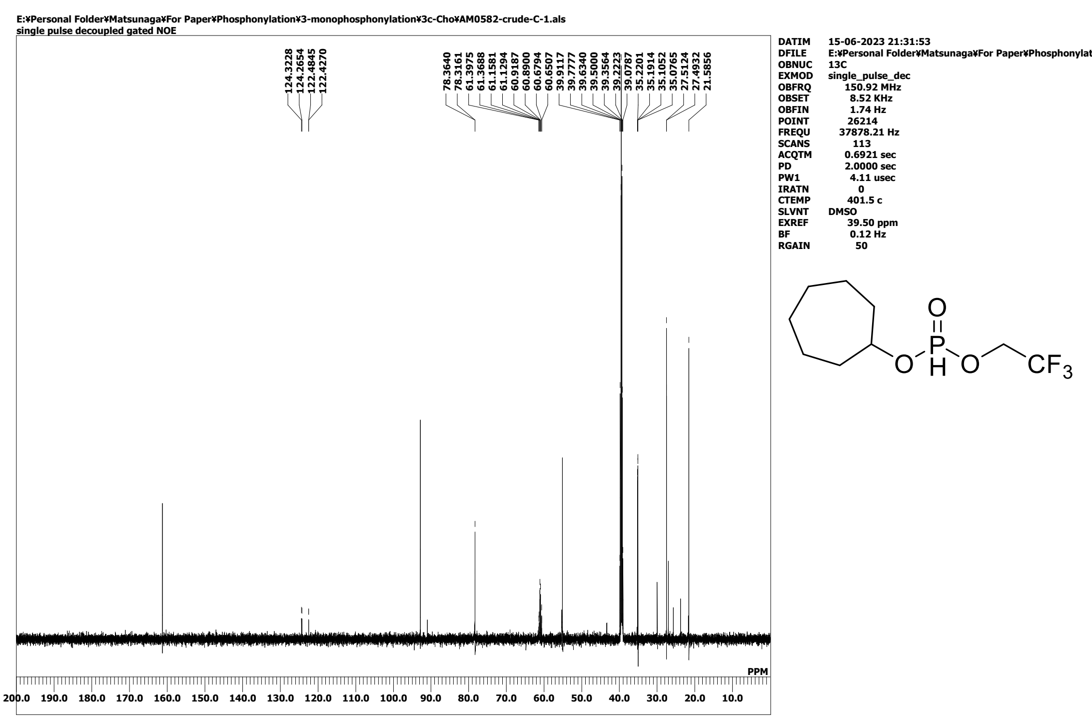
^{19}F NMR (565 MHz, DMSO-d_6) of **3b**



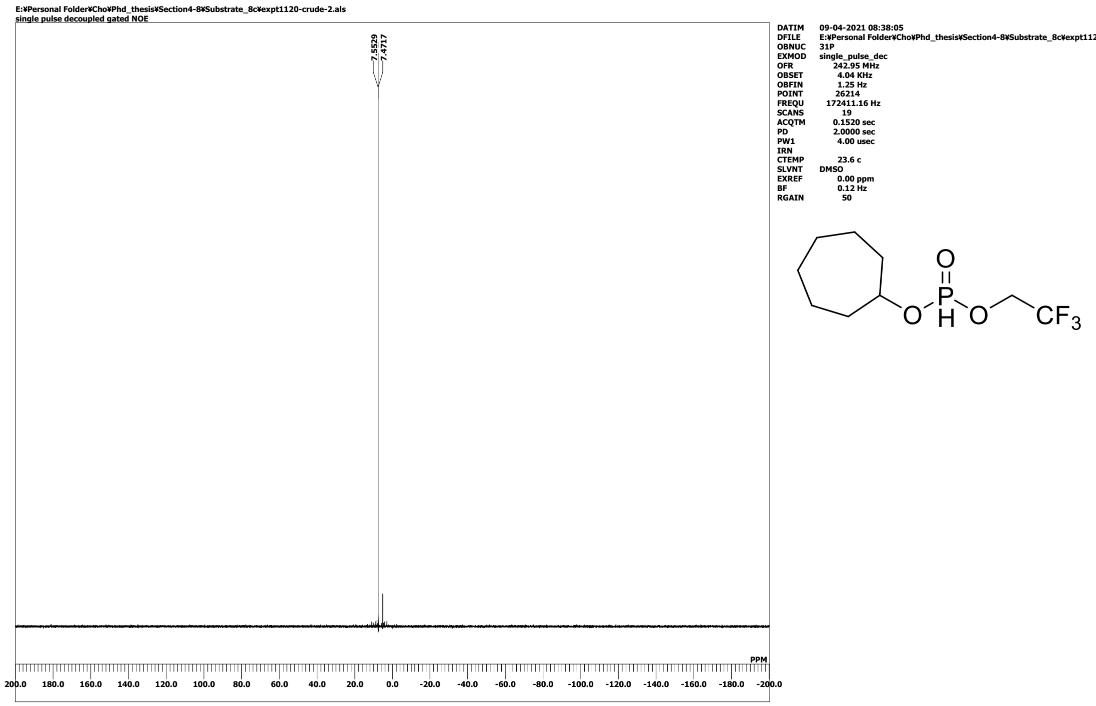
^{1}H NMR (500 MHz, DMSO-d_6) of **3c**



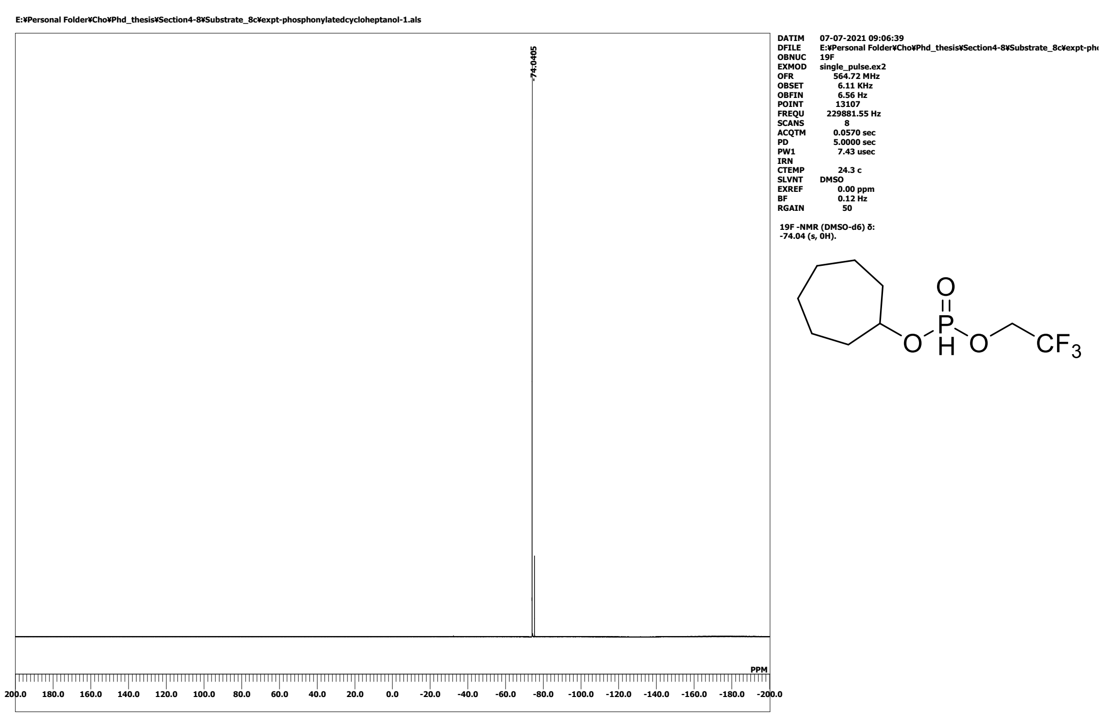
^{13}C NMR (151 MHz, DMSO-d_6) of **3c**



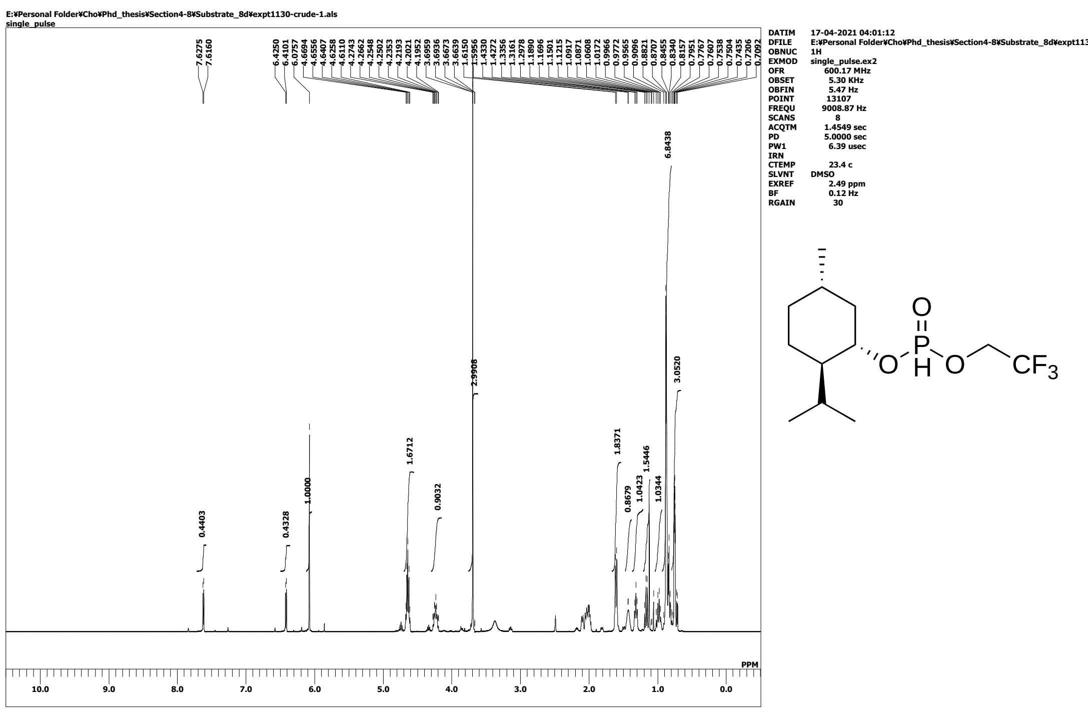
^{31}P NMR (243 MHz, DMSO-d_6) of **3c**



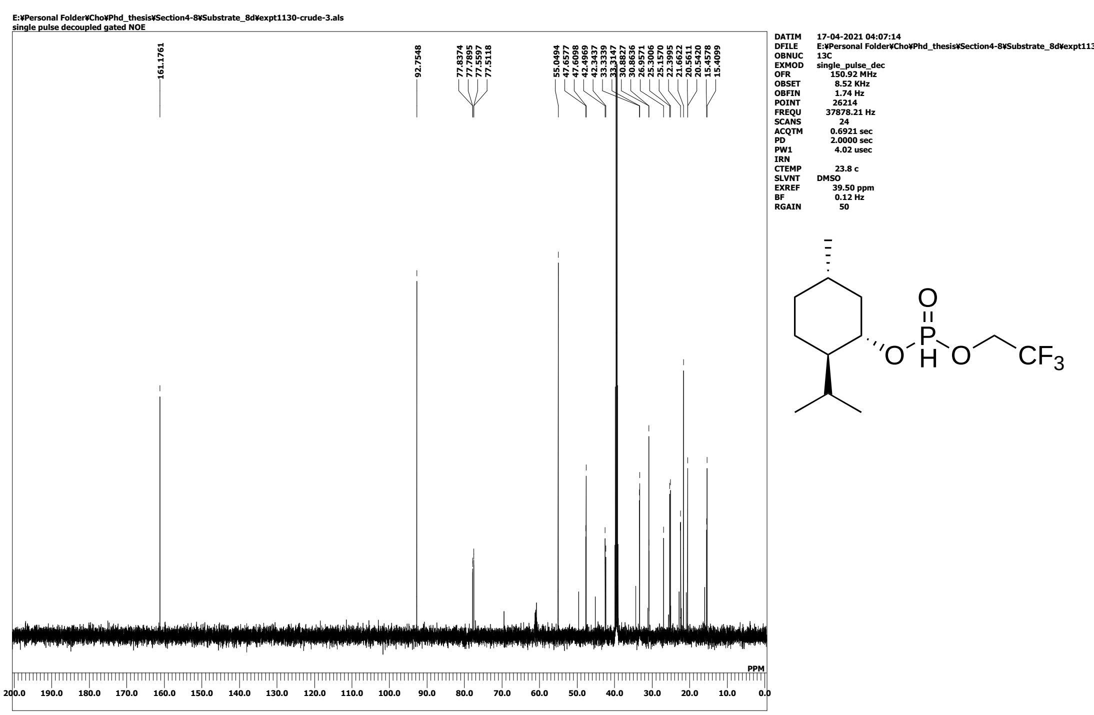
^{19}F NMR (565 MHz, DMSO-d_6) of **3c**



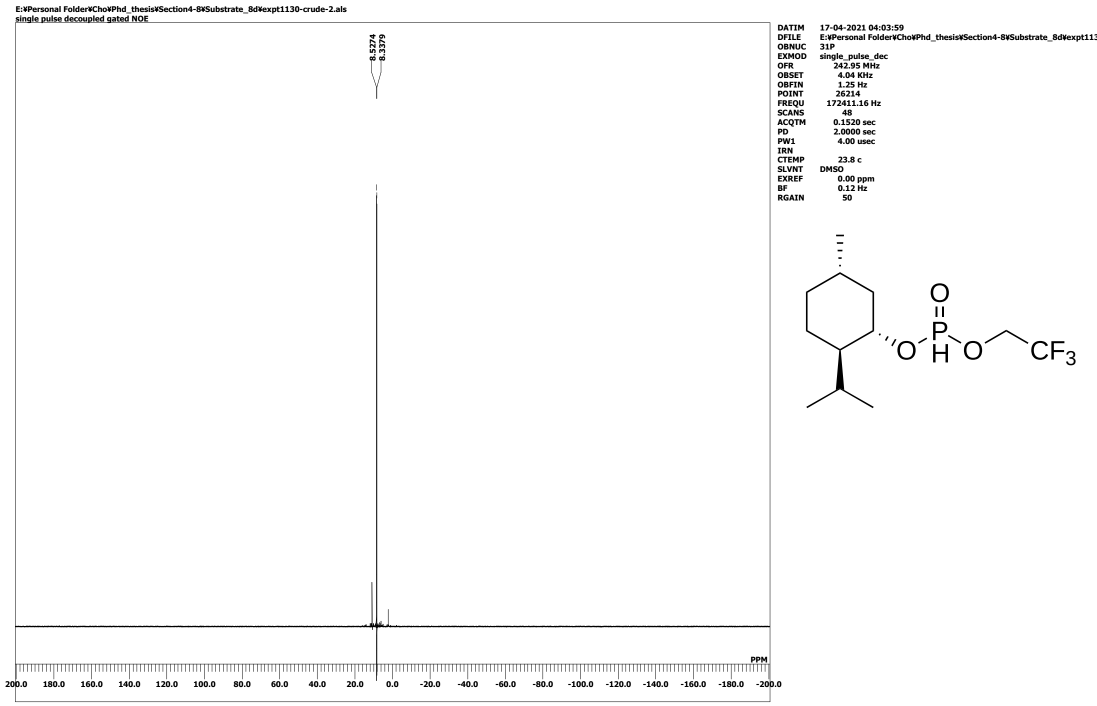
^{1}H NMR (600 MHz, DMSO-d_6) of **3d**



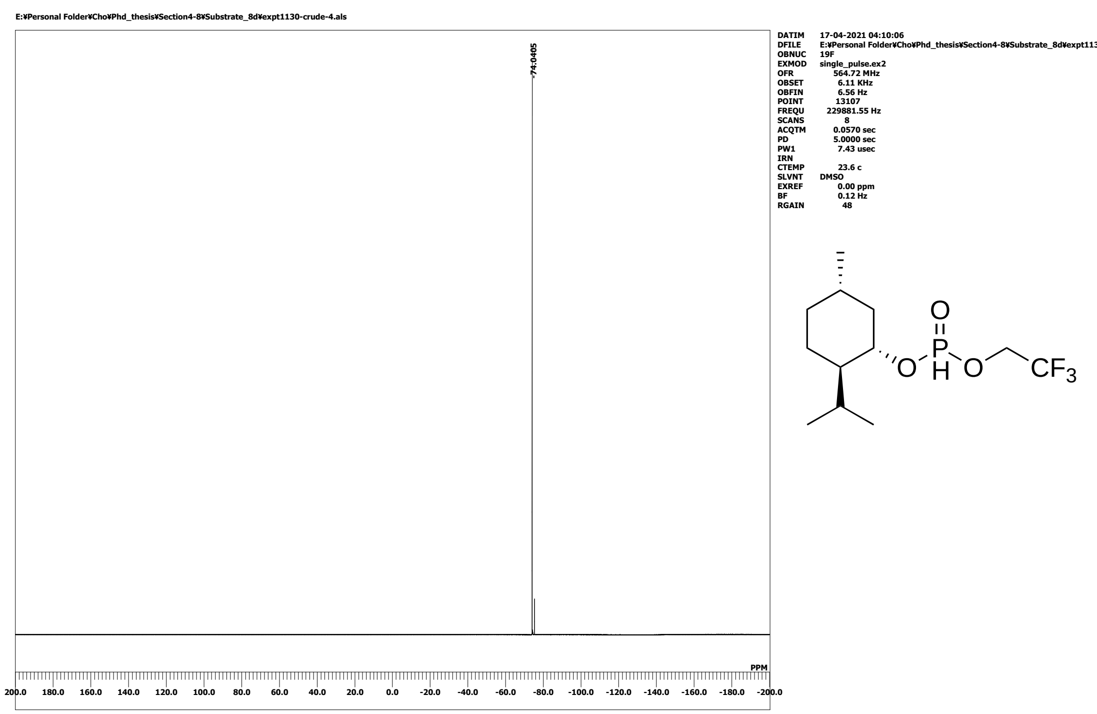
^{13}C NMR (151 MHz, DMSO-d_6) of **3d**



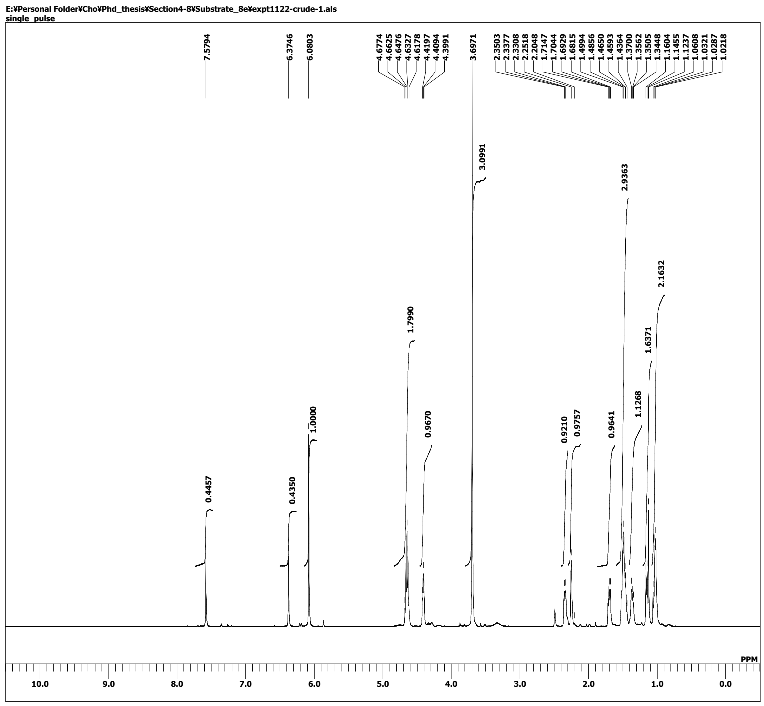
^{31}P NMR (243 MHz, DMSO-d_6) of **3d**

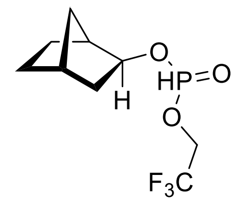


^{19}F NMR (565 MHz, DMSO-d_6) of **3d**

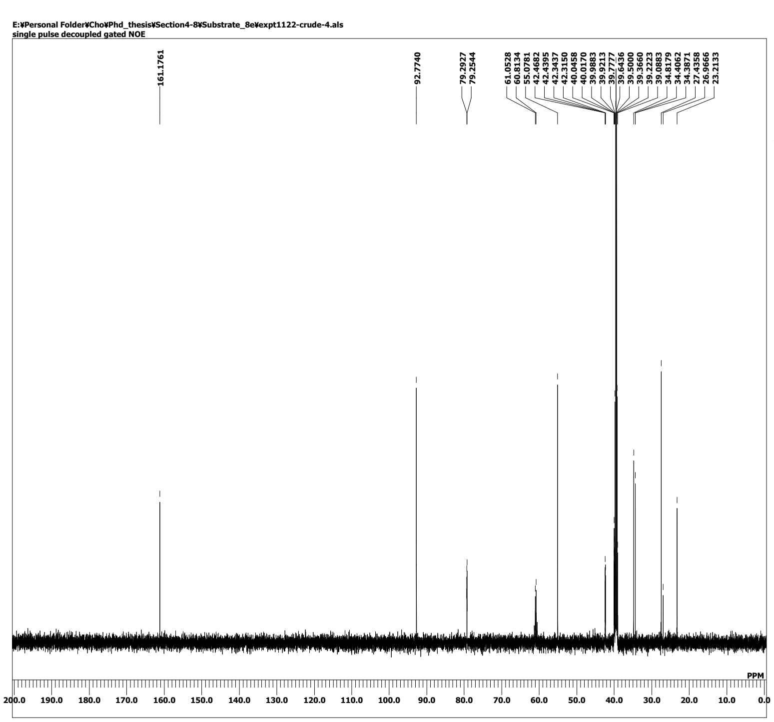


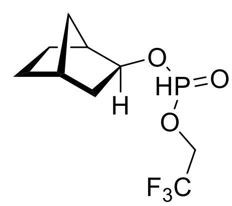
^{1}H NMR (600 MHz, DMSO-d_6) of **3e**



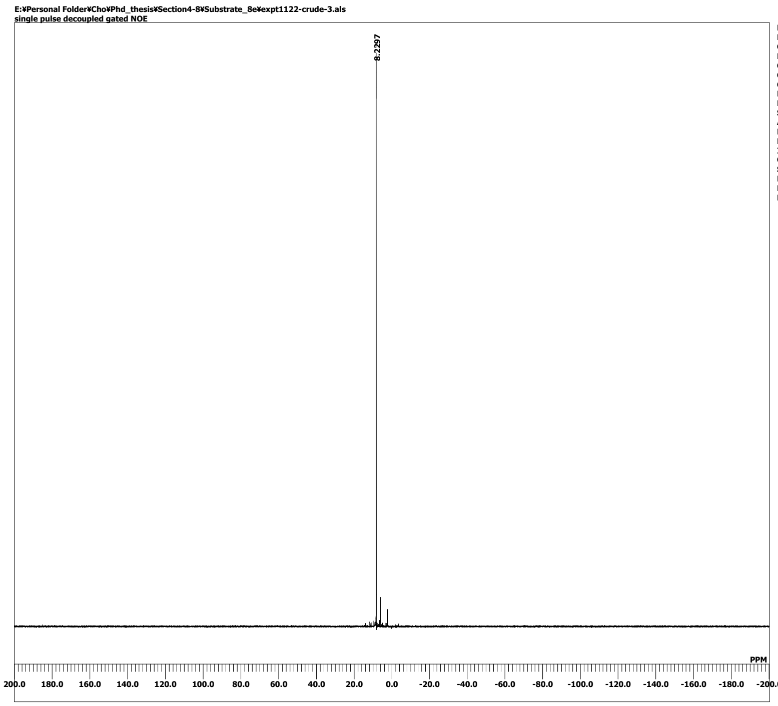


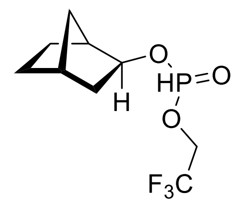
^{13}C NMR (151 MHz, DMSO-d_6) of **3e**



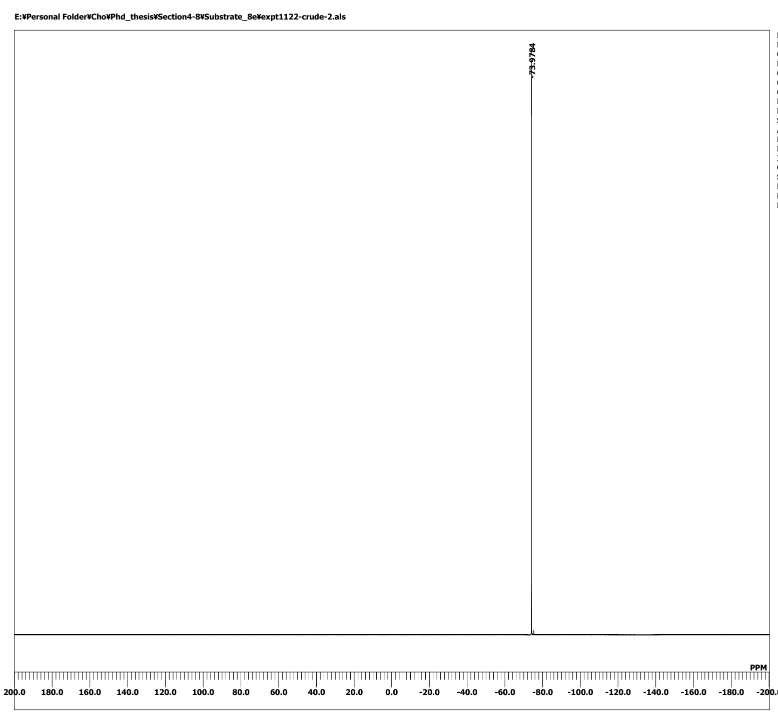


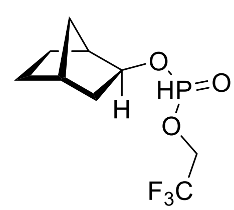
^{31}P NMR (243 MHz, DMSO-d_6) of **3e**



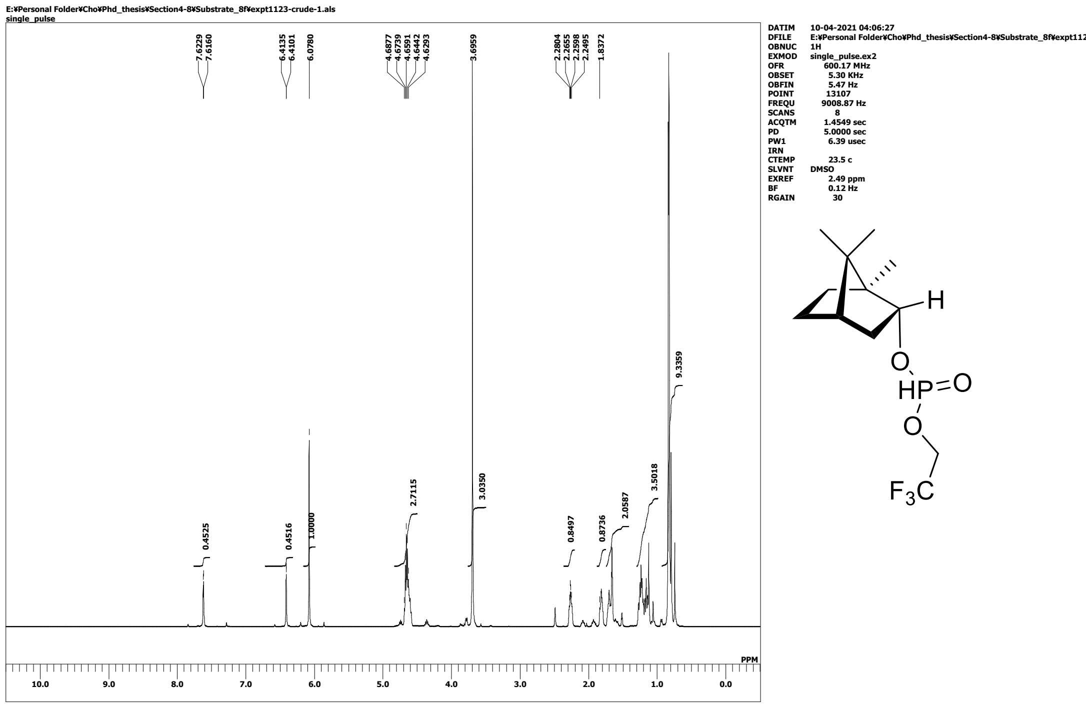


^{19}F NMR (565 MHz, DMSO-d_6) of **3e**

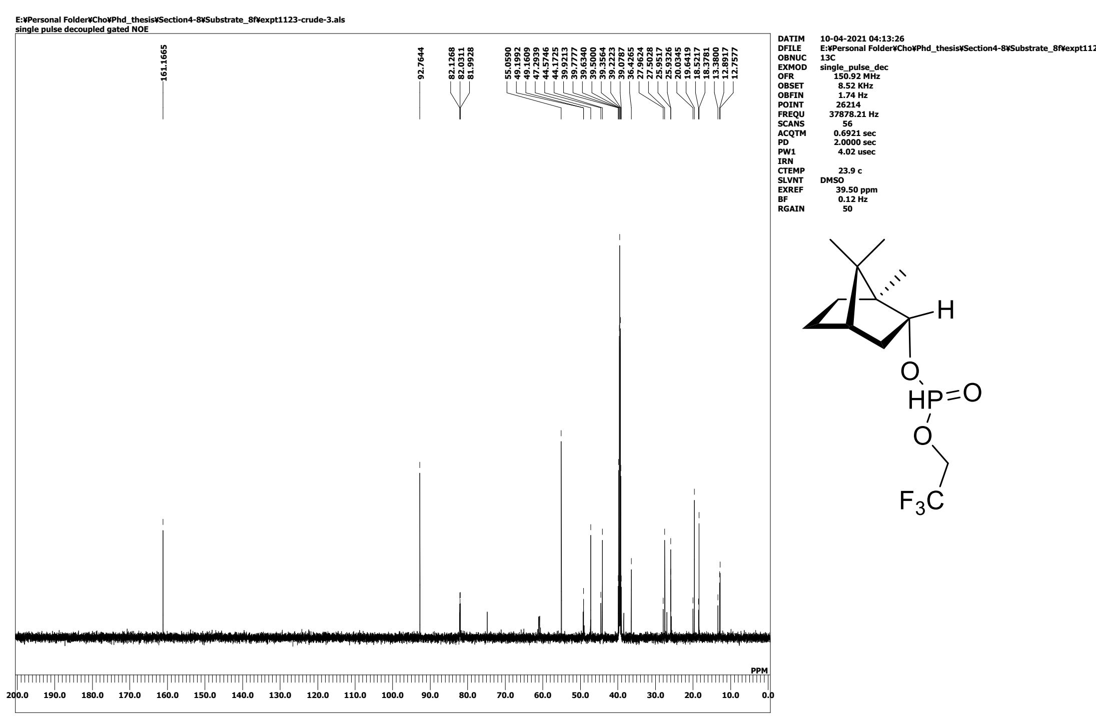




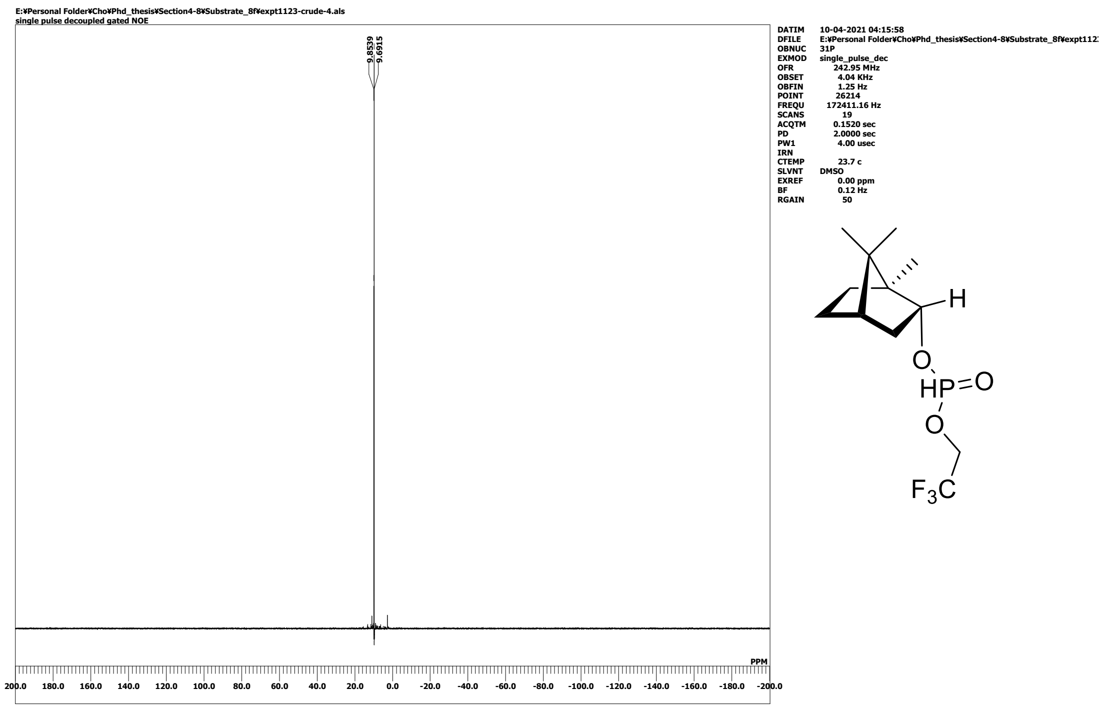
^{1}H NMR (600 MHz, DMSO-d_6) of **3f**



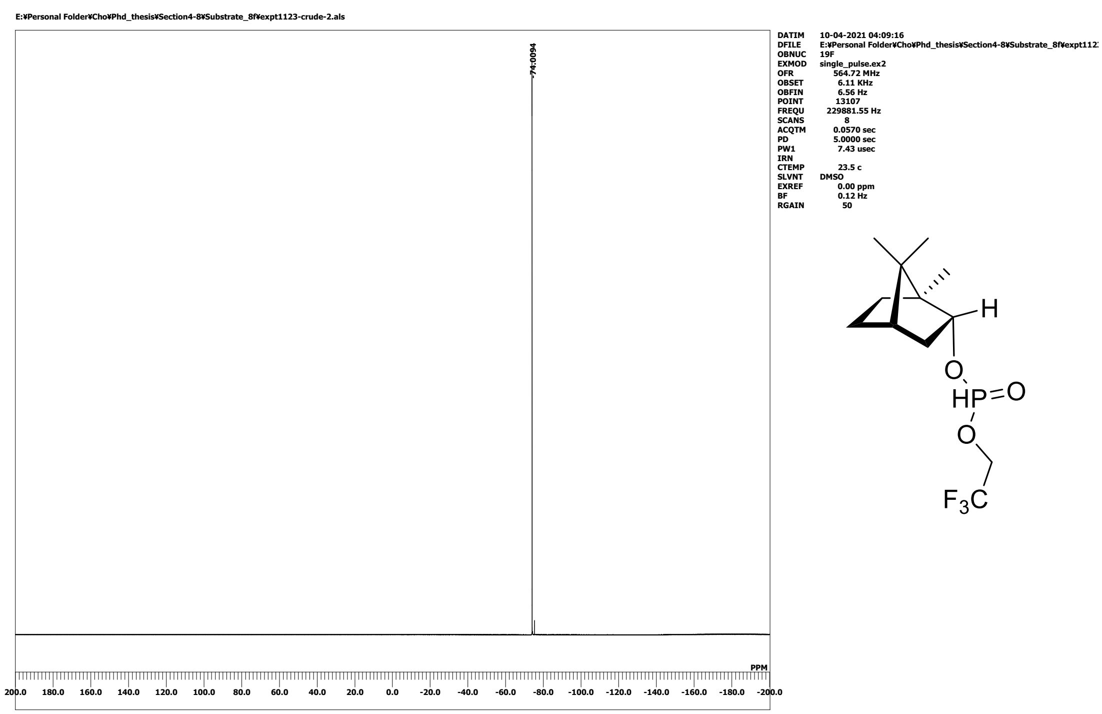
^{13}C NMR (151 MHz, DMSO-d_6) of **3f**



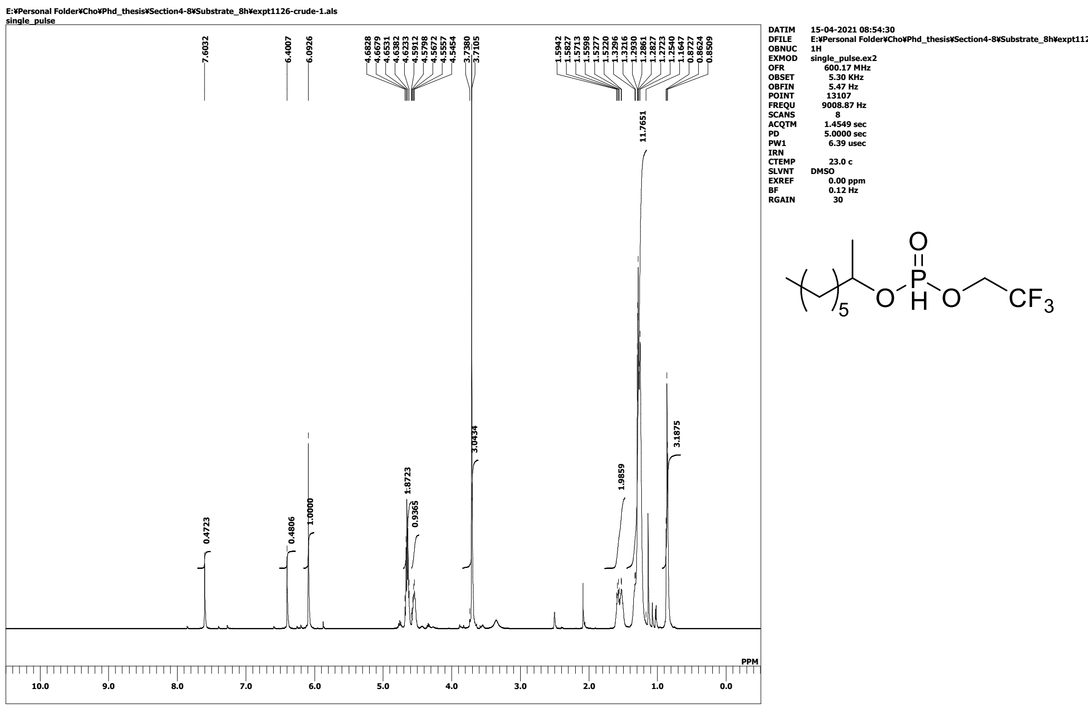
^{31}P NMR (243 MHz, DMSO-d_6) of **3f**



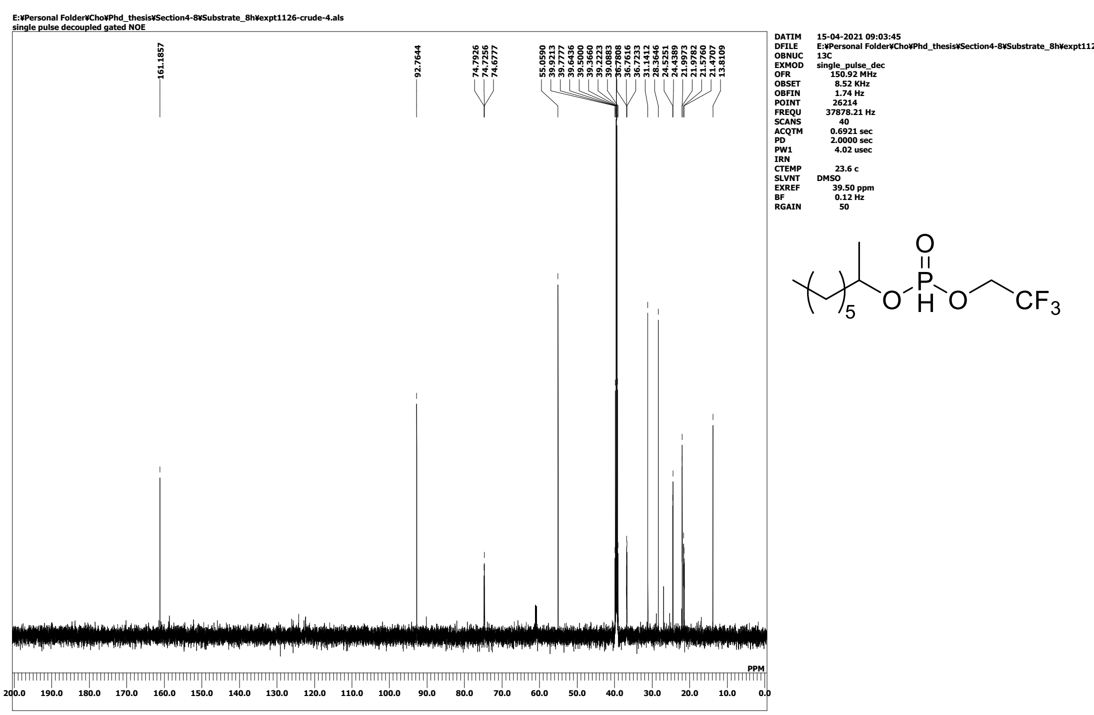
^{19}F NMR (565 MHz, DMSO-d_6) of **3f**



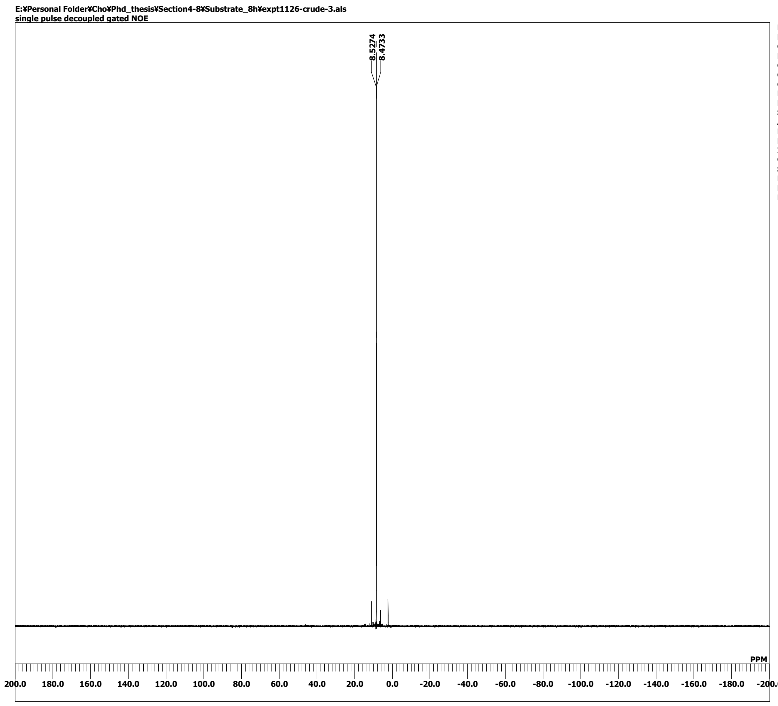
^{1}H NMR (600 MHz, DMSO-d_6) of **3g**

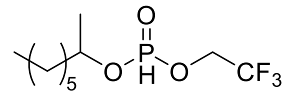


^{13}C NMR (151 MHz, DMSO-d_6) of **3g**

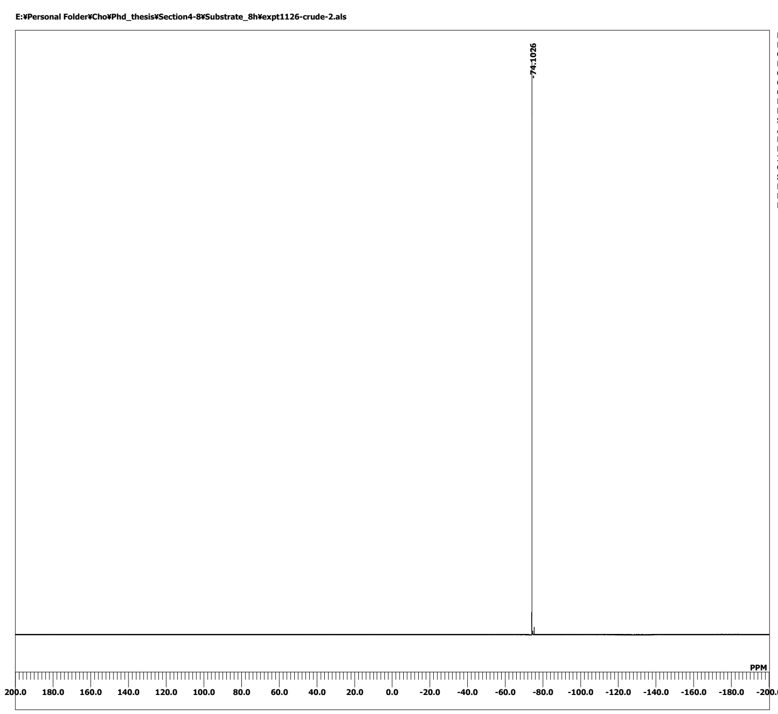


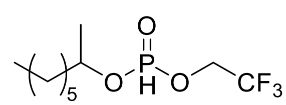
^{31}P NMR (243 MHz, DMSO-d_6) of **3g**



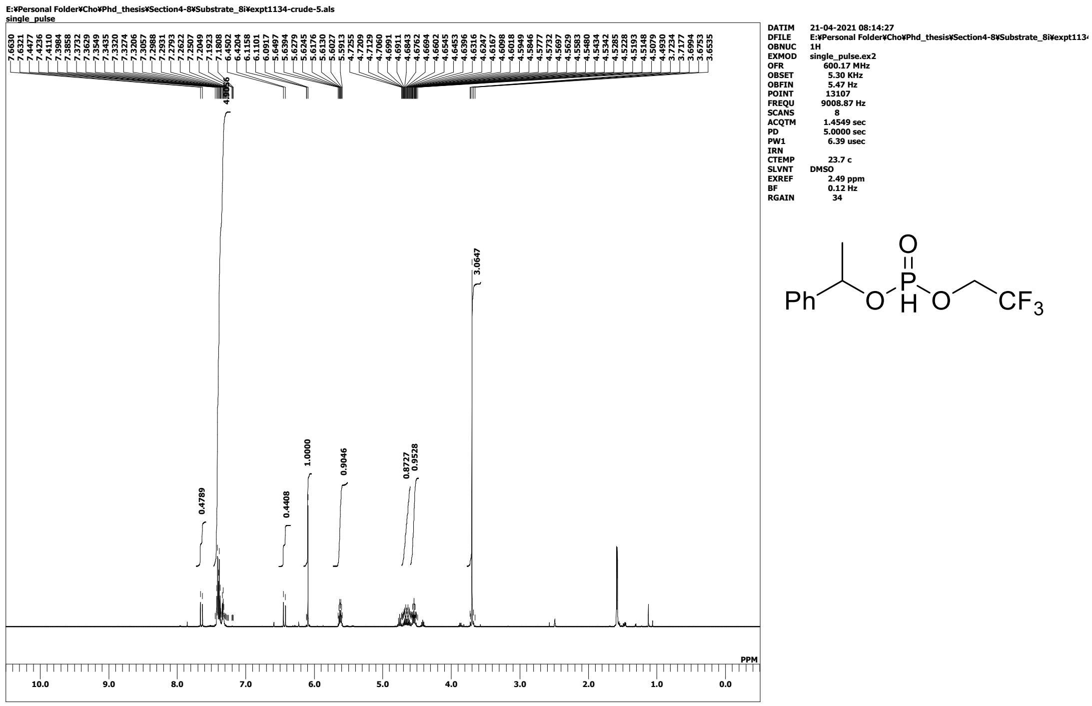


^{19}F NMR (565 MHz, DMSO-d_6) of **3g**

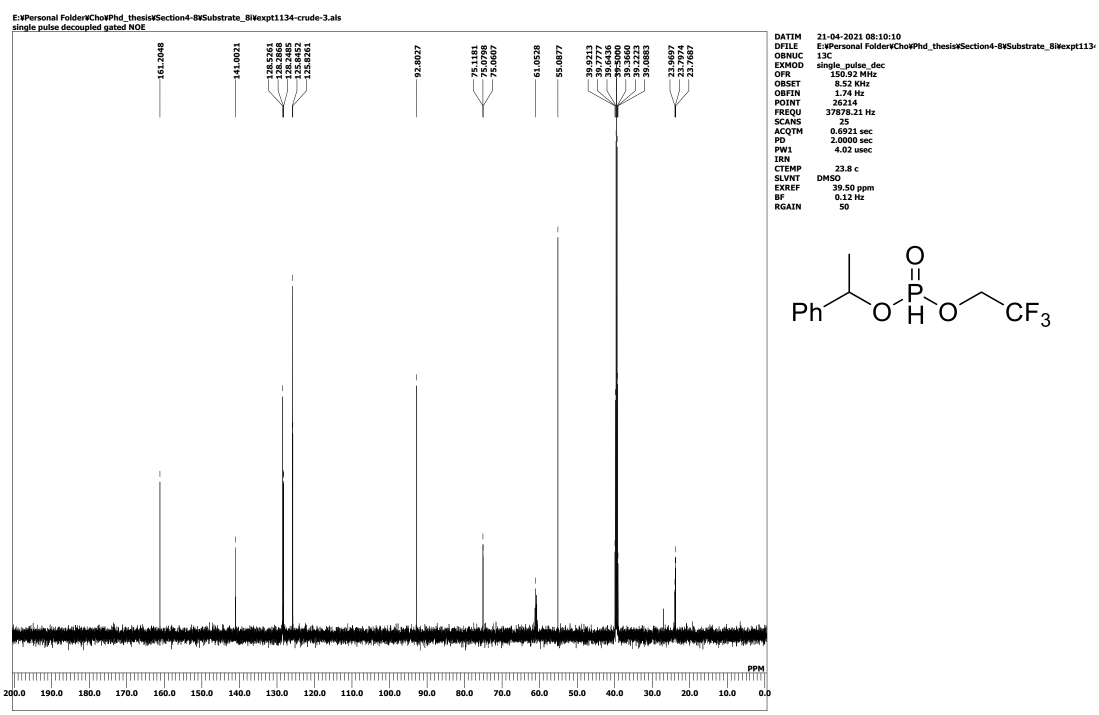




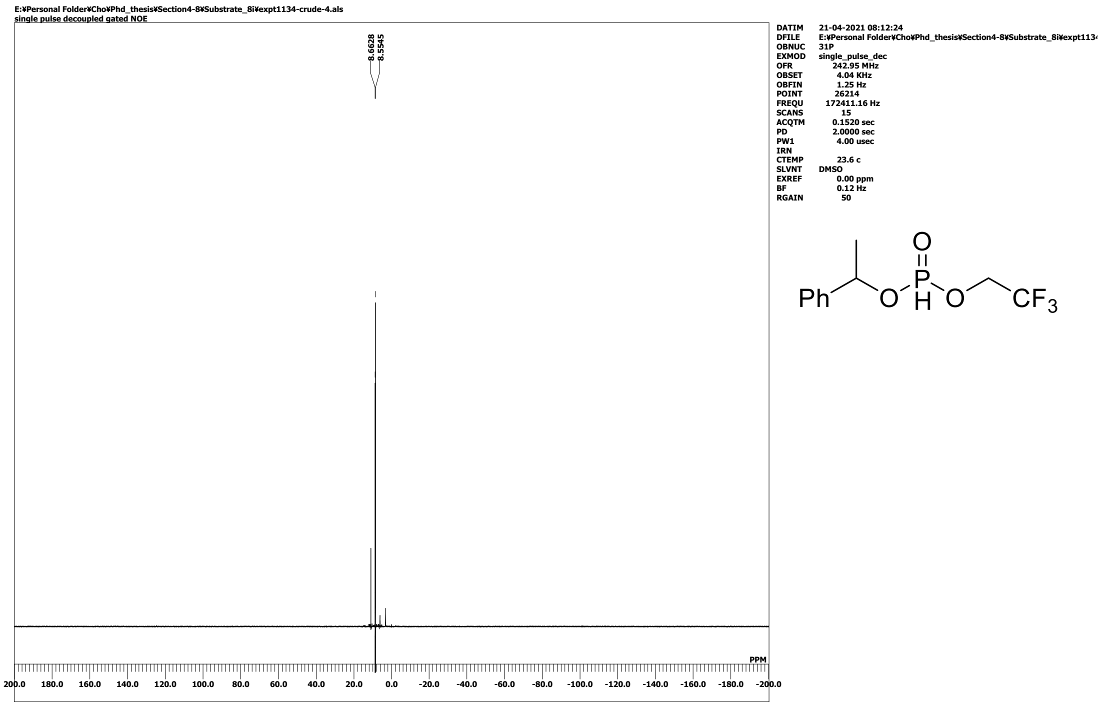
^{1}H NMR (600 MHz, DMSO-d_6) of **3h**



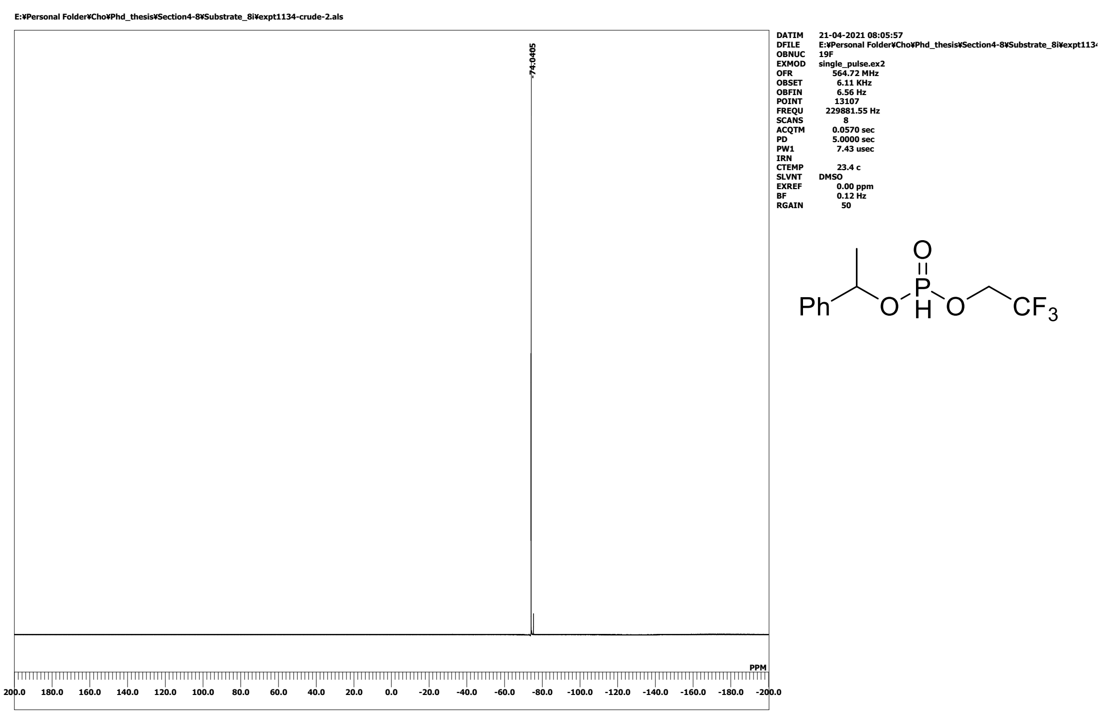
^{13}C NMR (151 MHz, DMSO-d_6) of **3h**



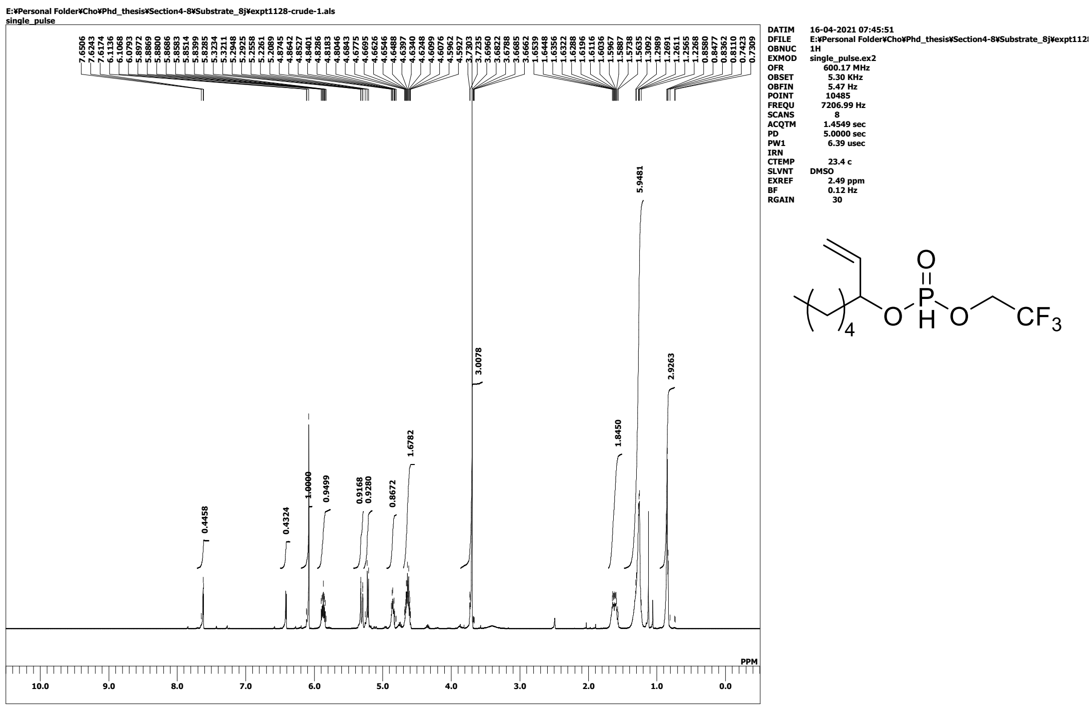
^{31}P NMR (243 MHz, DMSO-d_6) of **3h**



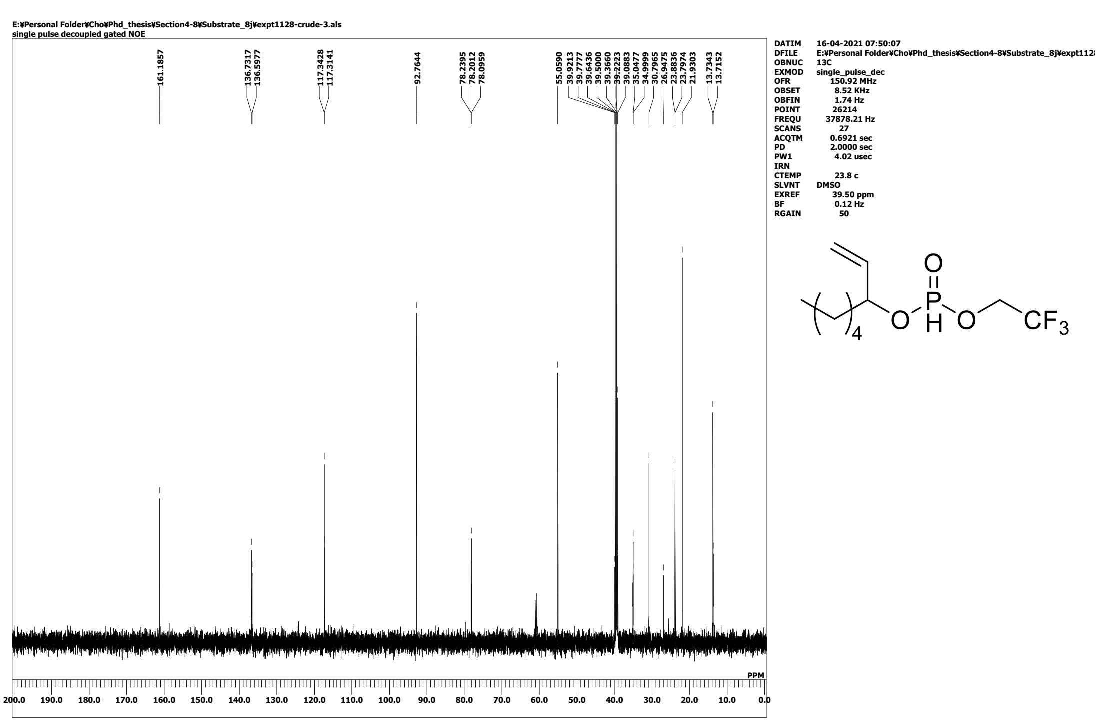
^{19}F NMR (565 MHz, DMSO-d_6) of **3h**



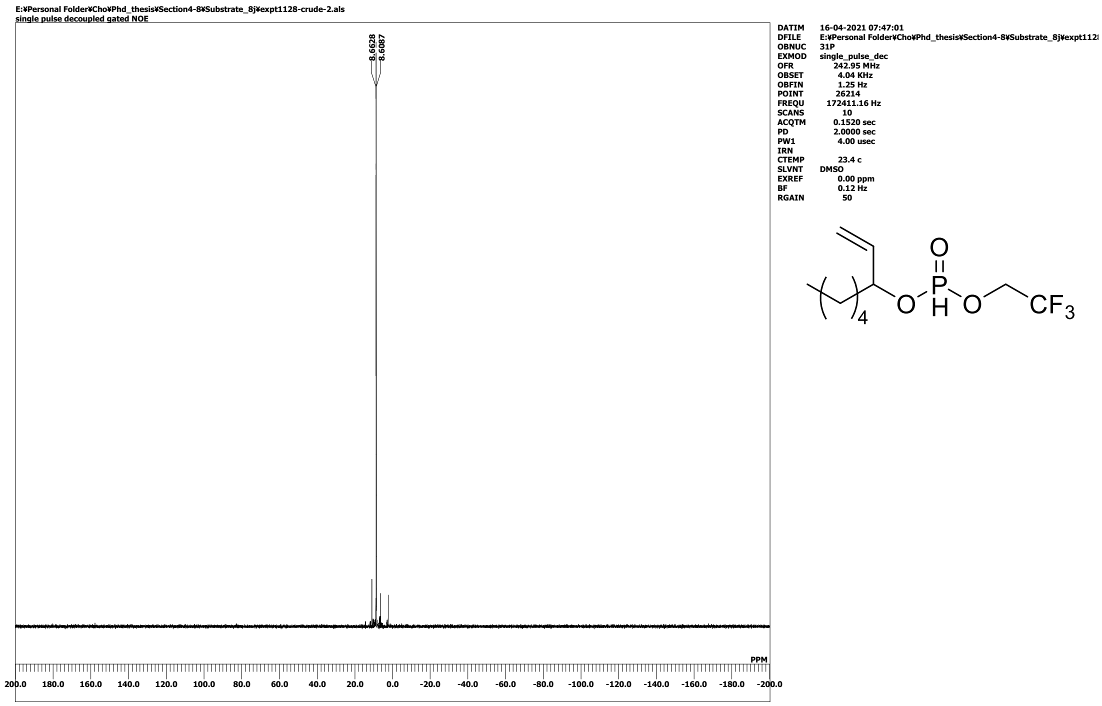
^{1}H NMR (600 MHz, DMSO-d_6) of **3i**



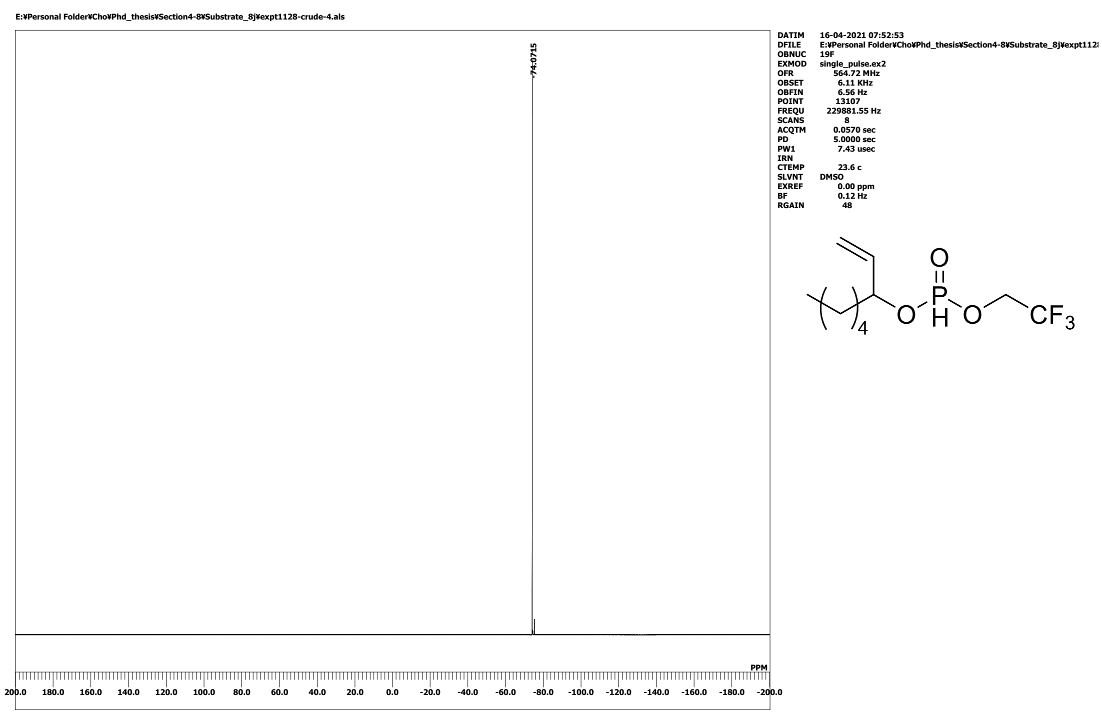
^{13}C NMR (151 MHz, DMSO-d_6) of **3i**



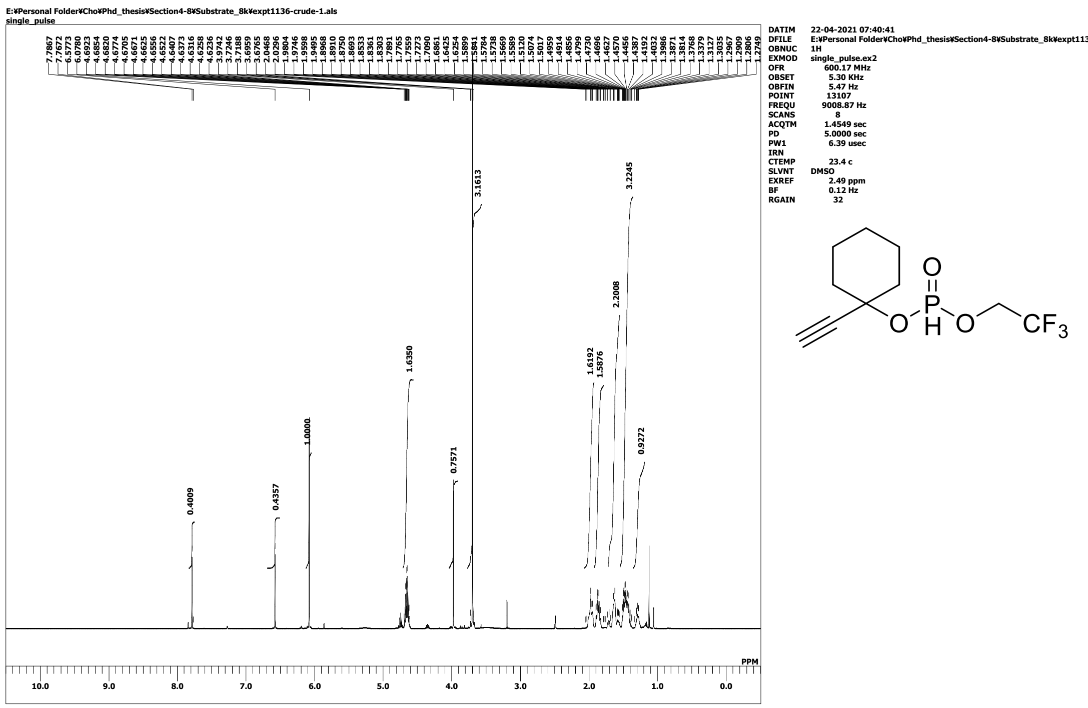
^{31}P NMR (243 MHz, DMSO-d_6) of **3i**



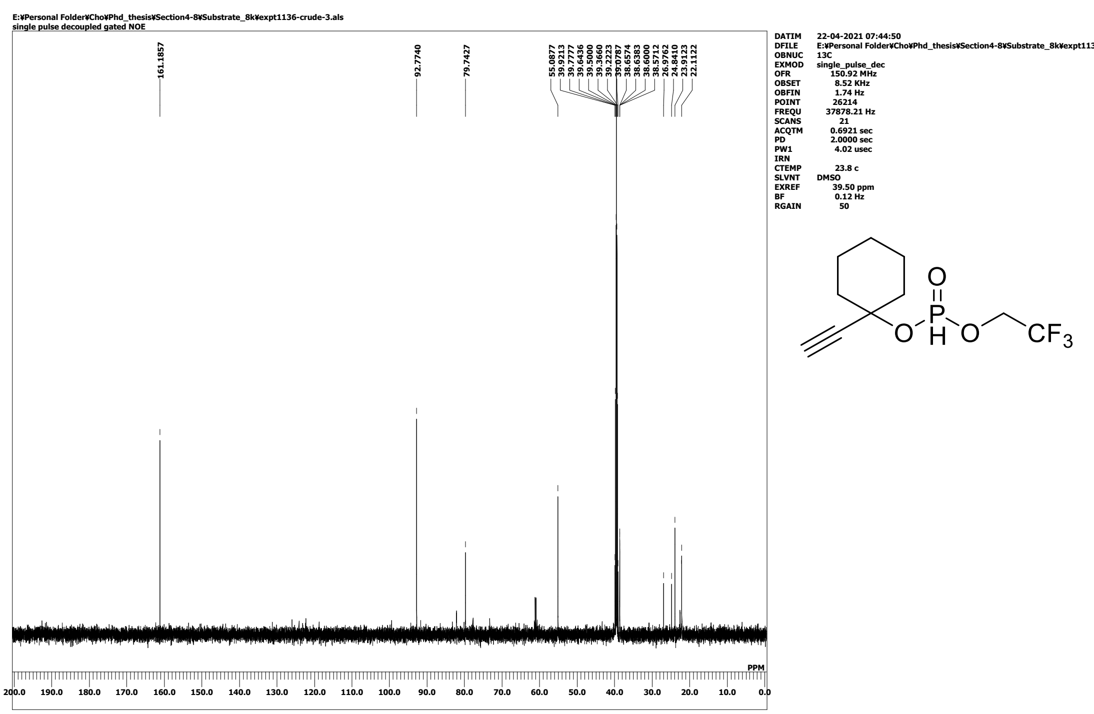
^{19}F NMR (565 MHz, DMSO-d_6) of **3i**



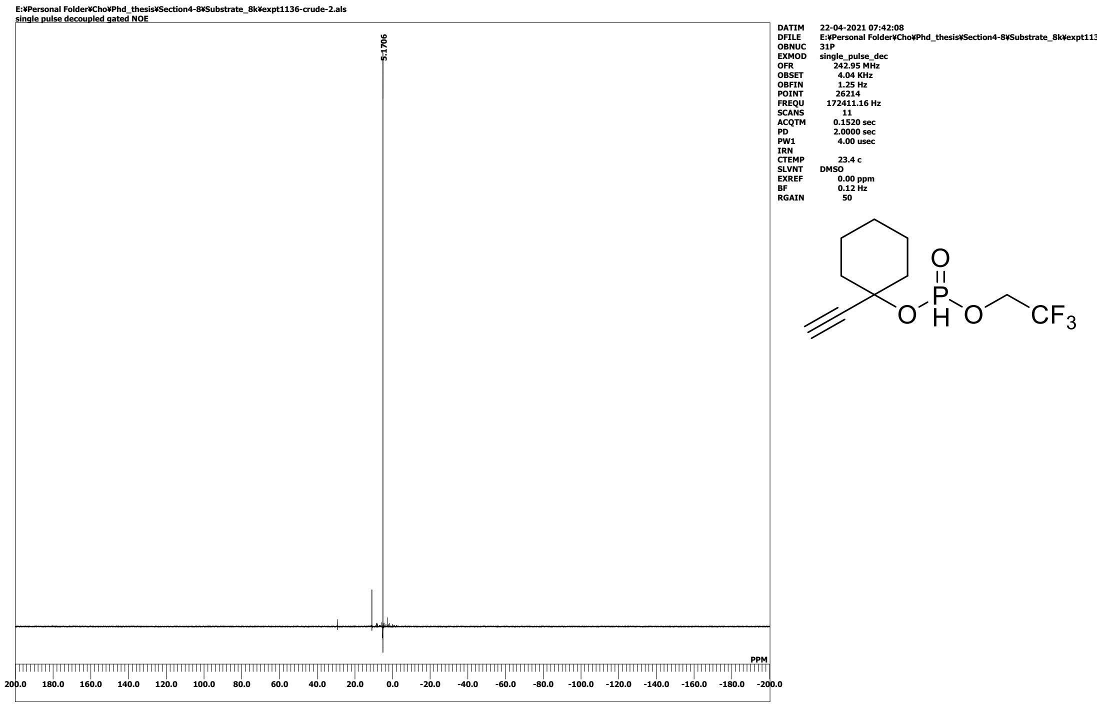
^{1}H NMR (600 MHz, DMSO-d_6) of **3j**



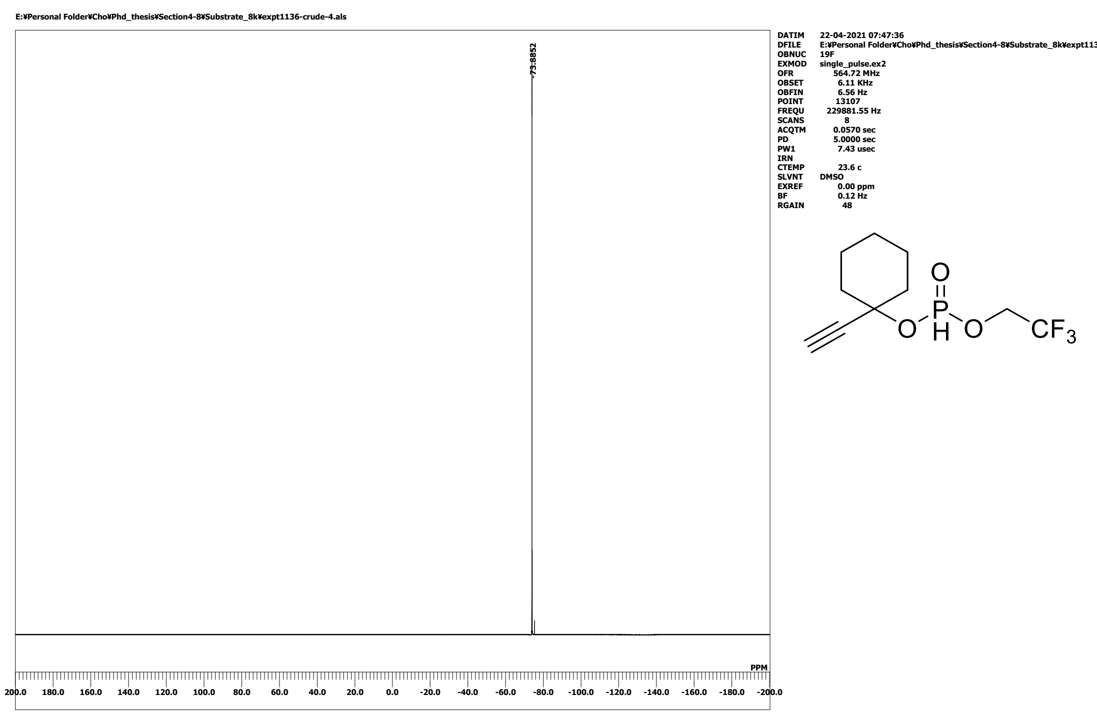
^{13}C NMR (151 MHz, DMSO-d_6) of **3j**



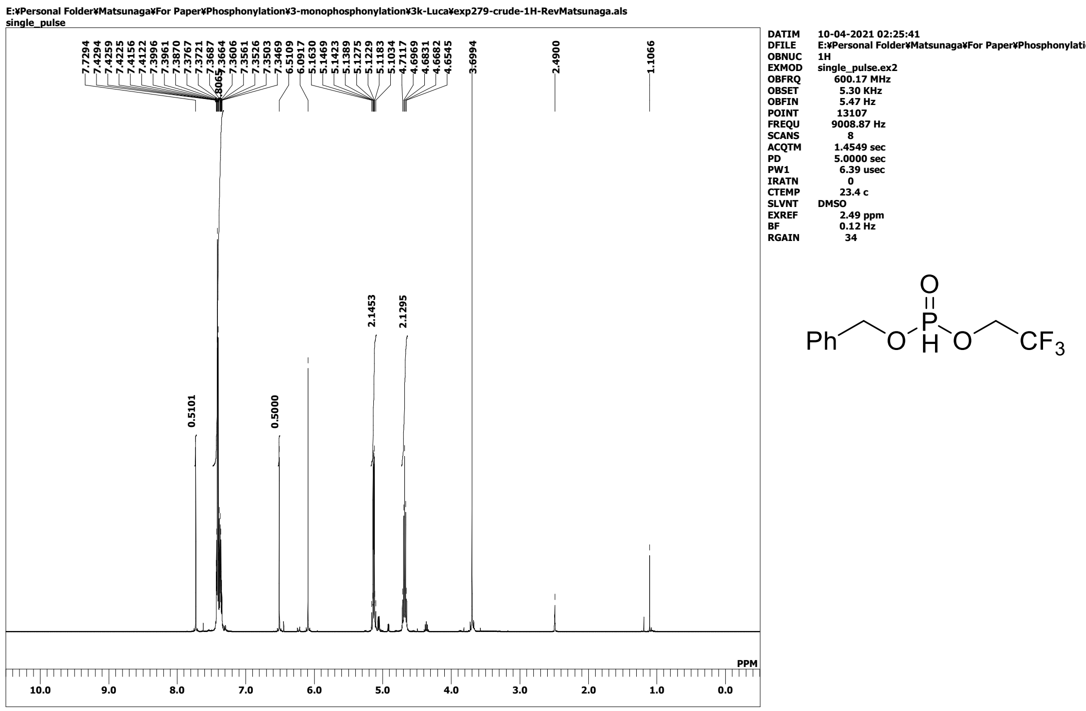
^{31}P NMR (243 MHz, DMSO-d_6) of **3j**



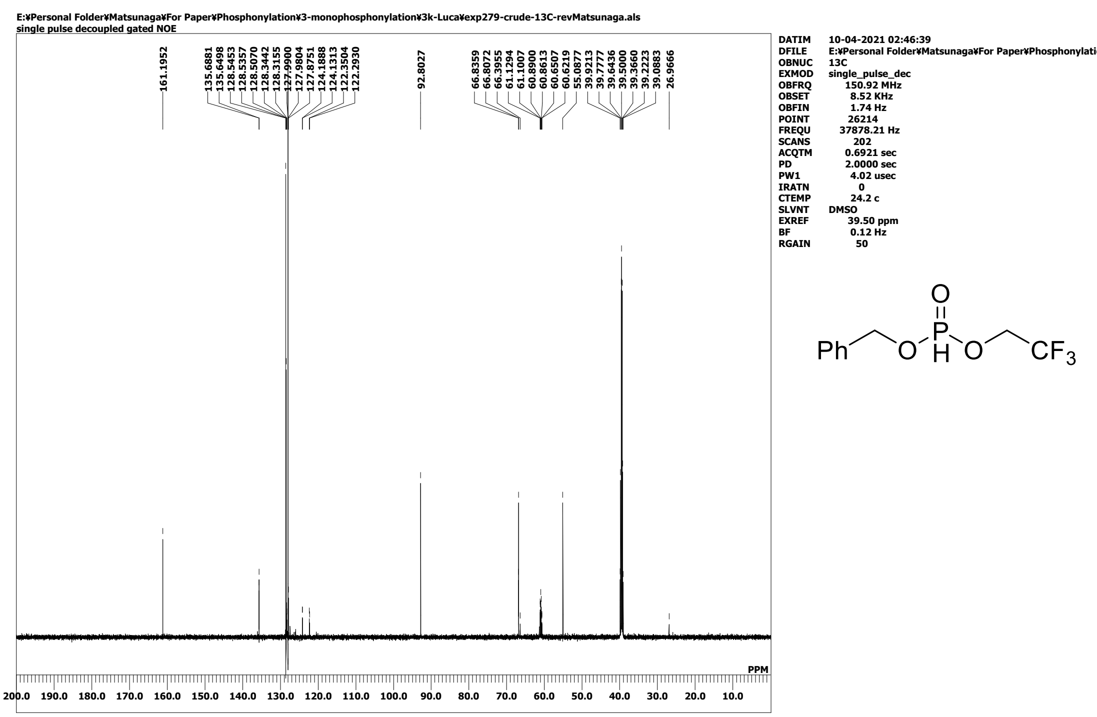
^{19}F NMR (565 MHz, DMSO-d_6) of **3j**



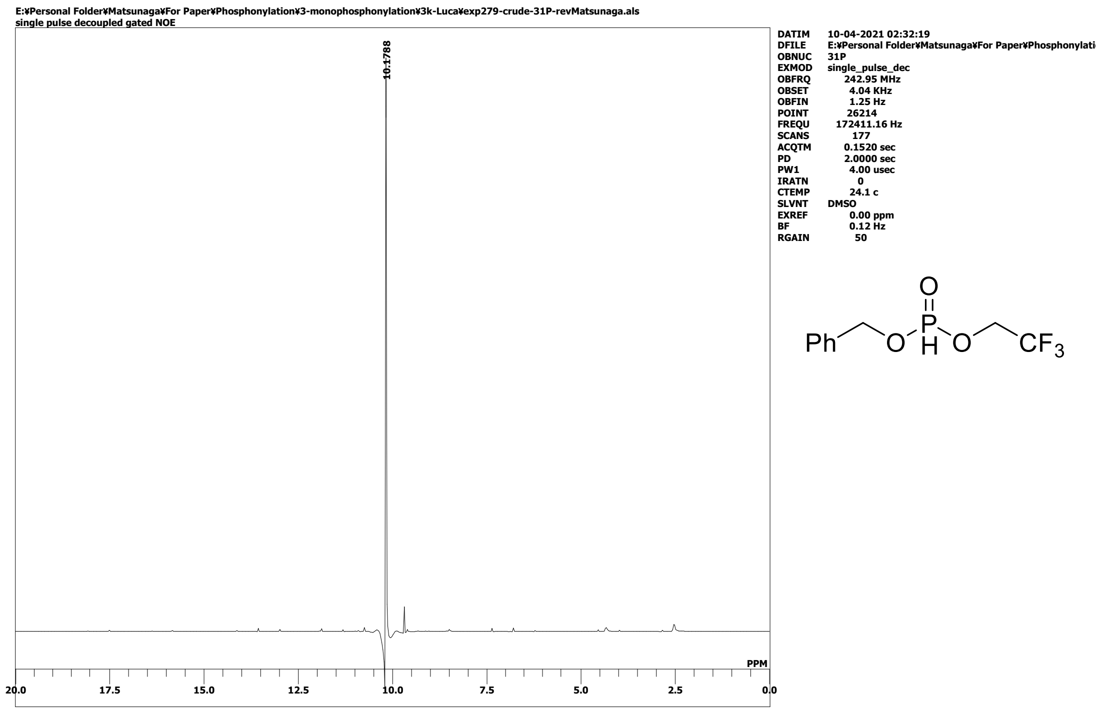
[1]H NMR (600 MHz, DMSO-d_6) of **3k**



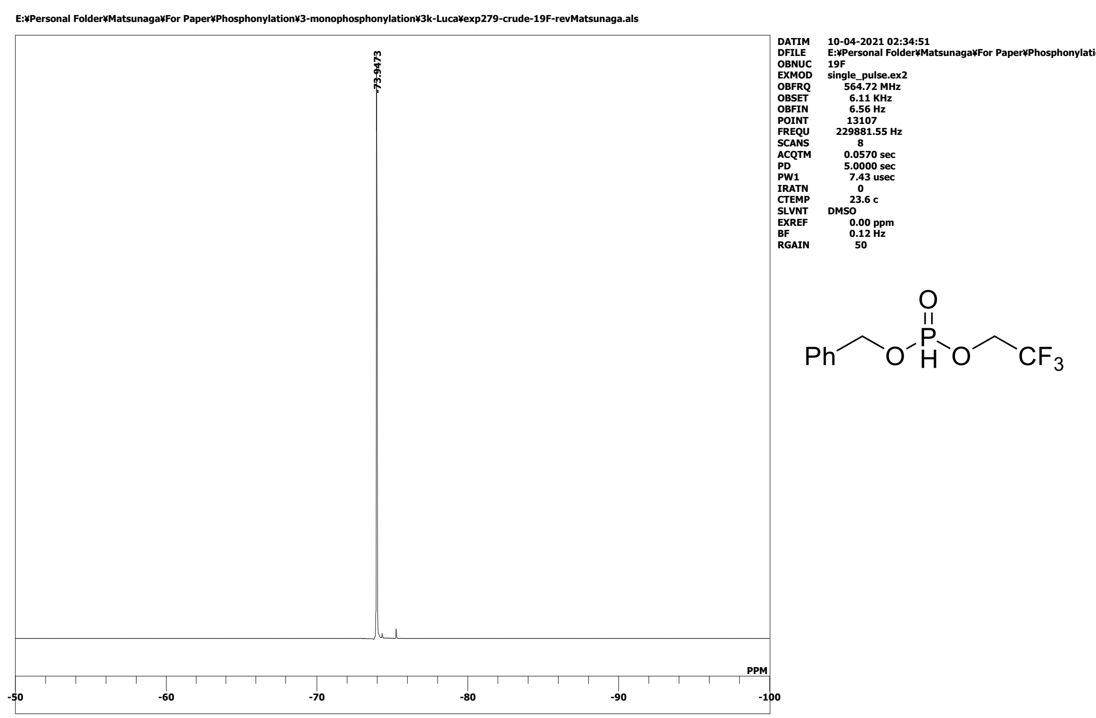
[13]C NMR (151 MHz, DMSO-d_6) of **3k**



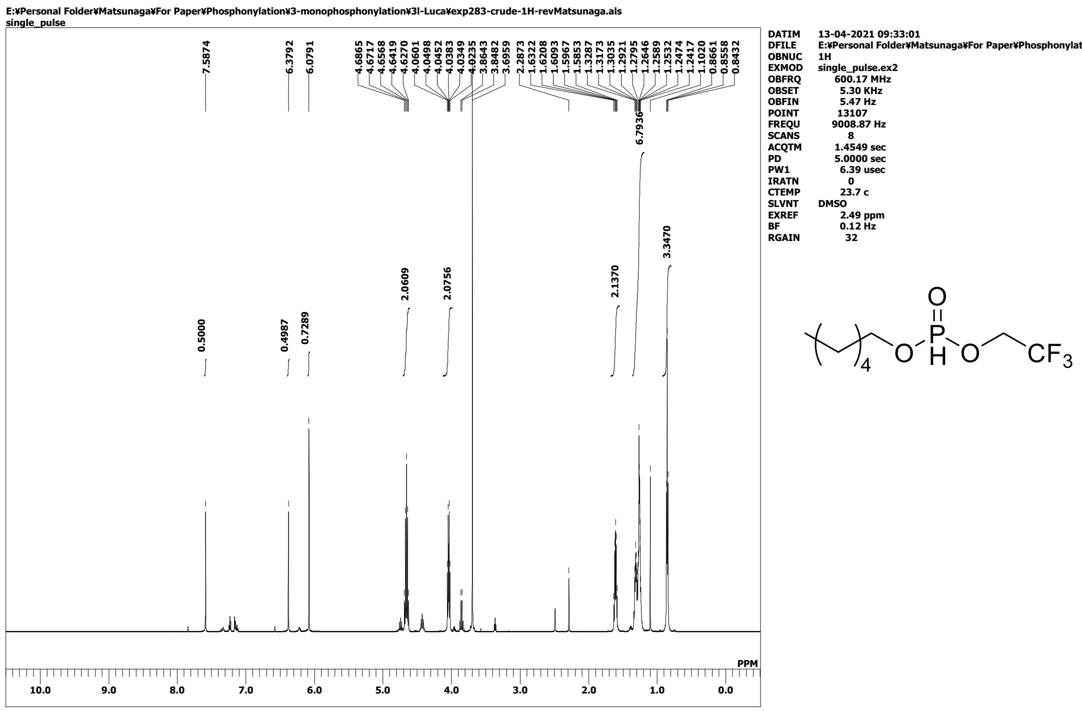
^{31}P NMR (243 MHz, DMSO-d_6) of **3k**



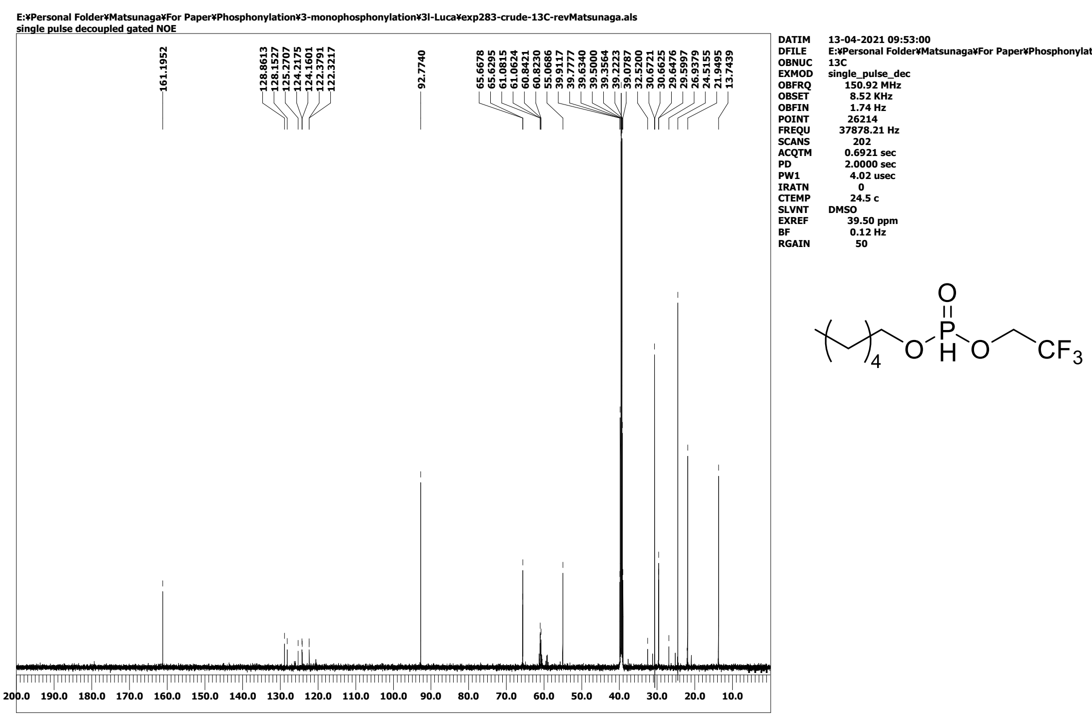
^{19}F NMR (565 MHz, DMSO-d_6) of **3k**



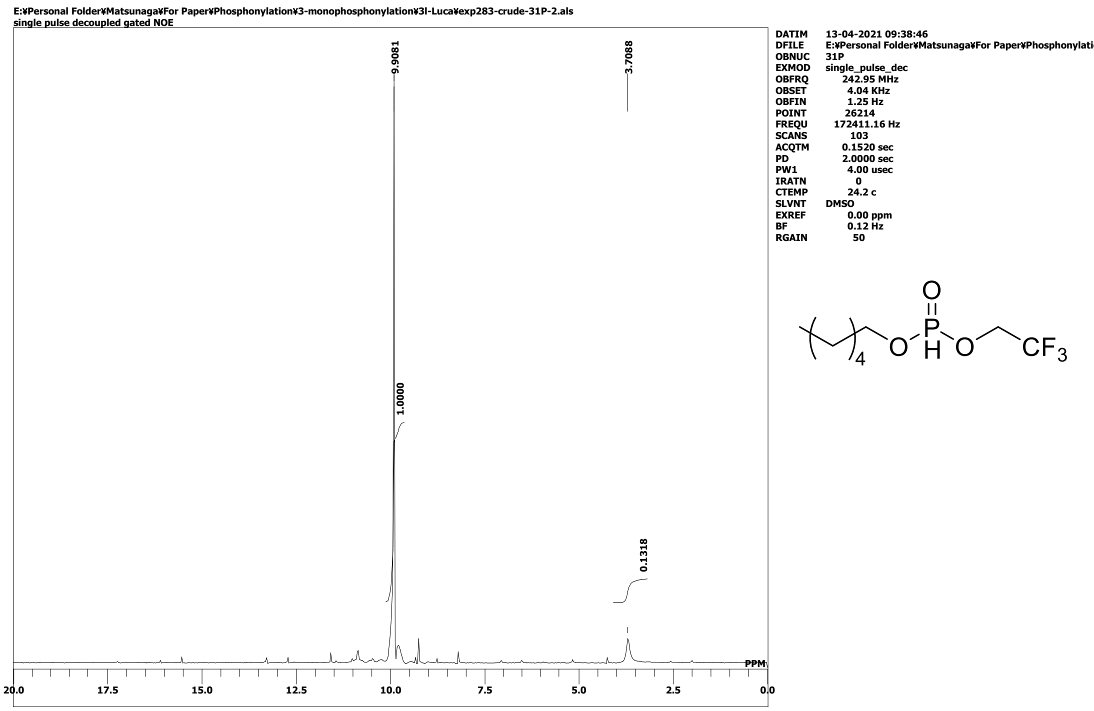
^{1}H NMR (600 MHz, DMSO-d_6) of **3l**



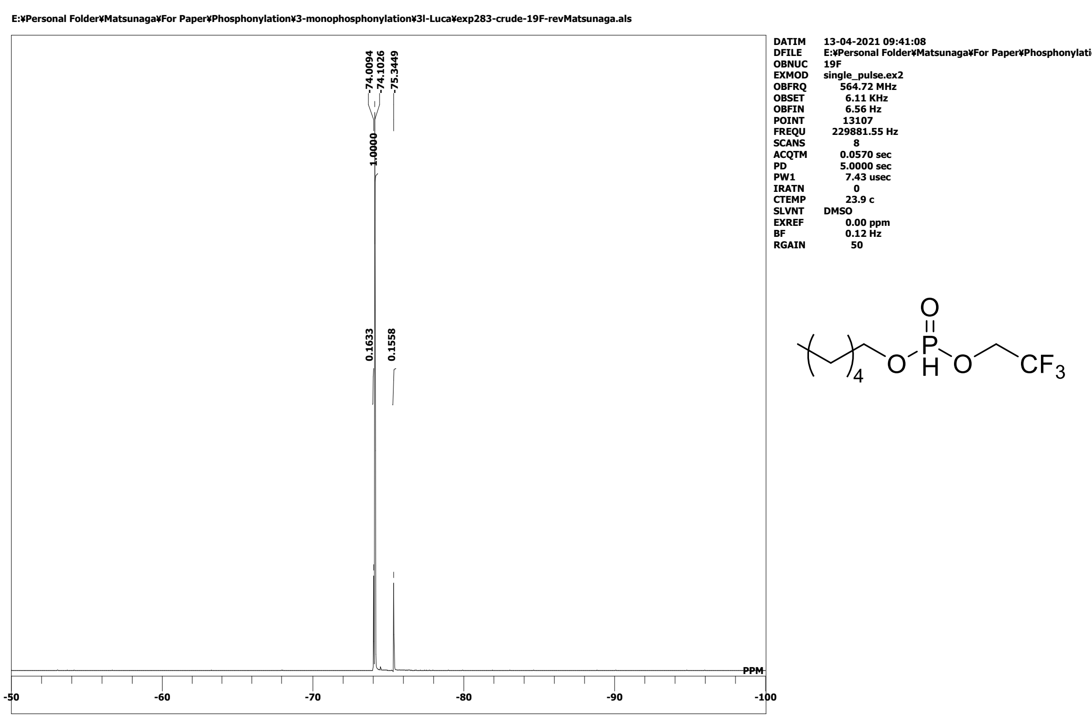
^{13}C NMR (151 MHz, DMSO-d_6) of **3l**



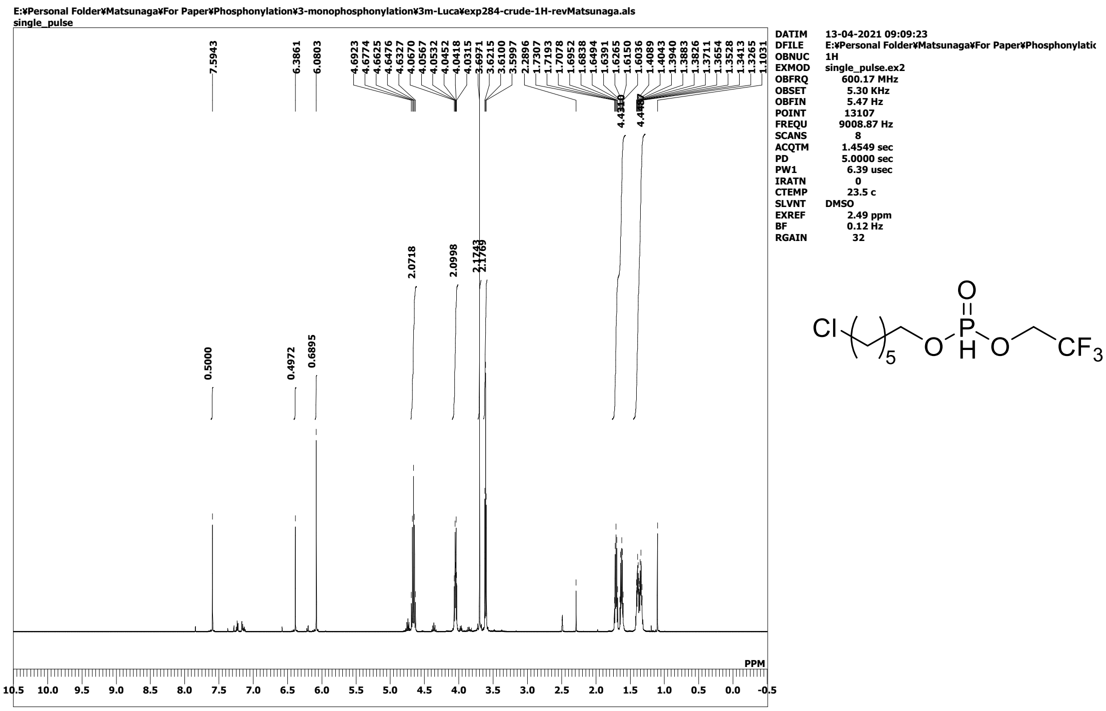
^{31}P NMR (243 MHz, DMSO-d_6) of **3l**



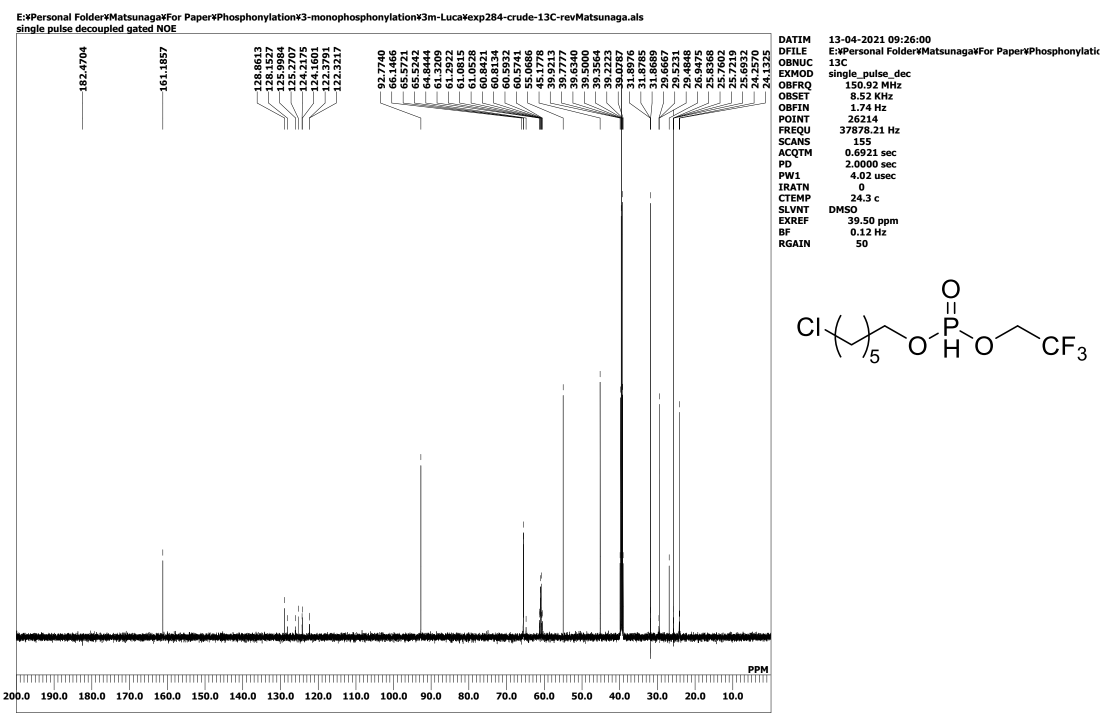
^{19}F NMR (565 MHz, DMSO-d_6) of **3l**



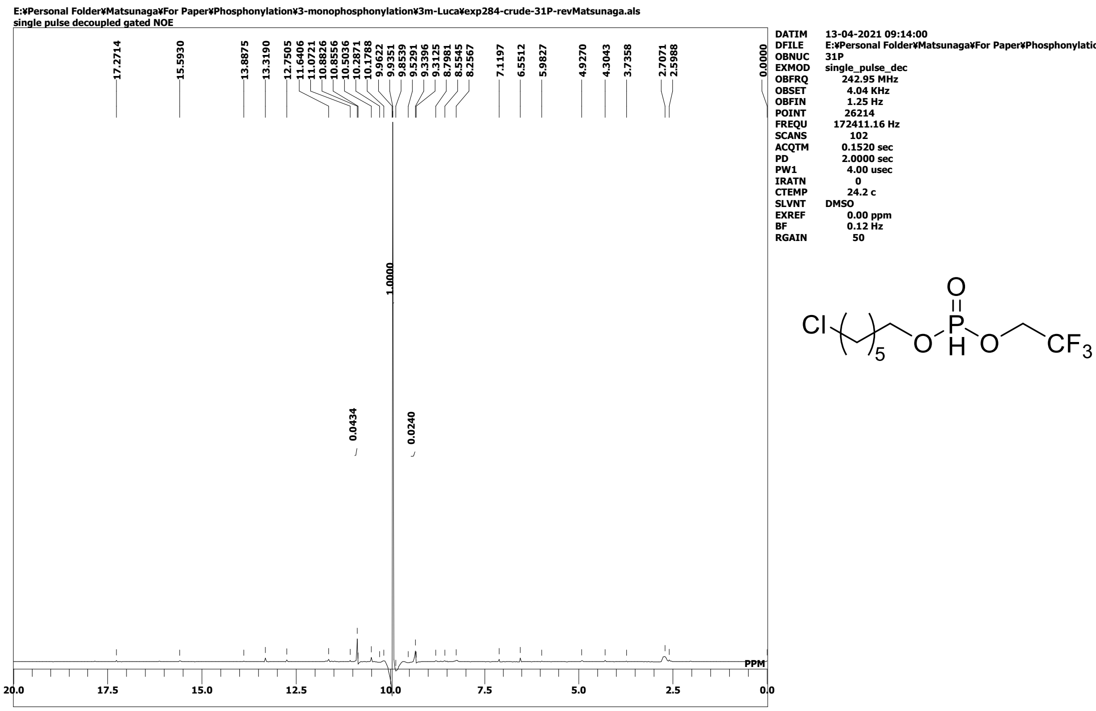
^{1}H NMR (600 MHz, DMSO-d_6) of **3m**



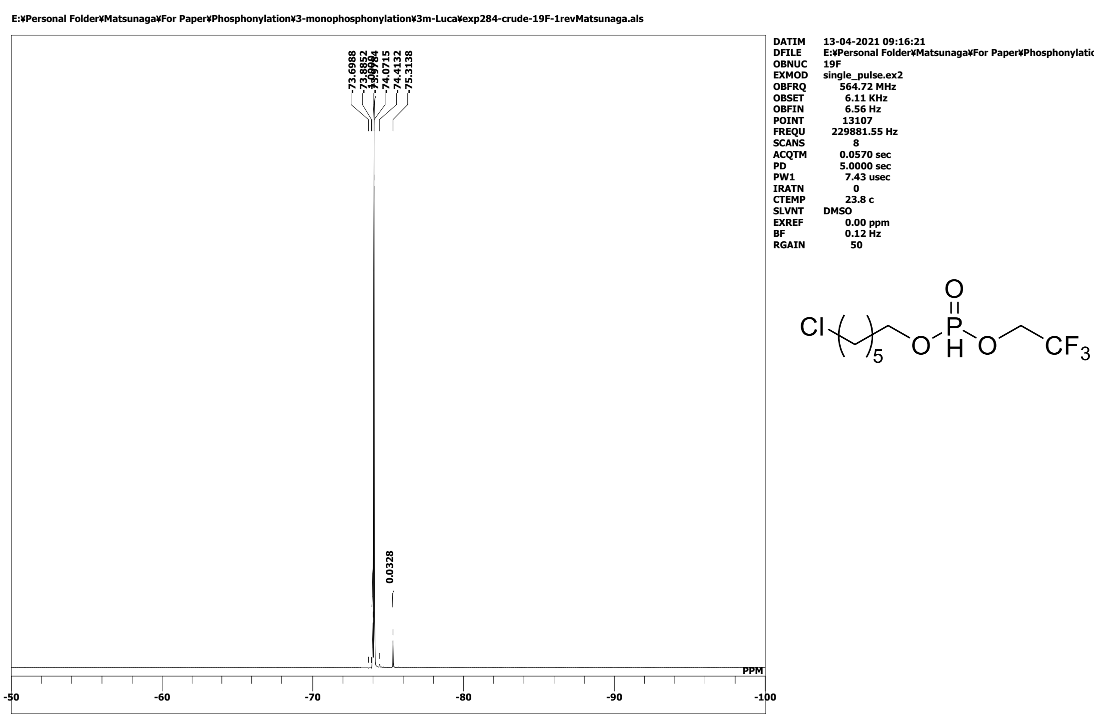
^{13}C NMR (151 MHz, DMSO-d_6) of **3m**



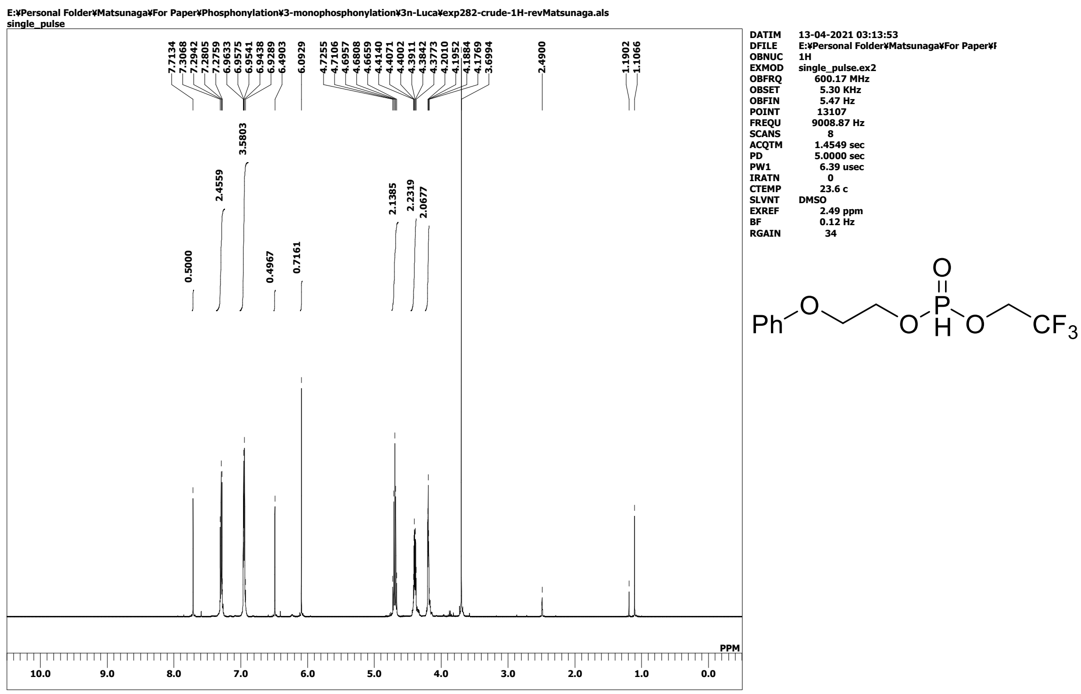
^{31}P NMR (243 MHz, DMSO-d_6) of **3m**



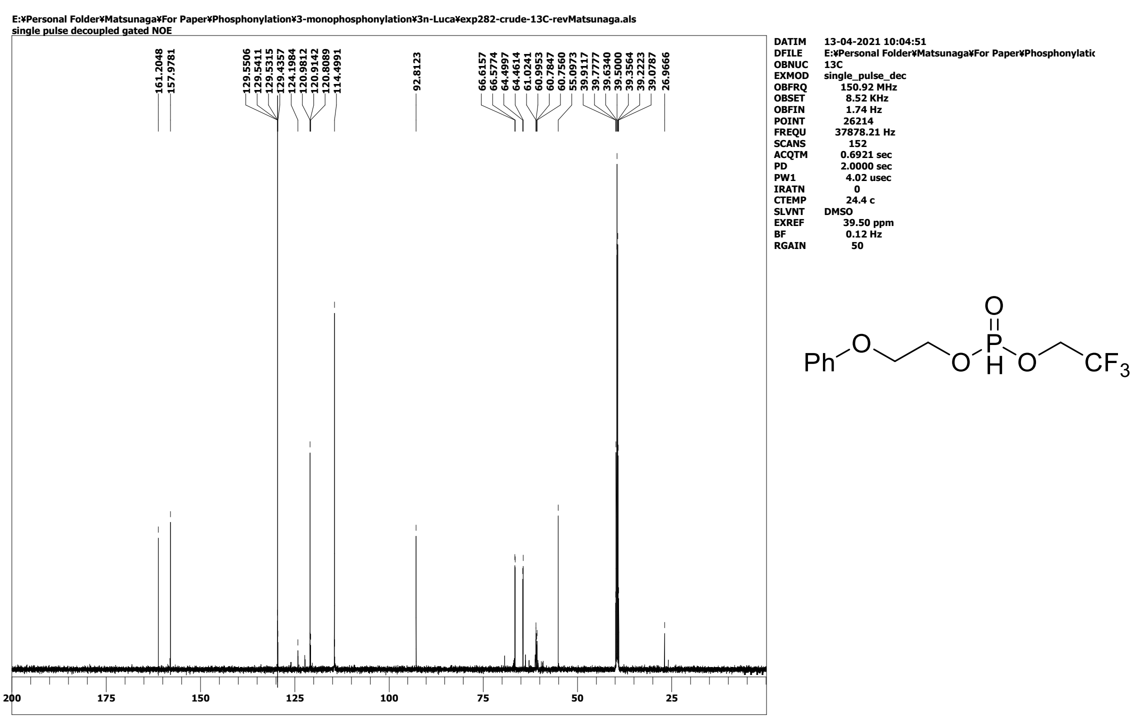
^{19}F NMR (565 MHz, DMSO-d_6) of **3m**



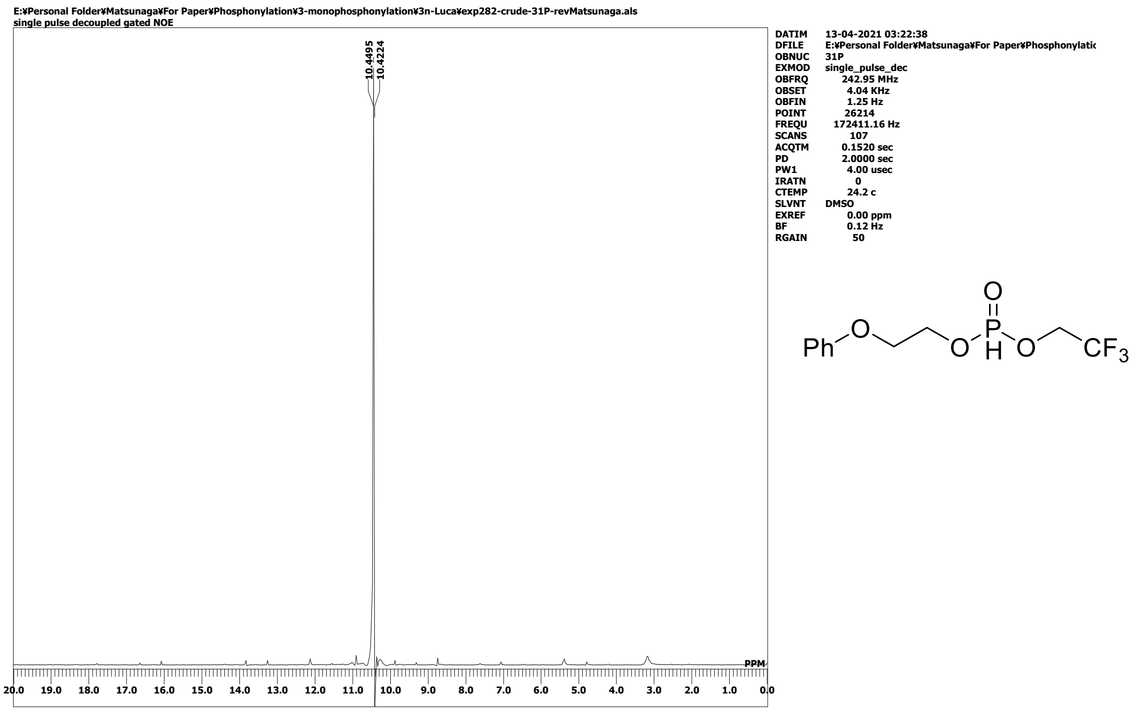
^{1}H NMR (600 MHz, DMSO-d_6) of **3n**



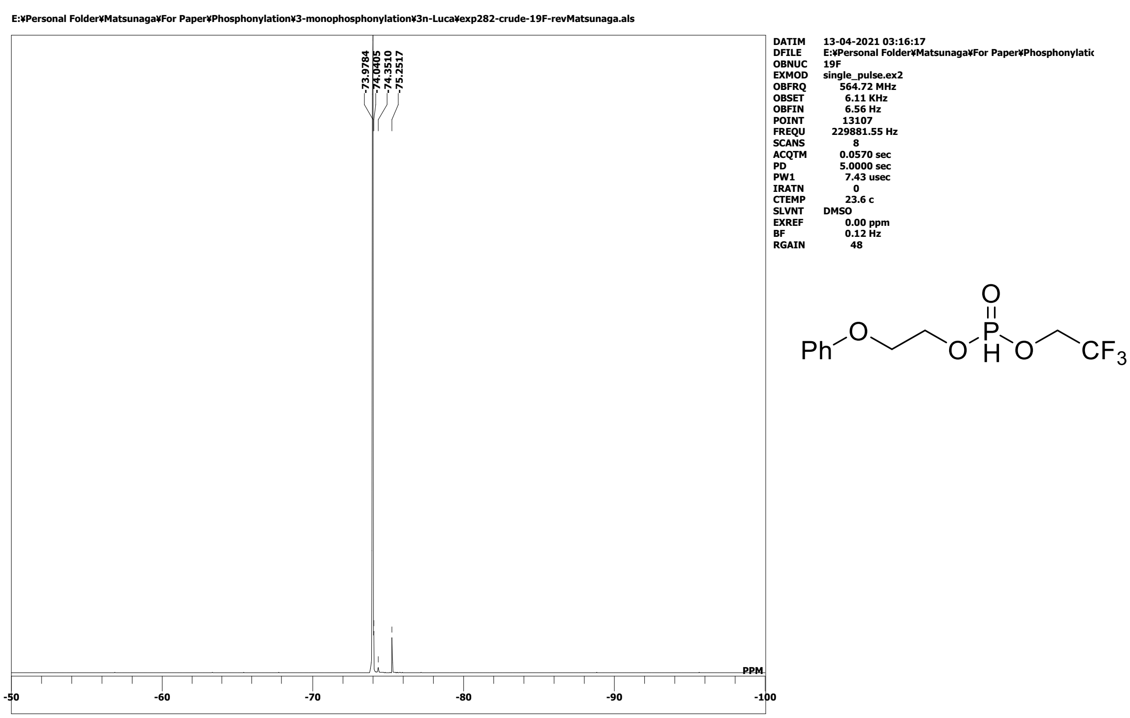
^{13}C NMR (151 MHz, DMSO-d_6) of **3n**



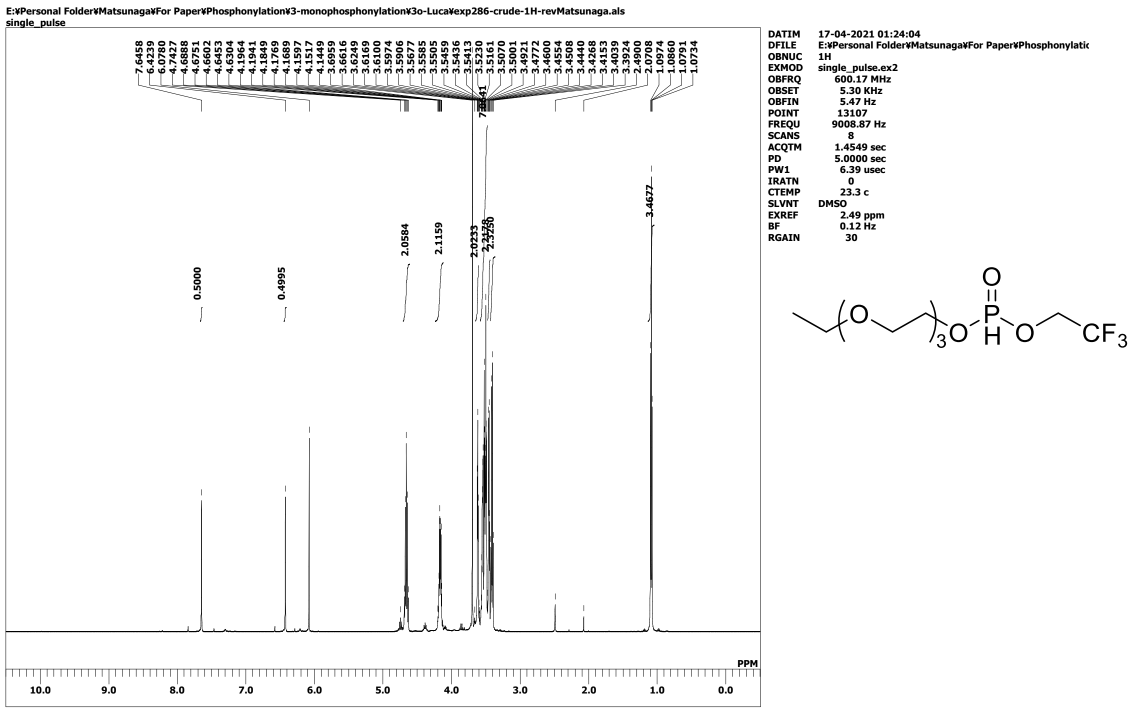
^{31}P NMR (243 MHz, DMSO-d_6) of **3n**



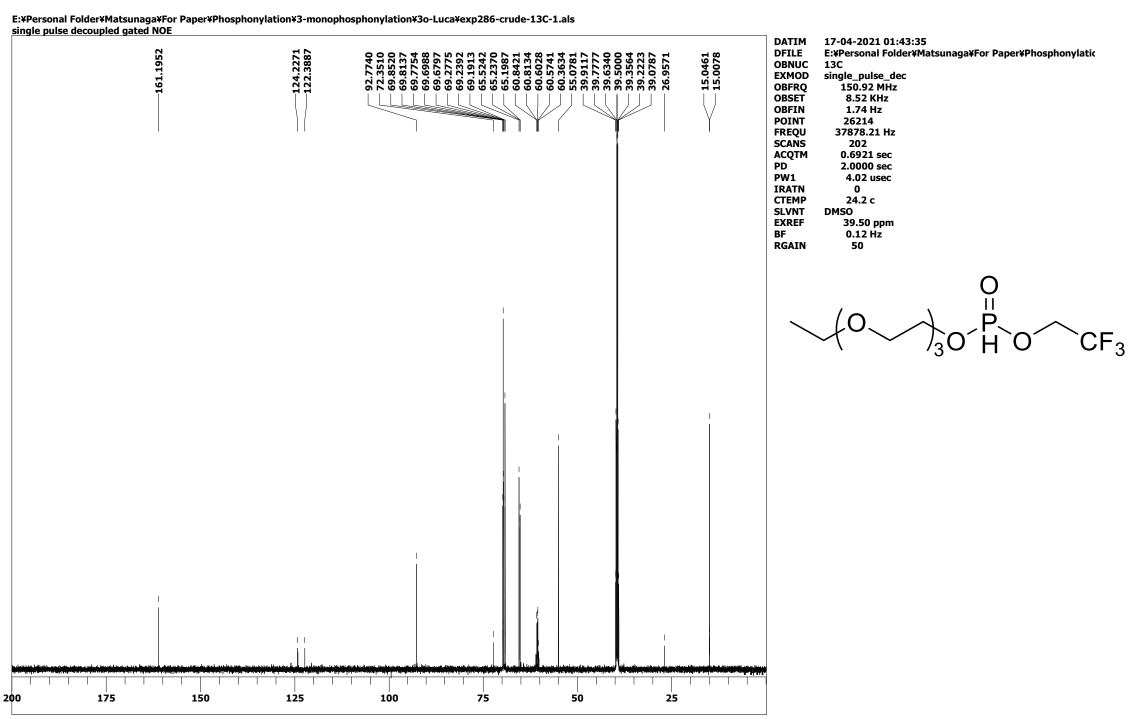
^{19}F NMR (565 MHz, DMSO-d_6) of **3n**



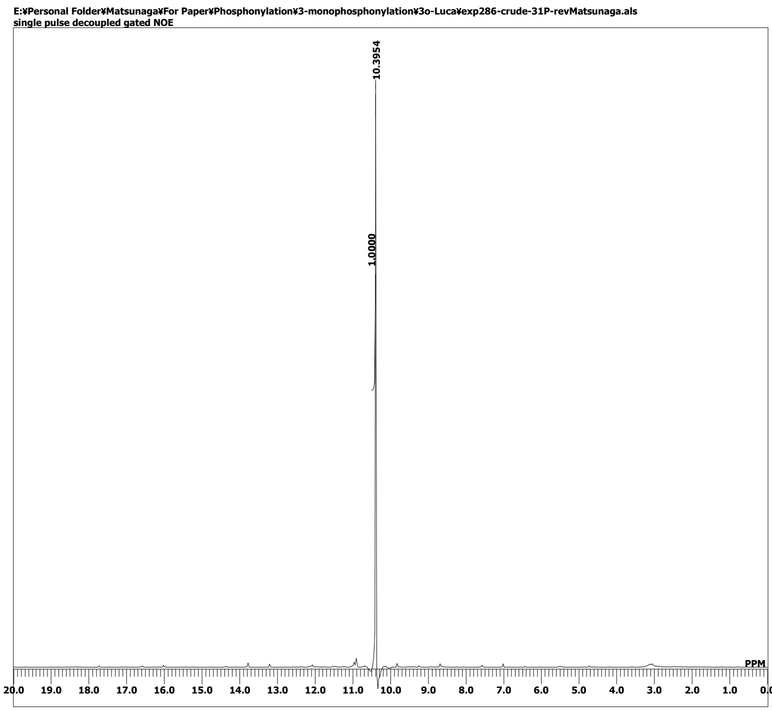
^{1}H NMR (600 MHz, DMSO-d_6) of **3o**

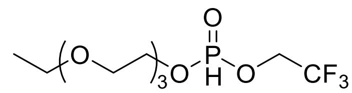


^{13}C NMR (151 MHz, DMSO-d_6) of **3o**



^{31}P NMR (243 MHz, DMSO-d_6) of **3o**





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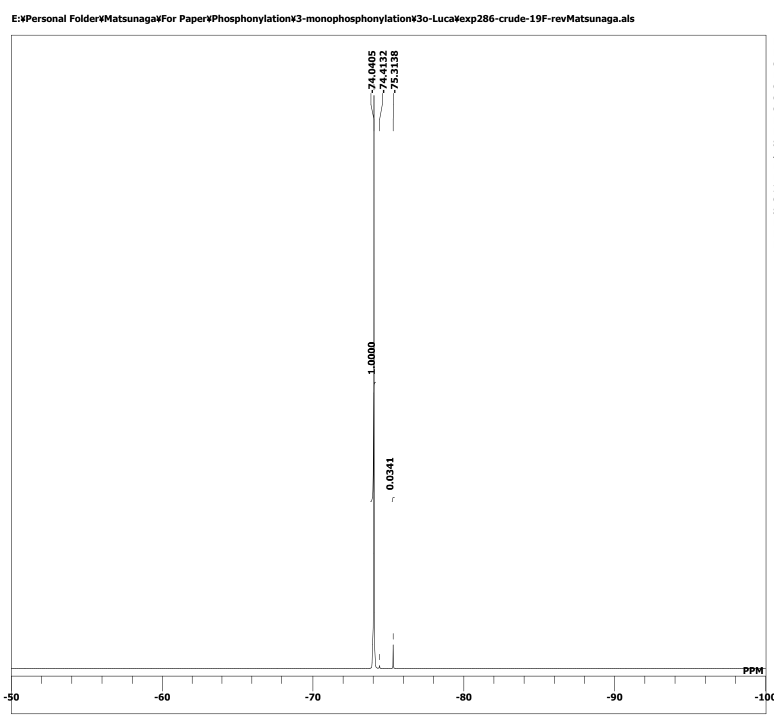
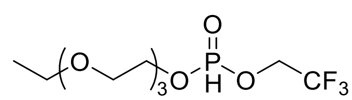
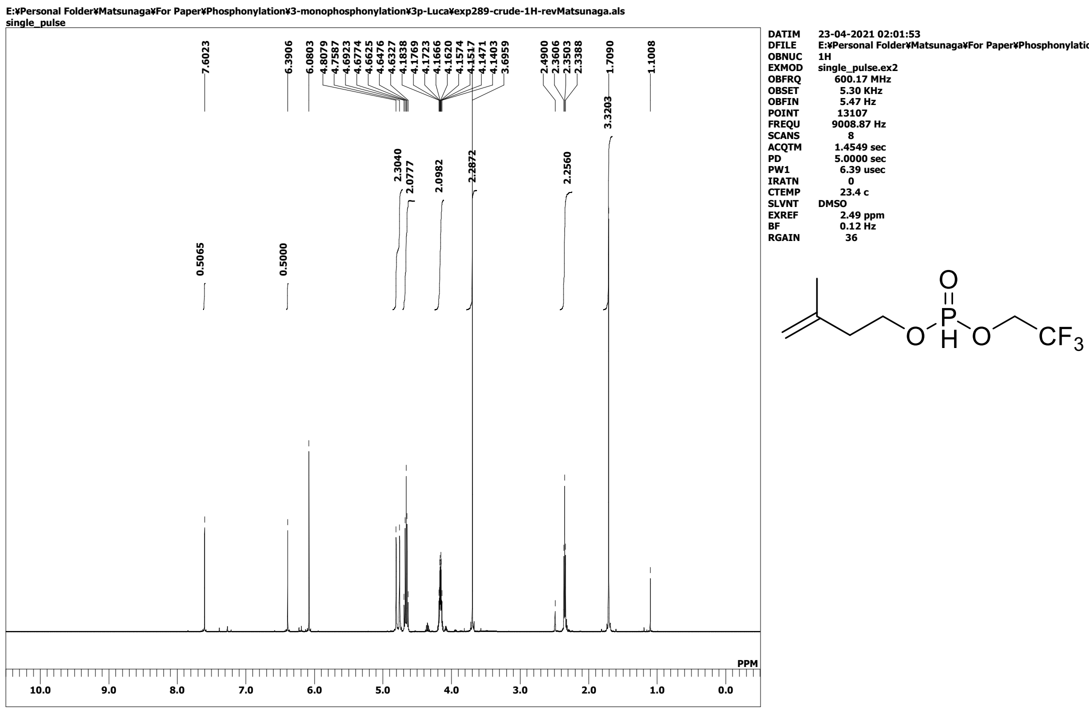
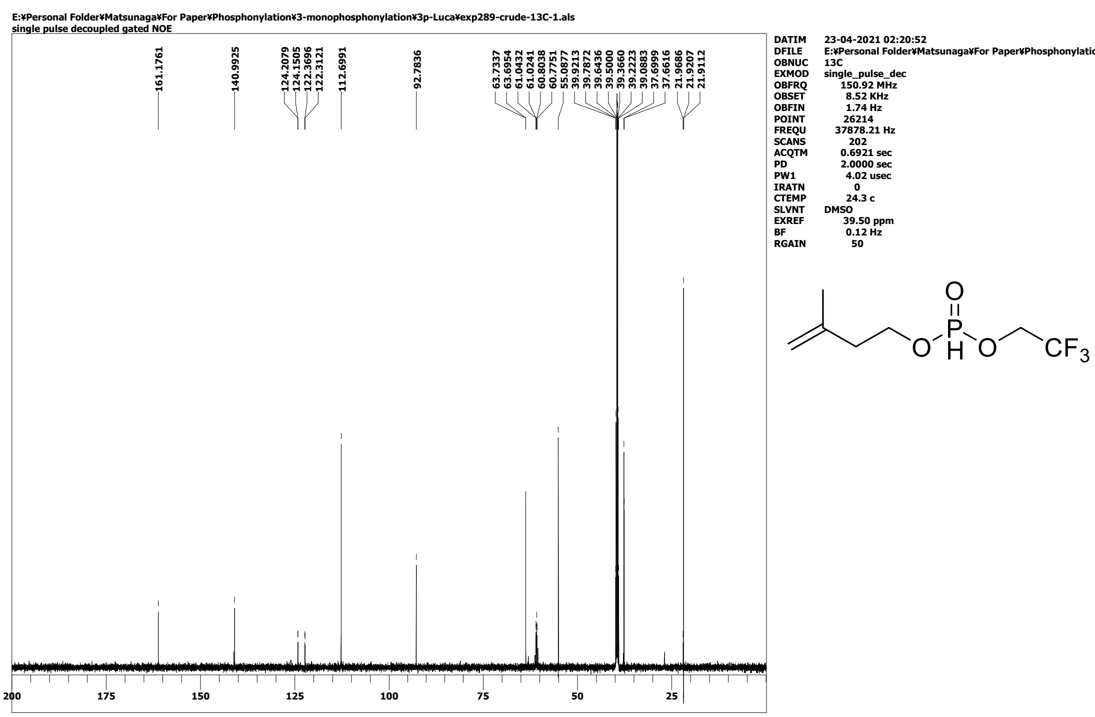




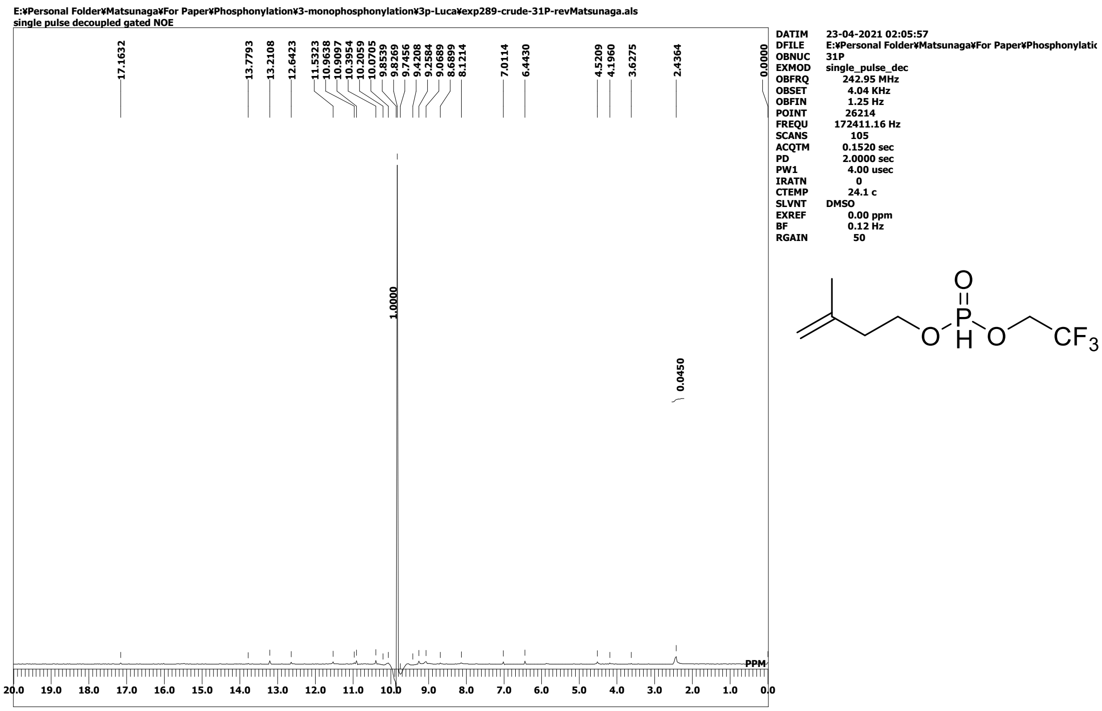
[1]H NMR (600 MHz, DMSO-d_6) of **3p**



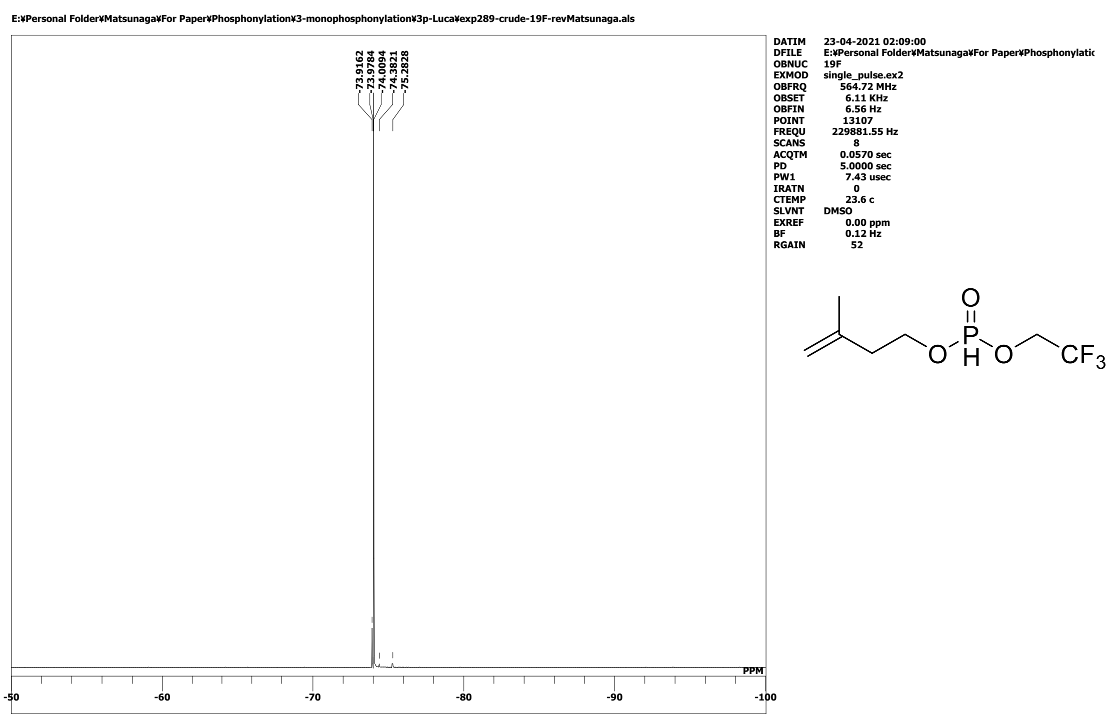
[13]C NMR (151 MHz, DMSO-d_6) of **3p**



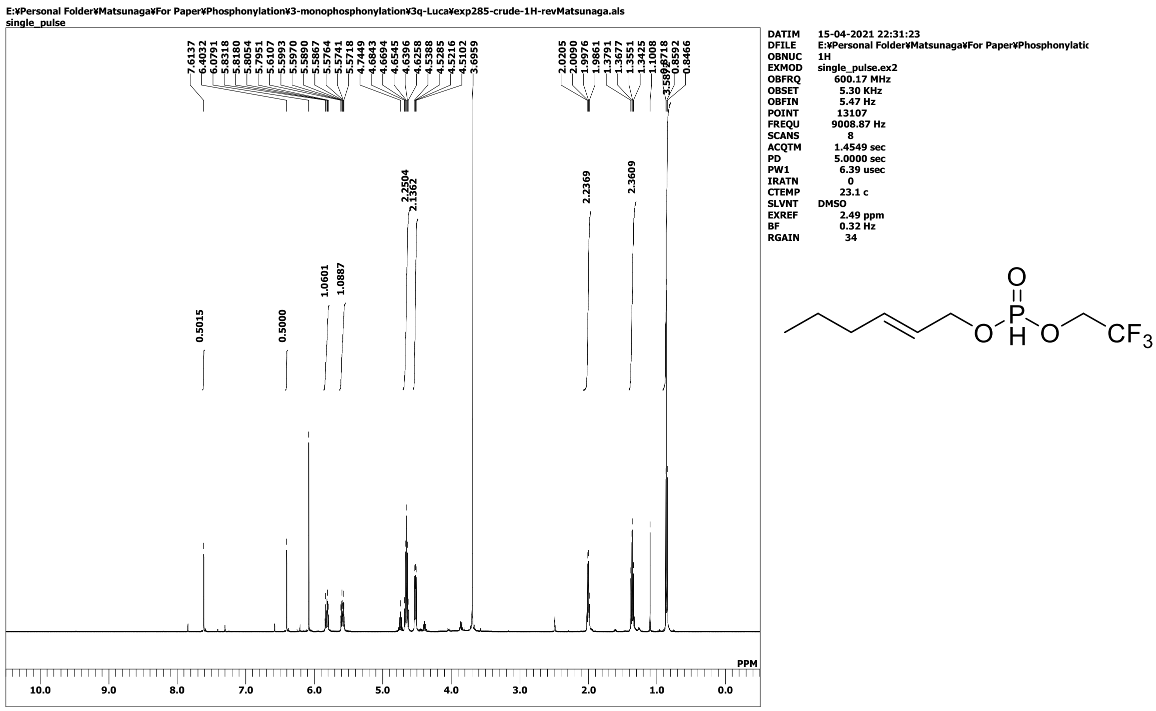
^{31}P NMR (243 MHz, DMSO-d_6) of **3p**



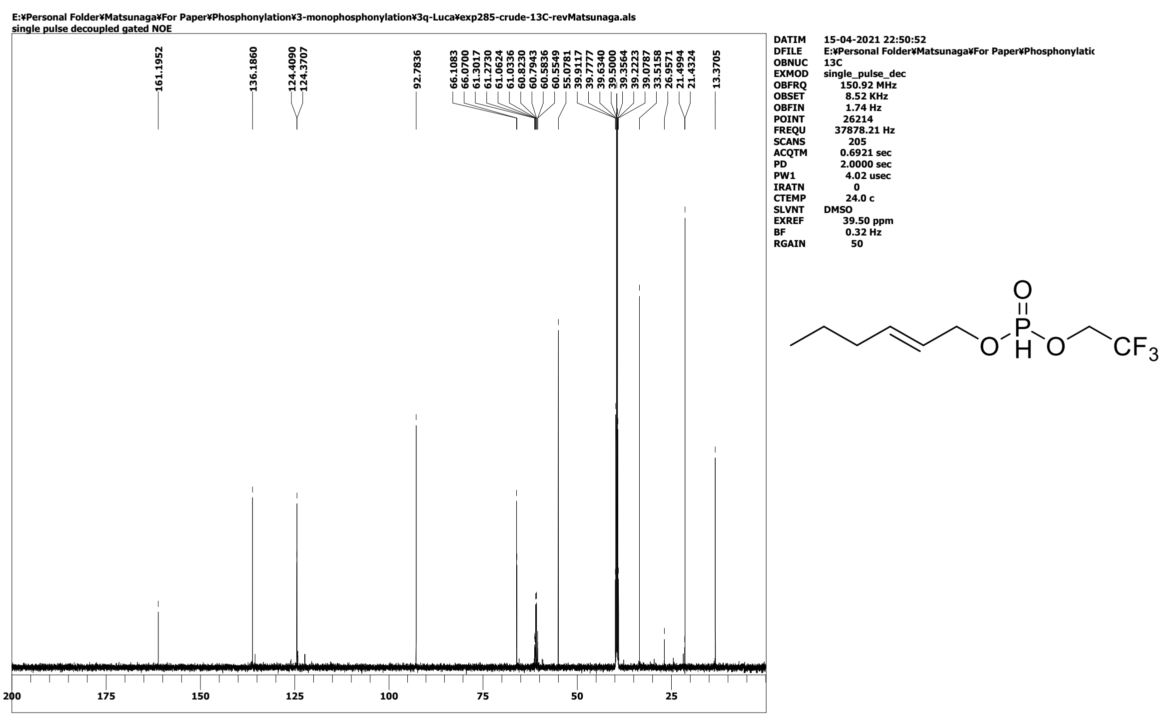
^{19}F NMR (565 MHz, DMSO-d_6) of **3p**



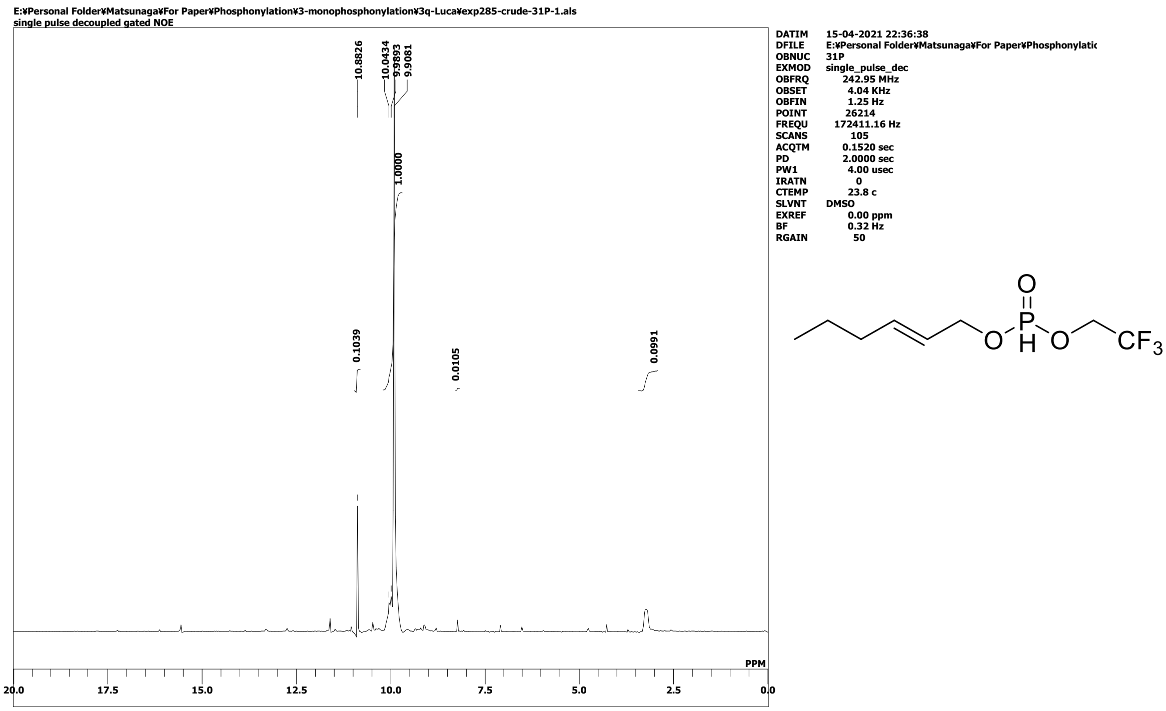
^{1}H NMR (600 MHz, DMSO-d_6) of **3q**



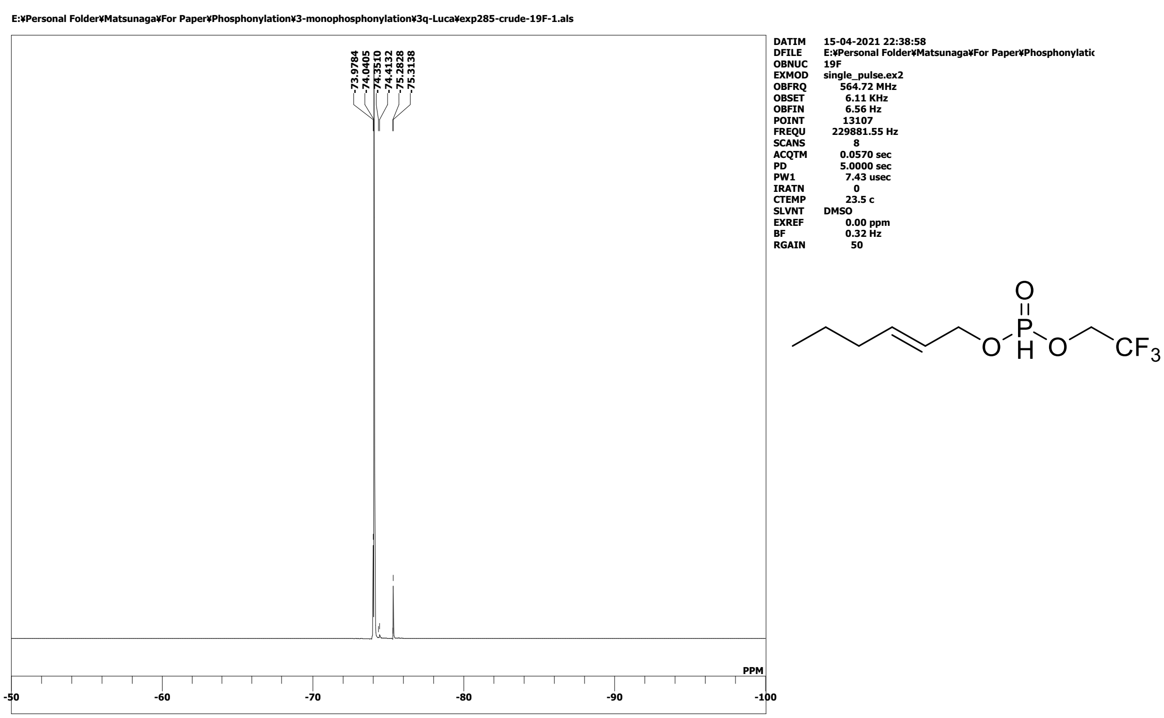
^{13}C NMR (151 MHz, DMSO-d_6) of **3q**



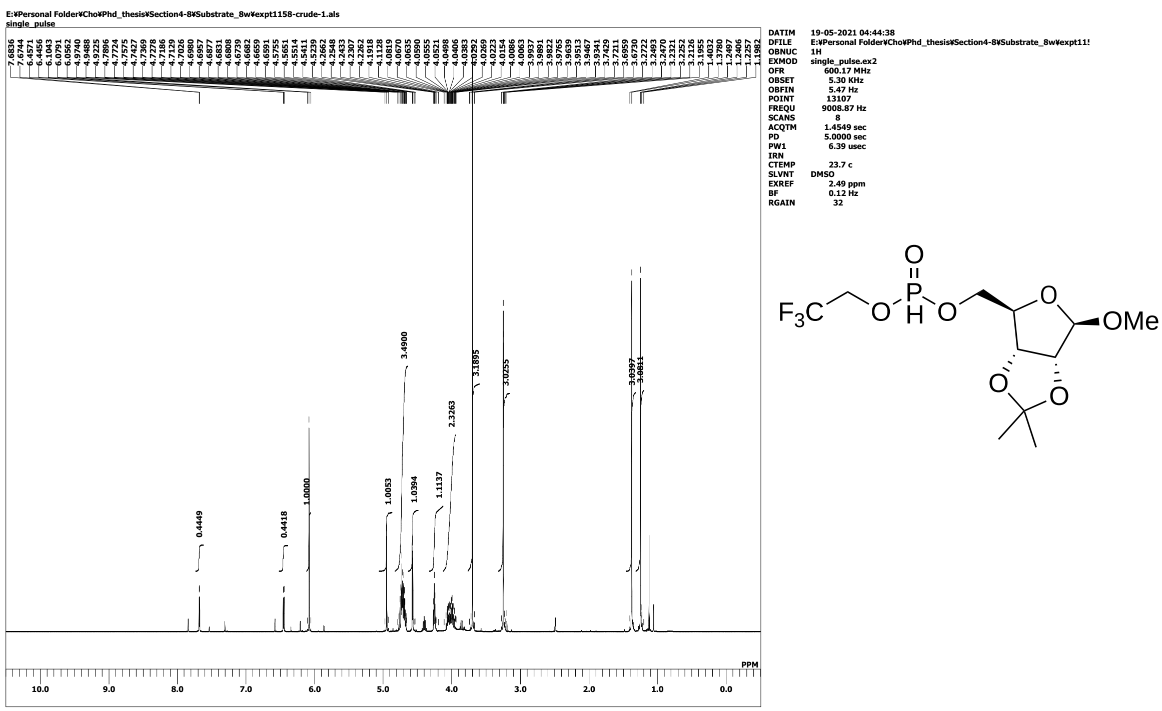
^{31}P NMR (243 MHz, DMSO-d_6) of **3q**



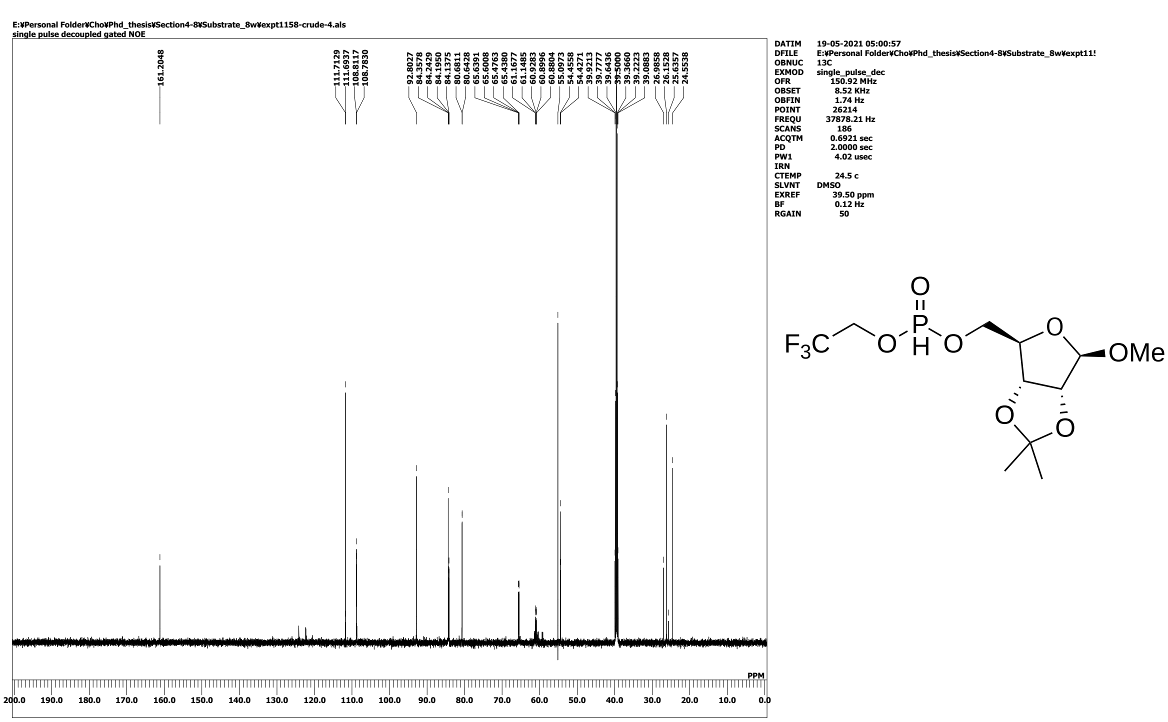
^{19}F NMR (565 MHz, DMSO-d_6) of **3q**



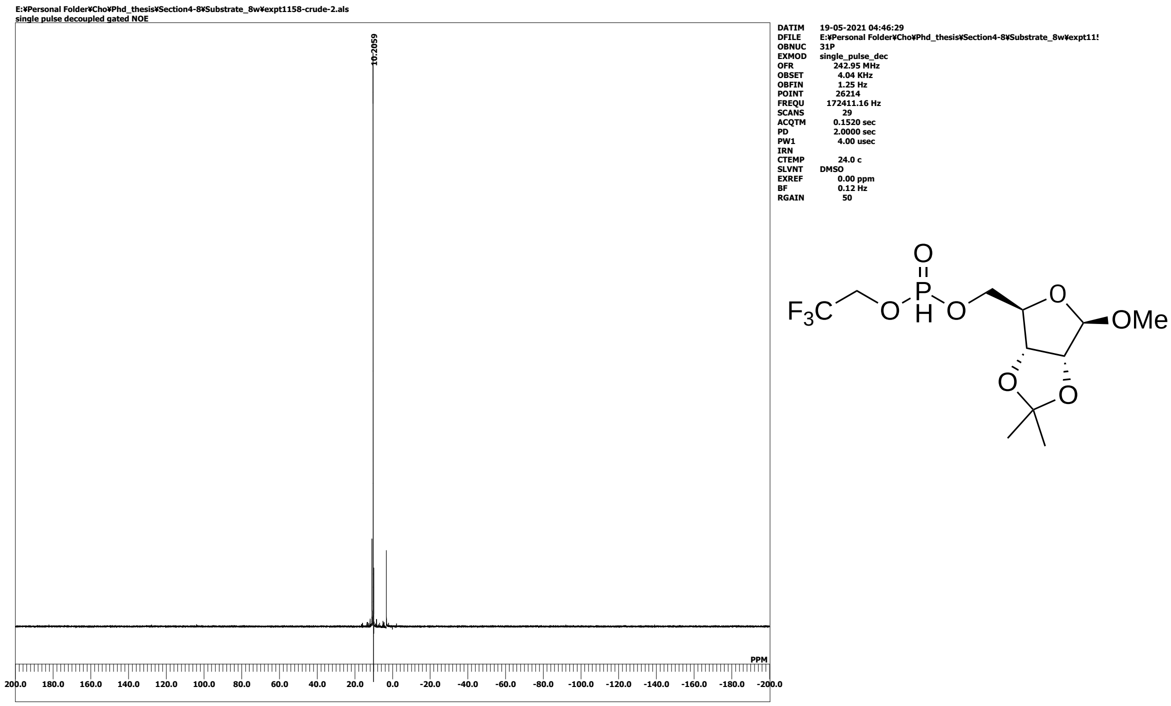
^{1}H NMR (600 MHz, DMSO-d_6) of **3r**



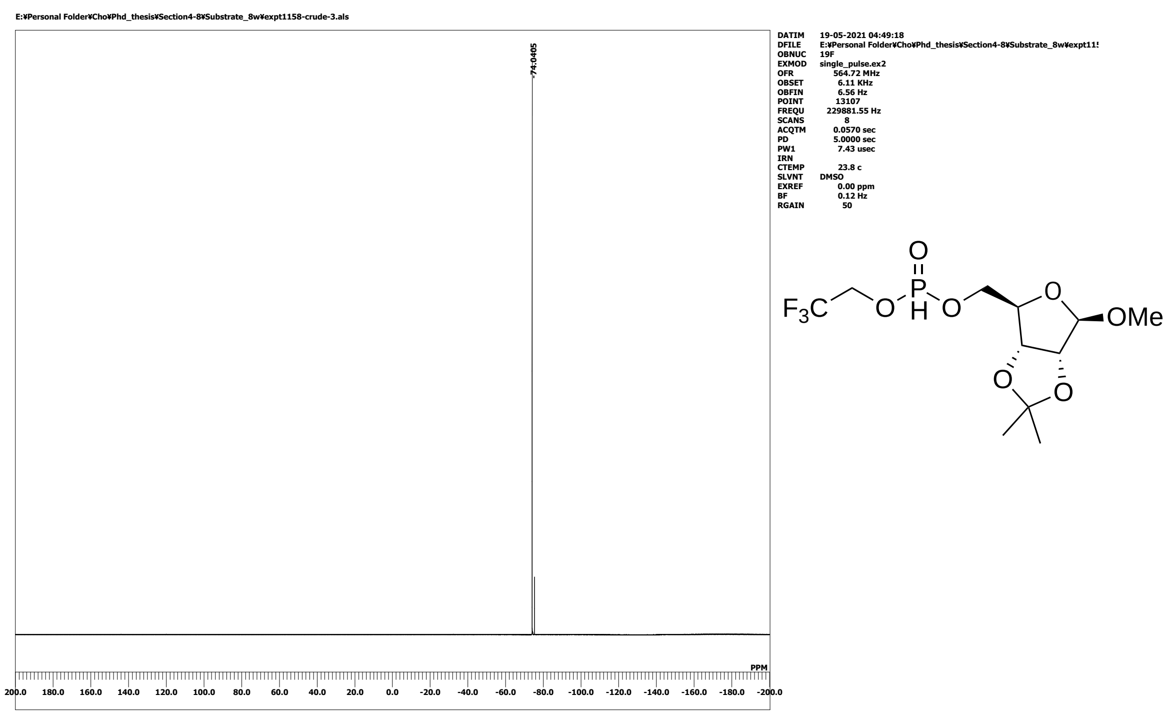
^{13}C NMR (151 MHz, DMSO-d_6) of **3r**



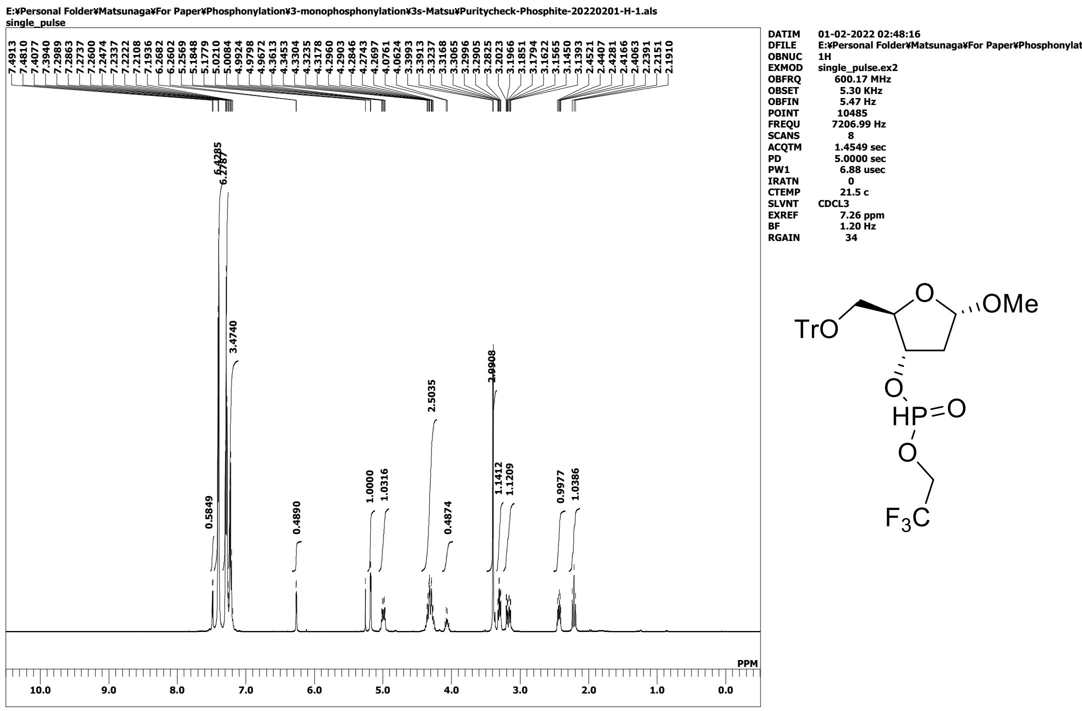
^{31}P NMR (243 MHz, DMSO-d_6) of **3r**



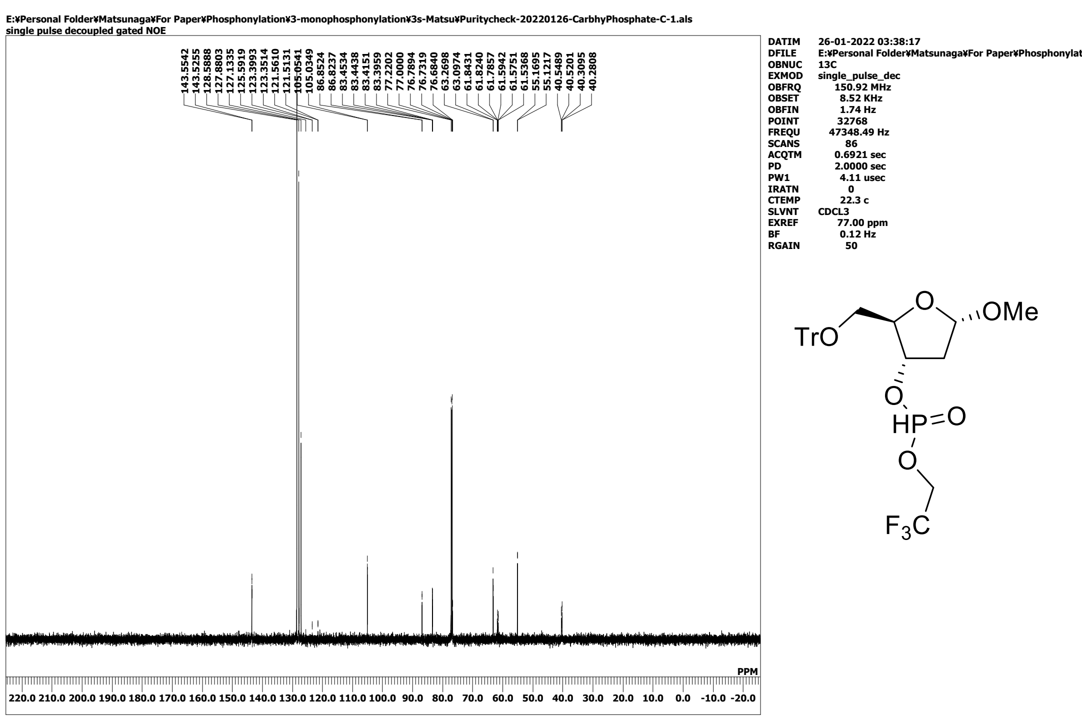
^{19}F NMR (565 MHz, DMSO-d_6) of **3r**



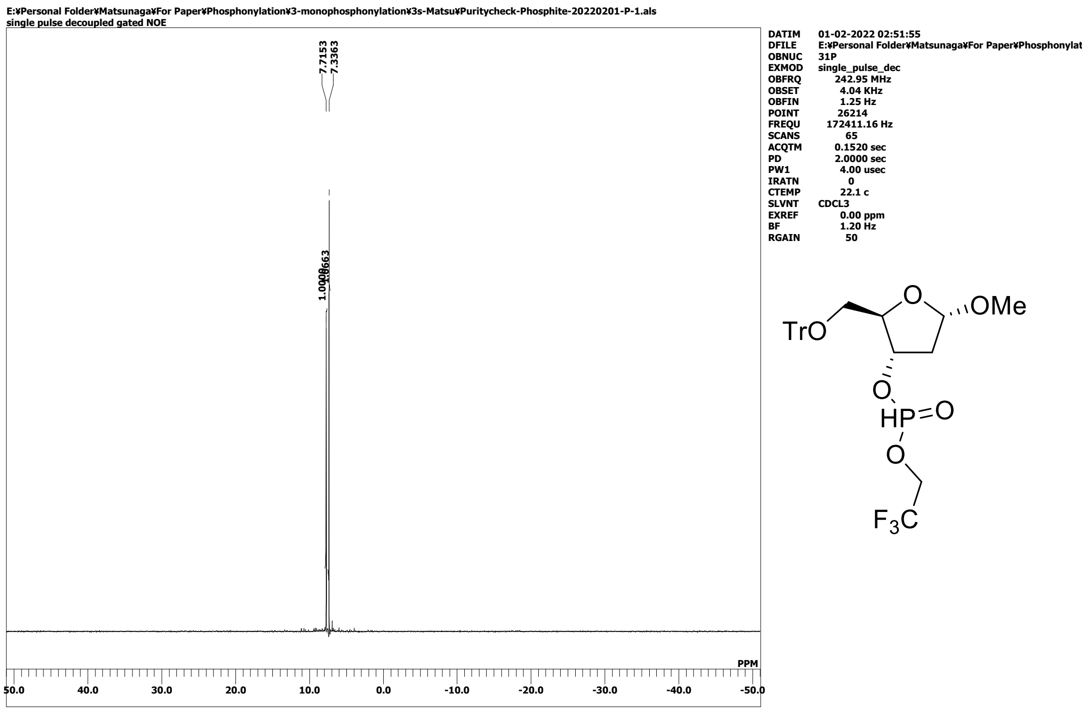
^{1}H NMR (600 MHz, $CDCl_3$) of **3s**



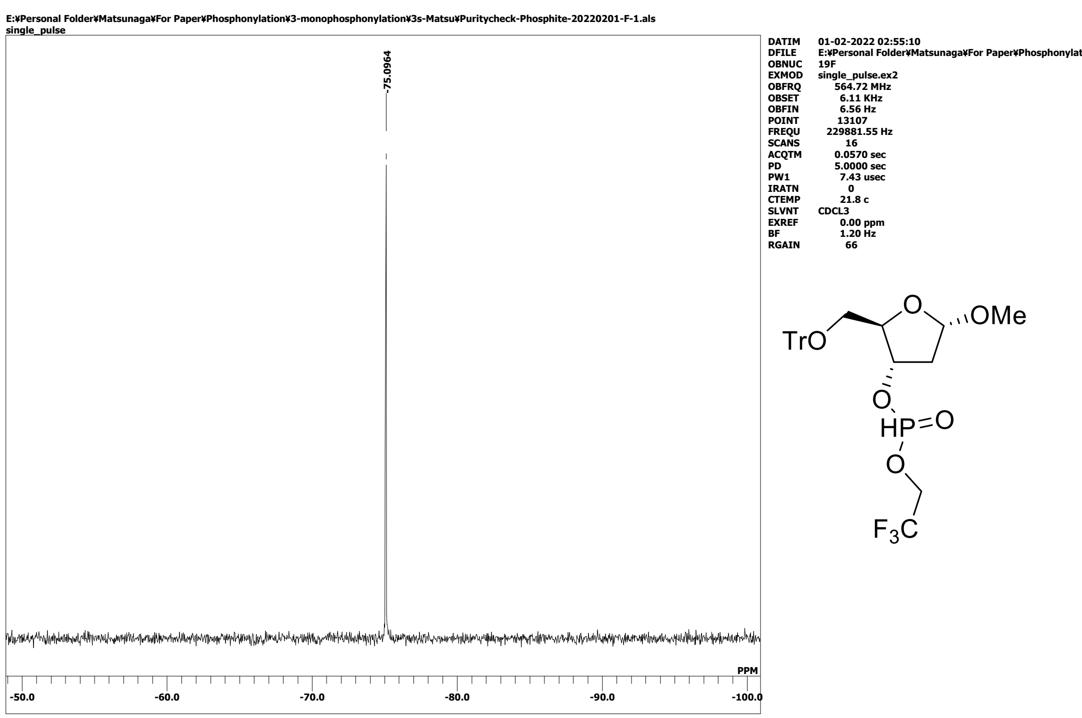
^{13}C NMR (151 MHz, $CDCl_3$) of **3s**



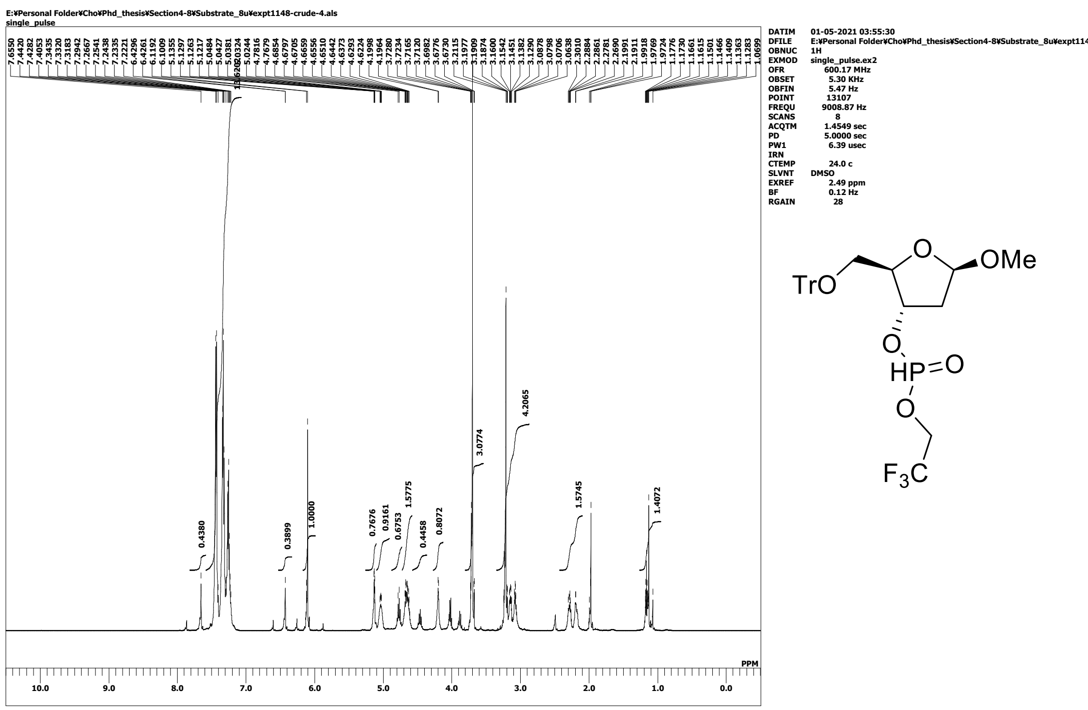
^{31}P NMR (243 MHz, $CDCl_3$) of **3s**



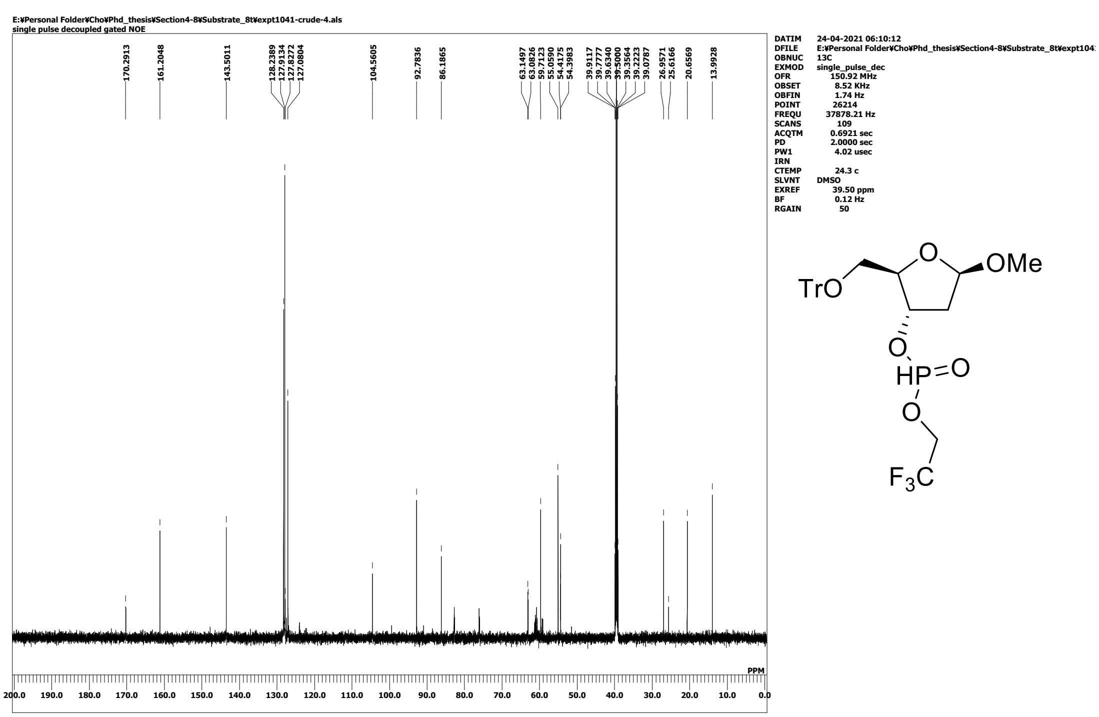
^{19}F NMR (565 MHz, $CDCl_3$) of **3s**



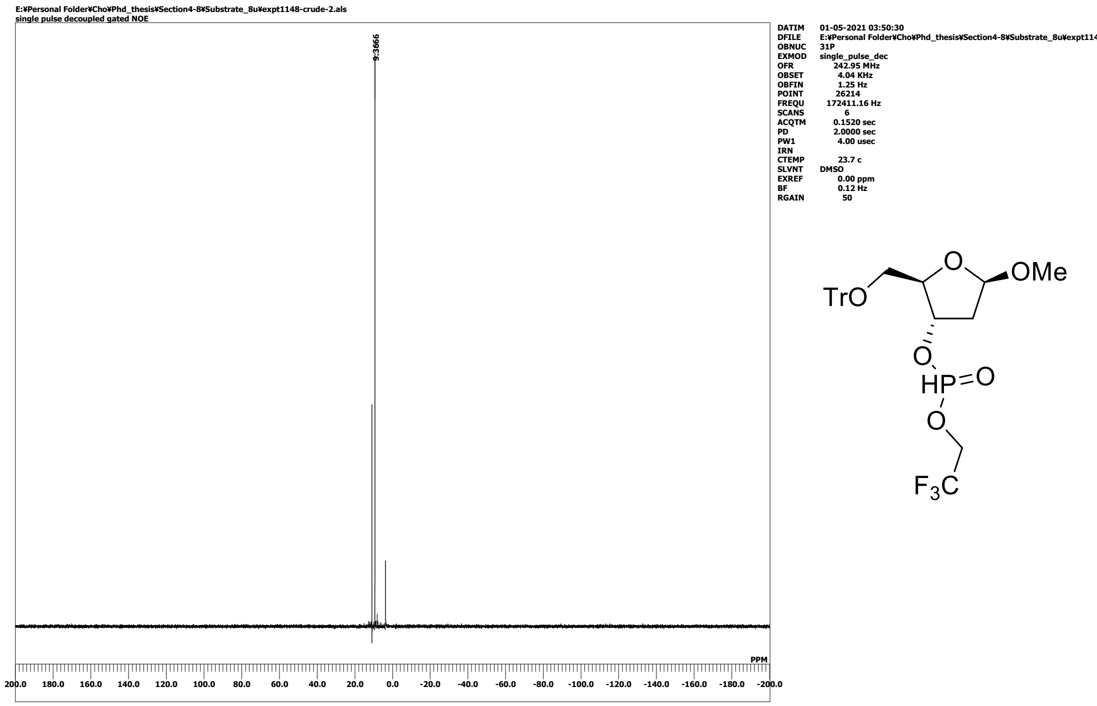
[1]H NMR (600 MHz, DMSO-d_6) of **3t**



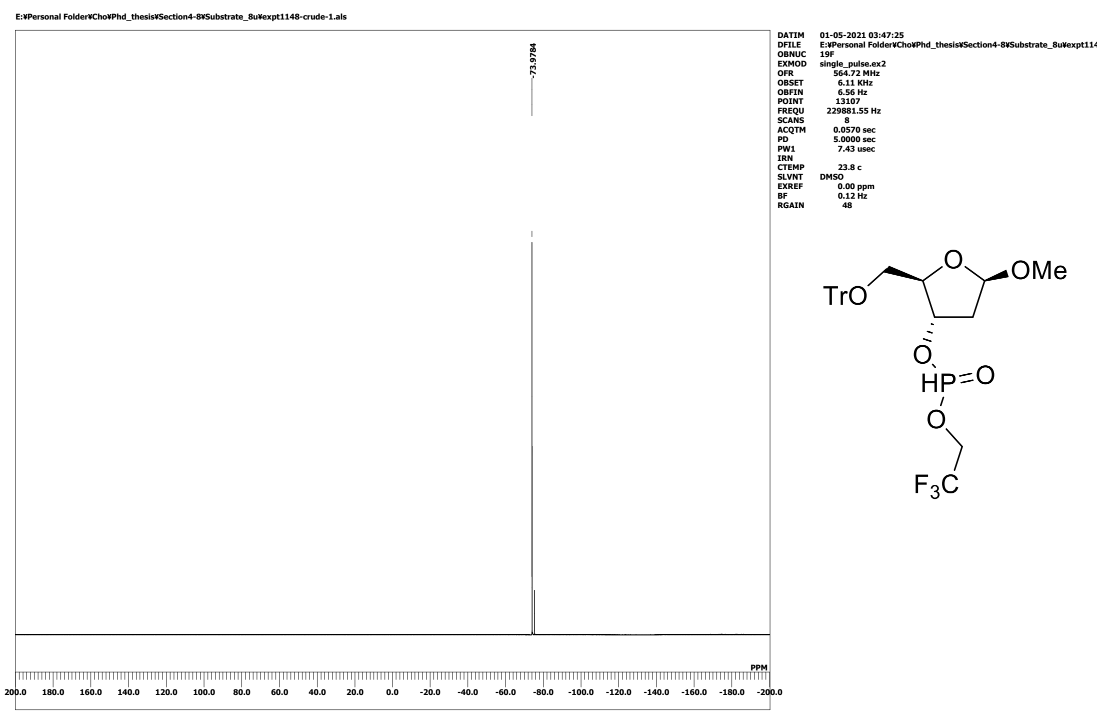
[13]C NMR (151 MHz, DMSO-d_6) of **3t**



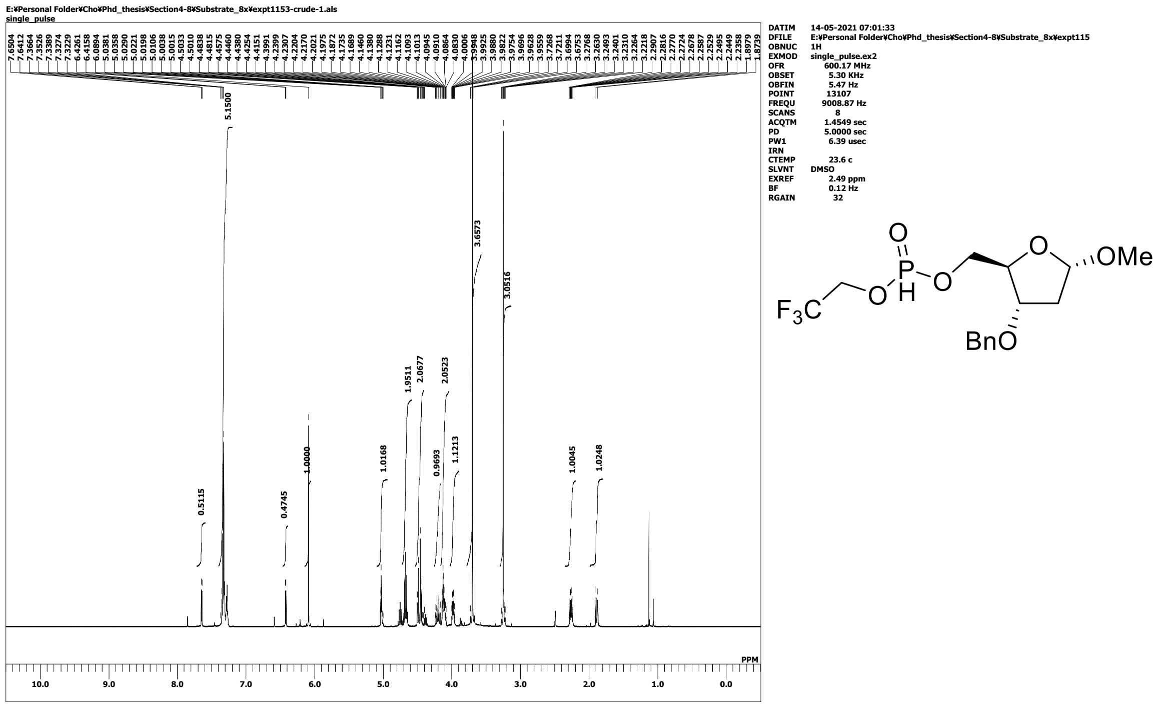
^{31}P NMR (243 MHz, DMSO-d_6) of **3t**



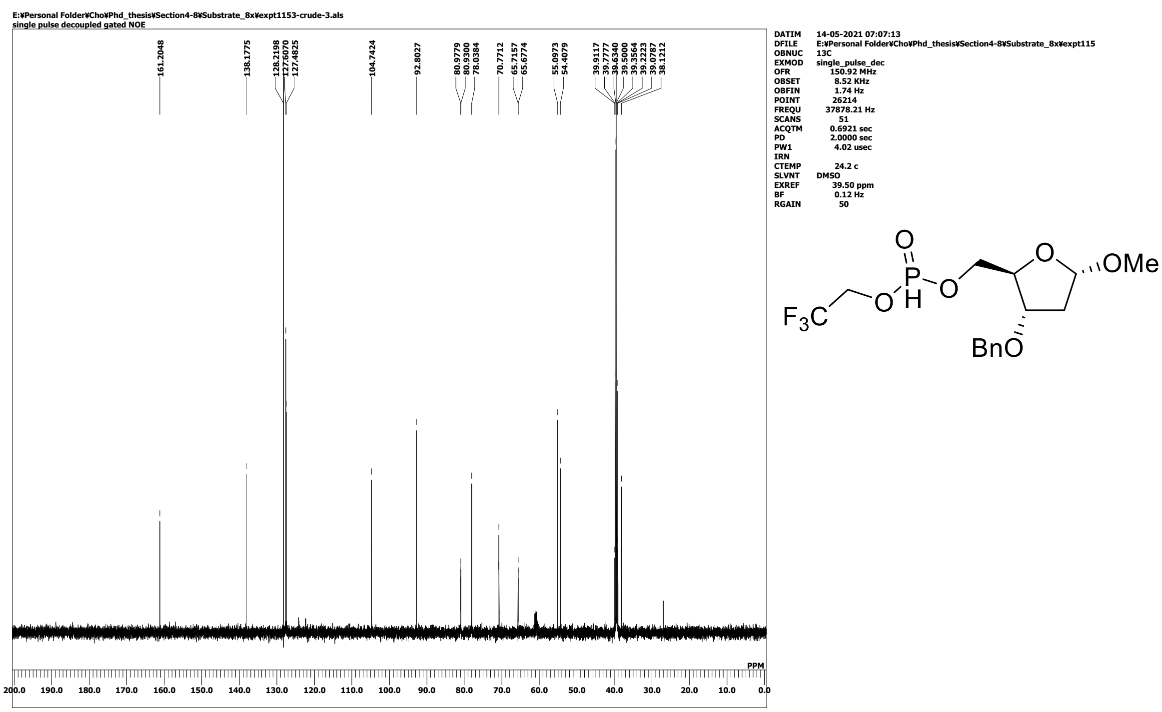
^{19}F NMR (565 MHz, DMSO-d_6) of **3t**



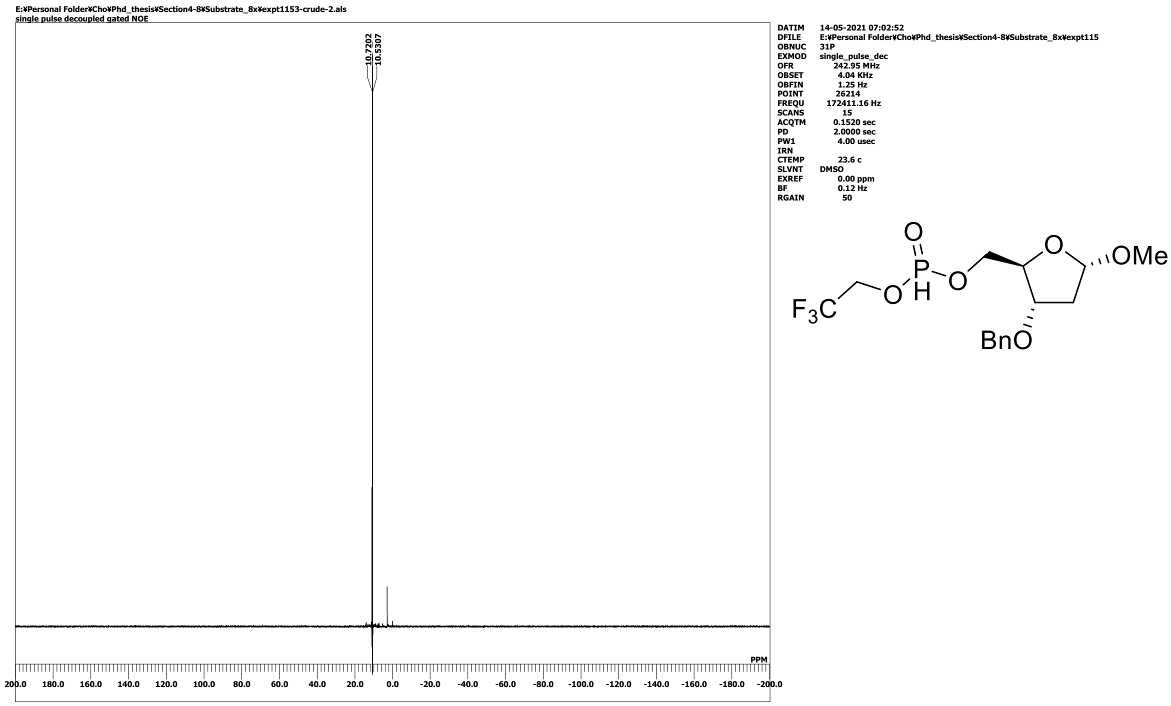
[1]H NMR (600 MHz, DMSO-d_6) of **3u**



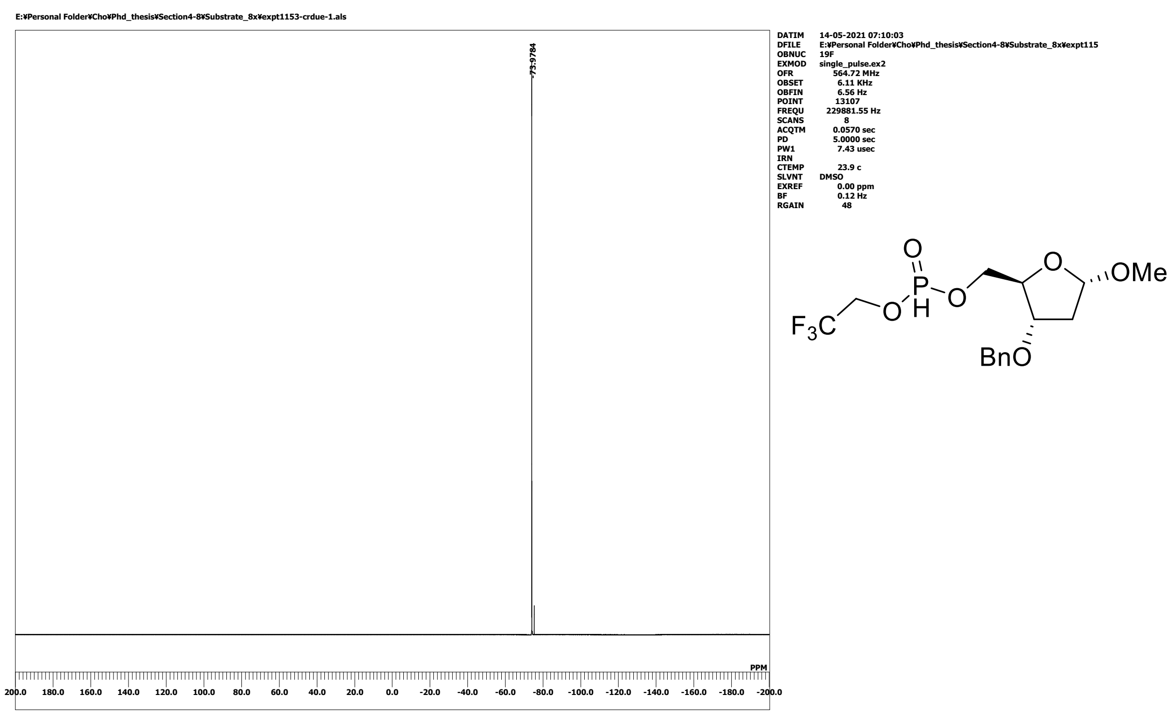
[13]C NMR (151 MHz, DMSO-d_6) of **3u**



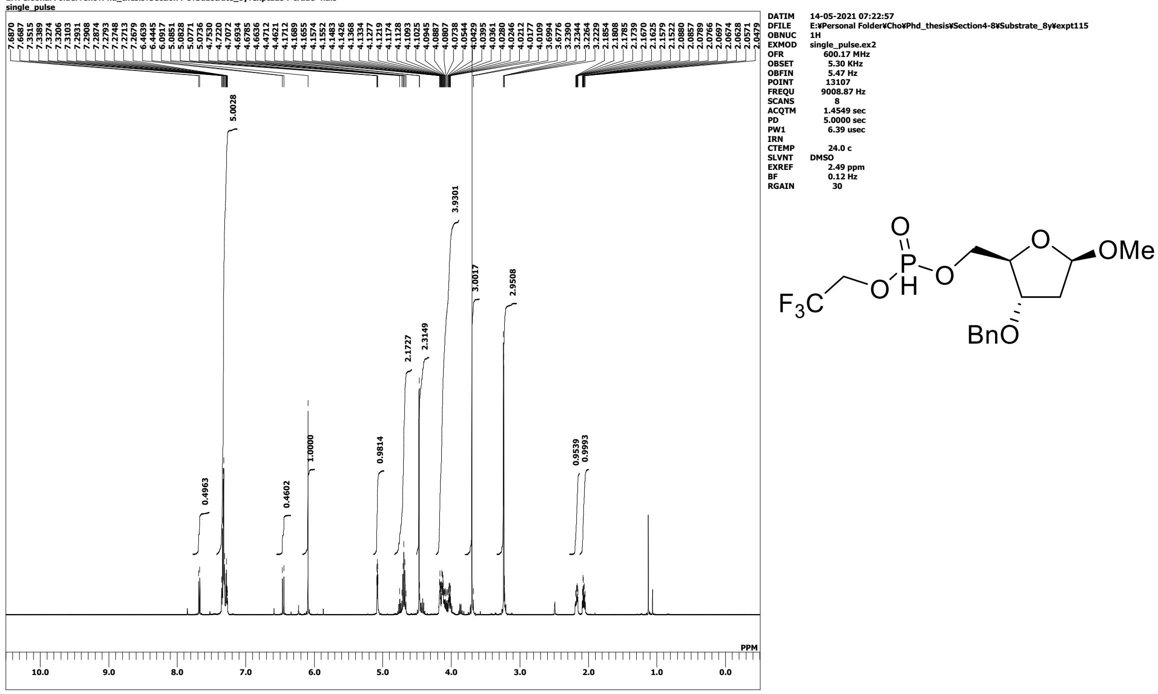
^{31}P NMR (243 MHz, DMSO-d_6) of **3u**



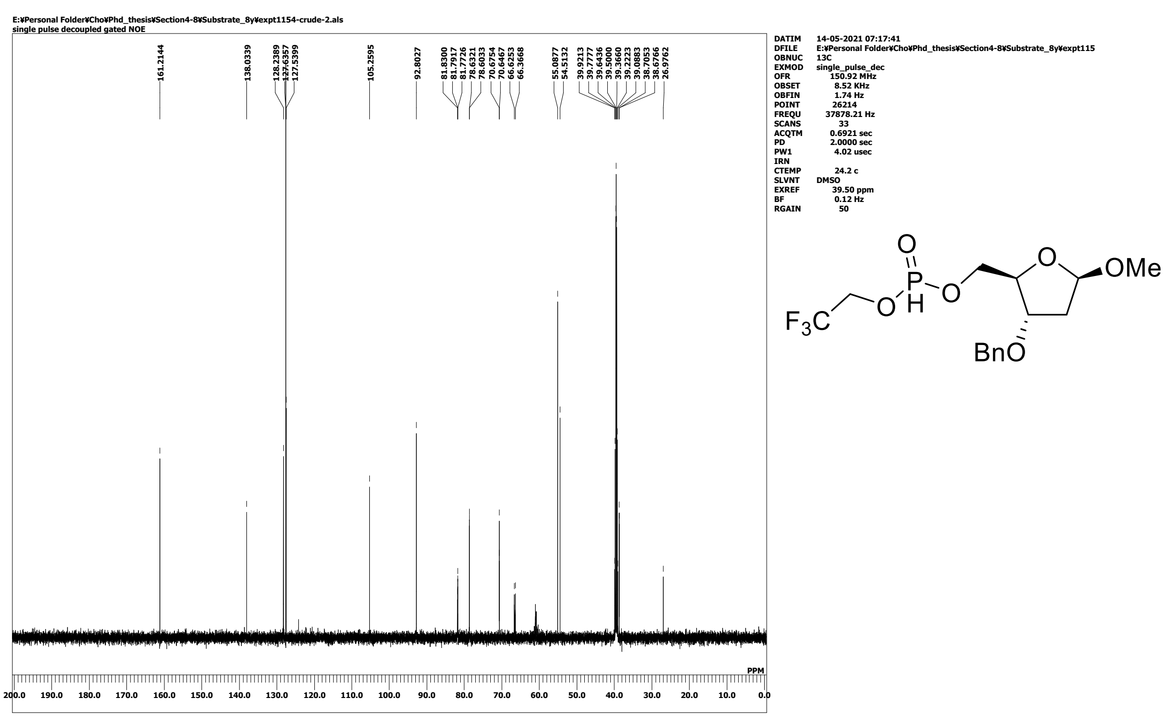
^{19}F NMR (565 MHz, DMSO-d_6) of **3u**



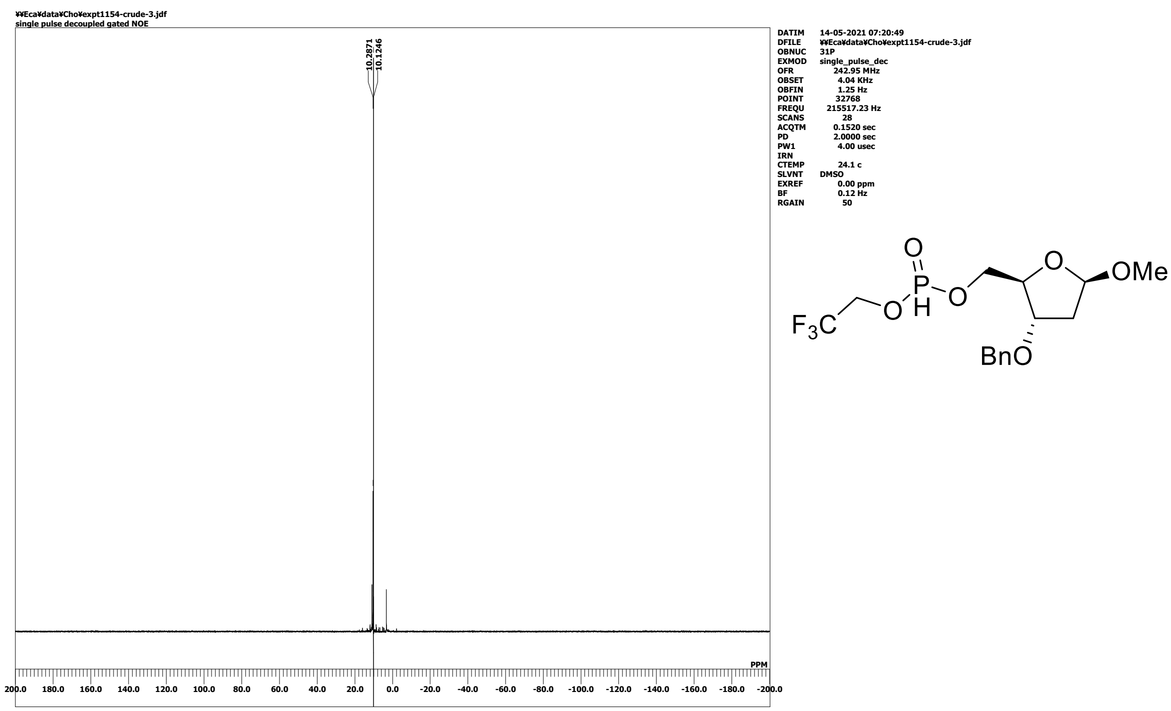
^{1}H NMR (600 MHz, DMSO-d_6) of **3v**



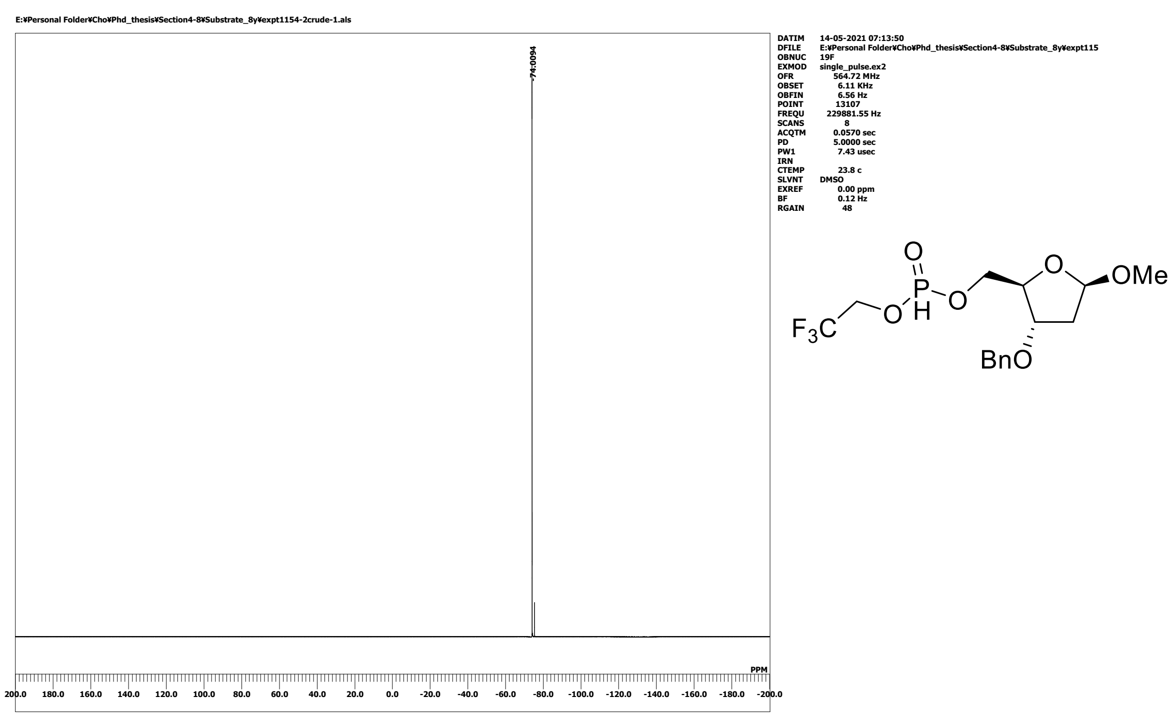
^{13}C NMR (151 MHz, DMSO-d_6) of **3v**



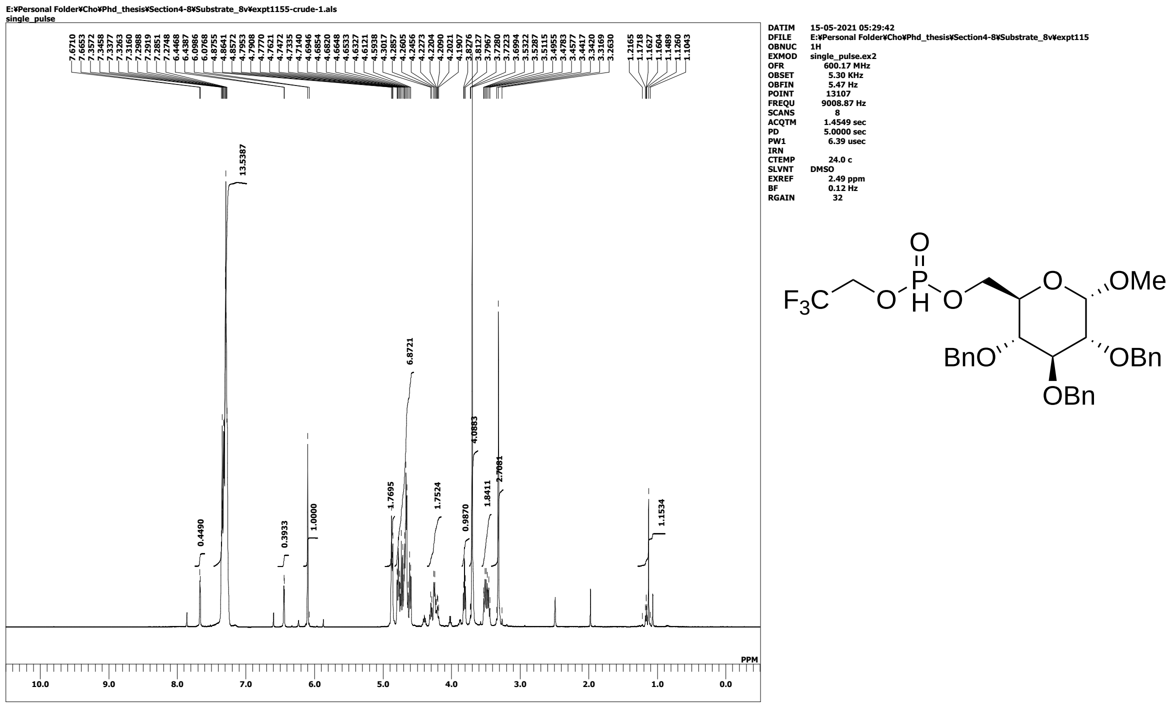
^{31}P NMR (243 MHz, DMSO-d_6) of **3v**



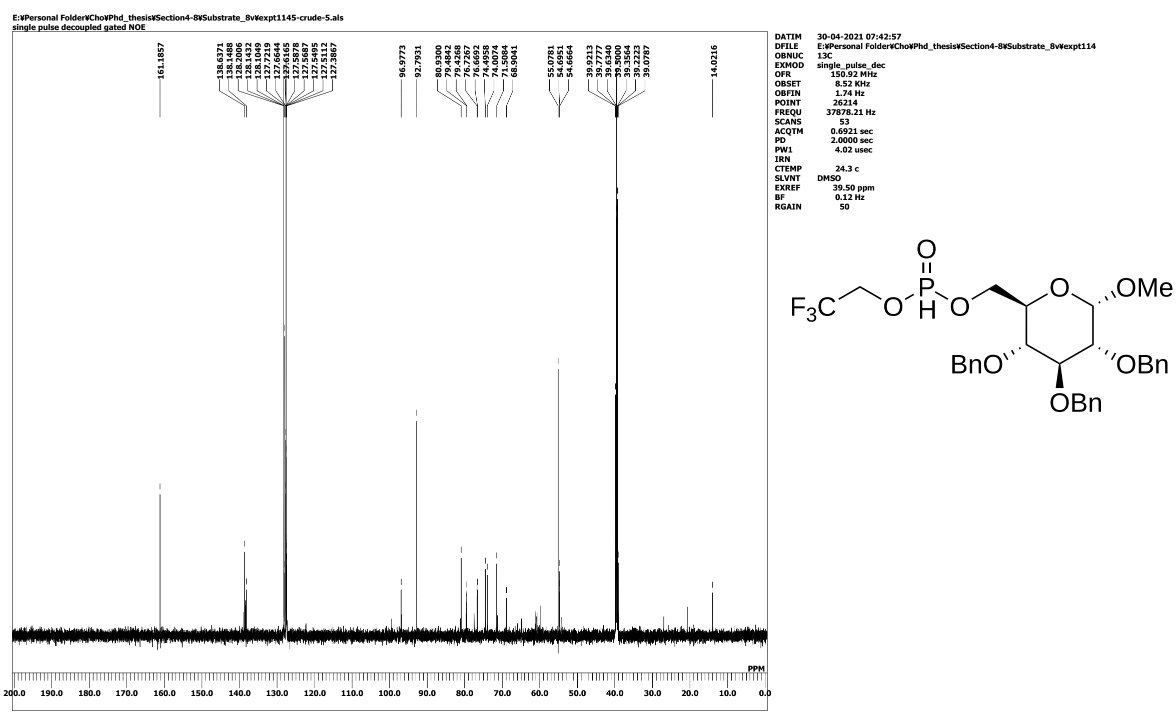
^{19}F NMR (565 MHz, DMSO-d_6) of **3v**



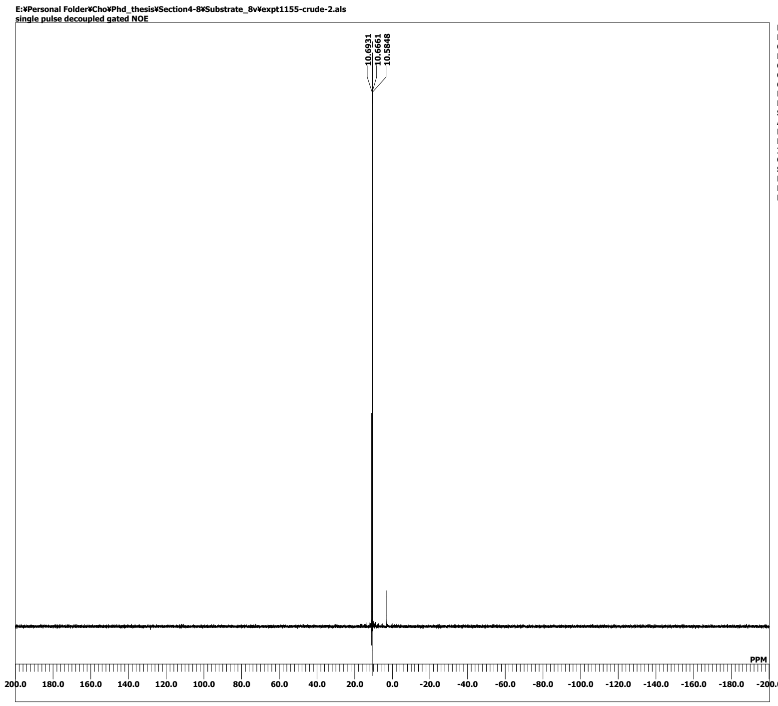
^{1}H NMR (600 MHz, DMSO-d_6) of **3w**

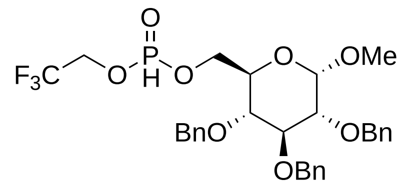


^{13}C NMR (151 MHz, DMSO-d_6) of **3w**

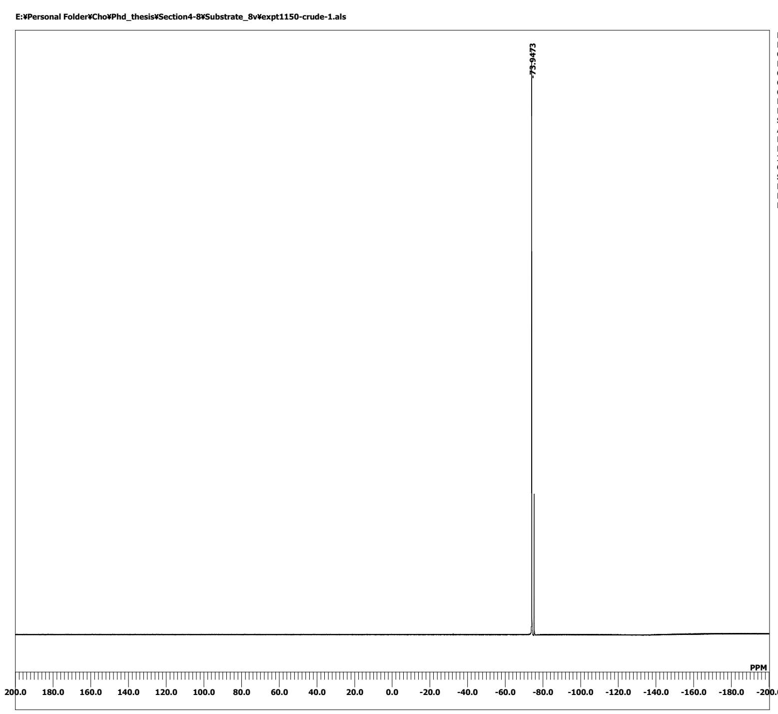


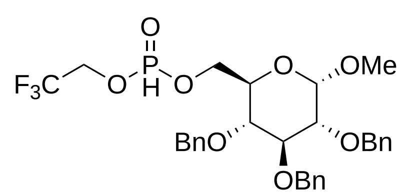
^{31}P NMR (243 MHz, DMSO-d_6) of **3w**



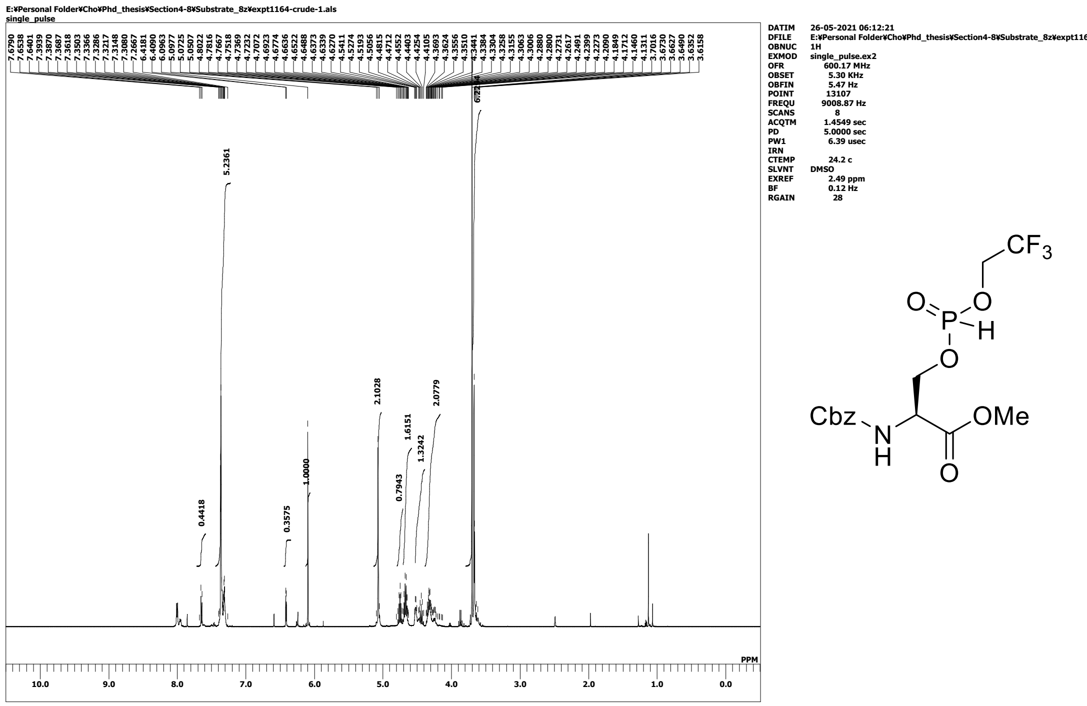


^{19}F NMR (565 MHz, DMSO-d_6) of **3w**

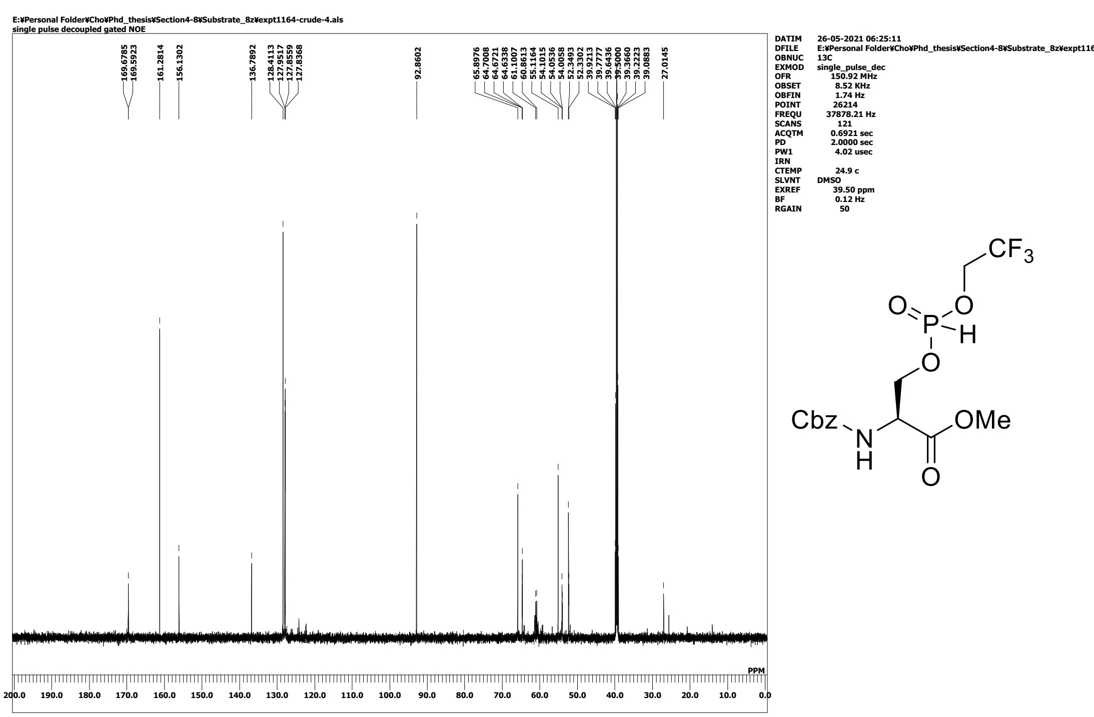




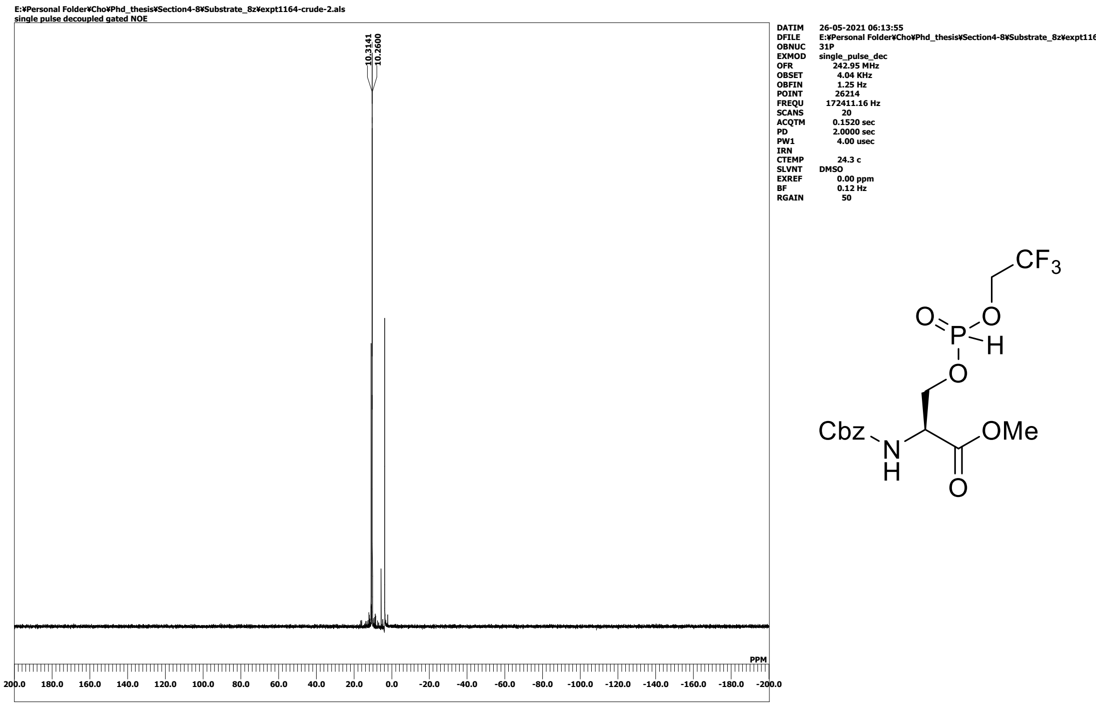
^{1}H NMR (600 MHz, DMSO-d_6) of **3x**



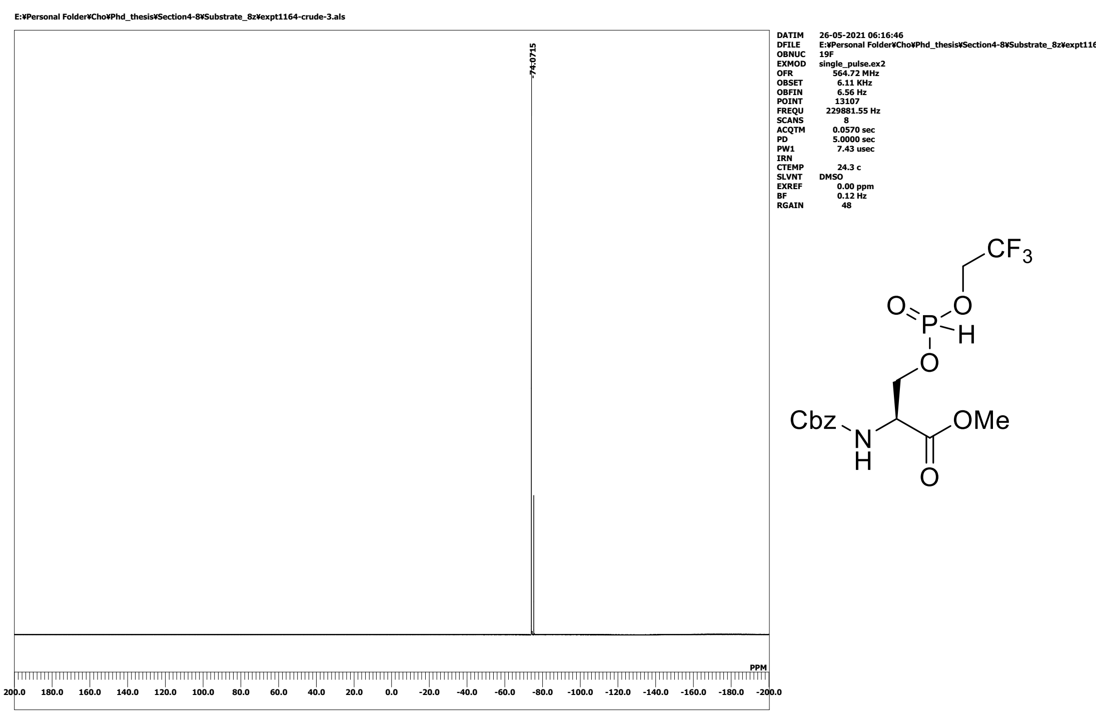
^{13}C NMR (151 MHz, DMSO-d_6) of **3x**



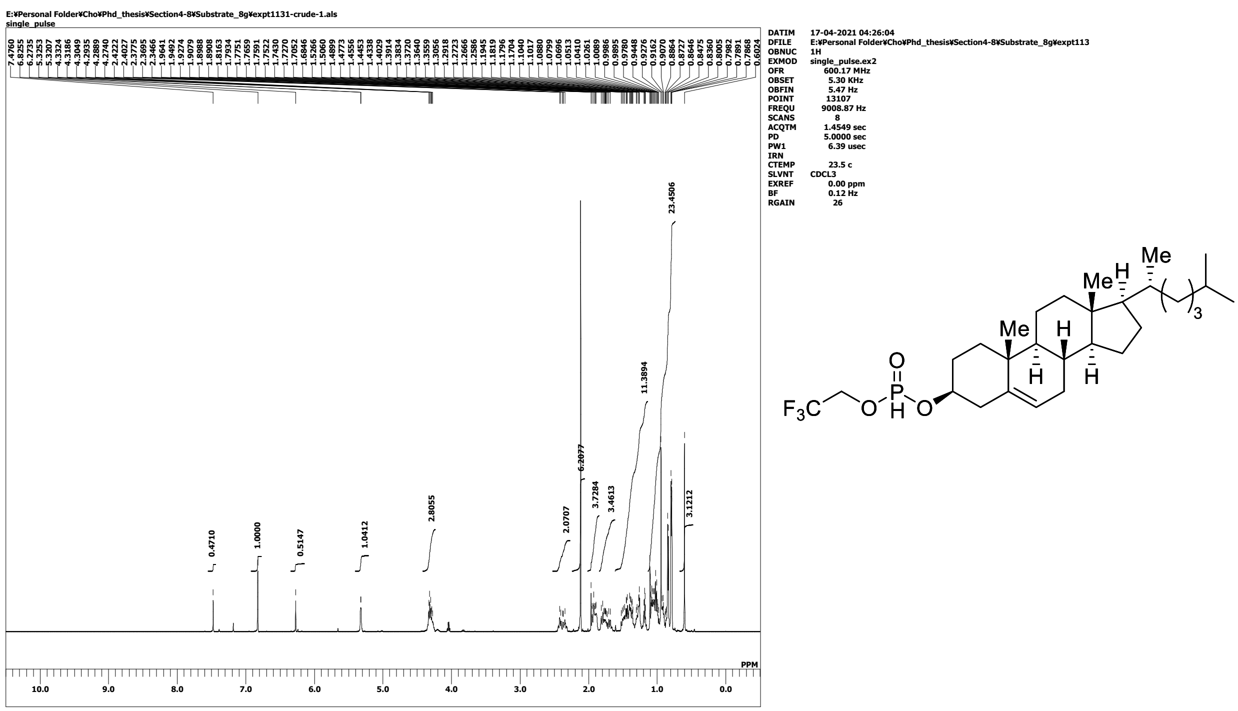
^{31}P NMR (243 MHz, DMSO-d_6) of **3x**



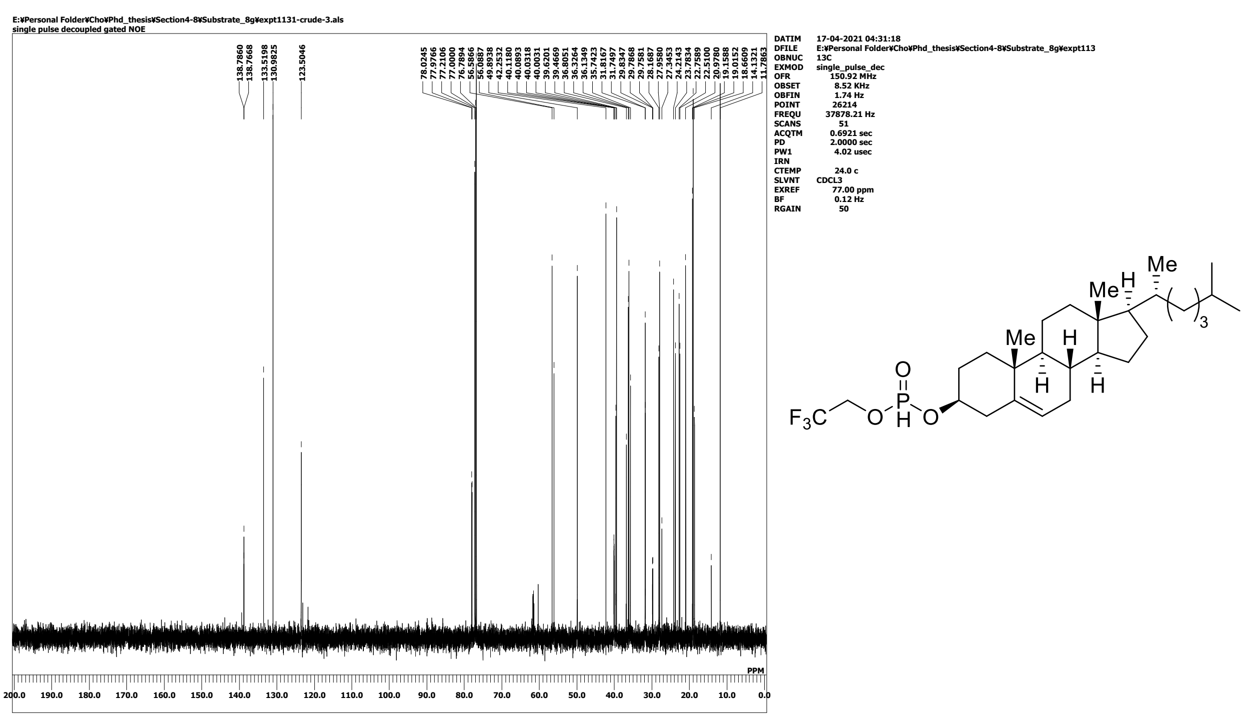
^{19}F NMR (565 MHz, DMSO-d_6) of **3x**



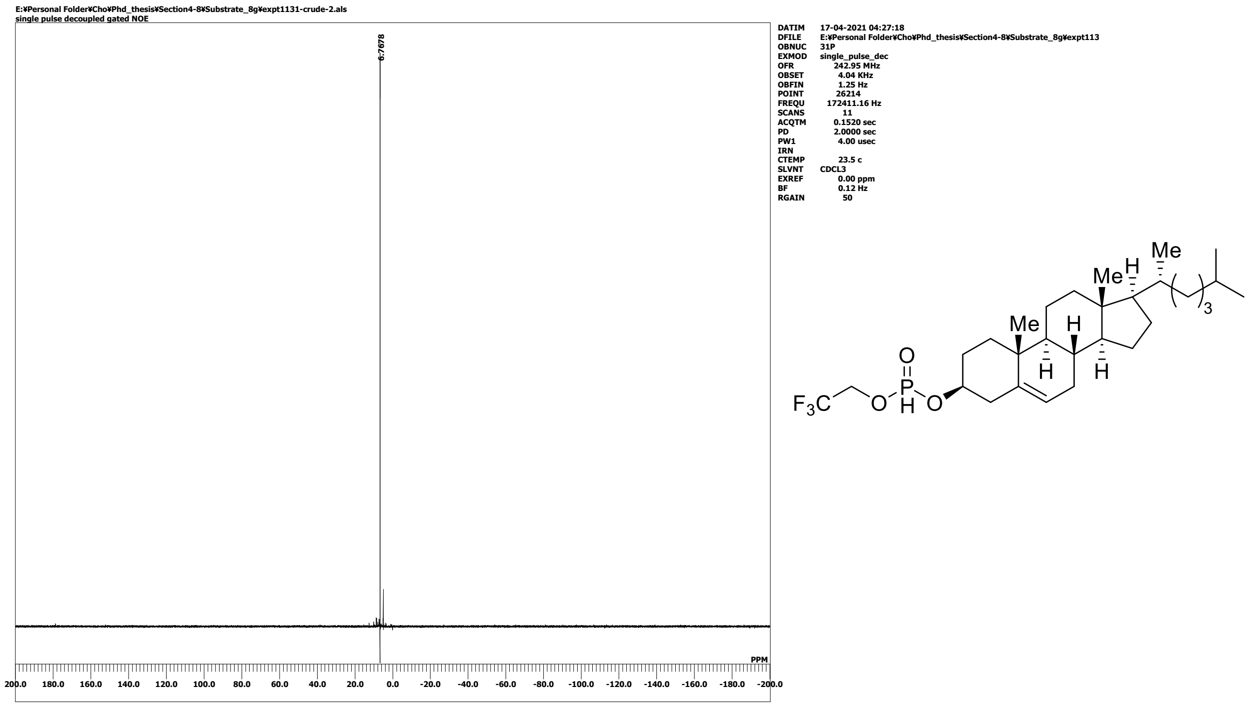
^{1}H NMR (600 MHz, $CDCl_3$) of **3y**



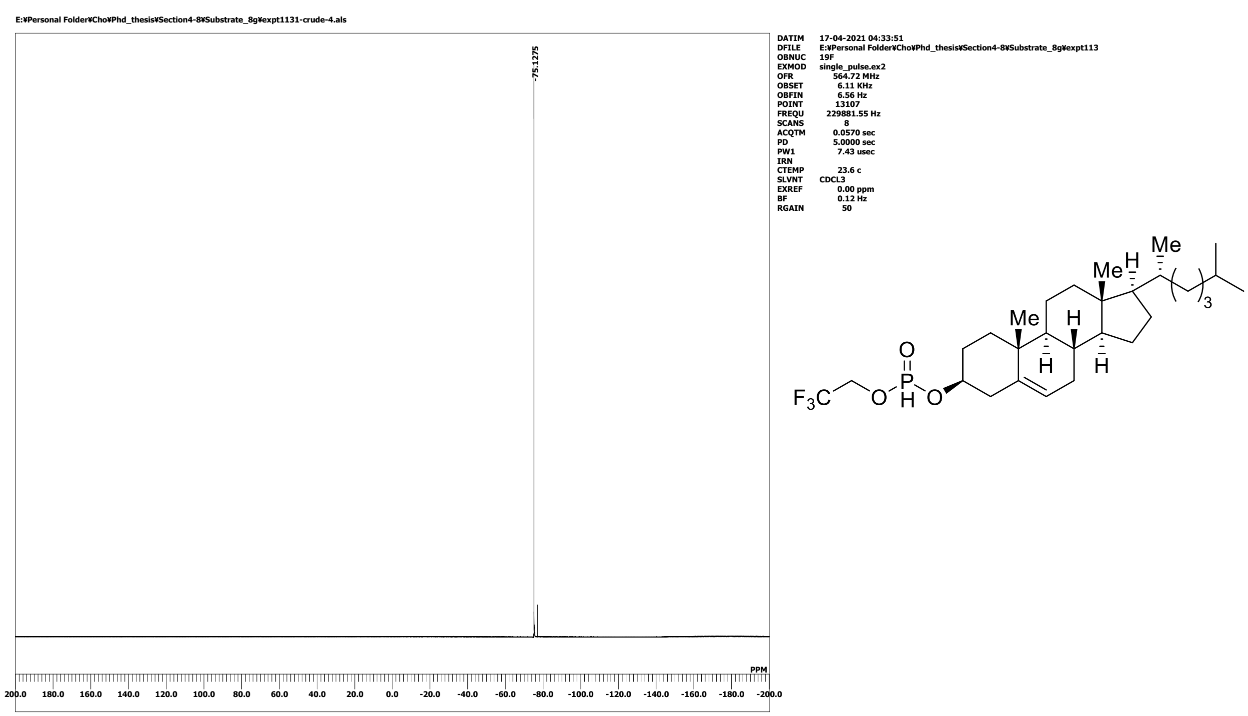
^{13}C NMR (151 MHz, $CDCl_3$) of **3y**



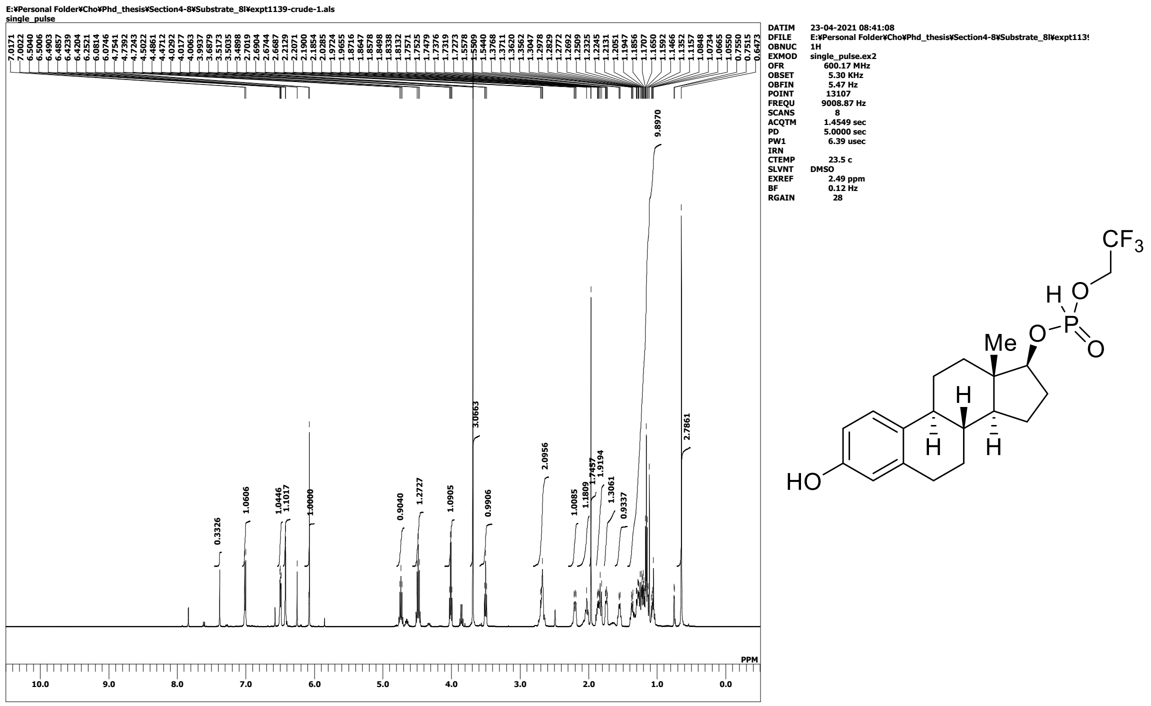
^{31}P NMR (243 MHz, $CDCl_3$) of **3y**



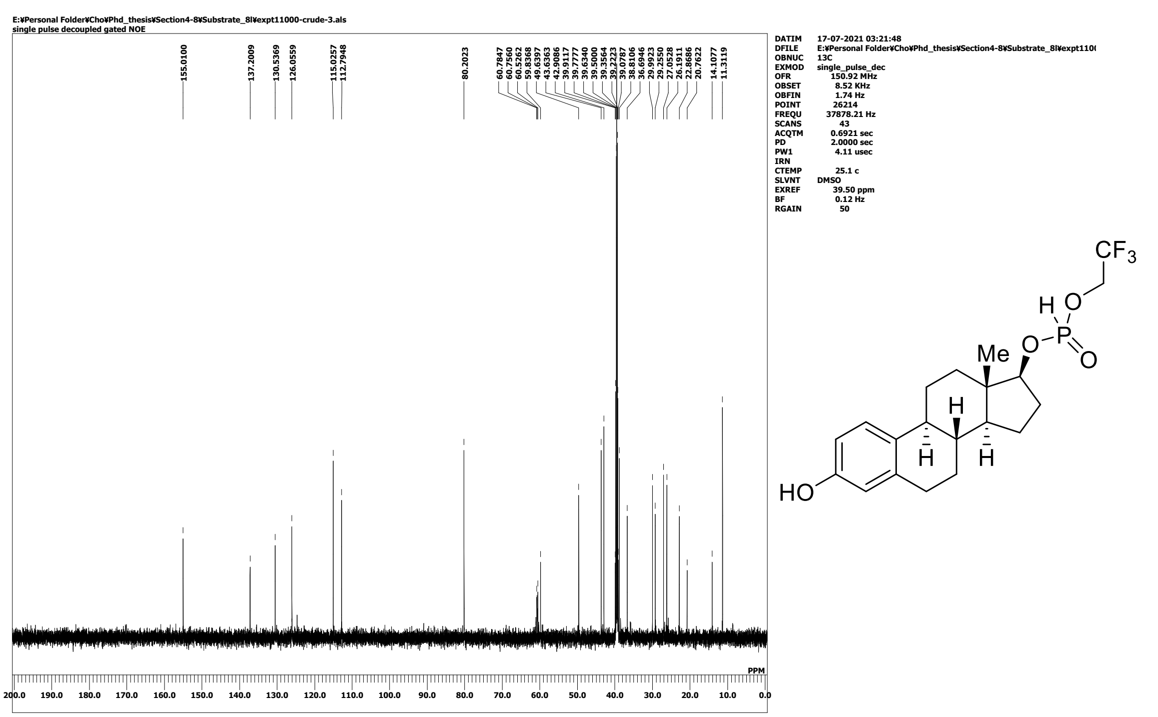
^{19}F NMR (565 MHz, $CDCl_3$) of **3y**



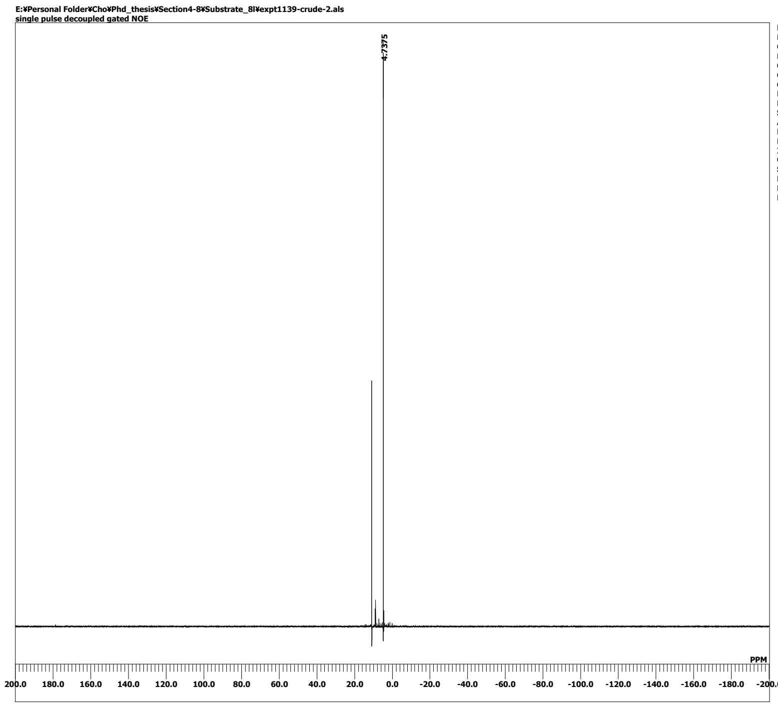
^{1}H NMR (600 MHz, DMSO-d_6) of **3z**

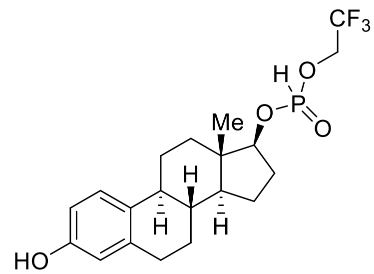


^{13}C NMR (151 MHz, DMSO-d_6) of **3z**

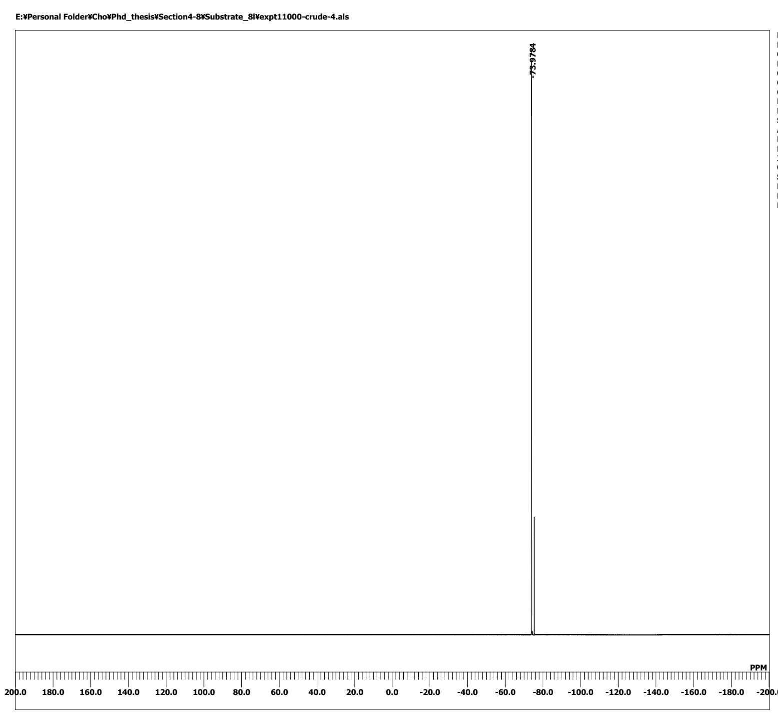


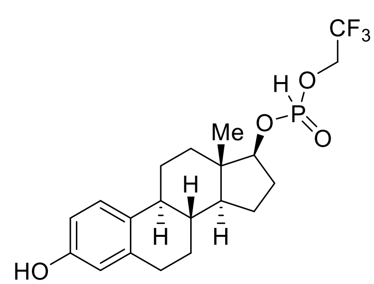
^{31}P NMR (243 MHz, DMSO-d_6) of **3z**



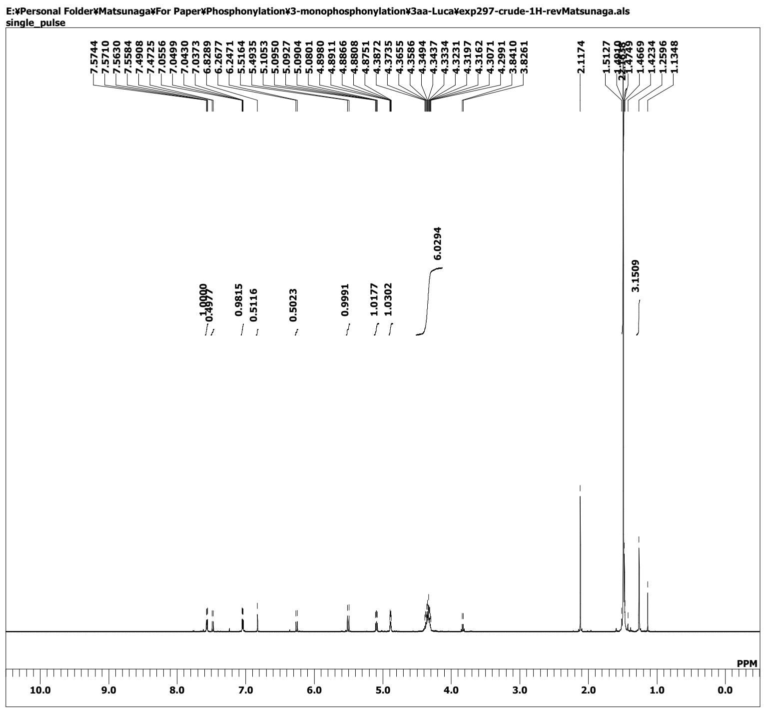


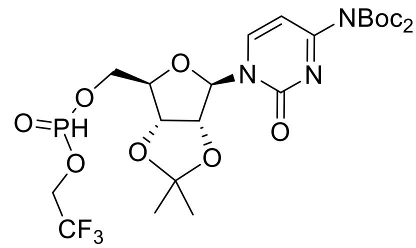
^{19}F NMR (565 MHz, DMSO-d_6) of **3z**



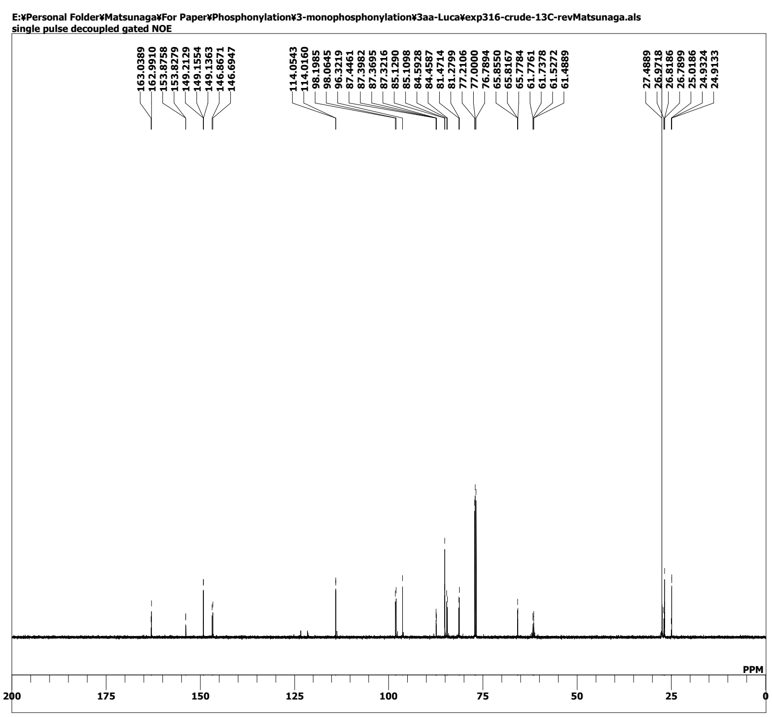


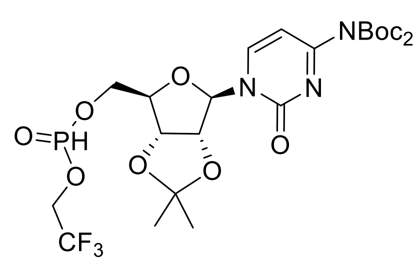
^{1}H NMR (600 MHz, $CDCl_3$) of **3aa**



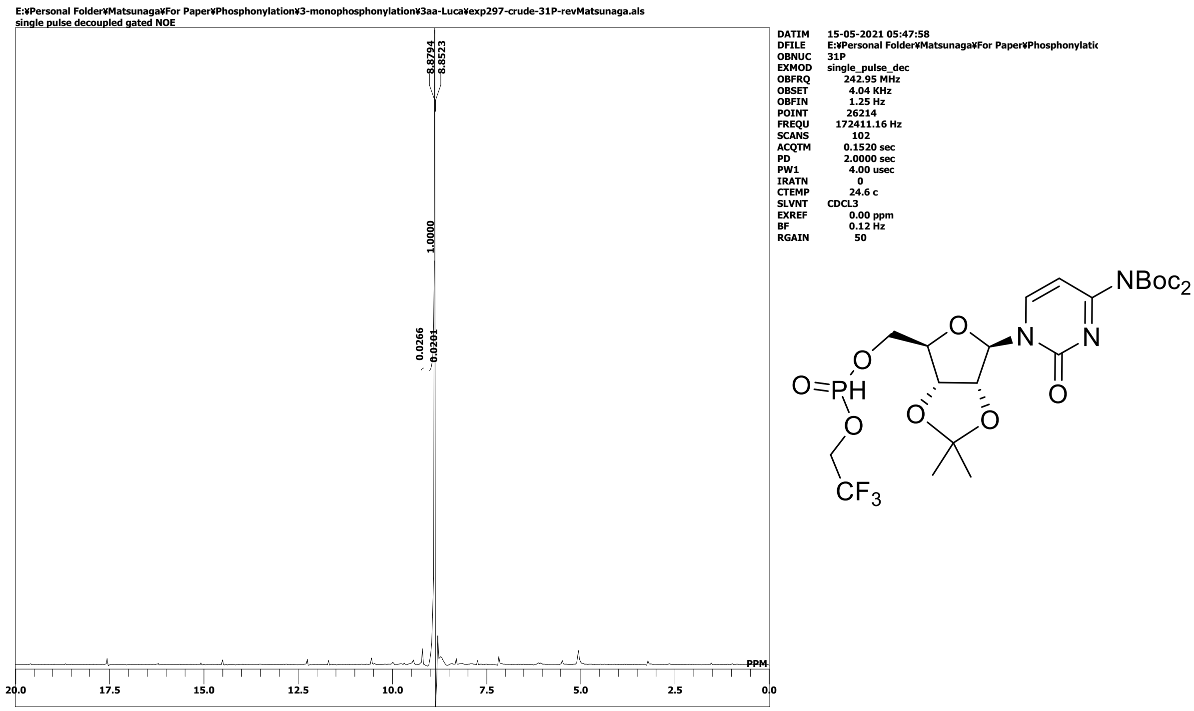


^{13}C NMR (151 MHz, $CDCl_3$) of **3aa**

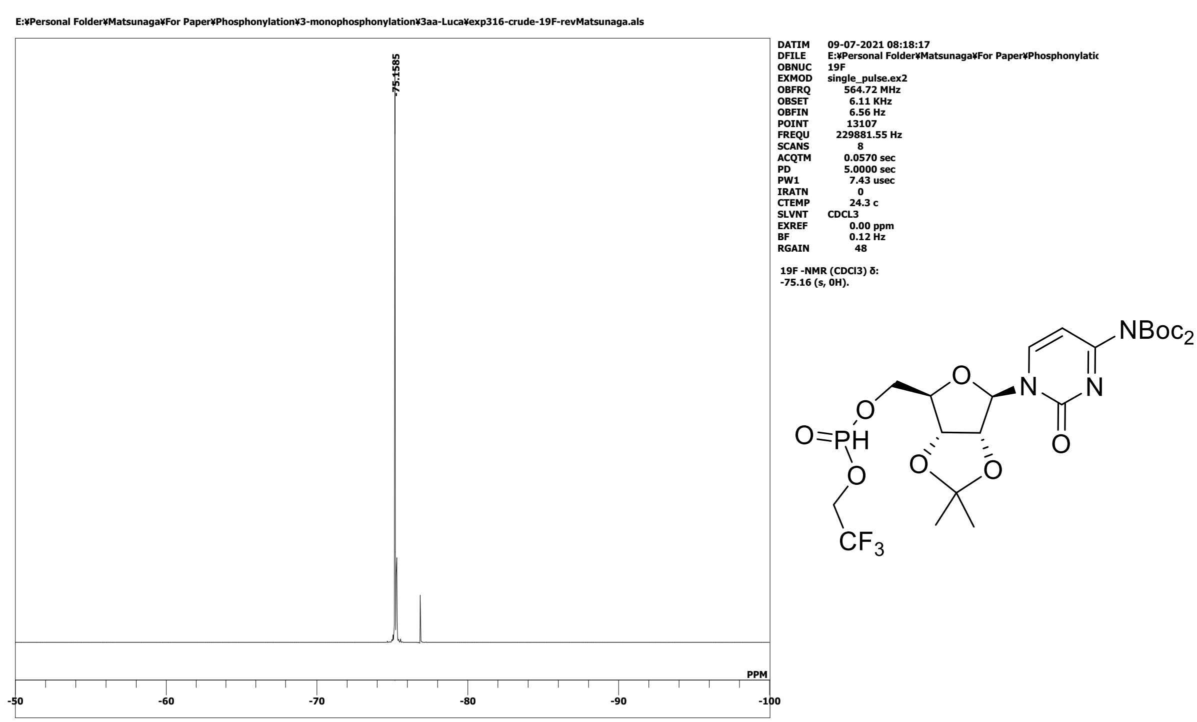




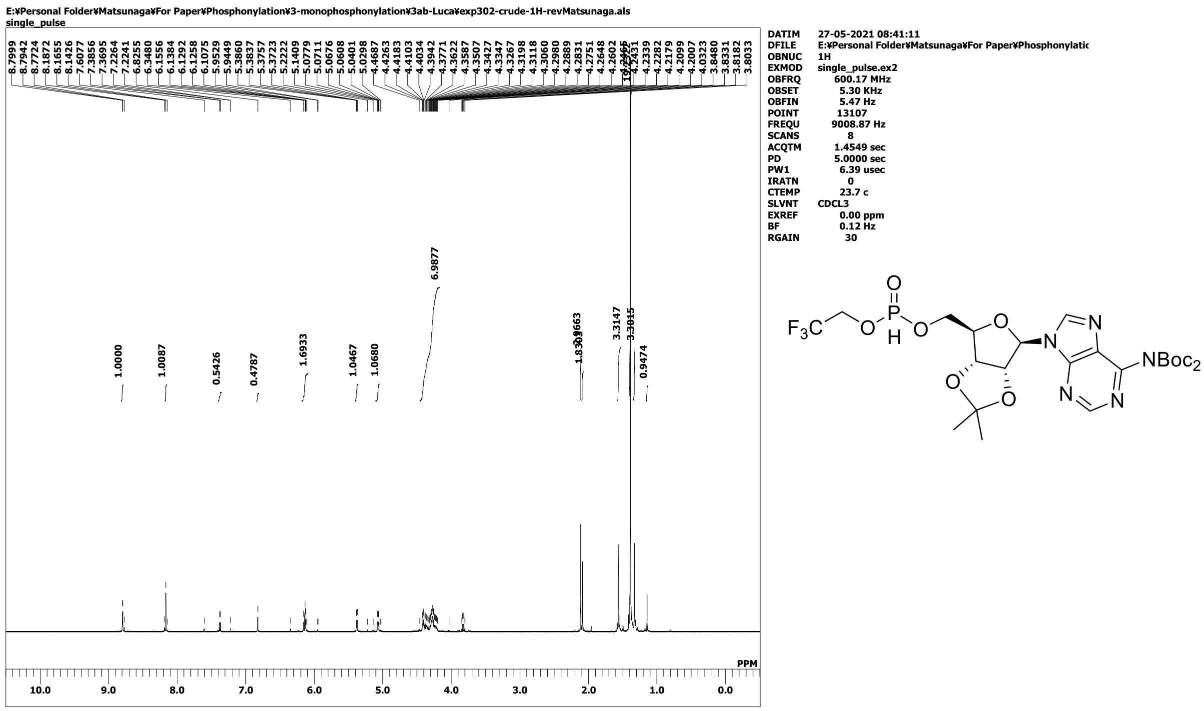
^{31}P NMR (243 MHz, $CDCl_3$) of **3aa**



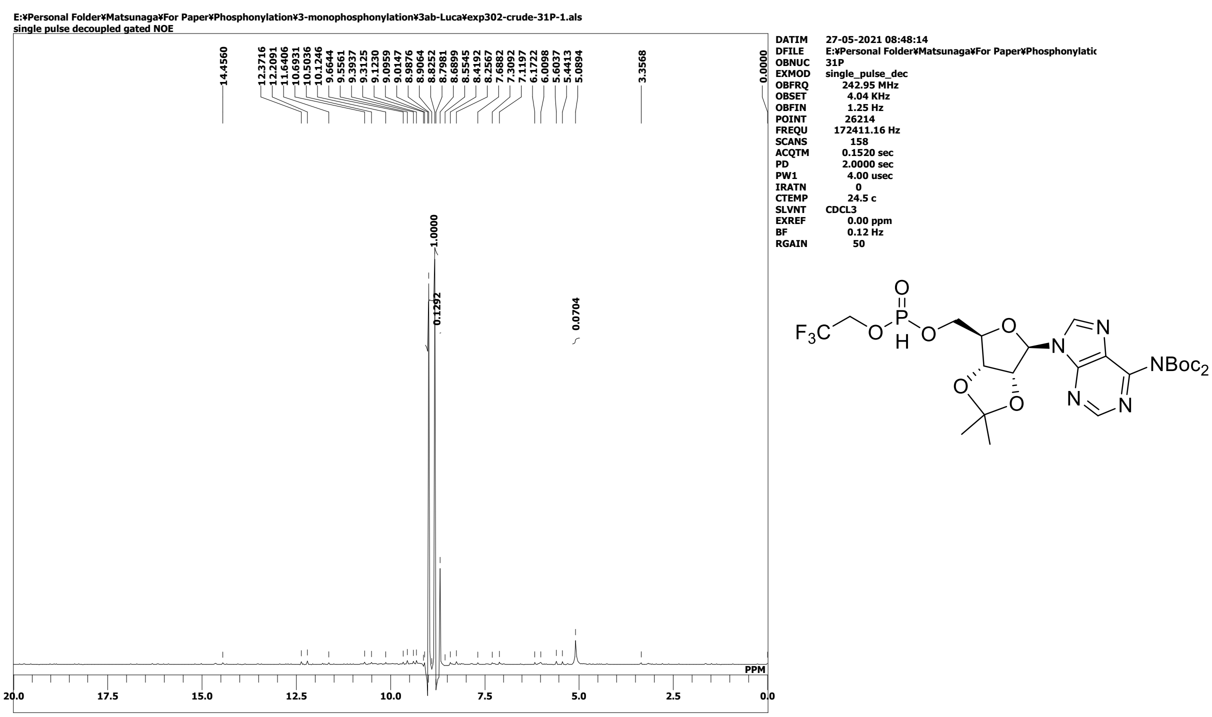
^{19}F NMR (565 MHz, $CDCl_3$) of **3aa**



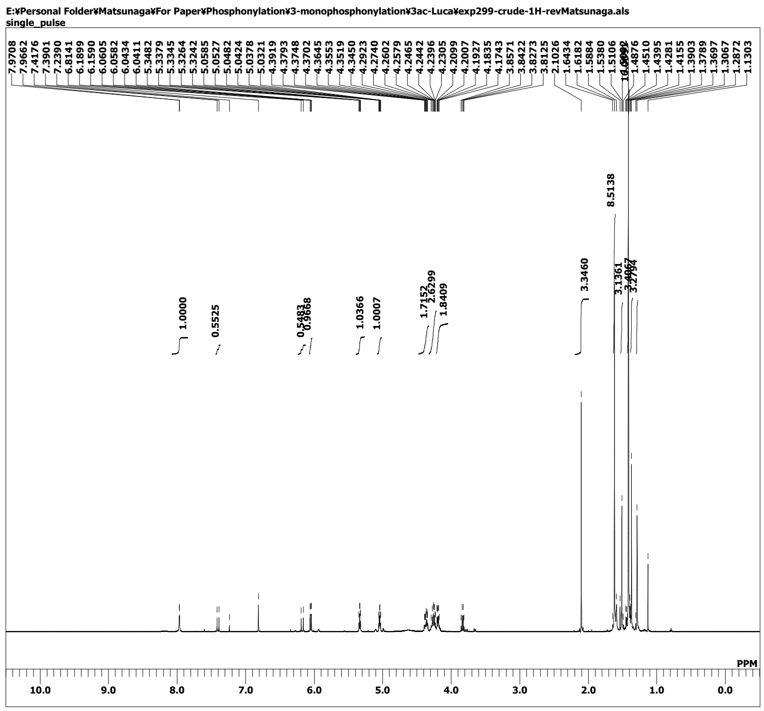
^{1}H NMR (600 MHz, $CDCl_3$) of **3ab**

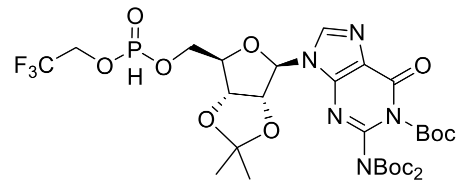


^{31}P NMR (243 MHz, $CDCl_3$) of **3ab**

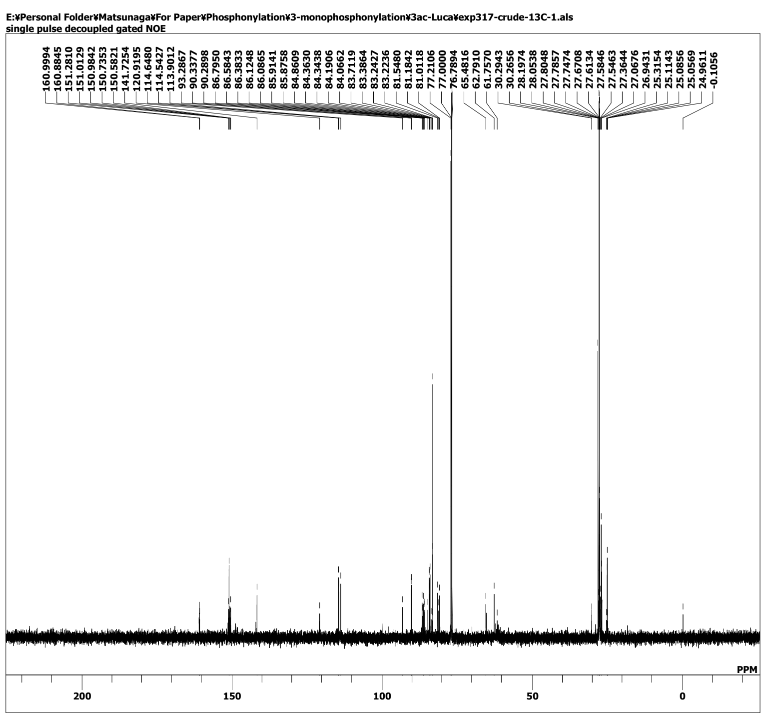


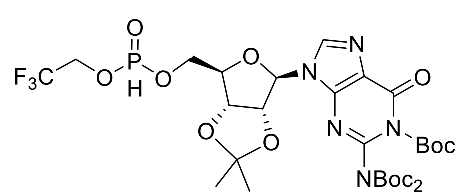
^{1}H NMR (600 MHz, $CDCl_3$) of **3ac**



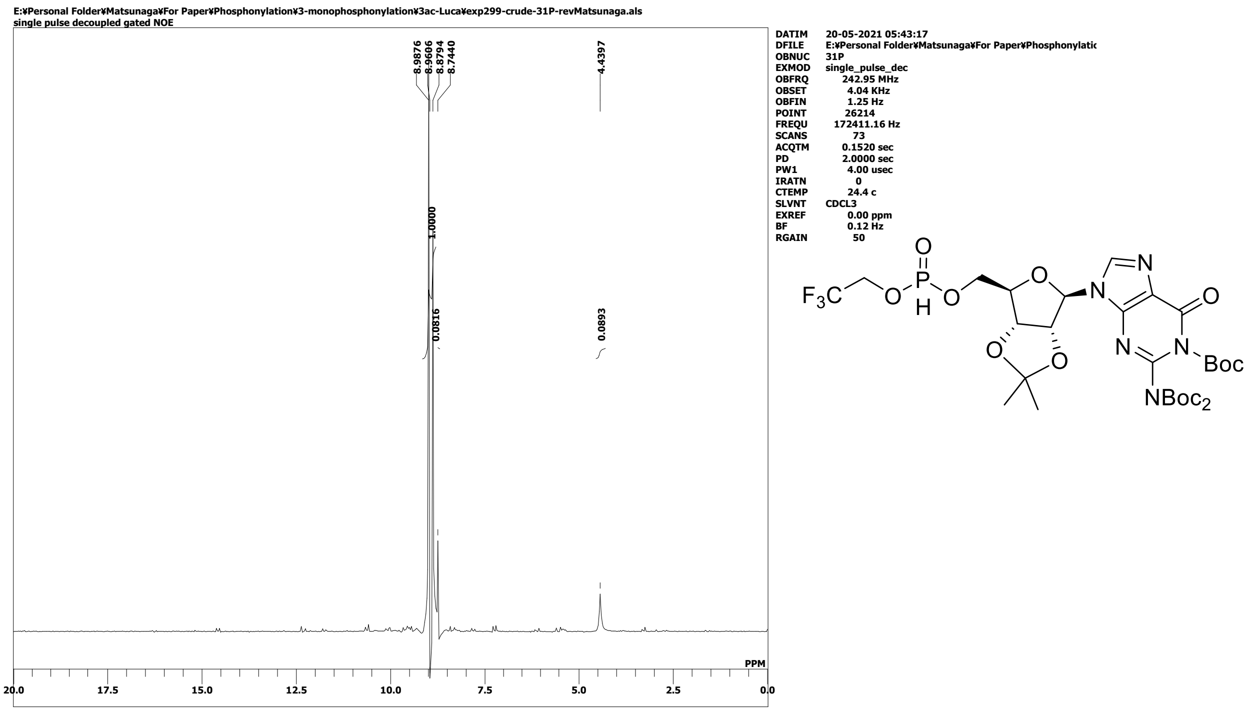


^{13}C NMR (151 MHz, $CDCl_3$) of **3ac**

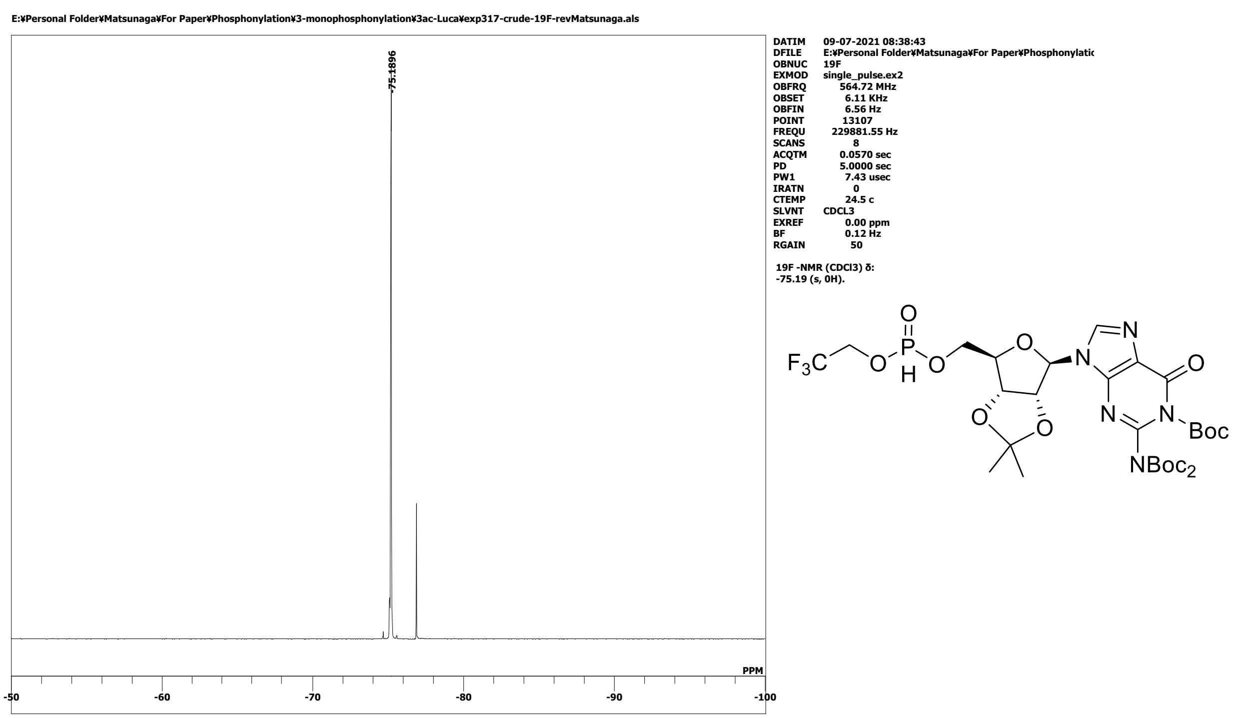




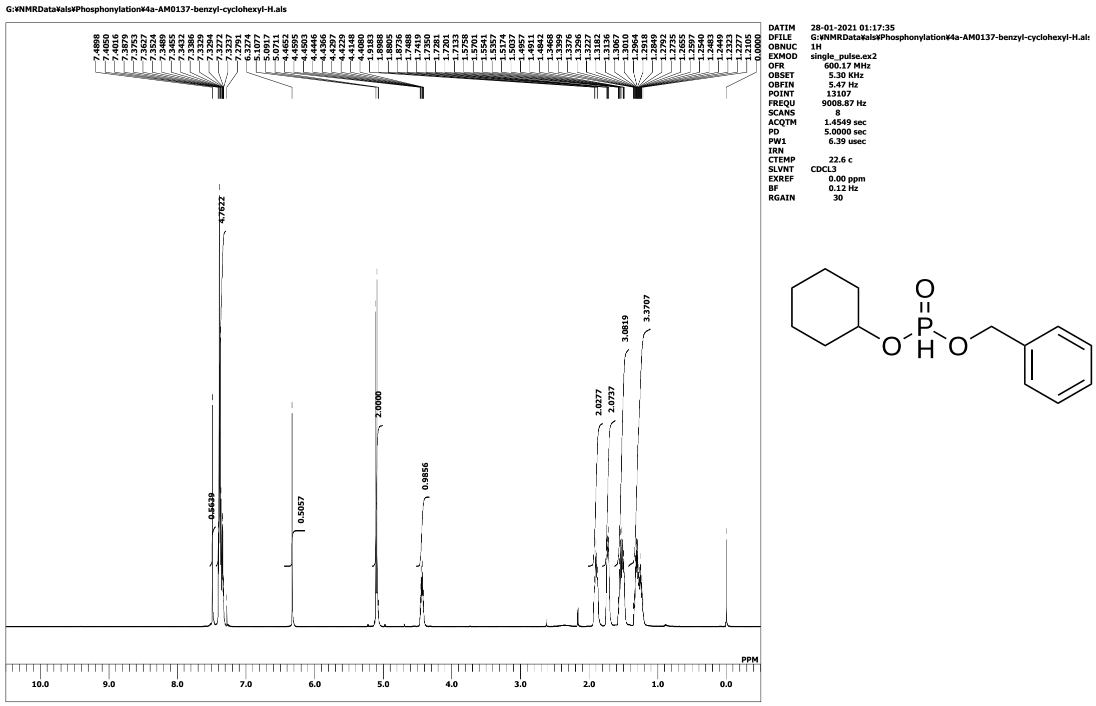
^{31}P NMR (243 MHz, $CDCl_3$) of **3ac**



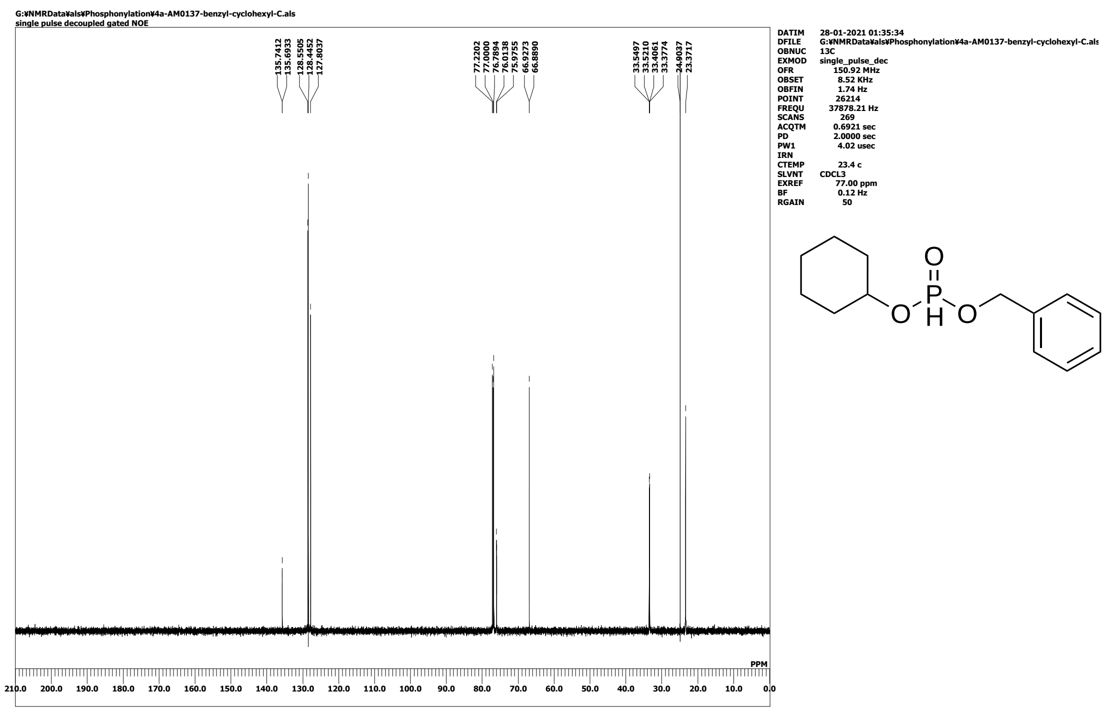
^{19}F NMR (565 MHz, $CDCl_3$) of **3ac**



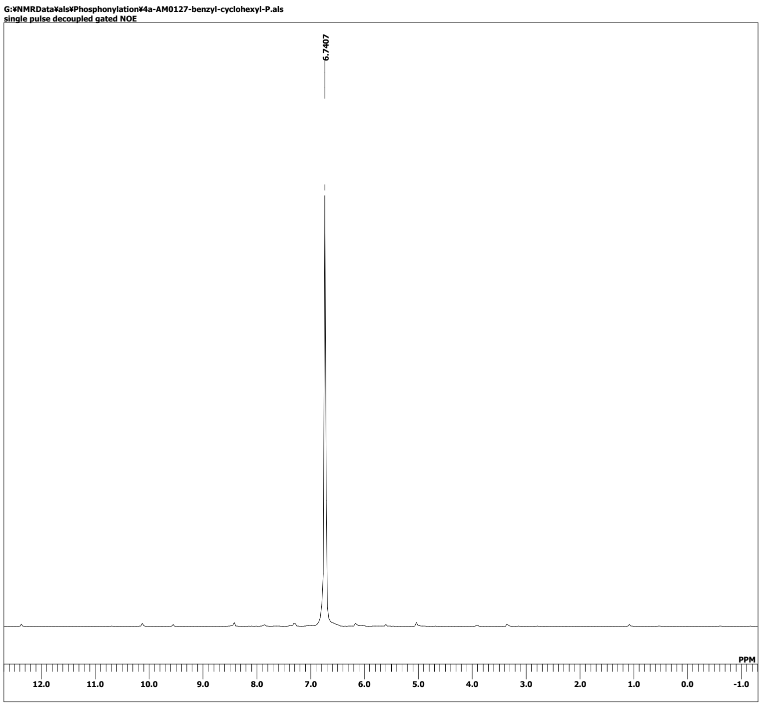
^1H NMR (600 MHz, $CDCl_3$) of **4a**

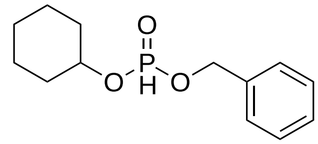


^{13}C NMR (151 MHz, $CDCl_3$) of **4a**

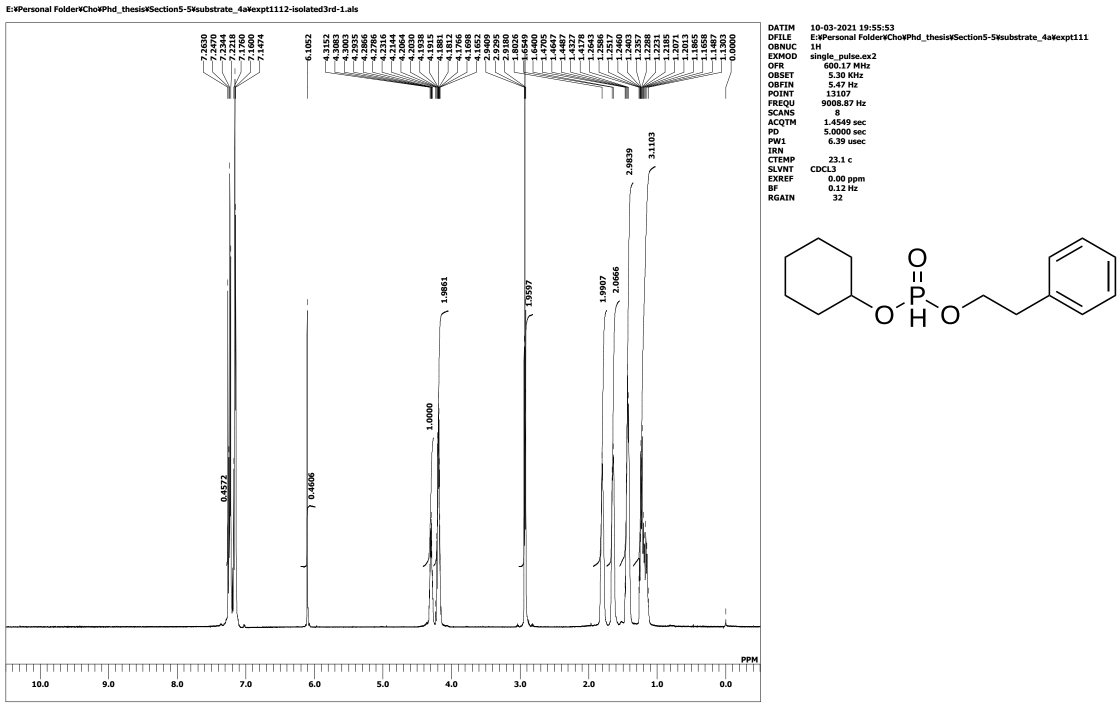


^{31}P NMR (243 MHz, $CDCl_3$) of **4a**

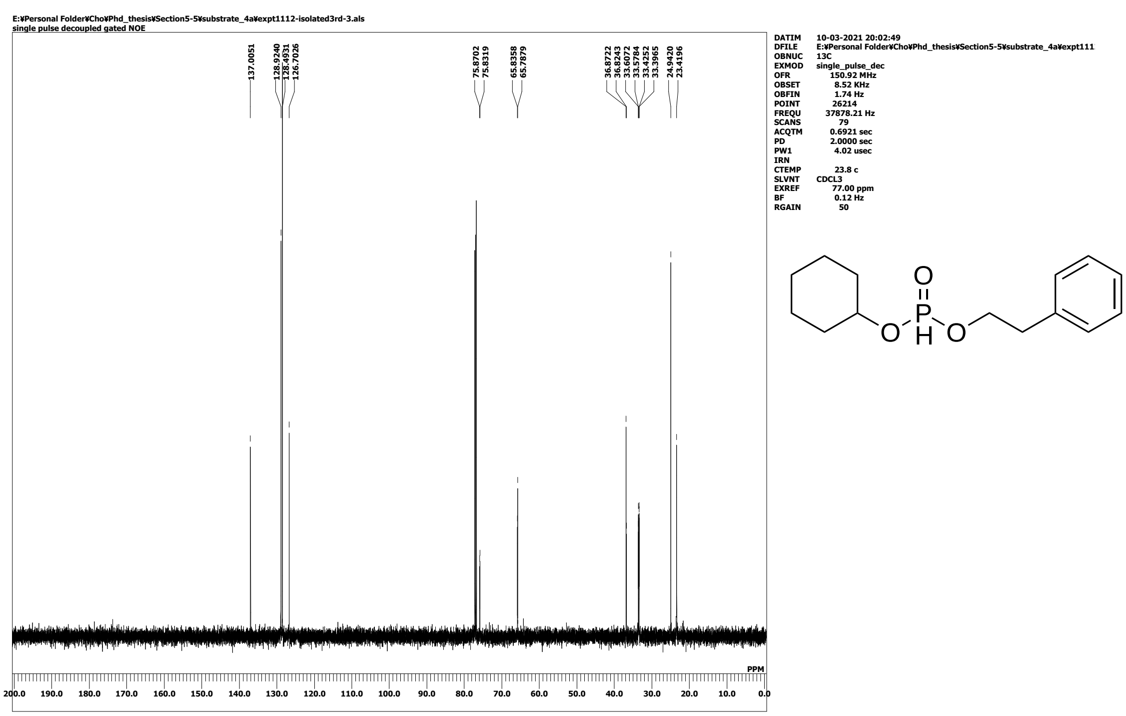




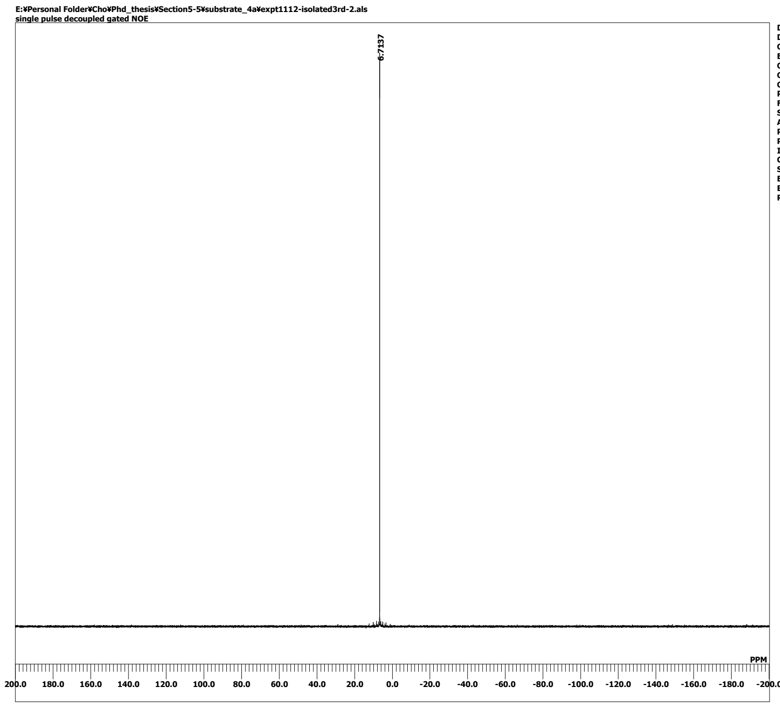
^{1}H NMR (600 MHz, $CDCl_3$) of **4b**



^{13}C NMR (151 MHz, $CDCl_3$) of **4b**



^{31}P NMR (243 MHz, $CDCl_3$) of **4b**



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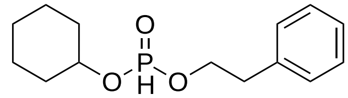

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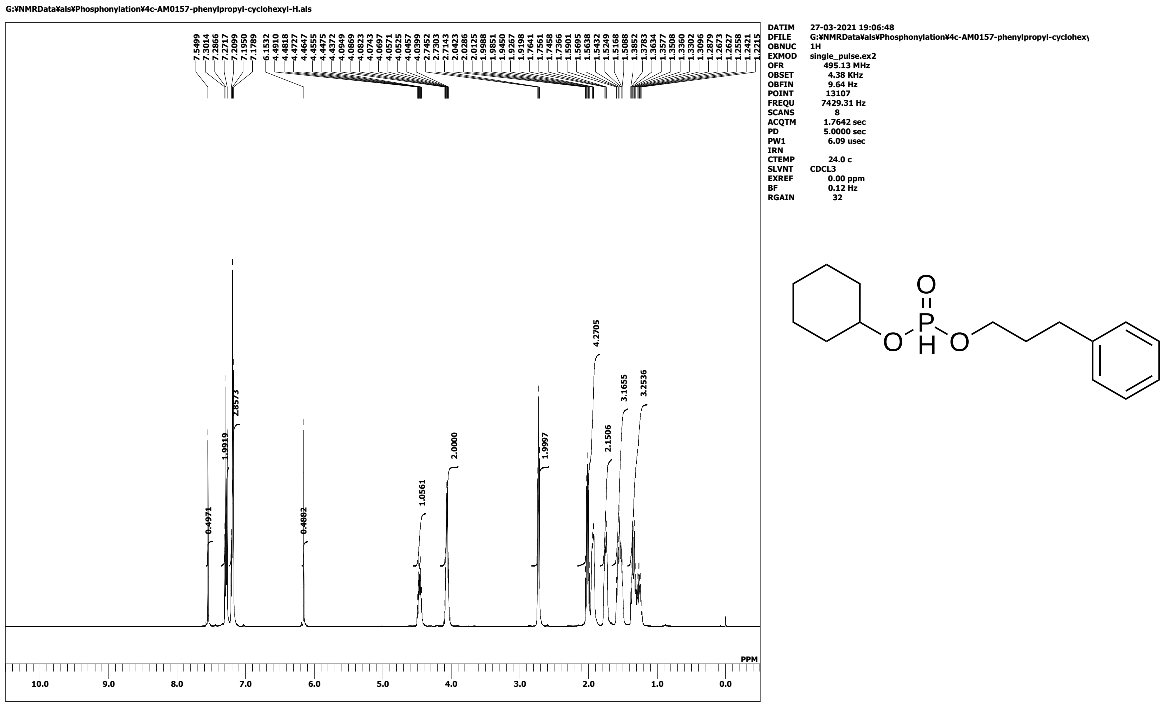

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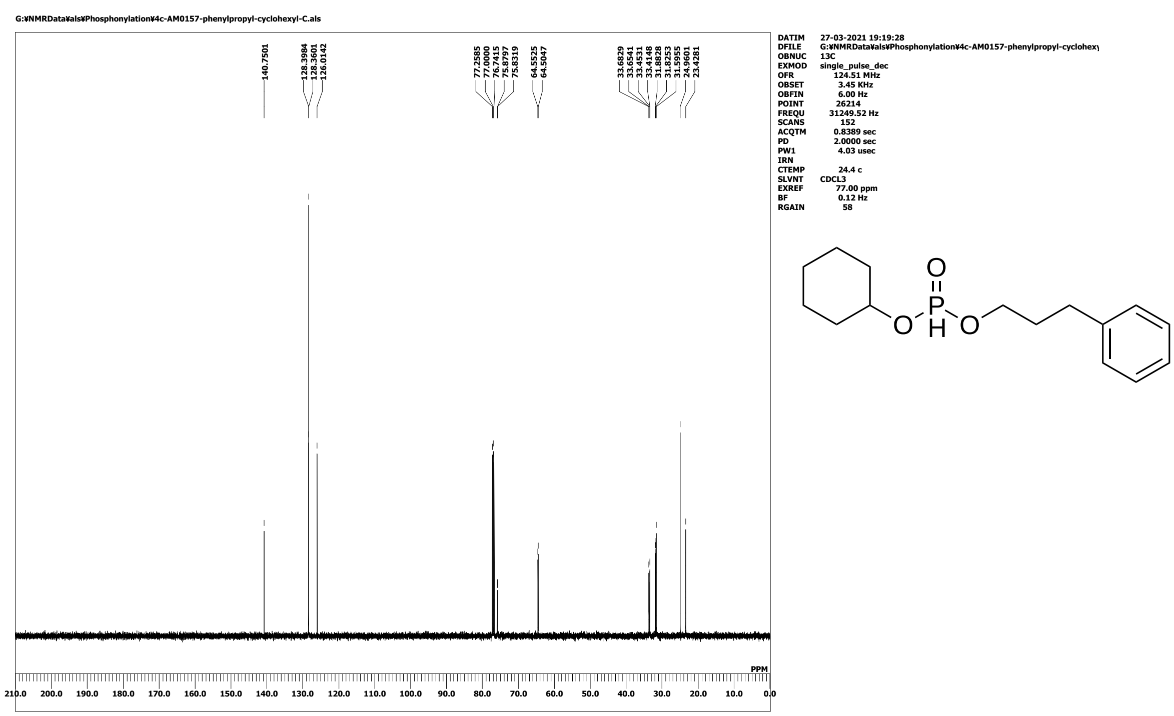

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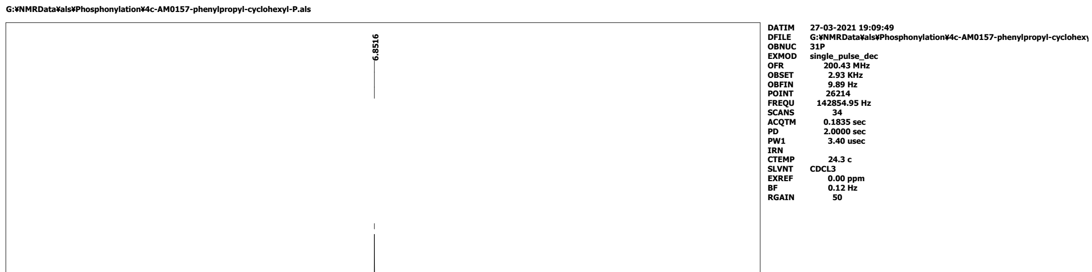
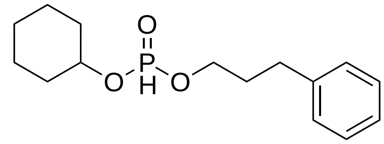
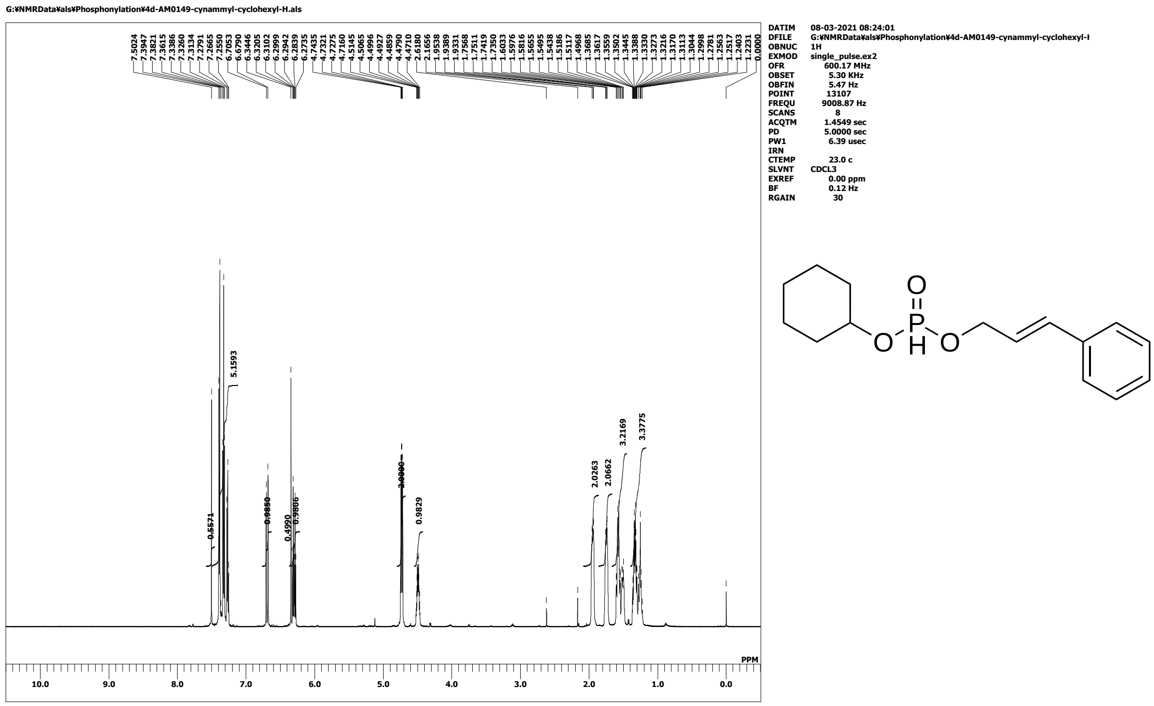
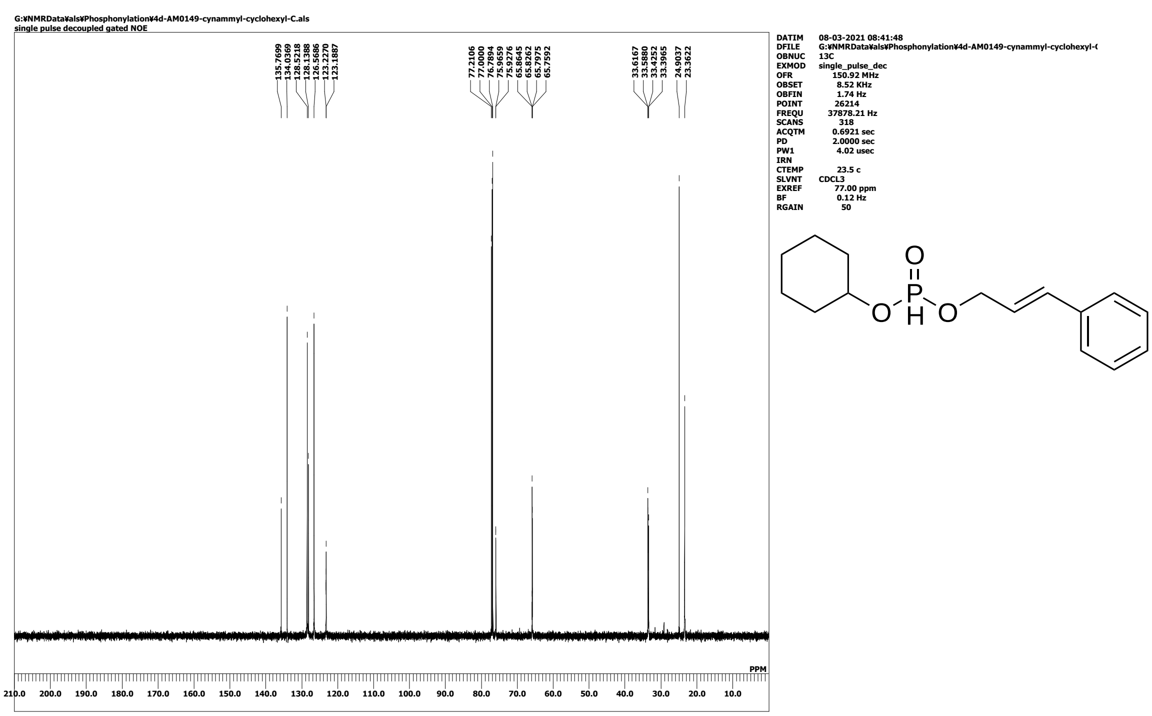




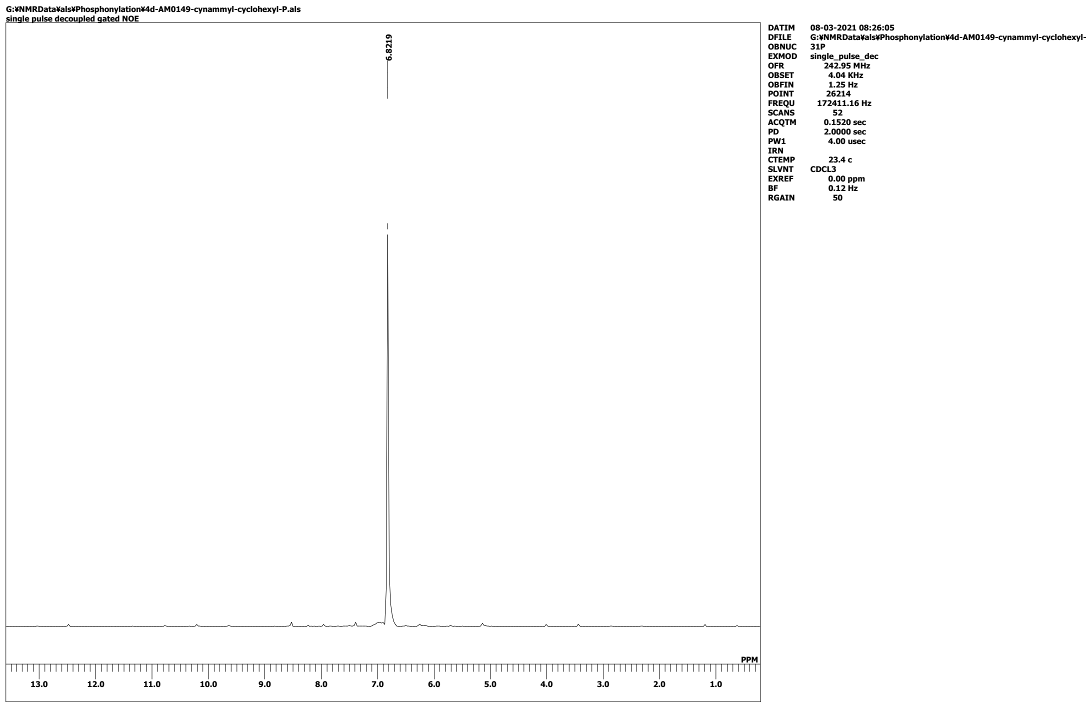
^{1}H NMR (600 MHz, $CDCl_3$) of **4d**



^{13}C NMR (151 MHz, $CDCl_3$) of **4d**



^{31}P NMR (243 MHz, $CDCl_3$) of **4d**



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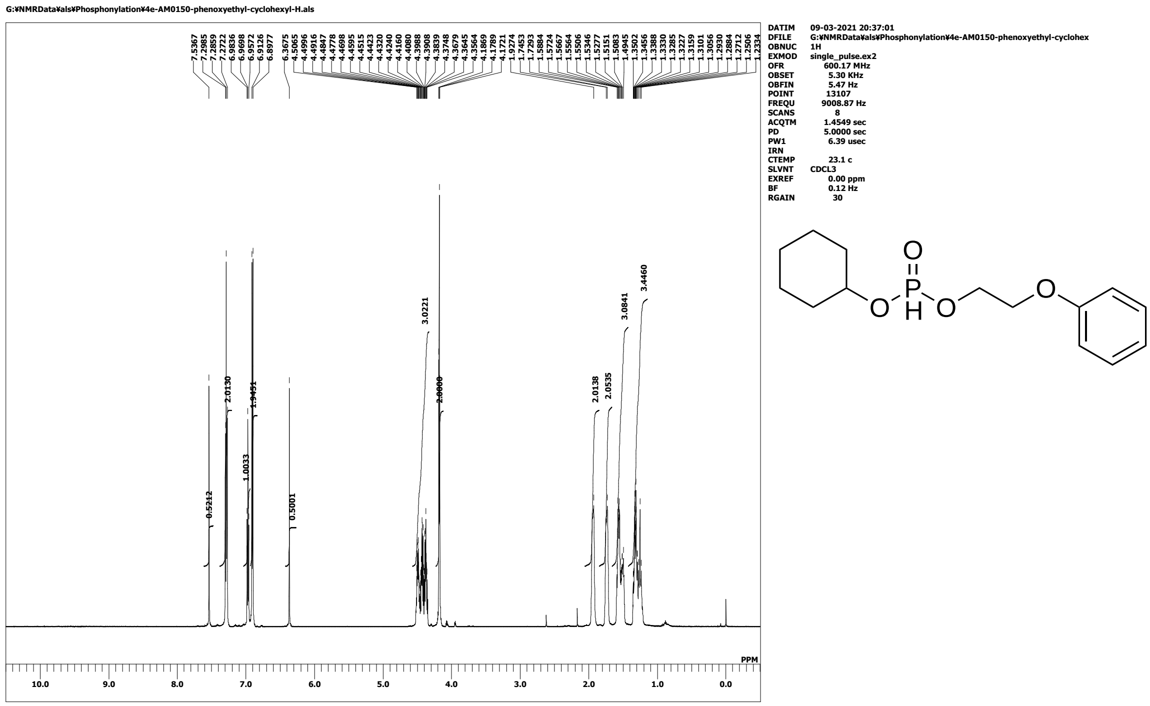

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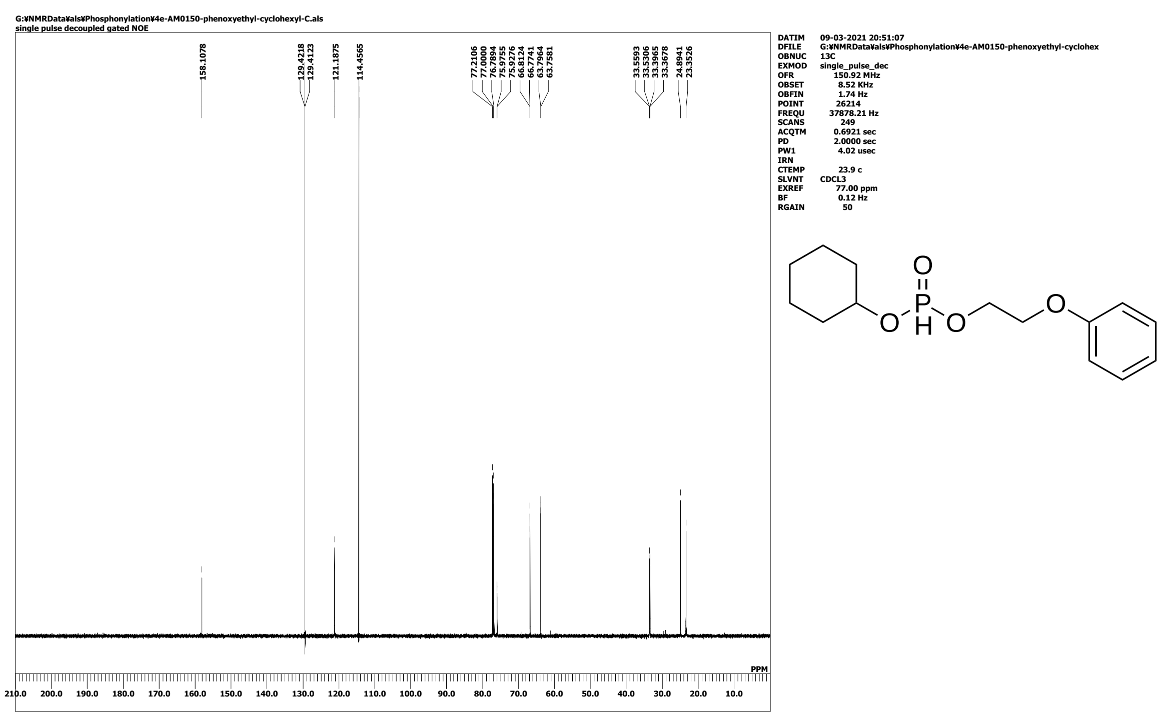

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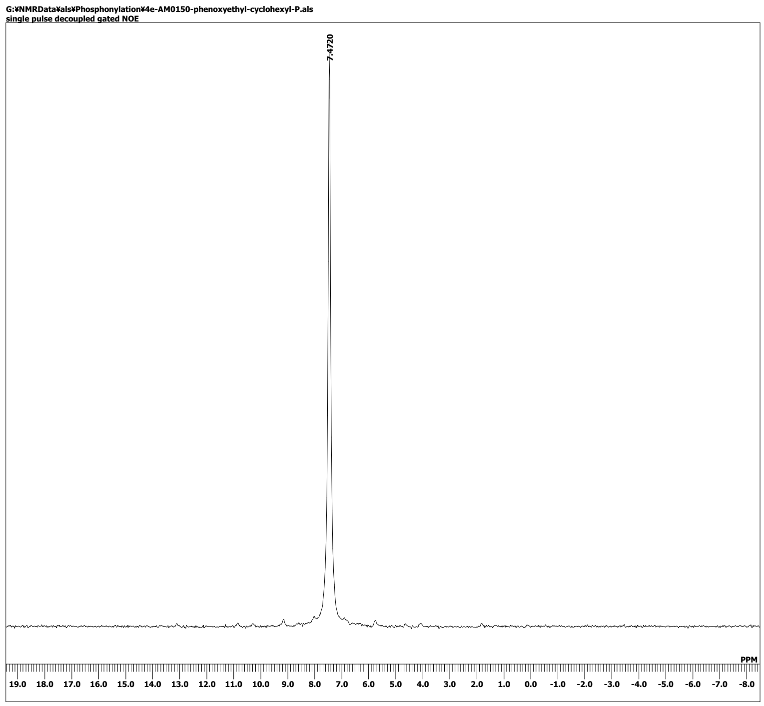

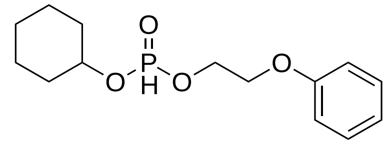

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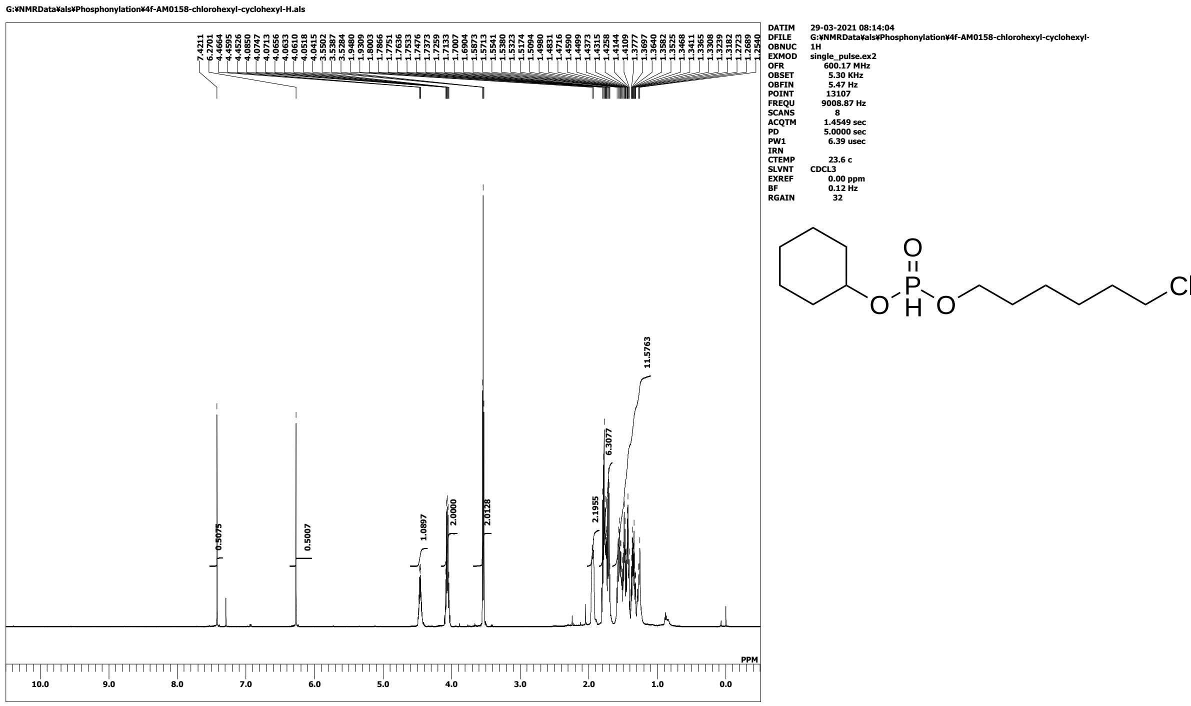

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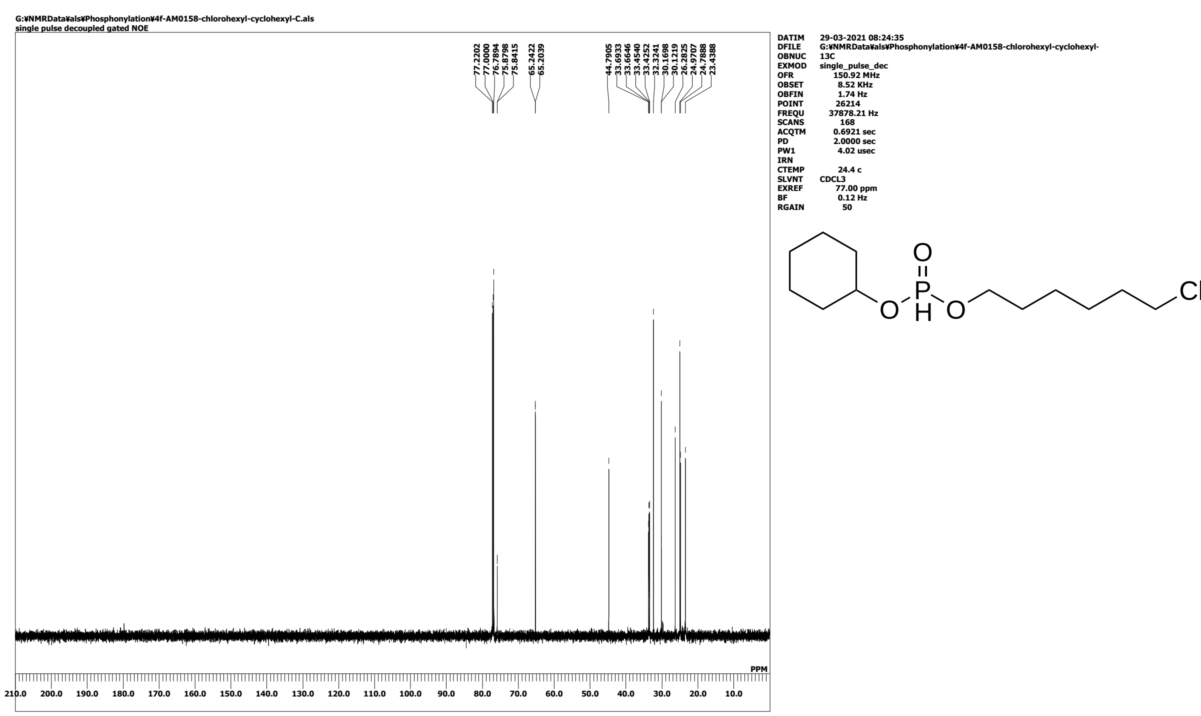

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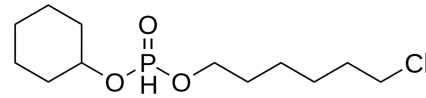
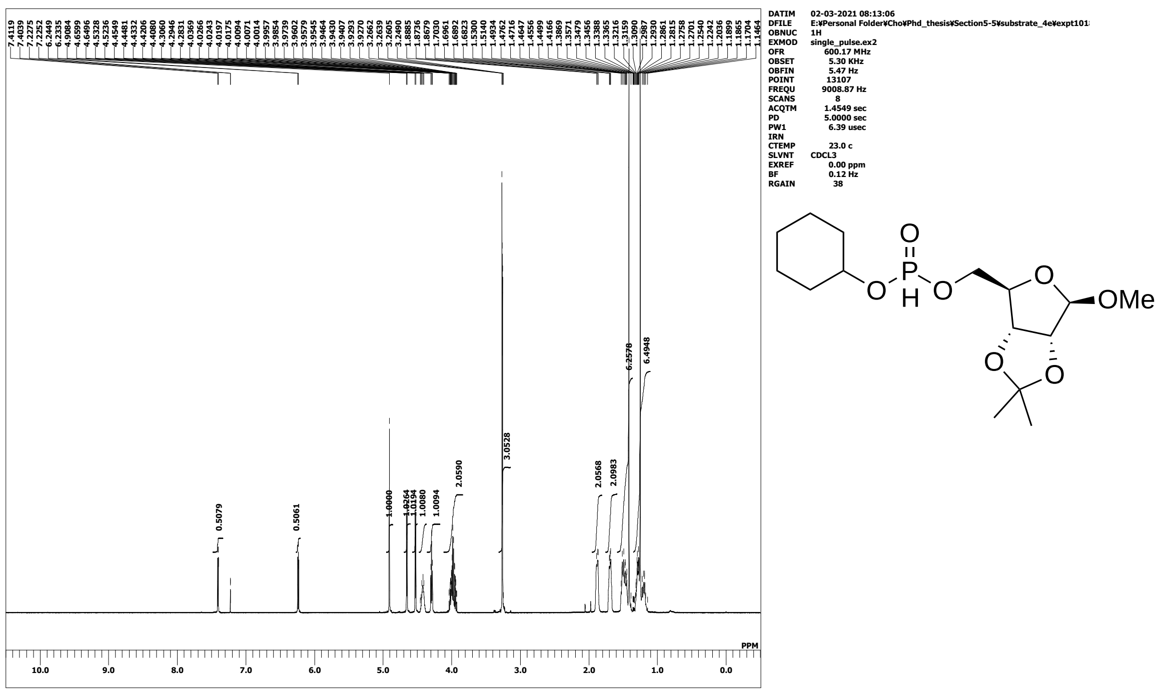
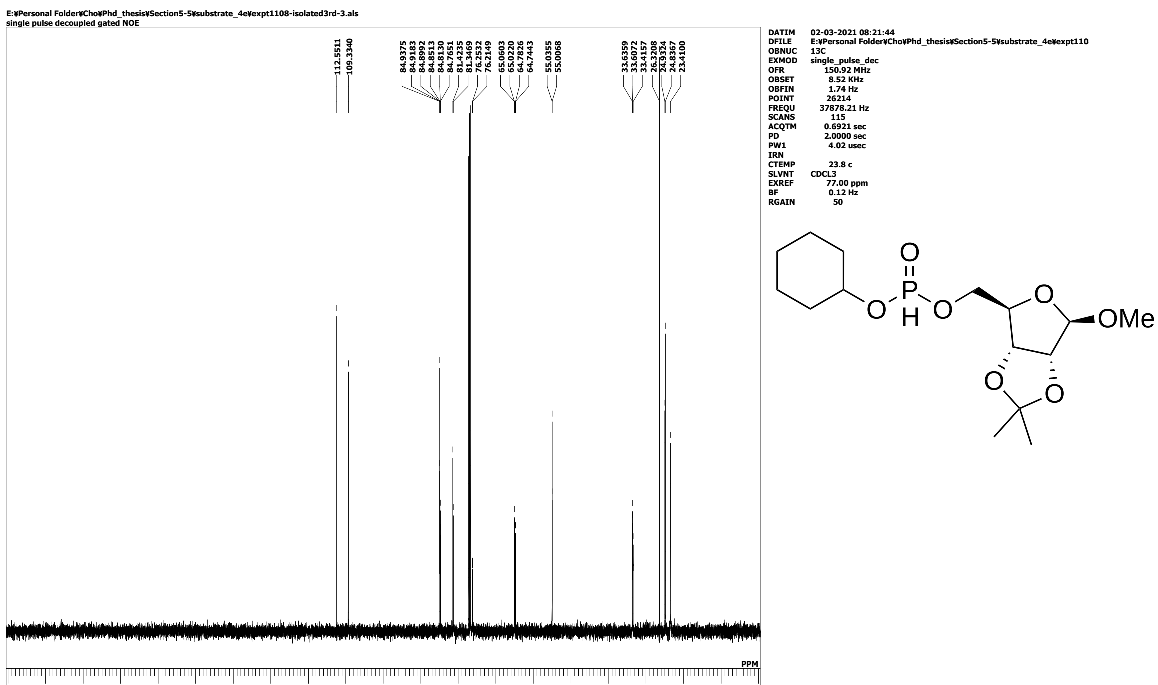


^{1}H NMR (600 MHz, $CDCl_3$) of **4g**



^{13}C NMR (151 MHz, $CDCl_3$) of **4a**



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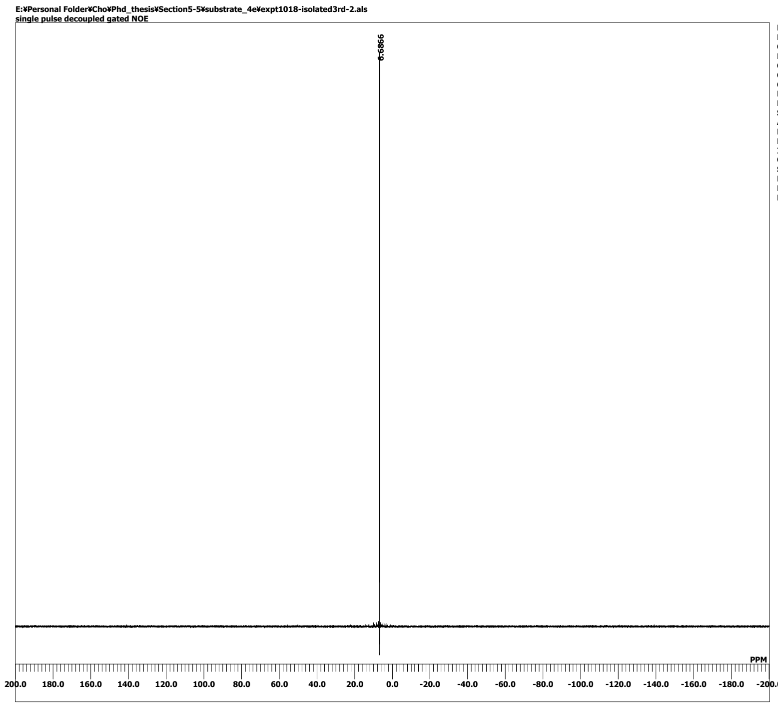

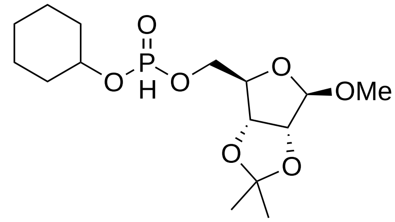

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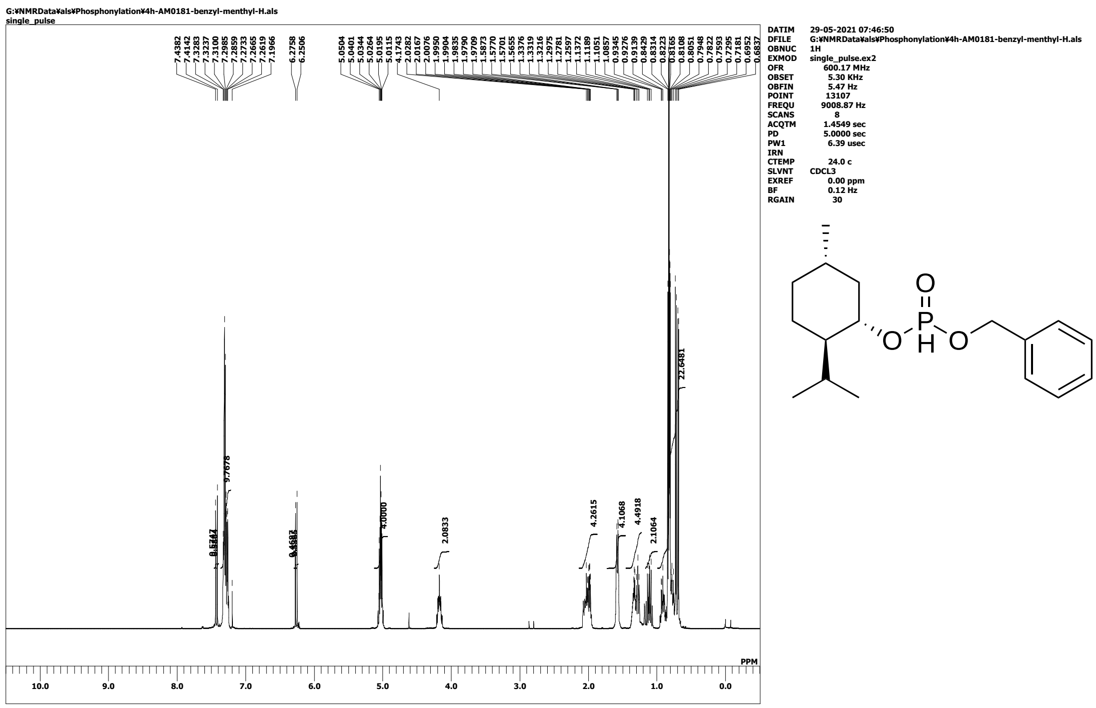

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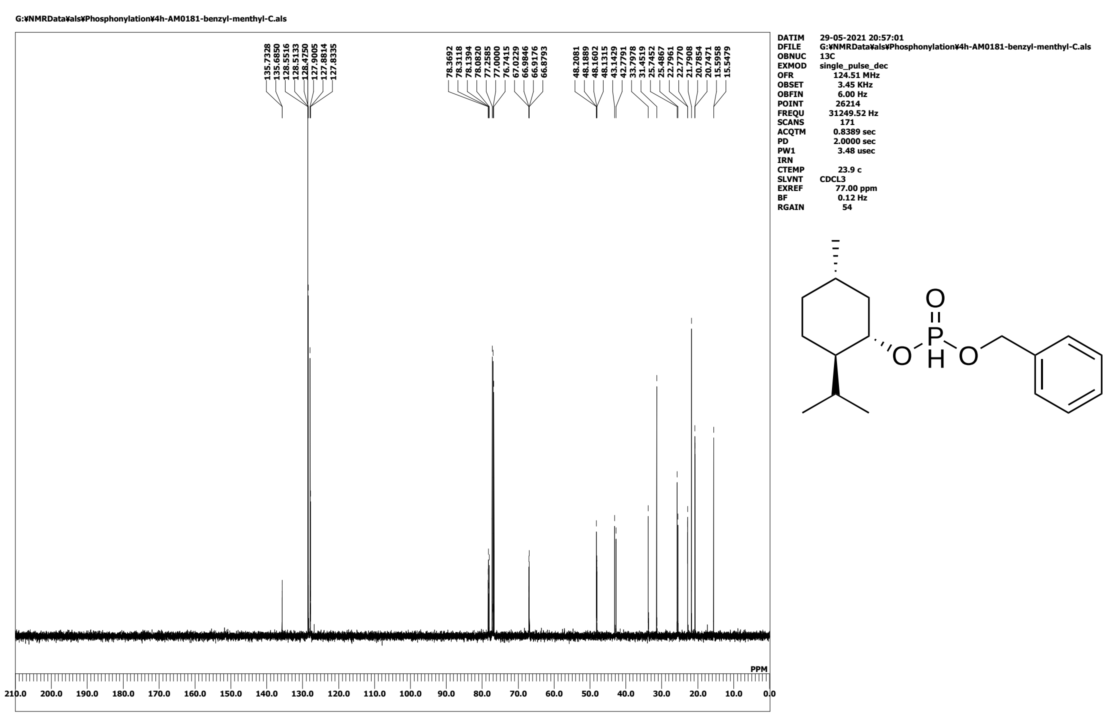

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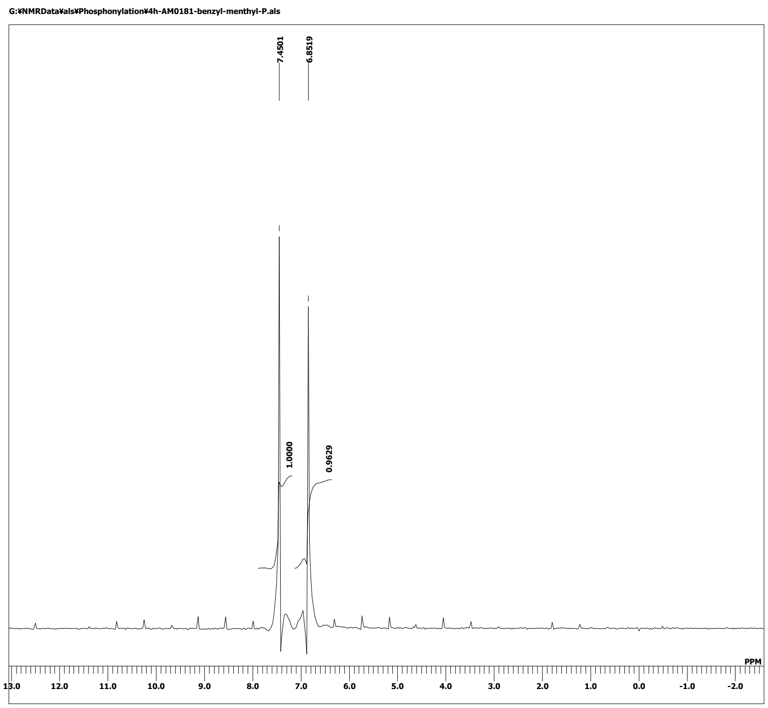

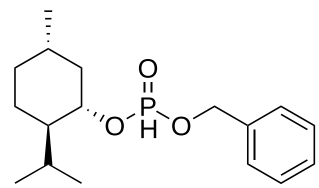

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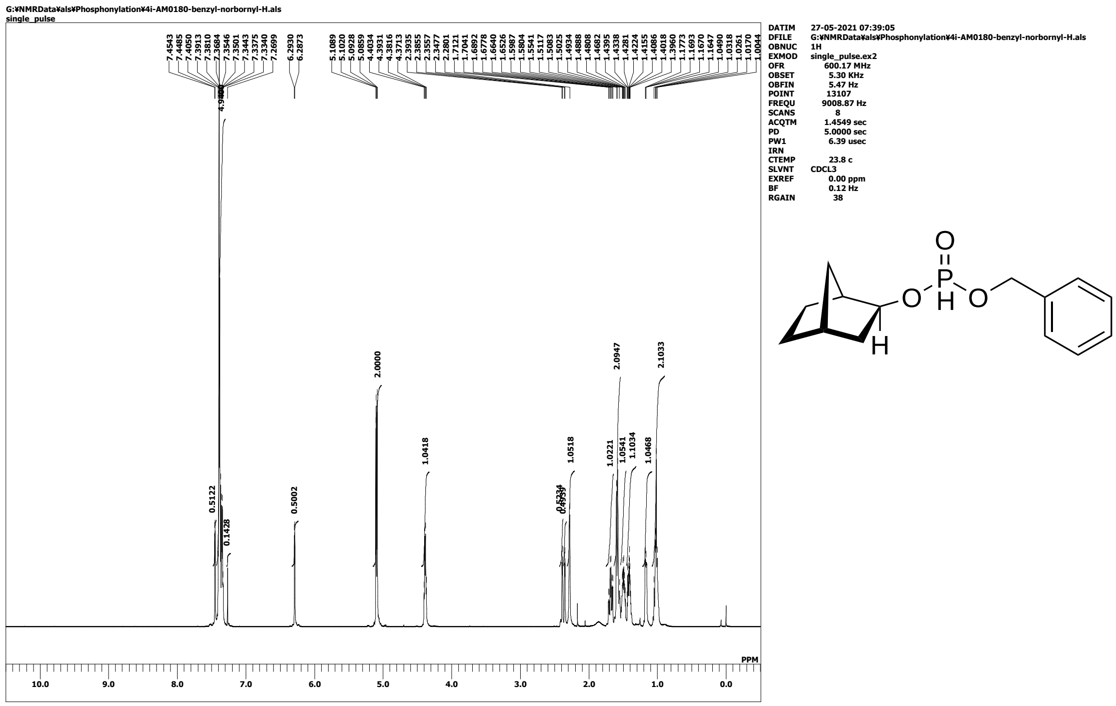
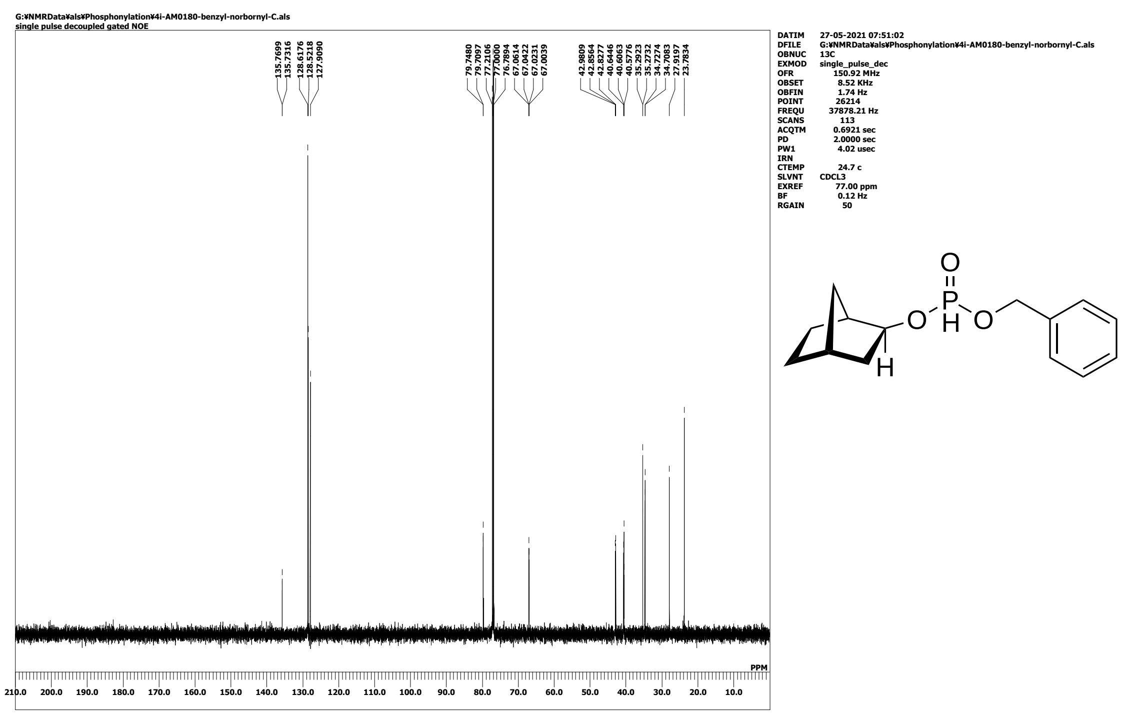
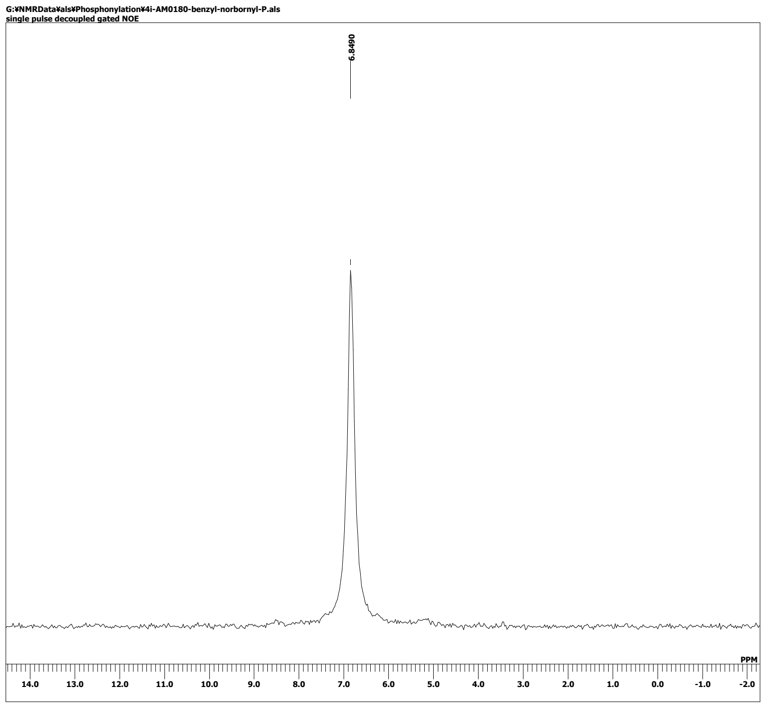
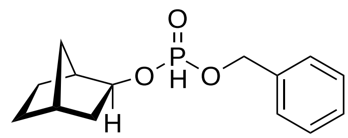


^{13}C NMR (151 MHz, $CDCl_3$) of **4i**



^{31}P NMR (243 MHz, $CDCl_3$) of **4i**





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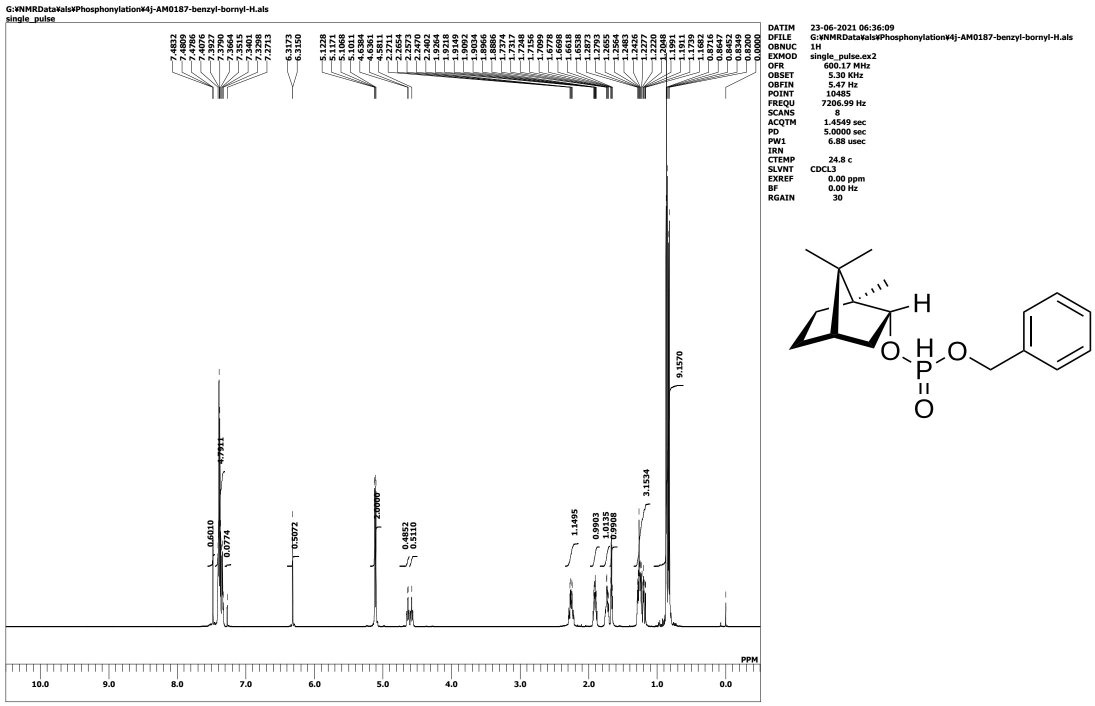

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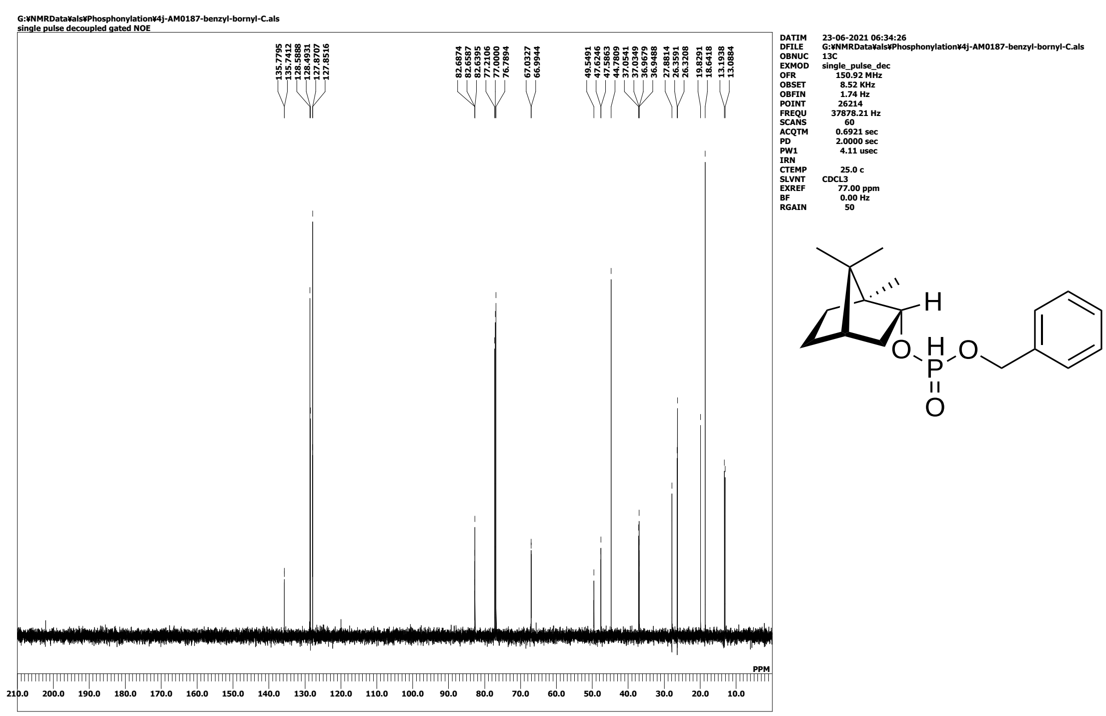

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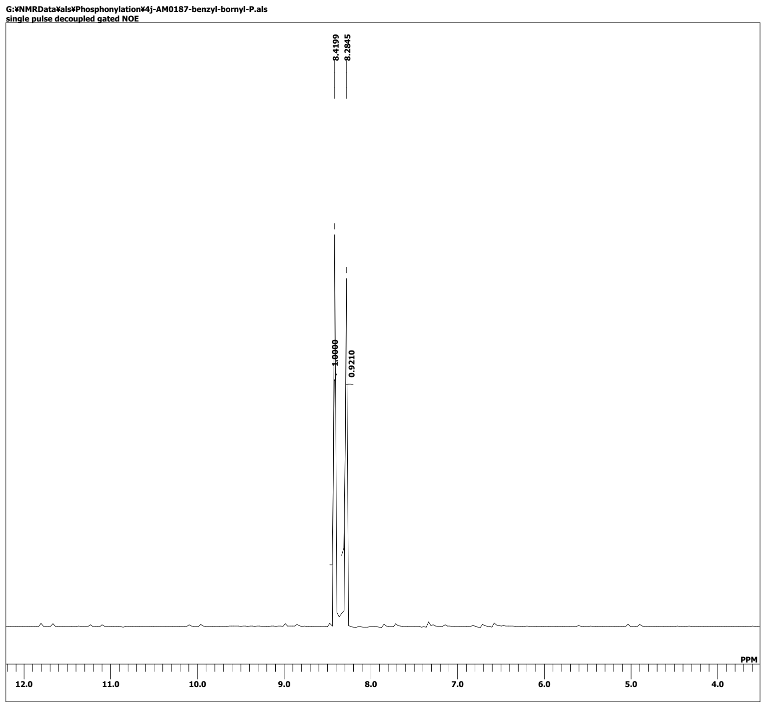

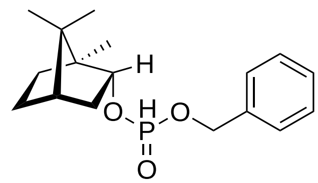

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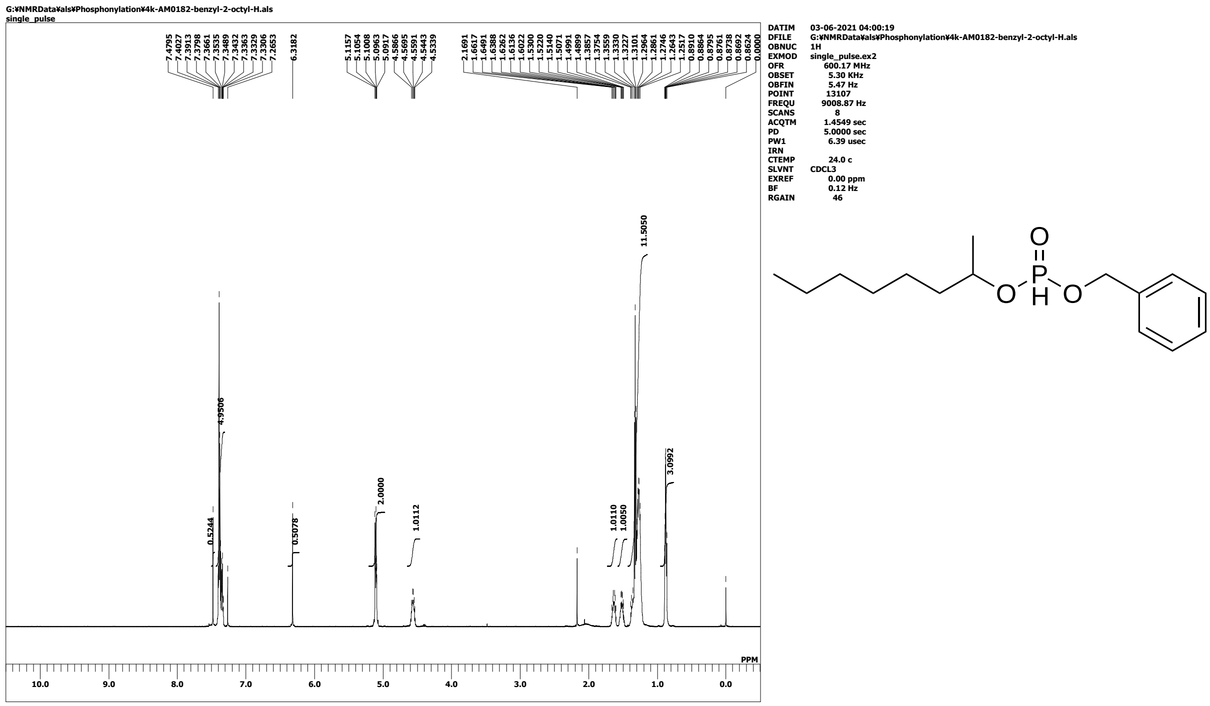

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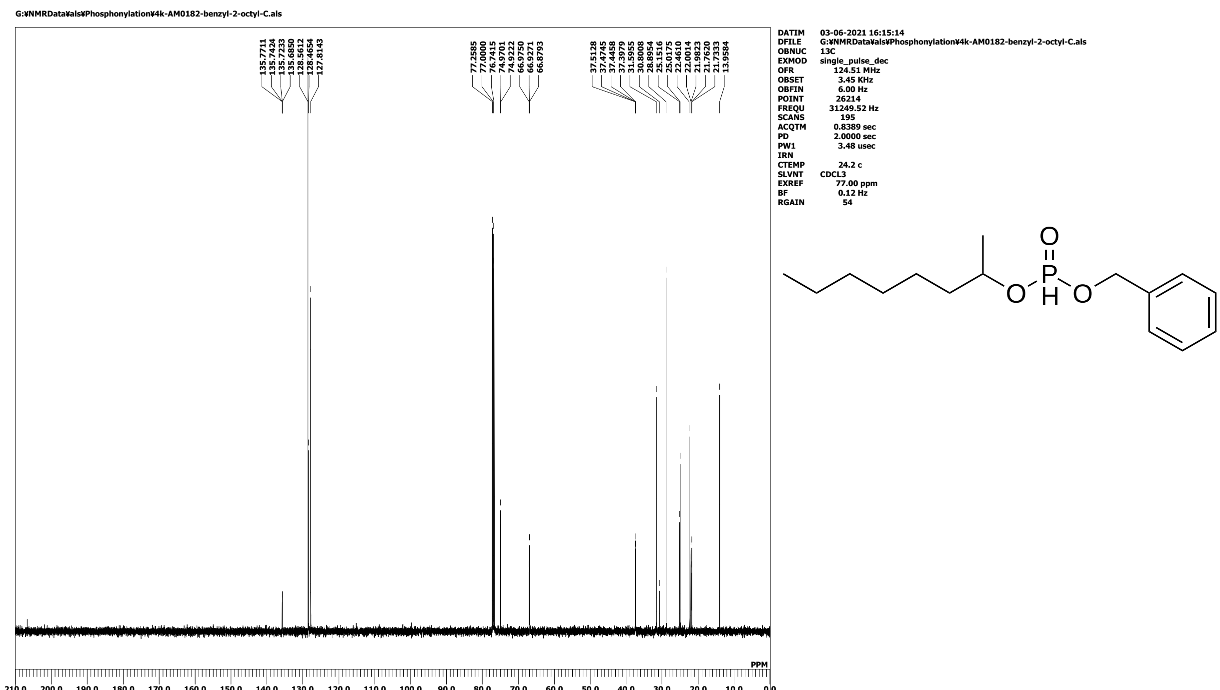
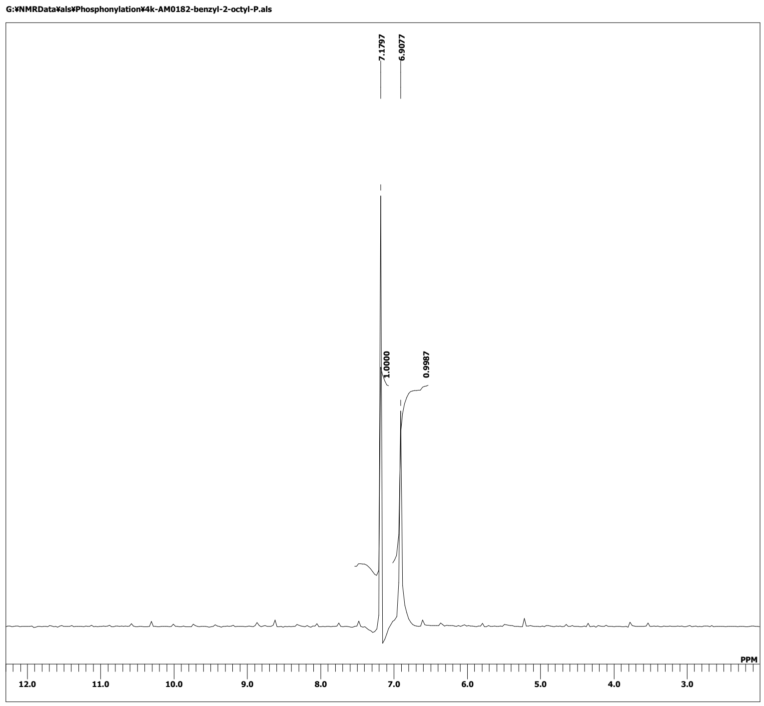
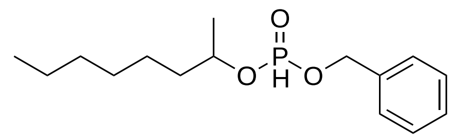
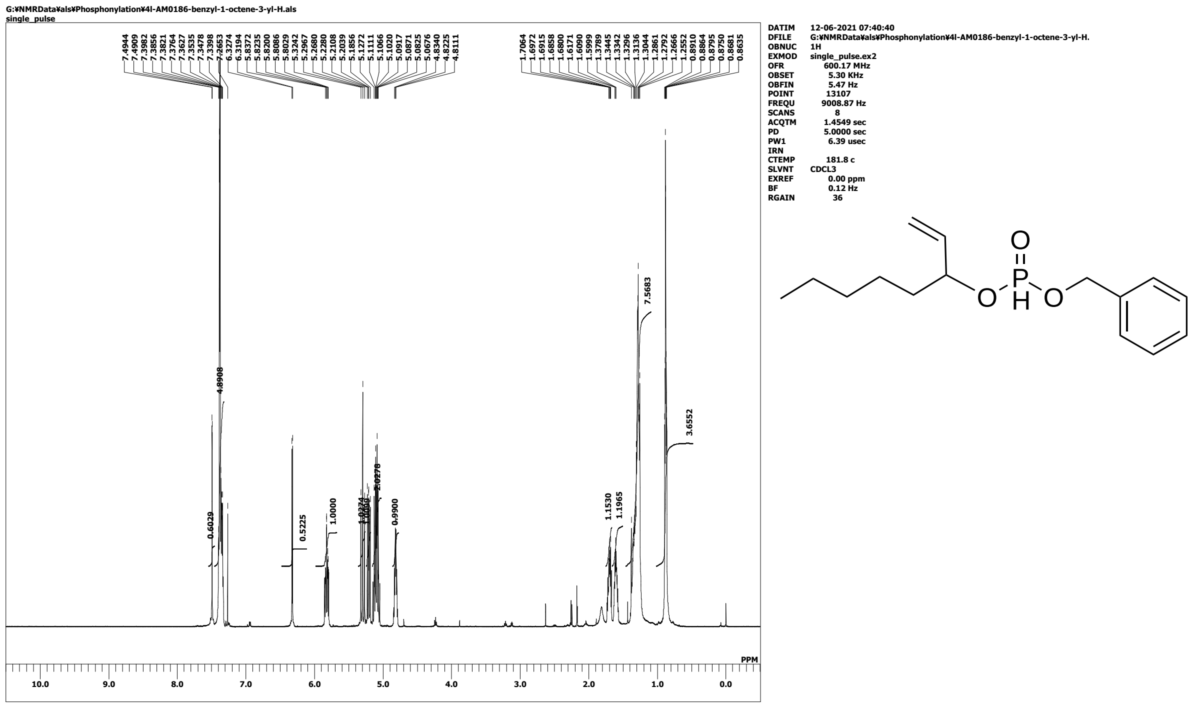


^{31}P NMR (243 MHz, $CDCl_3$) of **4k**

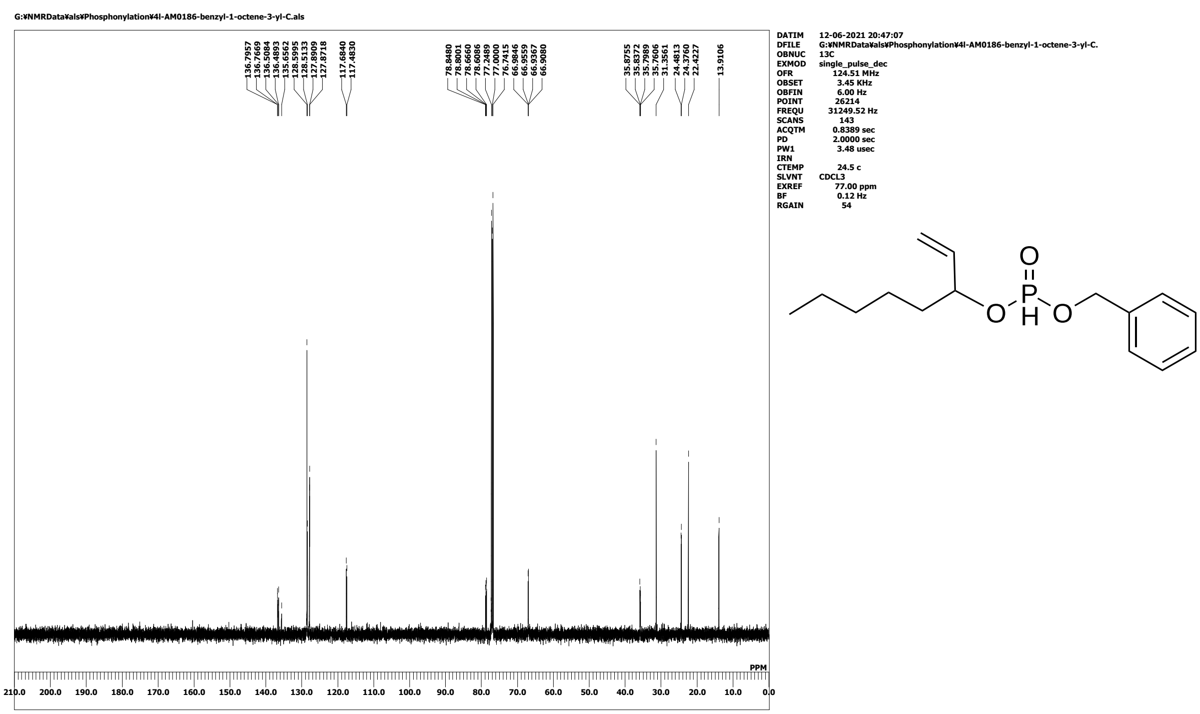




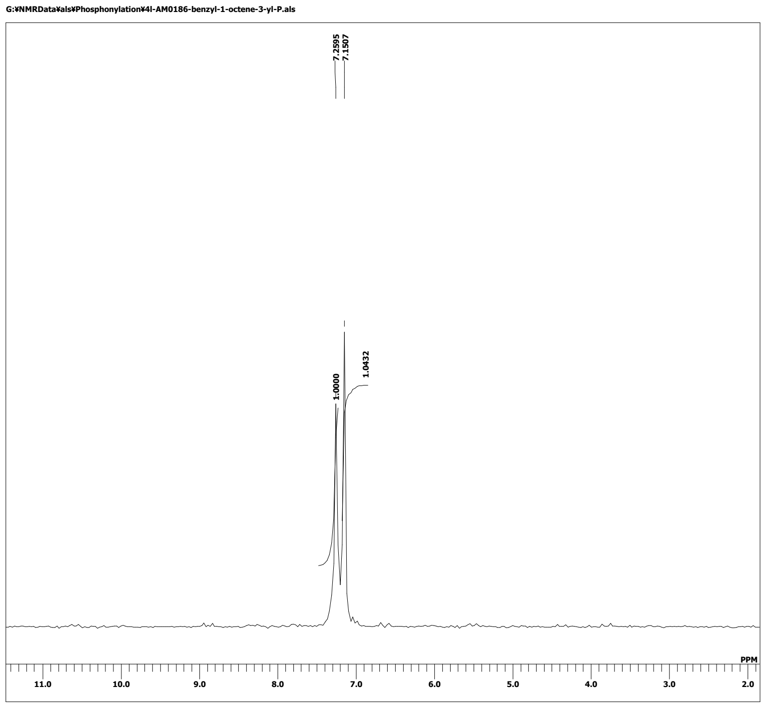
[1]H NMR (600 MHz, $CDCl_3$) of **4l**

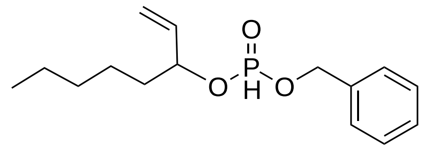


[13]C NMR (151 MHz, $CDCl_3$) of **4l**

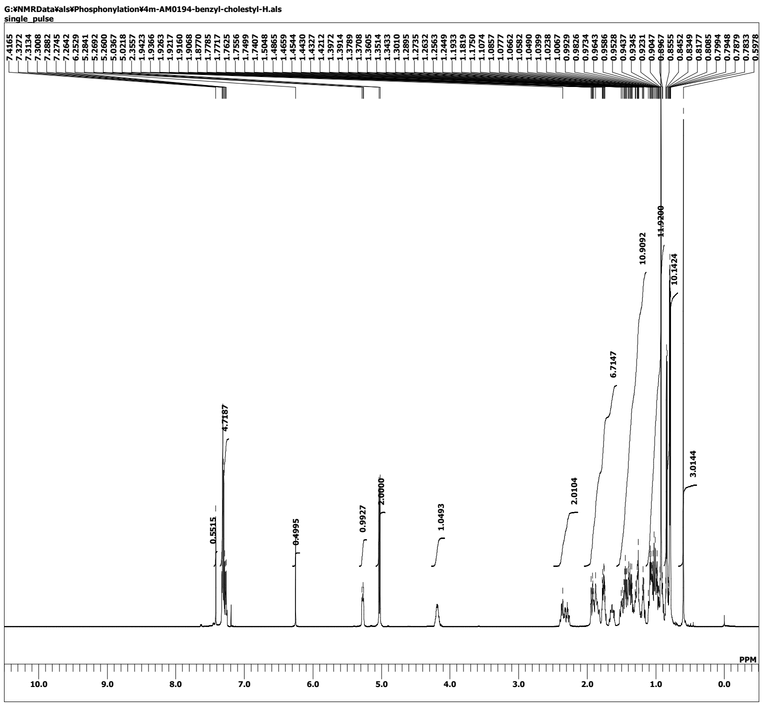


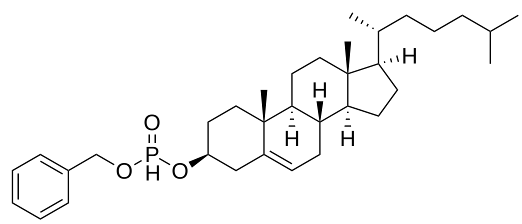
^{31}P NMR (243 MHz, $CDCl_3$) of **4l**



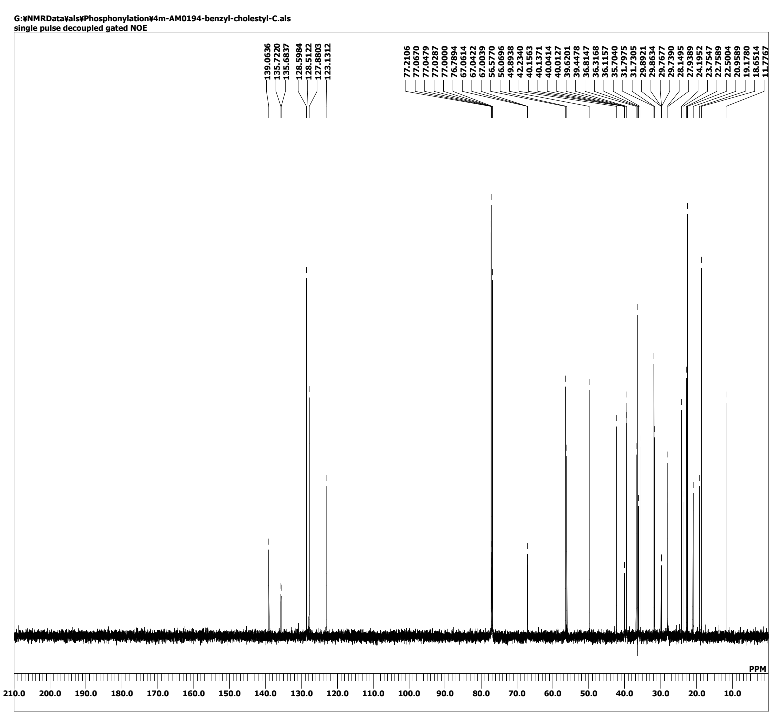


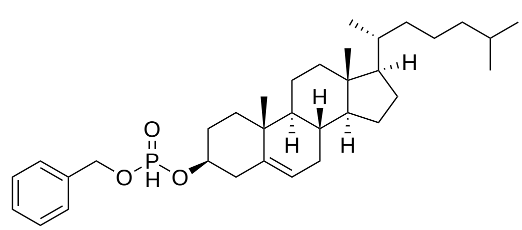
^{1}H NMR (600 MHz, $CDCl_3$) of **4m**



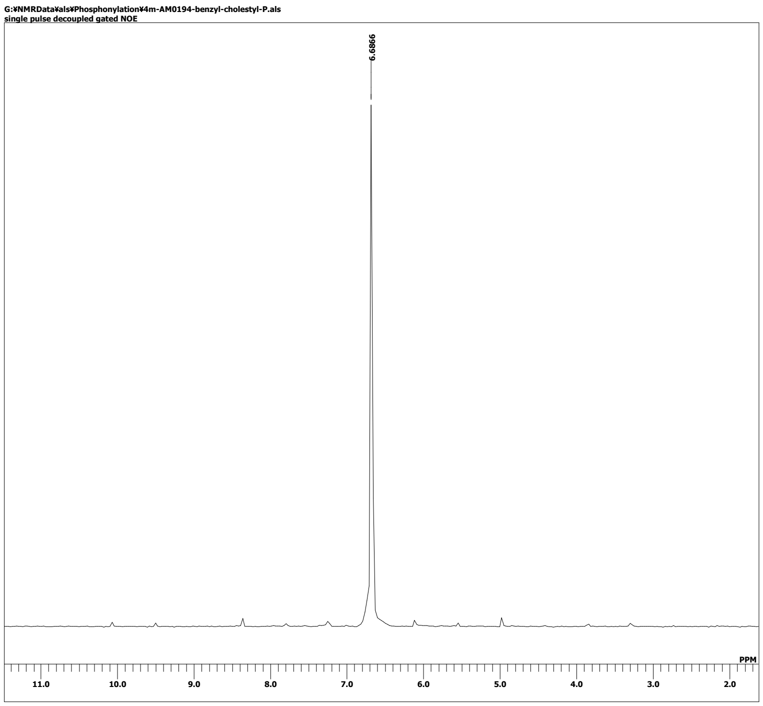


^{13}C NMR (151 MHz, $CDCl_3$) of **4m**





^{31}P NMR (243 MHz, $CDCl_3$) of **4m**



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EXMOD single_pulse_dec
OFR 242.95 MHz
OBSET 4.04 KHz
OBFIN 1.25 Hz
POINT 26214
FREQU 172411.16 Hz
SCANS 44
ACQTM 0.1520 sec
PD 2.0000 sec
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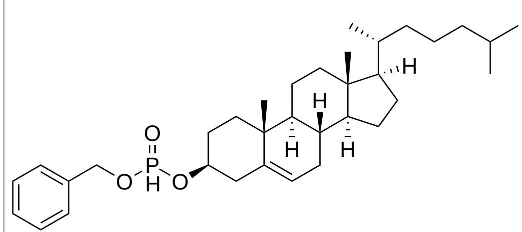
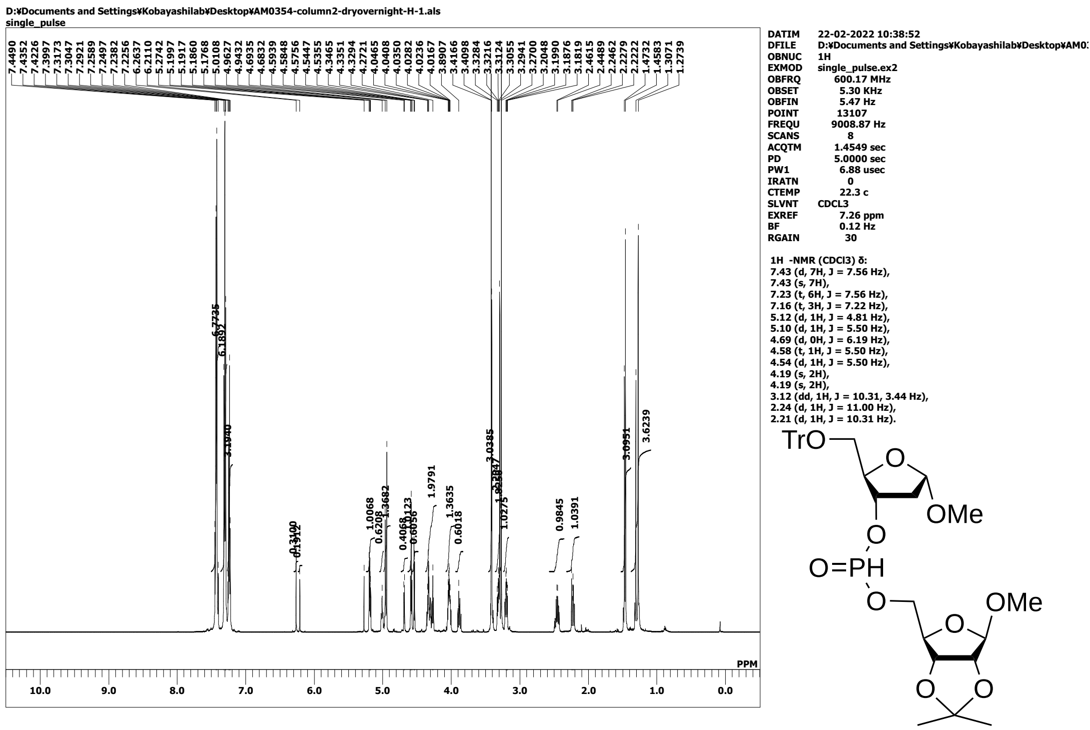
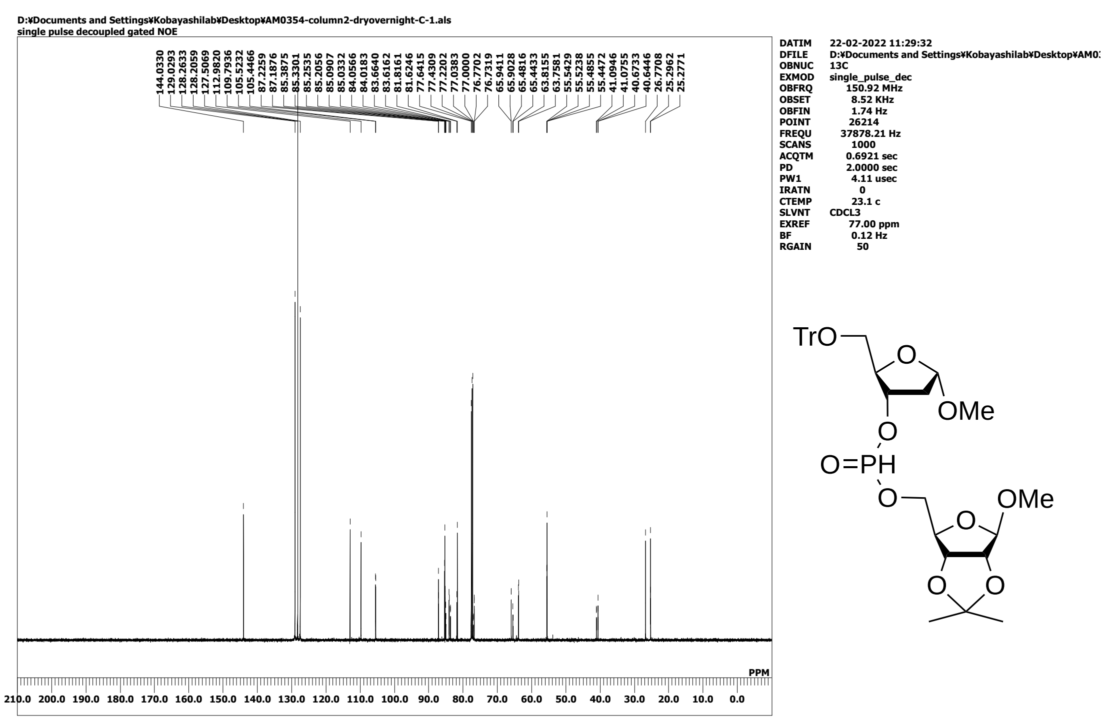


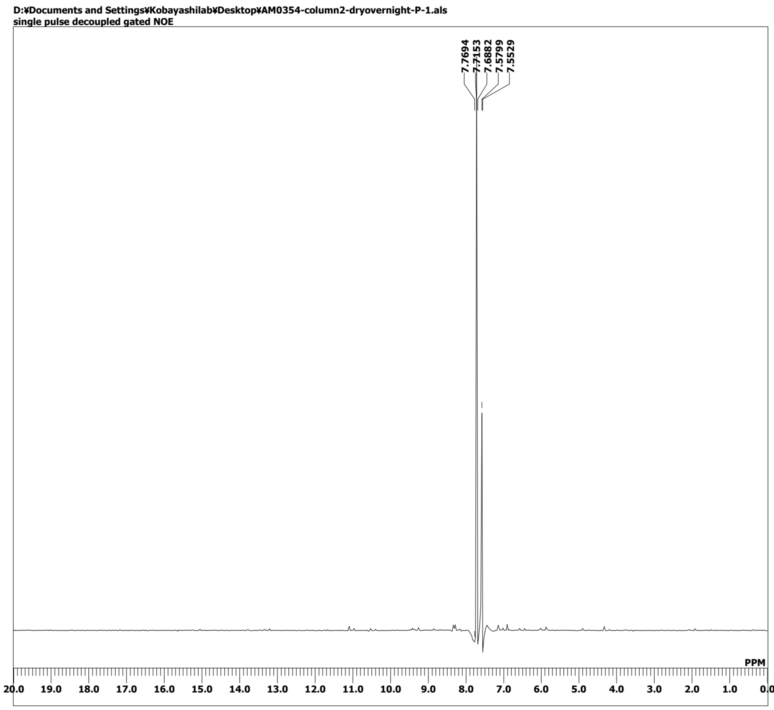
^{1}H NMR (600 MHz, $CDCl_3$) of **4n**

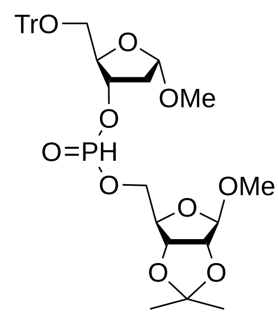


^{13}C NMR (151 MHz, $CDCl_3$) of **4n**

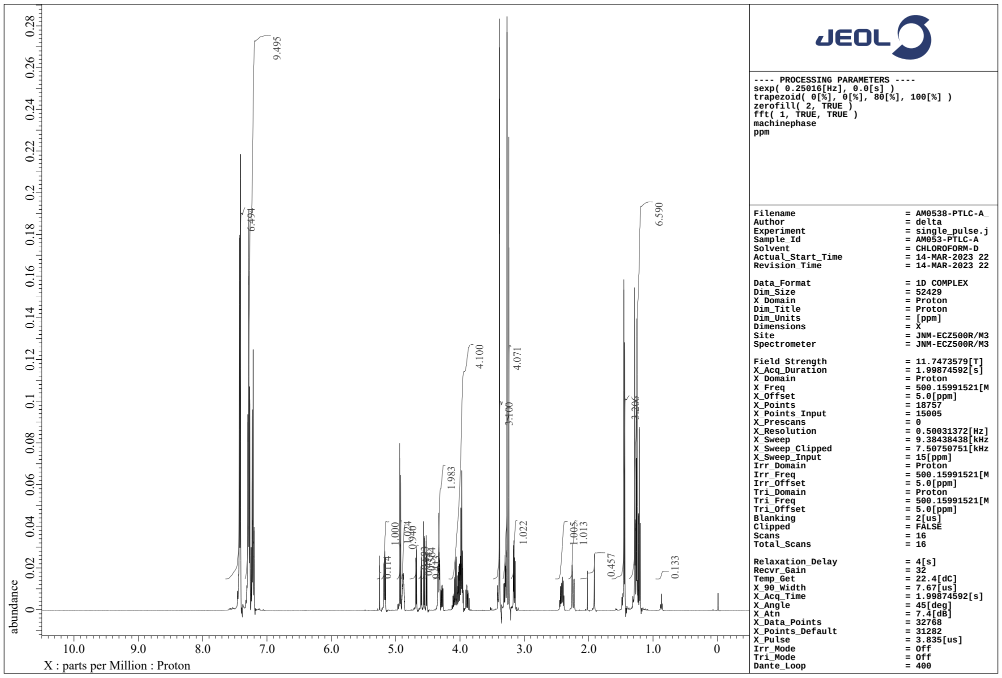


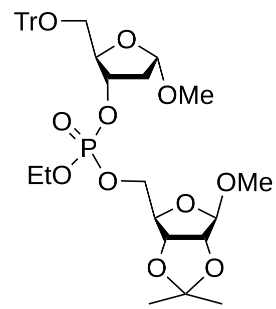
^{31}P NMR (243 MHz, $CDCl_3$) of **4n**



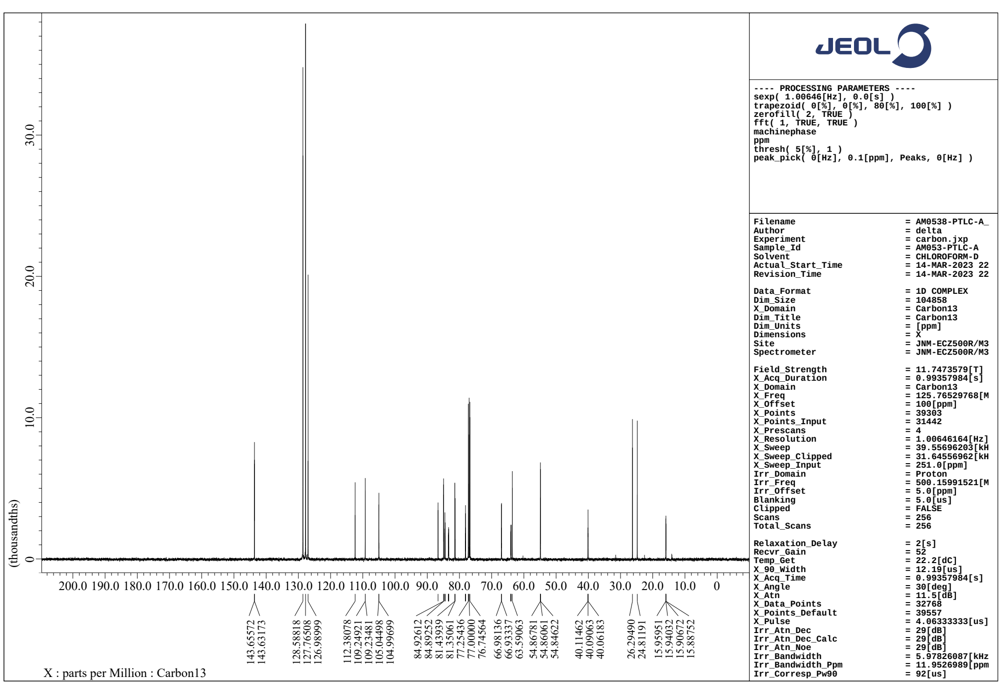


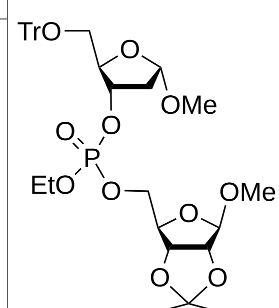
^{1}H NMR (500 MHz, $CDCl_3$) of **5a**



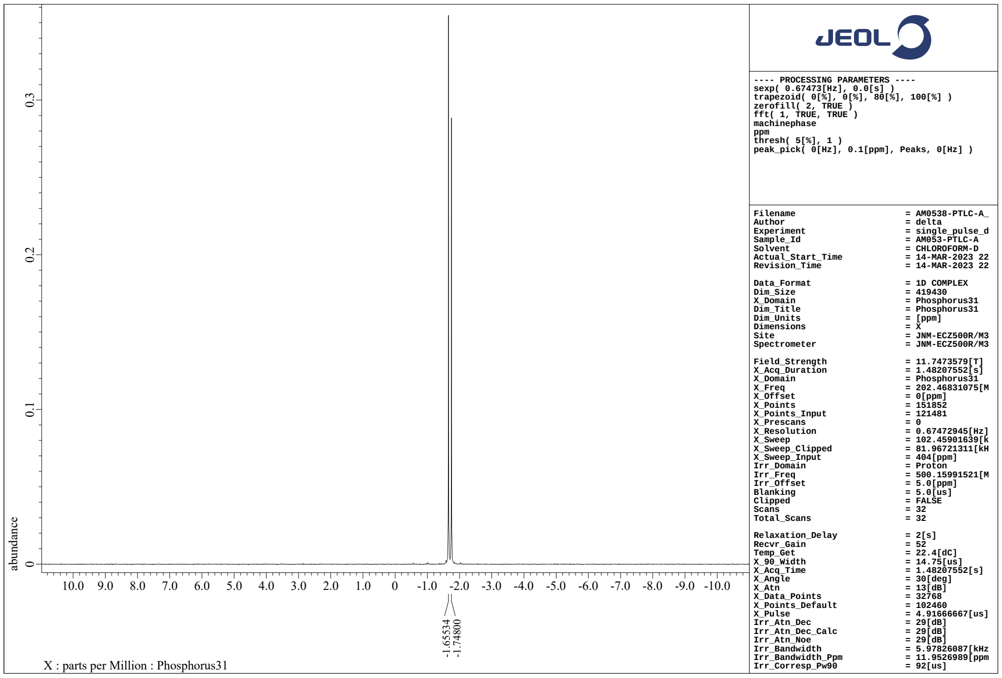


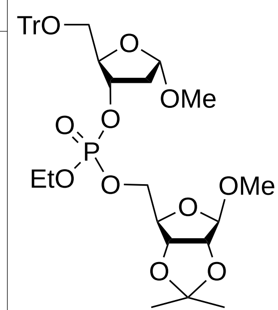
^{13}C NMR (126 MHz, $CDCl_3$) of **5a**



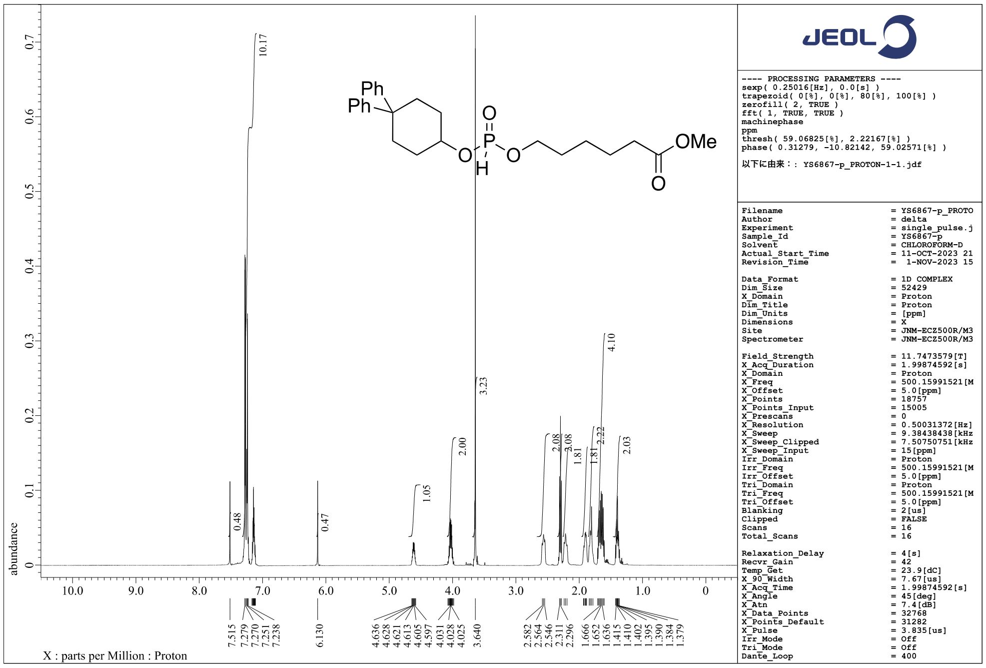


^{31}P NMR (243 MHz, $CDCl_3$) of **5a**

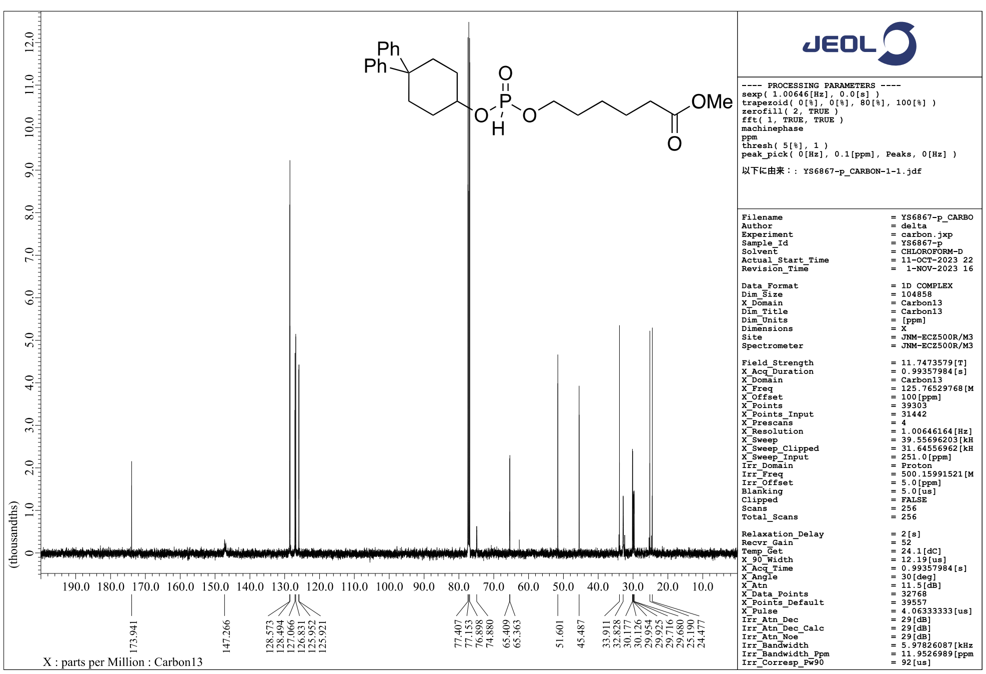




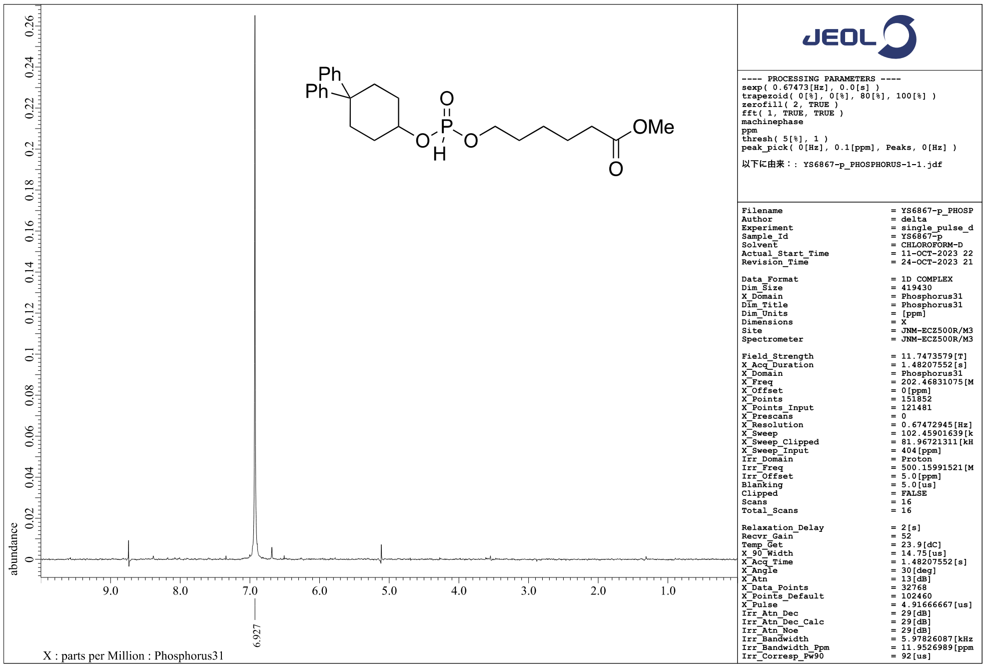
[1]H NMR (500 MHz, $CDCl_3$) of **4o**



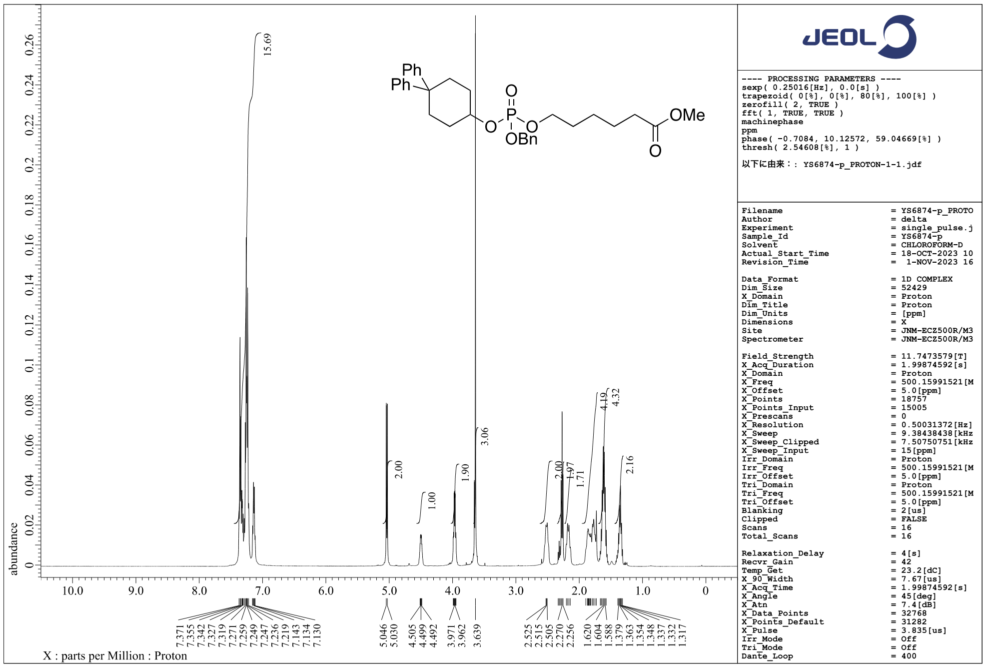
[13]C NMR (126 MHz, $CDCl_3$) of **4o**



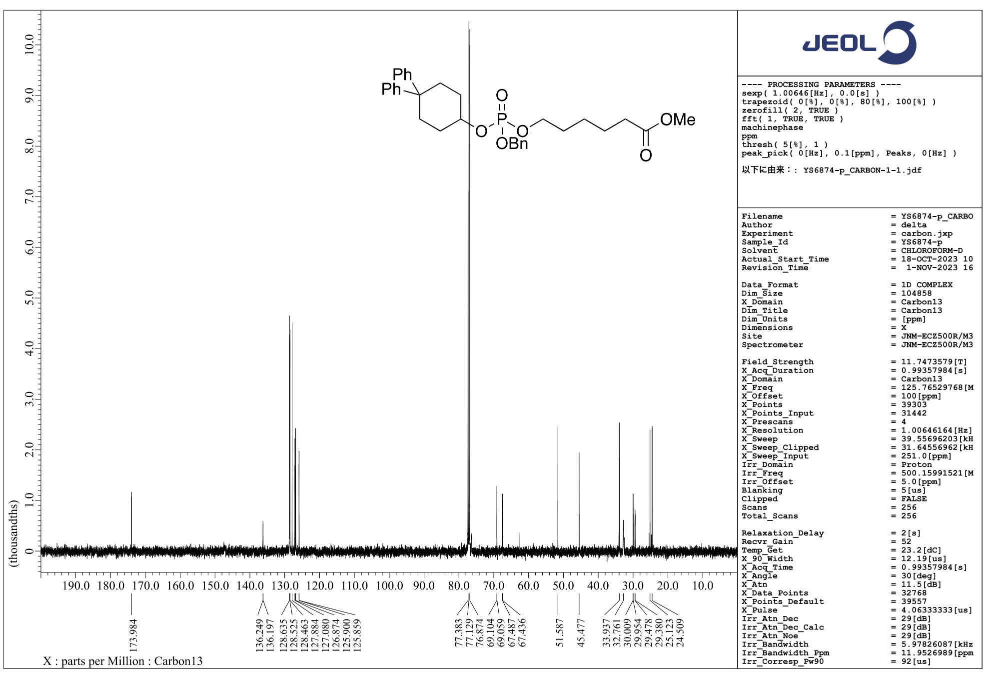
[31]P NMR (203 MHz, $CDCl_3$) of **4o**



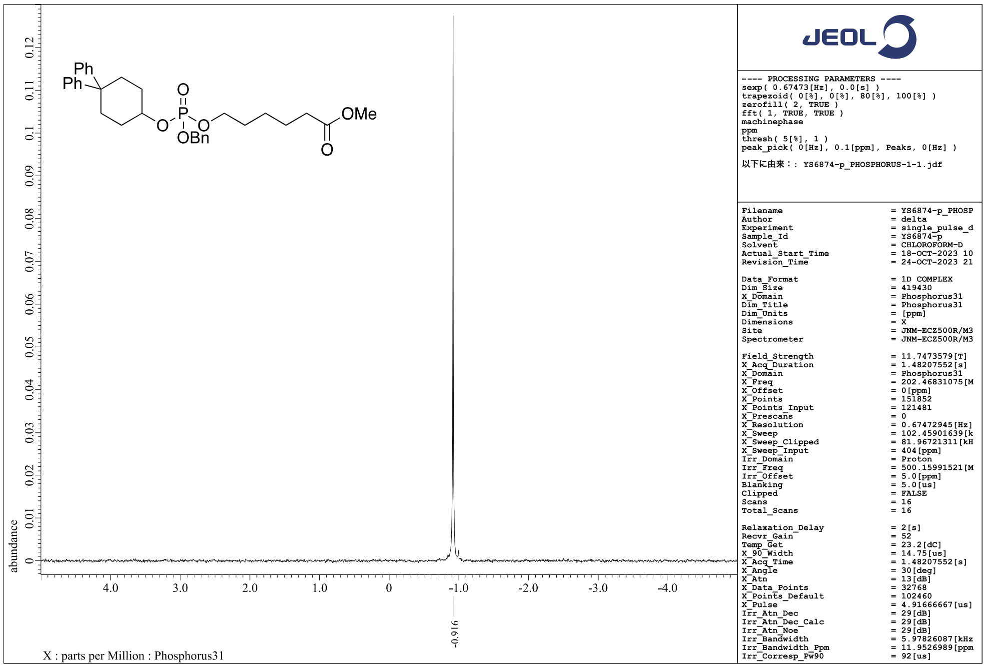
^{1}H NMR (500 MHz, $CDCl_3$) of **5b**



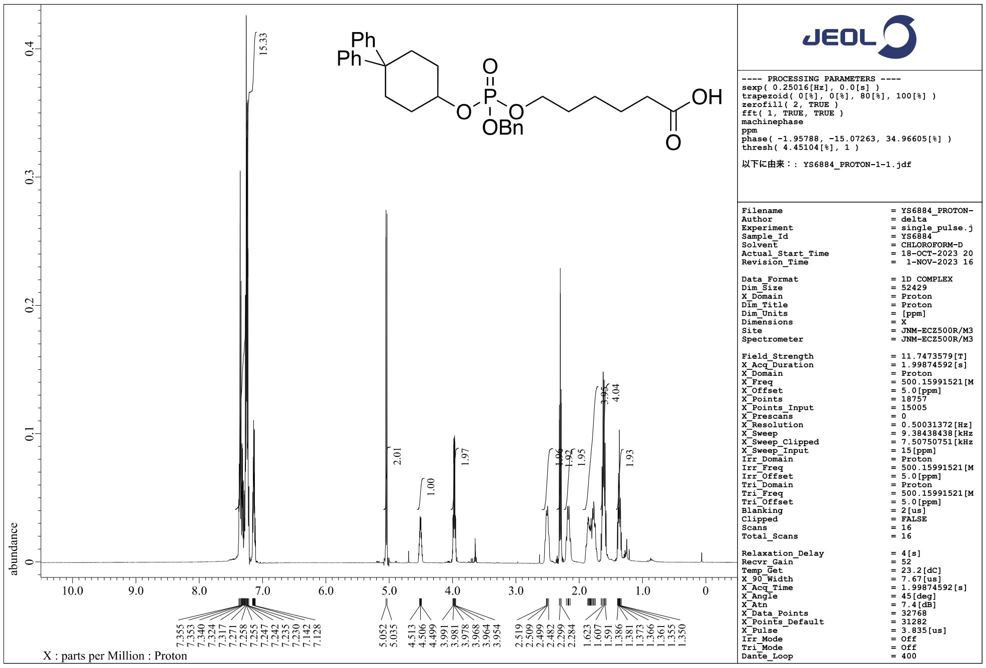
^{13}C NMR (126 MHz, $CDCl_3$) of **5b**



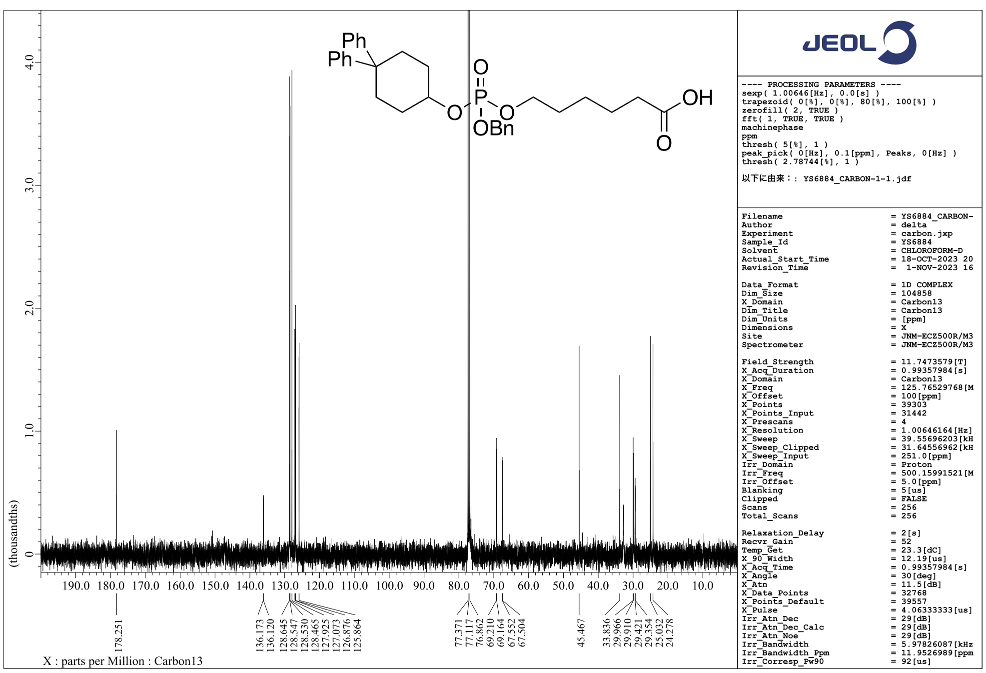
^{31}P NMR (203 MHz, $CDCl_3$) of **5b**



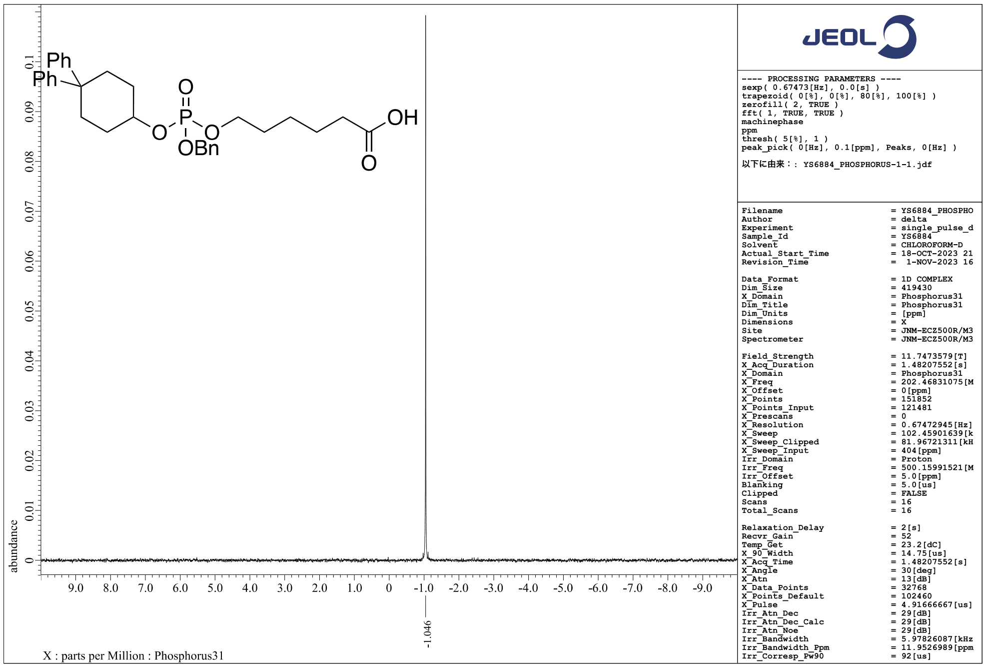
^{1}H NMR (500 MHz, $CDCl_3$) of **5c**



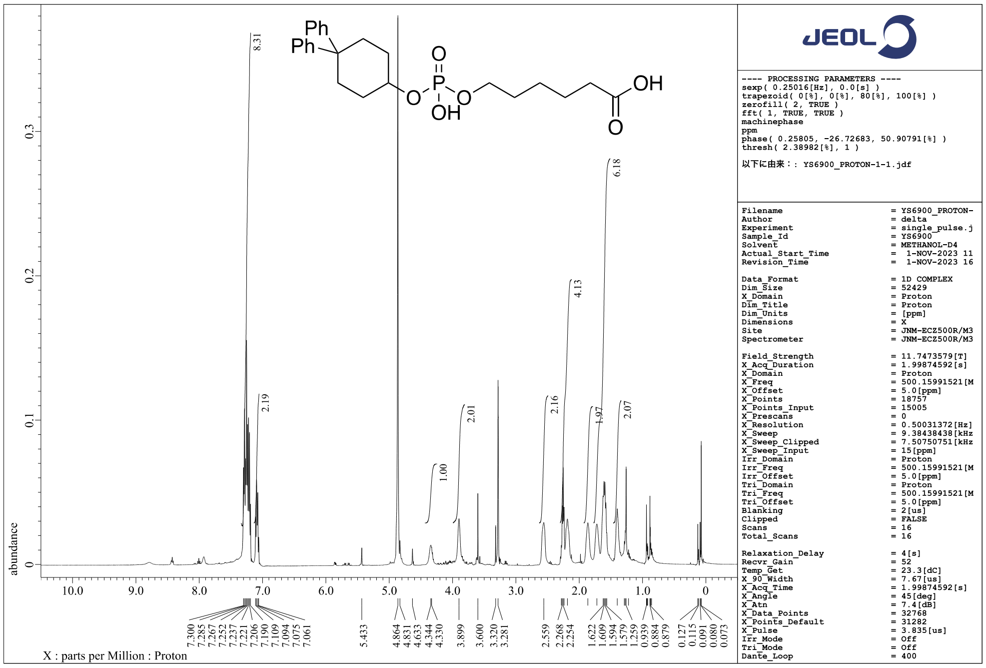
^{13}C NMR (126 MHz, $CDCl_3$) of **5c**



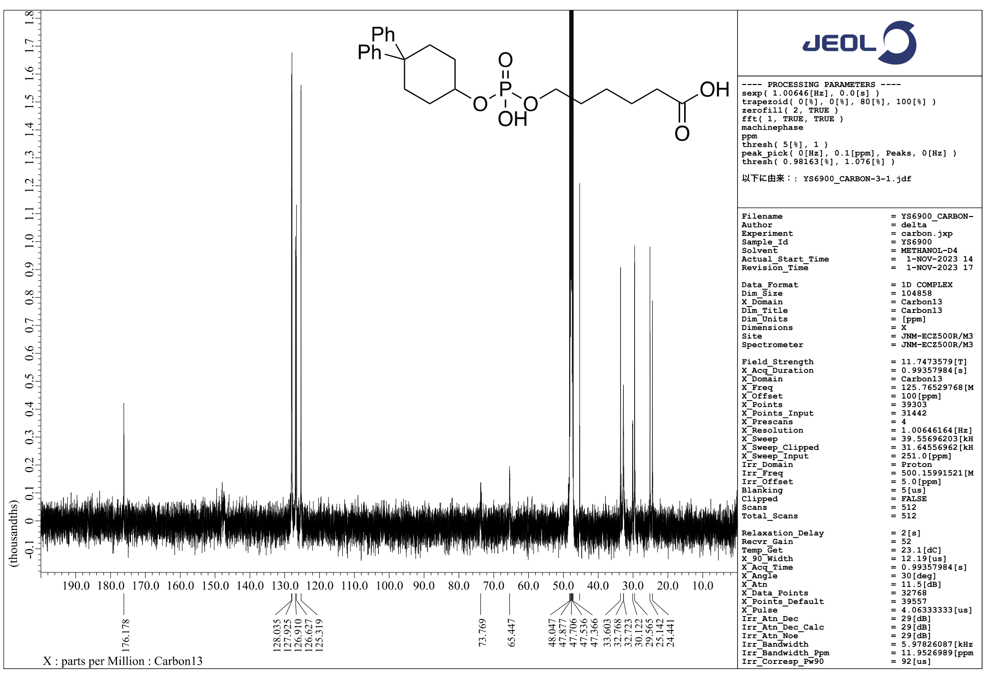
[31]P NMR (203 MHz, $CDCl_3$) of **5c**



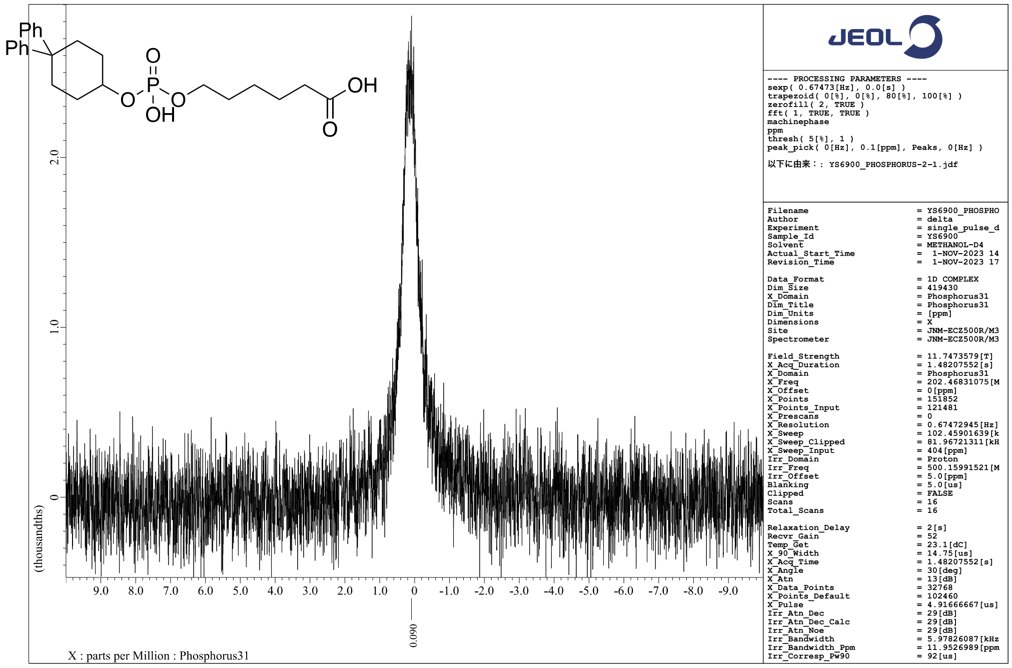
^{1}H NMR (500 MHz, MeOH-d$_4$) of **5d**

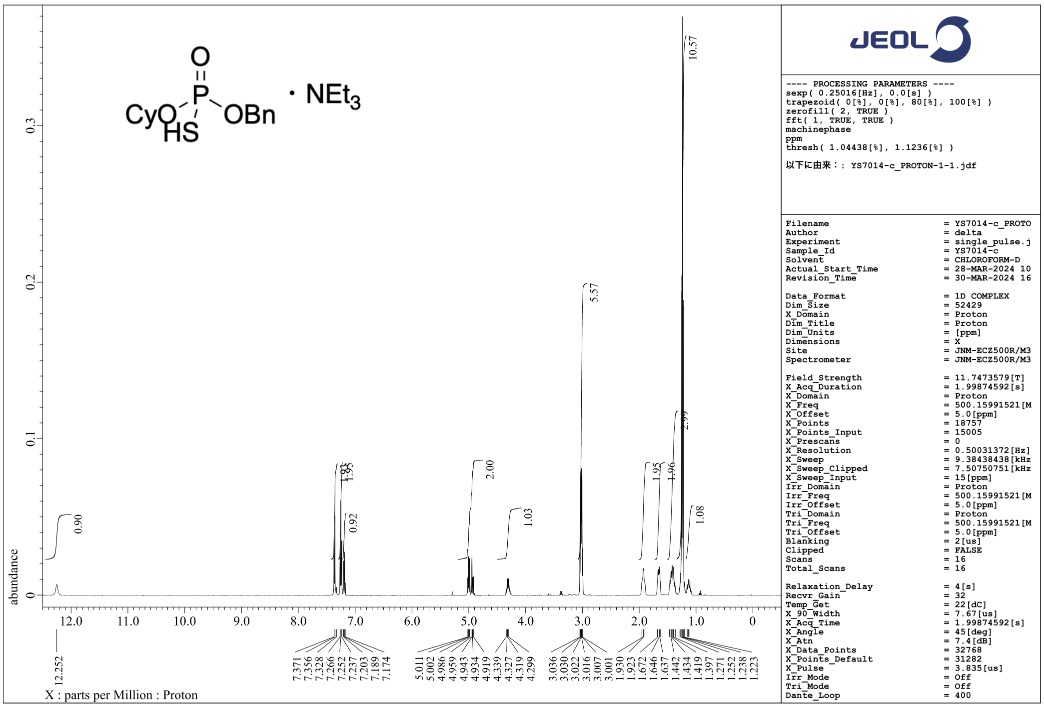


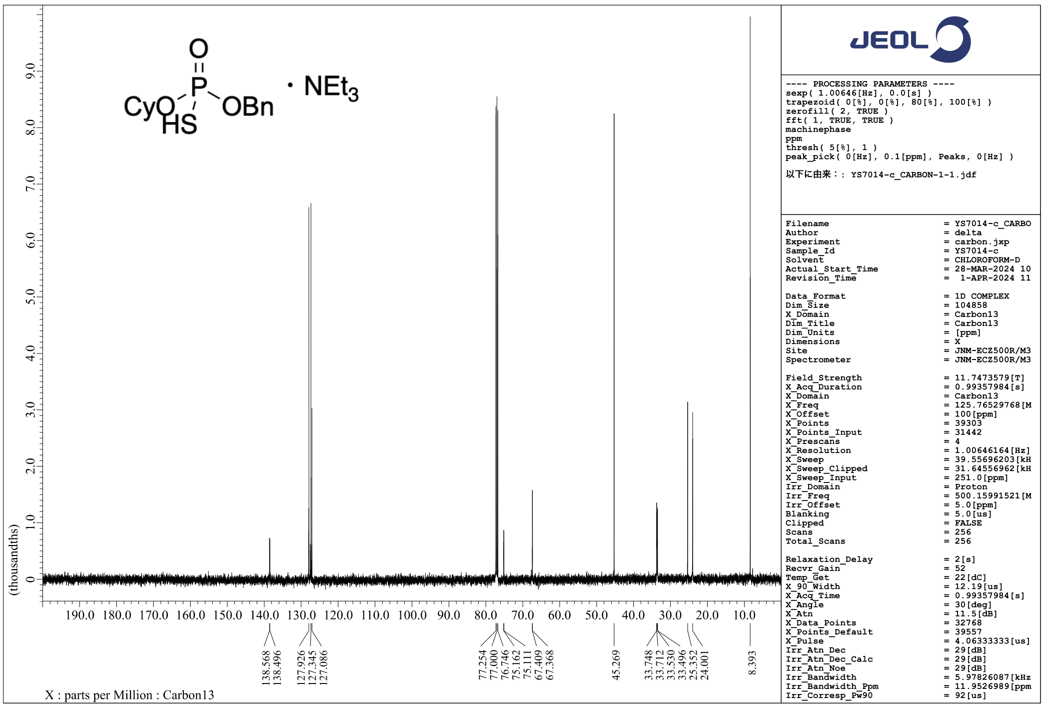
^{13}C NMR (126 MHz, MeOH-d$_4$) of **5d**

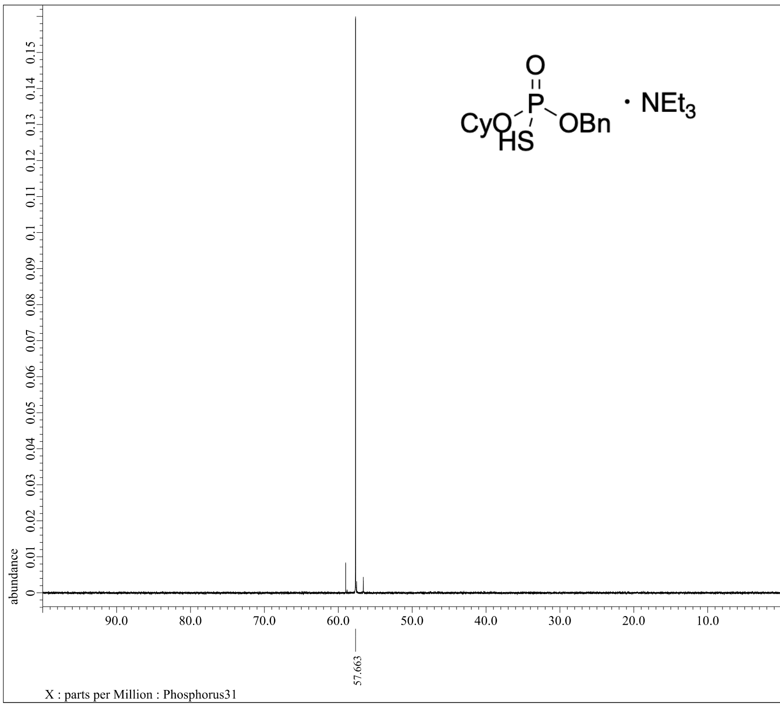


^{31}P NMR (203 MHz, MeOH-d_4) of **5d**




CyO P(=O)(HS) OBn · NEt3
abundance
X : parts per Million : Proton
0.90
0.92
1.93
1.95
2.00
1.03
5.57
1.95
1.96
2.99
10.57
1.08
12.252
7.371 7.356 7.328 7.266 7.252 7.237 7.203 7.189 7.174
5.011 5.002 4.995 4.986 4.943 4.934 4.919 4.339 4.327 4.319 4.299
3.036 3.030 3.022 3.016 3.007 3.001
1.930 1.923 1.672 1.646 1.637 1.442 1.434 1.419 1.397 1.271 1.252 1.238 1.223
JEOL
---- PROCESSING PARAMETERS ----
sexp(0.25016[Hz], 0.0[s])
trapezoid(0[%], 0[%], 80[%], 100[%])
zerofill(2, TRUE)
fft(1, TRUE, TRUE)
machinephase
ppm
thresh(1.04438[%], 1.1236[%])
以下に由来：: YS7014-c_PROTON-1-1.jdf
Filename = YS7014-c_PROTO
Author = delta
Experiment = single_pulse.j
Sample_Id = YS7014-c
Solvent = CHLOROFORM-D
Actual_Start_Time = 28-MAR-2024 10
Revision_Time = 30-MAR-2024 16
Field_Strength = 11.7473579[T]
X_Freq = 500.15991521[M
Scans = 16
Total_Scans = 16
Relaxation_Delay = 4[s]
Temp_Get = 22[dC]


CyO P(=O)(HS) OBn · NEt3
(thousandths)
X : parts per Million : Carbon13
138.568 138.496
127.926 127.345 127.086
77.254 77.000 76.746 75.162 75.111 67.409 67.368
45.269
33.748 33.712 33.530 33.496 25.352 24.001
8.393
JEOL
---- PROCESSING PARAMETERS ----
sexp(1.00646[Hz], 0.0[s])
trapezoid(0[%], 0[%], 80[%], 100[%])
zerofill(2, TRUE)
fft(1, TRUE, TRUE)
machinephase
ppm
thresh(5[%], 1)
peak_pick(0[Hz], 0.1[ppm], Peaks, 0[Hz])
以下に由来：: YS7014-c_CARBON-1-1.jdf
Filename = YS7014-c_CARBO
Author = delta
Experiment = carbon.jxp
Sample_Id = YS7014-c
Solvent = CHLOROFORM-D
Actual_Start_Time = 28-MAR-2024 10
Revision_Time = 1-APR-2024 11
Field_Strength = 11.7473579[T]
X_Freq = 125.76529768[M
Scans = 256
Total_Scans = 256
Relaxation_Delay = 2[s]
Temp_Get = 22[dC]




```
---- PROCESSING PARAMETERS ----
sexp( 0.67473[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 2, TRUE )
fft( 1, TRUE, TRUE )
machinephase
ppm
thresh( 5[%], 1 )
peak_pick( 0[Hz], 0.1[ppm], Peaks, 0[Hz] )

以下に由来：: YS7014-c_PHOSPHORUS-1-1.jdf
```

```
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Author                      = delta
Experiment                  = single_pulse_d
Sample_Id                   = YS7014-c
Solvent                     = CHLOROFORM-D
Actual_Start_Time           = 28-MAR-2024 10
Revision_Time               =  1-APR-2024 11

Data_Format                 = 1D COMPLEX
Dim_Size                    = 419430
X_Domain                    = Phosphorus31
Dim_Title                   = Phosphorus31
Dim_Units                   = [ppm]
Dimensions                  = X
Site                        = JNM-ECZ500R/M3
Spectrometer                = JNM-ECZ500R/M3

Field_Strength              = 11.7473579[T]
X_Acq_Duration              = 1.48207552[s]
X_Domain                    = Phosphorus31
X_Freq                      = 202.46831075[M
X_Offset                    = 0[ppm]
X_Points                    = 151852
X_Points_Input              = 121481
X_Prescans                  = 0
X_Resolution                = 0.67472945[Hz]
X_Sweep                     = 102.45901639[k
X_Sweep_Clipped             = 81.96721311[kH
X_Sweep_Input               = 404[ppm]
Irr_Domain                  = Proton
Irr_Freq                    = 500.15991521[M
Irr_Offset                  = 5.0[ppm]
Blanking                    = 5.0[us]
Clipped                     = FALSE
Scans                       = 16
Total_Scans                 = 16

Relaxation_Delay            = 2[s]
Recvr_Gain                  = 52
Temp_Get                    = 22[dC]
X_90_Width                  = 14.75[us]
X_Acq_Time                  = 1.48207552[s]
X_Angle                     = 30[deg]
X_Atn                       = 13[dB]
X_Data_Points               = 32768
X_Points_Default            = 102460
X_Pulse                     = 4.91666667[us]
Irr_Atn_Dec                 = 29[dB]
Irr_Atn_Dec_Calc            = 29[dB]
Irr_Atn_Noe                 = 29[dB]
Irr_Bandwidth               = 5.97826087[kHz
Irr_Bandwidth_Ppm           = 11.9526989[ppm
Irr_Corresp_Pw90            = 92[us]
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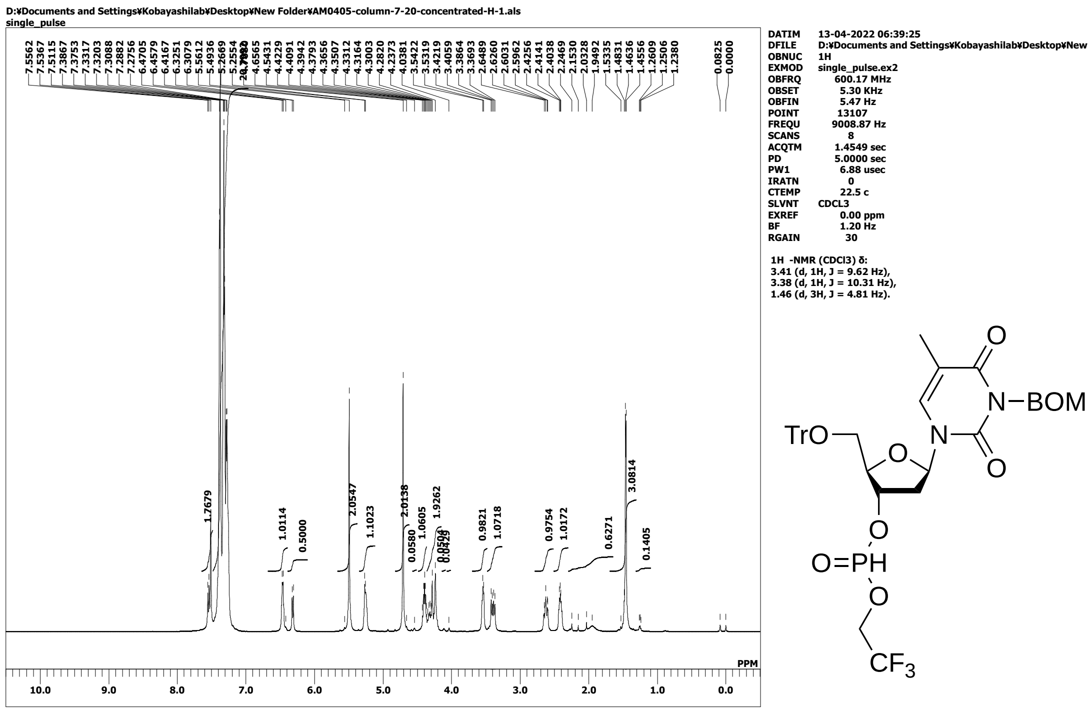
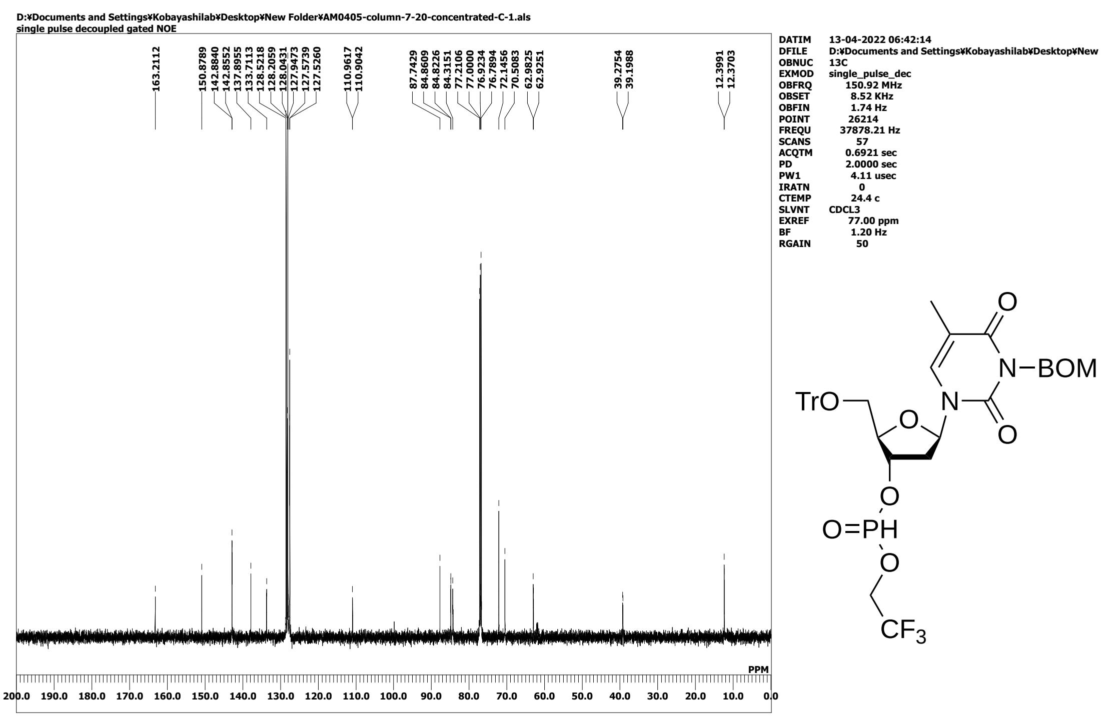
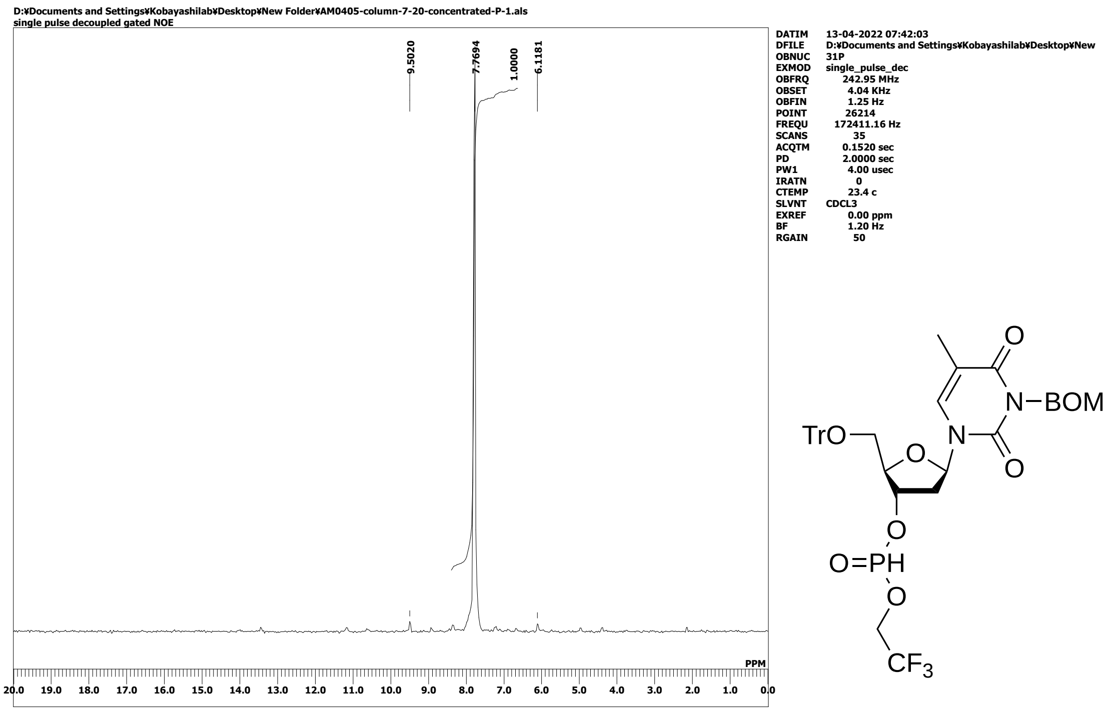
[1]H NMR (600 MHz, $CDCl_3$) of **3ad**



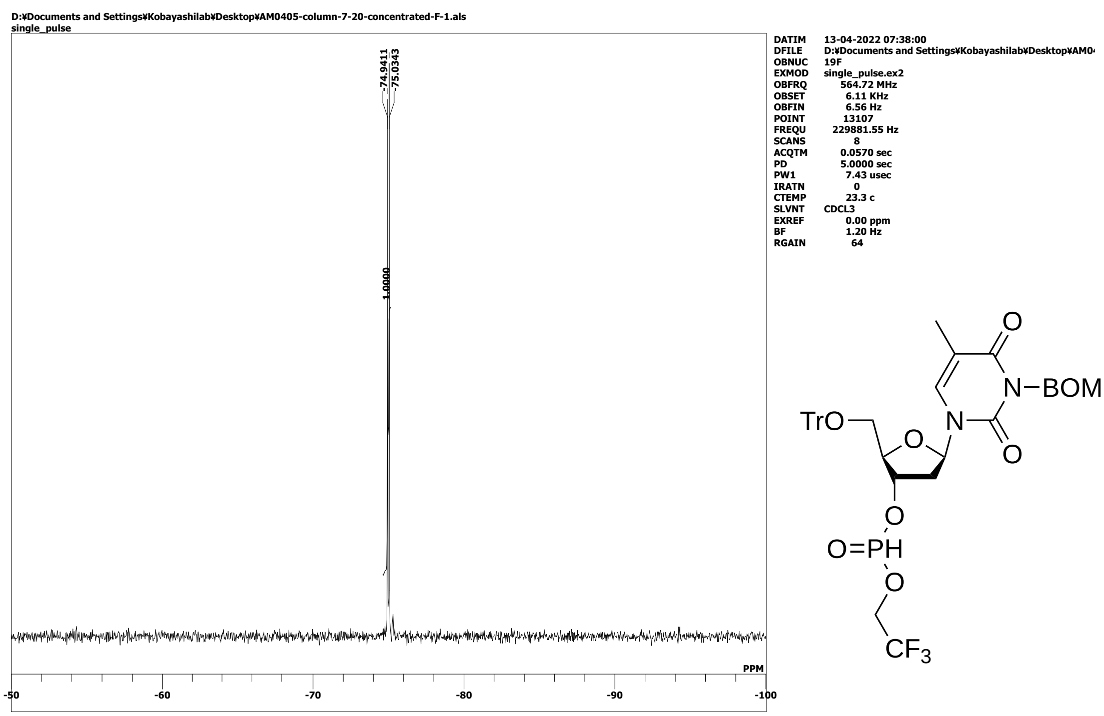
[13]C NMR (151 MHz, $CDCl_3$) of **3ad**



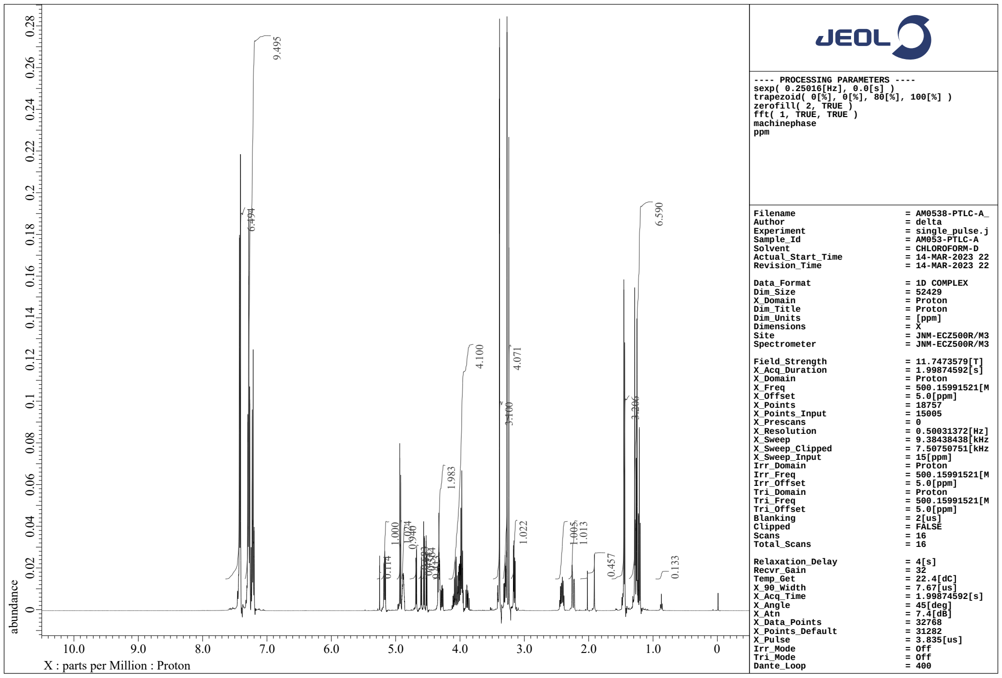
^{31}P NMR (243 MHz, $CDCl_3$) of **3ad**

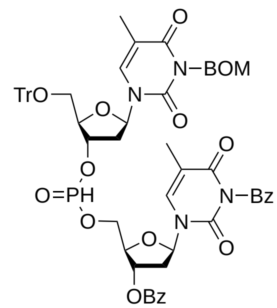


^{19}F NMR (565 MHz, $CDCl_3$) of **3ad**

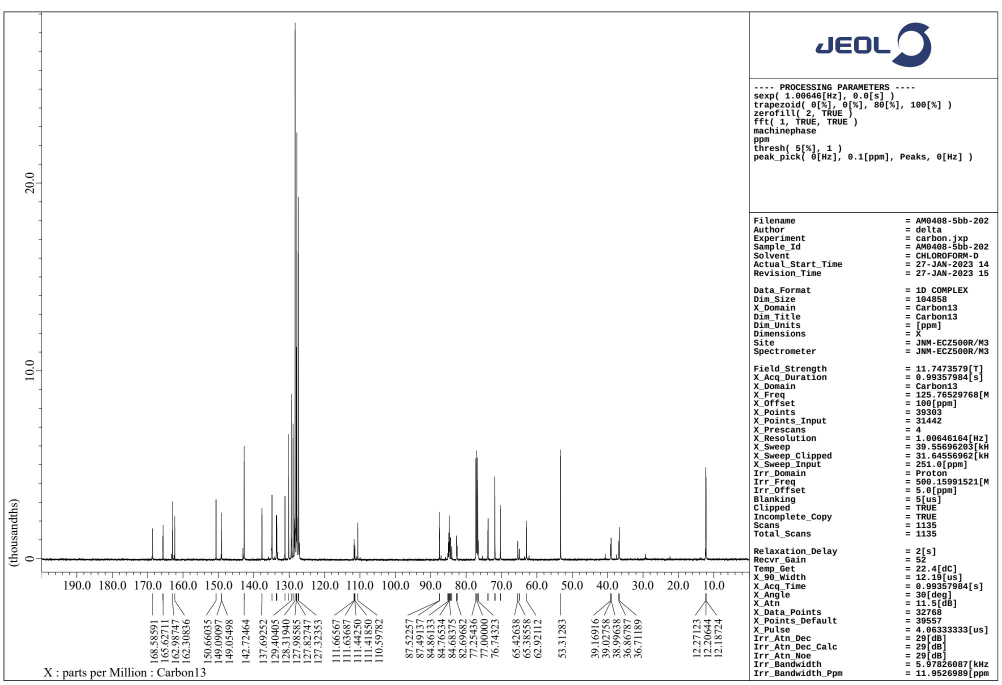


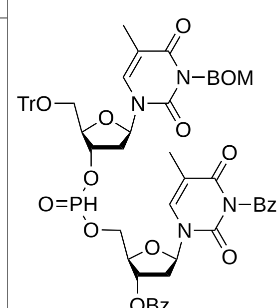
^{1}H NMR (500 MHz, $CDCl_3$) of **6a**



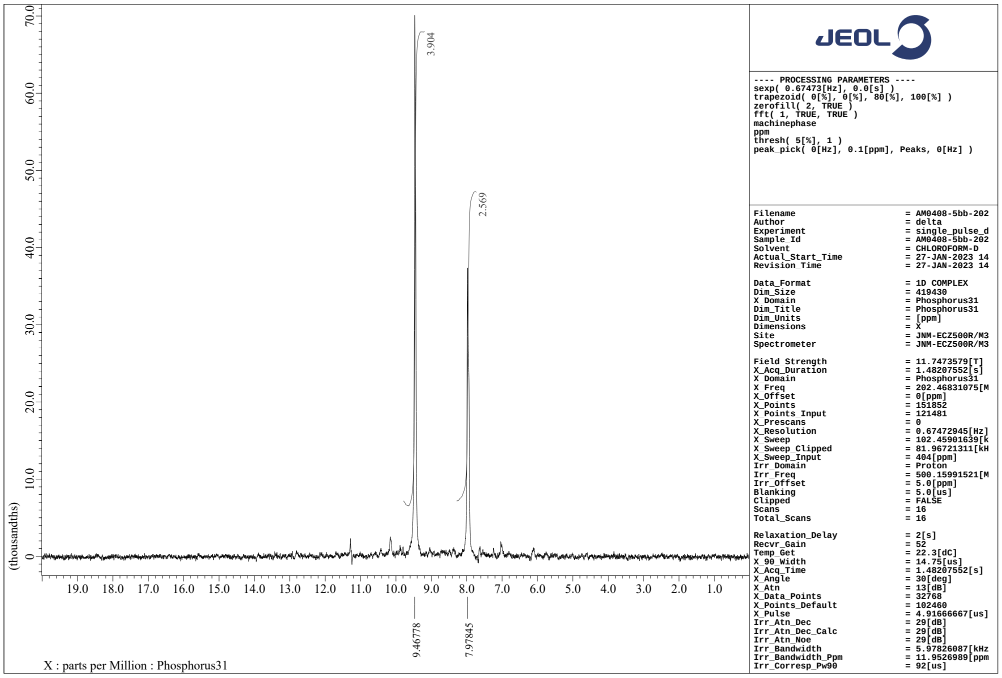


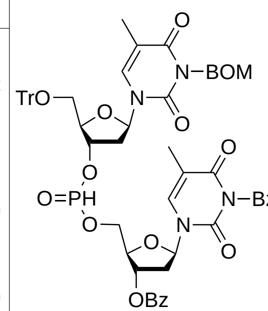
^{13}C NMR (126 MHz, $CDCl_3$) of **6a**



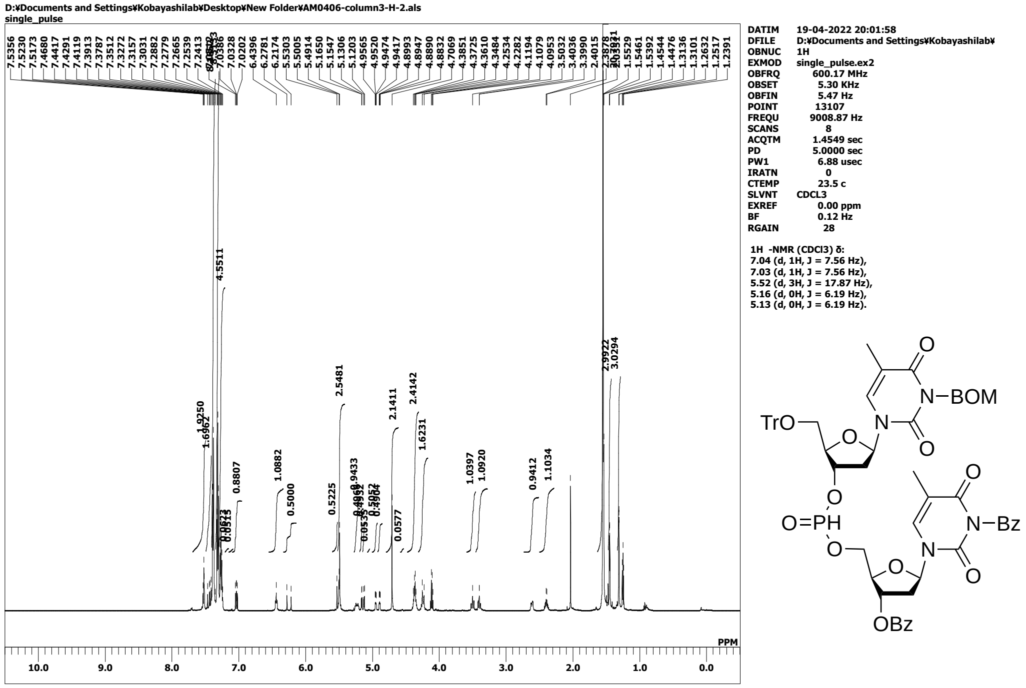


^{31}P NMR (202 MHz, $CDCl_3$) of **6a**

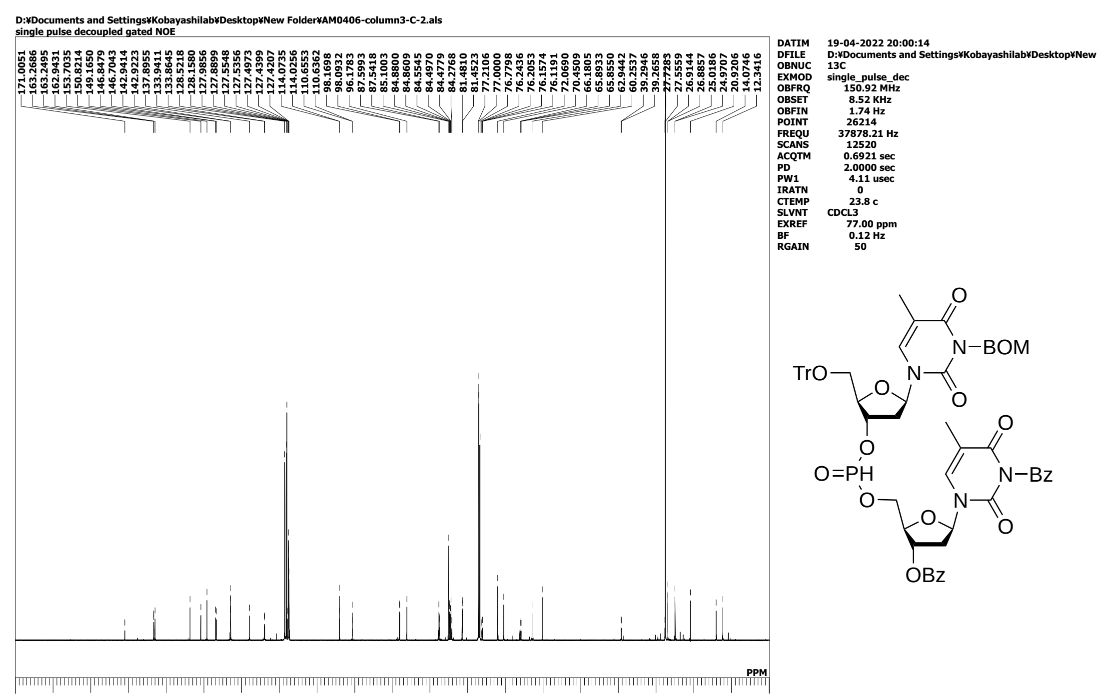




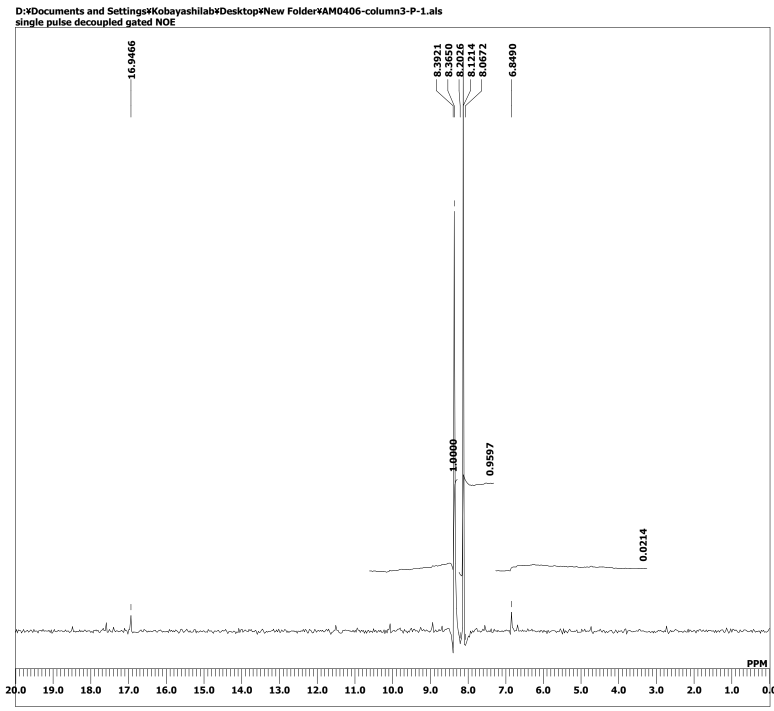
[1]H NMR (500 MHz, $CDCl_3$) of **6b**

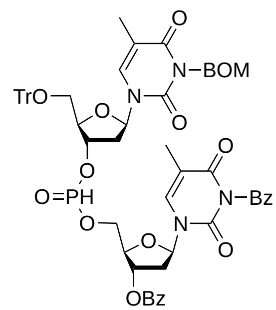


[13]C NMR (126 MHz, $CDCl_3$) of **6b**

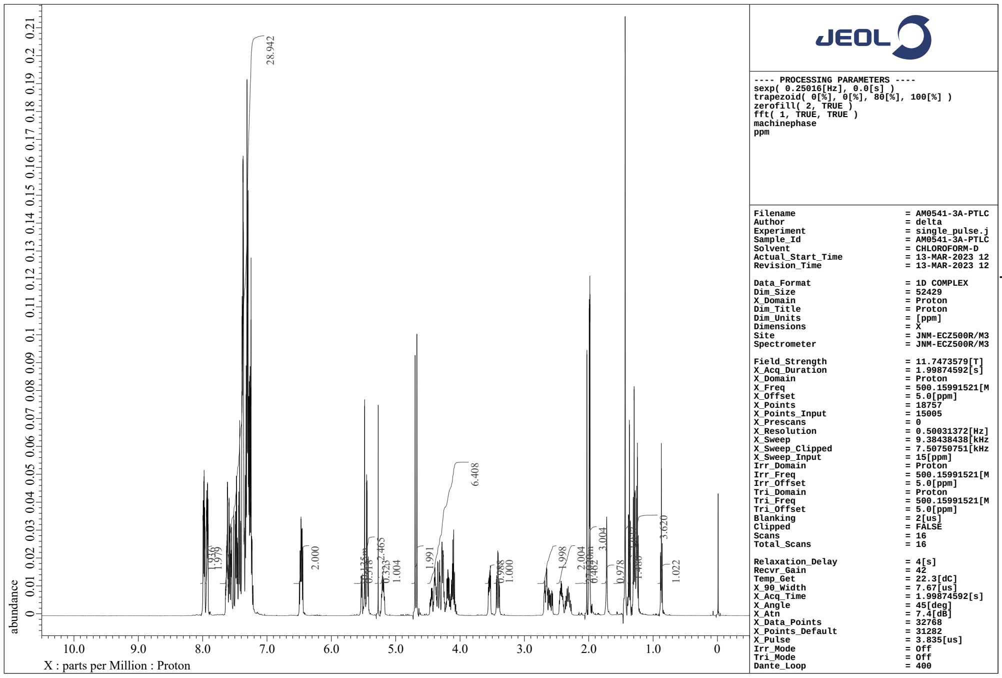


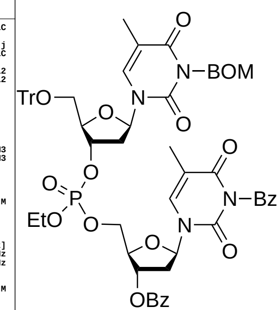
^{31}P NMR (202 MHz, $CDCl_3$) of **6b**



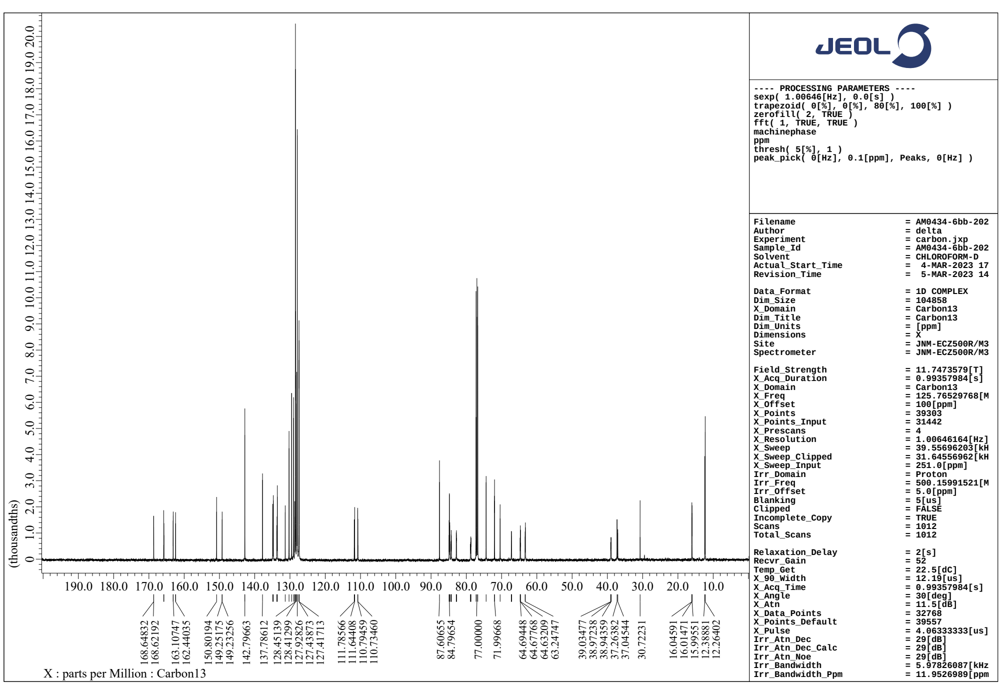


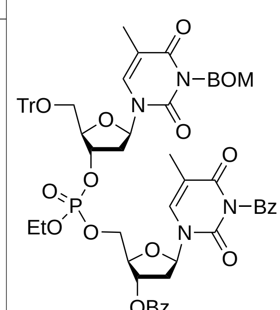
[1]H NMR (500 MHz, $CDCl_3$) of **7a**



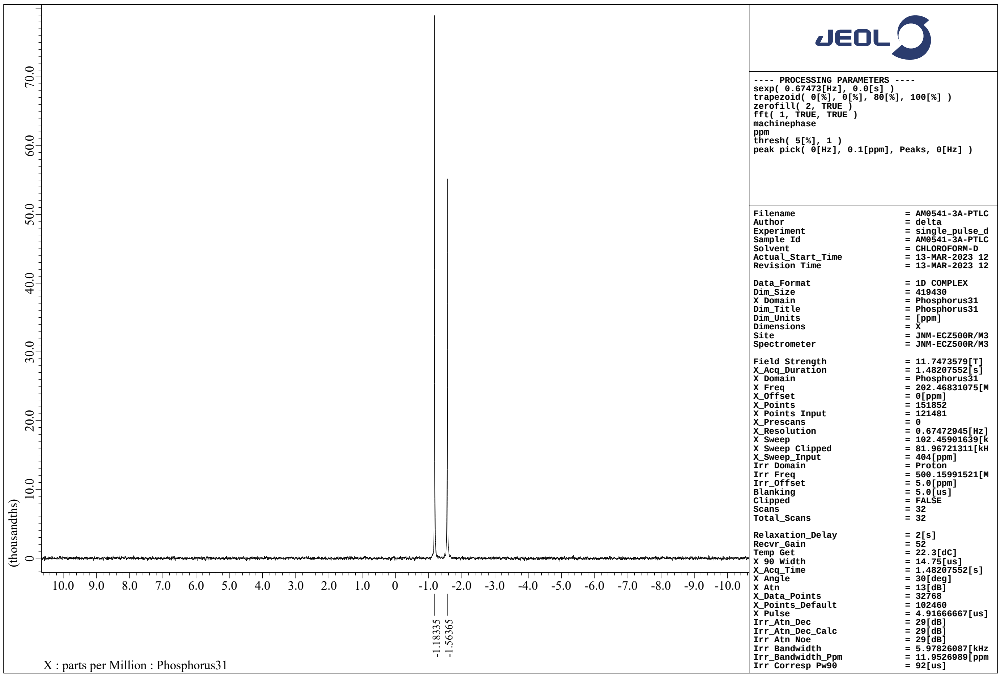


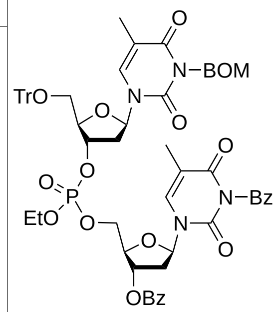
[13]C NMR (126 MHz, $CDCl_3$) of **7a**



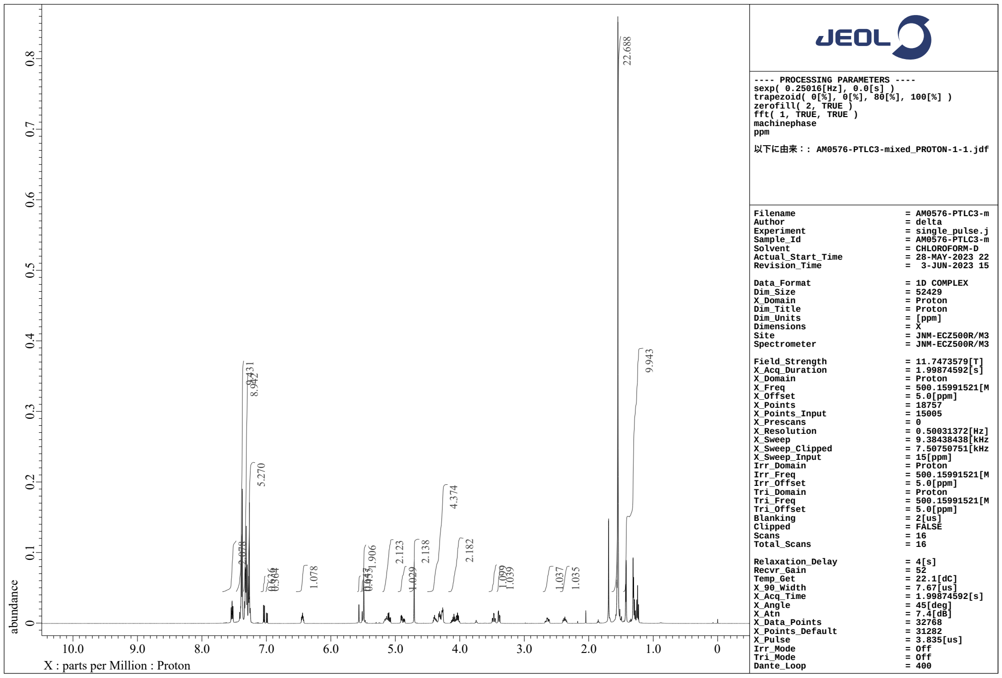


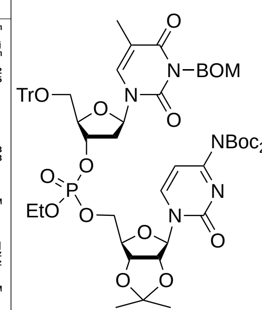
^{31}P NMR (202 MHz, $CDCl_3$) of **7a**



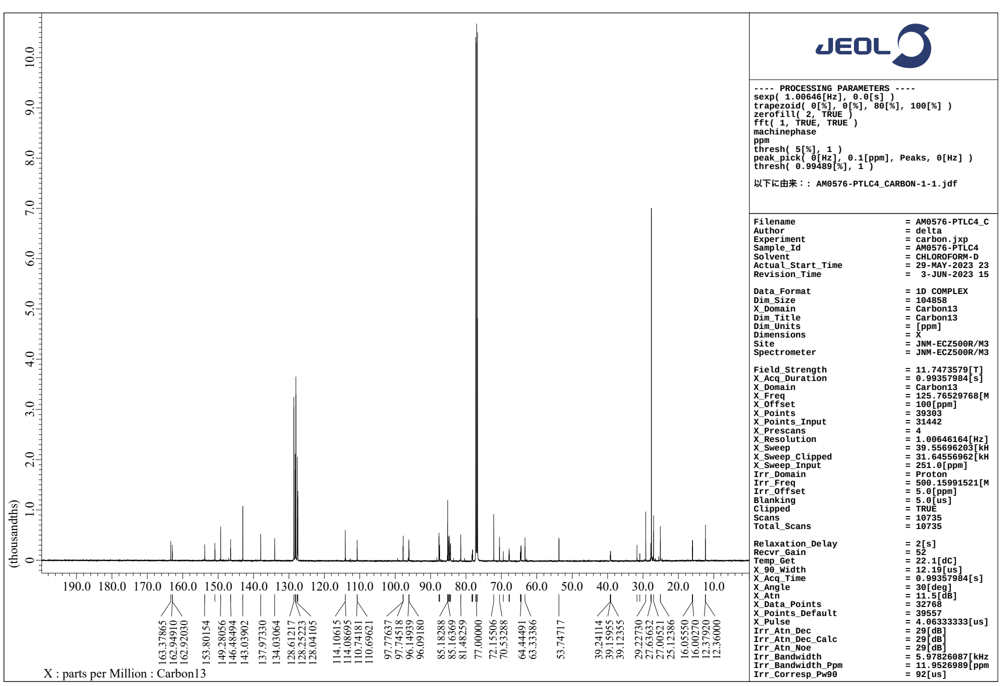


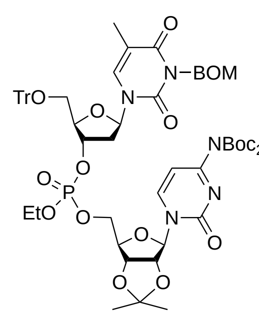
[1]H NMR (500 MHz, $CDCl_3$) of **7b**



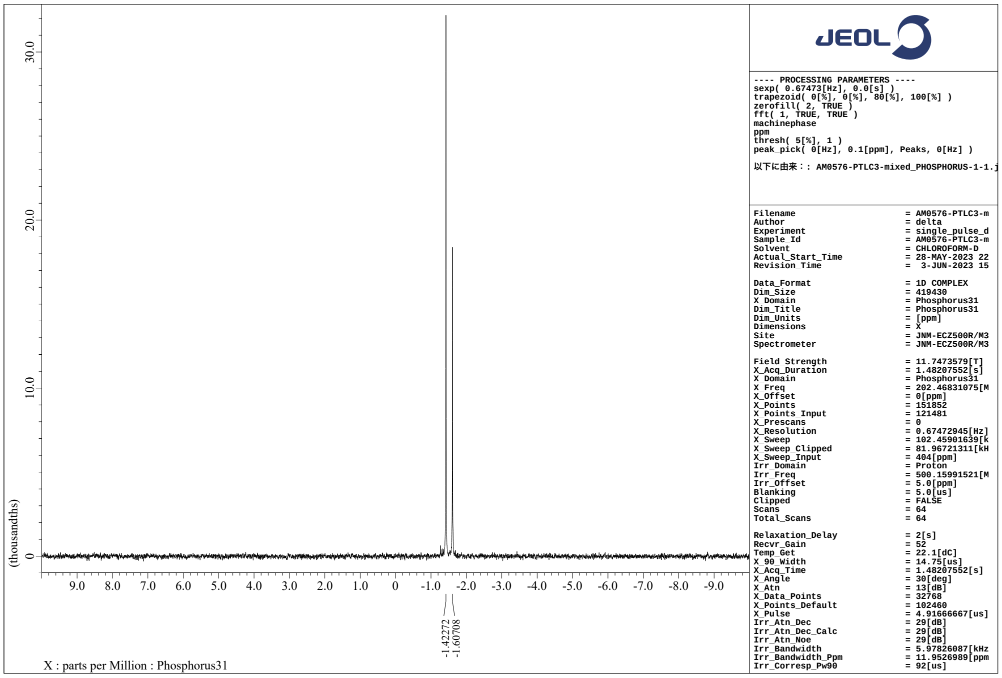


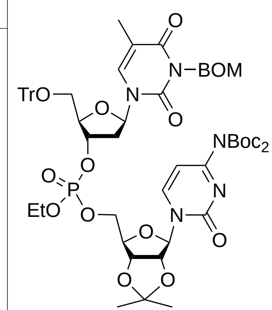
[13]C NMR (126 MHz, $CDCl_3$) of **7b**





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





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