Palladium-Catalyzed One-Pot Phosphorylation of Phenols Mediated by Sulfuryl Fluoride

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Contents

I. General Information.

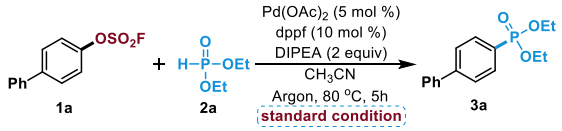
All commercially available organic compounds and DNA headpiece HP-NH_2 (5'- / 5phos / GAGTCA / iSp9 / iUniAmM / iSp9 / TGACTCCC-3', Figure 1) were purchased from commercial sources unless otherwise noted and used as received. The substrates **1** were prepared according to our previous paper.[1] ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and ^{19}F NMR spectra were recorded on Bruker AM-500 instruments. High-resolution mass spectra (HRMS-ESI) were obtained on an Agilent Technologies 6230 Accurate Mass TOF LC/MS instrument or an AB SCIEX 4600 QTOF MS instrument. All on-DNA reactions were performed in 1.5 mL or 5 mL Eppendorf tubes. On-DNA reaction were analyzed by LC-MS. Typically, samples were dissolved in an appropriate amount of distilled and deionized water (ddH_2O) and injected into a reverse-phase chromatography column (Xbridge Oligonucleotide BEH C18 column, 1.7 μm, 2.1×50 mm). The elution was carried out as followings: 5–95% solvent B over 4.5 min, 0.4 mL/min, λ = 260 nm; solvent A: 0.75% v/v hexafluoroisopropanol/ 0.038% v/v triethylamine in methanol/water = 5/95; solvent B: 0.75% v/v hexafluoroisopropanol/ 0.038% v/v triethylamine in methanol/water = 90/10. The effluents were analyzed by a Waters G2 TOF electrospray mass spectrometer in negative ion mode. Ignoring UV coefficient difference for all DNA products and assuming 100% of DNA total recovery, the yield of DNA products was determined from UV absorbance trace (260 nm) peak area using the equation below:

$$Yield\ (product, \%) = \frac{\%\ \text{UV (product)}}{\%\ \text{UV (DNA starting material before reaction)}} \times 100\%$$

Caution: Sulfuryl fluoride (SO_2F_2, MW = 102 g/mol, ρ = 4.17 g/cm3, bp = -55.20 °C) is a toxic gas that can resistant to hydrolysis up to 150 °C. The use of SO_2F_2 must be executed in a well ventilated fumehood. The excess SO_2F_2 can be quenched by basic aqueous medium.

II. Experimental Procedures and Characterizations:

Table S1. Screening of the reaction conditions

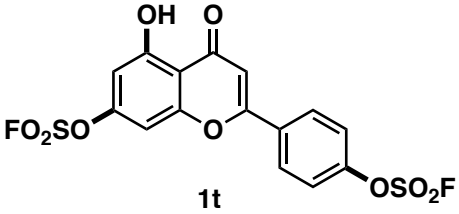


entry	Derivation from the standard conditions	Yield (%)[b]
1[a]	none	93 (87)[c]
2	without $Pd(OAc)_2$ and dppf, 80 °C	0
3	without dppf, 80 °C	5
4	dppp (instead of dppf), 80 °C	48
5	BINAP (instead of dppf), 80 °C	53
6	Xphos (instead of dppf), 80 °C	58
7	Xantophos (instead of dppf), 80 °C	75
8	$Pd(PPh_3)_2$ (instead of $Pd(OAc)_2$ and dppf), 80 °C	55
9	$Pd(OAc)_2$ (10 mol%) and dppf (20 mol%), 80 °C	95
10	$Pd(OAc)_2$ (2 mol%) and dppf (4 mol%), 80 °C	90
11	in the absence of argon, 80 °C	45
12	60 °C	92
13	40 °C	11
14	**2a** (2 equiv), CH_3CN-H_2O (4:1) as solvent, 80 °C	93
15	DMF as solvent, 80 °C	59
16	DMA as solvent, 80 °C	62
17	1,4-dioxane as solvent, 80 °C	47
18	Et_3N as base, 80 °C	90
19	Na_2CO_3 as base, 80 °C	34

[a]Standard conditions: **1a** (0.2 mmol), **2a** (0.25 mmol), DIPEA (0.4 mmol), $Pd(OAc)_2$ (5 mol %)/dppf (10 mol %) in CH_3CN (1 mL) were stirred at 80 °C for 5h under argon. [b]yield determined by LC-MS. [c]Isolated yield.

General Procedure for the Synthesis of Aryl Fluorosulfates

A 100 mL flask equipped with a magnetic stir bar was charged with the relative phenol (5 mmol, 1 equiv), Et_3N or DIPEA (10 mmol, 2 equiv) and DCM (25 mL). Sealed with a rubber septum, the flask was evacuated to low vacuum and backfilled with sulfuryl fluoride gas by a balloon. The resulting mixture was stirred at room temperature for 3~5 h. Upon completion, volatiles were removed in vacuo. The crude product was purified by flash chromatography on silica gel to give the desired aryl fluorosulfate.



1t

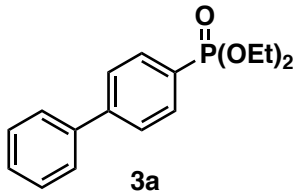
Yellow solid, 95% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.96 (s, 1H), 8.40 – 8.34 (m, 2H), 7.90 – 7.85 (m, 2H), 7.65 (d, J = 2.3 Hz, 1H), 7.35 (s, 1H), 7.18 (d, J = 2.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 183.08, 163.32, 162.01, 156.91, 153.57, 152.30, 131.57, 130.05, 122.60, 110.88, 107.86, 105.15, 101.92. ^{19}F NMR (376 MHz, DMSO) δ 40.56, 39.74. HRMS (ESI): Calcd for $C_{15}H_9F_2O_9S_2$: $[M+H]^+$ 434.9656, found: m/z 434.9650.

Standard Conditions: Procedure for the Phosphorylation of Fluorosulfates

A 25 mL flask equipped with a magnetic stir bar was charged with the relative fluorosulfate **1** (0.2 mmol), P(O)H compound **2** (0.25 mmol), $Pd(OAc)_2$ (5 mol %), dppf (10 mol %), DIPEA (0.4 mmol) and CH_3CN (1 mL). Sealed with a rubber septum, the flask was evacuated to low vacuum and backfilled with argon at room temperature. Then the resulting mixture was stirred at 80 ºC for 5h. Upon completion, volatiles were removed in vacuo. The crude product was purified by flash chromatography on silica gel to give the desired product **3**.

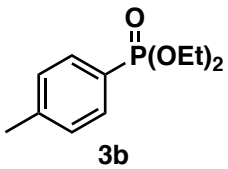
One-Pot Synthesis: Procedure for the Phosphorylation of Phenols

A 25 mL flask equipped with a magnetic stir bar was charged with the relative phenol (0.2 mmol), DIPEA (0.4 mmol) and CH_3CN (1 mL). Sealed with a rubber septum, the flask was evacuated to low vacuum and backfilled with sulfuryl fluoride gas by a balloon. The resulting mixture was stirred at room temperature for 3 h. Upon completion, the sulfuryl fluoride gas balloon was removed and the flask was purged with argon for 3 times. After that, TMSOH (0.6 mmol) was added and stirred for 30 min to remove the fluoride ion, followed by addition of P(O)H compound **2** (0.25 mmol)**,** $Pd(OAc)_2$ (5 mol %), dppf (10 mol %), DIPEA (0.4 mmol). Sealed with a rubber septum, the flask was evacuated to low vacuum and backfilled with argon at room temperature. Then resulting mixture was stirred at 80 ºC for 5h. Upon completion, volatiles were removed in vacuo. The crude product was purified by flash chromatography on silica gel to give the desired product **3**.



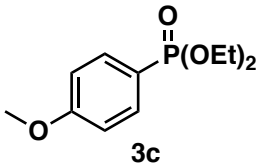
3a

Colorless oil, 87% yield, (90% for one-pot). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H), 7.70 – 7.67 (m, 2H), 7.62 – 7.59 (m, 2H), 7.49 – 7.44 (m, 2H), 7.42 – 7.38 (m, 1H), 4.23 – 4.05 (m, 4H), 1.35 (t, J = 7.1 Hz, 6H). These data are in agreement with literature data.[2]



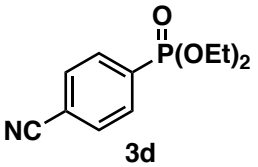
3b

Colorless oil, 92% yield, (91% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J = 12.9, 7.8 Hz, 2H), 7.29 – 7.26 (m, 2H), 4.22 – 3.99 (m, 4H), 2.40 (s, 3H), 1.31 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[3]



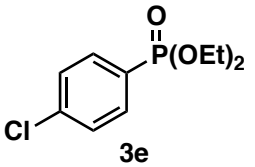
3c

Colorless oil, 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.70 (m, 2H), 7.01 – 6.91 (m, 2H), 4.17 – 3.97 (m, 4H), 3.85 (s, 3H), 1.31 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[4]



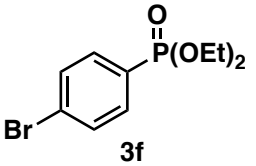
3d

Colorless oil, 84% yield, (90% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 12.9, 7.8 Hz, 2H), 7.76 (dd, J = 8.1, 2.8 Hz, 2H), 4.24 – 4.06 (m, 4H), 1.34 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[5]



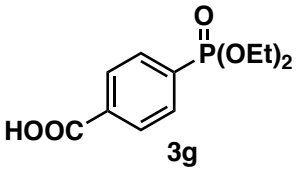
3e

Colorless oil, 93% yield, (88% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 12.5, 8.0 Hz, 2H), 7.45 (dd, J = 8.0, 2.1 Hz, 2H), 4.23 – 4.00 (m, 4H), 1.32 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[5]



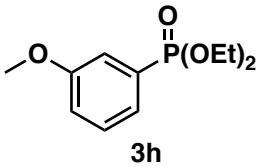
3f

Colorless oil, 90% yield, (87% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, J = 12.7, 8.2 Hz, 2H), 7.61 (dd, J = 8.3, 3.4 Hz, 2H), 4.20 – 4.02 (m, 4H), 1.32 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[6]



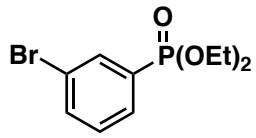
3g

White solid, 93% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.23 – 11.03 (m, 1H), 8.19 (dd, J = 8.1, 3.5 Hz, 2H), 7.93 (dd, J = 13.0, 7.9 Hz, 2H), 4.27 – 4.09 (m, 4H), 1.34 (t, J = 7.0 Hz, 6H). These data are in agreement with literature data.[7]



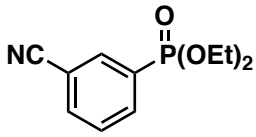
3h

Colorless oil, 82% yield, (80% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 3H), 7.11 – 7.05 (m, 1H), 4.19 – 4.03 (m, 4H), 3.84 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 6H). These data are in agreement with literature data.[8]



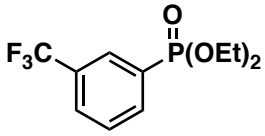
3i

Colorless oil, 93% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 12.5 Hz, 1H), 7.74 (dd, *J* = 12.4, 7.5 Hz, 1H), 7.68 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.35 (dt, *J* = 9.1, 4.5 Hz, 1H), 4.19 – 4.07 (m, 4H), 1.34 (t, *J* = 6.9 Hz, 6H). These data are in agreement with literature data.[9]



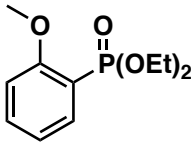
3j

Colorless oil, 85% yield, (82% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 13.3, 1.7 Hz, 1H), 8.06 – 8.01 (m, 1H), 7.82 (dq, *J* = 7.8, 1.2 Hz, 1H), 7.60 (td, *J* = 7.7, 3.5 Hz, 1H), 4.25 – 4.06 (m, 4H), 1.34 (t, *J* = 7.0 Hz, 6H). These data are in agreement with literature data.[10]



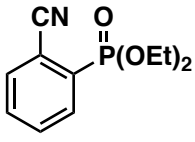
3k

Colorless oil, 92% yield, (89% for one-pot).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 13.6 Hz, 1H), 8.00 (dd, *J* = 13.0, 7.6 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.61 (td, *J* = 7.7, 3.7 Hz, 1H), 4.24 – 4.06 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 6H). These data are in agreement with literature data.[5]



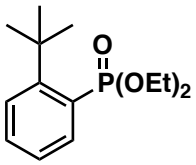
3l

Colorless oil, 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (ddd, *J* = 14.9, 7.6, 1.8 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.05 – 6.98 (m, 1H), 6.98 – 6.91 (m, 1H), 4.24 – 4.07 (m, 4H), 3.90 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 6H). These data are in agreement with literature data. These data are in agreement with literature data.[11]



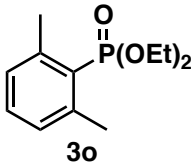
3m

Colorless oil, 67% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 14.1, 7.4 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.73 – 7.62 (m, 2H), 4.32 – 4.13 (m, 4H), 1.38 (t, *J* = 7.0 Hz, 6H). These data are in agreement with literature data.[12]



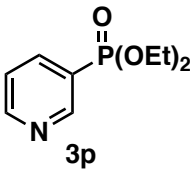
3n

Colorless oil, 53% yield. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.89 (ddd, J = 14.9, 7.8, 1.6 Hz, 1H), 7.60 (td, J = 7.8, 7.4, 1.3 Hz, 1H), 7.53 (tt, J = 8.4, 1.7 Hz, 1H), 7.35 (tdd, J = 7.4, 2.6, 1.3 Hz, 1H), 4.09 – 3.95 (m, 4H), 1.51 (s, 9H), 1.24 (t, J = 7.1 Hz, 6H). **^{13}C NMR** (126 MHz, DMSO) δ 155.02, 154.92, 135.76, 135.70, 132.80, 132.78, 127.89, 127.77, 127.63, 126.21, 126.14, 126.04, 61.97, 61.93, 37.14, 37.12, 32.05, 16.53, 16.48. ^{31}P NMR (202 MHz, DMSO) δ 19.88. **HRMS** (ESI): Calcd for $C_{14}H_{23}O_3P$: $[M+H]^+$ 271.1463, found: m/z 271.1458.



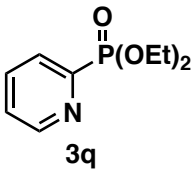
3o

Colorless oil, 58% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, 1H), 7.08 (dd, J = 7.6, 4.7 Hz, 2H), 4.16 (dp, J = 10.0, 7.2 Hz, 2H), 4.05 (dp, J = 10.0, 7.2 Hz, 2H), 2.64 (d, J = 1.6 Hz, 6H), 1.32 (t, J = 7.1 Hz, 6H). These data are in agreement with literature data.[13]



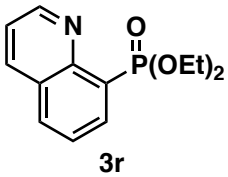
3p

Colorless oil, 90% yield, (82% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (dd, J = 6.6, 2.0 Hz, 1H), 8.77 (dt, J = 4.5, 2.1 Hz, 1H), 8.13 (ddt, J = 13.3, 7.8, 1.9 Hz, 1H), 7.43 (dt, J = 8.1, 4.1 Hz, 1H), 4.24 – 4.07 (m, 4H), 1.34 (t, J = 7.1 Hz, 6H). These data are in agreement with literature data.[14]



3q

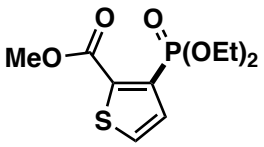
Colorless oil, 90% yield, (93% for one-pot). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, J = 4.6 Hz, 1H), 7.95 (t, J = 7.2 Hz, 1H), 7.79 (tdd, J = 7.6, 5.5, 1.5 Hz, 1H), 7.41 (dd, J = 8.5, 4.3 Hz, 1H), 4.29 – 4.14 (m, 4H), 1.32 (t, J = 7.1 Hz, 6H). These data are in agreement with literature data.[15]



3r

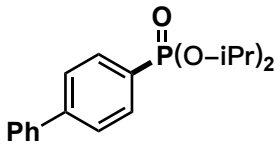
Colorless oil, 91% yield, (83% for one-pot). ^{1}H NMR (500 MHz, DMSO) δ 9.02 (dd, J = 4.2, 1.8 Hz, 1H), 8.47 (dt, J = 8.3, 2.1 Hz, 1H), 8.29 – 8.19 (m, 2H), 7.71 (ddd, J = 8.1, 7.1, 3.5 Hz, 1H),

7.63 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.17 (dqd, *J* = 8.7, 7.1, 3.8 Hz, 4H), 1.24 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 151.36, 147.86, 147.81, 137.18, 136.26, 136.20, 133.55, 133.52, 129.46, 128.43, 128.35, 127.98, 126.46, 126.33, 122.54, 62.33, 62.28, 16.79, 16.74. ^{31}P NMR (202 MHz, DMSO) δ 16.00. HRMS (ESI): Calcd for $C_{13}H_{17}NO_3P$: $[M+H]^+$ 266.0946, found: m/z 266.0934.



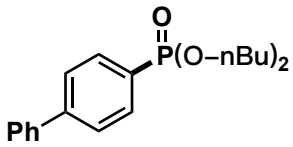
3s

Colorless oil, 83% yield, (70% for one-pot).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.42 (t, *J* = 4.8 Hz, 1H), 4.10 (dqd, *J* = 8.6, 7.0, 1.3 Hz, 4H), 3.85 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 161.03, 161.01, 138.47, 138.35, 135.64, 134.11, 133.91, 133.80, 133.08, 132.93, 62.65, 62.60, 53.16, 16.67, 16.62. ^{31}P NMR (202 MHz, DMSO) δ 9.20. HRMS (ESI): Calcd for $C_{10}H_{16}O_5PS$: $[M+H]^+$ 279.0456, found: m/z 279.0445.



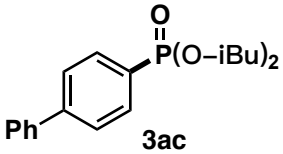
3aa

Colorless oil, 82% yield, (75% for one-pot).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H), 7.69 – 7.65 (m, 2H), 7.63 – 7.58 (m, 2H), 7.50 – 7.44 (m, 2H), 7.43 – 7.35 (m, 1H), 4.72 (dp, *J* = 7.8, 6.2 Hz, 2H), 1.39 (d, *J* = 6.2 Hz, 6H), 1.26 (d, *J* = 6.2 Hz, 6H). These data are in agreement with literature data.[16]



3ab

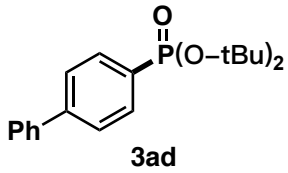
Colorless oil, 90% yield, (84% for one-pot).^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 – 7.80 (m, 2H), 7.82 – 7.76 (m, 2H), 7.76 – 7.71 (m, 2H), 7.51 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.47 – 7.40 (m, 1H), 4.06 – 3.92 (m, 4H), 1.60 (dq, *J* = 8.5, 6.5 Hz, 4H), 1.41 – 1.30 (m, 4H), 0.87 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 144.46, 144.44, 139.41, 132.44, 132.36, 129.56, 128.80, 128.32, 127.47, 127.44, 127.35, 126.82, 65.68, 65.63, 32.40, 32.36, 18.71, 13.84. ^{31}P NMR (202 MHz, DMSO) δ 17.96. HRMS (ESI): Calcd for $C_{20}H_{28}O_3P$: $[M+H]^+$ 347.1776, found: m/z 347.1763.



3ac

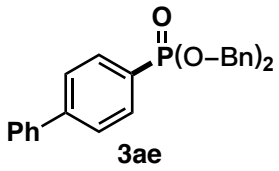
Colorless oil, 87% yield, (82% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 – 7.77 (m, 4H), 7.76 – 7.71 (m, 2H), 7.51 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.47 – 7.40 (m, 1H), 3.77 (qt, *J* = 9.8, 6.6 Hz, 4H), 1.89 (dh, *J* = 13.2, 6.6 Hz, 2H), 0.90 (d, *J* = 6.7 Hz, 12H). ^{13}C NMR (126 MHz, DMSO) δ

144.46, 144.44, 139.40, 132.45, 132.37, 129.58, 128.83, 128.24, 127.50, 127.45, 127.38, 126.73, 71.80, 71.75, 29.17, 29.12, 18.99. ^{31}P NMR (202 MHz, DMSO) δ 17.75. HRMS (ESI): Calcd for $C_{20}H_{28}O_3P$: $[M+H]^+$ 347.1776, found: m/z 347.1770.



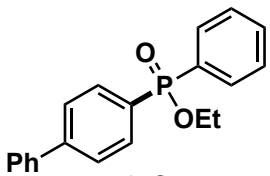
3ad

Colorless oil, 80% yield, (73% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 – 7.74 (m, 4H), 7.73 – 7.68 (m, 2H), 7.49 (dd, J = 8.4, 6.9 Hz, 2H), 7.44 – 7.38 (m, 1H), 1.42 (s, 18H). ^{13}C NMR (126 MHz, DMSO) δ 143.49, 143.47, 139.64, 133.70, 132.16, 132.07, 131.99, 129.50, 128.60, 127.38, 127.09, 126.97, 82.22, 82.16, 30.56, 30.53. ^{31}P NMR (202 MHz, DMSO) δ 9.76. HRMS (ESI): Calcd for $C_{20}H_{28}O_3P$: $[M+H]^+$ 347.1776, found: m/z 347.1768.



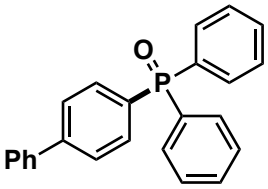
3ae

Colorless oil, 52% yield, (47% for one-pot).^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 – 7.82 (m, 4H), 7.75 – 7.70 (m, 2H), 7.51 (dd, J = 8.5, 6.9 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.40 – 7.31 (m, 10H), 5.10 (d, J = 8.0 Hz, 4H). ^{13}C NMR (126 MHz, DMSO) δ 144.71, 144.68, 139.36, 136.86, 136.81, 132.55, 132.47, 129.59, 128.95, 128.88, 128.71, 128.25, 127.79, 127.57, 127.47, 127.45, 126.28, 67.50, 67.46. ^{31}P NMR (202 MHz, DMSO) δ 18.96. HRMS (ESI): Calcd for $C_{26}H_{24}O_3P$: $[M+H]^+$ 415.1463, found: m/z 415.1456.



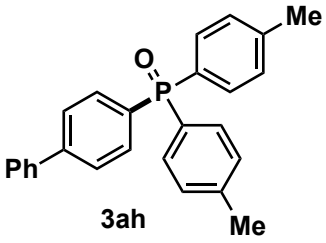
3af

Colorless oil, 93% yield, (97% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 – 7.78 (m, 6H), 7.72 – 7.66 (m, 2H), 7.62 – 7.57 (m, 1H), 7.54 (ddd, J = 8.5, 6.5, 3.4 Hz, 2H), 7.48 (dd, J = 8.4, 6.9 Hz, 2H), 7.43 – 7.37 (m, 1H), 4.06 – 3.97 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 144.28, 144.26, 139.45, 132.88, 132.74, 132.72, 132.43, 132.35, 131.80, 131.75, 131.67, 131.57, 130.48, 129.54, 129.34, 129.23, 128.78, 127.58, 127.48, 127.46, 61.31, 61.26, 40.51, 40.43, 40.34, 40.26, 40.17, 40.09, 40.00, 39.93, 39.84, 39.67, 39.51, 16.85, 16.80. ^{31}P NMR (202 MHz, DMSO) δ 29.52. HRMS (ESI): Calcd for $C_{20}H_{20}O_2P$: $[M+H]^+$ 323.1201, found: m/z 323.1197.



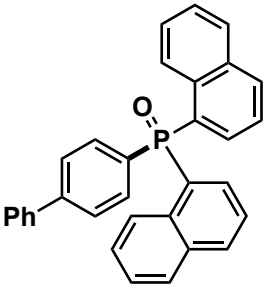
3ag

White solid, 90% yield, (91% for one-pot).[1]H NMR (500 MHz, Chloroform-*d*) δ 7.75 (tt, *J* = 17.1, 8.1 Hz, 8H), 7.65 – 7.56 (m, 4H), 7.53 – 77.45 (m, 6H), 7.42 (t, *J* = 7.3 Hz, 1H). These data are in agreement with literature data.[17]



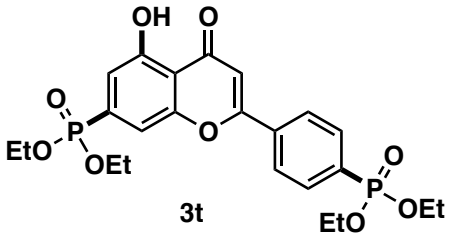
3ah

White solid, 91% yield, (88% for one-pot).[1]H NMR (500 MHz, DMSO-d_6) δ 7.81 (dd, *J* = 8.2, 2.4 Hz, 2H), 7.72 – 7.63 (m, 4H), 7.57 – 7.50 (m, 4H), 7.47 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.42 – 7.37 (m, 1H), 7.34 (dd, *J* = 8.2, 2.6 Hz, 4H), 2.34 (s, 6H). [13]C NMR (126 MHz, DMSO) δ 143.86, 143.84, 142.53, 142.51, 139.45, 132.98, 132.62, 132.54, 132.16, 132.04, 131.96, 130.64, 129.85, 129.80, 129.75, 129.54, 128.75, 127.45, 127.42, 127.32, 21.55. [31]P NMR (202 MHz, DMSO) δ 25.58. HRMS (ESI): Calcd for $C_{26}H_{24}OP$: $[M+H]^+$ 383.1563, found: m/z 383.1558



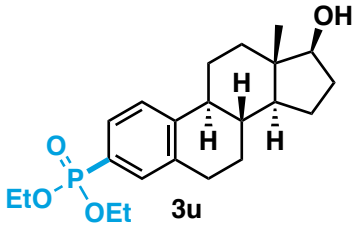
3ai

White solid, 90% yield. [1]H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.2 Hz, 2H), 8.06 – 7.97 (m, 2H), 7.93 (d, *J* = 7.9 Hz, 2H), 7.77 (dd, *J* = 11.8, 7.7 Hz, 2H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.3 Hz, 2H), 7.51 – 7.36 (m, 4H), 7.41 – 7.28 (m, 5H). [13]C NMR (126 MHz, $CDCl_3$) δ 139.89, 134.07, 133.32, 132.98, 128.97, 128.83, 128.18, 127.99, 127.52, 127.30, 126.62, 124.30. [31]P NMR (202 MHz, $CDCl_3$) δ 36.35. HRMS (ESI): Calcd for $C_{32}H_{24}OP$: $[M+H]^+$ 455.1565, found: m/z 455.1559.



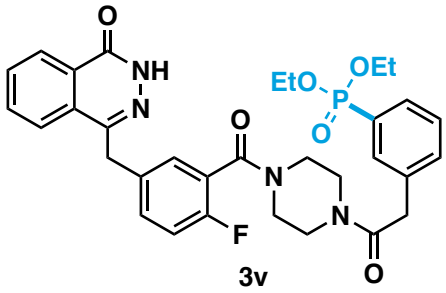
3t

Yellow solid, 90% yield, (93% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.57 (s, 1H), 8.27 (dd, J = 8.1, 3.5 Hz, 2H), 7.83 (dd, J = 12.7, 7.9 Hz, 2H), 7.49 (d, J = 14.5 Hz, 1H), 7.25 (s, 1H), 6.97 (d, J = 14.0 Hz, 1H), 4.03 (dddt, J = 14.8, 9.3, 7.1, 2.7 Hz, 8H), 1.21 (dt, J = 10.0, 7.0 Hz, 12H). ^{13}C NMR (126 MHz, DMSO) δ 183.48, 163.90, 160.37, 160.20, 156.21, 156.01, 137.48, 136.02, 134.36, 134.33, 133.63, 132.37, 132.29, 132.16, 127.56, 127.44, 113.23, 113.15, 112.87, 112.85, 111.11, 111.02, 107.96, 62.94, 62.90, 62.57, 62.53, 40.57, 40.47, 40.40, 40.31, 40.23, 40.14, 39.97, 39.90, 39.81, 39.64, 39.47, 16.66, 16.61. ^{31}P NMR (202 MHz, DMSO) δ 16.13, 14.46. HRMS (ESI): Calcd for $C_{23}H_{29}O_9P_2$: $[M+H]^+$ 511.1287, found: m/z 511.1280.



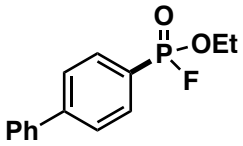
3u

White solid, 92% yield, (83% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.46 – 7.35 (m, 3H), 4.52 (s, 1H), 4.05 – 3.90 (m, 4H), 3.53 (t, J = 8.5 Hz, 1H), 2.85 (dt, J = 9.3, 4.6 Hz, 2H), 2.32 (dd, J = 14.0, 4.0 Hz, 1H), 2.23 (ddd, J = 13.8, 10.6, 3.9 Hz, 1H), 1.86 (dddd, J = 23.8, 12.1, 8.9, 4.1 Hz, 3H), 1.60 (dddd, J = 12.2, 9.8, 6.9, 3.2 Hz, 1H), 1.45 – 1.35 (m, 3H), 1.35 – 1.24 (m, 2H), 1.22 (td, J = 7.0, 1.1 Hz, 8H), 0.67 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.45, 137.47, 137.35, 132.19, 132.10, 128.88, 128.81, 126.38, 126.19, 126.07, 124.89, 80.44, 61.93, 61.89, 50.09, 44.53, 43.20, 38.34, 36.97, 30.32, 29.22, 26.93, 26.03, 23.22, 16.69, 16.64, 11.64. ^{31}P NMR (202 MHz, DMSO) δ 18.68. HRMS (ESI): Calcd for $C_{22}H_{34}O_4P$: $[M+H]^+$ 393.2195, found: m/z 393.2188.



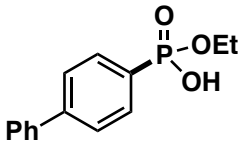
3v

Brown solid, 85% yield, (81% for one-pot). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.60 (s, 1H), 8.27 (d, J = 7.7 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.92 – 7.80 (m, 2H), 7.59 (dd, J = 14.3, 10.7 Hz, 2H), 7.46 (ddt, J = 15.3, 7.4, 3.8 Hz, 3H), 7.37 (ddd, J = 11.3, 6.4, 2.3 Hz, 1H), 7.24 (t, J = 9.0 Hz, 1H), 4.33 (s, 2H), 4.00 (dt, J = 14.8, 7.3 Hz, 4H), 3.87 (s, 1H), 3.80 (s, 1H), 3.58 (d, J = 16.4 Hz, 4H), 3.43 (dt, J = 19.8, 5.1 Hz, 2H), 3.18 – 3.13 (m, 2H), 1.21 (dt, J = 10.6, 7.0 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 169.32, 164.58, 159.87, 155.90, 145.32, 136.96, 135.35, 134.03, 133.96, 132.58, 132.29, 132.05, 129.83, 129.75, 129.55, 129.43, 129.19, 129.06, 128.38, 128.05, 126.56, 125.92, 124.09, 116.50, 116.33, 62.14, 62.09, 46.99, 46.69, 45.83, 45.36, 41.98, 41.69, 41.39, 36.92, 16.65, 16.60. ^{19}F NMR (471 MHz, DMSO) δ -119.77. ^{31}P NMR (202 MHz, DMSO) δ 18.04, 18.01. HRMS (ESI): Calcd for $C_{32}H_{35}FN_4O_6P$: $[M+H]^+$ 621.2278, found: m/z 621.2272.



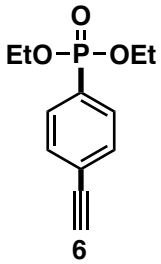
4

Colorless oil, 35% yield. ^{1}H NMR (500 MHz, DMSO) δ 7.92 (d, *J* = 11.5 Hz, 4H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 4.36 – 4.27 (m, 2H), 1.35 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 146.02, 145.99, 139.01, 132.65, 132.56, 129.66, 129.19, 127.96, 127.83, 127.60, 124.14, 123.89, 122.54, 122.30, 64.70, 64.65, 16.62, 16.57. ^{31}P NMR (202 MHz, DMSO) δ 17.06 (d, *J* = 1031.4 Hz). ^{19}F NMR (376 MHz, DMSO) δ -63.25 (d, *J* = 1031.4 Hz). HRMS (ESI): Calcd for $C_{14}H_{15}FO_2P$: $[M+H]^+$ 265.0794, found: m/z 265.0787.



5

Colorless oil, 15% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 – 7.74 (m, 4H), 7.73 – 7.68 (m, 2H), 7.49 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.44 – 7.37 (m, 1H), 3.96 – 3.87 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 143.67, 143.64, 139.66, 132.18, 132.10, 131.22, 129.76, 129.54, 128.64, 127.39, 127.18, 127.07, 61.20, 61.16, 40.55, 40.46, 40.38, 40.29, 40.21, 40.12, 40.05, 39.95, 39.88, 39.79, 39.62, 39.45, 16.75, 16.70. ^{31}P NMR (202 MHz, DMSO) δ 14.99, 14.98. HRMS (ESI): Calcd for $C_{14}H_{16}O_3P$: $[M+H]^+$ 263.0837, found: m/z 263.0823.



6

To a mixture of **3f** (87 mg, 0.3 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol) and CuI (11 mg, 0.06 mmol) in triethylamine (Et_3N) (1.5 mL) was added (trimethylsilyl)acetylene (85 μL mL, 0.6 mmol). The reaction mixture was stirred under argon atmosphere at 60 ºC for 6 h. After filtration, the filtrate was evaporated under reduced pressure, and dissolved in MeOH (1.5 mL). After that K_2CO_3 (124 mg, 0.9 mmol) was added. The mixture was stirred at room temperature for 3 h. After filtration, the filtrate was evaporated under reduced pressure. The crude product was diluted with dichloromethane, and was washed with water, and the dichloromethane layer was dried over $MgSO_4$. After the solvent was removed, the residue was purified by flash chromatography to give 46 mg of **6** as colorless oil in 65% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 2H), 7.62 – 7.54 (m, 2H), 4.25 – 4.03 (m, 4H), 3.26 (s, 1H), 1.33 (t, *J* = 7.0 Hz, 6H). These data are in agreement with literature data.[18]

III. The stability of 1a in the presence of TMSOH.

Procedure: To a solution of **1a** (0.2 mmol) in CH_3CN (1 mL) was added TMSOH (0.6 mmol) and DIPEA (0.4 mmol). The mixture was stirred at room temperature and analysis by LC-MS at 0.5h, 1h and 3h.

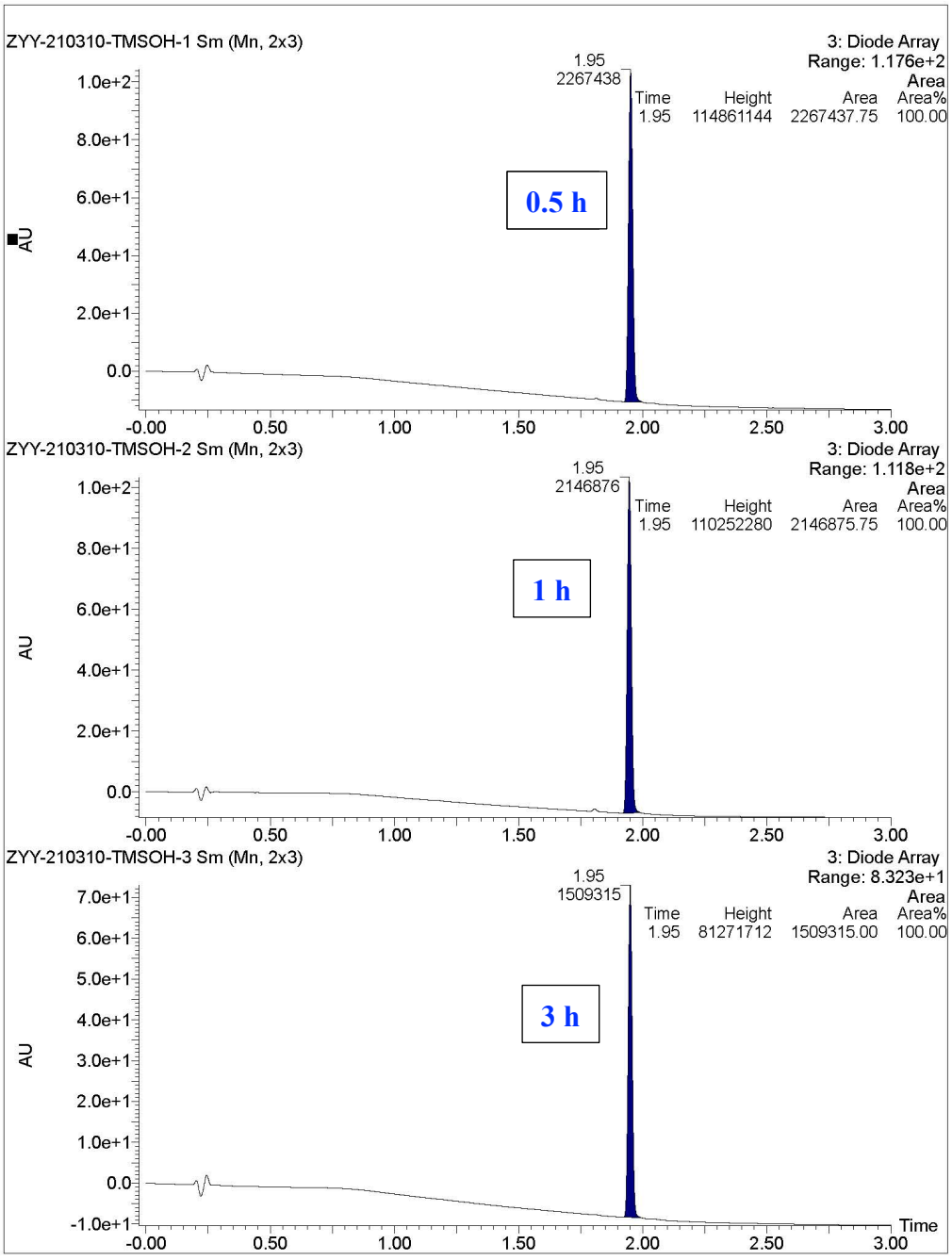
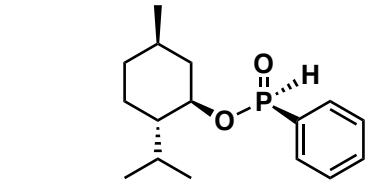


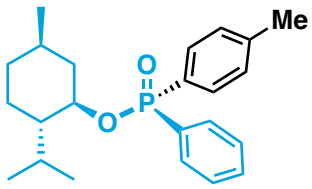
Figure 1. LC-MS analysis of the stability of **1a** in the presence of TMSOH and DIPEA.

IV. Synthesis of enantiomerically pure P-chiral 3aj.



(R_P)-(–)-menthyl benzylphosphinate

Synthesis of (Rp)-(–)-menthyl benzylphosphinate. (the synthesis was according to the literature procedures with slightly modification[19–21]) A solution of (–)-menthol (50 g, 0.32 mol) and pyridine (25 mL, 0.32 mol) in hexane (150 mL) was added dropwise to dichlorophenylphosphine (44 mL g, 0.32 mol) in hexane (150 mL) at 0°C. After stirring at room temperature for12 hours, the resulting pyridine hydrochloride was removed by filtration, and water (100 mL) was added slowly at 0°C. The two layers were separated, and the organic phase was washed with aqueous sodium bicarbonate solution (50 mL), dried over anhydrous Na_2SO_4, filtrated, and concentrated under reduced pressure to give 79 g of menthyl hydrogenophenylphosphinate with about 38% diastereomeric excess. The crude product was then diluted in hexane (10 mL) and stored at -40°C for 48h. The first batch was collected. After a second crystallization in hexane, 12.3 g (14% yield) of (*R*p)-(–)-menthyl benzylphosphinate was obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 552.5 Hz, 1H), 7.81 – 7.72 (m, 2H), 7.56 – 7.49 (m, 1H), 7.44 (td, *J* = 7.5, 3.2 Hz, 2H), 4.22 (qd, *J* = 10.5, 4.5 Hz, 1H), 2.20 – 2.07 (m, 2H), 1.69 (brs, 1H), 1.66 – 1.56 (m, 1H), 1.49 – 1.43 (m, 2H), 1.17 (td, *J* = 12.2, 10.9 Hz, 1H), 0.98 (qd, *J* = 13.6, 3.8 Hz, 1H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H). ^{31}P NMR (202 MHz, $CDCl_3$) δ 24.70. These data are in agreement with literature data.[21]



3aj

3aj (white solid, 85 % yield) was synthesized by using the one-pot procedure. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.79 (m, 2H), 7.68 – 7.62 (m, 2H), 7.52 – 7.46 (m, 1H), 7.45 – 7.38 (m, 2H), 7.22 (dd, *J* = 8.0, 3.2 Hz, 2H), 4.27 – 4.17 (m, 1H), 2.37 (s, 3H), 2.18 – 2.06 (m, 2H), 1.66 – 1.59 (m, 2H), 1.47 – 1.30 (m, 2H), 1.20 (td, *J* = 12.2, 10.8 Hz, 1H), 1.02 – 0.91 (m, 1H), 0.88 (d, *J* = 7.1 Hz, 2H), 0.83 (d, *J* = 6.4 Hz, 3H), 0.54 (d, *J* = 6.9 Hz, 3H). ^{31}P NMR (202 MHz, DMSO) δ 16.13, 14.46. ^{31}P NMR (202 MHz, $CDCl_3$) δ 29.77. These data are in agreement with literature data.[22]

V. Synthesis of DNA conjugated phosphine oxide D2.

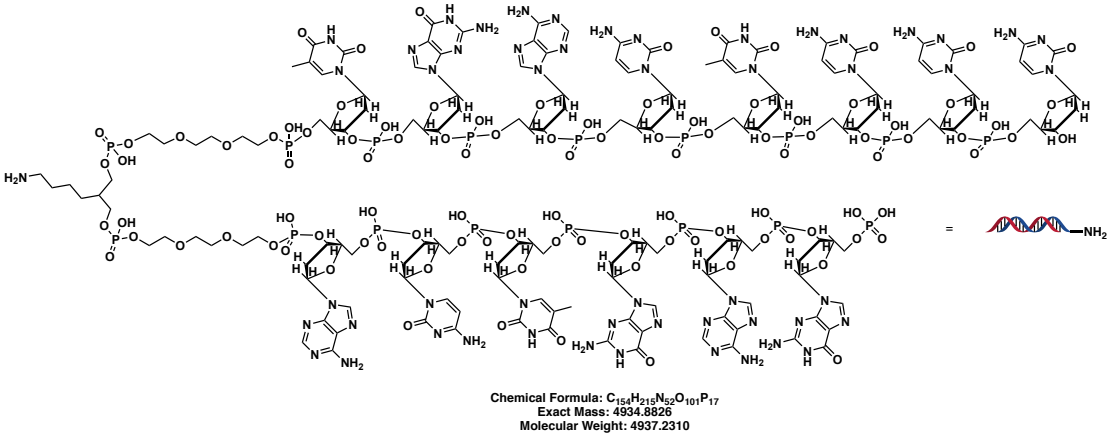


Figure 2. Structure of headpiece DNA (HP-DNA)

Synthesis of DNA conjugated aryl fluorosulfate D1:

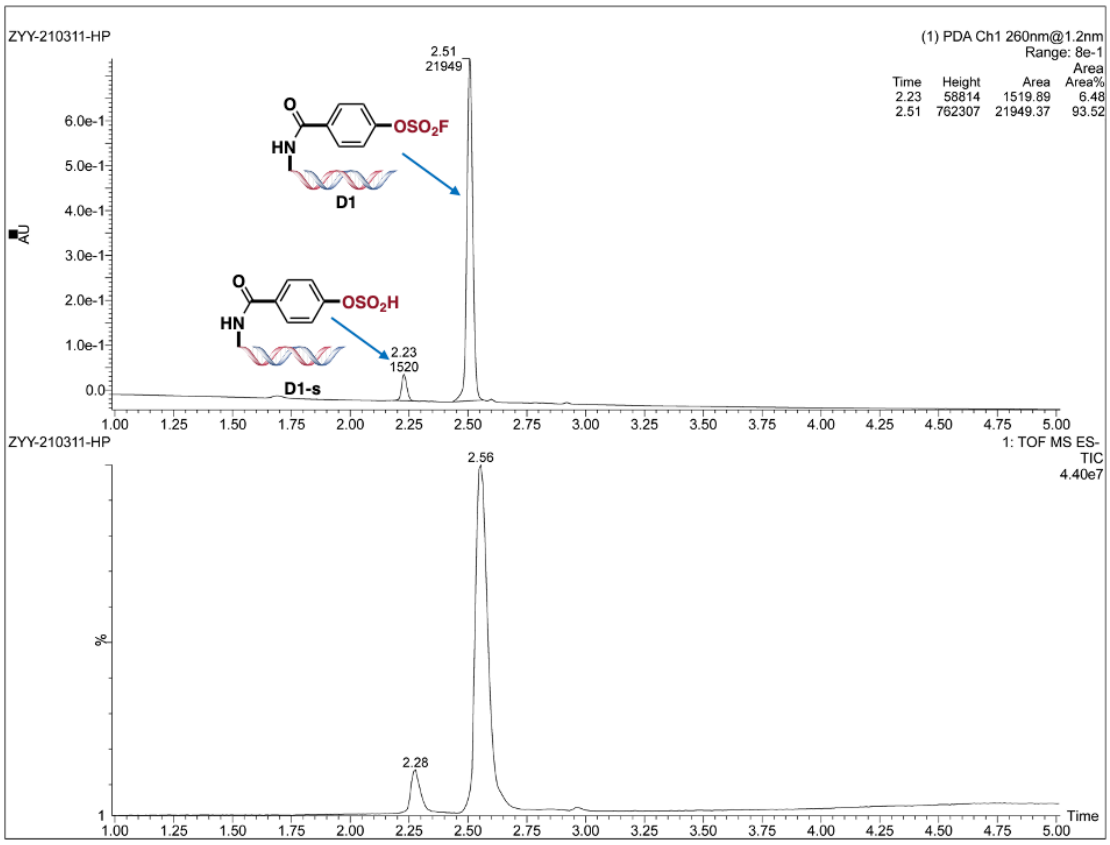
To a solution of DNA headpiece (100 nmol, 1 mM in water) in borate buffer 300 μL (250 mM, pH = 9.4), was added a mixture of DMA solution of HATU (100 μL, 200 m M in DMA), DIPEA (100 μL, 400 mM in DMA) and acid (100 μL, 200 mM in DMA). The resultant mixture was vortexed and incubated at 25 °C for 8 hours. Add 5 M NaCl solution (10% by volume) and cold ethanol (2.5 times by volume, ethanol stored at -20 °C) to the resultant supernatant. The mixture was vortexed and incubated at -80 °C for at least 30 minutes. The sample was centrifuged for 30 minutes at 4°C in a microcentrifuge at 12,000 rpm to remove the supernatant. The resulting pellet (precipitate) was re-dissolved in ddH_2O. Yield of **D1** 93.5%.

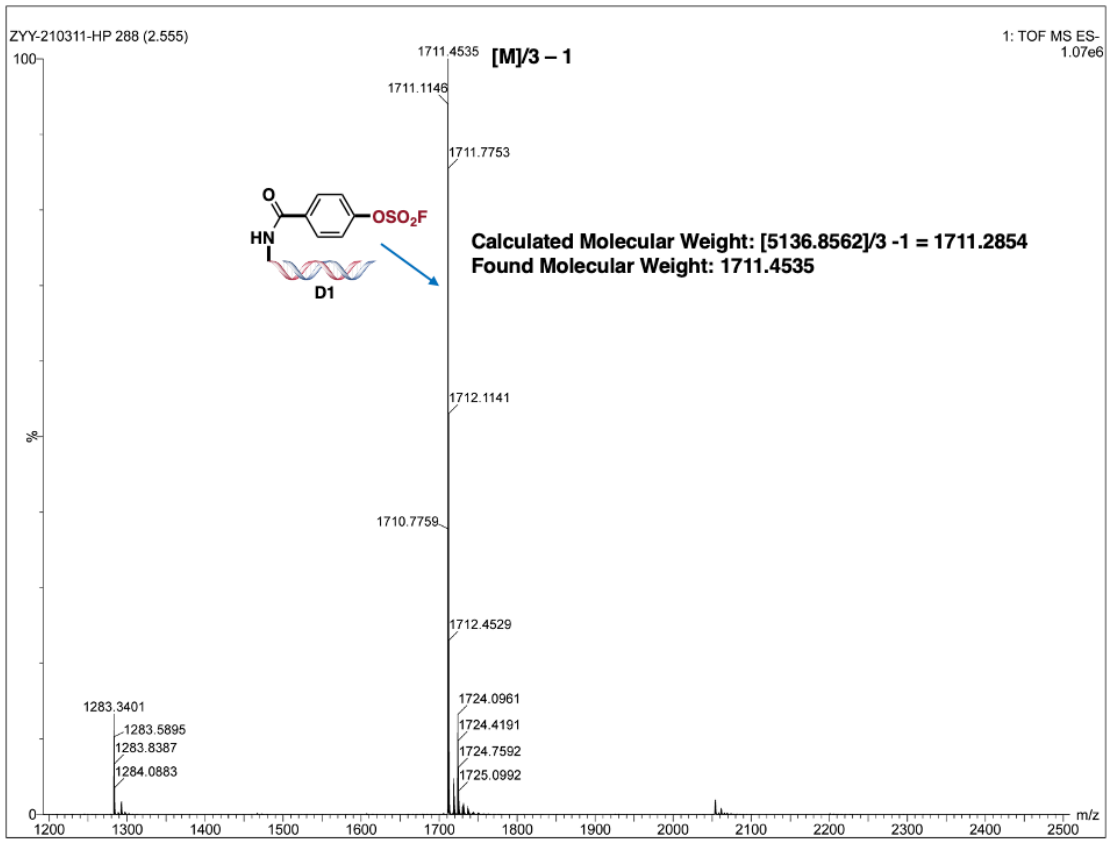
Synthesis of DNA conjugated phosphine oxide D2:

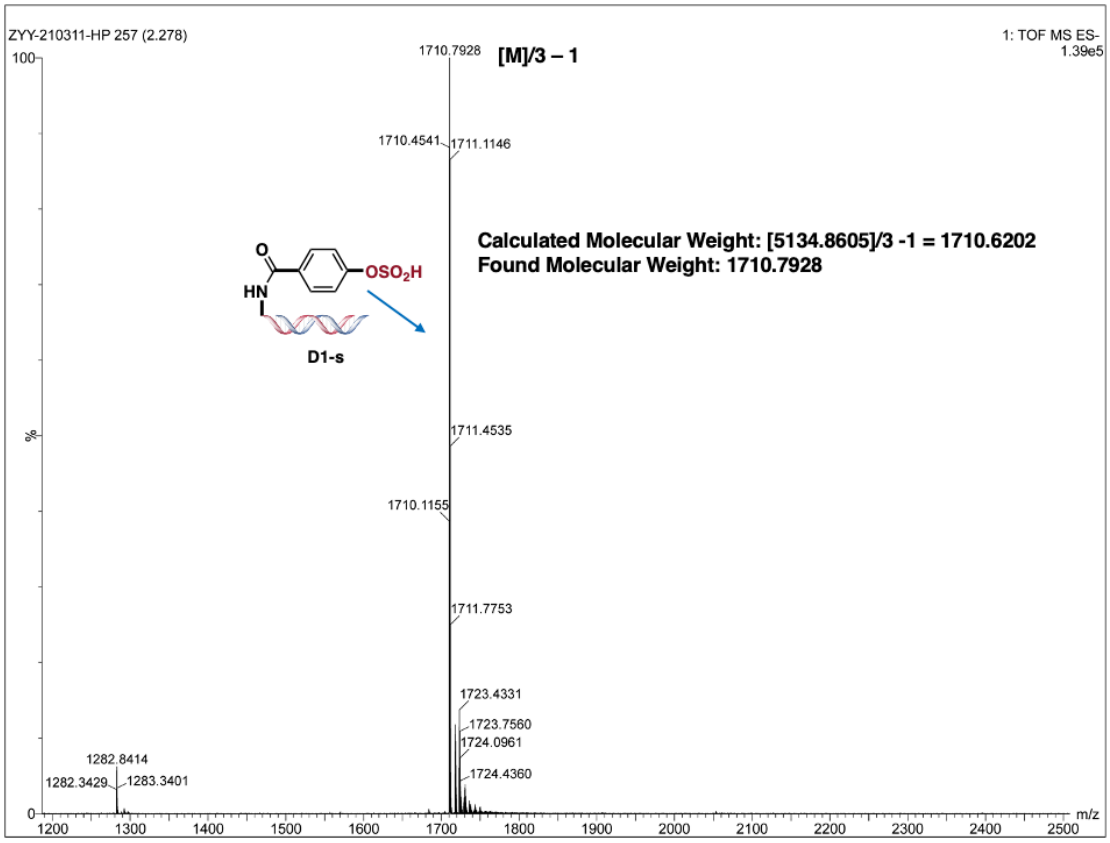
To the DNA conjugated aryl fluorosulfate **D1** (5 nmol, 5 μL, 1 mM in water), was added 500 equiv. of phosphines oxide (5 μL, 500 mM in DMF) followed by 500 equiv. of DIPEA (5 μL, 500 M in DMF), 20 equiv. of $Pd(OAc)_2$ (5 μL, 20 mM in DMF), 40 equiv. of dppf (5 μL, 40 mM in DMF) and 75μL ddH_2O. The mixture was vortexed and incubated at 80 °C for 2 hours. After reaction, 30 equiv. of scavenger sodium diethyldithiocarbamic acid (compared with $Pd(OAc)_2$, 3 μL, 1 M in ddH_2O) were added to the mixture, and the reaction mixture was heated at 60 °C for 30 minutes. The mixture was centrifuged at 4 °C for 10 min at 12,000 rpm, and the resultant supernatant was collected. Add 5 M NaCl solution (10% by volume) and cold ethanol (2.5 times by volume, ethanol stored at -20 °C) to the resultant supernatant. The mixture was vortexed and incubated at -80 °C for at least 30 minutes. The sample was centrifuged for 30 minutes at 4°C in a microcentrifuge at 12,000 rpm to remove the supernatant. The resulting pellet (precipitate) was re-dissolved in ddH_2O (300 μL) for LC-MS detection.

Yield of D2: $78.1\% = \frac{\text{73.04\% UV (product)}}{\text{93.52\% UV (DNA starting material before reaction)}} \times 100\%$

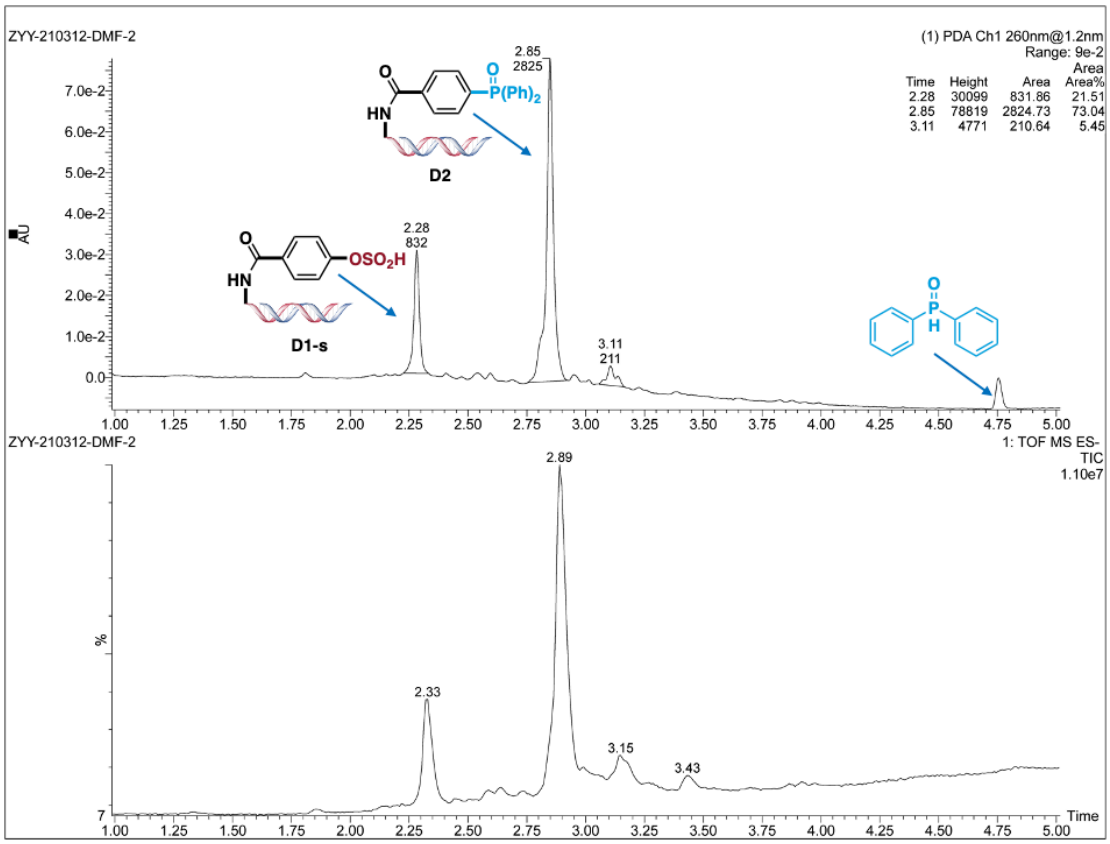
LC-MS analysis of D1

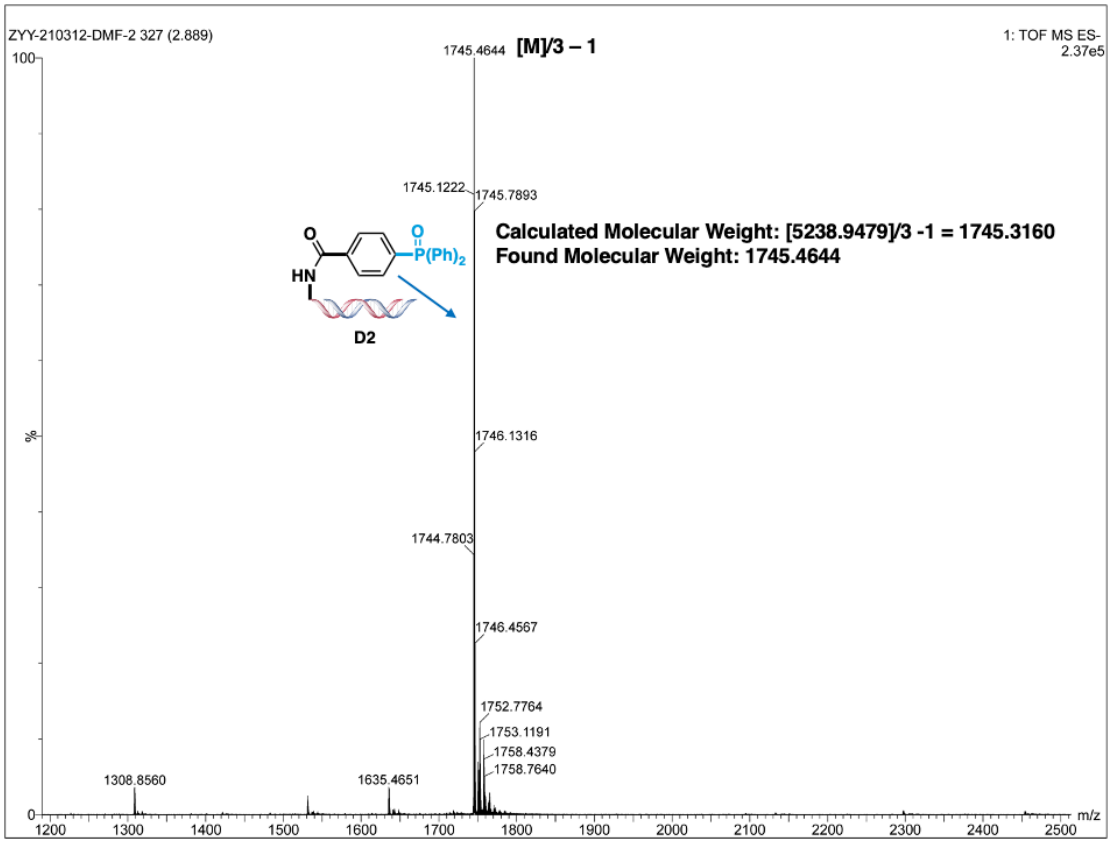


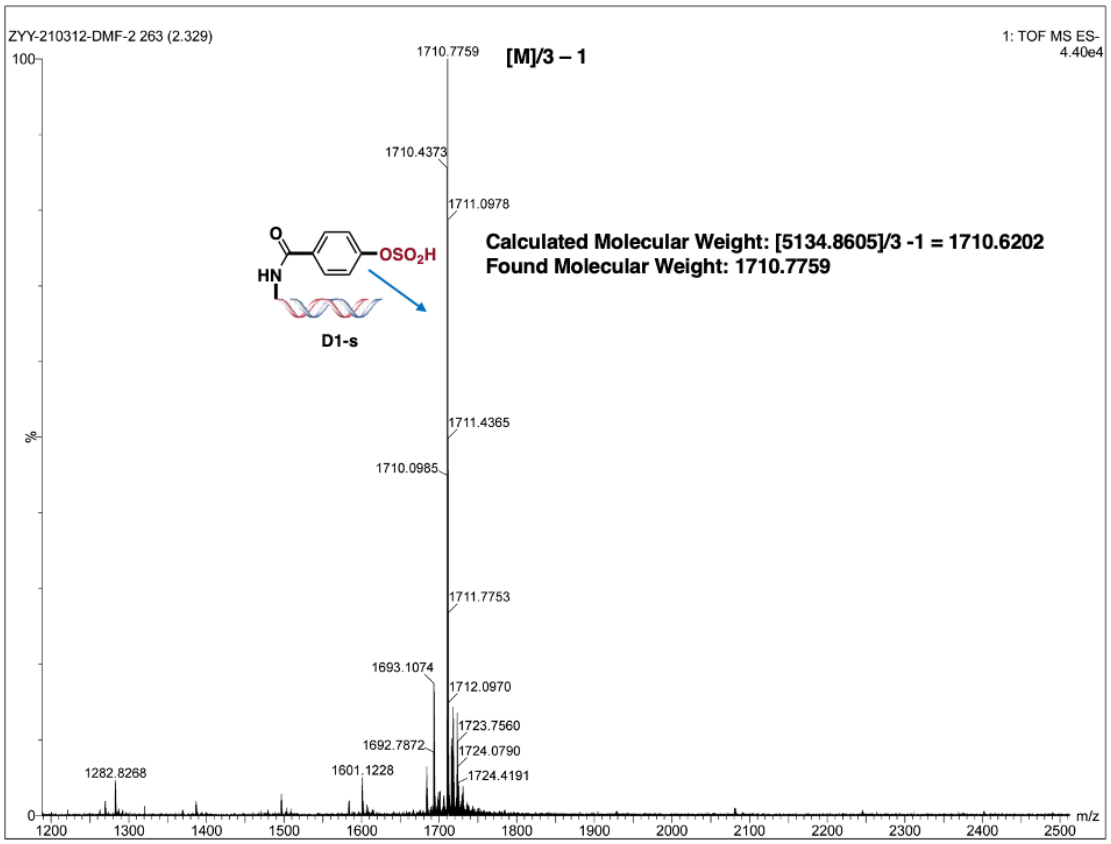




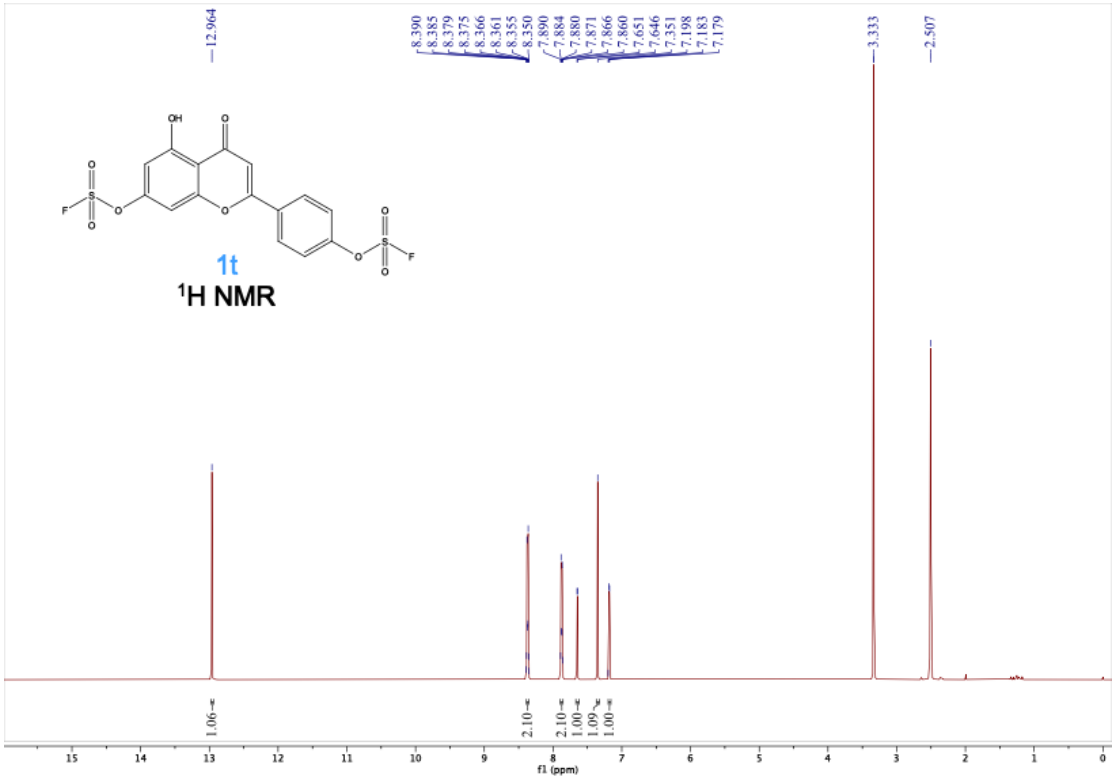
LC-MS analysis of D2

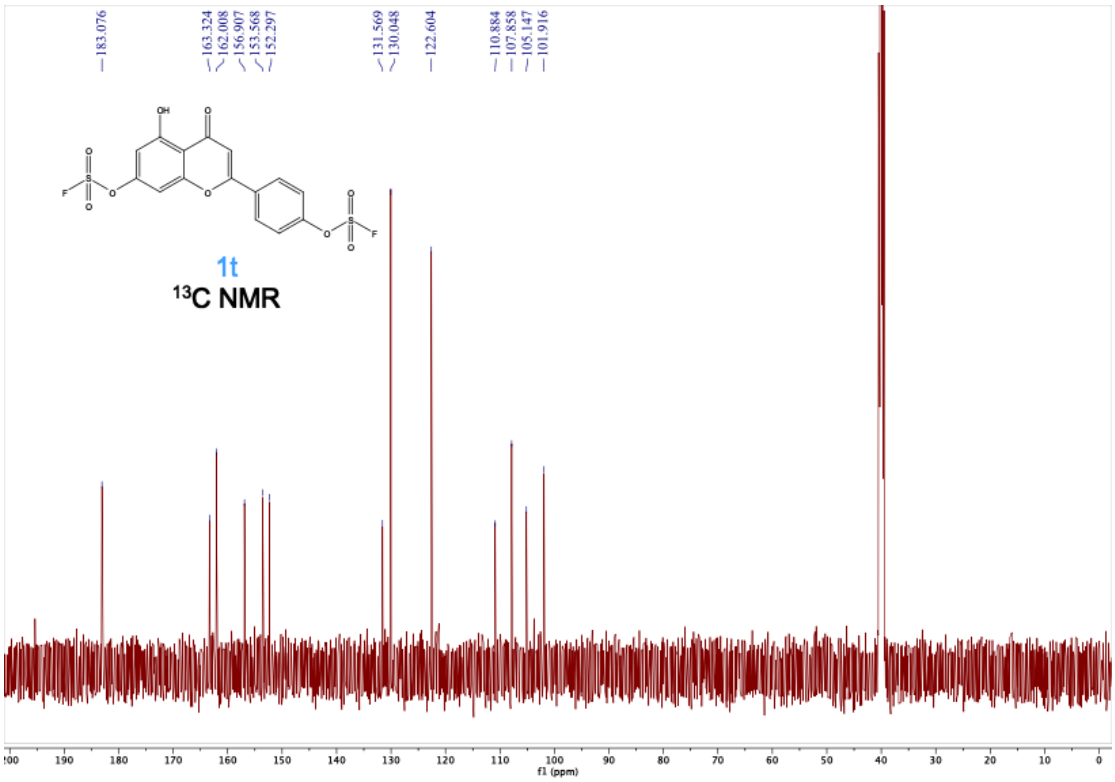


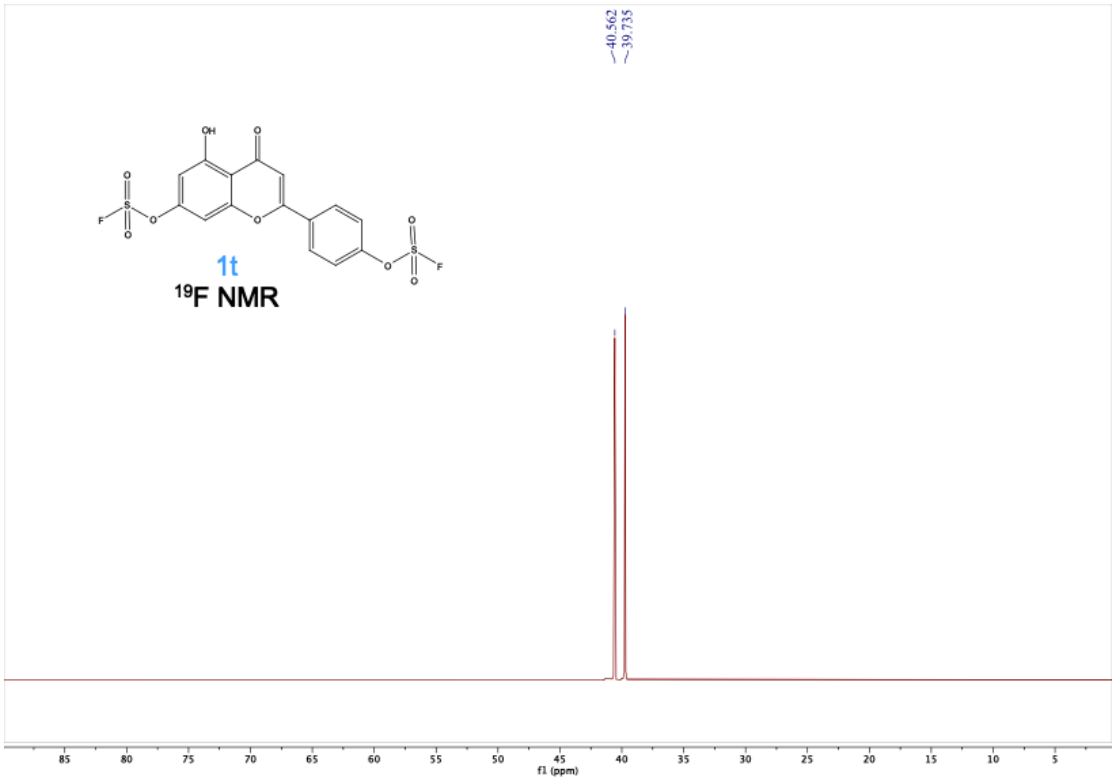

ZYY-210312-DMF-2 327 (2.889)
1: TOF MS ES-
2.37e5
[M]/3 – 1
1745.4644
1745.1222
1745.7893
Calculated Molecular Weight: [5238.9479]/3 -1 = 1745.3160
Found Molecular Weight: 1745.4644
D2
1746.1316
1744.7803
1746.4567
1752.7764
1753.1191
1758.4379
1758.7640
1308.8560
1635.4651
%
m/z

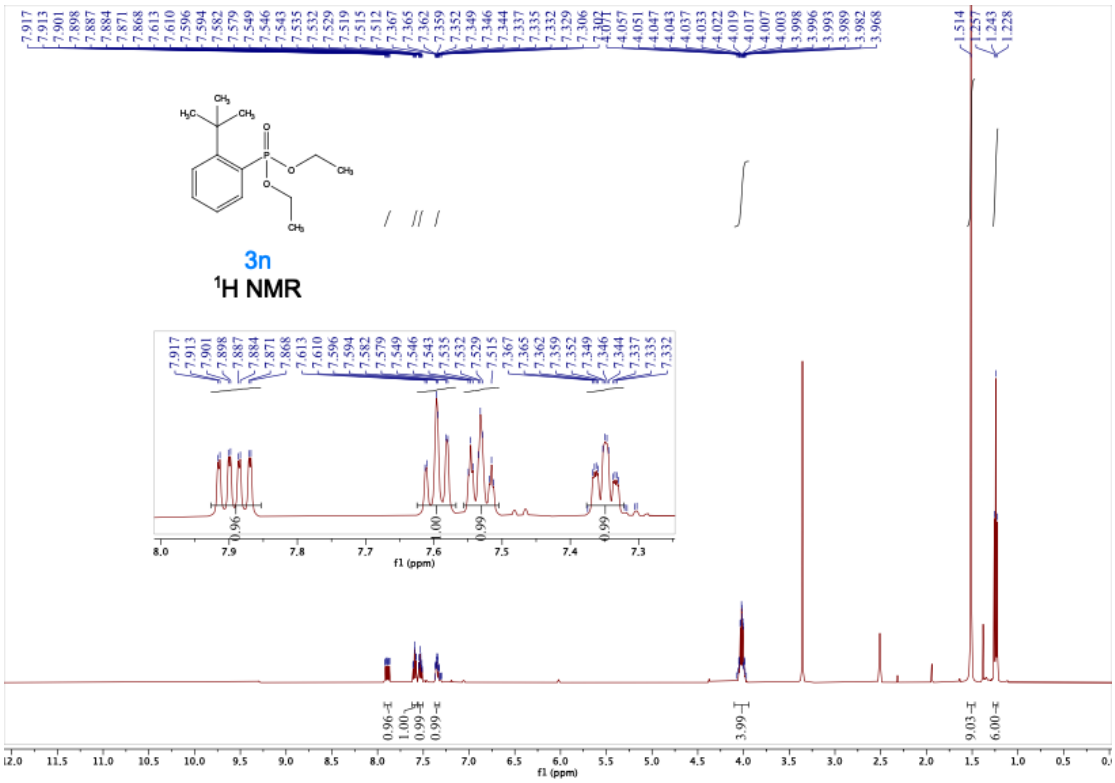

ZYY-210312-DMF-2 263 (2.329)
1: TOF MS ES-
4.40e4
[M]/3 – 1
1710.7759
1710.4373
1711.0978
Calculated Molecular Weight: [5134.8605]/3 -1 = 1710.6202
Found Molecular Weight: 1710.7759
D1-s
1711.4365
1710.0985
1711.7753
1693.1074
1712.0970
1723.7560
1692.7872
1724.0790
1724.4191
1282.8268
1601.1228
%
m/z

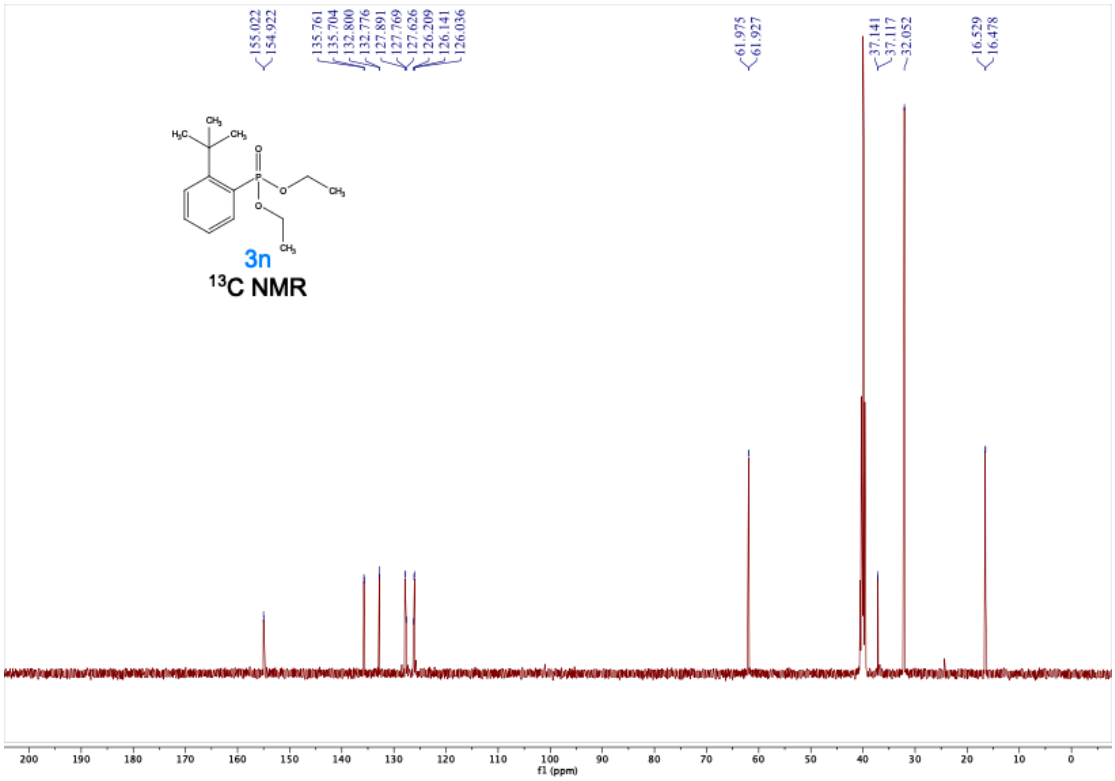
VI. Copies of ^{1}H NMR, ^{13}C NMR, ^{31}P NMR ^{19}F NMR Spectra

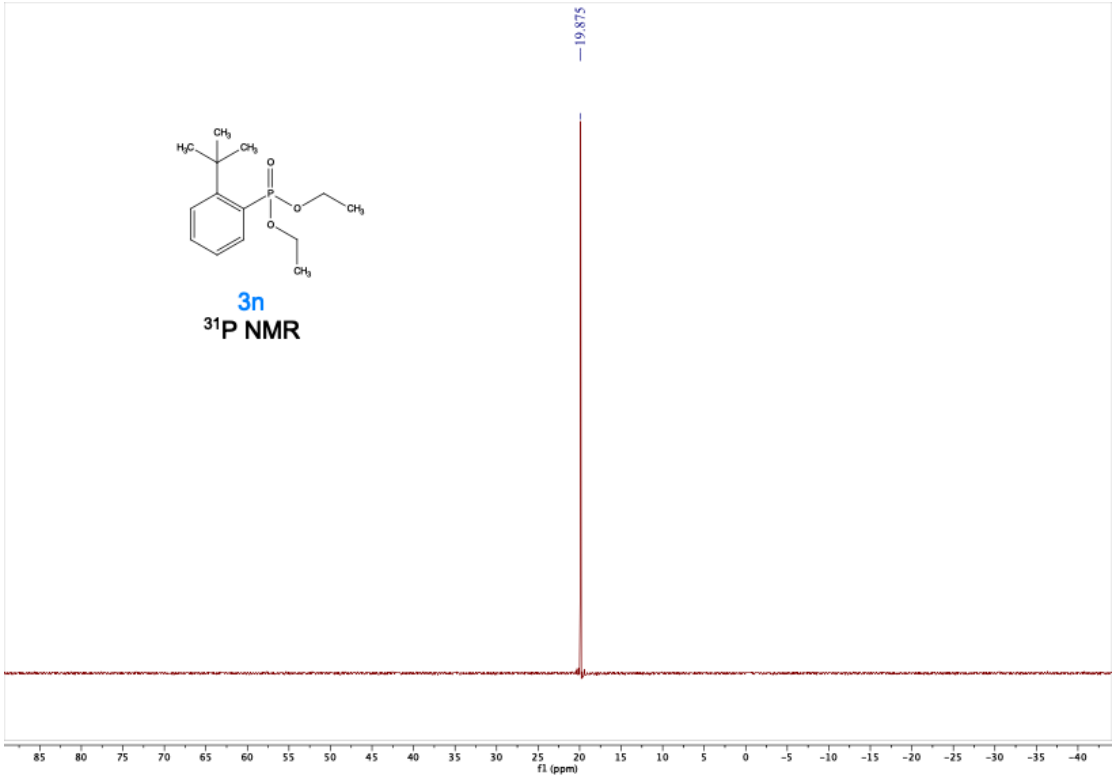


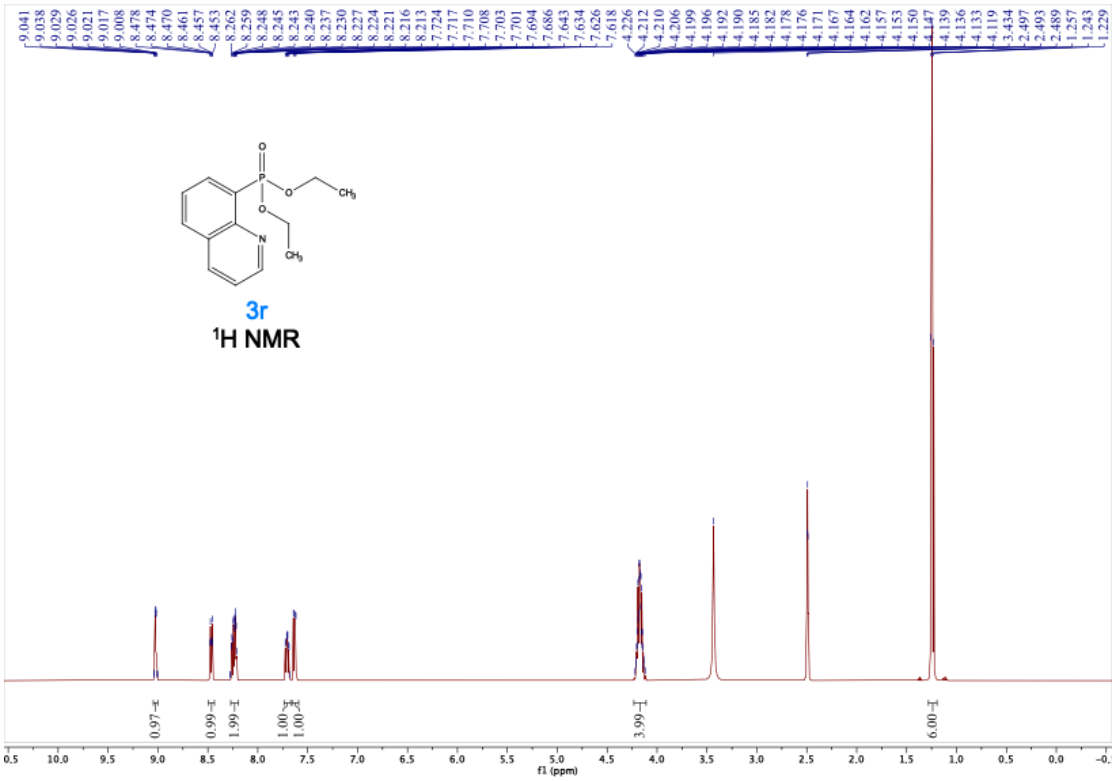


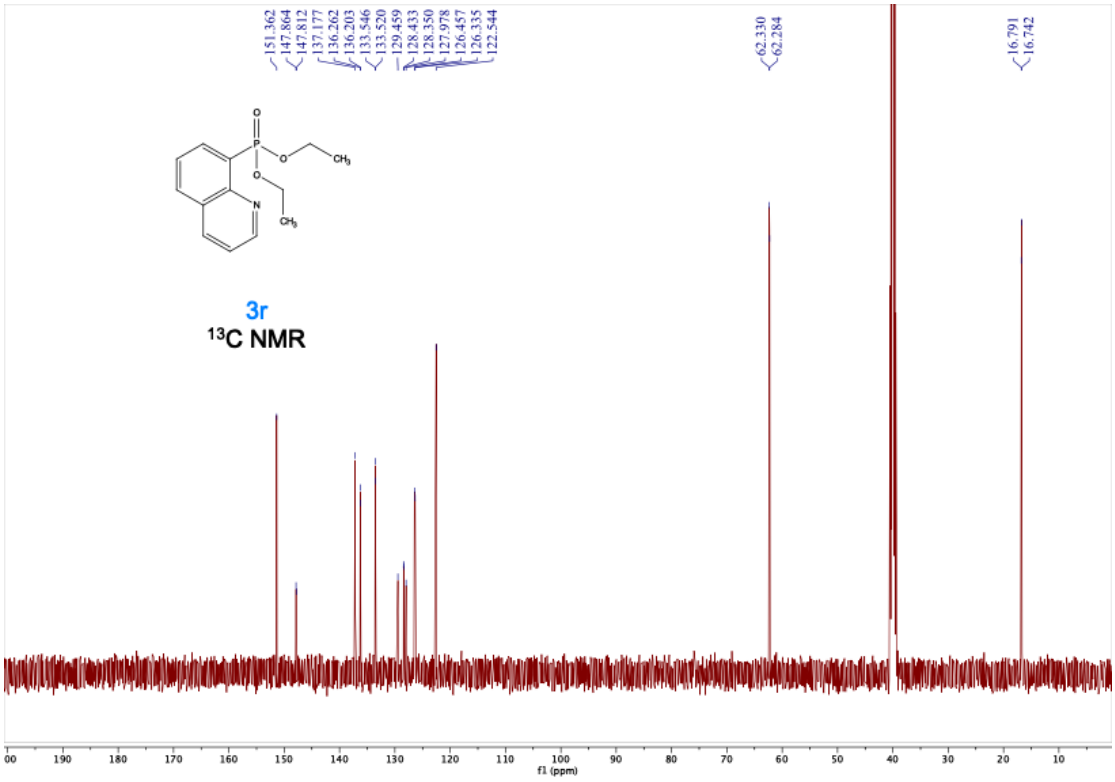

40.562
39.735
1t
19F NMR
f1 (ppm)

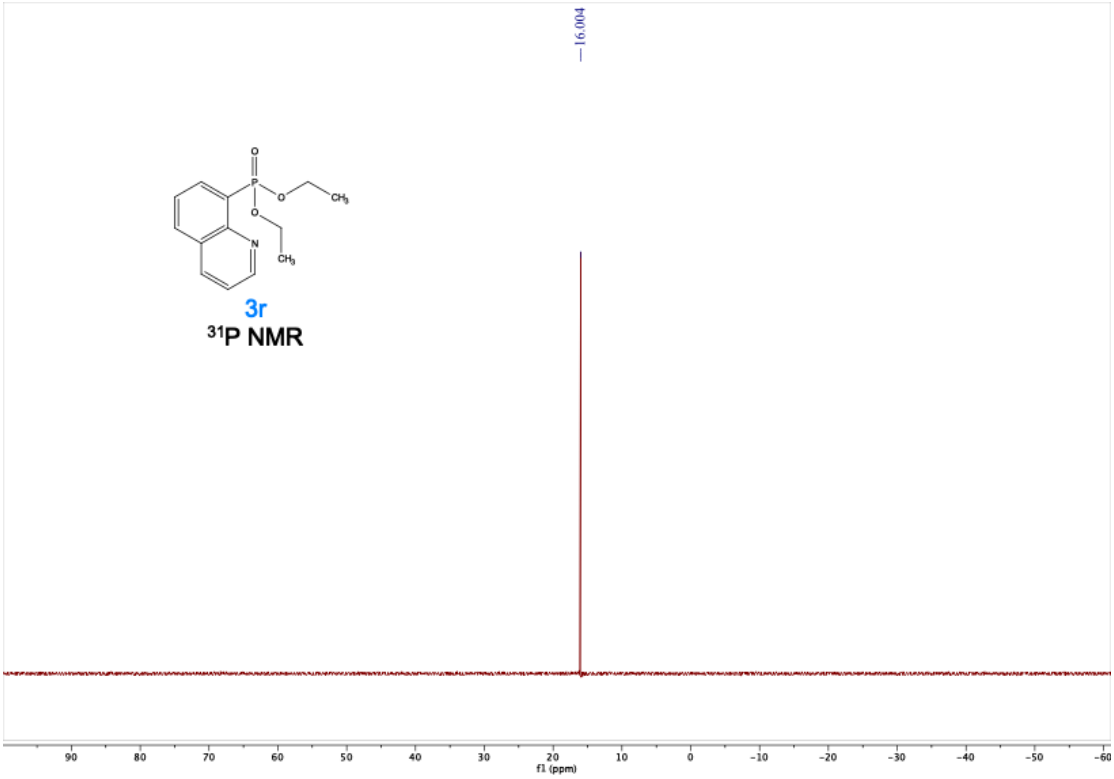

3n
1H NMR
f1 (ppm)


155.022
154.922
135.761
135.704
132.800
132.776
127.891
127.769
127.626
126.209
126.141
126.036
61.975
61.927
37.141
37.117
32.052
16.529
16.478
3n
13C NMR
f1 (ppm)


19.875
3n
31P NMR
f1 (ppm)

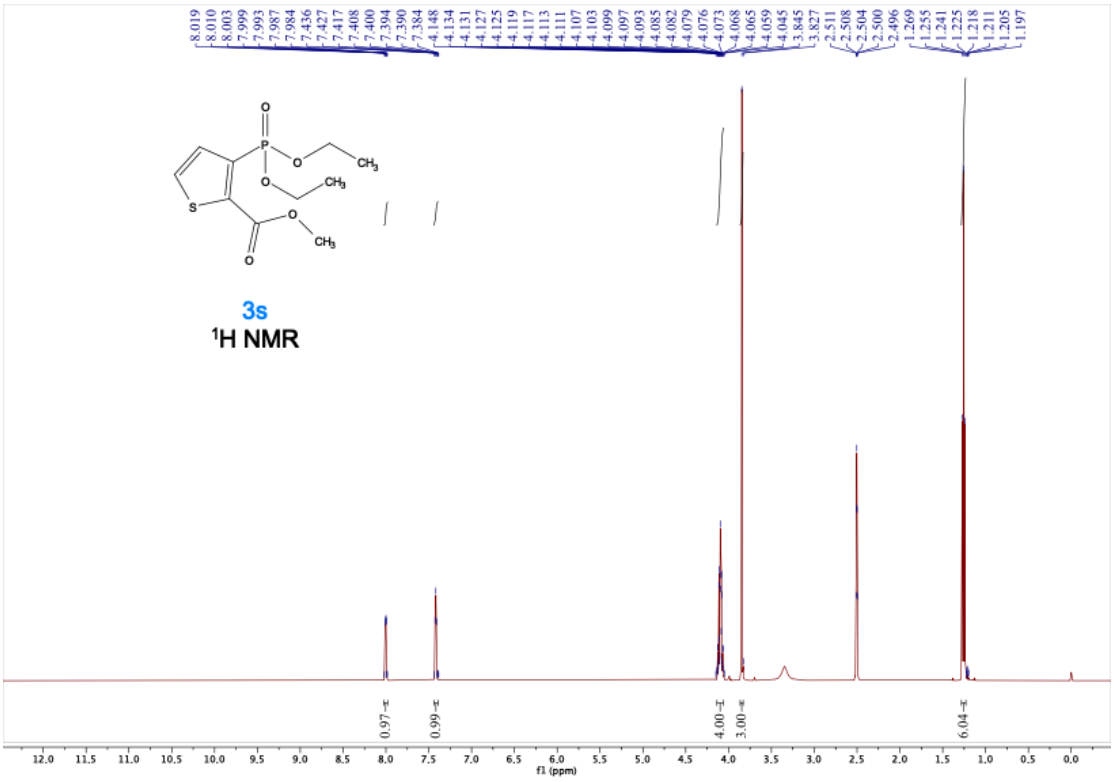

3r
1H NMR
f1 (ppm)


3r
13C NMR
f1 (ppm)



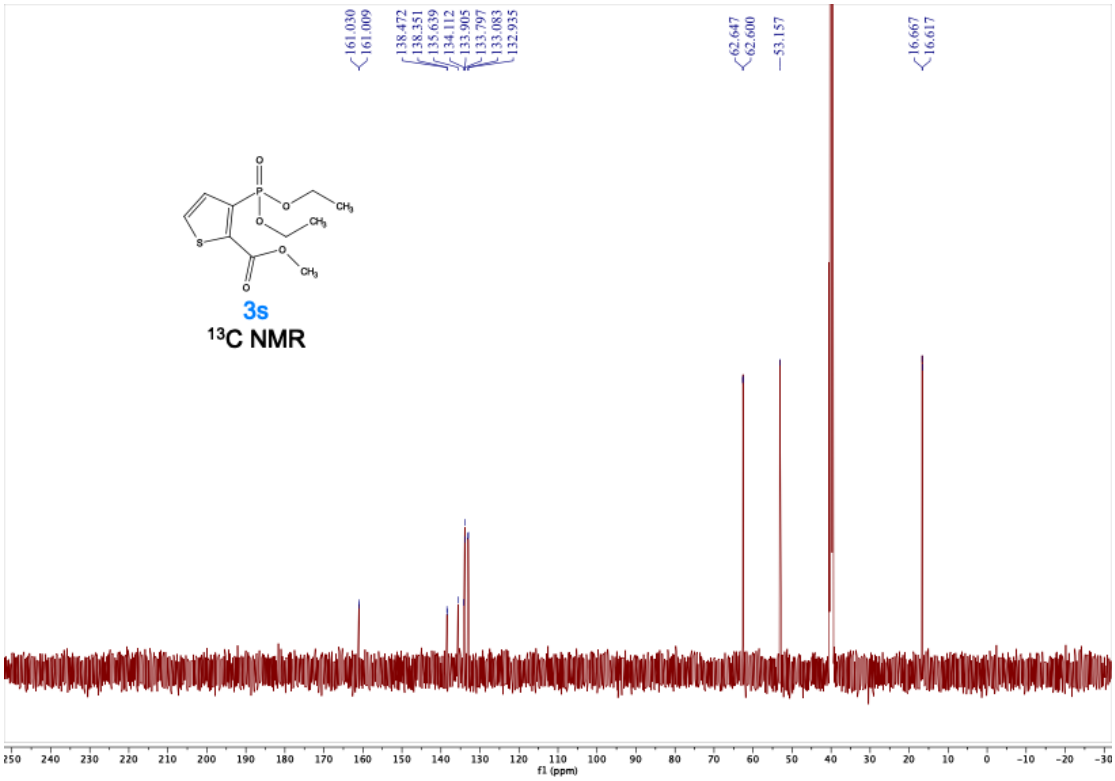
3r

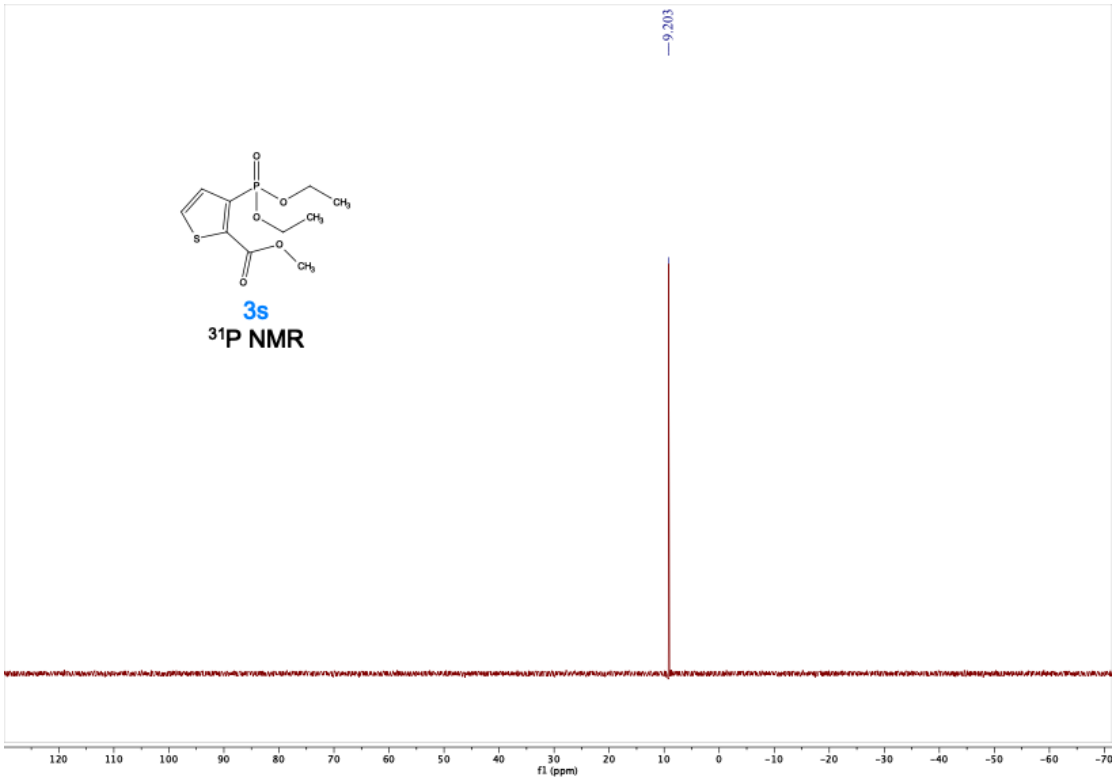
^{31}P NMR

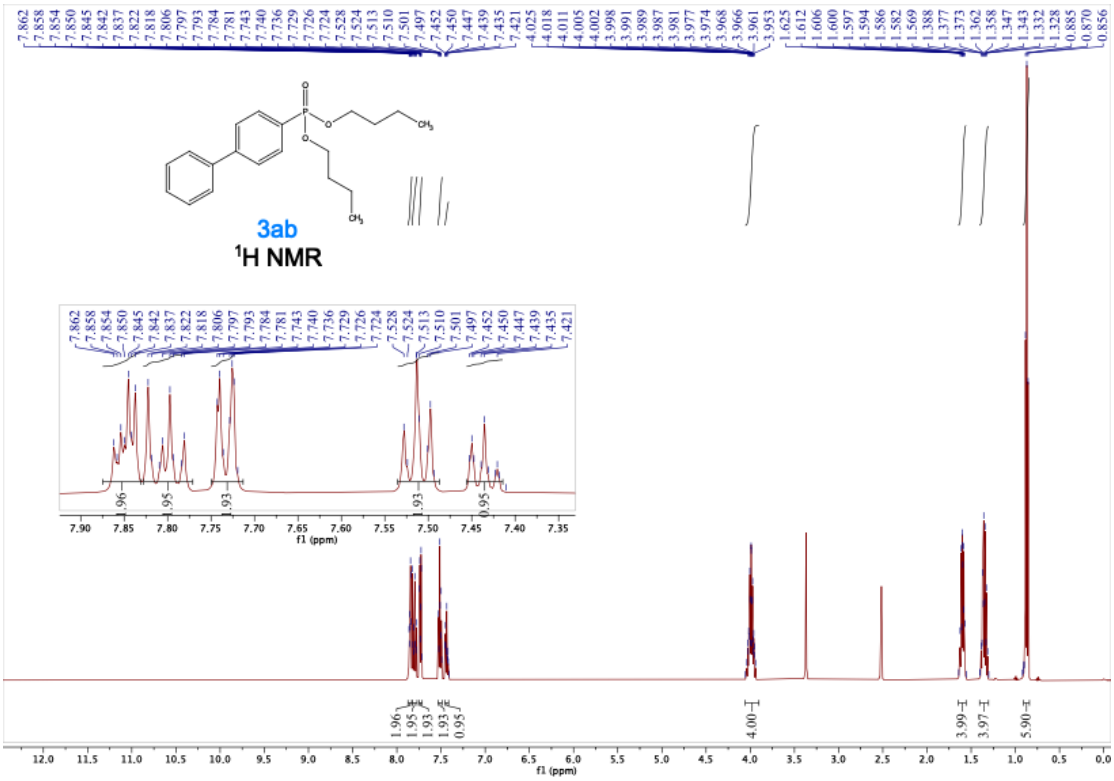


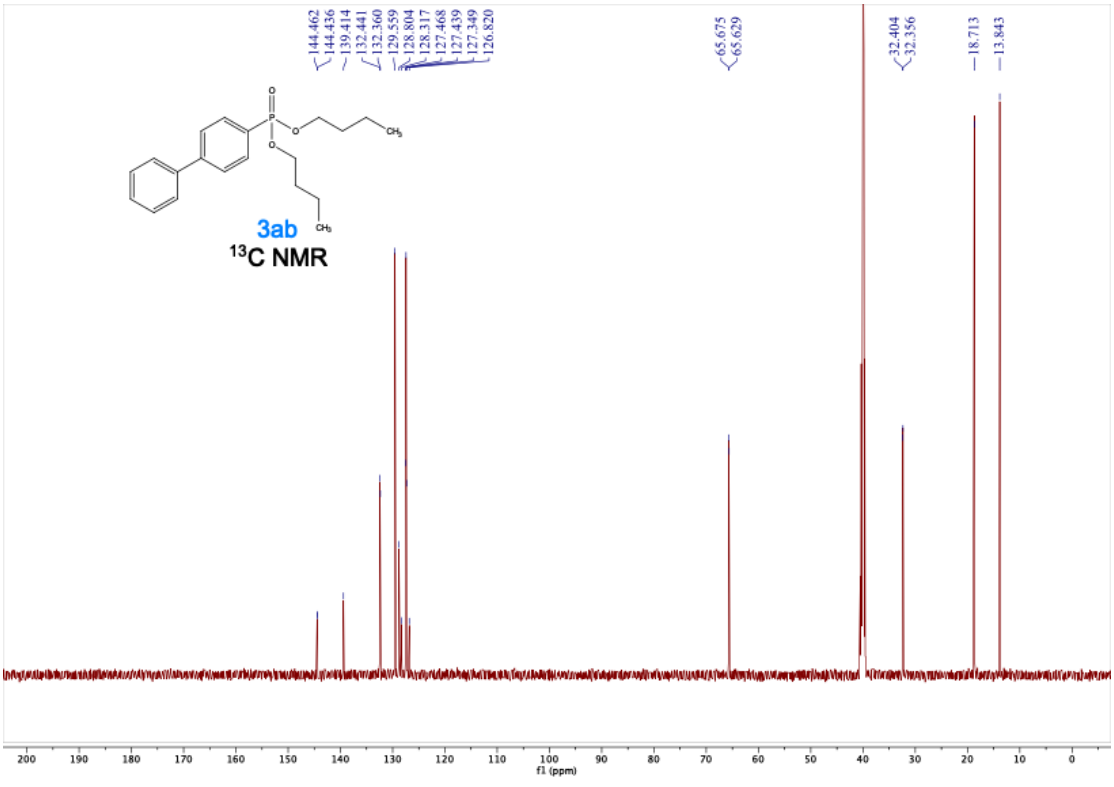
3s

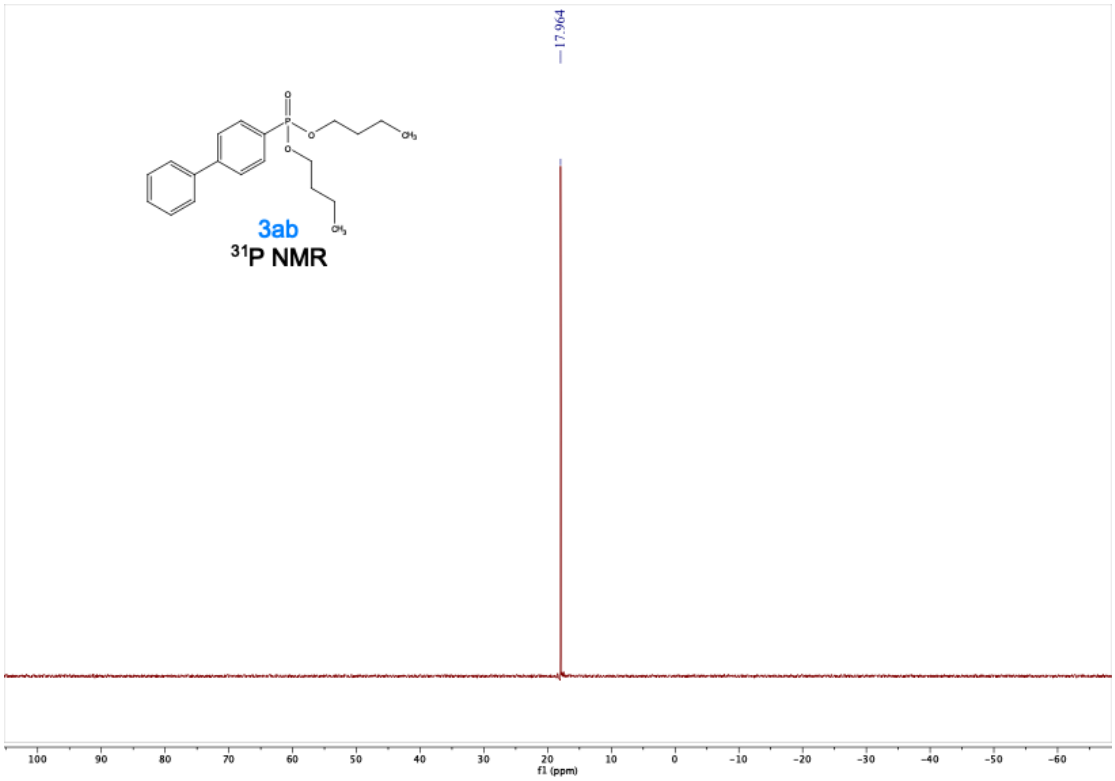
^{1}H NMR

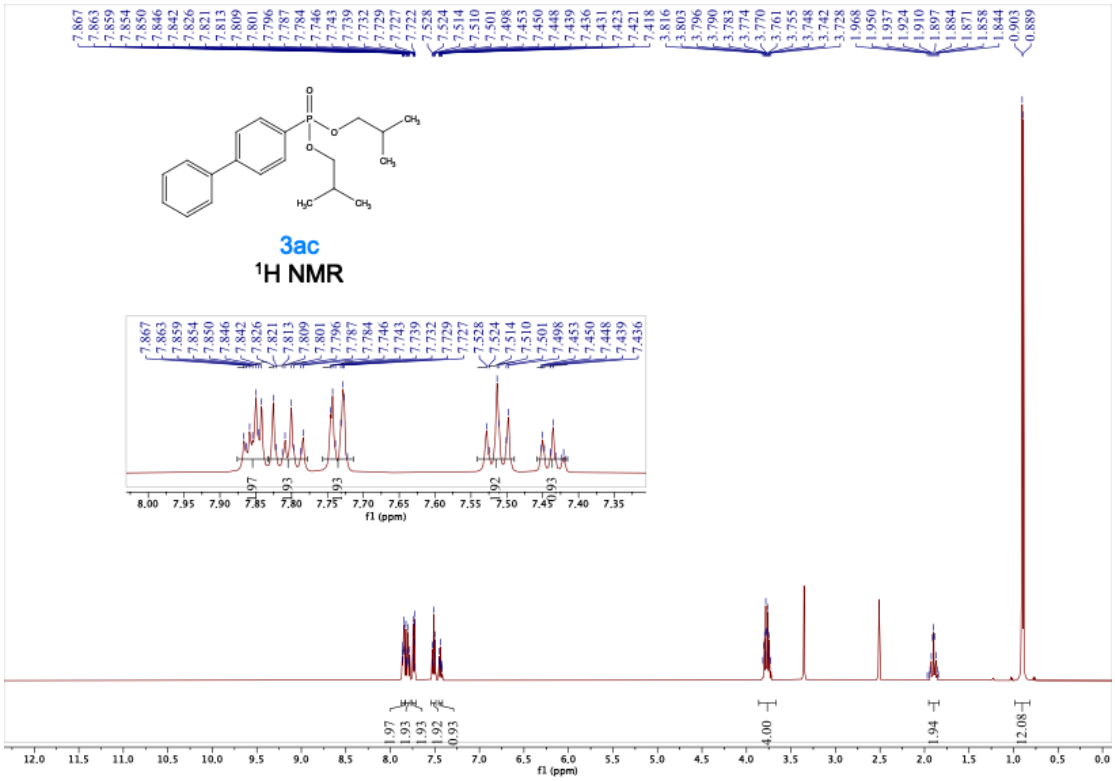

161.030
161.009
138.472
138.351
135.639
134.112
133.905
133.797
133.083
132.935
62.647
62.600
53.157
16.667
16.617
3s
13C NMR
f1 (ppm)

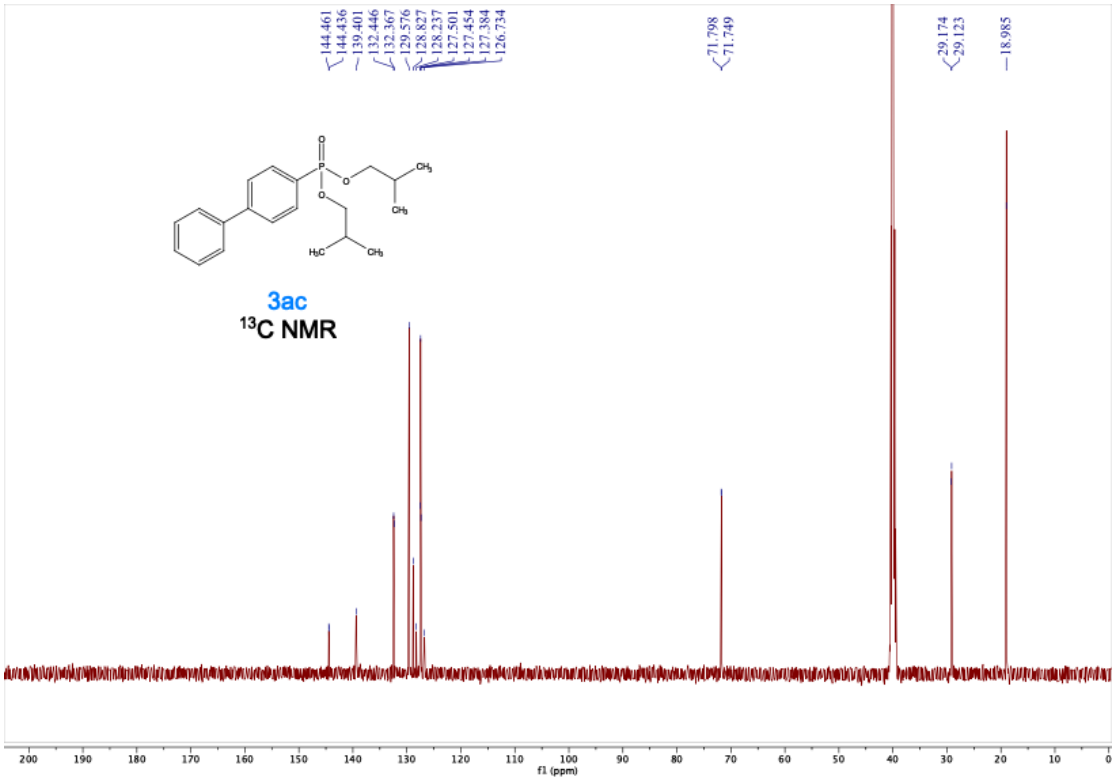

9.203
3s
31P NMR
f1 (ppm)

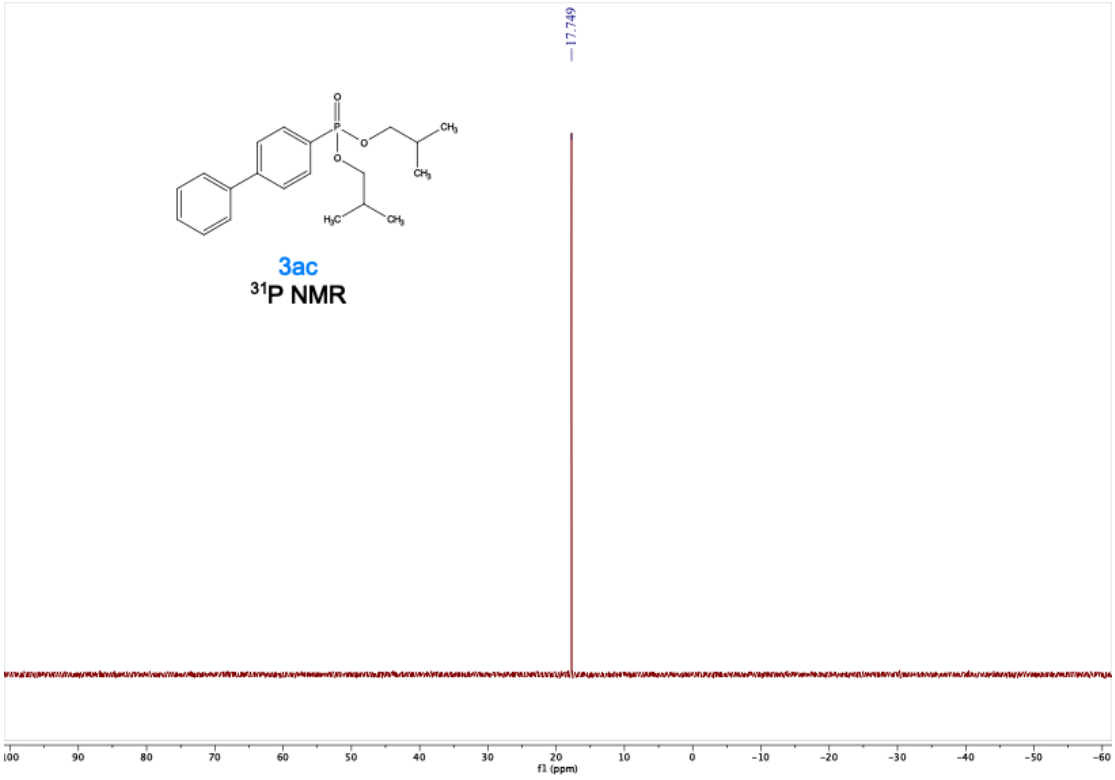

3ab
1H NMR
f1 (ppm)

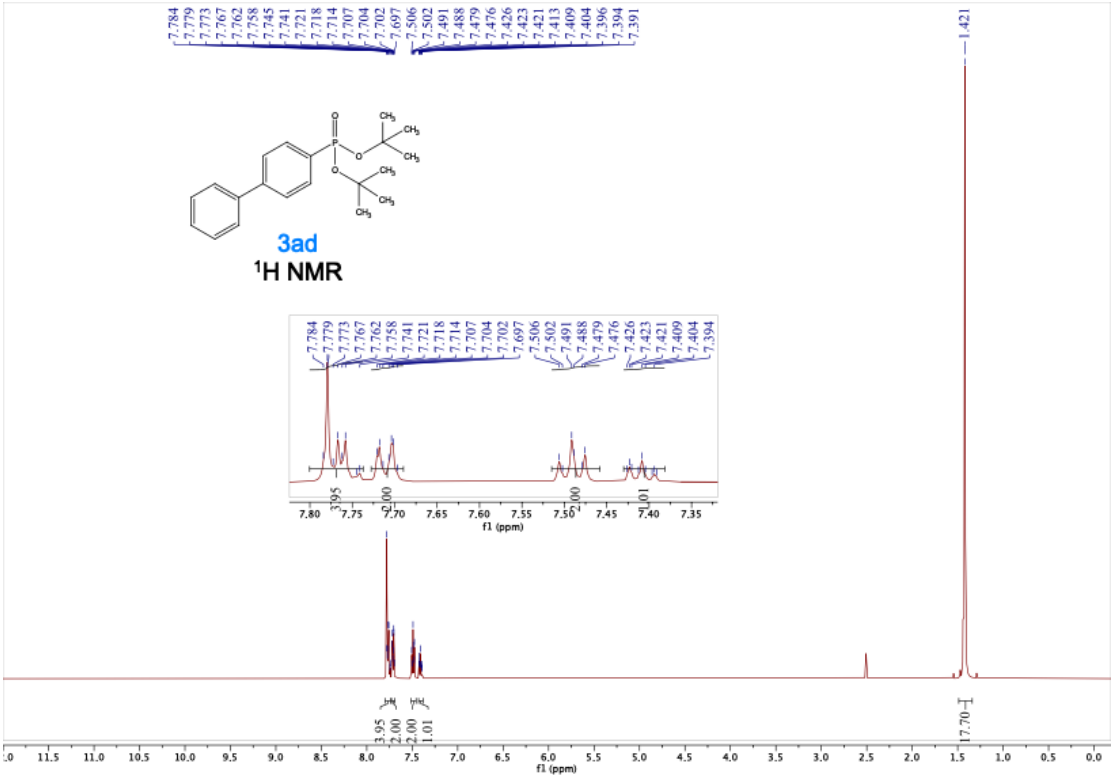

3ab
13C NMR
f1 (ppm)

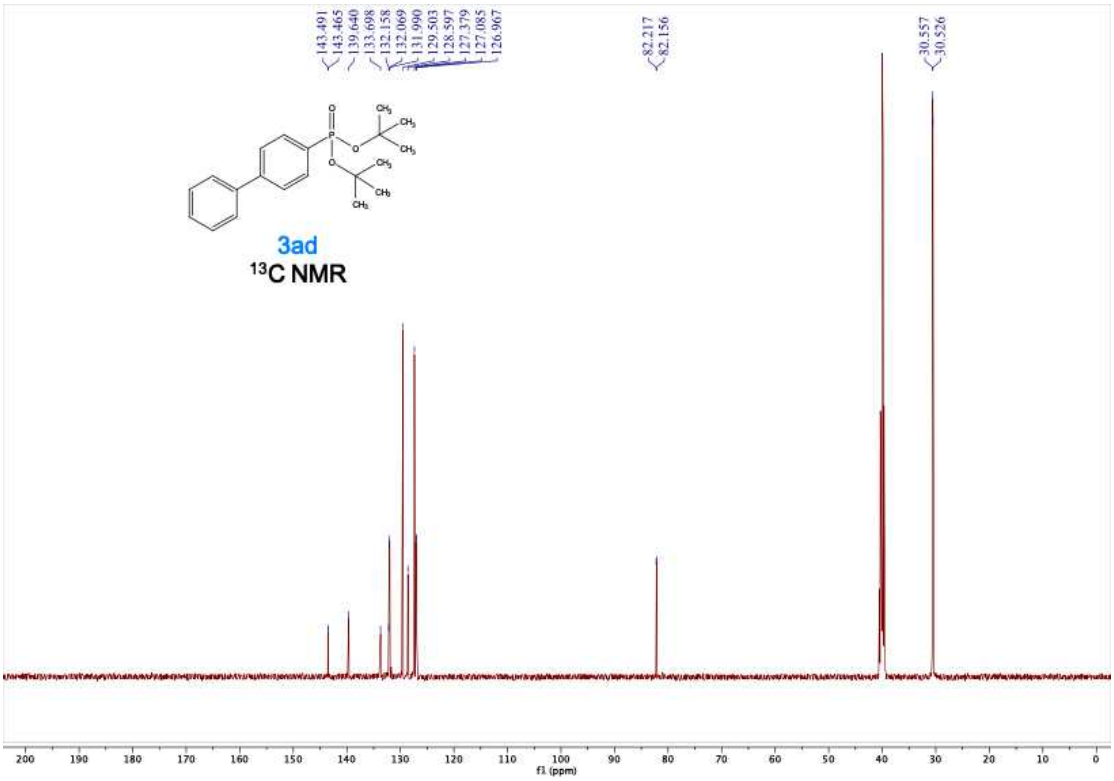

17.964
3ab
31P NMR
f1 (ppm)

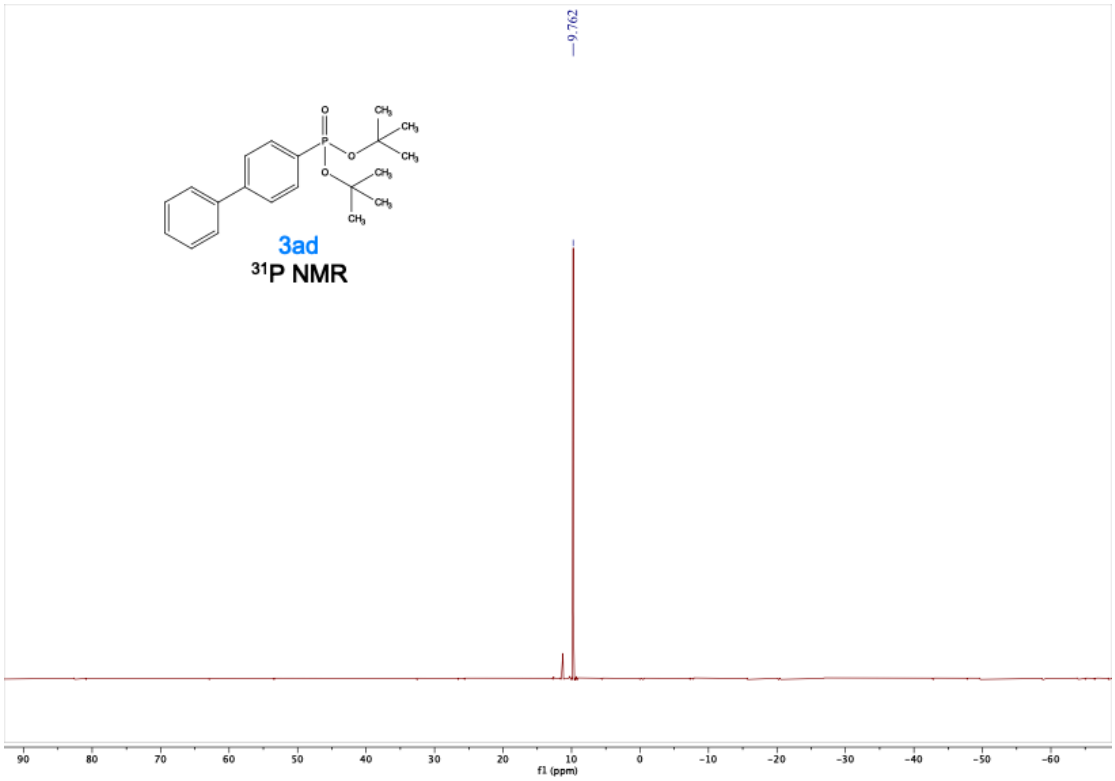

3ac
1H NMR
f1 (ppm)

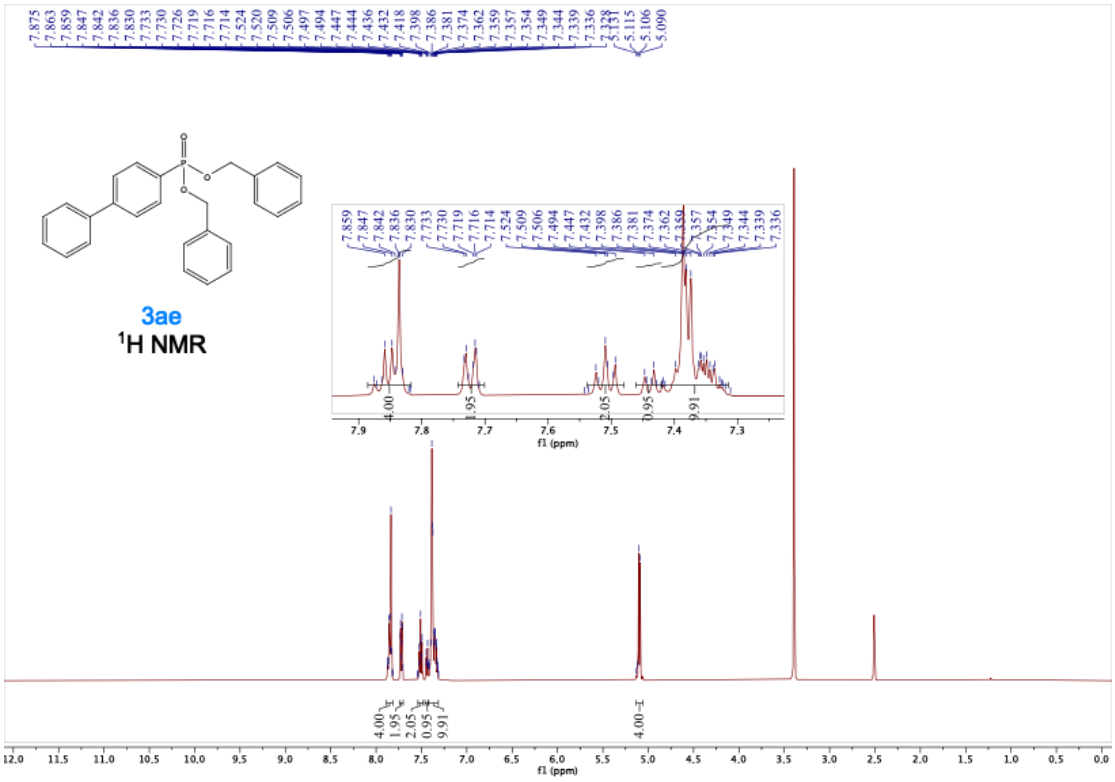

144.461
144.436
139.401
132.446
132.367
129.576
128.827
128.237
127.501
127.454
127.384
126.734
71.798
71.749
29.174
29.123
18.985
3ac
13C NMR
f1 (ppm)

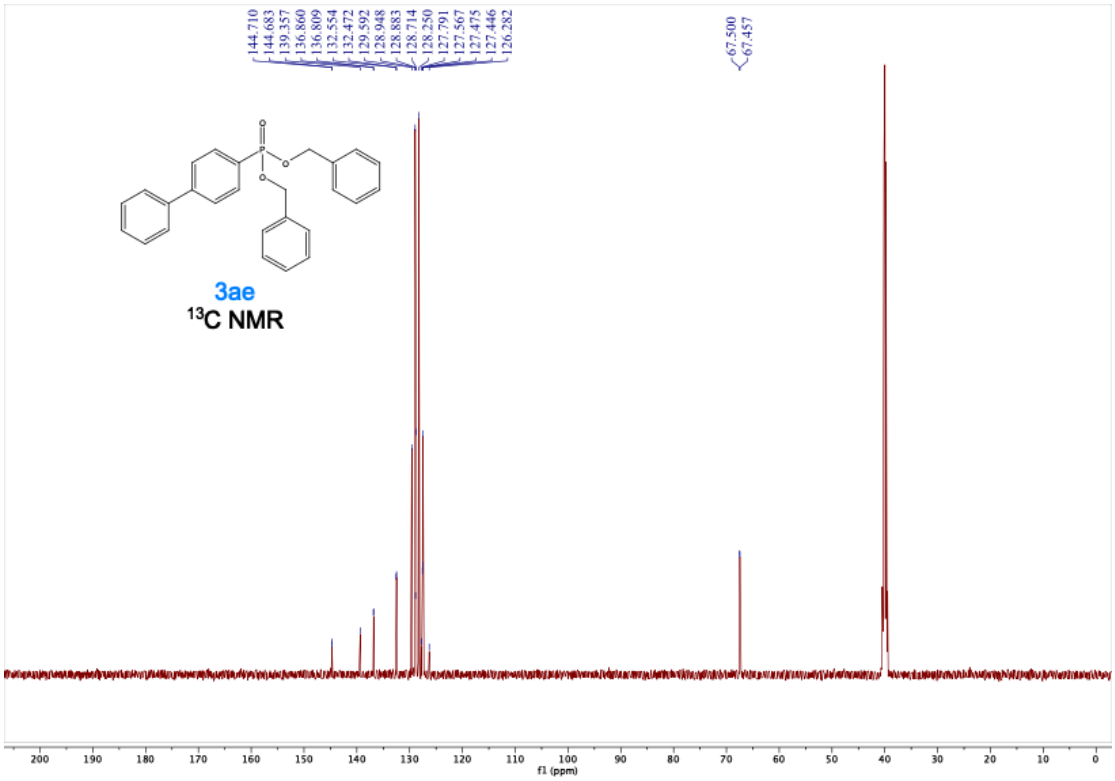

17.749
3ac
31P NMR
f1 (ppm)

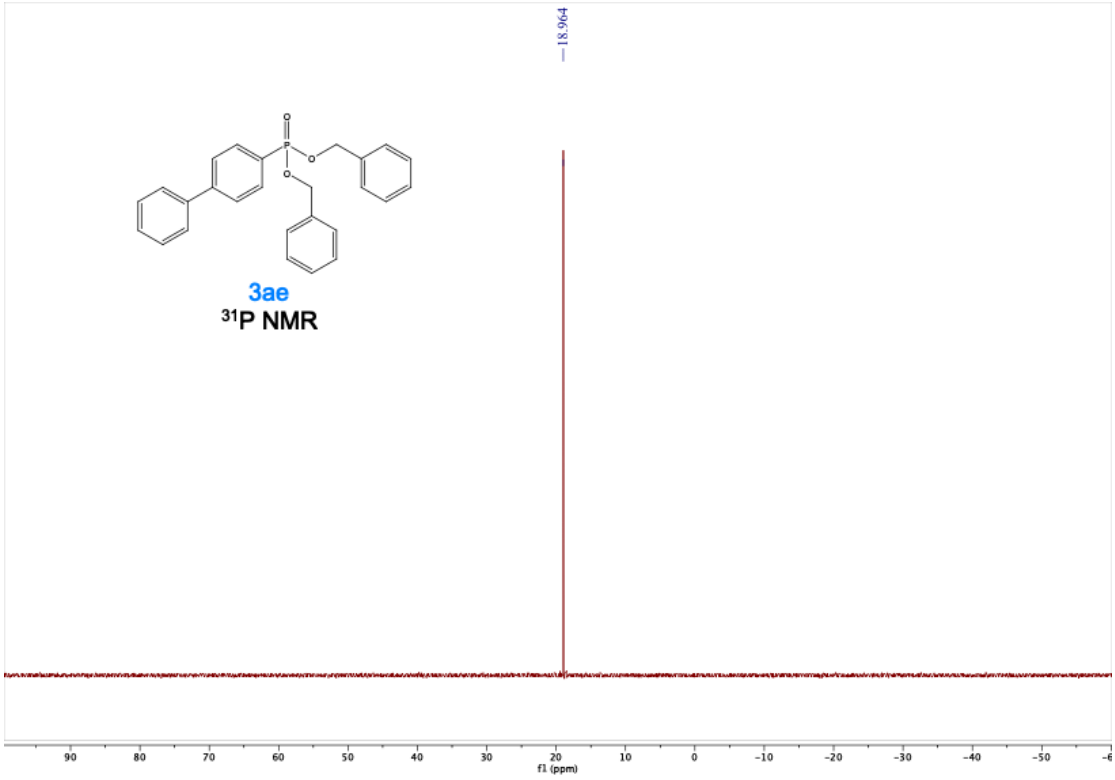

3ad
1H NMR

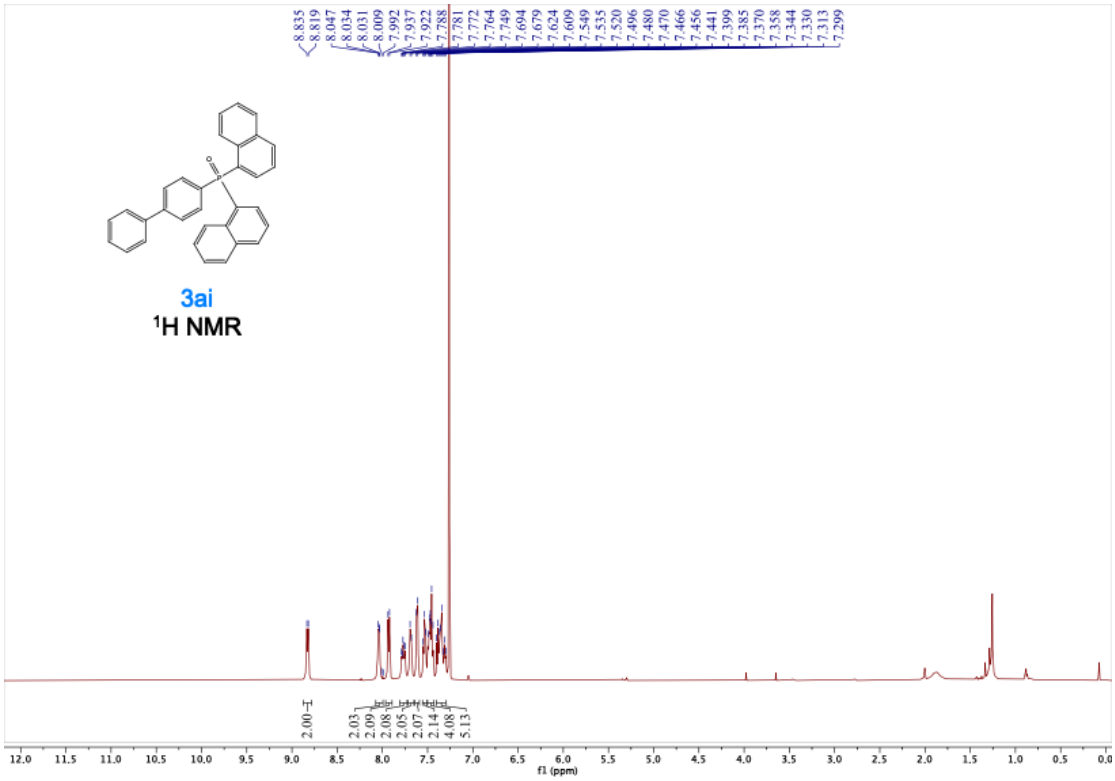

3ad
13C NMR

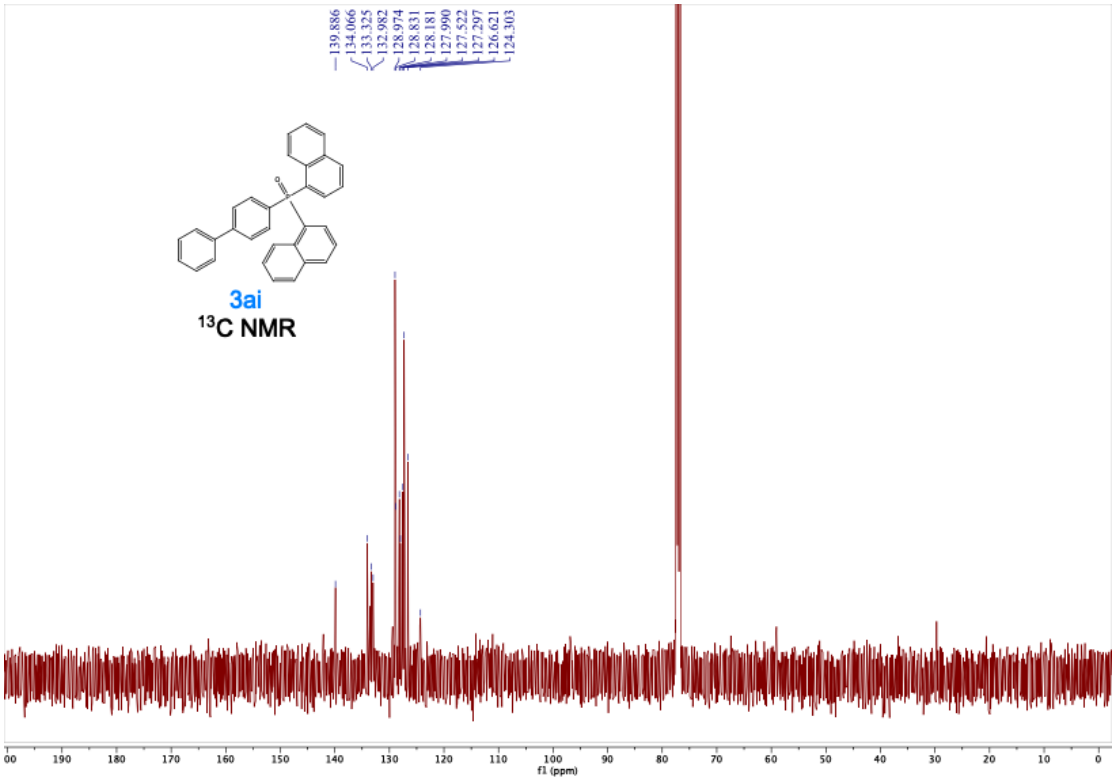

9.762
3ad
31P NMR
f1 (ppm)

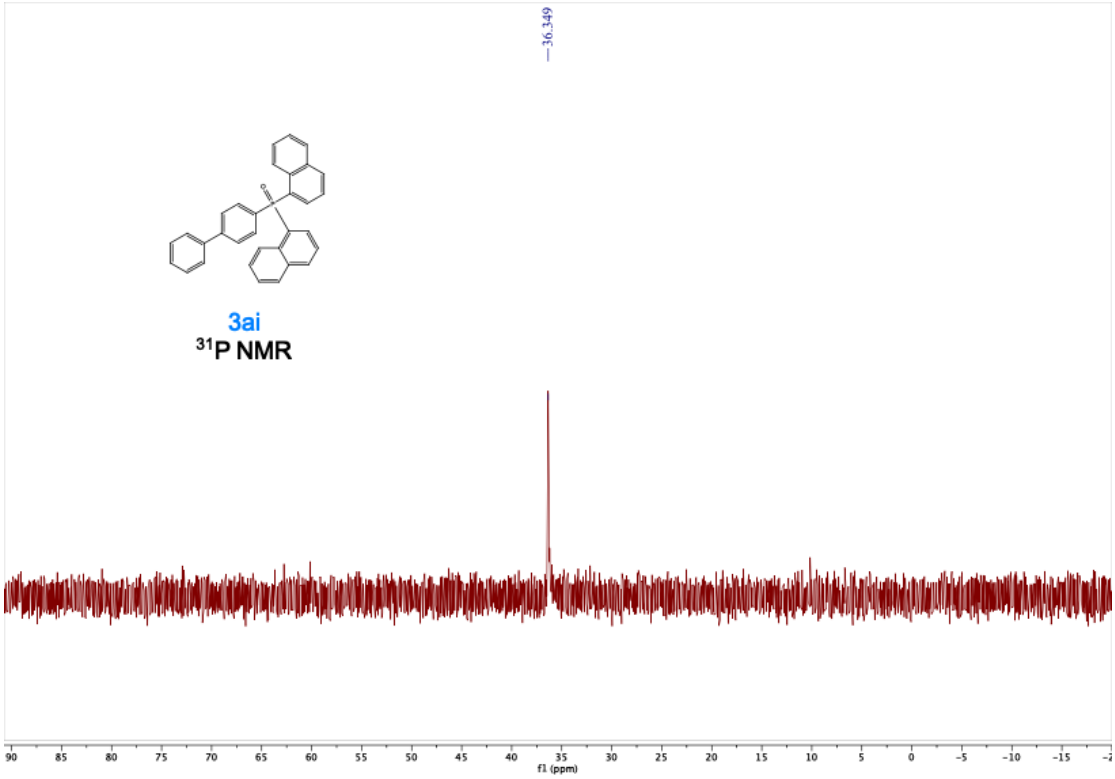

3ae
1H NMR
f1 (ppm)

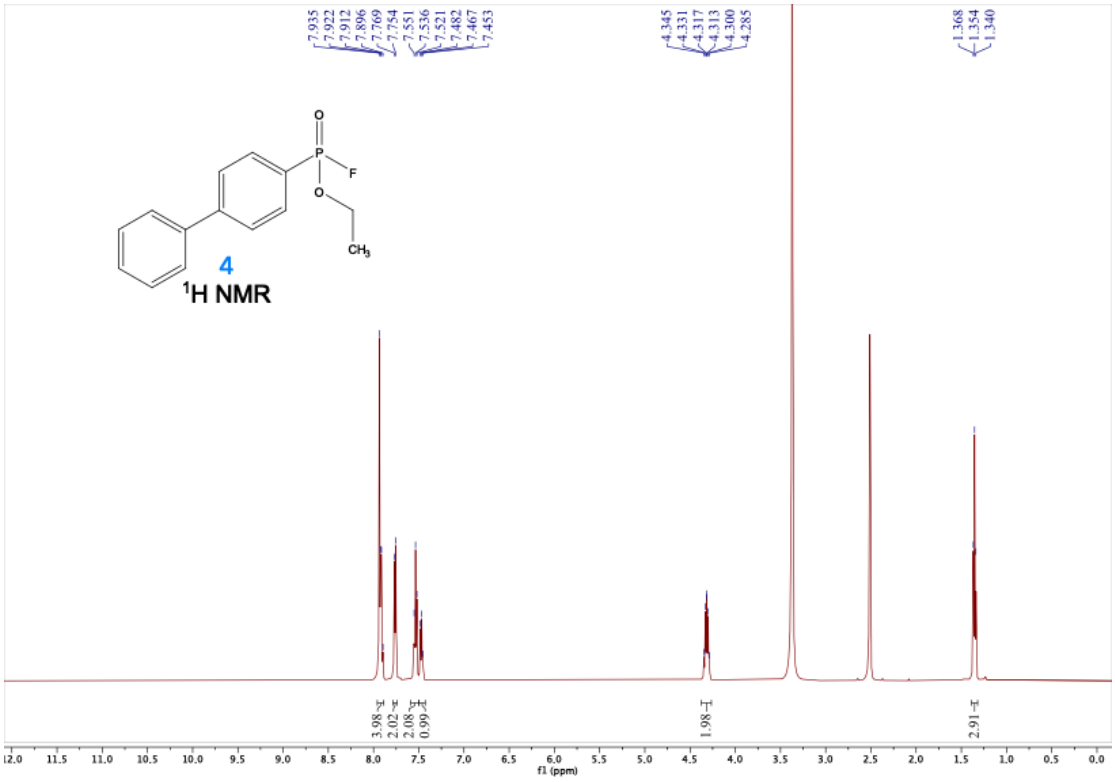

144.710
144.683
139.357
136.860
136.809
132.554
132.472
129.592
128.948
128.883
128.714
128.250
127.791
127.567
127.475
127.446
126.282
67.500
67.457
3ae
13C NMR
f1 (ppm)

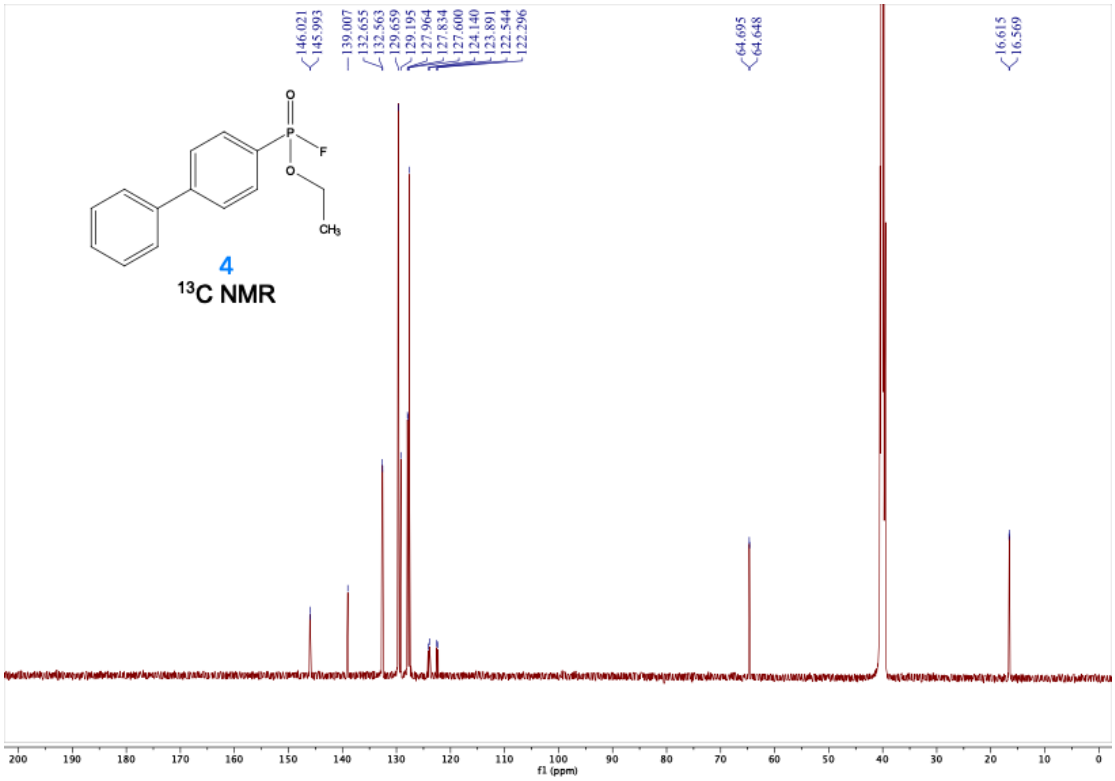

18.964
3ae
31P NMR
f1 (ppm)


3ai
1H NMR
f1 (ppm)


3ai
13C NMR
f1 (ppm)


36.349
3ai
31P NMR
f1 (ppm)


7.935
7.922
7.912
7.896
7.769
7.754
7.551
7.536
7.521
7.482
7.467
7.453
4.345
4.331
4.317
4.313
4.300
4.285
1.368
1.354
1.340
O
P
F
O
CH3
4
1H NMR
3.98
2.02
2.08
0.99
1.98
2.91
f1 (ppm)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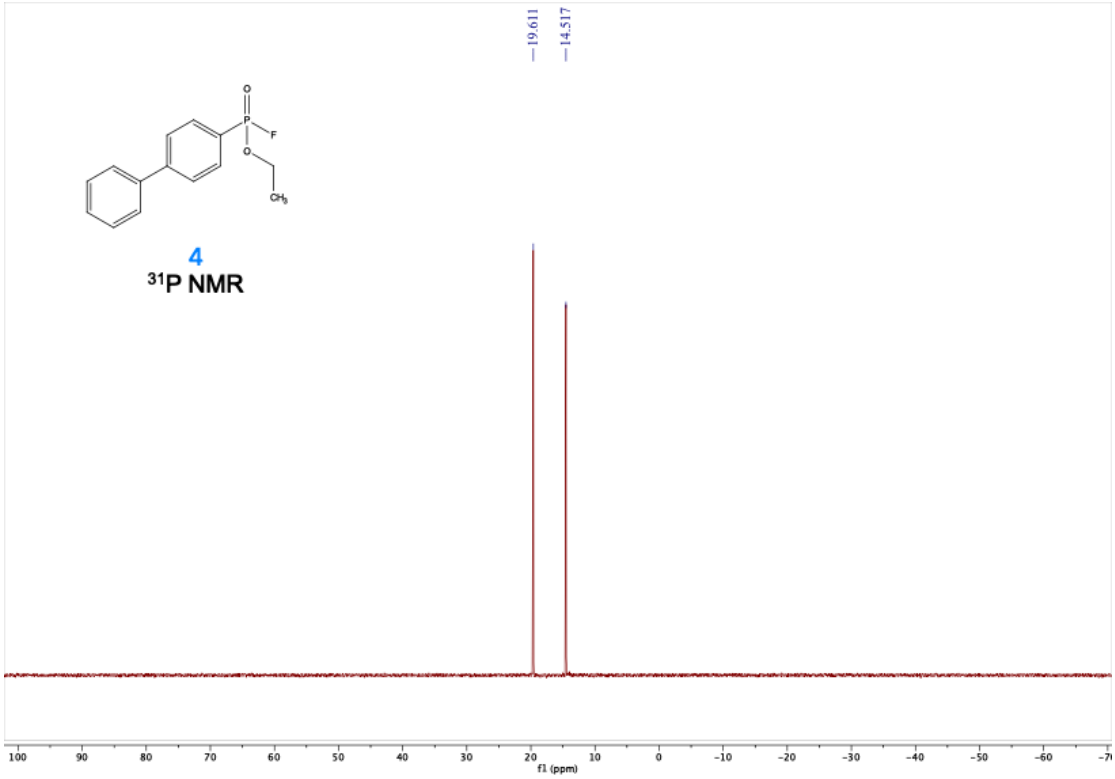
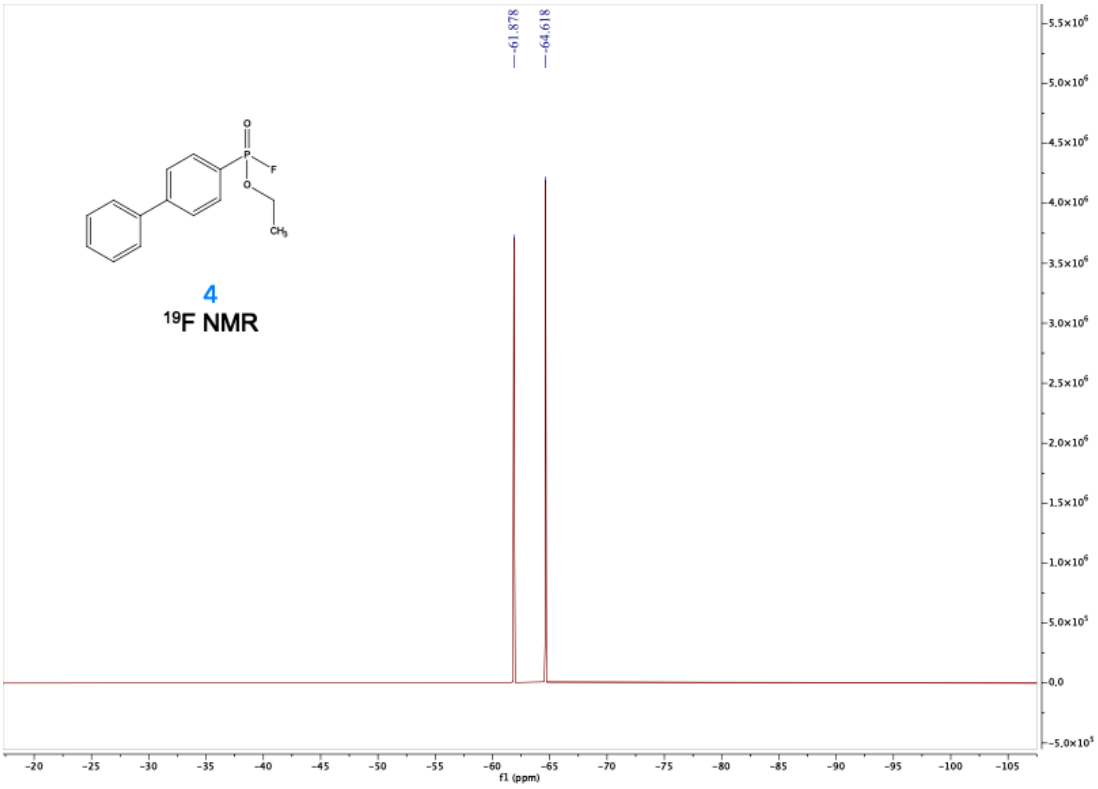
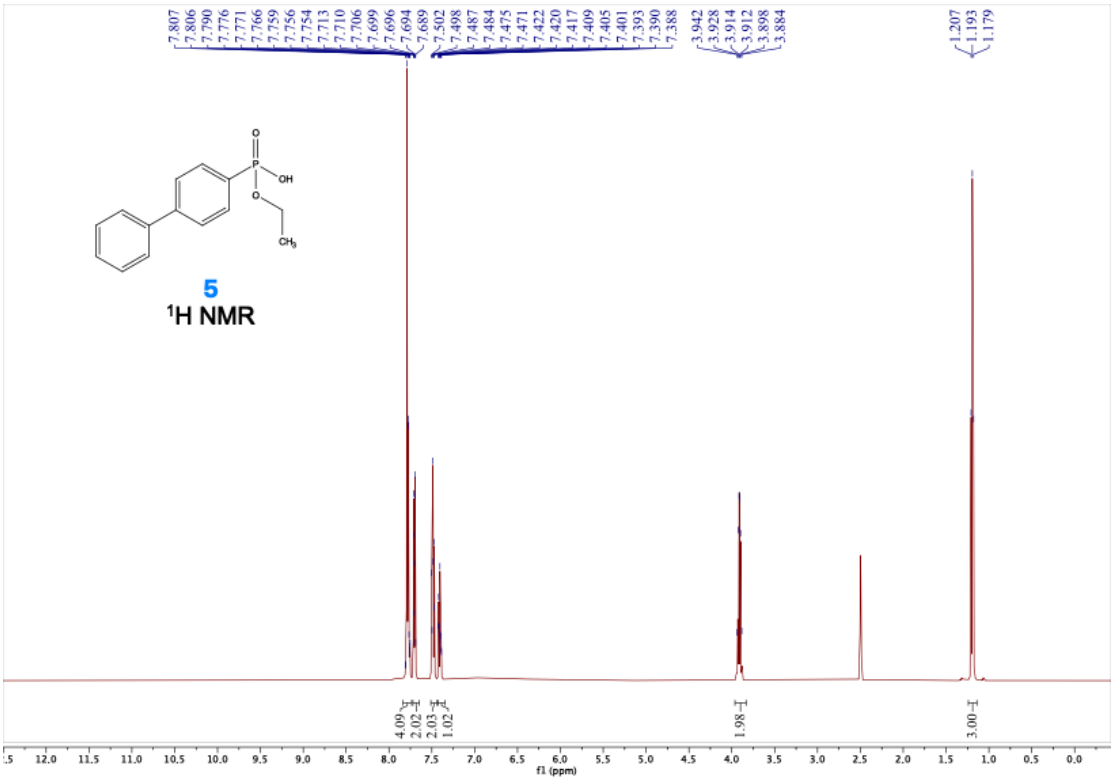
145.993
139.007
132.655
132.563
129.659
129.195
127.964
127.834
127.600
124.140
123.891
122.544
122.296
64.695
64.648
16.615
16.569
O
P
F
O
CH3
4
13C NMR
f1 (ppm)


19.611
14.517
O
P
F
O
CH3
4
31P NMR
f1 (ppm)


-61.878
-64.618
4
19F NMR
f1 (ppm)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7.806
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7.771
7.766
7.759
7.756
7.754
7.713
7.710
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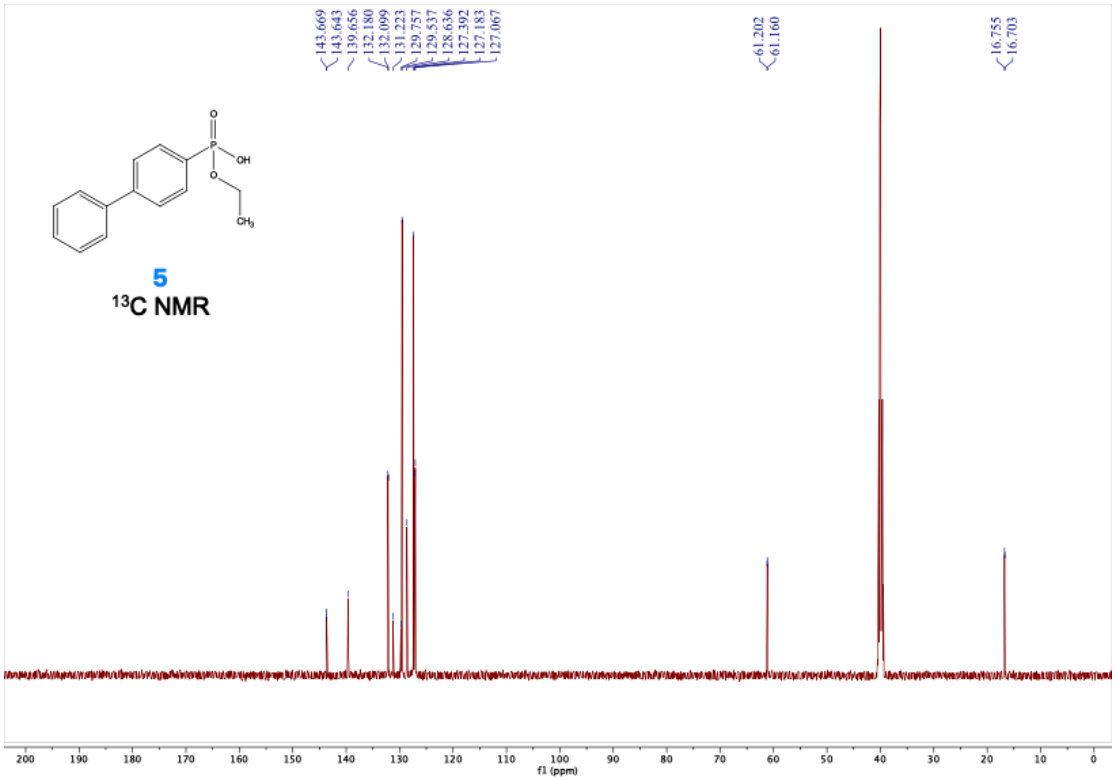
7.699
7.696
7.694
7.689
7.502
7.498
7.487
7.484
7.475
7.471
7.422
7.420
7.417
7.409
7.405
7.401
7.393
7.390
7.388
3.942
3.928
3.914
3.912
3.898
3.884
1.207
1.193
1.179
4.09
2.02
2.03
1.02
1.98
3.00
5
1H NMR
f1 (ppm)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132.099
131.223
129.757
129.537
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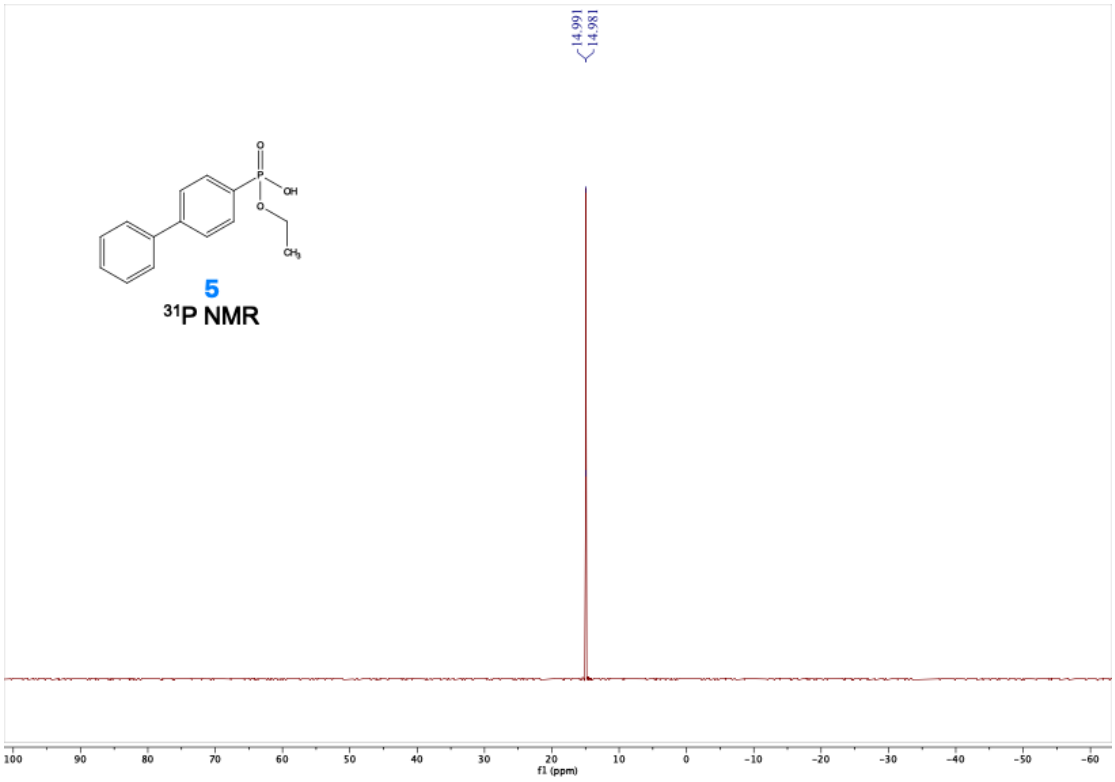
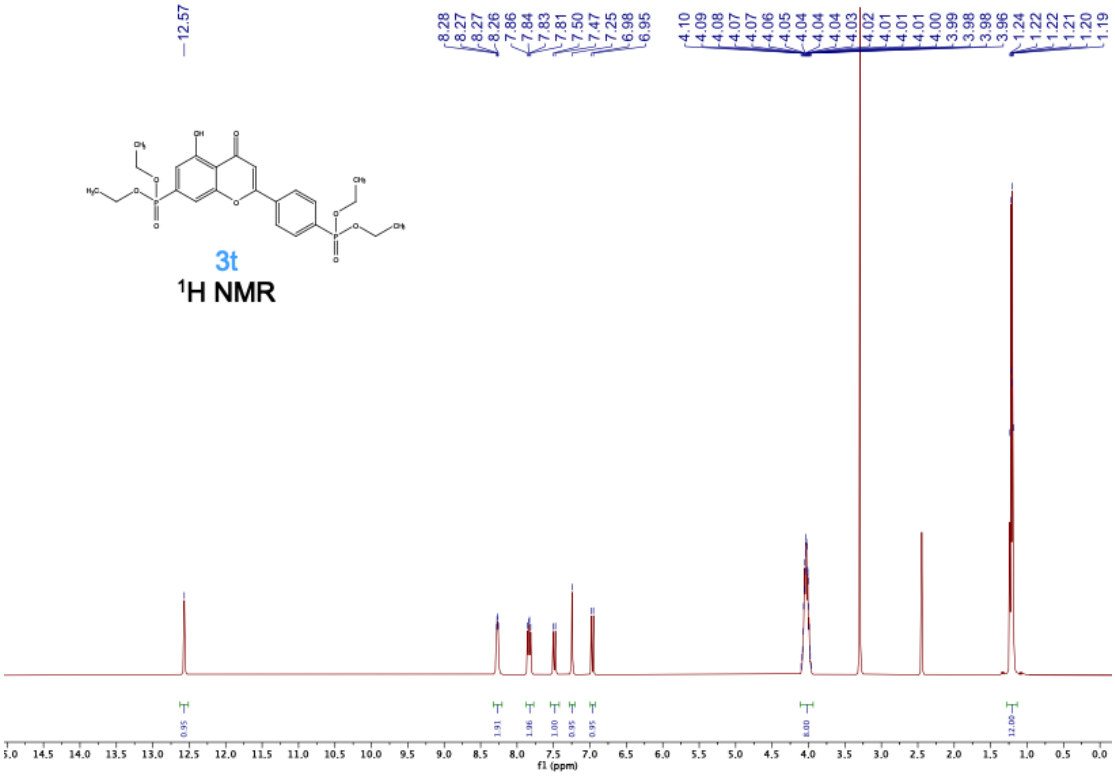
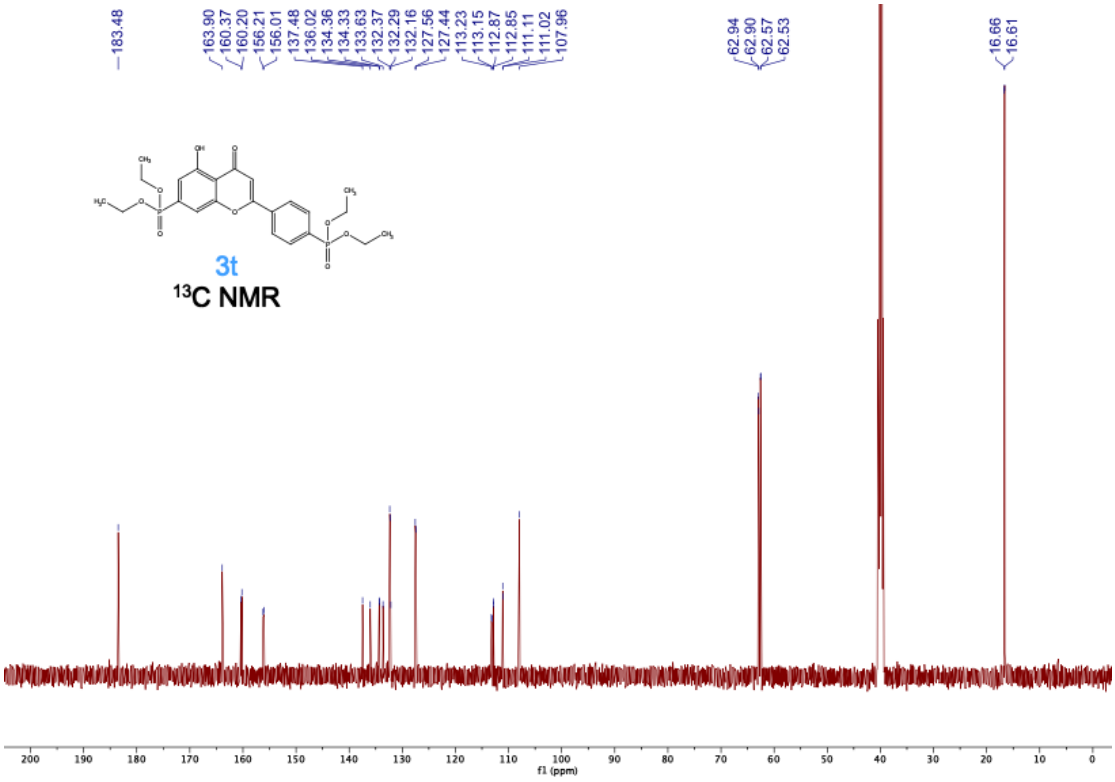
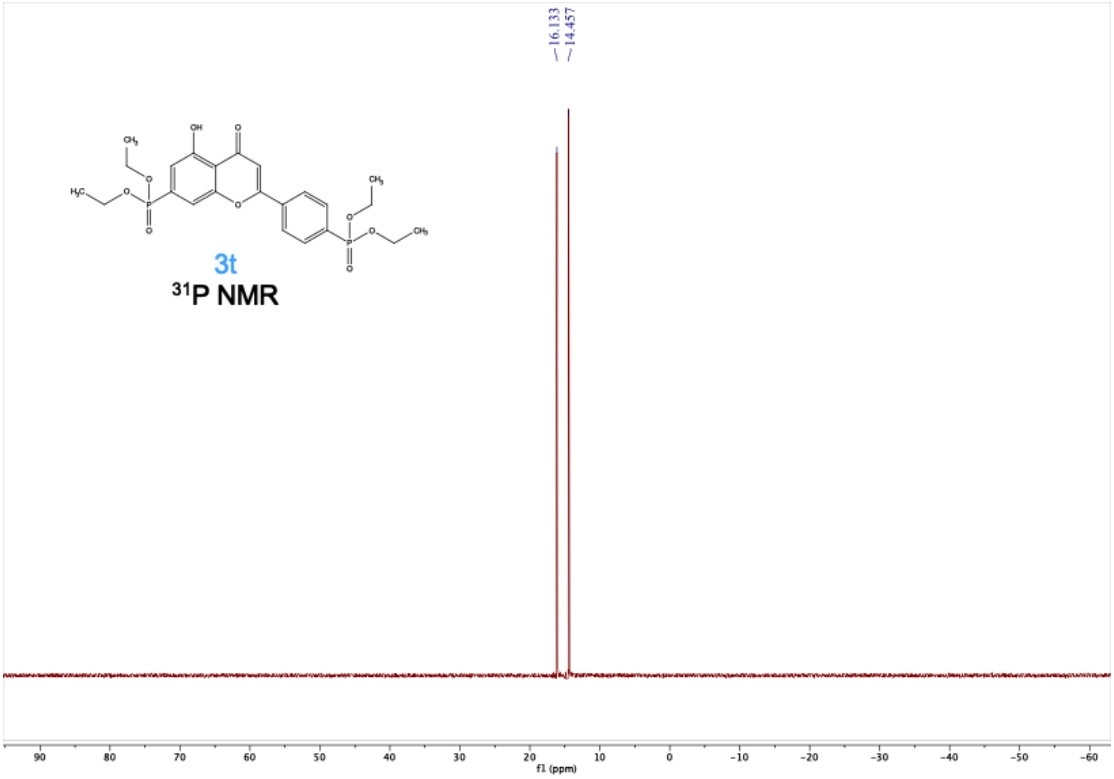
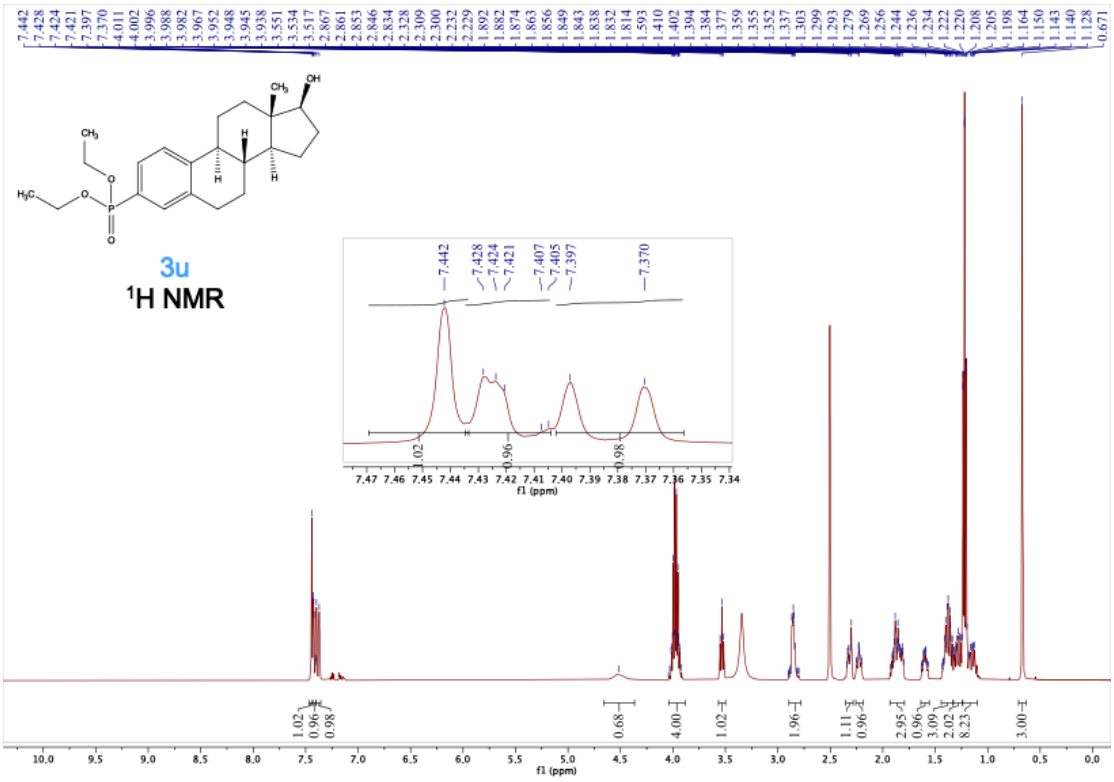
127.392
127.183
127.067
61.202
61.160
16.755
16.703
OH
CH3
5
13C NMR
f1 (ppm)

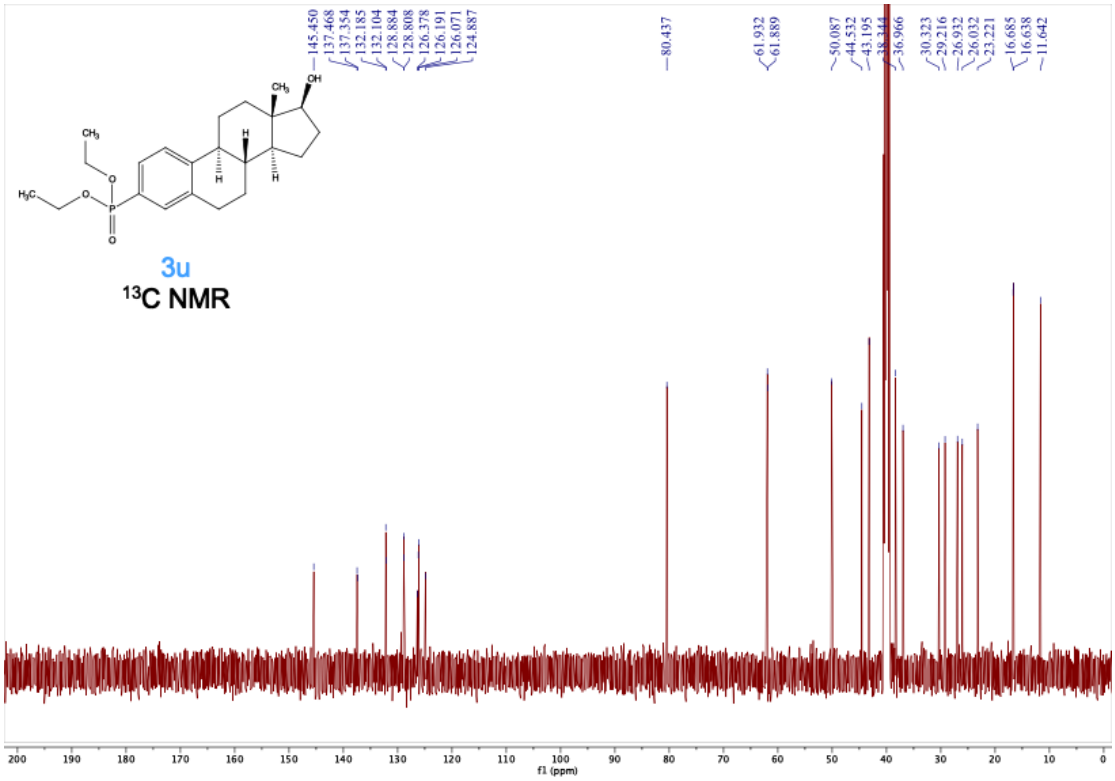

14.991
14.981
OH
CH3
5
31P NMR
f1 (ppm)

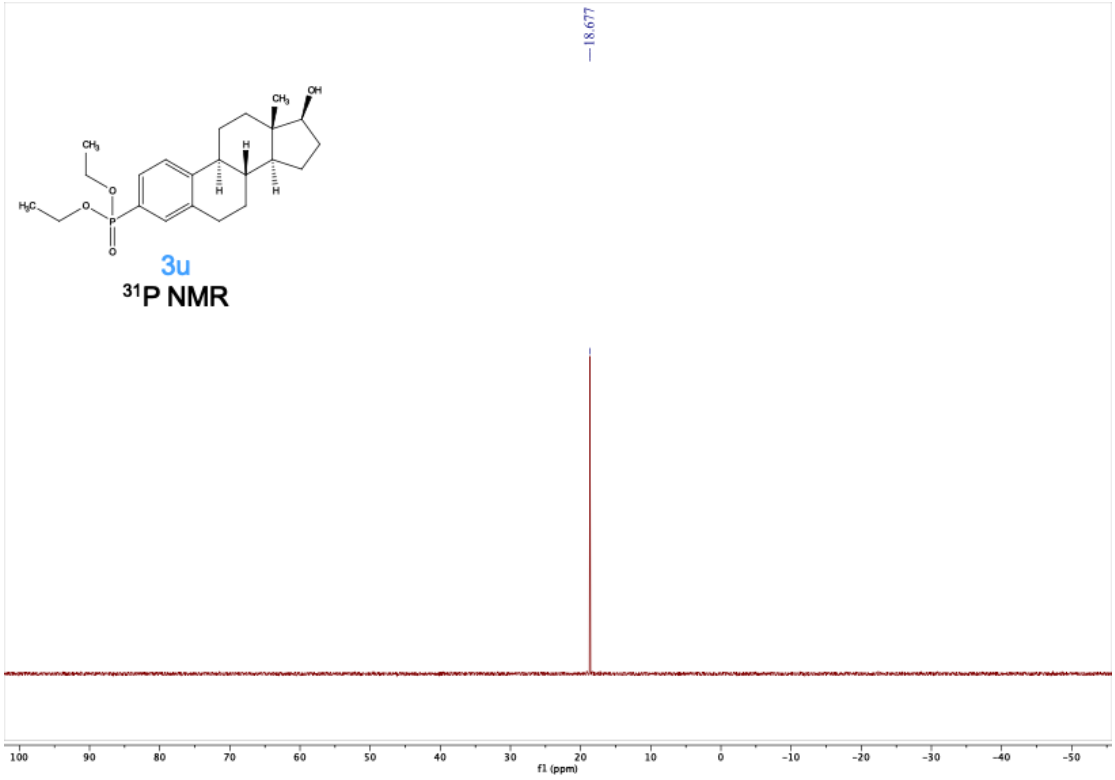

12.57
8.28
8.27
8.27
8.26
7.86
7.84
7.83
7.81
7.50
7.47
7.25
6.98
6.95
4.10
4.09
4.08
4.07
4.07
4.06
4.05
4.04
4.04
4.04
4.03
4.02
4.01
4.01
4.01
4.00
3.99
3.98
3.98
3.96
1.24
1.22
1.22
1.21
1.20
1.19
3t
1H NMR
f1 (ppm)

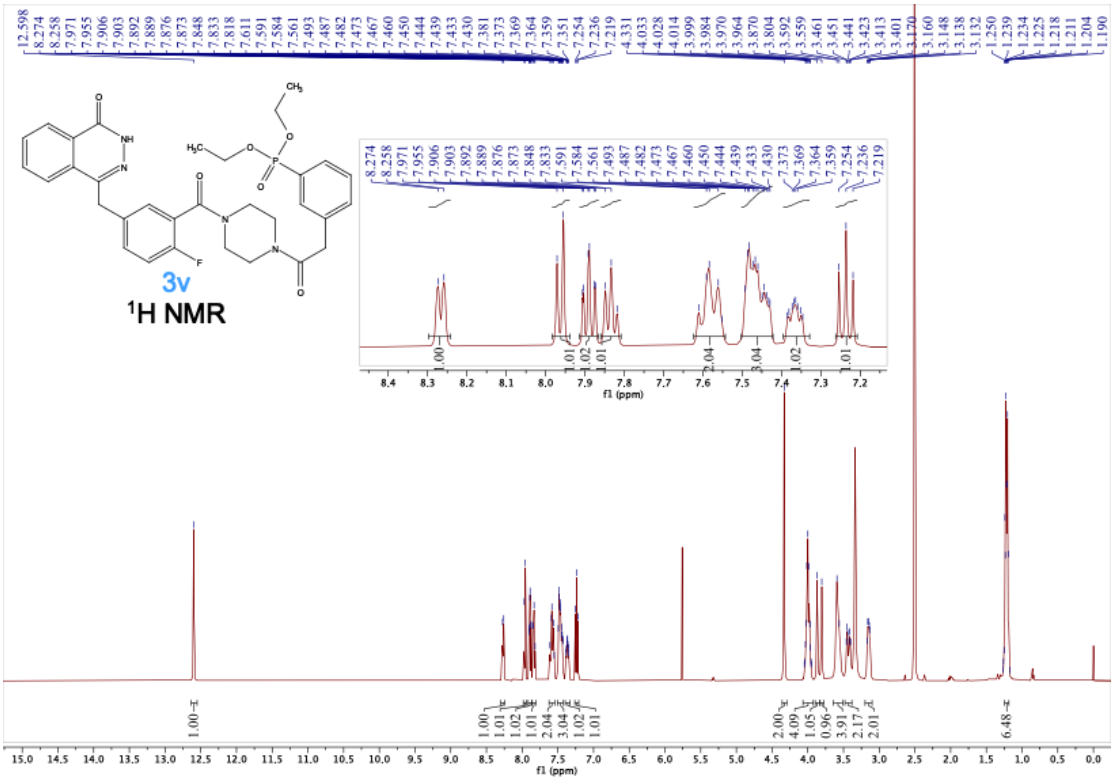

183.48
163.90
160.37
160.20
156.21
156.01
137.48
136.02
134.36
134.33
133.63
132.37
132.29
132.16
127.56
127.44
113.23
113.15
112.87
112.85
111.11
111.02
107.96
62.94
62.90
62.57
62.53
16.66
16.61
3t
13C NMR
f1 (ppm)

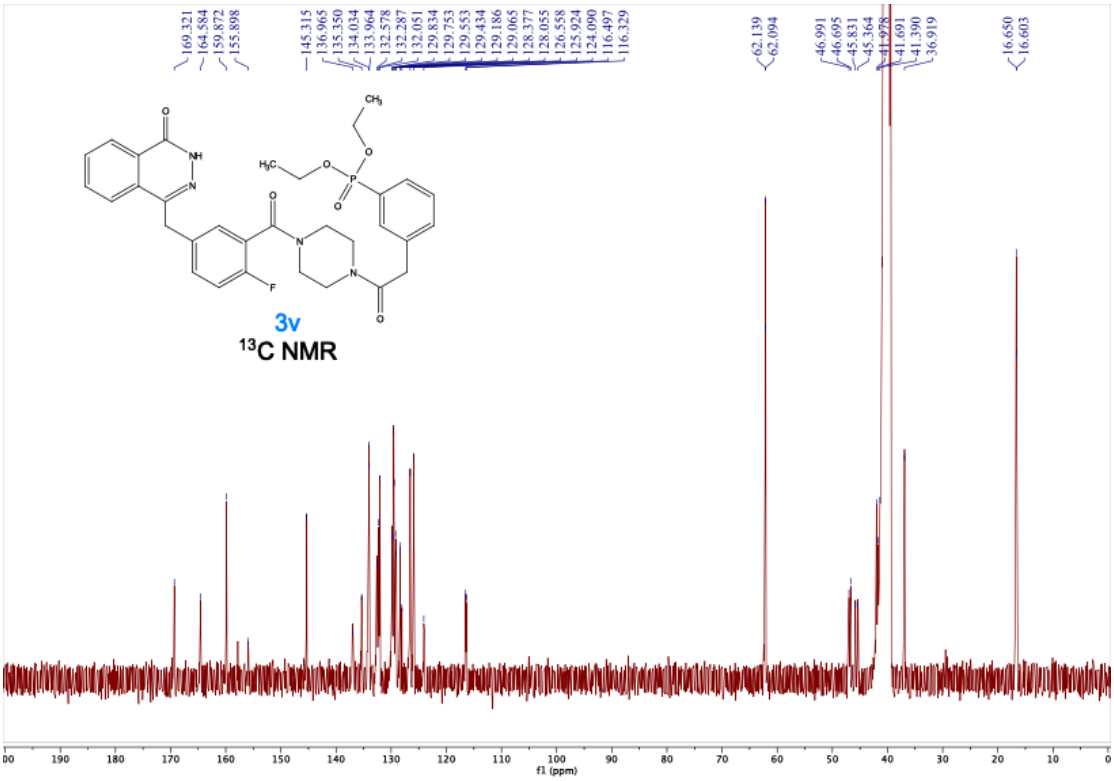

16.133
14.457
3t
31P NMR
f1 (ppm)

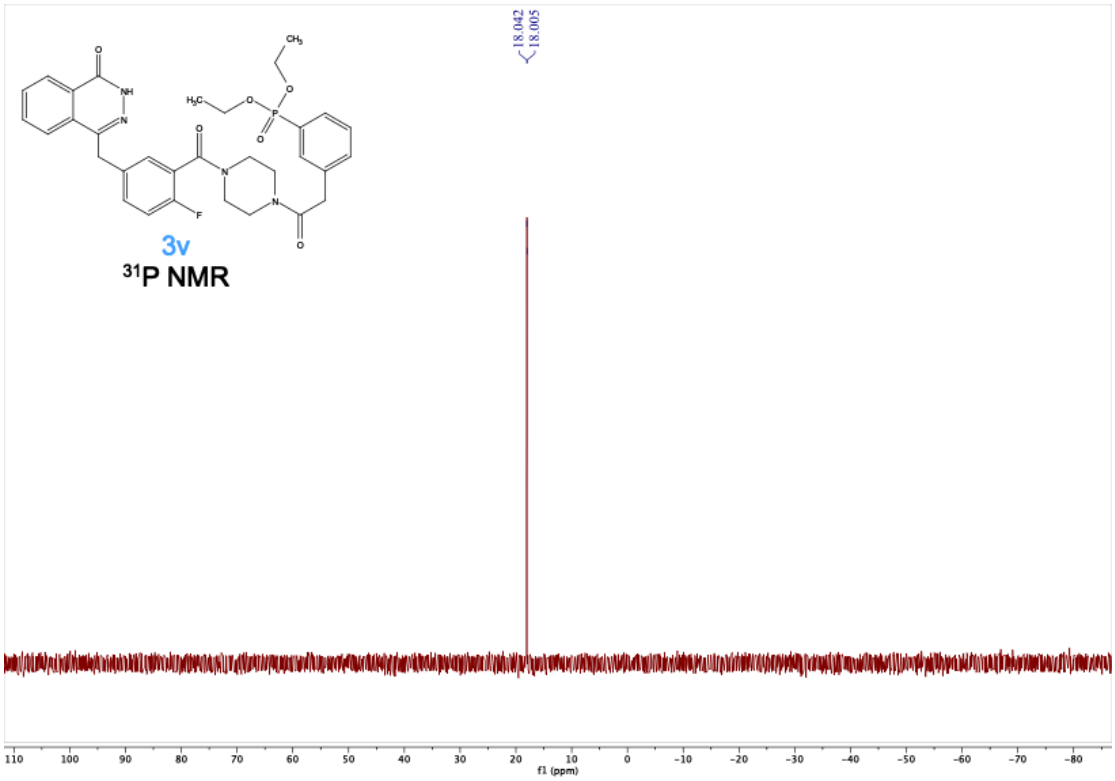

3u
1H NMR
7.442
7.428
7.424
7.421
7.407
7.405
7.397
7.370
1.02
0.96
0.98
f1 (ppm)

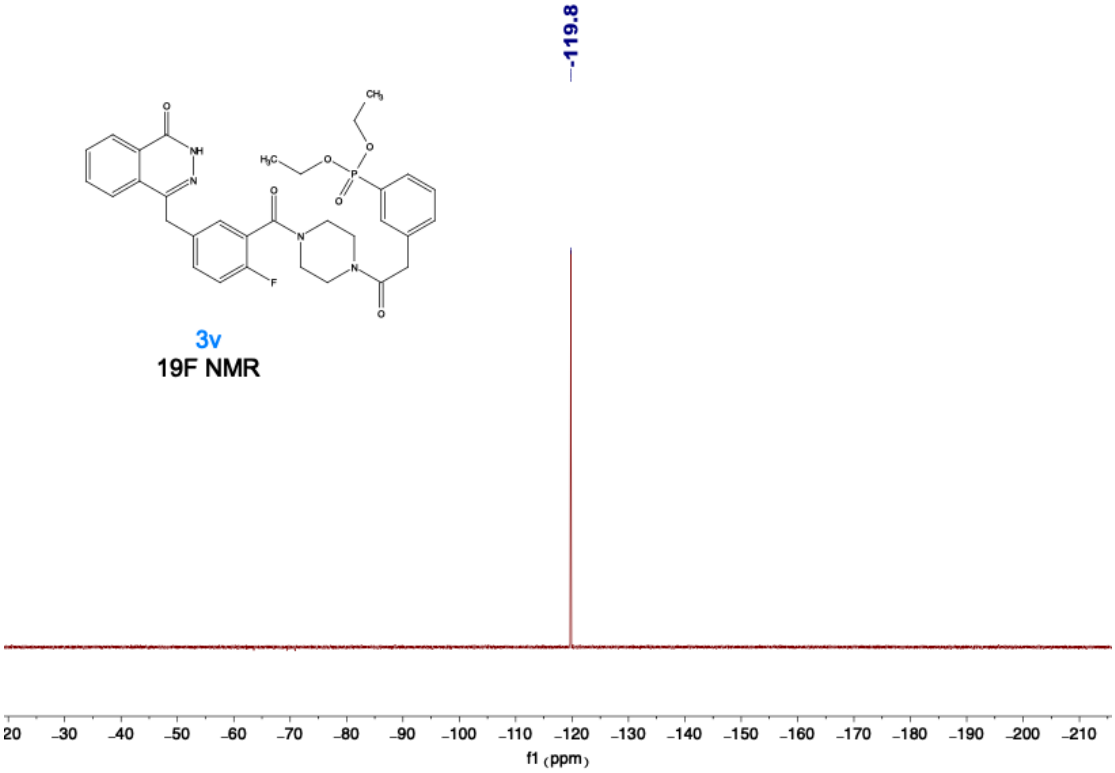

145.450
137.468
137.354
132.185
132.104
128.884
128.808
126.378
126.191
126.071
124.887
80.437
61.932
61.889
50.087
44.532
43.195
38.344
36.966
30.323
29.216
26.932
26.032
23.221
16.685
16.638
11.642
OH
CH3
H3C
O
P
H
3u
13C NMR
f1 (ppm)

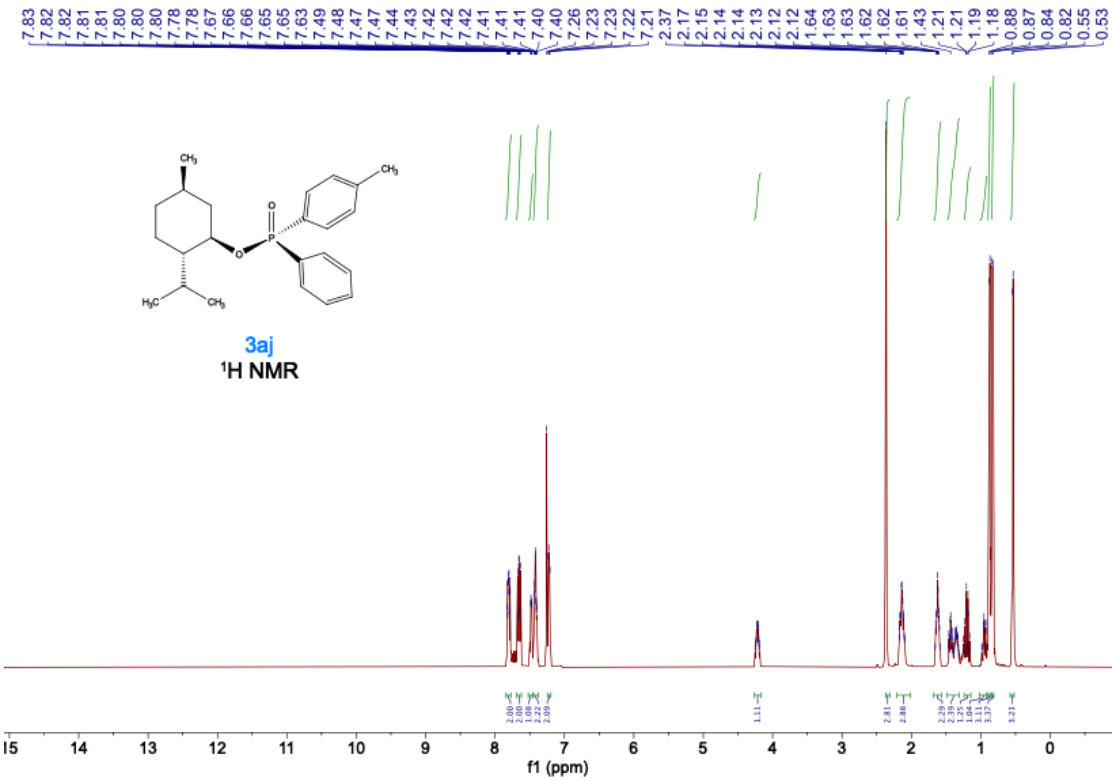

18.677
OH
CH3
H3C
O
P
H
3u
31P NMR
f1 (ppm)

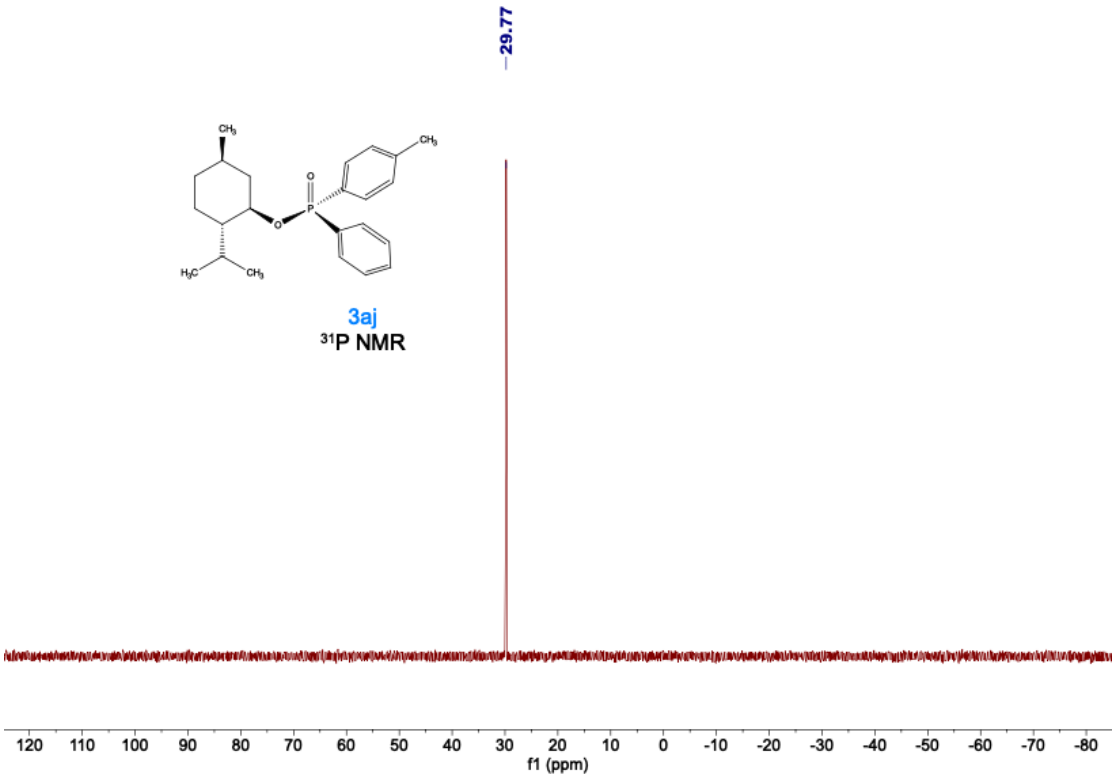

3v
^{1}H NMR
f1 (ppm)

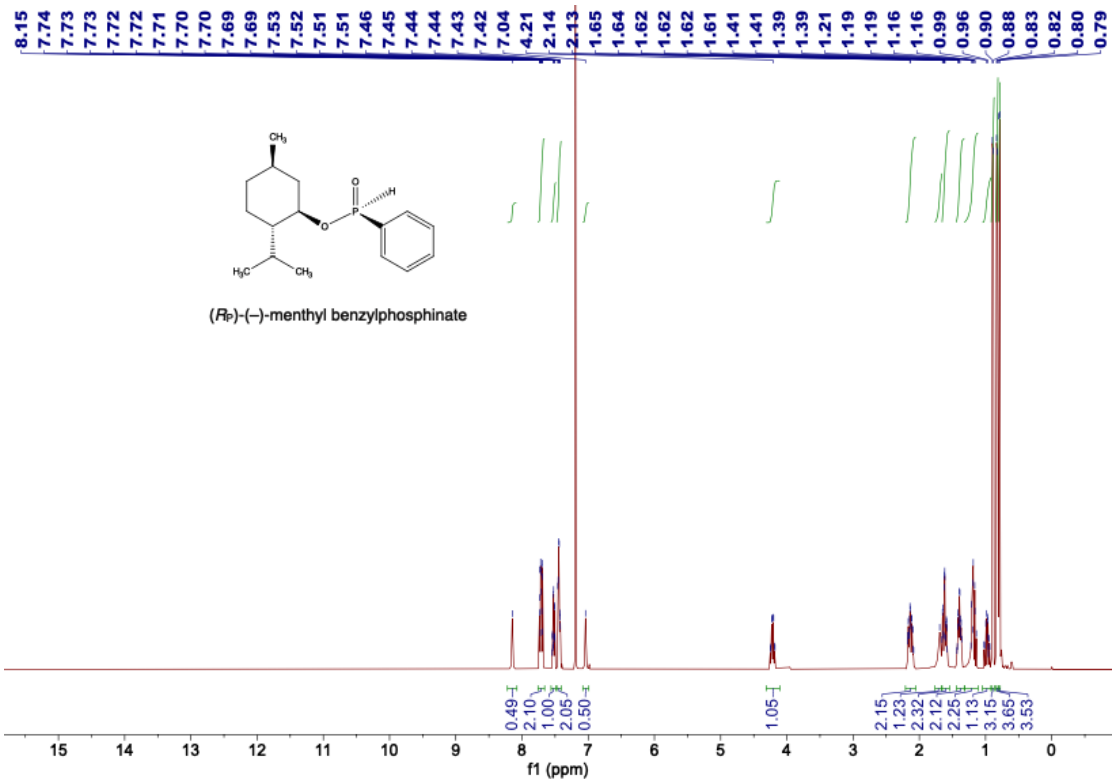

3v
^{13}C NMR
f1 (ppm)

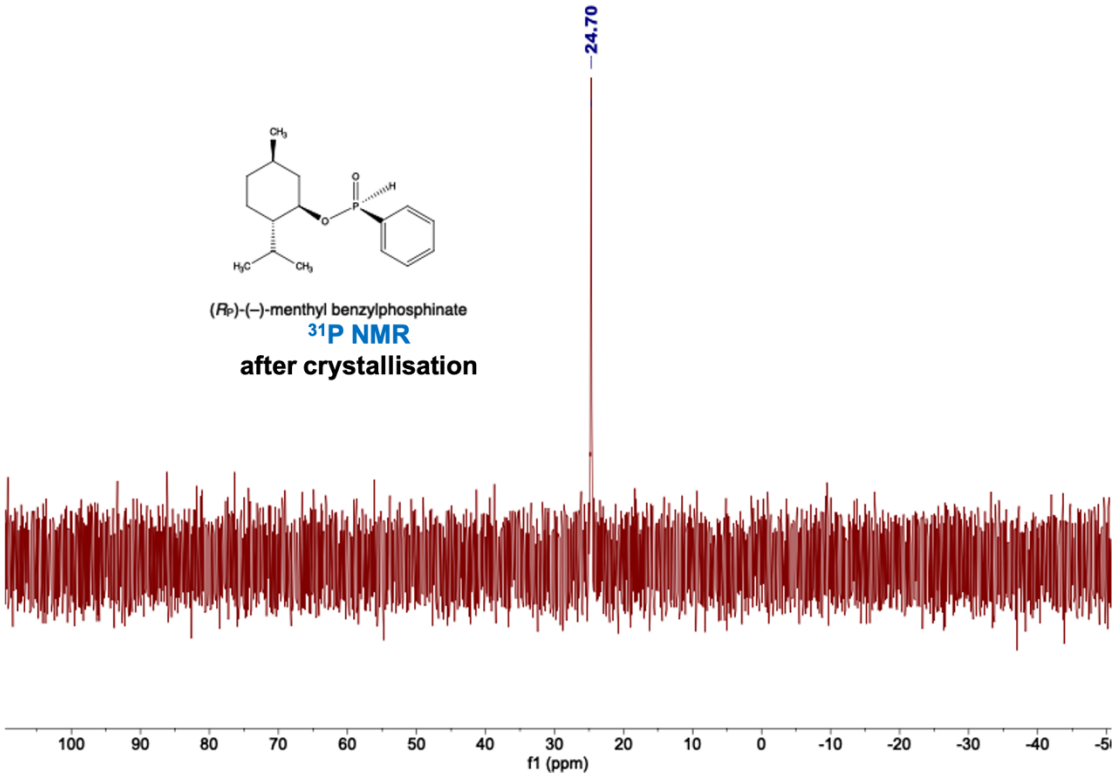

18.042
18.005
3v
31P NMR
f1 (ppm)

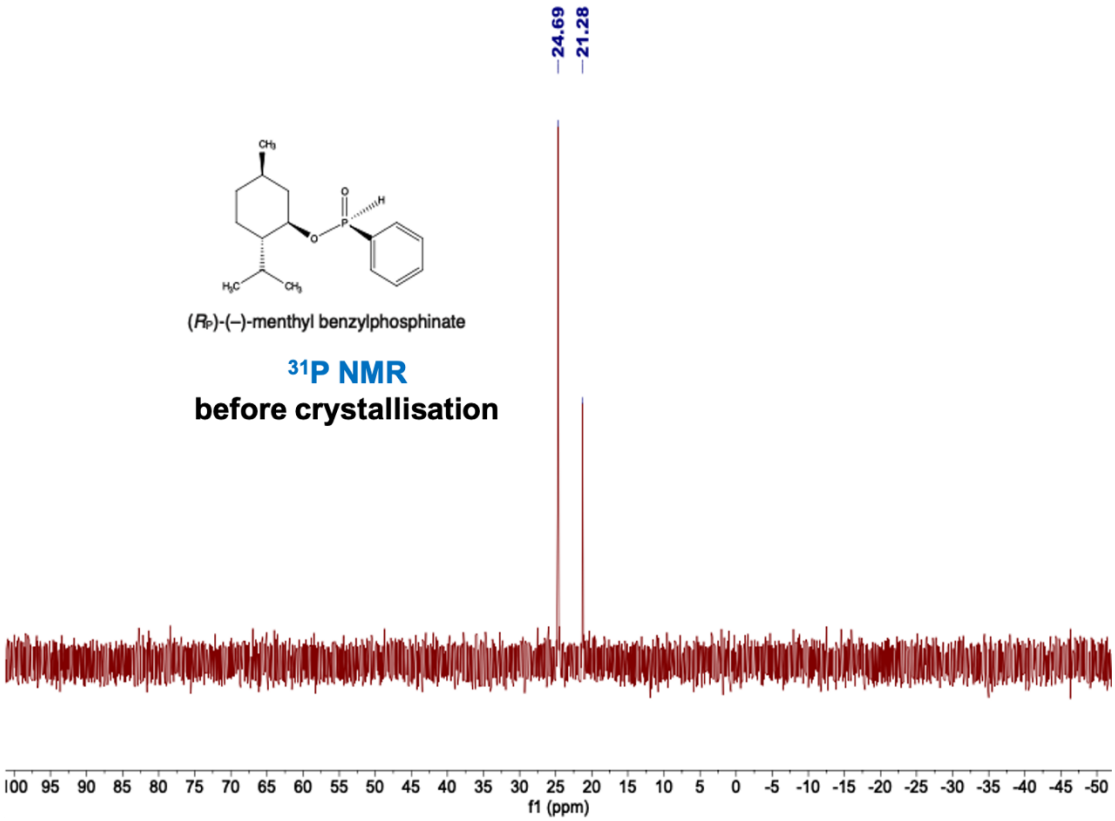

-119.8
3v
19F NMR
f1 (ppm)

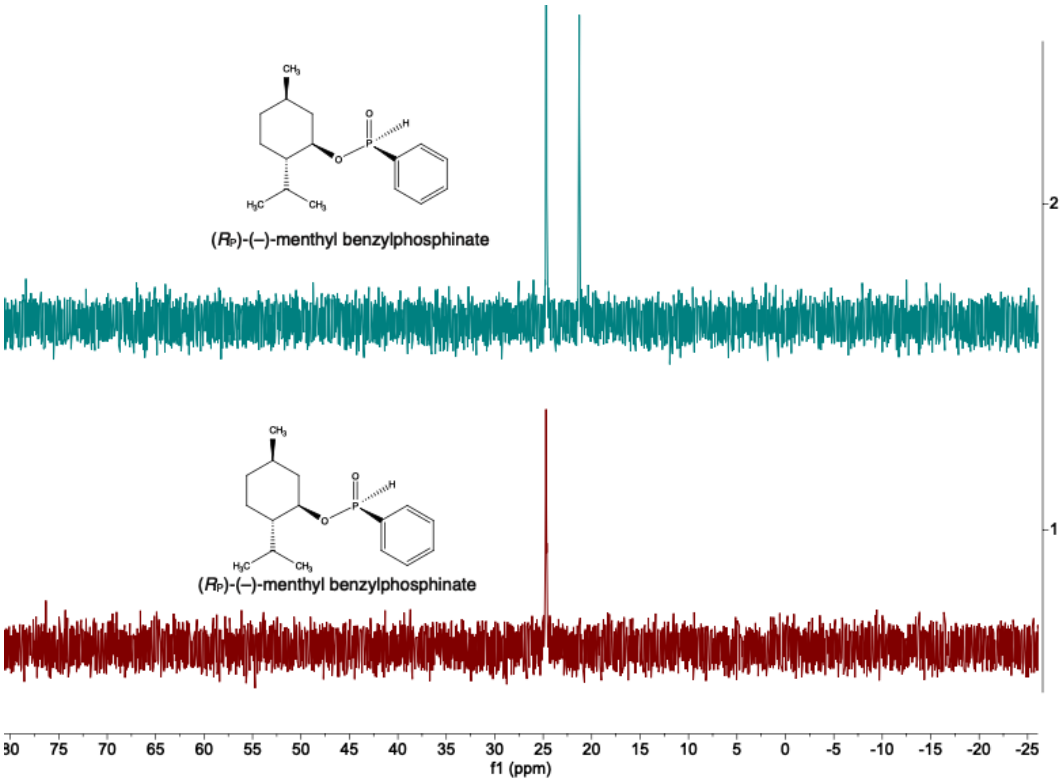

7.83 7.82 7.82 7.81 7.81 7.80 7.80 7.80 7.78 7.78 7.67 7.66 7.66 7.65 7.65 7.63 7.49 7.48 7.47 7.47 7.44 7.43 7.42 7.42 7.42 7.41 7.41 7.41 7.40 7.40 7.26 7.23 7.23 7.22 7.21 2.37 2.17 2.15 2.14 2.14 2.13 2.12 2.12 1.64 1.63 1.63 1.62 1.62 1.61 1.43 1.21 1.21 1.19 1.18 0.88 0.87 0.84 0.82 0.55 0.53
3aj
1H NMR
f1 (ppm)


29.77
3aj
31P NMR
f1 (ppm)


8.15 7.74 7.73 7.73 7.72 7.72 7.71 7.70 7.70 7.69 7.69 7.53 7.52 7.51 7.51 7.46 7.45 7.44 7.44 7.43 7.42 7.04 4.21 2.14 2.13 1.65 1.64 1.62 1.62 1.62 1.61 1.41 1.41 1.39 1.39 1.21 1.19 1.19 1.16 1.16 0.99 0.96 0.90 0.88 0.83 0.82 0.80 0.79
(RP)-(–)-menthyl benzylphosphinate
0.49 2.10 1.00 2.05 0.50 1.05 2.15 1.23 2.32 2.12 2.25 1.13 3.15 3.65 3.53
f1 (ppm)


24.70
(RP)-(–)-menthyl benzylphosphinate
31P NMR
after crystallisation
f1 (ppm)


24.69
21.28
(Rp)-(–)-menthyl benzylphosphinate
31P NMR
before crystallisation
f1 (ppm)


(Rp)-(–)-menthyl benzylphosphinate
(Rp)-(–)-menthyl benzylphosphinate
2
1
f1 (ppm)

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